

Mol-LLM: Multimodal Generalist Molecular LLM with Improved Graph Utilization

Chanhui Lee¹, Hanbum Ko¹, Yuheon Song², Yongjun Jeong¹
 Rodrigo Hormazabal^{3,4}, Sehui Han⁴, Kyunghoon Bae⁴, Sungbin Lim^{4,5*}, Sungwoong Kim^{1*}

¹Department of Artificial Intelligence, Korea University

²Department of Artificial Intelligence, UNIST

³Kim Jaechul Graduate School of AI, KAIST

⁴LG AI Research

⁵Department of Statistics, Korea University

Abstract

Recent advances in large language models (LLMs) have led to models that tackle diverse molecular tasks, such as chemical reaction prediction and molecular property prediction. Large-scale molecular instruction-tuning datasets have enabled sequence-only (e.g., SMILES or SELFIES) generalist molecular LLMs, and researchers are now exploring multimodal approaches that incorporate molecular structural information for further gains. However, a genuinely multimodal, generalist LLM that covers a broad spectrum of molecular tasks has yet to be fully investigated. We observe that naive next token prediction training ignores graph-structural information, limiting an LLM’s ability to exploit molecular graphs. To address this, we propose (i) Molecular structure Preference Optimization (MolPO), which facilitates graph usage by optimizing preferences between pairs of correct and perturbed molecular structures, and (ii) an advanced graph encoder with a tailored pre-training strategy to improve the effect of graph utilization by MolPO. Building on these contributions, we introduce Mol-LLM, the first multimodal generalist model that (a) handles a broad spectrum of molecular tasks among molecular LLMs, (b) explicitly leverages molecular-structure information, and (c) takes advantage of extensive instruction tuning. Mol-LLM attains state-of-the-art or comparable results across the most comprehensive molecular-LLM benchmark—even on out-of-distribution datasets for reaction and property prediction, where it surpasses prior generalist molecular LLMs by a large margin.²

1 Introduction

Large language models (LLMs) [1–4] have been widely used to tackle diverse tasks across multiple domains, such as mathematics and code generation, by leveraging their broad knowledge base. This achievement has recently motivated interest in applying LLMs to diverse molecular tasks—including molecular property prediction, chemical reaction prediction, description-guided molecule generation, and molecule captioning—all of which are essential in drug discovery and materials science [5–12]. In particular, most molecular LLMs tend to leverage only one of the two key components for improved molecular language modeling, either molecular structure information or multitask instruction-tuning, rather than combining both. Several studies [8, 10, 11] have moved away from conventional molecular language modeling based on 1D sequence such as SMILES [13] or SELFIES [14], and have instead developed multimodal LLMs that incorporate 2D molecular graphs as an additional input modality, thereby representing molecular structures and topologies more faithfully while achieving

*Corresponding Authors. {sungbin, swkim01}@korea.ac.kr.

²The model, code, and data will be publicly available.

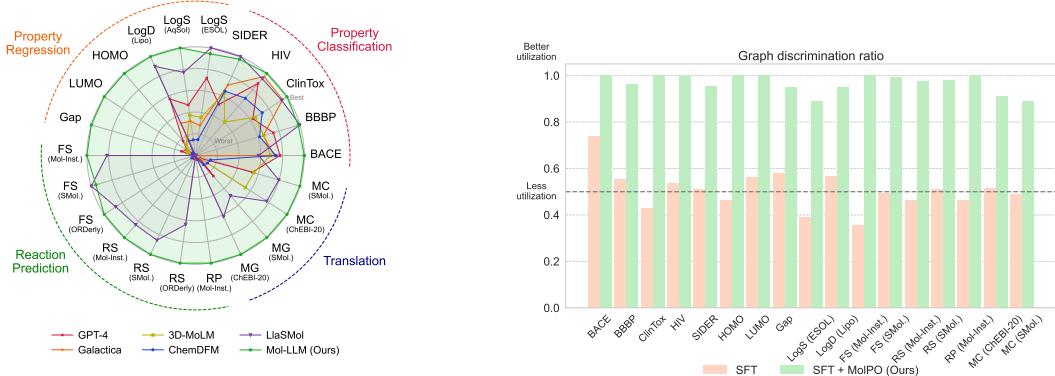


Figure 1: (Left) Performance comparison among generalist molecular LLMs with normalized primary metrics. (Right) Graph utilization comparison between SFT and proposed multimodal training (MolPO). Score closer to 1 indicate better use of graph, approaching 0.5 indicate less utilization.

better performance across diverse molecular tasks [15–17]. Meanwhile, other studies [5–7, 9] have constructed instruction-tuning datasets for multiple molecular tasks and fine-tuned LLMs on these datasets. This approach enables the models to acquire transferable and generalizable knowledge, allowing them to understand and perform various tasks based on natural language instructions.

However, it is uncertain whether the multimodal molecular LLMs effectively use molecular structural information when trained with naive supervised fine-tuning (SFT). To investigate this, we compare the likelihoods of the original and perturbed molecules, comparing how well the SFT model is at proper graph discrimination. Figure 1 shows that the SFT model hardly distinguishes between them on most molecular tasks, indicating that its molecular graph utilization is generally limited. Moreover, despite the potential for synergistic performance improvements by molecular graph structure utilization and multitask instruction-tuning, few studies have fully harnessed the benefits of both approaches, especially for a universal molecular LLM. Specifically, some recent studies [9, 11, 12, 18, 19] have attempted to combine molecule graph structure information with instruction-tuning, however, their instruction-tuning focuses solely on task-specific fine-tuning.

In this paper, we propose a generalist molecular LLM, called Mol-LLM, that leverages multimodal molecule and extensive instruction-tuning, addressing the broadest range of molecular tasks. In particular, while maintaining multimodal LLM architecture based on Q-Former [20], we introduce a novel multimodal instruction-tuning based on Molecular structure Preference Optimization (MolPO), where the molecular LLM learns to optimize the molecular structural preferences between the pairs of the correct (chosen) molecular graph and the perturbed (rejected) molecular graph. By creating rejected molecular graphs based on the substructures for molecular feature perturbation, the proposed MolPO mitigates the tendency to overlook graph information on various molecular tasks. Additionally, to further increase the effect of molecular graph utilization by advanced representation on a wide variety of molecular distributions, we introduce a new graph neural network (GNN) pre-training strategy and architecture. The proposed GNN pre-training framework combines two objectives: (i) functional group prediction, which teaches the model to accurately distinguish functional groups—the features that largely determine molecular properties—and (ii) SELFIES reconstruction, which helps the model preserve the molecular structure details from the molecular graph. Upon GINE [21], adopted by prior multimodal molecular LLMs [8, 9], we incorporate a transformer-based GNN named TokenGT [22], to enhance the expressive power. The resulting Mol-LLM shows strong performance and demonstrably better graph utilization on our benchmarks across a broad range of molecular tasks. To the best of our knowledge, Mol-LLM is not only the first versatile generalist multimodal molecular LLM on a wide range tasks with a single generalist model, but it also surpasses other generalist models: LlaSMol [5], ChemDFM [23], 3D-MoLM [12] on most benchmarks as shown in Figure 1, highlighting the power of graph modality synergized with extensive instruction-tuning.

In summary, our contributions are:

1. **Mol-LLM.** We present Mol-LLM, which sets a new state-of-the-art on both in-distribution and out-of-distribution molecular benchmarks relative to existing generalist models.

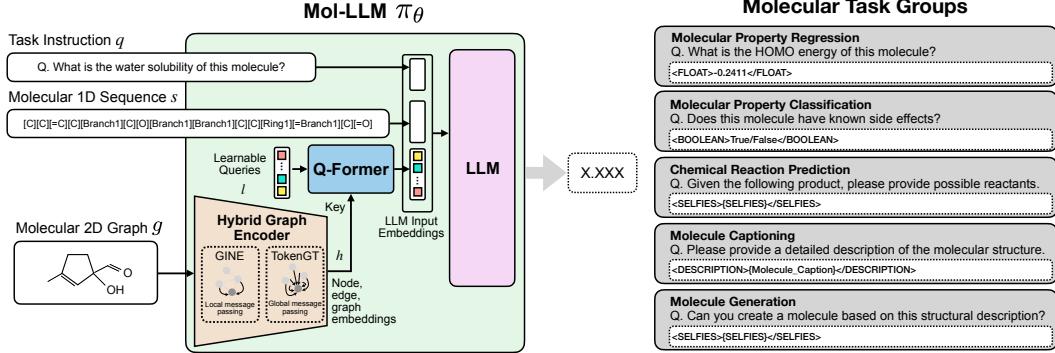


Figure 2: (Left) Overall structure of Mol-LLM. Molecular graph is encoded into a fixed-length token sequence by a hybrid graph encoder, followed by a Q-Former that outputs query embeddings to feed LLM, with corresponding task instruction and molecular 1D sequence. (Right) Representative downstream molecular tasks.

2. **Enhanced graph utilization.** To exploit 2D molecular graphs more effectively, we propose MolPO—a fine-tuning strategy that leverages perturbed molecules—alongside a GNN pre-training method and a hybrid graph encoder augmented with transformer architecture.
3. **Extensive instruction-tuning.** We construct a large, molecule-focused instruction-tuning dataset and employ multimodal training to build a generalist model with significantly enhanced molecular understanding.

2 Mol-LLM: Multimodal Generalist Molecular Large Language Model

This section introduces the model architecture, training strategy, and instruction-tuning dataset of Mol-LLM, a multimodal generalist molecular LLM. As depicted in Figure 2, Mol-LLM comprises a hybrid molecular graph encoder, a Q-Former for cross-modal projection between molecular graph and text, and a backbone LLM. Utilizing the multimodal framework, the LLM addresses molecular task instructions and 1D molecular sequences directly, while feeding 2D molecular graph embeddings to the LLM through the hybrid graph encoder and Q-Former. Such multimodal architectures are trained through three training stages, as depicted in Figure 3.

2.1 Model Architecture

Hybrid Graph Encoder Previous studies on multimodal molecular LLMs using 2D molecular graphs [8, 9] have adopted the GINE architecture [21], since it captures local graphical structure efficiently. However, addressing diverse molecular tasks across various data distributions requires the ability to process large molecules as well. This consideration led us to the simultaneous usage of TokenGT [22] as a graph encoder, which is designed to enhance global context understanding and mitigate over-smoothing [24] in large graphs via a transformer architecture. For a 2D molecular graph $G = (V, E)$, the GINE encoder f^G outputs a graph embedding $h_g^G \in \mathbb{R}^{1 \times d_g}$ and node embeddings $h_v^G \in \mathbb{R}^{|V| \times d_g}$, where d_g is the embedding dimension. Otherwise, the TokenGT encoder f^T outputs not only a graph embedding $h_g^T \in \mathbb{R}^{1 \times d_g}$ and node embeddings $h_v^T \in \mathbb{R}^{|V| \times d_g}$, but also edge embeddings $h_e^T \in \mathbb{R}^{|E| \times d_g}$. We then concatenate all the embeddings obtained by both encoders $h_g^G, h_v^G, h_g^T, h_v^T$, and h_e^T along the first dimension to obtain $h \in \mathbb{R}^{(2|V|+|E|+2) \times d_g}$, which is then used as the key for the Q-Former.

Cross-modal Projector (Q-Former) Querying transformer (Q-Former) [20] is a modality-bridging transformer that converts the varying number of concatenated embeddings for each molecular graph into a fixed-length token sequence, enabling efficient batch processing. Specifically, structural information is distilled via cross-attention between $N_q = 32$ learnable query vectors $l \in \mathbb{R}^{32 \times d_q}$, initialized randomly, and the concatenated molecular embeddings $h \in \mathbb{R}^{(2|V|+|E|+2) \times d_g}$, producing 32 tokens aligned with the text modality. The 32 tokens are concatenated with the task instruction as well as the SELFIES string before being fed to the LLM.

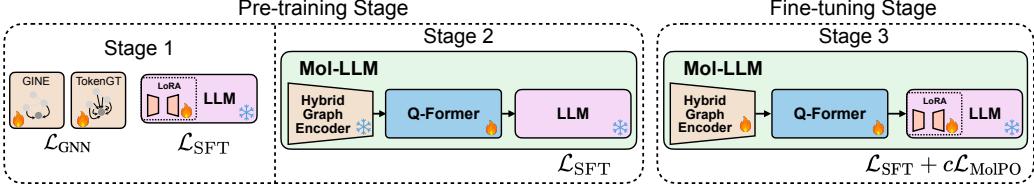


Figure 3: Overview of the three training stages and the loss function used at each stage. The training pipeline consists of a pre-training phase (Stages 1 and 2), followed by a fine-tuning phase (Stage 3). In Stage 1, all modules are trained independently and in parallel, whereas in Stages 2 and 3, the modules are trained in a unified architecture and loss function.

Backbone Large Language Model We adopt Mistral-7B-Instruct-v0.3 [25] as a backbone LLM, following Yu et al. [5]. In order to improve the efficiency in solving molecular tasks, we extend the token codebook with the 3K SELFIES vocabulary from BioT5+ [6] and add dedicated tokens for the digits 0–9, the decimal point, and the negative sign, thereby enabling direct number prediction for regression tasks. Additional task-specific vocabulary covers boolean labels, textual descriptions, and reaction routes, allowing Mol-LLM to natively produce the heterogeneous answer formats required by downstream applications. Examples of these extra tokens appear on the right side of Figure 2.

2.2 Multimodal Training

Stage 1 - Graph Encoder and LLM Pre-training The hybrid graph encoder comprises two GNNs, GINE and TokenGT. We pre-train these two GNNs in parallel with the LLM. The GNN pre-training comprises two complementary tasks: functional group prediction and SELFIES reconstruction. Functional group prediction strengthens representations of the functional groups that govern molecular properties, whereas SELFIES reconstruction encourages the encoder to preserve global structural information. Both tasks share the same graph-level embedding h_g produced by the GNN, as illustrated on the left side of Figure 4. After discarding extremely common or extremely rare functional groups, we retain $K = 72$ distinct groups (dataset construction details are given in Appendix B.1). For functional group prediction, h_g is passed through a three-layer MLP ($1024 \rightarrow 1024 \rightarrow 72$) f_θ^{MLP} and trained with the binary cross-entropy loss $\mathcal{L}_{\text{func}} = -\sum_{k=1}^K (y_{\text{func}}^{(k)} \log f_\theta^{\text{MLP}}(h_g)^{(k)} + (1 - y_{\text{func}}^{(k)}) \log(1 - f_\theta^{\text{MLP}}(h_g)^{(k)}))$, where superscript (k) is the value for functional group k . SELFIES reconstruction reuses h_g as a context for a GPT-2 decoder $\pi_\theta^{\text{GPT-2}}$ that learns to reproduce molecule’s SELFIES string s : $\mathcal{L}_{\text{recon}} = -\sum_t \log \pi_\theta^{\text{GPT-2}}(s_t | h_g, s_{<t})$. The graph encoder is optimized with the combined loss $\mathcal{L}_{\text{GNN}} = \mathcal{L}_{\text{func}} + \mathcal{L}_{\text{recon}}$. Additional training procedures and hyperparameters are provided in Appendix B.2.

