Accumulation of Beneficial Mutations in Low Dimensions

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EMORY
Evolutionary dynamics

• Rate of adaptation influenced by
  • Fitness Landscape
  • Time dependence
  • Spatial Structure
  • Heterogeneity
Evolutionary dynamics

- Rate of adaptation influenced by
  - Fitness Landscape
  - Time dependence
  - Spatial Structure
  - Heterogeneity
simple model

- $N$ (asexual) organisms
- For each generation, random number of kids
- fitness = mean number kids
- keep total $N$ fixed
- if $p(n) \sim$ poisson, conditional on $N$ being fixed $\rightarrow$ multinomial

- kids inherit fitness
mutation

- single mutant fitness $1 + s$
Fixation

• If mutant has fitness = 1 + s

• Then probability of fixation = 2s (for small s, large Ns)

• example: s = 0.05, probability of mutation dying is 90%!
Multiple mutations

- beneficial mutations arrive with some rate $U$, per individual
- $\log f' = \log f + s$
- $s \sim 0.01$
Mutation limited evolution

- fixation time $\ll$ mutation time

\[
\frac{2}{s} \ln N \ll \frac{1}{2sUN} \quad R = \frac{1}{t_{mut}} = 2sUN
\]
competing mutations

- fixation time \sim \text{mutation time}
Clonal Interference

- mutation A established
- before A fixates, B established
- who wins? A or B?
- one mutation is “wasted”
- probability of fixation reduced
Multiple Mutation Effect

- A and B compete
- A -> AC, AC has a better chance of winning
- mutation C is not wasted
Rate of Fixation

• With competing mutations:
  • $R$ is sublinear with $N$

• Bacterial experiments show multiple competing mutations are present

• distributed $s$? changing $U$? landscape?
Spatial Structure

- competition only between neighbors
- desegregation of 2 types

Hallatschek and Nelson, Physics Today 2009
Our model

• one dimension: one organism per site

• kids can only choose one of two parents:

\[
\begin{array}{cccc}
1.00 & 1.01 & 1.00 & 1.00 \\
\end{array}
\]

• \( p = 1.01/2.01 \)

• boundaries spread with speed \( s/2 \)
Surface growth

Log fitness

Lattice position

time

width
Surface growth

- width = std deviation of log f
- KPZ exponents: $\beta = \frac{1}{3}$, $\alpha = \frac{1}{2}$
Our model

• on a lattice, fixation probability is the same as in zero-D:
  • $p = 2s$
  • $R = 2sUN$ in mutation limited regime
• fixation time:
  • zero-D: $2/s \ln N$
  • one-D: $2/s N$
competition slows evolution

Fixation rate vs. Mutation rate $U$

- $\frac{1}{4N \log N}$
- $\frac{1}{4N^2}$
- zero-D interference
- zero-D
- ID lattice
- mutation limited

$N=512$
speed versus N

$U = 10^{-5}$

Fixation rate $\pi$

Population size $N$

- zero-D
- ID lattice

$x \times 10^{-4}$
Speed limit

- rate saturates with system size
- holds for:
  - distributed s
  - different wave speed
  - planar habitats

Martens, Hallatschek, Genetics, 2011
Summary

- Spatial structure increases fixation times. Threshold for interference lowered. Rate of fixation saturates.
- Rate of fixation reduced in bacterial experiment.
- Assumptions: homogenous spatial structure, no rough fitness landscape (epistasis), constant selection pressure.
- Harmful mutations?
Mixing

- competition/interference alleviated by:
  - spatial mixing
  - recombination

Martens, Hallatschek, Genetics, 2011