

None To Optima in Few Shots: Bayesian Optimization with MDP Priors

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Abstract

Bayesian Optimization (BO) is an efficient tool for optimizing black-box functions, but its theoretical guarantees typically hold in the asymptotic regime. In many critical real-world applications such as drug discovery or materials design, where each evaluation can be very costly and time-consuming, BO becomes impractical for many evaluations. In this paper, we introduce the Procedure-inFormed BO (ProfBO) algorithm, which solves black-box optimization with remarkably few function evaluations. At the heart of our algorithmic design are Markov Decision Process (MDP) priors that model optimization trajectories from related source tasks, thereby capturing procedural knowledge on efficient optimization. We embed these MDP priors into a prior-fitted neural network and employ model-agnostic meta-learning for fast adaptation to new target tasks. Experiments on real-world Covid and Cancer benchmarks and hyperparameter tuning tasks demonstrate that ProfBO consistently outperforms state-of-the-art methods by achieving high-quality solutions with significantly fewer evaluations, making it ready for practical deployment.

1 Introduction

Bayesian Optimization (BO) is an efficient machine learning-based approach for solving global optimization problems of black-box functions where the objective functions can be highly non-convex, and the functional form or derivative is not necessarily available. Owing to its ability to optimize black-box functions, BO is particularly suited for and has been applied in many critical real-world applications such as hyperparameter optimization [Snoek et al., 2012, Wu et al., 2020], neural architecture search [Kandasamy et al., 2018, Zhou et al., 2019], drug discovery [Pyzer-Knapp, 2018, Shields et al., 2021], and materials design [Khatamsaz et al., 2023, Tian et al., 2025].

In BO settings, the objective function can only be accessed by sequential, expensive and time-consuming evaluations. At each iteration all previous evaluations guide the selection process for the next query of the objective function. To study the data efficiency of BO, numerous theoretical studies focused on establishing asymptotic regret bounds [Srinivas et al., 2012, Chowdhury and Gopalan, 2017], such as cumulative regrets and simple regrets. However, asymptotic efficiency often proves impractical in real-world experimental design scenarios, primarily due to the high cost and long turnarounds of each function evaluation. In penicillin manufacturing, for example, the pharmaceutical goal is to identify the optimal experimental control parameters (e.g., temperature, humidity, biomass concentration) that maximize yield. Unfortunately, each evaluation via the wet

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labs can take days or weeks and incur substantial costs, severely limiting the number of feasible evaluations per year. Notably, Liang and Lai [2021] reported that even state-of-the-art BO algorithms require around 1,000 iterations to converge in a penicillin production simulator, equivalent to nearly 20 years if each evaluation takes one week. Also, Aldewachi et al. [2021] reported that developing a new drug cost approximately \$1.3 billion USD on average in 2018, while a failed Alzheimer’s disease drug development program could take up to 5 years and cost as much as \$2.5 billion.

Therefore, to significantly accelerate the scientific discovery processes mentioned above, an urgent and important question is:

Can we design a BO algorithm that is able to find the global optimum within very few shots, e.g., fewer than 20 evaluations?

In this paper, we answer this question affirmatively by proposing a few-shot BO method, the **Procedure-informed Bayesian Optimization** (PROFBO). How does PROFBO address the problem above that initially seems impossible? The key insight behind PROFBO is that, although the target task permits only a few evaluations, related source tasks often have existing evaluations that can serve as rich sources of prior information. Leveraging these existing evaluations enables us to both design and accelerate a BO algorithm for the target task. In practice, these related source tasks can be the docking scores of a set of molecules evaluated on different receptors [Liu et al., 2023], or evaluations of the same supervised-learning loss function on different datasets [Pineda-Arango et al., 2021].

The most straightforward way to exploit such source information is to directly predict the shape of the target objective function, as studied in Wistuba and Grabocka [2021], Falkner et al. [2018], Wang et al. [2024]. In this paper, however, we propose a framework that optimizes the target objective function by leveraging optimization trajectories of related source tasks in principled Bayesian perspective. Specifically, we use Markov Decision Process (MDP) [Bellman, 1958] priors to model source optimization trajectories, thereby capturing procedural knowledge on efficient optimization. We then embed these MDP priors into a Prior-Fitted Neural Network (PFN) [Müller et al., 2022] and employ Model-Agnostic Meta-Learning (MAML) [Finn et al., 2017] for fast adaptation to new target tasks.

The whole PROFBO framework works efficiently even with very few evaluations. See Figure 1 for an example showing that with only 3 evaluations, our PROFBO framework models the true objective function significantly better than the standard Gaussian Process (GP) model and the FSBO algorithm [Wistuba and Grabocka, 2021].

Contributions. Our contributions are summarized as follows:

1. With very few shots, our PROFBO framework can accurately and efficiently identify global optima of black-box functions. Its modular design allows easy adaptation to various configu-

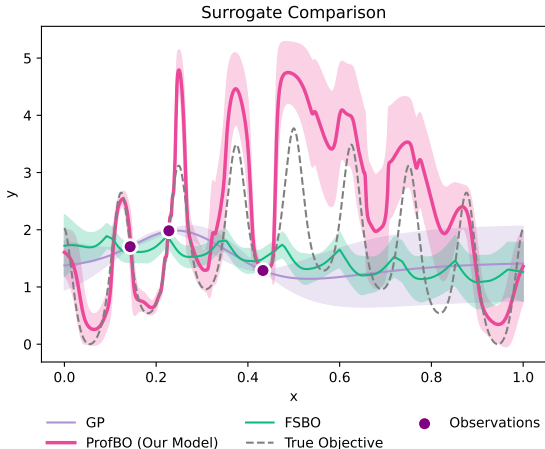


Figure 1: Comparison of function predictions with only 3 observation points. PROFBO models the true objective function curve significantly better than GP model and FSBO algorithm [Wistuba and Grabocka, 2021].

rations and input types by retraining the MDP priors part only. Both make PROFBO highly practical for a wide range of scientific and engineering applications.

2. While optimization trajectory information from source tasks is needed, the Bayesian framework underlying PROFBO *eliminates* all manual steps in prior design and posterior inference via the universal PFN inference.
3. The core design of the PROFBO algorithm lies in its use of MDP priors, which model optimization trajectories from source tasks, thereby capturing procedural knowledge of efficient optimization. These MDP priors are then embedded into a PFN, and MAML is employed for rapid adaptation to new target tasks.
4. We establish new real-world Covid and Cancer benchmarks for few-shot BO problems and show that PROFBO achieves better performances than all existing state-of-the-art baselines.

2 Related Works

Few-Shot Bayesian Optimization. In few-shot BO, people often leverage the knowledge in the evaluations of related tasks to improve the performance of BO. One common approach is meta-surrogate design, whose goal is to transfer-learn a BO surrogate that captures the shared features of multiple tasks’ response surfaces. The meta-surrogates can be synthesized from surrogates of related tasks. Falkner et al. [2018], Schilling [2016], Wistuba et al. [2016] used an ensemble surrogate with weights based on metrics like task similarity or model uncertainty from related task evaluations. Meta-prior design also induces the corresponding meta-surrogate, where knowledge from related tasks is transferred to the prior distribution of the target task. Swersky et al. [2013], Poloczek et al. [2016], Yogatama and Mann [2014], Law et al. [2019], Tighineanu et al. [2022], Wistuba and Grabocka [2021] proposed to design novel kernels for GP functional priors. Wang et al. [2024] proposed to obtain a target task prior by minimizing the KL divergence between it and its related tasks. Perrone et al. [2018] designed a linear function prior for the target objective whose feature is processed by a meta-trained neural network, and the inference is facilitated by Bayesian linear regression. However, most existing work relies on manually designed ensemble weights or tractable priors, and meta-learns only the response surface, while our approach *eliminates* those manual designs through the universal PFN inference, and introduces a trajectory surrogate that captures procedural information.

Acquisition function design is another important approach of few-shot BO, which also employs ensemble methods [Wistuba et al., 2017], similar to the surrogate design. Some work reframed BO as sequence modeling or Reinforcement Learning (RL). According to Bai et al. [2023], search space and initialization design [Wistuba et al., 2015a, Perrone et al., 2019, Li et al., 2022, Feurer et al., 2015, Wistuba et al., 2015b] also provide important information for few-shot BO, and their methods primarily leverage source-domain information to provide a warm start for the target task or narrow down the search space, which is far from the techniques used in our work.

Meta-Optimization with Sequence Modeling. An emerging trend in leveraging meta-data in optimization is to frame optimization as a generic sequential decision process, thus the knowledge transfer is not limited to BO components. Those methods have demonstrated state-of-the-art results in various hyperparameter optimization and drug discovery problems. The meta-acquisition learning method [Volpp et al., 2020, Hsieh et al., 2021] reframes BO (or optimization) as a MDP. Optimization trajectories are generated during their own training processes. They meta-train a RL agent on evaluations of related tasks and conduct optimization on target tasks. Iwata [2021],

Maraval et al. [2023] trained the acquisition function and surrogate model end-to-end, defining the state space solely as historical evaluations, which is consistent with this work. Unlike these approaches, we employ a lightweight RL agent to extract procedural experience, and generate optimization trajectories separately from the training process. And our agent is not used to optimize the target tasks, but serves as the prior distribution of the optimization trajectory.

The Transformer [Vaswani et al., 2017] architecture excels in sequence prediction and in-context learning. Transformer-based BO surrogate learning methods include Transformer Neural Process (TNP) [Nguyen and Grover, 2022, Müller et al., 2023], and leveraging the knowledge in Large Language Models (LLMs) to conduct in-context learning [Ramos et al., 2023, Liu et al., 2024]. Chen et al. [2022], Nguyen et al. [2024] framed optimization as a sequence prediction task, using LLMs to jointly predict the next query and response, leveraging evaluations of other optimization algorithms. Our approach also uses Transformer to facilitate in-context learning, but adopts a modular design that allows easy adaptation by retraining only the MDP priors for various configurations and input types.

