Quantum Alchemy: Treating chemically diverse compounds with perturbations

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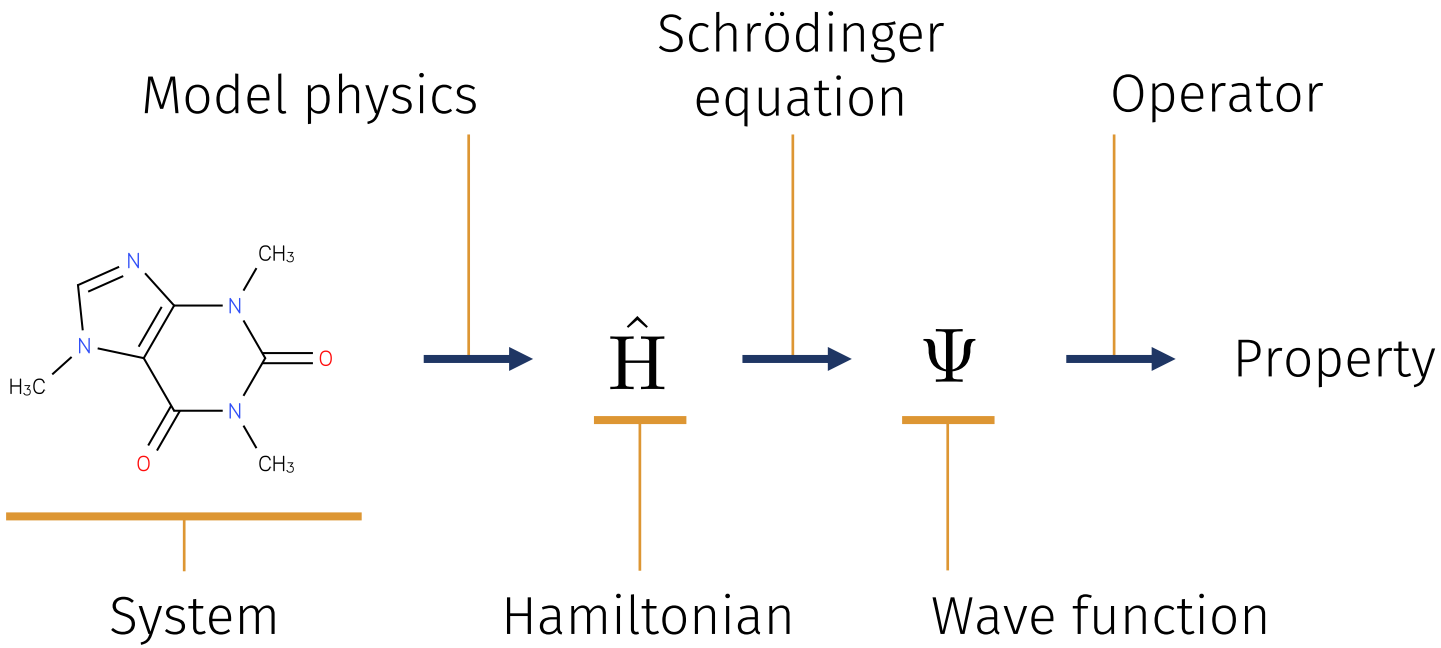
Solved?


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

Wave function

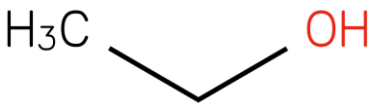
$$\Psi = \Psi(\mathbf{r}_1, \mathbf{r}_2, \mathbf{r}_3, \ldots, \mathbf{r}_n)$$

Methane

CH_4

N_2

Ethanol



Solved by approximations in computational chemistry?

