Reduction of conductance-based neuron models

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Abstract. We present a scheme for systematically reducing the number of differential equations required for biophysically realistic neuron models. The techniques are general, are designed to be applicable to a large set of such models and retain in the reduced system as high a degree of fidelity to the original system as possible. As examples, we provide reductions of the Hodgkin-Huxley system and the A-current model of Connor et al. (1977).

1 Introduction

Computational neuroscientists always face a difficult task in choosing the kind of model with which to approach a given problem. On the one hand are conductance-based models such as those epitomized by the seminal work of Hodgkin and Huxley (1952) that seek to reproduce physiological data with mathematical representations that can provide insight into the underlying biophysical mechanisms. The difficulty of developing and analyzing this kind of model has increased, as we now know that many neurons contain a large number of different voltage-dependent conductances (e.g., Yamada et al. 1989; Buchholtz et al. 1992; Golowasch et al. 1992). On the other hand we have abstract models such as those used by McCulloch and Pitts (1943); Hopfield (1982); FitzHugh (1961); and Lapicque (1907), which are mathematically and conceptually simple, although their parameters may bear no direct relationship to those of biological neurons. Indeed, despite the attractiveness of simple neuronal "caricatures" care must be exerted lest one is drawn to unwarranted conclusions based on the behavior of these abstract models.

Our aim is to provide methods that allow us to start with data-derived conductance-based models of the Hodgkin-Huxley type, and reduce these to the simplicity of neuronal caricatures while preserving a direct relationship between the parameters measured experimentally and the parameters in the simpler neuronal caricature. This will allow the modeler to use the simpler form for analysis without losing the ability to relate the results of the analysis to the currents that produced the model.

We present a change of variables and perturbation analysis that provide a power-series approximation of the original system whose leading term is a reduced system with fewer differential equations. There are basically two techniques. One, based on singular perturbation theory, is the elimination of "fast" variables by combining them with the membrane potential to form a single variable. The second technique is the combination of variables evolving on similar time scales and having similar effects.

Previous reduction schemes for the Hodgkin-Huxley system (HH) have exploited the rapidity of sodium current activation to eliminate the sodium activation as a dynamic variable. Our analysis goes one step further by including higher-order effects of this reduction. The similar time scales of the sodium inactivation h and potassium activation n have been used to combine h and n into a single "recovery" variable. Our treatment of these techniques is intended to improve upon prior work (FitzHugh 1961; Krinskii and Kozok 1973; Hindmarsh and Rose 1982; Rinzel 1985; Rose and Hindmarsh 1989) in two ways. First, we enhance the fidelity to the original system as much as possible, and second, we provide a systematic "recipe" which may be applied to any system with the appropriate characteristics.

In order to provide concrete examples of our method we will use HH, and a modification of HH to which the A current has been added (Connor et al. 1977). These reductions will be used to illustrate the advantages conferred by a visualizable configuration space in the analysis of several familiar phenomena.

2 Equivalent potentials

Dynamical systems that describe isopotential excitable neural membranes typically consist of two parts. The first is a differential equation expressing current conservation
Fig. 1. Behavior of the Hodgkin-Huxley (HH) dynamical variables exhibiting repetitive spiking behavior during application of a ramped depolarizing external current. For the sake of comparison, the HH system used here is as modified by Connor et al. (1977). The models called “HH” have \( g_A = 0 \) and the leak reversal potential is adjusted to give a resting potential of \(-68 \) mV.

\[
C \frac{dV}{dt} + I(V, \{x_i\}) = I_{\text{external}}(t)
\]

where \( V \) is the membrane potential, \( C \) is the membrane capacitance and \( I(V, \{x_i\}) \) is the total ionic current expressed as a function of \( V \) and the gating variables \( x_i \). Each member of the system of equations describing the dynamics of these gating variables has the form

\[
\frac{dx_i}{dt} = k_i(V)[\bar{x}_i(V) - x_i].
\]

providing the balance of the system’s description. In the HH system, for example, the gating variables are the sodium activation variable \( m \), the sodium inactivation variable \( h \), and the potassium activation variable \( n \). In this system, the current \( I(V, m, h, n) \) is

\[
I(V, m, h, n) = g_{\text{Na}} m^3 h (V - E_{\text{Na}}) + g_K n^4 (V - E_K) + g_{\text{leak}} (V - E_{\text{leak}})
\]

where \( g_{\text{carrier}} \) is the maximum conductance for that carrier, and \( E_{\text{carrier}} \) is its reversal potential. Figure 1 shows repetitive firing of the HH system under ramped current injection. We have plotted \( V, m, h \) and \( n \) each against time. To combine different variables together for the purpose of reduction, it helps to make them dimensionally equivalent. The membrane potential is ubiquitous in this system, entering the equations for each of the other variables, providing the sole link between these degrees of freedom and is, moreover, the sole mediator of external information to the system. This suggests that all the other variables might profitably be converted to equivalent potentials, defined for each of the gating variables as the potential \( v_i \) which makes \( \bar{x}_i(v_i) = x_i \):

\[
v_i = \bar{x}_i^{-1}(x_i)
\]

where the exponent \(-1\) refers to the functional inverse. In other words, the equivalent potential is the voltage which, in voltage clamp, would give the value \( x_i \) to the \( i \)th gating variable after equilibrium is reached. Note that equivalent potentials provide as complete and valid a description of the system as the gating variables. The equilibrium (and hence static) relationship used to define them does not compromise their dynamic variability in any way. The transformation requires that the functions \( \bar{x} \) are invertible. The class of models that we are considering does not include those that contain calcium-dependent conductances, since in these, some of the \( \bar{x} \) depend both on the membrane potential and on the calcium concentration. Further work may be required to reduce those variables that depend on the calcium concentration.

The chain rule may be applied to give us new equations of motion expressed in terms of the equivalent potentials:

\[
C \frac{dV}{dt} + F(V, \{v_i\}) = I_{\text{external}}(t)
\]

where

\[
F(V, \{v_i\}) = I(V, \{\bar{x}_i(v_i)\}),
\]

and

\[
\frac{dv_i}{dt} = \frac{k_i(V)}{\bar{x}_i(v_i)} [\bar{x}_i(V) - \bar{x}_i(v_i)]
\]

and the prime denotes differentiation. Note that for these variables, all of the surfaces on which the time derivatives of (1) vanish (its nullclines) are simply hypersurfaces given by \( v_i = V \), so that at equilibrium all of the equivalent potentials equal the (true) membrane potential. The only non-trivial nullcline is that for the current conservation equation. No approximations have yet been made; the new system is entirely equivalent to the original.

The evolution of the whole HH system expressed in equivalent potentials is shown in Fig. 2. The transformation to equivalent potentials reveals that of the four available degrees of freedom, only two are effectively utilized: \( v_m \) is nearly indistinguishable from \( V \); likewise with \( v_h \) and \( v_n \). The motions of the system within the four-dimensional configuration space are largely confined to a two-dimensional submanifold. Moreover we have at hand a convenient way of locating this manifold and formulating the appropriate dynamics on equivalent potentials.