

Simulating Stochastic Models

Models that are based on differential equations assume that the concentrations of molecular species change continuously in time. This is a reasonable approximation in many cases. However in some models, the number of molecules can be of the order of 10s of molecules. In such cases the use of differential equations is unreasonable. In addition to losing the assumption of continuity, such systems also show pronounced stochastic behavior because of the stochastic nature of molecular collisions.

New methods have been developed to model systems where the numbers of molecules is small. In the 1970s, **Dan Gillespie** developed what has become the standard method for simulating chemical models where the number of molecules is small, this method is now called the Gillespie method.

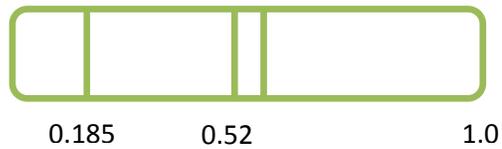
The Algorithm

The basis of the method is computing two values:

1. **When** will the next reaction take place?
2. **Which** reaction will take place?

The algorithm revolves around answering these two questions.

1. Initialize the number of molecules for each species in the model.
2. Calculate each reaction rate (called the propensity function), v_i
3. Calculate the sum of all reaction rates, $h = \sum v_i$
4. Generate two uniformly distributed random numbers: r_1 and r_2
5. Compute the time interval to the next reaction, $\tau = -(\ln r_1)/h$
6. Determine which reaction will 'fire' next. Divide each reaction rate by the total rate, h , and cumulatively order these number. For example if we have four reactions with rates, 0.34, 0.65, 0.1, 0.8, then the total rate is: 1.89. The normalized rates are therefore: 0.18, 0.34, 0.053, 0.42. We now form a cumulative list: 0.18, 0.52, 0.562, 1.0



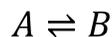
The second random number (r_2) can be used to locate the reaction that will 'fire'. For example if r_2 is 0.25, then the second reaction will fire, if r_2 is 0.02, then the third reaction will fire.

7. Compute the new time, $t = t + \tau$.

8. Compute the new molecule numbers by acting out the firing of the selected reaction. This will involve moving reactants from one side of a reaction to the other. Because the method is a discrete method, changes at each iteration only involve one molecule at a time modulated by the stoichiometry. Thus for a reaction such as $A \rightarrow B$, one molecule of A disappears while one molecule of B appears.

9. Goto 2.

Example, simulating an equilibration model:



1. Initialize the molecules numbers, $A = 10$, $B = 4$. Assume rate constants $k_1 = 0.2$ and $k_2 = 0.3$.

2. Calculate each reaction rate, forward and reverse:

$$v_1 = 10 \times 0.2 = 2$$

$$v_2 = 4 \times 0.3 = 1.2$$

3. Calculate the sum of the rates: $h = 2 + 1.2 = 3.2$

4. Generate two random numbers: 0.34 and 0.87

5. Compute the next time interval, $\tau = -\frac{\ln(0.34)}{3.2} = 0.337$

6. Determine which reaction will fire next, v_1 or v_2

Normalize rates, $nv_1 = \frac{2}{3.2} = 0.625$; $nv_2 = \frac{1.2}{3.2} = 0.375$

Form a cumulative list: 0.375, 1.0

The second random number (0.87) lies inside the second cumulative segment therefore the second reaction will 'fire' and so we subtract one molecule from B and add it to A: $B \leftarrow B - 1$; $A \leftarrow A + 1$

Using Jarnac to carry out Stochastic Simulations

Jarnac has built-in support for simulating stochastic models. To use Jarnac, declare a model in the usual way. When you come to simulating the model, use the following command:

```
m = gillespie (p, 100, [<p.time>, <p.A>, <p.B>]);
```

where p is the model you have defined and 100 is the amount of time to simulate for. The method returns a matrix of results which can be plotted using the graph command.