processes

MDPI

Supplemental Materials:

Derivation for the direct average formula

Let us consider the Equation (12)

$$Z_{n+1} = \overline{Z}_{n+1} + (I - hf'(\overline{Z}_{n+1}))^{-1} h(f(\overline{Z}_{n+1}) - f(Z_n))$$

h is the time step and is picked to be very small. f is the regular rate law and hence has the polynomial form. The system that we work on has low numbers in particles for most species. Therefore, $0 < hf' \ll 1$. Applying power expansion, we have:

$$(I - hf'(\overline{Z}_{n+1}))^{-1} \approx I + hf'(\overline{Z}_{n+1}) + h^2[f'(\overline{Z}_{n+1})]^2$$

Hence,

$$\begin{aligned}
&(I - hf'(\overline{Z}_{n+1}))^{-1} h(f(\overline{Z}_{n+1}) - f(Z_n)) \simeq \{I + hf'(\overline{Z}_{n+1}) + h^2[f'(\overline{Z}_{n+1})]^2\} h(f(\overline{Z}_{n+1} \\
&\simeq hf(\overline{Z}_{n+1}) - hf(Z_n)) + h^2 f'(\overline{Z}_{n+1}) f(\overline{Z}_{n+1}) - h^2 f'(\overline{Z}_{n+1}) f(Z_n)
\end{aligned}$$

Also using Taylor's expansion we have:

$$\begin{aligned}
f^j(\overline{Z}_{n+1}) \simeq\ & f^j(E\overline{Z}_{n+1}) + Df^j(Z)|_{E\overline{Z}_{n+1}} (\overline{Z}_{n+1} - E\overline{Z}_{n+1}) \\
& + 1/2(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T Hf^j(Z)|_{E\overline{Z}_{n+1}} (\overline{Z}_{n+1} - E\overline{Z}_{n+1})
\end{aligned}$$

$$\begin{aligned}
Df^j(\overline{Z}_{n+1}) \simeq\ & D(f^{j_1})^{,j_2}(Z)|_{E\overline{Z}_{n+1}} + DD(f^{j_1})^{,j_2}(Z)|_{E\overline{Z}_{n+1}} (\overline{Z}_{n+1} - E\overline{Z}_{n+1}) \\
& + 1/2(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T HD(f^{j_1})^{,j_2}(Z)|_{E\overline{Z}_{n+1}} (\overline{Z}_{n+1} - E\overline{Z}_{n+1})
\end{aligned}$$

$$\begin{aligned}
f^{j_1}(\overline{Z}_{n+1}) D(f^{j_2})^{j_3}(\overline{Z}_{n+1}) \simeq\ & f^{j_1}(E\overline{Z}_{n+1}) D(f^{j_2})^{j_3}(Z)|_{E\overline{Z}_{n+1}} + \\
& + [(D(f^{j_2})^{j_3}(Z) Df^{j_1}(Z)^T |_{E\overline{Z}_{n+1}} + f^{j_1}(E\overline{Z}_{n+1}) DD(f^{j_2})^{j_3}(Z)](\\
& + 1/2(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T \nabla[(D(f^{j_2})^{j_3}(Z) Df^{j_1}(E\overline{Z}_{n+1})^T |_{E\overline{Z}_{n+1}} \\
& + f^{j_1}(E\overline{Z}_{n+1}) DD(f^{j_2})^{j_3}(Z)]|_{E\overline{Z}_{n+1}} (\overline{Z}_{n+1} - E\overline{Z}_{n+1}) \\
\simeq\ & f^{j_1}(E\overline{Z}_{n+1}) D(f^{j_2})^{j_3}(Z)|_{E\overline{Z}_{n+1}} + \\
& + [(D(f^{j_2})^{j_3}(Z) Df^{j_1}(Z)|_{E\overline{Z}_{n+1}} + f^{j_1}(E\overline{Z}_{n+1}) DD(f^{j_2})^{j_3}(Z)|_{E} \\
& + 1/2(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T \{(DD(f^{j_2})^{j_3}(Z) Df^{j_1}(Z)^T |_{E\overline{Z}_{n+1}} + D(f \\
& + \mathrm{D}f^{j_1}(Z) DD(f^{j_2})^{j_3}(Z)]|_{E\overline{Z}_{n+1}} + f^{j_1}(\overline{EZ}_{n+1}) HD(f^{j_2})^{j_3}(Z)]|
\end{aligned}$$

