Colloquium du CERMICS

# Stuctured equations in Biology

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# Structured equations
## in biology

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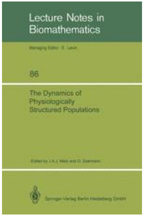
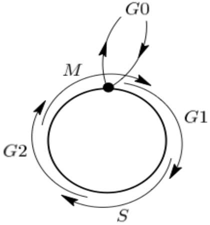


# Organisation of the talk

1. Why structured equations ?
2. Renewal and growth fragmentation eqs
3. Generalised relative entropy
4. Monge-Kantorovich distance

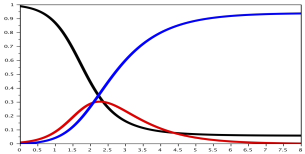
# Examples of stuctured equations

The standard SIR system

- $S(t)$ = Susceptible individuals
- $I(t)$ = Infectious individuals (who propagate the epidemic)
- $R(t)$ = Removed individuals

The SIR system (D. Bernouilli, 1760 ?) reads

$$\begin{cases} \dot{S}(t) = -\beta SI \\ \dot{I}(t) = \beta SI - \gamma I \\ \dot{R}(t) = \gamma I \end{cases}$$




It is easy to see that $S(t) \to S_\infty > S_{herd}$ (for $R_0 > 1$)

$$\ln S_\infty - \frac{\beta}{\gamma} S_\infty = \ln S^0 - \frac{\beta}{\gamma}[S^0 + I^0]$$

# Examples of stuctured equations

Heterogeneous population (contact matrices)

- $x$ = Social contacts
- $I(t,x)$ = immune system status

$$\begin{cases} \dot{S}(t,x) = -S(t,x)\int_\Omega \beta(x,y)I(t,y)\,dy \qquad (+\Delta S) \\ \dot{I}(t,x) = S(t,x)\int_\Omega \beta(x,y)I(t,y)\,dy - \gamma(x)I(t,x) \\ \dot{R}(t,x) = \gamma(x)I(t,x) \end{cases}$$

# Examples of stuctured equations

Heterogeneous population (contact matrices)

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**Theorem** (Almeida, Bliman, Nadin, BP, Vauchelet)
The solution converges to the UNIQUE steady state $S_\infty < S^0$ and

$$\ln S_\infty(x) - \int \frac{\beta(x,y)}{\gamma(y)} S_\infty(y)\,dy = \ln S^0(x) - \int \frac{\beta(x,y)}{\gamma(y)} (S^0(y) + I^0(y))\,dy$$

# Examples of stuctured equations

The Kermack-McKendrick renewal equation (1927)

$$\begin{cases} \frac{d}{dt}S(t) = B - \mu_S S(t) - I(t)S(t) \\ I(t) := \int_0^\infty \beta(s) n_I(t,s) ds \\ \frac{\partial}{\partial t} n_I(t,s) + \frac{\partial}{\partial s} n_I(t,s) + (\mu_I + \gamma(s)) n_I(t,s) = 0 \\ n_I(t, s=0) = I(t)S(t) \end{cases}$$

**Theorem** (Magal, McCluskey, Webb, 2010). Define

$$\mathcal{E}(t) = \int_0^\infty \psi(s) \bar{n}_I(s) \Big[ \frac{n_I(t,s)}{\bar{n}_I(s)} - \ln \frac{n_I(t,s)}{\bar{n}_I(s)} \Big] ds + \bar{S} \ln S(t) - S(t).$$

Then, we have

$$\frac{d}{dt}\mathcal{E}(t) \leq -D(t) \leq 0, \qquad D(t) = \frac{\mu_S}{S(t)} (\bar{S} - S(t))^2.$$

