Towards Physically Reliable Molecular Representation Learning

uai2023

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Molecular Energy Prediction Task

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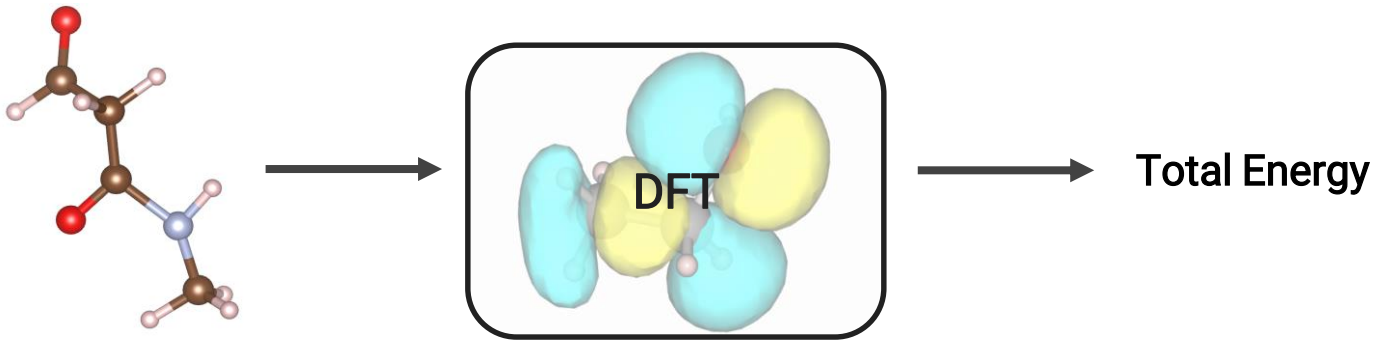

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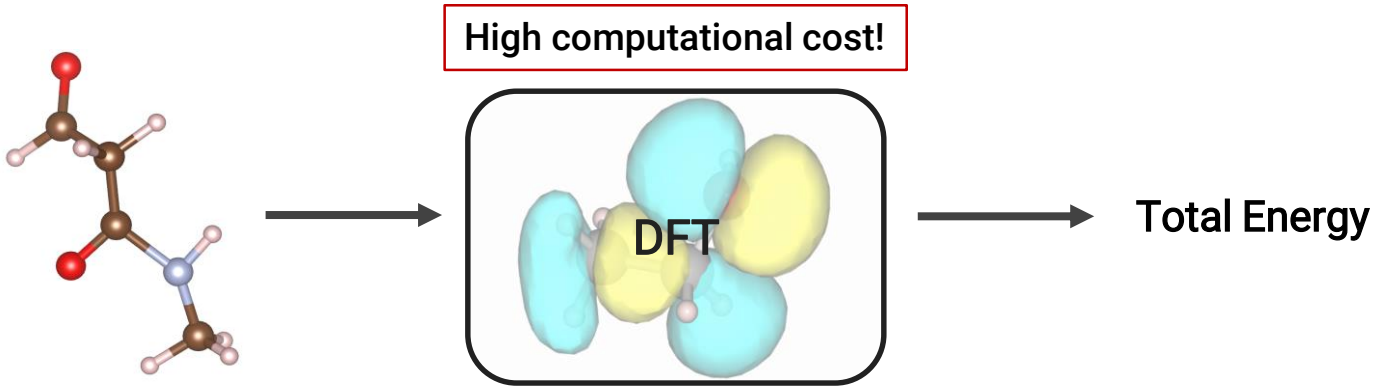

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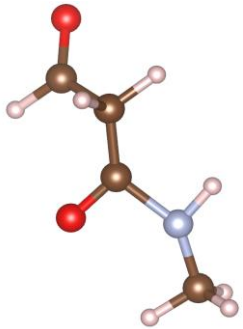
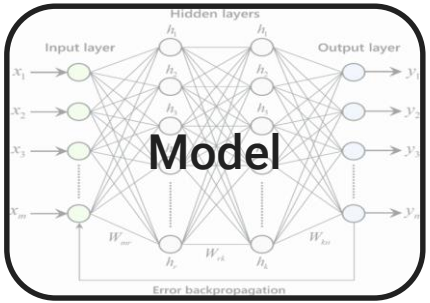


High computational cost!



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MXMNet (Zhang et al., 2020)
ForceNet (Hu et al., 2021)
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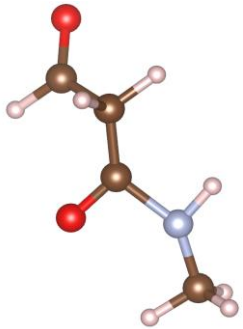

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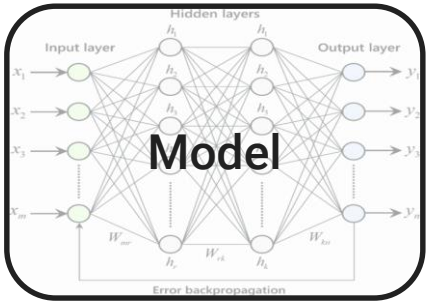

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Is small energy error enough for a physically reliable model?

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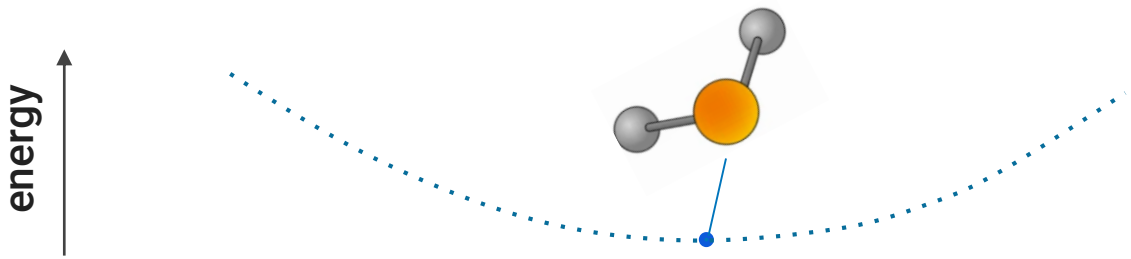

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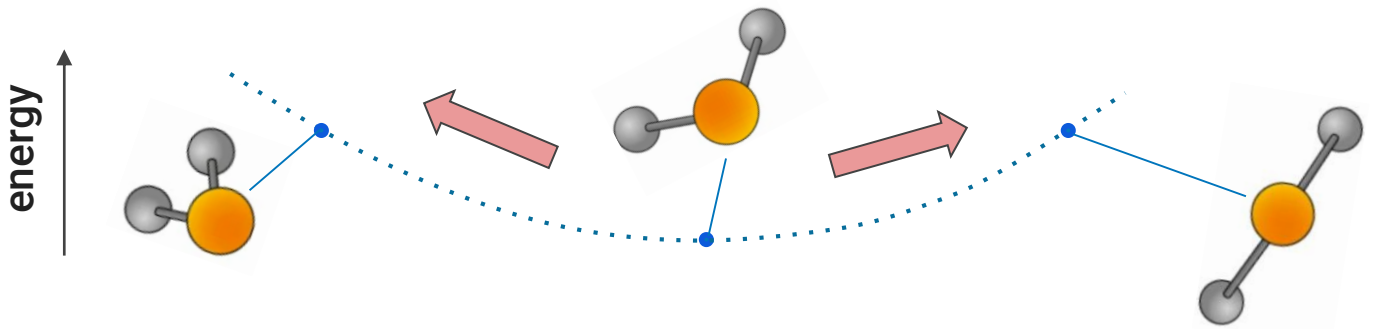

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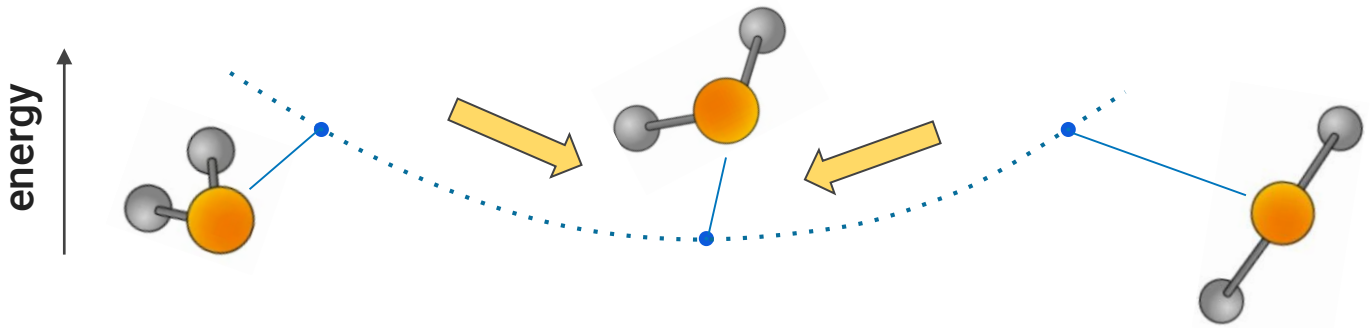
  - Once we optimize it again, the structure should be recovered if the perturbation is small enough.



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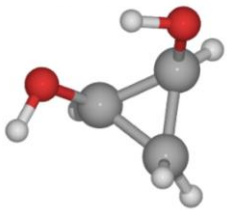	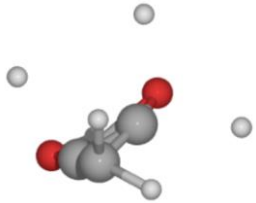	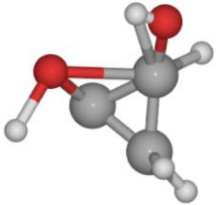	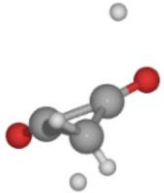	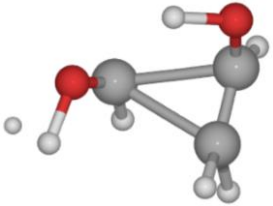	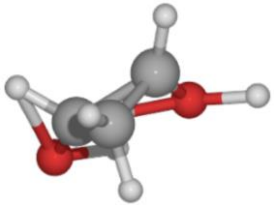
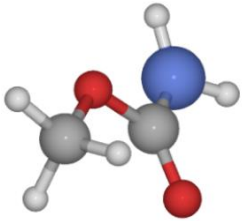	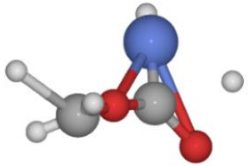	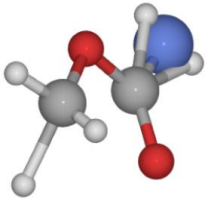	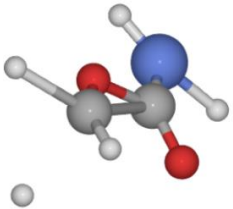	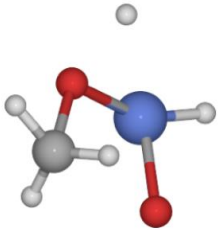	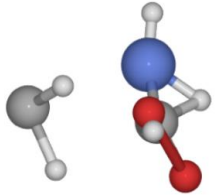

Conducted on QM9 dataset.

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  - Indicating they have been over-optimized only to energy estimation.

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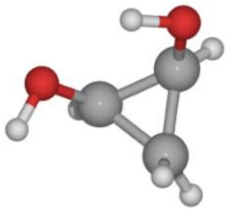	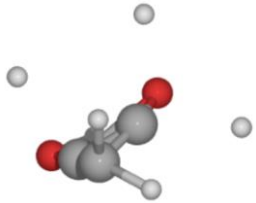	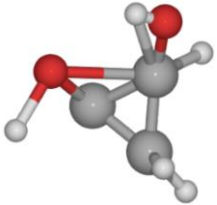	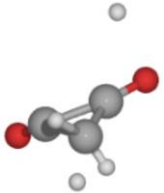	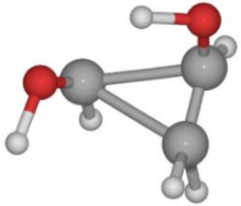	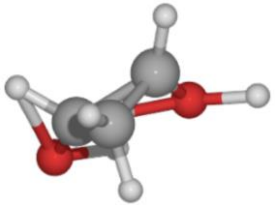
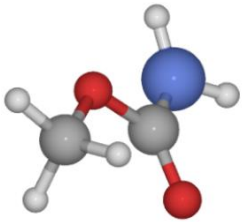	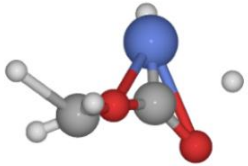	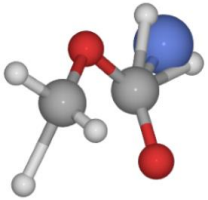	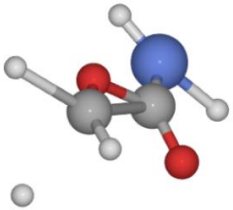	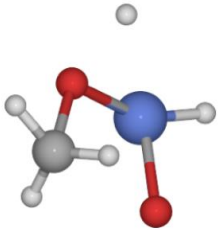	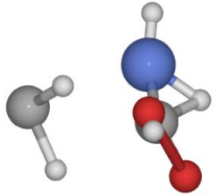

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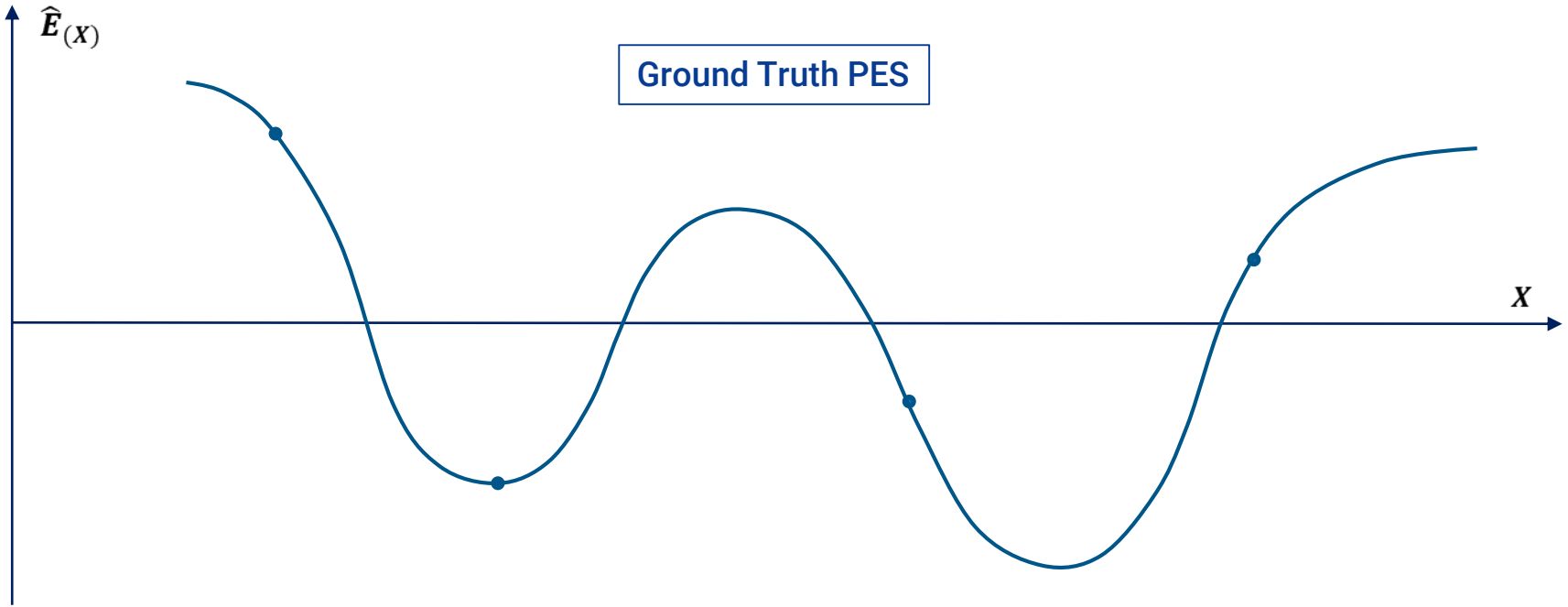

