Stochastic dynamics of adaptive trait and neutral marker driven by eco-evolutionary feedbacks

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How neutral diversity (molecular markers) is affected by selection and adaptation?

- Eco-evolutionary framework.
- How the ecological phenomena (which only depend on the trait values) will influence the generation and maintenance of neutral variation?
- How patterns of neutral molecular evolution could be used to infer the history of trait mutation that have driven past adaptation?
- Abundant literature on the impact of selection on neutral polymorphism. The models make the assumptions of constant population and selection.

  (Barton, Durrett-Schweinsberg, Etheridge-Pfaffelhüber-Wakolbinger and references therein).
- Our goal is to relax these assumptions.

The individual-based model

Our model:

Asexual population

Individual-based eco-evolutionary process of adaptive trait and neutral marker dynamics with varying population size (and selection).

Each individual is characterized

- by an adaptive trait which influences its intrinsic demographic rates and the ecological interactions.
  The ability of the individual to survive and reproduce depends on its trait.
- by a genetic marker supposed to be selectively neutral.

Trait and Marker Dynamics

The evolution of the trait and marker distribution results from three basic mechanisms.

- Heredity. Transmission of the ancestral trait and marker to the offsprings.
- Mutation. Generates variability in the trait and marker values.

  Main assumption: marker mutation process much faster than trait mutation process but much slower than the ecological time-scale of birth and death events.
- Selection. Acts on the death rates as the result of competition between individuals - for limited resources (depends only on the traits).

Three time scales: ecological birth and death, marker mutation, trait mutation.

Biological assumptions

- (1) large population
- (2) rare trait mutations
- (3) rare marker mutations
- (4) "small" marker mutation steps
- (5) marker mutation process much faster than trait mutation process

and long (evolutive) time scale.

Adaptive Dynamics framework: Successive invasions of successful trait mutants.

Description of the successive invasions of mutants:

- Game Theory - Dynamical Systems:
  Hofbauer-Sigmund 1990, Marrow-Law-Cannings 1992,
  Metz-Geritz-Meszéna et al. 1992, 1996, Dieckmann-Law 1996.
- PDE Approach. Perthame-Barles-Mirrahimi 07-10, Jabin, Desvillettes, Raoul, Mischler 08-10.
- Our Approach: **Individual-based model** (birth and death process with mutation and selection).
  (Bolker-Pacala 97, Kisdi 99, Dieckmann-Law 00, Fournier-M. 04, Ferrière-Champagnat-M. 06, Champagnat 06, Champagnat-M. 10)

Our aim: To explain by this adaptive dynamics framework the underlying dynamics of the neutral markers.

We will prove that if a trait mutant appears and sweeps through the population to fixation, the marker distribution undergoes a bottleneck and diffuses after the adaptive jump

Neutral diversity will be restored after each adaptive jump.

Individual-based model

- Trait under selection x in a subset $\mathcal{X}$ of $\mathbb{R}$ (rate of nutrient intake, body size at maturity, age at maturity ...).
- Neutral marker u in a subset $\mathcal{U}$ of $\mathbb{R}$.
- The type of an individual i : (x_i, u_i).
- K scales the size of the population.
- p_K scales the mutation probability of the traits under selection.
- q_K scales the mutation probability of the neutral markers.
- Population of $N^K(t)$ individuals weighted by $\frac{1}{K}$ with types $((x_1, u_1), \cdots, (x_{N^K(t)}, u_{N^K(t)}))$.

  It is represented by the point measure $\nu_t^K = \frac{1}{K} \sum_{i=1}^{N^K(t)} \delta_{(x_i,u_i)}$.

  $$\langle \nu_t^K, g \rangle = \frac{1}{K} \sum_{i=1}^{N^K(t)} g(x_i, u_i) \quad ; \quad N^K(t) = K \langle \nu_t^K, 1 \rangle.$$

Transitions

BIRTHS:

Each individual with characteristics (x, u) gives birth to a single individual at (inhomogeneous) rate $b(x)$; $0 \leq b(x) \leq \bar{b}$.

