

An attempt to give a clear semantics of the extension of PEPA for massively parallel processes and biological modelling

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Abstract

This paper is an attempt to give a clear semantics of an extension of PEPA that deals with massively parallel processes that can model both computer and biological systems. The semantics is defined as the expectation of the number of components in their different states with respect to time. Unfortunately, it is shown that it is not always possible to express the result of this semantics by a small set of coupled ordinary differential equations like in the previous works [2, 1, 4].

1 Introduction

PEPA is a stochastic process algebra defined by Jane Hillston [3] that permits to construct continuous time Markov chains (CTMCs) in a compact and elegant way. It uses a small set of operators that allow to define sequence, choice or synchronisation of actions. This makes it easy to define in a couple lines huge state space models, usable, then, as the input of many tools.

However, a model with too many states can be hard, even impossible, to analyse. For this reason recent works have been made to give PEPA an additional semantics. That semantics makes an abstraction of the exact description of the state space and considers instead the evolution of the number of identical components in their different states with respect to time [2, 1, 4]. The PEPA model is then interpreted as a set of coupled ordinary differential equations (ODEs) where each equation describes the evolution of the number of each component in each state. Such an abstraction may reduce greatly the size of the model since the size of the obtained ODE system might not depend on the number of identical components inside the PEPA model.

In this paper we express this semantics in terms of the expectation of the number of each component in their different states. We will show that, in the most obvious case (when the processes are independent), this semantics can be described by a small set of ODEs. For the other cases we do not know, but we give an example that cannot be expressed by a small set of ODEs, and that can let us think that in many cases this semantics cannot be reduced by small set of ODEs.

1.1 Outline

The paper is organised as follow : *Section 2* recalls what the process algebra PEPA is and defines two extensions of it. The first one completes the cooperation operator with another kind of interaction suitable to describe the multiplication of mass actions when modelling, for instance, kinetic reactions. *Section 3* gives the definition of the semantics of such a double extension (massively parallel processes and mass actions) in terms of the expectation of the number of each component in each state with respect to time. *Section 4* concludes.

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2 PEPA and its extensions

The definition of PEPA is only briefly recalled here. For further information the reader is invited to refer to [3]. A PEPA model is :

1. A set of declarations. A declaration is denoted :

$$C \stackrel{\text{def}}{=} S$$

where S is a PEPA term denoting a *sequential process* (or simply called a component) and follows the syntax :

$$S := (\alpha, r).S \mid S + S \mid C$$

2. A root term or system equation is a PEPA term obtained by the following rules :

$$P := P \underset{L}{\bowtie} P \mid P/L \mid S$$

where S is a PEPA term denoting a *sequential process*.

2.1 PEPA with the additional mass action cooperation

Here we define an extension of PEPA that can model, amongst others, the multiplication of the mass actions of biological kinetic reactions. To do that the cooperation synchronisation is extended with another kind of synchronisation. To represent this other kind, the cooperation operator is denoted in the following way :

$$P \underset{L}{\overset{H}{\bowtie}} Q$$

The cooperation operator uses two sets of actions, H and L .

- L contains the cooperating actions that follow the standard semantics of PEPA, that is, which respect the definition of the *bounded capacity* :
 - the resulting rate, denoted R , of the cooperation on the action α between two transitions of rates respectively, r_1 and r_2 placed on the components P and Q is defined by :

$$R = \frac{r_1}{r_\alpha(P)} \times \frac{r_2}{r_\alpha(Q)} \times \min(r_\alpha(P), r_\alpha(Q))$$

where $r_\alpha(P)$ and $r_\alpha(Q)$ denotes the apparent rate of α from P and Q respectively.

- H contains the cooperation actions that follow the multiplication of mass actions, as in biological kinetic reactions :
 - this time the resulting rate is :

$$R = r_1 \times r_2$$

- The apparent rate is defined consequently :

$$r_\alpha(P \underset{L}{\overset{H}{\bowtie}} Q) = r_\alpha(P) \times r_\alpha(Q)$$

Appendix A contains an example of a biological kinetic reaction that uses this kind of cooperation.

