Enzymology: recalls

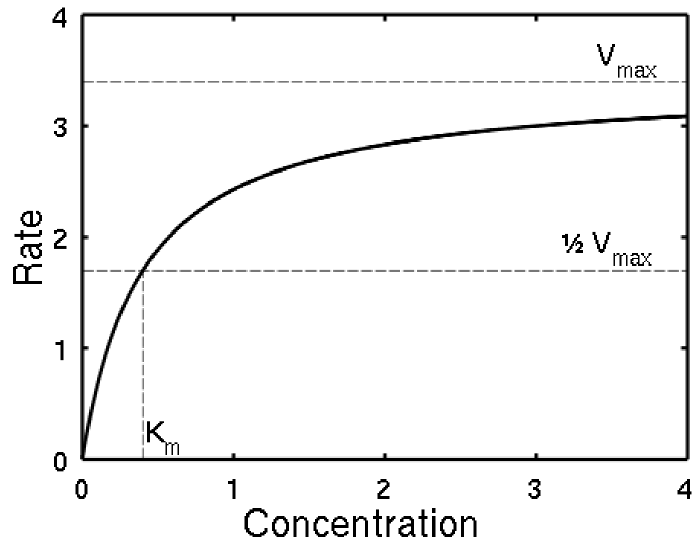
Michaelis-Menten kinetics

The model is an equation describing the rate of enzymatic reactions when the reaction is catalyzed by one enzyme acting on an unique substrate to give a product.

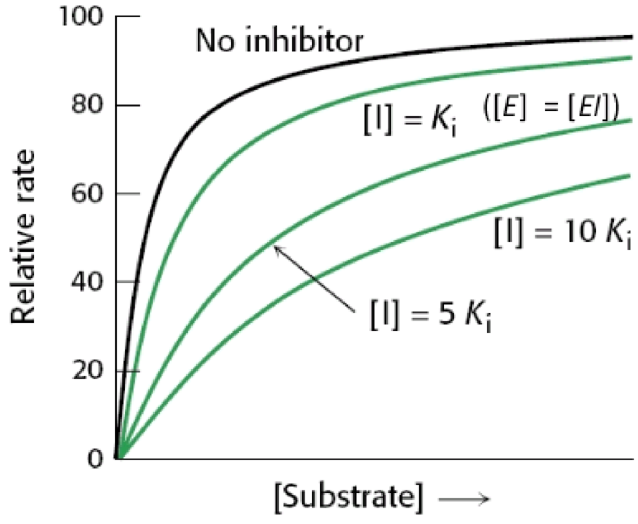
$$E + S \underset{k_{-1}}{\overset{k1}{\rightleftharpoons}} ES \overset{k_2}{\rightarrow} E + P$$

$$\frac{dP}{dt} = v_{\max} \frac{[S]}{K_m + [S]}$$

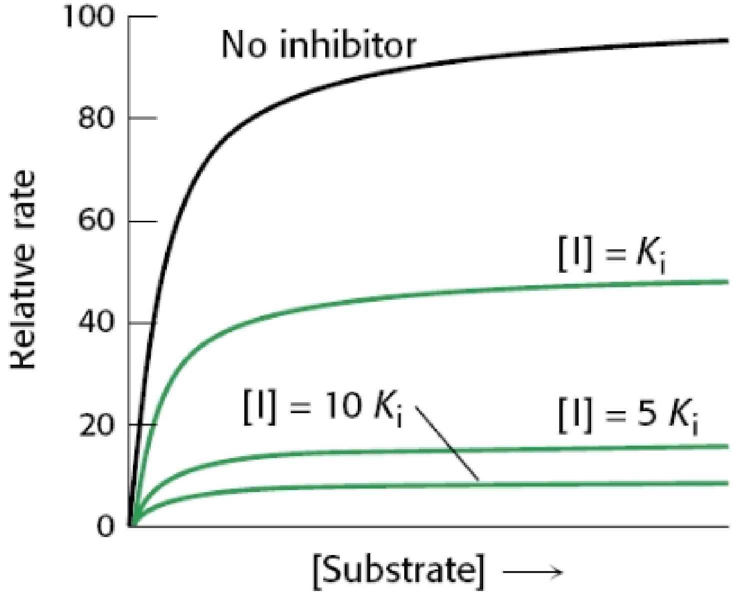
Where *P* is the product, *S* the substrate, v_{max} is the maximal synthesis rate of *P* and K_m is the required concentration of *S* for half-maximal synthesis rate ($v_{max}/2$)



