Abstract

Bayesian optimization is a coherent, ubiquitous approach to decision-making under uncertainty, with applications including multi-arm bandits, active learning, and black-box optimization. Bayesian optimization selects decisions (i.e., objective function queries) with maximal expected utility with respect to the posterior distribution of a Bayesian model, which quantifies reducible, epistemic uncertainty about query outcomes. In practice, subjectively implausible outcomes can occur regularly for two reasons: 1) model misspecification and 2) covariate shift. Conformal prediction is an uncertainty quantification method with coverage guarantees even for misspecified models and a simple mechanism to correct for covariate shift. We propose conformal Bayesian optimization, which directs queries towards regions of search space where the model predictions have guaranteed validity, and investigate its behavior on a suite of black-box optimization tasks and tabular ranking tasks. In many cases we find that query coverage can be significantly improved without harming sample-efficiency.

1 INTRODUCTION

Bayesian optimization (BayesOpt) is a popular strategy to focus data collection towards improving a specific objective, such as discovering useful new materials or drugs [51, 56]. BayesOpt relies on a Bayesian model of the objective (a surrogate model) to select new observations (queries) that maximize the user’s expected utility. If the surrogate does not fit the objective well, then the expected utility of a query may not correspond well at all to the actual utility, leading to little or no improvement in the objective value after many rounds of data collection.

The most practical way to check how well the surrogate fits the objective is to compute its accuracy on a random holdout subset of the training data. Unfortunately such a holdout set is not at all representative of points we are likely to query since the goal is to find queries that are better than the training data in some way. In other words there is feedback covariate shift between the likely query points and the existing training data which degrades the accuracy of the surrogate [21]. Even without covariate shift, we cannot guarantee the accuracy of the surrogate predictions at all, and instead can only hope that the predictions are accurate enough to provide a useful signal for data collection.

The crux of the issue is that the coverage (i.e., the frequency that a prediction set contains the true outcome over many repeated measurements) of Bayes credible prediction sets is directly tied to the correctness of our modeling assumptions, which we cannot entirely control [12, 17]. We would prefer the price of assumption error to be lost efficiency (i.e., wider prediction sets), rather than poor coverage.

Conformal prediction is a distribution-free uncertainty quantification method which provides prediction sets with reliable coverage under very mild assumptions [54]. In particular, conformal prediction can accommodate post hoc covariate shift (i.e., covariate shift that is only known after training the surrogate) and does not assume the surrogate is well-specified (e.g., we could use a linear model on data following a cubic trend). Furthermore, because conformal prediction sets are defined over observable outcomes, they cannot distinguish between epistemic and aleatoric uncertainty, a distinction that is important for effective exploration.

In this work we present conformal Bayesian optimization with a motivating example in Figure [1]. Conformal BayesOpt adjusts how far new queries will move from the training data by choosing an acceptable miscoverage tolerance \( \alpha \in (0, 1) \). If \( \alpha = 1 \) then we recover conventional BayesOpt, but if \( \alpha < 1 \) then the search will be directed to the region where conformal predictions are guaranteed coverage of at least \( 1 - \alpha \), keeping feedback covariate shift in check and accounting for potential error in modeling assumptions.
Figure 1: A motivating example of feedback covariate shift. We want $x^* \in [0, 1]^2$ which maximizes the Branin objective (a), starting from 8 examples in the upper right (the black dots). The upper-confidence bound (UCB) acquisition function (b) selects the next query (the red star) far from any training data, where we cannot guarantee reliable predictions. In higher dimensions, we will exhaust our query budget long before covering the whole search space with training data. Given a miscoverage tolerance $\alpha = 1/\sqrt{N}$, conformal UCB (c) directs the search to the region where conformal predictions are guaranteed coverage of at least $(1 - \alpha)$. (d) The dashed line is the set $x$ such that $w(x) \propto p_{\text{query}}(x)/p_{\text{train}}(x)$ is exactly $\alpha$.

In summary, our contributions are as follows:

- We show how to integrate conformal prediction into BayesOpt through the conformal Bayes posterior, with corresponding generalizations of common BayesOpt acquisition functions, enabling the reliable coverage of conformal prediction while still distinguishing between epistemic and aleatoric uncertainty in a principled way.

- An efficient, differentiable implementation of full conformal Bayes for Gaussian process (GP) regression models, which is necessary for effective query optimization, and a practical procedure to estimate the density ratio for BayesOpt query proposal distributions.

- Demonstrations on synthetic black-box optimization tasks and real tabular ranking tasks that conformal BayesOpt has superior sample-efficiency when the surrogate is misspecified and is comparable otherwise, while improving query coverage significantly. Note that while conformal BayesOpt has promising performance, our goal is not primarily to “beat” classical alternatives; rather, we show how to introduce conformal prediction into BayesOpt, and explore the corresponding empirical behaviour and results.\footnote{Code is available at \url{github.com/samuelstanton/conformal-bayesopt.git}}

2 PRELIMINARIES

In this work we will focus on black-box optimization problems of the form $\max_{x \in \mathcal{X}} (f^*_1(x), \ldots, f^*_m(x))$, where each $f^*_i : \mathcal{X} \to \mathbb{R}$ is an unknown function of decision variables $x \in \mathcal{X}$, and $m$ is the number of objectives. We do not observe $f^*$ directly, but instead receive noisy outcomes (i.e. labels) $y \in \mathcal{Y}$ according to some likelihood $p^*(y|f)$.

2.1 Bayesian optimization

BayesOpt alternates between inference and selection, inferring the expected utility of potential query points from available data, which then serves as a proxy objective to select the next batch of observations, which are fed back into the inference procedure, completing one iteration of a repeating loop \cite{boustanian2020}. Inference consists of applying Bayes rule to a prior $p(f)$, a likelihood $p(y|f)$ and dataset $D = \{(x_i, y_i)\}_{i=0}^{n-1}$ to obtain a Bayes posterior $p(f|D)$. The expected utility of $x$ is given by an acquisition function $a : \mathcal{X} \to \mathbb{R}$ with the general form

$$a(x) = \int u(f(x), D)p(f|D)df,$$

where $u$ is a user-specified utility function. For example, taking $u(f(x), D) = [f(x) - \max_{y \in \mathcal{Y}} y]_+$, where $[.]_+ = \max(\cdot, 0)$, yields the expected improvement (EI) acquisition function \cite{srinivas2012}. Since $a$ is the Bayesian posterior expectation of $u$, maximizers $x^* = \text{argmax}_{x \in \mathcal{X}} a(x)$ are \textit{Bayes-optimal} with respect to $u$. Bayes-optimality means a decision is \textit{coherent} with our posterior beliefs about $f^*$.

2.2 Bayesian inference and model misspecification

One way to assess the quality of our posterior beliefs is to check the coverage of the corresponding Bayes $\beta$-credible prediction sets, which are subsets $\mathcal{K}_\beta(x) \subseteq \mathcal{Y}$ satisfying

$$\beta = \int_{y \in \mathcal{K}_\beta(x)} \int p(y|f)p(f|D)dfdy,$$

where $\beta \in (0, 1]$ is the level of subjective credibility. $\beta$-credible sets may exhibit poor coverage, meaning the frequency of “implausible” events outside the set happening is much more than $1 - \beta$ \cite{srinivas2012}. Note that poor coverage does not necessarily imply that $\mathcal{K}_\beta(x)$ was computed incorrectly, it may simply indicate a faulty assumption.

For example, in BayesOpt it is very common to assume $f^* \sim \text{GP}(0, \kappa)$, where $\kappa$ is a Matérn kernel. Matérn kernels
Definition 2.1. In Appendix A.1 we discuss the assumptions underlying.
In Figure 2 we visualize the process of constructing $C_n(x_n)$ in the regression setting. First, (a) we choose some $y' \in \mathcal{Y}$ and
guess $y_n = y'$, computing conformal scores of $\{(x_0, y_0), \ldots, (x_{n-1}, y_{n-1})\}$ and $(x_n, y')$, (b) we note which examples
score better than our guess (shown in blue), and mask out the corresponding importance weights. (c) we compute the partial
sums $w_i$ of the masked importance weights, adding $y'$ to $C_n(x_n)$ if $w_n > \alpha$, (d) repeat steps (a–c) for many guesses of
$y_n$. Rejected and accepted guesses are shaded light and dark, respectively.

