Rate of Adaptation Under Weak Selection

Feng Yu

Department of Mathematics, University of Bristol, UK
Joint work with Alison Etheridge (Oxford)

CIRM, 25 May 2009

A problem in evolutionary genetics

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- We consider: accumulation of beneficial and deleterious mutations in asexual populations (with no recombination)
  - asexual reproduction: genetic information of the offspring differ from that of the parent only due to the effect of mutation
- Quantity of interest: mean fitness of the population
  - How does it evolve in time?
  - speed of increase of mean fitness = adaptation rate of the population

Outline of the talk

- Models
  - Strong selection: particle model
  - Weak selection: diffusion model

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  - Non-rigorous considerations lead to approximate asymptotic adaptation rate of $\mathcal{O}(\log N)$
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  - Weak selection: diffusion model
- Strong selection results:
  - Non-rigorous considerations lead to approximate asymptotic adaptation rate of $\mathcal{O}(\log N)$
  - Rigorous lower bound of $\mathcal{O}(\log^{1-\delta} N)$ on adaptation rate and brief discussion of its proof
- Weak selection results:
  - An expansion formula for the rate of adaptation
  - How to calculate each term in this expansion?

Model: strong selection

Assumption

- *Beneficial or deleterious mutations occur at rate* μ *per individual per generation (continuous time)*
- *Each mutation is assumed to be new and add* s *to the fitness of the individual (i.e. equal fitness strength)*
- *Examine the empirical measure* P_k *formed by the types of the* N *individuals* $(X_1, \ldots, X_N)$ *each with mass* $1/N$

Model: strong selection

Model

- *Mutation: for each individual i, at rate μq, X_i changes to $X_i + 1$; at rate $\mu(1-q)$, X_i changes to $X_i - 1$.*
- *Selection: for each pair of individuals (i,j), at rate $\frac{s}{N}(X_i - X_j)^+$, individual i replaces individual j.*
- *Resampling: for each pair of individuals (i,j), at rate $\frac{1}{N}$, individual i replaces individual j.*

Traveling wave

Adaptation rate = speed of the traveling wave

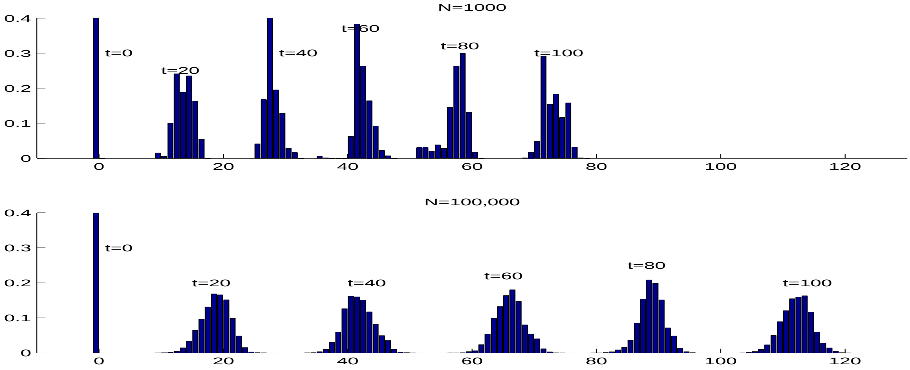
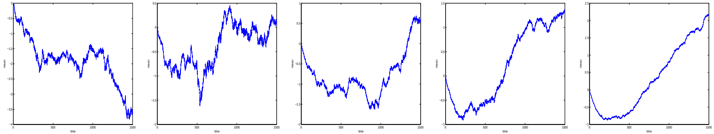


Figure: $N = 1,000$ and $N = 100,000$, $q = 1$, $\mu = 0.02$, $s = 0.02$

Special cases: $q = 1$; $q = 0$ (Muller's ratchet)

Strong selection model

- Simulation results
  - population sizes $N = 1, 2, 5, 10, 30 \times 10^3$; $\mu = 0.01$, $q = 0.01$, $s = 0.01$
  - Y-axis: mean fitness; X-axis: time



- Question: What is the asymptotic behaviour (as $N \to \infty$) of the wave speed for positive q?
  - Answer: As long as $q > 0$, the rate of adaptation is roughly $\mathcal{O}(\log N)$ as $N \to \infty$.

