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Short communication

Power series kinetic model based on generalized stoichiometric equations for microbial production of sodium gluconate

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ABSTRACT

Two main approaches are available for modeling of the fermentation process; these two are building an unstructured dynamic model and quantitative analysis of the metabolic network. The first one often employs several classic equations mostly derived from empirical knowledge and observation rather than mechanism knowledge. The second one is complicated because it requires sufficient biological information on cellular metabolic pathways. The objective of this article is to develop a kinetic model of the microbial production of sodium gluconate by using generalized stoichiometric equations and a typical enzyme kinetic structure called power series to overcome the shortcomings of previous methods.

The proposed kinetic model can describe the microbial growth of fungus as well as the interaction among dissolved oxygen, fungal metabolism, and product formation. Six batches were selected from seven batches of experimental sample data for modeling and analysis. The fitting precision was acceptable. The key parameters were analyzed based on the model. The main advantage of this model is that it has a simple structure based on the mechanism and can describe the fermentation process with sufficient accuracy.

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1. Introduction

Sodium gluconate is an important material widely utilized as a firming, stabilizing, or buffering agent in food, textile, pharmaceutical, and construction industries [1–3]. In recent years, it is also becoming a novel carbon source for fuels and chemicals production, such as ethanol production [4–6]. Many approaches for the production of sodium gluconate are available, such as biochemical fermentation, electrochemical oxidation, homogeneous chemical oxidation and heterogeneous catalysis oxidation. At present, microbial production of sodium gluconate or fermentation by *Aspergillus niger* is the most preferred method [7–10].

The fermentation process can be modeled by two different models: structured models based on the analysis of metabolic pathways and unstructured models in which biomass is described by one variable.

A structured model is difficult to build [11] because it requires sufficient biological information on intracellular metabolic pathways. Two approaches can be applied to build a structured model. One involves establishing flow equilibrium equations based on the cellular metabolic network by using stoichiometric coefficients and selecting an objective for optimization [12,13]. The problem becomes a linear optimization problem that fails to express many nonlinear features of the model. The other method involves kinetic analyses, such as enzyme kinetic analysis, metabolic control analysis [14], and biochemical system theory [15]. The problems include how to guarantee feasibility, obtain sufficient constraints, and reduce computational difficulty.

Unstructured models have simple forms. Previously proposed unstructured models can describe the fermentation process with satisfactory accuracy [16]. The Monod equation and the logistic equation can be utilized to describe the growth trend of cells with different properties. The Luedeking–Piret and Luedeking–Piret/like equations can be used to describe production formation and glucose consumption. However, these classic equations are mostly derived from empirical knowledge and observation rather than mechanism knowledge.

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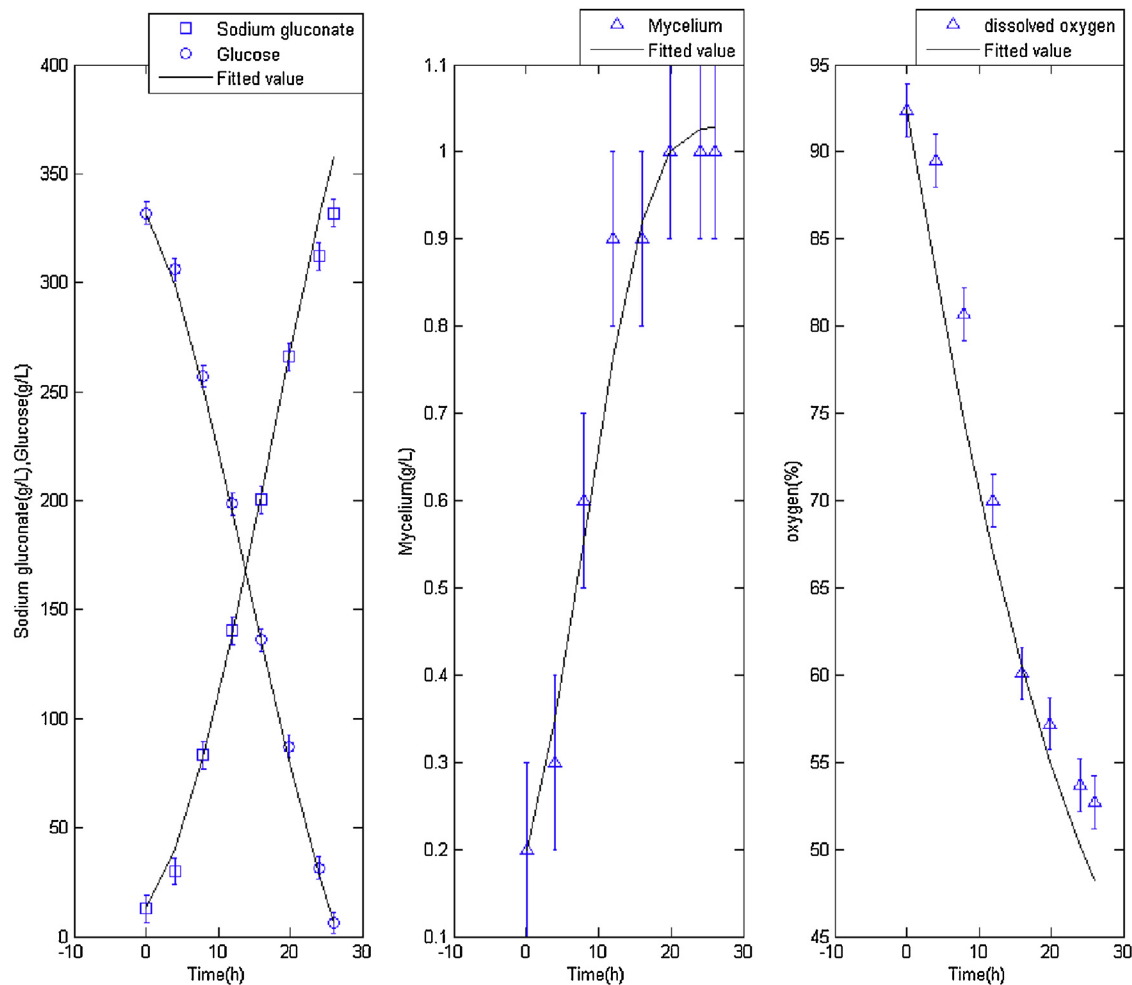

