Module:
Techniques in Neuroscience

Week 2
Electrophysiology: Looking at live neurons in action

Topic 1
An introduction to Electrophysiology – Part 1 of 3

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As the Italian physician, Luigi Galvani, discovered in 1790 while he was working on frogs, the nervous system uses electrical activity to perform its functions. This biological activity is studied and recorded by the science of electrophysiology. Electrophysiology uses a wide range of techniques that can be grouped under two headings: invasive and non-invasive.

In this topic, I will concentrate on the invasive techniques we use, while the non-invasive techniques will be covered by Dr Giampietro elsewhere on this module. This topic is divided into four parts: in the first part, I will briefly introduce the types of biological electrical activity; in the second part, extracellular recording; third part, intracellular recording; and finally, single channel recordings.

The biological electrical activity that we investigate in electrophysiology comes in a number of forms. There are large voltages that are generated by animals, such as electric eels or electric rays, which is used to stun prey, which can reach up to 700 volts. Then there is the negative resting membrane potential of about -70 millivolts, comparing the outside of both cells to the inside, and this is the membrane potential that most neurons have. There are also post-synaptic potentials, which are small variable changes in the membrane potential and that are in the range of one to 40 millivolts. And finally, there are the action potentials, which reach 100 millivolts, and they are large, fast and occur in an all-or-none fashion. Over the next few screens, I'll look at each of these in turn.

So first, let's look how electric fish, such as electric eels (Electrophorus) and rays (Torpedo) produce electricity. These fish possess specialist cells called electroplaques, which have membrane sodium-potassium exchanges. At rest, sodium-potassium exchanges use ATP to alter the ions distribution across the membrane. This generates a potential difference across the electroplaque. When the fish wants to give an electric shock, the electroplaques are activated by a nerve. The nerve releases acetylcholine onto nicotinic-type acetylcholine receptors that are ligand-gated ion channels. These channels allow the flow of sodium ions into the electroplaque, depolarising the electroplaque and generating a brief potential change of around 0.12 volts, or 120 millivolts.

Electroplaques are stacked in their thousands in electric organs and the sum of these can generate hundreds of volts. Small voltages are used to detect prey, while larger ones - up to 700 volts, as I said earlier - can stun. Similar to electroplaques, neurons also have sodium-potassium exchanges in their plasma membrane. These, as

before, generate high cytosolic potassium and low cytosolic sodium, using ATP as their energy source. In neurons, chloride ions are co-transported out of the cell using the potassium gradient as energy. There are many immobile negative ions, such as phosphate groups, found on proteins inside neurons. Overall, these all generate a resting membrane potential of between -60 and -80 millivolts inside the neuron.

Now let's take a closer look at the resting membrane potential, or Vm rest. The presence of the potential and concentration differences across the neuron's plasma membrane mean that there's a range of directions of movement for the different ions through their respective channels. For example, sodium ions move into the neuron, as both their concentration gradient and electrical gradients direct them inwards.

Conversely, the concentration for gradient for potassium ions makes them move out of the neuron, despite the inward electrical gradient of about -70 millivolts. Chloride ions move into the neuron down their concentration gradient, despite the electrical gradient of -70 millivolts, which would tend to keep them out. And finally, calcium ions move into the neuron down what is the highest concentration gradient of up to 10,000 to one, and also down the electrical gradient, which is into the neuron.

Next, let's look at post-synaptic potentials. The ion gradients in a neuron allow both depolarising and hyperpolarising potentials. Excitatory post-synaptic potentials, or EPSPs, are generated by the activation of ion channels that depolarise neurons, usually by transmitters that activate channels permeant to positive ions: sodium, potassium, and calcium. For example, when glutamate acts on ionotropic receptors, this activates sodium and calcium to flow into the cell, as shown in the picture on the left.

On the other hand, inhibitory post-synaptic potentials, or IPSPs, are generated by the activation of ion channels that hyperpolarise neurons, usually by neurotransmitters that activate channels permeant to negative ions, such as chloride - for example, when GABA acts on GABA A receptors and allows chloride into the neuron, as shown on the picture on the right.

Both EPSPs and IPSPs are graded in amplitude due to the concentration of the neurotransmitter, as well as time - the length of time the neurotransmitter is in the synaptic cleft. And both EPSPs and IPSPs are additive, but decay in amplitude as they move around the neuron.

Now, let's look at the fourth item in the list I gave you earlier, and this is the action potential. Action potentials require activation of voltage-gated sodium and voltage-gated potassium channels. At resting membrane potential, both sodium and potassium channels are closed in their resting state, as shown at point A. A depolarisation leads to the opening of the voltage-gated sodium channels, which lead to further depolarisation, and further voltage-gated sodium channels opening in an all-or-none way at B. At the peak of the action potential, C on the diagram, sodium channels close and go into their inactivated state, and the potassium channels start to open. Next, potassium ions move out and hyperpolarise the cell back around the resting membrane potential, and this is shown in D. At the resting membrane potential, both sodium and potassium channels return to the closed resting state at E, where we started.

Action potentials are all-or-none in terms of amplitude, around 100 millivolts. They are brief, lasting only between 0.5 and two milliseconds, and can travel fast at long distances in excitable tissues without changing amplitude. Here is a summary table of the biological activity covering the main points.