Competitive inhibition



Non competitive inhibition

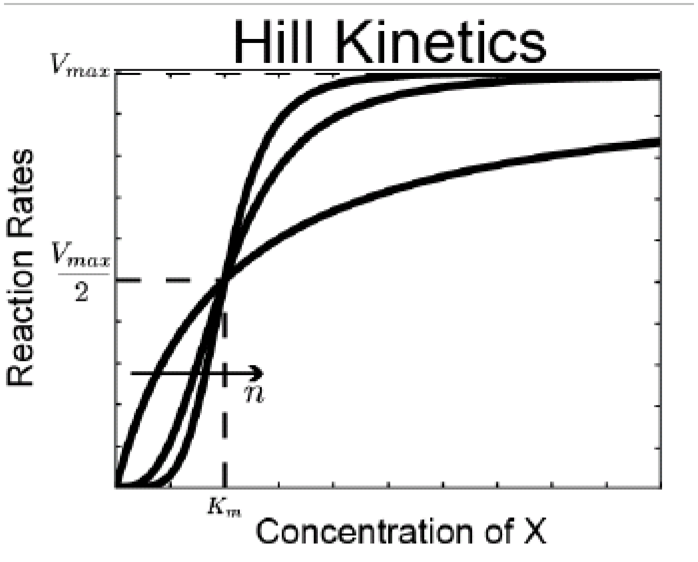


Hill function - Hill kinetics - Cooperativity

Many proteins have more than one binding site for their interaction partners. Binding of the first ligand may alter the bonding characteristics of all binding sites.

$$\frac{dP}{dt} = v_{\max} \frac{[X]^n}{K^n + [X]^n}$$

K is the Hill constant = concentration of X at which the reaction proceeds as half its maximum speed.
n is the Hill coefficient. The greater is *n*, the steeper is the response



The Hill coefficient comes from the fact that transcription factors can act as multimeres which leads to cooperative behaviour. Typical values for *n* are 1−4

Hill function – transcriptional regulator

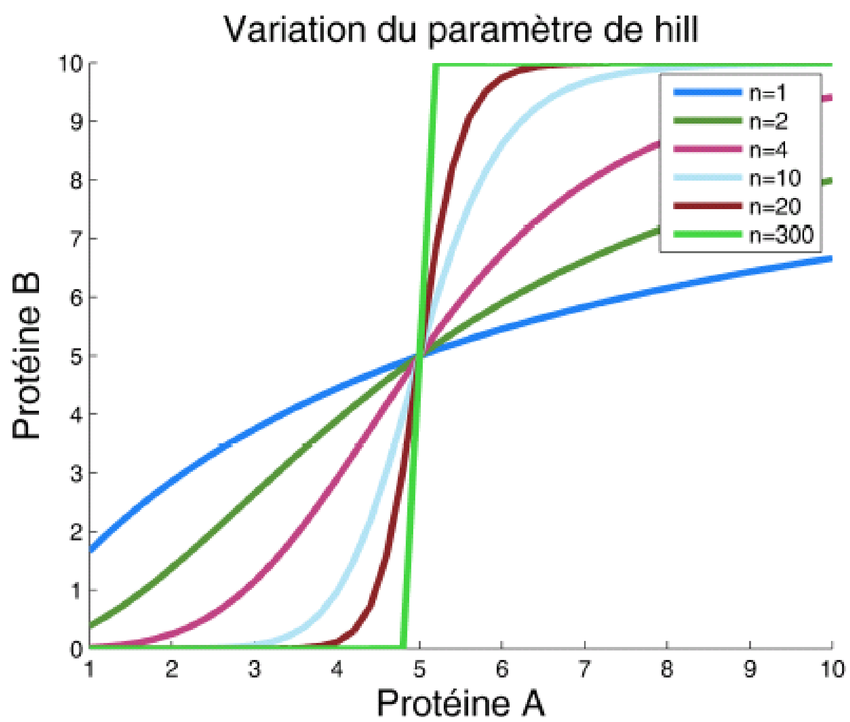
Case : rate of production of a protein Y controlled by a single transcription factor X

