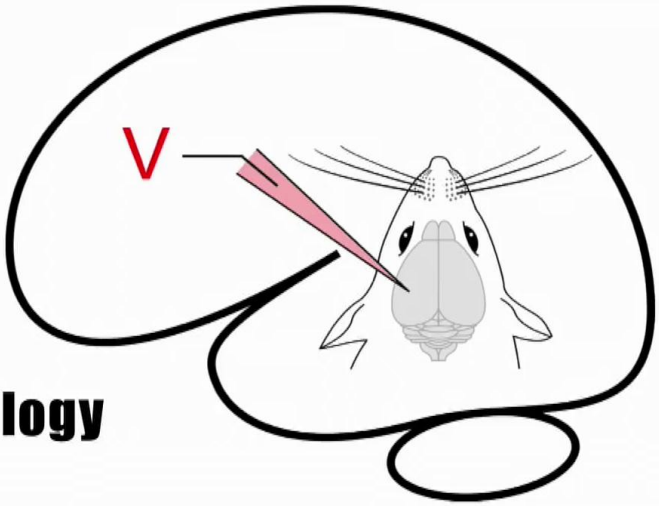
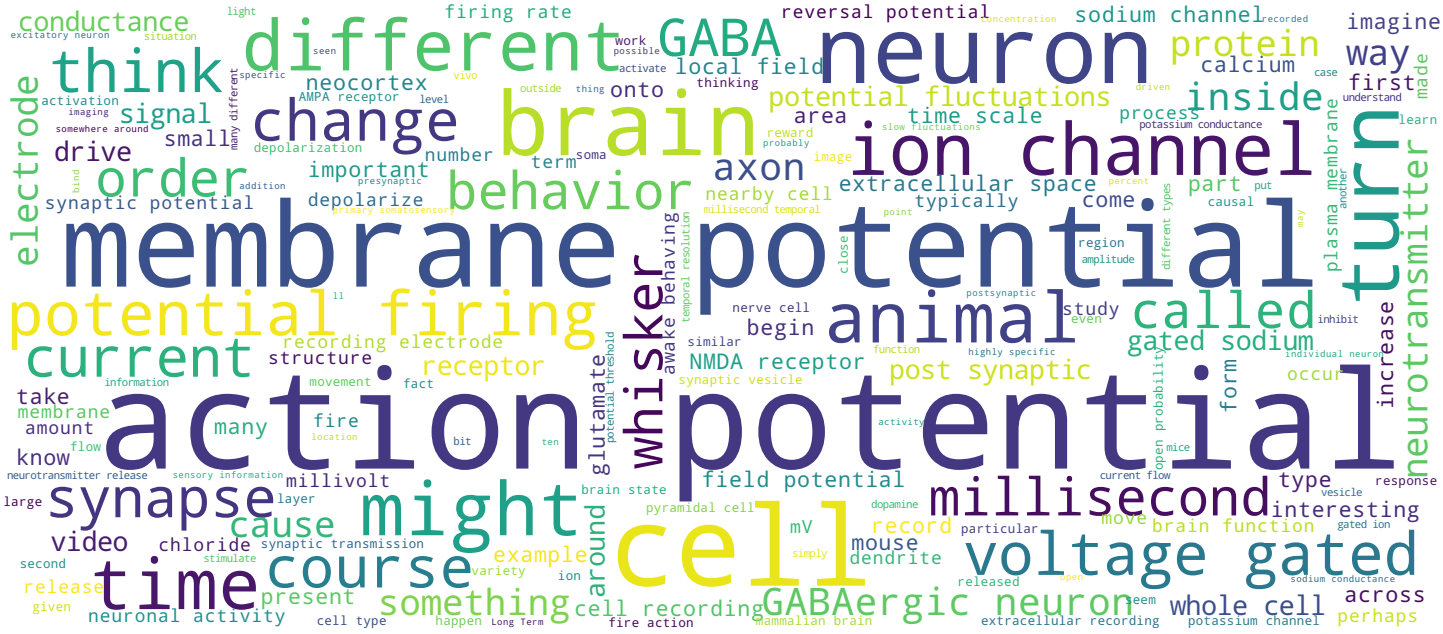


6.4 *In vivo* electrophysiology

Cellular Mechanisms of Brain Function

Prof. Carl Petersen



Search MOOC

Video

EPFL

In vivo electrophysiology

Cellular Mechanisms of Brain Function

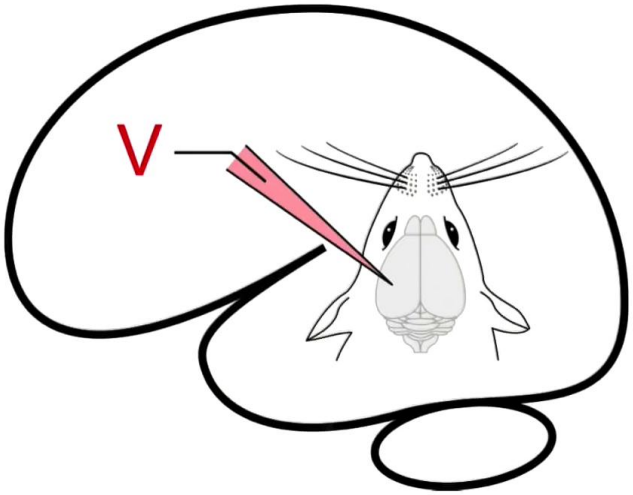
In the last video we discussed optical techniques for measuring brain function. And we found that this provided many exciting opportunities for measuring neuronal activity at a large number of different scales. There are however, also many limitations to optical measurements of neuronal activity, perhaps the most obvious one is that light doesn't penetrate very far into the brain, and so, imaging below 1 millimeter depth inside the brain, is extremely difficult unless one is prepared to take some more invasive techniques like endoscopy. Equally, if we think about two-photon calcium imaging as a way to resolve action potential firing in individual neurons, it turns out that the temporal resolution, because it's a scanning technique, is relatively low. And typically one has something like 100 millisecond temporal resolution and perhaps not even the ability to see every spike. Most of the calcium signals that are reported at the moment, are probably from bursts of action potentials. So although there's enormous excitement about imaging the brain in action, there are also many limitations. Whereas, electrophysiology is a much more invasive technique that involves the introduction of an electrode into the brain, it also has a number of advantages.

Notes

Summary

0m 05s

Extracellular and intracellular recordings



Cellular Mechanisms of Brain Function

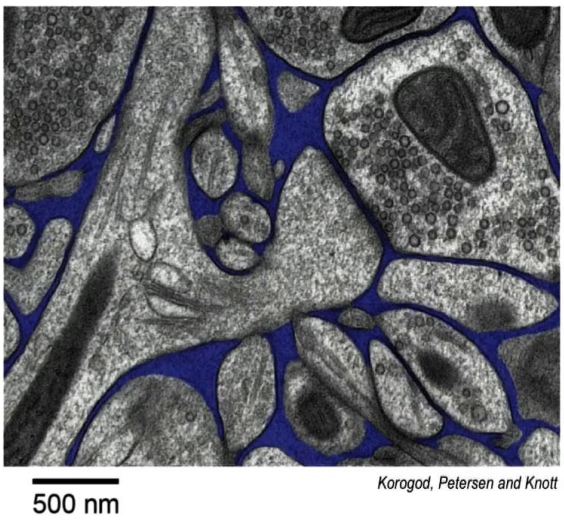
The temporal resolution of electrophysiology is unsurpassed, and it's easy to record signals at several kHz, and so, we can define neuronal activity with millisecond and submillisecond resolution. Equally, it's relatively easy to insert electrodes into any desired part of the brain, and so, we're not limited to studying the upper layers of the neocortex. If we insert an electrode into the brain, it could land either inside a cell, in which case we'd have an intracellular recording of membrane potential. Or, it could land in the extracellular space. And it turns out that are interesting electrophysiological signals in both of these compartments. It turns out that intracellular recording is much more difficult than extracellular recording. And we begin by thinking about extracellular signals in this video.

