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# A NEW MATHEMATICAL MODEL FOR PANCREATIC $\beta$ CELLS: GEOMETRIC ANALYSIS OF COUPLED BURSTERS

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Bursting is a type of electrical activity seen in many neurons and endocrine cells where episodes of action potential firing are interspersed by silent phases. Pancreatic  $\beta$ -cells show so-called square-wave bursting when stimulated by glucose, which causes  $\text{Ca}^{2+}$  oscillations and pulsatile insulin secretion.  $\beta$ -cells are electrically coupled within pancreatic islets, and excitation waves are observed to propagate through the  $\beta$ -cell population. When the islet is exposed to a glucose gradient, so that some cells would be active also when uncoupled while others would be below the activity threshold and thus silent,  $\text{Ca}^{2+}$  waves propagate only partly through the islet and stop approximately where the glucose concentration is at the threshold for cellular activity. Simulations of existing mathematical models of coupled  $\beta$ -cells produce waves that propagate too far into the region of “silent” cells, compared to experiments, unless unrealistic model assumptions are imposed. Here, we investigate why  $\beta$ -cell models fail to reproduce the experimentally observed wave properties and tend to synchronize the  $\beta$ -cell population too easily, by using a prototypical polynomial bursting model and slow/fast bifurcation analysis. Our analyses indicate how to modify the model so that the excitation waves stop at the border between “active” and “silent” cells. We verify this property by simulations using such a modified model for a chain, and for a cubic cluster, of coupled  $\beta$ -cells. Furthermore, we show how our one- and two-parameter bifurcation analyses allow us to predict where the simulated waves stop, for both the original model and the modified version. Our results indicate the geometrical structure that biophysical  $\beta$ -cell models should have to possess biologically realistic wave and synchronization properties.