Offer #2024-07290

PhD Position F/M Mathematical and physical modeling of the DNA transfection by means of pulsed electric fields (IDP 2024)

Contract type : Fixed-term contract

Level of qualifications required : Graduate degree or equivalent

Fonction : PhD Position

About the research centre or Inria department

The Inria center at the University of Bordeaux is one of the nine Inria centers in France and has about twenty research teams.. The Inria centre is a major and recognized player in the field of digital sciences. It is at the heart of a rich R&D and innovation ecosystem: highly innovative SMEs, large industrial groups, competitiveness clusters, research and higher education players, laboratories of excellence, technological research institute...

Context

The team MONC has developed a deep expertise on the modeling of electroporation from the cell scale to the tissue scale, including clinical application. The thesis proposal aims to push forward this expertise by addressing the problem of modelind DNA transfection by mean of electroporating fields, which is a booming subject in cancer immunotherapy. Roughly speaking, the goal is to develop a relevant and tractable model of DNA transfection by electroporation, to enable protocol optimization.

Assignment

The first goal of the thesis is to propose a new model of membrane based on local membrane composition – so called Landau Ginzburg models. A first work will consist in performing the mathematical analysis of the Cahn-Hilliard model to estimate the characteristic size of the defects, the characteristic time for the phase separation, and the duration and the amplitude of the electric fields to create defects. Alfaro et al. has studied the case of Allen-Cahn but the Cahn-Hilliard model with non local source term has not been investigated yet. In a second task, the goal is to derived rigorously a 2D model, thanks to an asymptotic analysis with respect to the thickness of the membrane.
The goal is to obtain a 2D surface effective model of the membrane to reduce the cost of computation.

The asymptotic model should be similar to a model A (or Allen-Cahn) type model for the phase order as in the recent PhD thesis of P. Jaramillo (Univ. Bordeaux, Dec. 2023), with source terms derived from the asymptotic expansion. Once the model of membrane permeabilisation will be obtained, the challenge of the PhD will consist in
describing the displacement of large charged molecules as DNA through the membrane. Interestingly, large molecules do not diffuse across the membrane but are internalized by electrophoretic forces. However due to their charge, DNA molecules behave like a dipole, that locally perturbs the electrostatic field. A moving source term has thus to be added in the above Poisson equation, and well-designed transmission conditions across the membrane are required for the DNA transport. From the numerical view point, specific well adapted numerical immersed boundary methods will be developed to tackle the numerical difficulties raised by the discontinuities across the membrane.

References (max 5):
– J.M. Escoffre, T. Portet, C. Favard, J. Teissié, D. S. Dean, M.-P. Rols, Electromediated formation of DNA complexes with cell membranes and its consequences for gene delivery, Biochimica et Biophysica Acta (BBA) - Biomembranes, Volume 1808, Issue6, 2011
– P. Jaramillo Aguayo, A. Collin, C. Poignard, Phase-field model of bilipid membrane electroporation, Journal of Mathematical Biology (2023) 87:18.
– M. Leguebe, A. Silve, L. Mir, and C. Poignard. Conducting and permeable states of cell membrane submitted to high voltage pulses: Mathematical and numerical studies validated by the experiments. Journal of Theoretical Biology, 360:83–94, Nov. 2014
– R. Smeets, U. Keyser, D.Krapf, et al., Salt Dependence of Ion Transport and DNA Translocation through Solid- State Nanopores Nano Letters, 6(1): 89–95, 2006.

Skills

Strong background in PDE and numerical analysis, with an appetite for biophysical problems.

Benefits package

- Subsidized meals
- Partial reimbursement of public transport costs
- Possibility of teleworking and flexible organization of working hours
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage

Remuneration

- 2100€ / month (before taxs) during the first 2 years,
- 2190€ / month (before taxs) during the third year.

General Information

- **Theme/Domain :** Modeling and Control for Life Sciences
- **Town/city :** Talence
- **Inria Center :** Centre Inria de l'université de Bordeaux
- **Starting date :** 2024-10-01
- **Duration of contract :** 3 years
- **Deadline to apply :** 2024-05-03

Contacts

- **Inria Team :** MONC
- **PhD Supervisor :**
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About Inria

Inria is the French national research institute dedicated to digital science and technology. It employs 2,600 people. Its 200 agile project teams, generally run jointly with academic partners, include more than 3,500 scientists and engineers working to meet the challenges of digital technology, often at the interface with other disciplines. The Institute also employs numerous talents in over forty different professions. 900 research support staff contribute to the preparation and development of scientific and entrepreneurial projects that have a worldwide impact.

Warning : you must enter your e-mail address in order to save your application to Inria. Applications must be submitted online on the Inria website. Processing of applications sent from other channels is not guaranteed.

Instruction to apply

Thank you to send:
- CV
- Cover letter
- Master marks and ranking
- Support letter(s)

Defence Security :
This position is likely to be situated in a restricted area (ZRR), as defined in Decree No. 2011-1425 relating to the protection of national scientific and technical potential (PPST).Authorisation to enter an area is granted by the director of the unit, following a favourable Ministerial decision, as defined in the decree of 3 July 2012 relating to the PPST. An unfavourable Ministerial decision in respect of a position situated in a ZRR would result in the cancellation of the appointment.

Recruitment Policy :
As part of its diversity policy, all Inria positions are accessible to people with disabilities.