

A Process Algebra Master Equation

Luca Cardelli

Microsoft Research

Abstract

A Master Equation provides a complete probabilistic description of the dynamics of stochastic processes. We give a master equation for a small stochastic process algebra (a subset of CCS with interaction rates). We show that it is equivalent to the standard Chemical Master Equation, connecting our process algebra to the stochastic chemistry of unary and binary reactions.

1 Introduction

The purpose of this paper is to establish a basic but precise connection between two well-known presentations of stochastic systems: by chemical reactions and by process algebra. After Regev and Shapiro's seminal proposal [11][12][13] to use stochastic process algebra [6][7][10] to represent biochemical systems, it has become common to translate biochemical pathways, given as sets of chemical reactions, into process algebra. A discussion of the advantages of that approach is beyond the scope of this paper, but it is related to the effort to obtain compositional and scalable representations of large biological systems, such as the ones found in systems biology [9]. Other discrete and stochastic frameworks have been used for the same purpose.

In view of the growing interest, formal connections between chemistry, differential equations, and various process algebras are now being established [1][2][3]. Here we provide a connection at the level of the stochastic interpretation of chemistry. The *chemical master equation* (CME) is a probabilistic description of the dynamics of chemical reactions over the discrete state space of molecule counts. It describes a continuous-time Markov chain, and it can be derived from the general Chapman-Kolmogorov equation for Markov chains [14], but it is defined directly over the structure of the chemical reactions. We give a related *process algebra master equation* (PME) directly over the structure of a small stochastic process algebra, again arising from the fact that the underlying dynamic system is a Markov chain, and the underlying state space is a process count. We can say that the CME is a semantics of chemical reactions, and the PME is therefore a corresponding process algebra semantics.

Our simplifying assumptions about stochastic chemistry are common ones. Individual molecules may spontaneously degrade into other molecules, at a certain rate; these are *unary reactions*. Pairs of molecules may collide and produce other molecules, at a certain rate; these are *binary reactions*. Binary reactions between molecules of the same chemical species are called *homeo (binary) reactions*, and otherwise *hetero (binary) reactions*. We can ignore reactions between three or more molecules, because of the unlikelihood, under normal biological conditions, of finding three or more of them at the same time in the same place, and with the right energy and orientation to produce a coordinated reaction ("Genuinely *trimolecular* reactions do not physically occur in dilute fluids with any appreciable frequency. Apparently trimolecular reactions in a fluid are usually the combined result of two bimolecular reactions and one monomolecular reaction, and involve an additional short-lived species." [5]). Reactions are assumed to occur with time-independent base rates, in constant volume, at constant temperature and pressure, and in a *well-stirred solution*, so that the probability of two molecules reacting is independent of their position. All these assumptions can be relaxed at the expense of added complexity.

On the other hand, systems are not assumed to be in chemical equilibrium: the dynamics, as opposed to the steady state, of such systems is of particular interest in many biological applications.

Correspondingly, we have simplifying assumptions about the process algebra. Interactions are binary (corresponding to collisions) or internal (corresponding to degradations). There is no message passing on interaction (nor channel passing), and there is no form of channel hiding. The remaining algebraic operators are guarded stochastic choice and parallel composition. The process algebra is thus reduced almost to a simple notion of interacting sequential automata, except that these automata (representing molecules) must be able to divide dynamically.

All these simplifying assumptions are in view of obtaining a correspondence between basic chemistry and basic process algebra, hopefully to be extended further. More advanced process algebra features are useful in modeling biochemistry. For example, the π -calculus notions of private channels and channels passing can conveniently represent complexation and polymerization. It will be interesting to see what kind of extended correspondences to chemistry can be established.

The paper is organized as follows. In Section 2 we define the process algebra master equation and we solve a simple example. In Section 3 we give the standard chemical master equation. In Section 4 we show that the chemical master equation and the process algebra master equation coincide under appropriate translations between chemistry and processes. Some notational difficulties are due to the existence of two established and conflicting sets of notations. We use “+” for chemical composition and “|” for process composition: when converting between chemistry and processes these symbols are implicitly converted. We use “ \oplus ” for stochastic choice in processes.

