Learning Reaction Barriers And Related Geometries

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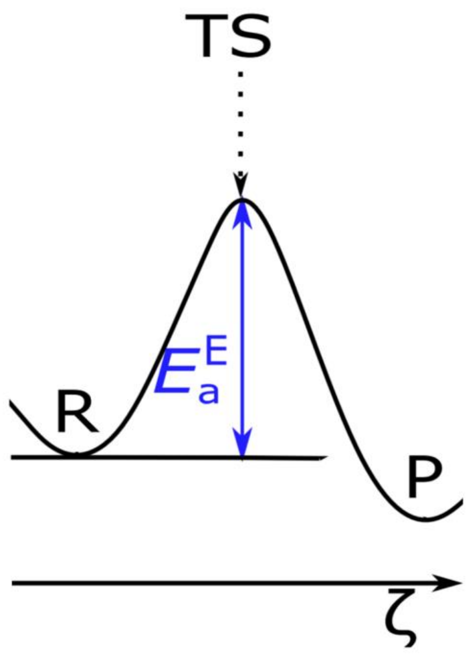
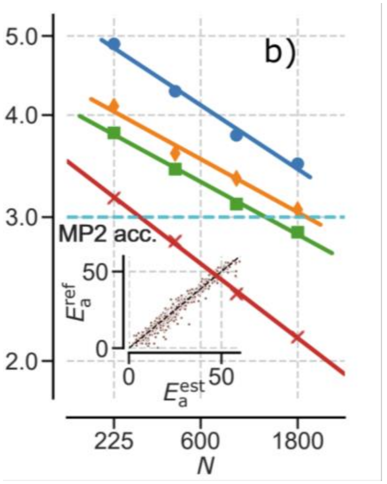
Introduction

- Reactions: complicated landscape
- Not only expensive but also hard problem
- Even if the reaction mechanism is known:
    - Find reactant (R)/product (P) complexes
    - Find transition state (TS) geometries
    - Describe energy near TS
    - Low level of automation available

- Machine learning: accelerate & less supervised



Overview



Energies with KRR

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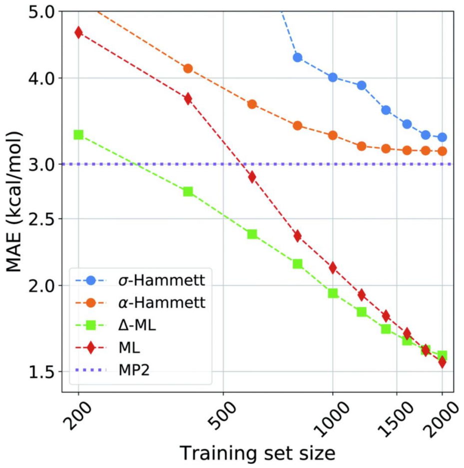
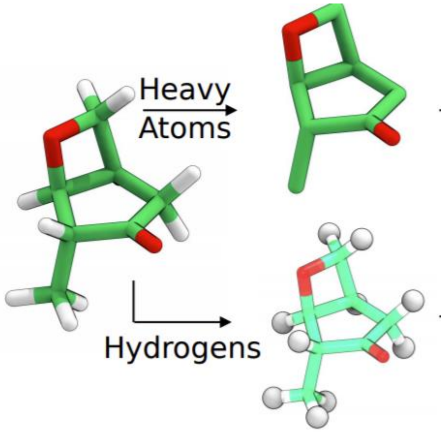


Detrending with Hammett's equation

chemspacelab/
Enhanced-Hammett



Geometries with Graph2Structure

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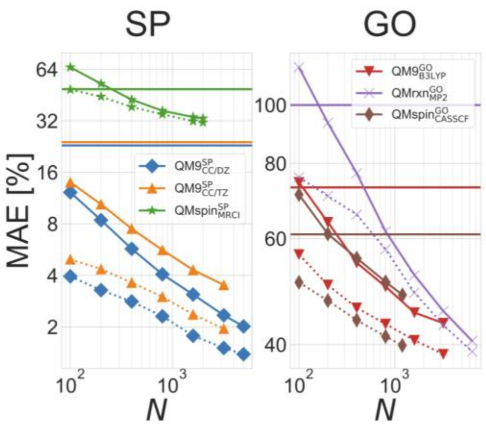

Estimate computational cost

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Kernel Ridge Regression

Idea

- Molecular representation for each molecule i — $\mathbf{M}_i$
  - CM, BoB, FCHL, SLATM, …
- Distance metric — $d_{ij} \equiv d(\mathbf{M}_i, \mathbf{M}_j)$
  - Typically L1 or L2 norm
- Kernel function — $k_{ij} \equiv k(d_{ij})$
  - Laplacian, Gaussian

Kernel Ridge Regression

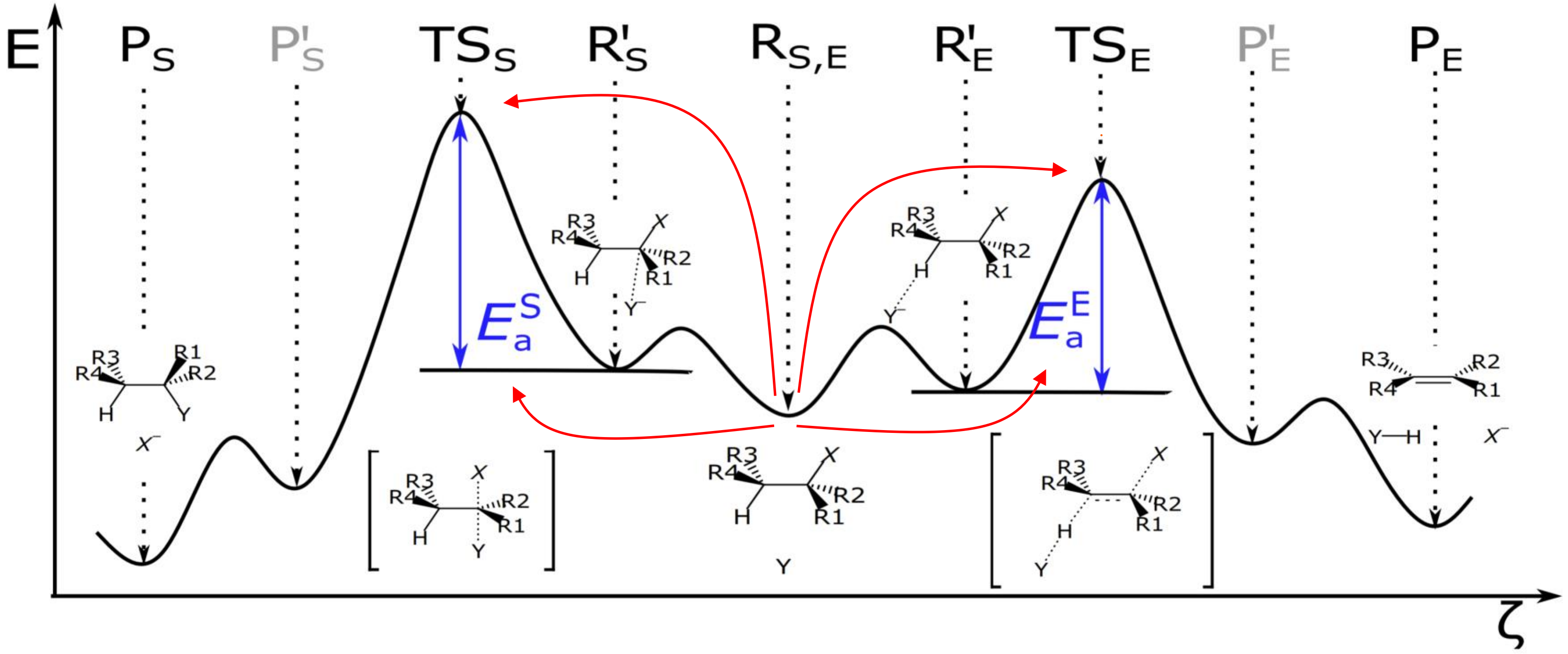
Procedure

- Get *i* data points with scalar property (label) $\{q_i\}$
  - E.g. atomisation energy
- Calculate all representations $\{\mathbf{M}_i\}$
  - typically ~1k
- Find distance and kernel matrices $\mathbf{D}, \mathbf{K}$
  - Symmetric
- Train model for predictions $\{\tilde{q}_i\}$
- Find best hyperparameters (cross-validation)

$$\arg\min_{\alpha} \sum_i (q_i - \tilde{q}_i)^2 + \lambda \sum_{ij} \alpha_i \alpha_j k_{ij}$$

$$\Rightarrow \alpha = (\mathbf{K} + \lambda \mathbf{I})^{-1} q \qquad \tilde{q}(\mathbf{M}) = \sum_i \alpha_i k(\mathbf{M}, \mathbf{M}_i)$$

