

Online model-based redesign of experiments for improving parameter precision in continuous flow reactors

Arun Pankajakshan*, Marco Quaglio*, Conor Waldron*, Enhong Cao*, Asterios Gavrilidis*, Federico Galvanin*

**Department of Chemical Engineering, University College London, London, WC1E, United Kingdom, e-mail: f.galvanin@ucl.ac.uk*

Abstract: Online model-based redesign of experiments (OMBRE) techniques reduce the experimental effort substantially for achieving high model reliability along with the precise estimation of model parameters. In dynamic systems, OMBRE techniques allow redesigning an experiment while it is still running and information gathered from samples collected at multiple time points is used to update the experimental conditions before the completion of the experiment. For processes evolving through a sequence of steady state experiments, significant time delays may exist when collecting new information from each single run, because measurements can be available only after steady state conditions are reached. In this work an online model-based optimal redesign technique is employed in continuous flow reactors for improving the accuracy of estimation of kinetic parameters with great benefit in terms of time and analytical resources during the model identification task. The proposed approach is applied to a simulated case study and compared with the conventional sequential model-based design of experiments (MBDoE) techniques as well as the offline optimal redesign of experiments.

Keywords: Online model-based redesign of experiments, Continuous flow reactors, identification of reaction kinetics.

1. INTRODUCTION

Online identification of deterministic process models in fully automated platforms is increasingly attracting the research attention as ideal approach for system identification with minimum materials, time and effort. One of the key areas of application of online model identification is the study of chemical reaction kinetics. Model-based design of experiments (MBDoE) techniques have been recognised as the cutting edge tools for the development and refinement of mechanistic process models (Asprey and Macchietto, 2000) and have been extensively applied in the study of kinetic phenomena. In the conventional MBDoE procedure, the model identification process is performed in a pure sequential manner involving: (i) design of experiments at the available parameter estimates, (ii) execution of all the designed experiments and (iii) parameter estimation and evaluation of parameter confidence region using the measurements from the designed experiments. This process is repeated until the parameters are estimated with minimum uncertainty. The drawback of the sequential procedure is that the parameter estimation and update of parameter estimates is repeated only after the completion of all the designed experiments. In other words, in the sequential approach parameter estimation is carried out only between successive experiment designs and creates unnecessarily delays in exploiting the information generated during the execution of designed experiments. This drawback has been overcome by the so called online model-based redesign of experiments (OMBRE) methods. The OMBRE method is an advanced form of MBDoE methods involving intermediate parameter estimations and experiment design at each of the updated parameter estimates, such that

the designed experiments replace some of the previously designed conditions, while the experiment is running at some conditions based on past design. Currently, OMBRE method appears to be the ideal method for online model identification. The idea of online model-based redesign of experiments is not new, as adaptive input design has been applied for linear time-invariant system identification (Hjalmarsson, 2005) and nonlinear batch systems (Stigter et al., 2006). Galvanin and co-workers (2009) proposed a general framework for online model-based redesign of experiments (OMBRE) for parameter estimation in dynamic systems and extended the formulation to dynamic systems in the presence of uncertainty (Galvanin et al., 2012) and variable updating policy (De Luca et al., 2016). Yakut et al. (2013) applied closed-loop online model-based redesign of experiments (CL-OMBRE) techniques to dynamic systems with integrating controller in the system to design the optimal experimental conditions within the safety constraints. The OMBRE method is particularly suitable for the identification of dynamic systems where information gathered from measurements at multiple time intervals allow to update the experimental settings of an experiment while it is still running. In steady state experiments, measurements are obtained only after attaining steady state conditions. This causes significant delays in accessing information from a single experiment. However, the benefits of steady state systems are the consistent data obtained at steady state conditions and the ease of control and operation of the process (Hone et al., 2017). In this work, we apply OMBRE techniques for designing a sequence of steady state experiments in continuous flow reactors to improve the

statistical quality of estimation of kinetic parameters with substantial savings of time.

