SOME APPLICATIONS OF MATHEMATICS TO BREEDING PROBLEMS III

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INTRODUCTION

Professor H. S. JENNINGS (1916, 1917) has published two papers in GENETICS, giving numerical results for different systems of breeding in which the inheritance of Mendelian factors is in question. The first paper deals with one-factor problems, the second with two-factor problems. The present author has dealt with more general one-factor problems (ROBBINS 1917, 1918) suggested by JENNINGS's work. Similarly the present paper follows JENNINGS's lead in two-factor problems.

Part I gives the results for random mating for the most general problem of two linked factors. Part II is a less satisfactory solution of the problem of selection with regard to one of two linked factors. Part III gives the results for the general problem of self-fertilization.

The work of JENNINGS on random mating shows how useful it is to deal with the four kinds of gametes involved instead of the ten kinds of individuals. Of course, at any stage of the game we can find the proportions of the different types of individuals from our knowledge of the gametes of the parents.

I. RANDOM MATING

a. Linkage r in each set of gametes

Let A, a represent respectively the dominant and recessive factors of a simple Mendelian pair; similarly let B, b represent respectively the dominant and recessive factors of a second simple Mendelian pair. With respect to these two sets of factors we will have four types of gametes. Let p_n, q_n, s_n, t_n be respectively proportional to the number of AB, Ab, aB, ab gametes that will combine to produce the $(n+1)$th generation. A zygote will be represented by the juxtaposition of the letters representing the gametes which unite to produce the zygote. If a zygote produces r gametes of each of the types which united to produce it, for each gamete of the type obtained by interchanging a pair of the factors in the original gametes, there is said to be a linkage r between the factors. For instance, if a zygote $ABab$ produces gametes in the proportion $rAB + Ab + aB + rab$, the factors have a linkage r. Using this notation, JENNINGS has expressed the proportions of gametes in the $(n+1)$th generation in terms of those in the nth generation in his table 9 (JENNINGS 1917, p. 144):

$$1)\quad \begin{cases} p_{n+1} = (r+1)\, p_n\, (p_n + q_n + s_n) + r\, p_n\, t_n + q_n\, s_n, \\ q_{n+1} = (r+1)\, q_n\, (p_n + q_n + t_n) + r\, q_n\, s_n + p_n\, t_n, \\ s_{n+1} = (r+1)\, s_n\, (p_n + s_n + t_n) + r\, q_n\, s_n + p_n\, t_n, \\ t_{n+1} = (r+1)\, t_n\, (q_n + s_n + t_n) + r\, p_n\, t_n + q_n\, s_n. \end{cases}$$

The form of these equations is decidedly simplified if we choose $p_n \ldots . t_n$ such that

$$2)\quad p_n + q_n + s_n + t_n = 1,$$

and use the notation $\Delta_n = q_n\, s_n - p_n\, t_n$. Then if we replace n by $n-1$ in equations 1) we obtain the following set:

$$3)\quad \begin{cases} p_n = p_{n-1} + \Delta_{n-1}/(1+r), \\ q_n = q_{n-1} - \Delta_{n-1}/(1+r), \\ s_n = s_{n-1} - \Delta_{n-1}/(1+r), \\ t_n = t_{n-1} + \Delta_{n-1}/(1+r). \end{cases}$$

These equations can be solved with little difficulty. From the first of equations 3) we have

$$4)\quad p_n = \frac{\Delta_{n-1}}{1+r} + \frac{\Delta_{n-2}}{1+r} + \ldots\ldots + \frac{\Delta_0}{1+r} + p_0.$$

If we can find Δ_n in terms of n we will have the desired solution for p_n. Calculating Δ_n from equations 3), i.e., forming $q_n\, s_n - p_n\, t_n$ and using Δ_{n-1} for $q_{n-1}\, s_{n-1} - p_{n-1}\, t_{n-1}$, we have

$$\Delta_n = \Delta_{n-1} - \frac{\Delta_{n-1}}{1+r} = \frac{r}{1+r} \cdot \Delta_{n-1}\, .$$

Whence,

5) $$\Delta_n = \left(\frac{r}{1+r}\right)^n \cdot \Delta_0 .$$

Substituting from 5) into 4) gives,

$$p_n = \frac{\Delta_0}{1+r}\left[\left(\frac{r}{1+r}\right)^{n-1} + \left(\frac{r}{1+r}\right)^{n-2} + \ldots\ldots + \frac{r}{1+r} + 1\right] + p_0 .$$

The bracket is a geometric progression. Summing it, p_n takes the closed form

$$p_n = \frac{\Delta_0}{(1+r)^n}\left[(1+r)^n - r^n\right] + p_0 .$$

Similar calculation for q_n, s_n, t_n gives us finally the set of solutions,

6) $$p_n = p_0 + \Delta_0 \left[1 - \left(\frac{r}{1+r}\right)^n\right],$$

7) $$q_n = q_0 - \Delta_0 \left[1 - \left(\frac{r}{1+r}\right)^n\right],$$

8) $$s_n = s_0 - \Delta_0 \left[1 - \left(\frac{r}{1+r}\right)^n\right],$$

9) $$t_n = t_0 + \Delta_0 \left[1 - \left(\frac{r}{1+r}\right)^n\right],$$

in which $\Delta_0 = q_0\, s_0 - p_0\, t_0$.

