Electronic Supplementary Material (ESI) for Reaction Chemistry & Engineering.

Nomenclature

Acronyms

DMF	Dimethylformamide
DMI	Demethylated Impurity
EVM	Error-in-Variables-Model
FPCA	Functional Principal Component Analysis
HIV	Human Immunodeficiency Virus
Int	Intermediate
lb	lower bound
MeCl	Methyl Chloride
MeF	Methyl Fluoride
MSD	Merck Sharp & Dohme
MSE	Mean-Squared-Error
NE	Not Estimated
ODE	Ordinary Differential Equation
P	Product
QS	Quaternary Salt
RMSE	Root-mean-squared Error
SM	Starting Material
THP	Tetrahydropyran
TMA	Trimethyl amine
ub	upper bound

Symbols

$C_{Cl^-}^{sat}$	Concentration of Cl^- ions in equilibrium with solid KCl
$C_{F^-}^{sat}$	Concentration of F^- ions in equilibrium with solid KF
$C_{m\,TMA0,i}$	Measured/ target value of initial concentration of TMA in Run i
$C_{TMA0,i}$	True value of initial concentration of TMA in Run i

C_{il}	Model prediction of the l^{th} measured concentration in the i^{th} experimental run
C_{SM0}	Initial concentration of SM
d	Vector of decision variables
E_f	Activation energy for the forward main reaction
E_{fs}	Activation energy for the side reaction
E_r	Activation energy for the reverse main reaction
$\boldsymbol{f}$	Vector of right-hand sides of ODEs
ΔH	Reaction enthalpy for main reaction
J_{EVM}	EVM objective function
J_{WLS}	WLS objective function
K	Equilibrium constant for the main reaction
k_f	Forward rate constant for the main reaction
$k_{f\,ref}$	Forward rate constant for the main reaction at T_{ref}
k_{fs}	Rate constant for the side reaction
$k_{fs\,ref}$	Rate constant for the side reaction at T_{ref}
$k_L a$	Mass transfer coefficient
k_r	Reverse main reaction rate constant
K_{ref}	Equilibrium constant for the main reaction at T_{ref}
$k_{r\,ref}$	Reverse main reaction rate constant at T_{ref}
R	Ideal gas constant
S_{KCl}	Solubility of solid KCl in the DMF solvent
S_{KF}	Solubility of solid KF in the DMF solvent
t	time
T	Temperature
t_f	Batch final time
T_{ref}	Reference temperature
V_s	Volume of solvent (DMF)

$\boldsymbol{x}$ Vector of state variables in ODE model,

$\boldsymbol{x} = [SM, TMA, QS1Cl, F^-, QS1F, Cl^-, Int, QS2Cl, QS2F, P, ClDMI, MeCl, MeF, QS3F, FDMI, QS3Cl]^T$

$y_{m,il}$ The l^{th} measured concentration in the i^{th} experimental run

Subscripts

i Counter for the number of experimental runs

l Counter for the number of sampling times

Greek symbols

Γ Coefficient to start mass transfer from solid KCl to reaction mixture

S1. Settings for experimental runs

Table S1 shows the experimental settings corresponding to 26 runs used for parameter estimation. The first 16 runs are corner-point runs and runs 17 to 24 are center-point replicate runs. The last two runs were conducted without KF. As a result, only the first two reactions (shown in the blue box in Scheme 1) take place. Prior to developing a mechanistic model to study the batch reactor, the empirical effect of each experimental factor on the measured responses was investigated. Fifteen empirical models of the following form:

$$y_m = \beta_0 + \beta_1 \frac{KF_0}{SM_0} + \beta_2 \frac{C_{TMA0}}{C_{SM0}} + \beta_3 T + \beta_4 V_s + \varepsilon \quad \text{(S1)}$$

were fitted using the available data. In these 15 models, y_m was the measured concentration of SM, Int, P, $ClDMI$ or $FDMI$ obtained at a particular sampling time ($t = 4.29\ h$, $12.29\ h$ or $22.29\ h$) in corner-point runs. For example, an empirical model that predicts measured concentration of P at $t = 4.29\ h$ is:

$$y_{mP\ 4.29} = \beta_0 + \beta_1 \frac{KF_0}{SM_0} + \beta_2 \frac{C_{TMA0}}{C_{SM0}} + \beta_3 T + \beta_4 V_s + \varepsilon \quad \text{(S2)}$$

The linear regression parameters $\beta_0, \beta_1, \ldots, \beta_4$ in Equation S2 were fitted using data from the 16 corner-point runs. The resulting estimate for parameter β_1 was not significantly different from zero at the 95 % confidence level, indicating that the ratio $\frac{KF_0}{SM_0}$ had negligible influence over the range of conditions encountered in the experiments. Note that estimates for β_1 were also not significant in the other 14 empirical models that were fitted. This result makes physical sense because solid KF was always present in the reactor throughout each run. As a result, the KF concentration in the reacting mixture depended on KF solubility rather than the total amount of KF added in each run. Note that the other parameters in Equation S2 were significantly different from zero, indicating that $\frac{C_{TMA0}}{C_{SM0}}$, T and V_s influence the amount of product that is formed after 4.29 hours in the batch reactor.

Table S1. Target experimental settings for 26 runs used in this study

Run #	T (°C)	C_{TMA0}/C_{SM0}	$V_s\ \left(\frac{L}{kgSM}\right)$	KF_0/SM_0
1	13	0.3	12	7
2	33	0.3	8	7
3	13	0.7	12	3
4	33	0.7	8	3
5	33	0.3	12	3
6	13	0.3	8	3
7	33	0.7	12	7

8	13	0.7	8	7
9	13	0.3	12	3
10	13	0.7	12	7
11	13	0.3	8	7
12	13	0.7	8	3
13	33	0.7	8	7
14	33	0.7	12	3
15	33	0.3	12	7
16	33	0.3	8	3
17	23	0.5	10	5
18	23	0.5	10	5
19	23	0.5	10	5
20	23	0.5	10	5
21	23	0.5	10	5
22	23	0.5	10	5
23	23	0.5	10	5
24	23	0.5	10	5
25	33	0.5	10	0
26	23	0.5	10	0

Using a basis of 1 g of SM, the initial concentration of SM in each run is:

$$C_{SM0} = \frac{1\ [g\ SM]}{MW_{SM}\ \left[\frac{g\ SM}{mol\ SM}\right]} \times \frac{1}{V_{rxn}[mL]} \times \frac{1000\ mL}{1\ L} \tag{S3}$$

where:

$$V_{rxn} = V_s + V_{SM0} \tag{S4}$$

and:

$$V_{SM0} = \frac{1\ [g\ SM]}{\rho_{SM}\ [\frac{g\ SM}{mL\ SM}]} \tag{S5}$$

In equation S3, $MW_{SM} = 273.1\ g/mol$ is the molar mass of SM, V_{rxn} is the volume of the reaction mixture, V_{SM0} is the initial volume of SM in the reactor, and $\rho_{SM} \approx 0.94\ g/mL$ is the density of SM.

S2. Unknown parameters and uncertain inputs

Table S2 shows a list of 39 unknown model parameters and 26 uncertain inputs, along with their initial guesses, lower bound (lb) and upper bound (ub). These bounds were selected to ensure that the estimated values for all estimated parameters and inputs are physically realistic.

Table S2. List of model unknown parameters and uncertain inputs

#	Parameter	Initial Guess	lb	ub
1	$k_{f1\,ref}\ \left(\frac{L}{molh}\right)$	10000	0	1000000
2	$E_{f1}\ \left(\frac{kJ}{mol}\right)$	50	0	500
3	$K_{1\,ref}\ \left(\frac{L}{mol}\right)$	100	0	10000
4	$\Delta H_1\ \left(\frac{kJ}{mol}\right)$	0	-500	500
5	$k_{f2\,ref}\ \left(\frac{L}{molh}\right)$	10000	0	1000000
6	$E_{f2}\ \left(\frac{kJ}{mol}\right)$	50	0	500
7	$K_{2\,ref}$	100	0	1000
8	$\Delta H_2\ \left(\frac{kJ}{mol}\right)$	0	-500	500
9	$k_{f3\,ref}\ \left(\frac{1}{h}\right)$	2500	0	25000
10	$E_{f3}\ \left(\frac{kJ}{mol}\right)$	50	0	500
11	$K_{3\,ref}\ \left(\frac{mol}{L}\right)$	100	0	1000
12	$\Delta H_3\ \left(\frac{kJ}{mol}\right)$	0	-500	500
13	$k_{f4\,ref}\ \left(\frac{L}{molh}\right)$	5	0	50
14	$E_{f4}\ \left(\frac{kJ}{mol}\right)$	50	0	500
15	$k_{f5\,ref}\ \left(\frac{L}{molh}\right)$	10000	0	1000000
16	$E_{f5}\ \left(\frac{kJ}{mol}\right)$	50	0	500
17	$K_{5\,ref}$	1	0	10

