Interfacing continuum and discrete methods: convective diffusion of microparticles and chemical species in microsystems

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Abstract: Convective transport of macromolecules or micro and nano-particles in microsystems is usually predicted by solving the Navier-Stokes equations for the carrier fluid and a concentration equation for the diffusing species. In the case of isolated particles—or molecules—or complicated geometries with extremely small apertures or microporous material, the concentration equation may be replaced by a Monte-Carlo model. In the limit of a large number of particles, we show that the two approaches lead to similar results.

Keywords: Convective transport, diffusion, random walk, microsystems for biotechnology.

1. Introduction

Many physical phenomena are mathematically governed by partial differential equations (PDE). In the case of microsystems, even with the scaling down linked to miniaturization, it is usual to use continuum modeling—like finite element method—to simulate the phenomena which are put to work, the limit being the transition to nanoscales. Nevertheless, two problems arise at very small scales: first, even if the liquid phase—carrier fluid—can be considered as a continuum, the transported species, targets, macromolecules, tracers or markers, may be in discrete amounts. Second, the geometrical scales can range in a large spectrum—with locally very small scales—making difficult the use of the continuum approach. Interfacing a usual PDE approach for the carrier phase and a discrete formulation for the transported particles may be the answer in such cases; besides, at larger scales and concentrations, it reveals the physical behavior often hidden in the continuum approach.

In this paper, we show the consistency of the two methods and illustrate some advantages of this interfacing in microfluidics.

2. Interfacing COMSOL and discrete Monte-Carlo model

2.1 Diffusion from a point source

Axi-symmetric diffusion of species from a point source is governed by the diffusion equation

$$\frac{\partial c}{\partial t} = \nabla.\left(-D\nabla c\right) + S = D\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial c}{\partial r}\right) + S \qquad (1)$$

Analytically, when the boundary conditions are not complicated, the solution can be written in term of Bessel functions [1]. However, a F.E.M. numerical scheme is often more convenient and versatile. Another way of apprehending the physics of the diffusion is to mimic the random walk of the diffusing species. This approach is inspired by the Langevin equation [2]. The random term is modeled as if the particles were moving by successive linear segments, and turning suddenly at a random angle. It is not required that the length of the linear segments be as small as the mean free path. A larger length (or time step) can be chosen under the condition that it is small compared to the characteristic dimensions of the problem. For simplicity we present here a 2D situation; the random walk is then described by

$$\begin{aligned} X_{i+1} &= X_i + \sqrt{4\,D\,\Delta t}\cos(\alpha) \\ Y_{i+1} &= Y_i + \sqrt{4\,D\,\Delta t}\sin(\alpha) \\ \alpha &= random\ (0, 2\pi) \end{aligned} \qquad (2)$$

The remaining difficulty is to describe precisely the computational domain boundaries and to specify conditions for the particles impacting the boundaries. This part can sometimes be complicated. In figure 1, we show the consistency of free 2D diffusion from a point source between Monte-Carlo and COMSOL models.

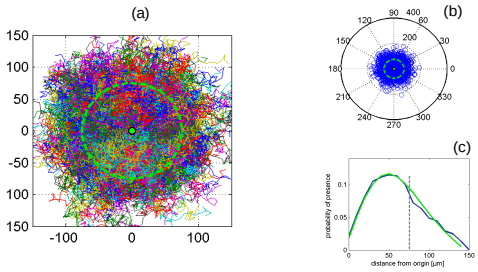

Figure 1. Diffusion of species from a point source: (a) random walks of particles, the green circle corresponds to the distance $l = \sqrt{4Dt}$, (b) end point at t=0.75 s (D= 10^{-9} m^2/s), (c) comparison with COMSOL for the integral of the concentration in function of the distance from the origin.

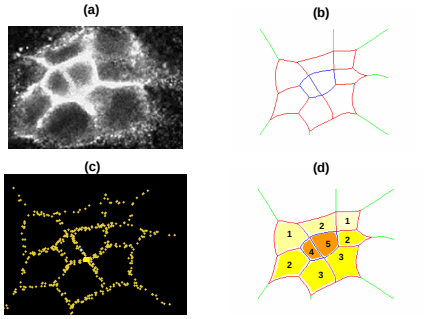

Figure 2. Diffusion in an extra cellular network of a tumor; (a) in vivo fluorescent image of diffusing drugs, (b) schematic of the network obtained with the Surface Evolver numerical software, (c) simulation of the diffusion with a Monte-Carlo model, (d) up-take calculation of diffusive species by the different cells based on a probabilistic model.

