Chapter 3

The Barnacle: Complexity in the Organism

Vignette no. 2: Barnacle. Crude introduction to the anatomy of Barnacle's nervous system. Introduction to neuroscience basics: neurons, synapses, axons, neurotransmitters. Biophysical motivation for neural computation. Boltzmann equation. Question: How to go from neural circuitry to elementary visual behavior. graded response and spiking neurons.

In the previous lecture we studied A. coli as a simple organism that was behaving in a complex envirnment, and sought to understand this behavior at a phenomenological level. At the same time we reviewed certain concepts from calculus and ended with the gradient ascent abstraction/algorithm. In this lecture we flip positions, and consider a simple environment and so that we can put the emphasis on the complexity of the organism. Our goal now is to introduce basic ideas from neuroscience. We introduce several basic aspects of neurons, the cells that comprise nervous systems; and briefly motivate their biophysics. To connect to the world we shall consider how signals can arise from light in a primitive photoreceptor unit. We conclude in the next chapter, by asking which behaviour can take advantage of this signal and for what purpose. So, this time we start with the cell and look 'inwards.' (Previously we 'looked' from the organism 'out' to the environment.) It's fascinating to think about the different levels of abstraction implied by these two perspectives. (We close with this thought.)

There are two fundamental continuations from the previous chapter. First, while *A. coli* were simple organisms, the need for some internal complexity became clear from the complexity of the behaviour that they exhibited: they needed to detect food molecules and move toward them which clearly involves a number of involved steps. Understanding this complexity within E. coli remains a fascinating area for research. While there are some analogies[1] from now on we shall focus on another – and for us, more important – class of cells with complex internal structure: NEURONS. These are one of the basic cell types from which nervous systems are built. We start on the basics

[1]The bacterium as a model neuron, D. E. Koshland, TINS, 1983, 133 - 137

Figure 3.1: Drawing of the barnacle *Semibalanus balanoides* from http://animaldiversity.ummz.umich.edu/site/resources/Grzimek_inverts/Thecostraca/Sem

of their internal structure, so that we can begin to understand the processes that drive them. Central to this is the perspective of physics and biophysics, and another analogy opens up. Previously we saw that A. coli explored their environment randomly and were "drawn" toward food sources. In this lecture IONS or charged collections of atoms will be center stage. As charges move around they can be measured as currents, and it is these currents and other electrical properties that support the abstraction toward which we are heading. Networks of such cells will provide the foundation for the information processing abstraction that will occupy us for the remainder of the class.

As will become clear, in this chapter we concentrate on the second "F": avoiding becoming food (avoiding predators and other dangers).

3.1 Barnacle Behaviour

Our second example of a biological phenomenon is the barnacle, a simple sea animal (e.g., *Cirripedia*) that lives in a castle-shaped shell. Their main behavour for eating is as follows: the barnacle plants its castle firmly in one spot and then extends a net of cirri out of the turret (opercular plates) to "fish for" whatever might be floating by. When an object is "caught" the cirri roll up, retract, and the opening is closed off. Several muscle groups work together to orchestrate this behaviour.

The size of the opening in the turret provides an example of Constraint C1, in that the barnacle will attempt to eat anything that will enter the turret. This is a type of *syntactic constraint*, in that a certain feature of the world (of the barnacle)—that edible items come in small sizes—has been realized as a functional constraint: those that fit through the turret. Of course there are more items that meet the syntactic size constraint than are edible, but this is of little consequence to the barnacle: if something fits in your mouth, try to eat it. Clearly the barnacle wins often enough to make the strategy evolutionarily successful.

The barnacle is visually unselective about mating (reproduction constraint) but it does use light to sense another basic aspect of its environment. Feeding involves physical contact; but waiting for physical contact with a preditor would be extremely dangerous. The visual sense permits preditor detection at a distance. To understand how this might work for the barnacle, and to conclude our discussion, we will try to infer the behaviour by observing its nervous system in operation.

Although a simple creature, the nervous system of the barnacle is already complex; it consists of several primitive "eyes", or primitive light sensing organs called OCELLI which provide the input to a neural network that ultimately controls the muscles; see Fig. 3.2.

An analogy: ocelli are a crude analog to the touch receptors on the surface of your body. It's an interesting thought exercise for you to ponder what happens to this 'pressure' signal: what is it used for; how is it processed? How much of your brain is necessary to process tactile information?

Before describing the nervous system of the barnacle in more detail, we introduce some of the basic components. We start with a very brief introduction to neurons and neuroscience, and include some snippets of statistical mechanics, which provides the basic framework for neuron biophysics. We then proceed to discussing the components of neurons and circuits of neurons.

3.2 Neuron: Basics

Neurons are specialized cells that will develop into a key building block for our information processing models.

There are three structural elements to neurons of fundamental importance; see Fig. 3.3. The CELL BODY, which we might at first glance think of as the information integration portion that connects the DENDRITES, or input units to the AXON, or output unit. This is a gross simplification, of course, because the organization of the dendrites into a complex tree of relationships; the position at which they attach to the cell body, and the length and branching structure of the axon, etc. etc., clearly matter. But we shall have to build our understanding gradually before we approach any of this complexity.

Approach: think of the neuron as a map:

$$\boxed{\text{neuron} : \text{input} \to \text{output}} \tag{3.1}$$

This point of view riases the questions: from what domain is the input drawn? The output? How does the transformation work? Is it like a computer? To answer these questions we need to look inside of the neuron.

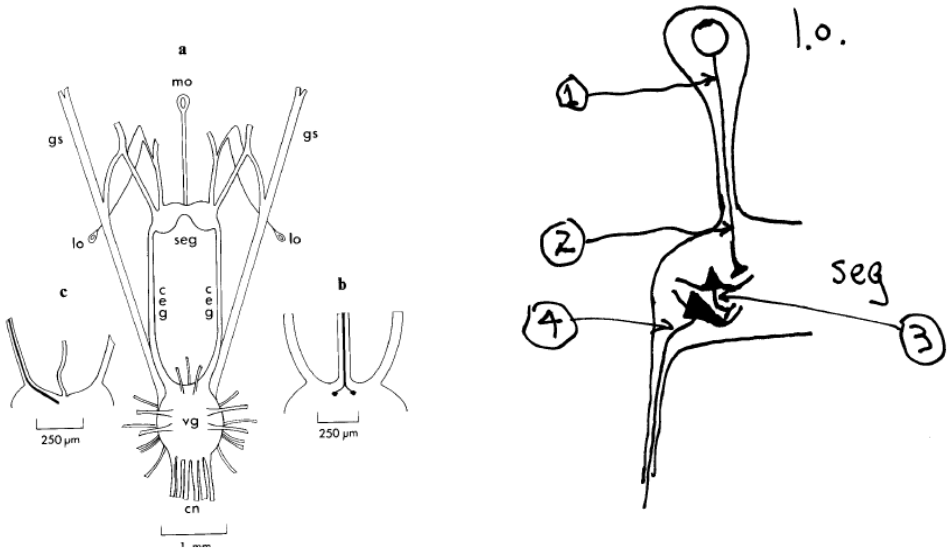
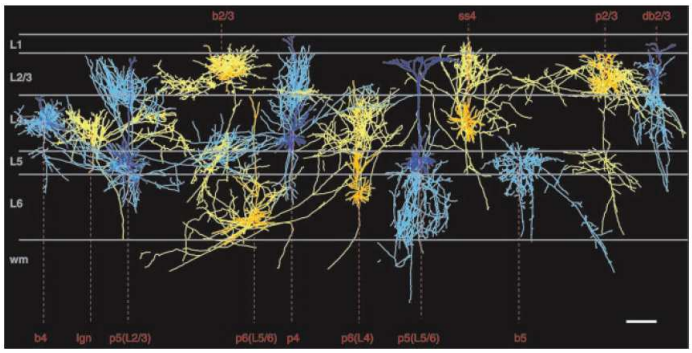


Figure 3.2: (LEFT) Drawing of the barnacle nervous system that participate in the visually-mediated withdrawal reflex. lo: lateral ocellus. mo: medial ocellus. seg:supra-oesophageal ganglion. vg: ventral ganglion. ceg: supra-oesophageal connectives. cn: cirral nerves. from Laughlin Fig1. (RIGHT) Drawing of the important stages that we shall consider in the barnacle nervous system. An ocellus, or photoreceptor cell (1) begins the transformation of light into electrical signals; these are modified by different neurons, or cells comprising the clusters known as ganglia. A few such neurons are labeled in sequence so that we can develop their properties in the course of this lecture. We think of this as a simple information processing network. Our challenge is to understand it "from 30,000 feet."



