

Asymptotic behavior of distributions of mRNA and protein levels in a model of stochastic gene expression

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Received 6 February 2006

Available online 4 January 2007

Submitted by H.A. Levine

Abstract

The paper is devoted to a stochastic process introduced in the recent paper by Lipniacki et al. [T. Lipniacki, P. Paszek, A. Marciniak-Czochra, A.R. Brasier, M. Kimmel, Transcriptional stochasticity in gene expression, J. Theor. Biol. 238 (2006) 348–367] in modelling gene expression in eukaryotes. Starting from the full generator of the process we show that its distributions satisfy a (Fokker–Planck-type) system of partial differential equations. Then, we construct a c_0 Markov semigroup in L^1 space corresponding to this system. The main result of the paper is asymptotic stability of the involved semigroup in the set of densities. © 2006 Elsevier Inc. All rights reserved.

Keywords: Piece-wise deterministic process; Stochastic gene expression; Semigroups of operators; Feller semigroups; Dual semigroups; Markov semigroups; Asymptotic stability

1. Introduction

Our article is devoted to mathematical aspects of the generalized stochastic process introduced in the recent model of gene expression by Lipniacki et al. [18]. First of all, we fill out some

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details needed for the construction of the process and show that it is an example of piece-wise deterministic processes of M.H.A. Davis [3,4]. Next, we construct a c_0 semigroup of Markov operators in the involved space $L^1(\mathcal{K} \times \{0, 1\})$ of absolutely integrable functions, related to the Fokker–Planck system of equations for the densities of the process; the system has the form:

$$\begin{aligned} \frac{\partial f_0}{\partial t} + \frac{\partial}{\partial x_1}(-x_1 f_0) + r \frac{\partial}{\partial x_2}((x_1 - x_2) f_0) &= q_1 f_1 - q_0 f_0, \\ \frac{\partial f_1}{\partial t} + \frac{\partial}{\partial x_1}((1 - x_1) f_1) + r \frac{\partial}{\partial x_2}((x_1 - x_2) f_1) &= q_0 f_0 - q_1 f_1, \end{aligned} \quad (1)$$

where $q_0 = q_0(x_1, x_2)$ and $q_1 = q_1(x_1, x_2)$ are given non-negative continuous functions defined on $[0, 1]^2$, $(x_1, x_2) \in [0, 1]^2$ and f_0, f_1 are real functions defined on $[0, \infty) \times [0, 1]^2$.

The most difficult part of the paper is to show asymptotic stability of the involved semigroup. The strategy of the proof is as follows. First we show that the transition function of the related stochastic process has a kernel (integral) part. Then we find a set E on which the density of the kernel part of the transition function is positive. Next we show that the set E is an “attractor.” Then we apply results concerning asymptotic behavior of partially integral Markov semigroups discussed in [21,24]. We show that the semigroup satisfies the “Foguel alternative,” i.e. it is either asymptotically stable or “sweeping.” Since the attractor E is a compact set, we obtain that the semigroup is asymptotically stable.

A similar technique was applied to study asymptotic behavior of a large class of transport equations. The paper [25] can be consulted for a survey of many results on this subject. A newer application of this method to a stochastic version of the Lotka–Volterra prey–predator model can be found in [26].

Other mathematical results concerning the involved model are presented in the companion paper [2].

2. The model of eukaryotic gene expression

2.1. The model

As reviewed recently in [13], stochasticity in gene expression arises from fluctuation in gene activity, mRNA transcription, or protein translation. Figure 1 illustrates the main steps in gene expression. Control of gene’s activity is mediated by proteins, called transcription factors, which may bind to the specific promoter regions and switch the gene *on* or *off*. When the gene is active mRNA transcription takes place. Next, mRNA is exported to the cytoplasm, where serves as a template for the protein translation.

Let us consider regulation of a single gene, having N homologous copies (alleles). The model introduced in [18] involves three classes of processes: allele activation/inactivation, mRNA transcription/decay, and protein translation/decay process (Fig. 1). It is assumed that, due to binding or dissociation of protein molecules, each of gene’s alleles may be transformed, independently of the remaining ones, into an active state (denoted by A) or into an inactive state (denoted by I), with intensities $q_0(x_2)$ and $q_1(x_2)$, respectively, where x_2 is the number of protein molecules. In the case of self repressing gene (switched off by its own product) it is natural to assume $q_0(x_2) = b_1 x_2 + b_2 x_2^2$ and $q_1(x_2) = c_0$, where b_1, b_2 and c_0 are constants. The linear and quadratic terms in this relation represent gene activation due to binding of protein monomers and protein dimers, respectively, while the constant c_0 corresponds to dissociation of regulatory

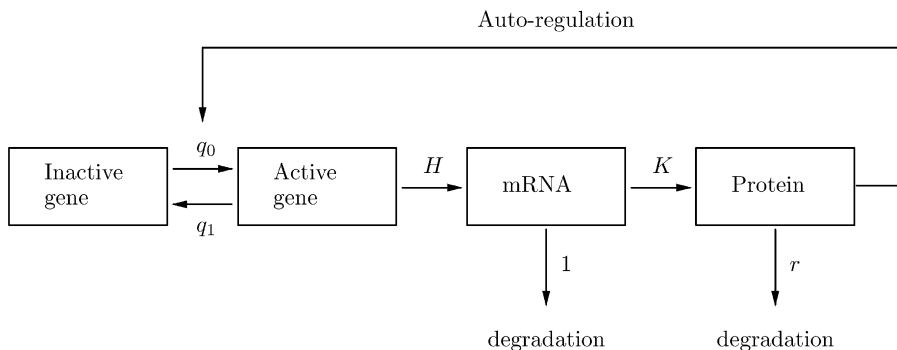


Fig. 1. Simplified diagram of auto-regulated gene expression.

proteins resulting in switching the gene on. In the case of self activating gene the activation intensity $q_1(x_2)$ should depend on the amount of the protein monomers or protein dimers, while the inactivation intensity may be assumed constant, since now inactivation is due to dissociation of regulatory protein. Furthermore, we assume that mRNA transcript molecules are synthesized at the rate $H\gamma(t)$, where H is a constant, $\gamma(t) = \sum_i g_i(t) \in \{0, 1, \dots, N\}$ and each g_i is a binary variable describing the state of the i th allele: $g_i(A) = 1$ and $g_i(I) = 0$. The protein translation proceeds with the rate $Kx_1(t)$, where K is a constant and $x_1(t)$ is the number of mRNA molecules. In addition, mRNA and protein molecules undergo the process of degradation. We chose the time scale so that the mRNA degradation rate is 1. Then, the reactions described above may be summarized as follows:



and



where r is the protein degradation rate and ϕ stands for degradation of gene products; it is described by the triple $(x_1(t), x_2(t), \gamma(t))$ of random variables with natural values.