18	$\Delta H_5 \left(\frac{kJ}{mol}\right)$	0	-500	500
19	$k_{f6\,ref} \left(\frac{1}{h}\right)$	2000	0	20000
20	$E_{f6} \left(\frac{kJ}{mol}\right)$	50	0	500
21	$k_{fs1\,ref} \left(\frac{1}{h}\right)$	0.5	0	5
22	$E_{fs1} \left(\frac{kJ}{mol}\right)$	50	0	500
23	$k_{fs2\,ref} \left(\frac{1}{h}\right)$	0.05	0	0.5
24	$E_{fs2} \left(\frac{kJ}{mol}\right)$	50	0	500
25	$k_{fs3\,ref} \left(\frac{L}{molh}\right)$	4000	0	40000
26	$E_{fs3} \left(\frac{kJ}{mol}\right)$	50	0	500
27	$K_{s3\,ref} \left(\frac{L}{mol}\right)$	0.01	0	1
28	$\Delta H_{s3} \left(\frac{kJ}{mol}\right)$	0	-500	500
29	$k_{fs4\,ref} \left(\frac{1}{h}\right)$	0.05	0	0.5
30	$E_{fs4} \left(\frac{kJ}{mol}\right)$	50	0	500
31	$k_{fs5\,ref} \left(\frac{L}{molh}\right)$	10000	0	1000000
32	$E_{fs5} \left(\frac{kJ}{mol}\right)$	50	0	500
33	$K_{s5\,ref}$	100	0	1000
34	$\Delta H_{s5} \left(\frac{kJ}{mol}\right)$	0	-500	500
35	$k_{fs6\,ref} \left(\frac{1}{h}\right)$	0.5	0	50
36	$E_{fs6} \left(\frac{kJ}{mol}\right)$	50	0	500
37	$S_{KCl} \left(\frac{mol}{L}\right)$	0.004	0.002	0.006
38	$S_{KF} \left(\frac{mol}{L}\right)$	0.0003	0.0001	0.0006
39	$k_L a \left(\frac{1}{h}\right)$	10000	1000	100000
40	$C_{TMA0,1} \left(\frac{mol}{L}\right)$	0.084	0.000	0.184
41	$C_{TMA0,2} \left(\frac{mol}{L}\right)$	0.120	0.021	0.221

42	$C_{TMA0,3}\left(\frac{mol}{L}\right)$	0.194	0.096	0.296
43	$C_{TMA0,4}\left(\frac{mol}{L}\right)$	0.280	0.183	0.383
44	$C_{TMA0,5}\left(\frac{mol}{L}\right)$	0.065	0.000	0.184
45	$C_{TMA0,6}\left(\frac{mol}{L}\right)$	0.120	0.021	0.221
46	$C_{TMA0,7}\left(\frac{mol}{L}\right)$	0.194	0.096	0.296
47	$C_{TMA0,8}\left(\frac{mol}{L}\right)$	0.273	0.183	0.383
48	$C_{TMA0,9}\left(\frac{mol}{L}\right)$	0.083	0.000	0.184
49	$C_{TMA0,10}\left(\frac{mol}{L}\right)$	0.195	0.096	0.296
50	$C_{TMA0,11}\left(\frac{mol}{L}\right)$	0.120	0.021	0.221
51	$C_{TMA0,12}\left(\frac{mol}{L}\right)$	0.281	0.183	0.383
52	$C_{TMA0,13}\left(\frac{mol}{L}\right)$	0.281	0.183	0.383
53	$C_{TMA0,14}\left(\frac{mol}{L}\right)$	0.195	0.096	0.296
54	$C_{TMA0,15}\left(\frac{mol}{L}\right)$	0.083	0.000	0.184
55	$C_{TMA0,16}\left(\frac{mol}{L}\right)$	0.120	0.021	0.221
56	$C_{TMA0,17}\left(\frac{mol}{L}\right)$	0.165	0.065	0.265
57	$C_{TMA0,18}\left(\frac{mol}{L}\right)$	0.163	0.065	0.265
58	$C_{TMA0,19}\left(\frac{mol}{L}\right)$	0.124	0.065	0.265
59	$C_{TMA0,20}\left(\frac{mol}{L}\right)$	0.160	0.065	0.265
60	$C_{TMA0,21}\left(\frac{mol}{L}\right)$	0.161	0.061	0.261
61	$C_{TMA0,22}\left(\frac{mol}{L}\right)$	0.162	0.065	0.265
62	$C_{TMA0,23}\left(\frac{mol}{L}\right)$	0.164	0.065	0.265
63	$C_{TMA0,24}\left(\frac{mol}{L}\right)$	0.164	0.064	0.264
64	$C_{TMA0,25}\left(\frac{mol}{L}\right)$	0.183	0.083	0.283
65	$C_{TMA0,26}\left(\frac{mol}{L}\right)$	0.183	0.083	0.283

S3. Output measurement variance calculations when all inputs are perfectly known

If n_q replicate runs are available for the q^{th} set of experimental settings, and each of these replicate runs involves n_t measurement times where concentrations of n_s species are obtained. The measurement variance for the k^{th} model response can be calculated from: [50]

$$\hat{\sigma}^2_{Y_{qk}} = \frac{\sum_{j=1}^{n_q}\left(y_{m,qjk} - \bar{y}_{m,qk}\right)^2}{n_q - 1} \qquad (q = 1, \ldots, N \; and \; k = 1, \ldots, n_s n_t) \tag{S6}$$

where $y_{m,qjk}$ is a data value obtained for the k^{th} model output in the j^{th} replicate run performed at the q^{th} set of experimental settings, $\bar{y}_{m,qk}$ is the average of the measurements for the k^{th} model output using the measurements from n_q replicate runs at the q^{th} set of experimental settings, and N is the number of target experimental settings. Variances obtained from Equation S7 can be statistically compared using F-tests, and if they are not significantly different, they can be pooled together. [50] For example, variance estimates for the k^{th} response from all N sets of run conditions can be pooled using:

$$\hat{\sigma}^2_{Y_k} = \frac{\sum_{q=1}^{N}(n_q - 1)\hat{\sigma}^2_{Y_{qk}}}{\sum_{q=1}^{N}(n_q - 1)} \tag{S7}$$

Note that variance estimates for measurements obtained at different sampling times may also be pooled together if the corresponding estimates are not significantly different. This approach was used to obtain the weighting factors in Equation 4.

Pooled variance estimates obtained from the above procedure were also used to obtain the scaling factors used for parameter subset selection. Because no replicate runs are available for

the last two runs in Table S1, we assumed that variances for $y_{m\,SM}$ and $y_{m\,ClDMI}$ in these runs are the same as the estimated variances from the first 24 runs. Unfortunately, there were no measured values for C_{QS1Cl} in data from the first 24 runs. This concentration was only measured for the last two runs. When estimating parameters, we assumed that the measurement variance of $y_{m\,QS1Cl}$ is equal to the measurement variance of $y_{m\,ClDMI}$ in the first 24 runs.

S4. Output measurement variance calculations when C_{TMA0} is uncertain

When accounting for uncertainty in the model inputs, output measurement variances need to be calculated while acknowledging that attempted replicate runs are pseudo-replicates that may have different input conditions. Abdi and McAuley proposed the following expression to be used when calculating output measurement variances from pseudo-replicates: [50]

$$\hat{\sigma}^2_{Y_{qk}} = \max\left(\frac{\sum_{j=1}^{n_q}\left(y_{m,qjk} - \bar{y}_{m,qk}\right)^2}{n_q - 1} - \left(\frac{\partial g_k}{\partial \boldsymbol{u}}|_{\boldsymbol{u_{mq}},\,\boldsymbol{x_q},\widehat{\boldsymbol{\theta}}}\right)\boldsymbol{\Sigma_U}\left(\frac{\partial g_k}{\partial \boldsymbol{u}}|_{\boldsymbol{u_{mq}},\,\boldsymbol{x_q},\widehat{\boldsymbol{\theta}}}\right)^T, \delta_k\right) \qquad \text{(S8)}$$

where g is a solution to model equations for obtaining the k^{th} model output, $\boldsymbol{u}$ is a vector of uncertain inputs, $\boldsymbol{u_{mq}}$ is a vector of measured uncertain inputs at the q^{th} set of experimental settings, $\boldsymbol{x_q}$ is the corresponding vector of perfectly known model inputs, $\widehat{\boldsymbol{\theta}}$ is a vector of parameter estimates, $\boldsymbol{\Sigma_U}$ is the covariance matrix for the uncertain inputs, and δ_k is a cut-off value to make sure that the new calculated variance is not negative. In Equation S8, the contribution of uncertain inputs to the output measurement variances is deducted so that a more accurate estimate of $\hat{\sigma}^2_{Y_{qk}}$ is computed than would be obtained using Equation S6. After the

estimates of $\hat{\sigma}^2_{Y_{qk}}$ were computed, pooling of variance estimates was performed to obtain the weighting factors in Equation 5.