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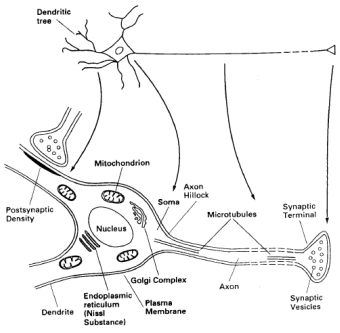

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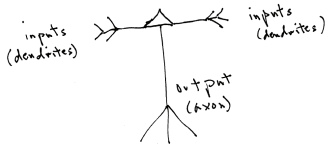

(c)

Figure 3.3: Neurons. (a) Some different anatomical types of neurons in the visual cortex. Eventually we shall have to worry about this complexity but for now we are seeking ways to abstract it to 'basics.' (b) Basic structural components of a neuron in correspondence to a sketch of a neuron. The overall cell anatomy is ressponsible for various metabolic and integrative functions. (c) Base-level simplification: a neuron 'transforms' the input (through the dendrites) into the output (carried by the axon).

3.2.1 Ions and Biophysics

It should come as no surprise that the cells of the barnacle are surrounded by an environment not unlike seawater. The remarkable point is that our neurons are as well! This implies there are many different ions in abundance, including sodium, potassium, calcium, chloride, etc., both within and surrounding the neurons. These ions follow a random walk driven by their thermal energy; however, because they are charged, they also create a physically-charged environment. Just as "food" "attracted" *A. coli*, electrical fields are now going to "push" the different ions around.

Neurons are cells encapsulated by a membrane and filled with ions. The neural membrane functions in a very special manner to control the flow of ions. By restricting the flow in certain ways, an ionic machine is created that works because of the concentration difference of different ions across the membrane; the concentractions within a neuron against those outside of it. This interplay provides a very powerful dynamic that provides the biophysical basis for information processing.

Thermal and electrostatic considerations interact; see Fig. 3.4. If it should happen that there was a local abundance of positively-charged ions, as an example, their mutual repulsion would drive them apart. At the same time, negative charges would be attractive. Thus one can think of a dynamic introduced by the forces between ions. A random walk respecting these forces would lead to a dynamic fluctuation around a net charge of 0, a charge distribution in balanced equilibrium. This playoff between diffusion and electrical forces brings us to physics.

3.2.2 Gases, Boltzmann and Statistical Mechanics

In this section we switch to considering some problems in physics that might seem a bit removed from neurobiology. Our goal is to give you the flavour of biophysics of neurons, so that you can appreciate a level of conceptualization one level "down" from where we will be concentrating in this class. This look down is into a world of atoms, ions, charges, forces and potentials. You may read this section quickly, just to get a feeling for the vocabulary of concepts that will be abstracted at the information processing level.

So, for a little while, let's do some physics. (If you know this material, you can skip it.) The discussion goes in three stages (Fig. 3.5), starting with a movable piston, going to a piston balanced by forces on both sides, and finally to a semi-permeable membrane. (Semi-[permeable means that different ions "pass through" it selectively.) Think of this piston or the semi-permeable membrane as a small section of the neuron's membrane.

We start with (Fig. 3.5(a). Molecules of an ideal gas in a volume exert a pressure on the container holding them. This can be seen by filling a box, one side of which is a frictionless piston, with the gas, and noting that the piston is forced out when

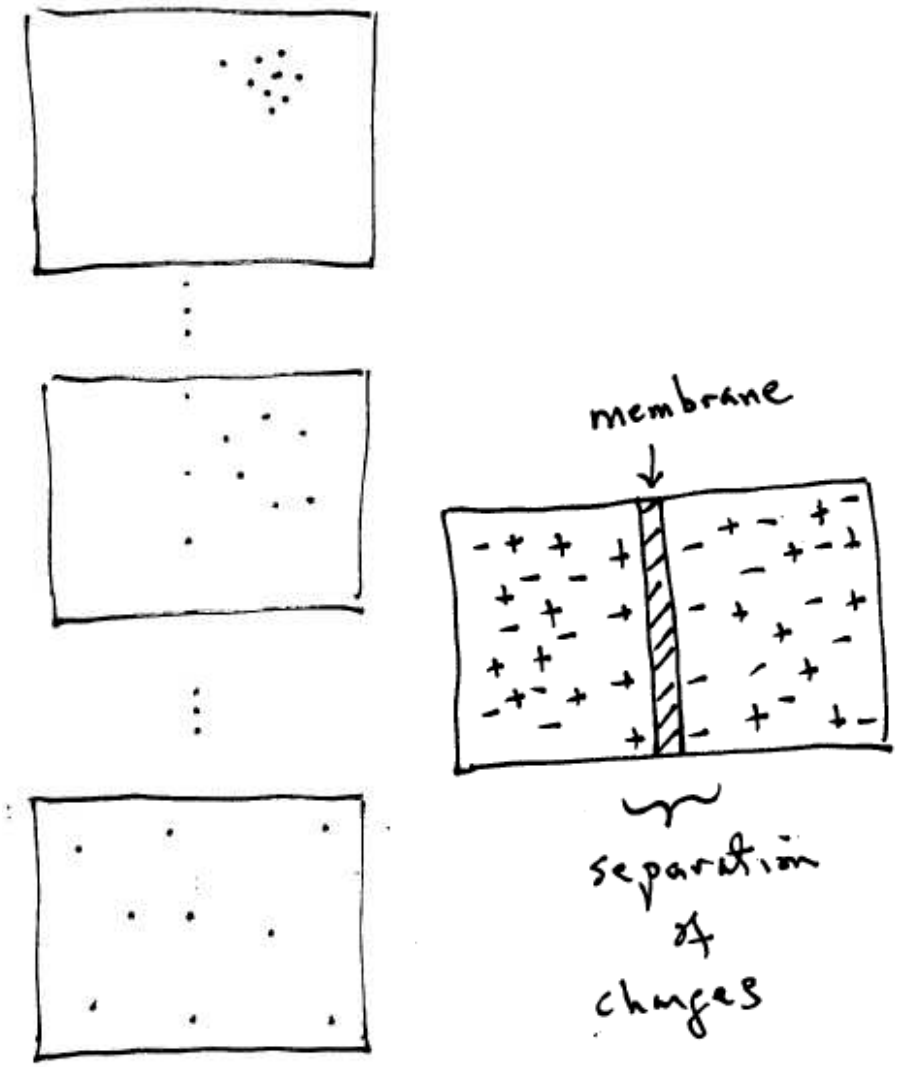

Figure 3.4: Two competing forces in the distribution of ions. (left) Diffusion: when a particle is placed in solution, it wanders around randomly due to thermal and other forces. When many such particles are placed in the same location, they each follow their own random path, diffusing until their concentration is about uniform. If the particles are identically-charged ions, electrostatic forces will repel them from one another. (right) If there is a membrane separating a mixture of ions, then charges will tend to organize on either side of it, introducing a potential difference, or voltage, across the membrane. Notice in particular how the charged ions remain mixed except near the membrane.

molecules collide with it. Pressure then is force/area:

$$P = F/A; \tag{3.2}$$

this is now much force F would need to be applied from the outside to keep the piston from moving.

This argument can be turned around – we could force the piston inward by an amount $-dx$, thereby doing an amount of *work*

$$F(-dx) = dW = -PAdx = -PdV \tag{3.3}$$

(The volume change, dV is the area times the length change; the minus sign is because the volume is reduced – compressed.)

Mechanics tells us that each collision between a molecule of gas and the piston transfers momentum; force is momentum per unit of time. If the piston were free, then each collision would give it a little more speed and the rate of acceleration is proportional to the force. Now, if the piston is a perfect "reflector" of the molecules, or every collision is elastic, then, on average, every molecule that hits it leaves with the same energy. If $\mathbf{v}$ is the velocity of an atom, then mv_x is its momentum in the x-direciton, and $2mv_x$ is the total momentum delivered to the piston by each particle (the 2 comes from the fact that it is reflected).

How many molecules will hit the piston in the time dt? Only those that are within distance $v_x dt$ of the piston (others will be too far away to collide in time dt). If there are $n = N/V$ molecules in a unit volume, and the volume is $Av_x dt$, then the force is

$$F = nv_x A \cdot 2mv_x \tag{3.4}$$

from molecules traveling only in the x-direction. On average, and considering all directions, this gives us:

$$P = \frac{2}{3} n < \frac{mv^2}{2} > \tag{3.5}$$

where the brackets $< \cdot >$ indicate an average over all velocities. The *kinetic energy* of the center-of-mass motion of the molecule is $< mv^2/2 >$.

