2012 RICARDO MILEDI NEUROSCIENCE TRAINING PROGRAM
Neuroscience: synapses, circuits and behavior

March 5 – 30, 2012 - Buenos Aires, Argentina

Instituto Leloir, CONICET
Facultad de Medicina and Facultad de Ciencias Exactas y Naturales, UBA
Instituto de Investigaciones en Ingeniería Genética y Biología Molecular (INGEBI, CONICET)
Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE, UBA-CONICET)

School Directors:

Alejandro Schinder and Osvaldo Uchitel

Organizing Committee:

Daniel Calvo, Arturo Romano

Organizing Institutions:

Society for Neuroscience (SFN)/The Grass Foundation
and Sociedad Argentina de Investigación en Neurociencias (SAN)

COURSE PROGRAM

LOCAL FACULTY

Daniel Calvo (INGEBI)
Fernanda Ceriani (Leloir)
Alejandro Delorenzi (IFIBYNE)
Belén Elgoyhen (INGEBI)
Tomás Falzone (F Medicina)
Diego Golombek (UNQUI)
Juan Goutman (INGEBI)
Eleonora Katz (INGEBI)
Emilio Kropff (Leloir)
Guillermo Lanuza (Leloir)
Fernanda Ledda (F Medicina)
Fernando Locatelli (IFIBYNE)
Antonia Marin-Burgin (Leloir)
Gustavo Murer (F Medicina)
Gustavo Paratcha (F Medicina)
M. Eugenia Pedreira (IFIBYNE)
Arturo Romano (IFIBYNE)
Marcelo Rubinstein (INGEBI)
Arleen Salles (Centro de Invest. Filosóficas)
Alejandro Schinder (Leloir)
Lidia Szczupak (IFIBYNE)
Daniel Tomsic (IFIBYNE)
Osvaldo Uchitel (IFIBYNE)
Francisco Urbano (IFIBYNE)

INVITED FACULTY

Carlos Aizenman (Brown University, Rhode Island, USA)
Benedikt Berninger (Helmholtz Zentrum, Munich)
Pablo Castillo (Albert Einstein College of Medicine, New York , USA)
Fabrizio Gabbiani (Baylor College of Medicine, Houston, TX, USA)
Guillermo González-Burgos (University of Pittsburgh School of Medicine, USA)
Francois Guillemot (National Institute for Medical Research, London, UK)
Isabel Llano (University of Paris)
Andreas Luthi (Friedrich Miescher Institute, Basel, Switzerland)
Alain Marty (University of Paris)

LAB INSTRUCTORS

Facundo Alvarez Heduán, Andrea Beltrán González, Estefanía Bello, Mariano Belluscio, Martín Berón de Astrada, Mariano Boccia, Barbara Braz, Abel Carcagno, Rodrigo Casas Cordero, Eric Casey, Lucas Cromberg, Ana Depetris-Chauvin, Daniela Di Bella, Mariano DiGuilmi, Mariela Escande, Noel Federman, Rodrigo Fernández, Cecilia Forcato, Lía Frenkel, Ramiro Freudenthal, Javier Gasulla, Carlota Gonzalez Inchauspe, Axel Gorostiza, Dolores Irala, María Eugenia Martín, Javier Maza, Lucas Mongiat, Nara Muraro, Gabriela Otero, Joaquin Piriz, María Laura Rodríguez, Elisa Schneider, Carolina Wedemeyer.

COURSE SECRETARY: **Silvina Ceriani**

SPONSORS OF THE MILEDI SCHOOL 2012

Miledi School at-a-glance

March 2012

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
				1	2	3
4 **ARRIVAL**	5 **RETREAT** Welcome by organizers Uchitel Round table	6 **RETREAT** D. Calvo – E. Katz – A. Marty (I) – I. Llano (I) – R. Schneggenburger (I)	7 **RETREAT** B. Berninger (I) – Llano (II) – N. Spitzer (I) – Marty (II) – Ralph (II)	8 **RETREAT** Spitzer (II) – Berninger (II) – talks by local faculty	9 **SYMPOSIUM**/LI Llano – Marty – Schneggenburger – Berninger – Spitzer **LABS BLOCK I**	10 SHORT TALKS Talks by students Free afternoon
11 **FREE DAY**	12 LECTURES/LAB I D Calvo E Katz **LABS BLOCK I**	13 LECTURES/LAB I G Paratcha/F Ledda T Falzone **LABS BLOCK I**	14 LECTURES/LAB I M Rubinstein G Lanuza **LABS BLOCK I**	15 LECTURES/LAB I A Schinder A Marín-Burgin **LABS BLOCK I**	16 LECTURES/LAB I F Urbano G Murer **LABS BLOCK I**	17 MEMORY LAB I **M Pedreira**
18 **FREE DAY**	19 LECTURES/LAB I M Pedreira A Romano **LABS BLOCK I**	20 LECTURES/LAB I A Delorenzi F Locatelli **LABS BLOCK I**	21 **RETREAT II** A Luthi – P Castillo – C Aizenman – O Uchitel	22 LECTURE/LAB II G González Burgos **LABS BLOCK II**	23 **SYMPOSIUM**/LII González Burgos – Castillo – Luthi – Aizenman **LABS BLOCK II**	24 STUDENTS/LMII **Students´ presentations for LAB BLOCK I** **MEMORY LAB II** **M Pedreira**
25 **FREE DAY**	26 LECTURE/LAB II F Ceriani D Golombek **LABS BLOCK II**	27 LECTURE/LAB II L Szczupak D Tomsic **LABS BLOCK II**	28 LECTURE/LAB II F Guillemot **LABS BLOCK II**	29 LECTURE/LAB II F Gabbiani **LABS BLOCK II**	30 **SYMPOSIUM** Guillemot – Gabbiani – Salles **Students´ presentations for LAB BLOCK II**	31 **DEPARTURE**