3 Preliminaries

3.1 Problem Statement

Let $[n]$ denote the set $\{1, \dots, n\}, n \in \mathbb{N}^+$. We consider the target problem of finding the global optimum of a black-box function $f : \mathcal{X} \rightarrow \mathbb{R}$:

$$x^* = \arg \max_{x \in \mathcal{X}} f(x), \quad (1)$$

where $\mathcal{X} \subseteq \mathbb{R}^d$ is the function domain and d is the input dimension. f is said to be a black-box function because its closed-form expression or the derivative is not necessarily known, and it can be a non-linear non-convex function. We learn from f only through sequential noisy evaluations. Throughout T iterations, at each iteration $t \in [T]$, its evaluation is given by $y_t = f(x_t) + \zeta_t$ where ζ_t is the noise. Our goal is to solve this problem within a few shots, e.g., $T \leq 20$.

Given the limited information gained from each evaluation, we assume access to historical source knowledge that can accelerate the target optimization process, enabling completion within only a few evaluations. Formally, historical knowledge can be $D^{(i)} = \{x_\tau^{(i)}, y_\tau^{(i)}\}_{\tau=1}^{n_i}, \forall i \in [N]$ generated by N source black-box functions $f^{(1)}, \dots, f^{(N)} : \mathcal{X} \rightarrow \mathbb{R}$ where n_i denotes the evaluation length of $f^{(i)}$. Additionally, we define $p(\mathcal{T}^{(i)})$ as the process of sampling from $f^{(i)}$, which can also be comprehended as the distribution of optimization trajectories of $f^{(i)}$ under some policy. $p(\cdot)$ or $p(\cdot|\cdot)$ denotes a (conditional) probability density function or its corresponding distribution. If p is a distribution of a function $f : \mathcal{X} \rightarrow \mathbb{R}$, it will specify the distribution of $f(x)$ with probability density function $p(\cdot|x)$ where $x \in \mathcal{X}$.

3.2 Background

Bayesian Optimization (BO). To solve eqn. (1), BO usually assumes f is drawn from a functional prior, e.g., a GP prior. At iteration t , conditioning on historical evaluations $D_{t-1} = \{x_\tau, y_\tau\}_{\tau=1}^{t-1}$, we denote the posterior predictive distribution as $p(\cdot|x, D_{t-1})$. Then the next query x_t is chosen by $x_t = \arg \max_{x \in \mathcal{X}} \alpha_t(x)$ where α_t is the acquisition function built on $p(\cdot|x, D_{t-1})$. Upper Confidence Bound (UCB) [Srinivas et al., 2012], Expected Improvement (EI) [Jones et al., 1998], Thompson sampling [Thompson, 1933], and knowledge gradient [Frazier et al., 2008] are commonly used as acquisition functions in practice.

Prior-Fitted Neural Networks (PFNs). The motivation of applying PFNs [Müller et al., 2022] in BO is to leverage the meta-trained Transformer architecture to perform principled Bayesian inference in a single forward pass, enabling superior few-shot learning and accurate predictions with interpretable uncertainty quantification. It outperforms traditional GP (see Figure 1), offering greater flexibility in the choice of prior and faster inference by avoiding the matrix inversion in GP posterior inference, thereby enabling our proposed MDP priors (Section 4.2). Given any observation set D and an inference location $x \in \mathcal{X}$, the PFN $q_\theta(\cdot|x, D)$ approximates $p(\cdot|x, D)$ through a bar distribution. In practice, we evaluate a sequence of queries $\{x_i\}_{i=1}^m$ in parallel. Figure 2 illustrates the forward pass and attention mask with three contextual observations and two inference locations. Our settings of PFN’s regression head and network structure are shown in Appendix A.1.

Markov Decision Process (MDP). An MDP [Sutton and Barto, 2018] is typically defined as a 5-tuple $\mathcal{M} = \{\mathcal{S}, \mathcal{A}, \mathcal{P}, \mathcal{R}, \gamma\}$ where \mathcal{S} is the state space, \mathcal{A} is the action space, \mathcal{P} is the transition probability space and $p(s_{t+1}|s_t, a_t) \in \mathcal{P}$ is the transition probability from state $s_t \in \mathcal{S}$ to state $s_{t+1} \in \mathcal{S}$ if the agent takes action $a_t \in \mathcal{A}$ at time t , $\mathcal{R} \subseteq \mathbb{R}$ is the reward space and $r_t(s_t, a_t) \in \mathcal{R}$ is the reward of taking action a_t at state s_t , and $\gamma \in (0, 1]$ is a discount factor. A classical RL problem is to train an agent by finding the optimal policy π^* that maximizes the expected cumulative discounted reward $\pi^* = \arg \max_{\pi} \mathbb{E} [\sum_{t=1}^{\infty} \gamma^{t-1} r_t]$ where the expectation is taken w.r.t. MDP.

Model-Agnostic Meta-Learning (MAML). MAML [Finn et al., 2017] is a gradient-based meta-learning framework designed to train a model M_θ that can rapidly adapt across a collection of tasks $\{\mathcal{T}^{(i)}\}_{i=1}^N$. Each task $\mathcal{T}^{(i)}$ specifies a loss $L^{(i)}(\theta)$. The meta-objective minimizes the meta loss defined as $L_{\text{meta}}(\theta) := \sum_{i=1}^N L^{(i)}(\theta - \beta \cdot \partial_\theta L^{(i)}(\theta))$ where β is an inner step size. By descending with respect to the meta loss, the model learns the common internal representation across N tasks.

4 The ProfBO Algorithm

In this section, we show details of our PROFBO algorithm, a Bayesian framework that can find high-quality solutions to the black-box function optimization problem within very few shots where T can be fewer than 20. The key design of PROFBO lies in how it can efficiently transfer the knowledge from historical optimization trajectories obtained from related source tasks to accelerate its optimization process in target task. The core procedure is summarized in Figure 2.

The PROFBO framework is grounded in a principled Bayesian perspective on optimization trajectories. Under the GP assumption in standard BO, at iteration t , all queries in D_{t-1} are treated as i.i.d. uniformly distributed, ignoring the fact that D_{t-1} is actually a BO trajectory. To fully make use of this information to accelerate the BO process in the target task, we aim to construct a new surrogate model that replaces GP with a set of optimization trajectory priors, $p(\mathcal{T}^{(i)}), \forall i \in [N]$ (Figure 2 right, Section 4.2). To facilitate posterior inference under such a prior, we introduce the PFN model $q_\theta(\cdot|x, D_{t-1})$ as a proxy for $p(\cdot|x, D_{t-1})$ (Figure 2 left-top, Section 4.1). By leveraging observations from the source tasks $\{D^{(i)}\}_{i=1}^N$, MAML enables the PFN model to rapidly adapt to the unknown trajectory of the target task f , while preventing it from learning spurious temporal correlations (Figure 2 left-bottom, Section 4.3).

4.1 The PFN Framework

First, we introduce the PFN framework used in the BO loop where the surrogate model $p(\cdot|x, D_{t-1})$ is obtained by updating the observation set D_{t-1} and conducting posterior inference. PFN conducts

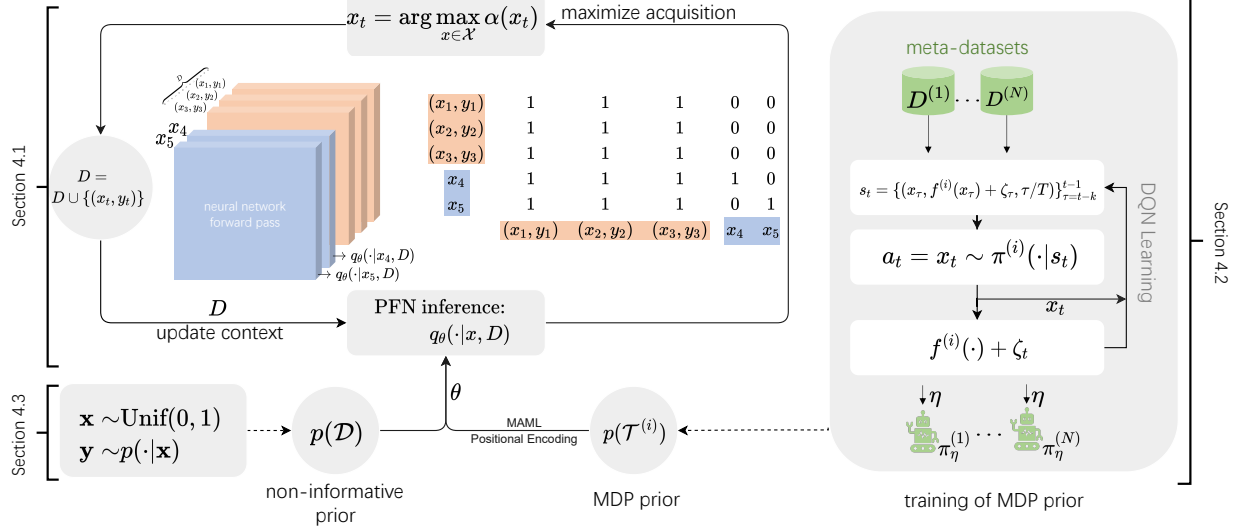


Figure 2: Overview of our PROFBO framework. [Left] The BO loop: a PFN [Müller et al., 2022] model pre-trained with a non-informative prior (e.g., GP) and fine-tuned with MDP priors from source tasks. Fine-tuning uses positional encoding and MAML [Finn et al., 2017] for better knowledge transfer. The PFN performs posterior inference on context D via Transformer attention, with outputs interpreted as logits of a bar distribution. [Right] MDP prior training: for each meta-dataset $D^{(i)}$, a Deep Q-Network (DQN) [Mnih et al., 2013] policy generates optimization trajectories of the corresponding objectives. Right flowchart is attributed to Figure 1 in Volpp et al. [2020].

simulation-based inference through the forward pass of a Transformer model. It directly takes D_{t-1}, x as inputs and outputs a discrete approximation of $p(\cdot|x, D_{t-1})$. Each query-evaluation pair in D_{t-1} attends to each other through the Transformer attention, and are attended by the position of the query x . The final layer of the query network is converted to logits of $p(\cdot|x, D_{t-1})$, through which we can compute approximated acquisition functions, such as UCB and EI.