Competing Reactions: E2 and S_N2

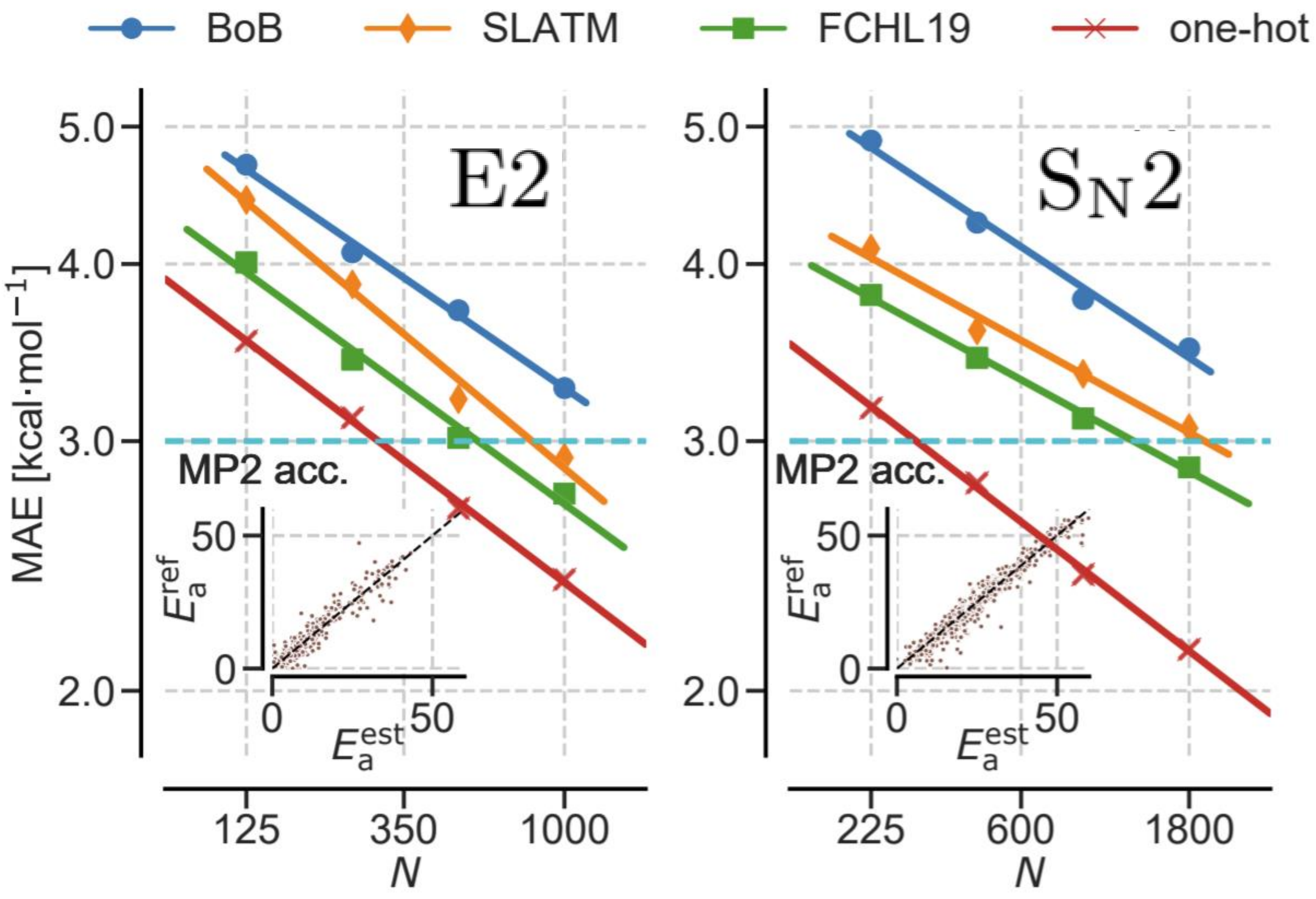


R	X	Y
H	F	H
NO_2	Cl	F
CN	Br	Cl
CH_3		Br
NH_2		

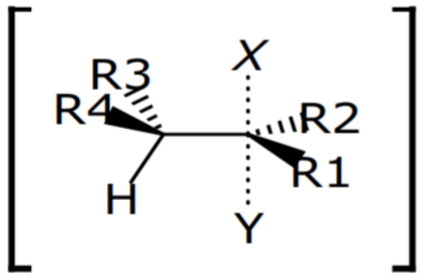
- Activation energies E_a
- Transition state geometries
- Dataset of 4.5k transition states, 143k reactant geometries, part MP2, part DF-LCCSD

GFvR, S. Heinen, M. Bragato, O. A. von Lilienfeld, *Mach. Learn.: Sci. Technol.* **2020** (*arXiv* 2006.00504).

Learning Activation Energies



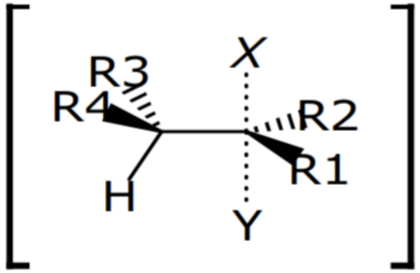
- Geometry-based representations on lowest conformer
  - BoB
  - SLATM
  - FCHL19
- Graph-based representations
  - One-hot

