# SEQUENTIAL EXPERIMENTAL DESIGN AND RESPONSE OPTIMISATION

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ABSTRACT. We consider the situation where one wants to maximise a function $f(\theta, \mathbf{x})$ with respect to $\mathbf{x}$, with $\theta$ unknown and estimated from observations $y_k$. This may correspond to the case of a regression model, where one observes $y_k = f(\theta, \mathbf{x}_k) + \epsilon_k$, with $\epsilon_k$ some random error, or to the Bernouilli case where $y_k \in \{0, 1\}$, with $\text{Prob}[y_k = 1|\theta, \mathbf{x}_k] = f(\theta, \mathbf{x}_k)$. Special attention is given to sequences given by $\mathbf{x}_{k+1} = \arg\max_{\mathbf{x}} f(\hat{\theta}^k, \mathbf{x}) + \alpha_k d_k(\mathbf{x})$, with $\hat{\theta}^k$ an estimated value of $\theta$ obtained from $(\mathbf{x}_1, y_1), \ldots, (\mathbf{x}_k, y_k)$ and $d_k(\mathbf{x})$ a penalty for poor estimation. Approximately optimal rules are suggested in the linear regression case with finite horizon case, where one wants to maximize $\sum_{i=1}^{N} w_i f(\theta, \mathbf{x}_i)$ with $\{w_i\}$ a weighting sequence. Various examples are presented, with a comparison with a Polya urn design and an up-and-down method for a binary response problem.

## 1. INTRODUCTION

We consider an optimisation problem, where one wants to maximise a function $f(\theta, \mathbf{x})$ with respect to $\mathbf{x} \in \mathcal{X} \subset \mathbb{R}^q$, where $\theta$ is an unknown vector of parameters, $\theta \in \mathbb{R}^p$. Two cases will be considered. The first one corresponds to a regression problem, where one observes

$$y_k = f(\theta, \mathbf{x}_k) + \epsilon_k \,, \;\; k = 1, 2, \ldots \tag{1.1}$$

with $\{\epsilon_i\}$ a martingale difference sequence with respect to an increasing sequence of $\sigma$-fields $\{\mathcal{F}_k\}$: $\epsilon_k$ is $\mathcal{F}_k$-measurable and $E\{\epsilon_k|\mathcal{F}_{k-1}\} = 0$. We also assume that $\sup_k E\{\epsilon_k^2|\mathcal{F}_{k-1}\} < \infty$ almost surely (a.s.).

In the second case, when the design variable is $\mathbf{x}_k$, one observes a Bernouilli response:

$$y_k \in \{0, 1\} \;\; \text{with} \;\; \text{Prob}[y_k = 1|\theta, \mathbf{x}_k] = f(\theta, \mathbf{x}_k) \,, \;\; k = 1, 2, \ldots \tag{1.2}$$

In both cases, the sequence of design points $\{\mathbf{x}_k\}$ and observations $\{y_k\}$ is used to estimate $\theta$. If the issue were only to determine the value $\mathbf{x}^*$ that maximises $f(\theta, \mathbf{x})$, one could resort to optimum-design theory for choosing an appropriate sequence of inputs $\{\mathbf{x}_k\}$, see, *e.g.*, [13, 22, 2, 3, 19, 21, 8]. However, here the objective is also to have each $f(\theta, \mathbf{x}_i)$ as large as possible. The sequence $\{\mathbf{x}_k\}$ must therefore fulfill two simultaneous (and generally opposite) objectives: (i) help to locate $\mathbf{x}^*$, (ii) be close to $\mathbf{x}^*$ in order to maximise $f(\theta, \mathbf{x}_k)$, $k = 1, 2, \ldots$ The problem is thus one of dual control (see the pioneer papers by Fel'dbaum (1960, 1961)).

A rather general formulation of the problem (see [14]) is:

$$\text{maximize} \;\; E\{\sum_{i=1}^{\infty} w_i y_i|\mathcal{F}_0\} / \sum_{i=1}^{\infty} w_i \tag{1.3}$$

with respect to $\mathbf{x}_1, \mathbf{x}_2, \ldots$, with $\{w_i\}$ a weighting (discount) sequence. For instance, the choice $w_i = 1$ for $i = N+1$ and $w_i = 0$ otherwise corresponds to a pure design problem, where emphasis is put on the estimation of $\mathbf{x}^*$ after $N$ observations; $w_i = 1, \ldots, N$, $w_{N+1} = K$ and $w_i = 0$ for $i > N+1$ corresponds to the case where the best guess for $\mathbf{x}^*$ at step $N$ is used for the next $K$ steps; the finite horizon case with no discount corresponds to $w_i = 1$, $i = 1, \ldots, N$, $w_i = 0$ for $i \geq N+1$, *etc.*

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In the two cases (1.1,1.2), $E\{y_i|\theta,\mathbf{x}_i\} = f(\theta,x_i)$, so that, when adopting a Bayesian approach, with $\pi(\theta) = \pi(\theta|\mathcal{F}_0)$ a given prior distribution for $\theta$, (1.3) becomes

$$\text{maximize} \quad E\{\sum_{i=1}^{\infty} w_i f(\theta,\mathbf{x}_i)|\mathcal{F}_0\}/\sum_{i=1}^{\infty} w_i\,. \tag{1.4}$$

We shall mainly consider design sequences that are constructed as follows: at step $k$, $\mathbf{x}_{k+1}$ maximizes the sum of the predicted value of $f$, that is, $f(\hat\theta^k,\mathbf{x})$ with $\hat\theta^k$ the estimated value of $\theta$, and a weighted penalty term $\alpha_k d_k(\mathbf{x})$, with $d_k(\mathbf{x})$ also a function of $(\mathbf{x}_i,y_i)$, $i=1,\ldots,k$:

$$\mathbf{x}_{k+1} = \arg\max_{\mathbf{x}\in\mathcal{X}} f(\hat\theta^k,\mathbf{x}) + \alpha_k d_k(\mathbf{x})\,. \tag{1.5}$$

In Section 2 we give an asymptotic result (infinite horizon, no discount) obtained for the regression problem (1.1) when $f(\theta,\mathbf{x})$ is linear in $\theta$ and $d_k(\mathbf{x})$ is the variance function used in the construction of $D$-optimum designs. Other penalty functions related to $L$-optimum design are then suggested. Section 3 is devoted to the finite horizon case: approximately optimal strategies are suggested, and a particular sequence of weights $\{\alpha_k\}$ and penalty function $d_k(\mathbf{x})$ for (1.5) are obtained through a series of approximations of the original problem (1.4). Extension to nonlinear problems is presented in Section 4, where the case of Bernouilli trials (1.2) is considered through an example. Finally, Section 5 concludes and points out some open issues and possible developments.

## 2. Some asymptotic results for linear response optimisation

### 2.1. $D$-optimum penalty.

Consider the case where the horizon is infinite ($N=\infty$) and there is no discount ($w_i=1$ for any $i$), and assume that the regression function is linear in $\theta$, that is, $f(\theta,\mathbf{x}) = \mathbf{r}^\top(\mathbf{x})\theta$. We use the penalty given by the variance function used in the sequential construction of $D$-optimum designs, see [24, 7],

$$d_k(\mathbf{x}) = d_k^D(\mathbf{x}) = \mathbf{r}^\top(\mathbf{x})\mathbf{M}_k^{-1}\mathbf{r}(\mathbf{x})\,, \tag{2.1}$$

with $\mathbf{M}_k$ the design matrix

$$\mathbf{M}_k = \sum_{i=1}^{k} \mathbf{r}(\mathbf{x}_i)\mathbf{r}^\top(\mathbf{x}_i)\,. \tag{2.2}$$

