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Chaos in the Hodgkin–Huxley Model[*]

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Abstract. The Hodgkin–Huxley model was developed to characterize the action potential of a squid axon. It has served as an archetype for compartmental models of the electrophysiology of biological membranes. Thus the dynamics of the Hodgkin–Huxley model have been extensively studied both with a view to their biological implications and as a test bed for numerical methods that can be applied to more complex models. This note demonstrates previously unobserved dynamics in the Hodgkin–Huxley model, namely, the existence of chaotic solutions in the model with its original parameters. The solutions are found by displaying rectangles in a cross-section whose images under the return map produce a Smale horseshoe. The chaotic solutions are highly unstable, but they are significant as they lie in the basin boundary that establishes the threshold of the system.

Key words. Hodgkin–Huxley, chaos, action potential, horseshoe

AMS subject classifications. 92C20, 37G35

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1. Introduction.

The Hodgkin–Huxley model [15] for the action potential of a space-clamped squid axon is defined by the four dimensional vector field

$$\begin{aligned}
\dot{v} &= I - \Big[120m^3h\,(v+115) + 36n^4\,(v-12) + 0.3\,(v+10.599)\Big],\\
\dot{m} &= (1-m)\,\Psi\left(\frac{v+25}{10}\right) - m\left(4\exp\frac{v}{18}\right),\\
\dot{n} &= (1-n)\,0.1\Psi\left(\frac{v+10}{10}\right) - n\left(0.125\exp\frac{v}{80}\right),\\
\dot{h} &= (1-h)\,0.07\exp\left(\frac{v}{20}\right) - \frac{h}{1+\exp\frac{v+30}{10}},\\
\Psi(x) &= \frac{x}{\exp(x)-1}
\end{aligned}$$

with variables (v, m, n, h) that represent membrane potential, activation of a sodium current, activation of a potassium current, and inactivation of the sodium current and a parameter I that represents injected current into the space-clamped axon. Recall that the Hodgkin–Huxley convention for membrane potential reverses the sign from modern conventions, and so the voltage spikes of action potentials are negative in the Hodgkin–Huxley model. While improved models for the membrane potential of the squid axon [3] have been formulated, the Hodgkin–Huxley model remains the paradigm for conductance-based models of neural

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systems. From a mathematical viewpoint, varied properties of the dynamics of the Hodgkin–Huxley vector field have been studied [13, 8, 11, 14, 16, 19, 5]. Nonetheless, we remain far from a comprehensive understanding of the dynamics displayed by this vector field. It has become conventional wisdom that the qualitative properties of the Hodgkin–Huxley model can be reduced to a two dimensional flow such as the Fitzhugh–Nagumo model [7]. Rinzel and Miller [19] first gave evidence that this is not always the case. Hassard [13] and Labouriau [16] also studied the Hopf bifurcation that plays an important role in locating regions of bistability in the Hodgkin–Huxley model. Doi and Kumagai [5] recently showed the existence of chaotic attractors in a modified Hodgkin–Huxley model that changes the time constant of one of the currents by a factor of 100. This note extends the work of Rinzel and Miller, demonstrating the existence of chaotic solutions in the Hodgkin–Huxley model with the "standard" parameters used by Hodgkin and Huxley.