We assume that the evaluations of f is generated by the process $p(\mathcal{D})$, which is similar to $p(\mathcal{T}^{(i)})$ defined in Section 3 corresponding to a certain process sampling from f . To train the PFN to conduct posterior inference for $p(\mathcal{D})$, one only need to minimize the KL divergence between the PFN approximation $q_\theta(\cdot|x, D)$ and the ground-truth $p(\cdot|x, D)$, where θ is the model parameter and D is any context. It is equivalent to a more tractable negative log-likelihood term $\mathbb{E}_{D \cup \{(x, y)\} \sim p(\mathcal{D})} [-\log q_\theta(y|x, D)]$ plus a constant, where $\{(x, y)\} \cup D$ are sampled from $p(\mathcal{D})$ ¹. In each gradient descent step, we aim to teach the model to make inference for context D at m inference locations, thus the step-wise loss is

$$\hat{\ell}_\theta(D \cup \{(x_i, y_i)\}_{i=1}^m) = \sum_{i=1}^m -\log q_\theta(y_i|x_i, D), \quad D \cup \{(x_i, y_i)\}_{i=1}^m \sim p(\mathcal{D}) \quad (2)$$

We use a fixed total sequence length for each training step, and m in each step is chosen to randomly split the sequence. The flexible choice of $p(\mathcal{D})$ provides the possibility to infer any complicated while easy-to-generate prior. Thus, we construct simulators of $p(\mathcal{T}^{(i)})$ based on meta-datasets of related tasks $D^{(i)}, \forall i \in [N]$ (Section 4.2) and train the PFN with the supervised loss in eqn. (2), yielding a desired trajectory surrogate for BO.

¹The derivation can also be found in Appendix A in Müller et al. [2022].

4.2 Modeling Optimization Trajectory with MDP

We propose a novel prior for Bayesian optimization that models $p(\mathcal{T}^{(i)})$, the prior distribution of optimization trajectories, with MDP [Bellman, 1958, Sutton and Barto, 2018]. In this MDP, at time t , the action a_t is defined as the next query point $x_t \in \mathcal{X}$. The state s_t consists of the previous k evaluations $\{x_\tau, f^{(i)}(x_\tau) + \zeta_\tau, \tau/T\}_{\tau=t-k}^{t-1}$, and the transition is adding a new evaluation $(x_t, f^{(i)}(x_t) + \zeta_t, t/T)$ while removing the oldest evaluation obtained at time $\tau = t - k$. The reward is the negative simple regret $r_t = \max_{\tau \leq t} f^{(i)}(x_\tau) - \max_{x \in \mathcal{X}} f^{(i)}(x)$. The agent thus performs T -shot optimization of f . We train an agent for each source task $f^{(i)}$ via a DQN policy [Mnih et al., 2013], and denote the resulting policy parametrized by η as $\pi_\eta^{(i)}$ (Figure 2 right). Trajectories sampled according to policy $\pi_\eta^{(i)}$ and state transition defined above are then used to train PFNs.

The DQN agent approximates the optimal Q-function with $Q_\eta(s, a)$ and updates η iteratively during training on dataset $D^{(i)}$ until surpassing random search (details in Appendix A.2). Its parametric nature allows efficient batched trajectory generation on GPUs, which is crucial for PFN training.

4.3 Model-Agnostic Meta-Learning for Trajectory Surrogate

Next, we show how PROFBO trains the PFN framework using MAML for trajectory surrogate, with details shown in Algorithm 1. Let $\text{GD}_\theta[f] := \theta - \beta \cdot \partial_\theta f$ denote the gradient descent operator where β is a learning rate. In the pre-training stage (Line 1–4), we train the PFN conventionally using synthetic samples from common function priors $p(\mathcal{D})$, such as GPs. As shown in Müller et al. [2023], PFNs trained with non-trajectory functional priors are well-suitable BO surrogates, as they generate sensible mean predictions with uncertainty quantification. Therefore, $p(\mathcal{D})$ provides a warm start for the following stage. Moreover, since trajectories may not cover the entire response surface of the objective, training with $p(\mathcal{D})$ stabilizes regions unexplored by $p(\mathcal{T}^{(i)})$ s. Each iteration involves gradient descent (Line 3) on the loss from a batch of samples (Line 2), enabling the PFN to infer across more diverse contexts.