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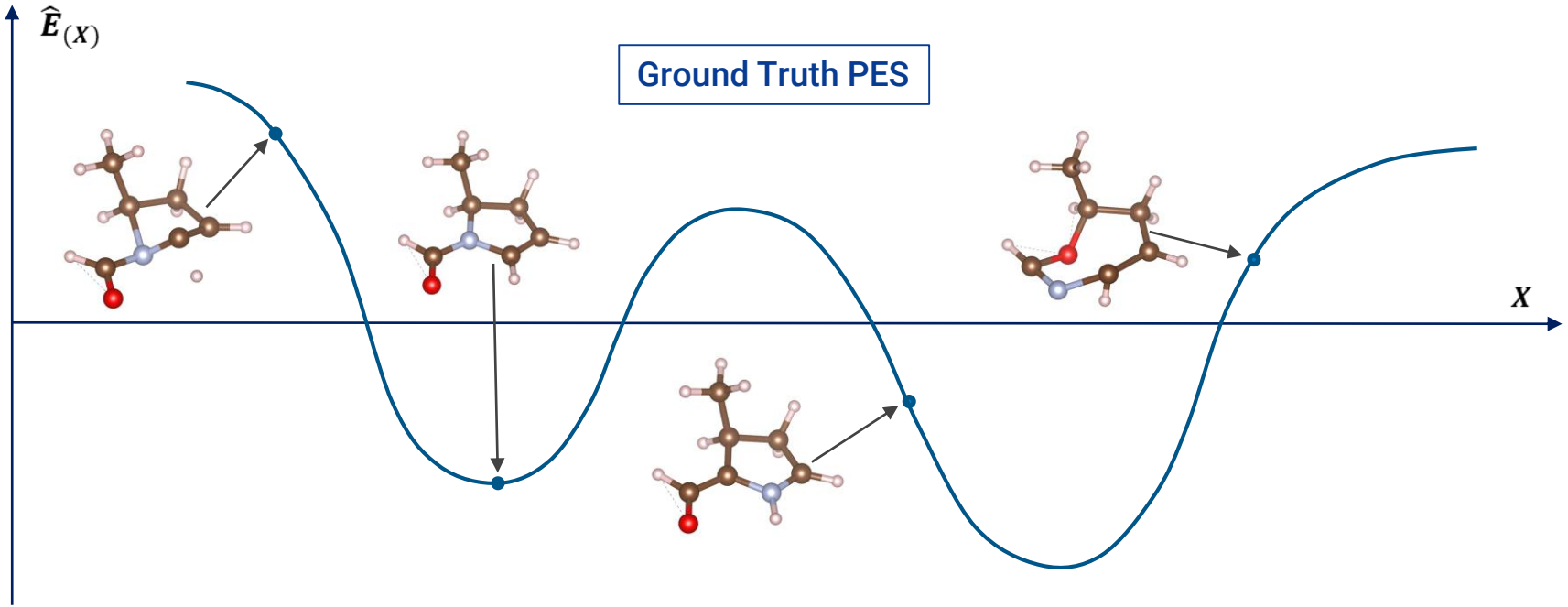

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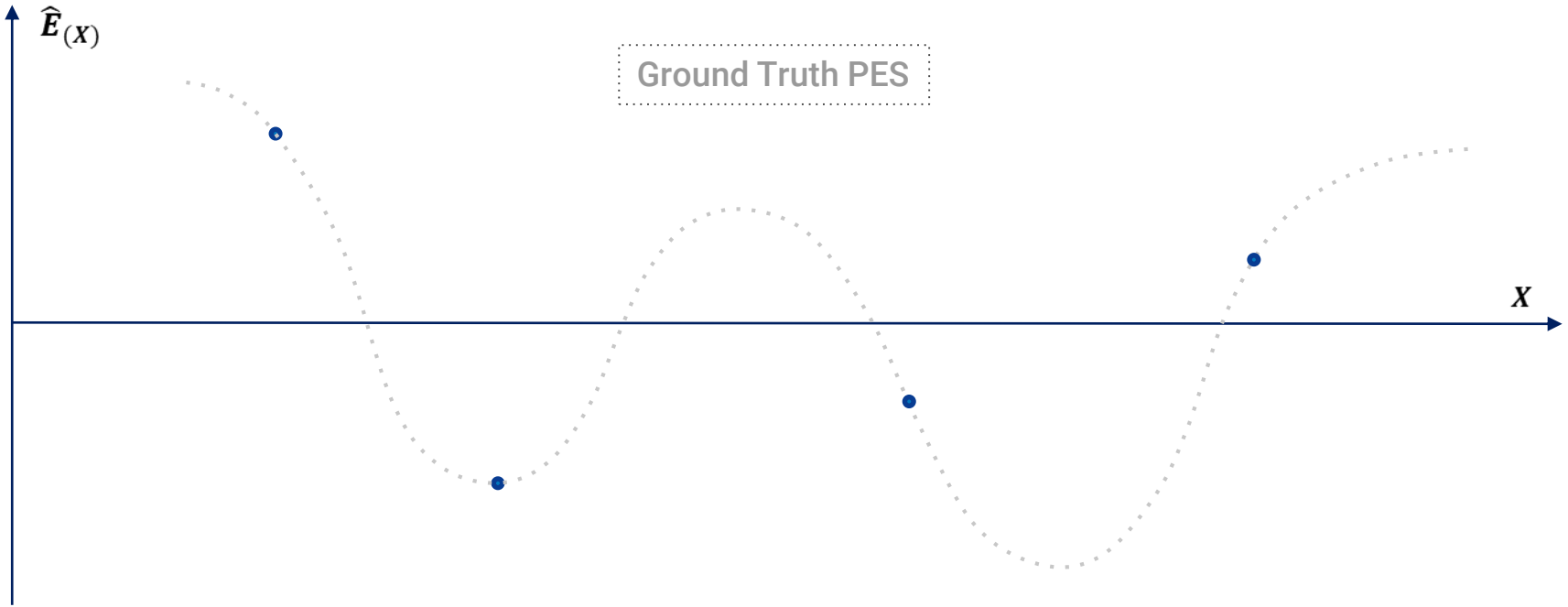

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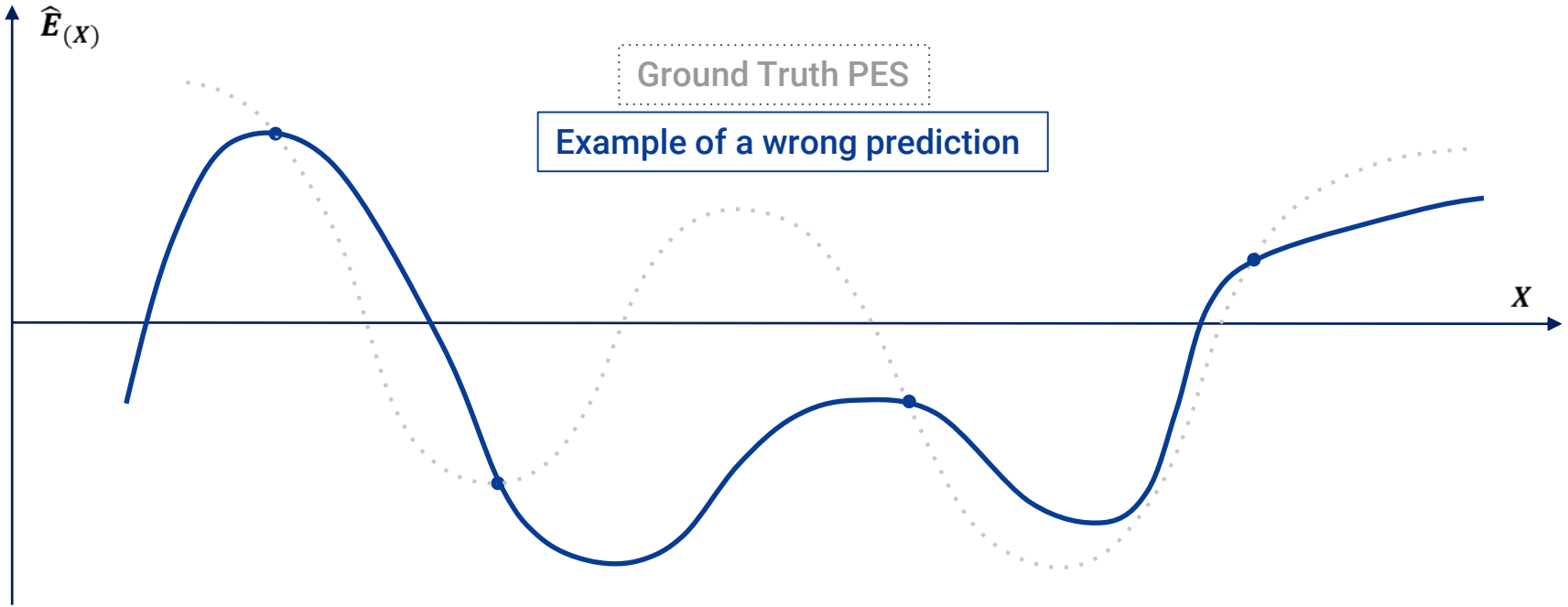

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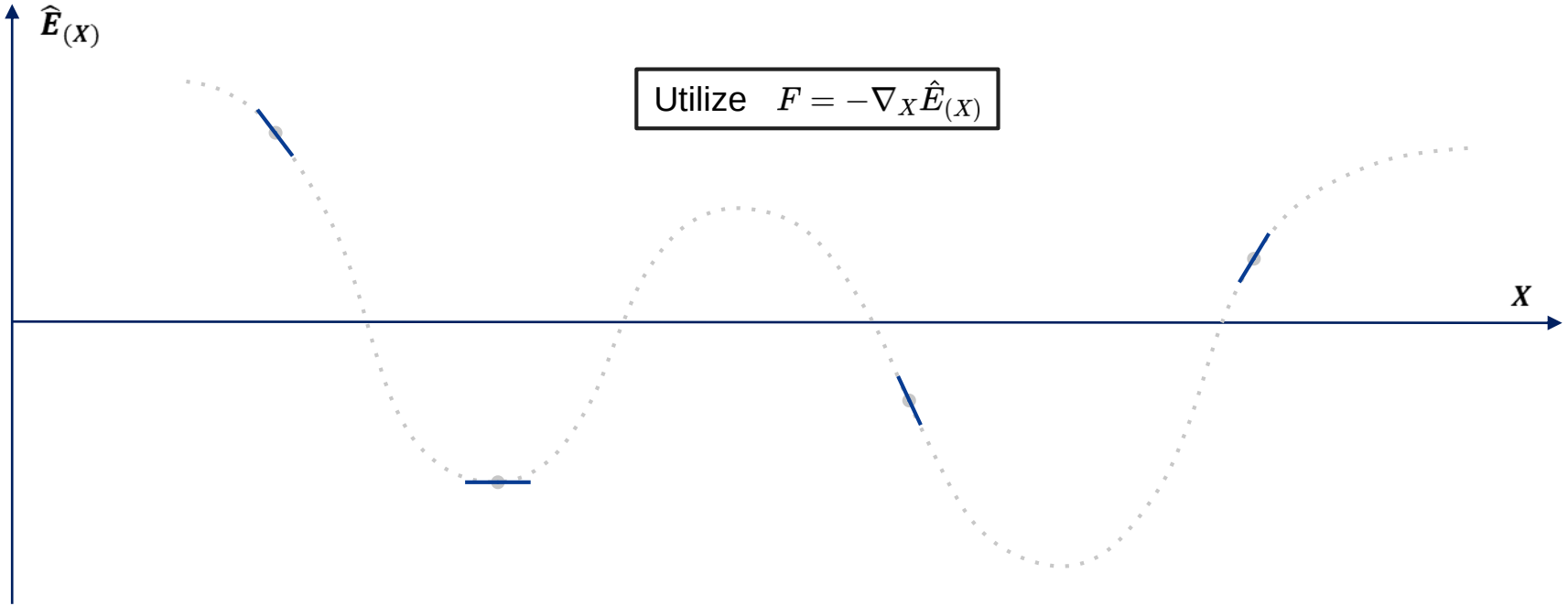

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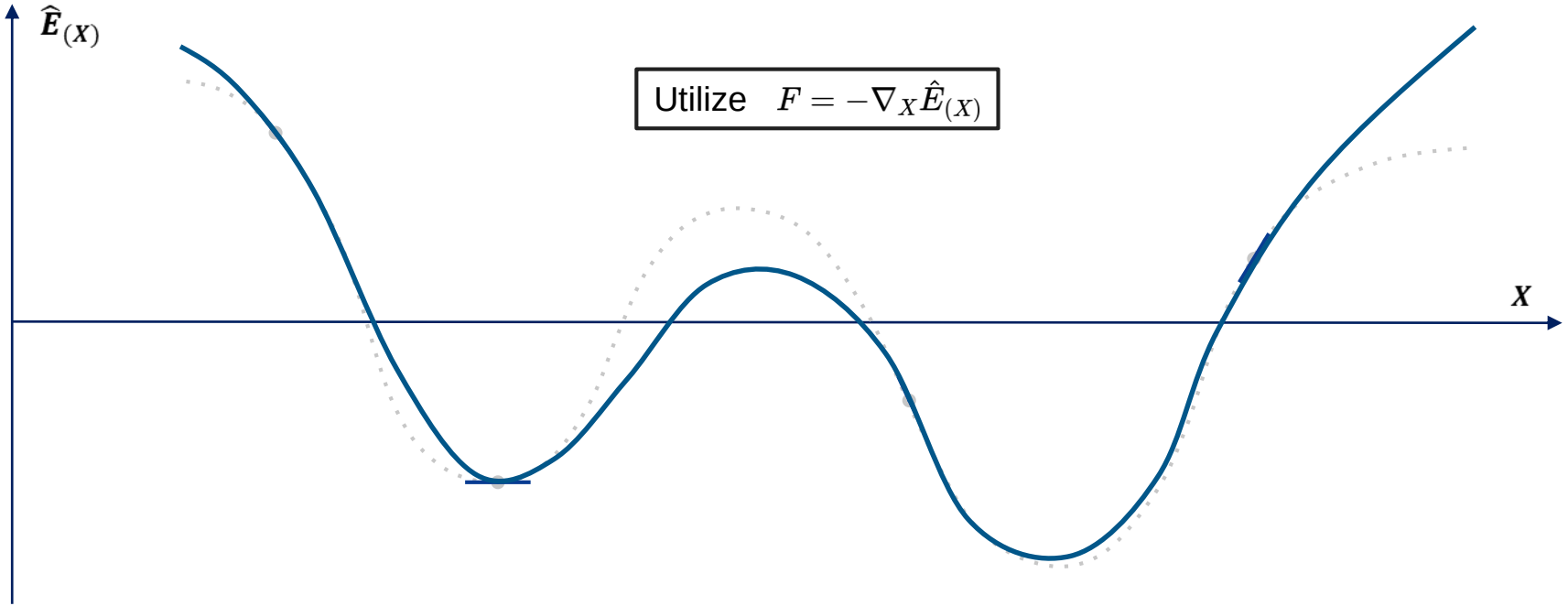

