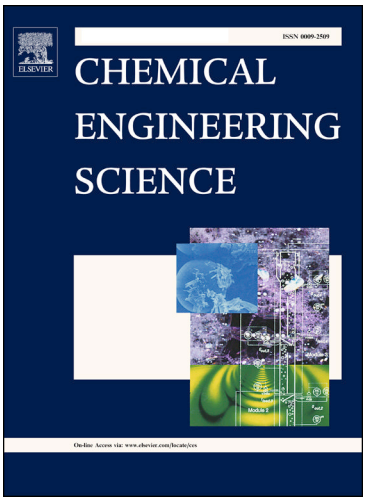

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Kinetic Model Discrimination of Penicillin G Acylase Thermal Deactivation by Non-Isothermal Continuous Activity Assay

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Abstract

A novel approach for the determination of a kinetic model of enzyme deactivation is presented incorporating time and temperature dependence into a single, continuous assay. A generic method for a non-isothermal, continuous activity assay is developed. Unique temperature profiles that enhance model discrimination with fewer experiments compared to linear temperature scans were used to differentiate kinetic models of penicillin G acylase (PGA) deactivation. Three models are examined in depth but the technique is generalizable to any kinetic deactivation model. Using the Akaike information criterion (AIC), the Lumry-Eyring model was found to best capture PGA deactivation behavior and the corresponding kinetic parameters are presented for the first time. Additionally, simulated experiments on lysozyme and TEM-1 beta-lactamase were used to develop temperature profiles that best differentiate the studied kinetic models. The results from the proposed approach were consistent with conventional, but tedious, isothermal batch experiments.

Keywords

Penicillin G acylase, Enzyme deactivation modeling, Lumry-Eyring mechanism, Model discrimination, Akaike Information Criterion