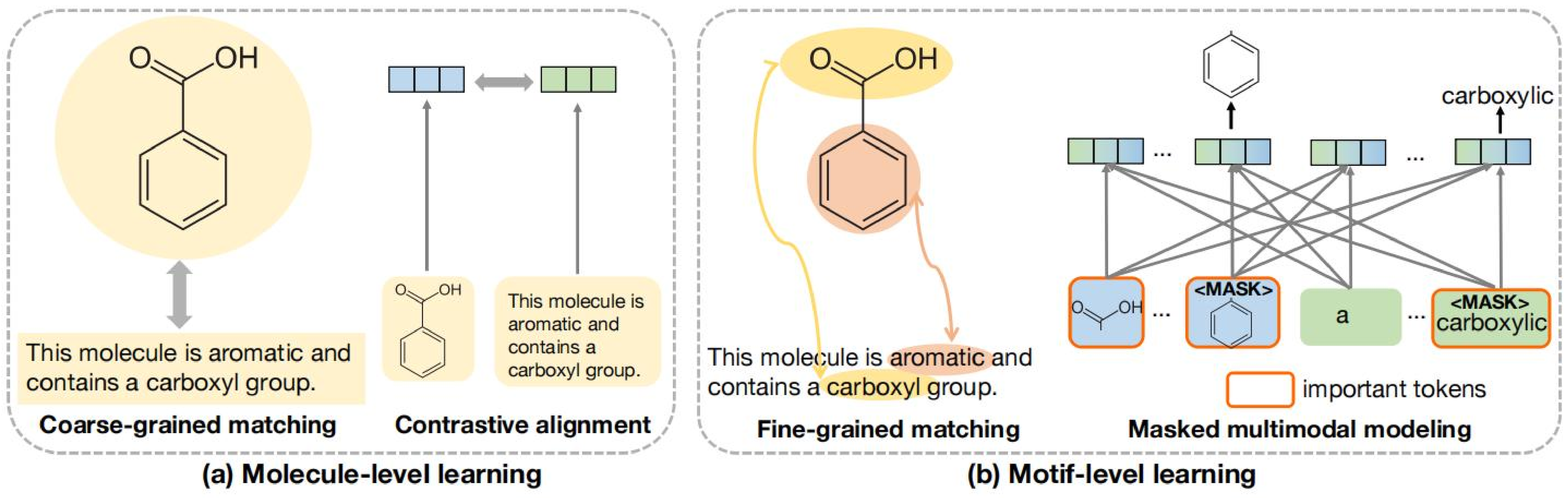
Advancing Molecular Graph-Text Pre-training via Fine-grained Alignment

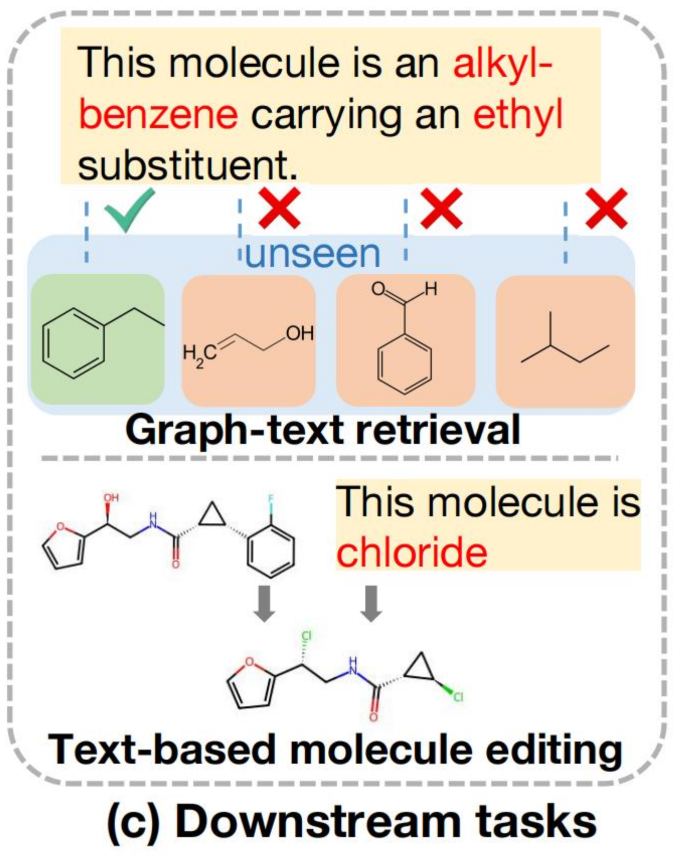
August 3-7, 2025 KDD2025

Yibo Li[1], Yuan Fang[2]*, Mengmei Zhang[3], Chuan Shi[1]*,
[1]Beijing University of Posts and Telecommunications
[2]Singapore Management University
[3]China Telecom Bestpay

