Nonnegative Compartment Dynamical System Modelling with Stochastic Differential Equations

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Abstract

Compartment models are widely used in various physical sciences and adequately describe many biological phenomena. Elements such as blood, gut, liver and lean tissue are characterized as homogeneous compartments, within which the drug resides for a time, later to transit to another compartment, perhaps recycling or eventually vanishing. We address the issue of compartment dynamical system modelling using multidimensional stochastic differential equations, rather than the classical approach based on the continuous-time Markov chain. Pure-jump processes are employed as perturbation to the deterministic compartmental dynamical system. Unlike with the Brownian motion, noise can be incorporated into both outflows and inter-compartmental flows without violating nonnegativity of the compartmental system, under mild technical conditions. The proposed formulation is easy to simulate, shares various essential properties with the corresponding deterministic ordinary differential equation, such as asymptotic behaviors in mean, steady states and average residence times, and can be made as close to the corresponding diffusion approximation as desired. Asymptotic mean-square stability of the steady state is proved to hold under some assumptions on the model structure. Numerical results are provided to illustrate the effectiveness of our formulation.

Keywords: Brownian motion; compartmental system; nonnegative system; Poisson process; mean-square stability; stochastic differential equation.

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1 Introduction

Quantitative modelling of the distribution over time of state in a system, for example, a drug or pollutant in a human or animal body, has often been carried out in terms of nonnegative compartmental models. Those models are composed of interconnected subsystems or compartments, which exchange variable nonnegative quantities of material with conservation laws describing transfer, accumulation, and elimination between the compartments and the environment, where there is assumed to be instantaneous mixing with material that enters an compartment so that all of the material of every compartment is at all times homogeneous. Compartment models are widely used in various physical sciences and adequately describe many biological phenomena. Elements such as blood, gut, liver and lean tissue are characterized as homogeneous compartments, within which the drug resides for a time, later to transit to another compartment, perhaps recycling or eventually vanishing. Since the state variables represent the amount of material contained in each compartment, they are obviously bounded to be nonnegative over time.

Classical approach in this area proposed deterministic descriptions of flows between compartments and stocks within them and the outside environment. Those frameworks assume that state variables are continuous and give the movement of material from compartment to compartment as deterministic continuous flows. With the mass balance requirements of compartmental systems, these assumptions lead to systems of...
ordinary differential equations. However, variations in compartment concentrations over replicated experiments suggest random fluctuations in the transfer mechanism of the system.

Stochastic compartment analysis has undergone over decades. There exists a large literature, which proposes mathematical formulation, explores the stochastic behavior and deals with statistical aspects of a variety of compartment models. Relevant publications, from classic to recent, include statistical inference \[3, 8, 7\]; stochastic parameters \[5\]; a formulation with Gaussian noise \[9\]; diffusion approximation \[13\]; non-Markovian processes \[14\]; continuous-time Markov chain models \[16, 21\]; residence times \[10, 23\], to mention just a few. The most popular approach seems to be the one based on the continuous-time Markov chain, where the state is expressed as integer valued stochastic processes with transition probabilities. The Kolmogorov equations for the rates of change of the state probabilities can then be derived, while the difficulty in solving such systems grow at an extraordinary speed with the number of compartments. It is moreover not very important to stick with the integer-valued state space, unless the primal interest lies in modelling the number of particles in each compartment.

In this paper, we employ stochastic differential equations to add stochasticity to deterministic linear compartmental dynamical systems. In the face of stochastic effects taking place in this direction, modelling nonnegative compartmental systems is often nontrivial. In particular, the positive invariance of the non-negative orthant along the solutions of stochastic dynamic equations should be properly established. Our approach based on the pure-jump process allows for noise on both outflows and inter-compartmental flows with maintaining essential features required for compartmental dynamical systems, such as nonnegativity, appropriate asymptotic behaviors, residence times, and mean-square stability of the steady state. The rest of this paper is organized as follows. Section 2 recalls some general notations and describes our problem setup and motivation, leaving the main results to Section 3 followed by numerical illustrations in Section 4. Section 5 gives some further remarks and indicates the direction of future research.

## 2 Background

Let us begin with notation and generalities which will be used throughout the paper. The vector \( x \) is said to be nonnegative if every component of \( x \) is nonnegative. We define \( \mathbb{R}_0 := \mathbb{R} \setminus \{0\} \) and let \( \mathbb{R}_n^\circ \) denote the nonnegative orthant of \( \mathbb{R}^n \). We write \( I_n \) for the identity matrix in \( \mathbb{R}^{n \times n} \). We say that a stochastic process \( \{L_t : t \geq 0\} \) in \( \mathbb{R} \) is a Lévy process, if its sample paths are almost surely right-continuous with left limits, if it is continuous in probability, and if it has stationary and independent increments. In this paper, we are particularly interested in one-dimensional pure-jump Lévy processes characterized in the form of the Lévy-Khintchine representation

\[
\mathbb{E} \left[ e^{iyL_t} \right] = \exp \left[ t \int_{\mathbb{R}_0} (e^{iyz} - 1) \nu(dz) \right],
\]

which is well defined if the so-called Lévy measure \( \nu \) satisfies \( \int_{|z| \leq 1} z \nu(dz) < +\infty \), that is, the Lévy process \( \{L_t : t \geq 0\} \) has finite variation. We also assume that \( \int_{\mathbb{R}_0} z \nu(dz) = 0 \) and \( \int_{\mathbb{R}_0} z^2 \nu(dz) < +\infty \), that is, the Lévy process is centered and is square-integrable, that is, for each \( t \geq 0 \),

\[
\mathbb{E} \left[ L_t \right] = t \int_{\mathbb{R}_0} z \nu(dz) = 0, \quad \text{Var} (L_t) = \mathbb{E} \left[ L_t^2 \right] = t \int_{\mathbb{R}_0} z^2 \nu(dz) < +\infty,
\]