$$f^j(Z_n) \simeq f^j(EZ_n) + Df^j(Z)|_{E\overline{Z}_{n+1}} (Z_n - EZ_n) + 1/2(Z_n - EZ_n)^T Hf^j(Z)|_{E\overline{Z}_{n+1}} (Z_n - EZ$$

$$
\begin{aligned}
f^{j_1}(Z_n)D(f^{j_2})^{j_3}(\overline{Z}_{n+1}) &= (f^{j_1}(EZ_n) + Df^{j_1}(Z)|_{E\overline{Z}_{n+1}}(Z_n - EZ_n) \\
&+1/2(Z_n - EZ_n)^T Hf^{j_1}(Z)|_{E\overline{Z}_{n+1}}(Z_n - EZ_n)) \\
&+(D(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}} + DD(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}(\overline{Z}_{n+1} - E\overline{Z}_{n} \\
&+1/2(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T HD(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}(\overline{Z}_{n+1} - E\overline{Z}_{n+1} \\
&\simeq f^{j_1}(EZ_n)D(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}} \\
&+[f^{j_1}(EZ_n)DD(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}](\overline{Z}_{n+1} - E\overline{Z}_{n+1}) \\
&+[D(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}} Df^{j_1}(Z)|_{E\overline{Z}_{n+1}}](Z_n - EZ_n) \\
&+1/2 f^{j_1}(EZ_n)(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T HD(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}(\overline{Z}_{n+1} \\
&+(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T Df^{j_1}(Z)|_{E\overline{Z}_{n+1}} DD(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}(Z_n \\
&+1/2(Z_n - EZ_n)^T Hf^{j_1}(Z)|_{E\overline{Z}_{n+1}} D(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}(Z_n -
\end{aligned}
$$

Applying the expected operator to both sides of the equation, we have:

$$
\begin{aligned}
EZ_{n+1}^j &= E\overline{Z}_{n+1}^j + E(I - hf'(\overline{Z}_{n+1}))^{-1} h(f(\overline{Z}_{n+1}) - f(Z_n))^{,j} \\
&= E\overline{Z}_{n+1}^j + E[hf(Z_n) - hf(Z_n)) + h^2 f'(Z_n)|_{\overline{Z}_{n+1}} f(\overline{Z}_{n+1}) - h^2 f'(Z_n)|_{\overline{Z}_{n+1}} f(\\
&= E\overline{Z}_{n+1}^j + h\{f^j(E\overline{Z}_{n+1}) + 1/2E[(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T Hf^j(Z)|_{E\overline{Z}_{n+1}}(\overline{Z}_{n+1} - E\overline{Z} \\
&- f^j(EZ_n) - 1/2(Z_n - EZ_n)^T Hf^j(Z)|_{EZ_n}(Z_n - EZ_n)\} + \\
&+ h^2\{f^j(\overline{EZ}_{n+1})D(f^{j_2})^{j_3}(\overline{Z}_{n+1})|_{E\overline{Z}_{n+1}} + \\
&+1/2E\{(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T\{(DD(f^{j_2})^{j_3}(Z)Df^j(Z)^T|_{E\overline{Z}_{n+1}} + D(f^{j_2})^{j_3}(Z)H_j \\
&+\mathrm{D}f^j(Z)DD(f^{j_2})^{j_3}(Z)]|_{E\overline{Z}_{n+1}} + f^j(E\overline{Z}_{n+1})HD(f^{j_2})^{j_3}(Z)]|_{E\overline{Z}_{n+1}}\}(\overline{Z}_{n+1} - \\
&- h^2\{f^{j_1}(EZ_n)D(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}} \\
&+1/2E\{f^{j_1}(EZ_n)(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T HD(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}(\overline{Z}_{n+1} - E\overline{Z}_{n+1}))\} \\
&+\mathrm{E}\{(\overline{Z}_{n+1} - E\overline{Z}_{n+1})^T Df^{j_1}(Z)|_{E\overline{Z}_{n+1}} DD(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}(Z_n - EZ_n)\} \\
&+1/2\{(Z_n - EZ_n)^T Hf^{j_1}(Z)|_{E\overline{Z}_{n+1}} D(f^{j_2})^{,j_3}(Z)|_{E\overline{Z}_{n+1}}(Z_n - EZ_n))\}\}
\end{aligned}
$$