Strong selection calculation

- The proportion of type-k individuals $P_k(t)$ satisfies

$$\begin{aligned} dP_k &= \bar{\mu}_k(P)\ dt + s\sum_{l\in\mathbb{Z}}(k-l)P_kP_l\ dt + dM_k^P \\ &= [\bar{\mu}_k(P) + s(k-m(P))P_k]\ dt + dM_k^P \\ \bar{\mu}_k(P) &= \mu(qP_{k-1} - P_k + (1-q)P_{k+1}) \end{aligned}$$

- M^P is a martingale (noise) with $\left\langle M_k^P \right\rangle(t) \le \frac{2\mu}{N}t + \frac{1}{N}\int_0^t \sum_{l\in\mathbb{Z}}(2+s(k-l)^+ + s(l-k)^+)P_k(s)P_l(s)\ ds$
- Mean fitness $m(P) = \sum_k kP_k$ satisfies ($c_2(P)$ is variance of P)

$$dm(P) = (\mu(2q-1) + sc_2(P))\ dt + dM^{P,m}$$

  - adaptation rate proportional to $c_2(P)$: Fisher's fundamental theorem

Cumulants

Recall the cumulant generating function for a (discrete) random variable with distribution function p_k:

$$g(x) = \log \sum_k p_k e^{kx} = mx + c_2 \frac{x^2}{2} + \ldots,$$

with $\kappa_1 = m = g'(0)$, $\kappa_2 = c_2 = g''(0)$, …, $\kappa_n = g^{(n)}(0)$

$$\kappa_n = L_n(m_1, \ldots, m_n) = \sum_{1 \le k \le n} (-1)^{k-1}(k-1)! B_{n,k}(m_1, \ldots, m_n),$$

where $B_{n,k}$ are the partial Bell polynomials

$$B_{n,k} = \sum \frac{n!}{j_1! \ldots j_{n-k+1}!} \left(\frac{x_1}{1!}\right)^{j_1} \left(\frac{x_2}{2!}\right)^{j_2} \ldots \left(\frac{x_{n-k+1}}{(n-k+1)!}\right)^{j_{n-k+1}},$$

with the sum taken over $j_1 + j_2 + \ldots = k$ and $j_1 + 2j_2 + 3j_3 + \ldots = n$.

Selection mechanism calculation

- Let $\mathcal{S}f(p) = \sum_k (k - m(p)) p_k \frac{\partial f(p)}{\partial p_k}$ be the generator associated with the selection mechanism, then

$$\mathcal{S}g(x) = \sum_k (k - m(p)) p_k e^{xk} e^{-g(p)} = g'(x) - m(p),$$

hence $\mathcal{S}\kappa_2 = \kappa_3$, $\mathcal{S}\kappa_3 = \kappa_4$, etc.

- With the selection mechanism alone, the cumulants roughly satisfy

$$\begin{aligned} d\kappa_2 &= s\kappa_3 \, dt + small \;\; noise \;\; terms \\ d\kappa_3 &= s\kappa_4 \, dt + small \;\; noise \;\; terms \\ d\kappa_4 &= s\kappa_5 \, dt + small \;\; noise \;\; terms \end{aligned}$$

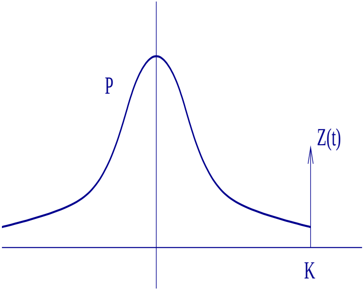
- If one assumes the stationary wave shape to be deterministic (set LHS of above equations to 0), then it is roughly Gaussian, which gives us a way to guess at the asymptotic adaptation rate

Strong selection: heuristics

- Suppose the stationary centred wave $\hat{P}_k$ (with $m(\hat{P}) = 0$) is Gaussian shaped with variance b^2, then the front is at K where

$$\frac{1}{\sqrt{2\pi}b} e^{-K^2/2b^2} = \frac{1}{N} \Rightarrow K \approx b\sqrt{2 \log N}$$

- Let $Z(t)$ be the number of fittest individuals with $Z(0) = 1$. Suppose there is only one individual at the front and that it doesn't die, then it grows roughly exponentially: $Z(t) = e^{sKt}$



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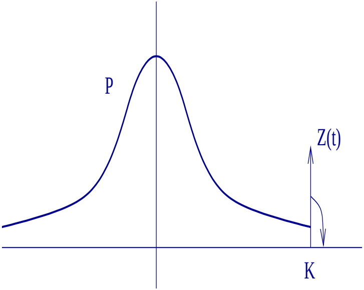