Processes similar to (2)–(4) have been intensively studied and simulated with help of Gillespie [9] algorithm. This is an exact numerical algorithm. However, it becomes very inefficient when number of molecules is large. In such a case, when the mRNA and protein synthesis rates (H and K) are large, the system (3)–(4) may be approximated by deterministic reaction-rate equations. To be more specific, we obtain:



$$\frac{dx_1}{dt} = \gamma(t) - x_1, \quad (6)$$

$$\frac{dx_2}{dt} = r(x_1 - x_2). \quad (7)$$

It should be noted here that in the above system non-dimensional units are used and that x_1 and x_2 are not integers anymore; rather $x_1, x_2 \in \mathbb{R}^+$. This approximation is much more computationally efficient than the Gillespie algorithm. We discuss accuracy of the algorithm in [17] and implement it to the analysis of regulatory network governing early immune response. Since

$\gamma(t) \in \{0, 1, \dots, N\}$ is a discrete random variable, Eqs. (6)–(7) generate stochastic trajectories, which can be described as piece-wise deterministic, time-continuous Markov process

$$p(t) = (x_1(t), x_2(t), \gamma(t)) = (x(t), \gamma(t)), \quad t \geq 0. \quad (8)$$

Introducing “partial” density functions of this process, $f_i(x_1, x_2, t)$,

$$\Pr[x(t) \in \mathcal{Y}, \gamma(t) = i] = \iint_{\mathcal{Y}} f_i(x_1, x_2, t) dx_1 dx_2, \quad i = 0, 1, \dots, N,$$

where \mathcal{Y} is a Borel subset of $\mathbb{R}^+ \times \mathbb{R}^+$, we are led (see [18]) to the following Fokker–Planck system of PDEs:

$$\frac{\partial f_i}{\partial t} + \frac{\partial}{\partial x_1}[(i - x_1)f_i] + r \frac{\partial}{\partial x_2}[(x_1 - x_2)f_i] = T_{i-1,i} + T_{i+1,i} - T_{i,i-1} - T_{i,i+1},$$

$i = 0, \dots, N$, where

$$T_{i,i+1} = (N - i)q_0 f_i, \quad T_{i+1,i} = (i + 1)q_1 f_{i+1}, \quad i = -1, 0, \dots, N,$$

with $f_{-1} = f_{N+1} = 0$. For $N = 1$, this system reduces to (1), except that in (1) we allow jump intensities q_0 and q_1 to depend on x_1 as well.

In [18], in the case of self repressing gene, i.e. a gene switched off by its own product (protein), we find the steady state solution of the system (1) numerically. Moreover, we observe that, numerically, solutions of (1) converge to this steady state solution. In the present paper we prove correctness of heuristic considerations and numerical results contained in [18] by showing asymptotic stability of the semigroup induced by (1) in the space $L^1([0, 1]^2 \times \{0, 1\})$ —see Section 2.5 for more information.

2.2. Two systems of ODEs

For fixed $i \in \{0, 1\}$ let us consider the following system of ODEs:

$$\begin{aligned} \frac{dx_1}{dt} &= i - x_1, \\ \frac{dx_2}{dt} &= r(x_1 - x_2), \end{aligned} \quad (9)$$

with initial condition $\bar{x} = (\bar{x}_1, \bar{x}_2) \in \mathbb{R}^2$, where, as before, $r > 0$ is a given constant. Its solution $\pi_t^i(\bar{x}) = (x_1^0(t), x_2^0(t))$ is given by

$$\pi_t^i(\bar{x}) = i v + e^{Mt}(\bar{x} - i v), \quad (10)$$

where π_t^i and $v = (1, 1)$ are treated as column-vectors,

$$M = \begin{bmatrix} -1 & 0 \\ r & -r \end{bmatrix}$$

and so

$$e^{Mt} = \begin{bmatrix} e^{-t} & 0 \\ r \frac{e^{-t} - e^{-rt}}{r-1} & e^{-rt} \end{bmatrix}, \quad r \neq 1,$$

and

$$e^{Mt} = \begin{bmatrix} e^{-t} & 0 \\ e^{-t} & e^{-t} \end{bmatrix} \quad \text{for } r = 1.$$

We note that this formula is valid not only for $t \geq 0$ but for all $t \in \mathbb{R}$. In other words, π_t^i s are flows (as opposed to semi-flows) inasmuch as $\{e^{Mt}\}_{t \in \mathbb{R}}$ is a group of matrices. We note that

$$\pi_t^0(v - \bar{x}) = v - \pi_t^1(\bar{x}). \quad (11)$$

2.3. Path-wise definition of process (8)

In this section, we give a path-wise definition of the process (8). Let $q_0 = q_0(x_1, x_2)$ and $q_1 = q_1(x_1, x_2)$ be two non-negative, continuous functions on \mathbb{R}^2 ; we assume throughout the paper that

$$q_i(i, i) \neq 0, \quad i = 0, 1. \quad (12)$$

Let $x = (x_1, x_2) \in \mathbb{R}^2$ be given. We define $F_{x,i}(t) = 1 - e^{-\int_0^t q_i(\pi_s^i) ds}$, $t \geq 0$. Since

$$\lim_{t \rightarrow \infty} \pi_t^i(x) = (i, i) \quad (13)$$

regardless of the choice of x , all F s are cumulative distribution functions. In our construction, $F_{x,i}$ is the cumulative distribution function of the first jump T_1 of the process that at $t = 0$ starts at the point $(x, i) \in \mathbb{R}^2 \times \{0, 1\}$. In other words, $\text{Prob}\{T_1 \leq t\} = F_{x,i}(t)$ and we define

$$p(t) = \begin{cases} (\pi_t^i(x), i), & t < T_1, \\ (\pi_{T_1}^i(x), 1 - i), & t = T_1. \end{cases} \quad (14)$$

After time T_1 , we restart the whole procedure with (x, i) replaced by the new initial condition $p(T_1)$, so that the process moves along the integral curves of one of systems (9) until the time T_2 of the second jump, and so on.

Since the semi-flows π_t^i are continuous and (13) holds, $F_{x,1}(t) < 1$ for all $t \geq 0$. Hence, $T_1 > 0$ and, more generally, $\Delta_k = T_k - T_{k-1} > 0$, $k \geq 1$, where $T_0 = 0$ (a.s.). Similarly, $\Delta_k < \infty$ a.s. Moreover, we show that

$$\lim_{k \rightarrow \infty} T_k = \infty \quad (\text{a.s.}), \quad (15)$$

so that our process is well-defined for all $t \geq 0$. To this end, we note first that there are infinitely many jumps. Indeed, supposing contrary we would have a time T_{k_0} of the last jump. Regardless, however, of the state of the process at T_{k_0} , by construction, the time Δ_{k_0+1} to the next jump would be, conditional on the state, independent of T_{k_0} and distributed according to one of the $F_{x,i}$ functions. In any case the time to the next jump would be finite: a contradiction. Next, we note that, in view of (13), the part $x(t)$ of the process (8) starting at $x \in \mathbb{R}^2$, stays in a compact set (depending on x). Let $\mu_x = \max q_i(y)$ over y in this set and $i = 0, 1$. Then, $F_{y,i}(t) \leq 1 - e^{-\mu_x t}$ for all y in this set. Hence, $\text{Prob}(\Delta_k \geq t) \leq 1 - e^{-\mu_x t}$ regardless of the values of Δ_i , $1 \leq i \leq k - 1$. Therefore, by induction $\text{Prob}(T_n \leq t) \leq (1 - e^{-\mu_x t})^n$, proving our claim.

Finally, we note that

$$\mathbb{E} N_t < \infty, \quad t > 0, \quad (16)$$

where $N_t = \max\{k \geq 0 \mid T_k < t\}$ is the number of jumps of the process up to the time t . Indeed, $\text{Prob}(N_t \geq n) = \text{Prob}(T_n < t) \leq (1 - e^{-\mu_x t})^n$ and so $\mathbb{E} N_t = \sum_{n=0}^{\infty} \text{Prob}(N_t \geq n) < \infty$.