SCHEDULE FOR LECTURES AND LAB SESSIONS

Typical lecture/lab day schedule for students

7.30 am breakfast
8.30 taxi to Leloir Institute
9.00 – 10.30 Lecture 1
10.30 – 11.00 coffee break
11.00 – 12.30 Lecture 2
12.30-13.30 Lunch at Leloir
13.30 - Taxi to labs/LABORATORY SESSIONS
21.00 Dinner at a restaurant near the hotel

LAB WORK IS DIVIDED IN 2 BLOCKS THAT ARE GROUPED TEMATHICALLY.
THE FIRST BLOCK WILL INCLUDE CELLULAR NEUROSCIENCE, DEVELOPMENT AND SYNAPTIC TRANSMISSION. IT WILL ENCOMPASS 8 AFTERNOON LAB SESSIONS STARTING ON FRIDAY MARCH 9 (THAT ONE IS A SHORT VISIT WITH MOSTLY LECTURE ABOUT THE LAB THEME) AND ENDING ON TUESDAY MARCH 20.
THE SECOND BLOCK WILL INCLUDE NEURAL CIRCUITS, LEARNING AND BEHAVIOR, TAKING 6 AFTERNOON LAB SESSIONS FROM THURSDAY MARCH 22 UNTIL THURSDAY MARCH 29.

STUDENTS WILL BE ASSIGNED TO SPECIFIC LABS FOR BLOCK 1 AND 2. THIS MEANS THAT EACH LAB WILL RECEIVE 2 OR 3 STUDENTS AND WILL KEEP THEM FOR THE ENTIRE BLOCK.

LABORATORY SESSIONS 1ST BLOCK (see lab session details in pg. 11)

Physiology, pharmacology and biophysics of ionotropic GABA receptors
Daniel Calvo, Javier Gasulla, Andrea Beltrán González (INGEBI) **2 students**

Synaptic transmission at the peripheral auditory system
Juan Goutman, Eleonora Katz, Belén Elgoyhen, Carolina Wedemeyer, Facundo Alvarez Heduan (INGEBI) **2 students**

Calcium channels, transmitter release and short term synaptic plasticity
Osvaldo Uchitel, Joaquin Piriz, Carlota Gonzalez Inchauspe, Mariano DiGuilmi (IFIBYNE) **2 students**

Synaptogenesis and neurogenesis in the adult mouse dentate gyrus
Alejandro Schinder, Antonia Marin-Burgin, Lucas Mongiat (LELOIR) **3 students**

Oscillations in thalamocortical neurons
Francisco Urbano, María Eugenia Martín (IFIBYNE) **2 students**

Neurogenesis and neuronal migration
Guille Lanuza, Abel Carcagno, Daniela Di Bella (LELOIR) **2 students**

Modulation of neuronal trafficking by neurotrophic factors
Tomás Falzone, Gustavo Paratcha, Fernanda Ledda, Gabriela Otero, Lucas Cromberg, Dolores Irala (FMED)
2 students

LABORATORY SESSIONS 2ND BLOCK (see lab session details in pg. 13)

Neural circuits in the leech
Lidia Szczupak, Elisa Schneider (IFIBYNE) **2 students**

Neuronal Activity Underlying Global Brain States
Gustavo Murer, Mariela Escande, Barbara Braz, Mariano Belluscio (FMED) **2 students**

In vivo intracellular recording of neuronal plasticity subserving long-term visual memory.
Daniel Tomsic, Martín Berón de Astrada (IFIBYNE) **2 students**

Molecular mechanisms in memory reconsolidation
Arturo Romano, Ramiro Freudenthal, Noel Federman, Mariano Boccia (IFIBYNE) **2 students**

The neuromodulatory state during consolidation and the memory expression: behaviour and calcium-imaging approaches
Alejandro Delorenzi, Fernando Locatelli, Javier Maza (IFIBYNE) **2 students**

Structure-function analysis of a circuit key to circadian behavior
Fernanda Ceriani, Nara Muraro, Lía Frenkel, Axel Gorostiza, Ana Depetris-Chauvin (LELOIR) **3 students**

Genetic Dissection of Dopamine D2 Receptor Function in the Mouse Brain
Marcelo Rubinstein, Estefanía Bello, Rodrigo Casas Cordero, Eric Casey (INGEBI) **2 students**

MEMORY LAB SESSIONS I AND II (ALL STUDENTS)

Reconsolidation of a declarative memory in humans: The effect of repeated triggering of the process on memory persistence.
María Eugenia Pedreira, Cecilia Forcato, María Laura Rodríguez, Rodrigo Fernández

COURSE SCHEDULE

FIRST WEEK: March 5 to 11

- **Monday March 5 – Thursday March 8: 3-day retreat at Tigre at Aires del Delta cabins (www.airesdeldelta.com.ar/english/default.php) for course students and faculty**

11.30 Trip to Aires del Delta (Bus + Boat)
18.00 **Welcome reception by course directors**, course description, handouts distribution
18.30 **Osvaldo Uchitel: Ricardo Miledi, science and history**
19.30 **past present and future of neuroscience and round table**

20.30 Dinner and beers

- **Tuesday March 6, Tigre**

8.30 breakfast
9.30 **Daniel Calvo: contribution of ion channels to neuronal excitability**
10.30 Eleo Katz: Neurons and excitability-action potential
11.30 break
12.00 Alain Marty (lecture I) Whole-cell recording
13.30 light lunch
15.00 **Isabel Llano (lecture I) Fluorescent indicators of calcium concentration**
16.30 mate break
17.00 Benedikt Berninger (lecture I) The glial nature of embryonic and adult neural stem cells
18.30 discussion and beers

