Bacterial Games

On the Role of Space and Stochasticity in Coevolutionary Dynamics

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Outline

- Introduction to Game Theory and Biological Model Systems
- May Leonard Model and Spatial Games

Introduction to Game Theory

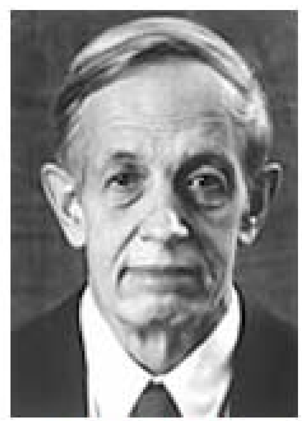
Game Theory

John Nash:
“An equilibrium is reached as soon as no party can increase its profit by unilaterally deciding differently.”

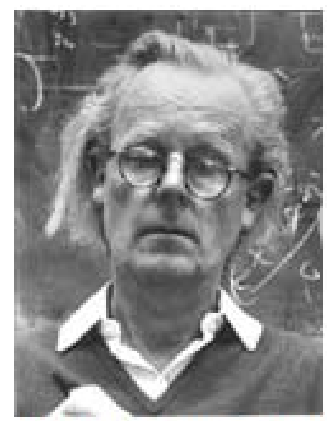
John Maynard-Smith and George R. Price:
“A strategy is called evolutionary stable if a population of individuals homogenously playing this strategy is able to outperform and eliminate a small amount of any mutant strategy introduced into the population.”

John von Neumann

Oskar Morgenstern



John Nash



John Maynard-Smith

Classical Formulation of Prisoner‘s Dilemma

``Two suspects of a crime are arrested by the police. The police have insufficient evidence for a conviction, and, having separated both prisoners, visit each of them to offer the same deal. If one testifies (defects from the other) for the prosecution against the other and the other remains silent (cooperates with the other), the betrayer goes free and the silent accomplice receives the full 10-year sentence. If both remain silent, both prisoners are sentenced to only 1 year in jail for a minor charge. If each betrays the other, each receives a five-year sentence. Each prisoner must choose to betray the other or to remain silent. Each one is assured that the other would not know about the betrayal before the end of the investigation. How should the prisoners act?''

Strategic Games

Mathematical description of strategic situations, in which an individual's success in making choices depends on the choices of others.

Prisoner's Dilemma:

P	Cooperator (C)	Defector (D)
C	1 year	10 years
D	0 years	5 years

(D,D) is a Nash equilibrium where unilateral deviation does not pay off.

Social Dilemmas

The fundamental problem of cooperation:

P	Cooperator (C)	Defector (D)
C	$b - c$	$-c$
D	b	0

General two-player games

P	Cooperator (C)	Defector (D)
C	$\mathcal{R}$eward	$\mathcal{S}$ uckers payoff
D	$\mathcal{T}$ emptation	$\mathcal{P}$ unishment

Social Dilemmas

The fundamental problem of cooperation:

P	Cooperator (C)	Defector (D)
C	$b - c$	$-c$
D	b	0

The snowdrift game:

P	Cooperator (C)	Defector (D)
C	$b - c/2$	$b - c$
D	b	0

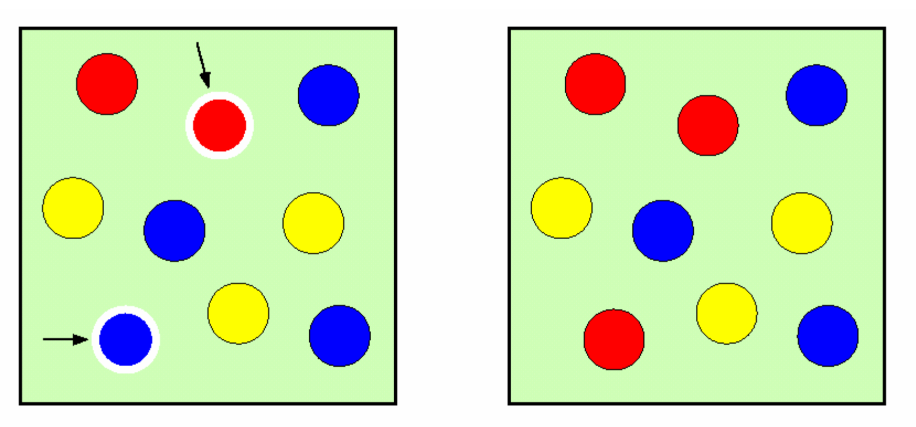
Evolutionary Game Theory

Consider a population of size N

N_i individuals play strategy A_i: $a_i = N_i/N$ (frequency)

Composition of the population is updated by some (evolutionary) rules: $N_i\ (t) \longrightarrow N_i\ (t+dt)$

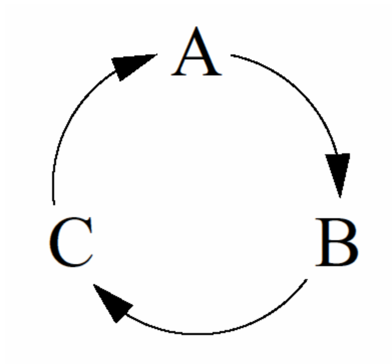
Moran process:



- pick two at random
- the fitter wins

Rate Equations

"Chemical" reactions:



$$A + B \xrightarrow{k_A} A + A$$
$$B + C \xrightarrow{k_B} B + B$$
$$C + A \xrightarrow{k_C} C + C$$

Rate equations:

$$\begin{aligned} \partial_t a &= a(k_A b - k_C c) \\ \partial_t b &= b(k_B c - k_A a) \\ \partial_t c &= c(k_C a - k_B b) \end{aligned}$$

Fitness and replicator equations

Payoff matrix:

$\mathbf{P}$	A	B
A	$p_{11} := \mathcal{R}$	$p_{12} := \mathcal{S}$
B	$p_{21} := \mathcal{T}$	$p_{22} := \mathcal{P}$

Frequencies: $a = N_A/N\,, \quad b = N_B/N = (1-a)$

Fitness = expected payoff:

$$f_A(a) = \mathcal{R}a + \mathcal{S}(1-a)\,, \quad f_B(a) = \mathcal{T}a + \mathcal{P}(1-a)$$

$$\bar{f}(a) = a f_A(a) + (1-a) f_B(a)$$

Replicator dynamics:

$$\partial_t a = \left[f_A(a) - \bar{f}(a)\right] a \qquad \partial_t a = \frac{f_A(a) - \bar{f}(a)}{\bar{f}(a)}\, a$$

Microbial Laboratory Communities:

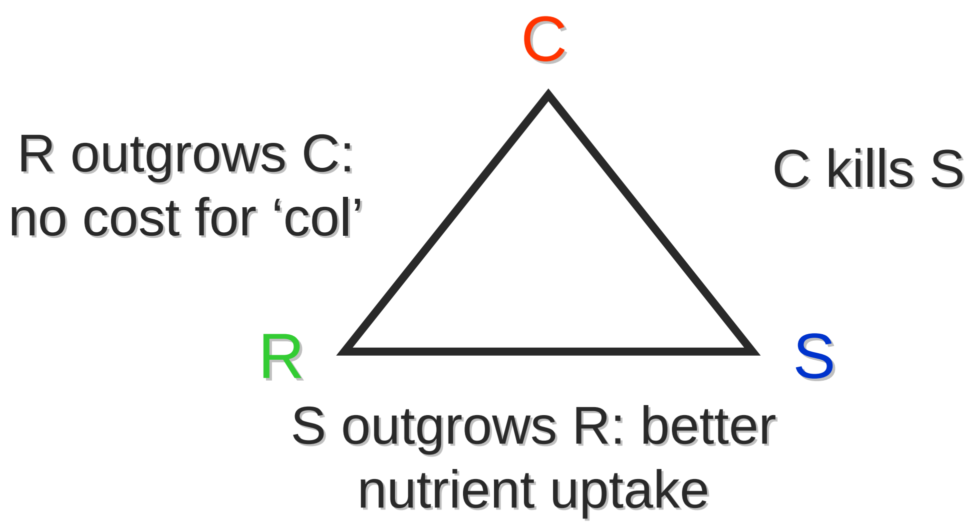
model systems for competition, cooperation, …

