

Latin American Training Program 2020

MOLECULES, CELLS AND CIRCUITS: UNDERSTANDING NERVOUS SYSTEM MECHANISMS

Montevideo, November 2-20, 2020

Preliminary program

INTRODUCTION

The aim of the Latin American Training Program (LATP) Course 2020 entitled “From Molecular and Cellular Neuroscience to Cognition: Clues to Understand Brain Diseases” is to provide the next generation of leading Latin American neuroscientists with intensive training on different aspects of neurobiology for three weeks. The selected students will be taught by leading neuroscientists from the region and overseas. A key feature of the LATP 2020 course is the strong hands-on lab activities that will give the students the opportunity to work side-by-side with expert neurobiologists and learn first-hand about state-of-the-art technologies (from electrophysiology, advanced imaging, chemogenetics and behavior analysis). In addition to lectures on fundamental topics of the neurosciences the students will actively engage in discussions about the development of professional skills. The overall goal of this course is to promote among Latin American students a broad knowledge in neuroscience within the context of critical thinking.

MODULE I. CELLULAR AND MOLECULAR NEUROBIOLOGY: NEURONS, GLIA AND PLASTICITY **November 2-7, 2020**

Coordination: Michel Borde and Raúl Russo

This module will focus on central aspects of cellular neurobiology such as the development of neural circuits, the biology of neural stem cells and neurogenesis, the biophysical basis of excitability and synaptic transmission together with the analysis of various forms of plasticity of neural circuits. Cutting edge experimental approaches will be discussed.

Monday November 2

09:00-09:10 | Opening Introduction to the School

09:10-10:00 | Cellular aspects of early neural development in vertebrates. *Flavio Zolessi*.

10:00-10:50 | Too hot or too cold: TRP channel in the nervous system. *Ramón Latorre*

10:50-11:20 | **Coffee break**

11:20-12:00 | The integrative properties of neurons: intrinsic properties and neuronal compartments. *Michel Borde*.

12:00-14:30 | **Lunch break**

14:30-19:00 | **Introduction to Hands-on lab activities I**

Tuesday November 3

09:00-9:50 | Presynaptic protein synthesis and synaptic function. *Pablo Castillo*.

9:50-10:40 | The axon: far more complex than a signal carrier. *Federico Trigo*.

10:40-11:10 | **Coffee break**

11:10-12:00 | Electrical synaptic transmission. *Alberto Pereda*.

12:00-14:30 | **Lunch break**

14:30-19:00 | Hands-on

Wednesday November 4

09:00-9:50 | The perfect damping machine: the Ca²⁺- and voltage -activated K⁺ (BK) channel.
Ramón Latorre

9:50-10:40 | Endocannabinoids as regulators of synaptic plasticity. *Pablo Castillo*.

10:40-11:10 | **Coffee break**

11:10-12:00 | Molecular complexity of electrical synapses. *Alberto Pereda*.

12:00-14:30 | **Lunch break**

14:30-19:00 | Hands-on

20:00-21:00 | PROFESSIONAL SKILLS I "How to write a paper". *Nick Spitzer* & "A look into the process of scientific publishing". *Pablo Castillo*.

Thursday November 5

09:00-9:50 | Tripartite synapse: synaptic regulation by astrocytes. *Alfonso Araque*.

9:50-10:40 | The role of transmitter plasticity in depression and PTSD. *Nick Spitzer*.

10:40-11:10 | **Coffee break**

11:10-12:00 | Neural Stem Cells; origin, self-renewal and key role in adult Neurogenesis. Arturo
Álvarez-Buylla

12:00-14:30 | **Lunch break**

14:30-19:00 | Hands-on

20:00-21:00 | Neuroscience by night: an informal open discussion. "*Synapse proposes, neuron disposes. Is that so?*". Active and passive intrinsic neuronal properties and synaptic integration and plasticity.
Sebastián Curti, Pablo Castillo and Alfonso Araque.

Friday November 6

09:00-9:50 | Exercise enhances motor skill learning by neurotransmitter switching in the adult midbrain. *Nick Spitzer*

9:50-10:40 | Astroglia-neuron networks in brain function. *Alfonso Araque*.

