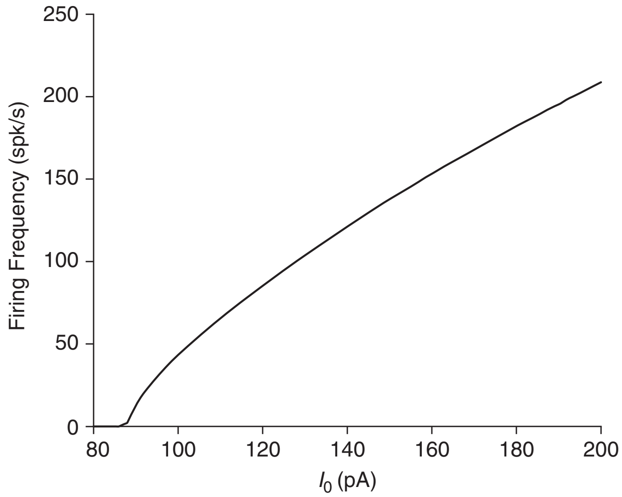

FIGURE 4.16 The number of spikes per second as a function of (constant) stimulus amplitude for the cell of §4.4 with the A-type potassium current. (`molifreq.m`)

5. One may excite a cell without impaling it, by instead upsetting the balance of extracellular ions. Modify `stE.m` to deliver a pulse of extracellular potassium ions, of concentration K_{stim}, in the time interval $[t_1, t_2]$, and so reproduce Figure 4.17. This stimulus resets the reversal potential, via (recall Eq. (4.2))

$$[K^+]_{out}(t) = 20 + K_{stim}\mathbb{1}_{(t_1,t_2)}(t), \quad E_K = 25.8\log([K^+]_{out}/400),$$

where $[K^+]_{out} = 20$ and $[K^+]_{in} = 400$ mM are drawn from Eq. (4.1).

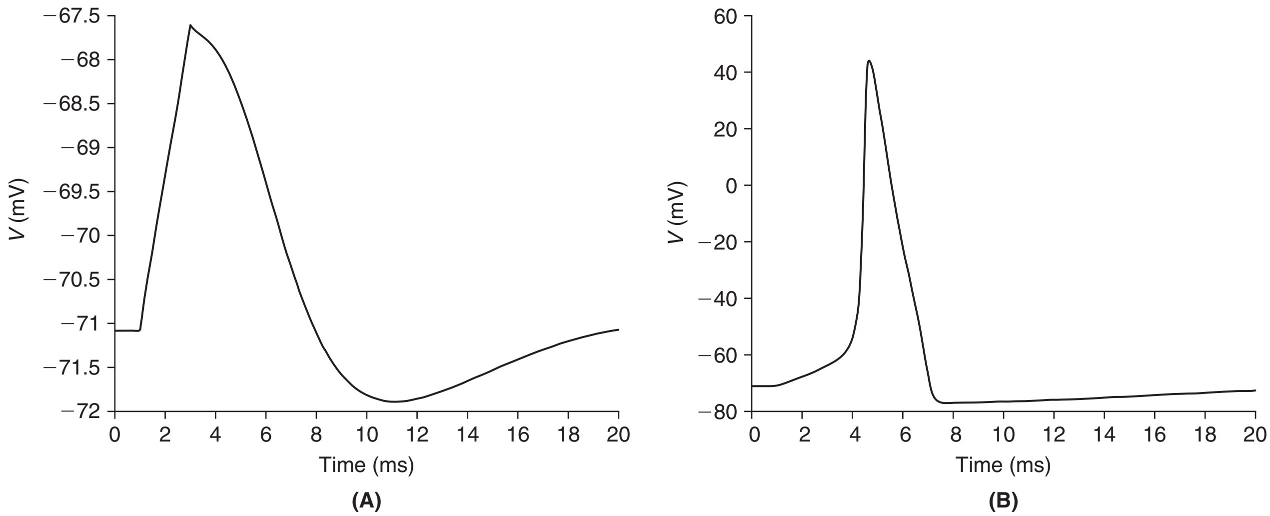

FIGURE 4.17 Depolarization of the Hodgkin–Huxley model by a 2 ms pulse of extracellular potassium ions. **A**. $K_{stim} = 5$ mM is subthreshold. **B**. $K_{stim} = 10$ mM elicits a spike. (`stEKstimdrive.m`)

6. Returning to Figure 4.6 we pursue a pair of simple observations. First, m, the gating variable of sodium activation is so fast that perhaps we can simply presume that it instantaneously reaches its steady-state level, $m_\infty(V(t))$. That is

$$m(t) \approx m_\infty(V(t)).$$

Second, we observe that $n+h$ is fairly flat. In, particular.