Assume that $\mathbf{r}(\mathbf{x})$ is continuous on $\mathcal{X}$ compact, that the first $K_0$ regressors $\mathbf{r}(\mathbf{x}_1),\ldots,\mathbf{r}(\mathbf{x}_{K_0})$ are such that $\mathbf{M}_{K_0}$ is positive definite. Also assume that $\theta$ in (1.1) takes a deterministic (but unknown) value $\bar\theta$ and that $\mathbf{r}^\top(\mathbf{x})\bar\theta$ has a unique global maximiser $\mathbf{x}^*$ in $\mathcal{X}$; that is:

$$\forall\beta>0\,,\ \exists\epsilon>0 \ \text{ such that } \mathbf{r}^\top(\mathbf{x})\bar\theta + \epsilon > \mathbf{r}^\top(\mathbf{x}^*)\bar\theta \Rightarrow \|\mathbf{x}-\mathbf{x}^*\| < \beta\,. \tag{2.3}$$

We estimate $\theta$ by least squares (LS):

$$\hat\theta^k = \arg\min_{\theta\in\Theta} \sum_{i=1}^{k} [y_i - \mathbf{r}^\top(\mathbf{x}_i)\theta]^2\,, \tag{2.4}$$

with $\Theta$ a compact subset of $\mathbb{R}^p$ such that $\bar\theta\in\Theta$. The difficulty is that for a suitable weighting sequence $\{\alpha_k\}$, the sequence $\{\mathbf{x}_k\}$ accumulates at the value $\mathbf{x}^*(\theta)$ that maximises $f(\theta,\mathbf{x})$, but, at the same time, when $p=\dim\theta>1$, a sequence too concentrated gives a singular design matrix, and thus does not yield consistent estimates. Using Bayesian estimation instead of LS does not help much since the arguments used in [15] to prove convergence of $\hat\theta^k$ cannot be used if $\xi_k$, the discrete measure having support points $\mathbf{x}_i$, $i=1,\ldots,k$, converges to a singular design. The following result is proved in [20].

**Theorem 2.1.** *Assume that sequence of weights $\{\alpha_k\}$ in (1.5) is such that $(\alpha_k/k)\log\alpha_k$ decreases monotonically and $\alpha_k/(\log k)^{1+\delta}$ increases monotonically to $\infty$ for some $\delta>0$. Then, the sequence $\{\mathbf{x}_k\}$ generated by (1.5,2.1) is such that $\hat\theta^k\to\bar\theta$, $(1/k)\sum_{i=1}^k \mathbf{r}^\top(\mathbf{x}_i)\bar\theta \to \mathbf{r}^\top(\mathbf{x}^*)\bar\theta$ and $\xi_k \xrightarrow{w} \xi_{\mathbf{x}^*}$ (in the sense of weak convergence of measures) almost surely (a.s.) as $k\to\infty$, with $\mathbf{x}^*=\mathbf{x}^*(\bar\theta)=\arg\max_{\mathbf{x}\in\mathcal{X}}\mathbf{r}^\top(\mathbf{x})\bar\theta$ and $\xi_{\mathbf{x}}$ the discrete measure that puts weight 1 at the point $\mathbf{x}$.*

One can note that from the Lebesgue dominated convergence theorem, Theorem 2.1 implies

$$E\{(1/k)\sum_{i=1}^{k}\mathbf{r}^\top(\mathbf{x}_i)\bar{\theta}\} \to E\{\mathbf{r}^\top[\mathbf{x}^*(\bar{\theta})]\bar{\theta}\}$$

when $\bar{\theta}$ has a prior $\pi(\bar{\theta})$ supported on $\Theta$ compact. Theorem 2.1 remains valid when $\hat{\theta}^k$ is replaced by

$$\tilde{\theta}^k = \arg\min_{\theta\in\Theta}\sum_{i=1}^{k}[y_i - \mathbf{r}^\top(\mathbf{x}_i)\theta]^2 + (\theta-\hat{\theta}^0)^\top\Omega^{-1}(\theta-\hat{\theta}^0)$$

and $\mathbf{M}_k$ by $\mathbf{M}'_k = \mathbf{M}_k + \Omega^{-1}$ in (2.1), with $\Omega$ non negative definite. Also, Theorem 2.1 is still valid with $\Theta = I\!R^p$ provided that the errors $\epsilon_i$ are independently identically distributed (i.i.d.) Gaussian variables $\mathcal{N}(0,\sigma^2)$. Indeed, for $k > K_0$ the LS estimator $\hat{\theta}^k$ coincides with the Bayesian estimator $E\{\theta|\mathcal{F}_k\}$ for the prior $\mathcal{N}(\hat{\theta}^{K_0},\sigma^2\mathbf{M}_{K_0}^{-1})$, with $\mathbf{M}_{K_0}$ positive definite. Then, from the martingale convergence theorem, a.s. $\hat{\theta}^\infty = \lim_{k\to\infty}\hat{\theta}^k$ exists and is finite, $\mathbf{r}^\top(\mathbf{x})\hat{\theta}^\infty$ is bounded on $\mathcal{X}$ a.s., and the same proof as in [20] is valid. Another situation where Theorem 2.1 is valid with $\Theta = I\!R^p$ is when the errors $\epsilon_i$ are bounded and $\hat{\theta}^k$ is replaced by $\tilde{\theta}^k$ with $\Omega$ positive definite. Indeed, one can then easily show that $\|\tilde{\theta}^k - \bar{\theta}\|$ remains bounded for all $k$, and again the same proof as in [20] applies.

2.2. ***L*-optimum penalty.** Using an idea similar to previous section, one can relate the penalty function to $L$-optimum design; that is, use

$$d_k(\mathbf{x}) = d_k^L(\mathbf{x}) = \mathbf{r}^\top(\mathbf{x})\mathbf{M}_k^{-1}\mathbf{H}\,\mathbf{M}_k^{-1}\mathbf{r}(\mathbf{x}) \tag{2.5}$$

in (1.5), with $\mathbf{H}$ a non negative definite matrix. It is shown in [23] that when $\mathbf{H}$ is positive definite and the sequence $\{\mathbf{x}_k\}$ is generated by $\mathbf{x}_{k+1} = \arg\max_{\mathbf{x}\in\mathcal{X}} d_k^L(\mathbf{x})$, the design measure $\xi_k$ converges to a $L$-optimum design measure $\xi_L^*$ that minimises $\mathrm{trace}\,\mathbf{H}\,\mathbf{I}^{-1}(\xi)$, where $\mathbf{I}(\xi) = \int_{\mathcal{X}}\mathbf{r}(\mathbf{x})\mathbf{r}^\top(\mathbf{x})\xi(d\mathbf{x})$. Further work is required to check if a property similar to Theorem 2.1 can be obtained in this case.

A case that has retained much attention in when the design objective is the estimation of the point $\mathbf{x}^*$ where $f(\theta,\mathbf{x})$ achieves its maximum, see [21], especially when $f$ is a quadratic function of a scalar variable $x$, see, *e.g.*, [8]. Assume that

$$f(\theta,x) = \theta_0 + \theta_1 x + \theta_2 x^2/2\,, \tag{2.6}$$

with $x\in\mathcal{X}$, a compact subset of the real line. One has $x^*(\theta) = -\theta_1/\theta_2$, and, in the case where the errors $\epsilon_i$ are i.i.d., the asymptotic variance of $x^*(\hat{\theta}^k)$, with $\hat{\theta}^k$ given by (2.4), is proportional to $\mathbf{c}^\top\mathbf{M}_k^{-1}\mathbf{c}$, with

$$\mathbf{c} = \mathbf{c}(\theta) = \frac{\partial x^*(\theta)}{\partial\theta} = (-1/\theta_2)\begin{pmatrix}0 & 1 & x^*\end{pmatrix}^\top .$$

