Program overview

Conceptual survey

The importance of thinking at the level of systems
The aim of the SysNeuro program is to provide students a view of the brain as a whole via unfolding, at least in part, its immense complexity. This is a major challenge of all time, but the right answer should be one that can integrate actual knowledge. As we are in the fortunate period of time when high performance tools (both hardware and software) and large datasets are getting more and more available, systems thinking is inevitable in brain research. Therefore, throughout the course students will learn how different approaches - reductionist, holist and functionalist - are all useful and necessary in understanding the brain.

Organizational perspective
The course introduces the students the different levels of organization all being complex systems themselves. Starting with molecular machineries at the subcellular level then turning to the cellular level explains why the neuron is considered as the unit of brain organization. In the next step it is shown how the milliards of neurons make up the cerebral cortex and how this evolutionarily new structure can perform diverse cognitive and other functions. Finally, whole brain functions and functioning will be approached via its role in behavior and pathology.

Importance of computation
How can we understand the complex networks of the brain? How new properties of brain structure and function emerge at higher levels of organization? How the understanding of dynamical systems helps understanding brain function? How structural specialization gives birth to specific functions? Why brain function is organized as it is and what is the essence of its operation? We aim to provide tools, rules and examples, which help answering these questions and also provide an outlook whereby the brain can be compared to other complex systems.

Interdisciplinary
Another notable feature of the Systems Neuroscience program is its interdisciplinary nature: it will introduce the students into several state of the art methods both experimental (molecular biology, cellular and extracellular physiology, different kinds of imaging) and theoretical (data and network analyses, simulation and modelling).

Detailed schedule

AOSANT560_1A (17-21 June 2019) Systems Biology: Neuronal genomics and proteonmics

By Gábor Juhász, PhD, DSc
Laboratory of Proteomics, Institute of Biology, Eötvös Loránd University, Budapest

The rapidly developing complexity based bio-molecular research will be summarized in one week curse. **The seminar series aims to give a survey on systems biology approach of biological functions**. We start at the definition of systems biology and a brief overview of its history from the Human Genome Program to modern stratified medicine. We discuss how systems biology was fueled by the up-coming medical revolution initiated by systems approach of biological functions in health and ill-health. Than we turn to the theoretical and practical consequences of changes in definition of phenotype. We also concern with the special features of experimental planning in systems biology to understand the unbiased research strategy.

Turning to **the high-throughput methods** we discuss next generation sequencing, proteomics and mass spectrometry of proteins, and we give a survey of recently developed sophisticated technologies and mathematical analysis of data.

As an important novel issue, we show the problems of **single cell transcriptomics** and genomics analyzing the individual cells in deep sequencing technology.

We also have a demonstration of **computerized literature handling** by search engines and discuss the Pathway Studio Platform and Ingenuity Platform.

We talk about **biobanks** and their use in biomarker discovery. The collection, storage and handling tissue and body fluid samples. The automated DNA and RNA separation from biobank samples.

As an important problem of systems biology research we talk about the reliability issues on the basis **of FDA Controlling Science Initiative** and EU recommendation for development of systems biology education, lab work and data processing in health industry. At the end we make a short summary of financing a business issues of systems biology based production of terranostics and diagnostic tools.

AOSANT560_4A (24-28. June 2019) Neocortex: from structure to function

by László Négyessy, PhD
Complex Systems and Computational Neuroscience Group, Wigner RCP, Hung. Acad. of Sciences, Budapest and
Department of Anatomy, Histology and Embryology, Semmelweis University, Budapest

Brain exerts the central regulatory role over body functions and behavior. What are the characteristics making the brain so special among the organs of the body? Why is the cerebral cortex so important within the brain? Such conceptual questions will be approached from an organizational view of brain's anatomy. This knowledge will be complemented by evolutionary and developmental hints, which finally leads to defining the situation of the cerebral cortex in our most complex organ the brain. In addition the central role of the cerebral cortex in integrative brain functions will also be introduced following another historical route the functional approach based on lesions and stimulations. The course will then turn on to the exploration of the structure and the functioning of the cerebral cortex as it is known today. It will be shown how the cortex is scaled up from its basic building blocks the neurons interconnected up to the full network of the cortical areas. Via this big leap the role of the 2D horizontal and 3D laminar organization will be discussed. Intermittently, a short, comprehensive intro will be given about the science of networks and its importance in neuroscience. It will be shown how the functional cortical systems subserving cognition are formed by subnetworks of the areas, and, vice versa, the cortical subnetworks responsible for different cognitive functions will be overviewed.

AOSANT560_3A (1-5. July 2019) Neurodynamics: from single neurons to motifs

by John Milton, MD, PhD
Claremont McKenna College, CA, USA

Can the behavior of large ensembles of neurons can be understood, at least in part, from the properties of smaller ensembles containing 2-5 neurons, currently referred to as motifs? Typically as we move up from the level of single neurons to the level of populations new phenomena emerge, for example, organized waves of neural activity. Curiously the properties at the lower level essential for understanding the emergent phenomena often did not really seem that important. For example, conduction time delays and the relative refractory period of a neuron play very important roles in generating traveling waves of synchronized activity in neural populations yet often receives scant attention by neuroscientists. The challenge is to identify prospectively which properties of neurons and motifs are the most relevant for the phenomena that spring up in larger populations. The solutions to this challenge would provide guidance to the efforts of present day neurobiologists and molecular biologists to understand collective phenomena such as the generation of epileptic seizures, the generation of the electroencephalogram, sleep wake cycles, cognition and, perhaps, even consciousness.

The goal of this week of lectures is to provide a foundation in neurodynamics of neurons and small neuronal motifs for neuroscientists who have only an introductory background in calculus.