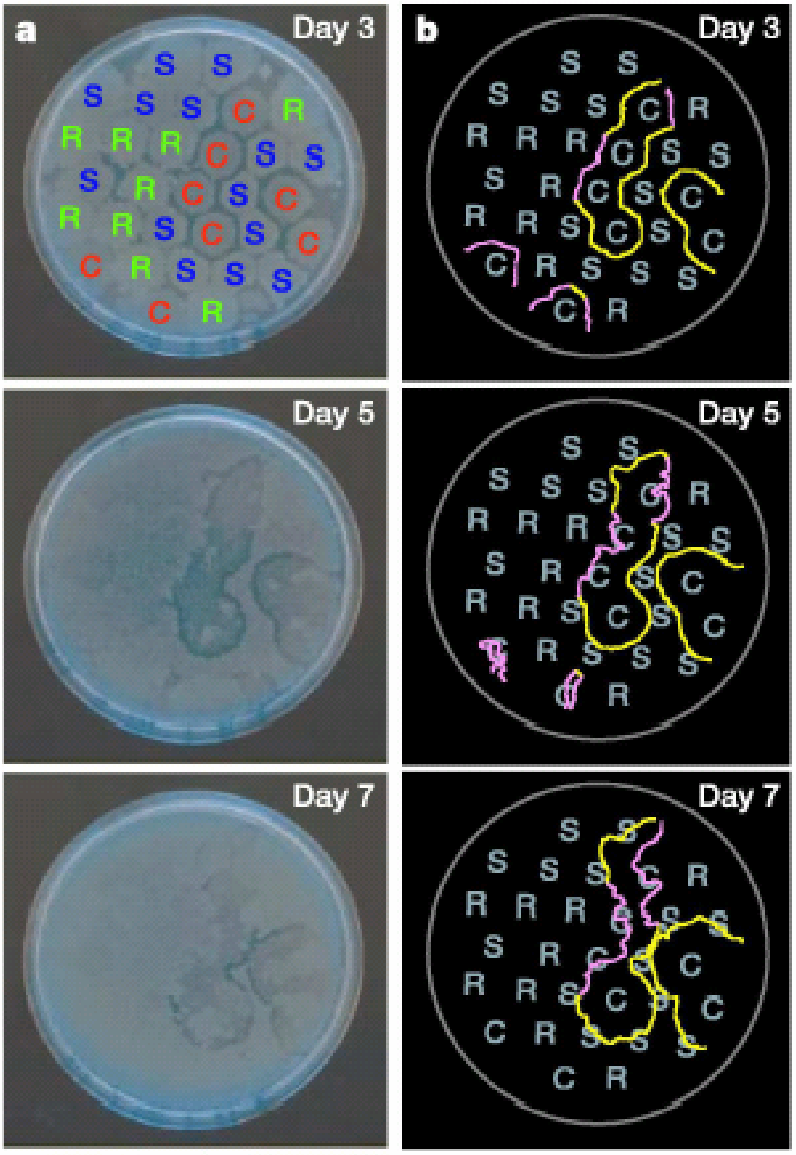
Colicinogenic Bacteria

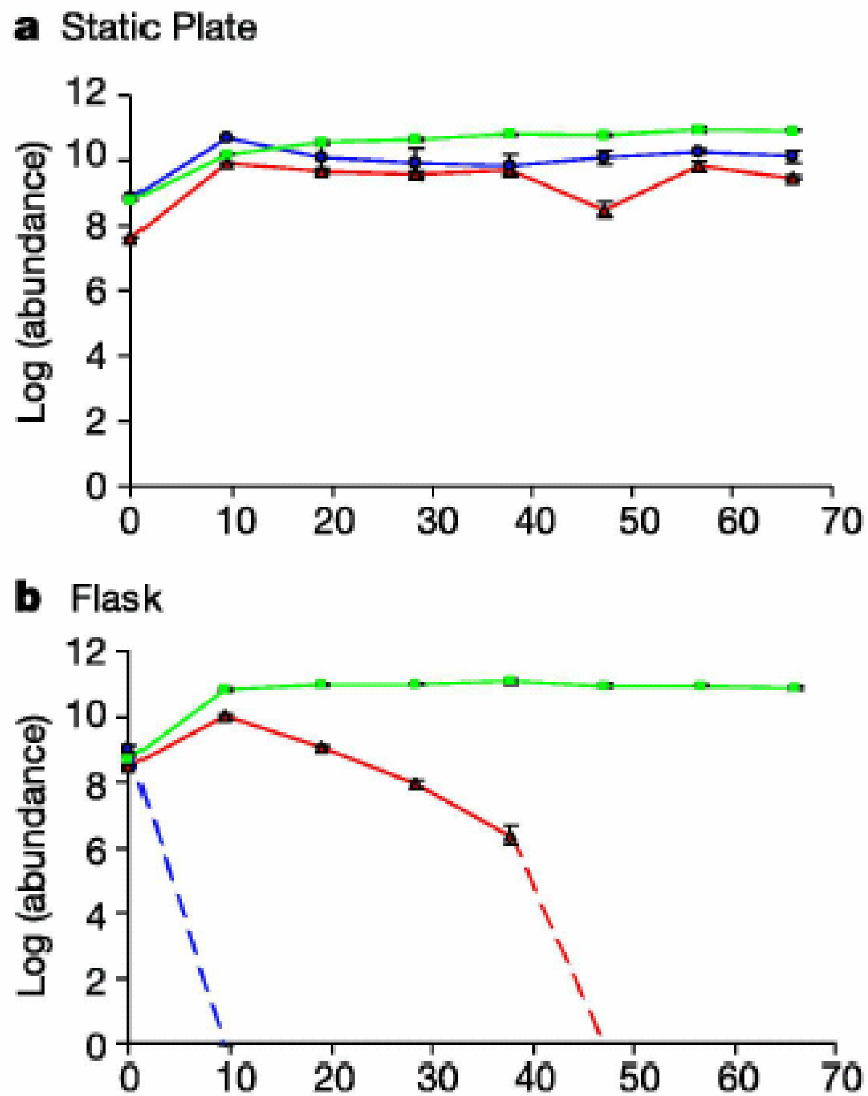
Toxin producing (colicinogenic) E.coli (C) carry a ‘col’ plasmid: genes for colicin, colicin specific immunity proteins, lysis protein

Colicin-sensitive bacteria (S)

Colicin-resistant bacteria (R) are mutations of S with altered cell membrane proteins that bind and translocate cocilin







B. Kerr et al., Nature 418, 171 (2002)

Elementary notes on extinction times

Linear Death Process

$$N \xrightarrow{\lambda} N - 1$$

Mean extinction time:

$$\begin{aligned} T &= \tau_{N_0} + \tau_{N_0-1} + \cdots + \tau_1 \\ &= \sum_{N=1}^{N_0} \frac{\tau}{N} \approx \tau \int_1^{N_0} \frac{1}{N} dN \\ &= \tau \ln N_0 \end{aligned}$$

For dynamics with drift towards an absorbing state the mean extinction time scales as $T \sim \ln N_0$

Linear Birth-Death Process

Deterministic description: $\partial_t N(t) = -(\lambda - \mu) N(t)$

Stochastic description (Master equation):

$$\partial_t P(N,t) = \lambda(N+1)P(N+1,t) + \lambda(N-1)P(N-1,t) - 2\lambda P(N,t)$$

$$\approx \lambda \partial_N^2 \left[N P(N,t) \right]$$

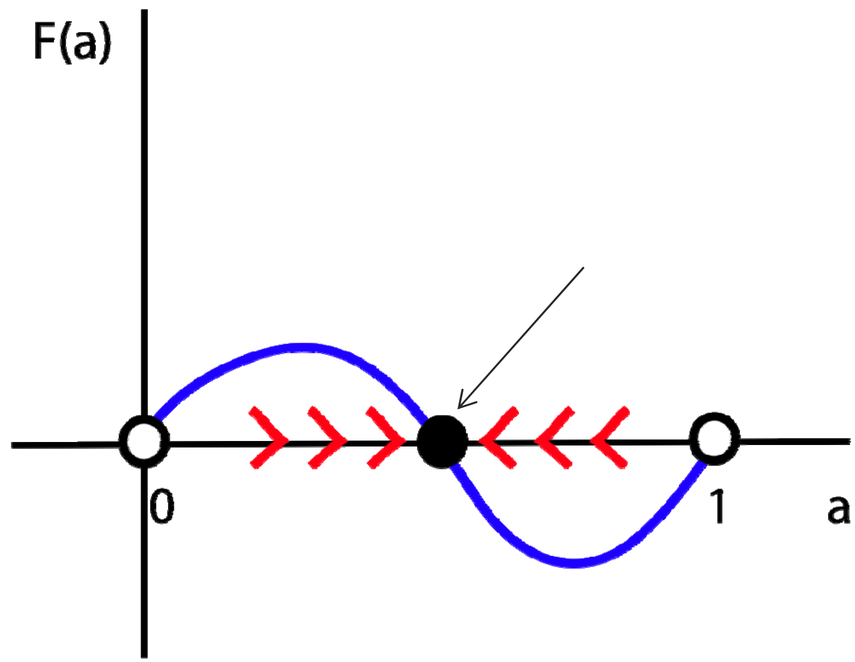
Frequency: $x = \frac{N}{N_0}$

$$\partial_t P(x,t) = D \partial_x^2 \left[x P(x,t) \right]$$

$$D = \frac{\lambda}{N_0}$$

For dynamics with diffusion towards an absorbing state the mean extinction time scales as $T \sim N_0$

Activated Dynamics



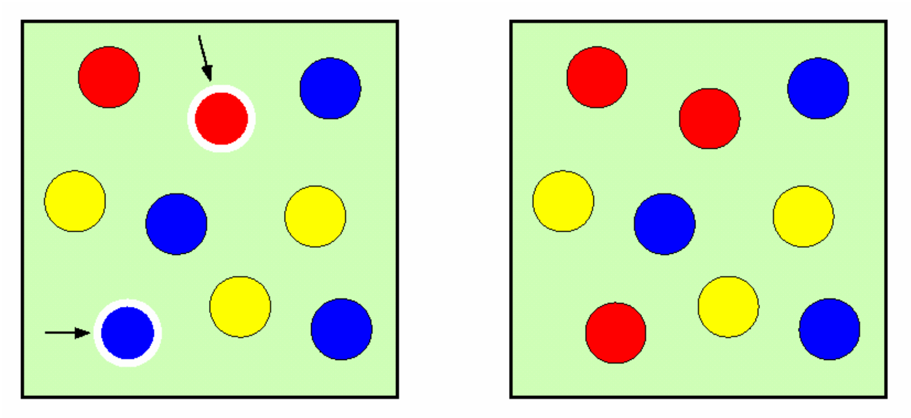
For dynamics with “barrier” towards the absorbing fixed points the mean extinction time scales as $T \sim e^{N_0}$

Stochastic Dynamics: Extinction Times

- Neutral game: $T \sim N$
- Stable reactive fixed point: $T \sim e^N$
- Unstable reactive fixed point: $T \sim \ln N$

The cyclic rock-scissors-paper game in well-mixed populations

The Rock-Scissors-Paper Game

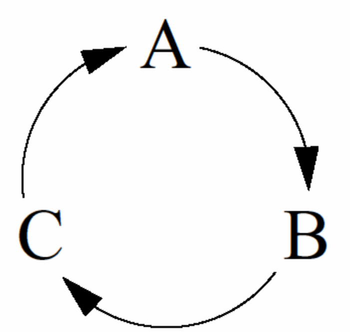


Consider a fixed population of N individuals in a well mixed environment ("urn model")

$$A + B \xrightarrow{k_A} A + A$$

$$B + C \xrightarrow{k_B} B + B$$

$$C + A \xrightarrow{k_C} C + C$$



Cyclic competition between three species A, B, C

T. Reichenbach, M. Mobilia and E. Frey, PRE (2006)

Deterministic Evolution

Rate equations:

$$\dot{a} = a(k_A b - k_C c)$$
$$\dot{b} = b(k_B c - k_A a)$$
$$\dot{c} = c(k_C a - k_B b)$$

$$a + b + c = 1$$

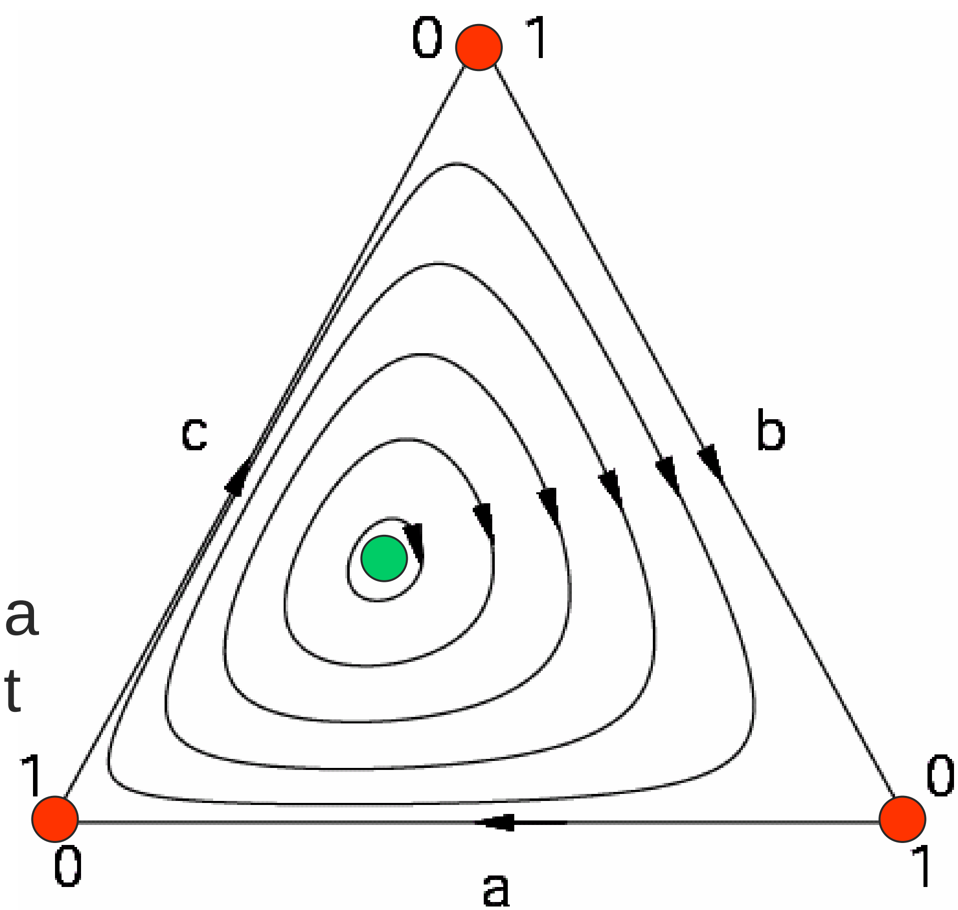
Constant of motion:

