Computation of approximate mean and covariance for a generic propensity function to be used in stochastic simulations

Following a procedure similar to one proposed in [1], we derive an ODE system of the mean and covariance of the number of molecules. For a chemical reaction system with $N_r$ reactions and $N_s$ species, the governing equation is the chemical master equation (CME; Equation (21)).

With simplified notation $P(x, t) \triangleq P(x, t \mid x_0, t_0)$, CME becomes

$$\frac{\partial P(x, t)}{\partial t} = \sum_{r=1}^{N_r} \left[ \alpha_r(x - v_r) P(x - v_r, t) - \alpha_r(x) P(x, t) \right] \quad (A.1)$$

By multiplying (A.1) with $x_s$ and then summing over all the possible states $x$, we obtain

$$\sum_x x_s \frac{\partial P(x, t)}{\partial t} = \sum_{r=1}^{N_r} \sum_x x_s \left[ \alpha_r(x - v_r) P(x - v_r, t) - \alpha_r(x) P(x, t) \right] \quad (A.2)$$

Because the sum in the first term of the right-hand side covers all $x$, we are allowed to renumber terms and to replace $x - v_r \rightarrow x$, which yields

$$\frac{\partial E[X_s]}{\partial t} = \sum_{r=1}^{N_r} \sum_x \left[ (x_s + v_{r,s}) \alpha_r(x) P(x_r, t) - x_s \alpha_r(x) P(x, t) \right]$$

$$= \sum_{r=1}^{N_r} \sum_x \left[ v_{r,s} \alpha_r(x) P(x_r, t) \right]$$

$$= \sum_{r=1}^{N_r} v_{r,s} E[\alpha_r(X)] \quad (A.3)$$

where $v_{r,s}$ is the $s^{th}$ component of vector $v_r$. 


Additional file 2
In order to obtain the second central moment, we denote \( \mu_s(t) = E[X_s(t)] \), multiply eqn. (A.1) by \((x_i - \mu_i)(x_j - \mu_j)\), and sum over all possible states. The result is

\[
\sum_x (x_i - \mu_i)(x_j - \mu_j) \frac{\partial P(x, t)}{\partial t} = \sum_{r=1}^N \sum_x (x_i - \mu_i)(x_j - \mu_j) \left[ \alpha_r(x - v_r)P(x - v_r, t) - \alpha_r(x)P(x, t) \right].
\]  

(A.4)

Again transforming the first term of the left-hand side with the replacement \( x - v_r \rightarrow x \) we obtain

\[
\frac{\partial E[(X_i - \mu_i)(X_j - \mu_j)\alpha_r(x)]}{\partial t} = \sum_{r=1}^N \sum_x \left( v_{r,i}(x_j - \mu_j) + v_{r,j}(x_i - \mu_i) + v_{r,i}v_{r,j} \alpha_r(x)P(x, t) \right) - (x_i - \mu_i)(x_j - \mu_j)\alpha_r(x)P(x, t)
\]  

(A.5)

\[
= \sum_{r=1}^N \sum_x \left( v_{r,i}E[(X_j - \mu_j)\alpha_r(X)] + v_{r,j}E[(X_i - \mu_i)\alpha_r(X)] + v_{r,i}v_{r,j}E[\alpha_r(X)] \right),
\]

where \( i, j = 1, \ldots, N_s \). With these results, we can now approximate the propensity function \( \alpha_r(x) \) using a second-order Taylor expansion at \( X = \mu \), which leads to the following result:

\[
\alpha_r(x) \approx \alpha_r(\mu) + \sum_{s=1}^{N_s} \frac{\partial \alpha_r(\mu)}{\partial X_s}(X_s - \mu_s) + \frac{1}{2} \sum_{m,n=1}^{N_s} \frac{\partial^2 \alpha_r(\mu)}{\partial X_m \partial X_n}(X_m - \mu_m)(X_n - \mu_n).
\]  

(A.6)

The approximation becomes exact when \( \alpha_r(x) \) is a linear or quadratic function, which is the case for elementary reactions. Furthermore, its expectation is
\[ E[\alpha_r(X)] \approx \alpha_r(\bm{\mu}) + \frac{1}{2} \sum_{m,n=1}^{N_r} \frac{\partial^2 \alpha_r(\bm{\mu})}{\partial X_m \partial X_n} E[(X_m - \mu_m)(X_n - \mu_n)]. \]  \hspace{1cm} (A.7)

Similarly,

\[ E[(X_i - \mu_i)\alpha_r(X)] \approx \sum_{s=1}^{N_r} \frac{\partial \alpha_r(\bm{\mu})}{\partial X_s} E[(X_i - \mu_i)(X_s - \mu_s)] \]
\[ + \frac{1}{2} \sum_{m,n=1}^{N_r} \frac{\partial^2 \alpha_r(\bm{\mu})}{\partial X_m \partial X_n} E[(X_i - \mu_i)(X_m - \mu_m)(X_n - \mu_n)]. \]  \hspace{1cm} (A.8)

