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This Week's Citation Classic®

Hubby J L & Lewontin R C. A molecular approach to the study of genic heterozygosity in natural populations. I. The number of alleles at different loci in *Drosophila pseudoobscura*. *Genetics* 54:577-94, 1966. **Lewontin R C & Hubby J L.** A molecular approach to the study of genic heterozygosity in natural populations. II. Amount of variation and degree of heterozygosity in natural populations of *Drosophila pseudoobscura*. *Genetics* 54:595-609, 1966.
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The separation of enzymes and other proteins by acrylamide gel electrophoresis was outlined as a method for determining the amount of genetic variation in any species. When applied to natural populations of *Drosophila pseudoobscura*, it was shown that very large amounts of genetic variation are present in the genome. [The *SCI*® indicates that these papers have been cited over 310 and 525 times, respectively, in 715 publications since 1966.]

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The leading experimental problem of evolutionary genetics for many years had been the assessment of genetic variation in natural populations. All of the theoretical structures of evolutionary genetics depended upon a knowledge of the numbers and frequencies of alleles segregating in populations, yet no method had been developed to determine these frequencies with the exception of special cases, such as lethal genes, which clearly did not represent "typical" genetic variation. The difficulty was that a simple gene substitution did not have a clear-cut phenotypic effect and that loci with no genetic variation could not be detected at all. One of us (R.C.L.), a population geneticist, had formulated the abstract requirement of the method for the solution of this problem. The other (J.L.H.), a biochemical geneticist, had developed the technique of acrylamide gel electrophoresis for the comparison of a large number of proteins and had applied the method previously to species comparisons. When we began to work together in Chicago, it became immediately apparent to us that we had a problem and a method that perfectly complemented each other.

Within a year the method had been adapted to the detection and separation of enzymes and proteins from single flies so that the genotype of an individual at a structural gene locus specifying the amino acid sequence of a given protein could be read directly on a slab gel. We then surveyed a large number of lines of *Drosophila pseudoobscura* from different natural populations and found an extraordinary amount of variation among the lines in the electrophoretic mobility of various protein molecules. Genetic tests showed the electrophoretic differences to be indeed the result of single allelic substitution. By equating nonvarying proteins in the gels with monomorphic genes, we were able to estimate both the average heterozygosity of the genome and the average proportion of polymorphic loci. We could determine the actual frequency distribution of various alleles at polymorphic loci. We found between one and eight alleles at various loci with an average heterozygosity per individual of 12 percent and with about one-third of loci polymorphic.

The large number of citations to these papers is the result of the application of the method over the last 12 years to literally hundreds of species of plants and animals in an attempt to get a general picture of genetic variation in living organisms, to look for evidence of natural selection, and to examine differences between populations and between species. Gel electrophoresis has been the chief method used by population geneticists since 1966.

The pattern of citation is very revealing for the sociology of science. The first of the two papers outlines the general problem, gives the general characteristics that a method would demand, and describes the actual method and the kinds of protein variations found. The second paper gave the detailed result of the application of the method to natural populations. The two papers were a genuinely collaborative effort in conception, execution, and writing and clearly form an indivisible pair, split into two papers for convenience, but published back-to-back in the same issue of the journal. The order of authors was alternated, with the biochemist, Hubby, being the senior author in the method paper and the population geneticist, Lewontin, as senior author in the application paper. Yet paper II has been cited over 50 percent more frequently than paper I. Moreover, many of the citations to paper II, in fact, refer to material given only in paper I. Citations to paper I virtually never stand alone but are nearly always paired with a citation to II, but the reverse is not true. Why? We seem to have a clear-cut case of Merton's "Matthew Effect"[1]—that the already better known investigator in a field gets the credit for joint work, irrespective of the order of authors on the paper, and so gets even better known by an autocatalytic process. In 1966 Lewontin had been a professional for a dozen years and was well known among population geneticists, to whom the paper was addressed, while Hubby's career had been much shorter and was known chiefly to biochemical geneticists. As a result, population geneticists have consistently regarded Lewontin as the senior member of the team and given him undue credit for what was a completely collaborative work that would have been impossible for either one of us alone.

1. **Merton R K.** The Matthew effect in science. *Science* 159:56-63, 1968. (Cited 170 times.)

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