

Module:
Techniques in Neuroscience

Week 2:
Electrophysiology: Looking at live neurons in action



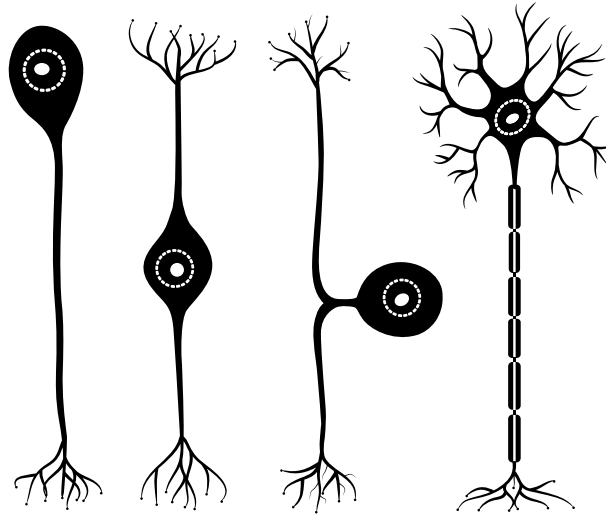
Dr Jonathan Robbins

Topic 1:
An introduction to electrophysiology
Part 3 of 3

Part 3

Intracellular recordings

current clamp
voltage clamp



sharp electrodes
patch clamp electrodes

Definitions to aid understanding

Definitions:

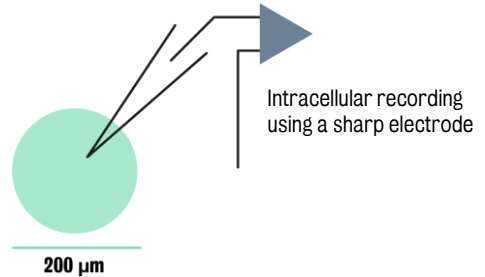
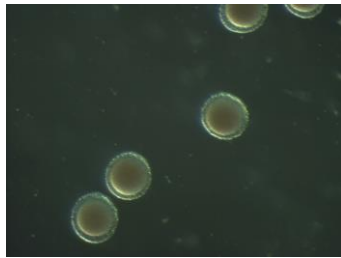
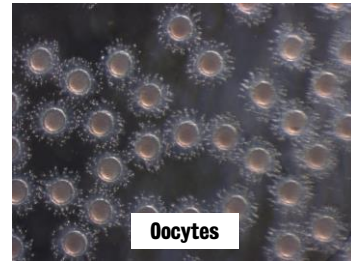
Voltage: the potential difference in charge between two points.

Current: the rate at which an electric charge is flowing.



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Using sharp electrodes



Perezoso (2007); Robbins (unpublished data)

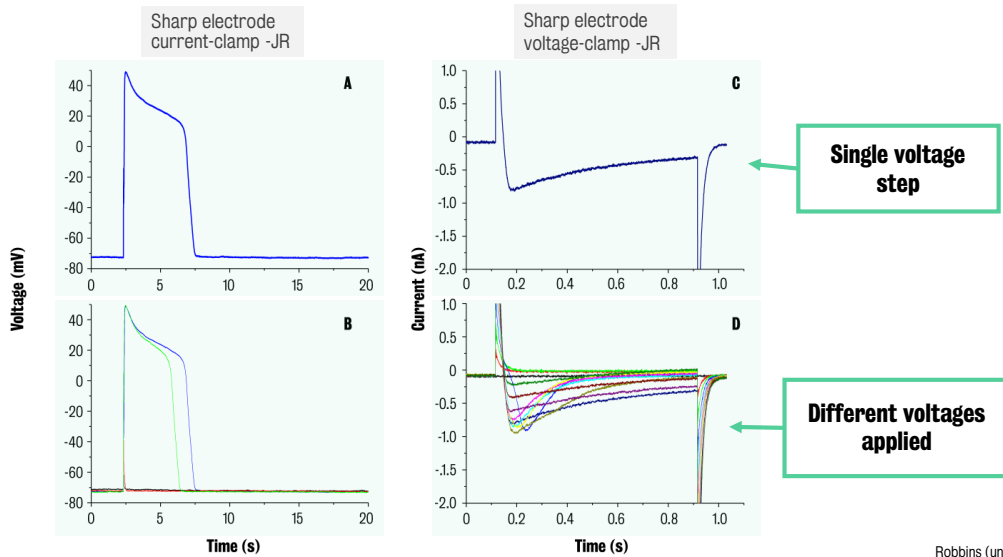
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Sharp electrodes with current clamp and voltage clamp