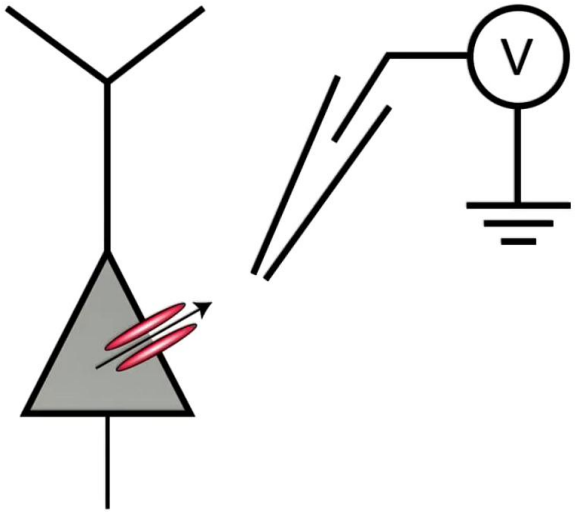
Notes

Summary

1m 29s

Extracellular potentials





Cellular Mechanisms of Brain Function

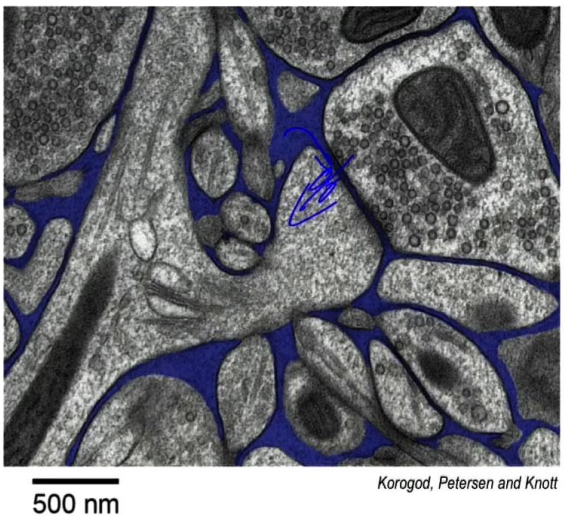
If we imagine taking either a glass electrode filled with extracellular fluid, or perhaps a metal electrode that has a small metal tip, then we insert that into the brain, and if it lands in the extracellular space, then we'll record an extracellular potential. Now to date we've considered the extracellular space as being at zero millivolts and isopotential. It turns out that that's not quite true. And the reason is somehow intuitively gathered if we look at this electron micrograph. The extracellular space that's drawn in here blue, and surrounding the cell compartments, has actually got relatively narrow diameters. Of course, it extends throughout the entire brain and so the blue forms one single extracellular compartment that accounts for about 20 percent of the volume of the neuropil. But nonetheless, the individual conduits through which extracellular currents need to flow, is actually relatively small. And so, there's some resistance involved in terms of extracellular currents. And if there's a resistance in currents then there must also be potential differences across space in the extracellular field.

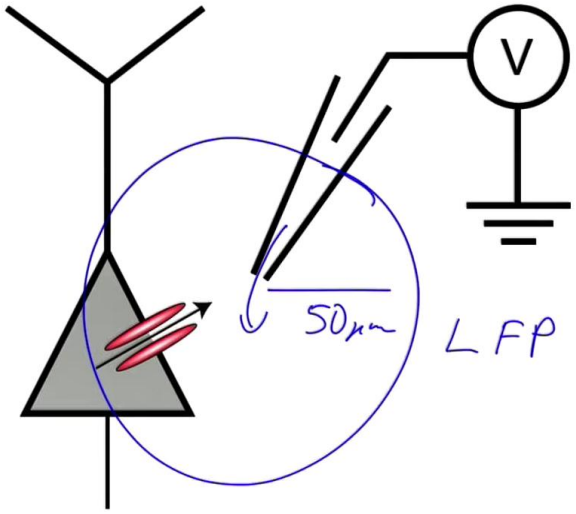
Notes

Summary

2m 23s

Extracellular potentials





Cellular Mechanisms of Brain Function

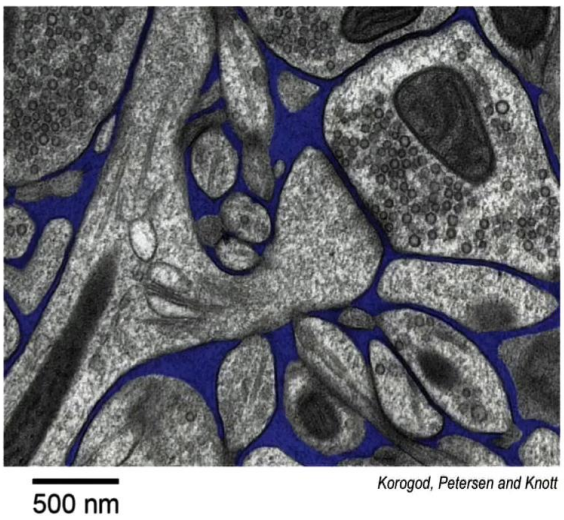
And so if we insert this electrode into the extracellular space, and we measure the potential relative to some remote area of the brain, it turns out that we'll see potentials that change over time. And there are two different types of potentials that are measured extracellularly. One type of potential results from synaptic transmission. And so here we see a synapse, and if glutamate is being released here, this will then activate AMPA receptors, and there'll be synaptic currents that flow in. And that synaptic current of course, needs to come from the extracellular space. And so there's a flow of current from the extracellular space into the cell, and so that could then be measured through a change in potential in the extracellular field. If many synapses are active simultaneously, then we'll see something on our extracellular recording electrode that samples a volume of something like 50 micrometers from around the recording tip. So that's one type of potential that's measured in the so called local field potential. And that's dominated by synaptic potentials. Another type of signal is when the cell fires an action potential.

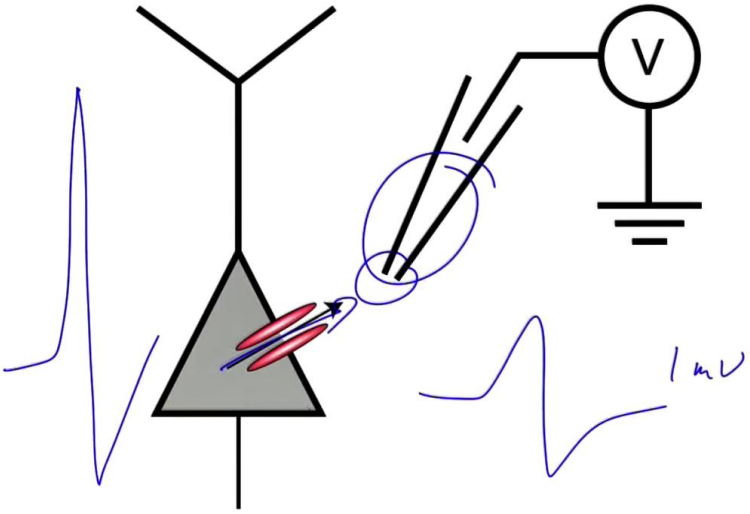
Notes

Summary

3m 41s

Extracellular potentials





Cellular Mechanisms of Brain Function

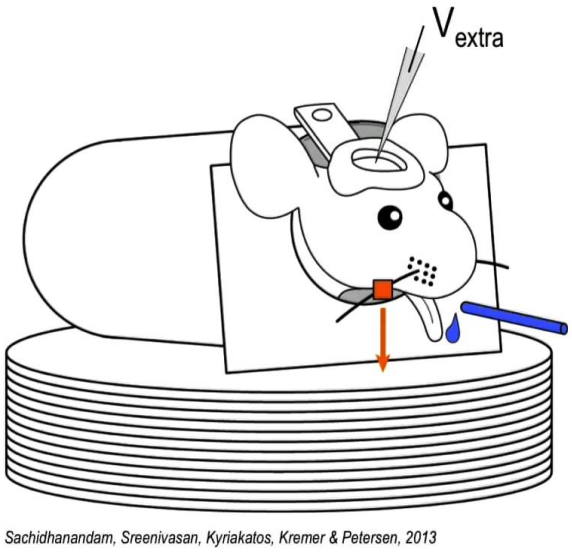
And particularly around the soma, there's a large number of voltage-gated sodium channels and potassium channels, because the surface area is so large, this creates a large, fast, inward current. On the rising phase of the action potential, sodium floods into the cell and again, those potentials are coming from extracelluar space and can be detected here in our extracellular recording electrode. Again, on the repolarizing phase, potassium leaves the cell, and again, that creates current flow in the extracellular space, causing potentials, and we see small signals in the extracellular space typically around 1 millivolt in amplitude but that depends very heavily on where that tip of the electrode is, relative to the somatic location. So extracellularly, we can record local field potentials that are summated, averaged synaptic potentials within a given volume of the brain. And action potentials that relate to the firing of spikes, and individual nerve cells that are very close to the recording tip of your electrode.

Notes

Summary

4m 59s

Extracellular recording of action potentials



Sachidhanandam, Sreenivasan, Kyriakatos, Kremer & Petersen, 2013

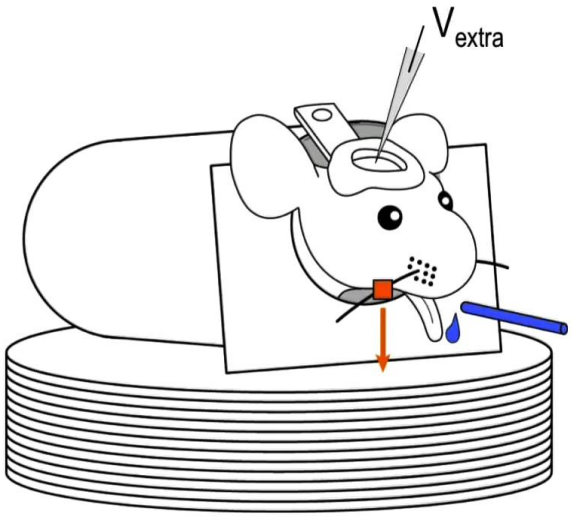
Here is an example of an extracellular recording of action potential firing in an awake behaving mouse. Similar to the imaging situation, it's easiest to record in head-restrained mice. And so here is the implanted metal head holder the head of the mouse is held still, the neurons are moving less than a few microns inside this awake behaving animal, We can insert our electrode, in this case a glass electrode, that we move into the brain, we touch some cellular membranes, we move around until we find cells that fire action potentials. That can typically take a bit of searching. The local field potential is always there as soon as you put the electrode into the brain. But finding cells that fire action potentials can sometimes take a bit of hunting. The animal here is trained to perform a very simple sensory motor task. We stimulate the whisker, that's of this orange time, that drives some action potential firing in the brain, we're recording in the somatosensory barrel cortex, where the whisker pathway signals to in the neocortex. Some action potentials are fired. And we can resolve these action potentials with millisecond temporal resolution.

