Mathematics and biology have not been easy bedfellows and there are many examples of biologists who have made terrible mistakes by ignoring mathematics and also mathematicians who have not fared very well when they have dipped their toes in the biological pool. Russ's work is a great example of the fruitful interaction between the two fields and it gives me enormous pleasure to call on him to deliver his lecture.

Russell Lande

Theoretical Population Biology:
(A) Evolution of correlated characters
(B) Stochastic demography and conservation

(A) Evolution of correlated characters: The fundamental principle of natural selection by which living organisms adapt to their environments was discovered by Darwin (1859), who integrated a wide variety of evidence supporting the theory of evolution. Differences in individual fitness due to variation among individuals in characters influencing survival and reproduction, combined with partial heritability of the variation, causes adaptive evolution. The validity of this theory is strongly confirmed by modern genetic data. Darwin and the early naturalists understood that natural selection acts simultaneously on many characters of an organism, and that hereditary constraints among characters prevent their independent evolution. *On the Origin of Species*, Darwin (1859) wrote that when man or nature selects on a given character, that character as well as other correlated characters evolve, due to 'correlation of growth'. We now know that genetic correlations between characters are caused by pleiotropy (a single gene influencing multiple characters) and linkage disequilibrium (nonrandom association between allelic forms of different genes, especially on the same chromosome).

Meanwhile, at his monastery, Mendel (1865) was hybridising mutant and wild-type plants, and breeding the offspring of hybrids. Having studied with the author of an early text on probability theory, Mendel was equipped to discover statistical laws governing the inheritance of single-gene visible mutations, such as the recessive mutation for wrinkled peas versus the dominant wild-type allele for smooth peas. In the terminology of Johannsen (1911), Mendel distinguished the phenotype of an individual that we perceive and measure, from its genotype that is inherited. Mendel also observed more complex averaging or blending inheritance in hybridising plant

varieties with different flower colours, and suggested this could be caused by the cumulative action of two or more independently inherited genes. Unfortunately, Mendel was diverted by a suggestion to investigate a species now known to be pseudogamous, asexual but requiring pollen to initiate seed. He became discouraged and quit his experiments.

Remarkably, a copy of Mendel's original paper was found in Darwin's library, but the pages remained uncut because Darwin lacked fluency in German. Mendel's work thus sank into obscurity until after his death. Even had he read Mendel's work, Darwin may not have appreciated its significance, because, as he later wrote in his autobiography, he felt that mathematics was like a sixth sense he was completely lacking. With no knowledge of the mechanism of inheritance and little quantitative ability, Darwin was confronted by a mathematical proof by engineer Jenkin that purely blending inheritance rapidly destroys heritable variation. Furthermore, the physicist Lord Kelvin seriously underestimated the age of the earth from radiative cooling, ignoring radioactive heating. Desperate for a mechanism to rapidly generate substantial heritable variation for natural selection, in later editions of *The Origin*, Darwin adopted Lamarck's erroneous theory of inheritance of acquired characters.

The biometrical school of evolution led by Galton and Pearson attempted to understand inheritance by statistical analysis of phenotypic variation and resemblance between relatives in quantitative (continuously varying) characters such as individual size, shape, and weight, and in threshold or meristic (countable) traits such as number of vertebrae, teeth, or flowers. They developed the terminology and mathematical theory of regression and correlation ('regression toward mediocrity' and the Pearson product-moment correlation), summarised in Galton's *Natural Inheritance* (1889). This work culminated in Pearson's (1903) attempt to understand natural selection on correlated characters by inventing the theory of multiple regression. The biometric school of evolution originated much of the foundation of modern statistics, but their work failed and fell into evolutionary obscurity because Pearson never accepted Mendelian genetics as the basis for quantitative inheritance.

Mendel's paper was rediscovered in 1900 by de Vries, Correns and von Tschermak. Bateson led the Mendelian school of evolution opposing the biometricians and blending inheritance. The biologist Castle (1903), mathematician Hardy (1908) and medical doctor Weinberg (1908) independently noticed that in the absence of evolutionary forces such as natural selection, Mendelian inheritance maintains a constant genetic variance in a large randomly mating population, in contrast to its rapid loss under purely blending inheritance. Yule (1906) sketched a theory for reconciling Mendelism with blending inheritance in quantitative characters. This was fully developed by

Fisher (1918) who invented the analysis of variance to statistically partition phenotypic variance among individuals in a population into genetic and environmental components, which he used to explain the observed degree of resemblance between relatives that share different fractions of their genome. Wright (1921) independently developed a similar theory of quantitative inheritance and invented path analysis to investigate networks of causation among observed variables. In this and subsequent work, Fisher, Wright and Haldane founded population genetics, and the modern synthetic theory of evolution, by incorporating Mendelian genetics into Darwin's theory.

