Additional Problems and Solutions to "Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting"

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Solutions to Chapter 2

- (Ex. 6) The following MATLAB program consists of three separate files:

  File `main.m`

```
function parameters = main();
% File main.m, created by Eugene Izhikevich. August 28, 2001
% Uses voltage-clamp data from N voltage-step experiments to
% determine (in)activation parameters of a transient current.
% Data provided by user:
global  v times current E p q
load v.dat        % N by 2 matrix of voltage steps
                  % [from, to; from, to;...]
load times.dat    % Time mesh of the voltage-clamped data
load current.dat  % Matrix of the current values.
E = 50;           % Reverse potential
p = 3;            % The number of activation gates
q = 1;            % The number of inactivation gates
% Guess of initial values of parameters
% activation   V_1/2    k     V_max    sigma    C_amp    C_base
par(1:6) = [   -50     20     -40       30       0.5     0.1];
% inactivation V_1/2    k     V_max    sigma    C_amp    C_base
par(7:12) =[   -60     -5     -70       20        5        1];
par(13) = 1;      % Maximal conductance g_max
% If E, p, or q are not known, add par(14)=60, etc.
% and modify test.m
parameters = fmins('test',par);
```

  File `test.m`

```
function err = test(par);
```

```
% File test.m, created by Eugene Izhikevich. August 28, 2001
% Calculates current traces I using parameters par and
% returns the error between I and current.dat
global  v times current E p q pars;
pars = par(1:6);      % Activation variable m
m0=1./(1+exp(-(v(:,1)-pars(1))/pars(2)));
[t,m] = ode15s('gate',times,m0);
pars = par(7:12);     % Inactivation variable h
h0=1./(1+exp(-(v(:,1)-pars(1))/pars(2)));
[t,h] = ode15s('gate',times,h0);
I = par(13)*(m.^p.*h.^q)'.*((v(:,2)-E)*ones(1,length(times)));
err = sum(sum((current-I).^2))
% Output (not needed)
format short, [par(1:6);par(7:12)]
plot(times,I,'.-'); hold on;
plot(times,current,'o'); hold off;
drawnow;
```

File `gate.m`

```
function dxdt = gate(t,x);
% File gate.m, created by Eugene Izhikevich. August 28,2001
% Calculates the derivative of the gate dx/dt
global  v pars
xinf = 1./(1+exp(-(v(:,2)-pars(1))/pars(2)));
tau=pars(6)+pars(5)*exp(-(pars(3)-v(:,2)).^2/pars(4)^2);
dxdt = (xinf-x)./tau;
```

The values of voltage steps are in the file `v.dat`. Each row corresponds to a separate experiment. The first number is the holding potential, the second number is the step potential, e.g.

```
-50 -80
-50 -60
-50 -40
-50 -20
-50   0
```

describes 5 voltage-clamp experiments consisting of stepping from -50 mV to $-80, -60, -40, -20$, and 0 mV, respectively. The values of the current are in the file `current.dat`. For example, we use Hodgkin-Huxley's transient current $I_{\mathrm{Na,p}}$ to generate the following data

```
-0.77 -0.27 -0.11 -0.02 -0.01 -0.01 -0.01 -0.01 -0.01 -.02 -.02 -.02 -.02 -.02
-0.66 -0.56 -0.49 -0.34 -0.24 -0.21 -0.20 -0.20 -0.22 -.24 -.26 -.28 -.30 -.32
-0.54 -0.60 -0.67 -0.83 -1.02 -1.11 -1.13 -1.08 -0.99 -.82 -.70 -.62 -.57 -.53
-0.42 -0.65 -0.89 -1.58 -2.24 -2.33 -2.14 -1.58 -1.10 -.54 -.29 -.18 -.13 -.10
-0.30 -1.07 -1.98 -3.74 -3.94 -3.32 -2.71 -1.79 -1.18 -.52 -.23 -.10 -.05 -.02
```

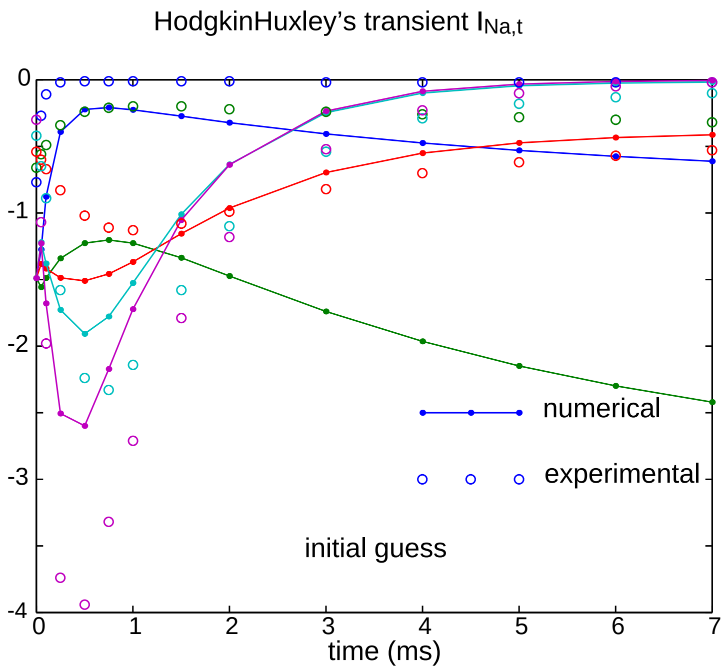

Figure 1: Initial output of the MATLAB numerical optimization procedure.