Notes

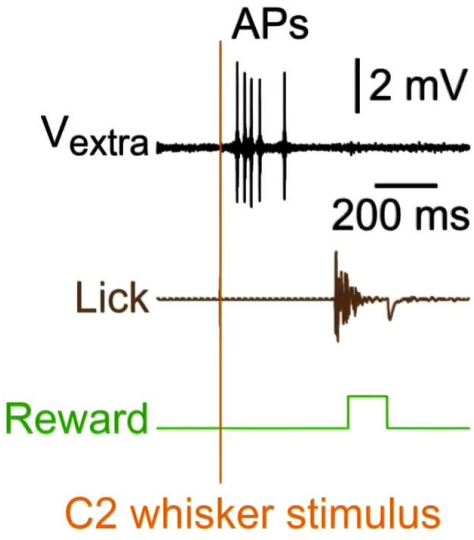
Summary

6m 12s

Extracellular recording of action potentials



Sachidhanandam, Sreenivasan, Kyriakatos, Kremer & Petersen, 2013



Cellular Mechanisms of Brain Function

And so we can follow here, a series of five action potentials that are evoked by the whisker stimulation and at some later time, the animal licks from this reward spout, when monitoring movements of this with piezo film and we see the tongue contacting here and reward is being delivered. This is what this animal was trained to perform, and so we can correlate the spiking activity in the brain with the behavioral performance of the animal. And sometimes the animal won't lick, and it turns out less spikes are fired in the brain at that time. And so we can begin to correlate the action potential firing in the brain with the behavior from the animal, fulfilling one of our needs, in terms of getting a causal and mechanistic understanding of how the brain works.

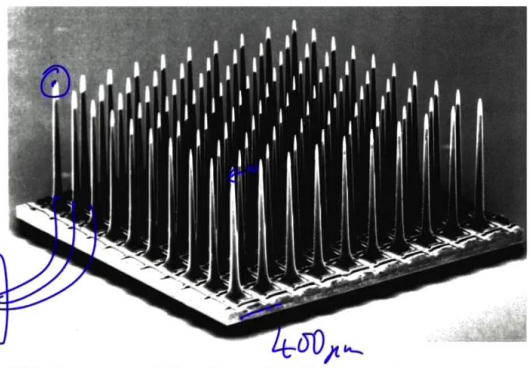
Notes

Summary

7m 27s

Multichannel extracellular recordings

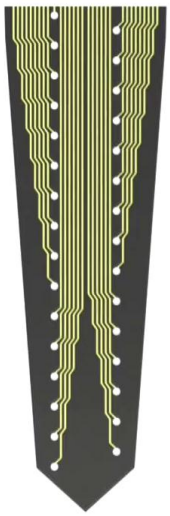
Electrode arrays



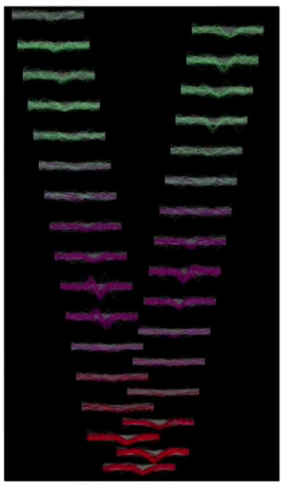
Utah array, Blackrock Microsystems

Hochberg et al., 2012
http://www.youtube.com/watch?v=ogBX18maUiM

Silicon probes



Neuronexus



Lapray and Petersen

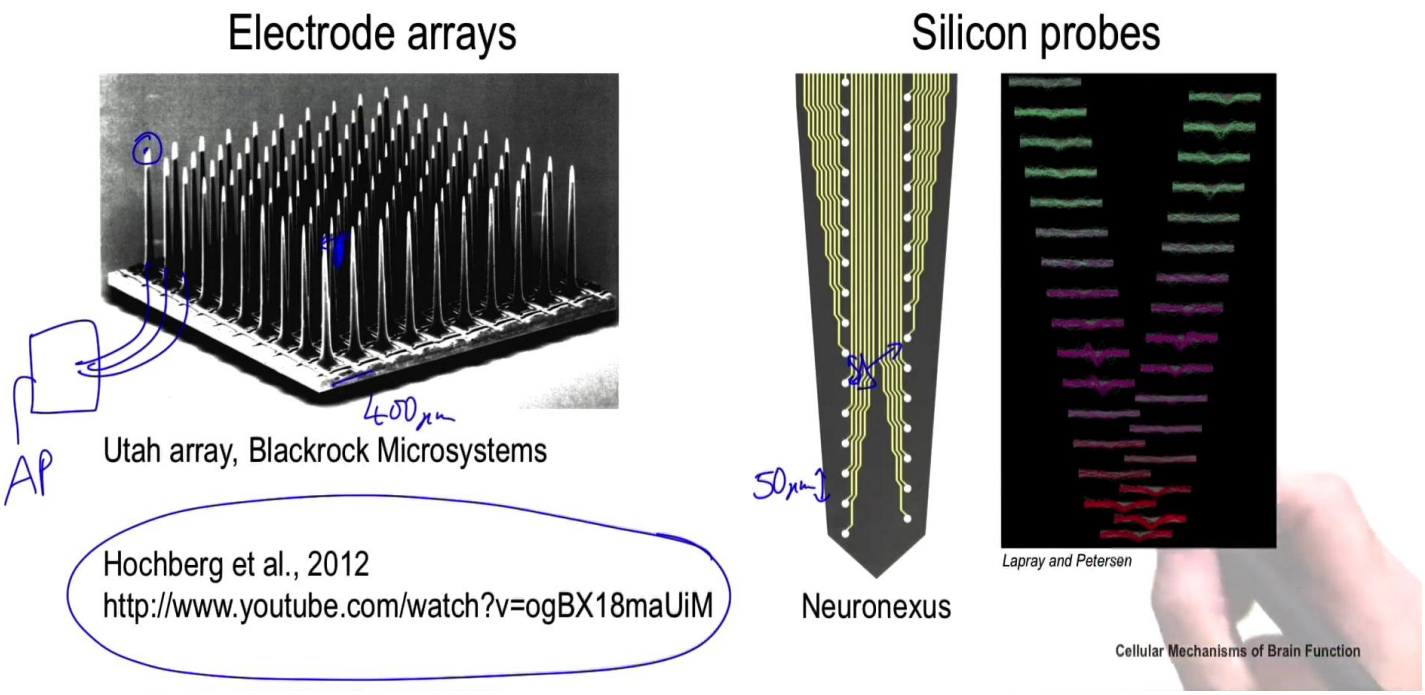
Now because extracellular recordings are technically, relatively easy to carry out, it's possible to record in parallel from many individual electrodes. And so scientists have developed electrode arrays where it become possible to record from many individual sites at the same time. This is the so called Utah array that has 10 by 10 electrodes spaced at 400 micrometers apart, so each electrode tip here, is 400 micrometers away from each other. And the exposed metal surface here, on the tip of the electrode, is where the potentials are being recorded. And of course, each one of these is then being fed into an amplifier and out come action potential waveforms with millisecond temporal precision. And so we can now measure across many millimeters of brain activity the action potential firing of cells near to these recording tips. And this recording technology, has already been tested in humans, in patients that have Tetraplegia. and there's a remarkable video that I encourage you to look at associated with the publication of Hochberg et al. in 2012, where they explain how they use this electrode array as a neuroprosthesis for driving a robotic arm.

Notes

Summary

8m 15s

Multichannel extracellular recordings



And a Tetraplegic woman has her first drink of coffee by controlling the robot through her neuronal activity and without any of her own muscle activity. So do have a look at this video if you have time. The electrode spacing here, is relatively far. 400 micrometers means there's a lot of neuronal tissue in-between these electrode sites that we have no access to from the electrophysiological data from this electrode array. And so, scientists have been working to make higher density recording probes and in particular, there's been a focus on silicon wafer probes where micro wires can be drawn in and exposed metal recording sites can be placed at relatively high density. And in this particular probe, the individual recording sites are around 50 micrometers away from each other. And now we're getting close to the scale of individual neurons. You can imagine a nerve cell being located somewhere around here, it would be a bit smaller than I've drawn, firing an action potential, and the action potential signal might be detected on multiples of these electrodes. In fact, that's what you see here. The purple traces here are recorded simultaneously and you'll see that there's an action potential waveform that's being recorded simultaneously on multiple different electrodes.

