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Title:

Diabetes and dynamics: The mathematical physiology of beta-cells and the Islets of Langerhans

Abstract:

The rapid increase in the occurrence of Type 2 Diabetes Mellitus (T2DM) is a major health concern throughout the developed nations, and most of the world. Impaired insulin secretion from the endocrine beta-cells of the pancreatic Islets of Langerhans is central to the development of T2DM and is the subject of much investigation. Despite great advances in the field, the mechanism underlying the pulsatility of insulin secretion remains controversial. The work of Sherman et al. has been systematically elucidating the biophysical basis of secretion for over two decades. In a recent development, calcium and metabolism have been proposed as being jointly implicated in controlling the network dynamics leading to hormone release. A mathematical framework, termed the Dual-Oscillator Model (DOM), has been put forward by the group that successfully explains much, but by no means all, available data on islet activity.

The physiology of beta cells and of islets is a complex problem that presents dynamical behavior at multiple scales, both temporal and spatial. We use a variety of mathematical tools, both numerical and analytical, to investigate their properties in models. Indeed, the geometric description of (classical) bursting pioneered by Rinzel is one of the most elegant examples of mathematical physiology. I will review the physiology of the system and recent models (DOM) and present some novel approaches to a geometric description of the complex bursting patterns that have been observed. I will also describe a new mathematical technique, adapted from homogenization theory that we have recently developed to describe islet behavior. Finally, I will indicate our current efforts to understand the substructure of the beta-cells as well. This work poses computational challenges that arise from the stiffness and size of the simulations: we are especially interested in the use of parallel codes to solve the associated PDEs, as well as the hybrid stochastic ODEs that emerge from a detailed consideration of the ion channel dynamics.

This is joint work, particularly with Arthur Sherman (NIDDK/NIH). The group works in close collaboration with Richard Bertram (Florida State University), and the experimental laboratory of Les Satin (Virginia Commonwealth University).