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Piecewise deterministic Markov processes in biological models

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Outline:

1. Piecewise deterministic Markov processes (PDMPs) and their examples.
2. Gene expression model.
3. Stochastic semigroups.
4. Asymptotic behaviour.
5. Comments.

References:

1. M. Tyran-Kamińska and R.R., in Semigroup of Operators Theory and Applications, Springer Proceedings in Mathematics & Statistics 113. (2015)

2. A. Bobrowski, T. Lipniacki, K. Pichór, and RR; J. Math. Anal. Appl. 333 (2007), 753-769.

3. K. Pichór R.R., (submitted 2015)

Davis (1984): "PDMPs is a general family of stochastic models covering virtually all non-difussion applications."

A continuous time Markov process $X(t)$ is a PDMP if there is an increasing sequence of random times (t_n), called jumps, such that sample paths of $X(t)$ are defined in a deterministic way in each interval (t_n, t_{n+1}).

Two types of jumps: the process can jump to a new point or can change the dynamics which defines its trajectories.

Examples:

1. Pure jump-type and velocity jump processes: Markov chains, kangaroo movement, phenotype-structured IBMs, dispersal of cells and insects, stochastic billiards.
2. Semiflows with jumps: cell cycle models.
3. Processes with switching dynamics: stochastic gene expression, neural activity (Stein).
4. Individual-based models (agent-based m.): structured population models, coagulation-fragmentation process.

Semiflows with jumps

Let π_t be a semiflow on E. The semiflow π_t describes the movement of a point between jumps, i.e. if x is the position of the point at time t, then $\pi_\tau x$ is its position at time $t+\tau$.
The point located at x can jump with an intensity $\lambda(x)$ to a point y. The location of y is described by a transition function $P(x,A)$, i.e., $P(x,A)$ is the probability that $y \in A$.
After the jump it continues movement according to the same principle.

Size-structured model of a cellular population.

The cell size (mass, volume) $x > 0$ grows with rate $g(x)$, i.e. $x' = g(x)$.
It splits with intensity $\varphi(x)$ into two daughter cells with size $x/2$, i.e., $P(x, A) = 1$ if $x/2 \in A$ and $P(x, A) = 0$ otherwise. After division we consider the size of a daughter cell, etc., and obtain a process $X(t)$, $t > 0$ which describes the size of consecutive descendants of a single cell. The process $X(t)$, $t > 0$ is a PDMP.

Processes with switching dynamics

A family of semiflows π_t^i, $i \in I = \{1, \dots, k\}$ on a topological space E.

The state of the system is a pair $(x, i) \in E \times I$.

If the system is at state (x, i) then x can move according to the semiflow π_t^i and after time t reaches the state $(\pi_t^i(x), i)$

or jump to the state (x, j) with a bounded and continuous intensity $q_{ji}(x)$.

The pair $(x(t), i(t))$ constitutes a Markov process $X(t)$ on $E \times I$.

Examples: gene regulatory systems.