2.4. Bibliographical remarks

The procedure presented above is a particular case of construction of the so-called *piece-wise deterministic process* of M.H.A. Davis [3,4], compare [1] and [18]; in particular, $p(t)$, $t \geq 0$, is a Markov process in $\mathbb{R}^2 \times \{0, 1\}$. To be more specific, $p(t)$, $t \geq 0$, is a piece-wise deterministic process with

- the countable set K equal to $\{0, 1\}$,
- sets M_i , $i \in K$, both equal to \mathbb{R}^2 ,
- the state space $E = \mathbb{R}^2 \times K$,
- the vector fields X_i in M_i , $i \in K$, given by $X_0 = (-x_1, r(x_1 - x_2))$, $X_1 = (1 - x_1, r(x_1 - x_2))$,
- the ‘rate’ function $\lambda : E \rightarrow \mathbb{R}^+$ given by $\lambda(x_1, x_2, i) = q_i(x_1, x_2)$,
- the transition measure $Q(x_1, x_2, i) = \delta_{(x_1, x_2, 1-i)}$ (the Dirac measure).

We note that in order to claim this, we needed to show (15).

Similar processes have been studied extensively in various contexts. Probably the oldest class of great proximity to $p(t)$, $t \geq 0$, would be that of *random evolutions of Griego and Hersh* [7,10,11,22]. In that terminology it would be desirable to call $x(t) = (x_1(t), x_2(t))$ and $\gamma(t)$, the *driven process* and the *driving process*, respectively—we note that, separately, neither $x(t)$ nor $\gamma(t)$ are Markov. In fact, $p(t)$, $t \geq 0$, would have been a typical example of a random evolution, were the intensities of jumps of $\gamma(t)$ independent of the state of $x(t)$. Other, often intersecting, classes of processes similar to this process include *randomly flashing diffusions*, *randomly controlled dynamical systems* [19,21] and *diffusion processes with state-dependent switching* [1,20].

2.5. A related Feller semigroup

Let $BM(E)$ be the space of bounded measurable functions on $E = \mathbb{R}^2 \times \{0, 1\}$ with supremum norm. By Theorem 2.1 of [4], the extended generator \mathcal{A} of the process $p(t)$, $t \geq 0$, as restricted to $BM(E)$ is given by

$$\mathcal{A}f(x, i) = X_i f(x, i) + \lambda(x, i)[f(x, 1-i) - f(x, i)], \quad (17)$$

and is well-defined for $f \in BM(E)$ such that $t \mapsto f(\pi_t^i, i)$ is absolutely continuous for $t \geq 0$, for all $i = 0, 1$ and initial conditions x for the flow π_t^i (note that condition (ii) in the above mentioned theorem is trivially satisfied since the sets M_i have no boundary, and that, by (16), condition (iii) of that theorem holds for all $f \in BM(E)$).

Clearly, $BM(E)$ is isometrically isomorphic to the Cartesian product $BM(\mathbb{R}^2) \times BM(\mathbb{R}^2)$ of two copies of the space $BM(\mathbb{R}^2)$ of bounded measurable functions on \mathbb{R}^2 . In other words, an element f of $BM(E)$ may be conveniently represented as a pair, say (f_0, f_1) of elements of $BM(\mathbb{R}^2)$, where $f_i(x) = f(x, i)$. In this setting (17) becomes

$$\mathcal{A}(f_0, f_1) = (X_0 f_0 + q_0 f_1 - q_0 f_0, X_1 f_1 + q_1 f_0 - q_1 f_1), \quad (18)$$

for all pairs (f_0, f_1) such that $t \mapsto f_i(\pi_t^i)$, $i = 0, 1$, is absolutely continuous for $t \geq 0$, for all initial conditions $x \in \mathbb{R}^2$. Here,

$$X_i f_i(x_1, x_2) = (i - x_1) \frac{\partial f_i(x_1, x_2)}{\partial x_1} + r(x_1 - x_2) \frac{\partial f_i(x_1, x_2)}{\partial x_2}, \quad i = 0, 1. \quad (19)$$

The state-space of the process (8) is $E = \mathbb{R}^2 \times \{0, 1\}$. However, we lose no information by considering the smaller state-space

$$S = \mathcal{K} \times \{0, 1\}, \quad (20)$$

where $\mathcal{K} = I \times I$ and $I = [0, 1]$ is the unit interval. To see that note that this set is an attractor for the process in the sense that all sample paths of the process tend to this set and once they get there, they remain there forever (use (10) or see [2] for more details).

Let $C(S)$ be the space of continuous functions on S . This space is isometrically isomorphic to the product $C(\mathcal{K}) \times C(\mathcal{K})$ of two copies of the space $C(\mathcal{K})$ of continuous functions on \mathcal{K} . Hence, by a slight abuse of language, we will say that a family $\{T(t), t \geq 0\}$ of linear operators $C(\mathcal{K}) \times C(\mathcal{K})$ is a Feller semigroup of operators in this space iff its isometrically isomorphic copy in $C(S)$ is a Feller semigroup. In other words, $\{T(t), t \geq 0\}$ is a Feller semigroup in $C(\mathcal{K}) \times C(\mathcal{K})$ iff

- (a) $T(0) = \text{Id}$,
- (b) $T(t+s) = T(t)T(s)$, $s, t \geq 0$,
- (c) for each $f \in C(\mathcal{K}) \times C(\mathcal{K})$, the map $t \mapsto T(t)f$ is strongly continuous,
- (d) all $T(t)$ map the set of pairs of non-negative functions into itself, and
- (e) $T(t)(1, 1) = (1, 1)$, where $1 \in C(\mathcal{K})$ is a function equal 1 for all $x \in \mathcal{K}$.

Let C^1 be the space of $f \in C(\mathcal{K})$ that admit a continuously differentiable extension to the whole of \mathbb{R}^2 . The operator \mathcal{A} in $C(\mathcal{K}) \times C(\mathcal{K})$ given formally by the same formula as (18), i.e.

$$\mathcal{A}(f_0, f_1) = (X_0 f - q_0 f_0 + q_0 f_1, X_1 f + q_1 f_0 - q_1 f_1), \quad (21)$$

but defined merely for $f_i \in C^1$, $i = 0, 1$, is closable and its closure generates a Feller semigroup $\{T(t)\}_{t \geq 0}$ in $C(\mathcal{K}) \times C(\mathcal{K})$ —see [2] (q_0 and q_1 are now two continuous non-negative functions on \mathcal{K}). From now on, we will focus on this semigroup, or, more precisely on the properties of its dual. Before we do that, however, we need to introduce some auxiliary results concerning Markov semigroups.

3. Markov semigroups

3.1. Basic definitions

Let (S, Σ, m) be a σ -finite measure space and let $D \subset L^1 = L^1(S, \Sigma, m)$ be the set densities, i.e.

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

A linear mapping $P: L^1 \rightarrow L^1$ is called a *Markov operator* if $P(D) \subset D$.

A family $\{P(t)\}_{t \geq 0}$ of Markov operators which satisfies conditions:

- (a) $P(0) = \text{Id}$,
- (b) $P(t+s) = P(t)P(s)$ for $s, t \geq 0$,
- (c) for each $f \in L^1$ the function $t \mapsto P(t)f$ is continuous with respect to the L^1 norm,

is called a *Markov semigroup*.

