

Asymptotic decomposition of stochastic semigroups and its applications

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Outline:

1. Stochastic semigroups.
2. Asymptotic decomposition and corollaries.
3. Piecewise deterministic Markov processes.
4. Applications to a gene expression model, to immunology, and to a kinetic equation.

References:

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Stochastic semigroups

(X, Σ, m) — σ -finite measure space.

$D = \{f \in L^1 : f \geq 0, \|f\| = 1\}$ — densities.

Stochastic operator (Markov operator):

$P: L^1 \rightarrow L^1$ linear, $P(D) \subset D$.

Stochastic semigroup : $\{P(t)\}_{t \geq 0}$,

$P(t)$ - stochastic 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.

Standard example - Fokker-Planck equation:

$(X_t)_{t \geq 0}$ diffusion process

f density of the distribution of X_0

$x \mapsto u(t, x)$ density of the distribution of X_t .

$$\frac{\partial u}{\partial t} = - \sum_{i=1}^n \frac{\partial (b^i(x)u)}{\partial x^i} + \frac{1}{2} \sum_{i,j=1}^n \frac{\partial^2 (a^{ij}(x)u)}{\partial x^i \partial x^j}.$$

$P(t)f(x) = u(t, x)$ a stochastic semigroup on $L^1(\mathbb{R}^n)$.

Asymptotic stability

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

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

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

Sweeping (zero-type property)

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

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

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

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

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

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.*

X separable metric space, $\Sigma = \mathcal{B}(X)$,
 $\{P(t)\}_{t \geq 0}$ stochastic semigroup with the kernel
part $k(t, x, y)$,
(K) for every $x_0 \in X$ there exist $r > 0$, $t > 0$,
and a function $\eta \geq 0$ s.t. $\int \eta dm > 0$ and

$$k(t, x, y) \geq \eta(y) \mathbf{1}_{B(x_0, r)}(x).$$

Theorem 2 *If (K) holds then:
there are a countable (possibly 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 ,
such that for every density f and every com-
pact set F we have*

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

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

Remark. Theorem 2 has a version for stochastic operators, but we replace the condition

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

by asymptotic periodicity.

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Corollary 1 Assume (K) and that $\{P(t)\}_{t \geq 0}$ has no invariant density. Then $\{P(t)\}_{t \geq 0}$ is sweeping with respect to compact sets.

Corollary 2 Assume (K) , and $\int_0^\infty P(t)f dt > 0$ a.e. for $f \in D$. Then $\{P(t)\}_{t \geq 0}$ is asymptotically stable or sweeping from compact sets.

Corollary 3 Let X be a compact space. Assume (K) , and that $\int_0^\infty P(t)f dt > 0$ a.e. for $f \in D$. Then $\{P(t)\}_{t \geq 0}$ is asymptotically stable.

Corollary 4 *If (K) holds and there exists a point x_0 such that for each $\varepsilon > 0$ and each density f we have*

$$\int_{B(x_0, \varepsilon)} P(t)f \, dt > 0 \quad \text{for some } t \geq 0. \quad (1)$$

Then there is at most one invariant density for this semigroup.

In particular, if X is compact then the stochastic semigroup is asymptotically stable.

SPRINGER BRIEFS IN APPLIED SCIENCES AND
TECHNOLOGY · MATHEMATICAL METHODS

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Piecewise Deterministic Processes in Biological Models

