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A dual approach to models with multilevel selection

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Outline

- The question of levels of selection
- Recent developments
- Wright-Fisher models with mutation and selection
- Interaction and replacement of demes (subpopulations)
- Multilevel Fleming-Viot process
- Set-valued dual dynamics
- Equilibria and fixation probabilities
- Phase transitions: e.g. Kimura's model, hunters-farmers model

The question of “levels of selection”

Wikipedia: *A unit of selection is a biological entity within the hierarchy of biological organisation (e.g. self-reproducing molecules, genes, cells, individuals, groups, species) that is subject to natural selection. For several decades there has been intense debate among evolutionary biologists about the extent to which evolution has been shaped by selective pressures acting at these different levels.*

Early history:

Wynne-Edwards (1962) (adaptations and social behaviour of animals)
W.D. Hamilton (1964) (kin selection and inclusive fitness)
G.C. Williams (1966) (highly critical of group selection)
John Maynard Smith (1964), (1976) - group selection and kin selection
D.S. Wilson (1975) - multideme model

Books

R.M. Brandon and R.N. Burian (1984)
E. Sober and D.S. Wilson (1998)
L. Keller (editor) Princeton Univ. Press (1999)
S. Okasha (Oxford Univ. Press 2006).

Mathematical models:

Motivated by K. Aoki (1982), Motoo Kimura (1983) introduced a *diffusion process model* and identified a condition for group selection to prevail over counteracting individual selection.

E.G. Leigh (2010)

These conditions (e.g. he quotes Kimura's conditions) seem so wonderfully improbable that, following Williams (1966), most biologists have focused almost exclusively on individual selection. Improbability, however, does not mean impossibility. Group selection capable of overwhelming selection within groups, played a crucial role in some major transitions …

Recent developments on multilevel selection

- Evolution of propagule size during evolution of multicellularity (Roze and Michod (2001))
- Plasmid replication in bacteria (Paulsson (2002))
- Prebiotic evolution (Hogeweg and Takeuchi (2003)))
- Evolution of cooperation (Traulsen and Nowak (2006))
- Animal science (Bijma, Muir and Arendonk (2007))
- Emergence of life (Szathmáry and Demeter (1987), Görnerup and Crutchfield (2008),
- Ecology - selection between species, major transitions (Leigh (2010))
- Host pathogen systems (Luo, Reed, Mattingly and Koelle (2012), Luo (2013)).
- Microbial social trait (de Vargas Roditi, Boyle and Xavier (2013))

Simple Model

- Level 2 unit is a population of N level 1 individuals undergoing mutation and selection.
- Each level 2 subpopulation described by K-type Wright-Fisher diffusions with mutation and selection
- Migration between subpopulations occur at rate c.
- There is some form of competition between demes (level 2 individuals) and the replacement of one deme by another with probabilities depending on the "fitness of the different demes".

System of interacting subpopulations (demes)

- Individual type space: $\mathbb{I}$, $|\mathbb{I}| = K$.
- Interacting subpopulations (demes): $\mu_\xi \in \mathcal{P}(\mathbb{I})$, $\xi \in \{1, \ldots, N\}$.
- Mutation rates $i \to j$: $\quad m_{i,j}$,
- Individual fitness of type j: $V_1(j) \in [0, 1]$, $j \in \mathbb{I}$
- Individual selection intensity s_1
- Genetic drift at each site: $\quad \gamma_1 \quad$ ("inverse population size")
- Migration rate between demes: $\xi \to \xi' \neq \xi$: $\frac{c}{N}$
- Deme fitness $V_2(\mu) \in [0, 1]$, $\mu \in \mathcal{P}(\mathbb{I})$
- Deme level selection intensity s_2
- Deme random sampling parameter γ_2

Stochastic dynamics $\gamma > 0$: Basic Tools

- Probability-valued Markov diffusion $X(t) \in \mathcal{P}(\mathbb{I}) = \Delta_{K-1}$
- Martingale problem with generator G to characterize the law of the process $P \in \mathcal{P}(C_{\Delta_{K-1}}([0,\infty)))$

$$M_F(t) := \qquad F(X(t)) - \int_0^t GF(X(s))ds$$

is a P **martingale** for all $F \in D(G)$.

