

IC-3i International PhD Program  
**PhD thesis project**  
 2016 Call for application



## Mechanosensing and dynamics of cell filopodia

### General information

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<b>Call</b>	2016
<b>Reference</b>	2015-08-BASSEREAU
<b>Keyword(s)</b>	Cell mechanics, Optical tweezers, Filopodia, Mechanosensing, Actin dynamics

### Director(s) and team

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<b>Thesis director(s)</b>	Patricia Bassereau, Guy Tran van Nhieu
<b>Research team</b>	<a href="#">Membranes and cellular functions</a>
<b>Research department</b>	<a href="#">Physical Chemistry</a>

### Description of the PhD thesis project

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Filopodia are very thin dynamic tubular protrusions at cell edge that allow cells to sense their surrounding and exert traction forces. They are involved in the migration of healthy cells as well as of metastatic cancer cells. Filopodia are also hijacked by pathogens during cell invasion. How filopodia sense the mechanical and biochemical properties of their environment is still unclear. Filopodia contain a discrete number of bundled actin filaments connected to the actin cortex at their base. They also contain many proteins linking actin filaments to plasma membrane, forming all together a membrane-confined complex array whose dynamics determine their elongation or retraction. Cytoskeletal linkers at the filopodial tip are key in regulating the transduction of forces associated with retraction in response to external and internal cues.

The general objective is to use a combination of mechanical (optical tweezers), advanced fluorescence microscopy and molecular approaches on single filopodia of living cells to decipher their sensing mechanisms.

Specific questions that will be addressed are:

- a) How is actin polymerization regulated at the filopodium tip following receptor-substrate interaction and filopodium retraction?
- b) Is the tip mechanosensitive?
- c) What regulates actin filament growth following rupture of the links between actin and membrane at the tip?

The project will be mainly developed at the Institut Curie for the experiments, with a participation of the L'Oréal company. The thesis will be supervised jointly by P. Bassereau (Biophysics, I. Curie) and G. Tran van Nhieu (Microbiology, Collège de France). P. Bassereau's group is expert in membrane mechanics, both on reconstituted systems and on cells. G. Tran van Nhieu is expert in bacterial pathogenesis, in particular in cytoskeletal reorganization induced by bacterial pathogens. Both groups have already successfully collaborated on the study of forces generated during filopodial capture and retraction.

## International, interdisciplinary & intersectorial aspects of the project

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The thesis will have the "Doctor Europaeus" label. It has interdisciplinary and international dimensions. Indeed, the project will be developed in 2 complementary groups, at the frontier between biophysics, cell biology and microbiology. It will also involve interactions with theoretician physicists at the Inst. Curie (J. Prost, J.F. Joanny) and at the Weizmann Inst. (IS) (N. Gov) on mechanics of cell protrusions. Collaborations with cell biologists already exist (P. Lappalainen, Helsinki, FI) or will be initiated with K. Rottner (Bonn, DE) and A. Bershadsky (Weizmann Inst., IS and Singapore). The French company L'Oréal will participate by involving one engineer as a mentor and member of the thesis committee and by offering to spend 3-4 weeks in their labs near Paris to run experiments.

## Recent publications

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1. Prevost C., Zhao H., Manzi J., Lemichez E., Lappalainen P., Callan-Jones A.\* , Bassereau P.\* (2015) IRSp53 senses negative membrane curvature and phase separates along membrane tubules, *Nat. Commun.*, 6, 8529
2. Renard H.-F., Simunovic M., Lemièrè J., Boucrot E., Garcia-Castillo M.-D., Arumugam S., Chambon V., Lamaze C., Wunder C., Kenworthy A., Schmidt A. A., McMahon H. T., Sykes C., Bassereau P., Johannes L. (2015) Additive Scission Functions of Endophilin-A2, Dynamin and Actin in Clathrin-Independent Endocytosis, *Nature*, 517, 493–496
3. Sanjay Datar A., Bornschlöggl T., Bassereau P.\* , Prost J.\* , Pullarkat P.\* (2015) Role of Cytoskeleton-Membrane Interaction in the Dynamics of Membrane Tethers in Neurons, *Biophys. J.*, 108, 489-497
4. Aimon S., Callan-Jones A., Berthaud A., Pinot M., Toombes G. E., Bassereau P. (2014) Membrane shape modulates trans-membrane protein distribution, *Dev. Cell*, 28, 212-218
5. Bornschlöggl T., Romero S., Vestergaard C., Joanny J. F., Tran Van Nhieu G.\* , Bassereau P.\* (2013) Filopodia retraction force is generated by cortical actin dynamics and controlled by reversible tethering at the tip, *PNAS*, 110, 18928-18933

## Expected profile of the candidate

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Applicants should have a background in physics, soft matter (chemical engineering), or biophysics with a strong interest for interdisciplinary research in cell biology and microbiology. Skills in instrumentation, in particular micromanipulation and optical microscopy, and some expertise in cell biology are a plus, but are not mandatory.