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# The renewal equation

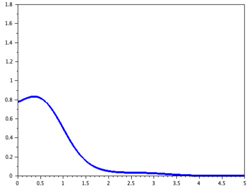
$$
\begin{cases}
\frac{\partial}{\partial t} n(t,x) + \frac{\partial}{\partial x} n(t,x) + d(x) n(t,x) = 0, \quad t \geq 0,\ x \geq 0 \\
N(t) := n(t, x=0) = \int_0^\infty b(y) n(t,y) dy \\
n(t=0,x) = n^0(x)
\end{cases}
$$

$$
b,\ d \in L^\infty_+(0,\infty).
$$

- Very useful (demography, cell cycle, anomalous diffusions)
- Very standard (Feller)
- Nonlinear versions are complex

# The renewal equation

$$
\begin{cases}
\frac{\partial}{\partial t} n(t,x) + \frac{\partial}{\partial x} n(t,x) + d(x) n(t,x) = 0, \quad t \geq 0,\ x \geq 0 \\
N(t) := n(t, x=0) = \int_0^\infty b(y, I(t)) n(t,y) dy \\
I(t) = \int q(x) n(t,x) dx
\end{cases}
$$



# Growth-fragmentation/TCP

Another useful equation

$$\begin{cases} \frac{\partial n(t,x)}{\partial t} + \frac{\partial [g(x)n(t,x)]}{\partial x} + b(x)n(t,x) = 2\int_x^\infty b(y)\kappa(x,y)n(t,y)dy \\ n(t,x=0)=0, \qquad g(0)>0, \\ n(t=0,x)=n^0(x). \end{cases}$$

- $b(y) =$ is the division rate of cells/polymers/messages of sizes $y$
- $\kappa(x,y)=0 \qquad$ for $x>y$
- $\int_0^y \kappa(x,y)dx = 1, \qquad \int_0^y x\,\kappa(x,y)dx = y/2$
- $\frac{d}{dt}\int_0^\infty n(t,x)dx = \int_0^\infty b(x)n(t,x)dx$
- $\frac{d}{dt}\int_0^\infty xn(t,x)dx = \int_0^\infty g(x)n(t,x)dx.$

# Many other structured equations

## Age and size structured

$$\begin{cases} \frac{\partial n(t,x,z)}{\partial t} + \frac{\partial n(t,x,z)}{\partial x} + \frac{\partial [g(z)\, n]}{\partial z} + d(x,z)\, n(t,x,z) = 0, \quad x > 0,\ z > 0, \\ n(t,x,z=0) = 0, \\ n(t,x=0,z) = \int_{x=0}^{\infty} \int_{z'=z}^{\infty} d(x',z')\kappa(z,z')n(t,x',z')dx'dz \end{cases}$$

## Age and space structured

$$\begin{cases} \frac{\partial n(t,x,z)}{\partial t} + \frac{\partial n(t,x,z)}{\partial x} + d(x)n(t,x,z) = 0, \quad x > 0,\ z \in \mathbb{R}^d \\ n(t,x=0,z) = \int_0^{\infty}\int_{\mathbb{R}^d} d(x)n(t,x,z+\varepsilon\eta)k(\eta)dxd\eta \end{cases}$$

- Doumic, M. ; Hoffmann, M. ; Krell, N. ; Robert, L. et al (2015)
- Berry, H. ; Lepoutre, T. ; González, A. ; Acta Appl. Math. (2016)
- Calvez, V. ; Gabriel, P. ; Mateos G. ; Asymptot. Anal. (2019)

- Franck M. ; Goudon T. ; KRM (2018)

# Which general tools ?

- Generalized relative entropy

- Modified Monge-Kantorovich distance

# Organisation of the talk

# Generalized relative entropy

All (linear) equations preserving positivity satisfy the GRE

$$\mathcal{L}\varphi + \lambda_0 \varphi = 0, \quad \varphi > 0, \qquad \mathcal{L}^* \psi + \lambda_0 \psi = 0, \quad \psi > 0,$$

Let

$$\frac{\partial n(t)}{\partial t} + \mathcal{L} n(t,x) = 0.$$

**GRE Principle.** For all $H(\cdot)$ convex, $u(t,x) = e^{-\lambda_0 t} \frac{n(t,x)}{\varphi(x)}$ satisfies

$$\frac{d}{dt} \int \psi(x)\varphi(x) H\big(u(t,x)\big)\, dx = -D_H(t) \leq 0$$

# Generalized relative entropy

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- $\int \psi(x) n(t,x) dx = e^{\lambda_0 t} \int \psi(x) n^0(x) dx$ Conservation law
- $u^0 \leq C^0 \Longrightarrow u(t,x) \leq C^0$
- $\frac{d}{dt} \ln n(t,x) \leq \max_x \frac{d}{dt} \ln n^0(x)$
- Explains Kermack-McKendrick $H(u) = u - \ln u$.

