HelixMO: Sample-Efficient Molecular Optimization in Scene-Sensitive Latent Space

Zhiyuan Chen*, Xiaomin Fang*, Zixu Hua, Yueyang Huang, Fan Wang, Hua Wu
Baidu Inc.

{chenzhiyuan05, fangxiaomin01, huazixu, huangyueyang, wang.fan, wu_hua}@baidu.com

Abstract—Efficient exploration of the chemical space to search for the candidate drugs that satisfy various constraints is a fundamental task of drug discovery. Advanced deep generative methods attempt to optimize the molecules in the compact latent space instead of the discrete original space, but the mapping between the original and latent spaces is always kept unchanged during the entire optimization process. The unchanged mapping makes those methods challenging to fast adapt to various optimization scenes and leads to the great demand for assessed molecules (samples) to provide optimization direction, which is a considerable expense for drug discovery. To this end, we design a sample-efficient molecular generative method, HelixMO, which explores the scene-sensitive latent space to promote sample efficiency. The scene-sensitive latent space focuses more on modeling the promising molecules by dynamically adjusting the space mapping by leveraging the correlations between the general and scene-specific characteristics during the optimization process. Extensive experiments demonstrate that HelixMO can achieve competitive performance with only a few assessed samples on four molecular optimization scenes. Ablation studies verify the positive impact of the scene-specific latent space, which is capable of identifying the critical characteristics of the promising molecules. We also deployed HelixMO on the website PaddleHelix (https://paddlehelix.baidu.com/app/drug/drugdesign/forecast) to provide drug design service.

Index Terms—Molecular optimization, Sample-efficient, Deep generative model, Latent space

I. INTRODUCTION

Efficiently exploring the chemical space to search for molecules that meet various requirements (e.g., bio-activities, druggability, and synthetics accessibility) is one of the most critical tasks in the drug discovery industry. High-throughput screening (HTS) [1] through laboratory experiments and visual screening (VS) [2] through in-silico experiments screen molecules from the molecular databases [3], [4] to find promising molecules for further validation. However, the entire chemical space is at the scale of 10^80 [5], far exceeding the scale of known molecules in the databases. Consequently, in many scenarios, the databases used may not contain the satisfactory molecules that can be developed into drugs. Thus, developing more efficient and effective chemical space exploration methods is appealing for drug discovery.

Advanced studies proposed various fantastic deep molecular generative models, e.g., recurrent-based models [6], [7], Variational AutoEncoder (VAE) [8]–[12], Generative Adversarial Network (GAN) [13]–[15], and Flow-based models [16]–[19], to generate novel molecules that are not contained in the molecular libraries. They attempt to apply these deep molecular generative models to design de-novo drugs to produce promising molecules that meet various constraints and could be developed into drugs. At each iteration, the generative methods query the scoring system, e.g., laboratory experiments, to assess the multiple properties of some candidate molecules and expect the assessed molecules to provide the direction for molecular optimization. Particularly, some methods [8]–[10], [19] explore in the compact chemical latent space instead of the discrete original space (input space). The mapping between the input and latent spaces is learned from large-scale molecular libraries. Although such methods have demonstrated their effectiveness, they still need to further improve the sample efficiency to enhance the practicability in drug discovery because a large number of laboratory experiments for sample assessments would be a great expense for the drug R & D institutions. We argue that designing a scene-sensitive latent space that can fast adapt to the optimization scenes during the exploration will likely benefit the sample efficiency. Previous latent-based works tend to keep the mapping of input and latent spaces unchanged during the whole exploration process. However, the distribution of the satisfactory molecules for a particular optimization scene is usually different from that of the molecules in the libraries
used for learning the initial mapping. Consequently, it is struggled to explore the promising molecules in the latent space based on the distribution of the molecular libraries. The promising molecules for a particular optimization scene could be far away from the center of the latent space, and it may take a great many steps to explore the space in order to find them (as shown in the top of Fig. 1).

