Applied Mathematics Seminar

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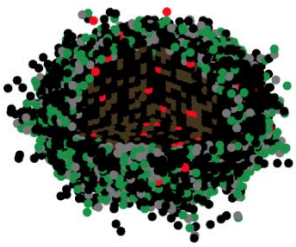
Friday, October 15, 2021

1-1:50pm - MAK B2124 or via zoom (request password from ortizron at gvsu dot edu)

A global method for simulating intracellular signaling in an ABM of tumor growth

Abstract: Systems biology often requires integrating data and information across spatio-temporal scales to gain a deeper, more robust understanding of the integrative functions of living systems. Agent-based models (ABMs) have become a valuable tool in translational systems biology, which has goals of predicting the effects of novel drugs and drug combinations by simulating virtual clinical trials. ABMs are a natural platform for capturing the multiple time and spatial scales associated with biological processes because they model each cell as an individual agent, allowing for the characterization of tissue heterogeneity that better reflects the complexity seen in living systems. However, a significant limitation of these models is that they can be computationally expensive, especially when they include the molecular level details of cell signaling or targeted therapeutics. The traditional approach to simulating this type of multiscale ABM is to solve a system of ordinary differential equations for the molecular events at every spatial location that houses a cell. This scales linearly with the number of agents modeled and can significantly add to the wall time necessary for simulations, which contributes to many ABMs being limited to around 10^5 cells. We propose a novel yet intuitive approach that reduces the time complexity for solving these equations from $O(N)$ to $O(1)$ where N is the number of agents. This results in a speedup of 1-2 orders of magnitude, allowing for more thorough explorations of ABMs with even larger numbers of agents than previously achievable. Using the molecular drivers of bladder cancer growth and targeted treatment as our test case, we show that our new method strongly agrees with the traditionally used approach across a broad range of parameter values. We also propose expected growth as a novel and simple metric for comparing between models or across parameter values. Finally, we show that our new simulation framework is robust to different assumptions about vasculature and even performs well when applied to treatments with larger therapeutic agents like monoclonal antibodies.
While we use cancer as an illustrative example, our new computational strategy for simulation of multiscale ABMs can easily be applied to a wide range of translational systems biology investigations.



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