At each birth time:

- with probability $(1 - p_K)(1 - q_K)$, the offsprings inherits of (x, u).
- Mutations on trait and marker occur independently with probability p_K and q_K.

$$p_K \sim \frac{1}{K^2} \ ; \ q_K = r_K \, p_K \ \ ; \ q_K \to 0 \ \ ; \ r_K \to +\infty.$$

- Trait mutation: the new trait is $x + \ell$ chosen according to $m(x, \ell) d\ell$.

- Marker mutation: the new marker is $u+h$ chosen according to $G_K(u,dh)$.

- $\exists$ $(A,\mathcal{D}(A))$ generator of a Feller semi-group such that $\forall g \in \mathcal{D}(A)$,

$$\lim_K \sup_u \left| \frac{r_K}{K} \int (g(u+h)-g(u))G_K(u,dh) - A\,g \right| = 0.$$

("Small" marker mutation steps)

DEATHS:

- Each individual with characteristics (x, u) dies at rate

$$d(x) + \eta(x) C * \nu_t^K(x) = d(x) + \frac{\eta(x)}{K} \sum_{i=1}^{N^K(t)} C(x - x_i).$$

- The term $\eta(x) C * \nu_t^K(x) = \frac{\eta(x)}{K} \sum_{i=1}^{N^K(t)} C(x - x_i)$ describes the competition pressure for external resources.

- Assumptions:

$$b(x) - d(x) > 0 \;\; ; \;\; \eta(x) C(x - y) \geq \underline{\eta} > 0.$$

- The demographic functions b, d, η, C and the mutation measures $m(.,\ell)d\ell$ and $G_K(.,h)dh$ are continuous functions.

Examples

- **Example 1**: $\mathcal{U} = [u_1, u_2]$ and $G_K \sim N(\mu_K, \sigma_K^2)$ with $\mu_K \to 0$ and $\sigma_K \to 0$ and

$$\lim_K \frac{r_K \mu_K}{K} = \mu \ ; \ \lim_K \frac{r_K \sigma_K^2}{K} = \sigma^2.$$

  Then $Af = \mu f' + \frac{\sigma^2}{2} f''$ for $f \in C^2$ and $f'(u_1) = f'(u_2) = 0$.

$$p_K = \frac{1}{K^2} \ ; \ r_K = K^{3/2} \ ; \ q_K = \frac{1}{\sqrt{K}} \ ; \ \mu_K = \frac{\mu}{\sqrt{K}} \ ; \ \sigma_K^2 = \frac{\sigma^2}{\sqrt{K}}$$

- **Example 2**:
  G_K is the law of a Pareto variable with index $\alpha \in (1, 2)$ divided by $K^{\frac{\eta}{\alpha}}$
  such that $\eta < 1$, $\lim_K \frac{r_K}{K^{1+\eta}} = \bar{r}$ and

$$Af = \bar{r} \int \left(f(u+h) - f(u) - hf'(u)1_{|h| \le 1}\right) \frac{dh}{|h|^{1+\alpha}}.$$

- **Example 3**: Discrete case $\mathcal{U} = \{a, A\}$.

  Marker mutation: the new marker h is chosen according to $G_K(u, dh)$:

$$G_K(u, dh) = 1_{u=a}\, q_a\, \delta_A(dh) + 1_{u=A}\, q_A\, \delta_a(dh) \;;\;\; \lim_K \frac{r_K}{K} = \bar{r} \,.$$

  Then

$$Af(u) = \bar{r}\left(1_{u=a}\, q_a\big(f(A) - f(a)\big) + 1_{u=A}\, q_A\big(f(a) - f(A)\big)\right).$$

$$p_K = \frac{1}{K^2} \quad ; \quad r_K = \bar{r}\, K \quad ; \quad q_K = \frac{\bar{r}}{K}.$$

Marker and trait population processes

$$\nu_t^K = \frac{1}{K} \sum_{i=1}^{N^K(t)} \delta_{(x_i,u_i)} \in \left\{ \frac{1}{K} \sum_{i=1}^{n} \delta_{(x_i,u_i)} \, ; \; n \geq 0, (x_1, u_1), \cdots, (x_n, u_n) \in \mathcal{X} \times \mathcal{U} \right\}.$$

