**DEVELOPMENT OF A GENE REGULATORY MODEL TO ENHANCE THE PREDICTION OF BIOETHANOL PRODUCTION BY *SACCHAROMYCES CEREVISIAE***

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**ABSTRACT**

The production of biofuels such as bioethanol from lignocellulosic biomass, constitutes a promising process holding numerous advantages including the reduction of fossil fuels and environmental pollution (Chen et al., 2021). Alcoholic fermentation is commonly performed by the industrial workhorse *Saccharomyces cerevisiae* (Nijland et al., 2020), utilizing glucose as the primary energy source via the pathway of glycolysis (Kim et al., 2021). Previous research has shown that the development of experimentally validated models of key genetic circuits (comprising groups of cellular elements that interact) could improve prediction of the kinetic properties of a microorganism (Koutinas et al., 2011). In order to predict the kinetics of the microorganism in relation to glucose uptake and consumption, a logic model was developed with the use of logic gates. In the logic model, the interacting molecular components were described as a combination of logic gates, producing an “electronic” representation following an analogy to electronic circuits (Chen et al., 2020). The logic model implemented included glucose sensing processes, activation of glucose/hexose transporters (HXTs) and glycolysis. The Rgt2 receptor, which is considered a glucose concentration sensor, is located on the plasma membrane of the cell detecting high glucose concentrations (>10 g/L) (Van Ende et al., 2019). Rgt2 is responsible for the expression of two glucose transporters within the cell, HXT1 and HXT3, which activate hexokinase 2 (HKX2), the first enzyme of glycolysis (Kim et al., 2021). Apart from the aforementioned intracellular components, PFK, TDH3 and PGK1 also comprise crucial enzymes for glycolysis (Songdech et al., 2020). The presentation will include construction of a Boolean model combining logic gates to describe important regulatory loops, while Hill functions will be used as input functions to the relevant genes, aiming to produce a dynamic mathematical model using ordinary differential equations to describe mRNA production from the genes involved in glycolysis. The mRNA production will be monitored using reverse transcription RT-PCR during bioethanol fermentations by *S. cerevisiae*. Simulations of the developed model predicting the dynamic behavior of the molecular system will be presented.

**KEYWORDS:** *Saccharomyces cerevisiae*, Mathematical modeling, Genetic circuit, Bioethanol, Glycolysis

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