Robust Sampling Time Designs for Parametric Uncertain Systems

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Abstract: Robust experimental design (RED) of sampling time scheduling has been discussed for parametric uncertain systems. Four RED methods, i.e., the pseudo-Bayesian design, the maximin design, the expectation-variance design, and the online experimental redesign, are investigated under the framework of model-based optimal experimental design (OED). Both the D-optimal and the E-optimal criteria are used as performance metrics. Two numerical procedures, the Powell’s method and the semi-definite programming (SDP), are employed to obtain the optimum solution for REDs. The robustness performance of the four REDs are compared using a benchmark enzyme reaction system. In comparison to a typical uniform sampling strategy, the sampling time profiles from REDs are more focused on regions where the dynamic system has higher parametric sensitivities, indicating choice of informative data for parameter identification. The designed sampling strategies are also assessed by bootstrap parameter estimation with randomly generated initial points, where the difference between the REDs can be observed.

Keywords: Optimal experimental design (OED); robust experimental design (RED); parametric uncertainty; sampling time scheduling; parameter estimation.

1. INTRODUCTION

Building mathematical models for complex systems from experimental data is widely explored in many sciences and engineering applications. Collecting data that contain the most relevant information about the system dynamics is crucial for model discrimination, parameter estimation and model validation (Morgan and Stallings, 2017). Optimal experimental design (OED) is a powerful tool developed to find the experimental settings under which the most informative data can be obtained for modelling. A standard OED method uses measures based on Fisher information matrix (FIM) mainly because, under certain assumptions, the inverse of FIM provides the lower bound for parameter estimation error covariance. A comprehensive review of OED can be found in (Franceschini and Macchietto, 2008). Since FIM is formulated on local parametric sensitivities, the reliability of OED can hardly be ensured when large uncertainty exists in initial modelling.

A few number of robust experimental design (RED) methods have been proposed for systems with large uncertainties such as the pseudo-Bayesian approach (Walter and Pronzato, 1987) and the maximin approach (Asprey and Macchietto, 2002; Dette et al., 2005). The maximin method maximises the information content for the possible worst performance within the uncertain region, while the pseudo-Bayesian design considers the averaged performance over the whole uncertain parameter space. An improved utility function is proposed for measurement set selection design that combines both the pseudo-Bayesian approach and the maximin method (Zhang and Drovandi, 2017).

Instead of a single experimental design as mentioned above, iterative design is an alternative option for RED. According to the time and experimental resources provided, OEDs can be performed in sequential (Walter and Pronzato, 1987), parallel (Galvanin et al., 2007), or hybrid procedures (Franceschini and Macchietto, 2008). The reproduced data is used for model update in each iteration to reduce the impact of model uncertainty. This iterative idea can also be applied to a single (batch) experimental design by dividing the whole experiment horizon into several sub-experiments. This is often called ”online” optimal experimental redesign which was first applied to linear systems (Mehra, 1974; Gerencsér and Hjalmarsson, 2005), and extended to nonlinear systems later on (Stigter et al., 2006; Galvanin et al., 2009). In a recent work (Wang and Yue, 2019), an auto-updating strategy is proposed to address the issue that an iterative scheme can become unreliable when it uses inadequate prior knowledge to assure practical identifiability.

The design of sampling time scheduling is of particular importance for dynamic systems with a long operating horizon. An equally-spaced sampling strategy is normally adopted in practice, which can become arduous and costly if the experiment takes a long time and the sampling frequency is high. OED on sampling time looks for a sampling profile that includes only the most informative data at the selected time points. A sampling time design is in principle improved utility function is proposed for measurement set selection design that combines both the pseudo-Bayesian approach and the maximin method (Zhang and Drovandi, 2017).
an infinite-dimensional non-convex dynamic optimisation problem. Partial derivatives are normally required to solve the problem, which is numerically cumbersome (Yu, 2018). Powell’s method (Powell, 1964) can be applied to update the selected sampling times iteratively to approach the optimum without using performance function derivatives. Another option is to transform the infinite continuous problem into a semi-definite programming (SDP) problem (Yu, 2018), which can be solved more easily.

In this work, several RED methods on sampling profile design are reviewed and compared for systems with parametric uncertainties. Key aspects in RED, such as problem formulation, optimisation algorithm, implementation readiness, computational load and robustness performance are assessed. The remaining of the paper is organized as follows. Section 2 gives the preliminaries on model assumptions, parameter estimation and typical OED formulation. In Section 3, four RED methods on sampling time scheduling are presented in optimisation framework. Two numerical methods employed for RED are discussed in Section 4. In Section 5, simulation studies are conducted on a benchmark enzyme reaction system, and the results are compared. Conclusions are made in Section 6.

