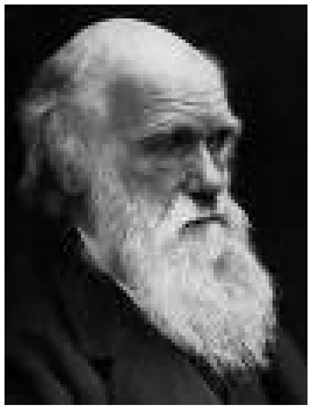
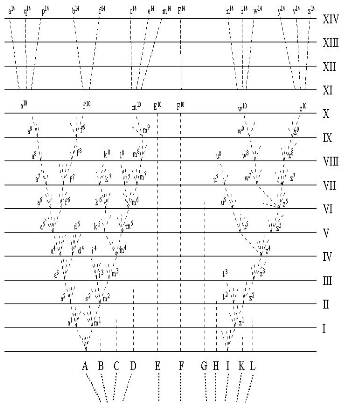
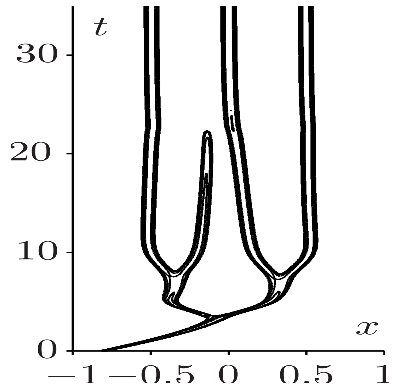
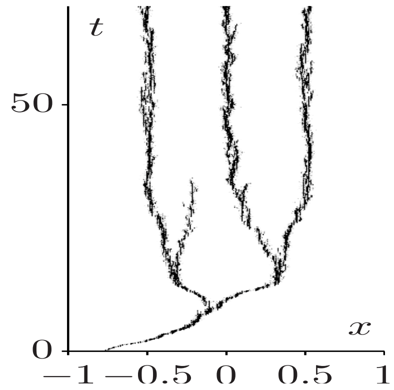
Adaptive evolution :
A population point of view

Benoît Perthame









Population formalism

$$\underbrace{\frac{\partial}{\partial t} n(x,t)}_{\text{variation of individuals}} = \overbrace{\int b(y) M(x,y) n(y,t)}^{\text{birth with mutations}} + n(x,t) \underbrace{R\big(x, I(t)\big)}_{\text{growth rate}}$$

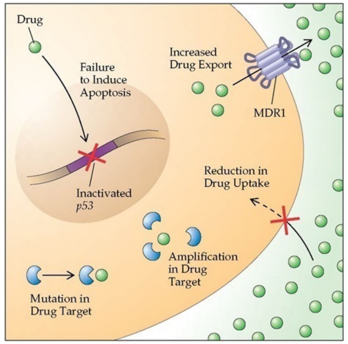
- $n(x,t) =$ number of indivuduals with trait x
- $x =$ phenotypical trait
- $I(t) = (I_1(t), ...I_J(t)) =$ environmental unknowns
- $R(x,I)$ of Lotka-Volterra type, can be negative

- Standard : Calsina, Cuadrado, Desvillettes, Raoul, Jabin, Mirrahimi, ...

Population formalism

The variable x can be

- Size of the adult individuals
- Cannibalism rate (and evolutionary suicide)
- Cooperative behaviour
- Dispersal rate
- Resistance to therapy



Chisholm,... Clairambault, *Emergence of reversible drug tolerance...*, Cancer Research, 2015

Population formalism

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- $n(x,t) =$ number of indivuduals with trait x
- $I(t) = (I_1(t), ...I_J(t)) =$ environmental unknowns

- interplay between population and environment

Rescaling

$$\varepsilon \frac{\partial}{\partial t} n_\varepsilon(x,t) = \int b(y) M_\varepsilon(x,y) n_\varepsilon(y,t)\,dy + n_\varepsilon(x,t) R\Big(x, I_\varepsilon(t)\Big),$$

- $M_\varepsilon(x,y)$ means mutations are rare/have small effect

Rescaling

$$\varepsilon \frac{\partial}{\partial t} n_\varepsilon(x,t) = \int b(y) M_\varepsilon(x,y) n_\varepsilon(y,t) dy + n_\varepsilon(x,t) R\Big(x, I_\varepsilon(t)\Big),$$

