1. Matrix Methods for Neuroscience

1.1. Nerve Fibers and the Strang Quartet

In our first such example we investigate the response of a nerve fiber to a constant current stimulus. Ideally, a nerve fiber is simply a cylinder of radius a and length ℓ that conducts electricity both along its length and across its lateral membrane. We denote by ρ_i the resistivity in Ωcm of the cytoplasm that fills the cell, and by ρ_m, the resistivity in Ωcm^2 of the cell's lateral membrane.
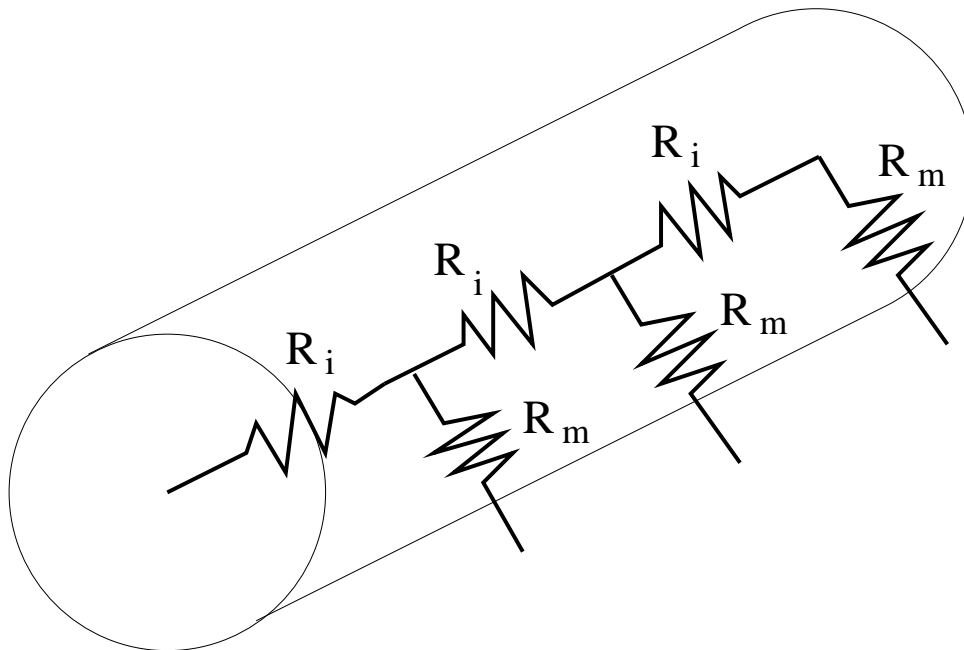

Figure 1.1. A 3 compartment model of a nerve cell.

Although current surely varies from point to point along the fiber it is hoped that these variations are regular enough to be captured by a multicompartment model. By that we mean that we choose a number N and divide the fiber into N segments each of length ℓ/N. Denoting a segment's axial resistance by