After the biometric and Mendelian schools of evolution were reconciled, academic geneticists concentrated increasingly on the genes, a reductionist trend greatly reinforced after 1953 by the discovery of the structure of DNA. Quantitative genetics became specialised for application to economic improvement of crop plants and domesticated animals by artificial selection (Smith 1936, Lush 1940, Falconer 1960). Its utility lies in predicting the evolutionary response of the mean phenotype to a known intensity of artificial selection on a character by experimentally estimating its 'heritability' (the proportion of phenotypic variance due to additive effects of genes) from the phenotypic resemblance between relatives such as siblings or parents and offspring. The theory of artificial selection focuses on truncation selection (breeding only individuals with phenotype above a threshold) on a single character, or linear combination of characters, such as the total economic value of an individual. In contrast, Darwin emphasized that natural selection acts subtly and simultaneously on many characters.

When I began Ph.D. thesis work in 1972, quantitative genetics had been largely ignored by evolutionary biologists for nearly half a century. Students of evolutionary biology routinely learned about Mendelian inheritance and population genetic models with discrete phenotypes or fitnesses determined by one or two genes. Typically only infrequent and brief exposure occurred for quantitative inheritance and artificial selection. Having begun to explore the arcane literature on quantitative genetics, and its history (Provine 1971), my main inspiration came in second year graduate school from reading a classic contribution to the modern evolutionary synthesis, *The Major Features of Evolution* (Simpson 1953), interpreting the fossil record using a vague phenotypic analogy to Wright's adaptive landscape for gene frequencies. The microscopic theory for describing evolution of gene frequencies was well developed, but a macroscopic theory of phenotypic evolution by natural selection was lacking.

I spent the next 12 years – and more – developing this theory. I formulated the basic dynamics of phenotypic evolution by natural selection, by random genetic drift due to finite population size, and by their interaction as in Wright's shifting balance

theory. My thesis developed a theory of the maintenance of genetic variation by mutation in a quantitative polygenic character under stabilising natural selection toward an intermediate optimum phenotype. It also derived the evolutionary dynamics of the mean phenotype of a single character by natural selection and random genetic drift, which as a postdoc I extended to correlated characters (1975, 1976, 1979). I applied the general theory to classical problems in evolution, including threshold and meristic characters (1978), sexual dimorphism and sexual selection (1980, 1981), life history evolution (1982), phenotypic plasticity (1985 with Via, 2009), maternal effects (1989 with Kirkpatrick) and fluctuating environments (2007, 2008).

The theory concerns a set of quantitative characters represented by the column vector, z, a linear array of measurements of an individual's phenotype, and the phenotypic and additive genetic covariance matrices, G and P, symmetric arrays with variances of single characters on the diagonal and covariances of pairs of characters off the diagonal. Both the phenotype and net additive genetic effect of an individual are assumed to have multivariate normal distributions in the population. Normality is theoretically expected from the Central Limit Theorem of statistics for variables resulting from many nearly additive independent factors, and is a good approximation whenever more than a few factors of comparable effect contribute to the variation. Empirically, phenotypic normality is often approximately valid for quantitative characters at least after suitable transformation of scale (e.g. to logarithms), and inheritance of quantitative characters is often multigenic.

In a general model of natural selection the expected fitness of individuals with phenotype z, $W(z)$, may take any functional form. The mean fitness in the population, $\bar{W}$, is a function of the mean phenotype, $\bar{z}$. In a randomly mating population with discrete non-overlapping generations, measured each generation before selection, the evolution of the mean phenotype across a generation is $\Delta\bar{z}=G\nabla\ln\bar{W}$. The selection gradient, $\nabla\ln\bar{W}$, is a vector pointing in the steepest uphill direction from any point on the adaptive landscape $\ln\bar{W}$, perpendicular to contours of constant mean fitness. However, the direction of phenotypic evolution is modified by the shape of the additive genetic covariance matrix, G. In a constant environment with constant G and P, the direction of evolution is always uphill on the phenotypic adaptive landscape, $\Delta\ln\bar{W}\geq 0$, although not in the steepest uphill direction. Evolution by natural selection in a constant environment thus improves the adaptation of the population to its environment (Fig. 1). As in Wright's theory, when phenotypic fitnesses are not constant, due to environmental change or intraspecific frequency-dependence caused by sexual selection or density-dependent resource competition, the mean fitness in the population does not always increase.