Trait marginal measure (on $\mathcal{X}$):

$$X_t^K(dx) = \frac{1}{K} \sum_{i=1}^{N^K(t)} \delta_{x_i} = \int_{\mathcal{U}} \nu_t^K(dx, du).$$

Marker distribution (probability on $\mathcal{U}$) for a given trait value x:

$$\pi_t^K(x, du) = \frac{\sum_{i=1}^{N^K(t)} \mathbf{1}_{x_i = x} \delta_{u_i}}{\sum_{i=1}^{N^K(t)} \mathbf{1}_{x_i = x}}.$$

We get

$$\nu_t^K(dx, du) = X_t^K(dx) \, \pi_t^K(x, du).$$

Behavior when K tends to infinity?

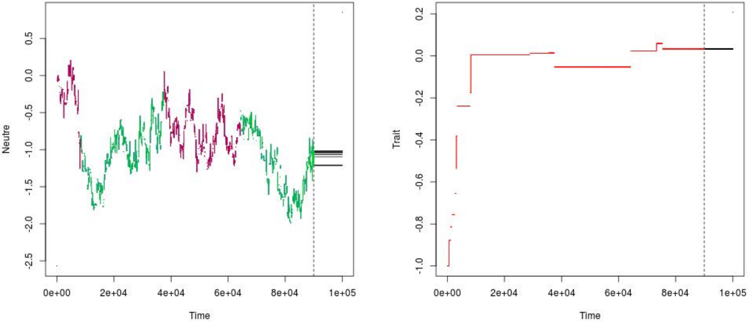
Example

Inspired by a model of beak's size. (Dieckmann-Doebeli 1999)

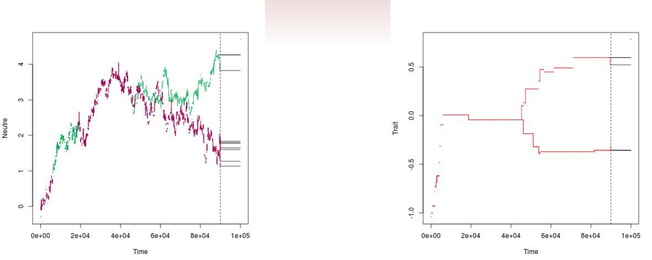
- $\mathcal{X} = [-2, 2]$; $\mathcal{U} = [-6, 6]$.
- $p_K = \frac{1}{K^2}$; $a_K = K^{3/2}$; $q_K = \frac{1}{\sqrt{K}}$.
- $m \sim N(0, 10^{-1})$ and $G_K \sim N(0, \frac{1}{\sqrt{K}})$ are two Gaussian laws conditioned to $[-2, 2]$ and $[-6, 6]$.
- $b(x) = \exp(-x^2/2\sigma_b^2)$; $\sigma_b = 0.9$. Maximum at 0.
- Symmetric competition for resources. $\eta(x) = 1$ and
$$C(x-y) = \exp(-(x-y)^2/2\sigma_C^2).$$
- Initial condition: $K = 1000$; $x_0 = -1, u_0 = 0$.

Simulations: Genealogies of the individuals

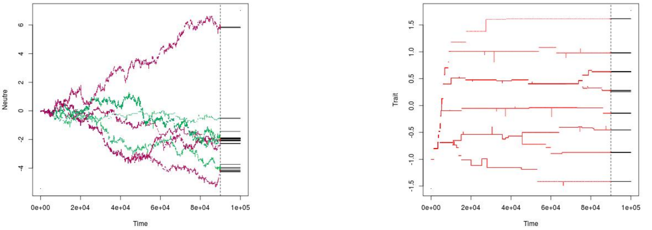
We only keep the trajectories of the individuals alive at time t.



(a) $\sigma_C = 0.8$



(b) $\sigma_C = 0.7$



(c) $\sigma_C = 0.3$

Ecological time scale - Invasion fitness function

Monomorphic initial population with fixed trait x.

When $K \longrightarrow \infty$, no mutation at this scale.