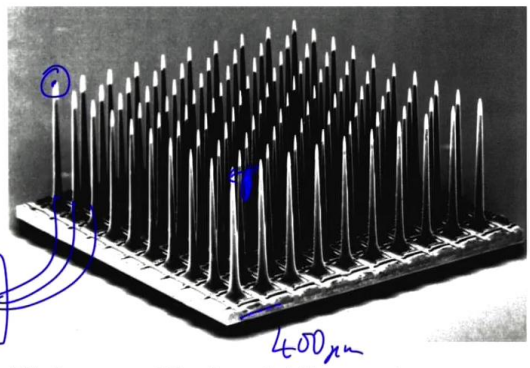
Notes

Summary

9m 40s

Multichannel extracellular recordings

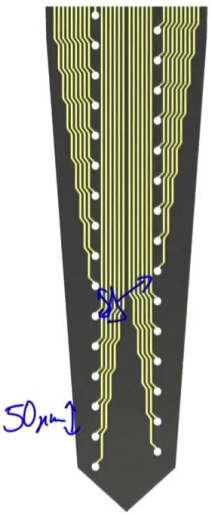
Electrode arrays

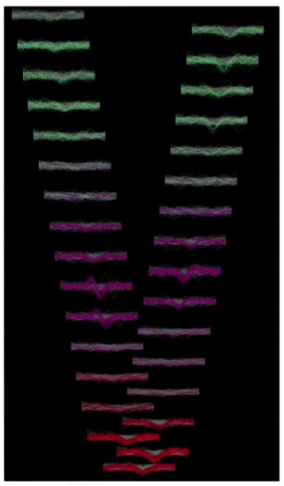


Utah array, Blackrock Microsystems

Hochberg et al., 2012
http://www.youtube.com/watch?v=ogBX18maUiM

Silicon probes





Lapray and Petersen

Neuronexus

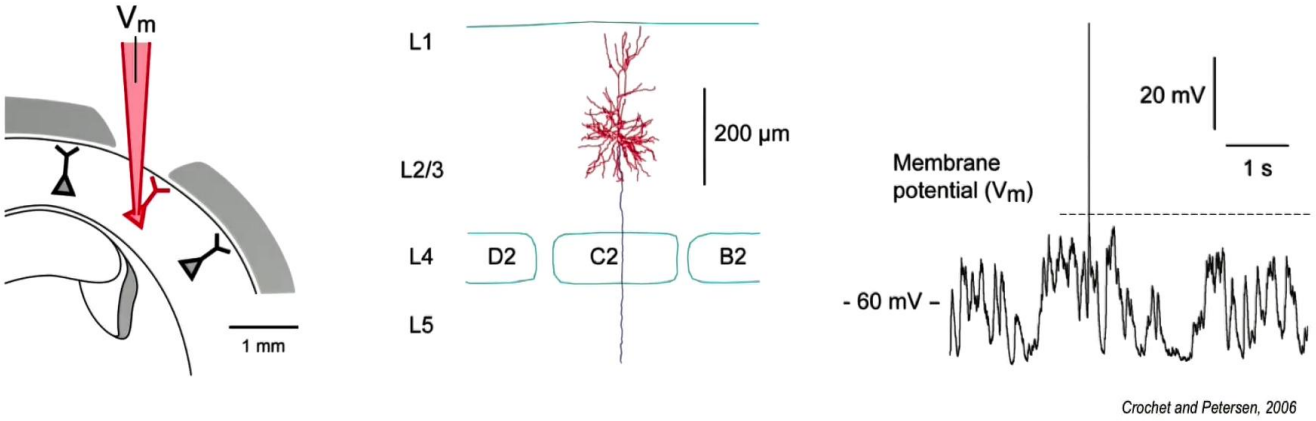
And that allows then, one to triangulate, and try to decipher the different action potential waveforms from many different neurons, sitting close to these different recording sites. And then one can then try and extract information from many neurons that are sitting in the vicinity of this silicon recording probe. So using multichannel extracellular recordings, it's possible to find and define the spike times of many different neurons with millisecond temporal precision in the living and behaving mammalian brain. Importantly, these technologies can also be applied to freely moving animals. And so one can study a variety of different behaviors using these extracellular recording techniques. However, if we want to get a causal and mechanistic understanding on how the brain works, we need to understand, what makes individual nerve cells fire action potentials. And for that we need access to the membrane potential. We need intracellular recordings.

Notes

Summary

11m 02s

In vivo whole-cell recordings



Crochet and Petersen, 2006

Cellular Mechanisms of Brain Function

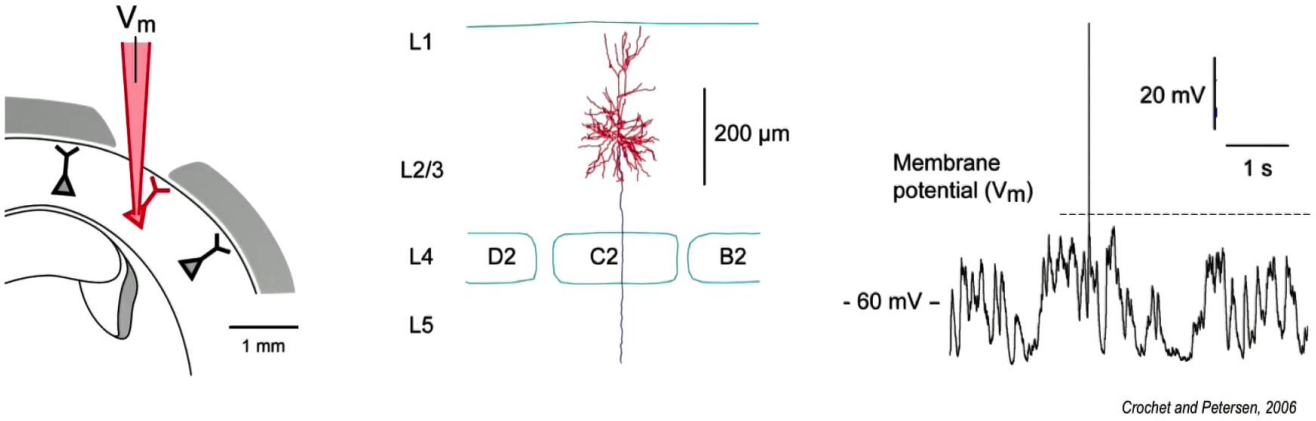
In turns out that the whole-cell recording technique that we've already seen working in brain slices also turns out to work well in *in vivo*. And so we can drill holes in the skull, make a so called craniotomy lower glass electrodes, filled now with a potassium-filled intracellular solution. We move that electrode up onto an individual neuron, we suck onto it, we get the gigaseal, we then break into the whole-cell recording configuration, and presumably, because of the mechanical stability of the whole-cell recording configuration this also turns out to work remarkably well *in vivo*, in awake, behaving animals, and so, although the brain is moving around by a few microns, it's possible to record membrane potential with very high quality in awake, behaving animals. Another nice feature of the *in vivo* whole-cell recording technique is that we can fill the cell with dye. And so the intracellular solution in the pipette, also fills the cell that we're recording from, that means we can visualize the structure and identify what cell it is we're recording from. And then this particular example, we're recording from a layer 2/3 pyramidal cell located in the C2 barrel column of mouse primary somatosensory cortex.

Notes

Summary

12m 03s

In vivo whole-cell recordings



Crochet and Petersen, 2006

Cellular Mechanisms of Brain Function

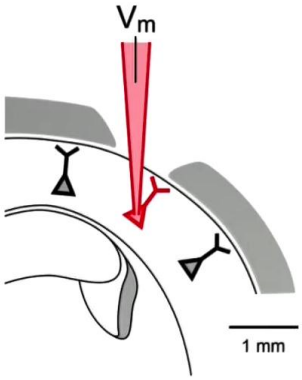
And it turns out that the membrane potential fluctuations that are recorded from the cell when an animal is awake but not doing anything, not performing any task, there are a variety of interesting membrane potential dynamics that can be recorded. There are membrane potential fluctuations that are occurring on relatively long time scales so it's worth looking here at the time scale-- this is one second. So there are fluctuations that are occurring on several second time scale. And these are huge in amplitude. So this is 20 milivolts on the Y axis, and so the fluctuations here, are from something like minus 70 to minus 50 millivolts so the membrane potential, swinging some 20 to 30 millivolts on this time scale in seconds. And there also much faster changes in membrane potential. So here, the membrane potential hyperpolarizes by more than 20 millivolt in just a few milliseconds. And so, membrane potential fluctuations, on a large scale of many tens of millivolt, occur on a variety of timescales, both slow at the second time scale, and also on the millisecond timescale. These membrane potential fluctuations are largely being driven by the synaptic inputs that are arriving on these neurons.

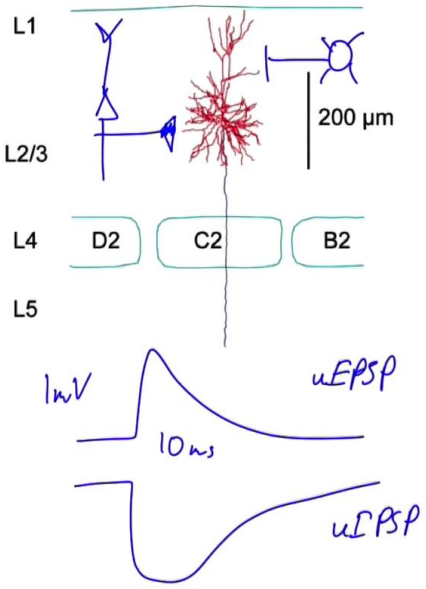
Notes

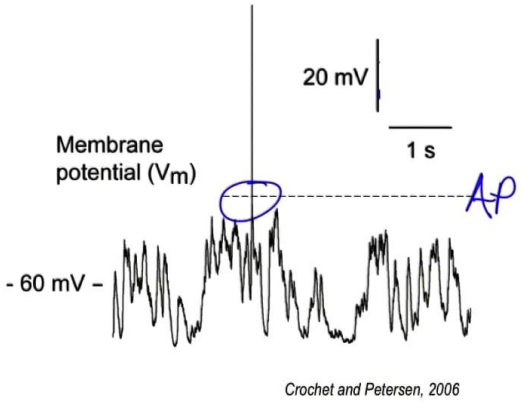
Summary

13m 26s

In vivo whole-cell recordings







Cellular Mechanisms of Brain Function

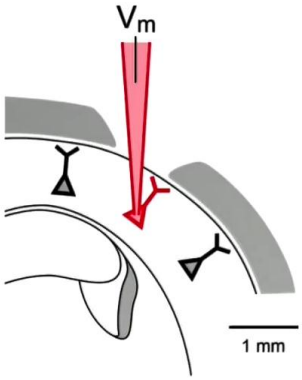
And so we know that there are many surrounding cells around the cell, some of which are synaptically connected and here would be a glutamatergic input, and from previous studies we know that the unitary EPSPs that are arriving from nearby cells typically have an amplitude of around one millivolt, and they last some 10 milliseconds or so. We also know that there are GABAergic neurons sitting around that release GABA and inhibit this neuron, and they typically have slightly longer time courses, also of around one millivolt in amplitude and perhaps some 10 to 20 milliseconds. And these unitary events, are then arriving across a somatodendritic arborization of the cell driving the membrane potential up and down through this neuronal computation of summation of post synaptic potentials. And every now and then, the membrane potential reaches the action potential threshhold. And when it hits threshold, an action potential is emitted, driven by the voltage-gated sodium channels, repolarized by voltage-gated potassium channels. And those action potentials, in layer 2/3 pyramidal cells turn out to be relatively rare events. We have a mean action potential firing rate, of a around 1 Hz.