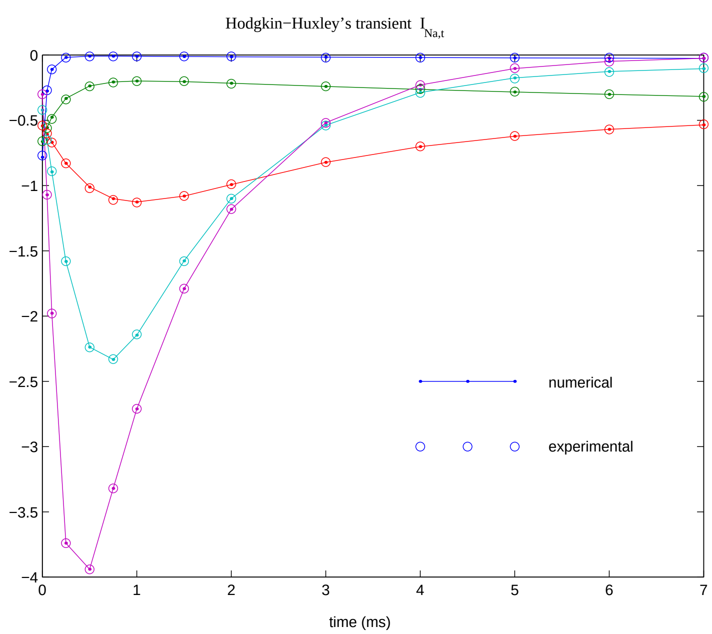

Figure 2: Final output of the MATLAB numerical optimization procedure.

which has 5 rows, each for each voltage step. The rows represent consecutive values taken at the time moments stored in the file `times.dat`, e.g.,

```
0 0.05 0.1 0.25 0.5 0.75 1 1.5 2 3 4 5 6 7
```

Thus, the first row of the file `current.dat` represents the values of the current right after the step from -50 mV to -80 mV, and taken at times 0 ms, 0.05 ms, 0.1 ms, etc. The current values are plotted as open circles in Fig. 1, which also depicts the current traces corresponding to the initial values of the parameters. The program `main.m` optimizes the values of parameters so that the numerical traces are close to the experimental values, as in Fig. 1.

- (Ex. 7) Instead of loading `v.dat`, use function $v(t)$ that returns the vector of voltage values at time t. Make appropriate modifications to the program, e.g., use `v(t)` instead of `v(:,2)` in `gate.m`, `v(0)` instead of `v(:,1)` in `test.m`, etc. The function

```
function voltage = v(t);
if (t==0)
   voltage = [-50;-50;-50;-50;-50];
else
   voltage = [-80;-60;-40;-20;0];
end;
```

  is equivalent to `v.dat` defined above. The function

```
function voltage = v(t);
if (t==0)
   voltage = [-10;-10;-10;-10;-10];
elseif (t<20)
   voltage = [-100;-80;-60;-40;-20];
else
   voltage = [50;50;50;50;50];
end;
```

  corresponds to the multiple voltage steps in Fig. 3.

1 Chapter 9

Simulate the canonical model for “Hopf/Hopf” bursting above with various choices of $\pm 1 \pm u$. Show that the model

$$z' = (u + i\omega)z - z|z|^2 \,,$$
$$u' = \mu(1 + u - a|z|^2) \,,$$

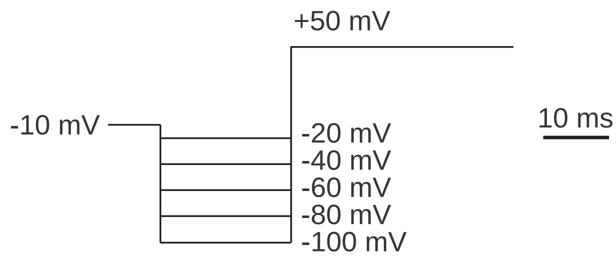

Figure 3: Multiple voltage steps are often needed to determine time constants of inactivation.