Choosing the $\mathbf{x}_k$'s to estimate $\mathbf{x}^*(\theta)$ corresponds to $c$-optimum design, that is, to $L$-optimum design with $\mathbf{H}$ given by the rank-one matrix $\mathbf{c}\mathbf{c}^\top$. Note that the dependence of $\mathbf{c}$ in $\theta$ makes the problem nonlinear. A Bayesian approach is used in [2, 5], based on a design criterion of the type $E\{\mathbf{c}^\top\mathbf{M}_k^{-1}\mathbf{c}\}$, where $E\{\cdot\}$ denotes the expectation w.r.t. $\theta$ for a given prior. Sequential approaches are considered in [13, 19]. One can also refer to [1] for the use of $c$-optimal design in the context of Bayesian estimation and to [4] for a survey on Bayesian experimental design. Following (2.5), a penalty function related to $c$-optimal design is thus

$$d_k(\mathbf{x}) = d_k^c(\mathbf{x}) = [\mathbf{r}^\top(\mathbf{x})\mathbf{M}_k^{-1}\mathbf{c}(\hat{\theta}^k)]^2\,. \tag{2.7}$$

Another approach, used in [21], is to derive the design criterion from the construction of a Bayesian risk. Assume that $\theta$ has a normal prior $\mathcal{N}(\hat{\theta}^0,\sigma^2\Omega)$, that the errors $\epsilon_i$ are i.i.d. $\mathcal{N}(0,\sigma^2)$ and that the discount factors $w_i$ satisfy $w_i = 1$ for $i = N+1$ and $w_i = 0$ otherwise. When $\mathbf{x}_1,\ldots,\mathbf{x}_N$ are all chosen at the same time (non sequential design), this corresponds to the following $L_B$-optimal design problem:

$$\text{minimise}\ \ \mathrm{trace}\,\mathbf{H}(\hat{\theta}^0)\,(\mathbf{M}_k+\Omega^{-1})^{-1}$$

with

$$\mathbf{H}(\hat{\theta}) = \frac{\partial^2 f[\theta,\mathbf{x}^*(\theta)]}{\partial\theta\partial\theta^\top}_{|\hat{\theta}}\,.$$

The matrix $\mathbf{H}$ can easily be proved to be non negative definite when $f$ is linear in $\theta$, see [21], and

$$\mathbf{H}(\hat{\theta}) = \frac{\partial \mathbf{r}(\mathbf{x})}{\partial \mathbf{x}^\top}_{|\mathbf{x}^*(\hat{\theta})} \frac{\partial \mathbf{x}^*(\theta)}{\partial \theta^\top}_{|\hat{\theta}}, \tag{2.8}$$

which can be expressed analytically when $f$ is quadratic in $\mathbf{x} \in I\!R^q$, $q \geq 1$. For instance, in the case where $f$ is given by (2.6) (with $\theta_2 < 0$ in order to have a function concave in $x$), one gets

$$\mathbf{H}(\hat{\theta}^0) = (-1/\hat{\theta}_2^0) \begin{pmatrix} 0 & 0 & 0 \\ 0 & 1 & \mathbf{x}^*(\hat{\theta}^0) \\ 0 & \mathbf{x}^*(\hat{\theta}^0) & [\mathbf{x}^*(\hat{\theta}^0)]^2 \end{pmatrix} = -\hat{\theta}_2^0\, \mathbf{c}(\hat{\theta}^0)\mathbf{c}^\top(\hat{\theta}^0)\,.$$

This suggests substitution of $\mathbf{H}(\hat{\theta}^k)$ for $\mathbf{H}$ in (2.5) in the case of sequential design. Again, in the infinite horizon case with no discount the choice of a weighting sequence $\{\alpha_k\}$ in (1.5) ensuring convergence to $\mathbf{x}^*(\hat{\theta}^k)$ to $\mathbf{x}^*(\bar{\theta})$ and of $\xi_k$ to $\xi_{\mathbf{x}^*(\bar{\theta})}$ remains an open issue.

## 3. Linear response optimisation with finite horizon

The following Lemma will be used to construct an approximate solution to the problem (1.4).

**Lemma 3.1.** *Let $g(\mathbf{x})$ and $h(\mathbf{x})$ be two times continuously differentiable functions on $\mathcal{X}$, a compact set of $I\!R^q$. Assume that $g$ has a unique global maximum at $\mathbf{x}^*$, an interior point of $\mathcal{X}$, with $\partial^2 g(\mathbf{x})/\partial\mathbf{x}\partial\mathbf{x}^\top_{|\mathbf{x}^*}$ negative definite, and let $\hat{\mathbf{x}}$ denote the point where $f(\mathbf{x}) = g(\mathbf{x}) + uh(\mathbf{x})$ reaches its maximum in $\mathcal{X}$. Then, $\|\hat{\mathbf{x}} - \mathbf{x}^*\| = O(u)$ and $|f(\mathbf{x}^*) - f(\hat{\mathbf{x}})| = O(u^2)$, $u \to 0$.*

*Proof.* For $u$ small enough, $\hat{\mathbf{x}}$ is an interior point of $\mathcal{X}$ so that

$$\begin{aligned} \frac{\partial f(\mathbf{x})}{\partial \mathbf{x}^\top}_{|\hat{\mathbf{x}}} = 0 &= \frac{\partial g(\mathbf{x})}{\partial \mathbf{x}^\top}_{|\mathbf{x}^*} + (\hat{\mathbf{x}} - \mathbf{x}^*)^\top \frac{\partial^2 g(\mathbf{x})}{\partial \mathbf{x}\partial \mathbf{x}^\top}_{|\mathbf{x}^*} + u\frac{\partial h(\mathbf{x})}{\partial \mathbf{x}^\top}_{|\hat{\mathbf{x}}} + o(\|\hat{\mathbf{x}} - \mathbf{x}^*\|) \\ &= (\hat{\mathbf{x}} - \mathbf{x}^*)^\top \frac{\partial^2 g(\mathbf{x})}{\partial \mathbf{x}\partial \mathbf{x}^\top}_{|\mathbf{x}^*} + u\frac{\partial h(\mathbf{x})}{\partial \mathbf{x}^\top}_{|\hat{\mathbf{x}}} + o(\|\hat{\mathbf{x}} - \mathbf{x}^*\|)\,, \end{aligned}$$

and $\|\hat{\mathbf{x}} - \mathbf{x}^*\| = O(u)$. Therefore,

$$\begin{aligned} f(\mathbf{x}^*) &= f(\hat{\mathbf{x}}) + (\mathbf{x}^* - \hat{\mathbf{x}})^\top \frac{\partial f(\mathbf{x})}{\partial \mathbf{x}^\top}_{|\hat{\mathbf{x}}} + \frac{1}{2}(\mathbf{x}^* - \hat{\mathbf{x}})^\top \frac{\partial^2 f(\mathbf{x})}{\partial \mathbf{x}\partial \mathbf{x}^\top}_{|\hat{\mathbf{x}}}(\mathbf{x}^* - \hat{\mathbf{x}}) + o(\|\hat{\mathbf{x}} - \mathbf{x}^*\|^2) \\ &= f(\hat{\mathbf{x}}) + O(u^2)\,. \end{aligned}$$

□

Next theorem shows how to construct an approximate solution to problem (1.4).

