Chapter 2
A System of Ordinary Differential Equations

Above, we introduced a very simple differential equation given by

$$y'(t) = y(t). \tag{2.1}$$

This is referred to as an *ordinary differential equation (ODE)* because it involves the derivative with respect to only one variable. If the derivative with respect to more than one variable is involved, the equation is referred to as a *partial differential equation (PDE)*. We will come back to PDEs in Chapter 3, and spend some time discussing how to solve them, but in this chapter, we will keep focusing on ODEs.

The ODE (2.1) is a *scalar* equation because there is only a single unknown function to be found. Now, we will start considering *systems* of ODEs. A typical system of ODEs can be written in the form

$$y'(t) = F(y(t)). \tag{2.2}$$

Here, y is a vector and F is vector valued function.

2.1 The FitzHugh-Nagumo Model

We will introduce numerical methods for systems of ODEs by considering the celebrated[1] FitzHugh-Nagumo model published by FitzHugh [1] in 1961 and, independently, by Nagumo et. al. [2] in 1962. The model is a system of ordinary differential equations with two unknowns, and is commonly used as a simple model for the action potentials of excitable pacemaker cells.

We consider the following version of the FitzHugh-Nagumo model,

$$v' = c_1 v(v-a)(1-v) - c_2 w, \tag{2.3}$$
$$w' = b(v - dw). \tag{2.4}$$

[1] These two papers together are cited more than 11,000 times.

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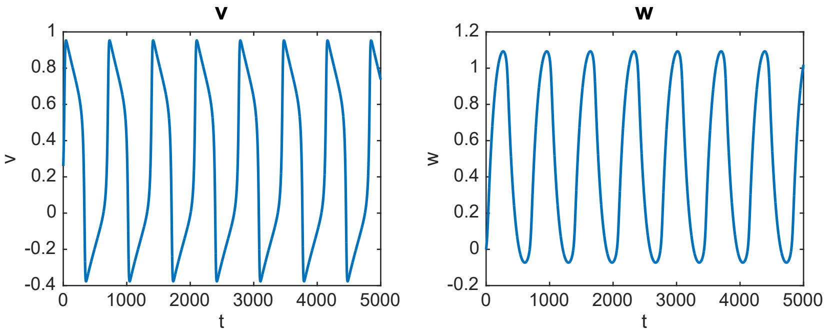

Fig. 2.1 Numerical solutions v_n (left) and w_n (right) of the FitzHugh-Nagumo model specified by (2.3)–(2.5). The numerical scheme used to compute the solutions is specified in (2.8)–(2.9), and we have used $\Delta t = 1$ and the initial conditions $v_0 = 0.26$ and $w_0 = 0$.

Here, the constants are given by

$$a = -0.12,\ c_1 = 0.175,\ c_2 = 0.03,\ b = 0.011,\ d = 0.55, \tag{2.5}$$

and the unknown functions are v and w. In order to solve the system of equations numerically, we use the steps introduced for the scalar equation in Chapter 1 and start by replacing derivatives by differences. The discrete system then reads

$$\frac{v_{n+1} - v_n}{\Delta t} = c_1 v_n (v_n - a)(1 - v_n) - c_2 w_n, \tag{2.6}$$

$$\frac{w_{n+1} - w_n}{\Delta t} = b(v_n - d w_n). \tag{2.7}$$

Again, we reorganize this system to write it in *computational form*,

$$v_{n+1} = v_n + \Delta t[c_1 v_n (v_n - a)(1 - v_n) - c_2 w_n], \tag{2.8}$$

$$w_{n+1} = w_n + \Delta t[b(v_n - d w_n)]. \tag{2.9}$$

This time, however, we note that we will need a piece of software to compute the solutions. But it is straightforward to implement this since the numerical solution at time t_{n+1} is an explicit function of the numerical solution at time t_n.

