DEPARTMENT OF
STATISTICS

Optimal experiment design

A thesis submitted in partial fulfillment of the requirements for
transfer of status from PRS to DPhil

November 2018

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Contents

Acknowledgements

I have been fortunate, in the first year of my DPhil, to have worked with a number of brilliant people. First and foremost, I would like to acknowledge the support, advice and patience of my supervisor, Yee Whye Teh. Also within Oxford, both Benjamin Bloem-Reddy and Tom Rainforth have been incredibly generous with their time and expertise. Without them, I would have struggled to achieve much in my first year. I would also like to thank Emile Mathieu for his unwavering support and friendship. I am grateful to Noah Goodman for taking a gamble on an unknown DPhil student and supporting my application to Uber Technologies for an internship. Noah's enthusiasm and guidance made my internship a joy, and also set me on a new and exciting research path. I'd like to extend my thanks to Martin Jankowiak and Eli Bingham, as well as the whole Pyro team, for their continued help and support.

Preface

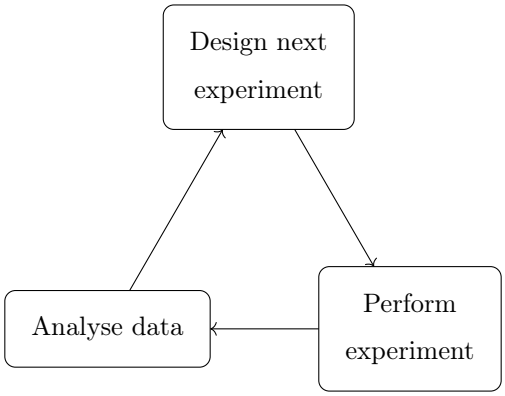
This thesis aims to describe the current work I am undertaking in my DPhil and possible future directions that I may take on broadly related topics. Optimal experiment design only entered into my research in June 2018. The initial work in my DPhil related to a question posed to me by Yee Whye Teh, namely, 'is probabilistic programming useful for Bayesian nonparametrics?'. Our NIPS workshop paper [Bloem-Reddy et al., 2017] and our open source contributions to the language Turing were related to this question. Subsequently, I worked on a project with Benjamin Bloem-Reddy about Bayesian nonparametric models of networks which resulted in a UAI paper and oral presentation [Bloem-Reddy et al., 2018]. During my internship at Uber and the past two months, I have worked on optimal experiment design. Chapter 2 will turn into a paper that we will submit to ICML 2019. We submitted a short version to the NIPS BDL workshop. Following ICML, I plan to continue research on optimal experiment design, as discussed in Chapter 3.

Chapter 1

Introduction and literature review

Much of machine learning is concerned with the analysis of given data. By contrast, the field of optimal experiment design (OED) is concerned with the creation of new data by experimentation or query. In many contexts, careful design of the experiment leads to more efficient learning. The gain in efficiency can be dramatic [Myung et al., 2013]. Learning more efficiently can translate into reduced costs, time saved, fewer lives risked or less damage to the environment.

Idealised active learning can be represented as follows

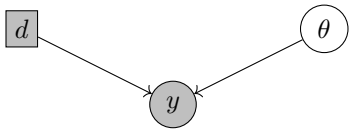


It is only within the context of a proposed data analysis that the optimality or suboptimality of an experiment design can be assessed.

1.1 Foundations

1.1.1 Problem specification

We assume the data analysis model for the experiment takes the form given by the graphical model



in which d represents the (non-random) design of the experiment, θ represents a latent variable and y represents the observed outcome of the experiment. The joint density is

$$p(y, \theta|d) = p(\theta)p(y|\theta, d) \tag{1.1}$$

We can generalize to the sequential design setting by standard Bayesian updating, namely at experiment iteration t, we replace $p(\theta)$ with $p(\theta|d_{1:t-1}, y_{1:t-1})$, where $d_{1:t-1}$ and $y_{1:t-1}$ are the designs and outcomes at previous steps of the experiment. The likelihood $p(y_t|\theta, d_t)$ is assumed unchanged. That is, experimentation does not change the behaviour of the underlying system from time to time, conditional upon θ.

A classical example is the linear regression model. In this case d is a design matrix X_d, θ is a coefficient vector with a Gaussian prior, and $y|\theta, d \sim N(X_d\theta, \sigma^2 I)$.

1.1.2 One-step design

We begin with the case of designing one experiment, after which we will collect and analyse our data. In selecting an optimal experiment design, we must first say with respect to what utility a design is considered optimal. We begin by very briefly discussing a range of choices for utility. We then focus on a natural Bayesian choice of utility, the expected information gain.

Suppose $\mathcal{D}$ is the space of admissible designs. We seek a utility $U : \mathcal{D} \to \mathbb{R}$. An optimal design would then be

$$d^* \in \text{argmax}_{d\in\mathcal{D}}\ U(d). \tag{1.2}$$

Suppose initially that we can assign a real-valued utility $U(y, \theta, d)$ to the event of observing y under design d when the true latent variable was θ. We can average over y to obtain

$$U(\theta, d) = \int p(y|\theta, d)\ U(y, \theta, d)\ dy \tag{1.3}$$

We can deal with θ in various ways

- The Bayesian approach [Chaloner and Verdinelli, 1995] places a prior $p(\theta)$ on θ and takes $U(d) = \int p(\theta)\ U(\theta, d)\ d\theta$
- The minimax approach [Fedorov, 1972] takes $U(d) = \inf_\theta U(\theta, d)$
- The local approach [Pronzato, 2010] begins with an estimate $\hat{\theta}$ and sets $U(d) = U(\hat{\theta}, d)$

Here, we primarily focus on the Bayesian approach. This is not an arbitrary decision, it can be motivated from decision theoretic considerations [Lindley, 1972]. See [Chaloner and Verdinelli, 1995] for further discussion of Bayesian experimental design.

Alternatively, we could take the (matrix-valued) 'utility'

$$U(y, \theta, d) = \left(\frac{\partial}{\partial\theta} \log p(y|\theta, d)\right)^2 \tag{1.4}$$

which leads to the the Fisher Information Matrix, used in many experiment design criteria [Pronzato, 2010], defined as

$$\mathcal{I}(\theta, d) = \int \left(\frac{\partial}{\partial \theta} \log p(y|\theta, d) \right)^2 p(y|\theta, d)\ dy \tag{1.5}$$

We can obtain a scalar utility from $\mathcal{I}(\theta, d)$ by choosing from the 'alphabetical' criteria [Box, 1982] which are defined as

- D-optimality $U(d, \theta) = \det\ \mathcal{I}(\theta, d)$
- A-optimality $U(d, \theta) = \text{tr}\ \mathcal{I}(\theta, d)$
- E-optimality $U(d, \theta) = \max_i \lambda_i$ where λ_i are the eigenvalues of $\mathcal{I}(\theta, d)$

Work dating back to [Lindley, 1956] instead uses an information-theoretic utility[1]

$$U(y, \theta, d) = \log \frac{p(\theta|y, d)}{p(\theta)} = \log \frac{p(y|\theta, d)}{p(y|d)} \tag{1.6}$$

and Lindley established that this is the only form that satisfies certain intuitive properties of an informative experiment. For this reason, we will focus on this utility. See [Chaloner and Verdinelli, 1995, Ryan et al., 2018] for a fuller discussion of utility functions used in experiment design.

With the information-theoretic utility and Bayesian averaging, we arrive at the following form for $U(d)$, called the **expected information gain (EIG)**

$$U(d) = \text{EIG}(d) = \iint p(y, \theta|d) \log \frac{p(\theta|y, d)}{p(\theta)}\ dy\ d\theta \tag{1.7}$$

The EIG can be interpreted in a number of ways

1. As the expectation of information gain. If we define

$$\text{IG}(y, d) = \text{KL}(\ p(\theta|y, d)\ ||\ p(\theta)\ ) \tag{1.8}$$

   then $\text{EIG}(d) = \mathbb{E}_{y \sim p(y|d)}[\text{IG}(y, d)]$.

2. From APE. Define the **average posterior entropy** (APE) as

$$\text{APE}(d) = \iint p(y, \theta|d) \log p(\theta|y, d)\ dy\ d\theta \tag{1.9}$$

$$= -\int p(y|d) H(\ p(\theta|y, d)\ )\, dy \tag{1.10}$$

   where H is the differential entropy. Then

$$\text{EIG}(d) = H(\ p(\theta)\ ) - \text{APE}(d) \tag{1.11}$$

[1] It can also be shown [Chaloner and Verdinelli, 1995] that this utility leads to a (modified form) of D-optimality for linear models.

and the prior entropy is a constant w.r.t. d. Thus EIG maximisation corresponds to APE minimisation.

3. Mutual information. Recall the mutual information is defined as

$$\mathrm{MI}(x, y) = \mathrm{KL}\left(p(x, y) \mid\mid p(x)p(y) \right) \tag{1.12}$$

then we have

$$\begin{aligned} \mathrm{MI}(y, \theta|d) &= \mathrm{KL}\left(p(y, \theta|d) \mid\mid p(y|d)p(\theta) \right) && (1.13)\\ &= \iint p(y, \theta|d) \log \frac{p(y, \theta|d)}{p(\theta)p(y|d)} dy\, d\theta && (1.14)\\ &= \mathrm{EIG}(d). && (1.15) \end{aligned}$$

4. Epistemic uncertainty. The total entropy or uncertainty in response y is

$$H_{tot}(d) = H\left(p(y|d) \right) \tag{1.16}$$

the aleatoric uncertainty under parameter θ is

$$H_{alea}(\theta, d) = H\left(p(y|\theta, d) \right) \tag{1.17}$$

Under prior $p(\theta)$, the expected aleatoric uncertainty is

$$H_{alea}(d) = \mathbb{E}_{\theta \sim p(\theta)} \left[H\left(p(y|\theta, d) \right) \right] \tag{1.18}$$

The epistemic uncertainty, under $p(\theta)$, is

$$\begin{aligned} H_{epist}(d) =& H_{tot}(d) - H_{alea}(d) && (1.19)\\ =& H\left(p(y|d) \right) - \mathbb{E}_{\theta \sim p(\theta)} \left[H\left(p(y|\theta, d) \right) \right] && (1.20)\\ =& -\int p(y|d) \log p(y|d) dy + \iint p(y, \theta|d) \log p(y|\theta, d) dy\, d\theta && (1.21)\\ =& \mathrm{EIG}(d) && (1.22) \end{aligned}$$

We shall see that the connection to mutual information in particular is handy for estimating EIG, because techniques for estimating MI have been developed in the recent past.

