**Question 1.**

**Part A.**

**Text, letter

Description automatically generated**

**Text, letter

Description automatically generated**

**Part B.**

Looking at the kinetic limit of transcription for gene , , the many genes () scenario differs from the single gene system only by the inclusion of in the denominator of the many gene scenario. For the many gene scenario to be approximately equivalent to the single gene system described in class, must approach zero. Since , , and can vary for each gene, there are many cases that allow for to be near zero.

For any gene , a low concentration of gene () would override the other constants and minimize the -ith term of the summation. Similarly, a large would also cause the -ith term to be small. In the expanded form of , it is visible that there are two terms, one that depends on (in the denominator) and one term that does not depend on . The -dependent term can approach zero when is large enough but the second, -independent term complicates things as must also be near zero for the -ith term to be small. As this third scenario demonstrates, there are likely many scenarios where the exact balance of , , and for each gene minimizes a term in the summation and this is further complicated when . Beyond minimizing the concentration of all genes except gene (essentially reducing this problem to the single-gene scenario), there appears to be no single scenario except setting that will ensure the many gene scenario is equivalent to the single-gene scenario we covered during class.

**Question 2.**

All code used for this question was prepared in MATLAB and is available in the attached GitHub repository.

**Part A.**

I have summarized the three-state model for PFK activity

Table

Description automatically generated with medium confidence

**Part B.**

To determine , I assumed that when [3’-5’-AMP] = 0 that state 2 would be completely non-active () so . This allowed for to be solved for using the initial rate provided and based on the constants provided.

Using the and values from before, I solved for the combined term for each rate in the provided dataset. I assumed that cannot be greater than 1 () and that at [3’-5’-AMP] = .99 mM, since the rate had essentially plateaued. As a result, I took the value of to be equal to the value of at [3’-5’-AMP] = .99 mM.

I then found the values for for each data point by dividing by . I adjusted the hill-type binding function provided to us to match that of other hill-type functions: . This assumes that is equivalent to , the 3’-5’-AMP concentration obtaining half-maximum response, rather than the dissociation constant . This is a matter of form though, where , but ensures the hill-type binding function works. To obtain a hill-plot, I used the log-form of the hill-type function: . I normalized the provided in this way to create a linear hill-plot, from which I took the slope as the order parameter and the x-intercept as the . In doing this, I excluded the first value where [3’-5’-AMP] = 0 and the final value where as the small denominator generates a large y-value that is inconsistent with the remaining data points.

The parameter values obtained through this process are summarized below, along with the hill-plot used to obtain some of them.

Chart, scatter chart

Description automatically generated

|  |  |  |
| --- | --- | --- |
| Parameter | Value | Units |
|  | .0451 | Dimensionless |
|  | 74.028 | Dimensionless |
|  | 2.337 | Dimensionless |
|  | .9534 | mM |

**Text, letter

Description automatically generated**

**Part C.**

The proposed model fits the experimental data well. The model is especially well fit at low and high concentrations and deviates when the change in PFK rate is high. The relatively low number of data points when the rate is rapidly changing likely contributes to this deviation and increasing the sampling could improve the accuracy of the model.

**Chart

Description automatically generated**