Stochastic modeling and eco-evolution of a diploid population

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Outline of the presentation

⓿ A diploid Mendelian population model

❶ Stochastic modeling of the mutational meltdown

- Motivations and references
- Fixation probability of a slightly non neutral allele
- Existence of a mutational meltdown
- Numerical results and biological interpretations

❷ Slow-fast dynamics, quasi-stationarity and measure-valued processes

- Slow-fast dynamics
- Quasi-stationary behavior of a diploid population
- Numerical results
- Multi-allelic model, measure-valued processes, allele continuum

Model

- 1 gene, 2 alleles: A and a.
- Diploid individuals: genotypes AA, Aa and aa.
- Population at time t:

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

- $(Z_t, t \geq 0)$ is a birth-and-death process with Mendelian reproduction and competition.

Birth and death rates

For any $(k, m, n) \in (\mathbb{Z}_+)^3$ such that $N = k + m + n$,

$$\begin{aligned}
\lambda_1(k,m,n) &= \frac{b_1}{N-1}\left[k(k-1) + km + \frac{m(m-1)}{4}\right] \\
\lambda_2(k,m,n) &= \frac{b_2}{N-1}\left[km + mn + \frac{m(m-1)}{2} + 2kn\right] \\
\lambda_3(k,m,n) &= \frac{b_3}{N-1}\left[n(n-1) + mn + \frac{m(m-1)}{2}\right] \\
\mu_1(k,m,n) &= k(d_1 + c_{11}(k-1) + c_{12}m + c_{13}n) \\
\mu_2(k,m,n) &= m(d_2 + c_{21}k + c_{22}(m-1) + c_{23}n) \\
\mu_3(k,m,n) &= n(d_3 + c_{31}k + c_{32}m + c_{33}(n-1))
\end{aligned}$$

Demographic parameters: $b_i > 0$, $d_i \geq 0$, $c_{ij} > 0$, for $i, j \in \{1, 2, 3\}$.

Motivations

Mutational meltdown:

- Lynch, Conery and Burger (1995).
- Observed in small populations.
- Combination of two phenomena that reinforce each other.

Small population size

Frequent deleterious mutation fixations

Demography

Genetics

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Demography Genetics

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Demography Genetics

Hypotheses for this work

- $b_i = b > 0$ and $c_{ij} = c > 0$ for all $i, j \in \{1, 2, 3\}$.
- $d_1 = d \geq 0$, $d_2 = d + \delta$ and $d_3 = d + \delta'$.
- No death when there are only 2 individuals left.

$$\Longrightarrow Z_t \in (\mathbb{Z}_+)^3_{**} = (\mathbb{Z}_+)^3 \setminus \{(0,0,0), (1,0,0), (0,1,0), (0,0,1)\}.$$

$(Z_t, t \geq 0)$ is a Markov process with 2 absorbing sets:

- $\Gamma_A = \{(k, 0, 0) : k \geq 2\}$: fixation of allele A,
- $\Gamma_a = \{(0, 0, n) : n \geq 2\}$: fixation of allele a.

Fixation probability of allele a

- Aim: Study the fixation probability of allele a if the population starts from the state $(k, m, n) \in (\mathbb{Z}_+)^3_{**}$:

$$u^{\delta,\delta'}_{k,m,n}$$

- Champagnat & Lambert (2007): haploid case.
- Neutral case ($\delta = \delta' = 0$): $\left(X_t = \frac{Z_t^2+2Z_t^3}{2(Z_t^1+Z_t^2+Z_t^3)}, t \geq 0\right)$ is a martingale.

$$\Longrightarrow \quad u^{0,0}_{k,m,n} = \frac{m+2n}{2(k+m+n)}.$$

Taylor expansion of $u_{k,m,n}^{\delta,\delta'}$

- Decomposition of u:

$$u_{k,m,n}^{\delta,\delta'} = \sum_{n'} \sum_{(i_1,...,i_l)\in C_{(k,m,n)\to(0,0,n')}} \pi_{i_1 i_2}^{\delta,\delta'} ... \pi_{i_{l-1} i_l}^{\delta,\delta'}.$$