**Theorem 3.2.** *Assume that $w_i > 0$, $i = 1, \ldots, N$ and $w_i = 0$ otherwise; that $f$ is linear in $\theta$, that is, $f(\theta, \mathbf{x}) = \mathbf{r}^\top(\mathbf{x})\theta$, with $\mathbf{r}$ two times continuously differentiable w.r.t. $\mathbf{x}$; that the errors $\epsilon_i$ are i.i.d. $\mathcal{N}(0, \sigma^2)$ and the prior distribution for $\theta$ is normal $\mathcal{N}(\hat{\theta}^0, \sigma^2\Omega)$. Denote $\mathbf{x}^*(\theta) = \arg\max_{\mathbf{x}\in\mathcal{X}} \mathbf{r}^\top(\mathbf{x})\theta$ and $\tilde{\theta}^k = E\{\theta|\mathcal{F}_k\}$, and assume that $f(\tilde{\theta}^j, \mathbf{x})$ has a unique global maximum at $\mathbf{x}^*(\tilde{\theta}^j)$ which lies in the interior of $\mathcal{X}$, with $\partial^2 f(\tilde{\theta}^j, \mathbf{x})/\partial\mathbf{x}\partial\mathbf{x}^\top_{|\mathbf{x}^*(\tilde{\theta}^j)}$ negative definite, $j = 0, \ldots, N-2$. Define $j_{k+1}(\mathbf{x})$ as the expected optimal gain to go at step $k$ when $\mathbf{x}$ is applied:*

$$j_{k+1}(\mathbf{x}) = E\{w_{k+1} f(\theta, \mathbf{x}) + \max_{\mathbf{z}\in\mathcal{X}} w_{k+2} j_{k+2}(\mathbf{z})|\mathcal{F}_k\}\,,\ j_N(\mathbf{x}) = E\{w_N f(\theta, \mathbf{x})|\mathcal{F}_{N-1}\}\,.$$

*It satisfies*

$$j_{k+1}(\mathbf{x}) = J_{k+1}(\mathbf{x}) + O(\sigma^4)\,,\ k = 0, \ldots, N-2\,, \tag{3.1}$$

*with*

$$\begin{aligned} J_{k+1}(\mathbf{x}) &= (w_N + \cdots + w_{k+2})\left\{\mathbf{r}^\top[\mathbf{x}^*(\tilde{\theta}^k)]\tilde{\theta}^k + \frac{\sigma^2}{2}\mathrm{trace}\,[\mathbf{H}(\tilde{\theta}^k)(\Omega^{-1} + \mathbf{M}_k)^{-1}]\right\} \\ &\quad -\frac{\sigma^2}{2}\mathrm{trace}\left\{\mathbf{H}(\tilde{\theta}^k)\sum_{j=0}^{N-k-2} w_{k+j+2}[\Omega_{j,k}^{-1} + \mathbf{r}(\mathbf{x})\mathbf{r}^\top(\mathbf{x})]^{-1}\right\} + w_{k+1}\mathbf{r}^\top(\mathbf{x})\tilde{\theta}^k\,, \end{aligned} \tag{3.2}$$

*where* $\Omega_{j,k} = \left\{\Omega^{-1} + \mathbf{M}_k + j\mathbf{r}[\mathbf{x}^*(\tilde\theta^k)]\mathbf{r}^\top[\mathbf{x}^*(\tilde\theta^k)]\right\}^{-1}$ *and* $\mathbf{M}_k$, $\mathbf{H}(\theta)$ *are respectively given by (2.2), (2.8). Moreover, the strategy defined by* $\mathbf{x}_N = \mathbf{x}^*(\tilde\theta^{N-1})$ *and* $\mathbf{x}_{k+1} = \arg\max_{\mathbf{x}\in\mathcal{X}} J_{k+1}(\mathbf{x})$, $k = 0,\ldots,N-2$, *satisfies*

(3.3)
$$\mathbf{x}_{k+1} = \arg\max_{\mathbf{x}\in\mathcal{X}} \left\{ w_{k+1}\mathbf{r}^\top(\mathbf{x})\tilde\theta^k + \frac{\sigma^2}{2}\sum_{j=0}^{N-k-2} w_{k+j+2}\frac{\mathbf{r}^\top(\mathbf{x})\Omega_{j,k}\mathbf{H}(\tilde\theta^k)\Omega_{j,k}\mathbf{r}(\mathbf{x})}{1+\mathbf{r}^\top(\mathbf{x})\Omega_{j,k}\mathbf{r}(\mathbf{x})} \right\}, \ k = 0,\ldots,N-2,$$

$$E\{\sum_{i=k+1}^{N} w_i f(\theta,\mathbf{x}_i)|\mathcal{F}_k\} = J_{k+1}(\mathbf{x}_{k+1}) + O(\sigma^4), \ k = 0,\ldots,N-2, \tag{3.4}$$

*and*

$$\|\hat{\mathbf{x}}_{k+1} - \mathbf{x}_{k+1}\| = O(\sigma^4), \ k = 0,\ldots,N-2, \ \hat{\mathbf{x}}_N = \mathbf{x}_N, \tag{3.5}$$

*where* $\hat{\mathbf{x}}_{k+1} = \arg\max_{\mathbf{x}\in\mathcal{X}} j_{k+1}(\mathbf{x})$ *corresponds to the optimum strategy.*

*Proof.* Straightforward matrix manipulation shows that $\mathbf{x}_{k+1}$ given by (3.3) maximises (3.2). We prove (3.1) and (3.4) by backward induction on $k$. For $k = N-2$, we have

$$\begin{aligned} j_{N-1}(\mathbf{x}) &= w_N E\{\mathbf{r}^\top[\mathbf{x}^*(\tilde\theta^{N-1})]\theta|\mathcal{F}_{N-2}\} + w_{N-1}\mathbf{r}^\top(\mathbf{x})\tilde\theta^{N-2} \\ &= w_N E\{\mathbf{r}^\top[\mathbf{x}^*(\tilde\theta^{N-1})]\tilde\theta^{N-1}|\mathcal{F}_{N-2}\} + w_{N-1}\mathbf{r}^\top(\mathbf{x})\tilde\theta^{N-2}. \end{aligned}$$

Since $\mathbf{x}^*(\tilde\theta^{N-2})$ is an interior point of $\mathcal{X}$, a second-order Taylor expansion around $\tilde\theta^{N-2}$ similar to that used in [21] gives

$$\begin{aligned} j_{N-1}(\mathbf{x}) &= w_N\{\mathbf{r}^\top[\mathbf{x}^*(\tilde\theta^{N-2})]\tilde\theta^{N-2} + \frac{\sigma^2}{2}\mathrm{trace}\,[\mathbf{H}(\tilde\theta^{N-2})(\Omega^{-1}+\mathbf{M}_{N-2})^{-1}]\} \\ &\quad -w_N\frac{\sigma^2}{2}\mathrm{trace}\,\{\mathbf{H}(\tilde\theta^{N-2})\left[\mathbf{r}(\mathbf{x})\mathbf{r}^\top(\mathbf{x}) + \Omega^{-1} + \mathbf{M}_{N-2}\right]^{-1}\} + w_{N-1}\mathbf{r}^\top(\mathbf{x})\tilde\theta^{N-2} + O(\sigma^4), \end{aligned}$$

which proves (3.1) for $k = N-2$. Since $E\{\sum_{i=N-1}^N w_i f(\theta,\mathbf{x}_i)|\mathcal{F}_{N-2}\} = j_{N-1}(\mathbf{x}_{N-1})$, it also proves (3.4) for $k = N-2$.

Assume that (3.1) is true at step $k$. At step $k-1$ we have $j_k(\mathbf{x}) = E\{w_k f(\theta,\mathbf{x}) + \max_{\mathbf{z}\in\mathcal{X}} j_{k+1}(\mathbf{z})|\mathcal{F}_{k-1}\}$. Using Lemma 3.1 with $u = \sigma^2$, we get

$$j_k(\mathbf{x}) = w_k\mathbf{r}^\top(\mathbf{x})\tilde\theta^{k-1} + E\{J_{k+1}[\mathbf{x}^*(\tilde\theta^k)]|\mathcal{F}_{k-1}\} + O(\sigma^4).$$