2.3 Conformal prediction

See Shafer and Vovk [44] for a complete tutorial on conformal prediction, or Angelopoulos and Bates [1] for a modern,
accessible introduction. Informally, a conformal prediction set $C_n(x) \subseteq \mathcal{Y}$ is a set of possible labels for a test point $x_n$.
Candidate labels $y'$ are included in $C_n(x)$ if the resulting pair $(x_n, y')$ is sufficiently similar to actual examples seen
in the past. The degree of similarity is measured by a score function $s$ and importance weights (IW$s$) $w$, and the similarity
threshold is determined by the miscoverage tolerance $\alpha$. In Figure 2 we visualize the process of constructing $C_n(x)$. In Appendix A.1 we discuss the assumptions underlying
conformal prediction in detail, the key distinction being that conformal prediction does not require a well-specified
model to produce valid predictions.

Definition 2.1. Let $\alpha \in (0, 1]$, $(x_i, y_i) \sim p(x)p(y|x)$ for $i < n$ and $(x_n, y_n) \sim p'(x)p(y|x)$, with $w_i \propto
p'(x)/p(x)$ s.t. $\sum_k w_k = 1$. The conformal prediction set corresponding to the score function $s$ is defined as

$$C_n(x_n) := \left\{y' \in \mathcal{Y} \middle| h^\top w > \alpha \right\},$$

where $D' = D \cup \{(x_n, y')\}$. In general the importance weights $w$ account for covariate shift [52]. In the special case
where $(x_0, y_0), \ldots, (x_n, y_n)$ are fully exchangeable (e.g. IID), then $w_i = 1/(n + 1)$, $\forall i$.

Conformal prediction enjoys a frequentist marginal coverage
guarantee on $C_n(x_n)$ with respect to the joint distribution
over $(x_0, y_0), \ldots, (x_n, y_n)$,

$$\mathbb{P}[y_n \in C_n(x_n)] \geq 1 - \alpha,$$

meaning if we repeatedly draw $n$ training examples from
$p(x, y)$, and draw a test example $(x_n, y_n)$ from $p'(x, y)$,
$C_n(x_n)$ will contain the observed label $y_n$ at least $(100 \times (1 - \alpha))\%$ of the time. A prediction set with a coverage guarantee like Eq. [4] is conservatively valid at the $1 - \alpha$ level. In Appendix [A.1] we discuss randomized conformal prediction which is exactly valid, meaning the long run frequency of errors converges to exactly $\alpha$.

Full conformal Bayes corresponds to the score function $s(x, y, D') = \log p(y|x, D')$. Conditioning an existing posterior $p(y|x, D)$ on an additional observation $(x', y')$ is commonly referred to as “retraining” in the conformal prediction literature. If the surrogate just so happens to be correctly specified (e.g. $f^* \sim p(f)$), then full conformal Bayes is the optimal choice of score function, meaning it provides the most efficient prediction sets (i.e. smallest by expected volume w.r.t. the prior $p(f)$) among all prediction sets that are valid at the $1 - \alpha$ level [29]. In the typical situation where we think our model assumptions are plausible but do not really believe them, full conformal Bayes rewards us if our assumptions turn out to be correct, yet it produces valid predictions as long as the true data generation process is some pseudo-exchangeable sequence.


3 RELATED WORK

Conformal prediction: Our work is related to Fannjiang et al. [21], who propose a black-box optimization method based on conformal prediction specifically to address feedback covariate shift. However, because they assume new queries are drawn from a closed-form proposal distribution, and because exact conformal prediction is not differentiable, their approach cannot be easily extended to most BayesOpt methods. Bai et al. [2] propose a differentiable approximation of conformal prediction, but it requires solving a minimax optimization subproblem. Stutz et al. [48] independently proposed a continuous relaxation of conformal prediction, like our work, but only for fully exchangeable classification data. We propose a more general form that allows for covariate shift, and we also provide an efficient discretization procedure for regression and show how to estimate the importance weights when the queries are drawn from an implicit density.

Robust BayesOpt: Since the seminal analysis of GP-UCB regret bounds by Srinivas et al. [45], follow-up work has proposed UCB variants for misspecified likelihoods [39], misspecified GP priors [9], or to guarantee \( f^*(x_j) > c \) for some threshold \( c \) [50]. These approaches are not easy to extend to other acquisition functions, and tend to rely on fairly strong assumptions on the smoothness of \( f \) or fix a specific kind of model misspecification. Wang et al. [57] prove regret bounds for GP-UCB when \( f^* \) is drawn from a GP with unknown mean and kernel functions, but assume we know the right hypothesis class of mean and kernel functions and have a collection of offline datasets available for pretraining.

Finally, Eriksson et al. [20] propose TuRBO, which is superficially similar since it constrains queries to a Latin hypercube trust region around the best known local optimum. While TuRBO can be very effective in practice, the size of the trust region is controlled by a heuristic with five hyperparameters in the multi-objective case [16]. Despite the additional complexity, the credible set coverage on queries in TuRBO trust regions can still vary wildly (see Section 5.3). In contrast, conformal prediction provides distribution-free coverage guarantees under very mild assumptions, and our approach can be applied to any reparameterizable acquisition function [59]. To our knowledge our approach is the first BayesOpt procedure to incorporate conformal prediction.

Algorithm 1 Differentiable conformal prediction masks

Data: train data \( D = \{ (x_i, y_i) \}_{i=0}^{n-1} \), test point \( x_n \), imp. weights \( w \), label candidates \( Y_{\text{cand}} \), score function \( s \), miscoverage tolerance \( \alpha \), relaxation strength \( \tau \).

\( m_j = 0, \forall j \in \{0, \ldots, k - 1\} \).

for \( y_j \in Y_{\text{cand}} \) do
\( s_j = [s(x_0, y_0) \cdots s(x_n, y_j)]^\top \).
\( h_j = \text{sigmoid}((s_j - s_j)/\tau) \).
\( w_j = 1^\top(h_j \odot w) \).
\( m_j \leftarrow \text{sigmoid}(w_j - \alpha)/\tau \).
end

Result: \( m \)

4 METHOD

We now describe the key ideas behind conformal Bayesian optimization. First in Section 4.1 we show how to efficiently compute \( C_\alpha(x) \), addressing differentiability and discretization of continuous outcomes. Our procedure is summarized in Algorithm 1. In Section 4.2 we introduce the conformal Bayes posterior \( p_\alpha(f(x)\mid D) \), allowing us to distinguish between aleatoric and epistemic uncertainty and combine to conformal prediction with many well-known BayesOpt utility functions. Finally in Section 4.3 we address feedback covariate shift without requiring closed-form expressions for \( p(x) \) and \( p'(x) \). In Appendix D.1 we provide a detailed overview of the whole method.

4.1 Full conformal Bayes with Gaussian processes

Efficient retraining: full conformal Bayes requires us to compute \( \log p(y_i \mid x_i, D') \forall i \leq n \) and \( \forall y' \in Y_{\text{cand}} \), where \( Y_{\text{cand}} \) is some discretization of \( \mathcal{Y} \). This incremental posterior update can be done very efficiently if the surrogate is a GP regression model [24][46][38], and we will later reuse the conditioned posteriors to estimate expectations w.r.t. \( p_\alpha(f(x)\mid D) \). Note that computing the GP posterior likelihood of training data can be numerically unstable, which we address in Appendix D. Other Bayesian predictive posteriors (e.g. from Bayesian neural networks) are conditioned on training data via iterative methods such as gradient descent, making full conformal Bayes very expensive [22].

