On the effects of migration in spatial Fleming-Viot models with selection and rare mutation

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Key object

Population in space under stochastic evolution

- resampling (pure genetic drift)
- mutation
- selection
- migration in geographic space

Phenomenon in focus:

- Invasion by rare fit mutants
- Successive hierarchically structured invasions drive evolution with increasing fitness in times of vastly different orders of time.
- Space determines a new faster speed of invasions.

Goal

- Model invasion by fitter rare mutants in a *spatial* context
- Exhibit stasis/punctuated equilibrium
- Exhibit longterm random effects of short scales on subsequent large scales
- Mathematical framework for quasi-equilibria

Mathematical Framework:

- Interacting collection of Fleming-Viot diffusions with selection and mutation
- Interaction via migration.

Scenario for stasis (punctuated equlibrium)

Phase 0:
M types of *lower* fitness in selection-mutation "equilibrium"

Phase 1:
$\uparrow$ rare mutation, *emergence* type of higher fitness

Phase 2:
Fixation on types of higher fitness

Phase 3:
Neutral equilibrium on types of higher fitness

Phase 4:
M types of *higher* fitness in selection-mutation, "equilibrium"

Phase 3,4:	very long time spans
Phase 1:	long time span (spatial effect)
Phase 0,2:	short time spans

Focus: Phase 1,2.

Two-type model

Space: $\{1, \cdots, N\}$ (hierarchical group)

State space: $[0, 1]^N$ or Δ_2^N

(1)

$$X(t) = \{(x_\ell^N(i,t))_{i=1,\cdots,N} \quad , \quad \ell = 1, 2\}.$$

Given are:

(2)
$$\{(w_i(t))_{t\geq 0}, \quad i = 1, \cdots, N\}$$
i.i.d.-standard Brownian motions,

the initial state $X(0)$ with

(3) $x_2(i, 0) = 0, \quad \forall i = 1, \cdots, N$

and parameters

(4) $c, d, m, s > 0.$

System of 2N coupled SDE

(5)

$$dx_2^N(i,t) = (c(\frac{1}{N}\sum_{j=1}^{N} x_2^N(j,t)) - x_2^N(i,t))dt$$
$$+\frac{m}{N}x_1^N(i,t)dt$$
$$+s(x_2^N(i,t)x_1^N(i,t))dt$$
$$+\sqrt{d \cdot x_2(i,t)x_1(i,t)}dw_i(t), \quad i \in \mathbb{N},$$

(6)

$$dx_1^N(i,t) = (c(\frac{1}{N}\sum_{j=1}^{N} x_1^N(j,t)) - x_1^N(i,t))dt$$
$$-\frac{m}{N}x_1^N(i,t)dt$$
$$-sx_2^N(i,t)x_1^N(i,t)dt$$
$$-\sqrt{d \cdot x_2^N(i,t)x_1^N(i,t)}dw_i(t), \quad i \in \mathbb{N}.$$

Global description:

(7) $$\Xi_t^N = \frac{1}{N} \sum_{i=1}^{N} \delta_{x_2^N(i,t)} \in \mathcal{P}([0,1])$$

Local description:

(8)
$$\{x_2^N(1,t), \cdots, x_2^N(L,t)\} \quad , \quad L \text{ fixed }, L \subseteq \mathbb{N}.$$

$N \to \infty$, what do we expect for phase 1,2?

$O(1)$: Some of the components of size order 1

$\frac{1}{\alpha} \log N$: positive fraction of sites reaches value ε

$O(1)$: If most components are $\geq \varepsilon$, then in finite (deterministic) time later fixation, meaning type-two mass $\geq 1 - \delta$.