To get the zygotic composition of the $(n+1)$th generation it is only necessary to substitute these values for p_n .... t_n in JENNINGS'S (1917) table (6).

DISCUSSION. 1. The sum $p_n + q_n$ represents the gametes *AB* and *Ab* in the *n*th generation; i.e., all the gametes having the factor *A*. Similarly $s_n + t_n$ represents all the gametes with the factor *a*. It is well known that for a single factor the proportions of dominants, recessives and heterozygous individuals is fixed after the first random mating. This is due to the fact that the proportions of dominant and recessive gametes never changes in random mating. Then in our problem we should expect $p_n + q_n$ to be constant, and our equations 6) and 7) show that $p_n + q_n = p_0 + q_0$. Similarly we have three other check equations.

2. *From equations* 6) *to* 9) *it is evident that the value of* Δ_0 *is quite important. Any two sets of initial conditions give results differing from the initial conditions by the same amounts if and only if* Δ_0 *is the same for both.*

3. *In the case* $\Delta_0 = 0$, *the proportions are fixed from the beginning.* This is shown by equations 6) to 9). *The only other case in which the proportions are fixed is that of complete linkage,* $r = \infty$. Then we have

$r/(1+r)$ approaches unity as a limit, and equation 6) becomes, $p_n = p_0$, and similarly, $q_n = q_0$, $s_n = s_0$, $t_n = t_0$. *It is also evident that the case of complete linkage is in essence a one-factor problem and that therefore the proportions should be fixed.*

4. *The results for independent factors are obtained by setting* $r = 1$:

$$p_n = p_0 + \Delta_0 \left(1 - \tfrac{1}{2}^n\right),$$
$$q_n = q_0 - \Delta_0 \left(1 - \tfrac{1}{2}^n\right),$$
$$s_n = s_0 - \Delta_0 \left(1 - \tfrac{1}{2}^n\right),$$
$$t_n = t_0 + \Delta_0 \left(1 - \tfrac{1}{2}^n\right).$$

b. Linkage r in one set of gametes and r′ in the other

We have a much more general problem than the one above if we assume that the degree of linkage is different in the different sexes. Consider the problem with linkages r and r' any two positive integers. Let p_n, q_n, s_n, t_n be the gametic proportions in the set of gametes of linkage r and p_n', q_n', s_n', t_n' the same for the set of linkage r'. Then a study of the crosses involved gives the following recurrences:

$$10)\quad \begin{cases} p_n = \dfrac{p_{n-1} + p_{n-1}'}{2} + \dfrac{d_{n-1}}{2(r+1)}, \\[2ex] q_n = \dfrac{q_{n-1} + q_{n-1}'}{2} - \dfrac{d_{n-1}}{2(r+1)}, \\[2ex] s_n = \dfrac{s_{n-1} + s_{n-1}'}{2} - \dfrac{d_{n-1}}{2(r+1)}, \\[2ex] t_n = \dfrac{t_{n-1} + t_{n-1}'}{2} + \dfrac{d_{n-1}}{2(r+1)}, \end{cases}$$

$$11)\quad \begin{cases} p_n' = \dfrac{p_{n-1} + p_{n-1}'}{2} + \dfrac{d_{n-1}}{2(r'+1)}, \\[2ex] q_n' = \dfrac{q_{n-1} + q_{n-1}'}{2} - \dfrac{d_{n-1}}{2(r'+1)}, \\[2ex] s_n' = \dfrac{s_{n-1} + s_{n-1}'}{2} - \dfrac{d_{n-1}}{2(r'+1)}, \\[2ex] t_n' = \dfrac{t_{n-1} + t_{n-1}'}{2} + \dfrac{d_{n-1}}{2(r'+1)}, \end{cases}$$

in which

$$d_n = q_n s_n' - p_n t_n' + q_n' s_n - p_n' t_n.$$

Substituting from equation 11) into equation 10) we have,

$$12)\quad \begin{cases} p_n = p_n' + \dfrac{(r'-r)\,d_{n-1}}{2(r+1)(r'+1)}, \\[2ex] q_n = q_n' - \dfrac{(r'-r)\,d_{n-1}}{2(r+1)(r'+1)}, \\[2ex] s_n = s_n' - \dfrac{(r'-r)\,d_{n-1}}{2(r+1)(r'+1)}, \\[2ex] t_n = t_n' + \dfrac{(r'-r)\,d_{n-1}}{2(r+1)(r'+1)}. \end{cases}$$

