
Federico Galvanin

FEDERICO GALVANIN, ENHONG CAO, NOOR AL-RIFAI, VIVEK DUA, ASTERIOS GAVRIILIDIS*
*Corresponding author
Department of Chemical Engineering, University College London,
Torrington Place, London WC1E 7JE, United Kingdom



# Optimal design of experiments
## for the identification of kinetic models of methanol oxidation over silver catalyst

**KEYWORDS: methanol oxidation, silver, microreaction technology, model-based design of experiments, model discrimination, kinetic modeling.**

Abstract

Partial oxidation of methanol to formaldehyde on silver catalyst represents an important industrial process due to the versatility of formaldehyde as an intermediate in chemical synthesis. The development of kinetic models is essential for a quantitative description of the changes in concentration of the chemical species involved in the process due to reaction as well as for process design and optimisation purposes. Microreactor platforms represent effective tools for the quick development of reliable kinetic models. However, the development and identification of kinetic models is strictly related to the execution of informative experiments, allowing either elucidation of the complex reaction pathways involved in the oxidation process or providing a precise estimation of the kinetic parameters for each candidate model. In this work a model-based design of experiments (MBDoE) procedure is proposed where experiments are optimally designed for both discriminating among competing models and for improving the estimation of kinetic parameters. The proposed methodology allows the most influential reaction pathways to be elucidated and provides a sequence of optimally informative experiments showing the key role of temperature in the kinetic model identification procedure.

**INTRODUCTION**

The partial oxidation of methanol to formaldehyde over a silver catalyst represents a reaction of high industrial significance due to the importance of formaldehyde as a precursor to the production of urea, formaldehyde resin, melamine resin, phenol formaldehyde resin, polyoxymethylene plastics, 1,4-butanediol, and methylene diphenyl diisocyanate. Under industrial conditions the silver catalyst process is usually carried out at atmospheric pressure and high temperatures ($T$ = 853-923 K); if steam is introduced with $H_2O/CH_3OH$ = 0.67 and $CH_3OH/O_2$ = 2.4-2.5 a high selectivity can be reached (~ 90%) (1). The overall oxidation process is usually regarded as an oxidative dehydrogenation, i.e. a combination of methanol oxidation ($CH_3OH + 1/2O_2 \rightarrow CH_2O + H_2O$) and dehydrogenation ($CH_3CH \rightarrow CH_2O + H_2$). The main by-products are $H_2$, $H_2O$, $CO_2$, CO, and methyl formate/formic acid.

Throughout the years, numerous research efforts have been devoted to this reaction system to understand the catalytic role of silver and the possible reaction mechanisms occurring on the catalyst surface (2,3). Methanol oxidative dehydrogenation on silver is strongly related to the presence of chemisorbed oxygen and it is driven by the different activity of oxygen species which are present on the catalyst surface and in the bulk (4). The accurate quantitative description of the concentration of the chemical species involved in the process is related to the availability of *i*) a reliable kinetic mechanism, defining the mathematical structure of the kinetic model (i.e. the set of constitutive equations); *ii*) the precise estimation of the set of kinetic parameters for the model. However, despite the industrial significance of this system, only a few attempts to model the kinetics have been reported in the scientific community (3,5,6) and a full understanding of the reaction on silver under industrial reaction conditions has yet to be established. Recently, a microkinetic model of methanol oxidation on silver, based on a Langmuir-Hinshelwood mechanism, has been proposed (5) in order to explain surface science experiments and kinetic experiments at industrially relevant conditions, applying physically realistic parameters. However, a simplification of the model was required in order to be applied for reactor engineering purposes (6), given the high number of kinetic parameters and the complexity of the rate expressions.

Microreactor platforms represent an ideal system for the study and determination of intrinsic reaction kinetics for strongly exothermic, endothermic, and fast catalytic reactions. With careful experimental design, microreactors allow these reactions to be performed isothermally and in the absence of mass transfer limitations, ensuring the rapid manipulation of reaction conditions and the precise control of the hydrodynamic environment (7). However, the quantity, quality, and speed of information generated by these systems

are affected by the experimental conditions realised during the trials. Design of experiments (DoE) (8) methodologies may help for designing preliminary screening and exploratory experiments, but these techniques are based on empirical models which do not imply a fundamental understanding of the chemical system. Conversely, model-based design of experiments (MBDoE) techniques, based on the phenomenological model of a system, have been proposed for designing a set of experiments yielding the most informative data to be used for the development of fundamental models. These techniques have been successfully adopted in a wide range of applications (9) including the investigation of chemical kinetics in catalytic systems (10,11) and microfluidic devices (12). According to MBDoE, experiments can be specifically designed for *i*) maximising the difference between model predictions, allowing a clear discrimination between candidate kinetic models (13); *ii*) improving the precision in parameter estimation for each candidate model (14). These two MBDoE objectives usually represent distinct sequential steps to be carried out in the conventional model building procedure (15). Some studies have tried to achieve these two goals simultaneously (16,17) by using a multi-objective approach where the objective functions were evaluated on a grid of experimental conditions, but no multi-objective optimisation was involved.