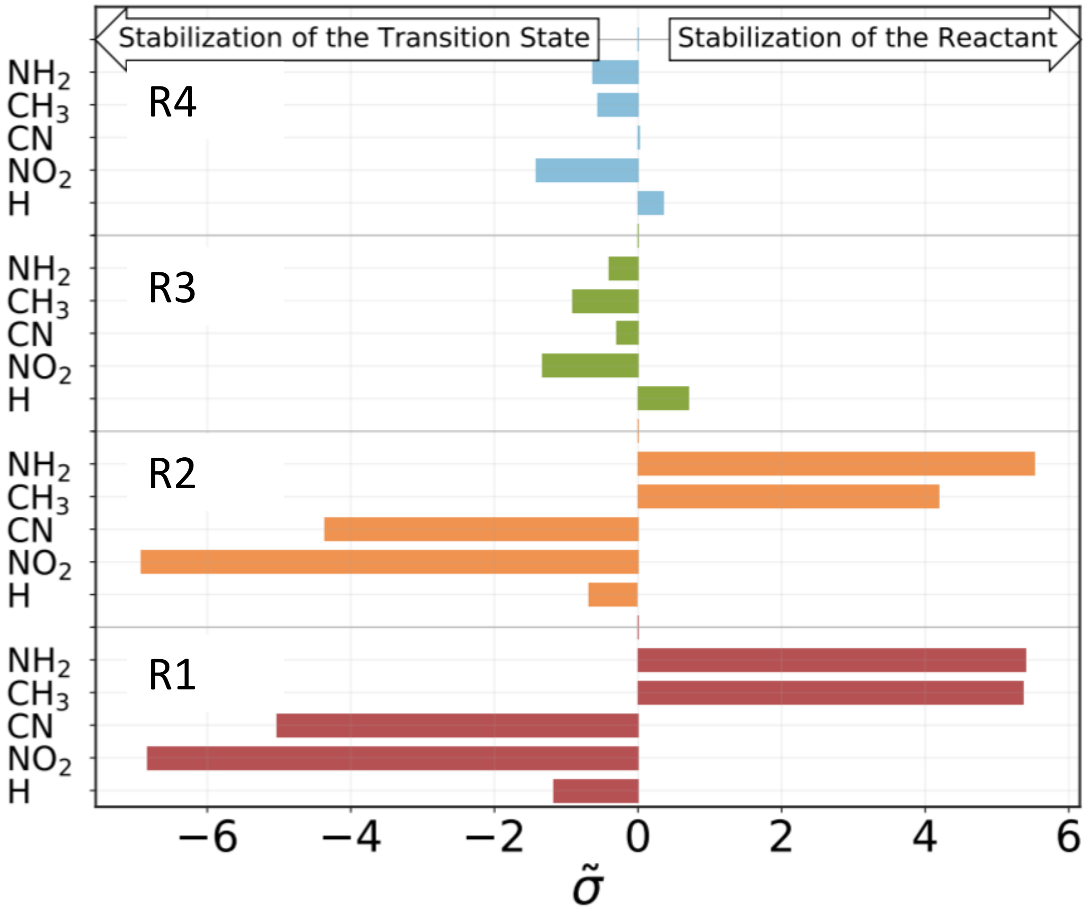


S. Heinen, GFvR, O. A. von Lilienfeld, *arXiv* 2009.13429.

Learning Activation Energies

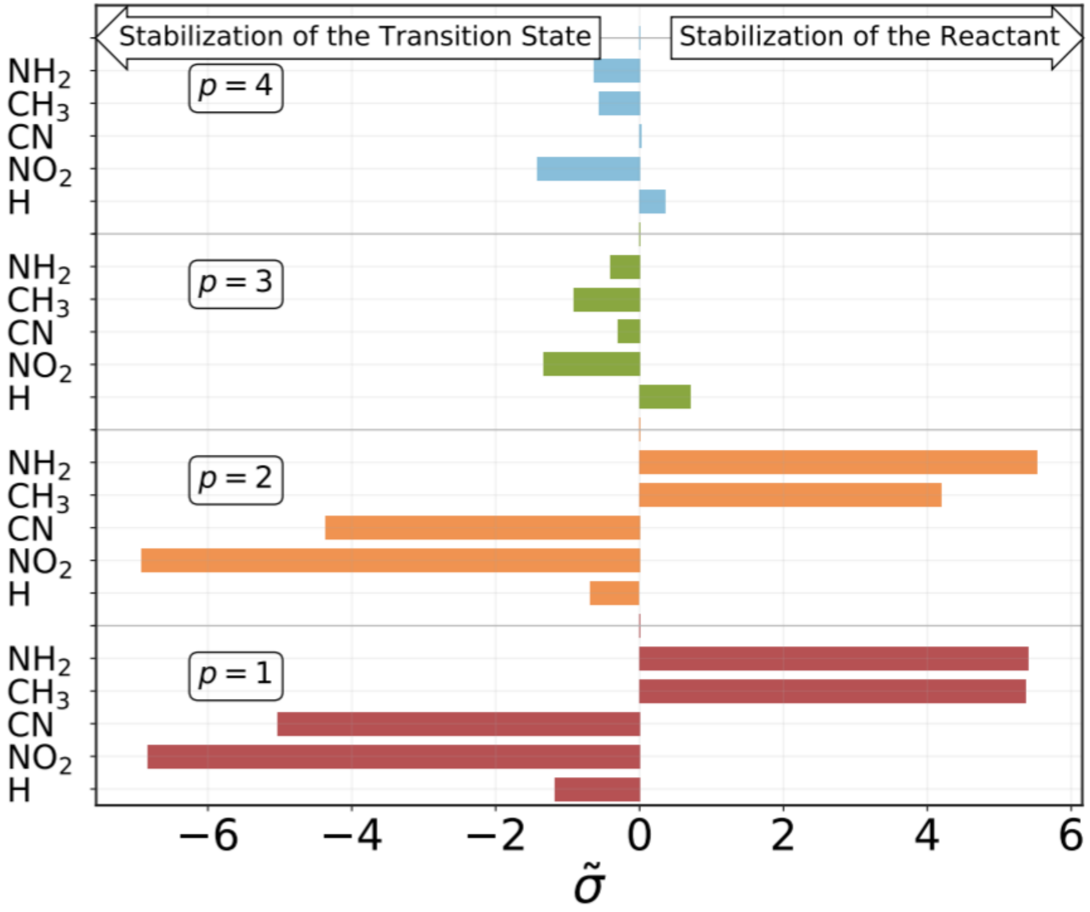
- Often in chemistry: trends obscure relevant detail
  - Electron density dominated by individual atoms
  - Energies dominated by elemental composition
  - Bond energies dominated by element pairs
  - ...





M. Bragato, GFVR, O. A. von Lilienfeld, *Chem. Sci. 2020 (arXiv 2004.14946).*

Learning Activation Energies



Hammett's equation (1935):

$$\log\left(\frac{K}{K_0}\right) \simeq \rho\sigma$$

Can be used to remove linear trends in the data

1. Find two aspects (e.g. solute/solvent) that are orthogonal and approximately balanced in the data set
2. Fit rho, sigma in a robust manner

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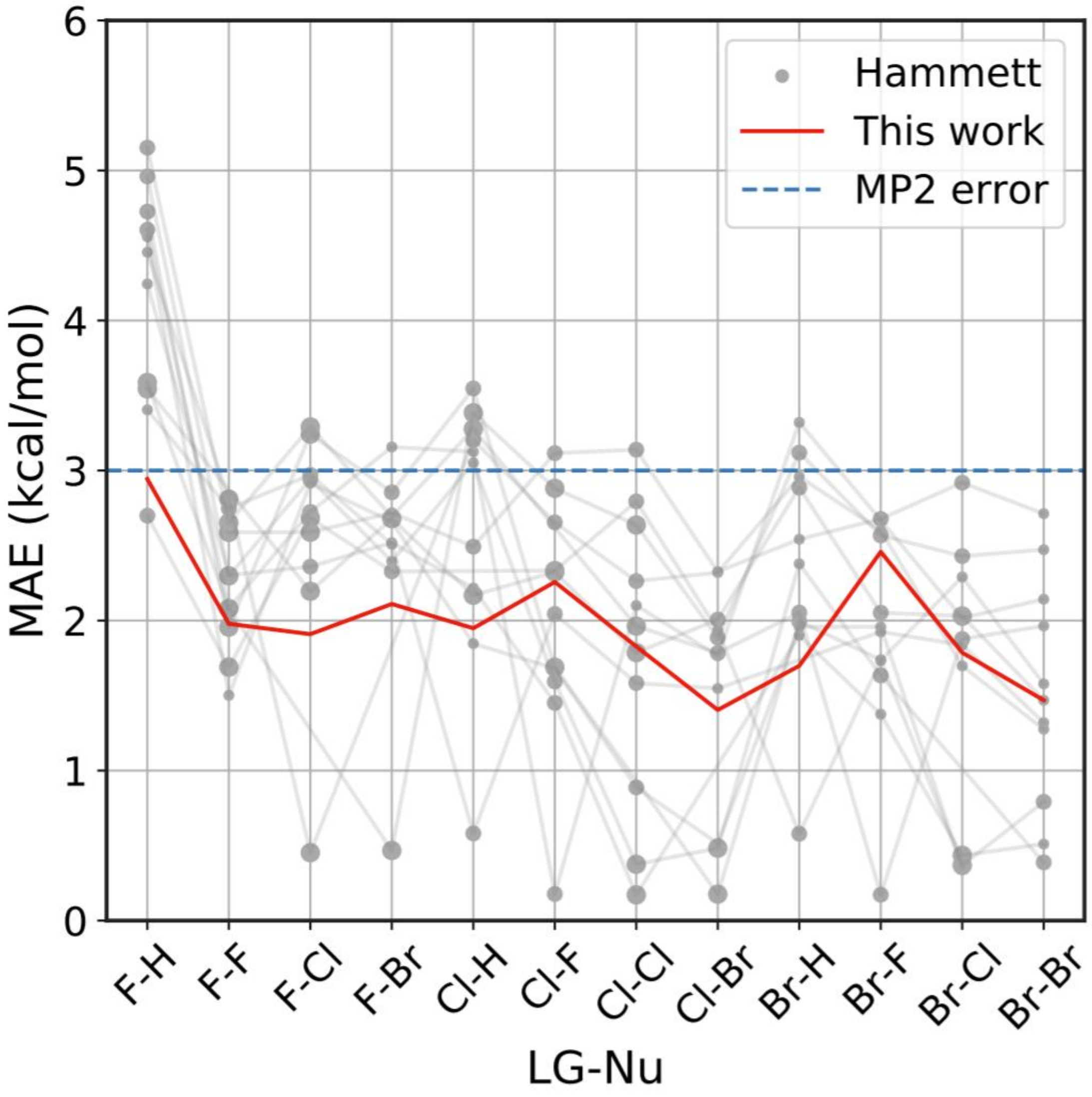
Learning Activation Energies