Gene expression model

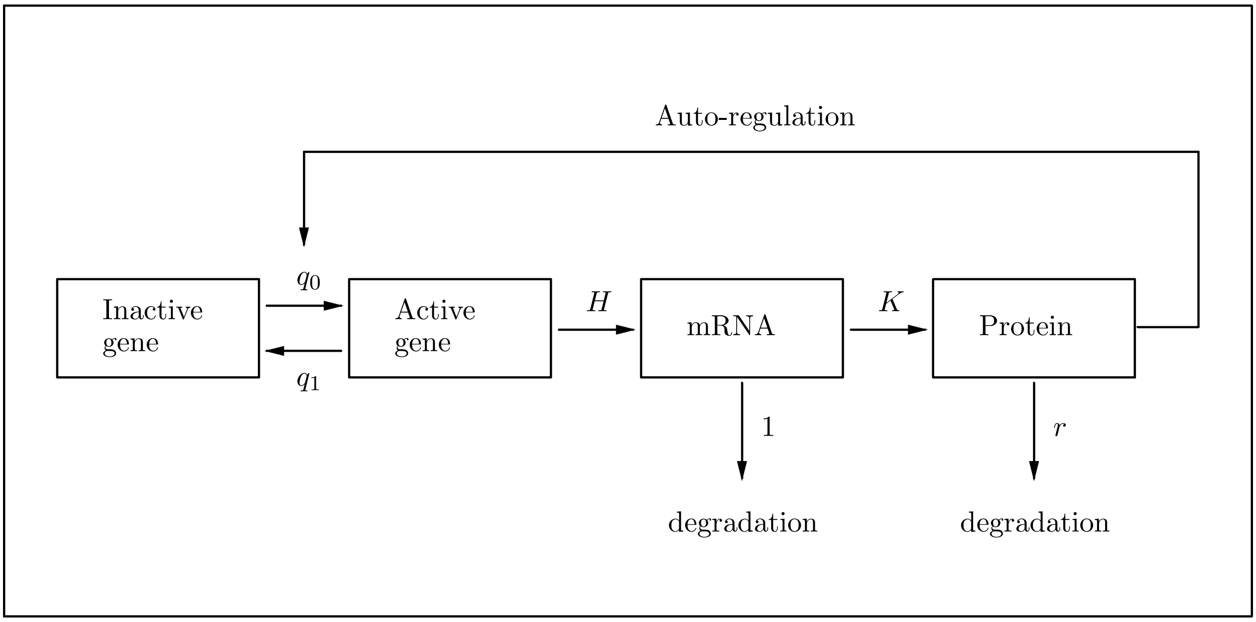


Fig. 1. Simplified diagram of auto-regulated gene expression.

x_1 the number of mRNA molecules,
x_2 the number of protein molecules,

$$I \xrightarrow{q_0(x_1,x_2)} A, \quad I \xleftarrow{q_1(x_1,x_2)} A,$$

$$A \xrightarrow{H\gamma(t)} \text{mRNA} \xrightarrow{1} \phi,$$

$$\text{mRNA} \xrightarrow{Kx_1(t)} \text{protein} \xrightarrow{r} \phi.$$

$$\frac{dx_1}{dt} = H\gamma(t) - x_1, \quad \frac{dx_2}{dt} = Kx_1 - rx_2,$$

$H = 1$, $K = r$.

Process

$$\xi(t) = (x_1(t), x_2(t), \gamma(t)),\ t \geq 0.$$

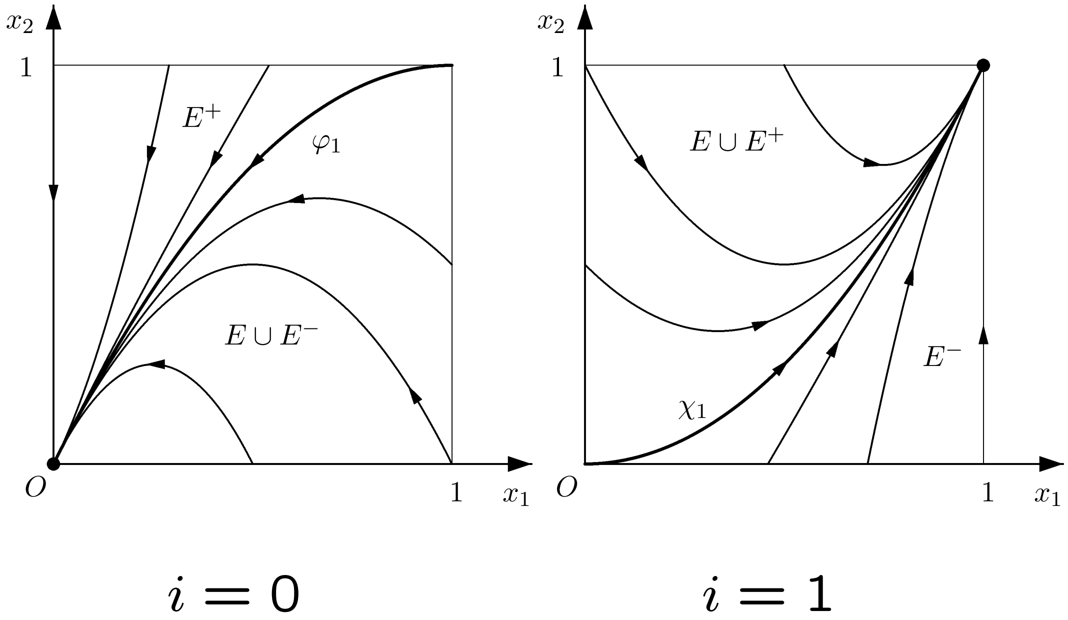
Partial density functions $f_i(x_1, x_2, t)$:

$$\mathrm{Pr}(\xi_t \in B \times \{i\}) = \iint_B f_i(x_1, x_2, t)\, \mathrm{d}x_1\, \mathrm{d}x_2,$$