Our Approaches

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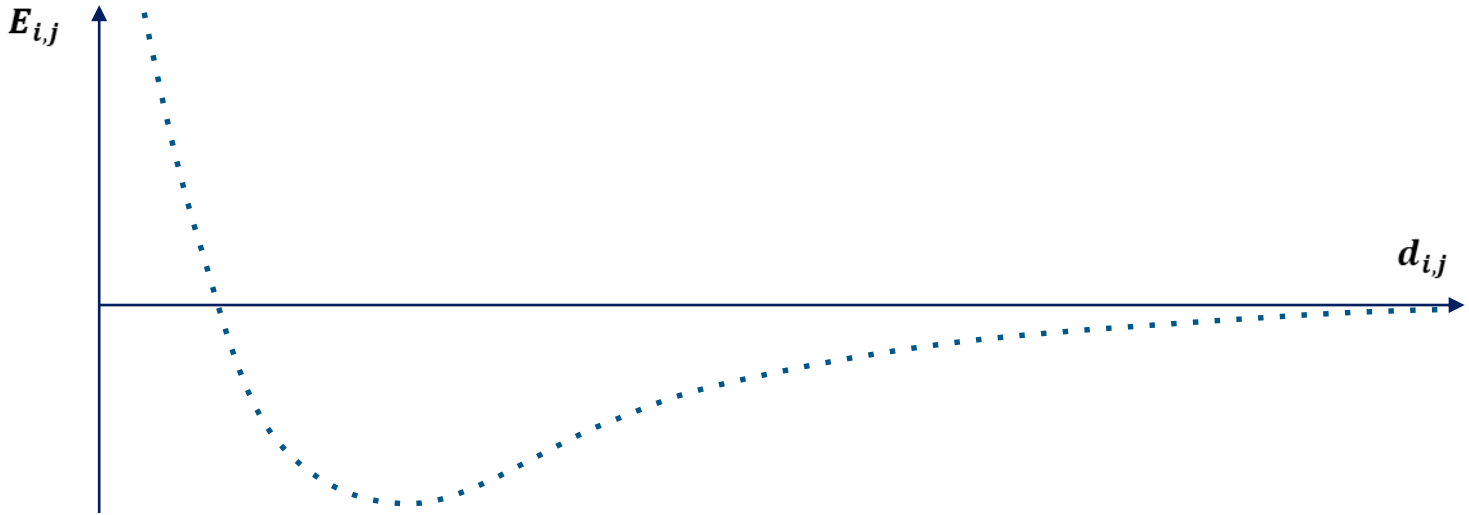

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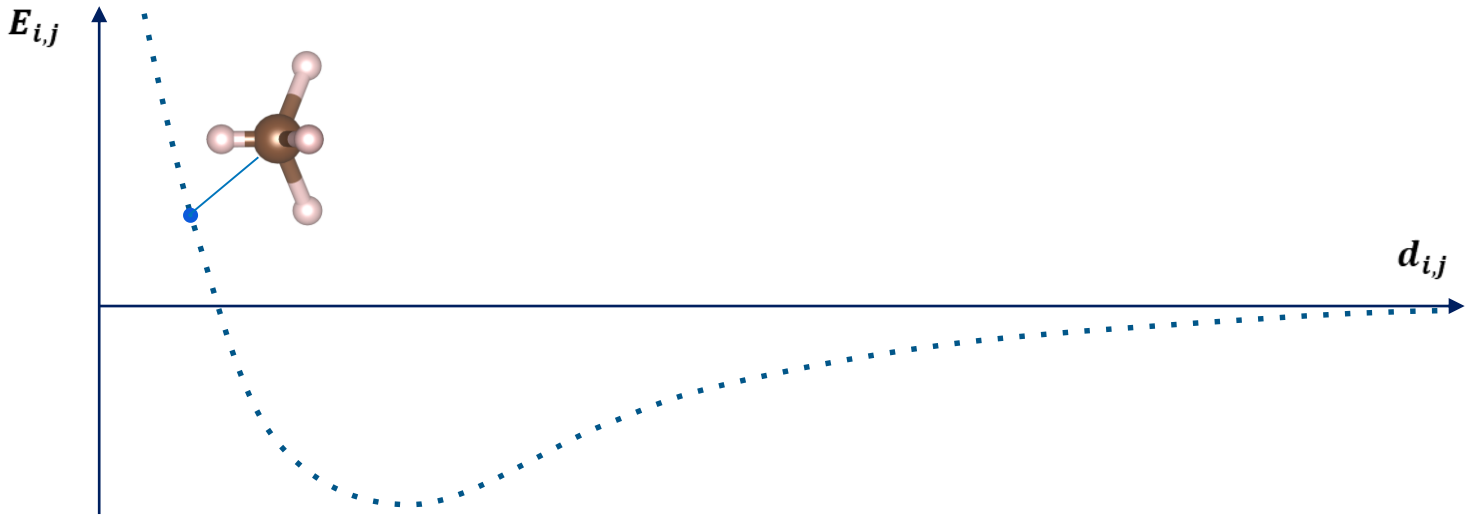

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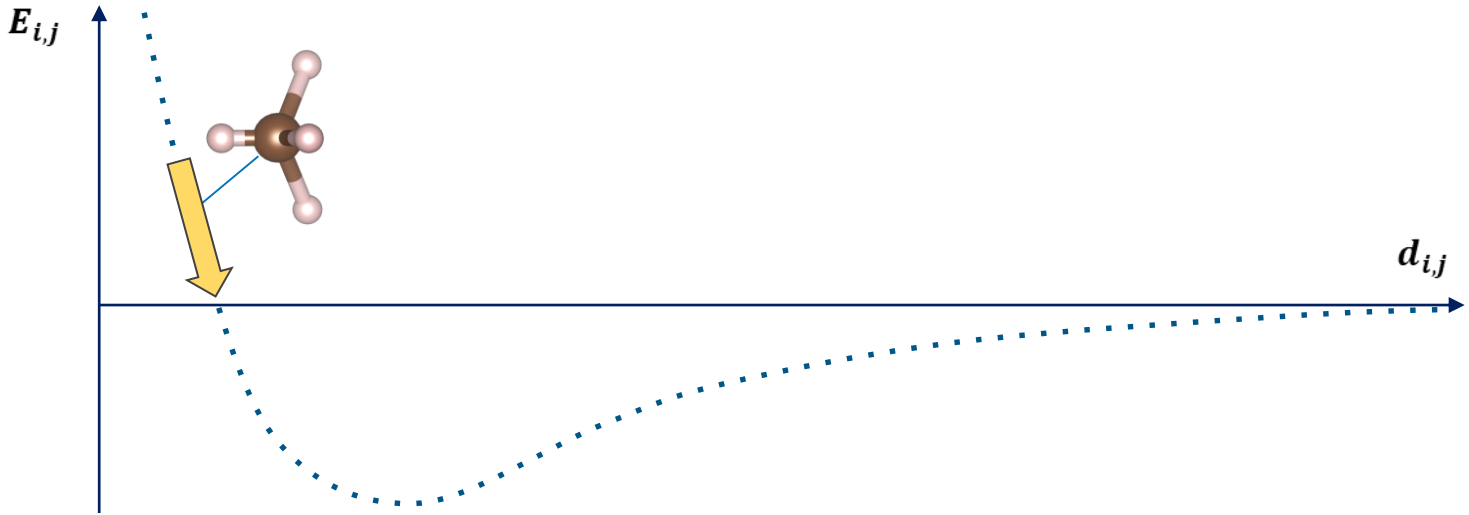

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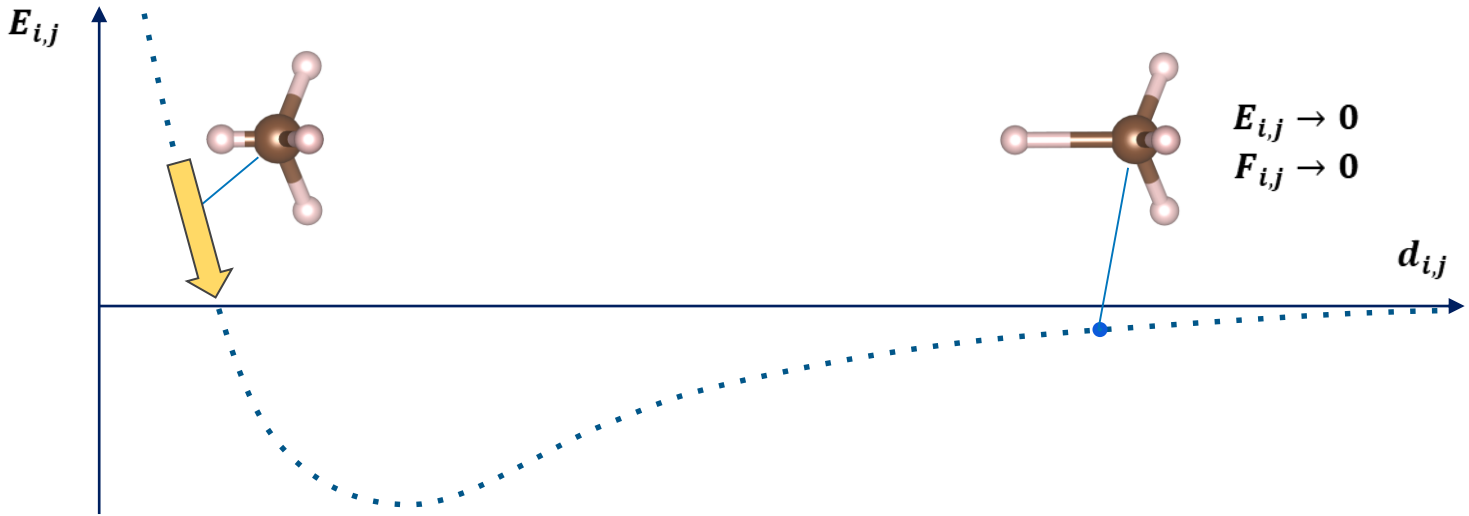

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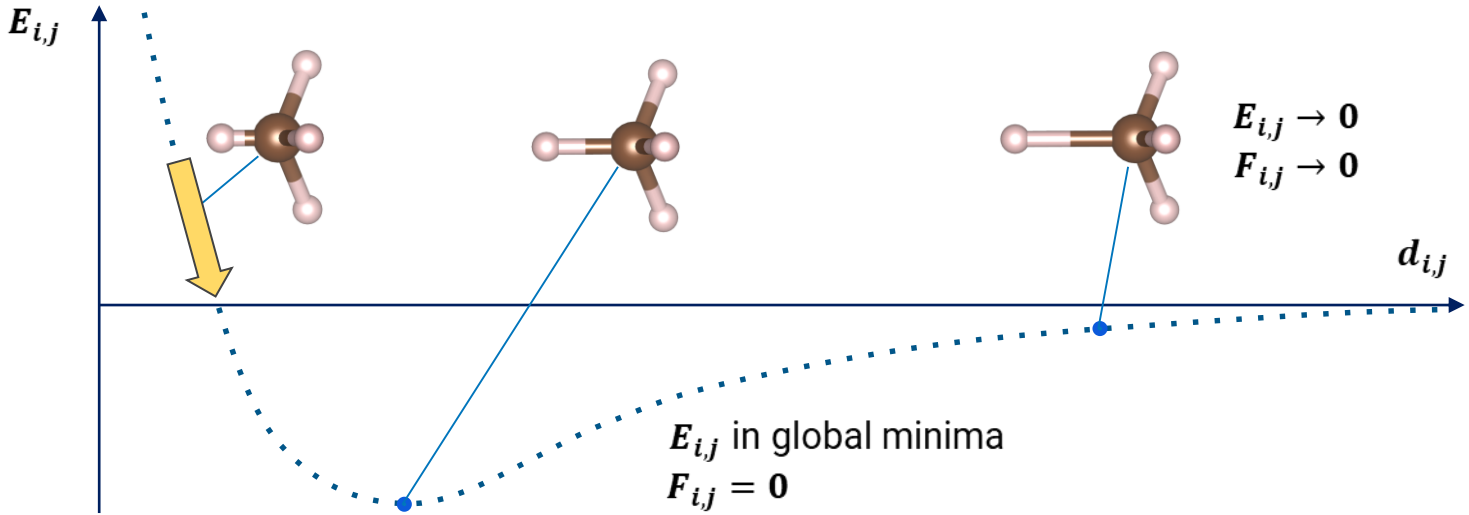

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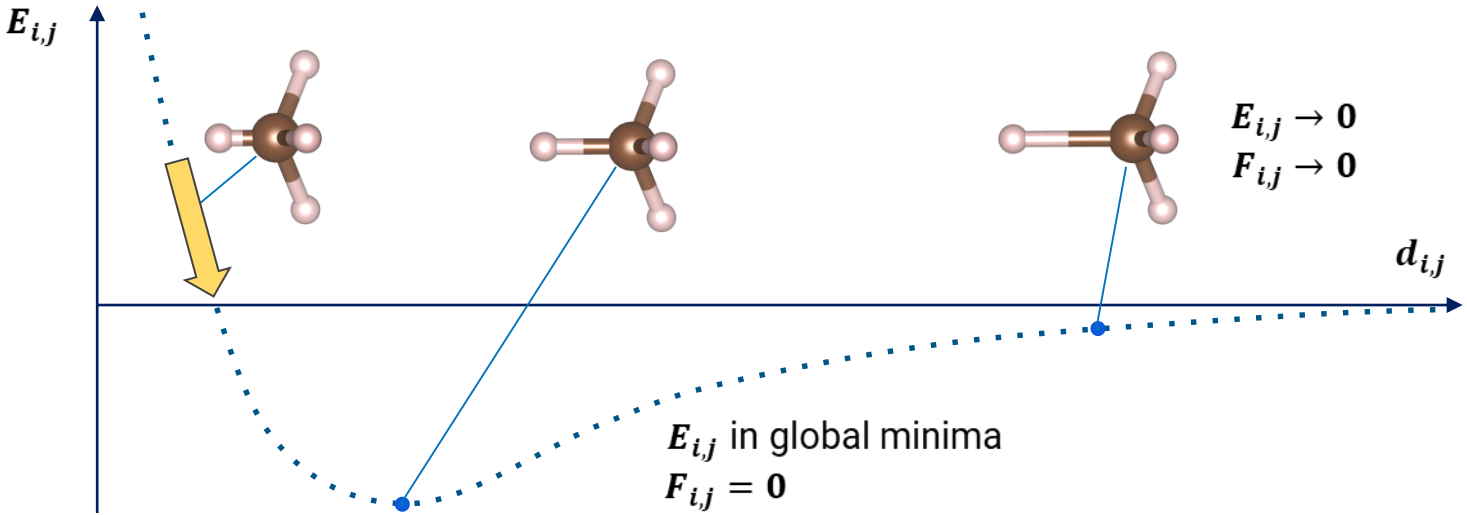

