Going EAST in Chemical Space: Challenges, Concepts, and Constraints

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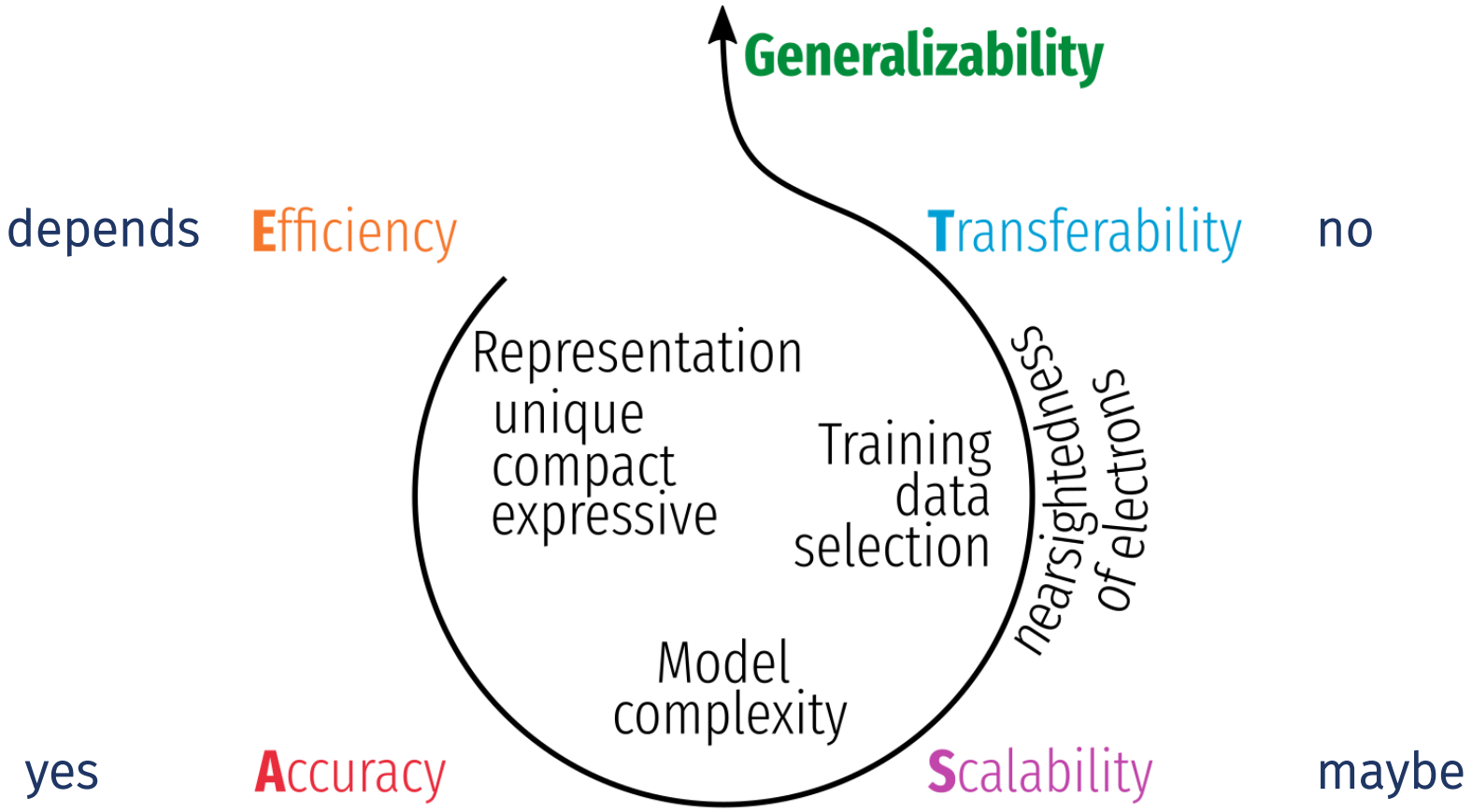
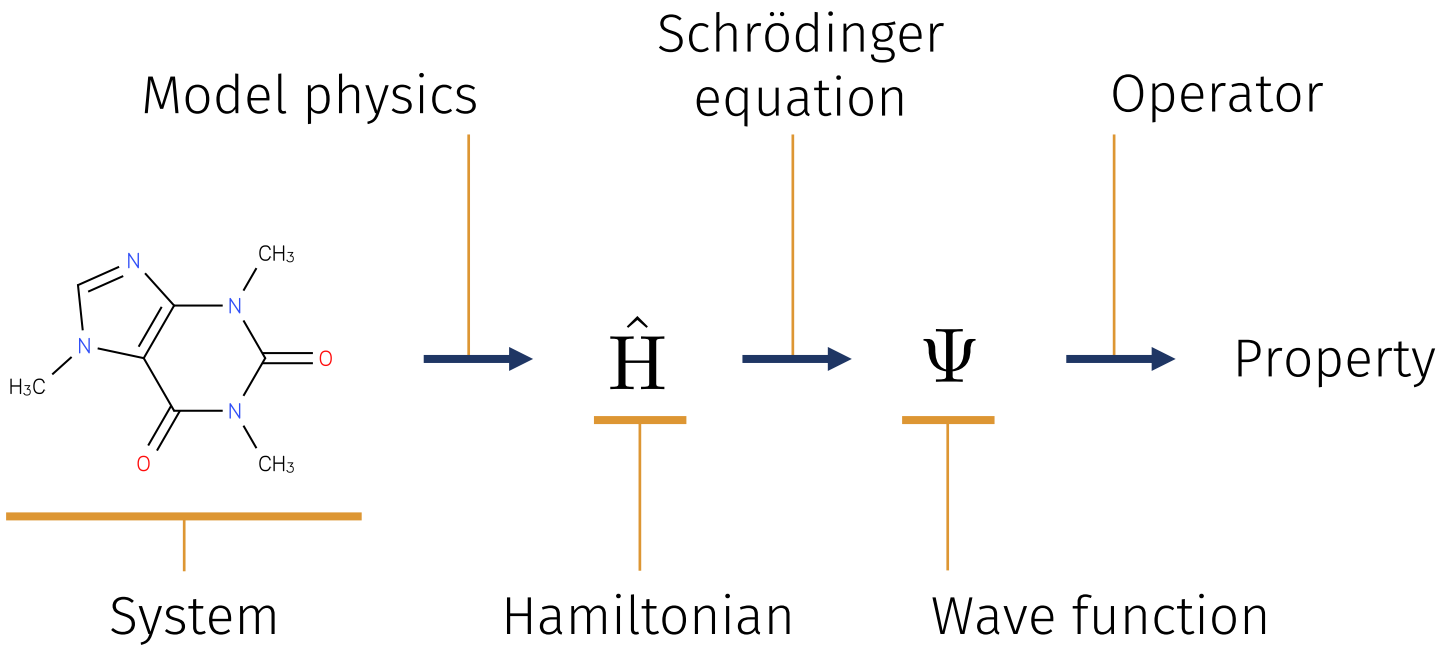
EAST



B. Huang, **GFvR**, A. von Lilienfeld, *Science*, **2023** (accepted).

Solved?


Model physics
Schrödinger equation
Operator
$\hat{H}$
Ψ
Property
System
Hamiltonian
Wave function

Cost

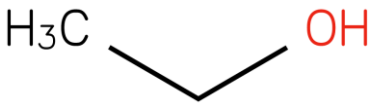
$$\Psi = \Psi(\mathbf{r}_1, \mathbf{r}_2, \mathbf{r}_3, \ldots, \mathbf{r}_n)$$

Methane

CH_4

N_2

Ethanol



Solved by approximations in computational chemistry?

