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A Plug-and-Play Quaternion Message-Passing Module for Molecular Conformation Representation

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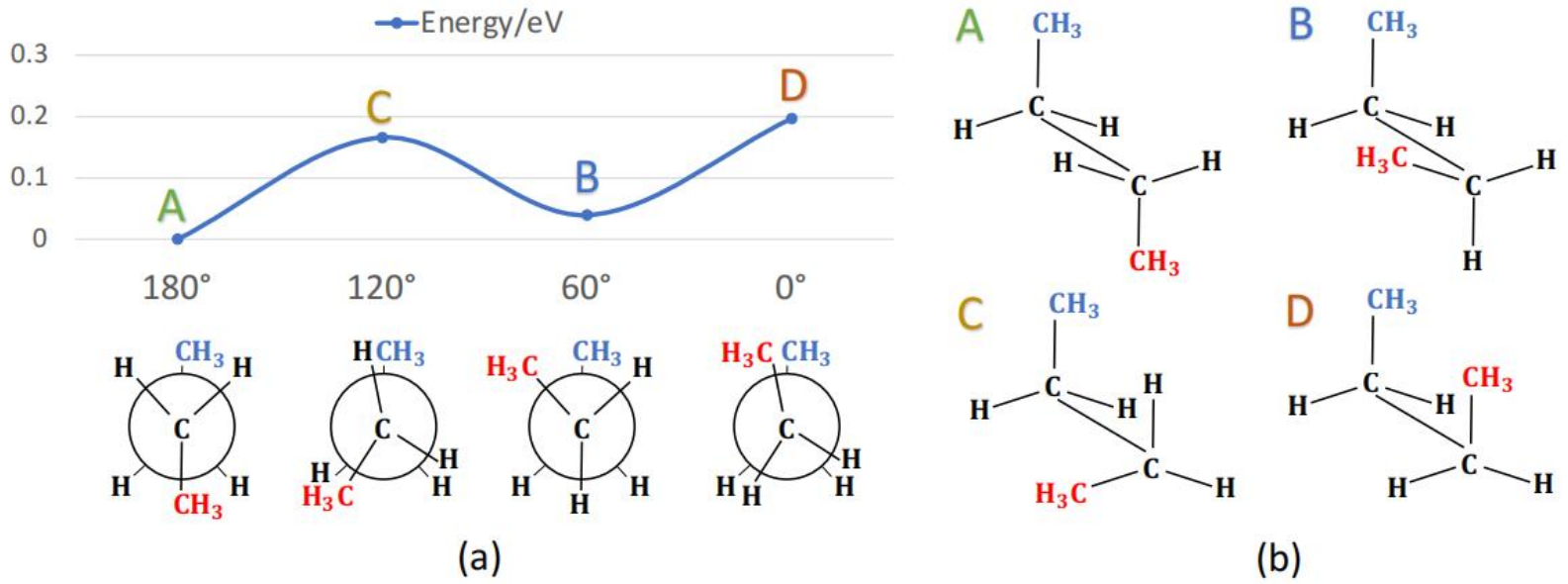
2023-6-13

- Introduction
- Method
- Experiment
- Conclusion

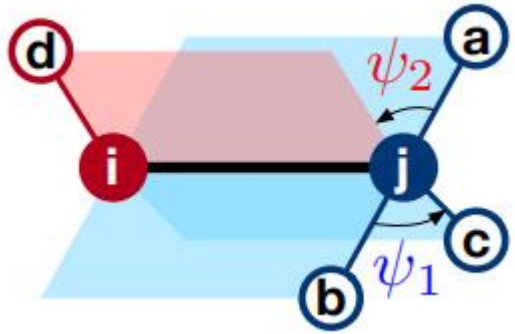
Introduction

- 3D molecular representation learning has shown great promise in molecular dynamics tasks, e.g., predicting the energy, atomic force, and other quantum mechanical properties of molecules.
- A real molecule exits as an ensemble of interconverting 3D structures, known as conformers. different conformers for the molecule show varying conformation energy.