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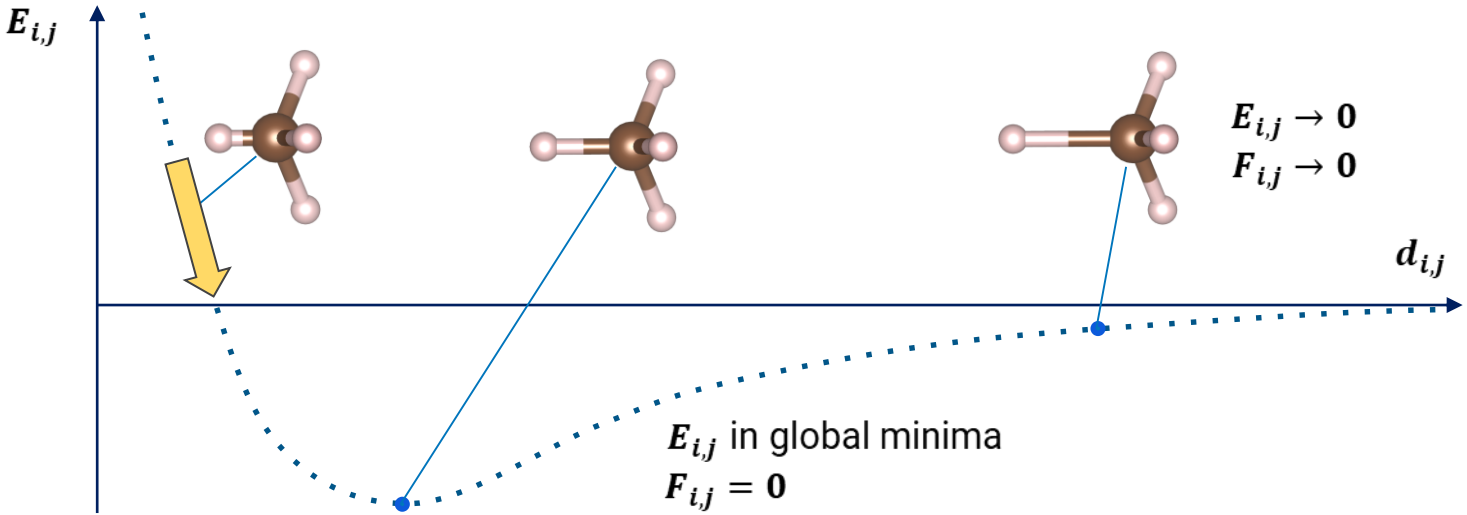

Our Approach 1: Physics-model Constraints

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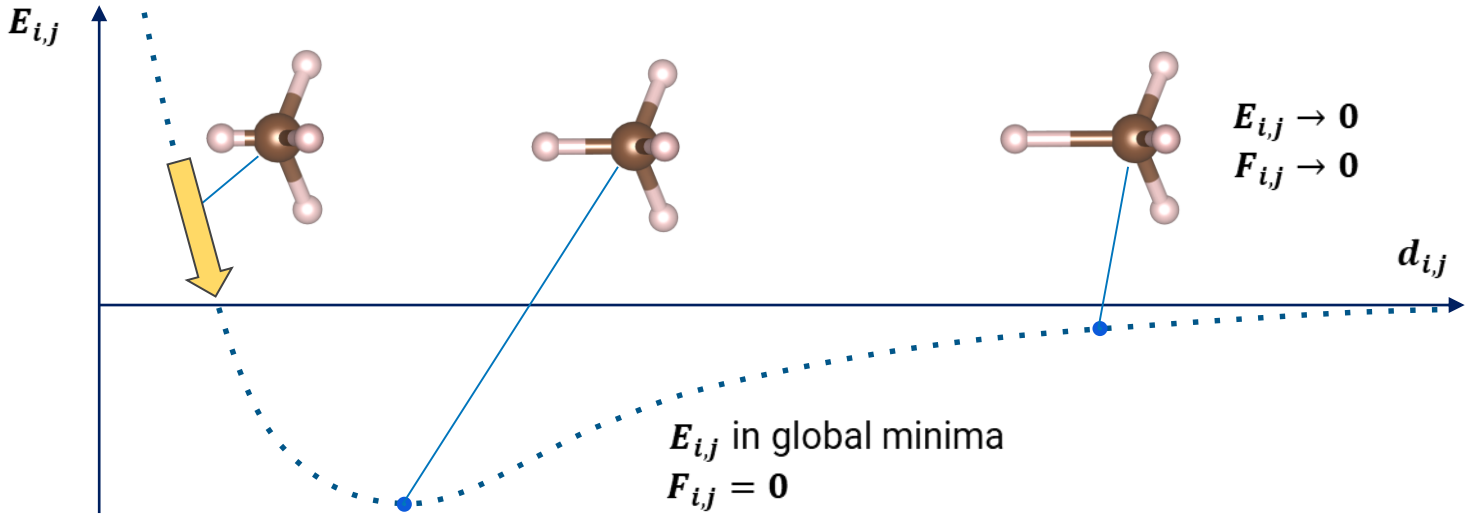

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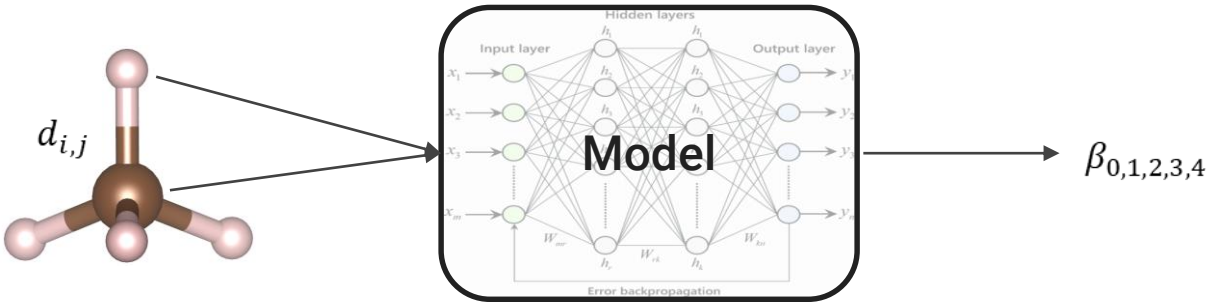
  - Parametrized by β, which depends on the species of pair of atoms



Our Approach 2: Physics-inspired Constraints

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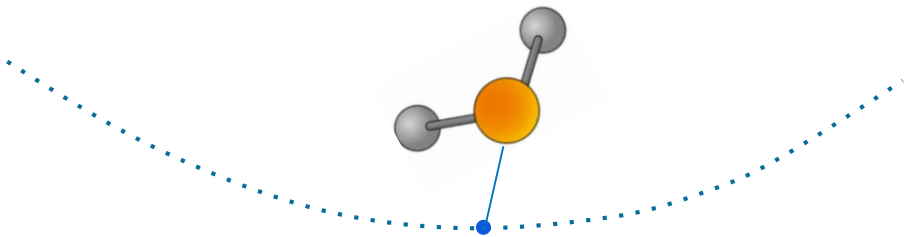

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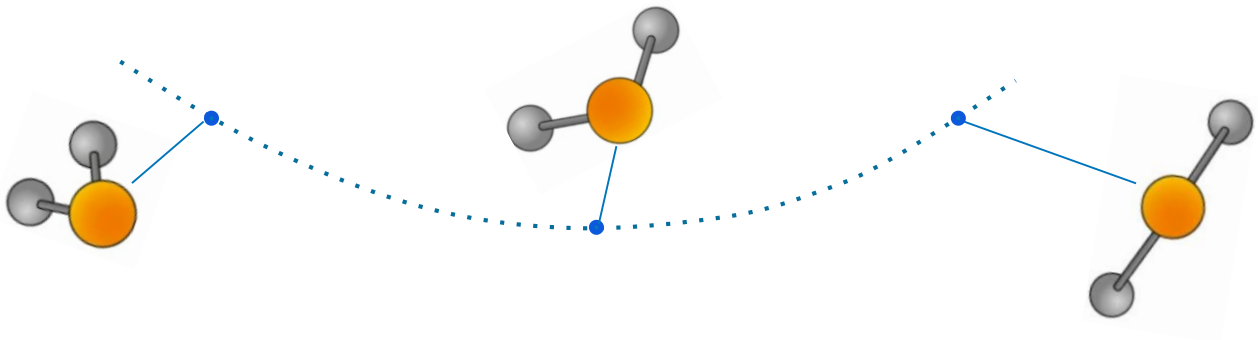

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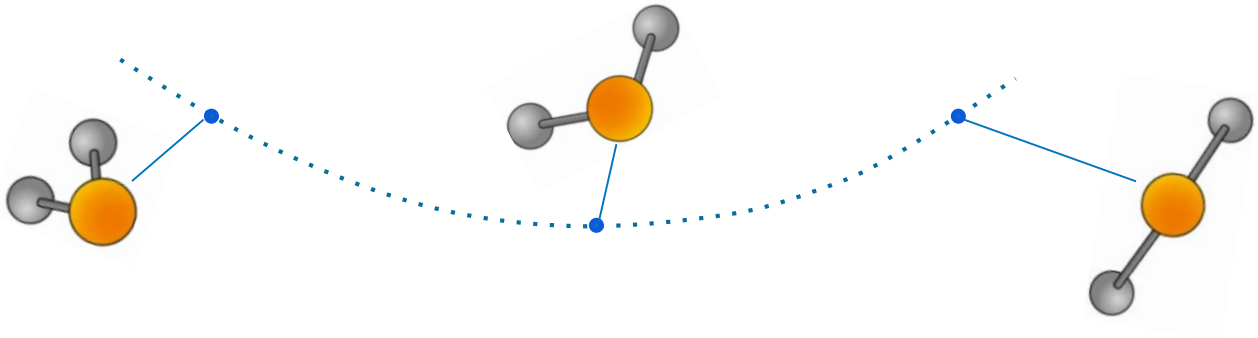

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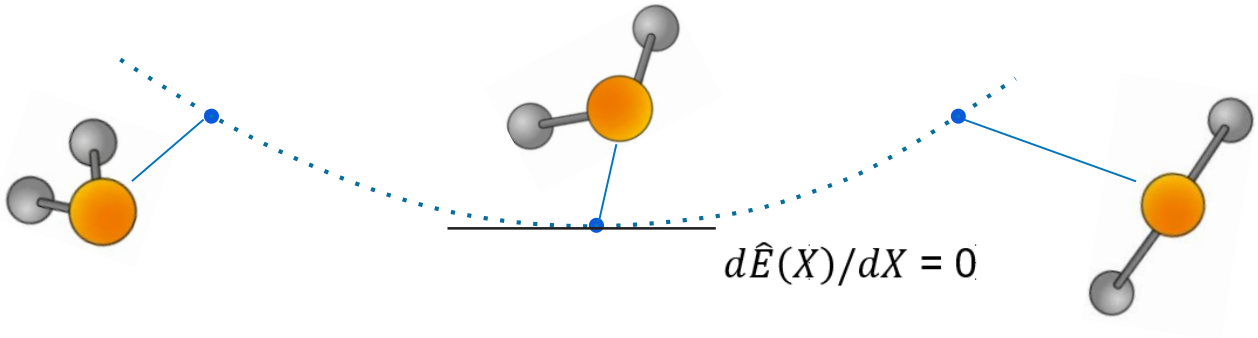

Our Approach 3: Masked Atomic Modeling

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Concurrently developed in G. Zhou et al., ICLR 2023 (Uni-Mol: A Universal 3D Molecular Representation Learning Framework).

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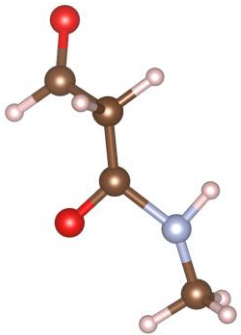

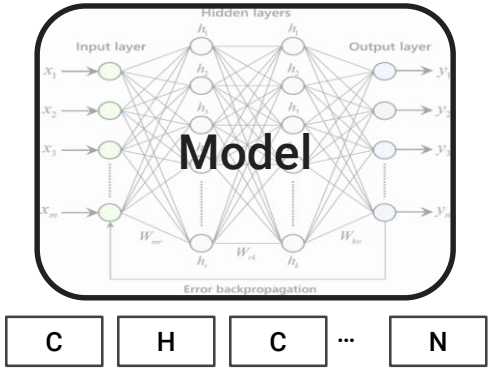

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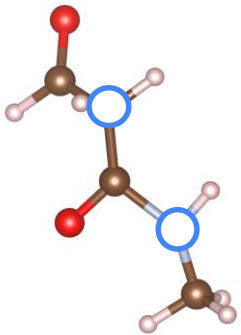

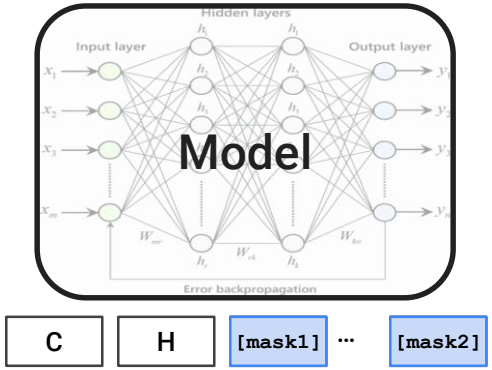

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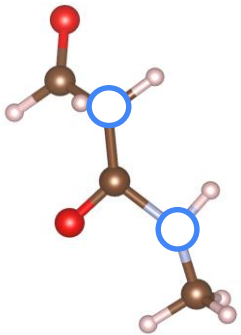

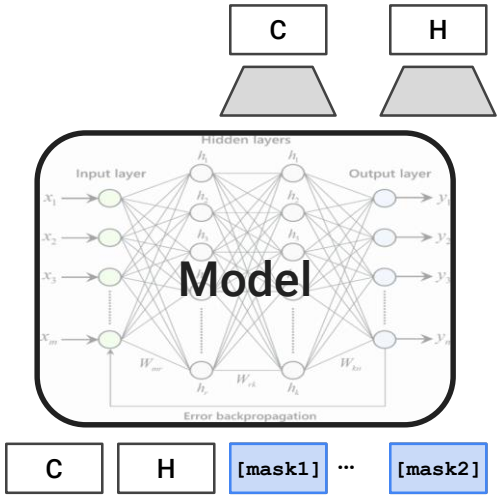

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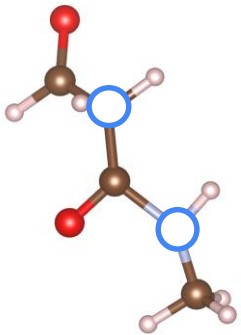
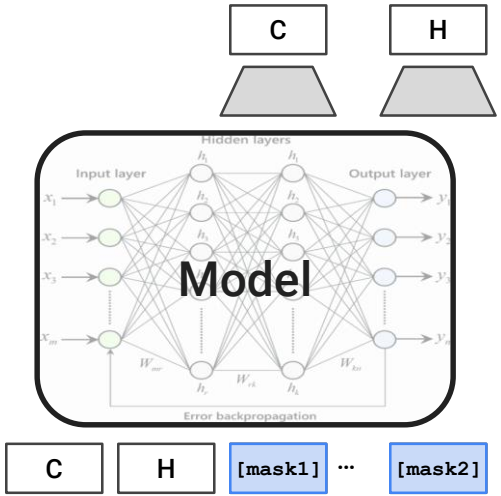
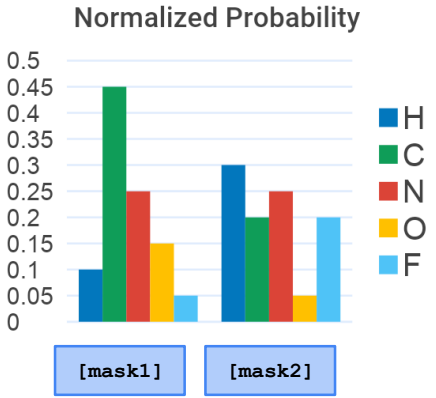
Our Approach 3: Masked Atomic Modeling

- Masked Atomic Modeling
  - Zero-out 30% of the entire atomic embeddings in a given molecule.
  - The model must learn fundamental bonding principles to recover them.







