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NEARLY CRITICAL BRANCHING PROCESSES
WITH ESCAPE MUTANTS

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BGW processes with mutation

Nearly critical case

Probability of escape

Mutation skeleton

Time to escape

Neutral mutation case

BGW PROCESSES WITH MUTATION

Bienaymé-Galton-Watson process $\{Z(n)\}_{n \geq 0}$

starts from one particle $Z(0) = 1$

particles reproduce independently

common offspring number distribution $p_k = \mathbb{P}(Z(1) = k)$

Extinction or escape from extinction depends on $m = \sum kp_k$

subcritical $m < 1 \Rightarrow$ extinction with probability 1

critical $m = 1, p_1 \neq 1 \Rightarrow$ extinction with probability 1

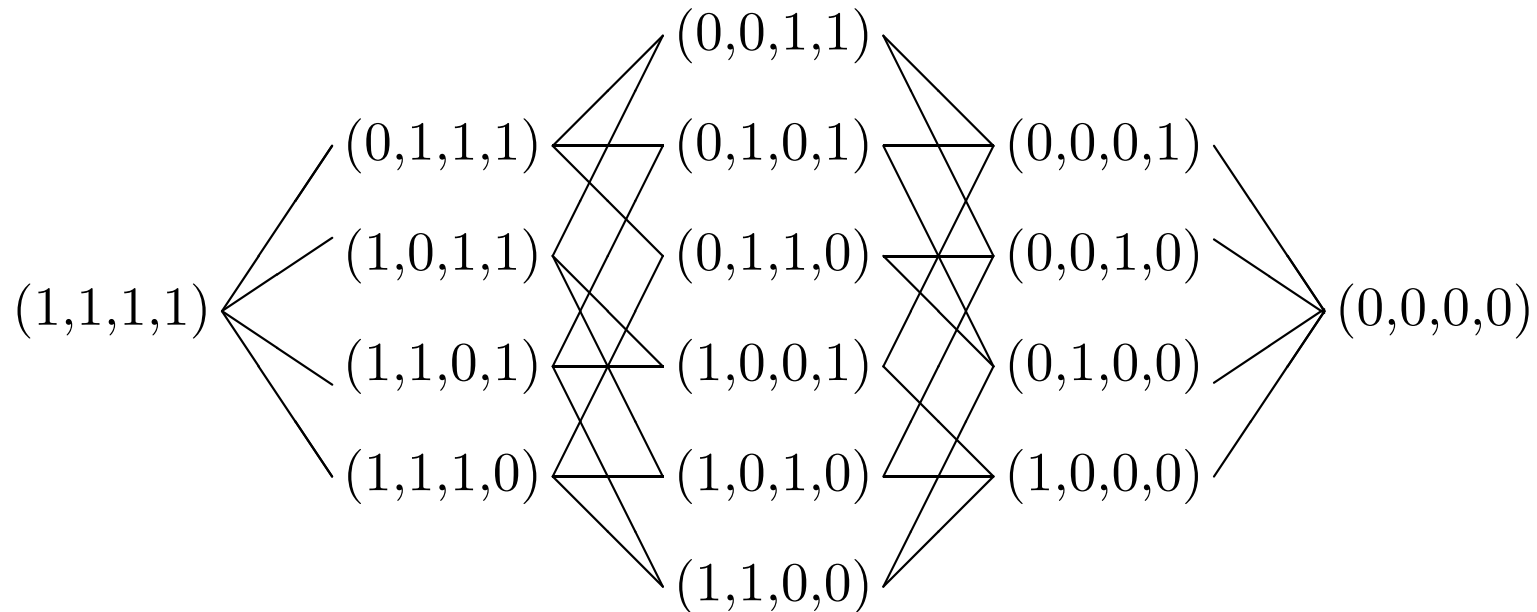
supercritical $m > 1 \Rightarrow$ escape with positive probability

S.Sagitov, M.C.Serra (2009) Multitype BGW processes escaping extinction

have studied the SUBCRITICAL case with escape mutants motivated by

*Y.Iwasa, F.Michor, M.A.Nowak (2004) Evolutionary dynamics of invasion
and escape*

BGW PROCESSES WITH MUTATION



The network of 0-1 sequences of length $L = 4$. Here the edges represent single point mutations of probability $\mu(1 - \mu)^{L-1}$. More generally, mutation between two given sequences which differ at i sites has probability $\mu^i(1 - \mu)^{L-i}$.

