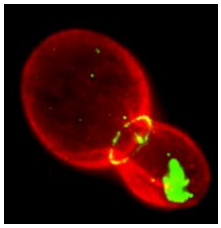
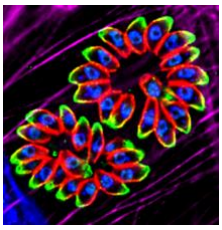
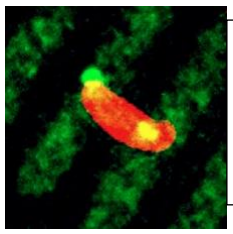
Institute for Advanced Biosciences
Site Santé
Allée des Alpes - 38700 La Tronche
iab.univ-grenoble-alpes.fr
CENTRE DE RECHERCHE UGA - INSERM U 1209 - CNRS UMR 5309

Research Engineer
(2 years' CDD- ANR- 2 positions funded)

Team « Biomechanics of Host-Parasite Interactions »-
IAB, CNRS UMR-5309, Inserm U-1209, Univ. Grenoble Alpes, Grenoble

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Apicomplexans *form a large phylum of* ***unicellular eukaryotic microbes****, some of which cause severe diseases in humans. Most successful is Toxoplasma, which parasitizes nearly a third of the human population, making it at risk of life-threatening complications, primarily encephalitis or pneumonia, in case of immune-suppression. This polarized parasite has evolved an impressive gliding motility strategy and ranks amongst the fastest non-swimming cells. Toxoplasma glides to navigate within the extracellular matrices as well as to move in and out human host cells in which they proliferate.*

The "Tardieux"' team uses multi-disciplinary approaches that combine nano-chemistry, micro-patterning, microfluidics, live imaging and Expansion Microscopy/EM & STED microscopy to interrogate the minimal biochemical and biophysical requirements for this microbe to achieve high-speed motility and invasion with the perspective of developing theoretical and experimental models for bio-engineering applications.

In order to decode the mechanics of motility evolved by the few micron-sized *Toxoplasma* parasite, we reconstitute extracellular matrix (ECM) mimicking environments and develop genetically engineered parasites that either lack molecular players (or candidates) of the motor engine or that express fluorescent/epitope tag reporters of interest compatible with **real time and super resolution imaging.** The team also applies **force microscopy** (flow forces/ TFM, AFM) and develops synthetic nanosensors and probes in order to dissect (i) the site and amplitude of adhesive, traction and dragging forces during movement but also (ii) to uncover the molecular engagement of the parasite surface-exposed adhesins with the substrate (ECM) ligands that account for a functional dynamic force transmission platform.

Primary objectives are to delve deeper into the components of the unique focal adhesion system recently uncovered by the team as necessary and sufficient for high-speed gliding. We intend to perform systematic screening of moieties and functionalized chemical groups under controlled molecule density and distribution as well as controlled viscoelastic properties of the substrates. Tunable surface chemistry coupled with Quartz Crystal Microbalance with Dissipation (QCMD) and Ellipsometry are developed in tight collaboration with the department of Molecular Chemistry (DCM, Grenoble) to meet our objectives.

Main objectives of the research engineer program

We plan molecularly and functionally characterizing the unique force transmission platform used by the polarized single-celled eukaryotic parasite to propel at very high speed in biochemically and biomechanically distinct ECMS. The candidate will,

- Use micropatterns and microfluidics chips under precise flow control optimize for high-speed high-resolution imaging of the parasite
- Use super resolution microscopy to get insights on the area of parasite surface-substrate contact
- Produce chemically and mechanically tunable functionalized surfaces and use QCM-D and ellipsometry
- Use bio-micro-rheology under various ECM mimicking 3D settings offered to the parasite.

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Hiring talented & highly motivated engineers and students.

- We are seeking for a highly motivated research-focusing engineer (School of engineers) candidate with solid training and experience in micro-fluidics and micro-patterning, as well as knowledge on organic chemistry and/or bio-engineering. The Applicant is invited to submit to Isabelle.tardieux@inserm.fr or Isabelle.tardieux@gmail.com

1- **A letter of motivation** where is demonstrating her/his strong interest in research **and a detailed CV**
2- **Two letters of recommendation** from renowned academics supporting the application (motivation and suitability for research) are required.

