A multi-type Λ-coalescent with mutation and selection.

Bob Griffiths

Department of Statistics
University of Oxford

Branching processes and their applications
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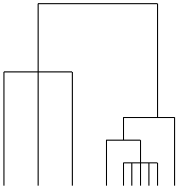
Joint research with Matthias Birkner,
Alison Etheridge and Luke Miller

Neutral Λ-coalescent



Multiple merger rate of k lineages while n individuals is

$$\lambda_{nk} = \int_0^1 y^k (1-y)^{n-k} \frac{F(dy)}{y^2},\ 2 \le k \le n$$

Pitman (1999) and Sagitov (1999).

Examples: F is Beta(2-γ,γ), $\gamma \in (0,2)$; F is uniform in (0,1); F has one atom at $\psi \in (0,1)$; F has one atom at 0.

Λ-Fleming-Viot population

$\mathbf{X}(t) = \big(X_1(t), \dots, X_d(t)\big)_{t \geq 0}$ are the frequencies of types in $[d] = \{1, \dots, d\}$.

The state space of $\{\mathbf{X}(t)\}_{t\geq 0}$ is $\Delta_\circ^d = \{\mathbf{x} \in \mathbb{R}_+^d; |\mathbf{x}| = 1\}$.

The generator of the process acting on $g \in C^2(\Delta_\circ^d)$ is

$$\mathcal{L}g(\mathbf{x}) = \int_{[0,1]} \sum_{i \in [d]} x_i \big[g(\mathbf{x}(1-y) + ye_i) - g(\mathbf{x})\big] \frac{F(dy)}{y^2}$$

where F is a probability measure. Birkner and Blath (2009).

Choose a type i individual with probability x_i and add in y individuals of the same type at rate $F(dy)/y^2$. Rescale the frequencies by $1 - y$ to add to 1.

The dual process back in time for a particular type is the Λ-coalescent tree.

Multi-type Λ-Fleming-Viot population

$$\mathcal{L}_{mt}g(\mathbf{x}) = \int_{\Delta^d} \sum_{i\in[d]} x_i \left(g(\mathbf{x}(1-|\mathbf{y}|)+\mathbf{y}) - g(\mathbf{x})\right) \frac{G_i(d\mathbf{y})}{|\mathbf{y}|^2},$$

where G_i are sub-stochastic measures, and $g \in C^2(\Delta^d_\circ)$.

$\Delta^d = \{\mathbf{y} \in \mathbb{R}^d_+; |\mathbf{y}| \le 1\}$, $\Delta^d_\circ = \{\mathbf{x} \in \mathbb{R}^d_+; |\mathbf{x}| = 1\}$.

Choose a type i individual with probability x_i and add in $\mathbf{y}$ individuals of the d types at rate $G_i(d\mathbf{y})/|\mathbf{y}|^2$. Rescale the frequencies by $1-|\mathbf{y}|$ to add to 1.

Mutation and fitness selection of offspring give rise to different reproduction measures G_i. $\int_{\Delta^d} G_i(d\mathbf{y})/|\mathbf{y}| < \infty$ is required.

The measures G_i

There is an assumption that $\exists$ a probability measure F on $[0,1]$ and sub-stochastic viability measures $V_i(\mathbf{w},\cdot)$ supported on $\{\mathbf{y} : \mathbf{y} \in \Delta^d; \mathbf{y} \le \mathbf{w}\}$ such that

$$\frac{G_i(d\mathbf{y})}{|\mathbf{y}|^2} = \int_{\mathbf{w}>\mathbf{y}}^{|\mathbf{w}|\le 1} V_i(\mathbf{w}, d\mathbf{y})\frac{F(d\mathbf{w})}{|\mathbf{w}|^2}$$

It is also assumed that

$$K_i(d\mathbf{y}) = \frac{F(d\mathbf{y}) - G_i(d\mathbf{y})}{|\mathbf{y}|} \qquad \left[G_i(d\mathbf{y}) = F(d\mathbf{y}) - |\mathbf{y}|K_i(d\mathbf{y})\right]$$

defines a finite signed measure on Δ^d.

Multi-type juvenile offspring from a type i individual are produced at rate $F(d\mathbf{w})/|\mathbf{w}|^2$, not depending on the type of the parent, then thinned by viability selection according to $V_i(\mathbf{w}, d\mathbf{y})$.

