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Nonlinear Mixed Effects Models for Kinetic Parameter Estimation with Batch Reactor Data

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Highlights

- Mixed effects models provide statistically superior parameter estimates for batch data.
- Confidence intervals from mixed effects models are not artificially compressed.
- Mixed effects models greatly reduce correlation between residuals.
- Better parameter estimates from mixed effects models will yield better decisions.

1. Introduction

Batch reactors are used extensively for the elucidation of chemical reaction mechanisms and estimation of the pertinent kinetic constants. Often, longitudinal measurements from batch reactions with multiple samples in a single batch will yield model parameter estimates with relatively small variances compared to the batch-to-batch variation that is observed from replicate or nearly replicate experiments. Standard fixed effects approaches, such as traditional nonlinear least squares or Bayesian estimation methods, assume fixed parameters and statistical independence between measurements within the sample and between different samples. However, for serially correlated measurements and significant correlation among samples such as those from batch reaction experiments, this assumption is not valid.

To circumvent these difficulties, numerous investigators have applied nonlinear mixed effects models in the biological, agricultural, and the environmental sciences [1]. Mixed effect models contain some parameters with a fixed and a random component. In this presentation, we introduce nonlinear mixed effects models, an approach commonly used in other fields but rarely mentioned in publications associated with the discovery of chemical reaction mechanisms. We illustrate this approach by comparing the results of parameter estimation using a mixed effects model with results from one or more of the commonly used fixed effects approaches. As our test case, we use single response data for the hydrogenation of acetophenone in a batch recycle trickle bed reactor [2].

2. Methods

The experimental system used in the collection of the data in this study has been described previously [2]. The single response data correspond to the concentration of acetophenone (the reactant) in a well-mixed vessel that serves both as the feed and the product vessel in this batch recycle system, which is integrated with a trickle bed reactor. The reactor operates in an integral mode with approximately 10% to 90% of acetophenone conversion per single pass.

For the analysis of the experimental data, we use a Langmuir-Hinshelwood rate law with three parameters and compare the nonlinear mixed effects approach with nonlinear least squares estimation. For the mixed effects model, we compare the results with a single random effect on the lumped rate constant, a single random effect on the acetophenone adsorption constant, or two random effects. The comparisons include the parameter means and confidence intervals, parity plots, lag plots for testing randomness, run sequence plots for testing data drift, and normal probability plots to assure that the errors are normally distributed.

3. Results and discussion

The mixed effects model with the two random effects provided the most statistically significant explanation of the observed data as assessed using the Akaike information criterion (AIC). Incorporation of the random effects into the fixed rate expression parameters not only improved model performance but also influenced the estimated values for the fixed parameters. The changes in the estimated parameter values obtained from fixed and mixed effects models are very important because these parameters are used for scaling up of reactors, optimization of existing reactors, and evaluation of catalyst performance. In addition, we observed that the confidence intervals were wider for the parameters with the mixed effects model than for the traditional nonlinear least squares fixed effects model. For the latter, the confidence intervals are very narrow and provide misleading estimates of the uncertainty in the parameter values and the predictive capabilities of the conditional model. This further substantiates the inferiority of fixed effects models for modeling batch reactor longitudinal experiments. Figure 1 displays lag plots for the nonlinear least squares fixed effect model and the mixed effects model with two random effects. The residuals of the fixed effects model are linearly correlated, with a Pearson correlation coefficient near unity, whereas this correlation is largely mitigated by the mixed effects model.

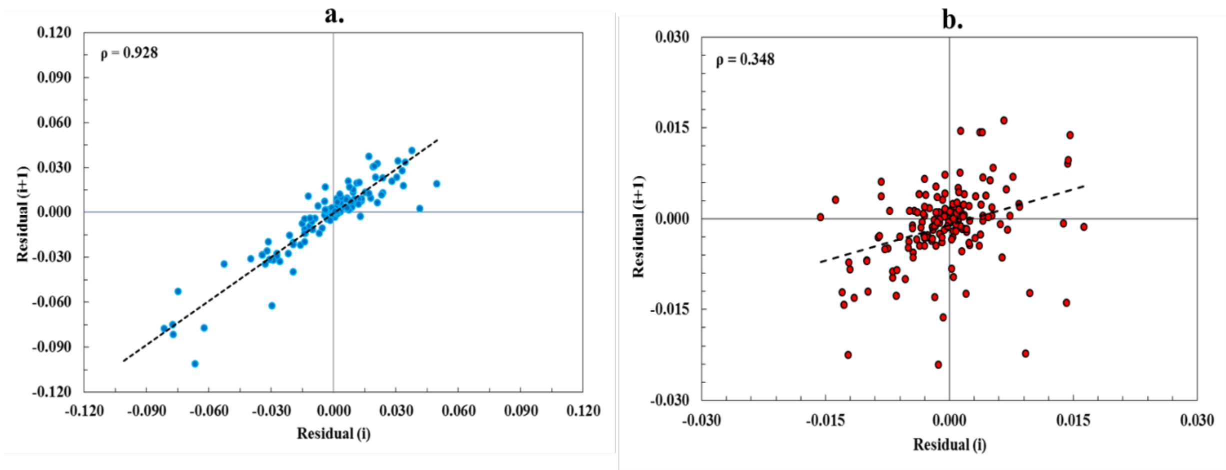

Figure 1. Lag plot for batch data from about 20 batch experiments fit with (a) a nonlinear least squares (fixed effects) model and (b) a mixed effects model with two random effects.

4. Conclusions

Using experimental data obtained with a batch recycle reactor, we demonstrate that assumptions of independent, normally distributed errors for longitudinal measurements from multiple batch experiments yield estimates that provide statistically inferior explanations of the observed data relative to models that incorporate batch-to-batch variation. Based on these experimental data and prior experience, the correlation between sequential residuals is strongly linear for fixed effects models. On the other hand, modeling batch reactor longitudinal experiments with mixed effects models offers a better explanation of the observed data by reducing or eliminating bias in the estimated parameters and providing confidence intervals that are more realistic. This enables better model predictive capability outside the scope of the experimental envelope.

References

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Keywords
Mixed effects; parameter estimation; batch reaction data