Strong selection: heuristics

- The probability that the front doesn't advance by 1 before time t is

$$\exp\left\{-q\mu\int_0^t Z(u)\ du\right\} = \exp\left\{-\frac{q\mu}{sK}(e^{sKt}-1)\right\}$$

- So *roughly* its takes on average $T = \frac{1}{sK-\mu}\log(sK-\mu)$ for the front to advance by 1, therefore (recall $K \approx b\sqrt{2\log N}$)

$$speed = \frac{1}{T} = \mu + sc_2 \quad \Rightarrow \quad \frac{sK-\mu}{\log(sK-\mu)} = \mu + s\frac{K^2}{2\log N}$$
$$\Rightarrow \quad K\log(sK) \approx 2\log N$$

Conclusion

K is roughly $\mathcal{O}(\log N)$, and wave speed is also roughly $\mathcal{O}(\log N)$.

Strong selection: rigorous results

Theorem

For any $\delta > 0$, there exists N large enough such that

$$\mathbb{E}^{\pi}[m(P(1))] \geq \log^{1-\delta} N.$$

Proof sketch

Study the centred distribution $\hat{P}$, which has a stationary measure π. Compare the selected model with a neutral model without the selection mechanism, which serves as a lower bound of the selected model.

Model: weak selection

Model (3 mechanisms)

- *Mutation: for each individual i, at rate μq, X_i changes to $X_i + 1$; at rate $\mu(1-q)$, X_i changes to $X_i - 1$.*
- *Selection: for each pair of individuals (i, j), at rate $\frac{s}{N}(X_i - X_j)^+$, individual i replaces individual j.*
- *Resampling: for each pair of individuals (i, j), at rate 1, individual i replaces individual j.*

Combine selection and resampling into a single mechanism

Model: weak selection

Model (2 mechanisms)

- *Mutation: for each individual i, at rate μq, X_i changes to $X_i + 1$; at rate $\mu(1-q)$, X_i changes to $X_i - 1$.*
- *Reproduction: For each pair of individuals (i,j), a reproduction event occurs at rate 1. With probability $\frac{1}{2}(1+\frac{s}{N}(X_i - X_j))$, individual i replaces individual j; with probability $\frac{1}{2}(1-\frac{s}{N}(X_i - X_j))$, individual j replaces individual i.*

Martingale problem

- Take limit $N \to \infty$ to obtain a process $P_k(t)$ (proportion of type-k individuals) that satisfies the martingale problem

$$\begin{aligned} P_k(t) &= P_k(0) + \mu \int_0^t (qP_{k-1}(u) - P_k(u) + (1-q)P_{k+1}(u))\, du \\ &\quad + s\int_0^t (k - m(P(u)))P_k(u)\, du + M_k(t), \end{aligned}$$

where $m(p) = \sum_k kp_k$ is the mean of the distribution p and M_k are martingales with quadratic variation process

$$\langle M_k, M_l \rangle (t) = \int_0^t P_k(u)(\delta_{kl} - P_l(u))\, du. \tag{1}$$

SDE representation

- Let $\{W_{kl} : k, l \in \mathbb{Z}, k > l\}$ are independent Brownian motions; for convenience, we define $W_{kl} = -W_{lk}$ for $k, l \in \mathbb{Z}$ and $k < l$ and $W_{kk} \equiv 0$ for $k \in \mathbb{Z}$, then

$$M_k(t) = \int_0^t \sum_{l \in \mathbb{Z}} \sqrt{P_k(u) P_l(u)}\, dW_{kl}(u).$$

- P_k satisfies the following infinite system of stochastic differential equations (SDE):

$$\begin{aligned} dP_k &= [\mu(qP_{k-1} - P_k + (1-q)P_{k+1}) + s(k - m(P))P_k]\, dt \\ &\quad + \sum_{l \in \mathbb{Z}} \sqrt{P_k P_l}\, dW_{kl} \end{aligned}$$

- Let $\mathbb{P}_s$ denote of the law of the solutions to the above system of SDE's

Girsanov transformation

- Idea: The transformation $\mathbb{P}_0$ to $\mathbb{P}_s$ is given by Dawson's Girsanov Theorem, in the infinite dimensional setting
- Let P_k satisfy the neutral SDE

$$dP_k = \mu(qP_{k-1} - P_k + (1-q)P_{k+1})\, dt + \sum_{l \in \mathbb{Z}} \sqrt{P_k P_l}\, dW_{kl}, \qquad (2)$$

