A simulation approach to detect oscillating behaviour in stochastic population models

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System parameters and deterministic limit. This work focuses on biological systems modelled as density dependent Markov processes[2]. The dynamics of such systems is often studied by considering the deterministic limit, which is obtained as the solution of a set of Ordinary Differential Equations (ODEs)[1]. The deterministic limit might not capture important system behaviours such as oscillations[2]. The method presented here averages the distances and angles of a number of stochastic simulations to easily detect oscillating behaviours.

System parameters: a) $s \in \mathbb{N}$ and $n \in \mathbb{N}$ are the number of species and events; c) $\mathbf{X}(t) \in \mathbb{N}^q_{\geq 0}$ is the state of the system at time t ($X_i(t)$ denotes the number of elements of species i at time t); d) $\nu \in \mathbb{N}^{q \times n}_{\geq 0}$ is the stoichiometry matrix, i.e., ν^j_i is the change produced in species i by event j; e) $V \in \mathbb{R}_{>0}$ is the system size; f) $W_j : \mathbb{R}^q_{\geq 0} \times \mathbb{R}_{>0} \to \mathbb{R}_{\geq 0}$ is the transition rate function, i.e, $W_j(\mathbf{X}(t), V)$ is the rate associated to event j for population $\mathbf{X}(t)$ and system size V (for conciseness, we will use $\mathbf{X}$ rather than $\mathbf{X}(t)$, and $W_j(\mathbf{X})$ rather than $W_j(\mathbf{X}(t), V)$).

The system is modelled as a jump Markov process in which events are exponentially distributed with rates $W_j(\mathbf{X})$. The occurrence of an event j changes the system state from $\mathbf{X}$ to $\mathbf{X} + \nu^j$. Functions $W_j(\mathbf{X})$ are assumed to be differentiable, nonnegative, time independent and to satisfy the mass-action law[2].

Deterministic limit: Under some conditions[1] on $W_j(\mathbf{X})$, the deterministic limit behaviour is given by the following set of ODEs: $\frac{dX_i}{dt} = \sum_{j=1}^{n} \nu^j_i W_j(\mathbf{X})$.

Method. Consider the trajectories obtained for two stochatic simulations. When computing the mean populations, one averages the cartesian coordinates of the populations in the phase space. Nevertheless, other coordinate systems, e.g., polar coordinates if $s = 2$, can be considered. Figure 1(a) shows the result of averaging the cartesian and polar coordinates of two states.

Let us describe how to average the polar coordinates of a number of stochastic simulations (for systems with $s > 2$, hyperspherical coordinates can be used). Assume that M stochastic simulations have been performed, and the trajectories have been resampled at same sampling times. Let (X^0_q, Y^0_q), (X^1_q, Y^1_q), $\ldots$, be the cartesian coordinates of simulation $q \in \{1 \ldots M\}$ at the sampling times. Let the origin of the polar coordinate system be the reference point a with cartesian coordinates (a_x, a_y). Each (X^k_q, Y^k_q) can be transformed to polar coordinates (ρ^k_q, θ^k_q) with origin at a by using: $\rho^k_q = \sqrt{(X^k_q - a_x)^2 + (Y^k_q - a_y)^2}$, $\theta^k_q = \operatorname{atan}(Y^k_q - a_y, X^k_q - a_x)$ where $\operatorname{atan}(y, x) : \mathbb{R} \times \mathbb{R} \to \mathbb{R}$ is the arctangent of a point with cartesian coordinates (x, y) that takes into account the quadrant. We will assume that the range of $\operatorname{atan}(y, x)$ is $(-\pi, \pi]$ and that $\operatorname{atan}(0, 0) = 0$. This straightforwad transformation to polar coordinates poses a problem when averaging θ: if at step k, θ^k_i is positive and close to π while θ^k_j is negative and

