Chapter 4

Numerical Solution of the Hodgkin-Huxley ODEs

In practice, complicated differential equations such as the Hodgkin-Huxley ODEs are almost always solved *numerically*, that is, approximate solutions are obtained on a computer.[7] The study of methods for the numerical solution of differential equations is the subject of a large and highly sophisticated branch of mathematics. However, here we will study only the two simplest methods: *Euler's method* and the *midpoint method*. Euler's method is explained here merely as a stepping stone to the midpoint method. For all simulations of this book, we will use the midpoint method, since it is far more efficient, and not much more complicated than Euler's method.

We write the Hodgkin-Huxley ODEs briefly as

$$\frac{dy}{dt} = F(y), \tag{4.1}$$

with

$$y = \begin{bmatrix} v \\ m \\ h \\ n \end{bmatrix}, \quad F(y) = \begin{bmatrix} \left(\overline{g}_{\mathrm{Na}} m^3 h (v_{\mathrm{Na}} - v) + \overline{g}_{\mathrm{K}} n^4 (v_{\mathrm{K}} - v) + \overline{g}_{\mathrm{L}} (v_{\mathrm{L}} - v) + I\right)/C \\ (m_\infty(v) - m)/\tau_m(v) \\ (h_\infty(v) - h)/\tau_h(v) \\ (n_\infty(v) - n)/\tau_n(v) \end{bmatrix}.$$

Suppose that in addition to the system of ODEs, (4.1), we are given the *initial condition*

$$y(0) = y_0, \tag{4.2}$$

Electronic supplementary material: The online version of this chapter (doi: 10.1007/978-3-319-51171-9_4) contains supplementary material, which is available to authorized users.

[7]This certainly does not mean that there are not mathematical methods that yield very valuable insight. You will see some of them later in this book. However, for most differential equations it is impossible to write down "explicit" solutions, that is, formulas representing solutions symbolically, and even when it is possible it may not always be useful.

C. Börgers, *An Introduction to Modeling Neuronal Dynamics*,
Texts in Applied Mathematics 66, DOI 10.1007/978-3-319-51171-9_4

i.e., we are given v, m, h, and n at time $t = 0$, and that we want to find $y(t)$, $0 \le t \le T$, for some $T > 0$.

The simplest idea for computing solutions to this problem is as follows. Choose a large integer M, and define $\Delta t = T/M$ and $t_k = k\Delta t$, $k = 0, 1, 2, \ldots, M$. Compute approximations

$$y_k \approx y(t_k), \quad k = 1, 2, \ldots, M,$$

from the equation

$$\frac{y_k - y_{k-1}}{\Delta t} = F(y_{k-1}), \quad k = 1, 2, \ldots, M. \tag{4.3}$$

This is called *Euler's method*, named after Leonhard Euler (1707–1783). Note the similarity between eqs. (4.1) and (4.3): One obtains (4.3) by replacing the derivative in (4.1) by a difference quotient. This is motivated by the fact that

$$\frac{y(t_k) - y(t_{k-1})}{\Delta t} \approx \frac{dy}{dt}(t_{k-1}) \tag{4.4}$$

for small Δt.

A small modification leads to a much more effective method: Write $t_{k-1/2} = (k - 1/2)\Delta t$, $k = 1, 2, \ldots, M$, and compute approximations

$$\hat{y}_{k-1/2} \approx y(t_{k-1/2}) \quad \text{and} \quad \hat{y}_k \approx y(t_k), \quad k = 1, 2, \ldots, M,$$

by

$$\frac{\hat{y}_{k-1/2} - \hat{y}_{k-1}}{\Delta t/2} = F(\hat{y}_{k-1}) \quad \text{and} \tag{4.5}$$

$$\frac{\hat{y}_k - \hat{y}_{k-1}}{\Delta t} = F(\hat{y}_{k-1/2}), \quad k = 1, 2, \ldots, M. \tag{4.6}$$

