

# Relating PDEs in Cylindrical Coordinates and CTMCs with Levels of Concentration

Andrea Degasperi<sup>1</sup> and Muffy Calder<sup>2</sup>

*Department of Computing Science  
University of Glasgow  
Glasgow, U.K.*

---

## Abstract

We present the derivation of a CTMC with levels model of diffusion in cylindrical coordinates from the partial differential equation for Fick's law. The resulting model abstracts both molar concentration, by discrete levels, *and* spatial location, by discrete compartments. We apply the results to the diffusion of nitric oxide in human vessels and illustrate with simulations in the PRISM tool.

*Keywords:* geometrical space, reaction-diffusion equations, cylindrical coordinates, partial differential equations, ordinary differential equations, continuous time Markov chains

---

## 1 Introduction

Formalisms such as process algebras and other calculi [15,19,11,6], rewriting rules [12,5] or languages [8,18], can be used to improve modelling and analysis of systems of biochemical reactions. Usually a model defined with these approaches uses mathematical techniques such as *ordinary differential equations* (ODEs), *continuous time Markov chains* (CTMCs), *CTMC with levels* [9] or *monte carlo simulations* as the underlying concrete semantics. In some cases, more than one mathematical semantics can be derived from the same formalism, e.g. Bio-PEPA [11], and they can be related to one another for a more robust interpretation of the result [9].

Recently, increasing interest has been given to the integration of location and movement in space within such formalisms. Spatial location and the diffusion of biochemical species can be represented in many ways. For example, space can be topological, i.e. hierarchical locations, or geometrical, i.e. a coordinate system of

---

<sup>1</sup> Email: [andrea@dcs.gla.ac.uk](mailto:andrea@dcs.gla.ac.uk)

<sup>2</sup> Email: [muffy@dcs.gla.ac.uk](mailto:muffy@dcs.gla.ac.uk)

spatial positions [13]. The diffusion of molecules can be described at a microscopic level by random walks, or at a macroscopic level by Fick’s law of diffusion [16,4].

In such scenarios, mathematical models are usually highly specific, incorporating assumptions that simplify the set of equations used. An example of this is the variety of mathematical models of nitric oxide (NO) transport and availability in blood vessels (see [20] for a complete review). These models all use sets of *partial differential equations* (PDEs), representing diffusion with Fick’s law in one dimensional cylindrical coordinates. More in detail, vessels are modelled as cylinders with concentric compartments representing layers of tissue. Subject of analysis is usually the distance at which NO can diffuse, from the layer of tissue where it is produced. To compute such distance, one can simplify the model considering only one dimension, the radius, as the other dimensions are invariants.

Our goal is to derive an approximation of models of NO transport and availability in blood vessels in terms of CTMC with levels. CTMC with levels are CTMCs whose states are characterised by the concentration of each species expressed in discrete levels. The motivation for this is the additional analysis available, e.g. testing of robustness under different degrees of stochasticity. Moreover, an approximation of PDEs in terms of such semantics ensures that we can use Bio-PEPA, which is based on CTMC with levels, and the tools developed for it to model and analyse this scenario. Before we can do so, the missing piece of the puzzle is a derivation of diffusion in one dimensional cylindrical coordinates in terms of CTMC with levels. In this paper we present such derivation, whose main novelties are:

- the rates of the resulting CTMC with levels are derived directly from the diffusion constant of the diffusing biochemical species. This derivation, trivial in case of Cartesian coordinates, requires additional assumptions in case of cylindrical coordinates;
- the rates of the CTMC with levels depend not only on the concentration of the species and the volumes of the compartments, but also on the spatial position.

The paper is organised as follows. In Section 2 we present the derivation of the PDEs to CTMC with levels. In Section 3 we present an example. In Section 4 we mention related work, while conclusions and future work are in Section 5.

## 2 Diffusion in a one-dimensional cylindrical vessel: relating PDEs, ODEs and CTMC models

The derivations in this section refer to a one-dimensional model in cylindrical coordinates. Although the only dimension considered is the radius, it is essential to note that the concentration at each point distant  $r$  from the centre represents the concentration at each point along the circumference of the circle with radius  $r$ . The length of the cylinder can be neglected, as it is an invariant for our derivations. For this reason we use the terms *area* and *volume* as synonymous.