Differentiable prediction masks: the definition of \( C_\alpha(x_n) \) in Eq. (3) can be broken down into a sequence of simple vector operations interspersed with Heaviside functions. The Heaviside function is piecewise constant, with ill-defined derivatives, so we replace it with its continuous relaxation, the sigmoid function. Informally, the output \( m_j \) of the final sigmoid can be interpreted as the probability of accepting some \( y_j \) into \( C_\alpha(x_n) \). The smoothness of the relaxation is controlled by a single hyperparameter \( \tau \in (0, +\infty) \). As \( \tau \to 0 \) the relaxation becomes exact but the gradients become very poorly behaved.

2BayesOpt proposal distributions are usually implicit, obtained through gradient-based optimization of the acquisition function.

3For example, it is commonly assumed that \( f^* \) has bounded RKHS norm w.r.t. the chosen GP kernel, that we know a good bound in order to set hyperparameters correctly, and that \( f^* \) is Lipschitz continuous.
In other words, \( \beta \) changes the truth along the boundary of \( C_{\alpha}(x) \) to capture all possible values of \( y \) and dense enough to pinpoint the boundary of \( C_{\alpha}(x) \). Even if we do not fully believe \( p(y|x, D) \), it is still our best guess of where \( y \) should be, so instead of a dense grid we populate \( Y_{\text{cand}} \) with proposals \( y_j \sim p(y|x, D) \). This approach not only reduces computational effort for low-dimensional \( y \), it also allows us to extend to tasks with multiple objectives and batched queries. In Figure 3 we visualize the computation of a conformal Bayes prediction set.

4.2 Conformal acquisition functions

By the sum rule of probability, we can rewrite \( p(f(x')|D) \) as an integral over all possible outcomes \( y'|x' \),

\[
p(f(x')|D) = \int_{y' \in Y} p(f(x')|D')p(y'|x', D)dy'. \tag{5}
\]

In other words, \( p(f(x')|D) \) can be seen as a Bayesian model average, where we condition each component model on a different potential observation \( (x', y') \), and weight the components by \( p(y'|x', D) \).

We are free to change the component weights to any other valid distribution over \( y' \) we like. Now we introduce the conformal Bayes predictive posterior \( p_\alpha(y'|x', D) \), defined as

\[
p_\alpha(y'|x', D) := \begin{cases} 
(1 - \alpha)/Z_1 & \text{if } y' \in C_{\alpha}(x'), \\
\alpha p(y'|x', D)/Z_2 & \text{else},
\end{cases}
\]

where \( Z_1, Z_2 \) are normalization constants. See Figure 4 for an illustration. We are partitioning the outcome space into two events, either \( y' \in C_{\alpha}(x) \) or it is not. Since \( C_{\alpha}(x') \) is a valid prediction set, \( y' \in C_{\alpha}(x') \) with frequency \( (1 - \alpha) \), and we do not consider any particular \( y' \in C_{\alpha}(x') \) to be more likely than another, since the coverage guarantee holds for \( C_{\alpha}(x') \) as a whole. We also expect that \( y' \in Y \setminus C_{\alpha}(x') \) with frequency \( \alpha \), and we weight each \( y' \not\in C_{\alpha}(x') \) by \( p(y'|x', D) \) to form a proper density (i.e. a density that integrates to 1).

If we had noiseless observations (i.e. \( y_i = f(x_i) \)), we could use \( p_\alpha(y'|x', D) \) directly when computing the acquisition value of new queries. However managing the explore-exploit tradeoff with noisy outcomes requires us to distinguish between epistemic and aleatoric uncertainty. If we do not, optimistic acquisition functions like UCB may direct us towards queries whose outcomes are uncertain due to measurement error. Substituting \( p_\alpha(y'|x', D) \) for \( p(y'|x', D) \) in Eq. (5) results in the conformal Bayes posterior \( p_\alpha(f(x')|D) \),

\[
p_\alpha(f(x')|D) := \frac{1 - \alpha}{Z_1} \int_{C_{\alpha}(x')} p(f(x')|D')dy' + \frac{\alpha}{Z_2} \int_{Y \setminus C_{\alpha}(x')} p(f(x')|D')p(y'|x', D)dy'. \tag{6}
\]

Given \( p_\alpha(f|D) \), we can "conformalize" any acquisition function written in the form of Eq. (1) by substituting \( p_\alpha(f|D) \) for \( p(f|D) \). In Appendix B.2 we show that

\[\
\]
Monte Carlo estimates of conformal acquisition values: in brief, given a query point \( x \) and utility function \( u \), we first draw a candidate grid \( Y_{\text{cand}} \) and compute the corresponding prediction mask \( m \) according to Section 4.1. Then we estimate the conformal acquisition value as follows:

\[
a_{\alpha}(x') = \int u(f(x'), D)p_\alpha(f(x')|D)df,
\]

\[
\approx (1 - \alpha)u^T v + \alpha u^T v',
\]

where \( u = [u(f^{(0)}, D), \ldots, u(f^{(k-1)}, D)]^T \),

\[
v_i = \frac{m_i}{p(y_i|\{x, D\})\left(\sum_j p(y_j|\{x, D\})\right)^{-1}},
\]

\[
v'_i = (1 - m_i)(1^T (1 - m))^{-1},
\]

and \( f^{(j)} \sim p(f|D \cup \{(x_j, y_j)\}), \forall y_j \in Y_{\text{cand}}, \) which is cheap since we already computed the conditioned posteriors when calculating \( m \). See Appendix B.3 for the full derivation.

4.3 Accounting for Feedback Covariate Shift

If we were merely ranking queries exchangeable with \( D \), then there would be no need to correct for covariate shift. However, our goal is to find queries with exceptional outcomes, and the more we optimize, the more severe we can expect the resulting feedback covariate shift to be.

Density ratio estimation: as we saw in Section 2.3 adapting \( C_\alpha(x) \) to covariate shift requires estimating importance weights \( w_i \propto r(x_i) = p'(x_i)/p(x_i) \), where \( p'(x) \) is the proposal distribution from which we draw candidate query points. If we know the densities \( p(x) \) and \( p(x') \) then we can compute \( r(x) \) very easily, but in general we only have samples from \( p(x) \). Furthermore if we wish to optimize queries with gradient based methods then \( p'(x) \) is implicitly defined as the distribution over iterates \( x_t \) induced by the gradient field \( \nabla x a_t \) and an initial distribution on \( x_0 \). Fortunately we can still obtain samples from \( p'(x) \) by sampling from the energy distribution, \( p'(x) \propto \exp\{a_t(x)\} \) via stochastic gradient Langevin dynamics (SGLD) [58].

Once we have samples from \( p(x) \) (which are already in \( D \)) and \( p'(x) \), we estimate \( r(x) \) with a probabilistic classifier [49]. We assign labels \( z \) to the samples, corresponding to the conditional distributions \( p(x|z) = p(x|z = 0) \) and \( p'(x|z = 1) = p(x|z = 1) \). By Bayes theorem, we rewrite \( r(x) \),

\[
r(x) = \frac{p(z = 0)p(x|z = 1)}{p(z = 1)p(x|z = 0)},
\]

such that we need only train a probabilistic classifier \( \hat{p}(z|x) \) to discriminate the sample labels. We estimate the prior ratio \( p(z = 0)/p(z = 1) \) empirically.

Which comes first, the acquisition function or the ratio estimator? To estimate \( r \) as just described we clearly must be able to compute \( \nabla x a_t \) to draw the required samples from \( p'(x) \propto \exp\{a_t(x)\} \). Here we find a second and more serious issue, since \( a_t \) itself then depends on \( r \). We need an estimator \( \hat{r} \) that simultaneously induces \( p'(x) \propto \exp\{a_t(x)\} \) and accurately estimates \( p'(x)/p(x) \). For example, we could assume \( \hat{r}(x) = 1, \forall x \), but the induced \( p' \) likely does not satisfy \( p'(x)/p(x) = 1, \forall x \).