❖ Motivation



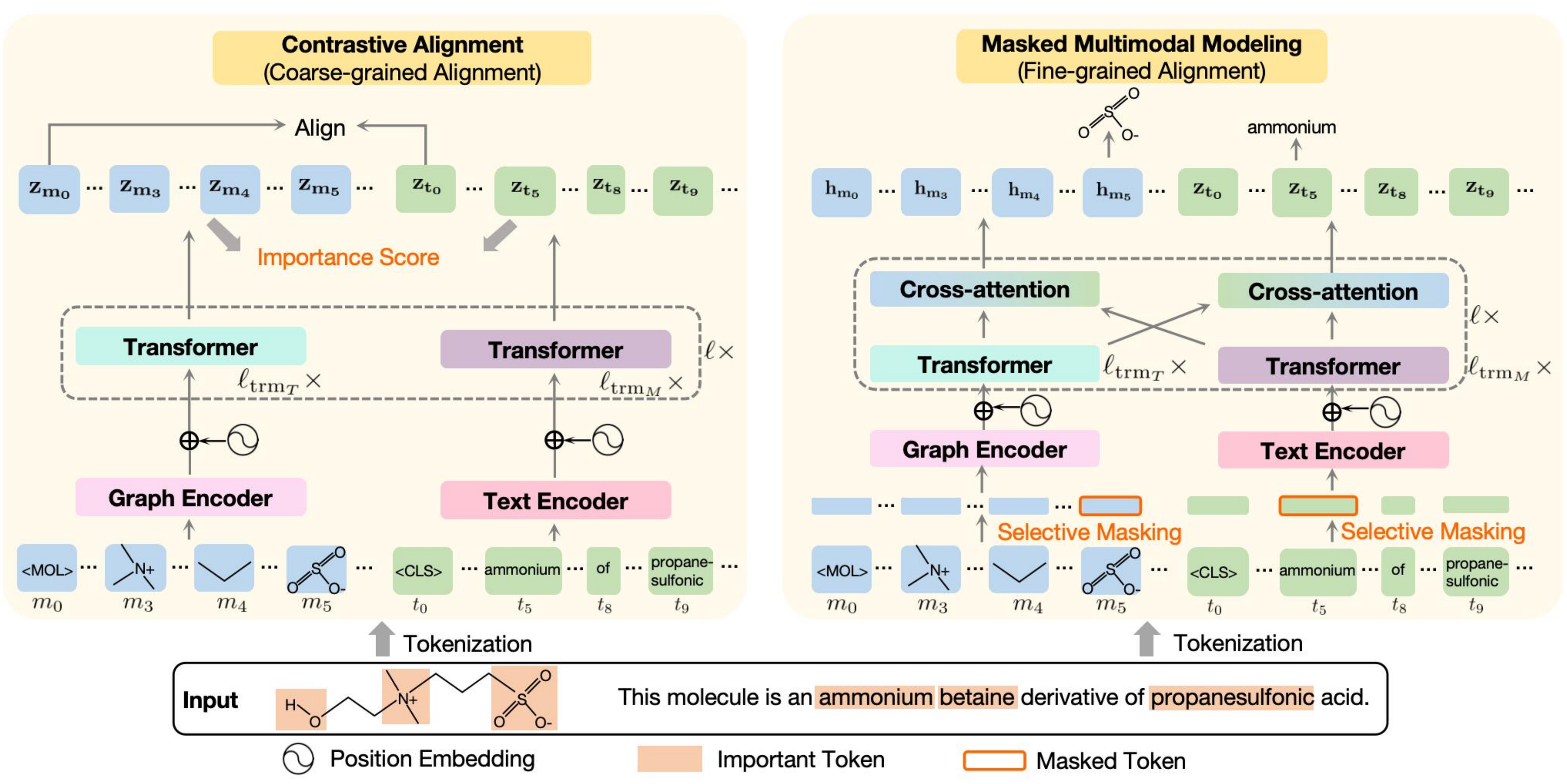
- **Traditional multimodal molecular learning frameworks fail to capture fine-grained knowledge of the sub-molecule level.**