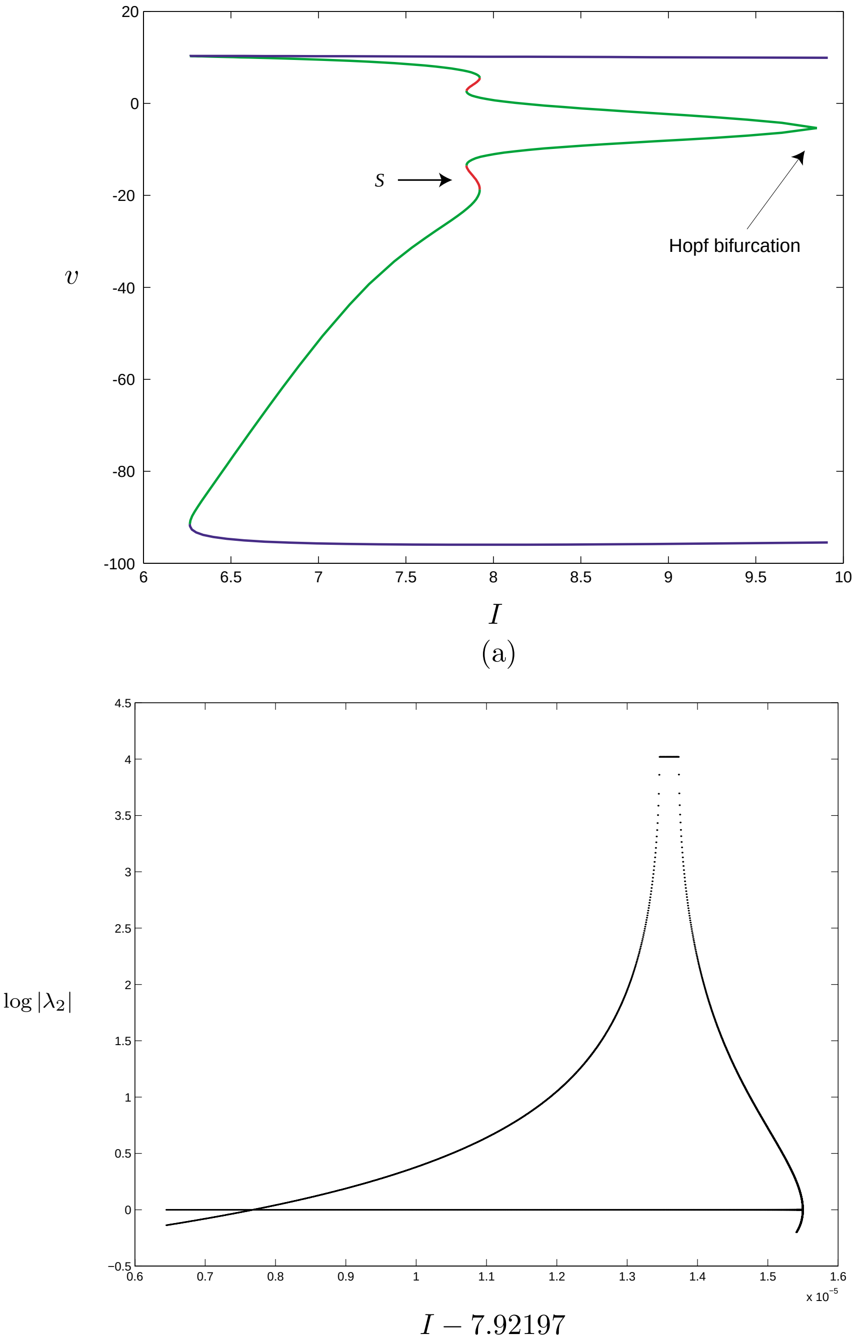
Extensive efforts have been made to discover chaos in many physical and biological systems, including neural systems [2]. Chaotic solutions to the Hodgkin–Huxley equations with periodic forcing [1] and greatly altered parameters [5] have been discovered but not in the original Hodgkin–Huxley model with its original parameters. The chaotic solutions we exhibit are highly unstable. We employed systematic methods to find them as described below. Note that, while we find our numerical evidence for the existence of chaos in the Hodgkin–Huxley model compelling, we do not give a rigorous proof that chaos exists in this system. The biological significance of chaos in the Hodgkin–Huxley system is related to the character of the threshold that separates states leading to repetitive firing from states that lead to a stable steady state. We return to this issue at the end of this note. (The implications of long-time unpredictability in deterministic chaotic systems have been widely discussed in a broad context by Stewart [21].)

