CHAPTER 1

INTRODUCTION

Both evolutionary genetics, and one of its sub-sets, the genetics of animal breeding, are based upon understanding changes in gene frequencies within populations. The theory concerning gene frequencies is extensive, and within the field of animal breeding, provides a basis for prediction, at least for simple genetic models and short time spans. In the wider evolutionary context, where fitness itself is the selected trait, and for less restrictive models in animal breeding, multi-locus models, involving epistasis and linkage, must be used for adequate prediction. Some theory concerning multi-locus systems has been developed, but its predictive power is largely untested, and little has been done to link the theory with observed data (Barker, 1979). Complete understanding of evolutionary change, and a wider scope for animal breeding theory, require inclusion of multi-locus and non-additive systems, and selection operating on such systems, in the body of theory.

The fullest attempt to incorporate non-additive genetic mechanisms into the theory of gene frequencies has been made by Sewall Wright. His early recognition of the importance of genetic interactions in control of a number of traits of guinea-pigs (Wright, 1920; 1922) and his observations on the population structure prevailing in the development of breeds of livestock (McPhee and Wright, 1925; 1926) led to his development of a theory which incorporates all the factors that may influence gene frequencies, and aims at explaining the development and selection of interaction systems. This "Shifting Balance Theory" evolved from simple recommendations regarding breeding structures in livestock species, into an extensive conceptual and theoretical framework, which has provided fertile grounds for interpretation and speculation, but also has been subject to criticism on various grounds. The theory is encapsulated by Wright (1977) as follows:" in a large but sub-divided population, there is continually shifting differentiation among the local races, even under static conditions, which through intergroup selection brings about indefinitely continuing, irreversible, adaptive and much more rapid evolution of the species as a whole."

The premises of the theory are as follows (Wright, 1977):

(i) a large amount of widespread polymorphism at many loci with respect to minor factors

(ii) pleiotropy in the effect of most allelic differences

(iii)multiple fitness peaks in the field of genotypic frequencies

(iv) multiple partially isolated demes.

Under appropriate conditions, the processes described in the Shifting Balance Theory allow for change of the sets of gene frequencies from one fitness peak to another. Wright (1977) gives the following full statement of the three stages involved in such changes:

"a) Phase of Random Drift: in each deme, the set of gene frequencies drifts at random in a multi-dimensional stochastic distribution about the equilibrium set characteristic of a particular fitness peak or goal. The set of equilibrium values is the resultant of three sorts of pressures on the gene frequencies: those due to recurrent mutations, to recurrent immigration from other demes, and to selection. The fluctuations in the gene frequencies responsible for the stochastic distribution (or random drift) may be due to accidents of sampling or to fluctuations in the coefficients measuring the various pressures.

b) Phase of Mass Selection: from time to time, the set of gene frequencies drifts fast enough to cross one of the innumerable two-factor saddles in the surface of fitness value in one of the demes. There ensues a period of relatively rapid change in this deme, dominated by selection among individuals (or families) until the set approaches the equilibrium associated with the newly controlling fitness peak, about which it now drifts at random and thus returns to the first phase, but at a higher level.

c) Phase of Interdeme Selection: a deme in which the set of gene frequencies comes under the control of a fitness peak superior to those controlling the sets at neighbouring demes tends to produce a greater surplus population and, by excess dispersion, systematically shifts the position of equilibrium of these towards its own position until the same saddle is crossed in them, and they all move autonomously to control by the same fitness peak. This process tends to spread through the species in concentric circles. Two such circles, spreading from different centres, may overlap and give rise to a new centre that combines the two different favourable interaction systems and becomes a still more active population source. The virtually infinite field of interaction systems may be explored in this way with only a small number of novel mutations, as alleles which had been rare come in time to displace the previously more abundant ones."

Experimental evaluation of this theory has been extremely limited, and has principally involved investigation of the effect of simplified models of this structure on responses to artificial selection. As will be discussed later, the relevance of these models to the Shifting Balance Theory is questionable. The work discussed in this thesis represents an attempt at a new and more relevant evaluation of the Shifting Balance Theory, both in terms of selection responses, and investigation of genetic changes taking place.

A general review of the development and refinement of the theory is presented, together with a brief review of related material in the field of animal breeding. The broader evolutionary field relating to the theory is then reviewed, including relevant theoretical and experimental material, and criticisms, misunderstandings or interpretations of the theory.

The experimental evaluation of the theory will be reviewed in chapter 3, which covers the design and results of the selection experiment which forms the basis of this thesis. Later chapters will deal with some investigations into the nature of genetic changes in selection lines, and with analysis of gene frequency distributions in the different population models.

1.1. Review of Literature

a) Wright's Shifting Balance Theory

Wright (1978) has outlined four distinct sources that contributed to his formulation of the Shifting Balance Theory:

(i) the work of Castle on the inheritance of colour in hooded rats (in which Wright acted as research assistant for a time), which suggested that the trait was influenced by multiple independent factors,

(ii) further investigations by Wright into colour and pattern of the guinea-pig coat,

(iii)studies of inbred lines of guinea-pigs for a number of traits (including fecundity, mortality, conformation and weight gain, as well as coat characteristics),

(iv) studies of the breeding structure of livestock breeds over the course of their development.

Together, these led to the recognition of the widespread importance of interaction systems, the differentiation amongst inbred lines resulting from cumulative sampling effects, and the way in which superior genotypes were spread from distinct nuclei throughout entire livestock breed populations, producing new sources of superior genotypes over time.

An early statement of a method of combining these effects (Wright, 1922) suggested that for improvement of traits of low heritability, a large number of inbred lines be formed, amongst which hereditary differences would be revealed. "Crosses amongst these lines ought to give full recovery of whatever vigour has been lost by inbreeding, and particular crosses may be safely expected to show a combination of desired characters distinctly superior to the original stock. Thus a cross-bred stock can be developed which can be maintained at a higher level than the original stock, a level which could not have been reached by selection alone." Further improvement could then be achieved by repetition of the process. This outline makes no direct reference to interaction systems, although Wright mentioned that successful "nicks" between promising families were often a basis for the development of livestock breeds. Also the significance of a combination of random (drift/inbreeding) and directed (selection) processes in achieving greater gains than possible by selection alone, a point that Wright has repeatedly stressed in later papers, is made clear in this outline.