- For all $(k,m,n) \in (\mathbb{Z}_+)^3_{**}$, $u_{k,m,n}^{\delta,\delta'}$ is a differentiable function of (δ,δ') in $(0,0)$:

$$u_{k,m,n}^{\delta,\delta'} = \frac{m+2n}{2(k+m+n)} - \delta v_{k,m,n} - \delta' w_{k,m,n} + o(|\delta|+|\delta'|).$$

- $|v_{k,m,n}| \leq C(k+m+n)$ and $|w_{k,m,n}| \leq C(k+m+n)$ for all $(k,m,n) \in (\mathbb{Z}_+)^3_{**}$.

Kolmogorov-forward equation

$$\begin{cases} (L^{\delta,\delta'}u(.,\delta,\delta'))(k,m,n)=0 \quad \forall(k,m,n)|N=k+m+n\geq 2 \\ u((0,0,n),\delta,\delta')=1 \quad \forall n\geq 2 \\ u((k,0,0),\delta,\delta')=0 \quad \forall k\geq 2 \end{cases}$$

$$u^{\delta,\delta'}_{k,m,n}=\frac{2n+m}{2(k+m+n)}-\delta v_{k,m,n}-\delta' w_{k,m,n}+o(|\delta|+|\delta'|).$$

$$\begin{cases} (L^{0,0}v)(k,m,n)=\frac{m(n-k)}{2N(N-1)} \quad \forall(k,m,n)|k+m+n\geq 3 \\ (L^{0,0}v)(k,m,n)=0 \quad \forall(k,m,n)|k+m+n=2 \\ v(2,0,0)=v(0,0,2)=0 \end{cases} \tag{S1}$$

The formula of $v_{k,m,n}$

Proposition (1.3.6)

For all (k,m,n) *such that* $N=k+m+n\geq 2$,

$$v(k,m,n)=(k-n)\left[\frac{m}{N}x_N+\frac{N^2-(k-n)^2}{N^2}y_N\right] \tag{1}$$

where the sequence of vectors $(z_N)_{N\geq 3}=\begin{pmatrix}x_N\\ y_N\end{pmatrix}_{N\geq 3}$ *is the unique bounded solution of the following system of equations:*

$$\begin{cases} B_N z_{N+1}=C_N z_N+D_N z_{N-1}+f_N & \text{for all } N\geq 4\\ B_3 z_4=\tilde{C}_3 z_3+f_3, \end{cases} \tag{S2}$$

where the matrices B_N, C_N, $\tilde{C}_3$, D_N *and the vectors* f_N *are known.*

Sketch of the proof

Proof.

- If (1) is true then $(S2)$ implies $(S1)$.
- $(S2)$ has a bounded solution $(z_N)_{N\geq 3}$ if b is small: for $N \geq 3$,

$$B_N z_{N+1} = (C_N + K_N) z_N + \sum_{k=3}^{N} (-1)^{N-k} E(k,N) f_k, \quad \text{if} \qquad \text{(S2')}$$

$$\begin{cases} K_3 = \tilde{C}_3 - C_3 \\ K_N = D_N (C_{N-1} + K_{N-1})^{-1} B_{N-1} & \forall N \geq 4 \\ E(k,k) = I_2 & \forall k \geq 3 \\ E(k,N) = D_N (C_{N-1} + K_{N-1})^{-1} E(k, N-1) & \forall k \in [\![3, N-1]\!]. \end{cases}$$

- For all $(k,m,n) \in (\mathbb{Z}_+)^3_{**}$, $v_{k,m,n}$ is an analytic function of b.

