CHEME5440 HW1

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Part A

Derivation of Transcription Rate Constant

The mass balances around the open and closed complex are:

$$\frac{d}{dt}(G_j : R_x)_C = k_+(G_j)(R_x) - k_-(G_j : R_x)_C - k_I(G_j : R_x)_C$$

$$\frac{d}{dt}(G_j : R_x)_O = k_I(G_j : R_x)_C - k_A(G_j : R_x)_O - k_{E,j}(G_j : R_x)_O$$

The total amount of RNA polymerase is:

$$R_{X,T} = R_X + (G_j : R_x)_C + (G_j : R_x)_O$$

Assuming steady-state, the amount of open and closed complexes are:

$$(G_j : R_x)_C = (\frac{k_+}{k_- + k_I})(G_j)(R_x)$$

$$(G_j : R_x)_O = (\frac{k_I}{k_A + k_E})(G_j : R_x)_c$$

Let the ratio of parameters be:

$$K_{X,j} = \frac{k_- + k_I}{k_+}$$

$$\tau_{X,j} = \frac{k_A + k_E}{k_I}$$

Replacing for terms in the expression for open complex and for the total amount of RNA polymerase, we get:

$$(G_j : R_x)_O = \frac{(G_j)(R_x)}{(K_{X,j})(\tau_{X,j})}$$

$$R_{X,T} = R_X + (G_j)(R_x)(K_{X,j}^{-1}) + (G_j)(R_x)(K_{X,j}^{-1})(\tau_{X,j}^{-1})$$

Rearranging, we get:

$$R_X = \frac{R_{X,T}(K_{X,j})(\tau_{X,j})}{(K_{X,j})(\tau_{X,j}) + (\tau_{X,j} + 1)G_j}$$

$$(G_j : R_x)_O = \frac{R_{X,T}G_j}{(K_{X,j})(\tau_{X,j}) + (\tau_{X,j} + 1)G_j}$$

Finally, we get an equation for the kinetic rate of transcription in terms of total RNA polymerase and other solvable parameters

$$r_{X,j} = k_{E,j}R_{X,T}(\frac{R_{X,T}G_j}{(K_{X,j})(\tau_{X,j}) + (\tau_{X,j} + 1)G_j})$$

List of Parameters Used from BioNumbers

Parameter	Value	Units	Source
e_x	27	nt/s	Proshkin S, et al. (2010)
L	924	nt	Xu L, et al. (2006)
K_xj	2.48e-8	M	McClure, et al. (1980)*
k_I	0.04	1/s	McClure, et al. (1980)
R_X,T	30	nM	Arkin A, et al. (1998)
$Radius_{cell}$	0.306	um	Rosenberger RF , et al. (1978)
$Length_{cell}$	2.62	um	Rosenberger RF , et al. (1978)

* Note: This parameter was calculated based on the intercept and slope obtained from Figure 2 in McClure, et al. (1980).

Part B

The constant $\tau_{X,j}$ is time constant which compares the initiation, elongation, and abortive constant as shown below.

$$\tau_{X,j} = \frac{k_A + k_E}{k_I}$$

Assuming that the abortive constant is negligibly small, then the time constant is a ratio between the elongation constant and initiation constant:

$$\tau_{X,j} = \frac{k_E}{k_I}$$

Using parameters determined from BioNumbers, this was determined to be:

$$\tau_{X,j} = 0.220$$

Since τ is less than one, transcription is elongation limited.

Part C

The following mass balance for the mRNA concentration was given:

$$\frac{dm_j}{dt} = r_{x,j} u_j(I) - (k^d_{x,j} - \mu) m_j$$

where the utility function u_j is a function of the inducer concentration:

$$u_j = \frac{W_1 + W_2 f_I}{1 + W_1 + W_2 f_I}$$

$$f_I = \frac{I^n}{K + I^n}$$

Using the given parameters and the steady state assumption for mRNA concentrations, the following equation was derived and plotted against inducer concentration:

$$m_j = \frac{r_{x,j} u_j}{k^d_{x,j} + \mu}$$

Please see HW1.jl file for actual plot.