The LLM pre-training serves two purposes: (i) injecting molecule-specific prior knowledge and (ii) reducing the compute required during later multimodal training. Accordingly, we pre-train the LLM on exactly the same dataset that will be used later for fine-tuning, optimizing a token-level cross-entropy objective. Given a training instance consisting of a task instruction q , a molecular SELFIES string s , and a ground truth answer y , we minimize $\mathcal{L}_{\text{SFT}} = -\sum_t \log \pi_\theta^{\text{LLM}}(y_t | s, q, y_{<t})$ where t indexes tokens.

Stage 2 - Q-Former Pre-training In Stage 2, only the Q-Former is updated, while both the GNN and the LLM remain frozen. Following Liu et al. [26], we simply reuse the fine-tuning dataset, in which molecular representations and natural language tokens appear in an interleaved format. For each training instance (s, q, y) , the SELFIES string s is converted into its corresponding molecular graph g . The combined model π_θ (GNN+Q-Former+LLM) is then trained for one epoch with the loss defined as $\mathcal{L}_{\text{SFT}} = -\sum_t \log \pi_\theta(y_t | s, q, g, y_{<t})$.

Stage 3 - MolPO: Molecular Structure Preference Optimization We observed that using only SFT training as in conventional multimodal Molecular LLMs [8, 9, 19, 12], result in a graph bypass phenomenon (Figure 1) in solving molecular tasks. To resolve the graph bypass issue, we propose Molecular structure Preference Optimization (MolPO). Rather than simply inputting multimodal molecules into the LLM without consideration for multimodal utilization, MolPO promotes the practical utilization of multimodal molecules by learning the preferences between an original (chosen)

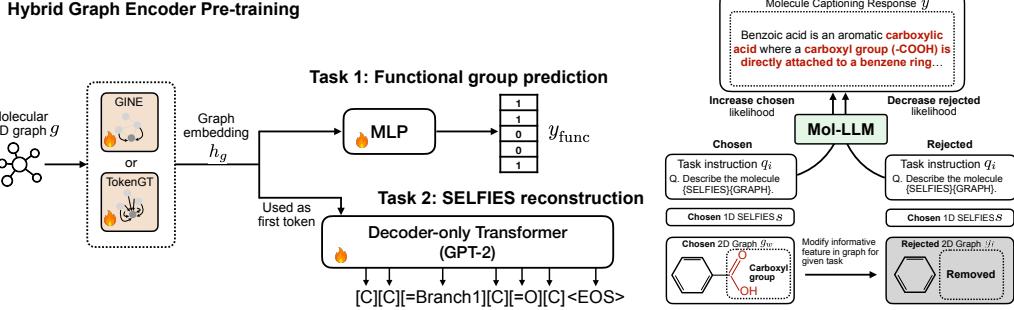


Figure 4: (Left) Overview of the two graph pre-training tasks for the proposed hybrid graph encoder. Two distinct GNN backbones, GINE and TokenGT, are trained independently. (Right) Illustration of the MolPO training objective, which contrasts a chosen molecule with a rejected molecule.

graph g_w and a perturbed (rejected) graph g_ℓ , which is inspired by mDPO [27]. Constructing g_ℓ , it is crucial to introduce perturbations that alter the relationship between the graph and the target. Since molecular features can generally be identified on a substructure basis, we substitute the substructures found in the original g_w as in Figure 4 right panel. This approach offers the advantage of being applicable to any molecular task without significant computational costs or requiring task-specific graph perturbation design (details in Appendix B.4). Based on the reward formulation $r_{w,i} = \frac{\beta}{|y|} \sum_t \log \pi_\theta(y_t | g_w, s, q_i, y_{<t})$ and $r_{\ell,i} = \frac{\beta}{|y|} \sum_t \log \pi_\theta(y_t | g_\ell, s, q_i, y_{<t})$ motivated from SimPO [28], the MolPO objective is defined as follows:

$$\mathcal{L}_{\text{MolPO}} = \mathbb{E}_{(s, q_i, g, y) \sim \mathcal{D}_{\text{tr}}} [-\log \sigma(\min(r_{w,i} - r_{\ell,i}, \lambda_{\text{clip}}|r_{w,i}|) - \gamma_i)], \quad (1)$$

where λ_{clip} is coefficient, and \mathcal{D}_{tr} denotes training dataset. $\gamma_i = \lambda_{\text{margin}} |\mathbb{E}_{(g_w, s, q_i, y)}[r_{w,i}]|$ is a task-adaptive target reward margin for each i -th molecular task, calculated during training. The entire training objective combined is $\mathcal{L}_{\text{SFT}} + c\mathcal{L}_{\text{MolPO}}$, where c is a constant.

In developing a generalist over diverse molecular tasks, we experimentally observed that adopting SimPO’s task-agnostic target reward margin γ results in inappropriate log-sigmoid values due to highly variant reward orders of magnitude across tasks. However, modeling the task-specific reward scale as a hyperparameter is not an ideal solution either, as it adds an additional burden of hyperparameter search for each molecular task. Instead, we introduce a task-adaptive target reward margin with only a task-agnostic hyperparameter λ_{margin} , where the expectation is estimated using an exponential moving average during training.

In addition, given that it is generally easier to lower the rejected reward than to increase the true chosen reward, the preference reward margin can be empirically manipulated by simply reducing $r_{\ell,i}$ without a corresponding enhancement of $r_{w,i}$. To fully harness the benefits of preference optimization without the drawbacks, we introduce margin clipping to appropriately control the influence of the reward margin on parameter updates. Specifically, the margin is constrained so that it cannot exceed a fraction, λ_{clip} of $|r_{w,i}|$. Through this simple margin clipping, the model is prevented from the circumventing unintended effect of preference optimization by solely reducing the rejected reward. Further details of MolPO training are provided in Appendix B.5.

2.3 Extensive Instruction-tuning Dataset

The instruction-tuning dataset for Mol-LLM spans five major molecular task groups: property regression, property classification, reaction prediction, description-guided molecule generation, and molecule captioning. Property regression consists of five tasks—LogS for water solubility (ESOL [5]), LogD for lipophilicity (Lipo [5]), HOMO [7], LUMO [7], and HOMO-LUMO gap [7], and property classification comprises BACE [6], BBBP [5], ClinTox [5], HIV [5], SIDER [5]. Reaction prediction covers forward synthesis (FS), retrosynthesis (RS), and reagent prediction (RP), with FS and RS each divided into Mol-Instructions [7] and SMolInstruct [5] subsets according to their dataset sources. The description-guided molecule generation and molecule captioning tasks are similarly split into ChEBI-20 [29] and SMolInstruct based on their origins. In addition, to enhance the understanding of IUPAC [30]—frequently used in molecular text captions—we incorporate an

Table 1: Performance comparison on molecular property prediction tasks from the MoleculeNet [41] benchmark. A superscript * indicates results evaluated with an official checkpoint, and "NA" denotes cases where no official checkpoint is available. **Boldface** highlights the best scores among generalist models. For semi-generalist models, each variant is annotated with the task group on which it is trained. GPT-4 is evaluated with 5-shots, except for classification performances borrowed from Zhao et al. [23] with zero-shot.

Task	LogS	LogD	HOMO	LUMO	Gap	BACE	BBBP	ClinTox	HIV	SIDER
Metric	RMSE (↓)	RMSE (↓)	MAE (↓)	MAE (↓)	MAE (↓)	ROC-AUC (↑)				
<i>Specialist Models</i>										
InstructMol	NA	NA	0.0048	0.0050	0.0061	82.1	72.4	NA	68.9	NA
MolCA	≥100	≥100	≥1	≥1	≥1	79.8	70.0	89.5	47.0	63.0
MolXPT	NA	NA	NA	NA	NA	88.4	80.0	95.3	78.1	71.7
<i>Semi-Generalist Models</i>										
Mol-Instructions*	4.81	≥100	0.0210	0.0210	0.0203	41.7	58.0	47.8	49.2	48.2
BioT5+*(Clas. & Trans.)	≥100	≥100	≥1	≥1	≥1	81.1	65.1	83.7	67.0	43.7
BioT5+*(Reg. & React.)	≥100	≥100	0.0022	0.0024	0.0028	65.5	51.5	51.0	58.8	52.5
<i>Generalist Models</i>										
GPT-4 (5-shot)	1.68	1.59	0.0227	0.0462	0.0395	62.5	61.5	51.6	65.9	40.5
Galactica	4.34	2.78	0.2329	0.0413	0.2497	58.4	53.5	78.4	72.2	55.9
3D-MoLM*	3.41	4.86	0.0299	0.0536	0.0673	55.5	53.8	53.7	30.6	49.7
ChemDFM*	8.19	6.21	0.1204	0.1262	0.1694	59.5	50.5	60.0	52.4	51.0
LlaSMol*	1.21	1.01	≥1	≥1	≥1	46.7	82.4	77.5	70.3	78.4
Mol-LLM (w/o Graph)	1.36	0.95	0.0044	0.0043	0.0055	80.8	84.3	85.0	76.5	76.1
Mol-LLM	1.28	0.91	0.0044	0.0043	0.0054	80.5	81.1	82.4	75.1	76.3

IUPAC and SELFIES translation dataset [5] to construct an 3.3M extensive instruction-tuning dataset (details in Appendix C.1).

3 Experiments

3.1 Experimental Setup

Baseline Models We group the molecular LLMs compared with Mol-LLM into three broad categories. Specialist models are trained for a single molecular task; semi-generalist models cover a specific task group within one model but do not span all task groups; and generalist models are designed to handle every molecular task group. Representative examples are MolCA [8] for the specialist category, BioT5+ [6] for the semi-generalist category, and Galactica [31] and LlaSMol [5] for the generalist category. Comprehensive details on all baseline models can be found in Appendix D.2.

Evaluation Benchmark In addition to the molecular tasks described in Section 2.3, we evaluate molecular LLM robustness to out-of-distribution (OOD) by proposing two evaluation benchmarks. For LogS prediction, we retain high-confidence solubility labels from AqSol [32], exclude every molecule that also appears in ESOL, and collect molecules of high consistency among labels to construct the OOD evaluation versus ESOL. For reaction prediction, we gather 23K FS and 59K RS data instances from the ORDerly [33] repository except USPTO [34], apply a scaffold split to remove motif overlap with Mol-Instructions [7] and SMolInstruct [5], and reserve 5K examples for evaluation in each task. Full OOD dataset construction details are provided in Appendix C.2.

Evaluation Metrics For property prediction tasks, we report the root mean squared error (RMSE) or mean absolute error (MAE) in regression, and in classification tasks, receiver operating characteristic area under the curve (ROC-AUC) using the predicted probability of the positive class (i.e., *True* token). For reaction prediction and description-guided molecule generation, we evaluate exact match with the target molecule (EXACT), textual similarity (BLEU) [35], molecular fingerprint similarity based on RDKit [36], MACCS keys [37], and Morgan [38] fingerprints (RDKit FTS, MACCS FTS, and MORGAN FTS, respectively), and the proportion of generated molecules that are chemically valid (VALIDITY). For the molecule captioning task, we measure similarity between the generated and reference descriptions using BLEU-2, BLEU-4, ROUGE-1 [39], ROUGE-2, ROUGE-L, and METEOR [40]. For a comprehensive assessment of the molecular LLM, we analyze a wide range of metrics for each molecular task. However, due to space limitations, the main paper reports only the primary metrics. The complete results are provided in Appendix D.3.

3.2 Results

Property Regression and Classification Table 1 summarizes the property regression and classification results. On most tasks, Mol-LLM outperforms every other generalist model, except for LogS,

Table 2: Performance comparison for reaction prediction tasks on Mol-Instructions [7] and SMolInstruct [5] datasets.

Dataset		Mol-Instructions / SMolInstruct					
Task	Forward Synthesis			Retrosynthesis		Reagent Prediction	
Metric	EXACT (\uparrow)	MACCS FTS (\uparrow)	EXACT (\uparrow)	MACCS FTS (\uparrow)	EXACT (\uparrow)	MACCS FTS (\uparrow)	
<i>Specialist Models</i>							
InstructMol	0.536 / NA	0.878 / NA	0.407 / NA	0.852 / NA	0.129	0.539	
MolCA*	0.000 / 0.000	0.494 / 0.357	0.000 / 0.000	0.880 / 0.760	0.000	0.115	
<i>Semi-Generalist Models</i>							
Mol-Instructions*	0.052 / 0.003	0.291 / 0.184	0.069 / 0.015	0.359 / 0.285	0.044	0.364	
BioT5+*(Cls. & Trans.)	0.000 / 0.000	0.152 / 0.187	0.001 / 0.000	0.195 / 0.170	0.000	0.056	
BioT5+*(Reg. & React.)	0.864 / 0.081	0.975 / 0.537	0.642 / 0.152	0.930 / 0.751	0.257	0.621	
<i>Generalist Models</i>							
GPT-4 (5-shot)	0.021 / 0.011	0.728 / 0.634	0.012 / 0.013	0.716 / 0.686	0.000	0.228	
Galactica	0.000 / 0.000	0.257 / 0.377	0.000 / 0.000	0.274 / 0.447	0.000	0.127	
3D-MoLM*	0.000 / 0.000	0.391 / 0.296	0.000 / 0.000	0.451 / 0.372	0.000	0.218	
ChemDFM*	0.000 / 0.002	0.142 / 0.178	0.000 / 0.000	0.440 / 0.443	0.000	0.099	
LlaSMol*	0.743 / 0.629	0.955 / 0.919	0.453 / 0.323	0.885 / 0.827	0.000	0.199	
Mol-LLM (w/o Graph)	0.893 / 0.584	0.983 / 0.904	0.510 / 0.363	0.886 / 0.828	0.202	0.586	
Mol-LLM	0.911 / 0.601	0.987 / 0.908	0.538 / 0.377	0.893 / 0.832	0.225	0.600	

Table 3: Performance comparison for molecule generation and molecule captioning on ChEBI-20 [29] and SMolInstruct [5] datasets.