S5. Best and worst fit to data using EVM parameter estimates

Figure S1 shows the model fit to data from run 1. This is the best fit obtained using EVM parameter estimates with a contribution to J_{EVM} of 13.4 compared to the overall J_{EVM} of 1552.2. Error bars in Figure S1 correspond to two standard deviations. As expected, EVM and WLS parameter estimates provide similar satisfactory fits to the data for this best case run. Notice that the target value and the estimated value of the initial concentration of TMA for run 1 are very close (see Table 10). As a contrast, Figure S2 shows the worst model fit to the data using EVM parameter estimates with a contribution to J_{EVM} of 275.0. Although EVM provides a better fit to the data for Int at lower reaction times for this run (run 12), WLS provides a better fit for P. Neither EVM nor WLS parameter estimates provide a good fit to the $FDMI$ data in the first half of the batch. Note that the EVM and WLS fits for run 8, which is the pseudo-replicate of run 12, is noticeably better with a contribution to J_{EVM} of 103.7 suggesting that the data from run 12 may be somewhat problematic. In future, it would be helpful to repeat run 12 to test this hypothesis.

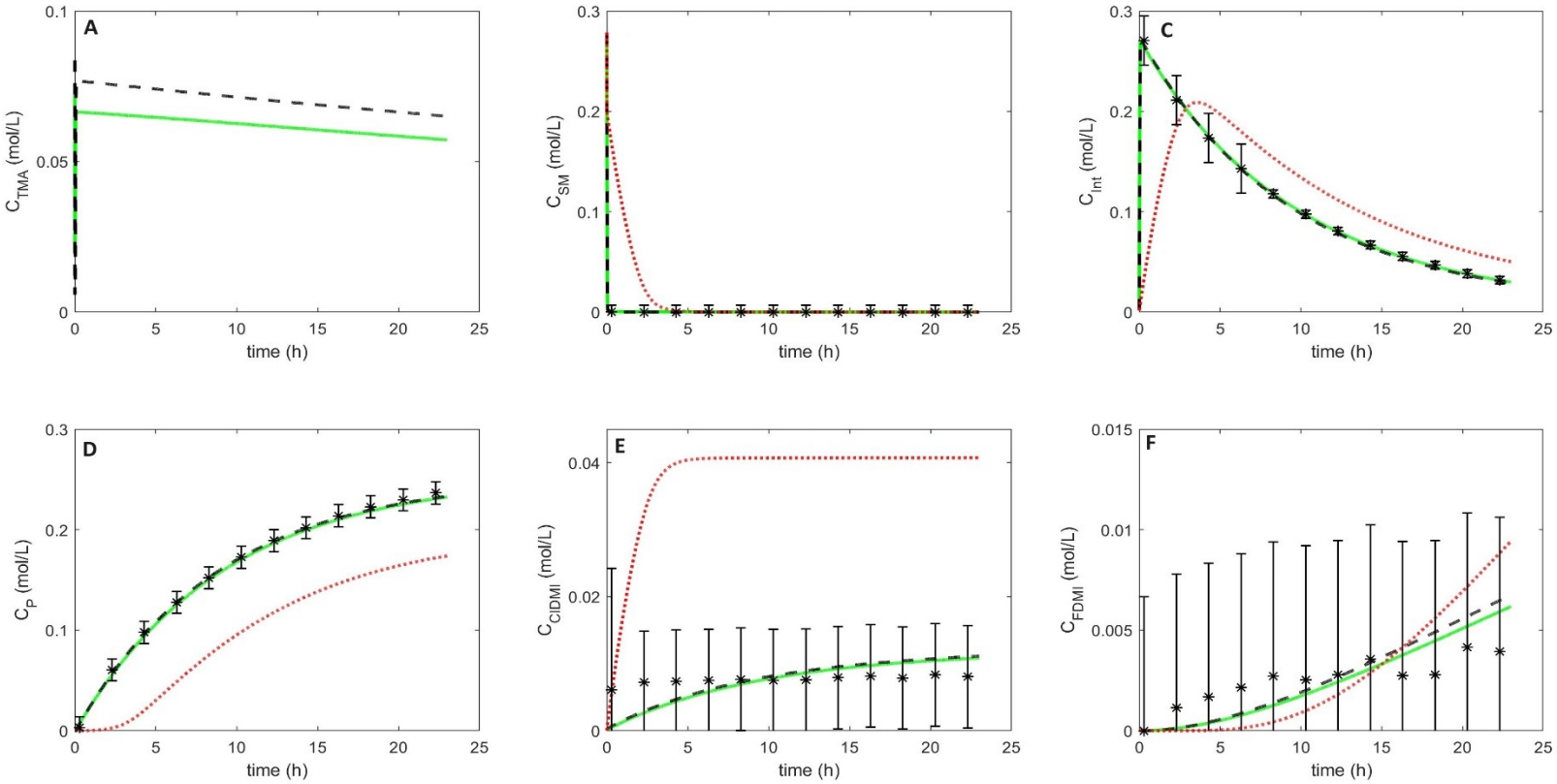

Figure S1. Comparison of model predictions using initial parameter guesses ··· , EVM parameter estimates —— , and WLS parameter estimates ---- with experimental data * for TMA, SM, Int, P, ClDMI, and FDMI from run 1

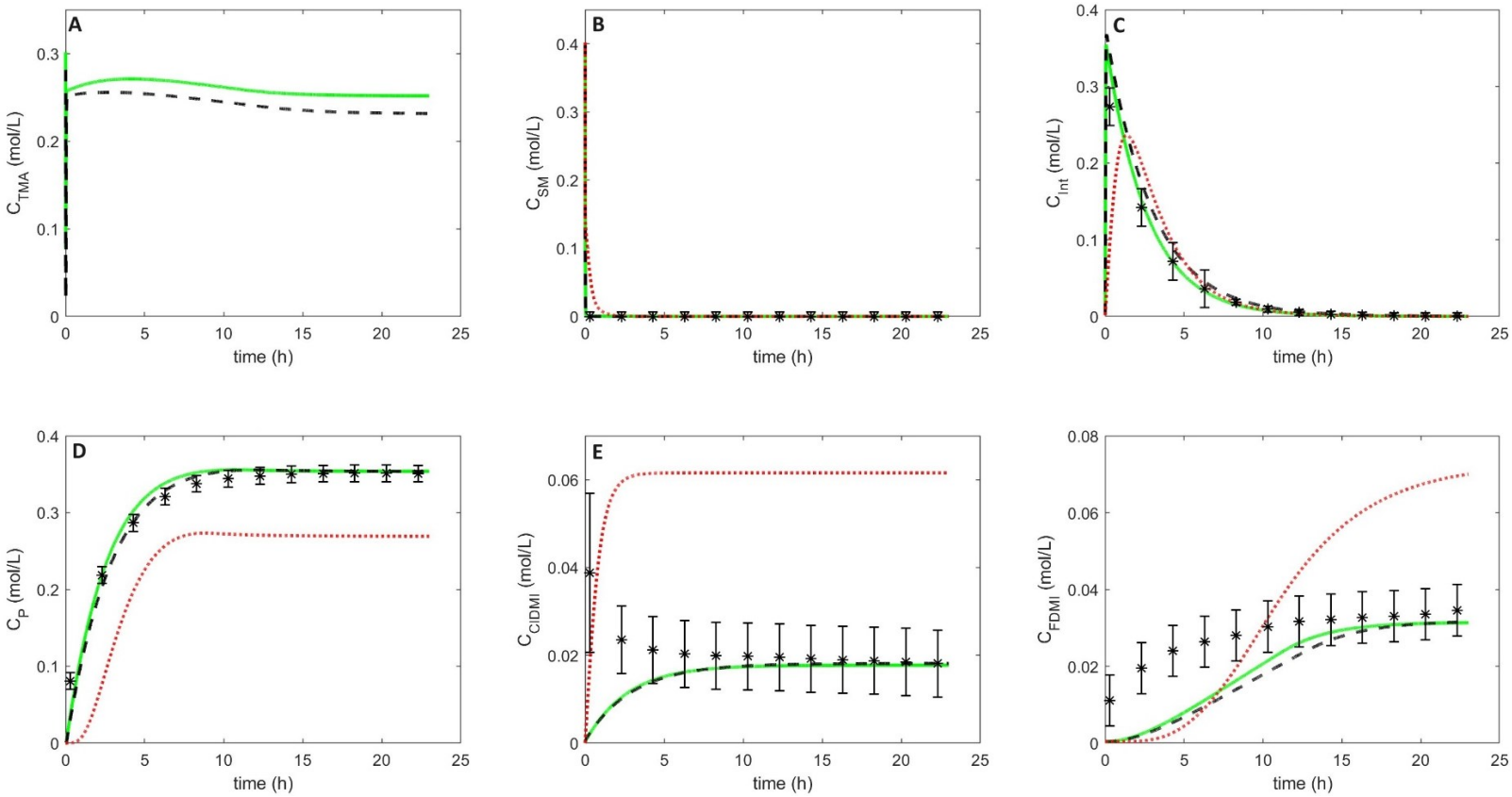

Figure S2. Comparison of model predictions using initial parameter guesses ··· , EVM parameter estimates —— , and WLS parameter estimates ---- with experimental data * for TMA, SM, Int, P, ClDMI, and FDMI from run 12