□

Mutations and mutational time scale

- Each individual mutates at rate $\mu_K = \frac{2\mu}{K}$, $K \to +\infty$.
- Each individual is characterized by its genotype $g = (x, x') \in \mathbf{G}$.
- $M(x_1, x_2)$ is the probability that a DNA strand x_1 mutates to x_2.
- Population at time t:

$$Z_t^K = \sum_{i=1}^{N_t^K} \delta_{g_t^{i,K}}$$

Theorem ((1.5.1), Convergence towards the TSS)

For all $0 < t_1 < ... < t_n$,

$$(Z_{Kt_1}^K, ..., Z_{Kt_n}^K) \longrightarrow (\tilde{N}_{t_1}\delta_{G_{t_1}}, ..., \tilde{N}_{t_n}\delta_{G_{t_n}}) \quad \textit{in law, when } K \to \infty.$$

Trait Substitution Sequence

- Conditionally to $(G_{t_1}, ..., G_{t_n}) = (g_1, ..., g_n)$, the random variables $\tilde{N}_{t_1}$, ..., $\tilde{N}_{t_n}$ are independent and $\tilde{N}_{t_i}$ has law $l(., b(g_i), d(g_i), c(g_i, g_i))$, with
$$l(N, b, d, c) := \frac{C}{N} \prod_{k=2}^{N-1} \frac{b}{d+kc}.$$
- $(G_t)_{t>0}$ jumps from genotype $g_1 = (x_1, x_1)$ to $g_2 = (x_2, x_2)$ at rate
$$2\mu M(x_1, x_2) \sum_{N=2}^{\infty} N l(N, b(g_1), d(g_1), c(g_1, g_1)) f((N-1, 1, 0), x_1, x_2).$$
- If $d(x_1, x_2) = d(g_1) + \delta$ and $d(g_2) = d(g_1) + \delta'$,
$$f((N-1, 1, 0), x_1, x_2) = u^{\delta, \delta'}_{N-1,1,0}.$$

Existence of a mutational meltdown

Jump rate of the process G: $\tau(b, d, c, \delta, \delta')$.

- Small population size $\Longleftrightarrow$ Frequent deleterious mutation fixations.
- More and more frequent fixations of deleterious mutations.

Theorem (1.5.2)

If $\delta > 0$ and $\delta' > \delta$, and if b is small enough, the mean time $T(b, d, c, \delta, \delta') = 1/\tau(b, d, c, \delta, \delta')$ is a decreasing function of d.

Distribution of the population size

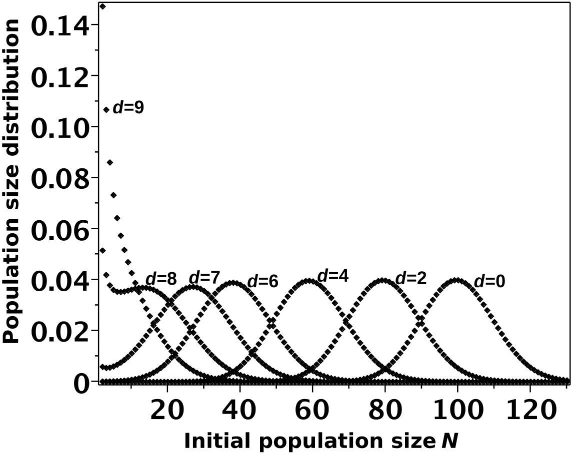

Figure: Distribution of the population size under different intrinsic death rates d. In this figure, $b = 10$ and $c = 0.1$.

Existence of a mutational meltdown

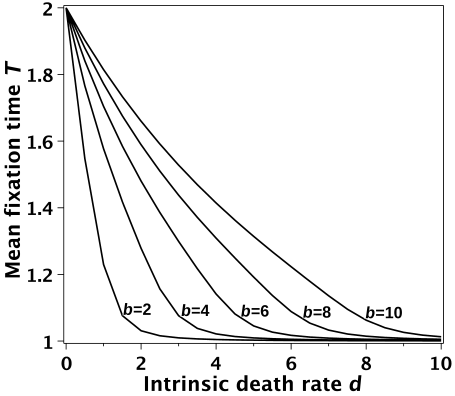

Figure: Relationship between the mean time to fixation of a deleterious mutation T and parameters b and d. Each curve corresponds to a fixed value of b. Other parameters are $\delta = 0.05$, $\delta' = 0.1$, $c = 0.1$ and $m = 1$.

