OBITUARY: *Motoo Kimura*

Motoo Kimura
1924–1994

Motoo Kimura died on 13 November 1994, his seventieth birthday. He was the leading theoretical population geneticist of the post-Fisherian era, and his work was fundamental in all areas of evolutionary population genetics. This account will focus on his work in the stochastic part of the theory, but it should be noted, for example, that by realizing the importance of using gametic as opposed to the traditional gene frequencies, Kimura was the first to provide the correct framework for the deterministic multi-locus analysis which now forms a significant part of evolutionary population genetics theory. Thus a much more complete account than this would be needed to describe his work in the entire body of the subject, as well as to describe his contributions to plant and animal breeding theory.

Kimura's contributions to stochastic theory can be divided, for convenience, into two parts. The first is his more formal purely mathematical work, which took up much of his time in the period 1954–1968, and which made his reputation, while the second is associated with his advocacy of the neutral, or 'non-Darwinian', theory of genetic evolution, which dominated the later part of his working life.

Kimura's research began with his association (as a graduate student) with James F. Crow, and also Sewall Wright, at the University of Wisconsin, in 1954. His first work took up a problem left unfinished by Fisher and Wright, namely finding the complete time-dependent solution of the forward Kolmogorov equation describing the stochastic changes in gene frequencies in a finite population in the absence of selection and mutation. His facility

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with manipulating the equations of diffusion theory and the various functions associated with them quickly became legendary as he solved increasingly complicated equations, involving many alleles (gene types), selection, and so on. Many years ago I wrote that this work heralded a rebirth in population genetics theory, which had been somewhat stagnant since the great days of Fisher and Wright, and I see no reason to change this opinion.

Three developments arising from this work should be noted. First, Kimura (at the same time as Moran) introduced the Kolmogorov backward equation and thus attacked, in a far more satisfactory manner than Fisher (who manipulated the forward equation for this purpose) problems of fixation probabilities and mean fixation times. Second, Kimura was a clear leader in noting that the theory must mirror the form of data arising from experimental studies, and thus introduced in turn theory relating to the infinitely many alleles model (which recognizes the gene as a segment of DNA with an effectively infinite number of possible base sequences), the infinitely many sites model (again with DNA in mind), and the charge-state model (which recognized the form of data obtained about levels of genetic variation in natural populations through the frequently-used technique of electrophoresis). His development of the properties of these models formed the brilliant centerpiece of his middle years. All the above relates to the prospective theory, in which properties of the future evolution of a population are considered. As a third major contribution, Kimura noted that with the advent of considerable genetic data describing the genetic make-up of contemporary populations, a retrospective theory (asking for properties of processes which would lead to these data) would be necessary, and initiated research into this theory.

The person with whom Kimura should be most closely compared is Fisher. Both had great insights, were dynamic leaders with an abundance of ideas and a marvellous facility in the mathematical analysis necessary to develop these ideas. They both went on from an early focus on more purely mathematical analyses to take up broad issues relating to the foundations, and the dominating questions, of their respective subjects. (Like Fisher, he also made a fair sprinkling of errors, some quite significant, and had these errors perpetuated beyond their normal lifespan because of his forceful and influential advocacy.) It is therefore of considerable interest to note that they came to diametrically opposite opinions on the evolutionary relevance of the stochastic theory which they had each done so much to develop. Fisher came to the view that, apart from special questions such as the survival probability of a new mutant, stochastic changes in gene frequency are of secondary importance, and that the more or less deterministic changes brought about by natural selection are of primary significance. In this he was no doubt influenced by the view that population sizes are usually very large (thus diminishing the importance of stochastic effects) and that mutation is recurrent, as well as by the concept of the gene current during his most active years (essentially as a billiard ball of one or other color, with no significant interior structure). He can thus be seen as perhaps the main upholder of the Darwinian theory when this theory is placed, as it must be, in a genetic hereditary context. To recast the Darwinian theory in Mendelian terms was, indeed, his avowed aim.

Kimura, by contrast, came to the opinion that stochastic factors have been of primary, rather than merely secondary, importance in genetic evolution, possibly because of the view that population sizes are, in effect, usually far smaller than Fisher imagined (the concept of the effective population size is central here), but probably more because of his view of the gene as a segment of DNA, with mutations being often to novel sequences rather than being recurrent. He thus advanced, in 1968, the neutral, or non-Darwinian, theory of evolution, claiming that much of the genetic variation within populations, and thus much of the genetic difference between populations, did not arise from selective processes but rather came about from purely random changes in gene frequencies among selectively equivalent alleles. Strictly, this should be called the extra-Darwinian theory, since Kimura admitted from the first that the gene frequency changes associated with the evolutionary development of all important physiological features of form and function are clearly directed by selective forces. His view thus was that, apart from these gene frequency changes, there has been a much larger number of changes having no selective significance, and occurring purely by chance. Correspondingly, he claimed that much of the genetic variation now known to exist in natural populations is purely random and without selective significance.

The assessment of this theory would take us too far afield, relying as it does on a large number of biological as opposed to purely mathematical factors such as the effective sizes of real populations, the numerical values of mutation rates and selective differences, as well as on a host of not easily quantified ecological considerations. Indeed, unlike a mathematical proposition, it is not even meaningful to ask if the non-Darwinian theory is correct or not. It is sufficient to say here that the theory, insofar as it can be analysed mathematically, relies on the stochastic theory of population genetics which Kimura himself did so much to develop, and in turn gave considerable incentive to develop the theory further. Further, some of the stochastic theory developed initially in connection with the non-Darwinian hypothesis has now found applications in areas of applied probability quite different from population genetics.

Kimura was a phenomenon which one does not expect to see repeated in one's own lifetime. He aspired to greatness and achieved it. His name will be linked with the famous trio of Fisher, Haldane and Wright to form a new quartet, whose lustre will be enhanced by his membership.

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Motoo Kimura was a member of the Applied Probability Editorial Board from its creation in 1964 through to the end of 1969.

For an autobiographical account see 'Diffusion models of population genetics in the age of molecular biology', in *The Craft of Probabilistic Modelling*, ed. J. Gani, pp. 150–165, Springer-Verlag, Heidelberg, 1986.

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