The forces of evolution, II

The deterministic model:
- \( F=ma \) for gene dynamics: review
- The algebra of natural selection: the lab

Why biology is not like physics: what goes off the rails - frequency dependent fitness

Does selection maximize fitness?
Does sex make you fitter?
The multivariate case: sickle cell anemia example
Change or die: the case for mutation
The dynamical system framework

The dynamical system framework
The dynamical system framework

\[ p: \text{some space} \]
\[ T: \text{some mapping, } Tp \rightarrow p \ (p' = Tp) \]
sequence \( p, Tp, T(Tp), \ldots T^k(p) = \text{orbit of } p \)
\[ p' - p = Tp - p \]

A selectional model of evolution

\{ \text{variation} \}
\{ \text{selection} \}
\{ \text{heredity} \}
New reality TV show: “Survivor”

Transformational Evolution - the main sequence
### Table

<table>
<thead>
<tr>
<th></th>
<th>Mortal</th>
<th>Immortal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variational</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transformational</td>
<td></td>
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</tr>
</tbody>
</table>

### Fisher’s proof of mud slides

- \( x \) = 1st parent's deviation from mean
- \( y \) = 2nd parent's deviation from mean
- variance = \( E(x^2) \)

\[
\begin{align*}
\text{var} \left( \frac{1}{2} (x + y) \right) &= E \left( \left[ \frac{1}{2} (x^2 + y^2) \right]^2 \right) = E \left[ \frac{1}{4} (x^2 + 2xy + y^2) \right] = \\
&= E \left[ \frac{1}{4} (2x^2) \right] = \frac{1}{2} E(x^2)
\end{align*}
\]
Gregor Mendel saves Darwin?

A MATHEMATICIAN’S APOLOGY
G.H. Hardy / Foreword by C.P. Snow
**Terminology**

\(A, a = \text{different forms of the same gene}
AKA “alleles”
\(p, q = \text{frequencies of alleles}
\)

Two chromosomes in each eukaryotic cell - diploid - so possible genotypes are:

\(AA = \text{homozygote } A\)
\(Aa = \text{heterozygote } A, a\)
\(aa = \text{homozygote } a\)

**Hardy-Weinberg as the simplest evolutionary dynamical system: “Newton’s First Law” of evolutionary biology**

\[
\begin{align*}
5 \text{ AA} & \quad 2 \text{ Aa} \quad 3 \text{ aa} \\
0.50 & \quad 0.20 \quad 0.30
\end{align*}
\]

Result:

\[
\begin{align*}
0.36 \text{ AA} & \quad 0.48 \text{ Aa} \quad 0.16 \text{ aa} \\
0.24 \text{ Aa} & \quad 0.16 \text{ aa}
\end{align*}
\]
How realistic are the H-W assumptions? What biological model are we proposing?

Model myth vs. reality

Phenotypic form

Gene

Epistasis

Phenotypic form Gene Gene Gene Gene

Pleiotropy

Phenotypic form Gene Phenotypic form Phenotypic form
New reality TV show: “Survivor”

Survivor by the ratings numbers

<table>
<thead>
<tr>
<th>Genotypes:</th>
<th>AA</th>
<th>Aa</th>
<th>aa</th>
</tr>
</thead>
<tbody>
<tr>
<td>relative fitnesses:</td>
<td>1</td>
<td>1</td>
<td>0.7 (assume these are viabilities)</td>
</tr>
</tbody>
</table>

Initial gene frequency of A = 0.2
Initial genotype frequencies (from Hardy–Weinberg)
(newborns) 0.04 0.32 0.64
x 1 x 1 x 0.7
Survivors (these are relative viabilities)
0.04 + 0.32 + 0.448 = Total: 0.808

genotype frequencies among the survivors: (divide by the total)
0.0495 0.396 0.554

gene frequency
A: 0.0495 + 0.5 x 0.396 = 0.2475
a: 0.554 + 0.5 x 0.396 = 0.7525

genotype frequencies: (among newborns)
0.0613 0.3725 0.5663
The algebra of selection - J.B.S. Haldane, 1924

1 gene in 2 different forms (alleles)

<table>
<thead>
<tr>
<th>genotype</th>
<th>AA</th>
<th>Aa</th>
<th>aa</th>
</tr>
</thead>
<tbody>
<tr>
<td>frequency</td>
<td>$p^2$</td>
<td>$2pq$</td>
<td>$q^2$</td>
</tr>
<tr>
<td>relative fitness</td>
<td>$w_{11}$</td>
<td>$w_{12}$</td>
<td>$w_{22}$</td>
</tr>
<tr>
<td>after selection</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\bar{w} \equiv \text{mean fitness} \equiv p^2 w_{11} + 2p(1-p)w_{12} + (1-p)^2 w_{22}$

$\bar{w}_1 \equiv \text{mean fitness of } A \equiv p^2 w_{11} + p(1-p)w_{12}$

**Algebra II**

$\bar{w} \equiv \text{mean fitness} \equiv p^2 w_{11} + 2p(1-p)w_{12} + (1-p)^2 w_{22}$

$\bar{w}_1 \equiv \text{mean fitness of } A \equiv p^2 w_{11} + p(1-p)w_{12}$

fitness ratios (scaled):

$$\frac{p^2 w_{11}}{\bar{w}} : \frac{2pq w_{12}}{\bar{w}} : \frac{q^2 w_{22}}{\bar{w}}$$
Newton’s F=ma for evolutionary systems