The application includes an interview to evaluate students' academic abilities, research interests and motivation.

Recent publications of the team' members related to the topic

- Vigetti L, Tardieux I. (2023). Fostering innovation to solve the biomechanics of microbe-host interactions: Focus on the adhesive forces underlying Apicomplexa parasite biology. Biol Cell. May 25:e202300016. doi: 10.1111/boc.202300016.
- Tolić, I.M., Tardieux, I. (2022). The power of parasite collectives. *Nat. Phys.* May 13; 18:491–492 https://doi.org/10.1038/s41567-022-01554-7
- Vigetti L, Labouré T, Roumégous C, Cannella D, Touquet B, Mayer C, Couté Y, Frénal K, Tardieux I, Renesto P. (2022). The BCC7 Protein Contributes to the *Toxoplasma* Basal Pole by Interfacing between the MyoC Motor and the IMC Membrane Network. *Int J Mol Sci.* May 26;23(11):5995. doi: 10.3390/ijms23115995.
- Tardieux I. (2021). Parasitism as a lifestyle: Ultimate intimacy between Apicomplexan protozoans and metazoan hosts. *Biol Cell.* Mar;113(3):131-132. doi: 10.1111/boc.202000128.
- Broncel M, Dominicus C, Vigetti L, Nofal SD, Bartlett EJ, Touquet B, Hunt A, Wallbank BA, Federico S, Matthews S, Young JC, Tate EW, Tardieux I, Treeck M (2020). Profiling of myristoylation in *Toxoplasma gondii* reveals an *N*-myristoylated protein important for host cell penetration. *Elife.* Jul 3;9:e57861. doi: 10.7554/eLife.57861.
- Pavlou G, Touquet B, Vigetti L, Renesto P, Bougdour A, Debarre D, Balland M, Tardieux I. (2020) Coupling Polar Adhesion with Traction, Spring, and Torque Forces Allows High-Speed Helical Migration of the Protozoan Parasite *Toxoplasma*. *ACS Nano.* Jun 23;14(6):7121-7139. doi: 10.1021/acsnano.0c01893. Epub 2020 Jun 1.
- Pavlou G, Milon G & Tardieux I (2019) Intracellular protozoan parasites: living probes of the host cell surface molecular repertoire. *Current Opinion in Microbiology*, review
- Pavlou G, Biesaga M, Touquet B, Lagal V, Balland M, Dufour A, Hakimi M-A & Tardieux I (**2018**) Toxoplasma Parasite Twisting Motion Mechanically Induces Host Cell Membrane Fission to Complete Invasion within a Protective Vacuole. *Cell Host Microbe* **24:** 81-96.e5
- Tardieux I (**2017**) Actin Nanobodies Uncover the Mystery of Actin Filament Dynamics in Toxoplasma gondii. *Trends in Parasitology* **33:** 579–581; review
- Tardieux I & Baum J (**2016**) Reassessing the mechanics of parasite motility and host-cell invasion. *J. Cell Biol.* **214:** 507–515; review
- Bichet M, Touquet B, Gonzalez V, Florent I, Meissner M & Tardieux I (**2016**) Genetic impairment of parasite myosin motors uncovers the contribution of host cell membrane dynamics to Toxoplasma invasion forces. *BMC Biol.* **14:** 97
- Bichet M, Joly C, Henni AH, Guilbert T, Xémard M, Tafani V, Lagal V, Charras G & Tardieux I (**2014**) The toxoplasma-host cell junction is anchored to the cell cortex to sustain parasite invasive force. *BMC Biol.* **12:** 773
- Lagal V, Abrivard M, Gonzalez V, Perazzi A, Popli S, Verzeroli E & Tardieux I (**2014**) Spire-1 contributes to the invadosome and its associated invasive properties. *J. Cell. Sci.* **127:** 328–340