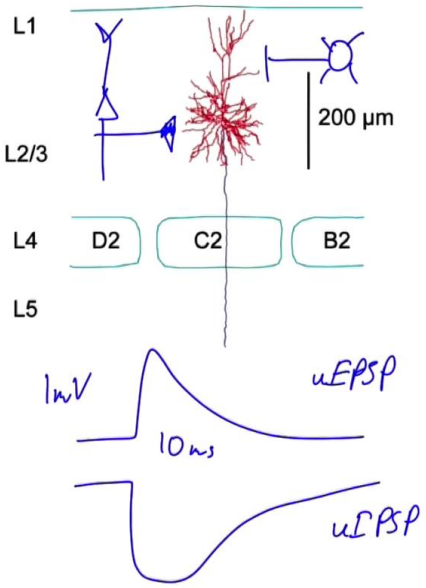
Notes

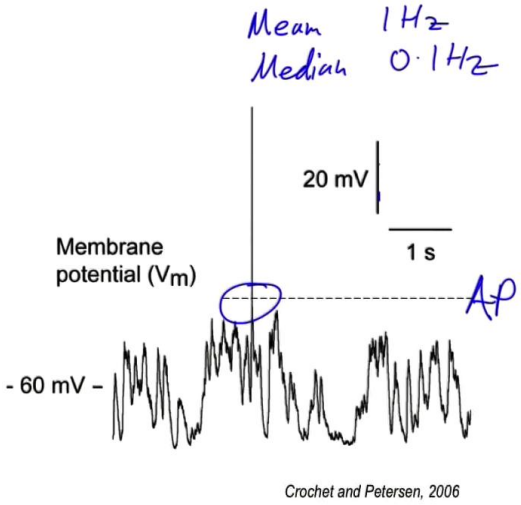
Summary

14m 42s

In vivo whole-cell recordings







Cellular Mechanisms of Brain Function

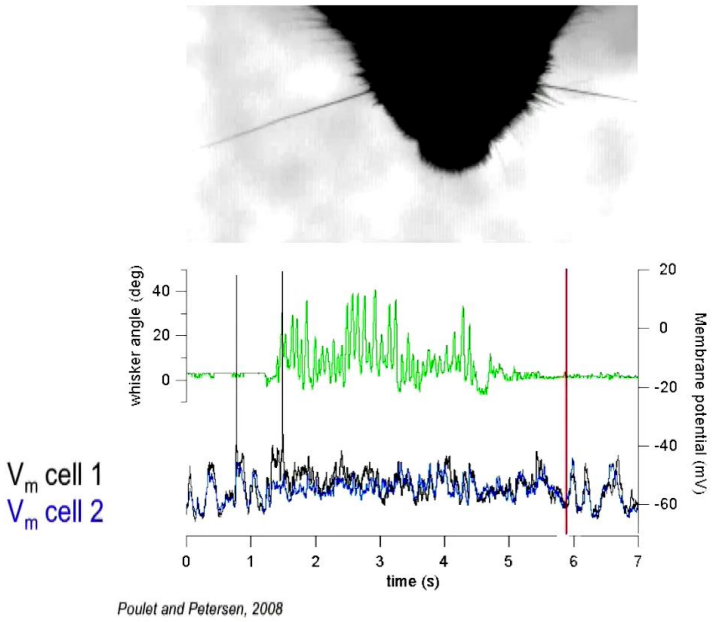
And we have median firing rates of around 0.1 Hz. when mice are resting. This implies that there are a few cells that are firing many action potentials and most of the cells that are firing very, very few action potentials. And we'll return to thinking a bit about what makes excitatory pyramidal cells fire an action potential First, we'll think about these membrane potential fluctuations that we see here in one individual cell. And when we see this pattern of fluctuations, we immediately wonder what's happening in all the other nearby cells. Are these fluctuations happening independently in nearby cells? Or, is there some degree of synchrony?

Notes

Summary

16m 09s

Dual whole-cell recordings



Poulet and Petersen, 2008

Cellular Mechanisms of Brain Function

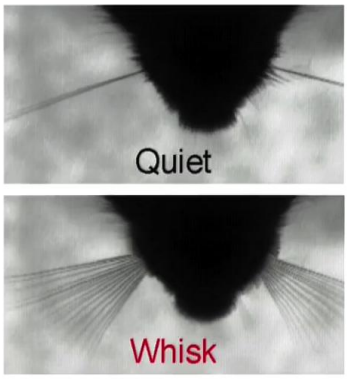
In order to resolve that question, we made dual whole-cell recordings, where we're recording both from a black cell, and a blue cell. And here, we're filming the behavior of the animal, at the beginning of the recording with the animal sitting still, and now it's beginning to actively move its whiskers around. And this is a so called active sensing system where the animal is scanning its immediate environment looking for objects to contact. While the animal sits still, and is not moving its whiskers here, at the beginning of the video, cell one and cell two, are hyperpolarizing and depolarizing almost synchronously with each other. While the animal is moving its whiskers however, the membrane potential fluctuations have lower variance, the slow fluctuations are gone, and if we now look carefully at the membrane potential of the black and blue trace, you might see that they're more independent from each other during this so called whisking period, compared to when the animal is quiet. And here, at the end of the video, the animal stops moving its whiskers, returns to quiet wakefulness, and the slow, highly synchronous fluctuations reappear.

Notes

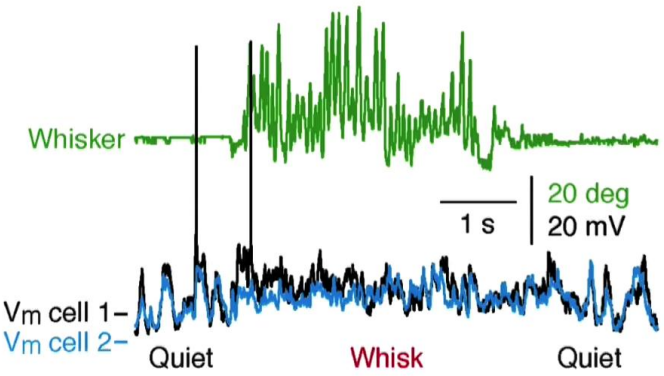
Summary

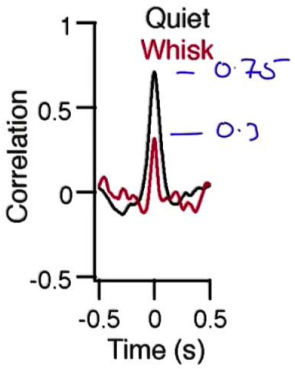
16m 55s

Dual whole-cell recordings



Poulet and Petersen, 2008





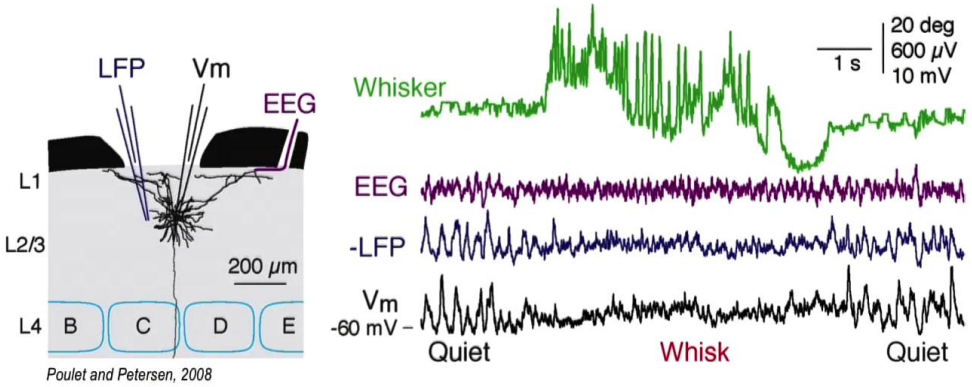
Here's that same data shown as a still image, and again, you see the two membrane potential fluctuations that are highly synchronized. When one cell depolarizes so does the other. When they both hyperpolarize synchronously action potentials however, occur independently, and in this particular trace, only the black cell fires two action potentials, and the blue cell didn't fire action potentials. We can look quantitatively at the correlation of the membrane potentials. And here you'll see that during the quiet phase, there's a very high cross-correlation of membrane potentials, sitting at around 0.75, and during this whisking phase, where it's obvious that the membrane potential fluctuations are less synchronized, it's about half of that. So we're down to somewhere around.3 in terms of the cross-correlation. And that's for one particular recording, but this turns out to be true across many different recordings. And this looks like two different brain states. When the animal is sitting quietly, we pick any two cells, and it turns out that they depolarize and hyperpolarize synchronously. When the animal is actively exploring its environment, those fluctuations are gone, and we get the so called the so-called desynchronized active brain state.