$$R_i = \frac{\rho_i \ell/N}{\pi a^2}$$

and membrane resistance by

$$R_m = \frac{\rho_m}{2\pi a \ell/N}$$

we arrive at the lumped circuit model of figure 1.1. For a fiber in culture we may assume a constant extracellular potential, e.g., zero. We accomplish this by connecting and grounding the extracellular nodes, see figure 1.2.
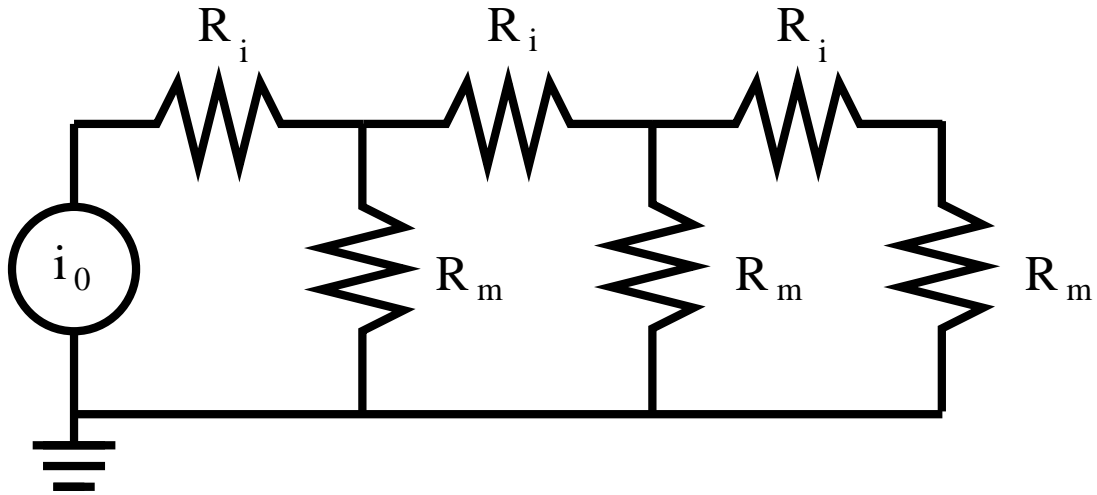
Figure 1.2. A rudimentary circuit model.

This figure also incorporates the exogeneous disturbance, a current stimulus between ground and the left end of the fiber. Our immediate goal is to compute the resulting currents through each resistor and the potential at each of the nodes. Our long–range goal is to provide a modeling methodology that can be used across the engineering and science disciplines. As an aid to computing the desired quantities we give them names. With respect to figure 1.3 we label the vector of potentials $x = [x_1 \ x_2 \ x_3 \ x_4]$ and vector of currents $y = [y_1 \ y_2 \ y_3 \ y_4 \ y_5 \ y_6]$. We have also (arbitrarily) assigned directions to the currents as a graphical aid in the consistent application of the basic circuit laws.
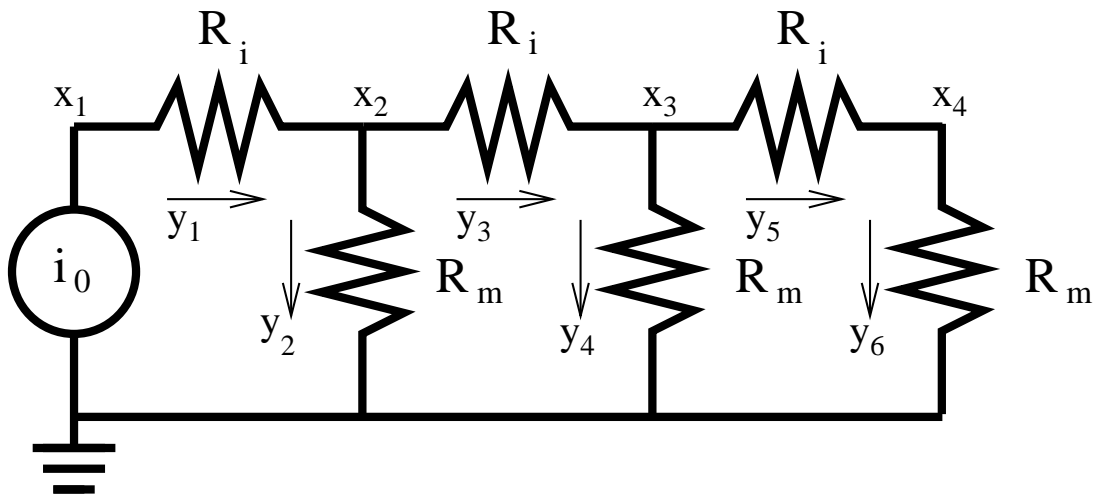

Figure 1.3. The fully dressed circuit model.

We incorporate the circuit laws in a modeling methodology that takes

the form of a Strang* Quartet

(S1) Express the voltage drops via $e = -Ax$.
(S2) Express Ohm's Law via $y = Ge$.
(S3) Express Kirchhoff's Current Law via $A^T y = -f$.
(S4) Combine the above into $A^T G A x = f$.