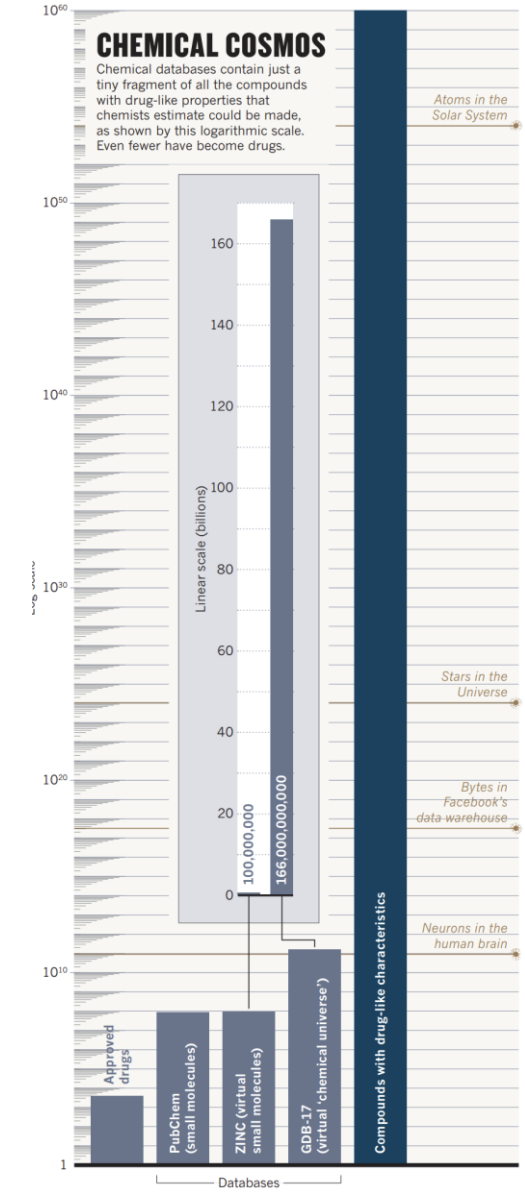
Scaling of Molecules

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



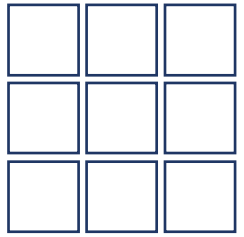
A. Mullard, *Nature*, 2017.

Scaling of Materials

Face centered cubic and 70 elements only

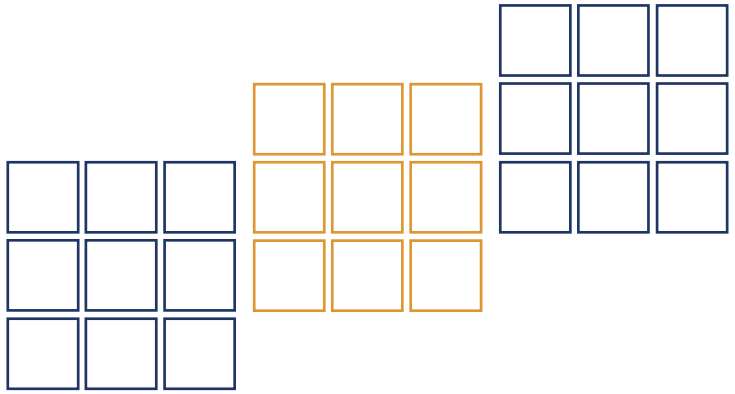
9 primitive cells

- Binary 10^{7}
- Ternary: 10^{13}
- Quaternary: 10^{15}



27 primitive cells

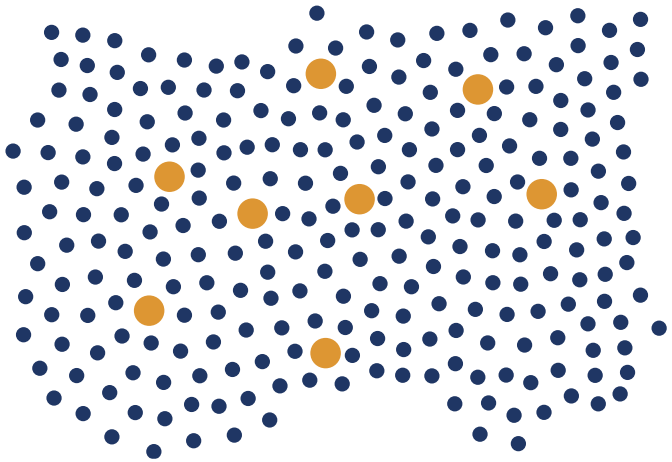
- Binary: ~ 10^{17}
- Ternary: ~ 10^{29}
- Quaternary: ~ 10^{36}

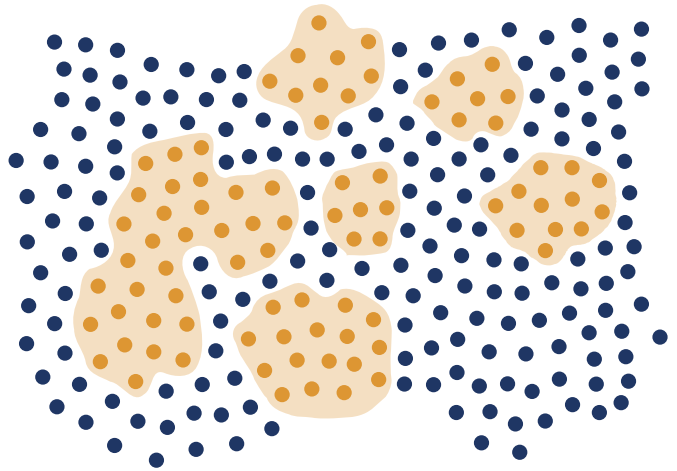


K. Shinohara, A. Seko, T. Horiyama, M. Ishihata, J. Honda, I. Tanaka, *J Chem Phys*, 2020.

Properties of domains?

Speed does not matter:
even enumeration is impossible.





Quantum Alchemy

Idea

Treat system changes perturbatively[1,2]
Build a Taylor/Padé approximant[3] : **often 100.000 times faster**

Steps

Choose system

Alter system, calculate property response functions

Predict many modified systems

1 | E. B. Wilson, *J. Chem. Phys.* 1962. 2 | GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.*, 2020. 3 | GFvR, *J. Chem. Phys.*, 2021.