The history of the British Shorthorn breed, and in particular the genetic structure within the breed during its development, was examined by McPhee and Wright (1925; 1926). It was apparent that at various stages, the relationship of the breed as a whole to one or a few outstanding individuals was quite high; these individuals, or their herds of origin, having acted as sources of genetic material for most of the rest of the breed for several generations.

A further statement of the Shifting Balance Theory was presented in 1931 in the extensive paper "Evolution in Mendelian Populations" (Wright, 1931). This includes description of the effects of individual factors affecting gene frequencies, and leads to a survey of potential for change under various combinations of these factors. The influence of population structures, ranging from large numbers of small isolated units, to single large populations, was discussed, with the conclusion being drawn that evolution within species would be most rapid and non-self-terminating in populations "subdivided into isolated and hence differentiating small groups, among which selection may be practised, but not to the extent of reduction to only one or two types. The crossing of superior types followed by another period of isolation, further crossing, and so on ad infinitum, presents a system by means of which an evolutionary advance through the field of possible combinations of genes present in the original stock and arising by occasional mutation, should be relatively rapid and practically unlimited". An extension of this was the suggestion that "complete isolation in this case ... originates new species differing for the most part in non-adaptive traits but capable of initiating an adaptive radiation as well as parallel ortho-genetic lines." This last represents a clear, albeit brief, statement of speciation via isolation.

The 1931 paper essentially provides the foundation for many later statements of the theory, both in animal breeding and evolutionary contexts. The importance of interactions becomes more clearly stated (e.g. compare Wright, 1939; with Wright, 1922), as does the notion of balance, or poise, amongst the forces affecting gene frequencies. The role of random forces, in particular of drift, is repeatedly outlined, in order to counter the misinterpretation of the theory as being one of evolutionary change by drift; rather than by combination of drift and selection. An example of this appears in Fisher and Ford (1950) where fluctuations in gene frequencies from year to year in even large populations were seen as refuting the need for small semi-isolated populations in order that saddles in the adaptive surface be crossed. These fluctuations were shown to be due to a range of causes including variation in selection coefficients. Clear interpretation of the significance of such changes with respect to the Shifting Balance Theory would require evidence that they were capable of moving populations from control by one selective peak to another. Neither the criticism, nor Wright's defence, namely that exclusive control of evolutionary change did not rest with drift alone in the theory, provide any evidence for or against the theory. The point presented by Fisher and Ford is important: the effects of fluctuations in gene frequencies should be evaluated simultaneously in large and in subdivided populations.

A second criticism made is that population structures actually found in nature do not include small enough units for drift to produce appreciable genetic differentiation (Simpson, 1953; Mayr, 1963). Accumulating evidence of genetic variation within structured populations effectively counters this criticism (e.g. Wright, 1978, for a review). The occurrence and duration of suitable population structuring has also been questioned (e.g. Simpson, 1953). This criticism remains unanswered, although Wright (1970) has pointed out that even if such conditions are only intermittently present, rapid change can occur during these periods.

While the specific effects of individual forces, and of combinations of these forces, have been extensively investigated by Wright (1931; 1955; 1956; 1960; 1963; 1965; 1970; 1977; 1980), no mathematical description of the operation of the entire three-stage process has been developed. The role of unique events, and the complexity of the multi-dimensional surface of selective peaks for even a small number of interacting loci render this task impossible; at best, potential paths for individual demes over simple surfaces can be modelled (for examples using simple interaction systems, see any of the papers noted above). These difficulties have meant that much of the discussion of the Shifting Balance Theory has been concerned with the degree to which any or all of its premises are met in specific populations. Some of these discussions will be mentioned later in this review.

Because the development and discussion of the theory has included both animal breeding and evolutionary topics, the remainder of this review will attempt to cover investigations into the effects of population structure and the Shifting Balance Theory in these areas, and the conclusions that have been reached as to its potential importance.

b) The Shifting Balance Theory and Animal Breeding

Lush (1933; 1947) restated Wright's conclusions regarding optimal breeding structure for livestock breeds, and showed how they were related conceptually to line-breeding and to family selection. These proposals were for improvement of overall merit, as a combination of many traits, and included the notion of testing crosses between strains/sub-groups, in order to determine those that produced the best combinations of traits. The system proposed was summarised as being "an alternation of line-breeding with tentative outcrosses, both accompanied at all times by intense selection. Most of the linebreeding would be done in the best of the herds with extreme outcrossing being confined to the poorer herds." The notion of relating degree of outcrossing to merit of the sub-group was included: "the more successful each sub-group was, the less readily would any outcrossing be done and the milder such outcrossing would be", (Lush, 1947). As will be apparent from the survey of experimental investigations of the Shifting Balance Theory, this particular aspect of the optimal structure has been either overlooked, or modelled in a greatly simplified and possibly inappropriate manner. Lush (1947) also raised a still unsolved question: namely, what is the general importance of epistasis? It was pointed out that if epistasis is not significant, then systems of mating that include inbreeding are not necessary for improvement programs.