The A in (S1) is the node–edge adjacency matrix – it encodes the network's connectivity. The G in (S2) is the diagonal matrix of edge conductances – it encodes the physics of the network. The f in (S3) is the vector of current sources – it encodes the network's stimuli. The culminating $A^T G A$ in (S4) is the symmetric matrix whose inverse, when applied to f, reveals the vector of potentials, x. In order to make these ideas our own we must work many, many examples.

1.2. Example 1

With respect to the circuit of figure 1.3, in accordance with step (S1), we express the six potentials differences (always tail minus head)

$$e_1 = x_1 - x_2$$
$$e_2 = x_2$$
$$e_3 = x_2 - x_3$$
$$e_4 = x_3$$
$$e_5 = x_3 - x_4$$
$$e_6 = x_4$$

Such long, tedious lists cry out for matrix representation, to wit

$$e = -Ax \quad \text{where} \quad A = \begin{pmatrix} -1 & 1 & 0 & 0 \\ 0 & -1 & 0 & 0 \\ 0 & -1 & 1 & 0 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & -1 & 1 \\ 0 & 0 & 0 & -1 \end{pmatrix}$$

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Step (S2), Ohm's law, states that the current along an edge is equal to the potential drop across the edge divided by the resistance of the edge. In our case,

$$y_j = e_j/R_i, \; j = 1, 3, 5 \quad \text{and} \quad y_j = e_j/R_m, \; j = 2, 4, 6$$

or, in matrix notation,

$$y = Ge$$

where

$$G = \begin{pmatrix} 1/R_i & 0 & 0 & 0 & 0 & 0 \\ 0 & 1/R_m & 0 & 0 & 0 & 0 \\ 0 & 0 & 1/R_i & 0 & 0 & 0 \\ 0 & 0 & 0 & 1/R_m & 0 & 0 \\ 0 & 0 & 0 & 0 & 1/R_i & 0 \\ 0 & 0 & 0 & 0 & 0 & 1/R_m \end{pmatrix}$$

Step (S3), Kirchhoff's Current Law, states that the sum of the currents into each node must be zero. In our case

$$i_0 - y_1 = 0$$
$$y_1 - y_2 - y_3 = 0$$
$$y_3 - y_4 - y_5 = 0$$
$$y_5 - y_6 = 0$$

or, in matrix terms

$$By = -f$$

where

$$B = \begin{pmatrix} -1 & 0 & 0 & 0 & 0 & 0 \\ 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & -1 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 \end{pmatrix} \quad \text{and} \quad f = \begin{pmatrix} i_0 \\ 0 \\ 0 \\ 0 \end{pmatrix}.$$

Turning back the page we recognize in B the **transpose** of A. Calling it such, we recall our main steps

$$e = -Ax, \quad y = Ge, \quad \text{and} \quad A^T y = -f.$$

On substitution of the first two into the third we arrive, in accordance with (S4), at

$$A^T G A x = f. \tag{1.1}$$

This is a system of four equations for the 4 unknown potentials, x_1 through x_4. Such systems are solved by Gaussian Elimination. We leave this task to MATLAB's backslash command (see `fib1.m`)
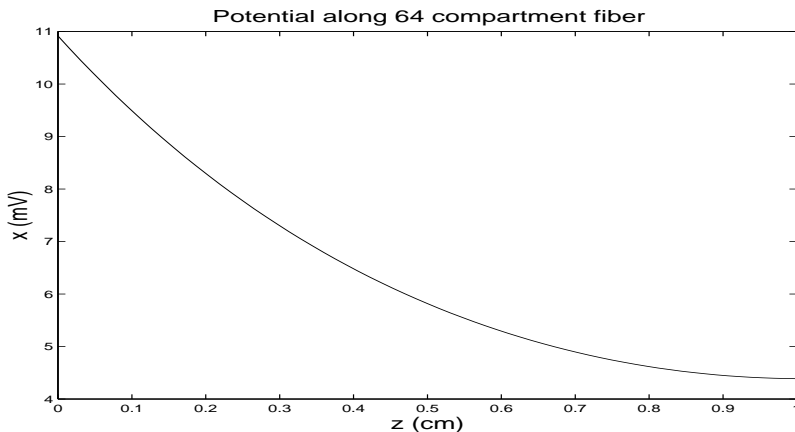