2 Processes

We now introduce our very basic stochastic process algebra. We present it in a normalized form that names the elementary reagents involved, and that prevents the construction of complex terms (each interaction is always followed by a solution, not by an arbitrary process).

2.1 A stochastic process algebra

We describe systems of interacting processes by the following syntax. A system E,P consists of a finite set of reagents (named molecules) E , and of a multiset P of initial molecules.

2.1-1 Definition: System of reagent species and initial solution

$E ::= 0 \mid X=M, E$	Reagents	(empty, or a reagent $X=M$ and Reagents E)
$M ::= 0 \mid \pi.P \oplus M$	Molecule	(empty, or an interaction $\pi.P$ and Molecule M)
$P ::= 0 \mid X \mid P$	Solution	(empty, or a variable X and Solution P)
$\pi ::= \tau_{(r)} \mid ?n_{(r)} \mid !n_{(r)}$	Interaction prefix	(delay, input, output)
$\text{Sys} ::= E,P$	System	(Reagents E with initial Solution P)

E is a finite set of *reagents* $X_i=M_i$, for distinct *species* X_i , and for *molecules* M_i that describe the interaction capabilities of the corresponding species; *species*(E) is the set of the species X_i in E . The possible process *interactions* π are: *delay* $\tau_{(r)}$ at *rate* r (where r is a positive real), *input* $?n_{(r)}$ on *channel* n at *rate* r , and *output* $!n_{(r)}$ on *channel* n at *rate* r (each channel always has the same rate). In the syntax of molecules, each interaction π leads to releasing a *solution* P , describing a multiset of molecules. We use \oplus for *choice*, $|$ for *parallel composition*, and 0 for the empty reagent, the empty molecule, and the empty solution. Trailing 0 's may be omitted. A system (E,P) is a set of reagents E together with *initial conditions*, which are a solution P . We write $E.X$ for the unique molecule associated to X in E , $M.i$ for the i -th summand $\pi_i.P_i$ in

molecule $M = \pi_1.P_1 \oplus \dots \oplus \pi_n.P_n \oplus 0$, and $E.X.i$ to refer to the i -th summand of molecule $E.X$.

A multiset ρ is a function from a set to integer numbers; negative counts are allowed, although they do not represent any legal state. A non-negative multiset ρ is also written with the notation $\{W, Y, Y, Z, Z, Z\}$. If $P = Y|W|Z|Z|Z|Y$ is a Solution, we write $P^\dagger = \{W, Y, Y, Z, Z, Z\}$ for the associated multiset, with the empty multiset $\{\} = 0^\dagger$. If ρ and ρ' are multisets, then $\rho^{\#X} = \rho(X)$ is the count of the X elements in ρ , $\rho + \rho'$ is multiset addition, and $\rho - \rho'$ is multiset subtraction.

2.1-2 Examples of systems of reagents E

Unary reaction

$X = \tau_{(r)}.0$ The reagent X that transitions to 0 after a stochastic delay of rate r .

Hetero binary reaction

$X = ?n_{(r)}.0,$ The reagent X that interacts with reagent Y on channel n
 $Y = !n_{(r)}.0$ at stochastic rate r , and then both reagents transition to 0 .

Homeo binary reaction

$X = ?n_{(r)}.0 \oplus !n_{(r)}.0$ The reagent X that interacts with another copy of X on channel n
at stochastic rate r , and then both copies transition to 0 .

2.2 The master equation

The master equation for our process algebra describes the conditional probability of a system being in state ρ at time t , given that it was in state ρ_0 at time t_0 . As we shall see, it has the same form as in chemistry. The master equation is the time differential of the conditional probability $\text{pr}(\rho, t)$: it sums the probabilities of entering a state minus the probabilities of exiting the state. That is, it sums all possible transitions $\iota \in \mathfrak{I}$ to the current state ρ , given by the probability of the previous state $\text{pr}(\rho - v_\iota, t)$ times the transition propensity from the previous state $a_\iota(\rho - v_\iota)$, minus all possible transitions ι out of the current state ρ , given by the probability of the current state $\text{pr}(\rho, t)$ times the transition propensity $a_\iota(\rho)$ from the current state to some other state. All these concepts are defined below.