The genetic structure of several livestock breeds/populations has been evaluated in the period since Wright's theory was formulated. Weiner (1953) and Robertson and Asker (1951) investigated the structure of dairy cattle breeds in Great Britain, and reported no evidence of significant genetic differentiation between herds, although hierachical structuring was evident, with genetic differences between herds at different levels. Larger differences between studs were reported in the Australian Merino (Short and Carter, 1955), and genetic differences between strains within Merinos for several traits were estimated by

Jackson and James (1970). The aim of the latter study was to compare two methods of choosing foundation animals for new studs: selecting from within one stud or within each of several studs. The general conclusion was that provided several traits were to be improved, and gains in the long term (more than three generations) were important, animals from several studs should be chosen. In order to reach these conclusions, estimates of the parameters `r', the correlation between estimated and true stud mean breeding value (equal to the square root of the between-stud heritability), and Ø, the ratio of between- to within-population genetic standard deviations, were required. r could not be estimated accurately without full knowledge of all genetic variances for each trait, and genetic relationships within studs, but was assumed to be high. The ratio of between stud genetic standard deviation to its within-stud phenotypic standard deviation (Øh) was found to be quite high (average value 0.74), with only small variation for a broad range of traits. Thus genetic differences between studs were quite large relative to the amount of genetic variation within them. Estimates of between-stud genetic variance components were presented, both as absolute values and as proportions of the total variance. These proportions ranged from 4 to 44%, and could be taken as estimates of between-stud heritability, suggesting that for some traits there was appreciable genetic differentiation between studs. Unfortunately, standard errors of the between-stud components were large for all traits evaluated, so that these values were not very useful.

Studies similar to those of Weiner (1953) and Robertson and Asker (1951) have been reported in Australian cattle populations (Barker, 1957; 1959; Barker and Allingham, 1959; Davey and Barker, 1963). For the Jersey breed, a high degree of subdivision into local strains was found, reflecting a greater use of home-bred sires, and migration mainly within local geographical areas, with two central regions acting as principal sources of immigrants to other regions. This suggested that the entire population would eventually be genetically more similar to those central regions. Regional subdivision did not imply significant genetic differentiation, but it was suggested that genotype by environment interactions could become important. Within the Hereford breed, genetic relationships to individual animals were never high, and little evidence of genetic differentiation between herds was found. The breed showed high levels of use of imported animals, similar to the situation in British Friesians (Robertson and Asker, 1951).

Jackson and James' (1970) paper was based on theory developed by James (1966) for determining whether foundation stock for breeding programmes should be based on one or several populations. A general formulation of the theory allowing selection of individuals from each of many populations by means of an index combining population and individual breeding values was outlined. James noted that population mean breeding value will not be known exactly, if at all, but that in general, higher proportions should be selected from populations having either higher mean breeding values or more genetic variance. Although overlooked at the time of formulation of my experimental design, this approach is essentially the one used here (Chapter 3) to determine contributions to a migrant pool in a model design to simulate the optimal model of Wright. James' approach differs from that of Wright, however, in that it is concerned solely with additive variance, and is a procedure for selecting individuals to form a single population, and not for determining gene flow patterns among semi-isolated population units maintained for some number of generations.

In animal breeding practice today, open nucleus, and by extension to the multi-breed situation, open synthetic schemes, represent attempts to maximise utilisation of genetic variation both within and between population units (herds/flocks in the case of open nucleus and breeds in the case of open synthetic schemes. In open nucleus systems, elite animals migrate into a nucleus where breeding effort is concentrated. An open synthetic is a breeding population based on more than one breed, and potentially receiving continuing inputs from other stocks). They differ from Wright's optimal designs in that only one population is treated as the centre for mixing different genotypes and as the source of superior genetic material for the remainder of the population. In this context, Wright's model could be viewed as a system having a number of open nuclei allowing simultaneous testing of many combinations of genotypes. This reflects the fact that open nucleus/synthetic schemes imply a single adaptive peak, whereas Wright's model assumes a number of such peaks in the adaptive surface. Theory has been developed for open nucleus/synthetic schemes (James, 1982; Taylor, 1976; Webb, 1976; Kinghorn, 1980; 1982), and limited data is available (e.g. Webb and King, 1976). One aspect which has relevance to Wright's model is the different methods of evaluating individuals for inclusion in the nucleus. Progeny sired by immigrants may show heterosis, depending on the trait and the nature of differences between population units, not available to progeny sired by individuals already in the nucleus. This will bias their estimated breeding value. There is also a possible bias due to differences in population means. Webb (1976) dealt with methods of removing these biases in theory and in practice. Kinghorn (1980; 1982) took the opposite approach, viewing maintainance of heterosis as desirable, and incorporating breed breeding values and individual phenotypic deviations from that mean. Simulation showed that inclusion of heterosis expression leads to greater selection responses over time. The models developed by Kinghorn were for single trait selection, but could be extended to the multi-trait case. Under such circumstances more than one adaptive peak may occur, and the situation would then more closely resemble the Wrightian model. The theoretical approach used in these studies would provide a useful basis for simulation of the operation of the Shifting Balance Theory, provided that the differences mentioned were taken into account.

c) Mathematical Theory of Structured Populations

Mathematical theory for one and two locus models in structured populations is extensive, and all aspects of the field contribute directly or indirectly to understanding of the Shifting Balance Theory. A small sample of this literature will be reviewed with the aim of illustrating the areas covered and their conclusions, together with discussion of their significance for the Shifting Balance Theory.

The effects of population subdivision on rate of spread of new mutant alleles, on degree of genetic differentiation and the behaviour of polymorphisms, both single and multi locus, and on the decay of genetic variability, have been studied extensively (e.g. Moran, 1959; Lewontin and Kojima, 1960; Maynard Smith, 1970; Maruyama, 1970; Rohlf and Schnell, 1971; Karlin, 1975; Slatkin, 1975, 1981; Prout, 1980; and for a review, see Christiansen and Feldman, 1975). Whilst the general conclusions from such studies, in terms of rates to fixation, genetic differentiation among sub-populations and conditions for existence and stability of polymorphisms, are of value, a general limitation in terms of the Shifting Balance Theory is that migration between demes is treated as independent of deme mean fitness (the case of migration being proportional to relative fitness was mentioned by Slatkin (1975) and discussed briefly by Rohlf and Schnell (1975), but in neither case were the consequences of such a model explored at any length). Since such a model for migration is essential to the phase of interdeme selection in the Shifting Balance Theory, these studies in general throw more light on the conditions existing in populations not actively "moving" through the three stages of the Shifting Balance Theory, and in this sense should be viewed as dealing with the background/framework conditions. It is within this framework that local populations may cross an adaptive saddle and so initiate the three stages of the Shifting Balance process.

