Lecture 6

The FitzHugh-Nagumo Model

6.1 The Nature of Excitable Cell Models

Classically, it was known that the cell membrane carries a potential across the inner and outer surfaces, hence a basic model for a cell membrane is that of a capacitor and resistor in parallel. The model equation takes the form

$$C_m \frac{dV}{dt} = - \frac{V - V_{eq}}{R} + I_{appl},$$

(6.1)

where $C_m$ is the membrane capacitance, $R$ the resistance, $V_{eq}$ the rest potential, $V$ the potential across the inner and outer surfaces, and $I_{appl}$ represents the applied current. In landmark patch clamp experiments in the early part of the 20th century, it was determined that many cell membranes are excitable, i.e., exhibit large excursions in potential if the applied current is sufficiently large. Examples include nerve cells and certain muscle cells, e.g., cardiac cells.

From 1948-1952, Hodgkin and Huxley conducted patch clamp experiments on the giant squid axon, a rather large part of nerve tissue suitable for experimentation given the technology of the time. Based on their experiments, they constructed a model for the patch clamp experiment in an attempt to give mathematical explanation for the axon’s excitable nature. A key part of their model assumptions was that the membrane contains channels for potassium and sodium ion flow. In effect, the $1/R$ factor in (6.1) became potential dependent for both channels. The underlying model equation is:

$$C_m \frac{dV}{dt} = - g_K n^4 (V - V_K) - g_{Na} m^3 h (V - V_{Na}) - g_L (V - V_L) + I_{appl},$$

(6.2)

Here the subscripts $K$, $Na$, and $L$ correspond to potassium, sodium, and leakage channels, respectively. The terms $g_K n^4$, $g_{Na} m^3 h$, and $g_L$ are the conductances...
(reciprocal of resistances). The variables $n$, $m$, and $h$ are hypothesized potential dependent gating variables whose dynamics were assumed to follow first order kinetics. The equations take the form

$$
\tau_w(V) \frac{dw}{dt} = w_\infty(V) - w, \quad w = n, m, h,
$$

(6.3)

where $\tau_w(V)$ and $w_\infty(V)$ are the time constant and rate constant determined from the experimental data.

Taken together, (6.2) and (6.3) represent a four dimensional dynamical system known as the Hodgkin-Huxley model. It does provide a basis for qualitative explanation of the formation of action potentials in the giant squid axon. Moreover, the model structure forms a basis for virtually all models of excitable membrane behaviour.

### 6.2 FitzHugh Model Reduction

In the mid-1950’s, FitzHugh sought to reduce the Hodgkin-Huxley model to a two variable model for which phase plane analysis applies. His general observation was that the gating variables $n$ and $h$ have slow kinetics relative to $m$. Moreover, for the parameter values specified by Hodgkin and Huxley, $n + h$ is approximately 0.8. This led to a two variable model, called the fast-slow phase plane model, of the form

$$
C_m \frac{dV}{dt} = -g_K n^4 (V - V_K) - g_{Na} m^3 n (V - V_{Na}) - g_L (V - V_L) + I_{app} \\
n_w(V) \frac{dn}{dt} = n_\infty(V) - n.
$$

In effect this provides a phase space qualitative explanation of the formation and decay of the action potential. (See Keener & Sneyd\(^1\).)

A further observation due to FitzHugh was that the $V$-nullcline had the shape of a cubic function and the $n$-nullcline could be approximated by a straight line, both within the physiological range of the variables. This suggested a polynomial model reduction of the form

$$
\frac{dv}{dt} = v(v - \alpha)(1 - v) - w + I \\
\frac{dw}{dt} = \varepsilon(v - \gamma w).
$$

(6.4)

Here, the model has been put in dimensionless form, $v$ represents the fast variable (potential), $w$ represents the slow variable (sodium gating variable), $\alpha$, $\gamma$, and $\varepsilon$ are constants with $0 < \alpha < 1$ and $\varepsilon \ll 1$ (accounting for the slow kinetics of the sodium channel). In 1964, Nagumo constructed a circuit using tunnel diodes for the nonlinear element (channel) whose model equations are those of FitzHugh (6.4). Hence the equations (6.4) have become known as the FitzHugh-Nagumo model.

### 6.3 Simulations and Phase Plane

We assume the parameters are such that precisely one equilibrium point exists. Further, we translate the model to place this equilibrium at $(0,0)$ as follows. Let

$$f(v) = v(v - \alpha)(1 - v),$$

and let $(v_{eq}, w_{eq})$ be the equilibrium point for (6.4). Then we can write the model equations in the form

$$\frac{dv}{dt} = f(v + v_{eq}) - f(v_{eq}) - w$$

$$\frac{dw}{dt} = \varepsilon(v - \gamma w).$$

Here we will illustrate the behaviour of the FitzHugh-Nagumo model using “typical” values for the parameters. Two Hopf bifurcation phenomena will be illustrated by varying $v_{eq}$ and by varying $\alpha$.