Grouping the terms $\mathbf{r}^\top[\mathbf{x}^*(\tilde\theta^k)]\tilde\theta^k$ and using a second-order Taylor expansion around $\tilde\theta^{k-1}$, we obtain

$$\begin{aligned} j_k(\mathbf{x}) &= (w_N + \cdots + w_{k+2} + w_{k+1})\left\{\mathbf{r}^\top[\mathbf{x}^*(\tilde\theta^{k-1})]\tilde\theta^{k-1} + \frac{\sigma^2}{2}\mathrm{trace}\,[\mathbf{H}(\tilde\theta^{k-1})(\Omega^{-1}+\mathbf{M}_{k-1})^{-1}]\right\} \\ &\quad -(w_N + \cdots + w_{k+2} + w_{k+1})\frac{\sigma^2}{2}\mathrm{trace}\,\{\mathbf{H}(\tilde\theta^{k-1})[\Omega^{-1}+\mathbf{M}_{k-1}+\mathbf{r}(\mathbf{x})\mathbf{r}^\top(\mathbf{x})]^{-1}\} \\ &\quad +(w_N + \cdots + w_{k+2})\frac{\sigma^2}{2}\mathrm{trace}\,\{\mathbf{H}(\tilde\theta^{k-1})[\Omega^{-1}+\mathbf{M}_{k-1}+\mathbf{r}(\mathbf{x})\mathbf{r}^\top(\mathbf{x})]^{-1}\} \\ &\quad -\frac{\sigma^2}{2}\mathrm{trace}\left\{\mathbf{H}(\tilde\theta^{k-1})\sum_{j=0}^{N-k-2} w_{k+j+2}[\Omega_{j+1,k-1}^{-1} + \mathbf{r}(\mathbf{x})\mathbf{r}^\top(\mathbf{x})]^{-1}\right\} + w_k\mathbf{r}^\top(\mathbf{x})\tilde\theta^{k-1} + O(\sigma^4). \end{aligned}$$

A simplification of the terms on the last three lines gives $j_k(\mathbf{x}) = J_k(\mathbf{x}) + O(\sigma^4)$, which proves (3.1). Since $\mathbf{x}_{k+1}$ maximises (3.2), similar arguments using (3.4) and Lemma 3.1 give $E\{\sum_{i=k}^N w_i f(\theta,\mathbf{x}_i)|\mathcal{F}_{k-1}\} = J_k(\mathbf{x}_k) + O(\sigma^4)$, and (3.4) is proved.

Finally, since $\mathbf{x}_{k+1}$ maximises $J_{k+1}(\mathbf{x})$, (3.1) and Lemma 3.1 with $u = \sigma^4$ give (3.5). □

*Remark* 3.3. The assumptions on $f(\tilde{\theta}^j,\mathbf{x})$ and $\mathbf{x}^*(\tilde{\theta}^j)$ for $j=0,\ldots,N-2$, in Theorem 3.2 are most often difficult, if not impossible, to check beforehand. Note, however, that it is always possible to apply the strategy and check them afterwards: if they are satisfied, then the Theorem applies.

The property stated in Theorem 3.2 suggests a simpler suboptimal strategy, as given in the following corollary.

**Corollary 3.4.** *Under the same conditions, and with the same notations, as in Theorem 3.2, the strategy defined by* $\mathbf{x}'_N=\mathbf{x}^*(\tilde{\theta}^{N-1})$ *and*

(3.6)

$$\mathbf{x}'_{k+1}=\arg\max_{\mathbf{x}\in\mathcal{X}}\left\{w_{k+1}\mathbf{r}^\top(\mathbf{x})\tilde{\theta}^k+\frac{\sigma^2}{2}\sum_{j=1}^{N-k-1} j\,w_{k+j+1}\,\frac{\mathbf{r}^\top(\mathbf{x})\Omega_{0,k}\mathbf{H}(\tilde{\theta}^k)\Omega_{0,k}\mathbf{r}(\mathbf{x})}{1+j\mathbf{r}^\top(\mathbf{x})\Omega_{0,k}\mathbf{r}(\mathbf{x})}\right\}\,,\ k=0,\ldots,N-2\,,$$

*is approximately optimal in the following sense:*

$$\max_{\mathbf{x}\in\mathcal{X}} j_{k+1}(\mathbf{x})-E\{\sum_{i=k+1}^{N} w_i f(\theta,\mathbf{x}'_i)|\mathcal{F}_k\}=O(\sigma^4)\,, \tag{3.7}$$

$$|\hat{\mathbf{x}}_{k+1}-\mathbf{x}'_{k+1}|=O(\sigma^2)\,, \tag{3.8}$$

*for* $k=0,\ldots,N-1$.

*Proof.* We first prove that $E\{\sum_{i=k+1}^N w_i f(\theta,\mathbf{x}'_i)|\mathcal{F}_k\}=J_{k+1}(\mathbf{x}'_{k+1})+O(\sigma^4)$, for $k=N-2,\ldots,1$.

For $k=N-2$ we have again $E\{\sum_{i=N-1}^N w_i f(\theta,\mathbf{x}'_i)|\mathcal{F}_{N-2}\}=j_{N-1}(\mathbf{x}'_{N-1})$ which equals $J_{N-1}(\mathbf{x}'_{N-1})+O(\sigma^4)$ from Theorem 3.2. Assume that the property is true at step $k$. At step $k-1$ we have

$$E\{w_k f(\theta,\mathbf{x})+\sum_{i=k+1}^N w_i f(\theta,\mathbf{x}'_i)|\mathcal{F}_{k-1}\}=w_k\mathbf{r}^\top(\mathbf{x})\tilde{\theta}^{k-1}+E\{J_{k+1}(\mathbf{x}'_{k+1})|\mathcal{F}_{k-1}\}+O(\sigma^4)\,,$$

and easy matrix manipulation using (3.6) and (3.2) shows that $\mathbf{x}'_{k+1}=\arg\max_{\mathbf{x}\in\mathcal{X}}[J_{k+1}(\mathbf{x})+\sigma^2h(\mathbf{x})]$, for some $h(\mathbf{x})$. Lemma 3.1 with $u=\sigma^2$ gives $J_{k+1}(\mathbf{x}'_{k+1})=J_{k+1}[\mathbf{x}^*(\tilde{\theta}^k)]+O(\sigma^4)$, and similarly to the proof of Theorem 3.2, $E\{w_k f(\theta,\mathbf{x})+\sum_{i=k+1}^N w_i f(\theta,\mathbf{x}'_i)|\mathcal{F}_{k-1}\}=J_k(\mathbf{x})+O(\sigma^4)$.

Finally, since the optimal strategy $\hat{\mathbf{x}}_{k+1}$ maximises $j_{k+1}(\mathbf{x})=J_{k+1}(\mathbf{x})+O(\sigma^4)$, whereas $\mathbf{x}'_{k+1}$ maximises a function that takes the form $J_{k+1}(\mathbf{x})+\sigma^2h(\mathbf{x})$, Lemma 3.1 gives (3.7-3.8). □

When $w_i=1$, $i=1,\ldots,N$ and $w_i=0$ otherwise, with $N$ large, the strategy (3.6) can be further approximated by

$$\mathbf{x}''_{k+1}=\arg\max_{\mathbf{x}\in\mathcal{X}}\left\{\mathbf{r}^\top(\mathbf{x})\tilde{\theta}^k+(N-k-1)\frac{\sigma^2}{2}\frac{\mathbf{r}^\top(\mathbf{x})\Omega_{0,k}\mathbf{H}(\tilde{\theta}^k)\Omega_{0,k}\mathbf{r}(\mathbf{x})}{\mathbf{r}^\top(\mathbf{x})\Omega_{0,k}\mathbf{r}(\mathbf{x})}\right\}\,,\ k=0,\ldots,N-2\,, \tag{3.9}$$

which has the form (1.5).

*Remark* 3.5. It is clear from the proof of Corollary 3.4 that properties similar to (3.7-3.8) can be obtained for other strategies than (3.6). What makes this strategy attractive is that it amounts to substituting $\mathbf{r}(\mathbf{x})$ for $\mathbf{r}[\mathbf{x}(\tilde{\theta}^k)]$ in $J_{k+1}(\mathbf{x})$ to construct $\mathbf{x}'_{k+1}$. This makes the rule (3.6) suboptimal compared to (3.3) that directly maximises $J_{k+1}(\mathbf{x})$ (compare (3.8) to (3.5)), but, on the other hand, $\mathbf{r}(\mathbf{x}'_{k+1})$ can be expected to be close to $\mathbf{r}[\mathbf{x}(\tilde{\theta}^k)]$ and the loss can be expected to be small.