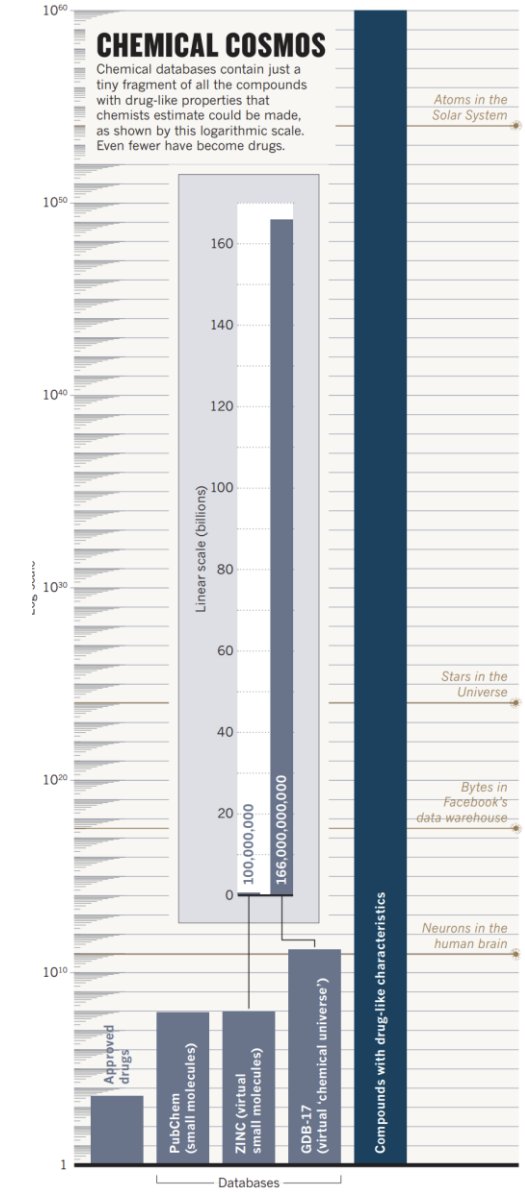
Scaling of Molecules

Commercial databases

- 164 million molecules
- 15k added daily

Scale

- One person: 1 million compounds/second
- 10 billion people on earth
- 10^{26} universe ages to go through



A. Mullard, *Nature*, 2017.

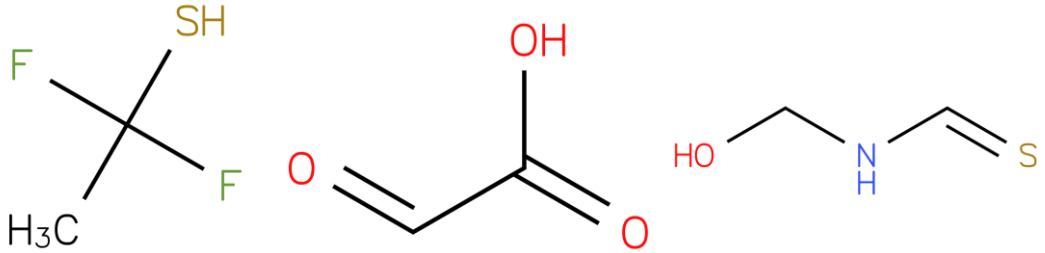
3D Geometries

Take some atoms from {C, O, N, F, S}, H-saturated

349:

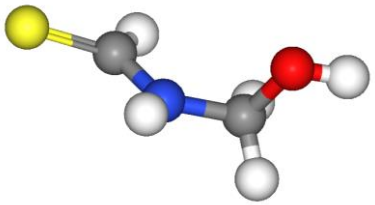
$C_2H_4F_2S$
$C_2H_2O_3$
C_2H_5NOS
...

9,917:



...

~52k:

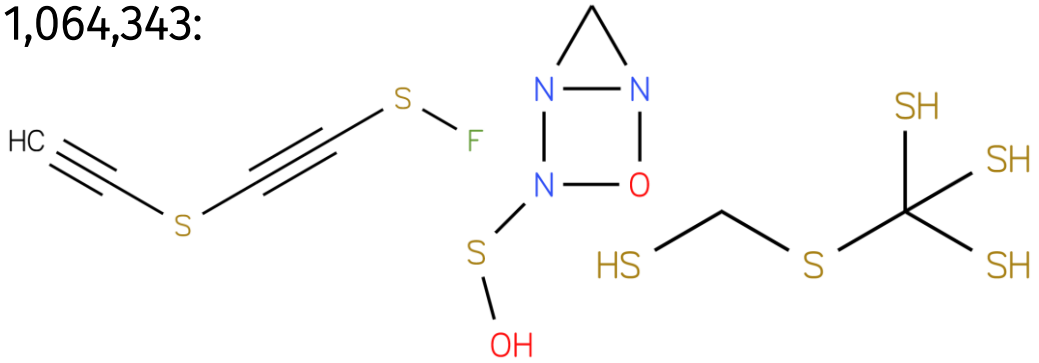


...

1,050:

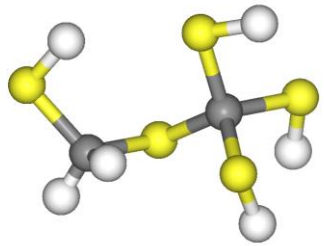
C_4HFS_2
$CH_3N_3O_2S$
$C_2H_6S_5$
...

1,064,343:



...

~23M:



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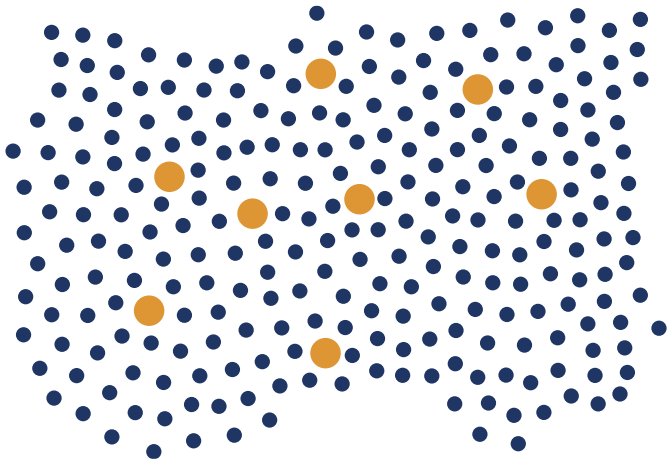
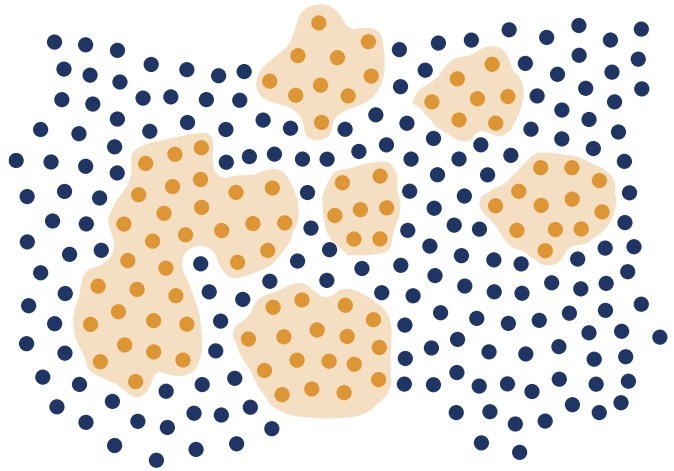
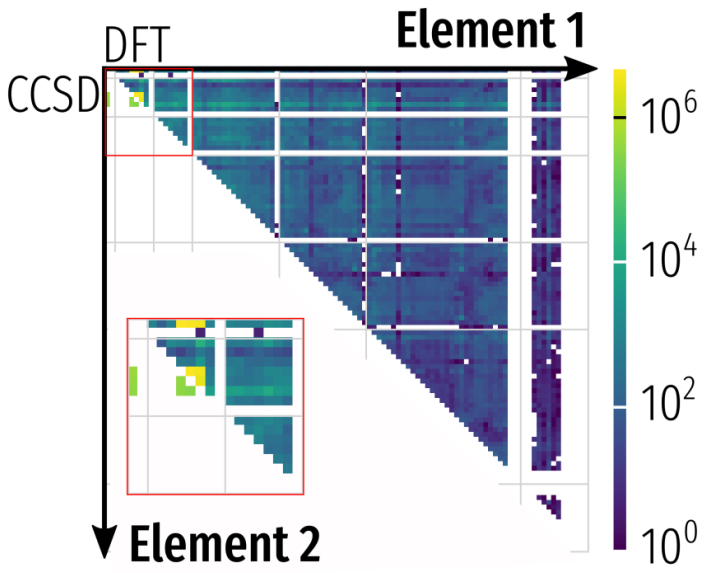
Constraint 1

