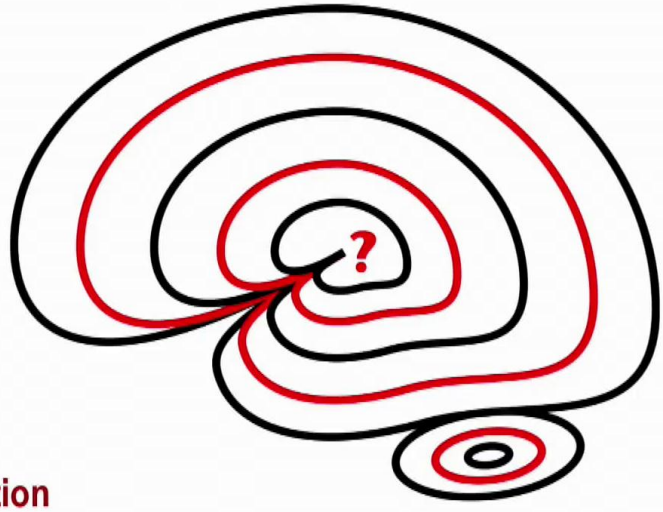
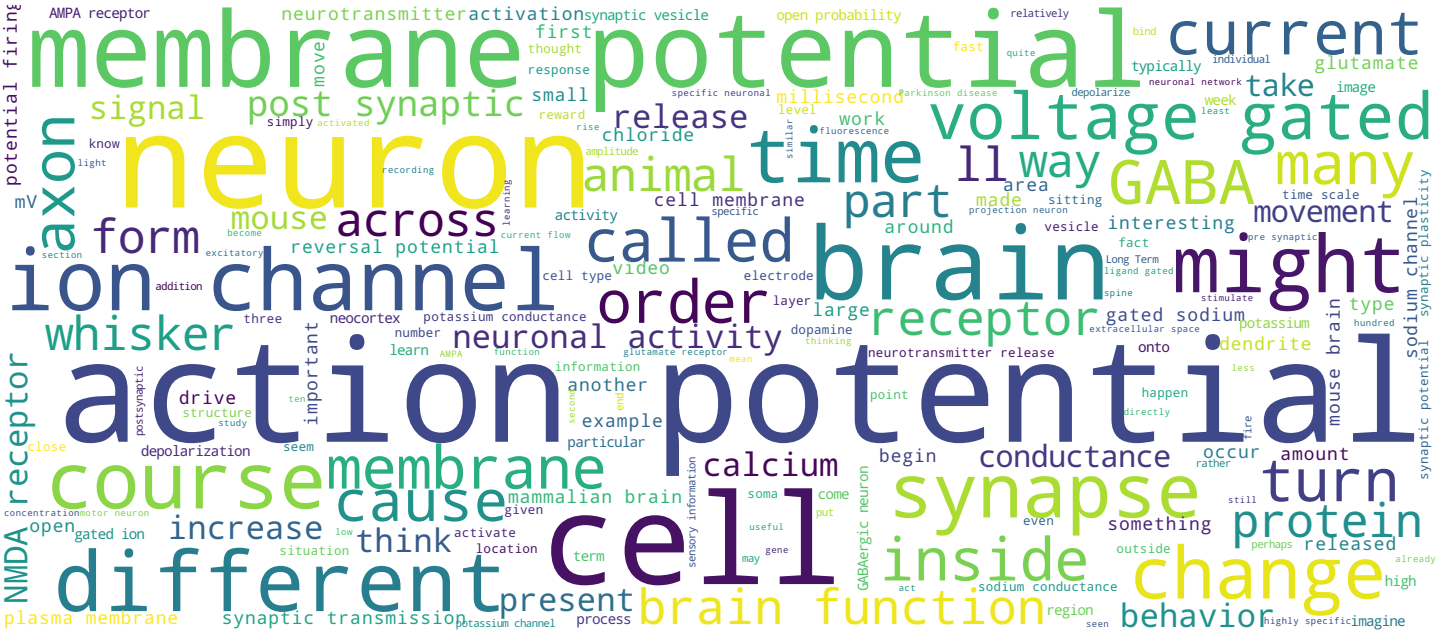
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE



1.1 Introduction

Cellular Mechanisms of Brain Function

Prof. Carl Petersen



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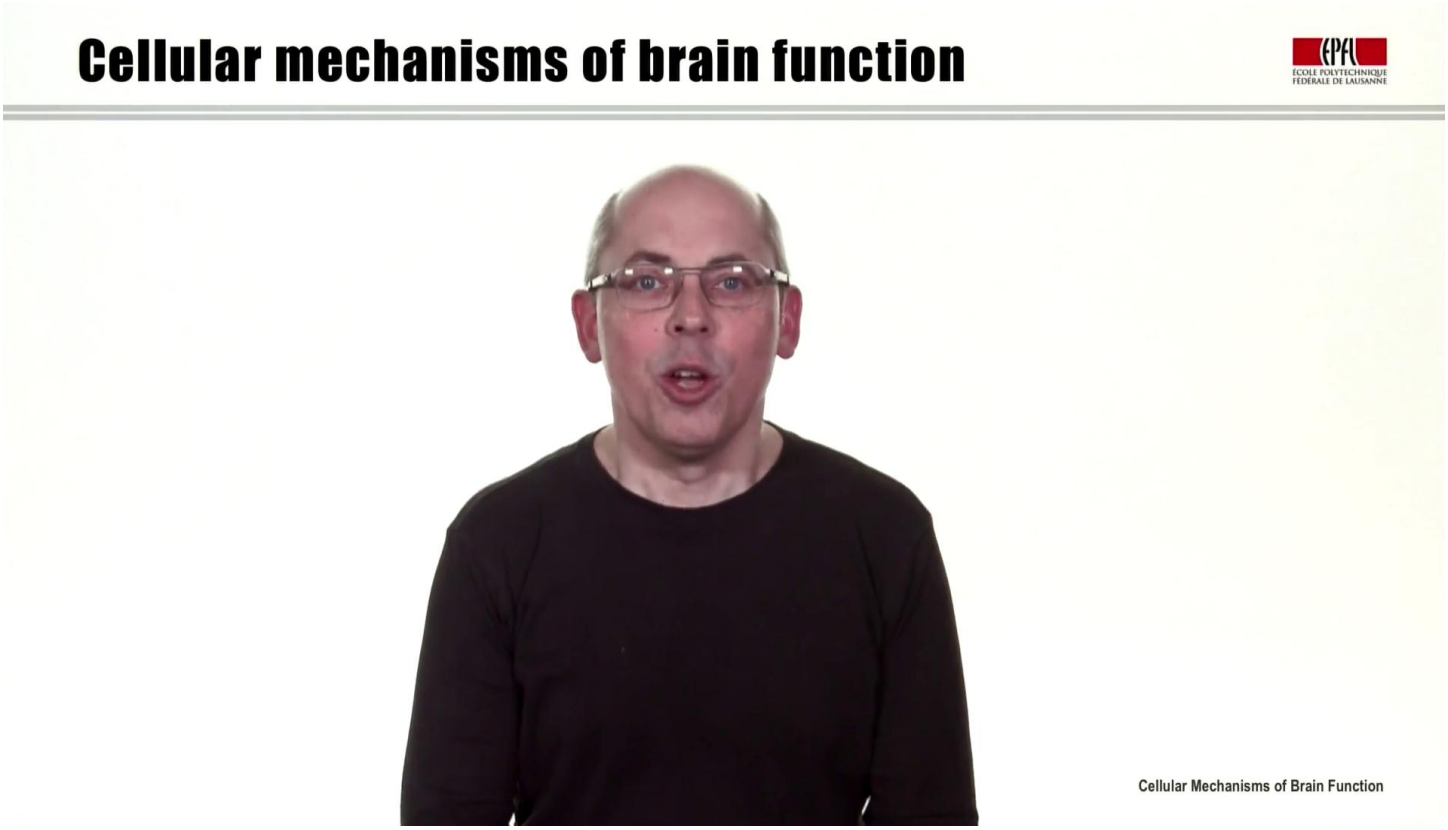
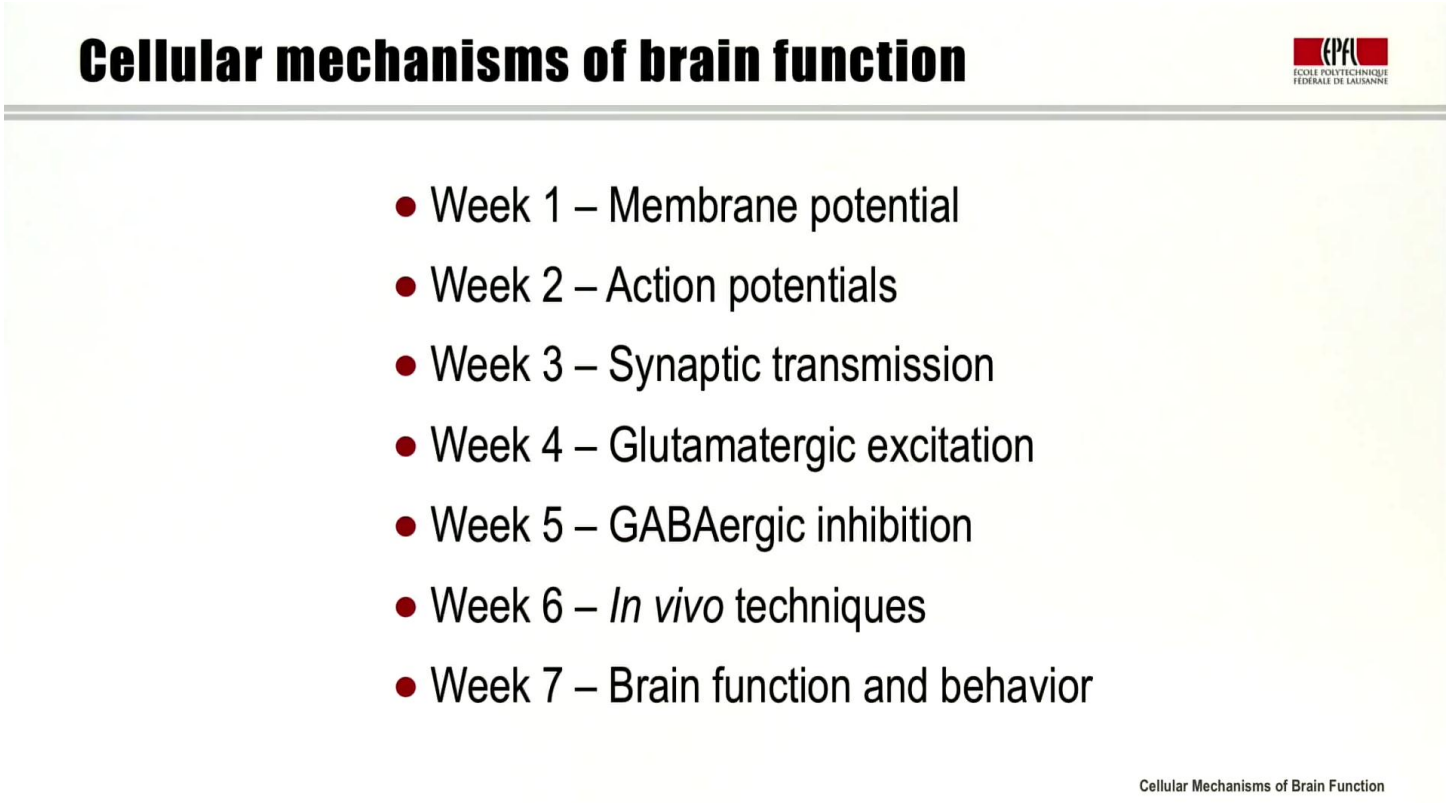