which ensure that the Lévy process \( \{L_t : t \geq 0\} \) is a square-integrable martingale with respect to its natural filtration. Finally, a matrix \( A \) in \( \mathbb{R}^{n \times n} \), with \( a_{k_1,k_2} \) being its \((k_1,k_2)\)-entry, is said to be compartmental if \( a_{k_1,k_2} \geq 0 \) for every \( k_1 \neq k_2 \) and if \( \sum_{m=1}^n a_{m,k_2} \leq 0 \), for every \( k_2 \). Henceforth, we write

\[
\mathcal{H}_n := \left\{ H \in \mathbb{R}^{n \times n} : H \text{ is compartmental} \right\}.
\]
To illustrate the concept of compartmental systems, we begin with the deterministic framework. Consider the deterministic linear system

$$\begin{align*}
    \dot{x}(t) &= Ax(t) + u(t), & x(0) = x_0 \in \mathbb{R}_+^n, \\
y(t) &= \langle c, x(t) \rangle,
\end{align*}$$

(2.3)

where \( c \in \mathbb{R}_+^n \), and \( u : [0, +\infty) \to \mathbb{R}^n \). We denote by \( x(t) \) the vector in \( \mathbb{R}^n \) representing the amount of resource present in each compartment at time \( t \). For \( k_1 \neq k_2 \), the entry \( a_{k_1, k_2} \) in the matrix \( A \) is the fractional transfer coefficient of the flow from the \( k_2 \)-nd to the \( k_1 \)-st compartment. The sum \( \sum_{m=1}^n a_{m, k_2} \) of the entries of the \( k_2 \)-nd column represents the fractional transfer coefficient of the outflow from the \( k_2 \)-nd compartment. The inflow vector \( u(t) \) indicates material injection from the environment. Since the output \( y(t) \) measures the material contained in some compartments, then at least one entry of \( c \) is strictly positive. The system (2.3) is said to be compartmental if \( A \in \mathcal{H}_n \). In short, compartmental systems satisfy the property that the state and output variables remain nonnegative. The system (2.3) is said to be outflow-closed if \( \sum_{m=1}^n a_{m, k_2} = 0 \) for every \( k_2 \) and is said to be inflow-closed if \( u(t) \equiv 0 \). Moreover, the system (2.3) is said to be outflow-connected if there is a path from every compartment to a compartment which has outflow and is said to have a trap if there exists a compartment (or a set of compartments) from which there are no transfers to the environment. In particular, it is well known that compartmental matrices have no eigenvalues with positive real part and no purely imaginary eigenvalues. If the system is outflow-closed, then each column of \( A \) sums to zero, which implies that \( A \) is singular for outflow-closed systems. Moreover, the system contains traps or is outflow-closed if and only if \( A \) is singular. The system is outflow-connected (and thus has no traps) if and only if \( A \) is nonsingular. To sum up, let us list three possible behaviors for the system (2.3).

(i) If \( u(t) \equiv 0 \) and \( A \) is singular, then the trajectories of \( x(t) \) lie on lower \( < n \) dimensional hyperplanes in the nonnegative orthant and tend exponentially to the zero set of \( A \) on each of these hyperplanes.

(ii) If \( u(t) \neq 0 \) and \( A \) is singular, then the trajectories of \( x(t) \) either lie on hyperplanes and tend to a solution \( x \) of \( Ax = -\lim_{t \to +\infty} u(t) \), or tend to infinity.

(iii) If the system has inflows with \( \lim_{t \to +\infty} u(t) = u \in \mathbb{R}^n \) and \( A \) is nonsingular, then \( x(t) \) tends exponentially to the steady state \( -A^{-1}u \in \mathbb{R}_+^n \).

See, for example, [11] for thorough details.

For the stochastic analogy of the deterministic system (2.3), the state variable \( x(t) \) is replaced with \( X_t \), which is an integer valued stochastic process, and the transfer coefficients are replaced by transition probabilities, so that \( a_{k_1, k_2} \Delta + o(\Delta) \) is the probability of transfer of one particle from the \( k_2 \)-nd to the \( k_1 \)-st in a short time interval \((t, t + \Delta)\). Such systems can be recast as continuous-time Markov chain. (See, for example, [21].) Let us summarize its basic properties and some points for consideration;

(i) With the transfer probabilities, the Kolmogorov equations for the rates of change of the state probabilities can be derived, while the difficulty in solving such systems grow at an extraordinary speed with the number of compartments;

(ii) The residence time distribution (roughly speaking, the fraction of particles that has left a outflow connected system without inflow in terms of time) remains the same as the one for the corresponding deterministic system on average. (See, for example, [10].) The stochastic analogy of this type is thus meant to express some random fluctuation around the deterministic system (2.3);

(iii) Nonnegativity of the system state is certainly preserved. It is however not very important to stick with the integer-valued state space \( X_t \), unless the primal element of modelling is the number of particles in each compartment. Indeed, this claim has long been supported by deterministic ordinary differential equation modelling, such as (2.3).
Alternatively, in the framework with stochastic differential equations, the first candidate as their driving noise would be Gaussian:

\[ dX_t = AX_t dt + \sum_{k=1}^{m} A_{w}^{(k)} X_t dW_t^{(k)} + u(t) dt, \quad X_0 = x_0 \in \mathbb{R}_+, \quad t > 0, \]

