**Modeling cell cycle and B cell birth-death dynamics**

We will pursue a birth-death dynamical model that combines an intracellular protein abundance dynamical model with a discrete Markov Chain model governed by hazard functions that are themselves functions of the intracellular protein abundances.

Before we get to the fully general model class, let’s examine a simple case.

Suppose there are two states referred to as  and , and that there are two control proteins whose concentrations are designated  and . The dynamics are set up as follows:

When the system is in state ,  increases linearly with rate which depends on the stimulus, and  does not change

.

We let the probability of making the  transition be proportional to the concentration of . Letting  denote the probability of the system’s being in state  at time  given that it is in state  at time , we have for  small,



When the system makes the  transition, the dynamical parameters change discontinuously, the value of  is instantaneously set to and the dynamical equations in state are

.

For the  transition, suppose that the transition is much sharper, as is the case in many cell-cycle models, such as



At the  transition division occurs,  is cut in half as the corresponding protein is divided to the two daughters, which then independently continue to grow and divide.

Suppose the initial value of  is . Then , the time to the transition, has cumulative distribution function



and the total time is

.

At the beginning of the next cell cycle (resetting the clock to ), we have .

From here, we want to generalize this construct to have any number of discrete states, any number of internal protein species, and realistic dynamics during the times spent in each of the states, and plausible discontinuous jumps during the state transitions.

**Generalization**

Suppose that the protein abundances of interest are denoted  for .

Suppose also that we have one or more discrete cell states defined functionally. Denote this state variable as . In the case of the cell cycle, for example, we may have the states . State transitions correspond to discontinuous changes of what are otherwise continuous state variables, discontinuous changes of parameter values, and to discontinuous changes in behavior.

In state the abundances evolve according to



where is the vector with components . The functions may change discontinuously when the state changes.

The state transition probabilities are given by



where  is the transition rate from  to in internal state .

Finally, there are rules giving the discontinuous changes that occur at transitions. If  is the state immediately prior to the state change, and  is the state immediately after the state change, we have

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