Mathematical physiology

PROBLEM SHEET 1.

1. Carrier-mediated transport of a substrate S by a carrier protein C is modelled as the (rapid) reaction system

$$S_i + C_i \underset{k_-}{\overset{k_+}{\rightleftharpoons}} P_i \underset{k}{\overset{k}{\rightleftharpoons}} P_e \underset{k_+}{\overset{k_-}{\rightleftharpoons}} S_e + C_e,$$

$$C_i \underset{k}{\overset{k}{\rightleftharpoons}} C_e.$$

Explain the meaning of these reactions. If a substrate flux J is supplied to the extra-cellular fluid and thus also (in a steady state) to the intra-cellular fluid, use steady state kinetics to show that

$$J = \frac{K^*(S_e - S_i)}{(K_m + S_i)(K_m + S_e) - K_d^2}, \quad K_m = \frac{k_- + k}{k_+}, \quad K_d = \frac{k}{k_+},$$

where K^* should be defined.

2. A membrane channel has N identical gates. If S_i is the proportion of channels with i open gates, write down rate equations for S_i in terms of the overall reaction rates R_i of $S_{i-1} \rightleftharpoons S_i$, $i = 1, 2, \ldots, N$. Derive a conservation law expressing the conservation of the total number of channels.

Suppose that

$$S_j = {}^N C_j n^j (1-n)^{N-j},$$

where ${}^N C_j$ is the binomial coefficient. Show that the equations are satisfied if

$$\dot{n} = \alpha(1-n) - \beta n, \quad (*)$$

where α and β are the gate opening and closing rates.

For the case $N = 2$, show that all initial states tend to this solution (*put* $S_0 = (1-n)^2 + y_0$, $S_2 = n^2 + y_2$, *where* n *satisfies* $(*)$, *and show that* $y_0, y_2 \to 0$.)

3. Suppose a membrane channel has three gates, two of which are controlled by a protein M, and the other is controlled by a protein H. Suppose that the fractions of open M and H gates are m and h respectively. By letting S_{ij} denote the density of channels with i open M-gates and j open H-gates, write down the rate equations for S_{ij}, assuming that the rates of M-gate opening and closing are α and β, and the rates of H-gate opening and closing are γ and δ, respectively.

Show that the equations have solutions in which $S_{00} = (1-m)^2(1-h)$, etc., providing m and h satisfy equations which you should find. [*There is no need to be exhaustive.*]