20.00 dinner

- **Wednesday March 7, Tigre**

8 am breakfast
9.00 Isabel (lecture II): Calcium and synaptic transmission
10.30 break
11.00 **Alain (lecture II): GABAergic synapses**
12.30 light lunch
14.00 **Juan Goutman: Control of presynaptic Ca, kinetic analysis of transmitter release and short-term plasticity at the calyx of Held**
15.30 break
16.00 **O Uchitel: Calcium channels are a headache. Electrophysiological studies in a migraine animal model**
17.30 mate break
18.00 A Schinder: Neurogenesis in the adult hippocampus
20.30 dinner
22.30 **Roundtable: How to plan a scientific career**

- **Thursday March 8, Tigre**

8 am breakfast

9.00 **Benedikt (lecture II) Cellular reprogramming: a novel approach towards modelling and cell therapy for neurodegenerative diseases**
10.30 break
11.00 Belén Elgoyhen: Nicotinic Receptors of Coclear Hair Cells
12.30 light lunch
14.00 - 14.50 **Eleonora Katz: Short-term plasticity at the olivocochlear outer hair cell synapse**
14.50 – 15.40 **Juan Goutman: Transmitter release at a single ribbon synapse**
15.40 – 16.30 **Tomás Falzone: Coordinated lysosome and proteasome retrograde axonal transport. From motor proteins to a regulated crosstalk in synaptic protein degradation**

17.30 departure to Le Batiment

21.00 Dinner at Arturito

IN ADDITION, THROUGHOUT THE RETREAT EACH STUDENT WILL BE ASSIGNED A TUTOR THAT WILL HELP HIM/HER TO POLISH THEIR 10 MIN PRESENTATION ABOUT THEIR OWN WORK, WHICH WILL OCCUR ON SATURDAY MORNING AT LELOIR.

STUDENTS WILL BE ASSIGNED TO LABS ALSO DURING THE RETREAT.

- **Friday March 9** **Open symposium at Leloir**

9.30 Isabel Llano: Presynaptic calcium signaling
10.10 Alain Marty: A direct estimate of the readily releasable pool of synaptic vesicles obtained with a new single-site calcium uncaging method
10.50 Coffee break
11.20 Benedikt Berninger: Direct conversion of somatic cells of astroglial and pericytic origin into functional neurons
12.00 To be announced

13.00 lunch at Leloir
14.00 First visit to labs "on site", talks about lab sessions

21.00 Dinner at Arturito

- **Saturday March 10**

9.30 Short talks (10 min) by students at Leloir x 15
FREE AFTERNOON

- **Sunday March 25 FREE DAY**

SECOND WEEK: March 12 to 18

Monday March 12 to Tuesday March 20: typical lecture/lab week

- **Monday March 12**

9.00 Daniel Calvo: Redox modulation of the GABAergic neurotransmission
10.30 Coffee Break
11.00 Eleonora Katz: From sound to synapses at the mammalian auditory periphery
12.30 Lunch at Leloir
Afternoon Lab block I
21.00 Dinner at Le Batiment or similar

- **Tuesday March 13**

9.00 Gustavo Paratcha/Fernanda Ledda: Neurotrophic Factors: A window into nervous system development
10.30 Coffee Break
11.00 Tomás Falzone: Neuronal Polarity: The Orchestrated Role of Microtubules, Molecular Motors and Cargos
12.30 Lunch at Leloir
Afternoon Lab block I
21.00 Dinner at Arturito

- **Wednesday March 14**

9.00 Marcelo Rubinstein: Transgenic and mutant mice to understand gene function in the mammalian brain (including 10 min of laboratory animals)
10.30 Coffee Break
11.00 Guillermo Lanuza: Neuronal subtype specification in the neural tube. Insights from developmental genetics.
12.30 Lunch at Leloir
Afternoon Lab block I
21.00 Dinner at Arturito

- **Thursday March 15**

9.00 Antonia Marin Burgin: Excitation/Inhibition balance in adult neurogenesis
10.30 Coffee Break
11.00 Emilio Kropff: Place cells and grid cells in the hippocampus
12.30 Lunch at Leloir
Afternoon Lab block I
21.00 Dinner at Arturito

- **Friday March 16**

9.00 Francisco Urbano: Thalamocortical interactions in health and disease
10.30 Coffee Break
11.00 Gustavo Murer: Neuronal activity underlying global brain states
- 12.30 Lunch at Leloir

Afternoon Lab block I
21.00 Dinner at Arturito

- **Saturday March 17**

10.00 Experiments by Eugenia Pedreira for ALL Students at IFIBYNE, part I
Consolidation of declarative memory in humans (I)

FREE AFTERNOON

- **Sunday March 18 FREE DAY**

THIRD WEEK: March 19 to 25

- **Monday March 19**

9.00 M. Eugenia Pedreira: Study of the different memory phases from the acquisition to extinction. Characterization of the diverse phases in a declarative memory in humans
10.30 Coffee Break
11.00 Arturo Romano: The molecular basis of the different phases of memory
12.30 Lunch at Leloir
Afternoon Lab block I
21.00 Dinner at Le Batiment or similar

- **Tuesday March 20**

9.00 Alejandro Delorenzi: Modulation of memory
10.30 Coffee Break
11.00 Fernando Locatelli: Olfaction: Sensation, perception and plasticity
12.30 Lunch at Leloir
Afternoon Lab block I LAST BLOCK I LAB SESSION
21.00 Dinner at Arturito

- **Wed March 21 Renovation of faculty, retreat in countryside with night barbecue**

Three talks by invited speakers (90 min each)
Andreas Luthi: Learning and memory: a circuits perspective
Pablo Castillo: Synaptic plasticity: basic rules and mechanisms
Carlos Aizenman: Regulation of Neuronal Excitability

