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Derivations for order reduction of the chemical master equation

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Abstract

This technical report contains supplemental derivations for the publications Haseltine, Rawlings, *J. Chem. Phys.* 123, 164115, (2005) and Mastny, Haseltine, Rawlings (2006). In both of these works the chemical master equation is partitioned on the basis of fast and slow reactions. Conditional probabilities are used to derive approximate, partitioned master equations. The first section of this report contains a derivation that proves the probability of all accessible states is non-zero at $t > t_0$. This derivation is essential to show that the conditional densities used in the above papers are well defined. The second section of this report shows the consistency of the net extent master equation and the irreversible extent master equation. The third section of this report shows how the chemical master equation of a lattice gas reaction can be reduced from the full configurational space to coverage space in the fast diffusion limit. The third section also shows how the reduced master equation can be reduced further to a set of differential equations in the thermodynamic limit.

1 Proof of the non-zero probability of accessible states

1.1 The chemical master equation

We model the state of the system, \mathbf{x} , using a net reaction extent for each reversible reaction. An extent of reaction model is consistent with a molecule balance model since

$$\mathbf{n} = \mathbf{n}_0 + \boldsymbol{\nu}^T \mathbf{x} \tag{1}$$

in which, assuming that there are m reaction extents and p chemical species:

- \mathbf{x} is the state of the system in terms of reaction extents (an m -vector),
- \mathbf{n} is the number of molecules of each species (a p -vector),
- \mathbf{n}_0 is the initial number of molecules (a p -vector), and
- $\boldsymbol{\nu}$ is the stoichiometric matrix (an $m \times p$ -matrix).

The upper and lower bounds of \mathbf{x} are constrained by the limiting reactant species. We arbitrarily set the initial condition to the origin. Given assumptions outlined by Gillespie (1992), the governing equation for this system is the chemical master equation

$$\frac{dP(\mathbf{x}; t)}{dt} = \sum_{k=1}^m a_k^f(\mathbf{x} - \mathbf{I}_k)P(\mathbf{x} - \mathbf{I}_k; t) + a_k^r(\mathbf{x} + \mathbf{I}_k)P(\mathbf{x} + \mathbf{I}_k; t) - (a_k^f(\mathbf{x}) + a_k^r(\mathbf{x}))P(\mathbf{x}; t) \quad (2)$$

in which

- $P(\mathbf{x}; t)$ is the probability that the system is in state \mathbf{x} at time t ,
- $a_k^f(\mathbf{x})dt$ is the probability to order dt that the k th forward reaction occurs in the time interval $[t, t + dt)$,
- $a_k^r(\mathbf{x})dt$ is the probability to order dt that the k th reverse reaction occurs in the time interval $[t, t + dt)$, and
- \mathbf{I}_k is the k^{th} column of the $(m \times m)$ -identity matrix \mathbf{I} .

Here, each net extent is characterized by a forward and reverse reaction with propensities $a_k^f(\mathbf{x})$ and $a_k^r(\mathbf{x})$, respectively. Potentially either or both of these propensities may be zero for a given \mathbf{x} . Also, we have implicitly conditioned the master equation (2) on a specific initial condition, i.e. \mathbf{n}_0 . Generalizing the analysis presented in this paper to a distribution of initial conditions $(\mathbf{n}_{0,1}, \dots, \mathbf{n}_{0,n})$ is straightforward due to the relation

$$P(\mathbf{x}|\mathbf{n}_{0,1}, \dots, \mathbf{n}_{0,n}; t) = \sum_j P(\mathbf{x}|\mathbf{n}_{0,j}; t)P(\mathbf{n}_{0,j}) \quad (3)$$

and the fact that the values of $P(\mathbf{n}_{0,j})$ are specified in the initial condition.

1.2 Probability of accessible states

Definition 1 (Accessibility from the initial condition). *A state \mathbf{x} is accessible from the initial condition \mathbf{x}_0 if there exists some sequence of reactions (v_1, v_2, \dots, v_n) such that*

$$\mathbf{x} = \mathbf{x}_0 + \sum_{j=1}^n \mathbf{I}_{v_j} \quad (4)$$

and

$$a_{v_j}(\mathbf{x}_j) > 0 \quad \forall \quad j = 1, \dots, n \quad (5)$$

Definition 2 (*n* steps removed). A state \mathbf{x} is *n* steps removed from \mathbf{x}_0 if \mathbf{x} is accessible from \mathbf{x}_0 in a minimum of *n* finite reactions.

The first definition states that there is some path in the reaction space that takes us to \mathbf{x} from \mathbf{x}_0 . The second definition states that every path to \mathbf{x} from \mathbf{x}_0 consists of at least *n* steps.

Assumption 1 (Conditions required for finite accessibility of accessible states).

1. Chemical elements are conserved in all reactions.
2. $P(\mathbf{x}, t) = \delta(\mathbf{x} - \mathbf{x}_0)$, $t = 0$.
3. There are a finite number of particles in \mathbf{x}_0 (i.e., $\|\mathbf{x}_0\| < \infty$).
4. There are a finite number of reactions, and $\|\boldsymbol{\nu}_j\| > 0 \quad \forall j$.

