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FitzHugh–Nagumo Model

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Definition

The FitzHugh–Nagumo (FHN) model is a mathematical model of neuronal excitability developed by Richard FitzHugh as a reduction of the Hodgkin and Huxley's model of action potential generation in the squid giant axon (FitzHugh 1955). Nagumo et al. subsequently designed, implemented, and analyzed an equivalent electric circuit (Nagumo et al. 1962).

In its basic form, the model consists of two coupled, nonlinear ordinary differential equations, one of which describes the fast evolution of the neuronal membrane voltage, the other representing the slower "recovery" action of sodium channel deinactivation and potassium channel deactivation. Phase plane analysis of the FHN model provides qualitative explanations of several aspects of the excitability exhibited by the Hodgkin–Huxley (HH) model, including all-or-none spiking, excitation block, and the apparent absence of a firing threshold. A version of the FHN equations which adds a spatial diffusion term models the propagation of an action potential along an axon as a traveling wave. Due to their relative simplicity and ease of geometric analysis, the FHN model and its variants are commonly used in neuroscience, chemistry, physics, and other disciplines as simple models of excitable dynamics, relaxation oscillations, and reaction–diffusion wave propagation.

Detailed Description

Mathematical Model

FitzHugh constructed the FHN equations by slightly modifying the cubic Bonhoeffer–van der Pol model of relaxation oscillations. The original van der Pol equation is a second-order linear differential equation:

$$\ddot{V} + \left(V^2 - 1\right)\dot{V} + \phi V = 0, \tag{1}$$

which may be written as two first-order equations by applying the Lienard transformation: $W = -\dot{V} + V - V^3/3$:

$$\dot{V} = V - V^3/3 - W \tag{2a}$$

$$\dot{W} = \phi V. \tag{2b}$$

For all $\phi > 0$, the origin in system Eq. 2 is an unstable fixed point surrounded by a globally stable limit cycle. FitzHugh's modification to Eq. 2 added linear terms which shifted the fixed point and made it stable (FitzHugh 1955):

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$$\dot{V} = V - V^3/3 - W + \mathrm{I} \tag{3a}$$

$$\dot{W} = \phi(V + a - bW). \tag{3b}$$

Here a, b, and ϕ are positive constants; FitzHugh's original values were $a = 0.7$, $b = 0.8$, and $\phi = 0.08$.

The variable V is taken to represent the membrane potential of the neuron, the parameter I is the applied current, and W is a "recovery" variable which represents the combined effects of sodium channel deinactivation and potassium channel deactivation.

There is a separation of timescales between the two variables that is set by the parameter ϕ, normally taken to be much smaller than unity in order to produce relaxation oscillations. That is, the evolution of V, as determined by Eq. 3a, occurs on a timescale of order $O(1)$, and, following Eq. 3b, W evolves on a timescale of order $\phi \ll 1$ (except at transitions; see below). Hence, V and W are referred to as the *fast* and *slow* variables, respectively.

Nagumo's Circuit Model

Using an electric circuit that included a tunnel diode, Nagumo, Arimoto, and Yoshizawa qualitatively modeled a number of axonal behaviors (Nagumo et al. 1962). The circuit consists of a capacitor (representing membrane capacitance) and a tunnel diode (representing the nonlinear dynamics of the fast membrane current) in parallel with a resistor (representing channel resistance), an inductor, and a battery (these last three components being in series). The dynamics of the tunnel-diode circuit shown in Fig. 1 are described by the equations:

$$C\dot{V} = I - F(V) - W \tag{4a}$$

$$L\dot{W} = E - RW + V, \tag{4b}$$

where C is the circuit's capacitance, R is the circuit's resistance, E is the battery's potential, L is the circuit's inductance, and I is an applied current. The variable V represents the voltage drop across the entire circuit, and the variable W represents the current through the resistor–inductor–battery circuit branch.