Dataset		ChEBI-20 / SMolInstruct					
Task	Molecule Generation			Molecule Captioning			
Metric	EXACT (\uparrow)	MACCS FTS (\uparrow)	VALIDITY (\uparrow)	BLEU-4 (\uparrow)	ROUGE-L (\uparrow)	METEOR (\uparrow)	
<i>Specialist Models</i>							
GIT-Mol	0.051 / NA	0.738 / NA	0.93 / NA	0.263 / NA	0.560 / NA	0.533 / NA	
InstructMol	NA / NA	NA / NA	NA / NA	0.371 / NA	0.502 / NA	0.509 / NA	
MolT5	0.311 / 0.317	0.834 / 0.879	0.91 / 0.95	0.508 / 0.366	0.594 / 0.501	0.614 / 0.515	
MolCA*	NA / NA	NA / NA	NA / NA	0.540 / 0.510	0.631 / 0.604	0.652 / 0.628	
MolXPT	0.215 / NA	0.859 / NA	0.98 / NA	0.505 / NA	0.597 / NA	0.626 / NA	
Text+Chem T5	0.322 / NA	0.901 / NA	0.94 / NA	0.542 / NA	0.622 / NA	0.648 / NA	
<i>Semi-Generalist Models</i>							
Mol-Instructions	0.016 / 0.045	0.167 / 0.475	1.00 / 1.00	0.171 / 0.020	0.289 / 0.217	0.271 / 0.124	
BioT5+*(Cls. & Trans.)	0.557 / 0.519	0.907 / 0.897	1.00 / 1.00	0.591 / 0.582	0.649 / 0.644	0.680 / 0.677	
BioT5+*(Reg. & React.)	0.537 / 0.416	0.897 / 0.867	1.00 / 1.00	0.216 / 0.221	0.364 / 0.364	0.323 / 0.321	
<i>Generalist Models</i>							
GPT-4 (5-shot)	0.092 / 0.027	0.745 / 0.726	0.65 / 0.74	0.158 / 0.125	0.303 / 0.273	0.320 / 0.274	
Galactica*	0.000 / 0.000	0.264 / 0.271	0.70 / 0.61	0.000 / 0.000	0.006 / 0.006	0.004 / 0.005	
3D-MoLM*	0.000 / 0.000	0.000 / 0.000	0.00 / 0.00	0.171 / 0.167	0.287 / 0.285	0.326 / 0.329	
ChemDFM*	0.018 / 0.041	0.165 / 0.297	0.19 / 0.13	0.031 / 0.035	0.101 / 0.108	0.078 / 0.085	
LlaSMol*	0.274 / 0.180	0.871 / 0.845	0.95 / 0.93	0.333 / 0.328	0.464 / 0.465	0.466 / 0.470	
Mol-LLM (w/o Graph)	0.431 / 0.362	0.903 / 0.888	1.00 / 1.00	0.482 / 0.477	0.509 / 0.490	0.587 / 0.585	
Mol-LLM	0.443 / 0.368	0.906 / 0.887	1.00 / 0.99	0.493 / 0.482	0.439 / 0.433	0.599 / 0.589	

ClinTox, and SIDER. Notably, even Mol-LLM (w/o Graph) performs on a par with the full model. We attribute this behavior to the small molecular sizes in MoleculeNet [41], which allow the LLM to infer structural information directly from the SELFIES representation.

Reaction Prediction The reaction prediction results are reported in Table 2. Except for the FS task of SMolInstruct dataset, Mol-LLM again leads all generalist models. Since successful reaction prediction depends on recognizing which functional groups can participate during a chemical reaction, these results suggest that pre-training of the GNN on functional group prediction helps Mol-LLM exploit structural cues more effectively. Consistent with this interpretation, omitting the graph input (w/o Graph variant) noticeably degrades performances.

Description-guided Molecule Generation Table 3 shows the results for description-guided molecule generation, whose input prompts contain no molecular graphs. Since both Mol-LLM and the w/o Graph variant receive identical inputs, their scores are nearly indistinguishable. This confirms that Mol-LLM’s ability to use graphs does not impede its instruction-following ability when

Table 4: Evaluation of OOD generalization for reaction prediction on the ORDerly dataset, which is non-USPTO, and LogS on the AqSol dataset.

Dataset	AqSol		ORDerly				
Task	LogS		Forward Synthesis		Retrosynthesis		
Metric	RMSE (↓)	EXACT (↑)	MACCS FTS (↑)	VALIDITY (↑)	EXACT (↑)	MACCS FTS (↑)	VALIDITY (↑)
<i>Semi-Generalist Models</i>							
BioT5+*(Reg. & React.)	1.81	0.095	0.628	1.00	0.139	0.678	1.00
<i>Generalist Models</i>							
GPT-4	2.17	0.000	0.723	0.87	0.000	0.672	0.65
Galactica*	3.20	0.000	0.322	0.49	0.000	0.398	0.38
3D-MoLM*	2.72	0.000	0.288	0.01	0.000	0.396	0.01
ChemDFM*	6.98	0.017	0.428	0.04	0.000	0.406	0.05
LlaSMol*	1.32	0.350	0.881	1.00	0.473	0.875	0.99
Mol-LLM (w/o Graph)	1.10	0.394	0.900	1.00	0.727	0.936	1.00
Mol-LLM	1.02	0.401	0.877	1.00	0.738	0.939	1.00

Table 5: An ablation study on MolPO’s effect on graph utilization. We report RMSE(↓) for LogS and LogD, and EXACT(↑) for FS, RS, RP, and T2M, each representing forward reaction prediction, retrosynthesis, reagent prediction, and molecule generation. "Mol-Inst." and "SMol." denote the Mol-Instructions and SMolInstruct datasets, respectively.

	LogS	LogD	FS (Mol-Inst.)	FS (SMol.)	RS (Mol-Inst.)	RS (SMol.)	RP (Mol-Inst.)	T2M (ChEBI-20)	T2M (SMol.)
Mol-LLM (w/o MolPO)	1.36	0.96	0.907	0.598	0.529	0.368	0.220	0.426	0.355
Mol-LLM	1.28	0.91	0.911	0.601	0.538	0.377	0.225	0.443	0.368

graphs are absent. On both the ChEBI-20 and SMolInstruct datasets, Mol-LLM nonetheless achieves the best results among generalist models.

Molecule Captioning As summarized in Table 3, Mol-LLM again surpasses all baselines. Compared with the w/o Graph variant, the full model obtains consistently higher BLEU and METEOR scores but slightly lower ROUGE scores on both ChEBI-20 and SMolInstruct. The pattern implies that Mol-LLM produces more concise captions: it captures the essential information while omitting peripheral details. We believe MolPO training encourages the model to rely on structural cues and focus on the core content.

Generalization Performance on Out-of-distribution Datasets Table 4 reports OOD results for AqSol. On the in-distribution training tasks (LogS and SIDER), Mol-LLM lags the generalist baseline LlaSMol only marginally. In contrast, it is markedly superior on the OOD AqSol benchmark, demonstrating stronger generalization. A similar trend appears in the reaction prediction FS and RS tasks: Mol-LLM is slightly weaker on in-distribution FS of SMolInstruct but outperforms competitors when evaluated OOD. These findings indicate that MolPO training confers broader generalization across both tasks and input distributions, whereas the semi-generalist BioT5+, which lacks large-scale instruction tuning, suffers a notable drop in performance.

3.3 Ablation Study

MolPO objective enhances molecular graph utilization and task performance. To examine whether incorporating the MolPO objective $\mathcal{L}_{\text{MolPO}}$ during Mol-LLM training leads the model to exploit molecular graph information more effectively than training with SFT alone, we first compare, for each task i , the log-likelihood $r_{w,i}$ obtained when the model is given the chosen graph g_w to the log-likelihood $r_{\ell,i}$ obtained when it is given the rejected graph g_ℓ . We then compute the graph discrimination ratio $\text{GDR} = \frac{1}{N_i} \sum_{n=1}^{N_i} \mathbb{I}[r_{w,i}(n) > r_{\ell,i}(n)]$, where N_i is the number of instances in task i , \mathbb{I} is the indicator function, and $r_{w,i}(n)$ is the log-likelihood for the n -th instance in task i . A GDR close to 1 indicates that the model can clearly identify the correct molecular graph (i.e., it effectively exploits molecular graph information); a value near 0.5 indicates random guessing, and a value near 0 indicates systematic confusion. Figure 1 shows the per-task GDRs—green bars for MolPO-trained models and orange bars for models trained without $\mathcal{L}_{\text{MolPO}}$. The consistently higher GDRs in the MolPO setting confirm that this objective helps the model make better use of molecular graph information. We also compare the multitask fine-tuning performance obtained when $\mathcal{L}_{\text{MolPO}}$ is combined with \mathcal{L}_{SFT} to that obtained when only \mathcal{L}_{SFT} is used. As shown in Table 5, leveraging the graph modality through the MolPO objective improves performances on most tasks.

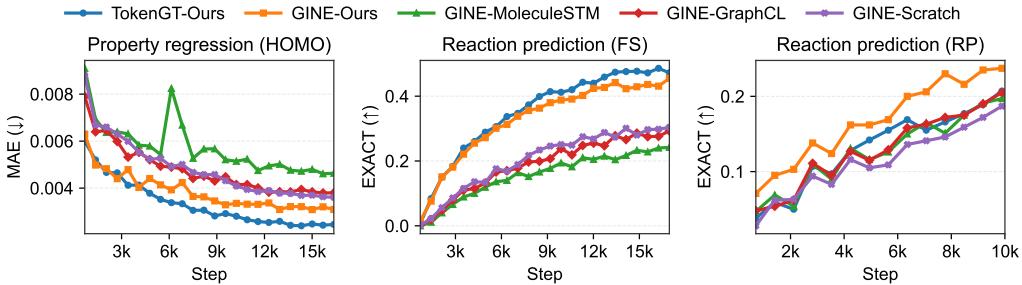


Figure 5: Comparison of fine-tuning performances on three tasks under different GNN architectures and initialization with (or without) pre-trained parameters. Each line is labeled as {GNN architecture}—{initialization}. *Ours* refers to models initialized with parameters obtained via our GNN pre-training method, whereas *Scratch* denotes models trained from random initialization. The x-axis denotes the number of training steps, and the y-axis shows the corresponding evaluation metric.

Our GNN pre-training improves molecular representation. To clearly demonstrate the effect of our GNN pre-training method, we frame the experiment as a single task setting and modify Mol-LLM so that, during fine-tuning, it receives only the task instruction and the 2D molecular graph as inputs, omitting the 1D sequence. The model is trained solely using the loss term \mathcal{L}_{SFT} , and its performance is then compared with different GNN architectures and weight initializations. Figure 5 presents the learning curves for property regression (HOMO) and reaction prediction (FS, RP). The GNN architectures (GINE, TokenGT) and their corresponding initializations are represented as {GNN architecture}—{initialization}. *Scratch* indicates that the GNN is trained from scratch without any pre-trained weights. The model whose GNN is initialized with the proposed pre-training method (*Ours*) consistently outperforms the others, indicating that it learns higher quality molecular representations. Moreover, the existing pre-trained models—MoleculeSTM [15] and GraphCL [42]—perform either worse than or roughly on par with the non-pretrained baseline *Scratch*, which is a surprising outcome.

4 Related Works

Molecular Large Language Models MolT5 [29] extends T5 [43] to bidirectional translation between SMILES strings and natural language, whereas MolXPT [44], built on the GPT architecture [45], unifies text–molecule translation with property prediction. MolCA [8] and GIT-Mol [10] fuse 2D molecular graphs with text via a Q-Former [20], while MoILM [46] further injects 3D geometric cues. UniMoT [11] discretizes Q-Former outputs into graph tokens while 3D-MolT5 [19] introduces 3D structure tokens, enabling generative reasoning over conformers. Although these models exploit molecule structures, each is tailored to a narrow set of tasks. Mol-LLM tackles this limitation by jointly processing text and graphs and by performing translation, prediction, and generation within a single generalist framework.

Instruction-tuning on Molecular Tasks Mol-Instructions [7] introduced the first broad instruction-tuning corpus, inspiring InstructMol [9] to fine-tune multimodal models with task-specific prompts and BioT5+ [6] to perform multitask tuning without structural inputs. LlaSMol [5] scales the idea to 3.3M examples across ten tasks, yielding a single model that matches—or exceeds—specialists. Subsequent work, including UniMoT [11], 3D-MolT5 [19] and 3D-MoLM, couples instruction tuning with 2D/3D structure encoders, yet still lacks a systematic strategy for exploiting multimodal inputs. Consequently, models remain sensitive to task distribution shifts. Mol-LLM fills this gap by unifying instruction tuning with structure-aware training, thereby improving robustness across in-distribution and out-of-distribution tasks.

Preference Optimization on Different Modality DPO [47] aligns language models with human preferences by maximizing the log-probability gap between preferred and rejected outputs; SimPO [28] removes the expensive reference model for lighter training. As multimodal LLMs rise, mDPO [27] adapts the idea to vision–language models by corrupting images to build preference pairs, and numerous follow-ups [48–51] confirm its effectiveness. Yet no study has demonstrated comparable gains for molecular data. Mol-LLM is the first to apply preference optimization to molecular

graphs and text jointly, showing that structure-aware preferences yield stronger generalization than sequence-only tuning while keeping training costs manageable.

5 Conclusion

We introduced MolPO, a multimodal training objective that leverages perturbed molecules to enhance the utility of 2D molecular graphs, together with a hybrid graph encoder pre-training strategy. We also curated a large-scale molecule instruction tuning dataset and, using the proposed methods, developed Mol-LLM, a multimodal generalist molecular large language model. Mol-LLM achieved state-of-the-art performances among generalist molecular models on property regression, property classification, reaction prediction, description-guided molecule generation, and molecule captioning tasks. We believe our approach can be extended beyond 2D molecular graphs to incorporate 3D structural information and molecular metadata, enabling real-world applications such as drug discovery and novel material discovery. A detailed discussion of the limitations are described in Appendix A.