Notes

Summary

18m 04s

Hans Berger observed brain state changes in human EEG recordings (1929).
He found prominent alpha waves in relaxed subjects with their eyes closed.
These slow oscillations disappeared upon eye opening.



Cellular Mechanisms of Brain Function

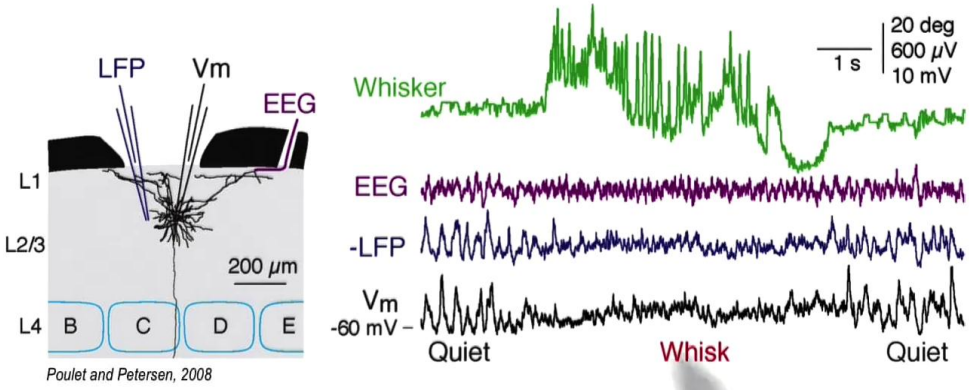
We think that these measurements that have been made in the whisker system of the mouse, may have some relevance to the very first human recordings of an electroencephalogram. Hans Berger in 1929 reported a very interesting pattern of activity across the occipital cortex of human subjects. When the subjects were relaxed with their eyes closed, he would see large amplitude slow fluctuations, so-called alpha waves, recorded in the EEG of the human subjects. When the subjects were alert, looking around with their eyes open, investigating the world around them, those slow fluctuations disappeared. And you could see rapid transitions comparing situations where the alert subject went into a relaxed state with eyes closed. The fast fluctuations transform into slow, highly synchronous alpha waves. And we think that's similar to what we're observing in the whisker system. When the animal is siting still, and not moving its whiskers, we equate this to the eyes closed situation. The mouse is siting there relaxed, not particularly interested in whisker sensory information.

Notes

Summary

19m 26s

Hans Berger observed brain state changes in human EEG recordings (1929).
He found prominent alpha waves in relaxed subjects with their eyes closed.
These slow oscillations disappeared upon eye opening.



Cellular Mechanisms of Brain Function

And the brain goes into slow, relaxed brain states, with slow, large amplitude oscillations in individual neurons, we now know those are highly synchronous with nearby neurons, and that gives rise to a local field potential because of the highly correlated synaptic inputs arriving on any cell you care to look at here. And so we see something in the local field potential, and even outside with the electroencephalogram, we can also record something that has some correlation to membrane potential and the local field potential. When the animal is actively exploring its world by moving its whiskers in the so called whisking state, we think this is similar to the actively exploring human, with the eyes open, looking at the world around them. In the mouse situation, this results in a desynchronized state, low membrane potential variance, low variance in the local field potential, the slow oscillations have disappeared, and that's because the level of individual cells does lower fluctuations in membrane potential and in addition, these fluctuations here, are now less synchronized with all its surrounding cells, so that tends to cancel out in the local field potential, giving rise to a more flat, so-called desychronized local field potential and electroencephalogram.

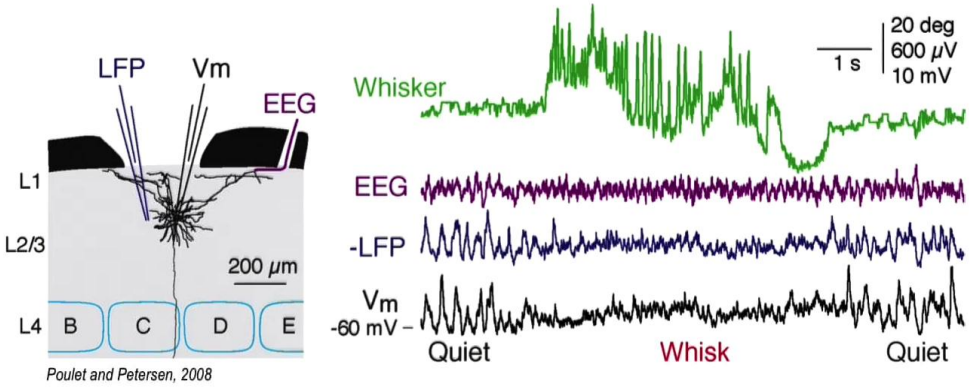
Notes

Summary

20m 43s

V_m, LFP and EEG

Hans Berger observed brain state changes in human EEG recordings (1929).
He found prominent alpha waves in relaxed subjects with their eyes closed.
These slow oscillations disappeared upon eye opening.



Poulet and Petersen, 2008

Cellular Mechanisms of Brain Function

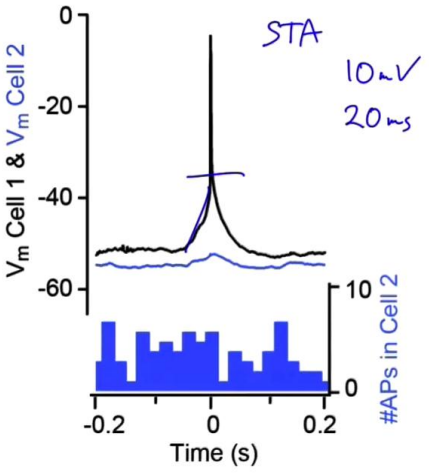
And so by recording in individual and dual recordings of cells in awake, behaving mice, we think we've come up with a cell explanation for some of the first human EEG recordings that reveal profound brain state changes depending upon the behavior of the human. And we now see the same thing in mice depending on the [unclear] behavior of the mice, there are also obvious brain state changes. And now in mice, we can of course go and look mechanistically and try to understand what's different about these two different brain states.

Notes

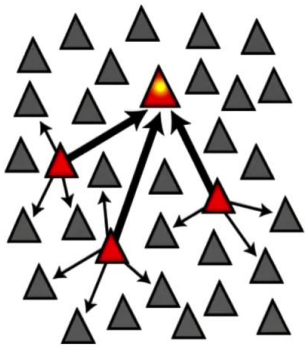
Summary

22m 02s

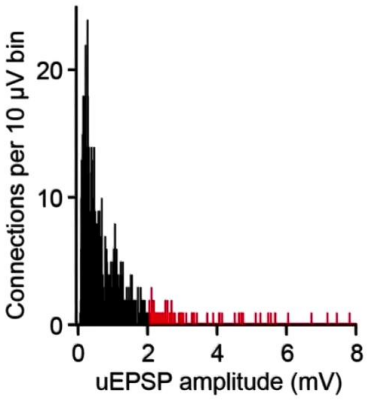
V_m dynamics driving action potential firing



Poulet and Petersen, 2008



The convergence of a few big uEPSPs could drive highly specific action potential firing.



Lefort, Tomm, Sarria and Petersen, 2009

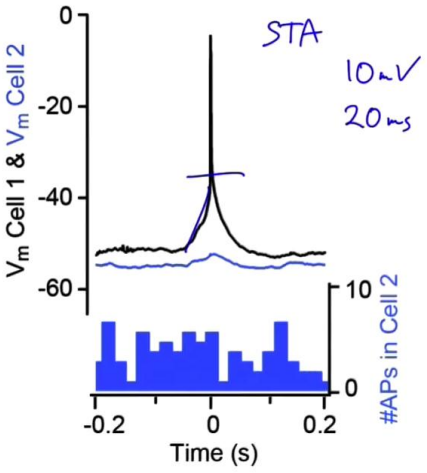
Using membrane potential recordings, we can also study what's happening to neuronal membrane potential that drives action potential firing. And so here, we now look in the black cell that we're recording from. We record the action potentials that occurred in that cell, and we align them all at time zero, and we generate the spike-triggered average waveform. When we do that we see that there's a large depolarization in the cell immediately before it hits action potential threshold. On average, it turns out, excitatory neurons in layer 2/3 of mouse barrel cortex at least, depolarize by 10 millivolts in the last 20 milliseconds before they hit action potential threshold. So there's an important depolarization that arrives immediately before action potential threshold on that tens of millisecond timescale. Now if you look at the second cell that we're recording simultaneously, it turns out that the action potential firing in the nearby cell is uncorrelated, and so in general, although the membrane potential fluctuations of neurons are highly correlated, it turns out that action potential firing in the neocortex is relatively asynchronous, and that there's no obvious correlation in the action potential firing times.