- **Thurdsay March 22**

9.00 Guillermo González Burgos 3-h lecture w/30 min break
GABAergic inhibition in cortical circuits: now that we know what we know, what do we know?
10.30 Coffee Break
Schizophrenia: are cognitive deficits the consequence of altered synaptic transmission in cortical circuits?
12.30 Lunch at Leloir
Afternoon Lab block II
21.00 Dinner at Arturito

- **Friday March 23 Open symposium at Leloir**

9.30 Guillermo González-Burgos: Endocannabinoid-mediated suppression of inhibition in prefrontal cortex: synthesis pathways, development and modulation by THC administration
10.15 Pablo Castillo: Activity-dependent synaptic plasticity expressed by NMDA receptors
11.00 Coffee break
11.30 Andreas Luthi: Defining the neuronal circuitry of fear and beyond
12.15 Carlos Aizenman: Functional regulation of a developing visual circuit

13.30 Lunch at Leloir

Afternoon Lab block II

21.00 Dinner at Arturito

- **Saturday March 24**

9.30 Student´s presentations LAB BLOCK I at IFIBYNE
13.00 Choripan Lunch at Costanera
14.30 Experiments by Eugenia Pedreira for ALL Students at IFIBYNE, part II
Consolidation of declarative memory in humans (II)

Sunday March 25 FREE DAY

FOURTH WEEK: March 26 to 30

- **Monday March 26**

9.00 Fernanda Ceriani: Neuronal control of circadian behavior in flies
10.30 Coffee Break
11.00 Diego Golombek: Circadian rhythms and clocks: a tale of extreme localization in the (mammalian) brain
12.30 Lunch at Leloir

Afternoon Lab block II

21.00 Dinner at Le Batiment or similar

- **Tuesday March 27**

9.00 Lidia Szczupak: Motor control in the leech nervous system. A model where single cells matter.
10.30 Coffee Break
11.00 Daniel Tomsic: Neuroethology of escape responses: from sensory ecology to neurons and back
12.30 Lunch in Leloir

Afternoon Lab block II

21.00 Dinner at Arturito

- **Wednesday March 28**

9.00-12.30 **Francois Guillemot: Signaling and transcriptional control of neuronal development from stem cells to synapses**
12.30 Lunch in Leloir

Afternoon Lab block II

21.00 Dinner at Arturito

- **Thursday March 29**

9.00 **Fabrizio Gabbiani: Introduction to Computational Neuroscience: Cellular and Synaptic Models.**

10.30 Coffee Break

11.00 Introduction to Computational Neuroscience: Coding and Systems

12.30 Lunch in Leloir

Afternoon Lab block II LAST LAB SESSION

21.00 Dinner at Arturito

- **Friday March 30 Open symposium at Leloir**

9.30 Francois Guillemot: Transcriptional control of neuronal stem cell fates

10.20 Fabrizio Gabbiani: Looming-sensitive neurons and neural computations underlying collision avoidance behaviors

11.10 Coffee break

11.40 Arleen Salles: Neuroethics

12.40 Lunch

14.00 Student´s presentations LAB BLOCK II at Leloir

21.00 Farewell dinner and party at Odu´s Place

LAB SESSIONS

LAB WORK BLOCK 1

Physiology, pharmacology and biophysics of ionotropic GABA receptors

Daniel Calvo, Javier Gasulla, Andrea Beltrán González (INGEBI)

Inhibitory neurotransmission in the central nervous system is mainly mediated by ionotropic GABA receptors. The aim of this lab practice will be to analyze the properties of different classes of ionotropic GABA receptors that mediate neuronal inhibition and to study their modulation by drugs. *Xenopus laevis* oocytes will be used as a model for expression of different combinations of $GABA_A$ and $GABA_C$ receptor subunits. Receptor activity will be elicited by application of GABA and monitored by electrophysiological recording. Experiments will show the influence of subunit composition in the physiological, pharmacological and biophysical properties of ionotropic GABA receptors. Modulation of responses mediated by the different GABA receptor subtypes will be also studied by using diverse pharmacological agents (neurosteroids, benzodiazepines and redox agents). Additionally, whole-cell patch-clamp recordings will be performed in mice brain slices to measure synaptic and tonic currents mediated by GABA receptors and their modulation assessed in the presence of some typical pharmacological agents.

Synaptic transmission at the peripheral auditory system

Juan Goutman, Eleonora Katz, Belén Elgoyhen, Carolina Wedemeyer, Facundo Alvarez Heduan (INGEBI)

The mammalian inner ear houses the structure responsible for detecting and transducing sounds into electrical signals: the cochlea. Two types of sensory cells present in the organ of Corti, the sensory epithelium of the cochlea, are responsible for transmitting acoustic information to the brain (inner hair cells, IHC) and for amplifying incoming sounds (outer hair cells, OHC). Both IHC and OHC receive synaptic connections that help bring the acoustic information to the brain or regulate the amplification of sounds, namely, afferent innervation to the IHC and efferent innervation to the OHC, respectively. We will do acute dissections of the organ of Corti of young mice and perform patch-clamp recordings on either IHC or OHC and investigate their peculiar electrical properties. We will also couple these recordings with stimulation of the efferent axons that reach the organ of Corti and study the biophysical and pharmacological properties of these synaptic connections. Finally, the ability of IHC to transmit information to the brain will be evaluated by measuring transient changes in their capacitance that result from the release of glutamate at the IHC-afferent synapse.

Calcium channels, transmitter release and short term synaptic plasticity

Osvaldo Uchitel, Joaquin Piriz, Carlota Gonzalez Inchauspe, Mariano DiGuilmi (IFIBYNE)

Neuromuscular junction and calyx of Held giant synapse will be used as models to analyze the basic properties of synaptic transmission and its modulation. Electrophysiological techniques including intracellular, extracellular and patch clamp whole cell techniques will be used to record pre and postsynaptic events. Vesicle recycling will be analyzed with image techniques with FM dyes at the neuromuscular junction. Presynaptic recording of Ca currents and presynaptic Ca concentration kinetics related to short term plasticity will be investigate using the calyx of Held giant synapse.