- Dual: Set-valued jump process $\mathcal{G}_t \in \{G \in 2^{\mathbb{I}^{\mathbb{N}}}, |G| < \infty\}$.
- Duality relation:

$$E_{X(0)}(F(X(t), \mathcal{G}_0)) = E_{\mathcal{G}_0}(F(X(0), \mathcal{G}_t))$$

Individual mutation-selection dynamics at a deme

The Wright-Fisher diffusion $X_t(1)$ satisfies the G^0-martingale problem where G^0 acting on a C^2-functions f on the simplex

$\Delta_{K-1} = \{(x_1, \ldots, x_K),\ x_i \geq 0, \sum_{i=1}^K x_1 = 1\} = \mathcal{P}(\mathbb{I})$ as follows:

$$
\begin{aligned}
G^0 f(\mathbf{x}) \qquad &= \sum_{i=1}^K \left(\sum_{j=1}^K (m_{ji} x_j - m_{ij} x_i) \right) \frac{\partial f(\mathbf{x})}{\partial x_i} \quad \text{mutation} \\
&+ s_1 \sum_{i=1}^K x_i \left(V_1(i) - \sum_{k=1}^K V_1(k) x_k \right) \frac{\partial f(\mathbf{x})}{\partial x_i} \quad \text{selection} \\
&+ \frac{\gamma_1}{2} \sum_{i,j=1}^K x_i (\delta_{ij} x_j - x_j) \frac{\partial^2 f(x)}{\partial x_i \partial x_j} \quad \text{genetic drift}
\end{aligned}
$$

Model of N interacting populations

A deme can be replaced with population $\mathbf{x}$ sampled from the empirical distribution of demes with weights proportional to the level 2 fitness

$$0 \leq V_2(\mathbf{x}) \leq 1, \quad \mathbf{x} \in \mathcal{P}(\mathbb{I}).$$

Individuals can migrate between demes at rate c

The generator for the interacting model: for $f \in C^2((\Delta_{K-1})^N)$

$$
\begin{aligned}
&G^{\text{int}} f(\mathbf{x}(1), \ldots, \mathbf{x}(N)) \\
&= \sum_{\xi=1}^{N} G_{\xi}^{0} f(\ldots, \mathbf{x}(\xi), \ldots) \qquad \text{mutation-selection dynamics at each site} \\
&\;+c \cdot \sum_{\xi=1}^{N} \left[\sum_{j=1}^{K} \left(\sum_{\xi'=1}^{N} \frac{1}{N} x_j(\xi') - x_j(\xi) \right) \frac{\partial f(\ldots, \mathbf{x}(\xi), \ldots)}{\partial x_j(\xi)} \right] \qquad \text{migration} \\
&+s_2 \sum_{\xi=1}^{N} \left(\frac{1}{N} \sum_{\xi'=1}^{N} V_2(\mathbf{x}(\xi'))[(\Phi_{\xi\xi'} f(...) - f(...)] \right) \quad \text{deme replacement} \\
&+\frac{1}{2}\gamma_2 \sum_{\xi=1}^{N} \sum_{\xi'=1}^{N} [\Phi_{\xi,\xi'} f(\ldots) - f(\ldots)] \quad \text{deme resampling}
\end{aligned}
$$

where $\Phi_{\xi\xi'} f(\ldots, \mathbf{x}(\xi), \ldots, \mathbf{x}(\xi'), \ldots) = f(\ldots, \mathbf{x}(\xi'), \ldots, \mathbf{x}(\xi'), \ldots)$

The martingale problem has a unique solution that defines a càdlàg strong Markov process with state space $(\Delta_{K-1})^N$.

Empirical Process

We assume that the initial state satisfies $(\mathbf{x}_1(0), \ldots, \mathbf{x}_N(0))$ is exchangeable.

$$\Xi^N(t) := \frac{1}{N}\sum_{j=1}^{N} \delta_{\mathbf{x}_j(t)} \in \mathcal{P}(\mathcal{P}(\mathbb{I})).$$

Then $\Xi^N(t)$ is a $\mathcal{P}(\mathcal{P}(\mathbb{I}))$-valued Markov process.

The multilevel Fleming-Viot process with selection at the deme level arises as the limit as $N \to \infty$.