Substituting these values of $p_n \ldots\ldots t_n$ into the equations 11) gives us,

$$13)\quad \begin{cases} p_n' = p_{n-1}' + \nabla_{n-1}, \\ q_n' = q_{n-1}' - \nabla_{n-1}, \\ s_n' = s_{n-1}' - \nabla_{n-1}, \\ t_n' = t_{n-1}' + \nabla_{n-1}. \end{cases}$$

where $n>1$ and

$$\nabla_{n-1} = \frac{1}{2(r'+1)}\left[\frac{r'-r}{2(r+1)}d_{n-2} + d_{n-1}\right].$$

It is evident that we can solve our problem if we can find ∇_{n-1}, and this depends upon finding d_n. If we let $D_n = q_n'\, s_n' - p_n'\, t_n'$, detailed computation from equations 12) and 13) show that

$$d_n = 2\,D_n - \frac{(r'-r)\,d_{n-1}}{2(r+1)(r'+1)}, \text{ and } D_n = D_{n-1} - \nabla_{n-1}.$$

From these last equations we find that

$$d_n = d_{n-1}\left[\frac{r}{2(r+1)} + \frac{r'}{2(r'+1)}\right] \text{ for } n>1\,.$$

Whence

$$d_n = d_1 .\, K^{n-1} \text{ where}$$

$$K = \frac{r}{2(r+1)} + \frac{r'}{2(r'+1)}.$$

Having d_n, we can calculate ∇_{n-1}, then solve equations 13) and finally equations 12).

$$p_n' - p_{n-1}' = \nabla_{n-1} = \frac{d_1\, r'K^{n-2}(r'+r+2)}{2(r'+1)(2rr'+r+r')}.$$

The solution of this equation is

14 a) $p_n' = c_1 - d_1 r' K^{n-2}/2(r'+1), \qquad n>1.$
in which[1]

$$d_1 = q_1 s_1' - p_1 t_1' + q_1' s_1 - p_1' t_1 \text{ and } c_1 = (p_1 + p_1' + d_1)/2.$$

Similarly,
14 b) $q_n' = c_2 + d_1 r' K^{n-2}/2(r'+1),$
14 c) $s_n' = c_3 + d_1 r' K^{n-2}/2(r'+1),$
14 d) $t_n' = c_4 - d_1 r' K^{n-2}/2(r'+1),$
in which $c_2 = (q_1 + q_1' - d_1)/2$; $c_3 = (s_1 + s_1' - d_1)/2$; $c_4 = (t_1 + t_1' + d_1)/2$.

Substituting into equations 12) we have,

$$15)\left\{\begin{aligned} p_n &= c_1 - d_1 r K^{n-2}/2(r+1), \\ q_n &= c_2 + d_1 r K^{n-2}/2(r+1), \\ s_n &= c_3 + d_1 r K^{n-2}/2(r+1), \\ t_n &= c_4 - d_1 r K^{n-2}/2(r+1). \end{aligned}\right.$$

Discussion. 1. It is evident that these results should reduce to those in the previous problem, linkage r in each sex, if we set $r'=r$. This can be easily verified and serves as a check on the calculations. *Equations 10) and 11) show that however different the original proportions may be in the two sexes, they are identical after the first cross, i.e.,* $p_1=p_1'$, *etc., if the linkage is the same in both sexes.*

2. *The results for the case of complete linkage in one set of gametes is given by making r' infinite in the above formulae. This gives:*

$$\begin{aligned} p_n' &= c_1 - d_1 K^{n-2}/2, \\ q_n' &= c_2 + d_1 K^{n-2}/2, \\ s_n' &= c_3 + d_1 K^{n-2}/2, \\ t_n' &= c_4 - d_1 K^{n-2}/2, \end{aligned}$$

in which $K = (2r+1)/2(r+1)$ *and* $c_1 \ldots c_4$ *are unchanged. The form of the equations for* $p_n \ldots t_n$ *does not change.*

3. *Setting* $r' = 1$ *will give the case of no linkage in one set of gametes. The equations become,*

$$\begin{aligned} p_n' &= c_1 - d_1 K^{n-2}/4, \\ q_n' &= c_2 + d_1 K^{n-2}/4, \\ s_n' &= c_3 + d_1 K^{n-2}/4, \\ t_n' &= c_4 - d_1 K^{n-2}/4, \end{aligned}$$

where $K = (3r+1)/4(r+1)$. *Here again the form of the equations for* $p_n \ldots\ldots t_n$ *remains unchanged.*

[1] Of course we can express c_1 and d_1 in terms of the original data, $p_0 \ldots t_0$, but so expressed they are cumbersome. The simpler is c_1 which is given by

$$c_1 = (2p_0 + 2p_0' + d_0 + q_0 s_0 - p_0 t_0 + q_0' s_0' - p_0' t_0')/4.$$

4. *Equations* 14) *and* 15) *show that if* $d_1 = 0$, *the proportions will be fixed after one random mating. In this case the proportions will be independent of the degree of linkage.* This last statement can easily be verified by calculating $c_1 \ldots c_4$ in terms of $p_0 \ldots t_0'$. The parts involving r and r' disappear—(see note 1).