1.1.3 Multi-step design

We turn to the case of multi-step, or adaptive, experiment design. In this context, we are able to base the next experiment on previous experimental designs and outcomes. Designing a sequence of multiple experiments, with a view to maximise expected utility can be viewed as a Partially Observable

Markov Decision Process (POMDP) [Marchant et al., 2014], and falls within the scope of reinforcement learning [Pang et al., 2018]. The problem is also referred to as *backward induction* or *stochastic dynamic programming*. The formal reframing of OED as a POMDP is laid out below.

Setup

Suppose we have a determinic, finite time horizon $t = 1, ..., T$. We specify as Partially Observable Markov Decision Process (POMDP) as follows.

- States $s_t = (\theta, h_t)$, where $h_t = d_{1:t}, y_{1:t}$ the history of designs d and outcomes y up to the current time. Here $y_t \sim p(y|\theta, d)$ is the outcome of performing the experiment using design d_t. The belief states $b_t(\theta)$, the states that we can actually observe, are the posterior for θ given the history h_t (and the prior $p(\theta)$). So $b_t(\theta) = p(\theta|h_t)$.
- Actions $a_t = d_{t+1}$. Transitions correspond to running the experiment and producing the outcome y_{t+1}.
- Observations $o_t = h_t$. Thus the only unobserved part of the state (θ, h_t) is the latent θ.
- Rewards $r_t = r(t, \theta, h_t)$. We take r to be a non-random function. Note that in many OED settings, we take $r_t = 0$ for $t < T$. Intuitively, this means we only care about our final understanding of or action upon the system, not the path taken to it. This is the choice made by [González et al., 2016] among others.

Under this set-up, the *optimal experiment design policy* is a map π from histories h_t to actions a_t which maximises the total reward

$$R_T = \mathbb{E}\left[\sum_{t=1}^{T} \gamma^t r_t \middle| \pi\right] \tag{1.23}$$

where $\gamma \in [0, 1]$ is the discount factor, often set to 1 in finite horizons.

Connection to EIG

In this section, we first show that when $T = 1$ our POMDP formulation, with an appropriate choice of reward, does give back the EIG maximisation approach we discussed previously. We then look at a general horizon T with an information-theoretic reward, and show that two different ways of writing down the information-theoretic reward are actually equivalent.

Horizon 1 Suppose $T = 1$. Choose the following reward function (which comes from the information-theoretic utility)

$$r(1, \theta, h) = \log \frac{p(\theta|y, d)}{p(\theta)} = \log \frac{p(y|\theta, d)}{p(y|d)} \tag{1.24}$$

The Q-function of action d_1 is the expected reward

$$Q(s_0, d_1) = E_{y \sim p(y|\theta,d)}[r(t, \theta, d_1, y)] \tag{1.25}$$

Since we do not know θ, we marginalise it out using our prior $p(\theta)$. This is equivalent to computing the Q-function on *belief states* rather than the original states. The Q-function of the belief state $p(\theta)$ and action d_1 is

$$Q(p(\theta), d_1) = E_{\theta \sim p(\theta)}\{E_{y \sim p(y|\theta,d)}[r(t, \theta, d_1, y)]\} \tag{1.26}$$

which reduces to the familiar expression

$$Q(p(\theta), d_1) = \iint p(y, \theta|d) \log \frac{p(\theta|y, d)}{p(\theta)} \, d\theta \, dy \tag{1.27}$$

Horizon T This formalism provides a convenient way to avoid the greedy approach to sequential design that is compatible with the information-theoretic objective of [Lindley, 1956].

Suppose the belief at time t is $b_t(\theta)$. We take the reward to be 0 at $t < T$ and

$$r(T, \theta, h_T) = r(T, \theta, b_T(\theta)) = \log \frac{b_T(\theta)}{p(\theta)} \tag{1.28}$$

we have updated b according to Bayes Theorem so

$$b_T(\theta) = p(\theta|y_{1:T}, d_{1:T}) \tag{1.29}$$

This reward structure represents the total information gained about θ from all experiments.

In fact, we can rewrite this reward to take non-zero values at earlier times, setting

$$r(t, \theta, h_t) = r(t, \theta, b_t(\theta)) = \log \frac{b_t(\theta)}{b_{t-1}(\theta)} \tag{1.30}$$

and this is equivalent to the previous formulation. To see this, consider the belief Q-function

$$\begin{aligned}
Q(b_t(\theta), d_{t+1}) &= \int b_t(\theta) \int p(y_{t+1}|\theta, d_{t+1}) \log \frac{b_{t+1}(\theta)}{b_t(\theta)} && (1.31)\\
&\quad + \int p(y_{t+2}|\theta, d_{t+1}, y_{t+1}) \log \frac{b_{t+2}(\theta)}{b_{t+1}(\theta)} + \dots \, dy_{t+2} \, dy_{t+1} \, d\theta && (1.32)\\
&= \int b_t(\theta) \int p(y_{t+1:t+2}|\theta, d_{t+1}) \log \frac{b_{t+2}(\theta)}{b_t(\theta)} + \dots \, dy_{t+1:t+2} \, d\theta && (1.33)\\
&= \dots && (1.34)\\
&= \int b_t(\theta) \int p(y_{t+1:T}|\theta, d_{t+1}) \log \frac{b_T(\theta)}{b_t(\theta)} \, dy_{t+1:T} \, d\theta && (1.35)
\end{aligned}$$

where $p(y_{t+1:T}|\theta, d_{t+1})$ assumes an optimal strategy after step $t+1$, under reward (1.30). We can now see by induction that the optimal strategy and Q-functions are the same for either choice of reward structure.

The greedy approach

In reinforcement learning and operational research, greediness refers to maximising the one-step-ahead reward, namely

$$a_t = \text{argmax}_{a_t \in \mathcal{A}} \left(\mathbb{E}[r_{t+1} | a_t] \right) \tag{1.36}$$

which, with the reward of (1.30), corresponds to one-step EIG maximisation at each step. The greedy approach is a commonly employed heuristic in many optimisation settings. We primarily focus on this form of multi-step optimisation because it removes all aspects of future planning beyond a single step from an already difficult problem.

Non-greedy approaches

Some have considered non-greedy strategies [González et al., 2016] [Pang et al., 2018]. See [Ryan et al., 2018, sec 6.1] for a summary of 'backwards induction' approaches.

Optional stopping

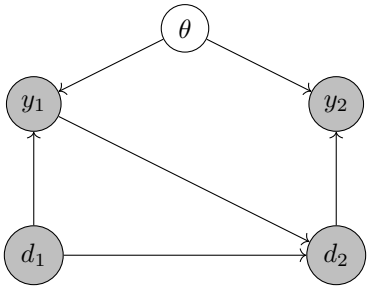
We finally mention another possible complication. Rather than a fixed and finite time horizon T, we may we allowed to continue experimentation indefinitely, choosing when to stop. One natural choice to stopping criterion is to terminate when the posterior entropy reaches a threshold value.

Optional stopping in Bayesian data analysis is a hotly debated topic
[Rouder, 2014, de Heide and Grünwald, 2017], but can be rigorously justified using martingale theory with certain stopping rules [Shafer et al., 2011] in the context of hypothesis testing. Of particular interest are stopping criteria based on non-negative supermartingales. We note in passing that the posterior entropy is a supermartingale (see (1.11)) and is non-negative if θ is discrete.

1.1.4 Theoretical considerations

The proposed experimentation strategy in which we design future experiments on the basis of previous observations may, at first sight, cause some consternation to the theoretical statistician. The first question we seek to answer is 'in what sense is the posterior obtained from multi-step OED the same as that obtained by a pre-ordained experimentation strategy?' The second line of questioning concerns the asymptotics of multi-step OED. 'Is multi-step OED statistically consistent and does it provide a faster convergence rate than other methods?'

To the first question, the answer is simply that the posterior is the same as if the experimentation strategy had been pre-ordained. Indeed, let us regard the designs as random variables and consider a 2-step experiment with the following graphical model



and the following conditional density for θ

$$p(\theta|y_1, d_1, y_2, d_2) = \frac{p(\theta, y_1, d_1, y_2, d_2)}{p(y_1, d_1, y_2, d_2)} \tag{1.37}$$

$$= \frac{p(\theta)p(d_1)p(y_1|\theta, d_1)p(d_2|y_1, d_1)p(y_2|\theta, d_2)}{\int p(\theta)p(d_1)p(y_1|\theta, d_1)p(d_2|y_1, d_1)p(y_2|\theta, d_2)d\theta} \tag{1.38}$$

$$= \frac{p(d_1)p(d_2|y_1, d_1)\ p(\theta)p(y_1|\theta, d_1)p(y_2|\theta, d_2)}{p(d_1)p(d_2|y_1, d_1)\ \int p(\theta)p(y_1|\theta, d_1)p(y_2|\theta, d_2)d\theta} \tag{1.39}$$

$$= \frac{p(\theta)p(y_1|\theta, d_1)p(y_2|\theta, d_2)}{\int p(\theta)p(y_1|\theta, d_1)p(y_2|\theta, d_2)d\theta} \tag{1.40}$$

showing that computing the posterior when regarding d_2 as a random variable that depends on y_1, d_1, (1.38), and computing it considering d_2 as a fixed and pre-ordained quantity, (1.40), actually give the same result. A related question from [Berry and Fristedt, 1985] was whether the map that takes the observed data to the posterior is a measurable function. This was addressed in [Berry and Fristedt, 1985, pp. 18-20] in the restricted setting of the multi-armed bandit.