Before we give the details of the derivation, we give a brief overview. First we introduce the PDE and we derive a numerical approximation in terms of ODEs. This

is obtained dividing the space in segments and through numerical approximations of first and second derivatives with respect to radial position. Second, we describe the diffusion in terms of ODEs with compartments, where the velocities of the transport reactions are in terms of mass action kinetic law. Third, we demonstrate that if we choose appropriately the kinetic constants for the transport mass action laws, the resulting equations are identical to the approximation of the PDE. Fourth, we derive the CTMC with levels from the ODEs, in analogy with the already proposed derivation in [10].

## 2.1 Partial Differential Equations

Modelling diffusions of species S is defined at a macroscopic level by Fick's equation, a Partial Differential Equation (PDE) of the form:

$$\frac{\delta[S]}{\delta t} = D_S \nabla^2[S] \quad (1)$$

where  $D_S$  is the diffusion coefficient of species S,  $[S]$  is the concentration of S (in molar, M) and  $\nabla^2$  is the Laplacian operator, which can be interpreted in different ways, depending on the coordinate system. Since we consider diffusion along with local biochemical interactions, we use the following reaction-diffusion equation [16,4]:

$$\frac{\delta[S]}{\delta t} = D_S \nabla^2[S] \pm \text{React} \quad (2)$$

where React represents other reactions involving species S.

We assume cylindrical coordinates and that the concentration changes only with respect to radial position and only because of diffusion or biochemical reactions. As a consequence Equation (2) can be simplified to a one dimensional form in cylindrical coordinates, where the only dimension considered is the radius:

$$\frac{\delta[S](r)}{\delta t} = D_S \cdot \left( \frac{\delta^2[S]}{\delta r^2} + \frac{1}{r} \cdot \frac{\delta[S]}{\delta r} \right) \pm \text{React} \quad (3)$$

Boundary conditions are:

$$\frac{\delta[S]}{\delta r} \Big|_{r=0} = 0 \qquad \frac{\delta[S]}{\delta r} \Big|_{r=R} = 0 \quad (4)$$

where  $r = 0$  represents the centre of the coordinate system while  $R$  is the radius of the circular region considered. At each moment  $t$  in time we can compute the concentration of S at any point  $r$  along the radius, starting from an initial concentration profile  $f(r)$ .

Consider now how to solve Equation (3) numerically. First, we divide the radius in  $K$  segments of length  $\Delta r = R/K$ . Each segment  $i$  is related to a variable  $[S_i]$ ,  $i = 1, \dots, K$ , that represents the average concentration in that segment. Second, we compute approximations of first and second order derivatives of  $[S]$  at radial positions using the  $[S_i]$ . These approximations represent derivatives at the middle point of the  $i$ th segment, at a distance  $r = \Delta r(2i - 1)/2$  from the centre of the coordinate system. Derivatives are computed using the central *finite difference*

method:

$$\frac{\delta[S](r)}{\delta r} \approx \frac{\delta[S_i]}{\delta r} = \frac{[S_{i+1}] - [S_{i-1}]}{2\Delta r} \quad \frac{\delta^2[S](r)}{\delta r^2} \approx \frac{\delta^2[S_i]}{\delta r^2} = \frac{[S_{i+1}] - 2[S_i] + [S_{i-1}]}{(\Delta r)^2} \quad (5)$$

We can now rewrite Equation (3) using the approximations in Equation (5):

$$\begin{aligned} \frac{\delta[S](r)}{\delta t} &\approx \frac{\delta[S_i]}{\delta t} = D_S \cdot \left( \frac{[S_{i+1}] - 2[S_i] + [S_{i-1}]}{(\Delta r)^2} + \frac{1}{\Delta r(2i-1)/2} \cdot \frac{[S_{i+1}] - [S_{i-1}]}{2\Delta r} \right) \pm \text{React} \\ &= \frac{D_S}{(\Delta r)^2} \cdot \left( \left(1 + \frac{1}{(2i-1)}\right)[S_{i+1}] - 2[S_i] + \left(1 - \frac{1}{(2i-1)}\right)[S_{i-1}] \right) \pm \text{React} \end{aligned}$$

And rewriting the last equation we obtain the final numerical approximation:

$$\begin{aligned} \frac{\delta[S_i]}{\delta t} &= \frac{D_S}{(\Delta r)^2} \cdot \left( \frac{2i}{(2i-1)}[S_{i+1}] - 2[S_i] + \frac{(2i-2)}{(2i-1)}[S_{i-1}] \right) \pm \text{React} \\ &\quad i = 2, \dots, (K-1) \end{aligned} \quad (6)$$