10:40-11:10 | **Coffee break**

11:10-12:00 | Neurogenesis in the adult hippocampus. *Alejandro Schinder*.

12:00-14:30 | **Lunch break**

14:30-19:00 | Hands-on

20:00-21:00 | Meet the PIs (Optional)

In this activity students will have the chance by their request, to meet principal investigators that participate in the course in an informal environment to discuss

about their science, future training possibilities and other aspects of interest for the young researchers.

Saturday November 7

Mini-Symposium I: Neural Stem Cells and Adult Neurogenesis

09:00-09:50 | Development of inhibitory neurons and the induction of critical period neural plasticity. *Arturo Álvarez-Buylla*

9:50-10:40 | Functional integration of newborn neurons in the hippocampal circuits of the adult and aging brain. *Alejandro Schinder*.

10:40-11:10 | **Coffee break**

11:10-11:40 | The central canal as a stem cell niche. *Raúl Russo*.

11:40-12:10 | Influence of neuroepithelial polarity on neuronal differentiation. *Flavio Zolessi*.

Afternoon

15:00-16:00 | Presentations of hands-on lab activities I

MODULE II. NEURODEGENERATIVE AND NEUROPSYCHIATRIC DISORDERS: NEW EXPERIMENTAL APPROACHES AND THERAPEUTIC STRATEGIES

November 9-14, 2020

Coordination: Patricia Cassina and Cecilia Scorza

This module will focus on the neural mechanisms involved in the physiopathology of neurodegenerative (Parkinson's Disease, Amyotrophic Lateral Sclerosis), metabolic and neuropsychiatric diseases (schizophrenia-psychosis and drug of abuse). Additionally, students will have the opportunity to learn new approaches to study these pathologies, from neuronal and astrocytes cultures to behavior, using techniques such as immunohistochemistry, confocal microscopy, flow cytometry, DREADD-based chemogenetic tools, behavioral test and molecular imagenology.

Monday November 9

09:00-09:10 | Welcome and Opening Module II

09:10-09:50 | A role for glial cells in brain pathologies. *Luis Barbeito*.

09:50-10:40 | Brain energy metabolism: astrocytes-neurons coupling. *JP Bolaños*.

10:40-11:10 | **Coffee break**

11:10-11:35 | Metabolic modulation as a strategy to reduce glial reactivity. *Patricia Cassina*.

11:35-12:00 | Molecular Imagenology in neurodegenerative diseases. *Eduardo Savio*

12:00-14:30 | **Lunch break**

14:30-19:00 | Introduction to hands-on activities II

Tuesday November 10

09:00-9:50 | Microglia in health and disease. *Hugo Peluffo*.

9:50-10:40 | New experimental approaches to modulate inflammation in Central Nervous System disorders. *Rubén López-Vales or Albert Quintana*.

10:40-11:10 | **Coffee break**

11:10-11:35 | Glial reactivity modulation in chronic pain. *Natalia Lago*

11:35-12:00 | Oligodendrocytes in neurometabolic diseases. *Silvia Olivera*.

12:00-14:30 | **Lunch break**

14:30-19:00 | Hands-on

Wednesday November 11

09:00-09:50 | Neuronal death mechanisms in Parkinson Disease. *Giselle Prunell*.
09:50-10:40 | Pathophysiology of Alzheimer disease. *Laura Morelli*.
10:40-11:10 | **Coffee break**
11:10-12:00 | Cannabinoids in neuropsychiatric disorders. *Francisco Guimaraes*.
12:30-14:30 | **Lunch break**
14:30-19:00 | Hands-on
20:00-21:00 | PROFESSIONAL SKILLS II "How to get a postdoc position". *Kuei Y. Tseng*.