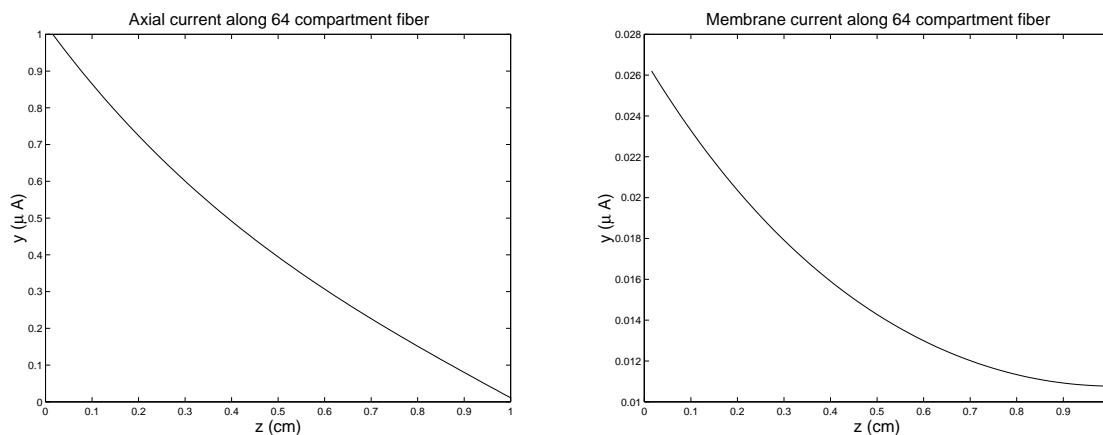
Figure 1.4. Results of a 64 compartment simulation.

Figure 1.5. Results of a 64 compartment simulation.

This program is a bit more ambitious than the above in that it allows us to specify the number of compartments and that rather than just spewing the x and y values it plots them as a function of distance along the fiber. We note that, as expected, everything tapers off with distance from the source and that the axial current is significantly greater than the membrane, or leakage, current.

1.3. Example 2

We have seen in the previous section how a current source may produce a potential difference across a cell's membrane. We note that, even in the absence of electrical stimuli, there is always a difference in potential between the inside and outside of a living cell. In fact, this difference is the biologist's

definition of 'living.' Life is maintained by the fact that the cell's interior is rich in potassium ions, K^+, and poor in sodium ions, Na^+, while in the exterior medium it is just the opposite. These concentration differences beget potential differences under the guise of the Nernst potentials

$$E_{Na} = \frac{RT}{F} \log\left(\frac{[Na]_o}{[Na]_i}\right) \quad \text{and} \quad E_K = \frac{RT}{F} \log\left(\frac{[K]_o}{[K]_i}\right)$$

where R is the gas constant, T is temperature, and F is the Faraday constant. Associated with these potentials are membrane resistances

$$\rho_{m,Na} \quad \text{and} \quad \rho_{m,K}$$

that together produce the ρ_m above via

$$1/\rho_m = 1/\rho_{m,Na} + 1/\rho_{m,K},$$

and produce the aforementioned rest potential

$$E_m = \rho_m(E_{Na}/\rho_{m,Na} + E_K/\rho_{m,K}).$$

With respect to our old circuit model, each compartment now sports a battery in series with its membrane resistance.
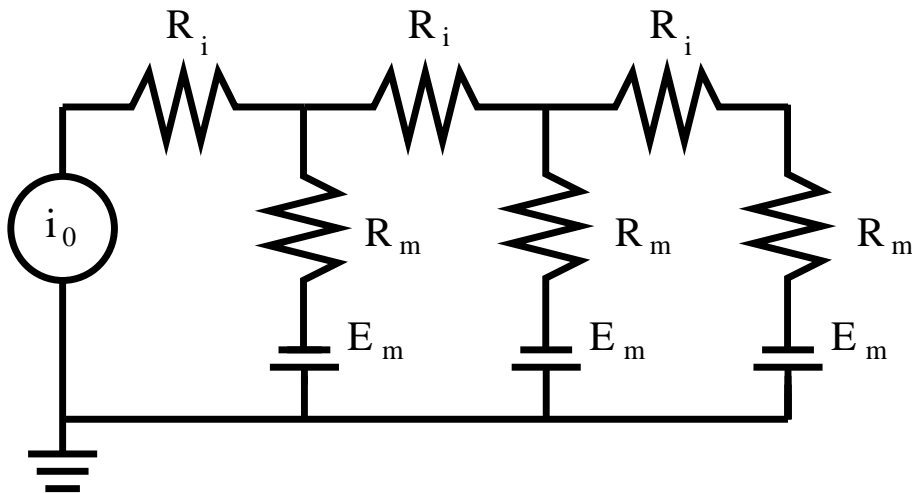