2.2-1 Process algebra master equation

$$\partial \text{pr}(\rho, t) / \partial t = \sum_{\iota \in \mathfrak{I}} a_\iota(\rho - v_\iota) \text{pr}(\rho - v_\iota, t) - a_\iota(\rho) \text{pr}(\rho, t)$$

- \mathfrak{I} is the finite set of *possible interactions* arising from a set of reagents E . Here $X.i$ is an ordered pair identifying a molecule summand in E , and $E.X.i$ is a molecule summand as previously defined.

$$\mathfrak{I} = \{ \{X.i\} \text{ s.t. } E.X.i = \tau_{(r)}.Q \} \cup \{ \{X.i, Y.j\} \text{ s.t. } E.X.i = ?n_{(r)}.Q \text{ and } E.Y.j = !n_{(r)}.R \} \quad (\text{for any } r, n, Q, R)$$

- $\rho \in \text{species}(E) \rightarrow \text{Nat}$ is a *reagent state* of the system: a multiset of reagent species. A general solution of the master equation (as a partial differential equation) is a function of ρ .
- let χ be a random variable whose values are states ρ . Then $\text{pr}(\rho, t) = \text{Pr}\{\chi(t) = \rho \mid \chi(0) = \rho_0\}$ is the conditional probability of the system being in state ρ at time t given that it was in state ρ_0 at time 0 . In a system E, P we have $\rho_0 = P^\dagger$, with $P^{\dagger \# X_i}$ being the initial number of X_i reagents.
- v_ι is the state change caused by an interaction $\iota \in \mathfrak{I}$. It is obtained from \mathfrak{I} and E :
$$v_\iota = -X^\dagger + Q^\dagger \quad \text{if } \iota = \{X.i\} \text{ s.t. } E.X.i = \tau_{(r)}.Q$$

$$v_\iota = -X^\dagger - Y^\dagger + Q^\dagger + R^\dagger \quad \text{if } \iota = \{X.i, Y.j\} \text{ s.t. } E.X.i = ?n_{(r)}.Q \text{ and } E.Y.j = !n_{(r)}.R$$
- $a_\iota(\rho)$ is the *propensity* of interaction ι in state ρ , defined by a base rate and a state-dependent count:
$$a_\iota(\rho) = r_\iota \cdot h_\iota(\rho)$$

- r_i is the stochastic rate of interaction ι ; homeo interactions can happen in 2 symmetric ways:

if $\iota = \{X.i\}$ s.t. $E.X.i = \tau_{(r)}.Q$	then	$r_i = r$
if $\iota = \{X.i, Y.j\}$ s.t. $X \neq Y$ and $E.X.i = ?n_{(r)}.Q$ and $E.Y.j = !n_{(r)}.R$	then	$r_i = r$
if $\iota = \{X.i, X.j\}$ s.t. $E.X.i = ?n_{(r)}.Q$ and $E.X.j = !n_{(r)}.R$	then	$r_i = 2r$
- $h_i(\rho)$ is the number of *distinct combinations* of reagents from state ρ that can participate in interaction ι ; it depends on the kind of interaction:

if $\iota = \{X.i\}$	then	$h_i(\rho) = \rho^{\#X}$
if $\iota = \{X.i, Y.j\}$ with $X \neq Y$	then	$h_i(\rho) = \rho^{\#X} \cdot \rho^{\#Y}$
if $\iota = \{X.i, X.j\}$	then	$h_i(\rho) = \rho^{\#X} \cdot (\rho^{\#X} - 1) / 2$
- Summarizing the last three points, we can compute the propensities $a_i(\rho)$ as follows:

if $\iota = \{X.i\}$ s.t. $E.X.i = \tau_{(r)}.Q$	then	$a_i(\rho) = r \cdot \rho^{\#X}$
if $\iota = \{X.i, Y.j\}$ s.t. $X \neq Y$ and $E.X.i = ?a_{(r)}.Q$ and $E.Y.j = !a_{(r)}.R$	then	$a_i(\rho) = r \cdot \rho^{\#X} \cdot \rho^{\#Y}$
if $\iota = \{X.i, X.j\}$ s.t. $E.X.i = ?a_{(r)}.Q$ and $E.X.j = !a_{(r)}.R$	then	$a_i(\rho) = r \cdot \rho^{\#X} \cdot (\rho^{\#X} - 1)$