Perspective shift

Few highly accurate calculations
instead of many intermediate ones

$$\hat{\mathrm{H}} = \hat{\mathrm{H}}(Z_i, \mathbf{R}_i, N_e, \sigma)$$

4N

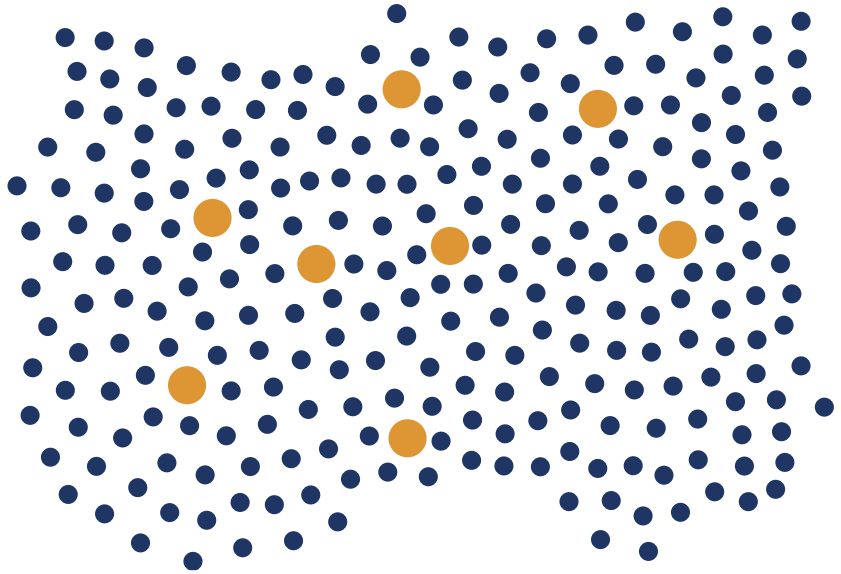
1D, close to $\sum_i Z_i$

1D

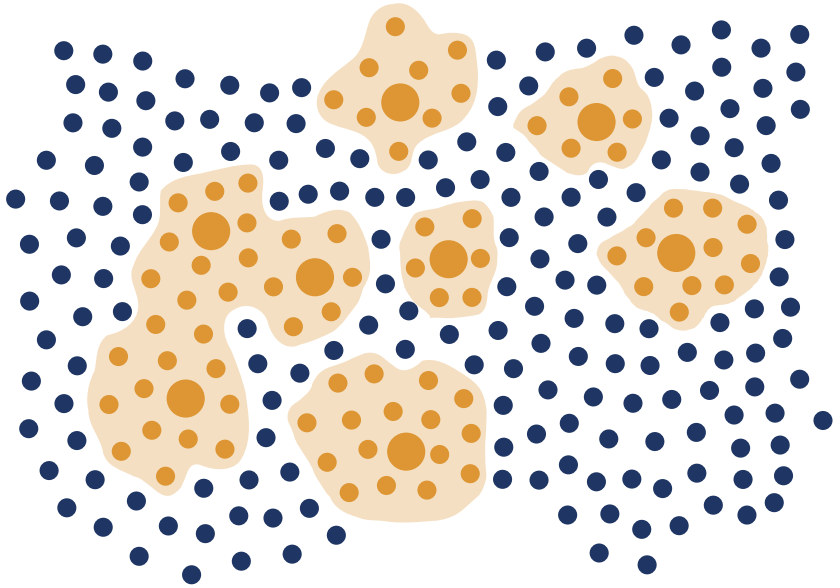
Joseph Wright, 1771

Motivation

Without Perturbation



With Perturbation



Systems
- Any
- Known
- Approximated

Requirements

Differentiable / Analytic

- ✓ Total Energy [1,2]
- ✓ Dipole moments [2]
- ✓ Deprotonation energies [3]
- ✓ Photoelectron circular dichroism [5]
- ✓ Electron density [1,2]
- ✓ Non-covalent interactions [1]
- ✓ Ionisation Energy [4]
- ✓ Orbital eigenvalues [2]
- ✓ Binding energies [1,2]
- ✓ Electron Affinity [4]

Converge quickly

NMR spectra (in progress)

1 | GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.*, 2020. 2 | GFvR, *J. Chem. Phys.*, 2021. 3 | GFvR, O. A. von Lilienfeld, *Phys. Chem. Chem. Phys.*, 2020. 4 | E Eikey, A Maldonado, C Griego, GFvR, J Keith, *J. Chem. Phys.*, 2022. 5 | GFvR, A Artemyev, B Lagutin, P Demekhin, *J. Chem. Phys.*, 2024.