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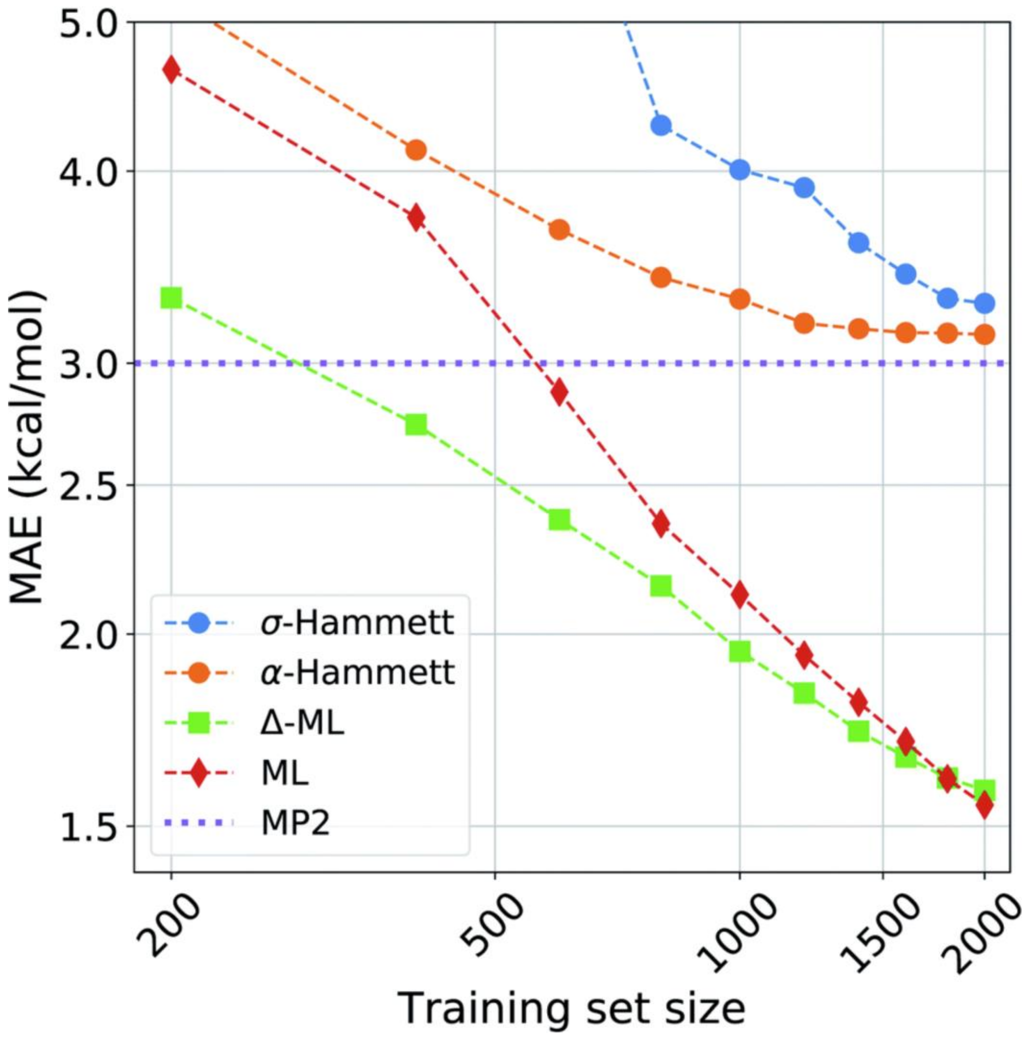
Learning Activation Energies

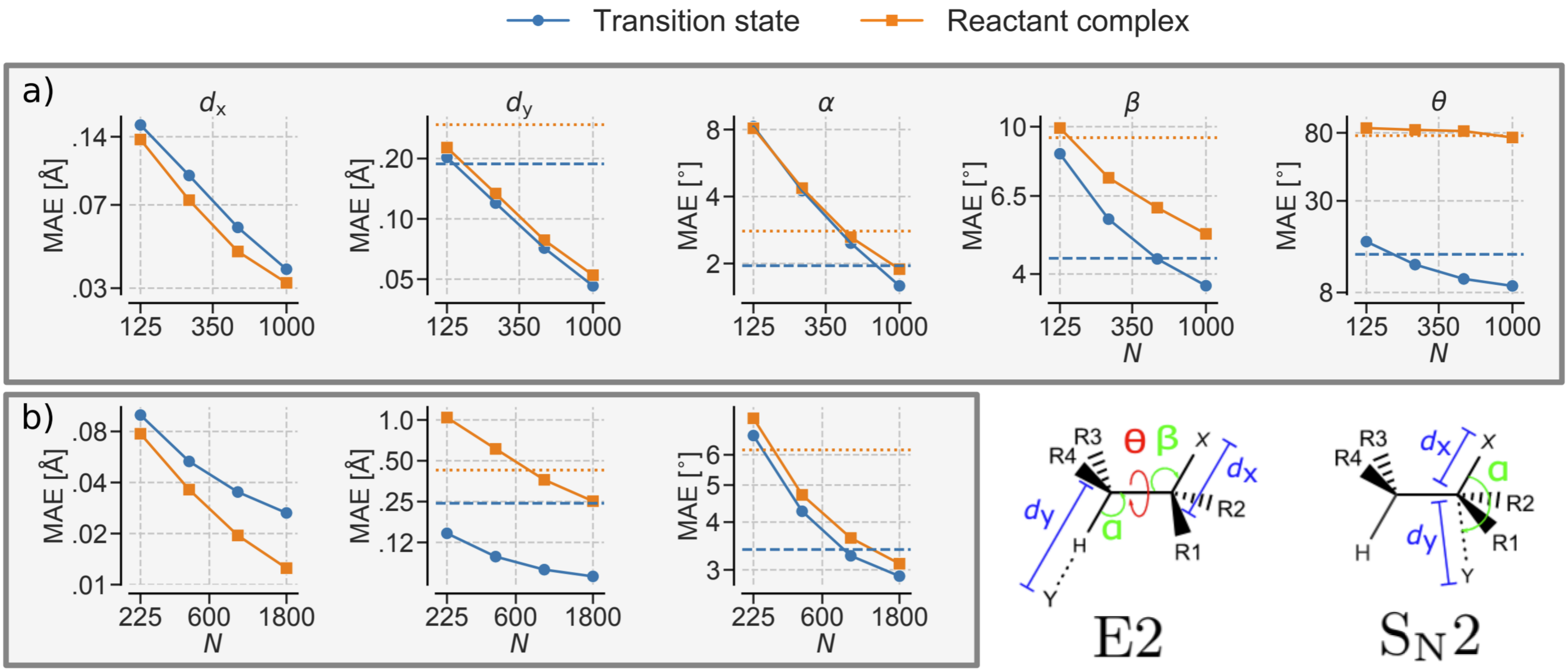


- Hammett nearly reaches MP2 accuracy
- Residuals are easier to learn
- Preprocessing of datasets most helpful for small training sets