In order to write Equation (6) also for  $i = 1$  and  $i = K$  we need to employ the boundary conditions (Equation (4)), from which we obtain:

$$\frac{[S_1] - [S_0]}{\Delta r} = 0 \quad \frac{[S_{K+1}] - [S_K]}{\Delta r} = 0$$

As a consequence, approximations in Equation (5) become:

$$\begin{aligned} \frac{\delta[S_1]}{\delta r} &= \frac{[S_2] - [S_1]}{2\Delta r} & \frac{\delta^2[S_1]}{\delta r^2} &= \frac{[S_2] - [S_1]}{(\Delta r)^2} \\ \frac{\delta[S_K]}{\delta r} &= \frac{[S_K] - [S_{K-1}]}{2\Delta r} & \frac{\delta^2[S_K]}{\delta r^2} &= \frac{[S_{K-1}] - [S_K]}{(\Delta r)^2} \end{aligned} \quad (7)$$

Employing Equation (7) we derive the two additional equations:

$$\begin{aligned} \frac{\delta[S_1]}{\delta t} &= \frac{2D_S}{(\Delta r)^2} \cdot ([S_2] - [S_1]) \pm \text{React} \\ \frac{\delta[S_K]}{\delta t} &= \frac{2K-2}{2K-1} \cdot \frac{D_S}{(\Delta r)^2} \cdot ([S_{K-1}] - [S_K]) \pm \text{React} \end{aligned} \quad (8)$$

As a final step, we derive the value of the  $[S_i]$  at time  $t = 0$ , using the initial condition  $f(r)$ ,  $r \in [0, R]$ . Notice that every point of the circumference with radius  $r$  has concentration  $f(r)$ . This means that each point in the  $i$ th segment has a different weight when we compute  $[S_i]$ , the average concentration of the segment. Since  $V_i = \pi(\Delta r)^2(2i-1)$  is the area of the ring whose average concentration is represented by  $[S_i]$ , such average concentration at time  $t = 0$  is given by:

$$[S_i](t=0) = \frac{1}{V_i} \int_{\Delta r(i-1)}^{\Delta r(i)} 2\pi r \cdot f(r) dr \quad (9)$$

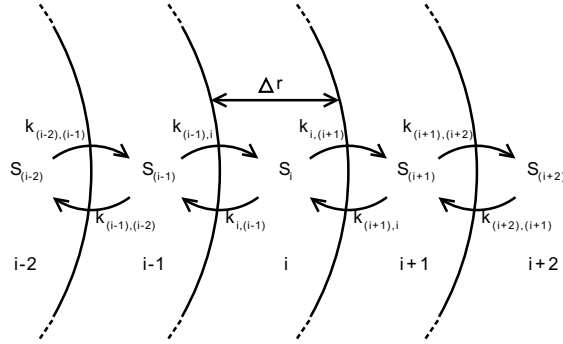


Fig. 1. Division of space in compartments.

## 2.2 Ordinary Differential Equations

In this section we derive an approximation of Equation (3) in terms of Ordinary Differential Equations (ODE), where we discretise the space into  $K$  compartments  $C_i$  with volume  $V_i$  ( $i = 1, \dots, K$ ). In order to represent a species  $S$  in the presence of compartments we need a variable  $S_i$  for each compartment  $C_i$ . We identify the average concentration of the species  $S$  in a compartment  $C_i$  by  $[S_i]$ . Concentration  $[S_i]$  can migrate from a compartment  $C_i$  to an adjacent compartment, i.e. either  $C_{i-1}$  or  $C_{i+1}$ , and the migration happens at a velocity given by the Mass Action law with kinetic constant  $k_{i,i-1}$  ( $i = 2, \dots, K$ ) or  $k_{i,i+1}$  ( $i = 1, \dots, (K-1)$ ) respectively (see Figure 1). In particular, we show that **the kinetic constants can be derived from the diffusion constant**  $D_S$  and the numerical solutions for the PDEs and ODEs are equivalent for a given  $K$ .