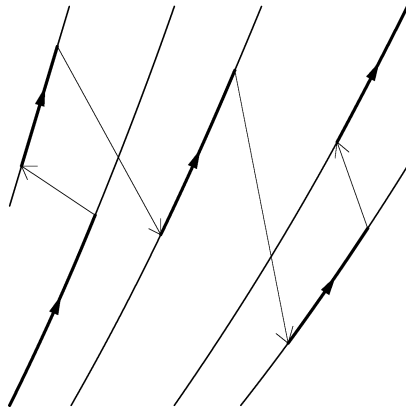
 Springer

Piecewise deterministic Markov processes

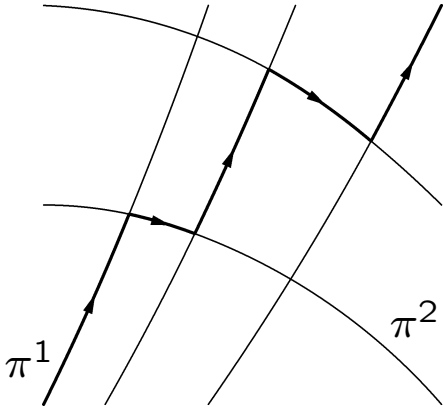
Davis (1984): "PDMPs is a general family of stochastic models covering virtually all non-diffusion applications."

A continuous time (homogeneous) 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.



Dynamical system with random jumps



Process with switching dynamics

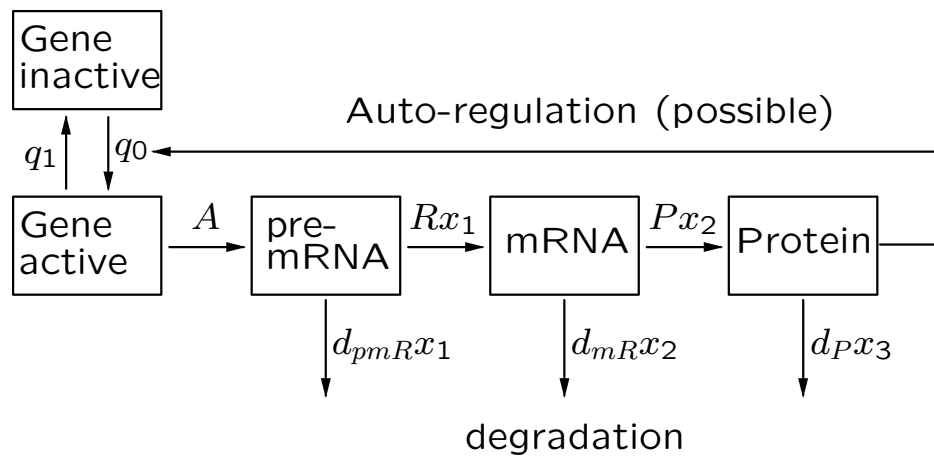


Examples:

1. Pure jump processes: Markov chains, kangaroo movement.
2. Velocity jump processes: dispersal of cells and insects, stochastic billiards.
3. Semiflows with jumps: cell cycle models, immune systems.
4. Processes with switching dynamics: stochastic gene expression.
5. Mixture of 3 and 4: neural activity model, production of subtilin.
6. Individual-based models (agent-based m.): structured population models, coagulation-fragmentation process.

Gene expression model





x_1, x_2, x_3 — the number of pre-mRNA, mRNA, protein molecules,

d_{pmR}, d_{mR}, d_P — degradation coefficients,
 A, Rx_1, Px_2 - velocities of transcription; conversion of pre-mRNA to mRNA; translation.

$$\begin{cases} x'_1 = A\gamma(t) - (d_{pmR} + R)x_1 \\ x'_2 = Rx_1 - d_{mR}x_2 \\ x'_3 = Px_2 - d_Px_3, \end{cases} \quad (2)$$

where $\gamma(t) = 1$ if a gene is active or
 $\gamma(t) = 0$ if it is inactive.