A Markov semigroup $\{P(t)\}_{t \geq 0}$ is called *partially integral* or *partially kernel* if there exist $t_0 > 0$ and a measurable function $k : \mathcal{S} \times \mathcal{S} \rightarrow [0, \infty)$, called a *kernel*, such that

$$\int_{\mathcal{S}} \int_{\mathcal{S}} k(p, q) m(dp) m(dq) > 0 \quad (22)$$

and

$$P(t_0)f(p) \geq \int_{\mathcal{S}} k(p, q) f(q) m(dq) \quad (23)$$

for every density f .

A density f_* is called *invariant* if $P(t)f_* = f_*$ for each $t > 0$. The Markov semigroup $\{P(t)\}_{t \geq 0}$ is called *asymptotically stable* if there is an invariant density f_* such that

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

A Markov semigroup $\{P(t)\}_{t \geq 0}$ is called *sweeping* with respect to a set $A \in \Sigma$ if for every $f \in D$,

$$\lim_{t \rightarrow \infty} \int_A P(t)f(p) m(dp) = 0. \quad (24)$$

Remark 1. The property of sweeping is also known as *zero type*. Some sufficient conditions for sweeping are given in [15,24]. It is clear that if a Markov semigroup is sweeping from any set of finite measure then it has no invariant density. But even an integral Markov semigroup with a strictly positive kernel and having no invariant density can be non-sweeping from compact sets (see [24, Remark 7]). Sweeping from compact sets is also not equivalent to sweeping from sets of finite measure (see [24, Remark 3]). A semigroup can be both recurrent and sweeping, i.e. the heat equation $\frac{\partial u}{\partial t} = \Delta u$ generates a Markov semigroup on $L^1(\mathbb{R}^n)$ which is sweeping for all $n \geq 1$ but recurrent for $n = 1, 2$ and transient for $n \geq 3$. Also dissipativity does not imply sweeping (see [15, Example 1]).

3.2. Some results based on the theory of Harris operators

We need some results concerning asymptotic stability and sweeping which are based on the theory of Harris operators [8].

Theorem 1. [21] *Let $\{P(t)\}_{t \geq 0}$ be an partially integral Markov semigroup. Assume that the semigroup $\{P(t)\}_{t \geq 0}$ has only one invariant density f_* . If $f_* > 0$ a.e. then the semigroup $\{P(t)\}_{t \geq 0}$ is asymptotically stable.*

Theorem 2. [24] *Let \mathcal{S} be a metric space and Σ be the σ -algebra of Borel sets. We assume that a Markov semigroup $\{P(t)\}_{t \geq 0}$ has the following properties:*

- (a) *for every $f \in D$ we have $\int_0^\infty P(t)f \, dt > 0$ a.e.,*
- (b) *for every $q_0 \in \mathcal{S}$ there exist $\kappa > 0$, $t > 0$, and a measurable function $\eta \geq 0$ such that $\int \eta \, dm > 0$ and*

$$P(t)f(p) \geq \eta(p) \int_{B(q_0, \kappa)} f(q) m(dq) \quad (25)$$

for $p \in \mathcal{S}$, where $B(q_0, \kappa)$ is the open ball with center q_0 and radius κ ,
(c) the semigroup $\{P(t)\}_{t \geq 0}$ has no invariant density.

Then the semigroup $\{P(t)\}_{t \geq 0}$ is sweeping with respect to compact sets.

From Theorems 1 and 2 it follows immediately

Corollary 1. Let \mathcal{S} be a compact metric space and Σ be the σ -algebra of Borel sets. Let $\{P(t)\}_{t \geq 0}$ be a Markov semigroup which satisfies conditions (a) and (b) of Theorem 2. Then the semigroup $\{P(t)\}_{t \geq 0}$ is asymptotically stable.

Proof. From condition (b) it follows that $\{P(t)\}_{t \geq 0}$ is a partially integral Markov semigroup. The semigroup $\{P(t)\}_{t \geq 0}$ has an invariant density f_* . Otherwise it fulfills all assumptions of Theorem 2 and is sweeping from all compact sets. But it is impossible because \mathcal{S} is compact. From condition (a) it follows that any invariant density is positive a.e. But this implies that f_* is a unique invariant density. Hence, by Theorem 1, the semigroup $\{P(t)\}_{t \geq 0}$ is asymptotically stable. \square

The property that a Markov semigroup $\{P(t)\}_{t \geq 0}$ is asymptotically stable or sweeping from a sufficiently large family of sets (e.g. from all compact sets) is called the *Foguel alternative* [16].

4. A Markov semigroup corresponding to process (8)

Let $\mathcal{B}(\mathcal{S})$ be the σ -algebra of Borel subsets of the space \mathcal{S} defined by (20) and let m be the product measure on $\mathcal{B}(\mathcal{S})$ given by $m(B \times \{i\}) = \nu(B)$ for each $B \in \mathcal{B}(\mathcal{K})$ and $i = 0, 1$, where ν is the Lebesgue measure on \mathcal{K} . The dual semigroup (see e.g. [14]) of the Feller semigroup in $C(\mathcal{S})$ acts in the space of finite Borel measures in \mathcal{S} . As we shall see, in the case of the semigroup $\{T(t)\}_{t \geq 0}$ related to the operator (21), the dual semigroup leaves the space of measures that are absolutely continuous with respect to m , invariant. This space is isometrically isomorphic to $L^1(\mathcal{S}) := L^1(\mathcal{S}, \mathcal{B}(\mathcal{S}), m)$. On the other hand, $L^1(\mathcal{S})$ is isometrically isomorphic to the product $L^1(\mathcal{K}) \times L^1(\mathcal{K})$. In what follows it will be convenient to not distinguish between these two spaces, and between isometrically isomorphic copies of operators in these spaces. In particular, by a usual abuse of language, we say that an operator in $L^1(\mathcal{K}) \times L^1(\mathcal{K})$ is a Markov operator while in fact it is its isometrically isomorphic copy in $L^1(\mathcal{S})$ that is Markov.

We start by rewriting (21) as follows: $\mathcal{A}(f_0, f_1) = (X_0 f, X_1 f) - \mu(f_0, f_1) + \mu \mathcal{B}(f_0, f_1)$, where $\mu = \max\{q_i(x) : x \in \mathcal{K}, i = 0, 1\}$ and

$$\mathcal{B}(f_0, f_1) = \mu^{-1}((\mu - q_0)f_0 + q_0 f_1, q_1 f_0 + (\mu - q_1)f_1). \quad (26)$$

Since \mathcal{B} is bounded, by the Phillips perturbation theorem [5,6,12],

$$T(t) = e^{-\mu t} \sum_{n=0}^{\infty} T_n(t), \quad (27)$$

where $T_0(t)(f_0, f_1) = (U_0(t)f_0, U_1(t)f_1)$, $t \geq 0$, $U_i(t)f_i(x) = f_i(\pi_t^i(x))$, $f_i \in C(\mathcal{K})$, $i = 0, 1$, and

$$T_{n+1}(t) = \mu \int_0^t T_0(t-s) \mathcal{B} T_n(s) ds, \quad n \geq 0.$$

We note that $\{T_0(t)\}_{t \geq 0}$ is a Feller semigroup, its dual leaves $L^1(\mathcal{K}) \times L^1(\mathcal{K})$ invariant, and the restriction of the dual to this space is a Markov semigroup given by $S_0(t)(h_0, h_1) = (V_0(t)h_0, V_1(t)h_1)$ where

$$V_i(t)h_i(x) = \begin{cases} h_i(\pi_{-t}^i x) \det[\frac{d}{dx} \pi_{-t}^i x], & \text{if } \pi_{-t}^i x \in \mathcal{K}, \\ 0, & \text{if } \pi_{-t}^i x \notin \mathcal{K}. \end{cases} \quad (28)$$