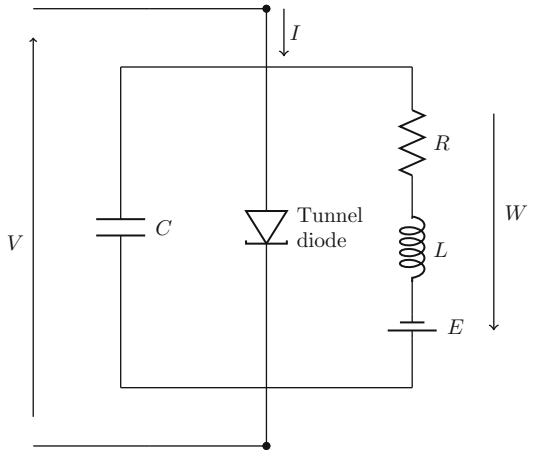

Fig. 1 Nagumo et al.'s electric circuit (Adapted from Nagumo et al. (1962))

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The $F(V)$ term expresses the current flowing through the tunnel diode as a function of voltage across it. When $F(V)$ is cubic, Eq. 4 may be easily transformed into Eq. 3; if R is eliminated from the circuit, one obtains the van der Pol Eq. 1. Thus FitzHugh's equations and Nagumo's circuit model are equivalent.

Phase Plane Analysis

The (fast) V-nullcline, given by

$$W = V - V^3/3 + I, \tag{5}$$

and the (slow) W-nullcline, given by

$$W = (V + a)/b, \tag{6}$$

are the phase plane structures which organize the FHN system's dynamics. The (left) local minimum and (right) local maximum of the cubic V-nullcline are typically referred to as its "knees." The knees divide the V-nullcline into three "branches," left, middle, and right.

The fixed point of the FHN system is located at the intersection of the nullclines. (Under conditions $1 - 2b/3 < a < 1$, $0 < b < 1$, and $b > \phi^2$, there is exactly one fixed point.) The fixed point is stable for low values of applied current I, when it lies on the left branch of the V-nullcline, so that the system remains at rest unless perturbed (quiescence), as shown in Fig. 2a. As I increases, the V-nullcline shifts upward, and the location of the equilibrium shifts toward the middle branch. As the fixed point reaches the left knee of the V-nullcline, it undergoes a Hopf bifurcation, and a limit cycle is born. Thus, for sufficiently large values of I, the FHN system simulates tonic spiking, as shown in Fig. 2b.

Near the V-nullcline, $\dot{V}$ is approximately zero, so that motion in the $\dot{W}$ direction predominates, though it is slow because the small parameter ϕ in the $\dot{W}$ equation keeps the magnitude of W very

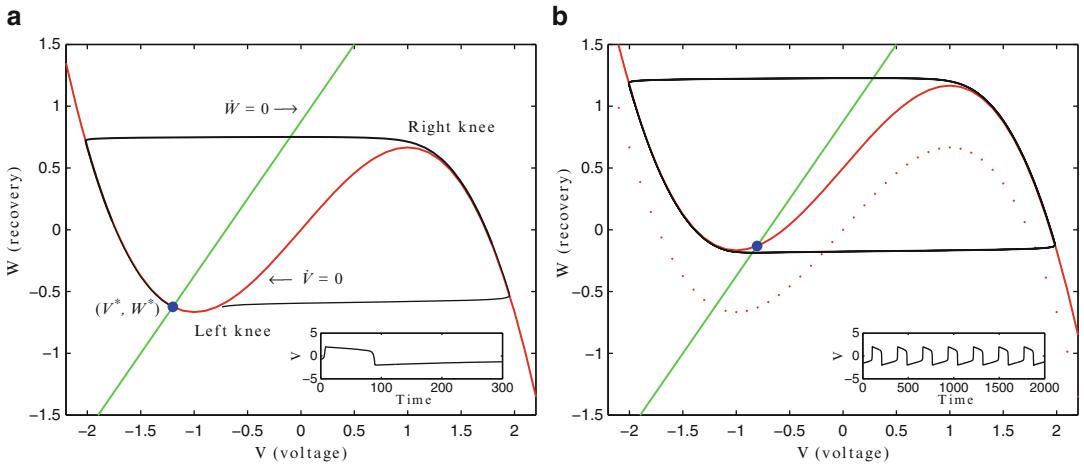

Fig. 2 Phase planes and sample trajectories for the FHN model Eq. 3 showing quiescence (**a**, *left*) and tonic spiking (**b**, *right*). The cubic fast nullcline ($\dot{V} = 0$) is *red*, the linear slow nullcline ($\dot{W} = 0$) is *green*, and the equilibrium point (V^*, W^*) is denoted by a *blue dot*. *Insets* show voltage versus time for the sample trajectories in *black*. The fast nullcline for $I = 0$ is shown as the *dotted red* cubic curve in **b** for comparison