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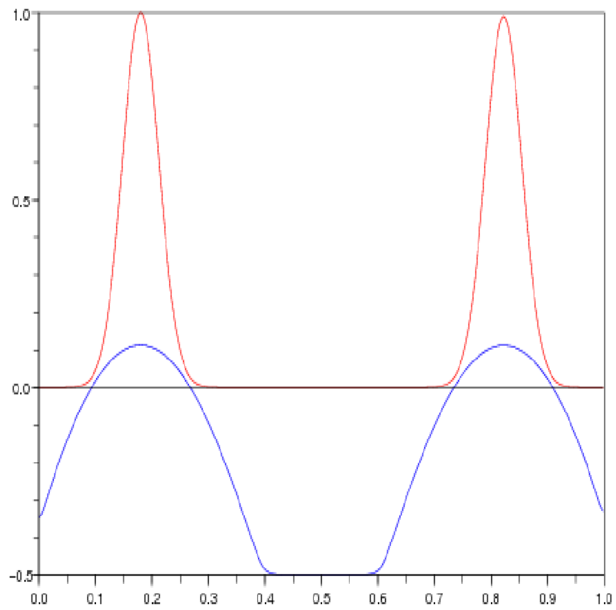
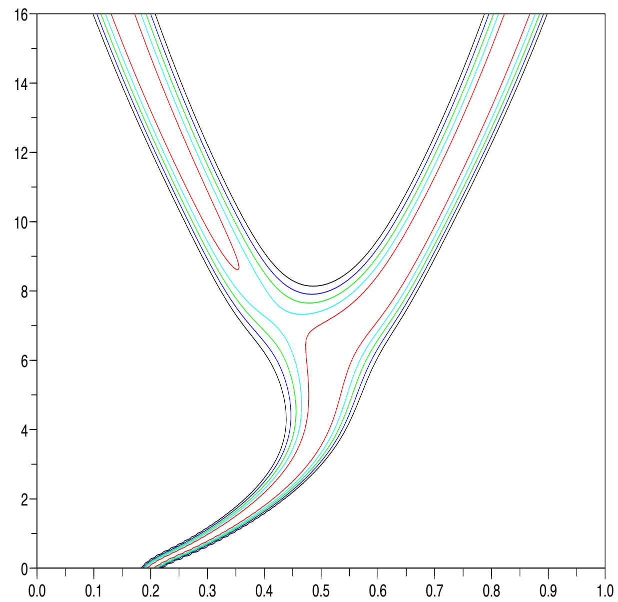
- $M_\varepsilon(x,y)$ means mutations are rare/have small effect
- $\varepsilon \frac{\partial}{\partial t} n_\varepsilon(x,t)$ means we consider a long time scale
- $M_\varepsilon(x,y) = \frac{1}{\varepsilon^d} M\left(\frac{x-y}{\varepsilon}\right)$

