The diffusion approximation for template coexistence in protocells

How do we explain the co-existence of distinct selfish genes or templates?

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Competition-only approach:

x_i frequency of templates of type *i*

$$\frac{dx_i}{dt} = \sum_j M_{ij} A_j x_j - \Phi(t) x_i$$

Eigen's quasispecies equation

A_i copies per unit of time produced by template *i*

M_{ij} probability of "mutation" from template *j* to *i*

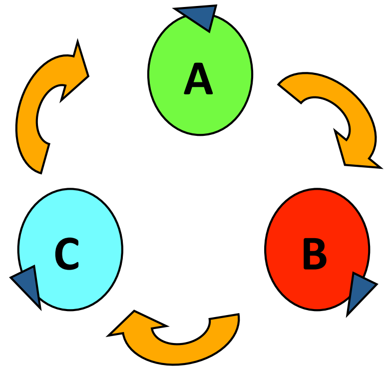
$$\frac{d \sum x_i}{dt} = 0 \Leftrightarrow \Phi(t)$$

zero-sum game:

only the most efficient template survives!

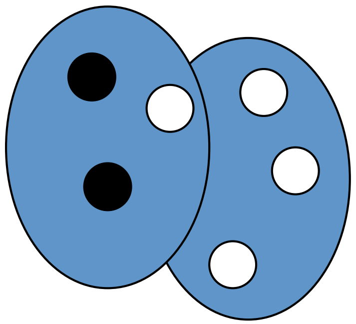
Two non-zero sum game solutions:

1) hypercycles:



$$\frac{dx_i}{dt} = A_i x_i + K_{ii+1} x_i x_{i+1} - \Phi(t) x_i$$

2) package models:



replication or survival of packages (vesicles) depends on their template composition!

two-level selection

Package model

a) individual selection for two template types (Wright-Fisher)

number of templates inside a vesicle: N

number of templates 1: $n_1 = n$ number of templates 2: n_2

frequencies: $x_1 = x = n_1/N$ $x_2 = 1 - x = n_2/N$

selection coefficient of template 1: $1 - s$ and of template 2: 1

$$x' = \frac{x(1-s)}{1-sx} \approx x - sx(1-x)$$

stochastic dynamics:

$$\binom{N}{n'}(x')^{n'}(1-x')^{N-n'}$$

$n \rightarrow n'$

diffusion approximation: $s \sim 1/N << 1$

$$M_{\delta x} = \langle (x' - x) \rangle = -sx(1-x)$$

$$V_{\delta x} = \langle (x' - x)^2 \rangle = x(1-x)/N$$

probability density that template 1 has frequency *x* at time *t*: $\varphi(x,t)$

$$\frac{\partial \varphi}{\partial t} = \frac{1}{2}\frac{\partial^2}{\partial x^2}\left[V_{\delta x}\varphi\right] - \frac{\partial}{\partial x}\left[M_{\delta x}\varphi\right]$$

b) vesicle selection (deterministic dynamics)

$\varphi(x,t)$ **fraction of vesicles in which template 1 has frequency *x* at time *t***

inter-vesicle selection coefficient: $c(x)$

$$\varphi(x,t+\Delta t) = \left[\varphi(x,t) + c(x)\varphi(x,t)\Delta t\right]\eta$$

$$\int \varphi(x,t+\Delta t)dx = 1 \Rightarrow \eta = \frac{1}{1+\bar{c}\Delta t}$$ with $$\bar{c} = \int_0^1 c(x)\varphi(x)dx$$

$$\frac{\partial\varphi}{\partial t} = \left[c(x) - \bar{c}\right]\varphi$$

c) Complete two-level selection dynamics

Kimura, PNAS **80** 6317 (1983)

$$\frac{\partial \varphi}{\partial t} = \frac{1}{2}\frac{\partial^2}{\partial x^2}\left[V_{\delta x}\varphi\right] - \frac{\partial}{\partial x}\left[M_{\delta x}\varphi\right] + \left[c(x) - \bar{c}\right]\varphi$$

$$V_{\delta x} = x(1-x)/N$$

$$\bar{c} = \int_0^1 c(x)\varphi(x)\,dx$$

$$M_{\delta x} = -sx(1-x)$$

$$c(x) = cx(1-x)$$

non-zero sum game!

d) Steady-state analysis $\frac{\partial \varphi}{\partial t} = 0$

$$\frac{d^2}{dx^2}\left[x(1-x)\varphi\right] + \frac{d}{dx}\left[Sx(1-x)\varphi\right] + \left[Cx(1-x) - \overline{C}\right]\varphi = 0$$

$$S = 2Ns \quad C = 2Nc \quad \overline{C} = C\int_0^1 x(1-x)\varphi(x)dx \qquad 1 = \int_0^1 \varphi(x)dx$$

solve recursively: fix $\overline{C}$ solve for φ recalculate $\overline{C}$ and so on…

bad idea!

not an initial value problem!