Figure 1.6. Circuit model with resting potentials.

Revisiting steps (S1–4) we note that in (S1) the even numbered voltage drops are now

$$e_2 = x_2 - E_m, \quad e_4 = x_3 - E_m \quad \text{and} \quad e_6 = x_4 - E_m.$$

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We accommodate such things by generalizing (S1) to

(S1') Express the voltage drops as $e = b - Ax$ where b is the vector of batteries.

No changes are necessary for (S2) and (S3). The final step now reads,

(S4') Combine (S1'), (S2) and (S3) to produce $A^T G A x = A^T G b + f$.

Returning to figure 1.6 we note that

$$b = -E_m [0\ 1\ 0\ 1\ 0\ 1]^T \quad \text{and} \quad A^T G b = (E_m / R_m)[0\ 1\ 1\ 1]^T.$$

This requires only minor changes to our old code. The new program is called `fib2.m` and results of its use are indicated in the next two figures.
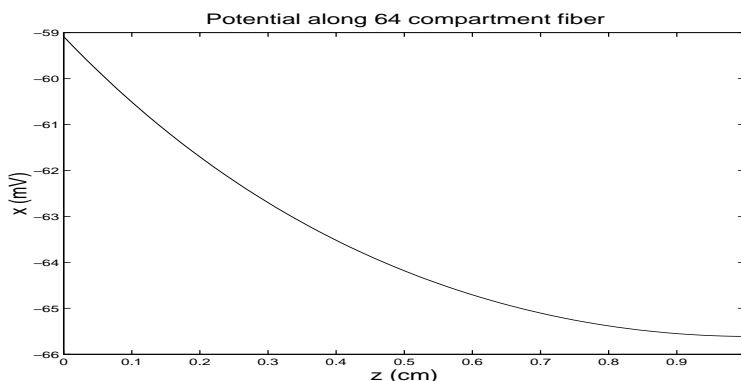

Figure 1.7. Results of a 64 compartment simulation with batteries.
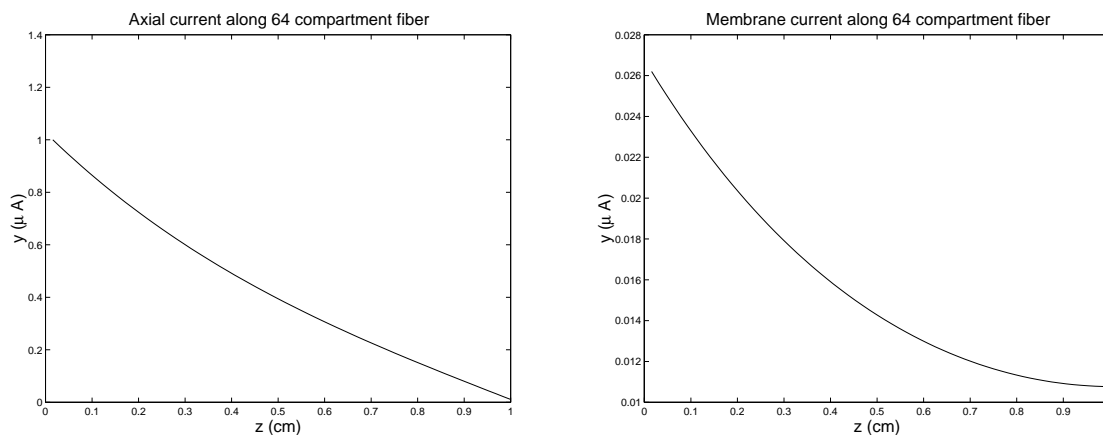

Figure 1.8. Results of a 64 compartment simulation with batteries.