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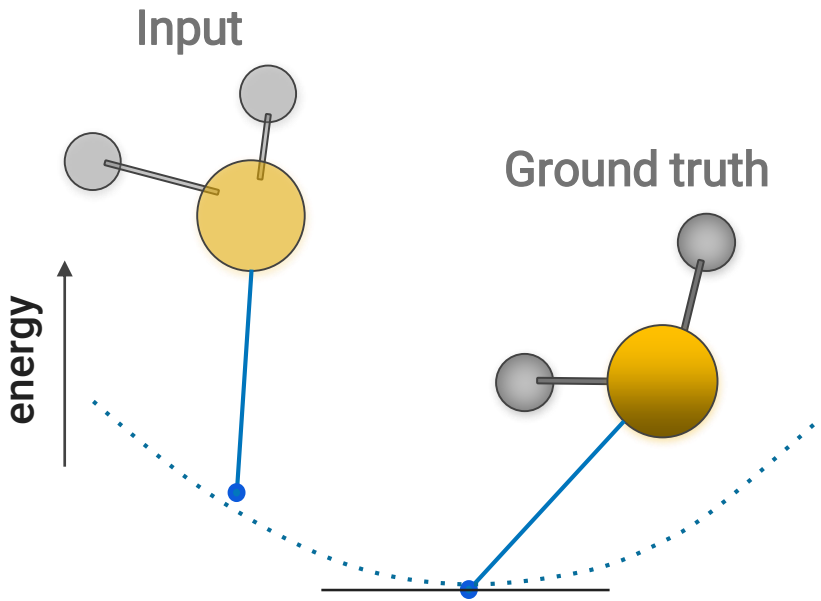
Experimental Results

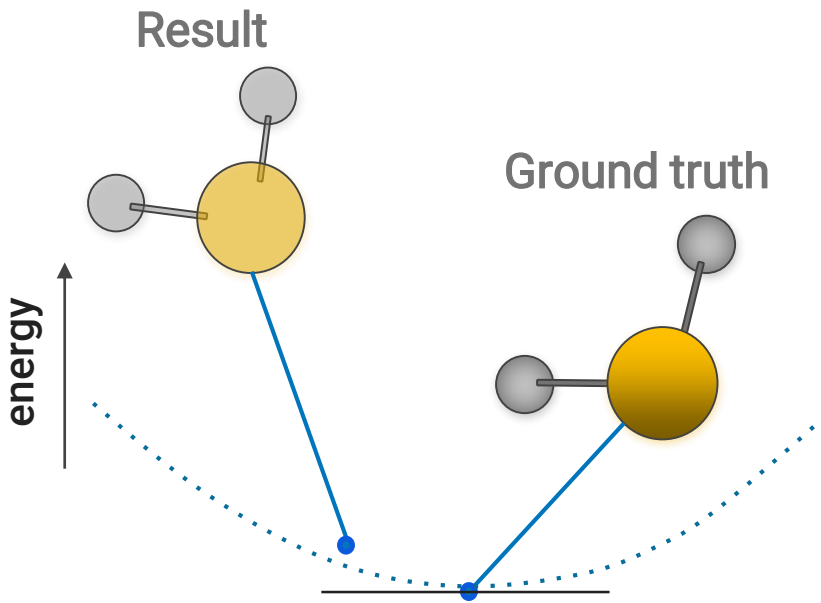
New metrics: ΔE and ΔP



New metrics: ΔE and ΔP

ΔP : Structural distortion

ΔE : Energy difference



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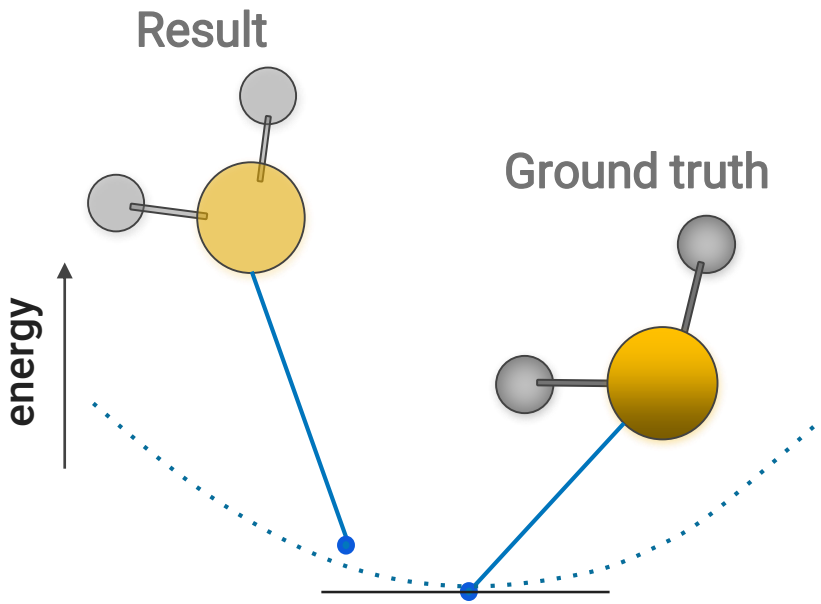
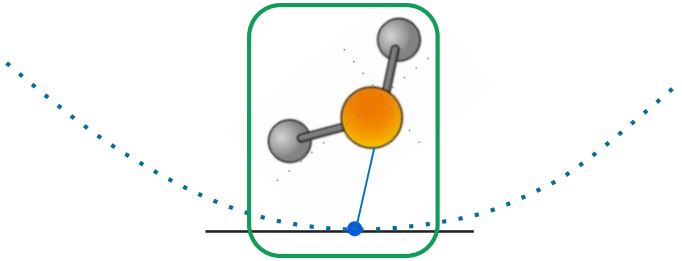


Ideal case: ΔE = 0 and ΔP = 0



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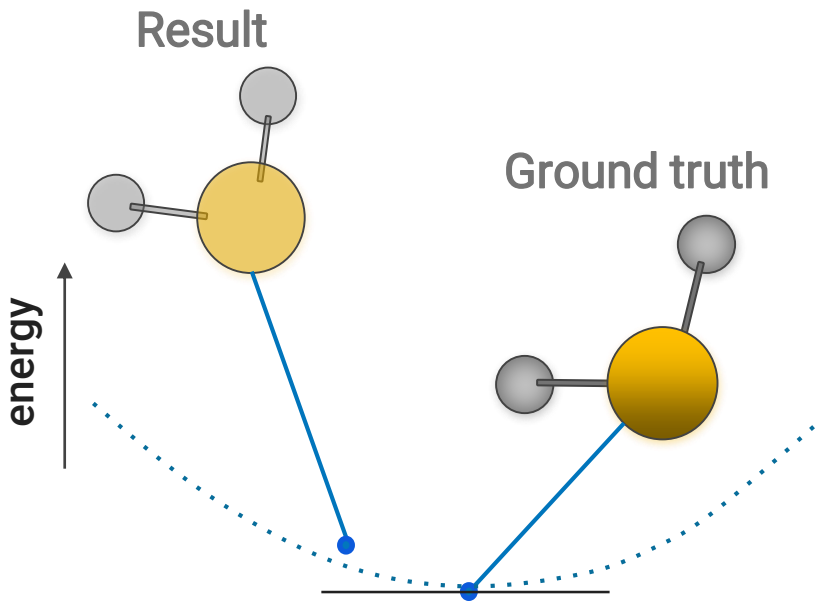

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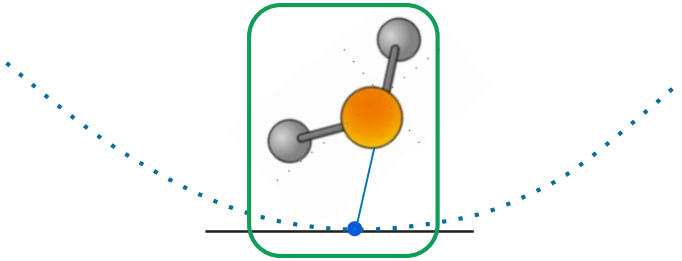

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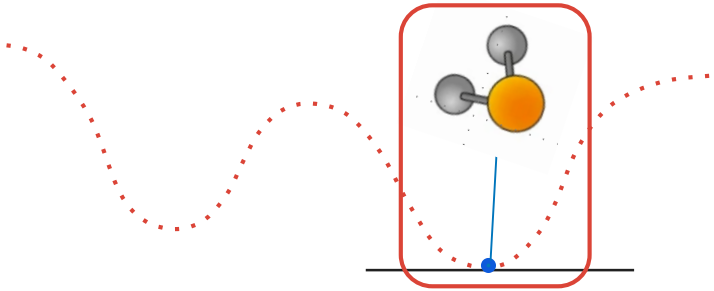
Problematic case: ΔE ≠ 0 and ΔP ≠ 0



Optimized structure ≠ Stable structure

Comparison with Other Models: Analysis

Dataset (Task) / Model	QM9 $\text{MAE}_\text{E}(\downarrow)$	QM9 $\text{MAE}_\text{F}(\downarrow)$	QM9 $\Delta P(\downarrow)$	OC20 (IS2RE) $\text{MAE}_\text{E}(\downarrow)$	OC20 (IS2RE) $\Delta P(\downarrow)$
SchNet [Schütt et al., 2018]	14.00	2.64	0.47	1.059	0.60
CGCNN [Xie and Grossman, 2018]	–	–	–	0.988	0.58
MXMNet [Zhang et al., 2020b]	**5.90**	1.83	1.57	–	–
DimeNet [Gasteiger et al., 2020]	8.02	1.79	0.58	1.012	0.55
ForceNet [Hu et al., 2021]	18.62	0.41	0.21	–	–
TorchMDNet (ET) [Thölke and De Fabritiis, 2022]	6.15	1.15	0.32	–	–
Ours ($\mathcal{L}_{\text{energy}}$ only)	8.35	1.28	1.23	–	–
Ours (full model)	15.16±0.539	**0.0057**±0.001	**0.0251**±0.01	**0.887**±0.024	**0.10**±0.01
p-value	–	0	3.2×10^{-7}	2.6×10^{-4}	7.0×10^{-8}

Comparison with Other Models: Analysis

Energy estimation error

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Dataset (Task) / Model	Energy estimation error QM9 $MAE_E(\downarrow)$	Net force (ideally 0) QM9 $MAE_F(\downarrow)$	Atom position distortion QM9 $\Delta P(\downarrow)$	OC20 (IS2RE) $MAE_E(\downarrow)$	OC20 (IS2RE) $\Delta P(\downarrow)$
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Force error and ΔP get considerably better than baselines with our full model!

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Baseline models fail to learn the actual energy surface, indicated by high force and position error.

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Baseline models fail to learn the actual energy surface, **indicated by high force and position error.**

It is same for our model when it is trained only on the energy loss. → **It is indeed important to** consider other physical constraints!

Energy estimation error — Net force (ideally 0) — Atom position distortion

Dataset (Task) / Model	QM9 $\text{MAE}_\text{E}(\downarrow)$	QM9 $\text{MAE}_\text{F}(\downarrow)$	QM9 $\Delta P(\downarrow)$	OC20 (IS2RE) $\text{MAE}_\text{E}(\downarrow)$	OC20 (IS2RE) $\Delta P(\downarrow)$
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MXMNet [Zhang et al., 2020b]	**5.90**	1.83	1.57	–	–
DimeNet [Gasteiger et al., 2020]	8.02	1.79	0.58	1.012	0.55
ForceNet [Hu et al., 2021]	18.62	0.41	0.21	–	–
TorchMDNet (ET) [Thölke and De Fabritiis, 2022]	6.15	1.15	0.32	–	–
Ours ($\mathcal{L}_{\text{energy}}$ only)	8.35	1.28	1.23	–	–
Ours (full model)	15.16±0.539	**0.0057**±0.001	**0.0251**±0.01	**0.887**±0.024	**0.10**±0.01
p-value	–	0	3.2×10^{-7}	2.6×10^{-4}	7.0×10^{-8}

We achieve comparable energy estimation to the baselines.

Force error and ΔP get considerably better than baselines with our full model!

Comparison with Other Models: Analysis

Baseline models fail to learn the actual energy surface, **indicated by high force and position error.**

It is same for our model when it is trained only on the energy loss. → **It is indeed important to** consider other physical constraints!

Energy estimation error — Net force (ideally 0) — Atom position distortion

Dataset (Task) / Model	QM9 $\text{MAE}_E(\downarrow)$	QM9 $\text{MAE}_F(\downarrow)$	QM9 $\Delta P(\downarrow)$	OC20 (IS2RE) $\text{MAE}_E(\downarrow)$	OC20 (IS2RE) $\Delta P(\downarrow)$
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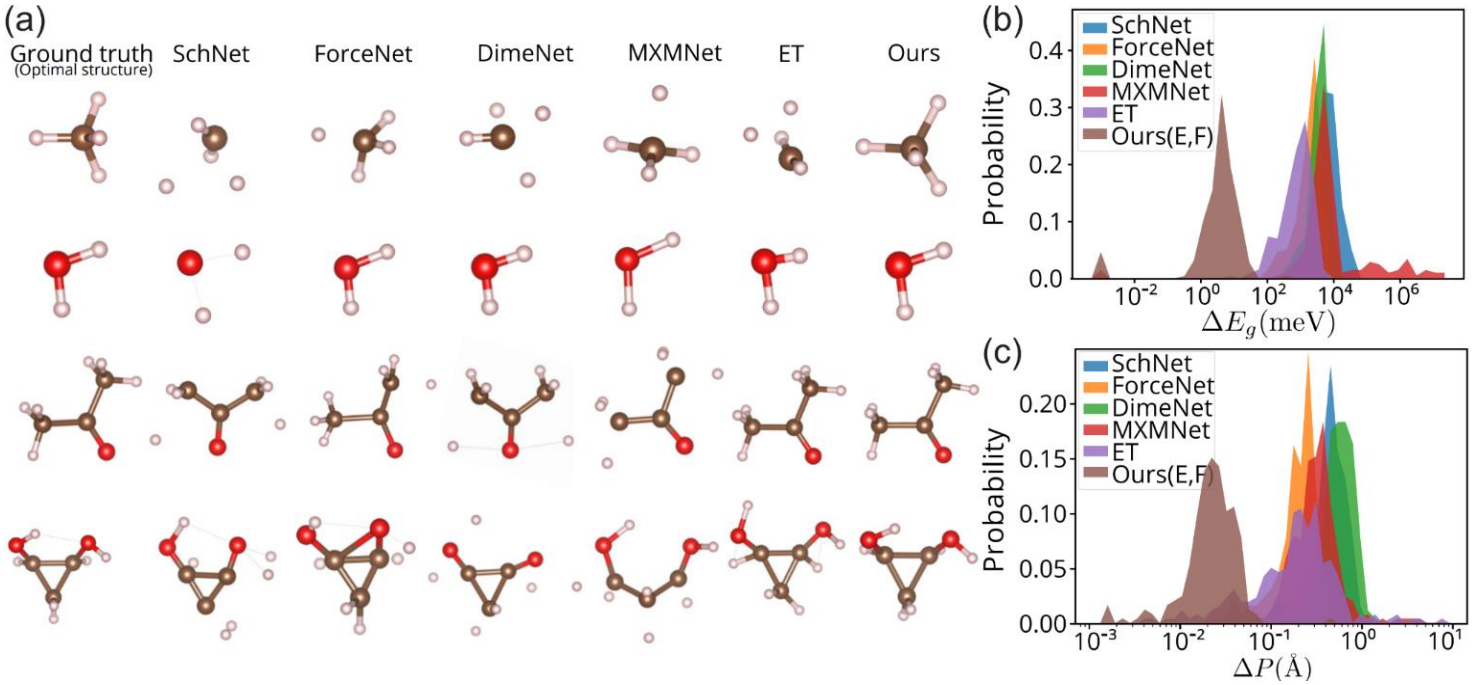
Similarly, our model outperforms baselines on OC20 dataset as well.

Qualitative Results: Structure Optimization

Reduced ΔP and ΔE more than 10x compared to other baselines.



Conducted on QM9 dataset.

