Likelihood-free Bayesian inference on the minimum clinically important difference

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Abstract

In applications where a likelihood that directly connects the data to the parameter of interest may not be available, one might think that a Bayesian analysis is out of reach. Here we consider a likelihood-free Bayesian approach based on the use of a suitable loss function. Our analysis is carried out in the context of a practically important likelihood-free example in medical statistics, namely, inference on the minimum clinically important difference, a threshold that defines a cutoff for clinical significance. We construct a likelihood-free posterior distribution for the minimum clinically important difference, prove its desirable asymptotic properties, and demonstrate with simulations that our new approach yields inference that generally outperforms that based on standard techniques.

Keywords and phrases: Clinical significance; loss function; M-estimation; model-free inference; posterior convergence rates.

1 Introduction

The standard Bayesian approach to statistical inference requires a likelihood function, describing the relationship between the observable data and a collection of unknown parameters, and a prior distribution for those parameters. Bayes theorem provides a conceptually simple procedure for combining the likelihood and prior to get a posterior, but actually obtaining a likelihood and prior, and performing the required posterior computations, can be costly in a variety of ways. By not requiring a full probability model connecting observable data to unknown parameters, all of these costs can be reduced, creating new opportunities for Bayesian inference. Here we address this interesting and important question, namely, how to carry out a Bayesian analysis when, for one reason or another, a genuine likelihood function is not available.

The problem we consider here has some connection to the more familiar problem of model misspecification, i.e., where a likelihood function is specified but turns out not to be the likelihood for the correct model. In such cases, there is a potential bias due to model misspecification, and the effect of this has been well-studied in the Bayesian
literature, for example, Berk (1966), Bunke and Milhaud (1998), Lee and MacEachern (2011), Kleijn and van der Vaart (2012), and Walker (2013); see Kleijn and van der Vaart (2006), De Blasi and Walker (2013), and Ramamoorthi et al. (2014) for results on misspecification in nonparametric problems. However, here we are not so much interested in the effect of a misspecified likelihood but, rather, what to do if one does not have a suitable likelihood in the first place. Bissiri et al. (2013) recently have discussed how, in cases where the parameter of interest is defined through a loss function rather than a likelihood, one can use that loss function to construct a posterior distribution. As an example, quantile regression is one where the connection between data and parameters is typically described via a loss function, called the “check loss” (e.g., Koenker 2005). Yu and Moyeed (2001) noted that Bayes estimators obtained by using an asymmetric Laplace likelihood—the negative logarithm of which resembles the check loss—had good empirical properties, and Sriram et al. (2013) established posterior consistency of the model using that loss function-motivated likelihood.

While the use of a loss function-motivated likelihood is not necessarily a new concept, we think this idea has considerable untapped potential, for at least two reasons. First, to our knowledge, model misspecification considerations primarily focus on the unfortunate case where the wrong likelihood is used, a consequence of having incomplete information about the data-generating mechanism. However, even if a genuine likelihood is or could be made available, one may choose not to use it. One case is when the genuine likelihood is too expensive to compute, and approximate Bayesian computation (e.g., Marin et al. 2012) and composite likelihood methods (e.g., Varin et al. 2011) are designed for such cases. Another case is when one may not wish to spend the resources needed to flesh out a full model, including priors for the model parameters, and then carry out the full posterior computations when, ultimately, it will be marginalized to the parameter of interest. The question is why not just do a sort of “implicit marginalization” first to get a posterior directly on the parameter of interest. This would simplify prior specifications and posterior computations and, given its connection to empirical risk optimization, would help popularize Bayesian methods in machine learning applications. Second, there are cases where any reasonable choice of likelihood would not yield a posterior with good concentration properties. The particular application to be considered here, discussed next, involves a loss function which is not smooth, and plugging in any smooth likelihood may lead to a bias which cannot be overcome, even asymptotically.

Here we will explore the development of a likelihood-free Bayesian analysis within the context of an interesting application in medical statistics. One objective of a clinical trial is assessing the efficacy of a treatment, but experts have observed that statistical significance alone does not necessarily imply efficacy. For instance, a study with high power may detect statistically significant differences, but these do not translate to practical differences noticeable by the patients. As a result, a cutoff value different than a statistical critical value is desired that would separate patients with and without clinically significant responses. This cutoff is called the “minimum clinically important difference,” or MCID for short. Accurate inference on the MCID is of significant importance to clinicians and health policy-makers to make educated judgments about the effectiveness of certain treatments. That the U. S. Food and Drug Administration (FDA) held a special
conference in 2012 concerning inference on the MCID is further justification of the importance of this application. More details on the MCID application, and the available results, are discussed in Section 2.

An important feature of the MCID problem is that the parameter of interest, $\theta$, is defined through a loss function, not a likelihood function; see Equation (1). If one did have a likelihood, then $\theta$ could be expressed as a function of the parameters of that likelihood function, but then it is not clear where the likelihood itself would come from. Moreover, it is not clear what is the advantage of going to the trouble to construct a model with associated parameters, introduce a prior for those parameters, and do the posterior computations, only to throw away that posterior, retaining only the marginal posterior distribution for $\theta$. Here, using some ideas in Bissiri et al. (2013), we construct, in Section 3.1, a likelihood-free posterior distribution directly on the MCID $\theta$ and, in Sections 3.2–3.3, we derive the asymptotic concentration properties of this posterior distribution. Our analysis is transparent, being based on some basic empirical process tools, and leads to some improvements on the available results for M-estimation of MCID. An important feature of the Bayesian approach is that the posterior distribution includes some measure of uncertainty, which can be converted into credible intervals, etc. Simulations results are presented in Section 4 and the take away message is that our proposed Bayesian posterior provides better inference on MCID, in terms of estimation accuracy and interval coverage and length, than the M-estimator of Hedayat et al. (2014). Some concluding remarks, including some broader perspective and new research questions, are given in Section 5. Technical details and proofs of the theoretical results are provided in the Appendix. While our work here focuses primarily on the MCID application, we believe that our analysis can be used as a template for others who want to carry out a Bayesian analysis but are discouraged by the efforts required to specify sampling models and prior distributions.

2 Minimum clinically important difference

2.1 Notation and definitions

In clinical trials for drugs or medical devices, it is standard to judge the effectiveness of the treatment based on statistical significance. However, it is possible that the treatment effect may be significantly different from zero in a statistical context, but the effect size is so small that the patients do not experience an improvement. To avoid the costs associated with bringing to market a treatment that is not clinically effective, it is advantageous to bring the patients’ assessment of the treatment effect into the analysis. While the need for a measure of clinical significance is well-documented (e.g., Kaul and Diamond 2010), it seems there is no universal definition of MCID and, consequently, there is no standard methodology to make inference on it. Recent efforts in this direction were made by Shiu and Gatsonis (2008) and Turner et al. (2010). Hedayat et al. (2014) provide a mathematically convenient formulation, described next, in which the MCID is expressed as a minimizer of a suitable loss function.