The ODE system described above is composed of the following equations:

$$V_1 \cdot \frac{\delta[S_1]}{\delta t} = k_{2,1}[S_2] - k_{1,2}[S_1] \pm V_1 \cdot \text{React}$$

$$V_i \cdot \frac{\delta[S_i]}{\delta t} = k_{i+1,i}[S_{i+1}] - k_{i,i+1}[S_i] - k_{i,i-1}[S_i] + k_{i-1,i}[S_{i-1}] \pm V_i \cdot \text{React}$$

$$i = 2, \dots, (K-1)$$

$$V_K \cdot \frac{\delta[S_K]}{\delta t} = k_{K-1,K}[S_{K-1}] - k_{K,K-1}[S_K] \pm V_K \cdot \text{React}$$

where volume  $V_i = \pi(\Delta r)^2(2i-1)$ . We can then rearrange the above equations:

$$\frac{\delta[S_1]}{\delta t} = \frac{k_{2,1}}{V_1}[S_2] - \frac{k_{1,2}}{V_1}[S_1] \pm \text{React} \quad (10)$$

$$\frac{\delta[S_i]}{\delta t} = \frac{k_{i+1,i}}{V_i}[S_{i+1}] - \frac{k_{i,i+1}}{V_i}[S_i] - \frac{k_{i,i-1}}{V_i}[S_i] + \frac{k_{i-1,i}}{V_i}[S_{i-1}] \pm \text{React}$$

$$i = 2, \dots, (K-1) \quad (11)$$

$$\frac{\delta[S_K]}{\delta t} = \frac{k_{K-1,K}}{V_K}[S_{K-1}] - \frac{k_{K,K-1}}{V_K}[S_K] \pm \text{React} \quad (12)$$

At this point, we choose the kinetic constants, parametric in  $D_S$ , that substituted in Equations (10), (11) and (12) yield Equations (6) and (8). We derive these

constants from inspection of Equation (6):

$$k_{i,i+1} = V_i \frac{D_S}{(\Delta r)^2} \frac{2i}{(2i-1)} = 2i\pi D_S \quad i = 1, \dots, (K-1) \quad (13)$$

$$k_{i,i-1} = V_i \frac{D_S}{(\Delta r)^2} \frac{(2i-2)}{(2i-1)} = (2i-2)\pi D_S \quad i = 2, \dots, K \quad (14)$$

Note that  $k_{i,i+1} = k_{i+1,i}$ . We can then substitute Equations (13) and (14) in Equation (11):

$$\begin{aligned} \frac{\delta[S_i]}{\delta t} &= \frac{(2(i+1)-2)\pi D_S}{\pi(\Delta r)^2(2i-1)}[S_{i+1}] - \frac{2i\pi D_S}{\pi(\Delta r)^2(2i-1)}[S_i] \\ &\quad - \frac{(2i-2)\pi D_S}{\pi(\Delta r)^2(2i-1)}[S_i] + \frac{(2(i-1))\pi D_S}{\pi(\Delta r)^2(2i-1)}[S_{i-1}] \pm \text{React} \\ &= \frac{D_S}{(\Delta r)^2} \cdot \left( \frac{2i}{(2i-1)}[S_{i+1}] - \frac{(2i+2i-2)}{(2i-1)}[S_i] + \frac{(2i-2)}{(2i-1)}[S_{i-1}] \right) \pm \text{React} \end{aligned}$$

And with a final rearrangement:

$$\frac{\delta[S_i]}{\delta t} = \frac{D_S}{(\Delta r)^2} \cdot \left( \frac{2i}{(2i-1)}[S_{i+1}] - 2[S_i] + \frac{(2i-2)}{(2i-1)}[S_{i-1}] \right) \pm \text{React} \quad i = 2, \dots, (K-1)$$

which is identical to Equation (6). In a similar way we can derive the two additional equations, starting from Equations (10) and (12):

$$\begin{aligned} \frac{\delta[S_1]}{\delta t} &= \frac{2D_S}{(\Delta r)^2} \cdot ([S_2] - [S_1]) \pm \text{React} \\ \frac{\delta[S_K]}{\delta t} &= \frac{2K-2}{2K-1} \cdot \frac{D_S}{(\Delta r)^2} \cdot ([S_{K-1}] - [S_K]) \pm \text{React} \end{aligned}$$

which are identical to Equation (8). Initial conditions are derived exactly as showed for the PDEs.

Thus we have shown that we can derive ODEs with compartments from PDEs in cylindrical coordinates. This is possible because of the correspondence we have found between the diffusion constant  $D_S$  in the PDE and the kinetic constants  $k_{i,j}$  of mass action transport reactions in the ODEs. At this point, we already know from [10] that we can derive the corresponding CTMC with levels.

### 2.3 Continuous Time Markov Chains with Levels of Concentration

In the previous two sections we related a continuous space PDE model with discrete space ODE models. Now we consider further discretisation: we relate the continuous concentration of the latter to the discrete concentration of a CTMC with levels model [9,10].

