Homework-3

Name: Ritu Kumari
Roll No.: 2016078

1.Answer- a) ODE study for negative regulation of tryptophan producing enzymes upon trpR binding with tryptophan molecules :

Let M = [mRNA],
E = [concentration of the enzyme produced by the operon genes]
T = [tryptophan] // [ ] denotes concentration

Then, we have-

$dM/dt = 1/(1+T^n) - \alpha M$

$dE/dt = M - \beta E$

$dT/dt = E - \gamma T$

The positive Hill constant n specifies the strength of the repression. The constants α, β, and γ are all positive and account for dilution by growth and enzymatic degradation. The parameter $\gamma > 0$ includes both of these effects as well as end product consumption.

Answer- b) ODE study incorporating transcriptional regulation of trpR :
Rate of decrease of repressor is proportional to the tryptophan level, i.e.
Let R=[repressor], t_r = [tryptophan]. Then we can write -

$$dR/dt = -k_r t_r$$

=> $$dt_r/dt = k - (k_d + k')t_r$$

Taking $k_d + k' = k''$, we have $dt_r/dt = k - k''t_r$

$$\int_{tr0}^{tr} dt_r / k-k''t_r = \int_0^t dt$$

$$-1/k'' = \ln((k-k''t_r) / (k-k''t_{r0})) = t$$

$$t_r = (k - k''(1 - t_{r0})e^{-k''t})/ k''$$

Using $k_d + k' = k''$ and differentiating ln(dr/dt), we have -

$$dr/dt = [-k_r(k - (k_d + k')(1 - t_{r0})e^{-(kd + k')t})] / (k_d + k')$$

Answer-c) Biological significance of the gene regulatory circuit that modulates the level of tryptophan inside a cell is vital to allow a cell to produce the gene products it needs when it needs them; in turn this gives cells the flexibility to adapt to a variable environment, external signals, damage to the cell etc. The cell can properly simulate its functions in order to produce tryptophan, thus ensuring proper usage of its energy.

Answer-(Challenge Problem)
The apo-repressor is activated by Trp (co-repressor). This process constitutes binding of two co-repressor molecules to two independent binding sites with identical affinities.
Let R=TrpR, T=Tryptophan. Then we have -

$$R + T \ {}^{2k0}\rightleftharpoons_{k1} \ RT$$

$$RT + T \ {}^{k0}\rightleftharpoons_{2k1} \ RT_2$$

The factor 2 multiplying with the constants k_0 and k_1 accounts for the fact that there are two identical and independent sites for Trp binding. So we have -

$$d[RT]/dt = -2k_0[R][T] + k_1[RT]$$

$$d[RT_2]/dt = -k_0 [RT][T] + 2k_1[RT_2]$$

References: PNAS 79: 3120-3124 (1982), PNAS 98:1364-1369 (2001)