As in [2] we check that the set $C^1 \times C^1$ is a core for the generator of $\{S_0(t)\}_{t \geq 0}$ and for $(h_0, h_1) \in C^1 \times C^1$ the generator is given by $\mathcal{G}_0(h_0, h_1) = (G_0 h_0, G_1 h_1)$ where

$$G_i h_i(x) = -\frac{\partial}{\partial x_1}((i - x_1)h_i(x)) + r \frac{\partial}{\partial x_2}((x_1 - x_2)h_i(x)). \quad (29)$$

Next, we note that \mathcal{B} leaves $L^1(\mathcal{K}) \times L^1(\mathcal{K})$ invariant, and the restriction of its dual to this space is a Markov operator Q given by

$$Q(h_0, h_1) = \mu^{-1}((\mu - q_0)h_0 + q_1 h_1, q_0 h_0 + (\mu - q_1)h_1). \quad (30)$$

Hence, by the Phillips perturbation theorem, the operator $\mathcal{G} - \mu \text{Id} + \mu Q$ is the generator of a Markov (see [16]) semigroup $\{P(t)\}_{t \geq 0}$ in $L^1(\mathcal{K}) \times L^1(\mathcal{K})$ given by

$$P(t) = e^{-\mu t} \sum_{n=0}^{\infty} S_n(t), \quad (31)$$

where

$$S_{n+1}(t) = \int_0^t S_n(t-s) Q S_0(s) ds, \quad n \geq 0. \quad (32)$$

(We note that the way the series is built here differs from the way it was built in (27)—both ways are allowed in the Phillips perturbation theorem, see e.g. [6, p. 161].) Comparing this with (27) we conclude that this semigroup is the restriction of the dual of the semigroup $\{T(t)\}_{t \geq 0}$ to the space $L^1(\mathcal{K}) \times L^1(\mathcal{K})$. In view of (29) and in terms of the process (8), our result states that if the distribution of $p(0)$ is absolutely continuous with respect to m , then so are the distributions of $p(t)$, $t \geq 0$. Moreover, if $(f_0, f_1) \in \mathcal{D}(\mathcal{G})$ is a density of $p(0)$ then the densities $f_i(t, \cdot)$ of $p(t)$ satisfy the system (1). On the other hand, the solutions to (1) are trajectories of the semigroup $\{P(t)\}_{t \geq 0}$.

Finally, we note that $\{P(t)\}_{t \geq 0}$ satisfies the integral equation

$$P(t)f = e^{-\mu t} S(t)f + \mu \int_0^t e^{-\mu s} S(s) Q P(t-s)f ds. \quad (33)$$

Here, and in what follows we write $S(t)$ instead of $S_0(t)$.

5. Asymptotic behavior of the semigroup related to process (8)

In this section we formulate and prove the main result of the paper.

Theorem 3. *Let*

$$E = \{(x_1, x_2): 0 \leq x_1 \leq 1, \chi_1(x_1) \leq x_2 \leq \varphi_1(x_1)\},$$

where

$$\varphi_C(x_1) = \begin{cases} \frac{C}{1-r} x_1^r + \frac{rx_1}{r-1}, & \text{for } r \neq 1, \\ -x_1 \log x_1 + Cx_1, & \text{for } r = 1, \end{cases}$$

and χ_C is the image of φ_C via the map $(x_1, x_2) \mapsto (1 - x_1, 1 - x_2)$. Suppose that the functions q_0 and q_1 are strictly positive in E , except perhaps at (i, i) where we may have $q_{1-i}(i, i) = 0$, $i = 0, 1$. Then, the semigroup $\{P(t)\}_{t \geq 0}$ given by (31) is asymptotically stable. Moreover, the invariant density f_* is supported by $\mathcal{E} = E \times \{0, 1\}$.

The proof of Theorem 3 is quite long, and so we divide it into lemmas. Before continuing we note that, as may be checked directly, the functions φ_C and χ_C are the phase curves of Eqs. (9) on the phase plane (x_1, x_2) ; in particular, φ_1 and χ_1 join points $(0, 0)$ and $(1, 1)$. Figures 2 and 3 show the phase portrait of Eq. (9) for $i = 0$ and $i = 1$, respectively.

Moreover, the set E is invariant with respect to the semi-flows π^i , i.e. if $x \in E$ then $\pi_t^i(x) \in E$, for $t \geq 0$, $i = 0, 1$. This statement is a direct consequence of geometric properties of the semi-flows (10); a rigorous proof may be based on simple application of the Darboux property or on the well-known theorem of M. Müller [27,28].

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

$$\lim_{t \rightarrow \infty} \int_{\mathcal{E}} P(t) f(p) m(dp) = 1. \quad (34)$$

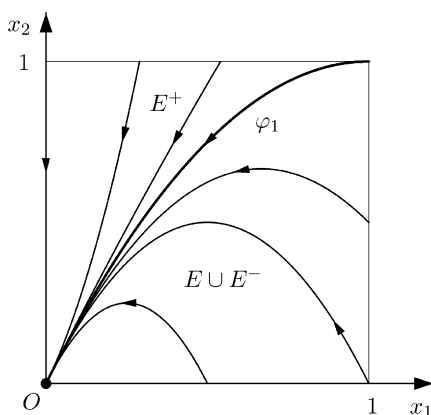
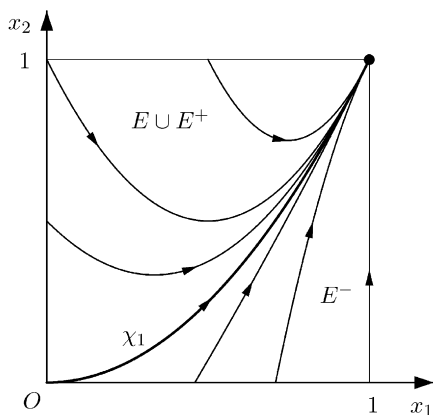
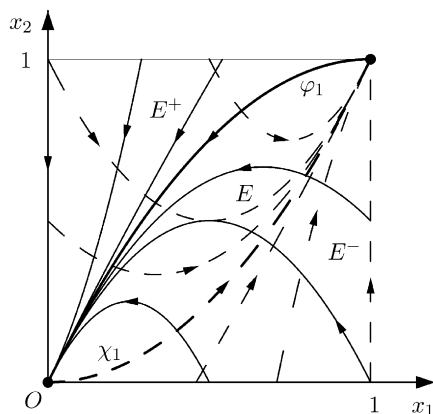


Fig. 2. Phase portrait of Eq. (9) for $i = 0$.

Fig. 3. Phase portrait of Eq. (9) for $i = 1$.Fig. 4. Action of semi-flows π^i , $i = 0, 1$.