2.2 PEPA for massively parallel processes and mass actions

The extension of PEPA for massively parallel processes has been defined in [2, 1, 4]. It consists of :

1. A additional notation which permits to define easier the parallelism of a certain number of identical, independent processes :

$$P[n] = \underbrace{P \parallel \dots \parallel P}_n$$

2. An algorithm to construct a set of coupled ODEs modelling the number of components in their different states with respect to time.

So the definition of PEPA for massively parallel processes and mass actions is :

1. a set of declarations, each noted :

$$C \stackrel{def}{=} S$$

with S a PEPA term designing a sequential process

$$S := (\alpha, r).S \mid S + S \mid C$$

2. a root term :

$$P := P \overset{H}{\underset{L}{\boxtimes}} P \mid P/L \mid (S_1[n_1] \parallel \dots \parallel S_k[n_k])$$

where $S_1, \dots, S_k$ define all states of the sequential process S . Also a mass of a sequential process can only be used once, no more. This is to ensure that the expectation of the states of this process will match with the mass action of the other processes (in other words the mass of a sequential process can not be split in two different areas).

3 Semantics of this double extension

In this section we defined the expectation of the number of each component in each state w.r.t. time of this double extension (mass actions and massive parallelism) and try to express this expectation as a small set of coupled ODEs. Unfortunately we succeed only for the simplest case when the processes are independent.

3.1 Definition of the semantics

We will now give the formal definition of such a semantics. In the other subsections we will try to identify in which cases this semantics can or cannot be expressed as simple¹ ODEs.

Definition 1 (Notation of the decomposition of a PEPA model in all its processes) *Let P be a PEPA model with the double extension defined above. Let's decompose P in n sequential processes (also called components) in the following manner :*

1. If $P = P_1 \overset{H}{\underset{L}{\boxtimes}} P_2$ then P_1 will be decomposed in n_1 components and P_2 in n_2 components. The decomposition of P will be the appending of the decomposition of P_1 and P_2 and the number of components will be $n = n_1 + n_2$.
2. If $P = P_1/L$ the decomposition of P will be the decomposition of P_1 .
3. If $P = (S^1[n_1] \parallel \dots \parallel S^k[n_k])$ the decomposition of P will be the $n = \sum_{i=1}^k n_i$ components, respectively n_i times S^i , for $i = 1, \dots, k$.

Let $X = (X_t)_{t \in \mathbb{R}_+}$ be the continuous time Markov chain (CTMC) of P . Let $X^i = (X_t^i)_{t \in \mathbb{R}_+}$ be the i^{th} random process of X according to this decomposition. It is important to remark that X^i captures the behaviour of S^i in interaction with the rest of P , which is different from the CTMC of S^i (unless S^i is independent from the others). X is entirely defined (admitted) by :

$$(X^1, \dots, X^n)$$

¹simple means the ODEs only contain functions describing the evolution of one component, not the evolution of some state in the whole process

Definition 2 (Semantics of the double extension of PEPA) Let $X = (X^1, \dots, X^n)$ be the stochastic process of P as defined above. Among the processes X^i some of them have the same state space because they are obtained from the same sequential process, denoted $S^i[n_i]$. Let $\mathbf{S}$ be the set of all states of all sequential processes. Since $\mathbf{S}$ is a set, multiple occurrences of the same state will be represented only once. Let there be $|\mathbf{S}|$ families of random variables, denoted $N^s = (N_t^s)_{t \in \mathbb{R}_+}$, one for each $s \in \mathbf{S}$. N^s represents the number of components of X in state s with respect to time. The semantics of PEPA for massively parallel processes is then given as the expectation of N^i :

$$\forall s \in \mathbf{S} \quad \mathbb{E}[N_t^s]$$

3.2 Methodology to express this semantics

In this subsection we give a methodology to find the ODEs of a given PEPA model. However in many cases this ODE system will be as big as the ODE system describing the CTMC of P . Let's first give the following proposition.