This talk focuses on the simple case $L = 1$

BGW PROCESSES WITH MUTATION

Conditional mutation probability

$$\mu \cdot a_k = \mathbb{P}(\text{mutation of a particle given it has } k \text{ siblings})$$

Assume $\sum k p_k a_k = 1$, then

μ is the total mutation rate per particle per generation

For a given escape probability α for a mutant particle describe

- asymptotical probability of escape as $\mu \rightarrow 0$
- the point process of mutation times
- time to escape = time to the first escape mutant

A small probability of back mutation does not change asymptotic results

NEARLY CRITICAL CASE, PROBABILITY OF ESCAPE

The critical reproduction law $\{p_k\}$ with mean $m = 1$ and variance σ^2 .

The nearly critical reproduction law $p_k^{(\mu)} \rightarrow p_k$ with mean $m^{(\mu)} \rightarrow 1$.

$$\text{Key assumption: } \frac{m^{(\mu)} - 1}{\sqrt{\mu}} \rightarrow \gamma \in (-\infty, \infty)$$

For a given escape probability α for a mutant particle

$$\mathbb{P}^\mu(\text{escape}) \sim c_\alpha \sqrt{\mu}$$

where

$$c_\alpha = \frac{\gamma + \sqrt{\gamma^2 + 2\alpha\sigma^2}}{\sigma^2}$$

There are two mutually exclusive ways to escape

r-escape: reproductive success of the wild-type particles

m-escape: escape solely through mutation

If $\alpha = 0$, then no m-escape and (Haldane's sieve)

$$\mathbb{P}^\mu(\text{r-escape}) \sim c_0 \sqrt{\mu}, \quad c_0 = \begin{cases} 0, & \text{if } \gamma \leq 0 \\ \frac{2\gamma}{\sigma^2}, & \text{if } \gamma > 0 \end{cases}$$

Thus (notice the symmetry between the sub- and supercritical cases: the latter conditioned on extinction becomes the former),

$$\mathbb{P}^\mu(\text{m-escape}) \sim (c_\alpha - c_0) \sqrt{\mu}, \quad c_\alpha - c_0 = \frac{\sqrt{\gamma^2 + 2\alpha\sigma^2} - |\gamma|}{\sigma^2}$$

If $\alpha = 1$, then $\{\text{escape}\} = \{\text{r-escape}\} \cup \{\text{mutation}\} = \{\text{mutation}\}$

and therefore for any α

$$\mathbb{P}^\mu(\text{mutation}) \sim c_1 \sqrt{\mu}$$

$$\mathbb{P}^\mu(\text{mutation without r-escape}) \sim (c_1 - c_0) \sqrt{\mu}$$

Wild type particles form a two-type BGW process $(Z_m(n), Z_u(n))$:

m-particles that have a mutation in their line of descent and
u-particles that have no mutation in their line of descent

$$\mathbb{P}^\mu(Z_m(0) = 1) = \mathbb{P}^\mu(\text{mutation}), \quad \mathbb{P}^\mu(Z_u(0) = 1) = \mathbb{P}^\mu(\text{no mutation})$$

The offspring distribution for a u-particle

$$\mathbb{E}_u^\mu \left(s_m^{Z_m(1)} s_u^{Z_u(1)} \right) \rightarrow f(s_u) = \sum p_k s_u^k$$

Probability generating functions for *size-biased* distributions describing the number of siblings to ...