Acknowledgments and Disclosure of Funding

LG AI Research supported this work. This work was also supported by Artificial intelligence industrial convergence cluster development project funded by the Ministry of Science and ICT(MSIT, Korea)&Gwangju Metropolitan City, the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIT) (No. RS-2024-00410082), Institute of Information communications Technology Planning Evaluation (IITP) grant funded by the Korea government(MSIT) (No. RS-2019-II190079, Artificial Intelligence Graduate School Program(Korea University); No.RS-2020-II201336, Artificial Intelligence Graduate School Program(UNIST); No. 2022-0-00612, Geometric and Physical Commonsense Reasoning based Behavior Intelligence for Embodied AI), and partly supported by the Institute of Information & Communications Technology Planning & Evaluation(IITP)-ITRC(Information Technology Research Center) grant funded by the Korea government(MSIT)(IITP-2025-RS-2024-00436857, 15%)

References

- [1] Tom B. Brown, Benjamin Mann, Nick Ryder, Melanie Subbiah, Jared Kaplan, Prafulla Dhariwal, Arvind Neelakantan, Pranav Shyam, Girish Sastry, Amanda Askell, Sandhini Agarwal, Ariel Herbert-Voss, Gretchen Krueger, Tom Henighan, Rewon Child, Aditya Ramesh, Daniel M. Ziegler, Jeffrey Wu, Clemens Winter, Christopher Hesse, Mark Chen, Eric Sigler, Mateusz Litwin, Scott Gray, Benjamin Chess, Jack Clark, Christopher Berner, Sam McCandlish, Alec Radford, Ilya Sutskever, and Dario Amodei. Language models are few-shot learners. In *NeurIPS*, 2023.
- [2] OpenAI. Gpt-4 technical report. *ArXiv*, abs/2303.08774, 2023.
- [3] Gemini Team Google. Gemini: A family of highly capable multimodal models. *ArXiv*, abs/2312.11805, 2023.
- [4] Hugo Touvron, Louis Martin, Kevin Stone, Peter Albert, Amjad Almahairi, Yasmine Babaei, Nikolay Bashlykov, Soumya Batra, Prajjwal Bhargava, Shruti Bhosale, Dan Bikel, Lukas Blecher, Cristian Canton Ferrer, Moya Chen, Guillem Cucurull, David Esiobu, Jude Fernandes, Jeremy Fu, Wenyin Fu, Brian Fuller, Cynthia Gao, Vedanuj Goswami, Naman Goyal, Anthony Hartshorn, Saghar Hosseini, Rui Hou, Hakan Inan, Marcin Kardas, Viktor Kerkez, Madian Khabsa, Isabel Kloumann, Artem Korenev, Punit Singh Koura, Marie-Anne Lachaux, Thibaut Lavril, Jenya Lee, Diana Liskovich, Yinghai Lu, Yuning Mao, Xavier Martinet, Todor Mihaylov, Pushkar Mishra, Igor Molybog, Yixin Nie, Andrew Poulton, Jeremy Reizenstein, Rashi Rungta, Kalyan Saladi, Alan Schelten, Ruan Silva, Eric Michael Smith, Ranjan Subramanian, Xiaoqing Ellen Tan, Binh Tang, Ross Taylor, Adina Williams, Jian Xiang Kuan, Puxin Xu, Zheng Yan, Iliyan Zarov, Yuchen Zhang, Angela Fan, Melanie Kambadur, Sharan Narang, Aurelien Rodriguez, Robert Stojnic, Sergey Edunov, and Thomas Scialom. Llama 2: Open foundation and fine-tuned chat models, 2023. URL <https://arxiv.org/abs/2307.09288>.
- [5] Botao Yu, Frazier N. Baker, Ziqi Chen, Xia Ning, and Huan Sun. Llasmol: Advancing large language models for chemistry with a large-scale, comprehensive, high-quality instruction tuning dataset. *ArXiv*, abs/2402.09391, 2024. URL <https://api.semanticscholar.org/CorpusID:267657622>.

- [6] Qizhi Pei, Lijun Wu, Kaiyuan Gao, Xiaozhuan Liang, Yin Fang, Jinhua Zhu, Shufang Xie, Tao Qin, and Rui Yan. Biot5+: Towards generalized biological understanding with iupac integration and multi-task tuning. *ArXiv*, abs/2402.17810, 2024. URL <https://api.semanticscholar.org/CorpusID:268041632>.
- [7] Yin Fang, Xiaozhuan Liang, Ningyu Zhang, Kangwei Liu, Rui Huang, Zuo Chen, Xiaohui Fan, and Huajun Chen. Mol-instructions: A large-scale biomolecular instruction dataset for large language models. *ArXiv*, abs/2306.08018, 2023. URL <https://api.semanticscholar.org/CorpusID:259164901>.
- [8] Zhiyuan Liu, Sihang Li, Yancheng Luo, Hao Fei, Yixin Cao, Kenji Kawaguchi, Xiang Wang, and Tat-Seng Chua. Molca: Molecular graph-language modeling with cross-modal projector and uni-modal adapter. *ArXiv*, abs/2310.12798, 2023. URL <https://api.semanticscholar.org/CorpusID:264306303>.
- [9] He Cao, Zijing Liu, Xingyu Lu, Yuan Yao, and Yu Li. Instructmol: Multi-modal integration for building a versatile and reliable molecular assistant in drug discovery. *ArXiv*, abs/2311.16208, 2023. URL <https://api.semanticscholar.org/CorpusID:265466509>.
- [10] Pengfei Liu, Yiming Ren, Jun Tao, and Zhixiang Ren. Git-mol: A multi-modal large language model for molecular science with graph, image, and text. *Computers in Biology and Medicine*, 171:108073, March 2024. ISSN 0010-4825. doi: 10.1016/j.combiomed.2024.108073. URL <http://dx.doi.org/10.1016/j.combiomed.2024.108073>.
- [11] Juzheng Zhang, Yatao Bian, Yongqiang Chen, and Quanming Yao. Unimot: Unified molecule-text language model with discrete token representation, 2024. URL <https://arxiv.org/abs/2408.00863>.
- [12] Sihang Li, Zhiyuan Liu, Yanchen Luo, Xiang Wang, Xiangnan He, Kenji Kawaguchi, Tat-Seng Chua, and Qi Tian. 3d-molm: Towards 3d molecule-text interpretation in language models. In *ICLR*, 2024.
- [13] David Weininger. Smiles, a chemical language and information system. 1. introduction to methodology and encoding rules. *J. Chem. Inf. Comput. Sci.*, 28(1):31–36, feb 1988. ISSN 0095-2338. doi: 10.1021/ci00057a005. URL <https://doi.org/10.1021/ci00057a005>.
- [14] Mario Krenn, Florian Häse, AkshatKumar Nigam, Pascal Friederich, and Alan Aspuru-Guzik. Self-referencing embedded strings (selfies): A 100string representation. *Machine Learning: Science and Technology*, 1(4):045024, October 2020. ISSN 2632-2153. doi: 10.1088/2632-2153/aba947. URL <http://dx.doi.org/10.1088/2632-2153/aba947>.
- [15] Shengchao Liu, Weili Nie, Chengpeng Wang, Jiarui Lu, Zhuoran Qiao, Ling Liu, Jian Tang, Chaowei Xiao, and Anima Anandkumar. Multi-modal molecule structure-text model for text-based retrieval and editing, 2024. URL <https://arxiv.org/abs/2212.10789>.
- [16] Yuyang Wang, Jianren Wang, Zhonglin Cao, and Amir Barati Farimani. Molecular contrastive learning of representations via graph neural networks. *Nature Machine Intelligence*, 4:279–287, 2022.
- [17] Bing Su, Dazhao Du, Zhao Yang, Yujie Zhou, Jiangmeng Li, Anyi Rao, Hao Sun, Zhiwu Lu, and Ji-Rong Wen. A molecular multimodal foundation model associating molecule graphs with natural language, 2022. URL <https://arxiv.org/abs/2209.05481>.
- [18] Youwei Liang, Ruiyi Zhang, Li Zhang, and Pengtao Xie. Drugchat: Towards enabling chatgpt-like capabilities on drug molecule graphs, 2023. URL <https://arxiv.org/abs/2309.03907>.
- [19] Qizhi Pei, Lijun Wu, Kaiyuan Gao, Jinhua Zhu, and Rui Yan. 3d-molt5: Towards unified 3d molecule-text modeling with 3d molecular tokenization, 2024. URL <https://arxiv.org/abs/2406.05797>.
- [20] Junnan Li, Dongxu Li, Silvio Savarese, and Steven Hoi. Blip-2: Bootstrapping language-image pre-training with frozen image encoders and large language models, 2023. URL <https://arxiv.org/abs/2301.12597>.

- [21] Weihua Hu, Bowen Liu, Joseph Gomes, Marinka Zitnik, Percy Liang, Vijay Pande, and Jure Leskovec. Strategies for pre-training graph neural networks. In *International Conference on Learning Representations*, 2020.
- [22] Jinwoo Kim, Dat Nguyen, Seonwoo Min, Sungjun Cho, Moontae Lee, Honglak Lee, and Seunghoon Hong. Pure transformers are powerful graph learners. *Advances in Neural Information Processing Systems*, 35:14582–14595, 2022.
- [23] Zihan Zhao, Da Ma, Lu Chen, Liangtai Sun, Zihao Li, Yi Xia, Bo Chen, Hongshen Xu, Zichen Zhu, Su Zhu, et al. Chemdfm: A large language foundation model for chemistry. *arXiv preprint arXiv:2401.14818*, 2024.
- [24] Qimai Li, Zhichao Han, and Xiao-Ming Wu. Deeper insights into graph convolutional networks for semi-supervised learning. In *Proceedings of the AAAI conference on artificial intelligence*, volume 32, 2018.
- [25] Albert Q. Jiang, Alexandre Sablayrolles, Arthur Mensch, Chris Bamford, Devendra Singh Chaplot, Diego de las Casas, Florian Bressand, Gianna Lengyel, Guillaume Lample, Lucile Saulnier, Lélio Renard Lavaud, Marie-Anne Lachaux, Pierre Stock, Teven Le Scao, Thibaut Lavril, Thomas Wang, Timothée Lacroix, and William El Sayed. Mistral 7b, 2023. URL <https://arxiv.org/abs/2310.06825>.
- [26] Haotian Liu, Chunyuan Li, Qingyang Wu, and Yong Jae Lee. Visual instruction tuning. *ArXiv*, abs/2304.08485, 2023. URL <https://api.semanticscholar.org/CorpusID:258179774>.
- [27] Fei Wang, Wenxuan Zhou, James Y. Huang, Nan Xu, Sheng Zhang, Hoifung Poon, and Muhaoo Chen. mdpo: Conditional preference optimization for multimodal large language models. *ArXiv*, abs/2406.11839, 2024. URL <https://api.semanticscholar.org/CorpusID:270560448>.
- [28] Yu Meng, Mengzhou Xia, and Danqi Chen. Simpo: Simple preference optimization with a reference-free reward. *ArXiv*, abs/2405.14734, 2024. URL <https://api.semanticscholar.org/CorpusID:269983560>.
- [29] Carl N. Edwards, T. Lai, Kevin Ros, Garrett Honke, and Heng Ji. Translation between molecules and natural language. *ArXiv*, abs/2204.11817, 2022. URL <https://api.semanticscholar.org/CorpusID:248376906>.
- [30] Henri A Favre and Warren H Powell. *Nomenclature of organic chemistry: IUPAC recommendations and preferred names 2013*. Royal Society of Chemistry, 2013.
- [31] Ross Taylor, Marcin Kardas, Guillem Cucurull, Thomas Scialom, Anthony S. Hartshorn, Elvis Saravia, Andrew Poultan, Viktor Kerkez, and Robert Stojnic. Galactica: A large language model for science. *ArXiv*, abs/2211.09085, 2022. URL <https://api.semanticscholar.org/CorpusID:253553203>.
- [32] Murat Cihan Sorkun, Abhishek Khetan, and Süleyman Er. Aqsoldb, a curated reference set of aqueous solubility and 2d descriptors for a diverse set of compounds. *Scientific Data*, 6, 2019. URL <https://api.semanticscholar.org/CorpusID:199491456>.
- [33] Daniel S. Wigh, Joe Arrowsmith, Alexander Pomberger, Kobi C. Felton, and Alexei A. Lapkin. Orderly: Data sets and benchmarks for chemical reaction data. *Journal of Chemical Information and Modeling*, 64:3790 – 3798, 2024. URL <https://api.semanticscholar.org/CorpusID:269325115>.
- [34] Jinmao Wei, Xiao-Jie Yuan, Qinghua Hu, and Shuqin Wang. A novel measure for evaluating classifiers. *Expert Syst. Appl.*, 37:3799–3809, 2010. URL <https://api.semanticscholar.org/CorpusID:9240275>.
- [35] Kishore Papineni, Salim Roukos, Todd Ward, and Wei-Jing Zhu. Bleu: a method for automatic evaluation of machine translation. In *Proceedings of the 40th annual meeting of the Association for Computational Linguistics*, pages 311–318, 2002.
- [36] Greg Landrum. Rdkit documentation. *Release*, 1(1-79):4, 2013.

