Master thesis

Analysis of circadian clock system with a Petri net inspired framework

Context

Understanding the mechanisms involved in **oscillatory** biological regulation is a fundamental issue to analyze living systems.
Time delays play a major role in the sustainability and control of oscillations, as shown for example in phenomena related to the mammalian **circadian clock**. This system controls most of our physiology over 24 hours. Mathematic modelling is key to understand the dynamics of circadian clocks and potential disruptive effects (for example shift work, jet-lag effects, etc.).

The Aim

The aim is to **formalize** and **verify** the properties of the circadian clock system taking into the account the **chronometric information** about various adaptive behaviors. However, the detailed biological data is not always available (or complete) and it contains both the quantative and qualitative metrics, therefore rendering such a formalization to be non-trivial.

Modelling

In previous works parametric time **Petri nets** were used to analyze some key properties of a small model of circadian rhythm (Comet et al., 2012). This research allowed to emphasize the benefits of Petri nets to study circadian clock. But this approach do not directly allow us to tackle noisy data, consider quantitative properties and capture some complex behaviors, like **aging**. The behavior of some parts of the circadian clock system has indeed been biologically proven to be dependent on the age of the subject.

One possible formalism to address such limits is the **Stochastic Petri nets** (+extensions) which benefits from expressive logics and well-established **model checking** procedures. The model checking of the selected properties can help to answer important biologically inspired questions, for instance related to the treatment of cancer and **sleep disorder**. This study involves the work on a detailed model of the circadian clock (which has already been established and which will be provided) where these methods will help to determine the values of parameters controlling the chronometric behaviour and propose the possible refinement of the model structure accounting for the aging factor.

Candidate

Successful candidates have a background in **Computer Science**. No specific skills in biology are required, even if we ask the applicant to have a motivation for applying computer science theory to the study of biological models.

Work place

Successful candidate has the opportunity to be directly advised in Saarland University (Saarbrucken, Germany) or in IRCCyN (Nantes, France).

References

(Schwind et al., 2013) Systems Resilience: A Challenge Problem for Dynamic Constraint-based Agent Systems.
(Andreychenko et al., 2015) A. Andreychenko, M. Magnin, and K. Inoue. Modeling and analysis of resilience properties in oscillatory biological systems using parametric time Petri nets.
(Comet et al., 2012) Simplified Models for the Mammalian Circadian Clock, 3rd International Conference on Computational Systems Biology and Bioinformatics, 2012.

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