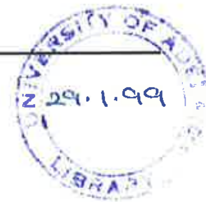

# GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO MORPHOLOGICAL VARIATION IN THE HUMAN PERMANENT DENTITION

## - A Study of Australian Twins

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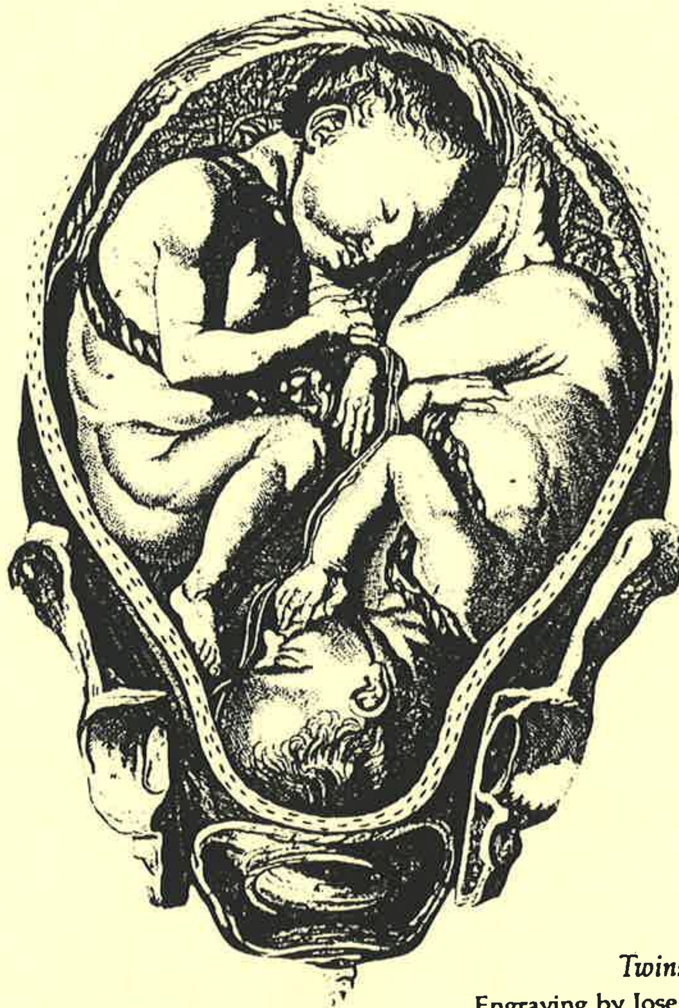
# Frontispiece



*Twins in Utero.*
Engraving by Josef von Morenheim, 1791.

"The problem of separating the effects of heredity and environment is one of the oldest, most difficult, and controversial subjects in the field of human genetics. In no aspect of human inheritance is the interplay of heredity and environment more involved than in problems relating to the dentition*. There are relatively few entities of great moment to the dentist that have been demonstrated to exhibit simple genetic transmission and hence might classify as the result of a single gene substitution. On the contrary, the genetics of the problems of most immediate concern to the dental profession are, for the most part, more complex, and involve genetic factors interacting with a variety of environmental factors." Niswander JD (1963)

* This is a moot point.

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# Declaration

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# Abstract

The aim of this thesis was to elucidate the nature and extent of genetic and environmental contributions to variation in permanent tooth crown size. Two crown diameters - the mesiodistal length (MD) and buccolingual breadth (BL) of 28 permanent teeth were recorded. Phenotypic variation among individuals for quantitative traits can be divided into additive and non-additive genetic factors, and individual and family environmental factors. The most common method used is the study of correlations among relatives, in particular, the classical twin method. In addition, twin studies may reveal evidence of contributions of sex-linked genes and sex hormones.

Sibling correlations were compared to find evidence of sex-linked genes contributing to tooth crown size. About half of the 56 crown diameters were in agreement with predictions. Alternative explanations were explored, and it was decided that the finding was consistent with a contribution of sex-linked genes to tooth crown size.

All 56 variables displayed significant sexual dimorphism, with males having larger teeth on average than females. The hypothesis that sex hormones contributed to sexual dimorphism was tested by comparing mean tooth size in female-male (opposite-sex or OS) twins with same-sex (SS) twins, and singletons. A multivariate ANOVA of 12 variables revealed a significant increase in tooth crown size of OS females, and no change in OS males. This is consistent with expectations if sex hormones diffused between twins in utero and influenced tooth size.

Most previous quantitative studies of tooth crown size have revealed a high degree of genetic determination. However, all of the statistical methods used had substantial difficulties in their application. Structural equation modelling analyses in this project revealed that most variation could be explained by additive genetic and unique environmental factors. In univariate analyses, canine and first premolar MD lengths showed substantial non-additive genetic variation, while common environmental variation was significant in the maxillary first molar. Multivariate analyses revealed several genetic and environmental factors applied to all variables in the analysis. Other additive genetic factors affected individual teeth or antimeric pairs of teeth, while non-additive genetic factors influenced groups of teeth. Common environment affected posterior teeth in the maxillary right quadrant. All findings were interpreted in the light of genetic, evolutionary and embryological principles.

# Acknowledgments

This thesis is dedicated to my parents, in recognition of their roles in the provision of my own genes and environment. In particular - for their encouragement of learning and of the pursuit of dreams, and for the appreciation of curiosity and wisdom which I received from them both.

My supervisors, Professor Grant Townsend (Univeristy of Adelaide) and Dr Nick Martin (Queensland Institute for Medical Research), devised the project. They provided the benefits of their knowledge and experience, maintained an open-door policy, and encouraged me to follow paths of my choosing. Assoc. Professor Mike Neale (Medical College of Virginia, USA) provided assistance and mentorship, and was considered an unofficial supervisor throughout the project.

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Sandra Pinkerton administered the twin study most efficiently, and patiently solved almost every problem I gave to her (including a few I dreamed up just to see if she could). Many people assisted with collection of data from the twins and their families, including dentists, dental students, finger printers, height and weight charters, handedness assessors, preparers of stone models, measurers of teeth, and data enterers.

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# Publications

## Publications produced during the period of candidature

### Written Papers

Dempsey PJ, Townsend GC, Richards LC (1993) Teeth, genes and the environment. *Perspectives in Human Biology* **4**:35-46.

Dempsey PJ, Townsend GC, Martin NG, Neale MC (1995) Genetic covariance structure of incisor crown size in twins. *Journal of Dental Research* **74**:1389-1398.

Dempsey PJ, Townsend GC, Richards LC (in press) Increased tooth crown size in females with twin brothers: evidence for hormonal diffusion between human twins in utero. *American Journal of Human Biology*.

Dempsey PJ, Townsend GC, Schwerdt W, Richards LC (submitted) Handedness in twins. *Perspectives in Human Biology*.

Pinkerton S, Townsend GC, Richards LC, Schwerdt W, Dempsey PJ (submitted) Expression of Carabelli trait in both dentitions of Australian twins. *Perspectives in Human Biology*.

Townsend GC, Dempsey PJ, Richards LC (submitted) Asymmetry in the deciduous dentition - fluctuating and directional components. *Perspectives in Human Biology*.

Dempsey PJ, Townsend GC, Martin NG (submitted) Insights into the genetic basis of human dental variation from statistical modelling analyses. *Perspectives in Human Biology*.

**Conference Presentations**

Dempsey PJ, Townsend GC, Martin NG (1993) Genetic covariance structure of incisor crown measurements in twins. International Association for Dental Research (ANZ division) meeting, Adelaide, Australia.

Dempsey PJ (1993) Genetic analysis of incisor crown size. Australasian Society for Human Biology meeting, Adelaide, Australia.

Dempsey PJ, Townsend GC, Richards LC (1994) Possible hormonal effects on tooth size in male-female twin pairs (abstract). *Journal of Dental Research* **73:**739.

Dempsey PJ, Townsend GC, Schwerdt W (1994) Dental asymmetry: are there differences between twins and singletons? IADR (ANZ division) Melbourne, Australia.

Dempsey PJ, Townsend GC, Martin NG (1995) Genetic and environmental contributions to variation in permanent tooth crown size (abstract). International Association for Dental Research (ANZ division) meeting, Singapore. Winner, IADR Travel Award. Presented also at IADR international meeting San Francisco USA, 1996.

Dempsey PJ, Townsend GC, Martin NG (1997) Multivariate genetic analysis of tooth crown size in twins (abstract). International Association for Dental Research (ANZ division) meeting, Dunedin, New Zealand.

# Abbreviations

## Study Subjects

| | |
|---|---|
| DZ | Dizygous Twins |
| MZ | Monozygous Twins |
| OS | Opposite-Sex Twins |
| SS | Same-Sex Twins |
| F | Female |
| M | Male |

## The Variables

| | |
|---|---|
| MD | Mesiodistal (length) |
| BL | Buccolingual (breadth) |
| Max | Maxillary (upper) |
| Man | Mandibular (lower) |
| I1 | Central Incisor |
| I2 | Lateral Incisor |
| C | Canine |
| P1 | First Premolar |
| P2 | Second Premolar |
| M1 | First Molar |
| M2 | Second Molar |

## Statistical Terms

| | |
|---|---|
| $\alpha$ | Alpha (significance) Level |
| AIC | Akaike's Information Criterion |
| CV | Coefficient of Variation |
| df | Degrees of Freedom |
| p | Estimated Probability |

# Chapter 1

# Introduction to the Project

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## The Question and the Field of Study

What is it that shapes our teeth - genes, environment, or both? How much does each contribute? What sort of genetic and environmental factors are acting? It is no longer a question of nature versus nurture, but how nature and nurture *interact* to shape the human tooth.

These questions, applied to traits with continuous distributions, form the basis of the scientific field known as quantitative genetics. Such traits may be referred to as continuous, quantitative, or metric traits. Sir Francis Galton is credited with having initiated the study of quantitative traits more than a century ago. The prevailing view at the time was that traits such as career status or mental ability were due to individual effort or environmental conditions. Galton (1869) began to study families to determine whether such complex traits could be due to genetic inheritance instead.

One aim of quantitative genetics is to find and quantify the factors contributing to variation in such multifactorial traits among individuals. This can be achieved through development of statistical models for phenotypic expression of a trait, which assume at least partial nonidentifiability of both genotypes and environments (Kempthorne 1957).

For human traits, the foremost method which has been developed is the study of correlation among individuals of known genetic relationship. When studying traits in domesticated animals, breeding and other experiments may be conducted to elucidate the contributing factors. In these cases, the correlation coefficient has been described as being more applicable to exploratory stages of a study than as an appropriate way of expressing results (Kempthorne 1957). In humans however, it is not possible to manipulate breeding conditions, and the correlation coefficient has proven very useful in demonstrating the existence of heredity, and estimating its intensity (Fisher, 1973).

Even so, the correlation coefficient alone has limited usefulness, since without knowledge of the presence or absence of a factor, and direction of causation between multiple factors,

"...calculation of the correlation coefficient, total or partial, will not advance us a step towards evaluating the importance of the causes at work" (Fisher 1973, p192).

Methods such as structural equation modelling (SEM) have been developed for disentangling the various effects of genes and environment from summary statistics, such as coefficients of correlation or covariance. In this thesis, SEM methods have been applied to measurements of tooth crowns from the permanent dentition. The sample comprises twin pairs and singletons. In addition, the degree of sexual dimorphism in the dentition was examined, and evidence for contributing factors was sought.

## Why Study Human Dental Morphology?

Having defined the *field* of study, it might be pertinent to discuss the *reasons* for choosing to study the permanent dentition. Human teeth are the subject of research in a wide variety of fields. There are at least two perspectives in this research - interest in the teeth themselves, and utilisation of teeth to answer more general questions in such areas as human embryology and development, evolution, social and cultural practices, migration histories, and health states.

Interest in the teeth themselves is most apparent in clinical dentistry, including orthodontic and other dental therapies. Clinicians seeking ways of effectively preventing or treating malformations and pathologies, are interested in the epidemiology of those conditions, and in the general embryology of the dentition. As stated by Corruccini *et al.* (1990): "A better understanding of the relative effects of

genetic and environmental influences on different occlusal features within and between different populations should ultimately improve theory in orthodontics."

In studying the contributions of genes and environment to human development (for example), the dentition provides an excellent model system. The reasons for this are numerous.

- Tooth crowns are visible externally, and can be measured noninvasively.

- Teeth are extremely durable (Kieser 1990) and tend to form the highest proportion of ancient remains.

- Teeth tend to remain relatively constant in size and shape with age, except for the effects of wear due to physical and chemical processes. These effects are generally minor (and to some extent, visible) compared with effects of age on other features, for example, body mass, musculature, or social attitudes.

- The teeth tend to form early, mostly before growth in other structures is completed, so that environmental influences are potentially fewer in number and easier to identify.

- The stages of odontogenesis are well documented. Comparisons of teeth with different timing and rates of development enable investigation of environmental effects occurring at different stages of development, involving both prenatal (and hence maternal) and early postnatal environments.

- The meristic nature of teeth means that aspects of development such as morphogenetic fields and patterns of symmetry or asymmetry can be examined.

- In addition, teeth have been described as "probably the greatest evolutionary diversification of the vertebrate skeleton" (Radinsky 1987).

The dentition provides a moderately simple and easily observed system from which information on a variety of developmental and evolutionary processes can be obtained. In particular, aspects of the embryology and early post-natal development of an individual are probably better indicated by the dentition than by most other adult features.

It is difficult to imagine a field of human research or dental practice which would not benefit from an understanding of the processes involved in tooth development. For instance, anthropologists and paleontologists studying hominid evolution, migration patterns, and relationships among groups of humans (whether extant or extinct) often utilise dental traits. These studies will be assisted by an understanding of genetic and environmental contributions to tooth morphology. Furthermore, forensic scientists faced with increasing numbers of individuals with few or no restorations in their teeth may be able to use dental traits to calculate the probability of familial relationship for a given set of remains.

## What Methods are Available?

The search for factors contributing to tooth crown size and shape began in the 1920s. Over this almost 80 year period, researchers have employed a wide variety of methods, including descriptive and correlational studies, quantitative genetic analyses, and molecular or biochemical methods. The vast majority of studies have been based on purely descriptive or correlational methods. For instance, patterns of tooth crown size and shape, variability, asymmetry, and rates of abnormality, have been described in detail for a wide variety of human populations. Correlations between these variables and various environmental and genetic factors also have been sought. The

descriptive patterns and correlations often have been interpreted as evidence of specific genetic and environmental factors. Quantitative genetic methods, using twins and other family pairings, also have been used extensively in past dental research.

Molecular and biochemical studies provide a sharp contrast to other methods. These studies seek the locations and base sequences of genes encoding specific proteins, and the mechanism of action of both regulatory and non-regulatory genes. While most other research has been conducted on humans, these studies generally involve animals such as mice. This is because the techniques tend to be more invasive, including such procedures as transplantation of dental tissues and subsequent histological investigation. The results gained tend to be specific, informative, and extremely accurate, compared with quantitative genetic analyses. In spite of this, relatively few analyses of tooth development (to date) are of this nature. This is due to the recency of their development, as well as to the complicated nature of quantitative traits, and the expense involved in a major study. Statistical analyses such as those of classical twin studies probably will remain of benefit for some time, because they are relatively inexpensive, and require smaller samples.

Since the methods employed in this thesis belong to the field of quantitative genetics, it is pertinent to consider the history of their development, and main underlying theories, especially as they apply to studies of twins.

## Quantitative Genetics

### A Brief History

Since excellent reviews of the developmental history of this scientific field have been published elsewhere (Plomin *et al.* 1990, Neale and Cardon 1992), only a brief account is included. As described previously, genetic studies of quanitative characters in humans were begun by Galton late last century. Galton not only found evidence that quanitative traits might be influenced by genetic factors, but believed that nature (genetics) predominated in the traits studied (Galton 1883). He was the first to propose using identical or monozygous (MZ) and fraternal or dizygous (DZ) twins to examine the relative powers of genes and environment. Another of Galton's contributions to the field was the development of the correlation coefficient - a measure of association between variables, which was independent of the scale of measurement.

It could be said that *modern* quantitative genetics commenced when it was first demonstrated that the range of phenotypes seen in quantitative characters could be explained by Mendelian principles applied to multiple gene loci simultaneously (Fisher 1918, Wright 1921b). Fisher (1918) demonstrated the partitioning of genetic sources of variation, while Wright developed the theories about components of environmental variation, and developed the technique of path analysis. It was the melding together of Fisher's biometrical genetic theory with Wright's path analysis that forms the basis of modern quantitative genetics (Martin *et al.* 1997).

### Comparing General Approaches

There are three main approaches to estimating genetic and environmental influences in humans - classical correlation analysis, Fisher's biometrical genetic procedure, and

multiple abstract variance analysis (MAVA, Cattell 1960,1965). The historical development of these techniques is described in Plomin *et al.* (1990), and Neale and Cardon (1992). The following comparison of the three approaches is summarised from Jinks and Fulker (1970).

The classical approach uses correlations between relatives to estimate various ratios describing the relative importance of genetic and environmental influences on trait variation. Such parameters include the *H* of Holzinger (1929), *E* of Neel and Schull (1954), *HR* of Nichols (1965), but the best-known example is probably Bulmer (1970) and Smith's (1974, 1975) heritability estimate: $h^2 = 2(r_{mz} - r_{dz})$.

MAVA is a more systematic and comprehensive approach which compares within- and between-family variances for twins, full-sibs and half-sibs. It leads to the estimation of nature:nurture ratios, and assesses correlations between genetic and environmental influences within the family and within the culture. The biometrical genetic approach incorporates and extends beyond the other two methods to an assessment of the kinds of gene action and mating system operating in the population.

The classical approach using correlations is not able to detect, estimate, or correct for the effects of genotype-environment correlation or genotype-environment interaction, whereas MAVA and biometrical genetics specifically recognise and seek to model and estimate these effects. The latter two differ in that modelling the interaction or correlation is difficult and subjective in MAVA. In biometrical genetics, a number of statistical tests have been designed to test the presence of these components before a model is constructed. These scaling tests provide evidence as to whether simple genetical models are adequate to account for most of the data, and if not, what kind of extension to the model is required. In addition to the insight which the procedure provides about gene action and mating systems, these tests represent the main advantage to the biometrical genetic approach.

It is this last method which forms the basis for the modelling analyses contained in this thesis. The main aim of the method is the partitioning of phenotypic variance into components for various genetic and environmental influences. The method used is based on path analysis, a method developed by Wright (1921a), which incorporates path diagrams for depicting causal structures among variables. The diagrams are visual representations of algebraic equations describing the relationships, but are easier to comprehend than a series of equations. Path analysis also has been described as a type of structured linear regression analysis of standardised variables in a closed system, which attempts to erect a causal structure compatible with observed data (Li, 1975).

**Partitioning Phenotypic Variance**

Phenotypic variation ($V_P$) among individuals may be decomposed into genetic ($V_G$) and environmental ($V_E$) components of variation, such that:

$$V_P = V_G + V_E$$

The total genetic effect on a phenotype ($V_G$) can be divided further, into additive effects of alleles at multiple loci ($V_A$), dominance effects at multiple loci ($V_D$), and epistatic interactions between loci ($V_I$). The total contribution of environment on the same phenotype may likewise be split into effects of common environment ($V_C$ - also called shared or family environment) and unique environment ($V_E$ - also known as specific, individual or random environment) (Mather and Jinks 1982). Thus, total phenotypic variation for a multifactorial trait has numerous components, and may be summarised as:

$$V_P = V_A + V_D + V_I + V_C + V_E$$

Additional factors which can influence phenotypic expression and correlations among relatives, are assortative mating, genotype-environment covariance (CovGE) or correlation (CorGE), and genotype by environment interaction (GxE). Genotype-environment correlation (CorGE) occurs when the environments an individual experiences are not a random sample of all environments, but are influenced by, or correlated with, the individual's genotype. Genotype by environment interaction (GxE) relates to the way genes and environment determine the phenotype. It describes the situation in which one genotype may be expressed the same way in two different environments, while expression of another genotype changes. The influences of these factors are described in detail elsewhere (Neale and Cardon 1992), and are considered further in chapter 6.

**Heritability Estimation**

Decomposition of $V_P$ into components of variance may be used to generate heritability estimates. The proportion of phenotypic variation due to all *genetic* sources of variance is referred to as broad-sense heritability, and is estimated as $V_G/V_P$. Narrow-sense heritability is the proportion of phenotypic variation due to additive genetic variance, and is estimated as $V_A/V_P$.

These estimates will vary from sample to sample, whether in different populations, different generations, even possibly in different groups of individuals within the same population and generation. Heritability estimates are dynamic, reflecting the processes which affected trait development in the given sample. A new environmental factor may decrease heritability in a sample relative to a former generation. Results thus apply to the sample in question, and their accuracy in estimating the true population values depends on the representativeness of the

sample. Wider application of results from the sample to the species level is probably better avoided, unless widespread samples reveal consistent results.

### Dominance and Natural Selection

Distinguishing dominance variance from total genetic variation allows one interesting insight. Fisher (1958) noted that most deleterious mutations were recessive. From this he postulated that advantageous alleles tend to become dominant, and developed the theory that moderate to strong selection leads to the presence of dominance variation, even if the selection was in the distant past. Thus, dominance variation was thought to indicate that a trait was related to selective fitness at some stage.

In more recent times, consideration has been given to the mechanism of dominance in metric characters (Kacser and Burns 1981, Dean *et al.* 1988). The conclusion was that dominance reflects enzyme activity levels. Advantageous alleles are dominant because they are associated with high levels of enzyme activity. Furthermore, neutral variation is believed to be reflected in low levels of dominance. In other words, instead of *becoming* dominant, advantageous alleles *are* dominant. Beyond this, the effect is the same - traits related to fitness will display dominance, as well as epistatic interaction variance, while those not related to fitness will display neutral, or additive genetic variation. A more complete review is contained in Falconer (1989).

## Family Studies

In any attempt to describe the covariance structure of a continuous trait, family groupings such as parent-offspring or siblings are examined. This is because the degree of genetic relationship between family members determines the number of genes they share on average. Thus, we can predict the correlation or covariance between them for that trait under various genetic and environmental models.

For instance, a model involving no contribution of individual environment to variation would yield an expected correlation coefficient of 1.00 between MZ twins. Presence of additive genetic variation tends to produce a DZ correlation of half the MZ value, since DZ twins and other full-siblings share about half of their genes on average. Family (shared) environment causes DZ correlations to be greater than half the MZ value, whereas non-additive genetic variation causes DZ correlations to be less than half the MZ value.

The most popular type of family study is probably the classical twin method, which may be defined as the study of MZ and DZ twins reared in the same home. It is one of the most powerful designs for detecting genetic and shared environmental effects (Neale and Cardon 1992).

**The Classical Twin Study**

Twin studies began with Galton's (1875) publication, "The history of twins as a criterion of the relative powers of nature and nurture". Galton was among the first to assert that twins were of two types - those that were formed from a single fertilised egg which had split, and those originating from two eggs, fertilised separately. The recognition that the first type of twinning process resulted in twins who shared the same genetic information, whereas the second type gave rise to two individuals who were no more alike than normal (full) siblings, was the first step in developing a method for estimating genetic and environmental contributions to variation among individuals. The basic twin method involves calculation of statistics such as concordance rates, correlation or covariance coefficients, and subsequent comparison using one of several formulae.

The twin method has been recognised as a powerful means of analysing the structure of phenotypic variation, yielding at its simplest step, estimates of heritability for a wide range of traits - including morphological, physiological, behavioural, psychological, and social characteristics. Heritability is perhaps the most widely calculated and best understood genetic statistic, but is of limited use in itself. Modern statistical methodology goes far beyond the estimation of heritability, to elucidation of other genetic components of variation, as well as various environmental components and interactions between components. Methods for doing this have been developed to a high degree, especially over the last forty years. A review of the development this methodology is contained in Neale and Cardon (1992).

**Twin Groups and the Twinning Process**

In general, twins are assumed to be of two types - identical and non-identical. The former are believed to be formed by the splitting of the zygote sometime after fertilisation, and thus are termed monozygous (MZ). The latter variably are called dizygous (DZ), fraternal, or non-identical twins, and form when two ova are released at ovulation, with each being fertilised by separate sperm. While MZ twins are assumed to be genetically identical, DZ twins share half their genes (on average), and are thus no more similar, genetically, than non-twin full siblings.

There are several advantages in studying DZ twins rather than singletons (Martin *et al.* 1997). Firstly, there is no confounding with age differences in expression of a trait due to either environment or age-related gene expression. DZ twins also match MZ twins as closely as possible in factors involved in twin gestation, birth and rearing. DZ twins are also more likely to have been sired by the same father than are non-twin siblings.

### Assumptions of Twin Studies

A number of assumptions exist in twin studies. Mostly they concern the degree to which twins are representative of the general population.

*1. MZ twins are genetically identical.*

Twin studies are based on the principal assumption that differences among MZ twins are caused exclusively by environment. However, a number of developmental disturbances have been postulated that may cause MZ twins to differ in genetic constitution or gene activity. Initially, the splitting of the embryo may result in unequal allocation of blastomeres, with one receiving more cells than the other (Machin 1996, Martin *et al.* 1997). Post-zygotic disturbances include chromosomal non-disjunction, somatic mutation, differential imprinting of genes, skewed X-inactivation in females, differential trinucleotide repeat expansion, and differences in timing of cellular events, such as gene imprinting or X-inactivation (Machin 1996, Martin *et al.* 1997). Any of these events might lead to a difference in phenotype between identical twins. Some have been demonstrated to have occurred, particularly non-disjunction (Kurosawa *et al.* 1992) and skewed X-inactivation (Richards *et al.* 1990, Trejo *et al.* 1994).

For the purposes of this study, MZ twins were assumed to be genetically identical, since karyotype analyses were not conducted to test for gross chromosomal changes, and it was not possible to detect other disturbances.

*2. Two types of twins - MZ and DZ*

It generally is assumed that non-MZ twins are formed from two separate ova fertilised by separate sperm, both from the same father. Several alternatives to this mode of producing non-identical twins have been suggested. These include cellular division of a single ovum, followed by fertilisation of each by separate sperm (monovular dispermy), fertilisation of the ovum and of one its polar body cells (polar body twinning), and production of DZ twins with different fathers (heteropaternal superfecundation).

It is believed that polar body twinning in humans is more likely to produce a chimeric individual than a set of twins, due to the close association between the ovum and polar body cells (Gartler *et al.* 1962), and one such chimeric individual has been described. It also has not been established whether monovular dispermic twins even exist (Elston and Boklage 1978). By comparison, heteropaternal superfecundation has been demonstrated to occur, although the frequency seems to be extremely low. For instance, DZ twins produced by heteropaternal superfecundation have been estimated at 1 per 13,000 cases of disputed parentage (Wenk *et al.* 1992).

The genetic effects of these methods of twin production vary. Division of a single ovum prior to fertilisation would produce two individuals who share an average of three quarters of their genes in common. Polar body twinning, if it produced twins at all, would reduce the similarity between them if it involved a primary oocyte and its polar body, or increase the similarity if it involved a seconday oocyte and its polar body. Heteropaternal superfecundation would lower the similarity, such that the individuals would share an average of one quarter of their genes in common.

Given the low frequencies of these types of twinning, and the difficulties that exist in detecting them, they were assumed to be absent from the twin sample obtained.

*3. Equal environmental similarity for MZ and DZ twins.*

This assumption applies to trait-relevant aspects of the environment twins share. If MZ twins are treated more similarly than are DZ twins, in ways that influence the trait under consideration, they would be expected to show greater similarity. This might then be interpreted as evidence of genetic variance. The assumption is difficult to test, especially given the partial nonidentifiability of environmental factors in tooth size determination. However, in one twin study, researchers tested the assumption by conducting a series of ingenious experiments utilising mistaken zygosity diagnosis. They demonstrated that the increased similarity of MZ twins was not due to their being treated similarly, as much as to their similar genes eliciting the same responses from the environment (Kendler *et al.* 1993a).

*4. Twins are representative of the general population.*

When estimating heritability from twins, it is a fundamental assumption that both MZ and DZ twins have the same genotypic and environmental variances as the singleton population from which they originate. If either of the twinning processes affect development of the trait being studied, then the results cannot be generalised to the rest of the population.

The splitting of an embryo during formation of MZ twins is perhaps the most disruptive event to their embryological development, possibly explaining the increased incidence of structural defects in MZ twins compared with DZ twins and singletons (Schinzel *et al.* 1979). Both types of twinning also have been associated

with malformations due to crowding in utero (Schinzel *et al.* 1979), and increased birth complications and neonatal mortality (Boklage 1985, Fraser *et al.* 1991).

Like assumption (3), this assumption is violated only if the zygosity affects the trait in question. Fortunately, it is not difficult to test for an association between twin zygosity (including singletons) and mean trait size or variance, and such an analysis is presented in chapter 3.

*5. Other twin study assumptions.*

Twin studies have been complicated by the assertion that a number of assumptions necessary to the interpretation of twin data exist, and should be tested before proceeding with data analysis. Christian and coworkers (Christian *et al.* 1974, Christian 1979) recommended testing for differences in means, variances and environmental covariances between zygosities, and using modified formulae if significant differences were found.

In the light of current biometrical genetic methods, some aspects of these tests seem inappropriate, and the assumptions they test, unnecessarily severe. For instance, the proposed test for equality of environmental covariances of MZ and DZ twins is an F test of among-DZ variances divided by within-DZ variances. If the calculated ratio is not appreciably greater than 1, it is assumed to be unlikely that any substantial proportion of the variance is genetic (Corruccini *et al.* 1990). However, the test appears to assume that genetic variation is additive. Significant non-additive genetic variation will cause within-DZ variances to rise, and the F ratio may then suggest that there is no significant genetic variation. In addition, Elston and Boklage (1978) criticize Christian analyses for assuming the differences in means or variances among twin types are due to differences in environmental contributions only, when

there are several possible sources of genetic variation which could lead to differences among zygosities.

**Other Family Studies**

By comparing associations between family members of different genetic and environmental relatedness, a clearer picture of genetic and environmental contributions to observed variability often can be obtained than by studying twins alone. For instance, parent-offspring comparisons can yield more information on traits which show dominance or epistatic interaction, than can twins raised together.

The literature on family studies of tooth size in the permanent dentition covers studies of twins, full and half siblings, and parent-offspring comparisons. The methods applied in these reports incorporate heritability estimation from either regression analysis of parents and offspring, or from components of variance generated by ANOVA. The latter may be followed by correlation analysis of multiple relationships, factor analysis, by examination of correlations of factor scores, and path analysis.

The correlation coefficients mostly were compared with expectations under various models of inheritance. For instance, Fisher's (1918) theory states that traits determined by many genes, each with small additive effects, would be reflected in correlation coefficients of 0.50 for parents and offspring, and full siblings, or 0.25 for half siblings. Midparent-offspring correlations likewise would be about 0.7. In addition, dominance would cause correlations to decrease, with larger decreases in parent-offspring than sibling correlations. Sibling correlations also were examined for evidence of genes on the sex chromosomes, since sex linkage (without dominance) has been postulated to lead to correlation coefficients of 0.75 for pairs of sisters, 0.50 for brothers, and 0.35 for sister-brother pairs (Mather and Jinks 1963).

## General Description of the Dentition

The mammalian dentition is described as heterodont, meaning that the teeth vary in shape and/or size, rather than being similar, repeated structures. They form four morphological classes - incisor, canine, premolar and molar. Within each class there are some differences in morphology and variability, although members of a given class are more similar to each other than to members of other classes. It is also a diphyodont dentition, having only two successive sets of teeth. These are referred to as the primary or deciduous dentition, and secondary or permanent dentition.

Although there are some variations on the theme, the typical human dental formula for both maxilla and mandible is two incisors, one canine, two premolars, and three molars. Since third molars often are extracted or fail to form, they are not studied by most researchers, and are not included in this thesis either. The two human premolars are actually the third and fourth in the classic mammalian dentition, the first and second having been 'lost' in the evolution of our species. However, for simplicity and to keep in line with most of the literature, they are referred to as first and second premolars.

## Embryology of the Dentition

Some aspects of tooth development are well known, such as which cells and tissues are involved, and the timing of formation. Descriptions have been published in many textbooks and journals, so only a brief version is presented here. Unless otherwise specified, the information presented is based on Sadler (1985) and Stock *et al.* (1997). Dental tissue forms within epithelial and mesenchyme cell layers. Epithelium is derived from embryonic ectoderm, while mesenchyme originates in the neural crest. Initally, the epithelium thickens to form a dental lamina, which pushes into the

mesenchyme to form a bud around which mesenchymal cells aggregate (bud stage). The epithelium at the tip of the bud invaginates to form a cap-shaped structure around the condensing mesenchyme (cap stage). The condensing mesenchyme is known as the dental papilla. A cluster of cells, the enamel knot, forms within the cap, facing the mesenchyme. As the indentation in the cap deepens, it takes on the shape of a bell (bell stage). The epithelial cells lining the inside of the bell (inner enamel epithelium) differentiate to become ameloblasts, and secrete the enamel proteins, enamelin and amelogenin. Similarly, a layer of mesenchymal cells differentiate into odontoblasts and secrete dentine. Each of these secretions is laid down initially at the junction of the cell layers, with progressive growth occurring away from the junction on each side. This mineralisation of the tooth progresses from the tip of the crown towards the cervical region. As this occurs, the final shape of the tooth emerges. Any major changes to the shape have to occur before this mineralisation spreads, when the tooth is still a mass of soft tissue.

At the tooth's centre, the remaining cells of the dental papilla form pulp, and eventually, a pulp chamber, containing blood vessels and nerves. The dental papilla and surrounding mesenchymal tissue (dental follicle) are responsible for producing the dentine of the crown and roots, as well as the cementum (outermost layer of the root), periodontal ligament which anchors the tooth, and the alveolar bone.

The interactions between epithelial and mesenchymal cell layers also have been studied in depth. Transplantation of premigratory cranial neural crest (CNC) cells and subsequent reunification with epithelium from a variety of body regions has demonstrated that the CNC cells have odontogenic potential, but only in the presence of epithelium from the dental arch (Lumsden 1988). This suggests that the CNC cells are not prespecified for differentiation before or even during their migration, and that "the oral epithelium is the earliest known site of tooth pattern" (Lumsden 1988, p155).

## What Genetic Factors have been Reported?

Of all the dental traits studied so far, very few exhibit simple genetic transmission or complete environmental determination. For the most part, they seem to involve a large number of genetic factors interacting with a variety of environmental factors (Niswander 1963). Since tooth crown size follows a continuous distribution, it also is assumed to be the result of actions and interactions among many genes and environmental factors. Some support for this notion has been provided by at least one study, in which there was no evidence of major gene effects (Kolakowski and Bailit 1981).

The genetic influences that have been identified to date have arisen from statistical analyses, studies of individuals with chromosomal anomalies, and from the more precise molecular studies of hormones, proteins and mapped genes. Given the long history of quantitative genetic methodology, compared with that of molecular techniques, there are many more studies based on the former than the latter. Indeed, much of the current genetic theory of tooth morphology arises from family studies.

### Statistical Factors - Family Studies

*Genetic Models Based on Correlation*

Correlation coefficients among full sibs, half sibs, and between parents and offspring mostly were found to be consistent with that expected in a trait with autosomal polygenic inheritance under Fisher's (1918) model (Bowden and Goose 1969, Townsend 1978, El-Nofely and Tawfik 1995), although there was some evidence that sex linked genes and non-genetic factors also played a role (El-Nofely and Tawfik 1995).

*Multivariate Genetic Factors*

Multivariate analyses have provided insights into common sources of variation for groups of variables. For instance, genetic factors applicable to the four tooth groups have been reported (Mizoguchi 1980). Further analyses suggested that there were two functional units in the dentition, corresponding to anterior (I1 to C) and posterior (P1 to M2) teeth (Potter *et al.* 1968, Mizoguchi 1981). Other reported factors have included independent genetic factors on each tooth (Lundström 1964, Moorrees 1964, Goose 1970), independent genetic determination of maxillary and mandibular dentitions (Potter *et al.* 1976), and independent genetic determination of mesiodistal (MD) and buccolingual (BL) diameters of anterior teeth (Potter *et al.* 1968, Townsend and Brown 1979). A more complete listing of statistical genetic factors is contained in chapters 7 and 8.

**Chromosomes**

Early family studies suggested an X-linked effect on permanent tooth crown size (Garn and Rohmann 1962, Alvesalo 1971). In particular, X chromosomal involvement is implicated by the existence of one form of amelogenesis imperfecta (defective enamel production) with X-linked dominant inheritance. The Y chromosome also was postulated to affect crown size, with its effect differing from that of the X chromosome (Alvesalo 1971, Alvesalo *et al.* 1991).

Subsequent studies of people with sex chromosomal anomalies have revealed a likely influence of the X chromosome on enamel deposition (amelogenesis), and of the Y chromosome on both amelogenesis and dentinogenesis (formation of dentin) (reviewed by Alvesalo *et al.* 1985, Townsend *et al.* 1986a, Alvesalo 1997). The Y chromosome seems to promote cell proliferation in the developing tooth germ,

resulting in a greater mass of cells forming the dentin, and thus a larger tooth (Alvesalo 1997). This role may be sufficient to explain the observed sexual dimorphism in human tooth crown size. These correlative studies also revealed the likely location of the X linked gene or genes as being on the short arm (Mayhall *et al.* 1991), while those on the Y were found to reside on the long arm (Alvesalo and de la Chapelle 1981).

**Hormones**

In contrast, knowledge about whether, and how, sex hormones affect tooth morphology is limited. There is indirect evidence of tooth development being affected by circulating sex and growth hormones (Garn et al., 1965a; Lorber et al., 1979). Androgens also have been implicated in tooth development in spotted hyenas (Frank et al., 1991) and in an observed (reverse) sexual dimorphism in molar tooth mass of mice (Heller and Blecher, 1982). However, there is indirect evidence against a significant role of androgens in tooth crown size in humans, from studies of 46,XY females (testicular feminization syndrome). The teeth of these females are not significantly different from those of normal males (Alvesalo and Varrela 1980). The syndrome is caused by a lack of androgen receptors (Alvesalo and Varrela 1980), so it seems unlikely that sexual dimorphism in tooth size is linked to production of androgens.

**Molecular Genetic Studies**

The two main aims of mplecular studies have been the mapping of loci for the human amelogenin gene, and the discovery of what substances initiate and guide embryonic development of dental tissues, mostly in mice.

*Amelogenin genes*

Amelogenin is the more abundant of the two enamel proteins, comprising as much as 90% of the enamel matrix (Fincham *et al.* 1992, Robinson *et al.* 1992). Alterations to the amelogenin gene are believed to be responsible for the X-linked condition, amelogenesis imperfecta (Lagerström *et al.* 1991). Evidence for chromosomal location of the amelogenin gene has been reported from investigations of chromosomal aneuploidies. For these reasons, the search for the gene has been relatively intense.

As in the chromosomal studies, molecular genetic investigations mapped human amelogenin genes to the X and Y chromosomes (Lau *et al.* 1989, 1990). It was demonstrated also that genes on both chromosomes are transcriptionally active, producing potentially functional proteins (Fincham *et al.* 1991, Nakahori *et al.*, 1991, Salido *et al.*, 1992, Gibson *et al.* 1992). The two genes (AMEL-X and AMEL-Y) differ in both chromosomal location and sequence. AMEL-X is situated at the distal end of the short arm (region Xp22.1 to 22.3), whereas AMEL-Y is close to the centromere on the long arm in region Yq11 (Lau *et al.* 1989, 1990, Lagerström *et al.* 1990). This difference in location supports the notion that there has been a pericentric inversion in the Y chromosome during primate evolution (Lau *et al.* 1989). There are several differences in base sequence and structure of the two genes (reviewed by Salido *et al.* 1992). Among these is the presence of 13 single amino acid substitutions and the deletion of a 21-amino acid domain in AMEL-Y relative to AMEL-X (Gibson *et al.* 1992). It has been postulated that the sequence differences explain the sexual dimorphism in human tooth size (Lau *et al.*, 1990, Fincham *et al.*, 1991).

*Homeobox genes, growth factors and other substances*

The other main branch of molecular genetic investigation has been the identification and localization of proteins and other substances present in embryonic dental tissues. At present most results come from studies of mice. Among the substances found to be present within developing dental mesenchyme, epithelium and enamel knot, are homeobox gene, growth factors and connective tissue molecules. Numerous reviews have been published (Weiss 1993, Thesleff 1995, Stock 1997), and unless otherwise referenced, the following information was taken from these reviews.

Among the proposed regulatory genes are Notch and homeobox genes Msx-1, Msx-2, Dlx cluster genes, Dbx, MHox, Mox2A, Pax-1, Pax-2 and Pax-6, and sonic hedgehog (Shh) (Vaahtokari *et al.* 1996), and genes from the more famous Hox cluster. There are also structural or connective tissue genes, such as syndecan (Salmivirta *et al.* 1991), collagens, amelogenin, osteonectin and tenascin. Several types of growth factors also have been identified - including EGR-1, EGF, bone morphogenetic proteins (BMP-2, BMP-4, and BMP-7), and FGF-4, a fibroblast growth factor (Vaahtokari *et al.* 1996).

Hox genes have been implicated in initiation of tooth formation and shape determination (MacKenzie *et al.* 1991, 1992). The BMPs may induce expression of Msx-1 (Vaahtokari *et al.* 1996), a critical event in tooth morphogenesis, since absence of Msx-1 is associated with agenesis of teeth (Satokata and Maas 1994). The precise influence of these molecules remains unclear, although the enamel knot has been portrayed as a signalling or organising centre providing positional information for tooth formation, and directing growth of the tooth cusps (Vaahtokari *et al.* 1996). All of the growth factors are expressed in the enamel knot in bud or cap stages, or both. BMP-4 is also expressed within the mesenchyme (Vaahtokari *et al.* 1996). The

enamel knot also expresses Shh (Vaahtokari *et al.* 1996). Msx-1 and Msx-2 are expressed in both incisors and molars of the mouse.

## What Environmental Factors have been Reported?

Environmental factors acting on the dentition may be divided into those occuring before birth (prenatal, maternal or uterine effects), and those after (postnatal effects). Environmental effects also may be divided into two groups depending on whether two members of the same family are exposed to them or not. The former class may be termed shared or family environment, and causes an increase in the correlation between relatives. The latter type is known as unique or individual environment, and decreases similarity among relatives. Environmental effects (especially prenatal) may be shared or unique among singleton siblings, but for twins they are more likely to be shared.

The permanent teeth begin to form in utero. At birth they are present essentially as soft tissue masses, the shape of which can still be modified. Calcification of the tooth crown ends this period of malleability. It begins at different times for different teeth, and also proceeds at tooth-specific rates. The first molars begin to calcify close to the time of birth, with other teeth starting later. Excluding the third molar, completion times vary from three or four years of age for the first molar, to between six and nine years of age for the second molar (Fanning 1971, Haavikko 1985, Smith 1991, Liversidge 1995). Thus, the type and magnitude of environmental influences might be expected to vary with the timing of calcification, and the length of time a tooth spends in soft tissue form. In particular, the first molars might be expected to display prenatal environmental effects more strongly than other teeth. Total environmental contributions to tooth crown characters might be expected to increase with length of time before completion of calcification.

**Prenatal (Maternal) Effects**

One important consideration is whether tooth crown size, which is finalised years after birth, can be affected by environmental conditions *in utero*. Numerous uterine conditions have been recorded previously as being associated with altered crown size in the permanent dentition. Mostly these involve maternal medical conditions, and intake of alcohol and nicotine. For example, average crown size was reported to be reduced in cases of maternal hypertension (Garn *et al.* 1979), and smoking (Heikkinen *et al.* 1994a, 1994b, 1995a, 1996). Conversely, maternal diabetes and hypothyroidism were correlated with increased crown size (Garn *et al.* 1979).

Even if the average sizes of tooth crowns are not altered by environmental conditions, there may be some loss of developmental stability, leading to increased asymmetry of right and left sides. When such asymmetry is random in direction, it is known as fluctuating asymmetry (FA). Studies of FA in tooth crown size suggest that overall developmental stability may be compromised under certain maternal conditions. FA has been demonstrated to increase with maternal alcohol consumption (Kieser 1992), and obesity (Kieser 1997). Although cigarette smoking alone was not associated with significant change in estimates of FA, smoking in combination with obesity was correlated with greater change than in obesity alone (Kieser 1997).

Other variables of the permanent dentition indicate an association with the uterine environment. Birth weight, used as an indicator of the quality of the uterine environment, and maternal age have been found to correlate negatively with dental development (Gyulavari 1966, Bailit and Sung 1968), although the correlations were reasonably low. Tooth eruption also correlated negatively with birth weight (Bailit *et al.* 1968). However, post natal influences could not be ruled out in these studies, and as Bailit *et al.* (1968) note, children from "disadvantaged homes" may have a poor pre- as well as post-natal environment.

As Garn *et al.* (1979, p. 675) state, "It should now be evident that a variety of definable factors operating well prior to birth may affect crown dimensions of ... permanent teeth in both sexes."

**Postnatal Effects**

Since the permanent teeth continue to grow and calcify after birth, it is conceivable that aspects of the post-natal environment also affect the final size and shape of teeth. In particular, nutrition and childhood disease processes might be expected to be important.

Numerous studies have revealed associations between the levels of nutritional elements and tooth morphology. The elements include fluoride, Vitamins A (in rats) and D, protein, sucrose:casein ratio (in rats), and phosphate (reviewed by Møller 1967). The most widely researched element, fluoride, has been shown to affect teeth adversely when the levels are too high *or* too low (Diefenbach *et al.* 1965).

There was no association between dental development and childhood illnesses in one study (Bailit *et al.* 1968), while in another, the levels of asymmetry in the dentition were shown to be associated with general levels of health and nutrition (Bailit *et al.* 1970).

Socioeconomic status has been shown to correlate with various indices of dental development although not consistently across all reports (reviewed by Bailit *et al.* 1968).

One artefactual source of postnatal environmental variation which may affect recorded tooth size is the deposition of calculus. This has been reported to correlate

positively with the BL diameters of anterior teeth (Kolakowski and Bailit 1981). These authors concluded that teeth with obvious calculus should be excluded from studies of crown size.

## Relative Levels of Genetic and Environmental Variation

In general, the estimates of genetic variation in tooth crown size have been moderate to high, and mostly additive in nature. Unique environmental contributions also have been shown to be significant, while very few studies have looked for (and found) significant common environment.

As stated by many authors, variation in tooth crown size appears to be mostly genetic in origin. How environment influences development of the permanent dentition, and how much it contributes, remain relatively unclear. However, there are indications from prior studies that the prenatal environment has more impact on dental development than the postnatal environment (Bailit *et al.* 1968).

To place some perspective, Garn (1977) pointed out that although the dentition is affected by conditions such as chromosomal aneuploidies, hormonal abnormalities, and body mass (and we could add level of nutrition), the degree of change is very small when compared with changes in skeletal components such as long bones, and physiological traits such as age at menarche.

### Estimates of Genetic Variation

Quantitative genetic analyses of data from related individuals have suggested a large genetic component to variation in human tooth crown size. Heritability has been estimated in numerous studies, as summarised in Tables 1.1 (for twins) and 1.2 (for other family studies). Although the average estimates indicate a moderately high

degree of genetic variance, the values range from near zero to more than one. Estimates also varied depending on the relationship and method used. For instance, half sibs gave substantially lower estimates than parent-offspring or full sibs in one study (Townsend 1978), but not in another (Townsend and Brown 1978b).

In mice, heritability of molar BL diameters was estimated using paternal half sib families, and a nested analysis of variance (ANOVA) (Bader 1965). This study revealed high levels of additive genetic contribution to all three molars with a distinctly lower value in the most distal tooth (0.66 for M1, 0.67 for M2 and 0.47 for M3).

Heritability estimates were reported to be greater in MD than BL dimensions (Moorrees 1964, Harzer 1987), and lower in distal than mesial members of tooth groups (Alvesalo and Tigerstedt 1974), although the latter is somewhat controversial.

**Estimates of Environmental Variation**

Few studies have attempted to estimate the percentage contribution of environmental factors to total variation. Using data from Australian Aboriginal families, total shared environmental contributions to the permanent teeth were estimated to average 6% in one study (Townsend 1978), and 18% for BL and 10% for MD diameters in another (Townsend 1978, 1992). A further pattern reported by Townsend was of higher values for BL than MD diameters. An earlier study of Caucasian adolescents yielded a suggestion that up to 50% of the variability in tooth crown diameters may be due to prenatal environmental factors (Garn *et al.* 1979).

In house mice, unique environmental effects have been estimated as explaining 17 to 26% of the variation in BL diameter of the molars, while common environment explained 16 to 27% (Bader 1965). For both types of environment, the highest value

was displayed by the third molar, with the first and second molars showing almost identical values. The factors involved were suggested to encompass cytoplasmic factors, uterine environment, and postnatal nutrition including the quality of maternal milk (Bader 1965). Significant postnatal maternal environment also has been reported in dentinal growth of second and third molars of male mice (Bae *et al.* 1996).

## Patterns of Variation within Tooth Classes

Teeth within each tooth class tend to be more similar to each other than to teeth in other fields, indicating that they develop as part of a system, rather than as individual units. However, it has been noted many times that teeth within each tooth class display different levels of variation. Observed patterns are remarkably constant over a variety of human populations studied, with maxillary central incisors, mandibular lateral incisors, canines, and first molars being the least variable teeth (reviewed by Kieser 1990).

How the tissues are induced to produce teeth of one class or another, and what produces the consistent patterns of variation, are questions which have been debated for many years. Two of the most common explanations are Butler's (1939) Field theory and Osborn's (1973) Clone theory.

### Morphogenetic Fields

Butler's (1939) Field theory states that tooth primordia grow within "fields" of diffusing morphogenetic substances, with one field for each tooth type. The theory includes the notion that teeth which form at the boundaries of a field may be influenced partly by substances diffusing from adjacent fields. This means that a tooth in the centre of a field (polar or key tooth) would show less variation than teeth

either side. The further one goes from the centre, the more variable the teeth should be. Initially, Butler identified three fields in mammals - incisor, canine and molar.

In 1945, Dahlberg argued that there were four morphogenetic fields in the mammalian dentition, corresponding to the four tooth classes. Within each field, he identified a "polar" tooth, which was more stable in its morphology - the central incisor, canine, first premolar and first molar. These teeth displayed lower coefficients of variation, and less chance of being missing, diminutive, or otherwise malformed. They also tended to be larger in size.

In a subsequent publication, Dahlberg (1949) stated that the field for mandibular incisors was reversed, with the lateral incisor being the polar tooth, because it was less variable than the central incisor. The process of deciding which teeth were polar seems somewhat circular (being based on variability levels). However, there are two aspects of embryology of the jaw which may explain the reversal of a morphogenetic field in the region of mandibular incisors - direction of ossification of the mandible, and position of the mental foramen. Ossification starts at the site of the mental foramen and proceeds both anteriorly through the canine and incisor regions, and posteriorly through the premolar and molar regions (Persson and Thilander 1985). The site of the (neurovascular) mental foramen may also explain the reversal in incisor field, if differentiation of odontogenetic tissues is controlled either neurally or by chemical messengers carried in the blood.

If this theory is correct, morphogenetic substances presumably diffuse distally along the tooth row, with the main centre of the field being at the mesial margin of the tooth group, except in the case of the mandibular incisors. In addition, polar teeth are somehow protected from the effects of diffusing morphogenetic substances mesial to their position, whereas distal teeth within each group are affected by substances diffusing from even more distal tooth groups. In short, later-forming teeth within a

group are affected by the field of the next-distal group, but earlier-forming teeth are not affected as much by substances from other groups.

Expansions of the field theory include the gradient prepattern (GP) model (Van Valen 1970), and the positional information (PI) model (Wolpert 1969). In the GP model, tooth primordia have identical prepatterns and are influenced by gradients of substances, but the magnitude of the response is determined by both the strength of substances, and the part of the primordium which is stimulated. The PI model simply states that tooth primordia gain information about their position from the concentration of morphogenetic substances surrounding them, and develop accordingly.

In addition to levels of variation being determined by position of a tooth within the morphogenetic gradient, predictions about levels of heritability have been generated from field theory. According to Falconer (1989), traits with low heritability tend to be strongly associated with reproductive fitness. These traits might be expected to exhibit more stability with time, and to be less variable in overall morphology. Thus the polar teeth might be expected to show lower levels of both variation and heritability, than other members of their tooth group. Some evidence supporting this prediction has been reported (Mizoguchi 1977).

**Osborn 's Clones**

An alternative to Butler's model was provided by Osborn's (1973, 1975, 1978) clone model. The field theory assumes that all tooth primordia are identical, and are reliant on surrounding tissues and diffusing substances to determine their shape and size. By contrast, Osborn's Clone model assumes that there are three clones of ectomesenchymal cells - incisor, canine, molar - from which all human teeth are derived. Each clone grows distally, and when it reaches a certain size, a tooth bud is

initiated in its centre. The clone continues to grow beyond the bud, and eventually creates other tooth buds until there is no more room. The increased variability of later-forming teeth in each of the three classes is explained as the result of the clonal origins: cells which give rise to the stable, polar teeth are younger than those which give rise to the more distal teeth. Changes in the genetic material accumulate as the clone grows.

**Other Explanations**

Alternatively, the odontogenetic process may be visualised as a progressive narrowing of potential developmental pathways, a process called epigenetic canalisation (Waddington 1942). In this model, phenotypic variability reflects the extent to which canalisation can withstand genetic or environmental disturbances. A further model of odontogenesis attempts to reconcile observed levels of variation with the length of time a developing tooth spends in soft tissue from, prior to calcification (Mizoguchi 1983). This model explains the higher variation of distal teeth as being due to environmental effects during the precalcific phase. Mizoguchi noted that the three least variable maxillary teeth (in order M1, C and I1), correspondingly had the shortest soft tissue stages, while second and third molars and maxillary lateral incisors exhibit long soft tissue stages and high rates of variability. This relationship has also been demonstrated in the fourth deciduous molar of the tree shrew, *Tupaia glis* (Gingerich 1974, Kondo *et al.* 1994). The patterns of variability may be explained then, by the potential for environmental factors to alter tooth shape during the prolonged soft tissue stage.

Therefore, dental variability might be attributable to concentration of a morphogenetic substance, age of primordial cell clones, degree of canalisation of development, environmental effects during the soft tissue stage, or a combination of these. Unfortunately, testing of the four models is difficult, since only the field and

environmental effects models generate predictions about levels of variation, and these generate similar predictions.

## Limitations of Previous Analyses

Given that there is already a wealth of information on genetic and environmental contributions to tooth crown size, it might be worth considering the merits of proceeding with another, albeit more modern, analysis. Further studies are warranted if there are more reliable or insightful methods available. Firstly, one could consider the inadequacies and limitations of previous methods, then look at a description of the approach used in this thesis, with its advantages, assumptions and limitations.

### Animal Studies

Although animal models provide insights into growth and development or the genetic basis of particular traits, the applicability of findings from animal studies is restricted in the extent to which humans and the experimental animals are similar. Since some experimental methods developed using animals cannot be applied to humans, it is difficult to test the degree of similarity. Even if the same molecules are found to be active in human tissues as in an animal model, it cannot be assumed that they provide the same function, or are regulated in similar ways.

### Descriptive and Correlational Studies

Descriptive patterns and correlations are, at most, evidence of *potential* sources of variation among individuals. It may be impossible to establish causation. For instance, research into chromosomal anomalies has revealed some fascinating correlations between the presence or absence of sex chromosomes and tooth size. However, since the precise nature of the connection between the anomaly and tooth

size is unknown, the genetic interpretation remains theoretical. Confirmation or disqualification of theories derived in this manner will require more precise techniques.

### Molecular Genetic Studies

The quality of information gained from molecular studies is excellent, but the process is relatively slow and expensive. In addition, the main focus has been to understand the genetic basis of diseases and extreme phenotypes, caused by a simple change in the DNA or in the regulation of gene expression. Variation which represents a range of normal functioning, rather than malformation or pathology, is a lesser focus of human molecular genetics. Molecular genetics as yet has not formed a solid foundation for understanding complex interactions among multiple genes, or between genes and the environment.
The situation is changing however, with interest in homeobox genes, and their contributions to the development of repeated structures like teeth and vertebrae, increasing.

### Quantitative Genetic Studies

Difficulties and limitations of former quantitative genetic studies (reviewed by Mizoguchi 1977) occurred in the areas of data collection (sample sizes and zygosity diagnosis) and statistical analysis (assumptions of the selected method).

#### *Zygosity Determination*

The earliest twin studies had difficulties establishing the true zygosity of twins in the sample. This has not been such a problem in studies of twins since the 1960s, because sufficient blood groups and enzyme polymorphisms have been identified to

minimise probability of incorrect diagnosis (Martin *et al.* 1997). Misdiagnosis has been further reduced by the introduction of testing for highly polymorphic DNA markers.

*Sample Sizes*

Another limitation was often one of small sample sizes. One estimate suggests that for a trait with high heritability, at least 200 pairs of twins are needed to obtain a reasonably accurate estimate of degree of genetic influence (Martin *et al.* 1978). The sample required is even greater if there is any common environment, non-additive genetic variation, or if heritability is moderate or low in magnitude (Martin *et al.* 1978). Many previous genetic analyses have shown deficiencies in this area, which is understandable given that twins are in low numbers within most populations.

*Statistical Methods*

Former studies also were plagued by obstacles such as being unable to distinguish or estimate heritability or other components of variation. Numerous components were assumed to be absent, particularly family environment, maternal effects, interactions between genes (epistasis), GxE and CorGE (reviewed by Mizoguchi 1977). In some cases heritability was not calculated because of reservations about the available methodologies (Osborne *et al.* 1958, Potter and Nance 1976). Generally, there was also no testing of models for goodness-of-fit. Many of the formulae encompassed several genetic and environmental components simultaneously, so the estimates which resulted from them are difficult to interpret, and of dubious value. In fact, complex genetic factors and interactions result in non-sensical values in most of the simple correlation-based estimates of heritability.

A second limitation of the statistical methods employed in the past is that they mostly involved single or multiple univariate analyses, without multivariate estimates of heritability. Given the high degree of intercorrelation among teeth (Potter *et al.* 1972), multivariate analyses of the dentition are preferred.

A further complication which has arisen occasionally is the decision to pool the sexes for analysis, in spite of significant sexual dimorphism in tooth crown size (reviewed by Mizoguchi 1977).

## Advantages of the New Approach

The current biometrical genetic methods have been assembled by workers in a number of fields, most notably agricultural and social sciences, over several decades. Their use is now reasonably widespread, and their applications almost unlimited in scope.

The advances in statistical analysis mean that a greater number of components of variation can be tested for, and estimated, than ever before. When applied to MZ and DZ twin pairs, the biometrical genetic modelling procedure allows testing for - and in most cases, estimation of - additive genetic, non-additive genetic, common environmental and unique environmental sources of variation. Both broad and narrow-sense heritabilities can be generated where both additive and non-additive genetic factors are estimated.

The process also can be extended to model means as well as variances and covariances. Other effects such as assortative mating, CorGE, and GxE can be incorporated, and a variety of types of heterogeneity between the sexes can be explored (Neale and Cardon 1992). The method also allows testing for age effects, co-twin interactions, and various inter-variable effects, such as an effect of earlier-developing teeth on later-developing ones.

The method provides efficient parameter estimates and a test of goodness-of-fit to the data. Different models can be compared so that the most parsimonious, and the best fitting, models can be identified.

Another advantage of modern methods arose with development of multivariate analyses, in which maximum likelihood analysis is blended with biometrical genetic concepts. Multivariate analyses allow exploration of the genetic basis of covariation between traits (Martin and Eaves 1977). "The aim is to determine in what combinations common genes pleiotropically influence a series of traits, and to what extent there are genetic effects specific to each trait ..." (Martin *et al.* 1997, pp 389-390).

A further reason for developing and applying such methods in the present project is because the subjects of study are humans. It is not viable to conduct breeding trials, or manipulative experiments in order to ascertain the type of genetic and environmental factors which may influence tooth morphology. The data we have are purely observational, and must be analysed carefully. Unless we continue to develop reliable, accurate statistical methods, the understanding of complex human traits may well remain beyond our grasp.

Overall, the procedures seem to be more reliable and less dependent on improbable assumptions. The advances are sufficiently significant that the results presented in this thesis are probably the most reliable (and complete) answers available on the topic.

The technique also has an advantage in connection with molecular genetic studies. Because the twin study is a powerful technique for demonstrating a genetic basis to complex traits, far from being superceded by molecular genetic techniques, it can

improve the efficiency of detection of quantitative trait loci (QTL) and assist in the understanding of developmental genetic mechanisms (Martin *et al.* 1997). Since simple, affordable molecular techniques to provide the same information will probably not be available in the foreseeable future, statistical analyses represent the best mode of enquiry.

## What Are The Limitations of This Study?

The potential limitations of this study include (1) the limitations inherent in any twin study, (2) sample size, and (3) nature of the measurement variables.

### Limitations of the Twin Model

When applied to data from twins raised together, the biometrical genetic method is restricted in several ways. Firstly, univariate models incorporating both common environment and non-additive genetic variation cannot be tested due to negative confounding (Grayson, 1989). Caution also must be applied with multivariate models, since very full models will be under-identified, leaving more parameters to be estimated than there are statistics or equations to solve. This difficulty can be resolved by including data from parent-offspring pairs. Secondly, dominance and epistatic interactions usually are not separable (Mather 1974). Thirdly, assortative mating cannot be tested, unless data is collected from parents of the twins (Neale and Cardon 1992).

Extending the twin model to include data from parents is one way to solve all three difficulties (Eaves *et al.* 1989). This extension does not form a part of the current work, but is a possible future direction, as data have been collected from the parents of some twins. Concerning assortative mating with respect to the dentition, it has been reported to be unlikely to occur (Potter *et al.* 1968, Hanihara *et al.* 1975). In

fact, family studies have revealed that correlations between parents were not significantly different from zero (Niswander and Chung 1965, Bowden and Goose 1969, Townsend and Brown 1978a, El-Nofely and Tawfik 1995). It also has been reported that there is no age effect on the dentition (Fujita 1960).

A further limitation involves the GIGO rule (garbage in, garbage out) of computer programming - the results are only as good as the models applied to the data.

**Sample size**

Sample sizes are important for (1) detection of heritability, (2) ability to detect common environment and non-additive genetic variation, and (3) ability to perform multivariate analyses.

The number of twins required if heritability is high is about 200 pairs (Martin *et al.* 1997). If moderate or low, and there is non-additive genetic variation or common environment, ten or twenty times this number are needed (Martin *et al.* 1997). The sample analysed here comprised 298 pairs of twins. Given the high degree of additive genetic contribution to variation (and low level of common environmental variation) in tooth crown size from most previous studies, it was expected that power would not be a major problem for this study.

Since the number of variables that may be modelled simultaneously is less than or equal to the number of twins in the smallest twin group, having a small sample size seriously restricts any multivariate analyses. In the data presented here, the smallest twin group was the DZ males, with a maximum of 45 pairs, yielding a maximum of 45 variables that could be analysed together. Since computing power did not permit analysis of more than 11 variables, these considerations did not limit the analysis.

### Nature of the Chosen Variables

Mesiodistal and buccolingual diameters are composite measurements, which may comprise the combined widths of two or more cusps. This makes it a little difficult to interpret results in terms of precise actions of genes, which may well control individual cusps and ridges. For example, path analysis was applied to correlations between the MD dimension of maxillary anterior teeth and nine dental traits including ridges, spines and shovelling (Mizoguchi 1978). The analysis revealed that three ridges loaded highly on the MD dimensions of the central incisor and canine, with some differences between sexes. Thus the resulting genetic and environmental influences on MD dimension may represent influences on three or more separate traits. Conversely, the gross diameters actually may represent the units of selection during evolution of the dentition. Cusps and other features may change in size or shape to accomodate required changes in overall tooth size.

Another consideration is that MD and BL diameters, even if analysed together, represent two-dimensional variables. Since teeth are three-dimensional, it may be more appropriate to study the 3-D shapes of whole tooth crowns, or of individual cusps or ridges. Such work has begun (e.g. Mayhall and Kanazawa 1989, Kanazawa *et al.* 1990, Mayhall and Alvesalo 1995, Pirttiniemi *et al.* 1998), and refinement of the methods involved may provide more biologically-sensible crown components for genetic analysis. In the meantime, raw diameters remain the most commonly-used indices of tooth crown size and shape.

## The Gaps in our Knowledge

So - where are the gaps in knowledge that this thesis seeks to fill? In part, the ground it covers is fresh and relatively unknown. Other paths already have been travelled by

a multitude of researchers. For the most part, the methods they used provided only partial or inaccurate answers, and the samples they collected, were often small. In the light of modern advances, even the ground that was well-trampled appears worth revisiting.

Both univariate and multivariate genetic analyses of tooth crown size are needed, using methods which provide the most reliable and accurate results possible. Evidence is sought of any genetic or environmental sources of phenotypic variation.

The wider questions which are of interest include how the dentition has been influenced by natural selection, the importance of the uterine environment during dental development, and the extent of sexual dimorphism, and nature of the factors which give rise to it.

It also is apparent that some dental genetic theories have been based on very small samples - in some cases, less than 20 pairs - or on unreplicated studies. Some of these studies have yielded conclusions which have become accepted dogma, sometimes even in the presence of evidence against them. In some cases, new information has arisen since the theories were generated, and so new hypotheses must be constructed and tested. Any additional studies at all are desirable, to enable development of a more sound basis to dental genetic theory. The controversial theories that have been generated in these ways include the levels of heritability in different teeth, as predicted by Butler's field theory, the evidence from sibling correlations of sex chromosomal involvement in tooth crown size, and even whether MZ and DZ twins and singletons are equivalent in their craniofacial development.

Current knowledge about the molecular basis of the patterning of the dentition also is very limited, especially when compared with other segmental systems in vertebrates, including the axial skeleton, digits and the brain (Stock *et al.* 1997). The more we can

learn about genetic and environmental influences on the dentition from family and other studies, the more we can direct the focus of analyses at the molecular level. The latest newcomer to the field of quantitative genetics is the search for quantitative trait loci (QTLs). These loci may be identified using relatively large samples of MZ and DZ twins. Before attempting to collect data from sufficient pairs of twins to identify QTLs, it is still an advantage to conduct a classical twin study to identify whether there is a significant contribution of genetic factors (Martin *et al.* 1997).

## Aims of This Thesis

The main objective of this project was to elucidate the nature and extent of genetic and environmental determination of permanent dental crown size, by comparing the phenotypic variation in MZ and DZ twins, and in unrelated singletons. Inherent within this study is an examination of the special nature of the twinning processes, and the implications they have, if any, on dental development. The analyses of tooth crown size involve nearly 300 pairs of twins, with more accurate zygosity determination using blood proteins or DNA, and exploration of sex differences in means and variances. The aims are :

- To look for effects of zygosity and birth order on tooth crown size;
- To test for sexual dimorphism in tooth crown size;
- To test for two possible causes of sexual dimorphism - sex chromosomes and sex hormones.
- To discover as much as possible about the nature of genetic and environmental factors influencing mesiodistal and buccolingual dimensions of individual permanent tooth crowns;

- To quantify their relative contributions;
- To identify pleiotropic effects of genes and environmental factors using multivariate analyses; and
- To examine patterns of variation and heritability within the dentition, for agreement with Butler's Field theory and other previous findings.

## Overview of The Thesis

The thesis is divided into nine chapters and five appendices. Following this introductory first chapter is a description of the study population, data collection and zygosity determination methods, definitions of the measured variables and dental nomenclature, and estimation of reliability of the measurement technique (Chapter 2). Chapter 3 details introductory exploratory analyses of the data, entailing testing of the data for normality, generation of descriptive statistics, testing for sex differences in means and variances, testing for effects of zygosity or birth order on mean tooth crown size, generation of correlation coefficients between different teeth, and between the two dimensions of each tooth. The magnitude of sexual dimorphism in the dentition is the subject of Chapter 4. In the following chapters, the use of sibling correlations to detect genes on the sex chromosomes is examined (Chapter 5), and evidence is sought of sex hormonal influences on the dentition, and diffusion of hormones between twins (Chapter 6). Chapters 7 and 8 contain the bulk of the biometrical genetic modelling, with univariate analyses of the 56 variables in the former, and multivariate analyses of (1) MD dimension of the eight incisors, (2) MD dimension of the maxillary right quadrant, and (3) BL dimension of the maxillary right quadrant in the latter. Chapter 7 also contains testing for GxE interactions and directional dominance. Both chapters involve modelling of means and covariances,

and examination of heritability estimates for agreement with patterns predicted by Butler's Field theory.

The appendices contain descriptive statistics for twins and singletons divided into eight groups on the basis of sex, zygosity, and sex of the co-twin (Appendix A), detailed description of the modelling process (Appendix B), and tables of inter-twin correlations (Appendix C).

**Table 1.1** : Summary of previous estimates of heritability for permanent tooth crown size, derived from twin studies.

| Author(s) | Year | Method [a] | Variables | Mean $h^2$ (SE) | Range |
|---|---|---|---|---|---|
| Rebich and Markovic | 1976 | $h^2 = (Var_{mz} - Var_{dz})$ | MD of I1 to M1 (maxilla) or M2 (mandible) | 0.88 | 0.71 to 0.97 |
| | | As above, using normalized data | All variables at once | 0.88 | -- |
| Mizoguchi | 1977 | $h^2 = 2(r_{mz} - r_{dz})$ | MD of I1 to M1 - females | 0.80 | 0.41 to 1.58 |
| | | | MD of I1 to M1 - males | 0.91 | 0.07 to 1.29 |
| Mizoguchi | 1980 | $h^2 = r_{mz}$ | MD of I1 to M2 - females | 0.79 (0.03) | 0.72 to 0.83 |
| | | | MD of I1 to M2 - males | 0.76 (0.04) | 0.60 to 0.85 |
| Townsend *et al.* | 1986c | Christian (1979) | MD of maxillary incisors | 0.34 | 0.21 to 0.42 |
| Harzer | 1987 | $h^2 = r_{mz}$ | MD of I1 to P2 | 0.73 | 0.64 to 0.88 |
| | | $h^2 =$ see paper | MD of I1 to P2 | 0.41 | 0.10 to 0.75 |
| | | $h^2 =$ see paper | MD of I1 to P2 | 0.63 | 0.38 to 0.81 |
| | | $h^2 = 2(r_{mz} - r_{dz})$ | MD of I1 to P2 | 0.51 | 0.20 to 0.90 |
| Boraas *et al.* | 1988 | $h^2 = 2(r_{mz} - r_{dz})$ | MD of maxillary incisors | 1.76 | |
| | | | MD of mandibular incisors | 0.60 | |
| Townsend | 1992 | $h^2 = 2(r_{mz} - r_{dz})$ | MD diameters | 0.90 (0.09) | |
| | | | BL diameters | 0.88 (0.09) | |

[a] Var= phenotypic variance, r = correlation coefficient.

**Table 1.2** : Summary of previous estimates of heritability for permanent tooth crown size derived from other family relationships.

| Author(s) | Year | Method [a] | Variables [b] | Mean $h^2$ (SE) | Range |
|---|---|---|---|---|---|
| Goose | 1971 | REG - Parent-Offspring | MD max I1, I2, C | 0.60 | -- |
| Alvesalo & Tigerstedt | 1974 | VC - Full Sibs | | 0.54 | 0.09 to 0.79 |
| | | | | 0.67 | 0.23 to 1.19 |
| Townsend | 1978 | VC - Parent-Offspring | | 0.64 (0.35) | -- |
| | | | | 0.57 (0.37) | -- |
| | | VC - Full Sibs | | 0.67 (0.12) | -- |
| | | | | 0.76 (0.12) | -- |
| | | VC - Half Sibs | | 0.47 (0.43) | -- |
| | | | | 0.41 (0.46) | -- |
| Townsend & Brown | 1978b | REG - Parent-Offspring | | 0.64 (0.35) | 0.21 to 1.54 |
| | | | | 0.57 (0.37) | 0.06 to 0.99 |
| | | VC - Full Sibs | | 0.72 (0.08) | 0.41 to 0.88 |
| | | | | 0.81 (0.08) | 0.58 to 1.01 |
| | | VC - Half Sibs | | 0.63 (0.30) | 0.17 to 1.25 |
| | | | | 0.66 (0.31) | -0.27 to 0.98 |

[a] REG = regression, VC = variance components.

[b] MD and BL of all 28 teeth (minus third molars) unless otherwise stated.

# Chapter 2

# Data Collection

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## Study Population

Twins and their families were located through the Australian National Health and Medical Research Council's Twin Registry, and through advertising. Singletons (or "non-twins") also participated, with most being first year dental students at the University of Adelaide. All subjects were of Caucasian descent. Data were obtained from 746 subjects, incorporating 149 MZ twin pairs, 149 DZ twin pairs, and 150 singletons (see Table 2.1). The twins were aged from 7 to 62 years, with 90% between 10 and 25 years. The mean age was 16.5 years. Singletons were aged between 17 and 25 years. Table 2.1 contains a summary of the sample classified by zygosity and sex.

## Data Collected from Subjects

Records obtained for each twin subject included alginate impressions and photographs of the dentition, and physical examination of the oral cavity. In addition, blood samples were collected for zygosity determination, as well as stereo facial photographs, finger and palm prints, and details regarding medical histories, birth weight and length, birth order for twins, and handedness. For singletons, only alginate impressions were obtained.

Twin zygosities were confirmed by examination of the blood antigens ABO, Rh, MNS, Jk and Fy, as well as serum enzyme polymorphisms ACP, AK1, ESD, GLO, GPT, PGD, PGM1 and PGP, and protein polymorphisms GC, HP, Pi and C3. The probability of dizygosity given concordance for all systems was less than 1%. Facial photographs and fingerprints provided confirmatory evidence of zygosity status. Data collection methods were approved by the Committee on the Ethics of Human

Experimentation, University of Adelaide (Approval No. H/07/84) and all participants were informed volunteers.

Models were made from the alginate dental impressions immediately after the impressions were obtained, using dental stone. Maximum mesiodistal (MD) and buccolingual (BL) crown diameters were recorded, following the definitions of Moorrees and Reed (1954). The MD dimension was taken to be the greatest distance between approximate surfaces, measured with the callipers held parallel to the occlusal and vestibular surfaces of the crown. For rotated or otherwise malpositioned teeth, the points on the approximate surfaces where it was considered that contact with adjacent teeth would normally occur, were used. The BL diameter was taken to be the greatest distance between the lingual and buccal surfaces of the tooth crown, measured in a plane perpendicular to that of the MD dimension (see Figure 2.1).

Measurements were recorded from all emerged and sufficiently-intact permanent teeth, except the third molars, yielding a maximum of 56 variables per subject. Measuring equipment comprised Mitutoyo digital vernier callipers, specially honed to produce finer points for more accurate measuring, and connected via a multiplexer unit to an Apple IIC computer. The callipers gave readings to the nearest 0.1mm. Data were subsequently transferred to a Unix machine (Sun Sparc Server 2) for analysis. Corrections for age were not considered necessary, since (1) the final size of dental crowns is determined before emergence of the teeth into the oral cavity, and (2) any teeth displaying significant attrition at measurement sites were excluded from subsequent analyses.

Dental nomenclature used in this thesis is depicted in Figures 2.1 and 2.2. *Mesial* means toward the midline or mid-saggital plane of the dental arch, *distal*, means

away from this midline. *Buccal* refers to the surface of the teeth facing the cheek or lip, while the tongue or palatal side is referred to as *lingual*. The terms mesiodistal and buccolingual reflect this terminology. The MD dimension is commonly referred to as a length, and the BL dimension is often referred to as crown breadth. In addition to dimension or diameter, the terms MD length and BL breadth are used throughout this thesis.

The incisors may be referred to either as central (I1) and lateral (I2), or first (I1) and second (I2). Premolars and molars are referred to either as first (P1 and M1) or second (P2 and M2). In addition to these classifications, the two incisors and one canine in each quadrant of the dentition may be referred to as *anterior* teeth, while the remaining premolars and molars are the *posterior* or cheek teeth.

## Reliability of the Measurement Technique

To estimate the reliability of the method, 50 models were measured independently by two investigators. The two sets of measurements ($x_1$ and $x_2$) were then used to calculate:

(1) Error Variance : $SE^2 = \{ \Sigma (x_1-x_2)^2 \} / 2n$ .......... (Eq 2.1)

(2) Dahlberg Statistic (TEM): $SE = \text{Sqrt } SE^2$ .............................. (Eq 2.2)

(3) Reliability : $R = (s^2 - SE^2)/s^2$ .......................... (Eq 2.3)

Inter- (or intra-) experimenter error variance ($SE^2$) may be estimated when the squared differences between two sets of measurements ($x_1$ and $x_2$) are summed over all cases (n) and divided by 2n (Equation 2.1). The square root of this (Equation 2.2) is variably referred to as the technical error of measurement (TEM), method error

statistic, or the Dahlberg statistic, since it was first suggested by Dahlberg (1940). In this thesis, TEM will be used to indicate the statistic.

The error variance and TEM incorporate both systematic and random errors (Houston 1983). In addition, we may estimate the proportion of total variance caused by random error alone, using the coefficient of reliability (Houston 1983). Reliability may be described as the proportion of observed variance due to true (phenotypic) variance as opposed to measurement error variance (Buschang *et al.*, 1987). Since observed variance ($s^2$) in any measurement is composed of true variance plus error variance ($s^2 = ST^2 + SE^2$), then true variance may be estimated as the difference between the observed ($s^2$) and error ($SE^2$) variances. Thus, reliability may be estimated as the ratio of true to observed variances (Equation 2.3).

Reliability calculated using repeated measures is the error from physically measuring the casts, and does not include error caused by all of the procedures used to measure the teeth - including impression- and model-making and storage. As for errors in the dental impressions, a certain amount of "linear distortion" of the impressions may have to be accepted due to syneresis (shrinkage due to water loss) or imbibition (expansion due to water uptake), no matter what materials and technique are used (Kieser, 1990). These effects remain unpredictable and not easily controlled, resulting in linear discrepancies estimated to be up to 0.06mm (Hollinger *et al.*, 1984). To minimise the error, impressions were sent (dampened) to the laboratory for model preparation immediately after they were obtained. Since these and other materials and techniques were not changed during data collection, this source of error was assumed to be small, and constant over all the models. Furthermore, at least one study has revealed that errors may actually be minimised by measuring casts instead

of taking intra-oral measurements, especially for the posterior teeth (Hunter and Priest 1960).

Accuracy of dental data has also been questioned at the level of interpretation of dental features. For instance, incomplete eruption of teeth into the oral cavity would increase inaccuracy in measuring BL diameters, particulary for the anterior teeth, so measurements were not recorded if eruption did not seem reasonably complete. Also, dental calculus has been postulated as a cause of increased variability of mandibular I1 BL breadth, relative to the I2 (Kolakowski and Bailit 1981). The increased variability has been shown to be a common feature of this tooth in other studies (eg Dahlberg 1949, Alvesalo and Tigerstedt 1974), but has not been demonstrated to be due to calculus.

The estimated TEM and reliability statistics for the 56 variables are listed in Table 2.2, and summarised in Table 2.3. For our repeated measures, the error variance was small, with all values being less than 0.013mm$^2$. The TEM averaged 0.06mm, with a range of 0.04 to 0.11mm. Estimated reliability ranged from 0.95 to 1.00 across the 56 variables, with an average value of 0.98. There do not appear to be any patterns among the reliability estimates which indicate significant levels of systematic or random errors, greater difficulty with measuring some teeth than others, or one dimension more than the other. Overall, the figures suggest a high degree of precision and repeatability of measurements, even when performed by the two different investigators.

