Overview

How the brain works remains one of the main mysteries of science. This course consists of 15 multimedia lectures introducing the study of the brain. We will discuss how modern multidisciplinary methods have provided fascinating insights into the operation of neurons and how neuronal mechanisms underlie cognition. We will also introduce a few concepts on the mechanisms of brain disease. Each class will consist of a 15 min introductory overview followed by a 10-15 min discussion of the video suggested during the previous class. I have selected videos from different sources (Stanford, MIT, UNC, Arizona State University, Hebrew University, University of Amsterdam, EPFL). I will then raise a research challenge, providing theoretical background and the methods to test hypotheses. A general or group-based discussion will follow.

Goals

Students will be acquainted with the basic concepts in neuroscience, including:

- Action potentials
- Synapses
- Neuronal circuits
- Integration
- Plasticity

as well as an understanding of the general principles of brain organization. Students will be able to discuss experimental approaches to solve outstanding questions in neuroscience.

Requirements

No prerequisites
Evaluation

Weekly quizzes (40%). Final exam (60%)

Contents

1- Introduction. Why it is exciting to study the brain.  
   Research Challenge: Curing Parkinson’s disease

2- Molecules, Synapses, Cells, Circuits, Systems and ...Behavior  
   Video: https://www.coursera.org/course/bluebrain  
   Research Challenge: What hallucinations tell us about how the brain works

3- Transfer of information: Neurotransmission and neuromodulation  
   Video: Karel Svoboda HHMI  
   http://youtu.be/I6-z0Yqj1dE?list=PL33580C2AB1361B04  
   Research Challenge: Timescales of neuronal activity. Modeling neurons

4- Plasticity of Neuronal systems  
   Video: Leslie Tolbert (U Arizona)  
   http://youtu.be/5E6Mz1MRR4U?list=PL33580C2AB1361B04  
   Research challenge: Learning and memory. How the brain is different from your computer?

5- A brief summary of neuroanatomy and methods  
   Video: Santiago Ramon y Cajal  
   http://youtu.be/70le2AmxeFw  
   Research challenge: Tracing long range neuronal connections

6- Sensory and motor systems  
   Video: Brain Matters Todd (Harvard)  
   http://youtu.be/YuoPMntgiQU  
   Research challenge: Phantom limbs

7- A primer on methods to record and visualize neuronal activity  
   Video: Reid (Allen Institute)  
   http://youtu.be/LoXye6KBeCI  
   Research challenge: Voltage sensors

8- Brain Basis of Cognition  
   Video: Eric Kandel (Columbia): Memories are made of this.  
   http://youtu.be/K0cnyqzqgkQ  
   Research challenge: Where do memories reside?
10. Cortical networks – out of the *Blue Brain Project*
   Video. Henry Markram (EPFL)
   Research challenge: Cortical columns

11. Brain states: sleep, awake and everything in between
    Video: Sleep and Dreams.
    Research challenge: Narcolepsy

12. Brains and emotions: A primer in Molecular Psychiatry
    Videos: Robert Sapolsky (Biology, Stanford)
    [http://youtu.be/eYG0ZuTv5rs](http://youtu.be/eYG0ZuTv5rs)
    Phillippe Goldin (Psychology, Stanford)
    [http://youtu.be/tShDYA3NFVs](http://youtu.be/tShDYA3NFVs)
    Research challenge: Anxiety and depression

13. Drugs and the brain
    Video. Addiction
    [http://youtu.be/H0xD0wyrIcE](http://youtu.be/H0xD0wyrIcE)
    Research challenge: Why do addicts relapse?

14. Neurodegeneration
    Video: Alzheimer’s disease
    [http://youtu.be/b0sYFLD6F-I](http://youtu.be/b0sYFLD6F-I)
    Research challenge: Can AD be cured?