Proposition 1 The expectation of the number components in a given state s is the sum of their probability to be in s :

$$\forall s \in \mathbf{S} \quad \mathbb{E}[N_t^s] = \sum_{i=1}^n \mathbb{P}(X_t^i = s)$$

Proof

Let there be $n \times |\mathbf{S}|$ families of binary random variables, denoted $B^{i,s} = (B_t^{i,s})_{t \in \mathbb{R}_+}$, such that $B_t^{i,s}$ is equal to 1 when X_t^i is in the state s , 0 otherwise :

$$B_t^{i,s} = \begin{cases} 1 & \text{if } X_t^i = s \\ 0 & \text{otherwise} \end{cases}$$

The expectation of $B_t^{i,s}$ is (by definition of the expectation) the probability of having $X_t^i = s$:

$$\mathbb{E}[B_t^{i,s}] = \mathbb{P}(X_t^i = s)$$

One can notice that $N_t^s = \sum_{i=1}^n B_t^{i,s}$, moreover since the expectation of the sum of random variables is the sum of their expectations, we obtain :

$$\mathbb{E}[N_t^s] = \mathbb{E}\left[\sum_{i=1}^n B_t^{i,s}\right] = \sum_{i=1}^n \mathbb{E}[B_t^{i,s}] = \sum_{i=1}^n \mathbb{P}(X_t^i = s)$$

□

So a possible methodology can be, for every state of $\mathbf{s}$, to express the sum $\sum_{i=1}^n \mathbb{P}(X_t^i = s)$. The probabilities $\mathbb{P}(X_t^i = s)$ can always be expressed by a set of ODEs (by summing the ODEs describing P), but the obtained set can be, depending on the model, reducible or not. For instance, if all processes are independent, their probabilities will simply be described by the ODEs of their individual CTMC. We want this probability to be expressed as simply as possible, but in the worst case it might be described by the ODEs of the whole CTMC of P .

In the next subsections we will give some examples when it is possible or not to express this expectation simply.

3.3 Expectation of a set of independent processes

We will now express the semantics of the most simple case : when all components are identical and independent.

Let $P = (S^1[n_1] || \dots || S^k[n_k])$. Let $X = (X^1, \dots, X^n)$, with $n = n_1 + \dots + n_k$. Each S^j with $1 \leq j \leq k$ corresponds to the same process starting at different states. $S^j[n_j]$ means n_j processes start at the state s_j . If X^i with $1 \leq i \leq n$ is independent from the others then X^i is just defined as the Markov process of some S^j . Let $\mathbf{Q}^i$ be its infinitesimal generator and π^i its initial distribution. Let $\{s_1, \dots, s_m\}$ be the state space of X^i . The probability $\mathbb{P}(X_t^i = s_h)$ with $1 \leq h \leq m$ is then defined by the ordinary differential equation system below :

$$\frac{d\mathbf{p}^i(t)}{dt} = \mathbf{p}^i(t) \cdot \mathbf{Q}^i \quad \mathbf{p}^i(0) = \pi^i$$

where $\mathbf{p}^i(t)$ is the following line vector :

$$\mathbf{p}^i(t) = (\mathbb{P}(X_t^i = s_1), \dots, \mathbb{P}(X_t^i = s_m))$$

Let's sum the ODEs of all processes $X^1, \dots, X^n$:

$$\sum_{i=1}^n \frac{d\mathbf{p}^i(t)}{dt} = \sum_{i=1}^n \mathbf{p}^i(t) \cdot \mathbf{Q}^i \quad \sum_{i=1}^n \mathbf{p}^i(0) = \sum_{i=1}^n \pi^i$$

Since the sum of the derivatives is the derivative of the sum and that all $\mathbf{Q}^i$ are identical, denoted $\mathbf{Q}$, we obtain :

$$\frac{d\sum_{i=1}^n \mathbf{p}^i(t)}{dt} = \left(\sum_{i=1}^n \mathbf{p}^i(t) \right) \cdot \mathbf{Q} \quad \sum_{i=1}^n \mathbf{p}^i(0) = \sum_{i=1}^n \pi^i$$