In this paper, a MBDoE procedure based on a multi-objective optimisation is proposed where experiments are optimally designed for improving the estimation of kinetic parameters as well as the simultaneous discrimination among competing kinetic models. MBDoE methodologies are exploited to design a sequence of experiments to be carried out in a specifically designed silicon-glass microreactor (18).

## OPTIMAL EXPERIMENTAL DESIGN PROCEDURE FOR THE IDENTIFICATION OF KINETIC MODELS

A sketch of the suggested procedure for the optimal design of experiments for the development of kinetic models of oxidative dehydrogenation of methanol on silver is shown in Figure 1. Insights from surface science and chemistry lead to the formulation of candidate kinetic mechanisms (Step 1) including the potential reactions taking place on the catalyst surface. Kinetic mechanisms represent the basis for the formulation of kinetic models (Step 2). Model reduction strategies based on the evaluation of the rate determining step (RDS) are used for the development of structurally identifiable models (19) (i.e. models where kinetic parameters can be uniquely determined from experimental data) with chemically consistent reaction rate expressions (10,20). Available historical data are then used for a preliminary model discrimination between candidate kinetic models (Step 3) based on a-posteriori statistics obtained after parameter estimation (21), allowing for a preliminary model selection and an initial estimation of kinetic parameters. Once a set of candidate kinetic models is defined, model-based design of experiment (MBDoE) techniques are applied for planning a sequence of optimally informative experiments allowing for the simultaneous discrimination among candidate models and for improving the precision of parameter estimation (Step 4). MBDoE optimisation computes both the experimental conditions yielding the minimum expected variability in the kinetic parameters and the ones providing the maximum discrimination power in terms of model predictions. The optimally designed experimental conditions are implemented in the microreactor system (Step 5), providing new experimental data to be used for parameter estimation (Step 6). The iteration of steps 4) to 6) represents the core of the MBDoE identification procedure, leading to the detection of the best model structure representing the system (i.e. inadequate models are rejected), elucidating the most plausible kinetic mechanism and ensuring at the same time a precise estimation of the kinetic parameters. The MBDoE procedure will stop when a model is found adequate to represent the system (from lack-of-fit $\chi^2$ tests based on a-posteriori statistics (21)) and a statistically satisfactory estimation of model parameters (based on *t*-test (14)) is achieved.

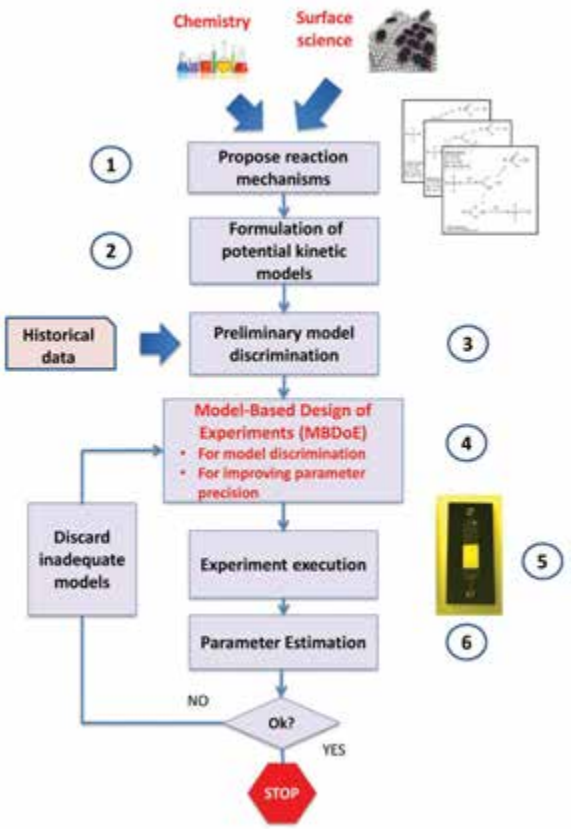



**Figure 1**. MBDoE procedure for simultaneous model discrimination and improvement of parameter precision.

### Formulation of competitive kinetic models of methanol oxidation on silver

The set of reactions involved in each proposed model is shown in Table 1. The simplified model proposed by Andreasen (6) is used as a reference model (Model 1) and two additional simplified kinetic models of increasing level of complexity (Model 2, Model 3) are considered. According to Model 1, methanol oxidative dehydrogenation (reaction 1) and formaldehyde partial oxidation (reaction 2) constitute the base (global) mechanism. Model 2 includes reactions 1-2 and the total oxidation reactions for both $CH_3OH$ and $CH_2O$ (reactions 3 and 4 respectively). Model 3 includes the total oxidation reactions 3,4 for $CH_3OH$ and $CH_2O$ (like Model 2) but global methanol oxidation (reaction 1 used in Model 1 and 2) is split into a dehydrogenation reaction (reaction 5)

and a selective oxidation step (reaction 6). Hydrogen oxidation (reaction 7) has also been included in each mechanism. This reaction is known to occur only at higher temperatures (22), and it has been primarily considered to represent the low hydrogen concentrations observed in the experiments.

