The dynamical effects of dendritic structure on neural systems

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The Dynamical Effects of Dendritic Structure on Neural Systems

by

Barry-Jon De Souza

A Doctoral Thesis

Submitted in partial fulfillment of the requirements

for the award of

Doctor of Philosophy in Mathematics of Loughborough University

March 2000

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Results! Why man, I have gotten a lot of results. I know several thousand things that won't work.

T.A. Edison

The interests of a writer and the interests of his readers are never the same, and if, on occasion they happen to coincide this is a lucky accident.

W.H. Auden
Abstract

The role of the dendritic tree and the way it functions within a neuron has been of interest to neurologists for over a century. As investigative techniques have become more sophisticated and thus revealing, our perception of the dendrites as being purely an information gathering component has changed to one where the dendritic tree may be viewed as a highly complex, nonlinear information processor [Mel (1994)]. In spite of this most mathematical studies of the dynamical behaviour of neural populations have neglected the influence of the dendritic tree. The aim of this thesis is to address this imbalance.

We thus re-examine, from a dendritic perspective, two important features of neurobiological systems: that of neural pattern formation and mode-locking. This is accomplished by including a simple representation of the dendritic tree [Rall (1959), Koch (1984)] into the standard mathematical models of neural pattern formation [Murray (1993), Ermentrout & Cowan (1979)] and mode-locking [Van Vreeswijk et al. (1994), Coombes & Bressloff (1999)]. We then fully investigate each model, through a mixture of analysis and computer simulation, emphasising the dynamical effects of the dendritic cable throughout.

Keywords

dendrites
cable theory
passive
quasi-active
spatial pattern formation
Turing instability
coupled neuronal oscillators
integrate-and-fire
mode-locking
phase-locking
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Contents

1 Introduction ............................................. 1
   1.1 Overview of thesis ..................................... 3

2 The Neuron: Structure and Function ......................... 7
   2.1 Neuronal Structure .................................... 7
      2.1.1 Soma ............................................... 8
      2.1.2 Axon ............................................... 8
      2.1.3 Dendrites ......................................... 9
      2.1.4 Synapses ......................................... 11
      2.1.5 Glia ............................................... 12
   2.2 Action Potentials: Generation and Propagation ............ 12
      2.2.1 Resting potential .................................. 12
      2.2.2 Action potential generation ......................... 13
      2.2.3 Action potential propagation ....................... 14
      2.2.4 Synaptic transmission ............................... 15
   2.3 Dendritic Information Processing ........................ 16
      2.3.1 Synaptic placement .................................. 17
      2.3.2 Passive membrane properties ....................... 17
3 Cable Theory for Dendritic Neurons

3.1 Introduction ................................................. 22

3.2 The Cable Equation ........................................... 23

3.2.1 Cable equation for passive dendrites ......................... 24

3.2.2 Boundary and initial conditions .............................. 25

3.3 Solution of the Passive Cable Equation ......................... 27

3.3.1 Steady-state solution ....................................... 27

3.3.2 Time-dependent solutions .................................... 28

3.4 Realistic Dendritic Models .................................... 32

3.4.1 Realistic dendritic morphologies ............................. 33

3.4.2 Compartmental modelling ................................. 35

3.4.3 Numerical methods ........................................... 38

3.5 Cable Theory for Quasi-Active Dendrites ....................... 39

3.5.1 Introduction .................................................. 39

3.5.2 Cable equation for quasi-active dendrites .................. 40

3.6 Solution of the Quasi-Active Cable Equation .................... 44

3.6.1 Steady-state solutions ...................................... 45

3.6.2 Time-dependent solutions .................................... 45

3.6.3 Numerical methods ........................................... 48

4 Neural Pattern Formation ........................................ 49

4.1 Introduction .................................................. 49

4.1.1 Ocular dominance stripes ................................. 49
4.1.2  Visual hallucination patterns ........................................ 51

4.2  Morphogenesis ................................................................. 52

4.2.1  Turing mechanisms ....................................................... 52

4.3  Simple Activation-Inhibition Model ...................................... 54

4.3.1  Introduction ................................................................. 54

4.3.2  The model ................................................................. 55

4.3.3  Linear stability analysis ................................................ 57

4.3.4  Numerical results ......................................................... 59

5  Neural Pattern Formation with Passive Dendritic Structure 61

5.1  Introduction ................................................................. 61

5.2  The model ................................................................. 62

5.3  Linear Stability Analysis ................................................ 66

5.3.1  Turing instability ....................................................... 67

5.3.2  Static network patterns ............................................... 68

5.3.3  Dynamic network patterns ........................................... 68

5.3.4  Dendritic patterns ...................................................... 76

5.4  Numerical results ......................................................... 77

5.4.1  Dynamic patterns (uncorrelated weights) ......................... 79

5.4.2  Static patterns (correlated weights) ................................ 79

5.5  Bifurcation analysis ...................................................... 83

6  Neural Pattern Formation with Quasi-Active dendritic structure 87

6.1  Introduction ................................................................. 87

6.2  The model ................................................................. 88
6.3 Linear stability analysis ........................................ 89
6.4 Numerical results ............................................... 94

7 The Dynamics of Coupled Neuronal Oscillators with Dendritic Structure ........................................... 96

7.1 Introduction ................................................... 96
7.2 Degrees of Locking Between Oscillators ......................... 97
  7.2.1 Definitions ................................................ 97
7.3 The Relevance of Neurobiological Rhythms ......................... 99
  7.3.1 Mode-locking .............................................. 99
  7.3.2 Phase-locking ............................................ 101
  7.3.3 Synchronization ........................................... 101
7.4 The Integrate-and-Fire Model ................................ 102
  7.4.1 Introduction and definition ................................ 102
  7.4.2 The Hodgkin-Huxley equations ............................. 103
7.5 Mode-Locking and Arnold tongues for an integrate-and-fire neuron with dendritic structure ...................... 108
  7.5.1 Introduction ............................................... 108
  7.5.2 Circle map dynamics ...................................... 108
  7.5.3 IF dynamics ............................................. 110
  7.5.4 Mode-locking considerations for a driven IF oscillator .... 112
  7.5.5 The model ................................................ 114
  7.5.6 Numerical considerations ................................ 117
  7.5.7 Mode-locked solutions and Arnold tongues ............... 118
7.6 Phase-locking between two integrate-and-fire neurons with dendritic structure .................................. 123
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.6.1</td>
<td>Introduction</td>
<td>123</td>
</tr>
<tr>
<td>7.6.2</td>
<td>The model</td>
<td>123</td>
</tr>
<tr>
<td>7.6.3</td>
<td>Phase-locked solutions</td>
<td>126</td>
</tr>
<tr>
<td>8</td>
<td>Conclusions</td>
<td>132</td>
</tr>
<tr>
<td>9</td>
<td>Bibliography</td>
<td>137</td>
</tr>
</tbody>
</table>
List of Figures

2.1 The neuron and its constituent parts. Reprinted from Llinás (1988) .... 9

2.2 Dendritic morphologies (the cells are not drawn to scale). (A) α motoneuron in spinal cord of cat (2.6 mm). (B) Spiking interneuron in mesothoracic ganglion of locust (0.54 mm). (C) Layer 5 neocortical pyramidal cell in rat (1.03 mm). (D) Retinal ganglion cell in postnatal cat (0.39 mm). (E) Amacrine cell in retina of larval tiger salamander (0.16 mm). (F) Cerebellar Purkinje cell in human. (G) Relay neuron in rat ventrobasal thalamus (0.35 mm). Reprinted from Mel (1993) ........ 10

2.3 A Synapse. As the diagram shows the synapse consists of two parts: the knoblike tip of an axon terminal and the receptor region on the surface of another neuron. The membranes are separated by a synaptic cleft some 20-30 nanometres across. Within the axon terminal, there exists stored vesicles of chemical transmitters. These are released upon the arrival of an action potential. Reprinted from Llinás (1988) .... 11

2.4 The generation of an action potential. As the action potential comes into existence and the membrane potential shifts rapidly from $-70 \, mV$ towards $+50 \, mV$, the closed sodium channels pop open and then close again. Meanwhile, the many fewer closed potassium channels pop open and then close again producing the afterpotential (see 6). Reprinted from Thompson (1993). 14
2.5 A back-propagating action potential. At the top of the Figure is a representation of a CA1 neuron with two whole cell recordings, one in the soma and one situated roughly 250 μm away from the soma in the dendrites. An action potential is fomented in the soma by current injection. As we have described, it begins in the axon and then propagates into the soma and eventually into the dendrites. The delay is naturally caused by the conduction time (the conduction velocity of back-propagation is about 0.3 m/s). One should also note that the action potential in the dendrites is smaller than that in the soma. This is due to the high density of A-type \( K^+ \) channels. The bottom part of the Figure, demonstrates the response in the soma and dendrites to a train of action potentials. The action potentials in the soma are all approximately the same size, whereas those in the dendrites undergo a frequency-dependent decline in amplitude because of slow inactivation of \( Na^+ \) channels and the high density of \( K^+ \) channels [Colbert et al. (1997)]. Reprinted from Shepherd (1998).

3.1 One dimensional view of cable. This diagram is based on one in Mel (1994).

3.2 (a) Ladder representation of a one-dimensional cable with frequency dependent membrane impedance \( z_m(\omega)\) and longitudinal resistance \( r_a\). (b) Electric circuit of a passive membrane. The parameters \( r, c \) are equivalent to \( R_m \) and \( C_m \).

3.3 Modulus of the transfer function \( |\hat{G}(0, \omega)|^2 \) (in units of \( 1/D^2 r_a \)) as a function of frequency (in units of \( 1/\tau \)) for a passive membrane. Here \( D = r_a = \tau = 1 \). The low-pass filtering properties can be seen clearly. The maximum is unmistakably located at zero.

3.4 Pictorial representation of a branching structure replaced by an equivalent cylinder. Here the two daughter branches are identical (both have diameter \( d_1 \) and length \( L_1 \)). Using the equivalent cylinder approximation, the uppermost structure can be replaced by an unbranched cylinder of length \( L_0 + L_1 \) and its diameter is the same as the parent branch.

3.5 Equivalent circuit for a compartmental model of a chain of successive cylindrical segments of a passive dendritic membrane [Bressloff & Coombes (1997)].

3.6 Effective impedance diagram associated with the linearized potassium current for the Hodgkin-Huxley system.
3.7 Electrical RLC circuit mimicking the linearized response of the Hodgkin-Huxley equations.

3.8 (a) Ladder representation of a one-dimensional cable with frequency dependent membrane impedance \( z_m(\omega) \) and longitudinal resistance \( r_a \). (b) Electric circuit of a linearized (quasi) active membrane.

3.9 Modulus of transfer function \( |\tilde{G}(0,\omega)|^2 \) (in units of \( 1/D^2r_a \)) as a function of frequency \( \omega \) (in units of \( 1/\tau \)) for various values of the inductive resistance \( r_l \). Here \( D = r_a = \tau = 1 \) and \( l = 0.2 \) Hm\(^2\). A transition from band-pass to low-pass can be seen as \( r_l \) increases. (a) \( r_l = 0.0 \), (b) \( r_l = 0.1 \), (c) \( r_l = 0.5 \), (d) \( r_l = 1.0 \) \( \Omega \)m\(^2\).

4.1 Spatial pattern of ocular dominance stripes in the visual cortex of a macaque monkey. The dark band areas receive input from one eye while the unshaded regions receive input from the other eye. Reprinted from Murray (1993).

4.2 Typical examples of the basic pattern types observed by hallucinating subjects. (a) lattice, (b) cobweb, (c) spiral, (d) tunnel or funnel. Reprinted from Ermentrout & Cowan (1979).

4.3 One-dimensional network of neurons. \( W(x - x') \) specifies the connectivity function from a neuron located at \( x' \) to a neuron at \( x \). \( f(U) \) is the output firing-rate function for a given somatic potential \( U \).

4.4 Mexican Hat Function \( J(x) \) given by equation (4.5) with \( \Lambda = +1 \), \( \gamma_1 = 0.2 \), \( \gamma_2 = 0.1 \) and \( \Gamma = 0.55 \).

4.5 The firing-rate function \( f(U) \) given by equation (4.6) with \( \kappa = 1 \).

4.6 Fourier transform of the Mexican Hat function \( \tilde{J}(p) \). A static Turing instability occurs at the critical point \( W = W_0 \) and the associated wave number is \( \pm p_c \). The parameter values are the same as for Figure (4.4).

4.7 Steady-state pattern arising from a static Turing instability in a one-dimensional array of neurons. The parameters took the following values: \( \Lambda = +1 \), \( \gamma_1 = 1.0 \), \( \gamma_2 = 0.5 \), \( \Gamma = 0.53 \) and \( W_0 = 10.0 \).
5.1 One-dimensional network of analog neurons with dendritic structure represented by a semi-infinite cable. \( W(\xi, x, x') \) specifies the axo-dendritic connections from neuron \( x' \) to neuron \( x \) and \( f(U) \) is the output firing-rate function for a given somatic potential \( U \).

5.2 Uncorrelated weights. Synaptic connections are located at the point \( \xi_0 \) on the dendritic cable irrespective of the positions of the neurons in the network.

5.3 Correlated weights. Synapses which are correlated with respect to the relative positions of the interacting cells in the network.

5.4 Plot of function \( H(\omega, \xi_0) \) against \( \omega \) (with \( \varepsilon = 1 \)) for \( \xi_0 = 2 \). The intercept \( \omega_0 \) determines the pair of pure imaginary roots at the Hopf bifurcation point associated with a dynamic Turing instability for uncorrelated weights.

5.5 Plot of \( \tilde{J}(p) \) given by equation (4.9) with \( \gamma_1 = 1.0, \gamma_2 = 0.5, \Gamma = 0.8 \) and \( \Lambda = +1 \) (short-range excitation, long-range inhibition).

5.6 Static Turing instability versus dynamic bulk instability for \( \tilde{J}(p) \) above [Figure (5.5)]. Plot of critical weights \( W_{0e} \) (dynamic) and \( W'_{0e} \) (static) as a function of the dendritic co-ordinate \( \xi_0 \). The system undergoes a static Turing instability for \( \xi_0 < \xi_{0e} \) and a dynamic bulk instability for \( \xi_0 > \xi_{0e} \) with \( \xi_{0e} \approx 3.2 \).

5.7 Plot of \( \tilde{J}(p) \) given by equation (4.9) with \( \gamma_1 = 1.0, \gamma_2 = 0.5, \Gamma = 0.53 \) and \( \Lambda = +1 \) (short-range excitation, long-range inhibition).

5.8 Plot of critical weights for \( \tilde{J}(p) \) as shown in Figure (5.7). In this case the system only undergoes a static Turing instability since \( W'_{0e} < W_{0e} \) for all \( \xi_0 \).

5.9 Plot of \( \tilde{J}(p) \) given by equation (4.9) with \( \gamma_1 = 1.0, \gamma_2 = 0.5, \Gamma = 0.53 \) and \( \Lambda = -1 \) (short-range inhibition, long-range excitation).

5.10 Dynamic Turing instability versus static bulk instability for \( \tilde{J}(p) \) as shown in Figure (5.9). Plot of critical weights \( W_{0e} \) (dynamic) and \( W'_{0e} \) (static) as a function of dendritic co-ordinate \( \xi_0 \). The system undergoes a static bulk instability for \( \xi_0 < \xi_{0e} \) and a dynamic Turing instability for \( \xi_0 > \xi_{0e} \) with \( \xi_{0e} \approx 1.9 \).

5.11 Plot of \( \tilde{J}(p) \) given by equation (4.9) with \( \gamma_1 = 1.0, \gamma_2 = 0.5, \Gamma = 0.8 \) and \( \Lambda = -1 \) (short-range inhibition, long-range excitation).
5.12 Plot of critical weights for $\bar{J}(\xi)$ as shown by Figure (5.11). Here the system only undergoes a static bulk instability since $W_{0c}'' < W_{0c}$.

5.13 Bulk instability in a one-dimensional network with an uncorrelated weight distribution given by equations (4.5) and (5.4), with $P(\xi) = \delta(\xi - \xi_0)$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.53$ and $\Lambda = -1$. Here $\xi_0 = 0.4 < \xi_{0c}$ and $W_0 = 40.0$. The steady-state somatic potential $U$ is plotted as a function of network co-ordinate $x$ and time $t$.

5.14 Dynamic Turing instability. Same as in Figure (5.13) with $\xi_0 = 2 > \xi_{0c}$ and $W_0 = 80$.

5.15 Steady-state pattern arising from a static Turing instability in a one-dimensional network with a correlated weight distribution given by equations (4.5) and (5.5), with $\alpha(x) = 0.1|x|$, $\gamma_1 = 0.2$, $\gamma_2 = 0.1$, $\Gamma = 0.9$, $\Lambda = +1$ and $W_0 = 50.0$. The steady-state dendritic potential $V(\xi, x)$ is plotted as a function of dendritic co-ordinate $\xi$ and network co-ordinate $x$.

5.16 Steady-state pattern arising from a static Turing instability. Same as in Figure (5.15) but from a different angle. This clearly shows the pattern along the dendritic cable.

5.17 Plot of $U(x)$ as a function of $x$. Same parameter values as Figure (5.15).

5.18 Plot of $V(\xi, x)$ as a function of $\xi$ for fixed $x$. Same parameter values as Figure (5.15).

6.1 One-dimensional network of analog neurons with quasi-active dendritic structure represented by a semi-infinite modified cable. $W(\xi_0, x, x')$ represents the connectivity function from neuron $x'$ to a point $\xi_0$ on the dendrite of neuron $x$ and $f(V(0, x'))$ is the output firing-rate, noting that the soma’s potential is approximated by $V(0)$.

6.2 Solution of equations (6.8) and (6.9). Here $f_1(\omega) = \tan(b(\omega)\xi_0)$ and $f_2(\omega) = -b(\omega)/a(\omega)$ with $\xi_0 = 1$. The inductive resistance $r_l = 10.0\ \Omega m^2$ for this plot thus representing the passive scenario.

6.3 Same as for Figure (6.2), this time however $r_l = 0.1\ \Omega m^2$, thereby representing the quasi-active scenario.
6.4 The function $b(\omega)$ plotted for the quasi-active case ($r_l = 0.1$) and passive case ($r_l = 10.0$). Here $r_l$ has units of $\Omega m^2$. The extra zero for $b(\omega)$ can clearly be seen for the quasi-active case.

6.5 Critical couplings $W_0^q$ and $W_0^p$ as a function of the inductive resistance $r_l$ (in units of $\Omega m^2$). There exists a critical inductive resistance $r_{lc} \approx 0.45$ such that for $r_l < r_{lc}$ a dynamic Turing instability occurs. Whereas if $r_l > r_{lc}$ a static Turing instability is observed.

6.6 Dynamic (time-periodic) instability in a one-dimensional network of analog neurons. We use an uncorrelated weight distribution together with a standard Mexican Hat function as specified by equation (6.3), with parameter values $\Lambda = +1$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$ and $\Gamma = 0.53$. Here $\xi_0 = 1.0$, $r_l = 0.1$ ($r_l < r_{lc}$) and $W_0 = 20.0$. The approximated somatic potential $V(0,x)$ is plotted as a function of network co-ordinate $x$ and time $t$. The distance $x$ is measured in units of $\Delta x$ where $\Delta x = 0.2$.

6.7 Static Turing instability. Same as Figure (6.6) but with $r_l = 10.0$ ($r_l > r_{lc}$).

7.1 An example of a 2:3 mode-locked solution that may arise in a periodically forced system. The forcing itself being a stream of spikes. Note that the system fires 3 spikes (with phases $\phi_0$, $\phi_1$, $\phi_2$) for every two periods of the driving signal.

7.2 A simple pictorial representation of phase-locking between two neurons, that is to say $\phi_1 - \phi_2 = \text{const}$. An entrainment condition has been applied, thus each neuron has the same period $T$.

7.3 The various degrees of locking of oscillators which we study and how they relate to one another. We again ask the reader to note that the phase-locking scenarios (the inner most circle) which we consider are all contained within a general entrainment regime.

7.4 A simple representation of Integrate-and-Fire dynamics.

7.5 Arnold tongues for the sine circle map. The dashed lines indicate the area of overlapping tongues. Reprinted from Jensen et al. (1984).

7.6 Mode-locking model. A periodic train of spikes is fed into the dendritic cable at a point $\xi_0$. We then compare the output train of spikes with the periodic input train of spikes.
7.7 The tongue structure for 1:1, 1:2 and 2:3 mode-locked solutions for a passive
cable. Here \( \epsilon = 4, l = 0.2 \) and \( r_I = 100.0 \Omega m^2 \).

7.8 Plot of average firing frequency versus dendritic location, obtained by di-
rectly simulating the equations of motion. The dominant solutions are
clearly shown to be 1:1, 1:2 and 2:3. The parameter values are the same as
for the ones above with \( \tau_s = 1 \).

7.9 Spike train pictures showing (a) 1:1 mode-locking (\( \xi_0 = 0.930 \)), (b) 2:3
mode-locking (\( \xi_0 = 0.675 \)) and (c) 1:2 mode-locking (\( \xi_0 = 0.435 \)). The
value of \( \tau_s \) remained at 1 throughout and the other parameter values re-
mained unchanged from Figure (7.7). The taller spikes represent the peri-
odic input whilst the smaller ones are the output from the neuron.

7.10 The effect of increasing \( \epsilon \) on the passive 1:1 tongue structure. Here \( l = 0.2 \)
and \( r_I = 100.0 \Omega m^2 \).

7.11 The effect of increasing \( r_I \) (in units of \( \Omega m^2 \)) on the 1:1 tongue structure.
Here \( \epsilon = 10 \) and \( l = 0.2 \).

7.12 Phase-locking model. A pair of identical IF neural oscillators coupled to-
gether via axo-dendritic synapses. The spike trains of each neuron is fed
into a point \( \xi_0 \) on the others dendritic cable.

7.13 Stability regions for the synchronous state in the weak coupling regime
plotted in (\( \xi_0, r_I \)) parameter space (\( r_I \) in units of \( 10^{-1} \Omega m^2 \) and \( \xi_0 \) in units
of \( \sigma \)). Black(white) denotes stability (instability). Here \( T_0 = 4.18879 \).

7.14 Bifurcation diagram for a weakly-coupled quasi-active system (\( r_I = 0.1 \Omega m^2 \)).
Stable branches are given by solid lines whereas the unstable ones are given
by the dashed ones.

7.15 Bifurcation diagram for a weakly-coupled passive system (\( r_I = 100 \Omega m^2 \)).
Stable branches are given by solid lines whereas the unstable ones are given
by the dashed ones.

7.16 Bifurcation diagram for a strongly coupled (\( \epsilon = 1.0 \)) quasi-active system
(\( r_I = 0.1 \)). Stable branches are given by solid lines whereas the unstable
ones are given by the dashed ones.
Chapter 1

Introduction

In any field find the most interesting thing, and then research it.

John Archibald Wheeler

The human brain is commonly described as the most complex system in the known universe. Its appearance belies the elaborate and intricate workings that characterise this complexity. Indeed from roughly three pounds of convoluted folds and flaccid matter has emerged such works as the micro-chip, Pet Sounds, calculus and War and Peace [Koch & Laurent (1999)]. It may be thought as paradoxical that the brain's complexity which obviously underlies these remarkable achievements prevents us, at present from fully comprehending it.

Our understanding of the brain is undoubtedly improving, however admittedly there is still much to learn. In a bid to concentrate and encourage the global scientific community, the former president of the United States, George Bush, during his term in office declared the 1990's as the 'Decade of the Brain'. Such initiatives as these have, to some extent fuelled both the scientists' and the public's interest in the brain. Indeed, it may appear to some that the brain has never been so popular. This may indeed be true, however the brain has always fascinated us and is not just some late 20th century phenomena. Such notions as degenerative neurological disorders, consciousness and artificial intelligence have intrigued the scientist and layman alike for centuries.

Neuroscience - the science of the brain, has its origins with the ancient Greeks. Hippocrates (460-379BC) the philosopher and physician for instance, proposed that the brain was the seat of intelligence and furthermore conjectured that epilepsy was a disturbance in the brain. The renowned Roman physician, Galen (130-200AD) was also particularly interested in nerve function and lectured extensively on the spinal cord.
After this initial excursion into neuroscience, the brain was not a topic of investigation until the 17th century. It was then that the subject of consciousness and the relationship between mind and body became the key issue in neuroscience. René Descartes (1596-1650) is in some circles thought of as the father of modern neuroscience. Although always destined to be associated with his pithy remark on consciousness, his research also included a theory on reflex actions.

As one looks back at the history of neuroscience [there are many excellent web sites on this subject see for example http://faculty.washington.edu/chudler/hist.html], it is apparent that major advances have been wholly dependent upon progress in other fields of science, most notably physics. For example, after Descartes the next leap forward coincided with progress in optics. Robert Hooke (1632-1703) and Antony van Leeuwenhoek (1632-1723) were both pioneers in microscopy and used their respective microscopes to give detailed descriptions of nerve fibres for the first time, amongst other minute entities such as bacteria and blood vessels [Rose & Bynum (1982)]. Further improvements towards the middle of the 19th century to microscopes enabled Remak (1815-1865), Purkinje (1787-1869) and Schwann (1810-1882) to describe in detail the anatomy of the most important cell in the brain - the neuron [Brazier (1988)]. The investigation of the physiological side of neurons was initiated primarily by Galvani (1737-1798) and Volta (1745-1827) towards the end of the 18th century [Brazier (1961)]. They made the important discovery that electric forces existed in nerve cells. Their work was extended by Du Bois-Reymond (1810-1882) amongst others, in measuring precisely the currents between cells. This was only made possible due to the considerable improvements made to galvanometers. Thus, this was the pattern that emerged for the rest of the 18th and 19th centuries. Advances in physics and chemistry led to revealing and remarkable insights into the anatomy and physiology of the neuron. Thus we may view neuroscience as an amalgam of science. One that draws upon advances in other fields such as biology, chemistry and physics to propel itself forward. As neuroscience entered the 20th century, it enjoyed a new phase as it drew upon this truly multidisciplinary approach, an approach which included mathematics for the first time.

The mathematical modelling of various neuronal functions did not begin in earnest until the late 1940's and early 1950's [Hodgkin & Rushton (1946), Davis & Lorente de Nó (1947)]. However there had been a few excursions before this, notably Herman around the turn of the century applying Kelvin's cable equation to action potential propagation [Koch (1999)] and Lapique who formulated a simple but powerful model of a spiking cell [Lapique (1907) (1926)].

As we emphasized in the opening paragraph, the brain's complexity presents a formidable barrier to the researcher. The primary aim of mathematical models is to reduce this
complexity by imposing constraints and assumptions thereby simplifying the system. Thus, what these models lose in specificity, they gain in insight and analytical tractability. In addition to this, the existence of these models opens a whole new way of researching the brain, as Koch & Segev (1989) point out in the book ‘Methods in neuronal modeling: from synapses to networks’,

"Thus the traditional Baconian dyad of theory and experiment must be modified to include computation. Computations are required for making predictions as well as evaluating data. This new triad of theory, computation and experiment then leads to a new cycle: mathematical theory, simulation of theory and prediction, experimental test, and analysis."

There are now a veritable plethora of mathematical models, ones which simulate a single neuron [Koch (1999)] to models of networks of neurons [Amari (1977)], from relatively simplistic mathematical definitions [Lapique (1907)] to more mathematically complex [Hodgkin & Huxley (1952d)]. With such a wide variety of models at one’s disposal, there exists an equally wide range of neurobiological features which these models can be applied to. From neuronal induced locomotion [Ito et al. (1998)] to memory and learning [Kairiss & Miranker (1998)]. The list is indeed expanding all the time.

The motivational force behind improving mathematical models is the need for the models to acquire greater verismilitude. However, one must acknowledge that there exists a difficult balancing act, especially in mathematical models of the brain, of on the one hand, trying to obtain biological realism for the model and on the other, keeping the model mathematically tractable. As our knowledge of dynamical systems has improved and coupled with the remarkable increase in computer power, so mathematical models are able to increase their level of realism but importantly retain their mathematical tractability. This is in some sense the essence of this thesis and it is the contents of this thesis which we now consider.

1.1 Overview of thesis

Two areas of neuroscience which have attracted much interest from the mathematical community are: neural pattern formation [Murray (1993)] and rhythmic patterns induced by various locking phenomena between coupled neuronal oscillators [Hoppensteadt & Izhikevich (1997)]. However, the vast majority of the mathematical models
which have been proposed for each of these features have neglected a key component of the neuron - the **dendritic tree**. Each neuron is essentially represented by a point processor without any extended spatial structure. This is surprising as a number of experimental studies [Mel (1993), Sheperd (1998)] have shown that the dendrites play an important role in the functioning of a neuron, particularly with reference to the neuron’s information processing capabilities [Fortune & Rose (1997), Johnston et al. (1996)]. This thesis therefore builds upon the standard models proposed for spatial patterns [Ermentrout & Cowan (1979), Murray (1993)] and the dynamics of coupled neuronal oscillators [Van Vreeswijk et al. (1994), Bressloff & Coombes (1999), Coombes & Bressloff (1999a)] by including a simple representation of a dendritic tree [Rall (1957)(1959), Koch (1984)] to probe what dynamical effects this inclusion has.

The thesis is thus organized as follows,

- **Chapter 2**
  
  We begin with a short discussion on the anatomy and physiology of the neuron. In particular we detail the role of the **dendritic tree** in information processing and emphasise how the physical properties of the dendrites are incorporated into this process.

- **Chapter 3**
  
  Within this chapter, we introduce the one-dimensional **cable equation**. This equation was initially formulated by Lord Kelvin (1855) and applied to passive unbranched dendrites by W.Rall (1957)(1959). We solve this equation for both steady-state and time-dependent cases utilising the Green’s function approach throughout. We then include a short section on how biological realism may be increased in this model by discussing the equivalent cylinder approximation and also the compartmental model approach. We continue this theme by exploring Koch’s model on **quasi-active** dendrites [Koch (1984)]. Again we solve the resultant model for steady-state and time-dependent domains.

- **Chapter 4**
  
  We introduce the concept of neurological based **spatial patterns** with particular reference to ocular dominance stripes and drug induced hallucination patterns. We then describe the theory, initially formulated by Turing (1952) which attempts to explain the process of pattern formation. We conclude the chapter by introducing a simple model which a number of authors have incorporated into their work [Ermentrout & Cowan (1979), Swindale (1980)]. It is an excellent pedagogical model and allows us to introduce a number of key concepts which are
needed for subsequent chapters. We analyse the model using both linear stability analysis and numerical simulations to calculate the conditions which engender pattern formation.

- **Chapter 5**

We augment the model presented in Chapter 4 by including a one-dimensional passive cable. Through a mixture of linear stability analysis, bifurcation theory and numerical simulations we analyse the model for several different axo-dendritic configurations. Hence we are able to establish conditions for the onset of a Turing instability leading to the formation of stable spatial patterns of network output activity. This chapter is essentially composed of the paper ‘Neural pattern formation in networks with dendritic structure’ by Bressloff & De Souza (1998).

- **Chapter 6**

A logical extension of the work on pattern formation is presented in this chapter. Essentially, we consider a network of neurons with quasi-active dendritic structure. We utilise both linear stability analysis and numerical simulations to examine the nature of the spatial pattern as we switch the dendritic membrane from quasi-active to passive.