2.2-2 Example

The analytical solution of master equations is in general very hard; see [8] for some solvable classes. As a simple example, let us solve the degradation, $\tau_{(r)}.0$, of a single molecule:

$$(E,P) = ((X = \tau_{(r)}.0), X)$$

The initial state is $P^t = \{X\}$. The reachable states are $\{X\}$ and $\{\}$; therefore, the probability $\text{pr}(\rho, t)$ is zero for any other state ρ . (N.B.: without this assumption the argument below goes into an infinite regression, and more general techniques such as [8] have to be used.) We have:

$$\mathfrak{S} = \{\{X.1\}\}, \text{ with a single possible interaction } \iota = \{X.1\}$$

$$\rho_0 = \{X\}, \quad v_i = -\{X\}, \quad r_i = r, \quad \{X\} - v_i = \{X, X\}, \quad \{\} - v_i = \{X\}$$

Let us work out the probability of state $\{X\}$:

$$a_i(\{X\}) = r_i \cdot h_i(\{X\}) = r \cdot \{X\}^{\#X} = r$$

$$a_i(\{X\} - v_i) = r_i \cdot h_i(\{X\} - v_i) = r \cdot \{X, X\}^{\#X} = 2r$$

$$d\text{pr}(\{X\}, t) / dt = \sum_{i \in \mathfrak{S}} a_i(\{X\} - v_i) \text{pr}(\{X\} - v_i, t) - a_i(\{X\}) \text{pr}(\{X\}, t) = -r \cdot \text{pr}(\{X\}, t)$$

The solution of that differential equation is an exponential function $\text{pr}(\{X\}, t) = Ce^{-rt}$. Since $\text{pr}(\{X\}, 0) = 1$, we have $Ce^{-r \cdot 0} = 1$, that is $C = 1$; hence:

$$\text{pr}(\{X\}, t) = e^{-rt}$$

Let us now work out the probability of state $\{\}$:

$$a_i(\{\}) = r_i \cdot h_i(\{\}) = r \cdot \{\}^{\#X} = 0$$

$$a_i(\{\} - v_i) = r_i \cdot h_i(\{\} - v_i) = r \cdot \{X\}^{\#X} = r$$

$$d\text{pr}(\{\}, t) / dt = \sum_{i \in \mathfrak{S}} a_i(\{\} - v_i) \text{pr}(\{\} - v_i, t) - a_i(\{\}) \text{pr}(\{\}, t) = r \cdot \text{pr}(\{X\}, t) = re^{-rt}$$

By integrating $\int re^{-rt} dt$ we obtain the following. Note that $\text{pr}(\{X\}, t) + \text{pr}(\{\}, t) = 1$, as expected.

$$\text{pr}(\{\}, t) = 1 - e^{-rt}$$

3 Chemistry

We now give the Chemical Master Equation for systems of chemical reactions, from [14] (which more generally treats reactions of any molecularity, not just unary/binary). Let M be the number of chemical reactions C , and N be the number of species X . Let $\gamma = N_A V$ where N_A is Avogadro's number, and V is the volume of the solution (assumed constant). The system of chemical reactions C and the vector of initial conditions S are written as follows, where s_{ij}, r_{ij} are the stoichiometric coefficients and k_j are the reaction rates:

3.1-1 Definition: System of chemical reactions and initial solution

$C_j: \sum_{i \in 1..N} s_{ij} X_i \rightarrow^{k_j} \sum_{i \in 1..N} r_{ij} X_i$	$j \in 1..M$	Chemical Reactions
$S_i: \text{the initial number of } X_i \text{ molecules}$	$i \in 1..N$	Initial Solution
$[X_i]_0 = S_i/\gamma$ is the initial concentration of X_i in <i>mol</i> .		