2. PRELIMINARIES

Consider a general nonlinear system with $n$ variables, $p$ parameters, and $m$ output variables.

$$
\dot{X}(t) = f(X(t), \theta), \quad X(t_0) = X_0
$$

$$
Y(t) = h(X(t)) + \xi(t)
$$

where $f(\cdot)$ are a set of continuous state transition functions that have first-order derivatives; $X \in \mathbb{R}^n$ is the state vector for $n$ state variables and $X_0$ is the initial condition of $X$; $\theta \in \mathbb{R}^p$ denotes the $p$ parameters; $Y \in \mathbb{R}^m$ is the vector for $m$ output variables, which is selected from the $n$ state variables (the selection function is denoted by $h(\cdot)$); $\xi \in \mathbb{R}^m$ is the vector of measurement errors, which are considered to be independent, identical distributed zero-mean Gaussian noise with variance $\sigma_j^2$ for $j = 1, \ldots, m$.

### 2.1 Sampling Time Points for Parameter Estimation

The sampling time points for measurement variables stay in a continuous bounded region (infinite time points available). In order to simplify the design problem, the continuous time region is relaxed to a discrete region with $N_t$ available time points. In parameter estimation, outputs are measured at $N_{sp}$ ($N_{sp} \leq N_t$) time points that are selected from the $N_t$ available time points. Taking the least square estimation (LSE) method, the parameter estimation can be formulated as:

$$
\hat{\theta} = \arg \min_{\theta \in \Theta} \frac{1}{2} \sum_{j=1}^{m} \sum_{i=1}^{N_t} \tilde{\omega}_i (y_j(t_i) - \tilde{y}_j(\theta, t_i))^2
$$

where $\tilde{y}_j$ and $\tilde{y}_j$ are measured and model prediction of the $j$th output; $\tilde{\omega}$ is the weight of the $i$th available sampling time point which is either 0 or 1 (1 means measurement is taken at this sampling time point and 0 not taken). The sampling time weighting vector, denoted as $\omega = [\omega_1, \omega_2, \cdots, \omega_N]$, should satisfy $1^T \omega = N_{sp}$, where 1 is a column vector of ones.

### 2.2 Optimal Experimental Design (OED)

For systems in Section 2.1, FIM can be written as

$$
\text{FIM}((\omega, \theta)) = \sum_{i=1}^{N_t} \tilde{\omega}_i \cdot S(t_i)^T \cdot \Sigma^{-1} \cdot S(t_i),
$$

where $S(t_i) = \frac{\partial X(t)}{\partial \theta}$, is the local parametric sensitivity matrix at time $t_i$, $\Sigma$ is the measurement error covariance matrix. According to the Cramer-Rao lower bound inequality, the inverse of FIM provides a lower bound for the parameter error covariance matrix from (2). The OED of sampling time scheduling can be written as the following integer programming problem:

$$
\arg \min_{\omega} \psi\left(\left(\text{FIM}(\omega, \theta)\right)^{-1}\right)
$$

subject to:

$$
\omega_i \in [0, 1], \quad 1^T \omega = N_{sp}
$$

where $\psi(\cdot)$ is a scaler function that is normally selected as determinant (D-optimal), L2 norm (E-optimal), or trace (A-optimal) of FIM. This would only work well when model uncertainty is small since FIM is formulated by local parametric sensitivities, which depend on the prior knowledge of model parameters.

An exhaustive searching method can be employed to solve (3) when $N_t$ is relatively small, but this method becomes computationally demanding for design with large $N_t$. The optimisation problem in (3) can be relaxed into an approximate continuous optimisation problem, which is convex for some design criteria.

$$
\arg \min_{\omega} \psi\left(\left(\text{FIM}(\omega, \theta)\right)^{-1}\right)
$$

subject to:

$$
\sum_{i=1}^{N_t} \omega_i = 1, \quad \omega_i \geq 0
$$

Here the weighting factors in $\omega = [\omega_1, \cdots, \omega_i]^T$ are real numbers rather than binary 0 or 1.

