Slow-fast stochastic dynamics and quasi-stationary behavior of a diploid population

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Motivation

- Consider a population of individuals that gets extinct a.s. in finite time
- One gene, two alleles.
- In a long-time scale, conditionally to the surviving of the population, which allele will remain?
- Can we observe a long-time coexistence of the two alleles?

Understand the quasi-stationary behavior of a diploid population.

Model

- Diploid individuals.
- 1 gene, 2 alleles, A and a: genotypes AA, Aa and aa.
- 3-type logistic birth-and-death process with Mendelian reproduction:

$$(Z_t, t \geq 0) = ((Z_t^1, Z_t^2, Z_t^3), t \geq 0).$$

- Population size at time t: $N_t = Z_t^1 + Z_t^2 + Z_t^3$.

Birth and death rates

If $Z_t = z = (z_1, z_2, z_3) \in (\mathbb{Z}_+)^3$ with $n = z_1 + z_2 + z_3$,

- Diploid Mendelian reproduction:

$$\lambda_1(z) = \frac{b_1}{n}\left[(z_1)^2 + z_1 z_2 + \frac{(z_2)^2}{4}\right]$$

- Competition and natural death:

$$\mu_1(z) = z_1(d_1 + c_{11}z_1 + c_{12}z_2 + c_{13}z_3)$$

Scaling

- Large population size assumption.
- Population represented by the pure jump process: $Z^K = Z/K \in (\mathbb{Z}_+/K)^3$, $K \longrightarrow +\infty$.
- Scaling of demographic parameters and hypotheses:

$$b_i^K = \gamma K + \beta_i$$
$$d_i^K = \gamma K + \delta_i$$
$$c_{ij}^K = \frac{\alpha_{ij}}{K}$$
$$Z_0^K \underset{K\to\infty}{\longrightarrow} Z_0 \quad \text{in law,}$$

$$\text{there exists } C \geq 0 \text{ such that for all } K \in \mathbb{N}^*, \mathbb{E}\left((N_0^K)^3\right) \leq C,$$

where $\gamma > 0$ and Z_0 is a $(\mathbb{R}_+)^3$-valued random variable.

Hardy-Weinberg deviation, new variables

- Deviation from Hardy-Weinberg equilibrium:

$$Y_t^K = \frac{4Z_t^{1,K}Z_t^{3,K} - (Z_t^{2,K})^2}{4N_t^K} = N_t^K(p_t^{AA,K} - (p_t^{A,K})^2)$$
$$= N_t^K(2p_t^{A,K}p_t^{a,K} - p_t^{Aa,K})$$
$$= N_t^K(p_t^{aa,K} - (p_t^{a,K})^2)$$

- $X_t^K = \frac{2Z_t^{1,K}+Z_t^{2,K}}{2N_t^K}$ = proportion of allele A at time t.
- $2Z_t^{1,K} + Z_t^{2,K} = N_t^{A,K}$ = number of alleles A divided by K at time t,
- $2Z_t^{3,K} + Z_t^{2,K} = N_t^{a,K}$ = number of alleles a divided by K at time t.

$$(Z_t^{1,K}, Z_t^{2,K}, Z_t^{3,K}) \longleftrightarrow (N_t^K, X_t^K, Y_t^K) \longleftrightarrow (N_t^{A,K}, N_t^{a,K}, Y_t^K)$$

Fast dynamics

Proposition

For all $s, t > 0$, $\sup_{t \leq u \leq t+s} \mathbb{E}((Y_u^K)^2) \longrightarrow 0$ *when* K *goes to infinity.*

Proof.

By Kolmogorov-forward equation,

$$\frac{d\mathbb{E}\left((Y_t^K)^2\right)}{dt} \leq -2\gamma K \mathbb{E}\left((Y_t^K)^2\right) + C_1.$$

□

- Y^K is a fast variable and the population converges to Hardy-Weinberg equilibrium.