Theorem 1 (Finite accessibility of all accessible states). Given assumptions 1, every accessible state from \mathbf{x}_0 is *n*-steps removed from \mathbf{x}_0 with finite *n*.

Proof. Proof by contradiction. Assume that there is a accessible state from \mathbf{x}_0 that is not finitely accessible. Since there are *m* reactions, then this state can be written as:

$$\mathbf{x} = \mathbf{x}_0 + \sum_{j=1}^m r_j \mathbf{I}_{v_j} \quad (6)$$

in which each r_j is a nonnegative, integer value. Then there exists some $r_j = \infty$. Since $\|v_j\| > 0$, either some component of $\mathbf{x}_i = \infty$ (which violates conservation of elements), or there is a combination of reactions for which

$$\mathbf{I}_{v_j} + \mathbf{I}_{v_k} + \dots + \mathbf{I}_{v_z} = \mathbf{0} \quad (7)$$

and

$$r_j = r_k = \dots = r_z = \infty \quad (8)$$

and the remaining *r*'s are finite.

However, the remaining *r*'s constitute a finitely-accessible state, which is a contradiction. Consequently, all accessible states are finitely accessible. \square

Assumption 2 (Linear independence of reactions). The reactions are linearly independent, i.e., the stoichiometric matrix $\boldsymbol{\nu}$ has full column rank and the corresponding \mathbf{I} has full rank.

Lemma 1 (Finite number of states). Given assumptions 1 and 2, if every state is finitely accessible, then there are a finite number of these states.

Proof. Proof by contradiction. Assume that every state is finitely accessible and that there are an infinite number of these states. Then there exists some combination of reactions and extents such that equations (7) and (8) hold. However, equation (7) implies that the reactions are linearly dependent, which is a contradiction. \square

Theorem 2 (Nonzero probability of finitely-accessible states for finite time).

Given assumptions 1 and 2, if every accessible state from \mathbf{x}_0 is finitely accessible, then $P(\mathbf{x}, t) > 0 \quad \forall \quad 0 < t < \infty$ and every accessible \mathbf{x} .

Proof. First stack probabilities for all accessible states into a vector \mathbf{P} . Consequently, the continuous-time master equation (2) can be recast as a vector-matrix problem, i.e.

$$\frac{d\mathbf{P}}{dt} = \mathbf{C}\mathbf{P} \quad (9)$$

in which \mathbf{C} is the matrix of reaction propensities. Also, \mathbf{P} has a finite number of elements as shown by lemma 1. The matrix \mathbf{C} can be decomposed as

$$\mathbf{C} = \mathbf{D} + \mathbf{B} \quad (10)$$

in which \mathbf{D} is a diagonal matrix in which

$$d_{ij} = \begin{cases} c_{ij} & \text{if } i = j \\ 0 & \text{otherwise} \end{cases} \quad (11)$$

and \mathbf{B} is a matrix in which

$$b_{ij} = \begin{cases} c_{ij} & \text{if } i \neq j \\ 0 & \text{otherwise} \end{cases} \quad (12)$$

Consequently, $d_{ij} \leq 0$ and $b_{ij} \geq 0$.

We want to show that $P(\mathbf{x}, t) > 0$ for \mathbf{x} accessible from \mathbf{x}_0 and $0 < t < \infty$. Defining

$$\mathbf{S} = \exp(\mathbf{C}t) = \exp(\mathbf{D}t) \exp(\mathbf{B}t) \quad (13)$$

then

$$\mathbf{P}(t) = \mathbf{S}(t)\mathbf{P}(t_0) \quad (14)$$

Consequently, we could also prove that $s_{ij} > 0$ in which the j th column corresponds to the initial condition $P(\mathbf{x}_0)$.

We use the definition of the Taylor-series expansion to determine $\exp(\mathbf{B}t)$

$$\bar{\mathbf{B}} = \exp(\mathbf{B}t) = \mathbf{I} + t\mathbf{B} + \frac{t^2}{2!}\mathbf{B}^2 + \dots \quad (15)$$

First, we know that $\bar{b}_{ij} \geq 0$ since $b_{ij} \geq 0 \forall i, j$. We want to show that $c_{ij} > 0$ for $0 < t < \infty$, in which column j corresponds to the initial condition. Define n_j to be the finite accessibility of \mathbf{x}_j . Since there are only a finite number of \mathbf{x}_j 's (due to the assumptions of conservation of elements, etc.) and they are all finitely accessible, we must show that $b_{i,j}^{n_j} > 0$. The interpretation of $b_{i,j}^{n_j}$ is that it gives all possible combinations of n_j reactions that can take you from state i to j . Since each state \mathbf{x}_j is finitely accessible,

$$b_{i,j}^{n_j} \geq \prod_{j=1}^{n_j} a_{v_j}(\mathbf{x}_{j-1}) > 0 \quad (16)$$

Since we are adding positive matrices, $b_{i,j}^{n_j} > 0$ implies that $\bar{b}_{ij} > 0$.