Let $Y \in \{-1, 1\}$ denote the patient reported outcome with 1 meaning that the treat-
ment was effective and $-1$ meaning that the treatment was not effective. Let $X$ be a continuous diagnostic measure taken on each patient. Let $P$ denote the joint distribution of $(X,Y)$, and $p$ the marginal density of $X$ with respect to Lebesgue measure. Given $\theta \in \mathbb{R}$, define the function $\ell_\theta$ by

$$\ell_\theta(x,y) = \frac{1}{2} \{1 - y \text{sign}(x - \theta)\}, \quad (x,y) \in \mathbb{R} \times \{-1,1\},$$

where $\text{sign}(0) = 1$, and write $L(\theta) = P\ell_\theta$ for the expectation of $\ell_\theta$ with respect to the joint distribution $P$. Then the MCID, denoted by $\theta^*$, is defined as

$$\theta^* = \arg\min_\theta L(\theta). \quad (1)$$

That is, the MCID is the minimizer of the expected loss $L$, and depends on the distribution $P$ in a somewhat complicated way; that is, we cannot easily think of a parametric model for $P$ that yields $\theta^*$ as a function of those parameters. The intuition behind this definition is the alternative expression for $L(\theta)$:

$$L(\theta) = P\{Y \neq \text{sign}(X - \theta)\},$$

i.e., $\theta^*$ minimizes, over $\theta$, the probability that $\text{sign}(X - \theta)$ disagrees with $Y$. In other words, $\text{sign}(X - \theta^*)$ is the best predictor of $Y$ in terms of minimum misclassification probability. Another representation of the MCID, as demonstrated by Hedayat et al. (2014), that will be convenient below is as a solution to the equation $\eta(\theta) = 1/2$, where

$$\eta(x) = P(Y = 1 \mid X = x) \quad (2)$$

is the conditional probability function. If $\eta$ is continuous and strictly increasing, then $\theta^*$ will be the unique solution to the equation $\eta(\theta) = 1/2$.

### 2.2 M-estimator and its large-sample properties

Hedayat et al. (2014) propose to estimate the MCID by minimizing an empirical risk. Let $P_n = n^{-1} \sum_{i=1}^n \delta_{(X_i,Y_i)}$ be the empirical measure, based on the observations $\{(X_i,Y_i) : i = 1,\ldots,n\}$. Then the empirical risk is $L_n(\theta) = P_n\ell_\theta$, and an M-estimator of MCID is obtained by minimizing $L_n(\theta)$, i.e.,

$$\hat{\theta}_n = \arg\min_\theta L_n(\theta). \quad (3)$$

Computation of the estimator is straightforward since it takes only finitely many values depending on the order statistics for the $X$-sample. Therefore, a simple grid search is guaranteed to quickly identify the minimizer $\hat{\theta}_n$. Consistency of $\hat{\theta}_n$ as an estimator of $\theta^*$, i.e., $\hat{\theta}_n - \theta^* = o_P(1)$ as $n \to \infty$, is established in Hedayat et al. (2014) under the condition that $\eta$ in (2) is continuous and strictly increasing; see our Theorem 2 below.

A shortcoming of this approach is that, due to the discontinuity of the loss function, an asymptotic normality result does not seem possible; see Section 2.3. Therefore, statistical inference on the MCID based on the loss minimizer $\hat{\theta}_n$ is not currently available. This provides some motivation for a Bayesian analysis, where credible intervals, etc, can be easily obtained, but some non-standard ideas are needed to deal with the fact that there is
no natural likelihood for \( \theta \); see Section 3. Bootstrap methods are available (see Section 4) but there is some general concern about the validity of the basic bootstrap in this case because, as Theorem 1 demonstrates, the rate is not the usual \( n^{-1/2} \).

Beyond consistency, convergence rates for the M-estimator \( \hat{\theta}_n \) have been studied by Hedayat et al. (2014). These rates rely heavily on the local behavior of the function \( \eta \) and of the marginal distribution of \( X \) around \( \theta^* \). Our assumptions here are slightly different than those in Hedayat et al., and we compare the two sets of conditions in Remark 1.

Assumption 1. Let \( p \) be the marginal density of \( X \), and assume that there exists an interval \( I \) around \( \theta^* \) such that

\[
p \text{ is continuous and bounded away from 0 and } \infty \text{ on } I.
\]  

(4)

Assumption 2. Fix two positive numbers \( M \) and \( \Delta \), with \( \Delta \) small. Let \( \gamma > 0 \) be the largest number such that

\[
\sup_{|x - \theta^*| \leq \varepsilon} |\eta(x) - \frac{1}{2}| \leq M\varepsilon^\gamma, \quad \forall \varepsilon \in (0, \Delta].
\]  

(5)

Assumption 1 is mild, given that the context assumes that \( X \) is a continuous random variable with a density. Assumption 2 is implied by a Hölder continuity condition on \( \eta \) which is, in general, weaker than differentiability; see Definition 1.2 in Tsybakov (2009). To get an idea of what role \( \gamma \) plays in determining the rate, note that \( \gamma \) will be large/small for functions \( \eta \) which are relatively flat/steep near \( \theta^* \). Since steep \( \eta \) means \( \theta^* \) is easier to identify, we expect that small \( \gamma \) will correspond to faster rates, which is indeed the case; see, also, the discussion in Tsybakov (2004). We will have more to say about \( \gamma \) in Remark 2 following the theorem statement. A similar result is given in Hedayat et al. (2014) but we have simplified the conditions and also improved the rate; the proof is a direct consequence of results presented in Section 3.

Theorem 1. Suppose that \( p \) is continuous and strictly increasing, and that (4) holds. For \( \gamma \) satisfying (5), define \( r(\gamma) = (1 + 4\gamma)^{-1} \). Then the M-estimator \( \hat{\theta}_n \) in (3) satisfies

\[
\hat{\theta}_n - \theta^* = O_P(n^{-r(\gamma)}) \text{ as } n \to \infty.
\]

Proof. See Appendix A.2

Remark 1. In place of our Assumption 1, Hedayat et al. (2014) impose a margin condition which assumes the existence of a constant \( \alpha > 0 \) such that

\[
P(|\eta(X) - \frac{1}{2}| \leq \varepsilon) \lesssim \varepsilon^\alpha,
\]  

(6)

where “\( \lesssim \)” denotes inequality up to a universal constant. Conditions such as this are common; see, for example, Equation (5) in Tsybakov (2004). However, given that \( X \) is assumed to be continuous with a Lebesgue density, if that density is well-behaved near \( \theta^* \), then it can be confirmed that (6) holds with \( \alpha = \gamma^{-1} \) and their rate result agrees with ours, except that we have removed their unnecessary logarithmic term. We believe that conditions on the density \( p \) of \( X \) are more natural than conditions on the distribution of \( \eta(X) \).
Remark 2. To get a better feel about the role $\gamma$ plays, consider the case where $\eta(x) = \Phi(x/\sigma)$ for some $\sigma > 0$, where $\Phi$ is the standard normal distribution function. In this case, $\theta^* = 0$. Since $\Phi$ is differentiable, if $\sigma$ is large then $\gamma = 1$. However, for small $\sigma$, $\eta$ is relatively steep near 0, so a better rate should be possible. Take $M$ and $\Delta$ fixed as in Assumption 2 in this case, if $M \geq (2\pi\sigma^2)^{-1/2}$ or, equivalently, if $\sigma \geq (2\pi M^2)^{-1/2}$, then $\gamma = 1$ so we take $M$ relatively small. If we set $\eta(\Delta) - \frac{1}{2}$ equal to $M\Delta\gamma$, we find that

$$\gamma(\sigma) = \frac{\log\{\Phi(\Delta/\sigma) - \frac{1}{2}\} - \log M}{\log \Delta}. \quad (7)$$