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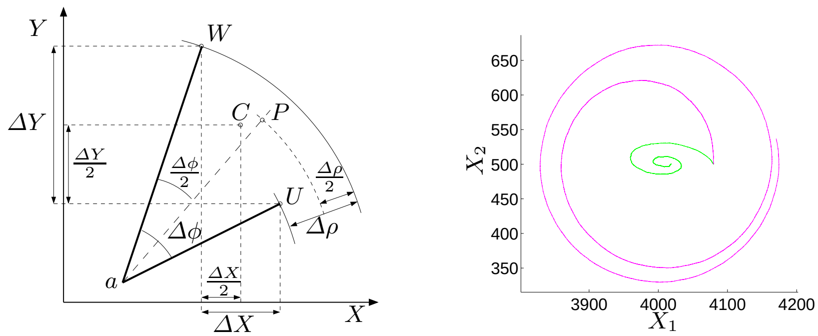

(a) (b)

Fig. 1. (a) Average cartesian (C) and polar (P) coordinates of U and W with respect to a; (b) Average cartesian and polar trajectories.

close to $-\pi$, the mean of will be close to 0 what is not a useful average. To overcome this problem, we define a new value ϕ_q^k to account for the overall angular distance run by the trajectory. Let us define $\phi_q^0 = \theta_q^0$, and for each $k \geq 0$, let us express ϕ_q^k as $\phi_q^k = z_q^k 2\pi + h_q^k$, with $z_q^k \in \mathbb{Z}$ and $-\pi < h_q^k \leq \pi$, i.e, z_q^k is the number of completed loops and h_q^k is the angular distance run on the current loop. The value of z_q^k is positive(negative) if the angular distance was run anticlockwise(clockwise). Then, for $k > 0$, ϕ_q^k can be computed as follows:

$$\phi_q^k = \begin{cases} z_q^{(k-1)} 2\pi + \theta_q^k + 2\pi & \text{if } h_q^{(k-1)} > \frac{\pi}{2} \text{ and } \theta_q^k < -\frac{\pi}{2} \\ z_q^{(k-1)} 2\pi + \theta_q^k - 2\pi & \text{if } h_q^{(k-1)} < -\frac{\pi}{2} \text{ and } \theta_q^k > \frac{\pi}{2} \\ z_q^{(k-1)} 2\pi + \theta_q^k & \text{otherwise} \end{cases}$$

The first(second) case of the expresion account for the discontinuity of the angle returned by atan when the trajectory moves from the second to the third(from the third to the second) quadrant. An average trajectory in polar coordinates is obtained as the mean of ρ_q^k and ϕ_q^k over all simulations.

Results. Consider the following system[2]: $s = 2$; $n = 5$; $\nu = \left(\begin{smallmatrix} 1 & -1 & -1 & 1 & 0 \\ 0 & 0 & 1 & -1 & -1 \end{smallmatrix}\right)$; $V = 5 \cdot 10^3$; $W_1 = \frac{X_1 + X_2}{1 + (0.4 \cdot (X_1 + X_2))/V}$, $W_2 = 0.2 \cdot X_1$, $W_3 = 10 \cdot X_1 \cdot X_2 / V$, $W_4 = 3 \cdot X_2$ and $W_5 = 5 \cdot X_2$ with initial populations $X_1(0) = 4080$ and $X_2(0) = 500$. The system has a unique non extinction fixed point $a = (4000, 502)$ which is taken as origin of the polar coordinate system. Figure 1(b) shows the average trajectories of 5000 simulations. The trajectory tending to a is the average of the cartesian coordinates, while the trajectory tending to a steady oscillation is the average of the polar coordinates. The interpretetation is that simulation trajectories tend to loop around the fixed point at an average distance of 170. Thus, while the cartesian mean informs about the trajectory of the *center of mass* of the simulations, the polar mean informs about the average *circular motion* what uncovers the undamped oscillations reported in[2].

References. 1. S. Ethier and T. Kurtz. *"Markov Processes: Characterization and Convergence"*. John Wiley, 1986.

2. M. Natiello and H. Solari. *"Blowing-up of Deterministic Fixed Points in Stochastic Population Dynamics"*. Mathematical Biosciences, 209(2):319335, 2007.