# Generalized relative entropy

**Examples.** $u(t,x) = e^{-\lambda_0 t} \frac{n(t,x)}{\varphi(x)}$

$$\frac{\partial n(t,x)}{\partial t} - \Delta n + \mathrm{div}(n \nabla V) = 0 \qquad \text{(Fokker-Planck)}$$

$$\lambda_0 = 0, \quad \psi = 1, \quad \varphi = e^V, \qquad D_H = \int \varphi H''(u) |\nabla u|^2$$

$$\begin{cases} \frac{\partial}{\partial t} n(t,x) + \frac{\partial}{\partial x} n(t,x) + d(x) n(t,x) = 0, & \text{(Renewal)} \\ N(t) := n(t, x=0) = \int_0^\infty b(y) n(t,y) dy \end{cases}$$

$$\varphi = e^{-\int_0^x d - \lambda_0 x}, \qquad D_H = \int b\varphi H(u) - H(\int b\varphi u)$$

# Generalized relative entropy

**Examples.** $u(t,x) = e^{-\lambda_0 t} \frac{n(t,x)}{\varphi(x)}$

In most of the cases, the spectral theory is not so easy

$$\frac{\partial n(t,x)}{\partial t} + \frac{\partial [g(x)n(t,x)]}{\partial x} + b(x)n(t,x) = 2\int_x^\infty b(y)\kappa(x,y)n(t,y)dy$$

$$D_H = 2 \iint \psi(x)\varphi(y)b(y)\kappa(x,y) \left[H(u(y)) - H(u(x)) - H'(u(x))(u(y) - u(x))\right] dxdy$$

# Generalized relative entropy

**Spectral gap.** Aim is to find $\lambda_1 > 0$ such that

$$\|e^{-\lambda_0 t} n(t,x) - \rho^0 \varphi\| \leq C e^{-\lambda_1 t}$$

- Poincaré inequality : when $\int \psi \varphi u(x) = 0$

$$\lambda_1 \int \psi \varphi H(u) dx \leq D_H(u)$$

- Doeblin's method
- Method of integral equation
- Bacry-Emery's method

(Ryzhik, BP, Doumic, Gabriel, Mischler, Cañizo, Yoldas, Laurencot)

# Organisation of the talk

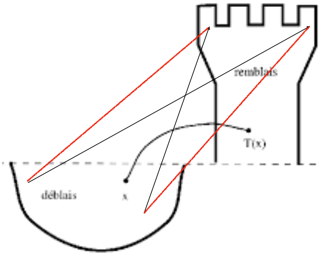
# Monge-Kantorovich distance

- $\Omega$ open subset of $\mathbb{R}^d$
- Cost function $c(x,y) \geq 0$, $x \in \Omega$, $y \in \Omega$
- $\mu_1$, $\mu_2$ probability measures on $\Omega$

• **Monge :** $T : \Omega \to \Omega, \qquad T_{\#}\mu_1 = \mu_2$

$$c(x,y) = |x - y|$$

$$d_{MK}(\mu_1,\mu_2) := \min_T \int_\Omega c(x, T(x))\mu_1(x)dx$$



# Monge-Kantorovich distance

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$$d_{MK}(\mu_1, \mu_2) := \min_T \int_\Omega c(x, T(x))\mu_1(x)dx$$

- **Kantorovich :**

$$d_{MK}(\mu_1, \mu_2) := \min_\mu \int_\Omega c(x,y)\mu(x,y)dxdy$$

$$\int_\Omega \mu(x,y)dy = \mu_1(x), \qquad \int_\Omega \mu(x,y)dx = \mu_2(y)$$

- Monge is equivalent to choose $\mu(x,y) = \mu_1(x)\delta(y = T(x))$.