Mean population size mean dynamics

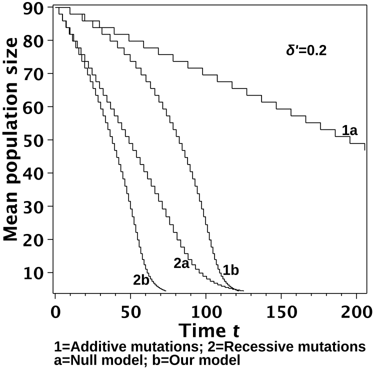

Figure: Mean temporal decrease in the mean population size in additive and recessive cases. $b = 10$, $c = 0.1$, $m = 1$, $D_0 = 1$ and $\delta' = 0.2$.

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- C.C., Méléard, S., Porcher, E., Robert, A. (2013): Quantifying the mutational meltdown in diploid populations. Am. Nat. 181(5):623-636.
- C.C.: Stochastic modeling of density-dependent diploid populations and extinction vortex. Adv. Appl. Probab., in press.

Large population size and allometry

- Each individual has size $1/K$, $K \to +\infty$.
- Z^K is a jump process with jump size equal to $1/K$.
- Demographic parameters depend on K. If $z = (z_1, z_2, z_3) \in (\mathbb{Z}_+)^3/K$ and $n = z_1 + z_2 + z_3$,

$$\begin{aligned}
\lambda_1^K(z) &= \frac{Kb_1^K}{n}\left(z_1 + \frac{z_2}{2}\right)^2, \\
\lambda_2^K(z) &= \frac{Kb_2^K}{n}2\left(z_1 + \frac{z_2}{2}\right)\left(z_3 + \frac{z_2}{2}\right), \\
\lambda_3^K(z) &= \frac{Kb_3^K}{n}\left(z_3 + \frac{z_2}{2}\right)^2. \\
\mu_1^K(z) &= Kz_1(d_1^K + K(c_{11}^K z_1 + c_{21}^K z_2 + c_{31}^K z_3)), \\
\mu_2^K(z) &= Kz_2(d_2^K + K(c_{12}^K z_1 + c_{22}^K z_2 + c_{32}^K z_3)), \\
\mu_3^K(z) &= Kz_3(d_3^K + K(c_{13}^K z_1 + c_{23}^K z_2 + c_{33}^K z_3)).
\end{aligned}$$

Demographic parameters scaling

Hypotheses:

$$\begin{aligned} b_i^K &= \gamma K + \beta_i \in [0, \infty[, \\ d_i^K &= \gamma K + \delta_i \in [0, \infty[, \\ c_{ij}^K &= \frac{\alpha_{ij}}{K} > 0, \\ Z_0^K &\underset{K \to \infty}{\longrightarrow} Z_0 \quad \text{in law}, \end{aligned}$$

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

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

Hardy-Weinberg deviation, new variables

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

$$X_t^K = \frac{2Z_t^{1,K} + Z_t^{2,K}}{2N_t^K}$$

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

Fast dynamics

Proposition (3.3.2)

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

Proof.

By Kolmogorov-forward equation,

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

□

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

Slow dynamics

Theorem (Theorem 3.3.3 and Corollary 3.3.4)

For all $\epsilon > 0$, $T^K_\epsilon = \inf\{t \in [0,T] : N^K_t \leq \epsilon\}$. $\{(N^K, X^K)_{.\wedge T^K_\epsilon}\}_{K\geq 1}$ *converges in law in* $\mathbb{D}([0,T], [\epsilon,\infty[\times[0,1])$ *toward a stopped continuous-time diffusion process* $(N,X)_{.\wedge T_\epsilon}$. *In the neutral case where* $\beta_i = \beta$, $\delta_i = \delta$ *and* $\alpha_{ij} = \alpha$,

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

Diploid vs haploid (1)

Haploid diffusion: Cattiaux & Méléard (2010).

