The Physics of Life: Spatial Population Genetics

I. Introduction to spatial population genetics

II. Pushed genetic waves and antagonistic interactions

III. Microbial interactions and expansions on liquid substrates
I. Introduction to spatial population genetics

Humans out of Africa; in 500 generations...

Large mammals expand over $\sim 10^4$ km

Bacteria (in a Petri dish) expand $\sim 1$ cm

K. Korolev et al., Reviews of Modern Physics 82, 1691 (2010)
II. **Pushed genetic waves and antagonistic interactions: Hybrid zones**

- Hybrid zones are narrow regions in which genetically distinct populations meet, mate and produce hybrids. Hundreds of examples known. (e.g., the grasshopper *Podisma pedestrís*, the butterfly *Heliconis.*) Hybrid zones can be a few hundred meters thick and hundreds of kilometers long.

Inferred profile from electrophoretic variations across the hybrid zone of the toads *Bombina bombina* and *Bombina variegata* near Cracow, Poland.

- Which way the interface moves depends on more than just the selective advantage – for example, recombination near the interface can break up favorable clusters of genes.

- In some cases, boundaries can exhibit a kind of surface tension, as well as a pressure to advance in a particular direction. This may promote sympatric speciation.
III. Microbial interactions and expansions on liquid substrates

... life probably evolved first in a liquid environment

• ~2-3 billion years ago, water covered most of the earth

• Fossilized, oxygen-producing cyanobacteria have been dated at ~2 billion years ago.

• Oxygenic cyanobacteria transformed the atmosphere via photosynthesis

• Spatial growth and evolutionary competition took place in liquid environments at both high and low Reynolds numbers

• These photosynthetic organisms may control their height to resist down welling currents and stay close to the ocean surface.

Cyanobacterium Synechococcus

www.dr-ralf-wagner.de/Blaualgen-englisch.htm

Bloom of cyanobacteria in Lake Atitlán, Guatemala

NASA Earth observatory
Range Expansions with Competition or Cooperation

Large mammals expand over $\sim 10^4$ km

Bacteria (in a Petri dish) expand $\sim 1$ cm

Red and Green Strains….
1. Could be neutral….
2. Could have different doubling times
3. One or both could secrete toxins that impede the other…
4. One or both could secrete amino acids useful to the other: mutualism
Gene Surfing and Survival of the Luckiest

Mutations and competition in a spreading population

FAS Center for Systems Biology

Lots of help in the lab from Pascal Hersen and Sharad Ramanathan

Oskar Hallatschek

Kirill Korolev

vs.
Gene Surfing and Survival of the Luckiest Mutations and competition in a spreading population

Surfing on the Einsbach, Englischer Garten, Munich...

Successful....

Unsuccessful....
Fisher Waves and Population Dynamics

\[ c(t) = \text{population of species at time } t \text{ in region } \Omega \]

\[ \frac{dc(t)}{dt} = \text{births} - \text{deaths} + \text{saturation} + \text{migration} \]

1798 T.R. Matthus

\[ \frac{dc(t)}{dt} = ac(t), \ a > 0 \]

1836 P.F. Verhulst

\[ \frac{dc(t)}{dt} = ac(t) - bc^2(t) \]

\[ c(t) = \frac{c(0)e^{at}}{1 + (c(0)b/a)(e^{at} - 1)} \]

stable population size: \( c^* = \frac{a}{b} \)

1937 R.A. Fisher, Kolmogorov et al.

\[ c = c(\vec{r}, t) \]

\[ \frac{\partial c(\vec{r}, t)}{\partial t} = D \nabla^2 c(\vec{r}, t) + ac(\vec{r}, t) - bc^2(\vec{r}, t) \]

J. Maynard Smith, Evolutionary Genetics
Wave Solutions to the Fisher-Kolmogorov et al. Equation

in one dimension:

\[
\frac{\partial c(x,t)}{\partial t} = D \frac{\partial^2 c(x,t)}{\partial x^2} + a c(x,t) - b c^2(x,t)
\]

* If \( c(x,0) \) is small \( (c(x,0) \ll \bar{c} = c^* = \frac{a}{b}) \), then early time behavior is given by the solution of the linear equation

\[
\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} + a c
\]

Namely,

\[
c(x,t) = c_0 e^{at} \frac{1}{\sqrt{4\pi Dt}} e^{-\frac{x^2}{4Dt}}
\]

\( \Rightarrow c(x,t) \) spreads out diffusively, but grows up exponentially as well...