3.1. **Example 1.** We assume that $f(\theta,x)$ is given by (2.6), with $\mathcal{X}=[-1,1]$, and that the observations $y_k$ are generated by (1.1) for $\theta=\bar{\theta}=(0\ 3.2\ -8)^\top$ with the errors $\epsilon_k$ i.i.d. $\mathcal{N}(0,\sigma^2)$, $\sigma=1$. The prior for $\theta$ is $\mathcal{N}(\hat{\theta}^0,\sigma^2\Omega)$, with $\hat{\theta}^0=(2\ -4\ -1)^\top$ and $\Omega=10^6\ \mathbf{I}_3$, with $\mathbf{I}_3$ the 3-dimensional identity matrix. Note that these numerical values give a prior guess for $x^*$ at -4, whereas the true location is at 0.4.

We take $w_i=1$, $i=1,\ldots,N$ and $w_i=0$ otherwise, with $N=100$, and compare four different strategies: $S_1$ corresponds to (1.5) with the penalty (2.1) and $\alpha_k=\sigma^2(\log k)^2$, and $S_2,S_3$ and $S_4$ correspond respectively to (3.9), (3.6) and (3.3). Table 1 presents the results obtained for 100 independent

| | mean | std |
|---|---|---|
| $S_1$ | 0.1788 | 0.0523 |
| $S_2$ | 0.3774 | 0.0289 |
| $S_3$ | 0.4234 | 0.0284 |
| $S_4$ | 0.4767 | 0.0484 |

TABLE 1. Empirical means and standard deviations (std) of $\sum_{i=1}^{N} f(\bar{\theta}, x_i)$ for strategies $S_1, \ldots, S_4$ in Example 1 (100 repetitions).

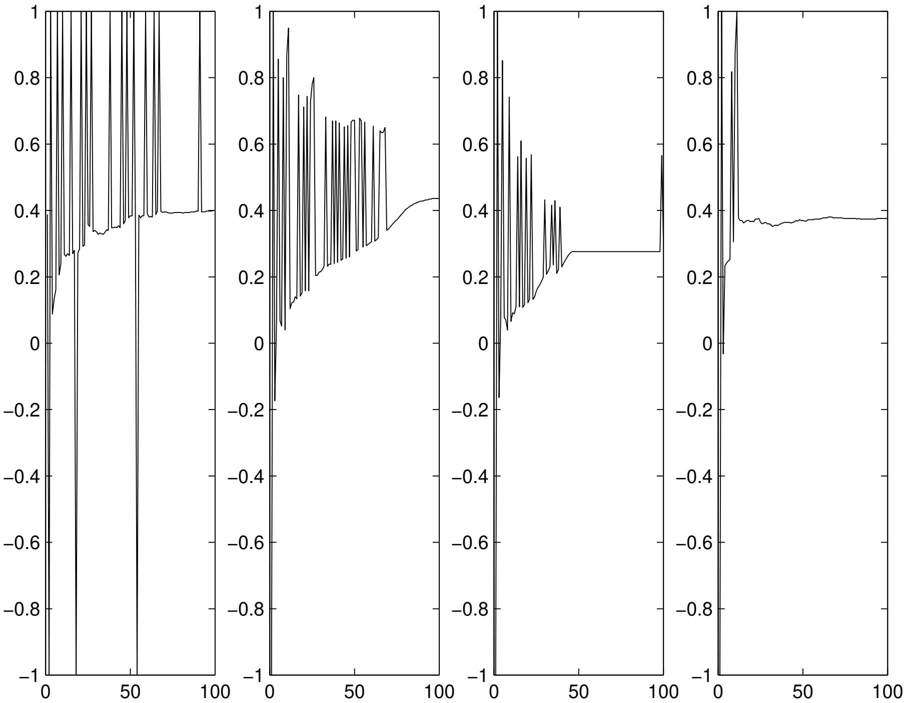

FIGURE 1. Sequences $\{x_k\}$ generated by strategies $S_1$ to $S_4$ (from left to right) in Example 1.

repetitions of the experiment (for each experiment, the same values of observations errors $\epsilon_k$ are used for the four strategies). As expected, performances improve from $S_1$ to $S_4$.

Figure 1 (resp. 2) presents a typical realization of the sequences $\{x_k\}$ (resp. $\{f(\bar{\theta}, x_k)\}$) generated by the four strategies. One can notice in Figure 1 that $x_k$ converges to $x^* = -\bar{\theta}_1/\bar{\theta}_2 = 0.4$ for $S_1$ (see Theorem 2.1), which does not seem to be the case for the other strategies. However, the performance measured in terms of (1.4) is much better for the other strategies, in particular $S_4$ that makes a particularly good compromise between estimation and optimisation, see Figure 2 where the optimum value $f[\bar{\theta}, x^*(\bar{\theta})]$ is indicated by the dashed line.

## 4. EXTENSION TO NONLINEAR SITUATIONS

4.1. **Nonlinear regression.** Whereas Theorem 2.1 relies on Corollary 3 of [18], deriving similar asymptotic results in the case of a nonlinear regression model would require to make use of Theorem 2 of [17]. The conditions in [17] being more stringent than those in [18], one may conjecture that $\alpha_k$ should increase faster than any power of $\log k$ when $k \to \infty$, compare with Theorem 2.1.

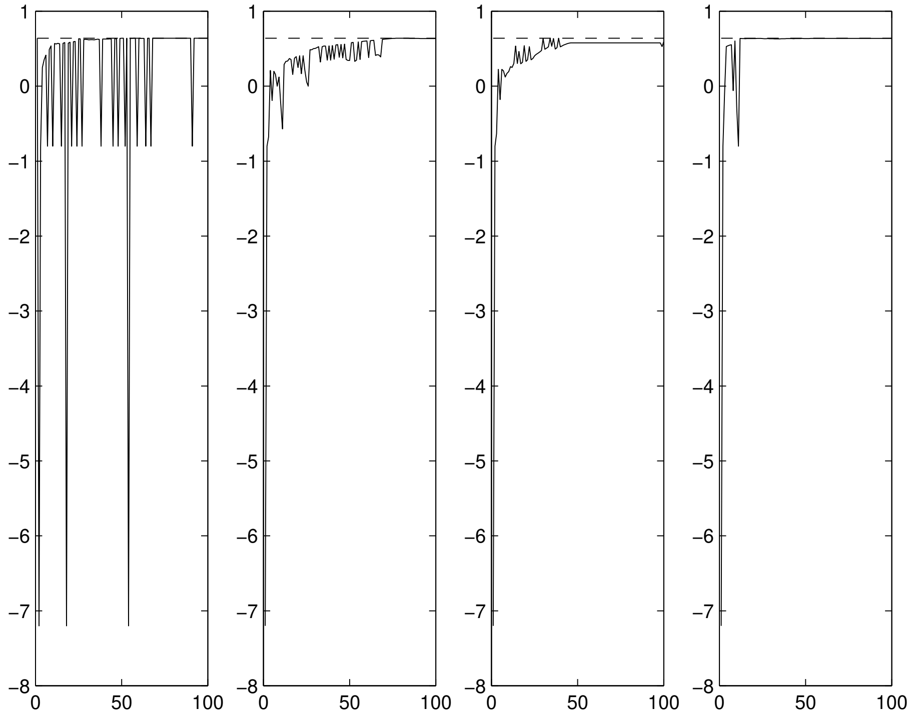


FIGURE 2. Sequences $\{f(\bar{\theta}, x_k)\}$ generated by strategies $S_1$ to $S_4$ (from left to right) in Example 1. The optimum value $f[\bar{\theta}, x^*(\bar{\theta})]$ is indicated by the dashed line.

In the case of finite horizon, the approaches of Section 3 can be used through a linearisation of the model response. Notice however that this implies that terms of order $O(\sigma^2)$ are neglected, so that the properties (3.4) and (3.5) are no longer true.