- $\tilde{P}_k = P_{k-m(P)}$ has a stationary distribution $\tilde{\mathbb{P}}$

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- $\tilde{P}_k = P_{k-m(P)}$ has a stationary distribution $\tilde{\mathbb{P}}$
- Define

$$\begin{aligned} a_n &= sn, \\ M(t) &= \sum_n n\, M_n(t) = m(P(t)) - (2q-1)\mu t \\ dZ &= Z \sum_n a_n\, dM_n = sZ\, dM, \end{aligned}$$

Girsanov transformation

- Then $\tilde{M}_k$ is a $\mathbb{P}_s$-martingale

$$\tilde{M}_k(t) = M_k(t) - s\int_0^t \sum_n a_n(u)\ d[M_k, M_n](u)$$

$$= M_k(t) - s\int_0^t \sum_n n(\delta_{kn} - P_k(u))P_n(u)\ du$$

$$= M_k(t) - s\int_0^t (k - m(P(u)))P_k(u)\ du$$

- Since $\langle M_k, M_l\rangle(t) = \left\langle \tilde{M}_k, \tilde{M}_l \right\rangle(t)$, we can write

$$\tilde{M}_k(t) = \int_0^t \sum_{l\in\mathbb{Z}} \sqrt{P_k(u)P_l(u)}\ d\tilde{W}_{kl}(u)$$

Girsanov transformation

- Thus

$$
\begin{aligned}
dP_k &= [\mu(qP_{k-1} - P_k + (1-q)P_{k+1}) + s(k - m(P))P_k]\, dt \\
&\quad + \sum_{l \in \mathbb{Z}} \sqrt{P_k P_l}\, d\tilde{W}_{kl},
\end{aligned}
$$

the same as the selected SDE

Change of measure

- The Radon-Nikodym derivative

$$
\begin{aligned}
\left.\frac{d\mathbb{P}_s}{d\mathbb{P}_0}\right|_{\mathcal{F}_t} &= Z(t) \\
&= \exp\left\{ \int_0^t \sum_k sk\ dM_k(u) - \frac{1}{2}\int_0^t \sum_{k,l} s^2 kl\ d\left\langle M_k, M_l \right\rangle (u) \right\} \\
&= \exp\left\{ sM(t) - \frac{s^2}{2}\int_0^t c_2(P(u))\ du \right\},
\end{aligned}
$$

where P solves the neutral SDE (2), $m(p) = mean\ of\ p$, and $c_2(p) = variance\ of\ p$

Change of measure

Proposition

The adaptation rate in the selected model (with selection coefficient s) is equal to

$$\lim_{t\to\infty}\frac{1}{t}\mathbb{E}_s[m(P(t))] = \lim_{t\to\infty}\frac{1}{t}\mathbb{E}_0[Z(t)m(P(t))]$$
$$= (2q-1)\mu + \lim_{t\to\infty}\frac{1}{t}\mathbb{E}_0[Z(t)M(t)]$$

Structure of $Z(t)$

- Recall $M = M^{(1)} = \sum_n n\ M_n$.
- Define

$$M^{(n)}(t) = \int_{\Delta_n(t)} dM(t_1)\dots dM(t_n)$$
$$\Delta_n(t) = \{0 < t_1 < \dots < t_n < t\}$$

- Example:

$$dM^{(n)} = M^{(n-1)}\ dM$$
$$M^{(2)}(t) = \int_0^t M(t_1)\ dM(t_1),$$
$$M^{(3)}(t) = \int_0^t M^{(2)}(t_1)\ dM(t_1), \dots$$

Structure of $Z(t)$

- Since Z satisfies $dZ = sZ\ dM$, we can write

$$Z = 1 + \sum_{n=1}^{\infty} s^n M^{(n)}$$

- Therefore the adaptation rate in the selected model can be written as

$$\begin{aligned} &(2q-1)\mu + \lim_{t\to\infty} \frac{1}{t} \mathbb{E}_s[M(t)] \\ &= (2q-1)\mu + \lim_{t\to\infty} \frac{1}{t} \sum_{n=1}^{\infty} s^n \mathbb{E}_0[M^{(n)}(t) M^{(1)}(t)] \end{aligned}$$