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small. Trajectories typically crawl down the left branch and up the right branch of the V-nullcline until they arrive at one of the knees. Once past a knee, the magnitude of $\dot{V}$ rapidly increases, while the magnitude of $\dot{W}$ remains small. The trajectory quickly traverses the region between the left and right branches, so that there is a large change in V in a very short time but very little change in W. Portions of trajectories between branches appear almost horizontal, and they become more nearly horizontal as ϕ decreases. These rapid changes in V as the trajectories switch branches mimic the rapid up- and downswings of depolarization and hyperpolarization during action potentials, as can be seen in the insets of Fig. 2a, b. The separation of timescales between the V and W variables, as set by ϕ, is necessary for this action potential-like behavior and is the essential characteristic of relaxation oscillations.

When a brief positive current stimulus is applied to the quiescent FHN system, the (unperturbed) fixed point (V^*, W^*) is no longer a fixed point of the perturbed system, and thus the system's state begins to change. (Compare the locations of the fast nullclines and equilibria in Fig. 2a, b.) If its trajectory moves sufficiently far away from the fixed point before the stimulus ends, it will continue to make a large excursion around the right branch of the V-nullcline before returning to the original fixed point, as described above. This behavior models the action potential response of real neurons to depolarizing current pulses. Shifting the initial condition from (V^*, W^*) to ($V^* + V_{stim}$, W^*) (to the right of the threshold curve near the middle branch of the fast nullcline; see below) produces a largely identical excursive trajectory (see Fig. 2a) and is the most common way to simulate single action potential production in response to external stimulus.

Geometric Explanation of Spike Generation Phenomena in the Hodgkin–Huxley Model

A number of phenomena which are characteristic of action potential generation in HH-style neuronal models – and, to some extent, in real neurons as well – were first explained by FitzHugh using the FHN model. FitzHugh varied I to simulate stimulation of a neuron by a constant current (setting $I = I_0$ for time $t > 0$) and by rectangular (constant step) currents of various durations (setting $I = I_0$ for time $T_{on} < t < T_{off}$) and then studied the FHN model's response. He discovered that sufficiently large constant current produces spike trains (tonic spiking) via the mechanism described above. He modeled and analyzed other action potential response phenomena with either brief, rectangular, depolarizing (positive) stimuli or with slow current ramps (linearly varying I).

Threshold Phenomena, Small-Amplitude Spikes, and Refractoriness

FitzHugh noted that in the FHN model no single value of V acts as a threshold separating all-or-none, action potential-like responses to stimulation from quiescent or subthreshold responses. Rather, a curve in the (V, W) plane forms a "quasi-type" threshold, such that for any given value of the recovery variable W_0, there is a corresponding membrane voltage V_0 which the stimulus must exceed in order to evoke an action potential response (FitzHugh 1955). Trajectories starting to the right of the threshold curve simulate action potentials, while those starting to left of the threshold curve return to the left branch of the fast nullcline without producing a large action potential-like excursion (Fig 3). Stimuli which fail to shift trajectories past the threshold curve result in small-amplitude trajectories or "bumps" in membrane potential, in both the HH and FHN models. Similar stimulation of biological neurons more typically produces either no response or a very negligible one.

The threshold curve lies near, but not on, the middle branch of the V-nullcline; it is very difficult to trace accurately using standard numerical integration techniques. (The threshold is in fact a canard trajectory which may be computed numerically using continuation methods (Desroches et al. 2013).) Because of the difficulty determining whether trajectories would veer to the left or

