Appendix 1: The Time Evolution Equation for the Mean

X ⇌ B Process:

In the main body of the paper we defined the two random variables $N_X(t + dt)$ and $N_X(t)$ as the number of molecules of X in $t + dt$ and t respectively, and established that since in dt at most one reaction can take place, the difference between them, *i.e.*,

$$dN_x(t) = N_X(t + dt) - N_X(t) \qquad (A.1)$$

can only take the values -1, 0 and 1.

In probability theory, the mean or expected value of a random variable Y is defined as

$$< Y > = \sum_{i=1}^{I} y_i P(Y = y_i) \qquad (A.2)$$

where I is the number of possible values of Y and P the probability of each value of Y.

For the following development, we need to calculate the mean of $dN(t)$

$$< dN_x(t) > = 0 \times P(dN_X(t) = 0) + 1 \times P(dN_X(t) = 1) + (-1) \times P(dN_X(t) = -1).$$

If we apply the theorem of total probability (1), we obtain for the mean:

$$< dN_X(t) >= P(dN_X(t) = 1) - P(dN_X(t) = -1) =$$

$$= \sum_{i=0}^{\infty} P(N_X(t) = i) P(dN_X(t) = 1 \mid N_X(t) = i) - \sum_{i=0}^{\infty} P(N_X(t) = i) P(dN_X(t) = -1 \mid N_X(t) = i) =$$

$$=< W_+(N_X(t)) > dt - < W_-(N_X(t)) > dt$$

For the first example, substituting the expressions of $W_+(N_x(t))$ and $W_-(N_X(t))$ (from Eqs. 7 and 8), taking into account that $< dN_X(t) >= d < N_X(t) >$, dividing by dt, and taking the limit $dt \to 0$, we obtain:

$$\frac{d < N_X(t) >}{dt} = k_2 N_B - k_1 < N_X(t) >$$

(A.3)

In this example $\frac{dN_X(t)}{dt}$ and $\frac{d < N_X(t) >}{dt}$ are equivalent, because $W_+(N_X(t))$ and $W_-(N_X(t))$ are linear functions of $N_X(t)$.

Schlögl Process:

In the reaction $A+2X \rightleftharpoons 3X$, the number of combinations of reactant molecules is $\frac{N_A N_X(t)(N_X(t) - 1)}{2!}$ for the forward reaction and $\frac{N(t)_X(N_X(t) - 1)(N_X(t) - 2)}{3!}$ for the reverse reaction.

In the reaction $B \rightleftharpoons X,$ the number of reactant molecules will be N_B and $N_x(t)$ for the forward and reverse reactions respectively.

Therefore, the positive functions $W_+(t)$ and $W_-(t)$ defined above will be:

$$W_+(N_X(t)) = \frac{k_1 N_A N_X(t)(N_X(t)-1)}{2!} + k_3 N_B \qquad \text{(A.4)}$$

$$W_-(N_X(t)) = \frac{k_2 N_X(t)(N_X(t)-1)(N_X(t)-2)}{3!} + k_4 N_X(t) \qquad \text{(A.5)}$$

.

To make the deterministic and average stochastic time evolutions equivalent, we have to make the approximations $<N_X{}^3(t)>=<N_X(t)>^3$ and $<N_X{}^2(t)>=<N_X(t)>^2$. The larger $N_X(t)$ is, the more precise the approximation will be (10).

Final State Calculation

The condition of final state in the stochastic approach, $W_+(N_X(t)) = W_-(N_X(t))$ implies

$$\frac{k_1 N_A N_X(t)(N_X(t)-1)}{2!} + k_3 N_B = \frac{k_2 N_X(t)(N_X(t)-1)(N_X(t)-2)}{3!} + k_4 N_X(t) \qquad \text{(A.6)}$$

which is also the final state condition of the deterministic approach. However, for $N_X(t) \gg 1$, we can approximate (10) $\dfrac{dN_X(t)}{dt}$ to :

$$(k_1 N_A / 2)(N_X(t))^2 + k_3 N_B - (k_2 / 6)(N_X(t))^3 - k_4 N_X(t)$$

(A.7)

This last approximation has been used in the paper.