We can now place the sum symbol inside each vector :

$$\begin{aligned} \frac{d(\sum_{i=1}^n \mathbb{P}(X_t^i = s_1), \dots, \sum_{i=1}^n \mathbb{P}(X_t^i = s_m))}{dt} &= \left(\sum_{i=1}^n \mathbb{P}(X_t^i = s_1), \dots, \sum_{i=1}^n \mathbb{P}(X_t^i = s_m) \right) \cdot \mathbf{Q} \\ \left(\sum_{i=1}^n \mathbb{P}(X_0^i = s_1), \dots, \sum_{i=1}^n \mathbb{P}(X_0^i = s_m) \right) &= \sum_{i=1}^n \pi^i \end{aligned}$$

We can now use *Proposition 1* :

$$\frac{d(\mathbb{E}[N_t^1], \dots, \mathbb{E}[N_t^m])}{dt} = (\mathbb{E}[N_t^1], \dots, \mathbb{E}[N_t^m]) \cdot \mathbf{Q} \quad (\mathbb{E}[N_0^1], \dots, \mathbb{E}[N_0^m]) = \sum_{i=1}^n \pi^i$$

π^i has 1 in its the entry corresponding to the initial state of the i^{th} process, 0 elsewhere. So the sum $\sum_{i=1}^n \pi^i$ is exactly $(n_1, \dots, n_m)$. Thus, we finally obtain the following ODE system to describe the expectation of the amount of every state of P :

$$\frac{d(\mathbb{E}[N_t^1], \dots, \mathbb{E}[N_t^m])}{dt} = (\mathbb{E}[N_t^1], \dots, \mathbb{E}[N_t^m]) \cdot \mathbf{Q} \quad (\mathbb{E}[N_0^1], \dots, \mathbb{E}[N_0^m]) = (n_1, \dots, n_m)$$

The case with non-identical independent processes is almost similar.

3.4 Example of a PEPA model not well expressed in this semantic

We will now give an example that shows that such a semantics is not always simply expressible. Let P be the PEPA model defined by the following declarations :

$$\begin{aligned} A &\stackrel{def}{=} (\alpha, r_\alpha).A' \\ A' &\stackrel{def}{=} (\tau, r_A).A \\ B &\stackrel{def}{=} (\alpha, r_\alpha).B' \\ B &\stackrel{def}{=} (\tau, r_B).B \end{aligned}$$

and the following root term $P = A \overset{\emptyset}{\boxtimes}_{\alpha} B$. The state space of P is $\{A \overset{\emptyset}{\boxtimes}_{\alpha} B, A' \overset{\emptyset}{\boxtimes}_{\alpha} B, A \overset{\emptyset}{\boxtimes}_{\alpha} B', A' \overset{\emptyset}{\boxtimes}_{\alpha} B'\}$. To simplify we will denote it $\{AA, A'B, AB', A'B'\}$. Let $X = (X^1, X^2)$ the CTMC of P . The set of ODEs describing completely P are :

$$\begin{aligned}\frac{d\mathbb{P}(X_t = AB)}{dt} &= -r_{\alpha} \times \mathbb{P}(X_t = AB) + r_A \times \mathbb{P}(X_t = A'B) + r_B \times \mathbb{P}(X_t = AB') \\ \frac{d\mathbb{P}(X_t = A'B)}{dt} &= -r_A \times \mathbb{P}(X_t = A'B) + r_B \times \mathbb{P}(X_t = A'B') \\ \frac{d\mathbb{P}(X_t = AB')}{dt} &= -r_B \times \mathbb{P}(X_t = AB') + r_A \times \mathbb{P}(X_t = A'B') \\ \frac{d\mathbb{P}(X_t = A'B')}{dt} &= r_{\alpha} \times \mathbb{P}(X_t = AB) - r_A \times \mathbb{P}(X_t = A'B') - r_B \times \mathbb{P}(X_t = A'B')\end{aligned}$$