Iterated Wiener-Itô integrals

- Let W be a Brownian motion. Define

$$J_n(f) = \int_{\Delta_n(t)} f(t_1, \dots, t_n) \, dW(t_1) \dots \, dW(t_n)$$

for a deterministic function f defined on $\Delta_n(t)$. Then Itô isometry implies

$$\begin{aligned} E[J_n(f)^2] &= \int_{\Delta_n(t)} f(t_1, \dots, t_n)^2 \, dt_1 \dots \, dt_n \\ E[J_m(f)J_n(g)] &= 0 \text{ if } m \neq n \\ J_n(g^{\otimes n}) &= \frac{\|g\|^n}{n!} H_n \left(\frac{\int_0^t g(u) \, dW(u)}{\|g\|} \right) \\ e^{\int_0^t g(u) \, dW(u) - \frac{1}{2}\|g\|^2} &= \sum_{n=0}^{\infty} \frac{\|g\|^n}{n!} H_n \left(\frac{\int_0^t g(u) \, dW(u)}{\|g\|} \right) \end{aligned}$$

Structure of M

- Crucial fact used:

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- But in our case,

$$\begin{aligned} d\langle M\rangle &= \sum_{k,l} kl\ d\langle M_k, M_l\rangle = \sum_{k,l} klP_k(\delta_{kl} - P_l)\ dt \\ &= \left(\sum_k k^2 P_k - \sum_{k,l} klP_k P_l\right)\ dt = c_2(P)\ dt, \end{aligned}$$

where we recall from (1)

$$d\langle M_k, M_l\rangle = P_k(\delta_{kl} - P_l)\ dt$$

Structure of M

- Crucial fact used:

$$d\langle W\rangle = dt$$

- But in our case,

$$d\langle M\rangle = \sum_{k,l} kl \; d\langle M_k, M_l\rangle = \sum_{k,l} klP_k(\delta_{kl} - P_l)\; dt$$
$$= \left(\sum_k k^2 P_k - \sum_{k,l} klP_kP_l\right)\; dt = c_2(P)\; dt,$$

where we recall from (1)

$$d\langle M_k, M_l\rangle = P_k(\delta_{kl} - P_l)\; dt$$

- More generally, since $dM^{(n)} = M^{(n-1)}\; dM^{(1)}$,

$$d\left\langle M^{(n)}, M^{(1)}\right\rangle = M^{(n-1)} d\left\langle M^{(1)}\right\rangle = M^{(n-1)} c_2\; dt$$

Terms in the expansion

Want to calculate

The adaptation rate in the selected model

$$(2q-1)\mu + \lim_{t\to\infty} \frac{1}{t} \sum_{n=1}^{\infty} s^n \mathbb{E}_0[M^{(n)}(t) M^{(1)}(t)]$$

Let $\mathcal{G}$ be the generator associated with the neutral SDE (2)

$$\begin{aligned} dP_k &= \mu(qP_{k-1} - P_k + (1-q)P_{k+1})\,dt + \sum_{l\in\mathbb{Z}} \sqrt{P_k P_l}\,dW_{kl} \\ \mathcal{G} &= \mathcal{R} + \mu\mathcal{M} \\ \mathcal{R}f(p) &= \frac{1}{2}\sum_{k,l} p_k(\delta_{kl} - p_l)\frac{\partial^2 f(p)}{\partial p_k \partial p_l} \\ \mathcal{M}f(p) &= \sum_k (qp_{k-1} - p_k + (1-q)p_{k+1})\frac{\partial f(p)}{\partial p_k} \end{aligned}$$

Terms in the expansion

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We set the initial condition for the neutral SDE to be its stationary distribution (on the centred process) $\tilde{\mathbb{P}}$:

$$\begin{aligned} d(M^{(n)}M^{(1)}) &= M^{(n)}\,dM^{(1)} + M^{(1)}\,dM^{(n)} + d\left\langle M^{(n)}, M^{(1)}\right\rangle \\ d\left\langle M^{(n)}, M^{(1)}\right\rangle &= M^{(n-1)}c_2\,dt \\ E[\left\langle M^{(n)}, M^{(1)}\right\rangle(t)] &= \int_0^t \mathbb{E}_0[M^{(n-1)}(u)c_2(u)]\,du = t\tilde{\mathbb{E}}_0[M^{(n-1)}c_2] \end{aligned}$$

Terms in the expansion

Want to calculate

The adaptation rate in the selected model

$$(2q-1)\mu + \lim_{t\to\infty} \frac{1}{t} \sum_{n=1}^{\infty} s^n \mathbb{E}_0[M^{(n-1)}\kappa_2]$$

- We use cumulants, because $\langle M, \kappa_n \rangle = \kappa_{n+1}$
- First term is $\tilde{\mathbb{E}}_0[\kappa_2]$

$$\mathcal{G}\kappa_2 = \mu - \kappa_2 \Rightarrow \tilde{\mathbb{E}}[\kappa_2] = \mu$$

