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Motoo Kimura: student, colleague, and friend

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Motoo Kimura's scientific life can be divided into two periods, before and after 1968. Prior to this year, he was mainly concerned with developing the mathematical theory of population genetics. In 1968 he published his neutral theory of molecular evolution. After that, although he continued to produce theoretical work, it was at a reduced rate, and his strongest interest was in finding evidence for his neutral theory. The neutral theory attracted wide attention from evolutionists and molecular biologists. Yet population geneticists are, if anything, more impressed by his earlier work. His creative insights made him the natural successor to the great pioneers Haldane, Fisher and Wright. The field had reached a plateau and Kimura gave it new life. The trio became a quartet.

Kimura came to the University of Wisconsin as my student in 1954. I was then a young faculty member and had the rare privilege of having early in my career two graduate students of the calibre of Motoo Kimura and Newton Morton. Not many teachers are so fortunate. And to add icing to the cake, Sewall Wright joined the Wisconsin Genetics Department at about the same time. Although they saw each other almost every day, Kimura and Morton pursued different problems. And neither of them worked closely with Wright; their methods were quite dissimilar. Yet it was an exciting time and we often discussed research problems.

The three poineers each had a distinctive style. Although Kimura admired both Wright and Haldane, and was led into population genetics theory by reading the works of these two, he is more comparable to Fisher. Fisher had an uncanny ability to solve difficult problems, usually in an original, highly creative way. Kimura was similar in finding ways to solve hard problems. Early in his career Kimura once told me that he could find ways to improve the mathematics of Wright and Haldane, but not that of Fisher. Later he went beyond Fisher in finding the complete solution of random drift from an arbitrary starting point and in using the Kolmogorov backward equation. Like Fisher's, Kimura's work often had elegance. And like Fisher, he was especially adept at finding approximate solutions to analytically intractable problems.

I'll mention one example. Two of our joint papers discussed the mutation load and the number of selectively maintained polymorphisms in a finite population. Kimura found approximate solutions. Although they were good enough for the problem at hand, I did not know how accurate they were. Now that computer routines are available for accurate numerical integration, I was able to check some of his approximations, and they are remarkably good.

Kimura was the first to use the Kolmogorov backward equation to solve important genetic problems. He had the unusual satisfaction of finding that his early theoretical work—solving such problems as the probability of fixation of a mutant gene, the time required for fixation or loss, and the number of individuals carrying the gene during the process—was preadapted for application to the neutral theory. Furthermore, he was

alert to changes in the field brought about by molecular advances. The infinitely-many-alleles model, more familiarly but less grammatically called the 'infinite-allele' model, is an example.

In considering those who might be thought of as successors to the great trio, another name comes forth—Gustave Malécot. Until recently, Malécot has not received proper recognition. There are two reasons. First, he wrote in French and most population geneticists do not read French easily, if at all. Second, he published in obscure journals. The result is that some of his great work remained unknown for many years. It is interesting to contrast Malécot and Kimura. Malécot brought generality and rigour to the field. The problems addressed were largely those already formulated by the pioneers. Kimura addressed new problems and these changed with advances in genetics. Especially in his later work, he always had genetical or evolutionary applications in mind. Malécot was a mathematician's population geneticist; Kimura was a biologist's.

Kimura was born in 1924. His early interest was primarily in botany and cytology, but he showed an early aptitude for mathematics. He finished high school and entered Kyoto University while Japan was at war. He was able to avoid immediate military service by enrolling in botany. He would have preferred to work in cytogenetics with Japan's leading geneticist, Hitoshi Kihara, but Kihara was in the Faculty of Agriculture. Curiously, botany students could defer their military service until after graduation, but agriculture students could not. After the War, Kimura was able to join Kihara's laboratory. Conditions, especially food shortages, were then even worse than during the War and Kimura's life, like that of millions of others in Japan, was one of hardship. Nevertheless, he was able to carry out his programme of self-study in population genetics. In 1949 he rejoined Kihara at the National Institute of Genetics in Mishima. Except for his graduate years in the US and several other short stays there and elsewhere, he remained at Mishima until his death in 1994.