2. PROCESS MODEL

We assume a process model described by a set of differential and algebraic equations (DAEs) in the form

$$\mathbf{f}(\dot{\mathbf{x}}(z, t), \mathbf{x}(z, t), \mathbf{u}(z, t), \mathbf{w}, \boldsymbol{\theta}, t, z) = 0 \quad (1)$$

$$\hat{\mathbf{y}}(z, t) = \mathbf{h}(\mathbf{x}(z, t), \mathbf{u}(z, t), \mathbf{w}, \boldsymbol{\theta}, t, z) \quad (2)$$

where $\mathbf{x}(z, t) \in \mathbf{R}^{N_x}$ is the time and space dependent vector of state variables, $\mathbf{u}(z, t) \in \mathbf{R}^{N_u}$ is the vector of time-dependent control variables (manipulated inputs) whereas $\mathbf{w} \in \mathbf{R}^{N_w}$ represents the vector of time-invariant controls, $\boldsymbol{\theta} \in \mathbf{R}^{N_\theta}$ is the set of unknown model parameters to be estimated within a continuous realisable set Θ , $\mathbf{y}(z, t) \in \mathbf{R}^{N_y}$ is the set of response variables (i.e. state variables that are measured in the process) and $\hat{\mathbf{y}}(z, t)$ represents the corresponding values of response variables predicted by the model, t is the time and z is the axial domain. The model-based experimental design procedure seeks the optimal value of experimental design vector $\boldsymbol{\phi} \in \mathbf{R}^{N_\phi}$, which minimises the uncertainty region of model parameters. The experimental design vector $\boldsymbol{\phi}$ consists of all set of conditions that characterise an experiment and is generally defined as

$$\boldsymbol{\phi} = \{\mathbf{y}_0, \mathbf{u}(t, z), \mathbf{w}, \mathbf{t}^{sp}, \tau\} \quad (3)$$

where \mathbf{y}_0 is the set of initial conditions of the measured variables; \mathbf{t}^{sp} is the vector of sampling times and τ is the duration of an experiment (for example reaction time in batch reactors or residence time in flow reactors).

3. METHODOLOGY

3.1 Model-based optimal experimental design procedure

The generic MBDoe procedure described in (Asprey and Macchietto, 2000) is given in Figure 1. The model identification procedure generally begins with the preliminary design of experiments. Usually, the set of preliminary experiments are designed by statistical design of experiments (DoE) methods without explicitly using the model structure. The second step is the execution of designed experiments. In the next step, a preliminary parameter estimation is carried out where the adequacy of the model to represent the experimental observations is tested by a chi-square goodness of fit test with $(N - N_\theta)$ degrees of freedom (N is the total number of measurements in all the performed experiments and N_θ is the number of model parameters) assuming 95 % significance. In case if the model fails the goodness of fit test, it is advised to revise the assumptions/modelling hypothesis considered while developing the model itself. Once the suitable model structure is identified (i.e. it passes the goodness of fit test),

the next set of experiments is designed to improve the precision in the estimation of model parameters. In this step, the precision in estimated parameter values is analysed by the statistical t -test and the new experiments are designed to minimise the uncertainty region of the model parameters. The procedure is repeated until desired precision on model parameters is achieved.

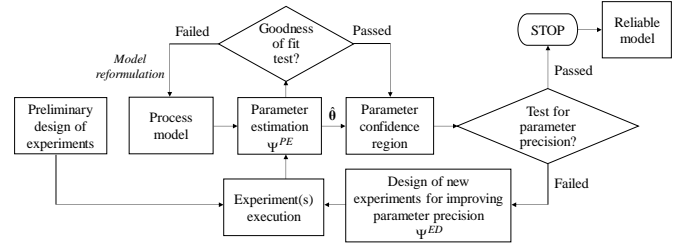


Figure 1. A simplified scheme illustrating the sequential procedure in optimal design of experiments