The behaviour of populations on adaptive surfaces, and properties of adaptive surfaces themselves, also have been investigated. Wright's adaptive topography (Wright, 1932) has been applied widely in biological studies (Frazzetta, 1975), and proved very useful in field studies (e.g. Lewontin and White, 1960). Behaviour of multi-locus polymorphisms on such surfaces together with the effects of linkage, recombination and interaction (e.g. Lewontin and Kojima, 1960), and the effects of a number of biologically significant situations e.g. epistasis, meiotic drive, fertility selection, differential selection between sexes, and gametic selection, in altering the behaviour of populations on such surfaces, have been evaluated (Curtsinger, 1983). These results extend those of Moran (1964), concerning the inapplicability of maximisation principles, and the consequences of that finding for the existence of adaptive topographies. Conrad (1978) discussed the evolution of adaptive landscapes, and some factors affecting their smoothness, or the ease with which populations may move over their surfaces. Barton (1983) investigated clines resulting from differential selection at many loci, showing that selection spread over a number of loci can be extremely effective in countering gene flow, and discussed the implications of these findings for speciation.

A particular aspect of population structuring that has been investigated extensively in recent years, is that of group selection for altruistic alleles/traits. Conditions under which alleles deleterious for individuals but increasing deme fitness can increase in frequency and spread throughout structured populations have been investigated by a number of authors (e.g. Leigh, 1983; Kimura, 1983). An extension of this model, perhaps more directly relevant to the Shifting Balance Theory, is the behaviour of favourable epistatic complexes composed of alleles that are individually neutral or even deleterious. The situation has been intensively investigated by Rutledge (1970).

His results show that survival of such complexes, and increases in their frequency to fixation, have higher probabilities in subdivided than in single large panmictic populations, and that the chance of their survival increases as the level of gene flow between demes increases. Migration rates used were much higher than those considered previously necessary for subdivision to be effective (e.g. by Simpson, 1953). The process of diffusion of the favourable combination into new demes was modelled, initially for the Island and Stepping Stone Models with equal deme size, but also for a modified Stepping Stone where deme size was proportional to frequency of the favourable combination -the island model being one where demes can receive immigrants from any other with equal probability, the stepping stone where migration is restricted to adjacent demes. This is the situation for phase 3 of the Shifting Balance Theory. For mathematical tractability, severe restrictions on this model were necessary, including setting the fitness of the repulsion gametes to zero (i.e. lethality), together with other restrictions imposed throughout the study (namely, constant sex ratio, discrete generations, no mutation, and all selection occurring in the haploid generation). In general, diffusion of the favourable combination was faster in the island model than the stepping stone . Relating deme fitness to frequency of the favourable combination resulted in an increased rate of replacement of alternative allele combinations, leading to fixation of the entire population for the favourable complex. It was necessary that migration rate, m, be small for this to occur, but not infinitessimally so; sufficient condition was that

$$m < S/(2+2S)$$

where S = selective advantage of favoured combination. While, as Rutledge concluded, his results need to be extended to less restrictive models, the finding that combinations of individually unfavourable alleles that are advantageous in combination, may be held at high frequency or reach fixation in subdivided populations, and can spread throughout entire structured systems, provides important theoretical support for Wright's model, and shows that the three stages of the Shifting Balance Theory can operate in the manner postulated by Wright. Results obtained in this thesis appear to provide experimental support for the conceptual model provided by Wright, and the theoretical results obtained by Rutledge, while using a far less restrictive model than his.

d) Structured Populations: Data

Experimental and natural population data exist that provide information on genetic structuring in natural populations, including the effects of migration as it operates in such circumstances. Lewontin and White (1960), and White et al (1963) estimated relative viabilities for inversion polymorphisms in morabine grasshoppers, and developed adaptive topographies for the species, upon which individual colonies could be sited. Movement of colonies on these surfaces was studied, and conclusions drawn regarding the stability of apparent equilibrium positions. Levin and Kerster (1974) and Allard (1975) reviewed work on gene flow in plant species, and suggested that levels of gene flow in natural populations are often very low, with inbreeding acting as a barrier to migration, protecting local co-adapted genomes. Similar conclusions were reported by Rasmussen (1970) and Anderson (1970), for small mammal populations, together with the suggestion that behavioural strategies may reduce effective gene flow considerably below that expected from observations on animal movement. Significant differentiation in the presence of movement of animals between demes and in the absence of differences in selective regime, were noted by Cheverud (1981) in Rhesus macaques. Behavioural patterns were involved as a factor limiting effective gene flow here also. These findings support the general conclusions of the review of Ehrlich and Raven (1969), that gene flow in nature may be more restricted than is commonly thought. Gene flow can however influence genetic composition in separate demes. For example, Smith and Patton (1984) obtained evidence for morphological change in pocket gopher colonies resulting from the influx of animals from neighbouring colonies.

Stable, structured polymorphisms have been observed in experimental situations. Endler (1973) produced clines in the frequency of the deleterious marker, Bar, in D. melanogaster populations, differing in selection pressure for the marker allele. While gene flow maintained the allele, albeit at low frequencies, in populations where the balance of selection (artificial vs natural) was overall against it, the clinal pattern was essentially the same as in the absence of migration. Thus gene flow appeared to moderate slightly the effects of the selection gradient. Using a circular stepping stone model, with a migration rate of $m = 0.03$, Altukhov and Bernashevskaya (1978) found that polymorphisms for two allozyme loci were more stable in a subdivided population than a single panmictic one. Further, the system became more stable over time, as correlations between deme allele frequencies increased in successive generations.

Genetic differentiation among demes/colonies, such as was observed by Altukhov and Bernashevskaya, in the absence of selective differences, have been interpreted quite differently by other authors. Extensive work on Cepea nemoralis in England and France (Cain, 1964; Cain and Currey, 1963; Lamotte, 1959) has revealed area effects in colour polymorphisms not readily explained by selective differences. Genetic drift has consistently been rejected as a contributing factor, although Wright (1978) discussed these results at length, and proposed an explanation that does not rule out sampling effects. A broader interpretation than that of Cain has been proposed for this polymorphism. This interpretation (Jones et al, 1977), attempts to integrate several possible factors, including selection and drift.