S6. Variance-covariance Matrices for the Parameter Estimates

Tables S3 and S4 show a portion of the variance-covariance matrices corresponding to WLS and EVM parameter estimates, respectively. In these tables, only strong correlation coefficients (greater than 0.8 or less than -0.8) are shown for simplicity. It is interesting that the number of large-magnitude covariances arising from EVM is smaller (i.e., 20) than the number arising from WLS (i.e., 23).

Table S3. Elements of variance-covariance matrix for WLS parameter estimates that indicate high correlation

	$k_{f2\,ref}$	$K_{s3\,ref}$	ΔH_1	E_{f5}	$k_L a$	ΔH_{s5}	S_{KCl}	ΔH_3	$K_{3\,ref}$	ΔH_2	$k_{fs2\,ref}$	$k_{f6\,ref}$	$k_{fs5\,ref}$	$K_{s5\,ref}$	S_{KF}	$k_{fs4\,ref}$	$K_{5\,ref}$	E_{fs2}
$k_{f2\,ref}$	1	-	-	-	0.99	-	-	-	-	-	-	-	-	-	-0.99	-	-	-
$K_{s3\,ref}$	-	1	-	-	-	-	-	-	-	-	-		-0.92	-	-	-	-	-
ΔH_1	-	-	1	-	-	-	-	0.91	-0.91	0.90	0.90	-	-	-	-	-	-	0.91
E_{f5}	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-0.87	-
$k_L a$	0.99	-	-	-	1	-	-	-	-	-	-	-	-	-	-0.99	-	-	-
ΔH_{s5}	-	-	-	-	-	1	-	-	-	-	-	-	-	-0.81	-	-	-	-
S_{KCl}	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-0.8	-	-
ΔH_3	-	-	0.91	-	-	-	-	1	-0.98	0.97	0.97	-	-	-	-	-	-	0.99
$K_{3\,ref}$	-	-	-0.91	-	-	-	-	-0.98	1	-0.99	-0.97	-	-	-	-	-	-	-0.99
ΔH_2	-	-	0.90	-	-	-	-	0.97	-0.99	1	0.99	-	-	-	-	-	-	0.99
$k_{fs2\,ref}$	-	-	0.90	-	-	-	-	0.97	-0.97	0.99	1	-	-	-	-	-	-	0.99
$k_{f6\,ref}$	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-0.86	-
$k_{fs5\,ref}$	-	-0.92	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-
$K_{s5\,ref}$	-	-	-	-	-	-0.81	-	-	-	-	-	-	-	1	-	-	-	-
S_{KF}	-0.99	-	-	-	-0.99	-	-	-	-	-	-	-	-	-	1	-	-	-
$k_{fs4\,ref}$	-	-	-	-	-	-	-0.8	-	-	-	-	-	-	-	-	1	-	-
$K_{5\,ref}$	-	-	-	-0.87	-	-	-	-	-	-	-	-0.86	-	-	-	-	1	-
E_{fs2}	-	-	0.91	-	-	-	-	0.99	-0.99	0.99	0.99	-	-	-	-	-	-	1

Table S4. Elements of variance-covariance matrix for EVM parameter estimates that indicate high correlation

	$k_{f2\,ref}$	E_{f2}	$C_{TMA0,11}$	$C_{TMA0,6}$	ΔH_1	$C_{TMA0,1}$	$C_{TMA0,9}$	$k_L a$	S_{KCl}	$K_{s5\,ref}$	$k_{fs4\,ref}$	$K_{3\,ref}$	ΔH_2	E_{fs4}	$k_{fs2\,ref}$	S_{KF}	E_{f1}	$k_{f3\,ref}$
$k_{f2\,ref}$	1	-	-	-	-	-	-	0.99	-	-0.82	-	-	-	-	-	-0.99	-	-
E_{f2}	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.88	0.84
$C_{TMA0,11}$	-	-	1	0.92	-	0.89	0.89	-	-	-	-	-	-	-	-	-	-	-
$C_{TMA0,6}$	-	-	0.92	1	-	0.89	0.89	-	-	-	-	-	-	-	-	-	-	-
ΔH_1	-	-	-	-	1	-	-	-	-	-	-	-0.91	-	-	-	-	-	-
$C_{TMA0,1}$	-	-	0.89	0.89	-	1	0.91	-	-	-	-	-	-	-	-	-	-	-
$C_{TMA0,9}$	-	-	0.89	0.89	-	0.91	1	-	-	-	-	-	-	-	-	-	-	-
$k_L a$	0.99	-	-	-	-	-	-	1	-	-0.82	-	-	-	-	-	-0.99		
S_{KCl}	-	-	-	-	-	-	-	-	1		-0.84	-	-	-	-	-	-	-
$K_{s5\,ref}$	-0.82	-	-	-	-	-	-	-0.82	-	1	-	-	-	-	-	0.82		
$k_{fs4\,ref}$	-	-	-	-	-	-	-	-	-0.84	-	1	-	-	-0.92	-	-	-	-
$K_{3\,ref}$	-	-	-	-	-0.91	-	-	-	-	-	-	1	-0.87	-	-0.84	-	-	-
ΔH_2	-	-	-	-	-	-	-	-	-	-	-	-0.87	1	-	0.89	-	-	-
E_{fs4}		-	-	-	-	-	-	-	-	-	-0.92	-	-	1	-	-	-	-
$k_{fs2\,ref}$	-	-	-	-	-	-	-	-	-	-	-	-0.84	0.89	-	1	-	-	-
S_{KF}	-0.99	-	-	-	-	-	-	-0.99	-	0.82		-	-	-	-	1	-	-
E_{f1}	-	0.88	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-
$k_{f3\,ref}$	-	0.84	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1

S7. Cross Validation Results

Figure S3 shows model predictions using EVM and WLS estimates for run 16 when parameters are estimated using data from the other runs. The predictions for C_{ClDMI} are noticeably better using the EVM parameter estimates. Predictions of other types of data are similar for this run.

