An Eco-Evolutionary approach of adaptation and recombination in a large population of varying size

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Two different ways of adaptation

- preexisting alleles that become advantageous after an environmental change (soft selective sweep)
- new mutation (hard selective sweep)

Question

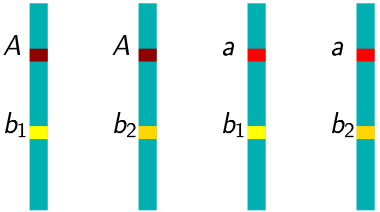
What is the effect of these two ways of adaptation on neutral diversity ?

1. Model
2. Soft selective sweep
3. Strong selective sweep

Eco-Evolutionary framework

- *Adaptive Dynamics : A Geometrical Study of the Consequences of Nearly Faithful Reproduction*, Metz and al [MGM$^+$96]
- Fournier and Méléard [FM04], Champagnat [Cha06], Champagnat and al [CFM06], Champagnat and Méléard [CM07, CM11], Champagnat and Lambert [CL07], Collet and al [CMM11], Coron [Cor12], Billiard and al [BFMT13]

Model



Ecological parameters

- sexual haploid population
- f_α and D_α birth rate and intrinsic death rate
- C_{α_1,α_2} competitive pressure felt by an individual carrying allele α_1 from an individual carrying allele α_2.
- $K \in \mathbb{N}$ rescales the competition between individuals. Related to the concept of carrying capacity,

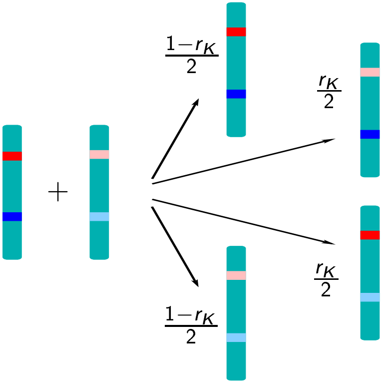
Death rate

Death rate

$$d^K_{\alpha\beta}(N) = \left[D_\alpha + C_{\alpha,A}N_A/K + C_{\alpha,a}N_a/K\right] N_{\alpha\beta}$$

Birth event

r_K = recombination probability per reproductive event.



Mate chosen uniformly among available gametes :

$$p_{\alpha\beta}(N) = f_\alpha N_{\alpha\beta}/(f_A N_A + f_a N_a)$$

Birth rate of Ab_1 individuals

$$Ab_1 \times Ab_1 : \frac{f_A N_{Ab_1} f_A N_{Ab_1}}{f_A N_A + f_a N_a}$$

$$Ab_1 \times Ab_2 : \frac{f_A N_{Ab_1} f_A N_{Ab_2}}{f_A N_A + f_a N_a}$$

$$Ab_1 \times ab_1 : \frac{f_A N_{Ab_1} f_a N_{ab_1}}{f_A N_A + f_a N_a}$$

$$Ab_1 \times ab_2 : (1 - r_K)\frac{f_A N_{Ab_1} f_a N_{ab_2}}{f_A N_A + f_a N_a}$$

$$Ab_2 \times ab_1 : r_K \frac{f_A N_{Ab_2} f_a N_{ab_1}}{f_A N_A + f_a N_a}$$

Birth rate

$$\bar{\alpha} = \{A, a\} \setminus \alpha, \quad \text{and} \quad \bar{\beta} = \{b_1, b_2\} \setminus \beta$$

Birth rate

$$b^K_{\alpha\beta}(N) = f_\alpha N_{\alpha\beta} + r_K f_a f_A \frac{N_{\bar{\alpha}\beta} N_{\alpha\bar{\beta}} - N_{\alpha\beta} N_{\bar{\alpha}\bar{\beta}}}{f_A N_A + f_a N_a}$$

Remark

$$\begin{aligned} P_{a,b_1} - P_{A,b_1} &= \frac{N_{ab_1}(N_{Ab_1} + N_{Ab_2}) - N_{Ab_1}(N_{ab_1} + N_{ab_2})}{N_A N_a} \\ &= \frac{N_{ab_1} N_{Ab_2} - N_{Ab_1} N_{ab_2}}{N_A N_a} \end{aligned}$$

Restriction to the trait population process [Cha06]

$$b_\alpha = f_\alpha N_\alpha, \quad d_\alpha = (D_\alpha + C_{\alpha,A} N_A / K + C_{\alpha,a} N_a / K) N_\alpha$$

If N_A and N_a are large, $(N_A/K, N_a/K)$ close to

$$\dot{n}_\alpha = (f_\alpha - D_\alpha - C_{\alpha,A} n_A - C_{\alpha,a} n_a) n_\alpha, \quad n_\alpha(0) = z_\alpha$$

Under the condition

$$f_A > D_A, \quad f_a > D_a, \quad \text{and} \quad f_a - D_a > (f_A - D_A). \sup \left\{ \frac{C_{a,A}}{C_{A,A}}, \frac{C_{a,a}}{C_{A,a}} \right\},$$