Thursday November 12

09:00-09:50 | Prefrontal Cortex dysfunction in neuropsychiatric disorders. *Kuei Y. Tseng*.
09:50-10:40 | Chemogenetics tools: DREADD vs Optogenetic. *Adriana Caballero*.
10:40-11:10 | **Coffee break**
11:10-12:00 | Application of DREADD in Neuroscience. *Kuei Y. Tseng*.
12:00-14:30 | **Lunch break**
14:30-19:00 | Hands-on

Friday November 13

09:00-09:50 | Psychotic-like effects induced by NMDA-R antagonists: role of GluNR2C. *Cecilia Scarza*.
09:50-10:40 | High frequency oscillations of the EEG in animal models of psychosis. *Pablo Torterolo*.
10:40-11:10 | **Coffee break**
11:10-12:00 | Psychedelic drugs. *Ignacio Carrera*
12:00-14:30 | **Lunch break**
14:30-19:00 | Hands-on
20:00-21:00 | Meet the PIs (Optional)

Saturday November 14

10:00-12:00 Presentations of hands-on lab activities I

MODULE III: NEURAL SYSTEMS, COGNITION, GENOMICS & BEHAVIOR.

November 16-20, 2020

Coordination: Leonel Gómez and Ana Silva

This module will focus on neural circuits solving problems integrating computational and behavioral perspectives. The neural and molecular mechanisms underlying behavior, perception, and cognition will be explored in iconic vertebrate model systems. We will combine multi-level experimental approaches with theoretical modeling and bioinformatic processing to highlight general strategies of neural computing across evolution.

Monday November 16

09:00-09:10 | Welcome and Opening Module III
09:10-09:50 | Neural Circuits. *Leonel Gómez - Ana Silva*

09:50-10:40 | Neuronal Networks. *Ruben Coen-Cagli*
10:40-11:10 | **Coffee break**
11:10-12:00 | Genomics of Behavior. *José Sotelo Silveira*
12:00-14:30 | **Lunch break**
14:30-19:00 | Introduction to hands-on lab activities III

Tuesday November 17

09:00-09:50 | *Cognitive and computational approaches to perception*. Neural models of perception. *Leonel Gómez*
09:50-10:40 | *Cognitive and computational approaches to perception*. Neural basis of early visual processing. *Ruben Coen-Cagli*
10:40-11:10 | **Coffee break**
11:10-12:00 | *Cognitive and computational approaches to perception*. Computing with auditory circuits. *José Luis Peña*
12:00-14:30 | **Lunch break**
14:30-19:00 | Hands-on

Wednesday November 18

09:00-09:50 | *Neural bases of perception*. Cognitive maps and where to find them. *Ignacio Sanguinetti*
09:50-10:40 | *Neural bases of perception*. The electric image. *Angel Caputi*
10:40-11:10 | **Coffee break**
11:10-12:00 | *Neural bases of perception*. Adaptive command for orienting behavior in premotor brainstem neurons of barn owls. *José Luis Peña*
12:00-14:30 | **Lunch break**
14:30-19:00 | Hands-on
20:00-21:00 | PROFESSIONAL SKILLS III "Women in Latin American Neuroscience". *Verónica Amarante, ECLAC-IBRO LARC*

Thursday November 19

09:00-09:50 | *Neural and molecular bases of social behavior*. Neuroendocrinological modulation of communication signals. *Vielka Salazar*
09:50-10:40 | *Neural and molecular bases of social behavior*. Seasonal changes of communication signals. *Laura Quintana*
10:40-11:10 | **Coffee break**
11:10-12:00 | *Neural bases and molecular of social behavior*. The social brain. *Lauren O'Connell*
12:00-14:30 | **Lunch break**
14:30-19:00 | Hands-on
20:00-21:00 | Meet the PIs (Optional)

Friday November 20

09:00-09:50 | *Neural and molecular bases of social behavior*. Agonistic behavior. *Ana Silva*
09:50-10:40 | *Neural and molecular bases of social behavior*. Neuroendocrinological bases of maternal care in mammals. *Natalia Uriarte*
10:40-11:10 | **Coffee break**

11:10-12:00 | Neural bases of social behavior. Neural basis of species differences in parental care strategies. *Lauren O'Connell*

12:00-14:30 | **Lunch break**

15:30-17:30 | Lab work student presentations III

17:30-18:00 | **BREAK**

18:00-19:00 | Closure Ceremony

Hands-on lab activities

We will organize 12 hands-on activities on the different topics addressed in the course in three sequential rounds. Each lab activity will be directed by at least one Local or Foreign Faculty and will have no more than 4 students in order to promote the proactive engagement of students with experimental activities. Students will be distributed in the hands-on activities according to their background so they can take advantage of theoretical and experimental training different from those of their home laboratories. At the end of each lab work session, students will analyze the data obtained, discuss it with their fellow students under the supervision of a faculty and produce a 10 min presentation for a general discussion.

