lec2.tex

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1 Repetition of lec1

In networks we have an adjacency matrix describing the conections between genes.

State od e.coli iis the concentration of all proteins expressed by the 4500 genes.

Polypeptide chain - aka protein

Transcription Factors regulate the gene expression (Promotor or repressor) TFs have an active and inactive form, the signals from environmant change the TF from inactive to active, starting regulation.

2 Transcription

2.1 3 state Hawley-McClure model

The rate of transcription varies by several orders of magnitude. Varies from secinds to minutes.

PNAS (1980)

-Initiation frequencies vary by a lot. (we know this from both in vivo and in vitro experiments (in silico means in simulation))

Some of these variations depend on RNAp-DNA interactions.

- Old model: DNA + RNAp in a "closed complex" New model: DNA + RNAp in an "open complex"

- Two possible rate limiting steps: –(1)Binding –(2) opening of the "DNA bubble" (open complex)

He wanted to find out which is which

McClure's big breakthrough was managing to measure the binding and opening of the DNA separately, that way they could figure out which one was limiting.

He designed an in vitro experiment where he could study (1) and (2) independently.

He didn't supply enough nucleotides (boulding blocks of RNA & DNA), didnt have all 4 base pairs. Then it produced lots of small pieces of RNa, then he measured those.

He had a solution with DNA + promoter + RNAp + nucleotides (not all) + ATP.

This led to lots of abotions and re-initiations

-¿ many small mRNAs

see fig.2.8 in book

2.2 3 state Hawley-McClure model of transription

see fig. 2.7, p. 26

(1) binding

binding constant

$$k = \frac{k_u}{k_b} \tag{1}$$

[concentration, M]

(2) closed complex

when it's bound, it's in this closed complex

(3) open complex

this is a non equilibrium process from (2) to (3), ignore the step back

then transcription starts, "elongation". $k_e \approx 30$ bp/s

Goal: relate τ to all rates k_o, k_u, k_b, k_e.

θ_c = prob. to be in closed complex θ_o = prob. to be in open complex

$$\frac{\mathrm{d}\theta_o}{\mathrm{d}t} = \theta_c k_o - k_e \theta_o \tag{2}$$

$$\frac{\mathrm{d}\theta_c}{\mathrm{d}t} = (\text{prob that the prom. free}) \cdot k_b[RNAp] - k_u\theta_c - k_o\theta_o \tag{3}$$

$$\frac{\mathrm{d}[RNAp]}{\mathrm{d}t} = \theta_o k_e \approx \bar{\theta_o} k_e \tag{4}$$

analyze these eqs in steady state,

$$\frac{\mathrm{d}\theta_c}{\mathrm{d}t} = \frac{\mathrm{d}\theta_o}{\mathrm{d}t} = 0 \tag{5}$$

$$[RNAp](t) \approx \bar{\theta_o} k_e \equiv \frac{t}{\tau} \tag{6}$$

solve for $\bar{\theta}_o$ and $\bar{\theta}_o$

$$\tau = \frac{1}{\bar{\theta}_o k_e} = \frac{1}{k_e} + \frac{1}{k_o} + \frac{1}{k_b RNAp}(1 - \frac{k_u}{k_o}) \tag{7}$$

bar denotes steady state

from Mcclures exp $k_o \approx .001 - .1/s$, $\frac{k_u}{k_b} \approx 1nM - 1\mu M$

2.3 Gene regulation - lac repressor (operon)

Humans have an operatror site for each gene that controls expression.

Bacteria have *Operons*, that are operator sites that can regulate several genes.