Terms in the expansion

Want to calculate

The adaptation rate in the selected model

$$(2q-1)\mu + \lim_{t\to\infty} \frac{1}{t} \sum_{n=1}^{\infty} s^n \mathbb{E}_0[M^{(n-1)}\kappa_2]$$

- Third term is $\tilde{\mathbb{E}}_0[M^{(2)}\kappa_2]$

$$\begin{aligned}
d(M^{(2)}\kappa_2) &= M^{(2)}\ d\kappa_2 + d\left\langle M^{(2)}, \kappa_2 \right\rangle + a\ martingale \\
&= (-M^{(2)}\kappa_2 + M^{(1)}\kappa_3)\ dt + a\ martingale \\
\tilde{\mathbb{E}}_0[M^{(2)}\kappa_2] &= \tilde{\mathbb{E}}_0[M^{(1)}\kappa_3] \\
d(M^{(1)}\kappa_3) &= -M^{(1)}\ d\kappa_3 + d\left\langle M^{(1)}, \kappa_3 \right\rangle + a\ martingale \\
&= (-3M^{(1)}\kappa_3 + \kappa_4)\ dt + a\ martingale \\
\tilde{\mathbb{E}}_0[M^{(1)}\kappa_3] &= \tilde{\mathbb{E}}_0[\kappa_4]/3 = -2\mu^2/3
\end{aligned}$$

Fourth term in the expansion

$$\begin{aligned}
d(M^{(3)}\kappa_2) &= M^{(3)}\ d\kappa_2 + d\left\langle M^{(3)}, \kappa_2 \right\rangle + a\ martingale \\
&= (-M^{(3)}\kappa_2 + M^{(2)}\kappa_3)\ dt + a\ martingale \\
\tilde{\mathbb{E}}_0[M^{(3)}\kappa_2] &= \tilde{\mathbb{E}}_0[M^{(2)}\kappa_3] \\
d(M^{(2)}\kappa_3) &= -M^{(2)}\ d\kappa_3 + d\left\langle M^{(2)}, \kappa_3 \right\rangle + a\ martingale \\
&= (-3M^{(2)}\kappa_3 + M^{(1)}\kappa_4)\ dt + a\ martingale \\
\tilde{\mathbb{E}}_0[M^{(2)}\kappa_3] &= \tilde{\mathbb{E}}_0[M^{(1)}\kappa_4]/3
\end{aligned}$$

Fourth and fifth terms in the expansion

$$
\begin{aligned}
d(M^{(1)}\kappa_4) &= -M^{(1)}\ d\kappa_4 + d\left\langle M^{(1)}, \kappa_4 \right\rangle + a\ martingale \\
&= (-M^{(1)}(7\kappa_4 + 12\kappa_2^2) + \kappa_5)\ dt + a\ martingale \\
d(M^{(1)}\kappa_2^2) &= -M^{(1)}\ d\kappa_2^2 + d\left\langle M^{(1)}, \kappa_2^2 \right\rangle + a\ martingale \\
&= (-M^{(1)}(-\frac{1}{2}\kappa_4 + 2\kappa_2^2) + 2\kappa_2\kappa_3)\ dt + a\ martinga \\
d(M^{(1)}(\frac{1}{10}\kappa_4 - \frac{3}{5}\kappa_2^2)) &= (-M^{(1)}\kappa_4 + (\frac{1}{10}\kappa_5 - \frac{6}{5}\kappa_2\kappa_3))\ dt \\
\tilde{\mathbb{E}}_0[M^{(1)}\kappa_4] &= \frac{1}{10}\tilde{\mathbb{E}}_0[\kappa_5 - 12\kappa_2\kappa_3] = (2q-1)(\frac{\mu^2}{3} + \frac{\mu}{20})
\end{aligned}
$$

$$
\tilde{\mathbb{E}}_0[M^{(4)}\kappa_2] = \frac{1}{51}\tilde{\mathbb{E}}_0\left[\frac{7}{5} + 38(\kappa_2 + (2q-1)\kappa_3) + \frac{7}{5}\kappa_6 + 38(\kappa_4\kappa_2 + \kappa_3^2)\right]
$$