To this end, we design a sample-efficient molecular optimization method, HelixMO, exploring the scene-sensitive latent space to search the promising molecules. The mapping of the input and latent spaces is dynamically adjusted to adapt to the particular optimization scene. The space mapping is dynamically tuned by leveraging the assessed samples during the exploration process to focus on modeling the promising molecules gradually. Three kinds of learning tasks, including the reconstruction task, the scene-specific property prediction tasks, and the general property prediction tasks, are designed to encourage the latent space to infer the critical characteristics of the promising molecules. The promising molecules will gradually gather together around the center of the latent space (as shown at the bottom of Fig. 1), and only a few steps (samples) are required to find the satisfactory molecules.

Compared with the advanced baseline methods, HelixMO achieves competitive performance with fewer assessed samples on four molecular optimization scenes with one or more optimization objectives, indicating its potential values in practice. We also analyze the impacts of the learning tasks on modeling scene-sensitive latent space, verifying that HelixMO will pay more attention to the promising molecules to promote search efficiency. Furthermore, we have already deployed HelixMO by taking molecular docking as the scoring system on the website PaddleHelix\(^1\) to provide drug design service.

Our main contributions can be summarized as follows:

- We designed a sample-efficient molecular optimization method, HelixMO, aiming to reduce the required number of assessed samples to improve the practicability in drug discovery.
- The optimization method exploits the scene-sensitive latent space, which is dynamically adjusted by various learning tasks on limited assessed samples to adapt to the particular optimization scenes.
- The proposed method can achieve competitive performance with fewer assessed samples than several baseline methods in four molecular optimization scenes, exhibiting the potential practical values.

II. PRELIMINARY

Since HelixMO explores the latent space to search the molecules that satisfy multiple constraints, we first introduce a typical generative method based on latent space exploration in this section, as demonstrated in Fig. 2. A genetic algorithm is adopted as the search algorithm to optimize the molecules according to the assessed results from the scoring system.

\(^{1}\)https://paddlehelix.baidu.com/app/drug/drugdesign/forecast

![Fig. 2. Framework of a typical molecular optimization method that is based on exploration in latent space.](image)

Usually, the molecular optimization process iterates multiple times until satisfactory molecules are found.

A. Scoring System

The scoring system assesses the molecules produced by the generative method at each iteration. An assessment of a molecule \(x\) is formalized as

\[
A(x) = a_1(x) \circ a_2(x) \circ \cdots \circ a_K(x),
\]

which is composed of one or multiple properties, e.g., bioactivity to a target protein, druggability, and synthetic accessibility. \(a_k(x)\) denotes the \(k\)-th objective, \(K\) is the number of properties, and \(\circ\) is an operator that combines the properties, such as summation and multiplication. When applying molecular optimization to drug development in practice, the properties of the molecules are evaluated by laboratory or in-silico experiments. Since those experiments are expensive and time-consuming, scoring functions [20] are usually used as alternatives for fast verification of the effectiveness of the molecular optimization methods. At the \(i\)-th iteration, the scoring system returns the overall assessed result \(A(x)\) as well as all the properties, i.e., \(a_1(x), \cdots, a_K(x)\) for each molecule in the molecular population \(x \in \mathcal{X}(i)\) to the generative method, where \(\mathcal{X}(i) = \{x_1^i, x_2^i, \cdots, x_N^i\}\), and \(N\) is the size of the population.

B. Generative Method

We apply a genetic algorithm to search the satisfactory molecules. The properties of the molecular population produced at each interaction will gradually improve and meet the constraints of the optimization scenes.

At the \(i\)-th iteration, the generative method produces a new molecular population \(\mathcal{X}(i)\) by perturbing the molecules in the last population \(\mathcal{X}(i-1)\) according to the corresponding results assessed by the scoring system. Note that at the 1-st iteration, the molecules in \(\mathcal{X}(0)\) are randomly selected from a drug-like molecular database.