Notes

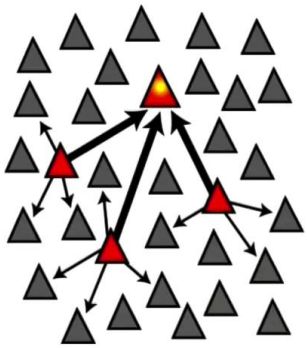
Summary

22m 36s

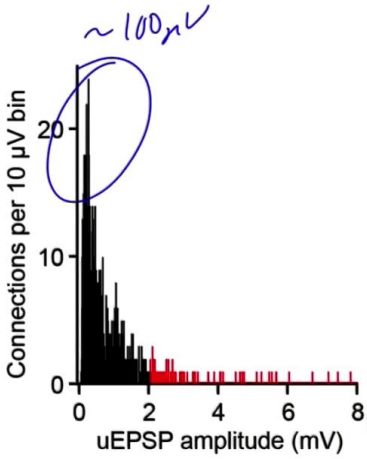
V_m dynamics driving action potential firing



Poulet and Petersen, 2008



The convergence of a few big uEPSPs could drive highly specific action potential firing.



Lefort, Tomm, Sarria and Petersen, 2009

Cellular Mechanisms of Brain Function

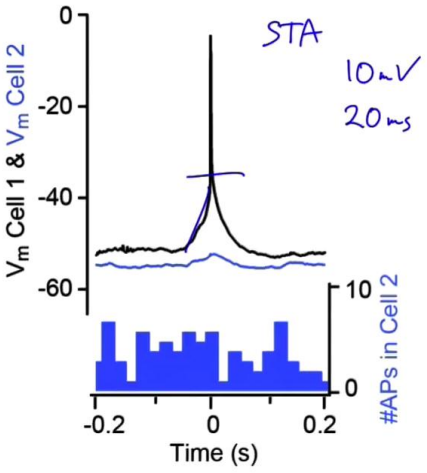
If you look at the membrane potential of the blue cell, it turns out that the membrane potential here isn't depolarizing very much at the time when the cell that fires an action potential depolarizes by some 10 millivolts. And so there's some highly specific input that arise in the cell that fires, that doesn't arrive in the neighboring nearby cells, and that's what then drives highly specific action potential firing with asynchronous firing in nearby cells. How might that come about? Well, we can return and think a little bit about neuronal networks that we've already studied in the neocortex. We know that the synaptic connectivity of exitatory cells is something like 10 percent of its nearest neighbors. And most of the synaptic connections that we've observed if we think about the histogram of the amplitude distributions, most of those synaptic connections are very small-- on the order of 100 microvolts or so. And so most of the output from a given cell onto its synaptic connected neighbors, is actually rather small. But, there's a small population of much larger excitatory potentials.

Notes

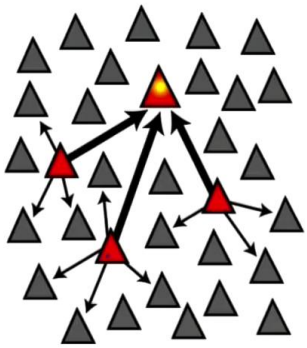
Summary

23m 56s

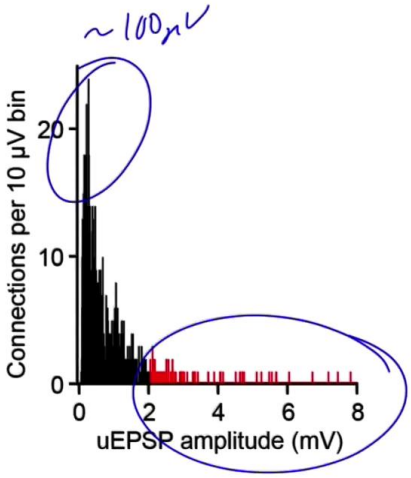
V_m dynamics driving action potential firing



Poulet and Petersen, 2008



The convergence of a few big uEPSPs could drive highly specific action potential firing.



Lefort, Tomm, Sarria and Petersen, 2009

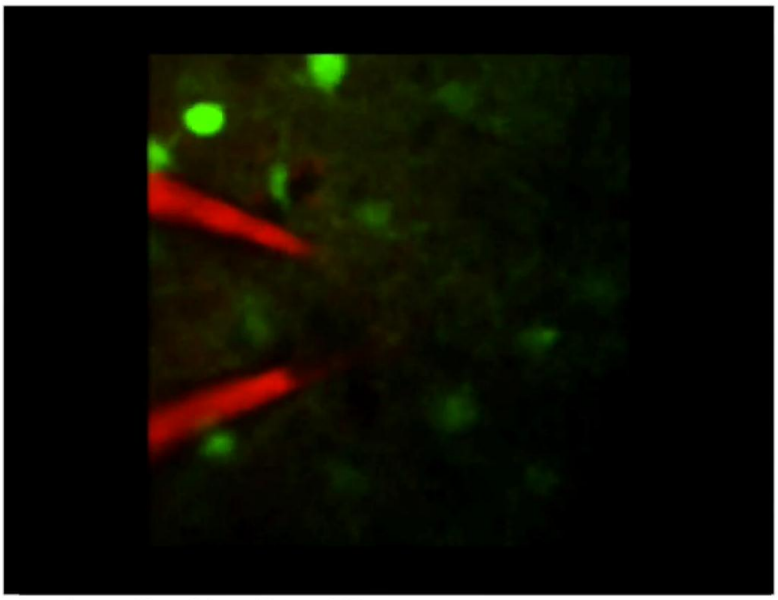
And if you now imagine that we're recording from this cell, and that's our black cell, and it's firing an action potential, we see that's it's depolarizing by some 10 millivolts in the 20 milliseconds before hitting spike. And that could then result from the firing of three nearby cells that happen to have these large, unitary inputs that converge onto the cell here, drive the spiking of that cell. Now, other cells nearby won't fire an action potential because they won't have that very sparse, large amplitude connection. So we probably only have these small, hundred microvolt connections with the rest of the neuronal circuit. And so other nearby cells, might just see very little depolarization. And so in this network which has relatively sparse overall firing of around 1 Hz mean firing rates, we can imagine that the convergence of just a few, big, unitary EPSPs could drive highly specifc action potential firing. And that could be one way in which specific firing of nerve cells can be driven within sparse activity networks. And that's a hypothesis that's currently being investigated by a number of different researchers.

Notes

Summary

25m 12s

Whole-cell recordings and two-photon imaging



Gentet, Avermann, Matyas, Staiger and Petersen, 2010

Cellular Mechanisms of Brain Function

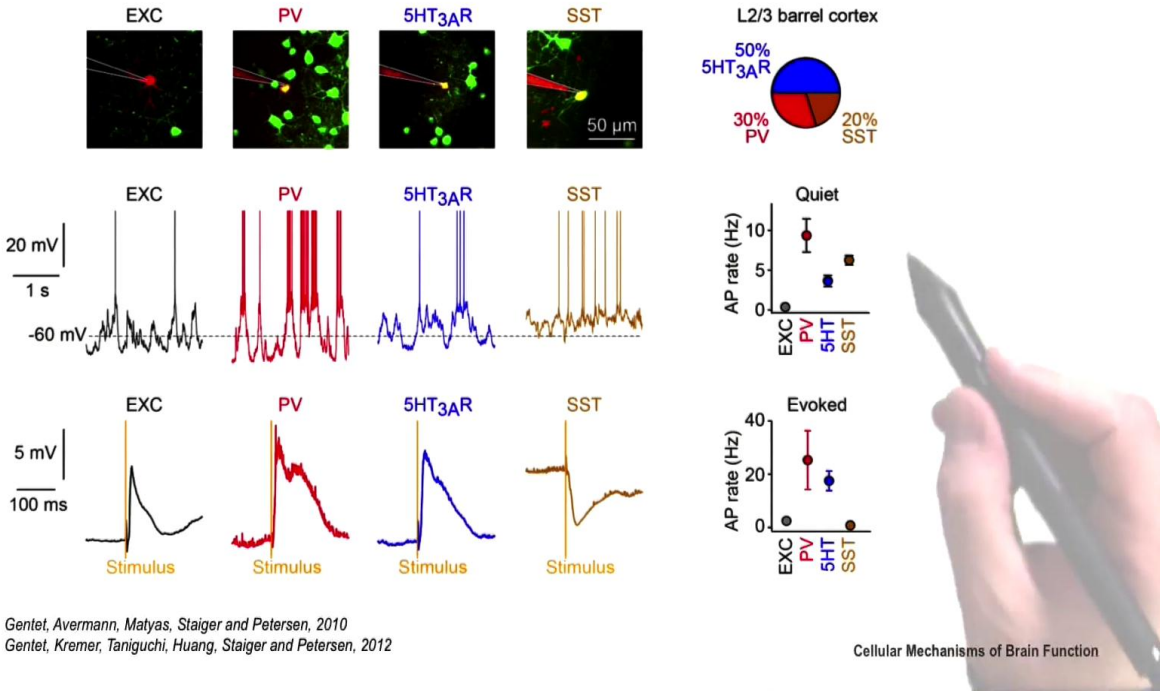
In order to learn more about the membrane potential dynamics of specific cell types, we can begin to combine the power of mouse genetics to photomicroscopy and whole-cell recordings. Here we're looking inside the brain of a mouse with a two-photon microscope, and the green blobs that you see are in fact, GABAergic neurons that are labeled in this transgenic mouse, in which all GABAergic neurons express green fluorescent protein. So the green blobs are around 10 micrometers in diameter, and we're focusing up and down, looking inside the brain of an awake, behaving mouse with a two-photon microscope. You also see that there are two red recording electrodes, and these are whole-cell patch clamp recording electrodes, that have been filled with a red fluorescent dye so we can see these recording electrodes that have been guided in. And two intracellular membrane potential recordings have been made with this patch clamp recording electrodes, and they're from two nearby GABAergic neurons. And so here we can begin to study the membrane potential dynamics in correlations of genetically-defined populations of neurons in the mammalian cortex during behavior.