**Table 2.1:** Sample Size and Sex/Zygosity Composition

| Zygosity | Sex | Pairs | Individuals |
|---|---|---|---|
| **MZ** | FF | 83 | 166 |
| | MM | 66 | 132 |
| **DZ** | FF | 49 | 98 |
| | MM | 44 | 88 |
| | MF | 56 | 112 |
| **Singleton** | F | -- | 75 |
| | M | -- | 75 |
| **Total:** | | | 746 |

**Table 2.2:** Sample size (N), TEM (in mm) and reliability (Rel).

| | Mesiodistal | | | Buccolingual | | |
|---|---|---|---|---|---|---|
| **Dim** | **N** | **TEM** | **Rel** | **N** | **TEM** | **Rel** |
| ***Maxilla, Right Side*** | | | | | | |
| **I1** | 50 | .06 | .99 | 50 | .06 | .98 |
| **I2** | 49 | .06 | .99 | 47 | .07 | .98 |
| **C** | 47 | .05 | .98 | 47 | .09 | .98 |
| **P1** | 46 | .04 | .99 | 46 | .08 | .98 |
| **P2** | 48 | .04 | .99 | 48 | .06 | .99 |
| **M1** | 50 | .08 | .98 | 50 | .04 | .99 |
| **M2** | 33 | .06 | .99 | 46 | .05 | 1.00 |
| ***Maxilla, Left Side*** | | | | | | |
| **I1** | 48 | .06 | .99 | 49 | .07 | .99 |
| **I2** | 49 | .04 | .99 | 48 | .08 | .98 |
| **C** | 48 | .06 | .97 | 48 | .07 | .98 |
| **P1** | 47 | .08 | .96 | 47 | .08 | .98 |
| **P2** | 48 | .05 | .99 | 48 | .06 | .99 |
| **M1** | 47 | .08 | .98 | 50 | .07 | .98 |
| **M2** | 34 | .08 | .98 | 42 | .08 | .99 |
| ***Mandible, Right Side*** | | | | | | |
| **I1** | 49 | .06 | .97 | 50 | .07 | .97 |
| **I2** | 49 | .05 | .98 | 50 | .06 | .98 |
| **C** | 48 | .07 | .97 | 46 | .05 | .99 |
| **P1** | 47 | .05 | .98 | 47 | .08 | .98 |
| **P2** | 48 | .06 | .98 | 47 | .09 | .98 |
| **M1** | 50 | .07 | .99 | 49 | .05 | .99 |
| **M2** | 31 | .08 | .99 | 45 | .07 | .99 |
| ***Mandible, Left Side*** | | | | | | |
| **I1** | 49 | .07 | .96 | 49 | .06 | .98 |
| **I2** | 49 | .05 | .98 | 50 | .06 | .98 |
| **C** | 50 | .07 | .95 | 46 | .07 | .99 |
| **P1** | 48 | .06 | .98 | 48 | .08 | .98 |
| **P2** | 49 | .06 | .98 | 48 | .07 | .98 |
| **M1** | 49 | .07 | .99 | 50 | .07 | .98 |
| **M2** | 36 | .11 | .97 | 47 | .05 | .99 |

**Table 2.3:** Range and average for TEM and Reliability.

| | | Min | Max | Mean |
|---|---|---|---|---|
| **TEM** | **MD** | .04 | .11 | .06 |
| | **BL** | .04 | .09 | .06 |
| **Reliability** | **MD** | .95 | .99 | .98 |
| | **BL** | .97 | 1.00 | .98 |

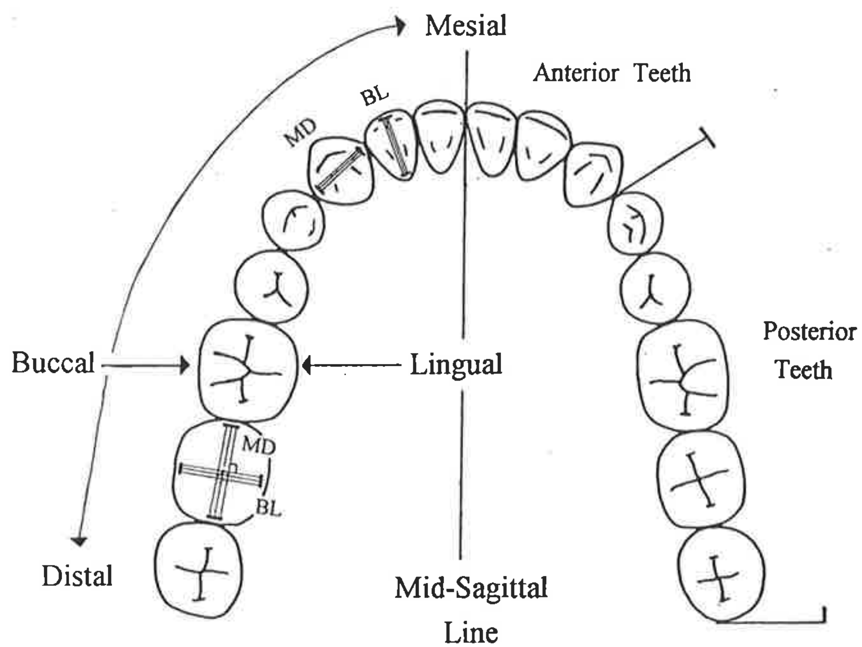


**Figure 2.1:** Dental nomenclature.

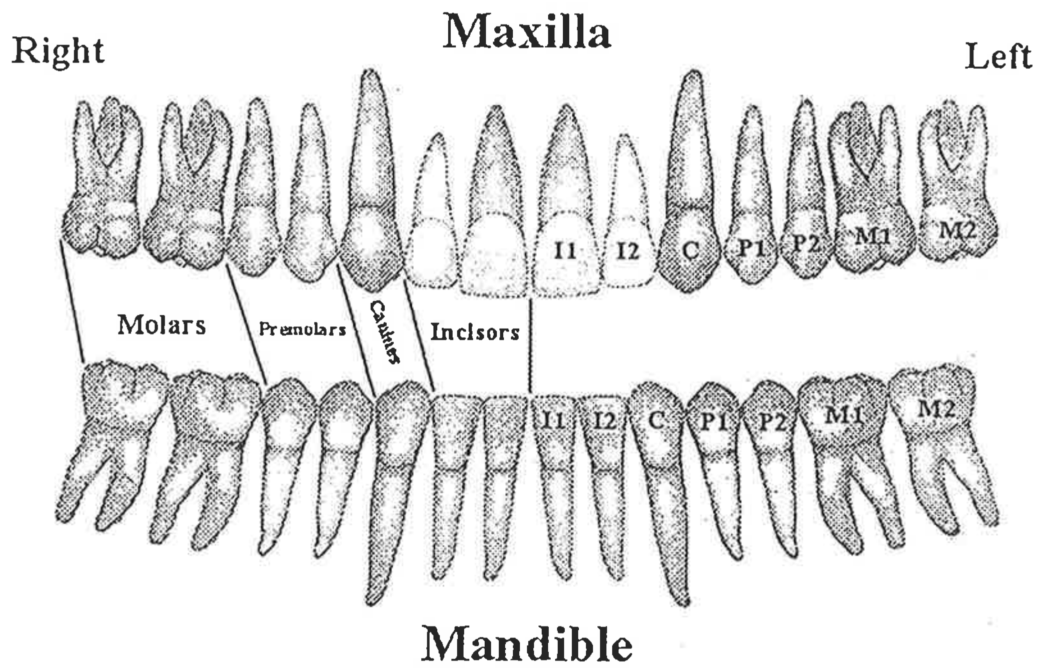


**Figure 2.2:** Map of the permanent dentition (excluding third molars).

# Chapter 3

# Exploring the Data

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## General Introduction

This chapter contains the results of basic analyses of the tooth size data, encompassing normality, descriptive statistics, differences between the sexes, effects of zygosity and birth order, and calculated correlations between the measured dimensions. Since most analyses were performed at least 56 times, the significance level chosen was $\alpha = 0.01$, unless otherwise stated. For all descriptive statistics, only the first member ("A" twin) of same sex twin pairs was used, since individual samples should be independent, and co-twins are not. Where the sexes were combined in a single analysis, the "B" twin from OS pairs was excluded also. A brief literature review precedes the data analysis in some sections.

## Normality of the Sample Distribution

The first step in data analysis entailed testing the distributions for normality. Since most studies of the dentition have revealed significant differences in tooth size between sexes, but not consistently among zygosities, normality was examined separately for each sex, regardless of zygosity. The program used was SPSSX (Release 4.0 for Sun4, SPSS Inc.), which produces a Kolmogorov-Smirnov (Lilliefors) test statistic, with a recommended alpha (significance) level of 0.2. Of the 112 variables (56 for each sex), 73 were significantly non-normal ($p < 0.2$). However, Norusis (1990) notes that almost any goodness-of-fit test of normality will result in rejection of the null hypothesis if the sample size is large enough, although "large enough" was not further defined. The alpha level itself generates an expected 22.4 Type I errors in 112 tests.

As a backup, normal, and detrended normal, probability plots and stemleaf plots were examined for each variable. Many variables exhibited one to a few extreme

values (high or low or both). However, the plots did not reveal any extreme or consistent non-normality in the data, and no transformation which was attempted ($log_{10}$, square and square root), produced significantly better results. There was also no sufficient reason to exclude the few outlying values. Overall, the data appeared to be approximately normally distributed, which is sufficient for most statistical tests.

To further examine the sample distribution, skewness and kurtosis were estimated for each variable within the sexes (Tables 3.1 and 3.2). Two-tailed tests of skewness ($\alpha = 0.01$) using tables of critical values from Zar (1984) revealed significant values in three variables - the MD diameter of mandibular left I2 and M2 in females, and maxillary left P2 in males. All exhibited positive skewness. In fact, most of the MD variables (25/28 for each sex) showed positive, but not significant, skewness. However, since most values were non-significant, transformations were not employed.

Significance of kurtosis was not attempted, as it cannot be assessed when n is less than 1000 (Zar 1984). However, zero was within the SE of most kurtosis estimates, indicating that a mesokurtotic shape of the sample distribution was possible. The only trends in the estimates were for significantly more negative than positive estimates among BL diameters of females (20/28 ($p<0.05$), 19/28 ($p<0.10$) for males), and more positive than negative estimates among MD diameters of females (20/28 ($p<0.05$), 14/28 ($p=1.0$) for males) than might be expected by chance.

## Sex Differences

### Introduction

Gender-related differences in the size of permanent tooth crowns have long been recognized to occur in humans. In short, males tend to have larger teeth than females.

This sexual dimorphism has been found to be significant for both MD and BL dimensions by univariate analyses (Seipel 1946, Moorrees 1959, Garn 1977) and multivariate analyses (Potter 1972, Boklage 1984).

In most analyses, the canines have been found to be the most sexually dimorphic teeth (both MD and BL diameters), and incisors have been reported as being the least dimorphic (Garn *et al.* 1964). A number of tests and calculations may be used to quantify this difference, but in this preliminary analysis phase, only tests of means, variances and coefficients of variation were conducted. The degree of sexual dimorphism in each tooth crown variable, and comparison of this among SS and OS twin pairs, will be described in Chapters 4 and 6, respectively.

**Analysis of Sex Differences**

Mean values, standard errors of the mean and standard deviations were calculated for each sex, using SS 'A' twins and all OS twins and singletons (see Tables 3.3 and 3.4). Male mean values were significantly greater than female means for all 56 variables (Student's t, $p<0.002$). In fact, all but two of the probability values were less than 0.001, with the remaining values being the BL dimension of mandibular right ($p=0.002$) and left ($p=0.001$) I2s. This supports previous conclusions that the incisors are the least sexually dimorphic teeth (Garn *et al.* 1964).

However, the intercorrelation of tooth crown diameters suggests that multivariate tests should be performed in preference to univariate tests (Potter 1972, Oxnard 1987, Harris and Rathbun 1991). To this end, a multivariate analysis of variance (MANOVA) procedure was employed. Since missing values lead to listwise deletion of individuals, the values for teeth were averaged over the four quadrants. That is, maxillary right and left and mandibular right and left teeth were averaged, yielding 14 variables - seven for MD and seven for BL diameters.

The SPSSX program included testing of MANOVA assumptions, including homogeneity of variances (univariate) and dispersion matrices (assessed by Box's M) between the sexes. Three of the variance comparisons - MD length of the canines, BL breadth of the I2s and canines - were significantly heterogeneous ($p<0.01$). Box's M indicated that the dispersion matrices were also significantly heterogeneous ($M=190.76$, $p<0.001$). However, violation of this assumption is not considered a problem if the groups have similar sample sizes, with the ratio of largest to smallest not exceeding 1.5 (Hair *et al.* 1995). Since the sample sizes in this study were approximately 237 for females and 211 for males, the impact of this violation is assumed to be minimal.

The exact F statistic generated by the MANOVA procedure was 12.27 ($p<0.001$), indicating a highly significant difference between sexes. Thus, both univariate and multivariate tests support the existence of sexual dimorphism for tooth size in humans.

The next question of interest was whether there were differences in variance which paralleled the mean differences between sexes. There was some indication from the MANOVA that this was the case, so variances for individual variables were calculated. Variance ratio (F) tests revealed a few significant differences in variance between females and males (Tables 3.5 and 3.6). The main tooth involved was the canine. Males showed significantly greater variance ($p<0.005$) for BL dimension of the four canines, with low but insignificant probabilities ($0.01<p<0.05$) for three out of four canine MD diameters. Significant differences were also found in the BL dimension of maxillary right and both mandibular I2s, and mandibular left M1, with males again displaying the greater variance. Thus, only eight of the 56 variables revealed evidence of a mean-variance relationship.

It also is of interest to compare coefficients of variation (CVs) between the sexes, to see if either sex is more variable when mean differences are removed. CVs may be compared if the variables are of the same dimensionality and complexity (Lande 1977). Since tooth crown diameters fit this criterion, CVs were compared using a variance ratio (F) test (2 tailed test, $\alpha = 0.01$) of squared CVs (Lande 1977). On inspection, male CVs generally were greater than those of females for BL dimensions, while female values were greater for most maxillary MD dimensions. Only two comparisons revealed a significant difference however - male CVs were significantly greater than female CVs for the BL diameters of both mandibular canines ($p<0.01$ for right and $p<0.001$ for left). Thus, by controlling for the difference in mean tooth size, most of the differences in variance disappeared. Only the mandibular canine BL diameters were more variable in males than females.

## Zygosity Differences

### Introduction

Twin studies were developed to analyse and estimate genetic and environmental contributions to variation in humans, but unless twins are representative of the whole population, the results cannot be applied more widely. Therefore, we should use whatever means are available to assess twin data for evidence of special effects of the twinning process. For example, it is a fundamental assumption of twin studies that zygosity itself does not influence the feature under study, so that means should be the same across the zygosity groups.

Criticisms of twin studies mostly have been based on the discovery of differences in means and variances between zygosity groups. In particular, Boklage and co-workers (Boklage 1984, Boklage *et al.* 1979) and Potter *et al.* (1979), have reported differences in means and/or variances between MZ and DZ twins using univariate

and multivariate analyses of the same 56 variables as used in this thesis. Boklage (1984) used discriminant function analysis to test for differences between zygosities. This procedure maximises the differences between the samples, and generally is used to provide information about minor differences between two populations. It is more appropriate to test for population mean differences using MANOVA than discriminant function analysis. The MANOVA performed by Boklage revealed no significant difference between zygosity groups. Univariate t' tests also showed no significant difference between means (Potter *et al.* 1979), although 13 to 15 of the 56 variables showed differences in variances between zygosities. The evidence for twins being non-representative of the general population then, is not conclusive.

**Analysis of Zygosity Differences**

Mean values, standard errors of the mean and standard deviations were calculated for the four "twin types" (MZ, DZSS, DZOS and Singleton) within each sex (see Appendix A). The data were then examined for any indication that mean tooth size might vary with zygosity. Given that sex is associated with differences in tooth size, two-way ANOVAs were performed for each of the tooth size (dependent) variables, using sex and zygosity (MZ, DZSS, DZOS, Singleton) as the independent variables. This allowed testing for significant interaction between sex and zygosity. Probability values associated with the F statistics for the effect of sex, zygosity and the interaction between them, are listed in Table 3.8. Unfortunately, multivariate testing using the 14 variables as in the previous section was not applicable, since tests of multivariate dispersion matrices revealed significant heterogeneity among the zygosity groups, and sample sizes varied too much to proceed (ratio of largest to smallest sample size = 2.96).

The difference in mean tooth size between the sexes was supported by the ANOVA. However, there was no consistent association between mean tooth size and zygosity.

Five F-values were significant - the MD dimension of the maxillary right I1 ($p<0.01$) and I2 ($p<0.001$), mandibular right I2 ($p<0.01$) and canine ($p<0.01$) and BL dimension of the mandibular left canine ($p<0.01$). Range tests of zygosity (Scheffe's test, $\alpha=0.01$) for these five variables within each sex revealed only one significant difference: DZOS males had significantly larger MD length of the maxillary right I2 than singleton males (by 0.3mm). Since the range tests were mostly nonsignificant, and the antimeres of these teeth showed no significance, the results were assumed to be of insufficient strength to warrant declaration of an association between zygosity and tooth crown size.

Only one of the 56 variables displayed a significant interaction between sex and zygosity: the BL dimension of the mandibular right M2 ($p<0.01$). The maximum difference in the average value for this variable was only 0.5mm, between MZ males (10.4mm) and singleton males (10.9mm). By comparison, the maximum difference between means in females was 0.2mm. The significance is assumed to be attributable to type I error, although it is noteworthy that the antimere also displayed a low but nonsignificant probability ($p<0.03$). In general, there appears to be no significant effect of zygosity on mean tooth size, or any interaction between sex and zygosity.

## Differences Due to Birth Order

### Introduction

One special aspect of being a twin is the higher probability of birth complications - in particular, blood gas level compromises. The second-born twin has been reported to undergo significant changes in blood gas concentrations compared with the first-born, and to be at a relative disadvantage. These differences include a lower $pO_2$ and pH, and higher $pCO_2$ (Nakano and Takemura 1988, Fuchi and Noda 1992). It is

therefore necessary to check whether birth order had an impact on the variables under study.

Previous studies of twins have revealed a significant difference in handedness between first- and second-born twins. However, the direction of the difference is not consistent. One report indicates that in 66% of twin pairs discordant for handedness, the non-righthanded one was the first-born (Christian *et al.* 1979), while in another, the non-righthanded one was the second-born in 60% of such cases (Boklage 1985). The latter study also reported that the effect of birth order was not significant for OS twin pairs, and that OS twins enjoyed a relatively lower perinatal mortality and higher birth weight. The suggestion was made that OS twins were not as stressed in utero as SS twins, and this was offered as evidence for oxygen stress causing non-righthandedness, and as a reason for the lack of effect of birth order on handedness in OS twin pairs (Boklage 1985).

In another study of birth order effects, a MANOVA procedure was applied to MD and BL dimensions of the tooth crowns, with sex, zygosity and birth order as the independent variables (Boklage 1984). Of these three variables, only sex was a significant contributor to mean tooth size.

**Analysis of Birth Order**

To investigate the impact, if any, of birth order on tooth size, multiple analysis of variance (MANOVA) was applied to MD and BL dimensions, averaged over the four quadrants, yielding 14 variables. Three MANOVA tests of the 14 variables were done in total - for all twins and for twins within each sex. Table 3.9 contains the results. Box's M test revealed homogeneity of variance-covariance matrices in the 3 analyses ($p>0.89$). Multivariate F tests revealed no significant effects of birth order

($p>0.68$). None of the 42 univariate F statistics was significant ($p>0.05$). Birth order of twins was not associated with a difference in MD or BL tooth crown size.

## Comparison of MD and BL Dimensions

### Introduction

Examining MD and BL dimensions - their mean values, levels of variation, and the degree of correlation between dimensions within a tooth, or between teeth within a dimension - is another way to gain insight into the kind of factors which influence tooth size and shape. For example, comparisons can yield evidence of evolutionary changes, sex effects, and genetic and environmental determination of the tooth diameters. The last option is the most relevant one for the current analysis. In particular, do different teeth, or different diameters within teeth, have the same determining factors - genetic, environmental, or both?

The following analyses have two main elements - correlation patterns among teeth within each of the two dimensions, and between the two dimensions within each tooth. There was one main aim: to look for evidence of genetic and environmental factors in the dentition. If two measurements or variables are highly correlated, then one possibility is that they share some determining factors, for example, a general "size" factor (Garn *et al.* 1968). A low correlation implies the inverse - that factors unique to at least one of the dimensions or variables have a stronger impact than any shared determinants.

### Inter-tooth comparisons

Firstly, Pearson correlation coefficients were calculated between all 28 variables within each of the two dimensions. The results are displayed in Tables 3.10 and 3.11.

All correlations were significant ($p<0.001$) and positive. The range of values was 0.27 to 0.93 for MD dimension, and 0.41 to 0.93 for BL dimension. In general, teeth showed higher correlations for BL than for MD diameter. The highest correlations were between antimeres ($r = 0.83$ to 0.93). The next highest correlations ($r = 0.70$ to 0.82) were between teeth within the incisor, premolar and molar tooth groups (e.g. maxillary left M1 with maxillary left M2), and between corresponding teeth in different quadrants (e.g. maxillary right I1 with mandibular right I1).

**Intra-tooth comparisons**

Mean MD and BL values from Tables 3.3 and 3.4 were examined by t-test ($\alpha = 0.01$) within each gender (using SS "A" twins, all OS twins and singletons), to see whether one dimension was significantly larger than the other. For most teeth, the BL dimension was greater than the MD dimension. The only exceptions were maxillary incisors and mandibular molars, for which the MD diameter was greater. The differences in means were significant ($p<0.001$) for all variables, except for the mandibular right M2 ($p>0.8$ for males and $p>0.05$ for females), and this was consistent across sexes.

Pearson correlation coefficients between the two dimensions were calculated using data from all singletons, and all "A" twins (see Table 3.12). All values were highly significant ($p<0.001$). The most obvious pattern was for lower correlations in the incisors ($r=0.35$ to 0.48) than in the other variables ($r = 0.55$ to 0.64 for canines, and $r = 0.55$ to 0.74 for posterior teeth).

**Discussion**

Few studies have analysed tooth size data in this manner, so available comparisons are limited. From the correlations between teeth, it would seem that different teeth

may have shared a moderate to high degree of common determination, with BL dimensions having been more strongly co-determined than MD dimensions. This finding is in agreement with correlations published for people of Japanese and Chinese origin (Yamada *et al.* 1986).

The correlations between MD and BL diameters within teeth were all positive and reasonably high (0.35 to 0.74), suggesting a moderate to high degree of determination of both dimensions by common factors also. These estimates are comparable to other studies of the dentition. For example, MD-BL correlations of 0.21 to 0.74 (Garn *et al.* 1968), and 0.10 to 0.74 (Yamada *et al.* 1986) have been reported for the permanent dentition, and 0.19 to 0.73 for the deciduous dentition (Farmer and Townsend 1993).

This topic will be discussed further in chapters 7 and 8, when theories of environmental and genetic contributions to tooth crown size are examined in more detail.

## Conclusions

- The tooth size data were approximately normally distributed, with no clear evidence of skewness or kurtosis;
- On average, tooth size was larger in males than in females;
- The BL diameter of mandibular canines was more variable in males than females;
- There was no significant effect of zygosity on mean tooth size, and no interaction between sex and zygosity affecting mean tooth size;

- There was no effect of birth order on mean tooth size;

- Intertooth correlations were reasonably high, suggesting moderate to strong common determinants ("size" factors); and

- BL and MD diameters also were reasonably highly correlated implying moderate to strong common determinants.

**Table 3.1:** Skewness and kurtosis, and standard errors (SE), for the MD dimension.

| | Females | | | | | Males | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Tooth** | **N** | **Skew**[a] | **SE** | **Kurt** | **SE** | **N** | **Skew** | **SE** | **Kurt** | **SE** |
| *Maxilla, Right Side* | | | | | | | | | | |
| **I1** | 257 | .08 | .15 | .01 | .30 | 231 | .08 | .16 | .13 | .32 |
| **I2** | 242 | -.13 | .16 | .39 | .31 | 226 | .31 | .16 | .95 | .32 |
| **C** | 233 | .09 | .16 | -.34 | .32 | 206 | .25 | .17 | -.19 | .34 |
| **P1** | 208 | -.07 | .17 | -.08 | .34 | 188 | .16 | .18 | -.11 | .35 |
| **P2** | 231 | .25 | .16 | -.23 | .32 | 197 | .33 | .17 | .34 | .34 |
| **M1** | 248 | .19 | .15 | .08 | .31 | 228 | .05 | .16 | -.49 | .32 |
| **M2** | 168 | .13 | .19 | 1.05 | .37 | 149 | .26 | .20 | 1.44 | .39 |
| *Maxilla, Left Side* | | | | | | | | | | |
| **I1** | 253 | .14 | .15 | .01 | .31 | 234 | .09 | .16 | .05 | .32 |
| **I2** | 246 | .00 | .16 | .17 | .31 | 230 | .30 | .16 | .30 | .32 |
| **C** | 236 | .17 | .16 | -.30 | .32 | 206 | .13 | .17 | -.31 | .34 |
| **P1** | 209 | .04 | .17 | .18 | .33 | 187 | .42 | .18 | .28 | .35 |
| **P2** | 230 | .09 | .16 | -.23 | .32 | 187 | *.51 | .18 | .44 | .35 |
| **M1** | 247 | .22 | .15 | .18 | .31 | 218 | .23 | .16 | -.37 | .33 |
| **M2** | 157 | -.32 | .19 | .54 | .38 | 133 | .11 | .21 | -.47 | .42 |
| *Mandible, Right Side* | | | | | | | | | | |
| **I1** | 260 | .14 | .15 | .35 | .30 | 233 | .25 | .16 | .54 | .32 |
| **I2** | 260 | .35 | .15 | .13 | .30 | 238 | .24 | .16 | .25 | .31 |
| **C** | 249 | .21 | .15 | .15 | .31 | 217 | -.20 | .17 | -.33 | .33 |
| **P1** | 227 | .01 | .16 | .12 | .32 | 204 | .10 | .17 | -.23 | .34 |
| **P2** | 227 | .41 | .16 | .42 | .32 | 199 | .13 | .17 | -.42 | .34 |
| **M1** | 239 | .20 | .16 | .08 | .31 | 226 | -.16 | .16 | -.34 | .32 |
| **M2** | 162 | .42 | .19 | .10 | .38 | 138 | .34 | .21 | -.18 | .41 |
| *Mandible, Left Side* | | | | | | | | | | |
| **I1** | 256 | .23 | .15 | .38 | .30 | 239 | .31 | .16 | .68 | .31 |
| **I2** | 257 | *.52 | .15 | .70 | .30 | 237 | .38 | .16 | .65 | .31 |
| **C** | 252 | .21 | .15 | .07 | .31 | 220 | .05 | .16 | -.26 | .33 |
| **P1** | 230 | .07 | .16 | -.08 | .32 | 205 | .17 | .17 | .03 | .34 |
| **P2** | 228 | .25 | .16 | -.05 | .32 | 195 | .13 | .17 | -.38 | .35 |
| **M1** | 240 | .12 | .16 | -.06 | .31 | 224 | -.27 | .16 | .02 | .32 |
| **M2** | 157 | *.71 | .19 | 1.28 | .38 | 137 | .23 | .21 | -.11 | .41 |

a * = $p<0.01$.

**Table 3.2:** Skewness and kurtosis, and standard errors (SE), for the BL dimension.

| | *Females* | | | | | *Males* | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Tooth** | **N** | **Skew[a]** | **SE** | **Kurt** | **SE** | **N** | **Skew** | **SE** | **Kurt** | **SE** |
| *Maxilla, Right Side* | | | | | | | | | | |
| **I1** | 246 | .04 | .16 | -.30 | .31 | 228 | .08 | .16 | -.22 | .32 |
| **I2** | 229 | -.03 | .16 | .09 | .32 | 209 | -.13 | .17 | -.12 | .33 |
| **C** | 219 | .05 | .16 | -.60 | .33 | 196 | -.11 | .17 | .18 | .35 |
| **P1** | 209 | -.40 | .17 | .10 | .33 | 190 | .19 | .18 | -.12 | .35 |
| **P2** | 231 | -.19 | .16 | -.28 | .32 | 201 | .11 | .17 | -.03 | .34 |
| **M1** | 251 | .09 | .15 | -.30 | .31 | 231 | .06 | .16 | -.37 | .32 |
| **M2** | 185 | .08 | .18 | .45 | .36 | 173 | .04 | .18 | -.53 | .37 |
| *Maxilla, Left Side* | | | | | | | | | | |
| **I1** | 248 | .03 | .15 | .04 | .31 | 226 | -.13 | .16 | -.27 | .32 |
| **I2** | 227 | -.02 | .16 | -.24 | .32 | 218 | -.13 | .16 | .20 | .33 |
| **C** | 221 | .04 | .16 | -.51 | .33 | 196 | -.02 | .17 | -.06 | .35 |
| **P1** | 214 | -.14 | .17 | -.09 | .33 | 193 | .14 | .17 | -.28 | .35 |
| **P2** | 234 | -.09 | .16 | -.25 | .32 | 191 | .26 | .18 | .27 | .35 |
| **M1** | 257 | .19 | .15 | .00 | .30 | 232 | .10 | .16 | -.35 | .32 |
| **M2** | 179 | .08 | .18 | -.18 | .36 | 162 | .17 | .19 | -.37 | .38 |
| *Mandible, Right Side* | | | | | | | | | | |
| **I1** | 258 | -.16 | .15 | .17 | .30 | 232 | -.33 | .16 | -.12 | .32 |
| **I2** | 250 | -.25 | .15 | .20 | .31 | 233 | -.23 | .16 | -.06 | .32 |
| **C** | 230 | -.28 | .16 | -.11 | .32 | 197 | -.33 | .17 | .03 | .34 |
| **P1** | 225 | .11 | .16 | -.19 | .32 | 202 | .14 | .17 | -.23 | .34 |
| **P2** | 228 | -.05 | .16 | -.15 | .32 | 199 | .03 | .17 | .05 | .34 |
| **M1** | 253 | -.05 | .15 | -.03 | .31 | 237 | .06 | .16 | -.32 | .31 |
| **M2** | 202 | -.02 | .17 | -.03 | .34 | 180 | .16 | .18 | -.36 | .36 |
| *Mandible, Left Side* | | | | | | | | | | |
| **I1** | 257 | -.12 | .15 | -.04 | .30 | 231 | -.37 | .16 | .36 | .32 |
| **I2** | 246 | -.05 | .16 | -.03 | .31 | 227 | -.37 | .16 | .36 | .32 |
| **C** | 231 | -.15 | .16 | -.54 | .32 | 191 | -.11 | .18 | -.28 | .35 |
| **P1** | 228 | .00 | .16 | -.25 | .32 | 204 | .09 | .17 | -.19 | .34 |
| **P2** | 227 | -.21 | .16 | -.10 | .32 | 195 | .09 | .17 | -.21 | .35 |
| **M1** | 248 | -.10 | .15 | -.06 | .31 | 227 | .05 | .16 | .10 | .32 |
| **M2** | 188 | -.10 | .18 | -.08 | .35 | 177 | -.05 | .18 | -.11 | .36 |

a * = $p<0.01$.

**Table 3.3:** Descriptive statistics for MD length: sample size (N), mean, standard error of the mean (SE), and standard deviation (SD).

| | *Females* | | | | *Males* | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **N** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 257 | 8.5 | .03 | .54 | 231 | 8.8 | .04 | .53 |
| **I2** | 242 | 6.6 | .03 | .52 | 226 | 6.8 | .04 | .54 |
| **C** | 233 | 7.5 | .02 | .37 | 206 | 8.0 | .03 | .45 |
| **P1** | 208 | 6.8 | .03 | .40 | 188 | 7.1 | .03 | .39 |
| **P2** | 231 | 6.6 | .03 | .42 | 197 | 6.8 | .03 | .40 |
| **M1** | 248 | 10.2 | .04 | .55 | 228 | 10.5 | .04 | .55 |
| **M2** | 168 | 9.8 | .05 | .62 | 149 | 10.3 | .05 | .63 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 253 | 8.5 | .03 | .54 | 234 | 8.8 | .03 | .53 |
| **I2** | 246 | 6.6 | .03 | .54 | 230 | 6.9 | .04 | .56 |
| **C** | 236 | 7.5 | .02 | .36 | 206 | 8.0 | .03 | .42 |
| **P1** | 209 | 6.8 | .03 | .39 | 187 | 7.1 | .03 | .40 |
| **P2** | 230 | 6.6 | .03 | .42 | 187 | 6.8 | .03 | .41 |
| **M1** | 247 | 10.2 | .03 | .54 | 218 | 10.5 | .04 | .52 |
| **M2** | 157 | 9.8 | .05 | .58 | 133 | 10.2 | .05 | .59 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 260 | 5.3 | .02 | .36 | 233 | 5.4 | .02 | .34 |
| **I2** | 260 | 5.8 | .02 | .39 | 238 | 6.0 | .03 | .39 |
| **C** | 249 | 6.5 | .02 | .34 | 217 | 7.0 | .03 | .38 |
| **P1** | 227 | 7.0 | .03 | .40 | 204 | 7.2 | .03 | .44 |
| **P2** | 227 | 7.0 | .03 | .45 | 199 | 7.3 | .03 | .42 |
| **M1** | 239 | 10.8 | .04 | .61 | 226 | 11.2 | .04 | .63 |
| **M2** | 162 | 10.3 | .05 | .61 | 138 | 10.8 | .06 | .66 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 256 | 5.3 | .02 | .36 | 239 | 5.4 | .02 | .34 |
| **I2** | 257 | 5.8 | .02 | .37 | 237 | 6.0 | .03 | .39 |
| **C** | 252 | 6.5 | .02 | .34 | 220 | 6.9 | .03 | .40 |
| **P1** | 230 | 6.9 | .03 | .42 | 205 | 7.2 | .03 | .42 |
| **P2** | 228 | 7.0 | .03 | .42 | 195 | 7.3 | .03 | .44 |
| **M1** | 240 | 10.8 | .04 | .65 | 224 | 11.2 | .04 | .60 |
| **M2** | 157 | 10.3 | .05 | .57 | 137 | 10.8 | .06 | .65 |

**Table 3.4:** Descriptive statistics for BL breadth: sample size (N), mean, standard error of the mean (SE), and standard deviation (SD).

| | *Females* | | | | *Males* | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **N** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 246 | 7.0 | .03 | .49 | 228 | 7.3 | .04 | .55 |
| **I2** | 229 | 6.2 | .03 | .48 | 209 | 6.5 | .04 | .59 |
| **C** | 219 | 8.0 | .04 | .53 | 196 | 8.4 | .05 | .66 |
| **P1** | 209 | 9.1 | .04 | .53 | 190 | 9.4 | .04 | .56 |
| **P2** | 231 | 9.2 | .04 | .56 | 201 | 9.6 | .04 | .59 |
| **M1** | 251 | 11.2 | .03 | .55 | 231 | 11.6 | .04 | .59 |
| **M2** | 185 | 10.9 | .05 | .71 | 173 | 11.6 | .06 | .78 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 248 | 7.1 | .03 | .49 | 226 | 7.4 | .04 | .57 |
| **I2** | 227 | 6.2 | .03 | .52 | 218 | 6.5 | .04 | .60 |
| **C** | 221 | 8.0 | .04 | .52 | 196 | 8.5 | .05 | .65 |
| **P1** | 214 | 9.1 | .04 | .52 | 193 | 9.4 | .04 | .54 |
| **P2** | 234 | 9.2 | .04 | .57 | 191 | 9.6 | .04 | .56 |
| **M1** | 257 | 11.2 | .03 | .54 | 232 | 11.7 | .03 | .53 |
| **M2** | 179 | 11.0 | .05 | .69 | 162 | 11.7 | .06 | .75 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 258 | 5.9 | .03 | .43 | 232 | 6.1 | .03 | .47 |
| **I2** | 250 | 6.3 | .03 | .42 | 233 | 6.4 | .03 | .50 |
| **C** | 230 | 7.3 | .03 | .51 | 197 | 7.8 | .05 | .68 |
| **P1** | 225 | 7.8 | .03 | .51 | 202 | 8.2 | .04 | .53 |
| **P2** | 228 | 8.5 | .03 | .49 | 199 | 8.8 | .04 | .58 |
| **M1** | 253 | 10.5 | .03 | .46 | 237 | 10.9 | .04 | .55 |
| **M2** | 202 | 10.2 | .04 | .54 | 180 | 10.7 | .05 | .62 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 257 | 5.9 | .03 | .42 | 231 | 6.1 | .03 | .45 |
| **I2** | 246 | 6.2 | .03 | .41 | 227 | 6.4 | .03 | .50 |
| **C** | 231 | 7.3 | .03 | .49 | 191 | 7.8 | .05 | .69 |
| **P1** | 228 | 7.7 | .03 | .52 | 204 | 8.1 | .04 | .55 |
| **P2** | 227 | 8.4 | .03 | .51 | 195 | 8.7 | .04 | .56 |
| **M1** | 248 | 10.4 | .03 | .45 | 227 | 10.8 | .04 | .55 |
| **M2** | 188 | 10.2 | .04 | .55 | 177 | 10.6 | .05 | .62 |

**Table 3.5 :** Variance in MD dimension in males and females, F ratio and significance.

| | *Males* | | *Females* | | |
|---|---|---|---|---|---|
| **Tooth** | **Var** | **df** | **Var** | **df** | **F** |
| *Maxilla, Right Side* | | | | | |
| **I1** | .28 | 231 | .29 | 257 | 1.04 |
| **I2** | .29 | 226 | .27 | 242 | 1.07 |
| **C** | .20 | 206 | .14 | 233 | 1.43 |
| **P1** | .15 | 188 | .16 | 208 | 1.07 |
| **P2** | .16 | 197 | .18 | 231 | 1.13 |
| **M1** | .30 | 228 | .30 | 248 | 1.00 |
| **M2** | .40 | 149 | .39 | 168 | 1.03 |
| *Maxilla, Left Side* | | | | | |
| **I1** | .28 | 234 | .29 | 253 | 1.04 |
| **I2** | .32 | 230 | .29 | 246 | 1.10 |
| **C** | .18 | 206 | .13 | 236 | 1.38 |
| **P1** | .16 | 187 | .15 | 209 | 1.07 |
| **P2** | .17 | 187 | .18 | 230 | 1.06 |
| **M1** | .27 | 218 | .29 | 247 | 1.07 |
| **M2** | .34 | 133 | .33 | 157 | 1.03 |
| *Mandible, Right Side* | | | | | |
| **I1** | .12 | 233 | .13 | 260 | 1.08 |
| **I2** | .15 | 238 | .15 | 260 | 1.00 |
| **C** | .14 | 217 | .12 | 249 | 1.17 |
| **P1** | .19 | 204 | .16 | 227 | 1.19 |
| **P2** | .18 | 199 | .20 | 227 | 1.11 |
| **M1** | .39 | 226 | .37 | 239 | 1.05 |
| **M2** | .44 | 138 | .37 | 162 | 1.19 |
| *Mandible, Left Side* | | | | | |
| **I1** | .11 | 239 | .13 | 256 | 1.18 |
| **I2** | .15 | 237 | .14 | 257 | 1.07 |
| **C** | .16 | 220 | .12 | 252 | 1.33 |
| **P1** | .17 | 205 | .18 | 230 | 1.06 |
| **P2** | .19 | 195 | .18 | 228 | 1.06 |
| **M1** | .36 | 224 | .42 | 240 | 1.17 |
| **M2** | .42 | 137 | .33 | 157 | 1.27 |

* = $p<0.01$; ** = $p<0.001$.

**Table 3.6 :** Variance in BL dimension in males and females, F ratio and significance.

| | *Males* | | *Females* | | |
|---|---|---|---|---|---|
| **Tooth** | **Var** | **df** | **Var** | **df** | **F** |
| *Maxilla, Right Side* | | | | | |
| **I1** | .30 | 228 | .24 | 246 | 1.25 |
| **I2** | .35 | 209 | .23 | 229 | 1.52 * |
| **C** | .44 | 196 | .28 | 219 | 1.57 * |
| **P1** | .31 | 190 | .28 | 209 | 1.11 |
| **P2** | .35 | 201 | .31 | 231 | 1.13 |
| **M1** | .35 | 231 | .31 | 251 | 1.13 |
| **M2** | .61 | 173 | .51 | 185 | 1.20 |
| *Maxilla, Left Side* | | | | | |
| **I1** | .32 | 226 | .24 | 248 | 1.33 |
| **I2** | .36 | 218 | .27 | 227 | 1.33 |
| **C** | .43 | 196 | .27 | 221 | 1.59 * |
| **P1** | .29 | 193 | .27 | 214 | 1.07 |
| **P2** | .32 | 191 | .32 | 234 | 1.00 |
| **M1** | .28 | 232 | .29 | 257 | 1.04 |
| **M2** | .57 | 162 | .48 | 179 | 1.19 |
| *Mandible, Right Side* | | | | | |
| **I1** | .22 | 232 | .19 | 258 | 1.16 |
| **I2** | .25 | 233 | .17 | 250 | 1.47 * |
| **C** | .46 | 197 | .26 | 230 | 1.77 ** |
| **P1** | .28 | 202 | .26 | 225 | 1.08 |
| **P2** | .34 | 199 | .24 | 228 | 1.42 |
| **M1** | .30 | 237 | .22 | 253 | 1.36 |
| **M2** | .38 | 180 | .30 | 202 | 1.27 |
| *Mandible, Left Side* | | | | | |
| **I1** | .20 | 231 | .17 | 257 | 1.18 |
| **I2** | .25 | 227 | .17 | 246 | 1.47 * |
| **C** | .47 | 191 | .24 | 231 | 1.96 ** |
| **P1** | .30 | 204 | .27 | 228 | 1.11 |
| **P2** | .31 | 195 | .26 | 227 | 1.19 |
| **M1** | .30 | 227 | .20 | 248 | 1.50 * |
| **M2** | .38 | 177 | .31 | 188 | 1.23 |

* = $p<0.01$; ** = $p<0.001$.

**Table 3.7:** Coefficients of variation (CV) for MD and BL tooth crown size.

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| | *Female* | | *Male* | | *Female* | | *Male* | |
| | **Right** | **Left** | **Right** | **Left** | **Right** | **Left** | **Right** | **Left** |
| ***Maxilla*** | | | | | | | | |
| **I1** | 6.4 | 6.4 | 6.1 | 6.1 | 7.0 | 6.9 | 7.6 | 7.8 |
| **I2** | 7.9 | 8.2 | 7.9 | 8.2 | 7.7 | 8.4 | 9.1 | 9.2 |
| **C** | 4.9 | 4.8 | 5.7 | 5.3 | 6.7 | 6.5 | 7.8 | 7.7 |
| **P1** | 5.9 | 5.7 | 5.5 | 5.7 | 5.9 | 5.7 | 6.0 | 5.7 |
| **P2** | 6.4 | 6.4 | 5.9 | 6.1 | 6.1 | 6.2 | 6.2 | 5.9 |
| **M1** | 5.4 | 5.3 | 5.2 | 5.0 | 4.9 | 4.8 | 5.1 | 4.6 |
| **M2** | 6.3 | 5.9 | 6.1 | 5.8 | 6.5 | 6.3 | 6.8 | 6.5 |
| ***Mandible*** | | | | | | | | |
| **I1** | 6.8 | 6.8 | 6.3 | 6.3 | 7.3 | 7.1 | 7.7 | 7.4 |
| **I2** | 6.7 | 6.3 | 6.5 | 6.5 | 6.7 | 6.6 | 7.8 | 7.9 |
| **C** | 5.2 | 5.2 | 5.5 | 5.8 | 7.0* | 6.7* | 8.7* | 8.9* |
| **P1** | 5.8 | 6.1 | 6.1 | 5.9 | 6.6 | 6.7 | 6.5 | 6.8 |
| **P2** | 6.4 | 6.0 | 5.8 | 6.1 | 5.8 | 6.1 | 6.6 | 6.5 |
| **M1** | 5.7 | 6.0 | 5.6 | 5.4 | 4.4 | 4.3 | 5.1 | 5.1 |
| **M2** | 6.0 | 5.6 | 6.1 | 6.0 | 5.3 | 5.4 | 5.8 | 5.9 |

* = significant difference in CVs between the sexes ($p<0.01$).

**Table 3.8 :** Probability values from the two-way ANOVA on sex and zygosity.

| | *Mesiodistal* | | | *Buccolingual* | | |
|---|---|---|---|---|---|---|
| **Tooth** | **Sex**[a] | **Zygos**[b] | **Interact**[b] | **Sex** | **Zygos** | **Interact** |
| *Maxilla, Right Side* | | | | | | |
| **I1** | .000 | .006* | .648 | .000 | .093 | .258 |
| **I2** | .000 | .000** | .412 | .000 | .670 | .363 |
| **C** | .000 | .974 | .279 | .000 | .021 | .446 |
| **P1** | .000 | .315 | .961 | .000 | .953 | .194 |
| **P2** | .000 | .275 | .963 | .000 | .906 | .515 |
| **M1** | .000 | .476 | .396 | .000 | .789 | .387 |
| **M2** | .000 | .196 | .649 | .000 | .376 | .093 |
| *Maxilla, Left Side* | | | | | | |
| **I1** | .000 | .022 | .979 | .000 | .016 | .489 |
| **I2** | .000 | .090 | .242 | .000 | .492 | .365 |
| **C** | .000 | .226 | .378 | .000 | .069 | .057 |
| **P1** | .000 | .290 | .882 | .000 | .986 | .356 |
| **P2** | .000 | .459 | .539 | .000 | .713 | .448 |
| **M1** | .000 | .112 | .339 | .000 | .861 | .148 |
| **M2** | .000 | .553 | .416 | .000 | .950 | .276 |
| *Mandible, Right Side* | | | | | | |
| **I1** | .001 | .723 | .495 | .000 | .251 | .299 |
| **I2** | .000 | .009* | .659 | .002 | .308 | .120 |
| **C** | .000 | .006* | .104 | .000 | .005* | .133 |
| **P1** | .000 | .145 | .928 | .000 | .982 | .436 |
| **P2** | .000 | .041 | .404 | .000 | .338 | .280 |
| **M1** | .000 | .815 | .732 | .000 | .998 | .216 |
| **M2** | .000 | .143 | .114 | .000 | .389 | .001* |
| *Mandible, Left Side* | | | | | | |
| **I1** | .000 | .780 | .898 | .000 | .487 | .472 |
| **I2** | .000 | .096 | .710 | .001 | .590 | .156 |
| **C** | .000 | .508 | .104 | .000 | .029 | .202 |
| **P1** | .000 | .449 | .571 | .000 | .907 | .077 |
| **P2** | .000 | .306 | .194 | .000 | .607 | .026 |
| **M1** | .000 | .934 | .438 | .000 | .922 | .050 |
| **M2** | .000 | .094 | .208 | .000 | .301 | .026 |

[a] All probabilities for Sex are <0.003.

[b] For the Zygosity and Interaction columns * = p<0.01, ** = p<0.001.

**Table 3.9:** Results of MANOVA on birth order in twins.

| Twin Group | Box's M | Prob | Exact F | df | Prob |
|---|---|---|---|---|---|
| **All twins** | 76.7 | 0.99 | 0.79 | 14, 322 | 0.69 |
| **Females** | 84.9 | 0.99 | 0.63 | 14, 125 | 0.84 |
| **Males** | 94.9 | 0.89 | 0.78 | 14, 182 | 0.69 |

**Table 3.10:** Inter-tooth correlations (x100) for MD dimension (all significant at $p<0.01$). Max = maxillary; Man = mandibular; R = right; L = left.

| | | *Maxillary Right* | | | | | | | *Maxillary Left* | | | | | | | *Mandibular Right* | | | | | | | *Mandibular Left* | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | I1 | I2 | C | P1 | P2 | M1 | M2 | I1 | I2 | C | P1 | P2 | M1 | M2 | I1 | I2 | C | P1 | P2 | M1 | M2 | I1 | I2 | C | P1 | P2 | M1 |
| Max R | I2 | 60 | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | C | 48 | 48 | | | | | | | | | | | | | | | | | | | | | | | | | |
| | P1 | 52 | 47 | 58 | | | | | | | | | | | | | | | | | | | | | | | | |
| | P2 | 46 | 42 | 50 | 70 | | | | | | | | | | | | | | | | | | | | | | | |
| | M1 | 58 | 45 | 50 | 56 | 58 | | | | | | | | | | | | | | | | | | | | | | |
| | M2 | 45 | 32 | 52 | 54 | 49 | 61 | | | | | | | | | | | | | | | | | | | | | |
| Max L | I1 | 92 | 58 | 49 | 52 | 47 | 58 | 44 | | | | | | | | | | | | | | | | | | | | |
| | I2 | 60 | 88 | 51 | 48 | 43 | 46 | 34 | 59 | | | | | | | | | | | | | | | | | | | |
| | C | 48 | 50 | 90 | 58 | 52 | 54 | 51 | 50 | 54 | | | | | | | | | | | | | | | | | | |
| | P1 | 52 | 48 | 60 | 88 | 72 | 57 | 53 | 52 | 49 | 60 | | | | | | | | | | | | | | | | | |
| | P2 | 48 | 44 | 52 | 68 | 85 | 58 | 46 | 49 | 43 | 52 | 72 | | | | | | | | | | | | | | | | |
| | M1 | 57 | 44 | 52 | 58 | 56 | 89 | 57 | 59 | 45 | 57 | 58 | 59 | | | | | | | | | | | | | | | |
| | M2 | 40 | 31 | 50 | 51 | 46 | 57 | 85 | 41 | 32 | 50 | 50 | 45 | 61 | | | | | | | | | | | | | | |
| Man R | I1 | 67 | 48 | 43 | 48 | 42 | 45 | 28 | 66 | 49 | 42 | 46 | 42 | 49 | 34 | | | | | | | | | | | | | |
| | I2 | 69 | 54 | 52 | 51 | 46 | 49 | 31 | 68 | 54 | 52 | 48 | 47 | 50 | 35 | 73 | | | | | | | | | | | | |
| | C | 52 | 51 | 77 | 57 | 50 | 52 | 51 | 52 | 51 | 76 | 57 | 46 | 51 | 45 | 48 | 60 | | | | | | | | | | | |
| | P1 | 50 | 47 | 52 | 76 | 63 | 56 | 49 | 51 | 47 | 56 | 73 | 62 | 56 | 47 | 51 | 52 | 56 | | | | | | | | | | |
| | P2 | 54 | 50 | 50 | 67 | 70 | 61 | 48 | 56 | 47 | 53 | 67 | 71 | 62 | 48 | 48 | 54 | 55 | 72 | | | | | | | | | |
| | M1 | 56 | 42 | 47 | 51 | 48 | 70 | 51 | 57 | 42 | 48 | 52 | 49 | 70 | 51 | 45 | 47 | 46 | 54 | 64 | | | | | | | | |
| | M2 | 49 | 44 | 49 | 54 | 53 | 62 | 59 | 49 | 42 | 51 | 52 | 56 | 64 | 61 | 40 | 46 | 49 | 54 | 63 | 65 | | | | | | | |
| Man L | I1 | 67 | 48 | 41 | 50 | 40 | 45 | 27 | 66 | 48 | 40 | 46 | 41 | 48 | 33 | 88 | 73 | 48 | 52 | 50 | 47 | 40 | | | | | | |
| | I2 | 67 | 56 | 55 | 50 | 47 | 50 | 36 | 67 | 56 | 54 | 48 | 46 | 51 | 35 | 73 | 86 | 62 | 53 | 52 | 48 | 53 | 71 | | | | | |
| | C | 51 | 47 | 76 | 57 | 54 | 52 | 49 | 51 | 50 | 75 | 57 | 52 | 51 | 44 | 48 | 60 | 88 | 59 | 58 | 48 | 46 | 48 | 62 | | | | |
| | P1 | 49 | 50 | 55 | 76 | 64 | 58 | 50 | 51 | 51 | 59 | 74 | 63 | 57 | 46 | 50 | 53 | 58 | 88 | 70 | 55 | 54 | 52 | 54 | 63 | | | |
| | P2 | 49 | 46 | 46 | 64 | 68 | 61 | 45 | 51 | 44 | 50 | 63 | 67 | 61 | 50 | 43 | 49 | 51 | 67 | 87 | 64 | 62 | 45 | 49 | 55 | 64 | | |
| | M1 | 55 | 40 | 46 | 53 | 49 | 71 | 49 | 56 | 43 | 46 | 53 | 49 | 69 | 52 | 45 | 47 | 47 | 53 | 60 | 93 | 62 | 47 | 48 | 50 | 56 | 62 | |
| | M2 | 48 | 42 | 47 | 53 | 54 | 62 | 56 | 50 | 43 | 51 | 52 | 56 | 68 | 59 | 40 | 43 | 51 | 55 | 65 | 66 | 88 | 43 | 50 | 52 | 56 | 64 | 63 |

Table 3.11: Inter-tooth correlations (x100) for BL dimension (all significant at p<0.01). Max = maxillary; Man = mandibular; R = right; L = left.

| | | *Maxillary Right* | | | | | | | *Maxillary Left* | | | | | | | *Mandibular Right* | | | | | | | *Mandibular Left* | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | I1 | I2 | C | P1 | P2 | M1 | M2 | I1 | I2 | C | P1 | P2 | M1 | M2 | I1 | I2 | C | P1 | P2 | M1 | M2 | I1 | I2 | C | P1 | P2 | M1 |
| **Max R** | I2 | 65 | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | C | 65 | 60 | | | | | | | | | | | | | | | | | | | | | | | | | |
| | P1 | 57 | 49 | 65 | | | | | | | | | | | | | | | | | | | | | | | | |
| | P2 | 53 | 45 | 60 | 79 | | | | | | | | | | | | | | | | | | | | | | | |
| | M1 | 57 | 50 | 64 | 65 | 63 | | | | | | | | | | | | | | | | | | | | | | |
| | M2 | 53 | 48 | 61 | 63 | 63 | 78 | | | | | | | | | | | | | | | | | | | | | |
| **Max L** | I1 | 90 | 64 | 67 | 51 | 50 | 54 | 50 | | | | | | | | | | | | | | | | | | | | |
| | I2 | 64 | 83 | 60 | 49 | 45 | 52 | 52 | 63 | | | | | | | | | | | | | | | | | | | |
| | C | 66 | 61 | 93 | 62 | 58 | 63 | 60 | 68 | 63 | | | | | | | | | | | | | | | | | | |
| | P1 | 57 | 48 | 63 | 92 | 79 | 63 | 62 | 50 | 48 | 62 | | | | | | | | | | | | | | | | | |
| | P2 | 56 | 48 | 58 | 80 | 93 | 64 | 64 | 51 | 48 | 57 | 82 | | | | | | | | | | | | | | | | |
| | M1 | 59 | 50 | 63 | 64 | 64 | 93 | 76 | 55 | 54 | 65 | 64 | 67 | | | | | | | | | | | | | | | |
| | M2 | 57 | 53 | 61 | 66 | 65 | 78 | 91 | 54 | 53 | 61 | 65 | 65 | 79 | | | | | | | | | | | | | | |
| **Man R** | I1 | 72 | 55 | 60 | 49 | 44 | 59 | 53 | 69 | 55 | 63 | 49 | 46 | 58 | 58 | | | | | | | | | | | | | |
| | I2 | 66 | 50 | 61 | 45 | 43 | 55 | 51 | 63 | 52 | 63 | 45 | 42 | 52 | 55 | 75 | | | | | | | | | | | | |
| | C | 64 | 55 | 79 | 53 | 50 | 56 | 58 | 65 | 58 | 82 | 53 | 49 | 55 | 59 | 65 | 70 | | | | | | | | | | | |
| | P1 | 55 | 49 | 60 | 70 | 65 | 60 | 60 | 53 | 51 | 60 | 68 | 68 | 61 | 61 | 53 | 57 | 58 | | | | | | | | | | |
| | P2 | 55 | 48 | 60 | 66 | 73 | 61 | 59 | 53 | 50 | 60 | 65 | 73 | 61 | 63 | 54 | 57 | 55 | 76 | | | | | | | | | |
| | M1 | 54 | 47 | 54 | 58 | 56 | 73 | 62 | 52 | 50 | 57 | 57 | 55 | 73 | 64 | 55 | 52 | 55 | 64 | 69 | | | | | | | | |
| | M2 | 59 | 52 | 55 | 57 | 54 | 69 | 72 | 56 | 51 | 58 | 58 | 57 | 69 | 75 | 56 | 56 | 59 | 62 | 64 | 78 | | | | | | | |
| **Man L** | I1 | 73 | 55 | 60 | 50 | 47 | 60 | 55 | 71 | 56 | 64 | 51 | 49 | 61 | 60 | 90 | 77 | 66 | 54 | 55 | 56 | 59 | | | | | | |
| | I2 | 69 | 53 | 60 | 44 | 42 | 53 | 51 | 67 | 52 | 64 | 44 | 41 | 51 | 55 | 76 | 88 | 70 | 54 | 51 | 53 | 56 | 78 | | | | | |
| | C | 64 | 57 | 79 | 56 | 52 | 56 | 60 | 64 | 56 | 81 | 55 | 52 | 57 | 61 | 63 | 69 | 91 | 60 | 58 | 55 | 64 | 65 | 69 | | | | |
| | P1 | 56 | 49 | 59 | 71 | 64 | 59 | 61 | 54 | 49 | 60 | 71 | 66 | 62 | 65 | 55 | 55 | 59 | 90 | 75 | 66 | 64 | 56 | 53 | 63 | | | |
| | P2 | 56 | 49 | 61 | 65 | 70 | 58 | 58 | 53 | 51 | 62 | 65 | 71 | 61 | 61 | 52 | 53 | 57 | 74 | 90 | 66 | 62 | 53 | 50 | 62 | 77 | | |
| | M1 | 54 | 45 | 54 | 56 | 53 | 73 | 62 | 53 | 48 | 56 | 56 | 54 | 73 | 64 | 59 | 52 | 53 | 63 | 67 | 91 | 78 | 58 | 54 | 54 | 66 | 66 | |
| | M2 | 53 | 50 | 54 | 55 | 52 | 67 | 69 | 54 | 46 | 54 | 55 | 56 | 68 | 71 | 55 | 54 | 55 | 56 | 64 | 74 | 90 | 55 | 55 | 60 | 60 | 63 | 78 |

**Table 3.12:** Pearson correlation coefficients (x100) of MD on BL diameter with respective sample sizes (N). In all cases, p<0.001.

| | Right | | Left | |
|---|---|---|---|---|
| | **N** | **Corr** | **N** | **Corr** |
| ***Maxilla*** | | | | |
| **I1** | 420 | 47 | 420 | 48 |
| **I2** | 392 | 45 | 395 | 45 |
| **C** | 372 | 63 | 374 | 64 |
| **P1** | 353 | 73 | 355 | 74 |
| **P2** | 381 | 67 | 374 | 70 |
| **M1** | 415 | 65 | 413 | 65 |
| **M2** | 273 | 60 | 248 | 55 |
| ***Mandible*** | | | | |
| **I1** | 429 | 41 | 433 | 44 |
| **I2** | 431 | 35 | 419 | 38 |
| **C** | 383 | 57 | 381 | 55 |
| **P1** | 384 | 62 | 389 | 62 |
| **P2** | 382 | 64 | 377 | 61 |
| **M1** | 414 | 60 | 407 | 62 |
| **M2** | 259 | 70 | 252 | 64 |

# Chapter 4

# Sexual Dimorphism in the Permanent Dentition

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## Introduction

Sexual dimorphism of human teeth has been found in the deciduous (Black III 1978, Farmer and Townsend 1993, El-Nofely 1995) and permanent dentitions (Seipel 1946, Moorrees 1959, Barrett *et al.* 1963, Garn *et al.* 1964b, 1967b, Alvesalo 1971, Hanihara 1978, Oxnard 1987, Yamada and Sakai 1992, El-Nofely 1995), although this chapter will only consider sexual dimorphism in the permanent dentition. The degree of dimorphism in permanent crown dimensions is generally reported to be greatest for the canines (Garn *et al.* 1964b, 1967b, Alvesalo 1971, Yamada and Sakai 1992, El-Nofely and Tawfik 1995). This is also true for all Pongid ape species (Hillson 1986). The permanent teeth which display the lowest level of sexual dimorphism vary between populations, but often involve the incisors (Garn *et al.* 1964b, 1967b, Yamada and Sakai 1992, Farmer and Townsend 1993). The BL diameter of tooth crowns tends to display a greater degree of sexual dimorphism than the MD dimension (Yamada and Sakai 1992, Farmer and Townsend 1993, El-Nofely and Tawfik 1995).

Although the sexual dimorphism in tooth size accompanies a sexual dimorphism in overall body size (and shape), the latter does not completely explain the former. In the human permanent dentition, low or insignificant correlations between sexual dimorphism in tooth and body size have been reported (Garn *et al.* 1967b, Hanihara 1978, Yamada and Sakai 1992). This is true also for Colobus monkeys (Yamada and Sakai 1983). On a broader scale, a study of 39 species of non-human primates revealed no relationship between sex differences in female and male allometry and the level of dental sexual dimorphism (Harvey *et al.* 1978).

In the same study, Harvey *et al.* demonstrated that sexual dimorphism was greatest in species in which sexual selection among males (in competing for females), and predator pressure, were likely to be greatest. Other interspecific comparisons among primates have shown that sexual dimorphism correlates with factors such as mating system (monogamy versus polygamy), habitat (terrestrial versus arboreal, and savannah versus forest), overall body size for the species, and average tooth size (reviewed by Oxnard 1984).

However, most studies do not provide strong, or even consistent, evidence for any of these factors individually. In a review of data from 34 genera of primates, Oxnard (1984) suggested that there was no single pattern of social organisation, ecological niche, feeding pattern, reproductive efficiency or developmental transformation pattern which was a good predictor of sexual dimorphism. Different combinations of these factors, and different weightings of them, were proposed to be important for different taxa (Oxnard 1984). Furthermore, few of the analyses have considered the role of phylogenetic relationships among the species studied. The observed correlations may have been due to a common ancestry, so the different species actually represented a single data point, instead of a group of independent observations (Harvey and Pagel 1991). Thus it is not clear what mechanism, or mechanisms, caused sexual dimorphism of tooth size in humans to arise, or to be reduced over evolutionary time.

Although there have been many investigations into sexual dimorphism of human teeth, the methods vary, making comparisons difficult. In most cases, mean tooth sizes for each sex (denoted F and M) have been reported, and one of several ratios has been calculated to give a sexual dimorphism index. These ratios are listed in Table 4.1.

The third equation, $(M/_{F}) - 1$ (Garn *et al.* 1967b), is the most commonly reported statistic, and represents the main basis for comparing values across studies. The values across a variety of populations range from 0.8 to 6.7 percent for MD length and 2.8 to 6.6 percent for BL breadth (Garn *et al.* 1967b, Townsend and Brown 1979b). In an analysis of the mathematical properties of various ratios and differences in sex means, this equation has been described as satisfying the criteria of a "good" index of sexual dimorphism (including proportional scaling and intuitiveness of the calculation) provided males were larger than females (Lovich and Gibbons 1992). In the case of human teeth, this proviso is generally true.

Another difficulty in comparing studies is the variety of tests used to estimate the significance of the sex difference. These tests range from univariate t tests (Potter 1972, Yamada and Sakai 1983, 1992, Farmer and Townsend 1993) to discriminant function analysis (Potter 1972, Black III 1978, Brown and Townsend 1979, Rosing *et al.* 1995), canonical variate analysis (Hanihara 1978, Oxnard 1987), principal component analysis (Farmer and Townsend 1993) and Mahalanobis' distance (Hanihara 1978, Yamada and Sakai 1983). Other gender comparisons include sex differences in variances and in correlations among teeth (Garn *et al.* 1965e).

Before proceeding with modelling genetic and environmental influences, I examined the differences between the sexes. Significance of the sex differences in tooth crown size was demonstrated in Chapter 3. In this chapter, the magnitude of sexual dimorphism is estimated for each variable, and a discriminant function analysis (DFA) performed to analyse the relative contributions of individual variables to the dimorphism. The following two chapters look for evidence of sex chromosome and sex hormone influences on the sexual dimorphism.

## Methods

In Chapter 3, t-tests revealed that average values for all variables were significantly larger in males than in females ($p<0.002$ in every case), and the MANOVA revealed a significant difference between sexes at the multivariate level ($p<0.001$). In the current chapter, the degree of sexual dimorphism in each of the 56 variables was estimated using the formula $(^{M}/_{F}-1)*100$ (Garn *et al.* 1967b), to allow comparisons with other reports. Discriminant function analysis was employed as well, to provide more information on the dimorphism, such as which variables were most important in defining the dimorphism, and how much variation in tooth crown size was explained by variation between the sexes.

The DFA was conducted using singletons and SS A twins, with the SS B twins being used as a holdout sample for classification analysis. The data entered were the averages for each tooth across the four quadrants of the oral cavity (as in Chapter 3), yielding 14 variables. To test the stability of the discriminant weights (standardized canonical DF coefficients) and loadings (correlations between independent variables and the discriminant function), the procedure was repeated using singletons and SS B twins for the DFA, and SS A twins as the holdout sample. Canonical correlation coefficients were squared to produce the percent variance in the dependent variable due to the discriminant function. Histograms were produced and examined, and the accuracy of classification of the holdout sample was tested using the proportional chance criterion ($C_{PRO}$), and Press's Q statistic (Hair Jr *et al.* 1995):

$$C_{PRO} = p^2 + q^2$$

where p = the proportion of males in the holdout sample, and q = the proportion of females;

$$\text{Press' } Q = \{(N-(nk))^2/N(k-1)\}$$

where N = total sample size, n = number of observations correctly classified and k = number of groups. The Q value is compared with a critical $\chi^2$ value with one degree of freedom.

The proportional chance criterion ($C_{PRO}$), represents the proportion of individuals who would be correctly classified by chance. According to Hair Jr *et al.* (1995), the actual percent correctly classified should exceed $C_{PRO}$ by 25%.

## Results

The estimated percent sexual dimorphism for MD and BL diameters of the 28 permanent teeth, and ranks of the antimere averages, are listed in Table 4.2. Values varied from 2.3 to 6.9 for MD length, and 2.6 to 7.7 for BL breadth. MD dimensions generally were less sexually dimorphic than BL ones, with average ranks of 23.3 for MD and 11.9 for BL. The canines and second molars displayed the greatest degree of sexual dimorphism, while the MD dimension of the central incisor and both premolars, and BL dimension of the mandibular lateral incisor, were the least dimorphic variables.

The results of the DFA are summarised in Tables 4.3 to 4.6. The prior probabilities were set at 0.5 for each gender, since the sex ratio is generally 1:1 in the population. Although Box's M test indicates that there was multivariate heteroscedasticity between sexes in the first group, the ratio of larger to smaller sample size is less than

1.5, so the violation is not considered a problem (Hair Jr *et al.* 1995). Wilk's lambda indicates that the discriminant functions had significant discriminatory power ($p<0.0001$) for each data subset, although only 35-39% of the variance in the dependent variable was explained by the discriminant function. Thus the sex difference was significant at a multivariate level. The discriminant weights and loadings, listed in tables 4.4 and 4.5 (respectively), were reasonably consistent (in sign and magnitude) across the two data subsets, with the greatest difference being 0.61 for BL5. The highest weights were exhibited by the canine MD dimension in both groups. As for the loadings, the MD and BL diameters of the canines had the highest values, with both dimensions of the two molars not far behind. There was no consistent pattern among the rest of the variables, except that BL diameters generally rated a little higher. These results are consistent with the estimated percent sexual dimorphism in Table 4.2.

Histograms of discriminant scores for individuals of each sex are displayed in Figures 4.1 and 4.2. Two groups are visible in both histograms, but there is also a high degree of overlap.

Results of classification of the holdout samples are contained in Tables 4.6. The proportional chance criterion ($C_{PRO}$ - multiplied by 1.25) was 63.3% for the SS B holdout sample and 63.0% for the SS A holdout sample. Since the actual proportions correctly classified were 75% for the former and 76.6% for the latter, the discriminant function was assumed to be of value. Press' Q statistic was 33.0 ($p<0.001$) for the former and 39.9 ($p<0.001$) for the latter, further indicating the significance of the accuracy of classification of the two holdout samples.

## Discussion

As previously reported in humans, sexual dimorphism of dental crown size was greatest in the canines, followed by the second molars. The dimorphism also generally was greater in BL than MD dimensions, although the canines were a notable exception to this rule. The *magnitude* of the dimorphism also was similar to previous accounts (Garn *et al.* 1967b, Townsend and Brown 1979b).

Comparing these results with those from Chapter 3, the DFA supports the importance of the canine and molars in defining the sexual dimorphism, and the greater dimorphism of BL than MD diameters. The main difference was that while univariate analyses gave the impression that the sexual dimorphism was very strong, the DFA indicated that the dimorphism was not strong when intercorrelations were taken into account. In fact, sex determinations probably could not be made confidently from dental diameters alone. The same conclusion was reached in a study comparing the usefulness of dental diameters with various cranial and post-cranial structures in sex determination (Brown and Townsend 1979).

Although gender differences in tooth crown diameters are present in a wide variety of human populations, the differences are only of the order of 2-8%. It is difficult to suggest why modern humans should display such a sexual dimorphism of tooth size. Given the magnitude of the differences, it is likely that the dimorphism is a remnant of a greater dimorphism in more ancient, ancestral hominids. Indeed, sexual dimorphism in tooth crown diameters of higher order primates has been reported to be at its greatest in the great apes, then diminishing through the Australopithecines, *Homo habilis*, *Homo erectus*, *Homo sapiens neanderthalensis* and finally, *Homo sapiens sapiens* (Oxnard 1987). The patterns of sexual dimorphism vary greatly within these groups, but elevated canine dimorphism has been reported in at least 10

modern human populations (Townsend and Brown 1979b), *Homo erectus* (Oxnard 1987), all Pongid apes (Hillson 1986) and three species of Colobus monkeys (Yamada and Sakai 1983).

Most sexually dimorphic traits arise through the direct actions of either gonadal hormones or genes (autosomal or sex-linked), or a combination of these. Since there is a consistent (though small) sexual dimorphism of tooth crown size, an investigation of genetic and hormonal factors was conducted. In Chapter 5, evidence for genetic contributions to sexual dimorphism is discussed, followed by examination of sibling correlations in search of evidence for sex-linked genes. In Chapter 6, OS twin pairs are compared with SS twin pairs and singletons to look for evidence of (1) a hormonal contribution to the sexual dimorphism, and (2) hormonal diffusion between human twins.

**Table 4.1:** Ratios commonly used to estimate sexual dimorphism in physical traits.

| **Authors** | **Equation** [a] |
|---|---|
| Smith (1980) | $F/M$ |
| Brace and Ryan (1980) | $M/F$ |
| Garn *et al.* (1967b) | $(M-F)/F$ or $(M/F) - 1$ |
| Yamada and Sakai (1983) | $(M-F)/\sigma$ |
| Harvey *et al.* (1978) | $RMTS = Obs(M)/Exp(M) \times Exp(F)/Obs(F)$ |

[a] F = female; M = male; $\sigma$ = unbiased population standard deviation; RMTS = Relative Male Tooth Size; Obs = observed value; and Exp = value expected given the body size.

**Table 4.2**: Estimated percent sexual dimorphism in MD and BL diameters of permanent tooth crowns, and ranks of the right-left averages. Percentages in bold are greater than 5.0. Ranks in italics are average ranks for the each quadrant of the table.

| | MD | | | BL | | |
|---|---|---|---|---|---|---|
| **Tooth** | **Right** | **Left** | **Rank** | **Right** | **Left** | **Rank** |
| **Maxilla** | | | *17.6* | | | *9.6* |
| **I1** | 3.0 | 2.7 | 26 | 4.1 | 3.7 | 14 |
| **I2** | 3.5 | 4.1 | 15.5 | 3.5 | 5.0 | 11 |
| **C** | **5.9** | **6.1** | 5 | **6.0** | **6.4** | 4 |
| **P1** | 3.2 | 3.5 | 23.5 | 3.7 | 3.9 | 15.5 |
| **P2** | 3.0 | 2.9 | 25 | 4.5 | 4.3 | 8 |
| **M1** | 3.7 | 3.6 | 19 | 3.9 | 4.5 | 12 |
| **M2** | 4.5 | 4.2 | 9.5 | **6.5** | **6.2** | 3 |
| **Mandible** | | | *28.9* | | | *14.2* |
| **I1** | 2.3 | 2.5 | 28 | 3.9 | 4.4 | 13 |
| **I2** | 3.3 | 3.6 | 21 | 2.7 | 2.6 | 27 |
| **C** | **6.9** | **6.8** | 2 | **7.7** | **7.1** | 1 |
| **P1** | 3.2 | 3.5 | 23.5 | **5.1** | **5.2** | 7 |
| **P2** | 3.9 | 3.6 | 17 | 3.7 | 3.5 | 20 |
| **M1** | 3.7 | 3.7 | 18 | 3.4 | 3.4 | 22 |
| **M2** | **5.2** | **5.4** | 6 | 4.7 | 4.0 | 9.5 |

**Table 4.3**: Statistics generated by the discriminant function analysis.

| | Singletons and SS A | | | Singletons and SS B | | |
|---|---|---|---|---|---|---|
| | **Female** | **Male** | **Prob** | **Female** | **Male** | **Prob** |
| **N** | 159 | 128 | ($\Sigma = 287$) | 151 | 127 | ($\Sigma = 278$) |
| **Prior Prob** | 0.5 | 0.5 | | 0.5 | 0.5 | |
| **Wilk's λ** | 0.613 | | < 0.0001 | 0.648 | | < 0.0001 |
| **Can. Corr.** | 0.622 | | | 0.594 | | |
| **% Variance** | 38.7 | | | 35.2 | | |
| **Box's M** | 192.23 | | < 0.0001 | 127.19 | | 0.1444 |

**Table 4.4**: Discriminant weights (standardized) from the DFA. Weight values in italics are greater than 5.0.

| | WEIGHTS | |
|---|---|---|
| | **SS A** | **SS B** |
| **MD I1** | -0.16 | -0.13 |
| **MD I2** | -0.24 | -0.23 |
| **MD C** | *0.88* | *0.84* |
| **MD P1** | -0.35 | *-0.82* |
| **MD P2** | 0.16 | 0.10 |
| **MD M1** | 0.20 | 0.27 |
| **MD M2** | 0.10 | 0.27 |
| **BL I1** | 0.08 | 0.25 |
| **BL I2** | -0.37 | -0.50 |
| **BL C** | 0.28 | 0.38 |
| **BL P1** | 0.32 | 0.16 |
| **BL P2** | *-0.52* | 0.11 |
| **BL M1** | 0.10 | -0.20 |
| **BL M2** | 0.36 | 0.32 |

**Table 4.5**: Discriminant loadings from the DFA, listed in order of magnitude.

| LOADINGS | | | |
|---|---|---|---|
| **SS A** | | **SS B** | |
| **MD C** | 0.78 | **MD C** | 0.72 |
| **BL C** | 0.64 | **BL C** | 0.66 |
| **BL M2** | 0.62 | **BL M2** | 0.61 |
| **BL M1** | 0.59 | **BL M1** | 0.57 |
| **MD M2** | 0.54 | **MD M2** | 0.57 |
| **MD M1** | 0.50 | **MD M1** | 0.52 |
| **BL P1** | 0.50 | **BL P2** | 0.48 |
| **BL I1** | 0.44 | **BL P1** | 0.48 |
| **MD P2** | 0.42 | **BL I1** | 0.46 |
| **BL I2** | 0.39 | **MD P2** | 0.42 |
| **BL P2** | 0.37 | **BL I2** | 0.37 |
| **MD P1** | 0.35 | **MD I1** | 0.30 |
| **MD I2** | 0.31 | **MD I2** | 0.28 |
| **MD I1** | 0.26 | **MD P1** | 0.27 |

**Table 4.6**: Reciprocal gender classifications of SSB and SSA twin holdout samples. Percentages in italics indicate correct allocation.

| Actual Gender | Total No. | Predicted Gender No. | | Predicted Gender % | | Correct % |
|---|---|---|---|---|---|---|
| | | Male | Female | Male | Female | |
| **SS B** | | | | | | 75.0 |
| **Male** | 54 | 37 | 17 | *68.5* | 31.5 | |
| **Female** | 78 | 16 | 62 | 20.5 | *79.5* | |
| **SS A** | | | | | | 76.6 |
| **Male** | 55 | 33 | 22 | *60.0* | 40.0 | |
| **Female** | 86 | 11 | 75 | 12.8 | *87.2* | |

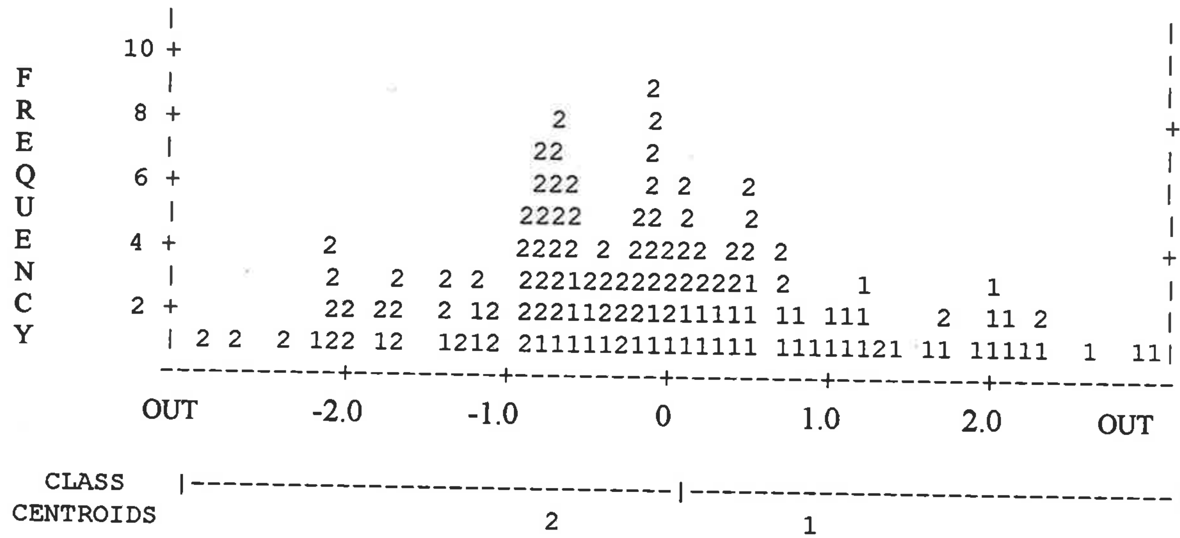


**Figure 4.1**: All-groups stacked histogram of canonical discriminant function for singletons and SS A twins.

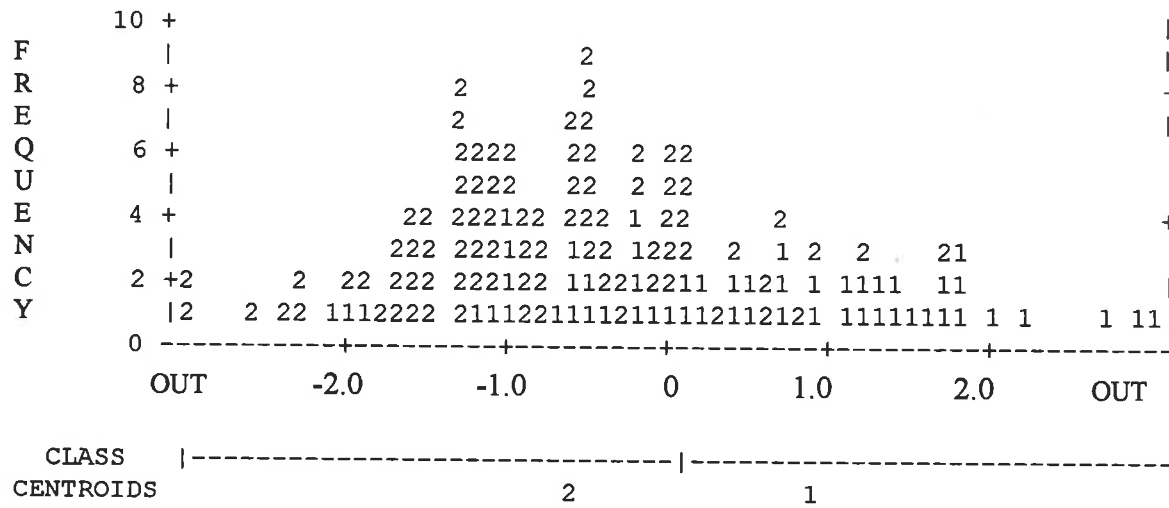


**Figure 4.2**: All-groups stacked histogram of canonical discriminant function for singletons and SS B twins.

## Chapter 5

# The Role of Sex Chromosomes

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## Introduction

As noted in Chapter 1, research into sex chromosomal anomalies such as Klinefelter (XXY) syndrome (Townsend and Alvesalo 1985b), XYY syndrome (Alvesalo *et al.* 1975, Townsend and Alvesalo 1985a) and Turner (XO) syndrome (Varrela *et al.* 1988, Townsend *et al.* 1984), have implicated the sex chromosomes as playing a role in the formation of dentine and enamel (reviewed by Alvesalo *et al.* 1985, Townsend *et al.* 1986a, Alvesalo 1997). Subsequent molecular genetic investigations resulted in the identification of amelogenin-producing genes on both X and Y chromosomes (Lau *et al.* 1989). Both chromosomes produce amelogenin proteins which are potentially functional (Nakahori *et al.* 1991, Salido *et al.* 1992). Amelogenin is one of the two protein groups which form enamel, and may account for as much as 90% of enamel material (Fincham *et al.* 1992, Robinson *et al.* 1992). Variations in these genes may affect the enamel structure and/or deposition.