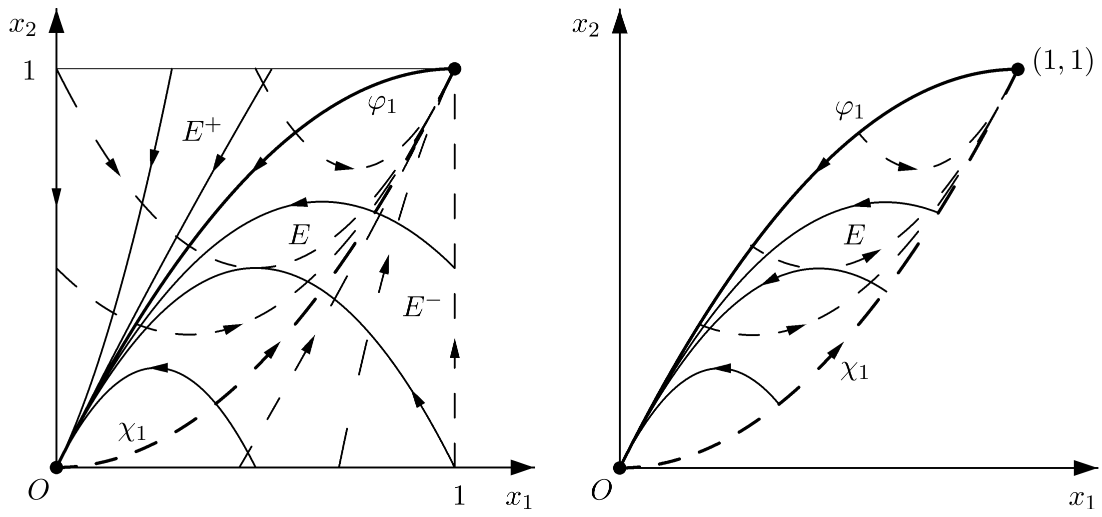
where B is a Borel subset of $\mathbb{R}_+ \times \mathbb{R}_+$,
$i = 0, 1$.

The state-space

$$\mathsf{E} = \mathbb{R}_+^2 \times \{0, 1\}, \quad \mathcal{S} = [0, 1] \times [0, 1] \times \{0, 1\}.$$



x_2
1
E^+
φ_1
$E \cup E^-$
O
1
x_1
x_2
1
$E \cup E^+$
E^-
χ_1
O
1
x_1
$i = 0$
$i = 1$


x_2
1
E^+
φ_1
E
E^-
χ_1
O
1
x_1
x_2
$(1,1)$
φ_1
E
χ_1
O
x_1

Fokker-Planck system of PDEs

(evolution equation on $L^1(\mathcal{S})$)

Let $\mathbf{x} = (x_1, x_2, i)$ and $u(\mathbf{x}, t) = u_i(x_1, x_2, t)$ be the density of ξ_t. Then

$$u'(t) = \mathcal{A}u = \mathcal{A}_0 u + \mathcal{K}u,$$

$$\begin{aligned}
\mathcal{A}_0 f(x_1, x_2, 0) &= \frac{\partial(x_1 f_0)}{\partial x_1} - r\frac{\partial((x_1 - x_2) f_0)}{\partial x_2} \\
\mathcal{A}_0 f(x_1, x_2, 1) &= -\frac{\partial((1 - x_1) f_1)}{\partial x_1} - r\frac{\partial((x_1 - x_2) f_1)}{\partial x_2}, \\
\mathcal{K} f(x_1, x_2, i) &= q_{1-i} f_{1-i} - q_i f_i.
\end{aligned}$$

Stochastic semigroups

(X, Σ, m) — σ-finite measure space.
$D = \{f \in L^1 : \ f \geq 0, \ \|f\| = 1\}$ – densities.
Markov (stochastic) operator:
$P : L^1 \to L^1$ linear, $P(D) \subset D$.
A linear, positive contraction $P : L^1 \to L^1$ is called *substochastic operator.*
Stochastic semigroup: $\{P(t)\}_{t \geq 0}$,
$P(t)$ - Markov operators,
$P(0) = Id$, $P(t+s) = P(t)P(s)$, $s, t \geq 0$,
(c) for each $f \in L^1$, the function $t \mapsto P(t)f$ is continuous.

If u is the solution of the F-P system with $u(\mathbf{x}, 0) = f(\mathbf{x})$ and $P(t)f(\mathbf{x}) = u(\mathbf{x}, t)$, then $\{P(t)\}_{t\geq 0}$ is a stochastic semigroup.

Asymptotic stability

f_* – *invariant* if $P(t)f_* = f_*$ for $t \geq 0$.

$\{P(t)\}$ – *asymptotically stable* if there is an invariant density f_* such that

$$\lim_{t\to\infty} \|P(t)f - f_*\| = 0 \quad \text{for} \quad f \in D.$$

Sweeping

$\{P(t)\}$ – *sweeping* with respect to a family of sets $\mathcal{F}$ if for $B \in \mathcal{F}$ and for $f \in D$

$$\lim_{t\to\infty} \int_B P(t)f(x)\, m(dx) = 0.$$

$\{P(t)\}$ – partially integral if there exist $t > 0$, $q(x,y) \geq 0$

$$\int_X \int_X q(x,y)\, m(dx)m(dy) > 0$$

$$P(t)f(x) \geq \int q(x,y)f(y)\, m(dy) \quad \text{for} \quad f \in D.$$

Theorem 1 *If a partially integral stochastic semigroup $\{P(t)\}_{t\geq 0}$ has a unique invariant density f_* and $f_* > 0$ then it is asymptotically stable.*

Let $\{P(t)\}_{t\geq 0}$ be a substochastic semigroup with the kernel part q. We say that it ha property (K) if :

for every $y_0 \in X$ there exist $\varepsilon > 0$, $t > 0$, and a measurable function $\eta \geq 0$ such that $\int \eta \, dm > 0$ and

$$q(t, x, y) \geq \eta(x)$$

for $x \in X$ and $y \in B(y_0, \varepsilon)$, where $B(y_0, \varepsilon)$ is the open ball with center y_0 and radius ε.