3.2 Parameter estimation

The parameter estimation problem seeks to find the optimal set of model parameters which produces the best fit to the experimental data within the prescribed tolerance. The parameter estimation (PE) problem is defined based on maximum log-likelihood criterion given in Bard (1974):

$$\hat{\boldsymbol{\theta}} = \arg \max_{\boldsymbol{\theta} \in \Theta} \Psi^{PE}(\boldsymbol{\phi}, \boldsymbol{\theta}) \quad (4)$$

$$\Psi^{PE}(\boldsymbol{\phi}, \boldsymbol{\theta}) = \frac{1}{2} \sum_{i=1}^{N_{\text{exp}}} \sum_{j=1}^{N_y} \left\{ -\ln(2\pi\sigma_j^2) - \left(\frac{\hat{y}_{ij}(\boldsymbol{\phi}_i, \boldsymbol{\theta}) - y_{ij}(\boldsymbol{\phi}_i)}{\sigma_j} \right)^2 \right\} \quad (5)$$

subject to Equation (1) and (2)

where $\boldsymbol{\phi}$ indicates the experimental design vector for all the experiments used for preliminary parameter estimation; $y_{ij}(\boldsymbol{\phi})$ is the measured value of the j -th response variable in the i -th experiment carried out at the conditions defined by design vector $\boldsymbol{\phi}_i$ and $\hat{y}_{ij}(\boldsymbol{\phi}_i, \boldsymbol{\theta})$ is the corresponding value predicted by the model; σ_j is the standard deviation of measurement error associated with the measurement of the j -th response variable (it is assumed that measurement errors are uncorrelated and independent from the experiments).

3.3 Optimal experimental design

The result of PE provides the estimate $\hat{\boldsymbol{\theta}}$, at which the experimental design (ED) problem seeks the optimal settings $\boldsymbol{\phi}^*$ of experiment design vector $\boldsymbol{\phi}$ which minimises the uncertainty region of model parameters defined by the $N_\theta \times N_\theta$ parameter variance-covariance matrix \mathbf{V}_θ . The variance-covariance matrix \mathbf{V}_θ is well approximated as the inverse of $N_\theta \times N_\theta$ Fisher information matrix \mathbf{H}_θ . The

information matrix for the design of j -th experiment is defined as given in Galvanin et al. (2009):

$$\mathbf{V}_{\theta|j} = (\mathbf{H}_{\theta|j})^{-1} \quad (6)$$

$$\begin{aligned} \mathbf{H}_{\theta|j} &= \sum_{k=0}^{j-1} \mathbf{H}_{\theta|k}(\boldsymbol{\theta}, \boldsymbol{\varphi}_k) + \mathbf{H}_{\theta}(\boldsymbol{\theta}, \boldsymbol{\varphi}_j) + (\mathbf{V}_{\theta}^0)^{-1} \\ &= \mathbf{H}_{\theta}(\boldsymbol{\theta}, \boldsymbol{\varphi}_j) + \mathbf{K} \end{aligned} \quad (7)$$

where \mathbf{K} denotes the constant contribution of Fisher information matrix comprising of information gathered from all the experiments prior to the design of j -th experiment and from the prior variance-covariance matrix of model parameters \mathbf{V}_{θ}^0 ; $\mathbf{H}_{\theta|k}$ denotes the information matrix of the k -th experiment. In flow reaction systems the information matrix for a single experiment is computed from the sensitivity coefficients evaluated at steady state conditions. The information matrix for a single experiment is

$$\mathbf{H}_{\theta}(\boldsymbol{\theta}, \boldsymbol{\varphi}) = \sum_{i=1}^{N_y} \frac{1}{\sigma_i^2} \mathbf{Q}_i^T \mathbf{Q}_i \quad (8)$$

where \mathbf{Q}_i is the matrix of the sensitivity coefficients q_{ij} defined as

$$q_{ij} = \frac{\partial \hat{y}_i(\boldsymbol{\tau})}{\partial \theta_j} \quad i = 1, \dots, N_y; j = 1, \dots, N_{\theta}. \quad (9)$$