The X- and Y-linked amelogenin genes differ in several ways. Firstly, they exhibit sequence differences, and these differences have been postulated to contribute to sexual dimorphism in tooth size (Lau *et al.* 1990; Fincham *et al.* 1991). In addition, the level of expression of the Y-linked gene is only about 10% that of the X-linked gene (Salido *et al.* 1992). Finally, the effect of the two differs - whereas X-linked genes appear to influence amelogenesis, the Y chromosome affects both amelogenesis and dentinogenesis. Part of this difference possibly involves the Y chromosome increasing mitotic activity in the dental lamina, from which the tooth germ develops (Alvesalo 1997). The result is a larger mass of dentinal tissue, and hence a larger tooth (Alvesalo 1997). This Y-linked cell-proliferation gene also has been postulated to contribute to sexual dimorphism in skeletal maturation (Alvesalo 1971, Alvesalo *et al.* 1991) and statural growth (Alvesalo *et al.* 1991) of humans.

Prior to this knowledge of the sex chromosomal location of genes affecting tooth size, numerous researchers were seeking evidence for such genes from family studies. Based on the theory of chromosomal inheritance, Garn and Rohmann (1962) predicted that X-linked inheritance would cause sisters to be more highly correlated than either brothers, or sisters and brothers. This is because sisters inherit the same paternal X chromosome, and have a 50 percent chance of inheriting the same maternal chromosome, whereas only half of brothers or sister-brother pairs share the same maternal X chromosome, and they do not share a paternal X. Their data on ossification of hand bones and calcification of five mandibular teeth supported their theory. Correlations for MD dimensions of permanent teeth in non-twin siblings also have been reported to be greater in sister-sister pairs than in brother-brother pairs, and greater in the latter than in sister-brother pairs (Lundström 1977).

Following this line of thought, Mather and Jinks (1963) extended the theory to state that pairs of brothers should exhibit higher correlations than male-female sibling pairs. Although the actual correlation values would vary as a function of the effects of autosomal genes and "non-heritable agencies", the relationship would hold if these effects were the same for both sexes (Mather and Jinks 1963). Thus, using S to represent a female sibling and B for a male sibling, the predicted pattern of correlations was SS>BB>SB. Several researchers have examined correlation patterns among siblings with some reporting evidence of the predicted pattern (Garn *et al.* 1965a), and some not supporting it (Bowden and Goose 1969, Townsend 1978, Townsend and Brown 1978a).

Concurrently with the publication of these papers in the early 1960s, the hypothesis of inactivation of one X chromosome in mammalian females was proposed (Lyon 1962; Beutler *et al.* 1962). It is unfortunate that the timing of publication did not

allow X-inactivation to be taken into account in discussion of these correlations. In subsequent publications, X-inactivation was ignored or postulated to be unsupported (eg Garn *et al.* 1965a, 1965e). Indeed, there appeared to be little or no evidence of it in the tooth size data analysed (Garn *et al.* 1965a), with correlation patterns mostly as predicted by Mather and Jinks (1963). However, other studies of tooth size in full-siblings, half-siblings and cousins failed to demonstrate consistently greater correlations between sisters than brothers or sister-brother pairs, or consistent evidence among cousins (Bowden and Goose 1969, Townsend and Brown 1978, Alvesalo 1971).

To complicate matters, X-inactivation in human females appears to be incomplete, and may not encompass the amelogenin gene. Comparing females with one, two, or three X chromosomes, or with a deletion of the short arm of one of the X chromosomes (46,X,i(Xq)), the order of tooth crown sizes from largest to smallest was XXX, XX, X0, 46X,i(Xq) (Alvesalo *et al.* 1987, Mayhall *et al.* 1991). Also, males with two X chromosomes (XXY) have larger teeth than XY males (Alvesalo and Portin 1980, Townsend and Alvesalo 1985). In addition, there is evidence that a region at the distal end of the short arm (where the amelogenin gene is believed to reside) is not inactivated (Lyon 1983, Therman 1983). Sibling correlations may be useful in determining whether X-inactivation occurs, if it leads to different expectations for the correlations.

Another aspect to be considered is the presence of the amelogenin gene on the Y chromosome, and what impact this has, if any, on expectations for sibling correlations. The Y chromosome is shared by brothers, making them more alike, and should decrease the similarity of sister-brother pairs.

The suggestion that both amelogenin genes are active in human females means that gene dosage compensation is nonexistent. However, compensation may be unnecessary for two reasons. Firstly, the gene on the Y chromosome is transcribed and produces a functional protein. Secondly, active genes on the otherwise-inactivated X chromosome have been reported to be less active than those on the fully-active X (Lyon 1983), and the amelogenin gene on the Y chromosome only exhibits about 10% the level of expression of the X-linked gene.

The first step in analysis of the data for evidence of sex chromosomal contributions then, was the reformulation of expected sibling correlations given X-inactivation and/or a Y-linked gene. Pearson product-moment correlation coefficients were then calculated and compared among the sibling groups. In the light of current knowledge of the role of sex chromosomes in tooth crown formation, it may seem superfluous to be following up on the principle of examining sibling correlations for evidence of sex chromosomal involvement. However, since examination of sibling correlations is a simple and inexpensive method, it is worth testing its value on a system we already understand reasonably well. If X inactivation and Y chromosomal involvement in a trait change the expected patterns of sibling correlations, then we may have a simple index for ascertaining the nature of sex chromosomal contributions.

## Methods

Since the correlation pattern - SS>BB>SB - predicted by Mather and Jinks (1963) did not account for X-inactivation or Y-linked genes, I recalculated the expected levels of similarity between siblings. In particular, the pattern is changed if Y chromosomal influences are included, since these will make brothers more alike, and sister-brother pairs even less alike.

The main assumptions are: (1) variation in the trait is caused (or contributed to) by a gene or tightly-linked gene complex on the X-chromosome, and by one or more genes on the Y chromosome, (2) the contributions of these genes sufficiently outweigh those of autosomal genes and environmental influences, and (3) if inactivation of one X chromosome (or of relevant parts of the chromosome) occurs in females, it occurs at random. Assumptions (1) and (3) seem likely, given that one transcriptionally active gene for tooth enamel has been located on each sex chromosome, and evidence for randomness of X-inactivation has been reported (Berkmann and Singer 1971, Tan *et al.* 1993, Bamforth *et al.* 1996). Assumption (2) is provided with some validity by the effects of sex chromosomal anomalies on teeth.

For simplicity, the X and Y chromosomes will be used to symbolise the genes (or gene complexes) of interest. Given the possibilities that X inactivation may exclude the amelogenin genes, and that the Y chromosome may contribute only a small amount towards tooth size, the expectations for sibling correlations were generated to take into account three situations: (1) X-inactivation and a significant contribution of the Y; (2) X-inactivation and no significant contribution of the Y; and (3) no inactivation and a significant contribution of the Y.

Four types of matings were examined - those in which the three X chromosomes (or genes of interest) were identical ($X_1X_1 \times X_1Y$), two matings with two X chromosomes the same ($X_1X_1 \times X_2Y$ and $X_1X_2 \times X_1Y$) and one in which the three X chromosomes were different ($X_1X_2 \times X_3Y$). Whether or not the three X chromosomes can be distinguished in this way will depend on the degree of polymorphism in the population - in both number and frequency of alleles.

For each of the three assumptions, and all four types of matings, the expected patterns of similarity between sibling pairs were derived. Firstly, the chromosomes

present in all possible pairs of siblings from each mating were listed, and the frequencies of each combination determined. Then, X-inactivation and/or Y chromosomal contributions were added, yielding even more combinations for some sibling pairs.

For instance, if the three X chromosomes in the mating were different, there would be four possible combinations of chromosomes in each pair of siblings (Table 5.1). Assuming both X-inactivation and Y-linkage, we expect the following patterns:

- For sisters, there are 16 possible combinations of active X chromosomes, four for each of the four pairs. They will express the same X chromosome in six of these 16 combinations - an expected proportion of 37.5%.

- Of the four types of brother pairs, two are identical. Thus 50% of all pairs of brothers will share the same X, and all will share the same Y chromosome.

- Among sister-brother pairs, of the eight possible combinations when X-inactivation is taken into account, only two pairs (25%) will express the same X chromosome, and none (0%) will share a Y chromosome.

Expectations for all mating types under the three assumptions are listed in Table 5.2, and summarised in Table 5.3. Overall, the order expected is **BB>SS>SB** if there is a Y chromosomal element. If there is no Y-linkage, and X-inactivation occurs, then **BB=SS>SB**. In this case, the mating $X_1X_2$ x $X_1Y$ produces a further exception: the order is **SS>BB=SB**.

Unlike the model of Mather and Jinks, brothers generally are expected to be more alike than sisters. Also, the presence of transcriptionally active gene(s) on the Y

chromosome might be expected to reduce further, the correlation between female-male sibling pairs. General predictions from this are (1) the correlation in SB is *always* less than those of BB and SS, because of the Y chromosome, (2) the BB correlation equals the SS one if there is X-inactivation and no significant contribution of the Y chromosome, (3) if allelic variation exists in the X-linked genes within a population, any sample will contain matings of most or all of the types listed, so we might expect the overall pattern to be **BB>SS>SB**. .

In order to test for these patterns, product moment correlations were calculated for sibling pairs, using DZ twins. No attempt was made to assess the significance of differences between coefficients, only the order was noted.

## Results

Of the 56 variables, 27 were in the order BB>SS>SB, as predicted under the assumption of X-inactivation and Y chromosome contribution (see tables 5.4 and 5.5 and figures 5.1 and 5.2). Twelve variables followed Mather and Jinks' prediction of SS>BB>SB, a further 12 were SS>SB>BB as reported by Garn and Rohmann (1962). Of the remaining five variables, three were BB>SB>SS, one was BB>SS=SB, and one was SB>BB>SS. Thus, brother pairs displayed the highest correlations for tooth size in 30 out of 56 variables, while sister pairs were the most highly correlated for 25 variables. SB pairs were the least similar group in 40 of the 56 variables. The pattern BB>SS>SB was revealed more often in MD dimensions than BL dimensions. In general, the variables which showed the new pattern were the MD dimensions of anterior teeth and premolars, and BL dimensions of mandibular posterior teeth. The results also showed a reasonable degree of bilateral symmetry, which was not unexpected given the level of correlation between antimeres.

## Discussion

From the comparison of sibling (DZ twin) correlations, there is some evidence for X and Y chromosome contributions to tooth crown size, but as in other studies, the evidence is inconsistent. Of the 56 variables, BB correlations were higher than SS correlations in 30, the reverse was true in 25, and SB correlations were the lowest in 40 variables. Prior analyses of the same variables in non-twin siblings yielded similar results (Alvesalo 1971, Townsend and Brown 1978). These results contradict the first report of sibling correlations for tooth crown size, in which SS correlations were the highest for 13 of 14 MD diameters, and BB were the highest in 1 variable (Garn *et al.* 1965a). Table 5.6 contains a summary of these analyses. While BB>SS can be accounted for by Y-linkage (with or without X-inactivation), only about half of the variables showed this pattern. Significant contributions of autosomal genes and/or environmental factors in some or all of the variables may be confounding the results.

The main difference between the study by Garn *et al.* (1965a) and the other three, is the method of correlation estimation. Garn *et al.* used weighted estimates of the correlation coefficient (ρ) based on Z scores of estimates for right and left sides. The same statistics were employed, and the same results obtained, in a comparison of sibling correlations for ossification of hand bones and calcification of five mandibular teeth (Garn and Rohmann 1962) although the multiple estimates were from serial longitudinal observations instead of right and left sides. Since the data from the present study and the other two investigations do not allow for multiple estimates of ρ, the correlations were compared directly. Whether, and how, this contributes to the differences in results is not clear. In any case, the results suggest that it is not only X- and Y-linked genes which influence variation in tooth crown size, but that autosomal genes and/or environmental factors are contributing also.

**Table 5.1:** Combinations of chromosomes in sibling pairs from the mating $X_1X_2$ x $X_3Y$.

| Siblings | Chromosome Combinations | | | |
|---|---|---|---|---|
| SS | $X_1X_3$ and $X_1X_3$ | $X_1X_3$ and $X_2X_3$ | $X_2X_3$ and $X_1X_3$ | $X_2X_3$ and $X_2X_3$ |
| BB | $X_1Y$ and $X_1Y$ | $X_1Y$ and $X_2Y$ | $X_2Y$ and $X_1Y$ | $X_2Y$ and $X_2Y$ |
| SB | $X_1X_3$ and $X_1Y$ | $X_1X_3$ and $X_2Y$ | $X_2X_3$ and $X_1Y$ | $X_2X_3$ and $X_2Y$ |

**Table 5.2:** Predicted percentage of siblings sharing and expressing the same chromosomes (or sex-linked genes) under different regimes of parental "genotypes", and three hupotheses about X-inactivation and Y chromosomal involvement.

| Parents | | BB | | SS | SB | |
|---|---|---|---|---|---|---|
| Mother | Father | X | Y | X | X | Y |
| **X-inactivation and significant Y** | | | | | | |
| $X_1X_1$ | $X_1Y$ | 100.0 | 100.0 | 100.0 | 100.0 | 0.0 |
| $X_1X_1$ | $X_2Y$ | 100.0 | 100.0 | 50.0 | 50.0 | 0.0 |
| $X_1X_2$ | $X_1Y$ | 50.0 | 100.0 | 60.0 | 50.0 | 0.0 |
| $X_1X_2$ | $X_3Y$ | 50.0 | 100.0 | 37.5 | 25.0 | 0.0 |
| **X-inactivation and no significant Y** | | | | | | |
| $X_1X_1$ | $X_1Y$ | 100.0 | --- | 100.0 | 100.0 | --- |
| $X_1X_1$ | $X_2Y$ | 100.0 | --- | 100.0 | 50.0 | --- |
| $X_1X_2$ | $X_1Y$ | 50.0 | --- | 62.5 | 50.0 | --- |
| $X_1X_2$ | $X_3Y$ | 50.0 | --- | 37.5 | 25.0 | --- |
| **No X-inactivation and significant Y** | | | | | | |
| $X_1X_1$ | $X_1Y$ | 100.0 | 100.0 | 100.0 | 100.0 | 0.0 |
| $X_1X_1$ | $X_2Y$ | 100.0 | 100.0 | 62.5 | 50.0 | 0.0 |
| $X_1X_2$ | $X_1Y$ | 50.0 | 100.0 | 62.5 | 50.0 | 0.0 |
| $X_1X_2$ | $X_3Y$ | 50.0 | 100.0 | 62.5 | 25.0 | 0.0 |

**Table 5.3**: Summary of expected order of correlations under the three assumptions.

| | **Assumption** | | |
|---|---|---|---|
| | **(1)** | **(2)** | **(3)** |
| **Mating** | **X-inactivation Y chromosome** | **X-inactivation No Y chromosome** | **No X-inactivation Y chromosome** |
| $X_1X_1 \times X_1Y$ | BB=SS>SB | BB=SS>SB | BB=SS>SB |
| $X_1X_1 \times X_2Y$ | BB>SS>SB | BB=SS>SB | BB>SS>SB |
| $X_1X_2 \times X_1Y$ | BB>SS>SB | SS>BB=SB | BB>SS>SB |
| $X_1X_2 \times X_3Y$ | BB>SS>SB | BB>SS>SB | BB>SS>SB |
| **Overall** | **BB>SS>SB** | **BB=SS>SB** | **BB>SS>SB** |

**Table 5.4:** Co-twin correlations and sample sizes for MD diameter of DZSS males (BB), females (SS) and DZOS twins (SB); (# = p< 0.05; * = p< 0.01; ** = p< 0.001).

| | BB | | SS | | SB | |
|---|---|---|---|---|---|---|
| **Tooth** | **Corr** | **N** | **Corr** | **N** | **Corr** | **N** |
| **Maxillary Right** | | | | | | |
| **I1** | .74 ** | 37 | .42 * | 45 | .30 # | 54 |
| **I2** | .53 * | 37 | .45 * | 42 | .10 | 45 |
| **C** | .28 | 28 | .22 | 40 | -.06 | 41 |
| **P1** | .26 | 27 | .22 | 29 | .13 | 25 |
| **P2** | .28 | 26 | .56 ** | 38 | .23 | 40 |
| **M1** | .59 ** | 40 | .55 ** | 40 | .54 ** | 47 |
| **M2** | .13 | 12 | .45 # | 20 | .32 | 21 |
| **Maxillary Left** | | | | | | |
| **I1** | .62 ** | 37 | .41* | 43 | .28 # | 53 |
| **I2** | .46 * | 38 | .41* | 44 | .25 | 45 |
| **C** | .42 # | 29 | .31 | 37 | .15 | 42 |
| **P1** | .31 | 26 | .33 | 31 | .14 | 26 |
| **P2** | .24 | 26 | .45 * | 37 | .40 # | 36 |
| **M1** | .54 * | 34 | .60 ** | 40 | .55 ** | 46 |
| **M2** | .63 | 9 | .20 | 16 | .18 | 17 |
| **Mandibular Right** | | | | | | |
| **I1** | .60 ** | 42 | .53 ** | 45 | .41* | 53 |
| **I2** | .46 * | 42 | .43 * | 46 | .38 * | 53 |
| **C** | .08 | 36 | .40 * | 42 | .20 | 46 |
| **P1** | .31 | 32 | .17 | 33 | .07 | 37 |
| **P2** | .26 | 27 | .56* | 33 | .22 | 37 |
| **M1** | .47 * | 39 | .32 | 36 | .33 # | 47 |
| **M2** | .49 | 12 | .57 # | 13 | .36 | 24 |
| **Mandibular Left** | | | | | | |
| **I1** | .56 ** | 43 | .53 ** | 45 | .17 | 52 |
| **I2** | .50 * | 43 | .38 * | 47 | .33 # | 54 |
| **C** | .29 | 37 | .28 | 44 | .12 | 45 |
| **P1** | .43 # | 32 | .39 # | 35 | .23 | 38 |
| **P2** | .55 * | 25 | .46 * | 34 | .35 # | 34 |
| **M1** | .34 # | 37 | .31 | 37 | .35 # | 46 |
| **M2** | .52 | 10 | .54 # | 15 | .51 # | 22 |

**Table 5.5:** Co-twin correlations and sample sizes for BL diameter of DZSS males (BB), females (SS) and DZOS twins (SB); (# = $p < 0.05$; * = $p < 0.01$; ** = $p < 0.001$).

| | BB | | SS | | SB | |
|---|---|---|---|---|---|---|
| **Tooth** | **Corr** | **N** | **Corr** | **N** | **Corr** | **N** |
| **Maxillary Right** | | | | | | |
| I1 | .59 ** | 38 | .49 * | 42 | .25 | 49 |
| I2 | .06 | 32 | .58 ** | 41 | .35 # | 41 |
| C | -.09 | 26 | .71 ** | 37 | .42 * | 40 |
| P1 | .14 | 26 | .43 # | 30 | .12 | 26 |
| P2 | .33 | 26 | .60 ** | 39 | .12 | 40 |
| M1 | .58 ** | 40 | .61 ** | 45 | .38 * | 50 |
| M2 | .50 # | 19 | .31 | 29 | .16 | 28 |
| **Maxillary Left** | | | | | | |
| I1 | .55 ** | 40 | .56 ** | 44 | .37 # | 47 |
| I2 | .14 | 33 | .36 # | 39 | .21 | 41 |
| C | .12 | 27 | .72 ** | 33 | .47 * | 39 |
| P1 | .27 | 27 | .68 ** | 30 | .21 | 28 |
| P2 | .27 | 27 | .51 * | 40 | .15 | 36 |
| M1 | .69 ** | 38 | .60 ** | 44 | .45 * | 52 |
| M2 | .43 | 19 | .47 # | 24 | .35 | 23 |
| **Mandibular Right** | | | | | | |
| I1 | .41 # | 38 | .57 ** | 45 | .44 * | 52 |
| I2 | .46 * | 41 | .43 * | 44 | .44 * | 48 |
| C | .35 | 26 | .59 ** | 36 | .44 * | 40 |
| P1 | .50 * | 32 | .48 * | 34 | .18 | 35 |
| P2 | .45 # | 25 | .33 | 33 | .16 | 37 |
| M1 | .68 ** | 41 | .56 ** | 42 | .24 | 53 |
| M2 | .66 * | 21 | .39 # | 30 | .54 * | 32 |
| **Mandibular Left** | | | | | | |
| I1 | .58 ** | 39 | .52 ** | 45 | .49 ** | 51 |
| I2 | .45 * | 40 | .55 ** | 44 | .47 * | 46 |
| C | .34 | 26 | .60 ** | 37 | .35 # | 39 |
| P1 | .51 * | 32 | .41 # | 36 | .41 # | 38 |
| P2 | .48 # | 23 | .43 # | 34 | .12 | 35 |
| M1 | .68 ** | 41 | .54 * | 44 | .23 | 49 |
| M2 | .63 * | 23 | .55 * | 28 | .38 # | 33 |

**Table 5.6:** Comparison of correlation patterns among siblings as evidence of X- and Y- linkage. Numbers are percentages of the variables showing each pattern.

| Authors | Number of Variables | BB>SS | SS>BB | SS,BB>SB |
|---|---|---|---|---|
| Garn *et al.* (1965a) | 14 | 7 | 93 | 64 |
| Alvesalo (1971) | 56 | 46 | 52 | 29 |
| Townsend and Brown (1978) | 56 | 41 | 29 | 41 |
| The current study | 56 | 54 | 45 | 71 |

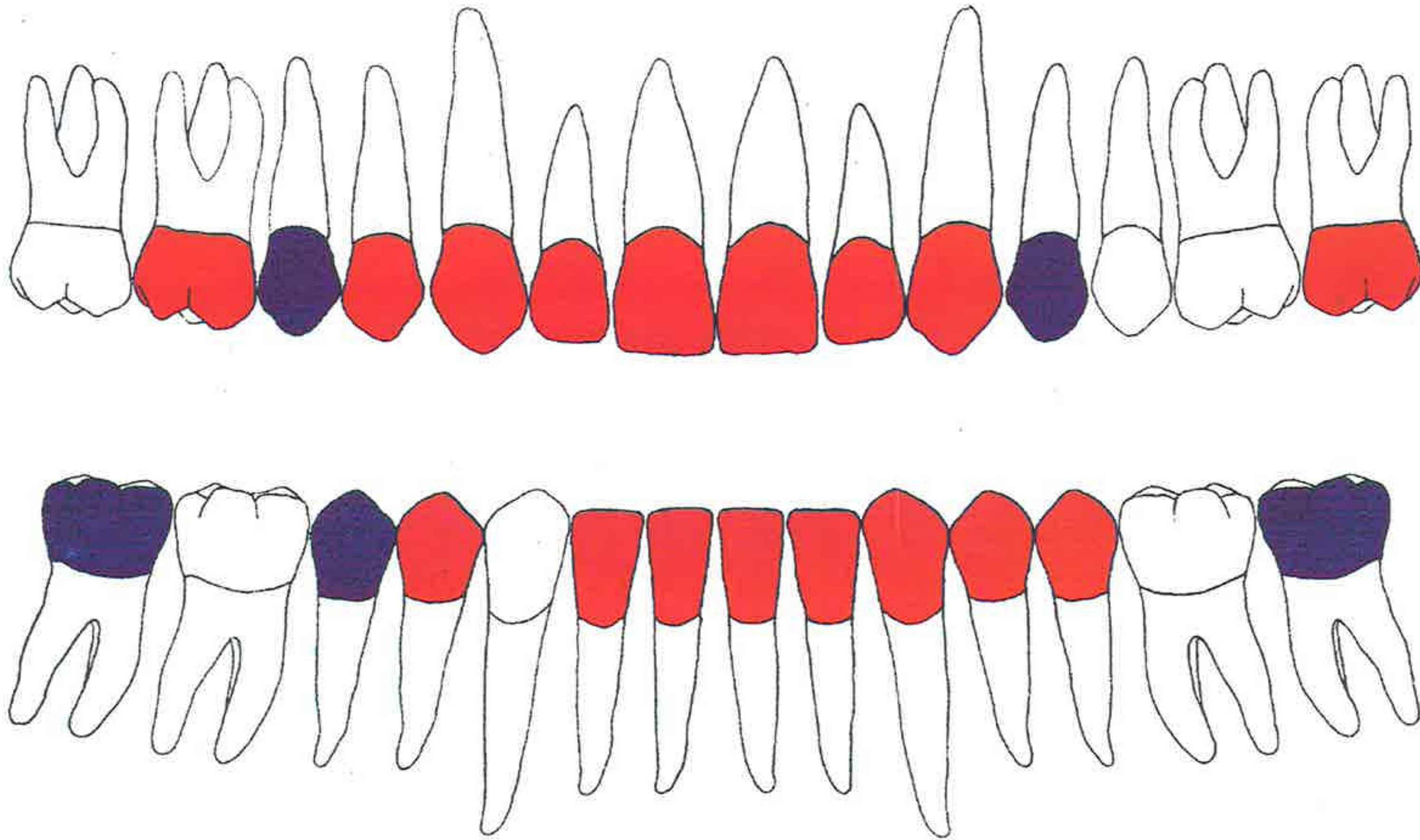

**Figure 5.1:** Order of correlations among DZSS females, DZSS males and DZOS twins for MD diameter. Red = BB>SS>SB; blue = SS>BB>SB (predicted by Mather & Jinks 1963). See text for further explanation.

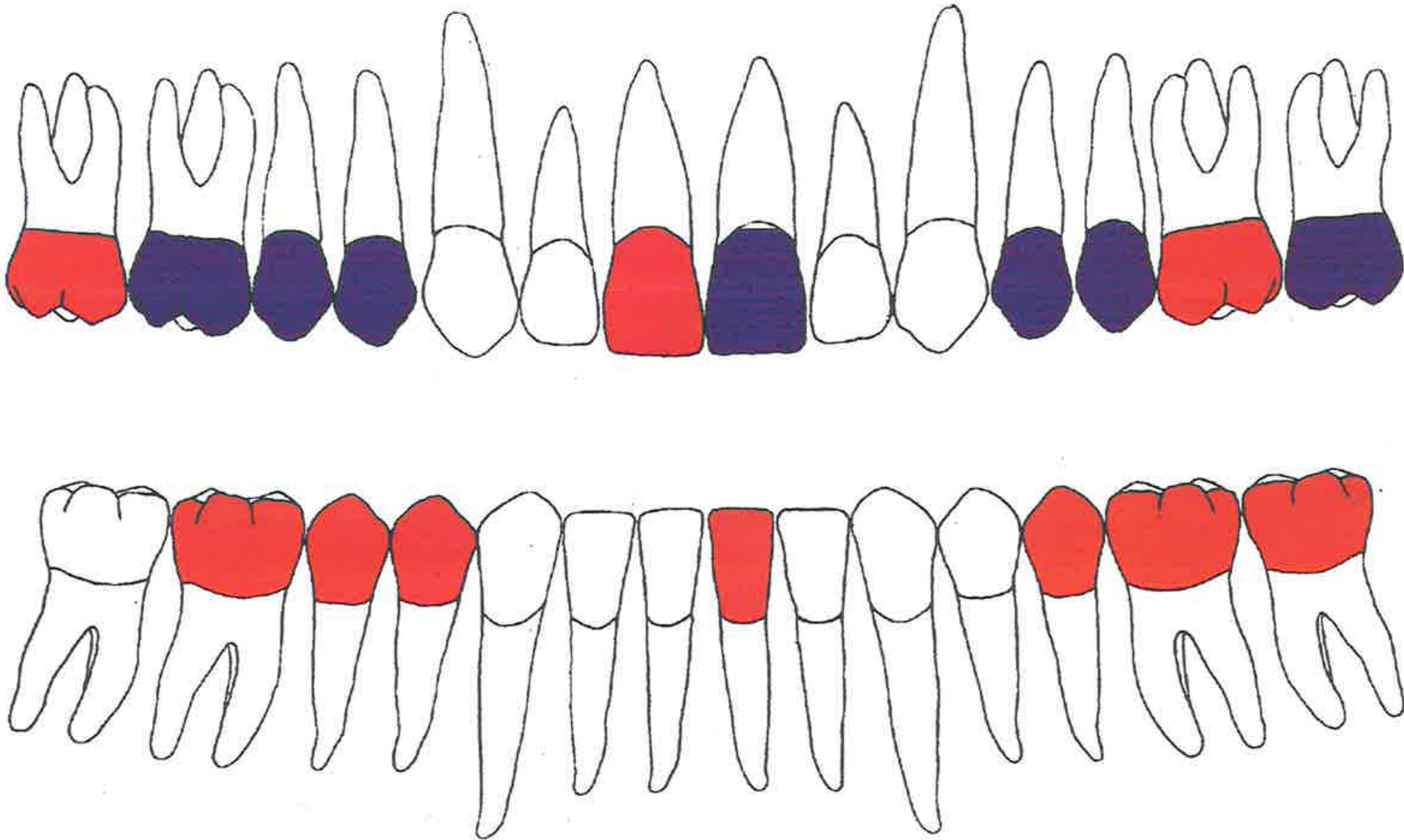

**Figure 5.2:** Order of correlations among DZSS females, DZSS males and DZOS twins for BL diameter. Red = BB>SS>SB; blue = SS>BB>SB (predicted by Mather & Jinks 1963). See text for further explanation.

# Chapter 6

# Sex Hormones, Twin Gestation and the Dentition

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## Introduction

When there is significant sexual dimorphism for a character, the role of sex hormones in the dimorphism might be investigated. Numerous sexually dimorphic traits in rodents and pigs have been found to be correlated with the sex of litter-mates and their position within the uterus. This finding has led to the suggestion that diffusion of sex hormones occurs between litter-mates, causing females to be masculinized and males feminized in both morphological and behavioral features. Additionally, some features have been found to be enhanced (made 'more female' or 'more male') by sharing prenatal circulation with members of the same sex. Reviews of this literature have been published by vom Saal (1989) and Miller (1994). Briefly, masculinization of females has been reported in numerous traits of rodents, including anogenital distances, copulatory behaviour, levels of aggression, body weight, activity levels, attractiveness to males, time of vaginal opening, and testosterone levels in blood serum and amniotic fluid. Conversely, feminization of male rodents has been noted in body weight, anogenital distance and parental behaviour.

In humans, opposite-sexed twin pairs provide a natural experiment to test whether such hormonal diffusion occurs, and whether primary or secondary sexual characteristics are affected by the hormones. The result would be phenotypes for both twins which are intermediate between the sexes, or a phenotype for one sex which more closely approximates that of the opposite sex. Comparing DZSS and DZOS twins thus can reveal three things - whether hormonal diffusion takes place in utero, whether hormones influence a particular character, and in which direction. A positive result (masculinization or feminization of an OS twin) answers all three questions, whereas a negative result (no change to either sex) does not allow us to determine whether hormonal diffusion is not occurring, hormones have no effect on the trait, or both.

Co-gestated human offspring do not usually share a placenta. If hormonal diffusion occurs, the hormones must pass from one foetus to the other via the maternal circulation, or directly through the foetal and placental membranes and amniotic fluid. Indirect evidence for the first path originates from several different studies. Firstly, steroids have been described as being able to cross the human placenta easily (Solomon 1988), and both cortisol and dehydro-epiandrosterone have been observed to pass from the maternal to foetal circulation (Schindler 1982). Since the sex hormones have a similar structure, it is assumed they also can diffuse across the placenta. Secondly, maternal testosterone levels in humans have been reported to be associated with sex of the foetus, suggesting that testosterone from a male foetus enters the maternal circulation (Meulenberg and Hofman 1991). Thirdly, injections of androgens into pregnant animals has been observed to produced masculinization of female offspring in rats, guinea pigs, rhesus monkeys (Phoenix *et al.* 1968) and cows (Jost 1972). As for the second path, testosterone has been shown to diffuse across the amniotic membranes separating rat foetuses (Fels and Bosch 1971), so at least in rodents, direct foetus-foetus diffusion appears to be possible.

Is there any evidence that sex hormones affect tooth crown size? Knowledge about whether, and how, sex hormones affect tooth morphology in humans is extremely limited. There is indirect evidence of tooth development being affected by circulating sex and growth hormones (Garn et al. 1965a; Lorber et al. 1979). Androgens also have been implicated in tooth development in spotted hyenas (Frank et al. 1991) and in a reverse sexual dimorphism of molar tooth mass in mice (Heller and Blecher 1982).

A further consideration is whether permanent tooth crown size, which is finalised after birth, can be affected by prenatal environmental conditions. Demonstrated associations between altered permanent tooth crown size and aspects of uterine

environment in humans, include the following maternal conditions: smoking (Heikkinen et al. 1994a, 1994b, 1995a, 1996), alcohol consumption (Kieser 1992), diabetes, hypothyroidism and hypertension (Garn et al. 1979), and obesity (Kieser et al. 1997). The reported effects include larger or smaller average tooth crown diameters or intercuspal distances, and increased levels of fluctuating asymmetry. In many of these studies, the permanent canine has been least affected. Maternal smoking also has been found to be associated with altered eruption timing of permanent teeth (Heikkinen et al. 1995b). It seems likely then, that prenatal influences on the developing dental crowns can have a measurable impact on final crown morphology.

Is there any evidence leading to an expectation about directionality of changes in OS twins? That is, would we expect both sexes to display an intermediate phenotype, or would the effect be restricted to one sex only? Foetal hormone levels suggest that either situation is possible. In humans, all of the sex hormones are present in both sexes. Differentiation is due to differences in the levels of each hormone, rather than the presence or absence of particular molecules *per se* (Wilson & Foster 1985). One examination of foetal hormone levels revealed that the two male hormones, testosterone and androstenedione, were present in male foetuses at significantly higher levels than in female foetuses, but the levels of progesterone and oestrogen were not significantly different (Carson *et al.* 1982). This contrasts with a study showing that estradiol levels were greater in female foetuses than in male foetuses (Reyes *et al.* 1974, in vom Saal 1989). The former finding leads to the prediction of masculinization of females but not feminization of males, while the second argues for both being possible.

Most published OS twin studies reveal evidence for masculinization of the females, but not feminization of the males. The traits that have demonstrated this effect include verbal ability (Record et al. 1970), mathematical performance and perceptual

speed (Fischbein 1978), otoacoustic emissions (McFadden 1993), spatial ability (Cole-Harding et al. 1988) and sensation seeking behavior involving measures of disinhibition, experience seeking, adventure seeking and boredom susceptibility (Resnick et al. 1993). Traits that have shown effects in both sexes include physical resemblance of twins to each parent (Zazzo 1960) and asymmetry in dental diameters (Boklage 1985), although the latter finding was based on only ten pairs of OS twins. Conversely, no such effects were found for psychological resemblance of twins to each parent (Zazzo 1960), shoulder:hip ratio in dizygous (DZ) OS twins (Dahlberg 1926, analysed by Miller 1994) or for most of a variety of reproductive traits (Loehlin and Martin 1998).

Most of these traits are physiological or psychological, with shoulder:hip ratio and dental asymmetry being the only clearly morphological variables. Further studies are needed of reliably-measured, sexually dimorphic morphological variables. A consistent sexual dimorphism in tooth crown size has been reported in most human populations, fossil hominids and extant primate species (reviewed by Oxnard 1984; Kieser 1990). On average, the dental crown diameters of human males are significantly larger than those of females, although the dimorphism is relatively small (generally less than 1mm, or 7% of the measured diameter). It is expressed most strongly in the canines and molars (Garn et al. 1964, 1967; Alvesalo 1971; Yamada and Sakai 1992), least in the incisors (Garn et al. 1964, 1967; Yamada and Sakai 1992), and more in buccolingual (BL) than mesiodistal (MD) diameters (Yamada and Sakai 1992). Such a consistent dimorphism is an obvious target for studying the role of sex hormones in development.

The aim in this chapter was to compare tooth crown diameters in SS and OS twins and singletons, to determine whether any systematic differences were evident. If the observed sexual dimorphism of tooth crown size was due, at least in part, to the actions of sex hormones diffusing between twins, we might expect females with twin

brothers to have larger teeth on average than other females. It is also possible that males with twin sisters might have smaller teeth on average than other males.

## Materials and Methods

SS twins and singletons were combined into a single group, denoted "NonOS", in order to compare them with OS twins. Means, standard errors, and standard deviations were calculated for OS twins and for NonOS individuals within each sex. Bar graphs were constructed to show the difference between OS and NonOS means (calculated as OS minus NonOS), and sign tests were performed to test for random distribution of positive and negative differences.

Because teeth show significant intercorrelations (Garn et al. 1965b), differences between OS and NonOS individuals were tested using MANOVAs. These multivariate tests require listwise deletion of individuals with missing values. The proportion of missing values ranged from 2 to 55%, depending on the tooth. To maximise our sample sizes, we selected three teeth with the highest proportion of values present - the central incisor, canine and first molar. MD and BL diameters of maxillary and mandibular teeth on the right side were used, yielding 12 variables. Missing values were then replaced by the value from the tooth on the left side, or if this was missing and the individual had a co-twin of the same sex, the value was taken from the co-twin. Overall, the proportion of values imputed ranged from 2 to 7%, and after this process, only 2 to 10% of values were still missing.

Initially, a MANOVA test of the difference between sexes was applied. Two further MANOVAs were applied to MZ twins, DZSS twins and singletons to determine whether the three groups could be pooled within each sex. The findings were positive for females ($p=0.47$), indicating that the three groups could be combined into a Non-OS group, and negative for the males ($p=0.03$). Among males, further MANOVA

tests revealed that MZ and DZSS twins could be pooled ($p=0.58$), forming a SS group, but singletons could not be added in ($p<0.001$). For the final analysis then, three MANOVA tests were employed, comparing OS females with Non-OS females, OS males with SS males, and OS males with singleton males.

## Results

Tables 6.1 and 6.2 contain descriptive statistics for the OS and NonOS individuals within each sex. Although our sample sizes were not large enough to provide the statistical power to disclose significant differences between individual crown size means in NonOS and OS females, 26 of the 28 differences between means were positive, indicating that the teeth of OS females were generally larger than those of Non-OS females (Fig.ure 6.1). The distribution of positive and negative values was not as expected if there were no systematic difference between OS and Non-OS female means, with the sign test for this being highly significant ($p<0.001$). Conversely, there was no significant difference from the expected number of positive and negative values in males (Figure 6.2), with 16 of the 28 means larger in OS males, and $p>0.50$ for the sign test.

As for the MANOVAs, the exact F statistic for the testing of female and male means was 15.05 ($p<0.001$), indicating a highly significant difference between sexes. There also were significant differences between means of OS and Non-OS females ($F=2.03$, $p=0.02$), and between male OS twins and singletons ($F=4.09$, $p<0.001$). However, there was no significant difference between SS and OS male twins ($F=0.68$, $p=0.77$).

## Discussion

### Masculinization of OS females

The bar graph, sign test, and MANOVA, indicated that OS female twins tended to have larger teeth than SS and singleton females. This may be taken as evidence of masculinization of female OS twins in utero.

OS females also displayed a trend toward greater variances than the other three groups of females combined. From Table 6.1, it can be seen that 21 of the 28 standard deviations were greater in OS than NonOS females. None of these differences were significant by univariate F test, but the sign test for this ratio was significant ($p=0.02$), whereas the equivalent test for males was not ($p>0.50$). In addition, of all the MANOVAs performed, only that of Non-OS and OS females came close to showing a significant difference in variances of the two groups (probability associated with Box's M test = 0.056). All others were associated with probabilities of at least 0.12. This intriguing trend may reflect a hormonal influence, since the amount of androgen an OS female receives from her brother will depend on how much he produces, and how much is retained by the mother's circulation. These factors would add to the variation from sources common to all types of twins and singletons. An alternative explanation is that it may simply be due to the difference in sample sizes between OS and Non-OS females.

The present finding is an important one. It provides evidence for masculinization of DZOS female twins for a morphological trait, measured with a high degree of reliability, and not likely to be influenced by cultural factors. Females from OS twin pairs in our sample had teeth which were consistently larger than those of females with a twin sister or, importantly, with no twin at all. Thus it cannot be argued that

OS females had larger teeth than those of SS females simply because OS twins have been reported to enjoy a relative protection from the stresses of twin pregnancy (Boklage 1985). In pondering similar findings for dental asymmetry displayed by OS twins, Boklage (1985) suggested that "something about the means of enacting the (sex) differences is diffusible." The actual mechanism for producing such effects in permanent teeth is unknown, but may involve increased proliferation of cells in the developing tooth germ prior to crown dimensions being fixed by calcification.

It is noteworthy that the difference between the averages for OS and Non-OS females was small, ranging from 0.01mm to 0.25mm. Although this difference is not of an order of magnitude that would enable females from DZ OS twin pairs to be distinguished from other females, it indicates a potential diffusion of hormones between twins in utero. Furthermore, this process may have greater impact on other morphological, physiological or behavioural traits.

Another important factor to consider is whether the effect demonstrated by teeth reflects a change in overall allometry. Given that there was no significant correlation between tooth crown size and birthweight in these twins, and that tooth crown size shows little or no correlation with adult body size (Garn 1958), it is unlikely that the effect presented here reflects an increase in body size in OS females. Nutrition also has been reported to influence tooth crown size (Niswander 1963; Moller 1967; Garn 1979), but would not be expected to differ between SS and OS twins, or to be better in OS twins than in singletons.

**Feminization of OS males**

Conversely, there was no evidence that feminization of male OS twins occurred. This finding is in agreement with most other investigations of OS twins, in which males were generally unaffected or only slightly affected by the presence of the female

twin. The one-sided nature of this effect is not surprising, since normal male development occurs in spite of exposure to maternal estrogen in utero. By comparison, the presence of "male" hormones induces the development of masculinity, so a chromosomally-female individual will develop as a male in the presence of androgens.

The fact that a number of studies have reported a shift in means of OS male twins towards those of females does not negate this, since virtually all of these have been behavioural traits, and may have been influenced by the presence of a twin sister post-natally. The only morphological study to show such a trend in males was that of dental asymmetry, from which Boklage (1985) concluded that allocation of twins to gender is likely to be correct unless the person has an OS twin, in which case the female shows the more profound effect of co-gestation with a male, even into adulthood. Since the study involved only ten OS twin pairs, the result is not particularly robust. The notion that effects are unidirectional is supported by the data presented in this paper, and by most previous studies.

**Singleton versus twin males**

The difference between singleton and twin males is not easily explained. Overall, it was caused by singletons having larger BL, and smaller MD diameters than SS or OS twins. There does not seem to be a good biological explanation for the result. For instance, the complications and added stresses of twin pregnancies might be expected to produce more consistent differences between twins and singletons across the variables studied, and to affect both sexes.

The result might be due to sampling error. For instance, singletons of both sexes were chosen from among the population of Caucasian dental students, and thus, may not be a representative sample of the wider population. From among this group, stone

models were selected with a bias towards individuals with most or all of their teeth present, to minimise the number of missing values. This may have resulted in selection of individuals with stronger, healthier teeth than average, although the difference was restricted to males. Having smaller MD diameters may also mean these individuals were less likely to suffer crowding of the dentition, and thus to have missing teeth due to extractions. Only further (random) sampling can resolve this point.

**Masculinization versus level of sexual dimorphism**

It is intriguing that the extent of masculinization of OS females was not proportional to the degree of sexual dimorphism. For instance, the greatest sexual dimorphism occurred in both diameters of the canines and first molars, and least in the central incisors. The variables which showed the greatest effect of masculinization were both diameters of maxillary second molars, followed by both diameters of maxillary central incisors. The effect was smallest for both diameters of maxillary canines and BL diameter of maxillary lateral incisors and maxillary and mandibular first molars. In fact the relationship appears to be somewhat negative. Adding weight to this notion is the finding that although BL dimensions were generally more sexually dimorphic than MD ones, MD dimensions showed a stronger effect in OS females. This suggests that sexually dimorphic traits may vary in the extent to which prenatal sex hormone levels influence the dimorphism.

If hormone production levels are genetically determined, hormonal exchange should not have a significant impact on MZ twins, but DZ twins may develop to be more alike than if they were singleton siblings. This would be reflected in genetic models as a contribution of common environment (some aspect of the environment which is common to both members of a twin pair). In our studies of tooth crown size in twins, we have shown a significant contribution of shared environment in the MD

dimension of maxillary central incisors (Dempsey et al. 1995, and Chapter 8). This effect only occurred in males, leading to the tempting suggestion that hormonal diffusion was causing the observed high degree of similarity between DZ SS males. The finding in this chapter that maxillary central incisors in OS females were strongly masculinized in both diameters lends support to the suggestion.

The same study revealed a significant contribution of non-additive genetic variation (dominance or epistatic interaction) to the MD dimension of canines, suggesting that there may have been strong selective pressures acting on these teeth in the recent or distant past (Fisher 1958). It also has been found that the canine is resilient in the presence of severe sex chromosomal anomalies (Townsend et al. 1986), and the current analysis suggests that the same is true in the presence of sex hormones. This suggests a mechanism for control of canine development which is independent of, or in addition to, hormonal and sex chromosomal control. So, the three pieces of evidence (from OS twins, studies of sex chromosome anomalies, and of quantitative genetics) lead us to propose that the size and degree of sexual dimorphism of canine tooth crowns is strongly controlled, via a mechanism not shared with other teeth.

## Conclusions

Females with twin brothers have teeth which are larger on average than those of females with twin sisters, or with no twin at all. Conversely, the tooth sizes of males with twin sisters do not differ from males with twin brothers. Singleton males revealed significantly different patterns of tooth crown size from twin males, and this may be due to sampling error - further sampling is required. The directionality of the effect is not unexpected given foetal levels of sex hormones, and exposure of male offspring to maternal oestrogen.

The magnitude of the effect across the dentition did not parallel the magnitude of sexual dimorphism for tooth crown size, suggesting that some teeth may be more affected by sex hormone levels than others. In particular, the maxillary central incisors were strongly influenced, while the maxillary canines were only weakly affected, if at all.

**Table 6.1**: Descriptive statistics for Non-OS and OS females

| | Non-OS Females | | | | OS Females | | | |
|---|---|---|---|---|---|---|---|---|
| **Variables** | **N** [a] | **Mean** | **SE** [b] | **SD** [c] | **N** | **Mean** | **SE** | **SD** |
| Maxilla, MD diameter | | | | | | | | |
| I1 | 206 | 8.47 | .04 | .52 | 56 | 8.67 | .08 | .58 |
| I2 | 200 | 6.56 | .04 | .50 | 55 | 6.61 | .08 | .62 |
| C | 197 | 7.51 | .03 | .36 | 47 | 7.54 | .06 | .42 |
| P1 | 188 | 6.83 | .03 | .39 | 46 | 6.89 | .06 | .42 |
| P2 | 198 | 6.58 | .03 | .42 | 46 | 6.64 | .06 | .42 |
| M1 | 201 | 10.17 | .04 | .55 | 56 | 10.30 | .07 | .56 |
| M2 | 158 | 9.81 | .05 | .61 | 39 | 10.06 | .10 | .64 |
| Mandible, MD diameter | | | | | | | | |
| I1 | 207 | 5.26 | .02 | .34 | 56 | 5.33 | .06 | .44 |
| I2 | 206 | 5.81 | .03 | .38 | 56 | 5.94 | .05 | .40 |
| C | 203 | 6.51 | .02 | .32 | 54 | 6.66 | .05 | .37 |
| P1 | 199 | 6.94 | .03 | .40 | 50 | 7.03 | .06 | .41 |
| P2 | 197 | 7.02 | .03 | .44 | 47 | 7.13 | .07 | .47 |
| M1 | 203 | 10.78 | .04 | .60 | 54 | 10.84 | .09 | .63 |
| M2 | 151 | 10.27 | .05 | .60 | 40 | 10.42 | .10 | .63 |
| Maxilla, BL diameter | | | | | | | | |
| I1 | 203 | 7.01 | .03 | .48 | 53 | 7.19 | .07 | .49 |
| I2 | 192 | 6.21 | .04 | .49 | 50 | 6.17 | .07 | .51 |
| C | 185 | 7.98 | .04 | .52 | 45 | 7.95 | .09 | .57 |
| P1 | 187 | 9.04 | .04 | .53 | 46 | 9.12 | .07 | .48 |
| P2 | 196 | 9.14 | .04 | .57 | 47 | 9.19 | .07 | .50 |
| M1 | 201 | 11.17 | .04 | .55 | 56 | 11.18 | .08 | .57 |
| M2 | 162 | 10.90 | .06 | .73 | 41 | 11.11 | .10 | .65 |
| Mandible, BL diameter | | | | | | | | |
| I1 | 206 | 5.89 | .03 | .41 | 56 | 5.93 | .07 | .49 |
| I2 | 204 | 6.27 | .03 | .43 | 54 | 6.36 | .05 | .37 |
| C | 197 | 7.28 | .04 | .50 | 46 | 7.44 | .08 | .52 |
| P1 | 198 | 7.80 | .04 | .52 | 47 | 7.84 | .08 | .55 |
| P2 | 198 | 8.41 | .04 | .50 | 47 | 8.55 | .07 | .49 |
| M1 | 206 | 10.53 | .03 | .46 | 56 | 10.56 | .06 | .45 |
| M2 | 172 | 10.22 | .04 | .54 | 43 | 10.24 | .09 | .57 |

[a] N = sample size. [b] SE = standard error of the mean. [c] SD = standard deviation.

**Table 6.2**: Descriptive statistics for Non-OS and OS males [a]

| | Non-OS Males | | | | OS Males | | | |
|---|---|---|---|---|---|---|---|---|
| **Variables** | **N** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** |
| Maxilla, MD diameter | | | | | | | | |
| I1 | 184 | 8.74 | .04 | .52 | 55 | 8.87 | .08 | .58 |
| I2 | 185 | 6.79 | .04 | .54 | 51 | 6.98 | .07 | .51 |
| C | 169 | 7.95 | .04 | .47 | 44 | 7.96 | .05 | .36 |
| P1 | 164 | 7.06 | .03 | .40 | 35 | 7.10 | .06 | .33 |
| P2 | 163 | 6.79 | .03 | .41 | 43 | 6.82 | .06 | .37 |
| M1 | 181 | 10.54 | .04 | .55 | 51 | 10.52 | .08 | .55 |
| M2 | 134 | 10.23 | .05 | .59 | 31 | 10.41 | .13 | .71 |
| Mandible, MD diameter | | | | | | | | |
| I1 | 182 | 5.38 | .02 | .33 | 55 | 5.41 | .05 | .36 |
| I2 | 184 | 6.00 | .03 | .39 | 55 | 6.13 | .05 | .39 |
| C | 176 | 6.95 | .03 | .40 | 48 | 7.05 | .04 | .30 |
| P1 | 170 | 7.16 | .04 | .46 | 44 | 7.23 | .05 | .34 |
| P2 | 168 | 7.28 | .03 | .44 | 42 | 7.36 | .06 | .37 |
| M1 | 180 | 11.18 | .05 | .62 | 52 | 11.14 | .09 | .67 |
| M2 | 125 | 10.78 | .06 | .65 | 33 | 10.80 | .12 | .70 |
| Maxilla, BL diameter | | | | | | | | |
| I1 | 183 | 7.30 | .04 | .56 | 51 | 7.28 | .08 | .55 |
| I2 | 179 | 6.44 | .04 | .60 | 45 | 6.52 | .08 | .55 |
| C | 156 | 8.47 | .05 | .67 | 42 | 8.35 | .09 | .60 |
| P1 | 163 | 9.37 | .04 | .56 | 35 | 9.41 | .09 | .54 |
| P2 | 165 | 9.55 | .05 | .61 | 44 | 9.52 | .08 | .53 |
| M1 | 181 | 11.61 | .04 | .60 | 54 | 11.54 | .08 | .57 |
| M2 | 155 | 11.57 | .06 | .80 | 34 | 11.49 | .10 | .60 |
| Mandible, BL diameter | | | | | | | | |
| I1 | 184 | 6.12 | .03 | .45 | 54 | 6.03 | .07 | .53 |
| I2 | 183 | 6.44 | .04 | .48 | 51 | 6.34 | .08 | .54 |
| C | 165 | 7.84 | .05 | .66 | 44 | 7.66 | .11 | .70 |
| P1 | 169 | 8.20 | .04 | .54 | 44 | 8.18 | .08 | .54 |
| P2 | 167 | 8.73 | .04 | .58 | 42 | 8.78 | .09 | .58 |
| M1 | 182 | 10.89 | .04 | .57 | 56 | 10.86 | .07 | .49 |
| M2 | 155 | 10.68 | .05 | .64 | 40 | 10.76 | .09 | .57 |

[a] See footnote in Table 1 for abbreviations.

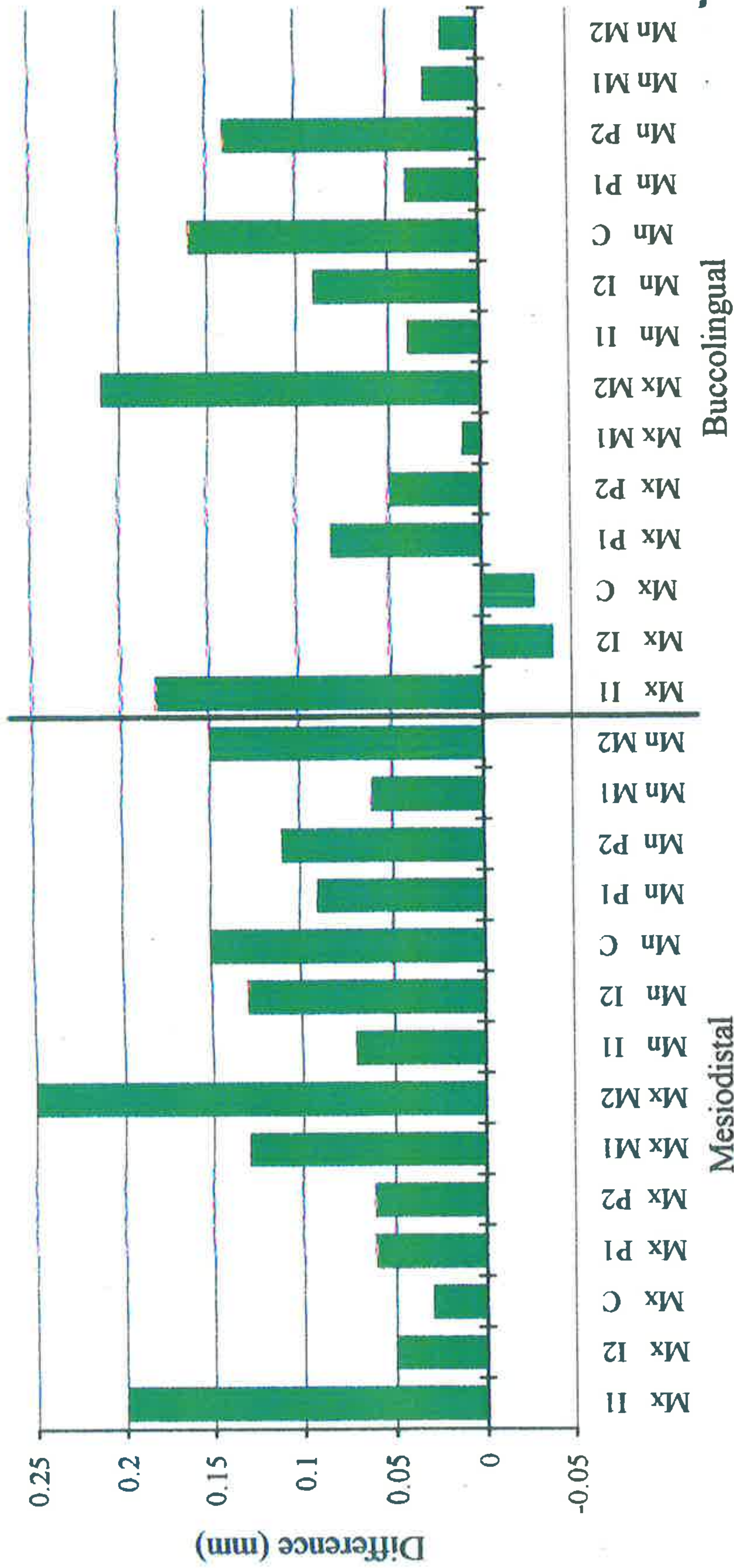


**Figure 6.1**: Bar chart showing difference in average tooth crown size between OS and Non-OS females.

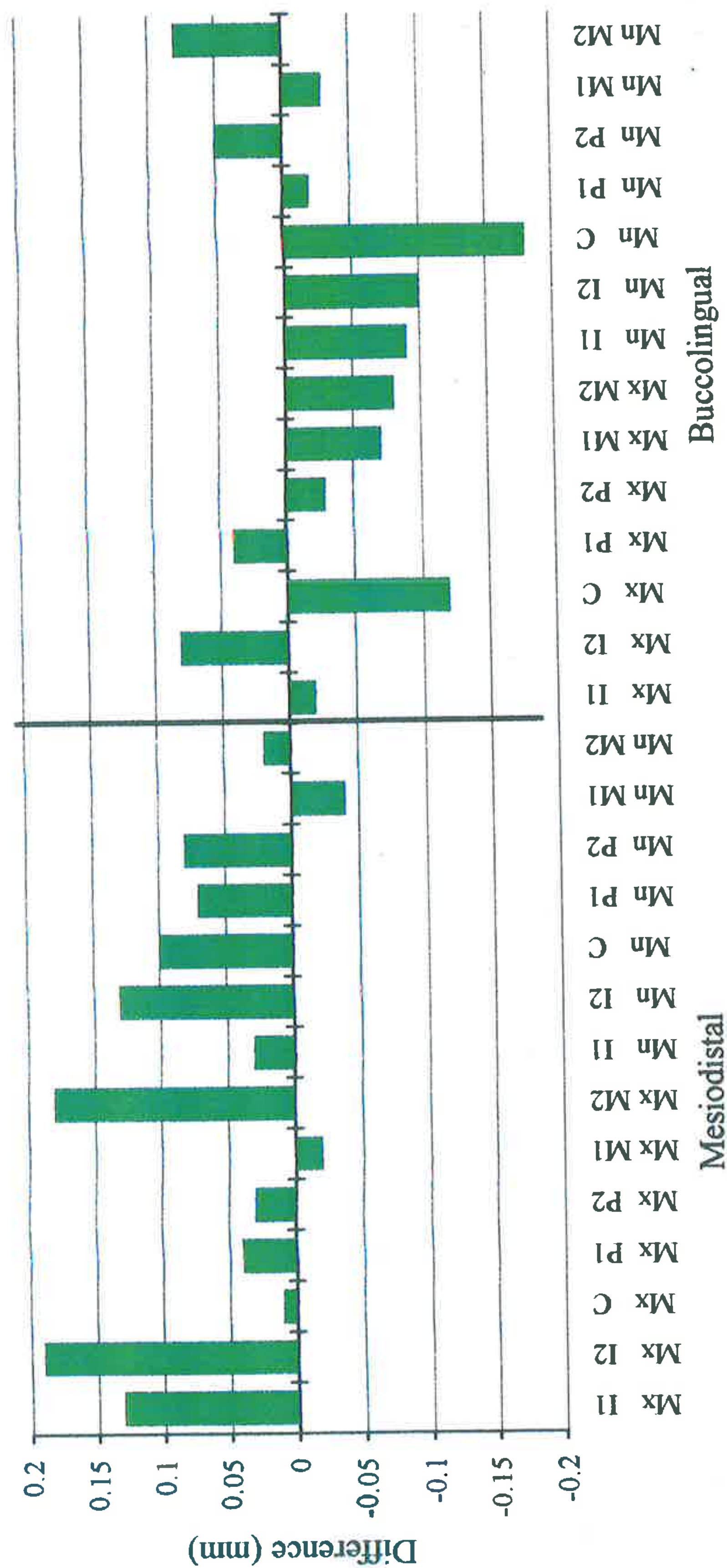


**Figure 6.2**: Bar chart showing difference in average tooth crown size between OS and Non-OS males.

# Chapter 7

# Genetic Modelling of Tooth Crown Size - the Univariate Analyses

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## Introduction

There have been a large number of reported investigations into genetic factors contributing to tooth crown size, with Korkhaus (1930) being one of the earliest. Most of the studies have utilised family data such as twins, triplets, full siblings, half siblings, cousins and parent-offspring pairings. Estimates for heritability from these studies range from 21% (Townsend *et al.* 1986) to 90% (Garn *et al.* 1965c), although most are over 60%. In fact, most researchers have reported significant genetic variation, including Lundström (1948), Osborne *et al.* (1958), Kraus *et al.* (1959), Garn *et al.* (1965c), Potter and Nance (1976), Rebich and Markovic (1976), Townsend (1978, 1992), Mizoguchi (1980), Sharma *et al.* (1985), and Harzer (1987). Such concordance between studies led Garn (1977, p67) to state that unless we discover a significant common environmental contribution, we can retain the notion that MD and BL crown dimensions "are to the largest extent gene-determined."

Typically, researchers have assumed a polygenic pattern of inheritance for crown diameters. Support for this assumption was provided by one study involving pedigree analysis and complex segregation analysis, which failed to reveal any major gene effects (Kolakowski and Bailit 1981). More detailed reviews of the role of genetic and environmental factors have been published by Potter (1976), Garn (1977), Kieser (1990) and Townsend (1992).

In spite of difficulties with statistical methods, and inabilities to detect, control for, or estimate various parameters, most studies have suggested a large genetic component to variation in tooth crown size. In addition, numerous reports have looked for patterns in the estimated heritabilities consistent with Butler's field theory (Butler 1939, Dahlberg 1945). The findings have been inconsistent, with some revealing lower heritabilities in distal members of tooth groups than in mesial members as

predicted (Moorrees 1964, Horowitz *et al.* 1958, Lundström 1964, Alvesalo and Tigerstedt 1974, Rebich and Markovic 1976, Mizoguchi 1977, Potter *et al.* 1978), and others revealing a different pattern or apparent lack of pattern (Mizoguchi 1977, Harzer 1987). The inconsistency may be due to differences in statistical methods or in the population from which the sample originated. Another reported trend is of greater heritability of MD than BL dimensions (Moorrees 1964, Harzer 1987).

Current biometrical genetic methodology represents a major breakthrough in estimating various genetic and environmental effects, since it allows testing for, and estimation of, the components which were previously assumed absent or undetectable. Since a detailed comparison of different methods was provided in Chapter 1, it suffices to say that the biometrical genetic approach used in this thesis is considered to have several advantages over both the correlation analyses and multiple abstract variance analyses employed in prior investigations (Jinks and Fulker 1970).

**Aims**

The aims of this study were:

- to quantify the relative contributions of various genetic and environmental factors to variation in mesiodistal and buccolingual dimensions of permanent tooth crowns; and
- to examine patterns of heritabilities for agreement with Butler's field theory and other previous findings.

## Materials and Methods

### General Approach to Modelling

The twin method may be employed to estimate the relative influences of additive genetic factors (A), non-additive genetic factors (D), the shared or common environment (C) and that part of the environment which is unique to each individual (E), to variation in the size of permanent tooth crowns. This involves comparing MZ twin variances and covariances with those of DZ twins.

Before attempting to estimate these four factors, the contribution of three additional cources of variance and covariance should be considered - assortative mating, genotype by environment interaction (GxE) and genotype-environment correlation (CorGE). Although the influences of these factors are described in detail elsewhere (Neale and Cardon 1992), each shall be described briefly.

Assortative mating mimics common environment, spuriously lowering the genetic contribution to variation. Data from spouses, or from parents of twins, are required to ascertain whether there is assortative mating. To date, the evidence published suggests that there is no assortative mating with respect to tooth crown size in humans (Niswander and Chung 1965, Bowden and Goose 1969, Townsend and Brown 1978a, El-Nofely and Tawfik 1995).

Genotype by environment interaction (GxE) relates to the way genes and environment determine the phenotype. It describes the situation in which one genotype may be expressed the same way in two different environments, while another genotype changes. The presence of GxE interactions may be indicated by

significant regression of MZ pair variances on MZ pair means (Jinks and Fulker 1970). This regression method was used to test for GxE interaction in the data, although there were a priori reasons for suspecting that there might not be sufficient power in the test. Fristly, since the effects of GxE interaction may be small compared with other genetic and environmental effects, large sample sizes may be needed (Neale and Cardon 1992). Secondly, in the absence of an identifiable environmental factor, adoption data may be the only method of detecting and estimating this interaction term (Neale and Cardon 1992).

Genotype-environment correlation (CorGE) occurs when the environments an individual experiences are not a random sample of all environments, but are influenced by, or correlated with, the individual's genotype. There are several types, each with a different effect. Genetic variance may be increased or decreased, and variances between MZ and DZ twins, or between twins and singletons, may be unequal. CorGE cannot be detected in cross-sectional studies (Neale and Cardon 1992). Again, adoption data may be necessary, and/or a variety of different familial relationships. Given that the data analysed *are* cross-sectional, this factor was not tested for, and must be assumed to have little or no impact.

CorGE includes sibling effects, wherein the phenotype of one sibling influences the phenotype of another. Sibling interactions in twins and other multiple gestations are possible, given that the permanent teeth are present in utero as soft tissue masses, and are thus still malleable depending on genetic or environmental conditions. Any substances diffusing from one twin to the other may have an effect, which most likely would mimic a sibling cooperation effect (Neale and Cardon 1992), and cause an increase in genetic contributions to variance. Evidence of an effect of sex hormones in Chapter 6 would probably qualify as sibling cooperation, except that the effect was restricted to OS females, not SS twins or OS males. In modelling analyses

then, it was not expected to affect the results, especially since the effect in OS females was relatively small. Conversely, a sibling competition effect may arise if a twin transfusion effect operated in utero. This would lead to a decrease in the estimated amount of genetic variance. These are perhaps the most likely sources of CorGE, since it is difficult to see how tooth crown size could be correlated with the range of environments to which the individual is exposed after birth.

There is some reassurance in noting that twin transfusion effect, and other sources of sibling interaction, have not been shown to influence tooth crown size substantially in twins. In fact, very few good examples of GxE interaction or CorGE have been demonstrated in humans. After 20 or more years of testing for them using well designed, powerful empirical studies (Martin *et al.* 1997), the assumption that they don't exist would not seem unrealistic.

The other four sources of variation in a pair of twins (A, D, C and E), and how they contribute to variances and covariances, are depicted in Figure 7.1. The genetic correlations $R_a$ and $R_d$, (indicated by two-headed arrows) between MZ twins are 1.0, since these twins are assumed to share all of their genes in common. As DZ twins share half of their genes in common on average, this value is $R_a = 0.5$ for additive genetic effects. For non-additive genetic effects, the expected DZ twin correlation is $R_d = 0.25$, because one quarter of all full-sib pairs receives the same genotype from their parents, and thus the same dominance deviation. Assuming that the shared environment for MZ twins is the same as that for DZ twins, the shared environmental correlation, is $R_c = 1.0$ for both twin types. By definition, unique environmental effects are uncorrelated between twins, constituting the only influence that causes MZ twins to differ, and incorporating measurement error.

Models with varying combinations of the four latent factors were applied to variance-covariance matrices for MZ and DZ SS twins within each sex, and OS twins. A maximum of three parameters can be modelled at one time, if the data are from twins raised together. This is because there are only three equations to solve - twin variance, MZ twin covariance and DZ twin covariance. Further details about the model fitting process are included in Appendix B.

Maximum likelihood (ML) procedures were applied using Mx (Neale 1995). This iterative process minimises the difference between observed and expected variance-covariance matrices, using the equations outlined in Appendix B. The output incorporates estimates for the parameters - $a$, $e$, and $c$ or $d$ - as well as a $\chi^2$ value for goodness-of-fit of the model to the data. This $\chi^2$ value also permits comparison of full models with simpler, nested models (e.g. an ACE with an AE model), to verify whether the more complex model provides a significantly better fit, and therefore, whether the extra parameter is significant. Akaike's Information Criterion (AIC) was calculated as $\chi^2$ minus twice the associated degrees of freedom. It allows comparison of models with different degrees of freedom, and is an indicator of relative parsimony. Initially, the simplest model which would explain the data was sought. Subsequently, more complicated models were checked to see if any were significantly better fitting. Given the number of $\chi^2$ tests performed, an alpha level of 0.01 was chosen for rejection of the null hypothesis.

Implicit in the model-fitting procedure were all the usual assumptions of the twin method - that mating was random, that trait-related shared environmental influences on MZ and DZ twins were equal, and that there was no GxE interaction or gene-environment covariation (Jinks and Fulker 1970). For further details on the methods, see Appendix B of this thesis, Neale and Cardon (1992) and Neale (1995).

The procedure entailed the following: examining twin similarity; testing for evidence of genotype by environment (GxE) interaction and directional dominance; modelling of means for each dental variable; modelling of covariances for each dental variable.

**Initial Examination of Co-twin Similarity**

To obtain a preliminary idea of the likelihood of genetic contributions to tooth crown size, co-twin similarity was examined. This was achieved firstly by calculating the absolute difference between co-twins for each of the 56 variables. The differences were summed over all 56 variables to give the total difference in tooth crown size between a pair of twins. These values were averaged over the twins within each of the five twin sex-zygosity groups, yielding the mean total difference in tooth crown size. In addition, product moment correlation coefficients were calculated between the twins for the 56 variables within each of the five twin groups. MZ and DZ correlation coefficients and mean total differences were compared to look for evidence of genetic and environmental components of variance.

**Testing for GxE Interaction and Directional Dominance**

Before proceeding with modelling of covariance structure, the data were explored to test for the presence of genotype by environment (GxE) interaction, and to determine the likelihood of detecting any non-additive genetic variation that may have existed. Dominance is most likely to be detected if it is directional, that is, if the dominance in most of the genes acts in the same direction - either enlarging or reducing tooth size. Directional dominance and GxE interaction were considered simultaneously because the methods for each were similar. The presence of GxE interactions may be indicated by significant regression of MZ pair variances on MZ pair means (Jinks and Fulker 1970). If there is no GxE interaction, directional dominance is indicated

by significant regression of DZ pair variances on DZ pair means, or significant coefficients of skewness evident in DZ twins only (Martin *et al.* 1978). The probability of detecting dominance by fitting models to twin data is generally low, even when there is complete dominance and high heritability, unless it has a strong directional component (Martin *et al.* 1982). To test for GxE interactions and directional dominance in the data, the absolute pair difference (which is proportional to the square root of the intrapair variance) was regressed onto pair sum, and onto the square of the pair sum. In case the relationship was not linear, square and logarithmic (log) transformations of the data also were tested for significant regression. In addition, coefficients of skewness were compared between MZ and DZ twin pairs.

**Data Preparation**

Variable length (VL) files of raw data were set up as described in Neale (1995) and utilised directly for the 56 univariate analyses. VL files are an efficient means of data entry which allow modelling of individuals with missing values.

**Univariate Modelling of Means**

The Mx program permits modelling of means, variances and covariances simultaneously. To simplify the process, a variety of mean models may be fitted while the variance-covariance matrix is held constant. Modelling of the latter can then proceed, incorporating the best mean model. For each of the 56 variables, five models of the means were fitted, each model building on the preceding one (see Table 7.1). In the first model, all twins were constrained to have the same mean. Then, female and male twins were allowed different means. For the third model, the opposite-sex females were allowed to vary from the same-sex females. The fourth model permitted the same for the males as well. The final model removed all

constraints of equality, except between co-twins of same-sex pairs, yielding six separate means.

Initially, the simplest model which would explain the data was sought. Secondly, the other (more complicated) models were checked to see if any provided a significantly better fit. Given the number of $\chi^2$ tests performed, an alpha ($\alpha$) level of 0.01 was chosen for rejection of the null hypothesis.

**Univariate Modelling of Covariances**

Once the appropriate mean model was found, models were fitted to covariances. Each variable was analysed separately, fitting a path coefficient model with unique environmental influences only (E model). Where this failed, the model was extended to include additive genetic variation (AE model), or shared environmental variation (CE model). Finally, ACE and ADE models were fitted, where D (non-additive genetic variation) incorporates both dominance and epistatic interaction variance, which cannot be separated when only MZ and DZ twins are used (Mather 1974). Path diagrams for these models are contained in Figures B.2 to B.6 of Appendix B. Path coefficients ($a$, $c$, $d$, $e$) were estimated, and $\chi^2$ values for goodness-of-fit of the models were calculated. Akaike's Information Criterion (AIC = $\chi^2$ minus two times the degrees of freedom) was used to indicate the parsimony of each model (Akaike 1987). The smaller or more negative the AIC, the better the parsimony and fit of a model. Various hypotheses were tested by setting different combinations of paths to zero, and examining the difference between resulting $\chi^2$ values or AIC values. The general approach was that of only accepting a more complex model when a simpler one had failed, or when the more complex model was significantly better by $\chi^2$ ($\alpha$=0.05). These $\chi^2$ values between two models have been denoted $\chi^2_{diff}$ throughout the thesis. In addition, comparisons of the $\chi^2$ and AIC values between complex and

simpler models indicate significance of the various components ($\alpha$=0.05). Only *e* could not be tested for its significance, since no model excluded it. Heritability ($h^2$) and "environmentality" ($e^2$) were estimated from the ratio of genetic or environmental variation to total phenotypic variation, using parameter estimates from the model chosen as the best using the above criteria.

In the second stage of modelling the covariances, variables without a satisfactory model (and their antimeres) were investigated to see if a suitable model could be found. Firstly, OS twins were removed from the analysis, then male and female SS twin pairs were analysed separately. Heterogeneity of the sexes was assessed by likelihood ratio $\chi^2$ ($\alpha$ = 0.05), subtracting the sum of the $\chi^2$ values for each sex from the $\chi^2$ for the four SS twin groups. The resulting value is itself distributed as $\chi^2$ :

$$\chi^2_{het} = \chi^2_{m\&f} - [\chi^2_m + \chi^2_f]$$

$$df = df_{m\&f} - [\ df_m + df_f]$$

A variety of sex-limitation models can be applied, so the variances, covariance and co-twin correlations were examined first to see which if any, was more likely. Possible models included heterogeneity, scalar sex-limitation, non-scalar sex-limitation, and general sex-limitation models. A more detailed description of all models, and the information which can be gleaned from examination of variances, covariance and co-twin correlations, is contained in Appendix B.

## Results

### Co-twin Similarity

Descriptive statistics on the total differences in tooth crown size are presented in Table 7.2 and Figure 7.2. The difference between MZ twins averaged about 9mm, that of DZ same-sex twins about 17mm, and that of opposite-sex twins, almost 21mm. Perhaps of more interest is the maximum total difference. No MZ twin pair exceeded 16mm total difference. DZ SS twins exhibited more than twice, and DZ OS twins four times, the maximum difference of MZ twin pairs. The pattern is similar for standard deviations, with greater variances accompanying the higher means. These results suggest the existence of a significant genetic component to tooth crown size. The greater maximum difference between DZ OS compared with DZ SS twins was expected, given the degree of difference between sexes. The minimum differences were less discriminating of twin type, because missing values decreased the total difference between twins. Examining these statistics also allowed the detection of a pair of DZ male twins who had been miskeyed as MZ twins during data entry.

Pearson correlation coefficients between co-twins in each of the five twin groups are listed in Appendix C, Tables C.1 to C.3. Figures 7.3 to 7.6 depict the correlation coefficients of DZSS and MZ twins, allowing visual comparisons. The coefficients ranged from 0.62 to 0.94 in MZ twins, 0.06 to 0.74 in DZ same-sexed twins, and 0.07 to 0.55 in DZ opposite-sexed twins. All MZ coefficients were significant ($p<0.01$), while about half the DZSS coefficients, and most of the DZOS coefficients were not significantly different from zero ($\alpha=0.01$), most likely due to the sample sizes. All of the MZ correlation coefficients were less than one, suggesting the

presence of unique environmental effects. The coefficients were greater in MZ than in DZ twins for all variables, indicating the presence of genetic factors. For most variables, additive genetic effects were indicated, since DZ coefficients were approximately half those of MZ twins. DZ coefficients which were less than one third the MZ coefficients were assumed to indicate non-additive genetic effects, and these occurred mostly among canines and premolars. DZ coefficients which were more than 0.7 times the MZ coefficients were assumed to indicate shared environmental effects. The molars, BL diameters of teeth in the canine region in females and MD dimension of male maxillary central incisors were the main variables in this category. Variables suggestive of non-additive genetic or shared environmental effects are presented in Figures 7.7 to 7.10.

**GxE Interaction and Directional Dominance**

Preliminary analyses of the data revealed no evidence of GxE interaction or directional dominance in any of the 56 variables. Not one of the 560 regressions was significant ($\alpha$=0.01). There also were similar degrees of skewness in MZ and DZ twin data within both sexes. Of the 56 variables in each group, significant skewness (2-tailed, $\alpha$=0.01) occurred in four variables for each of MZ and DZSS female twins, five variables for MZ male twins and two variables for DZ male twins. There was no clear pattern to the variables which showed skewness, except that first premolars and first molars were excluded from the list of variables with significant values. Given that two to three type I errors were expected within each group, two to five significant results is not a concern.

