Bayesian Experimental Design Literature Review

Connections with Bayesian Active Learning, Bayesian Optimisation and Bayesian Reinforcement Learning

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1 Introduction

If true knowledge arises from empirical observations, it is natural to ask which kinds of observations we should actively seek out to further our understanding of nature. In its broadest sense, this is the question that the design of experiments seeks to answer. An *experimental design* is an allocation of resources—e.g. time, human attention, chemical reagents, physical space—that will be used to obtain empirical observations. The *design space* is the set of designs that we could feasibly choose for the experiment; the problem of experimental design is to pick a design to use for the real experiment. The choice of design is an important one: we could easily waste resources on poorly designed experiments that do not further our understanding. By carefully designing experiments, we can efficiently gather empirical observations that lead to new ideas, hypotheses, conclusions and models.

It is therefore unsurprising that we find experimental design to be a key concern in scientific disciplines as diverse as psychology (Myung et al., 2013), bioinformatics (Vanlier et al., 2012), pharmacology (Lyu et al., 2019), physics (Dushenko et al., 2020), neuroscience (Shababo et al., 2013), astronomy (Loredo, 2004) and engineering (Papadimitriou, 2004). It is also is a natural abstraction for several central problems in machine learning, including active learning (Houlsby et al., 2011; Gal et al., 2017), Bayesian optimisation (Hernández-Lobato et al., 2014; Shahriari et al., 2015) and exploration (Sun et al., 2011; Shyam et al., 2019).

In many practical cases, experimental design is not used just once. Indeed, many experiments are naturally *adaptive*: they are an iterative process in which we can select the designs for later iterations on the basis of data already gathered. This allows feedback from the outcome of one experiment iteration to be used to guide the design of the next iteration. This setting can be particularly powerful because, as we gain some information about the system, it may become clearer how we should proceed to design our experiments to investigate further, thereby honing in quickly on the truth.

To choose between different possible experimental designs requires an objective function. In general, the objective depends not only on known quantities (such as the cost of the experiment), but also on the not-yet-observed outcome of the experiment and potentially on other unobserved quantities. For example, the objective function for a chemical experiment might reward correctly synthesising a product, something that will only be observed once the experiment is completed. To reason about objective functions that depend on unknowns in this way requires the incorporation of some *a priori* knowledge. This *a priori* knowledge is then used to select the design before commencing the experiment. In this work, we focus on the Bayesian approach to this problem (Lindley, 1956, 1972; Chaloner and Verdinelli, 1995; Ryan et al., 2016; Foster et al., 2019) in which *a priori* knowledge is encoded in two ways—first, the specification of a model for the experiment, and second in the prior distribution for the unknown parameters of that model. Typically, the model itself is assumed to be correct. The prior distribution explicitly represents initial beliefs about unknown parameters of the model. Furthermore, uncertainty in the prior is exactly the epistemic uncertainty that can be reduced by running experiments and collecting data, resulting in more precise *a posteriori* knowledge.

In this literature review, we begin with a brief survey of foundational concepts in Bayesian data analysis

(Sec. 2). We then turn to the core theory of Bayesian experimental design (Sec. 3), discussing criteria that have been used within the statistics community, with an emphasis on expected information gain. In Sec. 4, we discuss computational methods for Bayesian experimental that have been used within statistics, and in Sec. 5 we discuss active learning. We then discuss models in which the target of experimental design is embedded in a larger model (Sec. 6); Bayesian optimisation (Sec. 7) is a specific instance of this. Finally, we delve into the theory of the sequential experimental design problem (Sec. 8), and highlight connections with exploration and Bayesian reinforcement learning (Sec. 9).

2 Background on Bayesian statistics

We first introduce necessary notation and key concepts in Bayesian data analysis[1]. The first ingredient of any Bayesian analysis is a full probability model that places a joint distribution over all observable and unobservable quantities. We denote the parameters of interest, also called the latent variable of interest, by $\theta \in \Theta$. This may be a scalar, vector, or a function depending on the model. We denote the observed data, or outcome, as $y \in \mathcal{Y}$. The full probability model is simply a probability distribution $p(\theta, y)$ on $\Theta \times \mathcal{Y}$. Typically, the full probability model can be factorised as

$$p(\theta, y) = p(\theta)p(y|\theta) \tag{1}$$

where $p(\theta)$ denotes the *prior* on θ, and $p(y|\theta)$ is the *likelihood* function[2], or sampling distribution.

Since we are interested in experimental design, we also introduce the *design* or *covariate* $\xi \in \Xi$. This is not typically treated as a random variable, because it is assumed to be directly under the experimenter's control. Instead, for each possible design ξ, we have a different probability model $p(\theta, y|\xi)$. Different choices of ξ should not alter our prior $p(\theta)$, thus the change in the probability model is only felt through the likelihood, so we can write $p(\theta, y|\xi) = p(\theta)p(y|\theta, \xi)$. Intuitively, this says that the design of the experiment ξ does not change the natural environment, but it can change the outcome of an experiment that we choose to run.

Once we have chosen ξ and run our experiment to obtain y, we can make probability statements about θ by applying Bayes' Rule to calculate the posterior

$$p(\theta|\xi, y) = \frac{p(\theta)p(y|\theta, \xi)}{\int_\Theta p(\theta')p(y|\theta', \xi)d\theta'} = \frac{p(\theta)p(y|\theta, \xi)}{p(y|\xi)}. \tag{2}$$

In general, actually performing Bayesian inference to calculate $p(\theta|\xi, y)$ can be computationally challenging.

2.1 Explicit and implicit models

If the likelihood $p(y|\theta, \xi)$ is known in closed form, then the probability model is called an *explicit likelihood* model. Most Bayesian statistics assumes an explicit likelihood. If no closed form likelihood is available, the model is an *implicit likelihood* model (Sisson et al., 2018). Implicit models often arise when θ, y and ξ are related by a simulator (Alsing et al., 2019; Brehmer et al., 2018; Gonçalves et al., 2020) that can produce samples of $p(y|\theta, \xi)$, but does not have a closed form probability density.

Similarly, if $p(\theta)$ is known in closed form, then the model is said to have an *explicit prior*, otherwise, the prior is said to be *implicit*.

2.2 Sequential data collection

So far, we have considered choosing ξ, collecting y, and analysing the data by computing $p(\theta|\xi, y)$. A more realistic setting is to consider a sequence $\xi_1 \dots \xi_T$ of designs with corresponding outcomes $y_1, \dots, y_T$. This

[1] More details on Bayesian data analysis can be found in modern textbooks on the topic, such as Gelman et al. (2013) and Kruschke (2014).

[2] Strictly, the likelihood describes the sampling distribution $p(y|\theta)$ as a function of θ for a fixed y; we use likelihood in a slightly looser sense to refer to $p(y|\theta)$ in general.

means that we run T different experiments with T different designs, each with its own corresponding outcome. The value of θ, although unknown, is assumed to be the same across all the T experiments—that means that we are conducting multiple experiments in the same natural environment to gather further information about it, instead of starting afresh in a new environment for each new experiment.

In an *exchangeable* model (Bloem-Reddy and Teh, 2019), the order of the experiments does not matter. This is equivalent (Øksendal, 2003) to the following factorisation of the full probability model

$$p(\theta, y_{1:T}|\xi_{1:T}) = p(\theta)\prod_{t=1}^{T} p(y_t|\theta, \xi_t). \tag{3}$$

for some random variable θ. The question is whether we can identify this θ with the model parameters of interest θ. In general, this is valid when there are no other model parameters besides θ. Indeed, in a full statistical model with parameters θ (Cox, 2006), it is common to assume that the outcomes of different experiments are independent given θ, which is equivalent to the factorisation in equation (3). We discuss the case in which there are other model parameters aside from θ in Sec. 6.

In non-exchangeable models, there is no assumption of conditional independence between experiments. Such models are uncommon, but can arise in settings such as time series (Pole et al., 2018). In a non-exchangeable model, the distribution of y_t can, for example, be influenced by y_{t-1} as well as by θ and ξ_t. Without loss of generality, the probability model for a non-exchangeable model can be written

$$p(\theta, y_{1:T}|\xi_{1:T}) = p(\theta)\prod_{t=1}^{T} p(y_t|\theta, \xi_{1:t}, y_{1:t-1}). \tag{4}$$

which encodes only the assumption that future experiments cannot affect the outcome of earlier experiments.

Static and adaptive experiments An orthogonal distinction in sequential experiments is how the designs are generated. In a *static* experiment, also called fixed, batch, or open loop (DiStefano III et al., 2014), the designs $\xi_1, \ldots, \xi_T$ are chosen before the beginning of the experiment. In an *adaptive* experiment (Myung et al., 2013), each ξ_t is chosen depending on data already seen $\xi_1, \ldots, \xi_{t-1}, y_1, \ldots, y_{t-1}$. A simple consequence of the likelihood principle (Barnard et al., 1962; Birnbaum, 1962) is that the mode in which the ξ_t are generated does not affect the posterior distribution on θ calculated from the data. Indeed, suppose each new design is chosen adaptively from a density $p(\xi_t|\xi_{1:t-1}, y_{1:t-1})$. Then the resulting posterior distribution is

$$p(\theta|\xi_{1:T}, y_{1:T}) = \frac{p(\theta)\prod_{t=1}^{T} p(\xi_t|\xi_{1:t-1}, y_{1:t-1})p(y_t|\theta, \xi_{1:t}, y_{1:t-1})}{\int_\Theta p(\theta')\prod_{t=1}^{T} p(\xi_t|\xi_{1:t-1}, y_{1:t-1})p(y_t|\theta', \xi_{1:t}, y_{1:t-1})d\theta'} \tag{5}$$

$$= \frac{\prod_{t=1}^{T} p(\xi_t|\xi_{1:t-1}, y_{1:t-1})\ p(\theta)\prod_{t=1}^{T} p(y_t|\theta, \xi_{1:t}, y_{1:t-1})}{\prod_{t=1}^{T} p(\xi_t|\xi_{1:t-1}, y_{1:t-1})\ \int_\Theta p(\theta')\prod_{t=1}^{T} p(y_t|\theta', \xi_{1:t}, y_{1:t-1})d\theta'} \tag{6}$$

$$= \frac{p(\theta)\prod_{t=1}^{T} p(y_t|\theta, \xi_{1:t}, y_{1:t-1})}{\int_\Theta p(\theta')\prod_{t=1}^{T} p(y_t|\theta', \xi_{1:t}, y_{1:t-1})d\theta'}, \tag{7}$$

which is independent of the mechanism of choosing designs.

2.3 Bayesian decision making

After collecting data $\xi_{1:T}, y_{1:T}$, suppose that we must choose some decision δ, for example whether to prescribe a medication or not. The Bayesian approach to selecting the optimal decision (Lindley, 1972; Robert, 2007) is to specify a utility function $U(\delta, \theta)$ which should assign a value to the decision δ *in the case that* θ is the true value of the unobserved parameter. The optimal decision is then found by maximising expected utility under the current posterior

$$\delta^* = \underset{\delta\in\Delta}{\arg\max} \quad \mathbb{E}_{p(\theta|\xi_{1:T}, y_{1:T})}[U(\delta, \theta)] \tag{8}$$

For a more extensive discussion of Bayesian decision theory, see Berger (2013).

3 Bayesian Experimental Design

Experimental design with a Bayesian data analysis model means choosing the design using the likelihood model and the prior $p(\theta)$ as *a priori* information. What criterion should be used to select the design? Following from Bayesian decision theory, Lindley (1972) proposed a decision-theoretic approach to Bayesian experimental design that focuses on maximising a utility. Chaloner and Verdinelli (1995) provides a more recent summary of Lindley's approach.

First, let us restrict ourselves to a single design ξ with outcome y, leaving the sequential design problem to Sec. 8. In the spirit of Sec. 2.3, we consider a utility function $U(\theta, \xi, y)$ that may reflect the value of obtaining the data (ξ, y) when θ is the true value of the parameters, and may also incorporate costs of the experimental design and outcome. Whilst our discussion in Sec. 2.3 assumed that the data ξ, y had already been gathered, we now need to consider the choice of the design ξ. The order of operation for the experimenter is as follows:

1. choose design ξ;
2. perform experiment with design ξ, obtaining experimental outcome y;
3. compute the posterior $p(\theta|\xi, y)$;
4. the expected utility obtained is then $\mathbb{E}_{p(\theta|\xi,y)}[U(\theta, \xi, y)]$.

In order to choose ξ optimally, we should therefore consider the different possible observations y that could arise. Specifically, we will choose ξ to maximise the expected utility, taking an outer expectation over the observation y using the Bayesian marginal (also called prior predictive) distribution $p(y|\xi) = \mathbb{E}_{p(\theta)}[p(y|\theta, \xi)]$. This leads to the following method of choosing the optimal design

$$\xi^* = \arg\max_{\xi \in \Xi} \; \mathbb{E}_{p(y|\xi)} \left[\mathbb{E}_{p(\theta|\xi,y)}[U(\theta, \xi, y)] \right]. \tag{9}$$

Proposition 1 (Lindley (1972))**.** *It is not necessary to introduce randomness into the selection of* ξ*.*

Proof. Suppose we consider a randomised way of selecting ξ with distribution $p(\xi)$. The expected reward of this approach is

$$\mathbb{E}_{p(\xi)p(y|\xi)} \left[\mathbb{E}_{p(\theta|\xi,y)}[U(\theta, \xi, y)] \right] \leq \sup_{\xi \in \Xi} \mathbb{E}_{p(y|\xi)} \left[\mathbb{E}_{p(\theta|\xi,y)}[U(\theta, \xi, y)] \right] \tag{10}$$

where the righthand side is the expected utility using the non-random ξ^*. So a randomised design is not required. □

The remaining piece of the puzzle is to select a utility function. Some applications feature a highly problem-specific utility. In other cases, we can rely on general purpose utilities.

3.1 Expected Information Gain

Perhaps the most well-studied of all criteria for Bayesian experimental design is expected information gain (EIG). Within Bayesian experimental design, EIG appears to be dominant in a number of fields. EIG was proposed by Lindley (1956). Important statistical review papers (Chaloner and Verdinelli, 1995; Ryan et al., 2016) give EIG pride of place within Bayesian experimental design. In psychology, Myung et al. (2013) promote the use of EIG to run adaptive trials. Several toolboxes (Watson, 2017; Vincent and Rainforth, 2017) have been designed specifically for the problem of performing adaptive psychology trials using EIG as the criterion for selecting designs. Heck and Erdfelder (2019) suggest EIG for experimental design for cognitive models and Cavagnaro et al. (2010) consider its application in the context of model discrimination in cognitive science. Shababo et al. (2013) applied EIG maximisation within a Bayesian model of neural microcircuits to choose the right subset of neurons to stimulate in an experiment. Dushenko et al. (2020) proposed EIG as a criterion for designing measurement settings in magnetometry. In biochemistry, Busetto

et al. (2009) compared EIG with several other criteria for the design of experiments for biochemical dynamical systems, finding EIG to perform best. In pharmacology, Lyu et al. (2019); Foster et al. (2020) applied EIG maximisation to design experiments to calibrate a docking model. Loredo (2004) used EIG for active exploration, specifically investigating the scheduling of observations of a star to characterise the orbit of a planet. EIG has also been used in active learning, Bayesian optimisation and reinforcement learning. We discuss these fields separately in Sections 5, 7 and 9.

