

# INTERNSHIP PROPOSAL

(One page maximum)

Laboratory name: LPENS

CNRS identification code: UMR8023

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Internship location: 24 rue Lhomond, 75005 Paris

Thesis possibility after internship: YES

Funding: YES If YES, which type of funding: ERC

## **Creating a fusion pore under pressure**

Vesicles are membrane-bound spherical compartments that isolate the intravesicular from the extra-vesicular regions. Because of the stability of membranes, fusion of two vesicles requires the active intake of a large amount of energy, typically  $30 k_B T$ . In cells, fusion occurs to exchange materials between two compartments and is achieved by proteins that provide the energy. This is well-established and has been studied for decades. One case of fusion is out-of-the ordinary: neurotransmission. During neurotransmission, synaptic vesicles containing neurotransmitters are pre-bound to the target neuronal membrane and fuse less than 1ms after the arrival of the incoming signal. This exquisite sensitivity is obtained by a precise molecular choreography that we are barely discovering. This discovery led us to hypothesize that the synaptic vesicles are actual under high pressure, a couple of atmospheres. We predict that the effect of such pressure would be dramatic on the kinetics of the fusion pore and release of neurotransmitters. We want to test these predictions by using a unique microfluidic chip that we recently developed. This chip allows the monitoring of the fusion pore with a high precision (less than 1nm on the diameter with an acquisition rate of  $10\mu s$ ).

The goal of the internship is to use this microfluidic setup and monitor the kinetics of the fusion pore under various conditions that are expected to trigger or not the pressurization of the vesicle.

The internship will be performed in tight collaboration with the laboratory of Nobel Prize laureate Professor James Rothman at Yale University.

The internship can be followed by a PhD. The PhD will also involve theoretical predictions of fluid movements at nanometric scales (neurotransmitter release). Funds for the PhD are already secured.

Please, indicate which speciality(ies) seem(s) to be more adapted to the subject:

Condensed Matter Physics: NO      Soft Matter and Biological Physics: YES

Quantum Physics: NO      Theoretical Physics: NO