5. *The limiting population:*

a. *The gametic proportions approach limiting values as n increases.*

b. *The limiting values are equal in the two sexes;* i.e., *the limits of* p_n, q_n, s_n, t_n *are respectively the limits of* p_n', q_n', s_n', t_n'. *In case* r *and* r' *are not both infinite the limits of* p_n, q_n, s_n, t_n *are respectively* c_1, c_2, c_3, c_4. In case of complete linkage the limits are respectively $c_1 - d_1/2$, $c_2 + d_1/2$, $c_3 + d_1/2$, $c_4 - d_1/2$.

c. *The limiting values are independent of the linkage factors* r, r' *except in the sense that complete linkage in both sexes gives limits different from those for any other case.* As was pointed out above, the case of complete linkage in both sexes is really a one-factor problem, and the proportions are fixed after one random mating.

d. *The limiting proportions must be such that if used as initial proportions the population would remain fixed;* this follows because if after the limiting proportions had been reached one more random mating changed the proportions, our notion of limiting proportions would be violated. We can therefore check our limits by forming d_1 using $p_1 = p_1' = c_1$, $q_1 = q_1' = c_2$, $s_1 = s_1' = c_3$, $t_1 = t_1' = c_4$. From point 4 in the discussion, d_1 should vanish, and detailed calculation will show that it does.

e. *In the limiting population, the proportion of A B gametes is the product of the proportions of A gametes and B gametes.* Symbolically this is expressed by the equation $c_1 = (c_1 + c_2)(c_1 + c_3)$, which may be easily verified.

Two striking facts stand out as a result of this discussion:

1. *In random mating, the effect of incomplete linkage between two factors is only temporary.*

2. *Continued random mating results in a population in which the distribution of B factors among the A and a factors is the same as the distribution of the b factors among the A and a factors.*

II. SELECTION OF DOMINANTS WITH RESPECT TO ONE OF THE PAIRS OF CHARACTERS—LINKAGE r IN BOTH SETS OF GAMETES

In this problem we select for breeding purposes only the zygotes which have the factor *A*. A study of the crosses involved gives the following recurrence relations:

$$16)\quad \begin{cases} p_n = [(r+1)\ p_{n-1} + \delta_{n-1}]/D_{n-1}, \\ q_n = [(r+1)\ q_{n-1} - \delta_{n-1}]/D_{n-1}, \\ s_n = [(r+1)\ s_{n-1}\ l_{n-1} - \delta_{n-1}]/D_{n-1}, \\ t_n = [(r+1)\ t_{n-1}\ l_{n-1} + \delta_{n-1}]/D_{n-1}, \end{cases}$$

In which $\delta_n = q_n\ s_n - p_n\ t_n$; $D_n = l_n\ (1 + L_n)(r+1)$; $L_n = s_n + t_n$ and $l_n = p_n + q_n$.

The method of solving these equations is analogous to the methods used in the earlier problems, but there is more detail and the results are less satisfactory. It is convenient to solve first for L_n and l_n. It is evident that L_n and l_n give the gametic composition of the nth generation for the one factor problem and we could compute them from this standpoint, but it is easy to calculate them from the equations 16). We have

$$s_n + t_n = (r+1)l_{n-1}(s_{n-1} + t_{n-1})/D_{n-1} = (s_{n-1} + t_{n-1})/(1 + L_{n-1}).$$

Since $s_n + t_n = L_n$,

$$L_n = L_{n-1}/(1 + L_{n-1}).$$

Then

$$17)\quad \frac{1}{L_n} = \frac{1 + L_{n-1}}{L_{n-1}} = 1 + \frac{1}{L_{n-1}} = 2 + \frac{1}{L_{n-2}} = \ldots = n + \frac{1}{L_0}.$$

Whence,

$$18)\quad L_n = L_0/(n\ L_0 + 1).$$

$$19)\quad l_n = 1 - L_n = \frac{(n-1)L_0+1}{n\ L_0+1} = \frac{L_n}{L_{n-1}}.$$

Combining equations 17) and 19) we get,

$$20)\quad \frac{1}{1 + L_n} = \frac{L_{n+1}}{L_n} = l_{n+1}.$$

Equation 20) enables us to write D_n in the simpler form,

$$21)\quad D_n = (r+1)l_n/l_{n+1}.$$

It is at once apparent that L_n approaches zero as n increases and hence s_n and t_n do likewise. Therefore l_n approaches unity as n increases.