| Reactions | ID | Model 1 | Model 2 | Model 3 | Kinetic expression |
|---|---|---|---|---|---|
| $CH_3OH + 1/4O_2 \rightleftharpoons CH_2O + 1/2H_2 + 1/2H_2O$ | 1 | √ | √ | - | $r_1 = k_1 \frac{c_{CH_3OH} c_{O_2}^{1/4}}{c_{H_2O}^{1/2}}$ |
| $CH_2O + 1/2O_2 \rightleftharpoons H_2 + CO_2$ | 2 | √ | √ | √ | $r_2 = k_2 \frac{c_{CH_2O} c_{O_2}^{1/2}}{c_{H_2}^{1/2}}$ |
| $CH_3OH + 3/2O_2 \rightarrow 2H_2O + CO_2$ | 3 | - | √ | √ | $r_3 = k_3 c_{CH_3OH} c_{O_2}^{3/2}$ |
| $CH_2O + O_2 \rightarrow H_2O + CO_2$ | 4 | - | √ | √ | $r_4 = k_4 c_{CH_2O} c_{O_2}$ |
| $CH_3OH \rightleftharpoons CH_2O + H_2$ | 5 | - | - | √ | $r_5 = k_5 \frac{c_{CH_3OH}}{c_{CH_2O} c_{H_2}}$ |
| $CH_3OH + 1/2O_2 \rightleftharpoons CH_2O + H_2O$ | 6 | - | - | √ | $r_6 = k_6 \frac{c_{CH_3OH} c_{O_2}^{1/2}}{c_{CH_2O} c_{H_2O}}$ |
| $H_2 + 1/2O_2 \rightarrow H_2O$ | 7 | √ | √ | √ | $r_7 = k_7 c_{H_2} c_{O_2}^{1/2}$ |
| Number of kinetic parameters | | 6 | 10 | 12 | |

**Table 1.** Set of reactions involved in the proposed kinetic models.

The microchannel reactor is modelled as a dynamic plug flow reactor (PFR) in the form:

$$\frac{\partial c_i}{\partial t} = -u_z \frac{\partial c_i}{dz} + \sum_{j=1}^{N'} v_{ij} r_j \qquad \text{Eq. 1}$$

where $c_i$ is the species concentration, $r_j$ and $v_{ij}$ are the reaction rate and the stoichiometric coefficient of the *i*-th species in the *j*-th reaction respectively, *z* is the axial coordinate, $u_z$ is the flow velocity in the z-direction and *t* the integration time.

The microreactor was fabricated by photolithography and deep reacting ion etching. The reactor channel had a rectangular cross section with 8 mm width and 0.12 mm depth. The silver film catalyst was deposited on the channel floor by sputtering and was 12.5 mm long and 0.25 mm thick. In order to minimise heat losses, the microreactor assembly was insulated with ceramic insulation material. Even though some heat loss was present from the top of the reactor, the temperature at the catalyst location was constant. Mass transfer resistances can be neglected due to the small microchannel depth. The reactor and experimental setup have been described in detail in a previous publication (18).

The reaction was carried out at 725-826K and operation pressure ~1.6 atm. The residence time at reaction temperature was kept at ~6.5-7 ms to avoid formaldehyde decomposition. The effect of $O_2$, $CH_3OH$ and $H_2O$ concentrations was studied by varying each of these components (one at a time) and keeping the total flow constant (25.8-26.5 mL/min) using helium. The inlet and the effluent were analysed online using a ThermoQuest Trace gas chromatograph (GC) to determine the concentration of $CO_2$, $CH_3OH$ and $CH_2O$, while the non-condensable gases were analysed using a Shimadzu GC to determine $O_2$ and $H_2$. The GC analyses were assumed to be corrupted by Gaussian noise with zero mean and a standard deviation of 1% on the reading. A molar composition of the inlet gas mixture $CH_3OH$=10.4%, and ratios $CH_3OH/O_2$=2.25 and $CH_3OH/H_2O$=1.32 were used as a standard case. Experimental reproducibility was checked by performing the standard run at 783 K between each set of experiments. The variables which can be manipulated during the experiments are: inlet composition of reactants in terms of molar fractions ($\mathbf{y}^0 = [y^{CH3OH}, y^{O2}, y^{H2O}]$), temperature (*T*), total pressure (*P*) and volumetric flow rate (*F*).

**Preliminary model discrimination**

Preliminary data from $N_{exp}$= 21 one-factor-at-a-time (OFAT) preliminary experiments from the microreactor system were available for a first discrimination among the proposed competitive models (Model 1, Model 2 and Model 3) where the effect of temperature (*T*) and feed composition ($CH_3OH$, $O_2$ and $H_2O$ molar fraction $\mathbf{y}^0$) on final products ($CH_3OH$, $O_2$, $H_2O$, $CH_2O$, $H_2$, $CO_2$) was investigated:

1. Experiments E1-5: *T* varied from 725 to 826 K (inlet composition fixed at $y^{CH3OH}$=0.10, $y^{O2}$=0.04, $y^{H2O}$=0.07);
2. Experiments E6-9: *T* varied from 725 to 826 K (inlet composition fixed at $y^{CH3OH}$=0.15, $y^{O2}$=0.06, $y^{H2O}$=0.11);
3. Experiments E10-21: *T* kept at 733 K, variable $y^{CH3OH}$ (range 0.07-0.14, E10 to E14; $y^{O2}$=0.04, $y^{H2O}$=0.08), variable $y^{O2}$ (range 0.03-0.10, E15 to E17; variable $y^{CH3OH}$=0.10, $y^{H2O}$=0.08) and variable $y^{H2O}$ (range 0.02-0.22, E18 to E21; $y^{CH3OH}$=0.10, $y^{O2}$=0.04).

