Master de Sciences et Technologies
**Mention Biologie Intégrative et Physiologie**
**Parcours : Neurosciences**
Responsable : Professeur Régis Lambert

# Internship Proposal
# Academic Year 2019-2020

## 1. Host team :

Research Unit (e.g. Department or Institute) : Institut Pasteur
Research Unit Director : Pierre-Marie Lledo

Research Team Director : David DIGREGORIO
Team name : Unit of Dynamic Neuronal Imaging

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## 2. Internship project title:

Synaptic and circuit mechanisms of timing in the brain

## 3. Internship Description :

Critical and general to brain function is the necessity to represent changes in sensory stimuli over time, which in turn influence behavior. Time-dependent features such as delays, intervals and durations of stimuli have been shown to be encoded by both single neurons (e.g. integrators) and neuronal populations (population clocks) in multiple brain regions. However, a deep understanding of the causal mechanisms generating neural dynamics that encode *time* is lacking.

The cerebellum has long been thought to be a brain region necessary for learning temporal intervals in the subsecond range. Cerebellum's simple neuronal connectivity and cytoarchitecture has inspired elegant models of intrinsic temporal representations and time-dependent associative learning. Its simplicity also makes it a tractable experimental preparation to explore the synaptic and neuronal mechanisms underlying neural circuit dynamics driving behavior. We discovered that synapses conveying sensory information to the cerebellum exhibit diverse amplitudes and short-term plasticity in a sensory-specific manner and can be used to encode the timing of neuronal spikes. **We therefore hypothesize that synaptic diversity in the cerebellar cortex is a substrate for a population clock that is used to generate precisely timed behaviors.** In our research we focus particularly on non-motor cerebellum, where multisensory processing is thought to be important for cognitive behaviors, and is an area thought to be disrupted in autism and schizophrenia.

The topics of projects in the laboratory include: 1) identification of nanoscale mechanisms of functional synaptic diversity, 2) quantification of the multisensory synaptic diversity in non-motor cerebellum, 3) exploration of the influence of dendritic mechanisms for cerebellar cortical circuit function, 4) monitoring neuronal circuit behavior in awake behaving animals, and 5) establishment of a causal relationship

between synaptic and neuronal mechanisms during behavior. Mathematical modelling projects are also available.

Experimental projects in the laboratory will use one or more of the following imaging techniques: super-resolution imaging of macromolecular complexes in presynaptic terminals as well as two-photon imaging of neuronal and synaptic activity using state of the art fluorescence indicators for calcium, neurotransmitter, and membrane voltage both in acute brain slices and *in vivo*. Optogenetic strategies will be used to reversibly alter neuronal activity, and establish causal relationships between mechanisms and behavior. The laboratory is multidisciplinary with in situ and in vivo neurophysiologists, physicists (optics) and theoretical neuroscientists working in a highly collaborative environment. We are in search for highly motivated students interested in exploring **how cellular and molecular diversity of synapses contribute to the neural circuit dynamics controlling behavior**.