Now, $\mathbf{S} = \exp(\mathbf{D}t)\bar{\mathbf{B}}$. Since $\exp(\mathbf{D}t)$ is full rank with positive values on the diagonal, $\bar{b}_{ij} > 0$ implies that $s_{ij} > 0$ for $0 < t < \infty$. Therefore, we have shown that $P(\mathbf{x}_j, t) > 0$ for $0 < t < \infty$. \square

Here, we have shown that given the appropriate coordinate system and assumptions,

1. each state in the master equation can be accessed in a finite number of events,
2. the master equation contains a finite number of accessible states, and
3. the probability of being in any one of these states is nonzero for finite time.

Extension to initial condition distributions is straightforward. So is converting the proof from extent of reactions to molecules of species, or any other coordinate system which can be shown to have a finite number of states. Finally, any conditional probability is well defined for $0 < t < \infty$ since $P(\mathbf{x}, t) > 0$ for every \mathbf{x} .

2 Derivation of the net extent master equation from the irreversible extent master equation

We model the state of the system, \mathbf{y} , using a net reaction extent for each reaction. Here, reversible reactions are treated as two irreversible reactions. An extent of reaction model is consistent with a molecule balance model since

$$\mathbf{n} = \mathbf{n}_0 + \boldsymbol{\nu}^T \mathbf{y} \quad (17)$$

in which, assuming that there are m reaction extents and p chemical species:

- \mathbf{y} is the state of the system in terms of reaction extents (an $2m$ -vector),
- \mathbf{n} is the number of molecules of each species (a p -vector),
- \mathbf{n}_0 is the initial number of molecules (a p -vector), and
- $\boldsymbol{\nu}$ is the stoichiometric matrix (an $2m \times p$ -matrix).

The upper and lower bounds of \mathbf{y} are constrained by the limiting reactant species. We arbitrarily set the initial condition to the origin. The governing equation for this system is the chemical master equation

$$\frac{dP(\mathbf{y}; t)}{dt} = \sum_{k=1}^{2m} b_k(\mathbf{y} - \mathbf{I}_k^{2m})P(\mathbf{y} - \mathbf{I}_k^{2m}; t) - b_k(\mathbf{y})P(\mathbf{y}; t) \quad (18)$$

in which

- $P(\mathbf{y}; t)$ is the probability that the system is in state \mathbf{y} at time t ,
- $b_k(\mathbf{y})dt$ is the probability to order dt that the k th reaction occurs in the time interval $[t, t + dt)$,
- \mathbf{I}_k^{2m} is the k^{th} column of the $(2m \times 2m)$ -identity matrix \mathbf{I}^{2m} .

Define the net reaction extent vector as the m -vector \mathbf{x} . Partition the irreversible reaction extent vector so that $x_j = y_j - y_{m+j}$, that is, y_j and y_{m+j} are the forward and reverse reaction extents for the net extent x_j . We define

$$\mathbf{y}^f = \begin{bmatrix} y_1 \\ \dots \\ y_m \end{bmatrix} \quad (19a)$$

$$\mathbf{y}^r = \begin{bmatrix} y_{m+1} \\ \dots \\ y_{2m} \end{bmatrix} \quad (19b)$$

and consequently,

$$\mathbf{x} = \mathbf{y}^f - \mathbf{y}^r \quad (20)$$

We redefine the reactions propensities so that

$$a_j^f(\mathbf{x}) = b_j(\mathbf{y}) = b_j(\mathbf{y}^f, \mathbf{y}^r) \quad (21a)$$

$$a_j^r(\mathbf{x}) = b_{m+j}(\mathbf{y}) = b_{m+j}(\mathbf{y}^f, \mathbf{y}^r) \quad (21b)$$

Equation (21) takes advantage of the fact that the reaction propensities depend solely upon the net extent \mathbf{x} as opposed to the precise values of the forward (\mathbf{y}^f) and reverse (\mathbf{y}^r) extents; that is,

$$a_j^f(\mathbf{x}) = b_j(\mathbf{y}^f + k\mathbf{I}_j, \mathbf{y}^r + k\mathbf{I}_j) \quad \forall 1 \leq j \leq m, k \text{ such that } \mathbf{n} \text{ is accessible} \quad (22)$$

$$a_j^r(\mathbf{x}) = b_{m+j}(\mathbf{y}^f + k\mathbf{I}_j, \mathbf{y}^r + k\mathbf{I}_j) \quad \forall 1 \leq j \leq m, k \text{ such that } \mathbf{n} \text{ is accessible} \quad (23)$$

First define the distributions of \mathbf{x} , \mathbf{y}^f , and \mathbf{y}^r to be ζ , ξ , and η , respectively. We ultimately desire to determine an evolution equation for $P_\zeta(\mathbf{x})$ from the evolution equation of $P_{\xi,\eta}(\mathbf{y}^f, \mathbf{y}^r)$. To do so, we will first determine $P_{\zeta,\eta}(\mathbf{x}, \mathbf{y}^r)$ as a function of $P_{\xi,\eta}(\mathbf{y}^f, \mathbf{y}^r)$, then sum over \mathbf{y}^r to calculate the desired marginal $P_\zeta(\mathbf{x})$. It is clear that

$$\begin{bmatrix} \mathbf{x} \\ \mathbf{y}^r \end{bmatrix} = \begin{bmatrix} \mathbf{I} & -\mathbf{I} \\ \mathbf{0} & \mathbf{I} \end{bmatrix} \begin{bmatrix} \mathbf{y}^f \\ \mathbf{y}^r \end{bmatrix} \quad (24)$$

$$= \mathbf{J} \begin{bmatrix} \mathbf{y}^f \\ \mathbf{y}^r \end{bmatrix} \quad (25)$$