- $f_1(s) = f'(s) = \sum k p_k s^{k-1}$... one sampled particle
- $f_2(s) = \frac{f''(s)}{f''(1)} = \frac{1}{\sigma^2} \sum k(k-1) p_k s^{k-2}$... two sampled siblings
- $\psi(s) = \sum k p_k a_k s^{k-1}$... a mutant

The offspring distribution for an m-particle

$$\lambda_1 = \sqrt{\gamma^2 + 2\sigma^2}$$

$$\begin{aligned} \mathbb{E}_m^\mu \left(s_m^{Z_m(1)} s_u^{Z_u(1)} \right) &= (1 - \lambda_1 \sqrt{\mu}) s_m f_1^{(\mu)}(s_u) \\ &\quad + \lambda_1 \sqrt{\mu} \left\{ (1 - p)\psi(s_u) + p s_m^2 f_2(s_u) \right\} + o(\sqrt{\mu}) \end{aligned}$$

Mutation skeleton is the continuous time BP formed by m-particles:

exponentially distributed life times with parameter $\lambda_1 \sqrt{\mu}$

0 daughters with probab. $1 - p = \frac{1}{2} - \frac{\gamma}{2\lambda_1}$ (a mutation event)

2 daughters with probability $p = \frac{1}{2} + \frac{\gamma}{2\lambda_1}$

size-biased numbers of u-offspring given by $f_1^{(\mu)}(s) \rightarrow f_1(s)$,

$\psi(s)$, $f_2(s)$

If $\gamma > 0$, the mutation skeleton survives forever with probability

$$\frac{2\gamma}{\lambda_1 + \gamma} = \frac{c_0}{c_1} = \lim_{\mu \rightarrow 0} \mathbb{P}^\mu(\text{r-escape} | \text{mutation})$$

Let T_α be the time to escape and put

$$X(t) = \lim_{\mu \rightarrow 0} \mathbb{P}_m^\mu(T_\alpha > t/\sqrt{\mu})$$

Due to the branching property of the mutation skeleton

$$X(t) = e^{-\lambda_1 t} + (1-p)(1-e^{-\lambda_1 t})(1-\alpha) + p \int_0^t X^2(t-u)\lambda_1 e^{-\lambda_1 u} du$$

where $p = \frac{1}{2} + \frac{\gamma}{2\lambda_1}$. Multiply by $e^{\lambda_1 t}$ and take the derivative over t

$$X'(t) + \lambda_1 X(t) = (1-p)(1-\alpha)\lambda_1 + \lambda_1 p X^2(t)$$

Substitution $Z(t) = \lambda_1 p \left(\frac{1}{2p} - X(t) \right)$ gives

$$Z'(t) = \frac{\gamma^2 + 2\alpha\sigma^2}{4} - Z^2(t) \text{ with } Z(0) = -\frac{\gamma}{2}$$

After solving this ode we derive

$$1 - X(t) = \frac{c_\alpha}{c_1} \cdot \frac{1 - e^{-\lambda_\alpha t}}{1 + \frac{\lambda_\alpha + \gamma}{\lambda_\alpha - \gamma} e^{-\lambda_\alpha t}}$$

with

$$\lambda_\alpha = \sqrt{\gamma^2 + 2\alpha\sigma^2}, \quad c_\alpha = \frac{\gamma + \lambda_\alpha}{\sigma^2}$$