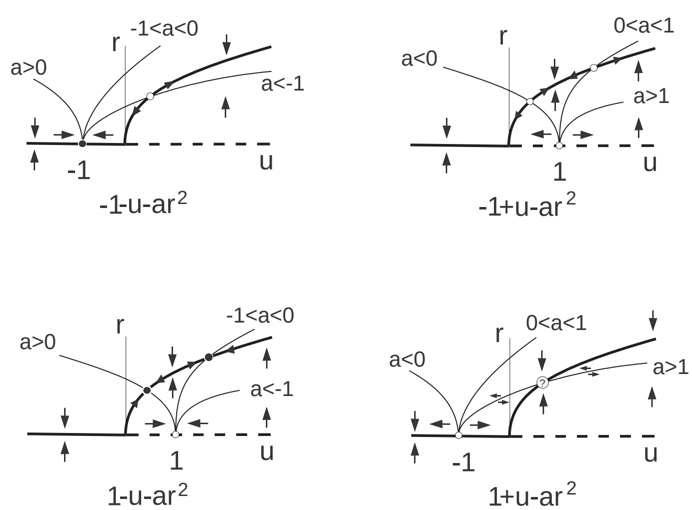

Figure 4: Intersections of nullclines $r' = 0$ (bold curve) and $u' = 0$ (thin curve) for various a and $\pm 1 \pm u - ar^2$

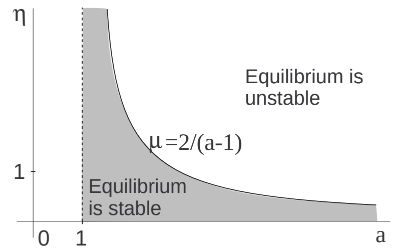

Figure 5: Region of stability of equilibrium.

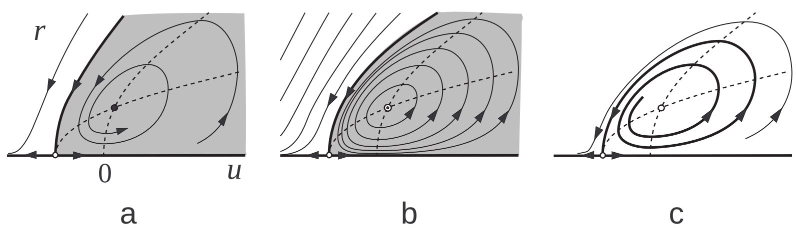

Figure 6: Phase portraits of the system for $a = 5$ and various μ. a. $\mu = 0.4$. b. $\mu = 0.5$. c. $\mu = 0.6$. Bold curves are separatrices of the saddle $(u, r) = (-1, 0)$, and dashed curves are nullclines of the system.

exhibits sustained bursting oscillations only when noise is added to the fast subsystem to alleviate the slow passage.

Solution: Phase portraits of the canonical model in polar coordinates $z = re^{\imath\omega t}$ are depicted in Fig. 4. The form

$$r' = ur - r^3$$
$$u' = \mu(\pm 1 \pm u - ar^2)$$

is the most interesting one. If $a \leq 1$, then this system does not have nontrivial equilibria and/or limit cycle attractors. If $a > 1$, then there is a unique nontrivial ($r \neq 0$) equilibrium, which is stable if and only if

$$\mu < \frac{2}{a-1} \; ;$$

see Figures 5, 6a and c. When $a > 1$ and $\mu = 2/(a-1)$, the system is a conservative dynamical system, which preserves the function

$$V(r, u) = e^{-u} r^{\mu} (1 + u - r^2)$$

along its trajectories; see Figure 6b.

Solutions of the system for $a = 19$ and various μ are depicted in Fig. 7. The model produces transient bursting behavior followed by either tonic spiking (when $\mu < 2/(a-1)$) or resting (when $\mu > 2/(a-1)$). Bursting persists when noise is added to the fast subsystem.

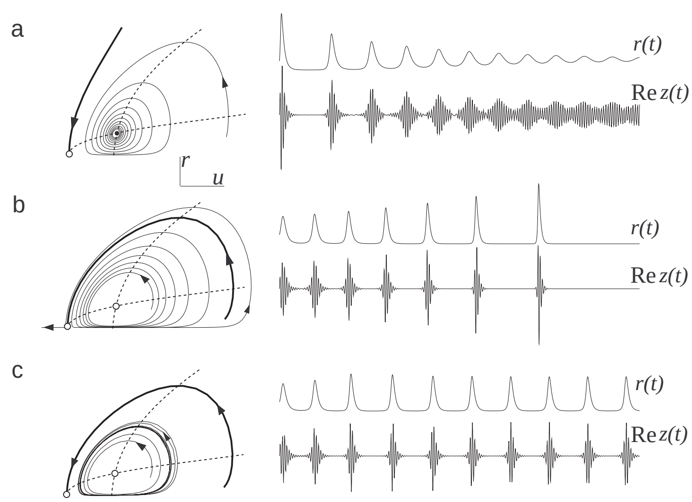

Figure 7: Simulations of the canonical model. Parameters: $\omega = 5$. a. $\mu = 1/12$. b. $\mu = 1/8$. c. $\mu = 1/8$, but additive noise of amplitude 10^{-3} is added to the right-hand side.