Synaptogenesis and neurogenesis in the adult mouse dentate gyrus

Alejandro Schinder, Antonia Marin-Burgin, Lucas Mongiat (LELOIR INSTITUTE)

Neurogenesis in the adult hippocampus will be used as a model system to study synapse formation, neuronal maturation and circuit assembly. Neurons will be labeled using a retrovirus to express GFP in

dividing progenitor cells of the adult dentate gyrus, as described in (Esposito et al., J Neurosci 2005). Students that join this lab practice will have the chance to do confocal imaging of immature synapses and electrophysiological recordings of spontaneous and evoked afferent activity in newly generated dentate granule cells in acute slices. Data analysis of whole cell recordings will involve the analysis of intrinsic neuronal and synaptic properties that differ between immature and mature neurons.

Oscillations in thalamocortical neurons

Francisco Urbano, María Eugenia Martín (IFIBYNE)

Thalamocortical neurons present transitions between gamma-band membrane potential oscillations (associated with wakefulness and consciousness) and low-frequency bursts (associated with somnolence and sleep) that occur rapidly. P/Q-type VGCCs located in the dendrites of neurons support the characteristic 35-45-Hz gamma-band oscillations while T-type calcium channels present on the soma support low-frequency burst activity. We will record neurons from the ventrobasal nucleus (VB) using coronal slices in combination with patch-clamp whole-cell recordings in current-clamp configuration. We will able to change the pattern of oscillations of VB neurons while injecting current to change membrane potential values. If possible, we will use thalamic slices from mice lacking P/Q-type calcium channels to illustrate how in the absence of these channels VB neurons cannot generate gamma-band oscillations. Finally, Lucifer yellow will be routinely added to the intracellular solution to illustrate the morphology of VB neurons during recordings.

Neurogenesis and neuronal migration

Guille Lanuza, Abel Carcagno, Daniela Di Bella (LELOIR)

The developing cerebral cortex will be used as a model to study embryonic neurogenesis and migration of post-mitotic cortical neurons. Student will pefrorm *in utero* electroporation in order to mark or manipulate defined sets of progenitors cells and neurons *in vivo*. *In utero* electroporation in the rodent has become a method of choice for gain- and loss-of-function studies in the embryonic brain. This technique will be combined with molecular genetic approaches in the mouse. Briefly, plasmids expressing GFP, Cre recombinase or proneural transcription factors will be transfected in the mouse telencephalon at different stages of development. Conditional reporter (or KO) alleles will allow to perform cell fate mappings and to gain experience in the use of loxp/Cre technology. Radial migration and formation of the layered structure will be analyzed by confocal microscopy.

Modulation of neuronal trafficking by neurotrophic factors

Tomás Falzone, Gustavo Paratcha, Fernanda Ledda, Gabriela Otero, Lucas Cromberg, Dolores Irala (FMED)

Signaling by neurotrophic factors in immature neurons is among the critical extracellular cues identified to control neuronal polarization and differentiation. Neurite outgrowth is supported by precise and coordinated regulation of neurotrophic factor over the transport machinery. Correct transport and positioning of proteins and organelles inside neurons depend on the orchestrated interaction of molecular motors with their cargo and microtubule tracks. During this laboratory practice student will learn to perform primary hippocampal and sensory dorsal root ganglia (DRG) neuronal cultures from newborn and embryonic mice, respectively. Polarized cultures will be used to register under an inverted fluorescent microscope the axonal transport dynamics of different intracellular cargos and its modulation by neurotrophic factors. Students will perform primary neuron transfection to observe the real-time dynamics of membrane fluorescently fused proteins. Stream acquisition and time-lapse movies using the specific delivery of organelle dyes will be performed. Two color movies will be set up to identify the movement of shared particles in a unifying moving organelle.

LAB WORK BLOCK 2

Electrical and chemical synapses in the nervous system of the leech

Szczupak L, Schneider E (IFIBYNE)

In this lab practice we will investigate properties of neurons and their connections using the stereotyped leech nervous system that allows recognizing individual neurons by their position and electrophysiological characteristics. The students will have the chance to perform electrophysiological experiments to understand basic resting and active properties of cells. Dual pair recordings using intracellular electrodes would be performed to study electrical, chemical and mixed connections between specific types of neurons. The analysis of the different types of synapses will include the study of their dynamic and plasticity mechanisms. In addition, we will fill neurons with small fluorescent dyes and use confocal microscopy to visualize their morphology and their dye-coupling with electrically connected pairs.

Neuronal Activity Underlying Global Brain States

Gustavo Murer, Mariela Escande, Barbara Braz, Mariano Belluscio (FMED)

The intact brain shows different "global states" (e.g., slow waves during sleep, "activation" during wakefulness), which are characterized by distinctive patterns of activity in the neocortex, thalamus, hippocampus and basal ganglia, and specific patterns of functional connectivity between these brain networks. Anesthetized rodents provide a system model to study how brain states are organized. Students attending our lab will record simultaneously the membrane potential of cortical neurons ("up and down states"), networks of spiking neurons in a nearby cortical area, and local field potentials in the hippocampus (theta rhythm, ripples) and neocortex (slow waves, "activation"). This will allow us to label the intracellularly recorded neurons and study their morphology postmortem, perform "spike sorting" to classify extracellularly recorded spikes and classify them as belonging to interneurons or pyramidal neurons, extract different frequency components in the signals by using wavelets, and computing measures of functional connectivity like cross-correlation and coherence.

In vivo intracellular recording of neuronal plasticity subserving long-term visual memory.

Daniel Tomsic, Martín Berón de Astrada (IFIBYNE)

Recording neuronal activity in vivo is fundamental to understand the working brain, but intracellular recording are rarely achieved in intact, behaving organisms. This can be done in crabs, allowing studying how visual processing in identified neurons relates to highly adaptive behaviors that involve long-term memory (Tomsic et al. J Neurosci 2003).