Then using the procedure outlined by Ross (1998) (which applies the inverse function theorem from calculus (Rudin, 1976)),

$$P_{\zeta,\eta}(\mathbf{x}, \mathbf{y}^r) = P_{\xi,\eta}(\mathbf{y}^f, \mathbf{y}^r) \|\mathbf{J}\|^{-1} \quad (26)$$

$$= P_{\xi,\eta}(\mathbf{x} + \mathbf{y}^r, \mathbf{y}^r) \quad (27)$$

in which $||\mathbf{J}||$ denotes the determinant of the matrix \mathbf{J} . We now manipulate the irreversible extent master equation (18) using equations (19), (21), and (27) to yield

$$\frac{dP(\mathbf{y}; t)}{dt} = \sum_{k=1}^{2m} b_k(\mathbf{y} - \mathbf{I}_k) P(\mathbf{y} - \mathbf{I}_k; t) - b_k(\mathbf{y}) P(\mathbf{y}; t) \quad (28)$$

$$\begin{aligned} \frac{dP_{\xi, \eta}(\mathbf{y}^f, \mathbf{y}^r; t)}{dt} &= \sum_{k=1}^m a_k^f(\mathbf{y}^f - \mathbf{I}_k, \mathbf{y}^r) P_{\xi, \eta}(\mathbf{y}^f - \mathbf{I}_k, \mathbf{y}^r; t) \\ &\quad + a_k^r(\mathbf{y}^f, \mathbf{y}^r - \mathbf{I}_k) P_{\xi, \eta}(\mathbf{y}^f, \mathbf{y}^r - \mathbf{I}_k; t) \\ &\quad - \left(a_k^f(\mathbf{y}^f, \mathbf{y}^r) + a_k^r(\mathbf{y}^f, \mathbf{y}^r) \right) P_{\xi, \eta}(\mathbf{y}^f, \mathbf{y}^r; t) \end{aligned} \quad (29)$$

$$\begin{aligned} \frac{dP_{\xi, \eta}(\mathbf{x} + \mathbf{y}^r, \mathbf{y}^r; t)}{dt} &= \sum_{k=1}^m a_k^f(\mathbf{x} - \mathbf{I}_k) P_{\xi, \eta}(\mathbf{x} + \mathbf{y}^r - \mathbf{I}_k, \mathbf{y}^r; t) \\ &\quad + a_k^r(\mathbf{x} + \mathbf{I}_k) P_{\xi, \eta}(\mathbf{x} + \mathbf{y}^r, \mathbf{y}^r - \mathbf{I}_k; t) \\ &\quad - \left(a_k^f(\mathbf{x}) + a_k^r(\mathbf{x}) \right) P_{\xi, \eta}(\mathbf{x} + \mathbf{y}^r, \mathbf{y}^r; t) \end{aligned} \quad (30)$$

$$\begin{aligned} \frac{dP_{\zeta, \eta}(\mathbf{x}, \mathbf{y}^r; t)}{dt} &= \sum_{k=1}^m a_k^f(\mathbf{x}^f - \mathbf{I}_k) P_{\zeta, \eta}(\mathbf{x} - \mathbf{I}_k, \mathbf{y}^r; t) \\ &\quad + a_k^r(\mathbf{x} + \mathbf{I}_k) P_{\zeta, \eta}(\mathbf{x} + \mathbf{I}_k, \mathbf{y}^r - \mathbf{I}_k; t) \\ &\quad - \left(a_k^f(\mathbf{x}) + a_k^r(\mathbf{x}) \right) P_{\zeta, \eta}(\mathbf{x}, \mathbf{y}^r; t) \end{aligned} \quad (31)$$

Summing the joint evolution equation (31) over all \mathbf{y}^r yields the desired marginal

$$\begin{aligned} \sum_{\mathbf{y}^r} \frac{dP_{\zeta, \eta}(\mathbf{x}, \mathbf{y}^r; t)}{dt} &= \sum_{\mathbf{y}^r} \sum_{k=1}^m a_k^f(\mathbf{x} - \mathbf{I}_k) P_{\zeta, \eta}(\mathbf{x} - \mathbf{I}_k, \mathbf{y}^r; t) \\ &\quad + a_k^r(\mathbf{x} + \mathbf{I}_k) P_{\zeta, \eta}(\mathbf{x} + \mathbf{I}_k, \mathbf{y}^r - \mathbf{I}_k; t) \\ &\quad - \left(a_k^f(\mathbf{x}) + a_k^r(\mathbf{x}) \right) P_{\zeta, \eta}(\mathbf{x}, \mathbf{y}^r; t) \end{aligned} \quad (32)$$

$$\begin{aligned} \frac{dP_{\zeta}(\mathbf{x}; t)}{dt} &= \sum_{k=1}^m a_k^f(\mathbf{x} - \mathbf{I}_k) P_{\zeta}(\mathbf{x} - \mathbf{I}_k; t) \\ &\quad + a_k^r(\mathbf{x} + \mathbf{I}_k) P_{\zeta}(\mathbf{x} + \mathbf{I}_k; t) \\ &\quad - \left(a_k^f(\mathbf{x}) + a_k^r(\mathbf{x}) \right) P_{\zeta}(\mathbf{x}; t) \end{aligned} \quad (33)$$

Thus the governing master equation for the net extent coordinate (i.e., equation (33)) can be derived from the master equation for the irreversible extent coordinate (i.e., equation (18)).

