Simulating mixed dimensional reaction transport systems in realistic cell geometries

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Abstract

Although cell signaling networks are typically modeled by assuming molecules are well-mixed within cellular compartments, spatial features of subcellular signaling are often fundamentally important. For instance, mechanotransduction pathways exhibit different behaviors depending on substrate dimensionality, the extent of cell spreading, and nuclear morphology. Such signaling networks translate mathematically into partial differential equations (PDEs) coupled across surfaces and volumes within a cell or subcellular region. Here, we present Spatial Modeling Algorithms for Reaction and Transport (SMART), our recently-developed finite-element based software that collects model specifications and assembles and solves the associated systems of PDEs. We leverage state-of-the-art mixed dimensional finite element approaches in FEniCS, allowing us to conduct simulations on complex, realistic cell geometries represented by tetrahedral meshes. Such geometries can be built up using mesh-generating software such as Gmsh, or directly derived from experimental images by converting segmented images into well-conditioned meshes using meshing tools such as GAMer2. We demonstrate the use of SMART in several biological test cases across temporal and spatial scales, including YAP/TAZ mechanotransduction on micropatterned substrates, calcium signaling within realistic dendritic spine and cardiomyocyte calcium release unit geometries, and ATP synthesis within a realistic mitochondrial geometry. Across these simulations, we find that signaling outputs are largely determined by local surface-area-to-volume ratios. For instance, in mechanotransduction simulations, we observe elevated cytoskeletal activation near highly curved membrane patches at the boundary of cell-substrate contact regions. Our findings demonstrate the importance of simulating reaction and diffusion within realistic cell geometries.

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