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Three Sexes

Essays in Theoretical Genetics

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Comments and suggestions are welcome. Please write to hubertk@pacbell.net.

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Introduction

In 1961 I received a PhD in mathematics from Saint Louis University (Missouri) and took my first (and only) permanent teaching position at Providence College (Rhode Island). I was hired to be the mathematics teacher in an experimental program for gifted science students, sponsored, as I recall, by the United States Department of Health. I taught only those students and was their only mathematics teacher for my first nine years at Providence College. (The program was then declared "successful"—and terminated.) In an attempt to find an area of science in which to apply myself, I began a study of genetics while attending a Summer Institute in Statistics in the Health Sciences in 1962 at Stanford University (California). My study resulted in three publications.

The first—very minor—result of my study was a bit of science-fiction whimsy in the campus newspaper. The student editor had been urging professors to contribute to the paper, known as *The Cowl*.[1] My article was designed to attract by its "science fiction" aspect, but also present some information in a way accessible to the students. It shows that I did not yet see the need for a simpler model. But this was still in the realm of science fiction. I don't recall if any students were interested by it. At any rate, no other professors followed my example.

The Hardy-Weinberg law describes the genetic equilibrium in a population by means of an algebraic equation. It states that genotypes (the genetic constitution of individual organisms) exist in certain frequencies that are a simple function of the allelic frequencies; namely, the square expansion of the sum of the allelic frequencies. It is so called because it was independently discovered in 1908 by the English mathematician G. H. Hardy and the German physician Wilhelm Weinberg. It established the mathematical basis for studying heredity in populations—naturally occurring populations, of course. One of my first efforts was to try to extend this law to the hypothetical three-sex situation I had described in the *Cowl* note earlier. After I had done this, I immediately asked, in the way typical of mathematicians, if my proof could be generalized to apply to any number of sexes. The answer was "yes" and the proof needed nothing deeper than elementary

1. The college was run by priests of the Dominican order whose habit included a cowl.

probability theory—though the manipulation of the required equations was a bit cumbersome.

After I had polished my proof to the degree of “elegance” expected in mathematics, I wrote the article for publication, leaving out any “science fiction” aspect by ascribing it to an interest in exobiology. At any rate, the role of mathematics was highly prized then in the study of genetics, especially human genetics, which is not an experimental science. It should be remembered that this was before the great surge in DNA studies, which are more strictly biological. The article duly appeared in *BioScience*.

Still, despite the success of my project, the question remained: Would it have any application? After all, if three sexes are possible, why haven’t any been found? In fact, organisms had been found in which three “sexes” occurred, but matings were always between two individuals. By then I had discovered examples of three-sex mating in science fiction, but the genetic/mathematical basis there was always vague. The basic problem with the model in my first article in the *Cowl* was that it required what I vaguely referred to as “certain inhibitory functions in the gametes.” My first discovery was that, without such “inhibitory functions,” there was essentially only one possible mathematical model for the three-sex situation. I was then able to show that, for this model, the three sexes would not reproduce in equal numbers.

The next step, of course, was to generalize this work from three to any number of sexes. I was soon convinced that all the results would hold, but finding the proof was harder than I expected. After much work, I had the beginning and ending of the proof, yet I lacked one crucial step in the middle. I spent many hours trying to bridge the gap. Finally I called for help from my best mathematics student, Paul Cull, who was then in graduate studies at the University of Chicago. He wrote back immediately with just the information I needed. So, after a bit more polishing to make the proof mathematically elegant, I added Cull’s name as co-author and submitted it for publication, this time to *Science*, which had a wider readership than *BioScience*.

This time the article was not immediately accepted. The editor returned it with the anonymous referee’s report that there was a mistake in the mathematical proof. I do not know why he thought the proof faulty. I made no changes in it, but sent my manuscript back to the editor with an explanation of the point I thought the referee has missed. The manuscript was again rejected. It had been sent back to the same referee, who now found the work “not sufficiently relevant.”

I immediately sent the article to *BioScience*, which was more receptive. It accepted the article in September 1969 and published it the following February. Alas, I was not given a chance to proofread the article and there was a misprint in it so that, as stated, the proof was invalid. No one ever mentioned this to me—in fact, I don’t recall anyone mentioning the article at all. Probably few people tried to follow the mathematical proof, and those few most likely realized that there was a misprint.[2] But Cull and I were both pleased with the publication.[3]

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2. The misprint was in the sentence: “The letter X will occur in exactly k sets, where $1 < k < n$.” The expression “$1 < k < n$” should be “$1 \leq k \leq n$.” I have corrected this in the article below.

