

Simulation of the Electrical Activity of the Pancreatic β Cells Induced by Ingesting of Glucose During an Oral Glucose Tolerance Test

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Introduction

Diabetes Mellitus is diagnosed when the levels of the glucose concentration in the blood exceed a certain limit after ingesting a standard glucose load. This excess in the glucose concentration in the blood is caused fundamentally by an insufficient insulin release. The β -cells store the insulin in packages, and when the glucose concentration in blood arises, the insulin is released by exocytosis. This process requires a pulsating elevation of the concentration of intracellular Ca^{++} . The pulsating elevation of $[\text{Ca}_i^{++}]$ in the β -cell is product of electrical activity in burst [2, 4]. When the glucose concentration is in its basal level, the β -cells shown a resting potential without electrical activity. The resting potential is mediated by K^+ channels. K_{ATP} channels are open in absence of ATP_i and they close on depending by the concentration of intracellular ATP_i [7]. When $[\text{glucose}]$ in blood is increased, and introduces into the β -cells causing an increase in the basal level of ATP_i [1], which diminishes the fraction of opened K_{ATP} channels, depolarized the cell [7]. This depolarization reaches a level threshold that generates burst of action potentials with the consequent pulsating elevation of Ca_i^{++} and insulin release [5].

Methods

Simulations were developed in MatLab v.7 (The MathWorks, Inc.). For the quantitative description of $[\text{glucose}]$ in blood during the oral glucose tolerance test, we used the model developed by Trujillo [6]. Mathematical model for the description of the electrical activity of the β -cells was taken from Godinez [4], that is a modified version of Chay [3] which describes the electrical properties of the β -cells and also considere the changes in $[\text{Ca}_i^{++}]$. To this model, we incorporate the change in the membrane resistance generated by the action of the glucose, for which the mathematical description reported by Fridlyand [5] was used. The model completed when incorporating the increase of the ATP_i according to the extracellular glucose levels, for which the data published by Ainscow [1] were used.

Results

We Simulate the electrical activity of a β -cells in absence of extracellular glucose (not shown); the membrane potential V_M is greater than -50mV and the concentration of Ca_i^{++} was 150nM.

Fig 1A, shows the results obtained at the beginning of the OGTT after a glucose load. At $t=0$ with normal glycemia, the β -cells are silent but show a reduction in the resting potential

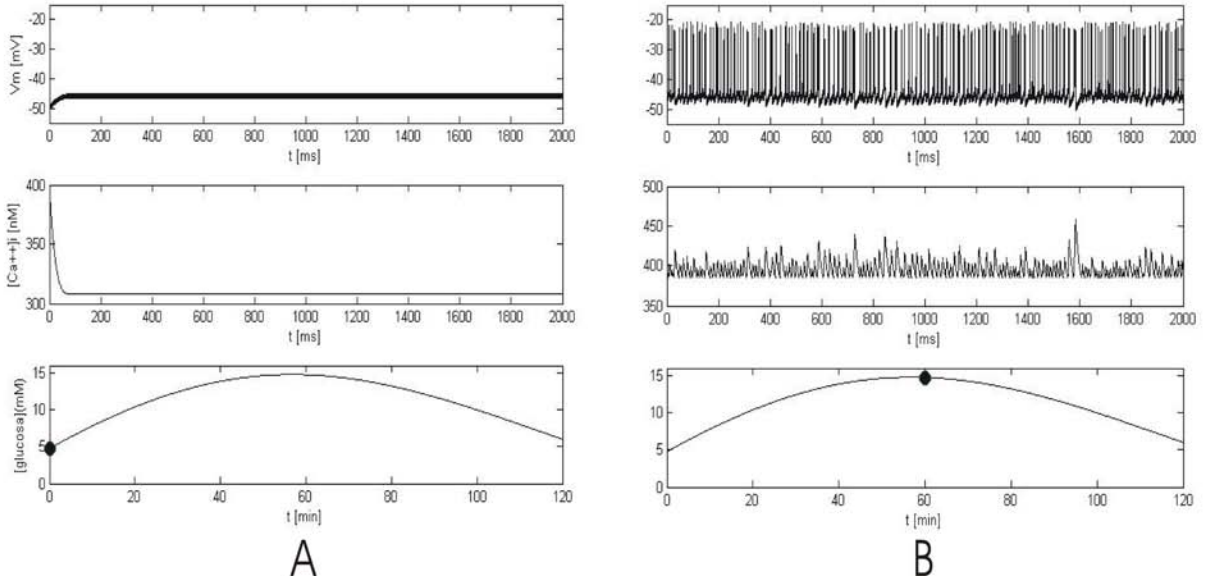


Figure 1: **A.** Reduction of resting potential (top), increase of Ca_i^{++} (middle) due an increase in blood glucose (5 mM) in oral glucose tolerance test at $t=0$ min (bottom). **B.** Burst of action potential (top), oscillations in Ca_i^{++} (middle) and maximum glycemia (15 mM) at $t=60$ min. after a glucose load (bottom).

and increases the basal level of Ca_i^{++} .

At $t=60$ min, when the maximum glucose is reached (Fig 1B), burst activity causes a depolarization. Associated to this type of electrical activity, an increase in the Ca_i^{++} is induced. The level average of the Ca_i^{++} was increased and it was accompanied by oscillations at the end of each burst of action potentials.

Discussion

Several models have been used to describe the electrical activity of pancreatic β -cells. Nevertheless, there is not a model of the electrical activity and the changes in $[\text{Ca}_i^{++}]$ in terms of the values of $[\text{glucose}]$ in blood. Our results indicate that the increase average of the ATP_i induced by hyperglycemia, is the factor that generates burst of action potentials and the oscillating increase of the Ca_i^{++} is product of the activation and inactivation of ionic channels. In addition, basal $[\text{ATP}_i]$ is critical for a suitable induction of the insulin release in response to an increase of glucose.

References

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