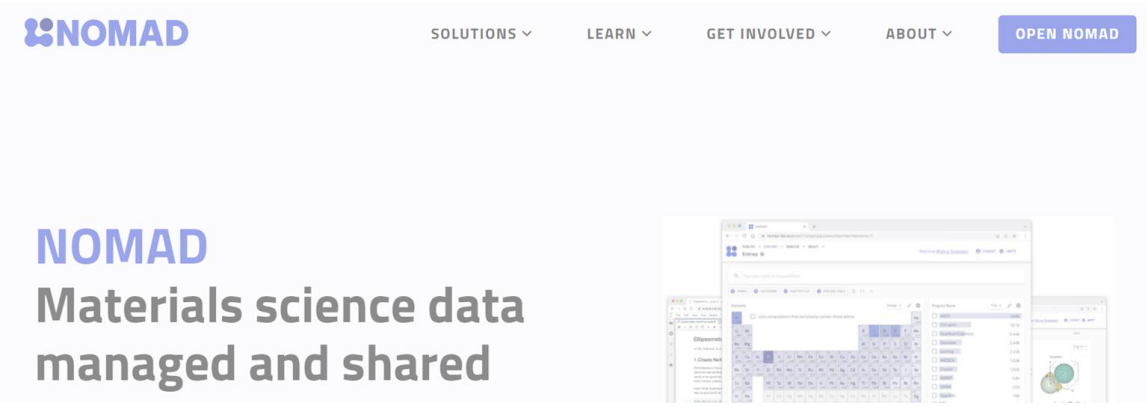
Speed does not matter:
even enumeration is impossible.