The experimental results of Altukhov and Bernashevskaya have been discussed in a broader context by Altukhov (Altukhov, 1982; 1985), where the stability inherent in subdivided systems renders them unsuitable for rapid adaptive evolution and speciation. Altukhov ascribed greater importance in these processes to saltational changes in monomorphic parts of the genome, and proposed that since species differ at monomorphic loci, the change from population to species is not a gradual transition, but a qualitative gap.

e) The Shifting Balance Theory and Evolutionary Theory

This last point leads to consideration of the place occupied by Wright's theory in the field of evolutionary theory; as an accepted model, a starting point for development of new models, and as is evident in the papers just discussed, rejected by some authors. In this context, it should be noted that the later of the papers of Altukhov referred to above seems to allow a greater role for Wright's model in evolutionary change, while at the same time suggesting that neither it nor Neo-Darwinism generally are capable of completely explaining new observations. Altukhov seems chiefly concerned to include chromosomal rearrangements or macromutations in order to explain an observation made in Salmonids and other species, namely, clear differences in monomorphic genes along with the absence of qualitative differences between "good" species in polymorphic ones.

Nei (1979) reviewed results at the molecular level in order to examine the relative usefulness of the Neutral Mutation Theory (Kimura, 1968) and Wright's Shifting Balance Theory to explain evolution at this level. He concluded that Wright's model is not supported by molecular data, but that under certain conditions mutation and random genetic drift could be important in morphological differentiation between populations.

Cavalli-Sforza (1969) reviewed results of work on structure in human populations, in particular the importance of migration and drift, and the levels of genetic differentiation amongst villages, towns and cities in the Parma valley in Italy. The results support the hypothesis that some of the differentiation results from drift and migration in the absence of any selection, and he concluded that "genetic drift can affect evolution on a small scale over a short period of time", and that the "relative importance of drift and selection in determining the course of evolution remains to be assessed".

Work on Hawaiian Drosophilidae has led Carson to ascribe great importance to founder events in small isolated populations. He has consistently supported the Shifting Balance Theory as both a mechanism for change within species and as a basic model allowing the possibility of occasional founder events (e.g. see Carson, 1965). He has developed the argument that speciation reflects profound reorganization of stabilized, co-adapted genetic systems, by means of stochastic processes occurring after drastic reductions in effective population size (bottlenecks, founder events). This extended model makes substantial use of the Shifting Balance Theory (Carson, 1982).

Templeton (1980; 1981; 1982) has extended ideas concerning speciation resulting from founder events to include genetic transilience, major changes in the "closed" system of genomes (Carson, 1975). He has developed theory regarding optimal situations for such changes to occur; these being that "founders have high reproductive values, in a low density environment with rapid increases in population size possible, have overlapping generations and have a hierachical population structure, at least temporarily" (Templeton, 1980). Laboratory studies (Templeton et al, 1976; Templeton, 1979) have been cited as providing evidence for this mode of speciation, although this conclusion has been reinterpreted more simply (Charlesworth et al, 1982). Templeton (1980) reviewed a number of other experimental designs that have involved "founder flush" phases, and used these designs, and the results obtained, to refine the theory of speciation by genetic transilience and methods of evaluating it experimentally. Templeton (1982) developed a new conceptual model of the operation of the Shifting Balance Theory, and pointed out that relatively rapid change followed by periods of stasis, at the macroevolutionary level, might reasonably be expected if the model operates as postulated. Barton and Charlesworth (1984) and Carson and Templeton (1984) summarise alternative viewpoints on Founder-flush theories, without any clear resolution of their differences.

The ideas of Carson and Templeton on rapid bursts of genetic change, often induced by severe sampling events, are in the vein of Simpson's "quantum evolution" (Simpson, 1953), Grant's "quantum speciation" (Grant and Flake, 1974; Grant, 1977), and Lewis "speciation by catastrophic selection" (Lewis, 1962). All these models involve populations subdivided into sub-units small enough that selection and drift can interact to allow the crossing of adaptive valleys, producing new species. Grant and Flake (1974) discussed the effects of various population structures on the costs-of-selection associated with such changes, and suggested that where populations are subdivided and different demes face different local selection pressures, individual demes may face lower costs of selection than would single large populations.

These ideas have been analysed and extended to include evolution by chromosomal rearrangement, in both peripheral and central populations, by Bush (1975; 1981) and co-workers (Bush et al, 1977). The latter study included an examination of the correlation between rates of chromosomal evolution and of speciation, and the effect on both of population structuring. The authors concluded that although sufficient data on effective population size, Ne, is lacking in many species, there is a suggestion that structuring into many small demes does accelerate rates of chromosomal evolution and speciation, as proposed by Wright (1931). They discussed means whereby such structuring may arise in the absence of extrinsic factors (physical barriers etc), including social structuring, and suggest that social factors may have contributed to rapid speciation rates in mammals.

Lande (1976, 1979, 1980) extended the theory of genetic change to include phenotypic variation and change in variously structured populations. This led to modification of views on the relative importance of natural selection and drift, and of the types of population structure conducive to adaptive change. His theoretical results indicate that only very weak selective forces are necessary to explain observed rates of phenotypic evolution, and also that random drift in even large populations ($Ne = 10^4-10^5$) cannot be discounted in contributing to these changes. These findings led to the conclusion that the "population structure most conducive to evolutionary radiation into new adaptive zones is that with several large stable centres to serve as reservoirs for colonization, and many small fully and partially isolated populations," (Lande, 1980). As Lande points out, "this conception is similar to Wright's shifting balance theory but includes the possibility of progressive evolution in fully isolated small populations". This model also includes crossing of valleys between adaptive phenotypic zones, in addition to Wright's "genetic fine-tuning within one phenotypic adaptive zone" (Lande, 1980). The limitations on Wright's model observed by Simpson (1953) and Mayr (1963), namely that the required population structure is restrictive, are thus relaxed.