- **Chapter 7**

In the last of the main chapters we consider the dynamical influence of dendrites on the dynamics of coupled neuronal oscillators. In particular we analyse the occurrence of rhythmic periodic patterns induced by some degree of locking between the oscillators. By locking we mean mode-locking (frequency-locking) or phase-locking. A number of authors have examined both of these phenomena [Van Vreeswijk et al. (1994), Coombes & Bressloff (1999a)] from a mathematical perspective, however generally the dendritic tree is not included in the formulation. As an introduction therefore we detail how the locking phenomena generate different rhythms and illustrate each of these rhythms’ relevance in a neruobiological environment. We then introduce the so-called Integrate-and-Fire (IF) model as the basic model with which we work and upon which we add biophysical detail. Before embarking on our main objectives, we explore the relationship between the IF model and the more biologically realistic Hodgkin-Huxley (HH) model [Hodgkin & Huxley (1952d), Abbott & Kepler (1990)]. Utilising Coombes & Bressloff’s (1999a) analytical framework we proceed to explore $q:p$ mode-locked solutions for one neuron with dendritic structure forced by a periodic train of spikes. We then examine the phase-locked solutions between two neurons in an entrainment regime, where both of the neurons have dendritic structure.
• Chapter 8
We conclude the thesis by summarising our results and proposing future work.
Chapter 2

The Neuron: Structure and Function

Much wonder groweth upon me, yea astonishment seizeth me. [Men go abroad] to wonder at the height of mountains, at the huge waves of the sea, at the long courses of rivers, at the vast compass of the oceans, at the circular motion of the stars; and they pass by themselves without wondering.

St. Augustine

The mathematical models presented in the latter chapters require the reader to be familiar with certain aspects of neurophysiology. A brief review of neuronal structure and function is thus provided to equip the reader with the necessary terminology.

2.1 Neuronal Structure

Like all the organs of the body, the brain is made up of discrete cellular elements. There are essentially two different types of cells within the brain: neurons and glia. However, it is the neurons that are of most interest. Their distinctive shape, and their ability to transmit information between themselves sets them apart from other cells. This is in spite of having the same biochemical apparatus, general organization and genes as other cells [Llinás (1988)].

There are approximately one hundred billion neurons in the brain, which is roughly the same number of stars in our galaxy. Surprisingly, within this population no two neurons have exactly the same form. They do however share certain structural features.
2.1.1 Soma

The body or soma of the cell is usually spherical or pyramidal in shape [Thompson (1993)]. At its centre lies the nucleus. This is surrounded by cytoplasmic material and bounded by a membrane. [Please refer to Figure (2.1)]

The cytoplasmic material consists of systems of membranes and a variety of organelles. The membranes themselves are comprised of two distinctive components: the endoplasmic reticulum and the Golgi apparatus. Their roles are clearly defined in the manufacture of chemical substances. Chemical transmitters are synthesized on the endoplasmic reticulum and packaged into vesicles on the Golgi apparatus. These vesicles are either released by the soma or transported to other parts of the neuron for later release. Ribosomes, mitochondria and microtubules are all termed as organelles [Stein (1982)]. However, the most important organelle in the cytoplasm is undoubtedly the mitochondria (from the Greek - for bread). Shaped like small sausages, their sole function is to convert glucose and water into adenosine triphosphate (ATP). Almost all processes carried out by the cell require energy. ATP is an ideal energy source. Its phosphate bond is a high energy bond which is readily accessible during almost all chemical reactions occurring in the cell.

Encasing all of this is the cell’s membrane. It is roughly five nanometres thick and consists of two layers of lipid molecules: fatty acids called phosphoglycerides. In addition to this various protein molecules are scattered throughout it. Membrane protein molecules of all cells may be classified into five classes: pumps, channels, receptors, enzymes and structural proteins. The proteins’ roles are however not mutually exclusive. Interestingly, differences between cells’ membranes may be attributed to differences between their associated proteins.

2.1.2 Axon

The axon is a thin, tube-like structure which extends away from the soma [see Figure (2.1)]. Its length and diameter can vary hugely between different neurons. For example, studies have found axonal lengths from several micrometers and one metre, whilst diameters have varied between several micrometres and a millimetre. The axon branches to form telodendria as it nears its target cells. At these ends contacts are made with other cells by means of synapses. There are several possible combinations of contacts: axon with axon, axon with soma, etc. The most likely and indeed frequent is that between the axon of one neuron with the dendrite of another.
Two essential functions are performed by the axon. One is axoplasmic transport. That is the transport of chemical substances from the cell body to the synaptic terminals and vice versa. The other function is to propagate information in the form of an action potential. This aspect will be discussed more fully in section (2.2).

### 2.1.3 Dendrites

These are delicate tube-like extensions which branch repeatedly to form a tree-like structure: the **dendritic tree** (from the Greek for tree) [see Figure (2.1)]. Dendritic trees may be viewed as the neural analogue of the root systems of terrestrial trees, as they are well suited for the penetration of a volume [Mel (1994)]. However, whereas root systems provide a strictly nutritive role, a dendritic tree exists to extract information from the volume in which it sits. Its complex morphology [see Figure (2.2) for examples of different dendritic morphologies] extends the receptive area of the neuron. In fact, in some neurons over 99% of their surface is accounted for by the dendritic tree [Shepherd
Figure 2.2: Dendritic morphologies (the cells are not drawn to scale). (A) α motoneuron in spinal cord of cat (2.6 mm). (B) Spiking interneuron in mesothoracic ganglion of locust (0.54 mm). (C) Layer 5 neocortical pyramidal cell in rat (1.03 mm). (D) Retinal ganglion cell in postnatal cat (0.39 mm). (E) Amacrine cell in retina of larval tiger salamander (0.16 mm). (F) Cerebellar Purkinje cell in human. (G) Relay neuron in rat ventrobasal thalamus (0.35 mm). Reprinted from Mel (1993).

The smallest compartment both structurally and functionally within the dendrites is the dendritic spine. It is a small \((1 - 2\mu m)\) thornlike protuberance. Although these structures have been extensively examined by both light and electron microscopy, physiological data has been hard to come by due to their tiny dimensions. As a direct result of this, theories proliferate as to the exact function of these minute appendages. Due to this ambiguity, we view them simply as sites for synaptic connections and neglect their role in our future models. For a comprehensive review of theories and experimental data see Shepherd (1996), Harris & Kater (1994), Segev & Rall (1988), Koch et al. (1992) and Miller et al. (1985).
2.1.4 Synapses

Synapses (from the Greek 'to clasp') are the contact points that enable neurons to form connections between each other in order to transmit and process information. There are essentially two different types of synapses: chemical and electrical. However in the following discussion we will concentrate on the chemical variety as they are much more prevalent in the mammalian brain.

Figure 2.3: A Synapse. As the diagram shows the synapse consists of two parts: the knoblike tip of an axon terminal and the receptor region on the surface of another neuron. The membranes are separated by a synaptic cleft some 20-30 nanometres across. Within the axon terminal, there exists stored vesicles of chemical transmitters. These are released upon the arrival of an action potential. Reprinted from Llinás (1988).

Chemical synapses may be identified by four common features [please refer to diagram above, Figure (2.3)].

- At a synapse, the axon enlarges to form a terminal button. This is sometimes termed as the pre-synaptic axon terminal.
• Inside this button, a large number of vesicles exist, each filled with chemical transmitter.

• Between the pre- and post-synaptic membranes exists a small space, termed the synaptic cleft. This space is always present and is generally twenty nanometres wide.

• On the post-synaptic side a dense staining band runs along the cell membrane. This defines the extent of the synapse.

2.1.5 Glia

As well as the neurons, the other cells in the brain are glia. They are even more numerous than the neurons, and perform a number of different functions. Some provide structural support, some provide insulation for axons in the form of the myelin sheath, while others act as the central nervous scavengers, analogous to the macrophages found in the rest of the body [Stein (1982)].

2.2 Action Potentials: Generation and Propagation

2.2.1 Resting potential

The fluid in which the neurons exist contains a number of different ions. Sodium($\text{Na}^+$), potassium($\text{K}^+$), chlorine($\text{Cl}^-$), calcium($\text{Ca}^{2+}$) and protein($\text{P}^2$) ions are all present. However the concentration of these ions are markedly different inside and outside the cell’s membrane. Particularly striking are the relative concentrations of $\text{Na}^+$ and $\text{K}^+$ ions; the intra-cellular fluid is ten times richer in $\text{K}^+$ whereas the extra-cellular fluid is ten times richer in $\text{Na}^+$. This anomaly is entirely due to the cell membrane’s properties. As we mentioned in (2.1.2), there are a number of intrinsic proteins embedded within the membrane. Some of these act as highly selective ionic channels, allowing only certain ions to pass freely. These channels may be further sub-divided into gated and non-gated. The gated channels have two stable states: open and closed. The opening/closing of the gate is entirely dependent upon a certain stimulus being applied. This stimulus may take the form of a potential difference for voltage-gated channels, or certain chemicals for the chemically-gated counterparts. The non-gated channels are simply water filled pores.
It has been shown that most of the $K^+$ channels are non-gated whereas the majority of the $Na^+$ channels are gated and closed in the resting state. This means that the $Na^+$ ions can cross the membrane only about one-twentieth as easily as the $K^+$ ions. In addition to this, negatively charged protein ions ($P^{2-}$) are prevented from leaving the cell due to their relatively large size. The net consequence of this, is an ionic imbalance which in turn creates a potential difference across the membrane. That is the interior of the cell is approximately 70$mV$ negative with respect to the exterior. This is known as the resting potential.

In order to correct any imbalance that may arise through ionic leakage, an intrinsic membrane protein called the sodium/potassium ATP pump exchanges sodium ions that have entered the cell for potassium ions outside it.

### 2.2.2 Action potential generation

An action potential is triggered by the soma’s response to synaptic activity. The precise meaning of this will be explained in the subsection on synaptic transmission (2.2.4) and to some extent in the section on information processing (2.3). However at this juncture we can still make the following remarks.

For an action potential (spike) to be generated, the initial requirement is for the membrane’s potential to be depolarized sufficiently. That is the potential must reach a certain threshold level. This level has been shown to be approximately $-55mV$. The new membrane potential causes both the voltage-gated sodium channels and potassium channels to open. Although these gates open at the same time, the influence of the sodium channels is much greater due to the significant imbalance of the concentration of sodium ions. The membrane potential sweeps toward $+50mV$ as the sodium ions cascade inwards. The figure of $+50mV$ represents the sodium equilibrium, and when this is reached the sodium gates are closed but not the potassium ones. The now positive membrane starts to attract $Cl^-$ ions and to repel $K^+$ ions from the intra-cellular fluid, thereby sending the potential to an even more negative value (roughly $-75mV$) than its resting state. It is only at this point do the $K^+$ gates close. Finally the resetting of the membrane is achieved by the sodium/potassium pump. The period when the $Na^+$ gates are open is termed the absolute refractory period. During this phase, the neuron may not emit another action potential. The whole process of action potential generation may be viewed pictorially below [see Figure (2.4)].
Figure 2.4: The generation of an action potential. As the action potential comes into existence and the membrane potential shifts rapidly from $-70 \text{ mV}$ towards $+50 \text{ mV}$, the closed sodium channels pop open and then close again. Meanwhile, the many fewer closed potassium channels pop open and then close again producing the afterpotential (see 6). Reprinted from Thompson (1993).

2.2.3 Action potential propagation

The neuron's membrane, being made of lipids, has a relatively high resistance compared to the intra- and extra-cellular fluids. That is the speed at which the electricity flows down the axon is much faster than the rate at which charge accumulates on the membrane.

The classical view states that when an action potential is initiated in the axon hillock, it also depolarizes the axonal membrane immediately adjacent to it. Eventually, the threshold for the $Na^+$ channels is reached and an action potential develops there. This process is repeated again and again thus allowing the action potential to move continuously down the axon.
The speed of propagation in a myelin coated axon is greatly increased, as the depolarization of the membrane need only occur at the nodes of ranvier (the breaks in the myelin sheath). Thus the action potential propagates by skipping from node to node. This is termed saltatory conduction. Apart from the advantage of increasing the speed, myelin also helps to conserve ATP. By confining the depolarization to small portions of the membrane, the amount of ions crossing the membrane is greatly reduced, thus less pumping needs to be done to reset the membrane to its resting potential.

2.2.4 Synaptic transmission

As stated in (2.1.4), chemical synapses are more prevalent within the mammalian brain than the electrical ones. The following discussion reflects this bias [Kandel et al. (1991)].

The arrival of an action potential at the terminal button, initiates the opening of the voltage gated $Ca^{2+}$ channels. The resulting flow of calcium ions into the cell triggers the release of the transmitter filled vesicles. The vesicles become attached on or near proteins which run the width of the synapse. It is only these vesicles that then fuse with the membrane. The other vesicles are held back in reserve. Once the transmitter has been spilt into the cleft, it diffuses across and attaches itself to receptors. These are intrinsic postsynaptic membrane proteins. The presence of the transmitter allows the chemically as opposed to voltage gated channels to open.

The influx of ions causes a small change in the potential of the membrane - a postsynaptic potential (PSP). If the sodium channels are activated then a depolarisation occurs, this is termed an excitatory postsynaptic potential (EPSP). If however, the chlorine channels are activated then a hyperpolarization occurs. This is termed an inhibitory postsynaptic potential (IPSP).

The opening of the specific ionic channels is wholly dependent upon which transmitter is released. For example, acetycholine (ACh) is an excitatory transmitter while $\gamma$-aminobutyric acid (GABA) is an inhibitory one [Kuffler & Nicholls (1984)]. These are by no means the only types of transmitter. Indeed over thirty are now known to exist, and no doubt more will soon be discovered.
2.3 Dendritic Information Processing

The question of how information is carried and decoded in the brain lies at the very forefront of theoretical neurobiology today. There is a general consensus that the neural system encodes information by using action potentials. The action potential is however an 'all-or-nothing' event. Information transmitted between neurons cannot therefore be encoded in the amplitude of the spike. Instead, it has been conjectured that a rate or a timing code is employed. By rate coding [Schadlen & Newsome (1994)] we mean that the mean firing frequency measured in a certain time window encodes the information [Koch (1999)]. Rate coding implies the brain uses first-order statistics [Deco & Schürmann (1999)]. Biological information is represented by coarse-grained temporal activities of neurons [Fukai (1996)]. Alternatively, higher order statistics may be employed as proposed by von der Malsburg (1981). This defines a timing code whereby the relative timing of spikes encodes the information [Gray & Singer (1987) (1989)]. We shall employ both types of codes in the course of this thesis. The choice of code is highly dependent upon what aspect of neurobiology we wish to explore and mathematical tractability considerations. The way in which the neuron then decodes this information is naturally equally as important and it is this question of information processing that we now address and in particular exactly what role the dendrites play.

For the vast majority of this century, the dendrites have been received solely as the information gathering component of the neuron [Mel (1994)]. As a direct result of this many neuroanatomical textbooks have represented the neuron as a single node with all inputs converging on to this node. This has had repercussions for not just experimental design in neurobiology but also for mathematical models [see section (4.3)]. However, as the investigative techniques have become more sophisticated and thus revealing, the dendrites may now be viewed as a highly complex, non-linear information processor. Indeed, it is they that co-ordinate and blend the plethora of inputs to eventually determine whether the neuron will fire an action potential at any given point in time and how it will respond to similar inputs in the future [Johnston & Wu (1995)].

The properties of dendrites that provides this integrative function as well as the nature of the integration itself are poorly understood. However, the physical features that we attribute to dendritic trees are shedding light on this area of neuroscience. The physical features are: dendritic branching, synaptic placement, passive membrane and active membrane properties [Shepherd (1998)].

We will concentrate on the last three features as our models are aimed at duplicating/simulating these features as opposed to the actual branching structure. If the
reader is interested in this particular aspect of dendritic integration, then the paper by Mainen and Sejnowski (1996) provides an excellent starting point.

We must stress however that the properties, although treated and discussed in an individual manner, must be viewed as components of the whole picture. Formulating a model which encompasses all of these features is to some extent our ultimate aim.

2.3.1 Synaptic placement

The activation of a single excitatory synapse will obviously not cause a neuron to fire. Many synapses have to be activated in order to exert a great enough influence and thus depolarize the neuron’s trigger zone sufficiently. The PSPs, both inhibitory and excitatory are summed together. However, this summation is not a simple addition of positive and negative voltages. Inhibitory synapses are generally located closer to the soma, thus their influence is much stronger than that of the excitatory synapses [Hirsch & Gilbert (1991), Kisvárday (1992)]. This is an important point and one that modellers have tended to neglect when constructing a variety of models [see section (4.3)].

Summation is achieved both spatially and temporally. For temporal summation each PSP adds to the cumulative total of its predecessors to yield a voltage change whose average reflects the frequency of the incoming impulses. Spatial summation corresponds to the integration of impulses from all over the dendritic tree. A neuron utilises both methods of summation in order to decide to fire an action potential at a given moment in time [Mitgaard (1994)].

2.3.2 Passive membrane properties

The passive electrical properties or electronic structure are determined by three electrical parameters $c_m$, $r_m$, and $r_i$ which are respectively the membrane capacitance, membrane resistance and internal resistance. The estimation of these parameters and their subsequent effect on information processing is still gathering much attention [Brown et al (1981), Spruston et al. (1994), Spruston & Johnston (1992)]. The studies have focused particularly on the hippocampal and cortical regions. Their results have generally concluded that the passive nature of the dendrites perform two important functions. Firstly, PSPs are attenuated with distance. The degree of attenuation is wholly dependent upon the values of the electrical parameters as well as the diameter of the dendrite. The PSPs attenuate more rapidly toward the soma than toward the dendritic
terminations. The voltage attenuation from distant synapses to the soma may be as much as a fifth. This is due to the somatic end having many dendrites attached to it thus presenting it as a large conductance load to the synaptic source. The dendritic terminations are however sealed ends and so little current is lost there. The obvious consequence of this is that a number of EPSPs must occur within a membrane time constant in order to displace the somatic potential across the threshold [Thurbon et al. (1994)].

Passive dendrites also behave as a low pass filter. That is, they attenuate high frequency components of an input waveform far more severely than slower or steady state events. As a result of this filtering the synaptic potentials are broadened as they spread from the distal locations. The broadening has the effect of delaying the signal, thus making the soma sensitive to the temporal order of synaptic events [Shepherd (1998)].

The idea of delays is an inherent one of biological systems [MacDonald (1989)]. The delay produced by dendritic processing is just one in the sequence of one neuron firing and another neuron's soma experiencing the effect of that spike. There is a finite delay as the action potential travels along the axon. In addition to this there is a set of distributed delays in the synaptic transmission of the spike and finally the dendritic processing delay. Throughout this thesis we will emphasise the dynamical importance of these delays with particular emphasis on the role of the dendrites.

2.3.3 Active membrane properties

The presence of voltage gated channels along the dendritic tree of many neurons, enables the dendrites to perform a number of different functions. The roles and distribution of these channels are however only recently being explored and as a result much still remains a mystery [Johnston et al. (1996)]. As with the soma, Na⁺, K⁺ and Ca²⁺ channels are all present and as one would expect, the opening or closing of specific channels underlies specific functions. There are many possible information processing activities which active membranes could support [Shepherd (1998), Koch (1999)]. However, we only feature three of the most important and indeed plausible processes.

Amplification of Synaptic Inputs

The proposal that dendrites could amplify or boost certain synaptic inputs has been around since the late 1950's and early 1960's [Mel (1993)]. Since then a wealth of experimental evidence has been accumulated to confirm this conjecture [Bernander et
al. (1994)]. For example, in pyramidal cells of the neocortex, synaptic inputs into the apical tuft at the distal end of the apical dendrite are greatly attenuated on route to the soma. This is chiefly due to the distance away from the soma. However important interareal projections make their synapses here so this apparent ineffectiveness of the distal apical input is somewhat counterintuitive. Thus, the apical dendrite makes use of active currents to selectively enhance signal transmission to the soma. This essentially reduces the location-dependent variability among inputs spread across the dendrites in terms of their ability to influence neuronal firing [Shepherd (1998)].

In addition to this the active properties of the dendrites change the filtering properties of the passive membrane to that of a band pass/high pass filter [Haag & Borst (1996)].

**Dendritic Action Potential Initiation**

The classical view of action potential initiations (section 2.2) predicts the site of initiations to the trigger zone or axon hillock. This however is not the complete picture. The spike initiation site is dependent upon the strength of synaptic stimulation. Evidence of this was provided by, among others, Turner and colleagues [Turner et al. (1991)]. Using a combination of inter- and extra-cellular recording, they showed that during high intensity synaptic stimulation, dendritic action potentials were recorded. These events are mediated by voltage activated Na\(^+\) channels or slower, regenerative Ca\(^{2+}\), often called Ca\(^{2+}\) spikes.

**Back Propagation of Action Potentials**

The concept of back-propagating action potentials was entertained by theoretical neurobiologists as early as the 1920's. Indeed Ràmon y Cayal (1923) remarked,

"Does the nervous impulse propagate in all directions, like sound or light, or does it consistantly flow in one direction, like the water running in a water mill?"

In fact action potentials once initiated in the axon will propagate into the dendritic tree in a retrograde fashion. However, the degree to which this back propagation occurs varies between different neurons. This variation can, in part, be attributed to the cell specific differences of density of the Na\(^+\) channels within the dendrites [Stuart et al. (1997)]. For example, in the cerebellar purkinje neurons, the low density of Na\(^+\)channels is reflected in the largely passive back propagation of an action potential. This is in direct contrast to the more active mechanisms shown in neocortical and hippocampal pyramidal cells.
Dendritic morphology is another factor that will influence the extent of back-propagation. In particular, the branching pattern plays an important role as the action potential may fail at the dendritic branch junction [Shepherd (1998)].

The back-propagating action potential is not like the action potential in the axon as it’s amplitude does not remain constant [see Figure (2.5)]. As the action potential propagates into the dendrites it’s amplitude decreases [Yuste & Tank (1996)]. This appears to be due to an increasing density of transient $K^+$ channels. The activation of these channels could shunt the membrane potential, thereby reducing the effectiveness of the back propagating action potential.

What functional significance could this antidromic spike have?

There are many theories that proliferate about the possible significance of these back-propagating action potentials [Stuart et al. (1997), Shepherd (1998)]. Perhaps the most plausible and indeed important concerns their possible role in Hebbian learning. Hebbian learning is perhaps the most influential learning theory in neuroscience. It was proposed in the late 1940s by the neuropsychologist Donald Hebb. Quoting from his book, 'The organization of behaviour' [Hebb (1949)],

“When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic changes take place in one or both cells such that A’s efficiency as one of the cells firing B, is increased.”

The above statement is essentially one that refers to changes at the synaptic level. That is the strength of a synapse is selectively increased if the two neurons on either side of it are activated synchronously [Stent (1973)]. Thus this Hebbian form of learning depends on interaction between presynaptic and postsynaptic activity [Haykin (1994)]. The back-propagating action potential, under physiological conditions, may provide this postsynaptic depolarization as well as informing the synapse that the neuron has just spiked. In addition to this the amplitude of the back-propagating action potential changes as it interacts with local EPSPs and IPSPs [Tsubokawa & Ross (1996)]. The EPSPs facilitate the action potential into specific branches of the tree and increase its amplitude [Markram et al. (1997)]. IPSPs, as would be expected, do it exactly the opposite. They reduce the action potentials amplitude and prevent it from propagating into certain areas of the tree. Thus, in a sense, Hebbian learning is controlled, by the way the EPSPs and IPSPs interact and direct the back-propagating action potential.
Figure 2.5: A back-propagating action potential. At the top of the Figure is a representation of a CA1 neuron with two whole cell recordings, one in the soma and one situated roughly 250 μm away from the soma in the dendrites. An action potential is fomented in the soma by current injection. As we have described, it begins in the axon and then propagates into the soma and eventually into the dendrites. The delay is naturally caused by the conduction time (the conduction velocity of back-propagation is about 0.3 m/s). One should also note that the action potential in the dendrites is smaller than that in the soma. This is due to the high density of A-type $K^+$ channels. The bottom part of the Figure, demonstrates the response in the soma and dendrites to a train of action potentials. the action potentials in the soma are all approximately the same size, whereas those in the dendrites undergo a frequency-dependent decline in amplitude because of slow inactivation of $Na^+$ channels and the high density of $K^+$ channels [Colbert et al. (1997)]. Reprinted from Shepherd (1998).
Chapter 3

Cable Theory for Dendritic Neurons

When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind. It may be the beginning of knowledge, but you have scarcely, in your thoughts advanced to the stage of science.

Lord Kelvin

3.1 Introduction

The incredibly long man-made transatlantic telegraph cables and the beautiful minute neuronal dendrites [see for examples Figure (2.2)] may at first glance seem as completely different as the environments in which they inhabit. However, at closer inspection their physical construction are remarkably similar. They both consist of a long, thin electrically conducting core surrounded by a thin membrane of relatively high resistance [Bressloff & Coombes (1997), Mel (1994)]. It is for this reason that the mathematical theory used to describe the flow of charge along electrical cables has been applied to dendritic trees. For obvious reasons, the mathematical theory is known as cable theory.

The theory was initially developed by Lord Kelvin during the mid 19th century [Kelvin (1855)]. The motivation behind the work was to help construct the first transatlantic telegraph cable [For a historical perspective see Rall (1977)]. By the turn of the century, Herman and others had constructed the so-called core conductor model, in the context
of studying the flow of current in nerve axons [Koch (1999)]. This work was continued by applying cable theory to the giant axon of a squid [Hodgkin & Rushton (1946), Davis & Lorente de Nó (1947)]. However it was only in the late 1950's that cable theory was applied to passive spatially extended dendrites. This was primarily achieved by W. Rall [Rall (1957, 1959)]. The rationale behind this step was to interpret intracellular recordings of individual neurons. Since this time, cable theory has played the most prominent part in the mathematical modelling of neurons with dendritic structure and has been an extremely valuable tool to both experimentalists and theoreticians [Segev (1995), Johnston & Wu (1995)].

3.2 The Cable Equation

The fundamental equation in cable theory is,

$$r_m c_m \frac{\partial V(\xi,t)}{\partial t} = -V(\xi,t) + \frac{r_m}{r_i} \frac{\partial^2 V(\xi,t)}{\partial \xi^2}$$

(3.1)

where $V(\xi,t)$ denotes the membrane potential at time $t$ and position $\xi$ along the cable relative to the resting potential of the membrane. The electrical parameters $r_m$, $r_i$ and $c_m$ are respectively, as stated before [subsection (2.3.2)], the membrane resistance (in units of $\Omega$), intracellular resistance (in units of $\Omega$/cm) and the membrane capacitance (in units of $F$/cm).

For an in depth derivation of equation (3.1), see Tuckwell (1988) or Rall (1989). However, for our purposes such a discussion is not warranted and so we make the following brief observations.

One may view the cable equation as essentially a balance between three kinds of electric current: axial, ionic and capacitive. Please refer to the diagram below [Figure (3.1)].

Kirchhoff's current law states that the net accumulation of axial current at $\xi$ (i.e. axial current entering - axial current leaving) is equal to the net current leaving the cell at position $\xi$ across the membrane. Two distinctive currents make up this outward flowing current. They are the capacitive and resistive currents. The capacitive current is proportional to the rate of change of the membrane voltage, that is the $\frac{\partial V}{\partial t}$ term in equation (3.1). Hence rapid changes in voltage are associated with large capacitative currents. The resistive current is, in accordance to Ohm's law, directly proportional to the membrane voltage (the $-V$ term). The net axial current is related to the curvature of the local membrane voltage (the $\frac{\partial^2 V}{\partial \xi^2}$ term). The cable equation simply states
that these three quantities are in balance.

### 3.2.1 Cable equation for passive dendrites

The equation (3.1) may be reformulated so that it incorporates the neurobiological parameters of the space (λ) and time (τ) constants. These represent respectively the length and time over which membrane potential decays to 1/e of its original value. We also include a source term, \( I_{\text{EXT}}(\xi, t) \). This corresponds to an external input injected into the cable. Thus setting \( \tau = r_m c_m \) and \( \lambda = \sqrt{r_m / r_i} \) and \( D = \lambda^2 / \tau \), where \( D \) is the diffusion coefficient, the equation now becomes,

\[
\frac{\partial V(\xi, t)}{\partial t} = -\frac{V(\xi, t)}{\tau} + D \frac{\partial^2 V(\xi, t)}{\partial \xi^2} + I_{\text{EXT}}(\xi, t) \tag{3.2}
\]

It is often useful to show the dependence of the space and time constants on the diameter of the cable, denoted by \( d \). Thus \( c_m = C_m \pi d \), where \( C_m \) is the membrane capacitance per unit area (\( F/cm^2 \)). Similarly \( r_m = R_m / \pi d \), where \( R_m \) is the membrane resistance times unit area (\( \Omega cm^2 \)). Thus the time constant remains unchanged, that is \( \tau = r_m c_m = R_m C_m \). We may now proceed to define the intracellular resistance (\( \Omega cm \)) and thus the space constant. \( r_i = R_i / (\pi d^2 / 4) \) and so \( \lambda = \sqrt{r_m / r_i} = \sqrt{R_m d / 4 R_i} \). Plausible values for these parameters gained from physiological experiments [Yuste & Tank (1996)] are as follows \( C_m = 0.7 - 2 \mu F/cm^2 \), \( R_m = 50 - 200 k\Omega cm^2 \) and \( R_i = 200 - 400 \Omega cm \).
3.2.2 Boundary and initial conditions

The equation (3.2) is a parabolic partial differential equation and as such has a unique solution if we specify suitable initial data and relevant boundary conditions. Tuckwell, in his book, 'Introduction to theoretical neurobiology (Volume I)' [Tuckwell (1988)] provides an excellent summary of such conditions, these will be briefly considered here.

Boundary Conditions

The domain over which the cable may extend may either be infinite \((-\infty, \infty)\), semi-infinite \([0, \infty)\) or finite \([-L, L]\). Invariably we choose not to investigate a finite cable but instead consider a semi-infinite cable as this simplifies our eventual analysis. In this case we require the potential at the infinite end to be bounded. That is, to be concise,

\[
\lim_{{\xi \to \infty}} |V(\xi, t)| < \infty \tag{3.3}
\]

We note that when we wish to simulate such a cable numerically, the semi-infinite domain becomes a finite one due to the constraints of the computer. In this case we will explicitly state which boundary condition to impose at the 'infinite' end.

This then leaves the \(\xi = 0\) end. The conditions on this side can, broadly speaking, be classified into five categories:

- **Killed end**
  A killed end essentially refers to a sudden ending of the nerve's membrane without a terminal covering membrane. This allows the intracellular fluid to adjoin the extracellular fluid. The boundary condition reflecting this case is
  
  \[
  V(0, t) = 0 \tag{3.4}
  \]

- **Sealed End**
  This infers that there is no longitudinal current at the end. That is, at the end \(\xi = 0\),
  
  \[
  \frac{\partial V}{\partial t} \bigg|_{\xi=0} = 0 \tag{3.5}
  \]
• **Voltage Clamp**

This is defined as the holding of an electrical potential at a particular value. If the voltage at the end $\xi = 0$ is clamped at some value $V_c$, say, then the corresponding boundary condition is,

$$V(0, t) = V_c$$

(3.6)

• **Current injection at an end**

If a current $I(t)$ is injected into the end $\xi = 0$, then the required boundary condition is,

$$\left. \frac{\partial V}{\partial t} \right|_{\xi = 0} = -r_i I(t)$$

(3.7)

The negative sign is due to the convention that longitudinal currents are positive in the positive $\xi$ direction.

• **Lumped Soma Termination**

We treat the soma as an equipotential surface, that is we regard it as a single resistor, $R_s$, in parallel with a single capacitor, $C_s$. Naturally, the boundary condition is only applicable at the $\xi = 0$ end. Thus the required boundary condition is,

$$C_s \frac{\partial V(0, t)}{\partial t} + \frac{V(0, t)}{R_s} - \frac{1}{r_i} \frac{\partial V(0, t)}{\partial \xi} = 0$$

(3.8)

**Initial conditions**

The initial data simply describes the depolarization present at the beginning of the experiment for all relevant values of $\xi$. Thus we have

$$V(\xi, 0) = v(\xi)$$

(3.9)

Often we will simply have a uniform resting state, such that,

$$V(\xi, 0) = 0$$

(3.10)
3.3 Solution of the Passive Cable Equation

In this section we consider both time-independent (steady-state) solutions as well as time-dependent solutions of the passive cable equation on a semi-infinite domain with a sealed end at $\xi = 0$. We assume the initial condition to be a uniform resting state. We state this system explicitly for future reference,

$$\frac{\partial V(\xi,t)}{\partial t} = -\frac{V(\xi,t)}{\tau} + D\frac{\partial^2 V(\xi,t)}{\partial \xi^2} + I_{EXT}(\xi,t), \quad \xi \in \mathbb{R}^+$$

(3.11)

$$\left. \frac{\partial V}{\partial t} \right|_{\xi=0} = 0, \quad \lim_{\xi \to \infty} |V(\xi,t)| < \infty, \quad V(\xi,0) = 0$$

(3.12)

The principle method of solution in both cases is by way of the Green's function.