$$K = a(t)^{k_B}\, b(t)^{k_C}\, c(t)^{k_A}$$

- cyclic trajectories around a neutrally stable fixed point
- coexistence

● absorbing fixed point

● reactive (center) fixed point



Stochastic Evolution

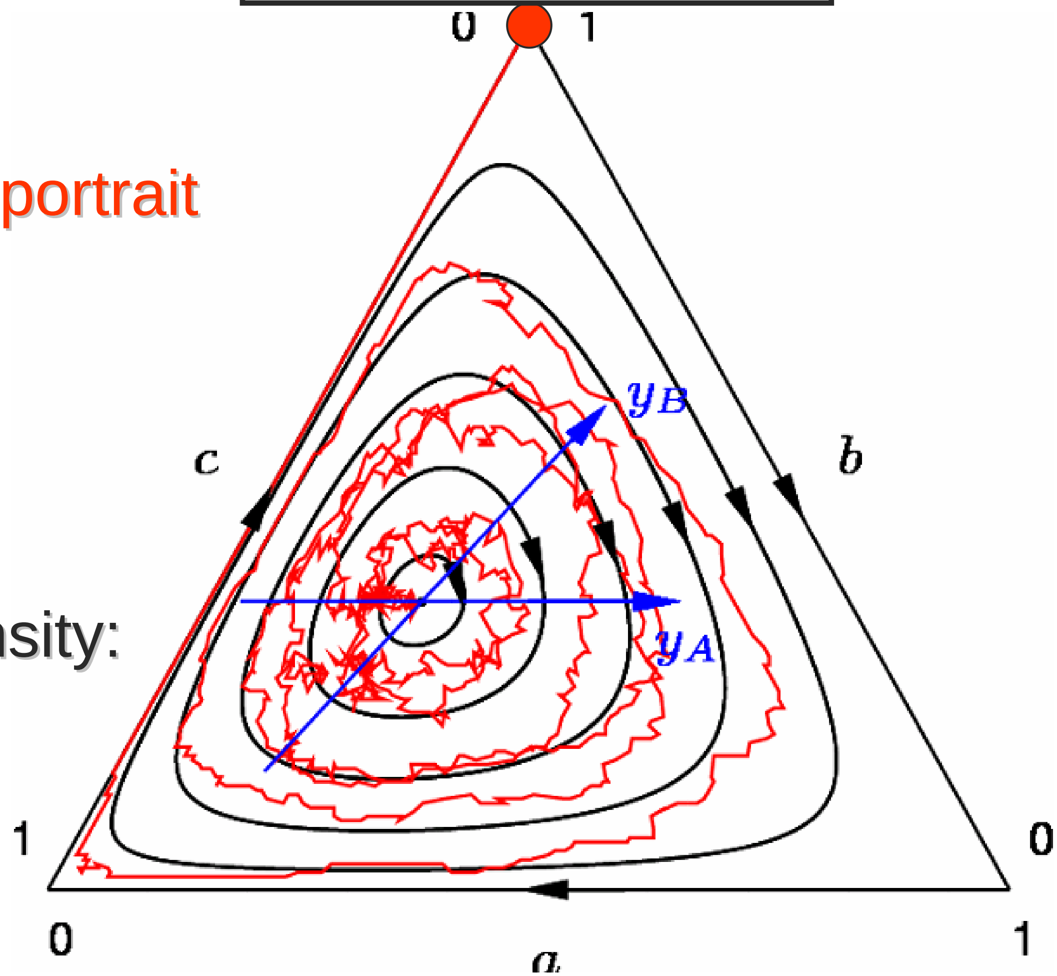
- processes are probabilistic
- K not a constant of motion
- <u>neutrally</u> stable cycles!
- "random walk" on phase portrait

$$T \sim N$$

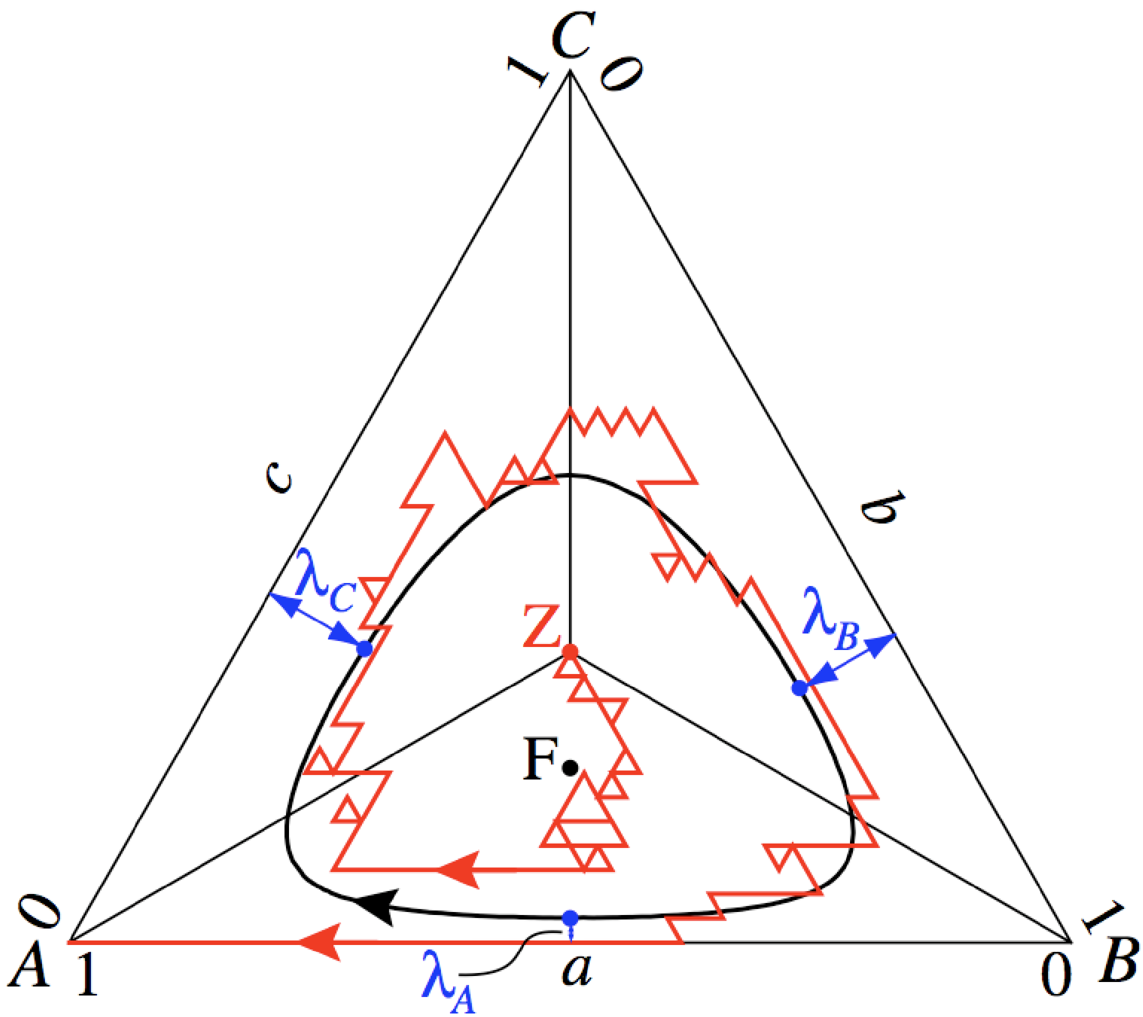
Stochastic description in terms of a probability density:

$$P(a,b,c;t) = P(\mathbf{x},t)$$

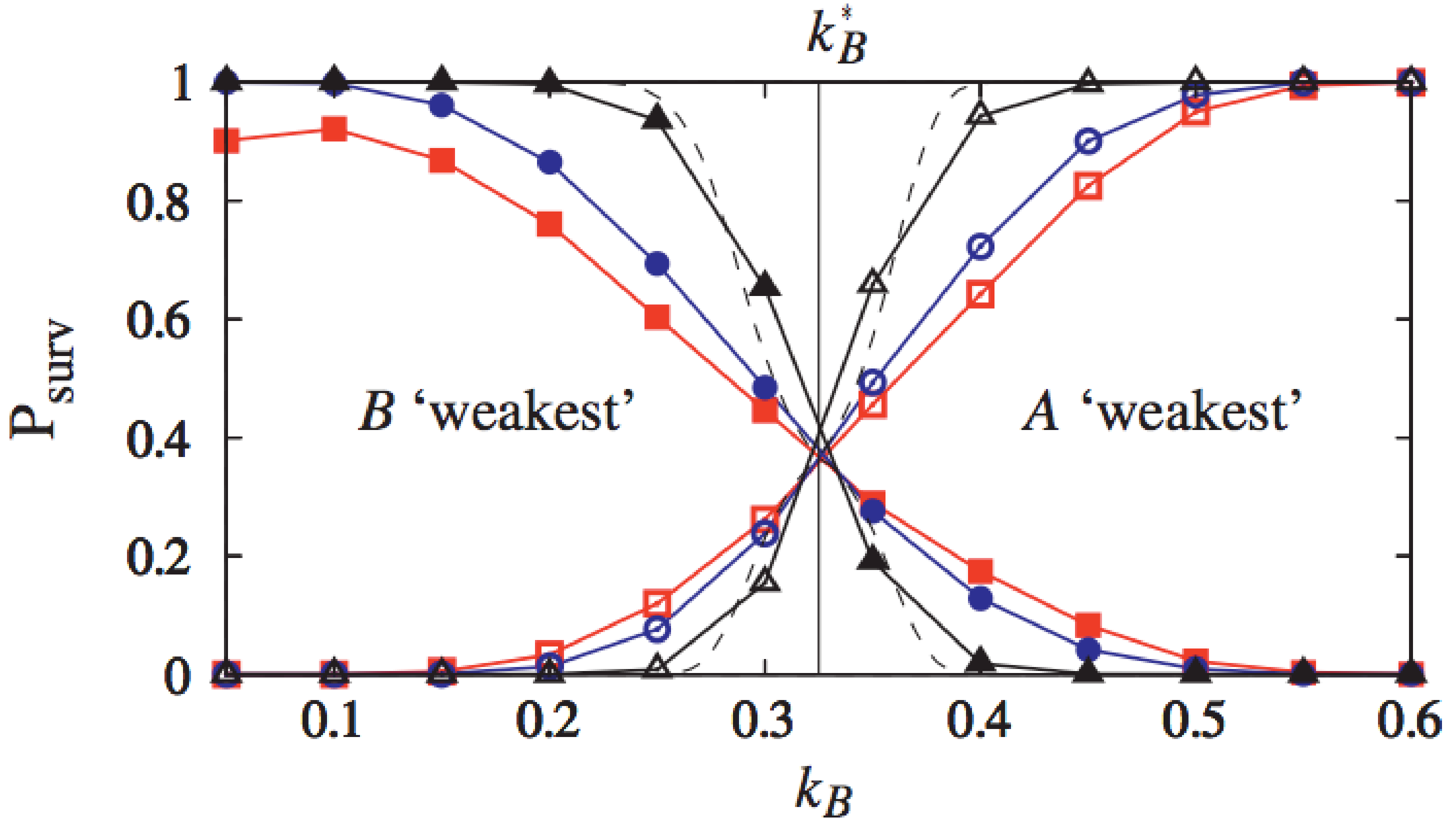
stochasticity causes loss of coexistence



„The Law of the Weakest“



M. Berr, T. Reichenbach, M. Schottenloher and E. Frey, PRL (2009)



Fix time scale: $k_A+k_B+k_C=1$
Fix $k_C=0.35$

As k_B passes through 0.325 species A becomes the weakest species.