Something to think about: One of the beautiful things about statistical mechanics is that it describes LOCAL quantities (velocity of an atom); one of the beautiful things about thermodynamics is that it describes GLOBAL properties (pressure). This transition between local and global is done in this example by an averaging operation. Now, looking ahead quite a bit: what is the relationship between the local pieces of an object, say short pieces of it's 'edges' and global object shape? Is the transition between them still one of averaging? Interesting (and subtle) questions to think about, indeed.

To understand the role of temperature in statistical mechanics, we move to a slightly more complex construction (Fig. 3.5(b). Here two monatomic gases are placed

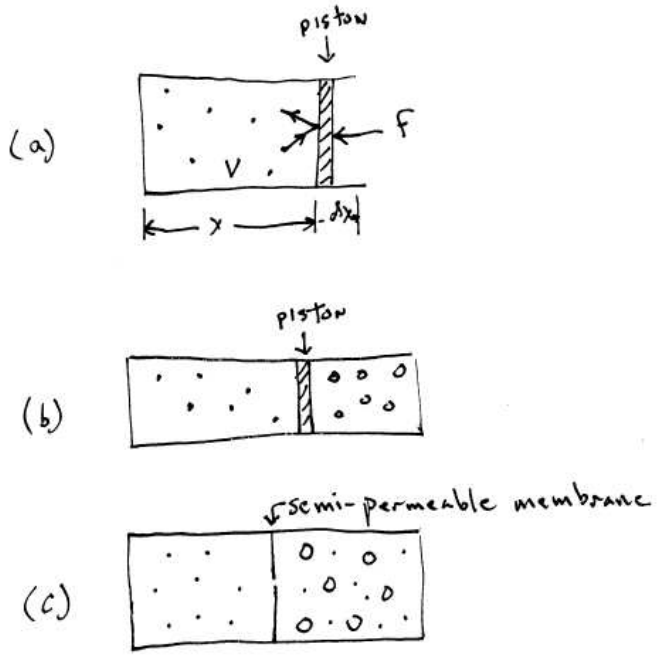

Figure 3.5: Gases, distributions of molecules, and forces. (a) Molecules of gas in a box exert pressure on a frictionless piston (hatched box) of area A, causing it to move a distance dx. A force F exactly balances the outward movement. (b) Two gases on either side of a frictionless piston. (c) Two gases mix through a semi-permeable membrane, depicted as a barrier through which "small" atoms can pass but not large ones. See text for development. (Figures after Feynman, 39-1, 2, 4).

on either side of the moveable piston, and arranged so that the pressures are equal. This means that the average kinetic energies on either side have to be equal, or

$$n_1 < m_1 v_1^2/2 >= n_2 < m_2 v_2^2/2 > . \tag{3.6}$$

To establish this balance, one could imagine a few molecules on the left side that were moving rapidly, and many molecules on the right that were moving slowly. However, energy will be transferred between them, so that when an instantaneous "fast" collision from the left causes the piston to be moving rapidly just at the instant a "slow" collision occurs from the right, energy would be transferred — the right molecule will emerge from the collision with a higher velocity. Equilibrium is achieved when the kinetic energies on both sides are equal; this mean kinetic energy is the *temperature*. Expressed in units of mean energy per degree Kelvin, we have: kinetic energy is $\frac{1}{2}kT$ in each direction, or $\frac{3}{2}kT$ averaged over all directions. k, the proportionality constant, is $k = 1.38 \times 10^{-23}$ joule/degree Kelvin.

We now construct another type of chamber to consider an ideal gas in a gravitational field held at constant temperature; see Fig. 3.6. Like our atmosphere gravity causes a decrease in pressure with height, but unlike our atmosphere (which gets colder with height) there is a mechanism to hold it at thermal equilibrium.

This variation in pressure is important: at a particular height the gas has to hold the weight of all the gas above it. In our diagram, the force from the gas below must exceed the force from the gas above the section $(h + dh)$ by

$$P_{h+dh} - P_h = dP = mgn\ dh \tag{3.7}$$

where g is the acceleration from gravity. Since $P = nkT$, and T is constant (by the construction of the chamber), we get:

$$\frac{dn}{dh} = -\frac{mg}{kT}n \tag{3.8}$$

which describes how the density of atoms changes.

This is another example of the type of DIFFERENTIAL EQUATION we saw at the end of the previous lecture. Here we moved to differentials in the density of atoms instead of infinitesimal steps in position, so now there is a derivative of n on the left side and an n on the right.

Let's look at this equation in slightly more detail. Suppose we have a substance x that is changing according to some reaction or process. One of the simplest types of such change is given by :

$$\frac{dx}{dt} = kx \tag{3.9}$$

which says that the rate a which a quantity x changes at every instant of time is proportional to the amount of x that is present at that instant. Since x is some type of stuff, we'll assume it's not a negative number. (k is the constant of proportionality.) Rearranging, we get that

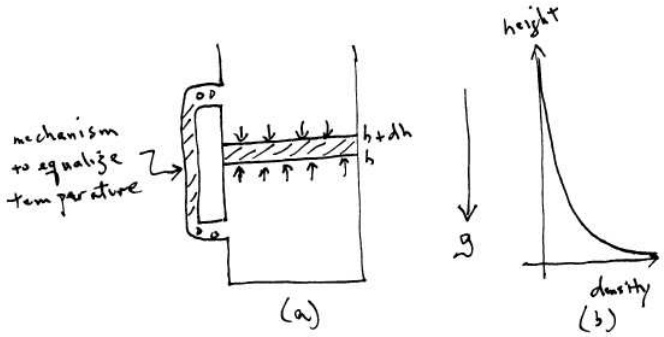

Figure 3.6: Construction for deriving Boltzmann's formula. (a) A chamber in which gas is distributed under a gravitational field while begin held at constant temperature. (b) The result is that density decreases exponentially with height. (Figure after Feynman, 40-1).

$$\frac{dx}{x} = k\ dt \tag{3.10}$$

or

$$\int \frac{dx}{x} = k \int dt \tag{3.11}$$

which implies

$$\ln x = k\ t + constant \tag{3.12}$$

The constant is evaluated from the initial conditions that $x = x_0$ when $t = 0$, the amount of x at the beginning.

This should all start to look a little familiar. We know from calculus that the function whose derivative is proportional to itself is the exponential, or $de^u = e^u du$. Thus, returning to our physics example, we have as a solution to this differential equation:

$$n = n_0 \exp\{-\frac{mg}{kT}h\} \tag{3.13}$$

where n_0, the constant of integration, is the density at $h = 0$. This says the density goes down exponentially with height; the constants describe the physics and units.

Something to think about. In the previous lecture we developed a differential equation that described the flow of A. coli along a path. (It's change in position at any moment of time followed a vector field.) What is the flow and what is the vector field implied by this one-dimensional ordinary differential equation?

Thus the density of atoms at a particular point is proportional to

$$e^{-\text{potential energy of each atom}/kT}. \tag{3.14}$$

We shall later see that this is the general principle in statistical mechanics, *Boltzmann's law*, which states that, quoting Feynman, "the probablity of finding molecules in a given spatial arrangement varies exponetially with the negative of the potential energy of at arrangement, divided by kT."

We're now ready to turn from idealized gas physics to biophysics. (We will discuss the exponential function more in Sec. 8.2.7.)

3.2.3 Channels and the Membrane Potential

We now get back to neuroscience, and this is material to which you should pay attention.

The membrane surrounding neurons is a complex molecular structure that is semi-permeable to different ions: some are allowed to pass through it readily; others with difficulty; and under certain conditions, some are not allowed to pass at all. It consists of a complex of lipids and other (alpha-helix) molecules arranged to provide channels.

We begin our more detailed analysis by noting a typical distribution of ions across the membrane; see the table below.

ion	outside conc (mM)	inside conc (mM)
Na^+	150	30
K^+	3	140
Ca^{++}	1.2	0.1μ M
Cl^-	130	8

To appreciate this ionic distribution, it helps to think of it as a simple physical system. Instead of concentrating on either side of the membrane, suppose the charges are distributed on two parallel conducting plates; a distance d apart, and of equal area A; see Fig. 3.7. Further suppose that equal and opposite charges have been placed on each of the plates and consider the work required to move a unit of charge from one plate to the other. The amount of work is proportional to the potential difference between the plates—the more charge, the more push for an appropriately-charged ion—and this push is the *electric field* E. (Notice that for neuroscience we have replaced the gravitational field from the previous section with the electric field induces by the distribution of charged particles. There is also some intuitive plausibility here, thinking back to the previous lecture. Thinking of A. coli swimming up a food potential, we now have the electric field as the gradient of the electrical potential; see Feynman, vol II.)