3.3.1 Steady-state solution

For a steady-state, the time dependence is removed from equation (3.11), thus transforming the partial differential equation into a second order ordinary differential equation. This simplification is valid if a current is applied to a nerve cylinder for a sufficiently long time. So as $t \to \infty$, $\frac{\partial V}{\partial t} \to 0$, the applied current density and membrane potential approach steady state values,

$$V(\xi,t) \longrightarrow \tilde{V}(\xi)$$

(3.13)

$$I_{EXT}(\xi,t) \longrightarrow \tilde{I}_{EXT}(\xi)$$

(3.14)

We obtain the following equation with this transformation,

$$D\frac{d^2 \tilde{V}(\xi)}{d\xi^2} - \frac{\tilde{V}(\xi)}{\tau} = -\tilde{I}_{EXT}(\xi)$$

(3.15)

The boundary conditions for this equation are obtained from those imposed on the partial differential equation (3.12) but are in the limiting form.

$$\left. \frac{d\tilde{V}}{d\xi} \right|_{\xi=0} = 0, \quad \lim_{\xi \to \infty} |\tilde{V}(\xi)| < \infty$$

(3.16)
Rearranging equation (3.15) we obtain,

$$\frac{d^2 \tilde{V}(\xi)}{d\xi^2} - \frac{\tilde{V}(\xi)}{\lambda^2} = -\frac{I_{\text{EXT}}(\xi)}{D} \tag{3.17}$$

The method of solution is by way of the Green's function method. The flexibility of this method makes it an attractive method of solution. This is especially true when we consider the full time-dependent system.

Recall, the Green's function, $\tilde{G}(\xi, \xi')$ for equation (3.17), with the given boundary condition is the solution of the equation,

$$\frac{d^2 \tilde{G}}{d\xi^2} - \frac{\tilde{G}}{\lambda^2} = \delta(\xi - \xi') \tag{3.18}$$

Then the solution to equation (3.17) is

$$\tilde{V}(\xi) = -\frac{1}{D} \int_{0}^{\infty} \tilde{G}(\xi, \xi') I_{\text{EXT}}(\xi') d\xi' \tag{3.19}$$

In general, obtaining the Green's function for a one-dimensional problem is trivial. This is the case for the problem posed above, so we will merely state the solution

$$\tilde{G}(\xi, \xi') = \begin{cases} 
-\lambda \exp(-\xi'/\lambda) \cosh(\xi'/\lambda) & 0 \leq \xi < \xi' \\
-\lambda \exp(-\xi/\lambda) \cosh(\xi/\lambda) & \xi' < \xi < \infty
\end{cases} \tag{3.20}$$

If the reader is interested in the steady-state problem both Tuckwell and Rall solve the steady-state system for a variety of domains and boundary conditions [Rall (1989), Tuckwell (1988)].

### 3.3.2 Time-dependent solutions

The steady state solutions are a gross simplification of this system. Indeed, steady state conditions will never prevail under natural conditions. That is not to say that steady state solutions are without their use. They can provide useful insights into the parameters of the system, input patterns and the effect of neuronal geometries [see section (3.4)].
Returning to the full system [equations (3.11) and (3.12)] however,

\[
\frac{\partial V(\xi, t)}{\partial t} = -\frac{V(\xi, t)}{\tau} + D \frac{\partial^2 V(\xi, t)}{\partial \xi^2} + I_{\text{EXT}}(\xi, t)
\]

The Green's function method, as we have seen is well suited for this case, and it is this one that we employ.

The Green's function, \(G(\xi, \xi', t, t')\) for equation (3.11) is,

\[
\frac{\partial G}{\partial t} + \frac{G}{\tau} - D \frac{\partial^2 G}{\partial \xi^2} = \delta(\xi - \xi')\delta(t)
\]  \hspace{1cm} (3.21)

with the same boundary conditions and initial condition as stated in equation (3.12). Hence the solution may be obtained as thus,

\[
V(\xi, t) = \int_0^\infty \int_0^t G(\xi - \xi', t - t') I_{\text{EXT}}(\xi', t') dt' d\xi'
\]  \hspace{1cm} (3.22)

To procure the fundamental solution, we note that there are a number of different methods at our disposal [Tuckwell (1988)]. However, we make use of the (semi) infinite domain to implement the Fourier transform method.

We note that a dichotomy exists, as to which variable (\(\xi\) or \(t\)), we wish to take the Fourier transform with respect to. However, in order to utilise Koch's elegant analysis of dendritic membranes [Koch (1984)], it is necessary to transform the equation with respect to time.

So, taking the Fourier transform of the homogeneous equation with respect to time yields,

\[
\frac{d^2 \tilde{V}(\xi, \omega)}{d\xi^2} - \left( \frac{1 + i\omega \tau}{D\tau} \right) \tilde{V}(\xi, \omega) = 0
\]  \hspace{1cm} (3.23)

where,

\[
\tilde{V}(\xi, \omega) = \int_{-\infty}^\infty V(\xi, t)e^{i\omega t} dt
\]  \hspace{1cm} (3.24)

We set,
\[ \gamma^2(\omega) = \frac{1 + i\omega\tau}{D\tau} \]  

(3.25)

In Koch's analysis [Koch (1984)], \( \gamma(\omega) \) is defined as the propagation constant. It is related to the underlying nature of the membrane. In order to investigate this particular feature further, let us again consider a linear, one-dimensional cable. We then represent this passive cable as an infinite ladder network, as illustrated below [Figure (3.2)].

(a)

(b)

Figure 3.2: (a) Ladder representation of a one-dimensional cable with frequency dependent membrane impedance \( z_m(\omega) \) and longitudinal resistance \( r_a \). (b) Electric circuit of a passive membrane. The parameters \( r, c \) are equivalent to \( R_m \) and \( C_m \).

Here \( z_m \) is the linearized, frequency dependent impedance and \( z_a \) denotes the serial impedance. As the diagram shows, the circuit for a passive membrane consists only of a resistor in parallel with a capacitor. Thus \( z_m \) is given by the following expression,

\[ z_m = \frac{r}{1 + i\omega\tau} \]  

(3.26)

where, \( \tau = rc \)

The serial impedance is simply given by an ohmic resistor, thus,
\[ z_a = r_a \]  
\[ (3.27) \]

Koch, then defines the propagation constant in terms of a ratio of these two impedances, so that,

\[ \gamma^2(\omega) = \frac{z_a(\omega)}{z_m(\omega)} = \frac{r_a(1 + i\omega T)}{r} \]  
\[ (3.28) \]

Comparison between this and the expression given by equation (3.25) reveals that \( D\tau = r/r_a \).

Solving equation (3.23) for an infinite cable if a \( \delta \)-current impulse is injected at the origin, yields the following solution, after the relevant boundary conditions have been applied,

\[ \tilde{V}(\xi, \omega) = \frac{1}{D\gamma(\omega)} e^{-\gamma(\omega)\xi} \]  
\[ (3.29) \]

As the Green's function is the response of the system to a \( \delta \)-input impulse, we are able to state the Fourier transform of the Green's function, simply as,

\[ \tilde{G}(\xi, \omega) = \frac{1}{D\gamma(\omega)} e^{-\gamma(\omega)\xi} \]  
\[ (3.30) \]

In certain parts of our analysis in future chapters, we require the real and imaginary components of the function \( \gamma(\omega) \). We state these here for future reference,

\[ \gamma(\omega) = a(\omega) + ib(\omega) \quad \text{where,} \]
\[ a(\omega) = \frac{1}{\sigma} \sqrt{\frac{1 + \sqrt{1 + (\omega^2\tau^2)}}{2}} \]  
\[ (3.31) \]
\[ b(\omega) = \frac{\text{sign}(\omega)}{\sigma} \sqrt{\frac{-1 + \sqrt{1 + (\omega^2\tau^2)}}{2}} \]  
\[ (3.32) \]

where \( \sigma = \sqrt{D\tau} \). The Fourier transform of the Green's function is also termed the transfer function or transfer impedance. It has been shown that if the membrane impedance \( z_m \) has low-pass filter characteristics then so does the transfer function. That is the transfer function reflects the filtering properties of the membrane impedance. Thus
has a maximum at zero. The amplitude $|\tilde{G}(0, \omega)|^2$ is plotted in Figure (3.3) as a function of $\omega$ to illustrate this point.

![Figure 3.3: Modulus of the transfer function $|\tilde{G}(0, \omega)|^2$ (in units of $1/D^2r_a$) as a function of frequency (in units of $1/\tau$) for a passive membrane. Here $D = r_a = \tau = 1$. The low-pass filtering properties can be seen clearly. The maximum is unmistakably located at zero.](image)

We can now invert this function (3.30) to obtain the Green’s function for the passive cable,

$$G(\xi, t) = \frac{1}{\sqrt{4\pi Dt}} e^{-t/\tau} e^{-\xi^2/4Dt} \tag{3.34}$$

To reiterate, this determines the membrane potential response at the end of the cable due to an instantaneous injection of unit current at the point $\xi$ at time $t$.

### 3.4 Realistic Dendritic Models

Thus far we have assumed the cable to be passive, unbranched and uniform in its electronic properties. In reality, however the cable branches repeatedly [see Figure(2.2)],
the membrane may be active and the parameters that define the electronic structure \( (R_i, R_m \text{ and } C_m) \) may vary along the cable. For example, a variation in \( R_i \) may occur due to the differing effects of organelles, the cytoskeleton or cytomatrix over different parts of the neuron [Shelton (1985)]. \( R_m \) may vary due to the uneven distribution of intrinsic proteins within the membrane [Trimmer (1991)]. It is less likely that \( C_m \) would vary. Although this is still possible, as non-uniform lipid composition would have an effect on the dielectric properties of the membrane. For this reason, one has to adopt a different strategy to model the dendrite. Within this section we review some of the methods which seek to add greater biological detail to the basic model. We ask the reader to note though that the concept and analysis of active membranes will be addressed in the next section.

3.4.1 Realistic dendritic morphologies

Thus far the intricate structure of the dendritic tree has been represented by an unbranched cable. Rall showed [Rall (1959)] that an extensively branched tree may be simplified and viewed as an equivalent cylinder if certain conditions were satisfied [Rall (1989), Mel (1994)]. The necessary conditions are,

- The values of \( R_m \) and \( R_i \) are the same in all branches
- All terminal branches end with the same distal boundary condition. This is usually taken to be a sealed end.
- All terminal tips lie at the same electronic distance, \( L \) say, away from the soma. \( L \) equals the sum of \( \xi/\lambda \) values along the path from \( \xi = 0 \) to the distal end of every terminal branch. \( L \) is then defined as the electronic length of the tree and importantly of the equivalent cylinder
- All branch points in the dendritic tree satisfy the so-called \( d^{3/2} \) law. When a dendritic "parent" branch connects to, say, two "daughter" branches then the following equation must hold true

\[
d_{\text{parent}}^{3/2} = d_1^{3/2} + d_1^{3/2} \quad (3.35)
\]

When all these conditions are met, the entire dendritic tree may be replaced by an equivalent cylinder subject to certain restricted input conditions [see Figure (3.4)]. Naturally, this again is an idealised model, however one that simplifies a highly complex
structure. Obviously the vast majority of dendritic trees will not be able to satisfy every condition. The major discrepancy surprisingly, is not that the dendrites do not obey the 3/2 power law at individual branch points. Indeed some natural dendritic trees do satisfy this condition, for example the motoneurons of the cat spinal cord. It is that many higher order branches are missing. This is due to the fact that their potential parent branches terminate at electronic distances away from the soma that are much less than for terminal branches. Thus the sum of $d^{3/2}$ decreases significantly for successively higher-order branches. The dendritic tree is now equivalent to a tapered core conductor or indeed several cylinders of different length placed electrically in parallel with a common soma.

![Diagram of a branching structure replaced by an equivalent cylinder.](image)

Figure 3.4: Pictorial representation of a branching structure replaced by an equivalent cylinder. Here the two daughter branches are identical (both have diameter $d_1$ and length $L_1$). Using the equivalent cylinder approximation, the uppermost structure can be replaced by an unbranched cylinder of length $L_0 + L_1$ and its diameter is the same as the parent branch.

Progress has been made for other realistic scenarios, for example by J.D.Evans and G.Major [Evans et al. (1992), Major et al. (1993), Evans & Kember (1994)]. They considered the problem of many equivalent cylinders connected to a soma, firstly with all the cylinders having the same space and time constants but then extending this case to each cylinder having its own specific time and space constant.
An alternative method introduced by Abbott and colleagues [Abbott et al. (1991), Abbott (1991), Cao & Abbott (1993)] uses a path integral approach, much the same as used in quantum mechanics and quantum field theory. Briefly, the voltage at $x$ in response to current injection at a point $y$ in an arbitrary tree is obtained by summing the Green's function of the cable along all possible paths between $x$ and $y$. The advantage of this method is that for relatively short times only a few paths need to be included.

### 3.4.2 Compartmental modelling

The methods discussed above have some drawbacks in that they do not cope well with multiple current inputs. Indeed, in the presence of $n$ current inputs, the order of $n^2$ extra computations have to be performed [Koch (1999)]. In addition to this, the models assume the membrane voltage behaves linearly and thus neglect the influence of voltage dependent membrane components. A different method is thus required. The strategy we employ is called compartmental modelling. This work was pioneered by Rall in his now landmark paper, 'Theoretical significance of dendritic trees for neuronal input-output relations' [Rall (1964)].

In the compartmental modelling approach, an unbranched region of a dendrite is partitioned into a number, $N$, of contiguous regions [Perkel & Mulloney (1980)]. Each region or compartment is considered small enough to be deemed isopotential. Thus non-uniformity in physical properties and differences in potential occur between compartments rather than within them [Bressloff & Coombes (1997)].

So formally we consider an unbranched, cylindrical region of a passive dendrite. A linked chain of equivalent electrical circuits represents this region as shown below [see Figure (3.5)].

We now consider the $\alpha$th compartment. As the diagram shows, it consists of a capacitor $C_{\alpha}$ in parallel with a resistor, $R_{\alpha}$. These electrical parameters are equivalent to the membrane capacitance and resistance in the previous sections. The membrane potential $V_{\alpha}(t)$ is defined as the displacement from the resting potential. In order to simplify matters, the resting potential is taken to be zero. This eliminates the need for there to be a battery in series with the membrane resistance. Each compartment is joined to its immediate neighbours by the junctional resistors $R_{\alpha,\alpha-1}$ and $R_{\alpha,\alpha+1}$. These parameters are related to the longitudinal resistances.

So relating the parameters used in the previous sections to the ones used in compart-
Figure 3.5: Equivalent circuit for a compartmental model of a chain of successive cylindrical segments of a passive dendritic membrane [Bressloff & Coombes (1997)].

In compartmental modelling, we set,

\[ R_m = R_2, \quad C_m = C_a, \quad R_4 = r_a \]  \hspace{1cm} (3.36)

Now suppose the cylinder has uniform diameter, \( d \) and let the length of the \( \alpha \)th compartment be \( l_\alpha \). Then the new parameters have the following relations,

\[ C_\alpha = c_\alpha l_\alpha \pi d, \quad R_\alpha = \frac{1}{g_\alpha l_\alpha \pi d}, \quad R_{\alpha \beta} = \frac{2r_\alpha l_\alpha + 2r_\beta l_\beta}{\pi d^2} \]  \hspace{1cm} (3.37)

where \( g_\alpha \) and \( c_\alpha \) are the membrane conductance and capacitance per unit area respectively.

Applying Kirchoff’s law to this system [Bressloff (1994)] we obtain the following equation,

\[ C_\alpha \frac{dV_\alpha}{dt} = -\frac{V_\alpha}{R_\alpha} + \sum_{\langle \beta, \alpha \rangle} \frac{V_\beta - V_\alpha}{R_{\alpha \beta}} + I_{EXT(\alpha)}(t), \quad t \geq 0 \]  \hspace{1cm} (3.38)
where \( I_\alpha(t) \) represents the net external input into the \( \alpha \)th compartment and \( \langle \beta; \alpha \rangle \) indicates that the sum over \( \beta \) only extends to the immediate neighbours of \( \alpha \).

We may now divide through by \( C\alpha \), and rewrite equation (3.38) as a linear matrix equation,

\[
\frac{dV}{dt} = QV + I(t), \quad Q_{\alpha\beta} = \frac{\delta_{\alpha\beta}}{\tau_\alpha} + \sum_{\beta' \neq \alpha} \frac{\delta_{\beta'\beta}}{\tau_{\alpha\beta'}}
\]

where the membrane time constant \( \tau_\alpha \) and the junctional time constant are given by,

\[
\frac{1}{\tau_\alpha} = \frac{1}{C\alpha} \left[ \sum_{\beta' \neq \alpha} \frac{1}{R_{\alpha\beta'}} + \frac{1}{R_\alpha} \right], \quad \frac{1}{\tau_{\alpha\beta}} = \frac{1}{C\alpha R_{\alpha\beta}}
\]

The matrix equation (3.39) may be solved formally as,

\[
V_\alpha(t) = \sum_\beta \int_0^t G_{\alpha\beta}(t - t')I_\beta(t') + \sum_\beta G_{\alpha\beta}(t)V_\beta(0), \quad t \geq 0
\]

with

\[
G_{\alpha\beta}(t) = [\exp(Qt)]_{\alpha\beta}
\]

The membrane potential of the \( \alpha \)th compartment at time \( t \) in response to a unit impulse stimulation of compartment \( \beta \) at time \( t - T \) is determined by the response function \( G_{\alpha\beta}(T) \). To obtain this function it is best to follow the recent approach as proposed by Bressloff and Taylor (1993). We leave this for the reader to pursue if he/she is particularly interested.

To summarize then, the compartmental modelling approach replaces the continuous partial differential equation of the analytical model [equation (3.11)] by a set of \( N \) ordinary differential equations. There are two key advantages of using this approach. Firstly, the flexibility of compartmental modelling ensures a far higher degree of resolution. The degree of resolution is obviously dependent on the amount of compartments we wish to divide the dendrite into. Secondly, the compartmental model can be implemented directly on a computer. It is this that we now consider.
3.4.3 Numerical methods

The implementation of the compartmental approach on a computer is undoubtedly the most common and efficient method of solution. We discretize both space and time to obtain a difference equation that may be solved iteratively. Consider equation (3.38), having expanded the summation,

\[ C \frac{dV_a}{dt} = -\frac{V_a}{R_a} + \frac{V_{a+1} - V_a}{R_{a,a+1}} + \frac{V_{a-1} - V_a}{R_{a,a-1}} + I_{\text{EXT}(a)}(t) \]  

(3.43)

We can now discretize time. Let \( V^n \) denote the membrane potential in the \( a \)th compartment at time level \( n \). We thus obtain,

\[ C \frac{V_a^{n+1} - V_a^n}{\Delta t} = -\frac{V_a^n}{R_a} + \frac{V_{a+1}^n - V_a^n}{R_{a,a+1}} + \frac{V_{a-1}^n - V_a^n}{R_{a,a-1}} + I_{\text{EXT}(a)}^n \]  

(3.44)

This then is our finite-difference scheme for a passive cable with non-uniform electronic structure. In subsequent chapters, our numerical simulations do not require such a high level of biological resolution as we assume the dendrite to be unbranched and uniform. Due to this simplification, we may apply the discretization process straight to the partial differential equation (3.11), to obtain the following explicit scheme,

\[ V^{n+1}_i = \left(1 - \frac{\Delta t}{\tau} \right) V^n_i + \frac{D\Delta t}{\Delta \xi^2} (V^n_{i+1} - 2V^n_i + V^n_{i-1}) + \Delta t I_{\text{EXT}(i)}^n \]  

(3.45)

The presence of the diffusive term naturally places a restriction on the relative sizes of \( \Delta t \) and \( \Delta \xi \) because of the explicit nature of the numerical scheme. That is to achieve numerical stability the inequality \( D\Delta t/\Delta \xi < 0.5 \) has to be satisfied. In the appropriate places we will state exactly which values of \( \Delta t \) and \( \Delta \xi \) we use.

As we are essentially dealing with a parabolic equation, alternative finite difference schemes can be employed. The backward-Euler scheme or the Crank-Nicolson method are both valid alternatives. Indeed both these schemes place no restrictions on the sizes of \( \Delta t \) and \( \Delta \xi \). This benefit comes with the cost of having to solve a tri-diagonal matrix at every new time-step as both methods are implicit. The author felt that the results achieved by the explicit method were good enough not to warrant an excursion into implicit numerical schemes. For a more in depth review of numerical methods used in neuronal modelling see Mascagni (1989) or Koch (1999).

As one can see, compartmental modelling and numerical modelling do have advantages
over analytical methods, however these methods should not be regarded as superior but much rather as complementary to the analytical methods. Indeed, in order to verify predictions or to confirm analytical results, numerical methods are usually the only solution.

3.5 Cable Theory for Quasi-Active Dendrites

3.5.1 Introduction

As we described in section (2.3.3) the active properties of dendrites support a number of unique processes vital for information decoding. These include amplification of synaptic inputs, back-propagation of action potentials and action potential initiation.

In general, linear cable theory fails to cope adequately with the complicated nonlinear processes which active membranes represent. The passive cable model also fails for small structures, such as spines. In this case, an electro-diffusion model has the necessary dexterity and finesse to cope with the rapid movement of ions across the membrane [Sejnowski & Quian (1992), Quian & Sejnowski (1989)]. Compartmental modelling is another valid method that has the required capability to enhance its resolution. It has successfully been employed by various authors [Jaegar et al. (1997), Jackson & Cauller (1997)]. However, as this method is implemented predominantly on a computer, most mathematical analytical insights are lost.

Progress may be made however, if we restrict the membrane's potential to relatively small deviations. As a consequence of this, it is then possible to linearize the nonlinear channel conductance [Koch (1999)]. The resultant membrane is then termed quasi-active or active-linearized [Koch (1984)]. We may distinguish between the two membranes (quasi-active and passive) by their filtering properties. The quasi-active membrane shows bandpass-like behaviour in its membrane impedance. That is the membrane impedance shows a prominent maximum at some nonzero resonant frequency. This is in direct contrast to a purely passive membrane which always behaves as a low pass filter [see Figure (3.3)].

Resonant-like behaviour has been shown to subserve specific neuronal functions. For example, rod photoreceptors of lower vertebrates have a receptive field which increases in size for increased temporal frequency of stimulus [Detwiler et al. (1978) (1980)]. Furthermore, hair cells in the vertebrate cochlea show their maximal sensitivity at some nonzero frequency value [Crawford & Fettiplace (1981)].
As described by Koch, the quasi-active membrane can be described in terms of resistors, capacitors and inductors. The addition of an inductance naturally changes the simple RC circuit which we represent the passive membrane [Figure (3.2)] by an RLC circuit. As shown by many electrical theory textbooks [Irwin (1996), Howatson (1996)], it is the presence of this inductance that allows resonance to become a feature of the system [Hoppensteadt (1997)].

3.5.2 Cable equation for quasi-active dendrites

We now elucidate on how an inductance-like behaviour can arise from the linearization of an active neural membrane. We initiate proceedings by considering the so-called Hodgkin-Huxley (HH) [Hodgkin & Huxley (1952 a,b,c,d)] system of equations. The HH model is truly able to mimic an active, excitable membrane. The equations are set out below,

\[ C \frac{dV}{dt} = -F + I(t) \]  \hspace{1cm} (3.46)

\[ F(V, m, h, n) = [g_Na m^4 h(V - V_{Na}) + g_K n^4 (V - V_K) + g_l (V - V_l)] \]  \hspace{1cm} (3.47)

In this model, the membrane current \( F \), arises from the conduction of sodium and potassium ions through voltage dependent channels in the membrane. Any other ionic currents are described by the Ohmic leakage contribution. \( F \) is thus a function of \( V \) and of three time- and voltage dependent conductance variables \( m \), \( h \) and \( n \). \( C \) is the membrane capacitance and \( I(t) \) is the input current. The various parameters in equation (3.47) take the following values \( g_l = 0.3 \text{ mmho/cm}^2 \), \( g_K = 0.36 \text{ mmho/cm}^2 \), \( g_{Na} = 120 \text{ mmho/cm}^2 \), \( V_l = -54.402 \text{ mV} \), \( V_K = -77 \text{ mV} \) and \( V_{Na} = 50 \text{ mV} \).

The conductance variables \( m \), \( h \) and \( n \) by definition take values between zero and one. Furthermore, they all approach asymptotic values \( \bar{m}(V) \), \( \bar{h}(V) \) and \( \bar{n}(V) \) with time constants \( \tau_m(V) \), \( \tau_h(V) \) and \( \tau_n(V) \) respectively,

\[ \tau_m \frac{dm}{dt} = \bar{m}(V) - m \hspace{1cm} \tau_h \frac{dh}{dt} = \bar{h}(V) - h \hspace{1cm} \tau_n \frac{dn}{dt} = \bar{n}(V) - n \]  \hspace{1cm} (3.48)

where for all three variables,

\[ \tau_{(m,h,n)} = \frac{1}{\alpha_{(m,h,n)} + \beta_{(m,h,n)}} \]  \hspace{1cm} (3.49)

\[ (\bar{m}(V), \bar{h}(V), \bar{n}(V)) = \frac{\alpha_{(m,h,n)}}{\alpha_{(m,h,n)} + \beta_{(m,h,n)}} \]  \hspace{1cm} (3.50)
and specifically,

\[
\alpha_m = \frac{0.1(V + 40)}{1 - \exp[-0.1(V + 40)]}
\]

(3.51)

\[
\alpha_h = 0.07 \exp[-0.05(V + 65)]
\]

(3.52)

\[
\alpha_n = \frac{0.01(V + 55)}{1 - \exp[-0.1(V + 55)]}
\]

(3.53)

\[
\beta_m = 4 \exp[-0.0556(V + 65)]
\]

(3.54)

\[
\beta_h = \frac{1}{1 + \exp[-0.1(V + 35)]}
\]

(3.55)

\[
\beta_n = 0.125 \exp[-0.125(V + 65)]
\]

(3.56)

We ask the reader to note that this model is described in more detail in Chapter 7 and in particular we analyse its relationship to the integrate-and-fire model. The quasi-active model is procured by linearizing each current around some fixed potential. In order to demonstrate this principle of linearization we follow Koch’s detailed analysis [Koch (1999)].

For simplicity we initially focus upon the potassium current:

\[
I_K = g_K n^4(V - V_K)
\]

(3.57)

Small perturbations of this current around some fixed potential \(V_r\) may be written

\[
\delta I_K = \frac{\delta V}{R_K} + 4g_K n^3(V - V_K)\delta n, \quad R_K^{-1} = g_K n^4(V_r)
\]

(3.58)

Using (3.48) and (3.49) and the fact that \(\delta n\) is small we may write

\[
\frac{d\delta n}{dt} = \delta \alpha_n - (\delta \alpha_n + \delta \beta_n)n - (\alpha_n + \beta_n)\delta n
\]

(3.59)

Since \(\alpha_n\) and \(\beta_n\) only depend upon the membrane potential \(V\) [see equations (3.53) and (3.56)] we have that

\[
\left(\frac{d}{dt} + \alpha_n + \beta_n\right) \delta n = \left[\frac{d\alpha_n}{dV} - (\alpha_n + \beta_n)\right] \delta V
\]

(3.60)

Combining (3.60) with (3.58) we arrive at the following equation for the first-order
variation of the potassium current

\[
\delta I_K = \frac{\delta V}{R_K} + \delta I
\]  

(3.61)

where \(\delta I\) satisfies

\[
\left(\frac{1}{r_n} + L_n \frac{d}{dt}\right) \delta I = \delta V
\]  

(3.62)

and

\[
\begin{align*}
    r_n^{-1} &= \frac{4g_K n^3 (V - V_K) [d\alpha_n/dV - n d(\alpha_n + \beta_n)/dV]}{\alpha_n + \beta_n} \\
    L_n &= \frac{r_n}{\alpha_n + \beta_n}
\end{align*}
\]  

(3.63) (3.64)

Hence, for a small perturbation \(\delta V\) around \(V_r\), the potassium current responds as though the resistance \(R_K\) is in parallel with a resistance \(r_n\) that is itself in series with an inductance \(L_n\) [see Figure (3.6)]. Such inductive terms account for the oscillatory overshoot commonly seen in response to depolarising current steps or even after the firing of an action potential. Koch terms this form of equivalent linear membrane circuit quasi-active to distinguish it from a truly active membrane.

Figure 3.6: Effective impedance diagram associated with the linearized potassium current for the Hodgkin-Huxley system.

The sodium and leak currents may be linearized along much the same lines as the potassium current. Indeed the linearization of the full HH set of equations leads to a system which is succinctly expressed in Fourier space as,
\[
\delta V(\omega) = K(\omega)[\delta I_K(\omega) + \delta I_{Na}(\omega) + \delta I_L(\omega)]
\]  

(3.65)

where \(K(\omega)\) is the (complex) impedance of the linearised Hodgkin-Huxley membrane and \(f(\omega) = \int_{-\infty}^{\infty} dt e^{-i\omega t} f(t)\). Koch (1984) has shown that the impedance of the quasi-active Hodgkin-Huxley system has the form

\[
K(\omega) = \frac{\beta_0 + \beta_1 \omega + \beta_2 \omega^2 + \beta_3 \omega^3}{\alpha_0 + \alpha_1 \omega + \alpha_2 \omega^2 + \alpha_3 \omega^3 + \alpha_4 \omega^4}
\]  

(3.66)

The \(\alpha_i\)'s and \(\beta_i\)'s are constants which depend on the values of the electrical components shown in Figure (3.7).

Utilising this theory we may now extend our analysis from purely passive cables to quasi-active ones. Consider then a linear one dimensional cable [Bressloff (1999)]. We represent this, as before, by a semi-infinite ladder network as shown below [Figure (3.8)].

With this configuration, the passive cable equation (3.2) describing the membrane potential, \(V(\xi, t)\) of a dendrite, is now supplemented by an equation describing the current, \(I(\xi, t)\), through the inductive branch of the equivalent circuit, so that the equations for the quasi-active system are [Bressloff (1999)],

\[
\frac{\partial V(\xi, t)}{\partial t} = \frac{-V(\xi, t)}{\tau} + D \frac{\partial^2 V(\xi, t)}{\partial \xi^2} + \frac{I(\xi, t)}{c} + I_{EXT}(\xi, t)
\]  

(3.67)

\[
l \frac{\partial I(\xi, t)}{\partial t} = -r_l I(\xi, t) + V(\xi, t)
\]  

(3.68)

43
Figure 3.8: (a) Ladder representation of a one-dimensional cable with frequency dependent membrane impedance $z_m(\omega)$ and longitudinal resistance $r_a$. (b) Electric circuit of a linearized (quasi) active membrane.

where $l$ is the inductance and $r_l$ is the resistor in series with said inductance [refer to Figure (3.8)]. Relating the other parameters used in these equations (3.67) and (3.68) to the parameters used in equation (3.2), it may be seen that $c = C_m$, $r = R_m$ and $r_a = R_a$. The biologically plausible values of the membrane parameters in the above equation are as follows [Koch (1984)]: $r = 0.3 \Omega m^2$, $c = 0.001 F m^{-2}$, $r_a = 2.8 \times 10^6 \Omega$, $r_l = 0.1 - 1.0 \Omega m^2$, $l = 6 \times 10^{-4} H m^2$. Invariably we rescale these parameters in our latter models, further details will be provided where necessary. We note that the parameter $r_l$ enables the system to switch between quasi-active ($r_l = 0$) and passive ($r_l \to \infty$). This feature of the model will be highlighted in the subsequent analysis.

