Gillespy2: Stochastic Modelling and Simulation

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Abstract

The dynamics of biological systems are very difficult to analyze due to their inherent stochasticity. Biochemical reactions fire in a non-deterministic way, which requires complex, probabilistic mathematical calculations to accurately represent. These computations are very taxing, and biologists rely on computer-driven methods for simulating these models. There are software libraries designed to meet this need, however many of these are difficult to use, or do not offer the versatility needed for a given system. This research will be contributing to the development of GillesPy2, a software package for building and simulating these models in the Python programming languages. GillesPy2 is the next-generation of the original GillesPy, an open-source cross-platform Python library used to model and simulate these systems with statistical accuracy. Users will be able run these simulations by creating models and selecting a solver that contains the best fitting algorithm for their need and model. This research will advance the development of GillesPy2 by implementing and testing the addition of two new solvers.

Description:

GillesPy2 currently includes solvers based on the Gillespie stochastic simulation algorithm(SSA), which produce exact results, but are computationally expensive. This research will result in the implementation of two additional solvers which provide algorithms that focus on reducing that computational cost and allowing users more versatility in their simulations. The first will be the hybrid solver, which partitions the system into fast and slow reactions to increase efficiency. The second will be the tau-leaping Solver, which will increase efficiency by "leaping" over many reactions based on reasonable approximation. This research will involve the research, design, and implementation of these solvers.

The hybrid solver improves on performance over the SSA direct method by separating the reactions into two subsets: "fast/continuous," and "slow/discrete." These reactions are then partitioned in the system and utilize different methods to calculate their trajectory. The "slow/discrete" reactions will continue to be updated with the standard SSA, an exact jump Markov process, while the "fast/continuous" reactions will be described over a predetermined time step interval by the chemical Langevin equation, a continuous Markov process. The use of the Langevin equation provides a significant improvement in computational efficiency, however, it only provides an accurate approximation for large quantities. For this reason, the assignment of "fast/continuous" reactions are reassessed at each time step, based on a pre-determined minimum for reactants, products, and reaction time. The slow reactions will be computed multiple times between each time step and will need to be considered when determining "fast/continuous" validity, as they will also affect the conditions of the fast reactions as they are fired. The hybrid solver will be ideal for very large models with many reactions occurring at different rates. This solver will yield a drastic improvement in performance over the SSA

and should maintain a high level of accuracy provided that the parameters are well-defined, and the conditions are met.

The second solver implemented will be the tau-leaping solver, which will also be implemented with a focus on performance improvement over the Gillespie SSA direct solver. The original SSA tracks every single reaction over a simulation, which requires an incredibly large amount of processing. The goal of the tau-leaping solver is to devise reasonable approximations of reactions over small time intervals, rather than calculate each singular event. The rate at which a reaction is fired is given by a propensity function. The propensity function for each reaction in a simulation is initialized with a base rate which is updated with each reaction based on the number of reactants available remaining. If the change in that propensity rate is small over some time interval, then a reasonable approximation can be made, and many reactions can be "leaped" over. As for the tau selection procedure, multiple solutions have been proposed. This research will involve the selection of an appropriate tau selection procedure as well as the development of the tau leaping solver into the GillesPy2 library.

GillesPy2 is a continued work under the direction and supervision of Dr. Brian Drawert and Dr. Kevin R. Sanft. This research will include the implementation of these solvers, and I will be continuing to contribute to this research this Fall with three credited research hours. The research will be presented at UNCA's Fall Undergraduate Research Symposium, and once completed, the research team for GillesPy2 will be publishing a paper in a high ranking scientific journal.

Timeline:

May 14th - June 8th (4 weeks): Research, development, and testing of hybrid solver.

June 11th - June 22nd (2 weeks): Research, development, and testing of tau-leaping solver.

June 25th – July 6th (2 weeks): Testing, Documentation, and release of GillesPy2 software.

July 9th - August 3rd (4 weeks): Collecting data and writing the paper.

Budget:

Student stipend: $1500

Resources

Abel, J.H, Drawert, B., Hellander, A., & Petzold, L.R. (2016) GillesPy: A Python Package for Stochastic Model Building and Simulation. *IEEE Life Sciences Letters*, *2(3)*, 35–38.

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Gillespie, Daniel T. (1977) Exact Stochastic Simulation of Coupled Chemical Reactions. *The Journal of Physical Chemistry 81(25)*, 2340-2361.

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