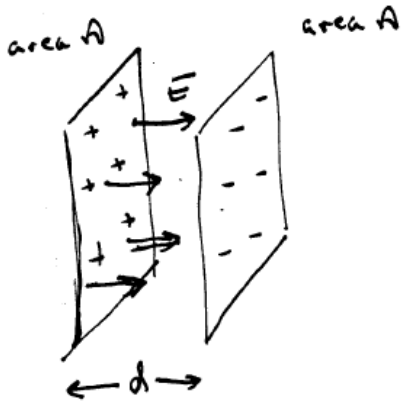

Figure 3.7: The parallel-plate condenser approximates the static distribution of charge across a membrane. Two plates are shown a distance d apart, and of equal area A.

In symbols, if we let V denote the work per unit charge in moving a small charge from one plate to another, we have:

$$V = Ed = \frac{\sigma}{\epsilon_0} d = \frac{d}{\epsilon_0 A} Q \tag{3.15}$$

where $\sigma = Q/A$ is the density of charge per unit area and ϵ_0 is a constant used to make the units into volts.

If there are equal charges (plus or minus) on each plate, then this equation tells us that the work goes up with the amount of charge (it's harder to push) and the distance (the amount it has to be moved).

We are now ready to return to the lipid bi-layer membrane. As the ions build up on either side of it there is a total charge difference; as above, this difference gives rise to a voltage or potential difference across it. Again,

$$\text{voltage} \propto \text{charge} \tag{3.16}$$

$$V \propto Q \tag{3.17}$$

$$V = c_m Q \tag{3.18}$$

where the capacitance across the membrane, c_m, is the constant of proportionality: more charge difference implies a higher voltage difference in constant proportion.

Ion transport across the membrane is accomplished by channels, or molecular complexes that function like gate-keepers, and there are many different types of them. See Fig. 3.8 for one example; we'll mention aspects several of them in this lecture.

The complex configuration of ions on either side of the cell membrane, and the potential difference arising from it, provide the absolutely fundamental link between

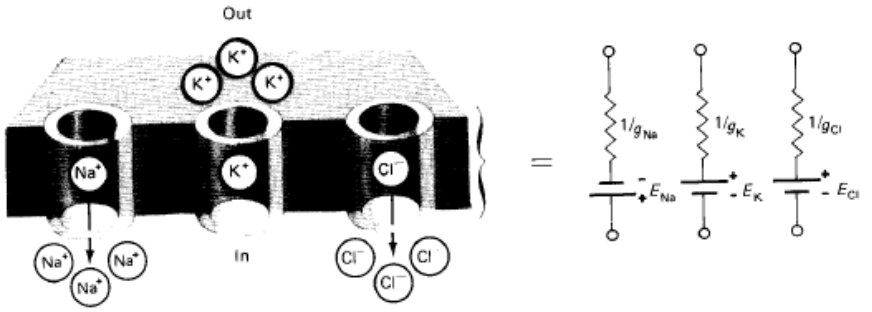

Figure 3.8: Illustration of potassium sodium and chlorine channels across the membrane, and their electrical equivalent circuits (from Kaz). Note how they resemble 'pores' through the membrane. Some channels are opened (or closed) by other molecules or a change in potential.

cellular biophysics and information processing: we can imagine the circuits developed by interacting components to a neuron, or many neurons, being designed to solve an information processing problem. For this reason we shall develop some of the "neuro-electric" properties of neurons a bit more.

We emphasize that the charge difference across the membrane, say the excess of positive ions on the outside relative to the inside, gives rise to a MEMBRANE POTENTIAL, or a voltage measured across the membrane). The constant of proportionality is called the CAPATICANCE.

Since different ions have different charges, the portion of the total potential for which they are responsible depends on their individual concentrations see Fig. 3.9. When the physical and thermodynamic forces balance the random diffusion, the inside and outside concentrations are related through a series of physical constants (e.g., temperature, because this is a measure of available thermal energy). However, the ions generally have to work against the membrane potential to get out; only those with sufficent thermal energy to cross this potential barrier will (on average) make it. Boltzmann distributions give us the exponential form for the probability that an ion will likely cross the membrane

$$[\text{outside conc of ion A}] \propto [\text{inside conc of ion A}] \exp(zFV/RT) \tag{3.19}$$

where V is the potential difference, or membrane voltage, T is temperature in absolute units, and z is the charge of the ion under consideration. (The other symbols are physical constants.) Note the inverse relationship between V and T.

An important balance condition arises when the membrane potential is in equilibrium with this energy. This NERNST EQUATION, written in terms of the potassium

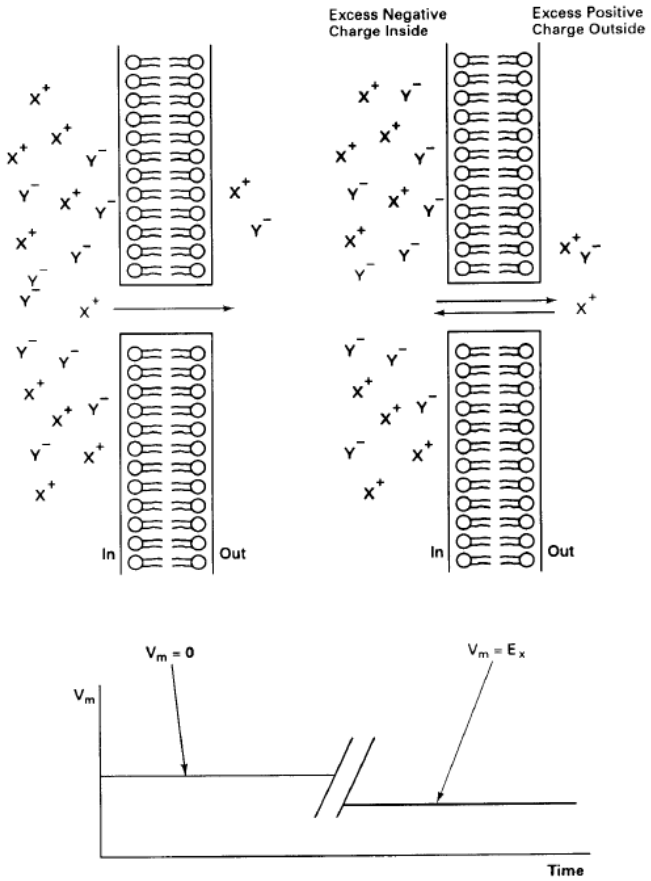

Figure 3.9: The distribution of ions on either side of a membrane with channels leads to equilibrium distributions in which charge and concentration are balanced together. The Nernst potential is the equilibrium at which those ions (of a particular species) are as likely to go in one direction as the other.

ion, is:

$$E_K = \frac{RT}{ZF} \log \frac{K_o}{K_i} \tag{3.20}$$

The Nernst, or equilibrium potential, denotes the equilibrium at which the diffusive flow of ions across a membrane exactly balances the electrostatic forces. For potassium, the Nernst potential is about -75mV; $E_{Na} \approx 50mV$, $E_{Ca} \approx 150mV$, and $E_{Cl} \approx -65mv$.

For the neurons we shall be considering, these different potentials combine to give a resting potential of about -65 mV (Goldman Equation here).

3.2.4 Potentials, Currents, Conductances

Because the proportion of charged ions gives rise directly to the voltage, but biological systems are normally in a state of flux for these ions, we seek to understand what happents when the ions change. To start, consider two different concentrations:

$$c_m V_1 = Q_1 \tag{3.21}$$
$$c_m V_2 = Q_2 \tag{3.22}$$

Subtracting them yields

$$c_m(V_2 - V_1) = Q_2 - Q_1 \tag{3.23}$$
$$c_m(\Delta V) = \Delta Q. \tag{3.24}$$
$$\tag{3.25}$$

Should the second charge distribution be the result of ions being "injected" into the cell, then we can think of an infinitesimal change in voltage with respect to time, or the time derivative of the above equation:

$$c_m \frac{dV}{dt} = \frac{dQ}{dt} = I. \tag{3.26}$$

Current, the flow of ions, is the rate of change of charge. Resistance to flow, R, can give rise to different potentials at different places in the neuron (think, for example, of the long axon):

$$I \propto \frac{V_2 - V_1}{R}. \tag{3.27}$$

Inserting an electrode into a cell is one way to change current; allowing the flow from other neurons is another way. As we shall see, one key idea in building a neural network is to vary the rate at which current can flow into one neuron from those downstream to it. This happens by, in cartoon terms, effectively varying, controlling or designing the "resistance" across the synapse.