Parsons (1983) surveyed data on genetic architetcture of morphological and ecobehavioural traits, including results of selection experiments, and suggested that combinations of few genes of large effects and long periods when stabilizing selection is operating can produce patterns of response marked by sudden bursts of change. By analogy, he suggests that patterns of stasis and short episodes of rapid change at the species level might therefore have a similar genetic basis.

Belief that such patterns at the species level reflect processes other than simple gradual adaptation, lies at the heart of the debate over the pattern of evolutionary change: "punctuated equlibrium" vs "gradualist Neo- Darwinism", (Gould, 1980; 1982; Stanley, 1979; 1982; Petry, 1981). Wright's ideas have been central to many of these arguments since they provide an explanation for patterns of change including both rapid bursts and long periods of relative stasis (Templeton, 1982). Wright's description of his model as being "two-level", that is, with selection acting at the level of individuals and demes (although via the same mechanism, differential fitness) is seen as placing a level between species and individual in a hierachy, at all levels of which drift and selection can interact, with the consequences depending on the level (Gould, 1982). However, the Shifting Balance Theory is seen as placing too much emphasis on change vis a vis stasis to fit with the fossil data and thus to be a satisfactory mechanism underlying punctuated equilibrium models (Gould, 1980). In this essay, Gould also reiterates the doubts raised by other authors regarding the likelihood and occurrence of suitable population structuring.

Critiques of punctuationist models also have included discussion of the Shifting Balance Theory. In an extensive refutation of punctuationist claims, Charlesworth et al (1982) cited the Shifting Balance Theory as "the only genetically credible alternative ... to the Darwinian process of step by step evolution under the guidance of natural selection", but pointed out the requirement for a favourable population structure, and the uncertainty regarding the existence of such structures. Similarly, Van Valen (1982) discussed the Shifting Balance Theory as a mechanism for rapid adaptive peak shift, but suggested that environmental variation on a time-scale to which selection can respond, may be more important, and that large effective populations, rather than small ones, would be more conducive to rapid change under selection.

In the Shifting Balance Theory, inbreeding in semi-isolated demes is viewed as providing a means by which populations can move off particular local adaptive peaks and across, or at least into, an adaptive valley, and come under control of a new, higher adaptive peak. Thus it is the dispersive action of drift arising from inbreeding that is central. An alternative interpretation of the effects of inbreeding under such circumstances has been proposed and developed by Shields (1982a,b; 1983). Seeking an explanation for widespread inbreeding and philopatry (tendency to breed at or near birth-site) in some groups of organisms, he postulated that philopatry has evolved as a mechanism favouring inbreeding in order to ensure preservation of co-adapted genomes. Under this hypothesis, the population structure required by the Shifting Balance Theory provides a balance between too strict inbreeding, resulting in excessive influence of stochastic processes, and over-wide outbreeding, which would destroy coadapted genomes. Requirements for both Shields' and Wright's models are similar, and are tested in similar ways (Shields, 1983). The major difference, as mentioned above, is that Wright suggests that appreciable drift would result from the inbreeding arising from the population structure. Shields' discussions of his and Wright's models include surveys of evidence on local effective population size, outbreeding depression, genetic differentiation within and between demes, and predictions of levels of inbreeding in low, medium, and high fecundity species.

Group selection studies are relevant to this discussion since they are based on genetic differentiation amongst population units, and include some form of inter-group selection. Wade (1978) reviewed the models used in theoretical and experimental studies of group selection, pointing out that many are based in principle upon the Shifting Balance Theory. His description of the mechanism of "group" selection in the Shifting Balance process, as operating via differential extinction of demes, is not correct. Wright saw differential migration as the principal mechanism of interdemic selection, with extinction and founding from other demes as the extreme of this process (Wright, 1978). Wade's review included discussion of the genetic basis of traits differing between groups, the models of group selection used and the inter-relationship between individual and group selection. Slatkin and Wade (1978), Wade (1977; 1979; 1982), McCauley and Wade (1980), and Wade and McCauley (1980; 1984) have investigated theoretically and experimentally group selection models, and their results suggest that significant genetic differentation can be generated in structured populations, and that this between-deme genetic variance is available to group selection. These experimental studies were based upon a populational trait, local deme growth, and therefore allow direct comparison with the predictions of the Shifting Balance Theory. Other group selection studies have been concerned with the fate of single, often altruistic alleles (Maynard Smith, 1964; 1976; Michod, 1980), a specific case within the general area of the effects of population structure on evolution.

Wright's most recent statements on the Shifting Balance Theory (1980; 1982a,b) have included discussions of group selectionist arguments and their relationship to his theory, and of the relationship between adaptive change within species under his model and macro-evolutionary change, with direct reference to the gradualist-punctuationist debate. In the latter context, he concluded that the population structure favourable for the operation of the Shifting Balance process is also favourable to incipient speciation, and that "the evolutionary processes indicated by the fossil record can be interpreted by the Shifting Balance Theory without involving any causes unknown to genetics or ecology".

Provine (1983; in press) discussed the sources and development of the Shifting Balance Theory in detail, and outlined the differing importance ascribed to random and directed processes by Wright during the long period since the theory was first formulated. He discussed some possible reasons for the widespread misinterpretation of the theory (see also Gould, 1983) and some reasons for the gradual changes in its formulation. Wade (1980) and Hartl (1979) in reviews of the Shifting Balance Theory, both stressed the nature of the theory as an attempt to integrate all the forces that can act on gene frequencies.

This review is by no means an exhaustive survey of all theoretical and experimental work relevant to the Shifting Balance Theory. Rather, it attempts to outline its essential principles, and give an impression of its position and role in animal breeding and evolutionary theory. It should be apparent from the review that while there is extensive theory, and experimental evidence, on individual elements of the theory, evaluation of the complete structure is extremely limited. This has not inhibited widespread utilisation and interpretation of the basic model. The lack of proper evaluation presumably reflects logistic difficulties entailed in experimental evaluation; Wright (Pers. comm.) has observed that adequate testing of the Shifting Balance process would be very difficult, if not impossible, due to the requirement for an enormous number of partially isolated local populations, and the rarity of demes acquiring by random drift "a significantly favourable interaction system of alleles at two loci that are otherwise slightly unfavourable". Similarly theoretical and simulation studies, while relatively simple in principle, also provide a number of problems (some of these will be discussed elsewhere in this thesis).