The two-level Fleming-Viot process

The domain $\mathcal{D}_2 \subset C(\mathcal{P}(\mathcal{P}(\mathbb{I})))$

$$H(\nu) = \prod_{k=1}^{K} \left[\int h_k(\mu_k) \nu(d\mu_k) \right]$$

$$h(\mu) = \sum_j h_j \mu^{\otimes}(\Pi_i A_{ij}) \quad \text{polynomial on } \mathcal{P}(\mathbb{I}).$$

The generator of the two-level Fleming-Viot process acting on $\mathcal{D}_2 \subset C(\mathcal{P}(\mathcal{P}(\mathbb{I}))$:

$$\begin{aligned}
G_2 H(\nu) \quad &= \int_{\mathcal{P}(\mathbb{I})} G^0 \frac{\delta H(\nu)}{\delta \nu(\mu)} \nu(d\mu) \\
&+ c \int_{\mathcal{P}(\mathbb{I})} \int_{\mathbb{I}} \left(\frac{\delta}{\delta \mu_1(x)} \frac{\delta H(\nu)}{\delta \nu(\mu_1)} \right) [\int \nu(d\mu_2)\mu_2(dx) - \mu_1(dx)] \nu(d\mu_1)) \\
&+ \frac{\gamma_2}{2} \int_{\mathcal{P}(\mathbb{I})} \int_{\mathcal{P}(\mathbb{I})} \frac{\delta^2 H(\nu)}{\delta(\nu(\mu_1))\delta(\nu(\mu_2))} \Big(\nu(d\mu_1)\delta_{\mu_1}(d\mu_2) - \nu(d\mu_1)\nu(d\mu_2) \Big) \\
&+ s_2 \left[\int_{\mathcal{P}(\mathbb{I})} \frac{\delta H(\nu)}{\delta \nu(\mu_1)} [V_2(\mu_1) - \int_{\mathcal{P}(\mathbb{I})} V_2(\mu_2)\nu(d\mu_2)] \nu(d\mu_1) \right]
\end{aligned}$$

This is the analogue of the multilevel branching and multilevel superprocess (e.g. D-Hochberg (1991), Y.Wu (1994), Gorostiza-Hochberg-Wakolbinger (1995), D-Hochberg-Vinogradov (1996)), D-Gorostiza-Wakolbinger (2004).

The Fleming-Viot limit and its equilibria

Theorem

$$\{\Xi^N(t)\}_{t\in[0,T]} \Rightarrow (\Xi_t)_{t\in[0,T]} \quad \text{as } N\to\infty$$

where $\Xi_t(dx) \in C([0,T],\mathcal{P}(\Delta_{K-1}))$ is solution to the $(G_2,\mathcal{D}_2)$ martingale problem. The martingale problem is well-posed.

The uniqueness is proved using the set-valued dual introduced below.

A class of fitness functions

$$V_2(\mu) = \sum_j a_j V_{2,j}(\mu), \quad V_{2,j}(\mu) = \mu^{\otimes}(\prod_i 1_{B_{ij}})$$

Using Bernstein approximation we can approximate any continuous function on $\mathcal{P}(\mathbb{I})$ in this way.

<u>Action of deme level selection</u>

$$h(\mu_1) \to V_{2,j}(\mu_1)h(\mu_1) + (1 - V_{2,j}(\mu_1))h(\mu_2)$$

$$\int h(\mu)\nu(d\mu) \to \int V_2(\mu_1)h(\mu_1)\nu(d\mu_1) + \int\int (1 - V_2(\mu_1))h(\mu_2)\nu(d\mu_1)\nu(d\mu_2)$$

Multilevel set-valued dual representation

The Set-Valued Process $\mathcal{G}_t$ (D-Greven (2011,2013))

Type space:

$$\mathbb{I} := \{1, \ldots, K\}$$

Geographic space (labels of demes)

$$S = \{1, \ldots, N\} \qquad \text{or } S = \mathbb{N}.$$

Local state space for a deme:

$$\begin{aligned} \mathcal{I} := \ & \text{algebra of subsets of } \mathbb{I}^{\mathbb{N}} \\ & \text{of the form } A \times \mathbb{I}^{\mathbb{N}},\ A \text{ is a subset of } \mathbb{I}^m, m \in \mathbb{N} \end{aligned}$$