A comparison of sharp electrodes in two different recording setups



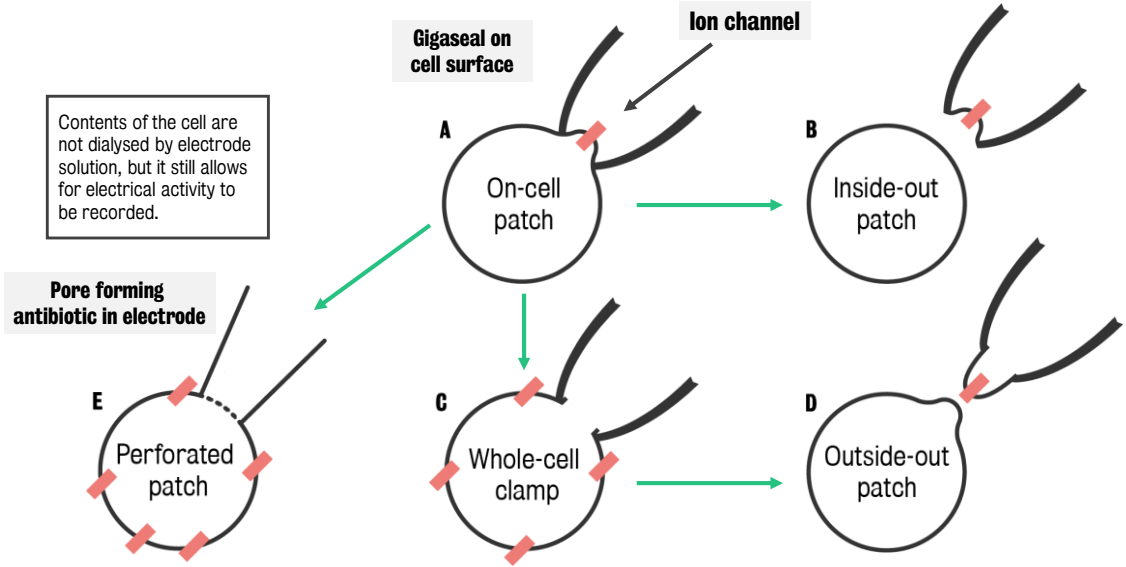
Robbins (unpublished data)

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Variants of the patch-clamp technique



Robbins (unpublished data)

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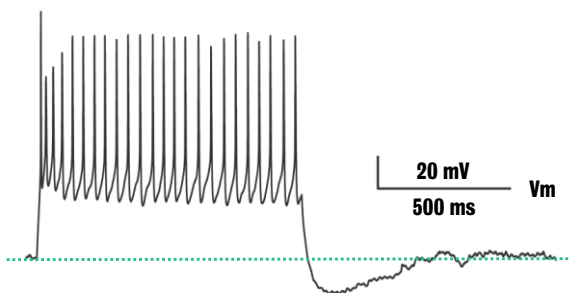
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Whole cell recording

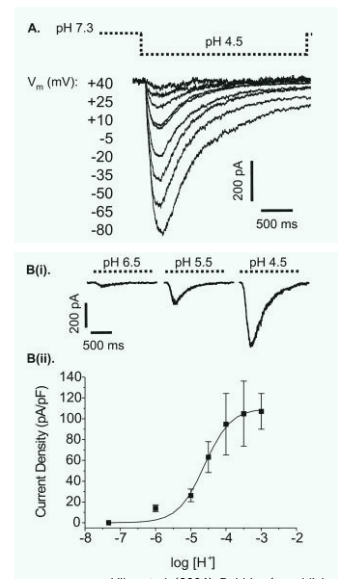
Recording of rat retinal ganglion cells

Current Clamp

Action potentials were recorded from a rat retinal ganglion neuron using the patch clamp technique.