Students will experience with several neurophysiological principles, ranging from intrinsic neuronal properties (e.g. measurements of input resistances, IPSP and EPSP reversal potentials, accommodation) to more integrative phenomena such as neuronal receptive fields and multimodal integration. In particular, they will be able to record, measure and analyze different kind of changes occurring in identified neurons during learning.

Molecular mechanisms in memory reconsolidation

Arturo Romano, Ramiro Freudenthal, Noel Federman, Mariano Boccia (IFIBYNE)

After learning, memory is labile and persists for a brief time. However, becomes stable and long-lasting by the process of consolidation. Long-term memory consolidation involves signaling pathways activation that lead to regulation of gene expression and *de novo* protein synthesis. Ones a memory is consolidated may be re-activated by retrieval and then, a new period of lability is induced. In order to re-stabilize the original trace, memory undergoes a consolidation-like process called reconsolidation. Students will participate in an

experiment that include training, memory reactivation and testing of animals, dissection of brain tissues and molecular techniques for determination of protein kinases and transcription factors activation during memory reconsolidation. They will participate in behavioral analysis and quantification of molecular processes obtained from experimental and control groups in order to determine a correlation between memory reconsolidation and activation of particular intracellular mechanisms.

The neuromodulatory state during consolidation and the memory expression: behaviour and calcium-imaging approaches

Alejandro Delorenzi, Fernando Locatelli, Javier Maza (IFIBYNE)

The generation of a memory should entail an evaluation of the experience, indicative of its biological meaning. For several decades is has been assumed that endogenous modulatory systems play a major role in this selection by affecting memory storage. Our recent results obtained investigating the retrieval and reconsolidation phases of memory point to a completely new an original interpretation of the neuromodulatory action on memory. Studying the role of the neuromodulator Angiotensin during reconsolidation in *Chasmagnathus* we obtained evidence of memory traces that are not expressed unless and enhancement treatment mediated by the neuromodulator is provided. Such unexpressed memories are however mRNA and protein synthesis dependent, indicating that they are in fact long-term consolidated memories. We conclude until now that the neuromodulatory state during consolidation or reconsolidation does not interfere with memory formation but determines that the formed memory is expressed or not. Students will participate in experiments that include training, memory assessment, and memory reactivation at short-term in vivo: the cellular basis of the neuromodulation will be studied by recording with calcium imaging visual interneurons that show plasticity during this learning paradigm. They will also participate in behavioral analysis studying the effect of angiotensins on *Chasmagnathus* cognitive performance showing how the neuromodulatory state during consolidation determines that the formed memory is expressed or not.

Structure-function analysis of a circuit key to circadian behavior

Fernanda Ceriani, Nara Muraro, Lía Frenkel, Axel Gorostiza, Ana Depetris-Chauvin (LELOIR)

Drosophila is a well-established model to study the cellular and molecular basis of behavior, and has led the way to understading the underpinnings of the circadian clock.

Clock output pathways are central to convey timing information from the circadian ¨pacemaker¨ cells to a diversity of physiological systems, ranging from cell-autonomous processes to behavior. The goal of the specific project is to interfere with intrinsic properties of the circadian circuit by genetic means and examine the impact of such alterations on its structure and function.

Students that participate in this project will receive training in basic fly husbandry, setup and analysis of a variety of adult behaviors (phototaxis, geotaxis, locomotor activity, learning and memory), as well as get familiarized with the dissection techniques for the adult brain, immunohistochemistry and confocal microscopy. Brain cultures will be employed to explore some of the basic physiological parameters.

Genetic Dissection of Dopamine D2 Receptor Function in the Mouse Brain

Marcelo Rubinstein, Estefanía Bello, Rodrigo Casas Cordero, Eric Casey (INGEBI)

Dopamine D2 receptors (D2R) are expressed postsynaptically in most dopamine (DA) target areas and mediate the extrapyramidal control of locomotor activity, spatio-temporal organization of goal-oriented behaviors and the reinforcing properties of natural rewards. Also, D2Rs are present in DA neurons where they act as autoreceptors controlling cell firing, DA synthesis and DA release. To understand the functional role of D2Rs in defined cell-types we are studying mutant mice selectively lacking D2 receptors generated by conditional gene targeting. In this lab module students will receive training in histochemical techniques

that will allow them to determine the spatial extent of gene mutations in the adult mouse brain (in situ hybridization, receptor binding autoradiography and immunohistochemistry). In addition, students will learn how to design behavioral experiments to study the effect of cell-restricted mutations in motor learning and operant procedures for self-administration of food. Students will set-up histochemical and behavioral experiments, collect the data, perform the statistical analysis, prepare publication quality figures and elaborate the interpretation of the results.

MEMORY RECONSOLIDATION LAB 1 AND 2 (ALL STUDENTS)

Reconsolidation of a declarative memory in humans: The effect of repeated triggering of the process on memory persistence.

María Eugenia Pedreira, Cecilia Forcato, María Laura Rodríguez, Rodrigo Fernández

The idea that memories are immutable after consolidation has been challenged. Several reports have shown that after the presentation of a specific reminder, reactivated old memories become labile and again susceptible to amnesic agents. Such vulnerability diminishes with the progress of time and implies a re-stabilization phase, usually referred to as reconsolidation. Two functions have been proposed for this process. One suggests that destabilization of the original memory after the reminder allows the integration of new information into the background of the original memory (memory updating), and the other suggests that the labilization-reconsolidation process strengthens the original memory (memory strengthening). We have previously reported the reconsolidation of human declarative memories, demonstrating memory updating and strengthening in the framework of reconsolidation. Indeed, when memory is labilized by the presentation of the proper reminder and the process is again triggered by the presentation of another reminder in the time window of the first, subjects can improve their performance at testing, and the improvement was reveal as an increase in the precision of the memory. It would also be expected that strengthening of the original memory by repeated labilization- reconsolidation processes maintain the memory available for longer periods. Therefore, we plan an experiment to evaluate the last proposal. The design will include two groups: A no-reminder group, which receive the training on day 1 and will be evaluated on day 7; and a double reminder group, which will be trained on day 1, confronted with two proper reminders on day 2, and evaluated on day 7. The results are going to be analyzed in the framework of our previous research. The students will learn to use the specific program used for the task, they will analyze the results and we will discuss them in comparison with previous results (Forcato et al 2011).