First, each molecule \(x \in \mathcal{X}(i)\) is encoded into a representation vector through the encoder \(z = \text{Enc}(x; \theta_{\text{Enc}})\), where \(\theta_{\text{Enc}}\) denotes the parameters. Second, we select the elite molecules from the molecular population. The assessment score from the scoring system is formalized as a fitness score of a molecule. The representation vectors from \(Z^i\) are selected with a probability proportional to their fitness scores. Third,
for each selected representation $z$, we randomly sample $C$ Gaussian noises $\epsilon_1, \epsilon_2, \ldots, \epsilon_C \sim \mathcal{N}(0, 1)$, where $C$ is a hyper-parameter to control the number of candidates and $I$ represents an identity matrix. The Gaussian noises are added to $z$:

$$z'_j = z + \sigma \cdot \epsilon_j, \text{ for } j = 1, \ldots, C,$$

where $z'_j$ is a perturbed representation vector, and $\sigma$ is the step size controlling the similarity degree between $z$ and $z'_j$. If $\sigma$ is too large, there will be a great difference between the original molecule and the perturbed one, and the perturbed molecule may fail to retain the characteristics of the original one. If $\sigma$ is too small, the perturbed molecule will be particularly similar to the candidate molecule, resulting in lower efficiency of chemical space exploration. Fourth, the perturbed representations are reconstructed into the perturbed molecules by decoder $Dec(z; \theta^{Dec})$, where $\theta^{Dec}$ denotes the parameters.

Finally, the scoring system is queried to assess the properties of the molecules $\mathcal{X}^{(i)}$, and the set of assessed results is denoted as $\{A(x^{(1)}), A(x^{(2)}), \ldots, A(x^{(N)})\}$ with $A(x)$ representing the assessed result of molecule $x$.

### III. Scene-Sensitive Latent Space

HelixMO searches the promising molecules in the scene-sensitive latent space. Since the distribution of molecules in the drug-like database used to obtain the initial mapping of the spaces is usually different from that of promising molecules of a particular optimization scene, we adjust the mapping of the input and latent spaces to encourage the latent space to focus more on modeling the promising molecules. The molecules with good properties tend to get together around the center of the latent space during the optimization process, and thus we can find the molecules that can satisfy multiple constraints more sample efficiently. The architecture of HelixMO is exhibited in Fig. 3. The mapping is dynamically adjusted in accordance with the potential of molecules discovered through three kinds of learning tasks, including the reconstruction task, scene-specific property prediction tasks, and general property prediction tasks, during the optimization process. Those learning tasks encourage the generative model to identify the promising molecules’ essential characteristics, e.g., the task-specific properties and the general properties. Those essential characteristics can effectively distinguish the high-potential molecules from the remaining ones.

#### A. Initial Mapping of Input and Latent Spaces

To obtain the initial mapping between the input space $\mathcal{X}$ and the latent space $\mathcal{Z}$, we adopt a widely used molecular generative model, Junction Tree Variational Autoencoder (JT-VAE) [10], as the backbone generative model. JT-VAE is trained on a large-scale molecular database, e.g., ZINC [3] and ChEMBL [21]. MOSES [22], containing about 250K molecules extracted from the ZINC database is utilized to obtain the initial mapping of the input and latent spaces. The encoder in JT-VAE can encode a molecule $x$ into a representation vector $z = Enc(x; \theta^{Enc})$, and the decoder in JT-VAE can reconstruct that molecule from the representation vector $x = Dec(z; \theta^{Dec})$. In such a method, we can obtain the initial mapping of the input and latent spaces.

#### B. Latent Space Adjustment

Previous works tend to keep the mapping unchanged during the whole optimization process. HelixMO gradually tunes the mapping during the optimization process to make it sensitive to particular optimization scenes.

To encourage the latent space to focus more on the modeling of the satisfactory molecules, i.e., the molecules with better properties, HelixMO takes advantage of the molecules produced at each iteration $\mathcal{X}^{(i)}$, and the parameters of the generative model are optimized with those produced molecules at each iteration. Since the properties of the molecules produced at each iteration are improved by the genetic algorithm, the generative model will gradually focus on the molecules with extraordinary properties.

