Mathematical Modelling of Reactive Inks for Additive Manufacturing of Charged Membranes

Xinhong Liu[1], Riju De[2], Alexander Pérez[3], John R. Hoffman[1], William A. Phillip[1], Alexander W. Dowling[1*]

[1]*Department of Chemical and Biomolecular Engineering, University of Notre Dame, Notre Dame, IN 46556, USA*
[2]*Department of Chemical Engineering Goa, BITS Pilani, Goa 403726, India*
[3]*Department of Mechanical Engineering, University of Puerto Rico-Mayagüez, Mayagüez, PR 00681, USA*
adowling@nd.edu

Abstract

Patterned charged membranes with engendered useful characteristics can offer selective transport of electrolytes. Chemical patterning across the membrane surface via a physical inkjet deposition process requires precise control of the reactive-ink formulation, which enables the introduction of charged functionality to the membrane. This study develops a new dynamic mathematical model for the primary step of the batch reactive-ink formulation considering an ink mixture of copper sulphate and ascorbic acid. Nonlinear least squares parameter estimation is performed to infer three kinetic model parameters by analysing data from nine dynamic experiments simultaneously. Global sensitivity and Fisher information matrix (FIM) analyses reveal only one kinetic parameter is identifiable from time-series pH measurements. The fitted model can capture the overall nonlinear dynamics of the batch reaction and works best for initial Cu^{2+} concentrations between 30 and 50 mM. Time-series Cu^{2+} or Cu^+ concentration measurements are recommended in future experiments to elucidate the kinetics of reactive-ink formulation.

Keywords: Sensitivity analysis, Parameter estimation, Additive manufacturing, Fisher information matrix, Nanostructured membrane, Data science

1. Introduction

A critical need for more selective membranes has emerged as their applications in modern separations and sensing processes continue to expand. To this end, membranes with chemically patterned surfaces such as charge-patterned mosaics and Janus membranes are an emerging approach for accessing higher selectivity (Qu et al., 2017). The state-of-the-art fabrication process of such membranes involves printing reactive inks on the nanostructured substrates, where the charged functionality is induced through the copper-catalysed azide-alkyne cycloaddition (CuAAC) reaction mechanism. Hoffman et al. (2019) demonstrated that this approach requires precise control of the reactive-ink formulation to ensure the membrane manufacturing process remains in the transport-limited regime. The reactive-ink formulation comprises of a sequence of reactions occurring between reactants, i.e., copper sulphate ($CuSO_4$), ascorbic acid (DH_2), and an alkyne, to facilitate the formation of the dinuclear-copper alkyne complex (DNCAC). The concentration of the DNCAC is essential for the CuAAC reaction to proceed and therefore should be optimized to achieve a smooth chemical patterning while ensuring a controlled charged functionalization rate of the membrane at the same time (Worrell et al., 2013).

Focusing on the primary step which involves the reaction between $CuSO_4$ and DH_2, there are only a few models available in the literature that explains the mechanism of the DH_2-$CuSO_4$ reaction (Shtamm et al., 1979; Xu and Jordan, 1990). However, these models are limited to either the final Cu^{2+} reduction or the Cu^+/hydronium ions (H^+) formation. None have discussed a comprehensive and detailed rate law-based model that captures all the species involved in the reaction to the best of our knowledge.

In this paper, we develop a first-principles-based kinetic model for reactive ink formulation. Considering the anaerobic reaction scheme for the ascorbic acid dissociation as reported in the literature, rate constants that are unavailable in the literature are posed as model parameters and related to known equilibrium constants from Shtamm et al. (1979). Parameter estimation is performed to identify kinetic rate constants from time-series pH data. Local and global sensitivity analyses are performed to determine which model parameters are identifiable and design future experiments.

2. Dynamic mathematical model for reactive-ink formulation

The simplest reactive-ink solution is an aqueous mixture of ascorbic acid and copper sulphate. The reaction scheme involves a sequential dissociation of ascorbic acid via two reversible reactions in equilibrium as given by Eqs. (I), (II) and a final forward reaction as in Eq. (III), which describes the conversion of Cu^{2+} to Cu^+. Shtamm et al. (1979) proposed the following reaction scheme for the reduction of Cu^{2+} to Cu^+:

$$DH_2 \underset{k_{b1}}{\overset{k_{f1}}{\Leftrightarrow}} DH^- + H^+ \tag{I}$$

$$Cu^{2+} + DH^- \underset{k_{b2}}{\overset{k_{f2}}{\Leftrightarrow}} CuDH^+ \tag{II}$$