Notes

Summary

26m 30s

Cell-type specific membrane potential dynamics



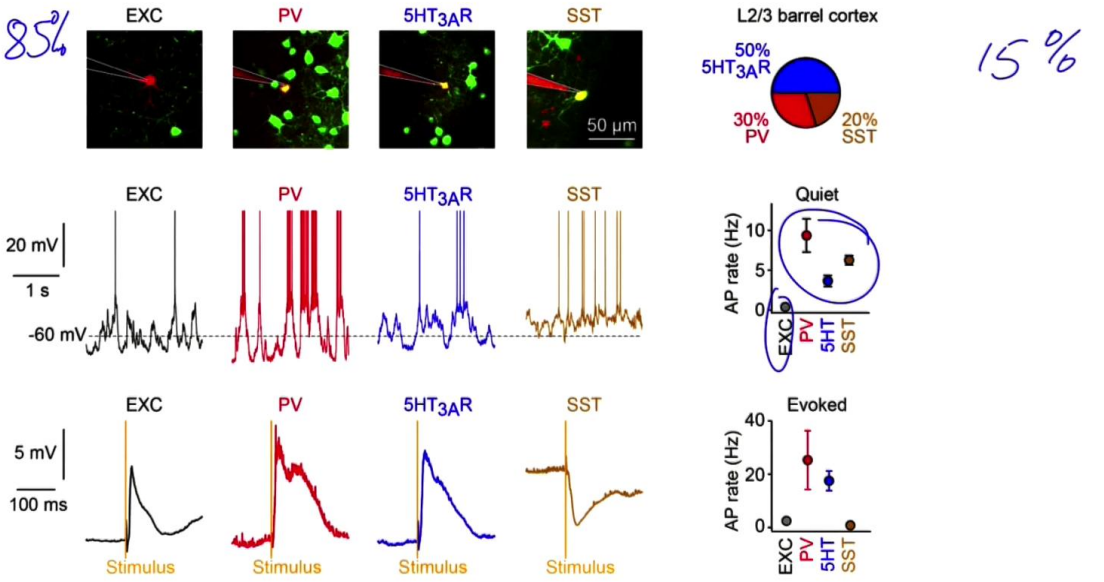
We can then target membrane potential recordings to a variety of genetically-defined types of cells in the layer 2/3 of the mouse barrel cortex. And here we compare four different types of cells. Excitatory pyramidal cells that we've been discussing mainly over this video that has slow membrane potential fluctuations and relatively low action potential firing rates. We can record from parvalbumin-expressing fast-biting GABAergic interneurons. They also have slow membrane potential fluctuations during quiet wakefulness. But they now fire action potentials at much higher rates. There are non-fast spiking GABAergic neurons that have also slow fluctuations and intermediate firing rates. And then there are somatostatin expressing GABAergic neurons that fire at relatively high rates during quiet wakefulness, and don't seem to have the slow fluctuations that the other neuronal cell types have. And the reason the somatostatin cells might not have these slow oscillations, might relate to the fact that they receive strongly facilitating glutamatergic inputs as we discussed a few weeks ago. Altogether, if we think about the action potential firing rates during quiet wakefulness, we'll see that there's a variety of different action potential firing rates in these different types of cells.

Notes

Summary

27m 51s

Cell-type specific membrane potential dynamics



Gentet, Avermann, Matyas, Staiger and Petersen, 2010
Gentet, Kremer, Taniguchi, Huang, Staiger and Petersen, 2012

Cellular Mechanisms of Brain Function

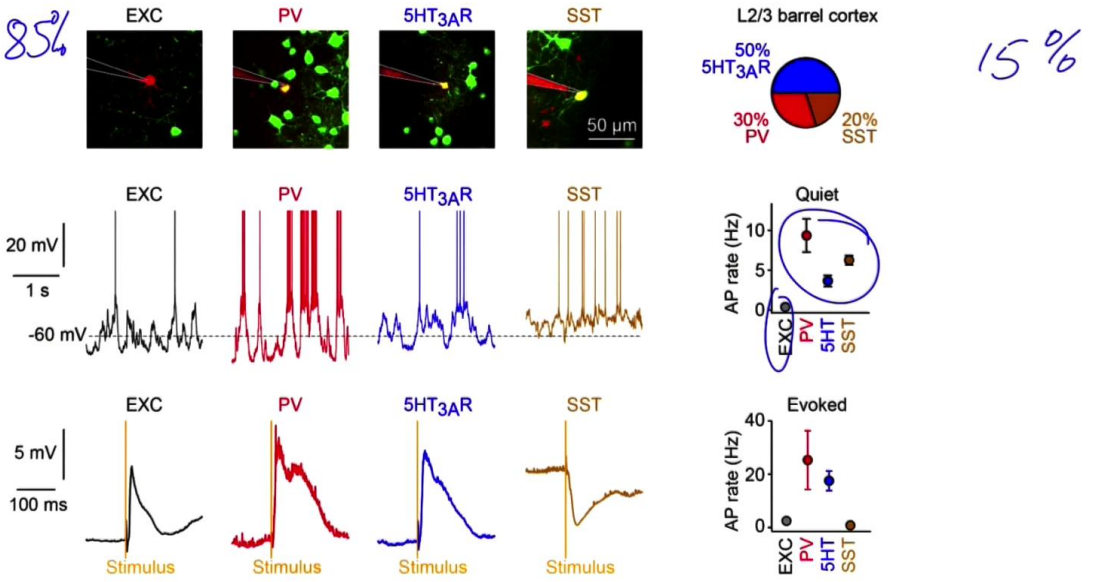
The excitatory pyramidal cells, as I've already mentioned, fire about 1 Hz action potential rates. The parvalbumin at around 10 herz. And the other two types of GABAergic neurons are somewhere in between. Given that the excitatory neurons make up some 85 percent of the population, and the GABAergic neurons make up only some sort of 15 percent of the population, it turns out that if we look at this, that the total number of glutamatergic spikes, compared to the number of GABAergic spikes, turns out to be roughly the same. There's about 10 times as many excitatory neurons, but the GABAergic neurons fire about 10 times as many action potentials. So spike for spike, it's about the same. We can also see what happens when we deliver a sensory stimulus. We're recording in primary somatosensory whisker cortex, and so we here deliver a brief one millisecond whisker stimulus. And that drives a depolarization in exitatory cells, fast spiking parvalbumin expressing cells, and also in the 5H/D3 non-fast-spiking GABAergic cells. They all depolarize in response to the sensory stimulus. The somatostatin cells, again, seems to be the odd ones out. They actually hyperpolarize and reduce their firing rates in response to this particular stimulus.

Notes

Summary

29m 14s

Cell-type specific membrane potential dynamics



Gentet, Avermann, Matyas, Staiger and Petersen, 2010
Gentet, Kremer, Taniguchi, Huang, Staiger and Petersen, 2012

Cellular Mechanisms of Brain Function

And so it turns out, that different cell types have different types of behaviors, and we can study that in detail by combining mouse genetics to photomicroscopy and whole-cell recordings, *in vivo*.

Notes

Summary

30m 32s

In vivo electrophysiology

- Action potentials can be recorded extracellularly in parallel from many neurons at the same time.
- Whole-cell recordings reveal membrane potential dynamics during behavior.
- Whole-cell recordings of specific cell-types through two-photon microscopy and genetics.

Cellular Mechanisms of Brain Function

So in this video we've seen that there are two important types of electrophysiological measurements that can be made in the awake, behaving, mammalian brain. We can record extracellularly, and pick up local field potentials that represent correlated synaptic potentials near to the recording electrode. And we can see spiking activity of neurons from the outside. And because the extracelluar recordings are relatively easy to make, we can record in parallel from many electrodes, and thus, get a feeling for the spiking activity of networks of neurons with millisecond temporal resolution. In order to understand how those spikes are driven, we can record intracellularly with a whole-cell recording technique. And that gives us then access to synaptic potentials and some causal and mechanistic insight into what's driving membrane potential fluctuations, and what drives action potential firing. By combining mouse genetics to get fluorescently-labeled specific cell types, two-photon microscopy to see them, and whole cell recordings that we can target to individual nerve cells. We can also begin to see now, the neuronal activity of highly specific, gentically-defined, populations of neurons.

Notes

Summary

30m 46s

In vivo electrophysiology

- Action potentials can be recorded extracellularly in parallel from many neurons at the same time.
- Whole-cell recordings reveal membrane potential dynamics during behavior.
- Whole-cell recordings of specific cell-types through two-photon microscopy and genetics.

Cellular Mechanisms of Brain Function

So we now seen that both optically and electrogeologically we have quite interesting techniques for measuring brain function during behavior. What we now need to do, if we want to get a causal and mechanistic insight into brain function, is to start taking control of those neurons. And that's what we'll learn about in the next video.

Notes

Summary

32m 00s