Slow dynamics

Theorem

The sequence of processes $\{((N_t^{A,K}, N_t^{a,K}), t \geq 0)\}_{K \geq 0}$ *converges in law in* $\mathbb{D}([0,T], (\mathbb{R}_+)^2)$ *toward a continuous-time diffusion process* (N^A, N^a) *such that in the neutral case where* $\beta_i = \beta$, $\delta_i = \delta$, $\alpha_{ij} = \alpha$ *for all* $i, j \in \{1, 2, 3\}$*:*

$$dN_t^A = \sqrt{\frac{4\gamma}{N_t^A + N_t^a}} N_t^A dB_t^1 + \sqrt{2\gamma \frac{N_t^A N_t^a}{N_t^A + N_t^a}} dB_t^2 + \left(\beta - \delta - \alpha \frac{N_t^A + N_t^a}{2}\right) N_t^A dt$$

$$dN_t^a = \sqrt{\frac{4\gamma}{N_t^A + N_t^a}} N_t^a dB_t^1 - \sqrt{2\gamma \frac{N_t^A N_t^a}{N_t^A + N_t^a}} dB_t^2 + \left(\beta - \delta - \alpha \frac{N_t^A + N_t^a}{2}\right) N_t^a dt$$

Comparison with the haploid case 1

Diploid population:

$$dN_t^A = \sqrt{\frac{4\gamma}{N_t^A + N_t^a}} N_t^A dB_t^1 + \sqrt{2\gamma \frac{N_t^A N_t^a}{N_t^A + N_t^a}} dB_t^2 + \left(\beta - \delta - \alpha \frac{N_t^A + N_t^a}{2}\right) N_t^A dt$$

$$dN_t^a = \sqrt{\frac{4\gamma}{N_t^A + N_t^a}} N_t^a dB_t^1 - \sqrt{2\gamma \frac{N_t^A N_t^a}{N_t^A + N_t^a}} dB_t^2 + \left(\beta - \delta - \alpha \frac{N_t^A + N_t^a}{2}\right) N_t^a dt$$

Haploid Lotka-Volterra diffusion (P. Cattiaux & S. Méléard (2010)):

$$dN_t^{A,h} = \sqrt{2\gamma N_t^{A,h}} dB_t^1 + (\beta - \delta - \alpha(N_t^{A,h} + N_t^{a,h}))N_t^{A,h} dt$$

$$dN_t^{a,h} = \sqrt{2\gamma N_t^{a,h}} dB_t^2 + (\beta - \delta - \alpha(N_t^{A,h} + N_t^{a,h}))N_t^{a,h} dt$$

Comparison with the haploid case 2

Diploid population:

$$dN_t = (\beta - \delta - \alpha N_t)N_t dt + \sqrt{2\gamma N_t} dB_t^1$$
$$dX_t = \sqrt{\frac{\gamma X_t(1 - X_t)}{N_t}} dB_t^2.$$

Haploid population (P. Cattiaux & S. Méléard (2010)):

$$dN_t^h = (\beta - \delta - \alpha N_t^h)N_t^h dt + \sqrt{2\gamma N_t^h} dW_t^1$$
$$dX_t^h = \sqrt{\frac{2\gamma X_t^h(1 - X_t^h)}{N_t^h}} dW_t^2.$$

Long time behavior of (N, X) and change of variables

- Cattiaux, Collet, Lambert, Martinez, Méléard, San Martín (2009): For all $(n,x) \in \mathbb{R} \times [0,1]$, $\mathbb{P}^{N,X}_{(n,x)}(T_0 < \infty) = 1$.
- Change of variables:

$$S^1_t = \sqrt{\frac{\gamma N_t}{2}} \cos\left(\frac{\arccos(2X_t - 1)}{\sqrt{2}}\right)$$
$$S^2_t = \sqrt{\frac{\gamma N_t}{2}} \sin\left(\frac{\arccos(2X_t - 1)}{\sqrt{2}}\right).$$