A plot of $\gamma(\sigma)$ as a function of $\sigma$, for the case $M = 0.5$ and $\Delta = 0.1$, is shown in Figure 1. So, we can see that, for these particular $(M, \Delta)$, if $\sigma$ is small, then $\gamma$ is also relatively small, indicating a faster rate of convergence than for $\sigma$ large. This is consistent with our intuition that $\eta$ functions which are steep near $\theta^*$ will have faster convergence rates.

2.3 On smoothed versions of the problem

It was mentioned above that the lack of smoothness of the loss function $L_n(\theta)$ causes some problems in terms of limit distribution theory, etc. It would, therefore, be tempting to replace that non-smooth loss function by something smooth, and hope that the approximation error is negligible. One idea would be to introduce a nice parametric model for this problem. For example, consider a binary regression model, where $\eta(x) = F(\beta_0 + \beta_1 x)$ and $F$ is some specified distribution function, such as logistic or normal. Then the MCID corresponds to the median lethal dose (e.g., Agresti 2002, Kelly 2001). Such a model is smooth so asymptotic normality holds. However, unless the true $P$ has the specified form, there will be non-zero bias that cannot be overcome, even asymptotically. Since the bias is unknown, sampling distribution concentration around the wrong point cannot be corrected, so is of little practical value.
A slightly less extreme smoothing of the problem is to make a minor adjustment to the original loss function $\ell_\theta$. As in [Hedayat et al. (2014)], introduce a smoothing parameter $\tau > 0$ and consider

$$\ell_\tau(x, y) = \min\{1, \left[1 - \tau^{-1} y \text{sign}(x - \theta)\right]^+\},$$

where $[\cdot]^+ = \max(\cdot, 0)$ denotes the positive part. Write $L^\tau(\theta) = P_{\ell_\theta}$. Based on arguments in [Hedayat et al. (2014)], it can be shown that $L^\tau(\theta)$ converges uniformly to $L(\theta)$ as $\tau \to 0$, so, for small $\tau$, the minimizer of $L^\tau$ would be close to $\theta^\star$. For fixed $\tau$, one can define $L^\tau_n(\theta) = P_{n\ell_\theta}$ just as before and consider an M-estimator $\hat{\theta}^\tau_n = \arg\min_\theta L^\tau_n(\theta)$. An asymptotic normality result for $\hat{\theta}^\tau_n$ is available, but the proper centering is not at $\theta^\star$ and the asymptotic variance is inversely proportional to $\tau$. So, one could take $\tau = \tau_n$ vanishing with $n$ in an effort to remove the bias, but a price must be paid in terms of the variance. Again, having an asymptotic normality result with either an unknown non-zero bias or a very large variance is of little practical value.

Based on these remarks, apparently there is no hope in trying to smooth out the problem to make it a standard one with asymptotic distribution theory. So, in order to construct useful interval estimates, etc, one needs some different ideas. This motivates our investigation into likelihood-free Bayesian analysis, discussed next.

3 A likelihood-free posterior for MCID

3.1 Motivation and construction

To carry out a standard Bayesian analysis in the MCID problem, one must start with a model for $P$, say, with joint density/mass function $f_\psi(x, y)$, depending on some parameter $\psi$ which might be different from $\theta$. For example, the binary regression model discussed above had slope and intercept parameters. Given a prior for $\psi$, a posterior distribution for $\psi$ can be readily obtained via Bayes theorem, which can be marginalized to get a posterior distribution for $\theta$. The issues with this standard approach are three-fold. First, as discussed above, if the posited model is wrong, then a bias may be introduced. Second, a prior for the full parameter $\psi$ must be specified, which is non-trivial because $\psi$ is not a “real” parameter so elicitation may not be possible, and it is not immediately clear if a default non-informative prior for $\psi$ will lead to a posterior for $\theta$ with good properties. Third, efforts to compute the posterior distribution for $\psi$, which sits on a space of dimension no less than that of $\theta$, are essentially wasted because only the marginal distribution of $\theta$ is of interest. In light of these challenges, an approach that yields a posterior distribution on $\theta$ directly is desirable.

For clarity, we give an illustration of the points just raised. In particular, one can do a Bayesian analysis of the MCID problem by starting with a standard logistic regression model for $Y$, given $X = x$, where the logit transform of the Bernoulli success probability is a linear function $\alpha + \beta x$. Then the MCID is just the median lethal dose, i.e., $\theta = -\alpha/\beta$. As a prior distribution for $(\alpha, \beta)$, which is not a “real” parameter, we consider the default, data-driven prior specified in [Robert and Casella (2004), Example 7.11]. Let us suppose that the true model generating data $(X,Y)$ has a distribution function $F$ for $X$ and, given $X = x$, $Y$ results from a Bernoulli trial with success probability $F(x)$. We will
Figure 2: Plots of (kernel estimates of) the posterior density for MCID. “Logistic” corresponds to the posterior based on the genuine Bayes logistic model; “loss” is the proposed likelihood-free Bayesian posterior; true MCID $\theta^*$ marked with a vertical dotted line.

consider two different forms of $F$, both two-component normal mixtures:

$$X \sim 0.7N(-1,1) + 0.3N(1,1) \quad \text{and} \quad X \sim 0.7N(-1,1) + 0.3N(5,1).$$

Plots of the marginal posterior density for $\theta$ are shown in Figure 2 for a typical data set of size $n = 500$ obtained from each of the two models, one for each marginal distribution for $X$. In Panel (a) we see that the posterior distribution, shown in gray, puts nearly all its mass on a narrow interval around the true MCID. However, in Panel (b) we see that the posterior distribution is clearly biased away from the true MCID. The distribution shown in black in each panel is our proposed method, described below, that constructs a posterior based on a loss function rather than a likelihood. Clearly, the loss-driven posterior centers around the true MCID in both cases. The point is that, while the standard Bayes approach can work well in some cases, there are cases where it fails and, since the the statistician does not know which of the two cases he/she is in, the standard Bayesian approach is dangerous. Therefore, there is a need for a model-free Bayesian approach and, to our knowledge, ours is the first attempt in this direction.