- [37] Joseph L Durant, Burton A Leland, Douglas R Henry, and James G Nourse. Reoptimization of mdl keys for use in drug discovery. *Journal of chemical information and computer sciences*, 42(6):1273–1280, 2002.
- [38] Harry L Morgan. The generation of a unique machine description for chemical structures-a technique developed at chemical abstracts service. *Journal of chemical documentation*, 5(2):107–113, 1965.
- [39] Chin-Yew Lin. Rouge: A package for automatic evaluation of summaries. In *Text summarization branches out*, pages 74–81, 2004.
- [40] Satanjeev Banerjee and Alon Lavie. Meteor: An automatic metric for mt evaluation with improved correlation with human judgments. In *Proceedings of the acl workshop on intrinsic and extrinsic evaluation measures for machine translation and/or summarization*, pages 65–72, 2005.
- [41] Zhenqin Wu, Bharath Ramsundar, Evan N. Feinberg, Joseph Gomes, Caleb Geniesse, Aneesh S. Pappu, Karl Leswing, and Vijay S. Pande. Moleculenet: a benchmark for molecular machine learning. *Chemical Science*, 9:513 – 530, 2017. URL <https://api.semanticscholar.org/CorpusID:217680306>.
- [42] Yuning You, Tianlong Chen, Yongduo Sui, Ting Chen, Zhangyang Wang, and Yang Shen. Graph contrastive learning with augmentations. *Advances in neural information processing systems*, 33:5812–5823, 2020.
- [43] Colin Raffel, Noam Shazeer, Adam Roberts, Katherine Lee, Sharan Narang, Michael Matena, Yanqi Zhou, Wei Li, and Peter J Liu. Exploring the limits of transfer learning with a unified text-to-text transformer. *Journal of machine learning research*, 21(140):1–67, 2020.
- [44] Zequn Liu, Wei Zhang, Yingce Xia, Lijun Wu, Shufang Xie, Tao Qin, Ming Zhang, and Tie-Yan Liu. Molxpt: Wrapping molecules with text for generative pre-training. In *ACL*, 2023.
- [45] Alec Radford, Jeffrey Wu, Rewon Child, David Luan, Dario Amodei, Ilya Sutskever, et al. Language models are unsupervised multitask learners. *OpenAI blog*, 1(8):9, 2019.
- [46] Xiangru Tang, Andrew Tran, Jeffrey Tan, and Mark B. Gerstein. Mollm: a unified language model for integrating biomedical text with 2d and 3d molecular representations. *Bioinformatics*, 40:i357 – i368, 2024. URL <https://api.semanticscholar.org/CorpusID:265455405>.
- [47] Rafael Rafailov, Archit Sharma, Eric Mitchell, Christopher D Manning, Stefano Ermon, and Chelsea Finn. Direct preference optimization: Your language model is secretly a reward model. In A. Oh, T. Naumann, A. Globerson, K. Saenko, M. Hardt, and S. Levine, editors, *Advances in Neural Information Processing Systems*, volume 36, pages 53728–53741. Curran Associates, Inc., 2023. URL https://proceedings.neurips.cc/paper_files/paper/2023/file/a85b405ed65c6477a4fe8302b5e06ce7-Paper-Conference.pdf.
- [48] Wenyi Xiao, Ziwei Huang, Leilei Gan, Wanggui He, Haoyuan Li, Zhelun Yu, Hao Jiang, Fei Wu, and Linchao Zhu. Detecting and mitigating hallucination in large vision language models via fine-grained ai feedback. *ArXiv*, abs/2404.14233, 2024. URL <https://api.semanticscholar.org/CorpusID:269293208>.
- [49] Yiyang Zhou, Chenhang Cui, Rafael Rafailov, Chelsea Finn, and Huaxiu Yao. Aligning modalities in vision large language models via preference fine-tuning. *ArXiv*, abs/2402.11411, 2024. URL <https://api.semanticscholar.org/CorpusID:267750239>.
- [50] Renjie Pi, Tianyang Han, Wei Xiong, Jipeng Zhang, Runtao Liu, Rui Pan, and Tong Zhang. Strengthening multimodal large language model with bootstrapped preference optimization. *ArXiv*, abs/2403.08730, 2024. URL <https://api.semanticscholar.org/CorpusID:268379605>.
- [51] Yihe Deng, Pan Lu, Fan Yin, Ziniu Hu, Sheng Shen, James Zou, Kai-Wei Chang, and Wei Wang. Enhancing large vision language models with self-training on image comprehension. *ArXiv*, abs/2405.19716, 2024. URL <https://api.semanticscholar.org/CorpusID:270123045>.

- [52] Iz Beltagy, Kyle Lo, and Arman Cohan. Scibert: A pretrained language model for scientific text. In *Conference on Empirical Methods in Natural Language Processing*, 2019. URL <https://api.semanticscholar.org/CorpusID:202558505>.
- [53] Carl Edwards, ChengXiang Zhai, and Heng Ji. Text2mol: Cross-modal molecule retrieval with natural language queries. In *Proceedings of the 2021 Conference on Empirical Methods in Natural Language Processing*, pages 595–607, 2021.
- [54] Sunghwan Kim, Jie Chen, Tiejun Cheng, Asta Gindulyte, Jia He, Siqian He, Qingliang Li, Benjamin A. Shoemaker, Paul A. Thiessen, Bo Yu, Leonid Y. Zaslavsky, Jian Zhang, and Evan E. Bolton. Pubchem 2023 update. *Nucleic acids research*, 2022. URL <https://api.semanticscholar.org/CorpusID:253182955>.

A Limitation

Performance Degradation from Limited Molecular Distribution in Classification Tasks When the training data lacks sufficient diversity, preference optimization approaches using input preference pairs could suffer performance degradation on test or out-of-distribution datasets. In the case of MolPO, if the training molecular distribution is too narrow or contains spurious patterns unrelated to the given molecular task, the model may inappropriately regard molecules in test set or out-of-distribution (OOD) dataset as rejected molecules, based solely on their non-in-distribution characteristics. This hypothesis is consistent with the observations in Table 1 for the classification datasets. The classification datasets are substantially smaller than the datasets in the other task groups. More than half of them contain only approximately 1K samples, compared with 3.3M samples in the entire training dataset, which explains why MolPO’s performance either remained unchanged or slightly decreased. The principled and necessary solution to this issue is basically to procure more diverse molecular distributions. We anticipate that the research community will pay more attention to developing diverse and comprehensive property classification datasets.

In-depth Analysis across Molecular Tasks Beyond the overall improvement in benchmark performance, an in-depth analysis is needed to understand what qualitative changes occur for each molecular task from the improved graph utilization by MolPO. It is necessary to identify trends that cannot be determined by performance metrics alone, such as which molecular features are difficult to capture with sequence-only approaches, and whether these identified molecular features have strong practical impact. Such analysis could be particularly interesting for property prediction tasks where spatial recognition of molecules is important.

Multi-step Reasoning and Multi-turn Interaction As demonstrated by recent successful LLMs [2, 3], impactful real-world applications of LLMs critically depend on multi-step reasoning capabilities and multi-turn interactions between LLMs and users. However, research on these two aspects remains significantly underdeveloped in the field of molecular LLMs. Such research requires different considerations from single-turn instruction tuning, beginning with dataset construction, and necessitates appropriate training objectives and reward modeling. It is an interesting direction to extend molecular LLMs to multi-step reasoning and multi-turn interaction for practical applications.

B Implementation Details

This section discusses the details of the Mol-LLM implementation. All the necessary materials to reproduce the results through Tables 1 to 4, including code, trained model, and test set, are available at <https://anonymous.4open.science/r/mol-llm-neurips2025-93EB>.

B.1 Functional Group Prediction Dataset for Graph Encoder Pre-training

As explained in Section 2.2, the proposed graph encoder pre-training conducts functional group prediction of a given molecule, a kind of self-supervision task carried out only with the input molecule. The principal challenge in constructing the functional group prediction dataset is the severe class imbalance: some groups occur in most molecules, whereas others are exceedingly rare. Leveraging the RDKit Fragments module³, we enumerate 87 functional groups and quantify their occurrences across the entire PubChem database, as summarized in the top panel of Figure 6. Figure 6 illustrates functional group imbalance, for example, `fr_NHO` (tertiary amines) appears in many molecules, whereas `fr_prisulfonamid` (primary sulfonamides) are scarce. This imbalance can cause overfitting to dominant classes instead of learning general chemical knowledge. To alleviate the overfitting problem, we remove the 11 most prevalent groups (from `fr_NHO` to `fr_aryl_methyl`) and the rarest group (`fr_prisulfonamid`), retaining 72 functional groups. The middle panel of Figure 6 shows the reduced yet still skewed distribution. To adjust the skewed distribution, we apply sparsity-aware importance sampling as follows. Given M molecules and G retained groups, let $x_{i,g} \in \{0, 1\}$ indicate the presence of group g in molecule i . Then we can define group frequencies as $c_g = \sum_{i=1}^M x_{i,g}$. Here, we implement importance sampling that favors rarer groups by introducing the scaling factor

³<https://www.rdkit.org/docs/source/rdkit.Chem.Fragments.html>

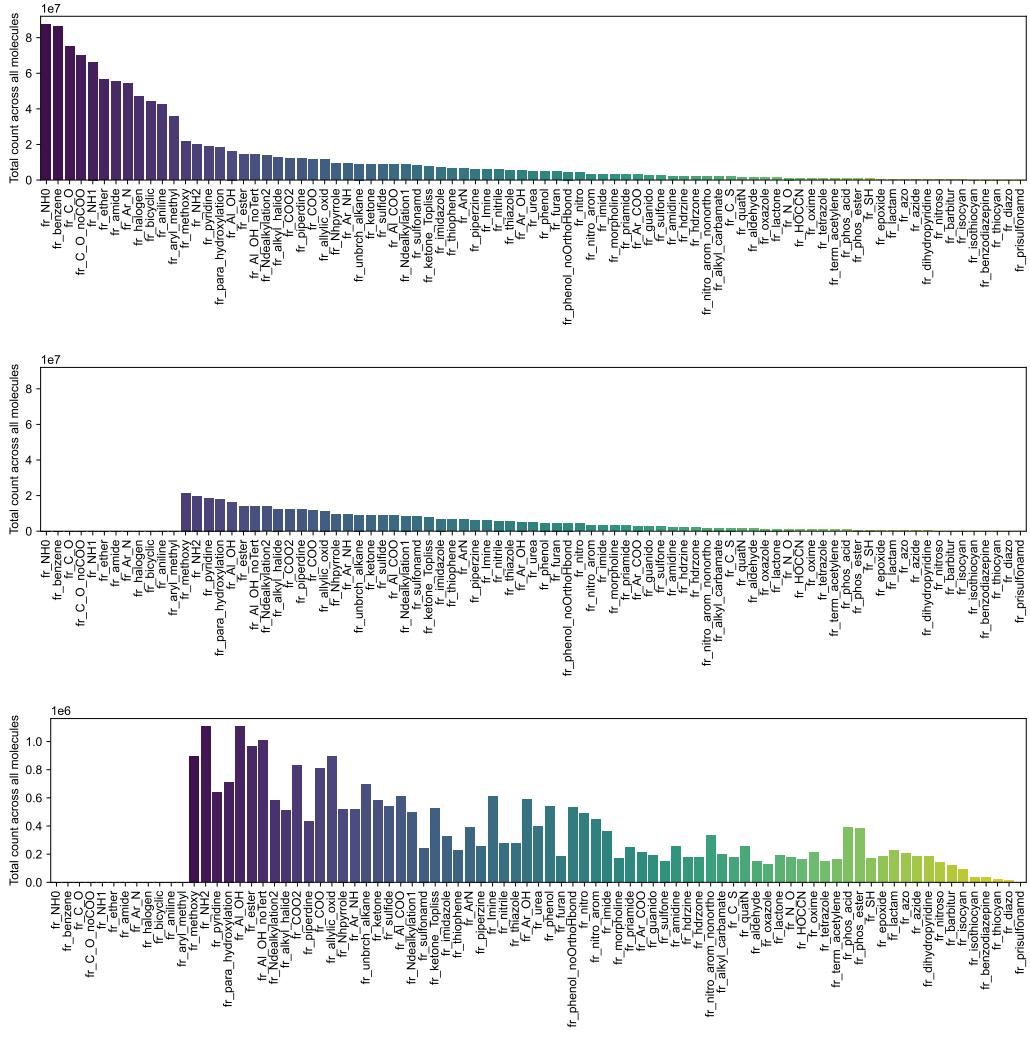


Figure 6: (Top) Distribution of functional groups present in molecules from the PubChem database. (Middle) Distribution of functional groups in PubChem molecules after excluding groups that are either overly common or extremely rare. (Bottom) Distribution of functional groups obtained after sampling 5M molecules from PubChem database, considering functional group sparsity. Since the number of molecules differs among panels, the y-axis scale varies across plots for visualization purposes.

$$\sigma_i = \left(\sum_g x_{i,g} s_g \right)^2.$$

Normalizing the scores yields a categorical distribution $p_i = \sigma_i / \sum_{j=1}^M \sigma_j$, from which we sample 5M molecules. The resulting distribution (bottom panel of Figure 6) is flatter than before, which enables the graph encoder to learn more unbiased chemical knowledge than when trained on the raw PubChem molecule distribution.

B.2 Details of Graph Encoder and Pre-training

Architecture Both GNN components of the hybrid graph encoder—GINE and TokenGT—use a hidden dimension $d_g = 1024$ and five message-passing layers. We replace the original transformer blocks of TokenGT with a BERT encoder implemented in FlashAttention-2 and configured

Table 6: Comparison of MAE (\downarrow) across different GNN training settings on the QM9 dataset.

Property	Description	GINE (Tuning)	GINE (Frozen)	GINE (Frozen MoleculeSTM)
μ	Dipole moment	0.5247	0.9616	1.0927
α	Isotropic polarizability	1.026	3.1919	3.3589
ϵ_{HOMO}	Highest occupied molecular orbital energy (HOMO)	0.1558	0.2864	0.357
ϵ_{LUMO}	Lowest unoccupied molecular orbital energy (LUMO)	0.1428	0.3555	0.4581
$\Delta\epsilon$	Gap between ϵ_{HOMO} and ϵ_{LUMO} (Gap)	0.1817	0.4003	0.3997
$\langle R^2 \rangle$	Electronic spatial extent	24.7215	94.5913	103.2612
$ZPVE$	Zero point vibrational energy	0.0471	0.3056	0.234
U_0	Internal energy at 0K	9,474.99	10,302.67	10,176.77
U	Internal energy at 298.15K	10,160.12	10,550.07	10,134.84
H	Enthalpy at 298.15K	10,295.32	10,466.08	10,057.47
G	Free energy at 298.15K	9,596.59	10,278.72	10,142.24
c_v	Heat capacity at 298.15K	0.5053	1.1965	1.4149
U_0^{ATOM}	Atomization energy at 0K	0.9713	3.6615	3.2477
U^{ATOM}	Atomization energy at 298.15K	0.8442	3.4631	3.309
H^{ATOM}	Atomization enthalpy at 298.15K	0.999	3.6308	3.2287
G^{ATOM}	Atomization free energy at 298.15K	1.0225	3.5317	3.4369
A	Rotational constant	0.9253	0.7283	1.0479
B	Rotational constant	0.1515	0.2428	0.2511
C	Rotational constant	0.0773	0.172	0.1368

with eight attention heads, thereby maximizing GPU throughput. Within TokenGT, the node- and edge-projection dimensions are both 64, and we adopt the graph laplacian eigenvector variant for node positional encoding.