chemspacelab/Enhanced-Hammett

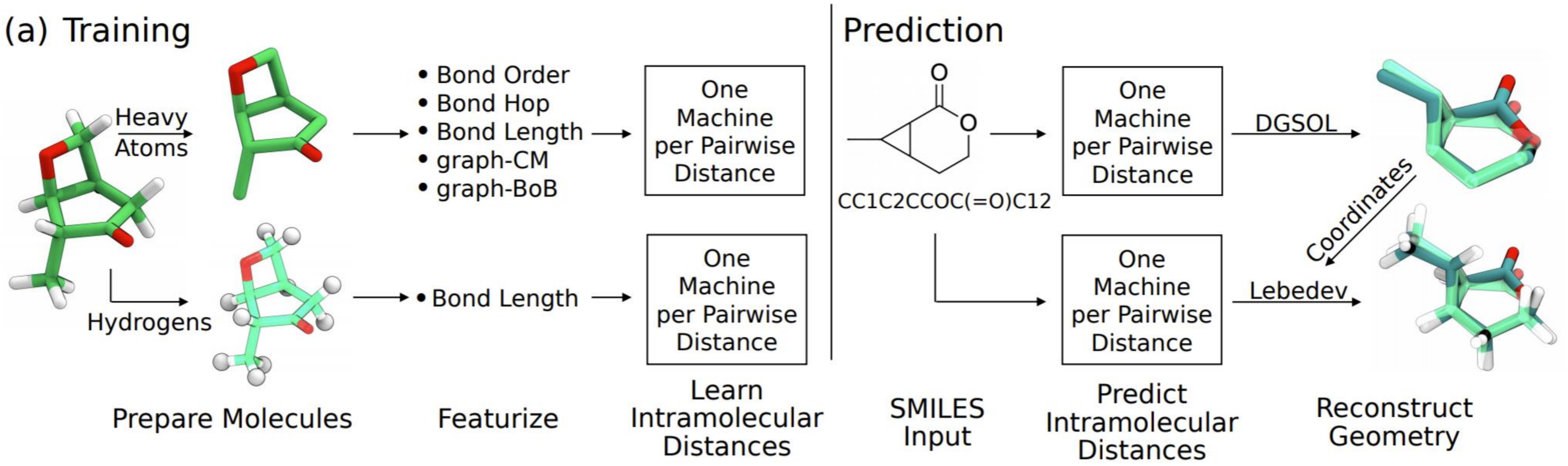
M. Bragato, GFVR, O. A. von Lilienfeld, *Chem. Sci. 2020 (arXiv 2004.14946).*

Learning Transition State Geometries



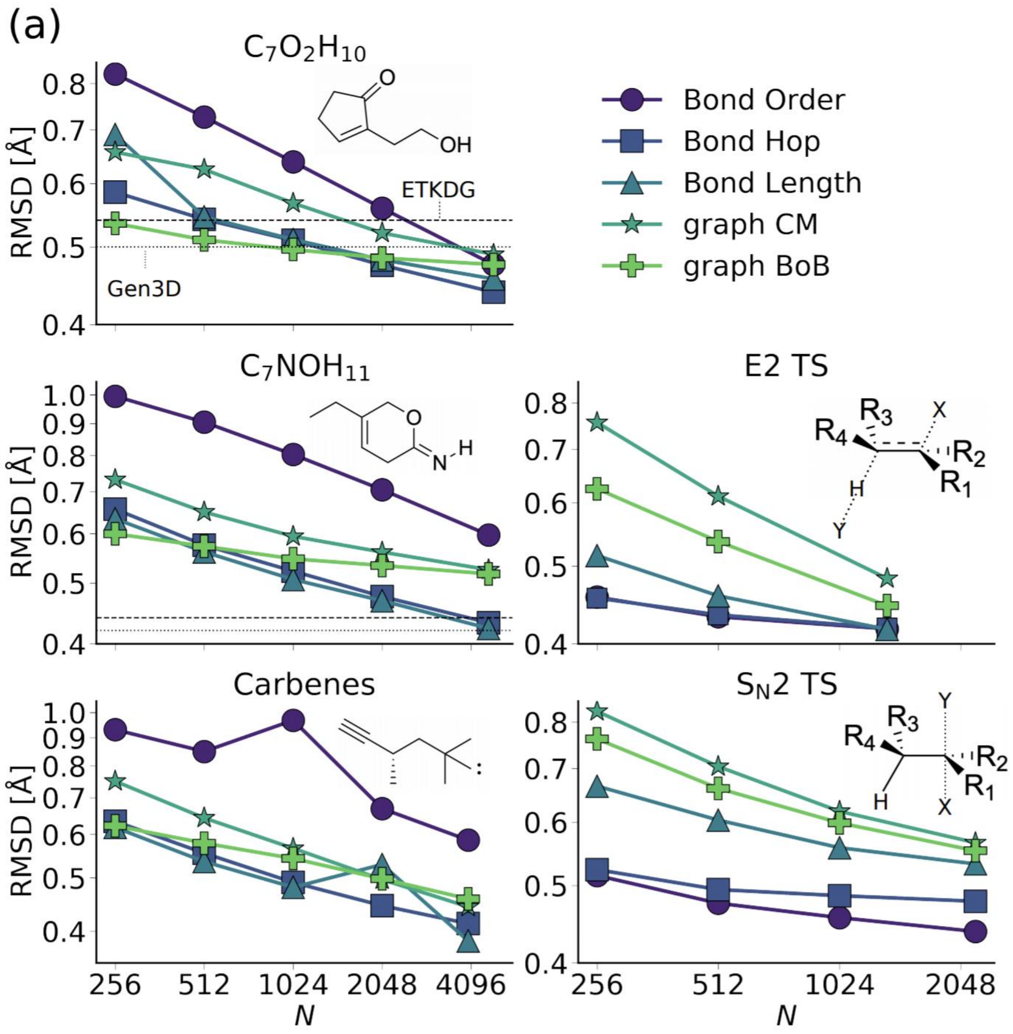
S. Heinen, GFvR, O. A. von Lilienfeld, *arXiv* 2009.13429.