3. Paul Cull received a PhD from the University of Chicago in 1970, the year the article was finally published. When he applied for a teaching position at Oregon State University he naturally listed this publication in his application. This had the odd effect that the letter I wrote in support of his application was rejected from consideration since I was a co-author of that publication. Happily he received the position without my support—and has gone on to have a successful career there.

Sex Life on Mars

By Hubert Kennedy

(A Study in Theoretical Genetics)

"Breathes there a man with soul so tough,
Who says two sexes aren't enough?"

When scientists succeeded, in 1970, in establishing contact with intelligent life on Mars, many interesting differences were discovered between the beings there and rational life on Earth. None, however, caused quite the stir as did the discovery of the existence of three sexes. Many people were skeptical. Many were openly enthusiastic. Clergymen warned from the pulpit of an increase in sex crimes, while college newspapers across the country called life on Mars a "picnic."

Philosophers quickly honed Ockham's Razor and joined the attack. "The purpose of having more than one sex," their leading spokesman said, "is to bring about the beautiful variety we see around us, and to further the possibilities for evolution. Now this is accomplished perfectly well with only two sexes, and since, as everyone knows, *entia non sunt multiplicanda praeter necessitatem*, the existence of three sexes is obviously impossible."

Finally, a newspaper feature story writer recalled that his mathematics professor at the small New England college he attended had mentioned that R. A. Fisher, as early as 1929 had suggested studying "the consequences experienced by organisms having three or more sexes." The reporter telephoned the professor and arranged to meet him in his office the next day. The following is a report of that interview.

Q. "Professor, were you surprised by the discovery of three sexes on Mars?"

A. “Well, no. Nothing surprises me very much anymore. Actually, some time ago I worked on a model for a population with three sexes, and the facts reported from Mars so far conform very closely to that model.”

Q. “Would you describe your model for our readers?”

A. “I’d be glad to.”

Q. “First of all, just what is a ‘model’?”

A. “In the sense in which I am using the word, a model is a hypothetical description of a situation, from which consequences may be deduced. These would then be looked for in the original and, if not found, the model might be modified. Until now, of course, no example of a population with three sexes had been found against which my model might be checked.”

Q. “Would you describe the parts of your model which agree with the Martian situation?”

A. “So far, everything agrees with my model; but all the facts aren’t in, of course. The family reproduction unit begins with the union of the three sexes. Of these, only one conceives and bears the children. This one we may call the female. The other two are essential to the production of the child, are, in a sense, “fathers” of the child. Their roles are quite similar and, hence, they may both be called “males.” To distinguish them, I have called one the delta-male and the other the epsilon-male.”

Q. “Doesn’t the existence of two ‘husbands’ in a family cause problems?”

A. “Yes and no. There are marital problems on Mars, often similar to those encountered here. But on the whole, this ménage a trois seems to work very well. Divorce rates, for example, are quite low.”

Q. “I mean, isn’t there a question of who’s boss?”

A. “Oh no. Naturally, the woman is. Their society is matriarchal in many respects—husbands take the wife’s name, and so on.”

Q. “You mean that when Miss Brown marries, there become two Mr. Browns?”

A. “Something like that. But they are always distinguished as, say, Delta Brown and Epsilon Brown.”

Q. “Are there equal numbers of deltas, epsilons, and females?”

A. “Not exactly, just as there are not equal numbers of males and females on Earth, but the proportion of each on Mars is very nearly one third.”

Q. “Would you explain the mechanism which insures this?”

A. “The sex-determining mechanism is very similar to that of human beings. As you know, in man one pair of chromosomes differentiates the sexes. In the females the two are alike, usually designated XX, but unlike in the males, usually designated XY. As a result of meiosis, the mature egg contains only one X chromosome, but there are two kinds of sperm produced by a male—those with an X chromosome and those with a Y chromosome. Fertilization with an ‘Y sperm’ leads to an XY zygote destined to become a male.

“The situation on Mars is only slightly more complicated. There are three types of sex chromosomes, X, Y, and Z. There, chromosomes occur in trios, not pairs, and each sex has a distinct combination of these three chromosomes. Due to certain inhibitory functions in the gametes, these can occur only in the combinations XYZ, XXY, and XXZ. The first of these is a female, the second, a delta-male, and the third, an epsilon-male. As a result of meiosis, each gamete contains only one sex chromosome. Thus the female produces three types of eggs. Fertilization requires the union of an egg with both a ‘delta sperm’ and an ‘epsilon sperm,’ but the sex into which the zygote will develop is determined by which type of egg is fertilized.”