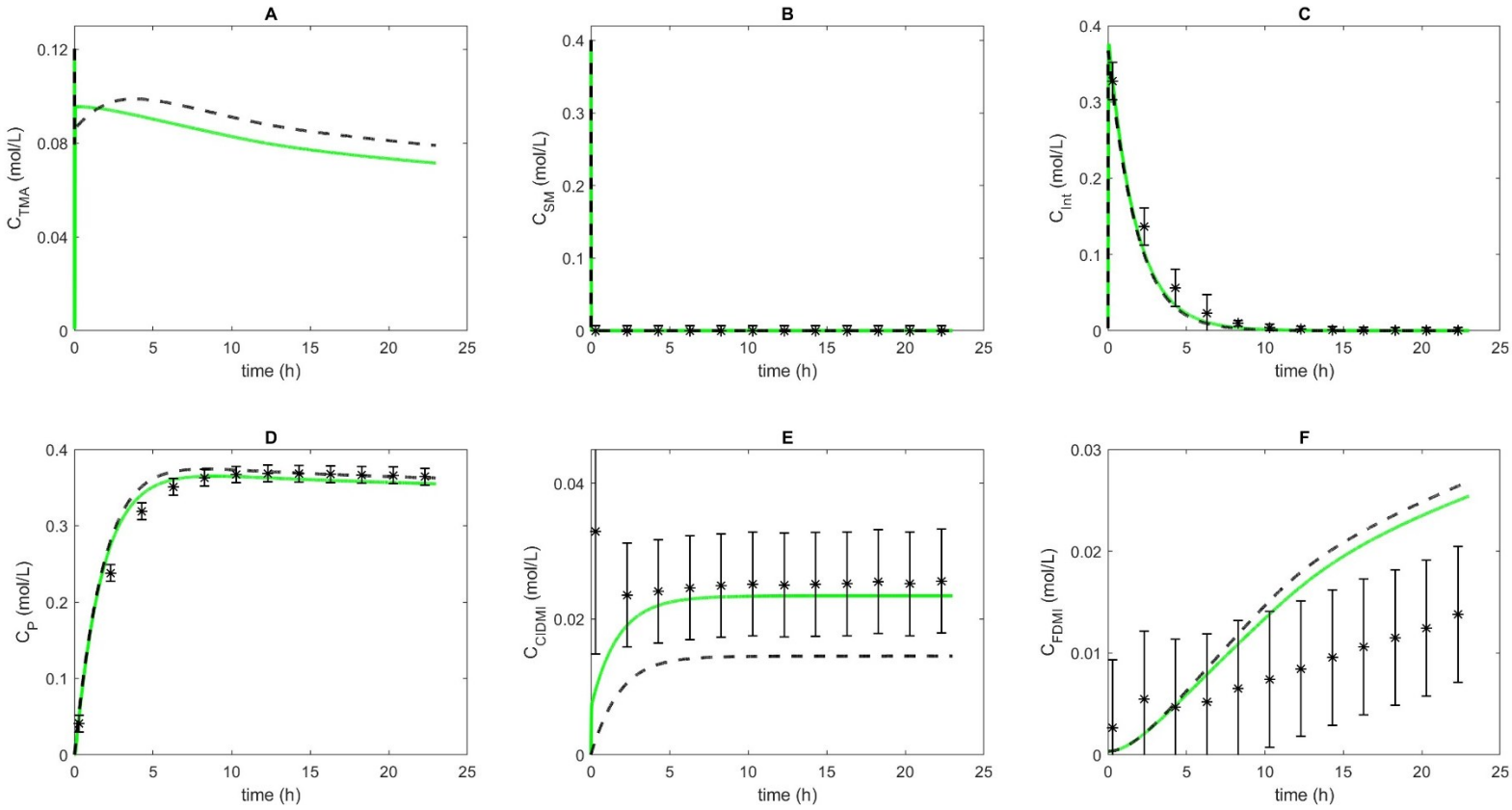

Figure S3. Comparison of model predictions using EVM parameter estimates —— and WLS parameter estimates ---- with experimental data * for TMA, SM, Int, P, ClDMI, and FDMI from run 16

S8. Optimization Results from Model using WLS Estimates

Table S5 shows results for the optimization problem when the model uses WLS parameter estimates. Optimization results are similar for both EVM and WLS case. However, compared to results from EVM estimates, model that uses WLS is less sensitive to changes in the reaction time and solvent volume.

Table S5. Results of solving the yield optimization problem using WLS estimates for model parameters

	Decision Variables				**Responses of Interest**	
Case #	$\boldsymbol{T}$ (℃)	$\frac{\boldsymbol{C_{TMA0}}}{\boldsymbol{C_{SM0}}}$	$\boldsymbol{t_f}$ $(\boldsymbol{h})$	$\boldsymbol{V_s}$ $(\boldsymbol{^{mL}/_{g\ SM}})$	**Optimized Yield**	**Quality Constraint** $\frac{\boldsymbol{C_{Int}(t_f)}}{\boldsymbol{C_{SM0}}}$
1	29.00	0.1320	48	12	0.9226	0.0065
2	28.77	0.2163	24	12	0.9216	0.0066
3	28.85	0.1098	48	8	0.9231	0.0066
4	28.61	0.1694	24	8	0.9210	0.0068

S9. Additional yield contours

Figure S4 shows four yield contours for Case 1 in Table 12. Error bars in this figure correspond to the uncertainties in T and $\frac{C_{SM0}}{C_{TMA0}}$. Similarly, Figure S5 shows yield contours corresponding to Case 4. Contours shown in Figures S4 and S5 confirm that the maximum yield is not very sensitive to the anticipated variability in the decision variables during commercial operation.

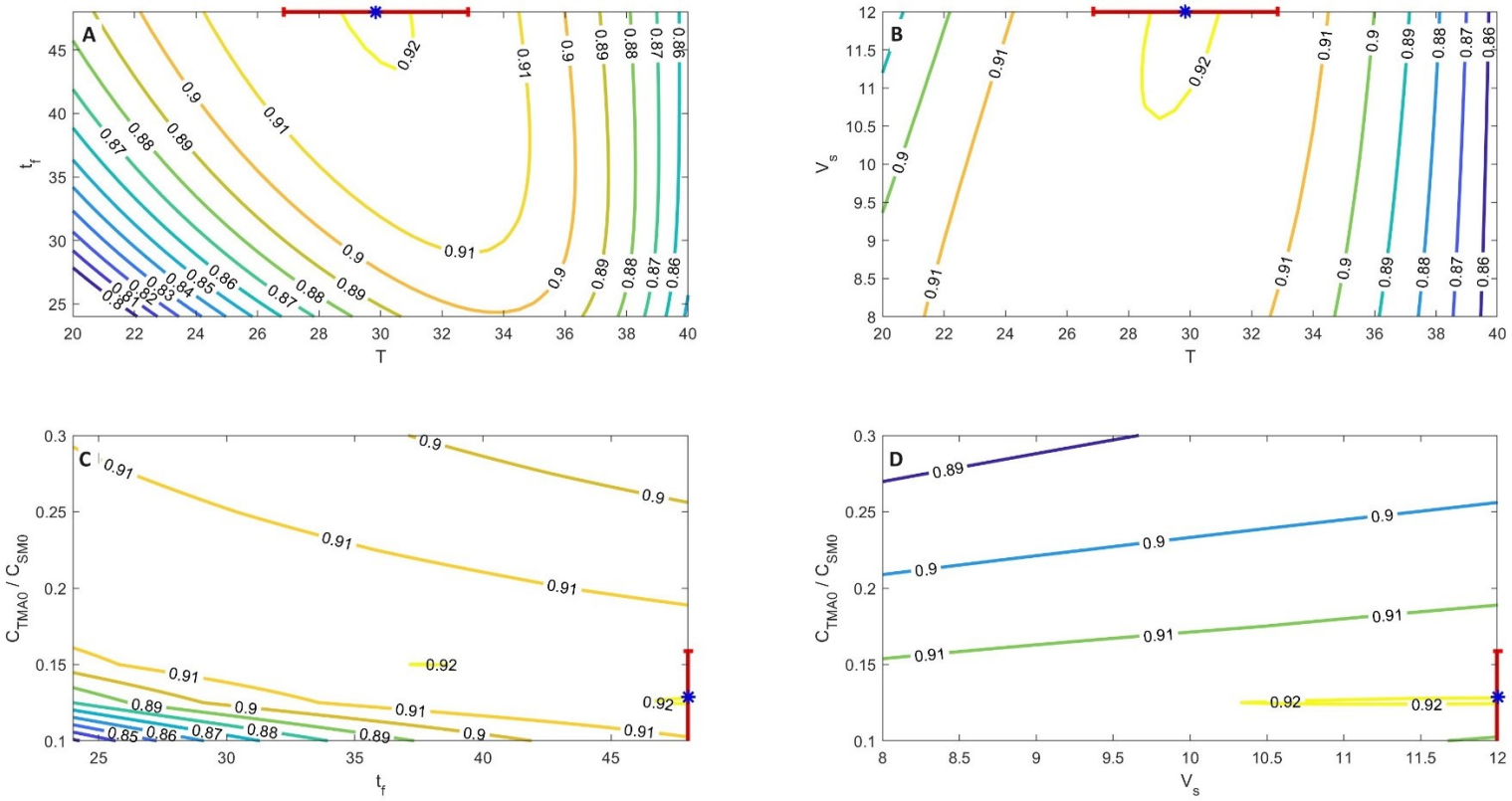

Figure S4. Yield contours for Case 1 in Table 12. * shows the optimization result for Case 1