State space:

$$\boxed{\mathsf{I} := \ \text{algebra of sets } = \{\mathsf{G} \in \mathcal{I}^{\mathsf{S}},\ |\mathsf{G}| < \infty\}}$$

$$\begin{aligned} |G| := \min\{j : \exists S_j = \{s_1, \ldots, s_j\} \subset \mathbb{N} : G = G_j \times ((\mathbb{I})^{\mathbb{N}})^{S \setminus S_j} \\ G_j \in \mathcal{I}^{S_j}\} \end{aligned}$$

The Dual Representation

$$\Xi(t) \in \mathcal{P}(\mathcal{P}(\mathbb{I})).$$

Set-valued Dual Process: $\mathcal{G}_t \in \mathsf{I}$

Define the function $F : \mathcal{P}(\mathcal{P}(\mathbb{I})) \otimes \mathsf{I} \to [0, 1]$ by

$$F(\Xi, \mathcal{G}) = \int X^*(x_1, \ldots, x_{|S|})(\mathcal{G})\Xi(d\mu_1), \ldots, \Xi(d\mu_{|S|})$$

where if $X = \prod_{j=1}^N \mathbf{x}_j$, then $X^*(x_1, \ldots, x_N) = \prod_{j=1}^N (\mathbf{x}_j)^{\mathbb{N}} \in \mathcal{P}((\mathbb{I}^{\mathbb{N}})^S)$.

$\boxed{\text{Dual Representation}}$

$$E_{X(0)}(F(\Xi(t), \mathcal{G}_0)) = E_{\mathcal{G}_0}(F(\Xi(0), \mathcal{G}_t))$$

Set-valued transitions - individual level

Examples:

Types $B \subset \mathbb{I}$ have fitness $s > 0$, B^c has fitness 0.

$$\mathcal{G}_0 = A \times \mathbb{I}^{\mathbb{N}}, \quad A \subset \mathbb{I}$$

Selection: $A \to B \cap A \cup B^c \times A$ at rate s

Coalescence: $A_1 \times A_2 \to A_1 \cap A_2$ at rate γ_1

Migration $(A_1)_1 \times (A_2)_1 \to (A_1)_1 \times (A_2)_2$ at rate c

here the subscript $()_i$ denotes the deme.

Mutation: $A \to A \cup \{j\}$ or $A \to A \backslash \{j\}$ at rates based on $\{m_{ij}\}$

Set-valued transitions - deme level selection

$$V_2(\mu) = \sum_j a_j V_{2,j}(\mu), \quad V_{2,j}(\mu) = \mu^{\otimes}(\prod_i 1_{B_{ij}})$$

$$\int h(\mu)\nu(d\mu) \to \int V_2(\mu_1)h(\mu_1)\nu(d\mu_1) + \int\int (1 - V_2(\mu_1))h(\mu_2)\nu(d\mu_1)\nu(d\mu_2)$$

Example: If $V_2(\mu) = \mu(B)$, then the set-valued process $\mathcal{G}_t$ the state space is

$$\left(\prod_{i=1}^{n} A_i\right)_1 \to (B)_1 \times \left(\prod_{i=1}^{n} A_i\right)_1 \cup (B^c)_1 \times \left(\prod_{i=1}^{n} A_i\right)_2$$

Set-valued transitions - deme level coalescence

Example

$$
\begin{aligned}
&\left(\prod_j B_j\right)_1 \times \left(\prod_i A_i\right)_1 \cup \left(\prod_j B_j\right)_1^c \times \left(\prod_i A_i\right)_2 \\
&\to \left(\prod_j B_j\right)_1 \times \left(\prod_i A_i\right)_1 \cup \left(\prod_j B_j\right)_1^c \times \left(\prod_i A_i\right)_1
\end{aligned}
$$

Applications

1. Equilibria and fixation probabilities

- Positive mutation rates on $\mathbb{I}$ and $\gamma_2 > 0$. The two level Fleming-Viot process has a unique equilibrium.

- Positive mutation rates on $\mathbb{I}$ and $\gamma_2 = 0$, $s_2 = 0$. Have deterministic McKean-Vlasov equation and convergence to a unique equilibrium.