(c) Downstream tasks

- **Motif-level knowledge is necessary for the generalization to unseen molecules.**
- **Motif-level knowledge bridges the gap for downstream tasks that require fine-grained knowledge.**

❖ FineMolTex



- **Contrastive Alignment:**

$$L_{\text{con}} = -\frac{1}{2}\mathbb{E}_{m_0,t_0}\left[\log \frac{\exp(\cos(\mathbf{z}_{m_0},\mathbf{z}_{t_0})/\tau)}{\exp(\cos(\mathbf{z}_{m_0},\mathbf{z}_{t_0})/\tau)+\sum_{t_0'}\exp(\cos(\mathbf{z}_{m_0},\mathbf{z}_{t_0'})/\tau)} + \log \frac{\exp(\cos(\mathbf{z}_{t_0},\mathbf{z}_{m_0})/\tau)}{\exp(\cos(\mathbf{z}_{t_0},\mathbf{z}_{m_0})/\tau)+\sum_{m_0'}\exp(\cos(\mathbf{z}_{t_0},\mathbf{z}_{m_0'})/\tau)}\right],$$

- **Masked Multimodal Modeling:**

$$L_{\text{pre}} = \beta\sum_i \mathrm{CE}(\hat{y}_{m_i}, y_{m_i}) + \alpha\sum_j \mathrm{CE}(\hat{y}_{t_j}, y_{t_j}).$$

- **Importance Score:**

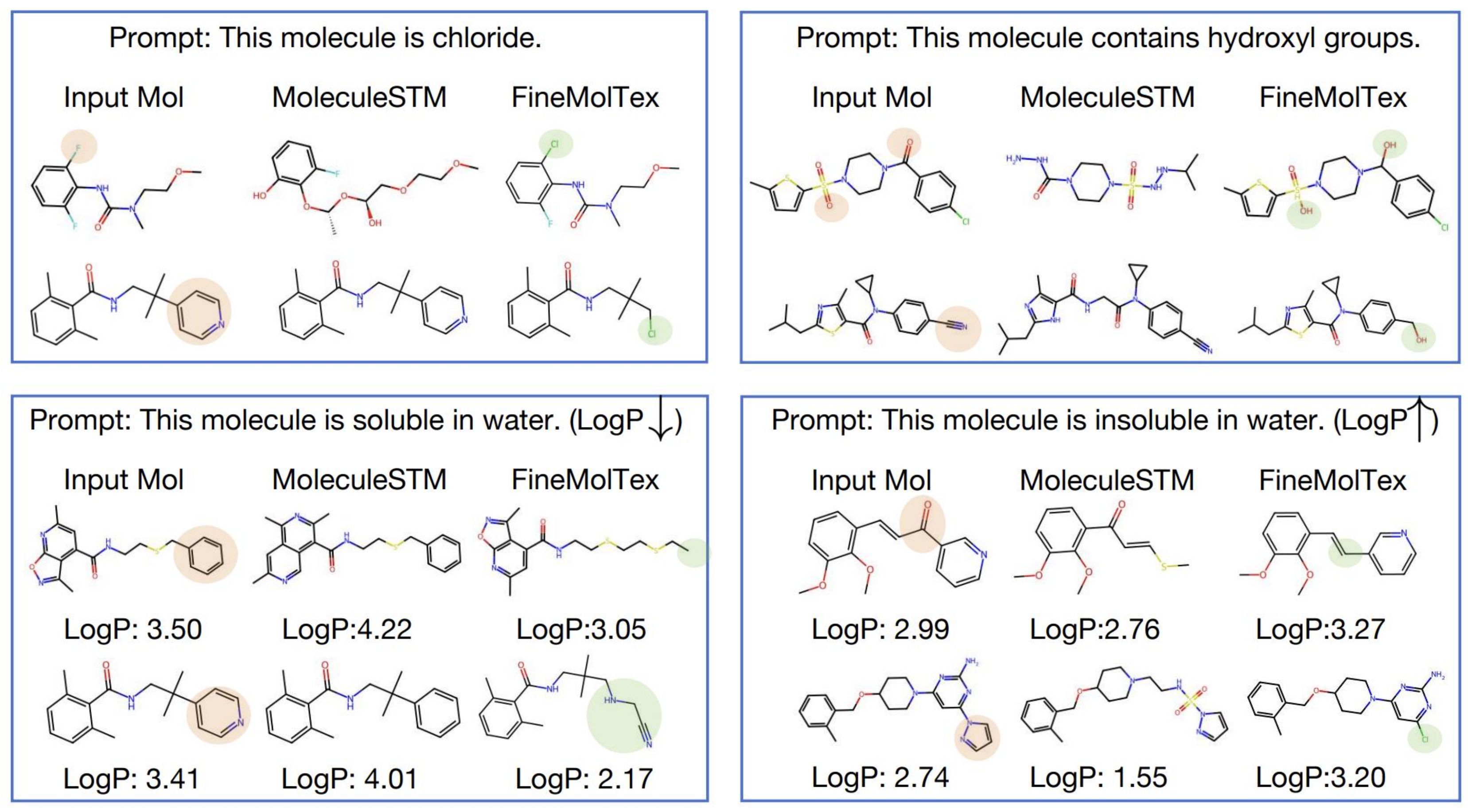
$$\omega_{t_i} = \frac{\exp(\cos(z_{t_i}, z_{t_0}))}{\sum_{j=1}^{N}\exp(\cos(z_{t_j}, z_{t_0}))},\quad \omega_{m_i} = \frac{\exp(\cos(z_{m_i}, z_{m_0}))}{\sum_{j=1}^{N}\exp(\cos(z_{m_j}, z_{m_0}))}$$