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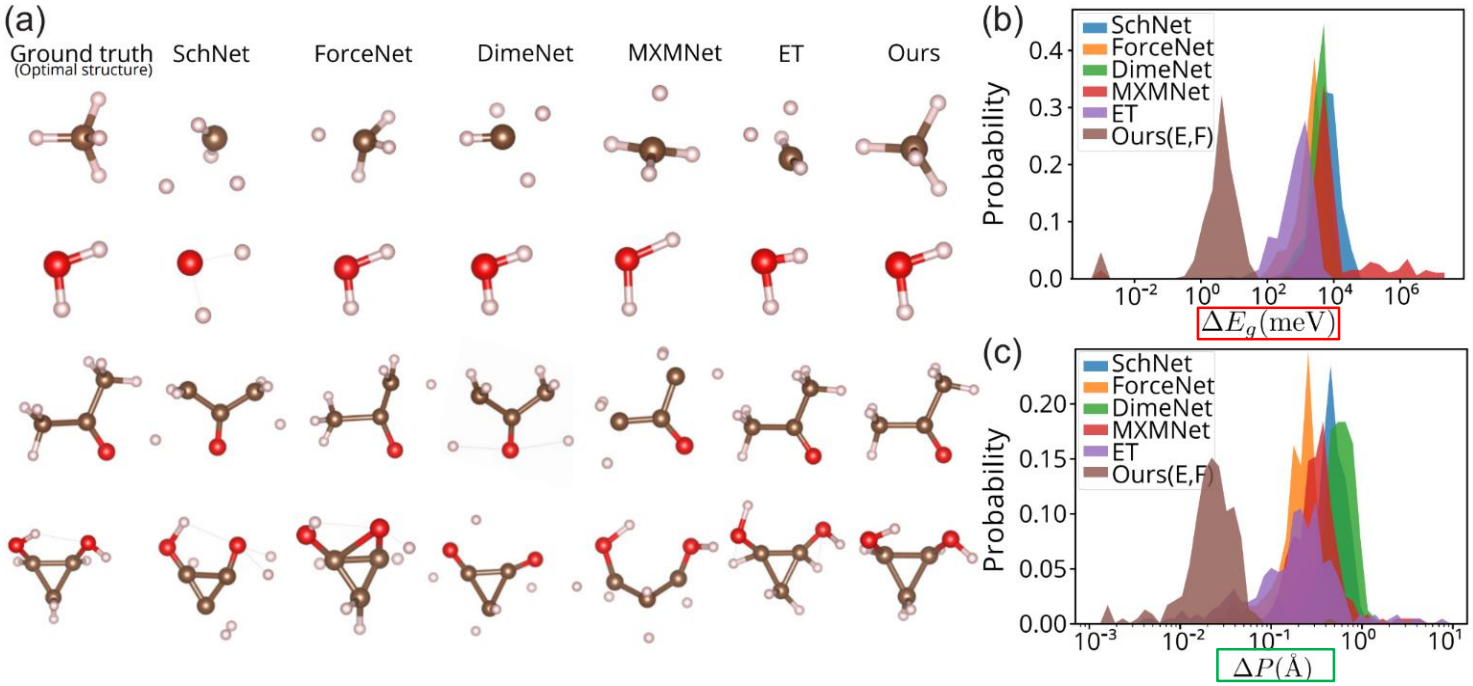

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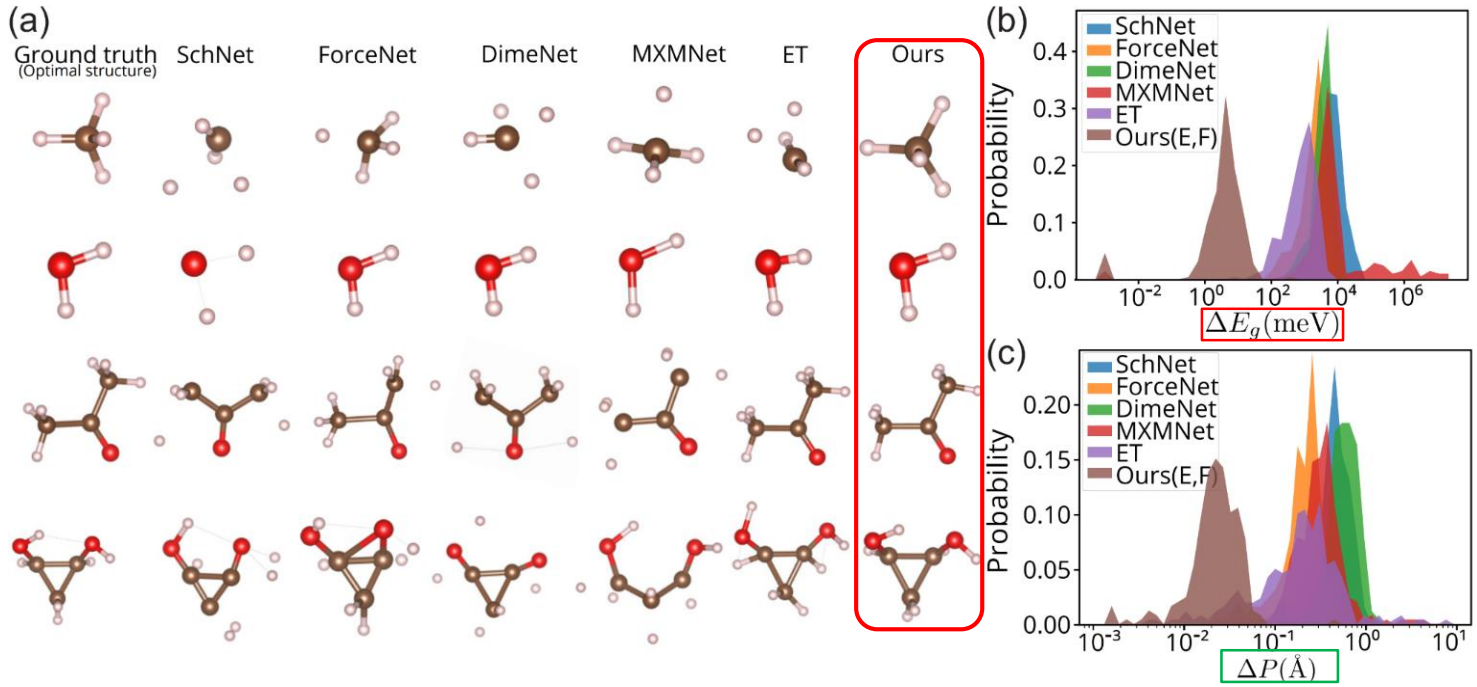

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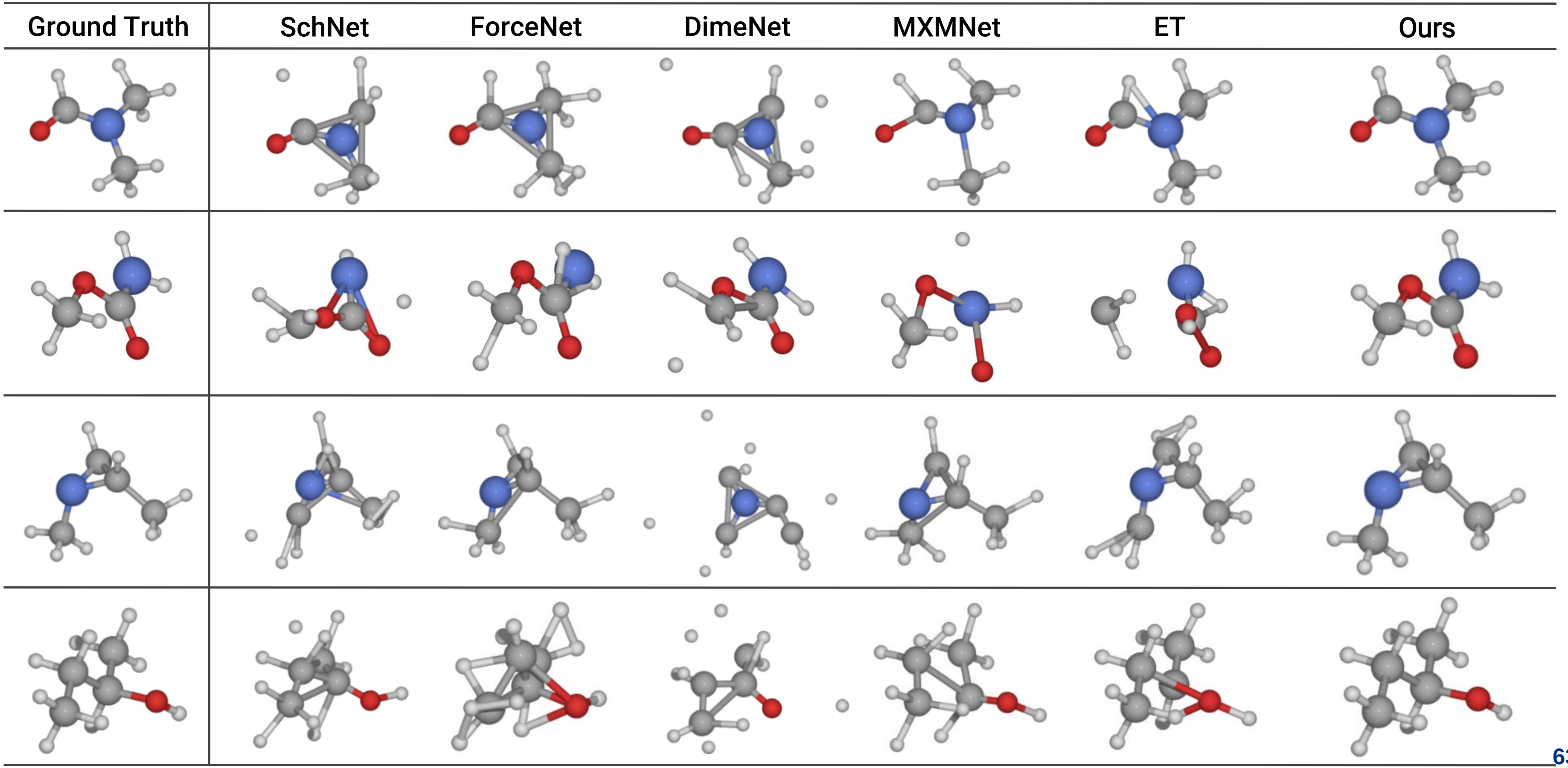

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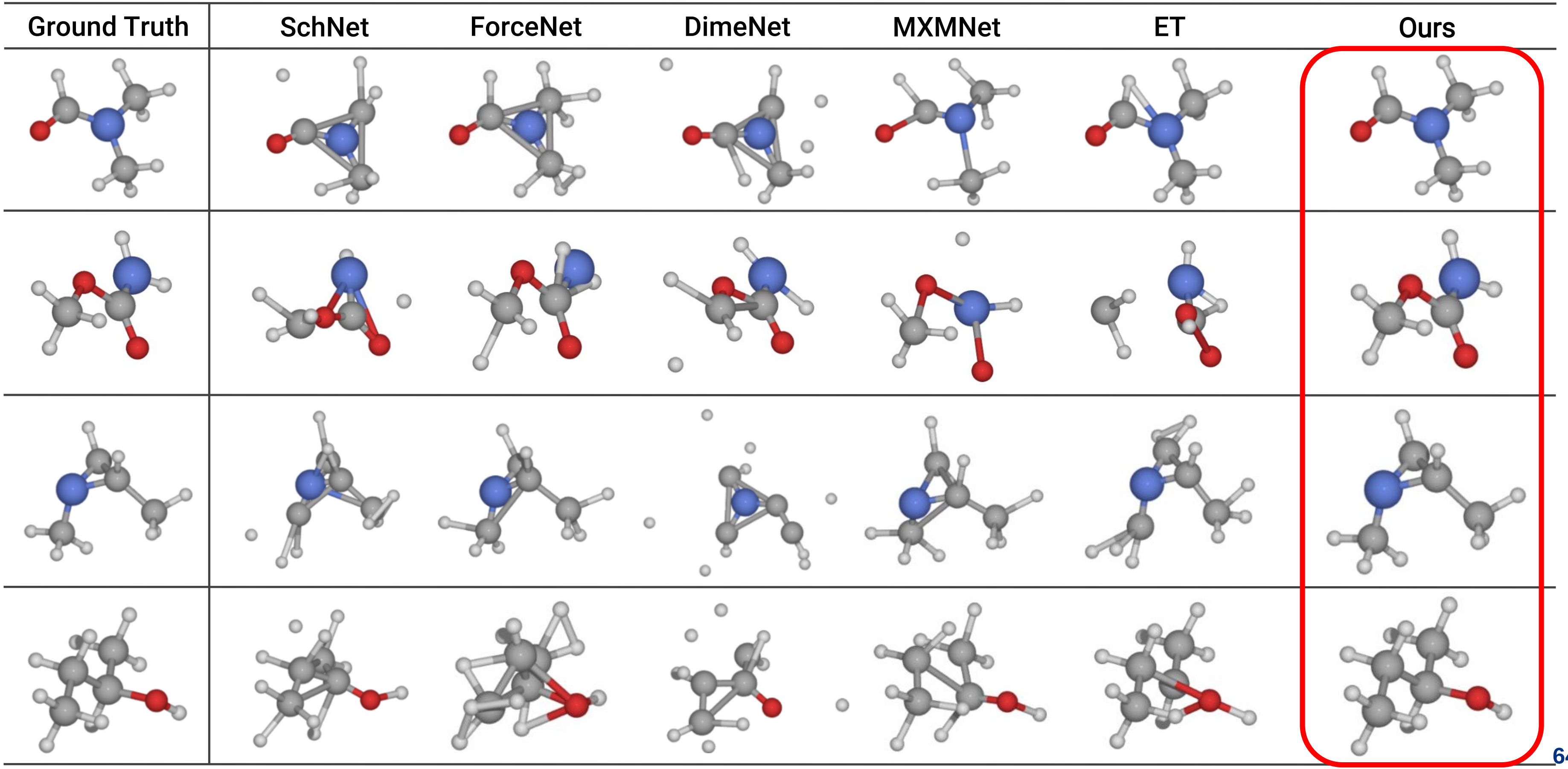
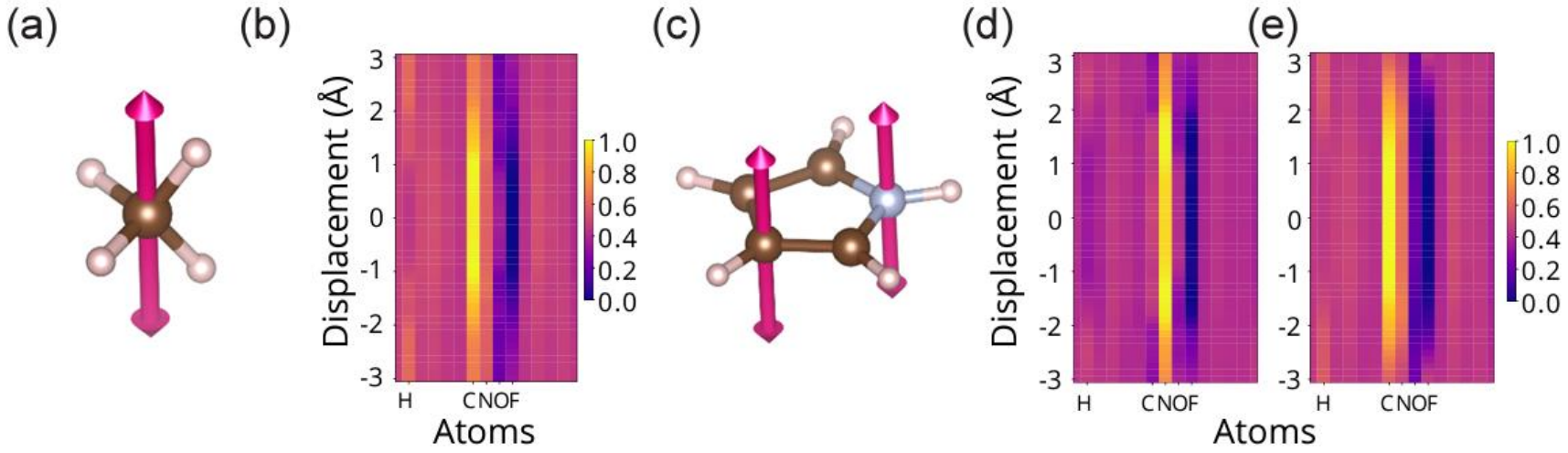


