

Assignment 7 Hodgkin Huxley Rate Functions

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Problem 1: Parameterizing Chemical Kinetics Classical chemical kinetics describes the transformation of a substance A into a substance B with forward rate constant k_f and backward rate constant k_b . Hodgkin and Huxley re-interpreted these rate constants as functions dependent on membrane voltage V_m : $\alpha(V_m)$ and $\beta(V_m)$, so their form of kinetics is:



Hodgkin Huxley modified this so that the forward and backward constants, which they called $\alpha(V_m)$ and $\beta(V_m)$, and are explicitly dependent on membrane voltage V_m .



The reverse reaction B turns back into A at the rate $\beta(V_m)$ moles per second.



The first order ordinary differential equation (ODE) for this system is Thus, the “standard” ODE for this system is

$$-\frac{dA}{dt} = \alpha A - \beta B \quad (0.4)$$

In other words, the “loss” of A is given by the forward production of A into B minus the backproduction of A from B .

Hodgkin and Huxley rewrite this scheme in terms of variables n^o (permissive state of gate variable n) and n^c (non-permissive state of gate variable n).

Lets call A by HH’s name n^c and B by n^o .

$$-\frac{dn^c}{dt} = \alpha n^c - \beta n^o \quad (0.5)$$

So, the Hodgkin Huxley idea is summarized as:

$$n^c \xrightleftharpoons[\beta(V_m)]{\alpha(V_m)} n^o \quad (0.6)$$

They were able to relate these hypothetical channels (e.g. n^{open} to observed values of membrane conductivity by separating the ion currents for sodium and potassium. They did this by making clamped voltage steps from resting potential V_r to a clamp voltage V_c , and assumed a specific form for the channel conductivities: $g_K = \bar{g}_K n^4$ and $g_{Na} = \bar{g}_{Na} m^3 h$. n^{open}, n^{closed} , interpreted as probabilities, are normalized as $n^{open} + n^{closed} = 1$

1. Rewrite the ODE describing the transformation of n^{closed} into n^{open} in an equation that only involves only n^{open} by using the normalization condition:

$$\frac{dn^o}{dt} = \alpha - (\alpha + \beta)n^o = (\alpha + \beta) * \left(\frac{\alpha}{\alpha + \beta} - n^o \right) \quad (0.7)$$

2. Since this is a first order ODE we expect an exponential solution in the form of $x = c_1 \exp^{-t/\tau} + c_2$. Show that the constant $c_2 = 0$, that the time constant $\tau(V_c) = \frac{1}{\alpha(V_c) + \beta(V_c)}$, and the constant $c_1 = n_0(V_c) - n_\infty(V_c)$, where n_∞ is the steady state value of n where $\frac{dn}{dt} = 0$ and n_0 is the initial value of $n(V_r)$, and so the solution is

$$n(V_c, t) = n_\infty(V_c) - (n_\infty(V_c) - n_0(V_c))e^{-\frac{t}{\tau(V_c)}} \quad (0.8)$$

3. Explain briefly how Hodgkin and Huxley were able to separately measure J_K and J_{Na} .

Computational study of the channel variables On the homework site, I've placed two matlab functions: alpha.m and beta.m. These represent the fits that Hodgkin and Huxley came up with in their kinetic model to reproduce their observations of the channel variables n, m, h . Write matlab code that plots out the values of $\alpha(V_c)$ and $\beta(V_c)$ and also τ and n_∞ . for each of the channels, using the functions supplied on the homework site for α and β .

Note: Here is some code to get started:

```
Vr = -65; Temp = 6.3; Cm = 1e-3;
```

Note that Cm is given in milliFarad units (You won't need Cm at the moment though). The motivation is that if time is given in milliseconds, voltage in millivolts, capacity in millifarads, current in milliamps and resistance or conductance in milliohms or millisiemens, then you can work directly in these "milli SI" units. An alternative is to convert everything to standard SI, but this is a bit of a savings when coding.

A good choice of voltage range is

```
nvsamples = 250; u = linspace(-100,50,nvsamples);
```

Also note that the alpha and beta functions are supplied with a parameter V_r and $Temp$. The reason is that original form of the functions HH fitted were based on a resting potential of zero. So, the functions were parameterized in terms of $V_r = 0$ (and $Temp$) but we would like to use the modern convention that V_r is, for example, $-65mV$. So, you should set a global Vr and Temp in your calling routine like

```
global Vr,Temp
```

This allows you to pass $V_r = -65mV$ to the functions I supplied without putting them in the call as function parameters, so we can plot everything with respect to the modern convention that resting potential is $-65mV$, but still use the HH functions, which were fit assuming $V_r = 0$. In this simple case, you could have just done that and avoided the global, but it when we expand the scope of this code, it will be increasingly easier to follow this approach.