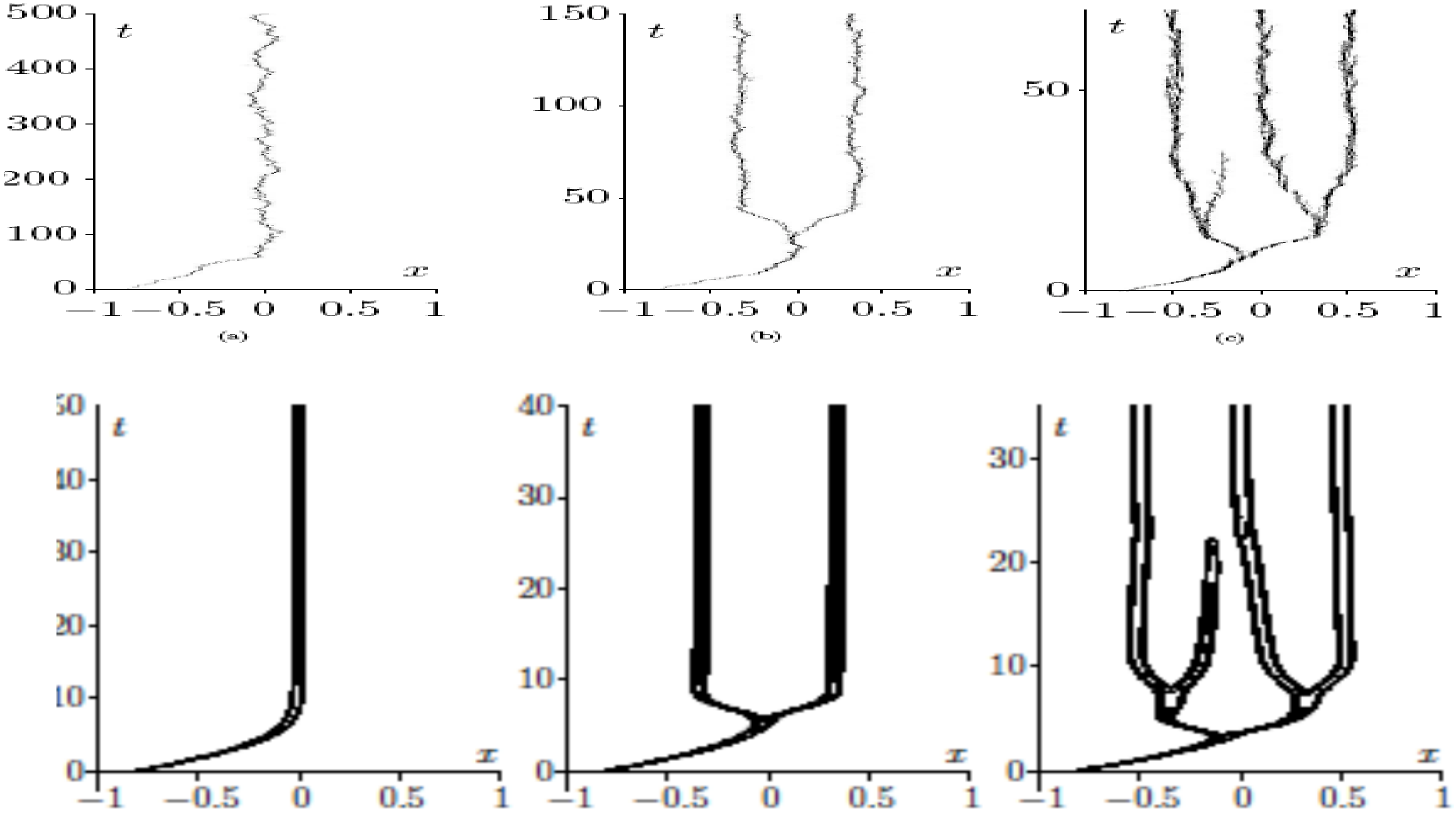
Examples of behaviors





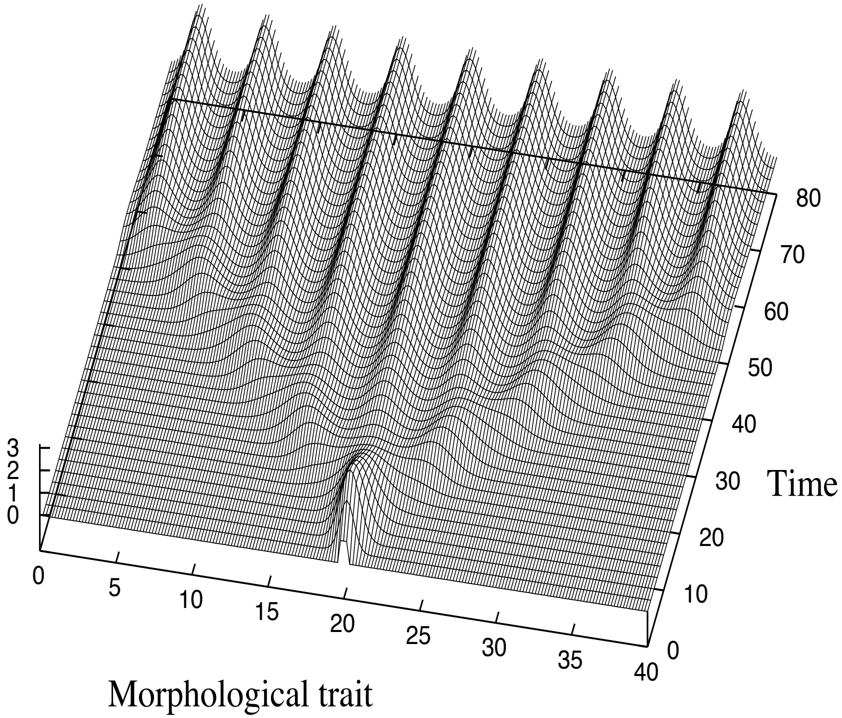
Branching can occur for more general right hand sides (convolution)

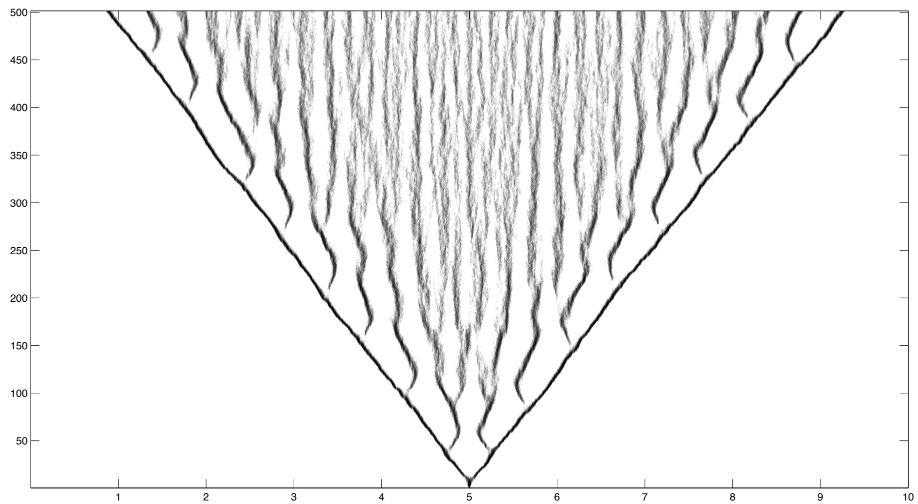
Examples of behaviors



Branching for a Gaussian convolution

Examples of behaviors





Branching for a non-Gaussian convolution

Rescaling

$$\varepsilon \frac{\partial}{\partial t} n_\varepsilon(x,t) = \int b(y) M_\varepsilon(x,y) n_\varepsilon(y,t) dy + n_\varepsilon(x,t) R\Big(x, I_\varepsilon(t)\Big),$$

- $M_\varepsilon(x,y)$ means mutations are rare/have small effect
- $\varepsilon \frac{\partial}{\partial t} n_\varepsilon(x,t)$ means we consider a long time scale
- Simple case $I_\varepsilon(t)$ is reduced to the knowledge of

$$\varrho_\varepsilon(t) = \int_{\mathbb{R}^d} n_\varepsilon(x,t) dx$$

Concentration phenomena

$$\begin{cases} \varepsilon \frac{\partial}{\partial t} n_\varepsilon(x,t) - \varepsilon^2 \Delta n_\varepsilon = n_\varepsilon(x,t) R\Big(x, \varrho_\varepsilon(t)\Big), & x \in \mathbb{R}, \\ \varrho_\varepsilon(t) = \int_{\mathbb{R}^d} n_\varepsilon(x,t)\, dx. \end{cases}$$

- $\exists \varrho_M > 0$ s.t. $\max_x R(x, \varrho_M) = 0$
- $R_\varrho < 0$
- $R_x > 0$

