June 3rd, 1938

My dear Ford,

There is one point in your book which I I had spotted earlier, where you say that heterozygosis is halved in each generation by brother and sister matings. This is true of self-fertilisation, but the effect of inbreeding sibs is quite a bit slower. I am enclosing a fuller discussion, which, though quite unsuitable for a popular book, may be of use to you some time.

Yours sincerely,

Brother and Sister inbreeding

For a single factor 6 types of matings are possible, let us assign the arbitrary frequencies, and calculate the new frequencies in the next generation.

Frequency	Matings	Derived matings
u	AA x AA	AA x AA
u'	aa x aa	aa x aa
v	AA x Aa	1/4(AA x AA) + ½(AA x Aa) + 1/4(Aa x Aa)
v'	aa x Aa	1/4(aa x aa) + ½(aa x Aa) + 1/4(Aa x Aa)
w	aa x AA	Aa x Aa
x	Aa x Aa	1/16(aa x aa) +1/16(AA x AA) +1/4(aa x Aa) +1/4(AA x Aa) +1/8(aa x AA +1/4(Aa x Aa)

Thus, if one new pair is chosen at random from the offspring of each pair, the frequencies expected in the second generation are

$$u_1 = u + 1/4\ v + 1/16\ x$$

$$u'_1 = u' + 1/4\ v' + 1/16\ x$$

$$v_1 = \tfrac{1}{2}v + 1/4\ x$$

$$v'_1 = \tfrac{1}{2}v' + 1/4\ x$$

$$w_1 = 1/8x$$

$$x_1 = 1/4\ v + 1/4\ v' + w + 1/4\ x$$

These are the primary equations, which deserve some discussion. The corresponding equations for other cases will be similar, though perhaps more complicated.

One approach which can, I think, only be ~~discerned~~ derived by rather elaborate methods, can, I think, be <u>exhibited</u> quite simply.

We may notice that

$$v_{,} - v'_{,} = \tfrac{1}{2}(v - v')$$

and hence infer that after n generations

$$v_n - v'_n = (v - v')/2^n \qquad \text{(a)}$$

this <u>component</u> is thus easily predicted without the rest of the solution.

Next

$$u_{,} - u'_{,} = u - u' + 1/4\,(v - v')$$

so that knowing $v - v'$ we can also predict $u - u'$; this may be put more neatly by observing that

$$u_{,} - u'_{,} + \tfrac{1}{2}(v_{,} - v'_{,}) = u - u' + \tfrac{1}{2}(v - v') \qquad \text{(b)}$$

so that this component simply remains constant.

With these two differences out of the way it is simpler now to write

$$U = u + u' \quad , \quad V = v + v'$$

so that

$$U_{,} = U + 1/4\,V + 1/8\,x$$

$$V_{,} = \tfrac{1}{2}V + \tfrac{1}{2}x$$

$$w_{,} = 1/8\,x$$

$$x_{,} = 1/4\,V + w + 1/4\,x$$

Then the next component to remove is

$$V_1 - x_1 - 4\,w_1 = 1/4(V - x - 4w)$$

so that

$$V_n - x_n - 4w_n = (V - x - 4w)/4^n \qquad \text{(c)}$$

dying away rapidly.

The last two components are more difficult, one can, however, verify that

$$\begin{aligned} & V_1(\sqrt{5}-1) - 4x_1 + 4w_1(\sqrt{5}+1) \\ &= \tfrac{1}{2}(\sqrt{5}-3)V + (\sqrt{5}-1)x - 4w \\ &= -\tfrac{1}{4}(\sqrt{5}-1)\{V(\sqrt{5}-1) - 4x + 4w(\sqrt{5}+1)\} \qquad \text{(d)} \end{aligned}$$

so that this component also decays in geometric progression, changing signs with each generation, the ratio being about −.309, so that here also the rate of decay is high.

Finally, changing the sign of $\sqrt{5}$ one has

$$\begin{aligned} & V_1(\sqrt{5}+1) + 4x_1 + 4w_1(\sqrt{5}-1) \\ &= \tfrac{1}{4}(\sqrt{5}+1)\{V(\sqrt{5}-1) + 4x + 4w(\sqrt{5}-1)\} \qquad \text{(e)} \end{aligned}$$

the decay being here in the ratio $\dfrac{\sqrt{5}+1}{4} = .809$

considerably slower than any other component.

The importance of the rate of decay is best brought out by considering how many generations are needed to decrease any component to 1/10 of its value

	Time in generations	Ratio of decrement
(c) $V - x - 4w$	1.661	.25
(d) $V(\sqrt{5}-1)-4x+4w(\sqrt{5}+1)$	1.961	-.309017
(a) $v - v'$	3.322	.50
(e) $V(\sqrt{5}+1)+4x+4w(\sqrt{5}-1)$	10.864	.809017

An important point in this sort of work is that the component having the slowest rate of decay becomes as time passes progressively the most important; the ratios of the frequencies thus tend to a condition in which (a), (c) (d) are all zero, this will be so if

$$\frac{w_n}{\sqrt{5}-1} = \frac{x_n}{8} = \frac{V_n}{4(\sqrt{5}+1)} = \frac{v_n}{2(\sqrt{5}+1)} = \frac{v'_n}{2(\sqrt{5}+1)}$$

1.236 8 12.944 6.472 6.472

The frequencies will necessarily tend to these ratios, all values decaying at the same slow rate, unless the frequencies of the matings initially were such as to make (e) vanish, and this cannot be, since all the coefficients in (e) are positive. After a large number _n_ of generations all the frequencies expected are therefore obtained by equating the fractions above to

$$(.309017)^n \; \frac{v(\sqrt{5} + 1) + 4x + 4w(\sqrt{5} - 1)}{80}$$