### 3. ROBUST EXPERIMENTAL DESIGN (RED)

#### 3.1 Maximin Robust Experimental Design

A maximin RED method optimizes the worst possible performance for any parameter values (Asprey and Macchietto, 2002) to ensure the design result is acceptable for all possible parameters. The RED problem is written as follows:

$$
\arg \min_{\omega} \arg \max_{\theta \in \Theta} \psi\left(\left(\text{FIM}(\omega, \theta)\right)^{-1}\right)
$$

where $\Theta$ is the admissible domain for $\theta$. With this RED method, only the upper and lower bounds of parameter uncertainty are required for robust design.

Exhaust searching algorithms can be used to solve this problem, which can be numerically demanding for high dimension systems. A more computationally efficient method has been proposed (Körkel et al., 2004; Flaherty et al., 2006), in which the first-order Taylor expansion is used to approximate either the parameter error covariance matrix or the FIM taking into account parameter uncertainties.
\[ \text{FIM}(\theta^* + \delta \theta) \approx \text{FIM}(\theta^*) + \frac{\partial \text{FIM}(\theta^*)}{\partial \theta} \bigg|_{\theta^*} \delta \theta + \cdots \]
\[ = \sum_{i=1}^{N_t} \omega_i \cdot \left\{ S^T(t_i, \theta^*) \Sigma^{-1} S(t_i, \theta^*) + \frac{dS^T(t_i, \theta)}{d\theta} |_{\theta^*} \delta \theta \right\} \]
\[ = \text{FIM}(\theta^*) + \Delta \]
\[ (6) \]

3.2 Pseudo-Bayesian Robust Experimental Design

In a pseudo-Bayesian design, the optimisation is made on the averaged or the expectation of the performance over the whole uncertain parameter regions (Walter and Pronzato, 1987). Assume that the distribution of parameter uncertainty can be described by its probability density function (PDF), i.e., \( \theta \sim p(\theta) \), the pseudo-Bayesian RED can be formulated as:
\[ \arg \min_{\omega} \int_{\Theta} \psi \left( \left( \text{FIM}(\omega, \theta) \right)^{-1} \right) p(\theta) d\theta \]
\[ (7) \]
In this design, the PDF of parameter distribution is required. The analytical solution of this optimisation problem is hard to find. Instead, the Monte-Carlo method can be used to solve this problem by sampling from the parameter uncertainty space. Assume that \( p(\theta) \) is of uniform distribution, and \( N_p \) sampling sets are taken for \( \theta \) in its distribution region, then (7) can be rewritten as:
\[ \arg \min_{\omega} \frac{1}{N_p} \sum_{i=1}^{N_p} \psi \left( \left( \text{FIM}(\omega, \theta_i) \right)^{-1} \right) \]
\[ (8) \]

3.3 Expectation and Variance Based Method

The pseudo-Bayesian design could be less sensitive to the outliers in parameter space due to its averaging algorithm. To tackle with this limitation, Zhang and Drovandi (2017) proposed a design method that combines the expectation and variance terms into the objective function:
\[ \arg \min_{\omega} \left( E + \lambda \frac{1}{N_p} \sum_{i=1}^{N_p} \psi \left( \left( \text{FIM}(\omega, \theta_i) \right)^{-1} \right) - E \right)^2 \]
\[ (9) \]
where \( E = \frac{1}{N_p} \sum_{i=1}^{N_p} \psi \left( \left( \text{FIM}(\omega, \theta_i) \right)^{-1} \right) \) and \( \lambda \) is a weighing factor defined by users to balance contributions between mean and variance. The idea of this RED method is that the design result should not only be a good choice for the averaged effect from parameter uncertainty, but also keeps the information content relatively stable for all possible parameters. A problem is that \( \psi \left( \left( \text{FIM}(\omega, \theta_i) \right)^{-1} \right) \) can differ largely for different parameter sets. To keep them on a comparable scale, logarithm or other scaling measures can be applied to \( \psi(\cdot) \).

3.4 Iterative Strategy—Online Experimental Redesign

In the online experimental redesign method, the whole experiment (process) is divided into several sub-experiments (in time zones). Model parameters are updated at the end of each sub-experiment with all data collected up to this time, and the updated model parameters are used as the prior information for the next sub-experiment. This RED method is easy to implement and is adjustable for changing operation conditions. With this design, the number of sub-experiments and the length of each sub-experiment need to be defined by users. The identifiability problem may appear if the length of a sub-experiment is too short to cover the dynamics. An auto-updating redesign method is proposed recently that not only ensures the identifiability but also improved the robustness performance under parametric uncertainty. The detailed design procedure can be found in Wang and Yue (2019).