### 3.6 Solution of the Quasi-Active Cable Equation

We apply the same methods of analysis as in the passive case. We consider the time-independent solutions first and then proceed to the complete time-dependent case. In both cases we employ the Green's function method of solution.
3.6.1 Steady-state solutions

We transform the two partial differential equations (3.67) and (3.68) into a single ordinary differential equation by removing the time-dependence in each equation and eliminating the inductive current term. The equation is thus,

$$\frac{d^2 \tilde{V}(\xi)}{dt^2} - \frac{1}{\lambda_a^2} \tilde{V}(\xi) = -\frac{\hat{I}_{\text{EXT}}(\xi)}{D}$$

where in (3.69), the parameter $\lambda_a$ is defined as,

$$\frac{1}{\lambda_a^2} = \frac{1}{\lambda^2} \left[ 1 + \frac{\tau}{ct} \right]$$

this is in exactly the same form as the passive case (c.f. equation (3.17)) we note that as $\tau \to \infty$ we recover the steady state passive equation (equation (3.17)). So trivially, the solution to the quasi-active steady state equation (3.69) is given by,

$$\tilde{V}(\xi) = -\frac{1}{D} \int_0^\infty G(\xi, \xi') \hat{I}_{\text{EXT}}(\xi') d\xi'$$

where,

$$G(\xi, \xi') = \begin{cases} -\lambda_a \exp\left(-\xi'/\lambda_a\right) \cosh(\xi/\lambda_a) & 0 \leq \xi < \xi' \\ -\lambda_a \exp\left(-\xi/\lambda_a\right) \cosh(\xi'/\lambda_a) & \xi' < \xi < \infty \end{cases}$$

3.6.2 Time-dependent solutions

As with the purely passive case, the time-dependent case is of most interest. We again follow Koch's analysis to study the membrane in the frequency domain. The beauty of this method is that it is surprisingly easy to extend the analysis on passive membranes to quasi-active ones. We need only change the form of the propagation constant, $\gamma(\omega)$, in the transfer function (the Fourier transform of the Green's function).

So, we first take the Fourier transform of both equations (3.67) and(3.68) with respect to time to obtain,

$$i\omega \tilde{V}(\xi, \omega) = -\frac{\tilde{V}(\xi, \omega)}{\tau} + D \frac{d^2 \tilde{V}(\xi, \omega)}{d\xi^2} - \frac{\tilde{I}(\xi, \omega)}{c}$$

$$i\omega \tilde{I}(\xi, \omega) = -\tau \tilde{I}(\xi, \omega) + \tilde{V}(\xi, \omega)$$
Rearranging the equations above (3.73) and (3.74) so that we eliminate \( l(\xi, \omega) \) and we obtain a linear equation in \( \tilde{V}(\xi, \omega) \),

\[
\frac{d^2 \tilde{V}(\xi, \omega)}{d\xi^2} - \frac{1}{D} \left[ \frac{1}{r} + \frac{1}{c} \left( \frac{1}{r_1 + i\omega l} \right) + i\omega \right] \tilde{V}(\xi, \omega) = 0
\]  

(3.75)

Following exactly the same pattern of analysis as for the passive case, we see that only the propagation constant has changed between the two cases [c.f. (3.23)],

\[
\gamma^2(\omega) = \frac{r_a}{z_m(\omega)}
\]

(3.76)

where,

\[
z_m(\omega) = \frac{r(r_1 + i\omega l)}{r + r_1 - \omega^2 l r + i\omega(l + r_1 r)}
\]

(3.77)

In the limit \( r_1 \to \infty \), we recover the passive membrane impedance equation (3.26).

Again we require the quasi-active propagation constant [as defined by equations (3.76) and (3.77)] to be broken down into its real and imaginary parts for certain analysis performed in the proceeding chapters. This procedure of representing \( \gamma(\omega) \) as \( a(\omega) + ib(\omega) \) is naturally a more involved process. However we accomplish this in two steps. Firstly decompose \( z_m(\omega) \) into real and imaginary parts, \( z_m(\omega) = r[u(\omega) + iv(\omega)] \), where

\[
u(\omega) = \frac{l(\xi, \omega) - lr \omega + l \omega^2 [l + r r l]}{Aw^4 + Bw^2 + C}
\]

(3.78)

\[
u(\omega) = \frac{lw[l + r(\xi, \omega) - lr l]}{Aw^4 + Bw^2 + C}
\]

(3.79)

and \( A = (r l)^2, B = l^2 + (r l)^2 - 2rr l \) and \( C = (r + r l)^2 \). Note that both \( u(\omega) \) and \( v(\omega) \) are dimensionless. Secondly we express \( a(\omega) \) and \( b(\omega) \) in terms of \( u(\omega) \) and \( v(\omega) \).

\[
a(\omega) = \frac{1}{\sigma} \sqrt{\frac{u(\omega) + \sqrt{u(\omega)^2 + v(\omega)^2}}{2[u(\omega)^2 + v(\omega)^2]}}
\]

(3.80)

\[
b(\omega) = \frac{-\text{sign}(v(\omega))}{\sigma} \sqrt{\frac{-u(\omega) + \sqrt{u(\omega)^2 + v(\omega)^2}}{2[u(\omega)^2 + v(\omega)^2]}}
\]

(3.81)

where \( \sigma = \sqrt{D r} \). As we mentioned in the introduction, the inclusion of an inductance within this electrical system can lead to resonant-like behaviour in which the impedance
|z_m(ω)| goes through a maximum at some non-zero frequency ω_{max}. We see that for the electrical circuit, shown in Figure (3.8), there exists a maximum at,

\[ \omega_{max} = \left[ -r_l/l^2 + ((r_l/l)^4 - E)^{1/2} \right]^{1/2} \quad (3.82) \]

provided that \( E \equiv (Br_l^2 - l^2C)/(AI^2) < 0 \) [Koch (1984)]. The ideal resonant circuit is the one with \( r_l = 0 \). In this case, \( \omega_{max} = 1/\sqrt{LC} \). In order to investigate how \( \omega_{max} \) varies with \( r_l \) we use the fact that the transfer function, \( \tilde{G}(ξ,ω) \), reflects the frequency filter characteristics of the membrane impedance, \( z_m(ω) \). That is if the impedance \( z_m(ω) \) has band-pass characteristics then so does the transfer function. So

\[ |\tilde{G}(ξ,ω)|^2 = \frac{1}{D^2 r_a} |z_m(ω)| e^{-2a(ω)} \quad (3.83) \]

has a maximum at \( \omega_{max} \), where \( a(ω) \) denotes the real part of \( γ(ω) \) [equation (3.80)]. The amplitude \( |\tilde{G}(0,ω)| \) is plotted below in Figure (3.9) as a function of \( ω \) and for various values of \( r_l \).

![Figure 3.9: Modulus of transfer function |\tilde{G}(0,ω)|^2 (in units of 1/D^2r_a) as a function of frequency ω (in units of 1/τ) for various values of the inductive resistance r_l. Here D = r_a = τ = 1 and l = 0.2 Hm^2. A transition from band-pass to low-pass can be seen as r_l increases. (a) r_l = 0.0, (b) r_l = 0.1, (c) r_l = 0.5, (d) r_l = 1.0 Ωm^2.](image)

As one can see, the value of \( \omega_{max} \) initially increases then decreases as \( r_l \) is increased from zero, until eventually the system acts as a low-pass filter, redolent of a passive
membrane [Figure (3.3)].

3.6.3 Numerical methods

For completeness we include the finite-difference scheme for the quasi-active system which we employ in future simulations. Discretizing both space and time in equations (3.67) and (3.68) with respective step lengths of $\Delta \xi$ and $\Delta t$ leads to the following explicit finite-difference scheme.

\[
V_i^{n+1} = \left(1 - \frac{\Delta t}{\tau}\right) V_i^n + \frac{D \Delta t}{\Delta \xi^2} (V_{i+1}^n - 2V_i^n + V_{i-1}^n) - \frac{\Delta t I_i^n}{c} + \Delta t I_{EXT(i)}^n \quad (3.84)
\]

\[
I_i^{n+1} = \frac{\Delta t V_i^n}{l} + \left(1 - \frac{\tau_i \Delta t}{l}\right) I_i^n \quad (3.85)
\]

As with the purely passive finite-difference scheme [equation (3.45)], $V_i^n$ represents the membrane voltage at time level $n$ in the $i$th compartment. Similarly $I_i^n$ denotes the current through the inductive branch of the $i$th compartment at time level $n$. 

48
Chapter 4

Neural Pattern Formation

A mathematician, like a painter or a poet, is a maker of patterns. If his patterns are more permanent than theirs it is because they are made with ideas.

G.H. Hardy

4.1 Introduction

A spatial pattern may be defined as a spatial inhomogeneity with a degree of regularity. That is to say, it is characterized by irregularity at the local scale and regularity at the global scale [Levin & Segel (1985)].

Spatial patterns are found in many different contexts throughout the sciences. For instance, the Belousov-Zhabotinski pattern in chemistry, Bénard convection cell patterns in fluid mechanics and the many obvious examples, such as animal coat markings, in biology [for further examples see Jäger & Murray (1984), Ball (1998)]. However, perhaps the most important and complex spatial patterning processes are those occurring in the nervous system. Two examples that have attracted much interest are patterns initiated through hallucinations and the ocular dominance stripes found in the visual cortex.

4.1.1 Ocular dominance stripes

The study of the mammalian visual cortex has steadily increased over the last twenty years. The interest has primarily been generated by the visual cortex's highly ordered
structure. Many theoretical neurobiologists are seeking to understand the processes which create this structure, as it has been conjectured that understanding this area of the brain, may actually shed light upon the whole of the cortex. For this reason, the discovery of the ocular dominance stripes has proved of great interest. Electrophysiological recordings conducted by Hubel and Wiesel showed that inputs from the left and right eyes were segregated into non-overlapping regions within layer IV of the cortex [Hubel & Wiesel (1962)(1972)]. They are characterized by their distinctive morphology and periodicity. For example, in the macaque monkey [see Figure (4.1) below], the ocular dominance stripes have periodicity of about 800$\mu m$ and width of around 400$\mu m$. They are often said to resemble the stripes of a zebra or indeed a fingerprint. However the process which underlies their development still remains somewhat of a mystery. Studies on newly born monkeys and monkeys which have been reared in the dark [Horton & Hocking (1996), LeVay et al. (1980)] have shown these primates have a nearly adult-like pattern of stripes despite no visual experience. This infers that the final outcome of segregation may be determined by patterns of neural activity.

Figure 4.1: Spatial pattern of ocular dominance stripes in the visual cortex of a macaque monkey. The dark band areas receive input from one eye while the unshaded regions receive input from the other eye. Reprinted from Murray (1993).

The ocular dominance stripes still remain an enigma from a functional point of view. Indeed, the stripes may be an incidental outcome of the visual cortex's development. This alternative idea has gained credance through the study of the marmoset and the three-eyed frog [Constantine-Paton (1983)]. Both species can be made to develop ocular dominance stripes where naturally they would not be present. This may infer that the stripes have no functional purpose. For an excellent review of this subject see
4.1.2 Visual hallucination patterns

Hallucinations may be induced by a number of different stimuli. Certain medical conditions such as epilepsy [Horwitz et al. (1967)] and migranes [Richards (1971)] have been known to provoke hallucinations. However, the most common form, especially since the 1960's have been drug induced hallucinations. Drugs such as LSD or mescaline often produce a bewildering array of visual hallucinations. Surprisingly during the initial stages of these drug induced hallucinations, many simple geometric shapes appear to the subject. These structures are apparently context free and independent of previous experiences [Siegel (1978)]. Extensive studies using mescaline based drugs were conducted by Klüver (1967). He concluded that the shapes could be classified into four categories of "form constants" regardless of the sensory input. These shapes may be viewed below [see Figure (4.2)]. The patterns are of two main types: small repetitive mosaics, such as lattices or honeycombs and the more global patterns such as the spiral, tunnel or funnel.

Figure 4.2: Typical examples of the basic pattern types observed by hallucinating subjects. (a) lattice, (b) cobweb, (c) spiral, (d) tunnel or funnel. Reprinted from Ermentrout & Cowan (1979).
It has been proposed that the origin of these patterns is cortical, as opposed to periphera1. Studies have shown that visual hallucinations may be elicited by electrically stimulating the sub-cortical regions of the temporal lobe [Horowitz et al. (1967), Penfield & Perot (1963)].

The two paradigms discussed above demonstrate the unique ability of populations of neurons to produce spatial patterns from their collective activity. The obvious question to ask now is: how do neurons form such spatial patterns?

4.2 Morphogenesis

The question of how collections of neuron can produce visual hallucinations or for that matter, ocular dominance stripes is a pertinent one. Indeed it forms the fundamental problem in development biology. That is, how are form and pattern generated from a comparatively featureless initial state? Although we are considering, neural based patterns, this question is equally relevant for animal markings, the vein structure of leaves or indeed the development of human embryos. This area of study is generally termed as morphogenesis. It has proved surprisingly difficult to obtain a general theory to explain the many examples of spatial patterns in nature. As Murray [Murray (1993)] states,

"Whatever pattern we observe in the animal world it is almost certain that the process that produced it is unknown."

However mathematical modelling has provided a variety of mechanisms which endeavour to explain the formation of spatial patterns within a biological environment. Without doubt the seminal contribution to this field of study was provided by Alan Turing [Turing (1952)], and it is this work which forms the basis of the pattern formation models we consider.

4.2.1 Turing mechanisms

In the now classical paper: 'The chemical basis of morphogenesis' [Turing (1952)], Turing studied a pair of reaction diffusion equations,

\[ \frac{\partial A}{\partial t} = F(A, B) + D_A \nabla^2 A \quad (4.1) \]
\[ \frac{\partial B}{\partial t} = G(A, B) + D_B \nabla^2 B \quad (4.2) \]
where \(A(x, t)\) and \(B(x, t)\) are the concentrations of two chemicals, \(F\) and \(G\) are the reaction functions (these are taken to be polynomials, although the exact form is unimportant). \(D_A\) and \(D_B\) are the diffusion coefficients of the respective chemicals. Through the analysis of these equations, Turing discovered a novel concept. That is, spatially inhomogeneous patterns can evolve through diffusion driven instabilities if and only if \(D_A \neq D_B\). This was a startling, even strange idea. Diffusion, up until this time, had always been thought of as a stabilising, smoothing mechanism. Murray provides an excellent example in his book [Murray (1993)], albeit unrealistic of how diffusion led instabilities may create patterns. We consider a synopsis of this example now.

Consider a large number of grasshoppers which inhabit a field of dry grass. These insects, when warmed, produce a lot of moisture through sweating. A fire is then started at the edge of the field, and the flame front starts to propagate with diffusion coefficient, \(D_F\), say. The grasshoppers once aware of the heat generated from the flames move quickly ahead of the flame front with diffusion coefficient, \(D_G\), say. We assume for the purpose of spatial pattern formation that \(D_G \neq D_F\) and that \(D_G \gg D_F\). The grasshoppers begin to sweat, due to the heat, and generate enough moisture to prevent the flames from entering these moistened areas. The charred area is thus confined to a distinct finite domain which is dependent upon both diffusion coefficients. By extending this example to a field in which a number of fires are started at random locations, we may finally see how this process would result in a final spatially inhomogeneous steady state distribution of charred and uncharred areas. The concept of competition between the grasshoppers and the fire is the key component of this analogy. A field set on light without any grasshoppers would just result in a charred field. Similarly, a field full of grasshoppers without any fire would just be a field full of grasshoppers.

Following the publication of Turing’s paper in 1952, there were only sporadic contributions from the scientific community which utilised Turing’s ideas [Wardlaw (1955)]. However by the early 1970’s, a number of theorists had begun to recognise the paper’s significance and had incorporated it into their own work. For example, Othmer and Scriven (1971) applied it to a cellular network.

The most salient contributions to this field were provided by two researchers, Gierer and Meinhardt, who surprisingly were initially unaware of Turing’s earlier findings. Using a variety of models aimed at explaining a number of key problems in development biology [Gierer & Meinhardt (1972)]. Meinhardt and Gierer’s conclusions were that in order to generate a diffusive based pattern, a combination of short-range activation (sometimes known as local self-enhancement) and long-range inhibition is needed. A substance, \(a\), is said to be autocatalytic or self-enhancing if a small increase of \(a\) over
its homogeneous steady-state concentration induces a further increase in a [Koch & Meinhardt (1994)]. Local enhancement is essential for the small local inhomogeneities to be amplified. However self-enhancement is not sufficient to generate stable patterns on its own. The self-enhancement of a has to complemented by a fast-diffusing antagonist, the inhibitor. The latter restricts the spread of the self-enhancing reaction into the surrounding area. This is achieved without choking the incipient local increase. The interaction between activator and inhibitor is the most important feature of this work as it is this competitive aspect of the model which underlies the formation of patterns [Meinhardt (1997), Oster & Murray (1989)]. This feature is evident in the simple grasshopper/fire analogy discussed above. The grasshoppers' 'sweat' provides the long-range inhibition whereas the fire acts as the local activator.

If we transpose the idea of the competitive interaction between activator and inhibitor to a neural environment, one may see immediately that the competition between excitatory and inhibitory inputs may act as the possible pattern formation mechanism. This in fact, lies at the very heart of the mathematical models proposed for the hallucinogenic patterns [Ermentrout and Cowan (1979) and as discussed above, the ocular dominance stripes [Swindale (1980) (1996), Harris et al. (1997)] and a variety of others [an der Heiden (1980), Amari (1982), Obermayer et al. (1995)]. In order to develop this idea further and introduce the necessary mathematical concepts for the latter models, we consider a simple model [Murray (1993)].

4.3 Simple Activation-Inhibition Model

4.3.1 Introduction

Although we deem this model to be simple, it in fact serves as an excellent pedagogical example and both Ermentrout and Cowan's model and Swindale's model are to some extent based upon it.

Before introducing the model, we make some general remarks regarding the modelling of neural systems. As with most biological systems, there are a number of inherent problems one encounters when trying to apply mathematics to describe it. The human cortex is a particularly complex example as we mentioned in Chapter 1. It is estimated to contain one hundred billion neurons each of which has the potential to make at least a thousand connections with other neurons. One can deduce immediately that the number of degrees of freedom is a phenomenally large number. Our philosophy, when modelling, is therefore to include enough biological detail whilst still making it
mathematically tractable. Simplification is therefore a necessity. Swindale (1996) puts it neatly when saying, “Models simplify reality by making assumptions. If they did not they would be of little use”. For this reason we employ the so-called “bottom-up” approach, starting with the simplest workable model and only then do we begin to add detail. For this initial model the assumptions are thus: the dendritic tree is neglected, each neuron is approximated as a point processor and we take the continuum limit and thus study neural networks in which space is continuous. This reduces dramatically the number of degrees of freedom [Haykin (1994)]. Furthermore, we choose to neglect the influence of noise, as a probabilistic treatment would then be warranted.

4.3.2 The model

Consider a population of neurons, represented as a one-dimensional network distributed along the x-axis. Let $U(x, t)$ denote the somatic membrane potential of the neuron located at the point $x$. Then the general equation of the neural network has the form,

$$
\frac{\partial U(x, t)}{\partial t} = -\frac{U(x, t)}{\tau_s} + \int_{-\infty}^{\infty} W(x, x') f(U(x', t)) dx' + I_{ext}(x)
$$

(4.3)

where $\tau_s$ denotes the membrane time constant for the soma. The convolution integral represents the combined inputs of neurons located at $x'$. A pictorial view of this system may be viewed below [see Figure (4.3)].

![Figure 4.3: One-dimensional network of neurons. $W(x - x')$ specifies the connectivity function from a neuron located at $x'$ to a neuron at $x$. $f(U)$ is the output firing-rate function for a given somatic potential $U$.](image)

The integral, as one may see, consists of a weighting or connectivity function, $W(x, x')$ and an output function, $f(U(x', t))$. The connectivity function, $W(x, x')$, determines the total strength of connection between a neuron located at $x'$ to a neuron located at $x$. The most typical form for $W(x, x')$ is one that is homogeneous, symmetric and
isotropic [Ermentrout (1998)]. That is, it is dependent only on the absolute spatial distance between \( x \) and \( x' \). We also include a bifurcation parameter, \( W_0 \), to facilitate analysis in the next section. Thus,

\[
W(x, x') = W_0 J(|x - x'|) = W_0 J(|x' - x|) \tag{4.4}
\]

There are many feasible choices for this function, \( J(x) \). Our choice is not completely free though, as we impose a condition that proximal cells exert more influence than distal ones and that as \( x \to \infty \) \( J(x) \to 0 \). Apart from this its form is wholly dependent upon exactly which type of connections we wish to model. These may be purely excitatory, purely inhibitory or perhaps more commonly a combination of both types of inputs. This in some respects utilises the Turing/Gierer/Meinhardt philosophy of a competition between activator and inhibitor. The choice of function most commonly used is shown below [see Figure (4.4)]. It is generally known as the Mexican Hat function for obvious reasons. It may be generated by a number of different means, however for simplicity we use the difference of two exponentials,

\[
J(x) = \Lambda [e^{-\gamma_1|x|} - e^{-\gamma_2|x|}] \tag{4.5}
\]

with the conditions \( \Gamma < 1, \gamma_1 > \gamma_2 > 0 \) and \( \Lambda = +1 \) being applied (the case of \( \Lambda = -1 \), which represents short-range inhibition and long-range excitation, will be considered in the following chapter). We note that this encapsulates the conditions expressed above as well as Gierer and Meinhardt's proposal of short-range activation and long-range (lateral) inhibition. We ask the reader to note that this weighting function allows the neuron to be connected to itself. This is a controversial issue and has not been completely resolved although some evidence has been provided [Tamas et al. (1997)].

The output function \( f(U(x', t)) \) may be interpreted as a short-time average firing rate in which details of individual spikes are neglected [see section (2.3)]. Its derivation is dependent upon certain statistical considerations [Amari (1977) (1980), Koch (1999)]. We are limited to its form (due to biological considerations), as the function must be strictly monotonically increasing and bounded. Thus, as our choice we take,

\[
f(U) = 1 + \tanh(\kappa U) \tag{4.6}
\]

where \( \kappa \) is the gain parameter. The advantage of using this analog model of output activity is purely a mathematical one. As \( f(U) \) is differentiable, we are able to employ
4.3.3 Linear stability analysis

Although pattern formation is principally a nonlinear phenomenon, a good indication of expected behaviour can be obtained by using linear stability analysis. Thus we begin by setting the external bias $I_{ext}(x) = -W_0 \int_{-\infty}^{\infty} J(x - x')$ in equation (4.3) so
that $U(x) = 0$ is the fixed point of the system. We then linearize the resultant equation about the zero homogeneous solution $U(x) \equiv 0$ obtaining

$$\frac{\partial U(x,t)}{\partial t} = -\frac{U(x,t)}{\tau_s} + W_0 \int_{-\infty}^{\infty} J(x-x')U(x',t)dx'$$ (4.7)

where a factor of $\kappa = f'(0)$ has been absorbed into $W_0$. Substitute into equation (4.7) a solution of the form $U(x, t) = U_0 \exp(\nu t + ipx)$, where $\nu$ is the growth factor and $p$ is the wave number of the pattern. This leads to the following characteristic equation,

$$\frac{1}{\tau_s} + \nu = W_0 \mathcal{J}(p)$$ (4.8)

where $\mathcal{J}(p)$ is the Fourier transform of $J(x)$. This is given by the formula,

$$\mathcal{J}(p) = 2\lambda \left[ \frac{\gamma_1}{p^2 + \gamma_1^2} - \frac{\gamma_1}{p^2 + \gamma_2^2} \right]$$ (4.9)

This is shown below in Figure (4.6)

![Figure 4.6: Fourier transform of the Mexican Hat function $\mathcal{J}(p)$. A static Turing instability occurs at the critical point $W = W_0c$ and the associated wave number is $\pm p_c$. The parameter values are the same as for Figure (4.4).](image)

Denote the solution of this characteristic equation (4.8) by $\nu(p)$. We may now state the conditions under which a Turing-like instability may arise.
(A) \( \text{Re} \, \nu(0) < 0 \) (the zero solution is stable to homogeneous perturbations)

(B) \( \exists \) at least one non-zero value of \( p \) for which \( \text{Re} \, \nu(p) \geq 0 \)

If \( \text{Re} \, \nu(p) \geq 0 \) over an interval \((p_1, p_2)\) then large scale patterns with wave numbers in this interval are expected to grow. This growth however is not unbounded, the nonlinearities within the system saturate it. We note that the pattern is stationary if \( \text{Im} \, \nu(p_c) = 0 \) at the bifurcation point. This we term as a static Turing instability. If, however \( \text{Im} \, \nu(p_c) \neq 0 \), then a time-periodic pattern may form. Naturally this is termed a dynamic Turing instability. For this simple example, however, \( \nu(p) \) is real for all \( p \). Hence a dynamic instability cannot occur.

Returning to equation (4.8) and taking \( W_0 \) as the bifurcation parameter, it is clear from Figure (4.6) that for sufficiently small \( W_0 \), the dispersion relation [equation (4.8)] satisfies \( \nu(p) < 0 \) \( \forall p \). However, as \( W_0 \) is increased a critical value \( W_{0c} \) is reached such that [this is shown on Figure (4.6)],

\[
\frac{1}{\tau_s} = W_{0c} \tilde{J}(p_c)
\]

where \( \tilde{J}(p_c) = \max_p[\tilde{J}(p)] \). Such a critical point satisfies the conditions for a Turing instability provided that \( p_c \neq 0 \). From equation (4.9), we obtain the result,

\[
p_c^2 = \frac{\gamma_1^2 \sqrt{\Gamma \gamma_2 / \gamma_1} - \gamma_2^2}{1 - \sqrt{\Gamma \gamma_2 / \gamma_1}}
\]

so that \( p_c \neq 0 \) when \( \Gamma > (\gamma_2 / \gamma_1)^3 \).

4.3.4 Numerical results

We employ a simple numerical scheme to simulate the model and thus validate the analytical result obtained in the previous section. We consider a one-dimensional chain of neurons labelled \( i = 1, \ldots, N \) and denote the somatic potential of the \( i \)th neuron at time level \( n \) by \( U_i^n \). The discretized version of equation (4.3) is

\[
U_i^{n+1} = \left( 1 - \frac{\Delta t}{\tau_s} \right) U_i^n + W_0 \sum_{j=1}^{N} J(|i-j|) \tanh(\kappa U_j^n)
\]

where \( J(|i-j|) \) is the discretized form of equation (4.5). That is
This numerical scheme is naturally an explicit scheme and is thus reasonably easy to implement. We set $\tau_s = \kappa = 1$, $\Delta t = 0.001$, $\Delta x = 0.2$ and take $N = 101$. We choose an initial condition for which the somatic membrane potential of each neuron is assigned a random value from the range $-0.2$ to $0.2$. The parameters defining the Mexican hat function take the following values: $\Lambda = +1$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.53$ and $W_0 = 10.0$. We then iterate this numerical scheme 10,000 times. The result can be seen below in Figure (4.7) where we plot the somatic potential $U$ as a function of $x$.

![Figure 4.7](image.png)

Figure 4.7: Steady-state pattern arising from a static Turing instability in a one-dimensional array of neurons. The parameters took the following values: $\Lambda = +1$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.53$ and $W_0 = 10.0$. 

\[
J(|i-j|) = \Lambda [e^{-\gamma_1|i-j|\Delta x} - \Gamma e^{-\gamma_2|i-j|\Delta x}]
\] (4.13)
Chapter 5

Neural Pattern Formation with Passive Dendritic Structure

5.1 Introduction

The work in this chapter has been presented in the paper Bressloff & De Souza (1998) which itself was an extension of the paper by Bressloff (1996). Essentially, we analyse a new model of neural pattern formation which takes into account the combined effect of diffusion along the dendritic tree and recurrent interactions via axo-dendritic synaptic connections. For concreteness, we take a one-dimensional recurrent network of analog neurons with the dendritic tree modelled as a semi-infinite uniform cable. Using a mixture of linear stability analysis, numerical simulations and bifurcation theory, we derive conditions for the onset of a Turing-like instability leading to the generation of stable spatial patterns.

The inclusion of the dendritic structure is important for a number of reasons. As discussed in section (2.3) the dendritic tree is responsible for much of the information processing which occurs within a neuron. Our model, although being a simple one-dimensional passive cable does have the capabilities to model some interesting features. For example, there has been reasonable evidence that the location of a synapse is often correlated with the relative positions of the interacting cells. Wilson and Bower (1992) amongst others [Shepherd (1998)] have shown that the recurrent collaterals of pyramidal cells in the olfactory cortex feed back onto the basal dendrites of nearby cells and onto the apical dendrites of distant pyramidal cells. Hence a synapse tends to be located further away from the soma as the separation between the neurons increases. This results in a reduction of effectiveness of the synaptic connection due to the diffusion
of the dendritic tree. As has been explained [subsection (2.3.3)], there are a number of mechanisms which could compensate for the reduction in long-range connections, such as the active properties of the dendrite's membrane and also an increase in the density of distal synapses. With our model we do not seek to model this aspect of information processing, instead we concentrate on the correlation of the location of the synapse with the relative position of the interacting cells and also the effect of diffusion which is the defining feature of passive membranes [see subsection (2.3.2)].

5.2 The model

Consider a one-dimensional network of analog neurons distributed along the x-axis. Let $U(x, t)$ denote the somatic membrane potential of the neuron located at $x \in \mathbb{R}$ at time $t$. Let $V(\xi, x, t)$ be the dendritic membrane potential at a point $\xi \in \mathbb{R}^+$ on the cable of said neuron and let $W(\xi, x', x)$ be the connection of a neuron at $x'$ impinging on a synapse located at $\xi$ on the dendritic cable of a neuron at $x$. The pictorial representation of the model may be seen below [Figure (5.1)]. The governing equations for $U$ and $V$ may be written down using standard cable theory [see section (3.2)] [Bressloff (1995)].

\[
\frac{\partial U(x, t)}{\partial t} = -\frac{U(x, t)}{\tau_s} + I_d(x, t) \quad (5.1)
\]

\[
\frac{\partial V(\xi, x, t)}{\partial t} = -\frac{V(\xi, x, t)}{\tau_d} + D \frac{\partial^2 V(\xi, x, t)}{\partial \xi^2} + \int_{-\infty}^{\infty} W(\xi, x', x) f(U(x', t)) dx' + I_{ext}(\xi, x) \quad (5.2)
\]

Equation (5.2) is supplemented by the boundary condition,

\[
-\frac{\partial V}{\partial \xi} \bigg|_{\xi=0} = I_d(x, t) = \rho_0 [V(0, x, t) - U(x, t)] \quad (5.3)
\]

Here $I(x, t)$ is the current density flowing to the soma from the cable at $\xi = 0$, $\rho_0$ is a conductance (in appropriate units), and $I_{ext}(\xi, x)$ is the external bias. The time constants for the soma and dendrites are $\tau_s$ and $\tau_d$ respectively. We ask the reader to be aware that throughout Chapter 3 the dendritic time constant, $\tau_d$ has just been referred to as just $\tau$. 
Figure 5.1: One-dimensional network of analog neurons with dendritic structure represented by a semi-infinite cable. $W(\xi, x, x')$ specifies the axo-dendritic connections from neuron $x'$ to neuron $x$ and $f(U)$ is the output firing-rate function for a given somatic potential $U$.

The connection function is essentially the same as in the previous section. We impose the homogeneity, isotropic and symmetric conditions, such that $W(\xi, x', x) = W(\xi, |x-x'|)$. However as explained above the inclusion of the dendritic structure means that there is an extra dimension and so we must also specify how the axon collaterals are distributed along the cable. We shall consider two types of weight distribution.

**Uncorrelated weights**

Suppose that the weight distribution has the product form

$$W(\xi, x) = P(\xi)w(x), \quad P(\xi) \geq 0, \quad \int_{0}^{\infty} P(\xi) d\xi = 1 \quad (5.4)$$

This infers that the distribution of axon collaterals across the dendritic tree is independent of the separation between the neuron and the corresponding pre-synaptic neuron. Although this is not biologically realistic, it facilitates our eventual analysis.

