Towards a bottom-up modelling approach to the pancreatic β-cell electrophysiology

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Glucose induced bursts of the membrane potential of pancreatic β-cells are at the origin of substantial intracellular calcium increases which, in turn, trigger exocytosis of insulin carrying vesicles. In the context of diabetes type II it is aimed to control vesicle exocytosis. This infers the necessity to understand the contribution and interplay of the different ion conducting transmembrane molecules to the β-cell electrophysiology. Traditional models of electrophysiology are based on whole cell currents [1,2]. These are successful phenomenological descriptions of the burst characteristics.

In this contribution a method will be described that allows to include a maximum of information about single transmembrane ion conducting molecules into the model [3]. The mostly measured characteristics of single channels and carrier proteins are directly used and incorporated into a model in which only the protein densities remain as free parameters. This approach aims at increasing the predictive power of the model and can be considered as a step towards a bottom-up model of β-cell electrophysiology. The model is based on its steady state at low glucose levels and develops bursts in response to elevated glucose metabolism. Novel conclusions about the interplay of the transmembrane currents and specific overexpression or inhibition experiments will be discussed. It will be shown that different proteins are responsible for bursting at different glucose levels. The role of sodium currents is revisited and a possible species-specific role is emphasised. Ambiguities of the single protein based approach and the potential of the model for future investigations will be discussed.

References:

[1] Sherman, A., J. Rinzel, and J. Keizer. Emergence of organized bursting in clusters of pancreatic beta-cells by channel sharing. Biophys. J. 54 (1988) 411425.

[2] Bertram, R., and A. Sherman. A calcium-based phantom bursting model for pancreatic islets. Bull. Math. Biol. 66 (2004) 13131344.

[3] Meyer-Hermann, M. The electrophysiology of the β-cell based on single transmembrane protein characteristics. Biophys. J. 93 (2007) 2952-2968.