The master equation describes the conditional probability of a chemical system being in state σ at time t , given that it was in state σ_0 at time 0:

3.1-2 Chemical master equation

$$\partial \text{pr}(\sigma, t) / \partial t = \sum_{i \in 1..M} a_i(\sigma - v_i) \text{pr}(\sigma - v_i, t) - a_i(\sigma) \text{pr}(\sigma, t)$$

- $\{X_i \mid i \in 1..N\}$ are the chemical species
- $\{C_j \mid j \in 1..M\}$ are the chemical reactions
- $\sigma \in \{1..N\} \rightarrow \text{Nat}$ is a *chemical state*: a vector of the number of molecules σ_i for each species X_i . There is an associated multiset which we also indicate by $\sigma \in \text{species} \rightarrow \text{Nat}$ such that $\sigma^{\#X_i} = \sigma_i$.
- let χ be a random variable whose values are states σ . Then, $\text{pr}(\sigma, t) = \text{Pr}\{\chi(t) = \sigma \mid \chi(0) = \sigma_0\}$ is the conditional probability of the system being in state σ at time t given that it was in state σ_0 at time 0. In a system C, S , the initial state is $\sigma_{0i} = S_i$ for each species X_i .
- $v_j = r_j - s_j$ is the vector of changes in the number of molecules caused by reaction j , where $r_j = (r_{1j} \dots r_{Nj})$ and $s_j = (s_{1j} \dots s_{Nj})$. Again there are associated multisets r_j, s_j such that $r_j^{\#X_i} = r_{ij}, s_j^{\#X_i} = s_{ij}$, and a multiset difference $v_j = r_j - s_j$.
- $a_j(\sigma)$ is the *propensity* of reaction j in state σ , defined as $a_j(\sigma) = c_j \cdot h_j(\sigma)$, where:
- $h_j(\sigma) = \prod_{i \in 1..N} (\sigma_i \text{ choose } s_{ij})$ is the number of distinct combinations of molecules from state σ that can participate in reaction C_j .
- c_j are the stochastic rates, related but not identical to the reaction rates k_j (we use also the letters r, s for stochastic rates). The general formula connecting the two is the following:

$$c_j = (k_j / (\gamma^{K_j-1})) \prod_{i \in 1..N} (s_{ij}!) \quad \text{for } \gamma = N_A V \text{ and } K_j = \sum_{i \in 1..N} (s_{ij}) \quad (K_j \text{ is the molecularity of } C_j)$$
- For the unary/binary reactions of interest to us, we can summarize the last three points as follows:

$X \xrightarrow{k_j} \dots$	$K_j=1$	$c_j = k_j$	$h_j(\sigma) = \sigma^{\#X}$	$a_j(\sigma) = k_j \cdot \sigma^{\#X}$
$X + Y \xrightarrow{k_j} \dots$	$K_j=2$	$c_j = k_j/\gamma$	$h_j(\sigma) = \sigma^{\#X} \cdot \sigma^{\#Y}$	$a_j(\sigma) = k_j \cdot \sigma^{\#X} \cdot \sigma^{\#Y} / \gamma$
$2X \xrightarrow{k_j} \dots$	$K_j=2$	$c_j = 2k_j/\gamma$	$h_j(\sigma) = \sigma^{\#X} \cdot (\sigma^{\#X}-1)/2$	$a_j(\sigma) = k_j \cdot \sigma^{\#X} \cdot (\sigma^{\#X}-1) / \gamma$

4 Equivalence of master equations

We translate systems of processes E, P to chemical systems C, S and back, under the restriction that chemical reactions have only one or two reagents (but any number of products). On the right side of the following tables, we note the conversions between stochastic rates r and mass action rates k from

[4][14]. In the case of $X+X$ homeo reactions we emphasize two separate phenomena: on one hand the conversion $r=2k/\gamma$ between stochastic and mass action rates, and on the other hand the rate $s=r/2$ of stochastic channels that implement an $X+X$ chemical interaction (resulting in $s=k/\gamma$). Chemical reactions in a set of reactions C are assumed to be uniquely tagged by tags “ n ” out of an arbitrary index set; these are used (or taken to be in bijection with) channel names in translation 4.1–1. The notation $\oplus \Pi$ of P is the choice-composition of one P for each element of the set satisfying the predicate Π ; suitable quantifications relating a P and its element are omitted. Recall that P can represent an arbitrary number of (or no) chemical products, while X and Y represent individual chemical species. Chemical “+” and process “|” are implicitly converted into each other.