# Monge-Kantorovich distance

- **Monge :** $T : \Omega \to \Omega, \qquad T_{\#}\mu_1 = \mu_2$

$$d_{MK}(\mu_1, \mu_2) := \min_T \int_\Omega c(x, T(x))\mu_1(x)dx$$

- **Kantorovich :** $d_{MK}(\mu_1, \mu_2) := \min_\mu \int_\Omega c(x, y)\mu(x, y)dxdy$

$$\int_\Omega \mu(x, y)dy = \mu_1(x), \qquad \int_\Omega \mu(x, y)dx = \mu_2(y)$$

- **Brenier :** For $\Omega = \mathbb{R}^d$, $c(x, y) = |x - y|^2$, $\mu_i$ 'smooth', $T$ is optimal if and only if

$$T(x) = \nabla\Phi(x) \qquad \text{with} \qquad \Phi : \mathbb{R}^d \to \mathbb{R} \ \text{ convex}$$

$$\det\, D^2\Phi(x) = \frac{\mu_1(x)}{\mu_2(T(x))} \qquad \text{Monge-Ampere eq.}$$

(Evans-Gangbo, Cafarelli-Feldman-McCann, Trudinger-Wang, Ambrosio)

## And PDEs ?

• **Otto :** Formal Riemanian metric.

**Theorem** The porous media equation

$$\frac{\partial n}{\partial t} - \Delta A(n) = 0$$

is non-expansive for the quadractic cost.

Proof uses the Monge-Ampere equation (see also Bolley-Carrillo)

No proof known by 'coupling'

• **Tanaka :** Homogeneous Boltzmann (new proof by 'coupling', Rousset, Fournier-BP)

# Coupling method : Fourier eq.

$$\partial_t n - \Delta n = 0, \qquad x \in \mathbb{R}^d,\ t \geq 0$$

**Theorem :** For costs $c(x-y)$, we have

$$d_{MK}(n_1(t), n_2(t)) \leq d_{MK}(n_1^0, n_2^0)$$

**Proof :** Consider $v$ solution of

$$\frac{\partial v}{\partial t} - \Delta_x v - \Delta_y v - 2\nabla_x \cdot \nabla_y v = 0, \quad x, y \in \mathbb{R}^d,\ t \geq 0$$

with a compatible initial data

$$\int v^0(x,y)dy = n_1^0(x) \qquad \int v^0(x,y)dx = n_2^0(y)$$

**Step 1.** $v \geq 0$ because $\begin{pmatrix} I & -I \\ -I & I \end{pmatrix}$ is nonnegative

# Coupling method : Fourier eq.

$$\partial_t n - \Delta n = 0, \qquad x \in \mathbb{R}^d, \; t \geq 0$$

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$$\int v^0(x,y)dy = n_1^0(x) \qquad \int v^0(x,y)dx = n_2^0(y)$$

**Step 2.** Marginals are correct. Integrate in $y$ :

$$\frac{\partial v_1(x,t)}{\partial t} - \Delta_x v_1 = 0$$

# Coupling method : Fourier eq.

$$\partial_t n - \Delta n = 0, \qquad x \in \mathbb{R}^d, \; t \geq 0$$

**Theorem :** For costs $c(x-y)$, we have

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**Proof :** Consider $v$ solution of

$$\frac{\partial v}{\partial t} - \Delta_x v - \Delta_y v - 2\nabla_x \cdot \nabla_y v = 0, \quad x, y \in \mathbb{R}^d, \; t \geq 0$$

**Step 3.** The distance diminishes

$$\frac{d}{dt} \int c(x-y) v(x,y,t) dxdy =$$
$$\int v(x,y,t) \Big( \Delta_x c(x-y) + \Delta_y c(x-y) + 2\nabla_x \nabla_y c(x-y|) \Big) dxdy$$
$$= \int v(x,y,t) \Big( \Delta_{x+y} c(x-y) \Big) dxdy = 0$$