E.coli

$$k_C \gg k_S > k_R$$

The resistant strain has the smallest growth rate and in this sense is the weakest.

Hence the resistant strain always survives!

In finite populations stochasticity causes loss of coexistence.

The typical extinction time T is proportional to the population size, T ~ N (neutrality).

The weakest always wins the game for large N

May-Leonard Model (well mixed)

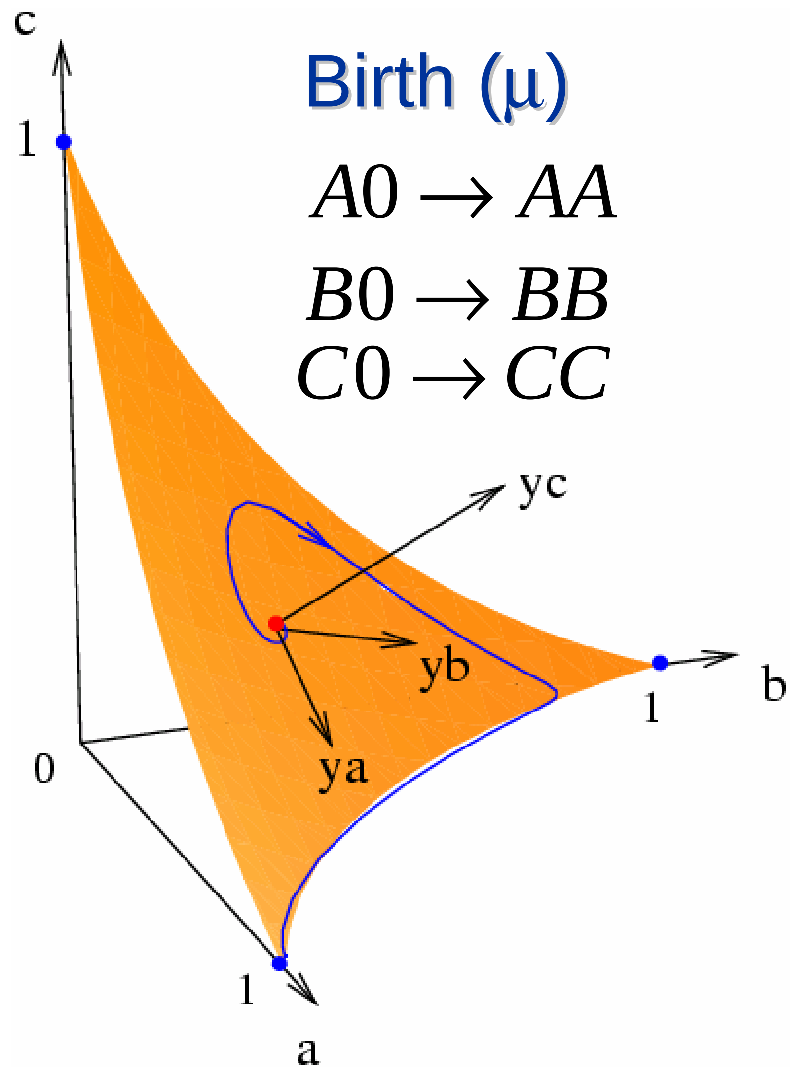
Species A,B,C and empty sites 0

Cyclic dominance (σ)

$$AB \rightarrow A0$$
$$BC \rightarrow B0$$
$$CA \rightarrow C0$$

Birth (μ)

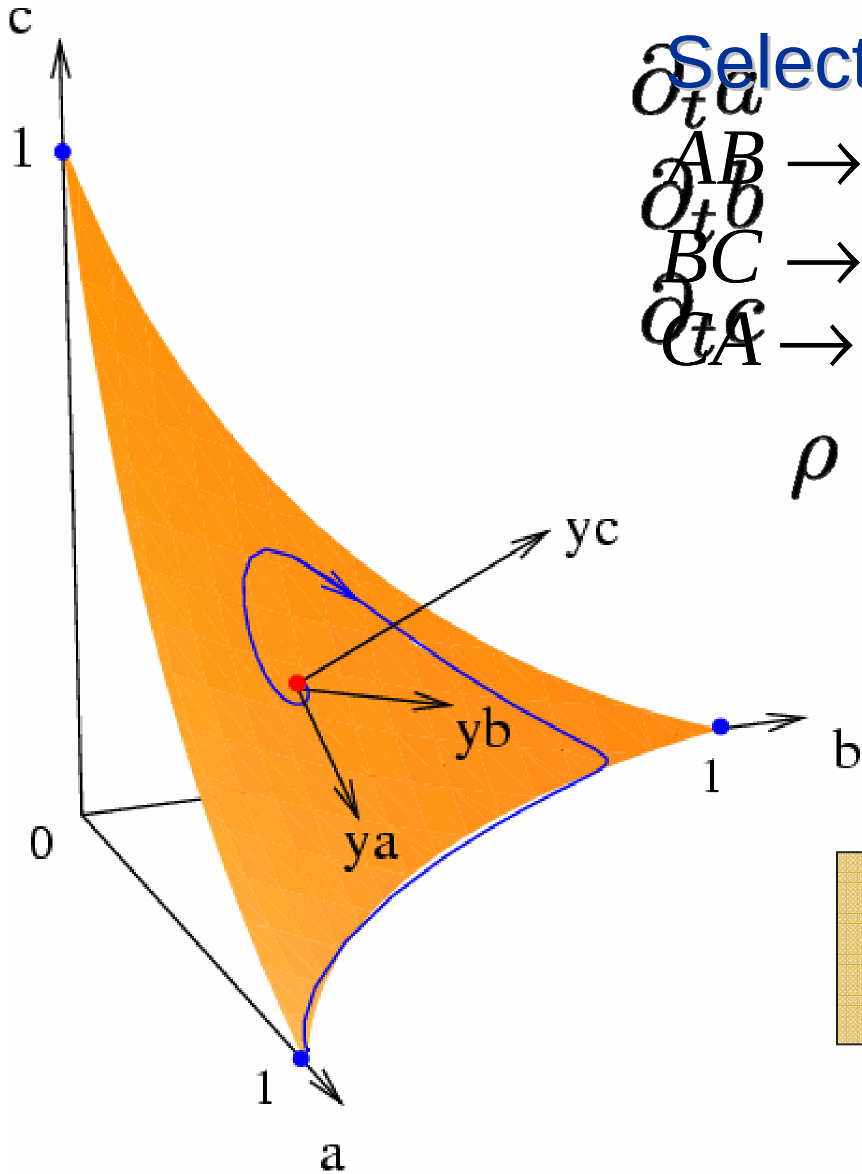
$$A0 \rightarrow AA$$
$$B0 \rightarrow BB$$
$$C0 \rightarrow CC$$



Without spatial structure coexistence fixed point is unstable

loss of biodiversity

May-Leonard Model



Selection (σ) | **Reproduction (μ)**

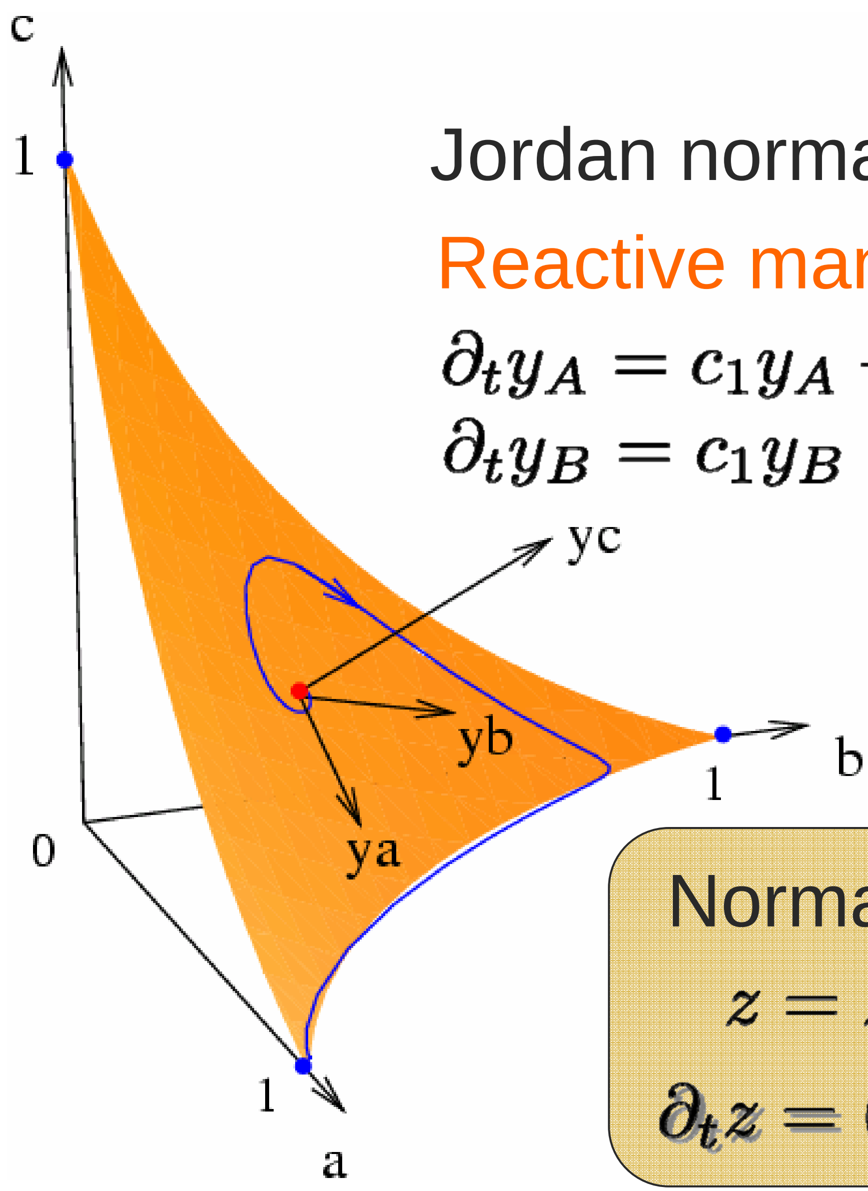
$$AB \to A0 \qquad A0 \to AA$$
$$BC \to B0 \qquad B0 \to BB$$
$$CA \to C0 \qquad C0 \to CC$$

$$\partial_t a = a[\mu(1-\rho) - \sigma c]$$
$$\partial_t b = b[\mu(1-\rho) - \sigma a]$$
$$\partial_t c = c[\mu(1-\rho) - \sigma b]$$

$$\rho = a + b + c$$

$$\partial_t \vec{a} = \vec{F}(\vec{a})$$

Nonlinear dynamics



$$\partial_t \vec{a} = \vec{F}(\vec{a})$$

Jordan normal form: $\partial_t \vec{y} = J\vec{y} + \vec{H}(\vec{y})$

Reactive manifold: $y_C = M(y_A, y_B)$

$$\partial_t y_A = c_1 y_A + \omega y_B + f(y^2, y^3) + o(y^3)$$
$$\partial_t y_B = c_1 y_B - \omega y_A + g(y^2, y^3) + o(y^3)$$

$$\vec{z} = \mathrm{NL}(\vec{y})$$

Normal form of nonlinear dynamics:

$$z = z_A + i z_B$$
$$\partial_t z = (c_1 - i\omega) z - c_2 (1 + i c_3) \mid z \mid^2 z$$