2. Evidence for chaos in the Hodgkin–Huxley system.

A stringent definition of chaos in a discrete dynamical system is that there is an invariant subset on which the transformation is hyperbolic and topologically equivalent to a subshift of finite type [10, 20]. Continuous time dynamical systems are reduced to discrete time maps through the introduction of cross-sections and Poincaré return maps [10]. We utilize the cross-section V given by a suitably chosen value $v = -4.5$ to define a Poincaré return map f for the Hodgkin–Huxley model. Specifically, $(\bar{m}, \bar{n}, \bar{h}) = f(m, n, h)$ if the trajectory beginning at $(-4.5, m, n, h)$ next intersects the cross-section V (with v increasing) at the point $(-4.5, \bar{m}, \bar{n}, \bar{h})$. To demonstrate that f has a chaotic invariant set, we follow the strategy described by Moser [18]. We find two subsets R_1 and R_2 of V and approximate splittings of the tangent bundles into stable and unstable directions on these sets so that the following hold:

1. The derivative of f maps expanding directions close to themselves, stretching the lengths of these vectors.
2. The sets $f(R_1)$ and $f(R_2)$ each intersect R_1 and R_2 so that their images stretch across R_1 and R_2 in the unstable directions and intersect the boundaries of R_1 and R_2 only on sets transverse to the unstable directions.

Using the more precise concept of invariant cone fields, Moser proved that a map f satisfying these properties has a "Smale horseshoe," a hyperbolic invariant set on which f is topologically equivalent to the shift on two symbols.



(a)

(b)

Figure 2.1. (a) *The amplitude of periodic orbits in the Hodgkin–Huxley model as a function of input current. Maximum and minimum values of* v *are plotted for each periodic orbit. Stable periodic orbits are shown in blue; those shown in green have a single positive unstable eigenvalue, while those shown in red have either two unstable eigenvalues or a negative unstable eigenvalue.* (b) *The magnitude of the second largest eigenvalue* λ_2 *of the return map for the periodic orbits along the vertical branch for a small interval centered at* $I = 7.92197$.

Table 2.1

	m	n	h
R_1	0.08510711565266	0.37702513977759	0.43770368051793
	0.08511751929147	0.37708261653418	0.43799786108786
	0.08506722811171	0.37702247883827	0.43770500525944
	0.08507763175053	0.37707995559486	0.43799918582936
	0.08506795096894	0.37673045670586	0.43526697935397
	0.08507180274587	0.37675541738823	0.43543828382985
	0.08502806342799	0.37672779576653	0.43526830409547
	0.08503191520493	0.37675275644891	0.43543960857136
R_2	0.08500054963158	0.37635307899354	0.43231650435083
	0.08500126298925	0.37635224747250	0.43225555564349
	0.08499057463645	0.37635239912448	0.43231667147632
	0.08499128799412	0.37635156760344	0.43225572276897
	0.08500090973955	0.37635423427118	0.43231211561955
	0.08500146426647	0.37635361157621	0.43226513798843
	0.08499093474442	0.37635355440212	0.43231228274504
	0.08499148927134	0.37635293170715	0.43226530511391

As a parameter of a dynamical system is varied, sets satisfying the above conditions are frequently created through the "period doubling route" to chaos [6]. Rinzel and Miller [19] located period doubling bifurcations in the Hodgkin–Huxley model by computing eigenvalues along a family of periodic orbits. As the parameter corresponding to external current is varied in the model, there is a Hopf bifurcation of steady states at $I \approx 9.78$. The bifurcation is subcritical, with a family of unstable periodic orbits collapsing to the equilibrium at the bifurcation. Beginning at this bifurcation, we followed the family of periodic orbits using continuation methods. Some of the observed phenomena along this family of periodic orbits are numerically sensitive, and so we used two continuation algorithms: a collocation method as implemented by Doedel in the program AUTO [4] and a multiple shooting method that employs Taylor series methods and automatic differentiation [12]. The results of the two methods agreed with one another qualitatively.

