A. Table of Notation

Table A. Summary of notation.

Symbol	Description
$\boldsymbol{f}_i$	Function associated with model $\mathcal{M}_i$
$f_{i,(e)}$	Dimension e of function $\boldsymbol{f}_i$; $e = 1, \ldots, E$
$\boldsymbol{x}$	Design variable, $\boldsymbol{x} \in \mathcal{X} \subset \mathbb{R}^d$
$\boldsymbol{\theta}_i$	Parameters of model $\mathcal{M}_i$, $\boldsymbol{\theta}_i \in \Theta_i \subset \mathbb{R}^{D_i}$
M	No. of models $\mathcal{M}_i$; $i = 1, \ldots, M$
E	No. of target dimensions; $\boldsymbol{f}_i : \mathbb{R}^{d+D_i} \to \mathbb{R}^E$
$\boldsymbol{\Sigma}_{\text{exp}}$	Measurement noise covariance
$\mathcal{D}_{\text{exp}}$	The set of experimental observations
$\mathcal{D}_{\text{sim},i}$	The set of simulated data for model $\mathcal{M}_i$

B. Design Criteria

We let $\Delta_{ij} = \boldsymbol{f}_i(\boldsymbol{x}, \hat{\boldsymbol{\theta}}_i) - \boldsymbol{f}_j(\boldsymbol{x}, \hat{\boldsymbol{\theta}}_j)$ and the covariance $\boldsymbol{\Sigma}_i = \boldsymbol{\Sigma}_{\text{exp}} + \breve{\boldsymbol{\Sigma}}_i(\boldsymbol{x})$, where $\breve{\boldsymbol{\Sigma}}_i(\boldsymbol{x})$ is the covariance of model $\mathcal{M}_i$'s marginal predictive distribution due to model parameter uncertainty.

For a single-response system, Box & Hill (1967) derive the design criterion D_{BH}, later generalised to a multi-response form by Prasad & Someswara Rao (1977)

$$D_{\text{BH}}(\boldsymbol{x}) = \sum_{i,j=1}^{M} \frac{\pi_{N,i}\pi_{N,j}}{2} \left\{ \Delta_{ij}^\top \left(\boldsymbol{\Sigma}_i^{-1} + \boldsymbol{\Sigma}_j^{-1} \right) \Delta_{ij} + \operatorname{tr}\left(\boldsymbol{\Sigma}_i \boldsymbol{\Sigma}_j^{-1} + \boldsymbol{\Sigma}_j \boldsymbol{\Sigma}_i^{-1} - 2\boldsymbol{I} \right) \right\} .$$

Buzzi-Ferraris et al. (1990) derive the design criterion D_{BF}

$$D_{\text{BF}}(\boldsymbol{x}) = \max_{1 \le i,j \le M} \left\{ \Delta_{ij}^\top \left(\boldsymbol{\Sigma}_i + \boldsymbol{\Sigma}_j \right)^{-1} \Delta_{ij} + \operatorname{tr}\left(2\boldsymbol{\Sigma}_{\text{exp}} \left(\boldsymbol{\Sigma}_i + \boldsymbol{\Sigma}_j \right)^{-1} \right) \right\} .$$

designed such that if $\max_{\boldsymbol{x}} D_{\text{BF}}(\boldsymbol{x}) < E$, the largest difference between model predictions is too small compared to the measurement noise variance to carry out model discrimination, and design of experiments terminates.

Michalik et al. (2010) proceed from the Akaike information criterion (AIC) as the model discrimination criterion to derive a design criterion D_{AW} from the Akaike weights

$$w_i(\boldsymbol{x}) = \frac{1}{\sum_{j=1}^{M} \exp\left(\frac{-1}{2} \Delta_{ij}^\top \boldsymbol{\Sigma}_i^{-1} \Delta_{ij} + D_i - D_j \right)} ,$$

yielding $D_{\text{AW}} = \sum_i w_i p(\mathcal{M}_i)$, where $p(\mathcal{M}_i)$ is the prior probability of model $\mathcal{M}_i$.