Ablation Study: Effect of MAM

Probability with dragging the atom of interest



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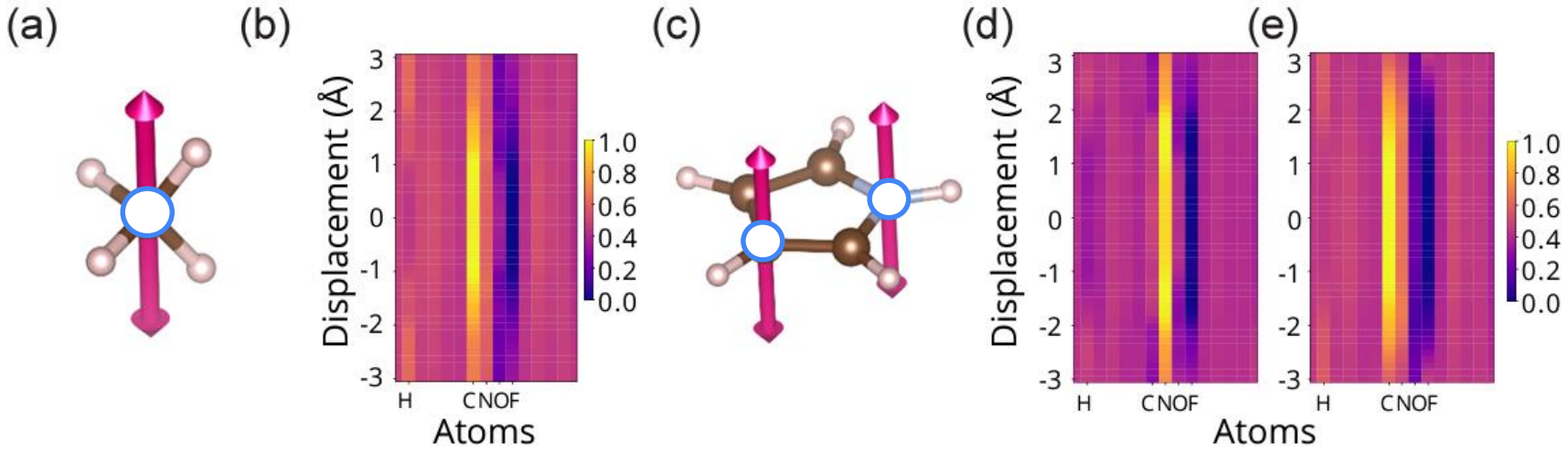

Results: Reaction Barrier Regression

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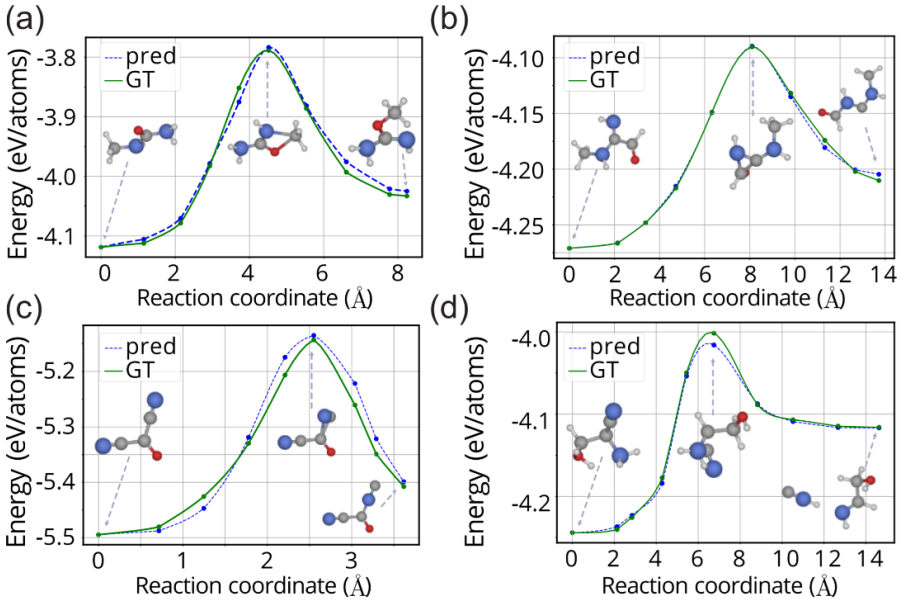

Conducted on Transition-1x dataset.

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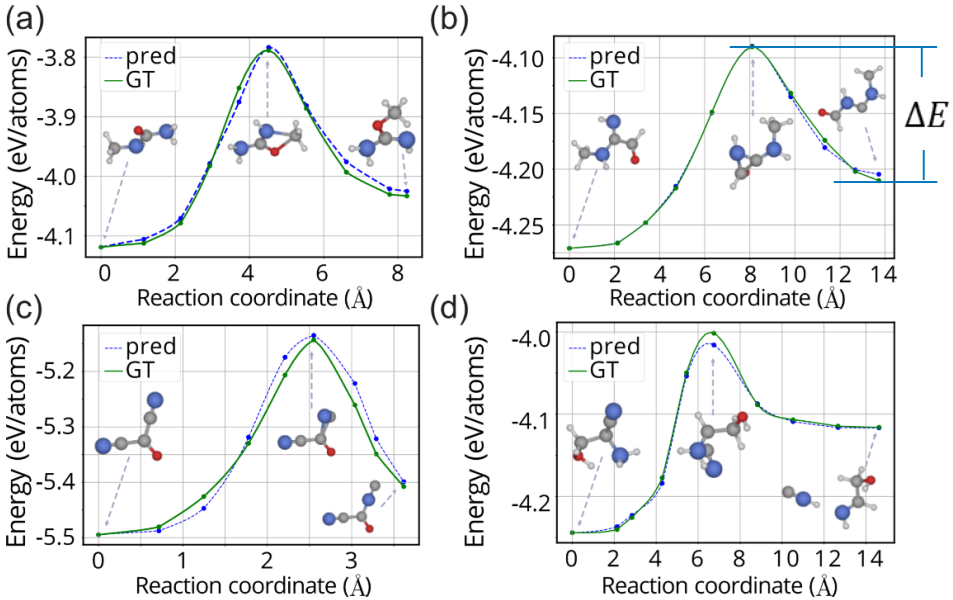

ΔE = Reaction barrier height

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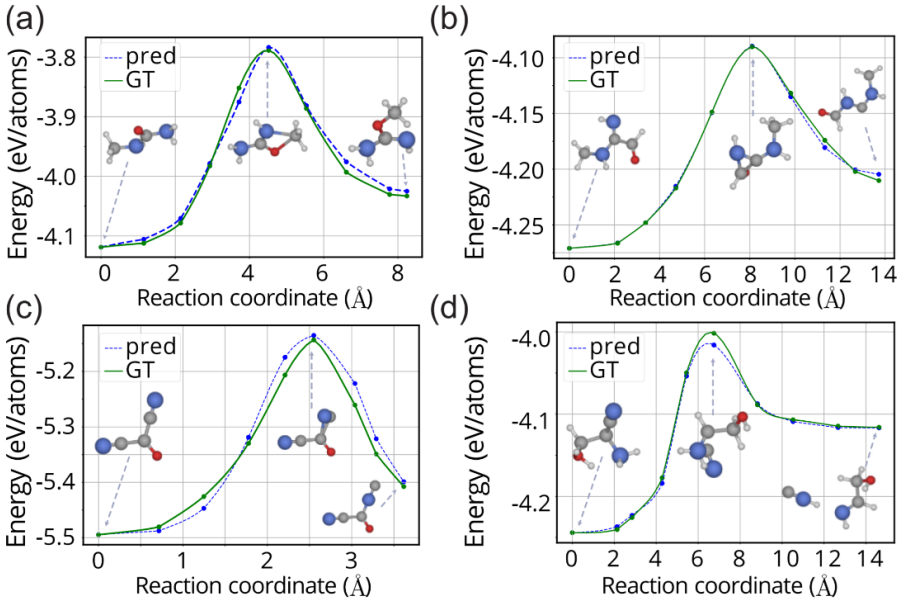

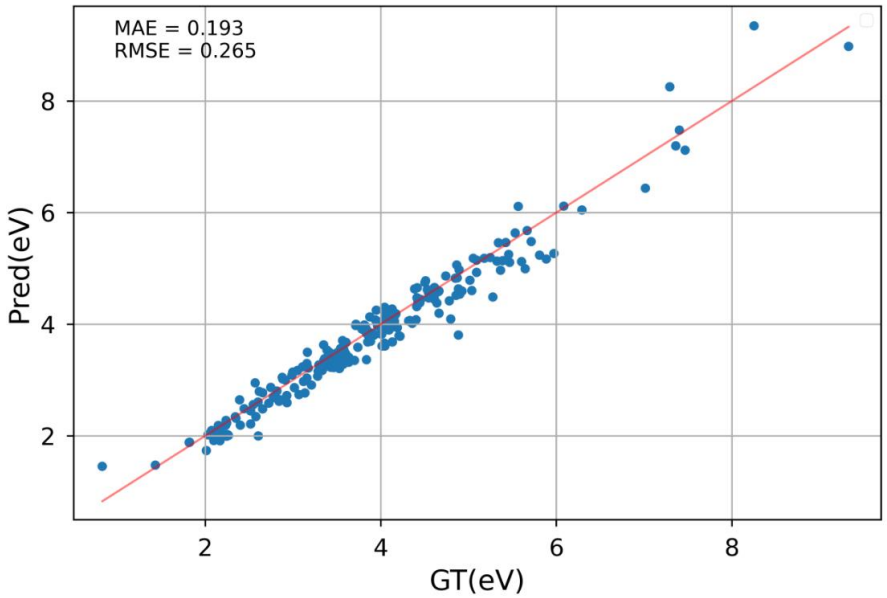

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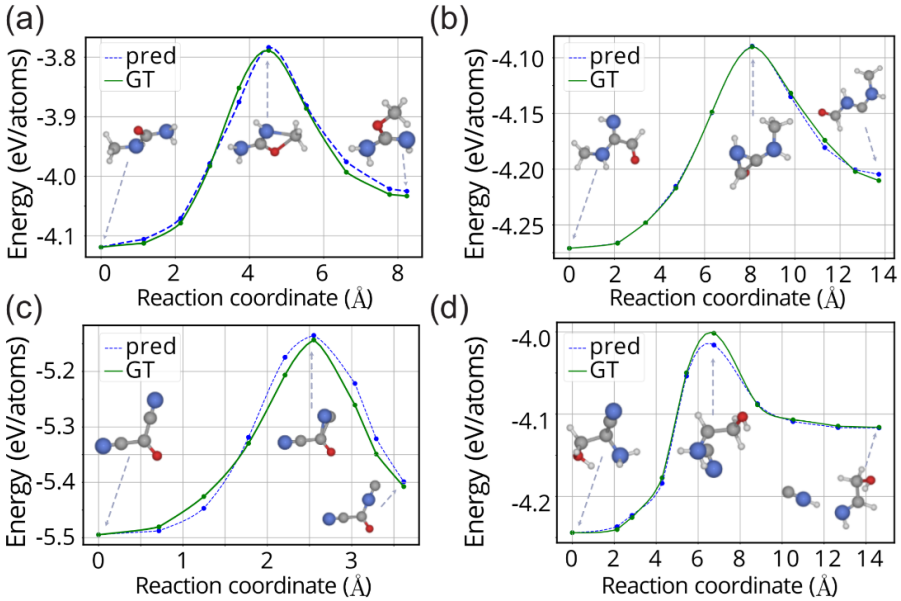

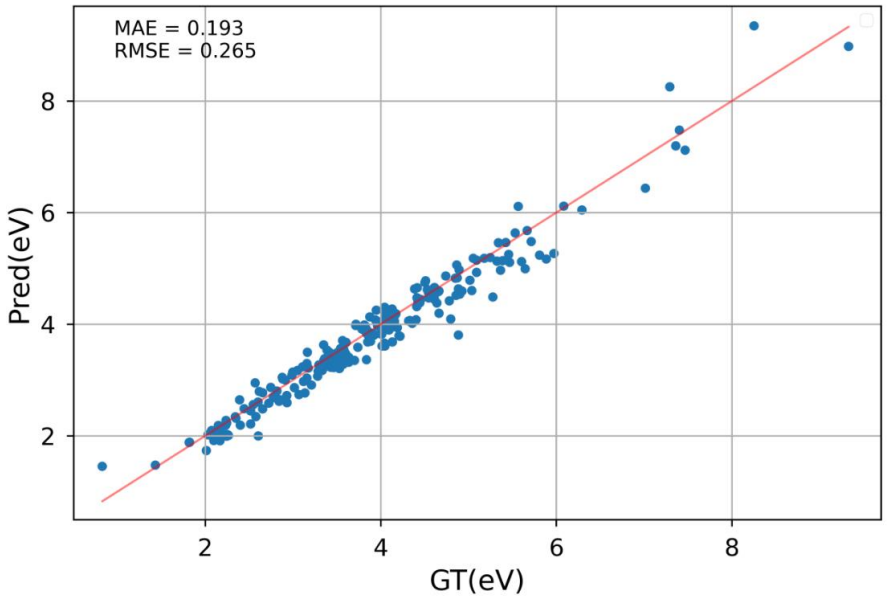

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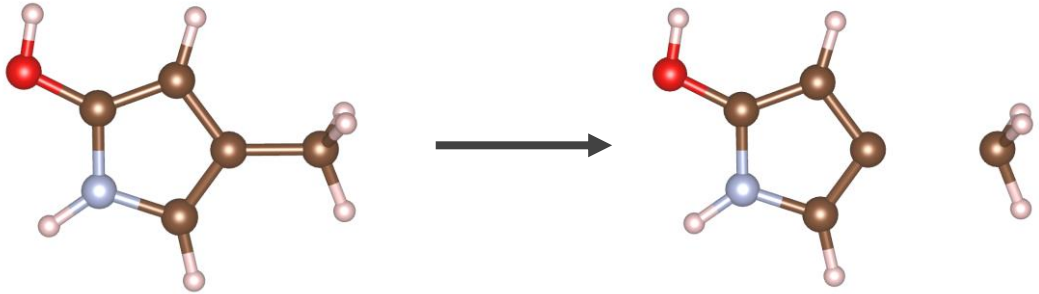
Results: Molecule Fragment Assembly

- A more challenging task to see generalization ability:
  - Split the molecule into functional groups, recover the initial state.