Under symmetric assumptions of the competition parameters the diffusion process $S = ((S^1_t, S^2_t), t \geq 0)$ satisfies

$$dS_t = dW_t - \nabla Q(S_t)dt.$$

Diffusion coefficient

$$Q(S) = \begin{cases} \frac{\ln\left(\left(S^1\right)^2 + \left(S^2\right)^2\right)}{2} + \frac{1}{2}\ln\left(\sin\left(\sqrt{2}\arctan\left(\frac{S^2}{S^1}\right)\right)\right) \\ \qquad - \left(\beta - \delta - \frac{\alpha\gamma}{4}\left(\left(S^1\right)^2 + \left(S^2\right)^2\right)\right)\frac{\left(S^1\right)^2 + \left(S^2\right)^2}{4} \\ \qquad \text{if } S^1 \geqslant 0 \\ \frac{\ln\left(\left(S^1\right)^2 + \left(S^2\right)^2\right)}{2} + \frac{1}{2}\ln\left(\sin\left(\sqrt{2}\left(\arctan\left(\frac{S^2}{S^1}\right) + \pi\right)\right)\right) \\ \qquad - \left(\beta - \delta - \frac{\alpha\gamma}{4}\left(\left(S^1\right)^2 + \left(S^2\right)^2\right)\right)\frac{\left(S^1\right)^2 + \left(S^2\right)^2}{4} \\ \qquad \text{if } S^1 \leqslant 0. \end{cases}$$

Definition space, absorbing sets

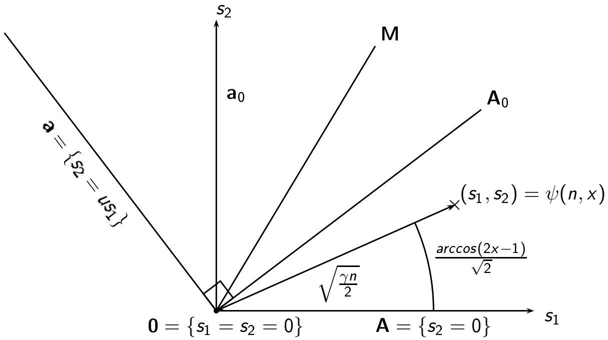

Figure : Set $\mathcal{D}$ of the values taken by S_t, for $t \geq 0$.

Absorption of the diffusion process S: properties

Theorem

(i) *For all* $s \in D \setminus \mathbf{0}$, $\mathbb{P}_s(T_{\mathbf{A}} \wedge T_{\mathbf{a}} < T_{\mathbf{0}}) = 1$.

- *Extended Girsanov Theorem (Cattiaux et al. (2009))* $\mathbb{P}_s(T_{\mathbf{A}} \wedge T_{\mathbf{a_0}} < T_{\mathbf{0}}) = 1$ *for all* $s \in \mathcal{D}_1$.
- *Martingale argument to conclude in the neutral case.*
- *Girsanov Theorem in the non-neutral case.*

(ii) *For all* $s \in D \setminus \partial D$, $\mathbb{P}_s(T_{\mathbf{A}} < T_{\mathbf{0}}) > 0$, *and* $\mathbb{P}_s(T_{\mathbf{a}} < T_{\mathbf{0}}) > 0$.

- *In the neutral case,* $\mathbb{P}_s(T_{\mathbf{a}} < T_{\mathbf{0}}) = 1/2$ *for all* $s \in \mathbf{M}$.
- *Girsanov Theorem:* $\mathbb{P}_s(T_{\mathbf{M}} < \infty) > 0$ *for all* $s \in \mathcal{D}$.
- *Strong Markov property to conclude.*
- *Girsanov Theorem in the non-neutral case.*

Quasi-stationary behavior

Theorem

(i) *There exists a unique distribution* ν_1 *on* $D \setminus \partial D$ *such that*
$$\lim_{t\to\infty} \mathbb{P}_s(S_t \in E | T_{\partial D} > t) = \nu_1(E) \quad \forall s \in D \setminus \partial D.$$

(ii) *There exists a unique distribution* ν *on* $D \setminus \mathbf{0}$ *such that*
$$\lim_{t\to\infty} \mathbb{P}_s(S_t \in E | T_0 > t) = \nu(E) \quad \forall s \in D \setminus \partial D.$$

$\Longrightarrow$ The law $\lim_{t\to\infty} \mathbb{P}(X_t \in .|N_t > 0)$ is well-defined.