There are several reasons for the dominance of the EIG. First, it has mathematical properties that make it very natural for describing information gained from experimentation. We discuss some key properties of the EIG in this section, and we discuss EIG in sequential settings in Sec. 8. More practically, EIG applies to a range of linear and nonlinear models (unlike some criteria which are more restricted in their applicability) and handles both continuous and discrete θ.

What does EIG measure? EIG quantifies the amount of information that the experiment with design ξ is expected to produce about the unknown parameter of interest θ. A higher EIG indicates that doing the experiment with design ξ is likely to produce data that will be helpful in reducing uncertainty about the true value of θ.

To precisely define EIG, we utilise the rigorous probabilistic definition of information that was first given by Shannon (1948). Lindley (1956) used this work to quantify the information provided by an experiment. Lindley began by considering the Shannon *entropy* of a random variable θ

$$H[p(\theta)] = -\mathbb{E}_{p(\theta)}[\log p(\theta)]. \tag{11}$$

One interpretation of entropy is uncertainty in what the true value of θ is. In the experimental design context, we measure the amount of information that is gained about θ by performing the experiment with design ξ and obtaining outcome y using the reduction in entropy from the prior to the posterior. This is referred to as the information gain (IG)

$$U_{\mathcal{I}}(\xi, y) = \mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|\xi, y)] - \mathbb{E}_{p(\theta)}[\log p(\theta)]. \tag{12}$$

To obtain an objective function for ξ, we can use this utility within the decision-theoretic framework laid out in the preceding section. We substitute $U_{\mathcal{I}}$ into equation (9). This gives the overall objective function to select ξ: the *expected information gain* (EIG), formed by taking the expectation of $U_{\mathcal{I}}$ over $p(y|\xi)$, giving

$$\mathcal{I}(\xi) = \mathbb{E}_{p(y|\xi)}\left[\mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|\xi, y)] - \mathbb{E}_{p(\theta)}[\log p(\theta)]\right]. \tag{13}$$

Proposition 2 (Lindley (1956))**.** *The EIG at design ξ, $\mathcal{I}(\xi)$, is the mutual information between y and θ under design ξ.*

Proof. By repeatedly using Bayes Theorem, we have

$$\begin{aligned}
\mathcal{I}(\xi) &= \mathbb{E}_{p(y|\xi)}\left[\mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|\xi, y)] - \mathbb{E}_{p(\theta)}[\log p(\theta)]\right] && (14)\\
&= \mathbb{E}_{p(y|\xi)p(\theta|\xi,y)}[\log p(\theta|\xi, y)] - \mathbb{E}_{p(\theta)}[\log p(\theta)] && (15)\\
&= \mathbb{E}_{p(\theta)p(y|\theta,\xi)}[\log p(\theta|\xi, y) - \log p(\theta)] && (16)\\
&= \mathbb{E}_{p(\theta)p(y|\theta,\xi)}\left[\log \frac{p(\theta|\xi, y)}{p(\theta)}\right] && (17)\\
&= \mathbb{E}_{p(\theta)p(y|\theta,\xi)}\left[\log \frac{p(\theta)p(y|\theta, \xi)}{p(\theta)p(y|\xi)}\right]. && (18)
\end{aligned}$$

□

Proposition 3. *EIG is unchanged under invertible reparametrisations of θ and y.*

Proof. This follows from the well-known property of mutual information (Cover, 1999). □

Proposition 4 (Bernardo (1979))**.** *EIG can equivalently be derived from the KL-divergence utility*

$$U_{KL}(\xi, y) = \mathrm{KL}\left(p(\theta|\xi, y)\|p(\theta)\right). \tag{19}$$

Proof. Substituting this utility into equation (9) gives us

$$I_{KL}(\xi) = \mathbb{E}_{p(y|\xi)}\left[\mathrm{KL}\left(p(\theta|\xi,y)\|p(\theta)\right)\right] \tag{20}$$

$$= \mathbb{E}_{p(y|\xi)p(\theta|y,\xi)}\left[\log\frac{p(\theta|y,\xi)}{p(\theta)}\right] \tag{21}$$

$$= \mathbb{E}_{p(\theta)p(y|\theta,\xi)}\left[\log\frac{p(\theta|y,\xi)}{p(\theta)}\right] = \mathcal{I}(\xi) \text{ by equation (17).} \tag{22}$$

□

Proposition 5 (Theorem 6 of Lindley (1956))**.** *EIG is convex in the likelihood.*

Proof. Let $\lambda \in [0,1]$ and ξ_0, ξ_1 be two designs. Suppose there exists a design ξ_λ with the following likelihood

$$p(y|\theta,\xi_\lambda) = \lambda p(y|\theta,\xi_0) + (1-\lambda)p(y|\theta,\xi_1). \tag{23}$$

We can interpret an experiment with likelihood $p(y|\theta,\xi_\lambda)$ as follows. With probability λ, the outcome y is sampled from $p(y|\theta,\xi_0)$, and with probability $1-\lambda$ it is sampled from $p(y|\theta,\xi_1)$, but it is unknown which of the two likelihoods was chosen. We could also consider a different experiment in which we observe y *and* the binary random variable u which indicates which likelihood was used. Intuitively, the latter experiment must contain at least as much information as the first. We can demonstrate this formally using the information chain rule. The expected information gain of the experiment with outcome u, y can be expanded as

$$I_{\xi,\lambda}(\theta;(u,y)) = I_\lambda(\theta;u) + I_{\xi,\lambda}(\theta;y|u), \tag{24}$$

we note θ and u are independent, and we expand the definition of the conditional mutual information

$$= \lambda I_{\xi_0}(\theta;y) + (1-\lambda)I_{\xi_1}(\theta;y). \tag{25}$$

We can also expand the same mutual information as

$$I_{\xi,\lambda}(\theta;(u,y)) = I_{\xi,\lambda}(\theta;y) + I_{\xi,\lambda}(\theta;u|y) \tag{26}$$

$$\geq I_{\xi,\lambda}(\theta;y) \tag{27}$$

since conditional mutual information is nonnegative. Finally, Proposition 2 tells us that $I_\lambda(\theta;y) = \mathcal{I}(\lambda)$. Hence,

$$\mathcal{I}(\xi_\lambda) \leq \lambda\mathcal{I}(\xi_0) + (1-\lambda)\mathcal{I}(\xi_1). \tag{28}$$

□

Proposition 6 (Sebastiani and Wynn (2000))**.** *EIG can be written as* $\mathcal{I}(\xi) = \mathbb{E}_{p(\theta)}\left[H[p(y|\xi)] - H[p(y|\theta,\xi)]\right]$. *Furthermore, when* $H[p(y|\theta,\xi)]$ *does not depend on* ξ*, EIG maximisation is equivalent to maximum entropy design which selects* ξ *to maximise* $H[p(y|\xi)]$.

Proof. Starting from Proposition 2, we have

$$\mathcal{I}(\xi) = \mathbb{E}_{p(\theta)p(y|\theta,\xi)}\left[\log\frac{p(\theta)p(y|\theta,\xi)}{p(\theta)p(y|\xi)}\right] \tag{29}$$

$$= \mathbb{E}_{p(\theta)p(y|\theta,\xi)}[\log p(y|\theta,\xi) - \log p(y|\xi)] \tag{30}$$

$$= \mathbb{E}_{p(\theta)p(y|\theta,\xi)}[\log p(y|\theta,\xi)] - \mathbb{E}_{p(y|\xi)}[\log p(y|\xi)] \tag{31}$$

$$= \mathbb{E}_{p(\theta)}\left[H[p(y|\xi)] - H[p(y|\theta,\xi)]\right]. \tag{32}$$

Now, if $H[p(y|\theta,\xi)]$ is independent of ξ, then we have $\mathcal{I}(\xi) = H[p(y|\xi)] + \text{const.}$, so EIG maximisation and maximum entropy design lead to the same optimal design. □

Remark 7 (Smith and Gal (2018))**.** *The EIG at design* ξ *can be interpreted as a measure of epistemic uncertainty in the outcome of performing an experiment with design* ξ.

Proof. Equation (32) breaks the EIG into two terms. The first is the total entropy $H[p(y|\xi)]$, called the predictive entropy. The second is $-\mathbb{E}_{p(\theta)}[H[p(y|\theta,\xi)]]$, which represents the expectation of the uncertainty in y *conditional on* θ. We can view this as a measure of aleatoric uncertainty—uncertainty which cannot be eliminated by knowing θ exactly. The EIG is the difference between the total and aleatoric uncertainties, hence we can interpret it as epistemic uncertainty—the part of $H[p(y|\xi)]$ that can be reduced by learning about θ. □

This interpretation does have its limitations. First, this definition of epistemic uncertainty is a model-dependent quantity—if we choose a more powerful model, then some variation that had previously been characterised as aleatoric would now be seen as epistemic. It also rests on our model's ability to accurately capture aleatoric uncertainty. Second, the interpretation does not hold true in the case that θ is a function of a larger set of model parameters ψ, as in Sec. 6. This is because the term $-\mathbb{E}_{p(\theta)}[H[p(y|\theta,\xi)]]$ no longer represents aleatoric uncertainty, as it also includes some uncertainty that arises from not knowing the true value of ψ.

Other important features of the EIG in sequential experiments will be discussed in Section 8.

3.2 Alphabetic criteria

The EIG is only one approach to assigning value to the design of an experiment. Whilst the EIG has a number of attractive properties, it is not the only criterion to have been explored in the literature. Perhaps the more classical approach to experimental design is to use one of the 'alphabetic' criteria. Unlike the EIG, the alphabetic criteria stem from research into *non-Bayesian linear models*, as it was in this context that the alphabetic criteria were originally proposed. Authors have then sought to generalise these alphabetic criteria, first to the Bayesian linear model, and then to general Bayesian models. Unfortunately, the resulting criteria do not always map onto Lindley's general Bayesian methodology as outlined in equation (9). As the focus in this review is on the EIG, we provide only a brief introduction to the alphabetic criteria, emphasising the historical development from linear models, and the connection to the EIG.

3.2.1 Non-Bayesian linear model

The alphabetic criteria were initially proposed in the context of non-Bayesian experimental design for the linear model

$$y|\theta,\xi \sim N(\xi\theta,\sigma^2) \tag{33}$$

where ξ is the $n \times p$ design matrix and θ is a p-vector. (In a linear model, we would conventionally replace $\theta \to \beta$ and $\xi \to X$.) The least squares estimator for θ is $\hat{\theta} = (\xi^\top\xi)^{-1}\xi^\top y$. In frequentist analysis of this estimator, the covariance matrix of $\hat{\theta}$ is proportional to $(\xi^\top\xi)^{-1}$. To guide the choice of ξ, Box (1982) discussed the following notions of optimality of ξ

A-optimality minimise $\mathrm{Tr}(\xi^\top\xi)^{-1}$, or more generally, minimise $\mathrm{Tr}\, A(\xi^\top\xi)^{-1}$ for a matrix A;

D-optimality minimise $\det(\xi^\top\xi)^{-1}$;

E-optimality minimise $\max_i \lambda_i$, where $\lambda_1,\ldots,\lambda_p$ are the eigenvalues of $(\xi^\top\xi)^{-1}$;

G-optimality minimise $\sup_{c\in\mathcal{C}} c^\top(\xi^\top\xi)^{-1}c$, where $\mathcal{C}$ is some target region for prediction.

Other alphabetic criteria include

c-optimality (Elfving, 1952) minimise $c^\top(\xi^\top\xi)^{-1}c$ for some vector c.

T-optimality (Atkinson and Fedorov, 1975) for model discrimination, which maximises the minimal deviation between a null model and an alternative.

Several key results relate these classical criteria, such as Kiefer and Wolfowitz (1959).

3.2.2 Bayesian linear model

The alphabetic criteria can be extended to Bayesian linear models (Chaloner and Verdinelli, 1995), using the observation that the posterior covariance matrix for θ is proportional to $(\xi^\top \xi + \Sigma_0^{-1})^{-1}$ when we augment the model in equation (33) with a Gaussian prior $\theta \sim N(0, \Sigma_0)$. This allows a direct generalisation of the alphabetic criteria with $(\xi^\top \xi + \Sigma_0^{-1})^{-1}$ playing the role of $(\xi^\top \xi)^{-1}$. For example, Bayesian A-optimality minimises $\mathrm{Tr}(\xi^\top \xi + \Sigma_0^{-1})^{-1}$, and Bayesian D-optimality minimises $\det(\xi^\top \xi + \Sigma_0^{-1})^{-1}$.

One may well ask how these alphabetic criteria relate to our preceding work on the EIG. Superficially, the alphabetic criteria are simply functionals of the Gram matrix $\xi^\top \xi$, whilst the EIG is defined in terms of posterior entropy. Fortunately, there is a point of close connection between the two for the Bayesian linear model.

Proposition 8 (Chaloner and Verdinelli (1995))**.** *For a Bayesian linear model, Bayesian D-optimality and EIG optimality are equivalent.*

Proof. In the Bayesian linear model, the posterior on θ is Gaussian with covariance matrix that is proportional to $(\xi^\top \xi + \Sigma_0^{-1})^{-1}$, and is independent of y. The entropy of this Gaussian posterior is $\frac{1}{2} \log\det(\xi^\top \xi + \Sigma_0^{-1})^{-1}$ + a constant. Substituting this into equation (13), the EIG for the Bayesian linear model is

$$\mathcal{I}(\xi) = \tfrac{1}{2} \log\det \Sigma_0 - \tfrac{1}{2} \log\det(\xi^\top \xi + \Sigma_0^{-1})^{-1} - \text{const} = -\tfrac{1}{2} \log\det(\xi^\top \xi + \Sigma_0^{-1})^{-1} + \text{const}'. \tag{34}$$

Thus, EIG optimality (maximise $\mathcal{I}(\xi)$) and Bayesian D-optimality (minimise $\det(\xi^\top \xi + \Sigma_0^{-1})^{-1}$) lead to the same optimal design. □

3.2.3 Bayesian non-linear models

The 'classical' approach (Tsutakawa, 1972; Chaloner and Verdinelli, 1995) to generalising the alphabetic criteria to non-linear Bayesian models is to consider the Fisher information matrix (FIM), which is defined as

$$M(\theta, \xi) = -\mathbb{E}_{p(y|\theta,\xi)} \left[\frac{\partial^2}{\partial \theta^2} \log p(y|\theta, \xi) \right] \tag{35}$$

where $\partial^2 / \partial \theta^2$ denotes the Hessian when θ is a vector. The FIM has two important properties that motivate its use to extend the alphabetic criteria:

1. the FIM for the linear regression model is proportional to $(\xi^\top \xi)$;
2. the inverse FIM is related to the asymptotic covariance matrix of the Bayesian posterior by the Bernstein–von Mises Theorem (Van der Vaart, 2000).

For non-linear models, the FIM generally depends on θ as well as ξ, so forming a criterion for ξ involves an integral over $p(\theta)$. For instance, Chaloner and Verdinelli (1995) gives a Bayesian non-linear version of D-optimality as

$$U_{\text{Bayesian-}D}(\theta, \xi) = \log\det M(\theta, \xi)^{-1}; \tag{36}$$

substituting this utility in equation (9), leads to the optimality condition

$$\xi^* = \arg\max_{\xi} \mathbb{E}_{p(\theta)}[\log\det M(\theta, \xi)^{-1}]. \tag{37}$$

Using the FIM is not the only way to generalise the alphabetic criteria to non-linear models. Indeed, Ryan et al. (2016) takes issue with the classical FIM approach, suggesting that "to qualify as a 'fully Bayesian design', one must obtain the design by using a design criterion that is a functional of the posterior distribution". Whilst the EIG satisfies this requirement, the FIM extensions of the alphabetic criteria do not.