Figure 2.1(a) plots the amplitude of the periodic orbits, showing the maximum and minimum values of v for each orbit versus the parameter I for this family of periodic orbits. The color coding corresponds to the number of eigenvalues with magnitude larger than one (blue $= 0$, green $= 1$, red $= 2$ or 1 unstable negative and 1 stable negative). The orbits grow in amplitude as I decreases from its value at the Hopf bifurcation. The branch has three turning points, all of which are saddle-node (or fold) bifurcations of periodic orbits. The first two turning points reached from the Hopf bifurcation bound a short branch of periodic orbits with two unstable eigenvalues. At the third turning point, the periodic orbits meet a family of stable periodic orbits. The amplitude of the stable periodic orbits does not change much. On the (red) branch S of periodic orbits, there is a parameter interval near $I \approx 7.92197$ inside which the unstable eigenvalues of the periodic orbit change dramatically. Figure 2.1(b) plots the log of the magnitude of the real part of one of these eigenvalues. Along the flat portion at the top of this graph, the eigenvalue is complex. This allows the eigenvalue to become real

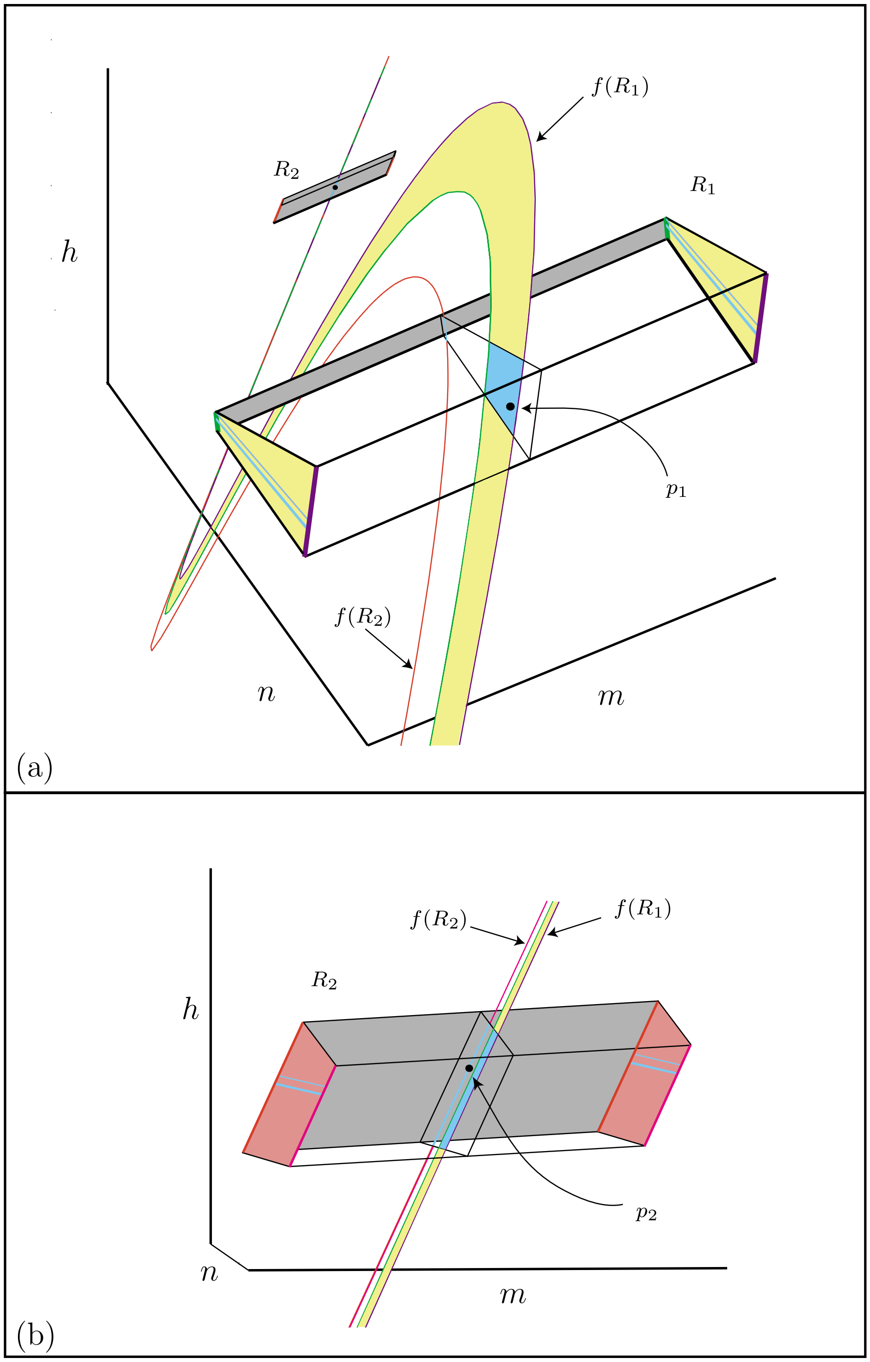


Figure 2.2. *Three dimensional boxes, and their images, which produce a horseshoe for the return map of the Hodgkin–Huxley model.* (a) *The ends of box* R_1 *transverse to the strong stable direction, and their images are shaded in yellow with the strips mapping into* R_1 *and* R_2 *shaded in light blue.* (b) *An expanded view of the region around* R_2*. The ends of box* R_2 *transverse to the strong stable direction, and their images are shaded in red with the strips mapping into* R_1 *and* R_2 *shaded in light blue.*

and negative without becoming stable along S. A period doubling bifurcation occurs on the part of S where the eigenvalue is negative and takes the value -1. We followed the doubled period orbits bifurcating from S and observed that they too undergo period doubling bifurcations. These computations suggest the existence of a period doubling cascade; we followed the cascade to its third period doubling. Nonetheless, these results prompted us to look for horseshoes in the return map f for values of I slightly larger than those at which the period doubling was found.

In the regime near the period doubling bifurcation, the periodic orbit of the family computed with continuation has a negative unstable characteristic multiplier, a negative stable characteristic multiplier, and a third positive characteristic multiplier of very small magnitude. We investigated these periodic orbits in more detail for the parameter $I = 7.8617827403$. The return map f has a fixed point p_1 at the intersection of the periodic orbit with the cross-section V. We find that

$$p_1 \approx (-4.5, 0.08508337639787, 0.37698374610906, 0.43727279295129).$$

