lec12.tex

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chapters 1-4 in uri alon's book "An introduction to systems biology. "

1 last lecture

–Feed forward loops (FFL)
x promotes y promotes z and x promotes z
x -¿ y -¿ z & x-¿z
(called a delay element)
– GRNs (gene regulatory networks)
S1, !2, ..., Sn
the layer separating the Signals from the genes (about 4500) is the transcirtion factors.
most common regulatory motif: auto-regulation, x -¿ x or x -— x
pro's
shorter respons times
good for homeostasis (can keep itself on a reasonable level)

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \beta f(x) - \alpha x \tag{1}$$

$$x(t_{1/2}) = \frac{\bar{x}}{2} \tag{2}$$

simple reg. : $t_{1/2} = \frac{\ln 2}{\alpha}$
self repression :

$$f(x) = \left(\frac{k}{x}\right)^2 \tag{3}$$

$t_{1/2} = [h = 1] = 0.2\frac{\ln 2}{\alpha}$
you should know this for exam: calc half times and response times

2 FFL

x-¿y-¿z and x-¿z

$$y(t) = \bar{y}(1 - e^{-\alpha t}) \tag{4}$$

where

$$\bar{y} = \frac{\beta_y}{\alpha_y} \tag{5}$$

add or subtract Y_0 in some way to get the appropriate behavior as $t \leftarrow \infty$.

prob of binding is associated with a binding const. K_{yz}. In order to have enough binding of $y*$, we must hace a concentration above a threshold level. this causes a delay in the production of z. the same is not true for x, we assume the productino of $x*$ is instantaneous.

effective response time for z is now response time plus delay, so $T_{ON} + \frac{\ln 2}{\alpha}$

we are assuming z behaves as an AND gate here.

now y is repressing z:

x-¿y-—z and x-¿z

z starts growing immediately and then backs down. Called pulse.

easy to calc delay time T_{ON}.

$$y * (t = TON) = k_{yz} \tag{6}$$

gives

$$TON = \frac{1}{\alpha_y} \ln\left(\frac{1}{1 - \frac{k_y z}{\bar{y}}}\right) \tag{7}$$

size of $k_y z$ is micromolar (??) $\frac{k_y z}{\bar{y}} \approx 1/3 \cdot 1/10$

Exam q: given a GRN, how does x affect z or what is the response time of z.

3 Feedback loops, FBL

4 Types of regulatory links

pretty obvious in the previous example.

Two main link types. The first is basically the previous:

i) binding to promotors. ex :

ii) small molecules binding to proteins and protein-protein binding. ex:

example of ii), the lac-operon.

when there's no lactose: lecrep blocks transcription of lac Z/Y/A.

lactose present: =¿ allo-lactose present =¿ lacrep falls off

this R-E-S system in fig 9 is a very common regulatory motif, e.g. metabolic regulation, stress-response systems.

4.1 Model R-E-S system

$$\begin{aligned} \frac{\mathrm{d}E}{\mathrm{d}t} &= \beta_E f(R) - \alpha_E E \\ \frac{\mathrm{d}S}{\mathrm{d}t} &= \beta_S - \gamma_{ES} E S \end{aligned} \tag{8}$$

wherre R is "free R", not bound,

$$\frac{R_{free}}{k_{ER} + R_{free}} \tag{9}$$

R + S forms a complex RS. with

$$\frac{RS}{R_{tot}} = \frac{k_{RS}}{k_{RS} + S} \tag{10}$$

$$R\frac{k_{RS}}{k_{RS} + S} = \#R\text{not bound by S} \tag{11}$$

heat-shoch response: when heat goes up in cell, they produce chaperone proteins that untwist proteins to avoid protein aggregates. This follows a similar regulation network.

common test for parkinsons : heat up e.coli, let cells divide and all the aggregates will be pushed to one side, collecting all aggregates in one cell .