To obtain the description of X^1 we just add the ODEs describing the probability of being in the states AB and AB' to get the probability of being in the state A and the probability of being in the states $A'B$ and $A'B'$ to get the probability of being in the state A' . It is similar for X^2 . Recalling that the derivative of the sum is the sum of the derivative we have :

$$\begin{aligned}\frac{d\mathbb{P}(X_t^1 = A)}{dt} &= \frac{d\mathbb{P}(X_t = AB)}{dt} + \frac{d\mathbb{P}(X_t = AB')}{dt} \\ \frac{d\mathbb{P}(X_t^1 = A')}{dt} &= \frac{d\mathbb{P}(X_t = A'B)}{dt} + \frac{d\mathbb{P}(X_t = A'B')}{dt} \\ \frac{d\mathbb{P}(X_t^2 = B)}{dt} &= \frac{d\mathbb{P}(X_t = AB)}{dt} + \frac{d\mathbb{P}(X_t = A'B)}{dt} \\ \frac{d\mathbb{P}(X_t^2 = B')}{dt} &= \frac{d\mathbb{P}(X_t = AB')}{dt} + \frac{d\mathbb{P}(X_t = A'B')}{dt}\end{aligned}$$

We replace the derivative by their functions and after simplification we obtain :

$$\begin{aligned}\frac{d\mathbb{P}(X_t^1 = A)}{dt} &= -r_{\alpha} \times \mathbb{P}(X_t = AB) + r_A \times (\mathbb{P}(X_t = A'B) + \mathbb{P}(X_t = A'B')) \\ \frac{d\mathbb{P}(X_t^1 = A')}{dt} &= r_{\alpha} \times \mathbb{P}(X_t = AB) - r_A \times (\mathbb{P}(X_t = A'B) + \mathbb{P}(X_t = A'B')) \\ \frac{d\mathbb{P}(X_t^2 = B)}{dt} &= -r_{\alpha} \times \mathbb{P}(X_t = AB) + r_B \times (\mathbb{P}(X_t = AB') + \mathbb{P}(X_t = A'B')) \\ \frac{d\mathbb{P}(X_t^2 = B')}{dt} &= r_{\alpha} \times \mathbb{P}(X_t = AB) - r_B \times (\mathbb{P}(X_t = AB') + \mathbb{P}(X_t = A'B'))\end{aligned}$$

We can simplify $\mathbb{P}(X_t = A'B) + \mathbb{P}(X_t = A'B')$ by $\mathbb{P}(X_t^1 = A')$. The others are simplified in the same way and we obtain :

$$\begin{aligned}\frac{d\mathbb{P}(X_t^1 = A)}{dt} &= -r_{\alpha} \times \mathbb{P}(X_t = AB) + r_A \times \mathbb{P}(X_t^1 = A') \\ \frac{d\mathbb{P}(X_t^1 = A')}{dt} &= r_{\alpha} \times \mathbb{P}(X_t = AB) - r_A \times \mathbb{P}(X_t^1 = A') \\ \frac{d\mathbb{P}(X_t^2 = B)}{dt} &= -r_{\alpha} \times \mathbb{P}(X_t = AB) + r_B \times \mathbb{P}(X_t^2 = B') \\ \frac{d\mathbb{P}(X_t^2 = B')}{dt} &= r_{\alpha} \times \mathbb{P}(X_t = AB) - r_B \times \mathbb{P}(X_t^2 = B')\end{aligned}$$

The probabilities of being in A , A' , B and B' also correspond to the expectation of the number of processes in these states (because they can not be more than one) :

$$\begin{aligned}\mathbb{E}[N_t^A] &= \mathbb{P}(X_t^1 = A) & \mathbb{E}[N_t^{A'}] &= \mathbb{P}(X_t^1 = A') \\ \mathbb{E}[N_t^B] &= \mathbb{P}(X_t^2 = B) & \mathbb{E}[N_t^{B'}] &= \mathbb{P}(X_t^2 = B')\end{aligned}$$

So the above ODEs describe the expectation of $N^A, \dots, N^{B'}$. The problem comes from the term $\mathbb{P}(X_t = AB)$. We have not found any way to simplify this term, and A, B are clearly neither independent nor equal. So it seems that the only way to know it, is to solve the ODEs describing the complete model P .