2.1.1 Numerical Computations

We assume that the solution is known initially, so we define (for instance) $v_0 = 0.26$ and $w_0 = 0$. Here, it is useful to note that if we put both v_0 and w_0 equal to zero, the solution will remain zero (for both v and w) for all time. But if we perturb v a little, we get very different solutions. In Fig. 2.1, we show the numerical solution from $t = 0$ to $t = T = 5000$. In the computation, we have used $N = 5000$ which

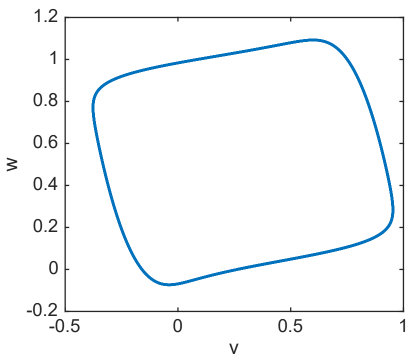

Fig. 2.2 The numerical solutions v_n and w_n of the FitzHugh-Nagumo model from Fig. 2.1 displayed in a parametric plot with v_n on the x-axis and w_n on the y-axis.

Table 2.1 Error of the numerical solution of the FitzHugh-Nagumo model specified by (2.3)–(2.5) at $t = T = 5000$ for different values of $\Delta t = \frac{T}{N}$. The error is defined as $E_N = |v - v_N| + |w - w_N|$, where v and w are the numerical solutions for a very fine resolution ($\Delta t = 0.001$), and v_N and w_N are the numerical solutions for larger values of Δt.

N	Δt	E_N	$E_N/\Delta t$
500	10	0.0923	0.0092
1000	5	0.0433	0.0087
5000	1	0.00727	0.0073
10000	0.5	0.00353	0.0071
50000	0.1	0.000682	0.0068

gives $\Delta t = T/N = 1$. In Fig. 2.2, we show the numerical solutions $(v_n, w_n)_{n=1}^N$ in a parametric plot, and we note that the solutions are periodic. In electrophysiology, such solutions are useful for studying pacemaker cells that keep on creating action potentials at a steady rate.

2.2 What Is the Error?

In the very simple equation in the previous chapter, we had a formula for the analytical solution and a formula for the numerical solution, and thus it was straightforward to find the error introduced by replacing a derivative by a difference. For the FitzHugh-Nagumo equations, this is harder. In numerical analysis there are techniques for proving error bounds for numerical methods. But the proofs tend to be very technical and often involve constants that need to be estimated. So we are looking for something simpler. If we just assume that we have convergence towards the correct solution as Δt tends to zero, we can compute an accurate approximation of the solution by using a very small Δt and then monitoring the convergence towards this highly resolved solution.

