Glycolytic oscillations in spatially ordered interacting cells

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1 Introduction

Glycolytic oscillations, and in particular the synchronisation of these oscillations, have been intensively analysed experimentally as well as theoretically. Because the cellular membrane is permeable for products of glycolysis as acetaldehyde/pyruvate, cells can interact via exchanging these compounds. Various theoretical models have been proposed to explain the synchronisation of glycolytic oscillations in yeast cells as observed experimentally [2]. There are, however, a number of discrepancies between model predictions and experimental results. For example, in existing models synchronisation occurs much slower than observed in populations of yeast cells [3]. In extension to previous models which considered stirred cell suspensions we study oscillations in spatially ordered cells. We aim to reproduce data of experiments where glucose is added to starved cells in a limited region of the cell layer initiating in this way a wave resulting from the propagation of glycolytic oscillations [1].

2 Method and Results

In a first model, oscillations in the individual cells result from an autocatalytic step in a simplified model of glycolysis. Cells are embedded in an extracellular medium in which the added glucose and the extracellular product Y^e can diffuse. The model takes into account special kinetic properties of glucose carriers in yeast cells. Intercellular coupling takes place via diffusion of the end product between neighboured compartments.

A schematic representation of the model is seen in Fig. 1. Here the parameter V_0 describes the constant glucose input flux. Variables G_i and X_i denote the extracellular and the intracellular substrate glucose of the i-th compartments, respectively, whereas Y_i and Y_i^e denote the intracellular and the extracellular product, respectively.

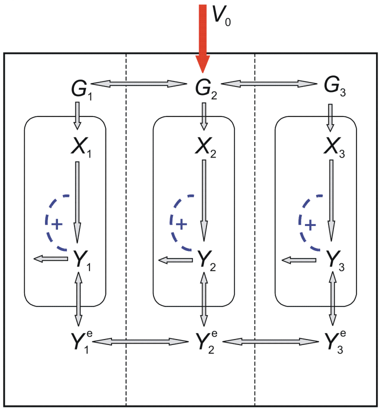

Figure 1: Schematic representation of the used glycolytic model.

Using bifurcation analysis we studied the dynamics for a small number of linearly ordered cells. Oscillations and waves of different type have been identified depending on the number of cells and the kinetic properties of the biochemical reactions as well as the transport processes.

For a first understanding we investigate two identical, coupled cells, both of them subject to a glucose input V_0. In this case there are two main oscillatory states: synchronous and asynchronous. Figure 2 shows a schematic bifurcation diagram with the glucose influx V_0 as bifurcation parameter. For small as well as for high values of V_0 there exists only one stable steady state. The stability changes at point B1 via a subcritical Hopf bifurcation leading to the branch b1. On this branch the cells oscillate synchronously as seen in Fig. 3a. These oscillations are stable at the solid part of branch b1 in Fig. 2 and become unstable at point B4.

A second branch b2 emerges at point B2 via a supercritical Hopf bifurcation. Here the cells oscillate asynchronously (see Fig. 3b), first unstable and beyond point B5 stable. On the asynchronous branch there is a further state with different amplitudes for each cell which is, however, unstable (branch b3). Between the two points B4 and B5, where neither the synchronous nor the asynchronous oscillations are stable, the two cells oscillate in a complex coupled state, shown in Fig. 3c. In this state the cells oscillate with a periodic amplitude, as it is known from the superposition of two oscillations with similar frequencies. Not included in Fig. 2, there are further oscillatory states at the left end of the stable part of branch b1, which are more complicated, however, all of them are unstable.

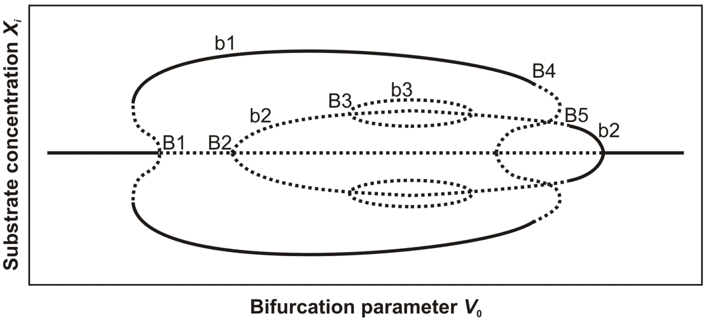

Figure 2: Schematic bifurcation diagram for two coupled identical cells (solid lines: stable states, broken lines: unstable states).

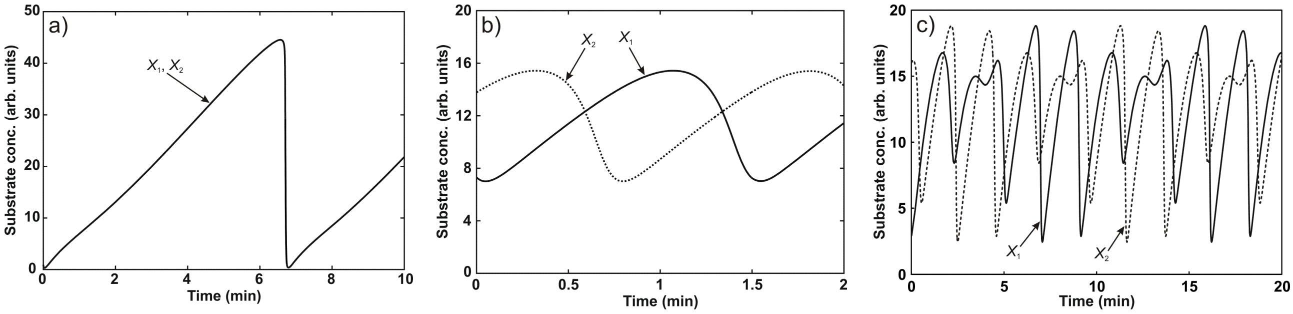

Figure 3: Oscillatory behaviour of two coupled identical cells;
a) synchronous oscillation; b) asynchronous oscillation; c) complex oscillations for parameter values at the transition from synchronous to asynchronous oscillations.

When extending the model for three interacting cells with a uniform glucose input we could find very different and complex oscillatory states. In a next step, we will apply this model to arrangements of a larger number of cells to describe glycolytic waves as obtained when glucose injection is confined to a limited number of neighboured cells.

References

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