MEASUREMENT, MATHEMATICS, AND MECHANISMS OF MAMMALIAN GROWTH

A thesis presented in partial fulfilment of
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Time goes, you say? Ah, no!

Alas, Time stays, we go.

H.A. Dobson

The Paradox of Time, stanza 1.

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by ROSS GRAHAM CLARK

Longitudinal growth experiments using rats, lambs, and heifers were analysed by establishing linear relationships between ages, live weights and body lengths in individual animals. Various analytical methods were investigated. Statistical and biological reasons forced the logarithmic transformation of weights and lengths, a three parameter logarithmic metameter was used if means and standard deviations were correlated on a two parameter logarithmic metameter. Age was transformed to give linear relationships. Changes to the experimental design and analysis of growth experiments were suggested.

Effects were demonstrated in individual animals that were previously only shown for grouped data and the techniques' sensitivity produced novel findings. Rats were ovariectomised at three ages and/or treated with oestrogen and slaughtered at four ages. The rat ovary inhibited growth pre-pubertally, and the response to ovariectomy or oestrogen was negatively related to the pre-treatment growth rate.

Compensatory growth occurred following weaning in rats and following birth in ruminants. Estimated initial weights explained more of the variation in subsequent growth rates than did observed weights. In rats pre-weaning growth lines diverged (compensation being negligible), birth and weaning weights being positively correlated, post-weaning growth rate was strongly negatively correlated with weaning weight. Estimated birth and final weights, and weaning and final weights, were unrelated; compensation being nearly complete.

Two sets of pre-weaning lamb live weights (collected by others) were, for individual animals, linearised. Pre-weaning compensation occurred, as it did in two independent sets of weighings from monozygotic twin heifers (also collected by others). Compensatory growth, between and within sets of twin, occurred rapidly to weaning, then slowed. The efficiency of identical twins for experimentation, using these methods, was shown, as were the disadvantages of using average daily gains.

The linear relationships did not explain all the systematic variation, short- and long-term oscillations in growth rate occurred. Long-term oscillations were related to live weight rather than to age. Neo-natal testosterone treatment of female rats transposed and advanced the pattern of growth. Both sex and strain affected the pattern of growth. The possible use of these techniques in animal breeding was discussed.

The logarithms of lengths and weights, assumed by many biologists to be linearly related (allometry), showed curvilinear relationships.

A technique of carcass analysis was developed and applied. Ovariectomy increased rat body weight and length but did not produce obesity (assayed by percentage composition and by allometry). Oestrogen stimulated fat deposition but inhibited linear growth. Body weight's response to oestrogen was adaptive,bone growth's non-adaptive. Similarly there was a large pre-pubertal sex difference in body length but a small difference in body weight. This separation of the mechanisms controlling bone growth and body weight increase was discussed. Part of the increased size of ovariectomised rats was attributed to increased skin size (and altered composition) and decreased tail length, giving decreased heat loss, and improved energy utilisation for growth.

Body growth occurs in two overlapping phases, of cell hypertrophy and cell hyperplasia, represented by different growth equations, and controlled by different mechanisms. A possible mechanism controlling cell hypertrophy, and directing compensatory growth, based on cartilage growth, would explain some of the effects described. The endocrinology of the mechanism, and oestrogen's interaction with it, were discussed.

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PREFACE

This thesis does not begin in the customary manner, with a large review of the relevant literature. The chief reason for this departure from custom being the paucity of literature relevant to the areas covered by Chapters One to Seven. Some parts of this thesis had been, or were about to be, published. Thus the present format reflects an attempt at minimising the amount of re-drafting of this published material. In addition the thesis evolved in a somewhat unusual manner, this also determined its form. The initial scope of the thesis was to investigate the effects of sex steriods on body growth, body composition, and the distribution of body fat in the laboratory rat. But the chief measure of body growth used, live weight, was found to be inadequately analysed in the current literature. This led to an extensive study of the statistical methods that could be applied to live weight data and to the eventual choice of what appears to be the most fruitful line of analysis. The statistical methods developed for analysing rat live weights were also applied to the live weights of domestic animals (sheep and cattle). Since what was, initially, a small part of the thesis grew, into perhaps the most important part, a re-structuring of the work was obviously necessary.

The studies in Chapters One to Seven will be presented in roughly the order that they were completed. This method of presentation does tend to give repetition as the same data is sometimes analysed and re-analysed in separate chapters. Essentially the same statistical techniques are also used and described in more than one chapter. So some parts of the chapters could have been combined but the lines of reasoning may have then become confused. Also a reader interested in the growth of a single species will, under the present format, generally find the information relevant concentrated in one chapter, or section, rather than scattered through the text. Although this lay-out entails some restatement of methods the general reader will note that different statistical problems occur in the various species and data sets and that their solution makes the whole relevant to the particular. The reader, it is hoped, will benefit from seeing the methods described in the order that they were developed, and applied, as the logical progression of the work should become clearer.