4.

$$ATP + D\text{-}\underbrace{\text{fractose-6-phosphate}} \xrightarrow{PFK} ADP + D - \text{fructose}1,6 \text{ biphosphate}$$

activated in presence of 3'-5'-AMP

$\hat{r}_j = r_j \, \nu(\cdots j)$ ~ control (dimensionless)

$\hat{r}_j$: overall rate of reaction $\hat{PFK}$ $\left[\frac{\mu M}{h}\right]$

r_j: kinetic limit (max rate of conversion in absense of allosteric regulation) $\left[\frac{\mu M}{h}\right]$

ν: describe influence of effector molecules

$$\nu(\cdots)_j = \frac{\sum_{i \in \{X\}} W_i f_i(\cdots)}{\sum_{j \in G} W_j f_j(\cdots)}$$

dimensionless weight

$\sum_{i \in \{X\}} W_i f_i(\cdots)$ — configs that lead to activity

$\sum_{j \in G} W_j f_j(\cdots)$ — all possible configs

$$f_i = \frac{\left(\frac{x}{K_i}\right)^{n_i}}{\left(1 + \left(\frac{x}{K_i}\right)^{n_i}\right)}$$

x [=] fraction of bond activator/inhibitor for config i

k_i [=] binding constant [=] mM

n_i [=] order parameter

kinetic limit for PFK (E, μM): $r_1 = k_{cat} E_1 \left(\frac{F6P}{K_{F6P} + F6P}\right)\left(\frac{ATP}{K_{ATP} + ATP}\right)$

(i) F6P conc is 0.1 mM (ii) ATP conc is 2.3 mM

(iii) E_1 (PFK) is 0.12 μM (iv) $K_{F6P} = 0.11$ mM, $K_{ATP} = 0.42$ mM

(v) $k_{cat} = 0.4 \frac{1}{s}$

(a) $r_1 = 0.4 \frac{1}{s} (0.12 \times 10^{-3} \text{ mM}) \left[\frac{0.1 \text{ mM}}{0.11 + 0.1 \text{ mM mM}}\right]\left[\frac{2.3 \text{ mM}}{0.42 + 2.3 \text{ mM mM}}\right] = 1.93 \times 10^{-5} \frac{\text{mM}}{s} = 0.0193 \frac{\mu M}{s}$

$$\left(0.0193 \frac{\mu M}{s}\right)\left(\frac{60 s}{\min}\right)\left(\frac{60 \min}{hr}\right) = 1619.58 \frac{\mu M}{hr}$$

$$\nu = \frac{W_1 + W_2 f_2}{1 + W_1 + W_2 f_2}$$

When there is no receptor, $f_i = 0$, and $\nu = \frac{W_1}{1 + W_1}$

therefore $\hat{r}_j = r_j \left(\frac{W_1}{W_1 + 1}\right)$ where

$$3.003 \frac{\mu M}{hr} = \left(69.58 \frac{\mu M}{hr}\right)\left(\frac{W_1}{W_1 + 1}\right)$$

$0.0431(W_1 + 1) = W_1$ $\Rightarrow$ $\boxed{W_1 = 0.0451}$

When the activator saturates, effector has max influence. We can assume this occurs when [PFK] = 0.99 mM, and $f_i = 1$

$$68.653 \frac{\mu M}{hr} = 69.58 \frac{\mu M}{hr} \left(\frac{0.0451 + W_2}{1 + 0.0451 + W_2}\right)$$

↳ $\boxed{W_2 = 74.0277}$

$0.9866(1.0451 + W_2) = 0.0451 + W_2$

$1.0311 + 0.9866 W_2 = 0.0451 + W_2$

4.(b) $f_i = \dfrac{\left(\frac{x_i}{K_i}\right)^n}{1+\left(\frac{x_1}{K_i}\right)^n}$, for $\nu = \dfrac{W_1 + W_2 f_2}{1+W_1+W_2 f_2}$

Look at excel for calculations and plots:

$\hat{r} = r\,\nu(\ldots)$

Using solver, $k = 0.657$ mM, and $n = 2.49$

If you fit for W_1, W_2, k, and n,

$W_1 = 0.0187$, $W_2 = 14.76$, $k = 0.286$

and $n = 2.794$.

(c) Plotted on excel and attached.

The proposed model describes the data to an extent. There is a large margin of error in the measured rate, so it is difficult for that to be captured in a model. If the parameters were recalculated with the max and min values in the 95% interval, it would provide a better understanding about the fit of the model and the range in which fitted parameters and constants would fall. It deviates and overestimates the rate from 0.2 - 1 μM and fits well in the 0.05 - 0.20 μM region. It also overestimates the 0 - 0.05 μM rate a bit.

(b)

Estimating the binding constants and order parameters from the data resulted in K = 0.657 mM and n = 2.48 for the data when W1 and W1 were set at the values from (a). I also tried fitting the W1 and W2 parameters to see if it would generate a better fit. Both plots have error bars, the original data, and the model.

(c)

The proposed model could describe the data, but the error margins for the measured data get larger as the overall rate increases.