Hands-on lab activities I (November 2-6)

1. Short- and long-term synaptic plasticity in rat hippocampal slices

Professors: Pablo Castillo, Michel Borde.

Location: Depto. de Fisiología, Fac. de Medicina, UdelaR.

Classical and novel forms of synaptic plasticity in the mammalian hippocampus will be analyzed *in vitro* with field potential recordings, current source density analysis (CSDA) and current and voltage-clamp intracellular recording techniques in the whole cell patch (WCP) configuration.

2. Membrane properties and electrical coupling in CNS neurons of the rat

Professors: Alberto Pereda, Sebastián Curti.

Location: Depto. de Fisiología, Fac. de Medicina, UdelaR.

In an *in vitro* preparation students will have the opportunity to gain insights in patch clamp whole cell recordings (voltage and current clamp configurations) from single cells and from electrically coupled pairs of neurons. Electrical transmission between neurons will be characterized through the evaluation of the coupling strength, its bi-directionality and the junctional conductance. Interaction of electric coupling with passive and active membrane properties of coupled neurons will also be analyzed.

3. Mapping Glutamate and GABA ionotropic receptors with laser photolysis

Professor: Federico Trigo

Location: Depto. de Neurofisiología Celular y Molecular, IIBCE.

In this hands-on section we will learn how to use a laser in order to photo-trigger the release of GABA and Glutamate in central nervous system neurons. We will learn the advantages and disadvantages of the technique as well as calibration methods. We will analyze the laser evoked currents and compare those with spontaneous EPSCs and IPSCs.

4. The intrinsic dynamics of neuronal firing: patch clamp recordings in slices

Professor: Raúl Russo.

Location: Depto. de Neurofisiología Celular y Molecular, IIBCE.

The students will learn the basics of patch clamp recordings of neurons in slices of the central nervous system. During the hands-on activity we will discuss the advantages and limitations of in vitro preparations as well as the fundamentals of current and voltage clamp. We will focus the activity on the intrinsic membrane properties of neurons: how they arise and their impact on neural integration.

Hands-on activities II (November 9-13)

5. Analysis of mitochondrial network in live glial cells in culture by confocal microscopy

Professors: Patricia Cassina, JP Bolaños

Location: Depto. de Histología & Embriología. Fac. de Medicina, UdelaR.

Mitochondria are organelles that have been primarily known as the 'power house of the cell'. However, recent advances in the field have revealed that mitochondria are also involved in many other cellular activities like lipid modifications, redox balance, calcium balance and even control cell death. These multifunctional organelles are motile and highly dynamic in shapes and forms; the dynamism is brought about by the mitochondria's ability to undergo fission and fusion with each other. Therefore it is very important to be able to image mitochondrial shape changes to relate to the variety of cellular functions these organelles have to accomplish.

6. Identification of different cells populations after Spinal Cord Injury by flow cytometry

Professors: Natalia Lago, Ruben López-Vales

Location: Institut Pasteur, Montevideo

The inflammatory response that occurs in the spinal cord following injury contributes importantly to spread tissue damage to healthy regions adjacent to the lesion site, and consequently, to increase neurological deficits. In the present practical activity, we will describe how to induce contusion injuries in the mouse spinal cord and a useful methodology to assess neuroinflammation in lesioned spinal cord tissue samples by flow cytometry.

7. Experimental models of Parkinson disease and neuroprotection

Professor: Giselle Prunell.

Location: Depto. de Neuroquímica, IIBCE.