This derivation demonstrates that the net and irreversible extent master equations are indeed consistent. However, there are several differences between these coordinate systems that deserve mention. First, given the assumptions outlined in section 1.2, the net extent coordinate yields a finite number of accessible states. On the other hand, the irreversible

extent coordinate yields an *infinite* number of accessible states because of the linear dependence given in equation (20). However, it is also clear that the irreversible extent coordinate master equation contains significantly more information than its counterpart. In particular, this coordinate system records *how many times* both the forward and reverse reactions have fired to produce a given net extent. Notably, exact simulations of the master equation provides precisely this information as well. Thus we may view the simulation as an exact realization of the irreversible extent master equation. Because the net extent master equation can be derived from the irreversible extent master equation, simulating the latter master equation then provides realizations of the former.

3 Lattice gas master equation order reduction

3.1 Notation

In this section of the report a diffusion event is an event that changes the position of an absorbed species but does not change the overall number of each type of species on the lattice. A reaction event changes the number of some of the species on the lattice, and can occur by adsorption/desorption or reaction. The notation listed below will be used for the balance of the report.

The following variables describe the lattice size and species considered:

- N_s is the number of sites on the lattice.
- p is the number of chemical species.

The following variables describe different ways to represent lattice configurations and numbers of possible lattice configurations:

- x is a state that represents a particular lattice configuration.
- n is a vector of dimension p containing the number of each species on the lattice.
- θ is a vector of dimension p containing the coverage of each species on the lattice (n/N_s).
- n_x represents the species numbers in state x .
- N_x is the number of possible x states.
- N_n is the number of possible n states.

The following are different types of probability distributions used to characterize lattice behavior. Although not explicitly written, all of the following probability densities are functions of time.

- $P_x(x)$ is the probability of have lattice configuration x .
- $P_{n,x}(n, x)$ is the joint probability of being in species number n and lattice configuration x .

- $P_n(n)$ is the marginal probability of being in species number n .
- $P_{x|n}(x|n)$ is the conditional probability of being in configuration x given species number n .
- \hat{P} denotes an approximate probability distribution, in which the above subscript notations apply.

The following are ways of characterizing transition rates from one state to another.

- $W_{\alpha,\beta}$ is the rate at which the system can move from lattice configuration β to configuration α , by any reaction or diffusion event.
- $K_{\alpha,\beta}$ is the rate at which the system can move from lattice configuration β to configuration α , by a reaction event.
- $D_{\alpha,\beta}$ is the rate at which the system can move from lattice configuration β to configuration α , by a diffusion event.

3.2 Probability state dimension

The difficulty that arises in solving the discrete master equation exactly is the dimension of the probability density. The dimension of the probability density is the number of accessible states or states that can be reached within the constraints of the mass balance and reaction mechanism. The probability density P_x has the dimension of the number of possible lattice configurations (N_x).

$$N_x = (p + 1)^{N_s}$$

The probability density P_n has the dimension of the number of possible combinations of species numbers on the lattice (N_n). N_n is proportional to N_s^p . For a system with two species $N_n = (N_s + 1)(N_s + 2)/2$.

Example	N_x	N_n
$N_s = 4, p = 1$	16	5
$N_s = 25, p = 2$	10^{12}	325
$N_s = 100, p = 2$	10^{48}	5050

Table 1: Comparison of the dimension of P_x and P_n for different lattice sizes and species numbers.

Table 1 compares the dimensions of P_x and P_n for a few cases. The dimension of P_n is significantly less than P_x because the states in P_n do not account for lattice positions of surface species. The numbers given in Table 1 demonstrate that, even for small lattices ($N_s = 25$), the probability density P_x cannot be stored a computer. This table also shows that for lattices with $O(100)$ sites, P_n has a state dimension small enough to enumerate and evaluate. One purpose of this paper is to show that the model in P_x can be accurately reduced to a model in P_n when diffusion events are much faster than reaction events. This order reduction facilitates the use of the chemical master equation to solve for the probability density of the surface reaction for small lattices.