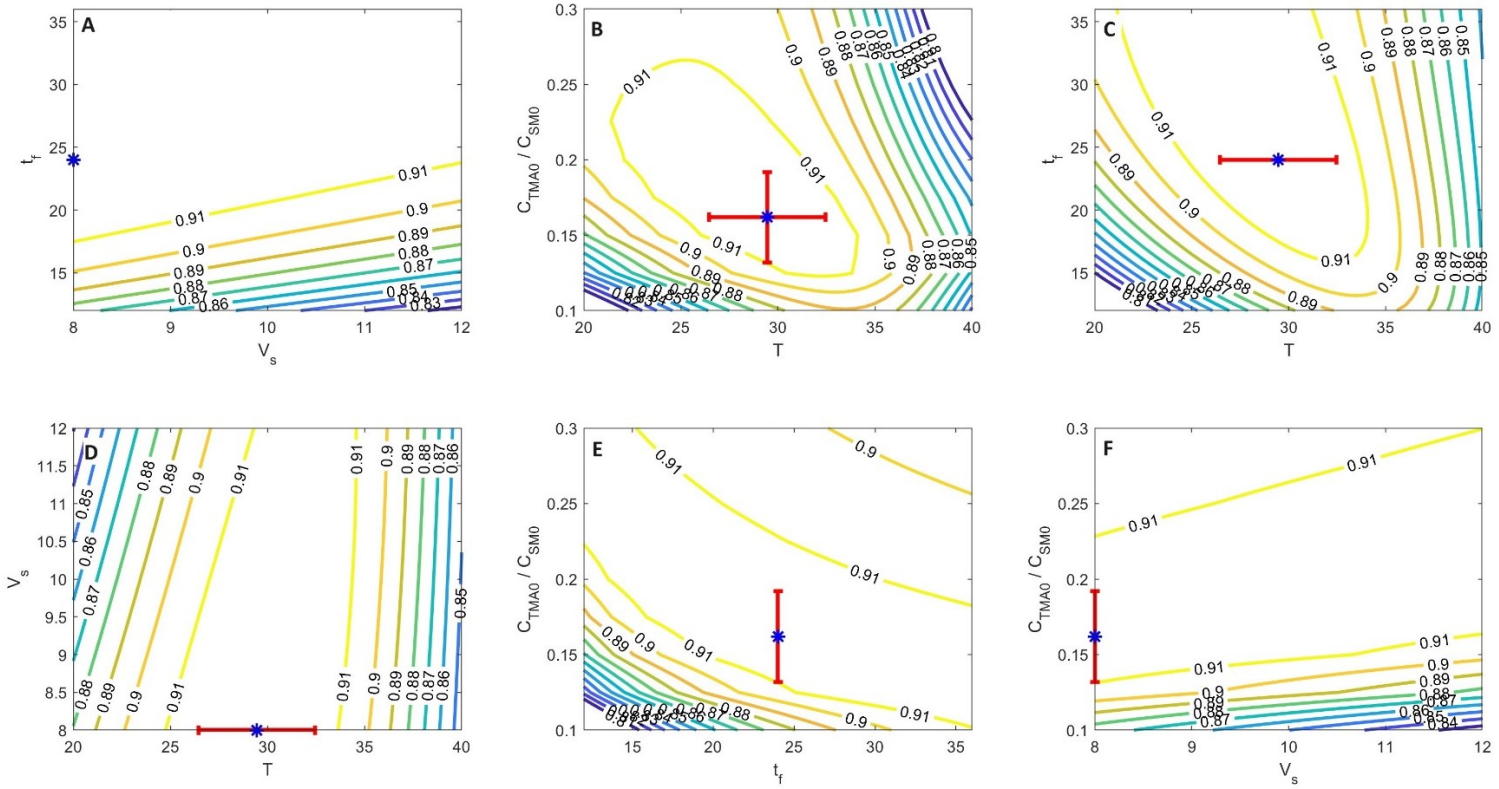

Figure S5. Yield contours for Case 4 in Table 12. * shows the optimization result for Case 4

S10. Numerical settings

Table S6 provides details of the solvers and numerical settings used for solving the model equations and for conducting parameter estimation and process optimization. To investigate the possibility of local minima, the parameter estimation and optimization problems were solved multiple times using different sets of initial guesses. No convergence to local minima was observed.

Table S6. details of solvers and numerical settings used in this study

For model equations	
Solver	*ode15s*
RelTol	10^{-10}
AbsTol	10^{-10}
For parameter estimation	
Solver	*lsqnonlin*
Algorithm	trust-region-reflective (default)
OptimalityTolerance	10^{-7}
StepTolerance	10^{-7}
FunctionTolerance	10^{-7}
For yield optimization	
Solver	*fmincon*
Algorithm	sqp
TolX	10^{-20}
TolFun	10^{-20}
ConstraintTolerance	10^{-20}

S11. Experimental data

Tables S7 to S32 provide experimental data from run 1 to run 26, respectively.

Table S7. Measured data corresponding to run 1

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2787	0.0004	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0016	0.2707	0.2114	0.1734	0.1429	0.1178	0.0977	0.0808	0.0668	0.0555	0.0467	0.0382	0.0318
C_P(mol/L)	0.0000	0.0031	0.0605	0.0979	0.1277	0.1521	0.1726	0.1891	0.2020	0.2139	0.2229	0.2296	0.2365
C_{ClDMI}(mol/L)	0.0000	0.0061	0.0072	0.0074	0.0075	0.0077	0.0075	0.0076	0.0079	0.0082	0.0079	0.0083	0.0080
C_{FDMI}(mol/L)	0.0000	0.0000	0.0011	0.0017	0.0021	0.0027	0.0025	0.0028	0.0036	0.0027	0.0028	0.0042	0.0039

Table S8. Measured data corresponding to run 2

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3992	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0045	0.3563	0.1507	0.0662	0.0293	0.0131	0.0061	0.0030	0.0015	0.0009	0.0005	0.0004	0.0003
C_P(mol/L)	0.0000	0.0317	0.2296	0.3134	0.3496	0.3644	0.3703	0.3724	0.3729	0.3722	0.3724	0.3712	0.3706
C_{ClDMI}(mol/L)	0.0000	0.0156	0.0198	0.0203	0.0207	0.0210	0.0211	0.0212	0.0212	0.0216	0.0213	0.0214	0.0214
C_{FDMI}(mol/L)	0.0003	0.0004	0.0040	0.0041	0.0044	0.0054	0.0065	0.0075	0.0084	0.0093	0.0098	0.0110	0.0118

Table S9. Measured data corresponding to run 3

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2768	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0026	0.2363	0.1406	0.0903	0.0578	0.0370	0.0237	0.0153	0.0098	0.0064	0.0044	0.0028	0.0018
C_P(mol/L)	0.0009	0.0295	0.1216	0.1716	0.2035	0.2240	0.2370	0.2451	0.2503	0.2530	0.2545	0.2533	0.2538
C_{ClDMI}(mol/L)	0.0000	0.0142	0.0131	0.0125	0.0123	0.0123	0.0123	0.0123	0.0122	0.0122	0.0122	0.0125	0.0125
C_{FDMI}(mol/L)	0.0000	0.0003	0.0050	0.0059	0.0067	0.0070	0.0073	0.0077	0.0080	0.0086	0.0092	0.0117	0.0121

Table S10. Measured data corresponding to run 4

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3997	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0031	0.2794	0.0327	0.0043	0.0008	0.0003	0.0003	0.0002	0.0002	0.0002	0.0000	0.0000	0.0000
C_P(mol/L)	0.0012	0.0851	0.3180	0.3447	0.3466	0.3448	0.3427	0.3409	0.3382	0.3363	0.3346	0.3307	0.3274
C_{ClDMI}(mol/L)	0.0000	0.0354	0.0379	0.0375	0.0371	0.0368	0.0365	0.0362	0.0359	0.0357	0.0359	0.0358	0.0362
C_{FDMI}(mol/L)	0.0000	0.0041	0.0154	0.0174	0.0195	0.0221	0.0245	0.0267	0.0296	0.0318	0.0335	0.0375	0.0404

Table S11. Measured data corresponding to run 5

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2154	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0628	0.2354	0.1110	0.0521	0.0245	0.0117	0.0057	0.0029	0.0015	0.0008	0.0004	0.0003	0.0000
C_P(mol/L)	0.0009	0.0313	0.1547	0.2124	0.2391	0.2509	0.2562	0.2586	0.2595	0.2603	0.2607	0.2598	0.2597
C_{ClDMI}(mol/L)	0.0011	0.0126	0.0114	0.0116	0.0118	0.0118	0.0119	0.0121	0.0121	0.0121	0.0121	0.0121	0.0122
C_{FDMI}(mol/L)	0.0000	0.0010	0.0032	0.0043	0.0049	0.0059	0.0065	0.0067	0.0071	0.0070	0.0071	0.0081	0.0084

Table S12. Measured data corresponding to run 6

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3984	0.0930	0.0002	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0040	0.2607	0.2713	0.2095	0.1624	0.1267	0.0981	0.0767	0.0600	0.0468	0.0362	0.0280	0.0220
C_P(mol/L)	0.0013	0.0015	0.1138	0.1752	0.2206	0.2564	0.2839	0.3052	0.3220	0.3349	0.3450	0.3516	0.3588
C_{ClDMI}(mol/L)	0.0000	0.0488	0.0152	0.0145	0.0148	0.0146	0.0149	0.0149	0.0149	0.0151	0.0150	0.0154	0.0149
C_{FDMI}(mol/L)	0.0003	0.0000	0.0035	0.0048	0.0061	0.0063	0.0070	0.0072	0.0071	0.0071	0.0078	0.0089	0.0083