❖ Experiments

- **RQ1. Can FineMolTex better generalize to unseen molecules?**

	Given Molecular Graph			Given Text		
T	4	10	20	4	10	20
KV-PLM	68.38±0.03	47.59±0.03	36.54±0.03	67.68±0.03	48.00±0.02	34.66±0.02
MolCA	83.75±0.54	74.25±0.26	66.14±0.21	81.27±0.33	69.46±0.17	62.13±0.16
MoMu-S	70.51±0.04	55.20±0.15	43.78±0.10	70.71±0.22	54.70±0.31	44.25±0.43
MoMu-K	69.40±0.11	53.14±0.26	42.32±0.28	68.71±0.03	53.29±0.05	43.83±0.12
3D-MoLM	81.35±0.14	73.65±0.13	64.79±0.15	79.78±0.22	62.38±0.16	53.43±0.11
MV-Mol	92.24±0.26	85.38±0.19	79.41±0.43	91.28±0.13	85.32±0.15	80.37±0.22
MoleculeSTM	92.14±0.02	86.27±0.02	81.08±0.05	91.44±0.02	86.76±0.03	81.68±0.03
FineMolTex	**96.78±0.05**	**92.48±0.02**	**87.94±0.14**	**96.29±0.12**	**91.65±0.15**	**85.07±0.11**

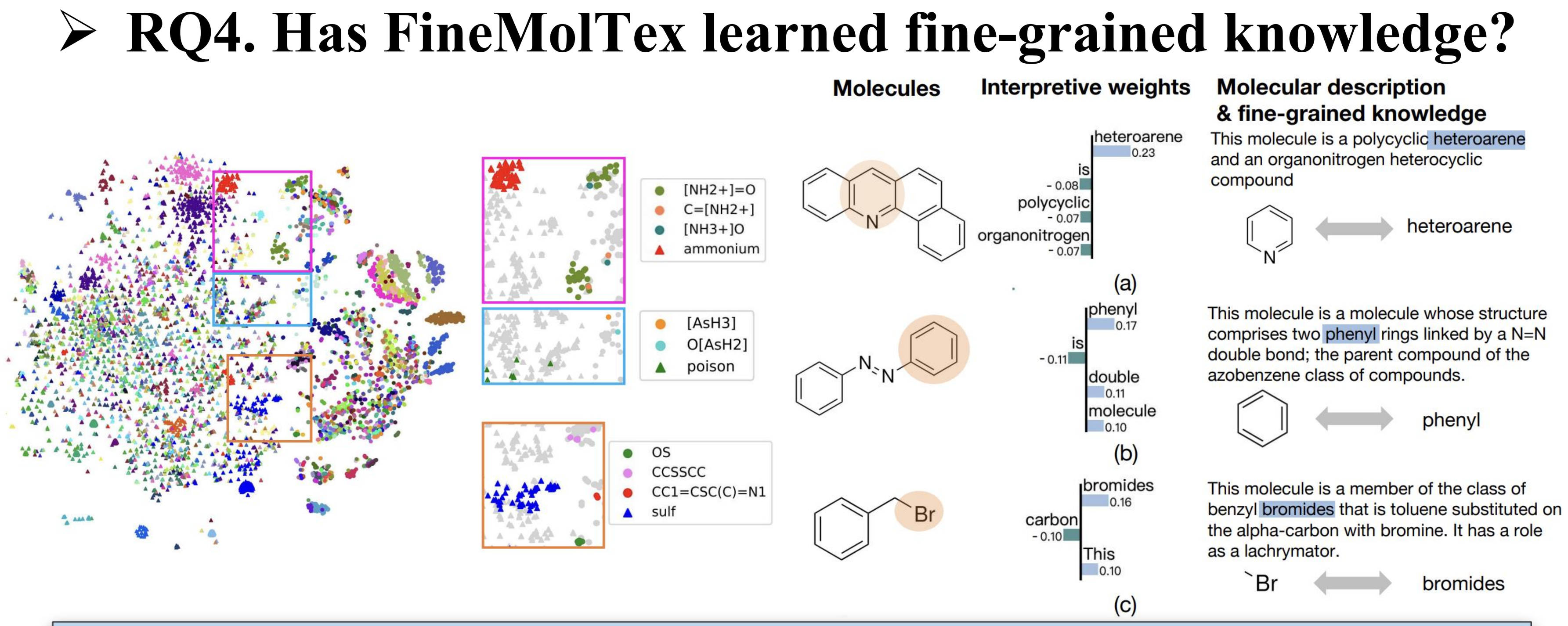
- **RQ2. Can FineMolTex bridge the gap to tasks centered on motiflevel knowledge?**