To solve these issues, we begin with an initial estimator \( \hat{r}_0(x) = 1, \forall x \), and for \( t \geq 0 \) we sample from \( p'(x) \propto \exp\{a_t(x)\} \) via SGLD using the current estimator \( \hat{r}_t \), then update the classifier on those new samples to produce an updated estimator \( \hat{r}_{t+1} \) for the next iteration. To keep the acquisition surface from changing too rapidly (potentially destabilizing our SGLD chain), we compute an exponential moving average of the classifier weights, and the averaged weights are used when computing gradients of \( a_t(x) \). Our approach is analogous to (and directly inspired by) bootstrapped deep Q-learning [41].
Figure 6: BayesOpt results on heteroscedastic, single-objective tasks sinc and double-knot (reporting median and its 95% conf. interval, estimated from 16 trials). (a) sinc(x) (left y axis) and ε(x) (right y axis). (b) the sinc task, best objective value found by conformal BayesOpt with homoscedastic likelihoods compared to baselines, risk-averse UCB and penalized EI, both with heteroscedastic likelihoods. (c) the double-knot task, same experiment as in panel (b). Conformal BayesOpt with a misspecified likelihood outperforms the specialized baselines on both tasks.

5 EXPERIMENTS

In Section 5.1 we report the empirical coverage of credible and conformal prediction sets in a simplified setting. In Section 5.2 we show that conformal BayesOpt is robust to a misspecified likelihood. Finally in Section 5.3 we evaluate conformal BayesOpt on synthetic black-box optimization tasks, comparing the query coverage of credible and conformal prediction sets. See Appendix C for results on multi-objective synthetic tasks and real ranking tasks using drug and antibody design data, and see Appendix D for all experimental details.

5.1 Do Our Approximations Impact Coverage?

First we compare the empirical coverage of Bayes credible sets and randomized conformal prediction sets, and evaluate the sensitivity of conformal prediction to continuous relaxation and density ratio estimation. We consider a simplified offline regression setting where \( p(x) \) and \( p'(x) \) are known 3D spherical Gaussian distributions with different means, \( f \) is the 3D Hartmann function, and \( y|x \sim \mathcal{N}(f(x), \sqrt{\delta}) \). If the exact validity guarantee of randomized conformal prediction holds, then over many trials the coverage should concentrate around \((1 - \alpha)\). Some deviation is to be expected due to sample variance and discretization error. In Figure 5a we see when we have the density ratio oracle and \( \tau = 0 \), that the distribution of conformal coverage is indeed concentrated around \((1 - \alpha)\), especially relative to the distribution of credible coverage. In the other panels of Figure 5 we show that empirical density ratio estimates and the continuous relaxation do not compromise validity. In particular increasing \( \tau \) makes the corresponding prediction sets more conservative, which is consistent with the limiting case \( \lim_{\tau \to \infty} C_\alpha(x) = \mathcal{Y}, \forall x \).

5.2 Model Misspecification and Sample-Efficiency

Recall from Section 2.2 that BayesOpt surrogates often use a homoscedastic likelihood \( p(y|f) = \mathcal{N}(f, \sigma^2) \), where \( \sigma^2 \) is a learned constant. In Figure 6a we plot sinc(x) = \((10 \sin(x) + 1) \sin(3x)/x\) on \([-10, 10]\) with \( y|x \sim \mathcal{N}(\text{sinc}(x), \epsilon(x)) \) and \( \epsilon(x) = 2/(1 + \exp(x/2)) \). In Figure 6b we compare conformal BayesOpt with \( p(y|f) = \mathcal{N}(f, \sigma^2) \) to two baselines specifically designed for tasks with heteroscedastic noise, specifically risk-averse UCB [39] and penalized EI [27], which both use heteroscedastic likelihoods. Both baselines require multiple replicates of each query to update their likelihoods, which significantly reduces sample efficiency. In Figure 6c we repeat the same experiment on a second heteroscedastic task double-knot\((x) := -x_1 \exp\{-x_1 - x_2\} \) on \([-2, 6]^2\), with \( y|x \sim \mathcal{N}(\text{sinc}(x), \epsilon(x)) \) and \( \epsilon(x) = |x|/2 \) [26]. Despite having a simpler, misspecified noise model, conformal BayesOpt finds a better solution with fewer queries.

5.3 Good Query Coverage and Good Sample-Efficiency Are Not Mutually Exclusive

We use the batch UCB acquisition function \((q = 3)\) to optimize two synthetic functions levy and ackley, taking \( \mathcal{X} \subset \mathbb{R}^2 \). For this experiment \( y|x \sim \mathcal{N}(f(x), (\sigma^*)^2) \). To simulate the covariate shift that occurs in many applied problems, we sampled the initial training data from a random orthant of the input space. In Figure 7 we compare the sample efficiency and coverage of standard BayesOpt, TuRBO [20], and conformal BayesOpt. Each method is comparable in terms of sample efficiency, and the credible set coverage for standard BayesOpt and TuRBO looks reasonable on a random subset of the training data, if a bit unpredictable. However if we look at the query coverage we see that the credible set coverage varies wildly. The difference between coverage on a random holdout set and coverage on the query set is due to feedback covariate shift. In contrast, we see that the conformal set coverage for both random holdout points and query points very consistently tracks \((1 - \alpha)\), where \( \alpha = 1/\sqrt{n} \). In other words, of the methods considered conformal BayesOpt is the only approach that improves the objective while reliably predicting the query outcomes.

In Figure 8 we preview results showing we can also improve query coverage in tabular ranking tasks related to drug design. See Appendix C.3 for the full experiment.
6 DISCUSSION

We have shown that a combination of model misspecification and optimization-induced covariate shift can make Bayesian predictions unreliable exactly where they are needed most — where the queries concentrate. Conformal prediction provides a principled solution to these issues, with distribution-free validity guarantees that help ensure robustness to model misspecification, and a natural mechanism to correct for covariate shift. To use conformal prediction inside of BayesOpt, we have developed differentiable and efficiently discretizable conformal prediction sets and coupled these with a practical density ratio estimation procedure, addressing key technical challenges in the conformal prediction literature. With the introduction of the conformal posterior, we have derived conformal generalizations of many popular acquisition functions, allowing us to accommodate features of practical tasks including batched queries, noisy observations, and multiple objectives. Empirically we find the combination of conformal prediction and BayesOpt to be very promising, since it improves query coverage and has sample-efficiency comparable to methods with no coverage guarantees at all.

Looking forward, although we focus on GP surrogates in the low-$n$ regime, we expect many of these ideas to transfer to much larger models and datasets by replacing full conformal Bayes with split conformal Bayes, and either augmenting GPs with deep kernel learning, or by replacing GPs entirely with linear models operating on pretrained representations learned by large self-supervised models. Extending conformal BayesOpt to discrete optimization, specifically biological sequence design, is a particularly exciting direction for future work. There are also intriguing theoretical directions, such as analyzing the effect of continuous relaxation and the effect of learned density ratio estimates on conformal coverage guarantees, and investigating whether the regret of conformal BayesOpt can be analyzed with milder assumptions than algorithms like GP-UCB [43].

As machine learning systems influence increasingly impactful applications, we must confront the reality that machine learning models will be built on faulty assumptions, and those models will be asked to rank potential decisions without sufficient training data. The solution is not to blind ourselves to the error in our assumptions, nor is it to paralyzed ourselves in pursuit of a perfect model. Instead we should develop methods that can gracefully accommodate imperfect models, balancing internal coherence with external validity.
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Appendices

The appendices are structured as follows:

- In Appendix A we describe the assumptions, limitations, and broader impacts of this work.
- In Appendix B we provide detailed derivations of the randomized differentiable conformal prediction, conformal Bayes posterior and of conformal acquisition functions.
- In Appendix C we include more experimental results, in particular multi-objective black-box optimization and single-objective tabular ranking tasks with real data.
- In Appendix D we give implementation details for all experiments.
A  ASSUMPTIONS, LIMITATIONS, AND BROADER IMPACTS

A.1  Assumptions

The assumptions underlying the coverage guarantee for conformal prediction are strikingly mild. All else equal, any real-valued, measurable score function will produce a valid prediction set \[ C_s(x) = Y, \forall x, \forall \alpha. \] There are trivial examples that produce trivially valid prediction sets \[ C_s(x) = Y, \forall x, \forall \alpha. \] In general if we choose \( s \) poorly we pay a price in terms of efficiency (i.e. the volume of the prediction sets), but validity is still maintained.