Theorem: *Assume that* $X_0^K(dy) = n_0^K \, \delta_x(dy)$ *and* $n_0^K \to n_0$.

Then $(N_t^K, t \geq 0)$ *converges to* $(n_t, t \geq 0)$, *where* n_t *is the solution of the (deterministic) logistic equation*

$$\dot{n}_t = \big(b(x) - d(x) - \eta(x)C(0)n_t\big)\, n_t,$$

which converges when t *tends to infinity to the charge capacity*

$$\hat{n}_x = \frac{b(x) - d(x)}{\eta(x)\, C(0)}.$$

The invasion fitness function is given by

$$f(y; x) = b(y) - d(y) - \eta(x)C(y - x)\hat{n}_x.$$

It represents the growth rate of a sub-population with trait mutant y in a resident trait-monomorphic population with trait x.

Evolutive time scale: asymptotic behavior of (X^K_{Kt}).

Trait Substitution Sequence: (Metz et al. 1996; Champagnat 06, Champagnat-Ferrière-M. 08).

Assume $\nu^K_0(dy) = n^K_0\,\delta_{x_0}(dy)$ and that $\lim_{K\to\infty} n^K_0 = \hat{n}_{x_0}$.

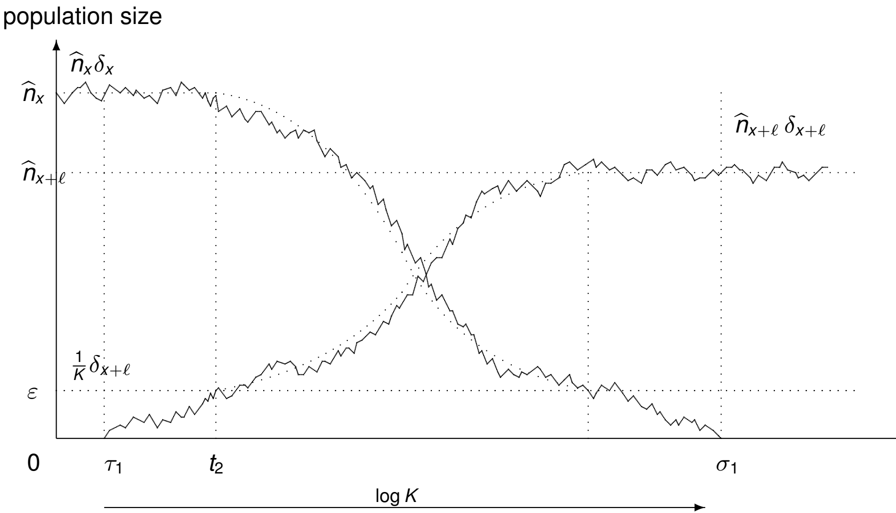
Assume "Invasion Implies Fixation".
(If $C = 1$, $x \mapsto \hat{n}_x$ is a monotonous function).

Theorem: *The population process* $(X^K_{Kt}, t \geq 0)$ *converges to a jump process* $(\hat{n}_{Y_t}\,\delta_{Y_t}; t \geq 0)$ *on monomorphic states, called Trait Substitution Sequence (TSS).*

- The TSS jumps from $\hat{n}_x$ individuals with trait x to $\hat{n}_{x+\ell}$ individuals with trait $x+\ell$ at rate

$$b(x)\;\hat{n}_x\,\frac{[f(x+\ell;x)]_+}{b(x+\ell)}\;m(x,\ell)d\ell.$$

- Each jump corresponds to a successful invasion of a new mutant trait.


population size
$\widehat{n}_x\delta_x$
$\widehat{n}_x$
$\widehat{n}_{x+\ell}\,\delta_{x+\ell}$
$\widehat{n}_{x+\ell}$
$\frac{1}{K}\delta_{x+\ell}$
ε
0
τ_1
t_2
σ_1
$\log K$

- The selection process has sufficient time between two trait mutations to eliminate disadvantaged traits.
- Since the population size is of order K, the duration for this competition phasis is of order log K.
- Succession of phases of trait mutant invasion, and phases of competition between traits.
- Convergence in the sense of finite dimensional distributions and convergence in law of the sequence of random measures $X^K_{Kt}(dx)dt$ to the random measure $\hat{n}_{Y_t}\,\delta_{Y_t}(dx)dt$.