Algorithm 1 PFN training of PROFBO

Inputs: Prior over general distribution $p(\mathcal{D})$; prior over source tasks $\{p(\mathcal{T}^{(i)})\}_{i=1}^N$, numbers of iterations K_1, K_2 , initialized PFNs parameter θ .

```

1: for  $j \in [K_1]$  do
2:   Sample  $D \cup \{(x_i, y_i)\}_{i=1}^m \sim p(\mathcal{D})$ 
3:   Update  $\theta = \text{GD}_\theta[\ell_\theta(D \cup \{(x_i, y_i)\}_{i=1}^m)]$  ▷ standard gradient descent
4: end for
5: for  $j \in [K_2]$  do
6:   sample a batch of priors  $\Pi \subset \{p(\mathcal{T}^{(i)})\}_{i=1}^N$  ▷ sample from MDP prior
7:   for  $p \in \Pi$  do
8:     sample  $D \cup \{(x_i, y_i)\}_{i=1}^m \sim p$ 
9:     Compute  $\theta_\pi = \text{GD}_\theta[\ell_\theta(D \cup \{(x_i, y_i)\}_{i=1}^m)]$  ▷ with positional encodings
10:  end for
11:  Update  $\theta = \text{GD}_\theta \left[ \sum_{\pi \in \Pi} \hat{\ell}_{\theta_\pi}(D \cup \{(x_i, y_i)\}_{i=1}^m) \right]$  ▷ MAML update
12: end for
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Output: q_θ

In the fine-tuning stage (Line 5–12), we fine-tune the PFN using samples from all $p(\mathcal{T}^{(i)})$, $\forall i \in [N]$, incorporating both MAML [Finn et al., 2017] and positional encoding. We introduce the positional

encoding to better capture sequential information in the MDP prior, unlike the original PFN [Müller et al., 2022] that omitted it for permutation-invariant priors. However, this also increases the risk of overfitting to spurious correlations. To address this, we combine positional encoding with MAML, which helps the model generalize well by focusing on common optimization patterns rather than overfitting task-specific details. Unlike its original purpose of warm-starting parameters, MAML in our method is creatively repurposed to extract features shared across trajectories. Fine-tuning with MAML involves three steps: sampling tasks (Line 8), computing task-specific updates (Line 9), and optimizing the total adapted loss (Line 11). In Section 5.4, we show through an ablation study that both MAML and positional encoding are crucial for building a robust trajectory surrogate.

The training cost in the first stage is incurred only once, since the base PFN can be stored and later fine-tuned for future problems. Thus, the cost for future problems is reduced to the fine-tuning stage.

5 Experiments

5.1 Experimental Setup

Baselines. We compare PROFBO with several few-shot BO methods using different techniques: BO with meta-learned GP (META-GP), few-shot deep kernel surrogate learning (FSBO) [Wistuba and Grabocka, 2021], pure transformer neural processes (TNP) [Nguyen and Grover, 2022, Müller et al., 2022], end-to-end meta-BO with transformer neural processes (NAP) [Maraval et al., 2023], random search (RANDOM), and BO with standard GP (GP). Table 1 shows a technical summary of them except RANDOM and GP since they do not use any listed techniques.

In TNP, we meta-train a TNP ² on original meta-data instead of MDP priors; for comparison, we also test a variant with MAML and positional encoding, denoted as TNP+. Similarly, we pre-train META-GP kernel parameters with meta-data before testing, and introduce a meta-trained version of our MDP prior, denoted as Meta-Acquisition Function (MAF), to align with RL-based methods. We also include OPTFORMER [Chen et al., 2022] when possible ³. As summarized in Table 1, these baselines fall into two main categories: *meta-surrogate learning* (META-GP, FSBO, TNP), which learn BO surrogates without sequential information, and *meta-trajectory learning* (MAF, OPTFORMER), which directly model trajectories. PROFBO and NAP use both approaches.

Techniques	META-GP	FSBO	TNP	MAF	NAP	OPTFORMER	PROFBO (Ours)
Meta-learn traj.	✗	✗	✗	✓	✓	✓	✓
Meta-learn surrog.	✓	✓	✓	✗	✓	✓	✓
MAML	✗	✗	✗	✗	✗	✗	✓
Positional encoding	✗	✗	✗	✗	✗	✓	✓

Table 1: Technical summary of all compared algorithms except RANDOM and GP. “✓” and “✗” denote a certain technique is used in an algorithm or not.

Evaluations. The objective function range of each task is normalized to $[0, 1]$, so the regret at iteration t is defined as $1 - \max_{0 \leq \tau \leq t} f(x_\tau)$ and we use the log-scaled version in our results. The

²Using the same architecture as our PFN, as in Maraval et al. [2023].

³OPTFORMER requires datasets with extensive optimization trajectories, which are unavailable in our drug discovery benchmarks.

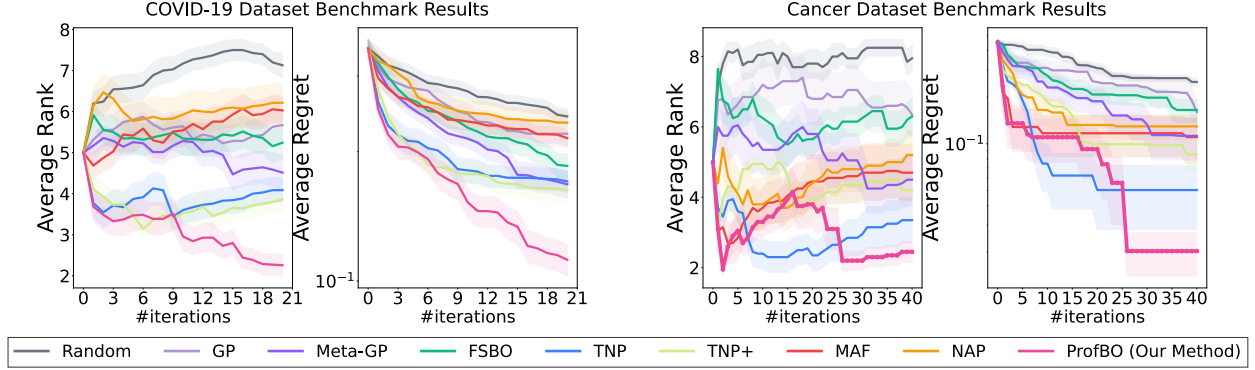


Figure 3: Strong performance of PROFBO on *Covid-B* (five problems) and *Cancer-B* (two problems) compared with other baseline methods.

rank is defined as the integer rank value of the method at a given iteration among all baselines in terms of regret performance. Both regret and rank are **the lower, the better**. As in existing literature [Müller et al., 2023, Wistuba and Grabecka, 2021], for each benchmark, we report the aggregated regret and aggregated rank, computed as the average regret and rank over five different initializations, with error bars denoting 95% confidence.

All the benchmarks contain a meta-training, meta-validation and meta-test dataset. We train the models with meta-training data. All the hyperparameters of our method (learning rate, acquisition function, MAML inner step size, fine-tuning epochs, etc.) are optimized on the validation set and the results are demonstrated on the test set. PROFBO uses the same pre-trained PFN for all benchmarks. We use an Adam optimizer for PFN training [Kingma and Ba, 2015]. Please refer to Appendix B for more detailed experimental settings and comparison.

5.2 Results on Real-World Drug Discovery

The docking score estimates how strongly a small molecule (ligand) binds to a target receptor (typically a protein) where lower scores indicate stronger predicted binding affinity. In drug discovery, a favorable docking score suggests effective interaction with the disease-related receptor, potentially blocking or modulating its function. In this paper, we establish two benchmarks, each consisting of multiple molecule search tasks that aim to minimize the docking score against Covid-19 or cancer receptors, denoted as *Covid-B* and *Cancer-B*. We use a 26D continuous embedding for both datasets, converted from their *mgn* feature [Nguyen et al., 2009]. *Covid-B* and *Cancer-B* contain 5 and 2 problems respectively. Check Appendix C for detailed dataset description.

In Figure 3, our method consistently and significantly outperforms baselines and meets the few-shot requirement by achieving strong performance within 20 or 40 iterations. In terms of average regret on both datasets, the gaps between PROFBO and other methods are even larger as T increases. While Maraval et al. [2023] reported state-of-the-art NAP’s superiority in a similar antibody design benchmark, in our experiments NAP performs comparably to the lighter MAF, likely due to the challenging high dimensionality of our benchmarks and the Transformer policy’s instability in few-shot settings. Notably, NAP required over 200 iterations to dominate in the 11D antibody design task, whereas we evaluate on 26D problems for few iterations.

5.3 Results on Hyperparameter Optimization