Substituting eqns. (A.5) and (A.6) into (A.1) and (A.3), we obtain

\[ \frac{\partial E[X_s]}{\partial t} \approx \sum_{r=1}^{N_r} \sum_{i=1}^{N_r} v_{r,i} \left\{ \alpha_r(\bm{\mu}) + \frac{1}{2} \sum_{m,n=1}^{N_r} \frac{\partial^2 \alpha_r(\bm{\mu})}{\partial X_m \partial X_n} E[(X_m - \mu_m)(X_n - \mu_n)] \right\}. \]  \hspace{1cm} (A.9)

and

\[ \frac{\partial E[(X_i - \mu_i)(X_j - \mu_j)]}{\partial t} \]
\[ = \sum_{r=1}^{N_r} \left\{ v_{r,i} \sum_{s=1}^{N_r} \frac{\partial \alpha_r(\bm{\mu})}{\partial X_s} E[(X_j - \mu_j)(X_s - \mu_s)] \right\} \]
\[ + v_{r,i} \sum_{m,n=1}^{N_r} \frac{\partial^2 \alpha_r(\bm{\mu})}{\partial X_m \partial X_n} E[(X_j - \mu_j)(X_m - \mu_m)(X_n - \mu_n)] \]
\[ + v_{r,i} \sum_{s=1}^{N_r} \frac{\partial \alpha_r(\bm{\mu})}{\partial X_s} E[(X_i - \mu_i)(X_s - \mu_s)] \]
\[ + v_{r,i} \sum_{m,n=1}^{N_r} \frac{\partial^2 \alpha_r(\bm{\mu})}{\partial X_m \partial X_n} E[(X_i - \mu_i)(X_m - \mu_m)(X_n - \mu_n)] \]
\[ + v_{r,i} v_{r,j} \left\{ \alpha_r(\bm{\mu}) + \frac{1}{2} \sum_{m,n=1}^{N_r} \frac{\partial^2 \alpha_r(\bm{\mu})}{\partial X_m \partial X_n} E[(X_m - \mu_m)(X_n - \mu_n)] \right\}. \]  \hspace{1cm} (A.10)
Finally, we denote $\sigma_{ij} = E[(X_i - \mu_i)(X_j - \mu_j)]$ and $\sigma_{ijk} = E[(X_i - \mu_i)(X_j - \mu_j)(X_k - \mu_k)]$ and obtain the mean and second central moment as

$$\frac{\partial \mu_j}{\partial t} \approx \sum_{r=1}^{N_r} \sum_{s=1}^{N_s} \nu_{r,s} \left\{ \alpha_{j}(\mu) + \frac{1}{2} \sum_{m,n=1}^{N_m} \frac{\partial^2 \alpha_{j}(\mu)}{\partial X_m \partial X_n} \sigma_{mn} \right\}$$

$$\frac{\partial \sigma_{ij}}{\partial t} \approx \sum_{r=1}^{N_r} \left\{ \nu_{r,j} \sum_{s=1}^{N_s} \frac{\partial \alpha_{j}(\mu)}{\partial X_s} \sigma_{js} + \nu_{r,j} \sum_{s=1}^{N_s} \frac{\partial \alpha_{j}(\mu)}{\partial X_s} \sigma_{is} + \nu_{r,i} \nu_{r,j} \left[ \alpha_{j}(\mu) + \frac{1}{2} \sum_{m,n=1}^{N_m} \frac{\partial^2 \alpha_{j}(\mu)}{\partial X_m \partial X_n} \sigma_{mn} \right] \right\} + \frac{1}{2} \sum_{m,n=1}^{N_m} \frac{\partial^2 \alpha_{j}(\mu)}{\partial X_m \partial X_n} \sigma_{mn}.$$

If the system is assumed to have a symmetric distribution such as multivariate normal distribution [2], then the third central moment is zero and we can obtain closed-form expressions for the mean and covariance equations, namely

$$\frac{\partial \mu_j}{\partial t} \approx \sum_{r=1}^{N_r} \sum_{s=1}^{N_s} \nu_{r,s} \left\{ \alpha_{j}(\mu) + \frac{1}{2} \sum_{m,n=1}^{N_m} \frac{\partial^2 \alpha_{j}(\mu)}{\partial X_m \partial X_n} \sigma_{mn} \right\}$$

(A.11)

$$\frac{\partial \sigma_{ij}}{\partial t} \approx \sum_{r=1}^{N_r} \left\{ \nu_{r,j} \sum_{s=1}^{N_s} \frac{\partial \alpha_{j}(\mu)}{\partial X_s} \sigma_{js} + \nu_{r,j} \sum_{s=1}^{N_s} \frac{\partial \alpha_{j}(\mu)}{\partial X_s} \sigma_{is} + \nu_{r,i} \nu_{r,j} \left[ \alpha_{j}(\mu) + \frac{1}{2} \sum_{m,n=1}^{N_m} \frac{\partial^2 \alpha_{j}(\mu)}{\partial X_m \partial X_n} \sigma_{mn} \right] \right\} + \frac{1}{2} \sum_{m,n=1}^{N_m} \frac{\partial^2 \alpha_{j}(\mu)}{\partial X_m \partial X_n} \sigma_{mn}.$$  

(A.12)

Reference