4.1–1 From chemical systems C,S to process systems $P_i(C,S)$

$$P_i(C) = \{ (X = \oplus ((n: X \rightarrow^k P) \in C) \text{ of } (\tau_{(r)}, P) \oplus \text{ with } r=k \\ \oplus ((n: X+Y \rightarrow^k P) \in C \text{ and } Y \neq X) \text{ of } (?n_{(r)}, P) \oplus \text{ with } r=k/\gamma \\ \oplus ((n: Y+X \rightarrow^k P) \in C \text{ and } Y \neq X) \text{ of } (!n_{(r)}, 0) \oplus \text{ with } r=k/\gamma \\ \oplus ((n: X+X \rightarrow^k P) \in C) \text{ of } (?n_{(r/2)}, P \oplus !n_{(r/2)}, 0)) \text{ with } r=2k/\gamma \\ \text{s.t. } X \text{ is a species in } C \}$$

$$P_i(C,S) = E,P \text{ where } E=P_i(C) \text{ and } P^{\#X_i} = S_i \text{ for all species } X_i$$

4.1–2 From process systems E,P to chemical systems $Ch_\gamma(E,P)$

$$Ch_\gamma(E) = \{ \{ \{X,i\}: X \rightarrow^k P \} \text{ s.t. } E.X.i = \tau_{(r)}, P \} \cup \text{ with } k=r \\ \{ \{ \{X,i,Y,j\}: X + Y \rightarrow^k P + Q \} \text{ s.t. } X \neq Y \text{ and } E.X.i = ?n_{(r)}, P \text{ and } E.Y.j = !n_{(r)}, Q \} \cup \text{ with } k=r\gamma \\ \{ \{ \{X,i,X,j\}: X + X \rightarrow^{2k} P + Q \} \text{ s.t. } E.X.i = ?n_{(r)}, P \text{ and } E.X.j = !n_{(r)}, Q \} \text{ with } k=r\gamma/2$$

$$Ch_\gamma(E,P) = C,S \text{ where } C=Ch_\gamma(E) \text{ and } S_i = P^{\#X_i} \text{ for all species } X_i$$

Reactions in $Ch_\gamma(E)$ are uniquely tagged by $\{X,i\}$ (a singleton containing an ordered pair of a species and an integer) or by $\{X,i,Y,j\}$ (a set containing two ordered pairs). Fact: there is a bijection between the tags of $Ch_\gamma(P_i(C))$ and those of C such that the corresponding reactions are equal. That is, $Ch_\gamma(P_i(C)) = C$ up to tags. E.g., if $(n: X \rightarrow^k P) \in C$ then $P_i(C).X.i = \tau_{(k)}, P$ for some i , and $(\{X,i\}: X \rightarrow^k P) \in Ch_\gamma(P_i(C))$, with the bijection relating n to $\{X,i\}$.

4.1–3 Example

As an example, and in particular an example of homeo reactions, consider the process system with one reagent X and two initial molecules:

$$(E,P) = (X = ?n_{(r)}, X \oplus !n_{(r)}, 0, X|X).$$

The corresponding chemical system is

$$Ch_\gamma(E,P) = (\{X,1,X,2\}: X + X \xrightarrow{r\gamma} X, \langle 2 \rangle).$$

The process master equation for (E,P) , expanding the definitions from Section 2 for $\Sigma_{i \in \{X,1,X,2\}}$ is:

$$\partial \text{pr}(\rho,t) / \partial t = (r \cdot (\rho^{\#X} + 1) \cdot \rho^{\#X}) \cdot \text{pr}(\rho + \downarrow X, t) - (r \cdot \rho^{\#X} \cdot (\rho^{\#X} - 1)) \cdot \text{pr}(\rho,t)$$

The chemical master equation for $Ch_\gamma(E,P)$ from Section 3 for $\Sigma_{j \in 1..1}$ and state vector $\sigma = \langle \sigma_1 \rangle$ is:

$$\partial \text{pr}(\sigma,t) / \partial t = (r \cdot (\sigma_1 + 1) \cdot \sigma_1) \cdot \text{pr}(\langle \sigma_1 + 1 \rangle, t) - (r \cdot \sigma_1 \cdot (\sigma_1 - 1)) \cdot \text{pr}(\sigma,t)$$

Therefore the two equations are identical if we identify (as we do) the molecule count vector σ with the multiset $\rho = \{X, \dots, X\}$ such that $\rho^{\#X} = \sigma_1$.