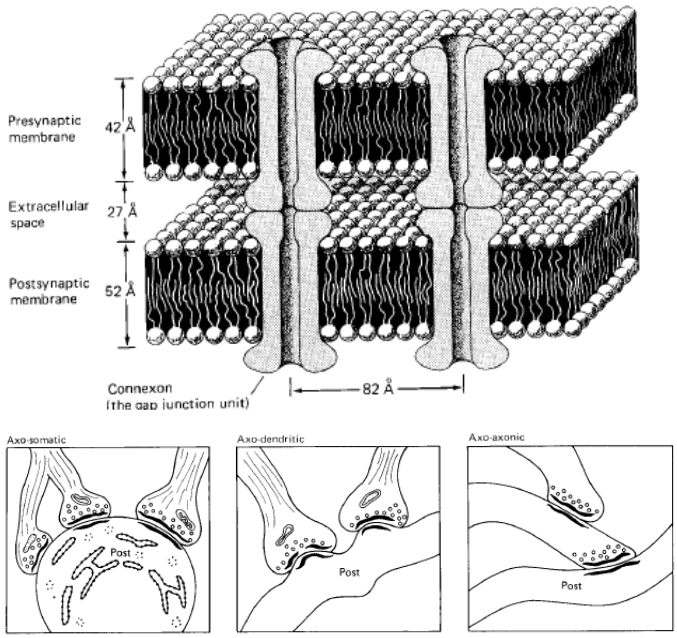

Figure 3.10: (TOP) A gap junction is a physical connection between channels that permits the direct flow of ions from one cell to the other. (BOTTOM) More general synapses have a synaptic cleft between them and may occur between different parts of neurons.

3.2.5 The Synapse

Neurons are not isolated; they are coupled in a manner that lets information be transferred from one to the other through the SYNAPSE.

The simplest synapse is the gap-junction. This is a direct connection that lets ions flow from one to the other; see Fig. 3.10. More generally there is a separation between the pre-synaptic neuron's axon (the output part) and the post-synaptic neuron's dendrite (the input part); of course in general networks more control is possible

More interesting are those synapses that allow some control over which ion can flow and when.

Neurotransmitters are molecules that bind to the synapse, thereby changing its configuration, and either opening it or closing it; Fig. 3.11. They are stored in vesicles and are dumped ectopically into the synaptic cleft.

They come in different varieties and, as we shall see, can either excite or inhibit function.

Remember, at equilibrium one can think of a neuron as sitting at - 65 mV. Now, if a channel opens that lets in positively-charged ions then the membrane will DEPOLARIZE, or become less negative; if it lets in negatively-charged ions it will HYPERPOLARIZE or become more negative.

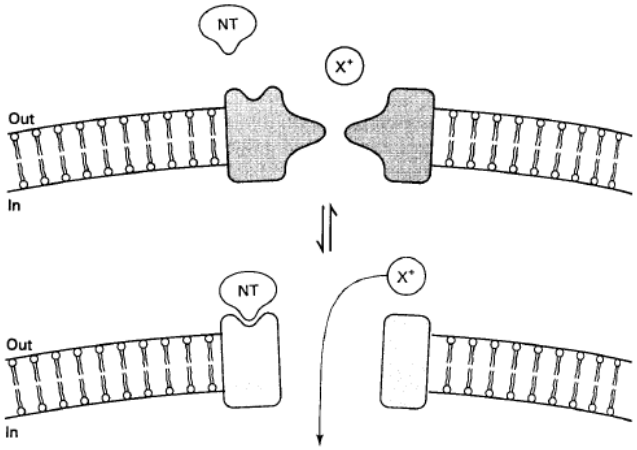

Figure 3.11: Neurotransmitters bind to synapses, thereby controlling their function. Figure from Kaz.

Now, thinking once again like a biophysicist, this change in potential can have another effect (different from forcing the movement of ions): it can effect the configuration of certain types of molecules that make up the channel – this gives rise to VOLTAGE-GATED CHANNELS. These open or close depending on membrane potential.

The dynamics of different channels are illustrated in Fig. 3.12.

There are many different classes of neurotransmitters, secondary messengers, and so on. We emphasize two: EXCITATORY NEUROTRANSMITTERS, such as glutamate, and INHIBITORY NEUROTRANSMITTERS, such as GABA (γ-aminobutryic acid). Among the glutamate receptors are AMPA, which activates quickly and NMDA, which is slower and involves calcium. In simple terms the former can be thought of as accomplishing some sort or neural transmission of information, while the latter may be involved in slower-scale events such as learning.

3.2.6 The Action Potential

Taken together one would expect some rather complex behaviour to emerge. Once channels open there is a new distribution of ions and potentials change effecting, in turn, other (e.g. voltage-gated) channels.

If sufficent currents add up to depolarize the neuron sufficently, a remarkable series of changes occur, the ACTION POTENTIAL. See Fig. 3.13. During the action potential sodium, potassium and chloride and calcium channels all open and ions are dumped across the membrane to result in a huge—but very brief—depolarization. This is followed by a short period of hyperpolarization, the RELATIVE REFRACTORY PERIOD. During the refractory period it is more difficult to cause a neuron to fire an

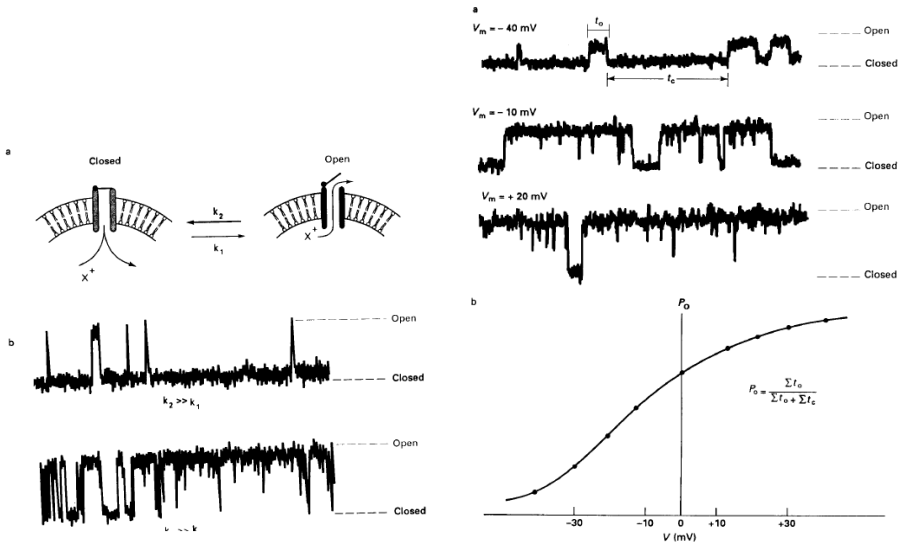

Figure 3.12: LEFT Individual channels can be thought of as pores with gates that open and close, allowing ions to pass through. Shown is a recording of current passing through a single ion channel. Notice how it is discrete – open or closed – and somewhat stochastic (opening or closing randomly in time). The ratio of the two constants, k_1 and k_2 gives the total amount of time the channel is open. With many channels opening and closing; and integration across time, the overall effect of current flow is smoothed into a more continuous variable. RIGHT For voltage-gated channels, the potential indicates the probability that the channel is open. The traces at the top go from a slightly depolarized state to a high depolarized state; notice how the channel switches from being predominantly closed to predominently open. This give rise to a "channel open probability" at the bottom, a sigmoidal function of the membrane voltage. Figure 4-4 and 4-5 from Kaz.

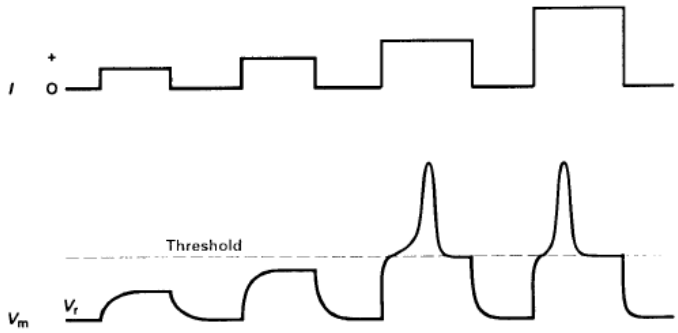

Figure 3.13: The action potential. The top curve is a series of current injections into a neuron; notice how they increase in magnitude. The bottom curve is the potential of the neuron; notice how current injection causes depolarization until threshold, when an action potential is triggered. Figure from Kaz.

action potential.