A powerful answer to the second question was given by [Paninski, 2005] and is a form of Bernstein–von Mises Theorem for EIG maximisation OED. Under relatively mild conditions, for any neighbourhood $\mathcal{U}$ of the true parameter value θ_0 we have

$$p(\mathcal{U}|y_{1:T}, d_{1:T}) \to 1 \text{ as } T \to \infty \text{ in probability.} \tag{1.41}$$

Under further conditions, we can show that the posteriors $p(\theta|y_{1:T}, d_{1:T})$ are asymptotically Normal with some covariance matrix Σ_{info}. The same result holds for i.i.d. sampling of designs, giving rise to some other covariance matrix Σ_{iid}. We have that $\det \Sigma_{\text{info}} \leq \det \Sigma_{\text{iid}}$. This led [Paninski, 2005] to say "Thus, information maximization is in a rigorous sense asymptotically more efficient than the i.i.d. sampling strategy." Related results were obtained by [Pronzato, 2010] and [Hu, 1998].

1.2 Estimation of EIG

The estimation of EIG, and quantities mathematically equivalent to it, has received attention from a diverse group of researchers.

1.2.1 Challenges in EIG estimation

Recall

$$\mathrm{EIG}(d) = \iint p(y,\theta|d) \log \frac{p(\theta|y,d)}{p(\theta)}\, dy\, d\theta = \iint p(y,\theta|d) \log \frac{p(y|\theta,d)}{p(y|d)}\, dy\, d\theta. \tag{1.42}$$

The computation of this integral is challenging since neither $p(\theta|y,d)$ nor $p(y|d)$ nor the outer integral can, in general, be found in closed form.

A further complication arises when the likelihood $p(y|\theta,d)$ cannot be computed pointwise. For example, this is the case in the presence of nuisance variables, also known as random effects. These are additional latent variables, ψ, that we do not consider variables of interest and so we do not want to waste resources reducing our uncertainty for them. Such models arise frequently in scientific applications, for instance accounting for individual variation between participants in a survey. With random effects ψ we have

$$p(y|\theta,d) = \int p(y|\theta,\psi,d)p(\psi|\theta)d\psi \tag{1.43}$$

which is typically intractable.

We survey existing approaches to EIG estimation.

1.2.2 Nested Monte Carlo

The estimator of [Vincent and Rainforth, 2017] and [Myung et al., 2013], among others, is a nested Monte Carlo (NMC) estimator

$$\mathrm{EIG}(d) \approx \frac{1}{N}\sum_{n=1}^{N}\left[\log p(y_n|\theta_n,d) - \log\left(\frac{1}{M}\sum_{m=1}^{M} p(y_n|\theta_m,d)\right)\right] \tag{1.44}$$

where

$$y_n, \theta_n \overset{\text{iid}}{\sim} p(y,\theta|d) \tag{1.45}$$

$$\theta_m \overset{\text{iid}}{\sim} p(\theta) \tag{1.46}$$

are all independent.

The drawbacks of such an estimator were noted in [Rainforth et al., 2018]. Most notably, while simple Monte Carlo estimators converge with a mean squared error rate $\mathcal{O}(N^{-1})$ in the total number of samples, NMC estimators converge at a much slower $\mathcal{O}(N^{-2/3})$ rate and are biased, though consistent [Rainforth et al., 2018].

A saving grace of the MC approach is a speed-up due to [Vincent and Rainforth, 2017] in the case that $\mathcal{Y}$, the sample space of y, is finite. Then

$$\mathrm{EIG}(d) \approx \sum_{y}\left[\frac{1}{N}\sum_{n=1}^{N} p(y|\theta_n,d)\log p(y|\theta_n,d) - \left(\frac{1}{N}\sum_{n=1}^{N} p(y|\theta_n,d)\right)\log\left(\frac{1}{N}\sum_{n=1}^{N} p(y|\theta_n,d)\right)\right] \tag{1.47}$$

where

$$\theta_n \overset{\text{iid}}{\sim} p(\theta). \tag{1.48}$$

Since this is a continuous function of vanilla Monte Carlo estimators, it converges at a rate $\mathcal{O}(N^{-1})$.

We finally mention that, whilst not present in the literature, NMC can be readily extended to the case of random effects

$$\text{EIG}(d) \approx \frac{1}{N}\sum_{n=1}^{N}\left[\log\left(\frac{1}{M'}\sum_{m'=1}^{M'} p(y_n|\theta_n, \psi_{nm'}, d)\right) - \log\left(\frac{1}{M}\sum_{m=1}^{M} p(y_n|\theta_m, \psi_m, d)\right)\right] \tag{1.49}$$

where

$$y_n, \theta_n \overset{\text{iid}}{\sim} p(y, \theta|d) \tag{1.50}$$

$$\psi_{nm'}|\theta_n \sim p(\psi|\theta_n) \tag{1.51}$$

$$\theta_m, \psi_m \overset{\text{iid}}{\sim} p(\theta, \psi) \tag{1.52}$$

and we note that we can replace $\psi_{nm'}$ with ψ_m when θ and ψ are independent under the prior $p(\theta, \psi)$. Again, when $\mathcal{Y}$ is finite a speed-up is possible, although we can no longer avoid nesting Monte Carlo estimators.

1.2.3 Inference based approaches

A number of authors [Long et al., 2013, Ryan et al., 2015] use some form of Laplace approximation to $p(\theta|y, d)$ to estimate expected information gain. In [Ouyang et al., 2016], probabilistic programming is used to completely solve the inference problem (in finite spaces) en route to estimating EIG.

1.2.4 Mutual information estimation

As mentioned previously, EIG estimation is mathematically equivalent to mutual information estimation, a topic that has received recent attention in part due to the connection with Generative Adversarial Networks (GANs) [Chen et al., 2016, Nowozin et al., 2016] and disentanglement [Chen et al., 2018]. In the following section, we drop d from our graphical model, and consider a joint density $p(y, \theta) = p(\theta)p(y|\theta)$.

Since $p(\theta|y)$ is typically an intractable, we might use an approximation $q(\theta|y)$. An idea used by [Barber and Agakov, 2004] and [Chen et al., 2016] is to bound the mutual information in terms of an amortised posterior $q(\theta|y)$ as

$$\text{MI}(y, \theta) = \int p(\theta)\int p(y|\theta)\log\frac{p(\theta|y)}{p(\theta)}\,dy\,d\theta \tag{1.53}$$

$$\geq \int p(\theta)\int p(y|\theta)\log\frac{q(\theta|y)}{p(\theta)}\,dy\,d\theta. \tag{1.54}$$

For a fuller derivation and discussion of this and related bounds, see Chapter 2 on variational optimal experiment design.

A more recent idea is to use the Donsker-Varadhan Representation of the KL divergence to estimate mutual information [Belghazi et al., 2018]. We have

$$\mathrm{MI}(y,\theta) = \mathrm{KL}\left(p(y,\theta) \;||\; p(y)p(\theta) \right) = \sup_T \left\{ \mathbb{E}_{p(y,\theta)}[T(y,\theta)] - \log\left(\mathbb{E}_{p(\theta)p(y)}[e^{T(y,\theta)}] \right) \right\} \tag{1.55}$$

where the supremum is taken over measurable T. Note that the optimising T is given by

$$T^*(y,\theta) = \log \frac{p(y,\theta)}{p(y)p(\theta)} + C \text{ where } C \text{ is any constant} \tag{1.56}$$

The importance of (1.55) is that we no longer need access to any densities to estimate the mutual information.

Practical implementations arising from both these objective functions follow from choosing a suitable parametric family for T (or, in the former case, for $q(\theta|y)$). One then optimises the bound w.r.t. the parameters of the family using finite sample approximations to the expectations. We note that such an idea is intimately connected with the GAN [Nowozin et al., 2016].

1.3 Optimisation of EIG

So far, little attention has been paid to the design d. We suppose now that $d \in \mathcal{D}$ and we seek

$$d^* \in \mathrm{argmax}_{d\in\mathcal{D}}\ \mathrm{EIG}(d) \tag{1.57}$$

the optimal design. As outlined in the previous section, we can have only approximate estimates of $\mathrm{EIG}(d)$. Thus we seek a global optimum of a unknown function which we have only noisy evaluations of. This puts us squarely in the domain of Bayesian optimisation [Shahriari et al., 2016]. When $\mathcal{D}$ is finite, we might instead call it a bandit problem.

Bayesian optimisation in its simplest form requires

1. A model of the unknown function
2. An acquisition rule to decide which design(s) should be queried at the next iteration

It is a fascinating fact that we are now back in the setting of OED. The variable of interest is the location of d^*, the maximiser of the unknown function. Other features of the function can be regarded as random effects. See [Hernández-Lobato et al., 2014] for further discussion on the connection between Bayesian optimisation and OED, in particular, the connection of EIG to Bayesian optimisation.

A popular approach to Bayesian optimisation is to choose a Gaussian process (GP) model of the unknown function, and an upper confidence bound (UCB) acquisition rule [Srinivas et al., 2009].

One aspect that sets EIG maximisation apart from conventional Bayesian optimisation is the ability for us to obtain more accurate estimates of the unknown function EIG by varying the amount of computational resources assigned to estimation. This was explored by [Vincent and Rainforth, 2017] in a finite $\mathcal{D}$ setting. The number of NMC samples was increased for the most promising designs.