Similarly, we can apply the same method to Equation (13):

$$
\begin{aligned}
g^{j_1}(Z_n)D(g^{j_2})^{j_3}(Z_n) &\simeq g^{j_1}((EZ_n)D(g^{j_2})^{j_3}((Z)|_{EZ_n} + \\
&+[(D(g^{j_2})^{j_3}(Z)Df^{j_1}(Z)^T|_{EZ_n} + g^{j_1}(EZ_n)DD(g^{j_2})^{j_3}(Z)](Z_n - EZ_n) + \\
&+1/2(Z_n - EZ_n)^T\nabla[(D(g^{j_2})^{j_3}(Z)Dg^{j_1}(Z)^T|_{E\overline{Z}_{n+1}} \\
&+ g^{j_1}(EZ_n)DD(g^{j_2})^{j_3}(Z)]|_{E\overline{Z}_{n+1}}(Z_n - EZ_n) \\
&\simeq g^{j_1}(EZ_n)D(g^{j_2})^{j_3}(Z)|_{EZ_n} + \\
&+[(D(g^{j_2})^{j_3}(Z)Dg^{j_1}(Z)^T|_{EZ_n} + g^{j_1}(EZ_n)DD(g^{j_2})^{j_3}(Z)](Z_n - EZ_n) + \\
&+1/2(Z_n - EZ_n)^T\{(DD(g^{j_2})^{j_3}(Z)Dg^{j_1}(Z)^T|_{EZ_n} + D(g^{j_2})^{j_3}(Z)Hg^{j_1}(Z)^T|_{EZ} \\
&+\mathrm{D}g^{j_1}(Z)DD(g^{j_2})^{j_3}(Z)]|_{EZ_n} + g^{j_1}(EZ_n)HD(g^{j_2})^{j_3}(Z)]|_{EZ_n}\}(Z_n - EZ_n)
\end{aligned}
$$

Applying the expected operator to both sides of the equation, we have:

$$
\begin{aligned}
E\overline{Z}_{n+1}^{j} &= EZ_n^j + hf^j(Z_n) + E\sum_{j_2=1}^{m}\sum_{j_1=1}^{m} g^{j_1} D(g^{j_2})^j (Z_n) EI_{(j_1,j_2)} \\
&= EZ_n^j + hf^j(Z_n) + g^{j_1}(EZ_n) D(g^{j_2})^j (Z)|_{EZ_n} \\
&+1/2E\{(Z_n - EZ_n)^T \{(DD(g^{j_2})^j (Z) Dg^{j_1}(Z)^T |_{EZ_n} + D(g^{j_2})^j (Z) Hg^{j_1}(Z)^T \\
&+\mathrm{D}g^{j_1}(Z) DD(g^{j_2})^j (Z)]|_{EZ_n} \\
&+ g^{j_1}(EZ_n) HD(g^{j_2})^j (Z)]|_{EZ_n}\}(Z_n - EZ_n)\} E(\int_{t_n}^{t_{n+1}}\int_{t_n}^{s_2} dW^{j_1}(s_1) dW^{j_2}(s_2))^j
\end{aligned} \tag{1}
$$

We can also evaluate the last term from the above equation

$$
E(\int_{t_n}^{t_{n+1}}\int_{t_n}^{s_2} dW^{j_1}(s_1) dW^{j_2}(s_2)) = \begin{cases} -h & \text{, if } j_1 \neq j_2 \\ 0 & \text{, if } j_1 = j_2 \end{cases} \tag{2}
$$

Reaction kinetics:

Table S1. Reactions and kinetic parameters.