4. NUMERICAL METHODS

For the OED problem in (4), if the D-optimal criterion is adopted, the OED can be proved to be convex and solved by Powell’s quadratically convergent method; if the E-optimal criterion is adopted, the OED can be transferred into a SDP problem. These two numerical algorithms will be used to solve the RED problems in this work.

4.1 Powell’s Method for D-optimal Design

The Powell’s quadratically convergent method first randomly selects the \( N_{tp} \) time points from the \( N_t \) available time points. It then gets rid of one point in the selection set and substitutes it with a non-selected point to reach minimum objective value. Repeat this process until all the selected \( N_{tp} \) time points are updated. In order to keep the algorithm reliable, the whole procedure will be repeated several times by taking different initially selected \( N_{tp} \) time points, and the updating process can also have several iterations.

A successful implementation of Powell’s method to solve the sampling time OED can be seen in a previous work Yu (2018). This method hasn’t been applied to RED, in which the objective function needs to be reformulated to incorporate parametric uncertainties.

Using the D-criterion for sampling scheduling, the maximin design objective function in RED can be written as:
\[ \det \left( \sup_{\theta \in \Xi} \left\{ \sum_{i=1}^{N_{tp}} \sum_{j=1}^{n} \frac{1}{\sigma_j^2} S_j(t_i, \theta)^T S_j(t_i, \theta) \right\} \right)^{-1} \]
\[ (10) \]
For the pseudo-Bayesian design, the D-optimal objective function in RED is written as:
\[ \det \left( \sum_{i=1}^{N_{tp}} \sum_{j=1}^{n} \frac{1}{\sigma_j^2} S_j(t_i, \theta)^T S_j(t_i, \theta) \right)^{-1} \]
\[ (11) \]
In the expectation-variance based method, using \( E \) to represent (11), the objective functions can be written as:
\[ E + \lambda \sqrt{N_p} \sqrt{ \sum_{i=1}^{N_{tp}} \left( \det \left( \sum_{i=1}^{N_{tp}} \sum_{j=1}^{n} \frac{1}{\sigma_j^2} S_j(t_i, \theta)^T S_j(t_i, \theta) \right)^{-1} \right)^2 - E } \]
\[ (12) \]
4.2 SDP for E-optimal Design

Using E-optimal criterion, the OED of measurement set selection can be transformed into SDP to get the optimal solution. This was extended to the OED of sampling time design (Yu, 2018), but hasn’t been explored to REDs of sampling time scheduling. In this section, the sampling time REDs with the maximin method and the pseudo-Bayesian method are transformed to SDP, which can be solved by established optimisation tools such as SeDuMi (Sturm, 1999).

Without loss of generality, FIM in (6) can be written as:

$$\text{FIM}(\theta^* + \delta\theta) = \sum_{i=1}^{N_t} \omega_i \left( \sum_{j=1}^{n} \frac{1}{\sigma_j^2} S_j^T(t_i) S_j(t_i) + \Delta_i \right)$$

(13)

where $\Delta_i$ is a $m \times m$ matrix at $t_i$. The maximin design problem in (5) can be cast as a standard SDP with the assumption on $\Delta_i$’s magnitude: $\|\text{blk} \, \text{diag}(\Delta_1, \cdots, \Delta_{N_t})\|_2 \leq \rho$. Following (Flaherty et al., 2006), assuming that $\Delta_1 = \cdots = \Delta_{N_t}$, the E-optimal maximin RED can be written as a regularised optimisation problem:

$$\arg \min_{\omega} -s$$

$$s.t. \sum_{i=1}^{N_t} \omega_i \left( \sum_{j=1}^{n} \frac{1}{\sigma_j^2} S_j^T(t_i) S_j(t_i) \right) - \rho \sqrt{N_t} \|\omega\|_2 J \geq s I$$

(14)

where $J, I \in \mathbb{R}^{m \times m}$ are unit matrix and identity matrix; the uncertainty bound $\rho$ is a regularisation parameter.

