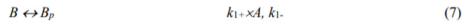
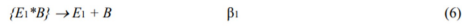
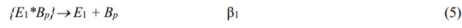
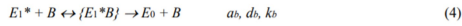
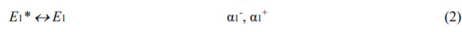
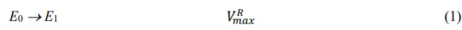


- Consider only two methylation states ($m=0, 1$).
- Allow only the $m=1$ state to be activated (i.e., set $\alpha_0^+ = 0$).
- Allow methylation to be zeroth order.
- Include the deactivation paths mediated by B and B_p (B acting as an "inhibitor").

Then the mass action kinetics are given by:



The simulated reference system (figure 3) had $M=2$ methylation sites ($m=0, 1, 2$) and the following parameters: $a_r = 0.2 \text{ s}^{-1} \cdot \mu\text{M}^{-1}$, $d_r = 0.1 \text{ s}^{-1}$ and $k_r = 0.1 \text{ s}^{-1}$, $a_b = 1 \text{ s}^{-1} \cdot \text{nM}^{-1}$, $d_b = 1 \text{ s}^{-1}$, $k_b = 0$, $a_{bp} = 0.1 \text{ s}^{-1} \cdot \text{nM}^{-1}$, $d_{bp} = 0.01 \text{ s}^{-1}$, $k_{bp} = 1 \text{ s}^{-1}$, $k_+ = 1 \text{ s}^{-1} \cdot \mu\text{M}^{-1}$, $k_- = 1 \text{ s}^{-1}$, $\alpha_0^+ = 10 \text{ s}^{-1}$, $\alpha_1^+ = 1/(1+\ell) \text{ s}^{-1}$, $\alpha_2^+ = 0$, $\alpha_0^- = 0$, $\alpha_1^- = \ell/(1+\ell) \text{ s}^{-1}$, $\alpha_2^- = 10 \text{ s}^{-1}$, $\beta_0 = 0$, $\beta_1 = 2.5\ell/(1+\ell) \text{ s}^{-1}$, and $\beta_2 = 25 \text{ s}^{-1}$. The concentration of receptors, CheR and CheB are $10 \mu\text{M}$, $0.2 \mu\text{M}$ and $2 \mu\text{M}$.

a) Express the balances in (a) as a series of ODEs for the seven species: $E_0, E_1, E_1^*, B, B_p, \{E_1^* B\}, \{E_1^* B_p\}$.

b) Using the parameter values (p. 877 of Barkai et al., 2001), justify the zeroth order approximation for methylation, give an expression for this rate, and find its numerical value for this rate.

Balances

$$E_0: \frac{dE_0}{dt} = -V_{max}^R + [E_1^* B_p] k_{bp} + [E_1^* B] k_b$$

$$E_1: \frac{dE_1}{dt} = V_{max}^R + E_1^* \alpha_1^- - E_1 \alpha_1^+ + [E_1^* B_p] \beta_1 + [E_1^* B] \beta_1$$

$$E_1^*: \frac{dE_1^*}{dt} = E_1 \alpha_1^+ - E_1^* \alpha_1^- - (E_1^*) (B_p) a_{bp} + [E_1^* B_p] d_{bp} - (E_1^*) (B) a_b + [E_1^* B] d_b$$

$$B: \frac{dB}{dt} = -(E_1^*) (B) a_b + [E_1^* B] d_b + [E_1^* B] k_b + [E_1^* B] \beta_1 - B \cdot k_{1+} \cdot E_1^* + B_p k_{1-}$$

$$B_p: \frac{dB_p}{dt} = -(E_1^*) (B_p) a_{bp} + [E_1^* B_p] d_{bp} + [E_1^* B_p] k_{bp} + [E_1^* B_p] \beta_1 + B \cdot k_{1+} \cdot E_1^* - B_p k_{1-}$$

$$[E_1^* B]: \frac{d[E_1^* B]}{dt} = (E_1^*) (B) a_b - [E_1^* B] d_b - [E_1^* B] k_b - [E_1^* B] \beta_1$$

$$[E_1^* B_p]: \frac{d[E_1^* B_p]}{dt} = (E_1^*) (B_p) a_{bp} - [E_1^* B_p] d_{bp} - [E_1^* B_p] k_{bp} - [E_1^* B_p] \beta_1$$

Methylation

methylation is most accurately described with m-m kinetics:

$$\frac{dE_{m+1}}{dt} = \frac{k_r (R) (E_m)}{\frac{k_r + d_r}{a_r} + (E_m)}$$

This expression can be simplified to the V_{\max} equation, based on the observation that $a_r \gg (K_r + \delta r)$, so $\frac{K_r + \delta r}{a_r} + E_m \approx E_m$

→

$$\frac{\delta E_{m+1}}{\delta t} \approx \frac{K_r(R) (E_m)}{(E_m)} = K_r(R)$$

therefore $V_{\max}^R = K_r(R) = (0.15^{-1}) (0.2 \mu M) = 20 nM \cdot s^{-1}$