Following an action potential, ION PUMPS return the concentrations to their resting levels.

The detailed biophysics are captured by the HODKIN-HUXLEY EQUATIONS.

Important for signal propagating along long sections of axon. Myelination. Nodes of Ranvier.

We are just beginning to get to an understanding of the questions posed at the beginning of this lecture (eq. 3.28)

$$\boxed{\text{neuron : current} \rightarrow \text{spikes}} \tag{3.28}$$

We will continue this analysis in the next lecture.

3.3 Aside: Neurotoxins, Pufferfish, and Disease

We have barely begun to scratch the surface of information about channels and neurotransmitters, and the story becomes extremely rich. I only mention two examples here.

In 1774 Captain James Cook reported that his crew had become ill after consuming some pufferfish. Eating *fugu* is now a great challenge for lovers of sushi. Two questions arise immediately: what is poisonous in the fish and why, in fact, doesn't the puffer die of its own poison?

The poison here is Tetrodotoxin (TTX). One hundred times more poisonous than potassium cyanide by weight, it is not destroyed by cooking.

TTX binds to the voltage-gated potassium channel, thereby blocking it and preventing normal neural function. Nerve and muscle paralysis–and often, death– ensues.

Many variations on the sodium channel have evolved, and pufferfish have one to which TTX does not bind.

Multiple sclerosis is a disease of the myelin sheath; when it breaks down the propagation of action potentials is disturbed and there may be ectopic transmission from one axon to another.

3.4 Notes

For an introduction to statistical mechanics, see Feynman Lectures on Physics, vol 1.

For an introduction to neuroscience, see Kandel and Schwartz or Purves et al.

For an introduction to computational neuroscience, see Sejnowski and Churchland or Abbott and Dayan.

Charming article about the evolution of eyes: Dawkins, R., The forty fold path to enlightenment, in **Climbing Mount Improbable**, Norton, New York, 1996.

Analysis of shadow reflex:

[**?**]

Stuart, A.E. Vision in barnacles, TINS, 1983, 6, 137-140.

Schnapp, B.J. and Stuart, A.E., 1983, Synaptic contacts between physiologically identified neurons in the visual system of the barnacle, J. Neurosci. 3, 1100 - 1115.

There's a lot more to the barnacle photoreceptor, such as spectral dependency at high light levels; see [**?**]

Chapter 4

The Barnacle 2: Integrate-and-Fire Models

continue Vignette no. 2: Barnacle. Spiking neurons. Integrate and Fire model. Firing rate as a code. Shadow reflex: if dI/dt¿threshold, then withdraw. Shadow reflex helps Barnacle avoid being food.

In this chapter we continue our discussion of neurons, but now put activity together across several neurons and across time. This opens an operational view into a simplified neural network. In fact, we leave out much of the basic biophysics from the last chapter and *lump* all of the details into a very simplied model. Technically it's called a single compartment: one set of dynamics handles it all.

We also introduce the first type of neural code: the way that action potentials can form a sequence (a spike train): fast spikes indicate high values while slow spikes indicate smaller ones.

4.1 Currents in a Neuron

We now put the pieces together for the simplest possible model for neural activity, in which it integrates the total synaptic current input and, when a threshold for depolarization is reached, the neuron "fires" an action potential. At this point the details of the action potential are ignored, the threshold is reset to a value below the resting level, and current integration starts up again. This is the integrate-and-fire model, first proposed by Lapicque in 1907.

Considering the neuron as a single compartment, we saw earlier that the change in membrane potential was proportional to current flow:

$$\boxed{c_m \frac{dV}{dt} = I,} \tag{4.1}$$

Basically, INTEGRATE AND FIRE is an algorithmic way of mapping from currents

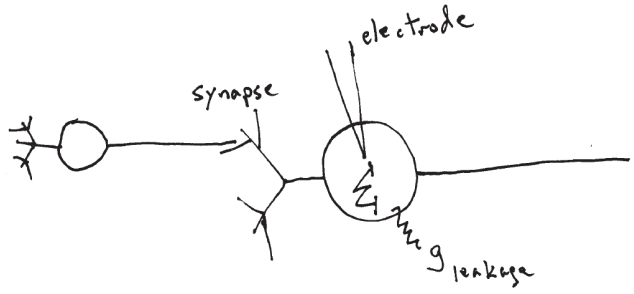

Figure 4.1: Sources of current 'into' a neuron include that from other neurons through synapses or that injected by an electrode (in the lab.). Loss of current 'out of' a neuron occurs by membrane leakage.

to frequency of firing. Why? From the above equation, we're looking for $V(t)$ but we have $\frac{dV}{dt}$; hence integrate! So our job boils down to finding the current flow.

Let's start by just thinking of those ions that "leak" out of the membrane. The force pushing them is in proportion to how much the membrane voltage, V, differs from the equilibrium potential, E_i, for an ion species (or collection of species). (Remember Nernst from the previous lecture.) Some leakage is due to the ion pumps that maintain concentration differences but we shall be vague about real membrane properties.

The conductance (per unit area) is denoted g_i, and in physical units is the inverse of resistance. According to OHM'S LAW (voltage equals current times resistance), we can write out the total leakage current as

$$i_m = \sum_i g_i(V - E_i) = g_{\text{leakage}}(V - E_i). \tag{4.2}$$

Now we're ready to introduce the synapse and other current "sources" (see Fig. 4.1). The total current entering a neuron consists of those currents that come from synapses, or equivalently, g_{synaptic} and those that are injected through electrodes, I_e (or written in density terms as I_e/A, where A is the membrane area), then we can combine the equations to give:

$$c_m \frac{dV}{dt} = -i_m + I_{\text{synapses}} + I_e/A = -g_{\text{leakage}}(V - E_i) + g_{\text{synaptic}}(V - E_i) + I_e/A. \tag{4.3}$$

By convention, we think of the current leaking across the membrane as positive outward, and the current entering (e.g. from an electrode) as positive inward, which accounts for the signs.

4.1.1 Dynamics: "charging up the neuron"

For a moment let's assume there is no synaptic activity. Notice that now, when the leakage current is balanced by the injected current, there is no change in potential, but if a strong current is injected the potential will depolarize. How fast does this happen?

Take our basic equation

$$c_m \frac{dV}{dt} = -g_{\text{leakage}}(V - E_i) + I_e/A \tag{4.4}$$

and multiply both sides by the specific membrane resistance, $r_m = 1/g_{\text{leakage}}$ to create the factor $c_m r_m = \tau_m$:

$$\tau_m \frac{dV}{dt} = E_L - V + R_m I_e = V_\infty - V \tag{4.5}$$

where $V_\infty = E_L + R_m I_e$. When I_e is a constant, i.e., is not a function of time, this differential equation has the same form that we encountered earlier, with a derivative on one side and the variable on the other. So it should come as no surprise that we can integrate it directly to get the voltage as an exponential function of time:

$$V(t) = V_\infty + (V(t_0) - V_\infty) \exp(-(t - t_0)/\tau_m \tag{4.6}$$

4.2 Integrate and Fire

The model we are developing has the input currents "charging up" the neuron, as if it's a capacitor. If the pre-synaptic neuron sends an isolated spike, then this will depolarize the neuron a little bit but it will "relax" back down to the resting potential. (We saw this is the last chapter.) But if the presynaptic neuron sends a string of action potentials closely space in time, or if many presynaptic neurons send a few spikes all closely arranged in time, then the threshold for firing will be reached an the neuron will initiate an action potential. If the spikes keep coming (or if current is continually injected via an electrode) then the neuron will continue to fire.

This is modeled most simply by integrate-and-fire; a model that is nice for theoretical studies. (Because none of the details of the actual currents carried by e.g. K and Na ions are modeled, nor are the dynamics of synapses, etc., this model is not physiologically accurate.) See Fig. 4.2.

Step 1. The neuron charges up according to the input currents minus the leakage currents: $C\frac{dV(t)}{dt} = I(t)$. This change in voltage determines the subthreshold dependence; it depends on the initial condition.