where \( \{W_t^{(k)} : t \geq 0\}_{k=1}^{m} \) is a sequence of mutually independent standard centered Brownian motions in \( \mathbb{R} \) and where \( A_{w}^{(k)} \) are in \( \mathbb{R}^{n \times n} \). This system can be thought of as a perturbation of the deterministic counterpart \( \dot{x}(t) = Ax(t) + u(t) \), as taking expectation yields \( \mathbb{E}[X_t] = X_0 + \mathbb{E}[\int_0^t (AX_t + u(s)) ds] \). The crucial drawback of this system based on a Brownian motion is that nonnegativity of the system is not guaranteed. The most straightforward sufficient condition, when \( u(t) \equiv 0 \), is that all the matrices are commuting, that is,

\[ A A_{w}^{(k)} = A_{w}^{(k)} A, \quad k = 1, \ldots, m, \quad \text{and} \quad A_{w}^{(k_1)} A_{w}^{(k_2)} = A_{w}^{(k_2)} A_{w}^{(k_1)}, \quad k_1 \neq k_2, \]

since then the resulting explicit fundamental solution

\[ X_t = \exp \left[ \left( A - \frac{1}{2} \sum_{k=1}^{m} (A_{w}^{(k)})^2 \right) t + \sum_{k=1}^{m} A_{w}^{(k)} W_t^{(k)} \right] X_0, \quad (2.4) \]

obviously indicates the almost sure nonnegativity of every component. (Note that the explicit solution \((2.4)\) happens to guarantee nonnegativity, while the existence of such an explicit solution is not essential to judge nonnegativity.) Nevertheless, such a set of conditions is not of practical use at all, that is, we may construct such commuting matrices, while estimated matrices are highly unlikely to be commuting. For example, suppose that all the matrices \( A_{w}^{(k)} \) have the form of \( \delta_k \mathbf{1}_n \) so that they are all commuting. This restriction is not of practical use either since then randomness is introduced only into the outflows, but not into the inter-compartmental flow. In general, it is difficult to derive even a necessary (and practical) condition for the system based on a Brownian motion to be nonnegative. It seems that this fact has long precluded one from formulating compartmental systems using stochastic differential equations.

### 3 Results

Instead of the continuous-time Markov chain or the stochastic differential equation driven by the Brownian motion, we propose the system

\[ dX_t = AX_t dt + \sum_{k=1}^{m_1} A_{\text{inter}}^{(k)} X_t dL_t^{(k)} + \sum_{k=1}^{m_2} A_{\text{out}}^{(k)} X_t dL_t^{(m_1+k)} + u(t) dt, \quad X_0 = x_0 \in \mathbb{R}_+, \quad (3.1) \]

where \( A_{\text{inter}}^{(k)}, A_{\text{out}}^{(k)} \in \mathbb{R}^{n \times n} \), where \( \{L_t^{(k)} : t \geq 0\}_{k=1}^{m_1+m_2} \) is a sequence of independent pure-jump Lévy processes satisfying \((2.1)\) and \((2.2)\), and where \( u(t) \) denotes the nonnegative deterministic inflow at time \( t \geq 0 \) from outside the system into each compartment. For simplicity, we will omit the output \( Y_t = \langle c, X_t \rangle \) hereafter. Note that pure-jump processes are employed in the system \((3.1)\) out of necessity, instead of the Brownian motion. We denote by \( \nu^{(k)} \) the Lévy measure of the Lévy process \( \{L_t^{(k)} : t \geq 0\} \) for each \( k = 1, \ldots, m_1 + m_2 \). Define for \( n \in \mathbb{N} \) and \( z \geq 0 \),

\[ \mathcal{H}_{n,z}^{\text{inter}} := \{ H \in \mathcal{H}_n : \text{outflow-closed}, \]

\[ \text{at most four entries are non-zero with absolute values no greater than } z > 0 \}, \]

\[ \mathcal{H}_{n,z}^{\text{out}} := \left\{ H \in \mathbb{R}^{n \times n} : H = \text{diag}[h_1, \ldots, h_n] \text{ with } \max_k |h_k| \leq z \right\}. \]
We mean by the notation $\mathcal{H}_{n,z}^{\text{inter}}$ and $\mathcal{H}_{n,z}^{\text{out}}$, respectively, the rate coefficient matrices for inter-compartmental flows and outflows. By assuming that $H \in \mathcal{H}_{n,z}^{\text{inter}}$ has at most four nonzero entries, the matrix $H \in \mathcal{H}_{n,z}^{\text{inter}}$ has at most two nonzero diagonal entries and two nonzero off-diagonal entries. This indicates that the matrix $H \in \mathcal{H}_{n,z}^{\text{inter}}$ may deal with at most one bridge between some two compartments. The following gives sufficient conditions for the system to be nonnegative and compartmental. (It is worth noting that the conditions in Theorem 3.1 guarantees the nonnegativity of the system $\text{(3.1)}$, while the existence of an explicit solution for the system $\text{(3.1)}$ is unknown here.)

**Theorem 3.1.** Let $\{z_k\}_{k=1,\ldots,m_1+m_2}$ be a sequence of positive constants. The system $\text{(3.1)}$ is nonnegative and compartmental if all the following conditions hold:

(i) $A \in \mathcal{H}_n$,  
(ii) $A_{\text{inter}}^{(k)} \in \mathcal{H}_{n,z}^{\text{inter}}$, $k = 1, \ldots, m_1$,  
(iii) $A_{\text{out}}^{(k)} \in \mathcal{H}_{n,z}^{\text{out}}$, $k = 1, \ldots, m_2$,  
(iv) $\nu^{(k)}(\mathbb{R} \setminus (-1/z_k, +1/z_k)) = 0$, $k = 1, \ldots, m_1 + m_2$.

Unlike in the case of continuous sample paths, we need to pay attention to the overshooting out of the nonnegative orthant due to jumps.