The experiment design problem for improving the accuracy of parameter estimation can be formulated as

$$\begin{aligned} \boldsymbol{\varphi}^* &= \arg \min_{\boldsymbol{\varphi} \in \Phi} \Psi^{ED}(\mathbf{V}_{\theta}(\boldsymbol{\varphi}, \hat{\boldsymbol{\theta}})) \\ \text{subject to:} \end{aligned} \quad (10)$$

$$\text{Equation (1) and } \boldsymbol{\varphi}_{\min} \leq \boldsymbol{\varphi} \leq \boldsymbol{\varphi}_{\max}$$

The exact form of the objective function of ED problem Ψ^{ED} depends on the choice of that measure of \mathbf{V}_{θ} which is minimised to obtain the optimal design vector (popular choices are the A-optimal, D-optimal and E-optimal designs, respectively minimising the trace, determinant and maximum eigenvalue of \mathbf{V}_{θ} and is equivalent to maximising corresponding measures of Fisher information matrix \mathbf{H}_{θ}) (Pukelsheim, 2006). The D-optimal design criterion was used in this work.

3.4 Standard sequential MBDoE vs offline/online redesign of steady state experiments

In this section, we compare a standard MBDoE procedure with the offline and online redesign of experiments for improving parameter precision in steady state experiments. For this, from a priori uncertainty of model parameters obtained after preliminary parameter estimation, we consider the case of designing three steady state experiments using the following approaches:

- Standard (sequential, offline) MBDoE;
- Offline redesign;

- Online redesign.

In the standard MBDoE approach, the three experiments are designed simultaneously by solving a single optimization problem in the (10) form. The approaches using offline and online redesign strategy in designing three experiments are explained using Figure 2a and 2b.

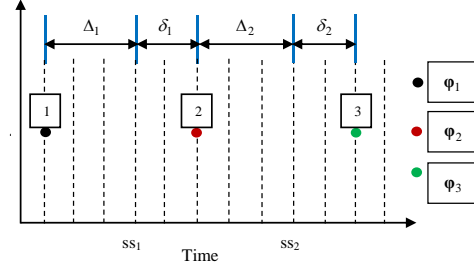


Figure 2a. Strategy for offline redesign of steady state experiments

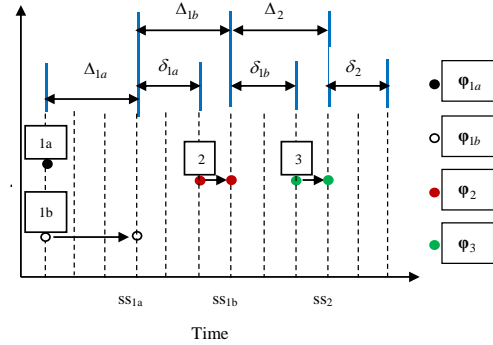


Figure 2b. Strategy for online redesign of steady state experiments

Figure 2a shows the offline redesign strategy for designing three steady state experiments. In the figure Δ_i represents the time required to reach steady state conditions for the i -th experiment with corresponding design vector $\boldsymbol{\varphi}_i$, δ_i represents the time required for analysis and computation of measurements from the i -th experiment. In the offline redesign procedure, only one experiment (experiment 1) is designed from the preliminary parameter estimation. The information from this experiment is accessed after a time delay of $(\Delta_1 + \delta_1)$. With this information, an intermediate parameter estimation is performed to design experiment 2 for improving the parameter precision. The information accessed from experiment 2 after the time delay of $(\Delta_2 + \delta_2)$ is used to design experiment 3. Thus, although no experiment is redesigned in this approach, intermediate parameter estimations are carried out offline.