The model used in this study represents the first attempt to combine the elements of the Shifting Balance process in the manner Wright has consistently outlined. The model is restricted and has several limitations, as will be discussed later, but it will be proposed that the results obtained from this study suggest that it is worthy of further investigation.

CHAPTER 2

BASE POPULATION PARAMETERS

2.1. Base Population

The population used in this study was derived from approximately fifty D.melanogaster females caught by trapping in the Armidale, N.S.W. area. After five generations establishment as a laboratory population, genetic parameters were estimated using an hierachical design based on Hill and Nicholas (1974).

2.1.1. Materials and Methods

The design consisted of 72 sires, 8 dams per sire and 3 male and 3 female progeny scored per dam. Mating and egg-lay took place on a yeasted medium (medium F1 of Claringbold and Barker, 1961) in 3x1-inch glass vials at 25±0.5oC and 70% relative humidity. All flies were stored prior to scoring on yeasted medium, under the same conditions as outlined above.

All flies (parents and progeny) were scored as 3-day old adults using a Mettler HL52 micro-balance. After scoring, flies were mated for 3 days, males discarded, females placed in individual vials to lay for 3 days, then discarded.

Results were analysed (by least squares analysis) using the programs LSML76 (Harvey, 1978) and NESREG (Hammond, Jackson and Miller, 1972). Heritabilities and genetic correlations were estimated from variance and covariance components and from parent-offspring regressions. Genetic parameters were calculated using the standard formulae of Falconer (1981) and Becker (1967). Sire-daughter and dam-son regression estimates of heritability were corrected for inequality of male and female variances as suggested by Falconer (1981). Standard errors of the genetic correlation estimates from the half-sib correlations were estimated by the method of Tallis (1959).

Genetic expectations for the heritability estimates are given in Table 2.1. These are taken from Bohidar (1964) and Becker (1967).

Table 2.1: Genetic Expectations for Heritability Estimates

Heritability Estimate	Genetic Component				
	V_A	V_{AA}	V_{AS}	V_D	V_M
Sire-Son	1	1/2			
Sire-Daughter	1	1/2	2		
Dam-Son	1	1/2	2		1
Dam-Daughter	1	1/2	1		1
Paternal 1/2-Brother	1	1/4			
Paternal 1/2-Sister	1	1/4	2		
Dams within Sires/Males	1	3/4	2	1	4
Dams within Sires/Females	1	3/4	1	1	4

V_A : Variance of Additive effects

V_{AA} : Variance due to Additive by Additive Epistasis

V_D : Variance of Dominance effects

V_M : Variance due to Maternal effects

2.1.2. Results

Population means and standard deviations, correlations between male and female bodyweight, analyses of variance, the sib based estimates of heritability, and the offspring-parent regression estimates of heritability, are presented in Tables 2.2-2.6 respectively.

Table 2.2: Base Population Parameters: Means and Standard Deviations (mg)

	Parents		Progeny	
Sex	Mean	Std. Dev.	Mean	Std. Dev.
Male	0.9839	0.1100	0.8938	0.0591
Female	1.5188	0.2160	1.4172	0.1221

Table 2.3: Base Population Parameters: Adult Bodyweight Correlation Between Sexes (Offspring-Parent)

	Sire	Dam	Sire & Dam
Phenotypic	0.368	0.365	0.365
Environmental	0.464	-0.825	-1.718
Genetic	0.226 (0.198)	0.599 (0.063)	0.541(0.066)

NB: standard errors of genetic correlations in brackets.

Table 2.4: Base Population Parameters: Analyses of Variance

(i) Separate Sexes

	Males			Females		
Source	df	Mean Square	Variance Component (x 10-3)	df	Mean Square	Variance Component (x 10-3)
Bet. Sires	69	0.500***	1.72	69	0.093*	2.14
Dams/Sires	255	0.027***	8.25	260	0.064**	16.54
Within Dams	609	0.004		640	0.015	

$*P<0.05$ $**P<0.01$ $***P<0.001$

(ii) Over Sexes

Source	df	Mean Square	Variance Component (x 10-3)
Bet. Sires	69	0.091*	1.08
Dams/Sires	271	0.060***	8.18
Sex	1	123.444***	
Within Dams	1562	0.015	

*P<0.05   **P<0.01   ***P<0.001   *P<0.05   ***P<0.001

Table 2.5: Base Population Parameters:
Sib Analysis Estimates of Heritability of Adult Bodyweight (StandardErrors)

	Sire	Dam	Sire & Dam
Male	0.499 (0.140)	2.457 (0.112)	1.478 (0.053)
Female	0.251 (0.102)	1.960 (0.130)	1.905 (0.073)
Pooled	0.381 (0.058)	1.377 (0.102)	0.779 (0.062)

Table 2.6: Base Population Parameters:
Offspring-Parent Estimates of Heritability (StandardError)

	Sire	Dam	Mid-Parent
Male	-0.074 (0.070)	0.043 (0.112)	-0.046 (0.029)
Female	0.186 (0.112)	0.044 (0.056)	0.048 (0.047)

In the sire analysis (Tables 2.4 & 2.5), the variance component due to dams within sires is much higher than that due to sires, for both male and female bodyweight (and bodyweight pooled over sexes). Consequently, the heritability estimates based on σ^2_D are much higher than those based on σ^2_S. The estimate based upon OD includes more non-additive genetic variance, including dominance and epistatic components, and common environmental effects. The dams' estimate for males also contains sex-linkage variance not included in the sires' estimate.