Data fitting results (Figure 2) shows the importance of including the total oxidation reactions in the model formulation for achieving a good representation of oxygen concentration (Figure 2a). Model 3, including distinct dehydrogenation and oxidation pathways, provides the best performance in terms of fitting formaldehyde data (Figure 2b).

**Model-based Design of Experiments (MBDoE)**

Eq. 1 and the power-law reaction rate expressions $r_j$ represent a system of differential and algebraic equations where the set of unknown kinetic model parameters (Arrhenius kinetic constants $A_i$ and $E_{a,i}$) have to be estimated in the most precise and accurate way. The variables optimised by MBDoE are:

1. Composition of reactants in terms of molar fractions $\mathbf{y}^0$: methanol ($y^{CH3OH}$ = 0.07-0.14), oxygen ($y^{O2}$ = 0.03-0.10) and water ($y^{H2O}$ = 0.02-0.22);
2. Temperature *T* (725 K < *T* < 826 K).

The ranges of operability (shown in parenthesis above) represent the currently investigated design space **D**, where *F* and *P* have been kept constant to *F* = 26.5 mL/min, *P* = 1.6 atm. MBDoE techniques for improving parameter estimation (MBDoE-PE) aim at decreasing the parameter uncertainty region predicted by each model through the solution of the optimisation problem:

$$\varphi^{MBDoE\text{-}PE} = \arg\min_{\varphi \in D} \left\{ \psi\left[ \mathbf{V}_\theta(\theta, \varphi) \right] \right\} = \arg\min_{\varphi \in D} \left\{ \psi\left[ \mathbf{H}_\theta^{-1}(\theta, \varphi) \right] \right\} \qquad \text{Eq. 2}$$

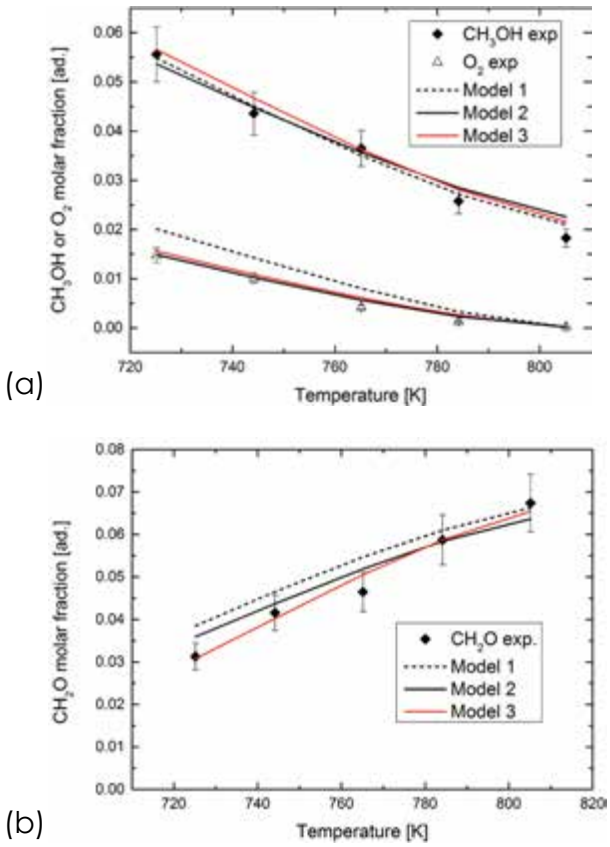



**Figure 2.** Preliminary model discrimination results for Model 1, 2 and 3: molar fractions as a function of temperature for selected species: (a) methanol and oxygen; (b) formaldehyde. Concentrations from experiments E1-E5 are shown, including error bars.

The design optimisation given by Eq. 2 is carried out by computing the $n_\varphi$-dimensional experiment design vector $\boldsymbol{\varphi}$, including all the variables which can be optimised during an experiment, i.e. $\boldsymbol{\varphi} = [\mathbf{y}^0, T]^T$. In Eq. 2 $\boldsymbol{\theta}$ is the $N_\theta$-dimensional vector of model parameters, $\mathbf{V}_\theta$ and $\mathbf{H}_\theta$ are the variance-covariance matrix of model parameters and the global Fisher Information Matrix (FIM), which is the sum of FIMs of candidate models. According to Eq. 2, the experiment is designed so as to minimise a measurement function ψ of $\mathbf{V}_\theta$, representing the chosen design criterion and the objective function to be optimised for improving parameter precision ($\psi = \psi^{MBDoE\text{-}PE}$) The most common design criteria are the A-, D-, E-optimal criteria, minimising the trace, the determinant and the maximum eigenvalue of $\mathbf{V}_\theta$ respectively, or its singular values (SV-optimal design) (14). In this work the A-optimal design criterion was used. However, the discussion that follows remains unchanged if D- and E-optimal design criteria are considered (See Section "MBDoE Results and Discussion").