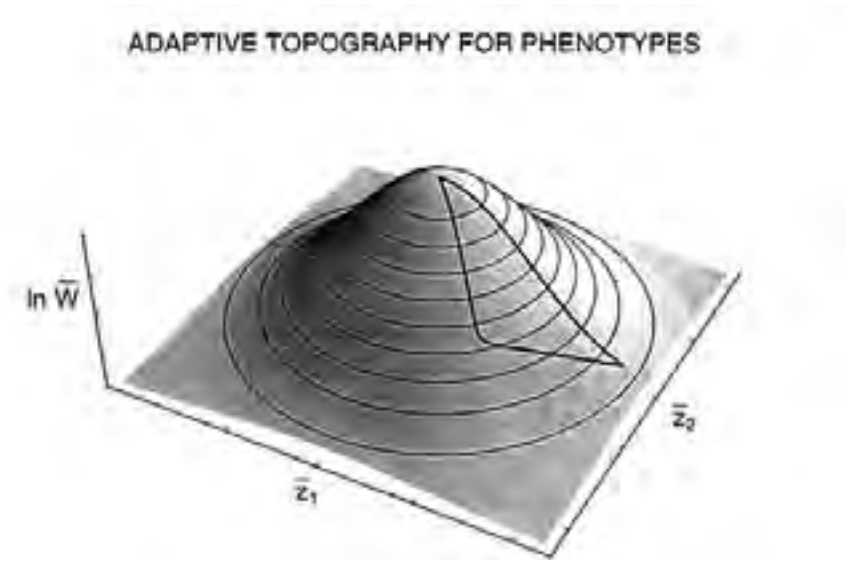

Fig. 1. *Phenotypic adaptive landscape,* $\ln\bar{W}$*, as a function of the mean phenotypes of two correlated quantitative characters,* $\bar{z}_1$ *and* $\bar{z}_2$*. For a population at any point on the adaptive landscape, the rate and direction of phenotypic evolution (long path),* $\Delta\bar{z}=G\nabla\ln\bar{W}$*, is the product of the matrix of heritable covariation of the characters, G, and the selection gradient vector,* $\nabla\ln\bar{W}$*, pointing in the steepest uphill direction (short path). In a constant environment with constant phenotypic and genetic variability the direction of evolution is always uphill.*

Darwin (1872) showed that sexual selection by inter-male conflict for resources or access to mates, and by female choice of mates, may often oppose natural selection. He emphasized that male secondary sexual characters are among the most rapidly evolving traits, often used to distinguish closely related species, with the same characters exaggerated in males typically reduced or rudimentary in females, which he termed the 'transference' of the character between the sexes. Fisher (1930) described how the similarity of pleiotropic effects of genes on male and female characters limits the rate of evolution of sexual dimorphism. He also proposed a mechanism for the origin and evolution of female mating preferences, which had puzzled Darwin. I developed quantitative genetic models showing how genetic correlations govern the evolutionary dynamics in these classical scenarios (1980, 1981), confirming Fisher's descriptions of the dynamics. For characters with small or moderate sexual dimorphism, such as male and female body weight in most animal species, a high genetic correlation between the sexes is usually observed. With

similar genetic and phenotypic variances in each sex, and comparable strengths of stabilising natural selection, sexual selection on males causes the average phenotype of both sexes to evolve rapidly almost in parallel, while sexual dimorphism evolves much more slowly.

Fisher's 'runaway process' concerns two sex-limited characters, a male morphological or behavioural trait, and a female mating preference for it mediated by emotion or sensory bias. Even though these characters are influenced by independent genes, a genetic correlation between them arises from assortative mating due to variation in both traits. This creates a positive feedback loop because natural and/or sexual selection directly for more extreme males also produces not only an increase in the male character but also an indirect, genetically correlated response increasing the female mating preference. This situation produces a potential instability which could cause the rapid origin of new secondary sexual characters in males and female mating preferences for them. Even when it is stable, the model indicates the possibility of rapid non-adaptive diversification in secondary sexual characters.