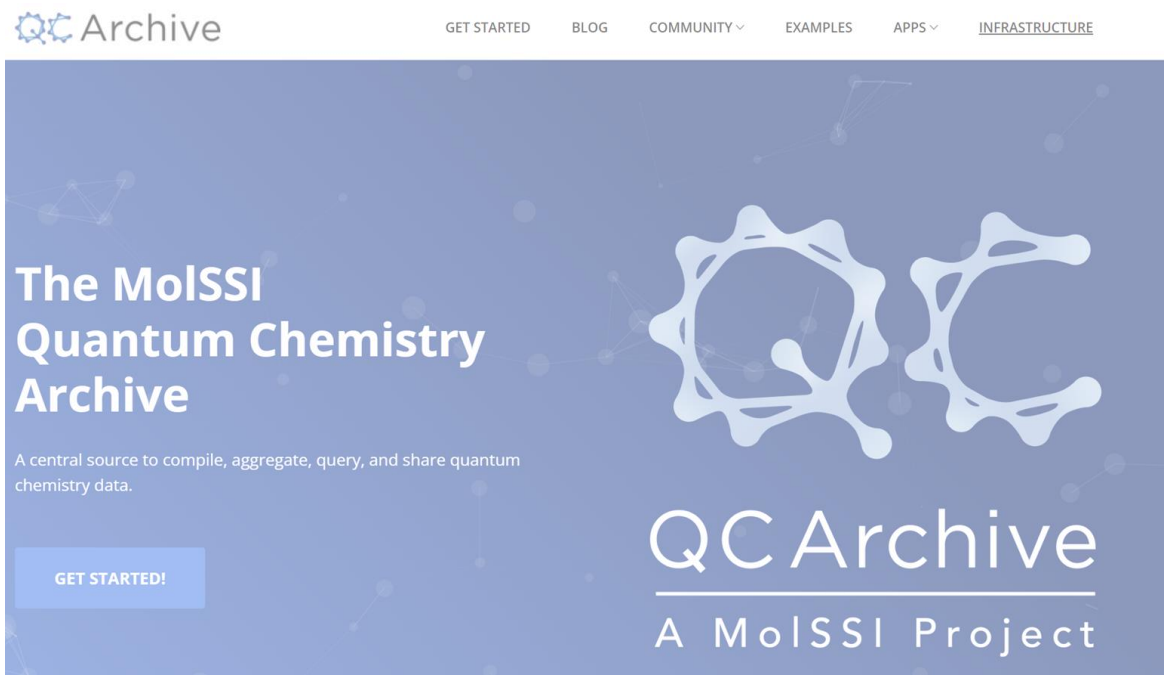




Data Availability



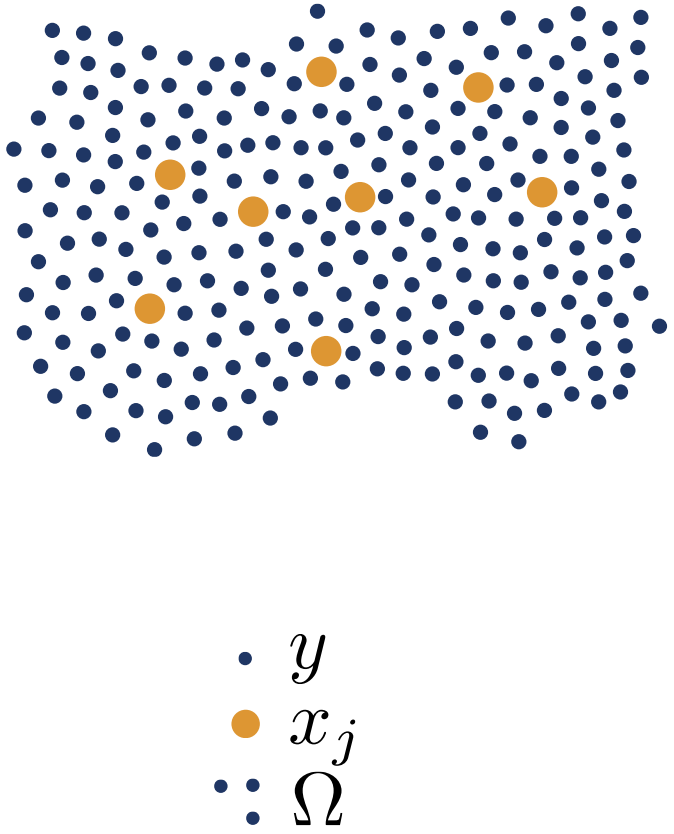




Fill Distance

$$h \equiv \sup_{y \in \Omega} \min_{x_j \in X} \|y - x_j\|_2$$

$$\text{Error} = a \exp(-c/h)$$

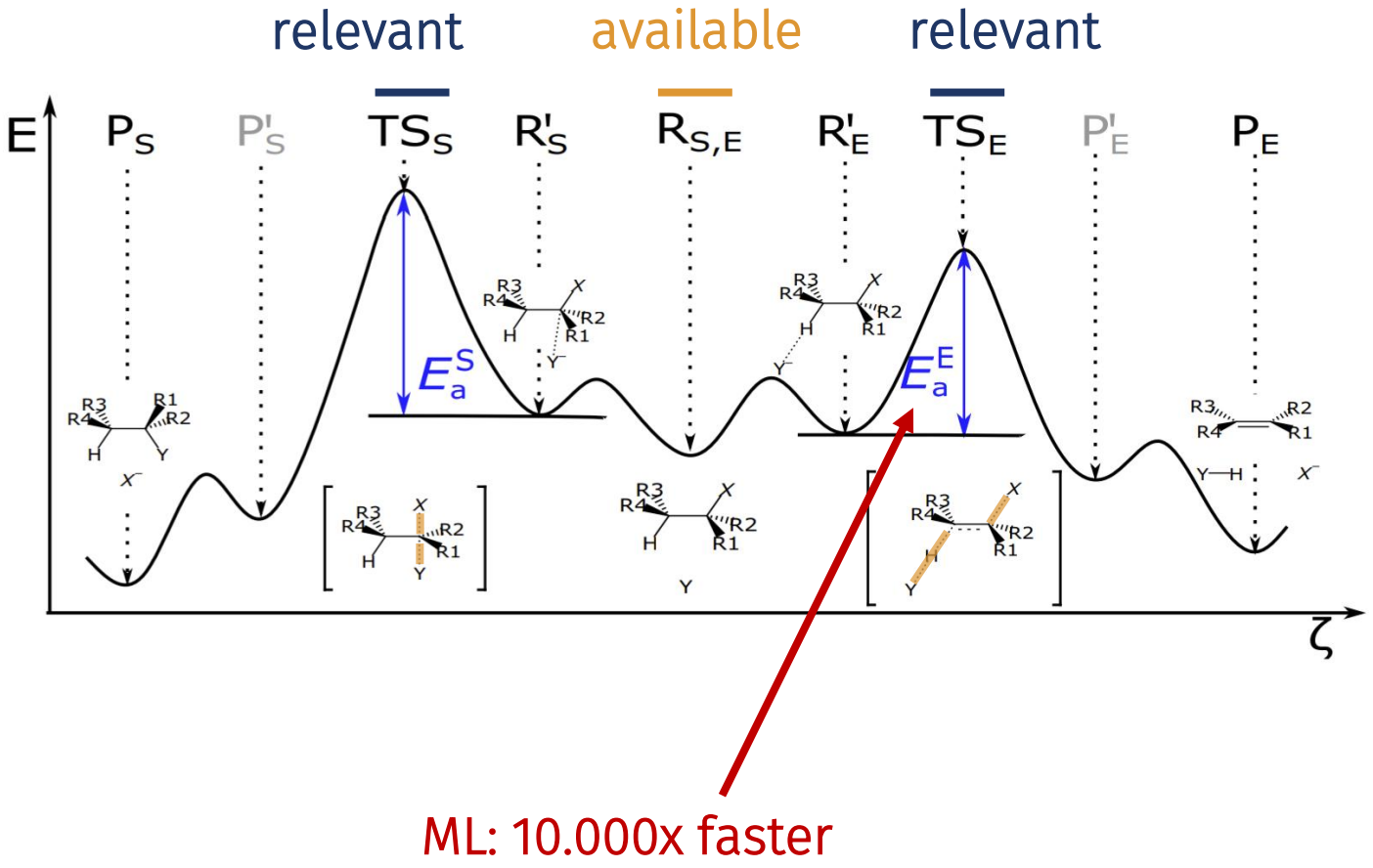


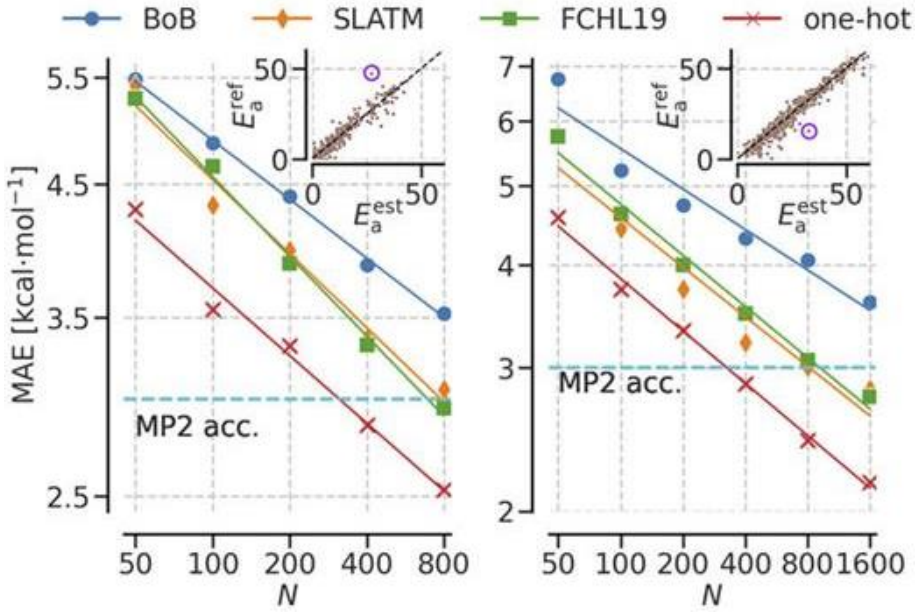
W.R. Madych, S.A. Nelson, *J Approx Theory*, 1992.

Constraint 2

Transferable models require a compact chemical space.
Or ludicrous amounts of data.

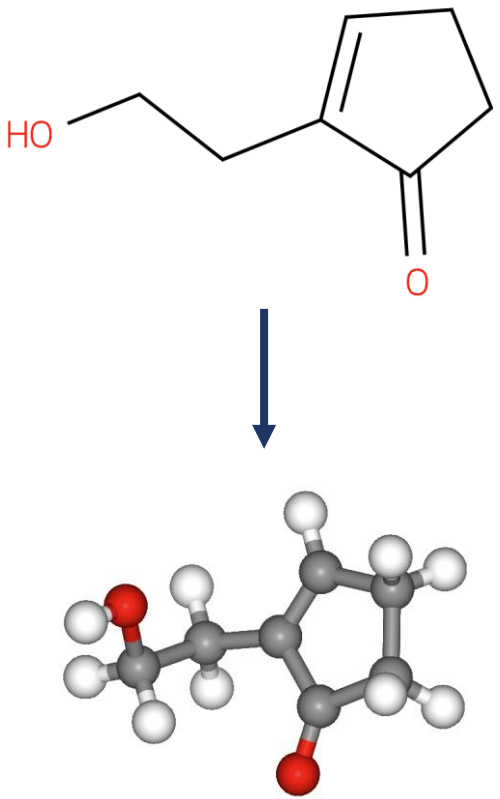
Concept: Avoid Knowing the PES



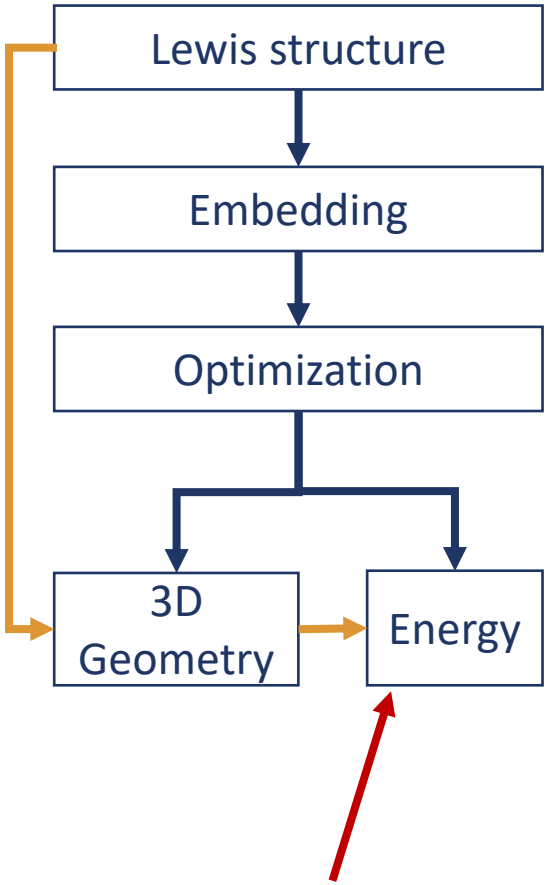


GFvR, S.N. Heinen, M. Bragato, O. A. von Lilienfeld, *Mach. Learn.: Sci. Technol.* 2020.
S.N. Heinen, GFvR, O. A. von Lilienfeld, *J. Chem. Phys.*, 2021.