$$h(t) \approx 0.87 - n(t). \tag{4.29}$$

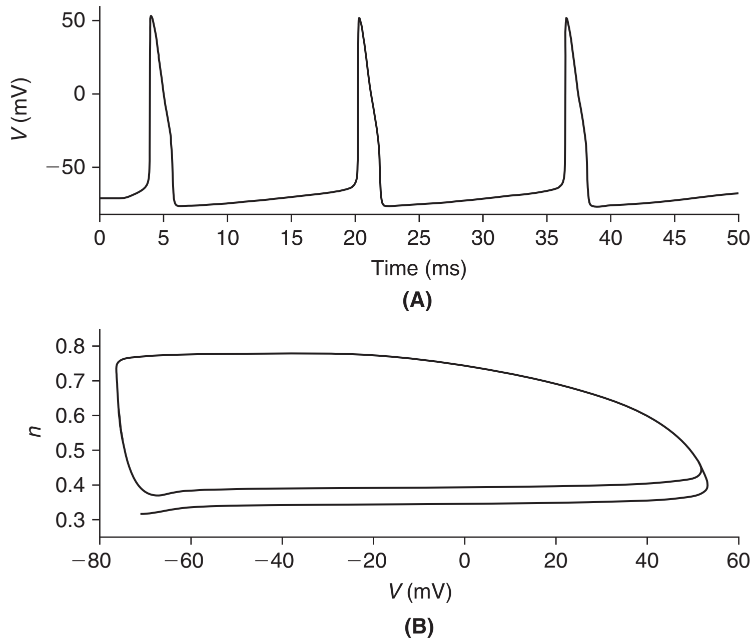

FIGURE 4.18 Response of the FitzHugh model, Eq. (4.30). **A**. Membrane potential as a function of time. **B**. Phase diagram of n and V. (stE2d.m)

With these approximations, the Hodgkin–Huxley system Eq. (4.15) reduces to

$$\begin{aligned} C_m V'(t) &= -\overline{g}_{Na} m_\infty^3(V)(0.87-n)(V-V_{Na}) - \overline{g}_K n^4 (V-V_K) - g_{Cl}(V-V_{Cl}) + I_{stim}/A \\ n'(t) &= \alpha_n(V)(1-n) - \beta_n(V)n. \end{aligned} \tag{4.30}$$

Modify stE.m to solve this two-variable reduced system and graph its response to $I_{stim} = 50\mathbb{1}_{(2,\infty)}(t)$ pA in the "phase plane" as in Figure 4.18. This reduced model is sometimes called the FitzHugh model.

7. One great feature of planar systems, like that of the previous exercise, is that the equations, when interpreted graphically, dictate how the solution must behave. The principal objects are the two nullclines. These are the curves on which V and n respectively, do not change. With reference to Eq. (4.30), the n nullcline is simply those points, (V,n), for which $n'(t)=0$, i.e., it is the graph of n_∞, namely $(V, n_\infty(V))$. The V nullcline is a bit more complicated. We recognize it as a quartic in n with coefficients that depend on V. We arrive at a very simple quartic if we replace our initial approximation, Eq. (4.29), with the arguably better

$$h(t) = 0.7 - n^2(t). \tag{4.31}$$

For in this case, the V nullcline is the set of points $(V, n_1(V, I_{stim}))$ where $n_1(V, I_{stim})$ is the lone positive root of the biquadratic

$$a(V)n^4 + b(V)n^2 + c(V) + I_{stim}/A, \tag{4.32}$$

for constant I_{stim}.

i. Please write out $a(V)$, $b(V)$, and $c(V)$ and argue that Eq. (4.32) indeed has only one root

$$n_1(V, I_{stim}) = \sqrt{\frac{-b(V) - \sqrt{b^2(V) - 4a(V)(c(V) + I_{stim}/A)}}{2a(V)}} \tag{4.33}$$

for each V for which $V_K < V < V_{Na}$.

ii. Graph, as in Figure 4.19A the n nullcline and V nullcline for $I_{stim} = 0$, 10, and 20 pA. Argue that these curves constrain the resulting dynamics by explaining why the solution, $(V(t), n(t))$ can only cross the n nullcline when moving horizontally and that it can only cross the V nullcline when moving vertically.