Pre-training GINE and TokenGT are pre-trained with the same set of hyperparameters. For SELFIES reconstruction, sequences are truncated to a maximum length of 512 tokens; tokens beyond this limit do not contribute to the loss calculation. The GPT-2 decoder used for reconstruction consists of six layers, eight attention heads, and an embedding size of 1024. We train for 50 epochs with a learning rate of 1×10^{-4} , a batch size of 64, and the AdamW optimizer. Training is performed on the 5M molecule dataset described in Appendix B.1, further augmented only by adding the corresponding SELFIES strings, and all experiments are run on four NVIDIA A100 GPUs.

B.3 Investigation of Graph Encoder Used in Prior Work

In Section 3.3, we show that the downstream performance of the LLM integrated with pre-trained GNNs used in Liu et al. [8], Cao et al. [9], which are MoleculeSTM [15] and GraphCL [42], does not improve from that of random initialization. To further investigate the graph representation of MoleculeSTM, we conducted an additional experiment evaluating MoleculeSTM in isolation from the LLM on the QM9 datasets. In this experiment, the graph embedding h_g is obtained by mean-pooling the node embeddings, and then passed to a simple MLP, a regression head, whose output is used for training over MSE minimization. While tuning the regression head, we compare three GNN tuning settings: tuning a randomly initialized GNN, freezing a randomly initialized GNN, and freezing a GNN initialized with MoleculeSTM. Table 6 reports the mean absolute error (MAE) for each property. It turns out that, when only the regression head is trained, the gap between random and MoleculeSTM initialization remains negligible w.r.t. the jointly training of GINE, reinforcing our observation that the current pre-trained GNN model fails to capture useful molecular representations. All models were trained for 1,500 epochs with a batch size of 128 using the Adam optimizer with a learning rate of 10^{-4} on four NVIDIA A100 GPUs.

B.4 Molecular Structure Preference Pair

To improve the graph utilization of our model, we create molecular structural preference pairs, which are required for Molecular Structure Preference Optimization (MoIPO). Specifically, as a generalist molecular LLM, it requires a preference pair generation method applicable across various molecular tasks. Therefore, we employed functional group-based substructure modification, which can alter molecular features based on only the input molecule, without requiring task-specific design. For this, we propose Molecular ACCess System (MACCS) [37] keys-based substructure modification method directly modifies molecular substructures by randomly removing and adding them. This approach first identifies the substructures of the molecule corresponding to MACCS keys, generating two lists: one containing the MACCS keys representing functional groups present in the molecule, and the other containing the keys for functional groups absent from the molecule. Then we sample random

Table 7: Model hyperparameters used for Mol-LLM architecture, evaluation, and training stages.

(a) Q-Former, LoRA, evaluation		(b) Training hyperparameters for each stage		
Parameter	Value	Parameter	Stage 1	Stage 2
<i>Q-Former</i>		max_length	512	
bert_hidden_dim	768	batch_size	968	1024
bert_name	scibert [52]	optimizer		adamw
num_query_token	32	scheduler	linear_warmup_cosine_lr	
bert_layers	5	weight_decay	0.05	
<i>LoRA</i>		min_lr		10^{-5}
lora_r	64	init_lr	10^{-4}	10^{-4}
lora_alpha	32	warmup_lr	10^{-5}	10^{-5}
lora_dropout	0.1	warmup_epochs	0.25	4×10^{-6}
<i>Evaluation</i>		gradient_clip_val	0.5	
gen_max_len	256	precision	bf16-mixed	
num_beams	1	c	NA	NA
		λ_{margin}	NA	0.25
		λ_{clip}	NA	1.0

keys from the present MACCS keys to remove from the original molecular graph. Subsequently, other random keys are chosen from the list of absent MACCS keys, and functional groups corresponding to the selected MACCS keys are attached at a random position in the molecule. We set the number of MACCS keys randomly selected to 30 percent of the number of each molecule’s present MACCS keys. This method effectively alters molecular structural information without task-specific design, at the same time, it does not require heavy computation.

B.5 Details of Mol-LLM

This section describes the details of the Mol-LLM architecture and training, including the hyperparameters listed in Table 7.

Architecture When using Q-Former as the cross-modal projector, instead of using randomly initialized weights, we initialize it, similarly to Liu et al. [8], using the parameters of a 12-layer pre-trained transformer encoder with an embedding dimension of 768. However, we observed that successful multi-task learning can be achieved without fully utilizing all 12 layers of the Q-Former while maintaining performance without significant performance degradation. Therefore, to reduce the pre-training cost of Q-Former, we use only 5 layers instead of all 12 layers. The number of Q-Former query tokens is set to 32 for multi-task learning, which is more than the eight used in prior work [8]. We set the LoRA rank to 64, alpha to 32, and the dropout rate to 0.1.

Three Stage Training For component ablation, we maintain identical hyperparameters for Mol-LLM, Mol-LLM (w/o Graph), and Mol-LLM (w/o MolPO), as specified in Table 7. In Stage 1, along with the GNN pre-training described in Appendix B.2, we fine-tune only the LoRA parameters of the LLM for 12 epochs. In Stage 2, we train the Q-Former for a single epoch to align the LLM and GNN embeddings learned in Stage 1. Next, in Stage 3, as described in Section 2, we train using the combined objective $\mathcal{L}_{\text{SFT}} + c\mathcal{L}_{\text{MolPO}}$, which combines both the SFT and MolPO objectives. Here, the scaling factor $c = 0.25$ is adjusted to ensure that the scales between \mathcal{L}_{SFT} and $c\mathcal{L}_{\text{MolPO}}$ do not differ significantly. For the hyperparameters used in $\mathcal{L}_{\text{MolPO}} = \mathbb{E}_{(s, q_i, g, y) \sim \mathcal{D}_{\text{tr}}}[-\log \sigma(\min(r_{w,i} - r_{\ell,i}, \lambda_{\text{clip}}|r_{w,i}|) - \gamma_i)]$, we use $\lambda_{\text{margin}} = 0.5$ and $\lambda_{\text{clip}} = 1.0$, respectively. For Stage 3, we initially trained the model for 6 epochs using the hyperparameters specified in Table 7; however, we observed that performance had not fully converged on several tasks. Therefore, we report experimental results based on the model trained for one additional epoch using a reduced initial learning rate of 2×10^{-5} (half of the original value) without a warm-up epoch.

Table 8: Details of Mol-LLM instruction-tuning training data and its sources.

Task	Data Sources	# Train	# Test	# All
Property Prediction (Regression)	MoleculeNet [41]	359,556	2,519	362,075
Property Prediction (Classification)	MoleculeNet [41]	59,607	7,460	67,067
Forward Reaction Prediction	USPTO [34]	1,079,379	5,062	1,084,441
Retrosynthesis	USPTO 500MT	968,943	5,156	974,099
Reagent Prediction	USPTO 500K	121,896	1,000	122,896
Molecule Captioning	ChEBI-20 [53]	58,763	5,793	64,556
Description-Guided Molecule Generation	ChEBI-20	58,763	5,838	64,601
Name Conversion	PubChem [54]	599,767	-	599,767
Overall		3,306,674	40,757	3,347,431

C Molecular Instruction-tuning Dataset

This section describes the construction details of our molecular instruction-tuning dataset, whose statistics are described in Table 8. It covers 21 tasks grouped into eight categories, comprising about 3.3M training and 40K test instances.

C.1 In-distribution Dataset Construction

We integrate molecules for each task from the molecule-oriented datasets Mol-Instructions [8] and SMolInstruct [5]. During this integration process, tasks present in both datasets, such as forward synthesis and molecule captioning, are deduplicated to ensure that molecules included in the test set of one dataset do not appear in the training set of the combined dataset. In this process, we exclude certain tasks that are not directly relevant (e.g., NC-I2F and NC-S2F). For tasks absent in both datasets, such as BACE, molecules are directly extracted from the original data sources to construct the dataset. Finally, we augment the resulting task-specific datasets with instructions using templates adopted and extended from SMolInstruct.

C.2 Out-of-distribution Dataset Construction

LogS - AqSol Dataset To evaluate Mol-LLM on OOD LogS prediction, we use the AqSol dataset [32], which contains multiple water solubility datasets in addition to ESOL. The AqSol dataset is constructed by curating data from 9 different water solubility datasets for 9,982 unique molecules. For our out-of-distribution evaluation on the ESOL dataset, we removed instances from the AqSol dataset that overlap with the ESOL dataset based on the molecule’s InChI. Notably, it is common for different prediction datasets to annotate different labels for the same molecule. This occurs due to experimental errors or when LogS labels are predicted based on different prediction models. To ensure high label reliability, we retain 925 molecules whose labels are either unique or have an inter-dataset standard deviation < 0.1 .

Reaction Prediction - ORDerly Dataset From Open Reaction Database (ORD) [33], we collected non-USPTO reaction data relevant to forward synthesis and retrosynthesis. Since all reactions in our instruction-tuning dataset are derived from USPTO data, the reactions extracted from non-USPTO sources constitute out-of-distribution (OOD) samples. Then, to ensure no duplication between the collected reaction data and those in Mol-Instructions [7] and SMolInstruct [5], we filtered out reactions from these non-USPTO sources whose input molecule scaffolds overlap with molecules used for reaction prediction training. During this, we first extract data for the forward synthesis task and subsequently ensure that the retrosynthesis reaction data extraction does not duplicate entries already obtained for the forward synthesis. Finally, we apply scaffold splitting to each dataset, resulting in 18K training samples and 5K test samples for forward synthesis, and 54K training samples and 5K test samples for retrosynthesis.

D Experimental Details

This section provides supplementary information necessary for understanding and reproducing the main experiments. In Appendix D.1, we detail the resource requirements and execution times needed to reproduce the main results, followed by Appendix D.2 where we define and categorize the baseline

Table 9: Numbers of training and evaluation of impactful molecular tasks, which consist of property classification, property regression, reaction prediction, molecule generation, and molecule captioning, of each model. BioT5+ comprises two separate models, each trained on a distinct group of tasks.

Model	# Train Tasks	# Eval Tasks
BioT5+ [6] (Mol-Instructions)	6	6
BioT5+ (ChEBI-20)	6	6
LlaSMol [5]	10	10
Mol-LLM (Ours)	23	15

Table 10: Summary of baseline models categorized by their input modality and model type.

Model	Input Modality	Task Coverage
InstructMol [9]	1D Sequence & 2D Graph	Specialist
MolCA [8]	1D Sequence & 2D Graph	Specialist
MolT5 [29]	1D Sequence Only	Specialist
MolXPT [44]	1D Sequence Only	Specialist
Mol-Instructions [7]	1D Sequence Only	Semi-Generalist
BioT5+ [6]	1D Sequence Only	Semi-Generalist
GPT-4 (5-shot) [2]	1D Sequence Only	Generalist
Galactica [31]	1D Sequence Only	Generalist
3D-MoLM [12]	1D Sequence & 3D Conformer	Generalist
ChemDFM [23]	1D Sequence Only	Generalist
LlaSMol [5]	1D Sequence Only	Generalist
Mol-LLM	1D Sequence & 2D Graph	Generalist

molecular language models based on modality and task coverage. In Appendix D.3, we include full experimental results, whose evaluation metrics are skipped in the main body due to the page limit.

D.1 Resources

All experiments, except for graph encoder pre-training, were conducted on 8 NVIDIA A100 80GB GPUs and an AMD EPYC 7713 64-Core processor with 512GB of RAM. Using this hardware configuration, Stage 1 required 6 days of training, Stage 2 required half a day, and Stage 3 required 12 days to complete. In Stage 1 graph encoder pre-training, GINE training took approximately 18 hours on 4 A100 GPUs, and TokenGT took 19 hours.

D.2 Baseline Models

As described in Section 3.1, we categorize the baseline models into three groups: specialist models, semi-generalist models, and generalist models, based on their level of specialization and task coverage. In addition to the three model categories, we provide a classification based on the type of input modalities. These categorizations are summarized in Table 10.

D.2.1 Categories by Input Modalities

1D Sequence Only Models that rely solely on 1D sequences (e.g., SMILES or SELFIES), which address molecules as strings. This category include Galactica 6.7B [31], GPT-4 [2], Mol-Instructions [7], BioT5+[6], LlaSMol [5], MolT5 [29], MolXPT [44], and ChemDFM [23].

1D Sequence & 2D Graph Models integrate string-based and graph-based representations to capture 2D molecular structure. Representative examples are InstructMol [9], MolCA [8], and GIT-Mol [10]. GIT-Mol additionally exploits molecular images, providing another route to leverage structural information.

1D Sequence & 3D Conformer Models incorporate 3D conformers alongside sequence information to enrich molecular 3D spatial representations 3D-MoLM [12] belongs to this category.

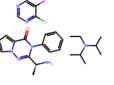
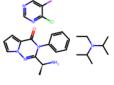
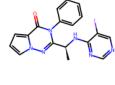
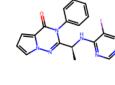
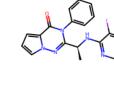
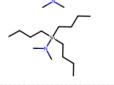
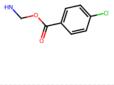
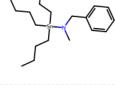
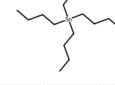
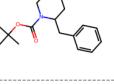
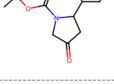
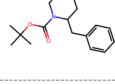
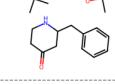
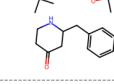
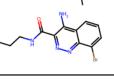
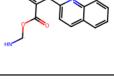
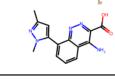
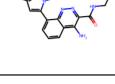
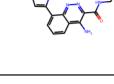
	Question	INPUT_MOLECULE	Galactica	LlaSMol	Mol-LLM (Ours)	Ground Truth
FS-InD	Please provide a feasible product that could be formed using these reactants and reagents: [INPUT_MOLECULE]					
FS-OOD	Please provide a feasible product that could be formed using these reactants and reagents: [INPUT_MOLECULE]					
RS-InD	Can you list the reactants that might result in the chemical product [INPUT_MOLECULE] ?					
RS-OOD	Can you list the reactants that might result in the chemical product [INPUT_MOLECULE] ?					

Figure 7: Comparison of predicted outputs by generalists on forward synthesis (FS) and retrosynthesis (RS), both in Mol-Instructions and ORDerly dataset. The upper two rows represent forward synthesis in Mol-Instructions (InD) and ORDerly (OOD) Datasets, respectively, and the lower two rows represent the retrosynthesis task in the same dataset order.