Generators

- $\mathcal{G}$ is the generator associated with the neutral SDE (2)

$$
\begin{aligned}
dP_k &= \mu(qP_{k-1} - P_k + (1-q)P_{k+1})\, dt + \sum_{l\in\mathbb{Z}} \sqrt{P_k P_l}\, dW_{kl} \\
\mathcal{G} &= \mathcal{R} + \mu\mathcal{M} \\
\mathcal{R}f(p) &= \frac{1}{2}\sum_{k,l} p_k(\delta_{kl} - p_l)\frac{\partial^2 f(p)}{\partial p_k \partial p_l} \\
\mathcal{M}f(p) &= \sum_k (qp_{k-1} - p_k + (1-q)p_{k+1})\frac{\partial f(p)}{\partial p_k}
\end{aligned}
$$

- $\mathcal{S}$ is the generator associated with the selection mechanism

$$
\begin{aligned}
\mathcal{S}f(p) &= \sum_k (k - m(p))p_k \frac{\partial f(p)}{\partial p_k} \\
d\left\langle M^{(n)}, f(p)\right\rangle &= M^{(n-1)}\mathcal{S}f(p)\, dt
\end{aligned}
$$

Generator calculation

- Let $g(x) = \log \sum_k P_k e^{kx}$, then

$$\begin{aligned} \mathcal{M}g(x) &= \sum_k (qP_{k-1} - P_k + (1-q)P_{k+1})e^{kx}e^{-g(x)} \\ &= \sum_k P_k(qe^x - 1 + (1-q)e^{-x})e^{kx}e^{-g(x)} \\ &= qe^x - 1 + (1-q)e^{-x} \end{aligned}$$

- Hence

$$\begin{aligned} \mathcal{M}\kappa_2 &= \left.\frac{\partial^2}{\partial x^2}\right|_{x=0} \mathcal{M}g(x) = 2q - 1 \\ \mathcal{M}\kappa_3 &= \left.\frac{\partial^3}{\partial x^3}\right|_{x=0} \mathcal{M}g(x) = 1 \\ &\vdots \end{aligned}$$

Generator calculation

- But

$$
\begin{aligned}
\mathcal{R}\kappa_2 &= -\kappa_2 \\
\mathcal{R}\kappa_3 &= -3\kappa_3 \\
\mathcal{R}\kappa_4 &= -(7\kappa_4 + 6\kappa_2^2) \\
\mathcal{R}\kappa_5 &= -(15\kappa_5 + 10\kappa_3\kappa_2) \\
&\vdots
\end{aligned}
$$

i.e. more complicated

Generator calculation

- Let $i = (i_1, i_2, \ldots, i_l)$ and $|i| = \sum_{j=1}^{l} i_j$,

$$\kappa_i = \kappa_{i_1}\kappa_{i_2}\ldots\kappa_{i_l}, \; K_n = span\{\kappa_i : |i| = n, \min i \geq 2\}$$

- Then

$$\begin{aligned} \mathcal{R}: \quad & K_n \to K_n \\ \mathcal{S}: \quad & K_n \to K_{n+1} \\ \mathcal{M}: \quad & K_n \to K_{n-2} \otimes \ldots \otimes K_2 \end{aligned}$$

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- For $k_n \in K_n$,

$$\begin{aligned} d(M^{(n)}\mathcal{R}^{-1}k_n) &= (M^{(n)}k_n + M^{(n)}\mathcal{M}\mathcal{R}^{-1}k_n)\,dt + M^{(n-1)}\mathcal{S}\mathcal{R}^{-1}k_n\,dt \\ \tilde{\mathbb{E}}[M^{(n)}k_n] &= \tilde{\mathbb{E}}[M^{(n)}\mathcal{M}(-\mathcal{R})^{-1}k_n] + \tilde{\mathbb{E}}[M^{(n-1)}\mathcal{S}(-\mathcal{R})^{-1}k_n] \quad (3) \end{aligned}$$

- In general, $\tilde{\mathbb{E}}_0[M^{(n)}\kappa_2]$ is a linear combination of the expectation of $\kappa_{n+2}, \kappa_n\kappa_2, \ldots, \kappa_{n+1}, \kappa_{n-1}\kappa_2, \ldots,$ and lower order terms.