3.3 Full master equation

The master equation of the full state is,

$$\frac{dP_x(x)}{dt} = \sum_{\beta} W_{x,\beta} P_x(\beta) - W_{\beta,x} P_x(x)$$

Since n is uniquely specified by x , the joint density can be written as

$$P_{n,x}(n, x) = P_x(x) \delta(n - n_x) \quad (34)$$

where $\delta(n - n_x)$ is a function of value one when the coverage n is the same as the coverage of configuration x and zero otherwise. The evolution equation of the joint density system is

$$\frac{dP_{n,x}(n, x)}{dt} = \sum_{\beta} (W_{x,\beta} P_x(\beta) - W_{\beta,x} P_x(x)) \delta(n - n_x) \quad (35)$$

The non-zero entries of W are rates constants of events that can transfer the system from one state to another. This matrix can be decomposed into the reaction event (K) and diffusion event (D) matrices.

$$W = K + D$$

Equation 35 can then be decomposed into two sums, one over the reaction events, and the other over diffusion events.

$$\begin{aligned} \frac{dP_{n,x}(n, x)}{dt} &= \sum_{\beta} (K_{x,\beta} P_x(\beta) - K_{\beta,x} P_x(x)) \delta(n - n_x) + \\ &\quad \sum_{\beta} (D_{x,\beta} P_x(\beta) - D_{\beta,x} P_x(x)) \delta(n - n_x) \end{aligned}$$

3.4 Evolution of n

Now we define the marginal density $P_n(n)$ as

$$P_n(n) = \sum_x P_{n,x}(n, x) = \sum_{\alpha} P_x(\alpha) \delta(n - n_{\alpha})$$

The evolution of P_n is then

$$\begin{aligned} \frac{dP_n(n)}{dt} &= \sum_{\alpha} \frac{dP_x(\alpha)}{dt} \delta(n - n_{\alpha}) \\ \frac{dP_n(n)}{dt} &= \sum_{\alpha} \left(\sum_{\beta} W_{\alpha,\beta} P_x(\beta) - W_{\beta,\alpha} P_x(\alpha) \right) \delta(n - n_{\alpha}) \end{aligned}$$

This summation can be broken into separate summations over diffusion and reaction events

$$\begin{aligned} \frac{dP_n(n)}{dt} &= \sum_{\alpha,\beta} (K_{\alpha,\beta}P_x(\beta) - K_{\beta,\alpha}P_x(\alpha))\delta(n - n_\alpha) + \\ &\quad \sum_{\alpha,\beta} (D_{\alpha,\beta}P_x(\beta) - D_{\beta,\alpha}P_x(\alpha))\delta(n - n_\alpha) \end{aligned} \quad (36)$$

Diffusion events do not change species numbers on the lattice; therefore all non-zero entries in the diffusion event matrix connect states with the same species numbers.

$$\text{If } D_{\alpha,\beta} \neq 0, \text{ then } n_\alpha = n_\beta \quad (37)$$

Thus, the summation over diffusion events in Equation 36 becomes zero.

$$\sum_{\alpha,\beta} (D_{\alpha,\beta}P_x(\beta) - D_{\beta,\alpha}P_x(\alpha))\delta(n - n_\alpha) = \sum_{\alpha,\beta} D_{\alpha,\beta}P_x(\beta)(\delta(n - n_\alpha) - \delta(n - n_\beta)) = 0$$

Therefore the resulting evolution equation for the P_n is:

$$\frac{dP_n(n)}{dt} = \sum_{\alpha,\beta} (K_{\alpha,\beta}P_x(\beta) - K_{\beta,\alpha}P_x(\alpha))\delta(n - n_\alpha) \quad (38)$$

With some further manipulations we cast Equation 38 in terms of the joint density for later use. Let $n_\alpha = \Delta n_{\alpha,\beta} + n_\beta$. Equation 38 now becomes

$$\frac{dP_n(n)}{dt} = \sum_{\alpha,\beta} K_{\alpha,\beta}P_x(\beta)\delta(n - \Delta n_{\alpha,\beta} - n_\beta) - K_{\beta,\alpha}P_x(\alpha)\delta(n - n_\alpha)$$

Using the definition of the joint density (Equation 34), the marginal density evolution equation becomes

$$\frac{dP_n(n)}{dt} = \sum_{\alpha,\beta} K_{\alpha,\beta}P_{n,x}(n - \Delta n_{\alpha,\beta}, \beta) - K_{\beta,\alpha}P_{n,x}(n, \alpha) \quad (39)$$

3.5 Fast time scale

Assumption 1: On the fast time scale the evolution of the joint density is affected by only diffusion events.

$$\begin{aligned} \frac{dP_{n,x}(n, x)}{dt} &\approx \frac{d\hat{P}_{n,x}(n, x)}{dt} \\ \frac{d\hat{P}_{n,x}(n, x)}{dt} &= \sum_{\beta} D_{x,\beta}P_x(\beta)\delta(n - n_x) - D_{\beta,x}P_x(x)\delta(n - n_x) \end{aligned} \quad (40)$$

From the arguments given in section 3.4, $d\hat{P}_n(n)/dt = 0$. The definition of the conditional density $\hat{P}_{x|n}(x|n)$ is

$$\hat{P}_{x|n}(x|n) = \frac{\hat{P}_{n,x}(n, x)}{\hat{P}_n(n)} \quad (41)$$

We know that $\hat{P}_n(n)$ is non-zero because there are a finite number of states in this master equation and every state can be reached in a finite number of steps from any initial condition, see Section 1.