Welcome to this course about the cellular mechanisms of brain function. Brain function governs our every thought and every action. Activity in our brain allows us to perceive the world and learn from our experiences. So, how does the brain do that? This course aims for a causal and mechanistic explanation of brain function, at the level of the brain's irreducible components: its neurons and synapses. The neurons are the excitable cells of the brain, and the synapses are the specializations where the neurons communicate with each other. In the same way that Newtonian and quantum mechanics provide equations for the laws of physics, here we seek the underlying laws governing neuronal activity: the biophysics of brain function. However, in contrast to physics, neuroscience is still a very young field. It's only just over a hundred years ago that the neurons of the brain were first described, and there's much that still remains unknown. Neuroscience is now undergoing a revolution, with an ever-increasing speed of discovery driven by new techniques and exciting hypotheses that are continuously being developed.

Notes

Summary

0m 05s



This course will take you through the basic principles of mammalian brain function, and try to assemble that knowledge into a coherent and up-to-date description of how neuronal activity can process sensory information, leading to subjective percepts and behavioral decisions. Here, in this introductory video, I'll give you a brief overview of the course. The course lasts seven weeks, and every week there'll be five videos, each lasting 15 to 30 minutes. At the end of each video, there'll be a short quiz to help you better understand the subject matter. If you have further questions or you want to go deeper, then you should write comments in the online discussion forum, which I hope will be a lively, fun, and interactive environment. We'll begin in weeks one to three with studying the basic principles of how neurons and synapses work. In weeks four and five, we'll think about how neurons are wired into networks of excitatory and inhibitory neurons. And finally, in weeks six and seven, we'll consider how to study neuronal network function in behaving animals, and how we can now begin to causally link brain function and behavior.

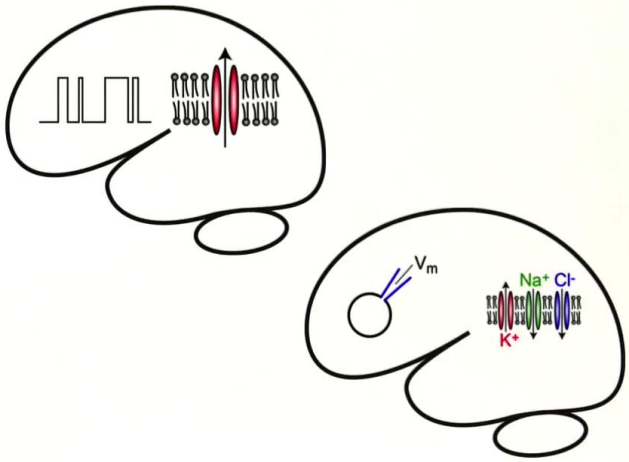
Notes

Summary

1m 28s

Week 1

- 1.1 Introduction
- 1.2 The cell membrane
- 1.3 Ion channels
- 1.4 Membrane potential
- 1.5 Cable properties



Cellular Mechanisms of Brain Function

The brain is essentially an electrical device. Electricity is not generated by the movement of electrons, as in an electronic computer, but rather by the movement of charged atoms: that is, ions. It's the movement of ions across the cell membrane that generates the electrical signals in the brain. These ionic currents flow across the elongated neuronal structures, and at synapses, these electrical signals are converted into the release of chemical messages: so-called neurotransmitters that affect specific target neurons. After this introductory video, there are four further videos of week one. We'll discuss the lipid bilayer of the cell membrane that electrically acts as a capacitor; and we will also discuss the protein ion channels that allow transport of speciifc ions across the cell membrane. The different concentrations of ions inside and outside of cells and the differential ion permeability of the cell membrane causes an electrical potential: the so-called membrane potential. Because neurons have long, elongated processes that act as cables, these electrical potentials have complex spaciotemporal dynamics.

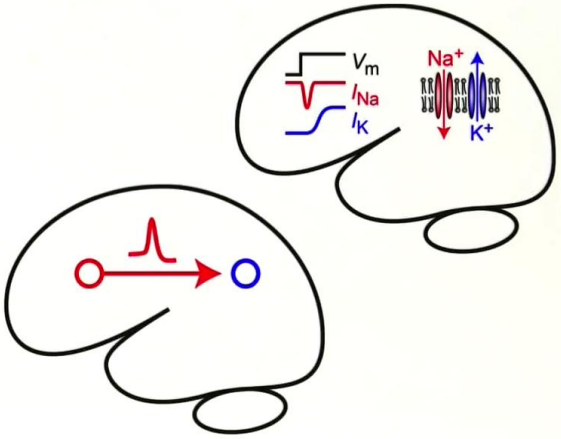
Notes

Summary

2m 46s

Week 2

- 2.1 Voltage-gated channels
- 2.2 Voltage-gating kinetics
- 2.3 The action potential
- 2.4 Action potential propagation
- 2.5 Whole-cell recordings



Cellular Mechanisms of Brain Function

In week two, we'll learn about nonlinear signal processing inside neurons generated by so-called voltage-gated ion channels with complex kinetics of activation and inactivation, depending upon the membrane potential. These nonlinear ionic conductances form the basis of an all-or-none digital signal, the action potential, which forms an important unit of information in the brain. The action potential actively propagates down the neuronal cables, and is therefore useful for transfering information from one part of the brain to another. At the end of week two, we'll make a lab excursion to see how neuronal membrane potential and action potentials can be measured in vitro in mouse brain slices using the whole-cell patch clamp recording technique.

