Metastablity and effective dynamics of mean-field models, with applications to the mathematical modeling of cardiac contraction at the mesoscale

Masters' internship and PhD thesis proposal

Within the project **MesoCardio**, funded by PEPR MATHS-VivES.

Position at CERMICS, École nationale des ponts et chaussées, under the supervision of Tony Lelièvre and Julien Reygner, jointly with Matthieu Caruel at MSME, Université Paris-Est Créteil.

Starting date: April 2026 for the internship, October 2026 for the PhD thesis.

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The MesoCardio project

The PhD is part of a large-scale initiative: the MesoCardio project. This project sets an interdisciplinary consortium to develop models of the cardiac contraction at the mesoscale, aiming at understanding the physiological mechanisms behind the regulation of the contraction. The consortium involves three mathematics labs (CERMICS, École nationale des ponts et chaussées; CMAP, École polytechnique; MΞDISIM, Inria Saclay), one biomechanics lab (MSME, Université Paris-Est Créteil) and one physiology lab (PhysioLab, University of Florence). The work program encompasses statistical mechanical modeling, mathematical analysis of stochastic systems, non-linear continuum mechanics and homogenization, the development of innovative numerical methods, and in situ experiments.

Muscle contraction is generated by nanoscale molecular motor proteins assembled in contractile units (Fig. 1 (a)). At the mesoscale, these units form a regular network supported by elastic cytoskeletal proteins (titin, M-line, Z disks) (Fig. 1 (b)). This network is the main constituent of the muscle fibers at the macroscale (Fig. 1 (c)). Currently, most mechanical models of the muscle tissue do not take into account the mesoscale level, and directly couple nanoscale mean-field-type molecular motor models with macroscale continuum mechanics balance laws. This approach is insufficient to model systems with low number of motors (fluctuations), and to understand the fundamental role played by cytoskeletal proteins in the regulation of the contraction (mechanical feedback) and in the preservation of the fibers' mechanical integrity (homogenization). This project aims at developing mathematical models able to capture these phenomena operating at the mesoscale.

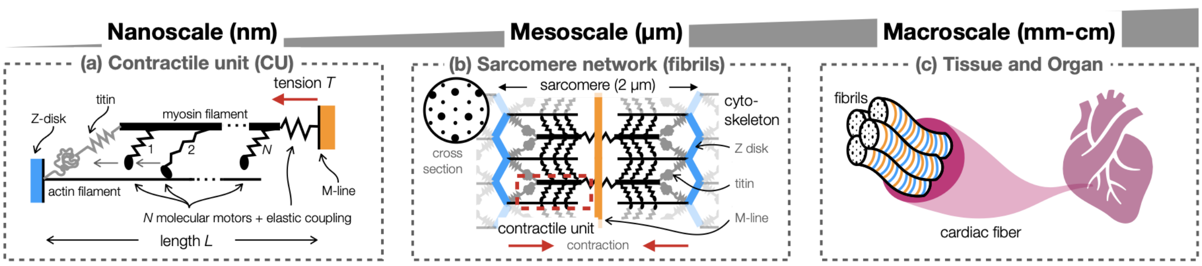

Figure 1: General context of the project. Muscle contraction is generated at the nanoscale by coupled molecular motors forming contractile units (a). These units for a regular network at the mesoscale (b), that constitutes the contractile apparatus of the tissue at the macroscale (c).

The project has three main objectives, organized in work packages (WP):

WP1. Develop a model reduction strategy to derive an effective model of a finite size contractile unit with several motors. This model can be used to model in an efficient way biological situations with a low number of motors involved (e.g. during activation) or specific in vitro experiments.

WP2. Formulate a stochastic model of interacting contractile units including activation mechanisms and perform associated validation experiments. The reduced formulations can be incorporated in this model to reduce the simulation cost.

WP3. Propose an homogenized formulation of this network of contractile units to be coupled with macroscopic balance laws in the framework of continuum mechanics.

Mean-field model of contractile unit

The internship and PhD project is the core of WP1. It deals with a stochastic model of contractile unit introduced in [3], which consists in a system of N jump-diffusion processes, representing molecular motors, and evolving according to mean-field interactions. The goals of the project are the following:

1. derive the $N \to +\infty$ limit of this process, under the form of a jump-diffusion process that interacts with its probability distribution, which is referred to as the *mean-field limit*;
2. understand and quantify the *finite-size effects*, namely the differences of behavior between the model of contractile unit and its mean-field limit, in particular over long time horizons;
3. derive an effective dynamics reproducing finite-size effects without having to simulate the whole system of N molecular motors.

The derivation of the $N \to +\infty$ limit of the system of molecular motors is expected to rely on standard techniques of *propagation of chaos* [1, 2]. The understanding of finite-size effects is related to the notion of *metastability*, as the system of molecular motors is expected to exhibit random changes between macroscopic states over long time scales. Such a phenomenon is known to arise in several other mean-field models, such as the *Curie–Weiss model* of ferromagnetism in statistical mechanics [4, 7, 6]. The derivation of effective dynamics is a standard issue in finite-dimensional molecular systems [5], but in the context of mean-field models it is a relatively open question.

Organization of the work

The 6-month Masters' internship will essentially be dedicated to the understanding of the stochastic model of contractive unit, and the derivation of its mean-field limit. The study of finite-size effects will be at the center of the PhD thesis. The overall project is balanced between the theoretical analysis of stochastic processes and the design of efficient numerical methods. The MesoCardio project is strongly interdisciplinary. The person recruited will interact with the doctoral candidate who will work in parallel on the formulation of larger scale models developed from physiological experiments (WP2). The results of WP2 will benefit from the model reduction strategy developed in WP1 and, in return, the person recruited on WP2 will provide physiological background and corresponding modeling elements to be included in WP1's model reduction pipeline.

Candidate profile

Candidates should be in the process of completing a Master's degree (M2) or an equivalent qualification in applied mathematics and/or modeling. They must have completed at least one advanced course in stochastic processes (Markov processes, diffusion processes). Familiarity with programming in Python, particularly for scientific computing, is also required. No prior knowledge of biology is necessary; however, candidates should demonstrate a genuine interest in the project's applicative aspects.

Practical aspects

The recruited person will be based at CERMICS, École nationale des ponts et chaussées, on the Cité Descartes campus in Marne-la-Vallée. The gross monthly salary is about 600€ for the internship, and 2300€ for the PhD thesis.

References

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[3] L.-P. Chaintron, F. Kimmig, M. Caruel, and P. Moireau. A jump–diffusion stochastic formalism for muscle contraction models at multiple timescales. *Journal of Applied Physics*, **134**(19):194901, (2023). DOI: 10.1063/5.0158191

[4] D. A. Dawson and J. Gärtner. Large deviations and tunnelling for particle systems with mean field interaction. *Canadian Mathematical Reports of the Academy of Sciences*, **8**(6):387–392, (1986).

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[6] P. Monmarché. Long-time propagation of chaos and exit times for metastable mean-field particle systems. *arXiv preprint*, arXiv:2503.00157, (2025). DOI: 10.48550/arXiv.2503.00157

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