16 July 1930.

Prof. C.G. Darwin, F.R.S.,
      The University,
            EDINBURGH.

Dear Professor Darwin,

I must have another shot about the runaway sexual
selection, but I will not take long because I think you will
see it better in three words than in three hundred. At the
bottom of page 137 you ask "But if there are fewer hens I
don't see how hen taste gets reinforced". My theory is
that tasteful hens don't rear more chicks, but their sons
are finer and get more grand-chicks; hence the prolegomena in
the middle of page 129. Now I'll promise not to worry you
any more about that unless you ask me. I make it exponential.

What I really want to interest you in is the problem at
the beginning of chapter VI which I have entirely failed to
solve and yet cannot resist having a qualitative shot at, as you
have seen. Start with a population of a billion asexual
organisms all dead alike, if that is the simplest way to start;
give each of them a fixed small chance of mutating in a number
of different mutations a,b,c,d,--- some advantageous, mostly
the reverse. Mutation pulls the average fitness down a bit,
but, by introducing diversity in fitness, it starts Natural

Selection, pulling the fitness up.   Assume the mutation rates
constant and the increments of fitness cumulative and go on
until a steady state is reached, always keeping the population
about a billion.   I should hope that the steady state would
be characterised by a definite form for the distribution in
fitness, certainly not symmetrical, and by a definite rate of
progress, the head advancing by favourable mutations and the
tail dying away exponentially.   I want to express the rate
of progress (and incidentally the distribution in fitness) in
terms of a given distribution of the fitness increments at
mutation and of a gross mutation rate, or, if you like, some
parameter which increases or decreases the mutation rates of
all the different mutations proportionally.   By common sense,
which I can persuade no sort of analysis to support, I believe
that there must be an optimum mutation rate, at which progress
will be most rapid, and that at very high mutation rates the
species would degenerate by being peppered with predominantly
deleterious mutations.   After some cogitation I believe that
the finiteness of the population is an essential element in
this conclusion, and that an analysis which ignores that will
miss the point.   I believe a solution of any particular case,
with the main features in it, would clear up the difficulty.
It really is a key problem because, apart from uni-gene orga-
nisms such as filter passers may be, it applies to genes
competing for the same locus and would throw light on a good

many organisms whose germ-plasm has got so tightly linked up that recombination is little more frequent than mutation.

As you will have noticed there are plenty of further puzzles touched on in the book to keep me busy but I don't know any other of the same importance where the mathematical data can be put so definitely.

May I thank you for the extraordinary kindness you have x shown in reviewing my book?   I only hope it may do half the good that you think it is capable of.   It will certainly be long before people widely realise how much there was in that subtle argument of Galton's about heiress marriages.

I enclose some notes on your marginal comments but don't think of answering these or bothering about them, except for your own convenience.

Yours sincerely,

Page 24. Of course it would be more logical to count age always from fertilisation but age from birth is so very familiar, both in common usage and in the actuarial notation that I felt bound to use it.

Page 26. It looks as though another "proportional to" will have to go in on line 10. $\int_0^\infty c^{-mx} l_x\, dx$ is not unity but about 50, or more exactly the reciprocal of the birth-rate, so one might use your expression in the margin if N were not the population, but the number of births per annum.

Page 27. Strictly the rate of interest is calculated so as to make the repayments just, so that there is no bad debt. Those dying childless are, so to speak, the bad part of the debt.

I am sorry about v_a. It __is__ unity by the definition on page 27 but when I came to make the graph I introduced a factor so as to make the total number of heads in the population in its steady state equal to the total value of such a population. That made v_a a trifle over 2, and the young ladies of eighteen not far from 3, which struck me as interesting from the point of view of an immigration agent since they only pay one fare, or less if they are young enough. Then of course for page 30 one ought either to put $v_a = 1$, or to differentiate the expression on page 27 as v_x / v_a

Page 30. I don't think the death-rate has fallen much in the 'sixties and after. The fact is that the number of births registered rose to a maximum in 1903 and has been since falling. Apart from the effects of very slight fluctuations in the death-rate the crest of

the wave must now be 27 years old and there is perhaps an excess
from 15 to 42.   The groups at these ages are falling off rapidly
in reproductive value (without producing many children either) but
are not dying much whereas we are short of people over 60 and under
5 who ordinarily have a high death-rate without the survivors
diminishing in reproductive value.

Pages 32, 33. Thanks for the hint about italics.   It is like electric
force and electric induction in a space of as many dimensions as
there are factors.   Homogamy works like a kind of specific inductive
capacity though I am not sure that there may not be other causes
for a to differ from α .

Page 35.   This is the variance in the value of p in a sample of
successful gametes from the practically infinite population of those
that might have been successful.

Page 40.   There is an assumption about isotropism.   A euclidean metric
can be chosen so that the surfaces of equal adaptation tend to be
hyper-spheres as O is approached; but then will mutations of the same
magnitude in different directions be represented by vectors of equal
length?   If we had an objective test of equality for different kinds
of change in the organism we might have to consider ellipsoidal
surfaces of equal adaptation.   As it is the only thing that worries
me is the idea that variations in different directions, in a metric
defined for convenience, may not be equally frequent so that a
species may approach its ideal obliquely, edging up towards the pole
at which its least frequent mutations point along AO.

Page 60. Biochemically dominance must be determined by a frightfully
complex, and perhaps equally delicate, series of reactions.   One has

a system with thousands of pairs of genes in it, all chemically different, which somehow develops into an organism.   If a pair AA is replaced by a pair of mutant genes aa the organism still develops, though somewhat abnormally.   Obviously A differs from a in the nature or the rate of some of the direct, or more probably very indirect, reactions it or its products undergo with the rest of the system or their products.   Dominance depends on how the system, starting with Aa, behaves, and I conceive that by appropriate changes in the rest of the system it may be made to behave just like AA, at any rate much more readily than aa could be made to do so. I do not imagine that there is a special class of mutation with specially high mutation rates needed to bring this about, but that within the existing genetic variability of the species there are usually gene substitutions already available which are capable of doing it. My strongest reason for thinking this is that the pure recessive so often modifies itself spontaneously when kept in stock, as in the cases on page 55, always in the direction of normality.   This experimental evidence bears directly on the modification of the homozygote suggested on page 64, the modification of dominance, i.e. of the heterozygote, being, as it were, a milder inference which seems to explain a good many odd facts.

Page 76.   The chance of success without selection is really not zero but $1/2n$ as shown on page 93.   Do you think I ought to qualify it here?   Of course the Poisson series can only be exact for an infinite population.

Page 97.   I take it that Hooker stressed the unreliability of varietal determinations and so did not want the individual cases exposed for

criticism, while he agreed with your grandfather that individual inaccuracies could not account for the aggregate results. Do you think a statistical summary of your grandfather's tables, by families for example, would be telling enough to inspire some botanist to work over for comparison the richer material now available?

Page 102. I am sure it could be done but hitherto I have shirked working out the reproductive values of the two homozygotes and the heterozygote for the case where a fixed fraction, say, θ, of the offspring are produced by self-fertilisation. The three genotypes still leaving offspring in the ratio a:b:c. It has always confused me when I have tried to think of it and the fact is that when I cannot get a grip of a thing in my head I can very seldom make it go on paper. But I suppose the reproductive values, i.e. the ultimate descendants, will be in a higher ratio than those in the first generation.