Nonlinear Dynamic Phenomena in Physiological Control Systems

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The purpose of this talk is to demonstrate the essential role that nonlinear dynamic phenomena play in normal physiological regulation and in the development of various diseases.

As an example we consider renal auto-regulation in normo- and hypertensive rats. Regulation of pressures and flows in the individual nephron involves the interaction between the tubuloglomerular feedback mechanism (TGF) and the oscillatory response of the activated afferent arteriole.
Early experiments by Leyssac and Holstein-Rathlou demonstrated that the TGF regulation tends to become unstable and generate self-sustained oscillations in the proximal tubular pressure with a characteristic period of 30-40 s. While for normal rats these oscillations have the typical appearance of a limit cycle, highly irregular oscillations are found for spontaneously hypertensive rats.

Coupling between nephrons occurs via a simple displacement of blood from one nephron to its neighbors as well as via contracting signals that propagate along the arteriolar wall. Together these mechanisms produce a wide variety of different nonlinear dynamic phenomena including intra- and internephron synchronization, generation of harmonics and subharmonics of the TGF-mediated oscillations as well as various form of deterministic chaos [1].

We present a model of the interacting feedback regulations in the individual nephron, of pairs of coupled nephrons, as well as of a tree of nephrons that share a common interlobular artery.

BioSim is an EU-sponsored Network of Excellence with a total funding of 10.7 mill. Euro over 5 years. The Network involves 26 academic partners, 10 industrial partners, and the regulatory agencies in Denmark, Holland, Sweden and Spain. The purpose of the Network is to illustrate how the use of mathematical models can reduce costs in the drug development process and improve treatment of patients in the health care sector.

[1] *E. Mosekilde*. Topics in Nonlinear Dynamics – With Applications to Physics, Biology and Economic Systems. World Scientific (2002), 3rd edition.