Advancing Bayesian Optimization via Learning Correlated Latent Space (Supplement)

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Summary. We provide additional experimental results/details and analysis in this supplement as: (A) analysis on regularization $\mathcal{L}_{\text{z}}$, (B) the proof of Theorem 1, (C) additional results on Guacamol Benchmarks, (D) additional results on DRD3 task, (E) efficiency analysis, and (F) implementation details.

A Analysis on Regularization $\mathcal{L}_{\mathbf{z}}$

Here, we analyze the necessity of regularization $\mathcal{L}_{\text{z}}$. Based on Theorem 1 in the main paper, to increase the correlation between the distance of latent vectors and the differences in their corresponding objective values, we need to keep the distance between the latent vectors $\mathbf{z}$ to be a *constant*. Figure 1 displays the box plot of distances between $\mathbf{z}$ at each iteration of BO. The box represents the first and third quartiles, and the whiskers represent the 10 and 90 percentiles. Each data point has a top-k score of objective value. As in Figure 1, the model only with Lipschitz regularization $\mathcal{L}_{\text{Lip}}$ (*i.e.*, without $\mathcal{L}_{\text{z}}$) increases the distance between the latent vectors $\|\mathbf{z}_i - \mathbf{z}_j\|_2$ since it is an easy way to minimize $\mathcal{L}_{\text{Lip}}$ given as

$$\mathcal{L}_{\text{Lip}} = \sum_{i,j \leq N} \max\left(0, \frac{|y_i - y_j|}{\|\mathbf{z}_i - \mathbf{z}_j\|_2} - L\right). \tag{1}$$

However, when applying both regularizations $\mathcal{L}_{\text{Lip}}$ and $\mathcal{L}_{\text{z}}$, we observe that the distance is preserved within a certain range, similar to the beginning of training.

B Proof of Theorem 1

Theorem 1. *Let $D_Z = d_Z(Z_1, Z_2)$ and $D_Y = d_Y(f(Z_1), f(Z_2))$ be random variables where Z_1, Z_2 are i.i.d. random variables, f is an L-Lipschitz continuous function, and d_Z, d_Y are distance functions. Then, the correlation between D_Z and D_Y is lower bounded as*

$$D_Y \leq LD_Z \Rightarrow \text{Corr}_{D_Z, D_Y} \geq \frac{\frac{1}{L}(\sigma^2_{D_Y} + \mu^2_{D_Y}) - L\mu^2_{D_Z}}{\sqrt{\sigma^2_{D_Z}\sigma^2_{D_Y}}},$$

where μ_{D_Z}, $\sigma^2_{D_Z}$, μ_{D_Y}, and $\sigma^2_{D_Y}$ are the mean and variance of D_Z and D_Y respectively.

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37th Conference on Neural Information Processing Systems (NeurIPS 2023).

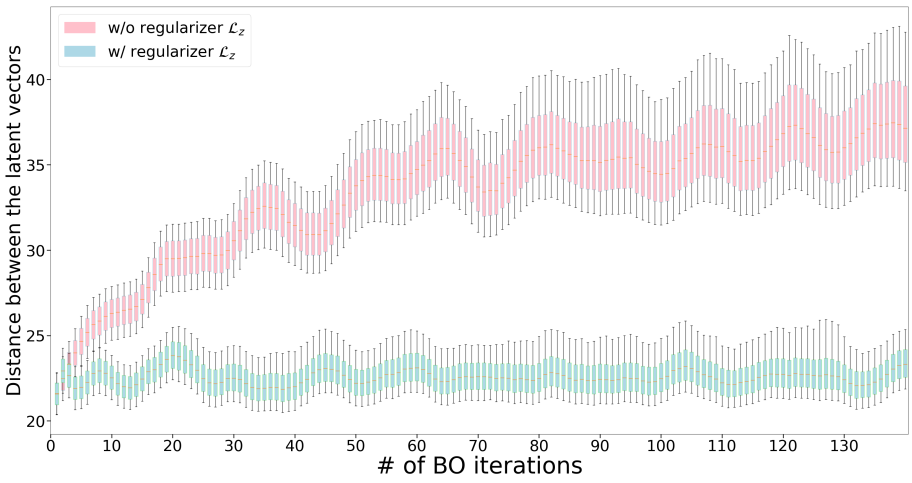


Figure 1: **Effects on Regularization $\mathcal{L}_z$.** The green and red box plots depict the distances of the latent vectors with and without regularization term $\mathcal{L}_z$, respectively.