Proof. Let

$$\begin{aligned} E^+ &= \{(x_1, x_2): 0 \leq x_1 \leq 1, \varphi_1(x_1) < x_2 \leq 1\}, \\ E^- &= \{(x_1, x_2): 0 \leq x_1 \leq 1, 0 \leq x_2 < \chi_1(x_1)\}. \end{aligned} \quad (35)$$

(Clearly, $\mathcal{K} = E \cup E^+ \cup E^-$.) Then, there exists $T > 0$ such that for every $x \in E^-$ and $y \in E^+$ we have $\pi_t^0(x) \in E$ and $\pi_t^1(y) \in E$ for $t \geq T$. Indeed, all points x from under diagonal $\mathcal{D} = \{(x_1, x_2); x_1 = x_2\}$ reach \mathcal{D} (under the action of the semi-flow π^0) at time $T_0(x_1, x_2) = \frac{\ln[(1-r)\frac{x_2}{x_1} + r]}{r-1} \leq \frac{\ln r}{r-1} = T_0$ for $r \neq 1$ and $T_0(x_1, x_2) = 1 - \frac{x_2}{x_1} \leq 1 = T_0$, and we have $T < T_0$. By (11), the same is true with points from above the diagonal under the action of the semi-flow π^1 . Figure 4 shows the action of both semi-flows.

Consider the stochastic process (8). We check that for almost every ω there exists $t_0 = t_0(\omega) > 0$ such that $x(t, \omega) \in E$ for $t \geq t_0$. Indeed, in Section 2.3 we showed that the driving process $\gamma(t)$ changes its values infinitely many times. As in that section, let $T_0 < T_1 < T_2 < \dots$ be the moments of jumps of the process and let $\Delta_n = T_n - T_{n-1}$, $n \geq 1$. Let T be as above. Since $q_i(x) \leq \mu$ we have $\text{Prob}(\Delta_n > T) \geq e^{-\mu T}$. Moreover, $p(t)$, $t \geq 0$, being a Feller càdlàg

process, is strong Markov and $T_n, n \geq 0$, are stopping times (see e.g. [23]). Conditioning on T_{n-1} , by induction we obtain $\text{Prob}(\Delta_i \leq T, i = 1, \dots, n) \leq (1 - e^{-\mu T})^n, n \geq 1$. This shows that at least two Δ_n s—one with odd and one with even index n —are greater than T . It means that for each $i = 0, 1$, in between of some jumps the semi-flow π_t^i acts for a time longer than T . Hence, $x(t) \in E$ for some and, hence, E being invariant, for all sufficiently large t and so $\lim_{t \rightarrow \infty} \text{Prob}(x(t) \in E) = 1$. Now if $p(0)$ has a density f then $\int_{\mathcal{E}} P(t)f(p)m(dp) = \text{Prob}(x(t) \in E)$ and condition (34) holds. \square

As a preparation for the crucial Lemma 3 we need the following technical result.

Lemma 2. *Let, for $x \in \mathcal{K}$, $i \in \{0, 1\}$ and $t > 0$, the set Λ_t and the function $\psi_{x,t,i} : \Lambda_t \rightarrow \mathbb{R}^2$ be defined by*

$$\Lambda_t = \{\tau = (\tau_1, \tau_2): \tau_1 > 0, \tau_2 > 0, \tau_1 + \tau_2 \leq t\} \quad \text{and} \\ \psi_{x,t,i}(\tau_1, \tau_2) = \pi_{t-\tau_1-\tau_2}^i \circ \pi_{\tau_2}^{1-i} \circ \pi_{\tau_1}^i(x). \quad (36)$$

Then,

$$\det \left[\frac{d\psi_{x,t,i}(\tau)}{d\tau} \right] \neq 0. \quad (37)$$

Proof. By (10),

$$\psi_{x,t,i}(\tau_1, \tau_2) = iv + e^{Mt}(x - iv) + (1 - 2i)[e^{M(t-\tau_1-\tau_2)} - e^{M(t-\tau_1)}]v.$$

Hence,

$$\frac{\partial}{\partial \tau_1} \psi_{x,t,i}(\tau_1, \tau_2) = (1 - 2i)Me^{M(t-\tau_1-\tau_2)}(e^{M\tau_2} - I)v, \\ \frac{\partial}{\partial \tau_2} \psi_{x,t,i}(\tau_1, \tau_2) = (2i - 1)Me^{M(t-\tau_1-\tau_2)}v.$$

Since $e^{M\tau_2}v$ equals $\left[\frac{r}{r-1}e^{-\tau_2} - \frac{1}{r-1}e^{-r\tau_2} \right]$ for $r \neq 1$ and $e^{-\tau_2} \left[\frac{1}{1+\tau_2} \right]$ for $r = 1$, the vectors $e^{M\tau_2}v$ and v are independent, and so are $e^{M\tau_2}v - v$ and v . Since the matrix $Me^{M(t-\tau_1-\tau_2)}$ is invertible, the vectors $\frac{\partial}{\partial \tau_1} \psi_{x,t,i}(\tau_1, \tau_2)$ and $\frac{\partial}{\partial \tau_2} \psi_{x,t,i}(\tau_1, \tau_2)$ are also independent. \square

Our next lemma is the core of the argument leading to Theorem 3. Roughly speaking the lemma stems from the fact that, if at $t = 0$ the process starts at a point $(x, i) \in \mathcal{S}$ and we know that up to time $t > 0$ there were exactly two jumps (in particular, $p(t)$ is back at $\mathcal{K} \times \{i\}$), then the distribution of the position of $x(t)$ in \mathcal{K} has a non-trivial absolutely continuous part. Such behavior of the process is intimately related to the fact that the semi-flows $\pi_t^i, i = 0, 1$, are in a sense “orthogonal”—see (37) and discussion in [21]. We note, however, that the results obtained in [21] cannot be applied directly to our case as they treat the situation where the intensities of jumps of the driving process do not depend on the state of the driven process: this dependence is the most interesting phenomenon of the model we are dealing with here.

Lemma 3. *Suppose that points x_0 and y_0 of \mathcal{K} , number $i \in \{0, 1\}$ and times $\tau_1^0, \tau_2^0, t > \tau_1^0 + \tau_2^0$ are chosen so that $x_0 = \psi_{y_0,t,i}(\tau_1, \tau_2)$ and*

$$q_i(\pi_{\tau_1^0}^i(y_0)) > 0, \quad q_{1-i}(\pi_{\tau_2^0}^{1-i} \circ \pi_{\tau_1^0}^i(y_0)) > 0. \quad (38)$$

Then, there exist neighborhoods $U \subset \mathcal{K}$ and $V \subset \mathcal{K}$ of y_0 and x_0 , respectively, and $\kappa > 0$ such that

$$P(t)f(x, i) \geq \kappa \int_{\mathcal{K}} \mathbf{1}_V(x) \mathbf{1}_U(y) f(y, i) dy, \quad (39)$$

for non-negative $f \in L^1(S)$ and v for almost all $x \in \mathcal{K}$.