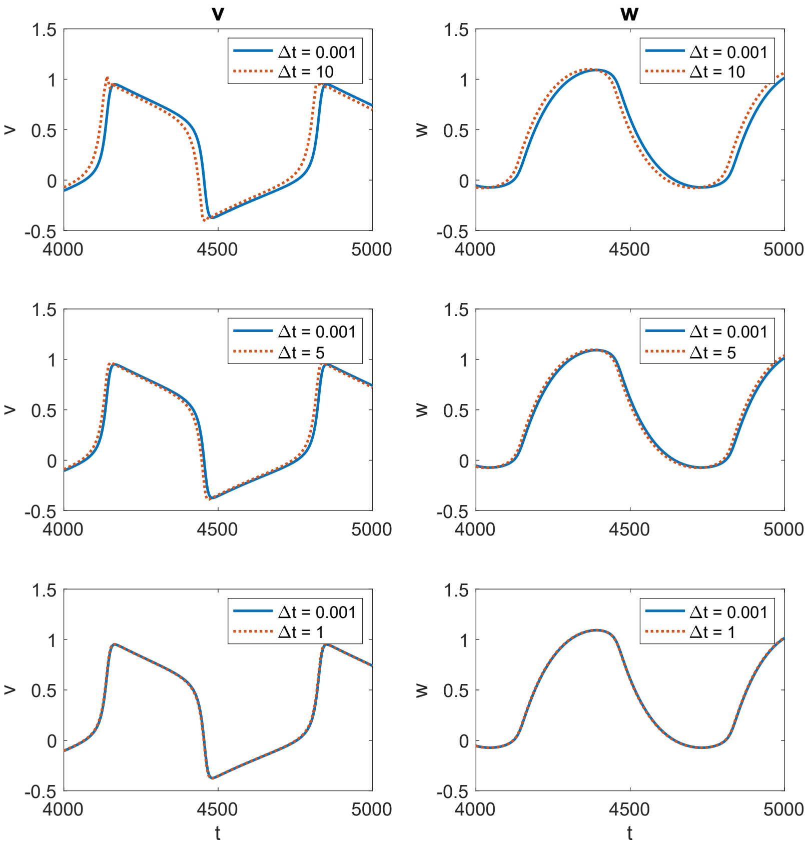

Fig. 2.3 Numerical solutions v_n (left) and w_n (right) of the FitzHugh-Nagumo model specified by (2.3)–(2.5). We compare the solutions for a very fine resolution ($\Delta t = 0.001$, solid blue line) to the solutions for three cases of coarser resolution (dotted orange line). In the upper panel, we consider $\Delta t = 10$, in the middle panel, we consider $\Delta t = 5$, and in the lower panel, we consider $\Delta t = 1$. To improve visibility, we only show the solutions from $t = 4000$ to $t = 5000$. As Δt is decreased, the coarse numerical solutions are more similar to the numerical solution computed with a very small Δt, and for $\Delta t = 1$ the two solutions are indistinguishable.

For simplicity, we assume that we are merely interested in the error at the final time $t = T = 5000$. We first compute the solution using an extremely fine resolution ($\Delta t = 0.001$) and regard that as the correct solution at time T. Then, we compute solutions for varying resolutions (different values of the time step Δt) and compare the "correct" and approximate solutions. In Fig. 2.3, we compare the solutions for a few different choices of Δt. The error defined by $E_N = |v - v_N| + |w - w_N|$, where (v, w) denotes the fine scale solution, is given in Table 2.1. Again, we observe that $E_N/\Delta t$ is more or less constant and we therefore conclude again that the error in the numerical solution is proportional to the time step Δt. In other words, the convergence is linear (or first order) in Δt.

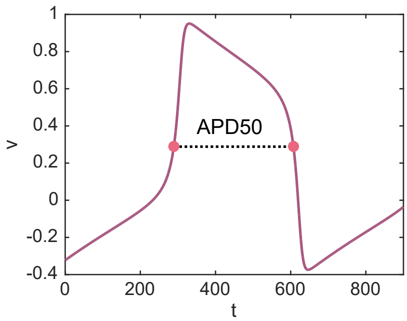

Fig. 2.4 Illustration of a definition of the action potential duration, APD50. The APD50 value is defined as the duration between the two times v crosses the threshold value defined at the center between the maximum and minimum value of v.

2.3 Upstroke Velocity and Action Potential Duration

In applications of the FitzHugh-Nagumo model, the unknown function v is often used to represent the membrane potential of an excitable cell, e.g., a neuron or a cardiac cell, firing a sequence of action potentials. A single action potential from the solution of the FitzHugh-Nagumo model is illustrated in Fig. 2.4. In general terms, the action potential first consists of a period during which the value of v increases slowly, followed by a more rapid increase (the upstroke). Then, v decreases relatively slowly for a while before it decreases rapidly back to the minimum value and starts increasing again. In this setting, we often refer to v increasing as *depolarization*, and v decreasing as *repolarization*. We will come back to these terms below where we introduce models with proper physical units.