Emergence - Fixation

Theorem 1

There exists $\alpha \in (0, s)$ such that:

(9) $\mathcal{L}[(\Xi^N_{\frac{1}{\alpha}\log N + t})_{t\in\mathbb{R}}] \underset{N\to\infty}{\Longrightarrow} \mathcal{L}[(\mathcal{L}_t)_{t\in\mathbb{R}}],$

(10)

$$\mathcal{L}[(x_2^N(1, \tfrac{1}{\alpha}\log N + t), \cdots, x_2^N(L, \tfrac{1}{\alpha}\log N + t)_{t\in\mathbb{R}}] \underset{N\to\infty}{\Longrightarrow} \mathcal{L}[(Y_t)_{t\in\mathbb{R}}].$$

Theorem 2

(11)

$\mathcal{L}_t \underset{t\to-\infty}{\Longrightarrow} \delta_0 \quad , \quad \mathcal{L}_t \underset{t\to\infty}{\Longrightarrow} \delta_1,$ (emergence-fixation)

$\mathcal{L}_t((0,1)) = 1 \quad a.s.,$ (true time-scale)

$\mathcal{L}_t$ is truely random (*rare* mutation effect)

Random Emergence
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Deterministic Fixation

Theorem 3

(a) $\left(e^{\alpha t}\int_0^1 x\mathcal{L}_t(dx)\right) \underset{t\to-\infty}{\Longrightarrow} {}^*\mathcal{W}$

$0 <^* \mathcal{W} < \infty$ a.s. $\quad , \quad Var({}^*\mathcal{W}) > 0.$

(b) $\exists!(\mathcal{L}_t^*)_{t\in\mathbb{R}} \quad , \quad e^{\alpha t}\int x\mathcal{L}_t^*(dx) \underset{t\to-\infty}{\longrightarrow} 1,$

$\mathcal{L}_t = \mathcal{L}^*_{t+{}^*\mathcal{E}}$ with ${}^*\mathcal{E} = \frac{\log^* \mathcal{W}}{\log \alpha}.$

$(\mathcal{L}_t^*)_{t\in\mathbb{R}}$: solves *McKean-Vlasov equation*,

$\mathcal{L}_t^* =$ Law $(\pi_1 \circ Y^*(t)).$

Growth rate: α

Growth constant is random: ${}^*\mathcal{W}$.
Time shift is random: ${}^*\mathcal{E}$.

${}^*\mathcal{E},{}^*\mathcal{W}$ reflect early events at time $O(1)$ somewhere in space.

α arises from interplay between migration and selection, which makes $\alpha < s$.

Propagation of chaos:

(12) $m = (m(t))_{t\in\mathbb{R}} : m(t) = \int\limits_0^1 x\mathcal{L}_t^*(dx)$

(13)

$$Y^{*,m}(t) = (y(1,t), \cdots, y(L,t)),$$

$$\{(y(i,t)_{t\geq 0}, \quad i = 1, \cdots, L\} \text{ i.i.d.}$$

$$dy(i,t) = c(m(t) - y(i,t)dt$$

$$+s(y(i,t)(1 - y(i,t))dt$$

$$+\sqrt{d \cdot y(i,t)(1 - y(i,t))}dw_i(t).$$

(14)

$$\mathcal{L}[(Y^*(t))_{t\in\mathbb{R}}] = \int_{\text{Path}} \mathcal{L}[(Y^{*,m}(t))_{t\in\mathbb{R}}]dm.$$

Theorem 4

(15) $\mathcal{L}[(Y_t)_{t\in\mathbb{R}}] = \mathcal{L}[(Y^*_{t+^*\mathcal{E}})_{t\in\mathbb{R}}].$

Droplet description

Droplet *total mass*:

(16) $\widehat{x}_2^N(t) = \sum_{i=1}^{N} x_2^N(i,t)$

Atomic random measure representation of droplet:

(17) $\beth_t^N = \sum_{i=1}^{N} x_2^N(i,t)\delta_{a(i)} \quad ,$

$\{a(\ell)\}_{\ell\in\mathbb{N}}$ i.i.d. $[0,1]$-valued according to uniform distribution.

Palm measure:

Typical configuration, i.e. configuration seen from a typical type-2 individual.