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

$$dX_t = \sqrt{\frac{\gamma X_t(1 - X_t)}{N_t}} dB_t^2$$

$$dN_t^h = (\beta - \delta - \alpha N_t^h)N_t^h dt + \sqrt{2\gamma N_t^h} d\tilde{B}_t^1$$

$$dX_t^h = \sqrt{\frac{2\gamma X_t^h(1 - X_t^h)}{N_t^h}} d\tilde{B}_t^2$$

Diploid vs haploid (2)

$$
\begin{aligned}
dN_t^A &= N_t^A \left[\left[\beta - \delta - \alpha \frac{(N_t^A + N_t^a)}{2}\right]\right] dt \\
&\quad + \sqrt{\frac{4\gamma}{N_t^A + N_t^a}} N_t^A dW_t^1 + \sqrt{2\gamma \frac{N_t^A N_t^a}{N_t^A + N_t^a}} dW_t^2 \\
dN_t^a &= N_t^a \left[\left[\beta - \delta - \alpha \frac{(N_t^A + N_t^a)}{2}\right]\right] dt \\
&\quad + \sqrt{\frac{4\gamma}{N_t^A + N_t^a}} N_t^a dW_t^1 - \sqrt{2\gamma \frac{N_t^A N_t^a}{N_t^A + N_t^a}} dW_t^2
\end{aligned}
$$

$$
\begin{aligned}
dN_t^{A,h} &= (\beta - \delta - \alpha(N_t^{A,h} + N_t^{a,h}))N_t^{A,h} dt + \sqrt{2\gamma N_t^{A,h}} d\tilde{W}_t^1 \\
dN_t^{a,h} &= (\beta - \delta - \alpha(N_t^{A,h} + N_t^{a,h}))N_t^{a,h} dt + \sqrt{2\gamma N_t^{a,h}} d\tilde{W}_t^2
\end{aligned}
$$

Long-time population behavior

- Extinction: $\mathbb{P}_x^N(T_0 < +\infty) = 1$ (Cattiaux et al. (2009)).
- Quasi-stationary behavior of the population?

- Cattiaux, P., Collet, P., Lambert, A., Martinez, S., Méléard, S. and San Martín, J. (2009): Quasi-stationary distributions and diffusion models in population dynamics. Ann. of Proba. 37(5):1926-1969.
- Villemonais, D. (2011): Distributions quasi-stationnaires et méthodes particulaires pour l'approximation de processus conditionnées. Thèse, École Polytechnique.
- Méléard, S. and Villemonais, D. (2012): Quasi-stationary distributions and population processes. Probab. Surv. 9:340-410.
- Cattiaux, P., and Méléard, S. (2010): Competitive or weak competitive stochastic Lotka-Volterra systems conditioned on non-extinction. J. Math. Biol. 60:797-829.
- C.C.: From diploid populations to Wright-Fisher diffusions and quasi-stationary distributions. Arxiv 1309.3405, Submitted.

Change of variables

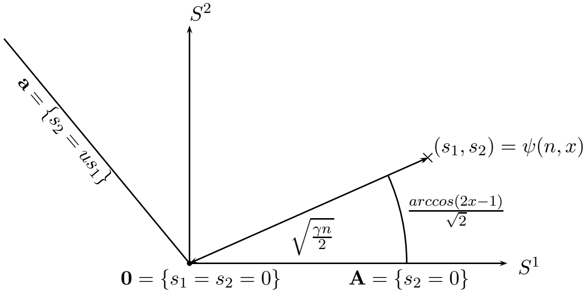
$$S_t^1 = \sqrt{\frac{2N_t}{\gamma}} \cos\left(\frac{\arccos(2X_t - 1)}{\sqrt{2}}\right)$$
$$S_t^2 = \sqrt{\frac{2N_t}{\gamma}} \sin\left(\frac{\arccos(2X_t - 1)}{\sqrt{2}}\right).$$

$$dS_t^1 = dW_t^1 - q_1(S_t)dt$$
$$dS_t^2 = dW_t^2 - q_2(S_t)dt,$$

If $\alpha_{ij} = \alpha_{ji}$ for all $i, j \in \{1, 2, 3\}$,

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

Absorption of the diffusion process S



Absorbing sets: $\mathbf{0}$, $\mathbf{A} \cup \mathbf{0}$, $\mathbf{a} \cup \mathbf{0}$, $\mathbf{A} \cup \mathbf{a} \cup \mathbf{0}$.