Theorem (d=1) For well-prepared initial data, we have

$$n_\varepsilon(x,t) \underset{\varepsilon_k \to 0}{\longrightarrow} \bar{\varrho}(t)\delta(x = \bar{x}(t)), \qquad \bar{x}(t),\ \ \bar{\varrho}(t) \in BV_{\text{loc}}(0,\infty)$$

$$R\Big(\bar{x}(t), \bar{\varrho}(t)\Big) = 0 \qquad \text{for a.e. } t > 0$$

$\bar{x}(t)$ is the fittest trait

Concentration phenomena

$$\begin{cases} \varepsilon \frac{\partial}{\partial t} n_\varepsilon(x,t) - \varepsilon^2 \Delta n_\varepsilon = n_\varepsilon(x,t) R\Big(x, \varrho_\varepsilon(t)\Big), & x \in \mathbb{R}, \\ \varrho_\varepsilon(t) = \int_{\mathbb{R}^d} n_\varepsilon(x,t)dx. \end{cases}$$

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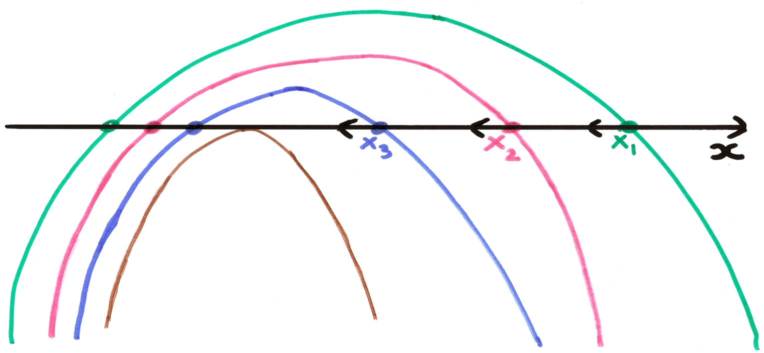
$$R\Big(\bar{x}(t), \bar{\varrho}(t)\Big) = 0 \qquad \text{for a.e. } t > 0$$

as $t \to \infty$ $\qquad R\Big(\bar{x}_\infty, \bar{\varrho}_\infty\Big) = 0 = \max_x R\Big(x, \bar{\varrho}_\infty\Big)$

Concentration phenomena, $d \geq 1$

$$\begin{cases} \varepsilon \frac{\partial}{\partial t} n_\varepsilon(x,t) - \varepsilon^2 \Delta n_\varepsilon = n_\varepsilon(x,t) R\Big(x, \varrho_\varepsilon(t)\Big), \quad x \in \mathbb{R}^d \\ \varrho_\varepsilon(t) = \int_{\mathbb{R}^d} n_\varepsilon(x,t)dx. \end{cases}$$



- $R_\varrho < 0$
- $\exists \varrho_M > 0$ s.t. $\max_x R(x, \varrho_M) = 0$
- $D_x^2 R \leq -KId$,

Theorem (Any dim.) For well-prepared initial data, we have

$$n_\varepsilon(x,t) \longrightarrow \bar{\varrho}(t)\delta(x = \bar{x}(t)), \qquad \bar{x}(t),\ \bar{\varrho}(t) \in C^1\Big([0,\infty)\Big)$$

$$R\Big(\bar{x}(t), \bar{\varrho}(t)\Big) = 0 \qquad \text{for all } t > 0$$

as $t \to \infty$ $\qquad R\Big(\bar{x}_\infty, \bar{\varrho}_\infty\Big) = 0 = \min_\rho \max_x R\Big(x, \varrho\Big)$

Concentration phenomena

Why is mathematics interesting ?

- Nonlocal nonlinearity drastically changes the picture
- Control in L^1 only
- Constrained Hamilton-Jacobi eq.
- Is there a simple rule for the dynamics of $\bar{x}(t)$?

Related approaches

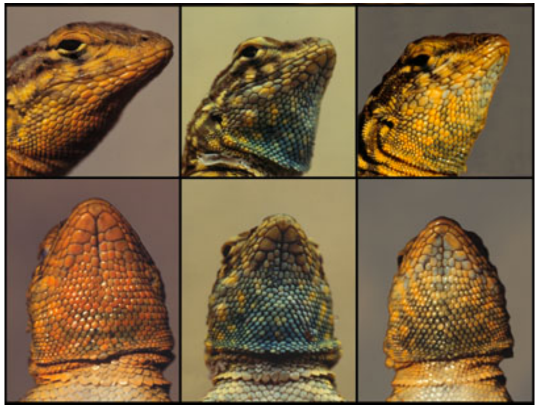
- **Evolutionary game theory**

Blue (stronger),

Orange (middle size),

Yellow (smaller)

compensate by mating **strategies**



from B. Sinervo. *http : //bio.research.ucsc.edu/barrylab*

NATURE VOL. 246 NOVEMBER 2 1973

The Logic of Animal Conflict

J. MAYNARD SMITH
School of Biological Sciences, University of Sussex, Falmer, Sussex BN1 9QG

G. R. PRICE
Galton Laboratory, University College London, 4 Stephenson Way, London NW1 2HE

J. Hofbauer- M. Nowak- K. Zigmund

Related approaches

- **Evolutionary game theory**

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Orange (middle size),

Yellow (smaller)