Concept: Avoid Knowing the PES



Traditional / G2S



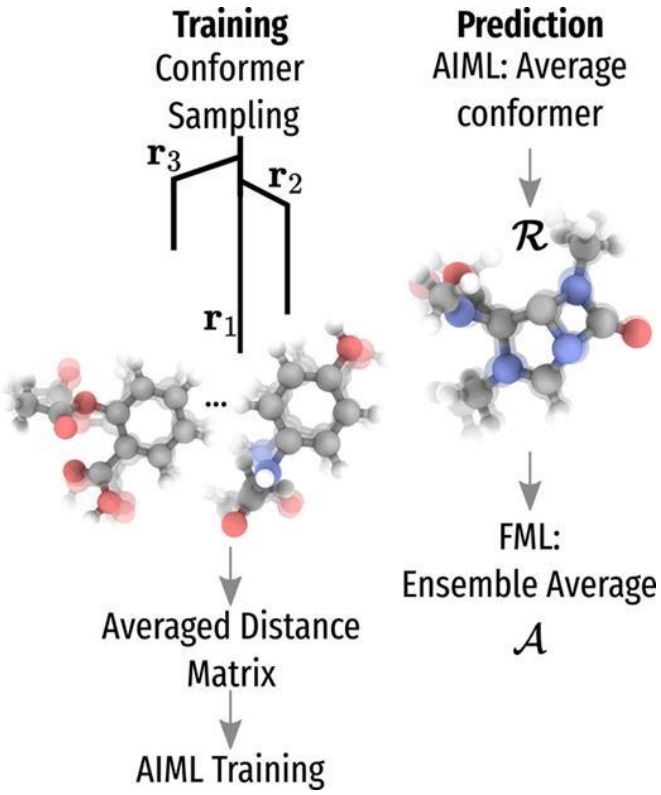
ML: 100.000x faster

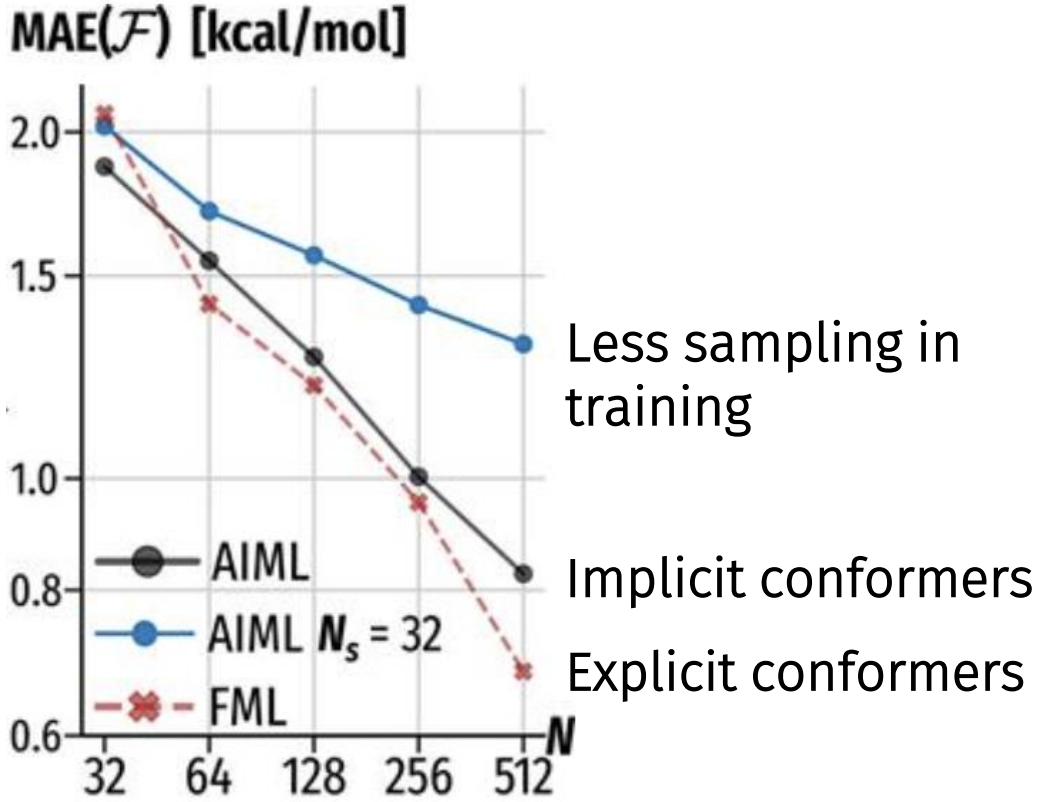
G2S

- Closer to DFT than common methods
  - Small molecules
- Applicable to complex chemical spaces
  - Transition state geometries
  - Carbenes
  - Elpasolite crystals

D. Lemm, **GFvR**, O. A. von Lilienfeld, *Nat. Commun.* **2021**.

Concept: Consider Ensembles





Less sampling in training

Implicit conformers

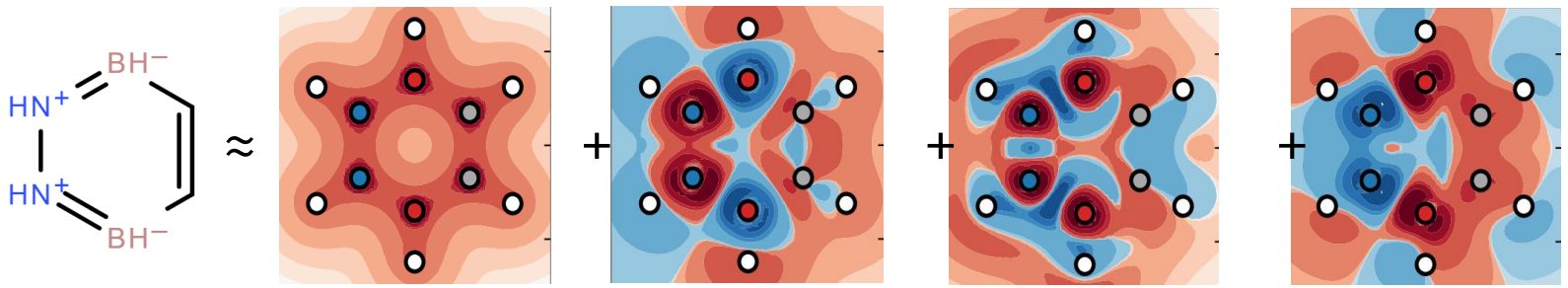
Explicit conformers

J Weinreich, D Lemm, GFvR, O. A. von Lilienfeld, J Chem Phys, 2022.

Quantum Alchemy

Taylor expansion

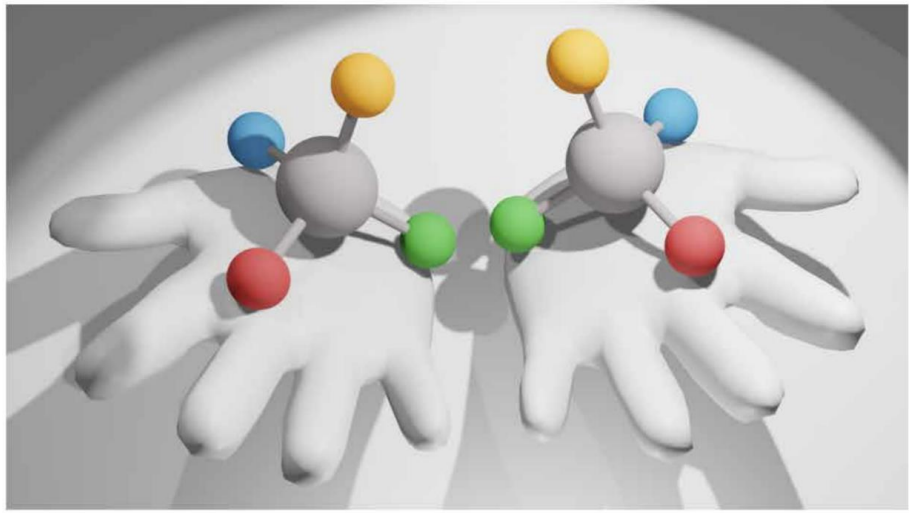
- Energy function of
  - Geometry — Forces, Vibrations
  - Nuclear charges — Alchemical changes
- Idea: obtain dominant leading derivatives, predict many systems