The critical assumption is that \( (x_0, y_0), \ldots, (x_n, y_n) \) are pseudo-exchangeable.\(^5\) A sequence of random variables is pseudo-exchangeable if the joint density can be factored into terms that only depend on the values of the sequence, not the ordering.\(^21\) Informally, we can see that BayesOpt satisfies pseudo-exchangeability because the likelihood of the training data is just the mixture of all the previous query likelihoods, and the query likelihoods do not depend on the order of the past observations. Because we make no assumptions about the data distribution beyond pseudo-exchangeability, conformal prediction belongs to a class of methods known as distribution-free uncertainty quantification.

A.2  Limitations

Marginal vs. conditional coverage guarantees: full and split conformal prediction sets have marginal coverage guarantee that is easy to confuse with conditional coverage guarantees.\(^1\) Marginal coverage guarantees must be interpreted with the same frequentist mindset as other frequentist measures of uncertainty, such as confidence intervals and \( p \)-values, with similar risks of misinterpretation by inexperienced users. We have attempted to make clear in the main text that the full conformal prediction coverage guarantee is only realized in the aggregate, as the average of coverages observed in many independent, parallel experiments. Coverage observed within any specific trial can (and does) vary substantially from the aggregate tendency. There is very recent work which seeks to provide a stronger validity guarantee that can be expected to hold for some \( (1 - \delta) \) fraction of trials, which we hope to apply to conformal BayesOpt in future work.\(^6\)

Approximation error: we have introduced some necessary approximations in this work, notably the discretization of continuous labels and the continuous relaxation of conformal prediction sets. While we have given empirical evidence that the error introduced by these approximations does not appear to be too severe, practitioners should be aware that some deviation from the expected coverage level may occur, as we discuss in Section 5. This limitation is analogous to the numeric limitations of linear algebra implemented with floating point arithmetic. We may be able to make use of Ndiaye\(^{42}\) to avoid discretizing continuous outcomes entirely, which we leave for future work.

A.3  Broader Impacts:

Potential negative social impacts: black-box optimization algorithms are application-agnostic. The same algorithms that are being used to design new therapeutics could in theory be used to discover new toxins for bioterror or biowarfare. Similarly, the same algorithms used to design new materials for scientific discovery could be used to design new weapons or rocket fuels. Our work is not particularly vulnerable to misuse relative to the large body of existing work on black-box optimization algorithms.

Machine learning research: phenomena like model misspecification and covariate shift are often blamed on complexity in the external world, but they are also induced by our own behavior, such as choosing a convenient likelihood for a model (even when a more sophisticated option is available) or actively selecting new training data. We hope this work spurs more interest in understanding how to reliably interact with the models we have today, in addition to work on “better” models for tomorrow.

Experimental design: applications like materials science and drug discovery require the coordination of large, interdisciplinary teams of scientists and engineers. If machine learning systems are to play a central role in that coordination, they must be reliable, in the sense that the systems have stable behavior and consistently valid predictions. That kind of reliability requires more than faith in an ad hoc collection of model assumptions with limited experimental validation. This work is a step towards machine learning systems with interpretable certificates of reliability that can serve as the foundation on which to build teams which push the boundaries of experimental science.

\(^5\)Note that every IID sequence of random variables is exchangeable, but not every exchangeable sequence is IID. Similarly pseudo-exchangeability does not mean every element of the sequence except for the last is IID.
B PROOFS AND DERIVATIONS

B.1 Smoothed conformal prediction

Algorithm 2 Randomized differentiable conformal prediction masks

Data: train data \( D = \{(x_i, y_i)\}_{i=1}^{n-1} \), test point \( x_n \), imp. weights \( w \), label candidates \( Y_{\text{cand}} \), score function \( s \), miscoverage tolerance \( \alpha \), relaxation strength \( \tau \).

\( m_j = 0, \forall j \in \{0, \ldots, k - 1\} \).

\textbf{for} \( y_j \in Y_{\text{cand}} \) \textbf{do}

\( s_j = [s(x_0, y_0) \cdots s(x_n, y_j)]^\top \).

\( h_j = \text{sigmoid}( (s_j - s_j) / \tau ) \).

\( \Delta_j = (h_j \odot w)_n \).

\( w_j = 1^\top (h_j \odot w) \).

\( \theta_j = \text{clip}((w_j - \alpha) / \Delta_j, 0, 1) \).

\( \eta_j \sim \text{Bernoulli}(\theta_j) \).

\( w'_j = w_j - (1 - \eta_j) \Delta_j \).

\( m_j \leftarrow \text{sigmoid}((w'_j - \alpha) / \tau) \).

\textbf{end}

\textbf{Result:} \( m \)

As discussed in Section 2.3 of the main text, standard conformal prediction (Definition 2.1) is \textit{conservatively valid}, meaning in the long run the coverage of conformal prediction sets is at least \( 1 - \alpha \). If the prediction sets are too conservative, they may be too wide to be helpful for decision-making. In the BayesOpt context we want prediction sets that are \textit{exactly valid}, neither underconfident nor overconfident. Fortunately with a small change (i.e. randomization) conformal prediction sets can be made exactly valid.

Informally, exact validity only requires that we treat an edge case more carefully (see “smoothed conformal predictors” in Vovk et al. [54] for more details). Specifically there will be some candidate labels \( y_j \) that are right on the boundary of the prediction set, and we will introduce randomness to sometimes include such points, and sometimes not, depending on exactly how close to the boundary the points are.

More precisely, there are occasions when

\[ \sum_{i=0}^{n-1} (h_j \odot w_j)_i < \alpha < \sum_{i=0}^{n} (h_j \odot w_j)_i = w_j. \]

In standard conformal prediction the corresponding label \( y_j \) would always be accepted into the prediction set. To make a smoothed conformal predictor, we flip a coin with bias \( \theta_j = \text{clip}((w_j - \alpha) / \Delta_j, 0, 1) \), where \( \Delta_j = (h_j \odot w)_n \). We call the outcome of the flip \( \eta_j \). If \( \eta_j = 1 \), then we accept \( y_j \), similarly if \( \eta_j = 0 \) we reject \( y_j \). Note if \( w_j - \alpha < 0 \) then \( y_j \) is always rejected, similarly if \( w_j - \alpha > \Delta_j \) then \( y_j \) is always accepted. We give the continuous relaxation of smoothed conformal prediction in Algorithm 2.

B.2 Characterizing the conformal Bayes posterior

All conditional distributions are also conditioned on \( D \), which we omit from the notation for the sake of clarity. Recall that the conformal Bayes posterior is written as

\[ p(f(x)|x) = \int_y p(f(x)|x,y)p(y|x)dy, \]

\[ = \int_{C_n(x)} p(f(x)|x,y)p(y|x)dy + \int_{Y\setminus C_n(x)} p(f(x)|x,y)p(y|x)dy. \]
Now we define a new conformal Bayes posterior distribution as a mixture distribution over \( y \),

\[
p_\alpha(y|x) = (1 - \alpha)q_1(y|x) + \alpha q_2(y|x)
\]

where the normalizing constants \( Z_1 \) ensure that \( \int p_\alpha(y|x)dy = 1 \) (assuming \( C_\alpha(x) \) is bounded and non-empty, so \( Z_1 \) is non-zero and finite). If \( C_\alpha(x) = \mathcal{Y} \) and \( \mathcal{Y} \) is unbounded then \( p_\alpha(y|x) \) is not a proper density.