[McLeod et al., 2017] tackled a more general problem of variable cost objectives, taking a GP based approach.

1.4 Applications

Optimal experiment design is a broadly applicable subject and has been re-discovered a number of times in various fields. The purpose of this section is twofold: firstly, to note specific problems tackled by OED and to identify the model $p(y, \theta|d)$ and design space $\mathcal{D}$ in use; secondly, to more broadly suggest which types of models and experiment design problems are relevant to a certain field.

1.4.1 Bayesian optimisation

We begin with a very brief section on Bayesian optimisation, as we discussed this area in 1.3.

In Bayesian optimisation, models are regression models and typically nonlinear in nature. Gaussian process models are popular. The parameter of interest is the location of the optimum [Hernández-Lobato et al., 2014]. The design space $\mathcal{D}$ consists of either single points in the input space $\mathcal{X}$ (single acquisition), or vectors with entries in $\mathcal{X}$ (multiple acquisition). A number of experiment design strategies, here referred to as acquisition rules, have been proposed. See [Ginsbourger et al., 2008, Azimi et al., 2012] for a discussion of single and multiple acquisition rules.

1.4.2 Active learning

Whilst active learning is formally as broad as OED, we can identify certain models of particular interest in this field.

Beginning with [Cohn et al., 1996], the authors look at models for regression such as the neural network, mixture of Gaussians and locally weighted regression. The entire function (or its governing parameters) was the variable of interest. The design space was simply the input space (single acquisition).

We note in passing that an OED treatment of neural networks and deep regression models requires a credible Bayesian approach to deep learning, something that remains an area of research [Gal and Ghahramani, 2016].

The connection between active learning and Bayesian optimal design was explored in [Golovin et al., 2010]. Here, the parameter space, termed the hypothesis space $\mathcal{H}$, as well as the test space (design space) and outcome space are all finite. The authors begin with a problem in which the outcome of an experiment is deterministic and the goal is to determine exactly which hypothesis is correct. In the noiseless setting, the sequential design can be encoded as a decision tree and the problem is called the Optimal Decision Tree problem. This problem is known to be NP-hard. The extension to probabilistic modelling comes when the outcome of a test is random. See [Nowak, 2009] for a related example.

Ideas from active learning also find themselves useful in the training of emulators in Approximate Bayesian Computation (ABC) [Lueckmann et al., 2018]. Here, the aim is to model an existing complex simulator with a simpler emulator. The acquisition process – making new queries to the simulator – corresponds to an OED problem.

1.4.3 Psychology

An important use of OED in psychology is to distinguish between competing theories. Here, the parameter space is a finite set of theories and all other variables in the model are regarded as random effects. For instance, [Ouyang et al., 2016] apply OED to the 5-4 experiment for category learning [Medin and Schaffer, 1978]. The experiment aimed to distinguish two competing models of category learning: the *exemplar model* and the *prototype model*.

In [Vincent and Rainforth, 2017], OED for delayed and risky choice (DARC) experiments was studied. In such experiments, we want to model how humans discount future rewards relative to present ones. A single experiment takes the following form: 'Would you prefer £A_1 at time t_1 or £A_2 at time t_2'? The parameter of interest is the discount factor and the model was a (non-linear) variant on probit regression.

Models employed in psychology (and other social sciences) may not be Bayesian. Those doing Bayesian data analysis typically use linear models and their extensions – generalized linear mixed models (GLMMs) [Kruschke, 2014, Gelman et al., 2013]. In many cases, the parameters of interest will be certain coefficients in these models.

1.4.4 Big data analysis

In most applications, we assume that experiments will be carried out after design. In [Drovandi et al., 2017], the authors instead assume that a large dataset already exists. The design therefore consists of points, or sets of points, in the existing dataset. The examples focused on logistic regression models. In general, such settings have a well-defined design space, the models to be fitted are regression models.

1.4.5 Natural science

Natural sciences typically have complex and powerful predictive models. In [Vanlier et al., 2012], a complex biochemical network was modelled with a differential equation. Highly non-linear equations for amplitude versus offset experiments are just one example from physics [van Den Berg et al., 2003]. On the other hand, with these well-developed theories the statistical models used in natural sciences can be very simple – Gaussian measurement error was incorporated in both these examples along with uniform or Gaussian priors on latent variables. The design spaces were the times at which to measure a response function, and the source-receiver distance respectively. The complexity in experiment design in both cases arose from the non-linearity.

Chapter 2

Estimating EIG

As outlined in Sections 1.2 and 1.3, the main technical barriers to OED using EIG maximisation are the estimation and optimisation of EIG. Here we address methods for estimation.

2.1 Variational optimal experiment design

Note: This section is broadly based on a paper recently submitted to the NIPS BDL workshop; we intend to submit a longer version to ICML 2019.

The core contribution of this section is to introduce efficient variational methods for EIG estimation that are applicable to a wide variety of models. The first method, which is related to amortised variational inference [Dayan et al., 1995, Kingma and Welling, 2014, Paige and Wood, 2016, Rezende et al., 2014, Stuhlmüller et al., 2013], employs an approximate posterior distribution, parameterised by the design and the experimental outcome. In a similar manner the second method employs a variational distribution for the marginal density over experimental outcomes for a given design. Both methods can benefit from recent advances in defining flexible families of amortised variational distributions using neural networks (e.g. normalising flows [Rezende and Mohamed, 2015, Tabak and Turner, 2013]). For this reason we developed our system in Pyro [Bingham et al., 2018], a deep probabilistic programming language that provides first class support for neural networks and variational methods.

The Nested Monte Carlo (NMC) approach (see Section 1.2.2) is inefficient because it constructs an independent estimate of $p(\theta|y,d)$ or $p(y|d)$ for each outcome y. Our key insight is that by taking a variational approach, we can instead learn an *amortized* approximation for either $p(\theta|y,d)$ or $p(y|d)$, and then use this approximation to efficiently estimate the EIG. In essence, the estimate of $p(y_1|d)$ provides information about $p(y_2|d)$ for similar y_1 and y_2 (presuming the density is smooth) and so it is more efficient to learn the functional form for $p(y|d)$ (or $p(\theta|y,d)$), than to treat separate values of y as distinct inference problems.

2.1.1 Bounding EIG

We construct a variational lower bound, $\mathcal{L}_p(d)$, using the amortized posterior $q_p(\theta|y,d)$:

$$\begin{aligned}
\text{EIG}(d) &= \iint p(y,\theta|d)\log\frac{p(\theta|y,d)q_p(\theta|y,d)}{q_p(\theta|y,d)}\,dy\,d\theta + H\left(\,p(\theta)\,\right) && (2.1)\\
&= \iint p(y,\theta|d)\log q_p(\theta|y,d)\,dy\,d\theta + H\left(\,p(\theta)\,\right) + \mathbb{E}_{p(y|d)}\left[\text{KL}\left(p(\theta|y,d)||q_p(\theta|y,d)\right)\right] && (2.2)\\
&\geq \iint p(y,\theta|d)\log q_p(\theta|y,d)\,dy\,d\theta + H\left(\,p(\theta)\,\right) \triangleq \mathcal{L}_p(d). && (2.3)
\end{aligned}$$

In analogy with variational inference, this bound is tight when $q_p(\theta|y,d) = p(\theta|y,d)$. Alternatively, we can instead introduce a marginal density $q_m(y|d)$, which results in an upper bound $\mathcal{U}_m(d)$:

$$\begin{aligned}
\text{EIG}(d) &= \iint p(y,\theta|d)\log p(y|\theta,d)\,dy\,d\theta - \int p(y|d)\log\frac{p(y|d)q_m(y|d)}{q_m(y|d)}dy && (2.4)\\
&= \iint p(y,\theta|d)\log p(y|\theta,d)\,dy\,d\theta - \int p(y|d)\log q_m(y|d)\,dy - \text{KL}\left(p(y|d)||q_m(y|d)\right) && (2.5)\\
&\leq \iint p(y,\theta|d)\log p(y|\theta,d)\,dy\,d\theta - \int p(y|d)\log q_m(y|d)\,dy \triangleq \mathcal{U}_m(d), && (2.6)
\end{aligned}$$

where the bound becomes tight for $q_m(y|d) = p(y|d)$.

2.1.2 Estimation

Just as in variational inference, the bounds in the previous section can be maximised with stochastic gradient methods [Robbins and Monro, 1951]. Concretely, suppose $\mathcal{Q}$ is a family of amortised variational approximations $q_p(\theta|y,d;\phi)$ indexed by ϕ. We can estimate EIG by maximizing the lower bound $\mathcal{L}_p(d;\phi)$:

$$\text{EIG}(d) \approx \max_\phi \mathcal{L}_p(d;\phi) = \max_\phi \left\{\iint p(y,\theta|d)\log q_p(\theta|y,d;\phi)\,dy\,d\theta\right\} + H\left(\,p(\theta)\,\right) \tag{2.7}$$

To do so only requires that we can generate samples from the model, $y_i,\theta_i \sim p(y,\theta|d)$; in a probabilistic programming context this corresponds to running the model forwards with no conditioning. We can then construct the required Monte Carlo estimates for the gradient as

$$\nabla_\phi \mathcal{L}_p(d;\phi) \approx \nabla_\phi \left\{\frac{1}{N}\sum_{i=1}^{N}\log q_p(\theta_i|y_i,d;\phi)\right\} \quad \text{where} \quad y_i,\theta_i \overset{\text{i.i.d.}}{\sim} p(y,\theta|d), \tag{2.8}$$

noting that no re-parameterization is required as $p(y,\theta|d)$ is independent of ϕ. An analogous scheme can be constructed for the upper bound $\mathcal{U}_m(d;\phi)$, except that we now perform a minimization.