By solving the FitzHugh-Nagumo model equations for different values of the model constants, or parameters, (a, c_1, c_2, b, and d), we could gain some insight into how the parameters affect the firing of action potentials. For example, we could investigate how the parameters affect the frequency of firing or the shape of the fired action potentials. Two properties that are of interest regarding the shape of the action potential are the *maximal upstroke velocity* and the *action potential duration*. The maximal upstroke velocity is often defined as the maximum value of the derivative of v with respect to time. Using a finite difference approximation of the derivative, this can be defined as

$$\max_n \left(\frac{v_{n+1} - v_n}{\Delta t} \right). \tag{2.10}$$

The action potential duration is often defined in terms of a given percentage of repolarization, for example APD50 or APD90, for 50% or 90% repolarization, respectively. Here, APD50 represents the duration from the start of the action potential until the membrane potential reaches a value that is 50% repolarized (i.e., at $v_{50} = 0.5\,(\max_n(v_n) + \min_n(v_n))$), at t_{50}^{down}. Similarly, APD90 is defined as the duration from the start of the action potential until the membrane potential reaches a value that is 90% repolarized (i.e., at $v_{90} = \max_n(v_n) - 0.9(\max_n(v_n) - \min_n(v_n))$), at t_{90}^{down}. The start of the action potential used in the definition of the action potential duration can, for example, be defined as the point in time when the maximal

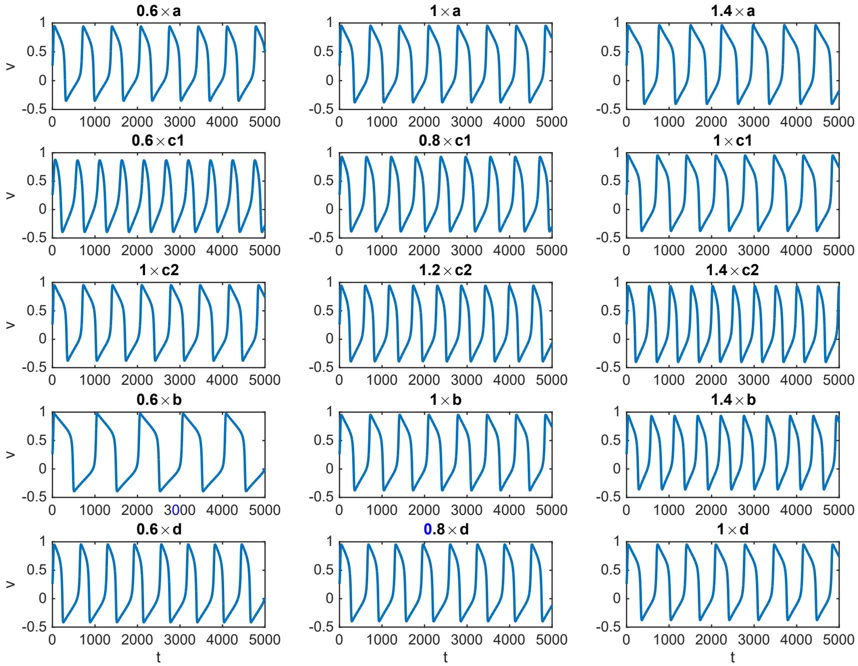

Fig. 2.5 The numerical solution, v_n, of the FitzHugh-Nagumo model, defined by the two equations $v' = c_1 v(v-a)(1-v) - c_2 w$, and $w' = b(v - dw)$. The parameters are as specified in (2.5), except that in each row of the figure, the value of either a, c_1, c_2, b, or d is adjusted. The title above each plot specifies the parameter change.

upstroke velocity occurs, or when the membrane potential crosses the 50% or 90% repolarization thresholds, v_{50} or v_{90}, during the upstroke, denoted by t_{50}^{up} or t_{90}^{up}, respectively. In the latter case, APD50 and APD90 can be defined as

$$\text{APD50} = t_{50}^{\text{down}} - t_{50}^{\text{up}}, \tag{2.11}$$

$$\text{APD90} = t_{90}^{\text{down}} - t_{90}^{\text{up}}. \tag{2.12}$$

Such a definition of APD50 is illustrated in Fig. 2.4.