For the pseudo-Bayesian Design, the E-optimal RED in (8) can be reformed as:

$$\arg \min_{\omega} -s$$

$$s.t. \frac{1}{N_p} \sum_{i=1}^{N_p} \sum_{l=1}^{N_t} \sum_{j=1}^{n} \omega_j \cdot \frac{1}{\sigma_j} S_j(t_i, \theta_l)^T S_j(t_i, \theta_l) \geq s I$$

(15)

5. CASE STUDY

5.1 System Settings

An enzyme reaction system is used for simulation studies. The reaction mechanism is shown in Fig. 1. This system has 10 state variables, among which 5 states, {S, N, P, Q, R}, are measurable. The 11 reaction rates, $[k_1, k_{-1}, k_2, k_{-2}, k_3, k_{-3}, k_4, k_{-4}, k_5W, k_{-5}, k_6]$, are model parameters. For this benchmark system, the model description, parameter nominal values and the initial conditions of state variables can be found in Yue et al. (2013). The parameters, $k_3, k_{-3}$ and $k_5W$ are the focus of parameter estimation because they are found to be most influential to system outputs through sensitivity analysis. The other 8 parameters are assumed known and set to their nominal values in the following study.

The experiment duration is 6,000 seconds and the 5 measurable variables are assumed to be sampled at the same time points. Assume that there are 201 sampling points available ($N_t = 201$), produced uniformly at $[0 : 30 : 6000]$.

Fig. 1. Enzyme reaction system(Yu, 2018)

30 : 6,000(s), among them 21 points will be selected for parameter estimation ($N_{sp} = 21$). For the three uncertain parameters $k_2, k_{-3}$ and $k_5W$, the nominal values are [100, 200, 5000], the lower and upper bounds are [50, 100, 2500] and [200, 400, 7500]. The parameters are uniformly distributed within the bounds. The same parameter samples which are generated by Latin hypercube sampling (LHS) are used for all REDs employing the Monte-Carlo method.

5.2 D-Optimal REDs Solved by Powell’s Algorithm

Four RED strategies, i.e., maximin design, pseudo-Bayesian design, expectation–variance method, and online experimental redesign are applied to D-optimal design of sampling time scheduling, which are solved by the Powell’s method. The design results are listed in Table 1.

Table 1. D-optimal RED results (Powell’s method)

<table>
<thead>
<tr>
<th>Design method</th>
<th>Sampling time points (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pseudo-Bayesian</td>
<td>[60, 340, 600, 660, 720, 1080, 1740, 2640, 2790, 3000, 3350, 3420, 4380, 4580, 4770, 4830, 5100, 5160, 5400, 5850, 5880]</td>
</tr>
<tr>
<td>maximin</td>
<td>[60, 90, 300 : 30 : 540, 2100 : 30 : 2280, 2340, 2370, 4980]</td>
</tr>
<tr>
<td>expectation–variance</td>
<td>[360, 450, 540, 690, 1440, 1860, 1890, 2250, 2400, 2460, 2610, 2850, 3120, 3240, 3300, 3390, 3690, 4020, 4500, 4530, 5580]</td>
</tr>
<tr>
<td>online redesign</td>
<td>[450, 580, 510, 1260, 1230, 1950, 1890, 2100, 2620, 3990, 3960, 4740, 4770, 5850 : 30 : 5970]</td>
</tr>
<tr>
<td>non–design</td>
<td>[0 : 300 : 6000]</td>
</tr>
</tbody>
</table>

The designed sampling profiles and the relative sensitivities of the 3 key parameters to the state, S, are shown in Fig. 2, from which it can be seen that the RED sampling profiles are more focused on the regions where parameter sensitivities are relatively high, e.g., $[300 – 2,500](s)$.

In order to explore the robust performance of REDs under parametric uncertainties, 1,000 parameter sets are drawn from the bounded region, and the statistics of logarithmic D-values ($\log|\det(\text{FIM}^{-1})|$) are used for comparison (Table 2). A smaller D-value corresponds to a possible smaller parameter estimation error using the collected experimental data. It can be seen from Table 2 that the pseudo-Bayesian design has the smallest mean, the largest maximum and the largest standard deviation of the D-value among all REDs, which means that it
Fig. 2. Sampling profiles and parameter relative sensitivities to S (D-optimal, Powell’s method)
achieves the best result at the averaged level within the uncertainty region, but has a large variation range. On
the contrary, the maximin design has the largest mean, but the smallest maximum of the D-value, which means
that it has the best performance at the worst parameter case. The expectation–variance based method has the
smallest standard deviation following its design nature. The statistics of the online redesign method fall in between
the other three REDs.

