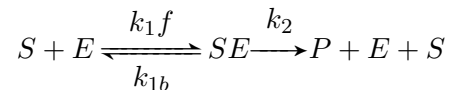


CS341 SYSTEMS BIOLOGY I

LECTURE 6

1. GENE REGULATION

We have been looking at enzyme-aided reactions, where E aids a reaction in which S is consumed and P is produced. In the case of gene regulation, we have a reaction more like this:



i.e. the S is not consumed by the final reaction. For transcriptional regulation, we think of the gene itself as E – we absolutely need it to accomplish the reaction, and there aren't very many in the system. And S is now a special kind of protein called a transcription factor. The transcription factor binds to the promoter region of the gene, RNA polymerase is recruited, and transcription begins. The transcription factor is now free to leave and repeat the whole process (or stay and repeat the whole process, but we won't get into that much detail).

We often draw the diagram for regulation as an arrow to a reaction, rather than as an arrow to a product.

Transcription factors can increase or decrease the rate of transcription. In fact, they can have such a strong effect, that they act more like switches – if there is enough TF then the gene suddenly turns on or off. This happens in the presence of a phenomenon called cooperativity – TF may recruit buddies to help get the gene going. To capture this situation, we use the Hill equation, which is similar to the M-M equation, but has exponents.

The Hill eq causes a sigmoidal relationship between the TF and the rate of transcription. The product of transcription is mRNA, so let's model that.

Transcription factor T up-regulates (activates) a gene, causing it to transcribe mRNA faster:

$$\frac{dM}{dt} = \frac{v_{max} \cdot T^n}{K^n + T^n}$$

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but we should design the model to reach a steady-state, rather than grow steadily over time. This means we should include degradation:

$$\frac{dM}{dt} = \frac{v_{max} \cdot T^n}{K^n + T^n} - d_M M$$

Transcription factor T down-regulates (represses) a gene, causing it to transcribe mRNA slower:

$$\frac{dM}{dt} = \frac{v_{max} K^n}{K^n + T^n} = \frac{v_{max}}{1 + \frac{T^n}{K^n}}$$

and with degradation, the model becomes

$$\frac{dM}{dt} = \frac{v_{max} K^n}{K^n + T^n} - d_M M = \frac{v_{max}}{1 + \frac{T^n}{K^n}} - d_M M$$

2. GENES REGULATED BY MORE THAN ONE TRANSCRIPTION FACTOR

When more than one TF regulates a gene, we need to know how they interact? There are generally three sets of interactions, or “gates”.

- (1) **AND** – multiply the regulation terms together
- (2) **OR** – use the max function, or do something a little more complicated if the binding is competitive (i.e. if the two transcription factors are vying for the same spot).
- (3) **SUM** – add the regulation terms together

Let’s examine the different gates in the presence of two activating signals.

If we have two activators that work with an AND gate, then we simply multiply the regulation terms together:

$$\frac{dM}{dt} = v_{max} \frac{T_1^{n_1}}{K_1^{n_1} + T_1^{n_1}} \frac{T_2^{n_2}}{K_2^{n_2} + T_2^{n_2}} - d_M M$$

If we have two competitive activators that work with a OR gate, then we simply add the regulation terms together:

$$\frac{dM}{dt} = v_{max} \left(\frac{(T_1/K_1)^{n_1}}{1 + (T_1/K_1)^{n_1} + (T_2/K_2)^{n_2}} + \frac{(T_2/K_2)^{n_2}}{1 + (T_1/K_1)^{n_1} + (T_2/K_2)^{n_2}} \right) - d_M M$$

If we have two activators that work with a SUM gate, then we simply add the regulation terms together:

$$\frac{dM}{dt} = v_{max} \left(\frac{T_1^{n_1}}{K_1^{n_1} + T_1^{n_1}} + \frac{T_2^{n_2}}{K_2^{n_2} + T_2^{n_2}} \right) - d_M M$$