Table S13. Measured data corresponding to run 7

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2772	0.0002	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0023	0.1948	0.0315	0.0053	0.0012	0.0004	0.0003	0.0002	0.0002	0.0002	0.0000	0.0000	0.0000
C_P(mol/L)	0.0008	0.0591	0.2239	0.2487	0.2496	0.2507	0.2487	0.2464	0.2472	0.2450	0.2441	0.2425	0.2410
C_{ClDMI}(mol/L)	0.0000	0.0215	0.0157	0.0154	0.0154	0.0152	0.0151	0.0152	0.0149	0.0149	0.0148	0.0148	0.0148
C_{FDMI}(mol/L)	0.0000	0.0047	0.0091	0.0109	0.0141	0.0139	0.0162	0.0184	0.0180	0.0202	0.0214	0.0230	0.0245

Table S14. Measured data corresponding to run 8

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3903	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0118	0.3017	0.1500	0.0752	0.0378	0.0191	0.0098	0.0052	0.0028	0.0016	0.0009	0.0006	0.0004
C_P(mol/L)	0.0015	0.0704	0.2216	0.2943	0.3315	0.3476	0.3556	0.3591	0.3593	0.3598	0.3594	0.3554	0.3536
C_{ClDMI}(mol/L)	0.0002	0.0258	0.0190	0.0181	0.0175	0.0176	0.0173	0.0170	0.0170	0.0169	0.0165	0.0167	0.0166
C_{FDMI}(mol/L)	0.0002	0.0061	0.0133	0.0163	0.0172	0.0197	0.0213	0.0226	0.0249	0.0257	0.0272	0.0313	0.0334

Table S15. Measured data corresponding to run 9

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2773	0.0003	0.0000	0.0003	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0028	0.2560	0.2094	0.1718	0.1395	0.1149	0.0946	0.0782	0.0645	0.0534	0.0442	0.0368	0.0305
C_P(mol/L)	0.0000	0.0110	0.0615	0.0991	0.1306	0.1548	0.1749	0.1914	0.2047	0.2156	0.2245	0.2322	0.2379
C_{ClDMI}(mol/L)	0.0000	0.0127	0.0080	0.0075	0.0078	0.0079	0.0079	0.0079	0.0079	0.0080	0.0081	0.0081	0.0082
C_{FDMI}(mol/L)	0.0002	0.0003	0.0013	0.0016	0.0024	0.0028	0.0029	0.0029	0.0031	0.0032	0.0034	0.0031	0.0037

Table S16. Measured data corresponding to run 10

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2785	0.0036	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0018	0.2089	0.1263	0.0736	0.0433	0.0255	0.0150	0.0089	0.0054	0.0033	0.0021	0.0014	0.0009
C_P(mol/L)	0.0000	0.0434	0.1327	0.1857	0.2168	0.2347	0.2448	0.2495	0.2527	0.2541	0.2553	0.2545	0.2541
C_{ClDMI}(mol/L)	0.0000	0.0203	0.0120	0.0102	0.0094	0.0091	0.0091	0.0091	0.0091	0.0091	0.0090	0.0090	0.0090
C_{FDMI}(mol/L)	0.0000	0.0040	0.0092	0.0108	0.0108	0.0109	0.0114	0.0127	0.0131	0.0138	0.0138	0.0154	0.0162

Table S17. Measured data corresponding to run 11

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.4006	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0032	0.3540	0.2675	0.2051	0.1574	0.1211	0.0937	0.0727	0.0562	0.0435	0.0341	0.0263	0.0206
C_P(mol/L)	0.0000	0.0297	0.1205	0.1830	0.2303	0.2653	0.2926	0.3131	0.3290	0.3410	0.3524	0.3581	0.3632
C_{ClDMI}(mol/L)	0.0000	0.0191	0.0121	0.0110	0.0107	0.0108	0.0107	0.0108	0.0109	0.0110	0.0109	0.0110	0.0113
C_{FDMI}(mol/L)	0.0002	0.0012	0.0038	0.0049	0.0056	0.0068	0.0070	0.0074	0.0080	0.0085	0.0065	0.0085	0.0090

Table S18. Measured data corresponding to run 12

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.4018	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0017	0.2732	0.1424	0.0720	0.0362	0.0184	0.0095	0.0051	0.0028	0.0015	0.0009	0.0006	0.0004
C_P(mol/L)	0.0000	0.0808	0.2186	0.2867	0.3210	0.3376	0.3444	0.3477	0.3499	0.3508	0.3513	0.3513	0.3508
C_{ClDMI}(mol/L)	0.0000	0.0388	0.0235	0.0212	0.0203	0.0199	0.0198	0.0195	0.0192	0.0190	0.0187	0.0185	0.0181
C_{FDMI}(mol/L)	0.0004	0.0111	0.0195	0.0240	0.0264	0.0280	0.0303	0.0317	0.0321	0.0327	0.0330	0.0336	0.0346

Table S19. Measured data corresponding to run 13

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.4018	0.0003	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0020	0.2338	0.0169	0.0016	0.0004	0.0003	0.0003	0.0003	0.0003	0.0002	0.0003	0.0003	0.0002
C_P(mol/L)	0.0000	0.1290	0.3525	0.3547	0.3507	0.3501	0.3454	0.3431	0.3393	0.3366	0.3329	0.3293	0.3262
C_{ClDMI}(mol/L)	0.0000	0.0286	0.0182	0.0193	0.0191	0.0184	0.0183	0.0181	0.0180	0.0180	0.0180	0.0181	0.0180
C_{FDMI}(mol/L)	0.0002	0.0122	0.0164	0.0284	0.0339	0.0352	0.0400	0.0425	0.0464	0.0492	0.0528	0.0563	0.0596

Table S20. Measured data corresponding to run 14

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2782	0.0001	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0019	0.1836	0.0236	0.0032	0.0007	0.0003	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0000
C_P(mol/L)	0.0000	0.0612	0.2271	0.2472	0.2463	0.2455	0.2440	0.2418	0.2395	0.2382	0.2362	0.2341	0.2324
C_{ClDMI}(mol/L)	0.0000	0.0283	0.0184	0.0181	0.0182	0.0180	0.0179	0.0181	0.0181	0.0180	0.0180	0.0180	0.0181
C_{FDMI}(mol/L)	0.0001	0.0072	0.0113	0.0118	0.0151	0.0165	0.0181	0.0202	0.0225	0.0239	0.0260	0.0280	0.0298

Table S21. Measured data corresponding to run 15

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2763	0.0004	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0032	0.2426	0.1199	0.0607	0.0306	0.0155	0.0080	0.0042	0.0023	0.0014	0.0008	0.0005	0.0003
C_P(mol/L)	0.0005	0.0277	0.1481	0.2067	0.2364	0.2509	0.2576	0.2605	0.2618	0.2621	0.2619	0.2614	0.2610
C_{ClDMI}(mol/L)	0.0000	0.0091	0.0097	0.0099	0.0104	0.0103	0.0104	0.0106	0.0105	0.0106	0.0106	0.0106	0.0106
C_{FDMI}(mol/L)	0.0003	0.0006	0.0025	0.0030	0.0029	0.0036	0.0043	0.0050	0.0056	0.0063	0.0070	0.0078	0.0083

Table S22. Measured data corresponding to run 16

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.4006	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0031	0.3274	0.1368	0.0563	0.0231	0.0097	0.0043	0.0020	0.0011	0.0006	0.0004	0.0003	0.0003
C_P(mol/L)	0.0000	0.0410	0.2381	0.3189	0.3511	0.3628	0.3671	0.3685	0.3682	0.3676	0.3666	0.3661	0.3643
C_{ClDMI}(mol/L)	0.0000	0.0329	0.0235	0.0241	0.0246	0.0249	0.0252	0.0250	0.0251	0.0252	0.0255	0.0252	0.0256
C_{FDMI}(mol/L)	0.0004	0.0027	0.0055	0.0047	0.0052	0.0065	0.0074	0.0085	0.0096	0.0106	0.0115	0.0124	0.0138

Table S23. Measured data corresponding to run 17

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3298	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0012	0.2832	0.1228	0.0558	0.0253	0.0117	0.0056	0.0028	0.0014	0.0008	0.0008	0.0000	0.0000
C_P(mol/L)	0.0000	0.0341	0.1872	0.2519	0.2813	0.2937	0.2988	0.2999	0.3010	0.3010	0.3008	0.2975	0.2963
C_{ClDMI}(mol/L)	0.0000	0.0130	0.0160	0.0163	0.0166	0.0164	0.0164	0.0169	0.0164	0.0164	0.0162	0.0168	0.0167
C_{FDMI}(mol/L)	0.0000	0.0007	0.0050	0.0069	0.0078	0.0092	0.0102	0.0113	0.0121	0.0128	0.0132	0.0166	0.0179