Bissiri et al. (2013) considered the problem of constructing a posterior distribution for parameters defined through a loss function, rather than a likelihood. They argue that one can use that loss function to construct a posterior, and still achieve coherent inference. Their approach boils down to treating the scaled loss function $nL_n(\theta)$ like a negative log-likelihood and constructing the posterior distribution as usual. That is, for our likelihood-free posterior distribution for $\theta$ we take

$$\Pi_n(A) = \frac{\int_A e^{-nL_n(\theta)} \Pi(d\theta)}{\int_{\mathbb{R}} e^{-nL_n(\theta)} \Pi(d\theta)}, \quad A \subset \mathbb{R},$$

where $L_n(\theta) = \mathbb{P}_n \ell_\theta$ is the empirical risk defined above, and $\Pi$ is the prior distribution for $\theta$. Note that the use of the actual loss function defining the MCID means that we
have not introduced any bias. Moreover, we are only required to do prior specification and posterior computations directly on the \( \theta \)-space, i.e., there are no additional nuisance parameters that need priors and then to be marginalized over.

Since the loss function \( L_n(\theta) \) is bounded away from zero and infinity, the tails of the posterior match those of the prior. However, data cannot support a value of \( \theta \) outside the range of the \( X \) observations, \([X_{(1)}, X_{(n)}]\), so, in practice, we will implicitly restrict the posterior to that range. This adjustment is not necessary for our asymptotic analysis.

### 3.2 Posterior consistency

As a first check that the loss function-driven posterior is behaving reasonably, we prove an asymptotic consistency theorem. Roughly, the theorem says that, if \( \eta \) in (2) is continuous and strictly increasing, and if the prior density \( \pi \) is positive in a neighborhood of \( \theta^* \), then the posterior will, with \( P \)-probability 1, as \( n \to \infty \), put all its mass on arbitrarily small neighborhoods of \( \theta^* \). Here and in what follows, it will be convenient to rewrite the posterior distribution in (8) as

\[
\Pi_n(A) = \frac{N_n(A)}{D_n} = \frac{\int_A e^{-n[L_n(\theta) - L_n(\theta^*)]} \pi(\theta) d\theta}{\int_{\mathbb{R}} e^{-n[L_n(\theta) - L_n(\theta^*)]} \pi(\theta) d\theta},
\]

Then the proofs that follow are all based on obtaining appropriate bounds on the numerator, \( N_n(A) \), for various subsets \( A \), and the denominator, \( D_n \).

**Theorem 2.** Let \( \eta \) in (2) be continuous and strictly increasing. If the prior density \( \pi \) is positive and continuous in a neighborhood of \( \theta^* \), then \( \Pi_n(\{\theta : |\theta - \theta^*| > \varepsilon\}) \to 0 \) \( P \)-almost surely as \( n \to \infty \) for any \( \varepsilon > 0 \).

**Proof.** See Appendix A.3.

An immediate consequence is that certain estimators based on the posterior distribution, such as the posterior mean, are consistent.

**Corollary 1.** If the prior mean for \( \theta \) exists, then, under the conditions of Theorem 2, the posterior mean \( \hat{\theta}_n \) satisfies \( |\hat{\theta}_n - \theta^*| \to 0 \) \( P \)-almost surely as \( n \to \infty \).

**Proof.** See Appendix A.3.

### 3.3 Posterior convergence rates

In this section we show that posterior consistency can be strengthened to a convergence rate using the same conditions, namely Assumptions 1–2, used to prove the convergence rate result for the M-estimator in Theorem 1. With the posterior probability expressed as in (8) we seek to bound the denominator \( D_n \) from below and the numerator \( N_n(A_n) \) from above, where \( A_n \) is a shrinking neighborhood of \( \theta^* \).

For bounding the denominator, we have the following result, whose proof follows that of Lemma 1 in Shen and Wasserman (2001) almost exactly; the only difference is that boundedness of \( \ell_n - \theta_0 \), can be used in place of a second Kullback–Leibler moment.

**Lemma 1.** For a vanishing sequence \( t_n \), set \( \Theta_n = \{\theta : L(\theta) - L(\theta^*) \leq t_n\} \). If \( nt_n \to \infty \), then \( D_n \geq \Pi(\Theta_n) e^{-2nt_n} \) with \( P \)-probability converging to 1 as \( n \to \infty \).
The next step is to bound the numerator $N_n(A_n)$, where $A_n$ is the complement of the shrinking neighborhood of $\theta^*$. Towards this, we have the following technical result which provides some uniform control on the empirical risk difference $L_n(\theta^*) - L_n(\theta)$ for $\theta$ outside a neighborhood of $\theta^*$. The proof of this result relies on some bracketing entropy calculations and a maximal inequality; see Appendix A.1.

**Lemma 2.** Under Assumptions 1–2 with $\gamma$ defined in (5), let $s_n = a_n n^{-r(\gamma)}$ where $r(\gamma) = (1 + 4\gamma)^{-1}$ and $a_n$ is any diverging sequence. Then there exists $K > 0$ such that

$$P\left( \sup_{|\theta - \theta^*| > s_n} \{L_n(\theta^*) - L_n(\theta)\} > -Ks_n^{1+2\gamma} \right) \to 0, \quad \text{as } n \to \infty.$$  

**Proof.** See Appendix A.4.

Lemma 2 is the driving force behind our convergence rate proofs for both the M-estimator and the likelihood-free Bayesian posterior. For the latter, the only condition required beyond Assumptions 1–2 is that the prior be well-behaved in a neighborhood of $\theta^*$, which can easily be arranged by assuming the prior density to be positive on the interval $\Theta \subseteq \mathbb{R}$ where $\theta^*$ resides. The precise result is next.

**Theorem 3.** Under Assumptions 1–2 with $\gamma$ defined in (5), write $r(\gamma) = (1 + 4\gamma)^{-1}$. Then $\Pi_n(A_n) \to 0$ in $P$-probability, where $A_n = \{\theta : |\theta - \theta^*| > a_n n^{-r(\gamma)}\}$ and $a_n$ is any diverging sequence.

**Proof.** See Appendix A.4.

The interpretation is that the posterior converges at a rate arbitrarily close to $n^{-r(\gamma)}$. This is the same as for the M-estimator in Theorem 1. Indeed, the posterior mean inherits the same rate of convergence from the posterior.

**Corollary 2.** Let $\gamma$ and $r(\gamma) = (1 + 4\gamma)^{-1}$ be as in Theorem 3. If the prior mean for $\theta$ exists, then the posterior mean $\hat{\theta}_n$ satisfies $\hat{\theta}_n - \theta^* = O_P(n^{-r(\gamma)})$ as $n \to \infty$.

**Proof.** See Appendix A.4.

### 3.4 On scaling the loss function

A subtle point is that the loss function $\ell_\theta$ has an arbitrary scale. That is, the problem of inference on the expected loss minimizer is unchanged if we replace $\ell_\theta$ with $\omega \ell_\theta$ for any $\omega > 0$. While this has no effect on the M-estimator, it does have an effect on our Bayesian approach. As Bissiri et al. (2013) explain, it is important to scale the loss in some way. In our case, we have found that scaling the loss by a sequence $\omega_n$ that vanishes at a certain rate provides good numerical results in terms of both estimation accuracy and credible interval coverage probability. We start with a result that says how fast the scale sequence can vanish without disrupting the posterior concentration.