The corresponding conformal Bayes posterior distribution over \( f \) is

\[
p_\alpha(f(x)|x) = \int p(f(x)|x,y)p_\alpha(y|x)dy
\]

\[
= \frac{1 - \alpha}{Z_1} \int_{C_\alpha(x)} p(f(x)|x,y)p_\alpha(y|x)dy + \frac{\alpha}{Z_2} \int_{\mathcal{Y}\setminus C_\alpha(x)} p(f(x)|x,y)p_\alpha(y|x)dy
\]

Finally we can rewrite both integrals over all \( \mathcal{Y} \) by introducing a binary mask.

**Definition B.1.**

\[
p_\alpha(f(x)|x) := \frac{1 - \alpha}{Z_1} \int_{C_\alpha(x)} m_\alpha(x,y)p(f(x)|x,y)dy + \frac{\alpha}{Z_2} \int_{\mathcal{Y}\setminus C_\alpha(x)} (1 - m_\alpha(x,y))p(f(x)|x,y)p(y|x)dy,
\]

\[
m_\alpha(x,y) := \begin{cases} 
1 & \text{if } y \in C_\alpha(x), \\
0 & \text{else}.
\end{cases}
\]

**Proposition B.1.** Let \( n > 1 \) and \( p_\alpha(f|D) \) be defined according to Definition B.1. Then \( p_\alpha(f|D) \) converges pointwise in \( x \) to \( p(f(x)|x, D) \) as \( \alpha \to 1 \),

\[
\lim_{\alpha \to 1} p_\alpha(f(x)|x) = p(f|x).
\]

**Proof:**

Let \( \varepsilon > 0 \), \( n > 2 \), and define \( \alpha_k = 1 - 1/(k+1) \) for \( k \in \mathbb{N} \).

\[
|p_{\alpha_k}(f(x)|x) - p(f(x)|x)| = |\Delta_1 + \Delta_2|,
\]

\[
\leq |\Delta_1| + |\Delta_2|,
\]

where

\[
\Delta_1 = \frac{1 - \alpha_k}{Z_1} \int_{C_{\alpha_k}(x)} p(f(x)|x,y)dy - \int_{C_{\alpha_k}(x)} p(f(x)|x,y)p(y|x)dy,
\]

\[
\Delta_2 = \frac{\alpha_k}{Z_2} \int_{\mathcal{Y}\setminus C_{\alpha_k}(x)} p(f(x)|x,y)p(y|x)dy - \int_{\mathcal{Y}\setminus C_{\alpha_k}(x)} p(f(x)|x,y)p(y|x)dy.
\]

Recalling the definition of \( C_\alpha(x) \) (Def. 2.1), we observe that \( C_{\alpha_k}(x) \supset C_{\alpha_{k+1}}(x), \forall k \in \mathbb{N} \). Furthermore we see that since the importance weights \( w \) must sum to 1 that \( \lim_{k \to \infty} C_{\alpha_k}(x) = \emptyset \).

\( A \supset B \) indicates that \( A \) is a strict superset of \( B \).
Bounding $|\Delta_1|$: 

$$
|\Delta_1| \leq |\mathcal{O}(1 - \alpha_k) - \mathcal{O}(1 - \alpha_k)|,
\Rightarrow |\Delta_1| \leq c_1(1 - \alpha_k).
$$

Bounding $|\Delta_2|$: 

$$
|\Delta_2| \leq |(\alpha_k - 1)\mathcal{O}(1)|,
\Rightarrow |\Delta_2| \leq c_2(1 - \alpha_k).
$$

Choose $k \in \mathbb{N}$ large enough that $(c_1 + c_2)(1 - \alpha_k) < \varepsilon$. ■

B.3 Monte Carlo integration of conformal acquisition functions

We want to integrate acquisition functions of the form

$$
a(x) = \int u(f(x), D)p_\alpha(f|D)df
\quad = \frac{1 - \alpha}{Z_1} \int \int u(f(x), D)m_\alpha(x, y)p(f(x)|x, y)dydf
\quad + \frac{\alpha}{Z_2} \int \int u(f(x), D)(1 - m_\alpha(x, y))p(f(x)|x, y)p(y|x)dydf,
$$

Suppose we have sampled $Y_{\text{cand}} = \{y_j\}_{j=0}^{k-1}$, with $y_j \sim p(y|x, \mathcal{D})$, and $\hat{f}^{(j)} \sim p(f(x)|\mathcal{D} \cup \{(x, y_j)\})$. Starting with the first term in the sum, we have

$$
\frac{1 - \alpha}{Z_1} \int \int u(f(x), D)m_\alpha(x, y)p(f(x)|x, y)dydf \approx \frac{1 - \alpha}{Z_1 k} \sum_{j=0}^{k-1} \frac{m_\alpha(x, y_j)}{p(y_j|x)} u(\hat{f}^{(j)}, \mathcal{D}).
$$

We estimate the normalization constant $Z_1$ as follows:

$$
Z_1 = \int_{\tilde{C}_\alpha(x)} 1dy = \int m_\alpha(x, y)dy
\quad \approx \frac{1}{k} \sum_{j=0}^{k-1} \frac{m_\alpha(x, y_j)}{p(y_j|x)}
$$

By similar logic the second term in the sum is estimated as follows:

$$
\frac{\alpha}{Z_2} \int \int u(f(x), D)(1 - m_\alpha(x, y))p(f(x)|x, y)p(y|x)dydf \approx \frac{\alpha}{Z_2 k} \sum_{j=0}^{k-1} (1 - m_\alpha(x, y_j))u(\hat{f}^{(j)}, \mathcal{D}),
$$

where

$$
Z_2 = \int_{Y \setminus \tilde{C}_\alpha(x)} p(y|x)dy = \int (1 - m_\alpha(x, y))p(y|x)dy
\quad \approx \frac{1}{k} \sum_{j=0}^{k-1} (1 - m_\alpha(x, y_j))
$$
When there are multiple objectives of interest, a single best design may not exist. Suppose there are multiple objectives, \( f : \mathcal{X} \rightarrow \mathbb{R}^m \). The goal of multi-objective optimization (MOO) is to identify the set of Pareto-optimal solutions such that improving one objective within the set leads to worsening another. We say that \( f \) is Pareto-optimal if for all \( x, x' \in \mathcal{X} \) and \( f_k(x) \geq f_k(x') \) for all \( k \in \{1, \ldots, m\} \) and \( f_k(x) > f_k(x') \) for some \( k \). The set of non-dominated solutions \( \mathcal{X}^* \) is defined in terms of the Pareto frontier (PF) \( \mathcal{P}^* \),

\[
\mathcal{X}^* = \{ x : f(x) \in \mathcal{P}^* \}, \quad \mathcal{P}^* = \{ f(x) : x \in \mathcal{X}, \not\exists x' \in \mathcal{X} \text{ s.t. } f(x') > f(x) \}.
\]

MOO algorithms typically aim to identify a finite approximation to \( \mathcal{X}^* \), which may be infinite, within a reasonable number of iterations. One way to measure the quality of an approximate PF \( \mathcal{P} \) is to compute the hypervolume \( HV(\mathcal{P}|r_{\text{ref}}) \) of the polytope bounded by \( \mathcal{P} \cup \{ r_{\text{ref}} \} \), where \( r_{\text{ref}} \in \mathbb{R}^m \) is a user-specified reference point.

\[
u_{\text{EHVI}}(f, \mathcal{D}) = HV(\mathcal{P}', \mathcal{P}|r_{\text{ref}}) = HV(\mathcal{P}'|r_{\text{ref}}) - HV(\mathcal{P}|r_{\text{ref}})+, \]

where \( \mathcal{P}' = \mathcal{P} \cup \{ f(x) \} \). If our measurements of \( f \) are noisy we cannot compute HV exactly and instead must substitute \( \tilde{f} \sim p(f|\mathcal{D}) \), i.e.

\[
u_{\text{NEHVI}}(f, \mathcal{D}) = HV(\mathcal{P}_{\tilde{f}}, \mathcal{P}|r_{\text{ref}}),
\]

where \( \mathcal{P}_{\tilde{f}} = \{ \tilde{f}(x) : x \in \mathcal{X}, \not\exists x' \in \mathcal{X} \text{ s.t. } \tilde{f}(x') > \tilde{f}(x) \} \) and \( \mathcal{P}' = \mathcal{P} \cup \{ \tilde{f}(x) \} \).