Introduction

- Geometries: bond distance (d), bond angle (θ), same-side dihedrals (ψ_1) and opposite-side dihedrals (ψ_2).
- Equivariant GNNs lack of bonds' rotation and torsion angles make them unable to distinguish molecular conformations.
- Ideal Invariant GNNs represent 3D structures of molecules by recording the dihedrals defined on each bond's 2-hop neighborhood, whose computational complexity can be as high as $O(ND^3)$ with N atoms and D degrees on average. **SphereNet** only considers ψ_1 which reduce the complexity to $O(ND^2)$ but can't distinguish conformations.



- **Motivation: Sensitive to local bond twisting, Invariant to global rotation and translation, Complexity is no larger than $O(ND^2)$.**

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Method: Notation

- A 3D molecule with N atoms and M chemical bonds as a graph $G(\mathcal{V}, \mathcal{E}, H^{(0)}, Z^{(0)}, X)$. $\mathcal{V}$ and $\mathcal{E}$ denote the set of atoms and that of bonds. $H^{(0)} \in \mathbb{R}^{N \times D_v}$ represents the atom feature matrix, and $Z^{(0)} \in \mathbb{R}^{N \times D_e}$ represents the bond feature matrix. The matrix $X \in \mathbb{R}^{N \times 3}$ contains the 3D coordinates.
- Extract SE(3) invariant information:
  - Bond Length Matrix: $D = [d_{ij}] \in \mathbb{R}^{N \times N}$. d
  - Bond Rotation Set: Two edges connected at atom j, (j, i), $(j, k) \in \mathcal{E}$. θ

$$\boldsymbol{u}_{kji} = \frac{\boldsymbol{p}_{jk} \times \boldsymbol{p}_{ji}}{\|\boldsymbol{p}_{jk} \times \boldsymbol{p}_{ji}\|_2}, \quad \text{and} \quad \theta_{kji} = \arccos\left(\frac{\langle \boldsymbol{p}_{jk}, \boldsymbol{p}_{ji} \rangle}{\|\boldsymbol{p}_{jk}\|_2 \|\boldsymbol{p}_{ji}\|_2}\right)$$

  - Bond Dihedral Set: same-side dihedral and opposite-side dihedral. ψ_1, ψ_2

Method: Quaternion

- Quaternion is a kind of hypercomplex number having one real part and three imaginary parts, denoted as $q = s + x\boldsymbol{i} + y\boldsymbol{j} + z\boldsymbol{k} \in \mathbb{H}$. The Hamilton product between two quaternions is

$$\begin{aligned} q_1 \otimes q_2 =& (s_1 s_2 - x_1 x_2 - y_1 y_2 - z_1 z_2) + (s_1 x_2 + x_1 s_2 + y_1 z_2 - z_1 y_2)\mathbf{i} + \\ & (s_1 y_2 - x_1 z_2 + y_1 s_2 + z_1 x_2)\mathbf{j} + (s_1 z_2 + x_1 y_2 - y_1 x_2 + z_1 s_2)\mathbf{k}. \\ =& [s_1 s_2 - \langle \boldsymbol{u}_1, \boldsymbol{u}_2 \rangle, \boldsymbol{u}_1 \times \boldsymbol{u}_2 + s_1 \boldsymbol{u}_2 + s_2 \boldsymbol{u}_1]. \end{aligned}$$

- Quaternion is a powerful mathematical tool to describe 3D rotations. Suppose that we rotate as a point $v_1 \in \mathbb{R}^3$ with an angle θ around a unit rotation axis u and obtain a point $v_2 \in \mathbb{R}^3$.

$$[0, \boldsymbol{v}_2^\top]^\top = q \otimes [0, \boldsymbol{v}_1^\top]^\top \otimes q^*, \text{ where } q = \left[\cos\frac{\theta}{2}, \sin\frac{\theta}{2}\boldsymbol{u}^\top\right]^\top,$$