**Proof.** We split the proof into three parts.

(I) Suppose $m_1 = 1$ and $m_2 = 0$, that is, there is only one inter-compartmental flow affected by noise and no outflows affected by noise. Assume that the noise occurs only on the inter-compartmental flow connecting the $k_1$-st and $k_2$-nd compartments, and let the $(k_1,k_1)$-, $(k_1,k_2)$-, $(k_2,k_1)$-, and $(k_2,k_2)$-entries of the matrix $A_{\text{inter}}^{(1)}$ be given respectively by

$$b_{k_1,k_1} = -s_1, \quad b_{k_2,k_1} = s_1, \quad b_{k_1,k_2} = s_2, \quad b_{k_2,k_2} = -s_2,$$

for some $s_1 \geq 0$ and $s_2 \geq 0$, while all the other entries of $A_{\text{inter}}^{(1)}$ are zero. Now, supposing the Lévy process $\{L^{(1)}_t: t \geq 0\}$ jumps at time $t$ with jump size $\Delta L^{(1)}_t$, it induces the jump of the $k_1$-st and $k_2$-nd compartments as

$$\Delta X_{t,k_1} = (b_{k_1,k_1}X_{t-k_1} + b_{k_1,k_2}X_{t-k_2})\Delta L^{(1)}_t,$$

$$\Delta X_{t,k_2} = (b_{k_2,k_1}X_{t-k_1} + b_{k_2,k_2}X_{t-k_2})\Delta L^{(1)}_t,$$

where $\Delta X_{t,k}$ denotes the jump of the state of the $k$-th compartment at time $t$. Clearly, the system remains nonnegative right after the jump $\Delta L_t$ occurs if and only if

$$X_{t-k_1} + \Delta X_{t,k_1} \geq 0, \quad X_{t-k_2} + \Delta X_{t,k_2} \geq 0, \quad a.s. \quad (3.4)$$

Plugging (3.2) and (3.3) into (3.4) yields

$$X_{t-k_1} \left(1 - s_1\Delta L^{(1)}_t\right) + s_2X_{t-k_2}\Delta L^{(1)}_t \geq 0, \quad a.s.,$$

$$X_{t-k_2} \left(1 - s_2\Delta L^{(1)}_t\right) + s_1X_{t-k_1}\Delta L^{(1)}_t \geq 0, \quad a.s.$$

Hence, for the nonnegativity of the states, it suffices to have

$$s_1\Delta L^{(1)}_t \in [0,1], \quad \text{and} \quad s_2\Delta L^{(1)}_t \in [0,1], \quad (3.5)$$

which indeed holds by the conditions (ii) and (iv).
Next, we extend the argument to the case $m_1 > 1$ and $m_2 = 0$, where each set of $A^{(k)}_{\text{inter}}$ and $L^{(k)}_t$ satisfies the condition (3.5). This is straightforward by noting that $\{L^{(k)}_t : t \geq 0\}_{k=1, \ldots, m_1}$ are independent subordinators, as mutually independent Lévy processes almost surely do not jump simultaneously. (As the simplest example, consider two independent standard Poisson processes, each of which jumps by one at the timings of successive summation of standard exponential random variables. Due to the smoothness of exponential distributions, the two Poisson processes jump at the same instant with probability zero.) Therefore, it is sufficient to have the condition (3.5) separately for $k = 1, \ldots, m_1$. Note that the inflow $u(t)$ does not affect any part of this argument as it is nonnegative.

(II) Suppose $m_1 = 0$ and $m_2 = 1$, that is, there are no inter-compartmental flows affected by noise and is one outflow affected by a random source. Let $A^{(1)}_{\text{out}} = \text{diag}[b_1, \ldots, b_n]$. Then, in a similar manner to the previous part (I), it holds that for every $k = 1, \ldots, n$,

$$\Delta X_{t,k} = b_k X_{t-k} \Delta L^{(1)}_t,$$

In the same spirit as (3.4), we can easily show that the condition (v) is sufficient. The extension to the case $m_1 = 0$ and $m_2 > 0$ follows immediately, as again mutually independent Lévy processes almost surely do not jump simultaneously.

(III) Suppose $m_1 > 0$ and $m_2 > 0$. Again, this general case follows immediately for the same reason that mutually independent Lévy processes almost surely do not jump simultaneously. The proof is complete. $\square$

Note that the definition of the set $\mathcal{H}_{n,c,z}^{\text{inter}}$ restricts our consideration to the case where each random source can affect at most one inter-compartmental flow. This restriction makes sufficient sense in practice, while from a technical point of view, it also seems sensible not to extend to the setting where one random source may affect more than one inter-compartmental flow, since then the condition is not as clear-cut as (3.5).

From a practical point of view, it seems more natural to assume that each outflow is affected independently by a single random source, that is, the matrices $A^{(k)}_{\text{out}}$ are simply diagonal with only one nonzero entry. (This is certainly covered by Theorem 3.1) Note that for the system based on a Brownian motion, it is still unclear even in such a simple setting whether nonnegativity is guaranteed, as all matrices are not necessarily commuting.

As all the driving noises $\{L^{(k)}_t : t \geq 0\}$ in the system (3.1) are martingales, it holds that $E[X_t] = X_0 + E \left[ \int_0^t (AX_s + u(s)) \, ds \right]$, just as in the aforementioned system based on a Brownian motion. If the expectation and the integral on the right hand side can be interchanged, then our system (3.1) behaves like the corresponding deterministic system (2.3) on average. In particular, the residence time distribution remains the same on average as the deterministic system as well. (This is also the case for the continuous-time Markov chain approach.) Hence, model identification techniques for the deterministic system based on residence times are in principle expected to apply to our system.

The continuous-time Markov chain model falls under the class of stochastic compartmental dynamical systems of which stochasticity is the major source of the trajectories. Our formulation can be modified to fall into the class as well, by setting $A \equiv 0$, changing the centered Lévy processes (2.2) into one-sided jumping Lévy processes and choosing $A^{(k)}_{\text{inter}}$ and $A^{(k)}_{\text{out}}$ appropriately. Through this, our model may recover the continuous-time Markov chain model.