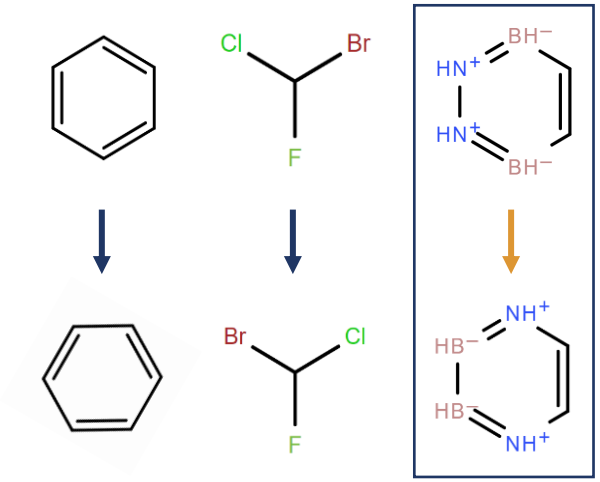


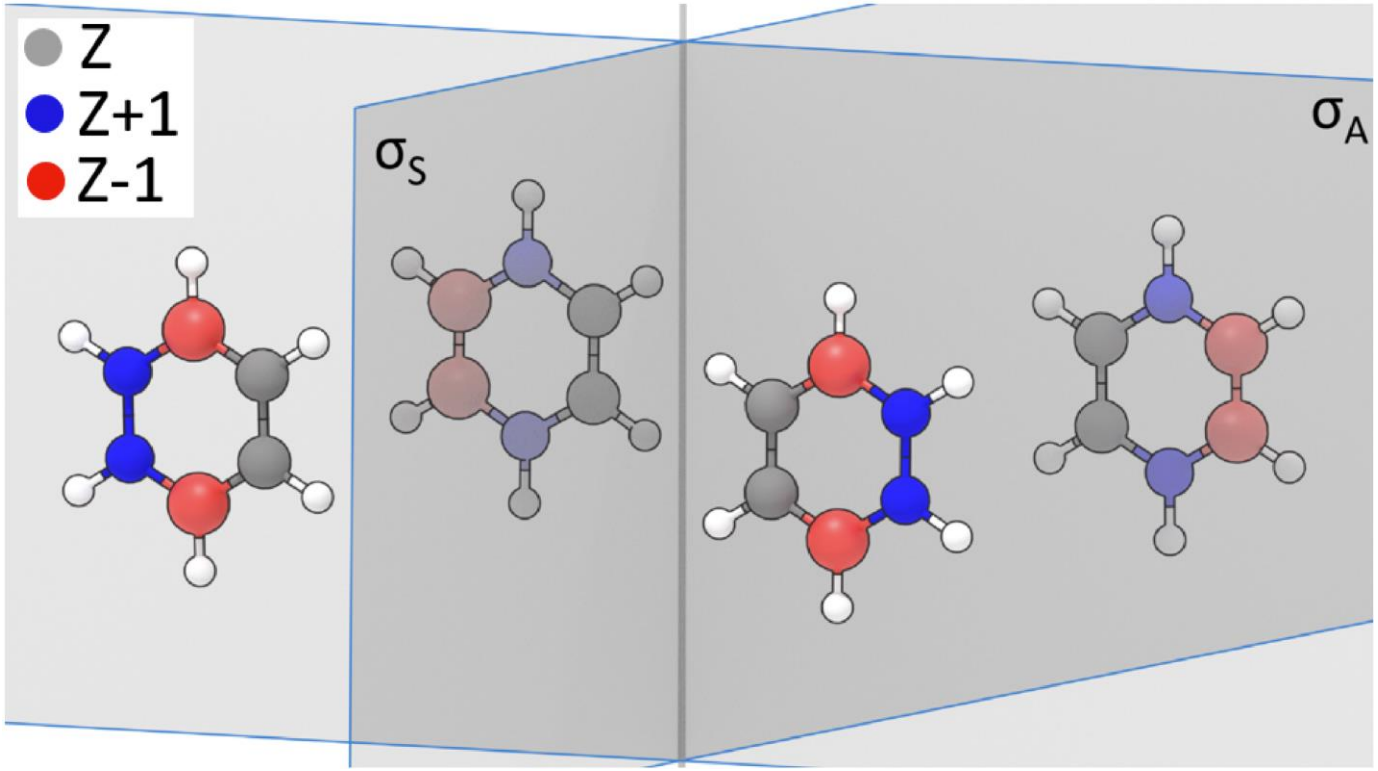
$$\hat{H}(\lambda) \equiv \lambda \hat{H}_{\mathrm{t}} + (1-\lambda)\hat{H}_{\mathrm{r}}$$

E. B. Wilson, *J. Chem. Phys.* 1962.
GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.*, 2020.

Concept: Use Symmetries





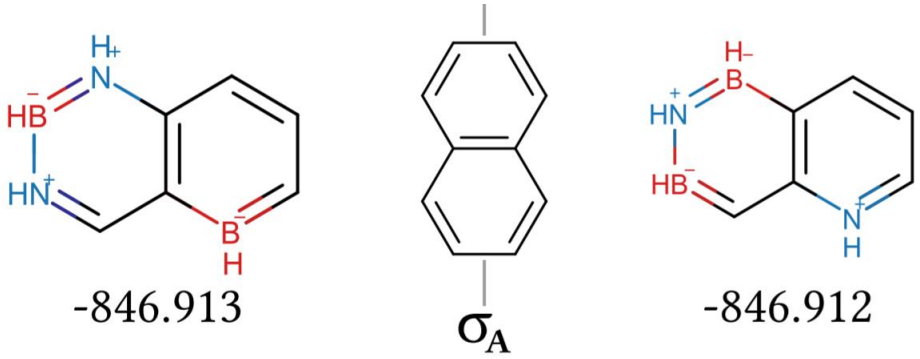


GFvR, O. A. von Lilienfeld, *Science Adv.* 2021.