The distribution $P(\xi)$ determines the probability density of these axon collaterals. For concreteness, we shall take $P(\xi) = \delta(\xi - \xi_0)$, $\xi_0 \geq 0$. This implies that the synaptic connections are located at the point $\xi_0$ on the dendritic cable irrespective of the positions of the neurons in the network [see Figure (5.2)].
Figure 5.2: Uncorrelated weights. Synaptic connections are located at the point $\xi_0$ on the dendritic cable irrespective of the positions of the neurons in the network.

**Correlated weights**

The synaptic organization of the brain, as described above, suggests that the decoupling of network and dendritic co-ordinates is an over simplification. In particular, a synapse tends to be located further away from the soma as the separation between cortical neurons increases. Motivated by this observation, we make the following assumption about the distribution $W(\xi, x)$: the average distance of a synapse from the soma $|\xi|$ increases with the separation $|x - x'|$ between neurons [see Figure (5.3)]. This property can be realized by a distribution of the form,

$$W(\xi, x) = W(x)\delta(\alpha(x) - \xi) \quad (5.5)$$

where network and dendritic co-ordinates are related according to $\xi = \alpha(x)$ for some given function $\alpha$. For concreteness we take $\alpha(x) = \xi_0 + \theta|x|$ with $\theta \geq 0$. Thus setting $\theta = 0$ recovers the uncorrelated case.

In order to simplify our analysis, we take the external bias to be

$$I_{ext}(\xi, t) = -\int_{-\infty}^{\infty} W(\xi, x, x')dx'$$

so that the homogeneous zero solution $U(x) = 0$, $V(\xi, x) = 0$ is a fixed point of the system. We set $\epsilon = 1/\tau_d$ and let $\epsilon = 1/\tau_e + \rho_0$, we can now rewrite equations (5.1) and (5.2) as,

$$\frac{\partial U(x, t)}{\partial t} = -\epsilon U(x, t) + \rho_0 V(0, x, t), \quad (5.6)$$

$$\frac{\partial V(\xi, x, t)}{\partial t} = -\epsilon V(\xi, x, t) + D \frac{\partial^2 V(\xi, x, t)}{\partial \xi^2} + \int_{-\infty}^{\infty} W(\xi, x', x)f(U(x', t))dx' \quad (5.7)$$

64
If one is only interested in output activity of the network as determined by the somatic potentials $U(x, t)$, then one can eliminate the dendritic potentials $V(\xi, x, t)$ as they appear linearly in the equation (5.7). We proceed by using a standard Green's function approach [see section (3.3)] and thereby obtain a solution for $V(0, x, t)$,

$$V(0, x, t) = \int_{-\infty}^{t} \int_{0}^{\infty} G(\xi', t - t') \left[ \int_{-\infty}^{\infty} W(\xi', x - x') f(U(x', t)) dx' \right] d\xi' dt'$$

$$- \rho_0 \int_{-\infty}^{t} G(0, t - t') [V(0, x, t') - U(x, t')] dt'$$  (5.8)

where $G/2$ is the fundamental solution of the one-dimensional cable equation [equation (3.34)].

$$G(\xi, t) = \frac{1}{\sqrt{\pi Dt}} \exp \left(-\frac{\xi^2}{4Dt} - \epsilon t\right)$$

To simplify our analysis, we shall assume that the second term on the right-hand side of the equation (5.8) is negligible compared to the first term arising from synaptic inputs. This approximation, which corresponds to replacing equation (5.3) by the homogeneous boundary condition $\partial V/\partial \xi|_{\xi=0} = 0$, does not alter the essential behaviour of the system. Substituting equation (5.8) into (5.6) leads to the following integro-differential equation for $U$,

$$\frac{\partial U(x, t)}{\partial t} = -\xi U(x, t) + \rho_0 \int_{-\infty}^{t} \int_{-\infty}^{\infty} K(x - x', t - t') f(U(x', t')) dx' dt'$$  (5.9)
where,

\[
K(x, t) = \int_0^\infty G(\xi, t)W(\xi, x)\,d\xi
\]  

(5.10)

We note that in the limit of zero diffusion \((D \to 0)\) with \(\epsilon \gg \dot{\epsilon}\), \(V\) can be treated as a fast variable in equation (5.7) so that equation (5.9) reduces to the simple activation/inhibition model [c.f. equation (4.3)] studied in the last chapter.

\[
\frac{\partial U(x, t)}{\partial t} = -\dot{\epsilon}U(x, t) + \rho_0 \int_{-\infty}^\infty W(x - x')f(U(x', t'))\,dx' 
\]  

(5.11)

with \(W(x) = W(0, x)/\epsilon\).

We consider the effect of each type of weight distribution upon the equation (5.9). Substituting the uncorrelated weight distribution (5.4) into equations (5.9) and (5.10) yields

\[
\frac{\partial U(x, t)}{\partial t} = -\dot{\epsilon}U(x, t) + \rho_0 \int_{-\infty}^\infty G(\xi_0, t - t') \left[ \int_{-\infty}^\infty W(x - x')f(U(x', t'))\,dx' \right] \,dt' 
\]  

(5.12)

We see that by comparing equations (5.11) and (5.12), the inclusion of the dendritic structure introduces a distribution of delays as determined by the kernel \(G(\xi_0, t)\).

The correlated weights produce a similar result. Substituting equation (5.4) into equations (5.9) and (5.10) gives

\[
\frac{\partial U(x, t)}{\partial t} = -\dot{\epsilon}U(x, t) + \rho_0 \int_{-\infty}^t \int_{-\infty}^\infty G(\alpha(x - x'), t - t') \left[ \int_{-\infty}^\infty W(x - x')f(U(x', t'))\,dx' \right] \,dt' 
\]  

(5.13)

As with the uncorrelated case, there is an effective distribution of delays as specified by \(G(\alpha(x), t)\).

### 5.3 Linear Stability Analysis

In the following sections we choose units of length and time such that the diffusion constant \(D = 1\) and the membrane time constants \(\dot{\epsilon}^{-1}, \epsilon^{-1}\) are of order one. The
distance $\xi$ along the dendritic cable is measured in terms of electronic length, which typically varies over the range 1-10 cm. Typical values of a membrane time constant are 5-20 ms. We shall also set $\rho_0 = 1$.

### 5.3.1 Turing instability

We follow exactly the same procedure of analysis as for the activation/inhibition model discussed in the last chapter [see section (4.3.3)]. So, linearizing about the zero fixed point $U(x) \equiv 0$ for the full model [equation (5.13)] gives,

$$\frac{\partial U(x,t)}{\partial t} = -\xi U(x,t) + \rho_0 \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} G(\alpha(x-x'), t-t') \left[ \int_{-\infty}^{\infty} W(x-x')U(x',t')dx' \right] dt'$$

(5.14)

We substitute into equation (5.14) a solution of the form $U(x,t) = U_0 \exp(\nu t + ipx)$ and thus obtain the following characteristic equation,

$$\Delta(\nu, p) \equiv \xi + \nu - W_0 \tilde{J}(\nu, p) = 0$$

(5.15)

where,

$$\tilde{J}(\nu, p) = \int_{-\infty}^{\infty} e^{ipx} \tilde{G}(\alpha(x), \nu)J(x)dx$$

(5.16)

and

$$\tilde{G}(\xi, \nu) = \frac{1}{\sqrt{\xi + \nu}} \exp(-|\xi|\sqrt{\xi + \nu})$$

(5.17)

is the Laplace transform of the fundamental solution $G(\xi, t)$ given by equation (3.34).

We highlight an important difference between the characteristic equation for the simplified model (4.8) and the one obtained above (5.15). There is an effective $\nu$-dependence on the right-hand side of equation (5.15); this will allow the formation of dynamic patterns. Also note from equation (5.15) that in the case of correlated weights there is an additional decay factor in the effective weight distribution that arises from diffusion along the dendritic cable. This latter feature means that $J(x)$ can be taken to be an increasing function of $|x|$, provided that the growth in $J(x)$ is non-exponential so that $\lim_{|x| \to \infty} \tilde{G}(\alpha(x), \nu)J(x) = 0$. For example, in Bressloff's paper, 'A new mechanism for neural pattern formation' [Bressloff (1996)], $J(x)$ was taken to be a linear function of $|x|$.  

67
5.3.2 Static network patterns

Let us first investigate the occurrence of static patterns. As before, we assume that $\nu$ is real and look for the onset of a Turing instability as specified by conditions (A) and (B) in section (4.4).

Assuming that the resting state is stable with respect to dynamic instabilities, then a static Turing instability will occur under almost identical lines to the reduced (activation-inhibition) model [equation (4.3)]. To illustrate this, consider $J(x)$ given by equation (4.5). Substituting into equation (5.16) with $\alpha(x) = \xi_0 + \theta |x|$ yields,

$$J(\nu, p) = \frac{2e^{-\xi_0 \sqrt{\epsilon + \nu}}}{\sqrt{\epsilon + \nu}} \left[ \frac{\theta \sqrt{\epsilon + \nu} + \gamma_1}{p^2 + (\theta \sqrt{\epsilon + \nu} + \gamma_2)^2} - \frac{\Gamma \theta \sqrt{\epsilon + \nu} + \gamma_1}{p^2 + (\theta \sqrt{\epsilon + \nu} + \gamma_2)^2} \right] \quad (5.18)$$

If we set $\nu = 0$ in equation (5.18) and compare with equation (4.9), we deduce that the inclusion of the dendritic cable, simply rescales the bifurcation parameter, $W_0$ by a factor $e^{-\xi_0 \sqrt{\epsilon}} / \sqrt{\epsilon}$ together with a change in the coherence lengths $\gamma_1^{-1}$ and $\gamma_2^{-1}$ according to $\gamma_1 \rightarrow \gamma_1 + \theta \sqrt{\epsilon}$. It follows that a Turing instability may be induced by changes in the dendritic location $\xi_0$.

5.3.3 Dynamic network patterns

The notion of synaptic placement was briefly touched upon when we discussed information processing [see section (2.3.1)]. As was stated, it is surprisingly difficult to find physiological and anatomical data [Swindale (1996)] to support the case of short-range excitation and long-range inhibition assumed in standard models of neural pattern formation. A canonical cortical circuit appears to possess short-range inhibition and long-range excitation [Shepherd (1998)]. This may be realized in our model by an inverted Mexican hat distribution and can be obtained by setting $\Lambda = -1$ in equation (4.5).

We shall show that if $\nu$ is allowed to be complex then it is possible for a Turing-like instability to occur for such a configuration due to a pair of complex roots $\pm i \omega$ crossing the imaginary axis. Such a scenario is a precursor for dynamic pattern formation in which there exists an oscillating, spatially varying pattern of network activity whose period in the time domain is $2\pi / \omega$. In the reduced system [equation (4.3)], in order to duplicate this dynamic pattern, one would require at least two distinct populations of neurons, one long-range inhibitory and the other short-range excitatory [Amari (1977), Ermentrout and Cowan (1980)].
A necessary condition for dynamic pattern formation is that there exists a pair $\omega, p \neq 0$ such that $\Delta(i\omega, p) = 0$, that is,

$$\dot{\varepsilon} + i\omega = W_0 \tilde{F}(i\omega, p) \quad (5.19)$$

Without loss of generality, we take $\omega, p \geq 0$. For simplicity, we shall consider the case of uncorrelated weights. Thus $\tilde{F}(\nu, p)$ is given by equation (5.16) with $\alpha(x) = \xi_0$. Setting $\nu = i\omega$ and equating real and imaginary parts gives the following pair of equations,

$$\frac{\dot{\varepsilon}}{W_0} = \tilde{J}_1(\omega, p) \quad (5.20)$$

$$\frac{\omega}{W_0} = -\tilde{J}_2(\omega, p) \quad (5.21)$$

with

$$\tilde{J}_k(\omega, p) = \tilde{J}(p) H_k(\omega, \xi_0), \quad k = 1, 2 \quad (5.22)$$

and where,

$$H_1(\omega, \xi_0) = \frac{1}{\sqrt{\varepsilon^2 + \omega^2}} e^{-A(\omega)\xi_0} \left[ A(\omega) \cos(B(\omega)\xi_0) - B(\omega) \sin(B(\omega)\xi_0) \right] \quad (5.23)$$

$$H_2(\omega, \xi_0) = \frac{1}{\sqrt{\varepsilon^2 + \omega^2}} e^{-A(\omega)\xi_0} \left[ A(\omega) \sin(B(\omega)\xi_0) + B(\omega) \cos(B(\omega)\xi_0) \right] \quad (5.24)$$

and $\sqrt{\varepsilon + i\omega} = A(\omega) + iB(\omega)$ where,

$$A(\omega) = \sqrt{\left[ \sqrt{\varepsilon^2 + \omega^2} + \varepsilon \right] / 2} \quad B(\omega) = \sqrt{\left[ \sqrt{\varepsilon^2 + \omega^2} - \varepsilon \right] / 2} \quad (5.25)$$

Equations (5.20)-(5.24) imply that,

$$-\frac{\omega}{\dot{\varepsilon}} = H(\omega, \xi_0) \equiv \frac{A(\omega) \sin(B(\omega)\xi_0) + B(\omega) \cos(B(\omega)\xi_0)}{A(\omega) \cos(B(\omega)\xi_0) - B(\omega) \sin(B(\omega)\xi_0)} \quad (5.26)$$

The function $H(\omega, \xi_0)$ is plotted as a function of $\omega$ in Figure (5.4) for $\xi_0 = 2$ and $\dot{\varepsilon} = 1$.

We are interested in the points of intersection of $H$ with the straight line through the origin having slope $-\dot{\varepsilon}$. We ignore the trivial solution $\omega = 0$ since this corresponds to a static instability. Although there is more than one non-zero solution, we need only consider the smallest solution $\omega_0$ since this will determine the stability or otherwise of
Figure 5.4: Plot of function $H(\omega, \xi_0)$ against $\omega$ (with $\hat{\epsilon} = 1$) for $\xi_0 = 2$. The intercept $\omega_0$ determines the pair of pure imaginary roots at the Hopf bifurcation point associated with a dynamic Turing instability for uncorrelated weights.

the resting state with respect to dynamic pattern formation. Since the point $\omega_0$ lies on the second branch of $H$, it follows that $H_1(\omega_0, \xi_0)$ is negative and $H_2(\omega_0, \xi_0)$ is positive.

We are now in a position to determine the critical value of $W_0$, for a dynamic Turing instability:

$$W_0 \tilde{J}(p_{\text{min}}) = -K_1(\xi_0)$$  \hspace{1cm} (5.27)

which should be contrasted with the condition for a static Turing instability, namely [c.f. equation (4.10)]

$$W'_0 \tilde{J}(p_{\text{max}}) = K_2(\xi_0)$$  \hspace{1cm} (5.28)

where,

$$\tilde{J}(p_{\text{min}}) = \min_p \tilde{J}(p) \quad \tilde{J}(p_{\text{max}}) = \max_p \tilde{J}(p)$$  \hspace{1cm} (5.29)

and

$$K_1(\xi_0) = \frac{\hat{\epsilon}}{|H_1(\omega_0, \xi_0)|} \quad K_2(\xi_0) = \frac{\hat{\epsilon}}{H_1(0, \xi_0)} = \hat{\epsilon} \sqrt{\xi_0} e^{\sqrt{\xi_0}}$$  \hspace{1cm} (5.30)
Assuming that $J(P_{\text{min}}) < 0 < J(P_{\text{max}})$, a dynamic Turing instability will occur if $W_0 < W'_0$ and $P_{\text{min}} \neq 0$, whereas a static Turing instability will occur if $W'_0 < W_0$ and $P_{\text{max}} \neq 0$.

In terms of the Mexican hat function (4.5) with $\Lambda = +1$ (short-range excitation, long-range inhibition), it is clear that a dynamic Turing instability is impossible since $P_{\text{min}} = 0$. However it is possible for a bulk oscillations to occur instead of static patterns when,

$$J(p_c) > \frac{K_2(\xi_0)|J(0)|}{K_1(\xi_0)}$$  \hspace{1cm} (5.31)

with $p_c$ given by equation (4.11). On the other hand, when $\Lambda = -1$ (short-range inhibition, long-range excitation) a dynamic instability can occur since $P_{\text{min}} = p_c$ and $P_{\text{max}} = 0$ and provided that

$$J(0) < \frac{K_2(\xi_0)|J(p_c)|}{K_1(\xi_0)}$$  \hspace{1cm} (5.32)

The different possible scenarios are illustrated in Figures (5.5)-(5.12). In particular, we ask the reader to note the transition from a static bulk instability to a dynamic Turing instability as $\xi_0$ is increased [see Figure (5.10)]. This in essence means that a sufficiently large effective delay needs to exist for a dynamic instability to occur. The correlated case may be examined in much the same way. However, for $\alpha(x) = \xi_0 + \theta |x|$, $\xi_0$ needs to be sufficiently large.
Figure 5.5: Plot of $\bar{J}(p)$ given by equation (4.9) with $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.8$ and $\Lambda = +1$ (short-range excitation, long-range inhibition).

Figure 5.6: Static Turing instability versus dynamic bulk instability for $\bar{J}(p)$ above [Figure (5.5)]. Plot of critical weights $W_{0e}^\prime$ (dynamic) and $W_{0e}^\prime$ (static) as a function of the dendritic co-ordinate $\xi_0$. The system undergoes a static Turing instability for $\xi_0 < \xi_{0e}$ and a dynamic bulk instability for $\xi_0 > \xi_{0e}$ with $\xi_{0e} \approx 3.2$. 
Figure 5.7: Plot of $\tilde{J}(p)$ given by equation (4.9) with $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.53$ and $\Lambda = +1$ (short-range excitation, long-range inhibition).

Figure 5.8: Plot of critical weights for $\tilde{J}(p)$ as shown in Figure (5.7). In this case the system only undergoes a static Turing instability since $W_{0e}' < W_{0e}$ for all $\xi_0$. 
Figure 5.9: Plot of $\tilde{J}(p)$ given by equation (4.9) with $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.53$ and $\Lambda = -1$ (short-range inhibition, long-range excitation).

Figure 5.10: Dynamic Turing instability versus static bulk instability for $\tilde{J}(p)$ as shown in Figure (5.9). Plot of critical weights $W_{0e}$ (dynamic) and $W'_{0e}$ (static) as a function of dendritic co-ordinate $\xi_0$. The system undergoes a static bulk instability for $\xi_0 < \xi_{0e}$ and a dynamic Turing instability for $\xi_0 > \xi_{0e}$ with $\xi_{0e} \approx 1.9$. 
1.2

Figure 5.11: Plot of $\tilde{J}(p)$ given by equation (4.9) with $\gamma_1 = 1.0, \gamma_2 = 0.5, \Gamma = 0.8$ and $\Lambda = -1$ (short-range inhibition, long-range excitation).

Figure 5.12: Plot of critical weights for $\tilde{J}(p)$ as shown by Figure (5.11). Here the system only undergoes a static bulk instability since $W'_{0_e} < W_{0_e}$. 
5.3.4 Dendritic patterns

An interesting feature of the model is that in the case of correlated weights, a spatially varying pattern also forms along the dendritic cable of each neuron. To show this, we return to the pair of equations (5.6) and (5.7). Linearizing equation (5.7) about the fixed point $U(x) \equiv 0$ and $V(\xi, x) \equiv 0$ yields (for $\kappa = \rho_0 = 1$).

\[
\frac{\partial V(\xi, x, t)}{\partial t} = -\epsilon V(\xi, x, t) + \frac{\partial^2 V(\xi, x, t)}{\partial \xi^2} + \int_{-\infty}^{\infty} W(\xi, x - x') U(x', t) dx' \quad (5.33)
\]

We now substitute the solution,

\[
U(x, t) = U_0 \exp(\nu t + ipx), \quad V(\xi, x, t) = V_0(\xi) \exp(\nu t + ipx) \quad (5.34)
\]

into equations (5.6) and (5.33)

\[
(\epsilon + \nu)V_0(\xi) = \frac{d^2 V_0(\xi)}{d\xi^2} + \tilde{W}(\xi, p) U_0 \quad \xi \geq 0 \quad (5.35)
\]

\[
(\epsilon + \nu)U_0 = V_0(0) \quad (5.36)
\]

where $\tilde{W}(\xi, p)$ is the Fourier transform of $W(\xi, x)$ with respect to $x$,

\[
\tilde{W}(\xi, p) = \int_{-\infty}^{\infty} W(\xi, x) e^{ipx} dx \quad (5.37)
\]

Substituting the particular form for $W(\xi, x)$ given by equation (5.5) into (5.37) shows that

\[
\tilde{W}(\xi, p) = 2W(\xi) \cos(p\xi) \quad (5.38)
\]

where we have set $a(x) = |x|$ for simplicity.

We now solve equation (5.35), with a sealed end at $\xi = 0$ [equation (3.5)], for $V_0(\xi)$ in terms of $U_0$. Thus,

\[
\frac{V_0(\xi)}{U_0} = \frac{1}{\sqrt{\epsilon + \nu}} \int_{0}^{\infty} [e^{-\sqrt{\epsilon + \nu}|\xi - \xi'|} + e^{-\sqrt{\epsilon + \nu}|\xi + \xi'|}]\cos(p\xi') W(\xi') d\xi' \quad (5.39)
\]

In the case of the function $W(\xi) = W_0 J(\xi)$ with $J$ given by equation (4.5), we find that equation (5.39) reduces to
\[ V_0(\xi) = \frac{W_0}{\sqrt{\varepsilon + \nu}} [V_0^{(1)}(\xi) - \Gamma V_0^{(2)}(\xi)] \]  
(5.40)

where,

\[ V_0^{(l)}(\xi) = v_0^{(l)} e^{-\gamma_1 \xi} \cos(p \xi) + v_1^{(l)} e^{\gamma_1 \xi} \sin(p \xi) + v_2^{(l)} e^{-\sqrt{\varepsilon + \nu} \xi}, \quad l = 1, 2 \]  
(5.41)

and

\[ v_0^{(l)} = \left[ \frac{\sqrt{\varepsilon + \nu - \gamma_1}}{(\sqrt{\varepsilon + \nu - \gamma_1})^2 + p^2} + \frac{\sqrt{\varepsilon + \nu + \gamma_1}}{(\sqrt{\varepsilon + \nu + \gamma_1})^2 + p^2} \right] \]  
(5.42)

\[ v_1^{(l)} = \left[ \frac{p}{(\sqrt{\varepsilon + \nu - \gamma_1})^2 + p^2} - \frac{p}{(\sqrt{\varepsilon + \nu + \gamma_1})^2 + p^2} \right] \]  
(5.43)

\[ v_2^{(l)} = \left[ \frac{\sqrt{\varepsilon + \nu + \gamma_1}}{(\sqrt{\varepsilon + \nu + \gamma_1})^2 + p^2} - \frac{\sqrt{\varepsilon + \nu - \gamma_1}}{(\sqrt{\varepsilon + \nu - \gamma_1})^2 + p^2} \right] \]  
(5.44)

First suppose that the network output activity undergoes a static instability, such that \( \nu = 0 \) and \( p = p_c \). It is clear from equations (5.40) and (5.41) that the amplitude \( V_0(\xi) \) will exhibit oscillatory spatial patterns along the dendritic cable whose period is \( 2\pi/p_c \) where \( p_c \) is the wave number of the pattern variation with respect to the network coordinate \( x \). Such an effect will be significant when there are long-range interactions for which \( \gamma_1,2 \ll p_c \). In the case of dynamic pattern formation, where \( \nu \approx i\omega \), there is an additional periodic component arising from terms of the form \( e^{-\sqrt{\varepsilon + \nu} \xi} = e^{A(\omega)\xi + B(\omega)\xi} \) with \( A(\omega) \) and \( B(\omega) \) given by equation (5.25). However, since \( A(\omega) > B(\omega) \) the decay factor tends to dominate.

The main feature of this analysis which we wish to stress is its possible implications for Hebbian learning. As we discussed in section (2.3.3), the modification of a synapse is dependent upon the level of pre-synaptic activity (network output patterns) and postsynaptic activity (dendritic patterns). Thus any analysis of learning should take into account the non-trivial relationship, which we have established, between the patterns of output activity and the patterns of dendritic activity. This may also explain how predominantly passive dendrites adopt the Hebbian learning mechanism without the aid of the the active mechanisms which direct the back-propagating action potential [see subsection (2.3.3)].

### 5.4 Numerical results

In this section we present some numerical results that confirm the validity of the analytical results obtained in the previous section. We consider a one-dimensional chain
of neurons labelled $i = 1, \ldots, N$. We firstly discretize both the continuous differential equations (5.6) and (5.7), thus obtaining the following finite-difference scheme [see subsection (3.4.3)],

$$U_i^{n+1} = (1 - \tilde{\epsilon} \Delta t) U_i^n + \Delta t V_i^n,$$

$$V_{i,m}^{n+1} = (1 - \epsilon \Delta t) V_{i,m}^n + \frac{\Delta t}{\Delta \xi} [V_{i,m+1}^n - 2V_{i,m}^n + V_{i,m-1}^n] + \sum_{j=1}^{N} W(m, i - j) \tanh(\kappa U_j^n)$$

where $U_i^n$ denotes the somatic membrane potential of the $i$th neuron at time level $n$ and $V_{i,m}^n$ denotes the dendritic membrane potential for the $m$th compartment of the $i$th neuron at time level $n$. The compartments are labelled $m = 1, \ldots, M - 1$. The length of each compartment is $\Delta \xi$ whilst a single time-step is of duration $\Delta t$.

Equation (5.46) is supplemented with zero-flux boundary conditions for $V_{i,m}^n$ at $m = 0, M - 1$. The connection weight $W(m, k)$ is taken to be of the form (c.f. equations (5.4) and (5.5))

$$W(m, k) = W(k) \delta_{m,m_0} \text{ (uncorrelated)} \quad W(m, k) = W(k) [\delta_{k,m} + \delta_{k,-m}] \text{ (correlated)}$$

and

$$W(k) = \Lambda W_0 [e^{-\gamma |k| \Delta \xi} - \Gamma e^{-\gamma \delta |k| \Delta \xi}]$$

The above finite-difference approximation is, as stated previously [see subsection (3.4.3)], an explicit numerical scheme. As discussed in section (3.4.3), the presence of the diffusive term places a restriction on the relative sizes of $\Delta t$ and $\Delta \xi$. That is to achieve numerical stability the inequality $\Delta t / \Delta \xi^2 < 0.5$ has to be satisfied. We shall choose $\Delta t = 0.001$ and $\Delta \xi = 0.2$. We also set $\epsilon = \tilde{\epsilon} = \kappa = 1$ and take $N = M = 100$. For our initial conditions, the somatic membrane potentials are assigned a random value from the range $-0.2$ to $0.2$, whilst the dendritic membrane potentials are all set to zero. We then iterate the equations over 10,000 time-steps for different values of $W_0$. 

78
5.4.1 Dynamic patterns (uncorrelated weights)

We first consider the case of dynamic pattern formation in a one-dimensional network with an uncorrelated weight distribution given by equations (4.5) and (5.4) with $P(\xi) = \delta(\xi - \xi_0)$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.53$ and $\Lambda = -1$. The steady-state somatic potential $U$ is plotted as a function of network co-ordinate $x$ and time $t$ in Figure (5.13) for $\xi_0 = 0.4$ and $W_0 = 40$. We see that the system exhibits a bulk instability, which is consistent with the analysis of subsection (5.3.3), since $\xi_0 < \xi_0$ and $W_0 > W_{0\text{c}}$ [see Figure (5.10)]. On the other hand, when $\xi_0 = 2.0$ and $W_0 = 80$, the system undergoes a dynamic Turing instability as shown in Figure (5.14). Here $\xi_0 > \xi_0$ and $W_0 > W_{0\text{c}}$. The frequency of oscillation for the given parameter values is $\omega \approx 2$ and the wave number is $p \approx 1$. These values are consistent with the typical frequencies (10-100 Hz) and length scales (1-10 cm) associated with cortical oscillations.

5.4.2 Static patterns (correlated weights)

As our second example, we consider the case of correlated weights with $\Lambda = +1$ (short-range excitation and long-range inhibition). Numerical simulations of the analog model confirm that a Turing instability occurs leading to the formation of stable stationary patterns. A typical pattern structure above the bifurcation point is illustrated in Figures (5.15)-(5.18) for $\gamma_1 = 0.2$, $\gamma_2 = 0.1$, $\Gamma = 0.9$ and $W_0 = 50$. From equation (5.18) with $\nu = 0$ we find that $W_{0\text{c}} \approx 11.4$ and $p_{\text{c}} \approx 1$. It is clear that the dendritic potential exhibits a spatially oscillating pattern with respect to $|\xi|$.
Figure 5.13: Bulk instability in a one-dimensional network with an uncorrelated weight distribution given by equations (4.5) and (5.4), with $P(\xi) = \delta(\xi - \xi_0)$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.53$ and $\Delta = -1$. Here $\xi_0 = 0.4 < \xi_{0e}$ and $W_0 = 40.0$. The steady-state somatic potential $U$ is plotted as a function of network co-ordinate $x$ and time $t$.

Figure 5.14: Dynamic Turing instability. Same as in Figure (5.13) with $\xi_0 = 2 > \xi_{0e}$ and $W_0 = 80$. 
Figure 5.15: Steady-state pattern arising from a static Turing instability in a one-dimensional network with an correlated weight distribution given by equations (4.5) and (5.5), with $\alpha(x) = 0.1|x|$, $\gamma_1 = 0.2$, $\gamma_2 = 0.1$, $\Gamma = 0.9$, $\Lambda = +1$ and $W_0 = 50.0$. The steady-state dendritic potential $V(\xi, x)$ is plotted as a function of dendritic co-ordinate $\xi$ and network co-ordinate $x$.

Figure 5.16: Steady-state pattern arising from a static Turing instability. Same as in Figure (5.15) but from a different angle. This clearly shows the pattern along the dendritic cable.
Figure 5.17: Plot of $U(x)$ as a function of $x$. Same parameter values as Figure (5.15).

Figure 5.18: Plot of $V(\xi, x)$ as a function of $\xi$ for fixed $x$. Same parameter values as Figure (5.15).
5.5 Bifurcation analysis

Within this section we establish the existence of spatial patterns at the nonlinear level using bifurcation theory. In particular, we use the method of harmonic balance [Allwright (1977)] to show that the formation of dynamic patterns corresponds to a supercritical Hopf bifurcation. We ask the reader to note that the case of static patterns was considered in Bressloff (1996).

To simplify our analysis we impose periodic boundary conditions such that $U(x + L) = U(x)$ $\forall x$. Since $W(\xi, x)$ is symmetric in $x$, we can also restrict ourselves to even solutions $U(-x) = U(x)$. We denote the solution space of continuous, bounded, periodic functions by $\mathcal{M}$. Define the inner product of two elements $U, V \in \mathcal{M}$ according to

$$\langle U, V \rangle = \int_{0}^{L} U^*(x)V(x)dx$$

where $U^*$ denotes the complex conjugate of $U$, so that $\mathcal{M}$ becomes a Hilbert space.

We now consider equation (5.9) in the form (setting $\varepsilon = 1$),

$$\frac{\partial U(x, t)}{\partial t} = -U(x, t) + W_0 \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} J(x - x', t - t')f(U(x', t'))dx'dt'$$

with $W_0$, as before, taken as the bifurcation parameter. For the sake of generality, we shall relax the condition that the nonlinear output function in equation (5.50) is given by $f(U) = \tanh(\kappa U)$, and take $f(U)$ to be any analytic function satisfying $f(0) = 0$. Suppose that as $W_0$ is increased from zero, a critical value $W_{0e}$ is reached signalling the onset of a dynamic Turing instability. We are assuming here that $W_{0e} < W_0^\ast$, where $W_0^\ast$ is the critical value for a static Turing instability. Introduce the linear operator $\hat{L}(s, W_0)$,

$$\hat{L}(s, W_0)U = (1 + s)U - f_1 W_0 \hat{L}_1(s)U$$

where,

$$\hat{L}_1(s)U(x) = \int_{0}^{\infty} e^{-st} \int_{-\infty}^{\infty} J(x - x', t)U(x')dx'$$
Then at some critical point, \( \tilde{U}(x) = \cos(p_c x) \) is a zero eigenfunction of \( \hat{L}(\omega_0, W_0) \) where \( p_c = 2\pi n_c / L \neq 0 \) for some integer \( n_c \).