The sets R_1 and R_2 of our construction intersect the unstable manifold of p_1 for the return map f. We found, as expected, that the unstable manifold has a bend. Starting in the unstable manifold, we used a shooting method to find a second fixed point of f:

$$p_2 \approx (-4.5, 0.08499590453730, 0.37635277095981, 0.43229451177364).$$

The unstable manifold of p_1 passes near p_2 and vice-versa. Near p_1, both unstable manifolds lie close to the plane of p_1 perpendicular to the strongly contracting eigenvector. To define R_1, we begin with two segments of the unstable manifolds of p_1 and p_2 near p_1. We enlarge the convex hull of these two segments in the plane perpendicular to the strongly contracting eigenvector of p_1 to form a quadrilateral. Finally, we construct a prism with this quadrilateral as base with edges parallel to the strongly contracting eigenvector of p_1. The set R_2 is obtained by an analogous procedure near p_2. Table 2.1 gives the coordinates of the vertices of R_1 and R_2. Figure 2.2 shows pictures of the sets R_1 and R_2 and their images under the return map f. (The scales of the coordinate axes in this figure are not uniform.) Each of $f(R_1)$ and $f(R_2)$ maps across both R_1 and R_2 in the unstable direction intersecting the boundaries of R_1 and R_2 in sets that are transverse to the unstable direction. These properties are evidence for the existence of a Smale horseshoe in V for the return map f.

3. Biological significance.

We turn now to the significance of these chaotic dynamics in the Hodgkin–Huxley model. The chaotic invariant set located above is a highly unstable structure associated with the "threshold" for action potentials. Action potentials of neurons are large all-or-nothing voltage spikes. We specify a minimum amplitude of voltage (say, $v = -50$) that must be reached to make the definition of action potential precise. In axons that are not space-clamped, like those represented by the Hodgkin–Huxley model, action potentials propagate along axons as traveling waves and stimulate synaptic currents in adjacent postsynaptic neurons. Threshold is the magnitude of an input that must be exceeded for an action potential to fire. This definition of threshold is based upon the assumption that there is a critical current input I_c above which the axon will fire an action potential when given a brief stimulus of magnitude I_c (with fixed duration) and below which it will not. The chaotic invariant set of the Hodgkin–Huxley model casts strong doubt on the validity of this assumption. It suggests that the boundary between initial states that lead to action potentials and those that do not is a fractal set. Related observations about fractal basin boundaries have been made for periodically forced neural models, for example, by Gong and Xu [9], but the firing of an action potential does not coincide with lying in one basin of attraction or another. There may be initial conditions leading to the firing of one or more action potentials followed by a decay in the quiescent equilibrium state.