The next step in the solution is to solve for δ_n. Computing δ_n from equations 16), i.e. calculating $q_n\ s_n - p_n\ t_n$ we get at once that

$$22)\quad \delta_n = \delta_{n-1}(r - L_{n-1})/D_{n-1}(1 + L_{n-1}).$$

Substituting from equations 20) and 21) for $1/(1+L_{n-1})$ and D_{n-1}, δ_n takes the form

$$\begin{aligned} \delta_n &= \delta_{n-1}\ l_n^2(r-L_{n-1})/l_{n-1}(r+1), \\ &= \delta_{n-2}\ l_n^2\ l_{n-1}(r-L_{n-1})(r-L_{n-2})/(r+1)^2\ l_{n-2}, \\ &= \delta_0 . l_n . l_n . l_{n-1}\ \ldots\ldots\ l_1(r-L_{n-1})\ \ldots\ldots\ (r-L_0)/(r+1)^n . l_0 \end{aligned}$$

From equation 20) we have,

$$l_n\, l_{n-1} \ldots\ldots l_1 = L_n/L_0.$$

Then we can write,

23) $$\delta_n = \delta_0 \; l_n L_n \prod_{i=0}^{i=n-1} (r - L_i) / \, l_0 \, L_0 \, (r+1)^n \, .$$

The first of equations 16) can be written

$$p_n - l_n \, p_{n-1}/l_{n-1} = \delta_{n-1} \, l_n / (r+1) l'_{n-1}.$$

The solution of this equation satisfying the initial conditions is,

24) $$p_n = \frac{p_0 \, l_n}{l_0} + \frac{l_n}{r+1}\left[\frac{\delta_{n-1}}{l_{n-1}} + \frac{\delta_{n-2}}{l_{n-2}} + \ldots\ldots + \frac{\delta_0}{l_0}\right].$$

Similarly the solutions of the other equations of set 16) are,

25) $$q_n = \frac{q_0 \, l_n}{l_0} - \frac{l_n}{r+1}\left[\frac{\delta_{n-1}}{l_{n-1}} + \frac{\delta_{n-2}}{l_{n-2}} + \ldots\ldots + \frac{\delta_0}{l_0}\right].$$

26) $$s_n = \frac{s_0 \, L_n}{L_0} - \frac{l_n}{r+1}\left[\frac{\delta_{n-1}}{l_{n-1}} + \frac{\delta_{n-2}}{l_{n-2}} + \ldots\ldots + \frac{\delta_0}{l_0}\right].$$

27) $$t_n = \frac{t_0 \, L_n}{L_0} + \frac{l_n}{r+1}\left[\frac{\delta_{n-1}}{l_{n-1}} + \frac{\delta_{n-2}}{l_{n-2}} + \ldots\ldots + \frac{\delta_0}{l_0}\right].$$

This seems to be about the most compact form into which the solution can be put. It will probably be a matter of opinion whether these equations are worth writing down. Certainly if one desires the composition of each generation, repeated use of the recurrence relation is easiest. But if one wishes the tenth generation and does not care about the preceding ones, it seems that the solutions 24) to 27) may be more useful. It should be noted that L_n and l_n are very simple functions of n and can be calculated rapidly, and that successive values of δ_n come rather easily if we use equation 22).

DISCUSSION. 1. *As noted above, s_n and t_n approach zero as n increases.*

2. *The proportions can be fixed only in the trivial case where $s_0 = t_0 = 0$.* This is shown by equation 18).

3. *If $p_i/q_i = s_i/t_i$ for any value of i it is true for all values of i.* This follows from equation 22), since if $p_i/q_i = s_i/t_i$, then $\delta_i = 0$. *In this special case, the equations 24) to 27) reduce to*

$$p_n = p_0 l_n / l_0 \, ; \; q_n = q_0 \, l_n / l_0 \, ;$$
$$s_n = s_0 \, L_n / L_0 \, ; \; t_n = t_0 \, L_n / L_0.$$

It is important to note that in this case, $\delta_i = 0$, the results are independent of the linkage factor. Furthermore we find that $p_n + s_n = p_0 + s_0$. This is readily shown as follows. From equations 24) and 26)

$$p_n + s_n = p_0\, l_n/l_0 + s_0\, L_n/L_0 \text{ when } \delta_0 = 0;$$
$$= p_0 l_n/l_0 + s_0(1 - l_n)/L_0$$
$$= l_n[p_0/l_0 - s_0/L_0] + s_0/L_0.$$

Since $p_0/q_0 = s_0/t_0$, then $p_0/(p_0 + q_0) = s_0/(s_0 + t_0)$; i.e., $p_0/l_0 - s_0/L_0 = 0$, and therefore

$$p_n + s_n = s_0/L_0.$$

Also since $p_0/(p_0 + q_0) = s_0/(s_0 + t_0)$, each fraction is equal to $(p_0 + s_0)/(p_0 + q_0 + s_0 + t_0) = \dfrac{p_0 + s_0}{1}$. Therefore,

$$p_n + s_n = p_0 + s_0.$$

This is an important fact. The sum $p_n + s_n$ represents the gametes with the factor B in the nth generation. We therefore have the conclusion, if $\delta_0 = 0$, selection of dominants with respect to A does not interfere with random mating with respect to B, regardless of the degree of linkage between A and B.