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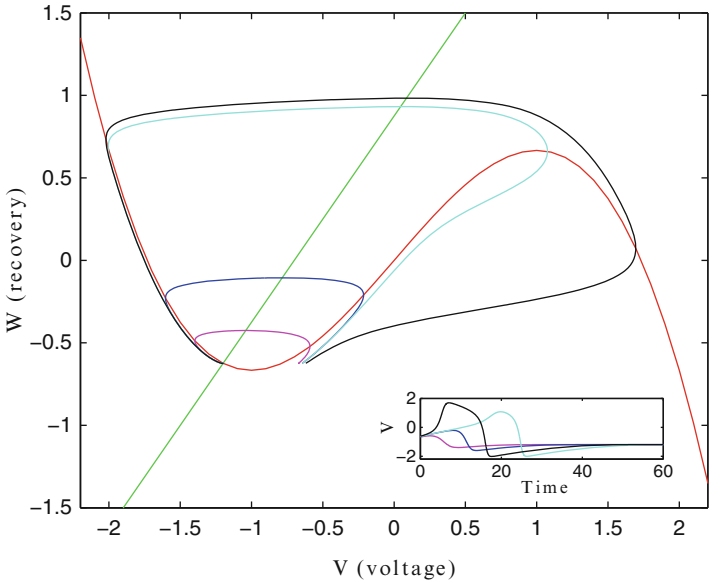

Fig. 3 Weak stimuli (current or voltage perturbations) fail to move the system across the quasi-threshold for firing an action potential, resulting in small-amplitude voltage "bumps" (*magenta*, *blue trajectories*). Sufficiently large stimuli cross the threshold to produce full action potential responses (*black trajectory*). For intermediate levels of stimulation which leave the system almost exactly at threshold, the system may track the quasi-threshold curve (near the middle branch of the *V*-nullcline) before turning *left* (no action potential) or *right* (near action potential, cyan trajectory)

right near the threshold curve, FitzHugh labeled that region of the phase plane "no man's land." The HH model has been shown numerically to have a complicated quasi-type spike threshold as well (Guckenheimer and Oliva 2002).

Stimulation by positive current has no discernible effect during the hyperpolarizing downswing of an action potential in both real and HH model neurons. During the repolarization phase, immediately following the downswing, much larger depolarizing input is needed to produce a second action potential than that required for generating the original action potential. These phenomena are termed absolute and relative refractoriness, respectively, and are typically explained in terms of the inactivation of the sodium channels required for depolarization. Phase plane analysis of the FHN model provides a complementary geometric explanation. The FHN model exhibits absolute refractoriness during the period that a trajectory is "jumping" from the right (depolarized) branch to the left (hyperpolarized) branch of the fast nullcline, and it exhibits relative refractoriness, while the trajectory crawls down the left branch of the fast nullcline toward the equilibrium point (repolarization).

FitzHugh summarized his exploration of the FHN model's response to brief depolarizing stimulus with a diagram similar to Fig. 4 (FitzHugh 1955, 1961).

Excitation Block

Applying positive external current shifts an HH neuron from quiescence to tonic spiking. In the FHN model, raising I moves the V-nullcline upward and induces repetitive firing as described above. If the magnitude of the stimulus is increased sufficiently, the fixed point will move to the right of the rightmost knee of the V-nullcline and become stable. The periodic orbit corresponding to repetitive spiking will be destroyed in a Hopf bifurcation, and the system will settle into a quiescent state at an elevated resting voltage. Thus, excitation of sufficient strength can block the production of spikes (Fig. 5).

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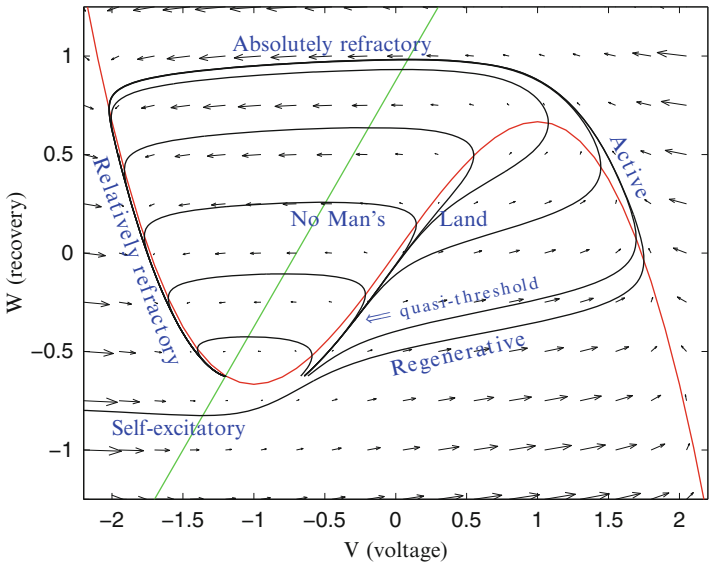