The organisation of the model is similar to the one just presented: space is divided in compartments  $C_i$ , with volume  $V_i = \pi(\Delta r)^2(2i-1)$ , each of which represents a ring where the average concentration of a species  $S$  is given by  $[S_i]$

( $i = 1, \dots, K$ ). However, this concentration is not expressed in a continuous form like in the ODE model, but by a discrete level  $\langle S_i \rangle = 0, \dots, N_i$ , with  $N_i$  the maximum level. The amount of concentration can be evaluated at any time using the relationship  $[S_i] = \langle S_i \rangle \cdot h_i$ , where  $h_i$  is called *step size* and is the amount of concentration represented by one level.

We shall now define states and transitions of a CTMC with levels derived from the models presented in the previous sections. A state of a CTMC with levels is defined by a vector of levels  $\sigma = (\langle S_1 \rangle, \dots, \langle S_K \rangle)$ .

In order for the state space of the CTMC to be finite, a maximum concentration  $M_i$  is fixed for each variable  $S_i$ , to be divided in  $N_i$  intervals representing  $h_i$  molar of concentration, with  $h_i = M_i/N_i$  and  $i = 1, \dots, K$ .

Transitions of the CTMC with levels and their activation in time are derived from the ODE model, using biochemical reactions and their velocities. We use the following additional notation:

$$\begin{aligned} R_{i,i+1} : S_i &\rightarrow S_{i+1} & v_{i,i+1} &= k_{i,i+1}[S_i] & i &= 1, \dots, (K-1) \\ R_{i,i-1} : S_i &\rightarrow S_{i-1} & v_{i,i-1} &= k_{i,i-1}[S_i] & i &= 2, \dots, K \end{aligned}$$

where the reaction  $R_{i,j}$  represents the transformation of  $S_i$  into  $S_j$  (i.e. the migration of  $S$  from  $C_i$  to  $C_j$ ), while  $v_{i,j}$  is the velocity of the reaction  $R_{i,j}$  expressed in *molar/s*,  $j \in \{i+1, i-1\}$ . Moreover, we assume that when a reaction  $R_{i,i+1}$  or  $R_{i,i-1}$  takes place, the CTMC will transit from a state  $\sigma = (\langle S_1 \rangle, \dots, \langle S_{i-1} \rangle, \langle S_i \rangle, \langle S_{i+1} \rangle, \dots, \langle S_K \rangle)$  to a state  $\sigma' = (\langle S_1 \rangle, \dots, \langle S_i \rangle - 1, \langle S_{i+1} \rangle + 1, \dots, \langle S_K \rangle)$  or  $\sigma'' = (\langle S_1 \rangle, \dots, \langle S_{i-1} \rangle + 1, \langle S_i \rangle - 1, \dots, \langle S_K \rangle)$  respectively. Reaction  $R_{i,j}$  cannot take place if  $\langle S_i \rangle = 0$  or if  $\langle S_j \rangle = N_j$ .

Now consider the ODE of a single reaction  $R_{i,i+1}$ . It is composed by two complementary equations:

$$V_i \cdot \frac{\delta[S_i]}{\delta t} = -k_{i,i+1}[S_i] \quad V_{i+1} \cdot \frac{\delta[S_{i+1}]}{\delta t} = k_{i,i+1}[S_i] \quad i = 1, \dots, (K-1) \quad (15)$$

Furthermore, Equation (15) can be written in the following difference form:

$$\begin{aligned} V_i \cdot \frac{\delta[S_i]}{\delta t} &\approx V_i \cdot \frac{\Delta \langle S_i \rangle \cdot h_i}{\Delta t} = -k_{i,i+1} \cdot \langle S_i \rangle \cdot h_i \\ V_{i+1} \cdot \frac{\delta[S_{i+1}]}{\delta t} &\approx V_{i+1} \cdot \frac{\Delta \langle S_{i+1} \rangle \cdot h_{i+1}}{\Delta t} = k_{i,i+1} \cdot \langle S_i \rangle \cdot h_i \end{aligned} \quad (16)$$

Our assumptions about the transitions on the CTMC state are that when reaction  $R_{i,i+1}$  takes place, one level of  $S_i$  is consumed and one level of  $S_{i+1}$  is produced. This implies that in Equation (16)  $\Delta \langle S_i \rangle = -1$  and  $\Delta \langle S_{i+1} \rangle = 1$ . Notice now that the only unknown term in Equation (16) is  $\Delta t$ , which can be regarded as the average time required to convert a level of  $S_i$  into a level of  $S_{i+1}$ . So we have:

$$\Delta t = \frac{V_i \cdot h_i}{k_{i,i+1} \cdot \langle S_i \rangle \cdot h_i} = \frac{V_{i+1} \cdot h_{i+1}}{k_{i,i+1} \cdot \langle S_i \rangle \cdot h_i} \quad i = 1, \dots, (K-1) \quad (17)$$