HPO-B [Pineda-Arango et al., 2021] is a benchmark of classification models’ hyperparameters and accuracies, widely used in few-shot BO. Following Maraval et al. [2023], we select 6 of the 16 problems, where each corresponds to the loss of a classification algorithm on different tasks, with input dimensions ranging from 2 to 18. We report results over 90 iterations to align with existing literature, though our focus is still on few-evaluation BO. Results on additional 13 problems with 25 iterations are provided in Appendix D, showing the consistent strong performances of PROFBO.

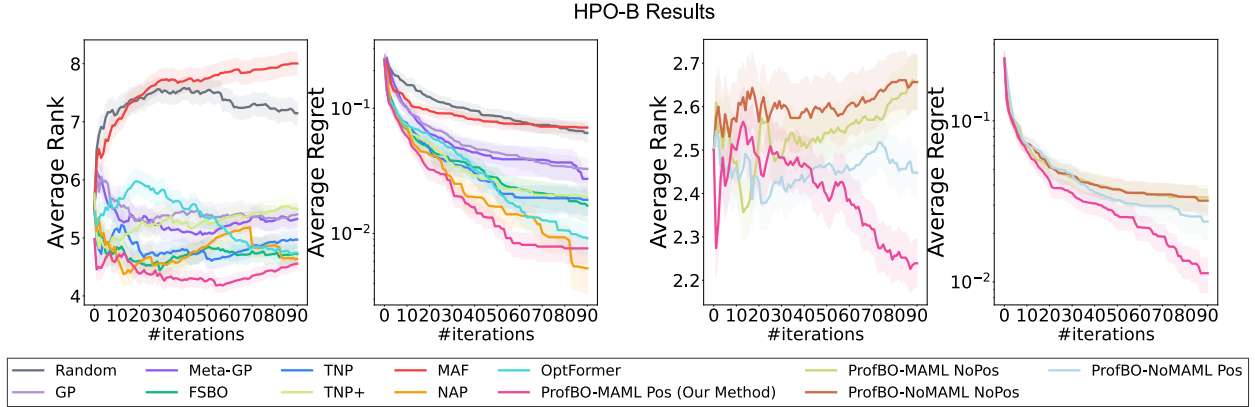


Figure 4: [Left two] Strong performances of PROFBO on *HPO-B* compared with other baseline methods. [Right two] Ablation study results of PROFBO with MAML and positional encoding enabled (“MAML”, “Pos”) or not (“NoMAML”, “NoPos”), showing both MAML and positional encoding are important technical components of PROFBO.

The *HPO-B* results are shown in the left two subfigures of Figure 4. PROFBO achieves strong performances, clearly leading in average rank and regret. Meta-surrogate learning methods (META-GP, FSBO, TNP, TNP+) overlook the procedural knowledge in optimization trajectories, while our surrogate leverages an MDP prior to capture this knowledge, yielding improved results. Among meta-trajectory learning methods, MAF performs even worse than RANDOM, OPTFORMER is competitive, and NAP, also directly modeling trajectories, outperforms both. We attribute this improvement to NAP’s supervised auxiliary loss, which helps the agent better learn inductive biases across tasks. PROFBO balances trajectory modeling and meta-learning by separating the two in a simple yet effective way. MAML enables efficient meta-learning of the trajectory surrogate, while PFN’s in-context learning accelerates adaptation to target tasks, yielding stronger performance than NAP and OPTFORMER, especially in the first 10 iterations.

5.4 Ablation Studies

To thoroughly understand the algorithmic design of PROFBO, we analyze the effectiveness of three key components in the fine-tuning of PROFBO: the MDP prior, MAML, and positional encoding added to PFN. The test setting is the same as Section 5.3. To ensure fair comparison, for each problem, all surrogates are trained with the same dataset pre-generated from our MDP prior.

To test the effectiveness of MDP prior, we compare PROFBO against TNP+. As discussed in Section 5.1, TNP+ is a meta-trained PFN using original meta-data instead of MDP priors, incorporating MAML and positional encoding, so TNP+ serves as the control group. Results shown in Figure 3, 4 provide compelling evidence for MDP priors’ great contributions across three bench-

marks. Without MDP priors, MAML and positional encoding provide little benefit to Transformer neural processes, as seen with TNP and TNP+⁴. This explains why MAML is effective with MDP priors: they encode richer sequential correlations but are more prone to overfitting, where MAML helps the surrogate extract common optimization patterns. This provides evidence for our claim in Section 4.3.

Next, to study the roles played by MAML and positional encoding, in the right two subfigures of Figure 4, we test four settings where MAML or positional encoding is enabled or not. The figures show that the performances of PROFBO indeed benefit from MAML, as the trials with MAML enabled are better than those without it under the same conditions. Also, vanilla PFN removes the positional encoding to make it permutation-invariant on the context, however, in our task we introduce the positional encoding back to PFN as it can help the surrogate better learn the optimization trajectories, which are also validated in Figure 4.

5.5 Computational Efficiency

NAP [Maraval et al., 2023] is one of the state-of-the-art methods in few-shot BO, and it implements a similar Transformer model to ours. NAP’s efficiency was investigated in the original paper, taking only 2% of OPTFORMER’s training time. However, PROFBO is even more efficient than NAP.

Both PROFBO and NAP use only the Transformer’s forward pass during test, resulting in similar test time, so we only compare the training time of them on the same device implementing a same Transformer architecture. NAP trains the model end-to-end, whereas PROFBO employs a two-stage training paradigm. We evaluate training time across five *Covid-B* problems, each with approximately 1M evaluations. NAP takes 3,925 seconds to finish the process, while PROFBO takes only 1,176 seconds, including 1,045 (MDP prior training) and 131 (fine-tuning) seconds, therefore, PROFBO is *3.34 times faster* than NAP. We attribute PROFBO’s efficiency to its lightweight RL agent (a MLP with hidden size 200-200-200-200), which trains faster than NAP’s Transformer policy. Additionally, supervised learning in PROFBO is less computationally intensive than RL in NAP.

6 Conclusion

In many real-world black-box optimization scenarios, such as drug screening in wet labs, traditional BO methods often fail to converge within a practical number of iterations due to costly evaluations. To solve this problem, we introduce PROFBO, a Bayesian framework that incorporates MDP priors to transfer procedural knowledge from source tasks. Integrated with PFNs and MAML, PROFBO can quickly adapt to the target task in few shots. Experiments on drug discovery and hyperparameter tuning tasks demonstrate consistent improved performances of PROFBO over existing methods. Moreover, its modular design and efficient training process make PROFBO practically ready for a wide range of critical applications. Overall, this work explores the potential of applying principled Bayesian inference to the optimization trajectory prior of real-world experiments, paving the way for more efficient and generalizable optimization strategies that further accelerate scientific discovery.

⁴Consistent with Wistuba and Grabcicka [2021], which showed that FSBO without MAML often outperforms its MAML-enhanced variant.

References

- Jasper Snoek, Hugo Larochelle, and Ryan P Adams. Practical bayesian optimization of machine learning algorithms. In *Advances in Neural Information Processing Systems*, volume 25, 2012.
- Jian Wu, Saul Toscano-Palmerin, Peter I Frazier, and Andrew Gordon Wilson. Practical multi-fidelity bayesian optimization for hyperparameter tuning. In *Uncertainty in Artificial Intelligence*, pages 788–798. PMLR, 2020.
- Kirthevasan Kandasamy, Willie Neiswanger, Jeff Schneider, Barnabas Poczos, and Eric P Xing. Neural architecture search with bayesian optimisation and optimal transport. *Advances in neural information processing systems*, 31, 2018.
- Hongpeng Zhou, Minghao Yang, Jun Wang, and Wei Pan. Bayesnas: A bayesian approach for neural architecture search. In *International conference on machine learning*, pages 7603–7613. PMLR, 2019.
- E. O. Pyzer-Knapp. Bayesian optimization for accelerated drug discovery. *IBM Journal of Research and Development*, 62(6):2:1–2:7, 2018.
- Benjamin J Shields, Jason Stevens, Jun Li, Marvin Parasram, Farhan Damani, Jesus I Martinez Alvarado, Jacob M Janey, Ryan P Adams, and Abigail G Doyle. Bayesian reaction optimization as a tool for chemical synthesis. *Nature*, 590(7844):89–96, 2021.