- General mutation rates on $\mathbb{I}$ and $\gamma_2 = 0$. Have infinite dimensional nonlinear dynamics.

- $\gamma_1 = \gamma_2 = 0$ - Deme dynamics is deterministic and deme level selection acts only on the initial randomness - e.g. case $\nu(d\mu) = \Xi_0(d\mu) = \delta_x m(dx)$ where $m \in \mathcal{M}([0,1])$. In this case deme level selection acts on the initial diversity of demes.

- No mutation on $\mathbb{I}$ and $\gamma_2 = 0$, $s_1, s_2 > 0$. Can compute fixation probabilities.

Parameter ranges and initial Conditions

Proposition
(a) Consider the case $\mathbb{I} = \{1, 2\}$, $\Xi_0 = \delta_\mu$ with no mutation and only level 2 selection and fitness function $V_2(\mu) = \mu(2)$, $s_2 > 0$ and $\gamma_2 = 0$. Then $\mu(t, 2) \to 1$ if and only if $\gamma_1 > 0$.
(This fact was first pointed out by John Maynard Smith.)

(b) Assume no mutation, $\gamma_1 > 0$, $\gamma_2 > 0$, $V_1, V_2 > 0$ – ultimate fixation of a single type. Can calculate the fixation probabilities using the set-valued dual equilibrium.

The proofs are obtained by showing that the growth of the set-valued process is described by a Crump-Mode-Jagers branching process.

2. Phase transition

Example: Kimura'smodel of the evolution of an altruistic trait

Consider the case $\mathbb{I} = \{1, 2\}$.

$$V_1(1) = 0,\ V_1(2) = 1,$$

the individual selection intensity is s_1, *and no mutation. The migration rate is* c, *the deme selection intensity is* s_2, *deme fitness is*

$$V_2(\mu) = \mu(1).$$

Then if $s_2 > \frac{2cs_1}{\gamma_1}$ *and* $\nu(\{\mu : \mu(1) > 0\}) > 0$, *then for* $\varepsilon > 0$,

$$\nu_t(\{\mu : \mu(2) > \varepsilon\}) \to 0,$$

if $s_2 < \frac{2cs_1}{\gamma_1}$ *and* $\nu(\{\mu : \mu(2) > 0\}) > 0$, *then for* $\varepsilon > 0$,

$$\nu_t(\{\mu : \mu(1) > \varepsilon\}) \to 0.$$

Kimura (1983) proved this by solving explicitly for the one dimensional diffusion in terms of hypergeometric functions.

Idea of the set-valued dual proof

Acting on $h(\mu) = \mu(1)$, $V_1(1) = 0, V_1(2) = 1$, $V_2(\mu) = \mu(1)$

- Each individual level selection operation acting on an active rank followed by a successful migration creates a factor smaller than 1. $(10)_1 \to (10)_1 \otimes (10)_1 \to (10)_1 \otimes (10)_2$. $p \to p^2$, rate $s_1 \frac{2c}{2c+\gamma_1}$

- Each deme level selection operation acting on an occupied site followed by a (level 1) coalescence creates a factor larger than 1. $(10) \to (10)_1 \otimes (10)_1 + (01)_1 \otimes (10)_2 \to (10)_1 + (01)_1 \otimes (10)_2$. $p \to p + p(1-p) = p(2-p) = 1-(1-p)^2$, rate $s_2 \frac{\gamma_1}{2c+\gamma_1}$
$(01) \to (10)_1 \otimes (01)_1 + (01)_1 \otimes (01)_2 \to (01)_1 \otimes (01)_2$.

- Get two competing CMJ branching processes. Then one can show that for large s_2 the second growth rate (related to the malthusian parameter) is larger than the first.

Conclusions and open problems

- These methods allow the analysis of multitype populations (i.e. not restricted to two-type level 1 populations).

- Can extend these methods to the case of countably many types (at least with bounded fitness function).

- Nonlinear dynamics in the case $\gamma_2 = 0$, mutation and general fitness functions.

- $\gamma_2 > 0$. Description of the genealogy.

- Extension to higher levels and generalized Fleming-Viot.

- Role of deme level selection on emergence of new types.

THANK YOU