Question: what happens for the marker distribution $\pi^K_t(x, dv)$ **?**

Fleming-Viot process (Dawson-Hochberg)

For $x \in \mathcal{X}$ and $u \in \mathcal{U}$, the Fleming-Viot process $(F_t^u(x, dv), t \geq 0)$ is

- a process with values in the probability measures on $\mathcal{U}$,
- started at time 0 with initial condition δ_u,
- associated with the (marker) mutation operator A,
- its law is characterized as the unique solution of the following martingale problem: For any $g \in \mathcal{D}(A)$,

$$\int_{\mathcal{U}} g(v)\, F_t^u(x, dv) = g(u) + b(x) \int_0^t \langle F_s^u(x, .), Ag\rangle\, ds + M_t^{(x,u)}(g).$$

$M^{(x,u)}(g)$ is a continuous square integrable martingale with quadratic variation

$$\frac{2\, b(x)}{\hat{n}_x} \int_0^t \Big(\langle F_s^u(x, .), g^2\rangle - \langle F_s^u(x, .), g\rangle^2 \Big) ds.$$

Substitution Fleming-Viot Process

Theorem: *Assume* $\nu_0^K(dy, dv) = n_0^K \, \delta_{(x_0,u_0)}(dy, dv)$ *and that* $\lim_{K\to\infty} n_0^K = \hat{n}_{x_0}$.

Assume that $x \mapsto \hat{n}_x$ *is a monotonous function. (Invasion implies fixation).*

The population process $(\nu_{Kt}^K, t \geq 0)$ *converges on* $M_F(\mathcal{X} \times \mathcal{U})$ *to the process* $(V_t, t \geq 0)$ *defined by*

$$V_t(dy, dv) = \hat{n}_{Y_t} \, \delta_{Y_t}(dy) \, F_t^{U_t}(Y_t, dv).$$

The process (Y_t, U_t) *started at* (x_0, u_0) *jumps from* (x, u) *to* $(x + \ell, v)$ *with the jump measure*

$$b(x) \, \hat{n}_x \, \frac{[f(x+\ell; x)]_+}{b(x+\ell)} \, F_t^u(x, dv) \, m(x, \ell) d\ell.$$

The convergence holds in the sense of finite dimensional distributions on $M_F(\mathcal{X} \times \mathcal{U})$ and in the sense of occupation measures.

Comments

- Three qualitative behaviors due to the three scales:

  - deterministic equilibrium for the transitory size of the population,

  - transitory diffusive behavior for the marker distribution,

  - jump process for the trait and marker distribution.

- After the jump (at time S), the marker dynamics is the Fleming-Viot process $F_t^v(Y_S, dw)$ started at δ_v at time S and parametrized by Y_S.

- The marker v has been chosen following the probability $F_t^{U_{S-}}(Y_{S-}, dv)$.

- Every jump creates a bottleneck for the genealogy of the marker.

- The distribution of the neutral marker depends on the ecological processes.

Extension to coexisting traits.

When "Invasion implies fixation" fails, several traits may coexist: the polymorphism evolution sequence (PES).
(Champagnat-M., PTRF 2011).

Between the jumps of the PES, the marker distribution is the sum of independent Fleming-Viot processes parametrized by the coexisting traits.

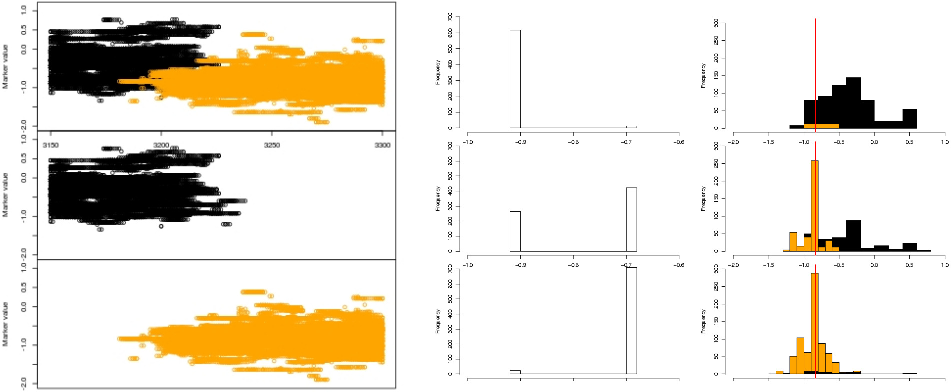
Thus, when there is a trait diversification, the distribution of the neutral diversity in one of the subpopulations does not evolve as completely forgetting the other ones. It depends on the complete trait distribution.