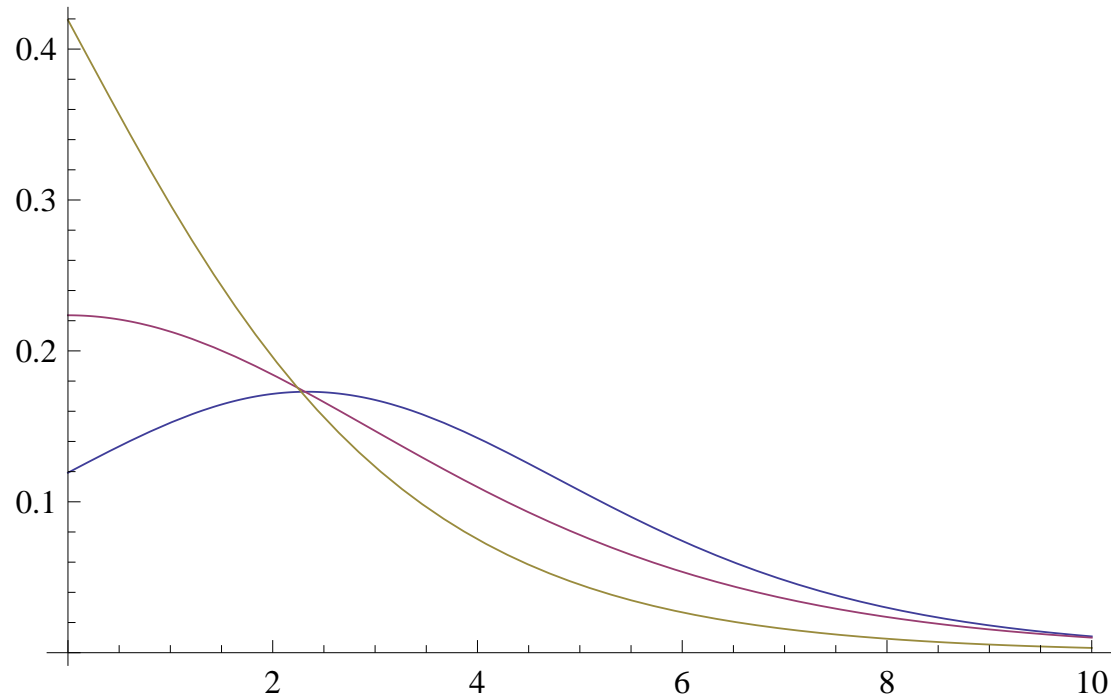
It follows

$$\mathbb{P}^\mu(T_\alpha \leq t/\sqrt{\mu}) \sim c_\alpha \sqrt{\mu} \cdot \frac{1 - e^{-\lambda_\alpha t}}{1 + \frac{\lambda_\alpha + \gamma}{\lambda_\alpha - \gamma} e^{-\lambda_\alpha t}}$$

Thus the *scaled time to escape* $T_\alpha \sqrt{\mu}$ *conditioned on escape* has a limit distribution with density

$$\phi(t) = 2(\lambda_\alpha - \gamma)e^{-\lambda_\alpha t} \left(\frac{\lambda_\alpha}{\lambda_\alpha - \gamma + (\lambda_\alpha + \gamma)e^{-\lambda_\alpha t}} \right)^2$$

TIME TO ESCAPE



Three density curves $\phi(t)$: subcritical, critical, and supercritical

if $\gamma \geq 0$, then $\phi(t)$ has its maximum at $t^* = \frac{1}{\lambda_\alpha} \ln \frac{\lambda_\alpha + \gamma}{\lambda_\alpha - \gamma}$

Parameter values: $\gamma = \pm 0.3$, $\alpha = 0.1$, $\sigma = 1$.

NEUTRAL MUTATION CASE

For a given escape probability α for a mutant particle

$$\mathbb{P}^\mu(\text{escape}) \sim \sqrt{\mu} \cdot \frac{\gamma + \sqrt{\gamma^2 + 2\alpha\sigma^2}}{\sigma^2}$$

If mutants form a nearly critical BP with $\alpha \sim c\sqrt{\mu}$, then

$$\frac{\gamma + \sqrt{\gamma^2 + 2\alpha\sigma^2}}{\sigma^2} \sim \begin{cases} \frac{2\gamma}{\sigma^2}, & \text{if } \gamma > 0 \\ \frac{\sqrt{2c}}{\sigma} \cdot \mu^{1/4}, & \text{if } \gamma = 0 \\ \frac{c}{|\gamma|} \cdot \sqrt{\mu}, & \text{if } \gamma < 0 \end{cases}$$

and

$$\mathbb{P}^\mu(\text{escape with neutral mutation}) \sim \begin{cases} \frac{2\gamma}{\sigma^2} \cdot \sqrt{\mu}, & \text{if } \gamma > 0 \\ \frac{\sqrt{2c}}{\sigma} \cdot \mu^{3/4}, & \text{if } \gamma = 0 \\ \frac{c}{|\gamma|} \cdot \mu, & \text{if } \gamma < 0 \end{cases}$$

NEUTRAL MUTATION CASE

Related work:

J.Schweinsberg (2008) The waiting time for m mutations

Moran model the same mutation rate for m consecutive mutations.

Varying mutation rates in the Moran model:

R.Durrett, D.Schmidt, J.Schweinsberg (2009) A waiting time problem arising from the study of multi-stage carcinogenesis

Motivated by

Y.Iwasa, F.Michor, M.A.Nowak (2004) Stochastic tunnels in evolutionary dynamics

THANK YOU!