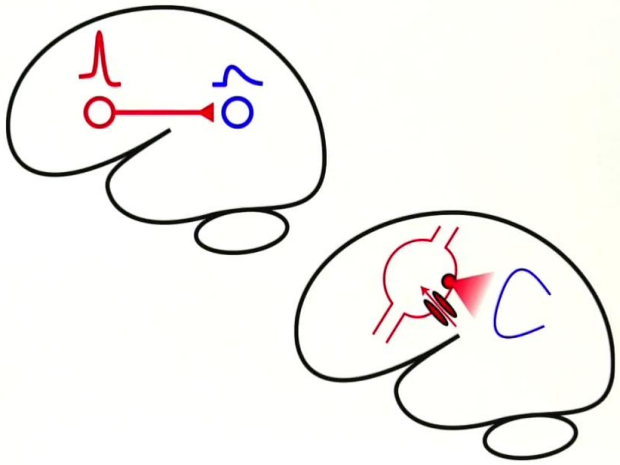
Notes

Summary

4m 05s

Week 3

- 3.1 Synaptic transmission
- 3.2 Neurotransmitter release
- 3.3 Presynaptic dynamics
- 3.4 Presynaptic modulation
- 3.5 Electron microscopy



Cellular Mechanisms of Brain Function

A key function of the action potential is to drive synaptic transmission: the release of a chemical substance, a neurotransmitter, sending a signal to other specific neurons. Synaptic transmission involves a complex cascade of molecular processes which are strongly influenced by recent patterns of activity, giving rise to interesting presynaptic dynamics. Synaptic transmission is also strongly regulated by the presence of other chemical substances, termed neuromodulators, which are present in the extracellular space of the brain. In the last video of week three, we'll make another lab excursion: this time, to see how we can image synapses at high resolution using electron microscopy.

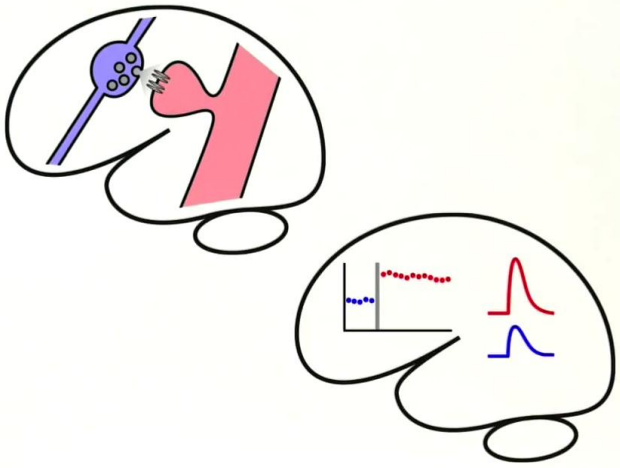
Notes

Summary

5m 00s

Week 4

- 4.1 Glutamate receptors
- 4.2 Postsynaptic potentials
- 4.3 Glutamatergic circuits
- 4.4 Synaptic plasticity
- 4.5 Dendritic spines



Cellular Mechanisms of Brain Function

Having got a basic understanding of the components of the brain, we'll next turn our attention to how the neurons work together in neuronal networks. We'll focus on the two most important neurotransmitters in the brain: the excitatory neurotransmitter glutamate and the inhibitory neurotransmitter GABA. These are released from different cell types in the brain which are wired together in highly-specific networks. In week four of the course, we will study the receptors that receive the glutamate signals from other neurons, and we'll discuss the excitatory electrical signals driven by the activation of the glutamate receptors: the so-called excitatory post-synaptic potentials. We'll also study examples of specific neuronal circuits used for signalling information from the sensory periphery to higher stations in the brain. These synaptic circuits are not written in stone; rather, they can change through a process known as synaptic plasticity. And these long-lasting, activity-dependent changes in synaptic strength are thought to underlie learning and memory. Much of this synaptic plasticity occurs at the specialized structures called dendritic spines that we'll study in some detail.