Proof. (i) Let $Q(t, \tau)$, $\tau \in \Lambda_t$, be the operator given by $Q(t, \tau) = S(t - \tau_1 - \tau_2)QS(\tau_2)QS(\tau_1)$ and $Q^*(t, \tau)$ be the adjoint of $Q(t, \tau)$ in $L^\infty(S)$. Then, $Q^*(t, \tau) = S^*(\tau_1)Q^*S^*(\tau_2)Q^*S^*(t - \tau_1 - \tau_2)$, where $S^*(\tau)$ and Q^* are the adjoint operators of $S(\tau)$ and Q , respectively. Also, $S^*(\tau)h(y, i) = h(\pi_\tau^i(y), i)$ and $Q^*h(y, i) \geq \mu^{-1}q_i(y)h(y, 1 - i)$ for $y \in \mathcal{K}$ and non-negative $h \in L^\infty(S)$ —see (30). As a short calculation proves, this implies

$$Q^*(t, \tau)h(y, i) \geq \mu^{-2}q_i(\pi_{\tau_1}^i(y))q_{1-i}(\pi_{\tau_2}^{1-i} \circ \pi_{\tau_1}^i(y))h(\psi_{y,t,i}(\tau_1, \tau_2), i). \quad (40)$$

(ii) Let $S_2(t)$ be given by (32)—recall that we have dropped the “b” sign. Then, by (31), $P(t)f \geq e^{-\mu t} \mu^2 S_2(t)f$ for $f \geq 0$. Moreover, $S_2(t) = \int_{\Lambda_t} Q(t, \tau) d\tau$. Hence, for every Borel set $B \subset S$,

$$\begin{aligned} \int_B P(t)f(p) m(dp) &\geq e^{-\mu t} \mu^2 \int_{\Lambda_t} \int_B Q(t, \tau) f(q) m(dq) d\tau \\ &= e^{-\mu t} \mu^2 \int_{\Lambda_t} \int_S f(q) Q^*(t, \tau) \mathbf{1}_B(q) m(dq) d\tau. \end{aligned} \quad (41)$$

(iii) By (38) and continuity, there exist $\delta > 0$, $\gamma > 0$ and a neighborhood $U_0 \subset \mathcal{K}$ of y_0 such that

$$q_i(\pi_{\tau_1}^i(y)) > \gamma \quad \text{and} \quad q_{1-i}(\pi_{\tau_2}^{1-i} \circ \pi_{\tau_1}^i(y)) > \gamma \quad (42)$$

for $y \in U_0$ and $(\tau_1, \tau_2) \in \Lambda_t^0$, where $\Lambda_t^0 = \{\tau \in \Lambda_t : |\tau_1 - \tau_1^0| < \delta, |\tau_2 - \tau_2^0| < \delta\}$. From (40) and (42) it follows that

$$Q^*(t, \tau)h(y, i) \geq \mu^{-2} \gamma^2 h(\psi_{y,t,i}(\tau_1, \tau_2), i) \quad (43)$$

for $y \in U_0$ and $\tau \in \Lambda_t^0$.

(iv) Let B be of the form $B = \Gamma \times \{i\}$ where Γ is a Borel subset of \mathcal{K} . Then, by (43), $Q^*(t, \tau) \mathbf{1}_B(y, i) \geq \mu^{-2} \gamma^2 \mathbf{1}_\Gamma(\psi_{y,t,i}(\tau_1, \tau_2))$ for $y \in U_0$ and $\tau \in \Lambda_t^0$. Combining this with (41),

$$\int_\Gamma P(t)f(x, i) dx \geq e^{-\mu t} \gamma^2 \int_{U_0} f(y, i) \int_{\Lambda_t^0} \mathbf{1}_\Gamma(\psi_{y,t,i}(\tau)) d\tau dy. \quad (44)$$

Substituting $x = \psi_{y,t,i}(\tau)$ to (44) and using (37),

$$\int_\Gamma P(t)f(x, i) dx \geq \kappa \int_{U_0} f(y, i) \int_{\psi_{y,t,i}(\Lambda_t^0)} \mathbf{1}_\Gamma(z) dz dy, \quad (45)$$

where κ is a positive constant.

Finally, we note that $x_0 \in \psi_{y_0,t,i}(\Lambda_t^0)$, and, by (37), without loss of generality we may assume that $\psi_{y_0,t,i}(\Lambda_t^0)$ is open. (In other words, we may always take a neighborhood smaller than Λ_t^0 such that its image via $\psi_{y_0,t,i}$ is open.) Hence, we may find neighborhoods $U \subset U_0$ and $V \subset \mathcal{K}$ of y_0 and x_0 , respectively, such that $V \subset \psi_{y,t,i}(\Lambda_t^0)$ for $y \in U$. Replacing in (45) $\psi_{y,t,i}(\Lambda_t^0)$ by V and U by U_0 , we obtain

$$\int_{\Gamma} P(t)f(x, i) dx \geq \kappa \int_{\Gamma} \int_U f(y, i) \mathbf{1}_V(x) dy dx. \quad (46)$$

This implies (39), Γ being arbitrary. \square

Proposition 1. For every $y_0 \in \mathcal{K}$, $i \in \{0, 1\}$ and $t > 0$ there exist $x_0 \in \mathcal{K}$ and neighborhoods $U \subset \mathcal{K}$ and $V \subset \mathcal{K}$ of y_0 and x_0 , respectively, such that (39) holds. In particular, operator $P(t)$ is partially integral with the kernel $k(p, q) \geq \kappa \mathbf{1}_{V \times \{i\}}(p) \mathbf{1}_{U \times \{i\}}(q)$.

Proof. For any $y_0 \in \mathcal{K}$, $i \in \{0, 1\}$ and $s > 0$ we have $q_i(\pi_s^i(y_0)) > 0$ and $q_{1-i}(\pi_s^{1-i} \circ \pi_s^i(y_0)) > 0$. Hence, for any $t > 0$ we see that y_0 , $\tau_1^0 = \tau_2^0 = \frac{t}{3}$ and $x_0 = \psi_{y_0,t,i}(\frac{t}{3}, \frac{t}{3})$ satisfy the assumptions of Lemma 3. Now, inequality (39) may be rewritten as $P(t)f(p) \geq \kappa \int_S \mathbf{1}_{V \times \{i\}}(p) \mathbf{1}_{U \times \{i\}}(q) f(q) m(dq)$. \square

Before we present Proposition 2 which constitutes the second major element of the structure of the proof of our main theorem, we present the following “communication lemma.” We omit its elementary proof—see Fig. 5.

Lemma 4. Fix $y_0 \in E$, $x_0 \in \text{Int } E$ and $i = 0, 1$. Then, τ_1 , τ_2 and $t > \tau_1 + \tau_2$ may be chosen so that $x_0 = \psi_{y_0,t,i}(\tau_1, \tau_2) = \pi_{t-\tau_1-\tau_2}^i \circ \pi_{\tau_2}^{1-i} \circ \pi_{\tau_1}^i(y_0)$; we note that then (38) holds by assumption.

Proposition 2. For every $q_0 \in \text{Int } \mathcal{E}$ and for every $p_0 \in \text{Int } \mathcal{E}$ there exist $t > 0$, $\kappa > 0$ and neighborhoods $U \subset \mathcal{S}$ and $V \subset \mathcal{S}$ of q_0 and p_0 , respectively, such that

$$P(t)f(p) \geq \kappa \int_S \mathbf{1}_V(p) \mathbf{1}_U(q) f(q) m(dq), \quad (47)$$

for m almost all $p \in \mathcal{S}$ and non-negative $f \in \mathcal{L}(\mathcal{S})$.

