# GILLESPY: A PYTHON PACKAGE FOR STOCHASTIC MODEL BUILDING AND SIMULATION

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*Abstract*

GillesPy is an open-source Python language package for model construction and simulation of stochastic biochemical systems. GillesPy consists of a pythonic framework for model building and an interface to the StochKit2 suite of efficient Gillespie stochastic simulation algorithms (SSAs). To enable intuitive model construction and seamless integration into the scientific Python stack, we present an easy to understand action-oriented programming interface. GillesPy also supports the import of legacy SBML models. Here, we describe the components of this package and provide a simple example relevant to the computational biology community.

*Keywords*

Stochastic systems, Gillespie algorithm, Python, open-source software

## Introduction

For many cellular processes, low copy numbers of genes and proteins have been shown to exhibit intrinsic stochastic noise, resulting in unique cellular behavior. While deterministic ordinary differential equation (ODE) models of biochemical processes have proven useful and accurate in the high-concentration limit, they fail to accurately capture stochastic fluctuations. Stochastic simulation algorithms (SSAs) address this issue by replacing deterministic ODEs with a set of propensity functions describing the probabilistic time evolution of the chemical reaction system. SSAs solve this chemical master equation (CME) with a Monte Carlo scheme to generate a trajectory that is a possible solution to the equations.

SSAs have improved significantly since the 1977 direct method (Gillespie). In addition to the direct method, many of these improved SSAs have been distributed in the popular StochKit2 software package (Sanft *et al.*, 2011). StochKit2 provides efficient implementation of SSAs including the direct method, optimized-direct method, composition-rejection method, and τ-leaping.

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With its wide variety of numerical libraries and statistical packages, Python has become one of the most commonly used and effective languages in computational biology. In order to facilitate stochastic model building and simulation, we have created the GillesPy package. GillesPy combines a Python model construction toolkit with the computational efficiency of the StochKit2 C-based SSAs.

## GillesPy Features

Biochemical models in GillesPy are constructed in an object-oriented fashion. Model objects are initialized, and filled with parameter, species, and reaction objects which describe how species interact. Once a model is completed, it may be simulated through the StochKitSolver.run() command. This command calls the StochKit2 C-solvers to simulate the provided model. StochKit2 selects the computationally-optimal SSA for solving each model, and returns simulation results to the Python interface.

The following section will demonstrate building and simulating a simple and biologically relevant example.

## Example: A Bistable Genetic Switch

Bistable stochastic genetic switches have been shown to play important roles in cellular differentiation. As the system has two equilibria, deterministic simulations fail to accurately capture the random switching between states. Here, we demonstrate using GillesPy to simulate a bistable switch from Gardener, Cantor, and Collins (2000). The deterministic equations comprising this switch are:

$$\frac{dU}{dt} = \frac{a_1}{1+V^B} - U \quad , \quad \frac{dV}{dt} = \frac{a_2}{1+U^y} - V \tag{1}$$

where $U$ and $V$ are co-repressor concentrations. Here, the parameters $a_1$ and $a_2$ are synthesis rates of $U$ and $V$ respectively. Parameters $B$ and $y$ represent the cooperativity of each repressor. Finally, we create a stochastic model from these equations by converting them to four stochastic reaction channels: creation and destruction of $U$ and $V$ respectively.

Constructing this model in Python starts with creating a Python object by inheriting from GillesPy's model class:

```
class BistableToggleSwitch(gillespy.Model):
```
We create and add parameters within this object by:

```
a1 = gillespy.Parameter('a1',expression=4)
self.add_parameter([a1,...])
```
and equivalently add species and reactions. We then simulate this model by invoking:

```
model = BistableToggleSwitch()
results = gillespy.StochKitSolver.run(model,
                t=100)
```
A single simulation showing $U$ and $V$ population over the course of 100s is shown as Figure 1.
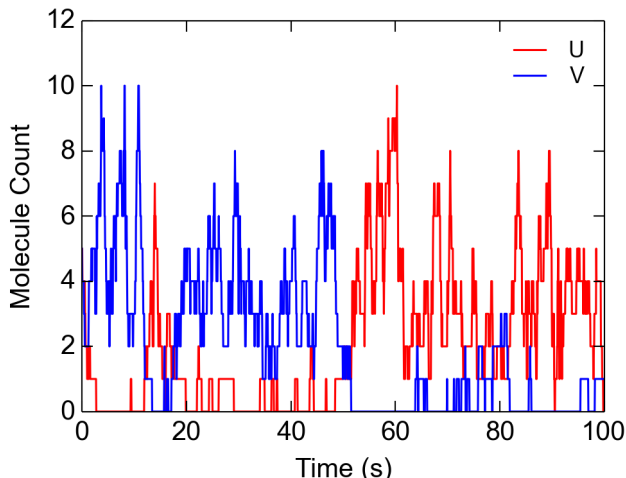


*Figure 1. Single trajectory plot of bistable genetic switch outputs. The genetic motif results in random switching between the two stable U (red) and V (blue) states.*

## Conclusion

GillesPy is an open source package for stochastic model building and simulation, and a Python interface to the StochKit2 solvers. GillesPy runs on Linux/Unix or Mac OS X. It is freely available under GPL version 3. Installation instructions and downloads are available at: http://github.com/JohnAbel/gillespy.

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