Normal form:

$$z = z_A + i z_B$$

$$\partial_t z = (c_1 - i\omega) z - c_2 \big(1 + i c_3\big) \mid z \mid^2 z$$

$$\begin{aligned}
\omega &= \frac{\sqrt{3}}{2} \frac{\mu\sigma}{3\mu + \sigma} \\
c_1 &= \frac{1}{2} \frac{\mu\sigma}{3\mu + \sigma} \\
c_2 &= \frac{\sigma(3\mu + \sigma)(48\mu + 11\sigma)}{56\mu(3\mu + 2\sigma)} \\
c_3 &= \frac{\sqrt{3}(18\mu + 5\sigma)}{48\mu + 11\sigma}
\end{aligned}$$

Polar coordinates

$$z_A = r\cos\phi \quad z_B = r\sin\phi$$

$$\begin{aligned} \partial_t r &= r[c_1 - c_2 r^2] \\ \partial_t \theta &= -\omega + c_2 c_3 r^2 \end{aligned}$$

Limit cycle: $r = \sqrt{c_1/c_2}$

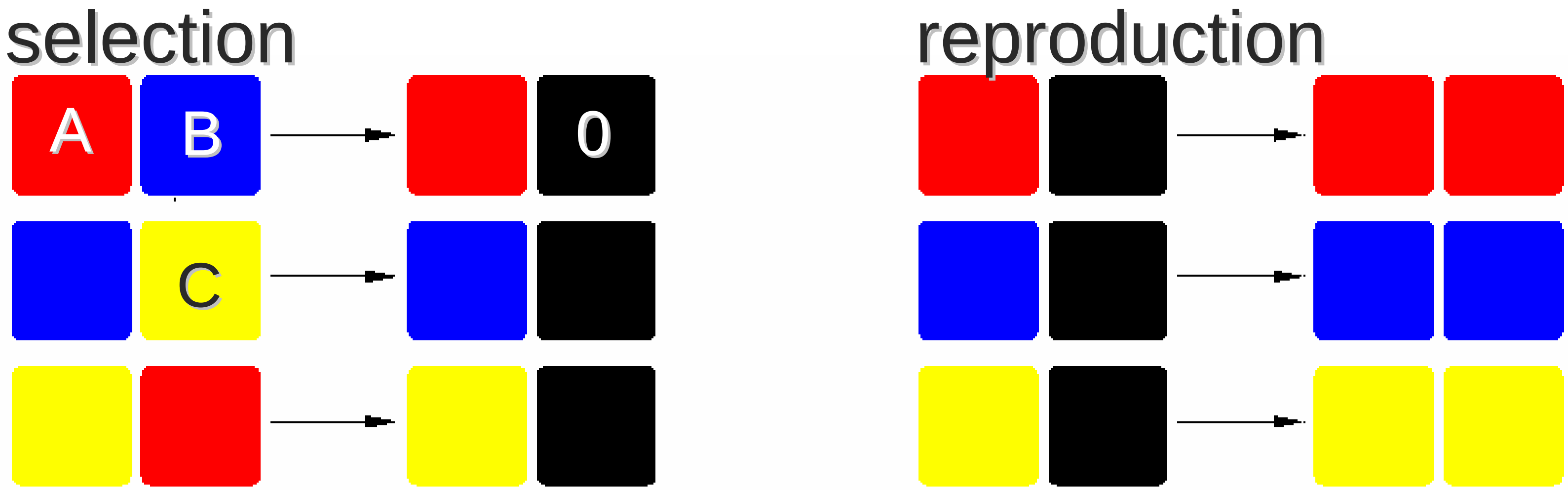
Mapping of the nonlinear rate equations to the reactive manifold and reducing it to normal form is essential for understanding its well-mixed dynamics...

... and also the spatial dynamics!

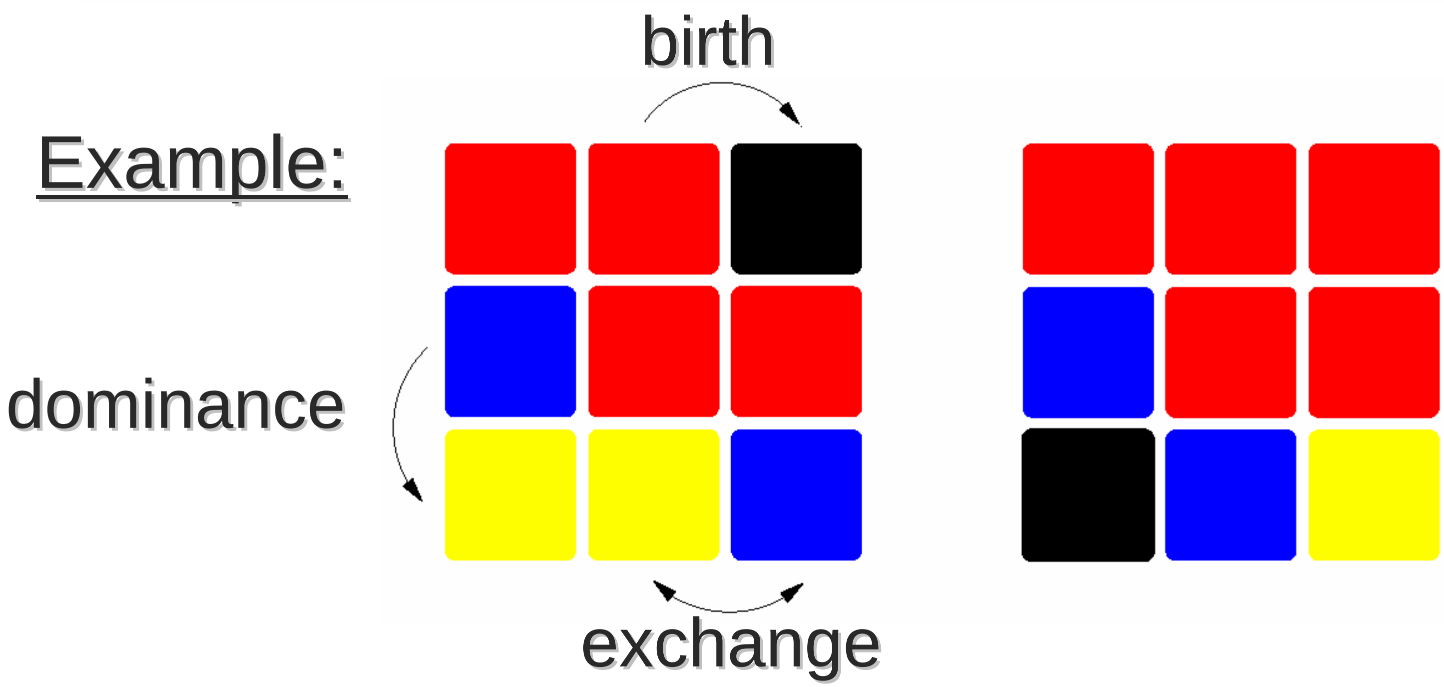
Spatial Games:

May-Leonard Model

Local Interaction Rules



Example:



May-Leonard Model on a Lattice (N=L^2)

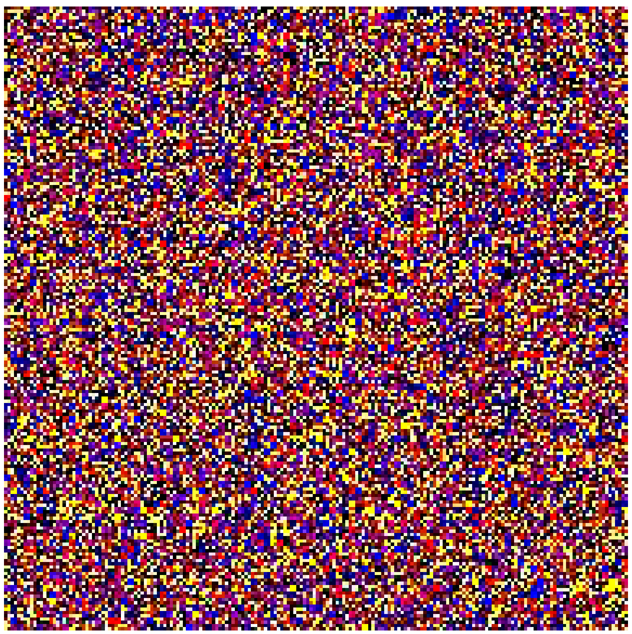
Add migration (ε)

$$A0 \rightarrow 0A$$

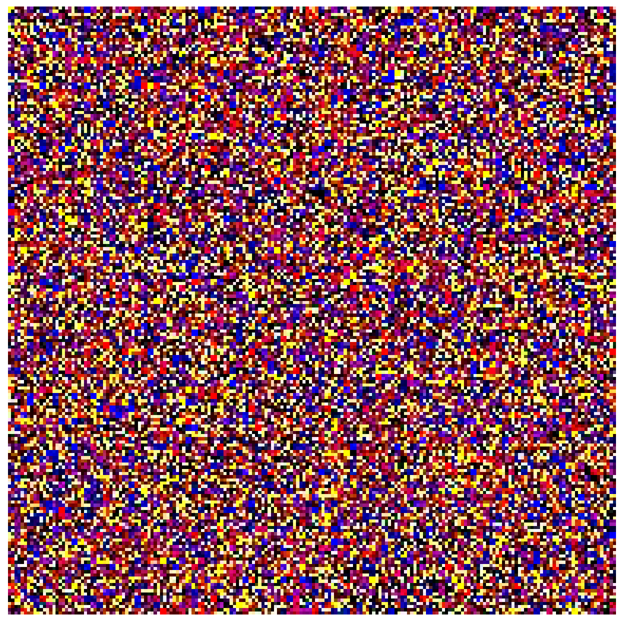
$$AB \rightarrow BA$$

...