By differentiating Equation 41, it can be shown that the conditional density evolution equation is

$$\frac{d\hat{P}_{x|n}(x|n)}{dt} = \frac{1}{\hat{P}_n(n)} \frac{d\hat{P}_{n,x}(n,x)}{dt} \quad (42)$$

Substituting Equation 40 into Equation 42, the conditional density evolution becomes

$$\frac{d\hat{P}_{x|n}(x|n)}{dt} = \frac{1}{\hat{P}_n(n)} \sum_{\beta} D_{x,\beta} \hat{P}_x(\beta) \delta(n - n_x) - D_{\beta,x} \hat{P}_x(x) \delta(n - n_x) \quad (43)$$

If $D_{x,\beta} \neq 0$, then $n_x = n_{\beta}$ and Equation 43 becomes

$$\begin{aligned} \frac{d\hat{P}_{x|n}(x|n)}{dt} &= \frac{1}{\hat{P}_n(n)} \sum_{\beta} D_{x,\beta} \hat{P}_x(\beta) \delta(n - n_{\beta}) - D_{\beta,x} \hat{P}_x(x) \delta(n - n_x) \\ \frac{d\hat{P}_{x|n}(x|n)}{dt} &= \sum_{\beta} D_{x,\beta} \frac{\hat{P}_{n,x}(n,\beta)}{\hat{P}_n(n)} - D_{\beta,x} \frac{\hat{P}_{n,x}(n,x)}{\hat{P}_n(n)} \\ \frac{d\hat{P}_{x|n}(x|n)}{dt} &= \sum_{\beta} D_{x,\beta} \hat{P}_{x|n}(\beta|n) - D_{\beta,x} \hat{P}_{x|n}(x|n) \end{aligned} \quad (44)$$

Equation 44 states that for a given n , the evolution of x is Markovian and depends only on diffusion events. Remember that this equation holds only for fast time scales, or a time scale during which no reaction events occur. Therefore, the KMC simulation that samples this master equation has a fixed n and employs only diffusion events.

3.6 Approximate evolution of n

Assumption 2: The joint density of being in state n, x is the probability of being in state n times the conditional density $x|n$ from the probability distribution from the fast time scale.

$$P_n(n) \approx \frac{\hat{P}_{n,x}(n,x)}{\hat{P}_{x|n}(x|n)}$$

Substituting this assumption into the marginal density evolution, Equation 39, gives

$$\frac{dP_n(n)}{dt} = \sum_{\alpha,\beta} K_{\alpha,\beta} \hat{P}_{x|n}(\beta|n - \Delta n_{\alpha,\beta}) P_{n,x}(n - \Delta n_{\alpha,\beta}) - K_{\beta,\alpha} \hat{P}_{x|n}(\beta|n) P_n(n) \quad (45)$$

We now collect terms in Equation 45, to make these summations computationally tractable. The elements of the reaction transition matrix K can be represented by summing over all

the types of reactions j .

$$K_{\alpha,\beta} = \sum_j k_j 1_j(\alpha \rightarrow \beta)$$

$$1_j(\alpha \rightarrow \beta) = \begin{cases} 1 & \text{if } \alpha \rightarrow \beta \text{ by rxn } j \\ 0 & \text{otherwise} \end{cases}$$

This alternative way of expressing K can be substituted into Equation 45

$$\begin{aligned} \frac{dP_n(n)}{dt} &= \sum_{\alpha,\beta} \left(\sum_j k_j 1_j(\alpha \rightarrow \beta) \right) \hat{P}_{x|n}(\beta|n - \Delta n_{\alpha,\beta}) P_{n,x}(n - \Delta n_{\alpha,\beta}) \\ &\quad - \left(\sum_j k_j 1_j(\beta \rightarrow \alpha) \right) \hat{P}_{x|n}(\beta|n) P_n(n) \end{aligned}$$

Next the order of summation can be changed in the following way

$$\begin{aligned} \frac{dP_n(n)}{dt} &= \sum_j k_j \left[\sum_{\beta} \left(\sum_{\alpha} 1_j(\alpha \rightarrow \beta) \right) \hat{P}_{x|n}(\beta|n - \nu_j) P_n(n - \nu_j) \right] \\ &\quad - \sum_j k_j \left[\sum_{\beta} \left(\sum_{\alpha} 1_j(\beta \rightarrow \alpha) \right) \hat{P}_{x|n}(\beta|n) P_n(n) \right] \end{aligned} \quad (46)$$

Let $s_{j,\beta} = \sum_{\alpha} 1_j(\alpha \rightarrow \beta)$. $s_{j,\beta}$ is the number of j reactions that can occur in state β . Substituting this term into Equation (46) gives

$$\frac{dP_n(n)}{dt} = \sum_j k_j \left[\sum_{\beta} s_{j,\beta} \hat{P}_{x|n}(\beta|n - \nu_j) P_n(n - \nu_j) - s_{j,\beta} \hat{P}_{x|n}(\beta|n) P_n(n) \right] \quad (47)$$

The last sum over the microscopic states in the marginal density can be removed in the following way

$$\frac{dP_n(n)}{dt} = \sum_j k_j [\langle s_j(n - \nu_j) \rangle P_n(n - \nu_j) - \langle s_j(n) \rangle P_n(n)] \quad (48)$$

In which $\langle s_j(n) \rangle$ is the average number of reaction j possible on the lattice, given n . Equation 47 is Markovian; therefore, if the terms $\langle s_j(n) \rangle$ are known for all n , then the master equation for the marginal density can be solved exactly. These terms are a function of the distribution of microscopic states sampled for a given n .