**Univariate Modelling of Means**

The results of modelling the means are contained in Tables 7.3 to 7.7. The model with two means - one for each sex - was the model-of-choice in this analysis, being sufficient for all variables. This is consistent with the significant sexual dimorphism for tooth size mentioned in Chapters 3 and 4. The simplest model - one mean for all twins - was sufficient for only 10/56 variables. Of these variables, 8 displayed a significantly better fit ($p<0.01$) under the two-mean model (see Table 7.8). The exceptions were the BL diameters of the two mandibular lateral incisors ($\chi^2_{diff}$ = 2.46 for 1df, $0.1<p<0.2$ for the right side and $\chi^2_{diff}$ = 3.39 for 1df, $0.05<p<0.1$ for the left). This finding is consistent with the low degree of sexual dimorphism in the mandibular lateral incisors (see Chapter 4). However, the AICs for these variables were still lower for the two-mean model than the one-mean version. For consistency, I decided to proceed with modelling the covariances using a mean model with a different parameter for the mean of each sex.

As for differences between MZ and DZSS twins, goodness-of-fit decreased for 47 of the 56 variables when means for MZ and DZ SS twins were allowed to vary (comparing Models 4 and 5). There was thus no sign of heterogeneity between these twin groups. The same could not be said for allowing SS and OS twins to have different means. Probabilities decreased in only 17 of the 56 variables in males, and 21 of the 56 variables in females. Overall, comparing Models 2 and 4, the probabilities declined for only 27 variables. Although the significance of the differences in fit was not assessed, these numbers suggest a trend toward larger differences between SS and OS twins than between MZ and DZ twins.

### Univariate Modelling of Covariances

In the covariance modelling phase, models with only a unique environmental factor (E) were rejected ($p<0.001$) for all variables (see Tables 7.9 to 7.13). Adding shared environment (C) did not result in an adequate fit, except for three maxillary variables - the right second premolar MD diameter, and both dimensions of the left second molar. The AE model however, was adequate for all but 2 of the 56 variables. The exceptions were the BL dimension of the maxillary left central incisor and right canine, for which there was no satisfactory model ($p<0.01$). The AE model was sufficient for the antimeres of these teeth, although the probabilities were very low ($0.02<p<0.05$ and $0.05<p<.10$ respectively).

Improvement in fit was achieved by addition of non-additive genetic variation to models for the MD dimension of the four canines, both of the maxillary first premolars and mandibular right first premolar, as well as the BL diameter of the maxillary right first premolar. The improvement was significant ($p<0.05$) for all but the mandibular right canine and maxillary right first premolar MD, although these almost attained significance ($0.05<p<0.10$ for both).

Likewise, improvement in fit was observed when shared environment was included in models for both BL and MD dimensions of the maxillary first molars. This was significant for the maxillary left variables, and almost so for the right side as well ($0.05<p<0.10$ for both).

**Heterogeneity Between Sexes**

Modelling of the covariances was extended for the two variables with no satisfactory model, and their antimeres. Firstly, the OS twins were removed from the analysis, then male and female SS twin pairs were analysed separately. The results are displayed in Table 7.14, excluding E and CE models, which were as poorly fitting as before. Excluding the OS twins did not improve the situation, but separate analyses for each sex resulted in considerably improved model fitting. For the BL dimension of the maxillary left central incisor, the AE model was best for both sexes, and *a* was the only significant parameter. For the antimere, the AE model was best in females while the ACE model was best in males - although again, *a* was the only significant parameter. For both maxillary canine BL breadths, the ACE model was best for females and AE for males. Significant parameters were *a* and *c* for females, and *a* for the left canine in males.

Tests of heterogeneity between sexes revealed significant heterogeneity for the two variables and their antimeres, whether using AE or ACE models (see Table 7.15). This suggests that sex-limited differences may exist in one or more of the parameters.

Standardised parameters from the models fitted to each sex separately are listed in Table 7.16. These were calculated as the ratio of squared parameter to total phenotypic variation, which was estimated for each sex separately. For the maxillary central incisors, the males displayed a much higher proportion of common environmental variation (30 and 43% for left and right teeth respectively) compared with the females (10 and 1%). The situation was not as clear in the canines. For the maxillary right canine, females displayed 10% higher additive genetic and 7% lower

unique environmental variation than the males, while the same figures were only 6 and 1% for the maxillary left canine, and common environment in females made up 7% more of the total variation than that in males. There were also greater differences in parameter values between right and left sides in males than in females.

In the next stage, models were fitted which attempted to encompass sex-limited gene or environmental contributions to these variables. Examination of the variances and co-twin correlations revealed little about the likely type of sex-limited effects which might have occurred. Thus, all types of models were fitted - heterogeneity, scalar sex limitation, nonscalar sex limitation and general sex limitation, with the results being listed in Tables 7.17 to 7.18.

The results of fitting sex-limitation models are contained in Tables 7.17 and 7.18. For both central incisors, the best model was a scalar sex-limitation AE model. The next best was a heterogeneity AE (for left tooth) and ACE (for right tooth) models. Estimated values for $k$, the scalar by which male statistics differed from those of females, was 1.23 for left and 1.16 for right central incisor.

The models for canines were again less consistent than for incisors. The best model for the maxillary right canine BL diameter was a general sex-limitation model with parameters $A_fA_m$ $C_fC_m$ $E_fE_m$. The next-best models were closely related - $A_fA_m$ $C_fC_m$ E and $A_fA_m$ $C_fC_m$ $E_fE_m$ $A'_m$. For the antimere, a scalar ACE model was the best (estimated $k = 1.19$) with scalar AE and heterogeneity ACE models the next best.

**Path Diagrams**

Path diagrams for all 56 variables appear in Figures 7.11 to 7.16, and estimated parameters (squared, standardised and x100) derived from the chosen model are

depicted in Figures 7.17 to 7.20. For variables with some influence of non-additive genetic variation, only the AE model-derived parameter estimates were used, as estimates of A and D were negatively confounded. In these variables, then, the heritability estimate is actually broad heritability or the ratio of total genetic to phenotypic variation.

Among the variables for which the AE or ADE models were chosen, heritability estimates ranged from 71 to 92% (most were over 80%), with unique environmental contributions of 8 to 29%. In the ACE models of the remaining variables - MD and BL diameters of maxillary first molars - additive genetic variation accounted for 56 to 61% of the variation, shared environment for 22 to 27%, and unique environment, 12 to 17%. Although additive genetic variation contributed most, there were substantial shared environmental contributions to variation in both dimensions of the maxillary first molars.

## Discussion

### Univariate Analyses of Covariance Structure

The main finding from univariate analyses was that the variation in crown size of most teeth was explicable by additive genetic and unique environmental variation, with no need for non-additive genetic or shared environmental variation. Most previous analyses of genetic structure of tooth crown size have yielded the same conclusion (*e.g.* Goose 1967, 1971, Potter *et al.* 1983). There was also a high degree of bilateral symmetry in the parameter estimates, with a maximum difference of 9% between sides.

## Common Environmental Variation

The first exception involved the presence of common environmental variation in both dimensions of the maxillary first molars. Although significance was only achieved for both diameters of the left first molar, the probability values for the right side were near enough to significant ($0.05<p<0.10$) to be considered as evidence of common environmental variation. Of more value is the observation that both antimeres indicate the effect. This contrasts with a prior analysis of genetic structure, involving MD diameters of maxillary first molars, in which no evidence was found for common environmental variation (Potter *et al.* 1983).

This tooth is exceptional among permanent teeth because it begins to calcify at birth, or soon after. The soft-tissue phase, in which a tooth's final form is still malleable, ends with calcification. Thus, if any aspect of the uterine environment affects tooth crown size, it might be expected to manifest itself as a common environmental factor, and most likely would be expressed in the deciduous teeth, and permanent first molars. The presence of significant common environment in this tooth, therefore, could be taken as indirect evidence for a prenatal common environmental influence contributing 22 to 27% of the total variation in maxillary first molar crown size.

These estimates are similar in magnitude to those from a study of Australian Aboriginal families (Townsend 1978, 1992). Common environmental contributions to the permanent teeth were estimated to average 18% for BL and 10% for MD diameters. A further pattern reported by Townsend was of higher values for BL than MD diameters, but there was no evidence of such a pattern in the current study.

Curiously, it seems we must look for an environmental factor which affects the maxillary teeth only. The effect was present in maxillary first molars alone, in spite of mandibular molars sharing the same timing of calcification. If the effect were trivial, it might be assumed that there was not sufficient power to detect it in all four first molars, but the effect was substantial in the maxillary teeth, and apparently absent in the mandibular molars.

**Non-Additive Genetic Variation**

The second exception concerned the presence of non-additive genetic variation in the canines and first premolars. This affected the MD diameters almost exclusively. The single BL diameter - that of the right maxillary first premolar- may indicate the presence of a low degree of non-additive genetic variation in BL diameters of first premolars, or it may be just an artefact of the correlation that exists between MD and BL diameters.

As outlined in Chapter 1, genes which are related to selective fitness tend to display non-additive genetic variation (Fisher 1958, Kacser and Burns 1981, Dean *et al.* 1988). Therefore, the presence of this type of variation may indicate selective pressures acting either currently or sometime in the past.

The canine generally is considered important to primates for purposes ranging from defence of territory and mates, and protection from predators, to purely dietary reasons (reviewed by Harvey *et al.* 1978, Oxnard 1984). It is the most sexually dimorphic tooth, even in humans. Evidence for natural selection on the canine is consistent with these observations. However, if selection were mainly for dietary reasons, the BL diameters also might be expected to reveal selective pressures. In addition, Harvey *et al.* (1978), argued that dietary selective pressures would act as

much on the premolars and molars as canines, so the absence of any evidence of non-additive genetic variation on the second premolars and molars could be taken as evidence supporting the importance of social roles in the selection for canine and first premolar MD length.

One further suggestion is that canines and first premolars may be "linked" in their functioning, and therefore in their evolution. Maxillary canines are larger and considerably stronger than other teeth, so the presence of strong mandibular canines and first premolars to occlude with might be an advantage.

**Sexual Dimorphism**

There was significant sexual dimorphism for tooth crown size, since the mean tooth sizes of the twins could be constrained to be equal across zygosities within each sex, but not across sexes. This dimorphism did not extend to covariance structure, except for BL breadths of the maxillary left central incisor and right canine, which required heterogeneous models for the sexes. From the co-twin correlations, the only observable difference was a slight increase in DZ male correlations compared with those of DZ females for the central incisors, suggesting a slightly stronger common environmental component of variation in males. The opposite pattern was evident in the maxillary canine BL dimension.

For maxillary central incisors, the best model was a scalar sex-limitation AE model ($p>0.05$). In this model, estimates for A, C and E were the same for the two sexes, except that male estimates were allowed to vary from female ones by a multiple, $k$. The value of $k$ averaged over the antimeres was 1.2, compared with the difference in means between sexes of 1.04 (from Chapter 4). Given the low probabilities associated with these models ($0.05<p<0.10$ for left, and $0.10<p<0.20$ for right,

central incisors), they should be viewed with caution. A number of other models also yielded similar goodness-of-fit, with the best model being chosen by AIC.

A similar situation exists for the BL diameter of maxillary canines. Although higher probabilities were achieved for canines ($p>0.30$ for right, $p>0.20$ for left) than for incisors, the best models for each antimere were quite inconsistent. For the maxillary right canine, the best models were general sex-limitation models, with 2 or more parameters having separate estimates in each of the sexes. For the antimere, a scalar ACE and AE models were the best (estimated $k = 1.19$).

Caution is therefore warranted in the extent to which these models are invoked in future discussions of dental genetics. It is possible that the models specified did not take into account some important factor, or that the data themselves were somehow problematic. The only way to resolve this would be to collect a second sample and repeat the modelling.

**Heritability Estimates**

The heritability estimates were moderate to high, with a minimum of 56% in the MD length of the maxillary first molar, reaching up to 91% in the BL diameter of the maxillary premolars. These estimates extend across most of the range of previously reported heritabilities. Shared environment contributed up to 27%, and unique environment, 29%, indicating that environmental influences on tooth crown size cannot be overlooked. The same sentiment has been expressed by Townsend (1978, 1992) and Potter *et al.* (1983).

There was no consistent pattern to the heritabilities, either comparing mesial and distal members of tooth groups, or MD and BL dimensions of individual teeth. Of

the 24 mesial:distal comparisons that could be made, 11 are in the predicted direction of mesial>distal (incorporating reversal for the mandibular incisors). Of the 28 MD:BL comparisons, 15 are in the direction BL>MD. These figures are very close to 50%, and are not significantly different from chance by a sign test ($p>0.50$).

There was thus no supporting evidence from this analysis of the morphogenetic fields described by Butler (1939) and Dahlberg (1945). These findings are in agreement with those of Mizoguchi (1977) and Harzer (1987).

**Table 7.1**: Mean models fitted to the dental variables within the six twin groups, and degrees of freedom associated with the $\chi^2$.

| Model No. | Means for: | df |
|---|---|---|
| 1 | All Twins | 8 |
| 2 | Females Males | 7 |
| 3 | SSF OSF Males | 6 |
| 4 | SSF OSF SSM OSM | 5 |
| 5 | MZF DZF OSF MZM DZM OSM | 3 |

**Table 7.2:** Descriptive statistics for total difference (mm) between co-twins: mean, standard deviation (SD), minimum, maximum and sample size (N).

| Twin Group | Mean | SD | Minimum | Maximum | N |
|---|---|---|---|---|---|
| **MZ Female** | 9.2 | 2.5 | 1.4 | 14.9 | 82 |
| **MZ Male** | 9.2 | 2.8 | 1.6 | 15.9 | 66 |
| **DZ Female** | 17.7 | 7.2 | 2.7 | 39.3 | 46 |
| **DZ Male** | 16.3 | 7.5 | 4.4 | 36.9 | 44 |
| **DZ Male/Female** | 20.8 | 12.5 | 3.9 | 60.7 | 57 |

**Table 7.3:** Results of fitting Model 1 (one mean for all individuals) to MD and BL mean diameters (df = 8).

| Variable | MD $\chi^2$ | MD AIC | MD Prob [a] | BL $\chi^2$ | BL AIC | BL Prob |
|---|---|---|---|---|---|---|
| *Maxilla, Right Side* | | | | | | |
| I1 | 36.79 | 20.79 | ** | 23.08 | 7.08 | * |
| I2 | 39.65 | 23.65 | ** | 18.26 | 2.26 | + |
| C | 101.88 | 85.88 | ** | 46.62 | 30.62 | ** |
| P1 | 32.27 | 16.27 | ** | 21.76 | 5.76 | * |
| P2 | 15.61 | -0.39 | + | 30.65 | 14.65 | ** |
| M1 | 31.70 | 15.70 | ** | 47.87 | 31.87 | ** |
| M2 | 20.66 | 4.66 | * | 31.27 | 15.27 | ** |
| *Maxilla, Left Side* | | | | | | |
| I1 | 39.95 | 23.95 | ** | 28.49 | 12.49 | ** |
| I2 | 34.13 | 18.13 | ** | 26.58 | 10.58 | ** |
| C | 111.02 | 95.02 | ** | 38.62 | 22.62 | ** |
| P1 | 35.64 | 19.64 | ** | 26.61 | 10.61 | ** |
| P2 | 21.91 | 5.91 | * | 32.42 | 16.42 | ** |
| M1 | 27.73 | 11.73 | ** | 61.87 | 45.87 | ** |
| M2 | 17.26 | 1.26 | + | 29.22 | 13.22 | ** |
| *Mandible, Right Side* | | | | | | |
| I1 | 18.10 | 2.10 | + | 22.04 | 6.04 | * |
| I2 | 39.97 | 23.97 | ** | 7.94 | -8.06 | 30 |
| C | 118.45 | 102.45 | ** | 34.39 | 18.39 | ** |
| P1 | 29.32 | 13.32 | ** | 38.97 | 22.97 | ** |
| P2 | 28.87 | 12.87 | ** | 12.38 | -3.62 | 10 |
| M1 | 30.08 | 14.08 | ** | 26.99 | 10.99 | ** |
| M2 | 26.69 | 10.69 | ** | 41.25 | 25.25 | ** |
| *Mandible, Left Side* | | | | | | |
| I1 | 18.50 | 2.50 | + | 25.41 | 9.41 | * |
| I2 | 31.67 | 15.67 | ** | 5.34 | -10.66 | 70 |
| C | 103.20 | 87.20 | ** | 28.59 | 12.59 | ** |
| P1 | 45.47 | 29.47 | ** | 38.06 | 22.06 | ** |
| P2 | 18.51 | 2.51 | + | 17.03 | 1.03 | + |
| M1 | 31.08 | 15.08 | ** | 27.70 | 11.70 | ** |
| M2 | 28.35 | 12.35 | ** | 32.83 | 16.83 | ** |

[a] Probability levels are expressed as percentages and are greater than the value specified unless significant: + = $p<0.05$, * = $p<0.01$, ** = $p<0.001$.

**Table 7.4:** Results of fitting Model 2 (means for females and males) to MD and BL mean diameters (df = 7). Probability levels are as defined for Table 7.3.

| | MD | | | BL | | |
|---|---|---|---|---|---|---|
| **Variable** | $\chi^2$ | **AIC** | **Prob** | $\chi^2$ | **AIC** | **Prob** |
| *Maxilla, Right Side* | | | | | | |
| **I1** | 13.46 | -0.54 | 5 | 10.62 | -3.38 | 10 |
| **I2** | 10.79 | -3.21 | 10 | 9.30 | -4.70 | 20 |
| **C** | 17.75 | 3.75 | + | 10.96 | -3.04 | 10 |
| **P1** | 9.35 | -4.65 | 20 | 4.98 | -9.02 | 50 |
| **P2** | 4.36 | -9.64 | 70 | 8.63 | -5.37 | 20 |
| **M1** | 9.12 | -4.88 | 20 | 8.16 | -5.84 | 30 |
| **M2** | 5.65 | -8.35 | 50 | 10.56 | -3.44 | 10 |
| *Maxilla, Left Side* | | | | | | |
| **I1** | 10.35 | -3.65 | 10 | 11.70 | -2.30 | 10 |
| **I2** | 11.64 | -2.36 | 10 | 10.38 | -3.62 | 10 |
| **C** | 17.86 | 3.86 | + | 9.84 | -4.16 | 10 |
| **P1** | 14.35 | 0.35 | + | 6.44 | -7.56 | 30 |
| **P2** | 9.52 | -4.48 | 20 | 7.78 | -6.22 | 30 |
| **M1** | 5.86 | -8.14 | 50 | 15.20 | 1.20 | + |
| **M2** | 3.32 | -10.68 | 80 | 9.25 | -4.75 | 20 |
| *Mandible, Right Side* | | | | | | |
| **I1** | 3.64 | -10.36 | 80 | 11.21 | -2.79 | 10 |
| **I2** | 15.52 | 1.52 | + | 5.48 | -8.52 | 50 |
| **C** | 9.95 | -4.05 | 10 | 3.93 | -10.07 | 70 |
| **P1** | 14.95 | 0.95 | + | 11.10 | -2.90 | 10 |
| **P2** | 12.10 | -1.90 | 5 | 5.05 | -8.95 | 50 |
| **M1** | 1.67 | -12.33 | 90 | 2.24 | -11.76 | 90 |
| **M2** | 7.75 | -6.25 | 30 | 9.97 | -4.03 | 10 |
| *Mandible, Left Side* | | | | | | |
| **I1** | 2.06 | -11.94 | 90 | 4.26 | -9.74 | 70 |
| **I2** | 7.80 | -6.20 | 30 | 1.95 | -12.05 | 90 |
| **C** | 11.69 | -2.31 | 10 | 2.95 | -11.05 | 80 |
| **P1** | 16.07 | 2.07 | + | 10.33 | -3.67 | 10 |
| **P2** | 5.87 | -8.13 | 50 | 8.20 | -5.80 | 30 |
| **M1** | 10.72 | -3.28 | 10 | 6.47 | -7.53 | 30 |
| **M2** | 10.36 | -3.64 | 10 | 10.47 | -3.53 | 10 |

**Table 7.5:** Results of fitting Model 3 (means for SSF, OSF and males) to MD and BL mean diameters (df = 6). Probability levels are as defined for Table 7.3.

| | MD | | | BL | | |
|---|---|---|---|---|---|---|
| **Variable** | $\chi^2$ | **AIC** | **Prob** | $\chi^2$ | **AIC** | **Prob** |
| *Maxilla, Right Side* | | | | | | |
| **I1** | 10.54 | -1.46 | 10 | 8.18 | -3.82 | 20 |
| **I2** | 10.66 | -1.34 | 5 | 8.02 | -3.98 | 20 |
| **C** | 17.74 | 5.74 | * | 10.41 | -1.59 | 10 |
| **P1** | 9.30 | -2.70 | 10 | 4.68 | -7.32 | 50 |
| **P2** | 4.14 | -7.86 | 50 | 8.40 | -3.60 | 20 |
| **M1** | 8.96 | -3.04 | 10 | 7.88 | -4.12 | 20 |
| **M2** | 5.13 | -6.87 | 50 | 10.47 | -1.53 | 10 |
| *Maxilla, Left Side* | | | | | | |
| **I1** | 7.95 | -4.05 | 20 | 11.27 | -0.73 | 5 |
| **I2** | 11.57 | -0.43 | 5 | 10.32 | -1.68 | 10 |
| **C** | 16.23 | 4.23 | + | 9.83 | -2.17 | 10 |
| **P1** | 13.89 | 1.89 | + | 5.47 | -6.53 | 30 |
| **P2** | 8.44 | -3.56 | 20 | 7.59 | -4.41 | 20 |
| **M1** | 5.01 | -6.99 | 50 | 15.20 | 3.20 | + |
| **M2** | 2.93 | -9.07 | 80 | 9.16 | -2.84 | 10 |
| *Mandible, Right Side* | | | | | | |
| **I1** | 2.44 | -9.56 | 80 | 11.19 | -0.81 | 5 |
| **I2** | 14.66 | 2.66 | + | 4.54 | -7.46 | 50 |
| **C** | 7.09 | -4.91 | 30 | 2.08 | -9.92 | 90 |
| **P1** | 14.95 | 2.95 | + | 8.91 | -3.09 | 10 |
| **P2** | 12.09 | 0.09 | 5 | 4.99 | -7.01 | 50 |
| **M1** | 1.64 | -10.36 | 90 | 2.11 | -9.89 | 90 |
| **M2** | 6.84 | -5.16 | 30 | 7.25 | -4.75 | 20 |
| *Mandible, Left Side* | | | | | | |
| **I1** | 2.00 | -10.00 | 90 | 3.97 | -8.03 | 50 |
| **I2** | 5.95 | -6.05 | 30 | 1.85 | -10.15 | 90 |
| **C** | 8.21 | -3.79 | 20 | 1.24 | -10.76 | 95 |
| **P1** | 15.02 | 3.02 | + | 8.59 | -3.41 | 10 |
| **P2** | 5.42 | -6.58 | 30 | 7.76 | -4.24 | 20 |
| **M1** | 10.62 | -1.38 | 10 | 5.75 | -6.25 | 30 |
| **M2** | 9.53 | -2.47 | 10 | 10.22 | -1.78 | 10 |

**Table 7.6:** Results of fitting Model 4 (means for SSF, OSF, SSM and OSM) to MD and BL mean diameters (df = 5). Probability levels are as defined for Table 7.3.

| | MD | | | BL | | |
|---|---|---|---|---|---|---|
| **Variable** | $\chi^2$ | **AIC** | **Prob** | $\chi^2$ | **AIC** | **Prob** |
| *Maxilla, Right Side* | | | | | | |
| **I1** | 10.39 | 0.39 | 5 | 7.90 | -2.10 | 10 |
| **I2** | 7.92 | -2.08 | 10 | 4.61 | -5.39 | 30 |
| **C** | 17.33 | 7.33 | * | 10.37 | 0.37 | 5 |
| **P1** | 9.28 | -0.72 | 5 | 4.50 | -5.50 | 30 |
| **P2** | 4.13 | -5.87 | 50 | 8.39 | -1.61 | 10 |
| **M1** | 8.44 | -1.56 | 10 | 7.78 | -2.22 | 10 |
| **M2** | 2.72 | -7.28 | 70 | 10.47 | 0.47 | 5 |
| *Maxilla, Left Side* | | | | | | |
| **I1** | 7.79 | -2.21 | 10 | 6.93 | -3.07 | 20 |
| **I2** | 8.43 | -1.57 | 10 | 4.27 | -5.73 | 50 |
| **C** | 16.22 | 6.22 | * | 9.24 | -0.76 | 5 |
| **P1** | 13.45 | 3.45 | + | 5.47 | -4.53 | 30 |
| **P2** | 8.09 | -1.91 | 10 | 7.28 | -2.72 | 20 |
| **M1** | 4.20 | -5.80 | 50 | 14.46 | 4.46 | + |
| **M2** | 2.80 | -7.20 | 70 | 9.15 | -0.85 | 10 |
| *Mandible, Right Side* | | | | | | |
| **I1** | 2.01 | -7.99 | 80 | 11.13 | 1.13 | + |
| **I2** | 12.73 | 2.73 | + | 3.96 | -6.04 | 50 |
| **C** | 6.70 | -3.30 | 20 | 1.98 | -8.02 | 80 |
| **P1** | 14.66 | 4.66 | + | 8.90 | -1.10 | 10 |
| **P2** | 11.21 | 1.21 | + | 4.41 | -5.59 | 30 |
| **M1** | 1.09 | -8.91 | 95 | 1.95 | -8.05 | 80 |
| **M2** | 6.69 | -3.31 | 20 | 3.50 | -6.50 | 50 |
| *Mandible, Left Side* | | | | | | |
| **I1** | 2.00 | -8.00 | 80 | 3.38 | -6.62 | 50 |
| **I2** | 5.63 | -4.27 | 30 | 1.85 | -8.15 | 80 |
| **C** | 7.18 | -2.82 | 20 | 1.16 | -8.84 | 90 |
| **P1** | 14.50 | 4.50 | + | 8.47 | -1.53 | 10 |
| **P2** | 5.05 | -4.95 | 30 | 7.24 | -2.76 | 20 |
| **M1** | 9.75 | -0.25 | 5 | 5.74 | -4.26 | 30 |
| **M2** | 7.76 | -2.24 | 10 | 5.05 | -4.95 | 30 |

**Table 7.7:** Results of fitting Model 5 (means for MZ, DZSS, and DZOS twins in each sex) to MD and BL mean diameters (df = 3). Probability levels are as defined for Table 7.3.

| | MD | | | BL | | |
|---|---|---|---|---|---|---|
| **Variable** | $\chi^2$ | **AIC** | **Prob** | $\chi^2$ | **AIC** | **Prob** |
| *Maxilla, Right Side* | | | | | | |
| **I1** | 9.43 | 3.43 | + | 6.53 | 0.53 | 5 |
| **I2** | 6.27 | 0.27 | 5 | 1.34 | -4.66 | 70 |
| **C** | 16.16 | 10.16 | * | 8.60 | 2.60 | + |
| **P1** | 9.08 | 3.08 | + | 4.09 | -1.91 | 20 |
| **P2** | 4.04 | -1.96 | 20 | 8.09 | 2.09 | + |
| **M1** | 8.35 | 2.35 | + | 7.72 | 1.72 | 5 |
| **M2** | 2.64 | -3.36 | 30 | 9.25 | 3.25 | + |
| *Maxilla, Left Side* | | | | | | |
| **I1** | 7.75 | 1.75 | 5 | 6.19 | 0.19 | 10 |
| **I2** | 7.67 | 1.67 | 5 | 4.07 | -1.93 | 20 |
| **C** | 16.08 | 10.08 | * | 6.59 | 0.59 | 5 |
| **P1** | 12.77 | 6.77 | * | 5.42 | -0.58 | 10 |
| **P2** | 7.93 | 1.93 | + | 6.47 | 0.47 | 5 |
| **M1** | 4.20 | -1.80 | 20 | 14.17 | 8.17 | * |
| **M2** | 1.72 | -4.28 | 50 | 9.12 | 3.12 | + |
| *Mandible, Right Side* | | | | | | |
| **I1** | 1.74 | -4.26 | 50 | 10.94 | 2.94 | + |
| **I2** | 12.63 | 6.63 | * | 3.86 | -2.14 | 20 |
| **C** | 5.39 | -0.61 | 10 | 1.07 | -4.93 | 70 |
| **P1** | 13.94 | 7.94 | * | 8.60 | 2.60 | + |
| **P2** | 10.09 | 4.09 | + | 2.67 | -3.33 | 30 |
| **M1** | 0.85 | -5.15 | 80 | 1.58 | -4.42 | 50 |
| **M2** | 5.24 | -0.76 | 10 | 1.43 | -4.57 | 50 |
| *Mandible, Left Side* | | | | | | |
| **I1** | 1.15 | -4.85 | 70 | 3.36 | -2.64 | 30 |
| **I2** | 5.11 | -0.89 | 10 | 1.66 | -4.34 | 50 |
| **C** | 6.86 | 0.86 | 5 | 1.01 | -4.99 | 70 |
| **P1** | 14.41 | 8.41 | * | 8.44 | 2.44 | + |
| **P2** | 3.22 | -2.78 | 30 | 6.16 | 0.16 | 10 |
| **M1** | 9.49 | 3.49 | + | 5.66 | -0.34 | 10 |
| **M2** | 3.06 | -2.94 | 30 | 3.85 | -2.15 | 20 |

**Table 7.8:** Testing for significant improvement in fit of Model 2 over Model 1, when the latter was sufficient to explain the variation in the data.

| Variable | | Model 1 [a] $\chi^2$ | Prob [c] | Model 2 [b] $\chi^2$ | Prob | Difference $\chi^2$ | Prob [d] |
|---|---|---|---|---|---|---|---|
| *Mesiodistal* | | | | | | | |
| Max R | P2 | 15.61 | + | 4.36 | 70 | 11.25 | ** |
| Max L | M2 | 17.26 | + | 3.32 | 80 | 13.94 | ** |
| Man R | I1 | 18.10 | + | 3.64 | 80 | 14.46 | ** |
| Man L | I1 | 18.50 | + | 2.06 | 90 | 16.44 | ** |
| Man L | P2 | 18.51 | + | 5.87 | 50 | 12.64 | ** |
| *Buccolingual* | | | | | | | |
| Max R | I2 | 18.26 | + | 9.30 | 20 | 8.96 | * |
| Man R | I2 | 7.94 | 30 | 5.48 | 50 | 2.46 | 10 |
| Man R | P2 | 12.38 | 10 | 5.05 | 50 | 7.33 | * |
| Man L | I2 | 5.34 | 70 | 1.95 | 90 | 3.39 | 5 |
| Man L | P2 | 17.03 | + | 8.20 | 30 | 8.83 | * |

[a] df = 8; [b] df = 7; [c] Probability levels are as defined for Table 7.3; [d] df = 1.

**Table 7.9:** Results of fitting E model of MD and BL diameters (df = 22).

| Variable | MD $\chi^2$ | MD AIC [a] | MD Prob [b] | BL $\chi^2$ | BL AIC | BL Prob |
|---|---|---|---|---|---|---|
| *Maxilla, Right Side* | | | | | | |
| I1 | 261.98 | | ** | 197.76 | | ** |
| I2 | 227.35 | | ** | 129.78 | | ** |
| C | 195.80 | | ** | 205.11 | | ** |
| P1 | 168.73 | | ** | 174.51 | | ** |
| P2 | 112.12 | | ** | 17526.91 | | ** |
| M1 | 237.45 | | ** | 236.97 | | ** |
| M2 | 100.44 | | ** | 169.31 | | ** |
| *Maxilla, Left Side* | | | | | | |
| I1 | 247.73 | | ** | 211.63 | | ** |
| I2 | 227.75 | | ** | 125.00 | | ** |
| C | 181.42 | | ** | 13542.07 | | ** |
| P1 | 157.70 | | ** | 217.35 | | ** |
| P2 | 140.86 | | ** | 31126.06 | | ** |
| M1 | 195.23 | | ** | 294.74 | | ** |
| M2 | 64.03 | | ** | 103.81 | | ** |
| *Mandible, Right Side* | | | | | | |
| I1 | 220.11 | | ** | 190.55 | | ** |
| I2 | 218.36 | | ** | 208.87 | | ** |
| C | 179.24 | | ** | 195.69 | | ** |
| P1 | 172.42 | | ** | 197.82 | | ** |
| P2 | 182.81 | | ** | 200.95 | | ** |
| M1 | 222.26 | | ** | 296.05 | | ** |
| M2 | 110.28 | | ** | 163.48 | | ** |
| *Mandible, Left Side* | | | | | | |
| I1 | 250.78 | | ** | 247.65 | | ** |
| I2 | 203.95 | | ** | 203.13 | | ** |
| C | 188.83 | | ** | 223.40 | | ** |
| P1 | 214.90 | | ** | 226.31 | | ** |
| P2 | 153.34 | | ** | 213.01 | | ** |
| M1 | 252.01 | | ** | 293.33 | | ** |
| M2 | 110.79 | | ** | 166.97 | | ** |

[a] AIC not calculated for significant values of $\chi^2$.

[b] Probability levels are as defined for Table 7.3.

**Table 7.10:** Results of fitting CE model of MD and BL diameters (df = 21).

| | MD | | | BL | | |
|---|---|---|---|---|---|---|
| **Variable** | $\chi^2$ | **AIC** [a] | **Prob** [b] | $\chi^2$ | **AIC** | **Prob** |
| *Maxilla, Right Side* | | | | | | |
| **I1** | 110.76 | | ** | 75.29 | | ** |
| **I2** | 98.32 | | ** | 50.85 | | ** |
| **C** | 120.80 | | ** | 71.22 | | ** |
| **P1** | 76.33 | | ** | 92.44 | | ** |
| **P2** | 32.25 | -9.75 | 5 | 134.29 | | ** |
| **M1** | 62.46 | | ** | 57.42 | | ** |
| **M2** | 48.69 | | ** | 75.09 | | ** |
| *Maxilla, Left Side* | | | | | | |
| **I1** | 112.15 | | ** | 75.52 | | ** |
| **I2** | 96.46 | | ** | 47.07 | | ** |
| **C** | 102.35 | | ** | 105.13 | | ** |
| **P1** | 77.80 | | ** | 90.64 | | ** |
| **P2** | 52.12 | | ** | 120.59 | | ** |
| **M1** | 41.92 | | * | 83.46 | | ** |
| **M2** | 26.27 | -15.73 | 10 | 33.15 | -8.85 | 2 |
| *Mandible, Right Side* | | | | | | |
| **I1** | 62.35 | | ** | 64.19 | | ** |
| **I2** | 75.68 | | ** | 57.41 | | ** |
| **C** | 83.65 | | ** | 68.03 | | ** |
| **P1** | 86.80 | | ** | 89.08 | | ** |
| **P2** | 94.56 | | ** | 89.14 | | ** |
| **M1** | 97.05 | | ** | 93.53 | | ** |
| **M2** | 49.62 | | ** | 41.16 | | * |
| *Mandible, Left Side* | | | | | | |
| **I1** | 108.29 | | ** | 91.81 | | ** |
| **I2** | 81.11 | | ** | 54.54 | | ** |
| **C** | 100.82 | | ** | 95.07 | | ** |
| **P1** | 98.71 | | ** | 92.38 | | ** |
| **P2** | 57.60 | | ** | 98.98 | | ** |
| **M1** | 128.99 | | ** | 108.23 | | ** |
| **M2** | 41.79 | | * | 49.97 | | ** |

[a] AIC not calculated for significant values of $\chi^2$.

[b] Probability levels are as defined for Table 7.3.

**Table 7.11:** Results of fitting AE model of MD and BL diameters (df = 21).

| Variable | MD $\chi^2$ | MD AIC | MD Prob [a] | BL $\chi^2$ | BL AIC | BL Prob |
|---|---|---|---|---|---|---|
| *Maxilla, Right Side* | | | | | | |
| **I1** | 30.69 | -11.31 | 5 | 35.10 | -6.90 | 2 |
| **I2** | 26.30 | -15.70 | 10 | 24.04 | -17.96 | 25 |
| **C** | 37.65 | -4.35 | 1 | 46.08 | 4.08 | * |
| **P1** | 23.71 | -18.29 | 25 | 19.16 | -22.84 | 50 |
| **P2** | 13.51 | -28.49 | 75 | 23.21 | -18.79 | 25 |
| **M1** | 24.82 | -17.18 | 25 | 28.00 | -14.00 | 10 |
| **M2** | 18.61 | -23.39 | 50 | 22.81 | -39.19 | 25 |
| *Maxilla, Left Side* | | | | | | |
| **I1** | 21.01 | -20.99 | 25 | 41.43 | -0.57 | * |
| **I2** | 18.10 | -23.90 | 50 | 19.84 | -22.16 | 50 |
| **C** | 35.95 | -6.05 | 1 | 31.62 | -10.38 | 5 |
| **P1** | 22.42 | -19.58 | 25 | 18.87 | -23.13 | 50 |
| **P2** | 15.81 | -26.19 | 75 | 22.21 | -19.79 | 25 |
| **M1** | 17.82 | -24.18 | 50 | 38.13 | -3.87 | 1 |
| **M2** | 13.49 | -28.51 | 75 | 16.16 | -25.84 | 75 |
| *Mandible, Right Side* | | | | | | |
| **I1** | 20.22 | -21.78 | 50 | 27.36 | -14.64 | 10 |
| **I2** | 19.44 | -22.56 | 50 | 21.71 | -20.29 | 25 |
| **C** | 28.92 | -13.08 | 10 | 28.02 | -13.98 | 10 |
| **P1** | 29.80 | -12.20 | 5 | 27.08 | -14.92 | 10 |
| **P2** | 29.44 | -12.56 | 10 | 17.23 | -24.77 | 50 |
| **M1** | 11.36 | -30.64 | 90 | 23.13 | -18.87 | 25 |
| **M2** | 20.36 | -21.64 | 25 | 23.73 | -18.27 | 25 |
| *Mandible, Left Side* | | | | | | |
| **I1** | 21.40 | -20.60 | 25 | 20.53 | -21.47 | 25 |
| **I2** | 13.54 | -28.46 | 75 | 20.74 | -21.26 | 25 |
| **C** | 34.23 | -7.77 | 1 | 36.62 | -5.38 | 1 |
| **P1** | 34.60 | -7.40 | 1 | 20.52 | -21.48 | 25 |
| **P2** | 17.81 | -24.19 | 50 | 26.12 | -15.88 | 10 |
| **M1** | 20.30 | -21.70 | 50 | 31.31 | -10.69 | 5 |
| **M2** | 17.79 | -24.21 | 50 | 24.48 | -17.52 | 25 |

[a] Probability levels are as defined for Table 7.3.

**Table 7.12:** Results of fitting ACE model of MD and BL diameters (df = 20).

| | MD | | | BL | | |
|---|---|---|---|---|---|---|
| **Variable** | $\chi^2$ [a] | **AIC** | **Prob** [b] | $\chi^2$ | **AIC** | **Prob** |
| *Maxilla, Right Side* | | | | | | |
| **I1** | 30.69 | -9.31 | 5 | 35.09 | -4.91 | 1 |
| **I2** | 26.30 | -13.70 | 10 | 24.04 | -15.96 | 10 |
| **C** | 37.65 | -2.35 | * | o 43.53 | 3.53 | * |
| **P1** | 23.71 | -16.29 | 25 | 19.16 | -20.84 | 50 |
| **P2** | 13.48 | -26.52 | 75 | 23.21 | -16.79 | 25 |
| **M1** | o 21.14 | -18.86 | 25 | o 24.23 | -15.77 | 10 |
| **M2** | 18.61 | -21.39 | 50 | 22.81 | -17.19 | 25 |
| *Maxilla, Left Side* | | | | | | |
| **I1** | 21.01 | -18.99 | 25 | 40.27 | 0.27 | * |
| **I2** | 18.10 | -21.90 | 50 | 19.84 | -20.16 | 25 |
| **C** | 35.95 | -4.05 | 1 | o 29.44 | -10.56 | 5 |
| **P1** | 22.42 | -17.58 | 25 | 18.87 | -21.13 | 50 |
| **P2** | 15.81 | -24.19 | 50 | 22.21 | -17.79 | 25 |
| **M1** | + 13.56 | -26.44 | 75 | + 33.75 | -6.25 | 2 |
| **M2** | 13.49 | -26.51 | 75 | 16.06 | -23.94 | 50 |
| *Mandible, Right Side* | | | | | | |
| **I1** | 19.29 | -20.71 | 50 | 26.86 | -13.14 | 10 |
| **I2** | 19.44 | -20.56 | 25 | 20.82 | -19.18 | 25 |
| **C** | 28.92 | -11.08 | 5 | 27.81 | -12.19 | 10 |
| **P1** | 29.80 | -10.20 | 5 | 27.08 | -12.92 | 10 |
| **P2** | 29.44 | -10.56 | 5 | 17.23 | -22.77 | 50 |
| **M1** | 11.36 | -28.64 | 90 | 21.72 | -18.28 | 25 |
| **M2** | 20.36 | -19.64 | 25 | o 20.91 | -19.09 | 25 |
| *Mandible, Left Side* | | | | | | |
| **I1** | 21.40 | -18.60 | 25 | 20.13 | -19.87 | 25 |
| **I2** | 13.54 | -26.46 | 75 | 19.07 | -20.93 | 50 |
| **C** | 34.23 | -5.77 | 1 | 36.62 | -3.38 | 1 |
| **P1** | 34.60 | -5.40 | 1 | 20.52 | -19.48 | 25 |
| **P2** | 17.81 | -22.19 | 50 | 26.12 | -13.88 | 10 |
| **M1** | 20.30 | -19.70 | 25 | 30.57 | -9.43 | 5 |
| **M2** | 17.41 | -22.59 | 50 | 22.65 | -17.35 | 25 |

[a] $\chi^2$ values (if lower) were compared with those from the AE model - probabilities for $\chi^2_{diff}$: o = not significantly different; + = p<0.05; * = p<0.01; ** = p<0.001.

[b] Probability levels are as defined for Table 7.3.

**Table 7.13:** Results of fitting ADE model of MD and BL diameters (df = 20).

| Variable | | | MD | | | | BL | |
|---|---|---|---|---|---|---|---|---|
| | | $\chi^2$ a | AIC | Prob b | | $\chi^2$ | AIC | Prob |
| *Maxilla, Right Side* | | | | | | | | |
| I1 | | 30.69 | -9.31 | 5 | | 35.10 | -4.90 | 1 |
| I2 | | 25.28 | -14.72 | 10 | | 23.81 | -16.19 | 25 |
| C | ** | 26.78 | -13.22 | 10 | | 46.08 | 6.08 | * |
| P1 | o | 20.14 | -19.86 | 25 | + | 14.35 | -25.65 | 75 |
| P2 | | 13.51 | -26.49 | 75 | | 22.04 | -17.96 | 25 |
| M1 | | 24.82 | -15.18 | 10 | | 28.00 | -12.00 | 10 |
| M2 | | 17.81 | -22.19 | 50 | | 22.07 | -17.93 | 25 |
| *Maxilla, Left Side* | | | | | | | | |
| I1 | | 20.78 | -19.22 | 25 | | 41.43 | 1.43 | * |
| I2 | | 17.12 | -22.88 | 50 | | 18.72 | -21.28 | 50 |
| C | + | 30.96 | -9.04 | 5 | | 31.62 | -8.38 | 2 |
| P1 | + | 18.47 | -21.53 | 50 | | 18.69 | -21.31 | 50 |
| P2 | | 15.55 | -24.45 | 50 | | 20.33 | -19.67 | 25 |
| M1 | | 17.82 | -22.18 | 50 | | 38.13 | -1.87 | * |
| M2 | | 13.30 | -26.70 | 75 | | 16.16 | -23.84 | 50 |
| *Mandible, Right Side* | | | | | | | | |
| I1 | | 20.22 | -19.78 | 25 | | 27.36 | -12.64 | 10 |
| I2 | | 19.39 | -20.61 | 25 | | 21.71 | -18.29 | 25 |
| C | o | 25.66 | -14.34 | 10 | | 28.02 | -11.98 | 10 |
| P1 | + | 23.76 | -16.24 | 25 | | 26.48 | -13.52 | 10 |
| P2 | | 27.73 | -12.27 | 10 | o | 15.15 | -24.85 | 75 |
| M1 | | 10.01 | -29.99 | 90 | | 23.13 | -16.87 | 25 |
| M2 | | 20.30 | -19.70 | 25 | | 23.73 | -16.27 | 25 |
| *Mandible, Left Side* | | | | | | | | |
| I1 | | 20.57 | -19.43 | 25 | | 20.53 | -19.47 | 25 |
| I2 | | 12.99 | -27.01 | 75 | | 20.74 | -19.26 | 25 |
| C | + | 29.01 | -10.99 | 5 | | 36.60 | -3.40 | 1 |
| P1 | | 32.98 | -7.02 | 1 | | 20.47 | -19.53 | 25 |
| P2 | | 17.81 | -22.19 | 50 | o | 23.84 | -16.16 | 10 |
| M1 | o | 17.04 | -22.96 | 50 | | 31.31 | -8.69 | 5 |
| M2 | | 17.79 | -22.21 | 50 | | 24.48 | -15.52 | 10 |

a $\chi^2$ values (if lower) were compared with those from the AE model - probabilities for $\chi^2_{diff}$: o = not significantly different; + = $p<0.05$; * = $p<0.01$; ** = $p<0.001$.
b Probability levels are as defined for Table 7.3.

**Table 7.14:** Results of AE, ACE and ADE models for different subsets of twin groups. The first group - All 5 - is as in Tables 5.11 to 7.13, and is included for comparison. Best fitting models are highlighted in italics.

| Twin groups | Param | df | $\chi^2$ | AIC | Prob [a] | $\chi^2$ | AIC | Prob |
|---|---|---|---|---|---|---|---|---|
| **Maxillary I1 BL** | | | | **Left** | | | **Right [b]** | |
| **All 5** | **AE** | 21 | 41.43 | -0.6 | * | *35.10* | *-6.9* | *2* |
| | **ACE** | 20 | 40.27 | 0.3 | * | 35.09 | -4.9 | 1 |
| | **ADE** | 20 | 41.43 | 1.4 | * | 35.10 | -4.9 | 1 |
| **4 x SS** | **AE** | 16 | *31.82* | *-0.2* | *1* | *27.97* | *-4.0* | *2* |
| | **ACE** | 15 | 30.29 | 0.3 | 1 | 26.57 | -3.4 | 2 |
| | **ADE** | 15 | 31.82 | 1.8 | * | 27.97 | -2.0 | 2 |
| **2 x Female** | **AE** | 7 | *9.89* | *-4.1* | *10* | *8.66* | *-5.3* | *20* |
| | **ACE** | 6 | 9.61 | -2.4 | 10 | 8.66 | -3.3 | 10 |
| | **ADE** | 6 | 9.89 | -2.1 | 10 | 8.66 | -3.3 | 10 |
| **2 x Male** | **AE** | 7 | *10.03* | *-4.0* | *10* | 11.89 | -2.1 | 10 |
| | **ACE** | 6 | 8.59 | -3.4 | 10 | *9.01* | *-3.0* | *10* |
| | **ADE** | 6 | 10.03 | -2.0 | 10 | 11.89 | -0.1 | 5 |
| **Maxillary Canine BL** | | | | **Right** | | | **Left [b]** | |
| **All 5** | **AE** | 21 | 46.08 | 4.1 | * | 31.62 | -10.4 | 5 |
| | **ACE** | 20 | 43.53 | 3.5 | * | *29.44* | *-10.6* | *5* |
| | **ADE** | 20 | 46.08 | 6.1 | ** | 31.62 | -8.4 | 2 |
| **4 x SS** | **AE** | 16 | 45.02 | 13.0 | ** | 30.67 | -1.3 | 1 |
| | **ACE** | 15 | 39.63 | 9.6 | ** | *25.69* | *-4.3* | *2* |
| | **ADE** | 15 | 45.02 | 15.02 | ** | 30.67 | 0.7 | * |
| **2 x Female** | **AE** | 7 | 14.43 | 0.4 | 2 | 10.75 | -3.3 | 10 |
| | **ACE** | 6 | *10.46* | *-1.5* | *10* | *6.57* | *-5.4* | *30* |
| | **ADE** | 6 | 14.43 | 2.4 | 2 | 10.75 | -1.3 | 5 |
| **2 x Male** | **AE** | 7 | *10.78* | *-3.2* | *10* | *10.98* | *-3.0* | *10* |
| | **ACE** | 6 | 9.72 | -2.3 | 10 | 9.83 | -2.2 | 10 |
| | **ADE** | 6 | 10.78 | -1.2 | 5 | 10.98 | -1.0 | 5 |

[a] Probability levels are as defined for Table 7.3.

[b] Antimeres included for comparison, even though suitable models were found for them.

**Table 7.15:** Results of heterogeneity testing between the sexes using AE and ACE models: $\chi^2$ for the 4 SS groups, minus the sum of $\chi^2$ values for females and males.

| | df | Central Incisor | | Canine | |
|---|---|---|---|---|---|
| | | Left | Right [b] | Right | Left [b] |
| **AE Model** | | | | | |
| Same sex $\chi^2$ | 16 | 31.82 | 27.97 | 45.02 | 30.67 |
| - F + M $\chi^2$ | 14 | 19.92 | 20.55 | 25.21 | 21.73 |
| $\chi^2_{het}$ | 2 | 11.90 | 7.42 | 19.81 | 8.94 |
| Prob [a] | | * | + | ** | + |
| **ACE Model** | | | | | |
| Same sex $\chi^2$ | 15 | 30.29 | 26.57 | 39.63 | 25.69 |
| - F + M $\chi^2$ | 12 | 18.20 | 17.67 | 20.18 | 16.40 |
| $\chi^2_{het}$ | 3 | 12.09 | 8.90 | 19.45 | 9.29 |
| Prob | | * | + | ** | + |

[a] Probability levels are as defined for Table 7.3.
[b] Antimeres included for comparison, even though suitable models were found for them.

**Table 7.16:** Standardised parameters $a = a^2/_p$, $c = c^2/_p$ and $e = e^2/_p$ for the four maxillary variables within each sex ($p$ = total phenotypic variation within each sex).

| | Females | | | Males | | |
|---|---|---|---|---|---|---|
| | *a* | *c* | *e* | *a* | *c* | *e* |
| **Central Incisor** | | | | | | |
| Left | 74 | 10 | 16 | 48 | 30 | 22 |
| Right [a] | 81 | 1 | 18 | 35 | 43 | 22 |
| **Canine** | | | | | | |
| Right | 46 | 42 | 12 | 36 | 45 | 19 |
| Left [a] | 46 | 45 | 9 | 52 | 38 | 10 |

[a] Antimeres included for comparison, even though suitable models were found for them.

**Table 7.17:** Results of sex-limitation models for the BL dimensions of maxillary central incisors. The first model - homogeneity - is as in Tables 5.11 to 7.13, and Table 7.14 ("All 5"), and is included for comparison. Adequate models with best fit by AIC are highlighted in italics for each model type, and bold italics for the best overall model.

| Model | | df | Left $\chi^2$ | Left AIC | Left Prob [a] | Right [b] $\chi^2$ | Right AIC | Right Prob |
|---|---|---|---|---|---|---|---|---|
| **Homo-geneity** | AE | 21 | 41.43 | -0.6 | * | *35.10* | *-6.9* | *2* |
| | ACE | 20 | 40.27 | 0.3 | * | 35.09 | -4.9 | 1 |
| | ADE | 20 | 41.43 | 1.4 | * | 35.10 | -4.9 | 1 |
| **Hetero-geneity** | AE | 19 | *27.40* | *-10.6* | *5* | 27.62 | -10.4 | 5 |
| | ACE | 17 | 25.54 | -8.5 | 5 | *23.13* | *-10.9* | *10* |
| | ADE | 17 | 27.40 | -6.6 | 5 | 26.77 | -7.2 | 5 |
| **Scalar** | AE | 20 | ***28.94*** | ***-11.1*** | ***5*** | ***28.79*** | ***-11.2*** | ***5*** |
| | ACE | 19 | 27.83 | -10.2 | 5 | 28.79 | -9.2 | .5 |
| | ADE | 19 | 28.94 | -9.1 | 5 | 28.79 | -9.2 | 5 |
| **Non-scalar** | AE | 18 | *27.40* | *-8.6* | *5* | *26.00* | *-10.0* | *5* |
| | ACE | 16 | 25.47 | -6.5 | 5 | 23.12 | -8.9 | 10 |
| | ADE | 16 | 27.40 | -4.6 | 2 | 26.00 | -6.0 | 5 |
| **General** | ACE | 20 | 45.80 | 5.8 | ** | 41.19 | 1.19 | * |
| | ACE + $A'_m$ | 19 | 34.30 | -3.7 | 1 | 33.64 | -4.4 | 2 |
| | $A_fA_mCE$ | 19 | 36.12 | -1.9 | 1 | 37.07 | -0.9 | * |
| | $A\ C_fC_m\ E$ | 19 | 41.20 | 3.2 | * | 35.64 | -2.4 | 1 |
| | $A\ C\ E_fE_m$ | 19 | 31.67 | -6.3 | 2 | 33.64 | -4.4 | 2 |
| | $A\ C_fC_m\ E_fE_m$ | 18 | 30.41 | -5.6 | 2 | 29.69 | -6.3 | 2 |
| | $A_fA_m\ C_fC_m\ E$ | 18 | 34.05 | -2.0 | 1 | 30.61 | -5.4 | 2 |
| | $A_fA_m\ C\ E_fE_m$ | 18 | *28.34* | *-7.7* | *5* | 32.38 | -3.6 | 1 |
| | $A_fA_m\ C_fC_m\ E_fE_m$ | 17 | 26.49 | -7.5 | 5 | *25.97* | *-8.0* | *5* |
| | $A_fA_m\ C_fC_m\ E_fE_m + A'_m$ | 16 | 25.47 | -6.5 | 5 | 25.97 | -6.0 | 5 |

[a] Probability levels are as defined for Table 7.3.

[b] Antimeres included for comparison, even though suitable models were found for them.

**Table 7.18:** Results of sex-limitation models for the BL dimensions of maxillary canines. The first model - homogeneity - is as in tables 5.11 to 7.13, and Table 7.14 ("All 5"), and is included for comparison. Adequate models with best fit by AIC are highlighted in italics for each model type, and bold italics for the best overall model.

| | | | | **Right** | | | **Left [b]** | |
|---|---|---|---|---|---|---|---|---|
| **Model** | | **df** | $\chi^2$ | **AIC** | **Prob [a]** | $\chi^2$ | **AIC** | **Prob** |
| **Homo-geneity** | AE | 21 | 46.08 | 4.1 | * | 31.62 | -10.4 | 5 |
| | ACE | 20 | 43.53 | 3.5 | * | *29.44* | *-10.6* | *5* |
| | ADE | 20 | 46.08 | 6.1 | ** | 31.62 | -8.4 | 2 |
| **Hetero-geneity** | AE | 19 | 61.12 | 23.1 | ** | 69.53 | 31.5 | ** |
| | ACE | 17 | *23.18* | *-10.8* | *10* | *19.86* | *-14.1* | *20* |
| | ADE | 17 | 28.29 | -5.7 | 2 | 24.22 | -9.8 | 10 |
| **Scalar** | AE | 20 | *32.32* | *-7.7* | *2* | 24.71 | -15.3 | 20 |
| | ACE | 19 | 30.43 | -7.6 | 2 | ***22.49*** | ***-15.5*** | ***20*** |
| | ADE | 19 | 32.32 | -5.7 | 2 | 24.71 | -13.3 | 10 |
| **Non-scalar** | AE | 18 | 28.23 | -7.8 | 5 | 24.20 | -11.8 | 10 |
| | ACE | 16 | *22.78* | *-9.2* | *10* | *18.40* | *-13.6* | *20* |
| | ADE | 16 | 28.29 | -3.7 | 2 | 24.22 | -7.8 | 5 |
| **General** | ACE | 20 | 38.74 | -1.3 | * | 51.46 | 11.5 | ** |
| | $ACE + A'_m$ | 19 | 26.50 | -11.5 | 10 | 38.33 | 0.3 | * |
| | $A_fA_mCE$ | 19 | 31.36 | -6.6 | 2 | 42.31 | -3.7 | * |
| | $A\,C_fC_m\,E$ | 19 | 48.51 | 10.5 | ** | 36.48 | -1.5 | * |
| | $A\,C\,E_fE_m$ | 19 | 34.15 | -3.9 | 1 | 33.50 | -4.5 | 2 |
| | $A\,C_fC_m\,E_fE_m$ | 18 | 32.24 | -3.8 | 2 | 34.04 | -2.0 | 1 |
| | $A_fA_m\,C_fC_m\,E$ | 18 | 22.37 | -13.6 | 20 | 34.97 | -1.0 | * |
| | $A_fA_m\,C\,E_fE_m$ | 18 | 28.04 | -8.0 | 5 | 31.27 | -4.7 | 2 |
| | $A_fA_m\,C_fC_m\,E_fE_m$ | 17 | ***19.03*** | ***-15.0*** | ***30*** | *23.42* | *-10.6* | *10* |
| | $A_fA_m\,C_fC_m\,E_fE_m + A'_m$ | 16 | 18.40 | -13.6 | 30 | 22.76 | -9.2 | 10 |

[a] Probability levels are as defined for Table 7.3.

[b] Antimeres included for comparison, even though suitable models were found for them.

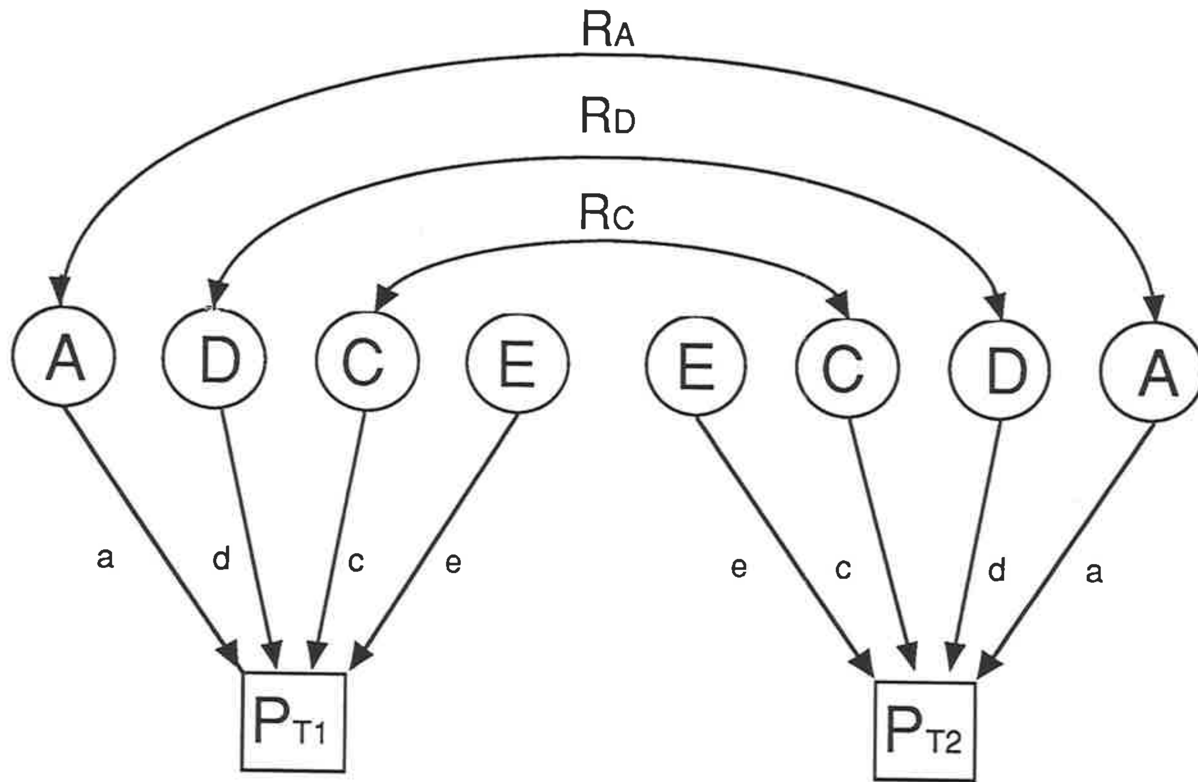


**Figure 7.1**: Path diagram indicating sources of variance and covariance for a trait in a pair of twins.

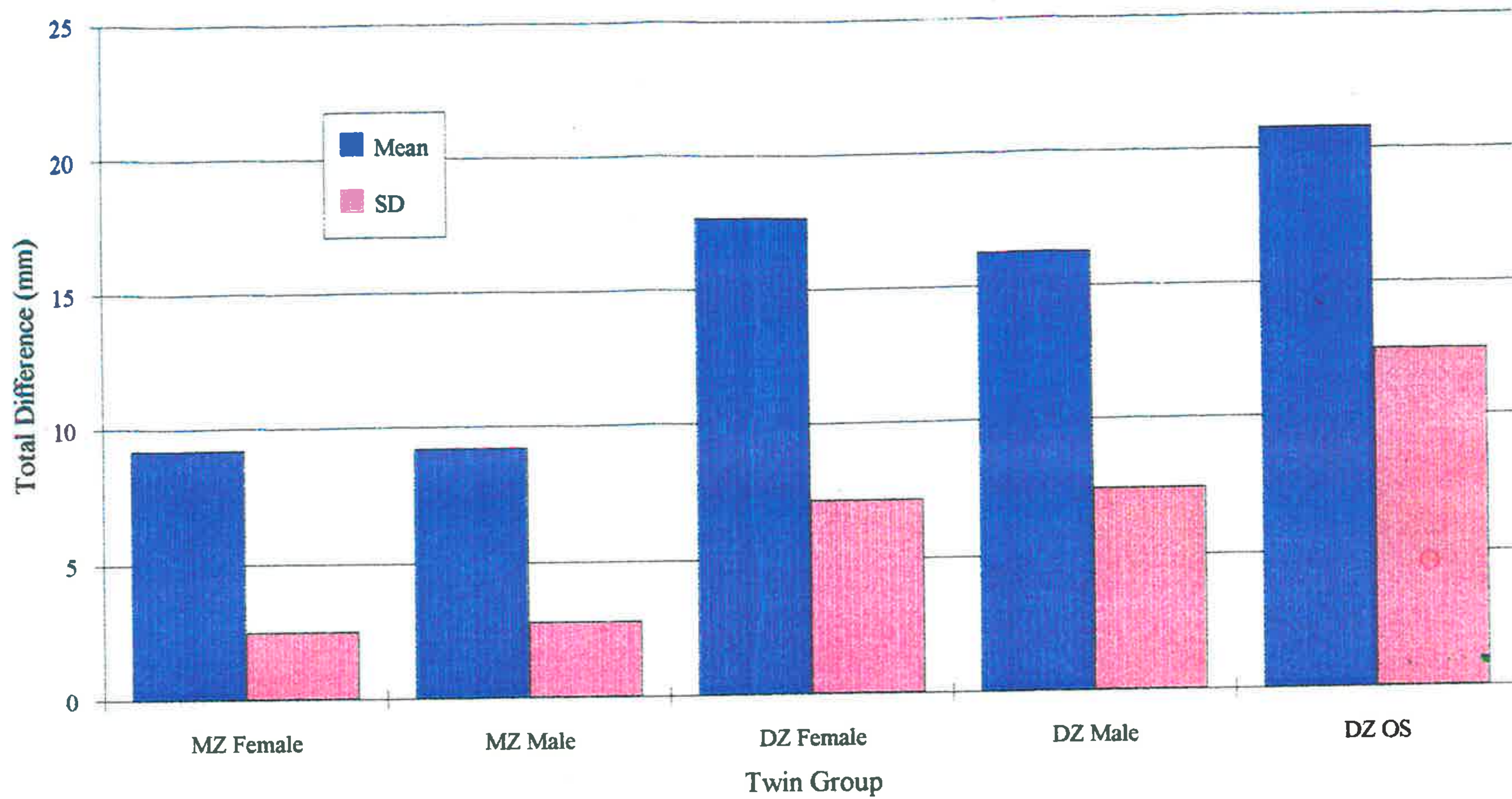


**Figure 7.2:** Bar graph of total differences in tooth crown size between co-twins.

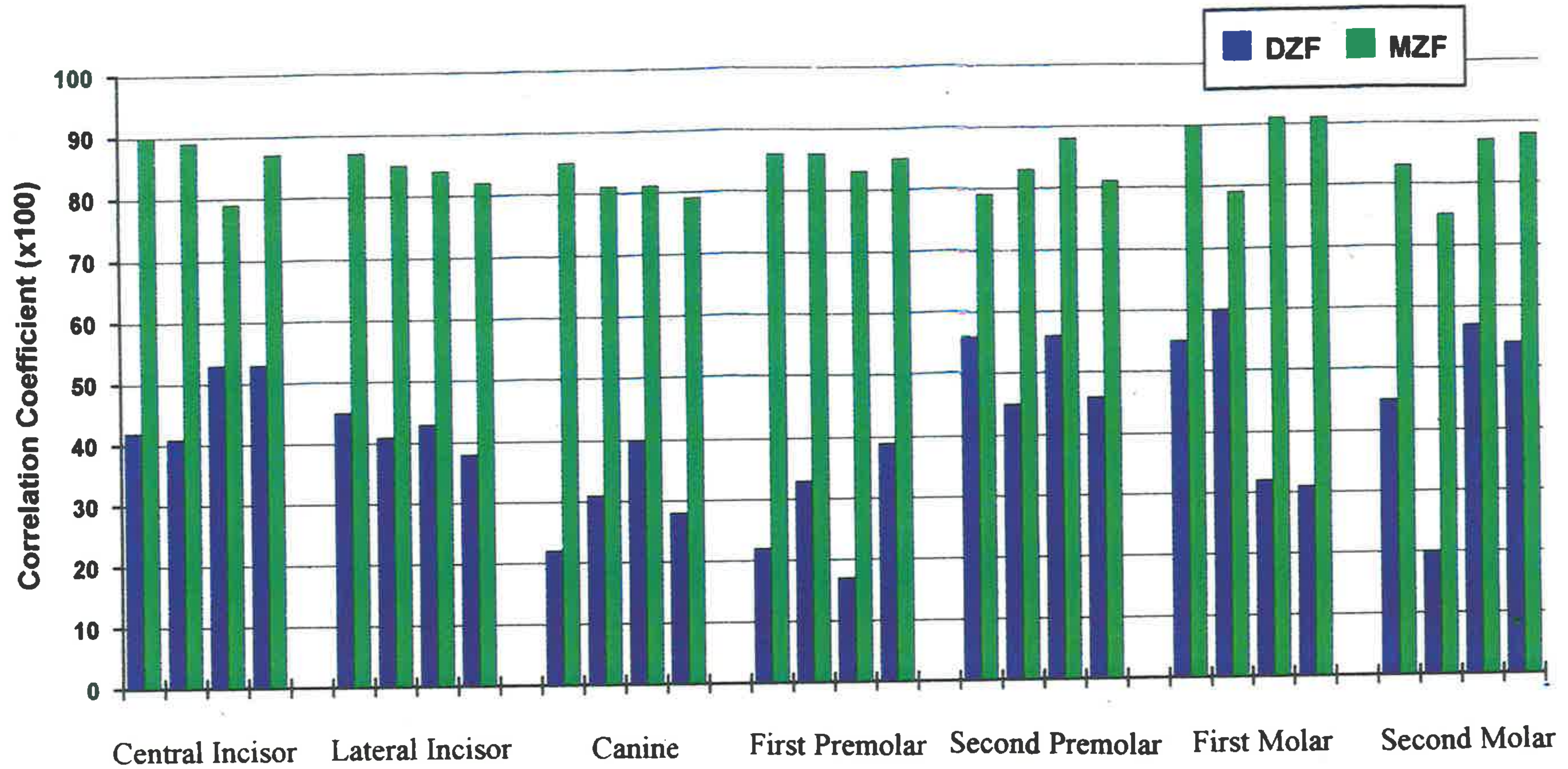


**Figure 7.3:** Bar graph of correlation coefficients for MD length in female MZ and DZ SS twin pairs. Order of bars for each tooth: maxillary right, maxillary left, mandibular right, mandibular left.

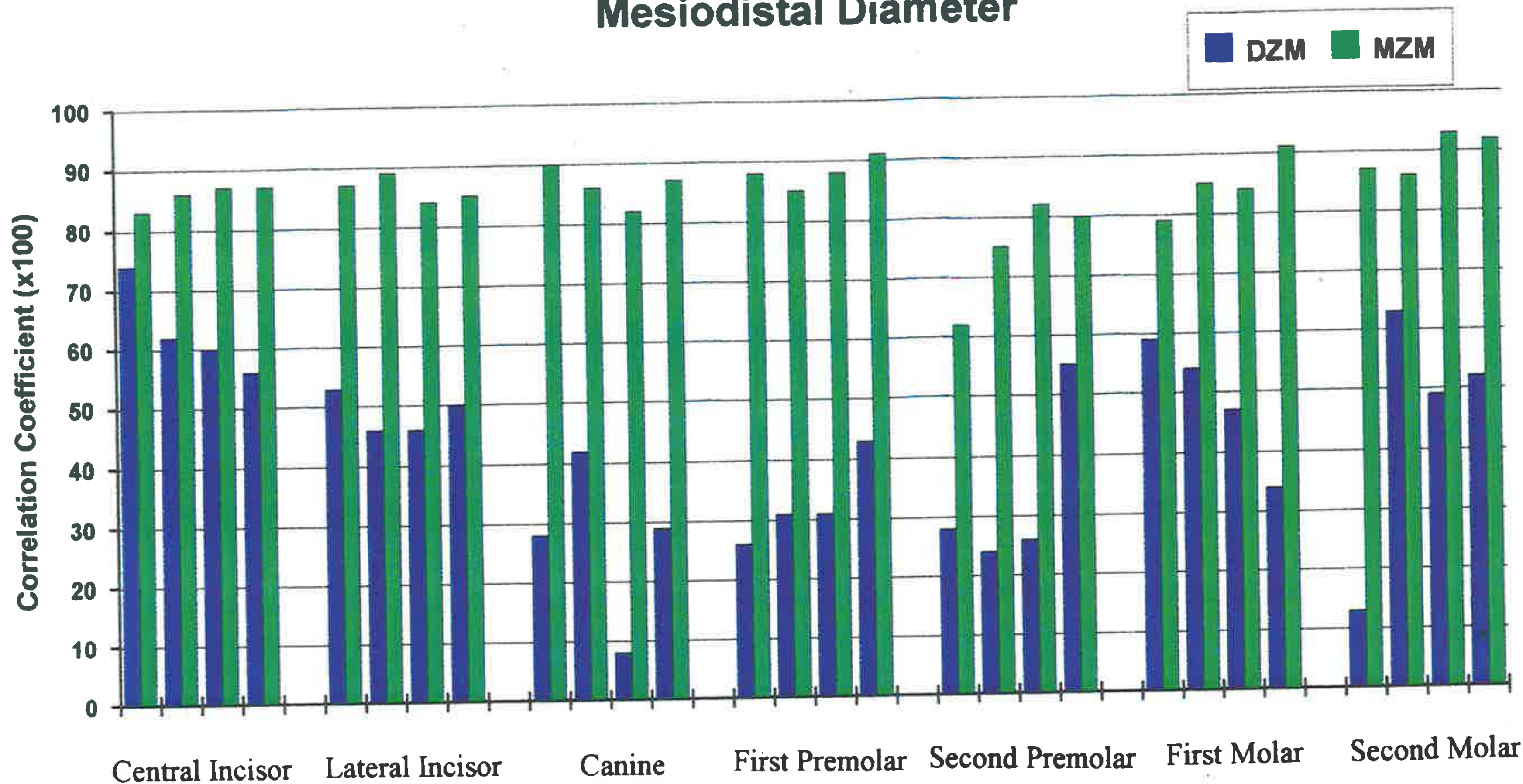


**Figure 7.4:** Bar graph of correlation coefficients for MD length in male MZ and DZ SS twin pairs. Order of bars for each tooth: maxillary right, maxillary left, mandibular right, mandibular left.

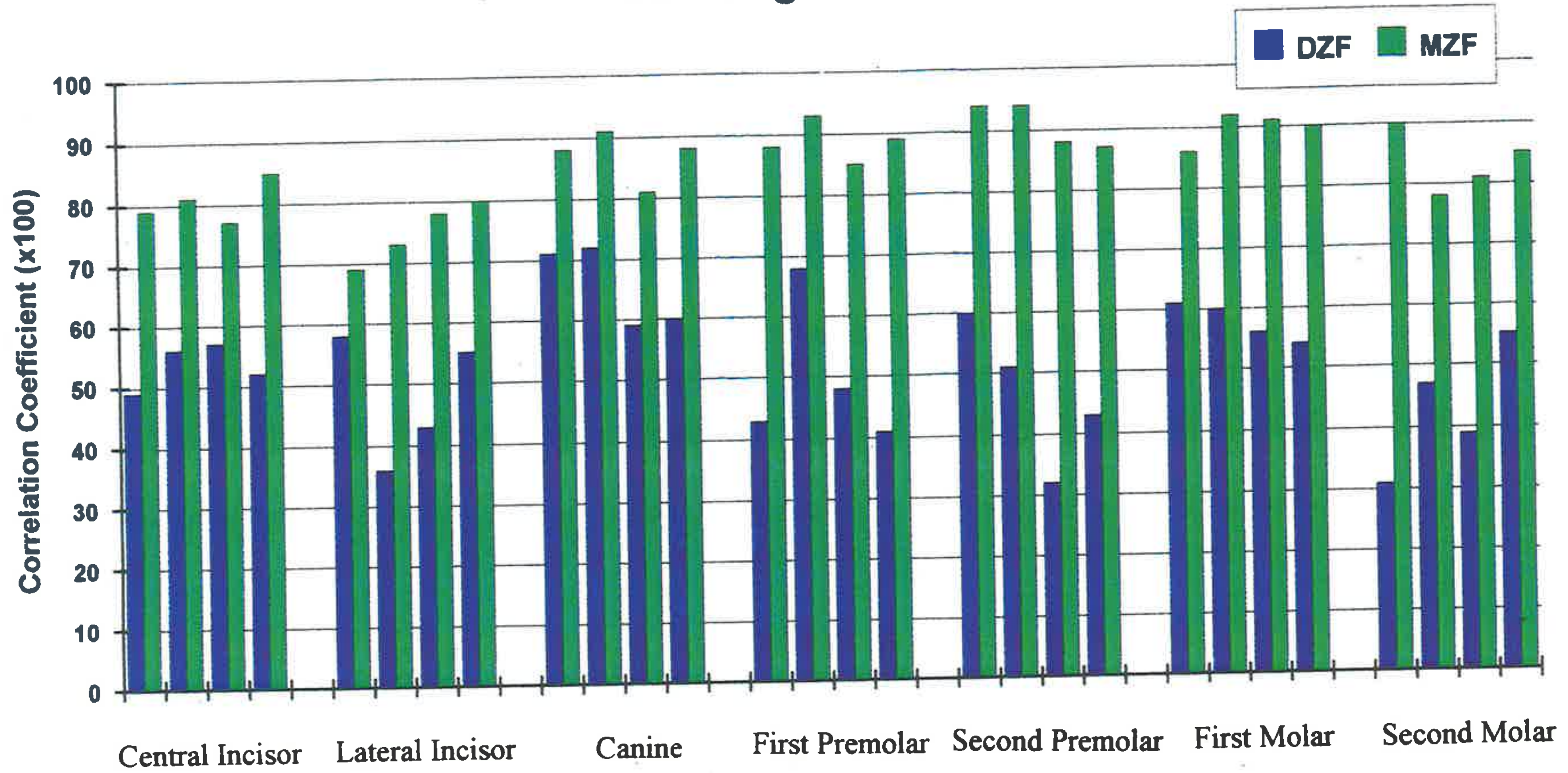


**Figure 7.5:** Bar graph of correlation coefficients for BL breadth in female MZ and DZ SS twin pairs. Order of bars for each tooth: maxillary right, maxillary left, mandibular right, mandibular left.

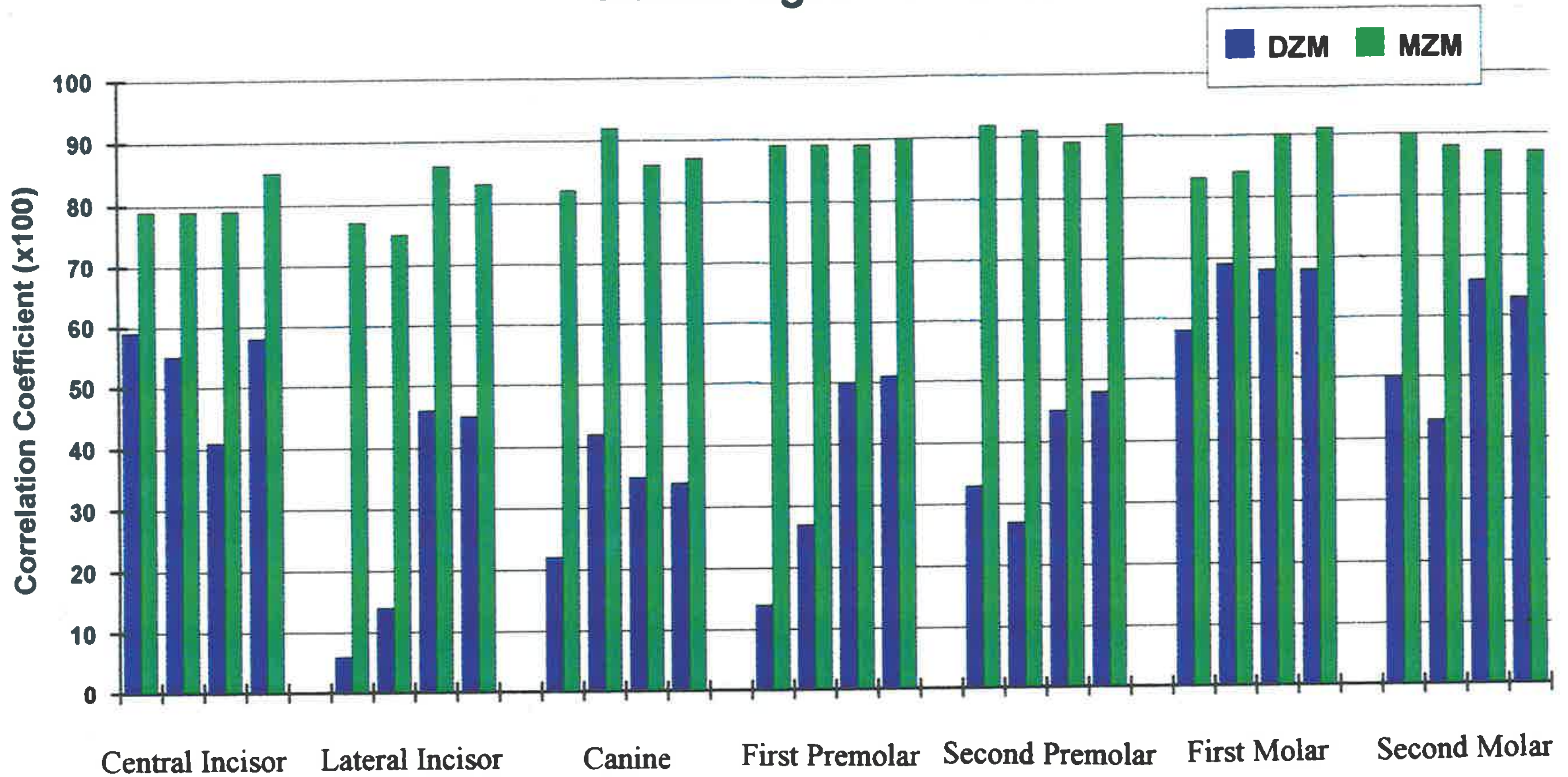


**Figure 7.6:** Bar graph of correlation coefficients for BL breadth in male MZ and DZ SS twin pairs. Order of bars for each tooth: maxillary right, maxillary left, mandibular right, mandibular left.