Theorem (3.4.7)

- *For all* $s \in \mathcal{D} \setminus \mathbf{0}$, $\mathbb{P}_s^S(T_\mathbf{A} \wedge T_\mathbf{a} < T_\mathbf{0}) = 1$.
- *For all* $s \in \mathcal{D} \setminus \partial\mathcal{D}$, $\mathbb{P}_s^S(T_\mathbf{A} < T_\mathbf{0}) > 0$, *and* $\mathbb{P}_s^S(T_\mathbf{a} < T_\mathbf{0}) > 0$.

Quasi-stationary behavior of (N, X)

Theorem (Theorem 3.4.10 and Corollary 3.4.11)

- *There exists a (unique) probability measure* $\nu^{N,X}$ *on* $\mathbb{R}_+^* \times]0,1[$ *such that for all* $F \subset \mathbb{R}_+^* \times]0,1[$ *and all* $(n,x) \in \mathbb{R}_+^* \times]0,1[$,

$$\lim_{t\to\infty} \mathbb{P}_{(n,x)}^{N,X}((N_t, X_t) \in F | T_0^N \wedge T_0^X \wedge T_1^X > t) = \nu^{N,X}(F).$$

- *There exists a (unique) probability measure* $\nu_0^{N,X}$ *on* $\mathbb{R}_+^* \times [0,1]$ *such that for all* $F \subset \mathbb{R}_+^* \times [0,1]$ *and* $(n,x) \in \mathbb{R}_+^* \times]0,1[$,

$$\lim_{t\to\infty} \mathbb{P}_{(n,x)}^{N,X}((N_t, X_t) \in F | T_0^N > t) = \nu_0^{N,X}(F).$$

Neutral case

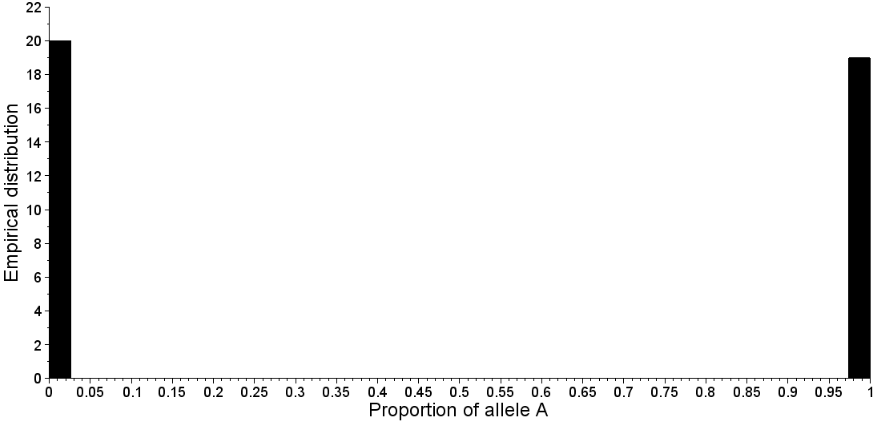


Figure: Distribution of the proportion X_t of allele A in the neutral case, knowing that $N_t \neq 0$. $\beta_i = 1 = \delta_i$, and $\alpha_{ij} = 0.1$ for all i, j, and $t = 40$.