An approach to generalising the alphabetic criteria that is consistent with Ryan's definition of 'fully Bayesian' is to look at the covariance matrix of the Bayesian posterior $\mathrm{Cov}_{p(\theta|y,\xi)}[\theta]$, which depends on ξ and y and is

a functional of the posterior. For example, Ryan et al. (2016) mention two scalar objectives that can arise from this covariance matrix. One is termed the Bayesian D-posterior precision

$$U_{D\text{-precision}}(\xi, y) = \frac{1}{\det \mathrm{Cov}_{p(\theta'|y,\xi)}[\theta']} \tag{38}$$

the other is quadratic loss

$$U_Q(\xi, y, \theta) = (\theta - \hat{\theta}(y, \xi))^\top A(\theta - \hat{\theta}(y, \xi)) \tag{39}$$

for some matrix A and for some posterior functional estimate $\hat{\theta}(y, \xi)$ of θ, such as the posterior mean. Both can be applied in the general framework of equation (9).

4 Computational methods for one-step design

Choosing Bayesian-optimal experimental designs brings tremendous promise for obtaining information more efficiently. The utilisation of this method, however, is practically limited by the difficulty of quickly obtaining accurate estimates of the design criterion. This is particularly true of the EIG, and we focus on computational methods for the EIG in this section. The mathematical problem that must be solved to find the optimal design is the EIG maximisation problem

$$\begin{aligned} \xi^* &= \arg\max_{\xi \in \Xi} \mathcal{I}(\xi) \\ &= \arg\max_{\xi \in \Xi} \mathbb{E}_{p(y|\xi)} \left[\mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|\xi, y)] - \mathbb{E}_{p(\theta)}[\log p(\theta)] \right]. \end{aligned} \tag{40}$$

Note that here we are restricting ourselves to one-step experimental design, with sequential and adaptive design being left to Sec. 8.

Computational methods for solving the EIG maximisation problem defined in equation (40) can generally be further broken down into two parts. First, they often make point estimates of the EIG criterion at various candidate designs ξ. The difficulty of this estimation procedure can immediately be seen from the definition of the EIG. It entails the calculation of the posterior entropy $-\mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|\xi, y)]$. For large-scale Bayesian models, density estimation of the posterior constitutes a complex computational task in of itself. However, for the EIG, the problem is more challenging because the posterior entropy occurs inside an expectation $\mathbb{E}_{p(y|\xi)}$ over the observation y. Thus, a direct approach to estimating the EIG amounts to *nested* estimation of potentially intractable posterior distributions. It is for this reason that EIG estimation is sometimes referred to as a 'double intractability' (Foster et al., 2019). In Sec. 4.1, we review methods that have been proposed for EIG estimation.

Second, there are still further difficulties in the problem of *optimising* the EIG objective function over the space Ξ of possible designs. In the most naive methods, the optimisation simply adds an additional layer of nesting onto the EIG estimation computations, with an outer optimiser searching over candidate designs and feeding them into the EIG estimation. Such optimisation procedures are generally best suited for smaller problems; for larger ones, more sophisticated approaches to the optimisation of the design have been studied. In Sec. 4.2 we review a range of techniques that have been proposed for this optimisation.

Computational advances, both in the estimation and the optimisation of EIG, have significantly broadened the range of Bayesian models and design spaces for which Bayesian experimental design is a realistic possibility for practitioners.

4.1 Point estimates of EIG

The EIG, $\mathcal{I}(\xi)$, represents the expected reduction in Shannon entropy between the prior and posterior (see Sec. 3.1). The first step in utilising EIG for experimental design is to compute an estimate of the EIG for a single design ξ. Since $\mathcal{I}(\xi) = \mathbb{E}_{p(y|\xi)}\left[H[p(\theta)] - H[p(\theta|\xi, y)]\right]$ involves an expectation over $y \sim p(y|\xi)$ of the posterior entropy $H[p(\theta|y, \xi)]$, a direct approach to its estimation requires repeated computations of the

posterior $p(\theta|y,\xi)$ with different simulated observations y. Given that calculating just one posterior can be intractable, it can readily be observed that EIG estimation is a computationally challenging problem.

A critical distinction when computing the EIG is whether the model has an explicit or an implicit likelihood (see Sec. 2.1 for a definition). In general, the explicit likelihood case contains strictly more information about the model, and so results in an easier, yet still doubly intractable, computational problem for the EIG. The implicit likelihood case is more challenging still, as the unknown likelihood typically has to be estimated in some way. We review computational methods for EIG estimation in both cases.

4.1.1 Explicit likelihood models

The existence of an explicit likelihood allows conventional approaches to posterior estimation, including MCMC, importance sampling, and Laplace approximation, to be used. Each leads to a family of well-studied approaches to EIG estimation. However, perhaps the most important computational methods are those which side-step direct estimation of the posterior, focusing on estimates of the marginal likelihoods $p(y|\xi)$ only. The Nested Monte Carlo estimator (Ryan, 2003) is the canonical method in this class, and been widely applied with a number of explicit likelihood models.

MCMC A natural approach that is mostly suited to low θ dimension problems, is to estimate the posterior using Markov Chain Monte Carlo (MCMC) (Andrieu et al., 2003). Unfortunately, MCMC only produces samples of the target density. This is problematic for EIG estimation, which also requires access to the posterior density $p(\theta|\xi,y)$. To overcome this, Heinrich et al. (2020) used MCMC to sample the posterior, and a Gaussian Mixture Model (Hastie et al., 2009, Sec. 6.8) to perform density estimation of the posterior. MCMC has also been applied to estimate non-EIG criteria for Bayesian experimental design (Wakefield, 1994; Han and Chaloner, 2004).

Importance sampling Another family of methods for EIG estimation is based on importance sampling. These methods begin with the key observation that estimating the posterior density is not actually required for EIG estimation, because we can write

$$\log \frac{p(\theta|\xi,y)}{p(\theta)} = \log \frac{p(y|\theta,\xi)}{p(y|\xi)}. \tag{41}$$

The approach of Cook et al. (2008); Ryan et al. (2014) is to estimate $p(y|\xi)$ using Monte Carlo samples from the prior, leading to the estimator

$$\log p(y|\xi) \approx \log\left(\frac{1}{N}\sum_{n=1}^{N} p(y|\theta_n,\xi)\right) \text{ where } \theta_1,\ldots,\theta_N \overset{\text{i.i.d.}}{\sim} p(\theta), \tag{42}$$

the other component of the likelihood ratio $p(y|\theta,\xi)/p(y|\xi)$ is the known likelihood. Cook et al. (2008); Ryan et al. (2014) then estimate $\mathbb{E}_{p(\theta|\xi,y)}[\log p(y|\theta,\xi)]$ for some fixed y by using importance sampling. Specifically, given some fixed y and the set of samples $\theta_1,\ldots,\theta_n$ drawn independently of $p(\theta)$, they use the estimator

$$\mathbb{E}_{p(\theta|\xi,y)}[\log p(y|\theta,\xi)] \approx \frac{1}{N}\sum_{n=1}^{N} \frac{p(y|\theta_n,\xi)}{\frac{1}{N}\sum_{p=1}^{N} p(y|\theta_p,\xi)} \log p(y|\theta_n,\xi). \tag{43}$$

The final estimator of EIG is formed by combining this estimator with the estimator in equation (42) for $\log p(y|\xi)$, and then taking the Monte Carlo integral over $y \sim p(y|\xi)$, giving

$$\mathcal{I}(\xi) \approx \frac{1}{M}\sum_{m=1}^{M}\left[\frac{1}{N}\sum_{n=1}^{N} \frac{p(y_m|\theta_n,\xi)}{\frac{1}{N}\sum_{p=1}^{N} p(y_m|\theta_p,\xi)} \log p(y_m|\theta_n,\xi) - \log\left(\frac{1}{N}\sum_{n=1}^{N} p(y_m|\theta_n,\xi)\right)\right] \tag{44}$$

where $y_1\ldots,y_m \overset{\text{i.i.d.}}{\sim} p(y|\xi)$ and $\theta_1,\ldots,\theta_n \overset{\text{i.i.d.}}{\sim} p(\theta)$ are independent.

Monte Carlo and Nested Monte Carlo Hamada et al. (2001); Ryan (2003) considered a closely related family of estimators. They also used equation (41) to avoid computing posterior densities. Unlike Cook et al. (2008); Ryan et al. (2014), they observed that $p(y|\xi)p(\theta|\xi,y) = p(\theta)p(y|\theta,\xi)$, allowing them to write the EIG as

$$\mathcal{I}(\xi) = \mathbb{E}_{p(\theta)p(y|\theta,\xi)}\left[\log \frac{p(y|\theta,\xi)}{p(y|\xi)}\right]. \tag{45}$$

The only unknown quantity in the integrand here is $p(y|\xi)$. Assuming some estimator $\hat{p}(y|\xi)$ for $p(y|\xi)$, we have the Monte Carlo estimator

$$\mathcal{I}(\xi) \approx \frac{1}{N}\sum_{n=1}^{N} \log \frac{p(y_n|\theta_n,\xi)}{\hat{p}(y_n|\xi)} \text{ where } \theta_n, y_n \overset{\text{i.i.d.}}{\sim} p(\theta)p(y|\theta,\xi). \tag{46}$$

In Hamada et al. (2001), $\hat{p}$ was computed by numerical integration, for a low dimensional θ. In Ryan (2003), two approaches for $\hat{p}$ were considered—the first was a Laplacian approximation using the posterior mode $\hat{\theta}$. The second was to use to an inner Monte Carlo estimation step to estimate $p(y|\xi)$ as in equation (42). This latter approach, also considered by Myung et al. (2013); Rainforth (2017), results in the double loop, or Nested Monte Carlo (NMC) estimator of EIG

$$\hat{\mathcal{I}}_{NMC}(\xi) = \frac{1}{N}\sum_{n=1}^{N} \log \frac{p(y_n|\theta_n,\xi)}{\frac{1}{M}\sum_{m=1}^{M} p(y_n|\theta'_m,\xi)} \text{ where } \theta_n, y_n \overset{\text{i.i.d.}}{\sim} p(\theta)p(y|\theta,\xi), \theta'_m \overset{\text{i.i.d.}}{\sim} p(\theta). \tag{47}$$

The asymptotic properties of this estimator were studied by Rainforth et al. (2018); Zheng et al. (2018); Beck et al. (2018), showing that $\hat{\mathcal{I}}_{NMC}(\xi)$ converges to $\mathcal{I}(\xi)$ with asymptotic error $\mathcal{O}(N^{-1}) + \mathcal{O}(M^{-2})$. Hence, it is optimal to set $M \propto \sqrt{N}$.

Laplace approximation Another important line of work (Lewi et al., 2009; Cavagnaro et al., 2010; Long et al., 2013) uses a Laplace approximation to the posterior to estimate the posterior entropy. The Laplace estimate uses the following Taylor expansion of a scalar function about a point $\hat{\theta}$

$$f(\theta) \approx f(\hat{\theta}) + (\theta-\hat{\theta})^\top \left.\frac{\partial f}{\partial \theta}\right|_{\hat{\theta}} + (\theta-\hat{\theta})^\top \left.\frac{\partial^2 f}{\partial \theta^2}\right|_{\hat{\theta}} (\theta-\hat{\theta}). \tag{48}$$

If we apply this approximation to the log posterior density $f(\theta) = \log p(\theta|\xi,y) = \log p(\theta) + \log p(y|\theta,\xi) + C$ at a point $\hat{\theta}$ for which the log posterior density has zero gradient, then we find the following Gaussian approximation

$$\log p(\theta|\xi,y) \approx (\theta-\hat{\theta})^\top \hat{\Sigma}^{-1}(\theta-\hat{\theta}) + C' \text{ where } \hat{\Sigma}^{-1} = \left.\frac{\partial^2 \log\left(p(\theta)p(y|\theta,\xi)\right)}{\partial \theta^2}\right|_{\hat{\theta}}. \tag{49}$$

One advantage of this approach is that the entropy of this Gaussian approximation is known in closed form. A drawback is that the Laplace approximation makes a strong structural assumption about the posterior. This was partially relaxed by Long (2021), who considered a multi-modal Laplace approximation. Another approach is to combine Laplace estimation and importance sampling (Ryan et al., 2015). Finally, Beck et al. (2018) analysed the standard Laplace estimator, and further proposed combining Laplace importance sampling with the NMC estimator.

4.1.2 Implicit likelihood models

When the likelihood is not available, EIG estimation is strictly more difficult than when the likelihood is known in closed form. A direct approach to re-use explicit likelihood EIG estimators is to approximate the likelihood, and use this surrogate approximation as if it were the true likelihood. Alternatively, authors have focused on existing methods for likelihood-free inference, which give posterior estimates for implicit likelihood models without requiring knowledge of the likelihood.

Approximating the likelihood In some models, the likelihood $p(y|\theta,\xi)$ can be computed, but it is too expensive to be used in extensive calculation. The approach of Huan and Marzouk (2013) is to approximate the likelihood using a polynomial chaos expansion. Here, it is necessary to use a small number of evaluations of the likelihood to compute the polynomial chaos coefficients, but once this is done, the surrogate polynomial chaos approximate likelihood can be used in place of the true likelihood for all other calculations. Huan and Marzouk (2013) specifically use the polynomial chaos approximation within a NMC estimator of the EIG.

Overstall and McGree (2020) also consider approximating the likelihood. They assume a parametric family for distributions over y with parameters ϕ, so that $y|\theta,\xi \sim \mathcal{H}_X(\phi_f(\theta,\xi))$. They estimate the function $\phi_f(\theta,\xi)$ using a Gaussian Process (Williams and Rasmussen, 2006), trained with data obtained by maximum likelihood estimation of ϕ_f. We note the close connections between this idea and Foster et al. (2019).

Approximate Bayesian Computation Approximate Bayesian Computation (ABC) (Csilléry et al., 2010) is a family of methods for performing inference without a tractable likelihood. In its simplest form, ABC simulates $(\tilde{\theta}_i, \tilde{y}_i)_{i=1}^N$ from the joint model $p(\theta, y|\xi)$. Given a metric ρ on $\mathcal{Y}$, a sample $\tilde{\theta}_i$ is accepted as a valid sample from $p(\theta|\xi, y)$ if

$$\rho(y, \tilde{y}_i) < \epsilon \tag{50}$$

for tolerance ϵ. Drovandi and Pettitt (2013), Hainy et al. (2016), Price et al. (2016) and Dehideniya et al. (2018) have applied ABC within the context of Bayesian experimental design.