Graph2Structure



D. Lemm, GFVR, O. A. von Lilienfeld, *Nat. Commun.* (accepted) *arXiv* 2102.02806.

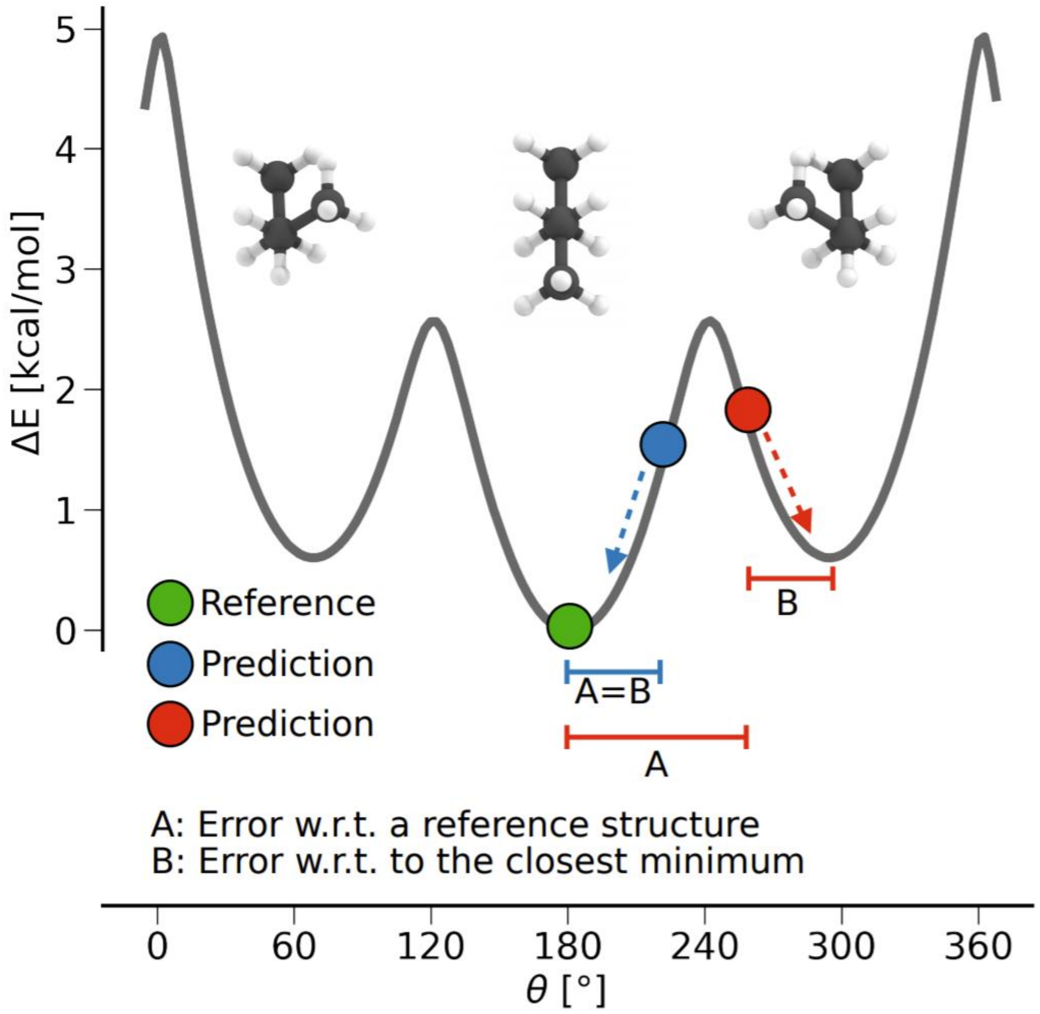
Graph2Structure



- Learns standard chemistry, but also carbenes, transition state geometries
- More accurate w.r.t. to QM calculations than state-of-the-art embedding methods (which only do standard chemistry)
- Can produce initial guesses for e.g. transition state searches

D. Lemm, GFVR, O. A. von Lilienfeld, *Nat. Commun.* (accepted) *arXiv* 2102.02806.

Graph2Structure



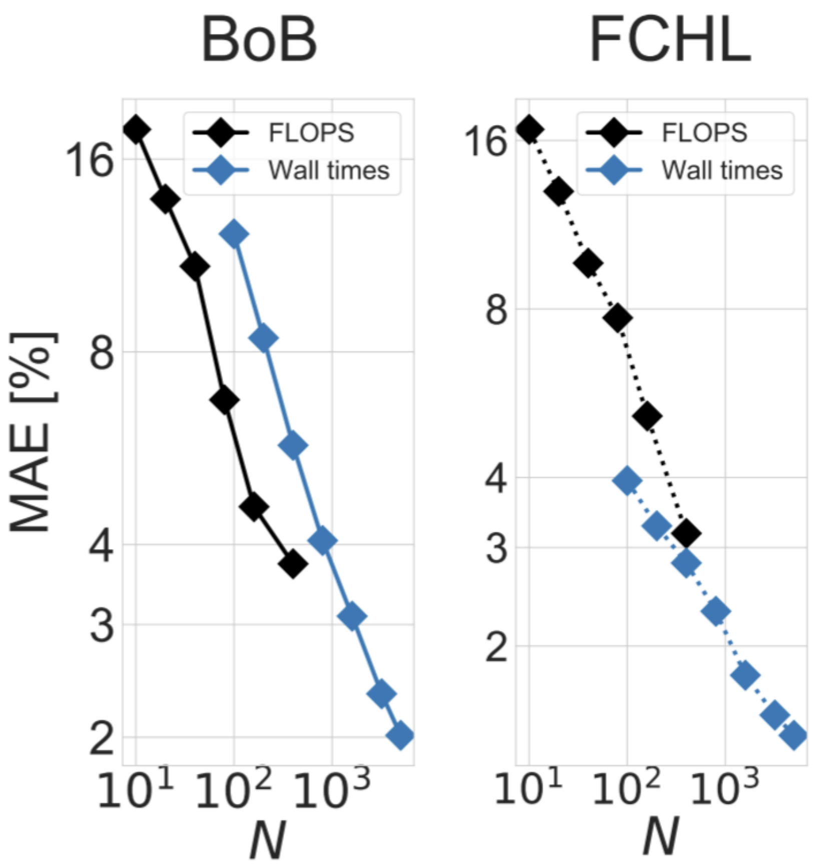
- Most efficient for cases with wide minima
- Multiple small minima e.g. stereoisomers account for most of the error

qmlcode/qml

D. Lemm, GFVR, O. A. von Lilienfeld, *Nat. Commun.* (accepted) *arXiv* 2102.02806.

Learning Computational Cost

- Training data expensive
- Not all training points equally expensive
  - Geometry optimisations may take longer
  - SCF might not converge or converge more slow
- Treating this as "molecular property"