Fig. 4 Phase plane map associating FHN system behavior with initial conditions (Adapted from Fitzhugh (1961))

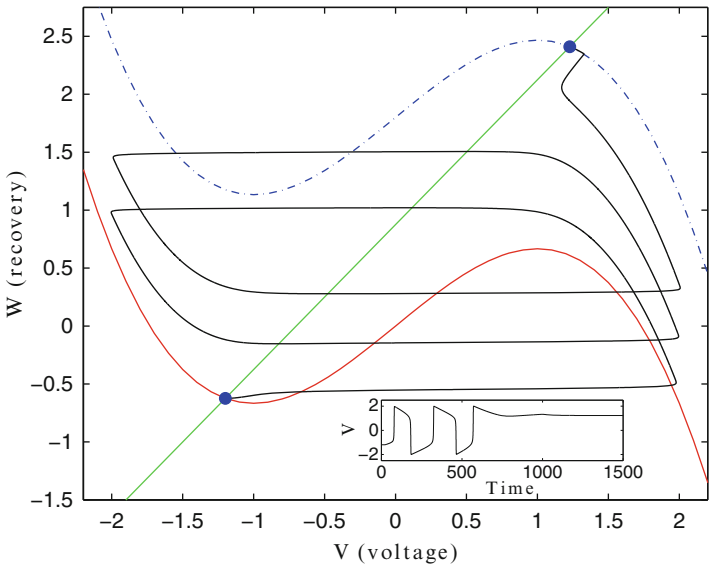

Fig. 5 Excitation block: as the applied current I is rapidly increased, the V-nullcline rises and the system passes through a bifurcation whereby the fixed point becomes unstable and a stable periodic orbit is born. So long as the fixed point remains between the two knees, the system spikes repetitively. Once I is sufficiently high for the fixed point to pass the *right knee*, the stable periodic orbit is destroyed, and the system is attracted to the new, depolarized stable equilibrium. Spiking stops and the membrane voltage remains at an elevated plateau

Post-inhibitory Rebound Spiking

This phenomenon is also called "anodal break excitation" in older literature. Applying hyperpolarizing current (decreasing I) moves the V-nullcline downward, maintaining the stability of the fixed point while shifting it down and to the left. When the hyperpolarizing current is turned off, the system is no longer at its fixed point but rather in a state where $\dot{V}$ and $\dot{W}$ are both positive (the

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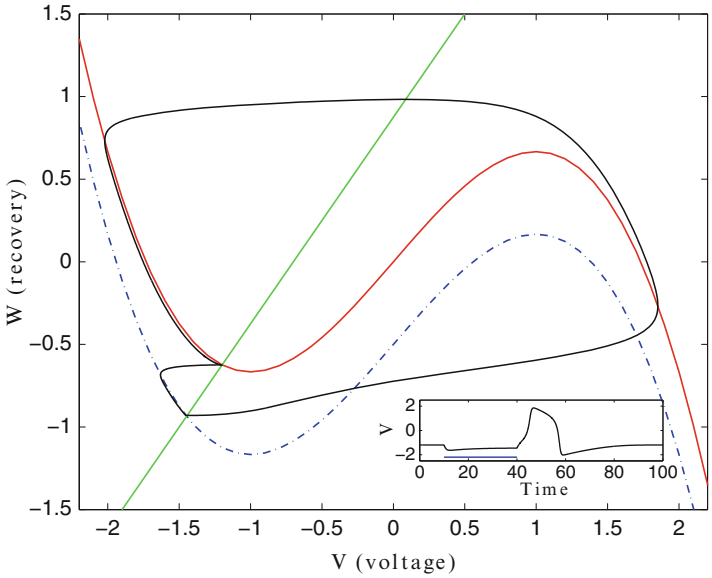

Fig. 6 Post-inhibitory rebound spiking: injecting negative (hyperpolarizing) applied current I lowers the *V*-nullcline (*red curve*) to a new, hyperpolarized level (*dotted blue curve*) and moves the stable fixed point to a lower voltage level in what would be the "self-excitatory" region of the phase plane, relative to the unperturbed system with $I = 0$. When the applied current is released, the *V*-nullcline and fixed point immediately return to their previous positions, and the system travels along a spike trajectory before returning to rest

"self-excitatory" region in Fig. 4). The system then follows a large excursive trajectory around the right branch of the *V*-nullcline, firing off an action potential in response to the release of inhibition (Fig 6).