Method: QMP

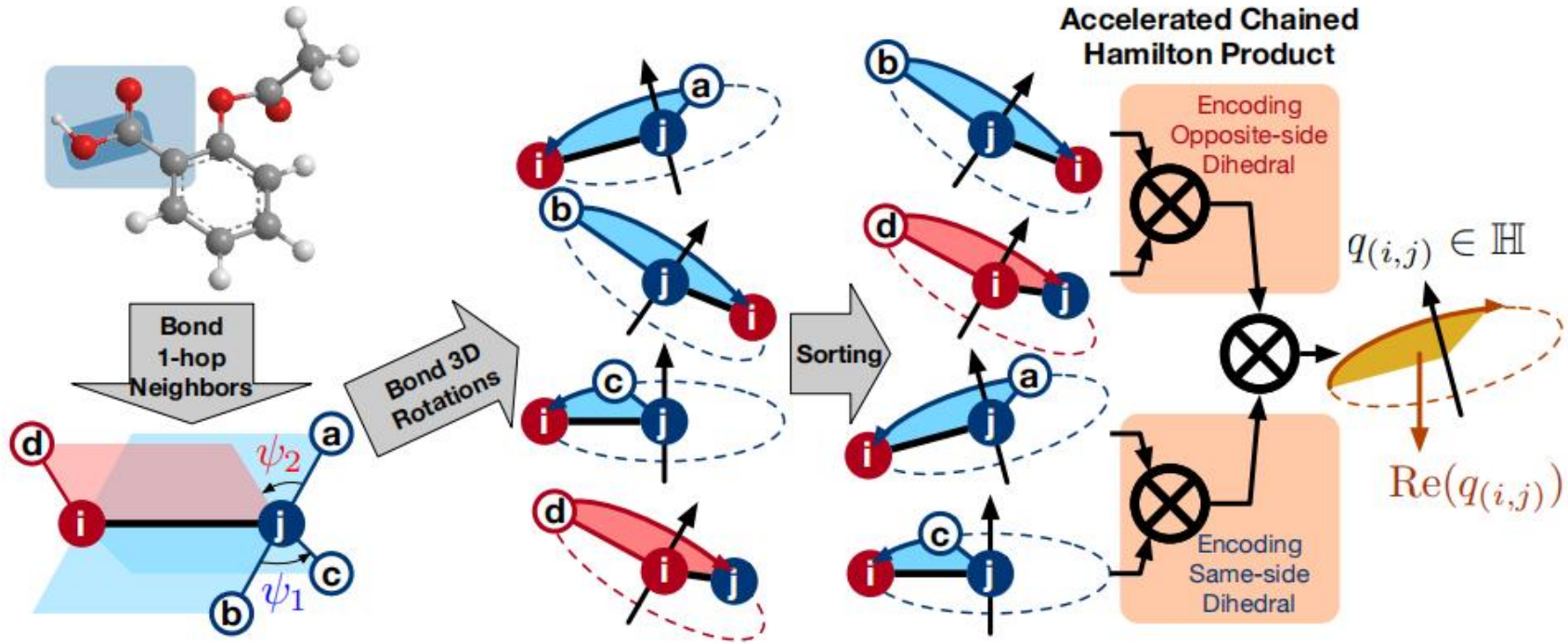


Figure 1: An illustration of our QMP module. Given a molecule, for each bond (i, j), we first obtain the 3D rotations from its 1-hop neighboring bonds to itself and sort them according to the rotation angles. Representing the sorted 3D rotations by a sequence of quaternions, we apply accelerated chained Hamilton product to obtain a quaternion $q_{(i,j)}$, whose real-part $\mathrm{Re}(q_{(i,j)})$ encodes all rotation angles, same-side dihedrals (e.g., the ψ_1 in blue), and opposite-side dihedrals (e.g., the ψ_2 in red) jointly. As shown in the orange blocks, the multiplications of quaternion pairs encode dihedrals.

Method: Merit

- **Global SE(3)-Invariance**

Real Part

$$\begin{bmatrix} s_1 \\ R(\boldsymbol{u}_1) \end{bmatrix} \otimes \begin{bmatrix} s_2 \\ R(\boldsymbol{u}_2) \end{bmatrix} = \begin{bmatrix} s_1 s_2 - \langle R(\boldsymbol{u}_1), R(\boldsymbol{u}_2) \rangle \\ R(\boldsymbol{u}_1) \times R(\boldsymbol{u}_2) + s_1 R(\boldsymbol{u}_2) + s_2 R(\boldsymbol{u}_1) \end{bmatrix}$$

$$= \begin{bmatrix} s_1 s_2 - \langle \boldsymbol{u}_1, \boldsymbol{u}_2 \rangle \\ R(\boldsymbol{u}_1 \times \boldsymbol{u}_2 + s_1 \boldsymbol{u}_2 + s_2 \boldsymbol{u}_1) \end{bmatrix},$$