\[
\int c(x,t) dx = c_0 e^{at}
\]

\( \Rightarrow c(x,t) \)

\( \Rightarrow \sqrt{2Dt} \)

\( \Rightarrow x \)

* but eventually \( c(x,t) \ll c^* \) & new behavior arises

\( \Rightarrow V \)

\( \Rightarrow W \)

\( \Rightarrow \frac{v}{w} = \frac{?}{?} \)
Dynamical Systems approach

Look for solutions of \( \frac{d}{dt} = G \) that interpolate

from \( c = c^* = \frac{a}{b} \) to \( c = 0 \) in the form of

a wave moving from left to right

\[
\begin{align*}
c^* &= \frac{a}{b} \\
\end{align*}
\]

\[
\begin{align*}
f(x,t) &= f(x-\nu t) = f(z) \\
\lim_{z \to -\infty} f(z) &= \frac{a}{b} \\
\lim_{z \to \infty} f(z) &= 0 \\
\end{align*}
\]

\[
\Rightarrow -\nu f''(z) = Df''(z) + af(z) - bf'^2(z)
\]

Regard \( z \) as a time-like variable and define a "momentum" variable \( g(z) = \frac{df}{dz} \)

Then \( (*) \) can be written as two ordinary differential equations

\[
\begin{align*}
g'(z) &= -\nu g(z) - \frac{a}{D} f(z) + \frac{b}{D} f'^2(z) \\
\end{align*}
\]

\[
\frac{df}{dz} = g(z)
\]

Fixed points are \((f^*, g^*) = (0, 0) \) & \((f^*, g^*) = (\frac{a}{b}, 0)\)

Phase Portrait

The solution we want is clearly the trajectory connecting the hyperbolic fixed point \((0, y_0)\) to the origin.
**Velocity selection problem**

However a solution seems to exist for a range of $V$'s!

* Can get a bound on $v$ by looking at the (right) foot of the wave & trying to solve the linear equation with $c(x,t) = c_0 e^{\frac{(x-vt)}{\xi}}$

$\Rightarrow \frac{V}{\xi} = \frac{D}{\xi^2} + a \Rightarrow V = \frac{D}{\xi^2} + a \xi$

"dispersion relation"

$\xi_{min} = \sqrt{\frac{D}{a}}$

$V_{min} = 2 \sqrt{Da}$

* Kolmogorov showed that the asymptotic velocities (moving right & left) for any initial condition with finite support is in fact $V = V_{min} = 2\sqrt{Da}$

$\xi = \xi_{min} = \sqrt{\frac{D}{a}}$

* More generally, velocity depends on the way $f(z)$ behaves as $z \rightarrow \pm \infty$

* Note that two exponential lengths appear for $V > V_{min}$.
Population & Genetic Waves In One Dimension

(R. A. Fisher, Kolmogorov-Petrovsky-Piscounov, 1937)

\[
\frac{\partial}{\partial t} c(x, t) = D \frac{\partial^2}{\partial x^2} c(x, t) + ac(x, t)[1 - bc(x, t)/a]; \quad \text{let } c(x, t) = f(x - vt)
\]

Schematic time development of a wavefront solution of Fisher’s equation on the infinite line. (J.D. Murray, Mathematical Biology)

Interface velocity = \(2\sqrt{Da}\) \quad Interface width = \(\sqrt{D/a}\)
*Genetic drift for a neutral mutation, (M. Kimura)*

Finite populations go to fixation for long times (using, e.g., Fisher-Wright population sampling)

\[
\frac{\partial u(p,t)}{\partial t} = \frac{\partial^2 [D_g u(p,t)]}{\partial p^2}
\]

\[
D_g(p) = \frac{p(1-p)}{2N}
\]

\[
\frac{\partial p(t)}{\partial t} = \sqrt{p(t)(1-p(t))}/N\quad \Gamma(t)
\]

\[
<\Gamma(t)\Gamma(t') >= \delta(t-t') \quad \text{(Ito calculus)}
\]
Fisher-Wright binomial statistics used:

\[ \frac{\partial u(p,t)}{\partial t} = \frac{\partial^2}{\partial p^2} \left[ \frac{p(1-p)}{4N} u(p,t) \right] \]

Allele frequencies diffuse due to genetic drift ....
M. Kimura, Genetics 47, 713 (1962)

u(p,t) = probability allele A has frequency p at time t.

See Populus program...

* Finite populations go to fixation for long times...