Suppose that \( W_0 \) is slightly above the critical value \( W_0^c \), so that we have \( \hat{L}(\alpha + i\tilde{\omega}, W_0)\tilde{U}(x) = 0 \) with \( \alpha > 0 \). This implies that the origin is unstable. The basic idea of harmonic balance is to try a periodic solution of equation (5.50) of the form

\[
U(x, t) = \text{Re}[u_0(x) + u_1(x)e^{i\omega t} + u_2(x)e^{2i\omega t} + \ldots]
\]  

and solve for \( \omega, u_0(x), u_1(x), \) etc. Following Allwright's work, it can be rigorously shown that for small amplitude oscillations, it is sufficient to consider only terms up to the second harmonic, that is \( u_0, u_1 \) and \( u_2 \), in order to determine the type of bifurcation. For our particular problem, this requires that the operators \( \hat{L}(ni\omega_0, W_0) \) have a bounded inverse \( \forall \) integers \( n \neq 1 \) (with respect to the \( L_2 \) norm \( \|U\| = \sqrt{\langle U, U \rangle} \)). This ensures that there are no resonances. We also make the hypothesis (justifiable a posteriori) that \( \|u_0\| = O(\|u_1\|^2) \) and \( \|u_2\| = O(\|u_3\|^2) \).

Substituting equation (5.53) into the Taylor expansion of \( f \) about \( U = 0 \),

\[
f(U(x, t)) = \text{Re}[U_0(x) + U_1(x)e^{i\omega t} + U_2(x)e^{2i\omega t}]
\]  

with

\[
U_0(x) = f_1u_0(x) + \frac{f_2}{4} u_1^*(x)u_1(x)
\]

\[
U_1(x) = f_1u_1(x) + \frac{f_2}{2} [2u_0(x)u_1(x) + u_1^*(x)u_2(x)] + \frac{f_3}{8} u_1^*(x)u_1(x)^2
\]  

\[
U_2(x) = f_1u_2(x) + \frac{f_2}{4} u_1(x)^2
\]  

Now substituting equations (5.53)-(5.55) into equation (5.50) leads to the harmonic balance equations,

\[
\hat{L}(0, W_0)u_0 = \frac{W_0f_2}{4} \hat{L}_1(0)u_1^* \]  

\[
\hat{L}(i\omega, W_0)u_1 = W_0\hat{L}_1(i\omega) \left[ \frac{f_2}{2} [2u_0u_1 + u_1^*u_2] + \frac{f_3}{8} u_1^*u_1^2 \right]
\]
\[ \hat{L}(2i\omega, W_0)u_2 = \frac{W_0f_3}{4} \hat{L}_1(2i\omega)u_1^2 \]  

(5.58)

Given the non-resonance condition, it is clear that when \( f(U) \) is an odd function of \( U \) so that \( f_2 = 0 \), both \( u_0 \) and \( u_2 \) are zero (at this level of approximation), which considerably simplifies the analysis. In particular, equation (5.57) becomes,

\[ \hat{L}(i\omega, W_0)u_1 = \frac{W_0f_3}{8} \hat{L}_1(i\omega)u_1^2 \]  

(5.59)

Try a solution of equation (5.59) of the form \( u_1(x) = [\bar{U}(x) + \delta U(x)]\eta \) for small \( \eta \) and write,

\[ \hat{L}(i\omega, W_0) \approx \hat{L}(s, W_0) - (\alpha - i\delta \omega)\hat{L}'(s, W_0), \quad s = \alpha + i\omega \]  

(5.60)

where \( \delta \omega = \bar{\omega} - \omega \) and \( \hat{L}' \) denotes differentiation with respect to the first argument. Substitute equation (5.60) into equation (5.59) and then take the inner product of both sides with respect to \( \bar{U} \). This gives

\[ \langle \bar{U}, \hat{L}(s, W_0)\delta U \rangle - (\alpha - i\delta \omega)\langle \bar{U}, \hat{L}'(s, W_0)\bar{U} \rangle = \eta^2 \frac{W_0f_3}{8} \langle \bar{U}, \hat{L}_1(i\omega)\bar{U}^3 \rangle \]  

(5.61)

Using the fact that \( \hat{L} \) is self-adjoint and \( \hat{L}(s, W_0)\bar{U} = 0 \), and determining \( \hat{L}' \) from equation (5.51), we obtain the result to \( O(\eta^3) \)

\[ -(\alpha - i\delta \omega)\langle \bar{U}, \bar{U} - f_1W_0\hat{L}_1'(s)\bar{U} \rangle = \eta^2 \frac{W_0f_3}{8} \langle \bar{U}, \hat{L}_1(i\omega)\bar{U}^3 \rangle \]  

(5.62)

It can be shown that \( \alpha \) and \( \delta \omega \) are both \( O(\eta^2) \). Thus taking the real part of equation (5.62) we find that,

\[ \alpha = \eta^2 \sigma_0 \]  

(5.63)

\[ \sigma_0 = -\frac{W_0f_3}{8} \text{Re} \left[ \frac{\langle \bar{U}, \hat{L}_1(i\omega)\bar{U}^3 \rangle}{\langle \bar{U}, \bar{U} - f_1W_0\hat{L}_1'(s)\bar{U} \rangle} \right] \]  

(5.64)

where, as a lowest order approximation, we have replaced \( s \) and \( i\bar{\omega} \) by \( i\omega_0 \) and \( W_0 \) by \( W_0 \). To have an oscillatory solution for small \( \eta^2 \) we require that \( \alpha \) and \( \sigma_0 \) have the same sign. Since \( \alpha > 0 \) for \( W_0 > W_0 \), the condition for a supercritical Hopf bifurcation is \( \sigma_0 > 0 \).
It follows from equation (5.62) and the definition $\bar{U}(x) = \cos(p_c x)$ that

$$
\langle \bar{U}, \bar{U} \rangle = \frac{L}{2}, \quad \langle \bar{U}, \bar{U}'(i\omega_0) \bar{U} \rangle = \frac{L}{2} \tilde{J}(i\omega_0, p_c)
$$

and

$$
\langle \bar{U}, \bar{L}_1(i\omega_0) \bar{U}^3 \rangle = \frac{3L}{8} \tilde{J}(i\omega_0, p_c)
$$

where $\tilde{J}(\nu, p)$ is obtained by Laplace transforming $J(x, t)$ with respect to $t$ and Fourier transforming with respect to $x$. In deriving equations (5.65) and (5.66), we have used the fact that $J(x, t)$ is an even function of $x$. If we now take $f(U) = \tanh(\kappa U)$ so that $f_1 = \kappa$ and $f_3 = -\kappa^3/3$, the coefficient $\sigma_0$ reduces to the form,

$$
\sigma_0 = \frac{\kappa^2}{32} \Re \left[ \frac{1 + i\omega_0}{1 - \kappa W_0 \tilde{J}(i\omega_0, p_c)} \right]
$$

on using the result that at the critical point $1 + i\omega_0 = \kappa W_0 \tilde{J}(i\omega_0, p_c)$.

For the sake of illustration, we shall evaluate $\sigma_0$ in the case of an uncorrelated weight distribution, $J(x, t) = G(\xi_0, t)J(x)$ [see equation (5.14)]. Using equation (5.22) we find that,

$$
\sigma_0 = \frac{\kappa^2}{32} \Re \left[ \frac{1 + i\omega_0}{1 - \kappa W_0 \tilde{J}(p_c)[H_1'(\omega_0, \xi_0) - iH_2'(\omega_0, \xi_0)]} \right]
$$

where $H'_k$ indicates differentiation with respect to the first argument. Thus

$$
\sigma_0 = \frac{\kappa^2}{32} \Re \left[ \frac{1 - \kappa W_0 \tilde{J}(p_c)[H_1'(\omega_0, \xi_0) - \omega_0 H_2'(\omega_0, \xi_0)]}{[1 - \kappa W_0 \tilde{J}(p_c)H_1'(\omega_0, \xi_0)]^2 + [\kappa W_0 \tilde{J}(p_c)H_2'(\omega_0, \xi_0)]^2} \right]
$$

Now suppose that $\tilde{J}(p)$ satisfies equation (4.9) with $\gamma_1 = 1.0$, $\gamma_2 = 0.5$, $\Gamma = 0.53$ and $\Lambda = -1$. Also take $\epsilon = \kappa = 1$. Then $\sigma_0$ can be calculated for a given $\xi_0$ by determining $W_0$ using equation (5.27) and $\omega_0$ using equation (5.26). Checking the sign of $\sigma_0$ for the case $\xi_0$ (where a dynamic Turing instability is expected to occur from Figure (5.6)), we find that $\sigma_0 > 0$, which shows that the bifurcation is supercritical.
Chapter 6

Neural Pattern Formation with Quasi-Active dendritic structure

6.1 Introduction

The physical features we utilise to classify dendrites, such as morphology and membrane properties subserve a variety of different means by which dendrites seek to process information [see section (2.3)]. In particular, there exist a variety of voltage-dependent ionic channels distributed along the dendritic tree which define the so-called active membrane properties. As we have discussed in subsection (2.3.3), these active properties support such processes amongst others as synaptic amplification, dendritic action potential initiation and Hebbian learning via back-propagation [Shepherd (1998)].

From a mathematical viewpoint, the highly complex, non-linear operations which occur in active membranes cannot be described fully by linear cable theory. However, for relatively small deviations of the membrane potential a linearization of the channel kinetics is valid [Koch (1984)]. The equations which emerge from this procedure [Koch (1999)] have been presented in section (3.5). The resultant model is defined as quasi-active.

It is a natural progression, therefore, to consider a network of neurons with quasi-active dendritic structure. Within this chapter we concentrate our efforts solely on analysing the effect of different membranes on the inducement of Turing-like instabilities as opposed to the effects of synaptic placement on a passive cable which was at the heart of the analysis presented in the last chapter.
6.2 The model

Consider then a one-dimensional network of analog neurons distributed along the $x$-axis. Let $V(\xi, x, t)$ denote the dendritic membrane potential at a point $\xi \in \mathbb{R}^+$ on the cable of a neuron located at $x \in \mathbb{R}$ at time $t$. Let $I(\xi, x, t)$ denote the current flowing through the inductive branch of a point $\xi \in \mathbb{R}^+$ on the cable of a neuron located at $x \in \mathbb{R}$ at time $t$ [please refer to Figure (6.1)]. We approximate the somatic potential, previously described by the variable $U(x, t)$ as $V(0, x, t)$. This simplification allows us to neglect equation (5.1). We thus need only two governing equations, as opposed to three. These equations may be written down using the quasi-active cable theory developed by Koch (1984) [see section (3.5) and more specifically equations (3.67) and (3.68)],

$$\frac{\partial V(\xi, x, t)}{\partial t} = \frac{V(\xi, x, t)}{\tau_d} + D \frac{\partial^2 V(\xi, x, t)}{\partial \xi^2} + \frac{I(\xi, x, t)}{c} + \int_{-\infty}^{\infty} W(\xi - x') f(V(0, x', t)) dx' + I_{ext}(\xi, x) \quad (6.1)$$

$$l \frac{\partial I(\xi, x, t)}{\partial t} = -r_l I(\xi, x, t) + V(\xi, x, t) \quad (6.2)$$

$\tau_d$ denotes the dendritic membrane time constant. As before it is defined as the product of the membrane leakage resistance, $r$ and membrane capacitance, $c$ for a cable of unit surface area, $l$ is the inductance in series with the resistor, $r_l$ [see Figure (3.8)]. As we have shown previously [see section (3.6)], varying the parameter $r_l$ can change the nature of the system from being quasi-active ($r_l = 0$) to passive ($r_l \to \infty$).

The argument of the output function has been modified slightly [c.f. equation (4.6)] in accordance with our initial assumption of approximating the somatic potential $U(x, t)$ with $V(0, x, t)$. However, its form may still be given by equation (4.6), that is $f(V(0, x, t)) = 1 + \tanh(\alpha V(0, x, t))$.

To simplify matters still further we assume the distribution of axon collaterals across the dendritic tree are independent of the separation between the neuron and the corresponding pre-synaptic neuron [equation (5.4)]. Thus the weighting function is of the form,

$$W(\xi, x - x') = W_0 \delta(\xi - \xi_0)J(x - x') \quad (6.3)$$

where $W_0$ is the bifurcation parameter as before and $J(x)$ is the standard Mexican-
that function [equation (4.5)] with parameter values $\Lambda = +1$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$ and $\Gamma = 0.53$. These are exactly the same values as Figure (5.7) in subsection (5.2.2). The logic behind this choice of parameters will become apparent in section (6.3). A pictorial representation of this model may be seen below in Figure (6.1).

Using a standard Green's function approach [Bressloff (1999)], we obtain the following solution for $V(0, x, t)$,

$$V(0, x, t) = W_0 \int_{-\infty}^{t} \int_{-\infty}^{\infty} G(\xi_0, t - t') J(x - x') f(V(0, x', t')) dx' dt' \quad (6.4)$$

where $G(\xi_0, t - t')$ is the fundamental solution for the one-dimensional quasi-active cable. We acknowledge that we have not stated explicitly the exact form of this function. However as we will show, the Fourier transform of this Green's function is all that is required for our analysis.

### 6.3 Linear stability analysis

In the following section, we choose units of length and time such that the diffusion coefficient $D = 1$ and the dendritic membrane time constant, $\tau_d$ is also of order one.
We take \( l = 0.2 \) throughout. The other parameter values will be stated where necessary.

In order to make the homogeneous zero solution a fixed point of the system we set the external bias to be \( I_{ext}(\xi, x) = -\int_{-\infty}^{\infty} W(\xi_0, x - x')dx' \).

As with the passive case, a good indication of the expected behaviour is given by linear stability analysis. We linearize about the fixed point \( V = 0 \) and absorb a factor of \( f'(0) \) into the bifurcation parameter, \( W_0 \), thus obtaining the following expression,

\[
V(0, x, t) = W_0 \int_{-\infty}^{t} \int_{-\infty}^{\infty} G(\xi_0, t - t')J(x - x')V(0, x', t')dx'dt' \tag{6.5}
\]

We look for solutions of the form \( V(0, x, t) = V_0 \exp(i\omega t + ipx) \). Substituting this expression into equation (6.5) yields,

\[
1 = W_0 \int_{-\infty}^{t} \int_{-\infty}^{\infty} G(\xi_0, t - t')J(x - x')e^{-i\omega(t-t')-ip(x-x')}dx'dt' \tag{6.6}
\]

We now take the Fourier transform of both \( G(\xi_0, t) \) and \( J(x) \) to obtain the characteristic equation,

\[
1 = W_0 \tilde{G}(\xi_0, \omega) \tilde{J}(p) \tag{6.7}
\]

where \( \tilde{G}(\xi_0, \omega) \) is the Fourier transform of the Green's function [equation (3.30)] and \( \tilde{J}(p) \) is the Fourier transform of the Mexican hat function [equation (4.9)]. Noting that \( \tilde{G}(\xi_0, \omega) = \exp(-\gamma(\omega)\xi_0)/\gamma(\omega) \), where \( \gamma(\omega) \) is the propagation constant [see equation (3.76)]. We substitute this expression into equation (6.7) and expand \( \gamma(\omega) \) in terms of its real and imaginary parts, \( a(\omega) \) and \( b(\omega) \). For the quasi-active system \( a(\omega) \) and \( b(\omega) \) have already been defined in section (3.6) in equations (3.80) and (3.81).

\[
1 = \frac{W_0 e^{-a(\omega)\xi_0} \tilde{J}(p) (a(\omega) \cos(b(\omega)\xi_0) - b(\omega) \sin(b(\omega)\xi_0))}{a(\omega)^2 + b(\omega)^2} \tag{6.8}
\]

\[
0 = b(\omega) \cos(b(\omega)\xi_0) + a(\omega) \sin(b(\omega)\xi_0) \tag{6.9}
\]

From the equations above (6.8) and (6.9), we may now determine graphically non-zero solutions of solutions of \( \omega \) by finding the intercepts of the functions \( f_1(\omega) = \tan(b(\omega)\xi_0) \) and \( f_2(\omega) = -b(\omega)/a(\omega) \). We note that the trivial solution \( \omega = 0 \) is a valid solution and corresponds to a static instability. In order to determine the effects of the inductive branch we plot the graph for \( r_1 = 10.0 \Omega m^2 \) and \( r_1 = 0.1 \Omega m^2 \), thereby simulating a
passive and quasi-active system respectively. The graphs may be seen in Figures (6.2) and (6.3).

Figure 6.2: Solution of equations (6.8) and (6.9). Here $f_1(\omega) = \tan(b(\omega)\xi_0)$ and $f_2(\omega) = -b(\omega)/\alpha(\omega)$ with $\xi_0 = 1$. The inductive resistance $r_l = 10.0 \Omega m^2$ for this plot thus representing the passive scenario.

Figure 6.3: Same as for Figure (6.2), this time however $r_l = 0.1 \Omega m^2$, thereby representing the quasi-active scenario.
Comparing the two graphs [Figures (6.2) and (6.3)] one can immediately see a difference. In the passive case the smallest non-zero solution is \( \omega = \omega_p \). However, in the quasi-active scenario, an additional non-zero solution exists [Bressloff (1999)], \( \omega = \omega_q \). This is a consequence of an additional zero for \( b(\omega) \) [see Figure (6.4)].

![Figure 6.4](image)

Figure 6.4: The function \( b(\omega) \) plotted for the quasi-active case (\( r_l = 0.1 \)) and passive case (\( r_l = 10.0 \)). Here \( r_l \) has units of \( \Omega m^2 \). The extra zero for \( b(\omega) \) can clearly be seen for the quasi-active case.

Setting \( \xi_0 = 1 \), as we have done in the Figures (6.2) and (6.3), we rearrange equation (6.8) to obtain the following expression,

\[
W_0 \tilde{J}(p) = H(\omega) = \frac{e^{a(\omega)(a(\omega)^2 + b(\omega)^2)}}{a(\omega) \cos(b(\omega)) - b(\omega) \sin(b(\omega))}
\]  

(6.10)

Evaluating \( H(\omega) \) at each of the solutions obtained from the graphs (i.e. \( \omega = 0, \omega_p, \omega_q \)), the following information is revealed. Firstly, both \( H(0) \) and \( H(\omega_q) \) are positive and \( H(\omega_q) < H(0) \). From this we can infer that a dynamic Turing instability can occur from a standard Mexican hat function in the quasi-active regime. Secondly \( H(\omega_p) < 0 \) and \( |H(\omega_p)| \gg H(\omega_q) \). This implies that a dynamic bulk instability is particularly hard to observe with the parameters we have chosen for \( \tilde{J}(p) \).

We are now in a position to determine the critical values of \( W_0 \) which induce dynamic and static Turing instabilities. Equation (6.10) shows that for \( \omega = 0 \) the critical value is (we note that \( b(0) = 0 \). See Figure (6.4))
\[ W_0^q = \frac{H(0)}{\tilde{J}(p_{\text{max}})} = \frac{a(0) \exp(a(0))}{\tilde{J}(p_{\text{max}})} \]  

(6.11)

where \( a(0) = \text{Re} \gamma(0) = (1/\sigma) \times \sqrt{(r + r_l)/r_l} \) and \( \tilde{J}(p_{\text{max}}) = \max_p \tilde{J}(p) \) [equation (5.29)].

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure65.png}
\caption{Critical couplings \( W_0^q \) and \( W_0^p \) as a function of the inductive resistance \( r_l \) (in units of \( \Omega m^2 \)). There exists a critical inductive resistance \( r_{lc} \approx 0.45 \) such that for \( r_l < r_{lc} \) a dynamic Turing instability occurs. Whereas if \( r_l > r_{lc} \) a static Turing instability is observed.}
\end{figure}

Similarly for \( \omega = \omega_q \), the critical value is (we note that \( b(\omega_q) = 0 \), see Figure (6.4)),

\[ W_0^q = \frac{H(\omega_q)}{\tilde{J}(p_{\text{max}})} = \frac{a(\omega_q) \exp(a(\omega_q))}{\tilde{J}(p_{\text{max}})} \]  

(6.12)

Finally for \( \omega = \omega_p \) we have the condition,

\[ W_0^p = \frac{H(\omega_p)}{\tilde{J}(p_{\text{min}})} = \frac{a(\omega_p) \exp(a(\omega_p))}{\cos(b(\omega_p))\tilde{J}(p_{\text{min}})} \]  

(6.13)

where \( \tilde{J}(p_{\text{min}}) = \min_p \tilde{J}(p) \) [equation (5.29)].

As we have stated before, a dynamic bulk instability will be hard to observe in this particular system as \( W_0^p \gg W_0^q \). Of most interest, however is the transition of a
dynamic Turing instability to a static Turing instability as we vary $\tau_1$. We therefore plot $W_0^s$ and $W_0^g$ as a function of $\tau_1$ [Figure (6.5)]. It can be seen from the graph, that beyond a certain value of $\tau_1$, a dynamic Turing instability cannot occur. This value we denote as $\tau_{1c}$ and its value has been found to be approximately $0.45 \, \Omega \, m^2$. From this critical point onwards a static Turing instability occurs.

### 6.4 Numerical results

Within this section we present the results of some numerical simulations which confirm the validity of the analytical results obtained in section (6.3). We accomplish this by firstly discretizing both space and time in equations (6.1) and (6.2). This to some extent has already been performed for a single cable in subsection (3.6.3). However for this specific model, where we consider a one-dimensional chain of neurons, we obtain a different finite difference scheme [see equations (3.84) and (3.85)]. The cable is now represented as a system of $N$ coupled electrical compartments of length $\Delta \xi$ labelled by $m = 0, \ldots, N - 1$. The temporal step length over which the equations are evolved is denoted by $\Delta t$. In order to ensure convergence we take $\Delta t = 0.001$ and $\Delta \xi = 0.2$. We have set $D = \tau_d = 1$ and take $l = 0.2$. The neurons in the chain are labelled $i = 1, \ldots, N$.

\begin{align}
V_{i,m}^{n+1} &= (1 - \Delta t)V_{i,m}^n + \frac{\Delta t}{\xi^2}(V_{i,m+1}^n - 2V_{i,m}^n + V_{i,m-1}^n) - \frac{\Delta tI_{i,m}^n}{c} \\
&\quad + \frac{W_0\Delta t}{\xi}\sum_{j=1}^{N}\delta_{m,m_0}J(i-j)\tanh(\kappa V_{j,0}^n) \\
I_{i,m}^{n+1} &= \frac{\Delta tV_{i,m}^n}{l} + \left(1 - \frac{\tau_1\Delta t}{l}\right)I_{i,m}^n
\end{align}

(6.14)

These equations are supplemented with zero-flux boundary conditions for both $V_{i,m}^n$ and $I_{i,m}^n$ at $m = 0, N - 1$. The term that represents the summation of the inputs comprises of two components: the output function, $\tanh(\kappa V_{j,0}^n)$ and the connectivity function, $W_0\delta_{m,m_0}J(i-j)/\xi$. This is the discrete approximation for equation (6.3), where $J(i-j)$ is given by,

\begin{equation}
J(i-j) = \Lambda[e^{-\gamma_1|i-j|\Delta \xi} - \Gamma e^{-\gamma_2|i-j|\Delta \xi}]
\end{equation}

(6.16)

with parameter values $\Lambda = +1$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$ and $\Gamma = 0.53$. 

94
We utilise this numerical scheme to simulate two cases which seek to confirm our analysis. We firstly simulate the quasi-active system with $r_l < r_c$ and then the passive case with $r_l > r_c$. The results can be seen below.

Figure 6.6: Dynamic (time-periodic) instability in a one-dimensional network of analog neurons. We use an uncorrelated weight distribution together with a standard Mexican Hat function as specified by equation (6.3), with parameter values $\Lambda = +1$, $\gamma_1 = 1.0$, $\gamma_2 = 0.5$ and $\Gamma = 0.53$. Here $\xi_0 = 1.0$, $r_l = 0.1$ ($r_l < r_c$) and $W_0 = 20.0$. The approximated somatic potential $V(0, x)$ is plotted as a function of network co-ordinate $x$ and time $t$. The distance $x$ is measured in units of $\Delta x$ where $\Delta x = 0.2$.

Figure 6.7: Static Turing instability. Same as Figure (6.6) but with $r_l = 10.0$ ($r_l > r_c$).
Chapter 7

The Dynamics of Coupled Neuronal Oscillators with Dendritic Structure

Observe due measure, for the right timing is in all things the most important factor.

Hesiod

7.1 Introduction

Dynamical systems with a high number of degrees of freedom are often seen to produce large scale rhythmic activity [Winfree (1980)]. Example systems are found throughout the field of science, and include Josephson junctions [Wiesenfeld (1992), Hadley et al. (1988)], lasers [Silber at al. (1993)], charge-density waves [Fisher (1985)] and oscillatory chemical reactions [Kuramoto (1984)].

The complexity of these systems makes analysis particularly hard. However, one promising strategy is to consider the dynamics of coupled systems made of many simple subunits whose properties we do understand [Matthews et al. (1991)]. For this reason the theory of coupled oscillator arrays [Watanabe & Strogatz (1993), Ashwin & Swift (1992), Swift et al. (1992), Nakagawa & Kuramoto (1994)] has been applied to such paradigms listed above [Watanabe & Strogatz (1994), Roy & Thornburg (1994)].

However, oscillatory systems in biology are somewhat different to an oscillatory chemical reaction say [Winfree (1987)]. The biological entities within the system communicate with each other through a brief episodic pulselike interaction as opposed to continuously interacting. The chirp of a cricket [Walker (1969), Sismondo (1990)],
the light flash of a firefly [Hanson et al. (1978), Buck (1988)] and of course the action potential of a neuron [see section (2.2)] are all such methods of communication. Large assemblies of these biologically realistic oscillators have only recently been studied [Mirollo & Strogatz (1990)]. Since Mirollo and Strogatz’s seminal work a stream of papers have ushered forth [a brief selection include Kuramoto (1991), Ermentrout & Kopell (1991), Ermentrout (1994)] concerned with the dynamics of biological oscillators with a particular slant on neurodynamics [Bressloff et al. (1997), Bressloff & Coombes (1999a)]. The model used in the vast majority of this body of work is the so-called Integrate-and-Fire (IF) model [see for example Tuckwell (1988), Van Vreeswijk & Abbott (1993), Corral et al. (1995), Bottani (1996), Burkitt & Clark (1999)]. Despite its relatively simplistic mathematical definition, it still captures the spiking and resetting nature of a neuron [see section (7.4) for a brief review of the IF model]. However, the influence of the dendritic tree has again been neglected in much of the work and it is this issue which we aim to address within this chapter.

7.2 Degrees of Locking Between Oscillators

When examining an array of coupled oscillators, we are particularly interested in rhythmic behaviour. To be more precise, rhythm induced by some degree of locking between oscillators. Such phenomena as synchronization, phase-locking and frequency-locking (mode-locking) are all examples of these locking patterns. These features are particularly relevant in a neurobiological environment where information is believed to be carried in the precise timing of spikes [see section (2.3)]. We examine the relevance of these rhythmic patterns to information processing in section (7.3).

Unfortunately, the phenomena listed above, do not have common definitions which are agreeable to all scientists [Hoppensteadt & Izhikevich (1997)]. We thus firstly clarify our definition regarding each degree of locking.

7.2.1 Definitions

The following definitions, are all applied to a neurobiological environment. We are thus comparing a neuron’s train of spikes to another, or to an external periodic drive.

- Mode-locking

If \( p \) spikes are fired within a window of time that is \( q \) times the input period (for integer \( q \)) the resulting train is shown to have an average firing rate of \( p/q \)
and is called a $q:p$ mode-locked state [Coombes & Bressloff (1999a)]. A pictorial representation of a 2:3 mode-locked state is shown in Figure (7.1).

Figure 7.1: An example of a 2:3 mode-locked solution that may arise in a periodically forced system. The forcing itself being a stream of spikes. Note that the system fires 3 spikes (with phases $\phi_0$, $\phi_1$, $\phi_2$) for every two periods of the driving signal.

- **Entrainment**
  If 1:1 frequency-locking exists then the system is said to be entrained.

- **Phase-locked**
  Firstly we note that phase-locking implies mode-locking. The reverse is not true however. Frequency-locking without phase-locking is defined as phase trapping [Hoppensteadt & Izhikevich (1997)]. For the analysis concerned with phase-locking considered later on in this chapter we impose an entrainment condition [see section (7.6)]. This is purely for facilitating our analysis.

Please refer to the diagram below [Figure (7.2)]. The state of each oscillator may be characterized by a constant phase $\phi_i$. Two neurons are said to be phase-locked if the phase difference $\phi_1 - \phi_2$ (also known as phase lag or phase lead) between them is constant. The phase difference is defined mod 1.

- **Synchronous**
  Synchronization occurs when $\phi_1 - \phi_2 = 0$. As the phase is defined mod 1, the phase difference could also equal 1.
Figure 7.2: A simple pictoral representation of phase-locking between two neurons, that is to say $\phi_1 - \phi_2 = \text{const}$. An entrainment condition has been applied, thus each neuron has the same period $T$.

- **Anti-synchronous**

  When $\phi_1 - \phi_2 = \frac{1}{2}$ the neurons are said to be anti-synchronous.

- **Asynchronous**

  When $0 < |\phi_1 - \phi_2| < \frac{1}{2}$, the neurons are said to be asynchronous.

We draw a diagram which encapsulates the various behaviours of the neurons and their relationship to each other in the Figure (7.3) below.

### 7.3 The Relevance of Neurobiological Rhythms

Rhythm is present at many different hierarchical levels within the brain. For example, it appears at the simple neuronal level, in the repetitive firing of a single cell and also in populations of neurons. The understanding of these different rhythms is central to our investigation of the brain. Within this section we therefore provide an assortment of neurobiological examples which illustrate the presence and role of these locking induced rhythms described in the section (7.2).

#### 7.3.1 Mode-locking

Vertebrate locomotion typically involves rhythmic, coordinated movements of such appendages as limbs or fins [Collins & Stewart (1992)]. It is known [Cohen et al.
Mode-locking

Entrainment

Anti-synchronous

Synchronous

Asynchronous

Figure 7.3: The various degrees of locking of oscillators which we study and how they relate to one another. We again ask the reader to note that the phase-locking scenarios (the inner most circle) which we consider are all contained within a general entrainment regime.

(1988) that networks of oscillatory neurons, called central pattern generators (CPGs) generate and control these movements. It would be fair to assume that mode-locking observed in limb movement implies mode-locking at the neuronal level. It is for this reason that the experiments carried out by Peper and colleagues (1995) are of particular interest. They studied the stability of particular ratios $N:M$ (3:8 and 5:8 were the actual ratios examined) of bimanual tapping. This was accomplished by asking a group of drummers to perform these particular rhythms and then gradually increasing their playing speed. Interestingly, abrupt transitions from the initial frequency ratios to other lower order frequency ratios (i.e. ratios with smaller values of $N$ and $M$) were induced. This feature is common to a number of biological systems where the most commonly observed stable behaviour corresponds to low-order ratios [Treffner & Turvey (1993)]. For example cardiac rhythms [Guevara & Glass (1982)], circadian control of ovulation [Winfree (1980)] and the coordination of breathing and locomotion in running [Bramble & Carrier (1983)].
7.3.2 Phase-locking

Phase-locking is also observed in animal locomotion. For example, during swimming freshwater turtles adopt leg movement patterns similar to that of a trotting terrestrial quadreped: diagonal legs move in phase and the two pairs of diagonal limbs move half a period out of phase with one another [Collins & Stewart (1992)].

Other species such as the lamprey display a different form of phase-locking. The undulatory motion of the lamprey is believed to be caused by a set of fixed phase differences distributed along a chain of CPGs. This manifests itself as a travelling wave along the length of the body [Cohen et al. (1982), Grillner (1981)].

7.3.3 Synchronization

Synchronization is a curious phenomenon within the context of the brain. Its presence may be perceived as being both constructive and destructive. Petsche and colleagues (1974), for example describe epileptic seizures involving whole regions of the brain. These seizures are characterised by large scale synchronous activity [Traub et al. (1987)]. We do not concentrate on this destructive behaviour but instead discuss the helpful contribution of synchronicity to visual processing.