$$Cu^{2+} + CuDH^+ \overset{k_{i1}}{\rightarrow} 2Cu^+ + D + H^+ \tag{III}$$

The equilibrium constants for reaction (I) and reaction (II) reported by Shtamm et al. (1979) are $K_{e1} = {k_{f1}}/{k_{b1}} = 5 \times 10^{-5}$ M and $K_{e2} = {k_{f2}}/{k_{b2}} = 200$ M^{-1}, respectively. Here, k_{f1} and k_{f2} denote the forward rate constant, whereas k_{b1} and k_{b2} symbolize the backward rate constants for reactions I and II, respectively. The rate constant for the final reaction (III) reported by Shtamm et al. (1979) is $k_{i1} = 6000$ mol^{-1}·L·min^{-1}. We consider a fully dynamic kinetic model for reactions (I) to (III) with five differential variables and five ordinary differential equations:

$$\frac{d[DH_2]}{dt} = -k_{b1}K_{e1}[DH_2] + k_{b1}[DH^-][H^+] \tag{1}$$

$$\frac{d[DH^-]}{dt} = k_{b1}K_{e1}[DH_2] - k_{b1}[DH^-][H^+] - k_{b2}K_{e2}[DH^-][Cu^{2+}] \\ + k_{b2}[CuDH^+] \tag{2}$$

$$\frac{d[H^+]}{dt} = k_{b1}K_{e1}[DH_2] - k_{b1}[DH^-][H^+] + k_{i1}[CuDH^+][Cu^{2+}] \tag{3}$$

$$\frac{d[Cu^{2+}]}{dt} = -k_{b2}K_{e2}[DH^-][Cu^{2+}] + k_{b2}[CuDH^+]$$
$$- k_{i1}[CuDH^+][Cu^{2+}] \tag{4}$$

$$\frac{d[CuDH^+]}{dt} = k_{b2}K_{e2}[DH^-][Cu^{2+}] - k_{b2}[CuDH^+]$$
$$- k_{i1}[CuDH^+][Cu^{2+}] \tag{5}$$

Here, $[DH_2]$, $[DH^-]$, $[H^+]$, $[Cu^{2+}]$, and $[CuDH^+]$ denote the concentrations of ascorbic acid, anion, hydrogen ion, cupric ion, and the complex, respectively, in unit of M. The model includes three unknown kinetic parameters, k_{b1} [mol^{-1}·L·min^{-1}], k_{b2} [min^{-1}] and k_{i1} [mol^{-1}·L·min^{-1}], that characterize the reaction progress.

3. Materials and methods

3.1. Materials

Initially, 200 mM ascorbic acid (DH$_2$) and copper sulphate (CuSO$_4$) solutions were prepared separately in 5 mL sample vials. Subsequently, the solutions were mixed to form 10 mL solutions. The pH of the mixtures was measured at every 1 min time interval for 5 min. The procedure was repeated in triplicate with CuSO$_4$ solutions at 200, 150, 100, 66.7, 50.0, 40.0, 33.3, 28.6, 25.0 mM for a total of (3 x 9 =) 27 experiments.

3.2. Parameter estimation with multi-start

To estimate the three unknown kinetic model parameters, $\boldsymbol{\theta} = \{\boldsymbol{k_{b1}, k_{b2}, k_{i1}}\}$, we solve the least-square nonlinear regression problem, shown in Eq. (6), which minimizes the square of the difference between the model predicted and the experimentally measured concentration of H$^+$ ions (residuals) for the 9 experimental conditions.

$$\widehat{\boldsymbol{\theta}} = \arg\min_{\boldsymbol{\theta}} \sum_{i=1}^{n_{exp}} \sum_{j=1}^{n_{tri}} \left([H^+]_{pred,i,j} - [H^+]_{exp,i,j}\right)^2 \tag{6}$$

Eq. (6) is solved numerically using scipy.optimize in Python with a customized multi-start strategy to help find the (near) global optima.

3.3. Local and global sensitivity analysis

The Fisher information matrix (FIM), which is defined as the inverse of the parameter covariance matrix, is computed at the best fit parameter values $\widehat{\boldsymbol{\theta}}$ based on local sensitivities of the model predictions to each parameter. The eigendecomposition of the FIM reveals which parameters are identifiable (Rothenberg and Thomas, 1971).

Similarly, a global sensitivity analysis is conducted via grid search by evaluating the objective function over a wide range of model parameters: k_{b1} = [400, 900] mol^{-1}·L·min^{-1}, k_{b2} = [1E-05, 1] min^{-1} and k_{i1} = [1, 6000] mol^{-1}·L·min^{-1}.