This is called the *midpoint method*. Equation (4.5) describes a step of Euler's method, with Δt replaced by $\Delta t/2$. Equation (4.6) is motivated by the fact that

$$\frac{y(t_k) - y(t_{k-1})}{\Delta t} \approx \frac{dy}{dt}(t_{k-1/2}) \tag{4.7}$$

for small Δt. The *central* difference approximation in (4.7) is much more accurate than the *one-sided* approximation in (4.4); see exercise 3. You might be concerned that whichever advantage is derived from using the central difference approximation in (4.6) is essentially squandered by using Euler's method to compute $\hat{y}_{k-1/2}$. However, this is not the case; the reason is, loosely speaking, that the right-hand side of eq. (4.6) is multiplied by Δt in the process of solving the equation for $\hat{y}_k$.

The theoretical analysis of Euler's method and the midpoint method relies on two assumptions. First, F must be sufficiently often differentiable.

(Twice is enough, but that is unimportant here: The right-hand side of the Hodgkin-Huxley equations is infinitely often differentiable with respect to v, m, h, and n.) In addition, one must assume that the solution $y(t)$ is defined for $0 \leq t \leq T$. See exercise 4 for an example illustrating that $y(t)$ is not guaranteed to be defined for $0 \leq t \leq T$ even if F is infinitely often differentiable. However, for the Hodgkin-Huxley equations, one can prove that all solutions are defined for all times; see exercise 5.

To characterize the accuracy of the approximations obtained using Euler's method and the midpoint method, we note first that y_k and $\hat{y}_k$ depend not only on k, but also on Δt, and we make this dependence clear now by writing $y_{k,\Delta t}$ and $\hat{y}_{k,\Delta t}$ instead of y_k and $\hat{y}_k$.

For Euler's method, there exists a constant $C > 0$ independent of Δt (but dependent on F, y_0, and T) so that

$$\max_{0 \leq k \leq M} |y(k\Delta t) - y_{k,\Delta t}| \leq C\Delta t. \tag{4.8}$$

Similarly, for the midpoint method,

$$\max_{0 \leq k \leq M} |y(k\Delta t) - \hat{y}_{k,\Delta t}| \leq \hat{C}\Delta t^2 \tag{4.9}$$

for a constant $\hat{C} > 0$ independent of Δt. The proofs of these results can be found in most textbooks on numerical analysis, for instance, in [78].

For small Δt, $\hat{C}\Delta t^2$ is much smaller than $C\Delta t$. (If Δt is small, Δt^2 is much smaller than Δt.) Therefore the midpoint method gives much better accuracy than Euler's method when Δt is small. One says that Euler's method is *first-order accurate*, and the midpoint method is *second-order accurate*. This terminology refers to the powers of Δt in eqs. (4.8) and (4.9).

Suppose that we want to compute the solution y up to some small error $\epsilon > 0$. If we use Euler's method, we should make sure that $C\Delta t \leq \epsilon$, so $\Delta t \leq \epsilon/C$. If we use the midpoint method, we need $\hat{C}\Delta t^2 \leq \epsilon$, so $\Delta t \leq \sqrt{\epsilon/\hat{C}}$. For small ϵ, the bound $\sqrt{\epsilon/\hat{C}}$ is much larger than the bound ϵ/C. This means that at least for stringent accuracy requirements (namely, for small ϵ), the midpoint method is much more efficient than Euler's method, since it allows much larger time steps than Euler's method.

In many places in this book, we will present computed solutions of systems of ODEs. All of these solutions were obtained using the midpoint method, most typically with $\Delta t = 0.01\,\text{ms}$.