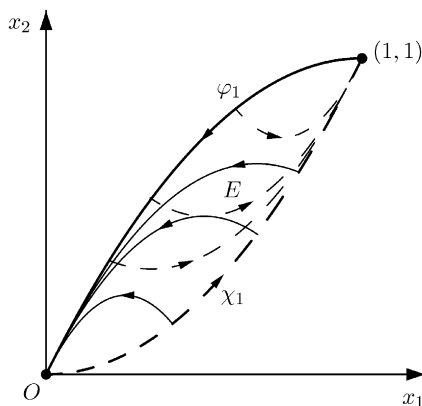


Fig. 5. Communication of states.

Proof. For p_0 and q_0 lying in the same square (i.e. for p_0 and q_0 having the same third coordinate) the claim follows directly by Lemmas 3 and 4.

To deal with the case where we have, say $p_0 = (x, i)$ and $q_0 = (y, 1 - i)$ we note that by (30) we have $Qf(x, i) \geq \mu^{-1} q_{1-i}(x) f(x, 1 - i)$. Hence, by (31) and (33),

$$\begin{aligned} P(s)f(x, i) &\geq \int_0^s e^{-\mu\tau} S(\tau)(q_{1-i}(x)P(s-\tau)f(x, 1-i)) d\tau \\ &\geq e^{-\mu s} \int_0^s V_i(\tau)(q_{1-i}(x)V_{1-i}(s-\tau)f(x, 1-i)) d\tau \end{aligned} \quad (48)$$

for $s \geq 0$. Since $q_{1-i}(x) > 0$ and $V_i(\tau)(x) = h(\pi_{-\tau}^i x)e^{(r+1)\tau}$, taking s sufficiently small and combining (39) with (48) we obtain

$$P(t+s)f(x, i) \geq \varepsilon' \int_{I \times I} \mathbf{1}_{V'}(x) \mathbf{1}_{U'}(y) f(y, 1-i) dy, \quad (49)$$

where U', V' are neighborhoods of y_0, x_0 and $\varepsilon' > 0$, which completes the proof. \square

Proof of Theorem 3. By Lemma 1, it suffices to investigate the restriction of the semigroup $\{P(t)\}_{t \geq 0}$ to the space $L^1(\mathcal{E})$. From Propositions 1 and 2 we obtain conditions (b) and (a) of Theorem 2, respectively. Finally, from Corollary 1 it follows immediately that the semigroup $\{P(t)\}_{t \geq 0}$ is asymptotically stable. \square

Acknowledgments

We thank J. Zabczyk for referring us to the work of M.H.A. Davis. This research was partially supported by the State Committee for Scientific Research (Poland) Grants No. 2 P03A 031 25 and 4 T07A 001 30.

References

- [1] G.P. Basak, A. Bisi, Stability of degenerate diffusions with state-dependent switching, *J. Math. Anal. Appl.* 240 (1999) 219–248.
- [2] A. Bobrowski, Degenerate convergence of semigroups related to a model of eukaryotic gene expression, *Semigroup Forum* (2005), in press.
- [3] M.H.A. Davis, Piece-wise deterministic Markov processes, *J. Roy. Stat. Soc. Ser. B* 46 (1984) 353–388.
- [4] M.H.A. Davis, *Lectures on Stochastic Control and Nonlinear Filtering*, Springer, 1984.
- [5] N. Dunford, J.T. Schwartz, *Linear Operators, Part I*, Interscience Publ., New York, 1968.
- [6] K.-J. Engel, R. Nagel, *One-parameter Semigroups for Linear Evolution Equations*, Springer, 2000.
- [7] S.N. Ethier, T.G. Kurtz, *Markov Processes. Characterization and Convergence*, Wiley, New York, 1986.
- [8] S.R. Foguel, Harris operators, *Israel J. Math.* 33 (1979) 281–309.
- [9] D.T. Gillespie, Exact stochastic simulations of coupled chemical reactions, *J. Phys. Chem.* 81 (1977) 2340–2361.
- [10] R.J. Griego, R. Hersh, Random evolutions, Markov chains, and systems of partial differential equations, *Proc. Natl. Acad. Sci. USA* 62 (1969) 305–308.
- [11] R.J. Griego, R. Hersh, Theory of random evolutions with applications to partial differential equations, *Trans. Amer. Math. Soc.* 156 (1971) 405–418.
- [12] E. Hille, R.S. Phillips, *Functional Analysis and Semigroups*, rev. ed., Amer. Math. Soc. Colloq. Publ., vol. 31, Amer. Math. Soc., Providence, RI, 1957.
- [13] M. Kaern, C.T. Elston, W.J. Blake, J.J. Collins, Stochasticity in gene expression: From theories to phenotypes, *Nature Review Genetics* 6 (2005) 451–464.

- [14] J. Kisyński, Semi-groups of operators and some of their applications to partial differential equations, in: *Control Theory and Topics in Functional Analysis*, International Atomic Energy Agency, Vienna, 1976, pp. 305–405.
- [15] T. Komorowski, J. Tyrcha, Asymptotic properties of some Markov operators, *Bull. Pol. Acad. Sci. Math.* 37 (1989) 221–228.
- [16] A. Lasota, M.C. Mackey, *Chaos, Fractals and Noise. Stochastic Aspects of Dynamics*, Appl. Math. Sci., vol. 97, Springer, New York, 1994.
- [17] T. Lipniacki, P. Paszek, A.R. Brasier, B. Luxon, M. Kimmel, Stochastic regulation in early immune response, *Biophys. J.* 90 (2006) 725–742.
- [18] T. Lipniacki, P. Paszek, A. Marciniak-Czochra, A.R. Brasier, M. Kimmel, Transcriptional stochasticity in gene expression, *J. Theor. Biol.* 238 (2006) 348–367.
- [19] J. Łuczka, R. Rudnicki, Randomly flashing diffusion: Asymptotic properties, *J. Stat. Phys.* 83 (1996) 1149–1164.
- [20] K. Pichór, R. Rudnicki, Stability of Markov semigroups and applications to parabolic systems, *J. Math. Anal. Appl.* 215 (1997) 56–74.
- [21] K. Pichór, R. Rudnicki, Continuous Markov semigroups and stability of transport equations, *J. Math. Anal. Appl.* 249 (2000) 668–685.
- [22] M. Pinsky, *Lectures on Random Evolutions*, World Scientific, Singapore, 1991.
- [23] D. Revuz, M. Yor, *Continuous Martingales and Brownian Motion*, Springer, 1999.
- [24] R. Rudnicki, On asymptotic stability and sweeping for Markov operators, *Bull. Pol. Acad. Sci. Math.* 43 (1995) 245–262.
- [25] R. Rudnicki, K. Pichór, M. Tyran-Kamińska, Markov semigroups and their applications, in: P. Garbaczewski, R. Olkiewicz (Eds.), *Dynamics of Dissipation*, in: *Lecture Notes in Phys.*, vol. 597, Springer, Berlin, 2002, pp. 215–238.
- [26] R. Rudnicki, Long-time behavior of a stochastic prey–predator model, *Stochastic Process. Appl.* 108 (2003) 93–107.
- [27] W. Walter, *Differential and Integral Inequalities*, *Ergeb. Math. Granzgeb.*, vol. 55, Springer, 1970.
- [28] W. Walter, *Differential inequalities and maximum principles: Theory, new methods and applications*, *Nonlinear Anal.* 30 (1997) 4695–4711.