- Danial Khatamsaz, Raymond Neuberger, Arunabha M Roy, Sina Hossein Zadeh, Richard Otis, and Raymundo Arróyave. A physics informed bayesian optimization approach for material design: application to niti shape memory alloys. *npj Computational Materials*, 9(1):221, 2023.
- Yuan Tian, Tongtong Li, Jianbo Pang, Yumei Zhou, Dezhen Xue, Xiangdong Ding, and Turab Lookman. Materials design with target-oriented bayesian optimization. *npj Computational Materials*, 11(1):209, 2025.
- Niranjan Srinivas, Andreas Krause, Sham M. Kakade, and Matthias W. Seeger. Information-theoretic regret bounds for gaussian process optimization in the bandit setting. *IEEE Transactions on Information Theory*, 58(5):3250–3265, 2012.
- Sayak Ray Chowdhury and Aditya Gopalan. On kernelized multi-armed bandits. In *International Conference on Machine Learning*, pages 844–853, 2017.
- Qiaohao Liang and Lipeng Lai. Scalable bayesian optimization accelerates process optimization of penicillin production. In *NeurIPS 2021 AI for Science Workshop*, 2021.
- H. Aldewachi, R. N. Al-Zidan, M. T. Conner, and M. M. Salman. High-throughput screening platforms in the discovery of novel drugs for neurodegenerative diseases. *Bioengineering*, 8(2):30, 2021.
- Martin Wistuba and Josif Grabocka. Few-shot bayesian optimization with deep kernel surrogates. In *International Conference on Learning Representations*, 2021.
- Xuefeng Liu, Songhao Jiang, Archit Vasan, Alexander Brace, Ozan Gokdemir, Thomas Brettin, Fangfang Xia, Ian Foster, and Rick Stevens. Drugimprover: Utilizing reinforcement learning for multi-objective alignment in drug optimization. In *NeurIPS 2023 Workshop on New Frontiers of AI for Drug Discovery and Development*, 2023.
- Sebastian Pineda-Arango, Hadi Jomaa, Martin Wistuba, and Josif Grabocka. HPO-B: A large-scale reproducible benchmark for black-box HPO based on OpenML. In *Conference on Neural*

- Information Processing Systems Track on Datasets and Benchmarks*, 2021.
- Stefan Falkner, Aaron Klein, and Frank Hutter. Practical transfer learning for bayesian optimization. *arXiv preprint arXiv:1802.02219*, 2018.
- Zi Wang, George E. Dahl, Kevin Swersky, Chansoo Lee, Zachary Nado, Justin Gilmer, Jasper Snoek, and Zoubin Ghahramani. Pre-trained gaussian processes for bayesian optimization. *Journal of Machine Learning Research*, 25:1–43, 2024.
- Richard Bellman. Dynamic programming and stochastic control processes. *Information and Control*, 1(3):228–239, 1958.
- Samuel Müller, Noah Hollmann, Sebastian Pineda Arango, Josif Grabocka, and Frank Hutter. Transformers can do bayesian inference. In *International Conference on Learning Representations*, 2022.
- Chelsea Finn, Pieter Abbeel, and Sergey Levine. Model-agnostic meta-learning for fast adaptation of deep networks. In *International conference on machine learning*, pages 1126–1135. PMLR, 2017.
- Nicolas Schilling. Scalable hyperparameter optimization with products of gaussian process experts. In *International Conference on Algorithmic Learning Theory*, pages 312–326, 2016.
- Martin Wistuba, Nicolas Schilling, and Lars Schmidt-Thieme. Two-stage transfer surrogate model for automatic hyperparameter optimization. In *Machine Learning and Knowledge Discovery in Databases*, pages 199–214, 2016.
- Kevin Swersky, Jasper Snoek, and Ryan P Adams. Multi-task bayesian optimization. In *Advances in Neural Information Processing Systems*, volume 26. Curran Associates, Inc., 2013.
- Matthias Poloczek, Jialei Wang, and Peter I Frazier. Warm starting bayesian optimization. In *Winter simulation conference*, pages 770–781. IEEE, 2016.
- Dani Yogatama and Gideon Mann. Efficient Transfer Learning Method for Automatic Hyperparameter Tuning. In *International Conference on Artificial Intelligence and Statistics*, pages 1077–1085, 2014.
- Ho Chung Law, Peilin Zhao, Leung Sing Chan, Junzhou Huang, and Dino Sejdinovic. Hyperparameter learning via distributional transfer. In *Advances in Neural Information Processing Systems*, volume 32, 2019.
- Petru Tighineanu, Kathrin Skubch, Paul Baireuther, Attila Reiss, Felix Berkenkamp, and Julia Vinogradska. Transfer learning with gaussian processes for bayesian optimization. In *International Conference on Artificial Intelligence and Statistics*, pages 6152–6181, 2022.
- Valerio Perrone, Rodolphe Jenatton, Matthias Seeger, and Cédric Archambeau. Scalable hyperparameter transfer learning. *Advances in Neural Information Processing Systems*, 31, 2018.
- Martin Wistuba, Nicolas Schilling, and Lars Schmidt-Thieme. Scalable gaussian process-based transfer surrogates for hyperparameter optimization. *Machine Learning*, 107:43–78, 2017.
- Tianyi Bai, Yang Li, Yu Shen, Xinyi Zhang, Wentao Zhang, and Bin Cui. Transfer learning for bayesian optimization: A survey, 2023.
- Martin Wistuba, Nicolas Schilling, and Lars Schmidt-Thieme. Hyperparameter search space pruning – a new component for sequential model-based hyperparameter optimization. In *Joint European Conference on Machine Learning and Knowledge Discovery in Databases*, 2015a.

- Valerio Perrone, Huibin Shen, Matthias Seeger, and Cédric Archambeau. Learning search spaces for bayesian optimization: Another view of hyperparameter transfer learning. In *Advances in Neural Information Processing Systems*, 2019.
- Yang Li, Yu Shen, Huaijun Jiang, Tianyi Bai, Wentao Zhang, Ce Zhang, and Bin Cui. Transfer learning based search space design for hyperparameter tuning. In *ACM SIGKDD Conference on Knowledge Discovery and Data Mining*, 2022.
- Matthias Feurer, Jost Springenberg, and Frank Hutter. Initializing bayesian hyperparameter optimization via meta-learning. In *AAAI Conference on Artificial Intelligence*, 2015.
- Martin Wistuba, Nicolas Schilling, and Lars Schmidt-Thieme. Learning hyperparameter optimization initializations. In *IEEE International Conference on Data Science and Advanced Analytics*, pages 1–10, 2015b.
- Michael Volpp, Lukas P. Fröhlich, Kirsten Fischer, Andreas Doerr, Stefan Falkner, Frank Hutter, and Christian Daniel. Meta-learning acquisition functions for transfer learning in bayesian optimization. In *International Conference on Learning Representations*, 2020.
- Bing-Jing Hsieh, Ping-Chun Hsieh, and Xi Liu. Reinforced few-shot acquisition function learning for bayesian optimization. *Advances in Neural Information Processing Systems*, 34:7718–7731, 2021.
- Tomoharu Iwata. End-to-end learning of deep kernel acquisition functions for bayesian optimization. *arXiv preprint arXiv:2111.00639*, 2021.
- Alexandre Max Maraval, Matthieu Zimmer, Antoine Grosnit, and Haitham Bou Ammar. End-to-end meta-bayesian optimisation with transformer neural processes. *Advances in Neural Information Processing Systems*, 34, 2023.
- Ashish Vaswani, Noam Shazeer, Niki Parmar, Jakob Uszkoreit, Llion Jones, Aidan N Gomez, Lukasz Kaiser, and Illia Polosukhin. Attention is all you need. *Advances in neural information processing systems*, 30, 2017.
- Tung Nguyen and Aditya Grover. Transformer neural processes: Uncertainty-aware meta learning via sequence modeling. In *International Conference on Machine Learning*, pages 16723–16738. PMLR, 2022.
- Samuel Müller, Matthias Feurer, Noah Hollmann, and Frank Hutter. Pfns4bo: In-context learning for bayesian optimization. In *International Conference on Machine Learning*, pages 25444–25470. PMLR, 2023.