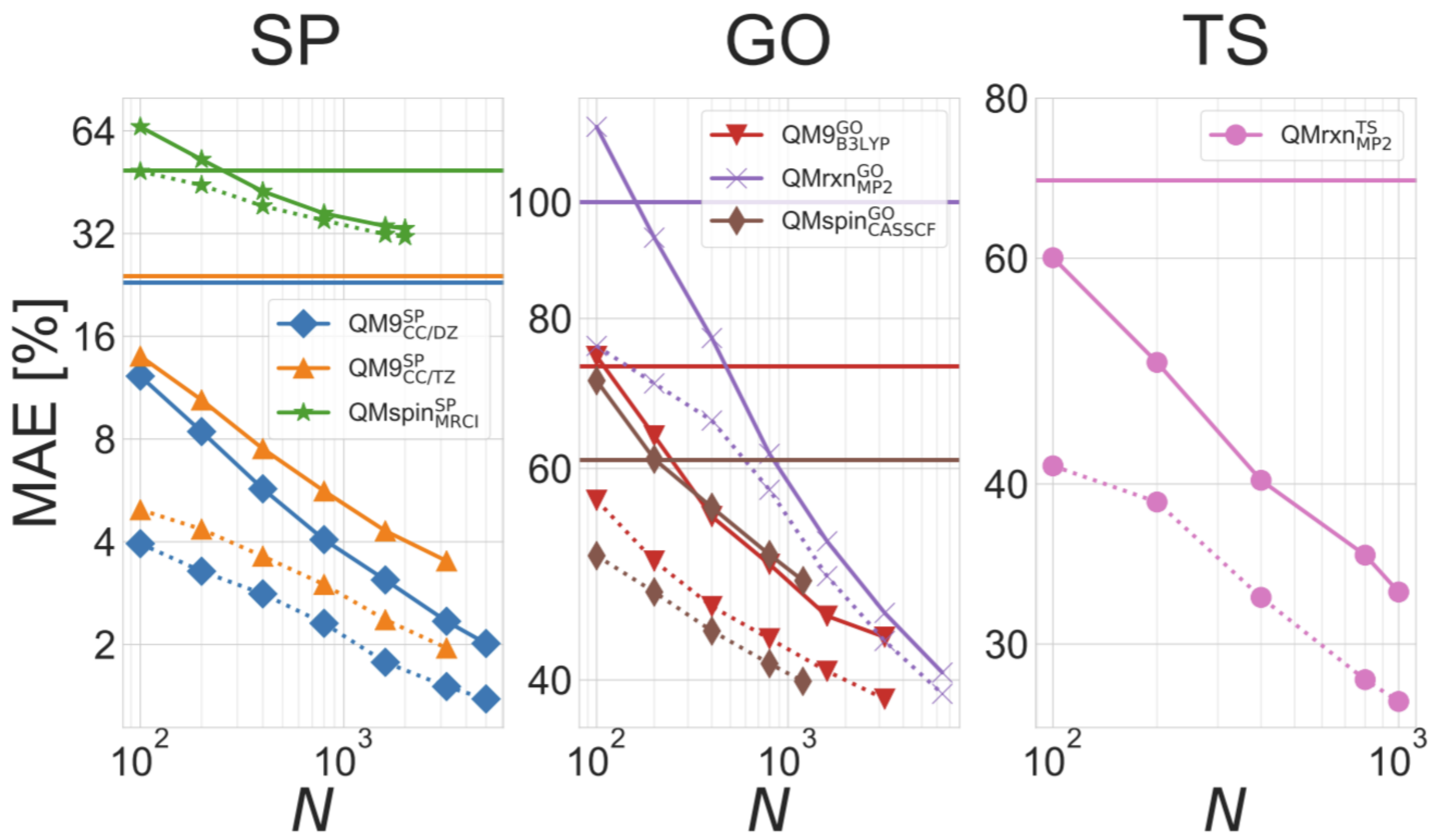


- Best case: controlled environment, single points (QM9)

S. Heinen, M. Schwilk, GFvR, O. A. von Lilienfeld, *Mach. Learn.: Sci. Technol.* **2020** (*arXiv* 1908.06714).

Learning Computational Cost

- Realistic case: I/O, noise: different machines



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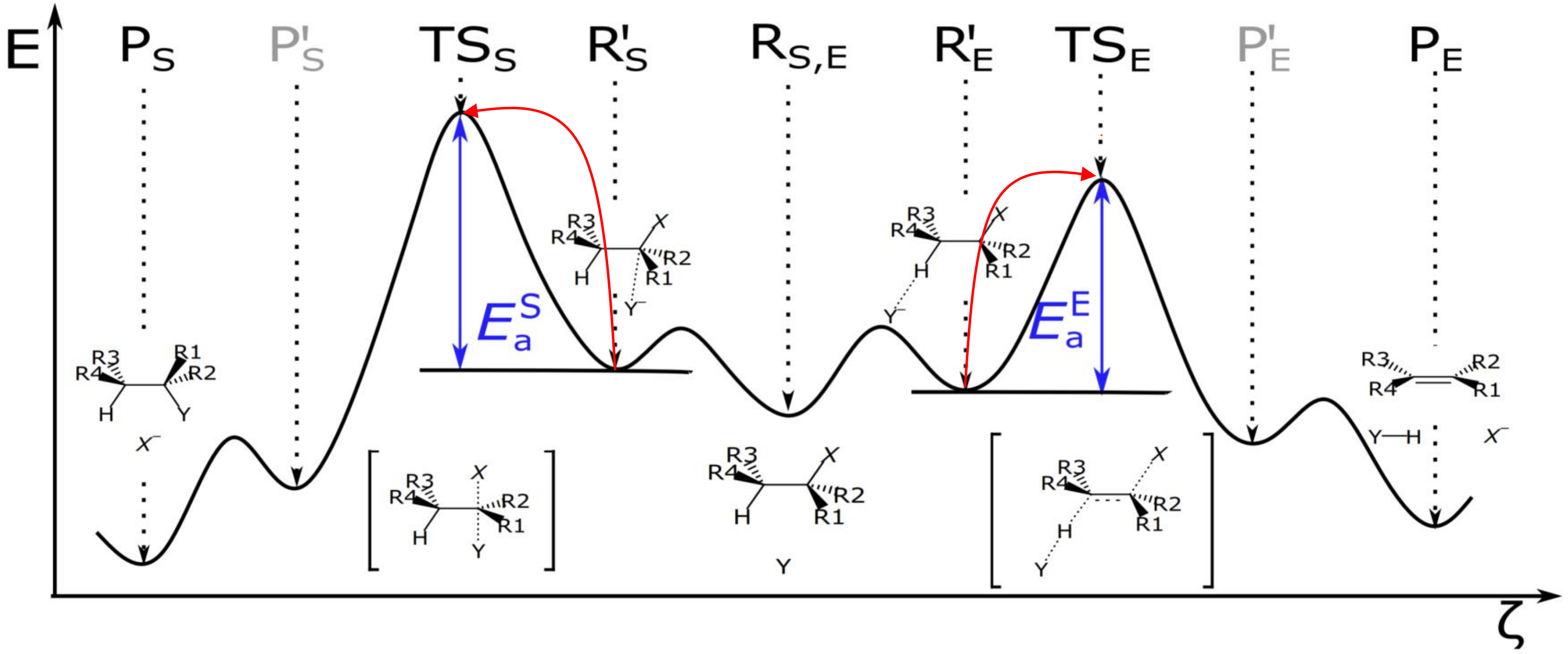
What about direct optimization?



S. Heinen, GFvR, O. A. von Lilienfeld, *in preparation*

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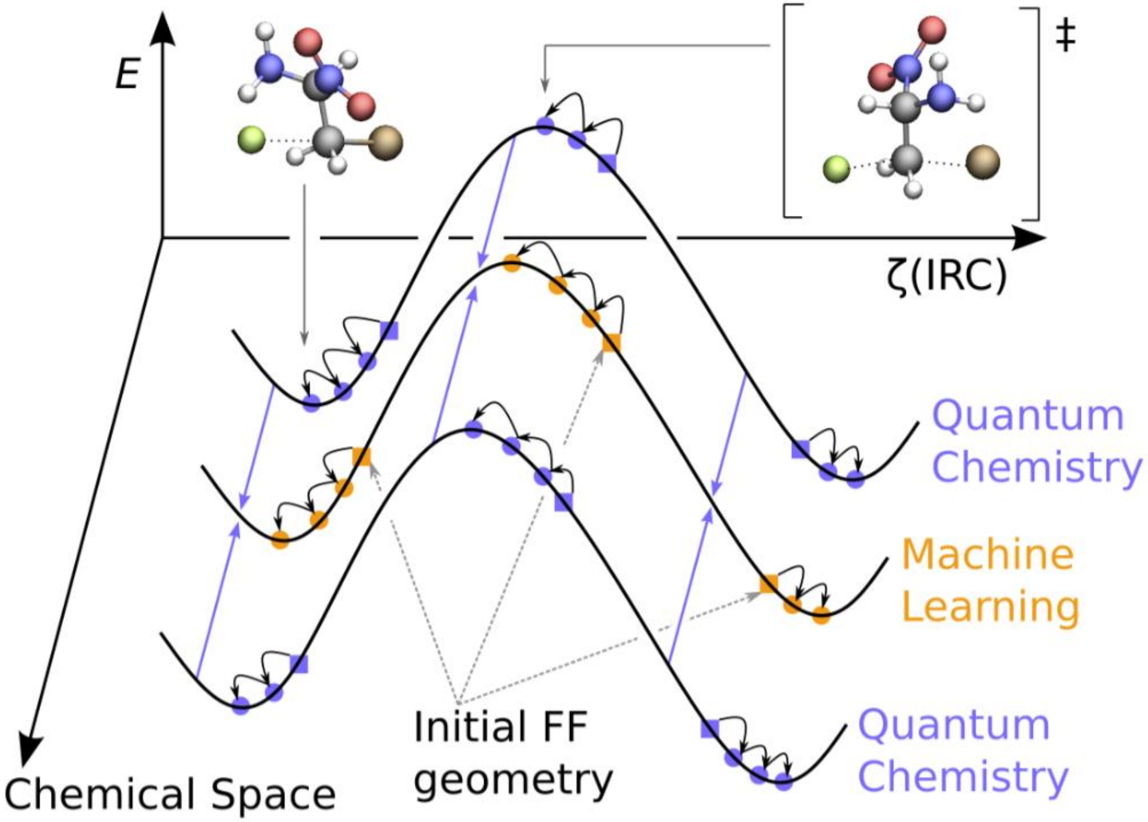