2.1.3 Convergence

Suppose that ϕ_n are the values obtained from the procedure outlined above. Disregarding Monte Carlo estimation error for a moment, we can see immediately from (2.2) that provided $\forall y:\ \text{KL}\left(\,p(\theta|y,d)\;||\;q_p(\theta|y,d;\phi_n)\,\right)\downarrow 0$ as $n\to\infty$ then by Monotone Convergence, the EIG estimates converge to $\text{EIG}(d)$ as $n\to\infty$. The condition rarely applies because it requires the approximating family to include the true posterior. If

KL ($p(\theta|y,d)$ || $q_p(\theta|y,d;\phi_n)$) is simply monotonic decreasing, then we have convergence to (2.7), the best estimate possible within the given variational family.

2.1.4 Accounting for random effects

Note that the lower bound $\mathcal{L}_p(d)$ can be computed whether or not the model contains random effects (see Section 1.2.1 for a discussion of random effects). On the other hand, the definition of $\mathcal{U}_m(d)$ involves $p(y|\theta,d)$ which is typically intractable in the case of random effects.

Fortunately, we can still make progress. Starting from

$$\text{EIG}(d) = \iint p(y,\theta|d) \log p(y|\theta,d) dy\, d\theta - \int p(y|d) \log p(y|d) dy \tag{2.9}$$

and we can bound each term separately in terms of two approximate densities: $q_m(y|d)$ for the marginal and $q_\ell(y|\theta,d)$ for the likelihood. Specifically, we have from Gibbs' inequality

$$-\int p(y|d) \log p(y|d) dy \leq -\int p(y|d) \log q_m(y|d) dy \tag{2.10}$$

$$\iint p(y,\theta|d) \log p(y|\theta,d) dy\, d\theta \geq \iint p(y,\theta,|d) \log q_\ell(y|\theta,d) dy\, d\theta\,. \tag{2.11}$$

Here we can no longer derive a direct bound on the EIG, but we can still use these inequalities to train an approximate marginal density q_m and an amortized approximate likelihood q_ℓ, which will yield the true EIG if they match the true marginal and likelihood respectively. Namely, suppose $\mathcal{Q}_1$ is a family of variational distributions $q_m(y|d;\phi_1)$ indexed by ϕ_1 and $\mathcal{Q}_2$ is a family of variational distributions $q_\ell(y|\theta,d;\phi_2)$ indexed by ϕ_2. Then a suitable objective for learning ϕ_1, ϕ_2 is

$$\mathcal{D}_{\phi_1,\phi_2}(d) \triangleq -\iint p(y,\theta,|d) \log q_\ell(y|\theta,d;\phi_2) dy\, d\theta - \int p(y|d) \log q_m(y|d;\phi_1) dy \tag{2.12}$$

$$\{\phi_1^*, \phi_2^*\} = \text{argmin}_{\phi_1,\phi_2} \mathcal{D}_{\phi_1,\phi_2}(d) \tag{2.13}$$

where the optimization can be performed using stochastic gradient methods, as in the main paper. Once these approximations have been learned, we can plug them back into (2.9) to give

$$\text{EIG}(d) \approx \iint p(y,\theta,|d) \log q_\ell(y|\theta,d;\phi_2^*) dy\, d\theta - \int p(y|d) \log q_m(y|d;\phi_1^*) dy \tag{2.14}$$

which can then itself be approximated by conventional Monte Carlo sampling.

2.1.5 Experiments

We validate our EIG estimators on a selection of Generalized Linear Mixed Models. These serve as useful benchmarks, since they are workhorse models in many different scientific disciplines. See Appendix 4.1 for a discussion of suitable variational families for these models. Our results are summarized in Table 2.1 and Fig. 2.1-2.4. In all four cases, both estimators (i.e. the posterior method based on q_p and the marginal

method[1] based on q_m) gave significantly lower variance than the NMC baseline, and in all but one case a significantly lower bias as well. We note that NMC especially struggles with random effects (LinReg + RE). More worryingly still, the bias of the NMC estimator can exhibit strong systematic variation as a function of the design, see Fig. 2.1-2.4. This is problematic because it can lead to the choice of a significantly suboptimal design. It is also worth emphasizing the utility of having multiple variational methods at our disposal: while the marginal method yields poor EIG estimates for the model with a large output dimension, the posterior method delivers high quality estimates. Finally, we consider an example ($\text{N}\Gamma^{-1}$Reg) that is not purely Gaussian. Here our method still performs well, despite the variational families not containing the true posterior or marginal.

	LinReg		LinReg + RE		LinReg large dim(y)		$\text{N}\Gamma^{-1}$Reg	
	bias	2std	bias	2std	bias	2std	bias	2std
NMC	1.37	1.93	5.33	3.84	3.13	2.97	3.39	3.20
Posterior	-0.23	0.25	-0.55	0.41	-0.29	0.31	-0.50	0.51
Marginal	0.34	0.15	0.36	0.20	4.57	0.29	1.59	0.64

Table 2.1: Bias and variance (we report 2σ) of EIG estimation averaged over 10 runs and 11 designs. Each method was run for 10 seconds. For more details on the models and experimental setup see Appendix 4.2. Note that the directions of the bias for the posterior and marginal match the fact that they are lower and upper bounds, as would be expected.

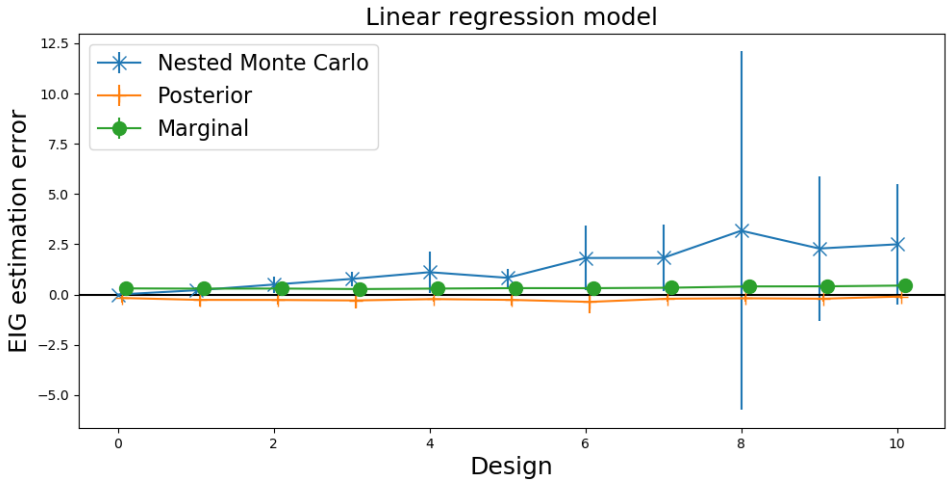


Figure 2.1: LinReg: EIG estimates for a linear regression model over 11 designs. We plot the mean and twice the standard deviation from 10 runs. Computational time was set to 10 seconds for comparison.

2.2 Extensions

2.2.1 Donsker-Varadhan

The bounds in Section 2.1.1 are partly inspired by the first bound described in Section 1.2.4. We also considered using bounds based upon the Donsker-Varadhan representation, mentioned in the same

[1] correcting for random effects as necessary

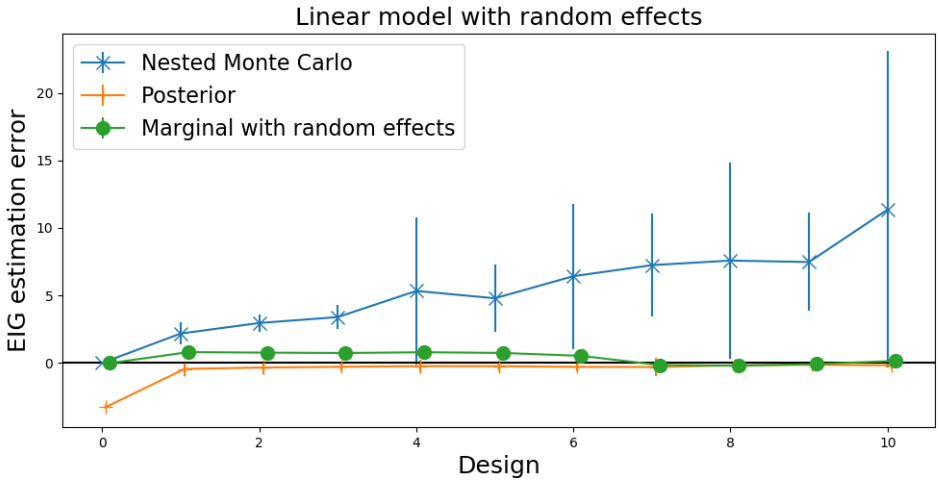


Figure 2.2: LinReg + RE: EIG estimates for a linear regression model with random effects. Settings as in Figure 2.1.