Numerical results 1: neutral case

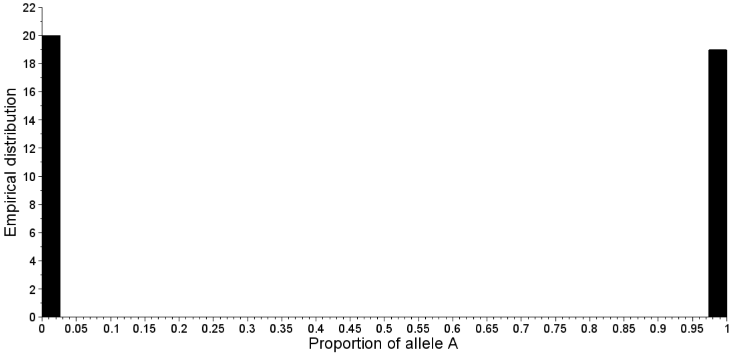

Figure : Distribution of the proportion X_t of allele A in a neutral case, knowing that $N_t \neq 0$. In this figure, $\beta_i = 1 = \delta_i$, and $\alpha_{ij} = 0.1$ for all i, j.

Numerical results 2: overdominance

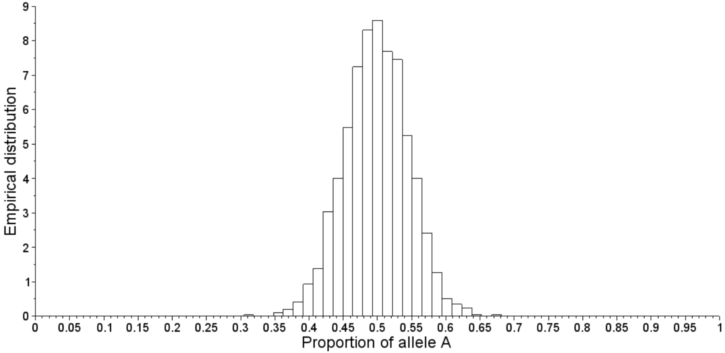

Figure : Distribution of the proportion X_t of allele A in an overdominance case, knowing that $N_t \neq 0$. $\beta_i = 1$ for all $i \neq 2$, $\beta_2 = 5$, $\delta_i = 0$ for all i, $\alpha_{ij} = 0.1$ for all (i,j), and $T = 100$.

Numerical results 3: separate niches

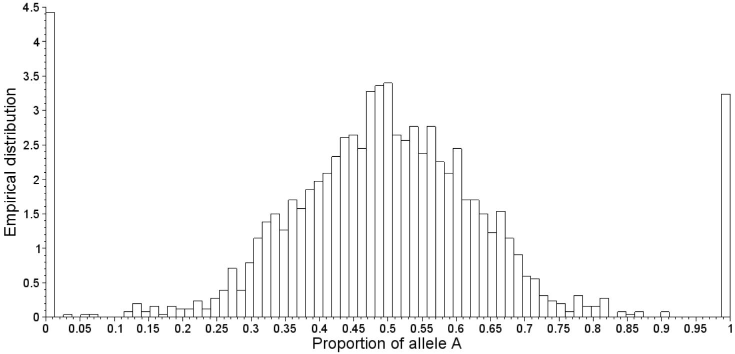

Figure : Distribution of the proportion X_t of allele A in a separate niches case, knowing that $N_t \neq 0$. $\beta_i = 1$, $\delta_i = 0$, $\alpha_{ii} = 0.1$ for all i, $\alpha_{ij} = 0$ for all $i \neq j$, and $T = 2500$.

New work and perspectives

- More alleles (joint work with Sylvie Méléard).
- What are the exact conditions for coexistence of the two alleles?

Bibliography

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