The concept of threshold is rarely given a precise mathematical meaning, even in the context of models. We propose the following definition for the Hodgkin–Huxley model: $v = v_t(m, n, h)$ is a threshold function if initial states with $v > v_t(m, n, h)$ yield action potentials, while initial states with $v < v_t(m, n, h)$ do not produce action potentials. We conjecture that no such function exists over a small range of steady input currents, all other model parameters taking the values assigned by Hodgkin and Huxley. Note that this definition is formulated in terms of initial conditions of the model with fixed parameters. All of the trajectories that appear to have local minima near the cutoff $v = -50$ for action potentials tend rapidly to the stable periodic orbit on their next oscillation.

The membrane oscillations within the horseshoe are intermediate in amplitude between action potentials and the resting membrane potential of the axon. The stable branch of periodic solutions in Figure 2.1(a) displays that the minimum of the action potentials is in the range $[-100, -90]$ mv for a Hodgkin–Huxley model that fires repetitively. The resting membrane potential is near 0. (With now standard conventions for membrane potential, v should be replaced by $v_o - v$ for a value of $v_o \approx -55$ in the Hodgkin–Huxley model.) Figure 3.1(a) displays two periods of the oscillations of the periodic orbits through points p_1 (blue) and p_2 (red) and the stable periodic orbit (black). Figure 3.1(b) shows the projections of these periodic orbits onto the (v, h) plane. Other trajectories in the horseshoe oscillate in an irregular pattern but with amplitudes that are approximated by the amplitudes of the orbits through p_1 and p_2.

The stable manifolds of unstable, chaotic invariant sets often form fractal basin boundaries of attractors in a dynamical system [17]. We conjecture that this is the case in the Hodgkin–Huxley model for the parameters used in this study; namely, the basin boundary between the basins of attraction of the stable equilibrium and stable periodic orbit is a fractal set that contains the stable manifold of the chaotic invariant we have discovered. Similar observations about fractal basin boundaries have been made for periodically forced neural models—for example, in the Fitzhugh–Nagumo model by Gong and Xu [9]. Initial states that lead to the stable rest state and those that lead to the periodic firing state are interleaved. Instead of a single sheet given by the graph of the threshold function v_t, we expect an infinite number of layers that lead to action potentials interspersed with layers that lead to a stable steady state. The trajectories tending to the stable steady state may show a transition with oscillations of smaller amplitude than the action potentials. There are also uncountable sheets that lie at threshold in the sense that they lead neither to the stable rest state nor to fully formed action potentials, but every neighborhood contains states that lead to action potentials and states that lead to the stable steady state. Due to the stiffness of the model and the fine scales on which the fractals appear, numerical calculation of the fractal basin boundaries of the Hodgkin–Huxley model with its standard parameter values appears difficult.

