Ca^{2+} Microdomains in the Pancreatic β-Cell: a Three-Dimensional Modeling Approach

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β-cells are responsible for secreting insulin as a response to an increase in blood glucose levels. Being electrically excitable, β-cells exhibit electrical activity in response to a glucose stimulus driven by a well established mechanism involving glucose metabolism, ionic channels and calcium signaling [1]. The purpose of β-cell electrical activity is to allow the influx of Ca^{2+} through ionic channels located in the plasma membrane in order to generate a high Ca^{2+} microdomain, which is the key signal triggering insulin exocytosis [2]. It is known that Ca^{2+} channels and insulin granules co-localize, and that they are not evenly distributed over the cell [3]. Accounting for these morphological characteristics we have developed a three-dimensional model of a β-cell. By including a mathematical description of the ionic channels, our model reproduces the electrical activity observed experimentally. This allow us to simulate the spatiotemporal distribution of Ca^{2+} in the microdomain generated by the electrical activity pattern. Our modeling approach enable us to evaluate the effect of distinct distributions of Ca^{2+} channels over the cell membrane. Besides reproducing experimental observations, we also assess the impact of impaired functioning of ionic channels on Ca^{2+} microdomains, which could ultimately affect insulin secretion.

References

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