Overdominance

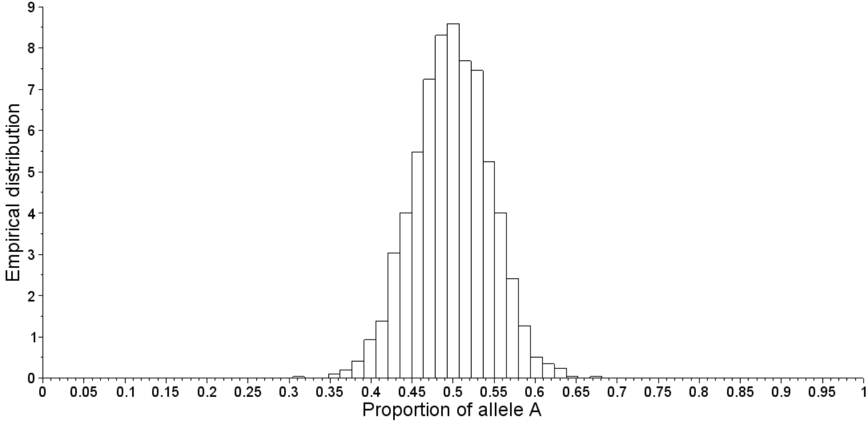


Figure: Distribution of the proportion X_t of allele A in an overdominance case, knowing that $N_t \neq 0$. $\beta_i = 1$ for all $i \neq 2$, $\beta_2 = 5$, $\delta_i = 0$ for all i, $\alpha_{ij} = 0.1$ for all (i,j), and $T = 100$.

Different niches

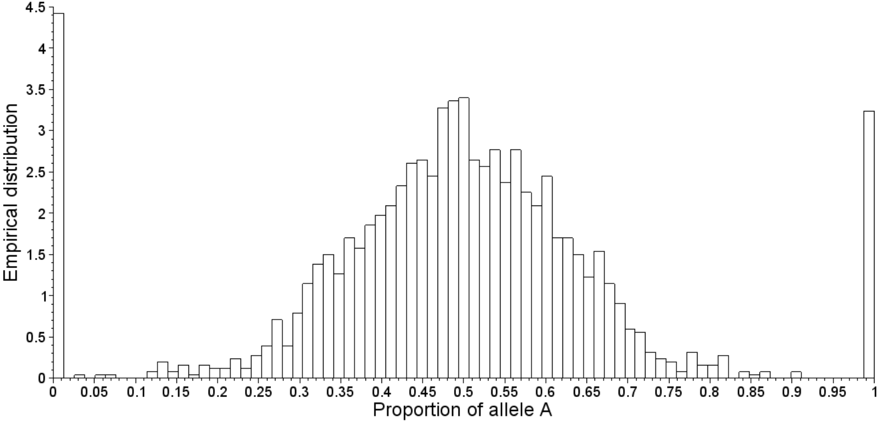


Figure: Distribution of the proportion X_t of allele A in a separate niches case, knowing that $N_t \neq 0$. $\beta_i = 1$, $\delta_i = 0$, $\alpha_{ii} = 0.1$ for all i, $\alpha_{ij} = 0$ for all $i \neq j$, and $T = 2500$.

Finite number of alleles

- 1 gene, L alleles $\in [\![1, L]\!]$.
- Population at time t:

$$\mathbf{X}^K(t) = (x_{ij}^K(t))_{1 \leq i,j \leq L} \in \mathcal{S}_L(\mathbb{Z}_+/2K).$$

- $x_{ii}^K(t) \in \mathbb{Z}_+/K$ is the rescaled number of individuals with genotype ii at time t.
- $x_{ij}^K(t) + x_{ji}^K(t) = 2x_{ij}^K(t) \in \mathbb{Z}_+/K$ is the rescaled number of individuals with genotype ij at time t.

Finite number of alleles

- Birth rates: if the population $\mathbf{x}$ has rescaled size $\phi_1(\mathbf{x}) \in \mathbb{Z}_+/K$,

$$\lambda_{ij}^K(\mathbf{x}) = b_{ij}^K K\phi_1(\mathbf{x})2p_ip_j = Kb_{ij}^K 2\frac{\left(\sum_{k=1}^L x_{ik}\right)\left(\sum_{l=1}^L x_{jl}\right)}{\phi_1(\mathbf{x})}$$

$$\lambda_{ii}^K(\mathbf{x}) = b_{ii}^K K\phi_1(\mathbf{x})(p_i)^2 = Kb_{ii}^K \frac{\left(\sum_{k=1}^L x_{ik}\right)^2}{\phi_1(\mathbf{x})}.$$

- Death rates:

$$\mu_{ij}^K(\mathbf{x}) = Kx_{\{ij\}}\left(d_{ij}^K + K\sum_{1\le k,l\le L} c_{ij,kl}^K x_{kl}\right),$$