Next, we demonstrate in a rigorous manner that the addition of jump-driven noise is not an unnecessary complication and provides a framework very close to the diffusion approximation without violating nonnegativity of the system. To this end, suppose that $\nu$ is a Lévy measure satisfying the condition (iv) of Theorem 3.1 and define a Lévy measure $\nu_n$ for each $n \in \mathbb{N}$ by

$$\nu_n(dz) := n(\mathcal{T}_{n-1/2} \nu)(dz),$$

where $\mathcal{T}_\nu$ denotes the transformation of the measure $\nu$ on $\mathbb{R}$ as $(\mathcal{T}_\nu \nu)(B) = \nu(r^{-1}B)$, $B \in \mathcal{B}(\mathbb{R})$. The above structure indicates that the intensity of jump increases in order $n$, while the jump size decreases in
order \( n^{-1/2} \). This ensures that for each \( n \in \mathbb{N} \), the Lévy process \( \{L_{t,n} : t \geq 0\} \) with Lévy measure \( \nu_n(dz) \) shares the same first and second moments with \( \{L_{t,1} : t \geq 0\} \), that is, for each \( t \geq 0 \),

\[
\mathbb{E}[L_{t,n}] = t \int_{\mathbb{R}_0} z n(\mathcal{F}_{n^{-1/2}}v)(dz) = t \sqrt{n} \int_{\mathbb{R}_0} z v(dz) = 0 = \mathbb{E}[L_{t,1}],
\]

\[
\text{Var}(L_{t,n}) = t \int_{\mathbb{R}_0} z^2 n(\mathcal{F}_{n^{-1/2}}v)(dz) = t \int_{\mathbb{R}_0} z^2 n v(dz) = \text{Var}(L_{t,1}).
\]

Note that the higher order moments do change. The following result tells us that the Lévy process converges to the Brownian motion not only for its marginals at fixed time by virtue of the central limit theorem, but also for sample path properties. In other words, each discontinuous sample path of \( \{L_{t,n} : t \geq 0\} \) converges in law to a continuous (nowhere differentiable) sample path of the Brownian motion.

**Proposition 3.2.** Let \( \{W_t : t \geq 0\} \) be a centered Brownian motion with \( \mathbb{E}[W_t^2] = \int_{\mathbb{R}_0} z^2 v(dz) \). It holds that as \( n \uparrow +\infty \),

\[
\{L_{t,n} : t \geq 0\} \rightarrow \{W_t : t \geq 0\},
\]

where the convergence is in the sense of the weak convergence of random processes in the space \( \mathbb{D}([0, +\infty), \mathbb{R}) \) of càdlàg functions from \( [0, +\infty) \) into \( \mathbb{R} \) equipped with the Skorohod topology.

**Proof of Proposition 3.2.** For the convergence of Lévy processes on the functional space \( \mathbb{D} \), it is sufficient to show the weak convergence of its marginals at unit time (rather than a whole sample path), due to the result of Skorohod [12, Theorem 15.17]. The limiting Gaussian variance is \( \int_{\mathbb{R}_0} z^2 v(dz) \), since for each \( \delta > 0 \), as \( n \uparrow +\infty \),

\[
\left| \int_{|z| \leq \delta} z^2 \nu_n(dz) - \int_{\mathbb{R}_0} z^2 v(dz) \right| = \left| \int_{|z| \geq \sqrt{n} \delta} z^2 v(dz) \right| \rightarrow 0,
\]

since the Lévy measure \( \nu \) has a bounded support. For the drift component, fix \( \delta > 0 \) and observe that as \( n \uparrow +\infty \),

\[
\int_{|z| > \delta} z \nu_n(dz) = \sqrt{n} \int_{|z| > \sqrt{n} \delta} z v(dz) \rightarrow 0,
\]

again as the Lévy measure \( \nu \) has a bounded support. Finally, let \( f \) be a bounded continuous function from \( \mathbb{R} \) to \( \mathbb{R} \) vanishing on a neighborhood of the origin. More precisely, there exist positive constants \( C \) and \( \delta \) such that \( |f| \leq C \) over \( \mathbb{R} \) and \( f(z) \equiv 0 \) on \( [-\delta, +\delta] \). Then, it holds that

\[
\int_{\mathbb{R}_0} f(z) \nu_n(dz) = n \int_{\mathbb{R}_0} f \left( n^{-1/2} z \right) v(dz) \leq n C v \left( (\sqrt{n} \delta, +\sqrt{n} \delta) \right) \rightarrow 0,
\]

where the last convergence holds again by the fact that the Lévy measure \( \nu \) has a bounded support. This completes the proof. \( \square \)

We have seen in Theorem 5.1 that our system (3.1) is nonnegative and compartmental as long as some technical conditions are satisfied. From a theoretical point of view, this brings the field of stochastic compartmental systems forward, as no such conditions have been known for diffusion approximation counterparts. Recall however that continuous-time systems based on a Brownian motion were originally proposed to provide a mathematically tractable diffusion approximation of an otherwise inherent discrete system of molecule dynamics at the sacrifice of nonnegativity. Our approach is thus something going back from such continuous approximations to a more or less discrete formulation. For example, the well-known Gillespie algorithm is an expensive simulation method for the discrete systems, which in some cases can be well approximated by much faster diffusion approximations. (See [22], for example.) If these diffusion approximations were inadequate, it would be reasonable to stick with the original discrete formulation. Indeed, Proposition 3.2 provides a positive answer to this question by showing that driving Lévy processes can be
made as close to the Brownian motion as desired without violating the nonnegativity. This fact does not necessarily imply a similar convergence of our system (3.1) to the corresponding system based on a Brownian motion. (Note that the result of Delgado and Jolis [4] is not applicable to our setting, as the limiting system should not be a Gaussian process.) Our approach is however not debased from a practical standpoint, as the noise terms are meant to act as a perturbation to the deterministic system (2.3), not as the major source of the trajectories, such as in the Black-Scholes model in mathematical finance.