Quantum Alchemy

Interpolate between molecular isoelectronic Hamiltonians

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

Taylor expansion around reference molecule

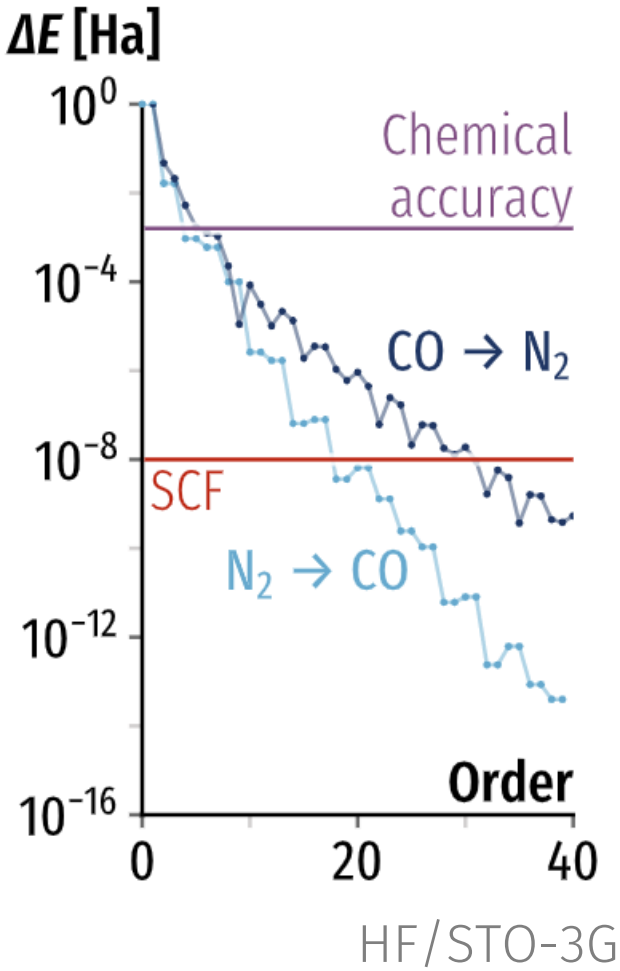
$$E_\mathrm{t} = E_\mathrm{r} + \Delta E^\mathrm{NN} + \int_\Omega d\mathbf{r} \sum_{n=0}^{\infty} \frac{1}{(n+1)!} \Delta v \frac{\partial^n \rho_\lambda(\mathbf{r})}{\partial \lambda^n}\bigg|_{\lambda=0}$$

- Gives consistent energies, densities, forces, …
- Uses the same derivatives for all predictions

GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.*, 2020.

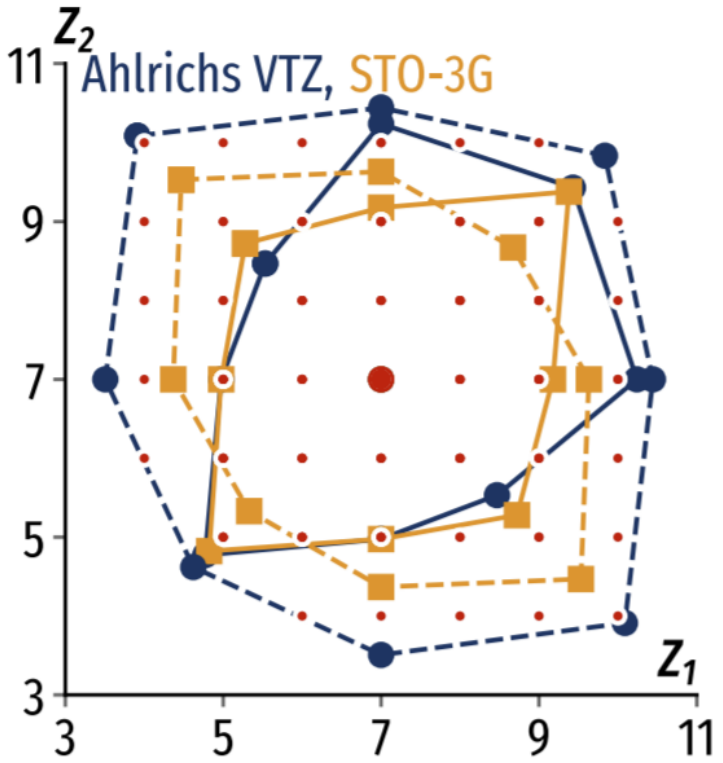
xkcd.com/2605

Convergence



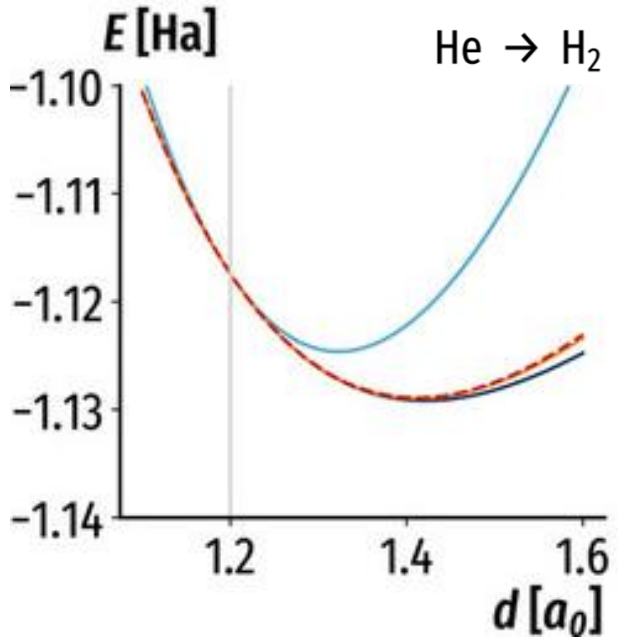
Taylor expansion

- First terms accurate enough
  - Truncate early
- Converges to the right value
- Large convergence radius
- Scales with chemical space