We assume that the gene is activated with rate $q_0(\mathbf{x})$ and inactivated with rate $q_1(\mathbf{x})$.

$$x'_1 = \gamma(t) - x_1; \quad x'_2 = \alpha(x_1 - x_2); \quad x'_3 = \beta(x_2 - x_3)$$

Processes with switching dynamics (PSD)

Markov process

$(x_1(t), x_2(t), x_3(t))$ is **not** a Markov process.

$$\xi_t = (x_1(t), x_2(t), x_3(t), \gamma(t)), t \geq 0.$$

The state-space

$$E = \mathbb{R}_+^3 \times \{0, 1\}.$$

Partial density functions $f_i(x_1, x_2, x_3, t)$:

$$\Pr(\xi_t \in B \times \{i\}) = \iint_B f_i(x_1, x_2, x_3, t) dx_1 dx_2 dx_3,$$

where B is a Borel subset of \mathbb{R}_+^3 , $i = 0, 1$.

f – density of $\xi(0)$, $P(t)f$ – density of ξ_t .

$$x'(t) = b_i(x(t)), \quad (3)$$

$i = 1, \dots, N$ and at point $x \in G \subset \mathbb{R}^d$ it can jump from j to i state with intensity $q_{ij}(x)$. $\xi_t = (x(t), i(t))$, $t \geq 0$, is a PDMP.

$$\text{prob}(\xi_t \in E \times \{i\}) = \int_E u(x, i, t) dx.$$

$$A_i f = - \sum_{k=1}^d \frac{\partial (b_i^k(x, i) f)}{\partial x_k}.$$

$$\frac{\partial u}{\partial t} = Mu + Au$$

where $Au = (A_1 u_1, \dots, A_N u_N)$, $u_i(x, t) = u(x, i, t)$
 $M = [m_{ij}(x)]$, $m_{ij}(x) = q_{ij}(x)$ for $i \neq j$
and $m_{ii}(x) = - \sum_{k \neq i} q_{ki}(x)$.

Applications to PSD – how to check (K)?

The system is governed by k flows π_t^i and each flow π_t^i is the solution of a differential equation $x' = b^i(x)$ on $G \subset \mathbb{R}^d$. All transition intensities $q_{ij}(x)$ are continuous and positive in a neighbourhood of y_0 .

(Hörmander condition) If vectors

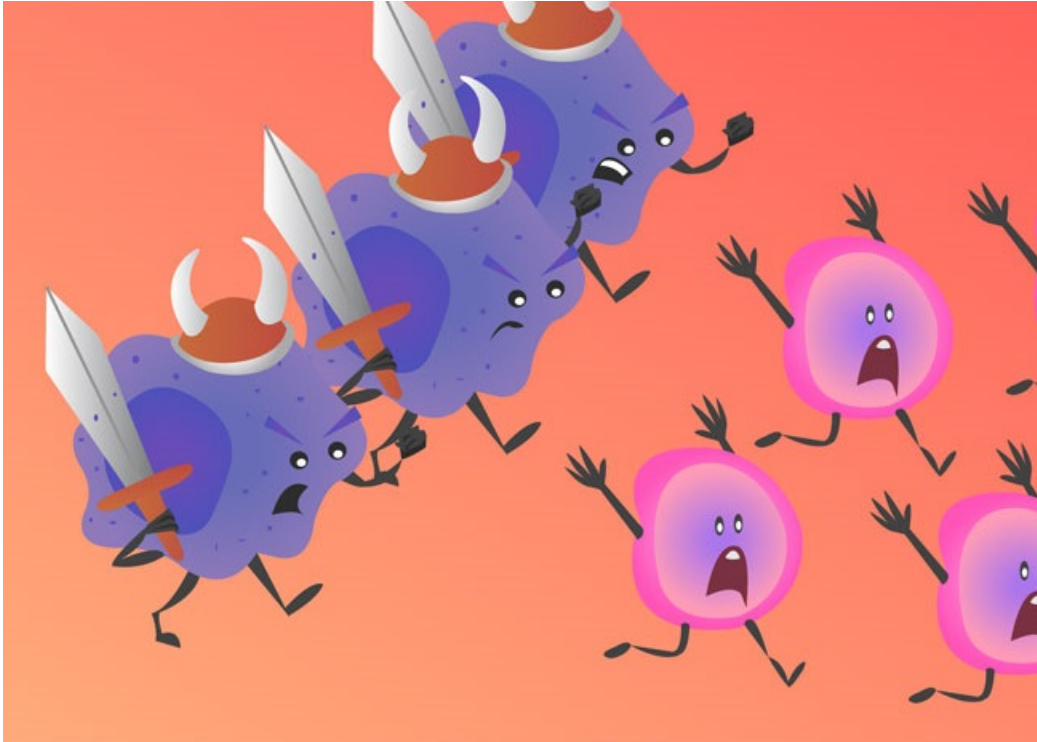
$$b^2(y_0) - b^1(y_0), \dots, b^k(y_0) - b^1(y_0), \\ [b^i, b^j](y_0)_{1 \leq i, j \leq k}, [b^i, [b^j, b^l]](y_0)_{1 \leq i, j, l \leq k}, \dots$$