Spike Accommodation

If the applied current I is raised slowly enough in the HH model, the neuron does not fire an action potential. Instead, the neuron remains quiescent, yet excitable, while the resting membrane potential rises. The same phenomenon is seen in the FHN model: as I increases, the *V*-nullcline shifts upward, and the equilibrium point shifts rightward, losing stability after it passes the left knee. If the shift is slow enough, the trajectory that began at the unperturbed fixed point will remain very close to the moving intersection (now unstable) of the fast and slow nullclines and will present itself as a slow rise in the resting membrane voltage over time (Fig. 7a). During this transition, very tiny perturbations may cause an action potential. Once the intersection of fast and slow nullclines passes the right knee, the fixed point will again be stable, and the system will remain at an elevating resting membrane potential. The maximum rate of change for I which will produce spike accommodation depends in part on the separation of timescales, as set by ϕ, since it determines the separation between the spike threshold curve and the middle branch of the *V*-nullcline (Fig. 7b).

Other Forms of the FHN Model

Alternative Formulations

Other formulations of the FHN equations are frequently encountered in the literature. FitzHugh also wrote his model as

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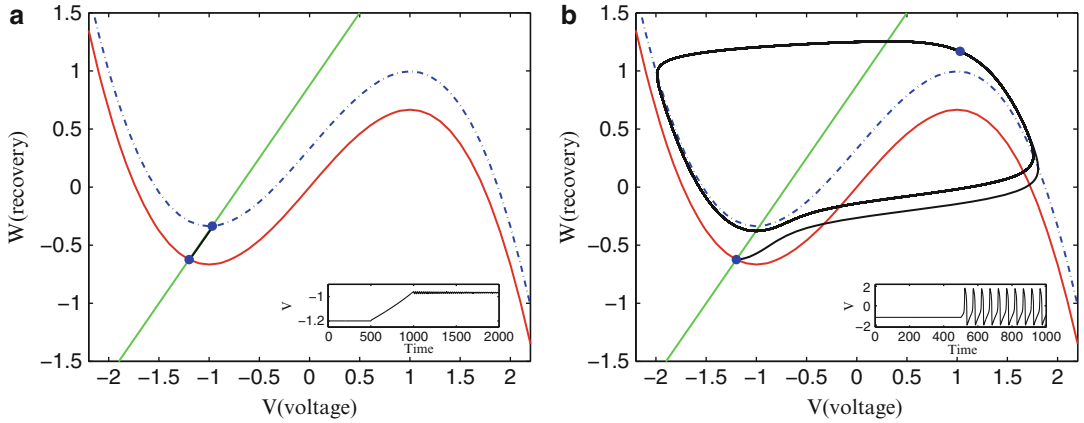

Fig. 7 Spike accommodation: increasing the applied current I raises the V-nullcline (*red curve*, $I = 0$) to a level where the fixed point is unstable (*dotted blue curve*, $I = 0.5$. When current is increased very slowly, the membrane voltage tracks the unstable fixed point (**a**, *left*). A more rapid current ramp produces a spike as the system is unable to track the unstable fixed point (**b**, *right*)

$$\dot{x}=c\left(y+x—x^3/3+z\right) \tag{7a}$$

$$\dot{y}=—x—a+by/c, \tag{7b}$$

with the constraints that a, b, and c were positive constants satisfying $1–2b/3 < a < 1$, $0 < b < 1$, and $b < c^2$ (FitzHugh 1961). This formulation produces a phase plane that is left–right reversed from the figures presented in this article for the FHN system Eq. 3.

Another common reformulation of Eq. 3 is

$$\dot{V}=V\ (1-V)(V-\alpha)-w+I \tag{8a}$$

$$\dot{W}=\epsilon(V-\gamma W), \tag{8b}$$

with $\epsilon \ll 1$ and $0 < \alpha < 1$. In this version, the horizontal intercepts of the V-nullcline are conveniently located at 0, α, and 1.

