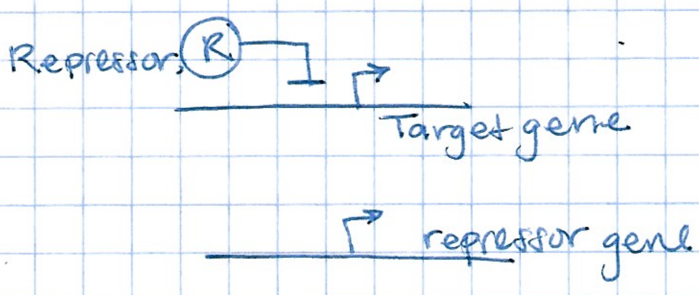
MODELING REPRESSORS AND ACTIVATOR WITH HILL FUNCTIONS

RECALL OUR TRANSCRIPTIONAL REPRESSOR SYSTEM



IF THE REPRESSOR GENE INHIBITS ITS OWN EXPRESSION THEN IT'S THE NEGATIVE AUTOREGULATION SYSTEM WE MODELED PREVIOUSLY.

FOR THE REPRESSOR

$$\frac{dm_r}{dt} = \alpha_m - \beta_m m_r$$

$$\frac{dp_r}{dt} = \alpha_p - \beta_p m_r$$

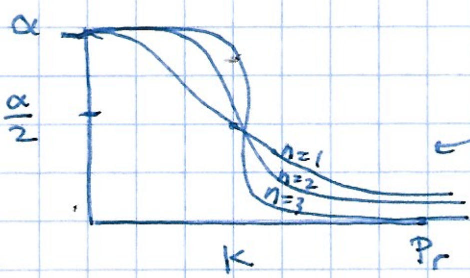
FOR THE TARGET GENE WE WILL CHOOSE TO MODEL GENE REGULATION BY THE REPRESSOR AS A HILL FUNCTION.

A. HILL FUNCTION

$$f(P_r) = \alpha_m \frac{1}{1 + (P_r/K)^n} + \alpha_0$$

repression

α_0 → BASAL EXPRESSION



n = HILL COEFFICIENT OFTEN CORRESPONDS TO "COOPERATIVITY" OR # OF MOLECULES THAT BIND (e.g.: REPRESSOR → PROMOTOR)

IF p → dimer $n=2$

p → tetramer $n=4$

NOTE: RESPONSE BECOMES MORE SWITCH-LIKE OR DIGITAL AS n INCREASES

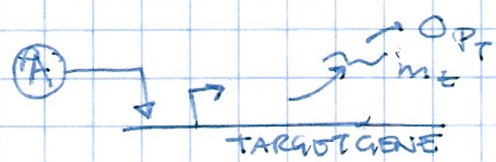
TARGET GENE

B. $$\frac{dm_t}{dt} = \left(\alpha_0 + \alpha_m \frac{1}{1+(P_r/K)^n}\right) - \beta m_t$$

$$\frac{dp_t}{dt} = \alpha_p m_t - \beta_p P_t$$

SEE MATLAB SCRIPTS FOR REPRESSOR

TRANSCRIPTIONAL ACTIVATOR CONTROLLING GENE EXPRESSION



$P_A \rightarrow P_T$

ACTIVATOR (P_A) INDUCES EXPRESSION OF THE TARGET GENE

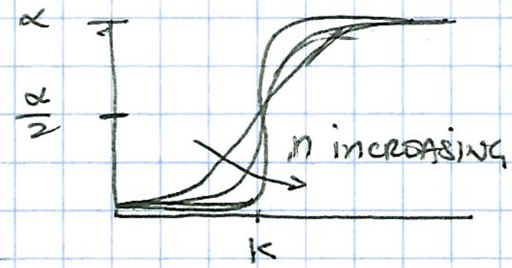
THE ACTIVATOR CAN BE MODELED AS SIMPLE CONSTITUTIVE EXPRESSION.

FOR THE TARGET

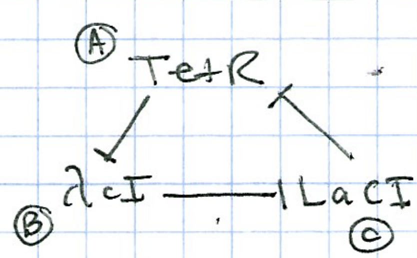
$$\frac{dm_t}{dt} = \alpha_0 + \alpha_m \frac{\left(\frac{P_a}{K}\right)^n}{1 + \left(P_a/K\right)^n} - \beta_m m_t$$

$$\frac{dP_t}{dt} = \alpha_p m_t + \beta_p P_t$$

HILL FUNCTION OF ACTIVATOR



CONNECTED REPRESSOR → REPRESSILATOR



ELOWITZ. NATURE 2000

A 3-RING SYSTEM OF REPRESSORS

SEE MATLAB CODE

SEE MATLAB FILES FOR REPRESSILATOR