

June 8, 1970

Professor Jack L. King
Department of Biological Sciences
University of California
Santa Barbara, California 93106

Dear Dr. King:

First of all, let me thank you for the courtesy of sending us your most interesting letter and several enclosures. They have been read and discussed by almost everyone in our group.

Now, let me start with a personal matter. I hope that you took my comment at the Boston meeting as a friendly one, as it was certainly intended to be. What I wanted to say was that you are not constrained to be a non-Darwinian, as others are by their past "sins." It is plain to me that Kimura, Crow, et al., have embraced the notion of prevalence of neutral mutations since they have given "proof" that polymorphisms cannot be as numerous as they are, and evolution cannot be as fast as it is. You are surely not in this predicament, since you, as well as Sved et al. have shown that the predicament does not exist. Reading the King-Jukes paper in "Science" one gets the impression that you are more "non-Darwinian" at the beginning and less so at the end, as though you wanted to throw a bombshell to stimulate discussion! And at the Boston meeting you were supposed to be the non-Darwinian, Mayr the Darwinian, and Fitch in the middle. So it looked to me as if you were to some extent playing the role of devil's advocate.

Let me say that I have not been and am not a hyperselectionist, like some of our, particularly British friends, who have a dogma that any and all genetic changes must be either adaptive or unadaptive. The problem has, of course, a fairly long history, which your label "non-Darwinian evolution" brushes aside. There were several non-Darwinian, i.e., non-selectionist, evolution theories before yours. Your theory, as you recognize, is a glorification of Sewall Wright's "random genetic drift" or "random walk". Random genetic drift was popular in the thirties and forties, very unpopular in the fifties and early sixties, and back in glory thanks to you, Jukes, and Kimura, for different reasons. I collaborated with Wright on several (4 if I am not mistaken) studies of random drift, while it was anathema to my friends Ford and Mayr. In two papers with O. Pavlovsky we have given, I believe, the only experimental verification of the variety of random drift called "founder principle." So, I am as convinced as you that some genetic variants (and, hence, mutational changes) are neutral, at least for a time and on the average.

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It is another matter to say that most genetic changes in evolution are "non-Darwinian." In talking about the evidence on which you and Jukes base your arguments I must, of course, freely admit the inadequacy of my knowledge of molecular genetics. God and the Columbia University Press willing, there will be in the Fall an opus called "Genetics of the Evolutionary Process," which started as an attempt to prepare a fourth edition of "Genetics and the Origin of Species" and evolved into a new book. For two years I was working hard, trying to learn a minimum necessary information to write the new book, and the King-Jukes article was an excellent goad. So, admitting the inadequacy of my knowledge, I still venture to say that the four "legs" on which in your words the non-Darwinian theory rests seem to me very shaky. Let me try to give you some arguments, none of which will be new to you.

The alleged uniformity of change in homologous proteins over time is not convincingly demonstrated, and need not be "non-Darwinian." Everybody (except possibly Kimura) knows that the dates of divergence of groups supplied by paleontologists are imprecise at best. To divide the number of substitutions by the number of years, gives you the average rate, and does not tell you whether one half of the substitutions happened in one-tenth of the time, or one-tenth of the substitutions in half of the time. Different proteins evolve admittedly at different rates. Why, then, should the same protein be assumed to evolve at a steady rate? Some works in this field (not yours!) seem to me classical examples of circular arguments.

The Poisson fit seemed to me the most solid of the four "legs" when I first read about it. It does not seem to any more. Anything can be fitted to anything by a process of elimination of what does not fit. You and Jukes were (to my knowledge) the first to recognize that this elimination process is evidence that some of the parts are protected by natural selection, and that the Poisson is applied to the remainder only. But how about their remainder - is it not possible that positions of different degree of stability and changeability are those in which changes are selectively less or more desirable? Let me say again, this does not deny that some changes may be truly neutral. But may they not be a minority only?

You so rightly mention the Ayala findings in connection with the T-mutator "leg". I appreciate that here one does no longer have random mutation, but biased towards GC increase. However this unusual mutational spectrum is submitted to rigorous selection. How many unfavorable mutations have been eliminated? Is there not an ample opportunity to select among the many mutations not merely a vigorous but even superior line?

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Dr. Jack King

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I have read with interest and profit for my education your paper on "Influence of the genetic code on protein evolution." This seems the strongest of the four "legs," but I must get a better education before being willing to stand on just one "leg." And on page 9 on that paper I find the sentence "Natural selection is very much involved in the patterns of non-Darwinian evolution, inasmuch as most mutations resulting in amino acid substitution appear to be deleterious and are eliminated by natural selection." Elimination, normalizing or stabilizing selection, is surely "Darwinian," and would it not be odd to have a dichotomy of selected vs. unselected, rather than a spectrum? So, we are back again to the question whether the truly neutral part of that spectrum is large or small. Personally, I vote for "small," without doubting that however small, it exists. In other words, there is your non-Darwinian evolution, or as I prefer to call evolution by random walk. You have done a most useful service to evolutionary biology, even if, as I hope, the phenomenon you have stressed will be a minor rather than a major one.

And finally, I beg you not to accuse Rollin Richmond of wishing to prohibit new ideas. He is a highly intelligent young scientist, and you will not want to hurt him, even if a part of his arguments are invalid. You will certainly not deny that molecular data should be considered in the light of what is already understood of the nature of evolution. In fact you do so consider them! But as you well know, there exist not a few molecular biologists who do not so consider them, for the good reason that they do not know, and even do not wish to know, what is already understood of the nature of evolution. Richmond's sentence you cite out of context, and most surely this gives a most unfair idea about what he means to say.

Let me conclude by saying again that your letter is deeply appreciated, and that I would like to hope that the opportunity may arise for us to meet and discuss things sitting around a table rather than by long letters.

With best wishes.

Sincerely,

Theodosius Dobzhansky

TD:gbz

Cc: Professor Jukes