Colloquium du CERMICS

École des Ponts
ParisTech

Stuctured equations in Biology

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Structured equations
in biology

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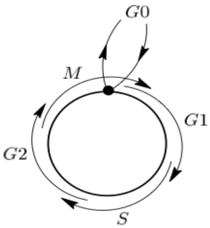


Organisation of the talk

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

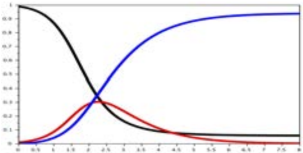
Examples of stuctured equations

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)

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

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

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

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

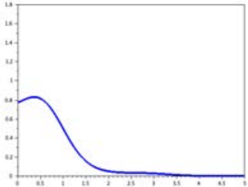
$$
\begin{cases}
\frac{\partial}{\partial t} n(t,x) + \frac{\partial}{\partial x} n(t,x) + d(x) n(t,x) = 0, \quad t \geq 0,\ x \geq 0 \\
N(t) := n(t, x=0) = \int_0^\infty b(y) n(t,y) dy \\
n(t=0,x) = n^0(x)
\end{cases}
$$

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

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

The renewal equation

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



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
- $u^0 \le C^0 \Longrightarrow u(t,x) \le C^0$
- $\frac{d}{dt} \ln n(t,x) \le \max_x \frac{d}{dt} \ln n^0(x)$
- Explains Kermack-McKendrick $H(u) = u - \ln u$.

Generalized relative entropy

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

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

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

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

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

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

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

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

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)

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4. Monge-Kantorovich distance

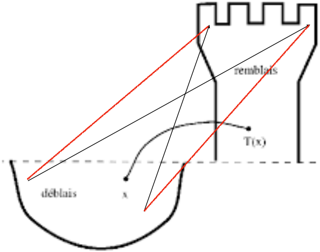
Monge-Kantorovich distance

- Ω open subset of $\mathbb{R}^d$
- Cost function $c(x,y) \geq 0$, $x \in \Omega$, $y \in \Omega$
- μ_1, μ_2 probability measures on Ω

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

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

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



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• **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 $\Omega = \mathbb{R}^d$, $c(x,y) = |x-y|^2$, μ_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)

Coupling method ?

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.

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

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

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

Step 3. The distance diminishes

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

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

$$\frac{\partial v}{\partial t} + \frac{\partial g(x)v}{\partial x} + \frac{\partial g(y)v}{\partial y} + \max(d(x), d(y))v$$
$$= b(x)\delta(x-y)\int \min(d(x'), d(y'))\, v(dx', dy', t)$$
$$+ b(x)\int \left(d(x') - d(y)\right)_+ v(dx', y, t)$$
$$+ b(y)\int \left(d(y') - d(x)\right)_+ v(x, dy', t).$$

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

$$c(x,y) \geq \int c(z,y)b(z)dz \frac{\left(d(x) - d(y)\right)_+}{\max(d(x), d(y))}$$
$$+ \int c(x,z)b(z)dz \frac{\left(d(y) - d(x)\right)_+}{\max(d(x), d(y))}$$

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