Generalized FitzHugh–Nagumo Systems

Planar dynamical systems which have:

I. A separation of timescales, i.e., one fast and one slow variable, say, v and w.
II. A "cubic-like" fast variable nullcline, say, $f(v,w) = 0$.
III. An approximately linear, monotonic slow variable nullcline, say, $g(v,w) = 0$, which intersects the fast variable nullcline exactly once, may be said to be "generalized FitzHugh–Nagumo systems." That is, they take the form:

$$\dot{v}=f\ (v,w) \tag{9a}$$

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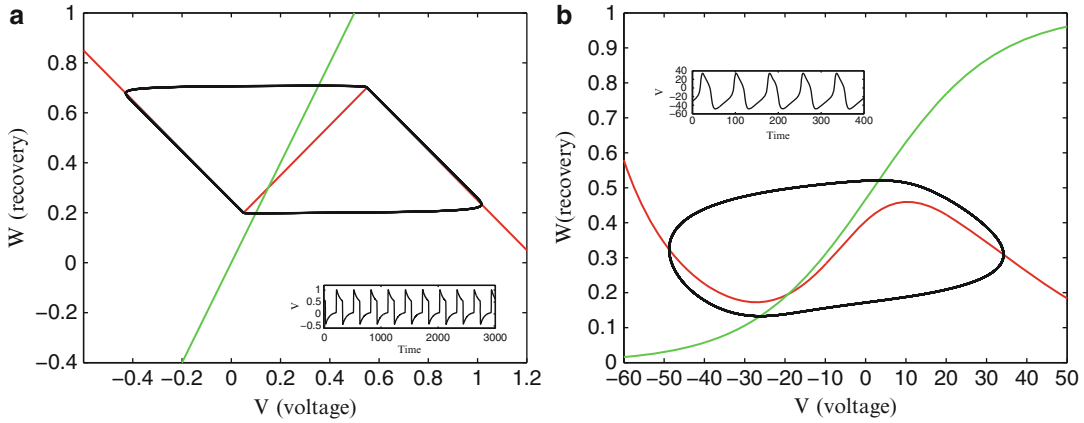

Fig. 8 Phase planes for the piecewise linear McKean model (**a**, *left*) and the biophysically realistic Morris–Lecar model (**b**, *right*). Note the cubic-like fast nullclines (*red*) and the (approximately) linear slow nullclines intersect exactly once; these are generalized FHN systems

$$\dot{w} = \epsilon g(v,w) \tag{9b}$$

with $0 < \epsilon \ll 1$. By "cubic-like," we mean that f is continuous; that there is a single, finite interval of w values for which $f(v,\ w) = 0$ is satisfied by three v values; and outside that interval $f(v,\ w) = 0$ generically takes a single v value (Keener and Sneyd 2009) (Fig. 7). Generalized FHN models exhibit dynamics that are equivalent or similar to the canonical FHN model within some range of parameters, but they may have different bifurcation structures. Examples of generalized FHN systems include the piecewise linear models of McKean (approximations of system (Eq. 8a; see Fig. 8a) (McKean 1970; Tonnelier 2003) and Rowat and Selverston (1997) and the Morris–Lecar model (Fig. 8b) (Morris and Lecar 1981)).

Fast–Slow Approximation of Hodgkin–Huxley Dynamics

FitzHugh intended his model to capture the qualitative dynamics of the Hodgkin–Huxley equations during action potential generation. The FHN model approximates the dynamics present in the fast–slow phase plane of the HH equations. The connection between the FHN and HH models can be seen in the following derivation, adapted from Keener and Sneyd (Keener and Sneyd 2009). (FitzHugh gave a similar explanation of the models' connection in FitzHugh (1961)).

The four-dimensional HH model (with variables V, m, n, h) may be reduced to a planar system with one fast variable (V, membrane voltage) and one slow variable (n, potassium activation) as follows. First, sodium activation m is assumed to equilibrate instantaneously, so that $m = m_\infty(V)$, i.e., the sodium activation timescale is faster than the membrane voltage timescale. Second, the levels of potassium channel activation and sodium channel inactivation are assumed to change on the same timescale and to maintain an approximately constant sum over the course of an action potential, i.e., $h(t) + n(t) \approx 0.8$.