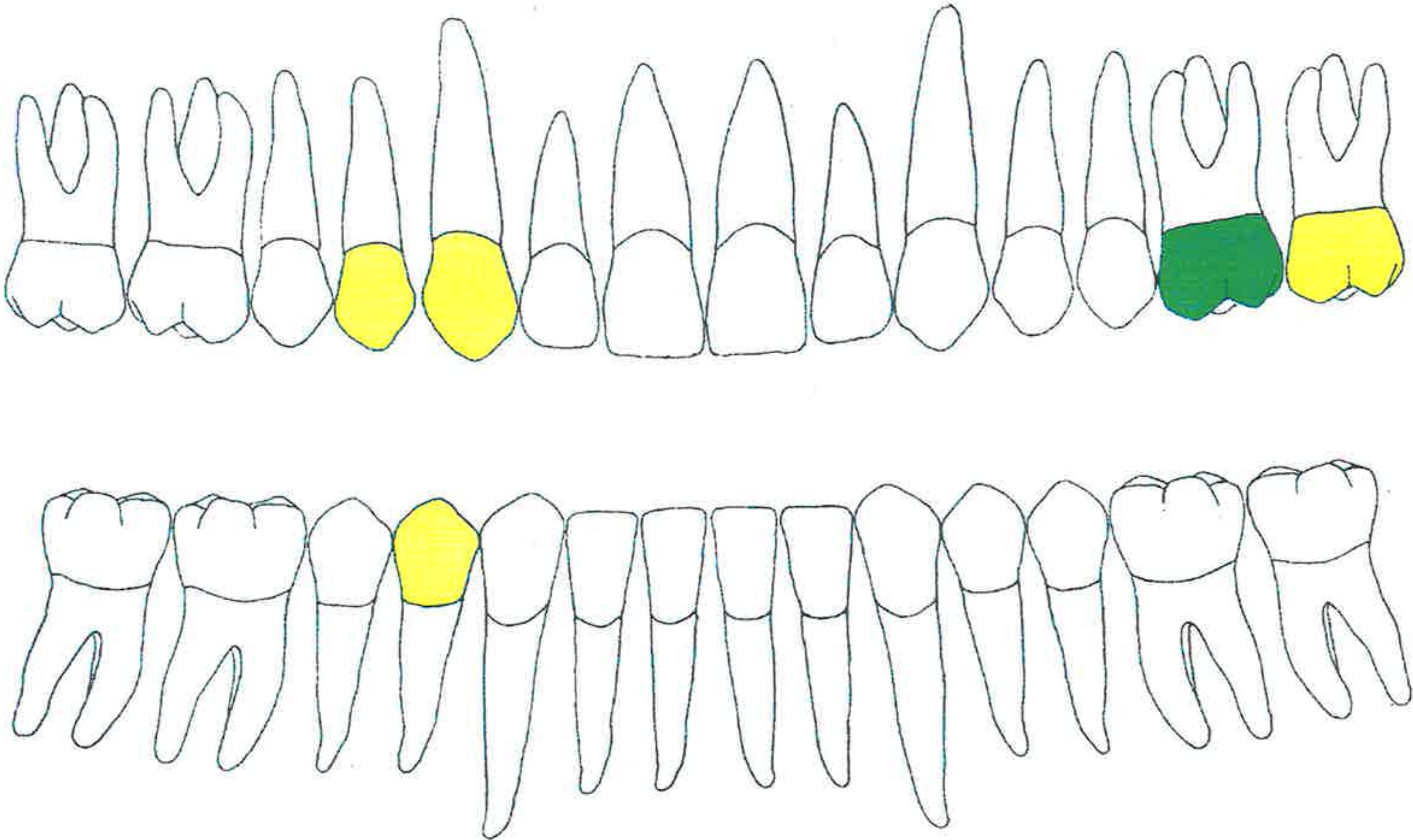

**Figure 7.7:** Non-additive genetic (yellow) and common environmental (green) influences on the MD dimensions, as suggested by co-twin correlations of females.

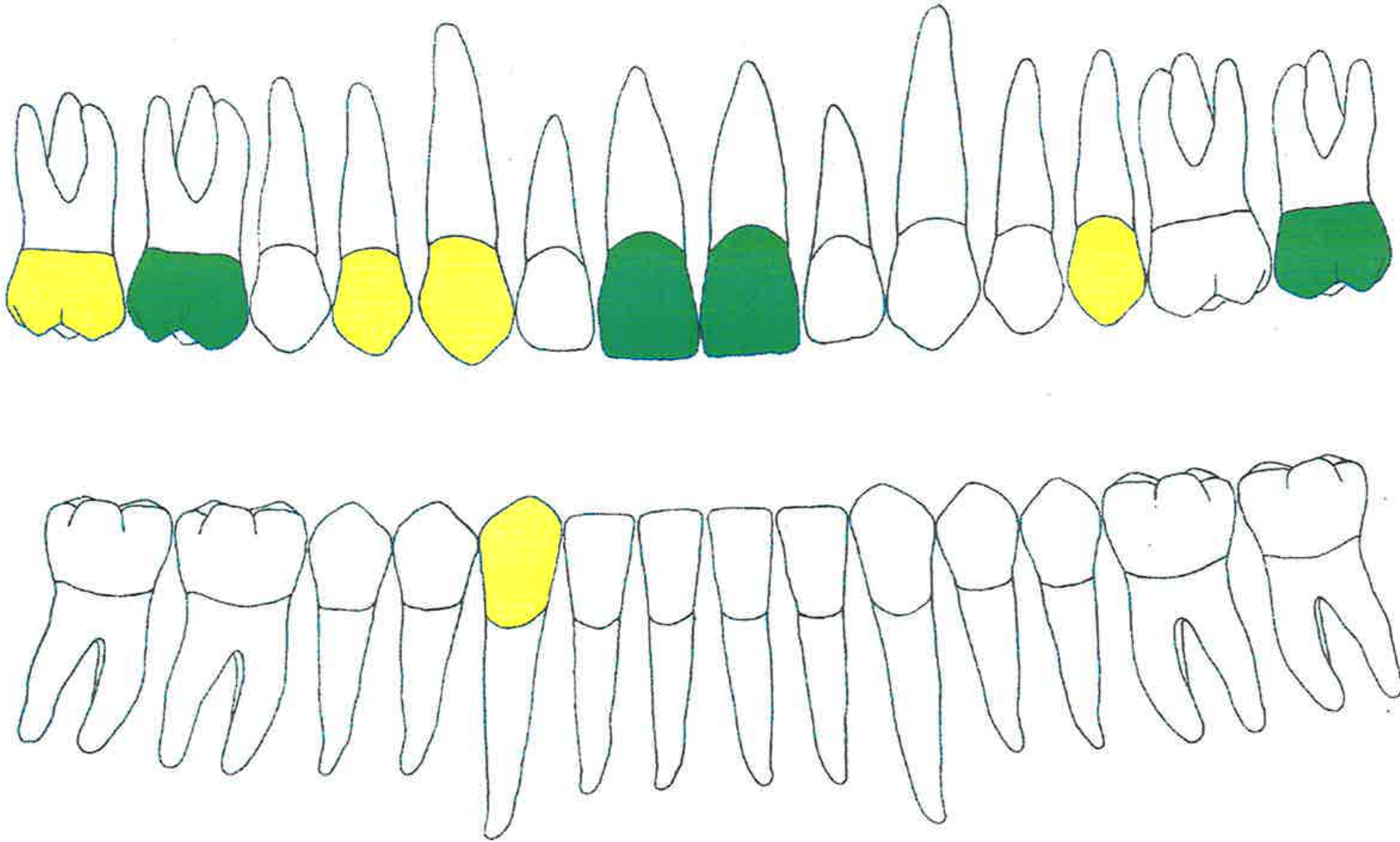

**Figure 7.8:** Non-additive genetic (yellow) and common environmental (green) influences on the MD dimension, as suggested by co-twin correlations of males.

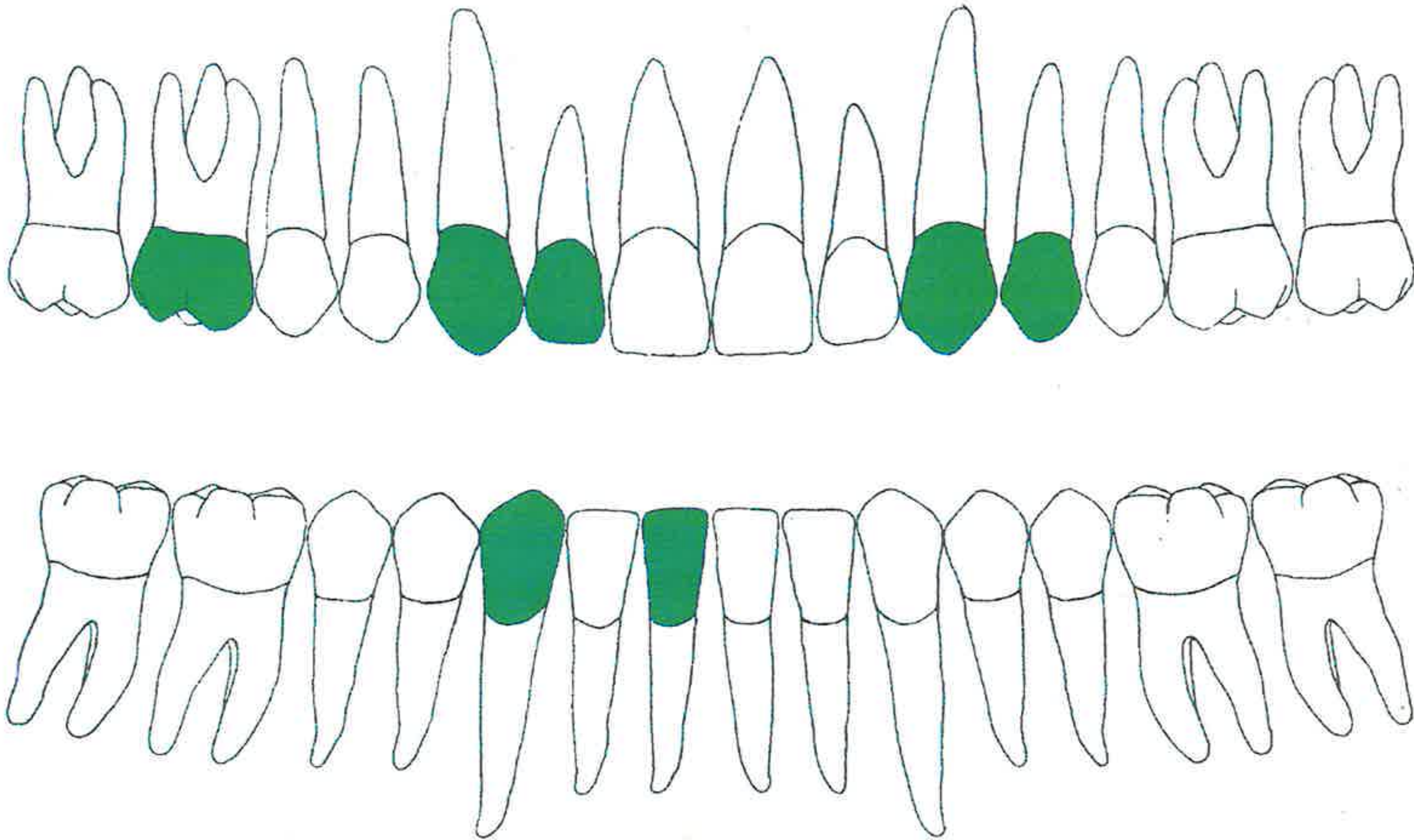

**Figure 7.9:** Non-additive genetic (yellow) and common environmental (green) influences on the BL dimension, as suggested by co-twin correlations of females.

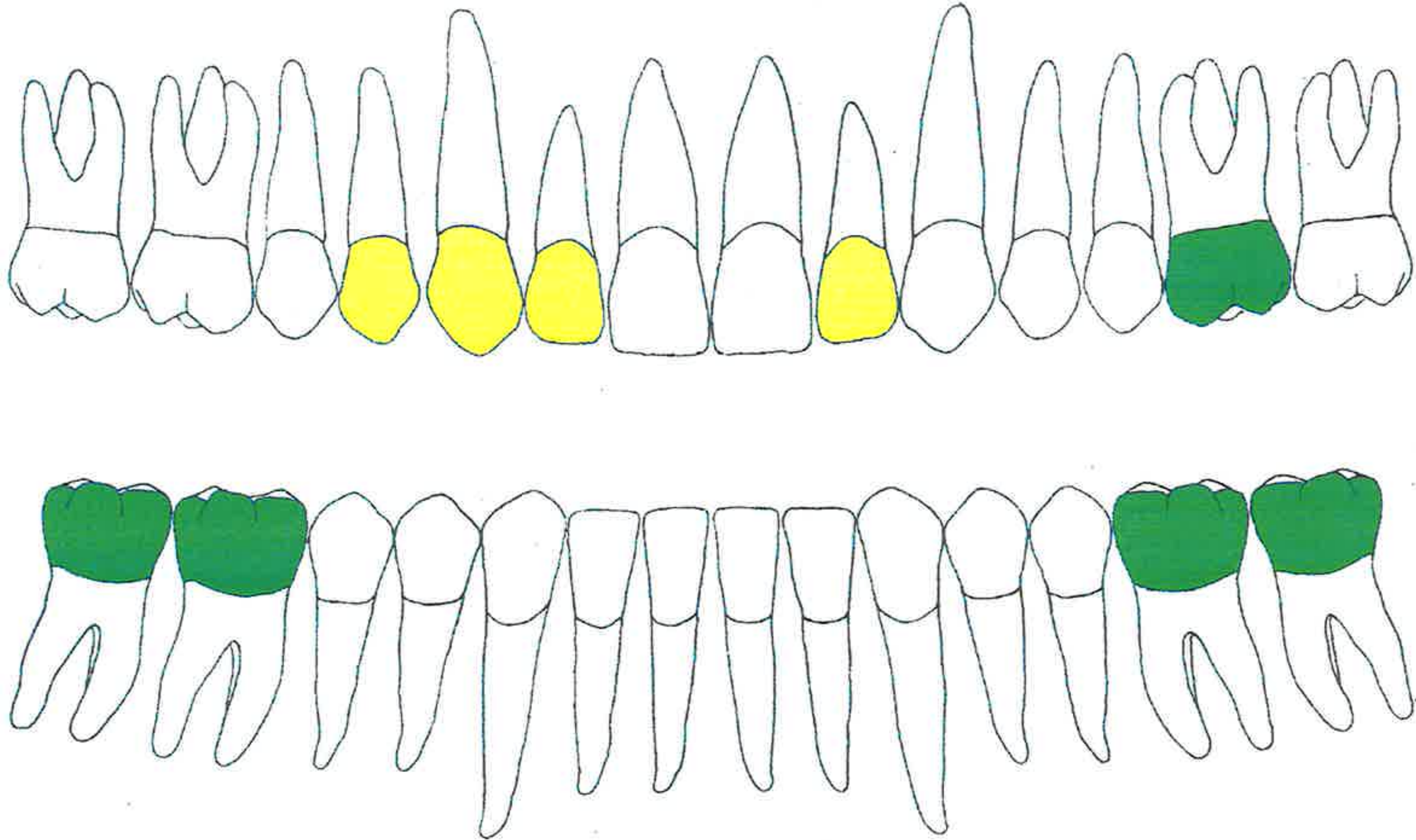

**Figure 7.10:** Non-additive genetic (yellow) and common environmental (green) influences on the BL dimension, as suggested by co-twin correlations of males.

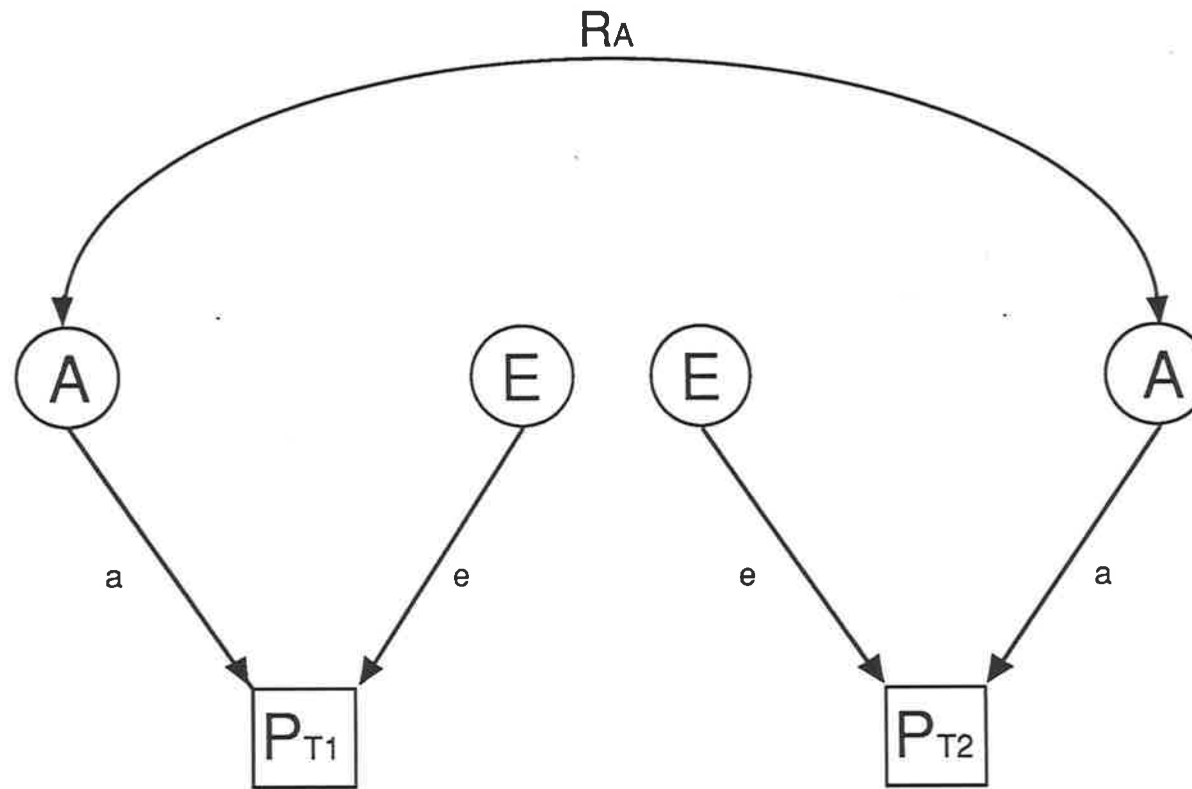


**Figure 7.11:** Path diagram for all variables other than those in Figures 7.12 to 7.16 - the AE homogeneity model.

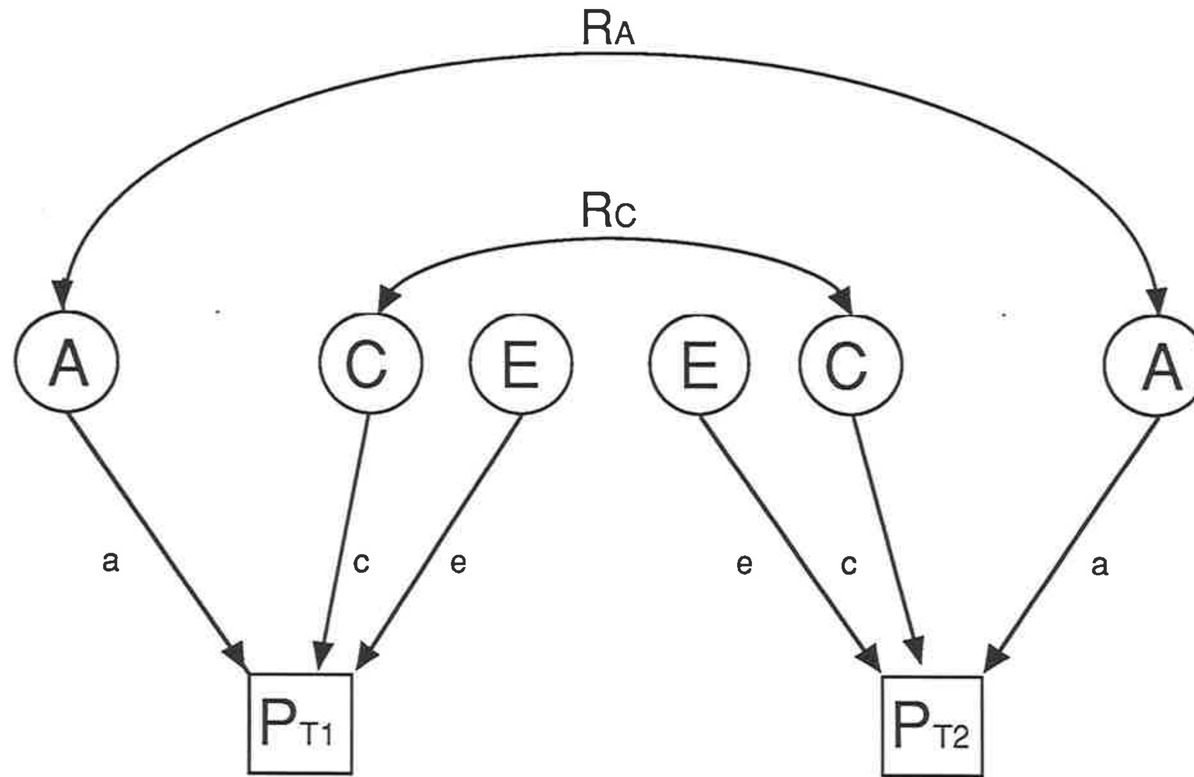


**Figure 7.12:** Path diagram for BL and MD dimensions of the maxillary first molars - the ACE homogeneity model.

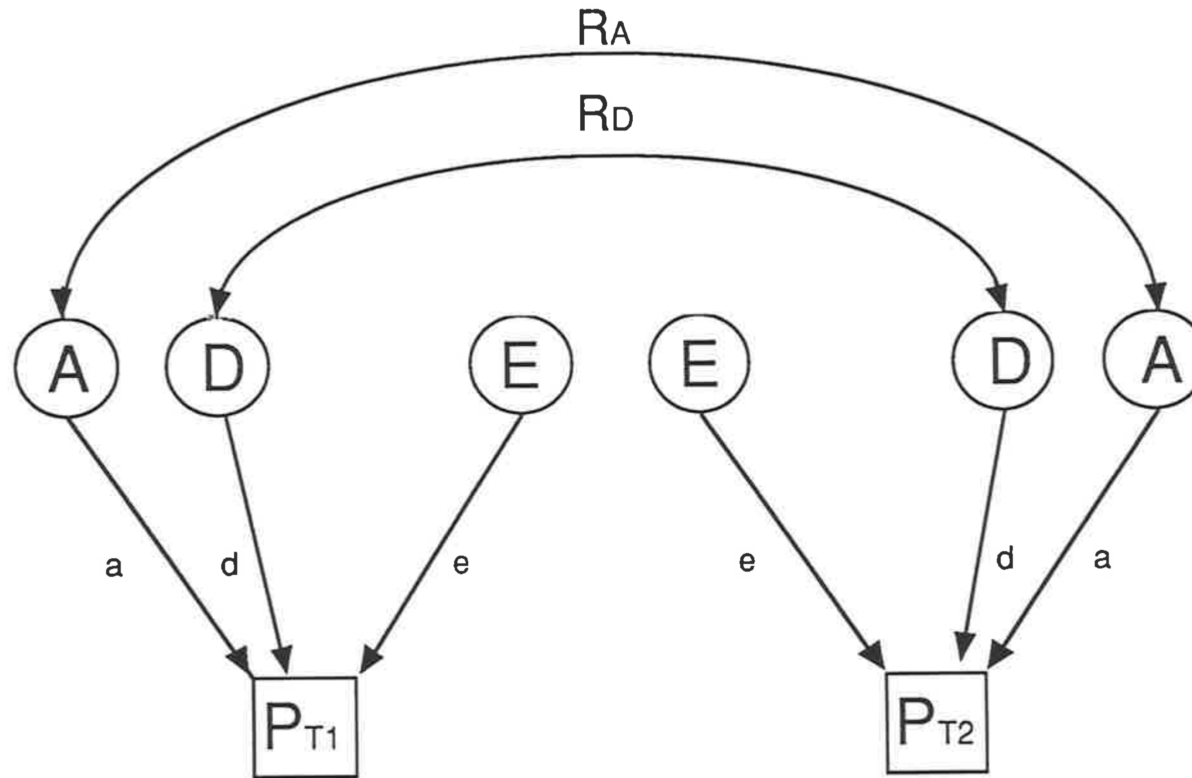


**Figure 7.13:** Path diagram for the MD dimension of all canines, both maxillary first premolars and mandibular right first premolar, as well as the BL diameter of the maxillary right first premolar - the ADE homogeneity model.

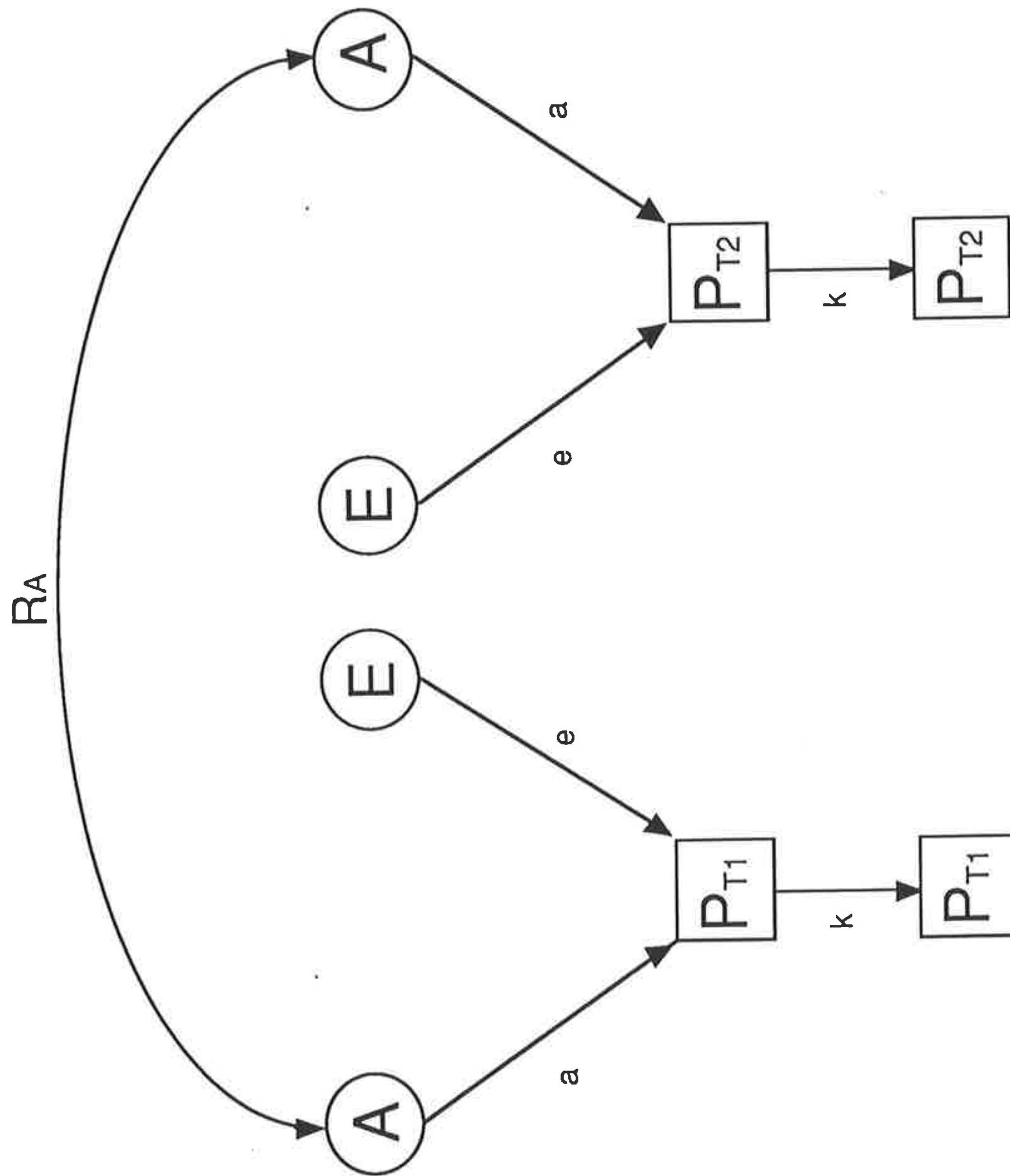


**Figure 7.14:** Path diagram for the BL dimension of the maxillary central incisors - the scalar sex-limitation AE model. k = 1 for females, k ≠ 1 for males.

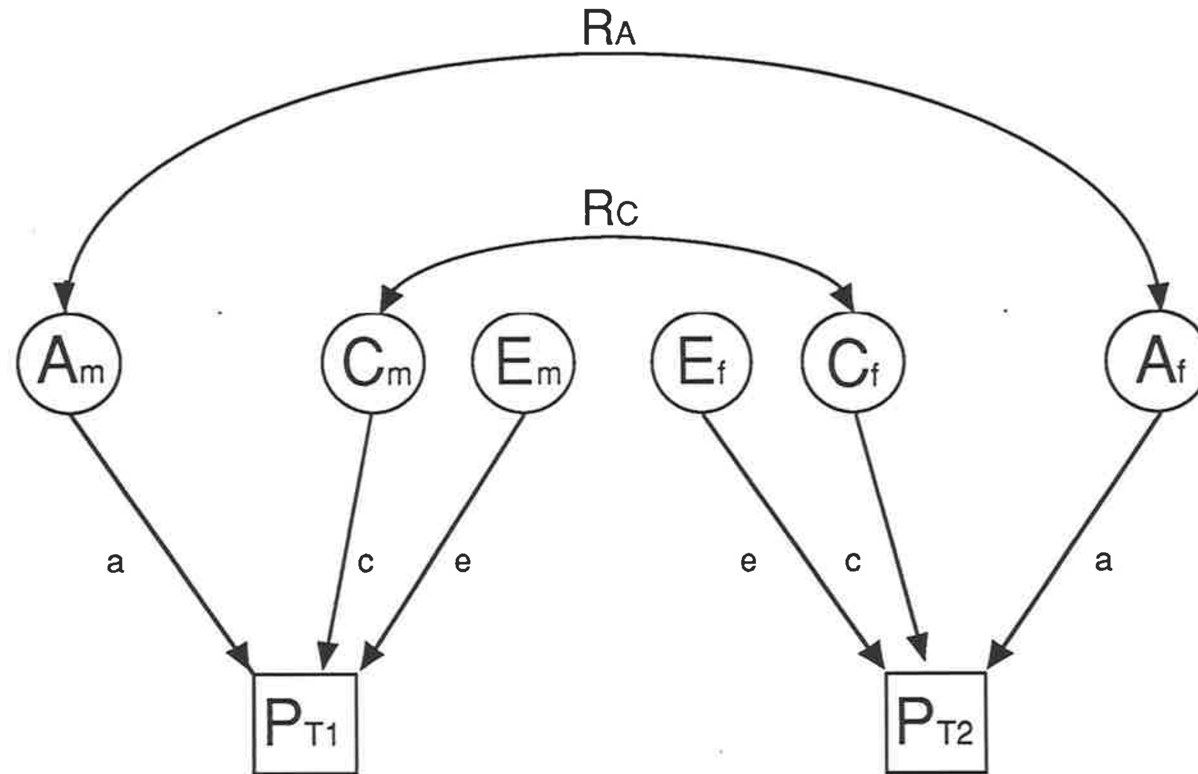


**Figure 7.15:** Path diagram for the BL dimension of the maxillary right canine - the general sex-limitation ACE model. A pair of DZ OS twins is depicted.

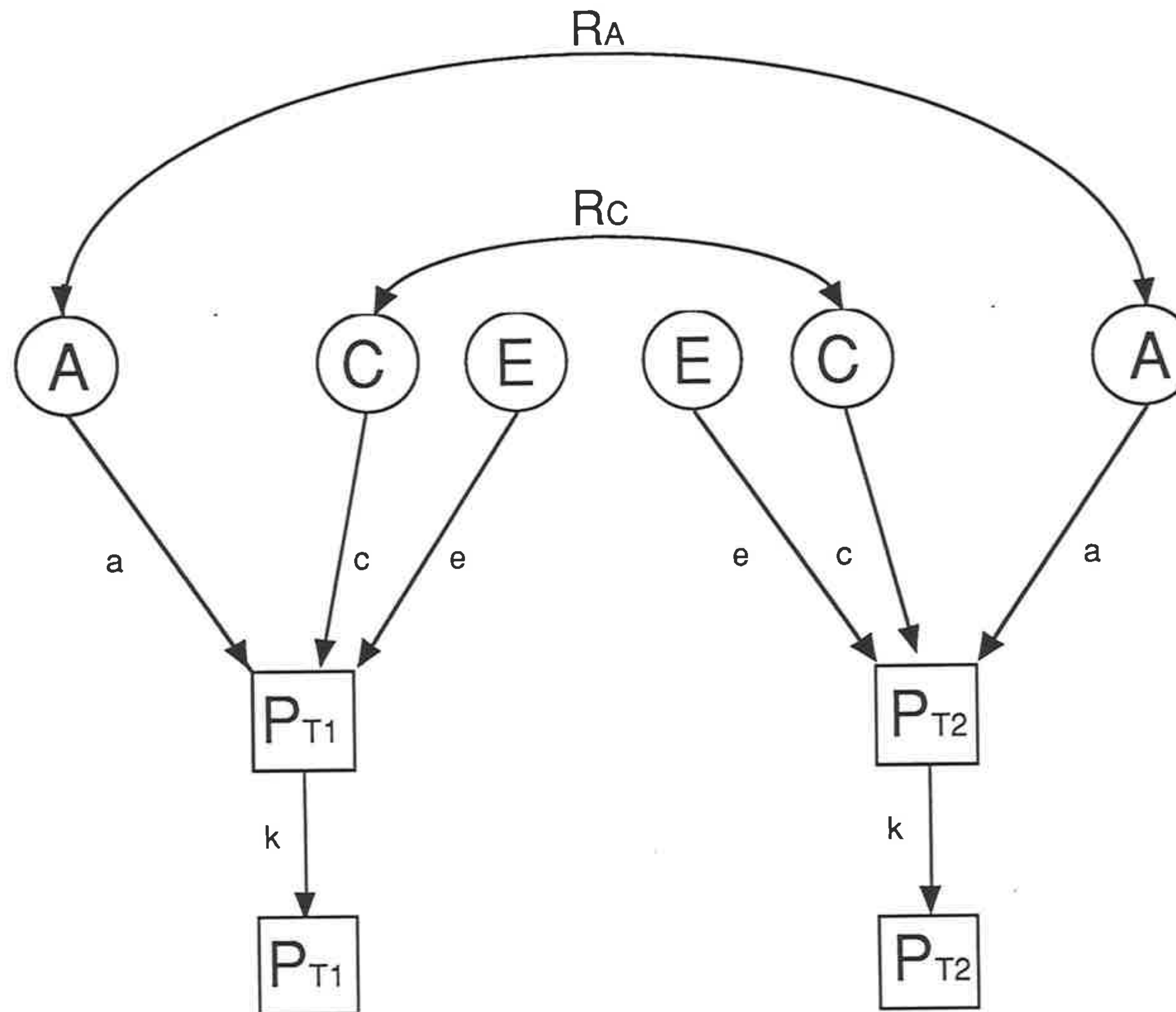


**Figure 7.16:** Path diagram for the BL dimension of the maxillary left canine - the scalar sex-limitation ACE model. $k = 1$ for females, $k \neq 1$ for males.

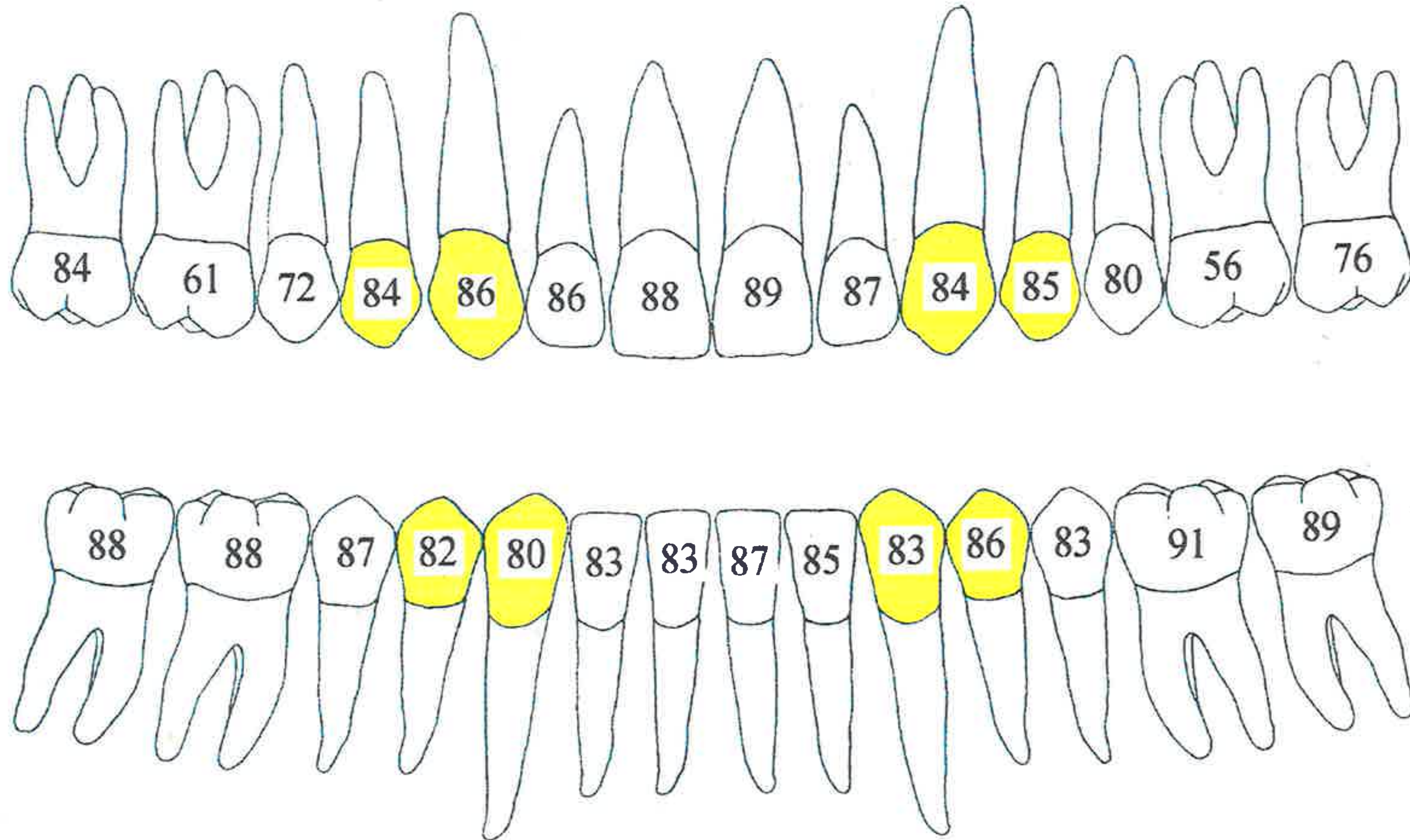


**Figure 7.17:** Heritability of MD diameter (black = additive genetic variation only, yellow = both additive and non-additive genetic variation).

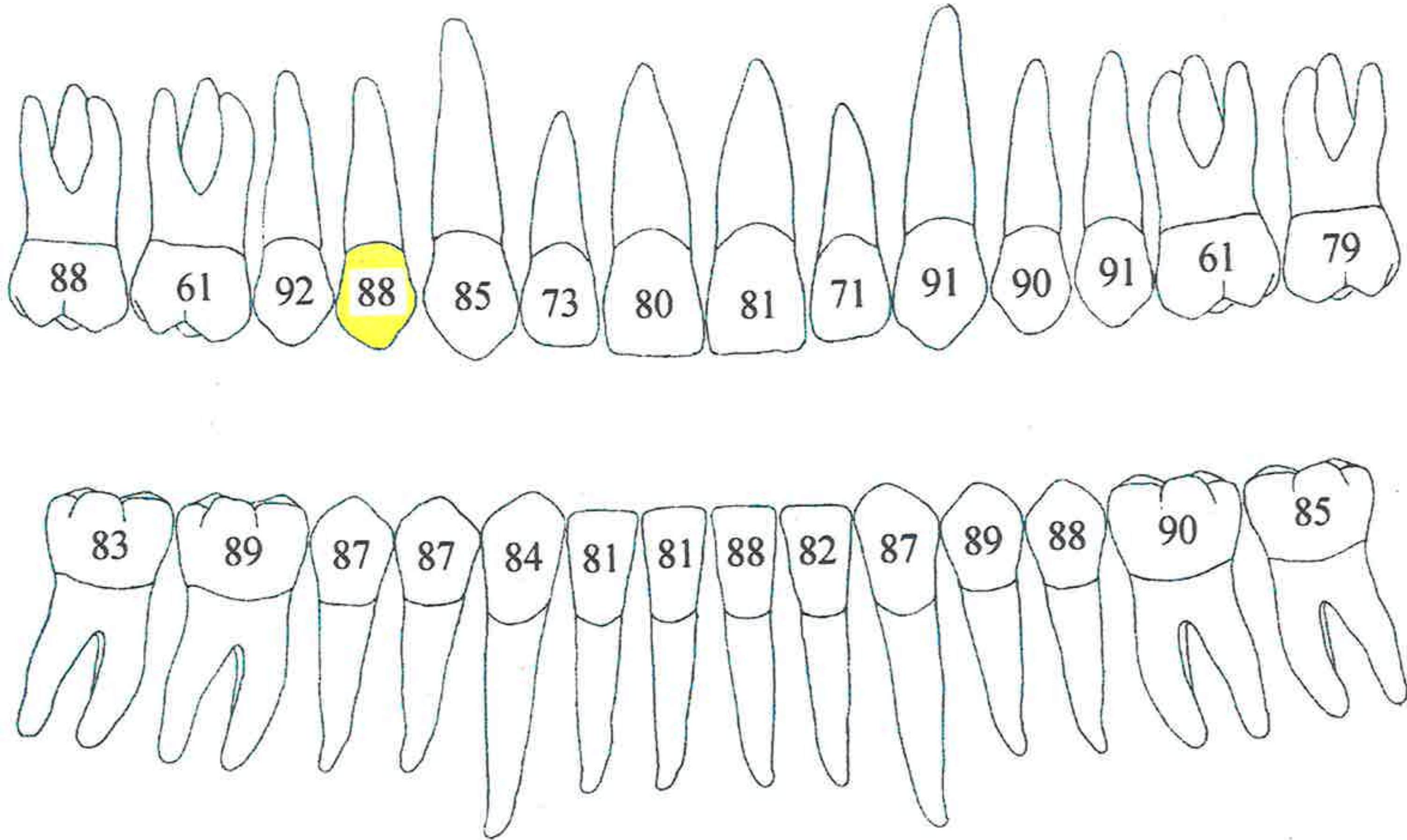


**Figure 7.18:** Heritability of BL diameter (black = additive genetic variation only, yellow = both additive and non-additive genetic variation).

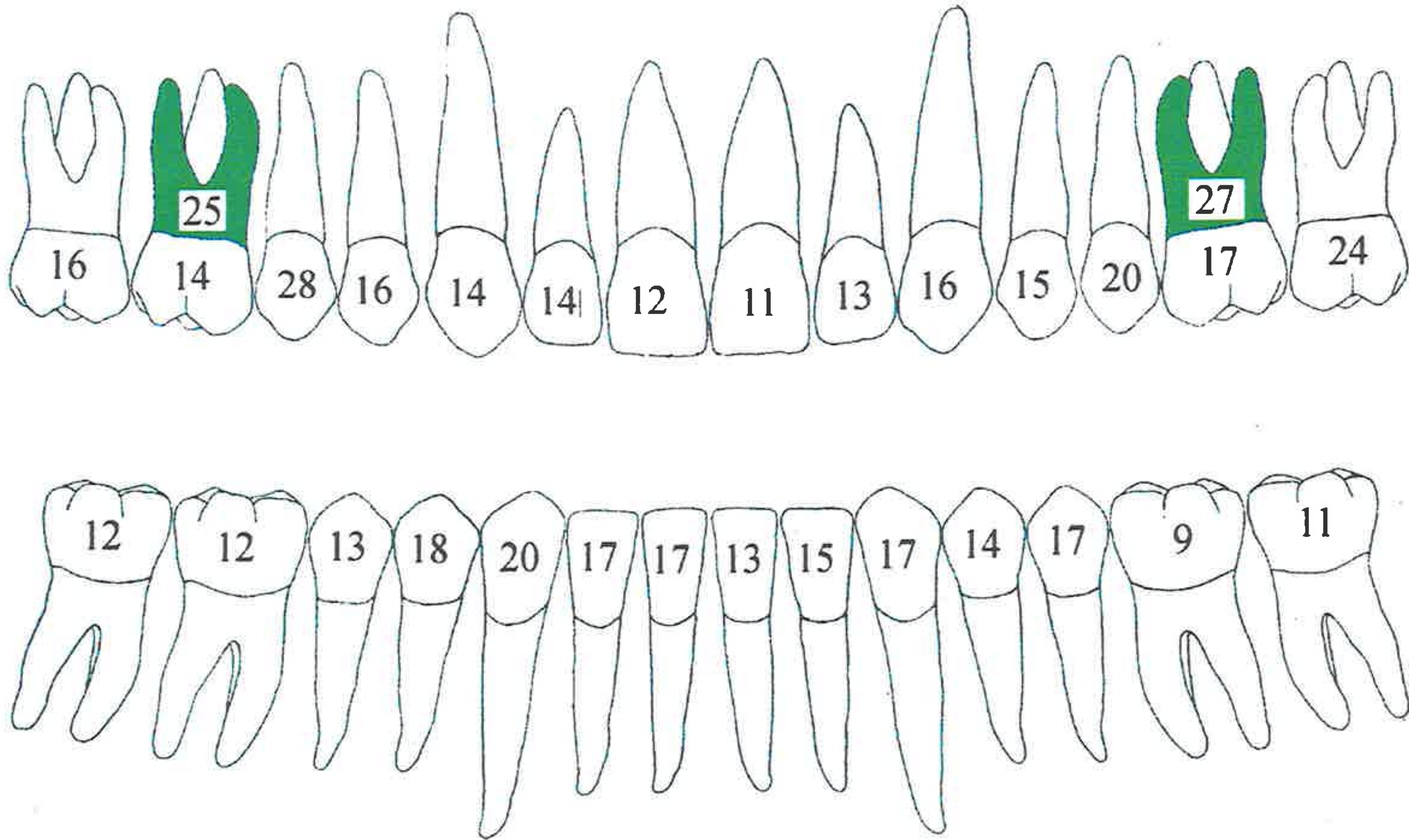


**Figure 7.19:** Environmentality of MD diameter (black = unique environmental variation, green = common environmental variation).

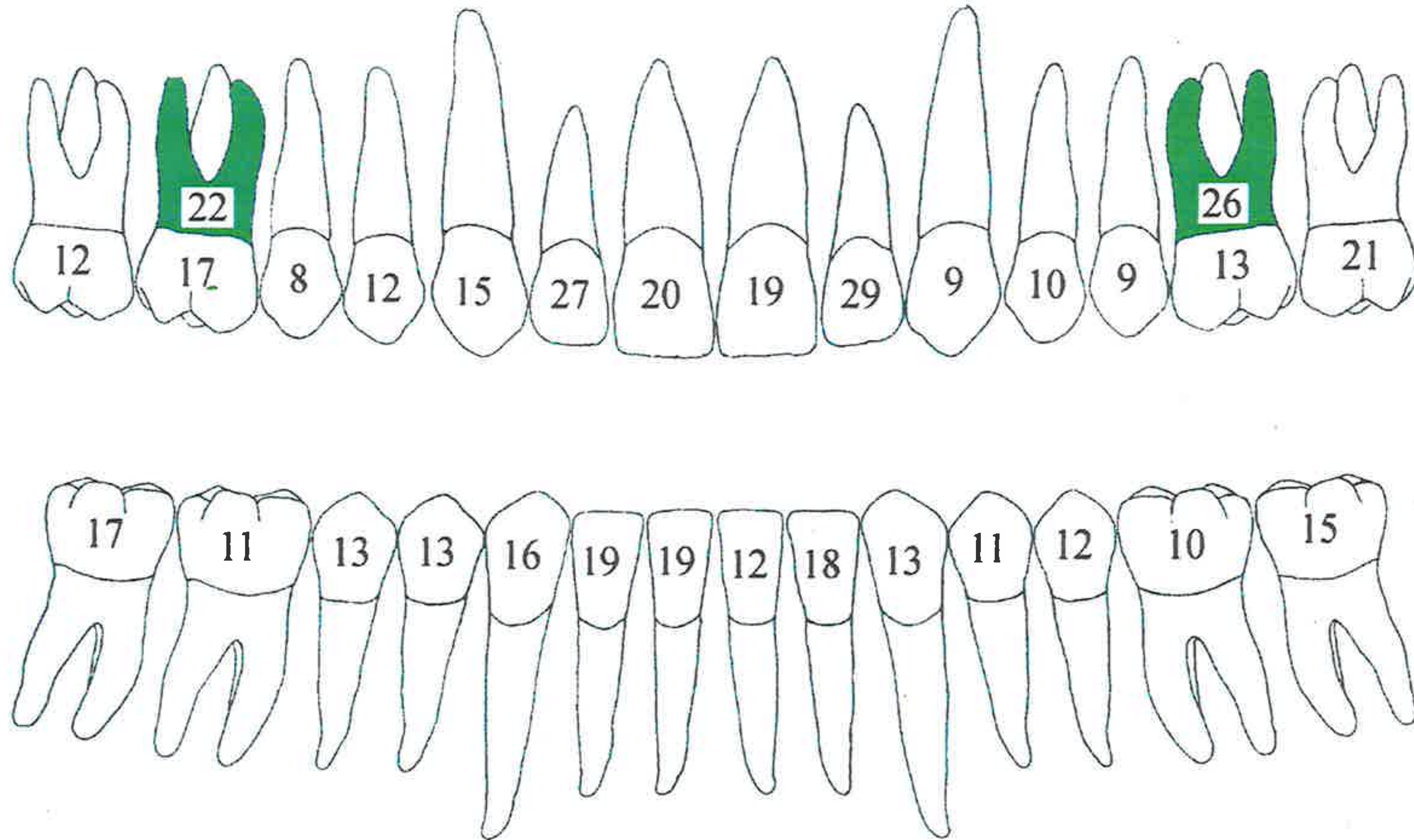


**Figure 7.20:** Environmentality of BL diameter (black = unique environmental variation, green = common environmental variation).

## Contemplating Heritability

"He had bought a large map representing the sea,
without the least vestige of land:
And the crew were much pleased
when they found it to be
A map they could all understand."

Lewis Carroll (1876) "The Hunting of the Snark"
London: MacMillan

# Chapter 8

# Multivariate Modelling Of Tooth Crown Size

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## Introduction

Univariate analyses can be extended to multivariate ones using the same basic process. The advantages include having increased power, and gaining the abilities to incorporate and account for correlations among the variables; determine whether different variables have common causal factors; and estimate the contributions of A, C, D, and E to the covariation among variables.

### Previous research

There have been numerous inter-tooth analyses yielding varied results, including a genetic factor influencing anterior teeth (Osborne and DeGeorge 1959), an additional genetic factor affecting the variability of the maxillary lateral incisors (Osborne and DeGeorge 1959, Horowitz *et al.* 1958) and independent genetic factors on each tooth (Lundström 1964, Moorrees 1964, Goose 1970). Genetic factors influencing teeth individually as well as collectively within the dentition also have been reported (Osborne *et al.* 1958). An extensive analysis of MD and BL dimensions in the permanent dentition of 75 pairs of twins using principal components analysis, discriminant function analysis and factor analysis revealed the following (Potter *et al.* 1976):

- a general genetic factor acting on maxillary teeth;
- a genetic factor acting on the anterior mandibular teeth;
- antimeres being associated with the same genetic factor;
- independent determination of maxillary and mandibular dentitions; and
- mandibular teeth being influenced by a wider range of factors than maxillary teeth

Subsequently, a series of multivariate investigations of tooth crown size in Japanese twins and/or singletons by Mizoguchi (1978, 1980, 1981, 1983) appeared in the literature. These reports yielded an interesting array of findings. Maximum likelihood factor analysis revealed four factors, interpreted as genetic in origin, applicable to the four tooth groups, and two environmental factors which were suggestive of environmental effects in the precalcification and calcification periods of tooth development, respectively (Mizoguchi 1980). Canonical correlation analysis of singleton adolescents revealed two groups or functional units in the dentition - those for anterior (I1 to C) and posterior (P1 to M2) teeth (Mizoguchi 1981). These last two findings were not considered by Mizoguchi to be at odds with one another. Rather, he suggested that relationships among teeth were primarily due to their membership in either anterior or posterior tooth groups, and then by compensatory interactions within their respective tooth groups (I, C, P and M) (Mizoguchi 1981).

Other factor analyses have revealed tooth group factors (Lombardi 1975), anterior and posterior tooth factors (Potter *et al.* 1968), or a combination of these (Townsend and Brown 1979a). The study by Potter *et al.* (1968) identified three factors - MD and BL of posterior teeth, BL of anterior teeth and MD of anterior teeth, suggesting independent determination of the two diameters of anterior teeth (Potter *et al.* 1968). Independent factors for MD and BL diameters in anterior teeth also were found by Townsend and Brown (1979a), along with a general size (MD and BL) factor for premolars and for molars.

All of these previous studies had substantial limitations, and several relied on assumptions which were unlikely to be true. These included absence of common environment or non-additive genetic variation, or a lack of interactions among factors. Notwithstanding this, they were preliminary explorations of dental development at a time when better methods were not widely available.

### Aims

The aims of the multivariate modelling were:

- to discover what genetic and environmental factors were required to explain variation in, and covariation among, MD and BL dimensions of permanent tooth crowns;
- to quantify the relative contributions of these factors;
- to test whether the size of each tooth was determined independently; and
- to examine heritability patterns

## Methods

The procedure entailed the following: data preparation, modelling of variance-covariance matrices for the eight incisors, modelling of means and variance-covariance matrices for the seven teeth (excluding the third molar) in the maxillary right quadrant of the oral cavity.

### Data Preparation

Unfortunately, it was not possible to model more than one or two variables at a time using VL files. The optimisation procedure was unable to operate and continually requested respecification of parameter starting values. For multivariate models then, variance-covariance and mean matrices were prepared using PRELIS (Version AIX-PRELIS 1.20, Jöreskog and Sörbom 1986) or Mx.

In order to produce positive-definite variance-covariance matrices, all individuals must have values for each variable. Since there were missing values in the data set, a

choice had to be made between listwise deletion of all individuals with at least one missing value, or imputation of the missing values. Listwise deletion would have resulted in the loss of a substantial amount of the data (eg 55% if the matrix included MD dimension of the lower right second molar). In fact, only a few individuals in our sample had all of their permanent teeth (not including the third molars) fully erupted and free of dental extraction, restoration or significant wear. The percentages of values missing for the 596 individual twins are listed in Table 8.1. The variables with the greatest proportion missing were the premolars (18 to 28%) and the second molar (33 to 55%). In general, there were more missing values for BL than MD dimensions. This was mainly due to incomplete eruption of teeth in juvenile and adolescent subjects, since the maximum BL dimension generally is closer to the cervical region of the tooth crown than is the maximum MD dimension.

Statistically, missing values are considered non-problematic if inferences drawn from a sample with missing values are the same as inferences based on a full distribution (Little and Rubin 1987, Brown 1994). This means that the values must be missing at random, so that the probability of absence of a variable is independent of the value of the variable. They also must be observed at random, meaning that the probability of absence of one variable is independent of the probability of absence of another. Data which fulfil these criteria are said to be missing completely at random (Little and Rubin 1987, Brown 1994).

In the data presented here, the pattern of missing values cannot be described as missing at random, since, in some cases, the value of the missing variable would make it more likely to be missing. For example, very small ("diminutive") or malformed ("peg-shaped") maxillary lateral incisors were excluded from the analysis. The missing values are also not observed at random since a variable is more likely to be missing if its antimere is missing, especially in young subjects, and if a

tooth is missing, then both MD and BL dimensions will be missing. This means that imputation of missing values could lead to biased results, and probably the loss of important information. Given that the alternative, listwise deletion, was even less viable, an imputation procedure was applied cautiously, checking the extent of the bias introduced using a univariate simulation study.

The imputation procedure followed a hierarchy of substitution: (1) missing values were substituted from the antimeric tooth when present; (2) if the antimere was absent, the value from the co-twin was used in same-sexed twin pairs; (3) where this was also missing, or the twins were opposite-sexed, the sex-specific mean was used. To reduce the impact of the imputations, twin pairs with less than 60 (50 for DZ male twins) of the 112 values present were removed. This left sample sizes of 79 MZ female, 60 MZ male, 45 DZ female, 41 DZ male and 47 DZ male-female twin pairs. The age range was consequently reduced to between 9 and 46 years. The percentages of values missing for the 596 original, and 544 remaining, individual twins are listed in Table 8.1.

In order to examine the effect of imputation, six variables were chosen, having between 2 and 29% of their values imputed. A full set of covariance models (E, AE, CE, ACE and ADE) was applied to each variable, with data being entered as VL files (no listwise deletion or imputation), raw imputed data, and variance-covariance matrices of imputed data. It was assumed there were four likely impacts of imputation: (1) an increase in bilateral symmetry due to substitution of values from the opposite side of the dentition; (2) an increase in common environmental component of variation due to substitution from the other twin and also due to substitution of the mean, since this would be done for both members of a SS twin pair; (3) a possible decrease in common environment due to inclusion of OS twins with substitution of their respective sex-means; and (4) a decrease in non-additive

genetic variation due to confounding with the (spurious) common environment (Martin *et al.* 1978). Since few of the imputations involved substitution from the other side (varying from 1 to 5% of the data set), it was assumed that the first impact was not likely to be significant. In addition, antimeres were not included in any of the multivariate analyses. As a result, only the effects on estimated common environmental variation and non-additive genetic variation were analysed.

**Choice of Data Subsets for Multivariate Analyses**

Which variables should be analysed together? Anything from two to 56 variables could have been chosen. It would have been ideal to study the 56 dimensions of the entire dentition, so that relationships among teeth, dimensions, and maxillary and mandibular arches could have been examined. The main restrictions involved the number of variables which could be analysed at one time by Mx (up to 11), and the amount of memory on the mainframe computer, while biological theory dictated which subsets of variables were of interest. The optimal groupings chosen from these criteria were the seven teeth within each oral quadrant, with MD and BL diameters being analysed separately. This allowed testing of Butler's field theory of development of the dentition, and testing for common and unique genes or groups of genes contributing to different tooth groups, and different members of the same tooth group.

In addition, the MD dimensions of the eight incisors were analysed early in the study. The advantages of analysing such tooth groups include the ability to test if antimeres, or maxillary and mandibular teeth, are determined by the same factors, thus testing two previous findings (Potter *et al.* 1976).

Next, consideration was given as to whether to analyse one or both sides of the dentition. Although it is of interest to determine whether both sides exhibit the same covariance structure, there is a certain degree of overlap in analysing both sides of the dentition. This is partly because of the high degree of bilateral symmetry, and partly because multivariate analyses were based on imputed data files, with missing values being substituted from the other side of the dental arch if that tooth was present and measurable. Since only 1 - 9% of values were substituted from the antimere, the second source of overlap was not considered serious.

The analyses of multivariate vectors of means and initial Cholesky decomposition of variance-covariance matrices were carried out on eight subgroups of data - MD and BL dimensions of the four oral quadrants. Constraints on time and computer space, and the principle of diminishing returns, resulted in the multivariate analyses of covariance structure being restricted to the MD diameters of the eight incisors, and MD and BL dimensions of the maxillary right quadrant.

Since the methods changed somewhat between the incisor analysis and that of the oral quadrants, the discussion section includes a comparison of strategies.

### Notation used for models of variance-covariance matrices

Due to the complexity of representing the factor structure of any given model, a system of notation was derived. For instance, Figure 8.1 depicts a model for the additive genetic variance component in this multivariate study. There is a general factor (subscript G) acting on all seven teeth, with specific factors (subscript S) acting on individual teeth. The path coefficients are numbered 1 to 7 for the former and 8 to 14 for the latter. An alternative way of depicting this model is with a matrix notation, as used by Mx (Figure 8.2).

Group factors (subscript R) also may be applied, and would appear as single latent factors with paths leading to at least two variables (see Figure 8.3). Any given path coefficient may be constrained to be the same as another by allocating the same number to each. Different numbers mean that the coefficients are allowed to vary. Thus in Figure 8.3, the estimated path coefficients for the general factor are constrained to be the same within incisor, premolar and molar tooth groups. The matrix notation for this model is depicted in Figure 8.4.

The figures depicting which models were fitted are presented in the Results section rather than in the Methods section. This enables easier cross-reference between the models and the results of fitting them. In specifying the models, the numbers 1-14 have been used in the representations of all four matrices, whereas in the programming they were 1-14 for A, 51-64 for E, 101-114 for D and 201-214 for C. The numbers 1-14 were chosen for simplicity, and are not meant to suggest equivalence of parameters *between* matrices.

**Incisors - Multivariate Modelling of Covariances**

The multivariate analysis of incisors was conducted for each sex separately, and comprised three main steps, each of which utilised the best model from the previous step. Only the covariance structure was explored. In the first stage, Cholesky decomposition models were applied to all eight variables. A Cholesky decomposition is a lower triangular matrix of variances and covariances, and corresponds to a principal components analysis. These models estimate all possible paths of covariation in an attempt to account for as much variation as possible, having as many factors as there are variables and as many loadings as there are observed correlations. Simpler models will display a worse fit than this by the $\chi^2$ criterion, but

are preferred if more parsimonious (as estimated by AIC) or more appropriate on theoretical grounds. See Appendix B for a more detailed description. As in the univariate analysis, E, CE, AE, ACE, and ADE models were applied.

In the second stage, principles of parsimony and biological theory were used to test models involving combinations of factors loading on all eight incisors ("general" factors) and factors loading on one or more pairs of incisors ("group" factors). Once a favourable genetic model was determined, the third step involved the same approach to elucidate the structure of the unique environmental covariation. Finally, $\chi^2$ tests of heterogeneity between male and female data were applied to the most parsimonious models, by adding the $\chi^2$ values for the fits of the model to male and female groups separately, and then subtracting this sum from the $\chi^2$ generated by fitting the model jointly to the four groups of SS twins. Heritability estimates also were obtained.

**Quadrants - Multivariate Modelling of Means**

Exploration of the data for the maxillary right quadrant followed a different path. Before analysing the covariance structure, the means were modelled multivariately, as in univariate analyses.

Eight models were included in the design, with model numbers reflecting the number of unconstrained means. As in the univariate phase, all twins were constrained to have the same mean in the first model (Model 1), then female and male twins were allowed different means, with the added constraint that the male mean equalled the female mean multiplied by a constant, k (Model 1k). Model 2 provided for two independent means for the sexes. For Model 3f, OS females were allowed to vary from SS females. Model 3m permitted OS males to vary from SS males, while

Model 4 permitted SS and OS twins to vary within both sexes. These models tested for differences in mean tooth crown size between SS and OS twins within each sex. Model 5 permitted MZ and DZ males to have separate means, while constraining MZ and DZ females to have the same mean. Model 6 removed all constraints of equality, except between co-twins of SS pairs, yielding six separate means. Including Models 5 and 6 allowed testing of the freeing of MZ and DZ SS twins within each sex separately.

Again, the simplest acceptable model was sought ($\alpha$=0.01), followed by models which were significantly better fitting ($\alpha$=0.01). AIC values were examined to see which model was best by this criterion, and models were checked across quadrants to look for patterns in their respective probabilities.

**Quadrants - Multivariate Modelling of Covariances**

Cholesky decomposition models for all parameters were applied to the data. As in previous analyses, E, CE, AE, ACE, and ADE models were applied. Since models fitted to a large number of variables or a large sample usually results in rejection of the model, the fits of these models to the data were compared with that of a null model - one with only a unique environmental specific factor. In a null model there is no covariance between variables or between twins. Mx provides a number of fit statistics comparing these two models. Provided many of the statistics are greater than 0.9, the model is considered to have a good fit. In addition, the latest version of Mx (1.41, June 1997) provides a measure of goodness-of-fit which is relatively independent of sample size - RMSEA. If this statistic is less than 0.1, the fit is considered good. A very good fit occurs when RMSEA falls below 0.05.

The various models were compared to see if any were adequate in comparison with null models; then if any were significantly better by $\chi^2$ ($\alpha$=0.05); and finally, which was best by AIC. Output from the chosen models was examined to look for patterns among the parameter estimates which were suggestive of important factors. These were then incorporated into a variety of models. The aim was to reduce the number of parameters as much as possible. As in the univariate analysis, biological principles also were built into models.

Details of the models fitted are listed in the results section. For each parameter, the first models were: general factor alone; specific factors alone; then general and specific factors. Substitution of group factors for specific factors was attempted in some cases, and various patterns of constraints within general and/or specific factors were tested. $\chi^2_{diff}$ coefficients were calculated to compare models ($\alpha$=0.05), and AIC and RMSEA were calculated and compared.

When a model was finally selected, multiple Mx runs using TH (for "try hard") = 10 were performed to force Mx to try to find a better solution. If all ten runs yielded the same parameter estimates and $\chi^2$ value, the model was deemed to be identified. Standardised parameter estimates were derived from this model and summed to give broad and narrow heritabilities for each variable. Path diagrams were constructed to illustrate each model.

## Results

### Impact of Imputations

The simplest adequate model and the parameters found to be significant, are listed in Table 8.2. Imputing effects occurred in two variables - the maxillary right canine MD

length (15% imputed) and mandibular left second molar (29% imputed). Using unimputed (VL) data, the canine displayed significant nonadditive genetic effects, and ADE was the only acceptable model by $\chi^2$ (p>0.01). In the parallel analyses of raw data and variance-covariance matrices, *d* was still significant, but the AE models were adequate (p>0.01). This is consistent with the prediction that where both nonadditive genetic and common environmental effects (even if spurious) coexist, they will inflate the additive genetic, and deflate the non-additive genetic, components of an ADE model, or deflate the common environmental component of an ACE model (Martin *et al.* 1978). For the second molar, a significant common environmental component was found in spite of lack of evidence for this in the co-twin correlations. This is assumed to be due to the imputations since there was no evidence of common environment when VL files were used.

The main effects of imputation seem to have been a slightly deflated estimate of nonadditive genetic variation, and a possible increase in common environment, which was not a problem until imputations from the other twin or the mean reached 29%. Since the trials were limited to univariate analysis involving six variables, caution was employed in interpreting the results of multivariate modelling, especially where common environment, nonadditive genetic variation and bilateral symmetry were concerned.

**Incisors - Multivariate Modelling of Covariances**

The models applied to the incisor data are listed in Figures 8.5 and 8.6. The results of the first stage were consistent with those of univariate analyses, in that AE models displayed the best fit for each sex (see Table 8.3). In the second stage, one of the best fitting models for additive genetic covariation (Model A4) comprised a general factor and four group factors, one each for the antimeric pairs of incisors. None of the more

complex models (Models A1 to A3) yielded significant improvements in fit. From Model A4, the general genetic factor alone was demonstrated to be insufficient, with the differences in $\chi^2$ values between Models A4 and A5 being 193.3 for females and 169.1 for males (8 df; $p<0.001$). The group factors for antimeric tooth pairs also were insufficient on their own, with $\chi^2_{diff}$ values between Models A4 and A6 being 183.2 for females and 173.1 for males (8 df; $p<0.001$).

For females, the fit improved when symmetry constraints were applied to the additive genetic factors (Model A9). The model for male data was improved by symmetry constraints on all but the general genetic factor, which was better left unconstrained (Model A8). The $\chi^2$ value increased by 18.2 (4 df; $p<0.001$) when the general genetic factor was constrained (Model A9).

The third step investigated the environmental covariation, using the best fitting model for additive genetic covariation. This equated to Model A9 for females, and Model A5 for males. Since heterogeneity testing for sex differences requires both sexes to have the same model, and the data for females displayed a better fit, Model A9 was chosen for both sexes.

The largest factor loadings from the Cholesky decomposition of unique environmental variation were on the diagonal of the matrix. This suggests that the effects of environment on each tooth separately, were greater than on any groupings of the teeth. The second highest loadings involved antimeric teeth. Exploration of the unique environmental covariation thus began with models comprising a general factor impacting on all eight incisors and eight specific factors, one for each tooth.

In applying these submodels for unique environmental covariation, the shift from Cholesky decomposition to one general and eight specific factors improved the fit for

males, but worsened it for females with $\chi^2_{diff}$ = 68.3 (20 df; p<0.001). As with additive genetic variation, the differences in $\chi^2$ values between models indicated that unique environmental covariation contained both group and specific factors. The model with a general factor alone (Model E2) was so unlikely it resulted in a nonsensical $\chi^2$ and probability level. Comparing Models E1 and E3 yielded $\chi^2_{diff}$ = 73.6 for females and $\chi^2_{diff}$ = 23.5 for males (8 df; p<0.01). Symmetry constraints on all factors improved the fit for both sexes (Model E4).

The path diagram for this model is depicted in Figure 8.7. The standardised estimates of additive genetic and unique environmental components are summarised in Figures 8.8 and 8.9. Broad heritability estimates ($h^2$) ranged from 0.81 to 0.91 in females, and from 0.84 to 0.89 in males (Figure 8.10).

Model E4 (incorporating A9) was used to test the data for heterogeneity of fit between sexes. This model produced a goodness-of-fit of $\chi^2$ = 338.3 for females, $\chi^2$ = 352.0 for males (256 df; p<0.001), and $\chi^2$ = 724.1 (528 df; p<0.01) when fitted to all four same-sexed matrices. Subtracting the sum of the $\chi^2$ values for the sexes considered separately from the third, joint fit, gave a heterogeneity chi-square of $\chi^2$ = 33.8 (16 df; p<0.01), indicating significant heterogeneity between female and male twins.

**Quadrants - Multivariate Modelling of Means**

The models and their designated numbers are listed in Table 8.4. The results of modelling the means are contained in Tables 8.5 and 8.6.

As in the univariate analysis, the model with a single mean for all twins was rejected confidently (p<0.001) in all eight analyses. Model 1k was also rejected (p<0.01) in

five analyses - the exceptions being the BL dimensions of maxillary right ($p=0.01$) and left ($p=0.06$) and mandibular right ($p=0.02$) quadrants. These models were associated with very low probabilities and all were significantly improved by more complex models - Model 2 in the mandibular right quadrant ($p<0.001$), Model 3f in the maxillary right quadrant ($p<0.01$), and Model 3m for the maxillary left quadrant ($p<0.01$). The simplest adequate model for the other five analyses was that of two means, one for each sex, the probabilities for which ranged from 0.111 to 0.845.

In six of the analyses, Model 2 was the best by AIC. The remaining two analyses were of the BL breadths of maxillary right and left quadrants. For the left quadrant, Model 3m was significantly better than Model 2 ($\chi^2_{diff} = 20.45$; $p<0.01$). The same was almost true for Models 2 and 3f in the right quadrant ($\chi^2_{diff} = 18.30$; $p<0.02$). This suggests a slight difference between mean BL breadths of maxillary teeth in SS and OS twins. The analysis for the left quadrant was the only one in which any model was significantly better than Model 2 when $\chi^2$ values were compared. For consistency, a model with separate means for each sex was chosen for the analysis of covariance structure which followed.

The degree of dimorphism as estimated by the parameter, $k$ in Model 1k ranged from 1.03 to 1.05, so female tooth crown size averaged over each of the quadrants, ranged from 95 to 97% of that in males.

In examining further patterns in the output, one consistent finding was that permitting MZ and DZ SS twins to have separate means tended to worsen the fit of the model within each sex. The differences were *not* significant ($p>0.05$) but were consistent. Of the 16 comparisons of Models 4 with 5, and 5 with 6, AIC values increased (became less negative) in all and the probabilities decreased in 14, indicating decreasing parsimony tended to be accompanied by decreasing goodness-

of-fit. Conversely, permitting SS and OS twins to have different means was mostly associated with a (non significant) decrease in parsimony accompanied by a slight increase in goodness-of-fit (Models 3f and 3m compared with 4).

In conclusion then, there was no clear evidence of a difference in the mean tooth sizes of MZ and DZSS twins, or of SS and OS twins within either sex, although there may have been a trend towards larger differences between SS and OS twins than between MZ and DZSS twins. This finding, and the choice of Model 2, parallel the findings of the univariate analyses.

### Quadrants - Multivariate Modelling of Covariances

*Cholesky decomposition of variance-covariance matrices*

All of the Cholesky decompositions resulted in probabilities which were less than 0.05, with most being less than 0.001 (Tables 8.7 and 8.8). In comparison with a null model however, AE, ACE and ADE models displayed a relatively good fit, while E and CE models did not. There was remarkably little variation in these statistics across the eight analyses, so statistics for only one quadrant are displayed, those of MD dimensions of teeth in the maxillary left quadrant (see Table 8.9). RMSEA values in Tables 8.7 and 8.8 reflected the comparisons with the null model, being 0.18 to 0.21 for E models and 0.11 to 0.14 for CE models, suggesting a poor fit. AE models ranged from RMSEA = 0.05 to 0.11, while ACE and ADE models yielded RMSEA = 0.06 to 0.11. The only quadrant without a good fit for the last three models was that of the BL diameters in the maxillary left quadrant (RMSEA>0.107). For this quadrant, AE was the best model.

When (Cholesky) AE models were compared with ACE and ADE models using $\chi^2$ of the differences, neither C nor D was significant in any of the analyses (p>0.95 for C in MD, p>0.10 for C in BL, p>0.70 for D in MD, p>0.80 for D in BL). Modelling thus proceeded in four main stages. Firstly, the structure of the A matrix was explored in an AE model, while the Cholesky decomposition model was retained for the E matrix. Using the best A matrix, the structure of the E matrix was investigated next. Although not significant, D and/or C may improve the fit of a model, so D factors were added to the best AE model, and then C factors were added to the best ADE model. The particular structures chosen for each model were derived partly from the results of the Cholesky decomposition analyses, and partly from knowledge of ontogenetic theories of, and correlations within, the dentition.

*Exploration of additive genetic variation - MD dimension*

The models fitted to the matrices of additive genetic variation are listed in Figure 8.11. The $\chi^2$, df and AIC for each model are contained in Table 8.10, while Table 8.11 has statistics for comparisons of models. Model A1 was the best by both RMSEA and AIC. Only Models A1 and A14 demonstrated a good fit to the data, with RMSEA > 0.1 for all other models. The results for Models A1 to A3 indicate that fitting both general and specific factors was better than either alone (p<0.001). Specific factors fitted better than group factors, but no probability was calculable because they had the same degrees of freedom. Removing equality constraints from all parameters in general and specific factors improved the fit of the model considerably (p<0.05 to p<0.001). Thus model A1 was chosen as the best model for additive genetic variation.

*Exploration of unique environmental variation - MD dimension*

The models fitted to the matrix of unique environmental variation are listed in Figure 8.12. The $\chi^2$, df and AIC for each model are contained in Table 8.12, while Table 8.13 has statistics for comparisons of models. Model E6 was the best by AIC and equal best by RMSEA. Models E1 and E4 to E9 displayed a good fit by RMSEA. Comparing Models E1 to E3, including both general and specific factors was better than either alone ($p<0.01$). For the general factor, equality constraints within the incisors and within the remaining five teeth were significantly better than having a constraint across the whole factor ($p<0.02$). Removing all constraints on the general factor did not significantly improve the fit ($p>0.30$). As for equality constraints on the specific factors, freeing all seven parameters proved significantly better than any pattern of constraints tested. Thus, model E6 was chosen as the best model for unique environmental variation.

*Exploration of non-additive genetic variation - MD dimension*

The models fitted to the matrix of non-additive genetic variation are listed in Figure 8.13. The $\chi^2$, df and AIC for each model are contained in Table 8.14, while Table 8.15 has statistics for comparisons of models. Model D17 was the best by AIC and RMSEA. Only model D3 (specific factors alone) did not have a good fit by RMSEA. Comparisons of Models D1 to D5 indicate that: addition of specific factors to a general factor did not improve the fit ($p>0.80$); tooth group factors were better than specific factors ($\chi^2_{diff}=28.83$, df=0, p incalculable); and fitting both general and group factors was better than fitting either alone ($p<0.001$). Exploring the pattern of group factors (D6 to D8), the best model had one factor for the incisors and another for the remaining five teeth (D6). The parameter estimates for first and second

molars in the second group factor were very low, and their inclusion did not significantly improve the fit of the model ($p>0.30$). The second premolar exhibited the next-lowest parameter estimate, but could not be excluded from the model without significantly affecting the goodness-of-fit ($p<0.001$). Constraining the general factor within anterior and posterior groupings was significantly better than constraining across the seven parameters ($p<0.01$), while freeing all seven did not improve the model further ($p>0.30$). As for the group factors, the incisor factor could be constrained without significant loss of goodness-of-fit ($p>0.20$), but the canine-premolar factor could not ($p<0.001$). Thus model D22 was chosen as the best model for non-additive genetic variation. Inclusion of D22 significantly improved the fit of the model when compared with the former AE model ($\chi^2_{diff} = 94.99$, df=6, $p<0.001$).

*Exploration of common environmental variation - MD dimension*

The models fitted to the matrix of common environmental variation are listed in Figure 8.14. The $\chi^2$, df and AIC for each model are contained in Table 8.16, while Table 8.17 has statistics for comparisons of models. Model C9 was the best by AIC. All models displayed a good fit by RMSEA, ranging from 76 to 79, with C8 being the best. The results for Models C1 to C5 indicate that combining general and specific factors, or general and group factors, was not significantly better than models with general, specific or group factors alone. Of the three, the general factor alone had the lowest AIC and RMSEA.

Within the general factor, the first molar had the highest parameter estimate (0.25). A model with this parameter alone (C12) resulted in a good fit by RMSEA (0.078). Adding the second premolar *or* second molar did not improve the fit ($p>0.10$, $p>0.70$, respectively). Significant improvement was achieved by adding the second

premolar *and* second molar (model C8, $p<0.05$) or first *and* second premolar (model C9, $p<0.02$) to the first molar. There was little difference in goodness-of-fit between Models C8 and C9, with C8 having a lower RMSEA, while C9 had a slightly lower AIC. This suggests that either the first premolar or second molar must be present with the second premolar and first molar, and since it was impossible to distinguish between C8 and C9, model C7 (covering first premolar to second molar) was retained. Including the incisors did not elevate the goodness-of-fit ($p<0.20$), while exclusion of the canine, which had the lowest parameter estimate, actually increased the goodness-of-fit of the model ($\chi^2_{diff}$= -2.28).