Q. “You mentioned that certain inhibitory functions in the gametes allow only these three types of zygotes to be produced.”

A. “This mechanism is not perfect, and occasionally other combinations do result. These produce some rather interesting syndromes, by the way. Ordinarily, however, an X egg can fertilized only by a Y delta sperm and a Z epsilon sperm, while a Y or Z egg can be fertilized only by an X delta sperm and an X epsilon sperm. Similar inhibitory mechanisms are not unknown on Earth—I am thinking, for example, of self-sterility in the plant Nicotiana.”

Q. “Are there other chromosomes besides the sex-chromosomes?”

A. “Yes, but we are not sure at present how many.”

Q. “And these also occur in trios?”

A. “Oh yes. As expected, a gamete contains one from each trio.”

Q. “This allows for Mendelian inheritance, does it not?”

A. “Exactly. It was, in fact the observation of the predicted Mendelian ratios which most confirmed my model.”

Q. “Assuming the correctness of your model, what other observations might be expected?”

A. “Some quite important ones. Many of the basic results in human genetics would apply—the Hardy-Weinberg Law, for instance, which says that genotypic proportions of a large random mating population are established in one generation. Our methods for calculating gene frequencies could be used, with the necessary modifications. Of course, all of these techniques are more complicated in the case of three sexes, but the basic methods do apply.”

Q. “One last question, Professor. Do you think a knowledge of Martian heredity will increase our knowledge of human heredity?”

A. “Indeed I do. Take the case of twin studies, for example. You know how important these have been. Results have been slower than we would like, however, and this is due in part to the relatively small numbers of twins. Among Martians, twins are much more common, accounting for something like five percent of all births. Twin studies on Mars should produce results much more quickly—results which could well guide human geneticists in their research.”

Q. “Thank you very much, Professor, for your discussion. I expect publication in about two weeks and would like to send you a copy. Should I send it to the college or to your home address?”

A. “Please sent it to the college; they will forward it to me. You see, I’m leaving next week. I’ve just accepted a position as visiting lecturer at the Martian State University.”

A generalized Hardy-Weinberg law

In 1908, independently of one another, the British mathematician G. H. Hardy and the German physician Wilhelm Weinberg enunciated a basic population law of Mendelian genetics which has since become known as the Hardy-Weinberg Law (Stern, 1943). Consider a large, freely interbreeding diploid population for which there are two alleles (A,a) at a particular locus and suppose there are p of A and q of a, where $p + q = 1$. The original formulations of the law state that if the three genotypes (AA,Aa,aa) are in the proportions p^2 of AA, $2pq$ of Aa, and q^2 of aa, then the genotypic proportions in the next generation will be the same as those in the preceding generation. This is so since, on the assumption that random mating is equivalent to random union of gametes, if the proportions of A and a genes in the population are p and q, then the proportions of the genotypes of the next generation will be given by the terms of the expansion of $(p + q)^2$, i.e., $(p + q)^2 = p^2 + 2pq + q^2$. That the proportion of A genes in this generation is again p is seen from the following. Since all genes of AA individuals are A and half of the genes of Aa individuals are A, the total proportion of A genes among the three genotypes is given by $p^2 + pq = p(p + q) = p$.

In 1909, Weinberg reformulated the law so as to apply to multiple alleles (although he was unaware of the existence of an instance of multiple alleles). The recent increased interest in exobiology (Levin, 1965) suggests that it may be worthwhile to state a generalization of the Hardy-Weinberg law which covers the case of multiple sexes. Consider a large, freely interbreeding population with s sexes for which the Mendelian model is valid, i.e., the production of a new individual requires the union of s gametes, one from each of the s sexes, such that each gamete carries a single gene for a particular locus. Suppose that there are n alleles, $A_1, A_2, \ldots, A_n$, and that the frequencies of these genes in the population are $p_1, p_2, \ldots, p_n$, respectively, where $p_1 + p_2 + \ldots + p_n = 1$. On the assumption, again, that random mating is the equivalent of random union of gametes, the frequencies of the various genotypes in the next generation will be given by the terms of the expansion of $(p_1 + p_2 + \ldots + p_n)^s$. The number of terms in this expansion is given by the formula

$$G = \frac{n(n+1)\ldots(n+s-1)}{1\cdot 2\ldots s},$$

that is, G is the number of distinct genotypes. For example, for seven alleles and seven sexes, there are 1716 different genotypes. We have just seen that the frequencies of the genotypes in the next generation depend only on the frequencies of the various genes in the preceding generation. We may show, then, that equilibrium has been reached in one generation by proving that the frequencies of the various genes are constant. As the same argument may be applied to each allele, we may without loss of generality show this only for A_1, which has frequency p_1. To this end, consider the expression for the frequencies of the various genotypes:

$$1 = [p_1 + (p_2 + \ldots + p_n)]^s$$

$$= \sum_{i=0}^{s} \frac{s!}{i!(s-i)!} p_1^i (p_2 + \ldots + p_n)^{s-i}.$$

The fraction of A_1 genes in genotypes whose frequencies are given by the expansion of

$$\frac{s!}{i!(s-i)!} p_1^i (p_2 + \ldots + p_n)^{s-i} \text{ is } \frac{i}{s}.$$