# Coupling method : Fourier eq.

$$\partial_t n - \Delta n = 0, \qquad x \in \mathbb{R}^d,\ t \geq 0$$

**Theorem :** For costs $c(x-y)$, we have

$$d_{MK}(n_1(t), n_2(t)) \leq d_{MK}(n_1^0, n_2^0)$$

**Step 4. Conclusion.** For all initial coupling $v^0$

$$d_{MK}(n_1(t), n_2(t)) \leq \int c(x-y)v(x,y,t)dxdy$$

$$\leq \int c(x-y)v^0(x,y)dxdy$$

$$\approx d_{MK}(n_1^0, n_2^0)$$

**Challenge :** $\partial_t n - \Delta(A(x)n) = 0$

# Structured equation

**Theorem.** (N. Fournier, BP)
The Renewal and Growth-Fragmentation equations (and many others) are non-expansive for the cost type[(1)]

$c(x-y) = \min(|x-y|, a)$, $a$ related to Lipschitz bounds on coef.

**History.**

Fournier and Locherbach (neuron networks)

Chafai, Malrieu, Paroux, Guillin, Zitt... (TCP connections)

Dobrushin, Vlasov equations. Functional anal. and its Appl. (1979)

# Structured equation

Renewal equation as an example.

$$\begin{cases} \frac{\partial n(x,t)}{\partial t} + \frac{\partial[g(x)n]}{\partial x} + d(x)n = b(x)N(t), \qquad t \geq 0,\ x \geq 0, \\ n(x=0,t) = 0, \qquad N(t) = \int_0^\infty d(x)n(x,t)dx. \end{cases}$$

$$g' \leq 0, \qquad g(0) \geq 0, \qquad \int_0^\infty b = 1$$

$$0 < a < 1 \qquad \text{and} \qquad a = \inf_{|x-y|<1} \frac{|x-y| \max(d(x), d(y))}{|d(x) - d(y)|}$$

Example : $d(x) = \alpha + \beta x^p,\ p \geq 1.$

$$c(x-y) = \min(|x-y|, a)$$

$$d_{MK}(n_1(t), n_2(t)) \leq d_{MK}(n_1^0, n_2^0)$$

# Structured equation

$$
\begin{aligned}
&\frac{\partial v}{\partial t} + \frac{\partial g(x) v}{\partial x} + \frac{\partial g(y) v}{\partial y} + \max(d(x), d(y)) v \\
&\quad = b(x)\delta(x-y) \int \min(d(x'), d(y'))\, v(dx', dy', t) \\
&\quad + b(x) \int \big(d(x') - d(y)\big)_+ \, v(dx', y, t) \\
&\quad + b(y) \int \big(d(y') - d(x)\big)_+ \, v(x, dy', t).
\end{aligned}
$$

with an initial data $v^0$ whose marginals are $n_1^0$ and $n_2^0$.

$$
\begin{aligned}
c(x,y) \geq &\int c(z,y) b(z) dz \frac{\big(d(x) - d(y)\big)_+}{\max(d(x), d(y))} \\
&+ \int c(x,z) b(z) dz \frac{\big(d(y) - d(x)\big)_+}{\max(d(x), d(y))}
\end{aligned}
$$

# Thank you

Entropy, Poincaré and Doeblin :

Perthame, B., Ryzhyk, L. Exponential decay for the fragmentation or cell-division equation. J. Diff. Eq. (2005)

Michel, P. ; Mischler, S., Perthame, B. General relative entropy inequality : an illustration on growth models. J. Math. Pures et Appl. (2005)

Recent theory : Laurençot, Doumic, Gabriel, Mischler, Canizo, Yoldas, Cloez, Monmarche and coll.

Monge-Kantorovich :

Fournier, N., Perthame, B. Transport distances for PDEs : the coupling method, EMS Surveys in Math. Sc. (2021)

Fournier, N., Perthame, B. Monge-Kantorovich distance and structured equations. SIMA. In press

**THANK YOU**