

**Heart rate variability:
what are essential ingredients to observe the HRV complexity**

The heart rhythm is a canonical example and a benchmark of modelling in biology. It is well known that the human heart does not beat at a constant rate, even for a subject in repose; rather, there is strong variability of the heart rate. Today, on the one hand, we have many tools to characterize the complexity of heart rate variability (HRV) as an integrative output of the cardio-vascular system (without, so far, an achievement of a satisfactory understanding). On the other hand, we currently have a very detailed model of the heart tissue, including the rhythm centre (sino-atrial node); we know some regulation mechanisms of cell activities and the basic regulatory networks.

The aim of the project is to develop a model which could reproduce *the complexity* of HRV. Starting from cell level (the bottom), it is suggested to select an essential level of complexity of the modelling and develop a model that could reproduce basic statistical features of HRV (the top).

Details. The project is based on the series of recent experiments where HRV has been measured for specific respiration patterns [1]. Respiration exerts a particularly strong influence in modulating the heart rate, masking activities of other regulatory networks. Moreover, a spontaneous respiration gives rise to a complex non-periodic signal which inevitably reflects in HRV. So, by removing the respiratory perturbation we can consider a residual HRV which would then reflect the intrinsic dynamics of the heart control system. The experiments have shown that the intrinsic dynamics is significantly simpler than HRV in the presence of respiration and it allows one to specify a number of key features of HRV without respiration. The features can easily be reproduced by a toy-model. However, it is not clear what a biologically relevant model is, especially the choice of regulatory networks which should be included into the model, and which details of the heart itself are necessary for modelling. On the base of available literature it is suggested to make the choice, formulate the model and carry out the computer simulations.

PhD project. The project can be considered as an introductory to a wide spectrum of open issues in the description of the cardio-vascular system, and, therefore, it is reasonable to expect different directions for further research. It can be a development of a combination of a time-series analysis with modelling for diagnosing the state of the cardio-vascular system. Another important problem is modelling the cardio-respiratory interaction for different respiration patterns and it's using for clinical purposes. An extension of current heart tissue models by including regulatory networks or by taking into account intracell processes, is another possible continuation of the project.

References

1. I.A. Khovanov, N.A. Khovanova, P.V.E. McClintock and A. Stefanovska, *Intrinsic dynamics of heart regulatory systems on short timescales: from experiment to modelling*, J. Stat. Mech. (2009) P01016.