- **Sensitivity to Local Torsions.**

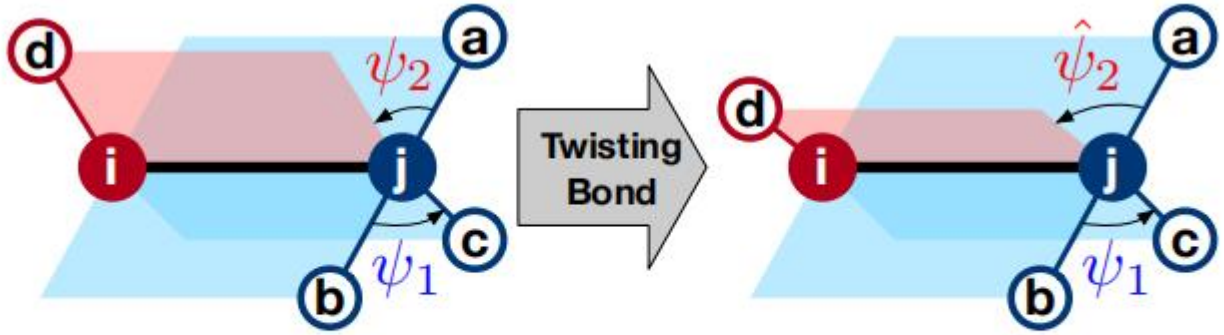


Figure 2: An illustration of the torsion caused by twisting bond. When twisting (i, j) with a torsion δ, the same-side dihedral ψ_1 is unchanged, while the opposite-side dihedral ψ_2 changes to $\hat{\psi}_2 = \psi_2 + \delta$.

Method: Merit

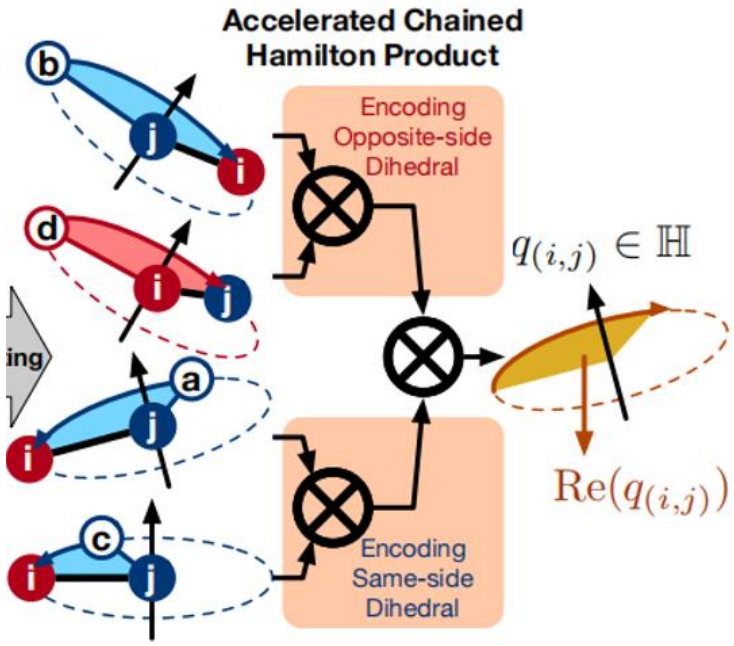
➢ **Accelerated Chained Hamilton Product.**

For a molecule with M bonds and N atoms that have D degrees on average. $M = O(ND)$.

In particular, for each bond, QMP records and merges $2K$ bond rotations from its 1-hop neighbors to itself. $K = O(D)$.

The computational complexity of QMP is $O(MK)$.