Such an approach has been used to predict the equivalent diffusion coefficient in porous networks of cells (fig.2) [3], and the subsequent cellular up-take by taking into account probabilities of penetration into the cells.

2.2 Convective transport

2.1. Introduction

A similar approach can be done for convective transport. This time, the random walk superposes to the convective transport, in agreement with Langevin's equation (drag term) [4,5]. First, the velocity field of the carrier fluid is computed by solving the Navier-Stokes equation (or the Stokes equation if the Reynolds number is sufficiently small). The fluid velocities at the nodes of the FEM model are then tabulated. Finally the Monte-Carlo model makes use of the interpolated velocities to calculate the random walk in the moving fluid

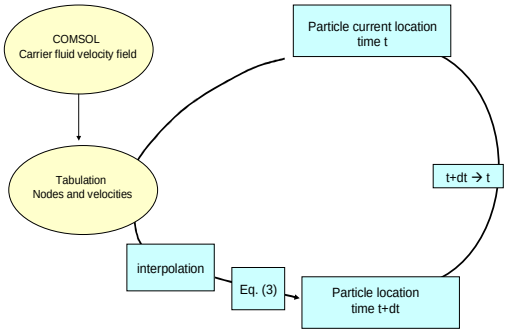

Figure 3. Principle of the coupling algorithm.

$$X_{i+1} = X_i + V_{x,i}\,\Delta t + \sqrt{4D\Delta t}\cos(\alpha)$$
$$Y_{i+1} = Y_i + V_{y,i}\,\Delta t + \sqrt{4D\Delta t}\sin(\alpha) \qquad (3)$$
$$\alpha = random\ (0, 2\pi)$$

The main difficulties at this stage are the interpolation algorithm for the velocities [V_x, V_y] and the proper geometrical boundary conditions at a solid wall. On one hand, it has been chosen to select the nearest neighboring nodes and calculate an averaged velocity. On the other hand, the boundary conditions are, for the moment, either an elastic rebound or a complete adsorption. Rigorously, when a nano-particle or a macro-molecule approaches a solid wall, a calculation of the molecular interactions should be done. But this solution is not tractable and simplified boundary conditions must be used (in the same manner than for mesoscale methods).

2.2. Straight micro-channel

The method has been first applied to convective diffusion of species in a straight micro-channel. Figure 4 shows the random walk of micro-particles in the channel (width 100 µm, average velocity 300 µm/s, and diffusion constant of 10^3 μ^2/s). Figure 5 compares the convection-diffusion solution obtained by using COMSOL or the coupling COMSOL-Monte-Carlo (for 1000 particles).

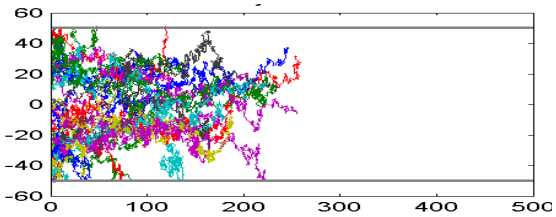

Figure 4. Convective diffusion of single micro-particles obtained by the coupled approach (not to scale).

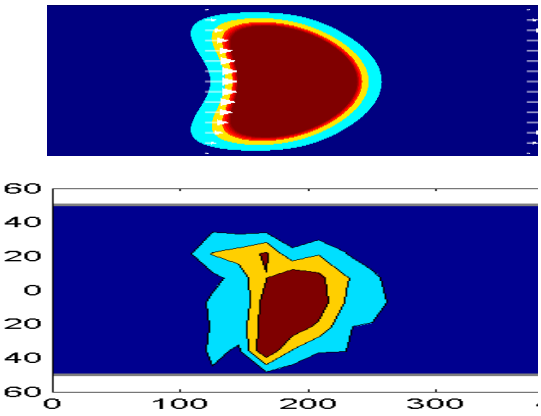

Figure 5. Concentration in a bolus moving through a micro-channel: top, COMSOL calculation; bottom, coupled COMSOL-Monte-Carlo calculation (1000 micro-particles).

2.3. Recirculation micro-chamber

Recirculation micro-chambers are used to trap biological objects like cells, or biochemical species [6-8]. It is of great importance to know if these objects are effectively trapped or can escape in the feeding channel (fig. 6).

Figure 7 shows the agreement between the COMSOL-multiphysics model and the COMSOL-Monte-Carlo approach.

The coupled COMSOL-Monte-Carlo gives very useful insight concerning the motion of the particles: the efficiency of trapping depends on the micro-chamber shape and dimensions, and on the diffusion constant of the particles (fig. 8).