Three kinds of learning tasks, including the reconstruction task, the scene-specific property prediction tasks, and the general property prediction tasks, guide the mapping adjustment by optimizing the parameters of the generative model $\Theta = \{\theta^{Enc}, \theta^{Dec}, \theta^{Spec}, \theta^{Gene}\}$. The overall loss function for model optimization is defined as:

$$L_{Total}(\mathcal{X}) = L_{Reco}(\mathcal{X}) + \frac{1}{K} \sum_{k=1}^{K} L_{Spec}^{(k)}(\mathcal{X}) + \frac{1}{S} \sum_{s=1}^{S} L_{Gene}^{(s)}(\mathcal{X}),$$

where $\mathcal{X} = \mathcal{X}^{(i)}$ at the $i$-th iteration. $L_{Reco}(\mathcal{X})$, $L_{Spec}^{(k)}(\mathcal{X})$, $L_{Gene}^{(s)}(\mathcal{X})$ denote the loss function of the reconstruction task, a scene-specific property prediction task, and a general property prediction task, respectively, where the detail definition will be introduced in the following subsections. $K$ is the number of the scene-specific properties used in the scene-specific property prediction tasks, and $S$ is the number of the general properties used in the general property prediction tasks. Those learning tasks attempt to mine knowledge from the limited samples assessed by the scoring system at each iteration. The knowledge is incorporated into the generative model to learn the scene-sensitive mapping between latent and input spaces.
C. Reconstruction Task

The reconstruction task is originally used to train the generative model, i.e., JT-VAE, to obtain the initial mapping of the input and latent spaces, which reconstructs the molecules from the latent representations. We also adopt the reconstruction task to tune the adjustment of the mapping of the input and latent spaces. The reconstruction task aims to minimize the distance between a input molecule \( x \in \mathcal{X} \) and the reconstructed molecule \( \hat{x} = \text{Dec}(\text{Enc}(x; \theta_{\text{Enc}}); \theta_{\text{Dec}}) \):

\[
L_{\text{Reco}}(\mathcal{X}) = \sum_{x \in \mathcal{X}} L_{\text{Dis}}(x, \hat{x}),
\]

where \( \mathcal{X} = \mathcal{X}^{(i)} \) at the i-th iteration, and \( L_{\text{Dis}}(\cdot) \) is a function measuring the distance between two molecules introduced in [10]. Using the reconstruction task to train on the produced molecules at each iteration can effectively lift the probability of the reconstruction of the promising molecules.

D. Scene-Specific Property Prediction Tasks

In order to guide the latent space to distinguish the molecules with superior properties from the remaining ones for the optimization scene, we introduce the scene-specific property prediction tasks. Those tasks attempt to estimate the properties, i.e., \( a_1(x), a_2(x), \cdots, a_K(x) \). For the \( k \)-th property, a Multilayer Perceptron (MLP), denoted by \( MLP^\text{Spec}(\cdot) \), takes the latent representation vector \( z \) of a molecule \( x \) as the input and outputs the estimated property:

\[
\hat{a}_k(x) = MLP^\text{Spec}_k(\text{Enc}(x; \theta_{\text{Enc}}); \theta^\text{Spec}_k),
\]

where \( \theta^\text{Spec}_k \) denotes the parameters of function \( MLP^\text{Spec}(\cdot) \). The parameters \( \theta_{\text{Enc}} \) and \( \theta^\text{Spec}_k \) are optimized by minimizing the distance between the estimated property \( \hat{a}_k(x) \) and the property return from the scoring system \( a_k(x) \) for a molecule \( x \). At the i-th iteration, the assessed molecules collected from the scoring systems, i.e., \( \mathcal{X}^{(i)} \), are utilized to optimize the parameters \( \theta_{\text{Enc}} \) and \( \theta^\text{Spec}_k \):