**Lemma 3.** Under Assumptions 1–2 with $\gamma$ defined in (5), write $r(\gamma) = (1 + 4\gamma)^{-1}$. Then the conclusion of Theorem 3 holds if the loss function is scaled by a sequence $\omega_n$ that vanishes no faster than $n^{-2\gamma(\gamma)}$. 

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This result follows immediately from the proof of Theorem 3 in Appendix A.4 and is, therefore, omitted. Instead, we give several remarks to explain how this result and the idea of scaling the loss by a vanishing sequence should be interpreted.

Remark 3. It may appear strange to have a scaling on the loss function that vanishes with $n$, as this suggests that the influence of the data should diminish as $n \to \infty$. Before addressing this, we should emphasize that the theory goes through without consideration of the scale, i.e., it holds for any scale, including those that are constant, those that increase, or those that decrease no faster than that specified in Lemma 3. So, this is a question about numerical finite-sample performance. Based on our experience, the posterior distribution actually tends to be quite narrow, so the posterior concentration rates seem to be driven primarily by the “center” of the posterior and, to a lesser extent, by the “spread.” So, the purpose of the vanishing scale is to increase the spread of the posterior so that it has a better chance to catch the true MCID in a credible interval in finite samples. The numerical results in Section 4 demonstrate that taking the scale to be vanishing accomplishes the goal of calibrating the credible intervals without having a negative effect on the accuracy of the posterior mean as a point estimator.

Remark 4. There are two limitations to the asymptotic result in Lemma 3. First, the bound on the rate of decay for $\omega_n$ depends on $\gamma$, which is a feature of the problem not known to the statistician. Since $\gamma = 1$ is a typical case, we propose to base our choice of the scale parameter on this, i.e., we take $\omega_n$ to vanish at the rate $n^{-2/5}$. Second, giving a rate of decay does not fully specify the sequence itself. Based on our experience, we have found that taking $\omega_n = 4n^{-2/5}$ gives a good balance of estimation accuracy and credible interval coverage over a range of different problems. This is the choice of scaling to be used in the numerical examples below.

4 Numerical examples

We consider three numerical examples to test the likelihood-free Bayesian model for the MCID. Each example has a different marginal distribution for $X$:

*Example 1.* $X \sim 0.7N(-1, 1) + 0.3N(1, 1)$;

*Example 2.* $X \sim N(1, 1)$;

*Example 3.* $X \sim \text{Unif}(-2, 4)$.

*Example 4.* $X \sim \text{Gamma}(2, 0.5)$.

The chosen examples cover a wide variety of distributions: bimodal, normal, flat, and skewed. In each example, we take $n$ independent samples from the respective marginal distributions, and then, given $X_i = x_i$, take $Y_i \sim 2\text{Ber}(F(x_i)) - 1$, $i = 1, \ldots, n$, where $F$ is the distribution function of $X$ and $\text{Ber}(p)$ denotes a Bernoulli distribution with success probability $p$. In our case, the relevant summaries are the bias and standard deviation of the estimators, and the coverage probability and length of the 95% interval estimates. We considered three sample sizes, namely, $n = 250, 500, 1000$, and the results in Tables 1–2 are based on 500 Monte Carlo samples. We compare the performance of our Bayesian MCID methodology, using the scaling rule in Remark 4 and a flat uniform prior for $\theta$, to that of the M-estimator and the corresponding percentile bootstrap confidence intervals.
Table 1: Approximate bias (and standard deviation) for point estimates.

| Example | Method      | $n = 250$          | $n = 500$          | $n = 1000$         |
|---------|-------------|-------------------|-------------------|-------------------|
| 1       | M-estimator | $-0.027 (0.289)$  | $-0.004 (0.221)$  | $-0.010 (0.181)$  |
|         | Posterior mean | $-0.044 (0.221)$  | $-0.005 (0.169)$  | $-0.005 (0.099)$  |
| 2       | M-estimator | $-0.001 (0.213)$  | 0.011 (0.158)     | $-0.001 (0.130)$  |
|         | Posterior mean | $-0.008 (0.171)$  | 0.005 (0.123)     | 0.002 (0.099)     |
| 3       | M-estimator | $-0.038 (0.370)$  | 0.017 (0.385)     | $-0.029 (0.308)$  |
|         | Posterior mean | 0.023 (0.347)     | 0.013 (0.289)     | $-0.001 (0.237)$  |
| 4       | M-estimator | $-0.044 (0.524)$  | $-0.050 (0.423)$  | $-0.019 (0.333)$  |
|         | Posterior mean | $-0.080 (0.405)$  | $-0.060 (0.336)$  | $-0.035 (0.258)$  |

Table 2: Approximate coverage probability (and mean length) of 95% intervals.

| Example | Method      | $n = 250$          | $n = 500$          | $n = 1000$         |
|---------|-------------|-------------------|-------------------|-------------------|
| 1       | Bootstrap   | 0.956 (1.039)     | 0.974 (0.827)     | 0.966 (0.646)     |
|         | Bayes       | 0.948 (0.941)     | 0.942 (0.698)     | 0.954 (0.587)     |
| 2       | Bootstrap   | 0.964 (0.745)     | 0.974 (0.610)     | 0.966 (0.481)     |
|         | Bayes       | 0.914 (0.649)     | 0.948 (0.508)     | 0.954 (0.419)     |
| 3       | Bootstrap   | 0.958 (1.363)     | 0.970 (1.380)     | 0.978 (1.149)     |
|         | Bayes       | 0.956 (1.531)     | 0.954 (1.175)     | 0.972 (0.993)     |
| 4       | Bootstrap   | 0.974 (1.957)     | 0.968 (1.534)     | 0.964 (1.200)     |
|         | Bayes       | 0.964 (1.762)     | 0.928 (1.266)     | 0.938 (1.055)     |

Hedayat et al. (2014) clearly demonstrated the superiority of their M-estimator over that of the estimators in Shiu and Gatsonis (2008) and Turner et al. (2010), so we will not consider these alternatives.

Table 1 shows the approximate bias and standard deviation for both the M-estimator and the posterior mean. Compared to the M-estimator, the posterior mean has smaller standard deviation in all cases, and similar bias; this conclusion holds for a wide range of scaling parameters, not just that in Remark 4. Table 2 shows the approximate coverage probability and length for the 95% interval estimates based on bootstrapping the M-estimator and on the likelihood-free Bayesian posterior sample. Here we see that the additional flexibility of being able to choose the scaling parameter/sequence provides approximately calibrated posterior credible intervals.