Proof. The correlation between D_Z and D_Y is:

$$\text{Corr}_{D_Z,D_Y} = \frac{\text{Cov}\,(D_Z, D_Y)}{\sqrt{\text{Var}\,(D_Z)\,\text{Var}(D_Y)}} \tag{2}$$

$$= \frac{\mathbb{E}[(D_Z - \mathbb{E}[D_Z])(D_Y - \mathbb{E}[D_Y])]}{\sqrt{\text{Var}\,(D_Z)\,\text{Var}(D_Y)}} \tag{3}$$

$$= \frac{\mathbb{E}[D_Z D_Y] - \mathbb{E}[D_Z]\mathbb{E}[D_Y]}{\sqrt{\text{Var}\,(D_Z)\,\text{Var}(D_Y)}}. \tag{4}$$

By L-Lipschitz continuity, we have:

$$d_Y(f(Z_1), f(Z_2)) \leq L d_Z(Z_1, Z_2) \Rightarrow D_Y \leq L D_Z. \tag{5}$$

Hence, the correlation is bounded as follows:

$$\text{Corr}_{D_Z,D_Y} = \frac{\mathbb{E}[D_Z D_Y] - \mathbb{E}[D_Z]\mathbb{E}[D_Y]}{\sqrt{\text{Var}\,(D_Z)\,\text{Var}(D_Y)}} \tag{6}$$

$$\geq \frac{\mathbb{E}[\frac{1}{L} D_Y D_Y] - \mathbb{E}[D_Z]\mathbb{E}[L D_Z]}{\sqrt{\text{Var}\,(D_Z)\,\text{Var}(D_Y)}} \tag{7}$$

$$= \frac{\frac{1}{L}\mathbb{E}[(D_Y)^2] - L\mathbb{E}[D_Z]\mathbb{E}[D_Z]}{\sqrt{\text{Var}\,(D_Z)\,\text{Var}(D_Y)}} \tag{8}$$

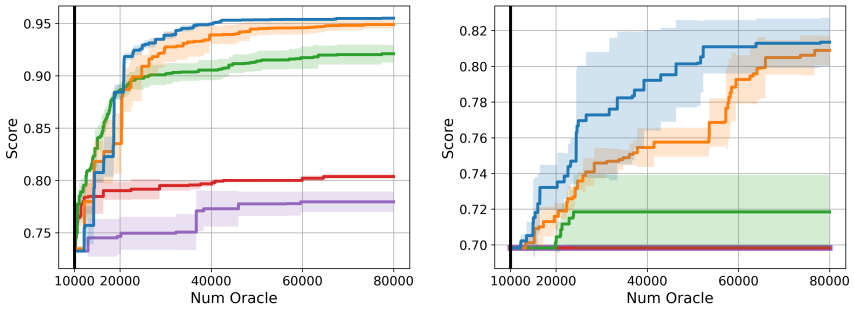
$$= \frac{\frac{1}{L}\left(\text{Var}[D_Y] + (\mathbb{E}[D_Y])^2\right) - L(\mathbb{E}[D_Z])^2}{\sqrt{\text{Var}\,(D_Z)\,\text{Var}(D_Y)}} \tag{9}$$

$$= \frac{\frac{1}{L}(\sigma^2_{D_Y} + \mu^2_{D_Y}) - L\mu^2_{D_Z}}{\sqrt{\sigma^2_{D_Z}\sigma^2_{D_Y}}}. \tag{10}$$

□

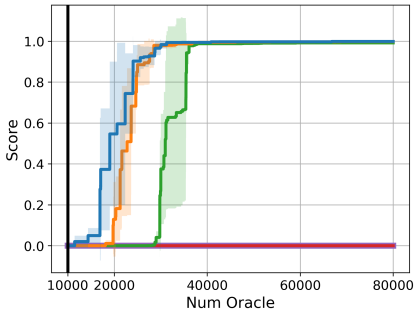
C Additional Results on Guacamol Benchmarks

In addition to the four tasks of the Guacamol benchmark that we previously mentioned, we also evaluate our model on three additional tasks: Ranolazine MPO, Aripiprazole similarity, and Valsartan SMART. The experimental settings for these additional tasks are the same with the settings applied



(a) Ranolazine MPO (rano)

(b) Aripiprazole similarity (adip)



(c) Valsartan SMART (valt)

Figure 2: **Optimization results with the additional three tasks on the Guacamol benchmark.** The lines and range are the mean and standard deviation of three repetitions with the same parameters.

to the initial four tasks. The results of the experiments are present in Figure 2. For the Valsartan SMART task, as depicted in Figure 2c, three models find the optimal point, note that our model finds the optimal point faster than other models.