Theorem 2 *Let* $\{P(t)\}_{t\geq 0}$ *be a substochastic semigroup on* $L^1(X)$*, where* X *is a separable metric space. If (K) holds then:*
there are a countable (possible empty) set I*, continuous positive functionals* α_i*,* $i \in I$*, and invariant densities* f_i^**,* $i \in I$*, with pairwise disjoint supports* A_i*,* $i \in I$*, such that for every density* f*, every compact set* F*, and* $i \in I$

$$\lim_{t\to\infty} \|\mathbf{1}_{A_i} P(t)f - \alpha_i(f) f_i^*\| = 0$$

and

$$\lim_{t\to\infty} \int_{F\cap Y} P(t)f(x)\, m(dx) = 0,\ Y = X \setminus \bigcup_{i\in I} A_i.$$

Corollary 1 *(a)* $\{P(t)\}_{t\geq 0}$ *satisfies (K),*
(b) $\{P(t)\}_{t\geq 0}$ *has no invariant density.*
Then $\{P(t)\}_{t\geq 0}$ *is sweeping with respect to compact sets.*

Corollary 2 X *– a compact metric space,*
$\{P(t)\}_{t\geq 0}$ *– a substochastic semigroup,*
$\{P(t)\}_{t\geq 0}$ *satisfies (K),*
$\int_0^\infty P(t)f\,dt > 0$ *a.e. for* $f \in D$.
Then it is asymptotically stable.

Theorem 3 *Suppose that the functions* q_0 *and* q_1 *are strictly positive in* E*. Then,* $\{P(t)\}_{t\geq 0}$ *is asymptotically stable.*

The idea of the proof of Theorem 3

1. For every density $f \in L^1(\mathcal{S})$

$$\lim_{t\to\infty} \int_{\mathcal{E}} P(t)f(\mathbf{x})\, m(d\mathbf{x}) = 1.$$

2. $\mu := \max\{q_i(x_1, x_2)\}$, $\mathcal{Q} := \mu^{-1}(\mu I + \mathcal{K})$.

$\mathcal{A} = \mathcal{A}_0 + \mu\mathcal{Q} - \mu I$, $\quad \mathcal{Q}$ is a Markov operator.

By the perturbation theorem

$$P(t)f = e^{-\mu t}S(t)f + \mu \int_0^t e^{-\mu s} S(s)\mathcal{Q}P(t-s)f\, ds,$$

$\{S(t)\}_{t\ge 0}$ – a M. semigroup generated by $\mathcal{A}_0$.
Using this formula we check assum. of Cor. 2.

How to check (a)?

The system is governed by k flows π_t^i and each flow π_t^i is defined as the solution of a system of differential equations $x' = b^i(x)$ on $G \subset \mathbb{R}^d$. All transition intensities $q_{ij}(x)$ are continuous and positive functions.

$$\psi_{x,t}(\tau_1, \ldots, \tau_d) = \pi^{i_{d+1}}_{t-\tau_1-\tau_2-\cdots-\tau_d} \circ \pi^{i_d}_{\tau_d} \circ \cdots \circ \pi^{i_2}_{\tau_2} \circ \pi^{i_1}_{\tau_1}(x).$$

$$\det \left[\frac{d\psi_{y_0,t_0}(\tau^0)}{d\tau} \right] \neq 0. \qquad (1)$$

Then there exists a continuous nonnegative kernel s.t. $k(t, x_0, y_0) > 0$.

Let $a(x)$ and $b(x)$ be two vector fields on $\mathbb{R}^d$. The *Lie bracket* $[a, b]$ is a vector field given by

$$[a, b]_j(x) = \sum_{k=1}^{d} \left(a_k \frac{\partial b_j}{\partial x_k}(x) - b_k \frac{\partial a_j}{\partial x_k}(x) \right).$$

(**Hörmander condition**) If vectors

$$b^2(y_0) - b^1(y_0), \dots, b^k(y_0) - b^1(y_0),$$
$$[b^i, b^j](y_0)_{1 \le i,j \le k},\ [b^i, [b^j, b^l]](y_0)_{1 \le i,j,l \le k}, \cdots$$

span the space $\mathbb{R}^d$ then (1) holds.

Thank you!