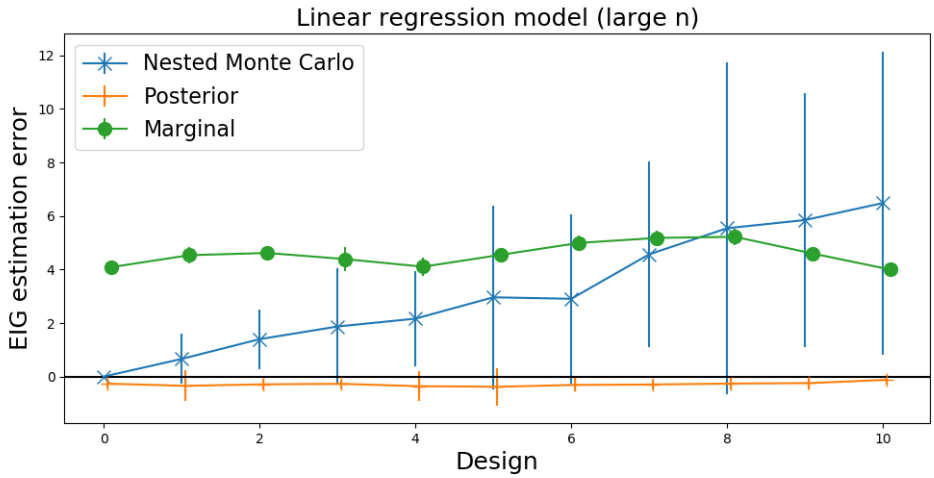


Figure 2.3: LinReg large $\dim(y)$: with settings as in Figure 2.1.

section. The Donsker-Varadhan representation gives

$$\text{EIG}(d) \leq \mathbb{E}_{p(y,\theta|d)}[T_d(y,\theta)] - \log\left(\mathbb{E}_{p(\theta)p(y|d)}[e^{T_d(y,\theta)}]\right) \tag{2.15}$$

Recall that the optimising T_d is given by

$$T_d^*(y,\theta) = \log \frac{p(y,\theta|d)}{p(y|d)p(\theta)} + C \text{ where } C \text{ is any constant.} \tag{2.16}$$

Whilst direction comparison between Donsker-Varadhan our previously proposed methods is difficult if T_d is a generic neural network, we can instead try either of

$$T_{p,d} = \log \frac{q_p(\theta|y,d)}{p(\theta)} \tag{2.17}$$

$$T_{m,d} = \log \frac{p(y|\theta,d)}{q_m(y|d)} \tag{2.18}$$

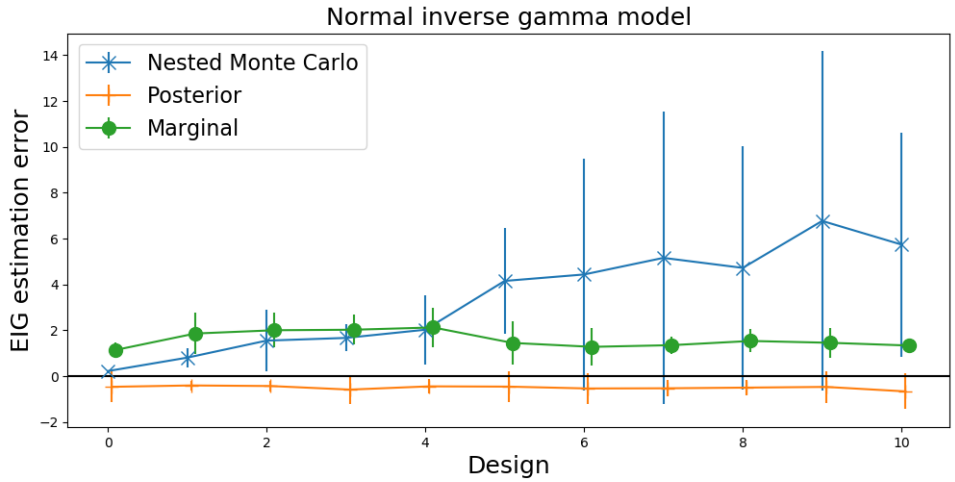


Figure 2.4: NΓ^{-1}Reg: EIG estimates for a Normal inverse-Gamma model. Settings as in Figure 2.1.

where q_p and q_m are the variational densities of Section 2.1.1. The form of T_d^* guarantees that the Donsker-Varadhan bound will be tight under the same conditions that give tightness in the bounds of the previous section.

When compared, the Donsker-Varadhan bound fared poorly against the simpler bounds in experiments. A single evaluation of the bound required many more samples to be numerically stable.

2.2.2 Analytic entropy

Our proposed method is based on taking Monte Carlo sums of log densities to approximate integrals such as

$$\text{APE}(d) \approx -\iint p(y, \theta|d) \log q_p(\theta|y, d; \phi)\, dy\, d\theta, \tag{2.19}$$

where the APE was defined in (1.9) and is simple $H\left(\, p(\theta)\, \right) - \text{EIG}(d)$. The above equation can be rewritten as

$$\text{APE}(d) \approx -\int p(y|d) \int p(\theta|y, d) \log q_p(\theta|y, d; \phi)\, d\theta\, dy. \tag{2.20}$$

We could instead have used the following

$$\text{APE}(d) \approx -\int p(y|d) \int q_p(\theta|y, d; \phi) \log q_p(\theta|y, d; \phi)\, d\theta\, dy = -\int p(y|d) H\left(\, q_p(\theta|y, d; \phi)\, \right) dy. \tag{2.21}$$

If the variational family $\mathcal{Q}$ for q_p had been chosen so that $H\left(\, q_p(\theta|y, d; \phi)\, \right)$ is easily calculable, the new approximation may have significantly lower Monte Carlo estimation error.

On the other hand, the new approximation does not bound $\text{APE}(d)$ and so an entirely different mechanism to *learn* q_p must be employed. A correct learning approach is suggested by [Piera and Parada, 2009], which showed that if $\text{KL}\left(\, q_n \,||\, p\, \right) \to 0$ then $H\left(\, q_n\, \right) \to H\left(\, p\, \right)$. In experiments, we trained q_p using (2.7) just as in the original method. We used the analytic entropy in the final step.

In practice, most computation time was spent learning q_p rather than making the final Monte Carlo estimate and so the gains from this alternative were negligible.

2.2.3 Experiments

We compare the two suggested extensions against the posterior method of Section 2.1. We used the same settings as the LinReg example. The biases and variances can be seen in Table 2.2 and Figure 2.5. We see poorer performance from Donsker-Varadhan and little to tell between posterior, and posterior using analytic entropy.

	LinReg2	
	bias	2std
Posterior	-0.24	0.32
Posterior, with analytic entropy	-0.33	0.53
Donsker-Varadhan	-0.46	1.01

Table 2.2: Bias and variance (we report 2σ) of EIG estimation averaged over 10 runs and 11 designs. Each method was run for 10 seconds. For more details on the models and experimental setup see Appendix 4.2.

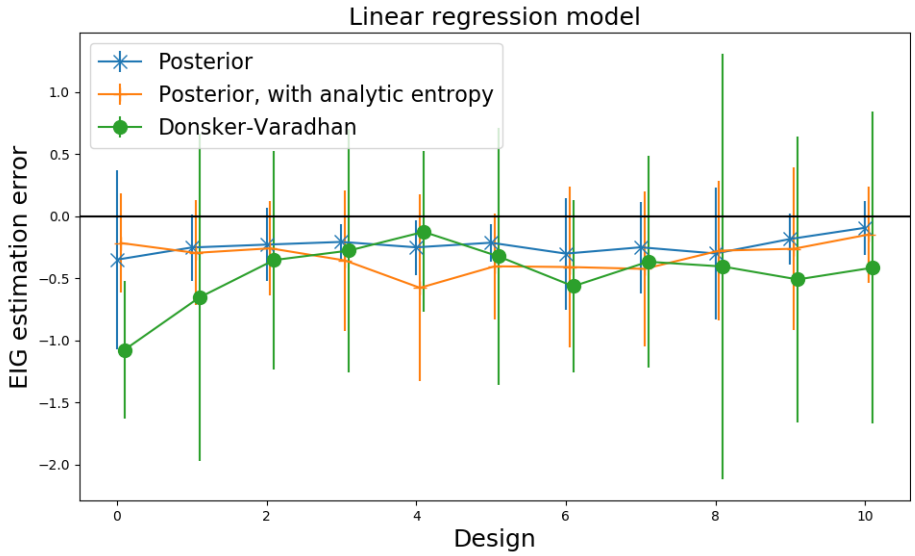


Figure 2.5: LinReg2: EIG estimates for a linear model, with extension methods. Settings as in Figure 2.1.

Chapter 3

Future directions

In this section, we outline ideas for future research in OED. Some ideas are next steps in the greedy EIG maximisation paradigm that has been adopted so far. The ultimate goal of this project would be a probabilistic programming framework that can efficiently design (near) optimal experiments for a wide variety of models and design spaces.

We also look beyond the current framework. Non-greedy strategies, and experiment design with costs both make OED more challenging. We also discuss designing experiments with causal inference in mind, or when models are misspecified. Could we design experiments to expose flaws in our models?

With such a diversity of interesting questions in this area, the difficulty is prioritisation. So far, we have sought to strike the balance between building things that work efficiently on some problems, and maintaining generality. Potential applications, interest and advice will guide future priorities.

3.1 Greedy EIG maximisation

3.1.1 Expanding the scope of variational OED

Variational optimal experiment design as outlined in Chapter 2, whilst a generally applicable idea, is currently limited in practice to (a subset of) GLMMs. The guides are highly structured and exploit knowledge of the models. If we are interested in OED for sequential human-in-the-loop experiments, there is a definite upper limit on acceptable computation time. This would encourage us to delve forwards with simpler models. The objective would be to drive computation time down as far as possible.

On the other hand, our literature review highlighted the interest in a number of other more complex models. When experiments are very expensive or timely, there is scope to allow a much longer OED computation time.

Among 'complex' models, nonlinear regression models are foremost. We can broadly divide these into parametric models (e.g. the differential equation model of [Vanlier et al., 2012]) and Bayesian non-parametric models where the Gaussian process is the leading example.

For highly nonlinear parametric models, it is likely that we dispense with assuming any knowledge of the nonlinearities and fall back on flexible approximators like deep neural networks.

For Gaussian processes on the other hand, it is likely we can exploit more structure. When considering Gaussian processes models, we should also make the further distinction between the case where θ, the variable of interest, represents the entire GP, and the case where θ represents the location of the optimum (as in Bayesian optimisation). The latter case has received a great deal of attention [Hernández-Lobato et al., 2014], and is a problem the community clearly cares about.