Our derivations hold for so-called composite acquisitions as well, so we could also extend to qParEGO and qNParEGO variants for multi-objective optimization.
B.6 Conformalizing Batch Acquisitions

In general batch acquisitions have the form

$$a(x_0, \ldots, x_{q-1}) = \int \max_{i<q} u(f(x_i), D)p(f|D)\,df.$$  \hfill (14)

Note that $f(x_0), \ldots, f(x_{q-1})$ are sampled jointly when estimating Eq. (14) with Monte Carlo. Increasing the query batch size to $q$ increases the dimensionality of the outcome to $q \times m$, where $m$ is the number of objectives. Our importance-sampling MC integration procedure introduced in Section 4.1 scales gracefully with higher outcome dimensionality, we simply sample the elements of $Y_{\text{cand}}$ from $p(y(x_0), \ldots, y(x_{q-1})|x_0:q-1, D)$.

The bigger challenge arises in computing the conformal masks for batched query outcomes. In our current implementation we compute the conformal scores (the Bayes posterior log-likelihood) pointwise for each query batch element, with corresponding pointwise conformal prediction masks. We apply the pointwise masks before computing $\max_{i<q} u$ across query batch elements. The alternative would be to compute a joint conformal score across all query batch elements (similarly computing joint scores for each of the previous query batches in the training data). Note that this second approach essentially reduces to replacing each datum $(x_i, y_i)$ in Eq. (3) with $(X_i, y_i) = ([x_0, \ldots, x_{q-1}]^\top, [y_0, \ldots, y_q]^\top)$. We leave the implementation of this second approach for future work.

B.7 Out-of-distribution queries

If $p'(x) \neq p(x)$, and $w(x, D) > \alpha$, then $C_\alpha(x) = \mathcal{Y}$, which makes $p_\alpha(x|D)$ an improper density. Intuitively the issue is there are not enough points in $D$ close enough to $x$ to guarantee a miscoverage rate of $\alpha$. Our solution is to set any conformal acquisition value $a_\alpha(x)$ to 0 if $w(x, D) > \alpha$. In practice we achieve this effect by introducing a second mask $m' = \text{sigmoid}(w_n - \alpha)/\tau_d$ which we apply to Eq. (7). For conformal EI and other similar acquisition functions, this mask simply means we will favor any point close enough to the dataset to guarantee coverage if it has positive expected improvement over any out-of-distribution point. For conformal UCB, this mask means all out-of-distribution points are assigned the value $\sum_{y_i \in D} y_i$ (assuming the labels have been zero-centered during preprocessing).
C ADDITIONAL EXPERIMENTAL RESULTS

C.1 Single-Objective Black-Box Optimization

Figure 9: BayesOpt best objective value found with conformal and standard acquisition functions on single-objective tasks Levy-$d$ and Ackley-$d$ (reporting median and its 95% conf. interval, estimated from 25 trials). qEI, qNEI, conformal qEI, and conformal qNEI all perform similarly, conformal qUCB is best everywhere except Ackley-20, where it comes second after qUCB.

Figure 10: BayesOpt empirical coverage of conformal and credible prediction sets evaluated on holdout data from single-objective task Levy-$d$ (reporting median and its 95% conf. interval, estimated from 25 trials). The conformal coverage curves track the target $1 - \alpha$ (black dashed line) well, significantly better than the credible curves, which tend to be overconfident. Median w/ 95% confidence interval is shown.

In Figure 9 we investigate the effect of the choice of acquisition function on sample-efficiency, comparing conventional and conformal versions. In particular we consider expected improvement (EI), noisy expected improvement (NEI) and upper confidence bound (UCB) alongside their conformal counterparts. No clear ranking emerges here, however UCB and conformal UCB both perform well in general.

In Figure 10, we investigate the sensitivity of coverage on random holdout data to the query batch size $q$ and the dimensionality of the inputs $d$. Here, we plot the median and its 95% confidence interval as shading, finding that the conformal sets are better calibrated in a frequentist sense than the equivalent coverage level of the Bayesian posterior.
C.2 Multi-Objective Black-Box Optimization

Figure 11: BayesOpt results on multi-objective tasks branin-currin and penicillin (reporting median and its 95% conf. interval, estimated from 25 trials). **Left two panels:** Both conformal and standard acquisitions find solution sets with similar hypervolumes. **Right two panels:** Credible and conformal empirical coverage curves. The conformal curves track the target $1 - \alpha$ (black dashed line) better than the credible curves, but both are underconfident.

To demonstrate that our approach scales to multi-objective tasks, we consider two tasks, branin-currin ($p = 2$) and penicillin ($p = 3$) [37]. The goal is not to find a single $x^*$, but rather to find the set of all non-dominated solutions, the Pareto front. By non-dominated, we mean the set of solutions with the property that the objective value cannot increase in one dimension without decreasing in another. We report results using the expected hypervolume improvement (EHVI) [18, 19, 13] and noisy expected hypervolume improvement (NEHVI) [14] as the base acquisition functions in Figure 11. Like the single-objective case conformal BayesOpt is comparable in terms of sample-efficiency as quantified by the solution hypervolume relative to a common reference point [8], and conformal set coverage tracks $(1 - \alpha)$ more closely than credible set coverage. All black-box functions used in this paper are synthetic with implementations coming from BoTorch [5]. The Penicillin function was originally proposed by Liang and Lai [37].
C.3 Tabular Ranking with Real-World Drug and Antibody Data

Figure 12: Result ranking tabular molecular datasets for drug-related properties such as solubility (logP) (a), empirical drug-likeness score (QED) (b), dopamine receptor (DRD3) binding affinity (c) and antibody stability (d). Across datasets, CUCB selects queries with more consistent coverage than UCB (bottom two rows), with identical sample efficiency (top row). The midpoint, lower, and upper bounds of each curve depict the 50%, 20%, and 80% quantiles, estimated from 4 trials.

Sometimes instead of solving $\max_{x \in X} a(x)$, the search space is restricted to a discrete subset of candidates $X_{\text{cand}} \subset X$. This restriction is particularly common for tasks with discrete decision variables, such as biological sequence design [47]. This existence of a fixed candidate set simplifies the computation of conformal acquisition functions substantially, since we can use samples from $X_{\text{cand}}$ directly when training the ratio estimator $\hat{r}$, rather than relying on bootstrapped SGLD as discussed in Section 4.3.

To emulate this kind of application, we compared standard and conformal UCB on a selection of small and large molecule ranking tasks. In particular, we ranked a subset of small molecules drawn from the ZINC dataset [34] for three target properties, penalized logP (solubility), QED (drug-likeness), and DRD3 (dopamine receptor) binding affinity [25, 31]. We also ranked a subset of large antibody molecules drawn from the OAS dataset [30] for stability. For simplicity we did not use sequence-based representations of the molecules, instead relying on RDKit chemical descriptors [35] and BioPython sequence descriptors [11] to generate continuous feature representations of the small and large molecules, respectively.