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

Geometry Relaxation



Taylor expansion

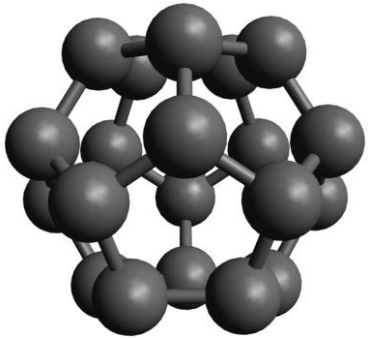
- Large changes still converge (more slowly)
- Geometric response can be recovered

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

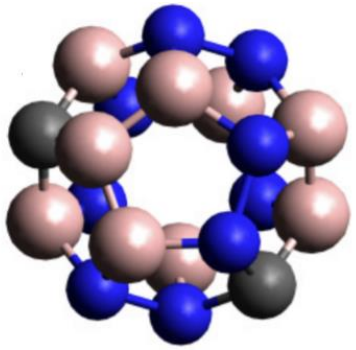
Covalent Interactions

Scaling with chemical space

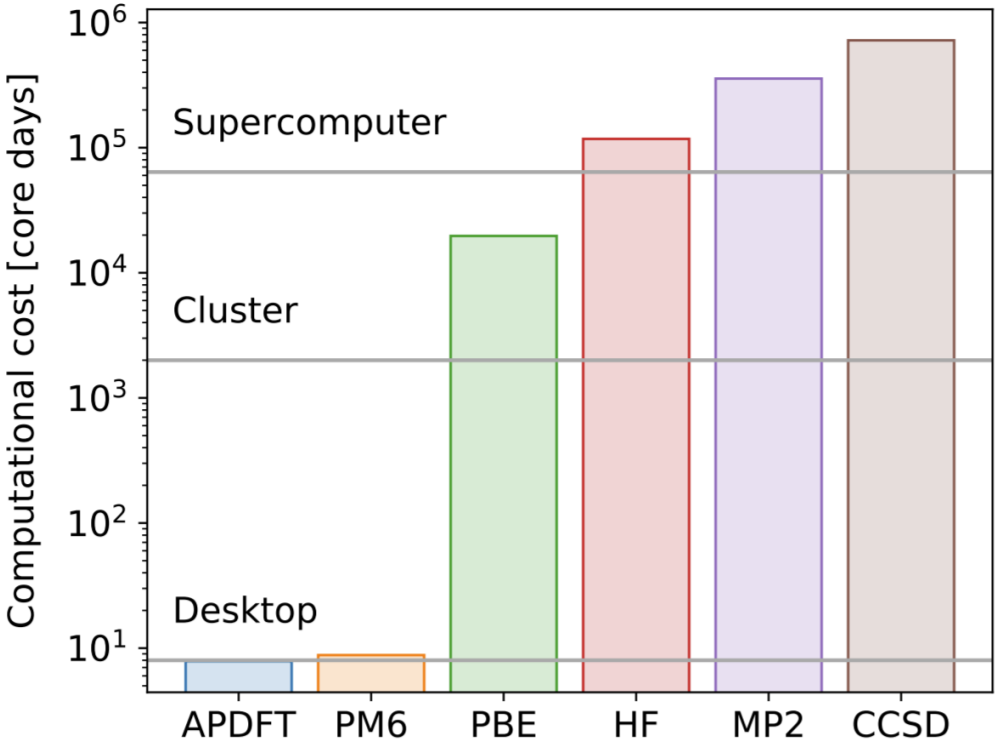
- 1 derivative for second order
- 5 derivatives for third order



C_{20}



$3.1 \cdot 10^6$ targets



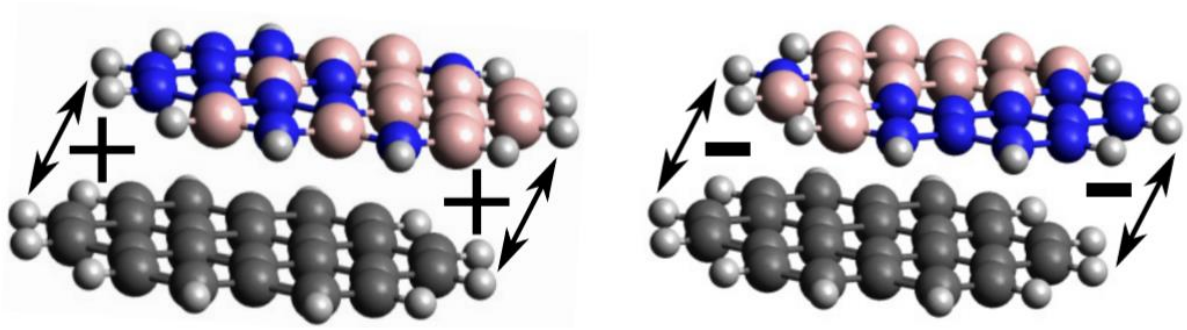
QA: 80.000x faster

GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.*, 2020.