Table 2. Statistics of D-values (logarithmic) of RED methods (Powell’s method)

<table>
<thead>
<tr>
<th>Design method</th>
<th>mean D</th>
<th>max D</th>
<th>std D</th>
</tr>
</thead>
<tbody>
<tr>
<td>pseudo — Bayesian</td>
<td>12.1776</td>
<td>17.9201</td>
<td>1.4941</td>
</tr>
<tr>
<td>maximin</td>
<td>13.2543</td>
<td>15.1271</td>
<td>1.0499</td>
</tr>
<tr>
<td>expectation — variance</td>
<td>12.2352</td>
<td>15.2357</td>
<td>0.7672</td>
</tr>
<tr>
<td>online redesign</td>
<td>12.4989</td>
<td>15.5762</td>
<td>1.5003</td>
</tr>
<tr>
<td>non — design</td>
<td>12.6441</td>
<td>16.5155</td>
<td>1.2802</td>
</tr>
</tbody>
</table>

To examine the data quality for parameter estimation from different REDs, 100 parameter estimations are obtained
by the bootstrap parameter estimation method (using random initial values for parameters taken from the uncer-
tainty region). The results are illustrated in Fig. 3, from which it can be seen that the pseudo-Bayesian design has
more extreme outliers than the other three REDs.

Fig. 3. Bootstrap parameter estimation of \( \{k_2, k_{-3}\} \) using sampling data obtained from D-optimal REDs

Fig. 4. Boxplots of \( k_2 \) estimation under D-optimal REDs and non-design

to see more clearly the outliers, a box-plot is produced for \( k_2 \) in Fig. 4. The red line inside each rectangular box
indicates the median level of the box. The "whiskers" below and above each box show the smallest and the
largest estimations that are not outliers, and the outliers are in red crosses. The circles besides all box-plots are esti-
mations obtained by corresponding RED samplings. Again Fig. 4 shows that with the pseudo-Bayesian design, the
parameter estimations have more outliers distributed in a wider range. For the maximin design, the estimations stay
closely around the nominal value. Most estimations using RED samplings have smaller estimation errors compared
to the results using the evenly spaced non-design sampling.

5.3 E-optimal REDs solved by SDP

In this section, the SDP algorithm is used to solve E-optimal REDs on sampling time scheduling. The sampling patterns for each RED method are listed in Table 3. Again the RED sampling profiles capture regions with more sensitive data compared to the non-designed strategy.

Table 3. E-optimal RED results (SDP)

<table>
<thead>
<tr>
<th>Design method</th>
<th>Sampling time points (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pseudo — Bayesian</td>
<td>[0, 30, 60, 120, 390, 450, 480, 510, 570, 840, 900, 990, 1050, 1080, 1200, 3180, 3300, 3390, 3480, 3510, 3540, 3750, 3960]</td>
</tr>
<tr>
<td>maximin</td>
<td>[30, 60, 90, 330 : 30 : 600, 3750 : 30 : 3960]</td>
</tr>
<tr>
<td>non — design</td>
<td>[0 : 300 : 6000]</td>
</tr>
</tbody>
</table>

Similarly, 1,000 parameter sets are drawn from the uncertainty space to examine the robustness. The statistical attributes of logarithmic E-values (\( \log \max \text{eig} (\text{FIM}^{-1}) \)) are shown in Table 4. The results are mostly consistent with D-optimal REDs solved by Powell’s method. The only exception is that, using the SDP solver, all REDs have better results than the non-design method in all aspects. Then 100 parameter estimations are obtained using the boot-
strap method taking arbitrary initial parameter settings. The box-plot for \( k_2 \) estimations with E-optimal REDs are shown in Fig. 5. In this case, the pseudo-Bayesian method has very few outliers, and the estimations are located close to the nominal value. With the maximin method, though
most of the estimations are tightly close to the nominal value, it has more outliers than the other two REDs. The non-design strategy has the worst performance compared to REDs in that it has more outliers, and many estimations stay far away from the nominal value.

Table 4. Statistics of E-values (logarithmic) of REDs (SDP)

<table>
<thead>
<tr>
<th>Design method</th>
<th>mean $E$</th>
<th>max $E$</th>
<th>std $E$</th>
</tr>
</thead>
<tbody>
<tr>
<td>pseudo – Bayesian</td>
<td>10.4834</td>
<td>12.6242</td>
<td>0.7608</td>
</tr>
<tr>
<td>maximin</td>
<td>10.6349</td>
<td>11.6682</td>
<td>0.6417</td>
</tr>
<tr>
<td>online redesign</td>
<td>10.6720</td>
<td>12.2990</td>
<td>0.8150</td>
</tr>
<tr>
<td>non – design</td>
<td>11.2688</td>
<td>12.7040</td>
<td>0.7778</td>
</tr>
</tbody>
</table>