We have listed in Section 2 three possible behaviors for the deterministic system (2.3). Among those, practically most important should be the case (iii), that is, the system with inflows and nonsingular $A$, as the system tends exponentially to a steady state in the nonnegative orthant. For simplicity (and without loss of much reality), we assume that the flow is nonnegative constant, that is, $u(t) \equiv u \in \mathbb{R}_+^f$. We then investigate an important question; whether this system is asymptotically stable around the steady state $x_e := -A^{-1}u$ of the deterministic system (2.3). This is indeed the case as soon as some technical conditions are satisfied.

**Theorem 3.3.** Consider the system (3.1) satisfying the conditions in Theorem 3.1 with nonsingular $A \in \mathcal{H}_n$ and $u(t) \equiv u \in \mathbb{R}_+^f$. Assume that there exist a positive definite matrix $P$ and a symmetric positive definite matrix $Z$ in $\mathbb{R}^{n \times n}$ such that the matrix

$$Z + (P + P^T)A + \sum_{k=1}^{m_1} (A_{\text{inter}}^{(k)})^\top PA_{\text{inter}}^{(k)} \int_{\mathbb{R}_0} z^2 v_k(dz) + \sum_{k=1}^{m_2} (A_{\text{out}}^{(k)})^\top PA_{\text{out}}^{(k)} \int_{\mathbb{R}_0} z^2 v_{m_1+k}(dz) =: Z + B_1,$$

is negative definite. Let $\theta_1 > 0$ and $\theta_2 > 0$ denote the greatest eigenvalues of $(-Z - B_1)^{-1}P$ and of $P^{-1}$, respectively, and define

$$B_2 := \sum_{k=1}^{m_1} (A_{\text{inter}}^{(k)})^\top PA_{\text{inter}}^{(k)} \int_{\mathbb{R}_0} z^2 v_k(dz) + \sum_{k=1}^{m_2} (A_{\text{out}}^{(k)})^\top PA_{\text{out}}^{(k)} \int_{\mathbb{R}_0} z^2 v_{m_1+k}(dz).$$

Then, it holds that for sufficiently large $t$,

$$\mathbb{E} \left[ \|X_t - x_e\|^2 \right] \leq \theta_1 \theta_2 \left( x_e, (B_2^+ Z + \mathbb{I}_n)B_2 x_e \right). \quad (3.7)$$

**Proof.** Define a Lyapunov function $V(x; x_e) := \langle x - x_e, P(x - x_e) \rangle$. It holds by the Ito formula that

$$dV(X_t; x_e) = \mathcal{A}V(X_t; x_e)dt + \sum_{k=1}^{m_1} \int_{\mathbb{R}_0} \left( V \left( X_t + A_{\text{inter}}^{(k)} X_{t-} z; x_e \right) - V(X_t; x_e) \right) (\mu_k - v_k)(dz, dt)
$$

$$+ \sum_{k=1}^{m_2} \int_{\mathbb{R}_0} \left( V \left( X_t + A_{\text{out}}^{(k)} X_{t-} z; x_e \right) - V(X_t; x_e) \right) (\mu_{m_1+k} - v_{m_1+k})(dz, dt),$$

where $\mathcal{A}V(x; x_e) := \langle (x - x_e), B_1(x - x_e) \rangle + \langle (x - x_e), B_2 x_e \rangle + \langle x_e, B_2 x_e \rangle$. Then, with a positive definite matrix $Z$, we get

$$\mathcal{A}V(x; x_e) = \langle x - x_e, B_1(x - x_e) \rangle + 2 \left( (Z^{-1/2})^\top (x - x_e), Z^{1/2} B_2 x_e \right) + \langle x_e, B_2 x_e \rangle
$$

\begin{align*}
&\leq \langle (x - x_e), (B_1 + Z)(x - x_e) \rangle + \langle x_e, (B_2^+ Z + \mathbb{I}_n)B_2 x_e \rangle \\
&\leq -\theta_1^{-1}V(x; x_e) + \langle x_e, (B_2^+ Z + \mathbb{I}_n)B_2 x_e \rangle,
\end{align*}

where we have used $\|x - y\|^2 = \|x\|^2 - 2\langle x, y \rangle + \|y\|^2 \geq 0$ and $\theta_1 \langle x - x_e, (-B_1 - Z)(x - x_e) \rangle \geq V(x; x_e)$ over $\mathbb{R}_+^f$. This indicates that the generator $\mathcal{A}V(x; x_e)$ is negative whenever $V(x; x_e)$ is above the threshold $\theta_1 \langle x_e, (B_2^+ Z + \mathbb{I}_n)B_2 x_e \rangle$. With this, it follows that

$$\mathbb{E} \left[ V \left( X_t; x_e \right) \right] = \mathbb{E} \left[ \int_0^t \mathcal{A}V \left( X_s; x_e \right) ds \right] \leq -\theta_1^{-1} \int_0^t \mathbb{E} \left[ V \left( X_s; x_e \right) \right] ds + t \langle x_e, (B_2^+ Z + \mathbb{I}_n)B_2 x_e \rangle,$$
which shows that $\mathbb{E}[V(X_t; x)]$ is asymptotically bounded by $\theta_1(x, (B_2^T Z + \mathbb{I}_n)B_2 x)$. Finally, the inequality \((3.7)\) holds by $\|x - x_0\|^2 \leq \theta_2 V(x, x_0)$.