The online strategy for designing three steady state experiments for improving parameter precision is illustrated in Figure 2b. As shown in the figure, in the online redesign strategy, in order to ensure that the experiment is running while the intermediate parameter estimation is carried out, from the preliminary parameter estimates, two experiments (1a and 1b) are designed simultaneously with respective

design vectors ϕ_{1a} and ϕ_{1b} . These experiments are shown by the black and white circles respectively. The measurements from the first experiment (experiment 1a) is available at the steady state time ss_{1a} and the second experiment (experiment 1b) is started at this time (the arrow in the figure starts at the point of design of an experiment and points to the time at which the designed experiments is actually executed). Thus, while the analysis of data from the first experiment is carried out, the second experiment is in progress. The information from the first experiment obtained at time $(\Delta_{1a} + \delta_{1a})$ is used to design the next single experiment (experiment 2) with design vector ϕ_2 . This experiment shown in red circle is started at time ss_{1b} ; when the experiment 1b is completed. The information from experiment 1b is used to design the next experiment (experiment 3) shown by the green circle. In this way, the information from the first experiment (experiment 1a) is used to design the third experiment (experiment 2) while the second experiment (experiment 1b) is running. In general, in the OMBRE approach for designing a sequence of steady state experiments, it is important to consider the time delays in deciding the optimal online design policy. For example, in experiments with analysis time δ equal to or greater than the time required to reach the steady state time Δ , the online design policy requires the design of at least two experiments each time for being able to run the experiments continuously.

3.4 Implementation of online optimal design

The standard MBDOE and two redesign approaches (both online as well as offline) for the design of steady state experiments were implemented as separate modules in Python (Van Rossum, 2003). The preliminary parameter estimation was performed using the measurements from a set of factorial experiments (which we call preliminary experiments). The experimental data was generated in-silico by adding random Gaussian noise to the true model. The parameter estimation was performed with the Nelder-Mead unconstrained optimization method. The optimization problem of experiment design was solved by minimising the determinant of the parameter variance-covariance matrix V_0 and was computed with the constrained optimization method SLSQP (Sequential Least Squares Programming). The initial guess for the design variables were chosen after trial and error approach starting with different random initial guess and selecting the best that produced the maximum value of trace of Fisher information matrix. The output of experiment design was used to generate the next experimental data from the true model. The parameter estimation was updated with the newly added experiment and the confidence in the estimated parameter values was verified using a t -test with 95 % significance. The parameter estimation and experiment design algorithm for offline and online redesign was iterated until the predefined experimental budget was reached.

4. CASE STUDY

We compare and demonstrate the online model-based redesign approach with a standard MBDOE approach in a

simulated case study of consecutive reactions taking place in a plug flow reactor. The reaction system is described by the following set of DAEs

$$\frac{-v}{A_c} \frac{dC_i}{dz} + \sum_{j=1}^{N_{reac}} \alpha_{ij} r_j = 0 \quad (11)$$

$$r_j = f(k_j, C_i) ; k_j = A_j \cdot \exp(-E_j/R \cdot T) \quad (12)$$

$$i = 1, \dots, N_{comp} ; j = 1, \dots, N_{reac}$$

$$i = 1, \dots, N_{comp} ; j = 1, \dots, N_{reac}$$

Equation (11) represents the reactor model of the plug flow reactor which describes the concentration profiles of reacting species along the reactor length; therefore the independent variable in Equation (1) is z . In Equation (11), C_i is the concentration (mol/L) of the i th component; r_j and α_{ij} are, respectively, the j -th reaction rate and the stoichiometric coefficient of the i -th component in the j -th reaction; v is the inlet volumetric flowrate of reactant A (ml/min); A_c is the reactor cross sectional area (assumed as 1.2 cm²); z is the axial coordinate along the length of the reactor; l is the length of reactor channel (25 cm). In Equation (12), the temperature dependency of reaction rate is described using Arrhenius law where, k_j denotes the reaction rate for the j -th reaction (min⁻¹), A_j the frequency factor and E_j the activation energy.