4. *The case of complete linkage, $r = \infty$, gives the same equations for p_n ..... t_n as does $\delta_0 = 0$. However, we do not have the other results that follow from $\delta_0 = 0$.*

5. *The case of no linkage, $r = 1$, simplifies considerably because the continued product for δ_n (equation 23) can be summed when $r = 1$:*

$$\delta_n = \delta_0\, l_n\, L_n\, l_{n-1} \ldots . l_0/l_0\, L_n\, 2^n.$$
$$= \delta_0\, L_n^2/L_0^2 \,.\, 2^n, \text{ (using equation 19))}.$$
$$\delta_n/l_n = \delta_0\, L_n^2/L_0^2 \,.\, 2^n \,.\, l_n.$$

Using equation 19) again, this becomes

$$\delta_n/l_n = \delta_0\, L_n\, L_{n-1}/L_0^2 \,.\, 2^n.$$

From equation 17) we have

$$1/L_n - 1/L_{n-1} = 1.$$

Whence,

$$L_n \,.\, L_{n-1} = L_{n-1} - L_n.$$

Substituting this value of $L_n\, L_{n-1}$ above, we have,

$$\delta_n/l_n = \delta_0(L_{n-1} - L_n)/L_0^2 \,.\, 2^n.$$

Using this value of δ_n/l_n, equations 24) to 27) may be written,

28) $$p_n = \left(p_0 + \frac{\delta_0}{2} + \frac{\delta_0\, l_0}{4 L_0}\right)\frac{l_n}{l_0} - \left(S_{n-1} + \frac{L_{n-1}}{2^{n-1}}\right) \cdot \frac{l_n\, \delta_0}{4 L_0^2}.$$

29) $$q_n = \left(q_0 - \frac{\delta_0}{2} - \frac{\delta_0\, l_0}{4 L_0}\right)\frac{l_n}{l_0} + \left(S_{n-1} + \frac{L_{n-1}}{2^{n-1}}\right) \cdot \frac{l_n\, \delta_0}{4 L_0^2}.$$

30) $$s_n = \left(s_0 - \frac{\delta_0}{2\, l_0} - \frac{\delta_0}{4}\right)\frac{L_n}{L_0} - \left(S_{n-1} - \frac{L_{n-1}}{2^{n-1}}\right) \cdot \frac{L_n\, \delta_0}{4 L_0^2}.$$

31) $$t_n = \left(t_0 + \frac{\delta_0}{2\,l_0} + \frac{\delta_0}{4}\right)\frac{L_n}{L_0} + \left(S_{n-1} - \frac{L_{n-1}}{2^{n-1}}\right) \cdot \frac{L_n\,\delta_0}{4\,L_0^2}\,.$$

in which $S_n = L_1/2 + L_2/4 + \ldots + L_n/2^n$.

The computation in this case is fairly simple and the formulae should be useful.

JENNINGS (1917) discusses this problem in section (26) of his paper. In the next to the last paragraph of this section he writes, "selection with reference to A and a is random mating with reference to B and b, if the two pairs are not linked." There is nothing in our equations 28) to 31) to suggest this, and as a matter of fact an example can easily be found for which this is not true. Suppose, for instance, that the breeding begins with a cross between $ABAb$ and $abab$ and suppose there is no linkage, $r = 1$. Then $p_0 = 1/4$; $q_0 = 1/4$; $s_0 = 0$; $t_0 = 1/2$. From equations 16) or equations 28) to 31), or from JENNINGS's equations of table 16, we calculate,

$$p_1 = 1/4,\quad q_1 = 5/12,\quad s_1 = 1/12,\quad t_1 = 1/4,$$
$$p_2 = 17/64,\quad q_2 = 31/64,\quad s_2 = 5/64,\quad t_2 = 11/64.$$

In random mating with respect to B and b, the proportion of each type of gamete remains fixed. The proportion of B gametes is given by $p_n + s_n$. In the above example,

$$p_0 + s_0 = 1/4;\; p_1 + s_1 = 1/3;\; p_2 + s_2 = 11/32.$$

Thus we see that we do not have random mating with respect to B and b.

6. *The proportions approach limiting values as n increases.* As has already been mentioned, s_n and t_n approach zero. That p_n and q_n approach limiting values is apparent when we notice from equations 24) and 25) that each increases or decreases continuously and lies between zero and unity. The limits of p_n and q_n are

$$\lim_{n=\infty} p_n = \frac{p_0}{l_0} + \frac{1}{r+1}\left[\frac{\delta_0}{l_0} + \frac{\delta_1}{l_1} + \frac{\delta_2}{l_2} + \ldots\right],$$
$$\lim_{n=\infty} q_n = \frac{q_0}{l_0} - \frac{1}{r+1}\left[\frac{\delta_0}{l_0} + \frac{\delta_1}{l_1} + \frac{\delta_2}{l_2} + \ldots\right].$$

We can say very little about these values because of their complicated form. However, we may note this one fact: *the limits of p_n and q_n depend upon the value of r and $\delta_0 = 0$.* This is worth noting since it was not the case in random mating.