* All finite populations eventually fixed with homozygous population of all (a/a) or all (A/A)
FIGURE 3.4  Random genetic drift in 107 actual populations of *Drosophila melanogaster*. Each of the initial 107 populations consisted of 16 $bw^{75}/bw$ heterozygotes ($N = 16$; $bw =$ brown eyes). From among the progeny in each generation, eight males and eight females were chosen at random to be the parents of the next generation. The horizontal axis of each curve gives the number of $bw^{75}$ alleles in the population, and the vertical axis gives the corresponding number of populations. (Data from Buri 1956.)
**Numerical solution by Kimura (1955)**

of Kolmogorov forward equation...

\[
\frac{\partial u(x, p, t)}{\partial t} = \frac{1}{4N} \left[ \frac{x(1-x)}{\partial x^2} u(x, p, t) \right]
\]

\[u(x, p, t=0) = \delta(x-p)\]

**Figure 3.7** Kimura’s (1955) solution to the diffusion equation for the particular case of \(N = 16\). This is the three-dimensional view of Figure 3.6, and represents the diffusion approximation to the exact solution obtained from the Wright-Fisher model in Figure 3.5.
**Genetic drift for a neutral mutation, (M. Kimura)**

Finite populations go to fixation for long times (using, e.g., Fisher-Wright population sampling)

\[
\frac{\partial u(p,t)}{\partial t} = \frac{\partial^2 [D_g u(p,t)]}{\partial p^2}
\]

\[
D_g(p) = p(1-p)/(4N)
\]

\(u(p,t)\) = probability allele \(A\) has frequency \(p\) at time \(t\).

Finite populations go to fixation for long times

Probability of fixation of a single neutral mutation in a population of size \(N\) is just \(1/N\)

But \(N\) is small in the vicinity of an expanding population front!
Successful Surfing (1d)

\[ c(x,t), \text{ population density} \]

\[ c_\infty \]

\[ x, \text{ comoving frame} \]

(O. Hallatschek)
Successful Surfing (1d)

\[ c(x, t), \text{ population density} \]

\[ C_\infty \]

\[ x, \text{ comoving frame} \]
Successful Surfing (1d)

\[ c(x, t), \text{ population density} \]
Successful Surfing (1d)

c(x,t), population density

$C_\infty$
Successful Surfing (1d)

\[ c(x,t), \text{ population density} \]
Often however ...

\[ c(x, t), \text{ population density} \]

\[ C_\infty \]

\[ x, \text{ comoving frame} \]

(O. Hallatschek)
Often however ...

\[ c(x,t), \text{ population density} \]
Often however ...

\[ c(x,t) \], population density

\[ C_\infty \]

\[ x \], comoving frame
Often however ...

$c(x,t)$, population density

$c_{\infty}$

$x$, comoving frame
Often however ...

\[ c(x, t), \text{ population density} \]

\[ C_\infty \]

\[ x, \text{ comoving frame} \]

... surfing is not achieved!
Gene Surfing in nonmotile E. coli

(thanks to Tom Shimizu, Berg Lab, for strains)

HCB1550/pVS130 Background DH5α

HCB1553/pVS133 Background DH5α

50-50 mixture, 1550/1553
Gene Surfing in nonmotile E. coli

50-50 mixture, 1550/1553

Cyan → Red

(thanks to Tom Shimizu, Berg Lab, for strains)
Genetic demixing in non-motile E. coli

(thanks to Tom Shimizu, Berg Lab, for strains)

Ori pBR

PTec99A: \text{yfp}^{A206K}

PTec99A: \text{ecfp}^{A206K}

Amp(R)

Ori pBR

HCB1553/pVS133
Background DH5α

HCB1550/pVS130
Background DH5α

P Tec

50-50 mixture, 1550/1553

Cyan \rightarrow Red
Gene surfing in the dilute limit: “survival of the luckiest”

95%-5% mixture, founder population ~ 500

98%-2% mixture, founder population ~ 5000
What would happen if we could “replay the tape of life”?

*E. coli* range expansions:
can infer the radius $R_0$
of the homeland from
data at the boundary:

$$N_{sec} = \sqrt{\pi R_0 v / 2D_w}$$
What would happen if we could “replay the tape of life”?

“Survival of the luckiest”
What would happen if we could “replay the tape of life”? 

Chiral range expansions
Linear Inoculations: “Genetic demixing” results from number fluctuations at the frontier

View from the top: razor blade inoculation

Side view as the population wave advances:

View of a “dust mote” on a Petri dish as the wave advances...

Fisher genetic waves
Thank you!

http://streetanatomy.com