Multi-type Moran model with viability selection

Fixed population of N individuals.
The type space is $[d] = \{1, \dots, d\}$.
Reproduction events occur at rate λ. a juvenile offspring are produced with probability distribution $\{r_a\}_{a \in [N-1]}$.
The distribution of the numbers of types $\mathbf{B}$ which survive to maturity from a juvenile offspring of a type i parent is $\{\mathcal{Q}_{ia}(\mathbf{B})\}$.
Probability that a type i parent produces $\mathbf{B}$ mature offspring is

$$p_i(\mathbf{B}) = \sum_{a=|\mathbf{B}|}^{N-1} r_a \mathcal{Q}_{ia}(\mathbf{B}).$$

$|\mathbf{B}|$ individuals are chosen to be killed, excluding the parent.
Viability selection and mutation where offspring are thinned according to $\mathcal{Q}_{ia}(\cdot)$.

Possible biological models

1. Mutation occurs independently to juvenile offspring according to a $d \times d$ type transition matrix U.
Mutation is followed by viability selection to form the mature offspring $\mathbf{B}$.

2. Selection occurs at the parental level, reducing the a juvenile offspring to $b \leq a$. Mutation then occurs according to a type transition matrix U to form the mature offspring $\mathbf{B}$, with $|\mathbf{B}| = b$.

The Moran model does not know the internal mechanism of reproduction. It only sees multi-type reproduction.

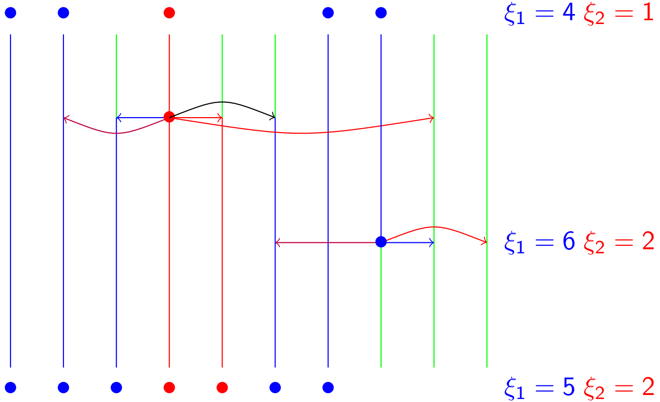
Real and virtual births

Reproduction

$$a \text{ juvenile offspring} \longrightarrow \begin{cases} \mathbf{B} \text{ mature offspring: Real births} \\ a - |\mathbf{B}| \text{ juveniles killed: Virtual births} \end{cases}$$

A concept of virtual births is needed for a dual process back in time.

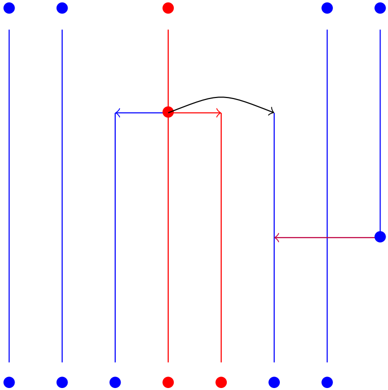
Dual Λ-branching-coalescing graph back in time



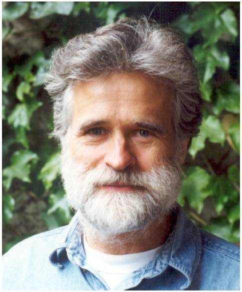
$\boldsymbol{\xi}(t)$ is the number of ancestral lines of the d types at time t back.

red →; blue →; virtual →; births

Branching-coalescing graph back in time





Dual process $\{\boldsymbol{\xi}(t)\}_{t\geq 0}$

Let $\mathbf{Z}(t)$ be the number of individuals of the d types at time $t \geq 0$ in the Moran model with viability selection.
Assume a stationary distribution exits for $\mathbf{Z}(t)$.

Theorem. $\{\mathbf{Z}(t)\}_{t\geq 0}$ is dual to the process $\{\boldsymbol{\xi}(t)\}_{t\geq 0}$ in $\Delta_N = \{\boldsymbol{\xi} \in \mathbb{Z}_+^d, |\boldsymbol{\xi}| \leq N\}$ with non-zero multi-type coalescence rates $q(\boldsymbol{\xi}, \boldsymbol{\xi} + \mathbf{e}_i - \mathbf{l})$ and branching rates $q(\boldsymbol{\xi}, \boldsymbol{\xi} + \mathbf{e}_i)$.

Coalescence occurs when forward in time a type i parent has $\mathbf{l}$ real offspring in the ancestral lines.

Branching occurs when a parent has at least one virtual offspring, but no real offspring in the $|\boldsymbol{\xi}|$ ancestral lineages.