Rearranging Equation (17) we obtain the following equality:

$$h_i = \frac{h_{i+1} \cdot V_{i+1}}{V_i} = h_{i+1} \cdot \frac{(2i+1)}{(2i-1)} \quad i = 1, \dots, (K-1)$$

As a main consequence, we have that once a step size  $h_i$  is chosen, the other step sizes are derived automatically. We suggest to compute  $h_1$  first, though it is possible to begin from other compartments. In particular, beginning from  $C_1$  will ensure that all the other  $h_i$  ( $i = 2, \dots, K$ ) will be smaller than  $h_1$ .

We can then use  $r_{i,i+1} = 1/\Delta t$  as the parameter of the exponential distribution of the time required for reaction  $R_{i,i+1}$ . Through manipulation of Equation (17) we have:

$$\begin{aligned} r_{i,i+1} &= \frac{k_{i,i+1} \langle S_i \rangle}{V_i} & i = 1, \dots, (K-1) \\ r_{i,i-1} &= \frac{k_{i,i-1} \langle S_i \rangle}{V_i} & i = 2, \dots, K \end{aligned} \quad (18)$$

## 2.4 Additional Notes

Although we have shown that the numerical solution for the PDE and the ODE model of diffusion are equivalent, a few further considerations are necessary. In the case of the PDE,  $K$  will be hidden to the modeller and in general is quite large, in order to obtain an output that is as close as possible to the analytical solution. When translating to ODEs, a lower  $K$  is advisable, as the modeller has to deal with compartments directly and a large amount of them would be difficult to manage.

Passing from the ODE to the CTMC with levels, we notice that the state space of the CTMC depends on  $K$  and, additionally, on the maximum number of levels  $N_i$ . Intuitively, larger  $K$  and  $N_i$  yield Markov chains whose output tends more and more to the output of the original PDE.

Finally we note the tension between complexity, ability of the CTMC to reproduce PDE output, and stochastic effects due to concentration discretisation. Managing this tension is the job of the modeller.

## 3 Example

We now turn our attention to an example, inspired by a series of publications about Nitric Oxide (NO) diffusion in human blood vessels. In particular, in [17] a vessel with a radius  $R$  of 138  $\mu m$  is defined; we consider NO having a diffusion constant  $D_{NO} = 3300 \mu m^2 s^{-1}$ .

As the initial concentration function  $f(x)$  at  $t = 0$  we choose:

$$f(r, \alpha, \beta) = \frac{\Gamma(\alpha + \beta)}{\Gamma(\alpha) \cdot \Gamma(\beta)} \cdot \left(\frac{r}{R}\right)^{\alpha-1} \cdot \left(\frac{R-r}{R}\right)^{\beta-1} \cdot 10$$

with  $\alpha = 1$  and  $\beta = 3$ , defined in  $[0, R]$ , with unit measure  $\mu molar$ . This choice is based on our experience of the concentration of NO in literature, as a result of measurements or as observed in other mathematical models. It is parametric in  $\alpha$



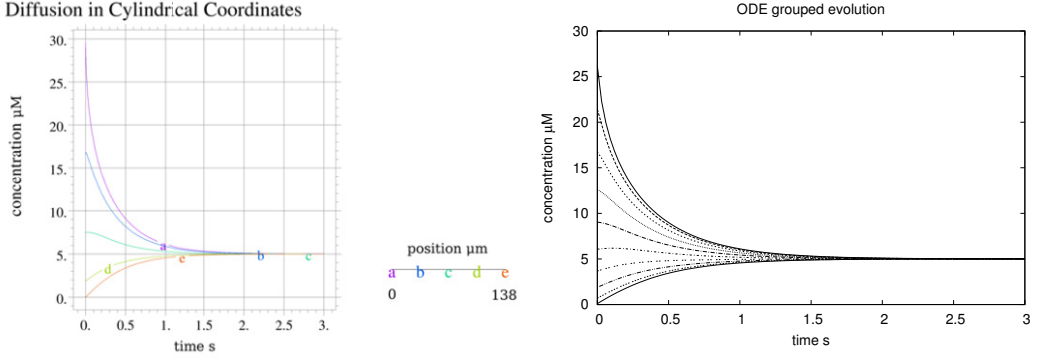


Fig. 2. PDE output (left) and ODE output (right) for the first 3 seconds of diffusion. Lines are the concentration at sample points along the radius (left) and the average concentration of compartments  $C_i$  ( $i = 1, \dots, 10$ ) (right).

and  $\beta$ , to allow the generation of a full range of initial conditions starting from the same function.