In a finite population, random genetic drift is caused by random sampling of gametes in Mendelian segregation and random variation in family size. This can make the mean phenotype move temporarily downhill on the adaptive landscape, possibly precipitating a shift to another adaptive peak or ecological niche. Stochastic phenotypic evolution by natural selection and random genetic drift can be approximated as a diffusion process. The (co)variance per generation produced by random genetic drift among replicate populations is the sampling (co)variance of the additive genetic component of the mean phenotype, G/N_e. Wright's effective population size, N_e, is generally less than the actual population size, N, by a quantifiable factor due to age structure, unequal sex ratio, variance in family size exceeding the mean, and/or temporal fluctuations in N. The stationary probability distribution of the mean phenotype, a constant times $\bar{W}^{2N_e}$, is independent of G (1979), resembling a greatly sharpened adaptive landscape. With two adaptive peaks, the expected waiting time until a peak shift by random genetic drift increases exponentially with the effective population size and the depth of the adaptive valley, but depends rather little on phenotypic distance between the adaptive peaks. When N_e and the adaptive valley are appreciable, the duration of the transition between adaptive peaks is much shorter than the expected waiting time until a peak shift, and nearly independent of N_e (1985).

The apotheosis of this work (1983 with Arnold) derived the now most commonly used method for measuring natural selection. In analysing stabilising selection on a single quantitative character, Haldane (1954) noted that natural selection generally

acts on the phenotype but evolutionary response also depends on genetic variation. This basic philosophy of quantitative genetics implies that selection can be measured by changes in the phenotype distribution within a generation due to differential survival and reproduction, regardless of the pattern of inheritance across generations. The selection gradient can be expressed in an alternate form, $\mathbf{V}\ln\bar{W} = P^{-1}\mathrm{Cov}[W/\bar{W}, z]$, which can be identified as the vector of partial regression coefficients in the best linear regression of individual relative fitness, $W/\bar{W}$, on the individual phenotypes, z. This confirms the interpretation that the elements of the selection gradient vector measure directional selection acting to change the mean phenotype of each character, separated from the effects of correlated characters that are included in the analysis. Similarly, stabilising and correlational selection appear as a matrix of curvature coefficients in the best quadratic regression of individual relative fitness on the characters. Invented 80 years earlier by Pearson in his failed approach to the same problem, the theory of multiple regression finally proved to be uniquely relevant for the measurement of natural selection.

(B) Stochastic demography and conservation: My expertise in population genetics garnered invitations to conservation meetings initially focusing on the genetics of small populations in captivity, but later also in wild populations. In the mid 1980s population genetics was being applied simplistically to the conservation of wild populations, to the near exclusion of ecology and demography. I also learned that my thesis work on mutation in quantitative characters was used to justify the rule that N_e above 500 suffices to maintain sufficient heritable variation for adaptive evolution and population persistence in the wild. To correct common misconceptions, I began working on theories of stochastic demography. Witnessing recent and projected anthropogenic destruction of biodiversity in the sixth mass extinction of life on earth, and not wishing to remain a spectator, I found practical applications for the theory in conservation.

I derived an extinction threshold, or minimum amount of suitable habitat for a territorial species in a fragmented environment (1987), and applied it and classical demography to data on the northern spotted owl (1988). This lead to my involvement as the key expert witness in the environmental court battle of the decade in the U.S., eventually resulting in listing the subspecies as threatened under the U.S. Endangered Species Act, preservation of millions of acres of old-growth forest, an ecosystem conservation plan spanning three states in the Pacific Northwest and a reorientation of endangered species management in U.S. government agencies. I also analysed population viability requirements of other threatened and endangered spe-

cies in publications, workshops and panels sometimes lasting for extended periods, including African elephants, Florida snail kite, Key deer, Florida panther and Pacific salmon species. Based on practical experience and theoretical expertise in conservation and extinction risk assessment, Mace and I (1991) suggested the initial version of the IUCN (World Conservation Union) Red List Criteria for classifying endangered species around the world. After numerous international meetings of taxonomic and conservation experts, the criteria were adopted in modified form by IUCN and used as a model for the Convention on International Trade in Endangered Species.

Stochasticity in population growth rate can be partitioned into two components that scale differently with population size. Demographic stochasticity is inversely proportional to population size, whereas environmental stochasticity affects a population independent of its size insofar as all individuals in it experience the same or similar environments. Demographic and environmental stochasticity also differ in spatial and temporal autocorrelation. I analysed how the different scaling laws affect population fluctuations in time and space, especially the dynamics of extinction, and derived statistical methods for estimating basic population parameters (summarized in 2003 with Engen & Sæther). Even the qualitative results of stochasticity are often non-intuitive, as in the following four examples:

(1) The optimal harvesting strategy for a population in a fluctuating environment depends on the goal. Let N signify population size and K its natural equilibrium in the average environment. To maximise the total cumulative harvest before eventual extinction (which is certain), the optimal strategy is immediate harvest when N exceeds K, and no harvest otherwise. Maximising the average annual harvest lowers the optimal harvesting threshold below K, but still involves frequent years of no harvest. From this standpoint, continual harvesting reduces the average harvest.