Duality equation

The dual equation is based on falling factorial moments, with notation $z_{[n]} = z(z-1)\cdots(z-n+1)$.

$$\mathbb{E}_{\mathbf{Z}(0)}\Big[\prod_{i=1}^{d} Z_i(t)_{[\xi_i(0)]}\Big] = \mathbb{E}_{\boldsymbol{\xi}(0)}\Big[\prod_{i=1}^{d} Z_i(0)_{[\xi_i(t)]}\Big]$$

$\mathbf{Z}(t)$ forward in time. $\boldsymbol{\xi}(t)$ backward in time.

This is a weak duality equation, however if virtual births are included in a forward model then the duality is a strong duality.

Typed lines and Bayes' factors

Let $\mathcal{H}(\boldsymbol{\xi})$ be the stationary sampling distribution

$$\mathcal{H}(\boldsymbol{\xi}) = \mathbb{E}\left[\frac{\binom{Z_1}{\xi_1}\cdots\binom{Z_d}{\xi_d}}{\binom{N}{|\boldsymbol{\xi}|}}\right]$$

where expectation is over $\mathbf{Z}$.

Rates in the dual process contain Bayes' factors

$$\begin{aligned}\boldsymbol{\xi} \to \boldsymbol{\xi} - \mathbf{l} + \mathbf{e}_i \quad &; \quad \mathcal{H}(i, \boldsymbol{\xi} - \mathbf{l})/\mathcal{H}(\boldsymbol{\xi}) \\ \boldsymbol{\xi} \to \boldsymbol{\xi} + \mathbf{e}_i \quad &; \quad \mathcal{H}(i, \boldsymbol{\xi})/\mathcal{H}(\boldsymbol{\xi})\end{aligned}$$

because of typed lines and time progressing backward.

$$\mathcal{H}(i, \boldsymbol{\xi}) = \frac{\xi_i + 1}{|\boldsymbol{\xi}| + 1}\mathcal{H}(\boldsymbol{\xi} + \mathbf{e}_i)$$

is the probability that the parent is of type i and a sample of size $|\boldsymbol{\xi}|$ from the remaining individuals in the population has configuration $\boldsymbol{\xi}$.

Timescale limit to Fleming-Viot process

Let U be the distribution of the juvenile offspring plus the continuing parent line, with $P(U = a + 1) = r_a$.
Choose

$$\frac{1}{\lambda^{(N)}} = c_N = \frac{\mathbb{E}\left[U(U-1)\right]}{N(N-1)}.$$

Assuming that $c_N \to 0$ in the Λ-coalescent limit there exists a probability measure F such that

$$\lim_{N\to\infty} \frac{1}{c_N} P(U > Nx) = \int_{(x,1]} \frac{F(dy)}{y^2}$$

If the mutation-selection distribution also converges the limit relative frequencies follow a Fleming-Viot process with generator

$$\mathcal{L}_{mt} g(\mathbf{x}) = \int_{\Delta^d} \sum_{i\in[d]} x_i \left(g(\mathbf{x}(1-|\mathbf{y}|)+\mathbf{y}) - g(\mathbf{x})\right) \frac{G_i(d\mathbf{y})}{|\mathbf{y}|^2}$$

Dual Process

The Fleming-Viot process is dual to the system of branching and coalescing lineages $\{\boldsymbol{\xi}(t)\}_{t\geq 0}$ which takes values in $\mathbb{Z}_+^d$.

The transition rates are, up to Bayes' factors,
for $0 \leq \mathbf{l} \leq \boldsymbol{\xi}$, $\mathbf{l} \neq \mathbf{0}, \mathbf{e}_i$, $|\mathbf{l}| \geq 1$

$$q(\boldsymbol{\xi}, \boldsymbol{\xi} - \mathbf{l} + \mathbf{e}_i) \quad \propto \quad \int_{\Delta^d} \left[\binom{|\boldsymbol{\xi}|}{\mathbf{l}, |\boldsymbol{\xi}| - |\mathbf{l}|} \prod_{j \in [d]} y_j^{l_j} \cdot (1 - |\mathbf{y}|)^{|\boldsymbol{\xi}| - |\mathbf{l}|} \right] \frac{G_i(d\mathbf{y})}{|\mathbf{y}|^2}$$

$$q(\boldsymbol{\xi}, \boldsymbol{\xi} + \mathbf{e}_i) \quad \propto \quad \int_{[0,1]} \left(1 - (1 - |\mathbf{y}|)^{|\boldsymbol{\xi}|} \right) \frac{K_i(d|\mathbf{y}|)}{|\mathbf{y}|}$$