Fig. 1. Fitting results for batch 1.

The proposed investigation approach attempts to combine structured and unstructured model features into a simple kinetic model that can describe the fermentation process with sufficient accuracy. Two main steps are required: describe the fermentation process through generalized stoichiometric equations and describe the relationship between reaction rate and metabolite concentration through the use of a power series structure. The parameters in the model can be categorized into two classes, namely, yield coefficients, which are determined by the structure of the generalized stoichiometric reactions, and kinetic rates, which are determined by specific metabolism pathways [17].

2. Experimental procedures

2.1. Microorganism

The industrial strain for the production of sodium gluconate, *Aspergillus niger* (AN151) was supplied by Shan Dong Fuyang Biological Technology Co., Ltd.

2.2. Culture methods

The *A. niger* strain was activated in a 250 mL flask (50 mL activation medium). The activation medium slant inoculated with AN151 strain was incubated at 35 °C until it was covered with dense spores. The spores were harvested by washing the slant with 50 mL sterilized water. The formulation of the strain activation culture medium is 60.0 g/L glucose, 0.20 g/L urea, 0.13 g/L KH_2PO_4, 0.15 g/L $MgSO_4$, 1.00 g/L corn steep liquor (Fu Yang Biology Co., Ltd., China), 5.00 g/L $CaCO_3$, and 20.0 g/L agar.

A total of 50 mL spore suspension was inoculated in a 15 L stirred bioreactor (9 L working volume) and cultivated for 18 h. Temperature and pressure were maintained at 38 °C and 0.1 MPa, respectively. The pH value was controlled at 5.5 by 7.5 M NaOH solution. Aeration and agitation rates were set to 0.8 vvm (air volume/culture volume/min) and 500 rpm, respectively. The formulation of the seed culture medium is 250 g/L glucose, 0.50 g/L KH_2PO_4, 1.80 g/L $(NH_4)_2HPO_4$, 0.19 g/L $MgSO_4$, 2.10 g/L corn steep liquor, and 0.20 mL/L polyether defoamer (Si Xin Scientific-Technological Application Research Institute Co., Ltd., Nanjing, China).

A total of 4.5 L seeds were transferred into 50 L stirred bioreactor (30 L working volume). The pH, temperature, and pressure values during fermentation were similar to those during seed cultivation. Aeration and agitation rates were set to 1.2 vvm and 550 rpm, respectively. The fermentation ended when the glucose concentration was lower than 3 g/L. The formulation of the fermentation culture medium is 330 g/L glucose, 0.55 g/L KH_2PO_4, 0.40 g/L $(NH_4)_2HPO_4$, 0.20 g/L $MgSO_4$, and 0.20 mL/L polyether defoamer.

All the culture media were sterilized at 115 °C for 20 min, and their initial pH were adjusted to 7.0 by using 1 M NaOH solution, so that gluconic acid can turn into sodium gluconate.

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