4 Conclusion

It is not clear yet what is the class of processes that be can expressed in this semantics and what is the class that cannot. But it might have something to do with the mixture of semi-dependent processes (ie those that are sometimes evolving alone and sometimes need to be synchronised with the others). The problem is that, certainly, the majority of practical interesting processes fall into this category. However, it may be possible to find that some simpler ODEs approximate this semantics. Maybe when the number of processes grows, the semantics in the previous works becomes a good approximation of this one?

5 Acknowledgement

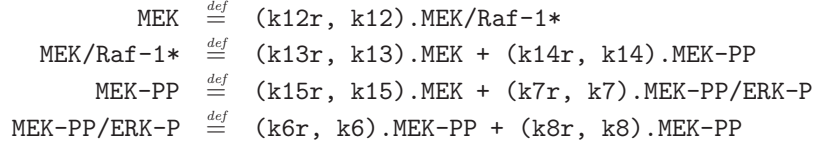
Thanks to Jane Hillston for our discussions about this problem and for her review.

References

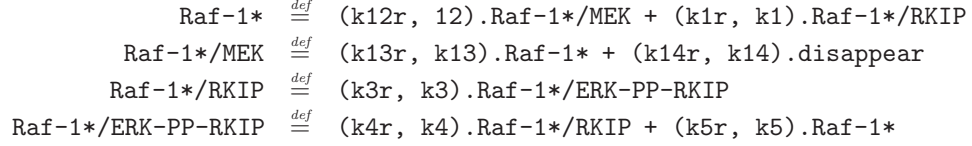
- [1] A. Benoit, M. Cole, S. Gilmore, and J. Hillston. Enhancing the effective utilisation of grid clusters by exploiting on-line performability analysis. *1st International Workshop on Grid Performability*, 2005.
- [2] M. Calder, S. Gilmore, and J. Hillston. Modelling the influence of RKIP on the ERK signaling pathway using the stochastic process algebra PEPA. *BioConcur*, 2004.
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- [4] J. Hillston. Fluid flow approximation of PEPA models. *QEST*, 2005.

A Example, modelling the influence of RKIP on ERK

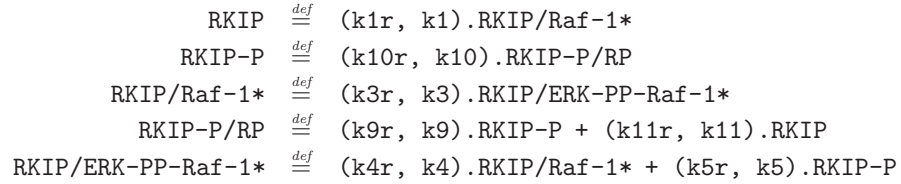
The code below models an example of biological kinetic reaction taken from [2]. Each reagent is modelled as a sequential component describing the evolution of it according to the different actions. The definition of MEK is given below :



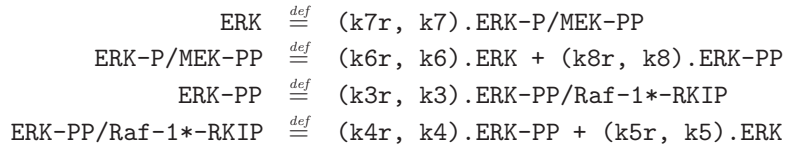
The definition of Raf-1* is given below :



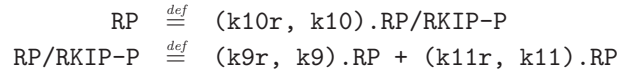
The definition of RKIP is given below :



The definition of ERK is given below :



The Definition of RP is given below :



The definition of system equation (root term) :