Testing constraints on model C7 (posterior tooth group factor), freeing the first premolar and first molar was the only model which led to a significant improvement in fit ($p<0.05$), while freeing all four did not ($p>0.50$). Thus model C17 was chosen as the best model of common environmental variation. Inclusion of C17 significantly improved the fit of the model when compared with the ADE model ($\chi^2_{diff}$ = 11.92, df=3, $p<0.01$).

*Final model - maxillary right MD dimension*

The final model for MD dimensions in the maxillary right quadrant is represented by a path diagram in Figure 8.15, while contributions of the four parameters are displayed in Figures 8.16 to 8.19. Parameter estimates are listed in Tables 8.18 (unstandardised), and 8.19 (standardised). Broad heritabilities are displayed in Figure 8.20.

*Exploration of additive genetic variation - BL dimension*

The models fitted to the matrix of additive genetic variation are listed in Figure 8.21. The $\chi^2$, df and AIC for each model are contained in Table 8.20, while Table 8.21 has statistics for comparisons of models. Model A5 was the best by AIC. The results for Models A1 to A20 indicate that both general and specific factors were required. Specific factors fitted better than group factors, but no probability was calculable because they had the same degrees of freedom. Equality constraints within the general factor could be applied to parameters such that I1=I2=C, and P1=P2=M1=M2. For the specific factors, freeing all seven parameters was significantly better than any pattern of constraints attempted. Thus model A5 was chosen as the best model for additive genetic variation.

*Exploration of unique environmental variation - BL dimension*

The models fitted to the matrix of unique environmental variation are listed in Figure 8.22. The $\chi^2$, df and AIC for each model are contained in Table 8.22 while Table 8.23 has statistics for comparisons of models. Model E14 was the best by AIC. The results for Models E1 to E15 indicate that general and specific factors were required. Tooth group factors were not tested since the loadings from the Cholesky decomposition strongly suggested specific factors were important. Equality constraints were successfully applied to general and specific factors such that for the general factor, I1=I2=C; P1=P2; and M1=M2. For specific factors, I1=I2; C=P1=P2; and M1=M2. Thus model E15 was chosen as the best model for unique environmental variation.

*Exploration of dominance genetic variation - BL dimension*

The models fitted to the matrix of non-additive genetic variation are listed in Figure 8.23. The $\chi^2$, df and AIC for each model are contained in Table 8.24, while Table 8.25 has statistics for comparisons of models. Model D22 was the best by AIC. The results for Models D1 to D22 indicate that tooth group factors gave a much better fit than tooth-specific factors, regardless of whether or not a general factor was present. Again, the comparison could not be assessed statistically, due to a lack of difference in degrees of freedom, but the $\chi^2_{diff}$ was 53.67 between the two when a general factor was present. Neither general nor group factors could be excluded without significant worsening of fit of the model. Of the four tooth group factors, only the molar factor was responsible for the improved fit of the general model, so the other factors were excluded. Within the general factor also, only the incisors and premolars were required. The canine and molars could be excluded without significant reduction in goodness-of-fit. Thus, two group factors remained - one including the incisors and premolars, and the other covering both molars. Equality constraints within the model were set up such that I1=I2; P1=P2; and M1=M2. Freeing the six parameters did not yield a significant improvement in fit. Thus model D22 was chosen as the best model for non-additive genetic variation. Comparing the best AE model with that including D22, there was significant improvement in fit by including this model of non additive genetic variation ($p<0.001$).

*Exploration of common environmental variation - BL dimension*

The models fitted to the matrix of common environmental variation are listed in Figure 8.24. The $\chi^2$, df and AIC for each model are contained in Table 8.26, while Table 8.27 has statistics for comparisons of models. Model C8 was the best by AIC. The results for Models C1 to C12 indicate that tooth group factors were preferable to tooth-specific factors, whether or not a general factor was present ($\chi^2_{diff}$ =12.74

when general factor was present). Once again, the comparison could not be assessed statistically, due to a lack of difference in degrees of freedom. The group factors could not be excluded from the general factor without significant reduction in fit. However, the general factor did not improve the fit of the group factors, and was excluded. Of the seven parameters in the group factors, only those of the two molars were significant. Allowing the two molar parameters to be unconstrained yielded a significant improvement in fit. Thus, model C8 was chosen as the best model for common environmental variation. Comparing the best ADE model with that including C8, there was significant improvement in fit by including common environmental variation ($p<0.001$).

*Final model - maxillary right BL dimension*

The final model for BL dimensions in the maxillary right quadrant is represented by a path diagram in Figure 8.25, while contributions of the four sources of variation are displayed in Figures 8.26 to 8.29. Parameter estimates are listed in Tables 8.28 (unstandardised), and 8.29 (standardised). Broad heritabilities are displayed in Figure 8.30.

## Discussion

### Sexual Dimorphism

There was significant sexual dimorphism for mean tooth crown size, since the means could be constrained to be equal across zygosities within each sex, but not across sexes. The degree of dimorphism was low, ranging from female means being 95 to 97% of male means. It was very similar in MD and BL diameters (95 to 96% in MD versus 96 to 97% for BL). These results are consistent with the univariate analysis

and with expectations from the exploratory data analyses in chapter 3. Modelling the variances and covariances did not reveal any sex-limited effects, even in BL diameters of the maxillary teeth.

**General Tooth Size Factors**

There were three general size factors influencing MD diameters of all seven teeth in the maxillary right quadrant - additive and non-additive genetic, and unique environmental factors. Of the three, unique environment was the lowest, accounting for at most 2% of the total variation. Additive genetic general factors contributed between 2 and 53% while non-additive genetic factors accounted for 14 to 54%. For BL diameters, only two general factors were required - additive genetic and unique environmental factors. Again, the latter accounted for at most 5% of the total variation, while the former contributed between 38 and 58%. A third potential general factor, non-additive genetic variation, was reduced to an incisor + premolar group factor when it was found that the canine and molars could be excluded. The incisor analysis also revealed significant additive genetic and unique environmental factors which impacted on the eight incisors mutually.

The incisor analysis incorporated right and left, as well as maxillary and mandibular teeth. Combining the incisor general factors with those from the quadrant analyses prompts the suggestion that they represent general size factors influencing all 28 permanent teeth. An expansion of the analysis to incorporate both diameters of the 28 permanent teeth would be required to confirm this.

The presence of general size factors of genetic origin would not be surprising, since there would be a need to coordinate the sizes of structures in the craniofacial region (as elsewhere) to ensure adequate functioning. Such a genetic factor has been

reported previously (Potter *et al.* 1976). The presence of a non-additive genetic size factor for MD, and possibly for BL, diameters, suggests that this coordination is, or was, related to fitness during human evolution (Fisher 1958).

The unique environmental (general) factors also may reflect a factor affecting more than just the teeth. Nutritional differences (in utero or post natally), twin transfusion syndrome, birth complications or neonatal health problems for one twin and not the other, are some of the environmental factors which could lead to an overall size difference (of the whole body, cranium, maxilla or mandible) between MZ twins, reflected also in the general size of their deciduous and permanent teeth. It also may be due, at least in part, to a consistent measurement error. However, this type of effect had the lowest contribution to correlations among teeth, being far lower than the unique environmental influences specific to each tooth, or any of the genetic factors. This is consistent with a statement by Potter *et al.* (1976) that the correlation among tooth dimensions is primarily genetic in origin.

**Factors Acting on Specific Teeth**

In addition to the general factors, there were additive genetic and unique environmental factors that were specific to each tooth (or each antimeric tooth pair for the incisor analysis). This was the case for both MD and BL diameters, but it is unclear whether the factors were the same ones for both dimensions, or separate ones for each. The implication is that there was a group of genes of additive effect specifically affecting each tooth (with possibly the same or different sets of genes for MD and BL dimensions). This is surprising, given the close similarity of, and correlation between, members of each tooth group, especially the premolars and molars. The finding correlates with those of Osborne *et al.* (1958), Lundström (1964), Moorrees (1964), and Goose (1970), but not with Potter *et al.* (1968),

Townsend and Brown (1979a) or Mizoguchi (1980, 1981) who found genetic factors corresponded with the four tooth groups, or with anterior and posterior teeth.

Unique environmental factors also impacted on each tooth individually, considerably more so than did the general unique environmental factor. This fits reasonably with expectations, given that the seven teeth vary considerably in the timing of their development, both in chronology and length of each stage in development. Hence, some teeth are exposed to different environmental factors or to the same ones for a longer time period.

**Non-additive Genetic Factors - Quadrant Analyses**

For MD diameters in the maxillary right quadrant, there was a general non-additive genetic factor. In addition, the incisors exhibited the presence of a non-additive genetic factor (about 21%), as did the canine and premolars combined (1 to 23%). The molars exhibited the lowest total non-additive genetic variation, about 15%, with the other teeth ranging from 40% (for second premolar) to 54% (for canine and first premolar).

Surprisingly, there was no significant non-additive genetic variation present in the BL diameter of the maxillary canine. Instead, there was a factor covering the incisors (8 to 9%) and premolars (13 to 15%), and a second one on the molars (7 to 9%). BL diameters thus showed substantially lower non-additive genetic variation than MD diameters. It is possibly the result of natural selection operating mainly on the MD diameters, since BL and MD diameters of each tooth are reasonably highly correlated ($r = 0.35$ to $0.74$ - see chapter 3).

As previously noted, the presence of dominance variation may indicate selective pressures acting either currently or sometime in the past (Fisher 1958). Accordingly, there may be, or may have been, a relationship between reproductive fitness and:

- MD diameters of maxillary teeth;
- MD diameters of maxillary incisors;
- MD diameters of maxillary canine and premolars;
- BL diameters of maxillary incisors and premolars;
- BL diameters of maxillary molars.

**Common Environmental Factors - Quadrant Analyses**

Common environment seemed to have an effect on MD diameters of posterior teeth, and on BL diameters of both molars. In both dimensions, the factors were most strongly concentrated on the first molar (29% for BL, 17% for MD). The BL diameter of the second molar was next highest (17%), followed by MD diameter of first premolar (6%), second premolar (0.1%) and second molar (0.04%). Although the standardised estimates for MD diameter of second premolar and second molar were low, they could not both be excluded from the analysis without significant worsening of fit.

Among these percentages there is evidence of a negative association with the chronological order of calcification. As the length of time a tooth takes to calcify increases, so the contribution of shared environment to total phenotypic variation decreases. The first molar begins calcification at about the time of birth and is the first tooth to be completely formed. The next posterior tooth to begin calcification is the first premolar, beginning at about 1.5 years of age (Logan & Kronfeld 1933, Haavikko 1985), and shows the third highest percent common environmental variation. Second premolars and second molars begin calcification at about 2.5 years.

This at first seems contradictory since it is most likely that a tooth will respond to environmental (and genetic) stimuli only until it has calcified. One possible explanation for the phenomenon is that the most potent source of common environmental variation for a pair of twins may occur in utero, or around the time of birth. Since the first molar begins to calcify at about the time of birth, it is most likely that uterine (maternal) or neonatal effects will be preserved in its final shape more readily than in other teeth. As the length of time prior to calcification increases, there is more chance that the effect will be negated by other genetic and environmental factors.

Spurious common environmental variation due to the imputation procedure is not likely to be the cause of this in all posterior teeth, since the first molar had one of the lowest rates of imputation (8% for MD, 4% for BL), and the second molar had the highest. Only the finding of significant common environmental variation in the BL diameter of the second molar (17% of total phenotypic variation) seems to require caution in its interpretation, since it may have been caused, or contributed to, by imputation.

Is there any evidence for post-natal common environmental effects? These would be indicated by higher contributions to later-forming teeth, and to BL than MD diameters. Since both phenomena were observed, the answer is yes. Firstly, second premolars and second molars exhibited low levels of common environmental variation in both multivariate and univariate analyses (possibly due to imputation-derived difficulties). For the univariate analyses, CE models were acceptable for three maxillary variables - the right second premolar MD diameter, and both dimensions of the left second molar. This coincides with the greater environmental variation in distal members of tooth groups predicted by Butler's field model of the

dentition (Butler 1939, Dahlberg 1945). Secondly, contributions to BL diameters were greater than to MD ones for both molars (29 versus 17% for first molar and 17 versus 0.04% for second molar). However, evidence for post-natal environment forming part of the common environmental effects in twins is weaker than that of pre- or peri-natal factors, and may be due to imputation-derived spurious common environmental variation.

**Functional Units in the Dentition**

Variable groupings within factors, as well as the patterns of equality constraints, may provide insight into functional units within the dentition. These may be defined as groups of teeth which interact during mastication or other tooth-related activities, and whose size and/or shape may have been partly determined by co-evolution.

In terms of which teeth were grouped together into the 19 factors, seven were general factors, five were tooth-specific (ie five matrices included seven tooth-specific factors), one contained antimeric pairs of incisors, and six involved subsets of the four tooth groups - two involved both molars, and one each were I1+I2, I1+I2+P1+P2, C+P1+P2, and P1+P2+M1+M2.

Of the 19 factor patterns across the analyses for both diameters, six were completely unconstrained (individual teeth were allowed their own loadings), one was unconstrained except that P2=M2, eight were constrained within tooth groups (I, C, P and M), one had tooth group constraints but I=C, two were constrained within anterior and posterior tooth groups, and one was constrained within incisors and within the other five teeth.

Thus there was some indication of the importance of the four tooth groups, or of the anterior and posterior tooth groups, providing support for Mizoguchi's (1980, 1981) suggestion of functional units in the dentition. In particular, four of the six factors which incorporated tooth groups came from the analyses of non-additive genetic variation in the quadrants. The members of these functional units thus may have coevolved in response to natural selection.

By contrast, there was evidence that variation in tooth crown size was more often the result of factors affecting the seven maxillary permanent teeth together, or each tooth individually, than in the four tooth groups, or in anterior/posterior tooth units. Evidence for Mizoguchi's theory mostly arose from patterns of constraints, suggesting that the various genetic and environmental influences often affected teeth within the two (anterior versus posterior) or four (I, C, P, M) tooth groups equally.

**Comparison with Previous Studies**

Some of the genetic factors reported by other researchers were in agreement with those derived in this study. For instance, a general genetic factor acting on maxillary teeth (Potter *et al.* 1976), independent genetic factors on each tooth (Lundström 1964, Moorrees 1964, Goose 1970) and a genetic factor affecting the variability of the maxillary lateral incisor (Osborne and DeGeorge 1959, Horowitz *et al.* 1958). The nearest correlate of the last factor was the additive genetic factor which was specific to the maxillary lateral incisors. Furthermore, the incisor analysis provided support for antimeres being associated with the same genetic factor (Potter *et al.* 1976).

Conversely, there was little or no evidence of an anterior tooth genetic factor (Osborne and DeGeorge 1959), or a genetic factor acting on the anterior mandibular

teeth (Potter *et al.* 1976). The closest findings were probably the general factors (both genetic and environmental) operating on the eight incisors. Since general factors also were present in the quadrant analyses, it might be assumed that these represent general factors operating on the whole dentition, rather than just on the anterior teeth. There also was no support for independent determination of maxillary and mandibular dentitions (Potter *et al.* 1976).

**Multivariate Estimates and Patterns of Heritability**

Estimates of heritability ranged from 81 to 91% for incisors, 70 to 89% for maxillary MD diameters, and 56 to 91% for BL diameters. Searches of the dental literature did not reveal any prior attempts to estimate heritability multivariately. This seems to be the first attempt to do so, hence the only comparisons possible are with univariate estimates. The values obtained were very similar to those derived from the univariate analyses in Chapter 7 (see Table 8.30), with differences in percentages mostly being less than 3%. Five variables had differences of 5% or more, with the two highest being the MD diameters of the first (11%) and second molar (8%). The multivariate analysis generated higher estimates for molars and the lateral incisor BL diameter. Overall, there was more concordance than might have been expected, given the extra non-additive genetic and common environmental factors identified in the multivariate analysis.

As described in the last chapter, a number of heritability patterns have been described in the human dentition. These include lower heritabilities in distal members of tooth groups than in mesial members (Moorrees 1964, Horowitz *et al.* 1958, Lundström 1964, Alvesalo and Tigerstedt 1974, Rebich and Markovic 1976, Mizoguchi 1977, Potter *et al.* 1978), and greater heritability of MD than BL dimensions (Moorrees 1964, Harzer 1987).

*Mesial versus Distal Teeth - Morphogenetic Field Theory*

Heritabilities also have been described as being higher in mesial than distal teeth within tooth groups (reversed in the mandibular incisors) according to the predictions of Butler's field theory. Lombardi (1975) maintained that MD and BL diameters should be analysed together to reveal true evidence of morphogenetic fields. However, no evidence for morphogenetic fields was revealed in his factor analysis of the permanent dentition, except when the dimensions were analysed separately. This suggests that there is no need to analyse the variables together, or no sign of morphogenetic fields in his data.

In the present multivariate analyses, no consistent pattern was found. In the incisor analysis, central incisors had a higher heritability than the laterals for both maxillary *and* mandibular teeth - there was no reversal of pattern in mandibular incisors. Although the significance of the differences was not tested, it is not likely they would have been significant, since the differences were only 3% for maxillary and 1% for mandibular incisors. In addition, only two of the six tooth pairs from the quadrant analyses displayed higher heritabilities in the mesial than distal member (two for MD and one for BL, differences ranged from 2 to 25%). Even if the differences were significant, the teeth with largest differences tended to show the reverse pattern (distal > mesial). There was thus no supporting evidence from this analysis of morphogenetic fields described by Butler (1939) and Dahlberg (1945). These findings are in agreement with those of the univariate analysis, and of Mizoguchi (1977) and Harzer (1987).

Little or no evidence was found to support the suggestion of compensatory interactions between earlier- and later-developing members of tooth groups (Sofaer

*et al.* 1971). These interactions among teeth have been postulated as being able to compensate for variability in amount of space in the jaws by maintenance of some phenotypic plasticity in later-forming teeth. That is, if earlier-forming teeth are relatively large, then later-forming teeth may compensate by being smaller. If this were the case, we might have expected to find a higher contribution of unique environmental variation on later forming teeth. This was the case only for MD diameters of maxillary right premolars. Mizoguchi (1983) also found no evidence of an influence between earlier- and later- developing teeth, except in the third molar.

*MD versus BL Diameters*

Why would MD and BL diameters have different heritabilities? There are at least three possibilities. Firstly, tooth crown calcification begins at the cuspal tip and moves towards the cervical region. Since MD and BL diameters often are measured at different heights on the tooth crown (especially in the incisors and canines), they can incorporate genetic and environmental influences operating at different times. BL diameters might be expected to exhibit a higher proportion of environmental variance (and hence lower heritability) since they remain in soft tissue form longer. Secondly, lower heritability of BL dimensions may be due to greater selective pressure on BL than MD diameters. Thirdly, lower heritability of MD diameters may be explained by the notion that phenotypic plasticity exists in teeth to allow later forming teeth to fit into an evolutionarily-reducing jaw length. This type of pressure, or compensatory interaction (Sofaer *et al.* 1971, Sofaer and MacLean 1972), would involve MD more than BL diameters, and should be reflected in greater environmental variation of MD diameters. The effect also would be strongest in later forming teeth.

A quick scan of Table 8.30 reveals that heritability estimates for MD diameters *were* larger than BL ones in five of the seven variables in the quadrant analyses, with the two premolars being the exceptions. The differences in heritability ranged from 1 to 14%, averaging 8.6%. No tests were performed for significance of the differences, but the differences were relatively small. It is unlikely that the difference between the two canine diameters (MD=87%, BL=86%) would have been significant.

Even looking at trends, there was no apparent association between differences in MD and BL heritabilities with differences in position each diameter was measured. Incisors and canines were no more different in their MD/BL heritabilities than premolars and molars. So, the overall trend as reported by other researchers was present, but it did not seem to be attributable to differences in timing of formation. Since MD diameters had higher heritabilities, the third effect listed above (phenotypic plasticity of MD diameters) is also unlikely.

The lower heritability of BL dimensions (if it exists) may reflect greater selective pressure on the BL diameters than on MD diameters, although this is not consistent with the finding of considerably lower contribution of non-additive genetic variation to total variation in BL diameters.

**Comparison of Methods - Incisors versus Quadrants**

There were several key differences in statistical procedure between the incisor and quadrant analyses. Firstly, there was no modelling of means or calculation of RMSEA for incisors. These facilities were later additions to Mx.

Secondly, the sexes were analysed separately in the incisor study. This permitted testing of heterogeneity between sexes. In the quadrant studies, greater emphasis was

given to fitting models parsimoniously. If the models did not fit the data well when all five twin groups were included, OS twins would have been excluded. If there was not sufficient improvement in fit, the sexes would have been analysed separately. Since there was no difficulty in finding adequate models for the five twin groups, it was deemed that there was no significant heterogeneity among the sexes or zygosities.

In both incisor and quadrant analyses, the AE Cholesky decomposition model was the best fitting model. Since adding C or D to these did not improve the fit, no further consideration was given to either in the incisor analysis. In the quadrant analysis, D and then C were added after the structure within A and E matrices was elucidated. The $\chi^2_{diff}$ tests indicated that the additions significantly improved the fit of AE and ADE models, respectively. This would seem to be a sensible way to proceed and is a refinement in procedure developed during the study.

## Conclusions

A number of conclusions can be drawn from the analyses in this chapter:

- There was significant sexual dimorphism in mean tooth size;
- These was no significant heterogeneity in covariance structure among sexes or zygosities;
- Most covariance structure could be explained by the presence of additive genetic and unique environmental variation, but including non-additive genetic and common environmental variation significantly improved the model;
- Additive genetic factors ranged from 26% (first premolar MD) to 86% (canine BL) of the variation;
- Non-additive genetic factors ranged from 7% (second molar BL) to 55% (canine MD) of the variation;

- Common environmental factors in the posterior teeth ranged from 0.04% (second molar MD) to 29% (first molar BL) of the variation;
- Unique environmental factors were mostly tooth-specific and ranged from 9% (second premolar BL) to 24% (central incisor BL) of the variation;
- There was evidence of general genetic and environmental factors determining overall tooth size;
- Beyond these, genetic and environmental factors were tooth-specific (mostly) or involved teeth within the four tooth groups;
- Symmetry between antimeres mostly had a genetic basis, since antimeres were influenced by the same tooth-specific genes, although both genetic and environmental factors had equal degrees of effect on the two sides;
- Some findings of previous studies were supported by this analysis, in spite of differences in methodologies and sample populations;
- There was a trend for heritabilities to be higher in MD than BL diameters; and
- There was no evidence of heritability patterns consistent with the presence of Butler's morphogenetic fields.

**Table 8.1:** Percentages of values that were missing before (original) and after (new) removal of twin pairs with many missing values.

| | Mesiodistal | | Buccolingual | |
|---|---|---|---|---|
| | **Original** | **New** | **Original** | **New** |
| *Maxilla* | | | | |
| **I1** | 4 | 3 | 6 | 3 |
| **I2** | 8 | 6 | 15 | 10 |
| **C** | 17 | 10 | 24 | 17 |
| **P1** | 28 | 22 | 27 | 20 |
| **P2** | 21 | 14 | 19 | 12 |
| **M1** | 9 | 8 | 5 | 4 |
| **M2** | 53 | 48 | 39 | 33 |
| *Mandible* | | | | |
| **I1** | 2 | 2 | 4 | 2 |
| **I2** | 2 | 1 | 6 | 3 |
| **C** | 9 | 3 | 21 | 14 |
| **P1** | 18 | 12 | 19 | 12 |
| **P2** | 22 | 15 | 21 | 14 |
| **M1** | 10 | 8 | 5 | 5 |
| **M2** | 55 | 50 | 33 | 26 |

**Table 8.2:** Results of modelling variables with different frequencies of missing values using variable length files (VL), raw imputed data (RAW) and imputed variance-covariance matrices (COV). Changes presumed to be due to imputation are highlighted in bold.

| | | | % | Simplest Adequate Model | | | Significant Path Coeffs | | |
|---|---|---|---|---|---|---|---|---|---|
| Variable | | | Imputed | VL | RAW | COV | VL | RAW | COV |
| Max R | I1 | MD | 2 | AE | AE | AE | *a* | *a* | *a* |
| Man L | M1 | MD | 7 | AE | none | AE | *a* | *a* | *a* |
| Max R | C | MD | 15 | ADE | **AE** | **AE** | *a,d* | *a,d* | *a,d* |
| Max L | P2 | BL | 15 | AE | AE | AE | *a* | *a* | *a* |
| Man R | P2 | BL | 17 | AE | AE | AE | *a* | *a* | *a* |
| Man L | M2 | BL | 29 | AE | ACE | ACE | *a* | *a,c* | *a,c* |

**Table 8.3** Results of the multivariate analysis of incisors in female and male twins. The best model in each section is highlighted in bold.

| | | Females | | | Males | | |
|---|---|---|---|---|---|---|---|
| **No.** | **df** | $\chi^2$ | **Prob** [a] | **AIC** | $\chi^2$ | **Prob** | **AIC** |
| **STEP 1: Cholesky models** | | | | | | | |
| **E** | 236 | 644.34 | ** | 172.34 | 647.98 | ** | 175.98 |
| **CE** | 200 | 360.71 | ** | -39.29 | 346.89 | ** | -53.11 |
| **AE** | **200** | **243.86** | **+** | **156.14** | **265.94** | ** | **134.06** |
| **ACE** | 164 | 236.74 | ** | -91.26 | 244.22 | ** | -83.78 |
| **ADE** | 164 | 236.65 | ** | -91.35 | 256.69 | ** | -71.31 |
| **STEP 2: Model 3, vary A.** | | | | | | | |
| **A1** | 206 | 243.86 | + | -168.14 | 271.11 | * | -140.89 |
| **A2** | 210 | 245.65 | + | -174.35 | 279.15 | * | -140.85 |
| **A3** | 212 | 244.63 | 0.062 | -179.37 | 276.19 | * | -147.81 |
| **A4** | 220 | 252.43 | 0.066 | -187.57 | **290.00** | * | **150.00** |
| **A5** | 228 | 445.76 | ** | -10.24 | 459.10 | ** | 3.10 |
| **A6** | 228 | 435.64 | ** | -20.36 | 463.06 | ** | 7.06 |
| **A7** | 224 | 254.20 | 0.081 | -193.80 | 311.46 | ** | -136.54 |
| **A8** | 224 | 257.11 | 0.064 | -190.89 | 299.15 | ** | -148.85 |
| **A9** | **228** | **258.96** | **0.078** | **197.04** | 317.32 | ** | -138.68 |
| **STEP 3: Model 15, vary E.** | | | | | | | |
| **E1** | 248 | 327.27 | * | -168.73 | 343.74 | ** | -152.26 |
| **E3** | 256 | 400.90 | ** | -111.10 | 367.28 | ** | -144.72 |
| **E4** | **256** | **338.34** | ** | **173.66** | **351.99** | ** | **160.01** |

[a] + = $p<0.05$; * = $p<0.01$; ** = $p<0.001$

**Table 8.4:** Mean models fitted to the six twin groups, and degrees of freedom associated with the $\chi^2$.

| Model | No. means | Means for | df |
|---|---|---|---|
| 1 | 1 | all twins | 63 |
| 1k | 1 | males=k(females) | 62 |
| 2 | 2 | females / males | 56 |
| 3f | 3 | ssf / osf / males | 49 |
| 3m | 3 | females / ssm / osm | 49 |
| 4 | 4 | ssf / osf / ssm / osm | 42 |
| 5 | 5 | ssf / osf / mzm / dzm / osm | 35 |
| 6 | 6 | mzf / dzf / osf / mzm / dzm / osm | 28 |

**Table 8.5**: Results of modelling mean MD diameters within each quadrant of the oral cavity. The simplest adequate model is indicated in bold.

| | | Right | | | Left | | |
|---|---|---|---|---|---|---|---|
| **Model** | **df** | **$\chi 2$** | **P [a]** | **AIC** | **$\chi 2$** | **P** | **AIC** |
| ***Maxilla*** | | | | | | | |
| **1** | 63 | 173.53 | ** | 47.53 | 170.80 | ** | 44.80 |
| **1a** | 62 | 96.55 | * | -27.45 | 103.35 | * | -20.65 |
| **2** | 56 | **67.25** | **.144** | **-44.75** | **69.17** | **.111** | **-42.83** |
| **3f** | 49 | 62.66 | .091 | -35.34 | 62.17 | .098 | -35.83 |
| **3m** | 49 | 55.18 | .252 | -42.82 | 60.94 | .118 | -37.06 |
| **4** | 42 | 49.15 | .209 | -34.85 | 51.47 | .150 | -32.53 |
| **5** | 35 | 47.35 | .079 | -22.65 | 50.28 | .046 | -19.72 |
| **6** | 28 | 38.38 | .091 | -17.62 | 44.69 | .024 | -11.31 |
| ***Mandible*** | | | | | | | |
| **1** | 63 | 157.73 | ** | 31.73 | 156.25 | ** | 30.25 |
| **1a** | 62 | 103.21 | * | -20.79 | 102.17 | * | -21.83 |
| **2** | 56 | **45.35** | **.845** | **-66.65** | **57.73** | **.411** | **-54.28** |
| **3f** | 49 | 40.31 | .807 | -57.69 | 48.39 | .498 | -49.61 |
| **3m** | 49 | 40.86 | .789 | -57.14 | 53.88 | .293 | -44.12 |
| **4** | 42 | 34.04 | .804 | -49.96 | 41.98 | .472 | -42.02 |
| **5** | 35 | 29.65 | .724 | -40.35 | 39.25 | .285 | -30.75 |
| **6** | 28 | 27.59 | .486 | -28.41 | 37.13 | .116 | -18.87 |

[a] Probabilities as estimated by Mx; *= p<0.01 ; **= p<0.001.

**Table 8.6** Results of modelling mean BL diameters within each quadrant of the oral cavity. The simplest adequate model is indicated in bold, and if any other AIC is lower, it is printed in bold italics.

| | | Right | | | Left | | |
|---|---|---|---|---|---|---|---|
| **Model** | **df** | **χ2** | **P** [a] | **AIC** | **χ2** | **P** | **AIC** |
| ***Maxilla*** | | | | | | | |
| **1** | 63 | 132.97 | ** | 6.97 | 131.94 | ** | 5.94 |
| **1a** | 62 | **90.85** | **.010** | **-33.15** | **79.89** | **.063** | **-44.11** |
| **2** | 56 | 81.39 | .015 | -30.61 | 68.88 | .116 | -43.13 |
| **3f** | 49 | 63.09 | .085 | ***-34.91*** | 59.92 | .137 | -38.09 |
| **3m** | 49 | 68.54 | .034 | -29.46 | 48.43 | .496 | ***-49.57*** |
| **4** | 42 | 54.83 | .089 | -29.17 | 40.18 | .551 | -43.82 |
| **5** | 35 | 50.64 | .042 | -19.36 | 35.93 | .425 | -34.07 |
| **6** | 28 | 42.54 | .039 | -13.46 | 31.41 | .299 | -24.60 |
| ***Mandible*** | | | | | | | |
| **1** | 63 | 108.43 | ** | -17.57 | 118.68 | ** | -7.32 |
| **1a** | 62 | **85.93** | **.024** | **-38.07** | 91.75 | * | -32.25 |
| **2** | 56 | 59.86 | .337 | ***-52.14*** | **51.23** | **.656** | **-60.77** |
| **3f** | 49 | 49.25 | .463 | -48.75 | 42.51 | .732 | -55.49 |
| **3m** | 49 | 48.98 | .474 | -49.02 | 42.36 | .737 | -55.64 |
| **4** | 42 | 41.43 | .496 | -42.57 | 35.81 | .738 | -48.19 |
| **5** | 35 | 28.96 | .754 | -41.04 | 30.79 | .672 | -39.21 |
| **6** | 28 | 23.75 | .695 | -32.25 | 27.42 | .496 | -28.58 |

[a] Probabilities as estimated by Mx; *= $p<0.01$ ; **= $p<0.001$.

**Table 8.7:** Results for the five Cholesky decomposition models in each of the four quadrants - MD dimension.

| Quadrant [a] | $\chi^2$ [b] | Prob [c] | AIC | RMSEA |
|---|---|---|---|---|
| **E model** | | | | |
| Max R | 1847.12 | ** | 853.12 | 194 |
| Max L | 1658.92 | ** | 664.92 | 179 |
| Man R | 1654.70 | ** | 660.70 | 182 |
| Man L | 1771.62 | ** | 777.62 | 187 |
| **CE model** | | | | |
| Max R | 982.33 | ** | 44.33 | 137 |
| Max L | 881.19 | ** | -56.81 | 120 |
| Man R | 886.16 | ** | -51.84 | 122 |
| Man L | 1003.70 | ** | 65.70 | 137 |
| **AE Model** | | | | |
| Max R | 633.87 | ** | -304.13 | 81 |
| Max L | 552.92 | * | -385.08 | 47 |
| Man R | 561.81 | * | -376.19 | 52 |
| Man L | 619.55 | ** | -318.45 | 78 |
| **ACE model** | | | | |
| Max R | 620.89 | ** | -261.11 | 87 |
| Max L | 539.12 | * | -342.88 | 56 |
| Man R | 546.03 | ** | -335.98 | 59 |
| Man L | 611.65 | ** | -270.35 | 86 |
| **ADE model** | | | | |
| Max R | 618.09 | ** | -263.91 | 87 |
| Max L | 531.15 | * | -350.85 | 56 |
| Man R | 543.62 | * | -338.38 | 56 |
| Man L | 597.09 | ** | -284.91 | 82 |

[a] Max = maxilla, Man = mandible.

[b] df are 497 for E, 469 for CE and AE, 441 for ACE and ADE models.

[c] Probability values: *= $p<0.01$ ; **= $p<0.001$.

**Table 8.8**: Results for the five Cholesky decomposition models in each of the four quadrants - BL dimension.

| Quadrant [a] | $\chi^2$ [b] | Prob [c] | AIC | RMSEA |
|---|---|---|---|---|
| **E model** | | | | |
| Max R | 1855.25 | ** | 861.25 | 197 |
| Max L | 1951.81 | ** | 957.81 | 209 |
| Man R | 1628.98 | ** | 634.98 | 184 |
| Man L | 1843.94 | ** | 849.94 | 200 |
| **CE model** | | | | |
| Max R | 1001.81 | ** | 63.81 | 140 |
| Max L | 1048.63 | ** | 110.63 | 144 |
| Man R | 798.11 | ** | -139.89 | 110 |
| Man L | 913.19 | ** | -24.81 | 126 |
| **AE Model** | | | | |
| Max R | 686.23 | ** | -251.77 | 93 |
| Max L | 753.05 | ** | -184.95 | 107 |
| Man R | 557.13 | * | -380.87 | 62 |
| Man L | 628.31 | ** | -309.69 | 78 |
| **ACE model** | | | | |
| Max R | 661.29 | ** | -220.71 | 96 |
| Max L | 717.41 | ** | -164.59 | 108 |
| Man R | 535.67 | * | -346.33 | 65 |
| Man L | 599.08 | ** | -282.92 | 82 |
| **ADE model** | | | | |
| Max R | 669.58 | ** | -212.42 | 98 |
| Max L | 731.95 | ** | -150.05 | 112 |
| Man R | 549.27 | ** | -332.74 | 68 |
| Man L | 621.75 | ** | -260.25 | 86 |

[a] Max = maxilla, Man = mandible.

[b] df are 497 for E, 469 for CE and AE, 441 for ACE and ADE models.

[c] Probability values: *= $p<0.01$ ; **= $p<0.001$.

**Table 8.9**: A typical pattern of fit statistics comparing cholesky decompositions with a null model of specific unique environmental factors. The data shown are for the MD dimensions of the teeth in the maxillary left quadrant.

| | MODELS | | | | |
|---|---|---|---|---|---|
| INDEX | E | CE | AE | ACE | ADE |
| Normed Fit | .46 | .71 | .82 | .82 | .83 |
| Normed Fit 2 | .55 | .84 | .97 | .96 | .97 |
| Tucker Lewis | .53 | .82 | .96 | .96 | .96 |
| Parsimonious Fit | .44 | .65 | .74 | .70 | .70 |
| Parsimonious Fit 2 | .72 | .26 | .30 | .12 | .12 |
| Relative Non-centrality | .54 | .84 | .97 | .96 | .97 |
| Centrality | .12 | .47 | .86 | .84 | .85 |

**Table 8.10:** Results of fitting the additive genetic models in Figure 8.11 to maxillary right MD dimensions. The best model by AIC is highlighted in bold.

| Model No. | df | $\chi^2$ [a] | AIC | RMSEA[b] |
|---|---|---|---|---|
| **A1** | **483** | **722.82** | **-243.18** | **97** |
| A2 | 490 | 1483.98 | 503.98 | 171 |
| A3 | 490 | 1043.49 | 63.49 | 139 |
| A4 | 489 | 771.72 | -206.28 | 105 |
| A5 | 488 | 770.97 | -205.03 | 105 |
| A6 | 488 | 746.74 | -229.26 | 100 |
| A7 | 487 | 743.04 | -230.96 | 100 |
| A8 | 487 | 743.18 | -230.82 | 100 |
| A9 | 486 | 741.23 | -230.77 | 100 |
| A10 | 489 | 840.67 | -137.33 | 116 |
| A11 | 488 | 840.66 | -135.34 | 117 |
| A12 | 488 | 838.91 | -137.10 | 116 |
| A13 | 487 | 838.01 | -135.99 | 117 |
| A14 | 486 | 731.99 | -240.01 | 98 |
| A15 | 483 | 770.71 | -195.29 | 105 |
| A16 | 483 | 749.27 | -216.73 | 102 |
| A17 | 483 | 829.95 | -136.05 | 115 |
| A18 | 483 | 1111.20 | 145.20 | 143 |
| A19 | 483 | 1108.27 | 142.27 | 143 |
| A20 | 483 | 990.57 | 24.57 | 132 |

[a] Probabilities associated with $\chi^2$ were all $p<0.001$.

[b] RMSEA values were multiplied by 1000, values<100 suggest a good fit.

**Table 8.11:** Comparing models to test for significance of factors and constraints.

| Compare | $\chi^2_{diff}$ | df | p [a] | Interpretation |
|---|---|---|---|---|
| A2 vs A1 | 761.16 | 7 | ** | Both general and specific factors better than general alone. |
| A3 vs A1 | 320.67 | 7 | ** | Both general and specific factors better than specific alone. |
| *General Factor* | | | | |
| A4 vs A5 | 0.75 | 1 | 30 | Constraints within anterior and posterior tooth groups not significantly better than constraints across entire quadrant. |
| A4 vs A6 | 24.98 | 1 | ** | Constraints within incisor and C to M2 tooth groups *were* significantly better than constraints across entire quadrant. |
| A6 vs A7 | 3.70 | 1 | 5 | Freeing C was not significantly better than constraints within incisor and C to M2 tooth groups. |
| A6 vs A8 | 3.56 | 1 | 5 | Freeing molars was not significantly better than constraints within incisor and C to M2 tooth groups. |
| A6 vs A9 | 5.51 | 2 | 5 | Freeing C and molars was not significantly better than constraints within incisor and C to M2 tooth groups. |
| A6 vs A1 | 23.92 | 5 | ** | Freeing all seven parameters *was* significantly better than constraints within incisor and C to M2 tooth groups. |
| | | | | Conclusion: General = 1 2 3 4 5 6 7 |
| *Specific Factors* | | | | |
| A10 vs A11 | 0.01 | 1 | 99 | Constraints within anterior and posterior tooth groups not significantly better than constraints across entire quadrant. |
| A10 vs A12 | 1.76 | 1 | 10 | Constraints within incisor, C to M2 tooth groups not significantly better than constraints across entire quadrant. |
| A10 vs A13 | 2.66 | 2 | 20 | Constraints within incisor, C & posterior tooth groups not significantly better than constraints across entire quadrant. |
| A10 vs A14 | 108.7 | 3 | ** | Constraints within I, C, P and M tooth groups *were* significantly better than constraints across entire quadrant. |
| A14 vs A1 | 9.20 | 3 | + | Removal of constraints *was* significantly better than constraints within I, C, P and M tooth groups |
| | | | | Conclusion: Specific = 8 9 10 11 12 13 14 |
| *Group Factors* | | | | |
| A15 vs A1 | 47.89 | 0 | - | Specific factors *were* better than any of the group factor structures. |
| A16 vs A1 | 26.45 | 0 | - | |
| A17 vs A1 | 107.13 | 0 | - | " |
| A18 vs A1 | 388.38 | 0 | - | " |
| A19 vs A1 | 385.45 | 0 | - | " |
| A20 vs A1 | 267.75 | 0 | - | " |

[a] Probabilities: + = $p<0.05$ ; *= $p<0.01$ ; **= $p<0.001$ ; - = incalculable.

**Table 8.12:** Results of fitting the unique environment models in Figure 8.12 to maxillary right MD dimensions. The best model by AIC is highlighted in bold.

| Model No. | df | $\chi^{2}$ [a] | AIC | RMSEA[b] |
|---|---|---|---|---|
| **E1** | 497 | 751.66 | -242.34 | 99 |
| **E2** | 504 | Incorrect | --------- | ---- |
| **E3** | 504 | 775.29 | -232.71 | 101 |
| **E4** | 503 | 761.38 | -244.62 | 99 |
| **E5** | 502 | 760.27 | -243.73 | 99 |
| **E6** | **502** | **755.44** | **-248.56** | **98** |
| **E7** | 501 | 754.31 | -247.69 | 98 |
| **E8** | 501 | 755.32 | -246.68 | 98 |
| **E9** | 500 | 752.90 | -247.10 | 98 |
| **E10** | 508 | 803.31 | -212.69 | 105 |
| **E11** | 507 | 802.87 | -211.13 | 105 |
| **E12** | 507 | 791.95 | -222.05 | 103 |
| **E13** | 506 | 777.46 | -234.54 | 101 |
| **E14** | 505 | 772.56 | -237.44 | 101 |

[a] Probabilities associated with $\chi^2$ were all $p<0.001$.

[b] RMSEA values were multiplied by 1000, values<100 suggest a good fit.

**Table 8.13:** Comparing models to test for significance of factors and constraints.

| Compare | $\chi^2_{diff}$ | df | P [a] | Interpretation |
|---|---|---|---|---|
| E2 vs E1 | ------- | 7 | | Both general and specific factors better than general alone. |
| E3 vs E1 | 23.63 | 7 | * | Both general and specific factors better than specific alone. |
| *General Factor* | | | | |
| E4 vs E5 | 1.11 | 1 | 20 | Constraints within anterior and posterior tooth groups not significantly better than constraints across entire quadrant. |
| E4 vs E6 | 5.94 | 1 | + | Constraints within incisor and C to M2 tooth groups *were* significantly better than constraints across entire quadrant. |
| E6 vs E7 | 1.13 | 1 | 20 | Freeing C was not significantly better than constraints within incisor and C to M2 tooth groups. |
| E6 vs E8 | 0.12 | 1 | 50 | Freeing molars was not significantly better than constraints within incisor and C to M2 tooth groups. |
| E6 vs E9 | 2.54 | 2 | 20 | Freeing C and molars was not significantly better than constraints within incisor and C to M2 tooth groups. |
| E6 vs E1 | 3.78 | 5 | 30 | Freeing all seven parameters not significantly better than constraints within incisor and C to M2 tooth groups. |
| | | | | Conclusion: General = 1 1 4 4 4 4 4 |
| *Specific Factors* | | | | |
| E10 vs E11 | 0.44 | 1 | 50 | Constraints within anterior and posterior tooth groups not significantly better than constraints across entire quadrant. |
| E10 vs E12 | 11.36 | 1 | ** | Constraints within incisor & C to M2 tooth groups *was* significantly better than constraints across entire quadrant. |
| E12 vs E13 | 14.49 | 1 | ** | Freeing C *was* significantly better than constraints within incisor and C to M2 tooth groups . |
| E13 vs E14 | 4.90 | 1 | + | Freeing C and molars *was* significantly better than constraints within incisor, C & posterior tooth groups. |
| E14 vs E6 | 17.12 | 3 | ** | Removal of constraints *was* significantly better than constraints within I, C, P and M tooth groups |
| | | | | Conclusion: Specific = 8 9 10 11 12 13 14 |

[a] Probabilities: + = $p<0.05$ ; *= $p<0.01$ ; **= $p<0.001$ ; - = incalculable.

**Table 8.14:** Results of fitting the non-additive genetic models in Figure 8.13 to maxillary right MD dimensions. The best model by AIC is highlighted in bold.

| Model No. | df | $\chi^2$ [a] | AIC | RMSEA[b] |
|---|---|---|---|---|
| **D1** | 488 | 686.32 | -289.69 | 88 |
| **D2** | 495 | 690.00 | -300.00 | 87 |
| **D3** | 495 | 751.94 | -238.06 | 100 |
| **D4** | 488 | 657.49 | -318.51 | 80 |
| **D5** | 495 | 689.79 | -300.21 | 86 |
| **D6** | 488 | 654.85 | -321.15 | 80 |
| **D7** | 488 | 652.19 | -323.82 | 79 |
| **D8** | 488 | 654.50 | -321.51 | 79 |
| **D9** | 490 | 653.96 | -326.04 | 78 |
| **D10** | 491 | 669.13 | -312.87 | 82 |
| **D11** | 492 | 676.44 | -307.56 | 84 |
| **D12** | 492 | 656.31 | -323.69 | 79 |
| **D13** | 496 | 665.65 | -326.35 | 80 |
| **D14** | 495 | 658.82 | -331.18 | 78 |
| **D15** | 495 | 661.38 | -328.62 | 79 |
| **D16** | 494 | 658.75 | -329.25 | 79 |
| **D17** | **494** | **655.36** | **-332.64** | **77** |
| **D18** | 493 | 655.25 | -330.75 | 78 |
| **D19** | 499 | 691.99 | -306.01 | 85 |
| **D20** | 498 | 690.03 | -305.97 | 85 |
| **D21** | 497 | 689.08 | -304.93 | 85 |
| **D22** | 496 | 660.45 | -331.56 | 78 |

[a] Probabilities associated with $\chi^2$ were all $p<0.001$.

[b] RMSEA values were multiplied by 1000, values<100 suggest a good fit.

**Table 8.15:** Comparing models to test for significance of factors and constraints.

| Compare | $\chi^2_{diff}$ | df | p [a] | Interpretation |
|---|---|---|---|---|
| D2 vs D1 | 3.68 | 7 | 80 | Specific factor does not improve general factor alone |
| D3 vs D1 | 65.62 | 7 | ** | Both general and specific factors better than specific alone |
| D4 vs D1 | 28.83 | 0 | - | Group factors better than specific factors |
| D2 vs D4 | 32.51 | 7 | ** | Both general and group factors better than general alone |
| D5 vs D4 | 32.30 | 7 | ** | Both general and group factors better than groups alone |
| *How many Group Factors?* | | | | |
| D4, 6, 7, 8 | | | | D7 had the lowest AIC and equal lowest RMSEA |
| D9 vs D7 | 1.77 | 2 | 30 | M1 and M2 in posterior tooth group factor not required |
| D10 vs D9 | 15.17 | 1 | ** | P2 in posterior tooth group factor *was* required |
| D11 vs D9 | 22.48 | 2 | ** | I and C+P groups significantly better than I2+C+P1 group |
| D9 vs D12 | 2.35 | 0 | - | Two group factors significantly better than one |
| | | | | Conclusion: Groups = 8 9 and 10 11 12 |
| *General Factor* | | | | |
| D13 vs D14 | 6.83 | 1 | * | Constraints within anterior & posterior tooth groups *were* significantly better than constraints across entire quadrant. |
| D14 vs D15 | 2.56 | 0 | - | Constraints within anterior & posterior tooth groups better than constraints across incisor & C to M2 tooth groups. |
| D14 vs D16 | 0.07 | 1 | 70 | Freeing C was not significantly better than constraints within anterior & posterior tooth groups. |
| D14 vs D17 | 3.46 | 1 | 5 | Freeing molars was not significantly better than constraints within anterior & posterior tooth groups. |
| D14 vs D18 | 3.57 | 2 | 10 | Freeing C and molars was not significantly better than constraints within anterior & posterior tooth groups. |
| D14 vs D9 | 4.86 | 5 | 30 | Freeing all seven parameters not significantly better than constraints within anterior & posterior tooth groups. |
| | | | | Conclusion: General = 1 1 1 4 4 4 4 |
| *Group Factor Constraints* | | | | |
| D19 vs D20 | 1.96 | 1 | 10 | Constraints within group factors not significantly better than constraints across both group factors. |
| D19 vs D21 | 2.91 | 2 | 20 | Freeing incisors not significantly better than constraints across both group factors. |
| D19 vs D22 | 31.54 | 3 | ** | Constraining incisors only *was* significantly better than constraints across both group factors. |
| D20 vs D22 | 29.58 | 2 | ** | Freeing C, P1 and P2 *was* better than constraining them |
| D22 vs D14 | 1.63 | 1 | 20 | Freeing all five parameters not significantly better than constraining incisors only. |
| | | | | Conclusion: Groups = 8 8 and 10 11 12 |
| E6 vs D22 | 94.99 | 6 | ** | Addition of D22 significantly improves the AE model |

[a] Probabilities: + = p<0.05 ; *= p<0.01 ; **= p<0.001 ; - = incalculable.

**Table 8.16:** Results of fitting the common environment models in Figure 8.14 to maxillary right MD dimensions. The best model by AIC is highlighted in bold.

| Model No. | df | $\chi^2$ [a] | AIC | RMSEA[b] |
|---|---|---|---|---|
| C1 | 482 | 643.62 | -320.38 | 79 |
| C2 | 489 | 648.01 | -329.99 | 77 |
| C3 | 489 | 654.08 | -323.92 | 79 |
| C4 | 482 | 640.56 | -323.44 | 79 |
| C5 | 489 | 650.38 | -327.62 | 78 |
| C6 | 490 | 645.73 | -334.27 | 77 |
| C7 | 492 | 648.23 | -335.77 | 77 |
| C8 | 493 | 648.58 | -337.43 | 76 |
| **C9** | **493** | **648.33** | **-337.67** | **77** |
| C10 | 494 | 653.86 | -334.15 | 78 |
| C11 | 494 | 655.29 | -332.71 | 77 |
| C12 | 495 | 656.26 | -333.74 | 78 |
| C13 | 495 | 658.67 | -331.34 | 78 |
| C14 | 494 | 656.99 | -331.01 | 78 |
| C15 | 494 | 656.40 | -331.60 | 78 |
| C16 | 494 | 653.71 | -334.29 | 78 |
| C17 | 493 | 648.53 | -337.47 | 77 |

[a] Probabilities associated with $\chi^2$ were all $p<0.001$.

[b] RMSEA values were multiplied by 1000, values<100 suggest a good fit.

**Table 8.17:** Comparing models to test for significance of factors and constraints.

| Compare | $\chi^2_{diff}$ | df | p [a] | Interpretation |
|---|---|---|---|---|
| C2 vs C1 | 4.39 | 7 | 70 | Specific factor does not improve general factor alone |
| C3 vs C1 | 10.46 | 7 | 10 | General factor does not improve specific factor alone |
| C2 vs C3 | 6.07 | 0 | - | General factor *was* better than specific factors |
| C1 vs C4 | 3.06 | 0 | - | Group factors *were* better than specific factors |
| C2 vs C4 | 7.45 | 7 | 30 | Both general & group factors not better than general alone |
| C5 vs C4 | 9.82 | 7 | 10 | Both general & group factors not better than groups alone |
| C1 to C5 | | | | General factor alone had the lowest AIC and RMSEA |
| *Group Factor* | | | | |
| C6 vs C2 | -2.28 | 1 | - | Exclusion of canine improved fit of model |
| C7 vs C6 | 2.50 | 2 | 20 | Exclusion of I1 and I2 did not worsen fit of model |
| C8 vs C7 | 0.35 | 1 | 50 | P1,P2,M1,M2 *not* significantly better than P2,M1,M2 |
| C9 vs C7 | 0.10 | 1 | 70 | P1,P2,M1,M2 *not* significantly better than P1,P2,M1 |
| C10 vs C8 | 5.28 | 1 | + | P2,M1,M2 *was* significantly better than P2,M1 |
| C10 vs C9 | 5.53 | 1 | + | P1,P2,M1 *was* significantly better than P2,M1 |
| C8 vs C9 | 0.25 | 0 | - | P1,P2,M1 very slightly better than P2,M1,M2 |
| C11 vs C8 | 6.71 | 1 | * | P2,M1,M2 *was* significantly better than M1,M2 |
| C12 vs C7 | 8.03 | 3 | + | P1,P2,M1,M2 *was* significantly better than M1 |
| | | | | Conclusion: Group = 4 5 6 7 |
| *Group Factor Constraints* | | | | |
| C13 vs C14 | 1.68 | 1 | 10 | Constraints (P1=M1 and P2=M2) were not significantly better than constraints across the entire factor |
| C13 vs C15 | 2.27 | 1 | 10 | Constraints (P1=P2 and M1=M2) were not significantly better than constraints across the entire factor |
| C13 vs C16 | 4.96 | 1 | + | Freeing M1 only *was* significantly better than constraints across the entire factor |
| C16 vs C17 | 5.18 | 1 | + | Freeing P1 & M1 (P2=M2) *was* significantly better than freeing M1 only |
| C17 vs C7 | 0.30 | 1 | 50 | Removing all constraints was not significantly better than freeing P1 & M1 only (constraining P2=M2) |
| | | | | Conclusion: Group = 4 5 6 5 |
| D22 vs C17 | 11.92 | 3 | * | Addition of C17 significantly improved the ADE model |

[a] Probabilities: + = p<0.05 ; *= p<0.01 ; **= p<0.001 ; - = incalculable.

**Table 8.18:** Unstandardised path coefficients (x100) for the model illustrated in Figure 8.15 - MD diameter.

| | Latent Factor | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | $A_G$ | $A_{S1(-7)}$ | $D_G$ | $D_{R1}$ | $D_{R2}$ | $C_R$ | $E_G$ | $E_{S(1-7)}$ |
| **I1** | 26 | 24 | 29 | 25 | --- | --- | 3 | 18 |
| **I2** | 8 | 30 | 29 | 25 | --- | --- | 3 | 20 |
| **C** | 5 | 22 | 29 | --- | - 3 | --- | 3 | 13 |
| **P1** | 14 | 13 | 21 | --- | 18 | - 9 | 5 | 13 |
| **P2** | 15 | 19 | 21 | --- | 14 | 1 | 5 | 18 |
| **M1** | 41 | 10 | 21 | --- | --- | 23 | 5 | 20 |
| **M2** | 18 | 42 | 21 | --- | --- | 1 | 5 | 17 |

**Table 8.19**: Standardised path coefficients (x100) for the model illustrated in Figure 8.15 - MD diameter.

| | Latent Factor | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | $A_G$ | $A_S$ | $D_G$ | $D_{R1}$ | $D_{R2}$ | $C_R$ | $E_G$ | $E_S$ | **Total** |
| **I1** | 22 | 19 | 28 | 20 | --- | --- | 0.3 | 11 | 100.3 |
| **I2** | 2 | 32 | 30 | 22 | --- | --- | 0.3 | 14 | 100.3 |
| **C** | 2 | 31 | 54 | --- | 1 | --- | 2.0 | 11 | 101.0 |
| **P1** | 14 | 12 | 31 | --- | 23 | 6.0 | 2.0 | 12 | 101.0 |
| **P2** | 14 | 23 | 28 | --- | 12 | 0.1 | 2.0 | 21 | 100.1 |
| **M1** | 53 | 3 | 14 | --- | --- | 17.0 | 1.0 | 13 | 101.0 |
| **M2** | 11 | 62 | 16 | --- | --- | <0.1 | 1.0 | 10 | 100.0 |

**Table 8.20:** Results of fitting the additive genetic models in Figure 8.21 to maxillary right BL dimensions. The best model by AIC is highlighted in bold.

| Model No. | df | $\chi^2$ [a] | AIC | RMSEA[b] |
|---|---|---|---|---|
| A1 | 483 | 817.18 | -148.82 | 114 |
| A2 | 490 | 1486.63 | 506.63 | 176 |
| A3 | 490 | 1146.94 | 166.94 | 148 |
| A4 | 489 | 844.93 | -133.07 | 116 |
| A5 | **488** | **823.42** | **-152.58** | **113** |
| A6 | 488 | 830.16 | -145.85 | 114 |
| A7 | 487 | 821.77 | -152.24 | 113 |
| A8 | 487 | 823.40 | -150.60 | 114 |
| A9 | 486 | 821.75 | -150.25 | 114 |
| A10 | 494 | 846.18 | -141.82 | 116 |
| A11 | 493 | 846.10 | -139.90 | 116 |
| A12 | 493 | 842.75 | -143.25 | 116 |
| A13 | 492 | 841.82 | -142.18 | 115 |
| A14 | 491 | 836.25 | -145.75 | 115 |
| A15 | 488 | 826.20 | -149.80 | 113 |
| A16 | 488 | 884.17 | -91.83 | 121 |
| A17 | 488 | 885.27 | -90.73 | 121 |
| A18 | 488 | 949.62 | -26.39 | 151 |
| A19 | 488 | 1173.63 | 197.63 | 135 |
| A20 | 488 | 1010.55 | 34.55 | 128 |

[a] Probabilities associated with $\chi^2$ were all $p<0.001$.

[b] RMSEA values were multiplied by 1000, values<100 suggest a good fit.

**Table 8.21:** Comparing models to test for significance of factors and constraints.

| Compare | $\chi^2_{diff}$ | df | P [a] | Interpretation |
|---|---|---|---|---|
| A2 vs A1 | 669.45 | 7 | ** | Both general and specific factors better than general alone. |
| A3 vs A1 | 326.76 | 7 | ** | Both general and specific factors better than specific alone. |
| *General Factor* | | | | |
| A4 vs A5 | 21.51 | 1 | ** | Constraints within anterior & posterior tooth groups *were* significantly better than constraints across entire quadrant. |
| A4 vs A6 | 14.77 | 1 | ** | Constraints within incisor and C to M2 tooth groups *were* significantly better than constraints across entire quadrant. |
| A5 vs A7 | 1.65 | 1 | 10 | Freeing C was not significantly better than constraints within anterior & posterior tooth groups. |
| A5 vs A8 | 0.02 | 1 | 80 | Freeing molars was not significantly better than constraints within anterior & posterior tooth groups. |
| A5 vs A9 | 1.67 | 1 | 10 | Freeing C and molars was not significantly better than constraints within anterior & posterior tooth groups. |
| A5 vs A1 | 6.24 | 5 | 20 | Freeing all seven parameters was not significantly better than constraints within anterior & posterior tooth groups. |
| | | | | Conclusion: General = 1 1 1 4 4 4 4 |
| *Specific Factors* | | | | |
| A10 vs A11 | 0.08 | 1 | 95 | Constraints within anterior and posterior tooth groups not significantly better than constraints across entire quadrant. |
| A10 vs A12 | 3.43 | 1 | 5 | Constraints within incisor, C to M2 tooth groups not significantly better than constraints across entire quadrant. |
| A10 vs A13 | 4.36 | 2 | + | Constraints within incisor, C & posterior tooth groups *were* significantly better than constraints across entire quadrant. |
| A13 vs A14 | 5.57 | 1 | + | Constraints within tooth groups *were* significantly better than constraints across entire quadrant. |
| A14 vs A5 | 12.83 | 3 | * | Removal of constraints *was* significantly better than constraints within tooth groups |
| | | | | Conclusion: Specific = 8 9 10 11 12 13 14 |
| *Group Factors* | | | | |
| A15 vs A5 | 2.78 | 0 | - | Specific factors *were* better than any of the group factor structures. |
| A16 vs A5 | 60.75 | 0 | - | " |
| A17 vs A5 | 61.85 | 0 | - | " |
| A18 vs A5 | 126.20 | 0 | - | " |
| A19 vs A5 | 350.21 | 0 | - | " |
| A20 vs A5 | 187.13 | 0 | - | " |

[a] Probabilities: + = p<0.05 ; *= p<0.01 ; **= p<0.001 ; - = incalculable.

**Table 8.22:** Results of fitting the unique environmental models in Figure 8.22 to maxillary right BL dimensions. The best model by AIC is highlighted in bold.

| Model No. | df | $\chi^2$ [a] | AIC | RMSEA[b] |
|---|---|---|---|---|
| E1 | 502 | 862.28 | -141.72 | 116 |
| E2 | 509 | * 83363.20 | -------- | ---- |
| E3 | 509 | 936.31 | -81.69 | 125 |
| E4 | 508 | 901.24 | -114.76 | 121 |
| E5 | 507 | 871.63 | -142.37 | 116 |
| E6 | 507 | 893.94 | -120.06 | 120 |
| E7 | 506 | 871.11 | -140.89 | 116 |
| E8 | 506 | 864.40 | -147.60 | 115 |
| E9 | 505 | 864.40 | -145.60 | 115 |
| E10 | 512 | 907.08 | -116.93 | 118 |
| E11 | 511 | 905.77 | -116.23 | 119 |
| E12 | 511 | 895.05 | -126.95 | 117 |
| E13 | 510 | 888.12 | -131.88 | 117 |
| **E14** | **510** | **871.51** | **-148.49** | **115** |
| E15 | 509 | 870.22 | -147.78 | 115 |

[a] Probabilities associated with $\chi^2$ were all $p<0.001$. * = Estimate is incorrect, but indicates how poorly the model fits the data

[b] RMSEA values were multiplied by 1000, values<100 suggest a good fit.

**Table 8.23:** Comparing models to test for significance of factors and constraints.

| Compare | $\chi^2_{diff}$ | df | P [a] | Interpretation |
|---|---|---|---|---|
| E2 vs E1 | -------- | 7 | | Both general and specific factors better than general alone. |
| E3 vs E1 | 74.03 | 7 | ** | Both general and specific factors better than specific alone. |
| *General Factor* | | | | |
| E4 vs E5 | 29.61 | 1 | ** | Constraints within anterior & posterior tooth groups *were* significantly better than constraints across entire quadrant. |
| E4 vs E6 | 7.30 | 1 | * | Constraints within incisor and C to M2 tooth groups *were* significantly better than constraints across entire quadrant. |
| E5 vs E7 | 0.52 | 1 | 30 | Freeing C was not significantly better than constraints within anterior & posterior tooth groups. |
| E5 vs E8 | 7.23 | 1 | * | Freeing molars *was* significantly better than constraints within anterior & posterior tooth groups. |
| E8 vs E9 | 0.00 | 1 | 100 | Freeing C was not significantly better than constraints within anterior, premolar and molar tooth groups. |
| E8 vs E1 | 2.12 | 4 | 70 | Freeing all seven parameters not significantly better than constraints within anterior, premolar & molar tooth groups. |
| | | | | Conclusion: General = 1 1 1 4 4 6 6 |
| *Specific Factors* | | | | |
| E10 vs E11 | 1.31 | 1 | 20 | Constraints within anterior and posterior tooth groups not significantly better than constraints across entire quadrant. |
| E10 vs E12 | 12.03 | 1 | ** | Constraints within incisor & C to M2 tooth groups *was* significantly better than constraints across entire quadrant. |
| E12 vs E13 | 6.93 | 1 | * | Freeing C *was* significantly better than constraints within incisor and C to M2 tooth groups . |
| E13 vs E14 | 16.61 | 0 | - | Freeing molars gave greater improvement in fit than freeing canines |
| E14 vs E15 | 1.29 | 1 | 20 | Freeing C & molars not significantly better than constraints within incisor, C to premolar, and molar tooth groups. |
| E14 vs E8 | 7.11 | 4 | 10 | Freeing all seven parameters was not significantly better than constraints within I, C to P, and M tooth groups |
| | | | | Conclusion: Specific = 8 8 11 11 11 13 13 |

[a] Probabilities: + = $p<0.05$ ; *= $p<0.01$ ; **= $p<0.001$ ; - = incalculable.

**Table 8.24:** Results of fitting the non-additive genetic models in Figure 8.23 to maxillary right BL dimensions. The best model by AIC is highlighted in bold.

| Model No. | df | $\chi^2$ [a] | AIC | RMSEA[b] |
|---|---|---|---|---|
| D1 | 496 | 780.86 | -211.14 | 103 |
| D2 | 503 | 783.38 | -222.62 | 102 |
| D3 | 503 | 868.49 | -137.51 | 116 |
| D4 | 496 | 727.19 | -264.81 | 92 |
| D5 | 503 | 733.80 | -264.20 | 94 |
| D6 | 496 | 725.61 | -266.39 | 92 |
| D7 | 501 | 761.44 | -240.56 | 99 |
| D8 | 498 | 727.61 | -268.39 | 92 |
| D9 | 499 | 729.23 | -268.77 | 92 |
| D10 | 500 | 733.80 | -266.20 | 92 |
| D11 | 501 | 733.80 | -268.20 | 92 |
| D12 | 502 | 733.81 | -270.19 | 91 |
| D13 | 503 | 736.34 | -269.67 | 92 |
| D14 | 504 | 738.77 | -269.23 | 92 |
| D15 | 504 | 744.36 | -263.64 | 94 |
| D16 | 506 | 786.58 | -225.42 | 102 |
| D17 | 506 | 792.07 | -219.93 | 102 |
| D18 | 506 | 773.99 | -238.01 | 99 |
| D19 | 509 | 847.63 | -170.37 | 111 |
| D20 | 508 | 835.87 | -180.13 | 109 |
| D21 | 507 | 832.98 | -181.02 | 108 |
| **D22** | **507** | **743.69** | **-270.31** | **93** |

[a] Probabilities associated with $\chi^2$ were all $p<0.001$.

[b] RMSEA values were multiplied by 1000, values<100 suggest a good fit.

**Table 8.25:** Comparing models to test for significance of factors and constraints.

| Compare | $\chi^2_{diff}$ | df | P [a] | Interpretation |
|---|---|---|---|---|
| D2 vs D1 | 2.52 | 7 | 90 | Specific factors do not improve general factor alone |
| D3 vs D1 | 87.63 | 7 | ** | Both general and specific factors better than specific alone |
| D4 vs D1 | 53.67 | 0 | - | Group factors better than specific factors |
| D2 vs D4 | 56.19 | 7 | ** | Both general and group factors better than general alone |
| D5 vs D4 | 17.17 | 7 | + | Both general and group factors better than groups alone |
| *Group Factors* | | | | |
| D6 vs D4 | 1.58 | 0 | - | Incisor & C to M2 groups *were* better than 4 tooth groups. |
| D7 vs D6 | 35.83 | 5 | ** | C to M2 factor significantly improves model D7 . |
| D8 vs D6 | 2.00 | 2 | 30 | Incisor group factor not required. |
| D9 vs D8 | 1.62 | 1 | 20 | Canine not required in group factor. |
| D10 vs D9 | 4.57 | 1 | + | P1 in posterior tooth group factor *was* required. |
| D11 vs D9 | 4.57 | 2 | 10 | Posterior tooth group factor not significantly better than molar tooth group factor. |
| | | | | Conclusion: Group = 13 14 (M1 M2) |
| *General Factor* | | | | |
| D12 vs D11 | 0.01 | 1 | 90 | Canine not required in general factor. |
| D13 vs D12 | 2.53 | 1 | 10 | M1 not required in general factor. |
| D14 vs D13 | 2.43 | 1 | 10 | M2 not required in general factor. |
| D15 vs D14 | 5.59 | 0 | - | Incisor/premolar factor better than separate I & P factors. |
| D16 vs D14 | 47.81 | 2 | ** | Molar factor significantly improved fit of the model. |
| D17 vs D14 | 53.30 | 2 | ** | Premolar factor significantly improved fit of the model. |
| D18 vs D14 | 35.22 | 2 | ** | Incisor factor significantly improved fit of the model. |
| | | | | Conclusion: Group factor 1 2 4 5 (I1 I2 P1 P2) |
| *Constraints* | | | | |
| D19 vs D20 | 11.76 | 1 | ** | Constraints within each of the group factors *were* significantly better than constraints across both factors. |
| D20 vs D21 | 2.89 | 1 | 5 | Freeing the molars was not significantly better than constraining them. |
| D20 vs D22 | 92.18 | 1 | ** | Constraints within tooth groups *were* significantly better than constraints within each of the group factors. |
| D22 vs D14 | 4.92 | 3 | 10 | Freeing all six parameters not significantly better than constraints within tooth groups. |
| | | | | Conclusion: Groups = 1 1 4 4 and 13 13 |
| E14 vs D22 | 127.82 | 3 | ** | Addition of D22 significantly improves the AE model |

[a] Probabilities: + = $p<0.05$ ; *= $p<0.01$ ; **= $p<0.001$ ; - = incalculable.

**Table 8.26** Results of fitting the common environment models in Figure 8.24 to maxillary right BL dimensions. The best model by AIC is highlighted in bold.

| Model No. | df | $\chi^2$ [a] | AIC | RMSEA[b] |
|---|---|---|---|---|
| C1 | 493 | 724.43 | -261.57 | 93 |
| C2 | 500 | 732.69 | -267.31 | 93 |
| C3 | 500 | 734.92 | -265.08 | 93 |
| C4 | 493 | 711.69 | -274.31 | 91 |
| C5 | 500 | 722.63 | -277.37 | 91 |
| C6 | 502 | 722.69 | -281.31 | 90 |
| C7 | 503 | 723.45 | -282.55 | 90 |
| **C8** | **505** | **724.57** | **-285.43** | **89** |
| C9 | 504 | 724.57 | -283.43 | 90 |
| C10 | 506 | 735.98 | -276.02 | 91 |
| C11 | 506 | 743.69 | -268.31 | 93 |
| C12 | 506 | 728.82 | -283.18 | 90 |

[a] Probabilities associated with $\chi^2$ were all $p<0.001$.

[b] RMSEA values were multiplied by 1000, values<100 suggest a good fit.

**Table 8.27:** Comparing models to test for significance of factors and constraints.

| **Compare** | $\chi^2_{diff}$ | **df** | **p** [a] | **Interpretation** |
|---|---|---|---|---|
| C2 vs C1 | 8.26 | 7 | 30 | Specific factors do not improve general factor alone |
| C3 vs C1 | 10.49 | 7 | 10 | General factor does not improve specific factors alone |
| C1 vs C4 | 12.74 | 0 | - | General + group factors *were* better than general + specific |
| C3 vs C5 | 12.29 | 0 | - | Group factors alone *were* better than specific factors alone |
| C2 vs C4 | 21.00 | 7 | * | General + group factors *were* better than general alone |
| C5 vs C4 | 10.94 | 7 | 10 | General + group factors were not better than groups alone |
| | | | | Conclusion: Tooth group factors - I, C, P, M |
| *Group Factors* | | | | |
| C6 vs C5 | 0.06 | 2 | 95 | Exclusion of I1 and I2 did not worsen fit of model |
| C7 vs C6 | 0.76 | 1 | 30 | Exclusion of canine did not worsen fit of model |
| C8 vs C7 | 1.12 | 2 | 50 | P1,P2,M1,M2 *not* significantly better than M1,M2 |
| C8 vs C9 | 0.00 | 1 | 100 | P2,M1,M2 *not* significantly better than M1, M2 |
| C8 vs C10 | 11.41 | 1 | ** | M1,M2 *was* significantly better than M1 |
| C8 vs C11 | 19.12 | 1 | ** | M1,M2 *was* significantly better than M2 |
| C8 vs C12 | 4.25 | 1 | + | Freeing M1 and M2 *was* significantly better than constraining them M1=M2 |
| | | | | Conclusion: Group = 13 14 (M1 M2) |
| D22 vs C8 | 19.12 | 2 | ** | Addition of C8 significantly improved the ADE model |

[a] Probabilities: + = p<0.05 ; *= p<0.01 ; **= p<0.001 ; - = incalculable.

**Table 8.28:** Unstandardised path coefficients (x100) for the model illustrated in Figure 8.25 - BL diameter.

| | Latent Factors | | | | | | |
|---|---|---|---|---|---|---|---|
| | $A_G$ | $A_S$ | $D_{R1}$ | $D_{R2}$ | $C_R$ | $E_G$ | $E_S$ |
| **I1** | 35 | 22 | -15 | -- | -- | 11 | 22 |
| **I2** | 35 | 27 | -15 | -- | -- | 11 | 22 |
| **C** | 35 | 34 | -- | -- | -- | 11 | 16 |
| **P1** | 39 | 21 | 20 | -- | -- | 4 | 16 |
| **P2** | 39 | 28 | 20 | -- | -- | 4 | 16 |
| **M1** | 39 | 8 | -- | 17 | 31 | 6 | 21 |
| **M2** | 39 | 38 | -- | 17 | 17 | 6 | 21 |

**Table 8.29**: Standardised path coefficients (x100) for the model illustrated in Figure 8.25 - BL diameter.

| | Latent Factor | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | $A_G$ | $A_S$ | $D_{R1}$ | $D_{R2}$ | $C_R$ | $E_G$ | $E_S$ | **Total** |
| **I1** | 48 | 19 | 9 | -- | -- | 5 | 19 | 100 |
| **I2** | 44 | 26 | 8 | -- | -- | 4 | 17 | 99 |
| **C** | 44 | 42 | -- | -- | -- | 4 | 9 | 99 |
| **P1** | 58 | 17 | 15 | -- | -- | 1 | 10 | 101 |
| **P2** | 51 | 26 | 13 | -- | -- | 1 | 9 | 100 |
| **M1** | 46 | 2 | -- | 9 | 29 | 1 | 13 | 100 |
| **M2** | 38 | 36 | -- | 7 | 7 | 1 | 11 | 100 |

**Table 8.30:** Comparison of heritability estimates from univariate and multivariate analyses.

| Variable | Heritability Estimate UVA | MVA |
|---|---|---|
| **Incisor MD Analysis**[a] | | |
| Max I1 | 89 | 90 |
| Max I2 | 87 | 87 |
| Man I1 | 85 | 84 |
| Man I2 | 84 | 83 |
| **Maxillary Right MD Analysis** | | |
| I1 | 89 | 89 |
| I2 | 87 | 86 |
| C | 85 | 87 |
| P1 | **85** | **80** |
| P2 | 76 | 78 |
| M1 | **59** | **70** |
| M2 | **80** | **88** |
| **Maxillary Right BL Analysis** | | |
| I1 | **81** | **76** |
| I2 | **72** | **78** |
| C | 88 | 86 |
| P1 | 89 | 89 |
| P2 | 92 | 91 |
| M1 | 59 | 56 |
| M2 | 84 | 81 |

[a] All univariate heritabilities are averaged over values for right and left sides. Multivariate heritabilities for incisor MD analysis are averaged over the sexes. Max = maxilla, Man = mandible. Heritabilities which show a difference of >3 are indicated in bold.

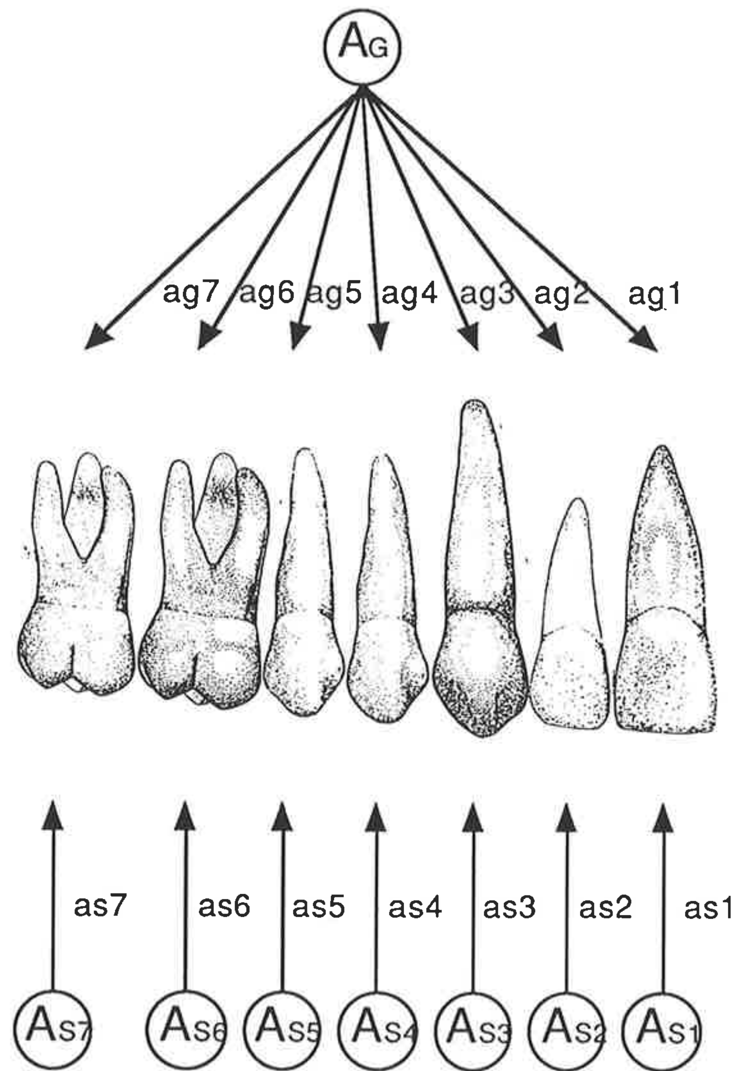



**Figure 8.1:** Diagrammatic representation of model for additive genetic variance of the maxillary right quadrant. Model contains a general factor plus seven specific factors.

**Figure 8.2:** Matrix representation of the model for additive genetic variance in Figure 8.1. Model contains a general factor plus seven specific factors.

| Tooth | General factor | Specific factors | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | $A_G$ | $A_{S1}$ | $A_{S2}$ | $A_{S3}$ | $A_{S4}$ | $A_{S5}$ | $A_{S6}$ | $A_{S7}$ |
| **I1** | 1 | 8 | | | | | | |
| **I2** | 2 | | 9 | | | | | |
| **C** | 3 | | | 10 | | | | |
| **P1** | 4 | | | | 11 | | | |
| **P2** | 5 | | | | | 12 | | |
| **M1** | 6 | | | | | | 13 | |
| **M2** | 7 | | | | | | | 14 |

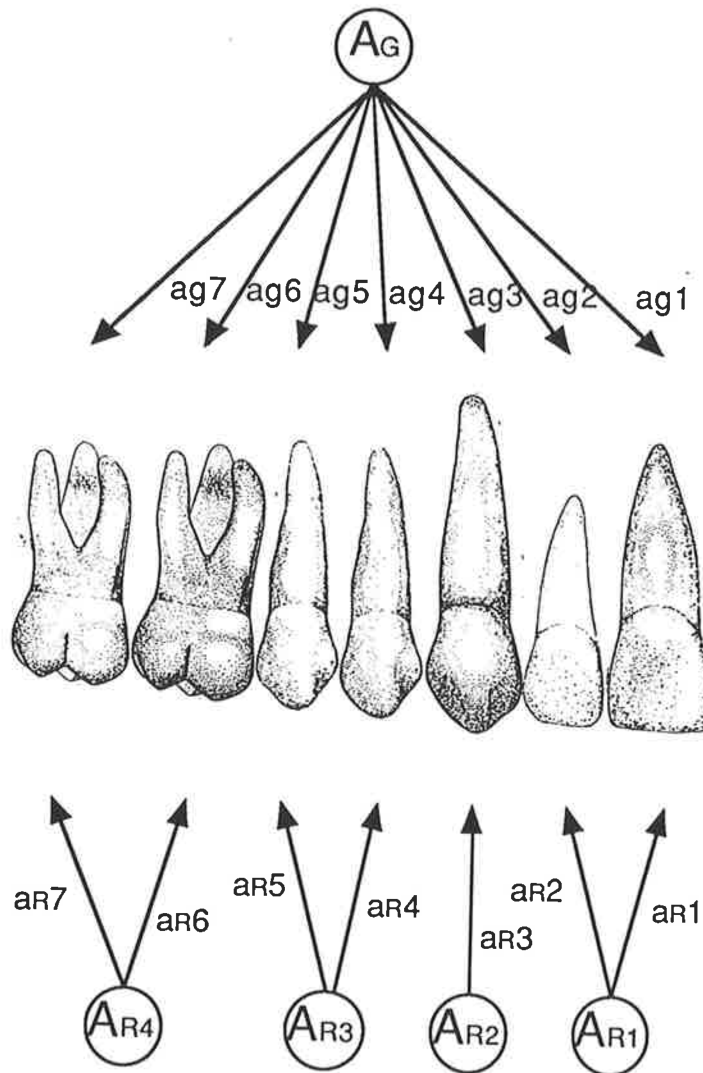



**Figure 8.3:** Diagrammatic representation of model for additive genetic variance of the maxillary right quadrant. Model contains a general factor plus group factors for each tooth group.