Thus the total proportion of A_1 genes among all genotypes is given by the sum:

$$\sum_{i=0}^{s} \frac{i}{s} \frac{s!}{i!(s-i)!} p_1^i (p_2 + \ldots + p_n)^{s-i}$$

$$= p_1 \sum_{i=1}^{s} \frac{(s-1)!}{(i-1)!(s-i)!} p_1^{i-1} (p_2 + \ldots + p_n)^{s-i}$$

$= p_1[p_1 + (p_2 + . . . + p_n)]^{s-i}$

$= p_1.$

That is, the frequency of the A_1 gene in the population is constant. Since a similar proof applies to each of the other alleles, we have proved a generalization of the Hardy-Weinberg Law for the cases of multiple alleles and multiple sexes.

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The Mendelian Model for Polysexual Populations

It has been shown (Kennedy, 1965), on the assumption that the sexes are reproduced in equal numbers, that a generalization of the Hardy-Weinberg law is valid for a population with n sexes for which the Mendelian model is valid, i.e., for which the production of a new individual requires the union of n gametes, one from each of the n sexes. The question remains, whether a population having more than two sexes is possible with a Mendelian model sex determination mechanism, and if so, whether the sexes would be reproduced in equal numbers. By "Mendelian model sex determination mechanism" we mean that: (a) each of the n gametes required for the production of a new individual contains one sex-determining chromosome: (b) distinct combinations of sex-determining chromosomes determine distinct sexes (i.e., no two combinations determine the same sex): and (c) all original combinations are possible and no new combinations are possible. We shall show that there is essentially one and only one model for a population with n sexes and that for $n > 1$ each such model has exactly two distinct kinds of sex-determining chromosomes. We shall further show that if $n > 2$, a population which followed this model would not reproduce the sexes in equal numbers.

To see that there is a model for a population with n sexes, consider the n sets of combinations of the two letters X and Y (which may represent distinct sex-determining chromosomes): $\{X^k, Y^{n-k}\}$, for $k = 1, 2, \ldots, n$, where the symbol X^k indicates that the set contains k X's. Clearly, each set is distinct from every other, and if one letter is selected from each set, then the set so constructed is the same as one of the original sets. Further, each of the original sets can be constructed by a proper choice of one letter from each set. Hence these sets satisfy the required conditions and so form a Mendelian model for n sexes.

Now, suppose there is a model satisfying the required conditions which contains more than two letters, say X, Y, Z, and possibly others. The letter X will occur in exactly k sets, where $1 \leq k \leq n$. By a proper choice of one letter from each set, we can construct k sets containing from 1 to k X's, and we can construct a set containing both Y and Z, which may or may not contain an X. If the set containing Y and Z has no X, we can now construct distinct sets $\{X^k, Y \ldots\}$ and $\{X^k, Z, \ldots\}$, where the three dots represent the same combination of letters in both sets. If the set containing Y and Z contains an X, we can construct distinct sets $\{X^{k-1}, Y, \ldots\}$ and $\{X^{k-1}, Z, \ldots\}$. In either case, we have constructed $k + 1$ distinct sets containing X's, contrary to the hypothesis that X occurs in exactly k sets. Hence, it is impossible to have a model containing more than two letters.

Thus, there is essentially only one model which satisfies the required conditions, so that we may speak of *the* Mendelian model for polysexual populations. If we add the further condition that: (d) the n sexes are reproduced in equal numbers, then the only possible populations are those with one or two sexes. To see this, note that for our Mendelian model the probability that a random choice of one letter from each set will produce the set $\{X, Y^{n-1}\}$ is $P(n) = n!/n^n$. In order to satisfy condition (d) we must also have $P(n) = 1/n$, but the only solutions of the equation $1/n = n!/n^n$ are $n = 1$ and $n = 2$.

In summary, for each number n there is one and only one Mendelian model for a population with n sexes; of these there are only two which further satisfy condition (d) above, namely that with one sex and that with two sexes. This may help to explain why no polysexual population has been discovered.

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