We now show that, in general, the chemical master equation and the process master equation are identical in the same sense under these translations.

4.1–4 Theorem

The Process Master Equation of E, P is the same as the Chemical Master Equation of $\text{Ch}_\gamma(E, P)$.

Proof

Take a set of reagents E , and consider $\text{Ch}_\gamma(E)$; those chemical reactions are indexed by the set:

$$\mathfrak{I} = \{\{X.i\} \text{ s.t. } E.X.i = \tau_{(r)}.Q\} \cup \{\{X.i, Y.j\} \text{ s.t. } E.X.i = ?a_{(r)}.Q \text{ and } E.Y.j = !a_{(r)}.R\}$$

Therefore, we write the chemical master equation for $\text{Ch}_\gamma(E)$ using \mathfrak{I} as the index set:

$$\partial \text{pr}(\sigma, t) / \partial t = \sum_{\iota \in \mathfrak{I}} a_\iota(\sigma - v_\iota) \text{pr}(\sigma - v_\iota, t) - a_\iota(\sigma) \text{pr}(\sigma, t)$$

The process algebra master equation for E is also a sum indexed by \mathfrak{I} :

$$\partial \text{pr}(\rho, t) / \partial t = \sum_{\iota \in \mathfrak{I}} a_\iota(\rho - v_\iota) \text{pr}(\rho - v_\iota, t) - a_\iota(\rho) \text{pr}(\rho, t)$$

We show that the corresponding elements of the summations are identical expressions in the respective state variables σ vs. ρ (we use different letters for the state variables just to disambiguate similar expressions from the two master equations). We have three cases:

(1) $\iota = \{X.i\}$. Then $X \rightarrow^k P \in \text{Ch}_\gamma(E)$ and $E.X.i = \tau_{(r)}.P$ with $k=r$. Hence:

$$\begin{array}{ll} \text{(CME)} & a_\iota(\sigma) = k \cdot \sigma^{\#X} \\ & v_\iota = r_1 - s_1 = -X^\dagger + P^\dagger \end{array} \quad \begin{array}{ll} \text{(PME)} & a_\iota(\rho) = r \cdot \rho^{\#X} = k \cdot \rho^{\#X} \\ & v_\iota = -X^\dagger + P^\dagger \end{array}$$

(2) $\iota = \{X.i, Y.j\}$ with $X \neq Y$. Then $X + Y \rightarrow^k P + Q \in \text{Ch}_\gamma(E)$ and $E.X.i = ?n_{(r)}.P$ and $E.Y.j = !n_{(r)}.Q$ with $k=r\gamma$. Hence:

$$\begin{array}{ll} \text{(CME)} & a_\iota(\sigma) = k \cdot \sigma^{\#X} \cdot \sigma^{\#Y} / \gamma \\ & v_\iota = r_1 - s_1 = -X^\dagger - Y^\dagger + P^\dagger + Q^\dagger \end{array} \quad \begin{array}{ll} \text{(PME)} & a_\iota(\rho) = r \cdot \rho^{\#X} \cdot \rho^{\#Y} = k \cdot \rho^{\#X} \cdot \rho^{\#Y} / \gamma \\ & v_\iota = -X^\dagger - Y^\dagger + P^\dagger + Q^\dagger \end{array}$$