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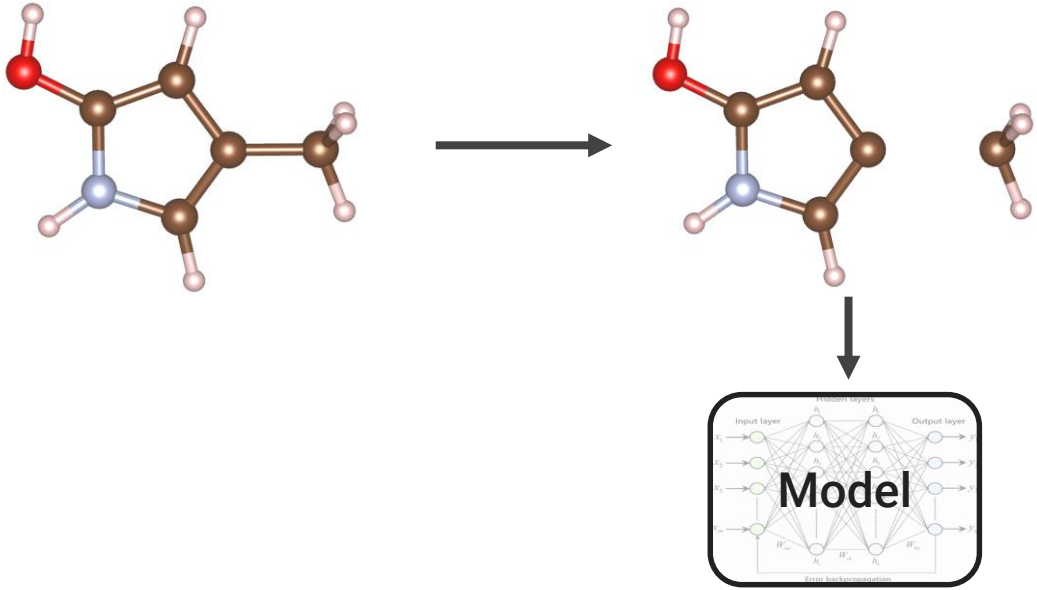

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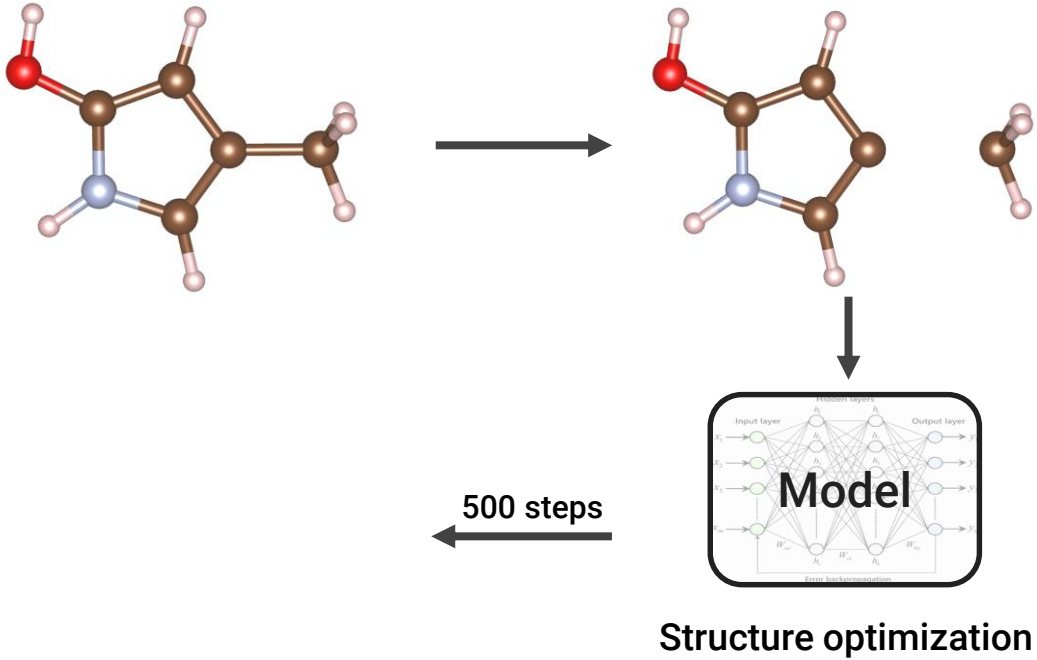

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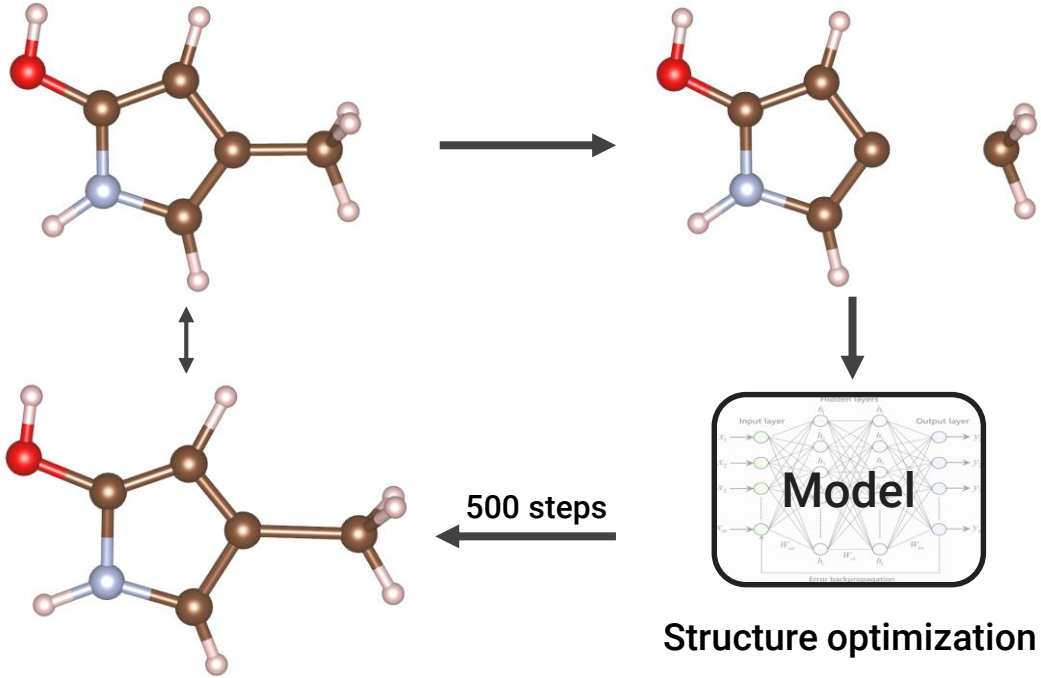

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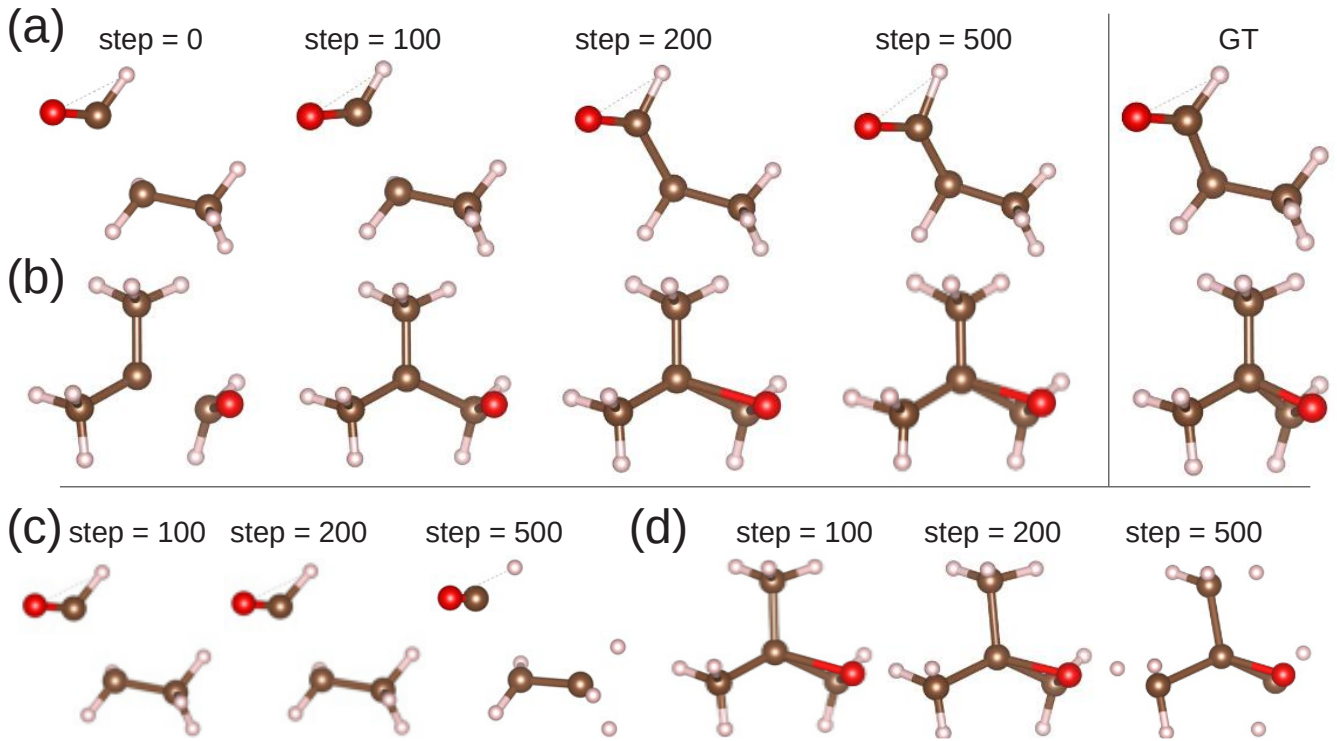

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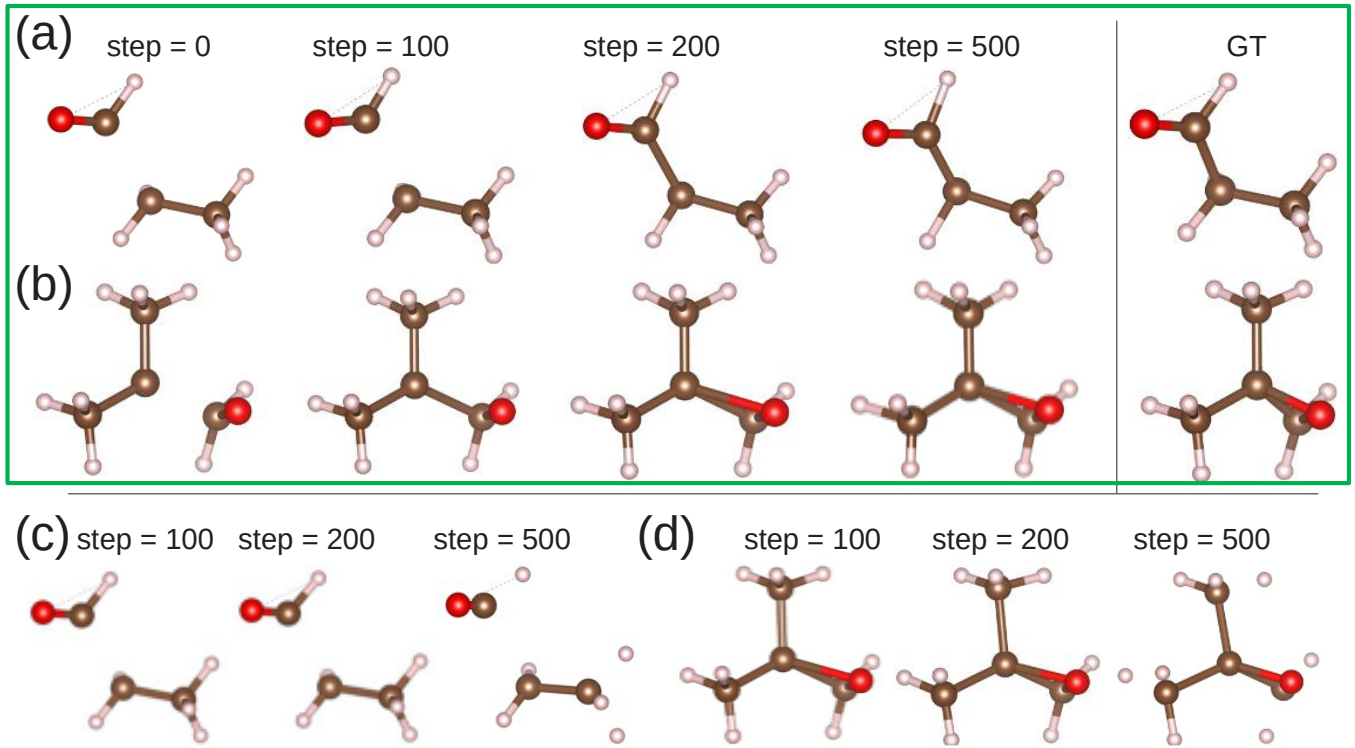
With inequality bound condition



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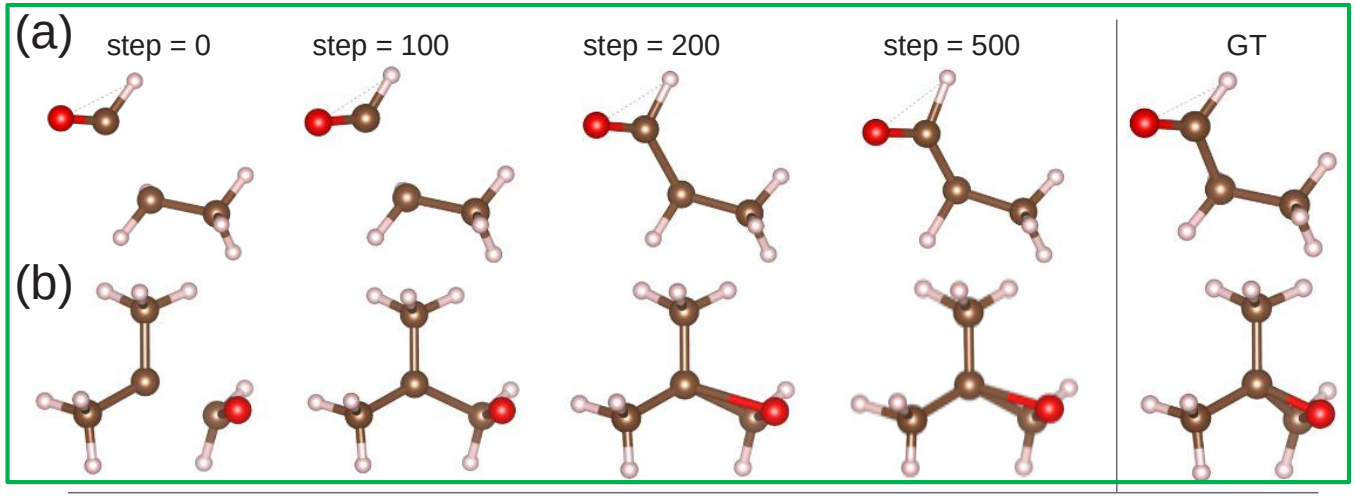

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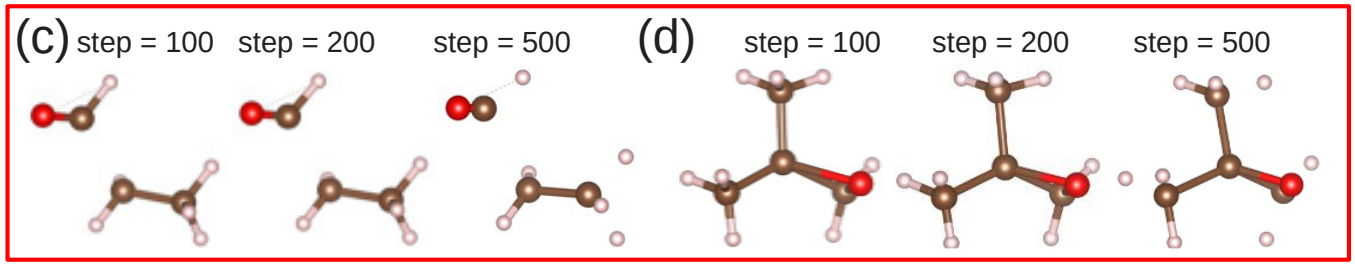

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  - Zero-force condition is fruitful for optimized structure only datasets (ex: QM9).
  - Masked atomic modeling helps the model to understand basic bonding nature in a molecule.

- Our model was able to generalize beyond stable structures, including reaction barrier prediction and molecule assembly task.

Any question?

Questions to: {jaguar6182, joonseok}@snu.ac.kr