- Mayk Caldas Ramos, Shane S Michtavy, Marc D Porosoff, and Andrew D White. Bayesian optimization of catalysts with in-context learning. *arXiv preprint arXiv:2304.05341*, 2023.
- Tennison Liu, Nicolás Astorga, Nabeel Seedat, and Mihaela van der Schaar. Large language models to enhance bayesian optimization. In *International Conference on Learning Representations*, 2024.
- Yutian Chen, Xiaoxi Song, Chung-Ching Lee, Zihang Wang, Ruoxi Zhang, David Dohan, Kenji Kawakami, Greg Kochanski, Arnaud Doucet, Marc’Aurelio Ranzato, et al. Towards learning universal hyperparameter optimizers with transformers. In *Advances in Neural Information Processing Systems*, volume 35, pages 32053–32068, 2022.
- Tung Nguyen, Qiuyi Zhang, Bangding Yang, Chansoo Lee, Jorg Bornschein, Yingjie Miao, Sagi Perel, Yutian Chen, and Xingyou Song. Predicting from strings: Language model embeddings

- for bayesian optimization. *arXiv preprint arXiv:2410.10190*, 2024.
- Donald R. Jones, Matthias Schonlau, and William J. Welch. Efficient global optimization of expensive black-box functions. *Journal of Global Optimization*, 13(4):455–492, 1998.
- William R Thompson. On the likelihood that one unknown probability exceeds another in view of the evidence of two samples. *Biometrika*, 25(3/4):285–294, 1933.
- Peter I Frazier, Warren B Powell, and Savas Dayanik. A knowledge-gradient policy for sequential information collection. *SIAM Journal on Control and Optimization*, 47(5):2410–2439, 2008.
- Richard S. Sutton and Andrew G. Barto. *Reinforcement Learning: An Introduction*. The MIT Press, 2018.
- Volodymyr Mnih, Koray Kavukcuoglu, David Silver, Alex Graves, Ioannis Antonoglou, Daan Wierstra, and Martin Riedmiller. Playing atari with deep reinforcement learning. *arXiv preprint arXiv:1312.5602*, 2013.
- Diederik P. Kingma and Jimmy Ba. Adam: A method for stochastic optimization. In *International Conference on Learning Representations*, 2015.
- Kong T. Nguyen, Lorenz C. Blum, Ruud van Deursen, and Jean-Louis Reymond. Classification of organic molecules by molecular quantum numbers. *ChemMedChem: Chemistry Enabling Drug Discovery*, 4(11):1803–1805, 2009.
- Maximilian Balandat, Brian Karrer, Daniel Jiang, Samuel Daulton, Ben Letham, Andrew G Wilson, and Eytan Bakshy. Botorch: A framework for efficient monte-carlo bayesian optimization. In *Advances in Neural Information Processing Systems*, volume 33, pages 21524–21538, 2020.
- Teague Sterling and John J. Irwin. Zinc 15 – ligand discovery for everyone. *Journal of Chemical Information and Modeling*, 55(11):2324–2337, 2015.

A Implementation Details of ProfBO

A.1 Settings of the PFN Training

The Transformer architecture [Vaswani et al., 2017] processes sequential data by embedding each element into a vector representation and employs a specialized attention mechanism to enable elements to attend to one another during the forward pass. PFNs utilize a tailored attention mask to allow context points in D to attend to each other and be attended by test locations during the forward pass.

The implementation of the PFN is adapted from the repository of PFNs4BO [Müller et al., 2023]⁵. Here we list the settings for the PFN used in our experiment (Table 2). Similar to Müller et al. [2023, 2022], our model takes contextual variables with dimension ≤ 26 by conducting a zero-padding to the missing dimensions and normalization to the existing dimension. We use a discrete bar distribution for the regression head of PFN, with 1,000 bars uniformly chosen from the interval $[-4.5, 4.5]$.

Hyperparameters	Choices
Embedding size	512
Number of self-attention layers	6
Number of heads	4
Activation function	GeLU
Feed forward NN size	1024
Number of discretized bars	1000
Pre-training learning rate	{1e-3, 1e-4, 3e-4, 1e-5}
Fine-tuning learning rate	3e-4
Batch size	128
Sequence length	40
Steps per epoch	100
Fine-tuning epoch	2
Maximum input size	26
Pre-training prior	GP
Acquisition function	{EI, PI, UCB}
Optimizer	Adam + Cosine Anneal

Table 2: PFN settings & Hyperparameters of PROFBO

A.2 Settings of the RL Training

We train our RL agent with the vanilla DQN algorithm, where there is a policy and target Q-network with identical architecture. The target network is a copy of the policy network initially, but it is updated at a specific frequency during the training process. The policy network is used to sample the trajectories, while the target network is treated as the “ground-truth”, and is used to calculate the Bellman equation as mentioned in Section 4.

In the main paper, where all baselines are discrete search problems, we developed an adapted training paradigm for the MDP prior to enable efficient learning from extensive molecule meta-data, demonstrating strong empirical performance in generating prior trajectories. Specifically,

⁵<https://github.com/automl/PFNs4BO>

we restricted the agent to interact with only 10% of the problem, updating to a new 10% subset and updating the target network every 50 epochs. Initially, training multiple RL agents with a dynamic action space per epoch was challenging. In this case, increasing the action space size slowed training without significant gains. Our approach ensures robust increases in cumulative reward while substantially reducing computational costs. Other training hyperparameters of the MDP prior are shown in Table 3. We note that the feed-forward NN of the agent has the same hidden size as the popular meta-learning neural acquisition methods [Hsieh et al., 2021, Volpp et al., 2020].

The sampling scheme of the final policy $\pi_\eta^{(i)}$ (i.e., $Q_\eta^{(i)}$) for task i is ϵ -greedy to balance exploration and exploitation:

$$a_t = \begin{cases} \text{Uniform}(\{x_\tau^{(i)}\}_{\tau=1}^{n_i}), \text{Pr} = \epsilon, \\ \arg \max_{a' \in \{x_\tau^{(i)}\}_{\tau=1}^{n_i}}, Q_\eta^{(i)}(s_t, a'), \text{Pr} = 1 - \epsilon. \end{cases}$$

Hyperparameters	Choices
Hidden size	[200, 200, 200, 200]
Activation function	ReLU
Episode length (T)	40
Epoch	250
Target update frequency	50
Discount factor (γ)	0.98
Maximum action sample size	$n_i/10$
History size (k)	10
Replay buffer size	10000
Learning rate	1e-3
Optimizer	Adam

Table 3: RL setting of PROFBO

B Experimental settings of other baselines

FSBO ⁶. FSBO meta-trains a deep kernel GP surrogate with the meta-dataset and performs few epochs of adaptation in each BO iteration. We adopted a deep kernel GP used in Wistuba and Grabocka [2021]. We trained the model with batch size 512 for 2000 iterations, so the total number of training data point is 1,024,000, the same as PROFBO. The learning rate is 1e-3.

NAP ⁷. We use a Transformer with the same architecture as PROFBO (Table 2). The training completely follows the settings mentioned in the original paper, where we perform RL on a conditional GP surrogate trained with meta-data and test on discrete problem. We use a different episode length, epochs, batch size for each benchmark, so that the episode length T matches the experimental results in Section 5 and the total training data is around 1M, please refer to our repository for details.

⁶<https://github.com/machinelearningnuremberg/FSBO>

⁷<https://github.com/huawei-noah/HEBO/tree/master/NAP>

OptFormer⁸. The results in *HPO-B* (Section 5.3) is produced by the authors of NAP based on the official codebase. Please refer to their paper for details.