	Reactions	Kinetic Parameters	Reaction Type
1	$X_4 + 4i \rightarrow X_4 i_4$	8.016×10^7 ($M^{-1}s^{-1}$)	1st order on i, 1st order on x_4
2	$X_4 + 4c \rightarrow X_4 c_4$	1.377×10^8 ($M^{-1}s^{-1}$)	1st order on c, 1st order on x_4
3	$B + X_4 \rightleftarrows BX_4$	F: 10^6 ($M^{-1}s^{-1}$) R: 10^{-1} (s^{-1})	(parameters base on the lacI)
4	$B + X_4 i_4 \rightleftarrows BX_4 i_4$	F: 10^8 ($M^{-1}s^{-1}$) R: 10^{-3} (s^{-1})	
5	$B + X_4 c_4 \rightleftarrows BX_4 c_4$	F: 10^9 ($M^{-1}s^{-1}$) R: 10^{-2} (s^{-1})	
6	$\xrightarrow{Pq-Induced} Q_{pre} \quad (Induced: B)$	0.1 (s^{-1})	1st order on B
7	$\xrightarrow{Pq-Induced} Q_{pre} \quad (Uninduced: BX_4 c_4)$	0.1(s^{-1})	1st order on $BX_4 c_4$
8	$\xrightarrow{Pq-Uninduced} Q_{pre} \quad (Uninduced: BX_4)$	0.000723 (s^{-1})	1st order on BX_4
9	$\xrightarrow{Pq-Uninduced} Q_{pre} \quad (Uninduced: BX_4 i_4)$	0.000723 (s^{-1})	1st order on $BX_4 i_4$
10	$\xrightarrow{Px-Induced} Q_a \quad (Induced: B)$	0.00121 (s^{-1})	1st order on B
11	$\xrightarrow{Px-Uninduced} Q_a \quad (Uninduced: BX_4 c_4)$	0.00121 (s^{-1})	1st order on $BX_4 c_4$
12	$\xrightarrow{Px-Uninduced} Q_a \quad (Uninduced: \mathrm{B} X_4)$	0.00823 (s^{-1})	1st order on BX_4
13	$\xrightarrow{Px-Uninduced} Q_a \quad (Uninduced: BX_4 i_4)$	0.00823 (s^{-1})	1st order on $BX_4 i_4$
14	$Q_{pre} \longrightarrow Q_L$ *	1 (s^{-1})	(the time for transcript the length from Px to pass IRS1, roughly 1s)
15	$Q_{pre} + Q_a \longrightarrow Q_s$	4.43×10^9 ($M^{-1}s^{-1}$)	From previous Kq = 4.43(nM^{-1}); $4.43 \times (6 \times 10^8)/0.6$, the latter is one reaction per second PS. 1nM ≈ 0.6 particle per cell for cell volume
16	$\xrightarrow{Q_s + Q_L} I_{ex}$	0.5(s^{-1}) × delta	delta is volume conversion factor, $\times 10^{-3}$ for 10^9 cells/ml
17	$I_{ex} \xrightarrow{uptake} i$	0.001 (s^{-1})	
18	$C_{ex} \xrightarrow{uptake} c$	0.001 (s^{-1})	
19	$\xrightarrow{Px-Induced} prgX \quad (Induced: B)$	0.000121 (s^{-1})	1st order on B

20	$\xrightarrow{Px-Induced} prgX \quad (Uninduced : BX_4c_4)$	0.000121 (s^{-1})	1st order on BX_4c_4
21	$\xrightarrow{Px-Uninduced} prgX \quad (Uninduced : BX_4)$	0.001021 (s^{-1})	1st order on BX_4
22	$\xrightarrow{Px-Induced} prgX \quad (Uninduced : BX_4i_4)$	0.001021 (s^{-1})	1st order on BX_4i_4
23	$\xrightarrow{prgX} X_2$	0.005 (s^{-1})	
24	$2X_2 \rightleftarrows X_4$	F: 1×10^5 ($M^{-1}s^{-1}$) R: 0.01 (s^{-1})	

Table S2. Degradation rates for different species.

Species	Degradation Rate (1/s)
X_4	1×10^{-5}
X_4i_4	1×10^{-5}
i	1×10^{-5}
X_4c_4	1×10^{-5}
c	1×10^{-5}
B	-
BX_4	-
BX_4i_4	-
BX_4c_4	-
Q_{pre}	-
Q_a	1×10^{-3}
Q_L	1×10^{-4}
Q_s	2×10^{-3}
I_{ex}	1×10^{-5}
C_{ex}	1×10^{-5}
$prgX$	2×10^{-4}
X_2	1×10^{-5}