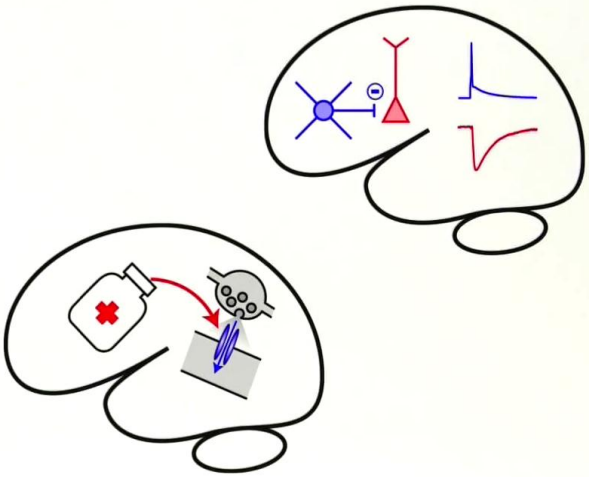
Notes

Summary

5m 48s

Week 5

- 5.1 GABAergic inhibition
- 5.2 Inhibitory synaptic conductances
- 5.3 Benzodiazepines
- 5.4 GABAergic projections
- 5.5 Neocortical inhibition



Cellular Mechanisms of Brain Function

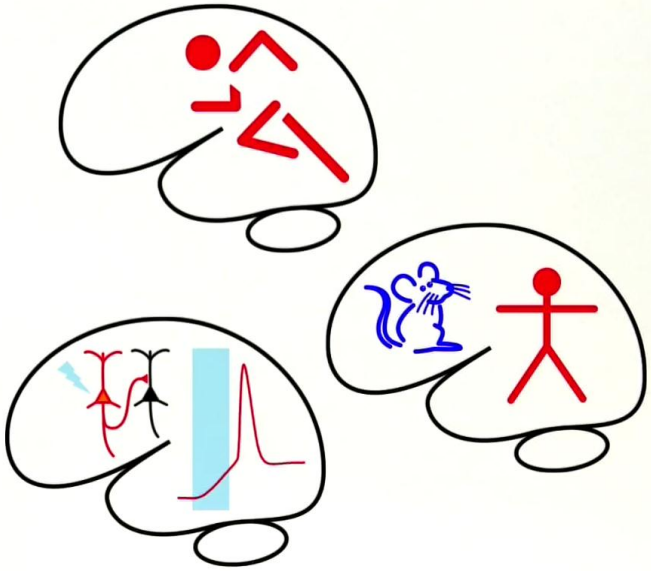
Whereas the neurotransmitter glutamate drives excitation of the neurons, the neurotransmitter GABA inhibits neurons. Neuronal networks, therefore, work through a dynamic process of integrating excitatory glutamatergic signals with inhibitory GABAergic signals. We'll study the synaptic conductances evoked by GABA and some specific neuronal circuits in the brain that use GABA. In addition, we'll introduce the field of neuropharmacology in the context of benzodiazepines, which act specifically at GABA receptors and are widely used as an anxiolytic medication. Neuropharmacology is of obvious importance because it provides the simplest means of treating brain disorders.

Notes

Summary

7m 06s

Brain function and behavior



The purpose of the brain is to govern behavior; so in order to understand brain function, we need to correlate and control neuronal activity in living animals during quantified behavior. This is an important challenge for modern, integrative neuroscience, and solving this will provide causal and mechanistic insight into deep questions about how our brains work. Breakthroughs in linking neuronal activity to behavior will also form the foundations necessary for developing rational therapies to treat the many brain diseases.

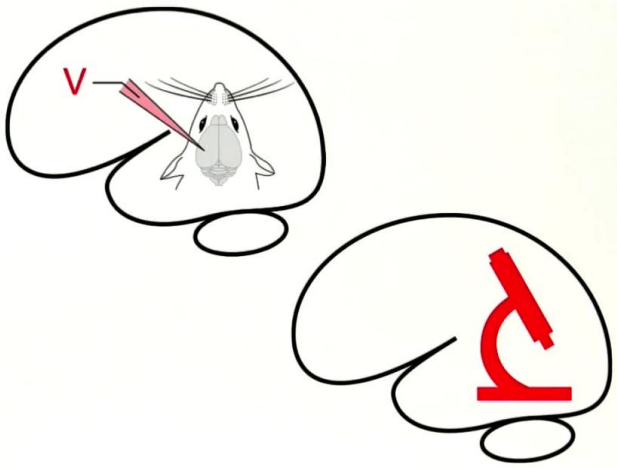
Notes

Summary

7m 58s

Week 6

- 6.1 Brain function and behavior
- 6.2 Man and mouse
- 6.3 Imaging the brain in action
- 6.4 *In vivo* electrophysiology
- 6.5 Controlling brain function