D Additional Results on DRD3 Task

We compare our results with the leaderboard[3] of the DRD3 task in Table 1. Note that we use a random initialized dataset of 100. We specifically compare the Top-1 scores as absolute values, which are also reported in our line plot.

Table 1: Optimization results with best score on TDC DRD3 task. Baselines are reported on leaderboard.

Oracle calls	CoBO (Ours)	Graph-GA[1]	SMILES-LSTM[2]	GCPN[3]	MARS[4]	MolDQN[5]
100	**-11.80**	-11.13	-11.77	-9.10	-7.02	-11.63
500	**-13.57**	-12.50	-11.37	-11.97	-9.83	-7.62
1000	**-13.97**	-13.23	-11.97	-12.03	-11.10	-7.80
3000	**-15.37**	-	-	-	-	-

E Efficiency Analysis

We conduct an efficiency analysis on every tasks: the Guacamol benchmarks, the DRD3 task, and the arithmetic fitting task. In our analysis, we compare our model with four baseline models. For a

[3] `https://tdcommons.ai/benchmark/docking_group/drd3/`

fair comparison, we set up experiments for every model in the same condition, as we use the CPU of AMD EPYC 7742 with a single NVIDIA RTX 2080 TI. Note that since these are CPU-intensive tasks, the CPU is crucial to the speed of execution. We report runtimes, the found best score, and the number of oracles, where we measure runtimes of executing a certain number of oracles as the wall clock time. The number of oracle calls increases each time as unique inputs are passed to the black-box objective function. Table 2, 3, 4 demonstrates that CoBO achieves comparable runtime with the same number of oracle calls, while outperforming the baselines by finding superior solutions.

F Implementation Details

In our implementation, we use PyTorch[4], BoTorch[5] and GPyTorch[6]. Additionally, we utilize the codebase[7] of [6] for the implementation. The SELFIES VAE is pretrained with 1.27M molecules in Guacamol benchmark and DRD3 task from [7] and the Grammar VAE is pretrained 40K expression in Arithmetic data from [8]. On the DRD3 task, we modify the evaluation metric from minimization to maximization by simply changing the sign of the objective values. In our experiments, we mainly employ NVIDIA V100 and Intel Xeon Gold 6230. In this setup, the pdop tasks with a budget of 70k oracle, took an average of 11 hours.

F.1 Hyperparameters

We grid search coefficients of our proposed regularizations $\mathcal{L}_{\text{Lip\_W}}$ and $\mathcal{L}_{\text{z}}$, in the range of [10,100,1000] for $\mathcal{L}_{\text{Lip\_W}}$ and [0.1,1] for $\mathcal{L}_{\text{z}}$. For some tasks, we didn't search for these hyper-parameters, and their coefficients are provided in Table 6. The selected coefficients from this search are presented in Table 5. For other hyperparameters, such as coefficients for other losses, batch size, and learning rate, we set values according to Table 7.

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Table 2: **Efficiency comparison on Guacamol benchmarks within 70k evaluation budget.**