LFIRE Another more recent approach to inference in intractable likelihood models is Likelihood-free Inference by Ratio Estimation (LFIRE) (Thomas et al., 2016). This method uses logistic regression to approximate the *likelihood ratio*

$$r(\xi, \theta, y) = \frac{p(y|\theta,\xi)}{p(y|\xi)}. \tag{51}$$

Importantly, this ratio is exactly the likelihood ratio that appears in the definition of the EIG, indeed we have $\mathcal{I}(\xi) = \mathbb{E}_{p(y|\xi)p(\theta|\xi,y)}[\log r(\xi,\theta,y)] = \mathbb{E}_{p(\theta)p(y|\theta,\xi)}[\log r(\xi,\theta,y)]$. Thus, if we are able to estimate $r(\xi,\theta,y)$ accurately, then EIG estimation can be performed by simple Monte Carlo integration. On this basis, LFIRE was applied in a Bayesian experimental design context by Kleinegesse and Gutmann (2018). They sampled $(\theta_i, y_i)_{i=1}^N$ from the joint model $p(\theta)p(y|\theta,\xi)$. For each θ_i, they trained a logistic regression model to distinguish samples from $p(y|\theta_i,\xi)$ and $p(y|\xi)$. This results in an estimate $\hat{r}(\xi,\theta_i,y)$ of $r(\xi,\theta_i,y)$ across different values of y. Finally, they form the Monte Carlo estimate of the EIG

$$\mathcal{I}(\xi) \approx \frac{1}{N}\sum_{i=1}^{N} \hat{r}(\xi,\theta_i,y_i). \tag{52}$$

4.2 Optimisation of EIG

We now turn to the problem of optimising the EIG over the design space Ξ. The simpler methods to perform this optimisation use point estimates of EIG. For finite Ξ, we can estimate EIG for every design. For infinite Ξ, we can use the EIG estimates at some design points to try and infer the EIG at others. Most simply, this could take the form of fitting a regression model to predict $\mathcal{I}(\xi)$ from ξ. More advanced methods use Bayesian optimisation—this both fits a Bayesian regression model of this form and uses Bayesian uncertainty estimates to propose new designs at which to compute the EIG. Another branch of thinking folds the EIG optimisation problem back into the problem of sampling from an unnormalised density. In this approach, the unnormalised density in question places high mass where the utility $U(\theta,\xi,y)$ is high. All aforementioned approaches are zeroth order methods—they do not make use of derivatives of $U(\theta,\xi,y)$. Using gradient information, albeit approximate, leads to a class of first order methods for EIG optimisation.

4.2.1 Discrete design space

For a small, discrete design space, the simplest option is to form separate estimates of $\mathcal{I}(\xi)$ for each $\xi \in \Xi$, and choose the design with the highest estimated EIG. This approach was taken by Carlin et al. (1998); Palmer and Müller (1998) and others. Vincent and Rainforth (2017) dynamically allocated resources between different discrete designs using ideas from the theory of bandit optimisation (Neufeld et al., 2014). In essence, this approach provides more accurate EIG estimates for designs that are likely to be optimal, spending less time on designs that are not promising.

4.2.2 Continuous design space

Discretisation Perhaps the simplest approach to continuous design optimisation is to discretise the design space, for example using uniformly or log-uniformly spaced points (Ryan, 2003; van den Berg et al., 2003; Watson, 2017; Vincent and Rainforth, 2017). Alternatively, a discrete set of candidate designs can be chosen by hand by the experimenter, and each evaluated (Han and Chaloner, 2004; Terejanu et al., 2012; Lyu et al., 2019).

Curve fitting Given a finite set of randomly sampled designs ξ_i with EIG estimates $\hat{\mathcal{I}}(\xi_i)$, Müller and Parmigiani (1995) proposed a curve fitting approach that fits a regression model to this data. The optimal design is then estimated as the optimum of the fitted regression model.

Bayesian optimisation Beyond simple curve fitting, Bayesian Optimisation (BO) (Snoek et al., 2012) is a well-established method for gradient-free optimisation. Like any other curve fitting approach, BO fits a model, specifically a Gaussian Process (GP), (Williams and Rasmussen, 2006) to the observed data $(\xi_i, \hat{\mathcal{I}}(\xi_i))$. However, BO iteratively suggests new designs at which to estimate the EIG, in order to efficiently seek the optimal design. We fully discuss BO and its connection with Bayesian experimental design itself in Sec. 7. For the purposes of solving the EIG optimisation problem, equation (40), we treat BO as a black box optimisation algorithm. The application of BO to optimising EIG over the design space was explored by Kleinegesse and Gutmann (2018); Foster et al. (2019); von Kügelgen et al. (2019).

Co-ordinate exchange The classical co-ordinate exchange algorithm for optimising design was proposed by Meyer and Nachtsheim (1995). Overstall and Woods (2017) proposed Approximate Co-ordinate Exchange. This is a two phase optimisation algorithm specifically designed for Bayesian experimental design. In the first phase, designs are optimised co-ordinate-wise by fitting a one-dimensional GP to the EIG surface for each co-ordinate in turn, with other elements of the design held fixed, and selecting the optimal value for that co-ordinate. In the second phase, different co-ordinates of the design are aggregated using a point exchange algorithm (Meyer and Nachtsheim, 1995; Atkinson et al., 2007).

Optimisation by sampling Clyde et al. (1996) proposed an approach to optimising the design that uses algorithms for sampling unnormalised densities. Their approach applies to any utility $U(\theta, \xi, y) > 0$ in the framework of equation (9). The authors define an augmented probability model on $\Xi \times \Theta \times \mathcal{Y}$ by

$$h(\xi, \theta, y) \propto p(\theta)p(y|\theta, \xi)U(\theta, \xi, y). \tag{53}$$

The marginal distribution for ξ is then

$$h(\xi) \propto \mathbb{E}_{p(\theta)p(y|\theta,\xi)}[U(\theta, \xi, y)], \tag{54}$$

this guarantees that high probability regions for ξ correspond to regions with a large utility. The core approach, then, is to sample from the joint density $h(\xi, \theta, y)$ using a technique such as MCMC—Clyde et al. (1996) used the Metropolis–Hastings algorithm (Hastings, 1970). MCMC on $h(\theta, \xi, y)$ was also used by Bielza et al. (1999); Müller (2005). Cook et al. (2008); Drovandi and Pettitt (2013) used the MCMC technique, and fitted a density estimator to the MCMC samples to improve their estimation of the optimal

design. Ryan et al. (2014) applied MCMC in combination with dimensionality reduction on the latent space to avoid problems with MCMC in higher dimensions.

An extension of this idea, inspired by simulated annealing (Van Laarhoven and Aarts, 1987), is to include the utility contributions from J independent (θ, y) pairs, to create an unnormalised density on $\Xi \times \Theta^J \times \mathcal{Y}^J$

$$h_J(\xi, \theta_{1:J}, y_{1:J}) = \prod_{j=1}^{J} p(\theta_j) p(y_j|\theta_j, \xi) U(\theta_j, \xi, y_j). \tag{55}$$

One can see that for larger J, the probability mass concentrates more strongly around the optimal ξ. The simulated annealing mechanism is applied by *increasing J during the course of optimisation.* This approach has been applied by Müller et al. (2004); Müller (2005); Stroud et al. (2001); Cook et al. (2008).

Alternatively, one can sample $h_J(\xi, \theta_{1:J}, y_{1:J})$ using Sequential Monte Carlo (SMC) (Doucet et al., 2000). This was the approach taken by Amzal et al. (2006); Kuck et al. (2006).

Evolutionary algorithms Another approach to solving equation (40) is to optimise over the design space using evolutionary algorithms (Eiben et al., 2003). Hamada et al. (2001) applied genetic algorithms to this problem, and Price et al. (2018) proposed the Induced Natural Selection Heuristic (INSH) method to optimise the design.

Gradient-based optimisation Whilst gradient-driven optimisation methods are commonplace in optimisation theory, their adoption in Bayesian experimental design has been limited. This is likely because, as with the EIG itself, estimating the gradient $\nabla_\xi \mathcal{I}$ is a computationally challenging problem, and it is rare that we can place a guarantee of accuracy on EIG gradient estimates. Standard stepwise optimisation methods are relatively data hungry, requiring the estimate of gradients at many design points. Given these challenges, approaches such as Bayesian optimisation, which emphasises optimisation with limited, expensive evaluations of the underlying objective function, predominate.

Nevertheless, Huan and Marzouk (2014) considered gradient-based methods for solving the EIG optimisation problem. They considered the Robbins–Monroe stochastic gradient descent (SGD) (Robbins and Monro, 1951) algorithm applied to the NMC estimator of the EIG, equation (47), resampling θ_n, y_n and θ'_m at each iteration. This leads to a gradient descent method with noisy and biased gradients. They also considered applying the SAA-BFGS algorithm (Fletcher, 2013) to the NMC estimator, without resampling at each iteration. Carlon et al. (2020) considered gradient optimisation of both NMC and Laplace estimators of the EIG using SGD.

Note: At the time of writing Chapter 3, we were not aware of the work of Huan and Marzouk (2014). This is an important piece of prior work for this chapter, which also deals with the stochastic gradient optimisation of the EIG. We regret the omission. The key distinctions between Chapter 3 and Huan and Marzouk (2014) are 1) the use of EIG lower bounds as surrogate differentiable objectives by the former as compared to the NMC surrogate used by the latter, 2) the simultaneous optimisation of a variational parameter to produce more accurate estimates of $\nabla_\xi \mathcal{I}$ of the former.

Other methods Huan and Marzouk (2013) proposed the Nelder–Mead simplex method (Nelder and Mead, 1965), a gradient-free optimisation algorithm, and simultaneous perturbation stochastic approximation (Spall, 1998) as two alternative optimisation algorithms for Bayesian experimental designs.

5 Bayesian Active Learning

Active learning allows a learning algorithm to "choose the data from which it learns" (Settles, 2009). In the Bayesian setting, the learning algorithm is a Bayesian model. In its most abstract form, then, Bayesian Active Learning is identical to Bayesian Experimental Design, but with different vocabulary: designs ξ are referred to as queries, observations y are referred to as labels and are often provided by a human labeller, the

Algorithm 1 Pool-based Bayesian active learning with greedy acquisition

Require: Acquisition function α, prior $p(\theta)$ on model weights, pool Ξ, initial dataset $\mathcal{D}_0$ may be empty.
for step $t = 1, \ldots, T$ **do**
  Find $\xi_t = \arg\max_{\xi \in \Xi} \alpha(\xi; \mathcal{D}_{t-1})$ by scoring each unlabelled element of the pool
  Obtain label y_t for query ξ_t
  Set $\mathcal{D}_t = \mathcal{D}_{t-1} \cup \{(\xi_t, y_t)\}$ and retrain model to compute $p(\theta|\mathcal{D}_t)$
end for

design criterion is referred to as the acquisition function. Queries are selected to maximise the acquisition function, typically in an iterative process.

Pool-based active learning However, this abstract similarity disguises the common differences in applications of active learning and experimental design. One hugely important sub-field of active learning, including Bayesian active learning, is *pool-based active learning* (Lewis and Gale, 1994). Here, the design space Ξ consists of unlabelled examples (such as images or sentences), the observation y is a human-provided label that corresponds to the unlabelled instance ξ, and the model is a classifier with parameters θ that predicts y from ξ. Pool-based active learning also applies less commonly to regression problems, for which y is a continuous label.

Sequential active learning with greedy acquisition In Sections 3 and 4, we focused on one-step design in which we begin with a prior $p(\theta)$, select a design ξ, obtain outcome y, and the experiment terminates. In active learning, we rarely want to acquire just one label or one batch of labels—the true power of the framework is apparent in a sequential setting (Lewis and Gale, 1994). This means that we pick design ξ_1 obtaining label y_1, then choose ξ_2 and receive label y_2, and so on. The dataset that we have after t experiments is $\mathcal{D}_t = \{(\xi_1, y_1), \ldots, (\xi_t, y_t)\}$. A simple approach to the sequential problem that is adopted in almost all of active learning (Gal et al., 2017) is *greedy acquisition*. In short, this strategy picks the next design to maximise the utility of the next label, without any consideration of how this will affect future queries.

However, it is still essential to incorporate all existing data $\mathcal{D}_t$ into the model before making this choice. To do this, we use the posterior[3] given existing data $p(\theta|\mathcal{D}_t)$ in place of the original prior $p(\theta)$. For the EIG, for example, at each step we would choose the design that maximises

$$\mathcal{I}(\xi; \mathcal{D}_t) = \mathbb{E}_{p(y|\xi, \mathcal{D}_t)} \left[\mathbb{E}_{p(\theta|\xi, y, \mathcal{D}_t)}[\log p(\theta|\xi, y, \mathcal{D}_t)] - \mathbb{E}_{p(\theta|\mathcal{D}_t)}[\log p(\theta|\mathcal{D}_t)] \right] \tag{56}$$

where $p(y|\xi, \mathcal{D}_t) = \mathbb{E}_{p(\theta|\mathcal{D}_t)}[p(y|\theta, \xi)]$. The high-level framework of greedy, sequential pool-based Bayesian active learning with a general acquisition function α is summarised in Algorithm 1. We discuss the theory of sequential experimentation in more detail in Sec. 8.

5.1 Acquisition functions

5.1.1 Bayesian Active Learning by Disagreement

A key point of intersection between Bayesian active learning and Bayesian experimental design is the Bayesian Active Learning by Disagreement (BALD) score (Houlsby et al., 2011), a widely adopted acquisition function within Bayesian Active Learning.

Proposition 9 (Houlsby et al. (2011))**.** *The BALD score is equivalent to the EIG.*

Proof. The BALD score is the mutual information between θ and y, but typically rearranged as

$$\alpha_{\text{BALD}}(\xi; \mathcal{D}_t) = \mathbb{E}_{p(\theta|\mathcal{D}_t)} \left[H[p(y|\xi, \mathcal{D}_t)] - H[p(y|\xi, \theta, \mathcal{D}_t)] \right]. \tag{57}$$

[3]In active learning, we make the assumption that θ represents the full set of model parameters (see Sec. 6).

We have

$$= \mathbb{E}_{p(\theta|\mathcal{D}_t)} \left[-\mathbb{E}_{p(y|\xi,\mathcal{D}_t)}[\log p(y|\xi,\mathcal{D}_t)] + \mathbb{E}_{p(y|\xi,\theta,\mathcal{D}_t)}[\log p(y|\xi,\theta,\mathcal{D}_t)] \right] \tag{58}$$

$$= \mathbb{E}_{p(\theta|\mathcal{D}_t)p(y|\xi,\theta,\mathcal{D}_t)} \left[-\log p(y|\xi,\mathcal{D}_t) + \log p(y|\xi,\theta,\mathcal{D}_t) \right] \tag{59}$$

$$= \mathbb{E}_{p(\theta|\mathcal{D}_t)p(y|\xi,\theta,\mathcal{D}_t)} \left[\log \frac{p(y|\xi,\theta,\mathcal{D}_t)}{p(y|\xi,\mathcal{D}_t)} \right] \tag{60}$$

applying Bayes Theorem gives

$$= \mathbb{E}_{p(\theta|\mathcal{D}_t)p(y|\xi,\theta,\mathcal{D}_t)} \left[\log \frac{p(\theta|\xi,y,\mathcal{D}_t)}{p(\theta|\mathcal{D}_t)} \right] \tag{61}$$

$$= \mathbb{E}_{p(y|\xi,\mathcal{D}_t)} \left[\mathbb{E}_{p(\theta|\xi,y,\mathcal{D}_t)}[\log p(\theta|\xi,y,\mathcal{D}_t)] - \mathbb{E}_{p(\theta|\mathcal{D}_t)}[\log p(\theta|\mathcal{D}_t)] \right] = \mathcal{I}(\xi;\mathcal{D}_t). \tag{62}$$

Note this is essentially the same proof as Proposition 6. □

The BALD score can be utilised directly in Algorithm 1. One important feature of writing EIG in BALD form is that it only depends on the actual experimental observation y, and does not require a probability density on θ. This can be important if we do not have a closed form density for θ either in the prior $p(\theta)$ or in the posterior $p(\theta|\mathcal{D}_t)$. This is particularly useful in active learning, where we may consider particularly complex models with high-dimensional θ.