In the first case, we take values: $\alpha = 0.139$, $\varepsilon = 0.008$, $\gamma = 2.54$. The plots are shown in Figures 6.1 and 6.2 where we have set $v_{eq} = 0.07$ and $v_{eq} = 0.15$, respectively. The phase portraits with nullclines are shown on the left. Note how the orbits are driven by the nullclines. Further, note the position of the knee of the $v$-nullcline in relation to the equilibrium point in the two figures. (In the limit cycle case, the knee is to the left.) Numerically, the actual bifurcation value is approximately $v_{eq} = 0.085$. 

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In our second case we take \( v_{eq} = 0 \) and allow \( \alpha \) to vary and take on negative values. The plots are shown in Figures 6.3 and 6.4 where we have set \( \alpha = 0.139 \) and \( \alpha = -0.139 \), respectively. The other parameters are \( \varepsilon = 0.008 \) and \( \gamma = 1.5 \). Again we note in the phase plots how the orbits follow the nullcline fields and the location of the knee of the \( v \)-nullcline for the limit cycle.
6.4 Bifurcation Analysis

Here we will present the bifurcation analysis corresponding to Figures 6.3 and 6.4. We will see that the bifurcation point is $\alpha_0 = -\varepsilon \gamma$ with a limit cycle bifurcating for $\alpha < \alpha_0$.

Computing the Jacobian we have

$$J = J(0, 0) = \begin{bmatrix} -\alpha & -1 \\ \varepsilon & -\varepsilon \gamma \end{bmatrix}.$$
Hence, $Tr(J) = -(\alpha + \varepsilon \gamma)$ and $\det(J) = \varepsilon (\alpha \gamma + 1)$. The eigenvalues are given by

$$\lambda = \frac{-(\alpha + \varepsilon \gamma) \pm \sqrt{(\alpha + \varepsilon \gamma)^2 - 4\varepsilon (\alpha \gamma + 1)}}{2},$$

and the condition for the eigenvalues to be complex reads:

$$\varepsilon \gamma - 2\varepsilon^{1/2} < \alpha < \varepsilon \gamma + 2\varepsilon^{1/2}.$$ 

At $\alpha = -\varepsilon \gamma$, the eigenvalues are $\lambda = \pm i \eta$, where $\eta = \sqrt{\varepsilon (1 - \varepsilon \gamma^2)}$. The corresponding eigenvectors are given by:

$$\begin{bmatrix} 1 \\ \varepsilon \gamma - i \eta \end{bmatrix} \text{ and } \begin{bmatrix} 1 \\ \varepsilon \gamma + i \eta \end{bmatrix}.$$ 

We can transform the model equations into suitable form using the transformation

$$T = \begin{bmatrix} 1 & 0 \\ \varepsilon \gamma & \eta \end{bmatrix}, \text{ with } T^{-1} = \frac{1}{\eta} \begin{bmatrix} \eta & 0 \\ -\varepsilon \gamma & 1 \end{bmatrix}.$$ 

Setting

$$\begin{bmatrix} v \\ w \end{bmatrix} = T \begin{bmatrix} x \\ y \end{bmatrix},$$

we obtain

$$\begin{bmatrix} \dot{x} \\ \dot{y} \end{bmatrix} = \begin{bmatrix} \frac{\mu}{\eta} & -\eta \\ -\varepsilon \mu \eta & 0 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} + \begin{bmatrix} (1 - (\mu + \varepsilon \gamma)x^2 - x^3) \\ -\varepsilon \gamma (1 - (\mu + \varepsilon \gamma)x^2 + \varepsilon \gamma x^3) \end{bmatrix},$$

(6.5)

where we have set $\mu = -(\alpha + \varepsilon \gamma)$. This is the form appropriate to apply Theorem 5.4. We have

$$d = \left. \frac{d}{d\mu} \text{Re}\lambda \right|_{\alpha=-\varepsilon \gamma} = \frac{1}{2} > 0.$$ 

Further, denoting the nonlinear terms in (6.5) by $f(x, y)$ and $g(x, y)$, then

$$a = \frac{1}{16} f_{xxx} + \frac{1}{16\eta} \left. (-f_{xx}g_{xx}) \right|_{(0, 0, -\varepsilon \gamma)}$$

$$= \frac{3}{8} + \frac{\gamma (1 - \varepsilon \gamma)^2}{4 (1 - \varepsilon \gamma^2)}.$$ 

For the parameters given above ($\varepsilon = 0.008$, $\gamma = 1.5$) we have $a = -0.02... < 0$. Consequently we can conclude that a limit cycle bifurcates for $\mu > 0$, i.e. $\alpha < -\varepsilon \gamma$.

This is what was desired.