(2) For a population in a fluctuating environment, let r denote the mean per capita rate of population growth when N is well below K. If both r and K are positive and neither is very small, then for any initial population size near K the population spends a long time fluctuating around K before eventual extinction. The expected duration of the final decline from K to extinction equals the mean time to grow from near extinction to K.

(3) The interaction of demographic and environmental stochasticity creates an Allee effect, resembling an unstable equilibrium at small population size below which populations tend to become rapidly extinct. Allee effects previously were attributed to behavioural or genetic problems in small or sparsely distributed populations, such as inbreeding or the difficulty of finding a mate. Even when r is positive at all population sizes in the average environment, the combination of demographic

and environmental stochasticity creates a critical size, N^*, below which most population trajectories decline quickly to extinction (Fig. 2).

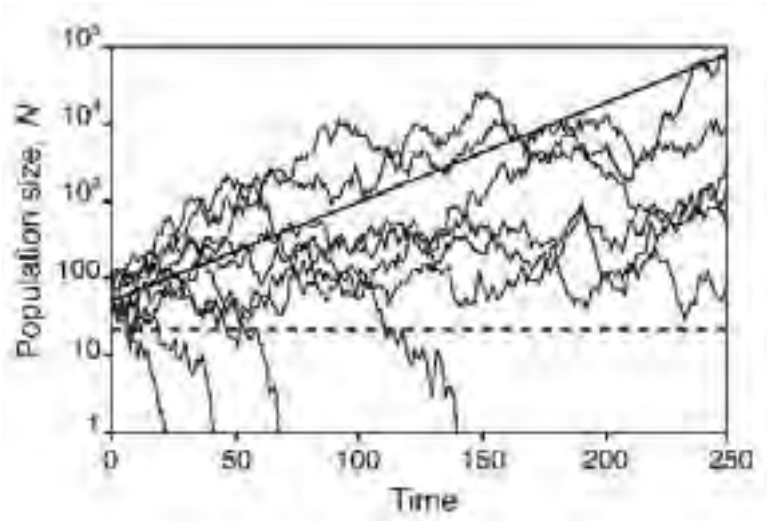

Fig. 2. *Simulated trajectories of stochastic exponential growth of population size on a log scale with demographic and environmental stochasticity in population growth rate. Environmental stochasticity causes all population trajectories eventually to increase more slowly than for deterministic exponential growth in the average environment (solid line). The interaction of both kinds of stochasticity produces a demographic Allee effect, such that populations falling below a critical size, N^* (dashed line), tend to become rapidly extinct.*

(4) In a spatially distributed population occupying a uniform habitat, spatially autocorrelated environmental stochasticity and random dispersal of individuals interact with the strength of density dependence in population growth rate to determine the spatial scale of synchrony in population fluctuations. As the strength of density dependence approaches 0, the amplitude and the temporal and spatial scales of population fluctuations increase toward infinity. In classical population models the strength of density dependence equals or is proportional to *r* (2003). Thus as a species becomes progressively threatened and endangered, and finally incapable of persistence, the population size (or its logarithm) should undergo fluctuations of increasing amplitude and scale in time and space, limited ultimately by habitat fragmentation and local extinction.

Interactions of evolutionary and demographic processes are now of great interest. I modeled evolution of a species' geographic range by adaptation of quantitative characters in a changing environment (1989 with Pease & Bull), and later applied this to coevolution of species competing for space and resources (2006 with Goldberg). Recently, I analysed how the magnitude of environmental stochasticity governs the classic tradeoff between *r*-selection for higher population growth rate and *K*-selection for larger population size (2009 with Engen & Sæther). I also investigated the potential for evolution of phenotypic plasticity to accelerate adaptation and prevent extinction following a rapid extreme change of environment, such as global warming (2009; 2010 with Chevin & Mace).

Much remains to be understood about extinction before ...

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Comments, Questions and Preliminary Discussion

Ulrich W. Suter: Thank you very much Russell Lande for this fascinating talk. We now have Brian Hollis with a short commentary and maybe a few questions. Dr. Hollis is a Post-Doc in the Department of Ecology and Evolution at the University of Lausanne.