D.2.2 Categories by Task Coverage

As described in Section 3.1, the baseline models are categorized as follows:

Specialist Models MolCA [8], InstructMol [9], MolXPT [44], GIT-Mol [10], and MolT5 [29] are optimized for individual molecular tasks without parameter or knowledge sharing across tasks.

Semi-Generalist Models BioT5+ [6] and Mol-Instructions [7] address related task groups within a single framework. For instance, BioT5+ trains two separate models: one for classification and translation, and the other for regression and reaction prediction, enabling knowledge sharing within each group while preserving task-specific optimization.

Generalist Models Galactica 6.7B [31], GPT-4 [2], LlaSMol [5], and ChemDFM [23] aim for broad generalization by simultaneously tackling all molecular task groups.

D.3 Full Experimental Results

Table 11 presents the complete results corresponding to Table 2. Table 13 and Table 12 show the full results for Table 3. In Figure 7, we also visualize predicted outputs by generalists, including Mol-LLM, Galactica [31], and LlaSMol [5] on forward reaction prediction and retrosynthesis on both Mol-Instructions and ORDerly datasets.

E Broader Impacts

We currently anticipate no major negative social impacts from this research; nevertheless, there is a possibility that it could be used to generate molecules harmful to humans or the environment. At present, training is carried out on eight NVIDIA A100 GPUs, but scaling to larger LLMs would require additional GPUs and would therefore increase carbon emissions. On the positive side, Mol-LLM enables researchers performing chemical experiments to predict experimental outcomes in advance.

Table 11: Performance comparison on reaction prediction task on Mol-Instructions [7] and SMolInstruct [5] datasets. FS, RS, RP each represent Forward synthesis, Retrosynthesis, and Reagent prediction.

Task	Dataset	Model	EXACT (\uparrow)	BLEU (\uparrow)	RDK FTS (\uparrow)	MACCS FTS (\uparrow)	MORGAN FTS (\uparrow)	VALIDITY (\uparrow)
<i>Specialist Models</i>								
Mol-Instructions	InstructMol	0.536	0.967	0.776	0.878	0.741	1.00	
	MolCA*	0.000	0.321	0.329	0.494	0.253	0.01	
<i>Semi-Generalist Models</i>								
FS	Mol-Instructions*	0.052	0.302	0.232	0.291	0.197	1.00	
	BioT5+*(Cl., & Trans.)	0.000	0.206	0.081	0.152	0.069	0.98	
	BioT5+*(Reg. & React.)	0.864	0.993	0.949	0.975	0.935	1.00	
<i>Generalist Models</i>								
SMolInstruct	GPT-4 (5-shot)	0.021	0.580	0.627	0.728	0.557	0.93	
	Galactica	0.000	0.468	0.156	0.257	0.097	0.95	
	3D-MoLM*	0.000	0.081	0.223	0.391	0.098	0.01	
	ChemDFM*	0.000	0.028	0.104	0.142	0.077	0.07	
	LlaSMol*	0.743	0.835	0.920	0.955	0.910	0.95	
	Mol-LLM (w/o Graph)	0.893	0.963	0.968	0.983	0.960	1.00	
	Mol-LLM	0.911	0.969	0.976	0.987	0.967	1.00	
<i>Specialist Models</i>								
Mol-Instructions	MolCA*	0.000	0.209	0.252	0.357	0.196	0.01	
	Mol-Instructions*	0.003	0.149	0.139	0.184	0.111	1.00	
	BioT5+*(Cl., & Trans.)	0.000	0.286	0.107	0.187	0.089	0.97	
<i>Semi-Generalist Models</i>								
RS	BioT5+*(Reg. & React.)	0.081	0.455	0.418	0.537	0.376	1.00	
	GPT-4 (5-shot)	0.011	0.451	0.520	0.634	0.440	0.87	
	Galactica*	0.000	0.241	0.292	0.377	0.202	0.36	
	3D-MoLM*	0.000	0.086	0.226	0.296	0.117	0.01	
	ChemDFM*	0.002	0.046	0.125	0.178	0.109	0.08	
	LlaSMol*	0.629	0.883	0.871	0.919	0.848	0.99	
	Mol-LLM (w/o Graph)	0.584	0.867	0.847	0.904	0.815	1.00	
<i>Generalist Models</i>								
RP	Mol-LLM	0.601	0.873	0.853	0.908	0.823	1.00	
	InstructMol	0.407	0.941	0.753	0.852	0.714	1.00	
	MolCA*	0.000	0.652	0.936	0.880	0.722	0.01	
	Mol-Instructions*	0.069	0.407	0.303	0.359	0.268	1.00	
	BioT5+*(Cl., & Trans.)	0.001	0.095	0.114	0.195	0.104	0.97	
	BioT5+*(Reg. & React.)	0.642	0.969	0.897	0.930	0.866	1.00	
	GPT-4 (5-shot)	0.012	0.573	0.531	0.716	0.506	0.77	
<i>Specialist Models</i>								
Mol-Instructions	MolCA*	0.000	0.503	0.716	0.760	0.589	0.01	
	Mol-Instructions*	0.015	0.402	0.223	0.285	0.191	1.00	
	BioT5+*(Reg. & React.)	0.000	0.085	0.095	0.170	0.085	0.97	
<i>Semi-Generalist Models</i>								
SMolInstruct	BioT5+*(Cl., & Trans.)	0.152	0.662	0.623	0.751	0.567	1.00	
	GPT-4 (5-shot)	0.013	0.523	0.499	0.686	0.465	0.76	
	Galactica*	0.000	0.346	0.341	0.447	0.272	0.43	
	3D-MoLM*	0.000	0.162	0.220	0.372	0.128	0.01	
	ChemDFM*	0.000	0.257	0.304	0.443	0.252	0.03	
	LlaSMol*	0.323	0.759	0.749	0.827	0.699	0.99	
	Mol-LLM (w/o Graph)	0.363	0.772	0.752	0.828	0.699	1.00	
<i>Generalist Models</i>								
RP	Mol-LLM	0.377	0.779	0.760	0.832	0.707	1.00	
	InstructMol	0.129	0.610	0.444	0.539	0.400	1.00	
	MolCA*	0.000	0.002	0.033	0.115	0.012	0.01	
	Mol-Instructions*	0.044	0.224	0.237	0.364	0.213	1.00	
	BioT5+*(Cl., & Trans.)	0.000	0.169	0.038	0.056	0.015	0.96	
	BioT5+*(Reg. & React.)	0.257	0.695	0.539	0.621	0.512	1.00	
	GPT-4 (5-shot)	0.000	0.133	0.077	0.228	0.071	0.72	
<i>Specialist Models</i>								
Mol-Instructions	Galactica	0.000	0.141	0.036	0.127	0.051	0.99	
	3D-MoLM*	0.000	0.042	0.039	0.218	0.077	0.01	
	ChemDFM*	0.000	0.014	0.033	0.099	0.027	0.06	
	LlaSMol*	0.000	0.050	0.041	0.199	0.050	0.93	
	Mol-LLM (w/o Graph)	0.202	0.557	0.497	0.586	0.461	1.00	
	Mol-LLM	0.225	0.578	0.517	0.600	0.485	1.00	

Table 12: Performance comparison on description-guided molecule generation task on ChEBI-20 [29] and SMolInstruct [5] datasets.

Dataset	Model	EXACT (\uparrow)	BLEU (\uparrow)	RDK FTS (\uparrow)	MACCS FTS (\uparrow)	MORGAN FTS (\uparrow)	VALIDITY (\uparrow)
<i>Specialist Models</i>							
ChEBI-20	GIT-Mol	0.051	0.756	0.582	0.738	0.519	0.93
	MolT5	0.311	0.854	0.746	0.834	0.684	0.91
	MolXPT	0.215	NA	0.757	0.859	0.667	0.98
	Text+Chem T5	0.322	0.853	0.816	0.901	0.757	0.94
<i>Semi-Generalist Models</i>							
ChEBI-20	Mol-Instructions*	0.016	0.042	0.132	0.167	0.090	1.00
	BioT5+*(Cl. & Trans.)	0.557	0.931	0.835	0.907	0.780	1.00
	BioT5+*(Reg. & React.)	0.537	0.821	0.831	0.897	0.773	1.00
<i>Generalist Models</i>							
ChEBI-20	GPT-4 (5-shot)	0.092	0.485	0.518	0.745	0.482	0.65
	Galactica*	0.000	0.189	0.142	0.264	0.057	0.70
	3D-MoLM*	0.000	0.000	0.000	0.000	0.000	0.00
	ChemDFM*	0.018	0.205	0.136	0.165	0.110	0.19
	LlaSMol*	0.274	0.644	0.755	0.871	0.679	0.95
	Mol-LLM (w/o Graph)	0.431	0.792	0.823	0.903	0.754	1.00
	Mol-LLM	0.443	0.795	0.829	0.906	0.761	1.00
<i>Specialist Models</i>							
SMolInstruct	MolT5	0.317	NA	0.802	0.879	0.732	0.95
	<i>Semi-Generalist Models</i>						
	Mol-Instructions*	0.045	0.507	0.366	0.475	0.272	1.00
SMolInstruct	BioT5+*(Cl. & Trans.)	0.519	0.918	0.822	0.897	0.757	1.00
	BioT5+*(Reg. & React.)	0.416	0.819	0.782	0.867	0.706	1.00
	<i>Generalist Models</i>						
	GPT-4 (5-shot)	0.027	0.404	0.482	0.726	0.368	0.74
	Galactica*	0.000	0.173	0.144	0.271	0.055	0.61
	3D-MoLM*	0.000	0.000	0.000	0.000	0.000	0.00
	ChemDFM*	0.041	0.069	0.230	0.297	0.189	0.13
SMolInstruct	LlaSMol*	0.180	0.718	0.712	0.845	0.623	0.93
	Mol-LLM (w/o Graph)	0.362	0.759	0.797	0.888	0.716	1.00
	Mol-LLM	0.368	0.761	0.800	0.887	0.721	0.99

Table 13: Performance comparison on molecule captioning task on ChEBI-20 [29] and SMolInstruct [5] datasets.

	Model	BLEU-2 (\uparrow)	BLEU-4 (\uparrow)	ROUGE-1 (\uparrow)	ROUGE-2 (\uparrow)	ROUGE-L (\uparrow)	METEOR (\uparrow)
<i>Specialist Models</i>							
ChEBI-20	GIT-Mol	0.352	0.263	0.575	0.485	0.560	0.533
	InstructMol	0.475	0.371	0.566	0.394	0.502	0.509
	MolT5	0.594	0.508	0.654	0.510	0.594	0.614
	MolCA*	0.623	0.540	0.693	0.553	0.631	0.652
	MolXPT	0.594	0.505	0.660	0.511	0.597	0.626
	Text+Chem T5	0.625	0.542	0.682	0.543	0.622	0.648
<i>Semi-Generalist Models</i>							
ChEBI-20	Mol-Instructions	0.249	0.171	0.331	0.206	0.289	0.271
	BioT5+*(Cl. & Trans.)	0.666	0.591	0.709	0.583	0.649	0.680
	BioT5+*(Reg. & React.)	0.249	0.216	0.387	0.302	0.364	0.323
<i>Generalist Models</i>							
ChEBI-20	GPT-4 (5-shot)	0.261	0.158	0.286	0.188	0.303	0.320
	Galactica*	0.001	0.000	0.006	0.000	0.006	0.004
	3D-MoLM*	0.252	0.171	0.361	0.184	0.287	0.326
	ChemDFM*	0.054	0.031	0.120	0.049	0.101	0.078
	LlaSMol*	0.432	0.333	0.522	0.356	0.464	0.466
	Mol-LLM (w/o Graph)	0.556	0.482	0.565	0.417	0.509	0.587
	Mol-LLM	0.566	0.493	0.493	0.336	0.439	0.599
<i>Specialist Models</i>							
SMolInstruct	MolT5	0.462	0.366	0.563	0.398	0.501	0.515
	MolCA*	0.599	0.510	0.665	0.519	0.604	0.628
<i>Semi-Generalist Models</i>							
SMolInstruct	Mol-Instructions	0.028	0.020	0.226	0.160	0.217	0.124
	BioT5+*(Cl. & Trans.)	0.656	0.582	0.702	0.576	0.644	0.677
	BioT5+*(Reg. & React.)	0.257	0.221	0.387	0.301	0.364	0.321
<i>Generalist Models</i>							
SMolInstruct	GPT-4 (5-shot)	0.220	0.125	0.352	0.156	0.273	0.274
	Galactica*	0.002	0.000	0.007	0.000	0.006	0.005
	3D-MoLM*	0.244	0.167	0.357	0.185	0.285	0.329
	ChemDFM*	0.057	0.035	0.128	0.054	0.108	0.085
	LlaSMol*	0.427	0.328	0.525	0.359	0.465	0.470
	Mol-LLM (w/o Graph)	0.554	0.477	0.544	0.393	0.490	0.585
	Mol-LLM	0.558	0.482	0.485	0.330	0.433	0.589

NeurIPS Paper Checklist

1. Claims

Question: Do the main claims made in the abstract and introduction accurately reflect the paper's contributions and scope?

Answer: [Yes]

Justification: The claims have been validated through extensive evaluation on various molecular tasks in Section 3 and Appendix D.3, comparing with a number of generalist baselines available, including in-domain and out-of-domain benchmarks.

Guidelines:

- The answer NA means that the abstract and introduction do not include the claims made in the paper.
- The abstract and/or introduction should clearly state the claims made, including the contributions made in the paper and important assumptions and limitations. A No or NA answer to this question will not be perceived well by the reviewers.
- The claims made should match theoretical and experimental results, and reflect how much the results can be expected to generalize to other settings.
- It is fine to include aspirational goals as motivation as long as it is clear that these goals are not attained by the paper.

2. Limitations

Question: Does the paper discuss the limitations of the work performed by the authors?

Answer: [Yes]

Justification: We discuss limitations in Section 5 and appendix A.