macroscopic diffusion $D = \frac{\varepsilon}{2L^2}$



$D = 3\times10^{-5}$



$D = 3\times10^{-4}$

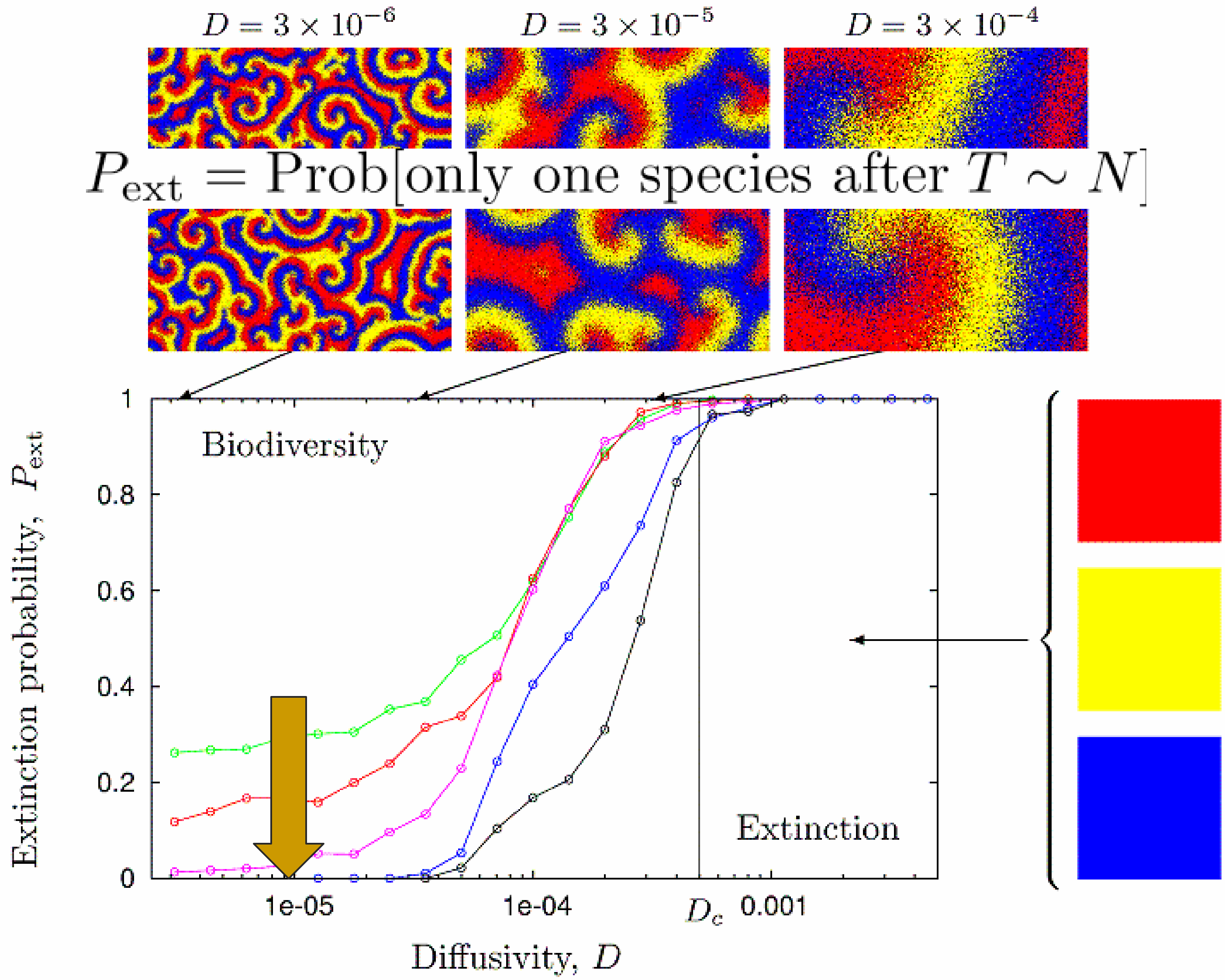
Stability of Biodiversity?

- For well mixed populations biodiversity is lost!
- Is there a critical value for the diffusivity *D* below which biodiversity is maintained?
- If yes, what is the nature of the transition?

Extensivity: let T be the typical extinction time and N the size of the population (system)

$T/N \longrightarrow \infty$		super-extensive / stable
$T/N \longrightarrow O(1)$		extensive / neutral / marginal
$T/N \longrightarrow 0$		sub-extensive / unstable

Diversity is lost above critical Diffusivity



T. Reichenbach, M. Mobilia and E. Frey, Nature (2007)

Loss of Biodiversity

- For large systems there is a well defined **threshold** value D_c (μ,σ) for the mobility.
- Loss of biodiversity seems to be related to the size of the spatial structures (spirals) in the population.

THEORETICAL ANALYSIS:

ROLE OF NONLINEARITY & NOISE

Reaction-Diffusion equation

$$\partial_t \vec{a}(\vec{r}, t) = D\nabla^2 \vec{a} + \vec{F}(\vec{a})$$

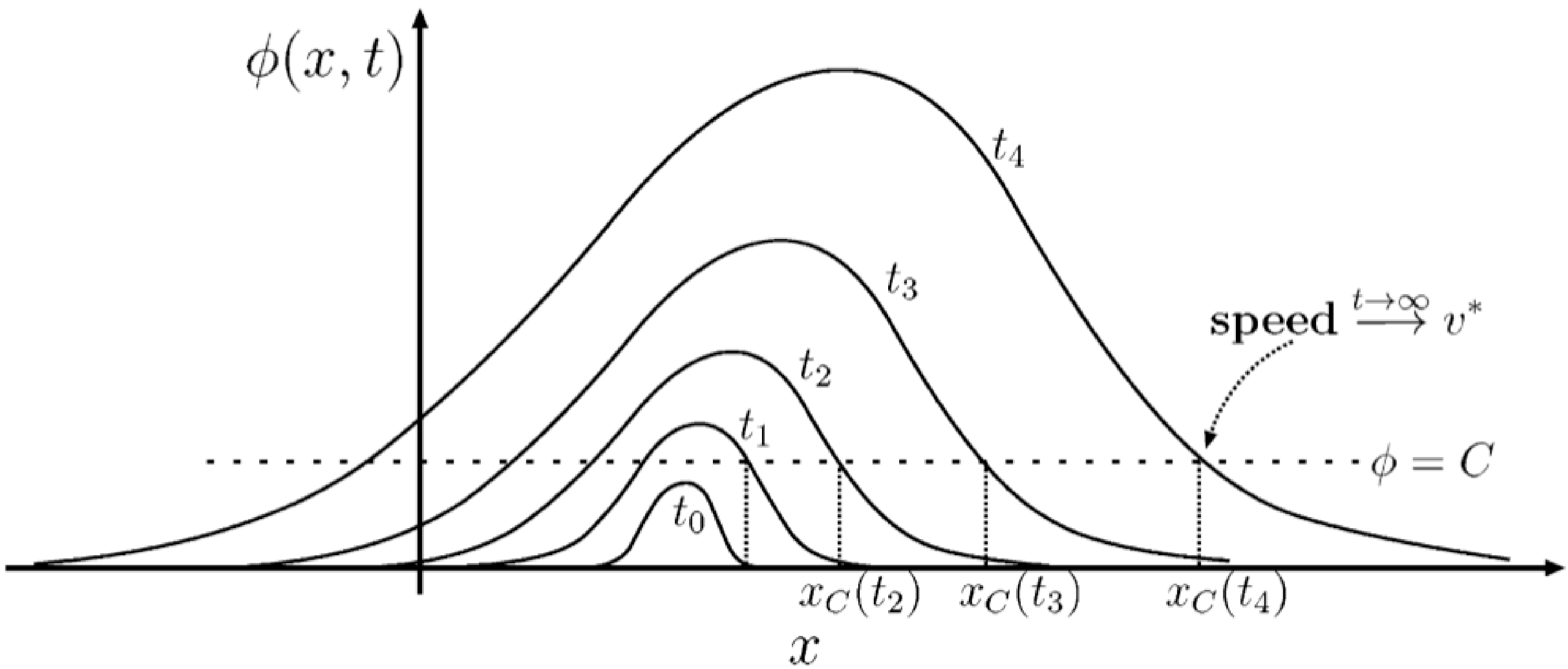
$$D = \frac{\epsilon}{2N}$$

$$\partial_t z \quad = \quad D\nabla^2 z + (c_1 - i\omega)z - c_2(1 + ic_3)|z|^2 z$$

Complex Ginzburg-Landau equation

→ spiral waves

Front propagation into unstable states



W. Van Saarloos, Phys. Rep. 386, 29 (2003)

What about noise?

Stochastic PDE

Look for a description in terms of local densities

$$\partial_t \vec{a}(\vec{r},t) = D\Delta\vec{a}(\vec{r},t) + \mathcal{A}[\vec{a}] + \mathcal{C}[\vec{a}]\cdot\vec{\xi}$$

$$\mathcal{A} = \vec{F}$$

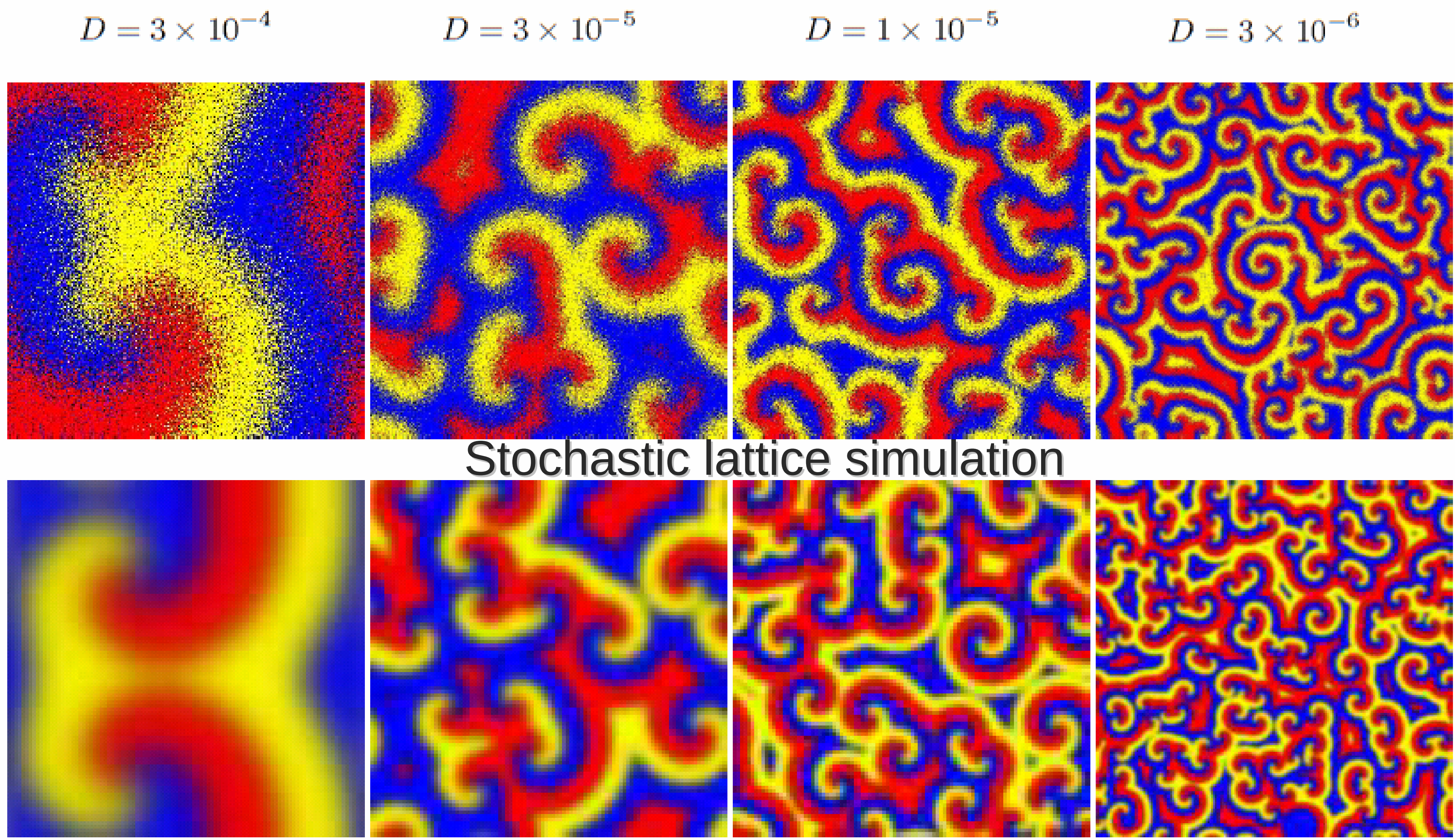
$$\mathcal{C}_A = \frac{1}{\sqrt{N}}\sqrt{a(\vec{r},t)\left[\mu(1-\rho(\vec{r},t)) + \sigma c(\vec{r},t)\right]}$$

$$\langle \xi_i(\vec{r},t)\xi_j(\vec{r}',t')\rangle = \delta_{ij}\delta(\vec{r}-\vec{r}')\delta(t-t')$$

- stochastic partial differential equation
- particle exchange = diffusion
- reactions = drift & multiplicative noise (~$N^{-1/2}$)

T. Reichenbach, M. Mobilia and E. Frey, PRL (2007)

How good is such a description?