4. Results and discussion

4.1. Parameter estimation with multi-start

Table 1 shows the parameters estimated from regressing time-series pH measurements from the 27 experiments simultaneously. When each dataset (experimental condition) is regressed independently, parameters k_{b1} varies from 260 to 1,100,00 mol⁻¹·L·min⁻¹ and k_{i1} varies from 12 to 6,000 mol⁻¹·L·min⁻¹. These non-unique parameters motivate both simultaneous regression (Table 1) as well as formal identifiability analysis.

Table 1. Parameter estimation and local sensitivity from analysing 9 experiments simultaneously.

Estimated parameters			Residuals squared	Eigenvalues of FIM	Eigenvectors of FIM		
k_{b1}	k_{b2}	k_{i1}					
(mol⁻¹·L·min⁻¹)	(min⁻¹)	(mol⁻¹·L·min⁻¹)	(M²)		k_{b1}	k_{b2}	k_{i1}
				2.18E-12	-1.00	1.55E-09	4.40E-04
17601.30	0.0074	105.69	68.62	2.74E-06	-4.40E-04	8.35E-07	-1.00
				2.84E+06	-1.92E-09	-1.00	-8.35E-07

4.2. Local and global sensitivity analysis

The eigenvalues and eigenvectors of the Fisher information matrix (FIM) are also reported in Table 1. Two eigenvalues are near zero, 2.18E-12 and 2.74E-06, which implies the FIM is near singular and model is partial non-identifiable. The corresponding eigenvectors are predominantly in the direction of k_{b1} and k_{i1}, respectively, which indicate these parameters cannot be reliably estimated from these data. Conversely, the eigenvector of the largest eigenvalue, 2.84E+06, is in the direction of k_{b2}. This difference of more than 12 orders of magnitude in eigenvalues implies only k_{b2} is identifiable based on the pH measurements from 9 experimental conditions considered in triplicate.
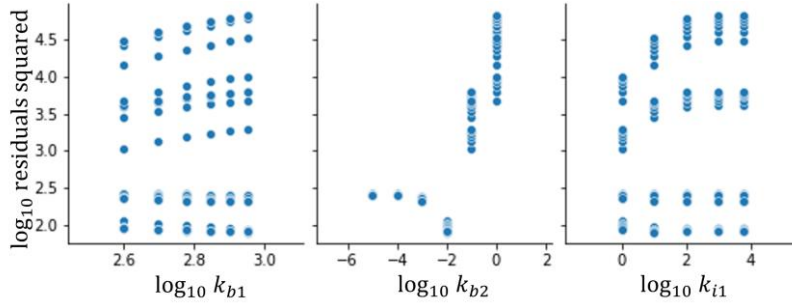

Fig. 1. Global sensitivity of the log₁₀-transformed sum of residuals squared for three model parameters.

Fig. 1 shows the results from a global sensitivity analysis which confirm that k_{b2} is the most sensitive model parameter. Parameters k_{b1}, k_{b2} and k_{i1} are varied with a grid search, and the log₁₀-transformed sum of residuals squared for the 27 experiments are computed. The plots with respect to k_{b1} and k_{i1} show the sum of residuals squared is only slightly impacted by the value of k_{b1} and k_{i1}. In other words, for a constant value of k_{b1} or k_{i1}, the sum of residuals squared changes by two orders of magnitude when varying the other two parameters. In a contrast, varying k_{b2} causes one to four orders of

magnitude changing in the sum of residuals squared. Moreover, the sum of residuals squared is minimized around $k_{b2} = 10^{-2}$ min^{-1}. For $k_{b2} \leq 10^{-2}$ min^{-1}, varying k_{b1} or k_{i1} has almost no impact on the sum of residuals squared, but the model becomes sensitive to k_{b1} and k_{i1} when $k_{b2} \geq 10^{-2}$ min^{-1}. A possible physical explanation for this result is that reaction (II) is rate limiting when $k_{b2} \leq 10^{-2}$ min^{-1}, hence the model predictions are not sensitive to the other reaction kinetic constants (provided they are sufficiently large to not be rate limiting).

4.3. Partial parameter estimation

The local and global sensitivity analyses above both show only k_{b2} can be reliably estimated from the available timeseries pH measurements from the 27 experiments. Since k_{b1} characterize the rate for the ascorbic acid dissociation, it only affects the beginning of Cu$^+$ formation and has little influence on the subsequent reaction progress. Therefore, we select $k_{b1} = 600$ mol^{-1}·L·min^{-1} for reasonable H$^+$ profiles and $k_{i1} = 6000$ mol^{-1}·L·min^{-1} based on literature (Shtamm et al., 1979).