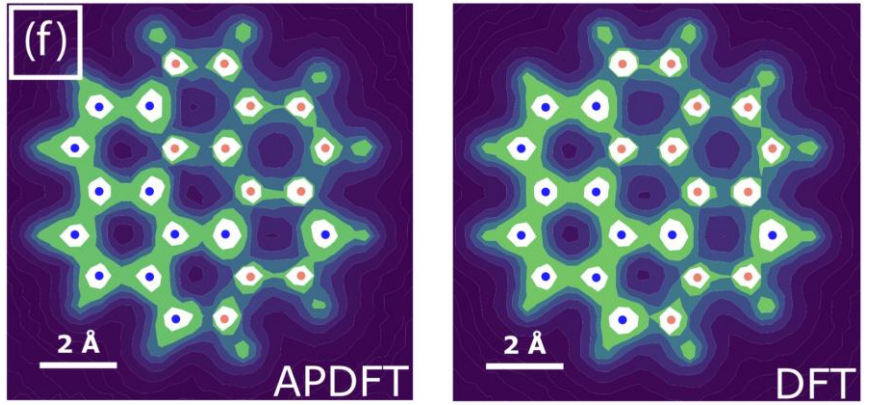
Non-covalent interactions

BN-doped coronene dimer

- Identify most/least attractive doping pattern
- Design case



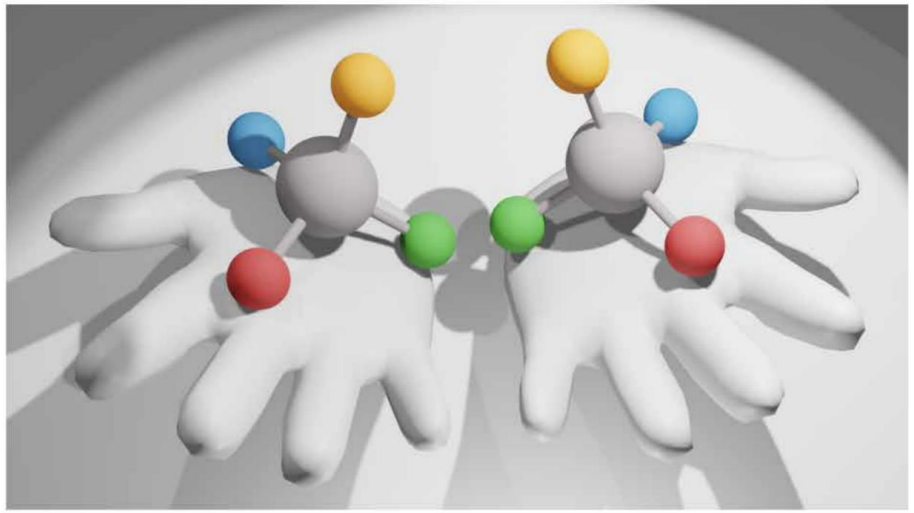
QA: 20.000x faster

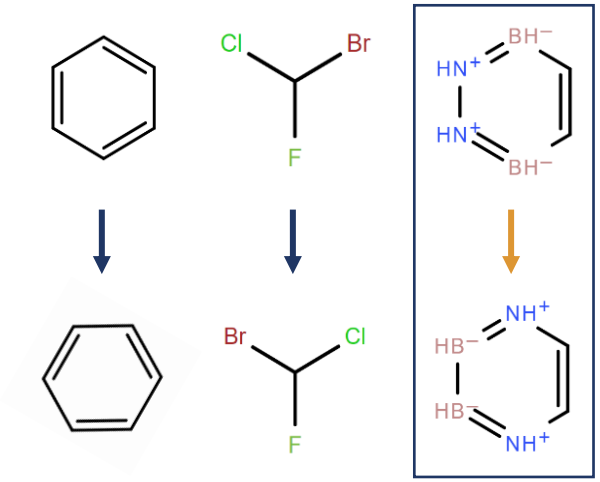