TNP. We used the same PFN architecture with a positional encoding as in Table 2. As mentioned in Section 5.4, we used 1M raw samples from meta-dataset to train the surrogate model with MAML and positional encoding.

Meta-GP. Like Maraval et al. [2023], we also pre-train the RBF kernel parameters of the GP with the meta-dataset and initialize the GP with pre-trained parameters at the test time. The implementation is based on BO package BoTorch [Balandat et al., 2020].

NAF. Please refer to Table 3 for the settings of the RL agent. We used a RL prior that learns from all the meta-datasets, instead of a single dataset. To do that, we train the RL agent to optimize $\mathcal{D}^{(i)}, i \in [N]$ for many i . Specifically, we sample i uniformly from $[N]$ in each outer loop and train the agent in the same way as described in Appendix A.2.

C Experimental Details of Benchmarks

C.1 HPO-B

Please refer to official repository⁹ and paper Pineda-Arango et al. [2021] for detailed explanation of the dataset. The six representative problems in Section 5.3 are 5860 (glmnet), 4796 (rpart.preproc), 5906 (xgboost), 5889 (ranger), 5859 (rpart), 5527 (svm). We also provide the aggregated results of 13 *HPO-B* problems in the following section of appendix (Figure 8).

C.2 Covid-B and Cancer-B

The *Covid-B* dataset comprises five problems as in Pineda-Arango et al. [2021] across 24 tasks. Each task within a problem optimizes the docking score for a shared Covid-19 receptor but targets different binding interactions. For instance, task NPRBD_6VYO_AB_1_F involves interactions with both chains A and B of the PDB structure 6VYO, while NPRBD_6VYO_A_1_F focuses solely on chain A. The validation set consists of unique datasets from Liu et al. [2023] that are distinct from their parent structure. The *Cancer-B* dataset differs from *Covid-B*, as it lacks related tasks from a common parent structure. Instead, it includes docking scores for 5 distinct cancer-target receptors, manually divided into source and target tasks. The validation set is a mixed random sample drawn from each dataset. The final dataset comprises three training sets and two test sets.

For both datasets, the problem for each task is a set of molecules, with size ranging from 2K to 150K and are stored as Simplified Molecular Input Line Entry System (SMILES). We first convert the molecules to their *mqn feature* (42D, integer) [Nguyen et al., 2009], then we use principle component analysis (PCA) to construct a 26D continuous representation for each molecule, where the percentage of explained variance in PCA are greater than 95% for all problems.

Covid-B. The *Covid-B* dataset is adapted from the Covid dataset used in DrugImprover [Liu et al., 2023]¹⁰. They were chosen by the authors from the Zinc 15 dataset [Sterling and Irwin, 2015], containing 11M drug-like molecules. The original dataset consists of 24 .csv files, each containing 1,000,000 molecular docking samples across various SARS-CoV-2 receptors. We identified five structural conditions shared by multiple receptors, each defined as a single *problem* (in *HPO-B*,

⁸<https://github.com/google-research/optformer>

⁹<https://github.com/machinelearningnuremberg/HPO-B>

¹⁰<https://github.com/xuefeng-cs/DrugImprover>

one learning algorithm corresponds to one problem). While different *datasets* in *HPO-B* share the same supervised loss but differ in training data, in *Covid-B* datasets correspond to the same structural condition under varying sub-conditions. Finally, we retain only the molecules common across their respective problems in each dataset. All the objective values are normalized to $[0, 1]$.

Problems	Meta-training		Meta-test	
	# Evaluations	# Datasets	# Evaluations	# Datasets
NPRBD	46,176	3	30,784	2
NSP10-16	202,254	1	202,254	1
NSP15	11,540	5	4,616	2
Nsp13.helicase	244,361	1	244,361	1
RDRP	106,266	3	35,422	1

Table 4: Statistics of each *Covid-B* problem in the meta-training and meta-test datasets.

We provide a list of problems of *Covid-B* and the size of each meta-train and meta-test dataset in Table 4. All the problems use a common meta-validation dataset, containing 4 datasets chosen as subsets of 3CLPro_7BQY_A_1_F, NSP16_6W61_A_1_H, PLPro_6W9C_A_2_F, NSP10_6W61_B_1_F and 1M evaluations in total.

Cancer-B. We also refer to Liu et al. [2023], Sterling and Irwin [2015] for the original five sets of molecules docked on different cancer proteins. In *Cancer-B*, we utilize three meta-training datasets (6T2W, NSUN2, RTCB), comprising 437,634 evaluations in total, and two meta-test datasets (WHSC, WRN), totaling 291,756 evaluations. The meta-validation set is constructed as a balanced mixture of random samples from these five datasets, totaling to 10,000 evaluations, with each dataset contributing an equal proportion. Molecules are also common in five .csv files.

D Additional experimental results

In this section, we present the additional experimental results.

D.1 Additional Baseline Comparison

In the following, we demonstrate the baseline comparison of regret and rank in each problem, i.e., the results in Section 5.2, 5.3 before aggregation w.r.t. problems.

Figure 5 demonstrates the results on 5 problems in *Covid-B*, where PROFBO shows superior performance in general, while NAP is the most unstable one. Figure 6 demonstrates the results on 2 problems in *Cancer-B*, where PROFBO demonstrates robust performances by being the best method after 30 iterations. Other methods suffer from instability in different problems.

Figure 7 shows the results on 6 *HPO-B* problems. We can see that the baselines’ performance stabilizes after 90 iterations, and PROFBO is consistently in the top 3 baselines except for Problem No. 5859. This shows that PROFBO is also prominent in problems that require long iterations. In Figure 8, we demonstrate the aggregated results of PROFBO on 13 problems of *HPO-B* for 25 iterations. We find PROFBO still excels in these problems, providing more solid evidence of its ability to adapt to problems with varying input dimensions and diverse meta-task dependencies.

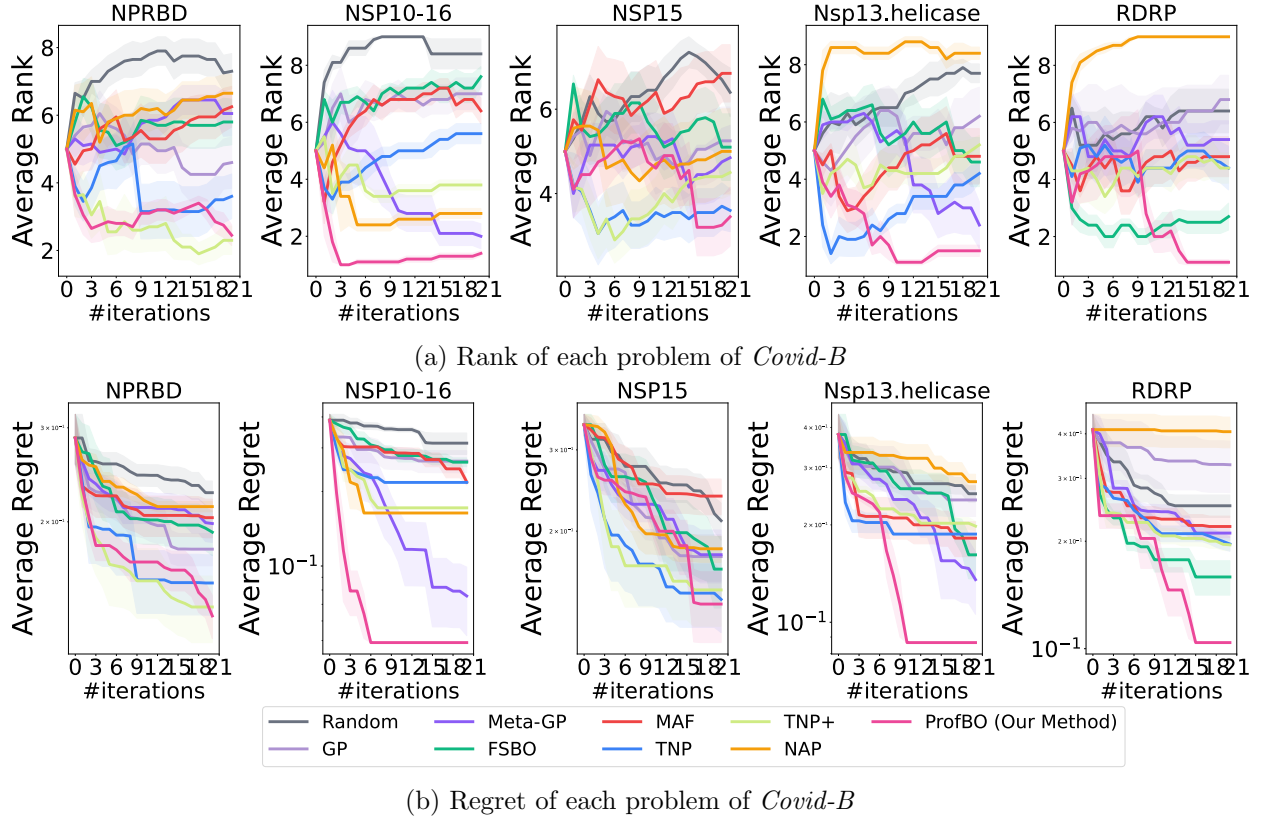


Figure 5: Performance comparisons on *Covid-B*.

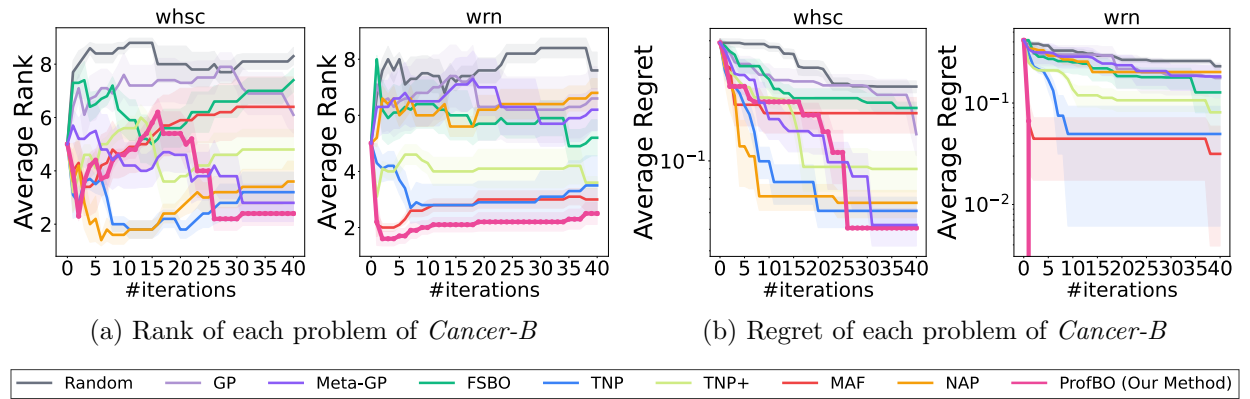
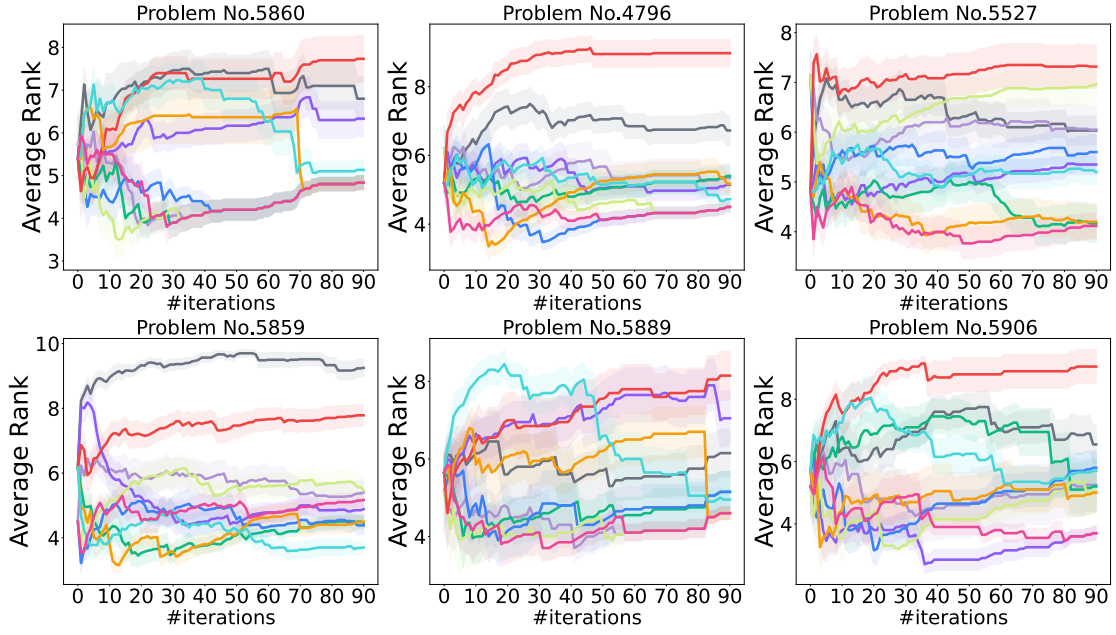
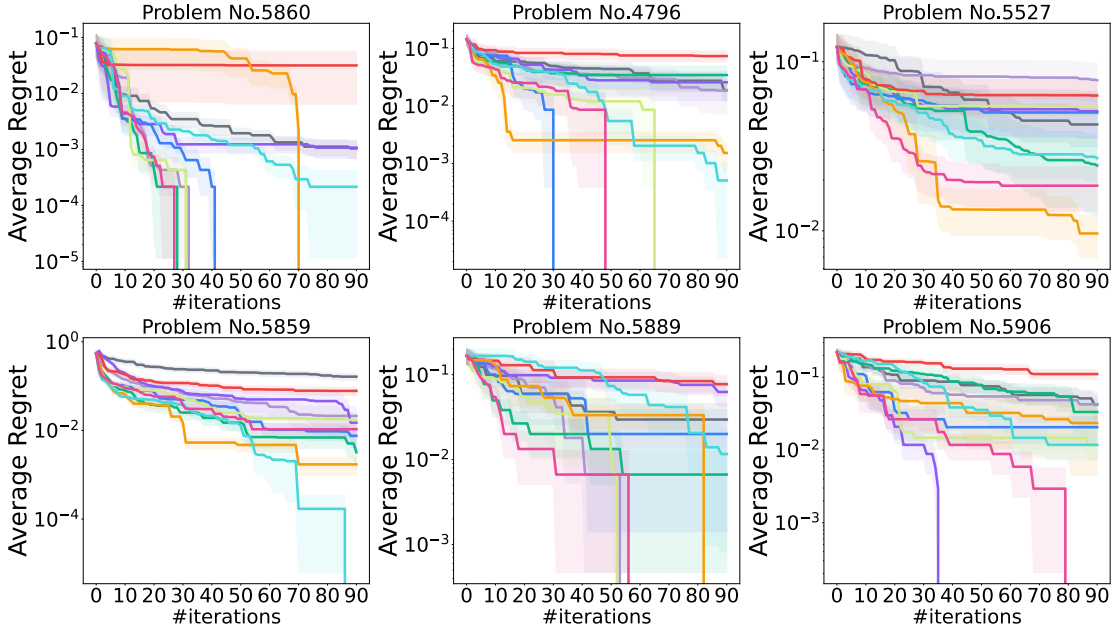


Figure 6: Performance comparisons on *Cancer-B*.



(a) Rank of each problem of $HPO-B$



(b) Regret of each problem of $HPO-B$

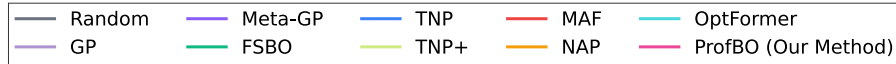


Figure 7: Performance comparisons on $HPO-B$.

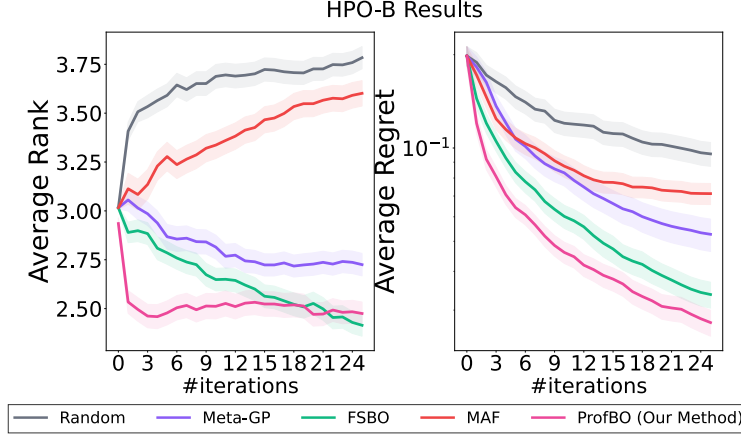


Figure 8: Aggregated results of *HPO-B* with 13 problems for 25 iterations.

D.2 Additional Function Prediction Comparison

In Figure 9, we demonstrate more visualizable comparison between PROFBO, FSBO, and GP, similar to Figure 1. In addition, we add META-GP to our comparison where the GP parameters are pretrained with meta-datasets. The settings for PROFBO, FSBO and GP are the same as mentioned in Figure 1. As we can see, PROFBO consistently models the true objective function much better than other methods, with only 3 evaluation points.

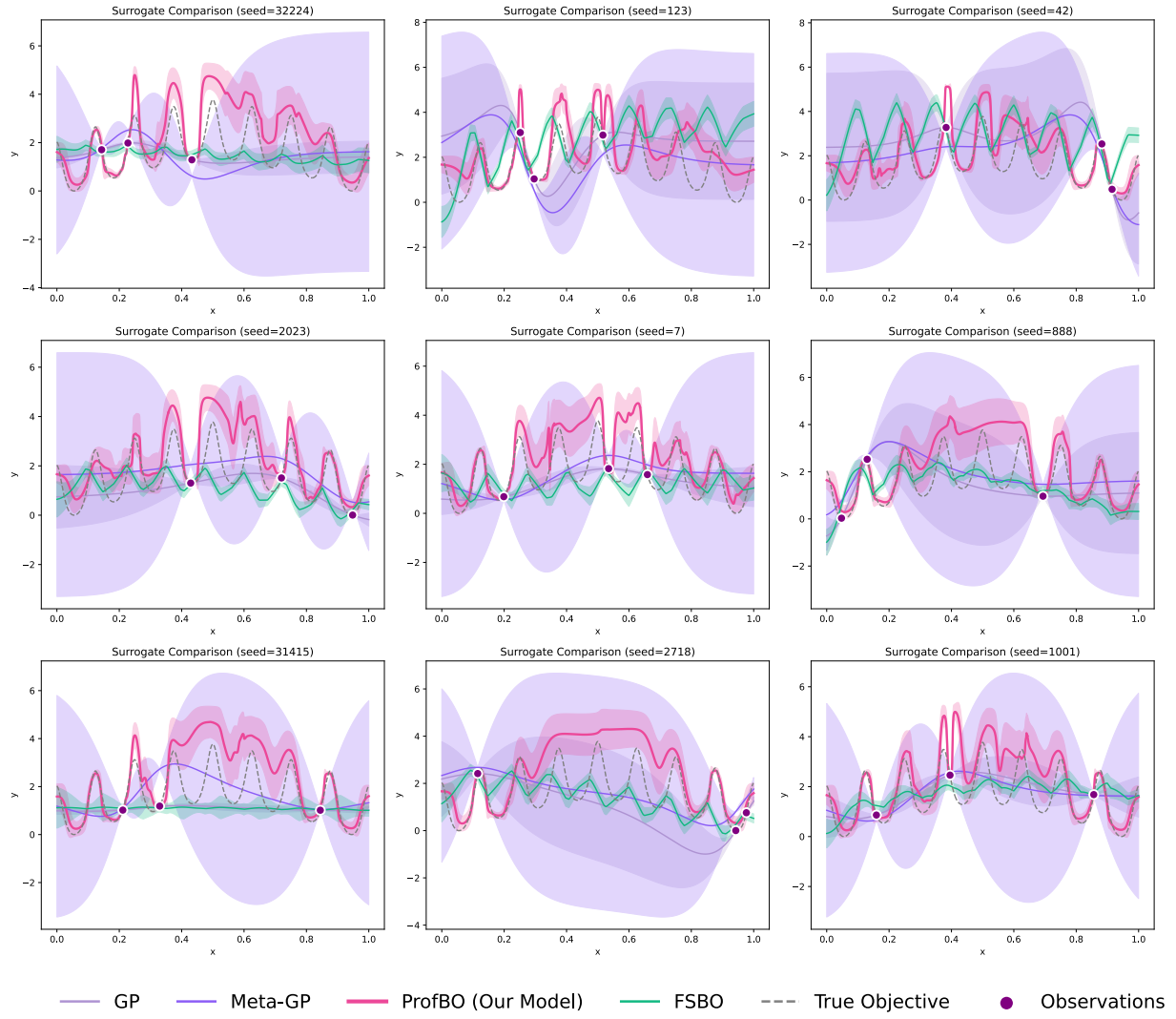


Figure 9: Function prediction comparison.