(3) $\iota = \{X.i, X.j\}$. Then $X + X \rightarrow^{2k} P + Q \in \text{Ch}_\gamma(E)$ and $E.X.i = ?n_{(r)}.P$ and $E.X.j = !n_{(r)}.Q$ with $k=r\gamma/2$. Hence:

$$\begin{array}{ll} \text{(CME)} & a_\iota(\sigma) = (2k) \cdot \sigma^{\#X} \cdot (\sigma^{\#X} - 1) / \gamma \\ & v_\iota = r_1 - s_1 = -X^\dagger - X^\dagger + P^\dagger + Q^\dagger \end{array} \quad \begin{array}{ll} \text{(PME)} & a_\iota(\rho) = r \cdot \rho^{\#X} \cdot (\rho^{\#X} - 1) = 2k \cdot \rho^{\#X} \cdot (\rho^{\#X} - 1) / \gamma \\ & v_\iota = -X^\dagger - X^\dagger + P^\dagger + Q^\dagger \end{array}$$

Moreover, the initial conditions of $\text{Ch}_\gamma(E, P)$ are S such that $S_i = P^{\dagger \#X_i}$ for all X_i . Hence, the initial conditions of the CME are $\sigma_{0i} = S_i = P^{\dagger \#X_i} = \rho_0^{\#X_i}$, which are the initial conditions of the PME. Therefore the two master equations are formally identical. \square

4.1–5 Theorem

The Chemical Master Equation of C, S is the same as the Process Master Equation of $\text{Pi}_\gamma(C, S)$.

Proof

We know from Theorem 4.1–4 that the PME of E, P is the same as the CME of $\text{Ch}_\gamma(E, P)$. Hence, for any chemical system C, S resulting in a process system $\text{Pi}_\gamma(C, S)$, we have that the PME of $\text{Pi}_\gamma(C, S)$ is the same as the CME of $\text{Ch}_\gamma(\text{Pi}_\gamma(C, S))$. Moreover, $\text{Ch}_\gamma(\text{Pi}_\gamma(C)) = C$ up to reaction labels (which are in bijection), and the initial conditions of $\text{Ch}_\gamma(\text{Pi}_\gamma(C, S))$ are S . Hence the CME of $\text{Ch}_\gamma(\text{Pi}_\gamma(C, S))$ is the same as the CME of C, S . Therefore, the PME of $\text{Pi}_\gamma(C, S)$ is the same as the CME of C, S . \square

References

- [1] L. Bortolussi, A. Policriti. Stochastic Concurrent Constraint Programming and Differential Equations. Proc. Fifth Workshop on Quantitative Aspects of Programming Languages, Braga, 2007.
- [2] M. Calder, S. Gilmore, J. Hillston: Automatically Deriving ODEs from Process Algebra Models of Signalling Pathways. Proc. Computational Methods in Systems Biology 2005, 204-215.

- [3] L. Cardelli: On Process Rate Semantics. Preprint available from <http://LucaCardelli.name>.
- [4] D.T. Gillespie. Exact Stochastic Simulation of Coupled Chemical Reactions. *Journal of Physical Chemistry* 81, pp. 2340–2361. 1977.
- [5] D.T. Gillespie. The chemical Langevin equation. *Journal of Chemical Physics* 113(1), 297-306, 2000.
- [6] H. Hermanns. *Interactive Markov Chains*. Springer LNCS, vol 2428, 2002.
- [7] J. Hillston. *A compositional approach to performance modelling*. Cambridge University Press, 1996.
- [8] T. Jahnke, W. Huisinga. Solving the chemical master equation for monomolecular reaction systems analytically. *Mathematical Biology* 54(1): 1-26. Jan 2007.
- [9] H. Kitano. A graphical notation for biochemical networks. *BioSilico* 1(5): 169-76. 2003.
- [10] C. Priami. Stochastic π -calculus. *The Computer Journal*, 38, pp 578–589, 1995.
- [11] C. Priami, A. Regev, E. Shapiro, W. Silverman. Application of a stochastic name-passing calculus to representation and simulation of molecular processes. *Information Processing Letters* 80, 25-31. 2001.
- [12] A. Regev. *Computational Systems Biology: A Calculus for Biomolecular knowledge*. Ph.D. Thesis, Tel Aviv University. 2002.
- [13] A. Regev, E. Shapiro. Cellular abstractions: Cells as computation. *Nature* 419 343. 2002.
- [14] M. Ullah, O. Wolkenhauer. A general derivation of the differential Chapman-Kolmogorov equation. <http://www.citebase.org/abstract?id=oai:arXiv.org:q-bio/0610003>. 2006.