- **RQ3. Can FineMolTex perform better on single-modality tasks?**

Model	BBBP	Tox21	ToxCast	Sider	ClinTox	MUV	HIV	Bace	Avg
AttrMask	67.8±2.6	75.0±0.2	63.6±0.8	58.1±1.2	75.4±8.8	73.8±1.2	75.4±0.5	80.3±0.0	71.2
ContextPred	63.1±3.5	74.3±0.2	61.6±0.5	60.3±0.8	80.3±3.8	71.4±1.4	70.7±3.6	78.8±0.4	70.1
InfoGraph	64.8±0.6	76.2±0.4	62.7±0.7	59.1±0.6	76.5±7.8	73.0±3.6	70.2±2.4	77.6±2.0	70.0
MolCLR	67.8±0.5	67.8±0.5	64.6±0.1	58.7±0.1	84.2±1.5	72.8±0.7	75.9±0.2	71.1±1.2	71.3
GraphMVP	68.1±1.4	77.1±0.4	65.1±0.3	60.6±0.1	84.7±3.1	74.4±2.0	77.7±2.5	80.5±2.7	73.5
GraphCL	69.7±0.7	73.9±0.7	62.4±0.6	60.5±0.9	76.0±2.7	69.8±2.7	78.5±1.2	75.4±1.4	70.8
KV-PLM	70.5±0.5	72.1±1.0	55.0±1.7	59.8±0.6	89.2±2.7	54.6±4.8	65.4±1.7	78.5±2.7	68.2
MoMu-S	70.5±2.0	75.6±0.3	63.4±0.5	60.5±0.9	79.9±4.1	70.5±1.4	75.9±0.8	76.7±2.1	71.6
MoMu-K	70.1±1.4	75.6±0.5	63.0±0.4	60.4±0.8	77.4±4.1	71.1±2.7	76.2±0.9	77.1±1.4	71.4
MolCA	70.0±0.5	**77.2±0.5**	64.5±0.8	63.0±1.7	89.5±0.7	72.1±1.3	77.2±0.6	79.8±0.5	74.2
MoleculeSTM	70.0±0.5	76.9±0.5	65.1±0.4	61.0±1.1	92.5±1.1	73.4±2.9	77.0±1.8	80.8±1.3	74.6
FineMolTex	**73.5±1.6**	77.1±1.2	**68.6±0.9**	**64.8±1.4**	**92.5±0.8**	**76.3±1.2**	**79.0±1.4**	**84.0±1.5**	**76.9**

- **RQ4. Has FineMolTex learned fine-grained knowledge?**



❖ Conclusion

- **We reveal that fine-grained motif-level knowledge is crucial for molecular representation learning.**
- **We propose FineMolTex to jointly learn both coarse- and fine-grained knowledge through a contrastive alignment. task and a masked multimodal learning task, respectively.**
- **Extensive experimental results verify the effectiveness of FineMolTex.**

- **Contact: liyibo@u.nus.edu**
- **Github: https://github.com/liushiliushi/FineMolTex**