	Model	CoBO (Ours)	LOL-BO	W-LBO	TuRBO-L	LS-BO
med2	Oracle calls	70k	70k	70k	70k	70k
	Wall clock time (min)	1057.8	1080.4	**175.8**	246.7	1580.3
	Found Best Score	**0.3828**	0.3530	0.3118	0.3118	0.3464
	Oracle calls	55k	33k	**70k**	48k	16k
	Wall clock time (min)	175.8	175.8	175.8	175.8	175.8
	Found Best Score	**0.3828**	0.3434	0.3118	0.3118	0.3295
adip	Oracle calls	70k	70k	70k	70k	70k
	Wall clock time (min)	4986.3	3340.7	**198.2**	236.3	1320.8
	Found Best Score	**0.8133**	0.8086	0.6983	0.6983	0.7186
	Oracle calls	32k	28k	**70k**	58k	13k
	Wall clock time (min)	198.2	198.2	198.2	198.2	198.2
	Found Best Score	**0.7921**	0.7466	0.6983	0.6983	0.7186
pdop	Oracle calls	70k	70k	70k	70k	70k
	Wall clock time (min)	1020.9	1920.4	**168.4**	268.1	840.6
	Found Best Score	**0.8343**	0.7959	0.5855	0.5736	0.6514
	Oracle calls	33k	28k	**70k**	38k	18k
	Wall clock time (min)	168.4	168.4	168.4	168.4	168.4
	Found Best Score	**0.8343**	0.7948	0.5855	0.5233	0.6312
rano	Oracle calls	70k	70k	70k	70k	70k
	Wall clock time (min)	3940.5	2820.9	340.6	**276.1**	2320.6
	Found Best Score	**0.9550**	0.9468	0.8045	0.7766	0.9226
	Oracle calls	42k	41k	55k	**70k**	21k
	Wall clock time (min)	276.1	276.1	276.1	276.1	276.1
	Found Best Score	**0.9486**	0.9433	0.8045	0.7766	0.9166
valt	Oracle calls	70k	70k	70k	70k	70k
	Wall clock time (min)	560.3	760.5	304.1	**234.2**	1940.4
	Found Best Score	**0.9982**	**0.9982**	4e-14	4e-33	0.9917
	Oracle calls	51k	38k	57k	**70k**	23k
	Wall clock time (min)	234.2	234.2	234.2	234.2	234.2
	Found Best Score	**0.9982**	0.9942	4.8532e-14	4875e-36	0.6533
zale	Oracle calls	70k	70k	70k	70k	70k
	Wall clock time (min)	374.7	1320.2	366.7	**150.4**	840.5
	Found Best Score	**0.7733**	0.7521	0.6024	0.5142	0.6366
	Oracle calls	46k	24k	35k	**70k**	11k
	Wall clock time (min)	150.4	150.4	150.4	150.4	150.4
	Found Best Score	**0.7733**	0.7415	0.5633	0.5142	0.5833
osmb	Oracle calls	70k	70k	70k	70k	70k
	Wall clock time (min)	477.6	840.1	372.2	**210.2**	743.4
	Found Best Score	**0.9267**	0.9233	0.8336	0.8481	0.8933
	Oracle calls	59k	43k	46k	**70k**	19k
	Wall clock time (min)	210.2	210.2	210.2	210.2	210.2
	Found Best Score	**0.9233**	0.9167	0.8332	0.8481	0.8866

Table 3: **Efficiency comparison on DRD3 benchmark within 3k evaluation budget.**

Model	CoBO (Ours)	LOL-BO	W-LBO	TuRBO-L	LS-BO
Oracle calls	3k	3k	3k	3k	3k
Wall clock time (hr)	86.4	65.7	40.7	**34.3**	67.4
Found Best Score	**-15.4**	-14.6	-12.3	-12.2	-13.9
Oracle calls	1.5k	1.5k	2.6k	**3k**	2.1k
Wall clock time (hr)	34.3	34.3	34.3	34.3	34.3
Found Best Score	**-14.5**	-14.2	-12.3	-12.2	-13.6

Table 4: **Efficiency comparison on arithmetic expression fitting task within 500 evaluation budget.**

Model	CoBO (Ours)	LOL-BO	W-LBO	TuRBO-L	LS-BO
Oracle calls	500	500	500	500	500
Wall clock time (min)	**5.4**	11.3	11.1	338.1	1620.7
Found Best Score	**0.1468**	0.4624	0.5848	0.7725	0.5533
Oracle calls	**500**	330	173	0	0
Wall clock time (min)	5.4	5.4	5.4	5.4	5.4
Found Best Score	**0.1468**	0.5467	1.0241	1.521	1.521

Table 5: **Coefficients of our proposed regularizations determined by grid search.**

	med2	osmb	pdop	zale	Arithmetic	DRD3
Coefficient of $\mathcal{L}_{\text{Lip\_W}}$	1e3	1e2	1e2	1e3	1e1	1e1
Coefficient of $\mathcal{L}_{\text{z}}$	1e0	1e0	1e-1	1e0	1e-1	1e0

Table 6: **Coefficients of our proposed regularizations w/o search.**

	rano	adip	valt
Coefficient of $\mathcal{L}_{\text{Lip\_W}}$	1e2	1e2	1e2
Coefficient of $\mathcal{L}_{\text{z}}$	1e-1	1e-1	1e-1

Table 7: **Other hyperparameters used in the experiments.**

Parameter	Guacamol	Arithmetic	DRD3
Learning rate	0.1	0.1	0.1
Coefficient of $\mathcal{L}_{\text{surr}}$	1	1	1
Coefficient of $\mathcal{L}_{\text{recon\_W}}$	1	1	1
Coefficient of $\mathcal{L}_{\text{KL}}$	0.1	0.1	0.1
Quantile of objective value for loss weighting	0.95	0.95	0.95
Standard deviation σ for loss weighting	0.1	0.1	0.1
# initial datapoints N	10000	40000	100
Latent update interval N_{fail}	10	10	10
Batch size	10	5	1
# top-k used training	1000	10	10

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