Building Reproducible Dynamical Models with Tellurium 2.0: A Case Study using EGFR/Erk

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Abstract:

Modelers in systems biology have long dreamed of a tool with the ability to support high-performance, feature-rich dynamical modeling, yet retain good interoperability with other tools. Tellurium realizes this dream by combining the latest technologies for high-performance simulation yet supports very high standards for interoperability by leveraging community standards (SBML, SED-ML, and the Combine archive) and supporting libraries. For example, Tellurium is one of the first tools to support the newly developed libCombine library for reading/writing Combine archives. Tellurium is available as a collection of Python packages, but also features a custom Jupyter/IPython notebook interface with special convenience functions for working with standards in systems biology. The notebook interface can be distributed as a self-contained desktop app / installer, obviating the need for users to know how to install Python packages or set up a Jupyter environment. We demonstrate the utility of Tellurium by constructing and simulating a model of the EGFR/Erk signaling pathway. We modeled the EGFR/Erk pathway using Antimony, which is interchangeable with SBML. We then performed sensitivity analysis on this model using libRoadRunner's built-in features for calculating steady state and determining local sensitivities. Our results help elucidate the role of negative feedback in this pathway. We show how in the presence of negative feedback, the pathway is more sensitive to changes in a number of the components of the pathway. This is a counter-intuitive result which we are continuing to investigate.