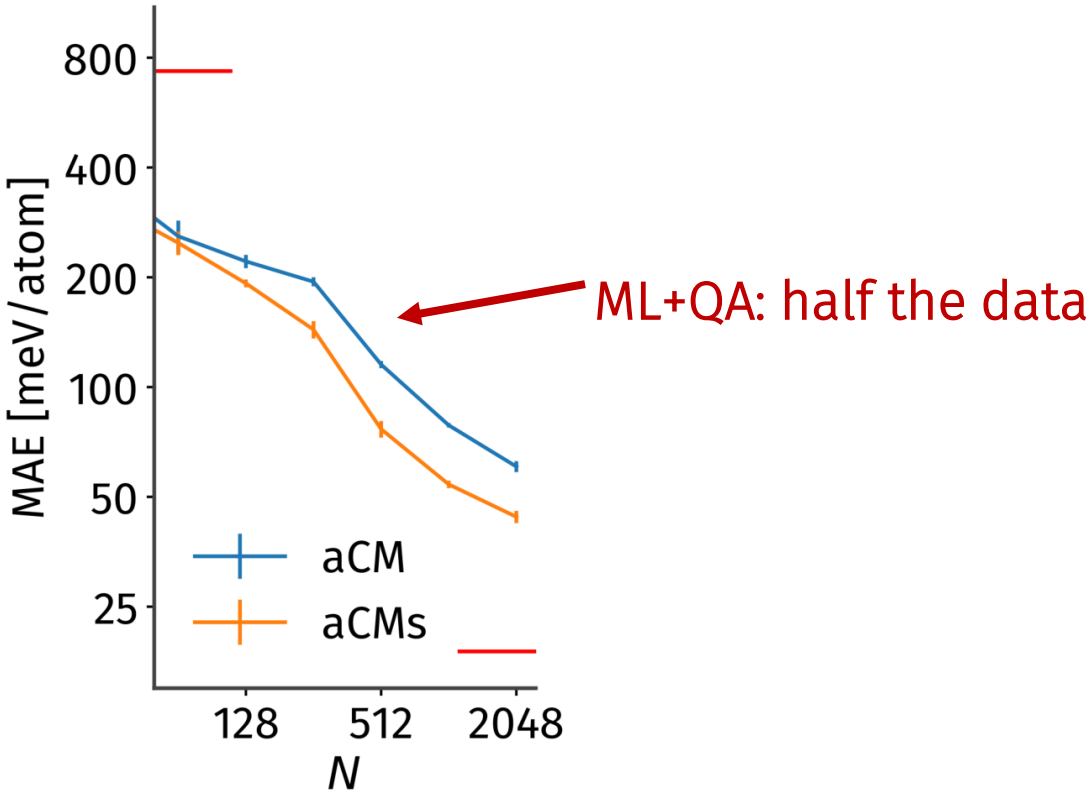
Concept: Use Symmetries

Alchemical Enantiomers

Electronic energy only

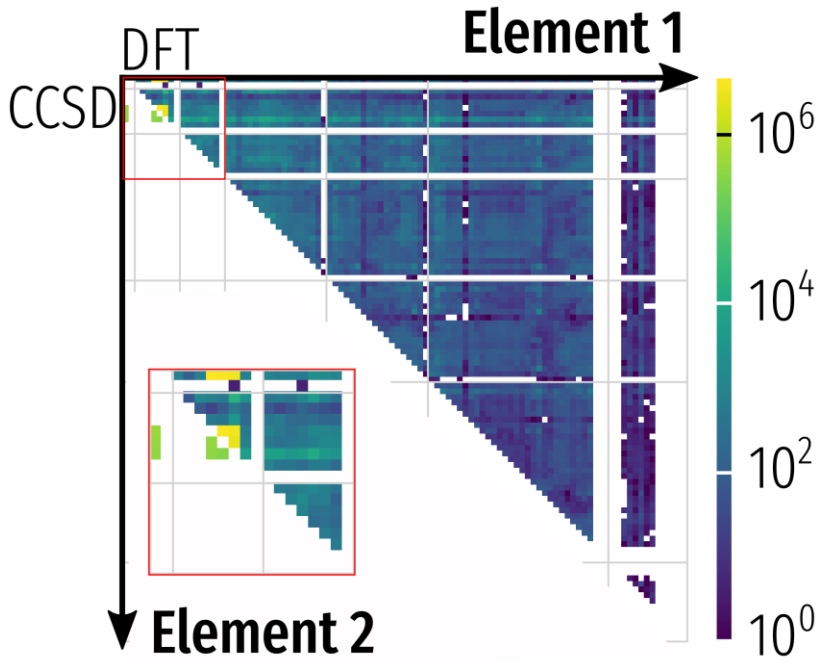


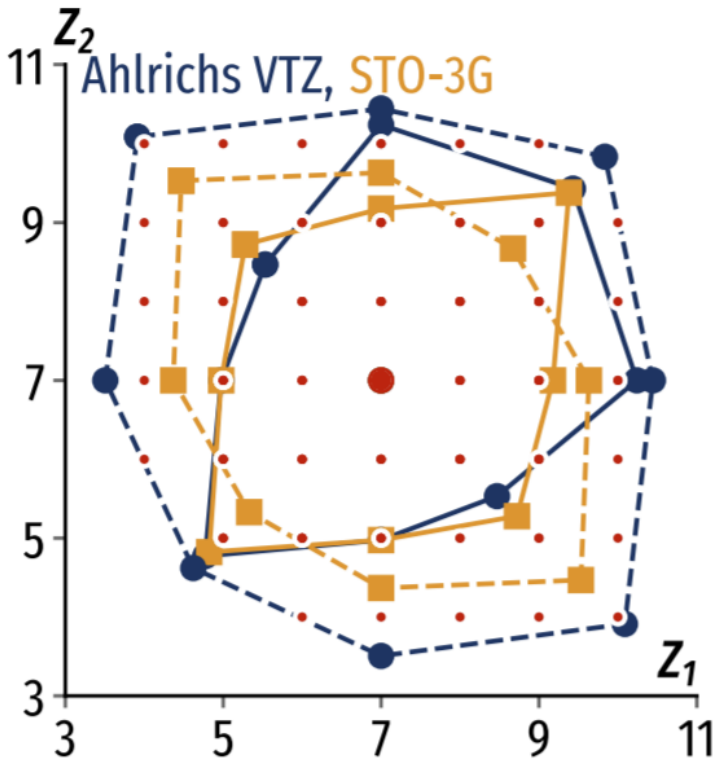
Speed up machine learning



GFvR, O. A. von Lilienfeld, *Science Adv.* 2021.

Challenge: Element Diversity

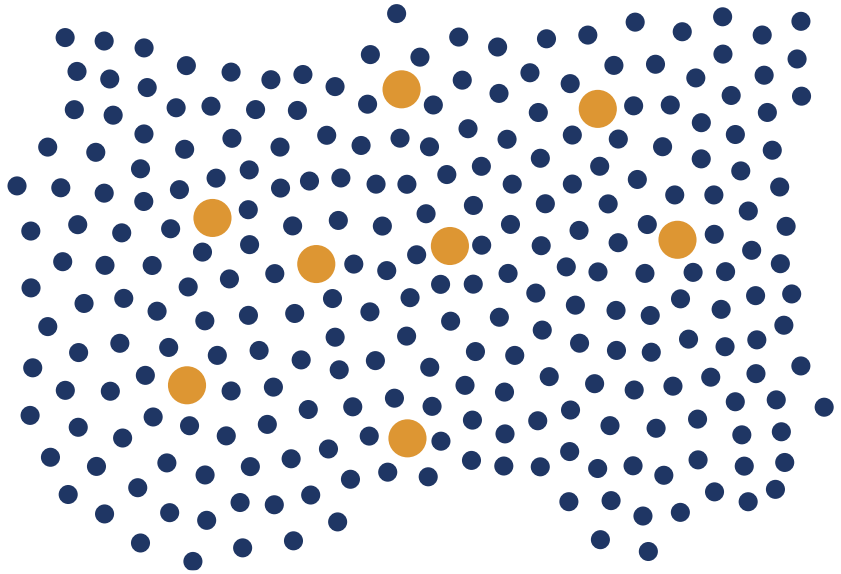




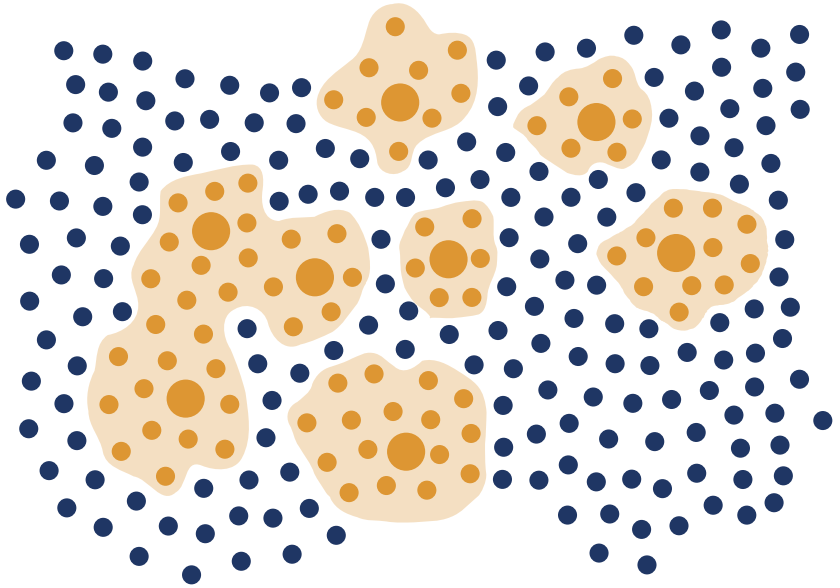
GFvR, *J. Chem. Phys.* 2021.