Basic dynamical system map: compute p’ from p

\[ p' = \frac{A \text{ survivors}}{\text{all survivors}} = \frac{p^2 w_{11} + \frac{1}{2} \times 2p(1-p)w_{12}}{p^2 w_{11} + 2p(1-p)w_{12} + (1-p)^2 w_{11}} \]

\[ p' = \frac{p(pw_{11} + p(1-p)w_{12})}{p^2 w_{11} + 2p(1-p)w_{12} + (1-p)^2 w_{11}} = p \frac{\bar{w}_1}{w} \]

\[ p' - p = \frac{p(1-p)\{w_{11}p + w_{12}(1-2p) - w_{22}(1-p)\}}{p^2 w_{11} + 2p(1-p)w_{12} + (1-p)^2 w_{11}} \]

Dynamics: Compute Δp and also w vs. p

gives the ‘jet fuel’ formula for gene frequency change under selection

\[ p' - p = \frac{p\bar{w}_1}{\bar{w}} - \frac{p\bar{w}}{\bar{w}} \Rightarrow \Delta p = \frac{p(\bar{w}_1 - \bar{w})}{\bar{w}} \text{ with 2 alleles,} \]

\[ \bar{w} = p\bar{w}_1 + (1-p)\bar{w}_2, \text{ so substituting:} \]

\[ \Delta p = \frac{p(1-p)(\bar{w}_1 - \bar{w}_2)}{\bar{w}} \text{ and now substitute for } (\bar{w}_1 - \bar{w}_2) = \frac{d\bar{w}}{dp} = \]

\[ \Delta p = \frac{p(1-p)}{\bar{w}} \frac{d\bar{w}}{dp} = \frac{p(1-p)}{dp} \frac{d\ln(\bar{w})}{dp} \]
The jet fuel formula for ‘evolutionary change’

\[ \Delta p = \frac{p(1-p)}{\bar{w}} \frac{dw}{dp} \]

Amount of change in \( p \) (variance component)

Direction of change (slope of \( \bar{w} \) wrt \( p \), + or –)

The shape of things now
Mean fitness always increases...

\[
\Delta \bar{w} = 2p(1 - p)\{w_{11}p + w_{12}(1 - 2p) - w_{22}(1 - p)\}^2 \\
\times \{w_{11}p^2 + (w_{12} + \frac{1}{2}w_{11} + \frac{1}{2}w_{22})p(1 - p) + w_{22}(1 - p)^2\} \bar{w}^{-2}
\]

But...this is not the same things as maximizing fitness...

\[
dp = kp(1 - p)dt \text{ or } \\
\int \frac{1}{p(1 - p)}dp = dt \text{ so } \\
t(p_1, p_2) = \int_{p_1}^{p_2} \frac{1}{p(1 - p)}dp
\]

<table>
<thead>
<tr>
<th></th>
<th>0.001-0.01</th>
<th>0.01-0.1</th>
<th>0.1-0.5</th>
<th>0.5-0.9</th>
<th>0.9-0.99</th>
<th>0.99-0.999</th>
</tr>
</thead>
<tbody>
<tr>
<td>(w_{11} &gt; w_{12} &gt; w_{22})</td>
<td>462</td>
<td>480</td>
<td>439</td>
<td>439</td>
<td>480</td>
<td>462</td>
</tr>
<tr>
<td>dominance, (w_{11} = w_{12} &gt; w_{22})</td>
<td>232</td>
<td>250</td>
<td>309</td>
<td>1.020</td>
<td>9.240</td>
<td>90,231</td>
</tr>
</tbody>
</table>
The shape of things now
Solving the fundamental recurrence equation

\[ p' - p = \frac{p(1 - p)\{w_{11} p + w_{12}(1 - 2p) - w_{22}(1 - p)\}}{p^2 w_{11} + 2p(1 - p)w_{12} + (1 - p)^2 w_{11}} \]

\[
\begin{array}{ccc}
  w_{11} & w_{12} & w_{22} \\
  1+s & 1+sh & 1 \text{ e.g.,} \\
  1 & 1 & 1 \\
  (1+s) & (1+s) & 1 \text{ "dominance"} \\
  1 & (1+s) & (1+s) \text{ "recessive"} \\
  1+s & 1+sh & 1 \text{ "heterozygote over/under dominant"} \\
\end{array}
\]

NB: only a few special cases have explicit solutions!

Dynamical system analysis of ‘adaptive topography’ or mean fitness vs. \( p \)

\[ \bar{w} = p^2 [(w_{11} - w_{12}) + (w_{22} - w_{12})] - 2p(w_{11} - w_{12}) + w_{22} \]

\[ w_{12} = \frac{w_{11} + w_{22}}{2} \]
One locus, 2 allele case: 7 graphs, p vs. w

'Degenerate' case: quadratic mean fitness, with
\[ w_{12} = \frac{w_{11} + w_{22}}{2} \]

Dynamical system analysis of 'adaptive topography' or mean fitness vs. \( \hat{p} \) - nondegenerate case
\[ \bar{w} = p^2 \left[ (w_{11} - w_{12}) + (w_{22} - w_{12}) \right] - 2p(w_{11} - w_{12}) + w_{22} \]

so in this case, formula for \( \bar{w} \) is a parabola.

There are 4 further subcases, depending on the ordering of the \( w_{ij} \)

\[ \hat{p} = \frac{w_{22} - w_{12}}{(w_{11} - w_{12}) + (w_{22} - w_{12})} \]
The four nonlinear cases - selection at one locus, 2 alleles - adaptive topography

\[ \hat{p} = \frac{w_{22} - w_{12}}{(w_{11} - w_{12}) + (w_{22} - w_{12})} = \frac{w_{22} - w_{12}}{w_{22} - w_{12}} = 1 \]

underdominance

overdominance