The runtime in practice is $\boldsymbol{O(MlogK) = O(NDlogD)}$



Method: Plug-and-Play

- **Plugging QMP into Representative Invariant GNNs.**

DimeNet, **DimeNet++** , and **SphereNet**

$$\text{Bond embedding: } \boldsymbol{z}_{ij}^{(l+1)} = f_e\left(\boldsymbol{z}_{ij}^{(l)} \oplus \sum\nolimits_{k\in\mathcal{N}_i\setminus\{j\}} f_{int}\left(\boldsymbol{z}_{ik}^{(l)}, b(\boldsymbol{D},\boldsymbol{\Theta},\boldsymbol{\Psi}_s)\right) \,\|\, \mathrm{Re}(q_{(i,j)})\right)$$

$$\text{Atom embedding: } \boldsymbol{h}_i^{(l+1)} = f_v\left(\boldsymbol{h}_i^{(l)}, \sum\nolimits_{j\in\mathcal{N}_i} \boldsymbol{z}_{ij}^{(l+1)}\right)$$

SchNet

$$\text{Bond embedding: } \boldsymbol{z}_{ij} = f_e\left(f_s(\boldsymbol{h}_j^{(l)}) \odot f_{cf}(b(\boldsymbol{D})) \,\|\, \mathrm{Re}(q_{(i,j)})\right)$$

$$\text{Atom embedding: } \boldsymbol{h}_i^{(l+1)} = f_v\left(\boldsymbol{h}_i^{(l)}, \sum\nolimits_{j\in\mathcal{N}_i} \boldsymbol{z}_{ij}\right)$$

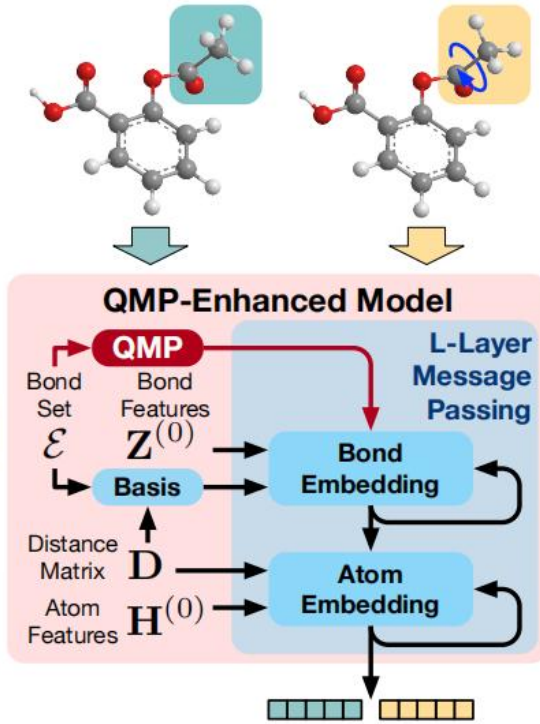


Figure 3: An illustration of how to plug our QMP into SE(3)-invariant GNNs. Given two molecular conformations, the QMP-enhanced model can capture bond torsions (i.e., the blue rotated arrow) and output different representations (i.e., the vectors with different colors).

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Experiment

■ MD17

Table 1: Results on MD17 in terms MAE of forces ($\frac{\text{kcal}}{\text{mol}\mathring{A}}$). The weight of force over energy (WoFE) in loss is set to 100. The best results are shown in bold, and the second best results are shown with underlines. ↑ indicates the performance is improved. The results of sGDML and DimeNet are quoted from [23].

	Force MAE							
Molecule	sGDML	DimeNet	SchNet	DimeNet++	SphereNet	Q-SchNet	Q-DimeNet++	Q-SphereNet
Aspirin	0.68	0.499	1.339	<u>0.325</u>	0.400	1.289↑	**0.316**↑	0.356↑
Benzene	0.20	0.187	0.346	<u>0.168</u>	0.193	0.316↑	**0.151**↑	0.177↑
Ethanol	0.33	0.230	0.738	<u>0.150</u>	0.181	0.468↑	**0.148**↑	0.169↑
Malonaldehyde	0.41	0.383	1.559	<u>0.263</u>	0.379	1.540↑	**0.241**↑	0.321↑
Naphthalene	0.11	0.215	0.723	**0.100**	0.159	0.521↑	<u>0.106</u>	0.138↑
Salicylic acid	0.28	0.374	1.001	**0.231**	0.261	0.971↑	<u>0.238</u>	0.321
Toluene	0.14	0.216	0.747	<u>0.117</u>	0.142	0.550↑	**0.107**↑	0.136↑
Uracil	0.24	0.301	1.351	<u>0.189</u>	0.228	1.010↑	**0.178**↑	0.241