We could instead ask: in which cases does OED deliver the greatest benefit? That is, under which conditions would an experimental program without OED, or with inaccurate OED, be inefficient? A partial answer to this question can be given by the interpretation of EIG as epistemic uncertainty in the response (see Section 1.1.2 for derivation)

$$\mathrm{EIG}(d) = H\left(\ p(y|d)\ \right) - \mathbb{E}_{p(\theta)}[H\left(\ p(y|\theta, d)\ \right)]. \tag{3.1}$$

Thus $\mathrm{EIG}(d)$ will be low whenever $p(y|d)$ is certain. This is intuitive – if our current model already accurately predicts y at query d, little we be gained from confirming that outcome. However, high uncertainty in $y|d$ is not enough. We also need the expected aleatoric uncertainty to be low. Put another way, if knowing the exact values of θ still fails to resolve the uncertainty in the outcome then querying at d will not tell us much about θ. We can manufacture interesting OED problems using these two insights. First, data censoring means that $H\left(\ p(y|d)\ \right)$ will be low unless we avoid the censored region. Secondly, allowing the strength of random effects to be higher for some d than others means $H\left(\ p(y|\theta, d)\ \right)$ will be high unless we avoid the noisy region.

One possible problem to explore is modelling distances, for instance using multi-dimensional scaling [Torgerson, 1952]. The design would be a pair $d = (x_1, x_2)$ of object to compare. This could become a very interesting problem if i) the response was censored for very dissimilar objects, ii) responses on previous objects allow us to accurately predict the outcome on some others. Both of these ideas could reduce $H\left(\ p(y|d)\ \right)$ for certain designs. One specific application is in psychology when studying the similarity between concepts [Shepard, 1962].

3.1.2 Importance weighting correction to variational OED

The variational methods of Section 2.1 are biased and, if $\mathcal{Q}$ is chosen poorly, do not converge to the true EIG. NMC, though sometimes very slow, is a consistent procedure. We explore the connection between the two here. We have

$$\mathrm{EIG}(d) = \iint p(y, \theta|d) \log p(y|\theta, d)\, dy\, d\theta - \int p(y|d) \log \left(\int p(y|\theta, d) p(\theta)\, d\theta \right) dy \tag{3.2}$$

and conventional NMC proceeds by estimating the integral $\int p(y|\theta, d)p(\theta)\, d\theta$ using fresh samples from $p(\theta)$. We could instead use $q_p(\theta|y, d)$ as a proposal

$$\int p(y|\theta, d)p(\theta)\, d\theta = \int p(y|\theta, d) \frac{p(\theta)}{q_p(\theta|y, d)} q_p(\theta|y, d)\, d\theta. \tag{3.3}$$

Using one Monte Carlo sample for this integral reduces to the estimators used in Section 2.1. If we instead used M samples, we would have a new NMC estimator

$$\text{EIG}(d) \approx \frac{1}{N}\sum_{n=1}^{N}\left[\log p(y_n|\theta_n, d) - \log\left(\frac{1}{M}\sum_{m=1}^{M} p(y_n|\theta_{nm}, d)\frac{p(\theta_{nm})}{q_p(\theta_{nm}|y_n, d)}\right)\right] \tag{3.4}$$

where

$$y_n, \theta_n \overset{\text{iid}}{\sim} p(y, \theta|d) \tag{3.5}$$

$$\theta_{nm}|y_n \overset{\text{iid}}{\sim} q_p(\theta|y_n, d). \tag{3.6}$$

and we would have a consistent estimator that likely converges much faster than conventional NMC. Note the connection with the IWAE [Burda et al., 2015], an importance weighting correction to the VAE ELBO.

It would also be interesting to see if we can find a correction that uses q_m, our approximation to the marginal, rather than q_p.

3.1.3 Estimating the gradient of EIG

Thus far, we have primarily focused on point estimation of $\text{EIG}(d)$. Many optimisation procedures (over d) rely instead on estimates of $\nabla_d \text{EIG}(d)$. We first note that, as EIG is an expectation over $p(y, \theta|d)$, the reparametrization trick and its extensions [Tucker et al., 2017, Rezende et al., 2014] would be attractive here.

Suppose that we use our variational OED estimates in place of true EIG evaluations. Then the global optimisation problem tackled is

$$\max_d \max_\phi \left\{\iint p(y, \theta|d) \log q_p(\theta|y, d; \phi)\, dy\, d\theta\right\} + H\left(\ p(\theta)\ \right). \tag{3.7}$$

Rather than a lengthy process of optimising ϕ at each step, we could iterate between gradient steps in ϕ and d space (or compute a combined gradient step) to reach the global optimum, as is done with the Generative Adversarial Network (GAN) [Goodfellow et al., 2014]. If successful, this approach could make finding local optima of EIG computationally similar in difficulty to evaluating EIG at a single point. Alternatively, using gradient information within Gaussian process driven Bayesian optimisation [Osborne et al., 2009] is possible, and may be preferable in OED where a global optimum is desired.

3.1.4 A sequential design framework in a probabilistic language

Implementation in Pyro has so far focused on EIG estimation procedures. Further software development will bring us closer to a functioning sequential design toolkit. An open question is, having designed and done an experiment, can we re-use computation from OED to compute the posterior more quickly? When using posterior variational OED, that based on q_p, we will already have an approximation to the posterior. An alternative approach using Population Monte Carlo (PMC) was outlined in

[Vincent and Rainforth, 2017].

3.1.5 Optional stopping

As was mentioned very briefly in Section 1.1.3, optional stopping might form part of sequential OED. Statistical analysis of optional stopping has a long history [Chernoff, 1972]. Which optional stopping rules are we allowed to use in EIG driven sequential experimentation with Bayesian data analysis? Which conclusions are we able to draw from our posterior when that posterior was created by optionally stopping?

3.1.6 EIG and power

Frequentist statisticians typically design experiments using a notion of statistical power (that is tied to a specific hypothesis). What is the connection between EIG and power?

Our interest in information arises from a belief that optimising overall information will allow us to tackle many downstream tasks. We would like to make a statement like the following: 'EIG optimisation is optimal when an unknown problem is to be solved using the final posterior'. Such a problem could be a hypothesis test. It could also be another kind of decision.

3.2 Beyond greedy EIG maximisation

3.2.1 Cost and non-greedy optimisation

Frequently, experimentation is not free and the cost varies with the design. This is particularly the case when the magnitude of the experiment is a design parameter. With the inclusion of costs, we might wish to optimise

$$U(d) = \mathrm{EIG}(d) - \lambda C(d) \tag{3.8}$$

where $C(d)$ is the cost of the design and λ is a constant that determines the trade-off between information and cost.

When designing a single experiment, the inclusion of cost seems relatively simple. In the multi-step case, the inclusion of cost may be more important. For example, in a sequential design problem with costs and a finite horizon T, it would make sense to perform cheaper experiments at early times. Once some aspects of the system are understood, we can proceed to more expensive experiments with less risk of performing the wrong experiment. In the case of a fixed budget, we would be happy to use up our entire budget at time T, but would be much more cautious at time 1.

Proceeding to the question of non-greedy optimisation more generally, it has been noted that we can view the problem as a POMDP and so generic methods like Partially Observable Monte Carlo Planning [Silver and Veness, 2010] are applicable. Suppose we wish to maximise total information gain, possibly including costs. Are there features of the problem that allow us to do significantly better than using generic POMDP solvers?

3.2.2 Causal inference

It is common in science that experiments are performed to learn causal structure or to estimate expectations defined using *do*-calculus [Pearl et al., 2009] such as $\mathbb{E}[Y|do(X = x)]$. Many flaws in scientific experiment design are the result, not of gaining too little information, but of making inappropriate causal assumptions or incorrectly estimating these sorts of expectations.

How does experiment design for causal inference intersect with experiment design for information? It is possible that causal statistics simply defines a subset $\mathcal{D}' \subseteq \mathcal{D}$ of designs that are valid from a causal inference perspective. We could then seek $\max_{d \in \mathcal{D}'} \text{EIG}(d)$. Alternatively, information about certain latent variables might be more valuable in determining the causal structure than others, altering the optimisation problem entirely.

3.2.3 Model misspecification

Box told us that all statistical models are wrong [Box, 1976]. How do we design experiments accounting for model misspecification? We could add independent noise to the outcome. This wouldn't change which design is optimal though. We could also encode our model uncertainty in a Bayesian hierarchical model where we sample some $V \in \{0, 1\}$ to decide if we trust our model. If untrusted, we fall back on some high variance model. This would only change design decisions if the fall back model depended on d or θ, or if V was regarded as part of θ.

If we have empirical samples of $y|d$, from previous experiments, we might stand a better chance of at least detecting model misspecification. It's possible that we could even make this the objective of the experimental program.

3.2.4 Experiment design for model criticism

Rather than assuming the model to be true and looking to gain information within the model, suppose instead that we have data from some prior experiments and seek a new experiment to best expose flaws in the whole model. Scientists often criticise models by comparing the posterior predictive and empirical distributions (possibly conditional on some input). Could we turn this into an objective function, similar to EIG, that would let us design experiments to quickly expose flaws in models?

3.2.5 Dynamic models

A foundational assumption in our sequential OED set-up was that experimentation does not change the underlying system. Many systems do change as we experiment with them. In such a system, would the latent variables of interest also change with time? If so, standard Bayesian data analysis would not be appropriate. If some time-invariant characteristics could be found then we might have a better chance. We could still formulate this model as a POMDP in the usual way if h_{t+1} depends only on h_t and θ. A first model to consider might be one with a Markovian structure, i.e. we would allow y_{t+1} to depend on θ and d_{t+1} as usual, but also on y_t and d_t. In such a setting it might be important to explore the entire state space or avoid absorbing states that would terminate learning.

3.2.6 Other criteria

Alternatives to EIG for one-step design abound [Chaloner and Verdinelli, 1995]. Particularly interesting are those employed in active learning that target expected misclassification or expected error on a test set. It could be interesting to explore these i) theoretically, to see if EIG is somehow connected to these other criteria, ii) empirically, to see if altering the criterion used actually changes the experiment design significantly.