Cellular models of neurodegeneration will be used during the laboratory module and the beneficial effects of natural products will be taken as an example of new potential therapies. The students will have the opportunity to work with primary neuronal cultures and a cell line to assess the neuroprotective activity of different natural products using biochemical and morphological approaches.

8. Chemogenetic tool DREADD in neurobiology of neuropsychiatric diseases

Professors: Kuei Y. Tseng, Adriana Caballero, Cecilia Scorza (DNFE-IIBCE)

Location: Depto de Neurofarmacología Experimental, IIBCE.

Designer Receptors Exclusively Activated by Designer Drugs (DREADD) is a chemogenetic-based tool which is now commonly used by neuroscientists to identify the circuitry and cellular signals involved in behavior, perceptions, emotions, and motor functions in different animal species. The students will be involved in the experimental approach to learn this technique, in

order to study the role of regions of the mesocorticolimbic circuit involved in the rewarding effects of psychostimulant drugs like cocaine and coca-paste.

Hands-on activities III (November 16-20)

9. Close loop behavior with bonsai.

Professors: Leonel Gómez, Juan Ignacio Sanguinetti

Location: Lab. Neurociencias, Fac. de Ciencias, Udelar.

Currently, despite the success of the reductionist approaches in neuroscience, many authors maintain that it is necessary to complement those strategies with studies that allow a careful theoretical and experimental decomposition of behavior to discover the component processes and its underlying algorithms. These studies provide a solid base for addressing the neural implementation of a behavior. Bonsai is a high-performance programming environment, fast to learn and easy to extend that allows the development of behavioral analysis projects based on the acquisition and processing of signals of different types: video, sound, neurophysiological records, etc. Using these tools, the students will be able to track, quantify and analyze different kinds of behavior guided by experimented instructors.

10. Structural plasticity in the rat's nervous system during motherhood

Professors: Natalia Uriarte, Javier Nogueira

Location: Sec. Fisiología, Fac. de Ciencias – Depto. Histología y Embriología, Fac. de Medicina, Udelar.

A remarkable reorganization of the extracellular matrix (ECM) occurs in the medial preoptic area (mPOA) of female rats during motherhood. Highly organized aggregations of ECM, perineuronal nets (PNNs) are expressed in mPOA and dynamically change during this period in response to gonadal hormones. As PNNs are proposed to play key roles in neural plasticity, and pregnancy and lactation are characterized by a significant increase in neuroplasticity, we proposed that these structures are involved in the expression of the behavioral flexibility during motherhood. Students will participate in experiments designed to assess the role of PNNs in the maternal behavior of lactating rats, which will include stereotaxic surgeries, behavioral recording and cytochemical detection of PNNs.

11. Transcriptomics of the dominant-subordinate status

Professors: Ana Silva, José Sotelo, Vielka Salazar

Location: Unid. Bases Neurales de la Conducta – Depto. De Genómica, IIBCE

The study of status-dependent gene expression profiles in the vertebrate brain has been challenged by several confounding factors. As the stereotypical type of aggression studied so far is the inter-male reproductive competition, it has been impossible to disentangle neuromolecular mechanisms driven by reproduction or by competence. Students will be involved in behavioral experiments of the best understood example of non-breeding dominance in fish, using the native weakly electric fish, *Gymnotus omarorum*. Further, students will analyze transcriptomic profiling of the brain region containing the preoptic area in both male dominants and subordinates identifying a set of differentially expressed genes and their correlation with behavioral traits.

12. Circadian and seasonal modulation of social behavior

Professors: Laura Quintana, Adriana Migliaro, Paula Pouso

Location: Unid. Bases Neurales de la Conducta, IIBCE

The electric behavior, the outcome of the electrogenic system of weakly electric fish, is a behavioral display with well-known circadian, social, and seasonal modulations. It is also an advantageous model to explore neuroendocrine mechanisms controlling the interplay of circadian (melatonin) and social (hypothalamic neuropeptides) modulators. Students will record the electric behavior during day and night, induce pharmacological modulations in *in vivo* and *in vitro* preparations, and explore the changes of the melatonergic and vasotocinergic systems between day and night and across seasons.

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