Voltage Clamp



Lilley et al. (2004); Robbins (unpublished data)

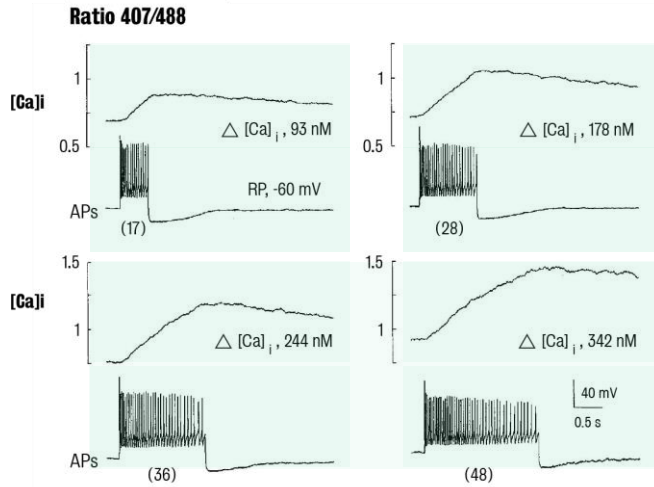
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Whole cell patch clamp in current clamp mode

Whole cell patch clamp (current clamp mode) with intracellular calcium measurement using Indo-1-SM/JT



Calcium entry during an action potential is related to the number of action potentials that are opened or activated in that cell.

Adapted from Trouslard et al. (1993)

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Single channel recording

Depolarised/channel open even more; current bigger

Vp -30

02 ← Both channels open
01 ← One channel open
C ← Both channels closed

Vp -20

One or both channels open; activity increase; channel current larger

Vp -10

Cell depolarised by 10mV

Single channel conductance quite low; time channel is open also low, channel almost closed most of time

200ms

1 pA

M. Passmore (unpublished data)

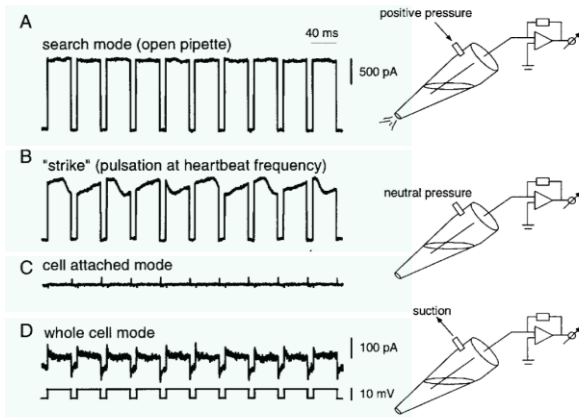
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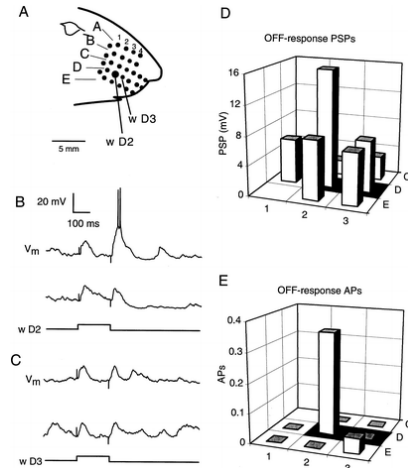
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In vivo patch clamp

Electrode in brain



Responses where whiskers of mouse were stimulated



Margrie et al. (2002)

Applications of the techniques

Humans (In vivo)	Non-humans (In vivo)	In vitro (can use human tissue)
Extracellular recording (only as part of treatment)	Extracellular recording (implanted /anaesthetic)	Extracellular recording
-	Intracellular recording (anaesthetic)	Intracellular recording
-	Single cell recording (anaesthetic)	Single cell recording

Summary on intracellular recordings



Technique	Advantages	Disadvantages
Current clamp	Records activity of the cell in 'physiological conditions' Detailed and high resolution recordings of voltages	Cannot control voltage
Voltage clamp	Can control the voltage Detailed and high resolution recordings of currents	Unstable
Sharp electrode	Reusable Simple electrode solution	High resistance Can be difficult to make Some damage to cell
Patch electrode	Low resistance Relatively easy to make Less damage to cell Dialysis of cell contents	Not reusable Dialysis of cell contents Complex electrode solution
Single channel	Allows the recording in real time of the functional activity of a single protein Elucidates drug action at molecular level	Complex and lengthy analysis

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Summary

- 1 Electrophysiology can record the electrical activity of whole brain tissue, a single neuron or a single ion channel.
- 2 Electrophysiology is a dynamic, functional, SI unit-based, real-time, hi-fidelity and high temporal resolution approach.
- 3 Many electrophysiological approaches can be used *in vivo*.
- 4 Electrophysiology can be used simultaneously or in conjunction with optical, molecular, biochemical and pharmacological techniques.
- 5 It is essential to the understanding of the nervous system.

References

Docherty, R. J., Charlesworth, G., Farrag, K., Bhattacharjee, A., & Costa, S. (2005). The use of the rat isolated vagus nerve for functional measurements of the effect of drugs in vitro. *Journal of pharmacological and toxicological methods*, 51(3), 235-242.

M. Passmore, G. (unpublished data)

Lilley, S., LeTissier, P., & Robbins, J. (2004). The discovery and characterization of a proton-gated sodium current in rat retinal ganglion cells. *Journal of Neuroscience*, 24(5), 1013-1022.

Lilley, S. J., & Robbins, J. (1998). The action of local anaesthetics on the compound action potential is altered by the nature of the permeant ion in frog nerve. *Neuroscience letters*, 252(1), 41-44.

Margrie, T. W., Brecht, M., & Sakmann, B. (2002). In vivo, low-resistance, whole-cell recordings from neurons in the anaesthetized and awake mammalian brain. *Pflügers Archiv European Journal of Physiology*, 444(4), 491-498.

O'keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford: Clarendon Press.

Perezoso. (2007). *Ciona intestinalis adult* [photograph]. Retrieved from <https://commons.wikimedia.org/wiki/File:Cionaintestinalis.jpg>

Quiroga, R. Q., Kraskov, A., Koch, C., & Fried, I. (2009). Explicit encoding of multimodal percepts by single neurons in the human brain. *Current Biology*, 19(15), 1308-1313.

Robbins, J. (unpublished data)

The Scripps Research Institute. (2008). Scientific Report 2008: Molecular and Integrative Neurosciences. *CNS Actions of Inflammatory Factors*. Retrieved from <https://www.scripps.edu/news/scientificreports/sr2008/mind08gruol.html>

References

Trouslard, J., Mirsky, R., Jessen, K. R., Burnstock, G., & Brown, D. A. (1993). Intracellular calcium changes associated with cholinergic nicotinic receptor activation in cultured myenteric plexus neurones. *Brain research*, 624(1), 103-108.

Wellcome Library. (2014). *Sciatic nerve, Galvani* [Etching]. Retrieved from https://commons.wikimedia.org/wiki/File:Sciatic_nerve,_Galvani_Wellcome_M0012614.jpg#/media/File:Sciatic_nerve,_Galvani_Wellcome_M0012614.jpg

Attributions

Portraits for Halle Berry and Michelle Pfeiffer adapted from:

Jeremiah, C. (2007). *Michelle Pfeiffer at the premiere of Stardust in Los Angeles*. Retrieved from https://commons.wikimedia.org/wiki/File:Michelle_Pfeiffer_2007.jpg
Marin, G. (2010). *Actress Halle Berry at the 2010* [photograph]. Retrieved from <https://commons.wikimedia.org/w/index.php?curid=16219454>
Skidmore, G. (2017). *Halle Berry speaking at the 2017 San Diego Comic-Con International in San Diego, California* [photograph]. Retrieved from <https://commons.wikimedia.org/w/index.php?curid=61271080>
US Navy (2006). *Halle Berry - USS Kearsarge*. Retrieved from https://commons.wikimedia.org/wiki/Halle_Berry#/media/File:Halle_Berry_-_USS_Kearsarge.jpg

End of topic