In Deep Bayesian Active Learning (Gal et al., 2017), for instance, the model that predicts y from ξ is a neural network with parameters θ. In order to treat this model in a Bayesian manner, methods for Bayesian deep learning must be utilised. Gal et al. (2017) specifically used Dropout as a way of estimating prior and posterior distributions on θ (Gal and Ghahramani, 2016). Here, fitting $p(\theta|\mathcal{D}_t)$ amounts to retraining the network with Dropout. Beluch et al. (2018) and Pop and Fulop (2018) used a simple ensemble of models, treating different members of the ensemble as posterior samples of θ. To fit $p(\theta|\mathcal{D}_t)$, each deterministic model in the ensemble is retrained separately.

A key computational insight when estimating $\mathcal{I}(\xi)$ for a classification model in which the observation space $\mathcal{Y}$ is finite was made by Houlsby et al. (2011); Gal et al. (2017). We have

$$\mathcal{I}(\xi) = \sum_{y \in \mathcal{Y}} \mathbb{E}_{p(\theta)} \left[p(y|\theta,\xi) \log \frac{p(y|\theta,\xi)}{\mathbb{E}_{p(\theta)}[p(y|\theta,\xi)]} \right] \tag{63}$$

which can simply be estimated with Monte Carlo using samples $\theta_1, \ldots, \theta_N \sim p(\theta)$. The same idea applied when we have $p(\theta|\mathcal{D}_t)$ in place of $p(\theta)$. This estimator was also used by Vincent and Rainforth (2017), who observed that, unlike the NMC estimator of equation (47), this estimator converges at the standard Monte Carlo rate with error $\mathcal{O}(N^{-1/2})$. This speed-up is a consequence of being able to sum over $\mathcal{Y}$.

BatchBALD In the pool-based active learning setting with a discrete pool of size p, each acquisition involves computing the BALD score for every element of the pool and choosing the best one (Algorithm 1), which is an $\mathcal{O}(p)$ operation. Kirsch et al. (2019) considered the problem of batch active learning, in which designs are k-subsets of the pool. This means that, at each iteration of active learning, k different unlabelled examples will be selected and labelled. Naively scoring each k-subset of the unlabelled pool costs $\binom{p}{k}$, which rapidly becomes prohibitive. BatchBALD instead creates the design by greedily adding elements from the pool one at a time, giving a more efficiently scalable algorithm. This approach can be justified theoretically using the notion of submodularity—see Sec. 8.1.1.

5.1.2 Other acquisition functions

Within the Bayesian active learning framework, a range of other acquisition functions and computational methods have been proposed. It is possible to extend most common *non-Bayesian* acquisition functions

for use with Bayesian models. These non-Bayesian acquisition rules are generally a function of the predictive distribution $p(y|\xi, \mathcal{D}_t)$. When using a Bayesian model we can use the Bayesian marginal (posterior predictive) $p(y|\xi, \mathcal{D}_t) = \mathbb{E}_{p(\theta|\mathcal{D}_t)}[p(y|\theta, \xi)]$ in place of the deterministic predictive distribution that arises in non-Bayesian models. Standard acquisition functions such as uncertainty sampling (Lewis and Gale, 1994), margin sampling (Scheffer et al., 2001), and variation ratios (Freeman, 1965) can be therefore be employed in this context. Of particular note is the maximum entropy sampling method (Shannon, 1948; Settles and Craven, 2008), which uses

$$\alpha_{\text{Entropy}}(\xi; \mathcal{D}_t) = H[p(y|\xi, \mathcal{D}_t)]. \tag{64}$$

As shown in Proposition 6, this approach is equivalent to EIG maximisation when the entropy $H[p(y|\theta, \xi)]$ does not depend on ξ. This can be interpreted as saying that, given the correct model, the level of noise is uniform across all examples in the pool Ξ. For instance, we could assume that every example has a true label that a human will assign with 100% accuracy. However, maximum entropy sampling (and, in general, rules based on uncertainty in the predictive distribution $p(y|\xi, \mathcal{D}_t)$) break down when there are designs ξ which are very ambiguous, e.g. the correct label is missing from the taxonomy. Maximum entropy and related acquisition rules can become fixated on ambiguous queries.

Active learning has also considered Bayesian-specific acquisition functions. Kendall et al. (2015) proposed the mean standard deviation (Mean STD) acquisition rule for classification models. Define $\sigma_y(\xi; \mathcal{D}_t)$ as the standard deviation over $\theta|\mathcal{D}_t$ of the probability of example ξ being assigned to class y, i.e.

$$\sigma_y(\xi; \mathcal{D}_t) = \sqrt{\text{Var}_{p(\theta|\mathcal{D}_t)}[p(y|\theta, \xi)]}, \tag{65}$$

then the MeanSTD acquisition function is,

$$\alpha_{\text{MeanSTD}}(\xi; \mathcal{D}_t) = \frac{1}{|\mathcal{Y}|} \sum_{y \in \mathcal{Y}} \sigma_y(\xi; \mathcal{D}_t). \tag{66}$$

Following Bayesian decision theory, Roy and McCallum (2001) considered minimising the Bayes posterior risk, focusing on log loss and 0/1 loss. Kapoor et al. (2007) considered a range of Bayesian acquisition functions for binary classification, focusing on a score which combines the mean and variance of the prediction. Yang et al. (2012) applied Bayesian active learning to metric learning, and used an acquisition function based on maximum entropy.

6 Embedded models

So far, we have assumed that θ, the parameters of interest, and θ, the full set of model parameters, are one and the same. In this section, we explore the case in which the parameters of interest and the full set of model parameters are different. Model selection (Vanlier et al., 2014; Drovandi et al., 2014), in which we are only interesting in deciding which model is correct and not interested in learning the exact model parameters, is one important example of this setting. Bayesian optimisation (Sec. 7) is also an example in which we have a probability model for an unknown function, but we are only interest in learning the location of the maximum of that function.

For this more general case, we assume that the model is fully specified by a set of parameters ψ, and that our parameters of interest θ are a function of the full parameter set $\theta = f_\theta(\psi)$. In this case, the full joint distribution of the model is $p(\psi, y|\xi)$, and we obtain a joint over $\Theta \times \mathcal{Y}$ by integrating

$$p(\theta, y|\xi) = \int_{f_\theta^{-1}(\{\theta\})} p(\psi, y|\xi)\, d\psi. \tag{67}$$

Semi-implicit likelihood The embedded model setting allows us to extend our discussion of explicit and implicit models (Sec. 2.1). It could be the case that we do have an explicit prior for ψ and an explicit

likelihood $p(y|\psi,\xi)$ for the observation y given the full set of parameters ψ. Then the likelihood $p(y|\theta,\xi)$ is given by

$$p(y|\theta,\xi) = \int_{f_\theta^{-1}(\{\theta\})} p(y|\psi,\xi)\, d\psi, \tag{68}$$

and the prior is given by

$$p(\theta) = \int_{f_\theta^{-1}(\{\theta\})} p(\psi)\, d\psi. \tag{69}$$

First, note that $p(\theta, y|\xi) \neq p(\theta)p(y|\theta,\xi)$ in an embedded model. Second, computing one or both of these integrals may be an intractable computation. We use the term *semi-implicit* for this case in which the likelihood or prior for ψ is explicit, but the likelihood or prior for θ involves an intractable integral. So a semi-implicit likelihood is one which is formed as an integral of an explicit likelihood $p(y|\psi,\xi)$ and a semi-implicit prior is one which is an integral of explicit prior $p(\psi)$.

Exchangeability In an exchangeable embedded model, it is no longer true that different experiments are independent *conditional on* θ. Intuitively, the reason for this is that one experiment gives us information about *all of* ψ. Without extra assumptions, information from the first experiment tells us something about ψ even when we condition on θ, and this influences the predictive distribution for the second experiment. More formally, the factorisation equation (3) must be replaced by a factorisation conditional on ψ, and the natural assumption to make is that experiments are independent conditional on ψ

$$p(\psi, y_{1:T}|\xi_{1:T}) = p(\psi)\prod_{t=1}^{T} p(y_t|\psi,\xi_t). \tag{70}$$

Sequential learning with greedy acquisition One of the consequences of equation (70) is that Algorithm 1 is not quite correct for an embedded model. Specifically, between iterations, it is necessary to update the full model on ψ by fitting $p(\psi|\mathcal{D}_t)$, it is not enough to update beliefs about θ.

6.1 Expected Information Gain for embedded models

The EIG can naturally extend to the case of embedded models. The definition of information gain on the parameter of interest θ remains the same: $U_{\mathcal{I}}(\xi, y) = \mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|y,\xi)] - \mathbb{E}_{p(\theta)}[\log p(\theta)]$. When we take the expectation over y, however, we use the Bayesian marginal that integrates over all of ψ, i.e. $p(y|\xi) = \mathbb{E}_{p(\psi)}[p(y|\psi,\xi)]$, to give

$$I(\xi) = \mathbb{E}_{p(\psi)p(\theta|\psi)p(y|\psi,\xi)}\left[\log \frac{p(\theta|y,\xi)}{p(\theta)}\right]. \tag{71}$$

where $p(\theta|\psi)$ is a delta function on $f_\theta(\psi)$. This is different to the definition in equation (17) because the expectation is taken over $p(\theta, y|\xi) \neq p(\theta)p(y|\theta,\xi)$ for an embedded model. The EIG in an embedded model can also be expressed in BALD form (Proposition 9) as

$$I(\xi) = H[p(y|\xi)] - \mathbb{E}_{p(\theta)}[H[p(y|\theta,\xi)]] \tag{72}$$

$$= H\left[\mathbb{E}_{p(\psi)}[p(y|\psi,\xi)]\right] - \mathbb{E}_{p(\psi)p(\theta|\psi)}[H[p(y|\theta,\xi)]], \tag{73}$$

where the second line emphasises the difference with the standard case.

6.2 Computational methods for semi-implicit likelihood models

The NMC estimator of the EIG (Ryan, 2003) can be extended to the semi-implicit case. The central idea is that we form a Monte Carlo estimator of both $p(y|\theta,\xi)$ and $p(y|\xi)$ using appropriate Monte Carlo integrals over ψ. As in the standard NMC estimator, we have

$$p(y|\xi) = \mathbb{E}_{p(\psi)}[p(y|\psi,\xi)] \approx \frac{1}{M}\sum_{m=1}^{M} p(y|\psi_m,\xi) \text{ where } \psi_1,\ldots,\psi_M \overset{\text{i.i.d.}}{\sim} p(\psi). \tag{74}$$

For $p(y|\theta,\xi)$, we need access to samples from the distribution $p(\psi|\theta)$. Then,

$$p(y|\theta,\xi) = \mathbb{E}_{p(\psi|\theta)}[p(y|\psi,\xi)] \approx \frac{1}{M}\sum_{m=1}^{M} p(y|\psi_m,\xi) \text{ where } \psi_1,\ldots,\psi_M \overset{\text{i.i.d.}}{\sim} p(\psi|\theta). \tag{75}$$

Combining, we have the semi-implicit NMC estimator of EIG

$$\hat{I}_{\text{SI-NMC}}(\xi) = \frac{1}{N}\sum_{n=1}^{N}\left[\log\left(\frac{1}{M}\sum_{m=1}^{M} p(y_n|\psi_{nm},\xi)\right) - \log\left(\frac{1}{M}\sum_{m=1}^{M} p(y_n|\psi_m,\xi)\right)\right] \tag{76}$$

where $\theta_n, y_n \overset{\text{i.i.d.}}{\sim} p(\theta,y|\xi)$, $\psi_m \overset{\text{i.i.d.}}{\sim} p(\psi)$ and $\psi_{nm} \overset{\text{i.i.d.}}{\sim} p(\psi|\theta_n)$.

Ma et al. (2018) considered information acquisition for imputation in a semi-implicit setting. They used a Partial VAE which facilitated estimation of the EIG using the conditional independence assumptions of the model. Extending this, Gong et al. (2019) considered a similar active imputation scenario. They used $\hat{I}_{\text{SI-NMC}}(\xi)$ to estimate an information criterion for experimental design. In their probabilistic model, they had $\psi = (\theta, z)$ with $p(\psi) = p(\theta)p(z)$. When conditioning on data $\mathcal{D}_t$, they used approximate inference in which the independence of θ and z was maintained. Under these conditions, sampling $p(\psi|\theta)$ amounted to fixing θ and taking new, independent samples of z. A simplified form of their estimator is

$$\hat{I}_{\text{Icebreaker}}(\xi) = \frac{1}{N}\sum_{n=1}^{N}\left[\log\left(\frac{1}{M}\sum_{m=1}^{M} p(y_n|\theta_n,z_m,\xi)\right) - \log\left(\frac{1}{ML}\sum_{m=1}^{M}\sum_{\ell=1}^{L} p(y_n|\theta_\ell,z_m,\xi)\right)\right] \tag{77}$$

where $\theta_n, y_n \overset{\text{i.i.d.}}{\sim} p(\theta,y|\xi)$, $z_m \overset{\text{i.i.d.}}{\sim} p(z)$ and $\theta'_\ell \overset{\text{i.i.d.}}{\sim} p(\theta)$. Overstall and Woods (2017) considered almost the same setting when estimating the EIG utility. Specifically, they considered a semi-implicit case in which ψ can be partitioned into parameters of interest and *independent* nuisance parameters, and used this semi-implicit NMC estimator for the EIG.

7 Bayesian Optimisation

Bayesian optimisation (BO) (Snoek et al., 2012; Shahriari et al., 2015) considers the problem of finding the maximiser of an unknown objective function

$$\xi^* = \arg\max_{\xi\in\Xi} f(\xi). \tag{78}$$

To deal with the unknown function in a Bayesian manner, we consider a statistical model for f with prior $p(f)$. We assume that we can obtain relatively expensive measurements from the true function f at design points ξ. These measurements may be corrupted by noise, meaning that we obtain observations

$$y|\xi, f \sim p(y|f(\xi)), \tag{79}$$

for example, $y = f(\xi) + \varepsilon$ for $\varepsilon \sim N(0,\sigma^2)$.

BO can naturally be cast within the framework of Bayesian experimental design. We have designs ξ and observations y connected by the Bayesian model on f and the noise model. The missing piece is to specify the parameter of interest θ. The parameter of interest is not f, because Bayesian optimisation is explicitly concerned with *maximising* f, meaning that any information about f in regions where it is well below its maximum is not useful. The most common formulation is to take to be the location of the maximiser of f (Hernández-Lobato et al., 2014), i.e. $\theta = \arg\max_{\xi\in\Xi} f(\xi)$. The fact that θ is not all of f means that BO is not an explicit likelihood (Sec. 2.1) experimental design problem, nor does it fit into the framework of Bayesian active learning (Sec. 5). BO is experimental design for an embedded model (Sec. 6), with the function f playing the role of the richer parameter set ψ. We will see that BO has its own character with a wide range of algorithms that apply specifically to the optimisation problem.

Algorithm 2 Bayesian Optimisation (Shahriari et al., 2015)

Require: Acquisition function α, prior $p(f)$ on function, design space Ξ, initial dataset $\mathcal{D}_0$ may be empty.
  for step $t = 1, \ldots, T$ **do**
    Find $\xi_t = \arg\max_{\xi \in \Xi} \alpha(\xi; \mathcal{D}_{t-1})$
    Obtain noisy measurement $y_t \sim p(y|f(\xi_t))$ at design ξ_t
    Set $\mathcal{D}_t = \mathcal{D}_{t-1} \cup \{(\xi_t, y_t)\}$ and retrain the model to compute $p(f|\mathcal{D}_t)$
  end for
  Use $p(f|\mathcal{D}_T)$ to estimate the maximiser of f.