It may be worth while to state without proof that in case $r = 1$, p_n lies between the values $p_0/l_0 + \delta_0/2l_0$ and $p_0/l_0 + \delta_0/2l_0 + \delta_0/2L_0$. Also, the difference between these two expressions, $\delta_0/2L_0$, lies between zero and 1/2.

Similar investigations can be carried through for the corresponding problem in which the linkage constant is different in the two sexes, but the results become complicated so rapidly that it would seem wiser to follow JENNINGS's method of repeated use of the recurrence relations.

III. SELF-FERTILIZATION

a. Linkage r in each set of gametes

In this problem we cannot deal with the types of gametes only. We must consider the different types of zygotes. We shall follow JENNINGS in letting c_n represent the proportion of the zygotes of the nth generation which have a composition indicated by *ABAB*, and use similar notation for other types as indicated in the following table:

$c_n = ABAB$		$i_n = ABAb$
$d_n = AbAb$	$g_n = ABab$	$j_n = ABaB$
$e_n = aBaB$	$h_n = AbaB$	$k_n = abAb$
$f_n = abab$		$l_n = abaB$

If we assume that

$$c_n + d_n + e_n + f_n + g_n + h_n + i_n + j_n + k_n + l_n = 1,$$

the recurrence relations for the problem are,

32) $c_n = c_{n-1} + r^2 g_{n-1}/R + h_{n-1}/R + (i_{n-1} + j_{n-1})/4,$

33) $d_n = d_{n-1} + g_{n-1}/R + r^2 h_{n-1}/R + (i_{n-1} + k_{n-1})/4,$

34) $e_n = e_{n-1} + g_{n-1}/R + r^2 h_{n-1}/R + (j_{n-1} + l_{n-1})/4,$

35) $f_n = f_{n-1} + r^2 g_{n-1}/R + h_{n-1}/R + (k_{n-1} + l_{n-1})/4,$

36) $g_n = 2[r^2 g_{n-1} + h_{n-1}]/R,$

37) $h_n = 2[g_{n-1} + r^2 h_{n-1}]/R,$

38) $i_n = 2r(g_{n-1} + h_{n-1})/R + i_{n-1}/2,$

39) $j_n = 2r(g_{n-1} + h_{n-1})/R + j_{n-1}/2,$

40) $k_n = 2r(g_{n-1} + h_{n-1})/R + k_{n-1}/2,$

41) $l_n = 2r(g_{n-1} + h_{n-1})/R + l_{n-1}/2,$

in which $R = 4(1 + r^2)$.

Adding 36) and 37) and using the notation $v = (r^2 + 1)/2(r + 1)^2$,

$$g_n + h_n = v(g_{n-1} + h_{n-1}).$$

Whence

42) $g_n + h_n = v^n(g_0 + h_0).$

Substituting from 42) into 38) gives,

$$i_n - i_{n-1}/2 = 2r(g_0 + h_0) \cdot v^{n-1}/R.$$

The solution of this equation is

43) $i_n = \dfrac{g_0 + h_0 + 2i_0}{2^{n+1}} - \dfrac{g_0 + h_0}{2} \cdot v^n.$

Similarly,

44) $$j_n = \frac{g_0 + h_0 + 2j_0}{2^{n+1}} - \frac{g_0 + h_0}{2} . v^n.$$

45) $$k_n = \frac{g_0 + h_0 + 2k_0}{2^{n+1}} - \frac{g_0 + h_0}{2} . v^n.$$

46) $$l_n = \frac{g_0 + h_0 + 2l_0}{2^{n+1}} - \frac{g_0 + h_0}{2} . v^n.$$

From equation 42) we get

$$h_n = v^n (g_0 + h_0) - g_n.$$

Substituting this value of h_n into equation 36) and simplifying we have,

$$g_n = [2(r^2 - 1) g_{n-1} + 2v^{n-1}(g_0 + h_0)]/R.$$

If we let $(r^2 - 1)/2(r + 1)^2 = w$, this equation takes the simpler form,

$$g_n - w\, g_{n-1} = (g_0 + h_0) v^{n-1}/2(r + 1)^2.$$

The solution is,

47) $g_n = (g_0 - h_0) w^n/2 + (g_0 + h_0) v^n/2.$

Substituting for g_n from equation 47) into equation 42) we have

48) $h_n = (h_0 - g_0) w^n/2 + (g_0 + h_0) v_n/2.$

We can now evaluate everything in equation 32) excepting c_n and c_{n-1} and have,

$$c_n - c_{n-1} = \frac{g_0 - h_0}{4} w^n + \frac{g_0 + h_0}{4} (v^n - v^{n-1}) + \frac{g_0 + h_0 + i_0 + j_0}{2^{n+1}}.$$

