Using COMSOL Multiphysics® Software for Benchmarking Problems in Cell Migration

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Abstract

Modeling of migrating cells often requires sophisticated numerical tools necessary for solving highly nonlinear partial and ordinary differential equations in domains with moving boundaries. We have recently developed a novel conservative method [1] for simulating reactions and transport in moving domains, which combines an Eulerian approach with tracking an explicit boundary. The latter is implemented by employing FronTier, a robust front-tracking technique [2]. Local mass conservation is ensured by finite-volume spatial discretization and natural-neighbor interpolation. Tests with exact kinematics indicated precise mass conservation and an order of convergence in space between one and two. The 'moving boundary' algorithm is currently being implemented in Virtual Cell (VCell), a general-purpose computational framework for simulating cellular phenomena in realistic geometries [3].

The algorithm was extended by coupling cell kinematics and intracellular dynamics and was validated using a set of benchmark problems. The COMSOL Multiphysics® software was extensively used to obtain alternative numerical solutions that served as reference solution where no exact analytic/closed-form solution was available.

The first test case was diffusion inside and expanding circle with the expansion velocity as a function of local concentration. An equivalent advection-diffusion problem was obtained by mapping onto a fixed domain, which was then solved with high precision using the Transport of Diluted Species interface of the COMSOL® software. Quantitative agreement was obtained in comparing the results of the two methods, see Figure 1(a-c). Furthermore, using the simulation result as a reference solution, we have shown that accuracy of our original algorithm is preserved if extrapolation near the boundary and the front-tracking routines are at least second-order accurate, see Figure 1(d).

In the second test case, we used a translating and (slightly) deforming cell example from the minimal models of actin-based motility. Briefly, the models included a viscoelastic equation for actin velocity and an advection-diffusion equation for myosin. Effect of cell-substrate adhesion on cell migration was also considered. We developed an equivalent numerical solution using the coefficient form PDE framework in the COMSOL Multiphysics® software. The moving domain problem was implemented in the moving mesh framework of the COMSOL® software that is based on Arbitrary Lagrangian-Eulerian (ALE) finite element methods. Several snapshots of the solution are shown in the top row of Figure 2. Great agreement was obtained in comparisons against the simulation results, see bottom row of Figure 2, with relative solution and interface position errors below 0.3%.

Given the fundamental differences between the two numerical methods, and the various spatial and temporal discretization schemes used in each one, these results validate both solutions.

Reference

[1] I. L, Novak, B. M, Slepchenko, A conservative algorithm for parabolic problems in domains with moving boundaries.
Journal of computational physics, 270, 203-213 (2014).
[2] D.C., Resasco et al., Virtual Cell: computational tools for modeling in cell biology, WIREs Syst. Biol. Med., 4, 129–140 (2012).
[3] J., Du et al., A simple package for front tracking, J. Comput. Phys., 213, 613–628 (2006).

Figures used in the abstract

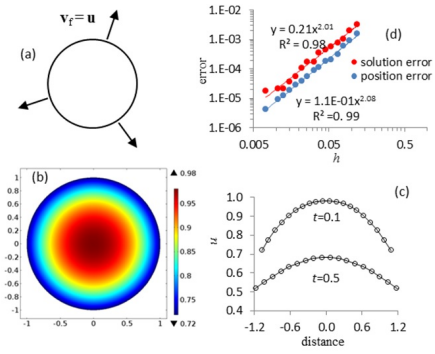

Figure 1. Expanding circle test: equation $\partial_t u = \Delta u$ is solved in an expanding circle (a), with boundary $(\nabla u + \boldsymbol{v}_f u)\boldsymbol{n}|_{\partial\Omega} = 0$ and initial condition $\Omega(0) = \{x, y \mid x^2 + y^2 < 1\}, u(x, y, 0) = 1$. The solution is tested against an equivalent problem solved in a fixed domain using COMSOL; a snapshot of the reference solution in (b) is shown for t = 0.1. Comparison of results obtained with our method (circles) against reference solution (curves) is shown for the equator at specific times (c), and convergence of position and solution errors is illustrated in (d).

Figure 1

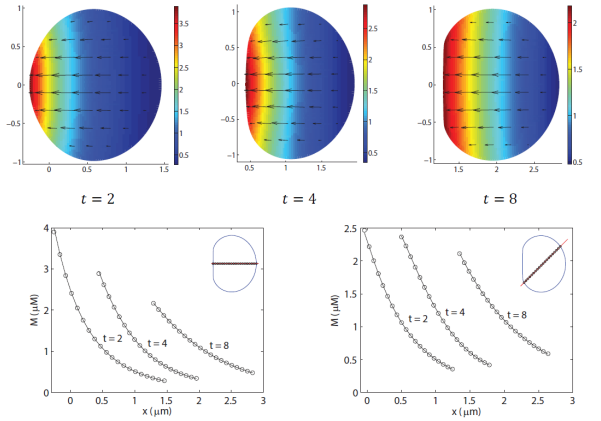

Figure 2. The moderate deformation migrating cell example. (top row) myosin distribution in pseudo-color and actin velocity vectors at different times; (bottom row) comparison of the myosin solutions obtained from the proposed method (circles) and the ALE method of COMSOL (solid lines) along different cut-lines for the time points shown in the top row. The insets show the cut-line defined for the last time point.

Figure 2