

# Week 1 Writeup

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## 1 Overview

The majority of the week was spent reading papers on various types of modeling, identifying the reactions involved in the synthesis of curli fibers, spider silk, cellulose, and alginate, and looking into cobrapy. Here I will focus on creating a gene circuit model of curli production.

## 2 Mass Action Kinetics

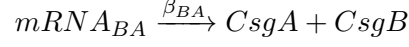
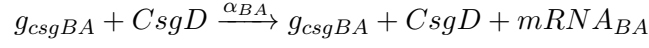
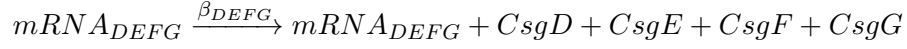
Mass Action Kinetics state that the rate of a reaction is the product of a rate constant ( $k$ ) and the mass of the substrate ( $S$ ). Several assumptions will be made in the following model:

1. Some of the molecular interactions, like polymerase or ribosome binding, will be ignored, as these would greatly increase the complexity of the model.
2. Transcription factor binding achieves equilibrium much faster than transcription, translation, and protein accumulation, so it can be considered to be at steady state on the time scale of proteins.
3. Spatial parameters, heat and diffusion gradients, transport times, etc. will not be considered to avoid partial differential equations.

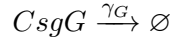
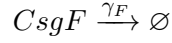
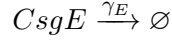
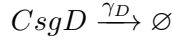
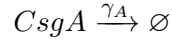
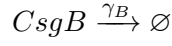
In the case of curli fibers, the main reactions are transcription, translation, secretion, nucleation, and polymerization. For now, I will focus on the transcription and translation aspects. This can be described using the following sets of chemical equations:

### Transcription & Translation





### Degradation



From these, we derive a system of differential equations to describe the rate of change of mRNA and protein levels over time:

$$\frac{d[mRNA_{DEFG}]}{dt} = \alpha_{DEFG}[g_{csgDEFG}] - \gamma_{DEFG}[mRNA_{DEFG}]$$

$$\frac{d[mRNA_{BA}]}{dt} = \alpha_{BA}[g_{csgBA}] - \gamma_{BA}[mRNA_{BA}]$$

$$\frac{d[CsgA]}{dt} = \beta_{BA}[mRNA_{BA}] - \gamma_{BA}[CsgA]$$

$$\frac{d[CsgB]}{dt} = \beta_{BA}[mRNA_{BA}] - \gamma_{BA}[CsgB]$$

$$\frac{d[CsgD]}{dt} = \beta_{DEFG}[mRNA_{DEFG}] - \gamma_{DEFG}[CsgD]$$

$$\frac{d[CsgE]}{dt} = \beta_{DEFG}[mRNA_{DEFG}] - \gamma_{DEFG}[CsgE]$$

$$\frac{d[CsgF]}{dt} = \beta_{DEFG}[mRNA_{DEFG}] - \gamma_{DEFG}[CsgF]$$

$$\frac{d[CsgG]}{dt} = \beta_{DEFG}[mRNA_{DEFG}] - \gamma_{DEFG}[CsgG]$$

### 3 Gene Regulation

The rate of transcription can be regulated by either activators or repressors. Thus, we must modify our differential equations to take this into account. We will define rate of transcription,  $\alpha$ , to be

$$\alpha = Bf(x)$$

where  $B$  is the basal expression rate when the gene is "on", and  $f(x)$  represents the probability of expression, a function of the concentration of  $x$ . This function  $f(x)$  can be described by the Hill function model:

$$f(x)_{activation} = \frac{x^n}{x^n + K^n}$$

$$f(x)_{repression} = \frac{1}{1 + (\frac{x}{K})^n}$$

Here  $x$  is the level of activator or repressor,  $n$  is the Hill coefficient, and the parameter  $K$  is the value of  $x$  where the probability  $f(x)$  is 0.5.

### 4 References

Csicsery, Nick and O’Laughlin, Ricky. (2013). *A Mathematical Model of a Synthetically Constructed Genetic Toggle Switch*.