Fitness and Inbreeding

Alan R. Rogers

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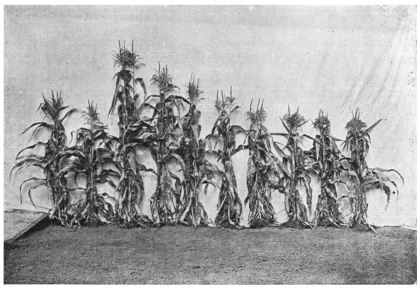
What inbreeding depression tells us



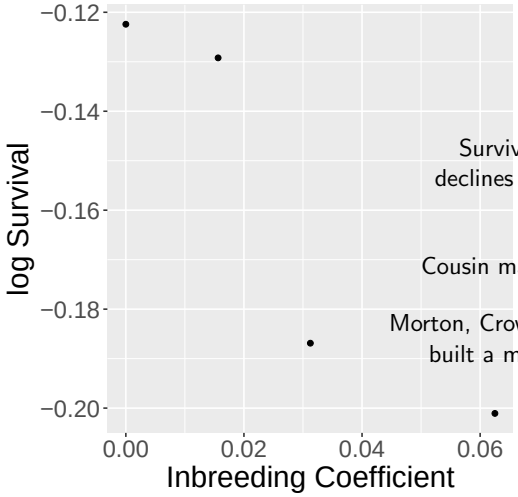
(Jones 1924)

Inbreeding depression is widespread in Nature.

Implies that deleterious alleles tend to be partially recessive,

or that there is widespread overdominance in fitness.

Measuring the effect



Survival of human children declines with their inbreeding coefficient.

Cousin mating $\Rightarrow F = 0.0625$.

Morton, Crow, and Muller (1956) built a model to estimate this effect.

Genotype frequencies and fitnesses

Genotype	Frequency	Fitness
A_1A_1	$p^2 + pqF$	1
A_1A_2	$2pq(1-F)$	$1 - hs$
A_2A_2	$q^2 + pqF$	$1 - s$

Mean fitness:

$$\begin{aligned} \bar{w} &= 1 - 2pq(1-F)hs - (q^2 + pqF)s \\ &= 1 - a - bF \qquad \Leftarrow \qquad \text{linear func of } F \end{aligned}$$

where

$$\begin{aligned} a &= 2pqsh + q^2 s \\ b &= 2pqs(1/2 - h) \end{aligned}$$

Why is inbreeding harmful?

We have just seen that mean fitness is

$$\bar{w} = 1 - a - bF$$

where

$$b = 2pqs(1/2 - h)$$

Fitness decreases with inbreeding if $b > 0$, which is true if $s > 0$ and $h < 1/2$, or in other words, if deleterious alleles are at least partially recessive.

If $h < 0$, then heterozygotes have higher fitness than either homozogte—the case of *overdominance*. Fitness declines with inbreeding in this case too, because $b > 0$.

Inbreeding depression is consistent with either hypothesiss.

Model of Morton, Crow, and Muller

Model

$$\begin{aligned} S &= \Pr[\text{survival}] \\ &= \prod_{i=1}^{L} 1 - a_i - b_i F \\ &\approx \prod_{i=1}^{L} e^{-a_i - b_i F} \\ &\approx e^{-A - BF} \end{aligned}$$

where $A = \sum a_i$ and $B = \sum b_i$.

Estimates

$$\begin{aligned} \hat{A} &= 0.1612 \\ \hat{B} &= 1.734 \end{aligned}$$

Example

For mating between full sibs, $F = 1/4$, and

$$\begin{aligned} S &= \exp\{-0.1612 - 1.734/4\} \\ &= 0.85 \end{aligned}$$

So we expect 15% mortality in the offspring of full-sib matings.

Discussion

Inbreeding reduces fitness if $h < 1/2$ at the average locus.

This is true if deleterious alleles tend to be recessive or if there is heterozygote advantage ($h < 0$).

Morton, Crow, and Muller did a "genome-wide" analysis long before there were genome-scale data.

Inbreeding and Genetic Drift

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Inbreeding and drift

Even under random mating, there is inbreeding in any finite population.

This "random inbreeding" is the same thing as genetic drift.

Number of ancestors

generation	year	ancestors
0	1994	1
1	1965	2
2	1936	4
3	1907	8
4	1878	16
5	1849	32
6	1820	64
7	1791	128
8	1762	256
9	1733	512
10	1704	1,024
11	1675	2,048
12	1646	4,096
13	1617	8,192
14	1588	16,384

Number of ancestors: II

generation	year	ancestors
15	1559	32,768
16	1530	65,536
17	1501	131,072
18	1472	262,144
19	1443	524,288
20	1414	1,048,576
21	1385	2,097,152
22	1356	4,194,304
23	1327	8,388,608
24	1298	16,777,216
25	1269	33,554,432
26	1240	67,108,864
27	1211	134,217,728
28	1182	268,435,456

Number of ancestors: III

generation	year	ancestors
29	1153	536,870,912
30	1124	1,073,741,824
31	1095	2,147,483,648
32	1066	4,294,967,296

If you were born in 1994, then you had over 4 billion ancestors in 1066.

But there were not that many people on the planet.

Many of your ancestors in 1066 were the same people—we are all inbred.

Let us build a model of this inbreeding.

Drift and inbreeding

Drift After t generations of genetic drift, the expected heterozygosity is

$$E[H(t)|p_0] = 2p_0q_0(1 - 1/2N)^t$$

Inbreeding If F_t is the average inbreeding coefficient in generation t, relative to generation 0,

$$E[H(t)|p_0] = 2p_0q_0(1 - F_t)$$

Equating these expressions gives

$$F_t = 1 - (1 - 1/2N)^t$$

Inbreeding *is* genetic drift.