Step 2. Suppose the voltage threshold for firing is given by V_{th}. Once the voltage reaches this, $V(t) = V_{th}$, the neuron fires and all the accumulated charge is shunted to ground; the voltage is reset to the resting level. (For mathematical simplicity you

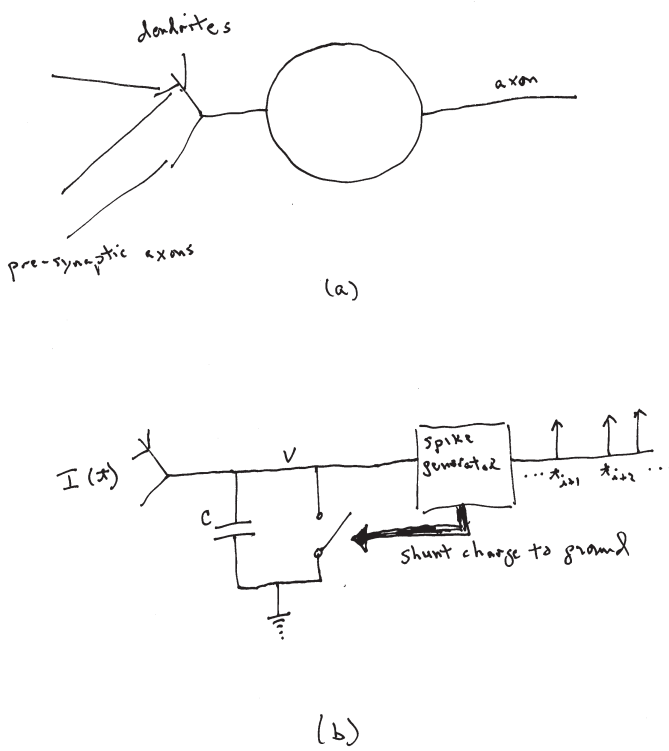

Figure 4.2: The integrate and fire model. The input current charges the capacitor C until threshold voltage is reached and an action potential fires; this then resets the neuron to base level voltage by closing the switch and shunting the charge to ground. Discussion follows Koch.

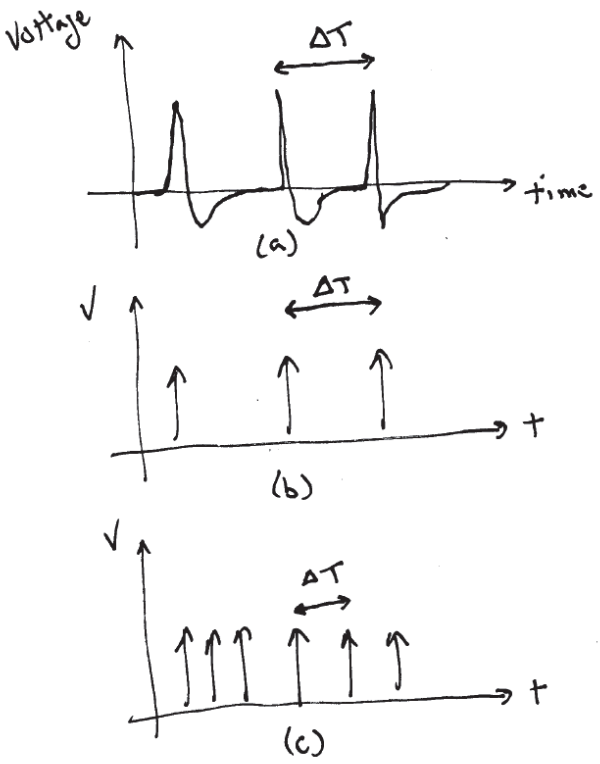

Figure 4.3: Spike frequency is the inverse of time between spikes. Normally an average is taken over several intervals, since there is some variation.

might think of this resting level as V = 0.) None of the time course details for an action potential are used: it is simply a "spike" at the correct instant of time. If the current stays on, the neuron then re-charges and another action potential is fired. The time between successive spikes i and $(i+1)$ is given by

$$\int_{t_i}^{t_{i+1}} I(t)dt = CV_{th} \tag{4.7}$$

4.2.1 Firing Rate

The activity of a neuron can be summarized as FIRING RATE, or the time interval between spikes; see Fig. 4.3.

For the simple integrate-and-fire model this is a straight line.

Adding in the leakage current gives the LEAKY INTEGRATE-AND-FIRE model (Fig. 4.4) and, slightly more biological, is the adapting leaky model. This models

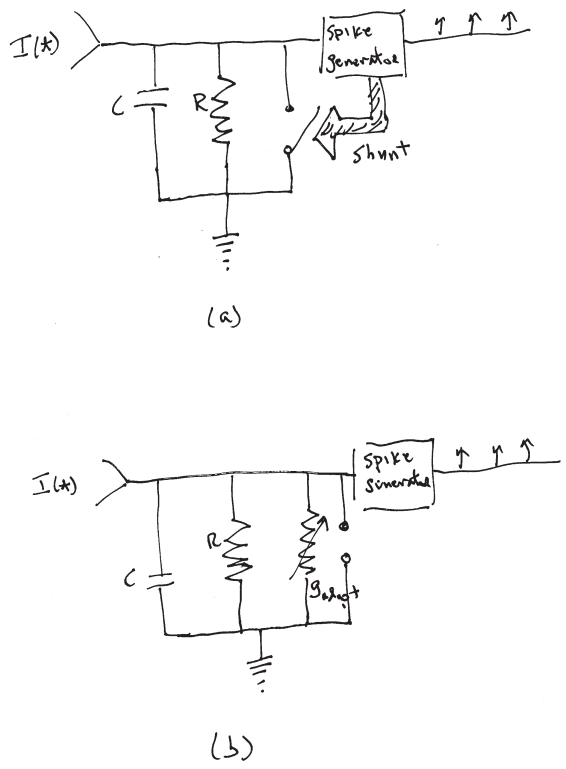

Figure 4.4: Adding the leakage current takes the form of a resistor. Adding adaptation takes the form of a variable conductance. Discussion follows Koch.

what happens in an actual neuron, where there is some SPIKE-RATE ADAPTATION; see Fig. 4.6. We now have a graph to represent the function at the end of our last lecture (eq. **??**, which we update to indicate the code:

$$\boxed{\text{neuron} : \text{current} \rightarrow \text{spikefiringrate}} \tag{4.8}$$

It is important to remember that this is the simplest model; it will turn out that there is more more information in spikes than the average inter-spike-interval. (Recall the initial transient vs the regular spiking rate in Fig. 4.6. This will appear in a real organism in the next lecture.)

Even in this simple model, a road ahead appears: to design neural networks, we need to specify which neurons are connected to which other neurons, and what is the synaptic 'weight' (g_{synaptic}) between them.

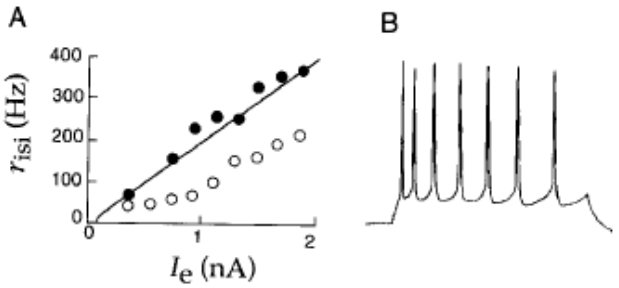

Figure 4.5: Firing rate is the average interspike interval and is well defined for the simple integrate and fire model. However real neurons do not fire at a constant rate; often they fire more rapidly with an initial transient and then settle to a relatively steady-state value. Data from McCormick. Figure from Abbott and Dayan.

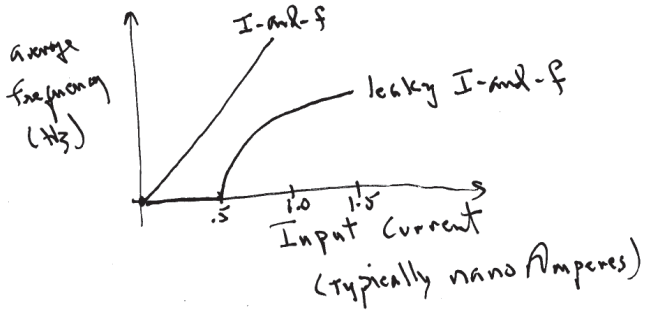

Figure 4.6: The input-output characterization of a simple neuron model is given by the frequency of spikes fired for a constant input current. The is called an F-I curve.

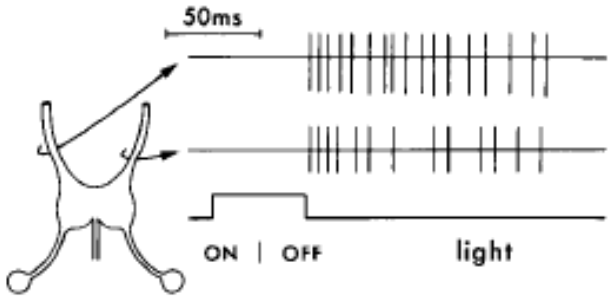

Figure 4.7: The shadow reflex abstracted. Notice the off-response and how, on multiple trials there is a stochastic variation around the expected response. Figure from Laughlin.