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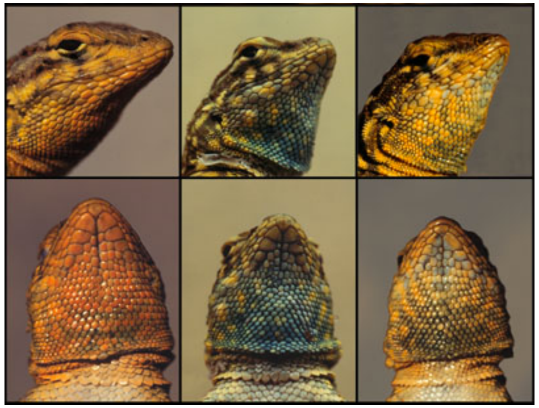
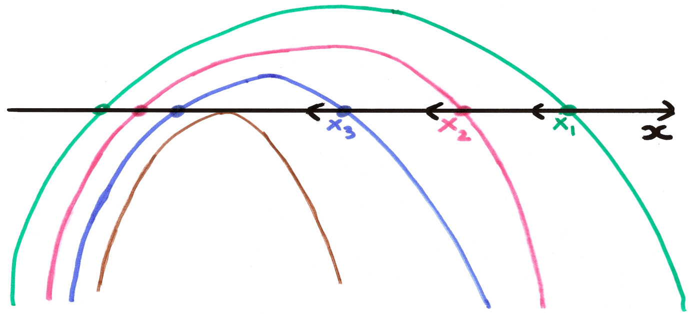


from B. Sinervo. $http://bio.research.ucsc.edu/barrylab$

The relation can be seen by

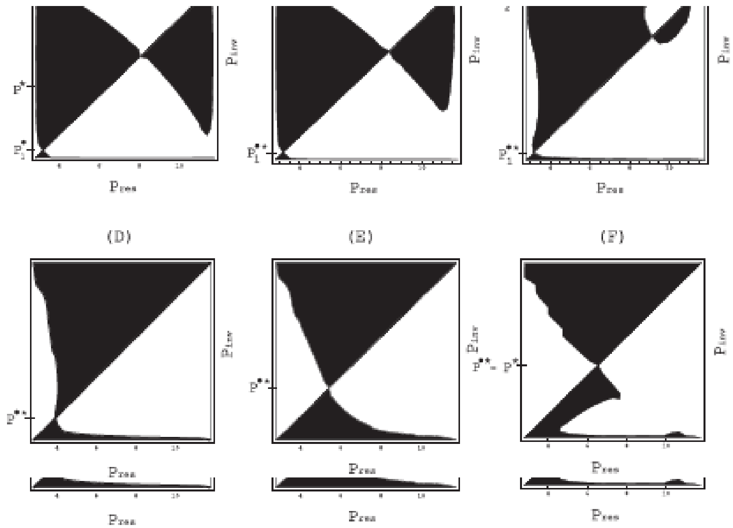
$$\max_{S} R(x, \bar{\varrho}_\infty) = 0 = R(\bar{x}_\infty, \bar{\varrho}_\infty)$$

$$\min_{\varrho} \max_{S} R(x, \varrho) = 0 = R(\bar{x}_\infty, \bar{\rho}_\infty)$$



Related approaches

- **Dynamical systems**



H. Metz, S. Geritz, G. Meszena, S. Kisdi, **O. Diekmann**

Can a mutant invade the resident population ?

Related approaches

- Stochastic models, Individual Based Models

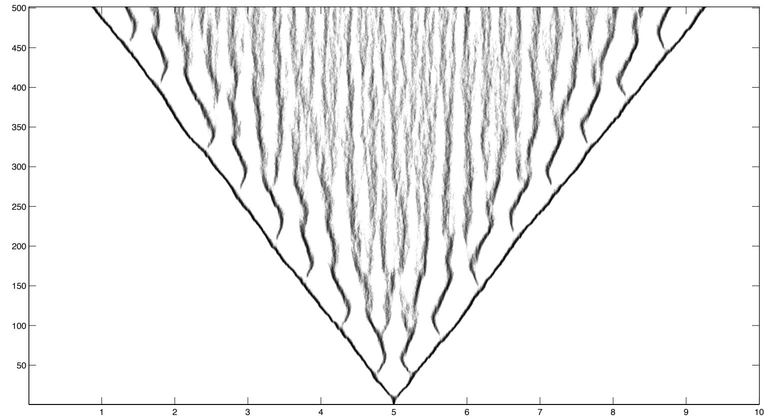
N individuals,

rescale mutation, birth, death rates

U. Dieckmann-R. Law, R. Ferriere

S. Billard, N. Champagnat

S. Méléard, V. C Tran



Asymptotics with mutations

$$\begin{cases} \varepsilon \frac{\partial}{\partial t} n_\varepsilon(t,x) - \varepsilon^2 \Delta n_\varepsilon = n_\varepsilon(t,x) R\Big(x, \varrho_\varepsilon(t)\Big), \\ \\ \varrho_\varepsilon(t) = \int_{\mathbb{R}^d} n_\varepsilon(t,x) dx. \end{cases}$$

Asymptotics with mutations

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In the limit one can expect

$$0 = n(t,x)R\Big(x, \varrho(t)\Big),$$

$$n(t,x) = \rho \delta_{\Gamma(t)}, \qquad \Gamma(t) \subset \Big\{R(\cdot, \rho(t)) = 0\Big\}.$$

Proof

Step 1. $\varrho_\varepsilon(t) \in_\mathrm{b} L^\infty, \qquad n_\varepsilon \in_\mathrm{b} L^\infty_t(L^1_x)$