The solution is

49) $$c_n = \frac{g_0 - h_0}{4} . w \frac{(1 - w^n)}{1 - w} + \frac{g_0 + h_0}{4} (v^n - 1) + (g_0 + h_0 + i_0 + j_0) \left(\frac{2^n - 1}{2^{n+1}}\right) + c_0 .$$

Similarly,

50) $$d_n = \frac{h_0 - g_0}{4} . w \frac{(1 - w^n)}{1 - w} + \frac{g_0 + h_0}{4} (v^n - 1) + (g_0 + h_0 + i_0 + k_0) \left(\frac{2^n - 1}{2^{n+1}}\right) + d_0 .$$

51) $$e_n = \frac{h_0 - g_0}{4} . w \frac{(1 - w^n)}{1 - w} + \frac{g_0 + h_0}{4} (v^n - 1) + (g_0 + h_0 + j_0 + l_0) \left(\frac{2^n - 1}{2^{n+1}}\right) + e_0 .$$

52) $$f_n = \frac{g_0 - h_0}{4} . w \frac{(1 - w^n)}{1 - w} + \frac{g_0 + h_0}{4} (v^n - 1) + (g_0 + h_0 + k_0 + l_0) \left(\frac{2^n - 1}{2^{n+1}}\right) + f_0 .$$

DISCUSSION. 1. It is easy to get the limiting population in this problem. Since v and w are proper fractions, v^n and w^n approach zero as n increases. Because of this, *the limits are zero for all but the homozygous types, c, d, e, f. For these four we have,*

$$\lim_{n=\infty} c_n = (g_0 - h_0)(r + 1)/2(r + 3) + (h_0 + i_0 + j_0)/2 + c_0.$$

$$\lim_{n=\infty} d_n = (h_0 - g_0)(r+1)/2(r+3) + (g_0 + i_0 + k_0)/2 + d_0.$$

$$\lim_{n=\infty} e_n = (h_0 - g_0)(r+1)/2(r+3) + (g_0 + j_0 + l_0)/2 + e_0.$$

$$\lim_{n=\infty} f_n = (g_0 - h_0)(r+1)/2(r+3) + (h_0 + k_0 + l_0)/2 + f_0.$$

In all the one-factor problems in self-fertilization or any other forms of inbreeding that have been discussed by JENNINGS (1916) *and by the present writer* (ROBBINS 1917, 1918) *the heterozygous type tends to disappear. Here in the two-factor problem in self-fertilization we note the same tendency.*

2. *In general the proportions in the limiting population depend upon the linkage factor r, but in case $h_0 = g_0$, i.e., when the two types ABab and AbaB appear in equal numbers, the limiting population is independent of the linkage factor.*

b. Linkage r in one set of gametes and r′ in the other set

The recurrence relations for this more general problem may be obtained by replacing r^2 by rr' and $2r$ by $r+r'$ in equations 32) to 41) above. The solutions have the same form as above, equations 43) to 52) but v and w have the values

$v = (rr' + 1)/2(r+1)(r'+1)$; $w = (rr' - 1)/2(r+1)(r'+1)$.

The limiting population takes the form obtained by replacing $(r+1)/2(r+3)$ in the previous limiting forms by $(rr' - 1)/(rr' + 2r + 2r' + 3)$.

DISCUSSION. 1. In case of no linkage in either set of gametes, $r = r' = 1$, the equations simplify considerably since $w = 0$ and $v = 1/4$.

2. In case of no linkage in one set of gametes and linkage r in the other set, $r' = 1$, we have $v = 1/4$; $w = (r-1)/4(r+1)$.

3. In case of complete linkage in both sets of gametes, $r = \infty$, we have $w = v = 1/2$. The value of each class except those which are homozygous reduces to its original value divided by 2^n. The homozygous classes have the values,

$$c_n = (g_0 + i_0 + j_0)\left(\frac{2^n - 1}{2^{n+1}}\right) + c_0 ,$$

$$d_n = (h_0 + i_0 + k_0)\left(\frac{2^n - 1}{2^{n+1}}\right) + d_0 ,$$

$$e_n = (h_0 + j_0 + l_0)\left(\frac{2^n - 1}{2^{n+1}}\right) + e_0 ,$$

$$f_n = (g_0 + k_0 + l_0)\left(\frac{2^n - 1}{2^{n+1}}\right) + f_0 .$$

4. In case of complete linkage in one set of gametes and r in the other we have $v = w = r/2(r+1)$.

5. In case of complete linkage in one set of gametes and no linkage in the other set, $v = w = 1/4$.

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