1.4. Nerve Fibers and the Dynamic Strang Quartet

A nerve fiber's natural electrical stimulus is not direct current but rather a short burst of current, the so–called nervous impulse. In such a dynamic environment the cell's membrane behaves not only like a leaky conductor but also like a charge separator, or capacitor.
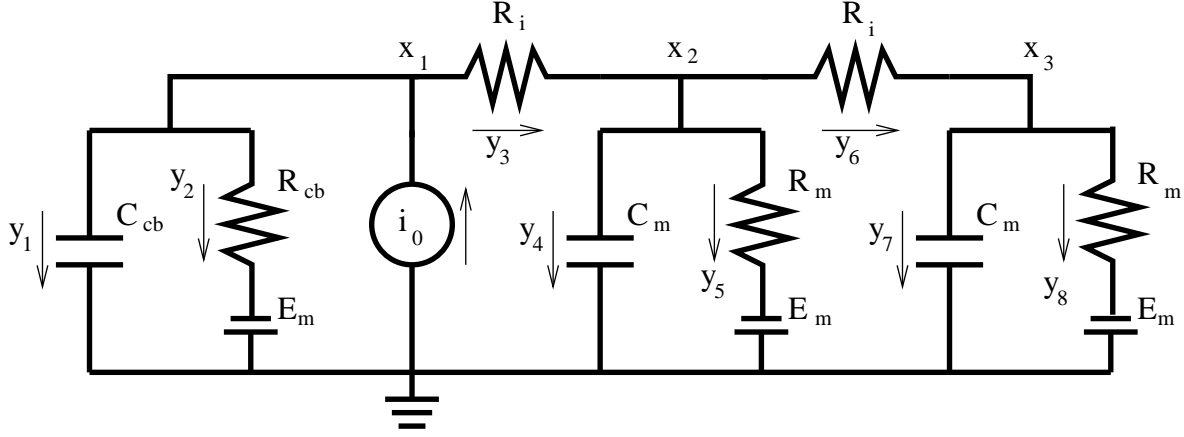
Figure 1.9. An RC model of a nerve fiber.

The typical value of a cell's membrane capacitance is

$$c = 1 \; (\mu F/cm^2)$$

where μF denotes micro–Farad. The capacitance of a single compartment is therefore

$$C_m = 2\pi a(\ell/N)c$$

and runs parallel to each R_m, see figure 1.9. This figure also differs from figure 1.4 in that it possesses two edges to the left of the stimuli. These edges serve to mimic that portion of the stimulus current that is shunted by the cell body. If A_{cb} denotes the surface area of the cell body then its capacitance and resistance are

$$C_{cb} = A_{cb}c \quad \text{and} \quad R_{cb} = A_{cb}\rho_m$$

respectively. We ask now how the static Strang Quartet should be augmented. Regarding (S1') we proceed as before. The voltage drops are

$$e_1 = x_1, \quad e_2 = x_1 - E_m, \quad e_3 = x_1 - x_2, \quad e_4 = x_2,$$
$$e_5 = x_2 - E_m, \quad e_6 = x_2 - x_3, \quad e_7 = x_3, \quad e_8 = x_3 - E_m,$$

and so

$$e = b - Ax \quad \text{where} \quad b = -E_m \begin{pmatrix} 0 \\ 1 \\ 0 \\ 0 \\ 1 \\ 0 \\ 0 \\ 1 \end{pmatrix} \quad \text{and} \quad A = \begin{pmatrix} -1 & 0 & 0 \\ -1 & 0 & 0 \\ -1 & 1 & 0 \\ 0 & -1 & 0 \\ 0 & -1 & 0 \\ 0 & -1 & 1 \\ 0 & 0 & -1 \\ 0 & 0 & -1 \end{pmatrix}$$