The model of beak's size

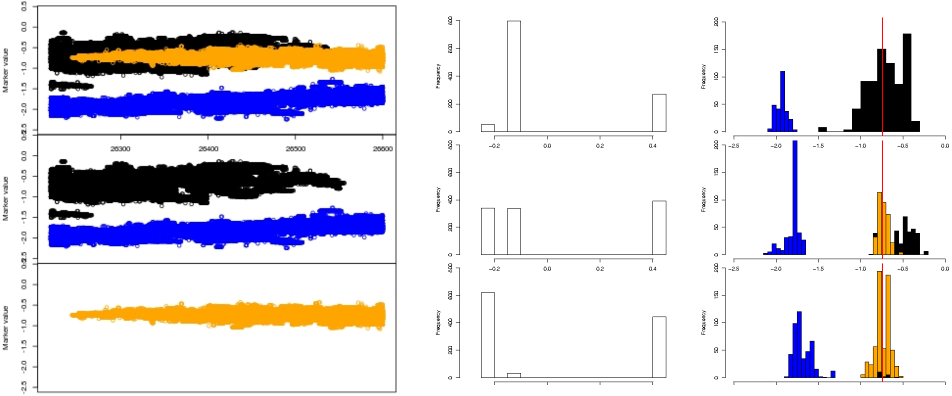
- $\mathcal{X} = [-1, 1]$; $\mathcal{U} = [-2, 2]$.
- $p_K = \frac{1}{K^2}$; $a_K = K^{3/2}$; $q_K = \frac{1}{\sqrt{K}}$.
- $m \sim N(0, 10^{-1})$ and $G_K \sim N(0, \frac{1}{\sqrt{K}})$ are two Gaussian laws conditioned to $[-1, 1]$ and $[-2, 2]$.
- $b(x) = \exp(-x^2/2\sigma_b^2)$; $\sigma_b = 0.9$. Maximum at 0.
- Symmetric competition for resources. $\eta(x) = 1$ and

$$C(x-y) = \exp(-(x-y)^2/2\sigma_C^2)\ ,\ \sigma_C = 0.8.$$

Individual-based Simulations



Coexistence case.



Wright-Fisher Evolutionary process

Discrete marker space $\mathcal{U} = \{A, a\}$, probabilities q_A and q_a to mutate from A to a and from a to A and $\lim_K \frac{r_K}{K} = \bar{r}$.

The process $(\nu^K_{Kt}, t \geq 0)$ converges to

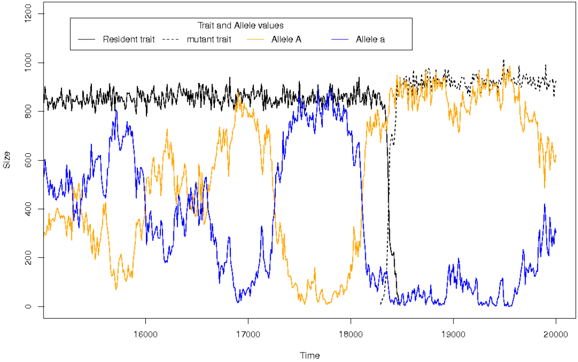
$$\hat{n}_{Y_t} \left(W^a_t \, \delta_{(Y_t, a)}(dy, du) + (1 - W^a_t) \, \delta_{(Y_t, A)}(dy, du) \right) ,$$

where between jumps,

$$dW^a_t = \bar{r} \, b(Y_t) \big(q_A (1 - W^a_t) - q_a W^a_t \big) dt + \sqrt{\frac{2b(Y_t)}{\widehat{n}_{Y_t}} \, W^a_t \, (1 - W^a_t)} dB_t .$$

The limiting process jumps with the TSS $(Y_t, t \geq 0)$.