Appendix 2: Fundamentals of the Algorithms of Generation of Sample Paths (Trajectories)

Let us define $a(N_X(t))$, a non negative function such that $a(N_X(t))dt$ is the probability that the number of molecules of X, which takes the value $N_X(t)$ at time t, undergoes a unitary increment (positive or negative) in the differential interval $(t, t+dt)$, so $a(N_X(t)) = W_+(N_X(t)) + W_-(N_X(t))$.

Let us also define two conditional probabilities:

- $w_+(N_X(t))$ as the probability that the process, which has undergone an increment of $+1$ or -1, undergoes an increment of $+1$, and

- $w_-(N_X(t))$ as the probability that the process, which has undergone an increment of $+1$ or -1, undergoes an increment of -1.

Evidently, $w_\pm(N_X(t))$ lies between 0 and 1 and $w_+(N_X(t)) + w_-(N_X(t)) = 1$; one can also see that $w_\pm(N_X(t)) = \dfrac{W_\pm(N_X(t))}{a(N_X(t))}$.

Let u be the random variable *"time to the next reaction given that the number of molecules of X at time t is $N_X(t)$"*.

Let $p_0(N_X(t), u)$ be the probability that the number of molecules of X, which takes the value $N_X(t)$ in time t, does not suffer any changes in $(t, t+u)$. We can then write:

$$p_0(N_X(t), u + du) = p_0(N_X(t), u)(1 - a(N_X(t))du) \tag{A.8}$$

which implies the differential equation:

$$\frac{dp_0(N_X(t), u)}{du} = -a(N_X(t))p_0(N_X(t), u) \tag{A.9}$$

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Its solution, with the initial condition $p_0(N_X(t),0) = 1$ is:

$$p_0(N_X(t),u) = \exp(-a(N_X(t)u)) \tag{A.10}$$

We see that the distribution of u is an exponential with mean $1/a(N_X(t))$. We use this result for the following algorithm of generation of sample paths.

Algorithms for the Generation of Sample Paths

1) Initialise $t = t_0$, $N_X(t) = N_X(0)$

2) Generate a value of u : we generate a number r of a uniform distribution in $(0,1)$ and then

$u = (1/a(N_X(t))) \log(1/r)$

3) Generate a second number r' from the uniform distribution in $(0,1)$. If $w\_(N_X(t)) > r'$,

then take $v = -1$; if not $v = 1$.

4) Update the process: $N_X(t) = N_X(t) + v$; $t = t + u$

5) Go back to 2).

Appendix 3: Probabilities for Final State Values

We recall here, following Gillespie (2), the formulas used to calculate, as a function of the initial state $N_X(0)$, the probability of reaching a final state .

We define the potential function as:

$$\phi(N) = \sum_{j=1}^{N} \log \frac{W_-(j)}{W_+(j)} \qquad (A.11)$$

for $N \geq 1$. The potential function has the following property: the process has a probabilistic tendency to move in the direction of decreasing $\phi(N)$.

We define the barrier function as:

$$\Psi(N) = \frac{1}{KW_+(0)} e^{\phi(N)} \qquad (A.12)$$

where $K = (1 + \sum_{n=1}^{N} \Pi \frac{W_+(n-1)}{W_-(n)})^{-1}$ is a normalising constant which will vanish in the formulae below. Then, it can be shown that the probability that the process, starting from any state $N_X(0) \in [N_1 + 1, N_3 - 1]$ will go first to final state N_3 rather than final state N_1

is

$$p_2(N_X(0); N_1, N_3) = \frac{\sum_{m=N_1}^{N_0-1} \Psi(m)}{\sum_{m=N_1}^{N_3-1} \Psi(m)}, \quad N_X(0) \in [N_1 + 1, N_3 - 1] \qquad (A.13)$$

Literature Cited

(1) Casella, G.; Berger, J. *Statistical Inference,* Duxbury Press, Belmont, 1990 .

 (2) Gillespie, D. *Markov Processes: an Introduction for Physical Scientists.* Academic Press, New York, 1984.