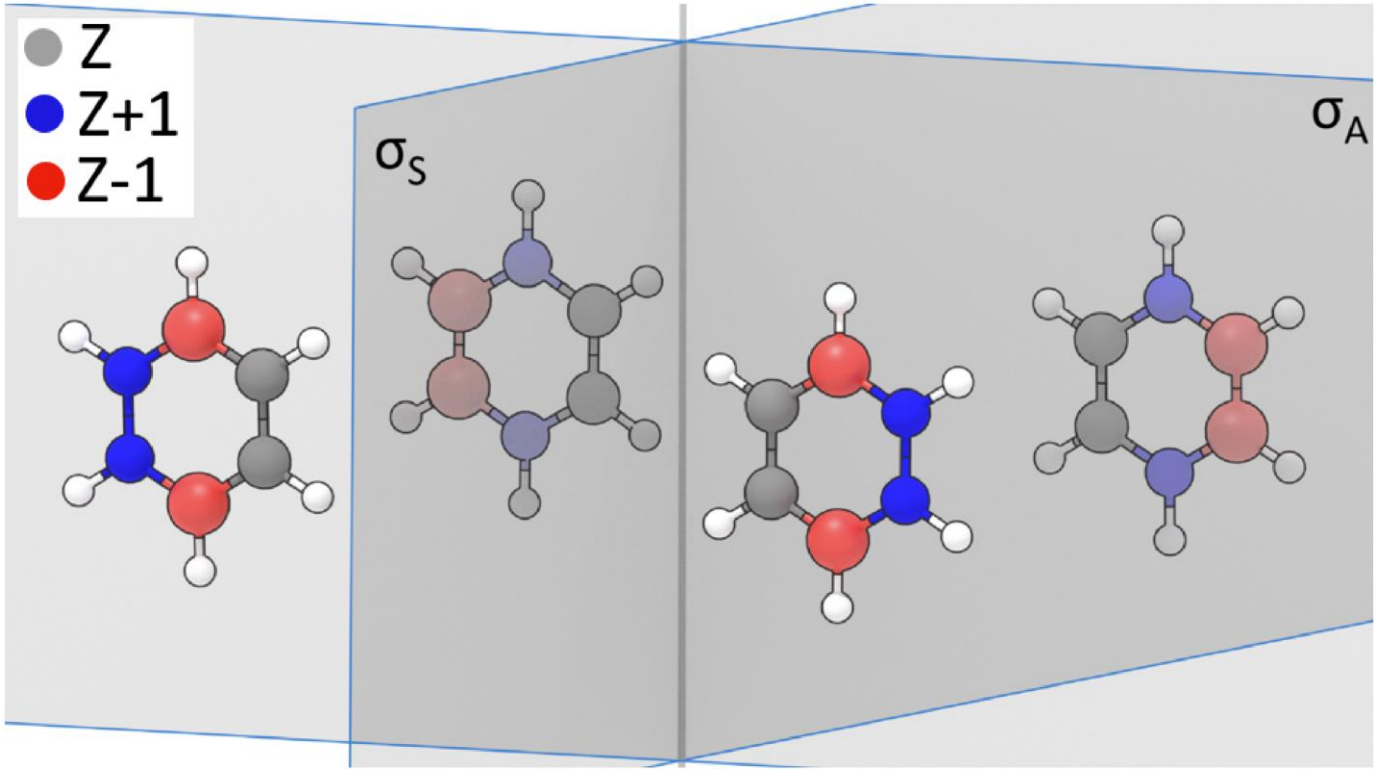
$2.8 \cdot 10^{10}$ targets

GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.*, 2020.

Alchemical Enantiomers





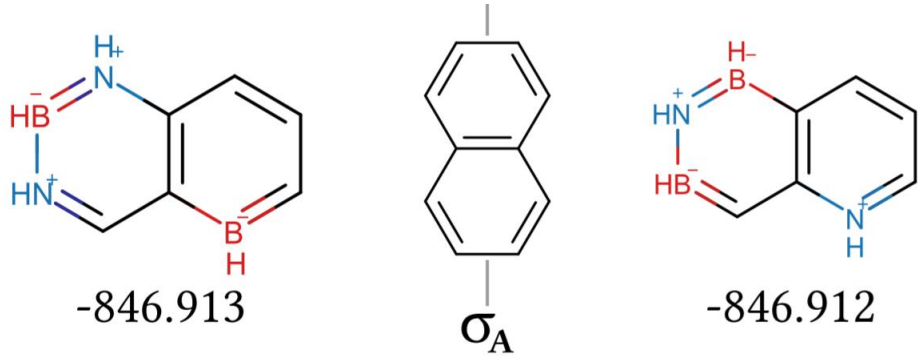


GFvR, O. A. von Lilienfeld, *Science Adv.* 2021.