Notice that the information so far is enough to solve Equation (1) in one dimensional cylindrical coordinates. We used the simulator FlexPDE [2] (Figure 2 on the left). By defining the number of compartments to be  $K = 10$ , we can compute the ODE solution as well. For this task we used the simulator Copasi [1] (Figure 2 on the right, where a line is drawn for the average concentration of each compartment).

The implementation of the CTMC model requires little additional information as well. We define a maximum number of levels  $N_1=10$  and a maximum concentration  $M_i=40 \mu\text{molar}$ ,  $i = 1, \dots, K$ . Here we used the Prism model checker [3]. The result was a CTMC with  $1.4 \cdot 10^{13}$  states and  $2.4 \cdot 10^{14}$  transitions. Large CTMCs are in fact expected, since the number of states grows exponentially with respect to the number of species in the model. In order to analyse transient properties of the chain, stochastic simulations or state-space reduction techniques are advised.

As a first exploration of the properties of the chain, we used stochastic simulations, taking average and standard deviation of model output from 100 runs. Some simulation results are shown in Figure 3.

## 4 Related Work

Translation from ODEs to CTMC with levels of concentration finds its roots in [7]. This has been then investigated further in [9], where a more solid theoretical link between the two approaches is introduced. Transport between compartments is finally considered in [10].

Our starting point for the translation of diffusion equations from PDEs to ODEs with compartments has been [14], which considers stochastic simulations of reaction-diffusion processes. However, in [14] only Cartesian coordinates are considered.

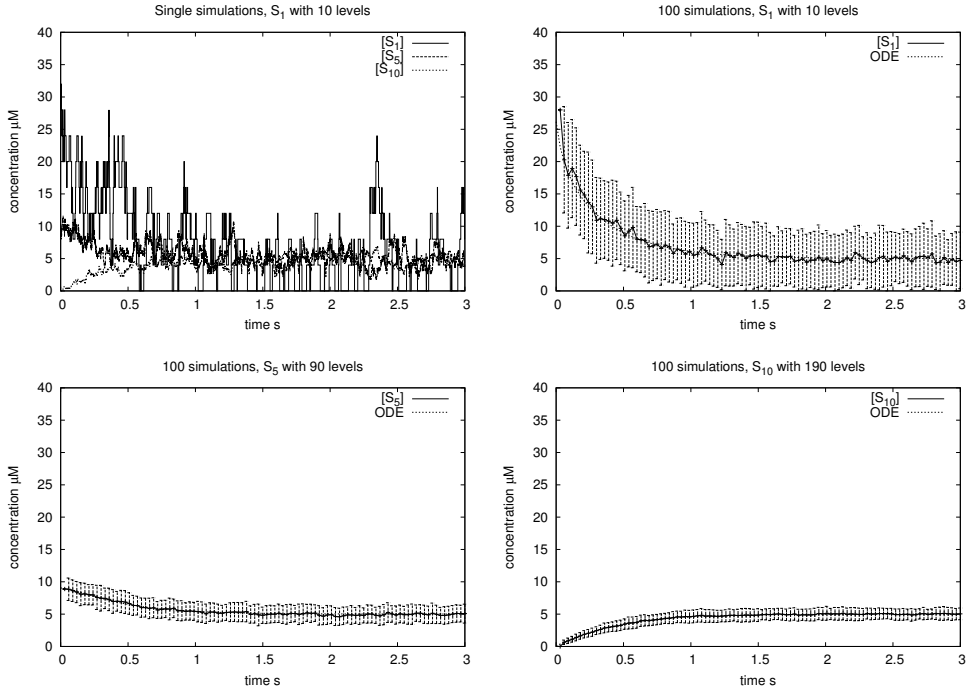


Fig. 3. CTMC stochastic simulations, average and standard deviation over 100 runs.  $S_1$ ,  $S_5$  and  $S_{10}$  are the average concentrations of compartments  $C_1$ ,  $C_5$  and  $C_{10}$ . Standard deviation over the 100 runs is shown.