Chapter 4

Appendix

4.1 Variational families for GLMMs

The success of variational OED relies heavily on a good choice of variational family (guide, in the language of Pyro). Here we briefly outline techniques that aid writing guides for Generalised Linear Mixed Models (GLMMs), which we define hierarchically as

$$\theta, \psi \sim N(\mu, \Sigma) \tag{4.1}$$

$$\eta = X_{d,\theta}\theta + X_{d,\psi}\psi \tag{4.2}$$

$$y \sim p(y|\eta) \text{ with } \mathbb{E}[y|\eta] = g^{-1}(\eta). \tag{4.3}$$

We first consider posterior guides, q_p, and propose a multivariate Gaussian approximation. It can be shown that the bound (2.3) is maximised when the mean and covariance of q_p match that of the true posterior. We have

$$\mathbb{E}(\theta|y,d) = \mathbb{E}(\mathbb{E}[\theta|\eta,d]|y,d) \tag{4.4}$$

$$\mathbb{E}[\theta|\eta,d] = G_d\eta \tag{4.5}$$

$$\implies \mathbb{E}(\theta|y,d) = G_d\mathbb{E}(\eta|y,d). \tag{4.6}$$

Similarly, the covariance $\mathbb{C}\text{ov}(\theta|y,d)$ is

$$\mathbb{C}\text{ov}(\theta|y,d) = \mathbb{E}(\mathbb{C}\text{ov}[\theta|\eta,d]|y,d) + \mathbb{C}\text{ov}(\mathbb{E}[\theta|\eta,d]|y,d) \tag{4.7}$$

$$\mathbb{C}\text{ov}[\theta|\eta,d] = H_d \tag{4.8}$$

$$\mathbb{C}\text{ov}(\mathbb{E}[\theta|\eta,y,d]|y,d) = G_d\mathbb{C}\text{ov}(\eta|y,d)G_d^T \text{ from (4.5)} \tag{4.9}$$

$$\implies \mathbb{C}\text{ov}(\theta|y,d) = H_d + G_d\mathbb{C}\text{ov}(\eta|y,d)G_d^T \tag{4.10}$$

The matrices G_d and H_d can be computed explicitly

$$H_d^{-1} = \Sigma_{\theta\theta}^{-1} + X_{d,\theta}^T(X_{d,\psi}[\Sigma_{\psi\psi} - \Sigma_{\psi\theta}\Sigma_{\theta\theta}^{-1}\Sigma_{\theta\psi}]X_{d,\psi}^T)^{-1}X_{d,\theta}, \tag{4.11}$$

$$G_d = H_d(\Sigma_{\theta\theta}^{-1}\mu_\theta + X_{d,\theta}^T(X_{d,\psi}[\Sigma_{\psi\psi} - \Sigma_{\psi\theta}\Sigma_{\theta\theta}^{-1}\Sigma_{\theta\psi}]X_{d,\psi}^T)^{-1}(\eta - X_{d,\psi}\mu_\psi)). \tag{4.12}$$

In some cases, $\eta|y, d$ may be significantly easier to learn than $\theta|y, d$.

Turning now to marginal guides, q_m, and likelihood guides, q_ℓ, we first note that the likelihood $p(y|\eta)$ is critical in determining the correct guide. A response y in $\{0, 1\}$ needs a very different guide to one in $\mathbb{R}$. Any suitable density estimator may be used for $q_m(y|d)$. For $q_\ell(y|\theta, d)$ we note that y depends on θ only through $X_{d,\theta}\theta$. In many cases, simply shifting certain parameters by $X_{d,\theta}\theta$ can give a good approximation. For logistic regression, for example, we wish to estimate

$$\int p(\epsilon)f(X_{d,\theta}\theta + \epsilon)d\epsilon = f(X_{d,\theta}\theta) + \tfrac{1}{2}\mathrm{Var}(\epsilon)f''(X_{d,\theta}\theta) + ... \tag{4.13}$$

where $\epsilon = X_{d,\psi}\psi$ assuming for now $\mu_\psi = 0$, and f is the logistic function. We approximate this as

$$\tfrac{1}{2}\left(f(X_{d,\theta}\theta + \phi) + f(X_{d,\theta}\theta - \phi)\right). \tag{4.14}$$

4.2 Experiment details

4.2.1 LinReg

A classical Bayesian linear regression model has the following form

$$\theta \sim N(\mu_\theta, \Sigma_{\theta\theta}) \tag{4.15}$$

$$y|\theta, d \sim N(X_d\theta, \sigma^2 I) \tag{4.16}$$

where X_d is the design matrix.

In our LinReg example, we took:

$$\mu_\theta = 0 \tag{4.17}$$

$$\Sigma_{\theta\theta} = \begin{pmatrix} 10^2 & 0 \\ 0 & 0.1^2 \end{pmatrix} \tag{4.18}$$

$$\sigma^2 = 1 \tag{4.19}$$

$$X_d = \begin{pmatrix} 1 & 0 \\ \vdots & \vdots \\ 1 & 0 \\ 0 & 1 \\ \vdots & \vdots \\ 0 & 1 \end{pmatrix} \text{ a } (10 \times 2) \text{ matrix} \tag{4.20}$$

with all 11 possible designs considered.

We chose families of variational distributions that include the true posterior (or true marginal). For the amortised posterior, we set $\phi = (\Lambda, \delta, \Sigma_\text{p})$ and let

$$q_p(\theta|y, d; \phi) \sim N(\mu_\text{p}, \Sigma_\text{p}) \tag{4.21}$$

$$\text{where } \mu_\text{p} = (X_d^T X_d + \Lambda)^{-1} X_d^T (y + \delta) \tag{4.22}$$

and Λ is a diagonal matrix and Σ_p is positive definite. For the marginal, we simple take $\phi = (\mu_\text{m}, \Sigma_\text{m})$ and

$$q_m(y|d; \phi) \sim N(\mu_\text{m}, \Sigma_\text{m}) \tag{4.23}$$

Finally, for each of our variational methods we used the Adam optimizer [Kingma and Ba, 2014] with a learning rate specified below. Each iteration used N_t samples, with T iterations in total. We used N samples for the final evaluation. NMC settings are N, M [Vincent and Rainforth, 2017] and we took the advice of the authors to set $N = M^2$.

The exact parameter settings, to get about 10 seconds of computation for each method, were

NMC		Posterior				Marginal			
N	M	N_t	T	lr	N	N_t	T	lr	N
110^2	110	10	1200	0.05	500	10	1200	0.05	500

4.2.2 LinReg + RE

In this experiment, we extended the model to include random effects. Specifically,

$$\theta \sim N(\mu_\theta, \Sigma_{\theta\theta}) \tag{4.24}$$

$$\psi \sim N(\mu_\psi, \Sigma_{\psi\psi}) \tag{4.25}$$

$$y|\theta, d \sim N(X_{d,\theta}\theta + X_{d,\psi}\psi, \sigma^2 I) \tag{4.26}$$

where

$$\mu_\psi = 0 \tag{4.27}$$

$$\Sigma_{\psi\psi} = I_{10} \tag{4.28}$$

$$X_{d,\psi} = I_{10} \tag{4.29}$$

and $X_{d,\theta}$ was the X_d from the previous example. Here θ is the random variable of interest, while ψ is a nuisance variable that needs to be integrated out. The variational distribution for the likelihood, q_ℓ, was the same as q_m, except that the mean was shifted by $X_{d,\theta}\theta$.

The exact parameter settings, to get about 10 seconds of computation for each method, were

NMC		Posterior				Marginal			
N	M	N_t	T	lr	N	N_t	T	lr	N
52^2	52	10	150	0.05	500	10	600	0.05	500

4.2.3 LinReg large $\dim(y)$

This experiment was identical to LinReg, except that we took X_d to have dimensions 20×2, with 11 designs as before. We also altered the marginal variational distribution to reflect the new dimension of y. Other than that, the specification of all variational distributions was identical.

The exact parameter settings, to get about 10 seconds of computation for each method, were

NMC		Posterior				Marginal			
N	M	N_t	T	lr	N	N_t	T	lr	N
90^2	90	10	1000	0.05	500	10	700	0.05	500

4.2.4 NΓ^{-1}Reg

We changed the model to

$$\sigma^2 \sim \Gamma^{-1}(\alpha, \beta) \tag{4.30}$$

$$\theta \sim N(\mu_\theta, \Sigma_{\theta\theta}) \tag{4.31}$$

$$y|\theta, \sigma^2, d \sim N(X_d\theta, \sigma^2 I) \tag{4.32}$$

where $\alpha = 3$ and $\beta = 2$.

We used a mean-field posterior variational distribution. For θ, we used the same variational distribution as for LinReg. For σ^2 we used an inverse Gamma variational distribution. We augmented the parameters ϕ with α_p, b_0 and took $\beta_\mathrm{p} = b_0 + \frac{1}{2}(y^T y - y^T X_d \mu_\mathrm{p})$. Then

$$q_p(\sigma^2|y, d; \phi) \sim \Gamma^{-1}(\alpha_\mathrm{p}, \beta_\mathrm{p}) \tag{4.33}$$

The marginal variational distribution was as in LinReg (a Gaussian).

The exact parameter settings, to get about 10 seconds of computation for each method, were

NMC		Posterior				Marginal			
N	M	N_t	T	lr	N	N_t	T	lr	N
110^2	110	10	800	0.05	500	10	1200	0.05	500

4.2.5 LinReg2

We used the model of LinReg, and the following parameter settings

Posterior				Posterior, with analytic entropy				Donsker-Varadhan			
N_t	T	lr	N	N_t	T	lr	N	N_t	T	lr	N
10	1200	0.05	500	10	1200	0.05	50	100	100	0.05	500

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