Table S24. Measured data corresponding to run 18

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3266	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0034	0.2901	0.1385	0.0705	0.0358	0.0182	0.0094	0.0050	0.0027	0.0015	0.0010	0.0006	0.0004
C_P(mol/L)	0.0010	0.0290	0.1721	0.2379	0.2716	0.2878	0.2958	0.2992	0.3006	0.3013	0.3013	0.2987	0.2980
C_{ClDMI}(mol/L)	0.0000	0.0112	0.0151	0.0153	0.0155	0.0156	0.0157	0.0157	0.0158	0.0158	0.0158	0.0158	0.0157
C_{FDMI}(mol/L)	0.0000	0.0007	0.0052	0.0072	0.0080	0.0093	0.0101	0.0110	0.0118	0.0123	0.0128	0.0158	0.0170

Table S25. Measured data corresponding to run 19

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.2474	0.0003	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0824	0.2839	0.1208	0.0542	0.0240	0.0109	0.0050	0.0025	0.0012	0.0007	0.0003	0.0003	0.0000
C_P(mol/L)	0.0010	0.0461	0.1952	0.2620	0.2905	0.3020	0.3064	0.3079	0.3079	0.3080	0.3074	0.3050	0.3053
C_{ClDMI}(mol/L)	0.0000	0.0003	0.0109	0.0096	0.0106	0.0115	0.0121	0.0123	0.0125	0.0121	0.0122	0.0125	0.0122
C_{FDMI}(mol/L)	0.0002	0.0004	0.0041	0.0052	0.0058	0.0066	0.0074	0.0083	0.0094	0.0102	0.0110	0.0132	0.0135

Table S26. Measured data corresponding to run 20

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3197	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0101	0.2609	0.1249	0.0591	0.0280	0.0134	0.0065	0.0033	0.0017	0.0010	0.0005	0.0004	0.0000
C_P(mol/L)	0.0012	0.0432	0.1823	0.2455	0.2749	0.2887	0.2944	0.2971	0.2975	0.2987	0.2983	0.2963	0.2962
C_{ClDMI}(mol/L)	0.0000	0.0243	0.0172	0.0176	0.0177	0.0176	0.0177	0.0176	0.0174	0.0174	0.0172	0.0173	0.0173
C_{FDMI}(mol/L)	0.0000	0.0026	0.0066	0.0087	0.0105	0.0113	0.0124	0.0130	0.0143	0.0139	0.0149	0.0170	0.0175

Table S27. Measured data corresponding to run 21

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3227	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0071	0.2588	0.1184	0.0534	0.0243	0.0112	0.0053	0.0026	0.0013	0.0007	0.0004	0.0003	0.0000
C_P(mol/L)	0.0010	0.0454	0.1903	0.2526	0.2804	0.2930	0.2984	0.3004	0.3006	0.3012	0.3008	0.2992	0.2985
C_{ClDMI}(mol/L)	0.0000	0.0236	0.0168	0.0173	0.0176	0.0175	0.0174	0.0173	0.0174	0.0172	0.0169	0.0170	0.0170
C_{FDMI}(mol/L)	0.0002	0.0032	0.0056	0.0076	0.0087	0.0092	0.0099	0.0106	0.0116	0.0119	0.0128	0.0144	0.0155

Table S28. Measured data corresponding to run 22

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3239	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0058	0.2646	0.1246	0.0583	0.0274	0.0131	0.0063	0.0032	0.0017	0.0009	0.0005	0.0004	0.0000
C_P(mol/L)	0.0011	0.0429	0.1843	0.2481	0.2777	0.2912	0.2979	0.3002	0.3008	0.3012	0.3007	0.2988	0.2982
C_{ClDMI}(mol/L)	0.0000	0.0204	0.0161	0.0162	0.0163	0.0166	0.0165	0.0164	0.0164	0.0163	0.0163	0.0165	0.0164
C_{FDMI}(mol/L)	0.0002	0.0031	0.0060	0.0083	0.0095	0.0100	0.0103	0.0112	0.0122	0.0125	0.0135	0.0153	0.0164

Table S29. Measured data corresponding to run 23

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3275	0.0002	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0033	0.2551	0.1241	0.0594	0.0279	0.0134	0.0065	0.0033	0.0017	0.0010	0.0006	0.0004	0.0003
C_P(mol/L)	0.0000	0.0532	0.1842	0.2474	0.2779	0.2924	0.2990	0.3017	0.3020	0.3019	0.3025	0.3010	0.3012
C_{ClDMI}(mol/L)	0.0000	0.0200	0.0159	0.0156	0.0156	0.0155	0.0154	0.0154	0.0154	0.0154	0.0154	0.0153	0.0152
C_{FDMI}(mol/L)	0.0002	0.0026	0.0068	0.0085	0.0096	0.0097	0.0100	0.0106	0.0118	0.0127	0.0125	0.0142	0.0142

Table S30. Measured data corresponding to run 24

time(h)	0	0.2917	2.2917	4.2917	6.2917	8.2917	10.2917	12.2917	14.2917	16.2917	18.2917	20.2917	22.2917
C_{SM}(mol/L)	0.3284	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
C_{Int}(mol/L)	0.0024	0.2612	0.1226	0.0569	0.0264	0.0123	0.0059	0.0030	0.0016	0.0009	0.0006	0.0004	0.0004
C_P(mol/L)	0.0000	0.0456	0.1881	0.2523	0.2818	0.2947	0.3000	0.3029	0.3024	0.3028	0.3021	0.3010	0.2998
C_{ClDMI}(mol/L)	0.0000	0.0211	0.0144	0.0144	0.0145	0.0146	0.0147	0.0147	0.0149	0.0147	0.0147	0.0147	0.0148
C_{FDMI}(mol/L)	0.0002	0.0029	0.0059	0.0074	0.0083	0.0093	0.0104	0.0104	0.0121	0.0126	0.0136	0.0148	0.0160

Table S31. Experimental data for run 25

Time (h)	C_{SM} (mol/ L)	C_{ClDMI} (mol/ L)	C_{QS1Cl} (mol/ L)
0.15	0.1696	0.0469	0.1495
0.23	0.1705	0.0641	0.1314
0.32	0.1711	0.0799	0.1151
0.48	0.1733	0.1253	0.0674
0.65	0.1737	0.1376	0.0547
0.82	0.1742	0.1474	0.0444
0.98	0.1743	0.1551	0.0366
1.15	0.1748	0.1600	0.0312
1.65	0.1751	0.1725	0.0184
2.15	0.1752	0.1786	0.0122
2.65	0.1751	0.1822	0.0087
3.15	0.1753	0.1842	0.0065
4.15	0.1753	0.1868	0.0040
5.15	0.1755	0.1879	0.0026
6.15	0.1748	0.1895	0.0018
7.15	0.1746	0.1900	0.0014
8.15	0.1741	0.1908	0.0012
9.15	0.1741	0.1911	0.0009
10.15	0.1744	0.1909	0.0007
11.15	0.1743	0.1911	0.0007
12.15	0.1742	0.1913	0.0005
13.15	0.1743	0.1912	0.0005
14.15	0.1743	0.1913	0.0004
15.15	0.1744	0.1913	0.0004

Table S32. Experimental data for run 26

Time (h)	C_{SM} (mol/ L)	C_{ClDMI} (mol/ L)	C_{QS1Cl} (mol/ L)
0.15	0.1740	0.0151	0.1770
0.23	0.1745	0.0215	0.1700
0.32	0.1746	0.0282	0.1632
0.48	0.1749	0.0383	0.1529
0.65	0.1753	0.0497	0.1410
0.82	0.1759	0.0590	0.1312
0.98	0.1763	0.0683	0.1214
1.15	0.1767	0.0753	0.1141
1.65	0.1780	0.0960	0.0920
2.15	0.1785	0.1122	0.0753
2.65	0.1789	0.1240	0.0631
3.15	0.1795	0.1340	0.0525
4.15	0.1804	0.1481	0.0376
5.15	0.1808	0.1575	0.0277
6.15	0.1809	0.1662	0.0189
7.15	0.1812	0.1698	0.0151
8.15	0.1812	0.1724	0.0124
9.15	0.1811	0.1746	0.0103
10.15	0.1813	0.1762	0.0086
11.15	0.1813	0.1774	0.0074
12.15	0.1811	0.1785	0.0064
13.15	0.1812	0.1792	0.0056
14.15	0.1812	0.1799	0.0050
15.15	0.1810	0.1805	0.0044