Step 2. A BV estimate

Step 3. Represent

$$n_\varepsilon(t,x) = \exp \frac{\varphi_\varepsilon(t,x)}{\varepsilon}$$

the 'fittest' trait $\bar{x}(t)$ is characterised by the Eikonal equation with constraints

$$\begin{cases} \frac{\partial}{\partial t}\varphi(t,x) = R\Big(x, \bar{\varrho}(t)\Big) + |\nabla\varphi(t,x)\Big)|^2 \\ \max_x \varphi(t,x) = 0 \qquad \Big(= \varphi(t,\bar{x}(t)) \Big). \end{cases}$$

Proof

Uniqueness

- $R(x, \varrho) = b(x)a(\varrho) - d(x)$
- J.-M. Roquejoffre et S. Mirrahimi
- P. E. Jabin Approach by modulation

Canonical equation

Any concentration point $x_i(t)$ will satisfy

(i) $$R\Big(\bar{x}_i(t), \bar{I}(t)\Big) = 0$$

(ii) $$\frac{d}{dt}\bar{x}_i(t) = \Big(- D^2\varphi(\bar{x}_i(t), t)\Big)^{-1}.\nabla R\Big(\bar{x}_i(t), \bar{I}(t)\Big)$$

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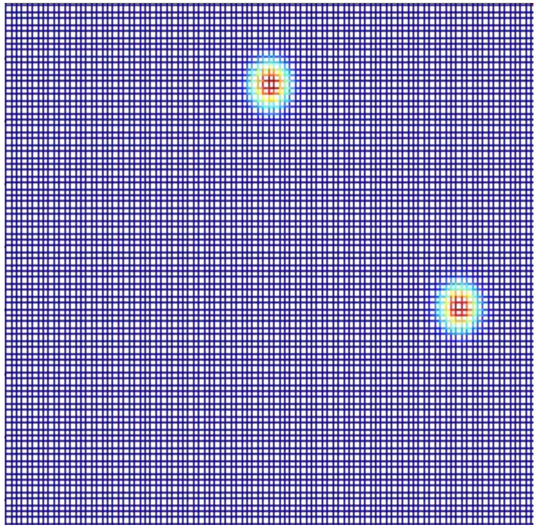
Conclusions :

- Gause's competitive exclusion principle
- $n_\varepsilon = \exp(\varphi/\varepsilon)$ the shape of φ plays a role

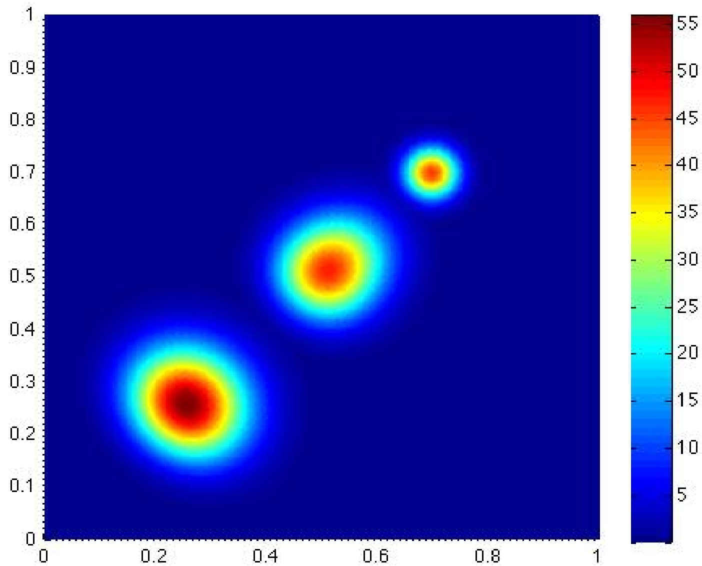
Canonical equation

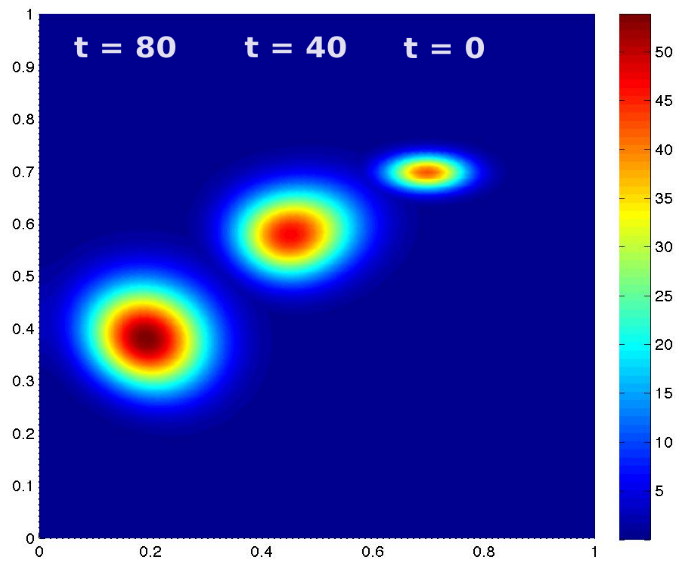


Canonical equation

$$\frac{d}{dt}\bar{x}(t) = \Big(- D^2\varphi(\bar{x}(t), t)\Big)^{-1} . \nabla R\Big(\bar{x}(t), \bar{\varrho}(t)\Big)$$

Effect of the matrix $\Big(- D^2\varphi(\bar{x}(t), t)\Big)$ (microstructure of the Dirac)