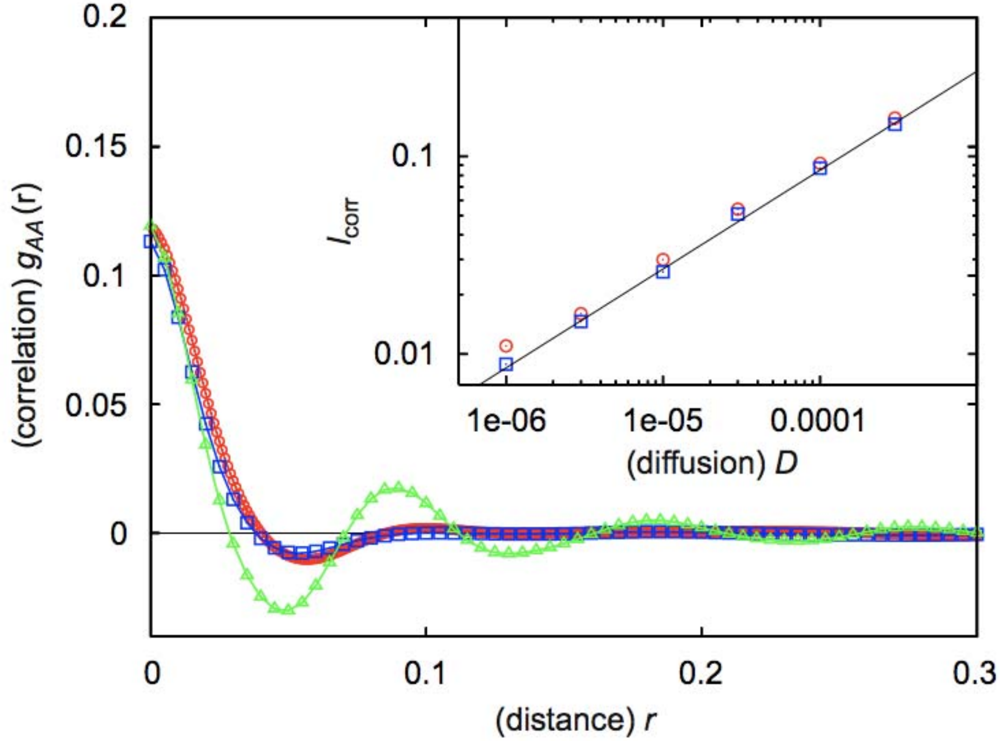


Stochastic lattice simulation

Stochastic reaction-diffusion equations

Spatial Correlations

$$g_{ij}(\mathbf{r},0) = \langle a_i(\mathbf{r},t)\, a_j(\mathbf{0},t)\rangle - \langle a_i(\mathbf{r},t)\rangle \langle a_j(\mathbf{0},t)\rangle$$



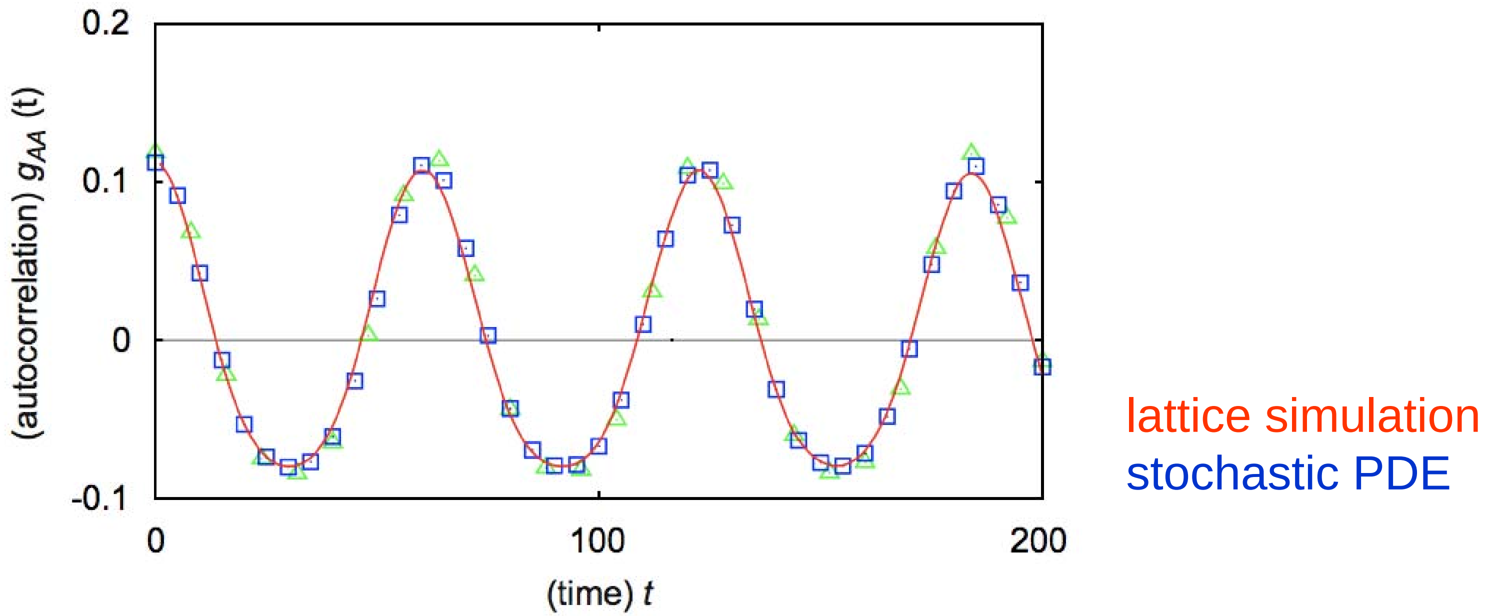
lattice simulation
stochastic PDE

$$l_{\mathrm{corr}} \sim \sqrt{D}$$

raising the diffusion constant *D* increases the size of the spirals

Temporal Correlations

$$g_{ij}(\mathbf{0},t) = \langle a_i(\mathbf{r},t)a_j(\mathbf{r},0)\rangle - \langle a_i(\mathbf{r},t)\rangle\langle a_j(\mathbf{r},0)\rangle$$

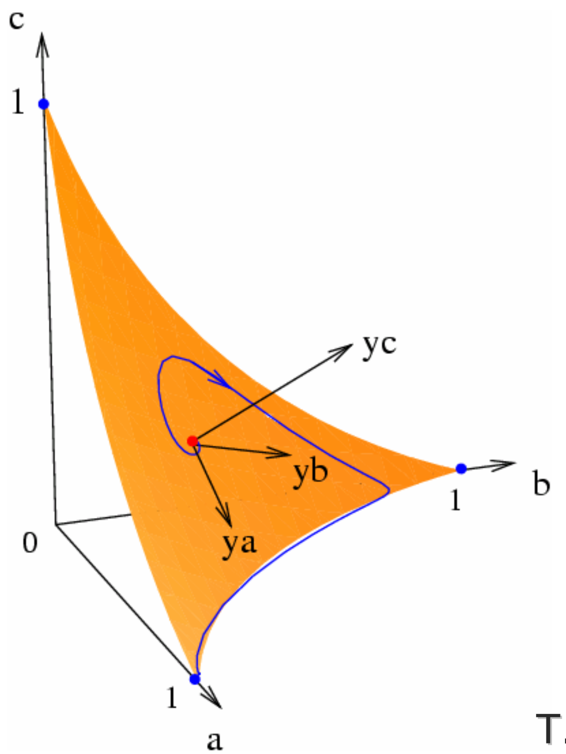


the rotation frequency is a function of the reaction rates μ and σ only

Complex Ginzburg Landau equation

$$\partial_t \vec{a}(\vec{r},t) = D\Delta\vec{a}(\vec{r},t) + \mathcal{A}[\vec{a}] + \mathcal{C}[\vec{a}]\cdot\vec{\xi}$$

$$\partial_t z \quad = \quad D\nabla^2 z + (c_1 - i\omega)z - c_2(1+ic_3)|z|^2 z$$

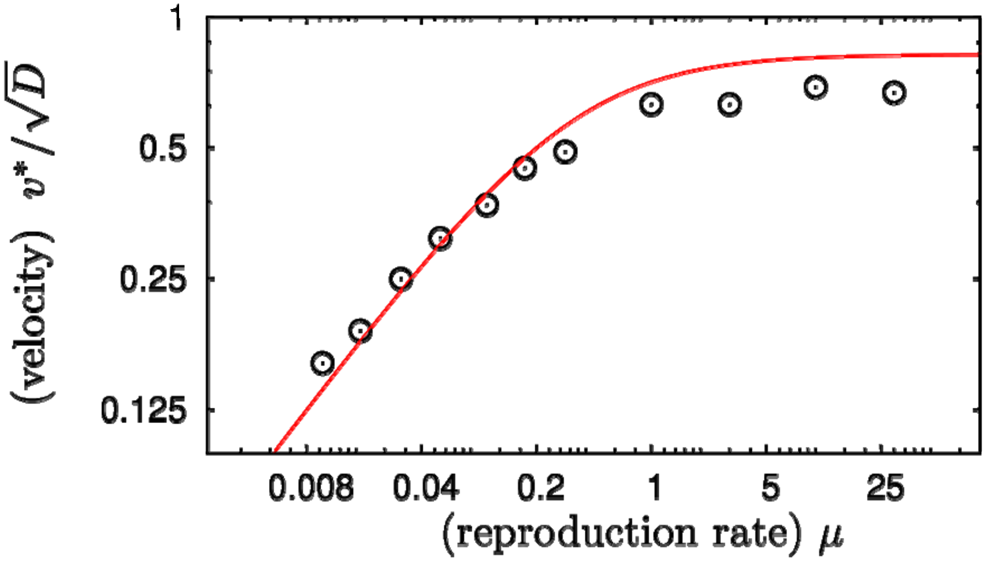


Project onto reactive manifold

Neglect the noise

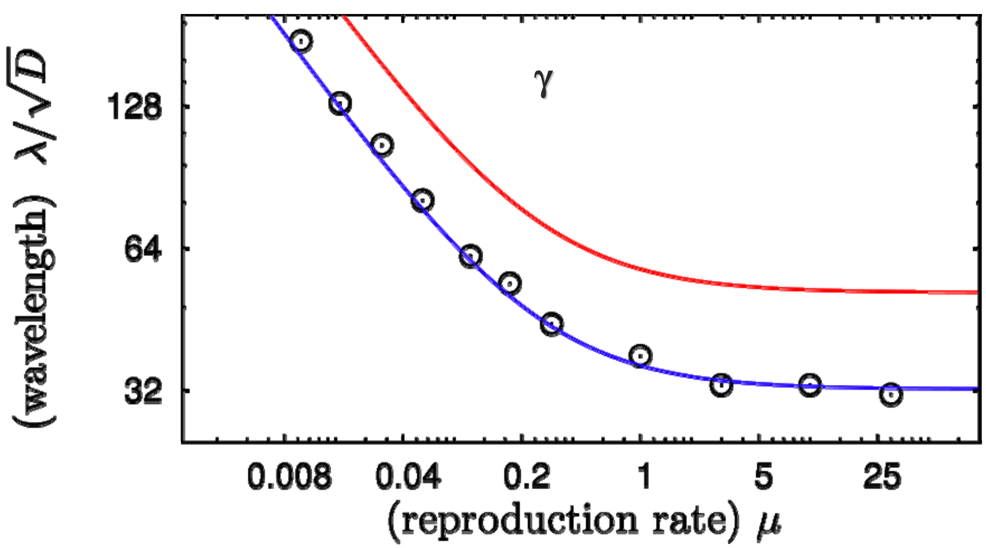
T. Reichenbach, M. Mobilia and E. Frey, J. Theor. Biol. 254, 368 (2008)