C. Case study from Vanlier et al. (2014)

There are nine chemical components with concentrations C_i, $i = 1, \ldots, 9$. The system of ordinary differential equations has the form

$$\begin{aligned}
\mathrm{d}C_1/\mathrm{d}t &= -g_1 + g_2 , \\
\mathrm{d}C_2/\mathrm{d}t &= g_1 - g_2 , \\
\mathrm{d}C_3/\mathrm{d}t &= -g_3 + g_4 , \\
\mathrm{d}C_4/\mathrm{d}t &= g_3 - g_4 - g_5 + g_6 , \\
\mathrm{d}C_5/\mathrm{d}t &= -g_9 + g_{10} , \\
\mathrm{d}C_6/\mathrm{d}t &= -g_5 + g_6 + g_9 - g_{10} , \\
\mathrm{d}C_7/\mathrm{d}t &= g_5 - g_6 , \\
\mathrm{d}C_8/\mathrm{d}t &= -g_7 + g_8 , \\
\mathrm{d}C_9/\mathrm{d}t &= g_7 - g_8 ,
\end{aligned}$$

i.e. the stoichiometry is the same for all models $\mathcal{M}_i$. But some of the fluxes $g_1, \ldots, g_{10}$ differ for the different models. For all models $\mathcal{M}_i$ the following fluxes are identical:

$$\begin{aligned}
g_2 &= \theta_{i,2} C_2 , & g_7 &= \theta_{i,7} C_8 , \\
g_4 &= \theta_{i,4} C_4 , & g_8 &= \theta_{i,8} C_9 , \\
g_5 &= \theta_{i,5} C_4 C_6 , & g_9 &= \theta_{i,10} C_5 , \\
g_6 &= \theta_{i,6} C_7 , & g_{10} &= \theta_{i,4} C_6 .
\end{aligned}$$

For flux g_1 the models differ in the following way:

$$\begin{aligned}
\mathcal{M}_i &: \quad g_1 = \theta_{i,1} C_1 , \quad i \in \{1, 3, 4\} \\
\mathcal{M}_2 &: \quad g_1 = \frac{\theta_{2,1} C_1}{\theta_{2,9} + C_7} .
\end{aligned}$$

For flux g_3 the models differ in the following way:

$$\begin{aligned}
\mathcal{M}_1 &: \ g_3 = \tfrac{\theta_{1,3} C_2 C_3}{\theta_{1,9} + C_7} , & \mathcal{M}_3 &: \ g_3 = \tfrac{\theta_{3,3} C_2 C_3}{\theta_{3,9} + C_9} , \\
\mathcal{M}_2 &: \ g_3 = \theta_{2,3} C_2 C_3 , & \mathcal{M}_4 &: \ g_3 = \tfrac{\theta_{4,3} C_2 C_3}{\theta_{4,9} + C_8} .
\end{aligned}$$

We assume that the only measured states are the concentrations C_4 and C_9, because these are the states from which Vanlier et al. (2014) collect their initial data. Similarly, we use the initial concentrations $C_4(t = 0)$ and $C_9(t = 0)$ as two of our design variables, the third design variable being the time point t at which to measure the concentrations.

Vanlier et al. (2014) look at times points in the range $t \in [0, 20]$, which we also adopt. We assume the initial concentrations $C_4(t = 0), C_9(t = 0) \in [0, 1]$ and fix all other initial concentrations to

$$\begin{aligned}
C_1(t = 0) = C_3(t = 0) = C_5(t = 0) = C_8(t = 0) = 1 , \\
C_2(t = 0) = C_6(t = 0) = C_7(t = 0) = 0.1 .
\end{aligned}$$

We assume the model parameter space $\boldsymbol{\theta} \in [0, 1]^{10}$. Simulations show that sampling from this parameter space gives a wide range of model realisations.

With reference to models $\mathcal{M}_1$ and $\mathcal{M}_2$ being similar, we see that the only difference between them is that the term $\theta_{i,9} + C_7$ divides g_1 and g_3 for $\mathcal{M}_1$ and $\mathcal{M}_2$, respectively. If C_7 is small compared to $\theta_{i,9}$, then the models are nearly identical.