Experiment

■ MD17@CCSD

Table 2: Results on MD17@CCSD in terms MAE of forces ($\frac{\text{kcal}}{\text{mol}\mathring{A}}$). The weight of force over energy (WoFE) in loss is set to 100. The best results are shown in bold and the second best results are shown with underlines. ↑ indicates the performance is improved.

	Force MAE					
Molecule	SchNet	DimeNet++	SphereNet	Q-SchNet	Q-DimeNet++	Q-SphereNet
Aspirin	1.471	<u>0.387</u>	0.458	1.298↑	**0.365**↑	0.475
Benzene	0.352	<u>0.049</u>	0.061	0.287↑	**0.048**↑	0.063
Ethanol	1.321	<u>0.129</u>	0.158	0.786↑	**0.108**↑	0.148↑
Malonaldehyde	1.531	**0.211**	0.289	1.086↑	<u>0.231</u>	0.264↑
Toluene	0.855	0.133	0.160	0.637↑	<u>0.128</u>↑	**0.052**↑

Experiment

■ OC20

Table 3: Results on OC20 IS2RE task in terms of energy MAE(eV) and the percentage of EwT of the ground truth energy. Performance is reported for models trained on the 10k training dataset. The best performance is shown in bold and the second best is shown with underlines. ↑ indicates the performance is improved.

		CGCNN	SchNet	DimeNet	DimeNet++	Q-SchNet	Q-DimeNet	Q-DimeNet++
Energy MAE	ID	0.9773	1.0480	0.9314	0.9261	1.0363↑	**0.9132**↑	0.9177↑
	OOD Ads	0.9818	1.0450	1.0720	0.9400	1.0640	0.9865↑	**0.9295** ↑
	OOD Cat	0.9269	1.0630	0.8945	0.8828	1.0370 ↑	**0.8753**↑	0.8816↑
	OOD Both	0.8828	1.0076	0.9643	0.8572	0.9646 ↑	0.9317↑	**0.8513**↑
	Average	0.9422	1.0409	0.9656	0.9015	1.0255 ↑	0.9267↑	**0.8950**↑
EwT (%)	ID	1.84	1.58	1.80	1.79	1.59↑	1.84↑	**1.91**↑
	OOD Ads	1.72	1.53	1.62	1.67	1.52	**1.85**↑	1.79↑
	OOD Cat	1.93	1.56	1.93	1.81	1.46	1.96↑	**2.13**↑
	OOD Both	1.69	1.48	1.57	**1.80**	1.61↑	1.70↑	1.75↑
	Average	1.80	1.54	1.73	1.77	1.55↑	1.84↑	**1.90**↑

Experiment

■ Ablation Study

Table 4: Effects of ablating components of QMP on force MAE for Aspirin MD17 dataset, backbone model is DimeNet++.

QMP Components			Force MAE
j-side	i-side	sorting	Aspirin
X	X	X	0.325
✓	X	✓	0.323
X	✓	✓	0.360
✓	✓	X	0.390
✓	✓	✓	**0.316**

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- Experiment
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Conclusion

- In this study, we have proposed an efficient and effective quaternion message-passing module for molecular conformation representation and analysis.
- With little computational cost, we can plug this module into most existing invariant GNNs by one-line code, achieving global SE(3)-invariance and enhancing their sensitivity to local bond torsions simultaneously.
- Experiments show that with the help of our QMP module, the enhanced models perform better on distinguishing molecular conformations, leading to consistent improvements in downstream tasks like predicting molecular energy and atomic force.
- In the future, we would like to utilize the imaginary part of our QMP to enhance equivariant GNNs. Additionally, we plan to leverage advanced mathematical tools from Clifford Algebra to design more hyper-complex neural networks for molecular modeling.

Thank You for listening!

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