In Fig. 2.5, we show the numerical solution, v_n, of the FitzHugh-Nagumo model with different choices of parameters. In each row, we consider three different values of one of the parameters a, c_1, c_2, b, or d, and keep the remaining values fixed at the values specified in (2.5). In the plots, we observe that increasing the value of c_1 appears to make the action potentials longer and the firing frequency slower, whereas the opposite effect is observed when c_2 or b are increased. In Fig. 2.6, we study the effects on the individual action potentials more closely. In the left panel, we have zoomed in on the points in time representing the action potential upstroke. We observe that decreasing the value of c_1 reduces the upstroke velocity, but changing the other parameters do not seem to have a significant effect on the upstroke. In the

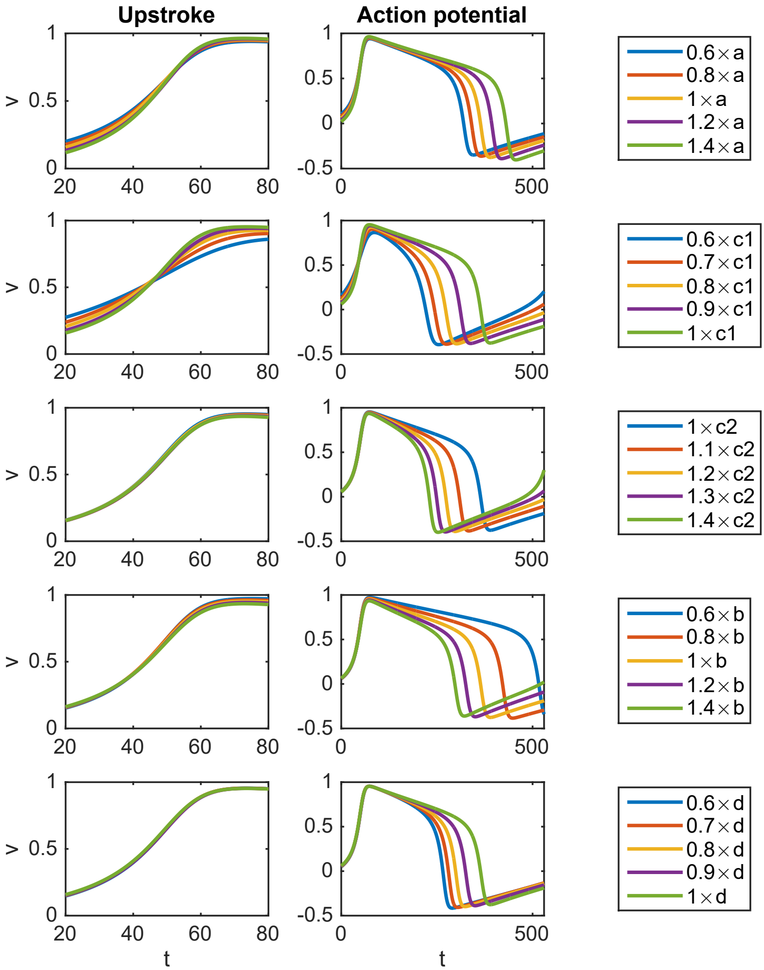

Fig. 2.6 The numerical solution, v_n, of the FitzHugh-Nagumo model, defined by the two equations $v' = c_1 v(v-a)(1-v) - c_2 w$, and $w' = b(v - dw)$. The parameters are as specified in (2.5), except that in each row, the value of either a, c_1, c_2, b, or d is adjusted. The legends at the right-hand side of each row specify the parameter changes. The time axes of the solutions are adjusted such that the maximal upstroke velocity occurs at the same time for all the parameter changes. The left panel shows the upstroke of the action potential and the right panel shows one action potential for each parameter set.

right panel, we consider a single action potential for the different parameter choices. We observe that all the parameters have a significant effect on the action potential duration.

References

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[2] Nagumo J, Arimoto S, Yoshizawa S (1962) An active pulse transmission line simulating nerve axon. Proceedings of the IRE 50(10):2061–2070

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