4.1 True model and generation of experimental data

A power law type kinetic model was assumed as the true model for the series reaction with four estimable model parameters $\theta = [A_1, E_1, A_2, E_2]$ corresponding to the two reaction rate constants k_1 and k_2 .

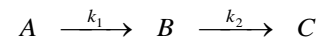


Table 1. Parameter values assumed for the true kinetic model

Parameter	Description	True value	Unit
A_1	Frequency factor for first reaction	8.0	min ⁻¹
E_1	Activation energy for first reaction	29000	J/mol
A_2	Frequency factor for second reaction	5.0	min ⁻¹
E_2	Activation energy for second reaction	35000	J/mol

The four model parameters $\theta = [A_1, E_1, A_2, E_2]$ were normalised with respect to the set of true values $\theta^0 = [8, 29000, 5, 35000]$ and the normalised values were considered to form the true parameter set, $\theta^* = [1.0, 1.0, 1.0, 1.0]$. It is assumed that the measurable response variables for the reaction are the concentration of three components: A, B and C. The experimental data was generated in-silico by adding Gaussian noise with standard deviation 0.03 mol/L to the true model. The initial concentration of reactant A (2 mol/L) was kept constant in all

the experiments. The experimental design vector ϕ was chosen as the conditions of reaction temperature (T) and feed flowrate (v) i.e. $\phi = [T, v]$. In the case study, nine preliminary experiments were designed using a three level-two-factor factorial design method assuming the levels of design variables as: reaction temperature T (333 – 373 K); volumetric flowrate v (0.004 – 0.008 ml/min). The data generated using these experiments were used for the preliminary parameter estimation. Further, the standard MBD_{oE} procedure was compared with the offline and online redesign procedure for the design of five additional experiments aimed to improve the precision of parameter estimation. The online strategy was implemented with the assumption that the steady state time for each experiment is three times the residence time observed at the lowest flowrate and the time for analysis of data from a single experiment is equal to twice the residence time of the reaction obtained at the lowest flowrate (see Figure 2a and 2b). It is also assumed that the analysis time includes the time for data processing and computational time and that the control action on manipulated inputs is extremely fast.

5. RESULTS AND DISCUSSION

From the nine factorial experiments, the values of model parameters were estimated and the results from preliminary parameter estimation are provided in Table 2.

Table 2. Parameter estimation from preliminary factorial experiments (Reference t -value: 2.068)

Weighted residuals	7.6
Reference χ^2	35.17
Preliminary estimate	[1.61, 1.05, 1.30, 1.02]
t -values	[2.05×10^{-7} , 1.48×10^{-6} , 8.21×10^{-9} , 7.91×10^{-8}]

Since the experimental data was generated from the true model and because of no other uncertainties, with the factorial experiments, the chi-square test was passed and the preliminary values of model parameters were obtained. At the preliminary parameter estimate, standard MBD_{oE} procedure was carried out to design the set of five experiments for improving parameter precision. In the design of experiments, the design space was extended from the initial levels assumed. The parameter estimates and the statistical quality of the estimates in terms of t -values are given in Table 3. With this approach, only two of the four parameters were estimated within the 95 % confidence region chosen.

Table 3. Parameter estimation from standard MBD_{oE} approach for designing five steady state experiments (Reference t -value: 2.02, Asterisk denotes t -values failing the test)

Estimate				t -values			
$\hat{\theta}_1$	$\hat{\theta}_2$	$\hat{\theta}_3$	$\hat{\theta}_4$	θ_1	θ_2	θ_3	θ_4
1.43	1.04	1.21	1.02	1.22*	9.35	0.79*	7.07

The results of parameter estimation and posterior statistics from designing five experiments, one at a time (offline

redesign approach) are shown in Table 4. With this approach, the statistical quality of the estimates was greatly improved, even if not significantly after the second experiment. The estimated values of model parameters were close to the known true value (unity for all parameters).

