Offer #2024-07381

PhD Position F/M Developing a deep learning framework to design cyclic peptides

Contract type : Fixed-term contract

Level of qualifications required : Graduate degree or equivalent

Fonction : PhD Position

Context

The main goal of this PhD project is to develope a deep learning framework for the design of cyclic peptides. This project has an important impact on designing theraputics to fight emerging diseases. Moreover, we will take advantage of the recent advances of deep learning methods, investigate several algorithms, and ultimately provide an open source application to the broad scientific community. This approach is a prerequisite for the design of new therapeutic peptides that target macromolecular complexes.

The PhD candidate will be hosted in the CAPSID team within LORIA at the Inria, Nancy - Grand Est site. The candidate will be supervised by Yasaman Karami (Inria researcher) with expertise in analyzing proteins conformational dynamics and peptide design [1] and Hamed Khakzad (CPJ Inria) expert in artificial intelligence and protein design [2]. CAPSID team (https://capsid.loria.fr/) is directed by Dr. Marie-Dominique Devignes and provides a multidisciplinary and international environment for students. The team benefits from experts in computational biology and structural bioinformatics, as well as in computer science. The group is equipped with a computational platform, MBI-DS4H (https://mbi-ds4h.loria.fr/) composed of 8 nodes and 12 GPUs, and provides technical support to the users.

[1] Y. Karami, et al. Exploring a Structural Data Mining Approach to Design Linkers for Head-to-Tail Peptide Cyclization. Journal of Chemical Information and Modeling 63.20: 6436-6450, 2023.

[2] Goverde, Casper A., et al. "De novo protein design by inversion of the AlphaFold structure prediction network." Protein Science 32.6 (2023): e4653.

Assignment

Proteins often interact closely with other proteins to form a protein-protein interaction (PPI) network. Finely orchestrated PPIs are at the heart of virtually all fundamental cellular processes [1]. A large number of PPIs contribute to life-threatening diseases [2], and more than half a million PPI dysregulations have been found to be involved in pathological events [3]. Targeting PPIs is one of the main therapeutic strategies to fight against several diseases, and numerous experimental and computational approached were developed in this direction. The advantages of peptides (that are protein fragments) such as small surface area, weak target affinity and low specificity [4], resulted in a shift of the recent developments toward considering peptides for targeting PPIs. One recent example is the Spike of SARS-CoV-2 that binds to the human ACE2 receptor, for which the use of peptides to inhibit the PPI formed between RBD and ACE2 is a very active field of research [5]. Moreover, the recent advances of machine learning and deep learning in the CASP competition and the outbreak of AlphaFold2 [6] for the prediction of protein structures have shown that, they can improve discovery and decision making when high-quality data are available. The main goal of this project is to design head-to-tail cyclic peptides for targeting defined sites in proteins of interest. To achieve this objective, we propose the development of a deep learning architecture. Within the aims of the project, we will investigate several facets of the algorithms and the design processes, and ultimately provide this application to the broad scientific community. The main goal of the PhD project is to develop a deep generative model to design cyclic peptide sequences toward specific target. To do so, the student requires to have extensive background in deep learning and computational biology.

[1] J. D Scott and T. Pawson. Cell signaling in space and time: where proteins come together and when they're apart. Science, 326(5957):1220–1224, 2009.
[2] M. R. Arkin, Y. Tang, and J. A Wells.Small-molecule inhibitors of protein-protein interactions: progressing toward the reality. Chemistry & biology, 21(9):1102–1114, 2014.
[3] W. Cabri, et al Therapeutic peptides targeting ppi in clinicaldevelopment: Overview, mechanism of action and perspectives. Frontiers in Molecular Biosciences, 8:697586, 2021.
[4] D. J. Craik, et al. The future of peptide-based drugs.Chemical biology & drug design, 81(1):136–147, 2013.
[5] D. Schutz, et al. Peptide and peptide-based inhibitors of sars-cov-2 entry.Advanced drug delivery reviews, 167:47–65, 2020.
[6] J. Jumper, et al. Highly accurate protein structure prediction with alphafold.Nature, 596(7873):583–589, 2021.

Main activities

- Literature review of the relevant studies
- Preparing a test set using existing databased of peptides and proteins
- Developing a generative model to design peptides
- Implementing the method and preparing a software using Python
- Validating the method and analysing the results
- Writing dissertation, scientific articles and presenting the work in international conferences

Skills

- Master's degree in Computer Science, Bioinformatics, Chemoinformatics or a related master program
- Proficiency in programming languages (Python, PyTorch or R) and good coding practices
- Skills in algorithm design and computational biology
- Experience in deep learning
- Ability to work independently and also to work in a team
- Excellent oral and written English skills

Benefits package

- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- Possibility of teleworking (after 6 months of employment) 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€ gross/month the 1st year

General Information

- **Theme/Domain :** Computational Biology
  Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Town/city :** Villers lès Nancy
- **Inria Center :** Centre Inria de l'Université de Lorraine
- **Starting date :** 2024-10-01
- **Duration of contract :** 3 years
- **Deadline to apply :** 2024-04-29

Contacts

- **Inria Team :** CAPSID
- **PhD Supervisor :**
  Karami Yasaman / yasaman.karami@inria.fr

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

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.