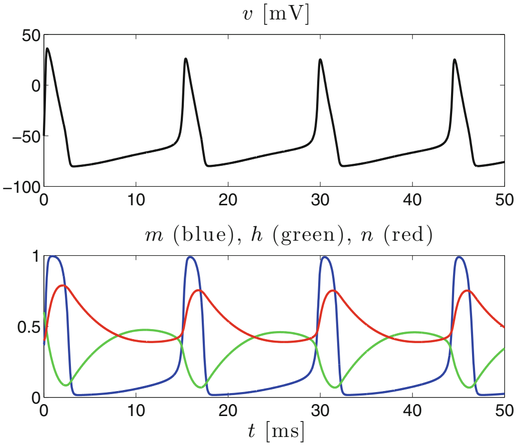

Figure 4.1. *A solution of the Hodgkin-Huxley ODEs with* $I = 10\,\mu\mathrm{A/cm}^2$. [HH_SOLUTION]

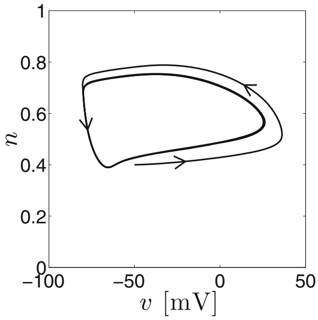

Figure 4.2. *Projection into the* (v, n)*-plane of the solution shown in Fig. 4.1. The arrows indicate the direction in which the point* (v, n) *moves.* [HH_LIMIT_CYCLE]

Figure 4.1 shows an example of a solution of the Hodgkin-Huxley ODEs, demonstrating that the model produces voltage spikes. We gave a heuristic explanation of the origins of the voltage spikes in Section 1.1 already. From a mathematical point of view, the spikes will be discussed in later sections.

Figure 4.2 shows, for the same solution, the curve $(v(t), n(t))$ in the (v, n)-plane. Periodic firing corresponds to a periodic solution of the Hodgkin-Huxley ODEs, represented by a closed loop in (v, m, h, n)-space. Solutions that start near the periodic solution converge to it. One therefore calls the periodic solution an *attracting limit cycle*.

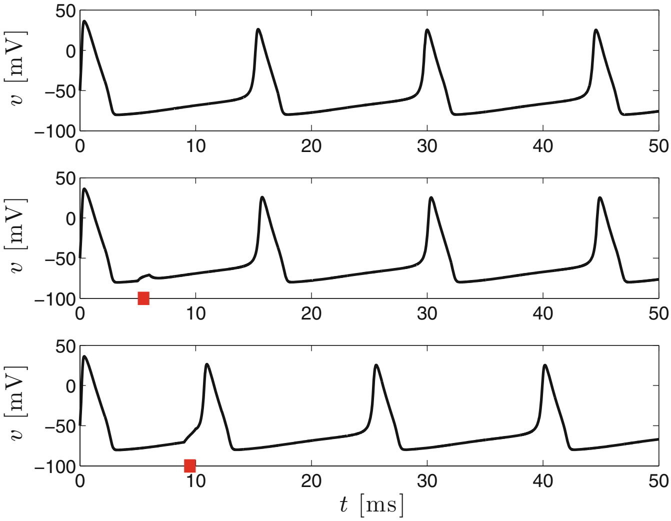

Figure 4.3. *An illustration of the refractoriness of the Hodgkin-Huxley neuron following an action potential. Top panel: Solution already shown in Fig. 4.1. Middle panel: Solution obtained when a brief strong pulse of input is added, raising I from 10 to 40 $\mu A/cm^2$ for t between 5 and 6 ms. Bottom panel: Same, with additional input pulse arriving later, between 9 and 10 ms. The time of the additional input pulse is indicated by a red bar in the middle and bottom panels.* [HH_REFRACTORINESS]

Figure 4.1 shows that it takes the gating variable, n, of the delayed rectifier current a few milliseconds to decay following a spike. This has an important consequence: Input arriving within a few milliseconds following a spike has very little effect. Positive charge injected at this time immediately leaks out. This is illustrated by Fig. 4.3. When the pulse comes soon after a spike (middle panel), it has almost no effect. When it comes just a few milliseconds later (bottom panel), it instantly triggers a new spike. One says that the neuron is *refractory* for a brief time following an action potential, the *refractory period*. It is not a sharply defined time interval: Immediately after a spike, the neuron is nearly insensitive even to strong input, then its input sensitivity gradually recovers.

