Offre n°2020-02988

Coupling and synchronization of circadian oscillators in peripheral organs: mathematical modeling and analysis

Le descriptif de l'offre ci-dessous est en Anglais

Type de contrat : Stage

Niveau de diplôme exigé : Bac + 4 ou équivalent

Autre diplôme apprécié : M1 or M2 student

Fonction : Stagiaire de la recherche

A propos du centre ou de la direction fonctionnelle

The Inria Sophia Antipolis - Méditerranée center counts 34 research teams as well as 7 support departments. The center's staff (about 500 people including 320 Inria employees) is made up of scientists of different nationalities (250 foreigners of 50 nationalities), engineers, technicians and administrative staff. 1/3 of the staff are civil servants, the others are contractual agents. The majority of the center's research teams are located in Sophia Antipolis and Nice in the Alpes-Maritimes. Four teams are based in Montpellier and two teams are hosted in Bologna in Italy and Athens. The Center is a founding member of Université Côte d'Azur and partner of the I-site MUSE supported by the University of Montpellier.

Contexte et atouts du poste

In mammalians, every cell contains its own circadian clock, a fundamental mechanism that controls many important cellular processes in a periodic way, with a 24 hour cycle. All the clocks are organized into a complex hierarchy that allows for the adaptation of the organism's behavior and physiology to the alternating day/night sequence. However, very little is known on the coupling and synchronization of circadian clocks within the same tissue or the same organ.

In the liver, a large number of processes and a significant fraction of its genes are regulated by the circadian clock in a rhythmic way. Notably, the amplitude of circadian oscillations in the liver is observed to increase in response to a temporary absence of nutrition intake (Panda, 2016). This increase in amplitude may be due to different causes: for instance, a direct increase in each cell, or the fact that cells become synchronized may both lead to an increase in the population amplitude. In the latter case, synchronization of the cells may possibly be due to intercellular communication, through the exchange of diffusible molecules.

To test these and other hypotheses, we will construct a mathematical model for the circadian clock in the liver and study the coupling of two or more similar cells interacting through the exchange of some molecules in a diffusive way.

This topic is part of the project SYNCHRO, in the "Masters Environneés" program at Université Cote d'Azur, in collaboration with the Circadian Systems Biology team of Franck Delaunay and Michele Teboul at Institut de Biology de Valrose. The Master student will thus frequently interact with a team of biologists with expertise in the mammalian circadian clock.

Mission confiée

In this project, we will use ordinary differential equations and piecewise linear systems to build a minimal mathematical model for the molecular oscillator in each cell, describing the concentration of the main proteins or metabolites involved in the oscillatory dynamics (see also Almeida et al. 2020). To characterize the intercellular interactions, we will assume that cells can exchange one of the metabolites in a diffusive way, so that the communication between two cells will be proportional to the difference between the concentration of that metabolite in each of the molecular oscillators.

There are several strategies to represent the network of intercellular communications among N identical systems. In an organ such as the liver, it may be assumed that all cells play a similar role in the network and communicate with all other cells, or at least with their near neighbors. At another level, we can consider that there exists a master oscillator whose role is to control and regulate all peripheral systems.

We will therefore study two well known network topologies, an "all-to-all" topology, where each oscillator is connected to all others, and a "star" topology, where one single oscillator is connected to all others (see also Chaves et al. 2019). Using both analytic results and numerical simulations, we will study the effects of cellular interactions in the synchronizations of the molecular oscillators, both in the amplitude and phase of oscillations. We will study the impact of diffusive coupling in enhancing or disturbing the synchronization of molecular oscillators in hepatocytes.

References

Almeida S, Chaves M, Delaunay F. Transcription-based circadian mechanism controls the duration of molecular clock states in response to signaling inputs. J Theor Biol. 2020;484:110015.

Chaves M, Scardovi L, Firippi E. Coupling and synchronization of piecewise linear genetic regulatory systems. Proc. IEEE Conference on Decision and Control (CDC19), Nice, France, 2019.

Panda S. Circadian physiology of metabolism. Science. 2016;354(6315):1008–1015.

Principales activités

- Mathematical modeling and analysis of the circadian oscillator system, by application of different techniques.
- Numerical simulations and analysis of the results.
- Writing a report on the project.

Compétences

The candidate should have some knowledge of ordinary differential equations and be familiar with a programming software such as Scilab, Matlab, Phyton, or equivalent

Avantages

- 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

Informations générales

- **Thème/Domaine :** Modélisation et commande pour le vivant
  Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Ville :** Sophia Antipolis
- **Centre Inria :** Centre Inria d'Université Côte d'Azur
- **Date de prise de fonction souhaitée :** 2021-01-18
- **Durée de contrat :** 6 mois
- **Date limite pour postuler :** 2020-11-03

Contacts

- **Équipe Inria :** BIOCORE
- **Recruteur :**
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A propos d'Inria

Inria est l'institut national de recherche dédié aux sciences et technologies du numérique. Il emploie 2600 personnes. Ses 215 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3900 scientifiques pour relever les défis du numérique, souvent à l'interface d'autres disciplines. L'institut fait appel à de nombreux talents dans plus d'une quarantaine de métiers différents. 900 personnels d'appui à la recherche et à l'innovation contribuent à faire émerger et grandir des projets scientifiques ou entrepreneuriaux qui impactent le monde. Inria travaille avec de nombreuses entreprises et a accompagné la création de plus de 200 start-up. L'institut s'efforce ainsi de répondre aux enjeux de la transformation numérique de la science, de la société et de l'économie.

L'essentiel pour réussir

The candidate should have a good motivation for mathematical modeling of biological systems.

Attention: Les candidatures doivent être déposées en ligne sur le site Inria. Le traitement des candidatures adressées par d'autres canaux n'est pas garanti.

Consignes pour postuler

Sécurité défense :
Ce poste est susceptible d'être affecté dans une zone à régime restrictif (ZRR), telle que définie dans le décret n°2011-1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L'autorisation d'accès à une zone est délivrée par le chef d'établissement, après avis ministériel favorable, tel que défini dans l'arrêté du 03 juillet 2012, relatif à la PPST. Un avis ministériel défavorable pour un poste affecté dans une ZRR aurait pour conséquence l'annulation du recrutement.

Politique de recrutement :
Dans le cadre de sa politique diversité, tous les postes Inria sont accessibles aux personnes en situation de handicap.