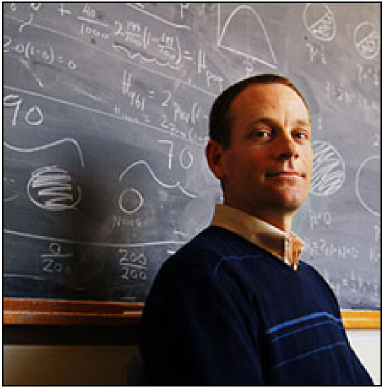
Recall that $K_i(d\mathbf{y}) = \dfrac{F(d\mathbf{y}) - G_i(d\mathbf{y})}{|\mathbf{y}|}$

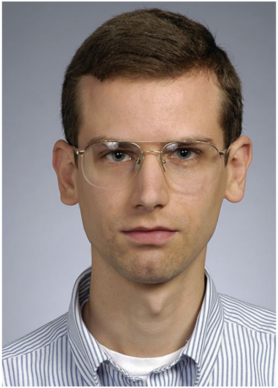
Example •

A two-type model with Beta measures and no mutation. The generator for X_1 acting on $g(x)$ is

$$x\int_0^1 [g((1-y)x+y)-g(x)]\,\frac{B_{2-\gamma_1,\gamma_1}(dy)}{y^2} \\ +(1-x)\int_0^1 [g((1-y)x)-g(x)]\,\frac{B_{2-\gamma_2,\gamma_2}(dy)}{y^2}$$

This model arises naturally from a continuous time Schweinsberg differential rates birth model or from a model with viability selection for the two types. The parameters $\gamma_1, \gamma_2 \in (0,1)$.





Two type Beta model: viability selection

The measures $G_i(dy) = B_{2-\gamma_i,\gamma_i}(dy)$, $i = 1, 2$.

Take $F = G_1$, no thinning of type 1 individuals.

A classical thinning identity for $Y_i \sim G_i$, $i = 1, 2$
and $U \sim B_{2-\gamma_2,\gamma_2}$ independent of Y_1 is that for $\gamma_2 > \gamma_1$

$$Y_2 =^{\mathcal{D}} Y_1 U$$

Let $f(y_2 \mid y_1)$ be the density of $Y_2 \mid Y_1 = y_1$, then

$$B_{2-\gamma_2,\gamma_2}(dy_2) = \int_{y_2}^{1} f(y_2 \mid y_1) dy_2 B_{2-\gamma_1,\gamma_1}(dy_1)$$

Example ●

If there is mutation, then viability selection on juvenile offspring a model is that type $i \in [d]$ individuals give birth to $|\mathbf{y}|$ offspring at rate $G_i(d|\mathbf{y}|)/|\mathbf{y}|^2$, and $\mathbf{y} = \sum_{j \in [d]} u_{ij} y_j \mathbf{e}_j$, where $\{u_{ij}\}$ is a stochastic matrix of mutation rates.

Example ●

If there is viability selection, then mutation $\mathbf{y} = |\mathbf{y}| \sum_{j \in [d]} u_{ij} \mathbf{e}_j$.

Weak selection theorem

Let G_i, $i \in [d]$ be a collection of sub-stochastic probability measures constructed from viability selection with measures $F(\cdot)$ and $V_i(\mathbf{x}, \cdot)$. A very weak mutation and selection model occurs by choosing $K_i(\cdot) = -\sigma_i \delta_{\epsilon(\mathbf{k}_i/\sigma_i)}(\cdot)$ with $\sigma_i \geq 0$, $|\mathbf{k}_i| = \sigma_i$, $i \in [d]$ and letting $\epsilon \to 0$. Then the limit generator equation is

$$\begin{aligned}
\mathcal{L}g(\mathbf{x}) &= \int_{\Delta^d} \sum_{i \in [d]} x_i \left(g(\mathbf{x}(1 - |\mathbf{y}|) + |\mathbf{y}|) - g(\mathbf{x}) \right) \frac{F(d|\mathbf{y}|)}{|\mathbf{y}|^2} \\
&\quad + \sum_{j \in [d]} \sum_{i \in [d]} (x_i \mu_{ij} - x_j \mu_{ji}) g_j(\mathbf{x}) \\
&\quad + \sum_{j \in [d]} x_j (\sigma_j - \sum_{i \in [d]} x_i \sigma_i) g_j(\mathbf{x})
\end{aligned}$$

representing a Λ-Fleming-Viot generator, where $\mu_{ij} = k_{ij}$ are mutation rates from i to j and σ_i are selection rates, $i, j \in [d]$.