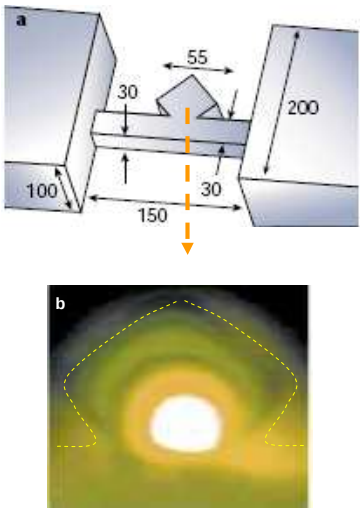

Figure 6. Schematic of a recirculation chamber [8]: For the right range of Reynolds numbers the particles are trapped inside the diamond shaped cavity.

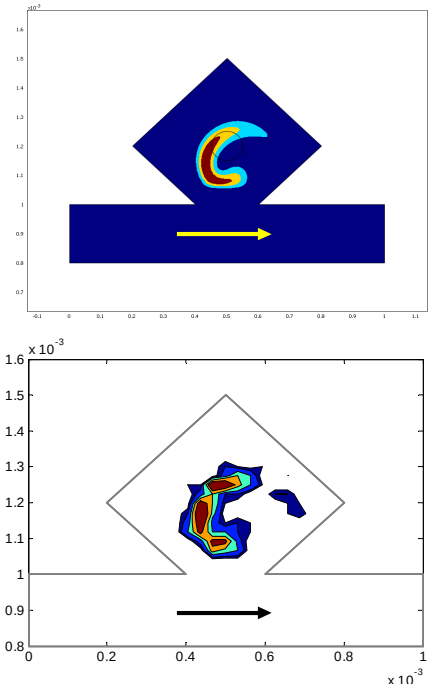

Figure 7. Left: COMSOL multiphysics model of a bolus of concentration in a recirculating chamber; right, same problem using the coupled COMSOL-Monte-Carlo approach.

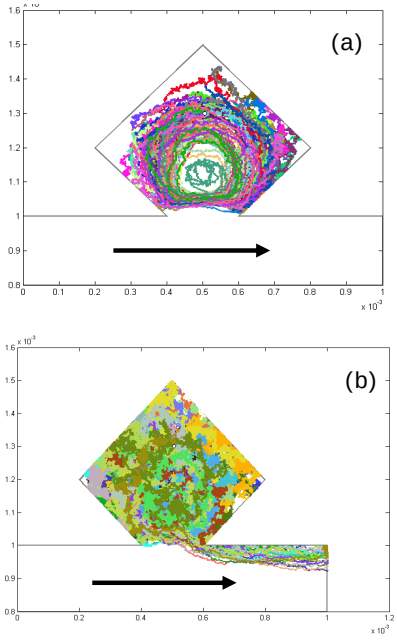

Figure 8. Random walk of particles trapped in a recirculation micro-chamber: (a) if the diffusion constant is small enough ($D=10^{-10}$ m^2/s) the particles are trapped; (b) they escape progressively when the diffusion coefficient is sufficiently large ($D=10^{-9}$ m^2/s).

2.4. Micro-pillars

In microsystems for Biotechnology such as proteomic reactors [9] and liquid-liquid extractors (LLE) [10,11], micro-pillars are often used: in proteomic reactor, the pillars are coated with ligands (enzymes) and the bio-reaction is realized upon contact of the proteins with the pillar surfaces; in LLEs, the pillars are used to stabilize interfaces between the liquids which are permeable to the targeted species. In both cases, the trajectories of proteins or biochemical species in the vicinity of pillars have a fundamental importance. Figure 9 shows the comparison between a concentration calculation with COMSOL and a COMSOL-Monte-Carlo method for a bolus of concentration entering a micro-channel obstructed by a pillar.

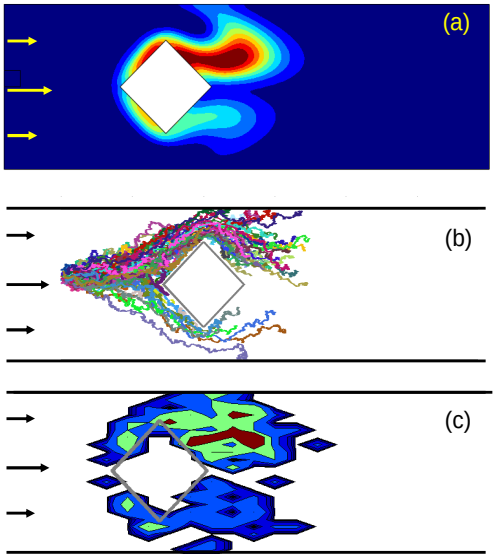

Figure 9. (a) concentration contour plot (COMSOL multiphysics); (b) plot of randomly selected trajectories; (c) concentration contour plots obtained by the coupled method with 200 molecules.