Starting with the 32 worst entries in our labeled dataset, we selected 128 candidates sequentially ($q = 1$), revealing the corresponding label and retraining the surrogate after each new selection. We share our results in Figure 12. Because selection is restricted to a prespecified candidate set, the coverage is less consistent than the black-box optimization setting, however we find that conformal UCB still selects queries with better coverage overall, without sacrificing sample-efficiency (measured by cumulative regret, i.e. the difference between the selected candidate label and the best possible label of the remaining candidates).
D IMPLEMENTATION DETAILS

D.1 Bringing Everything Together

Algorithm 3 Pseudocode for the conformal BayesOpt inner loop

Input: train data $\mathcal{D} = \{(x_i, y_i)\}_{i=0}^{n-1}$, initial solution $x_0$, score function $s$, miscoverage tolerance $\alpha$, sigmoid temperature $\tau_\sigma$, SGLD learning rate $\eta_\theta$, $\#$ SGLD steps $t_{\text{max}}$, SGLD temperature $\tau_{\text{SGLD}}$, classifier learning rate $\eta_\theta$, EMA parameter $\gamma$.

Initialize classifier $q_\theta$, set weight average $\bar{\theta} = 0$.

Initialize classifier dataset $\mathcal{D}' = \{(x_i, 0)\}_{i=0}^{n-1}$

for $t = 0, \ldots, t_{\text{max}} - 1$

Estimate $\hat{r}_t(x_i), \forall i \in \{0, \ldots, n\}$ with $q_\theta$.

$$(w_t)_i = \hat{r}_t(x_i)/\sum_k \hat{r}_t(x_k), \forall i \in \{0, \ldots, n\}.$$  

(Y_cand) 

$y_{\text{cand}} \leftarrow \{y_j\}_{j=0}^{m-1}$ s.t. $y_j \sim \hat{p}(y|x_t, \mathcal{D})$.

$m = \text{outcome\_mask}(\mathcal{D}, x_n, w_t, Y_{\text{cand}}, s, \alpha, \tau_\sigma)$.

Estimate acquisition value $a(x_n)$.

Update $x_n \leftarrow \text{sgld\_step}(x_n, a(x_n), \eta_\theta, \tau_{\text{SGLD}})$.

Update $\mathcal{D}' \leftarrow \mathcal{D}' \cup \{(x_n, 1)\}$.

Update $\theta \leftarrow \theta - \eta_\theta \nabla_\theta \ell(\theta, \mathcal{D}')$.

Update $\bar{\theta} \leftarrow (1 - \gamma)\bar{\theta} + \gamma\theta$.

end for

Return: $x_n$

In Algorithm 3 we summarize the entire conformal BayesOpt inner loop used to select new queries.

D.2 Stable Predictions on the Training Set

We found that computing the negative log likelihood (and its gradients) on our set of training data to be numerically unstable and so used stochastic diagonal estimation to estimate the posterior variances. Plugging in $K = \kappa(X, X)$ into that posterior mean and variance, we get that the posterior mean is $K(K + \sigma^2 I)^{-1} y$ and the posterior covariance is $\Sigma = \sigma^2 I + K - K(K + \sigma^2 I)^{-1} K$. Unfortunately, the second term ends up being unstable as it requires solving (and then subtracting) a (batched) system of size $n \times n$. To see the reason for instability, note that as $\sigma^2 I \rightarrow 0$ then the entire covariance matrix tends to zero.

We originally tried backpropagating through an eigendecomposition; however, this produced ill-defined gradients, see the explanation in Ionescu et al. [12]. Instead we computed a stochastic diagonal estimate, using the identities

$$\Sigma = \sigma^2 I + \sigma^2 K(K + \sigma^2 I)^{-1},$$  

$$\text{diag}(\Sigma)_i \approx \sigma^2 \left(1 + \left(\sum_{j=1}^{J} z^{(j)} \odot K(K + \sigma^2 I)^{-1} z^{(j)}\right)_i \left(\sum_{j=1}^{J} z^{(j)} \odot z^{(j)}\right)_i^{-1}\right),$$

where the probe vector $z^{(j)}$ has i.i.d Bernoulli entries and $\odot$ is the Hadamard product. This estimator comes from Bekas et al. [7] and is in spirit quite similar to Hutchinson’s trace estimator for the log determinant. We used $J = 10$ probe vectors.

D.3 Hyperparameters

For all GP models in this paper, we used the default single task GP (SingleTaskGP) model from BoTorch, which uses a scaled Matern-5/2 kernel with automatic relevance determination and a Gamma(3, 6) prior over the lengthscales and a Gamma(2, 0.15) prior over the output scales. We used constant means. For the likelihood, we used a softplus transformation to optimize the raw noise, constraining the noise to be between $5 \times 10^{-4}$ and 0.5. To fit the GP kernel hyperparameters $\phi$, we used BoTorch’s default fitting utility, fit_gpytorch_model, which uses L-BFGS-B to maximize the log-marginal likelihood $p(\mathcal{D}|\phi)$.

We used a simple schedule $\alpha = \max(0.05, 1/\sqrt{n})$. Note if $\alpha < 1/n$ then $C_\alpha(x) = \mathcal{Y}$, $\forall x \in \mathcal{X}$.

We initialized $D_0$ with 10 Sobol points drawn from a random orthant of the normalized input space. The input normalization was computed from 1000 Sobol points drawn from the unnormalized input space.
### Black-Box Optimization Hyperparameters

| Name                                      | Value |
|-------------------------------------------|-------|
| # Optimization rounds                    | 50    |
| \(q\) (query batch size)                 | \(\{1, 3\}\) |
| \(|D_0|\)                                 | 10    |
| \(\sigma\) (normalized measurement noise scale) | 0.1   |
| \(\tau_\sigma\) (sigmoid temp.)         | 1e-2  |
| \(k\) (i.e. \(|Y_{\text{cand}}|\))     | 256   |
| # SGLD chains                            | 5     |
| \(t_{\text{max}}\) (# SGLD total steps) | 100   |
| \(t_{\text{burn}}\) (# SGLD burn-in steps) | 25    |
| \(\eta_k\) (SGLD learning rate)         | 1e-3  |
| \(\tau_{\text{SGLD}}\) (SGLD temp.)    | 1e-3  |
| \(\eta_\theta\) (classifier learning rate) | 1e-3  |
| \(\gamma\) (classifier EMA weight)      | 2e-2  |
| \(\lambda\) (classifier weight decay)   | 1e-4  |
| Random seeds                             | \(\{0, \ldots, 24\}\) |

### Tabular Ranking Hyperparameters

| Name                                      | Value |
|-------------------------------------------|-------|
| # Optimization rounds                    | 128   |
| \(q\) (query batch size)                 | 1     |
| \(|D_0|\)                                 | 32    |
| \(\sigma\) (normalized measurement noise scale) | n/a |
| \(\tau_\sigma\) (sigmoid temp.)         | 1e-6  |
| \(k\) (i.e. \(|Y_{\text{cand}}|\))     | 64    |
| # number classifier gradient updates     | 256   |
| \(\eta_\theta\) (classifier learning rate) | 1e-3  |
| \(\gamma\) (classifier EMA weight)      | 1     |
| \(\lambda\) (classifier weight decay)   | 1e-4  |
| Random seeds                             | \(\{0, \ldots, 3\}\) |

### D.4 Compute

Our experiments were conducted on a range of NVIDIA GPUs, including RTX 2080 Tis, Titan RTXs, V100s, and A100s on internal clusters. All experiments used a single GPU at a time. It would require approximately 250 GPU hours to reproduce the experiments in this paper by our estimate,

\[
1 \text{ GPU hr/seed} \times 25 \text{ seeds per variant} \times 1 \text{ variant per experiment} \times 10 \text{ experiments} = 250 \text{ hrs}.
\]

Other experimental runs, e.g. debugging, probably consumed an order of magnitude more GPU hours.

### D.5 Software Packages

- Python 3, PSF License Agreement [53].
- Matplotlib, Matplotlib License Agreement.
- Seaborn, BSD License.
- NumPy, BSD License [28].
- PyTorch, BSD License [43].
- GPyTorch, MIT License [24].
- BoTorch, MIT License [5].