One of the most important, indeed critical jobs performed by our visual system is to group the myriad of features in a visual scene into the discrete objects that form the scene [Barinaga (1999)]. Anthony Movshon, a neuroscientist from New York, summarises it when saying

"It is very hard to analyze an image until you have broken it into the objects it contains."

Current theories assume the brain assembles objects with the help of visual cues such as colour, velocity, texture and continuity [Julesz (1981), Ballard et al. (1983)]. However, it is known that these cues are processed in different, spatially segregated areas of the brain [Zeki & Shipp (1988)]. The obvious question which arises from this is, how features belonging to the same object are marked and linked together [Ritz et al. (1994)]. This conundrum is generally known as the binding problem.

A theoretical solution to this problem has been proposed. Essentially, temporal coincidence of neural activity can code relevant information, that is synchronous firing binds together physically separated neurons perceiving the same object [Konig et al. (1992)].
Experimental evidence supports this conjecture. Gray and colleagues (1987)(1989), for example carried out experiments on the first visual cortical area of anesthesized cats. Using moving light bars as visual stimuli, it was found that groups of neurons in spatially remote columns (7mm apart) were synchronized.

7.4 The Integrate-and-Fire Model

The model we employ in trying to simulate the various rhythmic, periodic patterns, which we have just described, is called the Integrate-and-Fire (IF) model. In some ways the IF model can be thought of as a caricature of the more precise Hodgkin-Huxley (HH) neuronal model. This model was initially encountered in subsection (3.5.2). In this section, we firstly introduce the IF model before probing its relationship with the HH model.

7.4.1 Introduction and definition

The integrate-and-fire (IF) model is one of the oldest and most widely used of neuronal models. Its formulation was initially described by Lapique in the early part of this century [Lapique (1907)]. For this reason it is sometimes known as Lapique's model in some literature [Tuckwell (1988)], however we prefer the sobriquet of integrate-and-fire as it gives a clear inference as to the dynamics of the model. The model integrates the incoming PSPs and fires an action potential (spike) when the somatic potential reaches some threshold level. Immediately after a firing event the somatic potential is reset to some resting level. The equations which depict these actions are set out below [Coombes & Bressloff (1999a)],

\[
\frac{dU(t)}{dt} = -\frac{U(t)}{\tau_s} + A(t) \tag{7.1}
\]

subject to reset,

\[
U_-(T^n) \equiv \lim_{\delta \to 0} U(T^n - \delta) = 1, \quad U_+(T^n) \equiv \lim_{\delta \to 0} U(T^n + \delta) = 0 \tag{7.2}
\]

Here \(U(t)\) denotes the somatic potential, \(\tau_s\) is the somatic membrane time constant and \(A(t)\) is an applied signal. This input function is taken to be periodic in time such that \(A(t) = A(t + 1)\). The firing times, \(T^n\), are defined as,
A pictorial representation of the IF dynamics is provided below in Figure (7.4)

![Diagram of Integrate-and-Fire dynamics](image)

Figure 7.4: A simple representation of Integrate-and-Fire dynamics.

The IF model has admittedly a simplistic definition. One that captures only certain characteristics of a firing neuron. The simplistic definition is however misleading in terms of the prospective mathematical analysis. The reset condition induces harsh nonlinearities within the system, making analysis far from a trivial task. The IF model is however more mathematically tractable than the so-called Hodgkin-Huxley model (HH model). This is a far more detailed mathematical description of a spiking neuron and is given by a set of four non-linear ordinary differential equations. It is to this model we now turn our attention and in particular we analyse the relationship between the IF model and the more realistic Hodgkin-Huxley model, drawing heavily on Abbott & Kepler’s analysis (1990) which shows how the IF model may be derived from the more complex and realistic model.

### 7.4.2 The Hodgkin-Huxley equations

The work of A.L.Hodgkin and A.F.Huxley has long been recognised as an outstanding contribution to the field of mathematical biology. The four papers which they submitted in 1952 [Hodgkin & Huxley (1952 a,b,c,d)] were a culmination of many years theoretical and experimental work and revolutionised the study of electrically active cells.
They conducted a series of voltage-clamp experiments on the giant axon of a squid. The
description ‘giant’ is a relative one, as its diameter is only approximately 0.5 mm. This
is however much larger then most axons and was thus easier to perform experiments on.
The conditions one imposes on an axon during a voltage clamp experiment are entirely
artificial. The axon is immersed in fluids of various Na\(^+\) concentrations. Thus the
membrane potential of the axon has, at any given time, the same value along its entire
length. But more importantly, as time passes, the membrane potential remains fixed.
Thus the potential is independent of both space and time. This is in direct contrast
to a normally functioning axon [see section (2.2)] whereby the membrane potential is
either the same as the resting value or changes as an action potential propagates along
it. The data elicited from the collection of experiments however does shed light on how
the ionic conductances functioned. It is from this data that they proposed a system of
ordinary differential equations which formed the following phenomenological model of
the events underlying the generation of an action potential.

The equations are set out below,

\[
C \frac{dU}{dt} = -F + I(t) \quad \text{where,}
\]

\[
F(U, m, h, n) = [g_{Na}m^2h(U - U_{Na}) + g_Kn^4(U - U_K) + g_l(U - U_l)]
\quad (7.5)
\]

In this model, the membrane current \(F\), arises from the conduction of sodium and
potassium ions through voltage dependent channels in the membrane. Any other ionic
currents are described by the Ohmic leakage contribution. \(F\) is thus a function of \(U\)
and of three time- and voltage dependent conductance variables \(m\), \(h\) and \(n\). \(C\)
is the membrane capacitance and \(I(t)\) is the input current. The various parameters in
equation (7.5) take the following values \(g_l = 0.3\) mmho/cm\(^2\), \(g_K = 0.36\) mmho/cm\(^2\),
\(g_{Na} = 120\) mmho/cm\(^2\), \(U_l = -54.402\) mV, \(U_K = -77\) mV and \(U_{Na} = 50\) mV.

The conductance variables \(m\), \(h\) and \(n\) by definition take values between zero and one.
Furthermore, they all approach asymptotic values \(\bar{m}(U)\), \(\bar{h}(U)\) and \(\bar{n}(U)\) with time
constants \(\tau_m(U)\), \(\tau_h(U)\) and \(\tau_n(U)\) respectively,

\[
\tau_m \frac{dm}{dt} = \bar{m}(U) - m, \quad \tau_h \frac{dh}{dt} = \bar{h}(U) - h, \quad \tau_n \frac{dn}{dt} = \bar{n}(U) - n \quad (7.6)
\]

where for all three variables,

\[
\tau_{(m,h,n)} = \frac{1}{\alpha_{(m,h,n)} + \beta_{(m,h,n)}} \quad (7.7)
\]

\[
(\bar{m}(U), \bar{h}(U), \bar{n}(U)) = \frac{\alpha_{(m,h,n)}}{\alpha_{(m,h,n)} + \beta_{(m,h,n)}} \quad (7.8)
\]

104
and specifically,

\[
\begin{align*}
\alpha_m &= \frac{0.1(U + 40)}{1 - \exp[-0.1(U + 40)]} \\
\alpha_h &= 0.07 \exp[-0.05(U + 65)] \\
\alpha_n &= \frac{0.01(U + 55)}{1 - \exp[-0.1(U + 55)]} \\
\beta_m &= 4 \exp[-0.0556(U + 65)] \\
\beta_h &= \frac{1}{1 + \exp[-0.1(U + 35)]} \\
\beta_n &= 0.125 \exp[-0.125(U + 65)]
\end{align*}
\]  

Before discussing the derivation of the IF model from the HH model, we make some general remarks about this set of equations (7.4)-(7.14). Firstly, the derivation of this system was purely to fit the data gained from the voltage-clamp experiments. The best justification for the equations are simply that they work [Cronin (1987)]. Secondly, although the equations are elaborate, they interact in a fairly minimal way. The conductances \( m, h \) and \( n \) are not directly coupled to each other and only interact through \( U \). This feature is important for the reduction to the IF model. Our last remarks concern the HH models dynamics. If \( I(t) = 0 \), \( U \) remains at the resting value of \(-65 \text{ mV}\). An action potential will only occur for a sufficiently strong positive current \( I \) being applied for a sufficiently long time. The dynamics for each of the conductances is particularly fascinating during the course of an action potential. The rapid increase of the \( m \) variable triggers the initial sharp rise of the action potential. This acclivity terminates as the variables \( h \) and \( n \) adjust more slowly to the shift in the membrane potential. The sodium current which fomented the upward swing of the action potential is then shut off due to \( h \) decreasing. At the same time, \( n \) is increasing, thereby initiating a hyperpolarizing of the cell, due to a positive outward potassium current. The final stage is the readjustment of \( h \) and \( n \) back to their resting values. Thus the HH model is clearly able to duplicate three key features of action potential initiation: the action potential itself, the refactory period and the ability to integrate incoming PSPs.

From a mathematical viewpoint, once again biological realism comes at an expense. The four-dimensional nature of the phase-space makes it almost impossible to utilise traditional phase-space analysis. Any analysis of the model is done through numerical means [Cronin (1987)] or through a weak-coupling argument [Hansel et al. (1993), Hansel & Mato (1993)]. The temptation is therefore to decrease the number of dimensions whilst still capturing some key characteristics of the model and indeed the neuron.
Abbott & Kepler (1990) set out a systematic means by which the HH model may be reduced to a two-dimensional problem, which is in keeping with the Fitzhugh-Nagumo model but more accurate. Further simplifications then yield the IF model. The essence of their work is briefly considered now.

Firstly, we note that $\tau_m$ is much smaller than either $\tau_h$ or indeed $\tau_n$, this infers that $m$ reaches its asymptotic value faster than the other conductances. Thus Abbott & Kepler replaced the variable $m$ by its asymptotic value,

$$m \approx \bar{m}(U)$$ (7.15)

Thus $F$ [equation (7.5)] now becomes,

$$F(U, m, h, n) \approx F(U, \bar{m}(U), h, n)$$ (7.16)

It would help enormously if $h$ and $n$ could also be replaced by their respective asymptotic values. However, by doing this we would extirpate the model's ability to generate an action potential. Thus because of their longer time constants, $h$ and $n$ should reach their respective asymptotic values more tardily than $m$. In order to do this, Abbott and Kepler introduced an auxiliary voltage variable, $V$, which lags behind $U$. With this additional variable, we can replace $h$ and $n$ by their asymptotic values, not at $U$ but at $V$. Thus we may write,

$$h \approx \bar{h}(V) \quad n \approx \bar{n}(V)$$ (7.17)

so naturally $H$ [equation (7.16)] again changes to become,

$$H = F(U, \bar{m}(U), h, n) \approx F(U, \bar{m}(U), \bar{h}(V), \bar{n}(V)) \equiv f(U, V)$$ (7.18)

In order to diminish the impact of this approximation, the variable $V$ must be chosen carefully. As Abbott & Kepler state, the time-dependence of $V$ in $f$ should mimic the time-dependence induced into $F$ in the full model by the changing values of $h$ and $n$. Abbott & Kepler thus equated time derivatives of $F$ at constant $U$ in the full and reduced models,

$$\frac{\partial F}{\partial h} \frac{dh(U)}{dt} + \frac{\partial F}{\partial n} \frac{dn(U)}{dt} = \left( \frac{\partial f}{\partial h} \frac{d\bar{h}(V)}{dt} + \frac{\partial f}{\partial n} \frac{d\bar{n}(V)}{dt} \right) \frac{dU}{dt}$$ (7.19)

The original formulas for $dh/dt$ and $dn/dt$ [equation (7.6)] may now be incorporated into equation (7.17) so that,
\[ \tau_h(U) \frac{dh}{dt} \approx \bar{h}(U) - \bar{h}(V), \quad \tau_n(U) \frac{dn}{dt} \approx \bar{n}(U) - \bar{n}(V) \] (7.20)

Utilising these results, one can now solve equation (7.19) for \( dV/dt \) in terms of \( U \) and \( V \), and thus we obtain the following two dimensional system,

\[ C \frac{dU}{dt} = -f(U,V) + I(t) \] (7.21)
\[ \frac{dV}{dt} = g(U,V) \] (7.22)

where,

\[ g(U,V) = \frac{A}{B} \] (7.23)

with,

\[ A = \frac{\partial F}{\partial h} \left( \frac{\bar{h}(U)}{\tau_h(U)} \right) + \frac{\partial F}{\partial n} \left( \frac{\bar{n}(U)}{\tau_n(U)} \right) \] (7.24)

and

\[ B = \frac{\partial f}{\partial h} \frac{dh}{dV} + \frac{\partial f}{\partial n} \frac{dn}{dV} \] (7.25)

Finally for this system to be reduced to the IF model we ignore the dynamics of \( V \) (this essentially is accomplished by setting \( U = V \) and thus \( g(V,V) = 0 \)). This fairly crude simplification means the IF model cannot produce an action potential itself and the refractory period is not an automatic property of the model. This can be accomplished however by freezing the dynamics of \( U \) for a specified time. In our original notation of the firing times [equation (7.3)], now becomes, \( T^n = \inf\{t|U(t) \geq 1; t \geq T^{n-1} + \tau_r \} \), where \( \tau_r \) is the refractory period. Thus we obtain equation (7.1) with \((1/C)f(U) = U/\tau_s \) and \( A(t) = I(t)/C \). The notion of the threshold is simply obtained by stating that whenever \( dU/dt > 0 \) the system fires. The linear approximation for \( f(U) \) is the most common, we note though that a higher order polynomial can be used such as the cubic used in Abbott & Kepler's paper (1990).

If the reader is particularly interested in the HH model, then the book by Cronin, 'Mathematical aspects of Hodgkin-Huxley Neural theory' (1987) is an excellent starting point.
7.5 Mode-Locking and Arnold tongues for an integrate-and-fire neuron with dendritic structure

7.5.1 Introduction

The analysis performed in this section is very much an extension of the work undertaken by Coombes & Bressloff (1999a). We utilise their mathematical analysis and draw upon their analytical framework, thus we are able to extend their work to discover the effect of a simple one-dimensional dendritic cable on the mode-locking behaviour between a single neuron and a periodic drive. We firstly, however discuss the mathematical implications of mode-locking by way of circle map dynamics before returning to the IF system.

7.5.2 Circle map dynamics

Mode-locking is a resonant response occurring in systems of coupled oscillators or oscillators coupled to periodic external forces [Jensen et al. (1984)]. Generally speaking, resonances occur whenever the frequency of a harmonic of one oscillator, approaches some harmonic of another; and in the resonant region the frequencies of the two oscillators lock into some rational ratio.

An interesting and apparently simple model which elucidates this phenomenon is the so-called circle map. In general, circle maps are defined as,

$$\theta_{n+1} = f_\Omega(\theta_n) = \theta_n + \Omega + g(\theta_n)$$  \hspace{1cm} (7.26)

where,

$$g(\theta_n) = g(\theta_n + 1) \text{ mod } 1$$  \hspace{1cm} (7.27)

The mapping can be thought of as lifts of mappings from the circle onto itself, this is encapsulated in the periodic property in equation (7.27). The variable $\theta_n$ denotes the phase of the system. In addition to this $\Omega$ is the bias term and represents the frequency of the system in the absence of the non-linear coupling $g$.

In order to examine mode-locking in this system, it is natural to consider the iterations of the map, that is $\theta_1, \theta_2, \theta_3, \ldots$. The iteration of the map is conveniently described by the winding number. In short the winding number represents the mean number of
rotations per iteration. Mathematically it is defined as,

\[ W = \lim_{n \to \infty} \left[ \frac{f_n}{n} \right] \]  

(7.28)

So, for example, in the absence of the nonlinear coupling \( W = \Omega \). However, if we include the coupling term, \( W \) may converge onto a rational number, which describes a periodic solution or to an irrational which implies quasiperiodicity. We note that chaos may also be observed, but we shall consider this feature further on.

Jensen and colleagues (1984) summarize a number of important results for the circle map in which the coupling function is given by a sine function. Thus equation (7.26) becomes the so-called two-parameter sinusoidal circle map, discussed in detail by Arnold (1965),

\[ \theta_{n+1} = f_\Omega(\theta_n) = \theta_n + \Omega - \frac{K}{2\pi} \sin(2\pi\theta_n) \]  

(7.29)

where \( K \) can be thought of as the coupling strength. To summarize some well-known results then. For \( 0 < K < 1 \), the winding number locks-in at every single rational number \( P/Q \) in a nonzero interval of \( \Omega \). The regimes in \((\Omega, K)\) space where \( W \) assumes these rational numbers are called Arnold tongues [Arnold (1965)]. The widths of the tongues are proportional to the value of \( K \). So that for \( K \) close to zero, the tongues are very thin (at \( K = 0 \), the tongues are said to have zero measure), however, with increasing \( K \) the width of all the tongues increase. The stability of a particular mode-locked solution is therefore linked to the width of its tongue. The lower order tongues are fatter, therefore more stable. This is in keeping with the experiments conducted by Peper and colleagues (1995) [see subsection (7.3.1)]. Clearly at some value of \( K \) the tongues will begin to overlap. This critical point is found to be \( K = 1 \) (full measure). Interestingly for \( K > 1 \), the tongues overlap and the underlying map develops a local maximum (i.e. \( f'(\theta) = 0 \) thus it is now no longer invertible and chaotic solutions occur [Jensen et al. (1984)]. These features may may seen in Figure (7.5) below.

The most interesting aspect of this work on circle maps [Bohr et al. (1984), Glass & Bélair (1986), Knudsen et al. (1991)], is that the classical examples of oscillatory systems such as, Josephson junctions and charge density waves can in some respects be understood by reducing their behaviour to a circle map. This is shown by Coombes & Bressloff (1999a), amongst others [Keener et al. (1981)] to be the case in analysing the dynamics of IF oscillators.
7.5.3 IF dynamics

We initially consider Coombes & Bressloff's analysis (1999), valid for a point processor with no extended structure, before applying their theory to our model of an IF neuron with dendritic structure.

Returning to the model defined by equations (7.1) and (7.2), we find that by integrating equation (7.1) between reset and threshold, yields an implicit map of the firing times [Coombes & Bressloff (1999)].

\[
U_-(T_{m+1})e^{T_{m+1}/\tau} = U_+(T_m)e^{T_m/\tau} + \int_{T_m}^{T_{m+1}} e^{s/\tau} A(s)ds
\]

We now introduce the function,

\[
H(t) = \int_{-\infty}^{0} e^{s/\tau} A(t+s)ds = \frac{e^{-1/\tau}}{1-e^{-1/\tau}} \int_{0}^{1} e^{s/\tau} A(t+s)ds
\]

Hence \( H(t) = H(t+1) \) and defining \( F(t) = e^{t/\tau}[H(t) - 1], \) we obtain a map of the

---

Figure 7.5: Arnold tongues for the sine circle map. The dashed lines indicate the area of overlapping tongues. Reprinted from Jensen et al. (1984)
firing times [Keener et al. (1981)] from (7.30) as

\[ F(T^{n+1}) = F(T^n) + e^{T^n/\tau_s} \quad (7.32) \]

If \( F \) is invertible, that is to say if \( F'(t) \neq 0 \ \forall t \) and \( F^{-1} \) is defined on the range \( F(t) + e^{t/\tau_s} \) then we have an explicit map of the form,

\[ T^{n+1} = \Psi(T^n), \quad \Psi(t) = F^{-1}[F(t) + e^{t/\tau_s}] \quad (7.33) \]

If however \( F \) is not invertible then the mapping \( T^n \to T^{n+1} \) is defined by equation (7.3). We may deduce from this that in general the map of firing times is only available implicitly.

From equation (7.31), we ask the reader to note that \( \tau_s H'(t) + H(t) = \tau_s A(t) \) so that the condition \( F'(t) = e^{t/\tau_s}[A(t) - \tau_s^{-1}] \neq 0 \) is only valid for \( A(t) \neq \tau_s^{-1} \). If this condition is true and in addition to this \( F^{-1} \) is defined on the range of \( F(t) + e^{t/\tau_s} \), one may establish that \( F(\Psi(t) + 1) = e^{1/\tau_s}F(\Psi(t)) = F(\Psi(t+1)) \) and hence \( \Psi(t+1) = \Psi(t) + 1 \). This is an important statement as equation (7.33) may now be viewed as the iteration of a circle mapping (degree one lift) [see subsection (7.5.2)].

The function \( g(t) = \Psi(t) - k \) is now introduced, such that \( 0 \leq g(0) < 1 \). This then leads to the following mapping,

\[ T^{n+1} = g(T^n) + k \quad \text{with} \quad g(t+1) = g(t) + 1 \quad (7.34) \]

and defining

\[ \rho(t) = \lim_{n \to \infty} \inf \frac{g^n(t)}{n}, \quad \bar{\rho}(t) = \lim_{n \to \infty} \sup \frac{g^n(t)}{n} \quad (7.35) \]

allows the definition of the rotation interval of \( g \) as \( L(g) = [\rho_-, \rho_+] \) where

\[ \rho_- = \inf_{t \in \mathbb{R}} \rho(t), \quad \rho_+ = \sup_{t \in \mathbb{R}} \bar{\rho}(t) \quad (7.36) \]

The rotation number of \( g \) (if it exists) is denoted by \( \rho \), it is obtained as the rotation interval reduces to a single point (that is \( \rho_+ = \rho_- \)), thus the \( \lim \inf \) and \( \lim \sup \) in equation (7.35) may be replaced by a simple limit. The choice of \( k \) ensures that
\[ 0 \leq \rho < 1 \] so that \( \rho \) measures the average phase rotation per iteration [see equation (7.28) for the circle map equivalent].

If \( \rho \) exists and is rational then as we discussed in the previous subsection, this infers mode-locking exists. To be more concise, a rational \( \rho \) implies that there is an initial \( T^0 \) such that the sequence \( \{ T^n \mod 1 \} \) approaches a periodic sequence asymptotically for large enough \( n \). If however \( \rho \) is irrational, aperiodicity is observed. That is every solution is ergodic and the sequence \( \{ T^n \mod 1 \} \) is dense in the interval \([0,1)\) (assuming that \( \Psi(t) \) is continuous).

If the explicit map of firing times defined by equation (7.33) is to describe an invertible circle map we must also have the condition that \( \Psi'(t) \neq 0 \). This holds true whenever \( A(t) \neq 0 \) since \( \Psi'(t) = A(t)e^{it\tau}/F'(\Psi) \). If \( A(t) \neq \tau^{-1}a \) and \( A(t) \neq 0 \) then the firing map dynamics can always be reduced to an invertible map of the circle and so as we have discussed chaos will not feature [see subsection (7.5.2)].

### 7.5.4 Mode-locking considerations for a driven IF oscillator

Generally speaking we would expect an IF oscillator to fire one or more spikes at times which are integer multiples of the driving period. Thus the temporal pattern of spikes exhibit a bursting state whereby the inter-burst intervals are mainly influenced by the driving period and the intra-burst intervals being dependent upon the system parameters. It is therefore logical to seek mode-locked solutions of the form

\[
T^n = \left[ \frac{n}{p} \right] \Delta - \phi_{n(p)} \Delta, \quad n(p) = n \mod p \tag{7.37}
\]

where \([\cdot]\) signifies the integer part and \( \phi_{n(p)} \in [0,1) \) denote a collection of firing phases. \( \Delta \) is assumed to be rationally related to the forcing period (which for simplicity we have assumed to be one). Chow (1998) previously considered this type of assumption when analysing harmonic locking in two pulse-coupled spike response neurons. Within Coombes & Bressloff’s paper (1999a), they provide a systematic method of analysing such solutions. Firstly they distinguish three possible types of solution. These are

- **simple bursting**
  This is characterised by \( \Delta = 1 \) and \( p > 1 \).

- **skipping**
  This is defined as \( \Delta = q \) and \( p = 1 \), for \( q \in \mathbb{Z} \) and \( q > 1 \).
• mixed spike train

This is simply a spike train which combines elements of the first two solutions.

We are essentially interested in $q:p$ mode-locked behaviour. That is to reiterate we seek solutions of $p$ spikes fired in a window of time that is $q$ times the input period (for integer $q$). In order to determine this behaviour from a train of spikes we define the average firing $\langle \Delta \rangle$. This is defined in terms of the inter-spike-interval (ISI),

$$
\langle \Delta \rangle = \lim_{N \to \infty} \frac{1}{N} \sum_{n=1}^{N} \Delta_n = \frac{q}{p}
$$

This will be primarily used to verify solutions through direct simulation of the model.

Returning to equation (7.32), the $p$ firing phases may be calculated by the simultaneous solution of the $p$ equations,

$$
J_{n(p)}(\Phi, \Delta) = \frac{H(-\phi_{n+1}(p)\Delta) - 1}{H(-\phi_{n(p)}\Delta)} - \frac{\exp \left( \frac{\Delta}{\tau_s} \left( \frac{n}{p} - \phi_{n(p)} \right) \right)}{\exp \left( \frac{\Delta}{\tau_s} \left( \frac{n+1}{p} - \phi_{n+1(p)} \right) \right)} = 0 \tag{7.39}
$$

By perturbing the firing times such that $T^n \to T^n + \delta^n$ and expanding equation (7.32) to first order in the $\delta^n$'s (assuming $F'(T^n) \neq 0$) around a mode-locked solution we may determine the stability of the solutions.

Coombes & Bressloff denote a mode-locked solution by a set of phases $\Phi = (\phi_0, \ldots, \phi_{p-1})$ and the period $\Delta$. They established that $\delta^{n+1} = \kappa_{n(p)}(\Phi, \Delta) \delta^n$ where,

$$
\kappa_{n(p)}(\Phi, \Delta) = \exp \left[ -\frac{\Delta}{\tau_s} \left( \frac{(n+1)}{p} - \phi_{n+1}(p) - \left[ \frac{n}{p} + \phi_n(p) \right] \right) \right] \frac{A(-\phi_{n(p)}\Delta)}{A(-\phi_{n+1(p)}\Delta) - \tau_s^{-1}} \tag{7.40}
$$

The persistence of a mode-locked state with $p$ phases and period $\Delta$ is wholly dependent upon the behaviour of the map

$$
\delta^{n+1} = \left( \prod_{m=0}^{p-1} \kappa_m(\Phi, \Delta) \right) \delta^{n+1-p} \tag{7.41}
$$

This map has solutions of the form $\delta^n = \exp(n\nu/p)$ for $\nu \in \mathbb{C}$. Thus the stability of the mode-locked state is guaranteed for $\text{Re}(\nu(\Phi, \Delta)) < 0$ where,
where we define,

\[
\kappa(\Phi, \Delta) = \prod_{m=0}^{p-1} \kappa_m(\Phi, \Delta) = e^{-\Delta/\tau_s} \prod_{m=0}^{p-1} \left[ \frac{A(-\phi_m(p)\Delta)}{A(-\phi_{n+1}(p)\Delta) - \tau_s^{-1}} \right]
\]  

(7.43)

We are thus able to define the borders of the Arnold tongues by the condition \(\text{Re}(\nu(\Phi, \Delta)) = 0\), where the set of phases \(\Phi\) is obtained from the solution of equation (7.39).

7.5.5 The model

In the Coombes & Bressloff paper, 'Mode-locking and Arnold tongues in integrate-and-fire neural oscillators' (1999a) they considered mode-locking for any periodically forced IF oscillator without dendritic structure. For illustration purposes, they considered two different forms of forcing: sinusoidal and the more biologically realistic stream of pulses [see section (7.1)]. The forcing was delivered, however straight to the soma. It is perhaps not surprising to discover that the work in this section aims at discovering the effect of dendritic structure upon the mode-locking capabilities of a periodically forced IF oscillator. To aid our analysis we use a periodic stream of spikes as our forcing term and a one-dimensional quasi-active cable as our representaion of the dendritic tree. The model’s equations are thus using equations (7.1), (3.67) and (3.68) together with the reset condition expressed in equation (7.2),

\[
\frac{dU(t)}{dt} = -\frac{U(t)}{\tau_s} + \eta[V(0, t) - U(t)]
\]  

(7.44)

\[
\frac{\partial V(\xi, t)}{\partial t} = -\frac{V(\xi, t)}{\tau_d} + D \frac{\partial^2 V(\xi, t)}{\partial \xi^2} + \frac{I(\xi, t)}{c} + \epsilon \delta(\xi - \xi_0) \sum_{m \in \mathbb{Z}} \delta(t - mT)
\]  

(7.45)

\[
\frac{i \partial I(\xi, t)}{\partial t} = -\tau_i I(\xi, t) + V(\xi, t)
\]  

(7.46)

where \(\tau_s\) and \(\tau_d\) are respectively the somatic and dendritic membrane time constants, \(D\) is the diffusion coefficient, \(c\) is the membrane capacitance, \(l\) is the inductance, \(\tau_i\) is inductive resistance [please refer to Figure (3.8)]. Here \(\eta\) denotes the conductance (in appropriate units). The periodic input is described by the last term of equation (7.45). We represent them as a sequence of unit impulses or to be more precise a
A periodic train of spikes is fed into the dendritic cable at a point $\xi_0$. We then compare the output train of spikes with the periodic input train of spikes.

string of Dirac delta-functions. These are injected into the cable at a point $\xi_0$. The period of the forcing is denoted by $T$. This representation of the input has been used in other fields, for example the work Feingold and colleagues conducted on excitable electrical circuits (1988). The strength of coupling is denoted by $\epsilon$, it is taken to be always positive so that we are concerned with purely excitatory spikes. The model's configuration may be viewed in [Figure (7.6)].

We now set $\eta = \tau_d = D = 1$ (the other parameter values will be stated where needed) and assume the feedback current from the soma to the dendrite can be neglected. Using the standard Green's function approach adopted in earlier chapters we obtain the following standard equation [c.f. (7.1)],

\[ \frac{dU(t)}{dt} = -\frac{U(t)}{\tau_s} + A(t) \quad \text{where} \quad A(t) = \epsilon \sum_{m \in \mathbb{Z}} G(\xi_0, t + mT) \quad (7.47) \]

with $G(\xi_0, t)$ is the Green's function of the quasi-active cable. As we are in control over the drive we set $T = 1$ at this point. Furthermore since $A(t)$ is a periodic function, it may be represented as a Fourier series. That is,
\[ A(t) = \varepsilon \sum_{m \in \mathbb{Z}} \tilde{G}(\xi_0, \omega_m) e^{i \omega_m t} \quad \text{where} \quad \omega_m = 2\pi m \quad (7.48) \]

where \( \tilde{G}(\xi_0, \omega) = \exp(-\gamma(\omega)\xi_0) / \gamma(\omega) \) [see equation (3.30). Note we have already set \( D = 1 \)]. As \( A(t) \) is a real function, we rewrite the equation (7.48) as,

\[ A(t) = \varepsilon \sum_{m \in \mathbb{Z}} [A_r(\omega_m) \cos(\omega_m t) - A_i(\omega_m) \sin(\omega_m t)] \quad (7.49) \]

where,

\[ A_r(\omega) = \frac{e^{-a(\omega)\xi_0} [a(\omega) \cos(b(\omega)\xi_0) - b(\omega) \sin(b(\omega)\xi_0)]}{a(\omega)^2 + b(\omega)^2} \quad (7.50) \]

\[ A_i(\omega) = -\frac{e^{-a(\omega)\xi_0} [b(\omega) \cos(b(\omega)\xi_0) + a(\omega) \sin(b(\omega)\xi_0)]}{a(\omega)^2 + b(\omega)^2} \quad (7.51) \]

Here \( a(\omega) \) and \( b(\omega) \) are defined by equations (3.80) and (3.81).