To set up a BO system, we begin by specifying a Bayesian model for f with prior $p(f)$, and a measurement noise model $p(y|f(\xi))$. We then specify an acquisition function that guides our choice of designs at which we should take measurements. The acquisition function in BO plays the same role as the design criterion in Bayesian experimental design and the acquisition function in active learning—we select the design that maximises the acquisition function to obtain new measurements of f. As in active learning, BO typically adopts the *greedy acquisition* approach that was outlined in Sec. 5. The entire approach is summarised in Algorithm 2.

We begin by discussing common choices for the Bayesian model and acquisition function in BO. We focus specifically on the Entropy Search family of acquisition rules, highlighting the connection to experimental design with EIG.

7.1 Bayesian models for optimisation

7.1.1 Parametric models

When the design space Ξ is discrete, the function f can be characterised by a finite number of latent variables. This case is closely connected to theory of multi-armed bandits (Lai and Robbins, 1985): we can view each $\xi \in \Xi$ as an 'arm' of a bandit in a casino. Each arm has an unknown payout, and the aim is to identify the best arm. Our mathematical set-up specifically relates the pure exploration scenario (Bubeck et al., 2009), in which final knowledge of the location of the best arm is important, but function evaluations during the course of Algorithm 2 are not. Finite-dimensional models such as the Beta-Bernoulli (Shahriari et al., 2015) and the Gaussian (Hoffman et al., 2014) have been applied in the bandit context.

Both Bayesian linear and generalised linear models have been utilised within the Bayesian optimisation context (Russo and Van Roy, 2014; Shahriari et al., 2015). In the bandit context, these models are applied by associating each bandit arm with a feature vector $\mathbf{x}_\xi$, and assuming that the arm payout depends on this feature vector. For a linear model, for example, we would assume $f(\xi) = \langle \mathbf{x}_\xi, \mathbf{w} \rangle$. These models can also be applied to optimisation over continuous design spaces. Snoek et al. (2015) considered Bayesian optimisation using a Bayesian neural network as the model for f; they specifically took an 'adaptive basis regression' approach that is only Bayesian on the last layer of the network.

7.1.2 Nonparametric models

For continuous Bayesian optimisation, the Gaussian Process (GP) (Williams and Rasmussen, 2006) has proved an extremely popular Bayesian nonparametric model for the unknown function f (Osborne et al., 2009). The Gaussian process with a positive definite kernel k and mean function μ assumes the following multivariate Gaussian distribution for the finite-dimensional marginal distributions (Øksendal, 2003) of f

$$\begin{pmatrix} f(\xi_1) \\ \vdots \\ f(\xi_n) \end{pmatrix} \sim N\left(\begin{pmatrix} \mu(\xi_1) \\ \vdots \\ \mu(\xi_n) \end{pmatrix}, \begin{pmatrix} k(\xi_1, \xi_1) & \ldots & k(\xi_1, \xi_n) \\ \vdots & & \vdots \\ k(\xi_n, \xi_1) & \ldots & k(\xi_n, \xi_n) \end{pmatrix} \right). \tag{80}$$

Given a dataset of observations $\mathcal{D}_t = \{(\xi_i, y_i)\}_{i=1}^t$, the resulting posterior on f is also a Gaussian process. The mean and covariance structure of the posterior can be derived by computing the conditional form of

equation (80), however, the necessary matrix computations come at cubic cost $\mathcal{O}(t^3)$; we refer to Williams and Rasmussen (2006) for full details. As a mark of its popularity, BO with a GP model for f has been implemented in several software frameworks, such as BoTorch (Balandat et al., 2020).

Within Bayesian optimisation, several extensions of the GP have also been considered as models for f. Different variants of *sparse* GPs have been proposed (Quinonero-Candela and Rasmussen, 2005; Snelson and Ghahramani, 2006; Lázaro-Gredilla et al., 2010), aiming to reduce the computational burden of using the standard GP conditioning formula. Calandra et al. (2016) combined GPs with feature learning to propose the Manifold GP.

Beyond the GP family, Hutter et al. (2013) also considered a random forest model for f, but found GPs to be preferable. Focusing on the application of hyperparameter optimisation, Bergstra et al. (2011) proposed the Tree-structured Parzen Estimator model for f that combines a tree-structured hierarchy with mixture modelling. Finally, Neiswanger et al. (2019) considered Bayesian optimisation in which an arbitrary probabilistic program is used as the model for f.

7.2 Acquisition functions

7.2.1 The Entropy Search family

To define an information-theoretic acquisition function for Bayesian optimisation, we want to gain information about the random variable $\theta = \arg\max_{\xi\in\Xi} f(\xi)$. To this end, Villemonteix et al. (2009) proposed Stepwise Uncertainty Reduction (SUR). This method aims to reduce posterior entropy in θ using the acquisition rule

$$\alpha_{\mathrm{SUR}}(\xi;\mathcal{D}_t) := -\mathbb{E}_{p(y|\xi,\mathcal{D}_t)}[H[p(\theta|\mathcal{D}_t\cup\{(\xi,y)\})]]. \tag{81}$$

where $p(y|\xi,\mathcal{D}_t) = \mathbb{E}_{p(f|\mathcal{D}_t)}[p(y|f(\xi))]$. In practice, Villemonteix et al. (2009) estimated the acquisition function by discretising θ and using a GP model for f. Hennig and Schuler (2012) considered a closely related acquisition function called Entropy Search (ES) that maximises the KL-divergence between the posterior on θ and a base measure $b(\theta)$. This gives the acquisition function

$$\alpha_{\mathrm{ES}}(\xi;\mathcal{D}_t) := \mathbb{E}_{p(y|\xi,\mathcal{D}_t)}[\mathrm{KL}[p(\theta|\mathcal{D}_t\cup\{(\xi,y)\})\|b(\theta)]]. \tag{82}$$

The following Proposition, due to MacKay (1992), shows that these in information measures are equivalent, and are equivalent to the EIG.

Proposition 10 (MacKay (1992))**.** *Consider the general experimental design set-up of Sec. 3. The following acquisition functions all give the same optimal design*

$$\mathcal{I}(\xi) = \mathbb{E}_{p(y|\xi)}\left[\mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|\xi,y)] - \mathbb{E}_{p(\theta)}[\log p(\theta)]\right], \tag{83}$$

$$\mathcal{I}_2(\xi) = -\mathbb{E}_{p(y|\xi)}[H[p(\theta|\xi,y)]], \tag{84}$$

$$\mathcal{I}_3(\xi) = \mathbb{E}_{p(y|\xi)}[\mathrm{KL}[p(\theta|\xi,y)\|b(\theta)]] \tag{85}$$

where $p(y|\xi) = \mathbb{E}_{p(f)}[p(y|f(\xi))]$.

Proof. We have

$$\mathcal{I}(\xi) = \mathbb{E}_{p(y|\xi)}\left[\mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|\xi,y)] - \mathbb{E}_{p(\theta)}[\log p(\theta)]\right] \tag{86}$$

$$= \mathbb{E}_{p(y|\xi)}[-H[p(\theta|\xi,y)] + H[p(\theta)]] \tag{87}$$

$$= \mathcal{I}_2(\xi) + H[p(\theta)]. \tag{88}$$

and

$$\mathcal{I}(\xi) = \mathbb{E}_{p(y|\xi)}\left[\mathbb{E}_{p(\theta|\xi,y)}[\log p(\theta|\xi,y)] - \mathbb{E}_{p(\theta)}[\log p(\theta)]\right] \tag{89}$$

$$= \mathbb{E}_{p(y|\xi)}\left[\mathbb{E}_{p(\theta|\xi,y)}\left[\log\frac{p(\theta|\xi,y)}{b(\theta)}\right] - \mathbb{E}_{p(\theta)}\left[\log\frac{p(\theta)}{b(\theta)}\right]\right] \tag{90}$$

$$= \mathcal{I}_3(\xi) - \mathrm{KL}[p(\theta)\|b(\theta)]. \tag{91}$$

Since $H[p(\theta)]$ and $\mathrm{KL}[p(\theta)\|b(\theta)]$ do not depend on ξ, choosing ξ to maximise EIG is equivalent to maximising $\mathcal{I}_2$ and $\mathcal{I}_3$. □

Corollary 11. *Stepwise Uncertainty Reduction (Villemonteix et al., 2009) and Entropy Search (Hennig and Schuler, 2012) are equivalent to EIG maximisation when* $\theta = \arg\max_{\xi\in\Xi} f(\xi)$.

Proof. Note that $\mathcal{I}_2 = \alpha_{\mathrm{SUR}}$ and $\mathcal{I}_3 = \alpha_{\mathrm{ES}}$ when we replace the prior $p(\theta)$ with the posterior $p(\theta|\mathcal{D}_t)$. Since the result holds for a general experimental design set-up, it specifically holds in the BO case when $\theta = \arg\max_{\xi\in\Xi} f(\xi)$. □

Hernández-Lobato et al. (2014) proposed Predictive Entropy Search (PES). Like previous methods, PES uses the EIG (accounting for the embedded model, as in Sec. 6.1) as their acquisition function

$$\alpha_{\mathrm{PES}}(\xi;\mathcal{D}_t) = \mathcal{I}(\xi;\mathcal{D}_t) = H[p(\theta|\mathcal{D}_t)] - \mathbb{E}_{p(y|\xi,\mathcal{D}_t)}[H[p(\theta|\mathcal{D}_t \cup \{(\xi,y)\})]]. \tag{92}$$

However, the authors utilise the same insight as Houlsby et al. (2011) to write EIG in the equivalent form (see Proposition 9)

$$\mathcal{I}(\xi;\mathcal{D}_t) = H[p(y|\xi,\mathcal{D}_t)] - \mathbb{E}_{p(\theta|\mathcal{D}_t)}[H[p(y|\xi,\mathcal{D}_t,\theta)]]. \tag{93}$$

Within a GP model, the first term can be computed analytically, whilst the second is approximated by drawing samples of $\theta|\mathcal{D}_t$ and estimating $H[p(y|\xi,\mathcal{D}_t,\theta)]$ using expectation propagation (Minka, 2001). PES can be extended to batch acquisition in which we query f at multiple locations simultaneously on each iteration (Shah and Ghahramani, 2015).

In Maximum Entropy Search (MES) (Wang and Jegelka, 2017), the authors approach the problem differently. Instead of focusing on the latent variable of interest $\theta = \arg\max_{\xi\in\Xi} f(\xi)$, they instead formulate the problem with variable of interest $\theta_m = \max_{\xi\in\Xi} f(\xi)$. Here, θ_m is a one-dimensional random variable that represents the maximum *value* of the function f, rather than its arg max. The objective function for MES is then the EIG between a new observation y at design ξ and their parameter of interest θ_m

$$\alpha_{\mathrm{MES}}(\xi;\mathcal{D}_t) = H[p(y|\xi,\mathcal{D}_t)] - \mathbb{E}_{p(\theta_m|\mathcal{D}_t)}[H[p(y|\xi,\mathcal{D}_t,\theta_m)]]. \tag{94}$$

The MES objective may be easier to compute than PES with a GP model for f because θ_m is always one dimensional.

Computationally, a distinctive feature of BO with a GP model that sets it apart from computing the EIG in standard models (Sec. 4) is that many calculations can be performed analytically for the GP. For example, $H[p(y|\xi,\mathcal{D}_t)]$ is computed analytically in the PES acquisition function—this calculation would be intractable in a general model.

7.2.2 Other acquisition functions

Probability of improvement Perhaps the simplest acquisition rule, probability of improvement (Kushner, 1964) computes the probability that $f(\xi)$ is greater than some threshold τ

$$\alpha_{\mathrm{PI}}(\xi;\mathcal{D}_t) := \mathbb{P}(f(\xi) < \tau|\mathcal{D}_t). \tag{95}$$

Typically, the threshold τ is chosen adaptively to be the best objective value seen so far: $\tau_t = \max\{y_1,\ldots,y_t\}$.

Expected improvement A related acquisition rule is expected improvement (Mockus et al., 1978). This incorporates the amount by which the function value can be expected to increase at the location ξ, giving

$$\alpha_{\mathrm{EI}}(\xi;\mathcal{D}_t) := \mathbb{E}((f(\xi)-\tau)_+|\mathcal{D}_t) \tag{96}$$

where $x_+ = \max(0,x)$.

Upper confidence bound Starting with theoretical work on multi-armed bandits (Lai and Robbins, 1985), upper confidence bound (UCB) acquisition rules have been popular. Srinivas et al. (2009) explicitly considered the application of UCB functions with a GP model for BO. In its most general form, we let $q_p(\cdot)$ denote to the p-quantile of a univariate distribution. Then the UCB-p acquisition function is

$$\alpha_{\text{UCB-}p}(\xi; \mathcal{D}_t) := q_p(f(\xi)|\mathcal{D}_t). \tag{97}$$

In the Gaussian case, $f(\xi)|\mathcal{D}_t \sim N(\mu(\xi|\mathcal{D}_t), \sigma(\xi|\mathcal{D}_t)^2)$, an equivalent parametrisation of the UCB acquisition function is

$$\alpha_{\text{UCB-}p}(\xi; \mathcal{D}_t) = \mu(\xi|\mathcal{D}_t) + \beta_p \sigma(\xi|\mathcal{D}_t) \tag{98}$$

where β_p is the p-quantile of the standard Normal distribution.

Thompson sampling Thompson (1933) proposed a *stochastic* acquisition rule for Bayesian optimisation. Given a sample of the functional posterior $f_t \sim p(f|\mathcal{D}_t)$, Thompson Sampling chooses the maximiser of this sample as the next sampling location. This amounts to using the acquisition function

$$\alpha_{\text{TS}}(\xi; \mathcal{D}_t) = f_t(\xi) \text{ where } f_t \sim p(f|\mathcal{D}_t). \tag{99}$$

Hernández-Lobato et al. (2014) showed how the optimisation of a sample from the GP posterior can be approximately calculated.

8 Sequential Bayesian Experimental Design

We now lay out the theory of sequential experimentation more formally. Extending the basic sequential framework that we described for active learning in Sec. 5, we suppose that we have a sequence of T experiments. For each experiment, we pick ξ_t *adaptively* using the data that has already been observed[4] $\mathcal{D}_{t-1} = (\xi_1, y_1), \ldots, (\xi_{t-1}, y_{t-1})$. Given this design, we conduct an experiment using ξ_t and obtain outcome y_t. After each step of the experiment, our beliefs about θ are summarised by the posterior $p(\theta|\mathcal{D}_t)$, which is calculated as in Sec. 2.2. For an embedded model (Sec. 6), we would update our beliefs on the extended parameters ψ. For simplicity in this section, we assume we are not in an embedded model, unless otherwise stated, so the parameter θ is a full description of the model.

Policies and objectives The design ξ_t must be chosen on the basis of $\mathcal{D}_{t-1}$. A general abstraction to describe this is to introduce a *stochastic policy* $\pi(\xi|\mathcal{D}_{t-1})$ that maps from $\mathcal{D}_{t-1}$ to a distribution over designs. A special case of this is a deterministic policy, for which ξ_t is simply a function of $\mathcal{D}_{t-1}$.