An important point here is that we have used a flat non-informative prior for $\theta$, so one cannot expect the likelihood-free posterior to be substantially better than the M-estimator. However, if reliable prior information is available, then this can be readily incorporated in to our Bayesian analysis, naturally providing some improvements, while it is not clear how such information can be used to improve the M-estimator.
5 Conclusion

In certain applications, a likelihood function may not be available for a variety of reasons. In this paper, motivated by a real application in medical statistics, we have explored the use of a loss function-driven posterior distribution for Bayesian inference. The approach employed here is not specific to the MCID application. In fact, we expect that this approach would be quite attractive to those, particularly in the machine learning world, who are reluctant to adopt a Bayesian perspective because of concerns about modeling and unnecessary computations. As we have demonstrated, the proposed likelihood-free Bayesian approach is theoretically justified and provides quality point and interval estimates in practice. So, in a certain sense, our likelihood-free Bayesian approach provides the best of both worlds: that is, we get a theoretically justifiable posterior distribution without the unnecessary modeling and computations and without worry of bias due to an incorrectly specified model. The price that is paid is one of efficiency: if a standard Bayes model would work, then posterior normality results should be available. An important question, deserving further investigation, is in what cases will a standard Bayes model work. One surely will need to consider marginalization over the full parameter to the MCID $\theta$, and such questions have not been considered in the existing literature on Bayesian misspecification.

Although methods in Bissiri et al. (2013) and our own theoretical results (Lemma 3) can inform the choice of the scaling parameter, it seems that the “correct” choice of scaling yielding credible intervals with the right coverage probability is problem-specific. More work is needed to derive a general method for selecting the scaling when the goal is to produce credible intervals with good coverage properties.

The technical details in this paper were kept relatively simple due to the fact that $\theta$ is a scalar and the loss function $\ell_\theta$ is uniformly bounded. When one attempts to apply the methods used in this paper to other problems, proving posterior consistency and convergence rate theorems could be more difficult. The main challenge would be establishing a result like that in Lemma 2 but considerable work on bounding bracketing numbers has been done so we expect that there would be lots more applications that can be covered using these tools. For example, Hedayat et al. (2014) proposed a generalization of the MCID problem in which $\theta$ is actually a function of some other covariates, thereby making the MCID “personalized” in a certain sense. We are currently looking into how we can extend the likelihood-free Bayesian results presented here to this more interesting case. We would need a prior on the function $\theta$, such as a Gaussian process, and details about how to select the covariance function of the prior to adapt to the unknown smoothness of the MCID function $\theta^*$ remain to be worked out.

Beyond the theory, this likelihood-free Bayesian approach raises new questions about computation. For the MCID application presented here, the computation is straightforward since the parameter is one-dimensional. For higher-dimensional cases, where numerical integration is not feasible, one would need to employ some Monte Carlo methods. When the parameter is finite-dimensional, some standard techniques such as a Metropolis–Hastings sampler can be used. However, for infinite-dimensional problems, the standard Bayesian approach often makes use of special structure in the likelihood and/or prior. For example, for Bayesian nonparametric binary regression, Choudhuri et al. (2007) propose a Gaussian process prior for the regression function and then make
use of some latent structure in the likelihood to develop a Gibbs sampler for inference. This approach can be employed in the personalized MCID application mentioned above, but, as discussed above, inference will be biased if the true model is not of this form. So, one will need new computational techniques for likelihood-free Bayesian inference in nonparametric problems, and we are currently looking into this.

A Technical details and proofs

A.1 Preliminary results

Here, for the sake of completeness, we summarize some basic facts about the loss function $L_n(\theta) = \mathbb{P}_n \ell_\theta$ and its expectation $L(\theta) = \mathbb{E}_\theta$. Details will be given only for those results not taken directly from [Hedayat et al. (2014)].

First, we want to understand properties of the expected loss difference, $L(\theta) - L(\theta^*)$. By definition of $\theta^*$, we know the difference is non-negative and, if $\eta$ in (2) is strictly increasing, then the loss difference is strictly positive except at $\theta = \theta^*$. To see this, Hedayat et al. (2014) show that

$$L(\theta) - L(\theta^*) = 2 \int_{\theta^*}^{\theta} \{\eta(x) - \frac{1}{2}\} p(x) \, dx.$$  \hfill (9)

Moreover, by the assumed continuity of $\eta$ and $p$, we can see that the derivative of $L(\theta) - L(\theta^*)$ is zero only at $\theta = \theta^*$, which implies that the function is uniformly bounded away from zero outside an interval containing $\theta^*$. This latter point is important because asymptotic results of, say, the M-estimator require that the minimizer $\theta^*$ be “well-separated;” see Theorem 5.7 in van der Vaart (1998). Hedayat et al. (2014) go on to bound, under Assumptions 1–2, the loss difference outside a neighborhood of $\theta^*$:

$$\sup_{|\theta - \theta^*| > \varepsilon} \{L(\theta^*) - L(\theta)\} \leq -C\varepsilon^{1+2\gamma}, \quad \text{constant } C > 0. \hfill (10)$$

Second, we need some approximation properties of the class of functions $\mathcal{L}_\delta := \{\ell_\theta - \ell_{\theta^*} : |\theta - \theta^*| < \delta\}, \quad \delta > 0$.

Hedayat et al. (2014) shows, using the standard partition in the classical Glivenko–Cantelli theorem (e.g., van der Vaart 1998, Example 19.6), that the $L_1(\mathbb{P})$ $\varepsilon$-bracketing number $N_{l_1}(\varepsilon, \mathcal{L}_\infty, L_1(\mathbb{P}))$ is proportional to $\varepsilon^{-1}$. This is enough to show that the class $\mathcal{L}_\infty$ is Glivenko–Cantelli, from which a uniform law of large numbers follows.

**Lemma 4.** Let $\mathcal{G}_n f = n^{1/2}(\mathbb{P}_n f - Pf)$ be the empirical process. Then

$$\sup_{\theta} \left| n^{-1/2} \mathcal{G}_n(\ell_\theta - \ell_{\theta^*}) \right| \to 0, \quad P\text{-almost surely.}$$

However, better rates can be obtained by using a local bracketing, i.e., of $\mathcal{L}_\delta$ for finite $\delta$, and Assumptions 1–2. Such considerations allow us to remove the unnecessary logarithmic term on the rate presented in Theorem 1 of Hedayat et al. (2014).

**Lemma 5.** $N_{l_1}(\varepsilon, \mathcal{L}_\delta, L_1(\mathbb{P})) \lesssim \delta/\varepsilon$. 

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Proof. For the standard Glivenko–Cantelli theorem partition, which is used in Hedayat et al. (2014), one needs to partition the interval [0, 1] into $k$ intervals of length less than $\varepsilon$, so $k$ must be greater than $1/\varepsilon$, but can be taken less than $2/\varepsilon$. By Assumption 1, we have that $\delta \leq P(|X - \theta^*| < \delta) \leq \delta$. For the local bracketing, this means we only need to partition an interval of length proportional to $\delta$ into intervals of length less than $\varepsilon$. Therefore, the total number of intervals is $\lesssim \delta/\varepsilon$, as was to be shown. \hfill $\square$

From this and the fact that the brackets are pairs of indicator functions, we can get a bound on the $L_2(P)$ bracket number, i.e., $N_{\|.\|}(\varepsilon, \mathcal{L}_\delta, L_2(P)) \lesssim (\delta/\varepsilon)^2$; see Example 19.6 in van der Vaart (1998). Then the bracketing integral is

$$J_{\|.\|}(\delta, \mathcal{L}_\delta, L_2(P)) := \int_0^\delta \{\log N_{\|.\|}(\varepsilon, \mathcal{L}_\delta, L_2(P))\}^{1/2} d\varepsilon \lesssim \delta. \quad (11)$$

Finally, we will need a maximal inequality for the empirical process $G_n(\ell_\theta - \theta^*)$ for $\theta$ near $\theta^*$. Hedayat et al. (2014) show that $g(\theta) = I_{\{|\theta - \theta^*| \leq \delta\}}$ is an envelop function for $\mathcal{L}_\delta$, with $\|g\|_{L_2(P)} \lesssim \delta^{1/2}$. Then, given the bound (11) on the bracketing integral, the maximal inequality in Corollary 19.35 of van der Vaart (1998) gives the following.

