Title: Tunable resolution as a systems biology method for multi-scale, multi-compartment computational models

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The use of multi-scale mathematical and computational models to study complex biological processes is becoming increasingly productive in biomedical science. Multi-scale models span a range of time and/or length scales and can encompass multi-compartment (e.g. multi-organ) models. Advances in multi-scale modeling are enabling virtual experiments to explore and answer questions that are problematic to address in the wet-lab. The goal of these virtual experiments is to improve explanatory, mechanistic insight while reducing uncertainties. In wet-lab experiments, advances in technology now allow scientists to observe, measure, record, and analyze experiments at a variety of biological scales. We need the technical ability to mirror that same flexibility in virtual experiments. Here we present both a new approach and method, tunable resolution, to begin providing that flexibility. Tunable resolution involves fine-graining or coarse-graining of a multi-scale computational model at the user's discretion, allowing adjustment of the level of resolution specific to a question, an experiment, or a scale of interest. Tunable resolution enables new strategies for revising and validating mechanistic explanatory models. The tunable resolution approach can be applied to many model types, including differential equation, agent-based or hybrid models. We identify evolving principles for its use and application. We describe approaches to building tunable resolution models, including techniques for coarse-graining sub-models and linking dynamics at different scales, different than classical model reduction techniques. We demonstrate the tunable resolution approach with examples relevant to infectious disease modeling, illustrating principles at work.