MBDoE for model discrimination (MBDoE-MD) is formulated with the purpose of maximising the discriminating power (i.e. the relative difference between the predictions of candidate models):

$$\varphi^{MBDoE\text{-}MD} = \arg\max_{\varphi \in D} \left\{ \psi^{MBDoE\text{-}MD} \right\} = \arg\max_{\varphi \in D} \left[ \sum_{M=1}^{N_M} \sum_{N=1}^{N_M} P_M P_N \left[ \sum_{i=1}^{N_y} \frac{(\hat{y}_{M,i} - \hat{y}_{N,i})^2}{\sigma_{y,i}^2} \right]_{MN} \right] \quad \text{Eq. 3}$$

In Eq. 3 $\psi^{MBDoE\text{-}MD}$ is the discriminating power, $\sigma_{y,i}$ is the standard deviation of the *i*-th reading, $\hat{y}_{M,i}$ and $\hat{y}_{N,i}$ are the *i*-th predicted responses of model *M* and *N*, while $P_i$ is the relative probability of the *i*-th model to be the "true" model, as computed after maximum likelihood parameter estimation (13) from the following expression

$$P_i = 1 - \frac{SSWR_i}{SSWR^T} \quad \text{Eq. 4}$$

where $SSWR_i$ is the sum of squared weighted residuals for the *i*-th model, and $SSWR^T$ is the total sum of weighted residuals for the full set of candidate models. The probability $P_i$ reflects the confidence on the i-th model in such a way that MBDoE-based model discrimination will preferentially operate on the best candidate models representing the system. After the preliminary parameter estimation $P_1 = 0.26$, $P_2 = 0.34$ and $P_3 = 0.40$, reflecting the superiority of Model 3 on fitting the available experimental data.

## MBDoE RESULTS AND DISCUSSION

In order to show the potential of MBDoE techniques, a simulation study is presented here to compute the optimal experimental conditions to be used for both discriminating among competing models and improving the estimation of kinetic parameters. The optimal experimental conditions provided by MBDoE optimisation for improving parameter precision (MBDoE-PE, Eqs. 2) and for model discrimination (MBDoE-MD, Eq. 3) are, respectively:

1. MBDoE-PE: $\mathbf{y}^0 = [y^{CH3OH}, y^{O2}, y^{H2O}] = [0.14, 0.10, 0.22]$, $T = 732$ K;
2. MBDoE-MD: $\mathbf{y}^0 = [y^{CH3OH}, y^{O2}, y^{H2O}] = [0.14, 0.10, 0.22]$ , $T = 826$ K.

As can be observed from Figure 3a, the optimally designed conditions are far from the ones investigated by OFAT experiments in terms of inlet concentrations of reactants. In particular, the optimal operating region suggested by MBDoE (for both model discrimination and improving parameter precision) is the one at high concentrations of reactants. An A-optimal design criterion was used for MBDoE-PE, but optimisation results obtained from a D-optimal and E-optimal design were very similar to the ones obtained from the A-optimal (i.e. at the extremities of the design space). The difference was only of 3% on the optimal temperature value found from MBDoE-PE, whilst no difference on the solution was observed concerning the initial concentration of reactants. Reaction temperature *T* becomes a key factor for model discrimination: 1) at low T the confidence in the estimation of model parameters can be increased (MBDoE-PE); 2) at high T a clear distinction between model predictions along the microreactor can be realised (MBDoE-MD). Figure 3b shows the Pareto curve showing the trade-off solutions (points 1 to 4) between MBDoE-PE and MBDoE-MD in terms of objective functions ($\psi^{MBDoE\text{-}PE}$ and $\psi^{MBDoE\text{-}MD}$, Eq. 2 and Eq. 3 respectively) according to an ε-constraint multi-objective optimisation approach (23), where intermediate solutions 2 (T = 765 K) and 3 (T = 796 K) have been computed. Figure 3c shows the impact of the MBDoE-MD design on the prediction of formaldehyde molar fraction along the reactor for candidate kinetic models. The maximum discriminating power is obtained at the outlet of the reactor (point 2 in the figure, solid lines), where Model 1 formaldehyde molar fraction can be clearly distinguished from Model 2 and 3. However, note how a