Lemma 6. $P\{\sup_{|\theta - \theta^*| < \delta} |G_n(\ell_\theta - \ell_{\theta^*})| \} \lesssim \delta^{1/2}$.

A.2 Proofs from Section 2.2

Proof of Theorem 4. Similar to the proof of Theorem 2 in Wong and Shen (1995) and of Theorem 5.52 in van der Vaart (1998). The M-estimator $\hat{\theta}_n$, the global minimizer of $L_n$, satisfies $L_n(\hat{\theta}_n) \leq L_n(\theta^*) + \zeta_n$ for any $\zeta_n$. Take $\zeta_n = Ks_n^{1+2\gamma}$, where $s_n = a_n n^{-1/(1+4\gamma)}$ and $a_n$ is any divergent sequence. Then we have that

$$|\hat{\theta}_n - \theta^*| > s_n \implies \sup_{|\theta - \theta^*| > s_n} \{L_n(\theta^*) - L_n(\theta)\} \geq -Ks_n^{1+2\gamma}.$$ 

The latter event has vanishing $P$-probability according to Lemma 2 which implies that $P(|\hat{\theta}_n - \theta^*| > s_n) \to 0$. Therefore, $\hat{\theta}_n - \theta^* = o_P(s_n)$ or, since $a_n$ is arbitrary, $\hat{\theta}_n - \theta^* = O_P(n^{-1/(1+4\gamma)})$ as was to be shown. \hfill $\square$

A.3 Proofs from Section 3.2

Proof of Theorem 3. The denominator $D_n$ of the posterior distribution can be bounded below by $e^{-nc}$ for any $c > 0$, with $P$-probability 1 for all large $n$. The proof of this is exactly like that of Lemma 4.4.1 in Ghosh and Ramamoorthi (2003). For the numerator, we make use of the uniform law of large numbers in Lemma 1 in Appendix A.1. For given $\varepsilon > 0$, let $A = \{\theta : |\theta - \theta^*| > \varepsilon\}$. Then

$$N_n(A) = \int_A e^{-n[L_n(\theta) - L_n(\theta^*)]} \pi(\theta) d\theta \leq e^{n/2} \sup_{\theta} |G_n(\ell_\theta - \ell_{\theta^*})| \int_A e^{-n[L(\theta) - L(\theta^*)]} \pi(\theta) d\theta.$$
By the uniform law of large numbers, the first term is bounded above by \( e^{n^{1/2}b} \) for any \( b > 0 \), \( P \)-almost surely for all large \( n \). Also, because \( L(\theta) - L(\theta^*) \) is positive and bowl-shaped, for \( \theta \in A \), there exists a constant \( a > 0 \) such that \( L(\theta) - L(\theta^*) \geq a \) for \( \theta \in A \). Therefore,

\[
N_n(A) \leq e^{n^{1/2}b - na}, \quad P\text{-almost surely for all large } n.
\]

Then there exists \( d > 0 \) such that \( N_n(A) \leq e^{-nd} \) \( P \)-almost surely for all large \( n \). Now combine the bounds on \( N_n(A) \) and \( D_n \), with \( c = d/2 \), to complete the proof. \( \Box \)

Proof of Corollary 7. By Jensen’s inequality, \( \hat{\theta}_n - \theta^* \leq \int |\theta - \theta^*| \Pi_n(d\theta) \). Take any \( \varepsilon > 0 \) and partition \( \mathbb{R} \) as \( \{ \theta : |\theta - \theta^*| \leq \varepsilon \} \cup \{ \theta : |\theta - \theta^*| > \varepsilon \} \) and write

\[
\int |\theta - \theta^*| \Pi_n(d\theta) \leq \varepsilon + \int_{|\theta - \theta^*| > \varepsilon} |\theta - \theta^*| \Pi_n(d\theta).
\]

Just like in the proof of Theorem 2, the posterior measure away from \( \theta^* \) can be bounded by the prior measure times some \( Z_n \) such that \( Z_n \to 0 \) \( P \)-almost surely, uniformly in \( \theta \). Therefore, the second term in the above display is bounded by \( Z_n \cdot \int |\theta - \theta^*| \Pi(d\theta) \), which itself vanishes \( P \)-almost surely since the prior mean exists. Since \( \varepsilon > 0 \) is arbitrary, the claimed consistency follows. \( \Box \)

A.4 Proofs from Section 3.3

Proof of Lemma 3. Start with the identity

\[
L_n(\theta^*) - L_n(\theta) = \{ L(\theta^*) - L(\theta) \} - n^{-1/2} G_n(\ell_\theta - \ell_{\theta^*}),
\]

where \( G_n f = n^{1/2}(\mathbb{P}_n f - Pf) \) is the empirical process. Next, since the supremum of a sum is no more than the sum of the suprema, we get

\[
\sup_{|\theta - \theta^*| > \varepsilon} \{ L_n(\theta^*) - L_n(\theta) \} \leq \sup_{|\theta - \theta^*| > \varepsilon} \{ L(\theta^*) - L(\theta) \} + n^{-1/2} \sup_{|\theta - \theta^*| > \varepsilon} |G_n(\ell_\theta - \ell_{\theta^*})|;
\]

the second inequality comes from putting absolute value on the empirical process term. From (10), we get

\[
\sup_{|\theta - \theta^*| > \varepsilon} \{ L_n(\theta^*) - L_n(\theta) \} \leq -C\varepsilon^{1+2\gamma} + n^{-1/2} \sup_{|\theta - \theta^*| > \varepsilon} |G_n(\ell_\theta - \ell_{\theta^*})|.
\]

Now, following the proof of Theorem 5.52 from van der Vaart (1998) or of Theorem 1 in Wong and Shen (1995), introduce “shells” \( \theta : 2^m \varepsilon < |\theta - \theta^*| < 2^{m+1} \varepsilon \) for integers \( m \). On these shells, we can use both the bound in (10) and the maximal inequality in Lemma 3. That is,

\[
\sup_{|\theta - \theta^*| > s_n} \{ L_n(\theta^*) - L_n(\theta) \} > -Ks_n^{1+2\gamma}
\]

\[
\implies \sup_{2^m s_n < |\theta - \theta^*| \leq 2^{m+1} s_n} \{ L_n(\theta^*) - L_n(\theta) \} > -Ks_n^{1+2\gamma} \quad \exists m \geq 0
\]

\[
\implies n^{-1/2} \sup_{2^m s_n < |\theta - \theta^*| < 2^{m+1} s_n} |G_n(\ell_\theta - \ell_{\theta^*})| \geq C(2^m s_n)^{1+2\gamma} - Ks_n^{1+2\gamma}
\]

\[
\implies n^{-1/2} \sup_{|\theta - \theta^*| < 2^{m+1} s_n} |G_n(\ell_\theta - \ell_{\theta^*})| \geq C(2^m s_n)^{1+2\gamma} - Ks_n^{1+2\gamma},
\]