LECTURES AND SYMPOSIUM TALKS BY INVITED SPEAKERS

Except for the talks occurring at retreats, lectures will take place at Leloir Institute and are open to all local students, postdocs and investigators.

FIRST WEEK

Isabel Llano (University of Paris)

L1. Fluorescent indicators of calcium concentration

L2. Calcium and synaptic transmission

SYM. Presynaptic calcium signaling

Alain Marty (University of Paris)

L1. Whole-cell recording

L2. GABAergic synapses

SYM. A direct estimate of the readily releasable pool of synaptic vesicles obtained with a new single-site calcium uncaging method

Benedikt Berninger (Helmholtz Zentrum, Munich)

L1. The glial nature of embryonic and adult neural stem cells

L2. Cellular reprogramming: a novel approach towards modelling and cell therapy for neurodegenerative diseases

Sym. Direct conversion of somatic cells of astroglial and pericytic origin into functional neurons

THIRD WEEK

Carlos Aizenman (Brown University, Rhode Island, USA)

L1. Regulation of Neuronal Excitability

Sym. Functional regulation of a developing visual circuit

Pablo Castillo (Albert Einstein College of Medicine, New York , USA)

L1. Synaptic plasticity: basic rules and mechanisms

Sym. Activity-dependent synaptic plasticity expressed by NMDA receptors

Guillermo González-Burgos (University of Pittsburgh School of Medicine, USA)

L1. GABAergic inhibition in cortical circuits: now that we know what we know, what do we know?

L2. Schizophrenia: are cognitive deficits the consequence of altered synaptic transmission in cortical circuits?

Sym. Endocannabinoid-mediated suppression of inhibition in prefrontal cortex: synthesis pathways, development and modulation by THC administration

Andreas Luthi (Friedrich Miescher Institute, Basel, Switzerland)

L1. Learning and memory: a circuits perspective

Sym. Defining the neuronal circuitry of fear and beyond

FOURTH WEEK

Francois Guillemot (National Institute for Medical Research, London, UK)

L1. Signaling and transcriptional control of neuronal development from stem cells to synapses

Sym. Transcriptional control of neuronal stem cell fates

Fabrizio Gabbiani (Baylor College of Medicine, Houston, TX, USA)

L1. Introduction to Computational Neuroscience: Cellular and Synaptic Models.

L2. Introduction to Computational Neuroscience: Coding and Systems

Sym. Looming-sensitive neurons and neural computations underlying collision avoidance behaviors

LIST OF PARTICIPANTS

FACULTY

Aizenman, Carlos - USA
Brown University, Rhode Island
Carlos_Aizenman@brown.edu

Berninger, Benedikt - Germany
Helmholtz Zentrum, Munich
benedikt.berninger@helmholtz-muenchen.de

Calvo, Daniel - Argentina
Instituto de Investigación en Ingeniería Genética y Biología Molecular
danieljcalvo@gmail.com

Castillo, Pablo - USA
Albert Einstein College of Medicine, New York
pablo.castillo@einstein.yu.edu

Ceriani, María Fernanda - Argentina
Fundación Instituto Leloir
fceriani@leloir.org.ar

Delorenzi, Alejandro - Argentina
IFIBYNE - CONICET. FCEN -UBA
delorenzi@fbmc.fcen.uba.ar

Elgoyhen, Belén
Instituto de Investigación en Ingeniería Genética y Biología Molecular
abelgoyhen@gmail.com

Falzone, Tomás - Argentina
Facultad de Medicina, Universidad de Buenos Aires
tfalzone@fmed.uba.ar

Gabbiani, Frabrizio - USA
Baylor College of Medicine, Houston
gabbiani@cns.bcm.edu

Golombek, Diego - Argentina
Universidad Nacional de Quilmes
dgolombek@unq.edu.ar

Gonzalez-Burgos, Guillermo - USA
University of Pittsburgh School of Medicine
gburgos@pitt.edu

Goutman, Juan
Instituto de Investigación en Ingeniería Genética y Biología Molecular
jgoutman@gmail.com

Guillemot, Francois - UK
National Institute for Medical Research, London
fguille@nimr.mrc.ac.uk

Katz, Elenora - Argentina
Instituto de Investigación en Ingeniería Genética y Biología Molecular
eleokatz@gmail.com

Kropff, Emilio – Argentina
Fundación Instituto Leloir
kropff@gmail.com

Lanuza, Guillermo - Argentina
Fundación Instituto Leloir
GLanuza@Leloir.org.ar

Ledda, Fernanda - Argentina
Facultad de Medicina, Universidad de Buenos Aires
fernanda.ledda@ki.se

Llano, Isabel - France
University of Paris
isabel.llano@parisdescartes.fr

Locatelli, Fernando - Argentina
IFIBYNE - CONICET. FCEN –UBA
locatellif@yahoo.com.ar

Luthi, Andreas - Switzerland
Friedrich Miescher Institute, Basel
andreas.luthi@fmi.ch

Marin Burgin, Antonia - Argentina
Fundación Instituto Leloir
amburgin@leloir.org.ar

Marty, Alain - France
University of Paris
alain.marty@parisdescartes.fr

Murer, Gustavo - Argentina
Facultad de Medicina, Universidad de Buenos Aires
gmurer@fmed.uba.ar