4.2. **Example 2: Bernouilli trials.** We consider the situation defined by (1.2), with

$$f(\theta, x) = \frac{\theta_1 + \theta_2}{\theta_2} [1 - \exp(-x/\theta_1)] \exp(-x/\theta_2)\,,$$

with $\mathcal{X} = \{x_{\min}, x_{\min} + \delta, x_{\min} + 2\delta, \ldots, x_{\max}\}$, where $x_{\min} = 2, x_{\max} = 100, \delta = 2$, which gives $\#\mathcal{X} = 50$. This may correspond to a dose-response problem, where efficiency is small at low doses $x$ and toxic failures occur at large doses, see, *e.g.*, [16]. We assume that $\theta$ has a normal prior $\mathcal{N}(\hat{\theta}^0, \Omega)$, with $\hat{\theta}_0 = (70\ 70)^\top$ and $\Omega = 10^3 \mathbf{I}_2$. The observations are generated with $\theta = \bar{\theta} = (3\ 50)^\top$. Figure 3 presents the two probabilities $f(\bar{\theta}, x)$ (full line) and $f(\hat{\theta}^0, x)$ (dashed line) as functions of $x$. The prior guess $x^*(\hat{\theta}^0)$ is at 48.52, whereas the true value is at $x^*(\bar{\theta}) = 8.615$.

We estimate $\theta$ by the maximum *a posteriori* estimator and denote

$$\hat{\theta}^k = \arg\max \sum_{i=1}^{k} \log\{y_i f(\theta, x_i) + (1 - y_i)[1 - f(\theta, x_i)]\} - \frac{1}{2}(\theta - \hat{\theta}^0)^\top \Omega^{-1} (\theta - \hat{\theta}^0)\,.$$

The expression of $f(\theta, x)$ gives $x^*(\theta) = -\theta_1 \log[\theta_1/(\theta_1 + \theta_2)]$ and

$$\mathbf{c}(\theta) = \frac{\partial x^*(\theta)}{\partial \theta} = \begin{pmatrix} -\theta_2/(\theta_1 + \theta_2) - \log[\theta_1/(\theta_1 + \theta_2)] \\ \theta_1/(\theta_1 + \theta_2) \end{pmatrix}.$$

The design matrix $\mathbf{M}_k$ is replaced by $\mathbf{M}_k(\hat{\theta}^k)$, with

$$\mathbf{M}_k(\theta) = \sum_{i=1}^{k} \frac{\partial f(\theta, x_i)}{\partial \theta} \frac{\partial f(\theta, x_i)}{\partial \theta^\top} \frac{1}{f(\theta, x_i)[1 - f(\theta, x_i)]}\,,$$

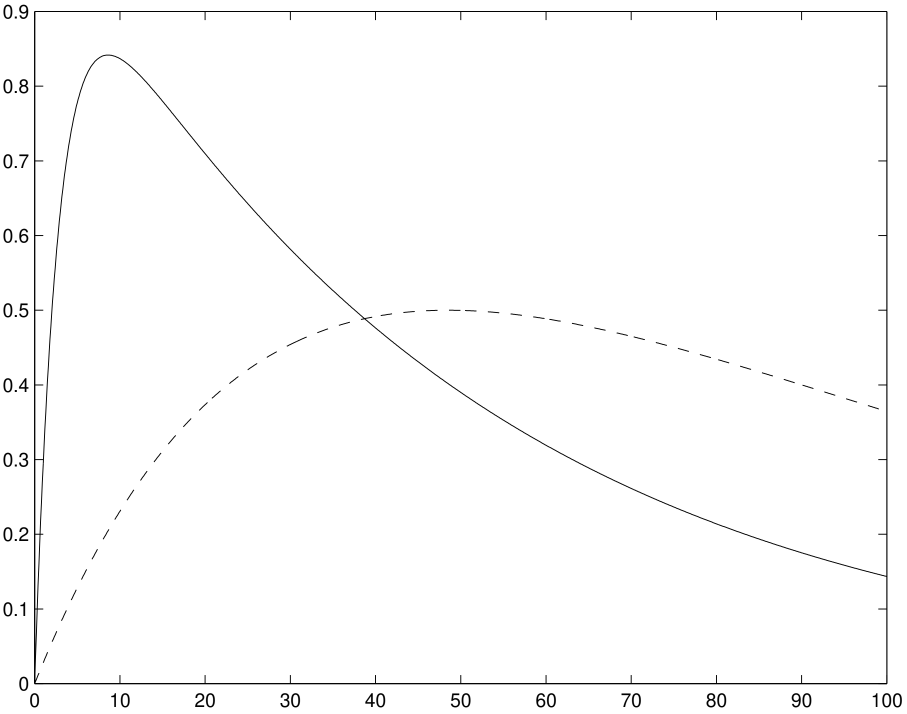


FIGURE 3. Probabilities $f(\bar{\theta}, x)$ (full line) and $f(\hat{\theta}^0, x)$ (dashed line) as functions of $x$ in Example 2.

that would be the Fisher information matrix evaluated at $\theta$ if the design levels $x_i$ were nonrandom constants. Note that it still has the form (2.2), with now

$$\mathbf{r}(x) = \mathbf{r}(\theta, x) = \frac{1}{\sqrt{f(\theta,x)[1-f(\theta,x)]}} \frac{\partial f(\theta, x)}{\partial \theta}.$$

We shall compare four strategies. $S_1$ and $S_2$ are defined by (1.5) with the weights $\alpha_k = k^{1/4}$, and penalty functions (2.1) and (2.7) respectively. $S_3$ corresponds to a randomized Polya urn design, see [6], and $S_4$ to an optimizing up-and-down design, see [16]. $S_3$ is initialized by putting one ball of each label in the urn, and $S_4$ samples by pairs, at $(P_k - \delta/2, P_k + \delta/2)$ at step $k$, and we take $P_1$ at the median of $\mathcal{X}$.

Figure 4 (resp. 5) presents a typical realization of the sequences $\{x_k\}$ (resp. $\{f(\bar{\theta}, x_k)\}$) generated by the four strategies. On Figure 5, the optimum value $f[\bar{\theta}, x^*(\bar{\theta})]$ is indicated by the dotted line. Figure 6 presents histograms of the values of $x_k$ generated by the four strategies.

Convergence to the maximum of $f(\theta, x)$ is faster for $S_1$ and $S_2$ than for $S_3$ and $S_4$. The difference in performance is even stronger when $\delta$ decreases, that is, when the number of points in $\mathcal{X}$ increases. Whereas the value of $\delta$ has no significant effect of $S_1$ and $S_2$, decreasing $\delta$ makes the behaviour of $S_3$ more erratic and increases the time $S_4$ requires to move away from the initial values of $x_k$. This effect is already apparent on Figures 4 to 6. A possible compromise strategy would be to start with $S_3$ or $S_4$ and a large value of $\delta$ (that is, few point in $\mathcal{X}$), and then decrease $\delta$ and switch to $S_1$ or $S_2$.

## 5. CONCLUSIONS AND FURTHER DEVELOPMENTS

We considered the problem of choosing a sequence of values $\mathbf{x}_k$ for $\mathbf{x}$ that maximize some function $f(\mathbf{x})$ in two different situations: $f(\mathbf{x}_k)$ is observed with errors (regression model), or binary responses are observed, the probability of a positive response at $\mathbf{x}_k$ being $f(\mathbf{x}_k)$. Assuming that a parametric form is known for $f$, that is, $f(\mathbf{x}) = f(\theta, \mathbf{x})$ with $\theta$ unknown, different strategies have been suggested.