3.7 Equilibrium assumption and simulation strategy

Assumption 3: On the slow time scale the x states reach equilibrium due to diffusion before reaction events occur that change n .

$$\frac{d\hat{P}_{x|n}(x|n)}{dt} = 0 \quad (49)$$

Without appealing to the mean field assumption, the $\langle s_j(n) \rangle$ terms in Equation 48 are not available analytically. In the previous section we defined $\langle s_j(n) \rangle$ as $\sum_{\alpha} s_j(\alpha) P_{x|n}(\alpha|n)$, or, in other words, the expectation of the number of reaction j from the probability density of the slow time scale. The master equation that governs the evolution of $P_{x|n}(\alpha|n)$ is Equation 44. This master equation evolves with only diffusion events. Therefore, we can determine $\langle s_j(n) \rangle$ by running a KMC simulation with only diffusion events and coverage n . When this KMC simulation reaches equilibrium, as in Equation 49, $s_j(n)$ can be measured over many sample times to determine $\langle s_j(n) \rangle$.

3.8 Large lattice limit and deterministic evolution equations

In the large lattice limit, the variables of interest are the fractional coverages of each species on the surface (θ_i) rather than species numbers. Instead of tracking the number of each type of reaction $s_j(n)$, we track $g_j(\theta) = s_j(n)/N_s$. When diffusion is much faster than reaction, the surface equilibrates between reaction events. Under equilibrated conditions, the results of equilibrium thermodynamics and statistical mechanics of the NVT ensemble apply to the surface. The theory of thermodynamics of small systems states that in the limit of large systems, observables such as $g_j(\theta)$, become intensive. In other words, $g_j(\theta)$ approaches a constant as the lattice size increases (Hill, 1963). Additionally, a classic result of statistical mechanics is that the probability distribution of an intensive variable becomes increasingly sharp as the system size increases. In the thermodynamic limit the probability distribution of this intensive variable is essentially a delta function (McQuarrie, 1973).

In the derivation given below we show that:

$$\frac{d\langle n \rangle}{dt} = \sum_j \nu_j k_j \langle s_j \rangle. \quad (50)$$

When divided by N_s Equation 50 becomes

$$\frac{d\langle \theta \rangle}{dt} = \sum_j \nu_j k_j \langle g_j \rangle \quad (51)$$

A system initialized with a specific coverage θ samples an equilibrated probability distribution for each g_j . If the lattice is large, the the probability distribution of each g_j is a delta function. Therefore, $\langle g_j \rangle$ can be written as $g_j(\theta)$, and the right hand side of Equation 51 becomes deterministic

$$\frac{d\theta}{dt} = \sum_j \nu_j k_j g_j(\theta)$$

3.8.1 Derivation of Equation (50)

Equation 48 can be expanded to a summation over the full n state and be rewritten as

$$\frac{dP_n(\alpha)}{dt} = \sum_{\beta} w_{\alpha,\beta} P_n(\beta) - w_{\beta,\alpha} P_n(\alpha)$$

The expectation of n is written as,

$$\langle n \rangle = \sum_n P_n(\alpha) n_\alpha$$

The rate of change of $\langle n \rangle$ is then

$$\frac{d\langle n \rangle}{dt} = \sum_\alpha \left(\sum_\beta w_{\alpha,\beta} P_n(\beta) - w_{\beta,\alpha} P_n(\alpha) \right) n_\alpha$$

These summations can be rearranged to give

$$\frac{d\langle n \rangle}{dt} = \sum_\alpha \sum_\beta w_{\alpha,\beta} P_n(\beta) (n_\alpha - n_\beta) \quad (52)$$

As done previously, we define an indicator function, by summing over all reaction types j .

$$w_{\alpha,\beta} (n_\alpha - n_\beta) = \sum_j k_j \nu_j 1_j(\alpha \rightarrow \beta)$$

Substituting this indicator function into Equation (52) gives

$$\begin{aligned} \frac{d\langle n \rangle}{dt} &= \sum_\alpha \sum_\beta \left(\sum_j k_j \nu_j 1_j(\alpha \rightarrow \beta) \right) P_n(\beta) \\ \frac{d\langle n \rangle}{dt} &= \sum_j k_j \nu_j \left(\sum_\alpha \sum_\beta 1_j(\alpha \rightarrow \beta) P_n(\beta) \right) \\ \frac{d\langle n \rangle}{dt} &= \sum_j k_j \nu_j \sum_\beta \left(\sum_\alpha 1_j(\alpha \rightarrow \beta) \right) P_n(\beta) \end{aligned}$$

By the previous definition of $s_j(n)$ this becomes

$$\begin{aligned} \frac{d\langle n \rangle}{dt} &= \sum_j k_j \nu_j \sum_\beta s_j(\beta) P_n(\beta) \\ \frac{d\langle n \rangle}{dt} &= \sum_j k_j \nu_j \langle s_j \rangle \end{aligned}$$

We have thus shown that if diffusion is much faster than reaction we can derive a set of differential equations that closes in the coverages. The functional form of $g_j(\theta)$ is unknown, but the numerical value of $g_j(\theta)$ can be found at a specific θ using a short, diffusion-only KMC simulation.

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