Challenge: Element Diversity

Without Perturbation



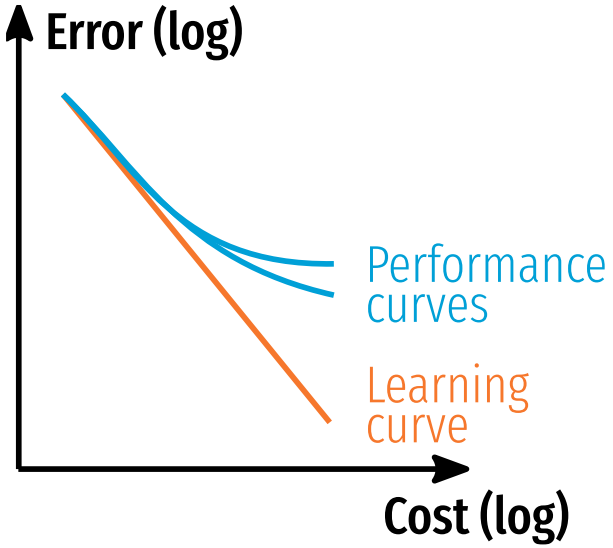
With Perturbation

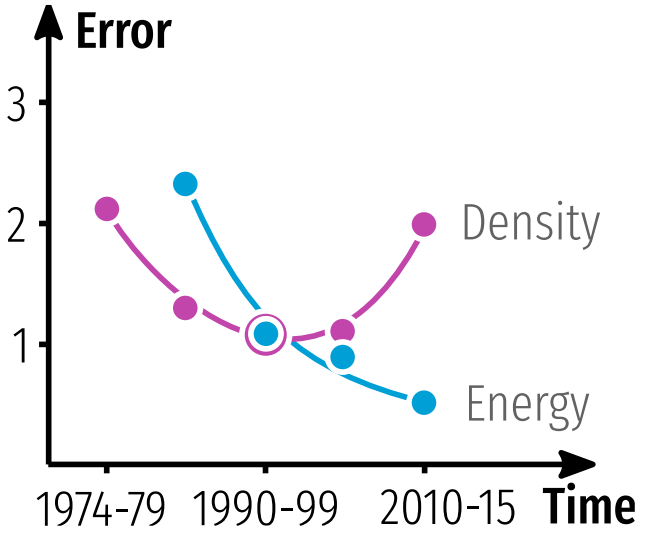


Systems/Molecules

- Any
- Known
- Approximated

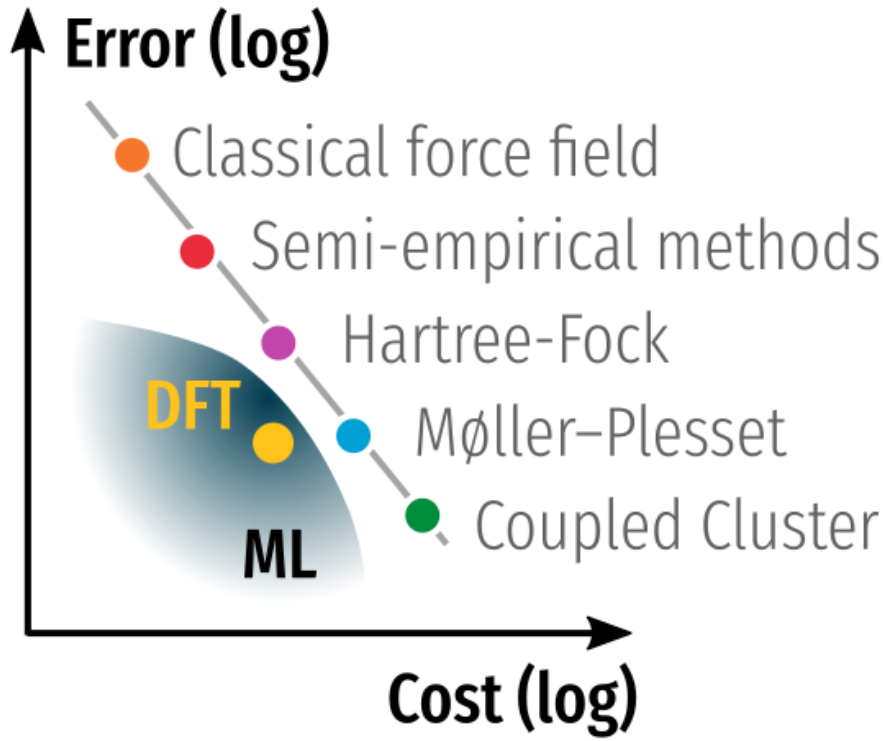
Challenge: Multi-Property Training





M.G. Medvedev et al., *Science*, 2017.

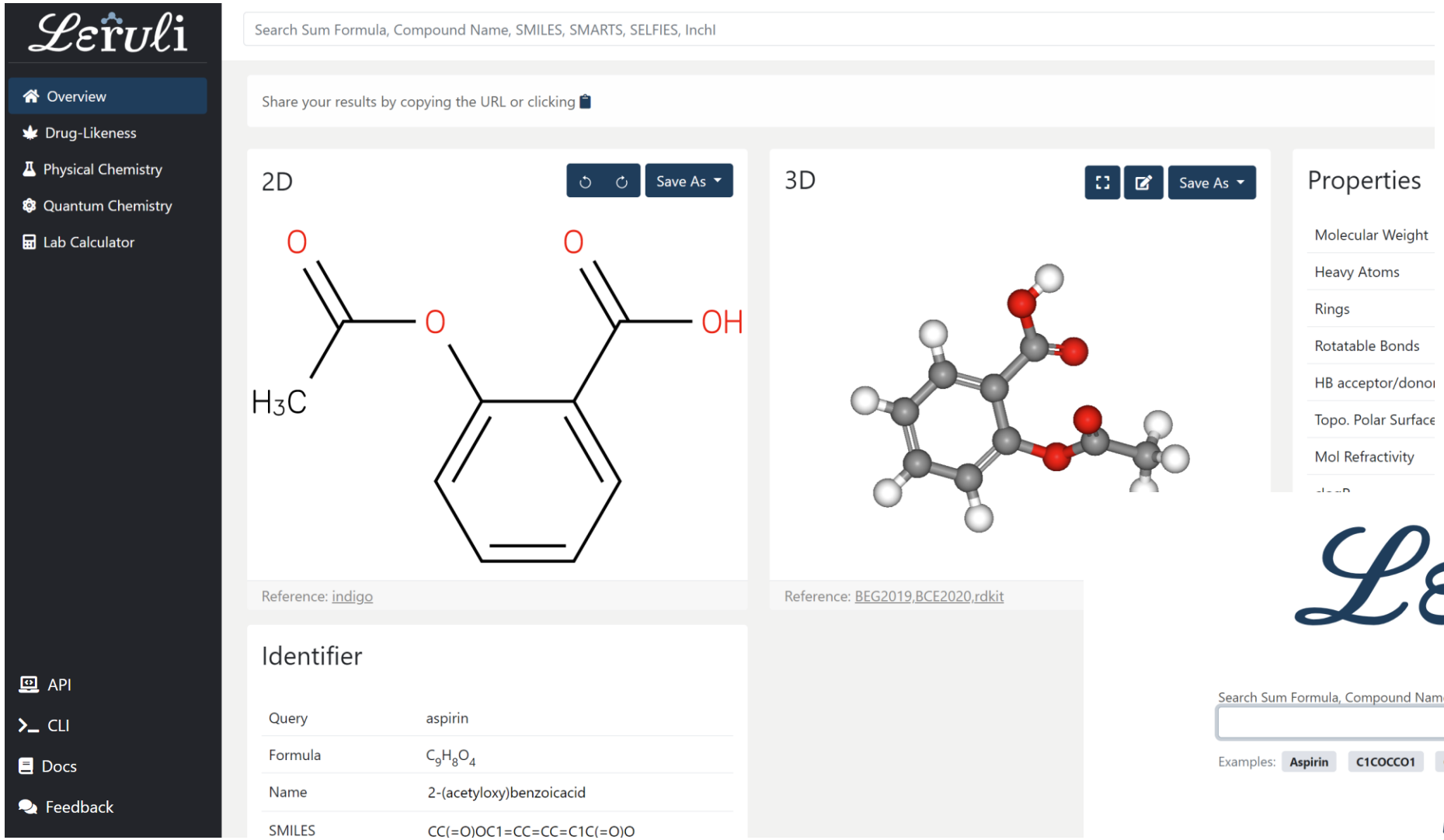
Challenge: Prediction Performance



How accurate can we be given
- an application and
- a compute budget?

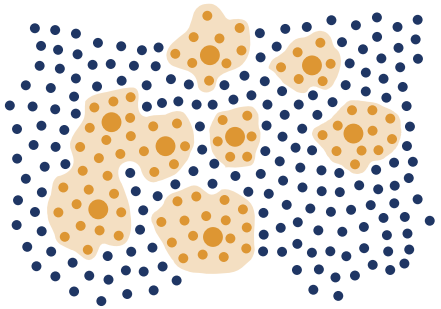
B. Huang, **GFvR**, A. von Lilienfeld, arXiv, **2023**.

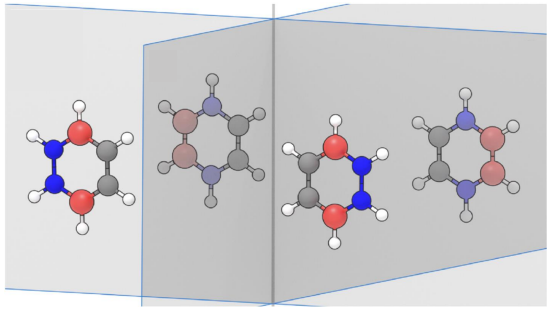
Challenge: Access to Models



Try it:
leruli.com

Summary





Concept | Avoid knowing the PES

Concept | Consider ensembles

Concept | Quantum Alchemy: derivatives and symmetry

Challenge | Element diversity

Challenge | Multi-property training

Challenge | Prediction performance

Challenge | Access to models

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Thanks

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Mario Krenn
Simon Krug
Dominik Lemm
Anatole von Lilienfeld
Alex Maldonado
Michael Sahre
Max Schwilk
Enrico Tapavicza
Jan Weinreich

We're hiring!