Compare CGLE and stochastic PDE's



spreading velocity

$$v^* = 2\sqrt{D}\sqrt{\frac{1}{2}\frac{\mu\sigma}{3\mu+\sigma}}$$

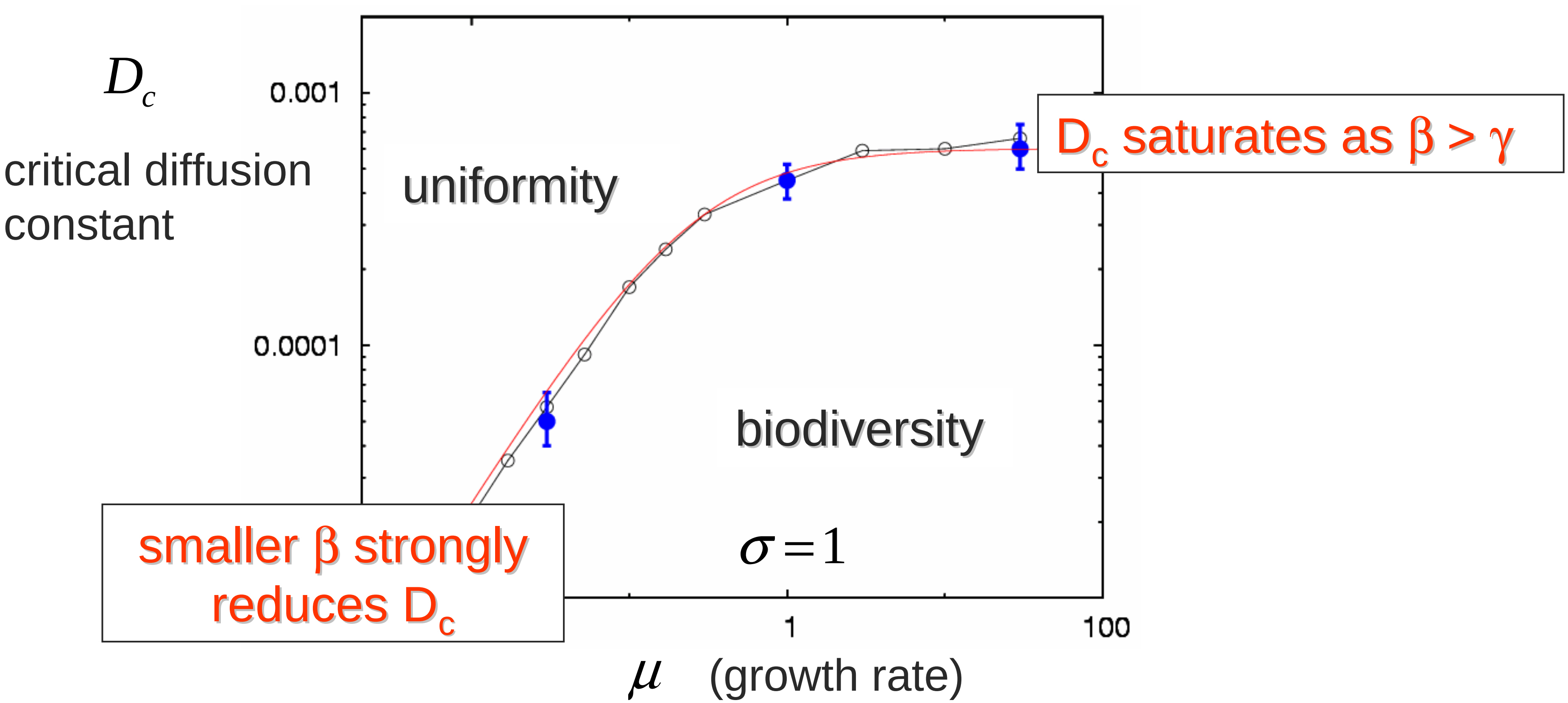


wavelength of spirals

$$\lambda = \frac{2\pi c_3\sqrt{D}}{\sqrt{c_1}\left(1-\sqrt{1+c_3^2}\right)}$$

State Diagram

The CGLE allows to calculate the state diagram



Direct vs. Indirect Dominance

Selection (σ)

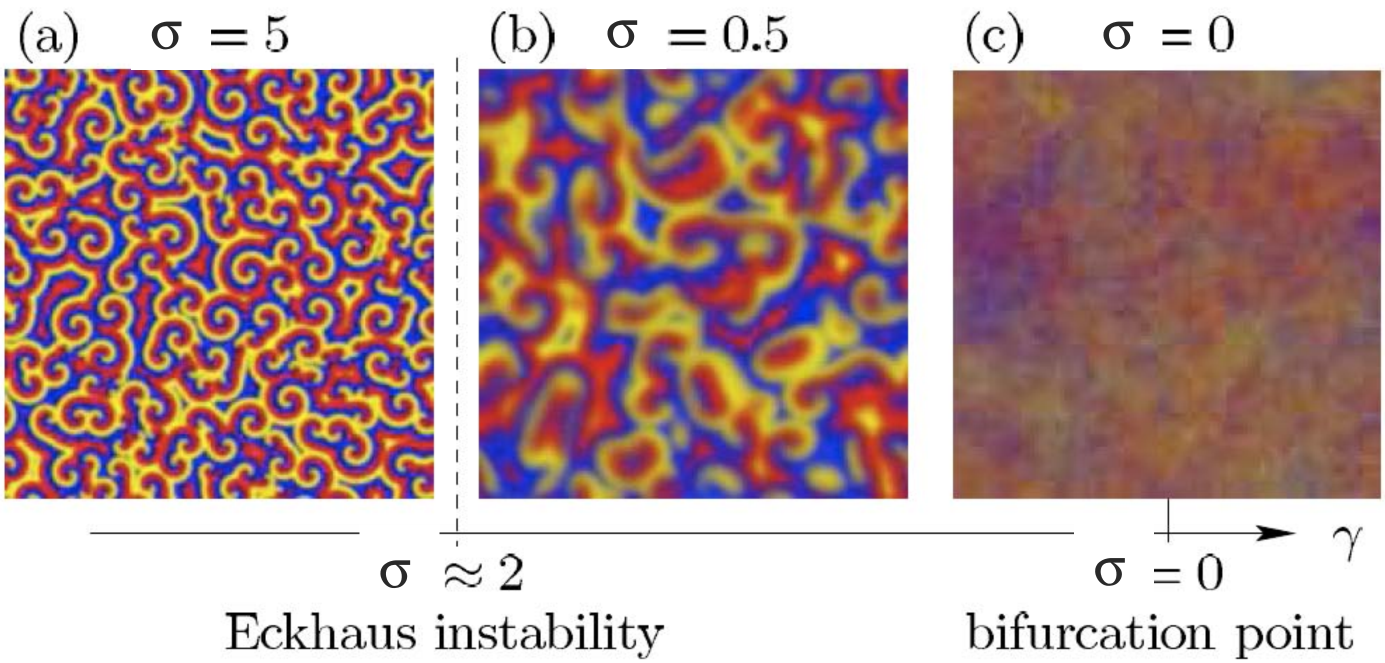
$$AB \rightarrow A0$$
$$BC \rightarrow B0$$
$$CA \rightarrow C0$$

Growth (μ)

$$A0 \rightarrow AA$$
$$B0 \rightarrow BB$$
$$C0 \rightarrow CC$$

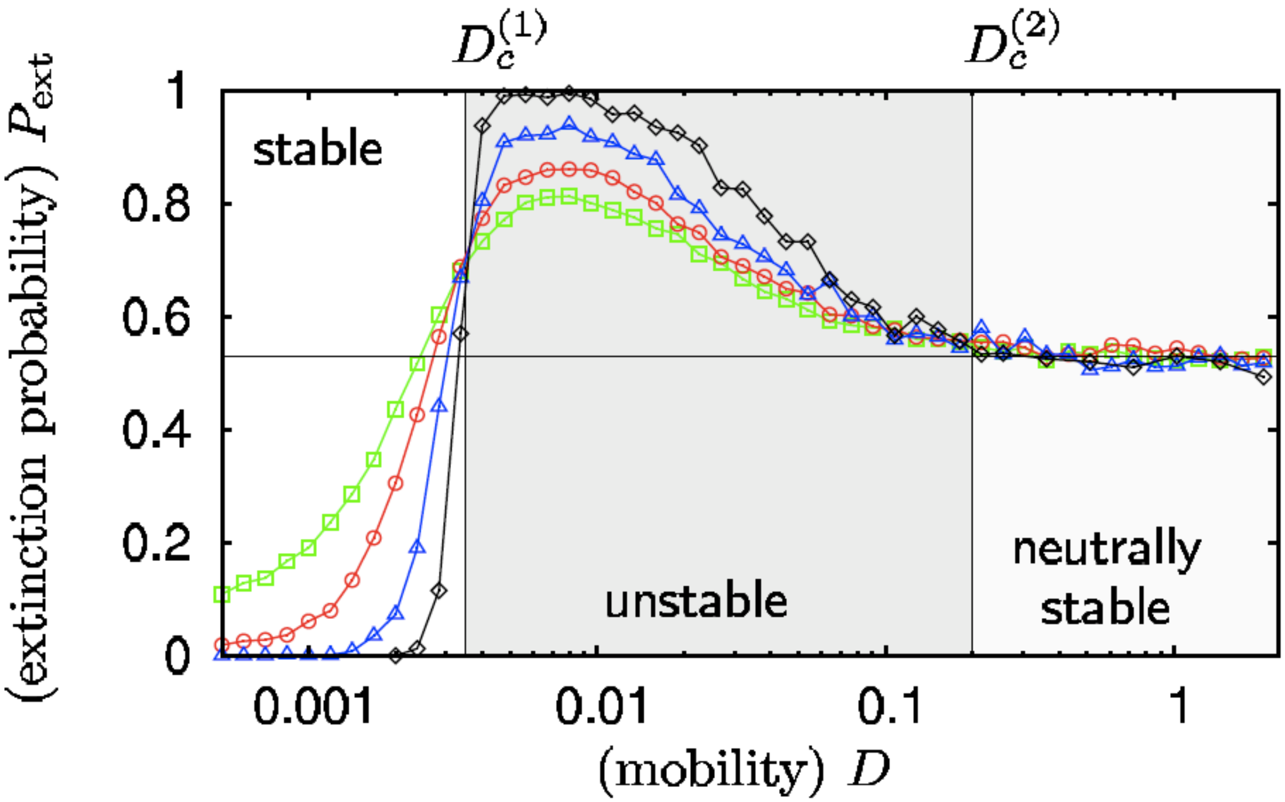
Direct dominance (1)

$$AB \rightarrow AA$$
$$BC \rightarrow BB$$
$$CA \rightarrow CC$$



T. Reichenbach, and E. Frey, PRL 101, 058102 (2008)

Stability Scenarios for Direct Dominance



Spatial structures are predominantly determined by noise

Patterns have an ambiguos impact on biodiversity (3 regimes)

Conclusions

- Well-mixed populations: law of the weakest.
- Local interaction: pattern formation and biodiversity.
- There is a mobility-threshold above which biodiversity is lost; need to characterize the transition in terms of extinction time scales.

Thanks to

- **Tobias Reichenbach** (Rockefeller, USA)
- Mauro Mobilia (Leeds, UK)
- Maximilian Berr (LMU)