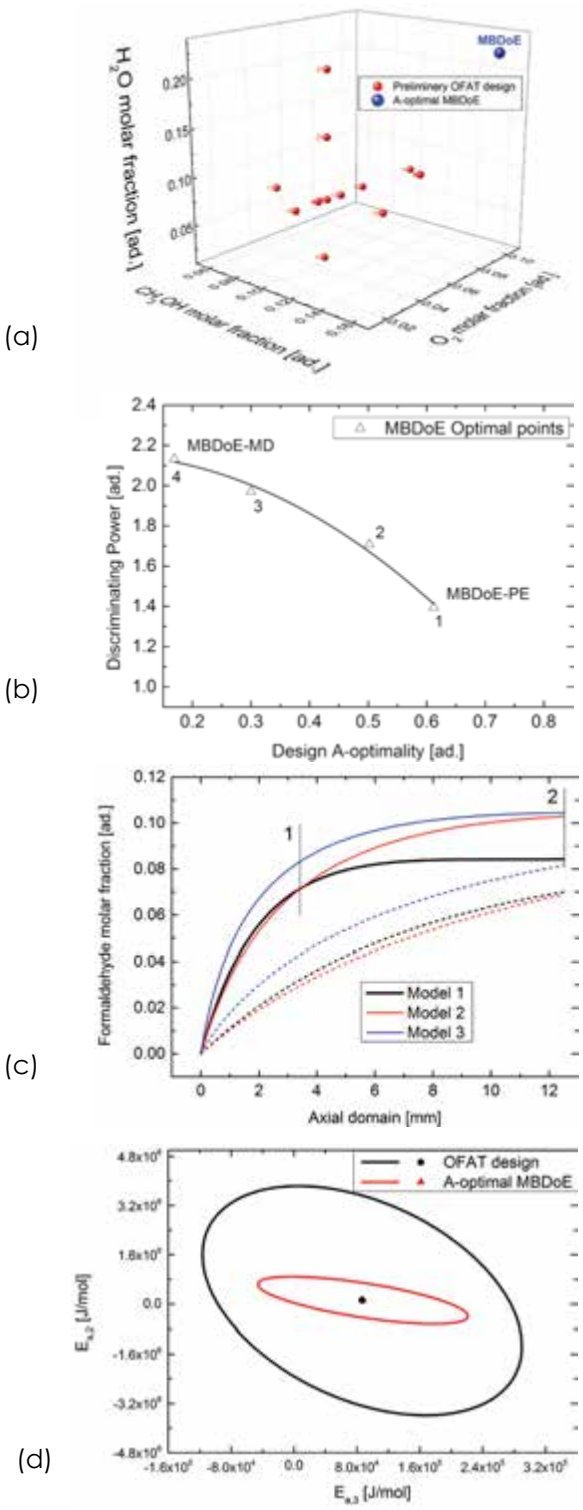



**Figure 3.** Experiments suggested by MBDoE for improving parameter precision and simultaneous model discrimination. (a) MBDoE optimal point and OFAT experiments in the space of reactants concentration. (b) Pareto plot for the simultaneous solution of the multi-objective optimisation problems given by Eq. 2 and Eq. 3. In the plot, points 1 to 4 are distinct solutions of the multi-objective optimisation problem given by the simultaneous solution of Eq. 2 and Eq. 3. (c) MBDoE-MD planned experiment: formaldehyde molar fraction profiles along the microreactor for candidate kinetic models at nominal flow rate (F = 26.5 mL/min, solid lines) and at increased flow rate (F = 106 mL/min, dashed lines). (d) MBDoE-PE planned experiment: impact on estimation precision for parameters $E_{a,2}$ and $E_{a,3}$ of Model 3.

net discrimination between Model 2 and 3 can only be obtained at point 1. For obtaining this condition at the outlet of the reactor, higher volumetric flow rate *F* has to be used (dashed lines). Figure 3d shows the effect of MBDoE-PE design on the parameter estimation confidence of activation energies $E_{a,2}$ (formaldehyde partial oxidation) and $E_{a,3}$ (methanol total oxidation) of Model 3.

Based on the solutions of the multi-objective MBDoE optimisation, a sequence of steady-state experiments (EXP1-4) is designed for improving the estimation of model parameters and the simultaneous discrimination among candidate models (MBDoE-SIM) minimising the experimental effort required for model identification. Suggested experiments in terms of temperature profile are given in Figure 4a. The first experiment (EXP1) starts at the MBDoE-PE planned experimental conditions ($\mathbf{y}^0$ = [0.14, 0.10, 0.22], $T_1$ = 732 K) and the temperature is increased to $T_2$ = 765 K until, after a transient phase $\Delta_1$ (in which the concentrations need to be stabilised) a new steady state is reached (EXP2). After a second transient ($\Delta_2$), the same approach is then used from EXP3 ($T_3$ = 796 K) to EXP4, where the temperature is increased until MBDoE-MD conditions ($\mathbf{y}^0$ = [0.14, 0.10, 0.22], $T_1$ = 826 K) are realised. As it becomes apparent from Figure 4b, this experiment allows a very clear distinction between model predictions in terms of formaldehyde selectivity. At $\mathbf{y}^0$, the increase in temperature designed by MBDoE-SIM is expected to increase the selectivity for Model 3, while a decrease in selectivity will be observed for Model 1 and 2.

## CONCLUSION

A MBDoE procedure has been proposed for the optimal design of experiments in microreactor platforms showing the best experimental conditions to be used for a precise estimation of the set of kinetic parameters of candidate kinetic models and for elucidating the different reaction pathways of proposed kinetic models based on historical data. A preliminary discrimination of simplified kinetic models of methanol oxidation on silver has been carried out, underlining a better representation of experimental results when dehydrogenation and a selective oxidation step are included in the model formulation. Furthermore, MBDoE results demonstrated the important role of temperature in the model discrimination task for this system. At high concentrations of the reactants, low temperature experiments provide the maximum confidence for the estimation of kinetic parameters, while high temperature ones support model discrimination. The management of this design variable allows designing a highly informative sequence of steady-state experiments providing at the same time a high discriminating power and an improvement of parametric precision.

## ACKNOWLEDGEMENTS

Funding from EPSRC grant (EP/J017833/1) is gratefully acknowledged.