4.3 The Barnacle – Again

The Ocelli are primitive light gathering organs. Photon causes a physical change in the receptor molecule that blocks a sodium channel; this causes the cell to depolarize. This GRADED POTENTIAL varies roughly with the log of light intensity. That is, the potential on the axon increases with brightness.

How is this encoded information processed within the SOG? It's tempting to look at the output from the network, which is cartooned in Fig. 4.7: strikingly, when the light is turned on there is little signal to the motor sysem; however, when the light is turned off there is a significant response. What might this mean?

Darwin had the answer:

> I found these species very sensitive to shadows ... They instantly perceived and drew in their cirri when my hand was passed between the basin in which they were kept and the window, even when this was tried rather late on a dusky evening; and likewise when my hand was passed between them and a single candle.[1]

Summary: the barnacle withdraws upon the cessation of light; in effect exhibiting a response to the light turning off or an sc off response. It makes sense as a protective strategy, since a predator would block the sun – or cast a shadow – which is an informative clue from the environment for initiating a protective maneuver. (For the barnacle, this means withdrawing its cirri, or feeding appendages, into its shell and closing off the opening.

This is an elaborate behaviour for a simple creature. Somehow the small changes in receptor potential have to be amplified into effective motor signals.

[1]Charles Darwin, 1854, A monograph on the subclass *Cirripedia*, Vol. 2, p. 94; quoted in Stuart, TINS, 1983, p. 137.

Two cells in the ganglion play a role in this. First, since the receptors depolarize to light but the animal responds only to decreases in light, the first cell in the ganglion (the second in the circuit) is called an "Inverter", or I cell. These second-order neurons influence third-order cells also found near the terminals from the receptors; these third-order cells are the first ones to exhibit spiking. Sometimes these are called "amplifier" or A-cells, because they amplify the small potential changes into behaviour-inducing spike trains. See Fig. 4.8.

Analogy between computers and barnacles as image analysis machines:

```
COMPUTER BARNACLE

sensor array ocelli

filters sog average response

computer f(t) = (dI > K) action potentials


GENERAL THEORETICAL VIEW EMERGING: measurement of features of the world and
then decisions on the basis of these measurements.
```

4.4 Levels of Explanation

The past two lectures covered several different levels of investigation at which we can talk about neural function – see Fig. 4.9. Think about how the notion of approximation holds between these levels. Which is the right one? Is there a right one?

4.5 Notes

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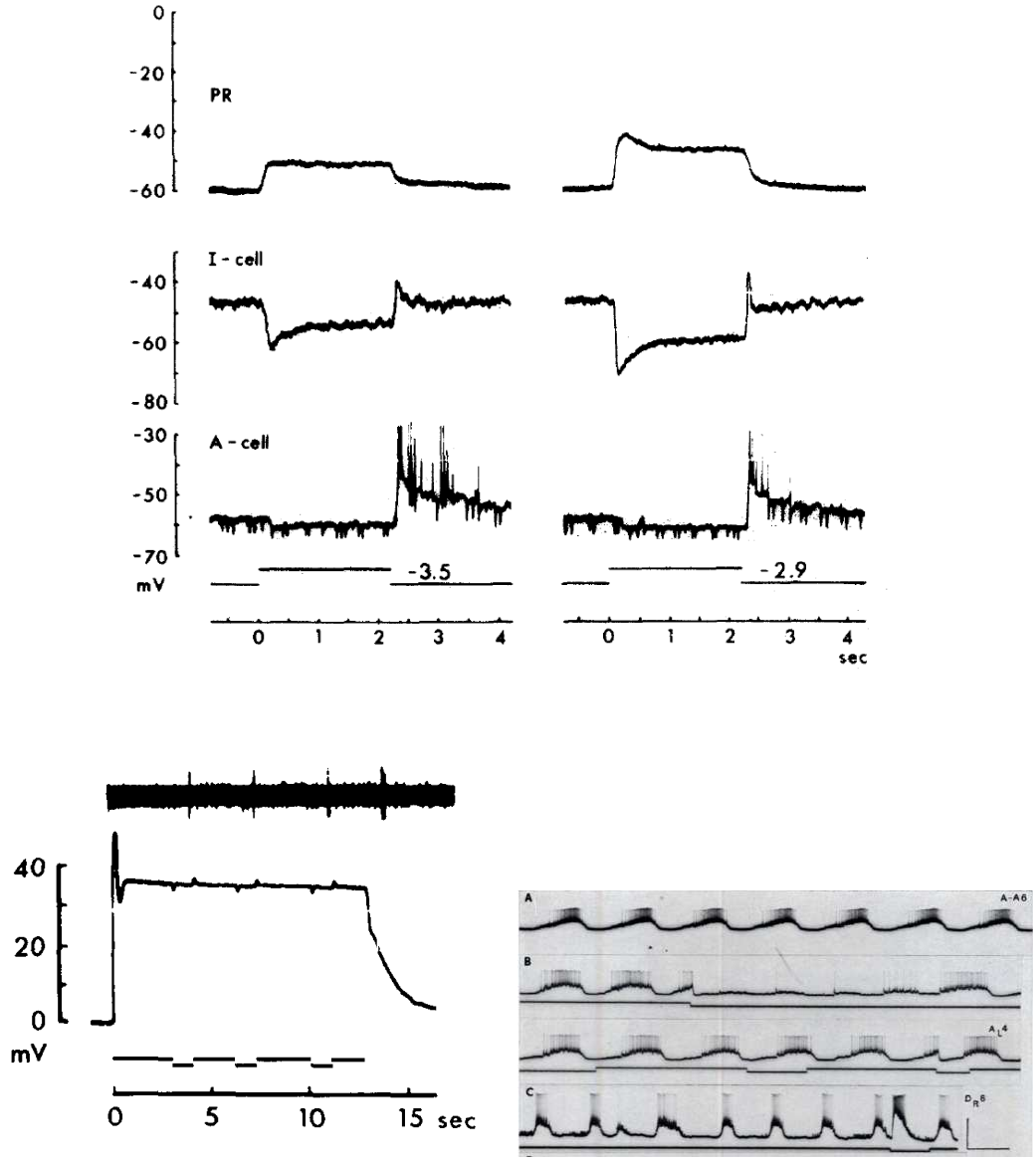

Figure 4.8: The actual responses in the barnacle's nervous system and the motor drive to withdraw. (top) Photoreceptor (PR), inverter (I), and amplifier (A) cell responses. When the light comes ON, the PR depolarizes, the I-cell hyperpolarizes, and the A-cell is quiet. When the light goes OFF, the opposite occurs except now the A-cell responds vigorously. Fig from Stuart. Different light intensities yield similar effects (left vs right traces). (BOTTOM) Other traces of the I and A levels (left) and PR and A levels (right). Figures from ** and Laughlin.

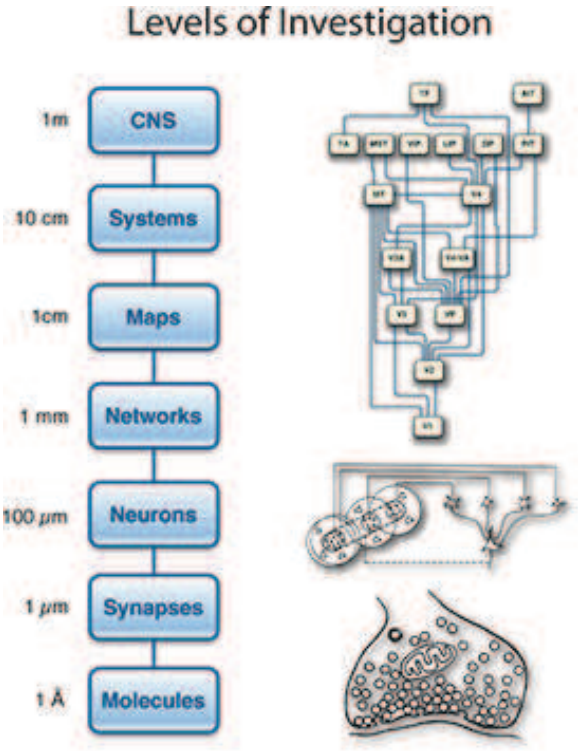

Figure 4.9: Different levels at which structure can be described in the nervous system. Figure from Sejnowski.

Schnapp, B.J. and Stuart, A.E., 1983, Synaptic contacts between physiologically identified neurons in the visual system of the barnacle, J. Neurosci. 3, 1100 - 1115.

There's a lot more to the barnacle photoreceptor, such as spectral dependency at high light levels; see [**?**]