Because the dam component estimates for both males and females were much larger than the sires' estimates, the most useful estimates for predictive purposes are those based on the sires' component. The average heritability of adult bodyweight, taken as the mean of the two sires' based values, was 0.38. The heritability estimate for males was significantly higher than that for females, and this observation, combined with the estimated genetic correlation between male and female bodyweight (Table 2.3), suggests that the measured trait involved both genes having similar effects in the two sexes, and genes whose effects were sex linked.

None of the offspring-parent regression estimates of heritability were significantly different from zero (Table 2.6), the only estimate approaching significance being that based on sire-daughter regression. On the basis of the genetic expectations from the different heritability estimates (Table 2.7), and evidence from the sib analysis of reasonable levels of additive genetic variance, it would be expected that the offspring-parent regression estimates should all be higher than was found. Two possible reasons for the discrepancy between estimates are genotype by environment interactions between parent and progeny generations, and natural selection favouring intermediates. The former suggestion is given some support by the fact that in both sexes, both the mean bodyweight in the progeny generation and its standard deviation were significantly lower than in the parental generation (Table 2.2). The most likely cause of the lower progeny mean weight is crowding during larval development. No standardization of egg numbers was carried out in the laying vials, so it may be that the progeny suffered greater crowding than the parental generation. Interactions with fitness may very well also have been important. The total number of dams mated in this experiment was 568, but a high proportion (207, or 36.4%) failed to produce any progeny at all. The mean bodyweight of dams producing progeny (1.5188 mg) was significantly higher than the mean weight for all 568 dams mated (1.4910 mg), suggesting some relationship between female bodyweight and egg production. Positive correlations between adult female bodyweight and fecundity have been reported previously (Martin and Bell, 1960). Unfortunately, no records were kept of total progeny per mating in the present study, so that this possible effect cannot be quantified. James (1966) has shown that in the absence of significant dominance, the strength of natural selection against extremes can be estimated as:

$$\mathrm{COV(HS)} = 1/2 \times (1-S) \times \mathrm{COV(PO)}$$

Since the covariance of parents and offspring in this study was effectively zero, and there was appreciable variation due to dominance (Table 2.7), it is impossible to estimate a coefficient of "homestatic strength" with any confidence. This source of bias may well however have influenced the results obtained.

Table 2.7: Base Population Parameters: Partitioning of Phenotypic Variance

Component	Male Bodyweight	Female Bodyweight
Additive Autosomal	0.499	0.251
Dominance	1.958	1.709
Additive x Additive	0.000	0.000
Sex Linkage i		0.006
ii	0.006	0.006
iii	0.003	0.003
Maternal iv	0.000	0.000
v	0.000	0.000

i V_{AS} = 1/2 [Paternal-1/2 Sister $\hat{h}^2$ - Paternal 1/2 Brother $\hat{h}^2$]

ii V_{AS} = $\hat{h}^2$ Dams/S. MALES - $\hat{h}^2$ DAMS/S. FEMALES

iii V_{AS} = 1/ 2 [$\hat{h}^2$ DAM-SON - $\hat{h}^2$ SIRE-SON] iv $V_M = \hat{h}^2$ DAM-SON $-$ $\hat{h}^2$ SIRE-DAUGHTER

v $V_M = \hat{h}^2$ DAM-DAUGHTER $-$ $\hat{h}^2$ SIRE-DAUGHTER

The discrepancies between the sib analysis and offspring-parent analysis estimates of heritability make the partitioning of phenotypic variance of very limited use. Any estimation involving offspring-parent regressions either becomes zero, or has its value inflated, and the partitioning of the dams' component estimate is made impossible. For these reasons, perhaps the only conclusion that can be drawn from these results is that there was some additive genetic variance for both male and female bodyweight, and that dominance, other non-additive genetic and common environmental effects were present, but were not easily separated or quantified.

2.1.3. Conclusions

Three main conclusions can be drawn from the results of this study. Firstly, there was significant additive genetic variation present in this population for both male and female bodyweight. The heritabilities of 50% and 25% for male and female bodyweight respectively are both sufficient to allow successful selection on the basis of individual phenotype (Falconer, 1981). Secondly, the difference between the heritabilities in the two sexes, together with the observed genetic correlation, suggest that the two sexes should be considered separately when examining responses to selection, prior to general statements on overall response. Thirdly, there appeared to be significant amounts of non-additive, sex-linkage and common environmental variance present for both male and female bodyweight, but the results obtained do not allow accurate estimation of these.

The estimates of heritability obtained are in reasonable agreement with previous reported results. Martin and Bell (1960) and Frahm and Kojima (1966) reported estimates of approximately 20% for heritability of adult bodyweight. Martin and Bell detected very little non-additive genetic variance, using a modified diallel, which would be expected to detect and more reliably estimate non-additive components (Sheridan et al, 1968). In contrast, Sheldon (1962), reported negligible additive genetic variation in an Oregon-RC laboratory stock. Although his diallel-based estimates had large sampling errors, appreciable non-additive genetic variation was detected. Further, in spite of apparent absence of additive variation, responses to selection were obtained over 40 generations, suggesting that the initial estimates of additive variance may not have been very precise. Finally, Katz and Young (1975) reported a base population estimate of 0.58 ± 0.22, which agrees closely with the estimate for male bodyweight obtained here.

For this study to have provided more useful information about the variance/covariance structure of adult bodyweight in this population, certain amendments to the design might have been useful. Some unknown proportion of the dams-within-sires component of variance was due to differences between vials, both for mating and more importantly for egg-lay and development. If each female had been allowed to lay in more than one vial, an estimate of the variation between vials could have been obtained. Secondly, some attempt should have been made to quantify the importance of interactions with fitness. It would have been valuable to either measure total progeny produced in each mating and include this in the model as a covariate, or standardise egg numbers per vial. Either procedure would reduce both the dams' and sires' (if there were differences between sires in number of progeny produced) components of variance, the former to a greater extent. The dams within sires component of variance would also be boosted by the likelihood that full sibs would tend to be closer in age than non-full-sibs. This effect could perhaps have been reduced by reducing the time allowed for mating and egg-lay, so that groups of full sibs would all be emerging over a shorter period of time. Finally, use of a diallel design might have been more useful in determining non-additive components of variance.