**Figure 8.4:** Matrix representation of the model for additive genetic variance in Figure 8.3. Model contains a general factor (constrained within tooth classes) plus group factors for each tooth class.

| Tooth | General factor | Group factors | | | |
|---|---|---|---|---|---|
| | AG | AR1 | AR2 | AR3 | AR4 |
| **I1** | 1 | 8 | | | |
| **I2** | 1 | 9 | | | |
| **C** | 3 | | 10 | | |
| **P1** | 4 | | | 11 | |
| **P2** | 4 | | | 12 | |
| **M1** | 6 | | | | 13 |
| **M2** | 6 | | | | 14 |

**Figure 8.5:** Models of additive genetic variation in the incisors. The best model is boxed.

Determination of number of factors

| | A1 | | | | |
|---|---|---|---|---|---|
| *UR I2* | 1 | | | | |
| *UR I1* | 2 | 9 | | | |
| *UL I1* | 3 | 10 | 16 | | |
| *UL I2* | 4 | 11 | 17 | 22 | |
| *LR I2* | 5 | 12 | 18 | 23 | 27 |
| *LR I1* | 6 | 13 | 19 | 24 | 28 |
| *LL I1* | 7 | 14 | 20 | 25 | 29 |
| *LL I2* | 8 | 15 | 21 | 26 | 30 |

| | A2 | | | |
|---|---|---|---|---|
| *UR I2* | 1 | | | |
| *UR I1* | 2 | 9 | | |
| *UL I1* | 3 | 10 | 16 | |
| *UL I2* | 4 | 11 | 17 | 22 |
| *LR I2* | 5 | 12 | 18 | 23 |
| *LR I1* | 6 | 13 | 19 | 24 |
| *LL I1* | 7 | 14 | 20 | 25 |
| *LL I2* | 8 | 15 | 21 | 26 |

| | A3 | | | | |
|---|---|---|---|---|---|
| *UR I2* | 1 | 9 | | 17 | |
| *UR I1* | 2 | 10 | | | 21 |
| *UL I1* | 3 | 11 | | | 22 |
| *UL I2* | 4 | 12 | | 18 | |
| *LR I2* | 5 | | 13 | 19 | |
| *LR I1* | 6 | | 14 | | 23 |
| *LL I1* | 7 | | 15 | | 24 |
| *LL I2* | 8 | | 16 | 20 | |

| | A4 | | | | |
|---|---|---|---|---|---|
| *UR I2* | 1 | 9 | | | |
| *UR I1* | 2 | | 11 | | |
| *UL I1* | 3 | | 12 | | |
| *UL I2* | 4 | 10 | | | |
| *LR I2* | 5 | | | 13 | |
| *LR I1* | 6 | | | | 15 |
| *LL I1* | 7 | | | | 16 |
| *LL I2* | 8 | | | 14 | |

| | A5 |
|---|---|
| *UR I2* | 1 |
| *UR I1* | 2 |
| *UL I1* | 3 |
| *UL I2* | 4 |
| *LR I2* | 5 |
| *LR I1* | 6 |
| *LL I1* | 7 |
| *LL I2* | 8 |

| | A6 | | | |
|---|---|---|---|---|
| *UR I2* | 9 | | | |
| *UR I1* | | 11 | | |
| *UL I1* | | 12 | | |
| *UL I2* | 10 | | | |
| *LR I2* | | | 13 | |
| *LR I1* | | | | 15 |
| *LL I1* | | | | 16 |
| *LL I2* | | | 14 | |

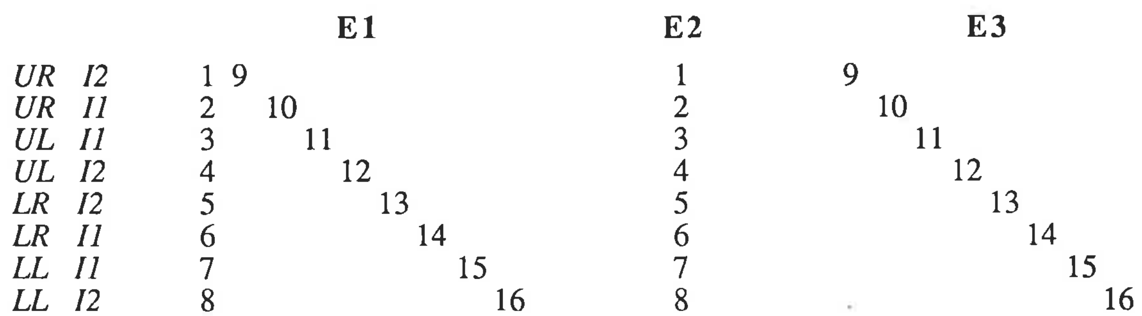
Testing symmetry of antimeres

| | A7 | | | | |
|---|---|---|---|---|---|
| *UR I2* | 1 | 9 | | | |
| *UR I1* | 2 | | 11 | | |
| *UL I1* | 2 | | 12 | | |
| *UL I2* | 1 | 10 | | | |
| *LR I2* | 5 | | | 13 | |
| *LR I1* | 6 | | | | 15 |
| *LL I1* | 6 | | | | 16 |
| *LL I2* | 5 | | | 14 | |

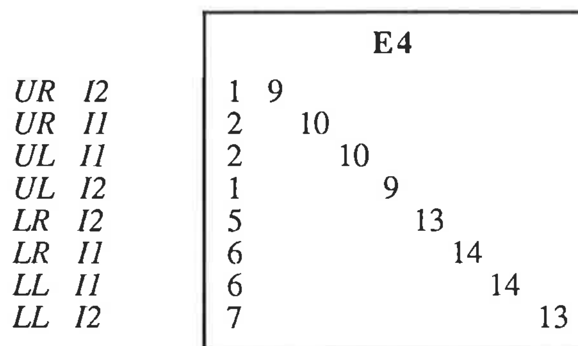
| | A8 | | | | |
|---|---|---|---|---|---|
| *UR I2* | 1 | 9 | | | |
| *UR I1* | 2 | | 11 | | |
| *UL I1* | 3 | | 11 | | |
| *UL I2* | 4 | 9 | | | |
| *LR I2* | 5 | | | 13 | |
| *LR I1* | 6 | | | | 15 |
| *LL I1* | 7 | | | | 15 |
| *LL I2* | 8 | | | 13 | |

| | A9 (boxed) | | | | |
|---|---|---|---|---|---|
| *UR I2* | 1 | 9 | | | |
| *UR I1* | 2 | | 11 | | |
| *UL I1* | 2 | | 11 | | |
| *UL I2* | 1 | 9 | | | |
| *LR I2* | 5 | | | 13 | |
| *LR I1* | 6 | | | | 15 |
| *LL I1* | 6 | | | | 15 |
| *LL I2* | 5 | | | 13 | |

**Figure 8.6** Models of unique environmental variation in the incisors.




Testing symmetry of antimeres



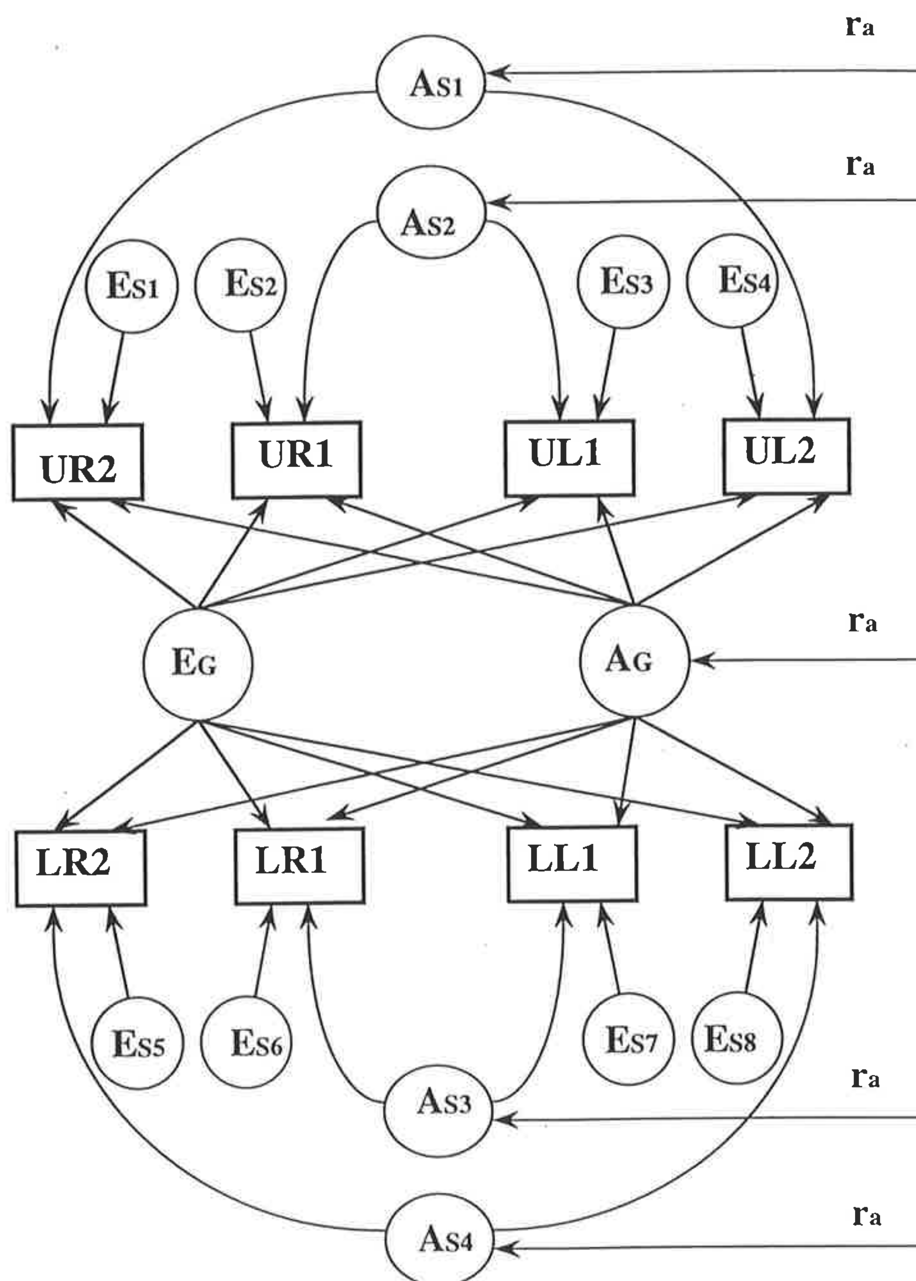



**Figure 8.7**: Path diagram of the best model for the incisors.

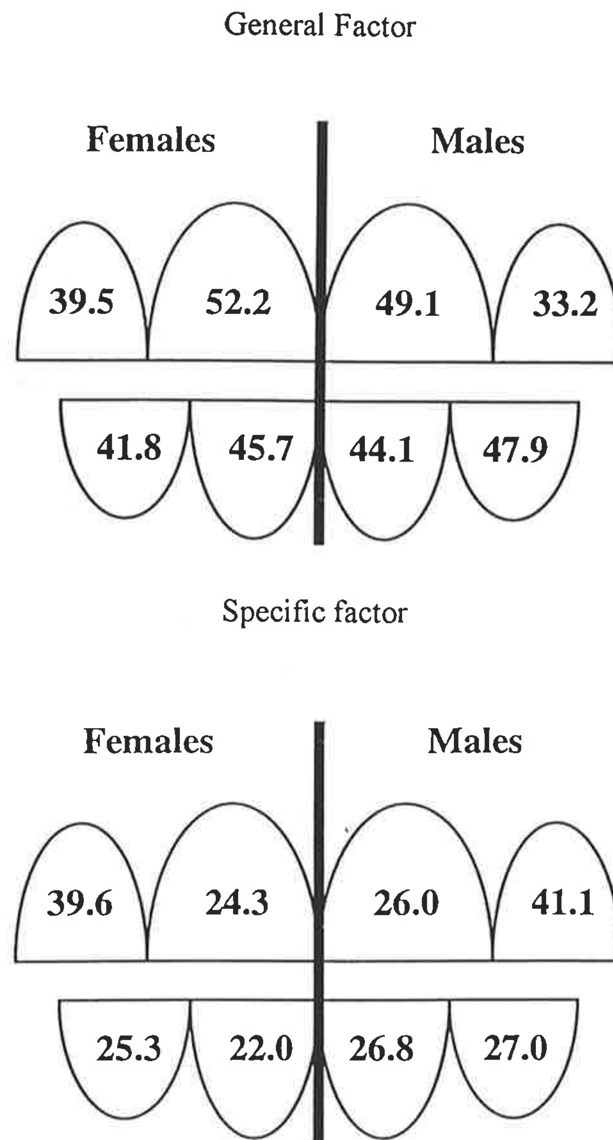



**Figure 8.8**: Standardised parameter estimates for additive genetic contributions to variation in the incisors, general and group factors. Only one side of the dentition is displayed within each sex, since the values are the same for antimeric pairs.

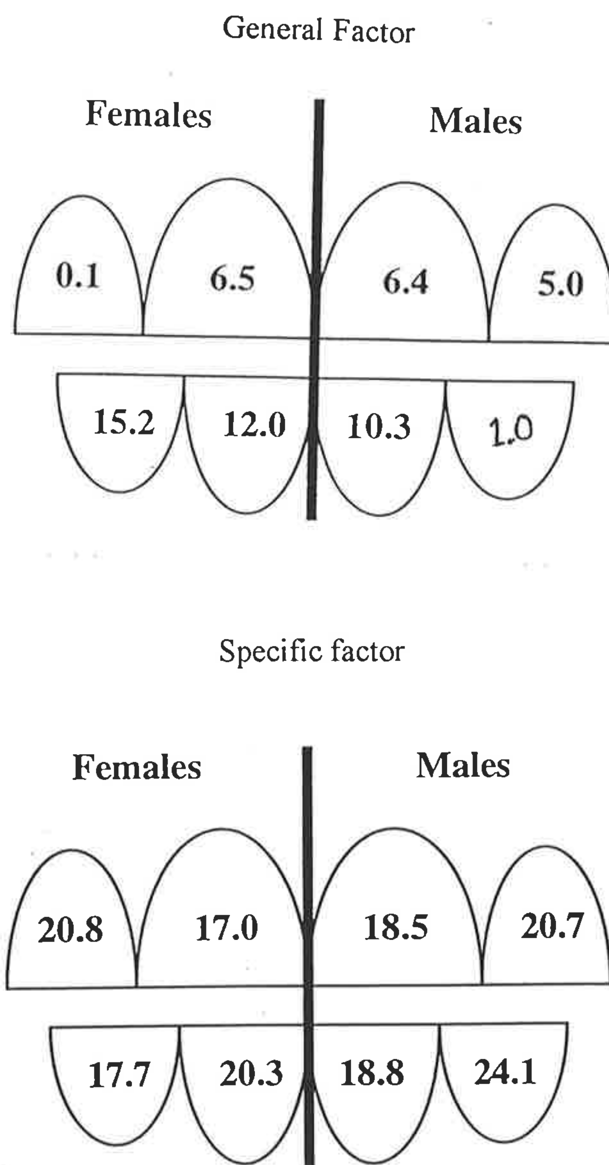



**Figure 8.9**: Standardised parameter estimates for unique environmental contributions to variation in the incisors, general and specific factors. Only one side of the dentition is displayed within each sex, since the values are the same for antimeric pairs.

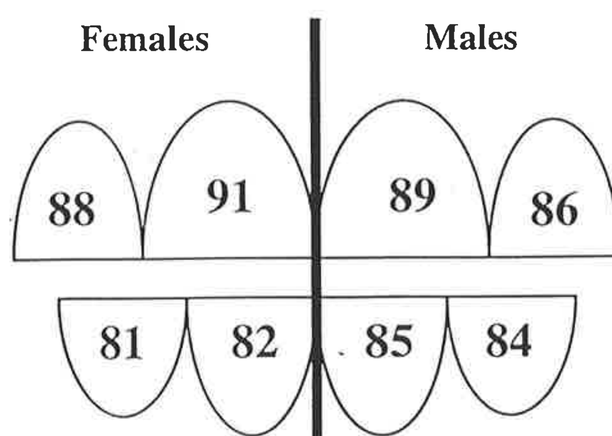
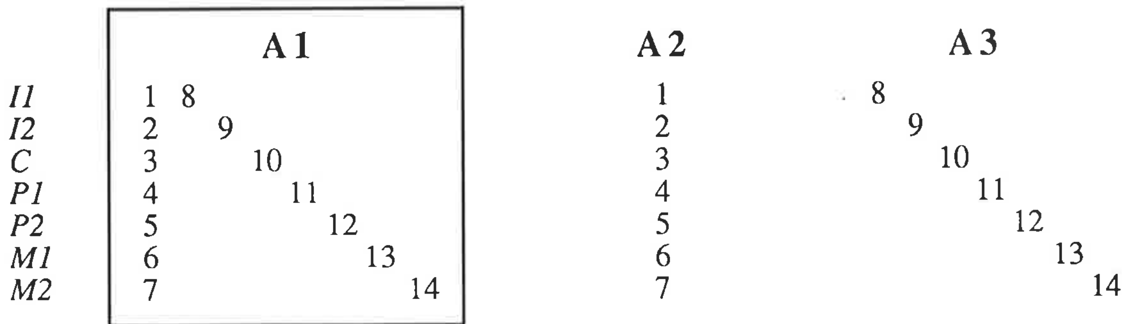



**Figure 8.10**: Heritability for the incisors in females and males.

**Figure 8.11:** Models of additive genetic contributions to variation in the maxillary right MD dimensions. The Cholesky decomposition suggested general, specific and posterior tooth group factors. For figure conventions, see Figures 8.1 to 8.4. The best model is boxed.

Testing the significance of general and specific factors




Modelling the general factor

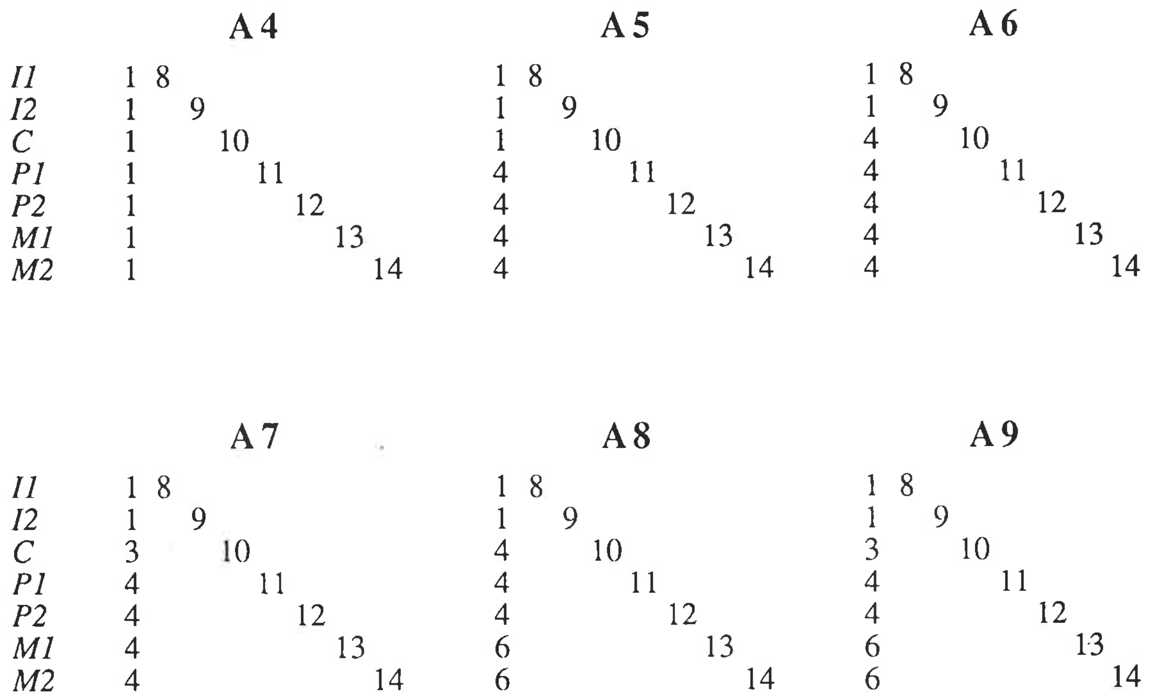


**Figure 8.11** (continued): Models of additive genetic factors - MD dimension.

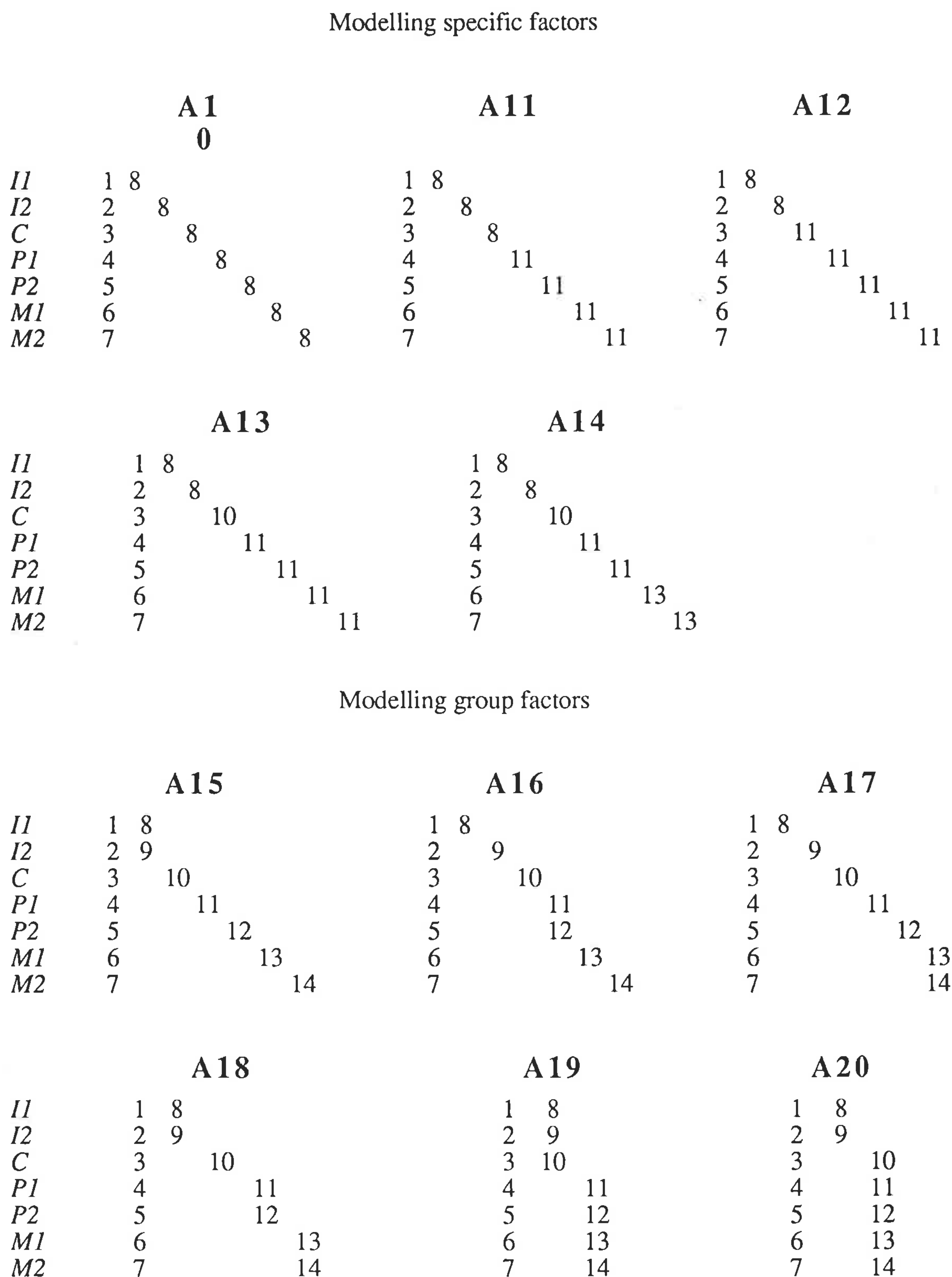


**Figure 8.12:** Models of unique environmental contributions to variation in the maxillary right MD dimensions. The Cholesky decomposition suggested specific factors were important. The best model is boxed.

Testing the significance of general and specific factors

| E1 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 2 | | 9 | | | | | |
| *C* | 3 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 5 | | | | | 12 | | |
| *M1* | 6 | | | | | | 13 | |
| *M2* | 7 | | | | | | | 14 |

| E2 | |
|---|---|
| *I1* | 1 |
| *I2* | 2 |
| *C* | 3 |
| *P1* | 4 |
| *P2* | 5 |
| *M1* | 6 |
| *M2* | 7 |

| E3 | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 8 | | | | | | |
| *I2* | | 9 | | | | | |
| *C* | | | 10 | | | | |
| *P1* | | | | 11 | | | |
| *P2* | | | | | 12 | | |
| *M1* | | | | | | 13 | |
| *M2* | | | | | | | 14 |

Modelling the general factor

| E4 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 9 | | | | | |
| *C* | 1 | | | 10 | | | | |
| *P1* | 1 | | | | 11 | | | |
| *P2* | 1 | | | | | 12 | | |
| *M1* | 1 | | | | | | 13 | |
| *M2* | 1 | | | | | | | 14 |

| E5 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 9 | | | | | |
| *C* | 1 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 12 | | |
| *M1* | 4 | | | | | | 13 | |
| *M2* | 4 | | | | | | | 14 |

| E6 (boxed) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 9 | | | | | |
| *C* | 4 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 12 | | |
| *M1* | 4 | | | | | | 13 | |
| *M2* | 4 | | | | | | | 14 |

| E7 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 9 | | | | | |
| *C* | 3 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 12 | | |
| *M1* | 4 | | | | | | 13 | |
| *M2* | 4 | | | | | | | 14 |

| E8 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 9 | | | | | |
| *C* | 4 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 12 | | |
| *M1* | 6 | | | | | | 13 | |
| *M2* | 6 | | | | | | | 14 |

| E9 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 9 | | | | | |
| *C* | 3 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 12 | | |
| *M1* | 6 | | | | | | 13 | |
| *M2* | 6 | | | | | | | 14 |

**Figure 8.12** (continued): Models of unique environmental factors - MD dimensions.

Modelling specific factors

**E10**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 8 | | | | |
| *C* | 4 | | | 8 | | | |
| *P1* | 4 | | | | 8 | | |
| *P2* | 4 | | | | | 8 | |
| *M1* | 4 | | | | | | 8 | |
| *M2* | 4 | | | | | | | 8 |

**E11**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 8 | | | | |
| *C* | 4 | | | 8 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 11 | |
| *M1* | 4 | | | | | | 11 | |
| *M2* | 4 | | | | | | | 11 |

**E12**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 8 | | | | |
| *C* | 4 | | | 11 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 11 | |
| *M1* | 4 | | | | | | 11 | |
| *M2* | 4 | | | | | | | 11 |

**E13**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 8 | | | | |
| *C* | 4 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 11 | |
| *M1* | 4 | | | | | | 11 | |
| *M2* | 4 | | | | | | | 11 |

**E14**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 8 | | | | |
| *C* | 4 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 11 | |
| *M1* | 4 | | | | | | 13 | |
| *M2* | 4 | | | | | | | 13 |

**Figure 8.13:** Models of nonadditive genetic contributions to variation in the maxillary right MD dimensions. The Cholesky decomposition suggested canine and premolar factors. The best model is boxed.

Testing the significance of general, specific or group factors

**D1**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 2 | | 9 | | | | | |
| *C* | 3 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 5 | | | | | 12 | | |
| *M1* | 6 | | | | | | 13 | |
| *M2* | 7 | | | | | | | 14 |

**D2**

| | |
|---|---|
| *I1* | 1 |
| *I2* | 2 |
| *C* | 3 |
| *P1* | 4 |
| *P2* | 5 |
| *M1* | 6 |
| *M2* | 7 |

**D3**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 8 | | | | | | |
| *I2* | | 9 | | | | | |
| *C* | | | 10 | | | | |
| *P1* | | | | 11 | | | |
| *P2* | | | | | 12 | | |
| *M1* | | | | | | 13 | |
| *M2* | | | | | | | 14 |

**D4**

| | | | | | |
|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | |
| *I2* | 2 | 9 | | | |
| *C* | 3 | | 10 | | |
| *P1* | 4 | | | 11 | |
| *P2* | 5 | | | 12 | |
| *M1* | 6 | | | | 13 |
| *M2* | 7 | | | | 14 |

**D5**

| | | | | |
|---|---|---|---|---|
| *I1* | 8 | | | |
| *I2* | 9 | | | |
| *C* | | 10 | | |
| *P1* | | | 11 | |
| *P2* | | | 12 | |
| *M1* | | | | 13 |
| *M2* | | | | 14 |

**D6**

| | | | |
|---|---|---|---|
| *I1* | 1 | 8 | |
| *I2* | 2 | 9 | |
| *C* | 3 | 10 | |
| *P1* | 4 | | 11 |
| *P2* | 5 | | 12 |
| *M1* | 6 | | 13 |
| *M2* | 7 | | 14 |

**D7**

| | | | |
|---|---|---|---|
| *I1* | 1 | 8 | |
| *I2* | 2 | 9 | |
| *C* | 3 | | 10 |
| *P1* | 4 | | 11 |
| *P2* | 5 | | 12 |
| *M1* | 6 | | 13 |
| *M2* | 7 | | 14 |

**D8**

| | | | | |
|---|---|---|---|---|
| *I1* | 1 | 8 | | |
| *I2* | 2 | 9 | | |
| *C* | 3 | | 10 | |
| *P1* | 4 | | | 11 |
| *P2* | 5 | | | 12 |
| *M1* | 6 | | | 13 |
| *M2* | 7 | | | 14 |

**D9**

| | | | |
|---|---|---|---|
| *I1* | 1 | 8 | |
| *I2* | 2 | 9 | |
| *C* | 3 | | 10 |
| *P1* | 4 | | 11 |
| *P2* | 5 | | 12 |
| *M1* | 6 | | |
| *M2* | 7 | | |

**D10**

| | | | |
|---|---|---|---|
| *I1* | 1 | 8 | |
| *I2* | 2 | 9 | |
| *C* | 3 | | 10 |
| *P1* | 4 | | 11 |
| *P2* | 5 | | |
| *M1* | 6 | | |
| *M2* | 7 | | |

**D11**

| | | |
|---|---|---|
| *I1* | 1 | |
| *I2* | 2 | 9 |
| *C* | 3 | 10 |
| *P1* | 4 | 11 |
| *P2* | 5 | |
| *M1* | 6 | |
| *M2* | 7 | |

**D12**

| | | |
|---|---|---|
| *I1* | 1 | 8 |
| *I2* | 2 | 9 |
| *C* | 3 | 10 |
| *P1* | 4 | 11 |
| *P2* | 5 | 12 |
| *M1* | 6 | |
| *M2* | 7 | |

**Figure 8.13** (continued): Models of non-additive genetic factors - MD dimensions.

Modelling the general factor

| | D13 | | | D14 | | | D15 | | |
|---|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | 1 | 8 | | 1 | 8 | |
| *I2* | 1 | 9 | | 1 | 9 | | 1 | 9 | |
| *C* | 1 | | 10 | 1 | | 10 | 4 | | 10 |
| *P1* | 1 | | 11 | 4 | | 11 | 4 | | 11 |
| *P2* | 1 | | 12 | 4 | | 12 | 4 | | 12 |
| *M1* | 1 | | | 4 | | | 4 | | |
| *M2* | 1 | | | 4 | | | 4 | | |

| | D16 | | | D17 | | | D18 | | |
|---|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | 1 | 8 | | 1 | 8 | |
| *I2* | 1 | 9 | | 1 | 9 | | 1 | 9 | |
| *C* | 3 | | 10 | 1 | | 10 | 3 | | 10 |
| *P1* | 4 | | 11 | 4 | | 11 | 4 | | 11 |
| *P2* | 4 | | 12 | 4 | | 12 | 4 | | 12 |
| *M1* | 4 | | | 6 | | | 6 | | |
| *M2* | 4 | | | 6 | | | 6 | | |

Modelling group factors

| | D19 | | | D20 | | | D21 | | | D22 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | 1 | 8 | | 1 | 8 | | 1 | 8 | |
| *I2* | 1 | 8 | | 1 | 8 | | 1 | 9 | | 1 | 8 | |
| *C* | 1 | | 8 | 1 | | 10 | 1 | | 10 | 1 | | 10 |
| *P1* | 4 | | 8 | 4 | | 10 | 4 | | 10 | 4 | | 11 |
| *P2* | 4 | | 8 | 4 | | 10 | 4 | | 10 | 4 | | 12 |
| *M1* | 4 | | | 4 | | | 4 | | | 4 | | |
| *M2* | 4 | | | 4 | | | 4 | | | 4 | | |

**Figure 8.14:** Models of common environmental contributions to variation in the maxillary right MD dimensions. The Cholesky decomposition suggested a general factor and a group factor for P2 and M1. The best model is boxed.

Testing the significance of general, specific or group factors

| | C1 | C2 | C3 | C4 |
|---|---|---|---|---|
| *I1* | 1 8 | 1 | 8 | 1 8 |
| *I2* | 2 9 | 2 | 9 | 2 9 |
| *C* | 3 10 | 3 | 10 | 3 10 |
| *P1* | 4 11 | 4 | 11 | 4 11 |
| *P2* | 5 12 | 5 | 12 | 5 12 |
| *M1* | 6 13 | 6 | 13 | 6 13 |
| *M2* | 7 14 | 7 | 14 | 7 14 |

Modelling the group factor

| | C5 | C6 | C7 | C8 | C9 | C10 |
|---|---|---|---|---|---|---|
| *I1* | 8 | 1 | | | | |
| *I2* | 9 | 2 | | | | |
| *C* | 10 | - | | | | |
| *P1* | 11 | 4 | 4 | | 4 | |
| *P2* | 12 | 5 | 5 | 5 | 5 | 5 |
| *M1* | 13 | 6 | 6 | 6 | 6 | 6 |
| *M2* | 14 | 7 | 7 | 7 | | |

| | C11 | C12 | C13 | C14 | C15 | C16 | **C17** (boxed) |
|---|---|---|---|---|---|---|---|
| *I1* | | | | | | | |
| *I2* | | | | | | | |
| *C* | | | | | | | |
| *P1* | | | 4 | 4 | 4 | 4 | 4 |
| *P2* | | | 4 | 5 | 4 | 4 | 5 |
| *M1* | 6 | 6 | 4 | 4 | 6 | 6 | 6 |
| *M2* | 7 | | 4 | 5 | 6 | 4 | 5 |

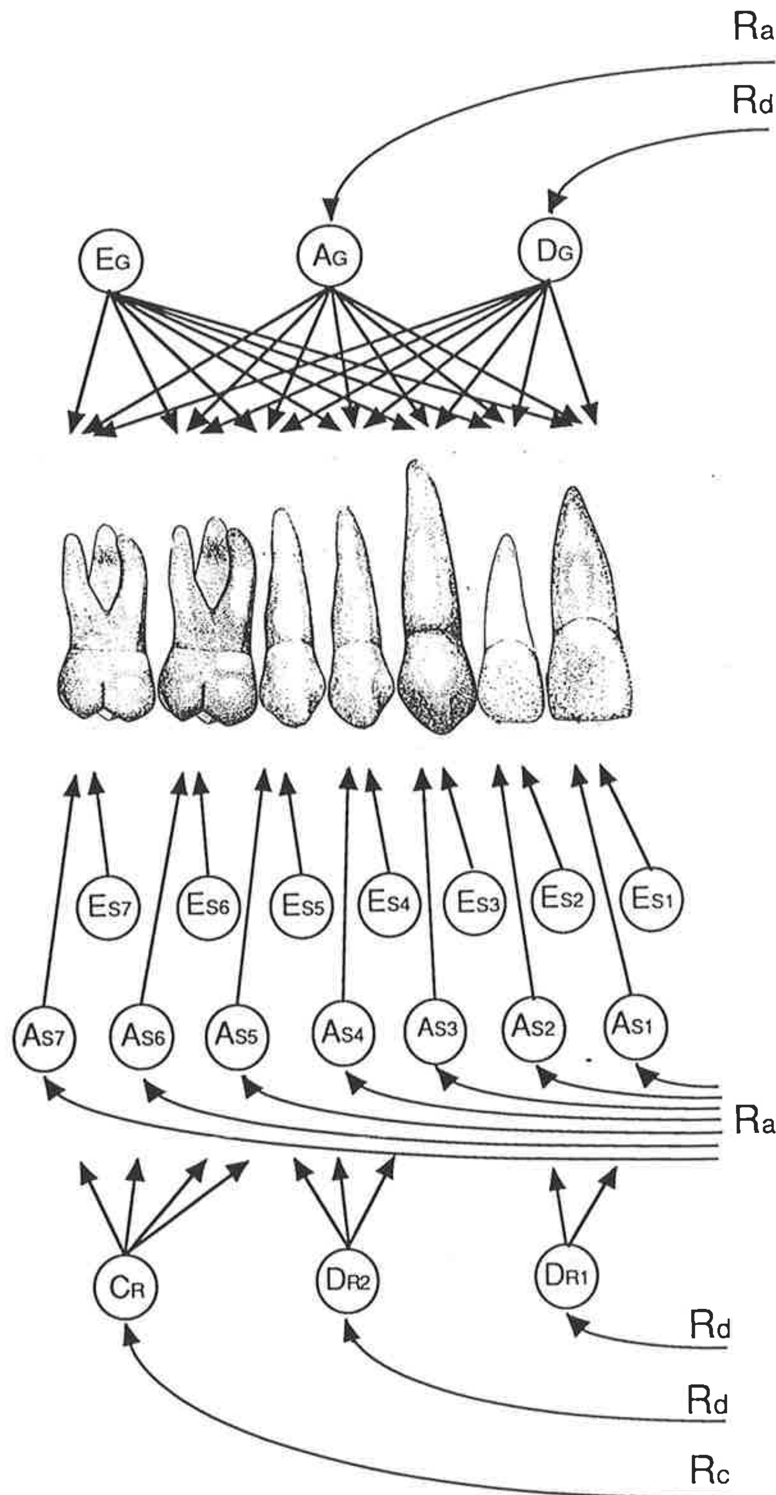



**Figure 8.15**: Path diagram for MD diameters of teeth in the maxillary right quadrant. Only half the path diagram is shown, the other half is the mirror image of this one, reflected along the righthand side of the page. Double headed arrows joining co-twins are correlations between them. The teeth left to right = M2 to I1. Circles = latent factors. Arrows from group factors are shortened for clarity. They should reach the teeth.

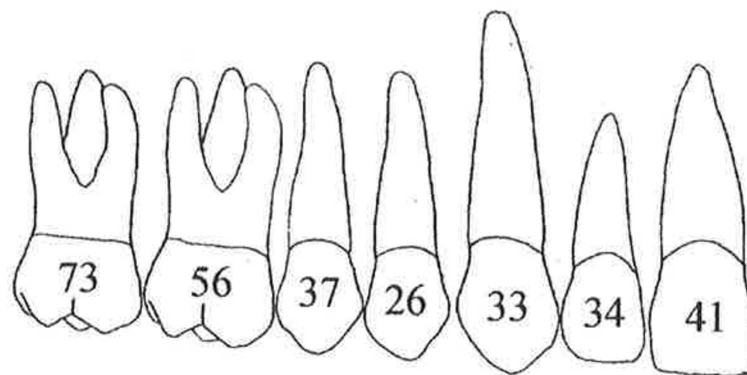



**Figure 8.16**: Percent contribution of all additive genetic factors to variation in the MD diameters of the seven permanent teeth in the maxillary right quadrant.

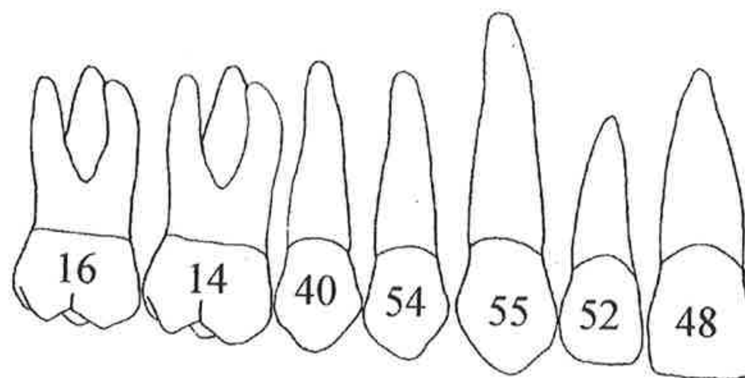



**Figure 8.17**: Percent contribution of all nonadditive genetic factors to variation in the MD diameters of the seven permanent teeth in the maxillary right quadrant.

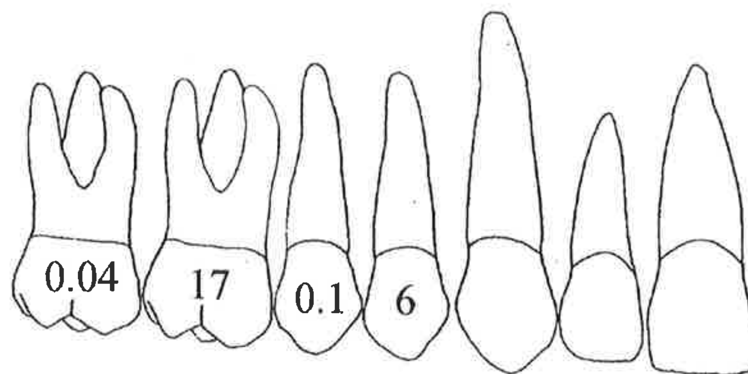



**Figure 8.18**: Percent contribution of all common environmental factors to variation in the MD diameters of the seven permanent teeth in the maxillary right quadrant.

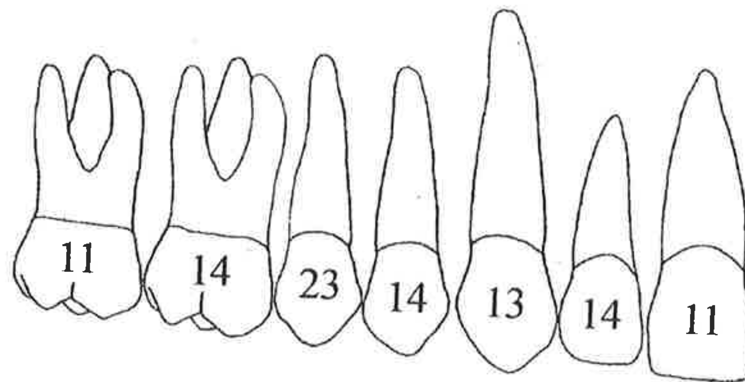



**Figure 8.19**: Percent contribution of all unique environmental factors to variation in the MD diameters of the seven permanent teeth in the maxillary right quadrant.

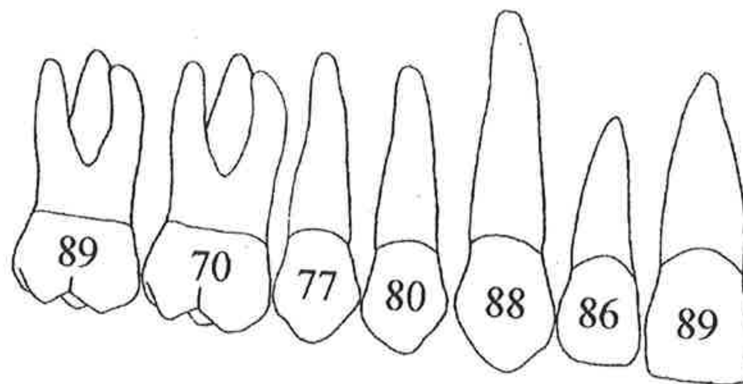
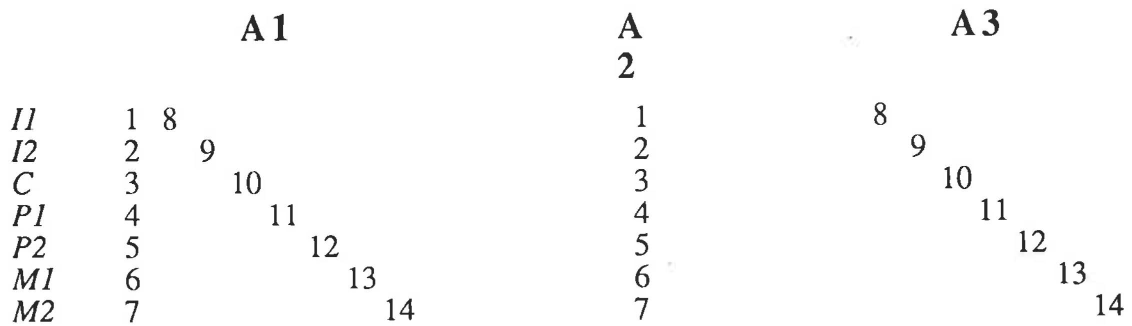



**Figure 8.20**: Broad heritability of the MD diameters of the seven permanent teeth in the maxillary right quadrant.

**Figure 8.21:** Models of additive genetic contributions to variation in the maxillary right BL dimensions. The Cholesky decomposition suggested general and either specific or tooth group factors. The best model is boxed.



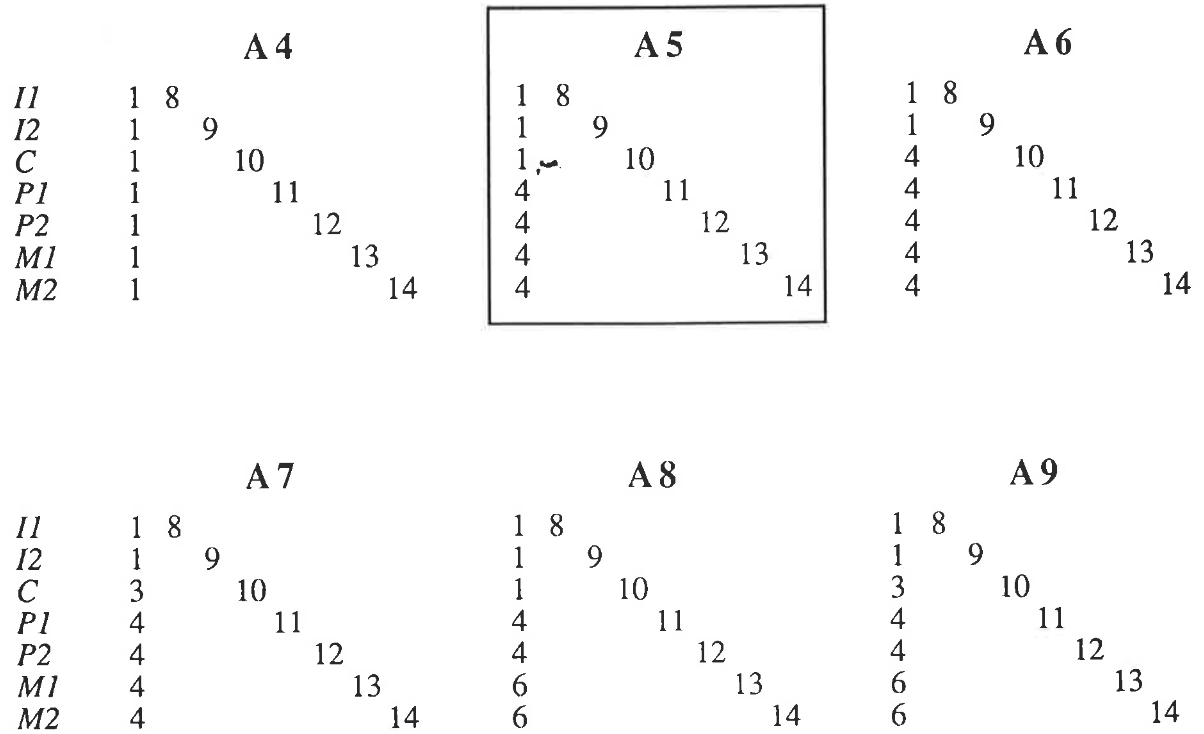



**Figure 8.21** (continued): Models of additive genetic factors - BL dimension.

Modelling specific factors

**A10**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 8 | | | | |
| *P1* | 4 | | | | 8 | | | |
| *P2* | 4 | | | | | 8 | | |
| *M1* | 4 | | | | | | 8 | |
| *M2* | 4 | | | | | | | 8 |

**A11**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 8 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 4 | | | | | | 11 | |
| *M2* | 4 | | | | | | | 11 |

**A12**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 11 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 4 | | | | | | 11 | |
| *M2* | 4 | | | | | | | 11 |

**A13**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 4 | | | | | | 11 | |
| *M2* | 4 | | | | | | | 11 |

**A14**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 4 | | | | | | 13 | |
| *M2* | 4 | | | | | | | 13 |

Modelling group factors

**A15**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | 9 | | | | | |
| *C* | 1 | | 10 | | | | |
| *P1* | 4 | | | 11 | | | |
| *P2* | 4 | | | | 12 | | |
| *M1* | 4 | | | | | 13 | |
| *M2* | 4 | | | | | | 14 |

**A16**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 9 | | | | |
| *C* | 1 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | 12 | | |
| *M1* | 4 | | | | | 13 | |
| *M2* | 4 | | | | | | 14 |

**A17**

| | | | | | | |
|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | |
| *I2* | 1 | | 9 | | | |
| *C* | 1 | | | 10 | | |
| *P1* | 4 | | | | 11 | |
| *P2* | 4 | | | | | 12 |
| *M1* | 4 | | | | | | 13 |
| *M2* | 4 | | | | | | 14 |

**A18**

| | | | | | |
|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | |
| *I2* | 1 | 9 | | | |
| *C* | 1 | | 10 | | |
| *P1* | 4 | | | 11 | |
| *P2* | 4 | | | 12 | |
| *M1* | 4 | | | | 13 |
| *M2* | 4 | | | | 14 |

**A19**

| | | | |
|---|---|---|---|
| *I1* | 1 | 8 | |
| *I2* | 1 | 9 | |
| *C* | 1 | 10 | |
| *P1* | 4 | | 11 |
| *P2* | 4 | | 12 |
| *M1* | 4 | | 13 |
| *M2* | 4 | | 14 |

**A20**

| | | | | |
|---|---|---|---|---|
| *I1* | 1 | 8 | | |
| *I2* | 1 | 9 | | |
| *C* | 1 | | 10 | |
| *P1* | 4 | | | 11 |
| *P2* | 4 | | | 12 |
| *M1* | 4 | | | 13 |
| *M2* | 4 | | | 14 |

**Figure 8.22:** Models of unique environmental contributions to variation in the maxillary right BL dimensions. The Cholesky decomposition suggested that specific factors were important. The best model is boxed.

Testing the significance of general and specific factors

**E1**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 2 | | 9 | | | | |
| *C* | 3 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 5 | | | | | 12 | |
| *M1* | 6 | | | | | | 13 |
| *M2* | 7 | | | | | | 14 |

**E2**

| | |
|---|---|
| *I1* | 1 |
| *I2* | 2 |
| *C* | 3 |
| *P1* | 4 |
| *P2* | 5 |
| *M1* | 6 |
| *M2* | 7 |

**E3**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 8 | | | | | | |
| *I2* | | 9 | | | | | |
| *C* | | | 10 | | | | |
| *P1* | | | | 11 | | | |
| *P2* | | | | | 12 | | |
| *M1* | | | | | | 13 | |
| *M2* | | | | | | | 14 |

Modelling the general factor

**E4**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 9 | | | | |
| *C* | 1 | | | 10 | | | |
| *P1* | 1 | | | | 11 | | |
| *P2* | 1 | | | | | 12 | |
| *M1* | 1 | | | | | | 13 |
| *M2* | 1 | | | | | | 14 |

**E5**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 9 | | | | |
| *C* | 1 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 12 | |
| *M1* | 4 | | | | | | 13 |
| *M2* | 4 | | | | | | 14 |

**E6**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 9 | | | | |
| *C* | 4 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 12 | |
| *M1* | 4 | | | | | | 13 |
| *M2* | 4 | | | | | | 14 |

**E7**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 9 | | | | |
| *C* | 3 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 12 | |
| *M1* | 4 | | | | | | 13 |
| *M2* | 4 | | | | | | 14 |

**E8**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 9 | | | | |
| *C* | 1 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 12 | |
| *M1* | 6 | | | | | | 13 |
| *M2* | 6 | | | | | | 14 |

**E9**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | |
| *I2* | 1 | | 9 | | | | |
| *C* | 3 | | | 10 | | | |
| *P1* | 4 | | | | 11 | | |
| *P2* | 4 | | | | | 12 | |
| *M1* | 6 | | | | | | 13 |
| *M2* | 6 | | | | | | 14 |

**Figure 8.22** (continued): Models of unique environmental factors - BL dimension.

Modelling specific factors

**E10**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 8 | | | | |
| *P1* | 4 | | | | 8 | | | |
| *P2* | 4 | | | | | 8 | | |
| *M1* | 6 | | | | | | 8 | |
| *M2* | 6 | | | | | | | 8 |

**E11**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 8 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 6 | | | | | | 11 | |
| *M2* | 6 | | | | | | | 11 |

**E12**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 11 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 6 | | | | | | 11 | |
| *M2* | 6 | | | | | | | 11 |

**E13**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 6 | | | | | | 11 | |
| *M2* | 6 | | | | | | | 11 |

**E14**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 11 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 6 | | | | | | 13 | |
| *M2* | 6 | | | | | | | 13 |

**E15**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 1 | | 8 | | | | | |
| *C* | 1 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 4 | | | | | 11 | | |
| *M1* | 6 | | | | | | 13 | |
| *M2* | 6 | | | | | | | 13 |

**Figure 8.23:** Models of nonadditive genetic contributions to variation in the maxillary right BL dimensions. The Cholesky decomposition suggested a general factor. The best model is boxed.

Testing the significance of general, specific or group factors

| | **D1** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 2 | | 9 | | | | | |
| *C* | 3 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 5 | | | | | 12 | | |
| *M1* | 6 | | | | | | 13 | |
| *M2* | 7 | | | | | | | 14 |

| | **D2** |
|---|---|
| *I1* | 1 |
| *I2* | 2 |
| *C* | 3 |
| *P1* | 4 |
| *P2* | 5 |
| *M1* | 6 |
| *M2* | 7 |

| | **D3** | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 8 | | | | | | |
| *I2* | | 9 | | | | | |
| *C* | | | 10 | | | | |
| *P1* | | | | 11 | | | |
| *P2* | | | | | 12 | | |
| *M1* | | | | | | 13 | |
| *M2* | | | | | | | 14 |

| | **D4** | | | | |
|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | |
| *I2* | 2 | 9 | | | |
| *C* | 3 | | 10 | | |
| *P1* | 4 | | | 11 | |
| *P2* | 5 | | | 12 | |
| *M1* | 6 | | | | 13 |
| *M2* | 7 | | | | 14 |

| | **D5** | | | |
|---|---|---|---|---|
| *I1* | 8 | | | |
| *I2* | 9 | | | |
| *C* | | 10 | | |
| *P1* | | | 11 | |
| *P2* | | | 12 | |
| *M1* | | | | 13 |
| *M2* | | | | 14 |

| | **D6** | | |
|---|---|---|---|
| *I1* | 1 | 8 | |
| *I2* | 2 | 9 | |
| *C* | 3 | | 10 |
| *P1* | 4 | | 11 |
| *P2* | 5 | | 12 |
| *M1* | 6 | | 13 |
| *M2* | 7 | | 14 |

| | **D7** | |
|---|---|---|
| *I1* | 1 | 8 |
| *I2* | 2 | 9 |
| *C* | 3 | |
| *P1* | 4 | |
| *P2* | 5 | |
| *M1* | 6 | |
| *M2* | 7 | |

| | **D8** | |
|---|---|---|
| *I1* | 1 | |
| *I2* | 2 | |
| *C* | 3 | 10 |
| *P1* | 4 | 11 |
| *P2* | 5 | 12 |
| *M1* | 6 | 13 |
| *M2* | 7 | 14 |

| | **D9** | |
|---|---|---|
| *I1* | 1 | |
| *I2* | 2 | |
| *C* | 3 | |
| *P1* | 4 | 11 |
| *P2* | 5 | 12 |
| *M1* | 6 | 13 |
| *M2* | 7 | 14 |

| | **D10** | |
|---|---|---|
| *I1* | 1 | |
| *I2* | 2 | |
| *C* | 3 | |
| *P1* | 4 | |
| *P2* | 5 | 12 |
| *M1* | 6 | 13 |
| *M2* | 7 | 14 |

| | **D11** | |
|---|---|---|
| *I1* | 1 | |
| *I2* | 2 | |
| *C* | 3 | |
| *P1* | 4 | |
| *P2* | 5 | |
| *M1* | 6 | 13 |
| *M2* | 7 | 14 |

| | **D12** | |
|---|---|---|
| *I1* | 1 | |
| *I2* | 2 | |
| *C* | | |
| *P1* | 4 | |
| *P2* | 5 | |
| *M1* | 6 | 13 |
| *M2* | 7 | 14 |

| | **D13** | |
|---|---|---|
| *I1* | 1 | |
| *I2* | 2 | |
| *C* | | |
| *P1* | 4 | |
| *P2* | 5 | |
| *M1* | | 13 |
| *M2* | 7 | 14 |

| | **D14** | |
|---|---|---|
| *I1* | 1 | |
| *I2* | 2 | |
| *C* | | |
| *P1* | 4 | |
| *P2* | 5 | |
| *M1* | | 6 |
| *M2* | | 7 |

**Figure 8.23** (continued): Models of non-additive genetic factors - BL dimension. .

| | **D15** | **D16** | **D17** | **D18** |
|---|---|---|---|---|
| *I1* | 1 | 1 | 1 | |
| *I2* | 2 | 2 | 2 | |
| *C* | | | | |
| *P1* | 4 | 4 | | 4 |
| *P2* | 5 | 5 | | 5 |
| *M1* | 6 | | 6 | 6 |
| *M2* | 7 | | 7 | 7 |

Can the factors be constrained?

| | **D19** | **D20** | **D21** | **D22** |
|---|---|---|---|---|
| *I1* | 1 | 1 | 1 | 1 |
| *I2* | 1 | 1 | 1 | 1 |
| *C* | | | | |
| *P1* | 1 | 1 | 1 | 4 |
| *P2* | 1 | 1 | 1 | 4 |
| *M1* | 1 | 6 | 6 | 6 |
| *M2* | 1 | 6 | 7 | 6 |

**Figure 8.24:** Models of common environmental contributions to variation in the maxillary right BL dimensions. The Cholesky decomposition suggested a general factor and a group factor for M1 and M2. The best model is boxed.

Testing the significance of general, specific or group factors

**C1**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | | | | |
| *I2* | 2 | | 9 | | | | | |
| *C* | 3 | | | 10 | | | | |
| *P1* | 4 | | | | 11 | | | |
| *P2* | 5 | | | | | 12 | | |
| *M1* | 6 | | | | | | 13 | |
| *M2* | 7 | | | | | | | 14 |

**C2**

| | |
|---|---|
| *I1* | 1 |
| *I2* | 2 |
| *C* | 3 |
| *P1* | 4 |
| *P2* | 5 |
| *M1* | 6 |
| *M2* | 7 |

**C3**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *I1* | 8 | | | | | | |
| *I2* | | 9 | | | | | |
| *C* | | | 10 | | | | |
| *P1* | | | | 11 | | | |
| *P2* | | | | | 12 | | |
| *M1* | | | | | | 13 | |
| *M2* | | | | | | | 14 |

**C4**

| | | | | | |
|---|---|---|---|---|---|
| *I1* | 1 | 8 | | | |
| *I2* | 2 | 9 | | | |
| *C* | 3 | | 10 | | |
| *P1* | 4 | | | 11 | |
| *P2* | 5 | | | 12 | |
| *M1* | 6 | | | | 13 |
| *M2* | 7 | | | | 14 |

Modelling the group factors

**C5**

| | | | | |
|---|---|---|---|---|
| *I1* | 8 | | | |
| *I2* | 9 | | | |
| *C* | | 10 | | |
| *P1* | | | 11 | |
| *P2* | | | 12 | |
| *M1* | | | | 13 |
| *M2* | | | | 14 |

**C6**

| | | | |
|---|---|---|---|
| *I1* | | | |
| *I2* | | | |
| *C* | 10 | | |
| *P1* | | 11 | |
| *P2* | | 12 | |
| *M1* | | | 13 |
| *M2* | | | 14 |

**C7**

| | | |
|---|---|---|
| *I1* | | |
| *I2* | | |
| *C* | | |
| *P1* | 11 | |
| *P2* | 12 | |
| *M1* | | 13 |
| *M2* | | 14 |

**C8** (boxed)

| | |
|---|---|
| *I1* | |
| *I2* | |
| *C* | |
| *P1* | |
| *P2* | |
| *M1* | 13 |
| *M2* | 14 |

**C9**

| | |
|---|---|
| *I1* | |
| *I2* | |
| *C* | |
| *P1* | |
| *P2* | 12 |
| *M1* | 13 |
| *M2* | 14 |

**C10**

| | |
|---|---|
| *I1* | |
| *I2* | |
| *C* | |
| *P1* | |
| *P2* | |
| *M1* | 13 |
| *M2* | |

**C11**

| | |
|---|---|
| *I1* | |
| *I2* | |
| *C* | |
| *P1* | |
| *P2* | |
| *M1* | |
| *M2* | 14 |

**C12**

| | |
|---|---|
| *I1* | |
| *I2* | |
| *C* | |
| *P1* | |
| *P2* | |
| *M1* | 13 |
| *M2* | 13 |

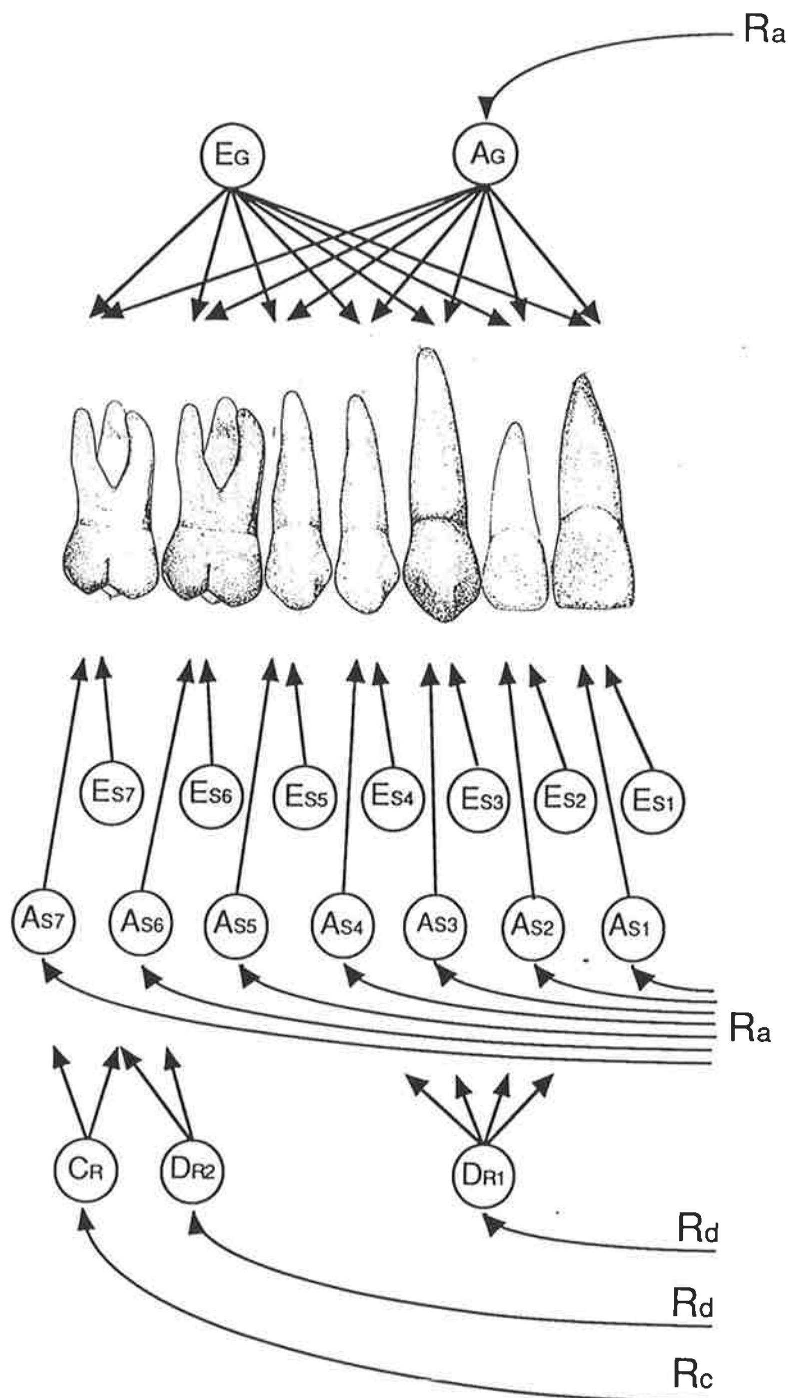



**Figure 8.25**: Path diagram for BL diameters of teeth in the maxillary right quadrant. Only half the path diagram is shown, the other half is the mirror image of this one, reflected along the righthand side of the page. Double headed arrows joining co-twins are correlations between them. The teeth left to right = M2 to I1. Circles = latent factors.

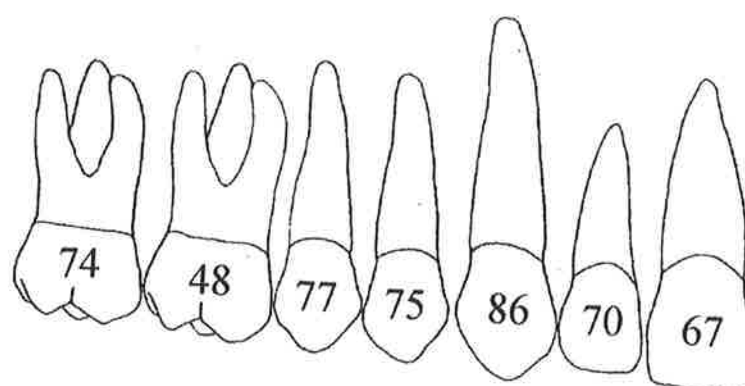



**Figure 8.26**: Percent contribution of all additive genetic factors to variation in the BL diameters of the seven permanent teeth in the maxillary right quadrant.

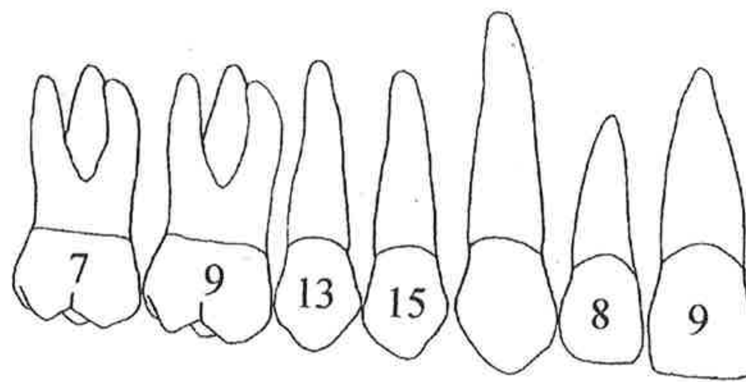



**Figure 8.27**: Percent contribution of all nonadditive genetic factors to variation in the BL diameters of the seven permanent teeth in the maxillary right quadrant.

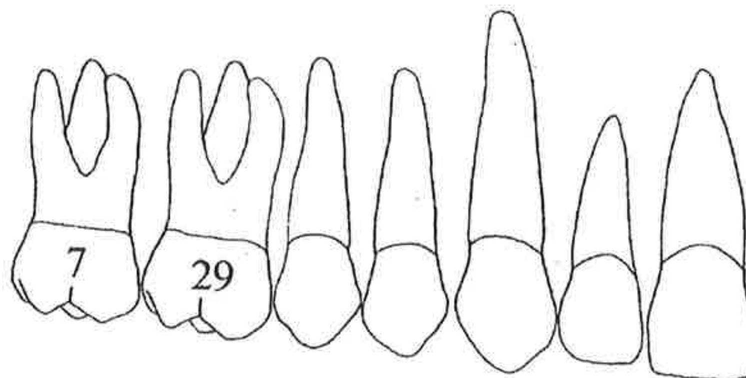



**Figure 8.28**: Percent contribution of all common environmental factors to variation in the BL diameters of the seven permanent teeth in the maxillary right quadrant.

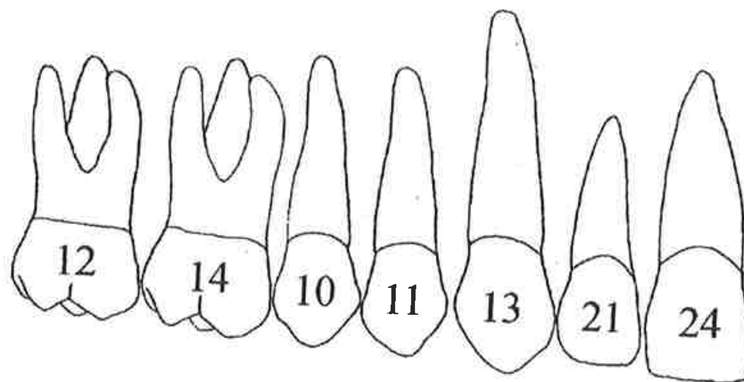



**Figure 8.29**: Percent contribution of all unique environmental factors to variation in the BL diameters of the seven permanent teeth in the maxillary right quadrant.

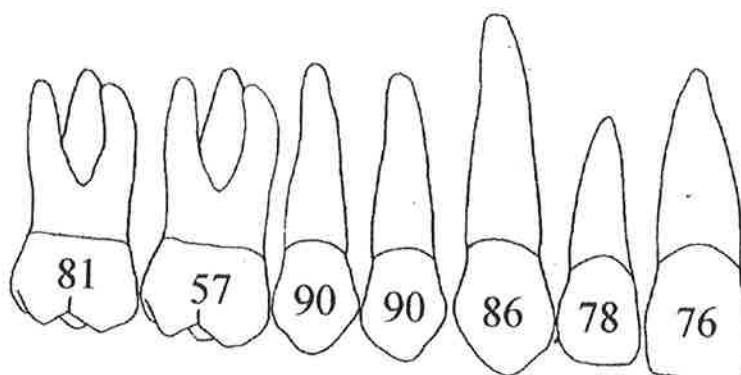



**Figure 8.30**: Broad heritability of the BL diameters of the seven permanent teeth in the maxillary right quadrant.

# Chapter 9

# Final Synthesis

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## Introduction

In this chapter I intend to draw together the findings of this study, and examine them in the light of dental genetic theory. At the outset, the main objective of this project was to elucidate the nature and extent of genetic and environmental determination of variability in permanent tooth crown size. My approach was to compare levels of covariation in MZ and DZ twins, and the patterns of numerous variables among twins and singletons. The following discussion draws together the findings of the main areas of research covered by this thesis - sexual dimorphism, and genetic and environmental contributions to variation in tooth crown size.

## Sexual Dimorphism

Mean sizes of permanent tooth crowns were significantly larger in males than females, a pattern shared with most other primates, and other published studies of tooth crown size in humans. Also consistent with previous reports, canines and molars were the most highly dimorphic teeth, while incisors were the least, and BL diameters were more highly dimorphic in general than MD diameters. The modelling analyses revealed dimorphism in the means of most of the 56 variables, while for the most part, there were no sexual differences in variances of, or covariances between, twins. The lack of a sex difference in variance is interesting, because it implies that there was no current differential selection occurring between the sexes (Arnold and Wade 1984), so whatever selection may have existed was the same for males and females.

### Sex Chromosomes

We know from molecular genetic research, and from studies of people with sex chromosome anomalies, that both sex chromosomes play a role in human tooth development. It also has been postulated that the presence of amelogenin genes on X

and Y chromosomes, and the differences in their DNA sequences, may cause the sexual dimorphism observed in mean tooth crown size. Before these studies were even contemplated, however, a method of comparing sibling correlations to test for sex chromosomal influences had been devised and employed. The first analysis of tooth crown size using this method confirmed evidence for sex chromosome effects, but the finding was not repeated in other studies. The predicted patterns of sibling correlations (SS>BB>SB) did not take into account Y-linked genes or X-inactivation, so the expectations may have been unrealistic, accounting for the inconclusive results. My reformulation of predicted pattern of correlations yielded an expectation of brothers (BB) being more highly correlated than sisters (SS), and sister-brother pairs (SB) showing the lowest correlations. This pattern was displayed by almost half of the 56 variables analysed in Chapter 5.

However, previous statistical and molecular analyses by others, and the biometrical analyses in this thesis, consistently support the notion that a variety of genes and environmental factors account for observed variation in tooth crown size. Sex chromosomal influences would have to be strong enough to override other genetic and environmental effects before sibling correlations would display the expected pattern consistently.

In addition, the same correlation patterns (BB>SS>SB) may be produced by genetic or environmental factors unrelated to sex-linked genes. For instance, SB correlations for any sexually dimorphic trait would be expected to be lower than BB or SS correlations, whether or not the dimorphism was due to sex-linked genes. My finding that SB correlations were lowest in nearly three quarters of the 56 variables thus may reflect the sexually dimorphic nature of tooth size. There also may be sex-limited genetic (autosomal) and environmental effects which could give rise to BB correlations being greater than those of SS and SB pairs. One possible scenario involves the diffusion of sex hormones between the twins. If male sex hormones promote tooth crown size as

suggested by the analyses in Chapter 6, then diffusion of male sex hormones between DZ twin brothers might be expected to increase the correlations between them, relative to females. This also assumes that the level of sex hormone produced by a male can differ from that produced by his DZ twin brother, perhaps under the influence of polymorphic genes, or because of differences in efficiency of placental exchange.

One of the benefits of conducting research using a variety of approaches is that possible alternative explanations may be supported or discarded by examination of the question from a different perspective. In this case, we can ask if there is evidence from biometrical modelling analyses of sex-limited genetic or environmental factors which might cause BB correlations to be greater than SS correlations. For instance, the sex hormone scenario described above. If strong enough in effect, this could produce a male-limited common environmental effect in biometrical modelling analyses. The only variables which suggested such factors might have occurred were the BL diameters of maxillary central incisors and canines, for which only one (maxillary right central incisor) exhibited higher correlations in BB pairs than SS or SB pairs. Thus, there is no evidence that the variables which exhibited the predicted pattern of sibling correlations did so for reasons other than a sex chromosomal influence. The conclusion that sex chromosomes influenced tooth crown size can be considered to be stronger in the presence of results from modelling analyses.

**Sex Hormones**

From the comparison of OS and SS twins and singletons, there was evidence that sexual dimorphism may have been due, at least in part, to male sex hormones (or another sexually dimorphic, diffusible molecule). In addition, the hormones may have affected tooth crown size in females from OS twin pairs. Surprisingly, the pattern did not correlate with the degree of sexual dimorphism in different teeth, suggesting that the influence of androgens may differ between teeth.

In conclusion, the data displayed sexual dimorphism for tooth crown size, with males having larger teeth on average than females, evidence of a contribution of the sex chromosomes to tooth crown size, and evidence consistent with a contribution of sex hormones to sexual dimorphism in tooth crown size. The genetic basis of the dimorphism probably involves a combination of genetic factors, including X- and Y-linked amelogenin genes, sex hormones, and other genes.

## Genetics of Tooth Crown Size

Variation in the size of permanent tooth crowns was found to be strongly influenced by genetic factors. All teeth had a relatively high degree of additive genetic variation (56 to 92% of variation in univariate analyses). Although non-additive genetic variation was not necessary in any of the analyses, its inclusion resulted in significant improvements in the fit of models.

### Additive Genetic Variation

The chosen biometrical models suggested that genes which contributed to variation additively, tended to do so in one of two ways. They either influenced individual tooth crowns (or at most, antimeric pairs of teeth), or acted pleiotropically, contributing to variation in most or all of the teeth within a quadrant together. The region of influence for these pleiotropic genes, of course, may be larger than a quadrant, extending around the dental arch, and/or incorporating both mandibular and maxillary dentitions. In addition, both MD and BL diameters may have been influenced simultaneously. Insights into the region of influence were gained from the multivariate analysis of incisor MD dimensions.

Within the incisor group, the general additive genetic factor affected the eight incisors together - right and left sides, maxilla and mandible. This suggests that pleiotropic influences on MD dimensions probably did extend throughout the whole dentition. Further evidence for a group of genes influencing all of the teeth, arises from the existence of strong intercorrelations among teeth. Since these intercorrelations extend to comparisons of MD and BL diameters of each tooth, the pleiotropic genes may affect both MD and BL dimensions.

The other additive genetic factors were shared by right and left members of each antimeric pair of incisors, suggesting that genes which contributed to variation in each tooth on one side of the dentition affected their antimere as well. Thus, even apparently tooth-specific groups of genes may have been pleiotropic in their influence. These findings are not surprising in bilaterally symmetrical organisms, and are supported by the high degree of bilateral symmetry exhibited in parameter estimates from modelling analyses, and by the finding that intercorrelations were highest between antimeric pairs of teeth.

It has been suggested that genes almost always have pleiotropic effects (Wright 1968), particularly those genes which are expressed early in development. This is certainly true of genes for skeletal components (Atchley and Hall 1991), so the finding of pleiotropic influences in the dentition is consistent with this idea. Conversely, the additive genetic factors which impacted on individual teeth and, presumably their antimeres, were not expected. Given the high degree of similarity among members within each tooth group - especially among premolars and among molars - it was expected that there would be evidence of variation due to incisor, premolar, and molar groups of genes. Thus, the multivariate analyses did not reveal evidence for genetic determinants of morphogenetic fields as described by Butler (1939), or for Osborn's clones (1973, 1975, 1978).