Kimura first studied cytogenetics, as did many Japanese biologists of that period. But while in Kyoto he discovered the work of Haldane and Wright and was immediately fascinated by it. He had always enjoyed mathematics and saw here an opportunity to apply his mathematical skills to biologically interesting problems. He was supported in this endeavour by Professor Taku Komai, who had studied with T.H. Morgan and was an admirer of Wright. Equally important was Kihara. Kihara realized Kimura's ability and assigned him no specific duties, thus freeing him to pursue his studies in population genetics. Kimura's idol was Sewall Wright and his great hope was one day to meet Wright and perhaps study with him.

I have the greatest admiration for Kimura's dogged persistence in these studies. He had little formal training in mathematics; he learned it by himself. None of his colleagues understood what he was doing, and the majority had neither interest nor appreciation. He worked entirely on his own. There were also physical difficulties, for books and journals were scarce in war-torn Japan. While in Mishima he often had to travel to Kyoto or Tokyo to read the important papers. There were no copying facilities, of course, so he copied the papers in longhand. On several of my visits to Mishima, I delighted in reading some of these, written in Kimura's neat, delicate hand. The most impressive was Wright's entire 63-page article 'Evolution in Mendelian populations', published in 1931. It was copied in full. I suppose this was done during Kimura's Kyoto days. Clearly he understood what he was doing, as his interspersed comments reveal.

Kimura's work in population genetics was recognized by Newton Morton and Duncan McDonald, who were with the Atomic Bomb Casualty Commission in Hiroshima. Morton called Kimura to my attention while McDonald arranged for him to have a fellowship in the US. Kimura wanted to study with Wright, but Wright was near retirement and was taking no more students. He recommended studying at Iowa State College with J. L. Lush. Kimura went there, but was dissatisfied with the direction of the work and, after a year, joined me at the University of Wisconsin. Soon after, Kimura's dream came true, for Wright moved from Chicago to Wisconsin. The Cold Spring Harbor Symposium of 1955 gave Kimura a chance to get acquainted with the leading population geneticists of the world, and his reputation increased rapidly.

Although Kimura had at last met Wright and had the opportunity to see him regularly, they never worked together. Kimura attended Wright's lectures, as did I. I remember them well. Despite his great abilities, Wright was prone to making algebraic errors at the blackboard. Those of us in the class, often Kimura, noticed these and called them to Wright's attention; but he preferred to correct them himself, often at the cost of considerable time.

Kimura's first accomplishment after coming to Wisconsin was to work out the complete process of random drift from an arbitrary starting point. Wright realized the importance of this, although his own interest was in populations near an equilibrium. When Kimura presented his work at the Cold Spring Harbor Symposium, very few of the audience understood it, both because of the mathematical complexity and because Kimura's English at that time was difficult to understand. Wright showed his great respect by taking the floor after Kimura's talk and telling the audience that only those who had tried to solve these difficult problems could fully appreciate the enormity of Kimura's accomplishments. Some of Kimura's most important research was done while he was still a graduate student.

I shall not describe Kimura's work. It is well documented and other authors in this collection discuss various aspects of it. A reprint edition of his most important papers has been published, with very helpful introductions and comments by Naoyuki Takahata (*Population Genetics, Molecular Evolution, and the Neutral Theory*, University of Chicago Press, 1994). Fortunately Kimura was able to see the book a few days before his death, which occurred on his 70th birthday in 1994.

Kimura and I met in 1953, the year before he came to Wisconsin as a student. It was the beginning of a close affiliation that continued through the rest of his life. Despite the width of the Pacific Ocean we remained in close contact. He made numerous trips to my institution and I made even more to his; and between these visits we had an extensive correspondence. We enjoyed collaboration, for what skills I possessed were complementary to his. The continuing association with him has been one of the enduring satisfactions of my life.

I should like to dedicate this article to Dr Hitoshi Kihara, for his pioneering work in the cytogenetics of wheat and also for his early support of Kimura. By freeing Kimura of other responsibilities and thereby encouraging his study of population genetics, Kihara played an indirect, but significant role in the history of population genetics and molecular evolution.