(18) $\mu_t^N := \mathcal{L}[\{x^N(i,t), i = 1, \cdots, N\}]$

Set

(19)

$$\widehat{\mu}_t(A) = \int \frac{x_2(1,t)}{\int x_2(1,t)d\mu_t(dX)} 1_A(X)d\mu(X).$$

Limiting droplet dynamic

Theorem 4

(20)

$$(a)\quad \widehat{\mu}_t^N \underset{N\to\infty}{\Longrightarrow} \widehat{\mu}_t^\infty \quad , \quad \forall t \geq 0.$$

$$(b)\quad \mathcal{L}[(\widehat{x}_2^N(t))_{t\geq 0}] \underset{N\to\infty}{\Longrightarrow} \mathcal{L}[(\widehat{x}_2(t))_{t\geq 0}] \quad , \quad \forall t \geq 0.$$

$$(c)\quad \mathcal{L}[(\daleth_t^N)_{t\geq 0}] \underset{N\to\infty}{\Longrightarrow} \mathcal{L}[(\daleth_t)_{t\geq 0}].$$

Remark: $(\daleth_t)_{t\geq 0}$ can be described by a stochastic equation using Ito's excursion theory of subcritical Feller diffusions.

Droplet growth

Theorem 5

There exists an $\alpha^* \in (0, s)$ such that:

$$\mathcal{L}[e^{-\alpha^* t} \daleth_t([0,1])], \underset{t\to\infty}{\Longrightarrow} \mathcal{L}[\mathcal{W}^*], \tag{21}$$
$$0 < \mathcal{W}^* < \infty \text{ a.s.},$$

(22)
$$\widehat{\mu}_t^{\infty} \underset{t\to\infty}{\Longrightarrow} \widehat{\mu}_{\infty}^{\infty} \quad , \quad \widehat{\mu}_{\infty}^{\infty} \text{ supported on } (0,1)^{\mathbb{N}}.$$

Theorem 6

Let $t_N = o(\frac{1}{\alpha^*} \log N)$. Then:

$$\mathcal{L}[e^{-\alpha^* t_N} \daleth_t^N([0,1])] \underset{N\to\infty}{\Longrightarrow} \mathcal{L}[\mathcal{W}^*]. \tag{23}$$

"Exit = entrance"

Theorem 7

(24) $\alpha^* = \alpha$

(25) $\mathcal{L}[^*\mathcal{W}] = \mathcal{L}[\mathcal{W}^*]$.

Remark on 2M types

M types on each of two levels:

- α gets smaller (Now effective fitness over lower order types is relevant).

- *random* frequencies of fitter types at fixation occurs

McKean-Vlasov equation:

(26) $\frac{d}{dt}\mathcal{L}_t = \mathcal{L}_t G^*$

with:

(27)

G^* adjoint operator to Generator G to (12), (13).

Limiting droplet dynamic

Theorem 8

(28)

$$\beth_t = \beth_{0,t} + \int_0^t \int_0^1 \int_0^{q(s,a)} \int_{W_0} w(t-s)\delta_a \, N(ds, da, dq, dw)$$
$$q(s,a) = m + c\beth_{s^-}^m([0,1]) \quad ,$$

and the intensity measure of the random measure N is:

(29) $dsdaduQ(dw)$.

The excursion measure Q arises from :

(30)

$$dy(t) = -cy(t)dt + sy(t)(1-y(t))dt + \sqrt{d \cdot y(t)(1-y(t))}\,dw(t)$$

$$y(0) = \varepsilon$$

Branching Approximation

(31)

$$dy(t) = a - cy(t)dt + sy(t)(1 - y(t))dt$$
$$+\sqrt{dy(t)(1 - y(t))}dw(t)$$

(32) a small : May survive.

(33) $\approx a - cy(t)dt + sy(t) + \sqrt{d \cdot y(t)}dw(t)$

(34)

$$\left.\begin{array}{ll} s < c & \text{subcritical branching} \\ s = c & \text{critical branching} \end{array}\right\} \text{extinction}$$

(35)

$$s > c \text{ supercritical branching } \} \begin{array}{l} \text{survival with} \\ \text{pos. probability,} \\ < 1 \text{ for } \varepsilon \text{ small} \\ \text{enough.} \end{array}$$