With this representation it is easier to calculate the function \( H(t) \), which is essential for our calculations. Thus from equation (7.31),

\[ H(t) = \varepsilon \tau_s \sum_{m \in \mathbb{Z}} \frac{\tilde{G}(\xi_0, \omega_m) e^{i \omega_m t}}{1 + i \omega_m \tau_s} \quad (7.52) \]

Once again we rewrite this in a more natural form,

\[ H(t) = \varepsilon \tau_s \sum_{m \in \mathbb{Z}} [H_r(\omega_m) \cos(\omega_m t) - H_i(\omega_m) \sin(\omega_m t)] \quad (7.53) \]

and where more specifically,

\[ H_r(\omega) = \frac{e^{-a(\omega)\xi_0} [(a(\omega) - \omega \tau_s b(\omega)) \cos(b(\omega)\xi_0) - (b(\omega) + \omega \tau_s a(\omega)) \sin(b(\omega)\xi_0)]}{(1 + (\omega \tau_s)^2)(a(\omega)^2 + b(\omega)^2)} \quad (7.54) \]

\[ H_i(\omega) = -\frac{e^{-a(\omega)\xi_0} [(a(\omega) - \omega \tau_s b(\omega)) \sin(b(\omega)\xi_0) + (b(\omega) + \omega \tau_s a(\omega)) \cos(b(\omega)\xi_0)]}{(1 + (\omega \tau_s)^2)(a(\omega)^2 + b(\omega)^2)} \quad (7.55) \]

The functions \( a(\omega) \) and \( b(\omega) \) are expressed in equation (3.80) and (3.81).
In our calculations, we naturally use a truncated Fourier series for both \( A(t) \) and \( H(t) \). In practice we took the following range \(-200 \leq m \leq 200\), as this was both computationally efficient and accurate. We say accurate in the sense that by increasing the range for \( m \) did not improve or change the answer significantly.

### 7.5.6 Numerical considerations

We briefly consider the finite-difference scheme which we employ to validate our theoretical predictions. Again we use a simple explicit numerical scheme [primarily equations (3.84) and (3.85)] to simulate the model described by equations (7.44)-(7.46). Thus discretizing both space and time with respective step lengths \( \Delta \xi \) and \( \Delta t \) yields the following equations (after setting \( \tau_d = D = 1 \))

\[
U^{n+1} = \left(1 - \frac{\Delta t}{\tau_s}\right) U^n + \Delta V_0^n \quad (7.56)
\]

\[
V_{i}^{n+1} = (1 - \Delta t)V_i^n + \frac{\Delta t}{\Delta \xi^2} (V_{i+1}^n - 2V_i^n + V_{i-1}^n) - \frac{\Delta t I_i^n}{c} + \frac{\epsilon \delta_{i,q} \delta_{n,q}}{\Delta \xi} \quad (7.57)
\]

\[
I_{i}^{n+1} = \frac{\Delta t V_i^n}{l} + \left(1 - \frac{\tau_i \Delta t}{l}\right) I_i^n \quad (7.58)
\]

where \( U^n \) denotes the somatic potential at time level \( n \), \( V_i^n \) represents the dendritic membrane voltage at time level \( n \) in the \( i \)th compartment. Similarly \( I_i^n \) denotes the current through the inductive branch of the \( i \)th compartment at time level \( n \). The discrete approximation to the \( \delta(\xi - \xi_0) \) term is represented by \( \delta_{i,p}/\Delta \xi \). Similarly \( \delta_{n,q}/\Delta t \) for \( q \in N \) represents the finite approximation to the stream of spikes. In practice we took \( \Delta t = 0.0001 \), \( \Delta \xi = 0.015 \) and \( i = 0, \ldots, 1000 \). We also assumed zero flux conditions at the ends of the cable. This numerical scheme was then iterated for approximately 500,000 times for different values of a certain parameters \((\tau_s, \xi_0)\).

Generally speaking the most important information to be gleaned from these simulations is the set of firing times. To improve the accuracy in calculating these times, we employ the same method as suggested by Hansel et al. (1998). Essentially, we linearly interpolate to recalculate the firing time. Thus if we denote the approximate firing time by \( T^* \), the more accurate firing time \( T_{acc} \) may be calculated by the following expression,

\[
T_{acc} = T^* + \frac{dt(1 - U(T^*))}{U(T^*) - U(T^* - \Delta t)} \quad (7.59)
\]
It is this more accurate firing time that we use for the spike train plots and for the evaluation of $\langle \Delta \rangle$ which together validate our theoretical predictions.

### 7.5.7 Mode-locked solutions and Arnold tongues

In order to plot the tongues we used the numerical continuation package XPP-Aut [see the following web address: ftp://ftp.math.pitt.edu/pub/bardware/tut/start.html]. Although primarily written for systems of ordinary differential equations, XPP-Aut can also compute solution branches for algebraic systems of the form (7.39) and (7.43). With this package we investigated the following aspects of our model. Firstly the existence of $q:p$ mode-locked solutions in a passive regime ($r_l \to \infty$, in practice we took $r_l = 100.0 \Omega m^2$). In Figure (7.7) we show three such tongues: 1:1, 1:2, 2:3, plotted in $(1/\tau_s, \xi_0)$ parameter space. The use of the numerical continuation package can be quite awkward and problematical. However we are aided when trying locate the approximate parameter regime where a higher order tongue is defined by the fact that if a $q:p$ and a $q':p'$ mode-locked solutions exist then another mode-locked solution $q + q':p + p'$ can be expected to be found in the intermediate parameter regime [Glass & Bélair (1986)]. This can clearly be seen in Figure (7.7) with the 2:3 tongue nestling between the 1:1 and 1:2 tongues. These figures are validated with direct numerical simulation of the model [the precise numerical scheme is detailed in equations (7.56)-(7.58)] to produce graphs of the average firing frequency $\langle \Delta \rangle$ against the dendritic location $\xi_0$ [see Figure (7.8)]. The resulting devil's staircase structure shows that the preferred mode-locked solutions are those with low ratios of $q$ to $p$ [see subsection (7.3.1)]. In addition to this, we also produce plots of spike trains which clearly show the specific mode-locking behaviour [see Figure (7.9)].
Figure 7.7: The tongue structure for 1:1, 1:2 and 2:3 mode-locked solutions for a passive cable. Here $\epsilon = 4$, $l = 0.2$ and $\tau_l = 100.0 \Omega m^2$.

Figure 7.8: Plot of average firing frequency versus dendritic location, obtained by directly simulating the equations of motion. The dominant solutions are clearly shown to be 1:1, 1:2 and 2:3. The parameter values are the same as for the ones above with $\tau_o = 1$. 
Figure 7.9: Spike train pictures showing (a) 1:1 mode-locking ($\xi_0 = 0.930$), (b) 2:3 mode-locking ($\xi_0 = 0.675$) and (c) 1:2 mode-locking ($\xi_0 = 0.435$). The value of $\tau_s$ remained at 1 throughout and the other parameter values remained unchanged from Figure (7.7). The taller spikes represent the periodic input whilst the smaller ones are the output from the neuron.

We may draw a number of conclusions from these Figures (7.7)-(7.9). Firstly, we see that type of mode-locking behaviour observed is very much dependent upon where the axon (connection) impinges on the dendrite. This again underlines the importance of the dendritic co-ordinate. In addition to this we see that the most stable and therefore most likely observed behaviour is that of entrainment (the 1:1 structure). Furthermore for small $\xi_0$ ($\xi_0 \approx 0.25$), that is where the axon impinges close to the neuron's soma, it is possible for the tongues to overlap [see Figure (7.7)]. In this case mode-locked solutions with different average firing frequencies co-exist at a point in parameter space leading to multi-stability. It would be helpful if one could draw the border whereby the underlying firing map is still reducible to the circle map dynamics. However we are unable to do this in this particular example. Thus instead we probed this area using our numerical scheme. It was found that the resulting behaviour was dependent upon the choice of initial conditions and that chaotic solutions did not exist.

We additionally scrutinized the effect of the other interesting parameters in the system i.e. the coupling strength, $\varepsilon$ and the parameter $\tau_1$ on the 1:1 tongue structure. The results may be viewed in Figures (7.10) and (7.11). Considering Figure (7.10) initially, we see that for progressively larger values of $\varepsilon$, the passive ($\tau_1 = 100.0 \Omega m^2$)
1:1 mode-locked region is found to occupy progressively smaller areas of parameter space, but these regions are located higher up the cable. Intuitively, one would expect this behaviour. The amount of attenuation an impulse receives as it traverses along the cable is wholly dependent upon where the impulse is initially injected along the cable. Naturally, impulses injected at large \( \xi_0 \) receive far greater attenuation en route to the soma than impulses injected close to the soma. Thus in order for the soma to experience the effect of distal injected impulses, the coupling strength \( \epsilon \) must be large enough to combat the attenuation which the passive cable represents.

We may now consider Figure (7.11) which concerns the effect of varying \( r_l \) on the 1:1 mode-locked structure with constant \( \epsilon \) (here \( \epsilon = 10.0 \)). One may see immediately that for progressively larger values of the inductive resistance \( r_l \) a similar scenario as for Figure (7.10) emerges. That is, as \( r_l \) is increased the regions of 1:1 mode-locking decrease in parameter space but are located at higher values of \( \xi_0 \). The enhancement in the quasi-active regime \( (r_l < 1.0 \, \Omega m^2) \), we conjecture is due to the resonant-like behaviour of quasi-active membranes. More specifically input signals with frequencies around \( \omega_{\text{max}} \) are treated preferentially in terms of smaller voltage attenuation to the soma than inputs that are faster or slower [Koch (1999)]. Thus as we have explained [see subsection (3.6)], the membrane essentially acts as a band-pass filter and it is this behaviour that enhances the tongue.

If we ruminate on these features, it is apparent that these findings may have possible implications for synaptic amplification previously discussed in subsection (2.3.3). As we have shown, by modulating the strength of coupling \( \epsilon \) and the inductive resistance \( r_l \), it is possible to alter not only the inherent stability of the tongue manifested in its width but also the relative position of the tongue along the cable. Thus for example, if the strength of coupling was relatively strong and the inductive resistance relatively small, it would be possible for a rich variety of dynamics to occur at distal locations. We conjecture that this endorses the current theories regarding synaptic amplification.
Figure 7.10: The effect of increasing $\epsilon$ on the passive 1:1 tongue structure. Here $l = 0.2$ and $r_l = 100.0 \Omega m^2$.

Figure 7.11: The effect of increasing $r_l$ (in units of $\Omega m^2$) on the 1:1 tongue structure. Here $\epsilon = 10$ and $l = 0.2$. 

122
7.6 Phase-locking between two integrate-and-fire neurons with dendritic structure

7.6.1 Introduction

As we discussed in section (7.2), phase-locking can be thought of as a subset of mode-locking [see Figure (7.3)]. Mathematically speaking, this requires us to impose greater restrictions upon the model in section (7.5) thus the possible behaviour is much more predictable making the analysis somewhat simpler. Due to this many more results have been obtained for phase-locking than for mode-locking. Central to this work is what effect the various neurobiological delays have on phase-locking behaviour [Ernst et al. (1995)]. This is not surprising since it is well known that delays can radically alter the dynamical behaviour of a system [see for example our work on pattern formation with passive dendrites - Chapter 5]. Axonal delays [Crook et al. (1997), Luzyanina (1995)] and synaptic delays [Van Vreeswijk et al. (1994)] have been considered in great depth, however dendritic delays have only recently been probed [Crook et al. (1998), Coombes & Lord (1997), Bressloff & Coombes (1997b)].

In this section then, we consider phase-locking in the entrainment regime of two neurons. This represents a major constraint and therefore a simplification. From a mathematical perspective this means both oscillators fire with the same frequency but the phase-difference between the two trains of spikes may be phase-locked for certain parameter values [see Figure (7.2)]. At this juncture, we must make the point that phase-locked behaviour for two neurons may be examined in a \( q \) mode-locked environment, but the analysis is very unwieldy. Considerable simplification is however possible in the weak-coupling regime. For more details see Coombes & Bressloff (1999a).

7.6.2 The model

We consider two IF neural oscillators \( (i = 1, 2) \) with dendritic structure. Their respective axons impinge at a point \( \xi_0 \) on the others dendritic tree. The equations which describe this particular system are essentially the same as the ones describing one externally driven neuron, just considered [equations (7.44)-(7.46)], but with a slight modification to the notation of the variables as we include a subscript to identify each neuron. The equations of motion are thus, [Bressloff (1999)],
\[
\frac{dU_i(t)}{dt} = -\frac{U_i(t)}{\tau_s} + I_{\text{ext}} + \eta[V_i(0,t) - U_i(t)] \tag{7.60}
\]

\[
\frac{\partial V_i(\xi,t)}{\partial t} = -\frac{V_i(\xi,t)}{\tau_d} + D \frac{\partial^2 V_i(\xi,t)}{\partial \xi^2} + \frac{I_s(\xi,t)}{c} + \varepsilon \delta(\xi - \xi_0) \sum_{m \in \mathbb{Z}} \delta(t - T_j^m) \tag{7.61}
\]

\[
I \frac{\partial I_i(\xi,t)}{\partial t} = -r_l I_i(\xi,t) + V_i(\xi,t) \tag{7.62}
\]

Equation (7.60) is also supplemented with the reset condition as expressed by equation (7.2). We include an external bias, \( I_{\text{ext}} \) in equation (7.60). This ensures that in the absence of any coupling (\( \varepsilon = 0 \)), the neurons fire at a constant rate \( T_0 = \tau_s \ln[\tau_s I_{\text{ext}}/(\tau_s I_{\text{ext}} - 1)] \). We model the train of spikes as before, by a series of Dirac-delta functions with a slight adjustment to the notation of firing times. Here \( T_j^m \) denote the \( m \)th firing time of the \( j \)th neuron. We ask the reader to note that the rest of the parameters have been defined before [see for example subsection (7.5.5)]. A pictorial view of the model can be seen below [Figure (7.12)].

![Figure 7.12: Phase-locking model. A pair of identical IF neural oscillators coupled together via axo-dendritic synapses. The spike trains of each neuron is fed into a point \( \xi_0 \) on the others dendritic cable.](image)

Using the Green's function approach, utilised in the last section and indeed in previous chapters, we find the system of equations (7.60)-(7.62) may be reduced to a single one,
Phase-locked solutions of equation (7.63) may be found by assuming the firing times take the form $T^m_j = (m - \phi_j)T \forall m \in \mathbb{Z}$ and $j = 1, 2$ and where $T$ is the self-consistent collective period. The phase is always in the range $0 \leq \phi_j < 1$.

We firstly set $\tau_s = \tau_d = D = 1$ and so we obtain by integrating equation (7.63) between two successive firing events the following pair of equations for $T$ and $\phi$ where $\phi = \phi_2 - \phi_1$.

\[ \frac{1}{1 - e^{-T}} = I_{ext} + \epsilon H_T(\pm \phi) \]  
\[ (7.64) \]

where,

\[ H_T(\phi) = \frac{e^{-T}}{(1 - e^{-T})} \int_0^T e^t \sum_{m \in \mathbb{Z}} G(\xi_0, [m - \phi]T + t) dt \]  
\[ (7.65) \]

This is principally the same as $H(t)$ defined by equation (7.31). However, the period $T$ is not ours to define any more, but must be calculated self-consistently.

We take advantage of the periodic properties of this function to represent it as a Fourier series as we have done previously,

\[ H_T(\phi) = \frac{1}{T} \sum_{m \in \mathbb{Z}} \frac{\tilde{G}(\xi_0, \omega_m)e^{i\omega_m\phi T}}{1 + i\omega_m} \quad \text{where} \quad \omega_m = \frac{2\pi m}{T} \]  
\[ (7.66) \]

and where more specifically,

\[ H_T(\phi) = \frac{1}{T} \sum_{m \in \mathbb{Z}} [H_T^r(\omega_m) \cos(\omega_m\phi T) - H_T^i(\omega_m) \sin(\omega_m\phi T)] \]  
\[ (7.67) \]

as $H_T(\phi)$ is a real function. The functions $H_T^r(\omega)$ and $H_T^i(\omega)$ are defined as follows,

\[ H_T^r(\omega) = \frac{e^{-a(\omega)\xi_0}[(a(\omega) - \omega b(\omega)) \cos(b(\omega)\xi_0) - (b(\omega) + \omega a(\omega)) \sin(b(\omega)\xi_0)]}{(1 + \omega^2)(a(\omega)^2 + b(\omega)^2)} \]  
\[ (7.68) \]

\[ H_T^i(\omega) = -\frac{e^{-a(\omega)\xi_0}[(a(\omega) - \omega b(\omega)) \sin(b(\omega)\xi_0) + (b(\omega) + \omega a(\omega)) \cos(b(\omega)\xi_0)]}{(1 + \omega^2)(a(\omega)^2 + b(\omega)^2)} \]  
\[ (7.69) \]
In our analysis, we naturally used a truncated Fourier series using the same level of truncation as the mode-locking case.

### 7.6.3 Phase-locked solutions

We may now use the pair of equations summarised in equation (7.64) in order to discover the phase-locked solutions. We reiterate that these equations determine both the relative phase $\phi$ and the collective period $T$.

In order to commence our analysis, we shall initially assume that the neurons are weakly coupled. As Bressloff et al. (1997) show, in the weak-coupling limit the phase-locked solutions of the IF model [equation (7.63)] converge to corresponding solutions of a phase-coupled model obtained from the former by an averaging procedure.

To begin then, we shall assume that in the absence of coupling ($\epsilon = 0$), each oscillator evolves according to,

$$\frac{dU_i(t)}{dt} = f(U_i), \text{ in our case } f(U) = -U + I_{ext} \quad (7.70)$$

for $i = 1, 2$. Then following the same lines of analysis as Van Vreeswijk et al. (1994) and Bressloff et al. (1997), we introduce a phase variable $\psi_i(t)$ and a nonlinear transform such that,

$$(\text{mod } 1) \psi_i(t) + \frac{t}{T_0} \equiv \Psi(U_i(t)) = \frac{1}{T_0} \int_0^{U_i(t)} \frac{dU'}{f(U')} \quad (7.71)$$

Under such a transformation equation (7.63) becomes,

$$\frac{d\psi_i(t)}{dt} = \epsilon F(\psi_i + t/T_0) \sum_{m \in \mathbb{Z}} G(\xi_0, t - T_j^n) \quad (7.72)$$

where,

$$F(z) = \frac{1}{T_0 f(\Psi^{-1}(z))} \quad \text{for } 0 \leq z < 1, \text{ for our case } F(z) = \frac{e^{zT_0}}{I_{ext}T_0} \quad (7.73)$$

and where $F(z + j) = F(z) \forall j \in \mathbb{Z}$. The function $F$ can be interpreted as the instantaneous phase-coupling response function of the system. When $\epsilon = 0$ then the phase variable $\psi_i(t)$ is constant in time and both the oscillators fire with period $T_0$. 126
Now, by increasing the value of \( \epsilon \) slightly such that the oscillators are weakly-coupled, to a first approximation, each oscillator still fires with period \( T_0 \), however the phases start to drift according to equation (7.72). The firing times may therefore be approximated by \( T_j^m = (j - \psi_i(t))T_0 \). With this assumption the right-hand side of equation (7.72) becomes a \( T_0 \) periodic function in \( t \). We are thus able to invoke the averaging theorem [Guckenheimer & Holmes (1983), Hoppensteadt & Izhikevich (1997)] as the conditions for this theorem are satisfied. Hence we obtain the following by averaging over a single period [Coombes & Lord (1997)],

\[
\frac{d\psi_i(t)}{dt} = K(\psi_j - \psi_i) \tag{7.74}
\]

with,

\[
K(\psi) = \frac{1}{T_0} \int_0^\infty F(t/T_0 - \psi)G(\xi_0,t)dt, \text{ in our case } K(\phi) = \frac{e^{T_0}H_{T_0}(\phi)}{I_{\text{ext}}T_0^2} \tag{7.75}
\]

The phase-interaction function, \( K(\phi) \) is thus proportional to the interaction function of the IF model, \( H_T(\phi) \) with \( T \) being replaced by \( T_0 \) [equation (7.75)]. Hence phase-locked solutions of the IF model converge to those of the phase-coupled model in the limit \( \epsilon \to 0 \). Thus the allowed solutions for \( \phi \) are given by the zeroes of \( L_{T_0}(\phi) \) where,

\[
L_T(\phi) = H_T(+\phi) - H_T(-\phi) \tag{7.76}
\]

In order to explore the different solutions to this equation (7.76), we apply aspects of group theory to predict solutions which are likely to exist. In particular we exploit the underlying symmetry of the system. By symmetrical, we mean the oscillators are identical and the coupling between them is the same. This approach is particularly helpful when considering a group of oscillators as opposed to just a pair [Bressloff & Coombes (1999a)]. However with just two IF oscillators, a group theoretic approach guarantees the existence of the synchronous solution \( \phi = 0 \) and the anti-synchronous \( \phi = 1/2 \). Moreover, we observe that if \( \phi \) is a solution then so must \( 1 - \phi \). For a far more in depth review of the group theoretic approach see Gaeta (1994) and Golubitsky et al. (1988).

The weak-coupling argument also permits us to calculate the stability of these solutions. With just two oscillators the required stability condition for a specified solution \( \bar{\phi} \) is given by a simple equation,
where we may state this expression exactly as shown below,

\[ \varepsilon \left. \frac{\partial L_{\phi}}{\partial \phi} \right|_{\phi=0} > 0 \]  \hspace{1cm} (7.77)

At this juncture, we must emphasize that this argument is only valid for a weak-coupling regime and not for arbitrary \( \varepsilon \) as a number of authors have implied [Van Vreeswijk et al. (1994)]. With this condition we are able to plot how a particular solution’s stability depends on the various parameters in the system. We choose \( \xi_0 \) and \( r_1 \), as it has been seen that varying each of these parameters can influence greatly the nature and stability of solutions. A natural choice of solution to investigate is \( \phi = 0 \), the synchronous state. The resulting plot is seen in Figure (7.13). The simplicity of the stability condition also allows us to easily see the effect of a weakly-coupled inhibitory system. The stability is simply reversed.

![Figure 7.13: Stability regions for the synchronous state in the weak coupling regime plotted in \((\xi_0, r_1)\) parameter space \((r_1\) in units of \(10^{-1} \Omega m^2\) and \(\xi_0\) in units of \(\sigma\)). Black(white) denotes stability (instability). Here \(T_0 = 4.18879\)](image)

We may draw two main conclusions from this plot. Firstly, as we have seen before in the context of the Arnold tongues, in the quasi-active regime (specifically \(0.025 < r_1 <\) \(\ldots\))
0.275) the synchronous region is greatly enhanced in parameter space. Secondly, for the inhibitory coupling, the synchronous solution is very much dominant in parameter space. This is in keeping with the results found in Van Vreeswijk et al. (1994) paper, 'When inhibition not excitation synchronizes neural firing'.

We may now compute all the solution branches to equation (7.76) with the aid of XPP-Aut. We still remain in the weakly coupled regime however we produce phase plots for both quasi-active and passive cases. These may be viewed below [see Figure (7.14) for the quasi-active case and Figure (7.15) for the passive one]. The value of $T_0$ was taken to be 2.39790. The stability of the various solutions was calculated using equation (7.78).

![Bifurcation diagram](image)

**Figure 7.14:** Bifurcation diagram for a weakly-coupled quasi-active system ($r_1 = 0.1 \Omega m^2$). Stable branches are given by solid lines whereas the unstable ones are given by the dashed ones.

From these Figures (7.14) and (7.15), we may deduce the following. For small values of $\xi_0$ only the anti-synchronous solution is stable. Increasing $\xi_0$ leads to the creation of two new unstable branches which eventually coexist with the synchronous solution. This pattern is repeated for larger values of $\xi_0$ however with the inter-change of solution stabilities. Furthermore, in the passive regime this interchanging occurs more often. Thus we may conclude that quasi-active membranes by enhancing the (anti-)synchronous solution reduce the need for the axon to make such a precise contact as is the case for passive membranes.

We may now turn our attention towards a more strongly-coupled system. In the Figure
Figure 7.15: Bifurcation diagram for a weakly-coupled passive system \((r_1 = 100 \Omega m^2)\). Stable branches are given by solid lines whereas the unstable ones are given by the dashed ones.

below [Figure (7.16)] it can be seen that the solutions from the weakly-coupled quasi-active system persist and we conjecture that the stability of these solutions remains the same. We must qualify this remark by stating that this is only true for neurons with purely excitatory connections. As Bressloff & Coombes (2000) show with strong purely inhibitory connections behaviour which is not predicted from the weak-coupling investigation is shown to occur, notably oscillator death.
Figure 7.16: Bifurcation diagram for a strongly coupled ($\epsilon = 1.0$) quasi-active system ($\tau_I = 0.1$). Stable branches are given by solid lines whereas the unstable ones are given by the dashed ones.
Chapter 8

Conclusions

It seemed that the next minute they would discover a solution. Yet it was clear to both of them that the end was still far far off and that the hardest and most complicated part was only just beginning.

from 'The Lady with the Dog' by A. Chekhov

To conclude this thesis, we summarize our results and propose possible extensions to this disquisition.

We began in Chapter 2 with a short discourse on the anatomy and physiology of a neuron. In addition to this we discussed how information is encoded and decoded within a neurological environment. The dendrites play the pre-eminent role in information processing. Interestingly, the physical features such as synaptic placement, morphology and membrane properties which one may use to classify and distinguish different dendritic trees actually aid the neuron in this processing of information. In section (2.3) we emphasized this aspect of the dendrites with particular reference to passive membrane properties, active membrane properties and synaptic placement.

In Chapter 3 we presented a mathematical representation of a simple uniform un-branched passive dendrite, commonly described as the cable equation. We went on to solve this equation for steady-state and time-dependent domains utilising the Green’s function method throughout. We then proffered how one might seek to add further biological detail by both analytical and numerical means. Continuing in this vein, we completed the chapter by introducing Koch’s quasi-active (active-linearized) model [Koch (1984) (1999)]. Again we solved the resultant model for both cases of time domains.
We addressed spatial neural patterns in Chapter 4. We elucidated upon the occurrences of these patterns within a neurological environment with particular allusion to ocular dominance stripes and drug induced hallucinations. We then embarked on a short discourse on the general mathematical theory which aims to describe pattern formation, formulated principally by Turing and contributed to by Gierer and Meinhardt. The major tenets of this theory and some useful mathematical modelling concepts were then incorporated into a simple pedagogical model: the activation-inhibition model. We analysed the model and authenticated our theoretical predictions through numerical simulation.

We augmented the activation-inhibition model in Chapter 5 through the inclusion of a one-dimensional passive cable. We used a combination of linear stability analysis, numerical simulations and bifurcation theory to gain the following original results,

- **Diffusion along the cable leads to an effective distributed system of delays that can induce spatial patterns of network activity. In the presence of long-range excitation and short-range inhibition dynamic (time-periodic) patterns may be generated. For short-range excitation and long-range inhibition static patterns can be induced.**

- **Associated with any spatial pattern of network output activity is a corresponding spatial pattern of activity along the dendrite of each neuron. In the case of correlated weight distributions, the latter can take the form of a spatial oscillatory pattern.**

As we discussed in Chapter 5, this second feature has implications for learning and adaptation which has many possible avenues of research.

We examined the dynamical influence of dendrites with quasi-active membranes on neural pattern formation in Chapter 6. Once again we used linear stability analysis and numerical simulations to analyse the model and thus we obtained the following result,

- **Dynamic (time-periodic) spatial patterns of network activity may be induced in the presence of short-range excitation and long-range inhibition for values of the inductive resistance $r_1$ smaller than $r_1c$ where $r_1c \approx 0.45$ $\Omega$m$^2$. For values greater than this critical value, the system adopts a passive nature and thus we obtain a static spatial pattern as in Chapter 5.**
In the last of the main chapters - Chapter 7, we turned our attention to assessing the influence of dendritic structure on the dynamics of coupled neuronal oscillators. More specifically, we were interested in rhythms fomented by locking between the oscillators. The scientific definitions of the different genres of locking are notoriously ambivalent and inconsistent. Thus we began by clearly delineating the different types of locking and moreover explaining their relationship to one another. The occurrence of these phenomena in a neurobiological environment was then considered with various examples given.

The familiar and widely-used Integrate-and-Fire (IF) model was introduced at this juncture. We showed in particular how the IF model may be considered as a reduction of the more biologically realistic Hodgkin-Huxley model. With this as our basic model we firstly analysed the behaviour of one IF neuronal oscillator with dendritic structure with a periodic train of spikes injected into the cable at a point $\xi_0$. Using analytical techniques developed by Coombes & Bressloff (1999a) we were able draw regions of mode-locked behaviour (Arnold tongues) and authenticate these through direct numerical integration. Through this procedure we gained the following results,

- The regions of $q:p$ mode-locked regions were highly dependent upon the point of contact between the input train of spikes and the dendritic cable. In addition to this low ratios of $q$ to $p$ were generally found to be the most stable.

- By modulating the strength of coupling $\epsilon$ or indeed the value of the inductive resistance $r_1$, one may alter the width of a particular tongue and in addition to this relocate the tongue to a different region in parameter space. We particularly note that in the quasi-active regime ($r_1 \approx 0.1 \text{m}^2$) the tongue is enhanced. We also note that for high values of $\epsilon$, the region of mode-locked solutions is generally located at higher values of $\xi_0$. This is particularly interesting with regards to synaptic amplification.

Our second model in this chapter concerned phase-locking between two IF neurons with dendritic structure in an entrainment regime. Their respective spike trains were fed into a point $\xi_0$ on the others dendritic cable. Through a weak-coupling regime argument we elicited the following results,

- The synchronous solution is enhanced in the quasi-active regime with excitatory coupling, although it is not the dominant solution in the $(r_1, \xi_0)$ parameter space. This is in contrast to the weakly inhibitory coupled system where the synchronous solution is the dominant solution.
• *Traversing along the cable (increasing $\xi_0$), alternating bands of anti-synchronous and synchronous solutions are predominantly found with asynchronous solutions existing but only for small parameter regimes. This "checkerboard" pattern is present in both passive and quasi-active systems. However the interchanging of solutions is much more prevalent in the passive case.*

Possible extensions of the work in this thesis are now considered. We believe that a number of avenues of research exist which are primarily motivated by our general quest of increasing the level of biological realism. However we restrict ourselves to the following on the basis of personal interest.

Firstly and perhaps most importantly we believe that the major area still left relatively unexplored is the morphology of the dendrites. That is to say why do neurons possess such strikingly different structures? As Koch (1999) discusses there are, at present two theories regarding this question. Firstly, one hypothesis is that the dendrites are a means of maximizing the probability that diffuse axonal trees contact as many neurons as possible (within some fixed volume). This then provokes the question of what sort of space-filling, fractal geometry will maximize the dendritic surface area for contacts with the largest number of axons? An alternative school of thought [Koch et al. (1982), Mel (1993)] proposes that the geometry of the dendritic tree coupled with the unique synaptic architecture implements specific logical computations.

Secondly, the beguiling nature of dendritic spines demands further investigation purely to decide their role in information processing and their dynamical influence in mathematical models. A number of researchers are and have been looking at this problem. Sample work includes Baer & Rinzel (1991), Kember & Evans (1995) and Coombes & Bressloff (1999b).

It would be foolish to confine ourselves to purely analytically tractable models as computational models do offer a whole range of exciting possibilities, for example the modelling of back-propagating action potentials is at present only researchable via this means [Mainen et al. (1995), Rapp et al. (1996), Egelman & Montague (1998)]. The implications of back-propagating action potentials [see subsection (2.3.3)] demands a deeper numerical examination.

With regards to our own work. The results on pattern formation with a correlated weight distribution should be incorporated into any analysis of learning and memory at the network level. Example works in which this could possibly be included are: Tank et al. (1995), Rosskhin & Tsitolovsky (1997), Kairiss & Miranker (1998), Edwards et al. (1999). In addition to this we acknowledge that further work on pattern formation
in higher dimensional networks should also be encouraged.

Lastly, the work on mode-locking could be further enhanced by studying a neuron forced by a quasi-periodic train of spikes which utilises the ideas developed by Glendinning & Wiersig (1999). In addition to this the presence of noise would also be worth investigating as Roper (1999) has shown.

From the results summarized above, we conclude that the excision of the dendritic tree in most mathematical models of neurons yields an over-simplified model and furthermore one that restricts itself from a rich variety of dynamics. It is hoped that more modellers will endeavour to include some representation of the tree in their future work.
Chapter 9

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