2.5. Diffusive transport through microscopic holes

In modern biosystems, it is frequent to use micro or even nano-holes forming a nanoporous membrane to filter out molecules [12,13]. Depending on their size, some molecules can percolate through the hole, larger ones do not. Micro-holes dimensions are meso-scale, at the border between microscopic and nanoscopic scales. Two types of problem arise with the continuum approach: first, difficulties with the meshing of very slender domains and the numerical stability conditions associated; second, the continuum hypothesis starts to be in difficulty for nanopores. The coupled approach appears to be a possible solution, as shown in figure 10.

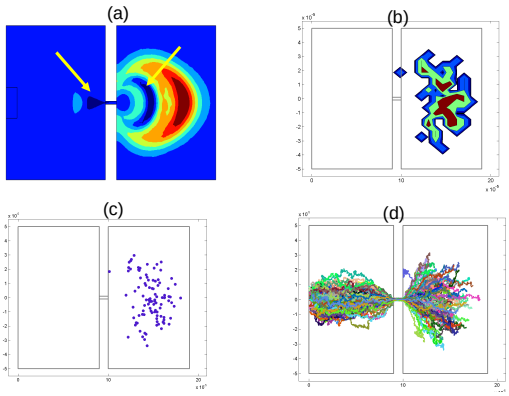

Figure 10. (a) Diffusive-convective transport of species through a microscopic pore (2 µm). (a) The continuum approach starts to show its limits with 'instabilities' due to insufficient meshing (yellow arrows); (b) the same calculation with the coupled approach (100 molecules only); (c) end points of molecules trajectories; (d) trajectories deduced from convective transport and random walk.

2.6. 3D approach

The numerical scheme proposed here can be applied to 3D geometries as well. The numerical scheme of equation (3) should be replaced by

$$\begin{aligned} X_{i+1} &= X_i + V_{x,i}\,\Delta t + \sqrt{4\,D\,dt}\,\cos(\alpha)\,\sin(\beta) \\ Y_{i+1} &= Y_i + V_{y,i}\,\Delta t + \sqrt{4\,D\,dt}\,\sin(\alpha)\,\sin(\beta) \\ Z_{i+1} &= Z_i + V_{z,i}\,\Delta t + \sqrt{4\,D\,dt}\,\cos(\beta) \\ \alpha &= random\ (0, 2\pi) \\ \beta &= a\cos\left(1 - 2\ random(0,1)\right) \end{aligned} \qquad (4)$$

where α and β are the directing angles.

Figure 11 shows the dispersion of a tracer in 3D straight and turning micro-channels.

7. Conclusions

In this work, we have demonstrated the consistency—for convective transport modeling of micro and nano-particles—of the continuum approach using a multiphysics PDE model and the coupled approach using a continuum PDE model for the carrier flow velocity field, interfaced with a Monte-Carlo model for the convective diffusion of micro and nano-particles.

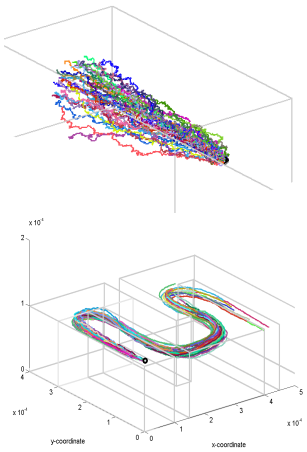

Figure 11. 3D dispersion of a tracer: (left) straight channel; (right) turning channel.

Rigorously the PDE approach based on the continuum assumption cannot be applied when the molecules of the transported species are in too small numbers—at the most, it defines only a probability of presence— or when the nanoscale is reached [4]. Besides, the PDE approach runs into difficulties for complicated geometries with very different scales. Interfacing Monte-Carlo diffusion with a PDE solution for the velocity field brings a new light for convective diffusion of solitary particles in the complex geometries of microsystems for biotechnology, especially when the carrier fluid seeps through small apertures, very narrow channels, restricted micro-chambers and micro-porous media. The remaining difficulty however is the same than that found in mesoscale computational approaches, i.e. to define and introduce the relevant boundary conditions at the wall.

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