Under these two assumptions, the HH equations reduce to

$$\dot{V} = f(V,n) \quad = -\Big(gK^{n^4}(V - E_K) + gNa^{m^3_\infty}(V)(0.8 - n)(V - E_{Na}), +gL(V - V_L)\Big)/C \tag{10a}$$

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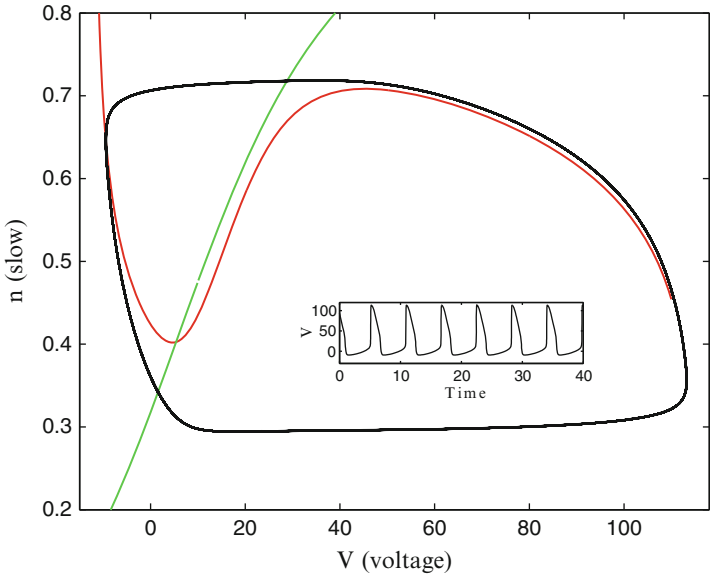

Fig. 9 Phase plane for the fast–slow reduction of the Hodgkin–Huxley equations with parameters set for tonic spiking. Note the *cubic*-like *shape* of the fast *V*-nullcline and the *linear shape* of the slow *n*-nullcline

$$\begin{aligned} \dot{n} &= g(V,n) \\ &= \alpha_n(V)(1-n) - \beta_n(V)n. \end{aligned} \tag{10b}$$

Now (I), there is a wide (though implicit) separation of timescales between the fast and slow variables; (II) $f(V, n) = 0$ is "cubic-like" according to the definition above; and (III) $g(V, n)$ is monotonically increasing, is approximately linear near $f(V, n) = 0$, and intersects $f(V, n) = 0$ exactly once. Thus, in the fast–slow phase plane, the HH model Eq. 10 is a generalized FHN system, and its behavior and analysis are essentially identical to that of the FHN model (Fig. 9). Note that the "recovery" role played by the slow variable n in the reduced HH Eq. 10 matches the physiological role played by potassium channels in helping to counteract excitation and reset the neuron's membrane potential back to the resting potential.

FitzHugh–Nagumo Model of Spike Propagation (Traveling Waves)

With the addition of a diffusion term, the FHN Eq. 3 may be adapted to provide a model of the spatial propagation of an action potential along an axon. Under appropriate boundary conditions to support a traveling wave solution (describing the propagation of the leading edge of the action potential), the equations become

$$V_t = V_{xx} + F(V) - W + I \tag{11a}$$

$$W_t = \phi(V + a - bW) \tag{11b}$$

where $F(V) = V^3/3 - V$.

For traveling wave solutions of the form $V = V(x - ct) = V(\xi)$ and $W = W(x - ct) = W(\xi)$, V and W must satisfy

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$$V_\xi = U \tag{12a}$$

$$U_\xi = W - F(V) - cU \tag{12b}$$

$$W_\xi = \frac{\phi}{c}(bW - V - a). \tag{12c}$$

Nagumo et al. first studied the system Eq. 12, taking $F(V)$ to be cubic and b = 0 (Nagumo et al. 1962). They found numerical evidence of two traveling wave solutions (homoclinic orbits) when ϕ was sufficiently small. Their numerical results indicated that only the higher-velocity solution was stable and that above a critical value of 0 no traveling wave solutions existed. FitzHugh's later numerical studies reached similar conclusions for $F(V) = V^3/3 - V$ and $b \neq 0$ (FitzHugh 1968). These numerical results have been confirmed analytically (see Scott (1975) for a fuller discussion).

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