MRI Master Class 2009/2010:
Numerical Bifurcation Analysis of Dynamical Systems
WEEK 13, Mar 30 and Apr 01: Willy Govaerts (Gent)
"Mathematical evolution models in the life sciences"

Elements of modelling

Chapter 1

The Hill function

The Hill function
$$H(n,T,x)=\frac{x^n}{T^n+x^n}$$
($T>0$, $n\geq 1$, $x\geq 0$) is a monotone function that maps $[0,\infty[$ onto $[0,1[$. The parameter T is called the threshold, the parameter n is called the Hill coefficient.

In some applications, this function is used to approximate the Heaviside function
$$H_T(x)=\begin{cases} = & 0 \text{ if } x<T\\ = & 1 \text{ of } x\geq T\end{cases}$$
by a smooth function. This approximation is best for large n since n determines the steepness of $H(n,T,x)$ for $x=T$.

On the other hand, the Hill function has some biochemical basis as well. In the case $n=1$ it appears naturally in the Michaelis-Menten equation. In the case where n is an integer value larger than 1 it appears in cooperative bindings and therefore n is often called a cooperativity coefficient. We now explain this.

In some cases a protein (E) is active only if a number n of its sites are bound to activating ligands (S) to form the complex nSE. These ligands can bind independently from each other. If for simplicity we take $n=2$ then we get the reaction equations
$$E+S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SE \tag{1.1}$$
$$SE+S \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} 2SE \tag{1.2}$$
Now if both these reactions attain an equilibrium, then by the law of mass action we must have
$$k_1[E][S]=k_{-1}[SE], k_2[SE][S]=k_{-2}[2SE],$$
and so
$$[2SE]=\frac{k_1k_2}{k_{-1}k_{-2}}[E][S]^2.$$
Clearly we also have
$$[E]+[SE]+[2SE]=E_0,$$

where E_0 is the initial concentration of protein E. Now in some cases the bindings cooperate, in the sense that once a site is bound, then the other sites bound much faster. Then we expect that at the end $[SE]$ is negligible and so we have

$$[2SE] = \frac{k_1 k_2}{k_{-1} k_{-2}}(E_0 - [2SE])[S]^2.$$

Solving this for $[2SE]$ we obtain

$$[2SE] = E_0 \frac{[S]^2}{T^2 + [S]^2},$$

where

$$T^2 = \frac{k_{-1} k_{-2}}{k_1 k_2}.$$

Chapter 2

Degradation rate and average life span.

Suppose that the size of a population $N(t)$ satisfies the equation

$$\frac{dN(t)}{dt} = -\alpha N(t),$$

where α is called the degradation rate. Prove that the average life span of a member of the population is $\frac{1}{\alpha}$ and that the half-life time $t_{\frac{1}{2}}$ when the population is halved, is given by $t_{\frac{1}{2}} = \frac{\ln 2}{\alpha}$.

Hint. Let the initial value be given by $N(0) = N_0$. Then at time t the population size is $N_0 e^{-\alpha t}$. The average life span is given by the limit of

$$\frac{\Delta_1 t_1 + \Delta_2 t_2 + \ldots + \Delta_n t_n}{\Delta_1 + \Delta_2 + \ldots + \Delta_n},$$

where $N_0 e^{-\alpha t_1} \in [N_0 - \Delta_1, N_0]$, $N_0 e^{-\alpha t_2} \in [N_0 - \Delta_1 - \Delta_2, N_0 - \Delta_1]$ etcetera and $\Delta_1 + \ldots + \Delta_n = N_0$, the limit being taken for $|\Delta| = \sup_i \Delta_i \to 0$. This is clearly equal to $\frac{A}{N_0}$ where A is the surface of the area under the curve $N_0 e^{-\alpha t}$ for $t \in [0, \infty]$. Hence the average life span is

$$\frac{\int_0^\infty N_0 e^{-\alpha t} dt}{N_0} = \frac{1}{\alpha}[-e^{-\alpha t}]_0^\infty = \frac{1}{\alpha}.$$

The thalf-life time $t_{\frac{1}{2}}$ is determined by the equation

$$N_0 e^{-\alpha t_{\frac{1}{2}}} = \frac{1}{2} N_0,$$

which implies

$$\alpha t_{\frac{1}{2}} = \ln 2.$$