## REFERENCES

1. Reuss, G., Disteldorf, W., Gamer, A. O., Albrecht, H. In: *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Wien, **15**, 737-768 (2012).

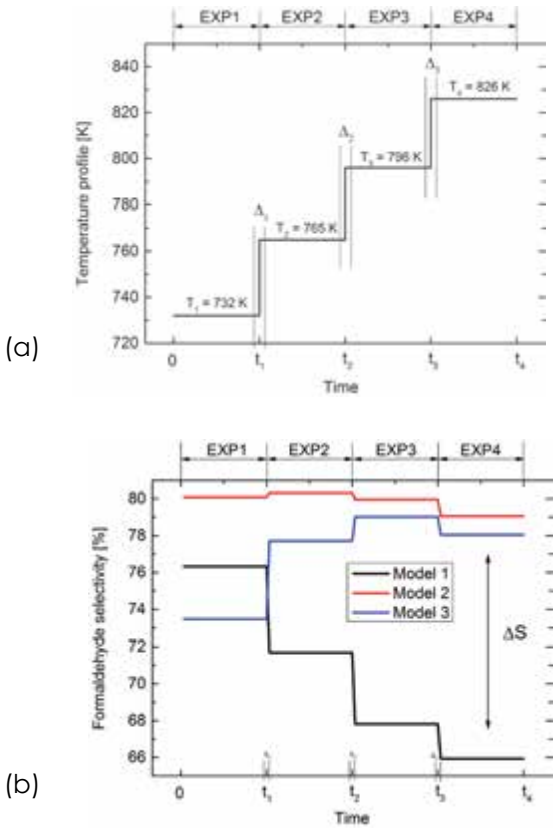


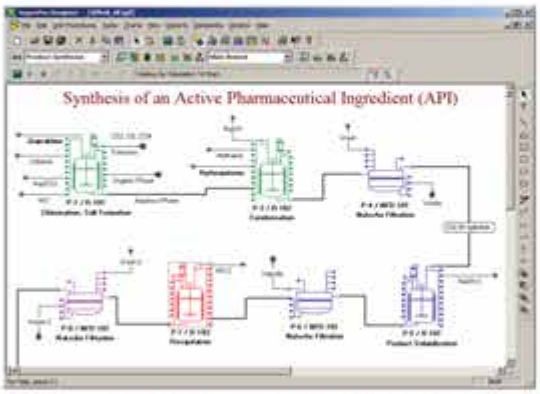

**Figure 4**. MBDoE results for improving parameter precision and simultaneous model discrimination (MBDoE-SIM). (a) Temperature profile for the sequence of steady-state experiments EXP1-4. (b) Formaldehyde selectivity for candidate models realised from the sequence of steady-state experiments EXP1-4.


2. Wachs, I. E., Madix, R. The oxidation of methanol on a silver (110) catalyst. J. Surf. Sci. **76**,531-539 (1978).
3. Robb, D. A., Harriott, P. The kinetics of methanol oxidation on a supported silver catalyst. J. Catal. **35**:176-183 (1974).
4. Montoya, A., Haynes, B. S. Methanol and Methoxide Decomposition on Silver J. Phys. Chem. **111**, 9867-9876 (2007).
5. Andreasen A, Lynggaard H, Stagelman C, Stolze P. A microkinetic model of the methanol oxidation over silver. Surf. Sci. **544**,5-12 (2003).
6. Andreasen, A., Lynggaard, H., Stagelman, C., Stolze, P. A simplified kinetic model of methanol oxidation on silver, Applied Cat. **189**, 267-275 (2005).
7. Al-Rifai , N., Cao, E., Dua, V., Gavriilidis, A. Microreactor technology aided catalytic process design, Curr. Opin. Chem. Eng. **2**, 1-8 (2013).
8. Montgomery, D. Design and analysis of experiments. Hoboken, NJ: John Wiley & Sons (2013).
9. Franceschini, G., Macchietto, S. Model-based design of experiments for parameter precision: state of the art, Chem. Eng. Sci. **63**, 4846-4872 (2008).
10. Prasad, V., Vlachos, D. G. Multiscale model and informatics-based optimal design of experiments: application to the catalytic decomposition of ammonia on ruthenium. Ind. Eng. Chem. Res. **47**, 6555-6567 (2008).
11. Schöneberger, J. C., Arellano-Garcia, H., Wozny, G., Körkel, S., Thielert, H. Model based experimental analysis of a fixed bed reactor for catalytic $SO_2$ oxidation. Ind. Eng. Chem. Res. **48**, 5165-5176 (2009).
12. Reizman, B. J., Jensen, K. F., An automated continuous-flow platform for the estimation of multistep reaction kinetics, Org. Process Des. Dev. **16**, 1770-1782 (2012).
13. Schwaab, M., Silva, F. M., Queipo, C. A., Barreto Jr., A. G., Pinto, J. C. A new approach for sequential experimental design for model discrimination, Chem. Eng. Sci. **61**, 5791-5806 (2006).
14. Galvanin, F., Bezzo, F., Macchietto, S., Model-based design of parallel experiments, Ind. Eng. Chem. Res., **46**, 871-877 (2007).
15. Asprey, S. P., Macchietto, S. Statistical tools for optimal dynamic model building, Computers Chem. Eng. **24**, 1261-1267 (2000).
16. Petrov, L. A., Eliyas, A. E., Maximov, C. S., Ind. Eng. Chem. Res., **30**, 636-645 (1991).
17. Akiti, T. T., Birchumshaw, L. D., Eckert, R. E., Can. J. Chem. Eng., **75**. 238-244 (1997).
18. Cao, E., Gavriilidis, A. Oxidative dehydrogenation of methanol in a microstructured reactor, Catal. Today **110**, 154-163 (2005).
19. Galvanin, F., Ballan, C.C., Barolo, M., Bezzo, F. A general model-based design of experiments approach to achieve practical identifiability of pharmacokinetic and pharmacodynamic models. J. Pharmacokinet. Pharmacodyn. **40**, 451–467 (2013).
20. Deshmukh, S. R., Vlachos, D. G. A reduced mechanism for methane and one-step rate expressions for fuel-lean catalytic combustion of small alkanes on noble metals. Combustion and Flame **149**, 366–383 (2007).
21. Stewart, W. E., Shon, Y., Box, G. E. P. Discrimination and goodness of fit of multiresponse mechanistic models. AIChE J. **44**, 1404-12 (1998).
22. H. Schubert, U. Tegtmeyer, R. Schlögl, On the mechanism of the selective oxidation of methanol over elemental silver, Catal. Lett. **28**, 383-390 (1998).
23. Mavrotas, G. Effective implementation of the ε-constraint method in multi-objective mathematical programming problems, Appl. Math. Comp. 213, 455-465 (2009).