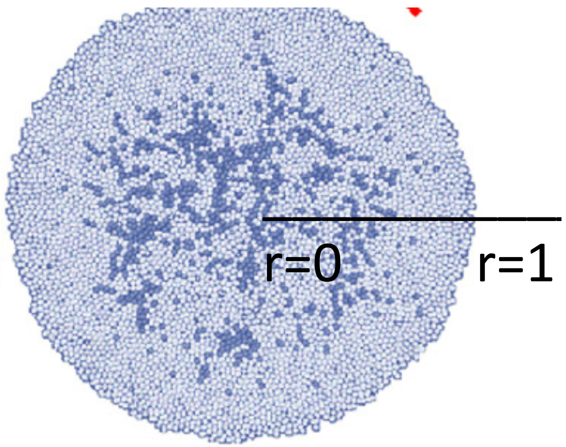




Space-trait concentration

Let $y \in \mathbb{R}$ a space variable

$$\begin{cases} \varepsilon \partial_t n_\varepsilon(y,x,t) = \Big[r(x) c_\varepsilon(y,t) - d(x) \varrho_\varepsilon(y,t) - \mu(x) \Big] n_\varepsilon(y,x,t) \\ -\Delta_y c_\varepsilon(y,t) + \Big[\varrho_\varepsilon(y,t) + \lambda \Big] \, c_\varepsilon(y,t) = \lambda c_B, \\ \varrho_\varepsilon(y,t) = \int n_\varepsilon(y,x,t) dx \end{cases}$$



Interpetation

- Nutrients/drugs are diffused and consumed by cells
- Local conditions select space-dependent traits

Space-trait concentration

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Theorem : For well-prepared initial data, as $\varepsilon_k \to 0$, we have

$$n_\varepsilon(y,x,t) \to \overline{\rho}(y,t) \delta\Big(x - \overline{X}(y,t) \Big)$$

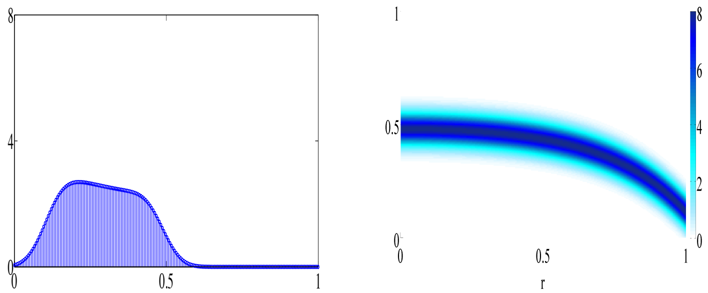
Difficulty : Space works well with L^∞. Traits with L^1

Outcome : Explains heterogeneity

Space-trait concentration

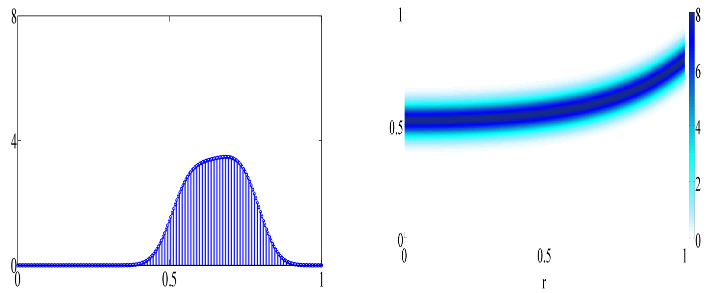
Let $x =$ resistance to drugs

$$\begin{cases} \varepsilon \partial_t n_\varepsilon(y,x,t) = \Big[r(x) c_\varepsilon(y,t) - d(x) \varrho_\varepsilon(y,t) - \mu(x) \Big] n_\varepsilon(y,x,t) \\ -\Delta_y c_\varepsilon(y,t) + \Big[\varrho_\varepsilon(y,t) + \lambda \Big] \, c_\varepsilon(y,t) = \lambda c_B, \\ \varrho_\varepsilon(y,t) = \int n_\varepsilon(y,x,t) dx \end{cases}$$



Without cytotoxic drug

High heterogeneity



With cytotoxic drug

Lower heterogeneity

Evolution of Dispersal

Selection without a proliferative advantage ?

- motility/dispersal of individuals is subject to variability
- no advantage regarding their reproductive rate

- $R(x, \rho) =$ Operator acting on the space variable

Hastings, *Theor. Popul. Biol.* 1983

Evolution of Dispersal

We model it for $y \in \Omega,\ x > 0$ + Neuman BC

$$\partial_t n(t,x,y) \overbrace{= x\partial^2_{yy} n(t,x,y)}^{\text{dispersion/motility}} + \underbrace{\overbrace{n(t,x,y)\,\big(K(y) - \rho(t,y)\big)}^{\text{reproduction}}}_{=R(x,\cdot)} \overbrace{+\varepsilon^2 \partial^2_{xx} n(t,x,y)}^{\text{mutations on motility}}$$

$$\rho(t,y) = \int_0^\infty n(t,x,y)\,dy$$

Evolution of Dispersal

$$\partial_t n(t,x,y) \overbrace{= x\partial^2_{yy} n(t,x,y)}^{\text{dispersion/motility}} + \overbrace{n(t,x,y)\,(K(y)-\rho(t,y))}^{\text{reproduction}} \overbrace{+\varepsilon^2 \partial^2_{xx} n(t,x,y)}^{\text{mutations on motility}}$$