Guidelines:

- The answer NA means that the paper has no limitation while the answer No means that the paper has limitations, but those are not discussed in the paper.
- The authors are encouraged to create a separate "Limitations" section in their paper.
- The paper should point out any strong assumptions and how robust the results are to violations of these assumptions (e.g., independence assumptions, noiseless settings, model well-specification, asymptotic approximations only holding locally). The authors should reflect on how these assumptions might be violated in practice and what the implications would be.
- The authors should reflect on the scope of the claims made, e.g., if the approach was only tested on a few datasets or with a few runs. In general, empirical results often depend on implicit assumptions, which should be articulated.
- The authors should reflect on the factors that influence the performance of the approach. For example, a facial recognition algorithm may perform poorly when image resolution is low or images are taken in low lighting. Or a speech-to-text system might not be used reliably to provide closed captions for online lectures because it fails to handle technical jargon.
- The authors should discuss the computational efficiency of the proposed algorithms and how they scale with dataset size.
- If applicable, the authors should discuss possible limitations of their approach to address problems of privacy and fairness.
- While the authors might fear that complete honesty about limitations might be used by reviewers as grounds for rejection, a worse outcome might be that reviewers discover limitations that aren't acknowledged in the paper. The authors should use their best judgment and recognize that individual actions in favor of transparency play an important role in developing norms that preserve the integrity of the community. Reviewers will be specifically instructed to not penalize honesty concerning limitations.

3. Theory assumptions and proofs

Question: For each theoretical result, does the paper provide the full set of assumptions and a complete (and correct) proof?

Answer: [NA]

Justification: The paper does not include theoretical results.

Guidelines:

- The answer NA means that the paper does not include theoretical results.
- All the theorems, formulas, and proofs in the paper should be numbered and cross-referenced.
- All assumptions should be clearly stated or referenced in the statement of any theorems.
- The proofs can either appear in the main paper or the supplemental material, but if they appear in the supplemental material, the authors are encouraged to provide a short proof sketch to provide intuition.
- Inversely, any informal proof provided in the core of the paper should be complemented by formal proofs provided in appendix or supplemental material.
- Theorems and Lemmas that the proof relies upon should be properly referenced.

4. Experimental result reproducibility

Question: Does the paper fully disclose all the information needed to reproduce the main experimental results of the paper to the extent that it affects the main claims and/or conclusions of the paper (regardless of whether the code and data are provided or not)?

Answer: [Yes]

Justification: We provide information on the full model architecture and training objective in Section 2. Appendix B includes further training details. Section 3 and Appendix D describe recipe for experiments reproduction.

Guidelines:

- The answer NA means that the paper does not include experiments.
- If the paper includes experiments, a No answer to this question will not be perceived well by the reviewers: Making the paper reproducible is important, regardless of whether the code and data are provided or not.
- If the contribution is a dataset and/or model, the authors should describe the steps taken to make their results reproducible or verifiable.
- Depending on the contribution, reproducibility can be accomplished in various ways. For example, if the contribution is a novel architecture, describing the architecture fully might suffice, or if the contribution is a specific model and empirical evaluation, it may be necessary to either make it possible for others to replicate the model with the same dataset, or provide access to the model. In general, releasing code and data is often one good way to accomplish this, but reproducibility can also be provided via detailed instructions for how to replicate the results, access to a hosted model (e.g., in the case of a large language model), releasing of a model checkpoint, or other means that are appropriate to the research performed.
- While NeurIPS does not require releasing code, the conference does require all submissions to provide some reasonable avenue for reproducibility, which may depend on the nature of the contribution. For example
 - (a) If the contribution is primarily a new algorithm, the paper should make it clear how to reproduce that algorithm.
 - (b) If the contribution is primarily a new model architecture, the paper should describe the architecture clearly and fully.
 - (c) If the contribution is a new model (e.g., a large language model), then there should either be a way to access this model for reproducing the results or a way to reproduce the model (e.g., with an open-source dataset or instructions for how to construct the dataset).
 - (d) We recognize that reproducibility may be tricky in some cases, in which case authors are welcome to describe the particular way they provide for reproducibility. In the case of closed-source models, it may be that access to the model is limited in some way (e.g., to registered users), but it should be possible for other researchers to have some path to reproducing or verifying the results.

5. Open access to data and code

Question: Does the paper provide open access to the data and code, with sufficient instructions to faithfully reproduce the main experimental results, as described in supplemental material?

Answer: [Yes]

Justification: Appendix B provides links to access source code, trained model, and data for result reproduction. In addition, the code, trained model, and data will be released publicly.

Guidelines:

- The answer NA means that paper does not include experiments requiring code.
- Please see the NeurIPS code and data submission guidelines (<https://nips.cc/public/guides/CodeSubmissionPolicy>) for more details.
- While we encourage the release of code and data, we understand that this might not be possible, so “No” is an acceptable answer. Papers cannot be rejected simply for not including code, unless this is central to the contribution (e.g., for a new open-source benchmark).
- The instructions should contain the exact command and environment needed to run to reproduce the results. See the NeurIPS code and data submission guidelines (<https://nips.cc/public/guides/CodeSubmissionPolicy>) for more details.
- The authors should provide instructions on data access and preparation, including how to access the raw data, preprocessed data, intermediate data, and generated data, etc.
- The authors should provide scripts to reproduce all experimental results for the new proposed method and baselines. If only a subset of experiments are reproducible, they should state which ones are omitted from the script and why.
- At submission time, to preserve anonymity, the authors should release anonymized versions (if applicable).
- Providing as much information as possible in supplemental material (appended to the paper) is recommended, but including URLs to data and code is permitted.

6. Experimental setting/details

Question: Does the paper specify all the training and test details (e.g., data splits, hyperparameters, how they were chosen, type of optimizer, etc.) necessary to understand the results?

Answer: [Yes]

Justification: All experimental settings are clearly specified. Details of data construction and splits are in Appendix C, hyperparameters, how they were chosen, and other training details are in Appendix B, and experimental details including evaluation configurations are in Appendix D.

Guidelines:

- The answer NA means that the paper does not include experiments.
- The experimental setting should be presented in the core of the paper to a level of detail that is necessary to appreciate the results and make sense of them.
- The full details can be provided either with the code, in appendix, or as supplemental material.

7. Experiment statistical significance

Question: Does the paper report error bars suitably and correctly defined or other appropriate information about the statistical significance of the experiments?

Answer: [No]

Justification: For generalist models, reporting results with such a statistical significance demands substantial resources. We note that the prior work we discussed in Section 4 similarly does not report statistical significance.

Guidelines:

- The answer NA means that the paper does not include experiments.
- The authors should answer “Yes” if the results are accompanied by error bars, confidence intervals, or statistical significance tests, at least for the experiments that support the main claims of the paper.
- The factors of variability that the error bars are capturing should be clearly stated (for example, train/test split, initialization, random drawing of some parameter, or overall run with given experimental conditions).
- The method for calculating the error bars should be explained (closed form formula, call to a library function, bootstrap, etc.)

- The assumptions made should be given (e.g., Normally distributed errors).
- It should be clear whether the error bar is the standard deviation or the standard error of the mean.
- It is OK to report 1-sigma error bars, but one should state it. The authors should preferably report a 2-sigma error bar than state that they have a 96% CI, if the hypothesis of Normality of errors is not verified.
- For asymmetric distributions, the authors should be careful not to show in tables or figures symmetric error bars that would yield results that are out of range (e.g. negative error rates).
- If error bars are reported in tables or plots, The authors should explain in the text how they were calculated and reference the corresponding figures or tables in the text.

8. Experiments compute resources

Question: For each experiment, does the paper provide sufficient information on the computer resources (type of compute workers, memory, time of execution) needed to reproduce the experiments?

Answer: [Yes]

Justification: Appendix D.1 provides sufficient resource information to reproduce the experiments, including workers, memory, and time of execution.

Guidelines:

- The answer NA means that the paper does not include experiments.
- The paper should indicate the type of compute workers CPU or GPU, internal cluster, or cloud provider, including relevant memory and storage.
- The paper should provide the amount of compute required for each of the individual experimental runs as well as estimate the total compute.
- The paper should disclose whether the full research project required more compute than the experiments reported in the paper (e.g., preliminary or failed experiments that didn't make it into the paper).

9. Code of ethics

Question: Does the research conducted in the paper conform, in every respect, with the NeurIPS Code of Ethics <https://neurips.cc/public/EthicsGuidelines>?

Answer: [Yes]

Justification: The research presented in this paper fully conforms to the NeurIPS Code of Ethics.

Guidelines:

- The answer NA means that the authors have not reviewed the NeurIPS Code of Ethics.
- If the authors answer No, they should explain the special circumstances that require a deviation from the Code of Ethics.
- The authors should make sure to preserve anonymity (e.g., if there is a special consideration due to laws or regulations in their jurisdiction).

10. Broader impacts

Question: Does the paper discuss both potential positive societal impacts and negative societal impacts of the work performed?

Answer: [Yes]

Justification: We discuss broader impacts in Appendix E.

Guidelines:

- The answer NA means that there is no societal impact of the work performed.
- If the authors answer NA or No, they should explain why their work has no societal impact or why the paper does not address societal impact.
- Examples of negative societal impacts include potential malicious or unintended uses (e.g., disinformation, generating fake profiles, surveillance), fairness considerations (e.g., deployment of technologies that could make decisions that unfairly impact specific groups), privacy considerations, and security considerations.

- The conference expects that many papers will be foundational research and not tied to particular applications, let alone deployments. However, if there is a direct path to any negative applications, the authors should point it out. For example, it is legitimate to point out that an improvement in the quality of generative models could be used to generate deepfakes for disinformation. On the other hand, it is not needed to point out that a generic algorithm for optimizing neural networks could enable people to train models that generate Deepfakes faster.
- The authors should consider possible harms that could arise when the technology is being used as intended and functioning correctly, harms that could arise when the technology is being used as intended but gives incorrect results, and harms following from (intentional or unintentional) misuse of the technology.
- If there are negative societal impacts, the authors could also discuss possible mitigation strategies (e.g., gated release of models, providing defenses in addition to attacks, mechanisms for monitoring misuse, mechanisms to monitor how a system learns from feedback over time, improving the efficiency and accessibility of ML).

11. Safeguards

Question: Does the paper describe safeguards that have been put in place for responsible release of data or models that have a high risk for misuse (e.g., pretrained language models, image generators, or scraped datasets)?

Answer: [NA]

Justification: Our model, Mol-LLM, does not have a high risk for misuse.

Guidelines:

- The answer NA means that the paper poses no such risks.
- Released models that have a high risk for misuse or dual-use should be released with necessary safeguards to allow for controlled use of the model, for example by requiring that users adhere to usage guidelines or restrictions to access the model or implementing safety filters.
- Datasets that have been scraped from the Internet could pose safety risks. The authors should describe how they avoided releasing unsafe images.
- We recognize that providing effective safeguards is challenging, and many papers do not require this, but we encourage authors to take this into account and make a best faith effort.

12. Licenses for existing assets

Question: Are the creators or original owners of assets (e.g., code, data, models), used in the paper, properly credited and are the license and terms of use explicitly mentioned and properly respected?

Answer: [Yes]

Justification: The backbone models of choice, including LLM and GNN, are credited in Section 2.1, and the datasets used are properly credited through Section 3.1 and Appendix C.

Guidelines:

- The answer NA means that the paper does not use existing assets.
- The authors should cite the original paper that produced the code package or dataset.
- The authors should state which version of the asset is used and, if possible, include a URL.
- The name of the license (e.g., CC-BY 4.0) should be included for each asset.
- For scraped data from a particular source (e.g., website), the copyright and terms of service of that source should be provided.
- If assets are released, the license, copyright information, and terms of use in the package should be provided. For popular datasets, paperswithcode.com/datasets has curated licenses for some datasets. Their licensing guide can help determine the license of a dataset.
- For existing datasets that are re-packaged, both the original license and the license of the derived asset (if it has changed) should be provided.
- If this information is not available online, the authors are encouraged to reach out to the asset's creators.

13. New assets

Question: Are new assets introduced in the paper well documented and is the documentation provided alongside the assets?

Answer: [Yes]

Justification: We release our model, code, and data along with comprehensive documentation, which is available in the code repository as detailed in Appendix B.

Guidelines:

- The answer NA means that the paper does not release new assets.
- Researchers should communicate the details of the dataset/code/model as part of their submissions via structured templates. This includes details about training, license, limitations, etc.
- The paper should discuss whether and how consent was obtained from people whose asset is used.
- At submission time, remember to anonymize your assets (if applicable). You can either create an anonymized URL or include an anonymized zip file.

14. Crowdsourcing and research with human subjects

Question: For crowdsourcing experiments and research with human subjects, does the paper include the full text of instructions given to participants and screenshots, if applicable, as well as details about compensation (if any)?

Answer: [NA]

Justification: This study does not require human subjects.

Guidelines:

- The answer NA means that the paper does not involve crowdsourcing nor research with human subjects.
- Including this information in the supplemental material is fine, but if the main contribution of the paper involves human subjects, then as much detail as possible should be included in the main paper.
- According to the NeurIPS Code of Ethics, workers involved in data collection, curation, or other labor should be paid at least the minimum wage in the country of the data collector.

15. Institutional review board (IRB) approvals or equivalent for research with human subjects

Question: Does the paper describe potential risks incurred by study participants, whether such risks were disclosed to the subjects, and whether Institutional Review Board (IRB) approvals (or an equivalent approval/review based on the requirements of your country or institution) were obtained?

Answer: [NA]

Justification: This study does not require human subjects.

Guidelines:

- The answer NA means that the paper does not involve crowdsourcing nor research with human subjects.
- Depending on the country in which research is conducted, IRB approval (or equivalent) may be required for any human subjects research. If you obtained IRB approval, you should clearly state this in the paper.
- We recognize that the procedures for this may vary significantly between institutions and locations, and we expect authors to adhere to the NeurIPS Code of Ethics and the guidelines for their institution.
- For initial submissions, do not include any information that would break anonymity (if applicable), such as the institution conducting the review.

16. Declaration of LLM usage

Question: Does the paper describe the usage of LLMs if it is an important, original, or non-standard component of the core methods in this research? Note that if the LLM is used only for writing, editing, or formatting purposes and does not impact the core methodology, scientific rigorosity, or originality of the research, declaration is not required.

Answer: [Yes]

Justification: Large language models (LLMs) are an integral component of the proposed method, as described in Section 2. Section 2 and Appendix B detail the implementation aspects of the method involving LLMs, while Appendix D.2 provides information on the usage of other baseline LLMs.

Guidelines:

- The answer NA means that the core method development in this research does not involve LLMs as any important, original, or non-standard components.
- Please refer to our LLM policy (<https://neurips.cc/Conferences/2025/LLM>) for what should or should not be described.