PaekJ-Prelim1

Justin Paek

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Problem 2b

```
data = read.table("Data-3-5-AMP.txt")
AMP_concs = data[,1]   #AMP conc. in mM
r_hats = data[,2]   #uM/hr
measured_rates = data[,3]   #uM/hr
```

Estimating W_1

Set up parameters

```
F6P_conc = 0.1   #mM
ATP_conc = 2.3  #mM
E1 = 0.12   #uM
K_F6P = 0.11  #mM
K_ATP = 0.42  #mM
kcat = 0.4*3600  #1/h

kinetic_limit = kcat*E1*(F6P_conc/(K_F6P+F6P_conc))*(ATP_conc/(K_ATP+ATP_conc))
```

To estimate W_1, we can consider the case where no AMP is present, so the only state that leads to activation is State 1. This means that $f_i = 0$, and $v(...)_j = \frac{W_1}{1+W_1}$. We can then solve for W_1:

$$\hat{r_j} = r_j \left(\frac{W_1}{1 + W_1} \right)$$

$$W_1 = \frac{\hat{r_j}}{r_j - \hat{r_j}}$$

```
r_hat_0 = r_hats[1]
W1 = r_hat_0/(kinetic_limit - r_hat_0)
W1
```

```
## [1] 0.04510578
```

Estimating W_2

To get an estimate of W_2, we can look at where the system approaches equilibrium. Here, the fraction of bound AMP approaches saturation. That is, $f_i \approx 1$. As such, the overall rate becomes:

$$\hat{r_j} = r_j \left(\frac{W_1 + W_2}{1 + W_1 + W_2} \right)$$

Solving for W_2 gives:

$$W_2 = \frac{\frac{\hat{r_j}}{r_j} + W_1\left(\frac{\hat{r_j}}{r_j} - 1\right)}{1 - \frac{\hat{r_j}}{r_j}}$$

```
ratio = r_hats[6]/kinetic_limit
W2 = (ratio + W1*(ratio-1))/(1-ratio)
W2
```

```
## [1] 74.02765
```

Estimating order parameter and binding constant

To obtain values for the order parameter n_i and the AMP binding constant K_i, we can fit the model to the experimental measured rate data and use non-linear least-squares regression. To do this, I used Microsoft Excel's solver function, which uses the GRG Nonlinear algorithm to find values of Ki and ni that minimized the sum of squared residuals. (file included in Github Repo)

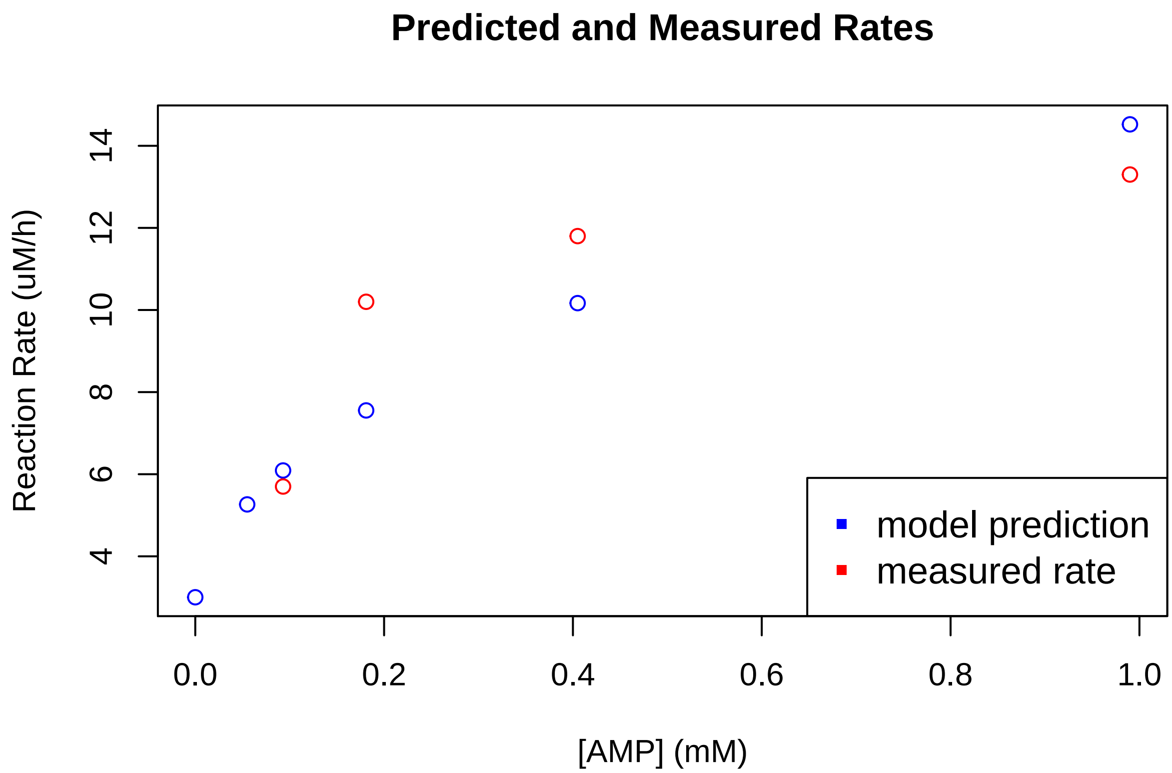
```
Ki = 12239.01119  #mM, determined from non-linear least-squares regression
ni = 0.617855636  #dimensionless, determined from non-linear least-squares regression
x = AMP_concs
fi = ((x/Ki)^ni)/(1+((x/Ki)^ni))
numerator = W1 + W2*fi
denominator = 1 + W1 + W2*fi
control = numerator/denominator
model_y = kinetic_limit*control
model_y
```

```
## [1]  3.003000  5.264625  6.090930  7.553657 10.167665 14.522426
```

```
measured_rates
```

```
## [1]  0.59  1.20  5.70 10.20 11.80 13.30
```

```
plot(AMP_concs, model_y, main = "Predicted and Measured Rates", ylab="Reaction Rate (uM/h)", xlab="[AMP
points(AMP_concs, measured_rates, col="red")
legend("bottomright", legend=c("model prediction", "measured rate"), col=c("blue","red"), pch = ".",
  pt.cex = 5,
  cex = 1.2,
  text.col = "black",
  horiz = F )
```



The model is not a particularly good fit. Specifically, the shape of the model predictions is not sigmoidal. This may be attributed to the fact that the regression was done in Microsoft Excel, with limited capacity for fitting highly complex non-linear functions, especially with only 6 data points given. The model can likely be improved if the regression was performed directly in R or in Julia, but unfortunately I was not able to get the regression working properly in either.