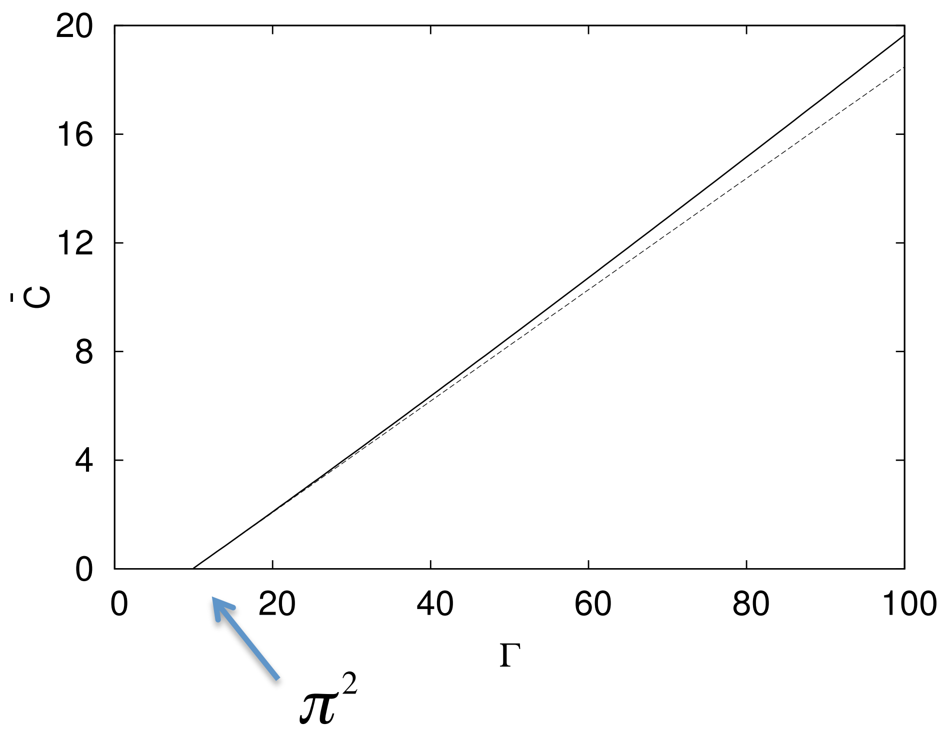
$$\varphi'(0) = \varphi(0)\frac{2 - S + \overline{C}}{2}$$

$$\varphi'(1) = -\varphi(1)\frac{2 + S + \overline{C}}{2}$$

Sturm-Liouville problem: $\overline{C}$ is the eigenvalue!

e) Numerical solution

$$\Gamma = C - S^2/4$$



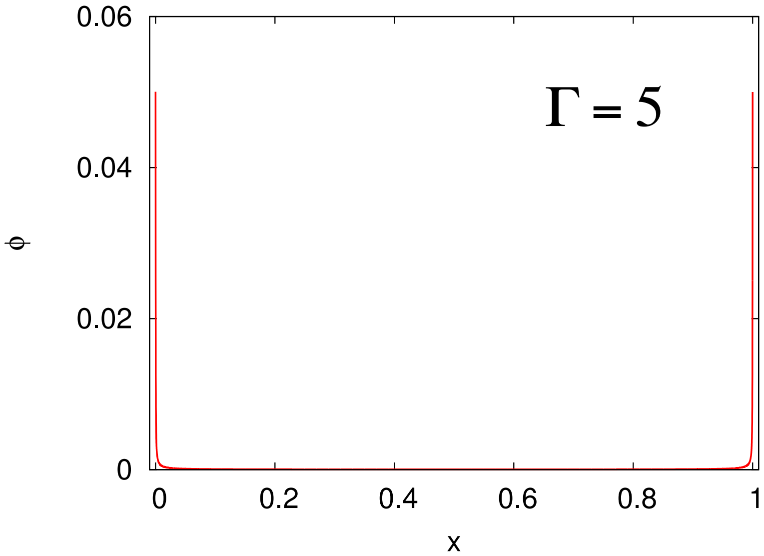
two regimes:

$\overline{C} = 0$ for $\Gamma < \Gamma_c = \pi^2$

$\overline{C} > 0$ otherwise

$$\overline{C} = \int_0^1 x(1-x)\varphi(x)dx$$

near the critical point: $\overline{C} \approx (\Gamma - \Gamma_c)\left[2\int_0^1 \frac{\sin^2(\pi x)}{x(1-x)}\right]^{-1}$