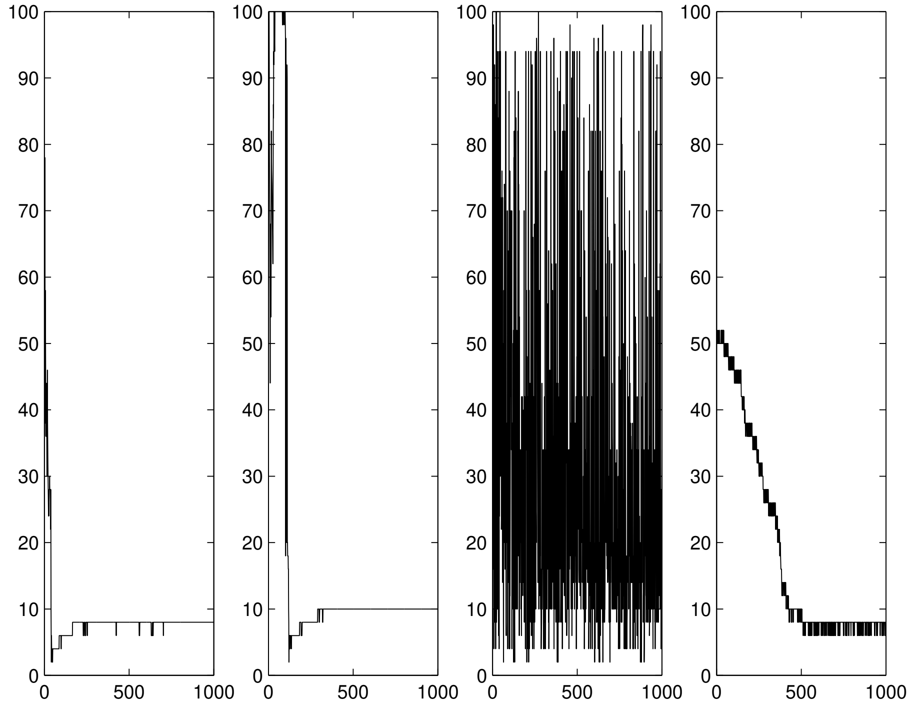


FIGURE 4. Sequences $\{x_k\}$ generated by strategies $S_1$ to $S_4$ (from left to right) in Example 2.

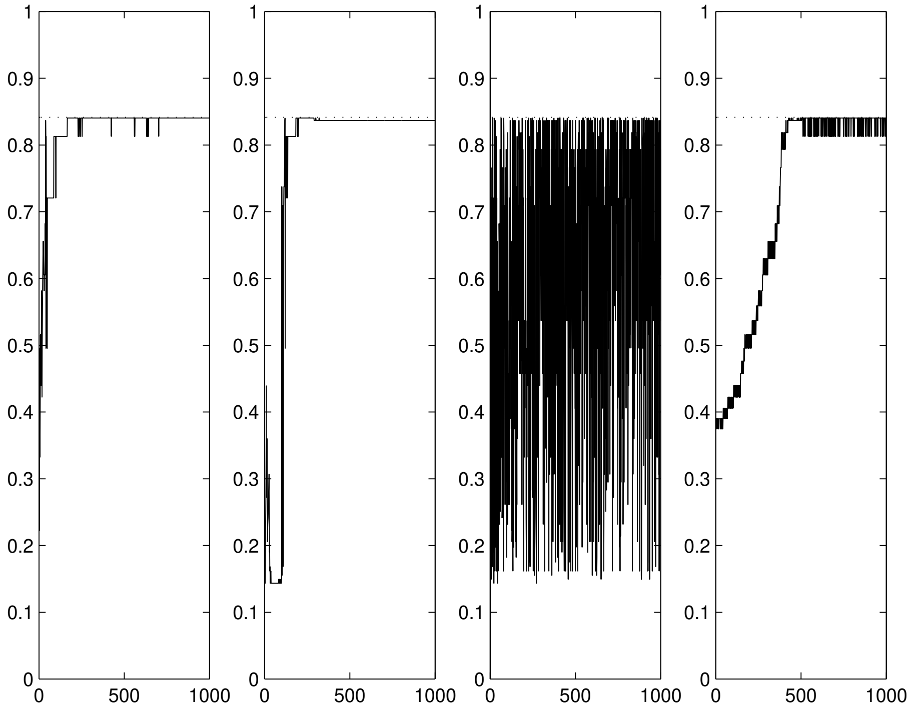


FIGURE 5. Sequences $\{f(\bar{\theta}, x_k)\}$ generated by strategies $S_1$ to $S_4$ (from left to right) in Example 2. The optimum value $f[\bar{\theta}, x^*(\bar{\theta})]$ is indicated by the dotted line.

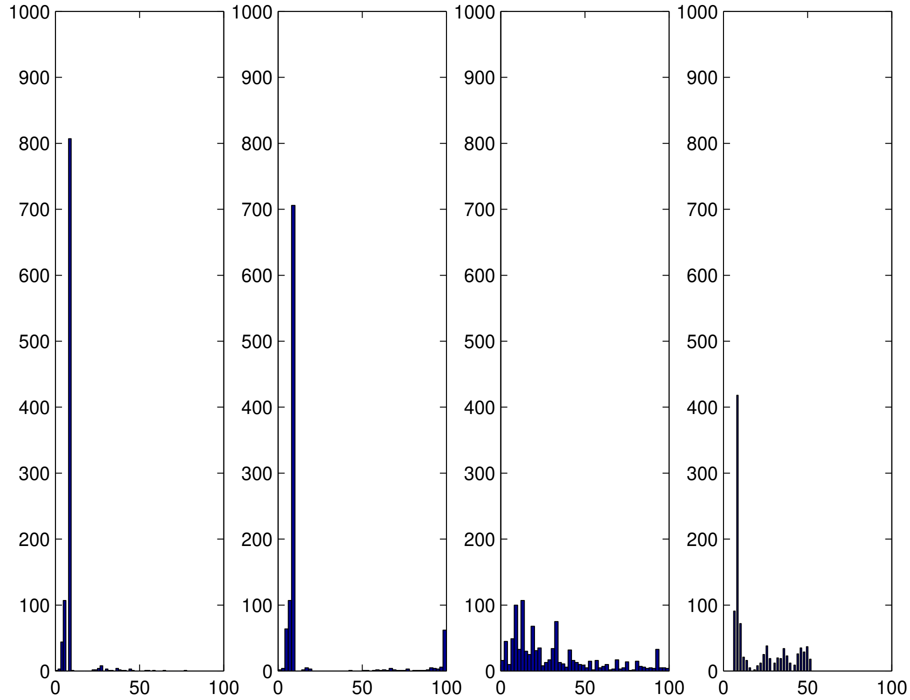


FIGURE 6. Histograms of the values of $x_k$ generated by strategies $S_1$ to $S_4$ (from left to right) in Example 2.

An approximately optimal strategy has been constructed in the case of a linear regression model with finite horizon. In more general situations, we considered sequences constructed according to the rule $\mathbf{x}_{k+1} = \arg\max_{\mathbf{x}} f(\hat{\theta}^k, \mathbf{x}) + \alpha_k d_k(\mathbf{x})$, with $\hat{\theta}^k$ an estimated value of $\theta$ obtained from $(\mathbf{x}_1, y_1), \ldots, (\mathbf{x}_k, y_k)$ and $d_k(\mathbf{x})$ a penalty for poor estimation. This is easily implemented in the case of binary responses, and numerical examples illustrate that such strategies may outperform more traditional ones, like Polya urn designs and up-and-down methods. Such a result should not be a surprise, since methods based on a parametric form of $f$ use more information than model-free approaches. On the other hand, their asymptotic behaviour is more difficult to study, due to the intricate connection between estimation of $\theta$ and optimisation. Only the linear regression case, with a penalty related to $D$-optimum design, seems to have been considered so far, see [20]. Extension to nonlinear regression problems is currently under study. In practice, it might be reasonable to start with a model-free approach, in order to gather enough information about the form of $f$, and then to switch to a parametric approach of the type considered here. This raises many issues (choice of model structure, choice of switching time, robustness with respect to model mis-specification, *etc.*) which deserve further studies.

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