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In (S2) we must now augment Ohm's law with voltage–current law obeyed by a capacitor, namely – the current through a capacitor is proportional to the time rate of change of the potential across it. This yields, (denoting d/dt by $'$),

$$y_1 = C_{cb}e_1', \quad y_2 = e_2/R_{cb}, \quad y_3 = e_3/R_i, \quad y_4 = C_m e_4',$$
$$y_5 = e_5/R_m, \quad y_6 = e_6/R_i, \quad y_7 = C_m e_7', \quad y_8 = e_8/R_m,$$

or, in matrix terms,

$$y = Ge + Ce'$$

where

$$G = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1/R_{cb} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1/R_i & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1/R_m & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1/R_i & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1/R_m \end{pmatrix}$$

and

$$C = \begin{pmatrix} C_{cb} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & C_m & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & C_m & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

are the conductance and capacitance matrices.

As Kirchhoff's Current law is insensitive to the type of device occupying an edge step (S3) proceeds exactly as above.

$$i_0 - y_1 - y_2 - y_3 = 0 \quad y_3 - y_4 - y_5 - y_6 = 0 \quad y_6 - y_7 - y_8 = 0,$$

or, in matrix terms,

$$A^T y = -f \quad \text{where} \quad f = [i_0 \ 0 \ 0]^T.$$

Step (S4) remains one of assembling,

$$A^T y = -f \Rightarrow A^T(Ge + Ce') = -f \Rightarrow A^T(G(b - Ax) + C(b' - Ax')) = -f,$$

becomes

$$A^T CAx' + A^T GAx = A^T Gb + f + A^T Cb'. \tag{1.2}$$

This is the general form of the potential equations for an RC circuit. Regarding the circuit of figure 1.9 we find

$$A^T CA = \begin{pmatrix} C_{cb} & 0 & 0 \\ 0 & C & 0 \\ 0 & 0 & C \end{pmatrix} \quad A^T GA = \begin{pmatrix} G_{cb} + G_i & -G_i & 0 \\ -G_i & 2G_i + G_m & -G_i \\ 0 & -G_i & G_i + G_m \end{pmatrix}$$

$$A^T Gb = E_m \begin{pmatrix} G_{cb} \\ G_m \\ G_m \end{pmatrix} \quad \text{and} \quad A^T Cb' = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}.$$

and an initial (rest) potential of $x(0) = E_m[1\ 1\ 1]^T$.

It is customary to write such systems in the form

$$x' = Bx + g. \tag{1.3}$$

where, with respect to our fiber problem

$$B = -(A^T CA)^{-1} A^T GA$$
$$= \begin{pmatrix} -(G_{cb} + G_i)/C_{cb} & G_i/C_{cb} & 0 \\ G_i/C_m & -(2G_i + G_m)/C_m & G_i/C_m \\ 0 & G_i/C_m & -(G_i + G_m)/C_m \end{pmatrix} \tag{1.4}$$

and

$$g = (A^T CA)^{-1}(A^T Gb + f) = \begin{pmatrix} (G_{cb}E_m + i_0)/C_{cb} \\ E_m G_m/C_m \\ E_m G_m/C_m \end{pmatrix}.$$

1.5. The Backward–Euler Method

We "solve" this system of differential equations by replacing the derivative with a finite difference quotient. That is, one chooses a small dt and 'replaces' (1.3) with

$$\frac{x(t) - x(t - dt)}{dt} = Bx(t) + g(t). \tag{1.5}$$

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The utility of (1.5) is that it gives a means of solving for x at the present time, t, from knowledge of x in the immediate past, $t - dt$. For example, as $x(0)$ is supposed known we write (1.5) as

$$(I/dt - B)x(dt) = x(0)/dt + g(dt).$$

Solving this for $x(dt)$ we return to (1.5) and find

$$(I/dt - B)x(2dt) = x(dt)/dt + g(2dt)$$

and solve for $x(2dt)$. The general step from past to present,

$$x(jdt) = (I/dt - B)\backslash(x((j-1)dt)/dt + g(jdt)), \qquad (1.6)$$

is repeated until some desired final time, Tdt, is reached. This equation has been implemented in `fib3.m` with $dt = 1$ and B and g as above.