We have only investigated in Theorem \([3.3]\) the mean-square stability of practical importance. The proof above can easily be extended to different modes of asymptotic stability with more theoretical flavors, such as the stability in probability due to $\mathcal{A}^2 V(x; 0) \leq 0$ and the almost sure exponential stability under some additional conditions on Lévy measures. We refer the reader to \([2]\) for details.

4 Numerical Illustrations

Consider the system \((3.1)\) with no inflows $u(t) \equiv 0$ and

$$A = \begin{bmatrix} -0.9 & 0.5 & 0.6 \\ 0.3 & -0.7 & 0.2 \\ 0.4 & 0.1 & -0.8 \end{bmatrix}. $$

This indicates that there are outflows from the first and second compartments with the fractional transfer coefficient of 0.1. The matrix $A$ is invertible and negative definite. As there are no inflows, this system would tend to zero at an exponentially fast rate without noise. For $k = 1, 2, 3$ and $n \in \mathbb{N}$, let $\{L_t^{(k)} : t \geq 0\}$ be iid Lévy processes respectively with Lévy measures $\nu_{\lambda, n}(dz) = n(\delta_{z+0.05/\sqrt{n}}(dz) + \delta_{z-0.05/\sqrt{n}}(dz))$ satisfying \((2.1)\) and \((2.2)\), where $\delta_c$ denotes the Dirac delta measure concentrated at $c \in \mathbb{R}$. That is to say, they are iid bilateral symmetric Poisson processes;

$$\left\{ L_t^{(k)} : t \geq 0 \right\} \overset{\mathcal{D}}{=} \left\{ N_{t,n,+0.05/\sqrt{n}} + N_{t,n,-0.05/\sqrt{n}} : t \geq 0 \right\}, \quad (4.1)$$

where $\{N_{t,\lambda, z} : t \geq 0\}$ denotes a Poisson process with intensity $\lambda$ and constant jump size $z \in \mathbb{R}_0$. Obviously, with larger $n$, Poisson processes consist of jumps of smaller size and tend to make jumps much more intensely. Recall that due to Theorem \([3.4]\) our approach requires all Lévy measures to have bounded support. This restriction looks apparently very strong. On the contrary, Proposition \([3.2]\) indicates that Lévy processes with unbounded jump size and/or with infinitely many jumps are not really needed. (Besides, the restriction of bounded support turns out to be useful in the proof of Proposition \([3.2]\). We will shortly observed in Figure \([1]\) and \([2]\) that the bilateral symmetric Poisson process \((4.1)\) does the job.) It is noteworthy that by taking $n$ sufficiently large in \((3.6)\), the condition \((iv)\) in Theorem \([3.1]\) is automatically satisfied. A whole sample path of $\{L_{t,n} : t \in [0, T]\}$ in \((4.1)\) over the finite horizon $[0, T]$ can be exactly generated as follows;

Step 1. Generate $N$ as a Poisson random variable with mean $2nT$.
Step 2. Let $\{T_k\}_{k=1}^{N}$ be a sequence of $N$ iid uniform random variables over $[0, T]$ sorted in ascending order.
Step 3. Let $\{J_k\}_{k=1}^{N}$ be a sequence of $N$ iid uniform random variables on $\{-0.05/\sqrt{n}, +0.05/\sqrt{n}\}$.
Step 4. Set $L_{t,n} = \sum_{k=1}^{N} J_k 1\{T_k \leq t\}$ for every $t \in [0, T]$.

We will generate sample paths of Poisson processes exactly with these steps throughout this section, while with a sufficiently small time stepsize $\Delta > 0$, it is usually sufficient to use the simplest Euler-Maruyama discretization,

$$X_{(n+1)\Delta} = X_{n\Delta} + (AX_{n\Delta} + u(n\Delta))\Delta + \sum_{k=1}^{m_1} A_{\text{inter}}^{(k)} X_{n\Delta} (L_{(n+1)\Delta}^{(k)} - L_{n\Delta}^{(k)}) + \sum_{k=1}^{m_2} A_{\text{out}}^{(k)} X_{n\Delta} (L_{(n+1)\Delta}^{(m_1+k)} - L_{n\Delta}^{(m_1+k)}),$$

which reduces sample path generation to random number generation.
We set the coefficient matrices as 
\[ A_{\text{inter}}^{(1)} = \begin{bmatrix} -0.1 & 0 & 0.5 \\ 0 & 0 & 0 \\ 0.1 & 0 & -0.5 \end{bmatrix}, \quad A_{\text{inter}}^{(2)} = \begin{bmatrix} -0.01 & 0.5 & 0 \\ 0.01 & -0.5 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \quad A_{\text{out}}^{(1)} = \begin{bmatrix} 0.01 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}. \]

The first noise \( \{L_1^{(1)} : t \geq 0\} \) affects the inter-compartmental flow between the first and third compartments; the second noise \( \{L_2^{(2)} : t \geq 0\} \) affects the one between the first and second compartments; the third noise \( \{L_3^{(3)} : t \geq 0\} \) is on the outflow from the first compartment, due to \( A_{\text{out}}^{(1)} \). One can check that all the conditions of Theorem 3.1 are satisfied. In Figure 1, we draw typical sample paths of the three compartments with the initial state \( X_0 = [1.6, 0.2, 0.8]^T \). Observe that nonnegativity of the system is preserved as Theorem 3.1 claims. To illustrate the effect of the scale \( n \) in (4.1), we give two figures corresponding to \( n = 1 \) and \( n = 20 \), respectively. As Proposition 3.2 indicates, the noise on the sample paths with a smaller scale (\( n = 1 \)) looks more Poisson, while it looks more Brownian with a larger scale (\( n = 20 \)). Note that this system is asymptotically mean-square stable around the steady state \( x_e \equiv 0 \) due to Theorem 3.3.