Table 4. Parameter estimation from offline optimal redesign of steady state experiments (Reference t -value: 2.07, Asterisk denotes t -values failing the test)

Exp. No.	Estimate				t -values			
	$\hat{\theta}_1$	$\hat{\theta}_2$	$\hat{\theta}_3$	$\hat{\theta}_4$	θ_1	θ_2	θ_3	θ_4
1	1.25	1.02	1.29	1.02	1.92*	16.05	0.86*	6.49
2	1.06	1.01	1.34	1.03	3.45	30.31	1.51*	9.56
3	0.97	0.99	1.17	1.01	3.16	29.91	1.35*	9.62
4	1.02	1.00	1.16	1.01	3.25	30.09	1.58*	10.74
5	0.97	0.99	1.02	1.00	3.29	31.61	1.54*	11.31

The results of parameter estimation in the online redesign approach (OMBRE) is provided in Table 5. No significant difference was observed in comparison with the offline redesign approach with respect to the precision of parameter estimation. This is also evident from the value of D-optimal objective function achieved at the end of the three experimental campaigns given in Table 6. The standard MBD_{oE} as well as offline and online redesign of experiments implemented in Python were computationally very fast and consumed a total CPU time of approximately 20 seconds on an Intel[®] Xenon[®] E5-1650, 3.5 GHz, RAM 32 GB. It shall be noted that in a real time implementation, the time required to complete the experimental design procedure using the online redesign approach will be much smaller compared to that in the offline approach. If, for example, the residence time and analysis time are assumed as constant and respectively equal to thrice and twice the residence time, and assuming an analysis time of 15 minutes, the design of five experiments by online redesign saves $4\delta = 3600$ seconds compared to the time required by a conventional offline redesign approach. Based on the online redesign procedure illustrated in Figure 2b, the general expression for the time savings t_n achieved in the online redesign approach compared to offline redesign approach for designing n steady state experiments is given by $t_n = (n - 1)\delta$. Thus the time savings is extremely large in cases of prolonged analysis time δ . The overall estimated time with the three experiment design approaches is given in Table 6 together with the value of the D-optimal design criterion. The online redesign approach is more effective on reducing the uncertainty region of model parameters, and allows at the same time to drastically decrease the required experimental time. It is assumed that the computational time is very small and negligible if compared to steady state time and analysis time and therefore the overall time for standard MBD_{oE} and offline redesign becomes approximately the same. The experimental settings in terms of design vector for the three different experimental design approaches are illustrated in Figure 3. In all the three approaches, high temperature is identified as the final optimal design condition. Interestingly, whilst the redesign policies generate very similar trends for the design variables, a conventional

MBDoe pushes towards the use of low flowrates as the optimal condition. It shall be also noted that in case of online redesign approach, there is an overlap of the designed experiments for the last two experiments.

Table 5. Parameter estimation from online optimal redesign of steady state experiments (Reference t -value: 2.07, Asterisk denotes t -values failing the test)

Exp. No.	Estimate				t -values			
	$\hat{\theta}_1$	$\hat{\theta}_2$	$\hat{\theta}_3$	$\hat{\theta}_4$	θ_1	θ_2	θ_3	θ_4
1	1.44	1.04	0.99	0.99	1.82*	15.24	0.21*	2.83
2	1.48	1.04	1.06	1.00	4.37	29.97	1.23*	9.46
3	1.39	1.03	1.12	1.01	4.23	30.25	1.29*	9.54
4	1.15	1.01	1.13	1.01	3.72	30.74	1.31*	9.61
5	1.03	1.00	1.04	1.00	3.49	31.79	1.49*	11.23

Table 6. Value of D-optimal design criterion and overall estimated experimental time after designing five steady state experiments using the three proposed approaches