\[
L_k^\text{Spec}(\mathcal{X}) = \sum_{x \in \mathcal{X}} H\text{uber}\_\text{loss}_\delta(\hat{a}_k(x), \tilde{a}_k(x)),
\]

where \( \mathcal{X} = \mathcal{X}^{(i)} \) at the i-th iteration, and \( H\text{uber}\_\text{loss}_\delta(\cdot) \) [23] is a loss function that measures the distance of two values with \( \delta \) controlling the impact of the outliers. As the number of iterations increases, the generative method would produce more satisfactory molecules, and the property values of the assessed molecules would become larger. To alleviate the negative impact caused by the changing scale of property values for model training, we normalize the property values by applying Gaussian Normalization, and the normalized property values are denoted as \( \tilde{a}_k(x) \) in Eq. 6. Through the scene-specific property prediction tasks, the model can infer the scene-specific properties of a molecule from its latent representation vector.

Note that the scene-specific property prediction tasks can serve as a coarse scoring system to screen out the perturbed molecules with the highest scores assessed by the coarse scoring system as the molecular population of the next iteration to improve the sample efficiency further.

E. General Property Prediction Tasks

We also introduce the general property prediction tasks to further enhance the capacity of the latent representations. Molecular fingerprints [24] can encode a molecule into a list of binary bits, describing the presence of the structure fragments in the molecule. The structure fragments of a molecule are strongly correlated to its general properties. Consequently, each binary bit can be simply regarded as a general property of a molecule. For the sake of identifying the assessed molecules’ general properties, the general property prediction tasks simultaneously estimate the binary bits of the molecular fingerprints from their latent representations:

\[
\hat{b}_1(x), \cdots, \hat{b}_S(x) = MLP^\text{Gene}(\text{Enc}(x; \theta_{\text{Enc}}); \theta^\text{Gene}),
\]

where \( \hat{b}_s(x) \) denotes the s-th estimated bit, and \( \theta^\text{Gene} \) represents the parameters of the general property prediction tasks, denoted by function \( MLP^\text{Gene} \). Cross-entropy is taken as the loss function to optimize the parameters \( \theta_{\text{Enc}} \) and \( \theta^\text{Gene} \) on the assessed molecules at the i-th iteration:

\[
L^\text{Gene}_s(\mathcal{X}) = \sum_{x \in \mathcal{X}} \text{Cross}\_\text{entropy}(b_s(x), \hat{b}_s(x)),
\]

where \( s \) is the index of the binary bits, and \( \mathcal{X} = \mathcal{X}^{(i)} \). We utilize the Morgan fingerprint with 2048 bits as the molecular general properties. Learning the latent representations in this way is equivalent to using the self-supervised learning (SSL) method [25] to learn valuable information from the unlabeled data, which has achieved great success in many domains.

IV. EXPERIMENTS

A. Experimental Settings

Following the previous work [26], the molecular optimization methods are compared through four molecular properties:

- **GSK3β** [27]: Inhibition against glycogen synthase kinase-3β;
- **JNK3** [27]: Inhibition against c-Jun N-terminal kinase-3;
- **QED** [28]: Quantitative Estimation of Drug-likeness;
- **SA** [29]: Synthetics Accessibility, indicating the difficulty of synthesizing a given molecule.

Each property is obtained through a scoring function. The properties compose four optimization scenes: two single-objective optimization scenes, including **GSK3β and JNK3**, and two multi-objective optimization scenes, including **GSK3β+JNK3** and **GSK3β+JNK3+QED+SA**. We use summation as the operator \( o \) to combine the properties in multi-objective optimization scenes.