![Typical sample paths](image)

Figure 1: Typical sample paths of the first compartment (\(-\circ\)-), the second (\(-\triangle\)-) and the third (\(-\diamond\)-), with the scale \( n = 1 \) (left) and \( n = 20 \) (right).

To illustrate the mean-square stability result in a more practical setting, we further introduce the nonzero constant inflow \( u(t) \equiv [0.1, 0.2, 0]^T \). The steady state of the corresponding deterministic system (2.3) is then given by 
\[ x_e = -A^{-1}u(t) = [1.0428571, 0.9142857, 0.6357143]^T, \]
and the second moments of the Lévy measures \( \nu_k \) are \( \int_{[0,\infty)} z^2 \nu_k(dz) = 0.005, k = 1, 2, 3 \). We set two positive definite matrices \( P = I_3 \), (that is, \( \theta_2 = 1 \)) and
\[ Z = \begin{bmatrix} 0.6981 & -0.1879 & -0.3631 \\ -0.1879 & 0.6559 & -0.3155 \\ -0.3631 & -0.3155 & 0.7160 \end{bmatrix}, \]
which satisfy the condition of Theorem 3.3 with \( \theta_1 = 8.1819 \). The upper bound in (3.7) is given by
\[ \theta_1 \theta_2 \left\langle x_e, (B_2^T Z + I_3)B_2 x_e \right\rangle = 0.0201, \quad (4.2) \]
where \( I_3 \) is the identity matrix in \( \mathbb{R}^{3 \times 3} \).
Remark 4.1. It is relatively easy to find a symmetric positive definite matrix $Z$, with a positive definite matrix $P$ given, through the following optimization problem formulation

$$\begin{align*}
\min \ & (\text{none}) \\
\text{s.t.} \ & \langle x, Zx \rangle \geq 0, \quad x \in \mathbb{R}^3, \quad (x, (Z + B_1)x) \leq 0, \quad x \in \mathbb{R}^3,
\end{align*}$$

(4.3)

where decision variables are the elements of the symmetric positive definite matrix $Z$. The constraint $\langle x, Zx \rangle \geq 0, x \in \mathbb{R}^3$ indicates that $Z$ is positive semi-definite, the other one $\langle x, (Z + B_1)x \rangle \leq 0, x \in \mathbb{R}^3$ indicates that $Z + B_1$ is negative semi-definite. Note that the optimization is not meant to optimize something but simply to find any feasible solution (that is, the elements of the matrix $Z$). This formulation is then rewritten as an optimization problem under a set of linear equalities and semi-definiteness constraints automatically by SOSTOOLS \[17\], which further sends the resulting optimization problem to an optimization solver, such as SeDuMi \[20\], on MATLAB.

The matrices $P$ and $Z$ satisfying the conditions of Theorem 3.3 are not unique. For example,

$$P = \begin{bmatrix}
1 & 0 & 0 \\
0 & 2 & 0 \\
0 & 0 & 3
\end{bmatrix}, \quad Z = \begin{bmatrix}
1.8470 & -0.2985 & -0.6499 \\
-0.2985 & 1.3512 & -0.5361 \\
-0.6499 & -0.5361 & 0.7910
\end{bmatrix},$$

satisfies the conditions of Theorem 3.3, as well. In this case, we have $(\theta_1, \theta_2) = (1.0301, 1)$ and the upper bound (3.7) is 0.0040, which is much smaller than the previous one 0.0201 in (4.2). It is not clear at the moment how to systematically find the matrices $P$ and $Z$ with minimization of the upper bound (3.7) of the long-run variance.

In Figure 2 we draw a typical set of sample paths of the three compartments $\{X_t: t \geq 0\}$ and a time series of the raw error $\{\|X_t - x_e\|^2: t \geq 0\}$. The expected error $E[\|X_t - x_e\|^2]$ should tend to be smaller than upper bound (3.7) in the long run. The upper bound 0.0040 of of the long-run variance looks very tight.

**Figure 2:** The left figure is a typical set of sample paths with the constant inflow of the first compartment (-o-), the second (-\(\triangle\)-) and the third (-\(\diamondsuit\)-), with the jump scale $n = 20$. The dotted lines indicate the steady state $x_e$. The right figure is a time series $\{\|X_t - x_e\|^2: t \geq 0\}$ of raw error with the dotted line indicating the upper bound of the long-run variance $\lim_{t \to +\infty} E[\|X_t - x_e\|^2]$.  

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5 Concluding Remarks

In this paper, we have achieved stochastic compartmental dynamical system modelling using multidimensional stochastic differential equations, instead of continuous-time Markov chains, with maintaining essential features required for compartmental dynamical systems, such as nonnegativity, appropriate asymptotic behaviors, residence times, and mean-square stability of the steady state. We have provided some simulation outputs to illustrate the effectiveness of our approach and to support the theoretical analysis. Encouraged by its simple model structure with handy simulation methods, our proposed system is expected to be one of standard stochastic compartment models in various fields of application.

There is certainly so much room for improvement through generalizations of model components. First, it is more or less straightforward to allow driving random processes to be time-dependent, that is, Lévy measures depend on time (but still deterministic). Such time-inhomogeneity is of major interest for applications in which the coefficients vary periodically or quasi-periodically. See, for example, [19] for works along this line. Next, instead of deterministic inflows, it might be worth injecting probabilistic flows as environmental stochasticity, as investigated in [18]. Such generalizations will certainly add realism and produce models which may better fit real data. The extension to nonlinear modelling, which causes serious mathematical intractability, would also be interesting, as real compartment systems are unlikely to operate in a simple linear manner. At last but not least, statistical inference and identification of the model structure is certainly a central issue for practical use, based on either partial or perfect information.

References


