Population Genetics of low-probability transitions

Stephen Proulx
UC Santa Barbara
Frequency/Density Dependence

- Alee effect
- Negative Frequency Dependence
- Stochastic selection
Stochastic selection

- Transitions between population states (fixation).
- Can lead to lower than “neutral” transition rates.
- In specific models it can also lead to alternative stable states.
Variability

Individual | Generational

Infinite pop size
- Max arithmetic mean
- Selection to reduce variance
  BUT: Emergent freq dep
  Common allele favored

Finite pop size
- Max geometric mean
- Selection to reduce variance
  BUT: Emergent freq dep
  Rare allele favored
\[ E[\Delta p] \approx \frac{p(1-p)}{\mu_1 p + \mu_2 (1-p)} \left( (\mu_1 - \mu_2) + \left( \frac{\mu_1}{\sigma_1^2} - \frac{\mu_2}{\sigma_2^2} \right) \left( \frac{\sigma_1^2 \sigma_2^2}{N(\mu_1 p + \mu_2 (1-p))^2} \right) \right) + \text{HOT} \]

Stochastic Price Equation

Rice 2007

\[ E[\Delta p] \approx \frac{\text{cov}(i, \mu_i)}{H(\bar{w})} - \frac{\text{cov}(i, \sigma_i^2)}{N \hat{\bar{w}}^2} \]

\[ = \frac{p(1-p)(\mu_1 - \mu_2)}{H(\bar{w})} - \frac{p(1-p)(\sigma_1^2 - \sigma_2^2)}{N(\mu_1 p + \mu_2 (1-p))^2} + \text{HOT} \]

Gillespie diffusion approx

\[ \mu_2 - \frac{\sigma_2^2}{n} < \mu_1 - \frac{\sigma_1^2}{n}. \]
• Rare strategy is at a disadvantage
• makes transition between states more difficult
• coalescent: (Taylor & Etheridge)

• Same mean: lower variance favored
• Higher mean is better
• If mean and variance both differ, then frequency dependence emerges
\[ p_{t+1} = p_t s_m \xi_t + \frac{p_t n_m}{p_t n_m + (1 - p_t)n_r} \left(1 - p_t s_m \xi_t - (1 - p_t)s_r \xi_t \right) \]

Surviving adults  
pop gen of new adults  
New empty space from dead adults
Lottery Competition

\[
p_{t+1} = p_t s_m \xi_t + \frac{p_t n_m}{p_t n_m + (1 - p_t) n_r} \left(1 - p_t s_m \xi_t - (1 - p_t) s_r \xi_t \right)
\]
Small population size

Large population size

Initial population state

Final population state
Ancestral gene functions in two contexts

Mutations can alter coding region

Mutations can alter regulatory region

Both kinds of mutation may affect a single allele
The DDC Model

All transitions are circum-neutral

Absorbing states

Force et al 1999
Proulx 2012
Matrix Model for the DDC Process

Proulx 2012

How many times does the process have to start over before “successful” duplication?

\[
\begin{pmatrix}
A & A|A & s_1|A & s_1|s_2 \\
1 - \mu_d & \mu_d & 0 & 0 \\
2\mu_k & -2\mu_k - 2\mu_s + 1 & 2\mu_s & 0 \\
\mu_k & 0 & -\mu_k - \frac{\mu_s}{2} + 1 & \frac{\mu_s}{2} \\
0 & 0 & 0 & 1 \\
\end{pmatrix}
\]
Estimating the Neutral Duplication Time

\[ T_{DDC} = 2N((2\gamma + 1)(2\gamma + 3)) + \frac{4\gamma^2 + 8\gamma + 7}{2\mu} \]

Drift to fixation is slower in large pops

High silencing rate means the cycle has to be repeated

Higher \( \mu \) buys more lottery tickets
Using the Origin-Fixation framework for gene interaction evolution

• Taking a step towards non-equilibrium dynamics

• Probability of a substitution may depend on an additional process component (mutation selection balance, stochastic tunneling)

• Likewise, a stable polymorphism might be an intermediate state from which further mutations can invade/replace

Example from Proulx 2012
Iwasa et al., 2004b. Stochastic tunnels …

Weissman et al TPB 2009

![Graph showing fitness vs. number of mutations with markers μ₀, μ₁, and μ₂.](image)
Mutation Network
Mutation Network

Good combination

X11

X10

X01

X00

X20

X02

X22
Frequency Dynamics

N=10^5

Recessive-lethal blinks in and out
Frequency Dynamics

- Black: neutral duplicate, transient
- Pink: recessive lethal
Frequency Dynamics

Secondary mutant appears
Frequency Dynamics

If one is good, two is even better!
Frequency Dynamics

Recombination occurs (could fix)
Frequency Dynamics

Mutation improves red function
Second mutation improves blue function and will become fixed
Approximate Waiting Times

Recessive Lethal
Tunneling
Duplication
Modification of second copy
Recombination

\[
T_{P_{1|2|3}} = \frac{1}{2} \left( \frac{1}{\bar{p}_s N \mu_c 2s_{sc}} + \frac{1}{p_{sc} N \mu_d 2s_{sc1|sc1}} + \frac{1}{(\bar{p}_s N \mu_c 2s_{sc}) + (p_{sc} N \mu_d 2s_{sc1|sc1})} \right)
\]

\[
+ \frac{1}{p_{sc1|sc1} (1 - p_{sc1|sc1}) N r 2s_{A|sc1}}.
\]

(7)
Stochastic Tuneling in general

- Cancer: Multiple mutations required, causes a difficult to reverse phase change in the organisms organization
- Invasion of diseases across species boundaries
- Colonization of sink habitats
Feedback through the environment

Dieckmann and Doebeli, 1999, Nature

Asexual

Sexual
Thanks!!!

- NSF
- Fred Adler
- Troy Day
- Patrick Phillips
- Kelly Thomasson
Three questions: I’m so confused…

• How can we incorporate analyses of non-equilibrium dynamics *and* be able to make general theory?
• How often do ecological feedbacks results in bi-stable evolutionary states?