**Non-Additive Genetic Variation**

Non-additive genetic factors (dominance and/or epistatic interactions) displayed a different pattern of occurrence from additive factors. They were strongly present in MD diameters of all four canines and three of the four first premolars in the univariate analyses. In the two multivariate analyses of the maxillary right quadrant, non-additive genetic factors incorporated interesting groups of variables. Among MD dimensions there was a general factor, a second factor acting on incisors, and a third on canine and both premolars. For BL dimensions there was one group factor influencing variation in incisors and premolars, and a second acting on molars. As outlined previously, the presence of non-additive genetic variation is suggestive of natural selection acting, or having acted, on these groups of teeth.

As was the case with additive genetic factors, the general non-additive genetic factor acting on MD dimensions may have been a more generally-acting (skeletal) factor. The groups factors were particularly intriguing, suggesting that natural selection, at some stage, may have acted on diameters of groups of teeth together. That is, the combined MD dimensions of both maxillary incisors, or of the canine and both premolars, may have been important at some point in our evolutionary history. This evidence of selection extended to both premolars and both incisors in the multivariate analyses, with a small amount being present in the molars as well.

The potential importance of the canine and first premolar as an adaptive complex was outlined in Chapter 7. In addition, the canine is the most sexually dimorphic permanent tooth. It also displayed high levels of non-additive genetic variation, suggesting a moderate to large influence of natural selection may have affected its development. Comparison of levels of sexual dimorphism in modern humans with other hominids and primates, revealed a pattern of increasing sexual dimorphism with evolutionary distance from modern humans. Thus the small amount of sexual dimorphism displayed in human

teeth may represent an exaptation (sensu Gould and Vrba 1982), that is, a feature derived from selection on the teeth of males of a common ancestor between modern humans and apes, but which is no longer under selection. It is possible that sexual selection for canine size operating in a common ancestor to modern primates is the source of the non-additive genetic variation displayed most strongly in canines and first premolars.

### Implications of Additive versus Non-Additive Genetic Variation

According to Fisher's fundamental theorem, the higher the proportion of additive genetic variation, the faster is the response to any natural selection applied to the population (Fisher 1930). Also, as noted previously, the presence of non-additive genetic variation is consistent with the population having been subjected to such selective pressures at some point. So the dentition may have responded to natural selection, and retains the ability to respond should new (or old) selective pressures arise.

## Environment and Tooth Crown Size

Unique environmental factors contributed between 8 and 29% of the variation in tooth crown diameters. The vast majority of this was tooth-specific and probably reflects the fact that teeth vary in the length of time spent in the soft tissue phase. Each tooth thus has a different range of environmental influences to which it is subjected. Environmental factors common to a pair of twins had their impact on maxillary molars and premolars, with the extent of the influence showing some association with timing of calcification. This suggested that the environmental aspect may have been pre- or peri-natal in its timing (see Chapter 8). The univariate analyses were different in that common environmental variation was restricted to both diameters of maxillary first molars. As with genetic factors, the multivariate analyses revealed complex

environmental factors acting on groups of teeth together, which were not found in univariate analyses.

Given that maxillary and mandibular first molars calcify at about the same time, it is curious that this influence of common environmental variation was only revealed in the maxillary first molars in the univariate analyses. One possibility is that there is a difference between maxillary and mandibular molar development such that it is an advantage for maxillary first molars to be more highly plastic in their shape before calcification begins. A second possibility is that common environmental variation does exist in mandibular teeth, and although not disclosed by a univariate approach, would be revealed in a multivariate analysis of mandibular teeth.

## Advantages of a Multidisciplinary Approach

Our current understanding of the genetics of tooth formation has arisen from a highly multidisciplinary approach. Statistical analyses such as the ones in this thesis have suggested that many genes and environmental factors are responsible for tooth development. They also have suggested that genes on both of the sex chromosomes may be involved in tooth development. Studies of individuals with sex chromosome anomalies have confirmed the role of both sex chromosomes, and provided suggestions of probable locations of these genes. Molecular genetic analyses have identified sex-linked amelogenin genes, the locations of which coincide with those suggested by the studies of sex chromosome anomalies. Descriptive studies of the functionality of the dentition have suggested the importance of the canines and premolars as a functional group. The results from this study revealed that natural selection in humans may have focused on canines and premolars. Further biochemical studies of dental ontogeny in mice have revealed a large array of genetically-programmed molecules including homeobox gene products and growth factors, with each tooth having a different combination of molecules directing its development. This is consistent with the finding

in this study of additive genetic factors influencing variation in individual teeth and their antimeres. If these genes control tooth development in humans as they do in mice, then each tooth along the tooth row may be influenced by some genes in common with the tooth before it, and also may be influenced by genes which the tooth before it doesn't express (reviewed by Weiss 1993, Thesleff 1995, Stock *et al.* 1997). This distribution of homeobox genes, combined with the presence of other molecules of varying distributions of expression, may explain why teeth displayed individual additive genetic factors, instead of tooth group factors. Tooth group factors were more evident among non-additive genetic sources of variation, and also may correlate with distributions of various molecules.

Thus, the findings of statistical and biochemical researches parallel each other, illustrating the benefits of tackling such questions from the different perspectives. Each perspective can add a different dimension to our understanding, and each can assist the other. For instance, biochemical analyses may identify a pattern of expression of a molecule which is consistent with a statistical factor. We may then be able to use statistics to estimate how important it is, or what other regions are influenced by the same factor or gene(s). This may suggest other regions where the gene is being expressed. In addition, patterns of gene expression discovered in biochemical analyses may assist in the application of biologically-sensible factor patterns to family data.

**Assessment of the Technique of Linear Structural Equation Modelling**

As described in the Introduction, the application of structural equation modelling to the data incorporated several advantages over previously used statistical methods applied to family data. These included the ability to test for and, in most cases, estimate additive genetic, non-additive genetic, common environmental and unique environmental sources of variation. The procedures were less dependent on improbable assumptions than methods used in earlier studies. Heritabilities were generated without

contamination by common environmental variation. Means as well as variances and covariances were modelled, with application of a variety of sex-limited models being possible. In general, the method provides efficient parameter estimates and a test of goodness-of-fit to the data. Different models were able to be compared statistically, so that the most parsimonious, and best fitting, models were identified. Multivariate analyses allowed exploration of the genetic basis of covariation between traits. There was considerable success in determining the combinations of traits pleiotropically influenced by common genes, and the extent to which genetic effects were specific to each trait. The resulting factor patterns, for the most part, complied with our current biological understanding of dental development, encouraging confidence in the methods as being reliable, accurate statistical methods for the understanding of complex human traits.

Limitations mentioned in the Introduction included sample sizes, general limitations of the classical twin study, and the composite nature of the chosen variables. However, sample sizes appear to have been sufficient for the detection of heritability, common environment and non-additive genetic variation, and for the performance of multivariate analyses. For univariate analyses there was an inability to model both common environment and non-additive genetic variation in the same model. This was not a problem in multivariate analyses, although caution had to be applied to ensure the models were not underidentified, leaving more parameters to be estimated than there were statistics or equations to solve. In the univariate analyses, estimates of non-additive genetic variation could not be separated from those of additive genetic variation, although the significance of each was assessable. Thus, only broad heritabilities could be generated for those variables with significant non-additive genetic variation. Because the study was restricted to MZ and DZ twins raised together, dominance and epistatic interaction variance could not be modelled separately.

## Comparison of Univariate and Multivariate Analyses

The differences between univariate and multivariate analyses show the value of the latter in revealing genetic and environmental covariances among variables. These relationships may provide insight into adaptive complexes within the dentition. It is quite likely that any system of repeated or meristic structures will have natural selection acting on individual as well as group subunits within it. For instance, the vertebrae may be divided along the length of the vertebral column into cervical, thoracic, lumbar, sacral and coccygeal vertebrae based on their morphology. The human dentition likewise is divided into four tooth types based on morphology. It is not surprising then, that natural selection may act on tooth groups individually or in combination, rather than on individual teeth. Environmental factors also may influence groups of teeth, because of their proximity to each other, or similarities in the timing of their development. Groups of teeth affected by the same environmental factor therefore may indicate a likely source, or timing, of environmental influence.

## Recommendations for Future Research

The multivariate analyses comprised seven or eight variables, with two revealing information on an entire quadrant while the other incorporated two teeth from each of the four quadrants. From these analyses, hypotheses were generated regarding the universality of general genetic and environmental factors across the dentition, incorporating both MD and BL diameters of the teeth, and perhaps throughout the craniofacial region, or even the entire skeleton. More widespread analyses encompassing greater numbers of variables would yield valuable information on the nature of such general factors. In addition, the identification of further adaptive complexes within the dentition, upon which natural selection operates, is possible. These include those in mandibular regions, and those which simultaneously encompass maxillary and mandibular teeth, or MD and BL diameters. Extension of the multivariate

analyses also may determine whether any common environmental variation exists in the posterior teeth of the mandible. Further investigations could test for interactions between earlier- and later-developing teeth, and also for any age-specific effects on the measured variables. Longitudinal analyses of deciduous and permanent dentitions of the same individuals also would enable exploration of a myriad of fascinating questions on genetic and environmental influences unique to each, and common to both.

## Specific Advantages of This Study

As far as I am aware, this study is the most thorough biometrical analysis of genetic and environmental contributions to variation in human teeth that has been undertaken to date. Its strengths are the application of the most advanced method - linear structural equation modelling - to more dental variables simultaneously than has been done before. The results are derived from one of the largest samples of twins that has been available for analysis of the human dentition. These strengths have allowed the critical assessment of the technique of linear structural equation modelling, and comparison of results with those derived from other methods. I also have been able to test several hypotheses about sources and patterns of variation derived from previous studies on smaller sample sizes. The results have provided support for some of these ideas, but other hypotheses have been found to be wanting.

The final goal of both molecular and quantitative approaches is the understanding of genetic and environmental contributions to variation in complex morphological traits. A great strength of this study is that there has been some correspondence between the hypothetical genetic architecture derived from it, and genetic determinants of tooth morphology known from molecular genetic studies. Such application of modern techniques of biometrical analysis thus help to bridge the gap between molecular and more traditional quantitative approaches. We are now a step closer to understanding the

genetic and environmental contributions to variation in morphology of tooth crowns in the human permanent dentition.

# Appendix A

**Table A.1:** Descriptive statistics for MZ females

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** | **N** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 8.50 | .06 | .56 | 79 | 7.01 | .05 | .43 | 78 |
| **I2** | 6.67 | .06 | .53 | 73 | 6.25 | .06 | .47 | 70 |
| **C** | 7.53 | .04 | .36 | 72 | 8.00 | .06 | .48 | 66 |
| **P1** | 6.86 | .06 | .46 | 62 | 9.10 | .08 | .60 | 64 |
| **P2** | 6.63 | .06 | .48 | 69 | 9.21 | .07 | .63 | 72 |
| **M1** | 10.25 | .07 | .61 | 77 | 11.24 | .07 | .62 | 80 |
| **M2** | 9.86 | .11 | .72 | 45 | 10.88 | .10 | .75 | 56 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 8.52 | .06 | .55 | 78 | 7.07 | .05 | .41 | 79 |
| **I2** | 6.60 | .06 | .54 | 74 | 6.23 | .07 | .57 | 68 |
| **C** | 7.50 | .04 | .32 | 72 | 8.00 | .06 | .47 | 67 |
| **P1** | 6.89 | .05 | .42 | 63 | 9.13 | .07 | .59 | 66 |
| **P2** | 6.69 | .05 | .43 | 71 | 9.23 | .07 | .63 | 73 |
| **M1** | 10.21 | .06 | .55 | 74 | 11.28 | .06 | .58 | 79 |
| **M2** | 9.91 | .09 | .60 | 40 | 11.06 | .11 | .76 | 50 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 5.25 | .04 | .36 | 80 | 5.90 | .04 | .39 | 80 |
| **I2** | 5.82 | .05 | .42 | 82 | 6.29 | .05 | .42 | 80 |
| **C** | 6.53 | .04 | .33 | 78 | 7.21 | .06 | .52 | 74 |
| **P1** | 6.98 | .05 | .42 | 70 | 7.86 | .06 | .52 | 70 |
| **P2** | 7.05 | .05 | .43 | 73 | 8.50 | .06 | .50 | 73 |
| **M1** | 10.84 | .07 | .61 | 75 | 10.58 | .06 | .49 | 78 |
| **M2** | 10.33 | .10 | .67 | 47 | 10.26 | .07 | .56 | 64 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 5.26 | .04 | .39 | 80 | 5.91 | .04 | .38 | 80 |
| **I2** | 5.80 | .04 | .38 | 79 | 6.24 | .04 | .39 | 77 |
| **C** | 6.48 | .04 | .36 | 80 | 7.24 | .06 | .50 | 74 |
| **P1** | 6.95 | .05 | .43 | 73 | 7.83 | .07 | .57 | 73 |
| **P2** | 7.05 | .05 | .41 | 71 | 8.49 | .07 | .57 | 74 |
| **M1** | 10.85 | .08 | .67 | 77 | 10.49 | .05 | .46 | 78 |
| **M2** | 10.25 | .09 | .57 | 44 | 10.21 | .08 | .60 | 60 |

**Table A.2:** Descriptive statistics for MZ males

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** | **N** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 8.75 | .06 | .48 | 64 | 7.23 | .07 | .58 | 62 |
| **I2** | 6.87 | .07 | .59 | 62 | 6.39 | .08 | .58 | 55 |
| **C** | 7.95 | .06 | .47 | 55 | 8.42 | .10 | .72 | 50 |
| **P1** | 7.10 | .06 | .42 | 50 | 9.27 | .08 | .54 | 49 |
| **P2** | 6.82 | .06 | .40 | 52 | 9.54 | .09 | .63 | 54 |
| **M1** | 10.55 | .07 | .59 | 63 | 11.52 | .07 | .59 | 64 |
| **M2** | 10.13 | .10 | .57 | 32 | 11.33 | .13 | .81 | 41 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 8.74 | .06 | .48 | 65 | 7.25 | .07 | .57 | 62 |
| **I2** | 6.81 | .08 | .64 | 66 | 6.42 | .08 | .62 | 62 |
| **C** | 7.97 | .06 | .46 | 56 | 8.42 | .10 | .68 | 51 |
| **P1** | 7.12 | .06 | .41 | 49 | 9.38 | .08 | .56 | 49 |
| **P2** | 6.79 | .06 | .40 | 47 | 9.54 | .09 | .62 | 48 |
| **M1** | 10.52 | .07 | .54 | 58 | 11.63 | .06 | .50 | 63 |
| **M2** | 10.16 | .11 | .56 | 26 | 11.58 | .13 | .80 | 38 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 5.42 | .05 | .37 | 65 | 6.04 | .06 | .45 | 66 |
| **I2** | 6.04 | .05 | .39 | 66 | 6.40 | .06 | .50 | 65 |
| **C** | 6.98 | .05 | .39 | 57 | 7.73 | .10 | .68 | 49 |
| **P1** | 7.20 | .06 | .46 | 52 | 8.13 | .07 | .49 | 51 |
| **P2** | 7.32 | .05 | .39 | 54 | 8.72 | .08 | .60 | 53 |
| **M1** | 11.18 | .08 | .63 | 60 | 10.84 | .07 | .58 | 65 |
| **M2** | 10.60 | .13 | .67 | 25 | 10.44 | .08 | .54 | 47 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 5.41 | .04 | .33 | 66 | 6.12 | .05 | .39 | 65 |
| **I2** | 6.05 | .05 | .38 | 66 | 6.30 | .06 | .52 | 65 |
| **C** | 6.92 | .05 | .39 | 59 | 7.67 | .10 | .69 | 50 |
| **P1** | 7.18 | .06 | .45 | 52 | 8.02 | .08 | .57 | 51 |
| **P2** | 7.29 | .06 | .40 | 51 | 8.63 | .07 | .54 | 52 |
| **M1** | 11.15 | .07 | .58 | 60 | 10.68 | .07 | .56 | 61 |
| **M2** | 10.54 | .13 | .64 | 24 | 10.34 | .08 | .55 | 45 |

**Table A.3:** Descriptive statistics for DZSS females

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** | **N** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 8.50 | .08 | .55 | 46 | 6.99 | .09 | .57 | 42 |
| **I2** | 6.54 | .07 | .49 | 45 | 6.19 | .08 | .55 | 42 |
| **C** | 7.45 | .06 | .37 | 42 | 7.93 | .08 | .49 | 38 |
| **P1** | 6.85 | .06 | .35 | 33 | 9.09 | .09 | .50 | 34 |
| **P2** | 6.62 | .06 | .41 | 41 | 9.17 | .09 | .59 | 42 |
| **M1** | 10.17 | .08 | .51 | 43 | 11.13 | .07 | .48 | 46 |
| **M2** | 9.75 | .12 | .60 | 26 | 10.94 | .13 | .72 | 33 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 8.49 | .08 | .55 | 45 | 7.06 | .09 | .59 | 44 |
| **I2** | 6.48 | .08 | .55 | 46 | 6.16 | .08 | .47 | 39 |
| **C** | 7.40 | .06 | .38 | 41 | 7.98 | .08 | .50 | 35 |
| **P1** | 6.80 | .06 | .38 | 35 | 9.12 | .09 | .50 | 34 |
| **P2** | 6.62 | .07 | .47 | 41 | 9.16 | .09 | .59 | 42 |
| **M1** | 10.19 | .07 | .49 | 43 | 11.14 | .07 | .48 | 46 |
| **M2** | 9.73 | .13 | .63 | 22 | 11.00 | .14 | .74 | 29 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 5.27 | .05 | .32 | 47 | 5.84 | .06 | .42 | 46 |
| **I2** | 5.82 | .05 | .35 | 47 | 6.23 | .07 | .45 | 44 |
| **C** | 6.49 | .05 | .31 | 43 | 7.29 | .08 | .49 | 39 |
| **P1** | 6.94 | .06 | .35 | 37 | 7.80 | .10 | .59 | 37 |
| **P2** | 7.15 | .08 | .45 | 35 | 8.49 | .08 | .47 | 36 |
| **M1** | 10.80 | .10 | .60 | 39 | 10.58 | .06 | .41 | 45 |
| **M2** | 10.45 | .10 | .49 | 26 | 10.30 | .08 | .49 | 34 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 5.30 | .05 | .34 | 46 | 5.85 | .06 | .43 | 46 |
| **I2** | 5.81 | .05 | .33 | 47 | 6.20 | .06 | .41 | 44 |
| **C** | 6.46 | .04 | .29 | 45 | 7.30 | .07 | .43 | 39 |
| **P1** | 6.88 | .07 | .43 | 38 | 7.77 | .09 | .57 | 38 |
| **P2** | 7.13 | .07 | .45 | 38 | 8.47 | .07 | .44 | 38 |
| **M1** | 10.79 | .11 | .68 | 39 | 10.46 | .05 | .34 | 46 |
| **M2** | 10.40 | .10 | .46 | 22 | 10.16 | .09 | .50 | 30 |

**Table A.4:** Descriptive statistics for DZSS males

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** | **N** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 8.84 | .09 | .56 | 40 | 7.18 | .09 | .56 | 42 |
| **I2** | 6.91 | .07 | .45 | 41 | 6.35 | .10 | .58 | 36 |
| **C** | 8.01 | .07 | .44 | 35 | 8.23 | .11 | .60 | 32 |
| **P1** | 7.08 | .06 | .32 | 33 | 9.35 | .08 | .49 | 36 |
| **P2** | 6.83 | .06 | .36 | 32 | 9.47 | .09 | .53 | 33 |
| **M1** | 10.55 | .08 | .55 | 43 | 11.57 | .10 | .65 | 42 |
| **M2** | 10.21 | .14 | .62 | 20 | 11.60 | .13 | .68 | 26 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 8.74 | .09 | .57 | 43 | 7.20 | .09 | .57 | 43 |
| **I2** | 6.96 | .09 | .55 | 42 | 6.46 | .09 | .55 | 37 |
| **C** | 7.94 | .07 | .40 | 34 | 8.22 | .11 | .62 | 31 |
| **P1** | 7.10 | .05 | .32 | 34 | 9.36 | .08 | .48 | 37 |
| **P2** | 6.80 | .07 | .40 | 31 | 9.43 | .09 | .53 | 31 |
| **M1** | 10.54 | .09 | .55 | 40 | 11.67 | .09 | .59 | 43 |
| **M2** | 10.12 | .13 | .54 | 16 | 11.60 | .13 | .65 | 25 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 5.41 | .04 | .30 | 44 | 6.09 | .07 | .45 | 41 |
| **I2** | 6.05 | .06 | .39 | 45 | 6.37 | .07 | .44 | 43 |
| **C** | 7.06 | .07 | .43 | 39 | 7.66 | .12 | .67 | 31 |
| **P1** | 7.20 | .06 | .35 | 37 | 8.22 | .08 | .53 | 39 |
| **P2** | 7.26 | .06 | .36 | 32 | 8.66 | .08 | .48 | 33 |
| **M1** | 11.21 | .10 | .63 | 42 | 10.84 | .08 | .56 | 44 |
| **M2** | 10.91 | .12 | .51 | 17 | 10.68 | .14 | .71 | 25 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 5.42 | .05 | .32 | 45 | 6.10 | .07 | .43 | 42 |
| **I2** | 6.02 | .06 | .39 | 45 | 6.30 | .07 | .46 | 42 |
| **C** | 6.98 | .07 | .44 | 39 | 7.66 | .12 | .66 | 29 |
| **P1** | 7.21 | .06 | .34 | 38 | 8.17 | .08 | .49 | 39 |
| **P2** | 7.16 | .06 | .35 | 33 | 8.59 | .08 | .43 | 33 |
| **M1** | 11.24 | .10 | .67 | 43 | 10.75 | .09 | .60 | 44 |
| **M2** | 10.93 | .13 | .57 | 18 | 10.58 | .14 | .75 | 28 |

**Table A.5:** Descriptive statistics for DZOS females

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** | **N** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 8.66 | .08 | .59 | 57 | 7.15 | .07 | .54 | 52 |
| **I2** | 6.63 | .09 | .63 | 49 | 6.20 | .08 | .51 | 45 |
| **C** | 7.53 | .06 | .41 | 45 | 7.94 | .09 | .58 | 42 |
| **P1** | 6.84 | .07 | .45 | 39 | 9.06 | .08 | .52 | 39 |
| **P2** | 6.63 | .06 | .43 | 45 | 9.17 | .08 | .52 | 44 |
| **M1** | 10.26 | .08 | .58 | 54 | 11.13 | .08 | .59 | 54 |
| **M2** | 10.00 | .12 | .68 | 30 | 11.08 | .11 | .64 | 35 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 8.64 | .08 | .56 | 56 | 7.19 | .07 | .51 | 51 |
| **I2** | 6.64 | .09 | .66 | 52 | 6.23 | .08 | .55 | 46 |
| **C** | 7.58 | .06 | .40 | 46 | 8.05 | .09 | .56 | 43 |
| **P1** | 6.84 | .07 | .45 | 37 | 9.06 | .08 | .49 | 40 |
| **P2** | 6.56 | .06 | .41 | 42 | 9.17 | .09 | .58 | 43 |
| **M1** | 10.29 | .09 | .62 | 54 | 11.21 | .08 | .59 | 56 |
| **M2** | 9.94 | .10 | .53 | 28 | 11.11 | .11 | .67 | 34 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 5.32 | .06 | .44 | 57 | 5.91 | .07 | .52 | 56 |
| **I2** | 5.92 | .06 | .41 | 56 | 6.35 | .06 | .41 | 52 |
| **C** | 6.65 | .05 | .38 | 52 | 7.38 | .08 | .54 | 44 |
| **P1** | 7.01 | .06 | .43 | 45 | 7.77 | .09 | .56 | 42 |
| **P2** | 7.10 | .07 | .49 | 45 | 8.53 | .08 | .52 | 45 |
| **M1** | 10.83 | .09 | .64 | 50 | 10.56 | .06 | .48 | 54 |
| **M2** | 10.32 | .12 | .68 | 30 | 10.21 | .09 | .58 | 38 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 5.29 | .06 | .41 | 54 | 5.91 | .07 | .49 | 55 |
| **I2** | 5.92 | .06 | .44 | 57 | 6.26 | .06 | .46 | 52 |
| **C** | 6.59 | .05 | .36 | 51 | 7.39 | .08 | .51 | 44 |
| **P1** | 6.89 | .07 | .44 | 43 | 7.72 | .08 | .53 | 42 |
| **P2** | 7.06 | .07 | .46 | 45 | 8.46 | .08 | .53 | 44 |
| **M1** | 10.81 | .09 | .63 | 51 | 10.42 | .07 | .48 | 53 |
| **M2** | 10.35 | .11 | .62 | 31 | 10.23 | .09 | .52 | 36 |

**Table A.6:** Descriptive statistics for DZOS males

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** | **N** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 8.84 | .08 | .62 | 55 | 7.26 | .08 | .58 | 52 |
| **I2** | 7.00 | .07 | .48 | 49 | 6.52 | .08 | .56 | 44 |
| **C** | 7.93 | .06 | .40 | 44 | 8.32 | .09 | .62 | 43 |
| **P1** | 7.07 | .06 | .35 | 34 | 9.37 | .10 | .58 | 35 |
| **P2** | 6.80 | .06 | .40 | 43 | 9.49 | .08 | .56 | 44 |
| **M1** | 10.47 | .08 | .58 | 51 | 11.50 | .08 | .59 | 54 |
| **M2** | 10.37 | .14 | .74 | 28 | 11.44 | .11 | .64 | 34 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 8.86 | .08 | .58 | 55 | 7.44 | .08 | .60 | 50 |
| **I2** | 7.00 | .08 | .55 | 48 | 6.61 | .08 | .51 | 45 |
| **C** | 7.97 | .06 | .40 | 43 | 8.38 | .09 | .60 | 41 |
| **P1** | 7.07 | .06 | .35 | 35 | 9.39 | .09 | .54 | 36 |
| **P2** | 6.76 | .06 | .41 | 41 | 9.55 | .07 | .49 | 42 |
| **M1** | 10.45 | .07 | .52 | 50 | 11.55 | .08 | .55 | 53 |
| **M2** | 10.12 | .12 | .60 | 24 | 11.46 | .12 | .66 | 28 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 5.39 | .05 | .38 | 54 | 6.03 | .08 | .55 | 53 |
| **I2** | 6.12 | .05 | .40 | 55 | 6.32 | .08 | .56 | 52 |
| **C** | 7.03 | .05 | .36 | 48 | 7.64 | .11 | .72 | 44 |
| **P1** | 7.20 | .06 | .37 | 44 | 8.19 | .08 | .53 | 42 |
| **P2** | 7.34 | .06 | .40 | 41 | 8.77 | .10 | .61 | 41 |
| **M1** | 11.11 | .10 | .72 | 52 | 10.85 | .07 | .51 | 57 |
| **M2** | 10.80 | .13 | .71 | 32 | 10.78 | .09 | .54 | 37 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 5.42 | .05 | .40 | 55 | 6.05 | .08 | .57 | 53 |
| **I2** | 6.07 | .06 | .44 | 55 | 6.33 | .08 | .55 | 48 |
| **C** | 6.87 | .06 | .42 | 49 | 7.67 | .11 | .73 | 41 |
| **P1** | 7.22 | .05 | .34 | 45 | 8.11 | .08 | .57 | 45 |
| **P2** | 7.30 | .08 | .52 | 38 | 8.72 | .09 | .56 | 39 |
| **M1** | 11.08 | .10 | .68 | 50 | 10.69 | .07 | .52 | 53 |
| **M2** | 10.91 | .14 | .73 | 29 | 10.70 | .09 | .53 | 37 |

**Table A.7:** Descriptive statistics for nontwin females

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** | **N** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 8.44 | .05 | .44 | 74 | 7.03 | .06 | .48 | 73 |
| **I2** | 6.45 | .05 | .43 | 74 | 6.20 | .05 | .43 | 72 |
| **C** | 7.54 | .04 | .36 | 73 | 8.03 | .07 | .56 | 72 |
| **P1** | 6.80 | .04 | .34 | 73 | 8.97 | .06 | .47 | 71 |
| **P2** | 6.54 | .04 | .36 | 75 | 9.09 | .06 | .49 | 72 |
| **M1** | 10.09 | .06 | .48 | 73 | 11.15 | .06 | .49 | 70 |
| **M2** | 9.80 | .06 | .52 | 66 | 10.83 | .09 | .71 | 60 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 8.43 | .06 | .50 | 73 | 7.05 | .06 | .48 | 73 |
| **I2** | 6.52 | .05 | .40 | 73 | 6.17 | .05 | .46 | 74 |
| **C** | 7.55 | .04 | .34 | 75 | 7.98 | .06 | .55 | 75 |
| **P1** | 6.79 | .04 | .33 | 73 | 9.00 | .06 | .48 | 73 |
| **P2** | 6.55 | .05 | .39 | 75 | 9.11 | .06 | .49 | 75 |
| **M1** | 10.05 | .05 | .46 | 75 | 11.13 | .06 | .50 | 75 |
| **M2** | 9.73 | .07 | .56 | 66 | 10.94 | .08 | .63 | 65 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 5.29 | .04 | .32 | 75 | 5.92 | .05 | .43 | 75 |
| **I2** | 5.81 | .04 | .36 | 74 | 6.28 | .05 | .41 | 74 |
| **C** | 6.52 | .04 | .30 | 75 | 7.38 | .06 | .48 | 73 |
| **P1** | 6.90 | .04 | .38 | 75 | 7.75 | .05 | .44 | 75 |
| **P2** | 6.91 | .05 | .41 | 73 | 8.33 | .05 | .45 | 73 |
| **M1** | 10.72 | .07 | .58 | 74 | 10.47 | .05 | .46 | 75 |
| **M2** | 10.07 | .07 | .53 | 59 | 10.09 | .06 | .53 | 66 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 5.28 | .04 | .32 | 75 | 5.90 | .05 | .41 | 75 |
| **I2** | 5.83 | .04 | .33 | 73 | 6.17 | .05 | .41 | 73 |
| **C** | 6.48 | .04 | .30 | 75 | 7.35 | .06 | .50 | 74 |
| **P1** | 6.89 | .05 | .40 | 75 | 7.65 | .05 | .44 | 74 |
| **P2** | 6.93 | .04 | .37 | 73 | 8.28 | .05 | .44 | 70 |
| **M1** | 10.73 | .07 | .63 | 72 | 10.29 | .06 | .47 | 70 |
| **M2** | 10.13 | .07 | .57 | 60 | 10.04 | .07 | .55 | 62 |

**Table A.8:** Descriptive statistics for nontwin males

| | Mesiodistal | | | | Buccolingual | | | |
|---|---|---|---|---|---|---|---|---|
| **Tooth** | **Mean** | **SE** | **SD** | **N** | **Mean** | **SE** | **SD** | **N** |
| *Maxilla, Right Side* | | | | | | | | |
| **I1** | 8.64 | .06 | .49 | 74 | 7.39 | .06 | .51 | 74 |
| **I2** | 6.66 | .06 | .54 | 75 | 6.53 | .07 | .62 | 74 |
| **C** | 7.91 | .06 | .49 | 74 | 8.61 | .08 | .65 | 72 |
| **P1** | 6.99 | .05 | .41 | 73 | 9.44 | .07 | .61 | 72 |
| **P2** | 6.75 | .05 | .44 | 72 | 9.60 | .08 | .64 | 72 |
| **M1** | 10.52 | .06 | .52 | 73 | 11.66 | .07 | .59 | 73 |
| **M2** | 10.30 | .08 | .63 | 70 | 11.70 | .10 | .84 | 73 |
| *Maxilla, Left Side* | | | | | | | | |
| **I1** | 8.68 | .06 | .51 | 73 | 7.41 | .06 | .55 | 73 |
| **I2** | 6.75 | .06 | .50 | 75 | 6.59 | .07 | .64 | 74 |
| **C** | 7.93 | .05 | .44 | 75 | 8.66 | .08 | .66 | 74 |
| **P1** | 7.02 | .05 | .44 | 71 | 9.47 | .07 | .57 | 73 |
| **P2** | 6.80 | .05 | .43 | 70 | 9.62 | .07 | .59 | 72 |
| **M1** | 10.45 | .06 | .52 | 72 | 11.71 | .06 | .55 | 75 |
| **M2** | 10.22 | .08 | .62 | 68 | 11.75 | .10 | .81 | 72 |
| *Mandible, Right Side* | | | | | | | | |
| **I1** | 5.35 | .04 | .31 | 72 | 6.21 | .05 | .44 | 74 |
| **I2** | 5.94 | .04 | .38 | 74 | 6.53 | .06 | .48 | 74 |
| **C** | 6.89 | .04 | .38 | 75 | 8.01 | .07 | .62 | 74 |
| **P1** | 7.10 | .06 | .50 | 72 | 8.22 | .07 | .58 | 72 |
| **P2** | 7.27 | .06 | .49 | 74 | 8.77 | .07 | .61 | 74 |
| **M1** | 11.17 | .07 | .59 | 74 | 10.96 | .07 | .56 | 73 |
| **M2** | 10.79 | .08 | .67 | 64 | 10.85 | .07 | .62 | 71 |
| *Mandible, Left Side* | | | | | | | | |
| **I1** | 5.37 | .04 | .31 | 75 | 6.20 | .05 | .42 | 73 |
| **I2** | 5.98 | .04 | .37 | 73 | 6.45 | .06 | .48 | 73 |
| **C** | 6.87 | .05 | .41 | 75 | 7.96 | .08 | .65 | 72 |
| **P1** | 7.10 | .06 | .47 | 72 | 8.19 | .07 | .56 | 71 |
| **P2** | 7.27 | .05 | .47 | 75 | 8.78 | .07 | .62 | 73 |
| **M1** | 11.20 | .06 | .55 | 73 | 10.82 | .07 | .56 | 71 |
| **M2** | 10.81 | .08 | .61 | 66 | 10.63 | .07 | .61 | 67 |

# Appendix B

# Detailed Modelling Methods

## B1 Definition of Structural Equation Modelling

Structural Equation Modelling (SEM) seeks to explain observed variables in terms of unobserved (latent) variables and their intercorrelations. It is an extension of a number of other multivariate analytic techniques, such as multiple linear regression and factor analysis, but it employs confirmatory (as opposed to exploratory) factor analysis. SEM allows construction of causal hypotheses, and tests competing models to see whether the hypotheses can be maintained.

The mathematical processes may seem complicated, but are necessary to elucidate the underlying causes of human variation, since control of environmental factors and manipulation of genotype through breeding experiments are not viable methods for the study of human characteristics. There are five main steps in modelling - specification of the model (hypothesis), identification or gathering of data and statistics, estimation of parameters, testing the goodness-of-fit of the model, and respecification of the model. Most of the following details are contained in Neale and Cardon (1992).

## B2 Specifying the Model

Most models contain linear equations relating observed and latent variables. For twins, the covariance between their phenotypes may be modelled in terms of such latent genetic variables as additive effects of multiple loci (A), nonadditive effects (dominance and epistatic interactions) of multiple loci (D). The latent environmental factors may be decomposed into shared (or family) environmental effects (C), and unique (nonshared) environmental effects (E). Setting the variances of these components to unity, we can derive the values of the path coefficients, or vice versa. In the analyses presented here, the former of these - the path coefficients model - was used.

### B2.1 Path diagrams

SEMs may be depicted in the form of path diagrams, devised by Sewall Wright (1921). These diagrams present relationships between variables in such a way that mathematical relationships can be represented, and expected values for various statistics derived. Since the principles, methods and assumptions of path analysis are covered in detail in other texts (Li 1975, Neale and Cardon 1992), the details will not be repeated here. Figure B.1 is a path diagram for a pair of twins indicating the contributions of A,C,D and E to twin variances and covariance for a trait. The correlations of A1 with A2, and D1 with D2 (indicated by double headed arrows) are fixed according to genetic theory. For instance, MZ twins inherit the same genes, while DZ twins will share half their genes on average, so that the correlation between additive genetic effects will be one for MZ twins and 0.5 for DZ twins. For nonadditive genetic variation, the respective correlations are 1 and 0.25. It is also assumed that shared environment will be perfectly correlated among both types of twins. By definition, the unique environmental influences are uncorrelated, and the shared environmental influences are perfectly correlated for all types of twins.

From the path model, the variance for a twin is expected to be $Var = a^2 + c^2 + d^2 + e^2$, while the covariance between co-twins will be $Cov_{12} = a^2 + c^2 + d^2$ for MZ twins reared together, and $0.5a^2 + c^2 + 0.25d^2$ for DZ twins reared together.

## B3 Identification

Identification of a model means that the unknown parameters have a unique solution. This is achieved using data from genetically related individuals, and by imposing constraints on certain parameters in the model, based on the principles of Mendelian inheritance (Rao 1991) as described in section B.2.1.

To achieve identification, one necessary condition is that the number of observed statistics is greater than or equal to the number of unknown parameters. With data from MZ and DZ twins reared together, for instance, we have two covariances ($Cov_{MZ}$ and $Cov_{DZ}$) and one variance, since we assume that the variance of twin 1 will equal that of twin 2, and that variance will not change as a function of zygosity. Thus, excluding models incorporating sex effects, models may only incorporate three or fewer unknown parameters. The model depicted in figure B.1 is therefore underidentified. The choice of subsets of parameters is made simpler by negative

confounding of genetic dominance with shared environmental influences (Grayson, 1989), so that a univariate model may not contain both D and C. Thus, ACE and ADE models are fitted, as are AE, CE and E models (see figures B.2 to B.6). No model appears without an E, since MZ correlations are rarely or never perfect ($r=1.0$), and also because unique environment incorporates measurement error. It would be unrealistic then, to assume that E would not be responsible for some of the observed variance in a trait. In addition, DE models are considered nonsensical, since even complete dominance at a locus results in a non-zero estimate for additive genetic variation.

### B3.1 Multivariate analyses

Multivariate analysis of twin data may begin with a Cholesky decomposition, in which any positive definite matrix may be transformed into the product of a lower triangular matrix and its transpose (Neale 1995). These models estimate all possible paths of covariation in an attempt to account for as much variation as possible, having as many factors as there are variables and as many loadings as there are observed correlations. The path diagram of a Cholesky decomposition of three variables (Y1, Y2, Y3) into three factors (F1, F2, F3) is shown in Figure B.7. The first factor (F1) loads on all the variables, the second (F2) loads on all but the first variable, the third (F3) loads on all but the first and second variables, and so on (Neale and Cardon, 1992). The Cholesky model is a unique factorisation of the covariance structure. It therefore provides a limiting test of how well any model with A, E, C or D factors will fit. Simpler models will display a worse fit than this by the $\chi^2$ criterion, but are preferred if more parsimonious (as estimated by AIC) or more appropriate on theoretical grounds. The first model again consisted of an E matrix alone, followed by AE, CE, ACE and ADE models.

## B4 Estimation of Parameters

SEM processes include optimization, an iterative process which attempts to find values for unknown parameters which minimise the function:

$$F = (s-\sigma)' W^{-1} (s-\sigma)$$

where s and $\sigma$ contain the nonduplicate elements of the observed variance-covariance matrix S and the expected (model) variance-covariance matrix $\Sigma$, and W is a positive

definite, symmetric, weight matrix, which varies according to which fit function is used (Browne 1984). The fit functions are listed in section B.5.

## B5 Testing Goodness-of-Fit and Respecifying the Model

The most commonly used statistic to assess goodness-of-fit of the model is $\chi^2$. In most cases, it is calculated as:

$$\chi^2 = F(N-1)$$

where F is the minimum of the fitting function (described below) and N is the number of observations on which S, the observed covariance matrix, is based (Neale and Cardon 1992). The df is calculated as the number of independent statistics minus the number of free parameters.

As for the fitting functions, the function used varies according to the type of input data. Since the univariate analyses utilised VL files, raw maximum likelihoods (RM) were calculated. The fit function then, was:

$$RM = -k\log(2\pi) + \log|\Sigma| + (x_i - \mu_i)' \Sigma^{-1} (x_i - \mu_i)$$

where $k$ = number of observed variables, $x_i$ = the observed mean vector, $\Sigma$ = the population covariance matrix, $\mu_i$ = the (column) vector of population means of the variables, $(x_i - \mu_i)'$ indicates the transpose of the matrix of difference between observed and population means, and $|\Sigma|$ and $\Sigma^{-1}$ denote the determinant and inverse of the matrix $\Sigma$, respectively (Neale 1995). Since no variance-covariance matrices were calculated, a full baseline model is constructed, which allows each twin group to have its own mean, variance and covariance. The SEM process in Mx generates a log-likelihood statistic for these baseline models and for subsequent nested models with fewer parameters. The difference between these statistics is distributed approximately as $\chi^2$ with df equal to the difference in number of parameters between the baseline and nested models.

For the multivariate analyses, models were fitted to variance-covariance matrices using the maximum likelihood (ML) fit function:

$$ML = df\,(\ln|\Sigma| - \ln|S| + (tr\,(S\Sigma^{-1})) - p)$$

where $\Sigma$ = the expected covariance matrix, S = the observed covariance matrix, tr(A) and |A| are the trace and determinant of the matrix A. The df is one less than the sample size used to calculate S, and $\Sigma$ and S are of order $p$ (Neale 1995).

Where models were fitted to both covariance matrices and mean vectors, the function was extended to (Neale 1995):

$$ML_{c+m} = df\,(\ln|\Sigma| - \ln|S| + (tr\,(S\Sigma^{-1})) - p + (x-\mu)'\,\Sigma^{-1}\,(x-\mu) + 1).$$

Firstly, a model with only unique environmental variation is tested. If this is insufficient ($p<0.01$) then CE, AE, ACE and ADE models are fitted. Even if two parameters are sufficient, the ACE and ADE models allow testing of significance of A, C and D. To achieve this, models may be compared in at least two ways. Firstly, a full or general model (e.g. ACE) may be compared with a nested model (e.g. AE) by calculating the difference between their $\chi^2$ values and their df, and using this as a $\chi^2$ value and df value. A significant value would indicate that the difference was significant, and the more general model had a better fit. It would also be said that C was a significant contributor to phenotypic variation. Secondly, Akaike's Information Criterion (AIC) may be calculated as:

$$AIC = \chi^2 - 2df$$

This statistic allows comparison of models with differing df, and incorporates the principle of parsimony as well as goodness-of-fit. The model with the lowest (largest negative) AIC value may be described as "the best by AIC" (Neale and Cardon 1992) and is usually considered both well-fitting and parsimonious.

Thirdly, RMSEA could be calculated as an alternative to probabilities associated with the $\chi^2$. It provides a measure of goodness-of-fit which is relatively independent of sample size (N). The formula is:

$$(((\chi^2 - df)/N)/df)^{0.5}$$

If the value obtained is less than 0.1, the fit is good. A very good fit occurs when RMSEA falls below 0.05.

## B6 Output

Besides the goodness-of-fit statistics, the output includes estimates of the path coefficients. Calculation groups within the program request standardisation of the path coefficients. Since total phenotypic variation equals the sum of the squared path coefficients, the proportion of phenotypic variation due to each latent factor is equal to the square of the path coefficient divided by the total phenotypic variation.

That is, since $P_{var} = a^2 + c^2 + d^2 + e^2$ ,
Proportion genetic variation (broad heritability) = $h^2 = (a^2 + d^2) / P_{var}$
Proportion additive genetic variation (narrow heritability) = $h^2 = a^2 / P_{var}$
Proportion shared environmental variation = $c^2 / P_{var}$
Proportion unique environmental variation = $e^2 / P_{var}$

Broad and narrow heritabilities are thus equal if there is no significant nonadditive genetic variance ($d = 0$).

## B7 Further modelling

Where standard models for covariance structure fail to fit the data ($p<0.01$), sex limitation models are attempted. These models allow males and females to have different values for path coefficients, or even include latent factors which are limited to one or other sex.

In the models fitted so far, the estimates of path coefficients have been constrained to be equal in all twins groups, so there is only one estimate of each of a,c,d and e. These models could be called "**homogeneity**" models. **Heterogeneity** models allow different path coefficient estimates for each sex (Figure B.8). **Scalar sex limitation** models are similar, but the coefficients for one gender are constrained to be a multiple (k) of the coefficients for the other (Figure B.9). Both of these models attempt to describe the situation in which the same genes and environmental affect both sexes, but to a different extent.

In order to model the situation in which *different* genes influence the trait in each sex, we fit **non-scalar sex-limitation** models (Figure B.10). This incorporates a coefficient, $r_g$, for the additive genetic correlation between OS twins, normally set at

0.5. Additionally, a **general sex-limitation** model can be constructed. These models contain a general genetic influence and a sex-specific one, so that in an ACE model with a male-specific additive genetic factor, the parameters are A, C, E and $A_m$ (Figure B.10).

A number of observations may be made from twin variances, covariances and correlations, which lead to prediction of which of the above models, if any, are likely to fit the data. This allows selection of one or a few possible models, and prevents the difficulties associated with fitting every possible kind of model to the data, until one fits. The following observations may be applied to such descriptive data before further modelling proceeds (taken from lecture notes provided at the 1996 International Workshop on Methodology of Twin and Family Studies held at the Institute for Behavior Genetics in Boulder, Colorado) :

(1) DZOS correlations being markedly lower than DZSS correlations suggests sex-specific effects of some kind;
(2) equal variances in all five twin groups, plus different correlation coefficients in each of the 3 DZ twin groups suggests a heterogeneity model;
(3) equal correlation coefficients across the sexes plus higher variance in one sex implies a scalar sex effect exists, with the scalar effect being on the sex with the higher variance;
(4) equal variances in all five twin groups, equal correlations across sexes, plus DZOS correlation being much less than that for DZSS twin pairs suggests a non-scalar sex effect; and
(5) equal variances *within* sexes, as opposed to *across* sexes, distinguishes the heterogeneity model from the general sex-limitation model.

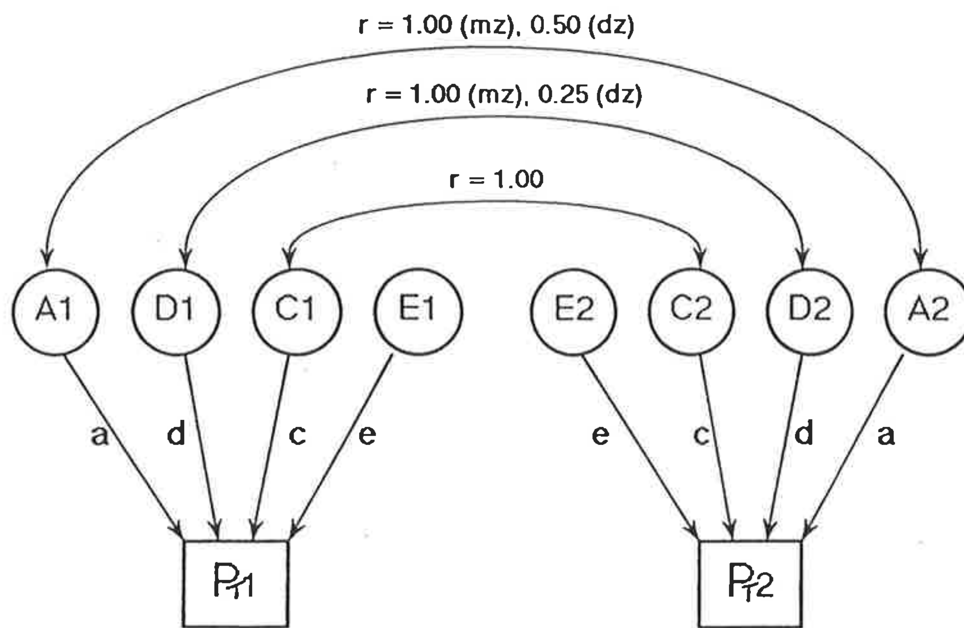


**Figure B.1:** path diagram for a single variable showing the main sources of variance and covariance. PT1 = phenotype of twin 1; PT2 = phenotype of twin 2; r = correlation between latent factors.

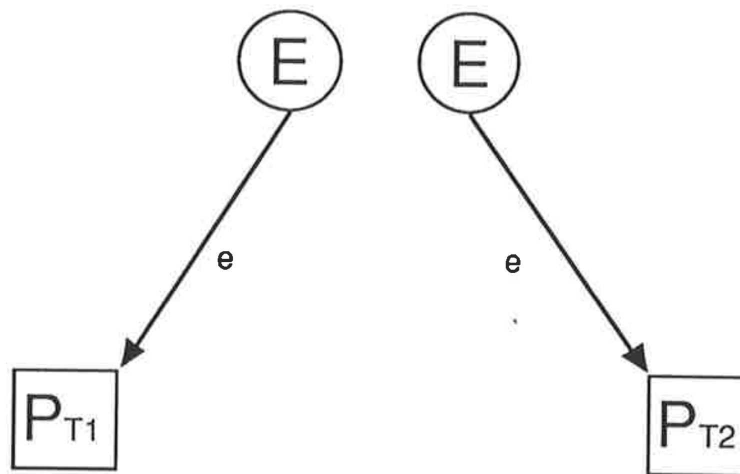


**Figure B.2:** An E model for a pair of twins.

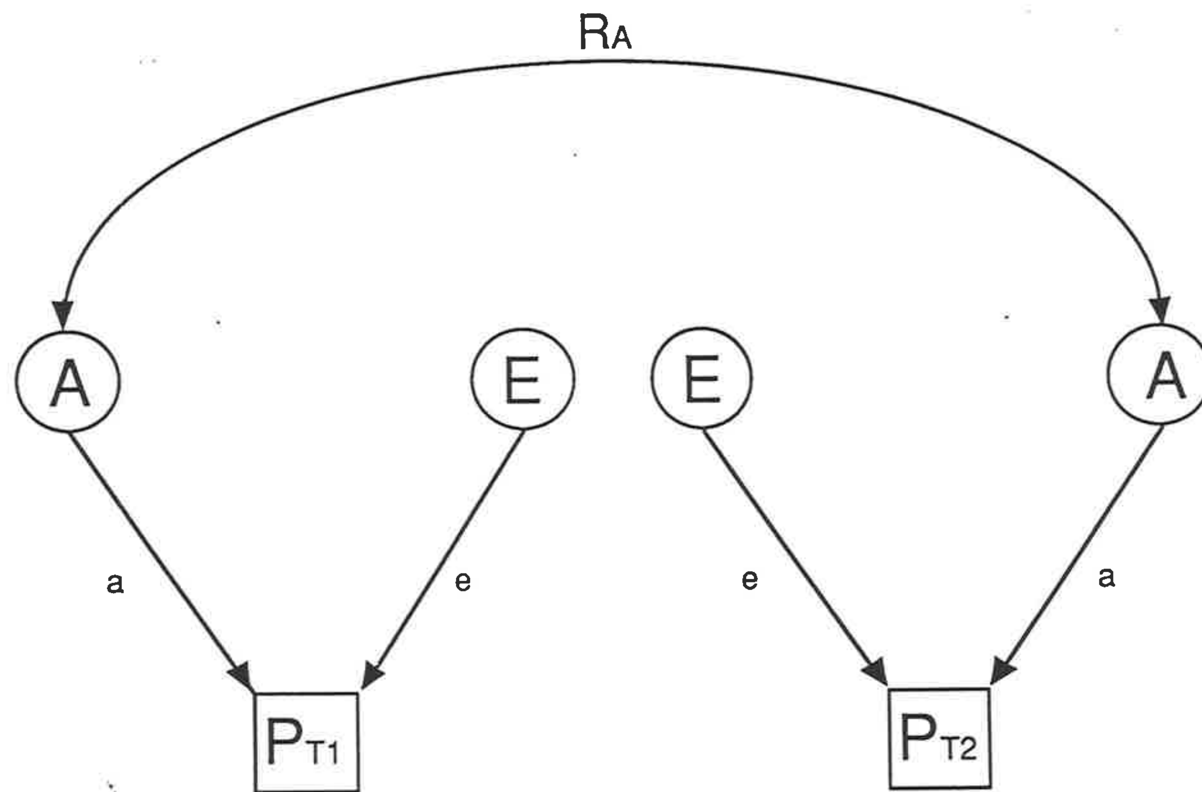


**Figure B.3:** An AE model for a pair of twins.

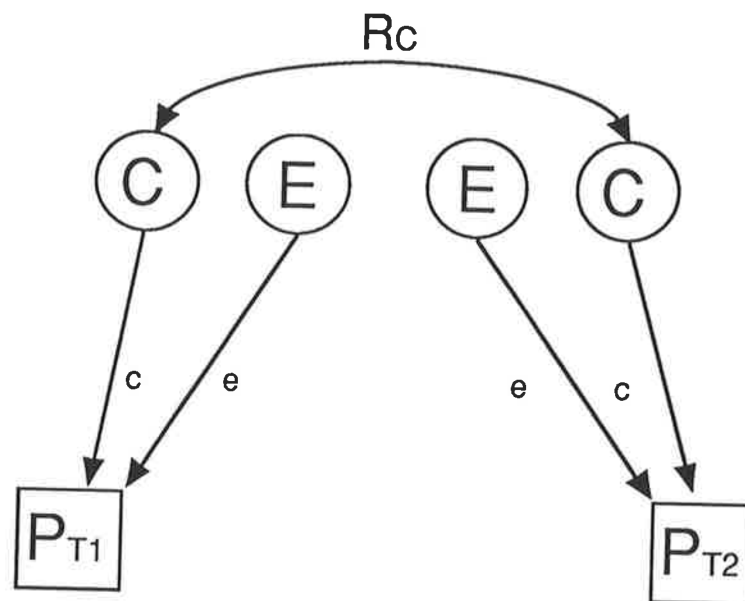


**Figure B.4:** A CE model for a pair of twins.

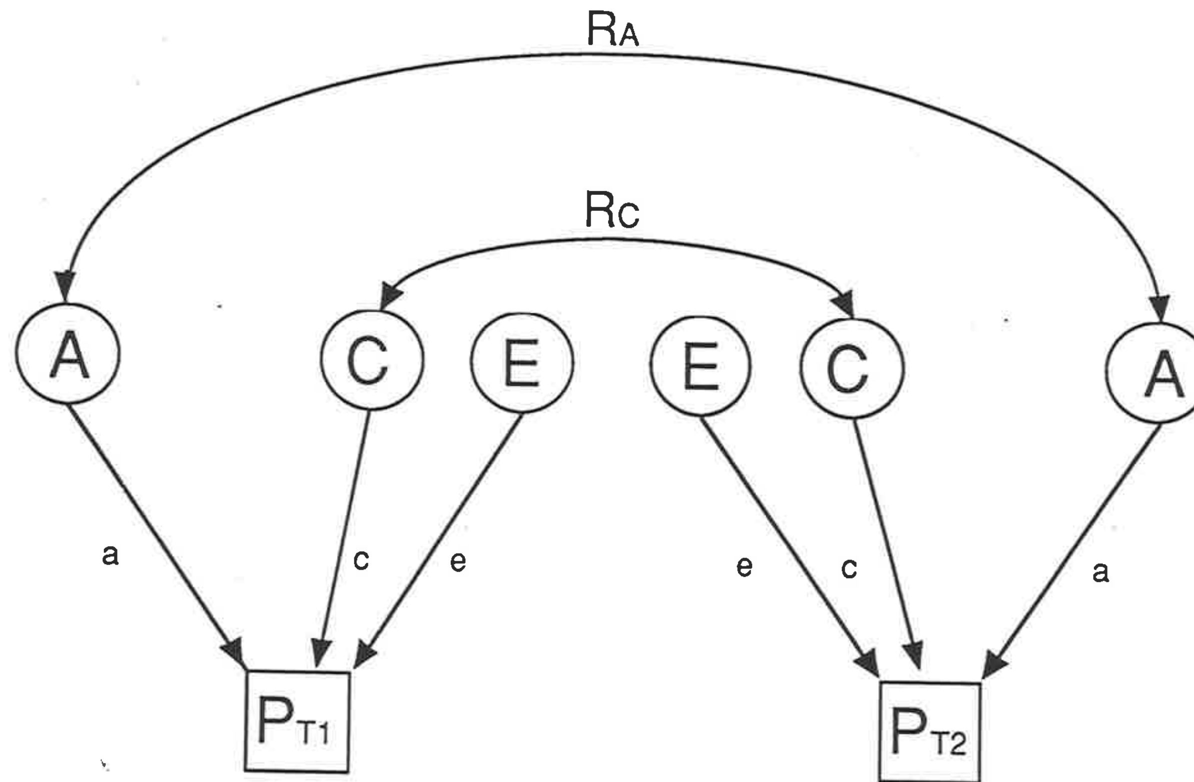


**Figure B.5:** An ACE model for a pair of twins.

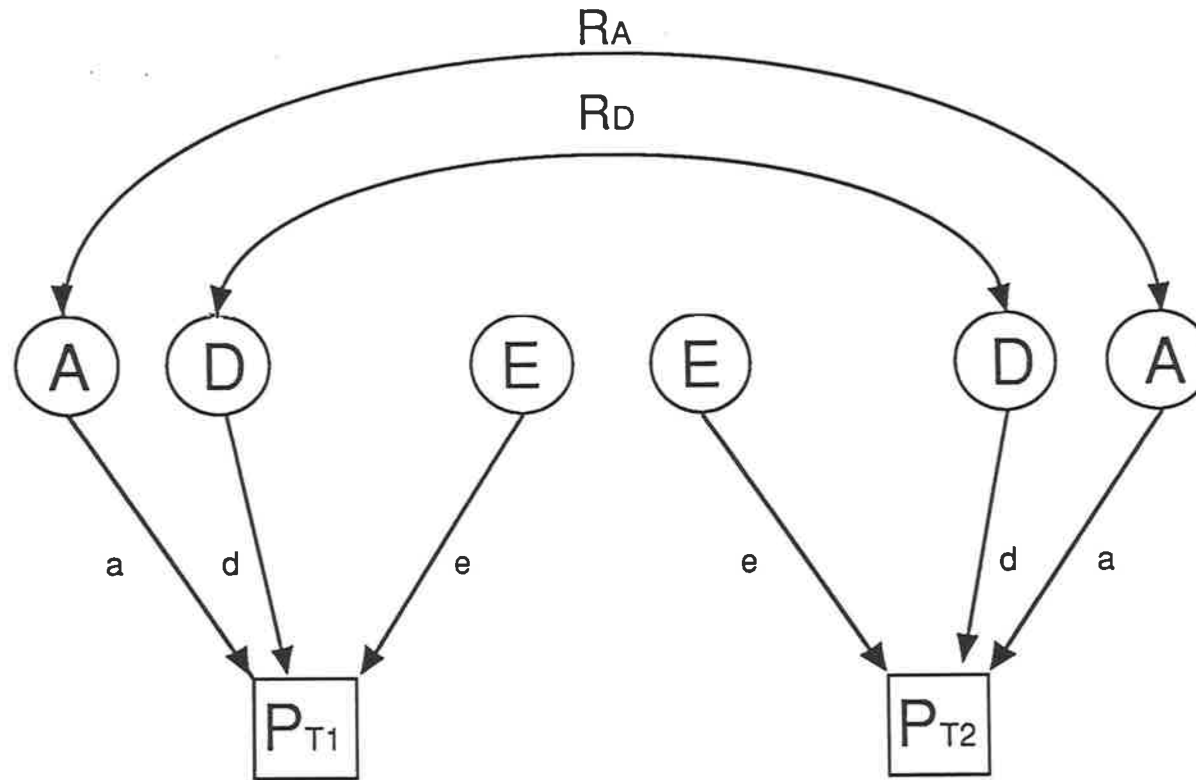


**Figure B.6:** An ADE model for a pair of twins.

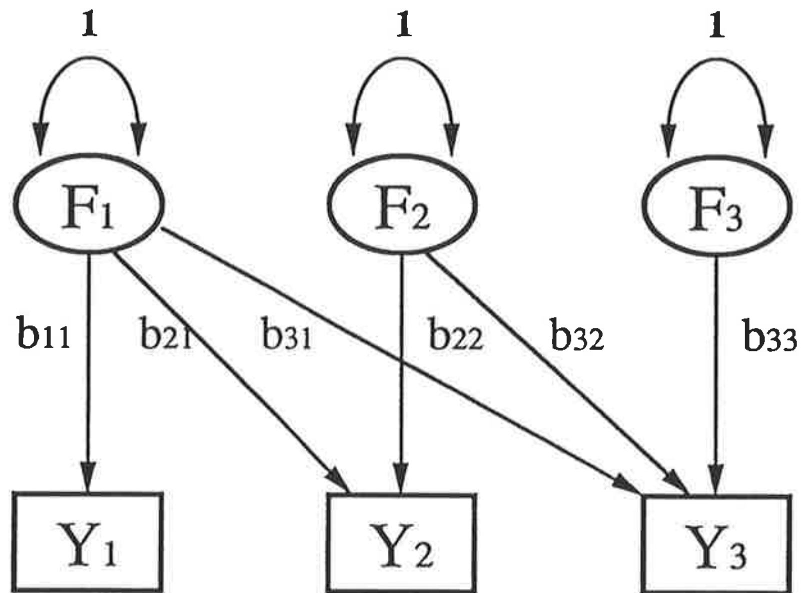


**Figure B.7:** Path diagram of Cholesky decomposition.

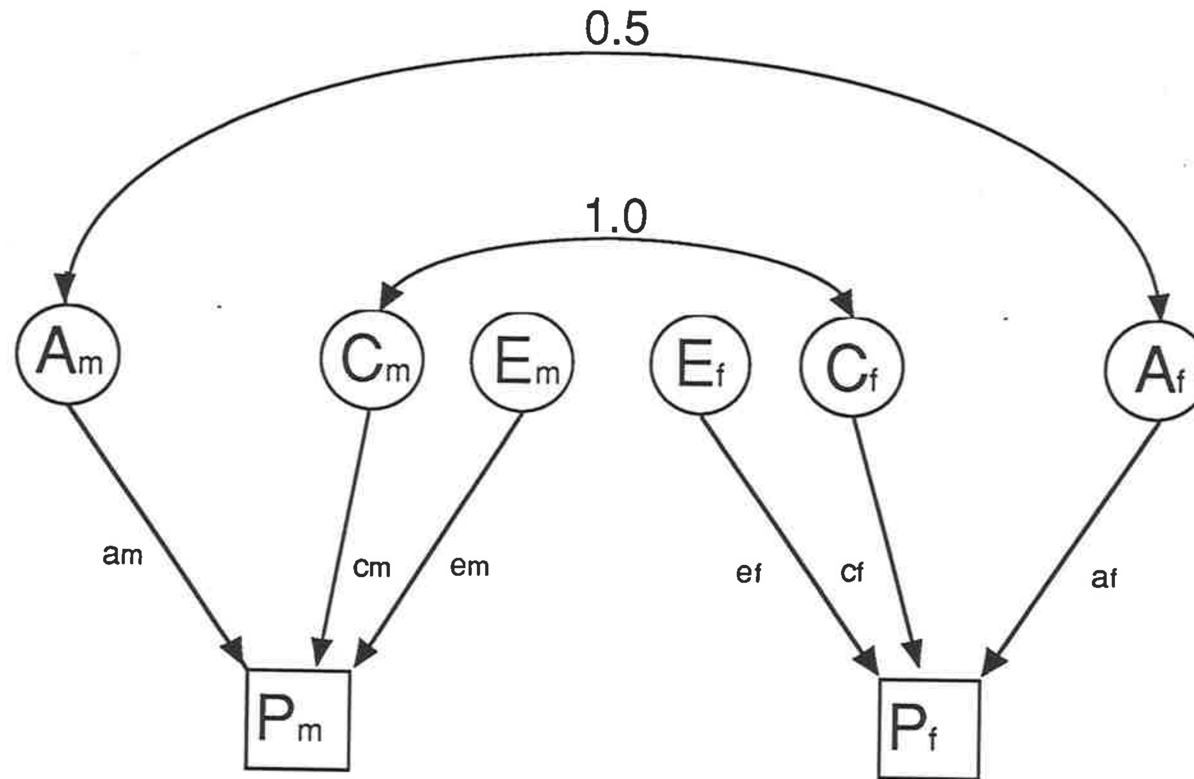


**Figure B.8:** Heterogeneity model for DZ OS twin pair.

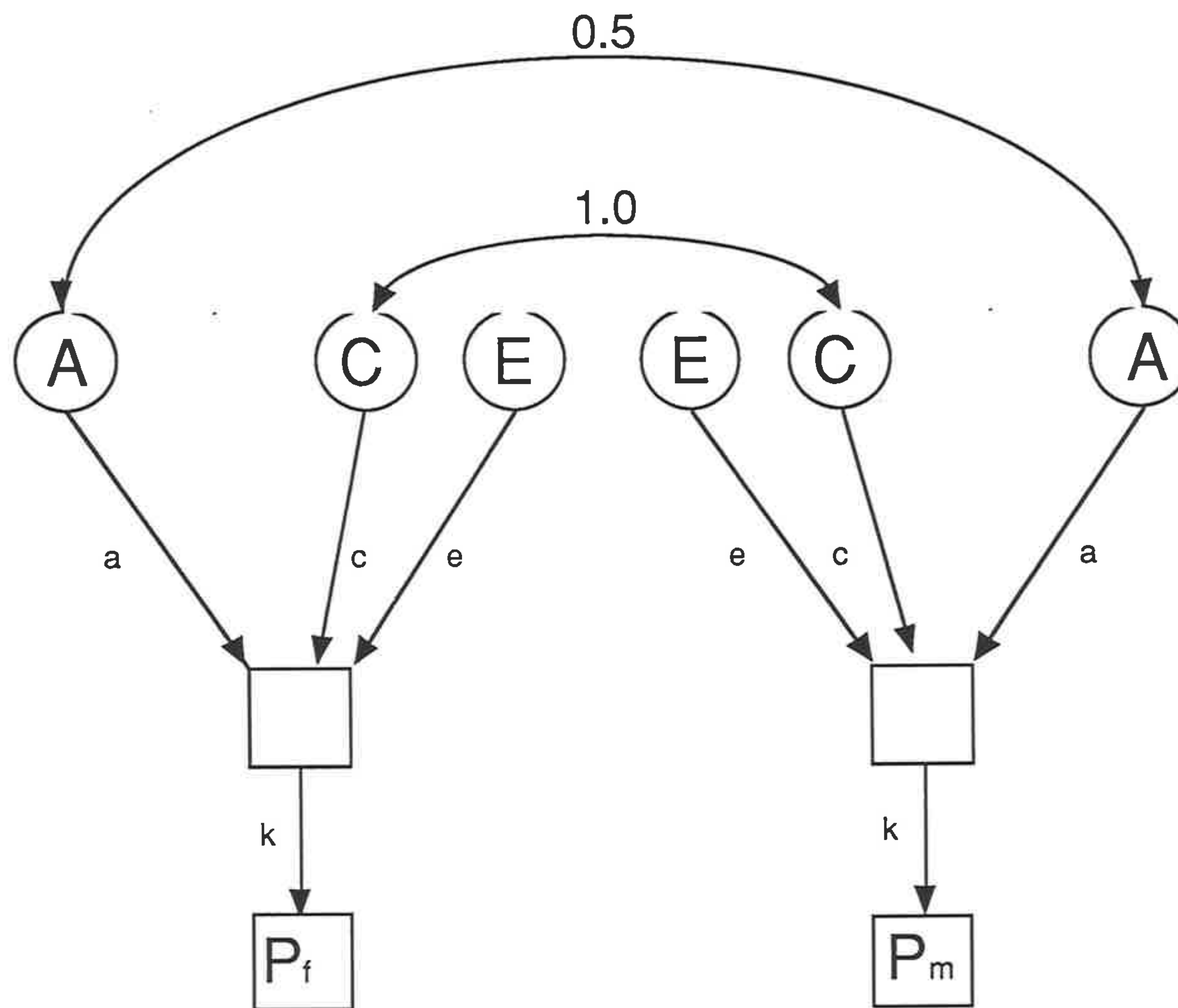


**Figure B.9:** Scalar sex limitation model for DZ OS twin pair.

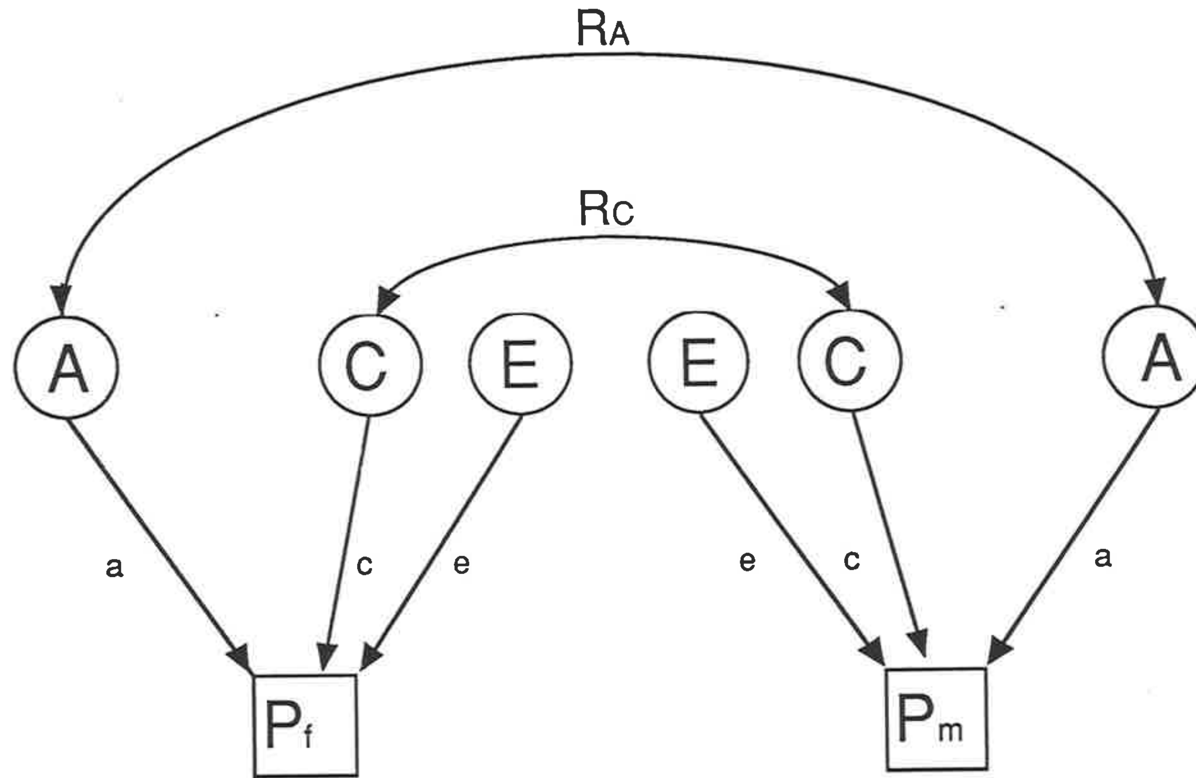


**Figure B.10:** Non-scalar sex limitation model for DZ OS twin pair.

# Appendix C

**Table C.1:** Correlation coefficients between co-twins for MD length. Significance (2-tailed) is indicated by # =p<0.05, * =p<0.01, ** =p<0.001.

| | MZF | DZF | MZM | DZM | DZOS |
|---|---|---|---|---|---|
| *Maxilla, Right Side* | | | | | |
| I1 | 90 ** | 42 * | 83 ** | 74 ** | 30 # |
| I2 | 87 ** | 45 * | 87 ** | 53 * | 10 |
| C | 85 ** | 22 | 90 ** | 28 | 6 |
| P1 | 86 ** | 22 | 88 ** | 26 | 13 |
| P2 | 79 ** | 56 ** | 62 ** | 28 | 23 |
| M1 | 90 ** | 55 ** | 79 ** | 59 ** | 54 ** |
| M2 | 83 ** | 45 # | 87 ** | 13 | 32 |
| *Maxilla, Left Side* | | | | | |
| I1 | 89 ** | 41 * | 86 ** | 62 ** | 28 # |
| I2 | 85 ** | 41 * | 89 ** | 46 * | 25 |
| C | 81 ** | 31 | 86 ** | 42 # | 15 |
| P1 | 86 ** | 33 | 85 ** | 31 | 14 |
| P2 | 83 ** | 45 * | 75 ** | 24 | 40 # |
| M1 | 79 ** | 60 ** | 85 ** | 54 * | 55 ** |
| M2 | 75 ** | 20 | 86 ** | 63 | 18 |
| *Mandible, Right Side* | | | | | |
| I1 | 79 ** | 53 ** | 87 ** | 60 ** | 41 * |
| I2 | 84 ** | 43 * | 84 ** | 46 * | 38 * |
| C | 81 ** | 40 * | 82 ** | 8 | 20 |
| P1 | 83 ** | 17 | 88 ** | 31 | 7 |
| P2 | 88 ** | 56 * | 82 ** | 26 | 22 |
| M1 | 91 ** | 32 | 84 ** | 47 * | 33 # |
| M2 | 87 ** | 57 # | 93 ** | 49 | 36 |
| *Mandible, Left Side* | | | | | |
| I1 | 87 ** | 53 ** | 87 ** | 56 ** | 17 |
| I2 | 82 ** | 38 * | 85 ** | 50 * | 33 # |
| C | 79 ** | 28 | 87 ** | 29 | 12 |
| P1 | 85 ** | 39 # | 91 ** | 43 # | 23 |
| P2 | 81 ** | 46 * | 80 ** | 55 * | 35 # |
| M1 | 91 ** | 31 | 91 ** | 34 # | 35 # |
| M2 | 88 ** | 54 # | 92 ** | 52 | 51 # |

**Table C.2:** Correlation coefficients between co-twins for BL diameter. Significance (2-tailed) is indicated by # =p<0.05, * =p<0.01, ** =p<0.001.

| | MZF | DZF | MZM | DZM | DZOS |
|---|---|---|---|---|---|
| *Maxilla, Right Side* | | | | | |
| I1 | 79 ** | 49 * | 79 ** | 59 ** | 25 |
| I2 | 69 ** | 58 ** | 77 ** | 6 | 35 # |
| C | 88 ** | 71 ** | 82 ** | 22 | 42 * |
| P1 | 88 ** | 43 # | 89 ** | 14 | 12 |
| P2 | 94 ** | 60 ** | 92 ** | 33 | 12 |
| M1 | 86 ** | 61 ** | 83 ** | 58 ** | 38 * |
| M2 | 90 ** | 31 | 90 ** | 50 # | 16 |
| *Maxilla, Left Side* | | | | | |
| I1 | 81 ** | 56 ** | 79 ** | 55 ** | 37 # |
| I2 | 73 ** | 36 # | 75 ** | 14 | 21 |
| C | 91 ** | 72 ** | 92 ** | 42 | 47 * |
| P1 | 93 ** | 68 ** | 89 ** | 27 | 21 |
| P2 | 94 ** | 51 * | 91 ** | 27 | 15 |
| M1 | 92 ** | 60 ** | 84 ** | 69 ** | 45 * |
| M2 | 78 ** | 47 # | 88 ** | 43 | 35 |
| *Mandible, Right Side* | | | | | |
| I1 | 77 ** | 57 ** | 79 ** | 41 # | 44 * |
| I2 | 78 ** | 43 * | 86 ** | 46 * | 44 * |
| C | 81 ** | 59 ** | 86 ** | 35 | 44 * |
| P1 | 85 ** | 48 * | 89 ** | 50 * | 18 |
| P2 | 88 ** | 32 | 89 ** | 45 # | 16 |
| M1 | 91 ** | 56 ** | 90 ** | 68 ** | 24 |
| M2 | 81 ** | 39 # | 87 ** | 66 * | 54 * |
| *Mandible, Left Side* | | | | | |
| I1 | 85 ** | 52 ** | 85 ** | 58 ** | 49 ** |
| I2 | 80 ** | 55 ** | 83 ** | 45 * | 47 * |
| C | 88 ** | 60 ** | 87 ** | 34 | 35 # |
| P1 | 89 ** | 41 # | 90 ** | 51 * | 41 # |
| P2 | 87 ** | 43 # | 92 ** | 48 # | 12 |
| M1 | 90 ** | 54 ** | 91 ** | 68 ** | 23 |
| M2 | 85 ** | 55 * | 87 ** | 63 * | 38 # |

**Table C.3:** Sample sizes associated with correlation coefficients in tables C.1 and C.2.

| | Mesiodistal | | | | | Buccolingual | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **mzf** | **dzf** | **mzm** | **dzm** | **dzos** | **mzf** | **dzf** | **mzm** | **dzm** | **dzos** |
| *Maxilla, Right Side* | | | | | | | | | | |
| **I1** | 80 | 45 | 63 | 37 | 54 | 78 | 42 | 60 | 38 | 49 |
| **I2** | 73 | 42 | 62 | 37 | 45 | 68 | 41 | 54 | 32 | 41 |
| **C** | 69 | 40 | 54 | 28 | 41 | 62 | 37 | 47 | 21 | 40 |
| **P1** | 58 | 29 | 46 | 27 | 25 | 59 | 30 | 44 | 26 | 26 |
| **P2** | 67 | 38 | 47 | 26 | 40 | 70 | 39 | 51 | 26 | 40 |
| **M1** | 74 | 40 | 56 | 40 | 47 | 78 | 45 | 59 | 40 | 50 |
| **M2** | 34 | 20 | 27 | 12 | 21 | 47 | 29 | 38 | 19 | 28 |
| *Maxilla, Left Side* | | | | | | | | | | |
| **I1** | 76 | 43 | 64 | 37 | 53 | 77 | 44 | 60 | 40 | 47 |
| **I2** | 74 | 44 | 64 | 38 | 45 | 67 | 39 | 60 | 33 | 41 |
| **C** | 72 | 37 | 54 | 29 | 42 | 66 | 33 | 47 | 22 | 39 |
| **P1** | 58 | 31 | 45 | 26 | 26 | 59 | 30 | 47 | 27 | 28 |
| **P2** | 65 | 37 | 46 | 26 | 36 | 69 | 40 | 45 | 27 | 36 |
| **M1** | 72 | 40 | 54 | 34 | 46 | 79 | 44 | 62 | 38 | 52 |
| **M2** | 32 | 16 | 19 | 9 | 17 | 45 | 24 | 28 | 19 | 23 |
| *Mandible, Right Side* | | | | | | | | | | |
| **I1** | 80 | 45 | 65 | 42 | 53 | 79 | 45 | 63 | 38 | 52 |
| **I2** | 82 | 46 | 65 | 42 | 53 | 78 | 44 | 64 | 41 | 48 |
| **C** | 78 | 42 | 57 | 36 | 46 | 71 | 36 | 49 | 26 | 40 |
| **P1** | 65 | 33 | 50 | 32 | 37 | 65 | 34 | 50 | 32 | 35 |
| **P2** | 64 | 33 | 48 | 27 | 37 | 69 | 33 | 50 | 25 | 37 |
| **M1** | 73 | 36 | 56 | 39 | 47 | 77 | 42 | 62 | 41 | 53 |
| **M2** | 34 | 13 | 17 | 12 | 24 | 54 | 30 | 41 | 21 | 32 |
| *Mandible, Left Side* | | | | | | | | | | |
| **I1** | 81 | 45 | 66 | 43 | 52 | 79 | 45 | 62 | 39 | 51 |
| **I2** | 79 | 47 | 63 | 43 | 54 | 75 | 44 | 62 | 40 | 46 |
| **C** | 76 | 44 | 58 | 37 | 45 | 69 | 37 | 47 | 26 | 39 |
| **P1** | 69 | 35 | 51 | 32 | 38 | 68 | 36 | 50 | 32 | 38 |
| **P2** | 67 | 34 | 45 | 25 | 34 | 71 | 34 | 46 | 23 | 35 |
| **M1** | 75 | 37 | 55 | 37 | 46 | 77 | 44 | 58 | 41 | 49 |
| **M2** | 32 | 15 | 17 | 10 | 22 | 53 | 28 | 38 | 23 | 33 |

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