Generator calculation

Theorem

The adaptation rate in the selected model (with selection coefficient s) is equal to

$$(2q-1)\mu + \sum_{n=1}^{\infty} s^n \tilde{\mathbb{E}}[M^{(n-1)}\kappa_2],$$

where $\tilde{\mathbb{E}}$ denotes expectation under the stationary distribution (on the centred process) and the terms in the above expansion can be calculated by solving the closed linear system (3). The first few terms of this expansion is

$$(2q-1)\mu + s\mu + s^2(2q-1)\frac{\mu}{3} - s^3\frac{2\mu}{3} + s^4(2q-1)(\frac{\mu^2}{9} + \frac{\mu}{60}) + \dots$$

Cumulants under resampling

We can apply Faà di Bruno's formula

$$
\begin{aligned}
\mathcal{R}g(x) &= 1 - e^{g(2x)-2g(x)} \\
\mathcal{R}\kappa_n &= -\frac{1}{2}\sum_{k=0}^{n} B_{n,k}\left(\frac{\partial}{\partial x}\bigg|_{x=0}(g(2x)-2g(x)),\right. \\
&\qquad \left. \ldots, \frac{\partial^{n-k+1}}{\partial x^{n-k+1}}\bigg|_{x=0}(g(2x)-2g(x))\right) \\
&= -\frac{1}{2}\sum_{k=0}^{n} B_{n,k}\left(0,(2^2-2)\kappa_2,\ldots,(2^{n-k+1}-2)\kappa_{n-k+1}\right)
\end{aligned}
$$

Cumulants under resampling

But $\kappa_{n_1}\kappa_{n_2}$ and $\kappa_{n_1}\kappa_{n_2}\kappa_{n_3}$ are more complicated (not triangular)

$$\begin{aligned}\mathcal{R}(\kappa_{n_1}\kappa_{n_2}) = {} & \kappa_{n_1}\mathcal{R}\kappa_{n_2} + \kappa_{n_2}\mathcal{R}\kappa_{n_1} \\ & + \text{a linear combination of } \{\kappa_{n'_1}\kappa_{n'_2} : n'_1 + n'_2 = n_1 + n_2\}\end{aligned}$$

$$\begin{aligned}\mathcal{R}(\kappa_{n_1}\kappa_{n_2}\kappa_{n_3}) = {} & \kappa_{n_1}\kappa_{n_2}\mathcal{R}\kappa_{n_3} + \kappa_{n_1}\kappa_{n_3}\mathcal{R}\kappa_{n_2} + \kappa_{n_2}\kappa_{n_3}\mathcal{R}\kappa_{n_1} \\ & +(\text{a linear combination of } \{\kappa_{n'_1}\kappa_{n'_2} : n'_1 + n'_2 = n_1 + n_2\})\kappa_{n_3} \\ & +(\text{a linear combination of } \{\kappa_{n'_1}\kappa_{n'_3} : n'_1 + n'_3 = n_1 + n_3\})\kappa_{n_2} \\ & +(\text{a linear combination of } \{\kappa_{n'_2}\kappa_{n'_3} : n'_2 + n'_3 = n_2 + n_3\})\kappa_{n_1}\end{aligned}$$

Moments under resampling

- Let

$$g_1(x) = \sum_k p_k e^{kx}$$

be the moment generating function, then $\mathcal{R}g_1 = 0$ and hence

$$\mathcal{R}m_n = 0$$

- Let

$$g_2(x_1, x_2) = g_1(x_1)g_1(x_2)$$

be the generating function for moments of the form $m_i m_j$, then

$$\begin{aligned} \frac{\partial}{\partial p_k} &= e^{kx_2} g_1(x_1) + e^{kx_1} g_1(x_2), \ \frac{\partial^2}{\partial p_k \partial p_l} = e^{kx_2 + lx_1} + e^{kx_1 + lx_2} \\ \mathcal{R}g_2 &= \sum_k p_k e^{k(x_1+x_2)} - \sum_{k,l} p_k p_l e^{kx_2 + lx_1} \\ &= g_1(x_1 + x_2) - g_1(x_1)g_1(x_2) \end{aligned}$$

Moments under resampling

$$\mathcal{R}(m_{n_1} m_{n_2}) = m_{n_1+n_2} - m_{n_1} m_{n_2}$$

- For higher order terms

$$\begin{aligned}\mathcal{R}(m_{n_1} m_{n_2} m_{n_3}) &= (m_{n_1+n_2} - m_{n_1} m_{n_2})m_{n_3} + (m_{n_1+n_3} - m_{n_1} m_{n_3})m_{n_2} \\ &\quad +(m_{n_2+n_3} - m_{n_2} m_{n_3})m_{n_1},\end{aligned}$$

  etc.
- $\mathcal{R}$ is triangular in $\{m_i : |i| = n\}$
- The hope: convert expressions in terms of cumulants into those involving moments, apply $\mathcal{R}^{-1}$, then convert these expressions back into cumulants

Conclusion

- An expansion formula for the rate of adaptation
- Each term in this expansion can be calculated explicitly, in theory
- Is there a nicer formula?

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Thank you!