A. 200 mM AA:200 mM Cu^{2+} B. 200 mM AA: 150 mM Cu^{2+} C. 200 mM AA: 100 mM Cu^{2+}

D. 200 mM AA: 66.7 mM Cu^{2+} E. 200 mM AA: 50 mM Cu^{2+} F. 200 mM AA: 40 mM Cu^{2+}

G. 200 mM AA: 33.3 mM Cu^{2+} H. 200 mM AA: 28.6 mM Cu^{2+} I. 200 mM AA: 25 mM Cu^{2+}
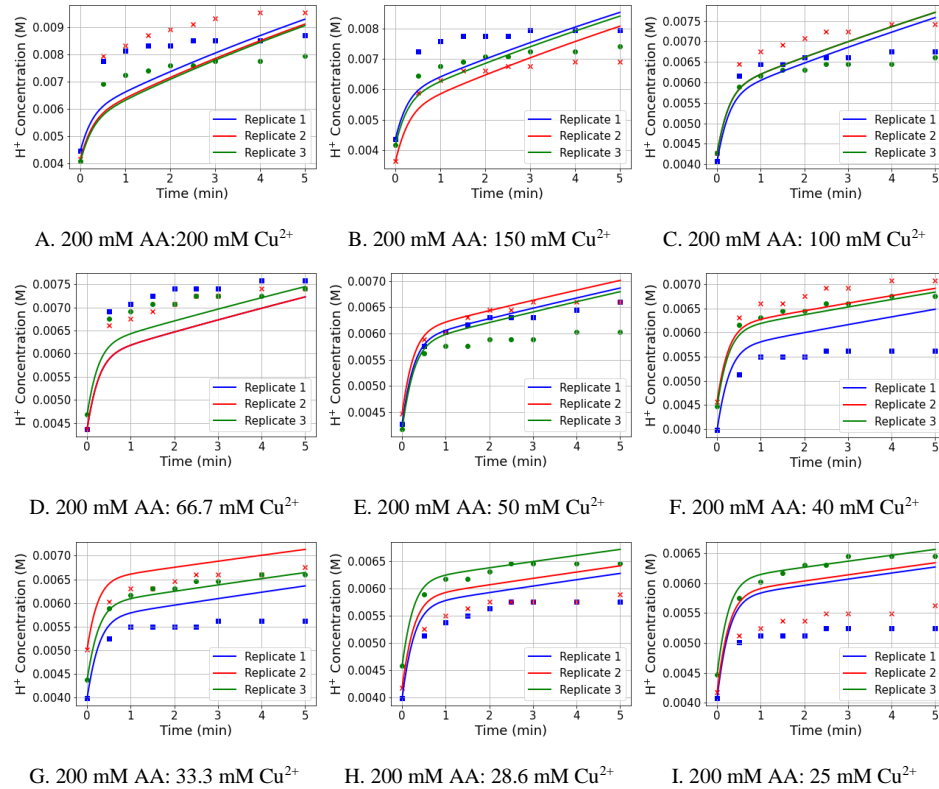
Fig. 2. Comparison for model predictions and experimental pH measurements for the 27 experiments (9 initial concentrations A-I repeated in triplicate).

Fig. 2 shows the results from partial parameter estimation with k_{b1} and k_{i1} fixed. The best fit value for k_{b2} is 0.0082 ± 0.0002 min^{-1}. As seen in Fig. 2, the continuous H$^+$ concentrations predicted from the fitted model match the overall the reaction progress as measured by the timeseries pH data. Experiments with initial Cu^{2+} concentrations between

28.6 and 50 mM (Fig. 2E-H) are best predicted with their relative sum of residuals squared less than 4%. However, for the experiments conducted with higher $[Cu^{2+}]_0$, the model overestimates the H⁺ concentration after 5 minutes (Fig. 2A-D). Also, the relative sum of residuals squared increases monotonically from 7 % to 44 % as $[Cu^{2+}]_0$ increases from 66.7 to 200 mM, respectively. Similarly, for $[Cu^{2+}]_0 = 25.0$ mM, the model overestimates the H⁺ concentration and the relative sum of residuals squared equals 11%. Together, these results suggest that copper complexes, which are not modeled, are important.

5. Conclusions

We developed a mathematical model for the Cu-DH₂ reaction system. Local and global sensitivity analysis reveals that only reaction rate parameter, k_{b2}, can be identified from timeseries pH measurements. Partial parameter estimation is performed to estimate k_{b2}, which is, to our knowledge, one of the first reported values for k_{b2} in literature.

While the fitted model captures the overall nonlinear dynamics of the batch reaction, several extensions should be considered as future work. We hypothesize measuring timeseries Cu²⁺ or Cu⁺ concentrations will enable some of the remaining model parameters to be identified. Likewise, adding intermediate chemical species such as complexes to the model may improve the quality of fit. Ultimately, a predicted dynamic model, such as the one presented in this paper, may be used to optimize the ink formulations for additive manufacturing of chemically patterned membranes.

Acknowledgments

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