$$\rho(t,y) = \int_0^\infty n(t,x,y)\,dy$$

Theorem (P. E. Souganidis, BP and K. Y. Lam, Y. Lou) The ESS are of the form

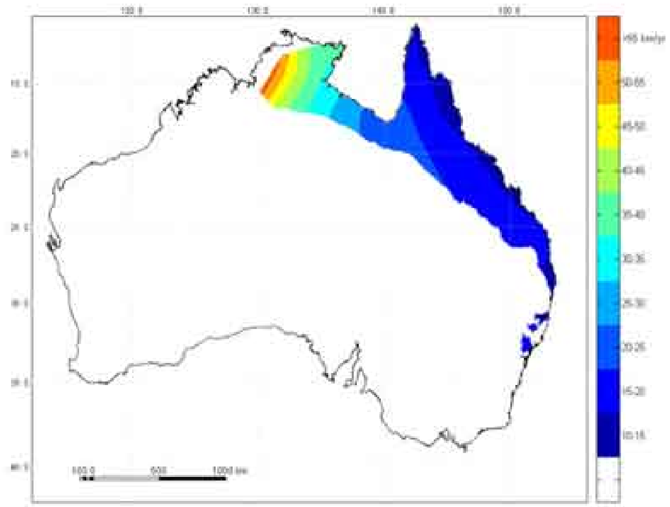
$$n(t,x,y) \approx \bar{\rho}_\infty(y)\delta\Big(x=0\Big) \qquad \varepsilon \to 0, \quad t \to \infty$$

and the constrained H.-J. eq.

$$\begin{cases} \frac{\partial}{\partial t} u(x,t) = \Lambda(x,\varrho(\cdot,t)) + |\nabla u|^2 \\ \max_x u(x,t) = 0 = u(\bar{X}(t),t), \end{cases}$$

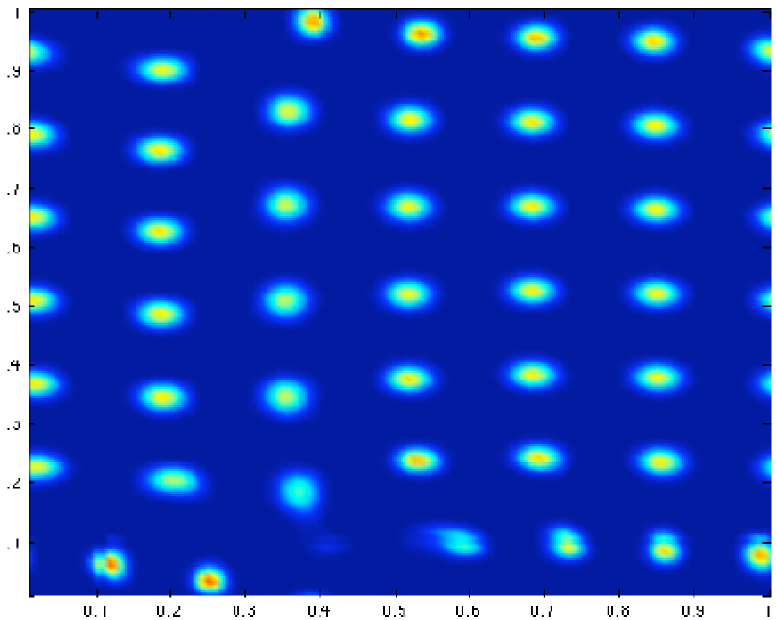
Evolution of Dispersal

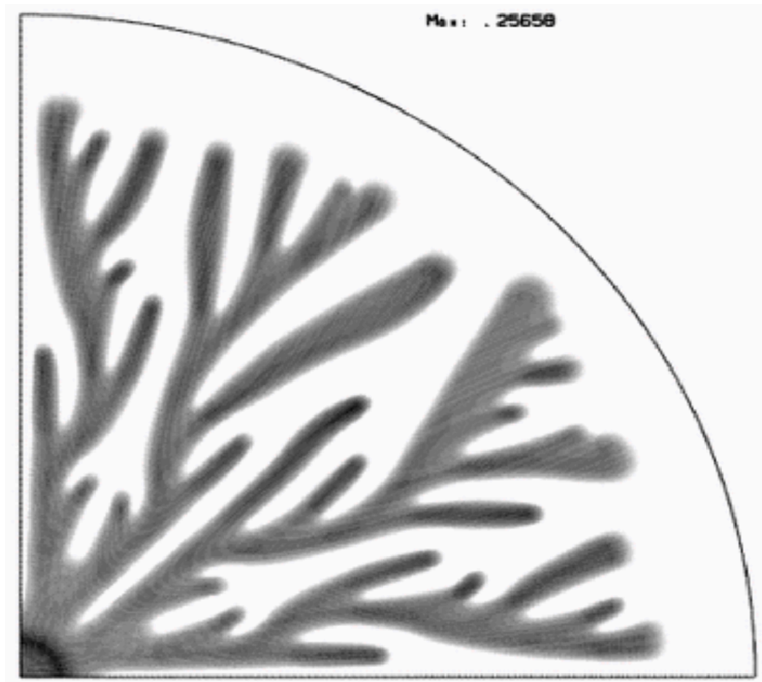
- Same question for traveling waves
- Accelerating waves
- Example cane toads invasion in Australia



J. Berestycki, E. Bouin, V. Calvez, C. Mouhot, G. Raoul, L. Ryzhik., C. Henderson

Turing (dentritic) patterns





Thanks to my collaborators

O. Diekmann, P.-E. Jabin, S. Mischler,

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G. Barles, S. Mirrahimi, P. E. Souganidis, A. Lorz, T. Lorenzi, Thanks to my collaborators

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THANK YOU ALL