- Scaling:

$$b_{ij}^K = \gamma K + \beta_{ij}, \quad d_{ij}^K = \gamma K + \delta_{ij} \quad \text{and} \quad c_{ij,kl}^K = \frac{\alpha_{ij,kl}}{K}.$$

Slow-fast dynamics and measure-valued process

- Fast dynamics: convergence toward Hardy-Weinberg equilibrium.
- Slow dynamics: $\{(N^K(t\wedge T^K_\epsilon), p^K_2(t\wedge T^K_\epsilon), p^K_3(t\wedge T^K_\epsilon), ..., p^K_L(t\wedge T^K_\epsilon))_{0\leq t\leq T}\}_{K\geq 1}$ converges in law in $\mathbb{D}([0,T],[\epsilon,\infty[\times[0,1]^{L-1})$ toward a stopped diffusion process $(N(t\wedge T_\epsilon), p_2(t\wedge T_\epsilon), ..., p_L(t\wedge T_\epsilon))_{0\leq t\leq T}$.
- Measure-valued process:

$$\eta^L_t = \sum_{i=1}^{L} x^L_i(t)\delta_{\frac{i}{L}} \in \mathcal{M}_F([0,1]) \quad \text{with } x^L_i(t) = N(t)p_i(t)$$

$$\zeta^L_t = \left(\frac{\langle \eta^L_t, 1\rangle}{2}, \frac{\eta^L_t}{\langle \eta^L_t, 1\rangle}\right) \in \mathbb{R}^*_+ \times \mathcal{P}([0,1]) \cup \{0\} \times p_\partial.$$

Allele continuum and convergence

Theorem (4.4.1)

The sequence $(\zeta^L_{t\wedge T^L_\epsilon}, t \geq 0)$ *converges in law in* $\mathbb{D}([0,T],[\epsilon,+\infty[\times\mathcal{P}([0,1]))$ *towards the unique continuous-time stopped process* $(\zeta_{t\wedge T_\epsilon}, t\in[0,T]) = ((n_{t\wedge T_\epsilon}, p_{t\wedge T_\epsilon}), t\in[0,T])$ *such that*

$$\sup_{t\in[0,T_\epsilon]} \mathbb{E}(n_t^3) < +\infty,$$

and solution of the martingale problem: for all functions $f\in\mathcal{C}^2_b(\mathbb{R}^*_+\times\mathbb{R},\mathbb{R})$ *and* G *measurable on* $[0,1]$*, if* $H(n,p) = f(n,\langle p, G\rangle)$*, then the process* $(m^H_t, t\in[0,T])$ *such that* $t\in[0,T]$*,*

$$m^H_t = H(n_t,p_t) - H(n_0,p_0) - \int_0^{t\wedge T_\epsilon} \mathcal{L}^\zeta H(n_s,p_s)ds$$

is a continuous martingale.

Generator

$$H(n,p) = f(n, \langle p, G\rangle),$$

$$\begin{aligned}
\mathcal{L}^{\zeta} H(n,p) = {} & n\int_0^1\int_0^1 \beta_{xy} - \delta_{xy} - \left(\int_0^1\int_0^1 \alpha_{xy,uv}\, n\, dp(u)dp(v)\right) dp(x)dp(y)\,\partial_1 f(n, \langle p, G\rangle) \\
& + \gamma n\, \partial^2_{11} f(n, \langle p, G\rangle) \\
& + \int_0^1 G(x) \Bigg[\int_0^1 \int_0^1 \Bigg(\beta_{xz} - \beta_{yz}) - (\delta_{xz} - \delta_{yz}) \\
& \quad - \int_0^1\int_0^1 (\alpha_{xz,uv} - \alpha_{yz,uv})\, n\, dp(u)dp(v)\Bigg) dp(y)dp(z)\Bigg] dp(x)\,\partial_2 f(n, \langle p, G\rangle) \\
& + \frac{\gamma}{n}\left(\langle p, G^2\rangle - \langle p, G\rangle^2\right)\, \partial^2_{22} f(n, \langle p, G\rangle).
\end{aligned}$$