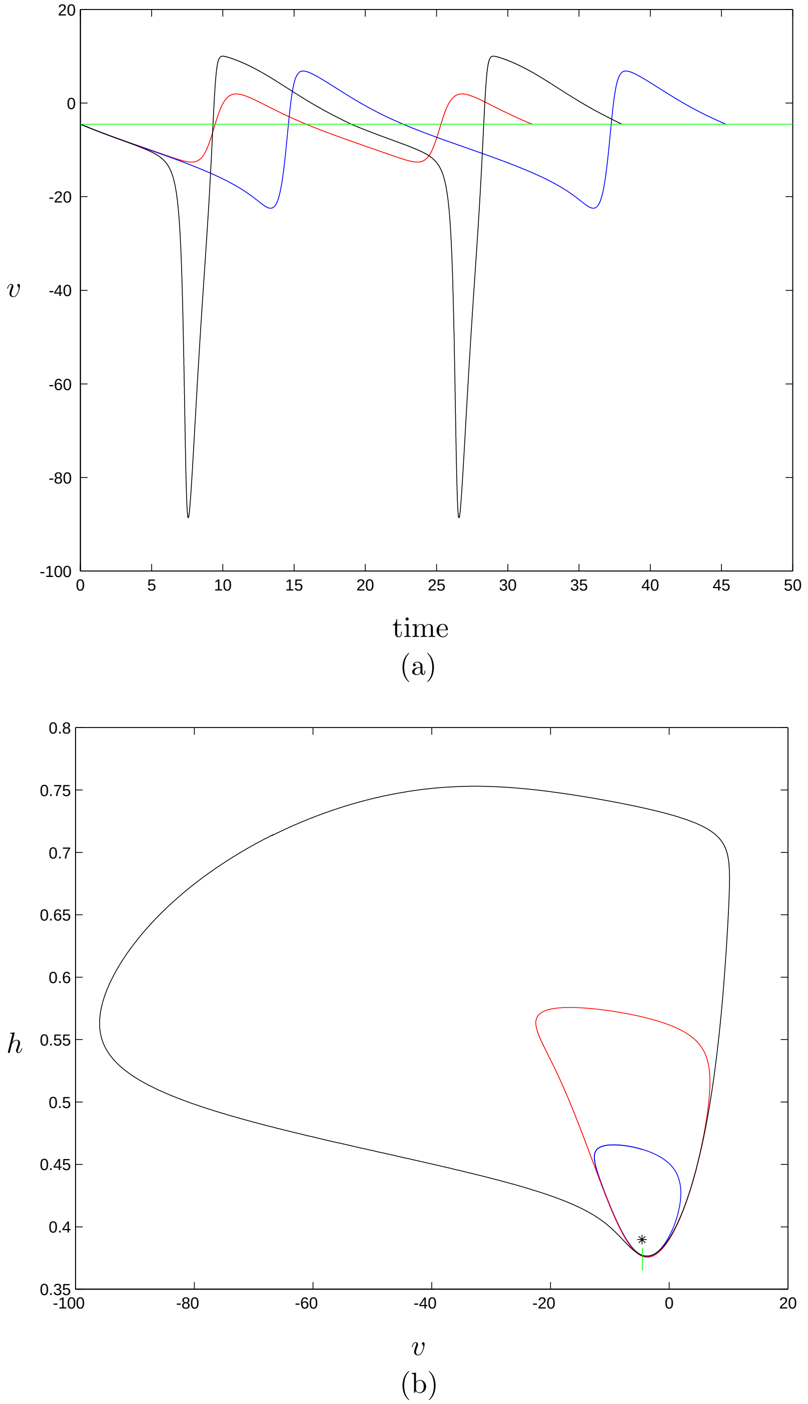


Figure 3.1. (a) *Two cycles of three periodic orbits of the Hodgkin–Huxley model with external current* $I = 14.2211827403$*. The stable periodic orbit is shown in black, and two unstable periodic orbits are shown in red and blue. The green horizontal line is at the value* $v = -4.5$ *of the cross-section used in our computations of a return map.* (b) *Projection of the three periodic orbits onto the* (v, h) *plane. The green segment is the cross-section used to obtain return maps.*

If our conjectural description of the phase space of the Hodgkin–Huxley model is correct, then there is a degree of unpredictability about how the system will respond to stimulation. Brief current inputs to the axon that evolve to the stable steady state and those that evolve to the firing state are finely interleaved with each other as the amplitude of the current input is varied. The nonlinear dynamics underlying action potentials yield an inherent lack of predictability in determining how large an input is required to cross the threshold for firing action potentials. Due to the extreme Lyapunov exponents associated to the chaotic invariant set, the fractal, interleaved structure of the membrane threshold is hardly observable in the Hodgkin–Huxley model even in computer simulation. Inherent noise in the membrane has a far larger scale than the fractal structure in the Hodgkin–Huxley model for its standard parameters. However, we believe that the phenomenon seen here on fine scales may well be present on larger scales in other neural systems or for different parameter values of the Hodgkin–Huxley model. The significance of our results is that they establish the subtlety of the concept of threshold: the excitability of a neural membrane to fire an action potential may be more complex than a smooth hypersurface that divides subthreshold and suprathreshold membrane potentials.