## 5 Conclusions and Future Work

We presented a derivation of Fick's law of diffusion in one-dimensional cylindrical coordinates from partial differential equations to CTMC with levels. As an intermediate step, we converted the PDEs to ordinary differential equations with compartments, where transport velocities are implemented with mass action kinetic law. The novelties of this derivation are that the kinetic constants are derived directly from the diffusion constant and that they are dependent on the radial position. Although this derivation is trivial in case of Cartesian coordinates, additional assumptions have to be considered in case of cylindrical coordinates. We then illustrated the result with an example, where we showed the consistency between simulations of PDEs, ODEs and CTMC.

In the future, we plan to develop and analyse a complete CTMC with levels model of NO transport and bioavailability in blood vessels, where diffusion is implemented using the derivation presented here.

## Acknowledgement

Andrea Degasperi is supported by a Lord Kelvin / Adam Smith Scholarship of the University of Glasgow and by the EPSRC funded [SIGNAL project](#).

## References

- [1] *Copasi web site* (2010).  
URL <http://www.copasi.org/tiki-index.php>
- [2] *FlexPDE web site* (2010).  
URL <http://www.pdesolutions.com/>
- [3] *PRISM web site* (2010).  
URL <http://www.prismmodelchecker.org/>
- [4] Berg, H. C., “Random Walks in Biology,” Princeton University Press, 1993.
- [5] Blinov, M. L., J. R. Faeder, B. Goldstein and W. S. Hlavacek, *BioNetGen: software for rule-based modeling of signal transduction based on the interactions of molecular domains*, *Bioinformatics* **20** (2004), pp. 3289–3291.
- [6] Bortolussi, L., *Stochastic concurrent constraint programming*, *Electronic Notes in Theoretical Computer Science* **164** (2006), pp. 65–80.
- [7] Calder, M., S. Gilmore and J. Hillston, *Modelling the influence of RKIP on the ERK signalling pathway using the stochastic process algebra PEPA*, *Lecture Notes in Computer Science* **4230** (2006), pp. 1–23.
- [8] Calzone, L., F. Fages and S. Soliman, *Biocham: An environment for modelling biological systems and formalizing experimental knowledge*, *Bioinformatics* **22** (2006), pp. 1805–1807.
- [9] Ciocchetta, F., A. Degasperi, J. Hillston and M. Calder, *Some investigations concerning the CTMC and the ODE model derived from bio-pepa*, *ENTCS* **229** (2009), pp. 145–163.
- [10] Ciocchetta, F. and M. L. Guerriero, *Modelling biological compartments in bio-pepa*, *Electr. Notes Theor. Comput. Sci.* **227** (2009), pp. 77–95.
- [11] Ciocchetta, F. and J. Hillston, *Bio-PEPA: A framework for the modelling and analysis of biological systems*, *Theoretical Computer Science* **410** (2009), pp. 3065–3084.
- [12] Danos, V., J. Feret, W. Fontana, R. Harmer and J. Krivine, *Rule-based modelling of cellular signalling*, *Lecture Notes in Computer Science* (2007), pp. 17–41.
- [13] Degasperi, A. and M. Calder, *On the formalisation of gradient diffusion models of biological systems*, *PASTA Workshop 2009* (2009).  
URL [http://www.dcs.gla.ac.uk/~andrea/files/DegasperiCalder\\_Bio-PASTA2009.pdf](http://www.dcs.gla.ac.uk/~andrea/files/DegasperiCalder_Bio-PASTA2009.pdf)
- [14] Erban, R., J. Chapman and P. Maini, *A practical guide to stochastic simulations of reaction-diffusion processes*, *ArXiv e-prints* (2007), pp. 1–35.
- [15] Hillston, J., “A Compositional Approach to Performance Modelling,” Cambridge University Press, 1996.
- [16] Jones, D. S. and B. D. Sleeman, “Differential Equations and Mathematical Biology,” George Allen & Unwin Ltd, 1983.
- [17] Lamkin-Kennard, K. A., D. G. Buerk and D. Jaron, *Interactions between NO and O<sub>2</sub> in the microcirculation: a mathematical analysis*, *Microvascular Research* **68** (2004), pp. 38–50.
- [18] Pedersen, M. and G. Plotkin, *A language for biochemical systems*, *Lecture Notes in Bioinformatics* **5307** (2008), pp. 63–82.
- [19] Priami, C. and P. Quaglia, *Beta-binders for biological interactions*, *LNCS* **3082** (2005), pp. 20–33.
- [20] Tsoukias, N. M., *Nitric oxide bioavailability in the microcirculation: Insights from mathematical models*, *Microcirculation* **15** (2008), pp. 813–834.