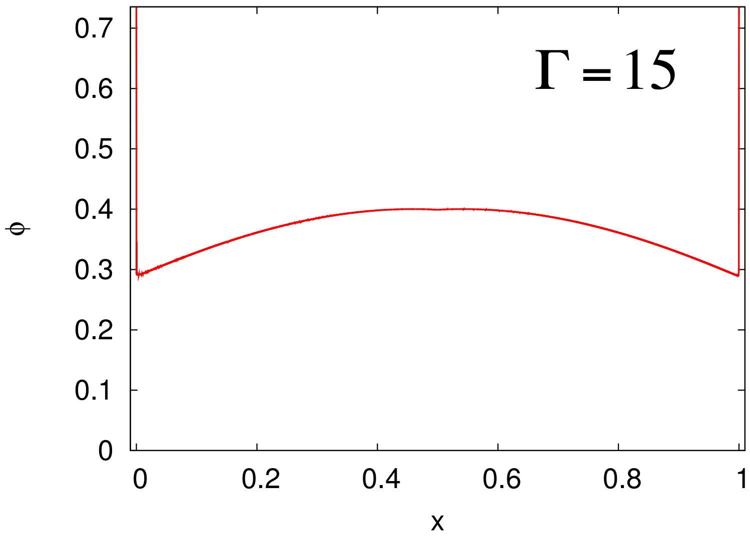


non-ergodic segregating phase

$$\overline{C} = 0$$

$$\varphi = A_0\delta(x) + A_1\delta(x-1)$$

$$A_0 + A_1 = 1$$



ergodic coexistence phase

$$\overline{C} > 0$$

$$\varphi = A_0\delta(x) + A_1\delta(x-1) + B\eta(x)$$

$$A_0 + A_1 + B = 1$$

$$A_0 = B\eta(0)/\overline{C} \qquad A_1 = B\eta(1)/\overline{C}$$

$$\overline{C} = B\int_0^1 x(1-x)\eta(x)\,dx$$

f) transition line $\bar{C} = 0$

$$\frac{d^2}{dx^2}\left[x(1-x)\eta\right] + S\frac{d}{dx}\left[x(1-x)\eta\right] + Cx(1-x)\eta = 0$$

$\rho(x) = x(1-x)\eta(x)$ **damped harmonic oscillator**

$\rho(x) = \exp(-Sx/2)\left[A\cos wx + B\sin wx\right]$ $w^2 = C - S^2/4 = \Gamma$

η is normalizable: $\rho(0) = \rho(1) = 0 \Rightarrow A = 0 = \sin w$

transition line: $w = \pi \Rightarrow$

$$\Gamma_c = \pi^2$$

$$C_c = \pi^2 + S^2/4$$

$$\eta_c(x) = A\exp(-Sx/2)\frac{\sin \pi x}{x(1-x)}$$

get *A* from normalization

$$A_0^c = \frac{1}{1+\exp(-S/2)} \qquad A_1^c = \frac{\exp(-S/2)}{1+\exp(-S/2)}$$

independent on the initial conditions

g) Delta weights for the non-ergodic regime (S=0)

$$\langle f(x)\rangle_t = \int_0^1 f(x)\varphi(x,t)\,dx$$

expected value of a regular function *f* at time *t*

$$\frac{d}{dt}\langle f\rangle_t = \left\langle x(1-x)\frac{\partial^2 f}{\partial x^2}\right\rangle_t + C\langle x(1-x)f\rangle_t - \overline{C}\langle f\rangle_t$$

choosing $f(x) = \sin\left(\sqrt{C}x + \theta\right)$ with θ arbitrary yields:

$$\frac{d}{dt}\left\langle \sin\left(\sqrt{C}x+\theta\right)\right\rangle_t = -\overline{C}(t)\left\langle \sin\left(\sqrt{C}x+\theta\right)\right\rangle_t$$ whose solution is

$$\frac{\left\langle \sin\left(\sqrt{C}x+\theta\right)\right\rangle_t}{\left\langle \sin\left(\sqrt{C}x+\theta\right)\right\rangle_0} = \exp\left[-\int_0^t \overline{C}(\tau)\,d\tau\right]$$ independent on θ

$\theta = 0$ $$\frac{\left\langle \sin\left(\sqrt{C}x\right)\right\rangle_t}{\left\langle \sin\left(\sqrt{C}x\right)\right\rangle_0} = \frac{\left\langle \cos\left[\sqrt{C}\left(x-1/2\right)\right]\right\rangle_t}{\left\langle \cos\left[\sqrt{C}\left(x-1/2\right)\right]\right\rangle_0}$$ $\theta = \left(\pi - \sqrt{C}\right)/2$

$t \to \infty$ $\varphi = A_0\delta(x) + A_1\delta(x-1)$ $t = 0$ $\varphi(x,0)$

$$A_1 = \frac{\cos\left(\sqrt{C}/2\right)\int_0^1 \sin\left(\sqrt{C}\,x/2\right)\varphi(x,0)\,dx}{\sin\left(\sqrt{C}/2\right)\int_0^1 \cos\left[\sqrt{C}\left(x-1/2\right)\right]\varphi(x,0)\,dx} \qquad A_0 = 1 - A_1$$

for $C \to 0$: $A_1 = \int_0^1 x\varphi(x,0)\,dx$

for $C \to \pi^2$: $A_1 = 1/2$

Fixation probability in presence of group selection!!

thanks!

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