# Module:
# Techniques in Neuroscience

## Week 2
## Electrophysiology: Looking at live neurons in action

## Topic 1
## An introduction to electrophysiology – Part 2 of 3

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In this part of the topic, I will cover the electrophysiological techniques we use to record electrical activity of nervous tissue. So, I'll talk about extracellular, intracellular and single channel recording in that order. Extracellular recording, which we abbreviate to ER includes five recording types: field potentials, whole nerve activity, multi-unit activity, single unit activity, and finally, the use of multi-electrode arrays, or MEAs.

Intracellular recording, or IR, is used to record activity within single cells and involves the use of either sharp electrodes or patch suction electrodes. Single channel recording, or SCR, is used for recording the activity of single ion channels and uses patch clamp-type electrodes. We will look at each of these in turn, starting with extracellular recordings.

So, let's look in more detail at extracellular recording. As I indicated earlier, there are five versions of extracellular recordings that we're going to show you: firstly, field potentials; then, whole nerve recordings; multicellular recordings, or multi-unit recordings; single unit recordings; and MEAs. In each case, the electrode is outside but very close to the neuron. Under these conditions, electrodes pick up only field potentials and low frequency filtered action potentials. You cannot record membrane potential, or VM rest, or post-synaptic potentials using these techniques. Here, I'm going to illustrate field potentials recorded from a rat's brain slice.

This is a slice of the rat's brain. It is in fact a slice of the hippocampus area, and we have placed three electrodes into the tissue but not into the cells. One is a stimulating electrode in red, and the two recording electrodes are shown in blue. When we stimulate the stimulating electrode, this activates the Schaffer collaterals and causes neurotransmitter release onto the Purkinje neurons in the area called CA1, which is where the two electrodes in blue are positioned. The signal from the blue recording electrode on the left show something called an FEPSP, and this is a field excitatory post-synaptic potential, and this is the effect of glutamate receptors opening and causing a depolarisation of the neuron at this point. The other electrode, which is on the right, this is recording the action potential known as the somatic population spike, so it's in fact the sum of many action potentials of CA1 cells in this area.

So here, we can record both the incoming EPSP and the resultant action potential generated by it in the dendrites of the neuron. In a similar way to the previous example, the compound action potential of a whole nerve can be

recorded extracellularly. In the example shown here, the action potential of the sciatic nerve of the frog is being recorded. Here you can see that the nerve has been isolated and placed on platinum wires at one end for stimulating and the other for recording. The outer chambers are sealed with silicone grease - SG in the figure - and filled with olive oil to electrically isolate the nerves. Only the action potential traveling down the individual axons will be recorded.

You can see that increasing the intensity of the stimulation from 1.2 volts to five volts in the graph increases the compound action potential size; because the stronger the stimulation, the more axons are recruited to fire action potentials, meaning that the compound action potential gets larger and eventually all the axons will be recruited and the compound action potential will be maximal.

I have recorded two videos for you: a recreation of Galvani's experiment on frogs, where I stimulate the nerve to cause the frog leg to twitch; the isolation of the whole nerve from a frog and recording of the action potential, as I highlighted to in the previous slide. Similar compound action potentials can be recorded from rats- in this case, the isolated vagus nerve of one.

Here, you can see the different types of axons from A-beta, A-delta and C fibres. These different axons can be separated by the intensity of the stimulus and their conduction velocity - AB fibres being the fastest and C fibres the slowest.

Now, I'll move onto multi-unit extracellular recordings, and these can be done *in vivo*. Here, an electrode is placed in an anaesthetised rat brain; the recording area is called the lateral geniculate nucleus or LGN, which is part of the visual pathway. With the electrode in place, a flash of light is used to activate the neurons. The largest action potentials you see here are from one neuron very close to the electrode, but the smaller action potentials here are from a cell that is further away from the electrode. Therefore, you are simultaneously recording from two different cells.

Here is an example of a single unit recordings, this time done in a human brain, and at the medial temporal lobe. This patient gave consent for this and was having a deep brain stimulation electrode implanted, so the recording wasn't done without good reason. As we see at stimulus one, we have a picture of Halle Berry and we can see the neuron that was being recorded from the subject responded with action potentials. Stimulus 2 is a different picture of Halle Berry and the neuron still responds. Stimulus 3 is a very different picture of Halle Berry, but the neuron still responds. They even put a picture of Halle Berry's name up and it responded, however, it did not respond to a picture of Michelle Pfeiffer. Therefore, this neuron was called a Halle Berry neuron, and it is an example of association neurons that may exist in the human brain.

And this is my final example of extracellular recording where we can use multi-electrode arrays, or MEAs. These electrodes, rather than being sharp pointed things, are actually electrodes that are bedded in the bottom of this dish shown in the picture. There are, in fact, 64 of them in the bottom of the dish shown on the first square here, and if we look at those individually, they are inert to the cells - so don't affect the cells - but they can pick up extracellular electrical activity neurons.

What we can do is actually grow the neurons inside these dishes in an incubator and we can monitor, then, the electrical activity in a very non-invasive manner. In this slide, I show a picture of an MEA with cells that are growing on it. These cells are called NG108-15 cells and you can see the cells are growing on the multi-electrode array and the black circles are where the electrodes are. So, you can see the cells are very happy in this dish and they're happily growing on the electrodes, so we can record their electrical activity.

In this slide, I can show you examples of the action potential activity from the MEAs that you've just seen. On the top left, you can see there is no action potential activity, but just some background noise. In the middle left, where it says '12 millimolar potassium chloride', this is what's been applied to those cells and made them depolarised and start to fire action potentials. As I said in the middle trace, you can see two action potentials, and after a period of time, the action potential activity increases on the bottom trace in the left. On the right, we've applied a more natural neurotransmitter, ATP. The right top trace just shows the background activity in control situations. Then, I apply one millimolar ATP in the middle trace and the action potentials start to fire, and finally, is a trace a few seconds later where there's high levels of action potential activity. And this shows we can record, in a non-invasive manner, action potential activity from multi-electrode arrays.

In this slide, I have given you all the main points about the extracellular recordings, particularly comparing their advantages of the different technique to their disadvantages.