15. Beyond the brain: Neuroscience and society, economy and the law.
    Videos: Ken Foster (Bioengineering U Penn)

Suggested reading:

Opto 205
A Master course on Optogenetics, Chemogenetics and Biophotonics

Overview

The ability to manipulate the activity of genetically defined neurons has revolutionized neuroscience, as it is now possible to interrogate the function of neuronal circuits in behavior with unprecedented specificity and temporal precision.

Optogenetics is based on the targeting of light-sensitive opsin molecules in specific neuronal populations to enable excitation or inhibition of neuronal circuits. In the past few years, optogenetic techniques have been used to uncover new components of sensory, motor and limbic processing. The recent determination of the crystal structure of channelrhodopsin 2 will allow the design of new optogenetic probes with different current properties and activation spectra. Also, new devices to increase the efficiency of light delivery in the brain are being developed. Combination of genetically encoded optical sensors of neuronal activity (e.g. GCamp6) with optogenetic actuators is leading to all-optical control and functional interrogation of neuronal circuits during complex behavioral tasks.

An essentially different and complementary approach to manipulating cell-type specific neuronal activity is the use of modified designer receptors (DREADDs). When expressed in neurons, DREADDs do not bind endogenous ligands, but are sensitive to the orally available ligand clozapine N-oxide (CNO) which is otherwise pharmacologically inert. DREADDs are particularly attractive to study the function of modulators with longer time scales.

This masters course will highlight advances in understanding of CNS function enabled by opto- and pharmacogenetic methods while emphasizing in the complexities of functional analysis of neuronal circuits.

Goals

By the end of the course the students should be familiar with the basics of optogenetics, light delivery, chemical genetics and ready to implement these methods in experimental designs.
Requirements

A degree in Biology, Chemistry, Physics, Biochemistry or Neuroscience is required. This course is aimed at graduate students who plan to engage in research including optogenetics and derived methods.

Evaluation

One quiz (20%) and a final exam (80%).

Contents

1. *Introduction to optogenetics, Historical considerations.*

Suggested reading:


2. *Channelrhodopsin 2. Discovery, crystal structure, photocycle. Mutations and variants*


Suggested reading:

3. *Inhibitory opsins. Proton and chloride pumps*

Suggested reading:

4. Chemogenetics: Excitatory and Inhibitory DREADDs

Suggested reading:

5. In vitro applications of ChR2. Photostimulation of single synapses using multi-photon microscopy


6. In vivo applications 1. Circuit mapping, CRACM,


7. In vivo applications 2. Closed loop control. Illumination of terminals


8. **Devices: Light delivery**


9. **Animal models: Zebrafish, C elegans, Drosophila**


10. **Experimental design. Limitations and perspectives**


Opto 301
A PhD Practical course on optogenetics

Overview

Optogenetics is based on the targeting of light-sensitive opsins molecules in specific neuronal populations to enable excitation or inhibition of neuronal circuits. In the past few years, optogenetic techniques have been used to uncover new components of sensory, motor and limbic processing.

This PhD level course will be oriented toward the practical aspects of optogenetics. Pros and cons of different viral vectors with distinct Boolean logic (AND, OR, NOR, XOR, etc), light delivery devices, optical controllers, LEDs vs Lasers, etc will be discussed. The final session will include a general discussion and the students will be encouraged to present their own optical devices.

Goals

This is a practical course directed towards students already using or planning to use optogenetics for their experiments. By the end of the course, attendees will be able to conduct in vivo experiments using different ways of light delivery and increase confidence in the technical aspect of optogenetics.

Requirements

Enrollment in a PhD Biosciences Graduate Program

Evaluation

Final test will consist of the design of an experiment to interrogate different aspects of a functional neuronal circuit. (100%).
Contents

1. Introduction. Channelrhodopsin
3. Viral vectors. AAV, Lentivirus, CAV, retrograde viruses. Viral Boolean Logical Operators
4. Light delivery. Cannulas, Optical implants
5. Pulse controllers, Commutators, Closed loop operation; All optical recording/actuation.
6. Future developments. Open discussion

Recommended references:

