***IN VIVO* ELECTROPHYSIOLOGY**

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Relevant Journal Articles

Khodagholy, D., Doublet, T., Quilichini, P., Gurfinkel, M., Leleux, P., Ghestem, A., Ismailova, E., Hervé, T., Sanaur, S., Bernard, C., & Malliaras, G. G. (2013). In vivo recordings of brain activity using organic transistors. *Nature communications*, *4*, 1575. https://doi.org/10.1038/ncomms2573

- Here they used a device called a transistor array or more specifically organic electrochemical transistor (OECT) for recording brain activity with superior signal-to-noise ratio, they recorded ECoG (non-invasive) on the somatosensory cortex of rats, and confirmed the results with electrode recordings. The arrays are made of biocompatible-only materials to the brain, thus the glial response is minimal. They perfused a GABA A receptor antagonist (Bicuculline) on the surface of the brain and recorded the spikes (epileptiform activity) from the transistor, a surface electrode, and a Ir-penetrating electrode. The transistor and electrode recordings confirms that both devices record LFPs, with higher SNR from the transistor, showing it can record small and more local activities, the next question is what new information can be revealed by higher SNR?

John I. Broussard, Kechun Yang, Amber T. Levine, Theodoros Tsetsenis, Daniel Jenson, Fei Cao, Isabella Garcia, Benjamin R. Arenkiel, Fu-Ming Zhou, Mariella De Biasi, John A. Dani. (2016). Dopamine Regulates Aversive Contextual Learning and Associated In Vivo Synaptic Plasticity in the Hippocampus. *Cell Reports*, 14 (8), 1930-1939. https://doi.org/10.1016/j.celrep.2016.01.070.

- They looked at dopamine innervation of the hippocampus from the midbrain to observe learning during inhibitory avoidance (IA) training, in this experiment mice received a footshock upon entering the dark side of a training chamber from the lighted side (we know that mice prefer the dark site, unless they're trained to avoid it by fear conditioning), showing the synaptic plasticity in the CA1 circuit with a D1 dopamine receptor agonist and antagonist *in vivo* in freely moving mice and in ex vivo hippocampal slices. The results indicate that dopamine-receptor signaling during an aversive contextual learning regulates memory retention, and likely underlie learning. They identified a sparse direct projection of midbrain dopamine neurons to the hippocampus from the ventral tegmental area (VTA) and the substantia nigra (SN), injecting a D1/D5 receptor antagonist prior training, inhibiting D1-like receptor showed it prevents IA long-term synaptic potentiation (decreased approach latency compared to control), they also observed an increased in the AMPA/NMDA ratio in the CA1 area of pyramidal neurons but not from dentate gyrus granule cells, demonstrating an association between learned avoidance and the CA1 area. Dopamine agonist enhanced retention of a footshock when tested 72 hr after training, suggesting that elevated dopamine activity enhances retention at a longer retention interval. They also showed that beta adrenergic signaling did not significantly influence memory retention.

Rey, H. G., Pedreira, C., & Quian Quiroga, R. (2015). Past, present and future of spike sorting techniques. *Brain research bulletin*, *119*(Pt B), 106–117. https://doi.org/10.1016/j.brainresbull.2015.04.007

- This paper describes different strategies to do spike sorting after data collection from extracellular recordings. This analysis part is crucial for the understanding of the signals detected, how to you know where the spike is coming from? Because the electrical potential changes measured reflect the dynamics of the neural tissue surrounding the electrode and so the signals obtained can come from different neurons plus background activity from neurons further away (Local Field Potentials, LFP). The detected spikes are grouped based on their shapes, each then associated to a single unit (neuron), or if superimposed then multiunit. The goal is to build an algorithm to validate spike sorting automatically of large neural populations. They discuss current spike sorting strategies, challenges, and an alternative approach. They also mention that the development of spike sorting algorithms should go in hand with developments in recording techniques, for example using a wireless interface with the capacity to transmit full broadband signals.

Henze, D. A., Borhegyi, Z., Csicsvari, J., Mamiya, A., Harris, K. D., & Buzsáki, G. (2000). Intracellular features predicted by extracellular recordings in the hippocampus in vivo. *Journal of neurophysiology*, *84*(1), 390–400. https://doi.org/10.1152/jn.2000.84.1.390

- Here they used a multichannel tetrode array to detect and record extracellularly and a micropipette to record intracellularly from hippocampal CA1 pyramidal cells and interneurons in anesthetized rats. The goal of this paper was to show the relationship between intracellular action potentials and extracellular spikes, by recording both simultaneously. The results showed that extracellularly recorded spike reveals information about the shape of the intracellular action potential and membrane polarization, and that a single tetrode placed in the CA1 pyramidal layer should be able to simultaneously record from ~100 neurons.

Montezinho, L. P., Castro, M. M., Duarte, C. B., Penschuck, S., Geraldes, C. F., & Mørk, A. (2006). The interaction between dopamine D2-like and beta-adrenergic receptors in the prefrontal cortex is altered by mood-stabilizing agents. *Journal of neurochemistry*, *96*(5), 1336–1348. https://doi.org/10.1111/j.1471-4159.2005.03654.x

- Here researchers studied the effects of three mood-stabilizing drugs (lithium, carbamazepine, and valproate) on the dopaminergic and adrenergic systems, particularly on D2-like and B-adrenergic receptors, in vitro and vivo data was collected from cortical neurons and prefrontal cortex in rats. D2 and B-adrenergic receptors are G-coupled receptors that transduce extracellular stimuli to intracellular signaling events. For the *in vivo* part, they implanted cannulas into the brain, positioning the probe tip in the PFC, basal cAMP levels were taken in freely-moving rats, then compared to data obtained in cultured cortical neurons. Both in vivo and in vitro showed that there is a cross-talk between D2-like and B-adrenergic receptor activities in the rat brain cortical regions, when D2 is activated, B-adrenergic receptors are inhibited, both are co-localized in the PFC and protein levels changed by each drug.

Relevant Websites

https://www.jove.com/video/55940

- This is a video article from JOVE that shows a multi-site *in vivo* electrophysiological recording method.

https://www.psychogenics.com/services/in-vivo-electrophysiology/

- This is a research company that carries out preclinical research and development in CNS and orphan disorders. Here I found a summary of *in vivo* Electrophysiology.

https://youtu.be/SBSJGdLhgE4

- I used YouTube to watch videos of *in vivo* techniques, this video is called "Observing the freely behaving brain in action" and it is from a neuroscience research institute called Caesar that is associated with the Max Planck Society.

https://www.researchgate.net/post/Can-any-one-suggest-some-basic-in-vivo-electrophysiology-book-or-papers

- I used this website to find out what researchers were talking about *in vivo* electrophysiology techniques.

https://acroscell.creative-bioarray.com/neuronal-in-vivo-assays.html

- I used this website to read about neuronal in vivo assays, animal behavior testing, and basic neuronal activity.

Florida State University Libraries (fsu.edu)

- I used FSU library to find books relevant to my topic, for example I used the following e-book: Carter, Jennifer Shieh, Farra, N., & Harris, G. (2015). Guide To Research Techniques In Neuroscience (Second Edition.). Academic Press.
    - I used chapter 3 & 4.