In the sequential setting, it no longer makes sense to talk of the optimality of individual designs. Indeed, we cannot say whether a design ξ_2 will be optimal until we have observed the outcome y_1. Instead, we can describe optimality in terms of the *policy*—the policy which makes the best decision for ξ_2 for every possible value of y_1 would be an optimal policy.

Optimality also requires a criterion, so we must extend the utility-based approach of Sec. 3 based on Lindley (1972) to the sequential setting. Perhaps the most natural extension of Lindley's original theory, which is used implicitly by Huan and Marzouk (2016); Foster et al. (2021) is to consider a final utility, or reward, which is obtained after all data has been collected. In this *terminal reward* framework, we assume that we have a utility function $U(\theta, \mathcal{D}_T)$. Once we have collected all our data, we have expected utility $\mathbb{E}_{p(\theta|\mathcal{D}_T)}[U(\theta, \mathcal{D}_T)]$. The optimal policy, therefore, is the natural counterpart to equation (9), namely

$$\pi^* = \arg\max_{\pi} \mathbb{E}_{p(\mathcal{D}_T|\pi)} \left[\mathbb{E}_{p(\theta|\mathcal{D}_T)}[U(\theta, \mathcal{D}_T)] \right] \tag{100}$$

[4]For an exchangeable model, the order of the data does not matter, so we could write $\mathcal{D}_{t-1} = \{(\xi_1, y_1), \ldots, (\xi_{t-1}, y_{t-1})\}$, which we implicitly assumed was the case in Sections 5 and 7. For a non-exchangeable model, we need to know the order that data was collected to conduct valid inference.

Algorithm 3 Terminal reward Sequential Bayesian Experimental Design

Require: Prior $p(\theta)$, model $p(y|\xi,\theta)$, initial data $\mathcal{D}_0$ may be empty.
  for step $t = 1, \ldots, T$ **do**
    Use policy to compute design $\xi_t \sim \pi(\xi|\mathcal{D}_{t-1})$
    Obtain experimental observation $y_t \sim p(y|\theta, \xi_t)$ with design ξ_t
    Set $\mathcal{D}_t = (\xi_1, y_1), \ldots, (\xi_t, y_t)$
  end for
  Obtain reward $U(\theta, \mathcal{D}_T)$

where $p(\mathcal{D}_T|\pi) = \mathbb{E}_{p(\theta)}\left[\prod_{t=1}^{T} \pi(\xi_t|\mathcal{D}_{t-1})p(y_t|\theta,\xi_t)\right]$ for an exchangeable model[5]. The whole sequential experiment process is described in Algorithm 3.

Sequential EIG The natural extension of EIG to the sequential setting is to let (Foster et al., 2021)

$$U_{\mathcal{I}}(\mathcal{D}_T) = H[p(\theta)] - H[p(\theta|\mathcal{D}_T)] \tag{101}$$

or equivalently (Huan and Marzouk, 2016)

$$U_{\mathrm{KL}}(\mathcal{D}_T) = \mathrm{KL}[p(\theta|\mathcal{D}_T)\|p(\theta)]. \tag{102}$$

The intuition behind this utility is to reduce our uncertainty in the value of θ from the sum total of all our experiments. It is in the sequential setting that the naturalness of using information-theoretic objectives for experimental design becomes most apparent.

Example 12 (Shannon (1948); Lindley (1956))**.** *Consider a model with $\theta = (L, R)$ where L and R are discrete random variables with independent uniform priors $\theta \sim \mathrm{Unif}(n_L) \times \mathrm{Unif}(n_R)$. Suppose we have two experimental designs at our disposal: ξ_L and ξ_R which produce noiseless outcomes giving the values of L and R respectively. Then, the utility of the sequence of experiments ξ_L, ξ_R is equal to sum of the utilities of the separate experiments ξ_L and ξ_R, i.e.*

$$U_{\mathcal{I}}((\xi_L, L), (\xi_R, R)) = U_{\mathcal{I}}((\xi_L, L)) + U_{\mathcal{I}}((\xi_R, R)). \tag{103}$$

Proof. Direct calculation using equation (101) gives

$$U_{\mathcal{I}}((\xi_L, L), (\xi_R, R)) = \log(n_L n_R) = \log n_L + \log n_R \tag{104}$$
$$U_{\mathcal{I}}((\xi_L, L)) = \log n_L \tag{105}$$
$$U_{\mathcal{I}}((\xi_R, R)) = \log n_R. \tag{106}$$

□

Shannon (1948) showed that this property (along with other technical requirements) can only be satisfied by utilities based on entropy, making the EIG arguably the most natural criterion for sequential Bayesian experimental design.

Static and batch policies One simple approximation to the optimal policy is to select all designs $\xi_1, \ldots, \xi_T$ before the start of the experiment. This is known as *static* design, also called *open-loop* design (DiStefano III et al., 2014). In effect, static design collapses the sequential design problem back into the one-step problem of Sec. 3, albeit with a larger design space

$$\Xi^T = \{(\xi_1, \ldots, \xi_T) : \xi_t \in \Xi \text{ for all } t\} \tag{107}$$

[5]For a non-exchangeable model, it would be $p(\mathcal{D}_T|\pi) = \mathbb{E}_{p(\theta)}\left[\prod_{t=1}^{T} \pi(\xi_t|\mathcal{D}_{t-1})p(y_t|\theta,\xi_t,\mathcal{D}_{t-1})\right]$

and corresponding observation space. The probabilistic model is also augmented as in Sec. 2.2. Unfortunately, static design may be arbitrarily worse than the performance of the best fully adaptive policy.

Rather than choosing all T designs upfront, we could instead choose design in batches of B. There can be practical benefits for choosing designs in batches (Lyu et al., 2019), as opposed to choosing them individually. Mathematically, this *batch* design procedure fits back into the sequential theory we have already laid out, with batches of designs being chosen from the new design space Ξ^B. Static design corresponds to the case $B = T$ in which we stop after one batch. Batch design in active learning is discussed on page 16.

8.1 Greedy design policies

Designing a policy to solve equation (100) can be challenging. One common approximate strategy is *greedy* design (also called *myopic* design). A greedy policy can be characterised as choosing each design ξ_t assuming that this is the final experiment—i.e. that once ξ_t has been chosen and y_t observed, the sequence of experiments will terminate. This means that the greedy policy will choose ξ_t to maximise

$$\xi_t^* = \arg\max_{\xi \in \Xi} \mathbb{E}_{p(y|\xi_t, \mathcal{D}_{t-1})} \left[\mathbb{E}_{p(\theta|\mathcal{D}_t)}[U(\theta, \mathcal{D}_t)] \right]. \tag{108}$$

where $p(y|\xi_t, \mathcal{D}_{t-1}) = \mathbb{E}_{p(\theta|\mathcal{D}_{t-1})}[p(y|\theta, \xi)]$. We can see that this amounts to solving the one-step design optimisation problem of equation (9) at each t, with the important distinction that we *replace the original prior $p(\theta)$ with the posterior given existing data $p(\theta|\mathcal{D}_{t-1})$*. This agrees exactly with the greedy acquisition strategy described in Section 5.

There is a subtle distinction when θ is embedded in a larger model with parameters ψ (Sec. 6)—we must update our beliefs about all the parameters to $p(\psi|\mathcal{D}_{t-1})$ and use the predictive distribution $p(y|\xi_t, \mathcal{D}_{t-1}) = \mathbb{E}_{p(\psi|\mathcal{D}_{t-1})}[p(y|\psi, \theta)]$ for y. This agrees with the greedy acquisition strategy of Section 7, where we update the full model on the unknown function f at each step.

The greedy (myopic) approach to experimental design is very widely adopted (Cavagnaro et al., 2010; Drovandi et al., 2014; McGree et al., 2012; Myung et al., 2013; Foster et al., 2019). As noted, it is also the typical sequential optimisation strategy in Bayesian active learning and Bayesian optimisation. One benefit of the greedy strategy is its simplicity—it effectively reduces the sequential experimental design problem to repeated applications of one-step design. It is typically observed that greedy optimisation for experimental design does not fail as catastrophically as greedy policies can do in general reinforcement learning tasks (Bakker et al., 2020). We explore a possible theoretical explanation for this phenomenon.

8.1.1 Submodularity

How much do we lose by using a greedy approach? A key theoretical tool for studying greedy policies is the notion of *submodularity* (Krause and Golovin, 2014). In short, if a utility function obeys submodularity (and a number of other conditions), then the theorem of Nemhauser et al. (1978) proves that a greedy strategy can achieve at least $(1 - 1/e) \approx 63\%$ of the best possible utility.

To precisely define submodularity, we must first define several other concepts. For any (finite) set V, the *power set* of V is $2^V = \{S : S \subseteq V\}$. A *set function* is any function $g : 2^V \to \mathbb{R}$. The *discrete derivative* of g is defined as

$$\Delta_g(e|S) = g(S \cup \{e\}) - g(S), \tag{109}$$

i.e. the extra value of adding element e to the set $S \subseteq V$. A set function $g : 2^V$ is *submodular* if, for every $A \subseteq B \subseteq V$ and for every $e \in V \setminus B$,

$$\Delta_g(e|B) \leq \Delta_g(e|A). \tag{110}$$

Intuitively, the value of adding e to the larger set B is smaller than the value of adding e to the smaller set A. Submodularity captures the intuitive notion of 'diminishing returns'. We also define a set function to be *monotone* if, for $A \subseteq B \subseteq V$, we have

$$g(A) \leq g(B). \tag{111}$$

The *greedy strategy* to maximise a monotone set function is to increment S by adding elements one at a time, following the rule

$$S_t = S_{t-1} \cup \{e_t\} \quad \text{where} \quad e_t = \arg\max_{e \in V} \Delta_g(e|S_{t-1}). \tag{112}$$

The following theorem of Nemhauser et al. (1978) shows that the greedy strategy performs near-optimally for submodular set functions.

Theorem 13 (Nemhauser et al. (1978))**.** *Let g be a monotone, submodular set function $g : 2^V \to \mathbb{R}$. Let $(S_t)_{t \geq 0}$ be obtained by the greedy strategy of equation (112). Then for any $t \leq |V|$ we have*

$$g(S_t) \geq (1 - 1/e) \max_{S \subseteq V, |S| = t} g(S). \tag{113}$$

This theorem proves that the greedy strategy can achieve at least $(1 - 1/e)$ of the best possible performance.

Submodularity for static experimental design There is a direct connection between the theory of submodularity and the *greedy construction of static experimental designs*. Indeed, the static experimental design problem is to choose $(\xi_1, \ldots, \xi_T)$ where each $\xi_t \in \Xi$. We assign a value to each static design following equation (100)

$$g(\xi_1, \ldots, \xi_T) = \mathbb{E}_{p(y_1, \ldots, y_T | \xi_1, \ldots, \xi_T)} \left[\mathbb{E}_{p(\theta | \mathcal{D}_T)} [U(\theta, \mathcal{D}_T)] \right]. \tag{114}$$

Suppose we could show that g is a monotone, submodular set function. Then the result of Theorem 13 would apply, meaning that we could construct a static design greedily by adding one element at a time.

To satisfy these conditions, we first need g to be invariant to the order of $\xi_1, \ldots, \xi_T$; we therefore assume that the model is exchangeable (Sec. 2.2). For the properties of submodularity and monotonicity, we need to choose a utility U, here we focus on the EIG with $U_{\mathcal{I}} = H[p(\theta)] - H[p(\theta|\mathcal{D}_T)]$. Then the function g becomes the mutual information between θ and $y_1, \ldots, y_T$ given $\xi_1, \ldots, \xi_T$.

Proposition 14 (Krause and Guestrin (2012))**.** *Suppose that, for any k and for designs $\xi_1, \ldots, \xi_k$, the random variables $y_1|\xi_1, \ldots, y_k|\xi_k$ are independent conditional on θ. Then the mutual information*

$$g(\{\xi_1, \ldots, \xi_k\}) = \mathbb{E}_{p(y_1, \ldots, y_k | \xi_1, \ldots, \xi_k)} \left[H[p(\theta)] - H[p(\theta | \mathcal{D}_k)] \right] \tag{115}$$

is a monontone, submodular set function.

The conditional independence assumption is equivalent to assuming an exchangeable model (Sec. 2.2) in which θ is the only model parameter (Sec. 6). Proposition 14 was also proved by Kirsch et al. (2019) in the context of BatchBALD for active learning.

8.1.2 Adaptive submodularity

The limitation of submodularity as a tool for analysing experimental design is that it does not consider *adaptive* design policies where the choice of a later design could be conditional on the outcome of earlier experiments. To address this limitation, Golovin and Krause (2011) introduced the notion of *adaptive submodularity*.

To define adaptive submodularity within our framework for experimental design, we focus on a discrete design space $|\Xi| < \infty$. We can then define the *conditional expected marginal benefit* of a design ξ as

$$\Delta(\xi | \mathcal{D}_t) = \mathbb{E}_{p(\theta | \mathcal{D}_t) p(y | \theta, \xi)} [U(\theta, \mathcal{D}_t \cup \{(\xi, y)\}) - U(\theta, \mathcal{D}_t)]. \tag{116}$$

The utility U is *adaptive monotone* with respect to model $p(\theta)p(y|\theta, \xi)$ if the conditional expected marginal benefit of all designs is positive. That is, for all $t \geq 0, \mathcal{D}_t$ and $\xi \notin \mathcal{D}_t$ we have

$$\Delta(\xi | \mathcal{D}_t) \geq 0. \tag{117}$$

Furthermore, the utility U is *adaptive submodular* with respect to model $p(\theta)p(y|\theta,\xi)$ if for all $s \leq t$ and all nested datasets $\mathcal{D}_s \subseteq \mathcal{D}_t$ and for all designs $\xi \notin \mathcal{D}_t$ we have

$$\Delta(\xi|\mathcal{D}_t) \leq \Delta(\xi|\mathcal{D}_s). \tag{118}$$

This is a natural generalisation of submodularity for set functions, and again it captures the principle of 'diminishing returns'. Golovin and Krause (2011) were able to generalise the result of Nemhauser et al. (1978) to the adaptive case for noiseless experiments in which $p(y|\theta,\xi)$ is deterministic.

Theorem 15 (Golovin and Krause (2011))**.** *Let π^{greedy} be the greedy policy of equation (108). Assume U is adaptive monotone and adaptive submodular for model $p(\theta)p(y|\theta,\xi)$. Then,*

$$\mathbb{E}_{p(\mathcal{D}_T|\pi^{greedy})}\left[\mathbb{E}_{p(\theta|\mathcal{D}_T)}[U(\theta,\mathcal{D}_T)]\right] \geq (1-1/e)\sup_{\pi}\mathbb{E}_{p(\mathcal{D}_T|\pi)}\left[\mathbb{E}_{p(\theta|\mathcal{D}_T)}[U(\theta,\mathcal{D}_T)]\right]. \tag{119}$$

Golovin et al. (2010) explored the applicability of this framework to Bayesian active learning and Bayesian experimental design, focusing on the noiseless case in which $p(y|\theta,\xi)$ is deterministic. They proved that the information gain utility $U_{\mathcal{I}}$ is adaptive monotone and adaptive submodular, so the result of Theorem 15 applies in this case.