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If \( K \leq C/2 \), then \( C(2^m s)^{(1+2\gamma)} - K s^{1+2\gamma} \geq C(2^m s)^{1+2\gamma}/2 \) for all \( m \geq 0 \).

\[
P\left( \sup_{|\theta - \theta^*| > s_n} \{L_n(\theta^*) - L_n(\theta)\} > -K s_n^{1+2\gamma} \right)
\leq \sum_{m \geq 0} P\left(n^{-1/2} \sup_{|\theta - \theta^*| < 2^{m+1}s_n} |G_n(\ell_\theta - \ell_{\theta^*})| \geq C(2^m s_n)^{1+2\gamma}/2 \right)
\]

To the summands, apply Markov’s inequality and Lemma 6 to get

\[
P\left(n^{-1/2} \sup_{|\theta - \theta^*| < 2^{m+1}s_n} |G_n(\ell_\theta - \ell_{\theta^*})| \geq C(2^m s_n)^{1+2\gamma}/2 \right) \leq \frac{C'(2^{m+1}s_n)^{1/2}}{n^{1/2}(2^m s_n)^{1+2\gamma}(C/2)}.
\]

For \( s_n = a_n n^{-\gamma} \), the upper bound satisfies

\[
\leq a_{n}^{-1/2+2\gamma}(2^{1/2+2\gamma})^{-m}.
\]

Since \( \gamma > 0 \), the sum over \( m \geq 0 \) converges, so

\[
P\left( \sup_{|\theta - \theta^*| > s_n} \{L_n(\theta^*) - L_n(\theta)\} > -K s_n^{1+2\gamma} \right) \leq a_{n}^{-1/2+2\gamma}.
\]

Then the upper bound vanishes since \( a_n \to \infty \), completing the proof. \( \square \)

**Proof of Theorem 3.** From Lemma 2 we get an exponential bound on the numerator \( N_n(A_n) \), i.e.,

\[
N_n(A_n) \leq e^{-Kn s_n^{1+2\gamma}}, \quad \text{with P-probability approaching 1}.
\]

For the denominator \( D_n \), for a suitable sequence \( t_n \), we have

\[
D_n \geq \Pi(\Theta_n)e^{-2nt_n},
\]

where \( \Theta_n = \{ \theta : L(\theta) - L(\theta^*) \leq t_n \} \). We claim that

\[
\Theta_n \supseteq \{ \theta : |\theta - \theta^*| \leq t_n^{1/(1+\gamma)} \}.
\]

To see this, first note that if \( \theta \) is close to \( \theta^* \), then by [9] and Assumption 2

\[
L(\theta) - L(\theta^*) \lesssim |\theta - \theta^*|^\gamma \int_{\theta^*}^\theta p(x) \, dx.
\]

The remaining term in the upper bound is the marginal \( P \)-probability assigned to the small interval around \( \theta^* \) which, by Assumption 1, can be bounded by a constant times \( |\theta - \theta^*| \). Therefore,\n
\[
L(\theta) - L(\theta^*) \lesssim |\theta - \theta^*|^{1+\gamma},
\]

so if \( |\theta - \theta^*| \lesssim t_n^{1/(1+\gamma)} \), then \( L(\theta) - L(\theta^*) \leq t_n \). If the prior density is bounded away from zero in a neighborhood of \( \theta^* \), then we can bound \( \Pi(\Theta_n) \leq t_n^{1/(1+\gamma)} \). So, if we take

\[
t_n = n^{-(1-\beta)}
\]

for some \( \beta > 0 \) to be identified, then by Lemma 1 we get

\[
D_n \geq e^{-H n^\beta}, \quad \text{with P-probability approaching 1}.
\]

Put together the bounds on the numerator and denominator we get that, for some constant \( M \),

\[
\frac{N_n(A_n)}{D_n} \lesssim \exp \left\{ -M \left( a_{n}^{1+2\gamma} n^{2\gamma/(1+4\gamma)} - n^\beta \right) \right\}.
\]

Therefore, we can take \( \beta < 2\gamma/(1+4\gamma) \) and the upper bound vanishes. \( \square \)
Proof of Corollary 2. The proof here is similar to that of Corollary 1. Set $s_n = a_n n^{-r(\gamma)}$ for $a_n$ an arbitrary divergent sequence. Next, define $\tilde{s}_n = a_n n^{-r(\gamma)}$, where $a_n$ is such that $\tilde{a}_n/a_n \to 0$, e.g., $\tilde{a}_n = \log a_n$. Now partition $\mathbb{R}$ as $\{\theta : |\theta - \theta^*| \leq \tilde{s}_n\} \cup \{\theta : |\theta - \theta^*| > \tilde{s}_n\}$, and write

$$|\tilde{\theta}_n - \theta^*| \leq \int |\theta - \theta^*| \Pi_n(d\theta) \leq \tilde{s}_n + \int_{|\theta - \theta^*| > \tilde{s}_n} |\theta - \theta^*| \Pi_n(d\theta),$$

(12)

where the first inequality is by Jensen. From the proof of Theorem 3, the posterior measure away from $\theta^*$ is bounded by the prior measure times some $Z_n = o_P(1)$, uniformly in $\theta$. That is,

$$\int_{|\theta - \theta^*| > \tilde{s}_n} |\theta - \theta^*| \Pi_n(d\theta) \leq Z_n \int |\theta - \theta^*| \Pi(d\theta).$$

In fact, we can bound $Z_n$ more precisely:

$$Z_n \lesssim \exp\{-M(a_n^{1+2\gamma} n^{2r(\gamma)} - n^\beta)\},$$

for any sufficiently small $\beta > 0$. Dividing through (12) by $s_n$ we get that $s_n^{-1} |\tilde{\theta}_n - \theta^*|$ is bounded by a constant times

$$\tilde{a}_n/a_n + e^{-\zeta_n} \int |\theta - \theta^*| \Pi(d\theta),$$

where

$$\zeta_n = M a_n^{1+2\gamma} n^{2r(\gamma)} + \log a_n - M n^\beta - r(\gamma) \log n.$$ 

The first term in the upper bound goes to zero by the choice of $\tilde{a}_n$. The second term goes to zero provided that the prior mean exists and $\zeta_n \to \infty$ as $n \to \infty$. We assumed the former condition, and the latter condition can be easily arranged by choosing $\beta$ sufficiently small, so $\tilde{\theta}_n - \theta^* = o_P(s_n)$, as was to be proved.

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