# Intelligen Suite®

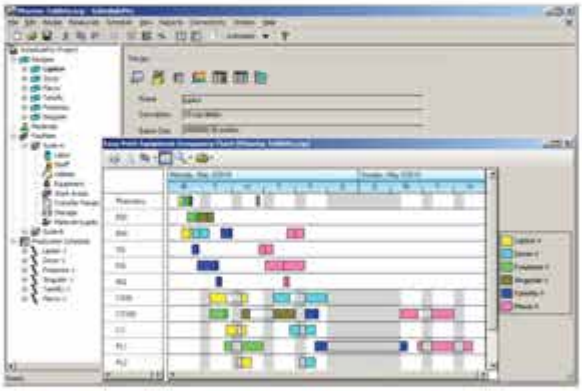
## The Market-Leading Engineering Suite for Modeling, Evaluation, Scheduling, and Debottlenecking of Multi-Product Facilities

## SuperPro®

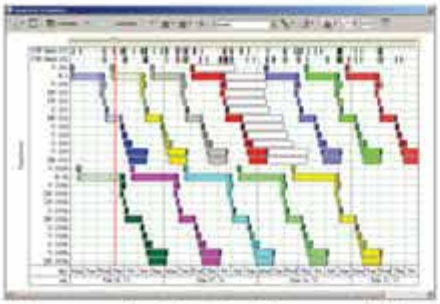



Use SuperPro Designer to model, evaluate, and optimize batch and continuous processes


## SchedulePro®

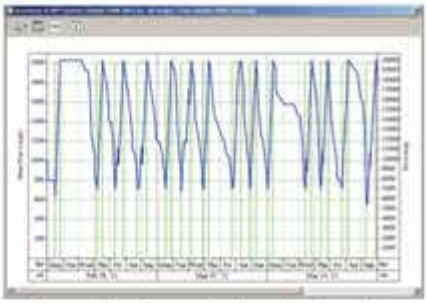


Migrate to SchedulePro to model, schedule, and debottleneck multi-product facilities



Easy production tracking, conflict resolution and rescheduling

Tracking demand for resources (e.g., labor, materials, utilities, etc.)



Managing inventories for input, intermediate, and output materials

**SuperPro Designer** is a comprehensive process simulator that facilitates modeling, cost analysis, debottlenecking, cycle time reduction, and environmental impact assessment of integrated biochemical, bio-fuel, fine chemical, pharmaceutical (bulk & fine), food, consumer product, mineral processing, water purification, wastewater treatment, and related processes. Its development was initiated at the Massachusetts Institute of Technology (MIT). SuperPro is already in use at more than 500 companies and 900 universities around the globe (including 18 of the top 20 pharmaceutical companies and 9 of the top 10 biopharmaceutical companies).

**SchedulePro** is a versatile production planning, scheduling, and resource management tool. It generates feasible production schedules for multi-product facilities that do not violate constraints related to the limited availability of equipment, labor, utilities, and inventories of materials. It can be used in conjunction with SuperPro (by importing its recipes) or independently (by creating recipes directly in SchedulePro). Any industry that manufactures multiple products by sharing production lines and resources can benefit from the use of SchedulePro. Engineering companies use it as a modeling tool to size shared utilities, determine equipment requirements, reduce cycle times, and debottleneck facilities.

***Visit our website to download detailed product literature and functional evaluation versions of our tools***

**INTELLIGEN, INC. • 2326 Morse Avenue • Scotch Plains, NJ 07076 • USA**
**Tel: (908) 654-0088 • Fax: (908) 654-3866**
**Email: info@intelligen.com • Website: www.intelligen.com**
***Intelligen also has offices in Europe and representatives in countries around the world***