span the space \mathbb{R}^d then (K) holds for any point x which is connected with y_0 .

Assume that G is a bounded set and there exist $x_0 \in G$ and $i_0 \in I$ such that starting from any state $(x, i) \in X$ we are able to go arbitrarily close to (x_0, i_0) by a cumulative flow and that the Hörmander's condition holds. Then the semigroup $\{P(t)\}_{t \geq 0}$ is asymptotically stable.

Corollary 5 *The semigroup generated by the gene expression model is asymptotically stable.*

Dynamics of antibody levels



The immune status x is the concentration of specific antibodies, which appear after infection with a pathogen and remain in serum, providing protection against future attacks of that same pathogen.

$x(t)$ is a stochastic process whose trajectories are decreasing functions $x(t)$ between subsequent infections:

$$x'(t) = g(x(t)), \quad g < 0, \quad (4)$$

If x is the concentration of antibodies at the moment of infection, then $Q(x) > x$ is the concentration of antibodies just after clearance of infection.

The moments of infections are independent of the state of the immune system and they are distributed according to a Poisson process $(N_t)_{t \geq 0}$ with rate $\Lambda > 0$.

$$\xi_{t_n} = Q(\xi_{t_n^-}), \quad \xi'_t = g(\xi_t) \text{ for } t \in [t_{n-1}, t_n),$$

The process $(\xi_t)_{t \geq 0}$ satisfies the stochastic differential equation

$$d\xi_t = g(\xi_t) dt + (Q(\xi_t) - \xi_t) dN_t.$$

If f is the density distribution of x before an infection then $P_Q f$ is the density distribution of x just after clearance of infection:

$$P_Q f(x) = \sum_{i \in I_x} f(\varphi_i(x)) |\varphi_i'(x)|, \quad (5)$$

where φ_i are the right-inverse functions of $Q|_{(a_i, b_i)}$.

$$P_Q^* f(x) = f(Q(x)).$$

The density of ξ_t is given by $u(t)(x)$ and

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

$$\mathcal{A}f(x) = -\frac{d}{dx}(g(x)f(x)) + \Lambda P_Q f(x) - \Lambda f(x).$$

\mathcal{A} is a generator of a semigroup $\{U(t)\}_{t \geq 0}$.

Results:

Theorem 3 *The semigroup $\{U(t)\}_{t \geq 0}$ satisfies the Foguel alternative, i.e. it is asymptotically stable or for every $f \in L^1[0, \infty)$ and $M > 0$*

$$\lim_{t \rightarrow \infty} \int_0^M U(t)f(x) dx = 0.$$

The proof of (K) is based on the Dyson-Phillips expansion.

Asymptotic stability — if we have V such that:

$$\limsup_{x \rightarrow \infty} [g(x)V'(x) + \Lambda V(Q(x)) - \Lambda V(x)] < 0.$$