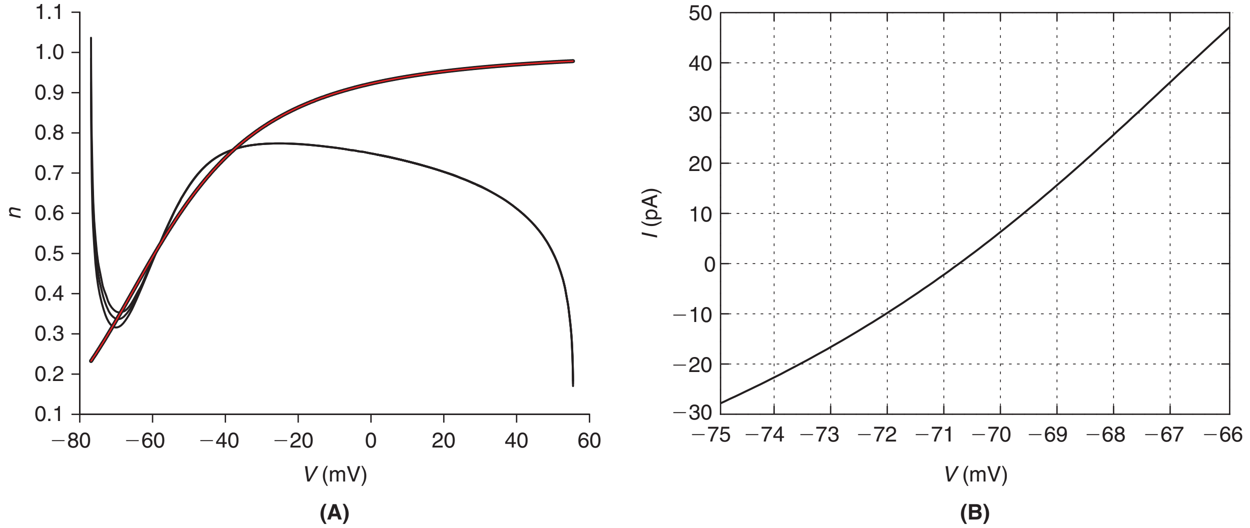

FIGURE 4.19 **A**. The n nullcline (red) and V nullclines (black) for $I_{stim} = 0$, 10, and 20 pA. The three V nullclines coincide outside of the interval $-75 < V < -55$ mV. In this interval, increasing I_{stim} serves to "lift" the V nullcline and so produce more depolarized rest states. **B**. The $I - V$ rest curve associated with Eq. (4.34). (`fhpp.m`)

iii. Next argue that the system is at rest only where its two nullclines cross. Argue that this occurs when V and I_{stim} satisfy

$$I_{stim} = -A(a(V)n_\infty^4(V) + b(V)n_\infty^2(V) + c(V)), \tag{4.34}$$

and graph this as in Figure 4.19B.

iv. Now address, as in Figure 4.20, the stability of a pair of rest states by incrementing I_{stim} by 1 pA at the 2 ms mark.

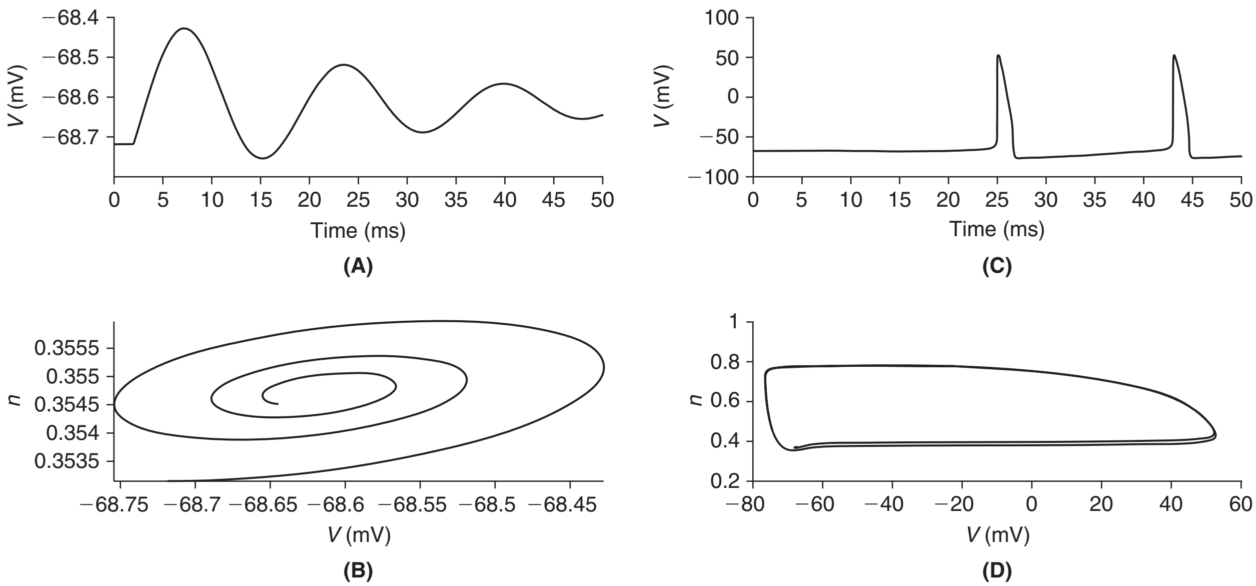

FIGURE 4.20 Voltage traces and phase planes of the modified FitzHugh system for $I_{stim} = 20 + \mathbb{1}_{(2,\infty)}(t)$ pA (**A**, **B**) and $I_{stim} = 30 + \mathbb{1}_{(2,\infty)}(t)$ pA (**C**, **D**). In the former case the incremental current brought us to a nearby rest state, while in the latter the same increment produced a large excursion and eventual periodic spiking. The mathematics developed in the next chapter will permit us to take a closer look at this threshold. (`fhpp.m`)