

## Exact Methods for Computing Biological System Dynamics

Drew Endy (<http://mit.edu/endy/>)

### Goals Covered Last Time

I. How is reaction time updated w/o resampling?

J. Back to the biology! What is this stuff good for? [Genetic Memory]

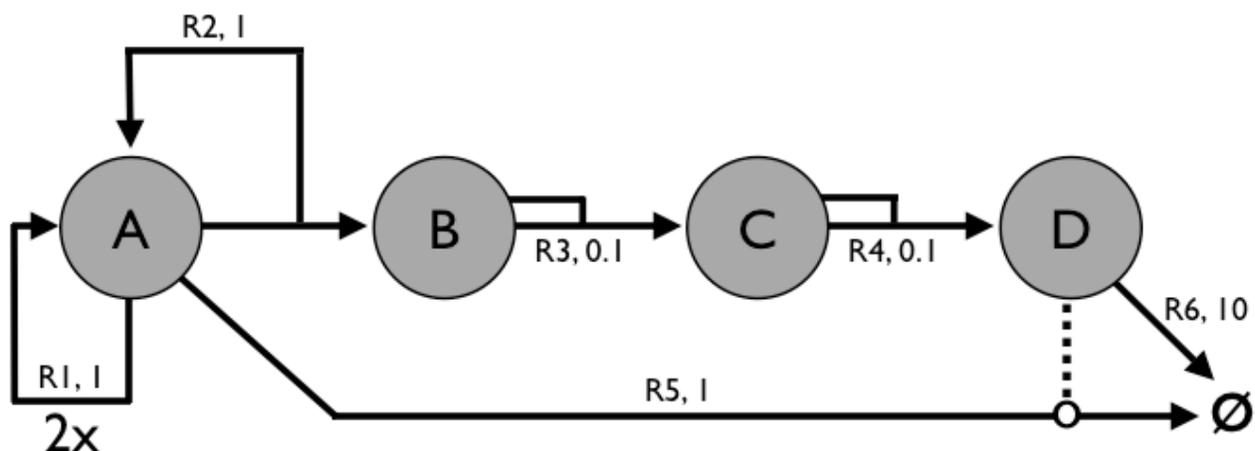
### Goals for Today

K. Discuss dynamics of 'simple' system from HW10

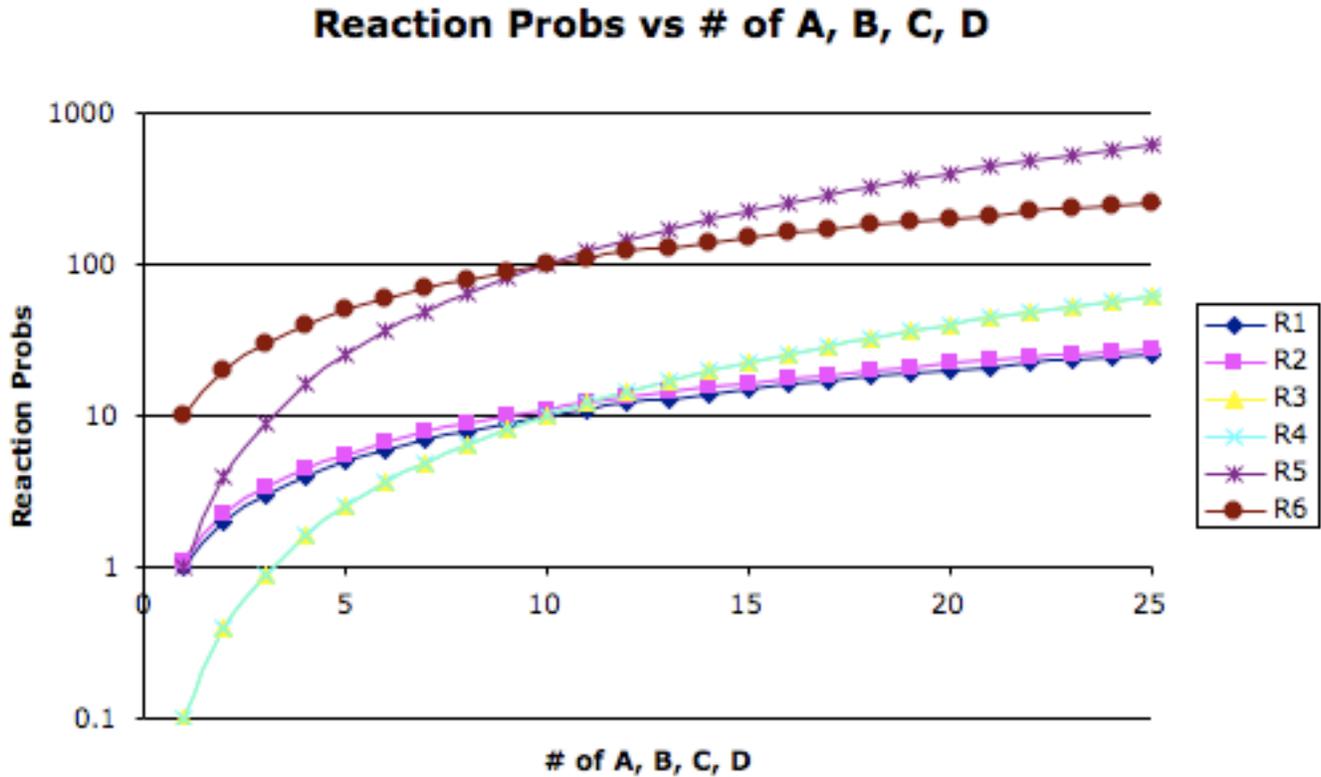
L. Review of key concepts from this module

**74. How else could we store state inside cells?** In the above latch we are storing state via the levels of proteins. Is this the best way to go? How else could we store state? One idea is to write to DNA. For example, there are enzymes that let you switch the orientation of DNA. These enzymes are called invertases. (could also consider using phage integrases).

**75. What do we expect this system to do?** Oscillate.



**76. Why?** Consider how the reaction probabilities change as a function of varying numbers of the reactants? Below is a plot of everything collapsed onto one independent axis. See the point where A is degraded faster than D? This is because the  $A+D \rightarrow D$  reaction is 2nd order. To get a still clearer sense of this you could try plotting reaction prob surfaces with two independent axis (# of A, # of D).



**77. What is the absolutely certain ( $p=100\%$ ) final state of this system?**

$\#A=\#B=\#C=\#D=0$ . Why? Because if ever the # of A goes to zero then the degradation of D will eventually deplete the system (NOTE: there may be one molecule of B and C left over, since they require two molecules to react).

## 78. Key Concepts

Exact, discrete reaction event simulators. Needed when the precise timing of individual reactions events matters (e.g., when the occurrence of one reaction has a major impact on the probability that other reactions occur). Such situations can arise given low number of reactants (e.g., DNA present at low or single copy number inside cells), whenever the system of interest contains sharp, switch-like behavior, et cetera.

Underlying assumptions of the computational methods. System volume in which most reaction events are non-reactive and thus the volume is self-mixing. We can define a small slice of time in which only a single (i.e., one and only) elementary chemical reaction event occurs (i.e., an instantaneous physical event).

Different algorithms for implementing the method. The choice of algorithm can have dramatic impacts on computational cost. As a developer or user of computational methods you will want to be aware of what your methods cost and why.

In considering costs of computational methods remember that Useful Results per Real World (time, energy, etc) = Useful Results per Computing Unit (i.e., software) x Computing Units per Real World (i.e., hardware). Sometimes it is best to make investments to improve hardware, sometimes software, sometimes both. Choose wisely.