Design type	Standard MBDoE	Offline redesign	Online redesign
D-optimal value	2.24×10^{-12}	2.38×10^{-13}	3.15×10^{-13}
Total time	$5\Delta + 5\delta$	$5\Delta + 5\delta$	$5\Delta + \delta$

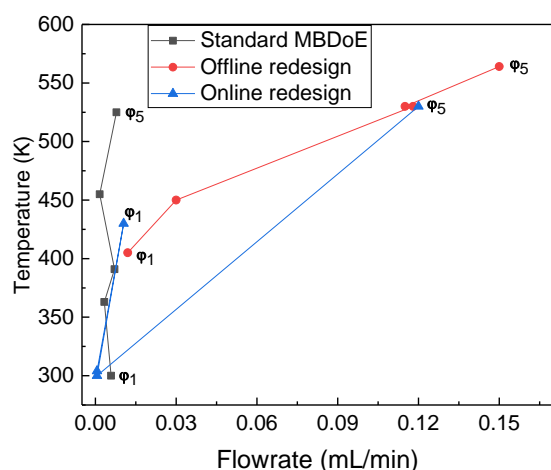


Figure 3. Profile of experimental design variables for the three approaches for designing five steady state experiments. Each point in the profile denotes an experiment.

6. CONCLUSIONS

An online redesign strategy was implemented for designing optimal experimental conditions in a continuous flow reactor. The strategy was compared with the conventional MBDoE procedure and with the offline redesign of experiments. The simulation study demonstrates the advantage of substantial savings in time along with the precise estimation of parameters in the online model-based redesign of experiments techniques applied to steady state experiments. Compared to an offline model-based redesign approach, the same precision of parameter estimation was achieved with the newly proposed online model-based redesign approach, but with a substantial time saving, equivalent to four times

the analysis time. In the real time implementation of online model-based redesign of steady state experiments it is important to consider the time delays along with the information content for the optimal design of steady state experiments in order to minimise the time and material use for the identification of reliable kinetic models.

REFERENCES

- Asprey, S.P. and Macchietto, S. (2000). Statistical tools for optimal dynamic model building. *Comput. Chem. Eng.*, 24, 1261-1267.
- Bard, Y. (1974). *Nonlinear parameter estimation*, Academic Press
- Hjalmarsson, H. (2005). Adaptive input design in system identification. *In: Proc. 44th IEEE Conference on Decision and Control*, Seville, Spain.
- Stigter, J.D., Vries, D., and Keesman, K.J. (2006). On adaptive optimal input design: a bioreactor case study. *AIChE J.*, 52, 3290-3296.
- Galvanin, F., Barolo, M., and Bezzo, F. (2009). Online Model-Based Redesign of Experiments for Parameter Estimation in Dynamic Systems. *Ind. Eng. Chem. Res.* 48, 4415-4427.
- Galvanin, F., Barolo, M., Pannocchia, G., and Bezzo, F. (2012). Online model-based redesign of experiments with erratic models: a disturbance estimation approach. *Comput. Chem. Eng.*, 42, 138-151.
- De-Luca, R., Galvanin, F., and Bezzo, F. (2016). A methodology for direct exploitation of available information in the online model-based redesign of experiments. *Comput. Chem. Eng.*, 91, 195-205.
- Yakut, N., Barz, T., Cardenas, D.C.L., and Wozvy, G. (2013). Online Model-Based Redesign of Experiments for Parameter Estimation Applied to Closed-Loop Controller Tuning, *AIDIC Conference Series*, 11, 421-430.
- Hone, C.A., Holmes, N., Akien, G.R., Bourne, R.A and Muller, F.L. (2017). Rapid multistep kinetic model generation from transient flow data, *React. Chem. Eng.*, 2, 103-108.
- Pukelsheim, F. (2006). *Optimal Design of Experiments*. Society for Industrial and Applied Mathematics, New York, United States of America.
- Van Rossum, G. and Drake, F.L. (2003). *The Python Language Reference Manual*. Network Theory Ltd., Bristol, United Kingdom.