REFERENCES

[1] K. Aihara and G. Matsumoto, *Chaotic oscillations and bifurcations in squid giant axons*, in Chaos, A. Holden, ed., Manchester University Press, Manchester, UK, 1986, pp. 257–269.

[2] D. Campbell and H. Rose, eds., *Order in chaos*, Phys. D, 7 (1983), pp. 1–362.

[3] J. R. Clay, *Excitability of the squid giant axon revisited*, J. Neurophysiol., 80 (1998), pp. 903–913.

[4] E. Doedel, H. B. Keller, and J. P. Kernévez, *Numerical analysis and control of bifurcation problems* I, Internat. J. Bifur. Chaos Appl. Sci. Engrg., 1 (1991), pp. 493–520.

[5] S. Doi and S. Kumagai, *Nonlinear dynamics of small-scale biophysical neural networks*, in Biophysical Neural Networks, R. R. Poznanski, ed., Mary Ann Liebert, Inc., Larchmont, NY, 2001, pp. 261–301.

[6] J.-P. Eckmann, *Roads to turbulence in dissipative dynamical systems*, Rev. Modern Phys., 53 (1981), pp. 643–654.

[7] R. Fitzhugh, *Impulses and physiological states in models of nerve membrane*, Biophys. J., 1 (1961), pp. 445–466.

[8] H. Fukai, T. Nomura, S. Doi, and S. Sato, *Hopf bifurcations in multiple-parameter space of the Hodgkin-Huxley equations*, I, II, Biol. Cybern., 82 (2000), pp. 215–222; 223–229.

[9] P.-L. Gong and J.-X. Xu, *Global dynamics and stochastic resonance of the forced Fitzhgh-Nagumo neuron model*, Phys. Rev. E. (3), 63 (2001), pp. 1–10.

[10] J. Guckenheimer and P. Holmes, *Nonlinear Oscillations, Dynamical Systems, and Bifurcations of Vector Fields*, Springer-Verlag, New York, 1983.

[11] J. Guckenheimer and I. S. Labouriau, *Bifurcation of the Hodgkin–Huxley equations: A new twist*, Bull. Math. Biol., 55 (1993), pp. 937–952.

[12] J. Guckenheimer and B. Meloon, *Computing periodic orbits and their bifurcations with automatic differentiation*, SIAM J. Sci. Comput., 22 (2000), pp. 951–985.

[13] B. Hassard, *Bifurcation of periodic solutions of the Hodgkin-Huxley model for the squid giant axon*, J. Theoret. Biol., 71 (1978), pp. 401–420.

[14] B. Hassard and L.-J. Shiau, *A special point of Z_2-codimension three Hopf bifurcation in the Hodgkin-Huxley model*, Appl. Math. Lett., 9 (1996), pp. 31–34.

[15] A. L. Hodgkin and A. F. Huxley, *A quantitative description of membrane current and its applications to conduction and excitation in nerve*, J. Physiol. (Lond.), 116 (1952), pp. 500–544.

[16] I. S. Labouriau, *Degenerate Hopf bifurcation and nerve impulse* II, SIAM J. Math. Anal., 20 (1989), pp. 1–12.

[17] S. W. McDonald, C. Grebogi, E. Ott, and J. A. Yorke, *Fractal basin boundaries*, Phys. D, 17 (1985), pp. 125–153.

[18] J. Moser, *Stable and Random Motions in Dynamical Systems*, Princeton University Press, Princeton, NJ, 1973.

[19] J. Rinzel and R. Miller, *Numerical calculation of stable and unstable periodic solutions to the Hodgkin-Huxley equations*, Math. Biosci., 49 (1980), pp. 27–59.

[20] S. Smale, *Diffeomorphisms with many periodic points*, in Differential and Combinatorial Topology (A Symposium in Honor of Marston Morse), Princeton University Press, Princeton, NJ, 1965, pp. 63–80.

[21] I. N. Stewart, *Does God Play Dice?: The Mathematics of Chaos*, Basil Blackwell, Oxford, UK, 1989.