AOSANT560_2A (8-12. July 2019) Computational Models in Systems Neuroscience

By Mihály Bányai, PhD
Wigner RCP, Computational Systems Neuroscience Lab, Budapest

The purpose of this course is to introduce a mathematical modelling approach to understand brain functionality. We will explore how to build formal theories about the brain with an emphasis on being able to predict measurements. Mathematical tools required to formulate and evaluate hypotheses will be discussed together with interdisciplinary approaches to cognition and cortical computation both on the behavioral and neural levels. We will review state-of-the-art models aiming to predict biophysical quantities in the sensory and decision making systems of the brain. We will elaborate on the strong ties that connect neuroscience to machine learning and artificial intelligence. Recent advancements in the latter fields are discussed.

AOSANT560_5A (15-19. July 2019) Learning and Navigation in the brain and in artificial neural networks

By Zoltán Somogyvári, PhD
Complex Systems and Computational Neuroscience Group, Wigner RCP, Hungarian Academy of Sciences, Budapest

During this course, we will study classical learning theories through artificial neural network models. Learning methods, networks and rules, their capabilities and limitations will be discussed. By applying these theories, high level cognitive functions will be approached. As an example, navigation will be our working horse, a task which should be solved by all moving animals. Thus, the possible navigation strategies, applied by different species, will be reviewed, then the underlying neural structures and activity patterns will be described. Finally, neural models of the navigation (some of them are applicable and actually were applied in robots) will be introduced.

AOSANT560_6A (22-26. July 2019)

6.1. Brain imaging: from normal to pathological

By Lajos Kozák, MD, PhD
MR Research Center, Semmelweis University, Budapest

Blood-oxygenation level dependent (BOLD) functional MRI (fMRI) provides a highly flexible, high spatial resolution, and non-invasive and safe means for measuring and describing neural activity in humans. Due to its favorable properties it became a widely used method for investigating and describing functional networks in healthy individuals and patients. Functional MRI started off as a brain mapping tool, i.e. relatively simple paradigms were used to localize brain areas involved in various cognitive functions. Later on, as the method evolved and became an important tool of cognitive science, paradigms became increasingly complex and the description of functional networks and the investigation of network hierarchies became available. Recently, data-driven approaches lead to the era of paradigm-less or resting-state fMRI which in conjunction with diffusion tensor imaging (DTI) (an MRI-based tool for the in-vivo non-invasive mapping of white matter structure) became the most important tool for large scale whole brain analysis of functional and structural connectivity networks of the brain.

The course starts with an introduction of the physical and physiological background of fMRI and DTI, then we will continue with the basics of data acquisition and classical generalized linear model (GLM) based analysis, paradigm design for brain mapping, dynamic connectivity (dynamic causal modelling, DCM) analysis and data-driven methods (independent component analysis, ICA), with a focus on basic research and clinical applications. We will demonstrate and discuss relevant publications related to fMRI detectable differences between healthy and diseased brains, and the cognitive and possible structural correlates of such differences. Special focus will be given to functional brain mapping as a tool for pre-surgical evaluation and decision-making in brain tumor and epilepsy patients.

6.2. Neural rhythms: normal and pathological

By Dániel Fabó MD PhD
Department of Functional Neurosurgery and Department of Epilepsy, National Institute of Clinical Neuroscience, Budapest

Brain is a very complex oscillator. This fact has been obvious from the very first electroencephalographic recording of Berger's, when the alpha oscillation was recorded. Since then the functional implications of brain oscillations changed significantly, from being idling rhythms to harboring essential functions. Parallel with the physiological studies, investigations of the pathological brain states resulted in numerous other oscillations, the registration of which became basic tools of classical neurological diagnostics.

The idea of the underlying mechanisms, how pathological brain oscillations are organized, evolved also significantly. Now many think that derailed physiological oscillators produce the altered rhythms, chaining together the investigation of pathologies with the understanding of physiological functions. It is studied intensively if these failed rhythms are causes or consequences of the diseases and the symptoms. Nevertheless which situation is the case, a new therapeutic strategy has been emerged from these thoughts called neuromodulation. Through these techniques new rhythms are delivered into some parts of the nervous system of various patients resulting the easing or elimination of the symptoms.

During this course we set sail adrift these waves to get better insight into the normal and abnormal functions of the brain. We proceed through wake and sleep oscillations to the pathophysiological features of epilepsy. We will see how these oscillations can be recorded in humans at various scales, beside the bed or within the operating room and we will glance at the exciting horizons opened by neuro-modulatory techniques such as deep brain stimulation.

AOSANT560_7A (29. July-2. August 2019) Statistics of the Brain

By Gergő Orbán, PhD
Computational Systems Neuroscience Lab, Wigner RCP, Hungarian Academy of Sciences, Budapest

Perception relies on internal models to interpret stimuli coming from the external world. These internal models represent our knowledge about the dependencies and interplay of the features of the environment. Characterization of these models is challenging and requires advanced techniques. A particularly promising way to understand the internal models applied by the nervous system is to identify the computational problem these internal models need to solve. The nervous system is bound to use available information efficiently in order to make decisions or execute motor plans. In a general setting the information collected by our senses is incomplete, noisy, or ambiguous and computational strategies applied by the nervous system need to overcome these limitations as well as possible. We adopt a Bayesian perspective to construct ideal observer models which define the optimal strategy to interpret stimuli. Whether the generation of stimuli involved a stochastic component or not, a Bayesian treatment assumes a probabilistic process underlying the stimulus. We will explore how humans adopt these optimal strategies, how computations can be identified by psychophysical experiments, how internal models characteristic to each individual can be revealed and what approximations are made once computations become intractable.