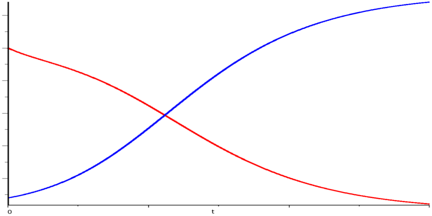
- unique attracting stable equilibrium $(0, \bar{n}_a) = (0, (f_a - D_a)/C_{a,a})$
- non-stable equilibrium $((f_A - D_A)/C_{A,A}, 0) = (\bar{n}_A, 0)$

Invasion fitness

$$S_{\alpha\bar{\alpha}} = f_\alpha - D_\alpha - \frac{C_{\alpha,\bar{\alpha}}}{K} K \bar{n}_{\bar{\alpha}}$$

Assumption 1

$$\bar{n}_A > 0, \quad \bar{n}_a > 0, \quad \text{and} \quad S_{Aa} < 0 < S_{aA}.$$



Assumption 2 : Initial condition

$$\left(z_{Ab_1}K, z_{Ab_2}K, z_{ab_1}K, z_{ab_2}K\right), \quad z_{\alpha\beta} > 0$$

Assumption 3

$$\lim_{K\to\infty} r_K = r \in [0,1].$$

Theorem

For z in $\mathbb{R}_+^{4*}$ and under Assumptions 1 and 2 :

$$\mathbb{P}(Fix^K) \to 1, \quad (K \to \infty)$$

Moreover, if Assumption 3 holds, there exists $F(z,r) \in [0,1]$ s.t.

$$\mathbb{P}\left(\left|P^K_{a,b_1}(T^K_{\mathrm{Fix}}) - \left[\frac{z_{Ab_1}}{z_A}F(z,r) + \frac{z_{ab_1}}{z_a}(1-F(z,r))\right]\right| \mathbb{1}_{Fix^K} > \varepsilon\right) \underset{K\to\infty}{\to} 0.$$

$$F(z,r) = \int_0^\infty \frac{rf_A f_a n_A(s)}{f_A n_A(s) + f_a n_a s)} \exp\Big(- rf_A f_a \int_0^s \frac{n_A(u) + n_a(u)}{f_A n_A(u) + f_a n_a(u)} du \Big) ds,$$

Possible detection

- less alleles with extreme proportions
- comparison between a migrant and a non-migrant populations

Sketch of proof for the standing variation

Steps

- We study the sequence of processes with $r_K = r$
- We couple sequences of processes with recombination probabilities r and r_K
- We study the end of the sweep

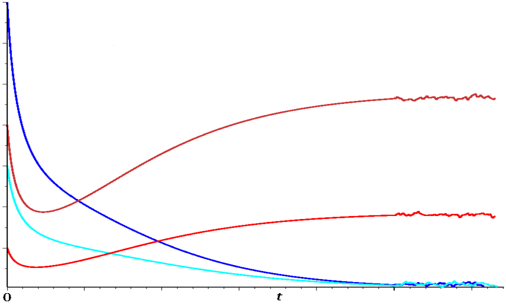


Figure: When r is constant we can compare process with a four dimensional dynamical system on a finite time interval

$$\dot{n}_{\alpha\beta} = \left(f_\alpha - \left(D_\alpha + C_{\alpha,A} n_A + C_{\alpha,a} n_a\right)\right) n_{\alpha\beta} + \frac{r f_A f_a \left(n_{\bar{\alpha}\beta} n_{\alpha\bar{\beta}} - n_{\alpha\beta} n_{\bar{\alpha}\bar{\beta}}\right)}{f_A n_A + f_a n_a}.$$

Change of variables

$$n_\alpha = n_{\alpha b_1} + n_{\alpha b_2}, \quad p_{\alpha,b_1} = n_{\alpha b_1}/n_\alpha, \quad \text{and} \quad d = p_{a,b_1} - p_{A,b_1},$$

New system

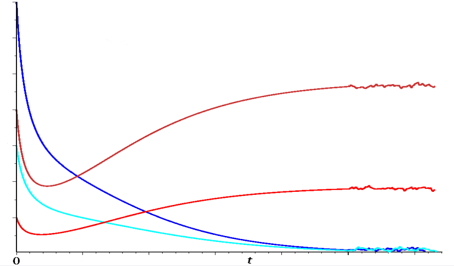
$$\left\{ \begin{array}{l} \dot{n}_A = (f_A - (D_A + C_{A,A} n_A + C_{A,a} n_a)) n_A \\ \dot{n}_a = (f_a - (D_a + C_{a,A} n_A + C_{a,a} n_a)) n_a \\ \dot{d} = -d \Big(r f_A f_a (n_A + n_a)/(f_A n_A + f_a n_a) \Big) \\ \dot{p}_{a,b_1} = -d \Big(r f_A f_a n_A/(f_A n_A + f_a n_a) \Big). \end{array} \right.$$

Coupling

We use the same Poisson point process to construct the two sequences of processes.

Extinction of the *A*-population

During the last period, *A*-individuals are very few and do not influence the neutral proportion in the *a*-population.