The strength of the effect of the transcription factor on the transcription rate of its target gene is described by an **input function.** In our case, the number of proteins *Y* produced per unit time is a function of the concentration of *X* under its active form X^*. The input function $f(X^*)$ is a monotonic, S-shaped function. A useful function that describes many real gene input functions is the Hill function.
For an activator, the Hill function is a curve that rises from 0 and approaches a maximal saturated level. It is given by:

$$\frac{d[Y]}{dt} = f(X^*) = \frac{\beta_{\max}\left[X^*\right]^n}{K^n + \left[X^*\right]^n}$$

With β_{max} is maximal transcription rate of the promoter-transcription factor complex
X^* is the concentration of the active form of X
K is the activation coefficient, i.e., the required concentration of X* to reach the half-maximal expression ($\beta_{max}/2$)
and n is the Hill coefficient that governs the steepness of the curve, the higher n, the more step-like the input function. This coefficient comes from the fact the transcription factors can act as multimeres which leads to cooperative behaviour. Typical values for n are 1−4

Hill function – transcriptional regulator



When *n* = 1-> equation of Michaelis and Menten
When *n* increases, the curve becomes a sigmoid
When *n* -> ∞, the curve becomes a step function

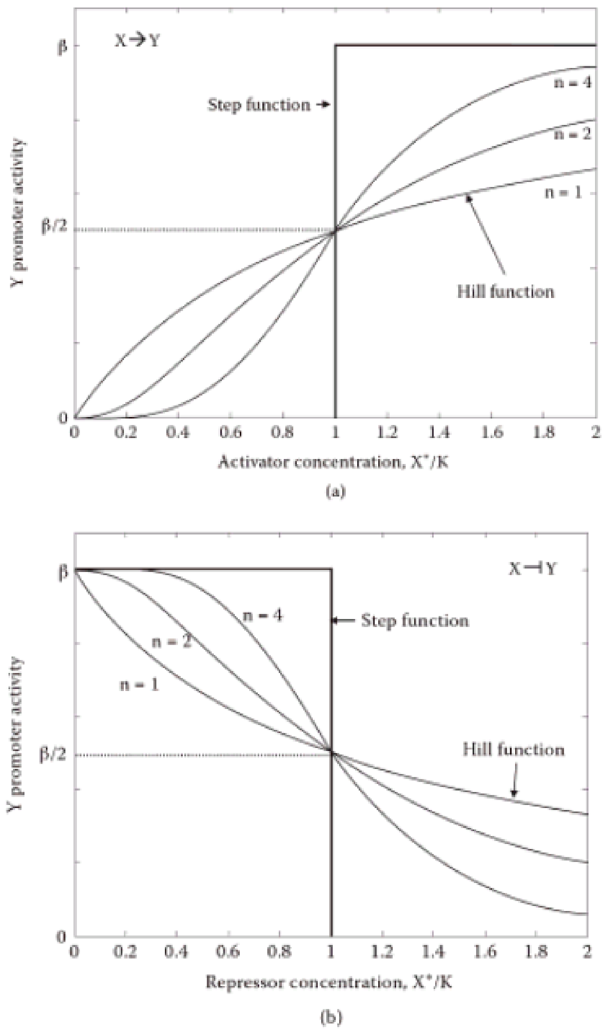
Hill function – transcriptional regulator

For repressors the Hill function decreases with the concentration of active repressor X^*. It is a decreasing S-shaped curve:

$$\frac{d[Y]}{dt} = f(X^*) = \frac{\beta_{\max}}{1 + \left(\frac{[X^*]}{K}\right)^n}$$