Cellular Mechanisms of Brain Function

Up to this point in the course, we will largely have covered principles of neuroscience derived from reduced, in vitro preparations. In order to investigate mammalian brain function during behavior in mechanistic detail, we need to make invasive, in vivo measurements and manipulations. The overall organization of the mammalian brain is similar across a wide range of species, and currently, substantial effort goes into understanding the mouse brain. What we learn from studying the mouse brain will in many cases likely be directly analogous to what happens in the human brain. We'll describe techniques for optical imaging of the mouse brain, resolving signals at millisecond temporal resolution and with cellular and subcellular spatial resolution. Electrophysiological measurements can also be made in behaving mice, allowing action potential firing and membrane potential dynamics to be studied during quantified behavior. In order to gain causal insight, these methods for correlating neuronal activity with behavior must now be complemented by manipulations of neuronal activity. Over the last few years, the development of optogenetics is providing tools that allow neuroscientists to control highly-specific neuronal activity with millisecond precision. We are now in a position to investigate the causal, neuronal mechanisms underlying behavior.

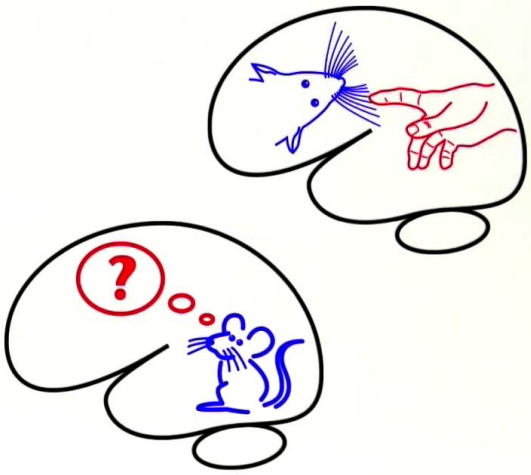
Notes

Summary

8m 32s

Week 7

- 7.1 Sensorimotor interactions
- 7.2 Sensory perception
- 7.3 Learning
- 7.4 Brain dysfunction
- 7.5 Concluding remarks



Cellular Mechanisms of Brain Function

In the final week of the course, we'll begin by considering behavior as a result of movements driven by specific motor neurons. Sensory input provides important information for guiding motor control, and so the simplest behaviors can be regarded as sensorimotor interactions. We'll also learn that sensory perception is an active process whereby we make movements to gain specific information: like moving our eyes to look at an interesting object, or touching a surface to feel its shape and texture. Sensory perception is also an active process from an internal, computational perspective whereby the neurons in our brains generate sensory percepts derived from our past experiences and current expectations. We'll also study aspects of reward-based learning, in which the brain tries to organize behavior to maximize reward. Finally, we'll discuss how the cellular mechanisms of some brain diseases are beginning to be understood, giving hope for future treatments.

Notes

Summary

10m 00s

Cellular mechanisms of brain function

- Unitary elements of the brain, neurons and synapses, are beginning to be understood in biophysical detail.
- Neuronal networks involving specific cell-types are being delineated at high resolution.
- The next major challenge for neuroscience is to causally link neuronal function to behavior.

Cellular Mechanisms of Brain Function

So, in this course, you'll see that the unitary elements of the brain, the neurons and synapses, are beginning to be understood in biophysical detail. We already have quite a good quantitative description of membrane potential, action potentials, and synaptic transmission. Neuroscientists have also made good progress in delineating the synaptic connectivity of specific neuronal cell types. We're thus learning a lot about the rules underlying the wiring diagram of the mammalian brain. The next major challenge for modern neuroscience is now to causally link neuronal activity to behavior. This requires in vivo measurements and manipulations to correlate and perturb brain function during behavior. Fortunately, enormous progress has been made, and many neuroscientists think that we'll have a deep understanding of how the basic operating principles of the mammalian brain govern behavior within the next 50 years, and hopefully within our lifetimes.

Notes

Summary

11m 08s