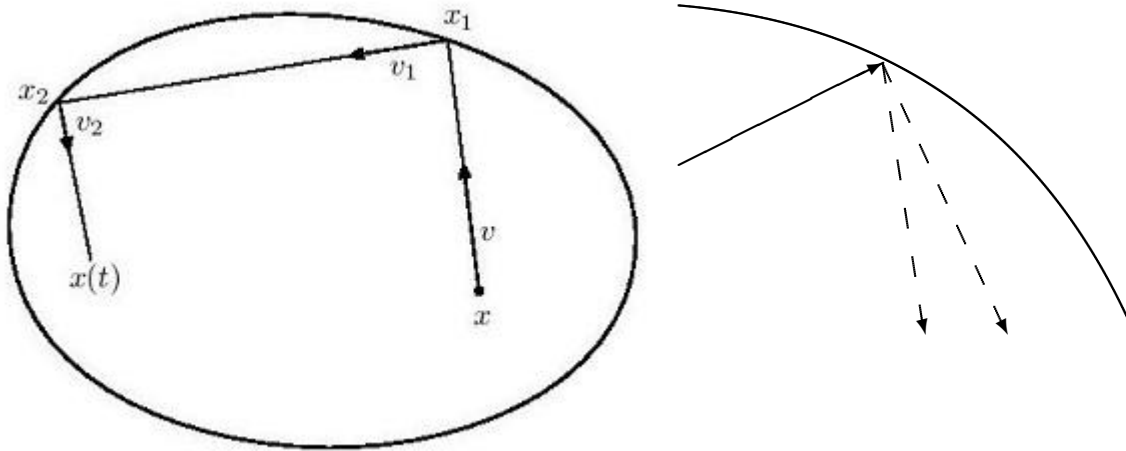
Example: if $\lim_{x \rightarrow \infty} g(x) = -\infty$ and $Q(x) \leq x + L$, then $V(x) = x$ is OK.

1) $a > \Lambda \log b$, $g(x) \leq -ax$ and $Q(x) \leq bx$ for a sufficiently large x , then $\{U(t)\}_{t \geq 0}$ is asymptotically stable.

2) If $a < \Lambda \log b$, $g(x) \geq -ax$ and $Q(x) \geq bx$ then the semigroup is sweeping from compact sets.

Sweeping can be interpreted as asymptotic permanent immunity of the population.

Collisionless kinetic equations



$$\partial_t u(t, x, v) + v \cdot \nabla_x u(t, x, v) = 0, \quad (x, v) \in \Omega \times V, \quad t \geq 0$$

$$\psi|_{\Gamma_-} = H(\psi|_{\Gamma_+}),$$

where

$$\Gamma_{\pm} = \{(x, v) \in \partial\Omega \times V; \pm v \cdot n(x) > 0\}$$

$n(x)$ – the outward unit normal at $x \in \partial\Omega$

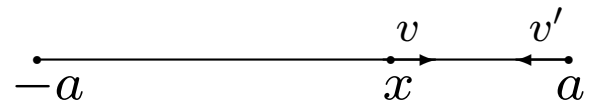
H is a linear boundary operator relating the outgoing and incoming fluxes.

$f(x, v) = u(0, x, v)$, $P(t)f(x, v) = u(t, x, v)$ stochastic semigroup on $L^1(\Omega \times V)$.

Main result: Sufficient conditions for asymptotic stability of $\{P(t)\}_{t \geq 0}$.

Steps of the proof: Existence of invariant density, checking the semigroup is partially integral and irreducible.

One dimensional stochastic billiard



Stochastic process $\xi(t) = (x(t), v(t))$ with values in $X = [-a, a] \times ([-1, 0) \cup (0, 1])$.

$$\frac{\partial u}{\partial t}(t, x, v) + v \frac{\partial f}{\partial x}(t, x, v) = 0$$

f -invariant density $\Rightarrow f$ is a function of v and satisfies some integral equation.

Special case: velocity after hitting a boundary point is uniformly distributed.

Then the semigroup is sweeping from compact sets and, consequently, the distribution of velocity converges to δ_0 .

It is interesting that in this case

$$f(t, x, v) \sim \frac{c}{|v|} (\log t)^{-1} \quad \text{when } t \rightarrow \infty$$

for $|v| \geq \varepsilon$ i $x \in [-a, a]$, where c is some constant.