At jump time t, the process $(W^a_t, 1 - W^a_t)$ goes to $(1, 0)$ with probability W^a_t and to $(0, 1)$ with probability $1 - W^a_t$.



A mutant trait appears around time 18290.
At that time, the *A*-allele frequency is 85%.
After fixation time around 18490, the *a*-allele population is extinct.
It is regenerated by mutation but gets extinct 3 times before time 19600.

Marker Distribution in a mutant trait population

Let us consider a mutant (y, v) appearing in a monomorphic population with trait x_0 and marker distribution $\pi^K(x_0, du)$. Assume that $f(y; x_0) > 0$.

Let $\varepsilon > 0$ and consider a sequence $(t_K; K \in \mathbb{N}^*)$ such that $\lim_{K\to+\infty} t_K/\log K = +\infty \quad ; \quad \lim_{K\to+\infty} t_K/K = 0$. (for example $t_K = \sqrt{K}\log K$).
Then

$$\lim_{K\to+\infty} \mathbb{P}\big(\langle \nu^K_{t_K}, 1_y\rangle > \varepsilon\big) = \frac{f(y;x_0)}{b(y)} = \lim_{K\to+\infty} \mathbb{P}\big(\pi^K_{t_K}(y, du) = \delta_v(du)\big);$$

$$\lim_{K\to+\infty} \mathbb{P}\big(\langle \nu^K_{t_K}, 1_y\rangle = 0\big) = 1 - \frac{f(y;x_0)}{b(y)}.$$

The fixation of the mutant creates a genetical bottleneck.

Idea: The rate of marker mutations can be large: of order $Kq_K \approx \sqrt{K}$. But until time s_K, $\log K \ll s_K \ll (\log K)^2$, the marker mutation frequency is small and between s_K and t_K, the mutant markers remain in negligible proportion.

Marker distribution in a trait-monomorphic population - time scale Kt

$\nu_0^K(dy,dv) = n_0^K\,\delta_{(x_0,u_0)}(dy,dv)$ and $n_0^K \to \hat{n}_{x_0}$. Let τ^K be the time of first trait mutation.

Proposition

(i) $\lim_{K\to\infty} \frac{\tau^K}{K} = \tau$.
(ii) The process $(\pi^K_{K(t\wedge\tau^K)}(x_0,dv), t\geq 0)$ converges in law to the Fleming-Viot process $(F_t^{u_0}(x_0,dv), t\geq 0)$ started at δ_{u_0} and parametrized by x_0 and stopped at τ.

Proof:

$$\langle \pi^K_{K(t\wedge\tau^K)}(x_0,\cdot), g\rangle = g(u_0) + H^{K,g}_{K(t\wedge\tau^K)}$$

$$+\, b(x_0)\,q_K(1-p_K)\,\frac{r_K}{K}\int_0^{t\wedge\tau^K} ds\left(1-\frac{1}{K\langle\nu^K_{Ks},1\rangle+1}\right)$$

$$\int_{\mathcal{U}}\pi^K_{Ks}(x_0,dv)\Big[\int_{\mathcal{U}}\big(g(v+h)-g(v)\big)G_K(v,h)dh\Big]$$

The process $H^{K,g}$ is a square integrable martingale.

Computation shows that its quadratic variation behaves as

$$\int_0^t \left\{ \frac{b(x_0) + d(x_0) + \eta(0)\langle \nu^K_{Ks}, 1\rangle}{\langle \nu^K_{Ks}, 1\rangle} \left(\langle \pi^K_{Ks}(x_0, .), g^2\rangle - \langle \pi^K_{Ks}(x_0, .), g\rangle^2 \right), \right.$$

as K tends to infinity.

Remark: Fundamental to choose $\frac{1}{K^2 p_K} \sim 1$ to get a non degenerate limiting quadratic variation process.