B. Overall Evaluation

To verify that HelixMO has a great advantage in sample efficiency, we evaluate the performance of HelixMO and several typical baseline methods when the number of requests for the scoring system \( l \) the number of assessed samples
(Cost for molecular optimization) is set to be a specific number. We compare HelixMO with Molecular Database (ChEMBL), MARS [30], and Scene-Insensitive Latent Space (SILS). ChEMBL is a database of bioactive molecules with drug-like properties, which is used as a naive baseline based on virtual screening in our paper. We randomly sampled some molecules from the molecular database, and the top sampled molecules were evaluated. MARS explores the input space for molecular optimization, modeling the probability of adding/deleting fragments to/from the original molecules to produce new molecules. SILS takes JT-VAE [10] as the model backbone and explores the unchanged latent space for molecular optimization by a genetic algorithm, just like HelixMO. ILS is a scene-insensitive ablation version of HelixMO. We use the default hyper-parameters that are recommended in the corresponding literature. For each method, the average property scores (Aps) of the top-100 molecules under different Costs (2K, 4K, 6K, 8K, and 10K) are reported in Fig. 4. We operated five runs on HelixMO for each optimization scene and reported its average performance.

From the figure, we can draw the following conclusions:

- Compared with the baseline methods, HelixMO demonstrates its effectiveness and efficiency in finding satisfactory molecules on four optimization scenes. The Aps scores of HelixMO significantly surpass those of the baseline methods in almost all the cases.
- Although SILS is also based on latent space exploration, HelixMO still shows superior sample efficiency. The dynamically adjusted latent space used by HelixMO can effectively identify the promising molecules by analyzing the information of molecules produced at each iteration, reducing the number of search steps required.
- Interestingly, although ChEMBL only randomly samples molecules from the database without reliance on the deep generative model, the Aps scores of ChEMBL are higher than those of MARS and SILS when only 2K assessed samples are available on four optimization scenes. We speculate that in the early stage of molecular optimization, the properties of the molecules in the regions explored by those two methods are unsatisfactory and even inferior to the drug-like molecules in ChEMBL.

Besides, we comprehensively evaluate HelixMO and more advanced baseline methods (RationaleRL [31] and MolEvol [32]) from three perspectives: (1) Cost: assessed samples required for molecular optimization; (2) Aps: average property score of the top-100 molecules; and (3) Novelty (Nov): the ratio of generated molecules not present in the known active molecule set toward targets GSK3β and JNK3. The overall evaluation of HelixMO and the baseline methods on four optimization scenes are exhibited in Fig. 5.

1) As exhibited in Fig. 5(a), RationaleRL, MolEvol, and MARS require millions of assessed samples to search the satisfactory molecules. In contrast, the methods that explore the latent space, including SILS and HelixMO, require only tens of thousands of assessed molecules for chemical space exploration. Especially by applying the scene-sensitive latent space, only 10K assessed samples are required to achieve competitive performance with the baseline methods. These results demonstrate the sample efficiency of HelixMO. (2) As exhibited in Fig. 5(b), the Aps scores of HelixMO are comparable to those of the optimal baseline methods on all the optimization scenes in general. For optimization scenes GSK3β and JNK3 with only one optimization objective, HelixMO surpasses all the baseline methods, except ChEMBL. For the more difficult scenes with multiple optimization objectives, HelixMO achieves the highest Aps scores on GSK3β+JNK3 and GSK3β+JNK3+QED+SA. These results indicate that HelixMO is capable of discovering those molecules with satisfactory properties. (3) Although the Aps scores of the top molecules in the drug-like database ChEMBL are excellent on four optimization scenes, as shown in Fig. 5(c), the Nov scores of the top molecules are the worst among all the methods. Many top molecules in ChEMBL have already been contained in the known active molecule set toward targets GSK3β and JNK3 since a virtual screening method cannot design de novo molecules that are not in the screening database.