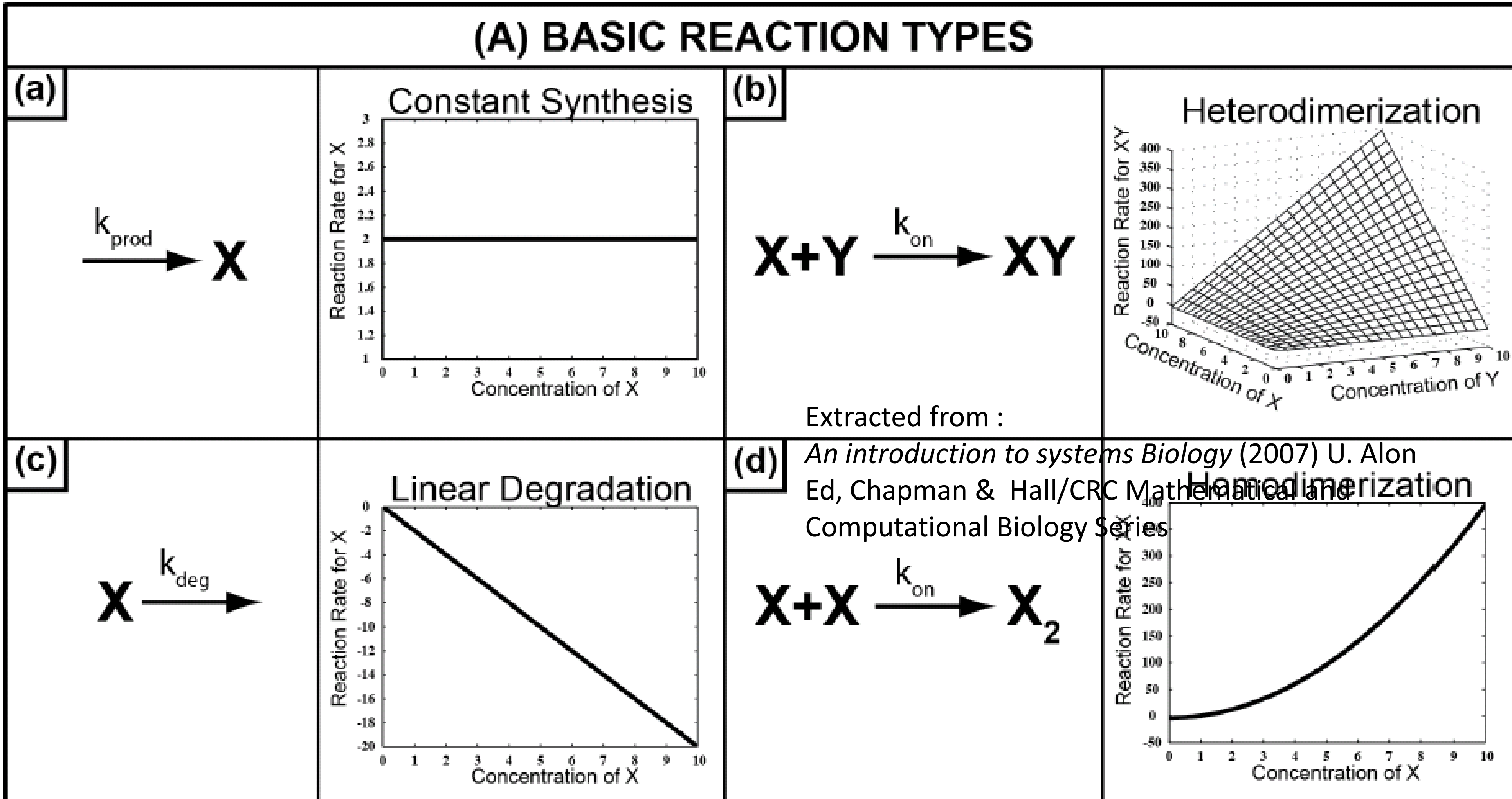
The maximal production rate β_{max} is obtained when $X^* = 0$ (no repressor). Half-maximal repression is reached when the concentration of X^* is equal to K. K is the repression coefficient. Again, the Hill coefficient n determines the steepness of the curve.

Hill function – transcriptional regulator



FIGu r E 2.4 (a) Input functions for activator X described by Hill functions with Hill coefficient n = 1, 2, and 4. Promoter activity is plotted as a function of the concentration of X in its active form (X*). Also shown is a step function, also called a logic input function. The maximal promoter activity is β, and K is the threshold for activation of a target gene (the concentration of X* needed for 50% maximal activation). (b) Input functions for repressor X described by Hill functions with Hill coefficient n = 1, 2, and 4. Also shown is the corresponding logic input function (step function). The maximal unrepressed promoter activity is β, and K is the threshold for repression of a target gene (the concentration of X* needed for 50% maximal repression).

Extracted from :
An introduction to systems Biology (2007) U. Alon Ed, Chapman & Hall/CRC Mathematical and Computational Biology Series



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Extracted from a chapter book from Iber and Fengos: *Predictive models for cellular signaling networks*