Paratcha, Gustavo - Argentina
Facultad de Medicina, Universidad de Buenos Aires
gustavo.paratcha@ki.se

Pedreira, María Eugenia - Argentina
IFIBYNE - CONICET. FCEN -UBA
mpedreira@fbmc.fcen.uba.ar

Romano, Arturo - Argentina
IFIBYNE - CONICET. FCEN -UBA
aromano@fbmc.fcen.uba.ar

Rubinstein, Marcelo - Argentina
Instituto de Investigación en Ingeniería Genética y Biología Molecular
mrubins78@gmail.com

Salles, Arleen - Argentina
Centro de Investigaciones Filosóficas
arleenl60@gmail.com

Schinder, Alejandro - Argentina
Fundación Instituto Leloir
aschinder@leloir.org.ar

Szczupak, Lidia - Argentina
IFIBYNE - CONICET. FCEN -UBA
szczupak@retina.ar
Tomsic, Daniel - Argentina
IFIBYNE - CONICET. FCEN -UBA
tomsic@fbmc.fcen.uba.ar

Uchitel, Osvaldo - Argentina
IFIBYNE - CONICET. FCEN -UBA
odu@fbmc.fcen.uba.ar

Urbano, Francisco - Argentina
IFIBYNE - CONICET. FCEN -UBA
fjurbano@fbmc.fcen.uba.ar

STUDENTS

Arneodo, Ezequiel - Argentina
Physics Department, FCEyN, Universidad de Buenos Aires
enogmelimon@gmail.com

Barros, Taís Adelita - Brazil
Federal University of São Paulo (UNIFESP)
taisadelita@hotmail.com

Cabral, Agustina - Argentina
Laboratory of Neurophysiology, Institute of Cell Biology, La Plata
agustinacabral177@hotmail.com

Cuesta, Santiago - Argentina
Facultad de Ciencias Bioquímicas y Farmacéuticas de Rosario
cuestasantiago@hotmail.com

Cuestas Torres, Diana Marcela - Colombia
School of Medicine, Universidad Nacional de Colombia
dmcuestast@gmail.com

Espirito Santo Araujo, Sheila - Brazil
Federal University of Rio de Janeiro-UFRJ/ Carlos Chagas Filho Biophysics Institute
sheila.tutora@gmail.com

Fontanet, Paula - Argentina
Facultad de Medicina, Universidad de Buenos Aires
paulafontanet@gmail.com

Gandini del Valle, María Alejandra - Mexico
Center for Research and Advanced Studies, National Polytechnic
Institutegandinivalle@hotmail.com

Gazarini, Lucas - Brazil
Federal University of Santa Catarina
lgazarini@gmail.com

Lazaroni, Thiago - Brazil
Universidade Federal de Minas Gerais
tln.lazaroni@gmail.com

Martínez Silva, María de Lourdes - Mexico
Department of Physiology, Biophysics and Neuroscience, Research and Advanced Studies Center
celulula@hotmail.com

Posada Duque, Rafael Andrés - Colombia
University of Antioquia
rafaposada1@gmail.com

Raineri Andersen, Mariana - Argentina
Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires
marurainerí@gmail.com

Serrano González, Felipe Andrés - Chile
Pontificia Universidad Católica de Chile
serranofeli@gmail.com

Suarez, Luis - Argentina
IFIBYNE - CONICET. FCEN -UBA
lsuarez@fbmc.fcen.uba.ar

ATTENDING STUDENTS

Boffi , Juan Carlos - Argentina
Instituto de Investigación en Ingeniería Genética y Biología Molecular
juancarlosboffi@yahoo.com.ar

Fustiñana, María Sol - Argentina
IFIBYNE - CONICET. FCEN -UBA
msfusti@gmail.com

Gasulla, Javier - Argentina
Instituto de Investigación en Ingeniería Genética y Biología Molecular
jgasulla81@yahoo.com.ar

Gonzalez, Laura - Argentina
IFIBYNE - CONICET. FCEN -UBA
laurag@qb.fcen.uba.ar

Snitcofsky, Marina - Argentina
Facultad de Medicina, Universidad de Buenos Aires
marinaveterinaria@yahoo.com.ar

CONTACT PHONES AND ADDRESSES

(A) FUNDACIÓN INSTITUTO LELOIR
Av. Patricias Argentinas 435
Contact: Alejandro Schinder
Phone: 5238-7500, int: 3307
Cell: 15-6363-3334

(B) LE BATIMENT
Paraguay 2862
Phone: 4964-9300

(C) FACULTAD DE MEDICINA-UBA
Paraguay 2155
Contact: Gustavo Murer
Phone: 5950-9500, int: 2137
Cell: 15-4408-9617
Contact: Tomás Falzone
Phone: 5950-9500, int: 2216

(D) INGEBI
Vuelta de Obligado 2490
Contact: Daniel Calvo
Phone: 4783-2871
Cell: 15-5497-6576

(E) IFIBYNE, FCEN- UBA
Pabellón II, Ciudad Universitaria, Núñez
Contact: Osvaldo Uchitel
Phone: 4576-3368/3386
Cell: 15-5405-5861
Contact: Arturo Romano
Phone: 4576-3348
Cell: 15-6735-7234

RESTAURANTE ARTURITO
San Luis 2999, Abasto
4961-4280

MILEDI COURSE SECRETARY
Silvina Ceriani
Cell: 15-6-729-1565

In case of emergency please contact O. Uchitel, A. Schinder or S. Ceriani

(A) FUNDACIÓN INSTITUTO LELOIR
(B) LE BATIMENT
(C) FACULTAD DE MEDICINA, UBA
(D) INGEBI
(E) CIUDAD UNIVERSITARIA - IFIBYNE-FCEN , UBA