Organizational remarks

Tomorrow recitation 10/17/07 topic
‘PS #2 Support’

Office Hours M 4 – 6 PM, Rm. 68-377

PS#2 due R 10/18/07 (< 3 PM)

Main points of last 2 lectures:

L9: Biological background
what is the function of the individual molecules?

L10: modeling of all possible chemotactic reactions
why doesn’t this model reproduce experimentally observed perfect adaptation?

L10-L11: strip down full model to essentials based on assumptions that are experimentally justified (or sometimes not)
**First reduction**

\[
\alpha \equiv \frac{[3]}{[2]+[3]}
\]

in steady state:

\[
k_{\text{phos}} = (1-\alpha) k_{\text{eff1}}(L) + \alpha k_{\text{eff2}}(L)
\]

fine-tune: net phosphorylation rate and \( k_{\text{eff1}} \) and \( k_{\text{eff2}} \) so that \( \alpha \) falls in safe zone

**Second reduction**

additional assumption:
- CheB only demethylates phosphorylated receptors

experimental backup:
- not possible to directly measure if CheB demethylates only active receptors
- rate of methylation drops immediately after addition of ligand indicates that CheB works on active receptors
Third reduction:

**additional assumption:**
- $[\text{CheR}] < [\text{receptors}]$,
- methylation operates at saturation ($r_{in}$ is independent of receptor concentrations)

**experimental backup:**
- Michaelis constant of CheR binding $<< [\text{receptors}]$
  - so $R_{tot} \sim R_{bnd}$

Fourth reduction:

**additional assumption:**
- demethylation is identical for bound and unbound receptors, so $k_{eff4}$ is independent of $L$.

**experimental backup:**
- kinetics of demethylation almost independent of level of methylation and ligand binding.

This final module obeys perfect adaptation for any value of $L$.

$\left[ \frac{3}{p} \right] = \frac{2r_{in}}{k_{eff4}}$

**Stability Analysis:**

$\dot{C} = -(k_{pt} - k_{eff4})C^* + k_{eff2}C + r_{in}$

This circuit is asymptotically stable when:

$\frac{a}{b} \leq c$
Nullclines:

\[
\begin{align*}
\dot{x} &= 0 \\
\dot{y} &= 0
\end{align*}
\]

\[
\begin{align*}
y &= \frac{-r_{in} - a}{b} x = \frac{-r_{in} + k_{pt} + k_{eff4} a}{k_{eff2} b} x \\
y &= \frac{-r_{in} - c}{d} x = \frac{r_{in} + k_{pt} - k_{eff2} a}{k_{eff2}} x
\end{align*}
\]

fixed point (stable or unstable?)

\[
\begin{align*}
(x^*, y^*) &= \left( \frac{2r_{in}}{k_{eff4}}, \frac{r_{in} k_{eff4} + r_{in} k_{pt}}{k_{eff4} k_{eff2}(L)} \right) \\
\dot{x} &= -(k_{pt} + k_{eff4}) x + k_{eff2} y + r_{in} \\
\dot{y} &= k_{pt} x - k_{eff2} y + r_{in}
\end{align*}
\]

increased ligand concentration
Dynamical response of switches, chemotactic network and oscillators

two stable fixed points
one stable fixed point
unstable fixed point

nullclines:
\[
\begin{align*}
    \frac{du}{dt} &= \frac{\alpha_1}{1 + v^\beta} - u \\
    \frac{dv}{dt} &= \frac{\alpha_2}{1 + u} - v
\end{align*}
\]
Adaptation (one stable fixed point)

\[(x^*, y^*) = \left( \frac{2r_{in}}{k_{eff}^4}, \frac{r_{in}k_{eff}^4 + 2r_{in}k_{pt}}{k_{eff}^4 k_{eff}^4 (L)} \right) \]

\[
\dot{x} = -(k_{pt} + k_{eff}^4)x + k_{eff}^2 y + r_{in} \\
\dot{y} = k_{pt} x - k_{eff}^2 y + r_{in}
\]

increased ligand concentration

\[(x^*, y^*) = \left( \frac{2r_{in}}{k_{eff}^4}, \frac{r_{in}k_{eff}^4 + 2r_{in}k_{pt}}{k_{eff}^4 k_{eff}^4 (L)} \right) \]

Oscillator (unstable fixed point)

\[
\dot{x} = -(k_{pt} + k_{eff}^4)x + k_{eff}^2 y + r_{in} \\
\dot{y} = k_{pt} x - k_{eff}^2 y + r_{in}
\]

\[
\dot{x} > 0, \quad \dot{y} < 0 \\
\dot{x} < 0, \quad \dot{y} > 0
\]