C. Ablation Studies

HelixMO makes efforts to fine-tune the mapping between the input space and latent space through three kinds of learning tasks for the sake of making the latent space sensitive to the optimization scenes. To explore the impacts of the learning tasks on the latent space, we compare multiple ablation versions of HelixMO with different settings:

- None: The latent space is kept unchanged during the molecular exploration process (refer to SILS in the last subsection);
The scene-sensitive latent space is the primary factor for the high sample efficiency of HelixMO. A scene-sensitive mapping between the input and latent space should focus more on modeling the promising molecules for the particular optimization scenes rather than molecules in the drug-like database. The VAE-style backbone model used by HelixMO assumes the molecules follow the normal distribution in the latent space. Therefore, the attention degree of the model to a molecule is inversely proportional to the distance of the molecule from the center of the latent space (the norm of the representation vector). We believe that the closer the promising molecules are to the center of the latent space, the faster the genetic algorithm will find these molecules that meet the property constraints. Fig. 6(b) shows the average norms of the representation vectors in various latent spaces of 500 promising molecules for optimization scene $GSK3\beta+JNK3+QED+SA$. More concretely, we calculated the average norm of the encoded representation vectors of the promising molecules at multiple iterations for each ablation version of HelixMO. For $Spec$, $Spec+Reco$, and $Spec+Reco+Gene$, the average norms decrease with the increase of iteration, which means the dynamically adjusted latent spaces of these methods gradually pay more attention to the promising molecules. Significantly, the average norm for $Spec+Reco+Gene$ at the last iteration is the lowest, indicating that the general property prediction tasks only bring a little improvement in the Aps scores. Although the general property prediction tasks can not explicitly promote the Aps scores, it still plays roles in better space mapping and enhancement of the robustness for molecular optimization.

Fig. 6(a) exhibits the Aps scores of ablation versions of HelixMO on optimization scene $GSK3\beta+JNK3+QED+SA$. (1) $Spec$ achieves better Aps scores than $None$. The scene-specific property prediction tasks in $Spec$ encourage the model to infer the properties of the molecules from the latent space, and thus the model is capable of distinguishing the satisfactory molecules from the others. Besides, the scene-specific property prediction tasks serve as a coarse scoring system to provide direction to choosing the candidate molecules with more potential. (2) The significant improvement of $Spec+Reco$ compared with $Spec$ indicates that the reconstruction task contributes to the improvement during the molecular exploration process. It is difficult for the generative model to sample/reconstruct a molecule that is out of the distribution of the molecules in a database used to obtain the initial mapping. Since the distribution of the satisfactory molecules for a particular optimization scene is usually different from that of the molecules in the database, fine-tune the latent space precipitate to enhance the success rate of reconstructing a satisfactory molecule. (3) By comparing $Spec+Reco$ and $Spec+Reco+Gene$, we observe that the general property prediction tasks only bring a little improvement in the Aps scores. Although the general property prediction tasks can not explicitly promote the Aps scores, it still plays roles in better space mapping and enhancement of the robustness for molecular optimization.
that the general property prediction tasks can strengthen the modeling ability for the molecules that meet the requirements of the optimization scenes.

Besides, the general property prediction tasks can be regarded as auxiliary self-supervised learning tasks, which can improve the robustness of the generative model. Fig. 6(c) shows the average Aps scores as well as the standard deviation of the Aps scores of five independent runs of Spec+Rec+Gene and Spec+Reco at multiple iterations on optimization scene GSK3β+JNK3+QED+SA. Spec+Rec+Gene with the general property prediction tasks can not only find satisfactory molecules with fewer assessed samples but also has better robustness, where the deviation of the Aps is smaller than that of Spec+Reco during the molecular exploration process.

V. CONCLUSIONS

The development of deep generative models makes it possible to search the entire chemical space to find potential drugs. Due to the low sample efficiency, employing the existing generative methods in practical applications is still challenging. In order to reduce the number of the required assessed samples, we developed HelixMO, attempting to explore the scene-sensitive latent space to efficiently search the satisfactory molecules. The mapping of the input and latent spaces is dynamically adjusted to focus on modeling the promising molecules by three well-designed learning tasks. In this way, HelixMO is capable of achieving competitive performance with fewer assessed samples than the mainstream methods. We also deploy HelixMO as an online service, expecting to provide experimental inspiration for drug R & D researchers.

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