A key results of Chen et al. (2015) did away with the noiseless assumption. Instead, they assumed that different experimental outcomes are independent conditional on θ. This matches exactly with the factorisation equation (3). They also assume that θ takes finitely many values $|\Theta| < \infty$. The key bound is as follows

Theorem 16 (Theorem 2 of Chen et al. (2015))**.** *Let π^{greedy} be the adaptive greedy experimental design policy. Assume that observations y are conditionally independent given θ. Then, for any $\delta > 0$*

$$\mathbb{E}_{p(\mathcal{D}_T|\pi^{greedy})}\left[U_{\mathcal{I}}(\mathcal{D}_T)\right] \geq \left(1-\exp\left[-\frac{1}{\gamma\max\{\log|\Theta|,\log(1/\delta)\}}\right]\right)\left(\sup_{\pi}\mathbb{E}_{p(\mathcal{D}_T|\pi)}\left[U_{\mathcal{I}}(\mathcal{D}_T)\right]-\delta\right) \tag{120}$$

where γ is a constant that depends on the noise distribution (see Chen et al. (2015)), and $U_{\mathcal{I}}$ is the information gain defined in equation (101).

Chen et al. (2017) went on to consider the case of noisy and correlated experimental outcomes (violating both the noiseless and the conditionally independent assumptions).

Finally, we note that the expected information gain is *not* adaptive submodular without assumption. This is elucidated by the following example, in which outcomes are not independent conditional on θ.

Example 17 (Inspired by Theorem 9 of Golovin et al. (2010))**.** *Consider a model with prior $\theta \sim \text{Unif}(\{-1,1\})$ and with $v \sim \text{Unif}(\{-1,1\})$. We have two potentially useful designs. ξ_v reports the value of v. $\xi_{\theta v}$ reports the value of θv. We also have M 'dummy' designs $\xi_1^d,\ldots,\xi_M^d$ which report nothing. Clearly, the optimal strategy to learn θ is to conduct experiments with ξ_v and $\xi_{\theta v}$ in any order, since $v \cdot \theta v = \theta v^2 = \theta$. However, if we analyse a one-step optimal greedy strategy, we observe that every design apart from $\xi_{\theta v}$ is independent of the value of θ, and hence has EIG 0. We can also verify that, without knowing v, the posterior on θ given the outcome of design $\xi_{\theta v}$ is still $\text{Unif}(\{-1,1\})$, hence the EIG of this design is also 0. Thus the greedy strategy will pick a design at random. If M is very large, the greedy strategy is likely to keep picking dummy designs.*

8.1.3 Asymptotic theory

A celebrated result of asymptotic statistics is the Bernstein–von Mises Theorem (Van der Vaart, 2000). In our experimental design set-up, this says that, under certain technical conditions and with i.i.d. random designs $\xi_t \overset{\text{i.i.d.}}{\sim} p(\xi)$, the posterior distribution $p(\theta|\mathcal{D}_t)$ is asymptotically Gaussian centred on the true value θ^* of the parameters of interest and with covariance matrix $t^{-1}M(\theta^*)^{-1}$. (Here, $M(\theta)$ is the Fisher information matrix, taking the expectation over $\xi \sim p(\xi)$.)

Paninski (2005) showed that a closely related result holds when designs are not random, but are chosen by greedy maximisation of the EIG.

Theorem 18 (Theorem 1 of Paninski (2005)). *Under certain technical conditions, the posterior distributions with greedy EIG maximisation are asymptotically Gaussian with mean θ^* and with covariance matrix $t^{-1}\Sigma_{info}$. Furthermore, if $t^{-1}\Sigma_{iid}$ is the asymptotic covariance with i.i.d. random designs, then*

$$\det \Sigma_{info} \leq \det \Sigma_{iid}. \tag{121}$$

This result tells us that the EIG maximisation strategy is no worse than i.i.d. sampling of designs, and that it will recover the true value θ^* in the limit as $t \to \infty$, i.e. the procedure is statistically consistent.

8.2 Non-greedy design policies

Whilst greedy policies enjoy computational tractability and some theoretical guarantees, a more direct approach to the problem of sequential experimental design is to seek the optimal policy that maximises equation (108). As we discuss in Sec. 9, finding this optimal policy can be cast in the language of reinforcement learning. In this section, we focus on computational approaches that have been suggested in the literature that specifically address non-greedy experimental design. These can generally be organised under two headings.

Forward sampling The forward sampling, or lookahead, family approaches relax the greedy assumption that the next experiment will be the last one. Instead, they assume that there will be m more experiments, and take account of these m future steps when deciding on the next experimental design. As m grows larger, this approach more closely approximates the truly optimal decision. However, with a larger m, the number of future outcomes to consider may grow exponentially. Such approaches either try to limit the number of outcomes considered, or else use a smaller value of m.

Backwards induction An alternative solution is to begin at the end. Classical optimisation theory (Bellman, 1966) shows that sequential optimisation problems are often more easily solved by starting with the final decision to be made at time T. For this final decision, the greedy solution is exactly optimal. The values of designs at later steps can be propagated backwards to inform earlier decisions. (See Sec. 9 for a fuller discussion.)

Non-greedy optimisation has typically been confined to low-dimensional cases within experimental design (Ryan et al., 2016). In medicine, Whitehead and Brunier (1995) and Whitehead and Williamson (1998) used a multi-step lookahead when finding optimal treatment doses. Berry and Ho (1988) explored optimal stopping when testing a one-sided hypothesis. Lewis and Berry (1994) applied backwards induction in a Bayesian clinical trials setting. Carlin et al. (1998) used forward sampling in a closely related clinical trial design problem. Brockwell and Kadane (2003) implemented backwards induction on a grid, and applied this to clinical trial planning. Müller et al. (2006) explored forward sampling for dose-response finding in clinical trials.

The main work to tackle the more general sequential experimental design problem, using the EIG utility, was Huan and Marzouk (2016). They used approximate dynamic programming to perform backwards induction by estimating the *value function*. The value function was then used to select optimal designs at each stage. The intermediate posterior distributions were estimated on a dynamically adapted grid.

In another line of work, González et al. (2016) build a predictor of future query locations given the current data. This allows them to use a forward sampling approach that is restricted to a single future trajectory. Jiang et al. (2020) use a related approach in which the future query locations are learned by repeatedly solving the *static* design optimisation problem with $T - t$ designs, but only using one of these designs at each step.

9 Bayesian Reinforcement Learning

Reinforcement learning (RL) (Sutton, 1990; Szepesvári, 2010) has a number of important and fascinating connections to sequential Bayesian experimental design. First, the problem of sequential experimental design

is a reinforcement learning problem. Specifically, we will show how the set-up of the preceding section can be cast as a Bayes Adaptive Markov Decision Process (BAMDP) (Ross et al., 2007; Guez et al., 2012; Ghavamzadeh et al., 2016). Second, the problem of making sequential decision to learn about a model is deeply connected to *exploration* in model-based reinforcement learning (Sun et al., 2011; Shyam et al., 2019; Sekar et al., 2020).

9.1 Sequential Bayesian Experimental Design as a BAMDP

The BAMDP is a generalisation of the Markov Decision Process (Bellman, 1957; Duff, 2002) that accommodates an unknown transition model. Adopting the notation of Guez et al. (2012), a BAMDP can be described by its augmented state space S^+, action space A, augmented transition model $\mathcal{P}^+$, reward function R^+ and discount factor γ. The augmented state space consists of the *history* of all states and actions previously visited $h_t = s_1 a_1 \dots a_{t-1} s_t$. This data is used to update the transition model in a Bayesian manner, using

$$p(\mathcal{P}|h_t) \propto p(\mathcal{P}) p(h_t|\mathcal{P}). \tag{122}$$

For a sampled transition model, the probability of moving from s_t to s_{t+1} when action a_t was used is

$$p(s_{t+1}|s_t, a_t, \mathcal{P}) = \mathcal{P}(s_t, a_t, s_{t+1}). \tag{123}$$

The BAMDP transition model is therefore given by the marginal (Guez et al., 2012)

$$p(s_{t+1}|a_t, h_t) = \int p(\mathcal{P}|h_t) \mathcal{P}(s_t, a_t, s_{t+1}) \, d\mathcal{P}. \tag{124}$$

The reward for using action a in state s is sampled as $r \sim R(s, a)$. Planning in a BAMDP means finding the policy that maximises

$$\mathcal{J}(\pi) = \mathbb{E}_\pi \left[\sum_{t=1}^{T} \gamma^{-t} r_t \right]. \tag{125}$$

To set up sequential Bayesian experimental design in this framework, we associate the augmented history states with the data $\mathcal{D}_t$ up to time t. The actions of the BAMDP are the experimental designs ξ_t. The transition model is associated with the model parameters θ (we assume in this section that we are not considering an embedded model). The 'transitions' of a sequential experiment are given by

$$p(\mathcal{D}_{t+1}|\mathcal{D}_t, \xi_{t+1}) = \mathbb{E}_{p(\theta|\mathcal{D}_t)}[p(y_{t+1}|\theta, \xi)] = \int p(\theta|\mathcal{D}_t) p(y_{t+1}|\theta, \xi_{t+1}) \, d\theta \tag{126}$$

which agrees with equation (124) if we take $\mathcal{P}_\theta(y_{t+1}, \xi_{t+1}, y_t) = p(y_{t+1}|\theta, \xi_{t+1})$. Note that we write a_t as ξ_{t+1}, and that in the exchangeable experimental design case the transition model does not depend explicitly on y_t.

The only minor distinction from the set-up of Guez et al. (2012) is that the rewards in experimental design depend on the augmented state $\mathcal{D}_t$ rather than the state s_t. We can take the reward function for experimental design to be $R(\mathcal{D}_t) = \mathbf{1}[t = T]\mathbb{E}_{p(\theta|\mathcal{D}_t)}[U(\theta, \mathcal{D}_t)]$. Setting the discount factor $\gamma = 1$, we see that the BAMDP objective equation (125) is the same as the sequential experimental design problem equation (100). This shows the close connection between these two fields. For completeness, the value function and Q-function (Szepesvári, 2010) for Bayesian experimental design are given by

$$V^\pi(\mathcal{D}_t) = \mathbb{E}_{p(\mathcal{D}_T|\mathcal{D}_t, \pi)} \left[\mathbb{E}_{p(\theta|\mathcal{D}_T)}[U(\theta, \mathcal{D}_T)] \right] \tag{127}$$

$$Q^\pi(\mathcal{D}_t, \xi_{t+1}) = \mathbb{E}_{p(\mathcal{D}_T|\mathcal{D}_t, \xi_{t+1}, \pi)} \left[\mathbb{E}_{p(\theta|\mathcal{D}_T)}[U(\theta, \mathcal{D}_T)] \right] \tag{128}$$

where

$$p(\mathcal{D}_T|\mathcal{D}_t, \pi) = \mathbb{E}_{p(\theta|\mathcal{D}_t)} \left[\prod_{\tau=t+1}^{T} \pi(\xi_\tau|\mathcal{D}_{\tau-1}) p(y_\tau|\theta, \xi_\tau) \right] \tag{129}$$

$$p(\mathcal{D}_T|\mathcal{D}_t, \xi_{t+1}, \pi) = \mathbb{E}_{p(\theta|\mathcal{D}_t)} \left[p(y_{t+1}|\theta, \xi_{t+1}) \prod_{\tau=t+2}^{T} \pi(\xi_\tau|\mathcal{D}_{\tau-1}) p(y_\tau|\theta, \xi_\tau) \right]. \tag{130}$$

Belief states In the previous section, we followed Guez et al. (2012) and took the state space for experimental design to be the dataset $\mathcal{D}_t$. We see from equation (126) that the transition model only depends on $\mathcal{D}_t$ via the posterior $p(\theta|\mathcal{D}_t)$. Furthermore, our choice of reward function only depends on $p(\theta|\mathcal{D}_t)$ (plus an indicator that we have reached the final stage). Thus, it is sufficient to take $p(\theta|\mathcal{D}_t)$ as our augmented state. Posterior distributions treated as states are referred to as *belief states* (Igl et al., 2018). They have been utilised extensively in Bayesian RL (Igl et al., 2018; Zintgraf et al., 2019; Ghavamzadeh et al., 2016) and are beginning to be used in Bayesian experimental design (Huan and Marzouk, 2016).

9.2 Exploration

We have seen the close connection between sequential Bayesian experimental design and Bayesian RL. We associated the transition model of an unknown MDP with the model parameter θ. In this framing, we have a new interpretation of objective functions for experimental design—they encourage the collection of data to improve knowledge of the transition model and are motivated by model-derived quantities, rather than by an external reward signal. Utility functions for experimental design can thus be reinterpreted as rewards for *exploration* behaviour that leads to improved knowledge in a model of the environment.

The experimental design scenario is most closely connected with model-based reinforcement learning (Sutton, 1990). Specifically, we consider reinforcement learning settings in which we have a Bayesian parametric model of the environment with parameter θ. A range of authors have considered 'intrinsic rewards' (Singh et al., 2005)—unlike external rewards which are separate from the model and environment dynamics, intrinsic rewards encourage behaviour to learn about the environment. For example, Itti and Baldi (2006) used surprisal as an intrinsic reward—agents are encouraged to take actions for which the outcome is not predictable, and hence will be surprising. Mathematically, surprisal can be defined using predictive entropy. Empowerment (Klyubin et al., 2005; Salge et al., 2014; Mohamed and Rezende, 2015) is another intrinsic reward signal that is based on conditional mutual information between state and action variables. Sajid et al. (2021) studied curiosity-driven exploration and the connection with free energy minimisation.

One line of research uses EIG as an intrinsic reward signal (Storck et al., 1995). This curiosity-driven exploration (Schmidhuber, 2010; Sun et al., 2011) is therefore the closest part of the RL literature to sequential experimental design. Specifically, Sun et al. (2011) utilise information gain as a reward. Given history h and h' such that h is a prefix of h' they define

$$\mathrm{IG}(h'\|h) = \mathrm{KL}\left(p(\theta|h')\|p(\theta|h)\right). \tag{131}$$

To motivate this choice, Sun et al. (2011) proved the following result (a more formal version of Example 12)

Proposition 19 (Sun et al. (2011))**.** *Let $h \subseteq h' \subseteq h''$ be histories such that h a prefix of h' and h' a prefix of h''. Suppose h' has been observed. Then,*

$$\mathbb{E}_{h''|h'}[\mathrm{IG}(h''\|h)] = \mathrm{IG}(h'\|h) + \mathbb{E}_{h''|h'}[\mathrm{IG}(h''\|h')] \tag{132}$$

so the information gain is additive in expectation.

Information gain for exploration was applied to robotics by Fung et al. (2016).

9.2.1 Computational approaches to exploration in Bayesian RL with EIG

To utilise information gain as an intrinsic reward for exploration requires approximation and optimisation of this quantity. Storck et al. (1995) focused on the tabular setting with finite states and actions, in which the transition model can be described with a finite number of parameters. Sun et al. (2011) also focused on the finite space case for their computations. Houthooft et al. (2016) tackled the continuous space problem. They used variational inference (Rezende et al., 2014; Kingma and Welling, 2014) to estimate the posterior distributions $p(\theta|\mathcal{D}_t)$. They then used the variational approximate posterior as a surrogate for the true posterior when computing the information gain reward. Information gain was combined with an external reward signal to balance exploration and exploitation. Shyam et al. (2019) used an ensemble to approximate

the distribution $p(\theta|\mathcal{D}_t)$, to estimate information gain they replaced Shannon entropy with Rényi entropy which can be calculated for a mixture of Gaussians. Sekar et al. (2020) used a closely related approach. Rather than the Rényi entropy, they used the empirical variance of ensemble means as a way of estimating the intractable marginal entropy that occurs in the EIG.

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