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SMART: Spatial Modelling Algorithms for Reactions and Transport

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Summary

Biological cells respond to stimuli through chains of chemical reactions generally referred to as *cell signaling pathways*. The propagation of the chemical substances and the cell signalling pathways can be represented by coupled nonlinear systems of reaction-transport equations within intracellular, subcellular and extracellular spaces. The geometries of real biological cells are complicated; subcellular structures such as the endoplasmic reticulum are highly curved and tortuous. *Spatial Modelling Algorithms for Reactions and Transport* (SMART) is a high-performance finite-element-based simulation package for describing, modelling and simulating spatially-varying reaction-transport processes with specific features targeting signaling pathways in biological cell geometries. SMART is based on the FEniCS finite element library, provides a symbolic representation framework for specifying reaction pathways, supports general 2D and 3D geometry specifications, and supports parallelism via MPI.

Statement of need

The traditional approach to modelling cell signalling pathways is to assume that the substances are well-mixed within the cell body or a subcellular compartment. In this case, the governing biophysical equations reduce to ordinary differential equations, for which a plethora of simulation tools exist. This approach has successfully recapitulated many cell-wide signaling events, from calcium elevations in neurons to models of cell mechanotransduction. However, such models obviously neglect many spatial aspects of cell signaling, which are crucially important on short timescales or for slower diffusing species. Recently, there has been increased interest in spatiotemporal modeling of cell signaling.

- Describe in 1-2 sentences which frameworks that exist in addition to SMART
- State in 1-2 sentences why these are insufficient
- Describe in 1-2 sentence key SMART features that addresses these insufficiencies.
- Include citations, see how to format citations in text.

Other software tools currently used to model signaling networks in cells either primarily focus on assembling non-spatial models or are restricted to finite-volume methods (Cowan et al., 2012) or stochastic, particle-based simulations (Kerr et al., 2008). Alternatively, there exist many mature platforms such as COMSOL that use the finite element method to solve various PDEs. However, these programs are not open source, they grant the user less control over the choice of solution methods, and they are not wel SMART leverages state-of-the-art finite element software (FEniCS) which is compatible with meshing software such as Gmsh or the newly developed GAMer 2 (Lee et al., 2020), allowing users to solve highly nonlinear systems

of PDEs within complex cellular geometries.

Scientific impact and examples of SMART use

- Detail one existing and some upcoming use cases for SMART.
- Include 1-2 figures, and 2-3 references.

SMART offers the unique opportunity to model signaling networks spatially in realistic cell geometries; for instance, using recent electron micrographs of ER geometry in Purkinje neurons, we were able to predict the emergent calcium dynamics within realistic cell volumes (Fig 1). ...[mention another example?] In the near future, SMART can be used to solve coupled mechano-chemical systems; for instance, we plan to explore coupling between calcium release and contraction within single skeletal muscle fibers.

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