$$J(\boldsymbol{\alpha}) = \left\| \begin{bmatrix} \mathbf{y} \\ \mathbf{f} \end{bmatrix} - \begin{bmatrix} \mathbf{K} \\ -\frac{\partial}{\partial \mathbf{r}}\mathbf{K} \end{bmatrix} \boldsymbol{\alpha} \right\|_2^2$$

$$L(\alpha) = 0.01 \sum_i (y_i - y_i^{\mathrm{est}})^2 + \sum_i \frac{1}{n_i} ||\mathbf{f}_i - \mathbf{f}_i^{\mathrm{est}}||^2$$

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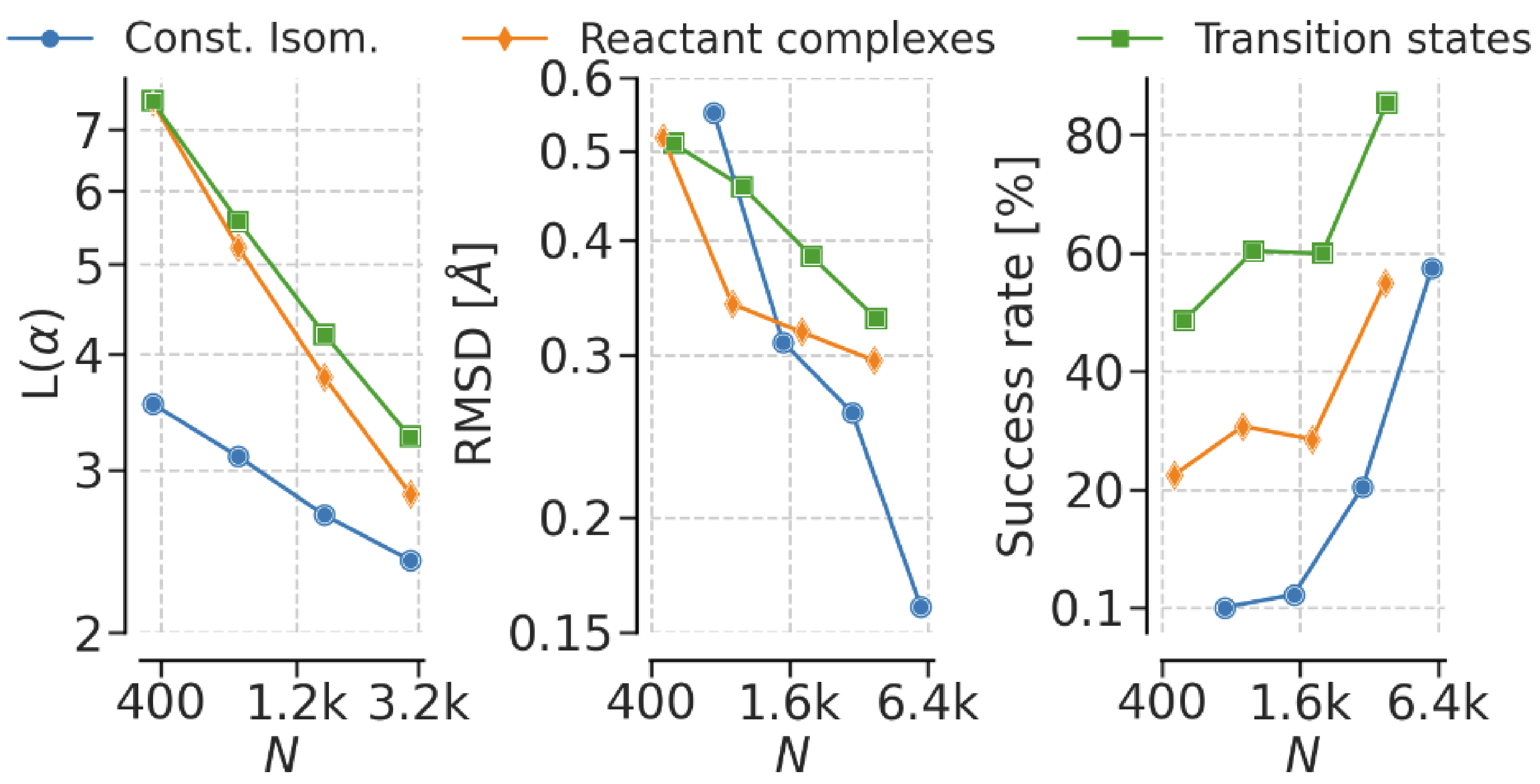

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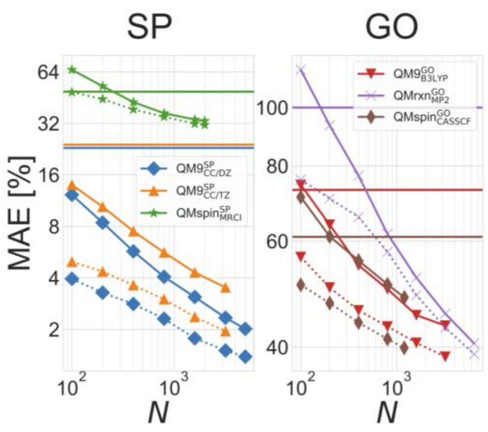
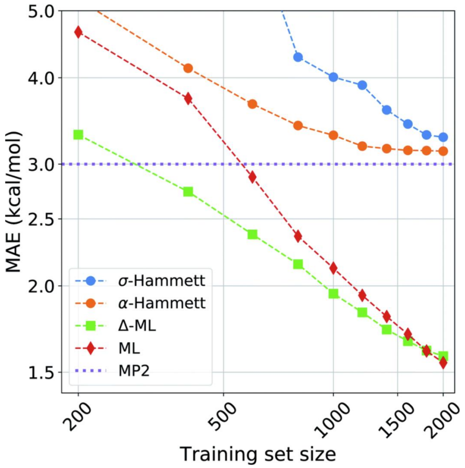
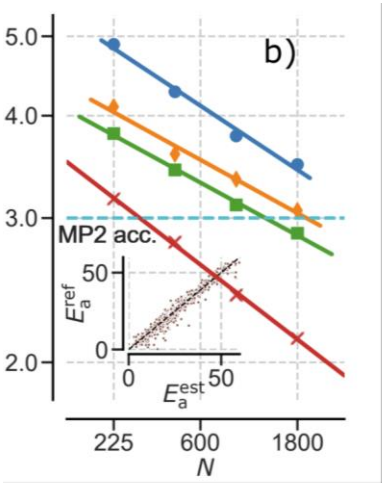
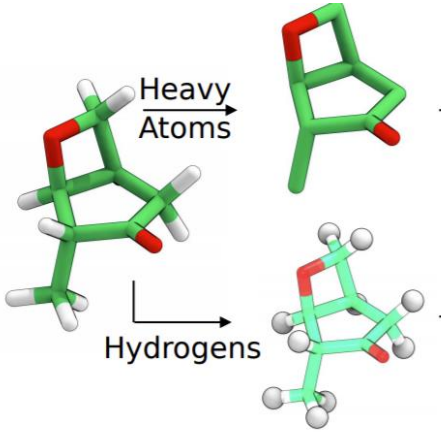
Summary









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Energies with KRR

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Geometries with Graph2Structure

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Acknowledgements


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