1.6. Exercises

[1] In order to refresh your matrix-vector multiply skills please calculate, by hand, the product $A^T G A$ in the 3 compartment case and write out the 4 equations in (1.1). The second equation should read

$$(-x_1 + 2x_2 - x_3)/R_i + x_2/R_m = 0. \qquad (1.7)$$

[2] We began our discussion with the 'hope' that a multicompartment model could indeed adequately capture the fiber's true potential and current profiles. In order to check this one should run `fib1.m` with increasing values of N until one can no longer detect changes in the computed potentials.

(a) Please run `fib1.m` with $N = 8, 16, 32$ and 64. Plot all of the potentials on the **same** (use `hold`) graph, using different line types for each. (You may wish to alter `fib1.m` so that it accepts N as an argument).

Let us now interpret this convergence. The main observation is that the difference equation, (1.7), approaches a differential equation. We can see this by noting that

$$dz \equiv \ell/N$$

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acts as a spatial 'step' size and that x_k, the potential at $(k-1)dz$, is approximately the value of the true potential at $(k-1)dz$. In a slight abuse of notation, we denote the latter

$$x((k-1)dz).$$

Applying these conventions to (1.7) and recalling the definitions of R_i and R_m we see (1.7) become

$$\frac{\pi a^2}{\rho_i} \frac{-x(0) + 2x(dz) - x(2dz)}{dz} + \frac{2\pi a\,dz}{\rho_m} x(dz) = 0,$$

or, after multiplying through by $\rho_m/(\pi a\,dz)$,

$$\frac{a\rho_m}{\rho_i} \frac{-x(0) + 2x(dz) - x(2dz)}{dz^2} + 2x(dz) = 0.$$

We note that a similar equation holds at each node (save the ends) and that as $N \to \infty$ and therefore $dz \to 0$ we arrive at

$$\frac{d^2 x(z)}{dz^2} - \frac{2\rho_i}{a\rho_m} x(z) = 0. \tag{1.8}$$

(b) With $\mu \equiv 2\rho_i/(a\rho_m)$ show that

$$x(z) = \alpha \sinh(\sqrt{\mu}z) + \beta \cosh(\sqrt{\mu}z) \tag{1.9}$$

satisfies (1.8) regardless of α and β.

We shall determine α and β by paying attention to the ends of the fiber. At the near end we find

$$\frac{\pi a^2}{\rho_i} \frac{x(0) - x(dz)}{dz} = i_0,$$

which, as $dz \to 0$ becomes

$$\frac{dx(0)}{dz} = -\frac{\rho_i i_0}{\pi a^2}. \tag{1.10}$$

At the far end, we interpret the condition that no axial current may leave the last node to mean

$$\frac{dx(\ell)}{dz} = 0. \tag{1.11}$$

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(c) Substitute (1.9) into (1.10) and (1.11) and solve for α and β and write out the final $x(z)$.

(d) Substitute into x the ℓ, a, ρ_i and ρ_m values used in `fib1.m`, plot the resulting function (using, e.g., `ezplot`) and compare this to the plot achieved in part (a).

[3] Adapt the Backward Euler portion of `fib3.m` so that one may specify an arbitrary number of compartments, as in `fib1.m`. Submit your well documented M-file along with a plot of x_1 and x_{10} *versus* time (on the same well labeled graph) for a nine compartment fiber of length $\ell = 1$ *cm*.

[4] We expect that the Backward Euler solution should approach the true solution as the time step, dt, approaches zero. To see this let us return to (1.6) and assume, for now, that $g \equiv 0$. In this case, one can reverse the above steps and arrive at the representation

$$x(jdt) = ((I - dtB)^{-1})^j x(0). \tag{1.12}$$

Now, for a fixed time t suppose that $dt = t/j$ and show (at least when B is one-by-one) that

$$\lim_{j \to \infty} ((I - (t/j)B)^{-1})^j x(0) = \exp(Bt)x(0).$$

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