Exercises

4.1. Consider an initial-value problem

$$\frac{dy}{dt} = -cy \quad \text{for } t \geq 0, \qquad y(0) = y_0,$$

with $c > 0$ and y_0 given.

(a) Write down a formula for $y(t)$, and show that $\lim_{t\to\infty} y(t) = 0$.

(b) Denote by y_k, $k = 1, 2, 3, \ldots$, the approximations to $y(k\Delta t)$ obtained using Euler's method. Write down an explicit, simple formula for y_k.

(c) Prove that

$$\lim_{k\to\infty} y_k = 0 \quad \text{if } \Delta t < 2/c,$$

but

$$\lim_{k\to\infty} |y_k| = \infty \quad \text{if } \Delta t > 2/c.$$

One says that $2/c$ is a *stability threshold*.

(d) We write $y_{k,\Delta t}$ instead of y_k to make clear that y_k does not only depend on k, but also on Δt. Let $T > 0$ and $\Delta t = T/M$, where M is a positive integer. Then $y_{M,\Delta t} = y_{M,T/M}$ is an approximation for $y(T)$. Show explicitly, without using (4.8), that

$$\lim_{M\to\infty} y_{M,T/M} = y(T).$$

(L'Hospital's rule will be useful here.)

4.2. For the initial-value problem in exercise 1, denote by $\hat{y}_k$, $k = 1, 2, 3, \ldots$, the approximations of $y(k\Delta t)$ obtained using the midpoint method. Write down an explicit, simple formula for $\hat{y}_k$.

4.3. Let $y = y(t)$ be a function that is as often differentiable as you wish. (Three times will be enough, but that is unimportant here. Solutions of the Hodgkin-Huxley equations are infinitely often differentiable.) Let t be fixed, and let $\Delta t_{\max} > 0$ be any positive number.

(a) Using Taylor's theorem, show that there exists a constant C, independent of Δt, so that

$$\left| \frac{y(t) - y(t-\Delta t)}{\Delta t} - y'(t-\Delta t) \right| \leq C\Delta t$$

for all Δt with $0 < \Delta t \leq \Delta t_{\max}$, where $y' = dy/dt$.

(b) Using Taylor's theorem, show that there exists a constant $\hat{C}$, independent of Δt, so that

$$\left| \frac{y(t) - y(t-\Delta t)}{\Delta t} - y'(t-\Delta t/2) \right| \leq \hat{C}\Delta t^2$$

for all Δt with $0 < \Delta t \leq \Delta t_{\max}$, where again $y' = dy/dt$.

4.4. Using separation of variables, find a solution of the initial-value problem

$$\frac{dy}{dt} = y^2, \quad y(0) = 1.$$

Show that the limit of $y(t)$ as $t \to 1$ from the left is ∞. This is called *blow-up in finite time*.

4.5. Suppose that v, m, h, and n solve the Hodgkin-Huxley ODEs, eqs. (3.8) and (3.9). Define

$$A = \min\left(v_{\mathrm{K}}, v_{\mathrm{L}} + \frac{I}{\overline{g}_{\mathrm{L}}}\right), \qquad B = \max\left(v_{\mathrm{Na}}, v_{\mathrm{L}} + \frac{I}{\overline{g}_{\mathrm{L}}}\right).$$

Explain: If $A \leq v(0) \leq B$ and $0 \leq x \leq 1$ for $x = m$, h, and n, then $A \leq v(t) \leq B$ and $0 \leq x \leq 1$ for all $t \geq 0$. So there is no blow-up in finite time (see exercise 4) for the Hodgkin-Huxley ODEs.