1. Model
2. Soft selective sweep
3. Strong selective sweep

Assumption 4

There exists $z_{Ab_1} \in]0, \bar{n}_A[$ such that $N^{(z^{(K)},K)}(0) = \lfloor z^{(K)} K \rfloor$ with

$$z^{(K)} = (z_{Ab_1}, \bar{n}_A - z_{Ab_1}, K^{-1}, 0)$$

Thanks to [Cha06]

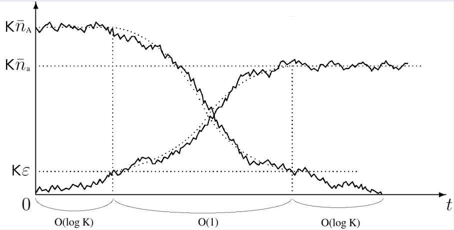


Figure: Trait dynamics ; $\mathbb{P}(Fix) \sim S_{aA}/f_a$

Assumption 5 : Strong recombination

$$\lim_{K\to\infty} r_K \log K = \infty$$

Assumption 6 : Weak recombination

$$\limsup_{K\to\infty} \quad r_K \log K < \infty$$

Theorem

Under Assumptions 1, 4 and 5,

$$\mathbb{P}\left(\left|P^K_{a,b_1}(T^K_{\text{Fix}}) - \frac{z_{Ab_1}}{z_A}\right|\mathbb{1}_{Fix^K} > \varepsilon\right) \underset{K\to\infty}{\to} 0.$$

Under Assumptions 1, 4 and 6,

$$\mathbb{P}\left(\left|P^K_{a,b_1}(T^K_{\text{Fix}}) - \left[\frac{z_{Ab_1}}{z_A} + \frac{z_{Ab_2}}{z_A}\exp\left(-\frac{f_a r_K \log K}{S_{aA}}\right)\right]\right|\mathbb{1}_{Fix^K} > \varepsilon\right) \underset{K\to\infty}{\to} 0.$$

Remarks

- The two regimes are consistent :

$$\lim_{r_K \log K \to \infty} \left\{ \frac{z_{Ab_1}}{z_A} + \frac{z_{Ab_2}}{z_A} \exp\left(- \frac{f_a r_K \log K}{S_{aA}} \right) \right\} = \frac{z_{Ab_1}}{z_A}$$

- The weak recombination case is also consistent with the works of Schweinsberg and Durrett [SD05] (constant population size) and Etheridge, Pfaffelhuber and Wakolbinger [EPW06] (Wright-Fisher diffusion approximation) if we take S_{aA}/f_a instead of s, but we have not the convergence rate.

Sketch of proof for the strong recombination ($r_K \log K \to \infty$)

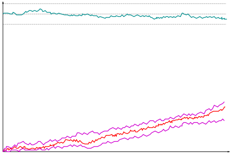
Recall birth rate

$$b^K_{\alpha\beta}(N) = f_\alpha N_{\alpha\beta} + r_K f_a f_A \frac{N_{\bar\alpha\beta}N_{\alpha\bar\beta} - N_{\alpha\beta}N_{\bar\alpha\bar\beta}}{f_A N_A + f_a N_a}$$

$$\begin{aligned} P_{a,b_1} - P_{A,b_1} &= \frac{N_{ab_1}(N_{Ab_1}+N_{Ab_2}) - N_{Ab_1}(N_{ab_1}+N_{ab_2})}{N_A N_a} \\ &= \frac{N_{ab_1}N_{Ab_2} - N_{Ab_1}N_{ab_2}}{N_A N_a} \end{aligned}$$

$$\mathbb{E}[(P_{A,b_1} - P_{a,b_1})^2(t)] \leq c\Big(1/(r_K K) - e^{-A_0 S_{aA} t/2} + e^{-c r_K f_a t}\Big).$$

Sketch of proof for the weak recombination ($\limsup r_K \log K < \infty$)



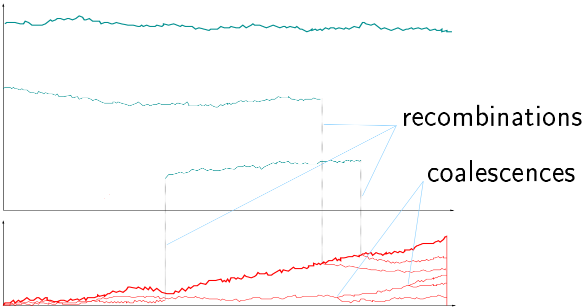
- $s_-(\varepsilon) := \frac{S_{aA} - \varepsilon(2C_{a,A}C_{A,a}/C_{A,A} + C_{a,a})}{f_a}$
- $s_+(\varepsilon) := \frac{S_{aA} + 2\varepsilon C_{a,A}C_{A,a}/C_{A,A}}{f_a}$

Coupling with two birth and death processes

$$b_a^K(N(t)) = f_a N_a(t),$$

$$f_a(1 - s_+(\varepsilon))N_a(t) \leq d_a^K(N(t)) \leq f_a(1 - s_-(\varepsilon))N_a(t).$$

Steps (following method in [SD05])



- Fluctuations of a-population size
- Negligible events : two recombinations or a coalescence then a recombination
- Approximation of the probability to undergo a recombination

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