Alchemical Enantiomers

Fundamentally new symmetry

Electronic energy only



Bond energy rules

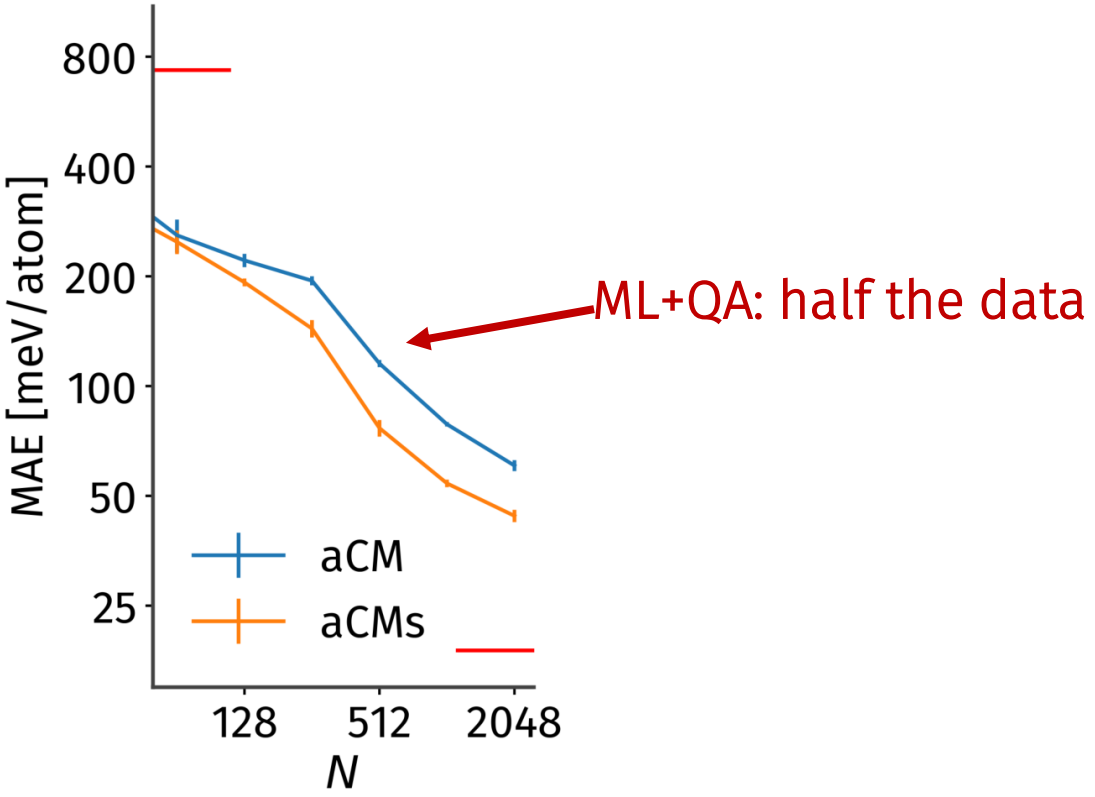
Consecutive Elements

Q R S

B C N

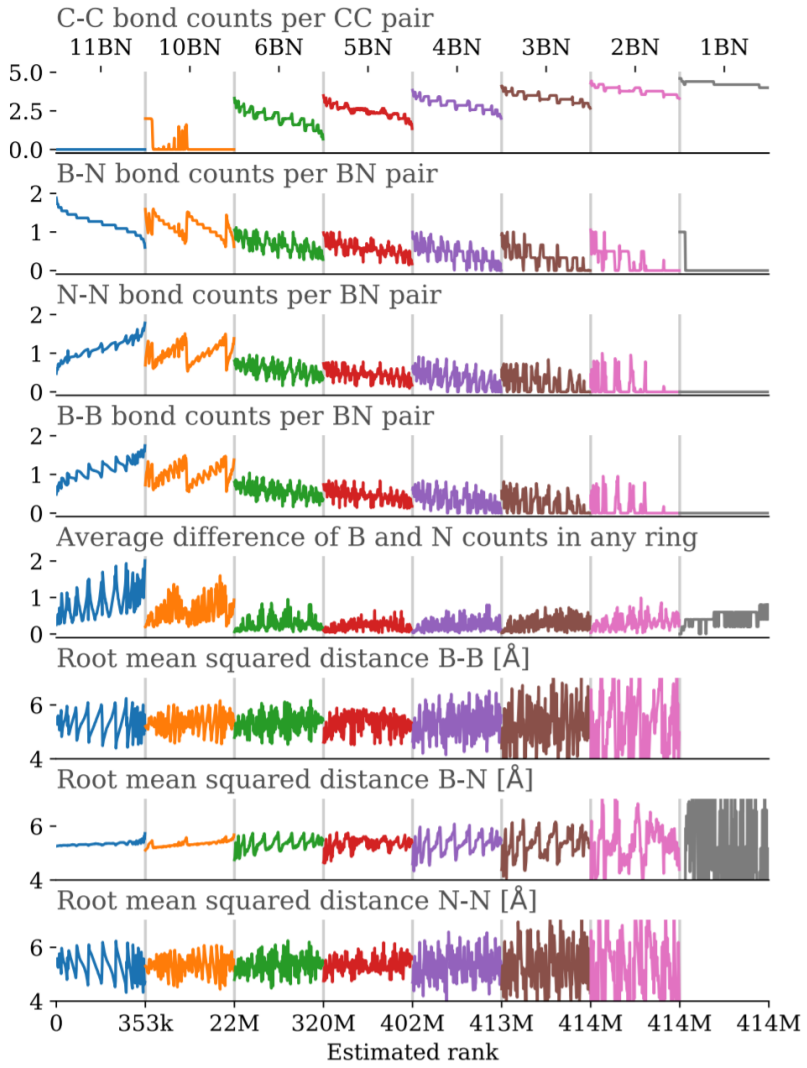
$$E_{\mathrm{QR}} \simeq E_{\mathrm{SR}} + 0.5(E_{\mathrm{QQ}} - E_{\mathrm{SS}})$$

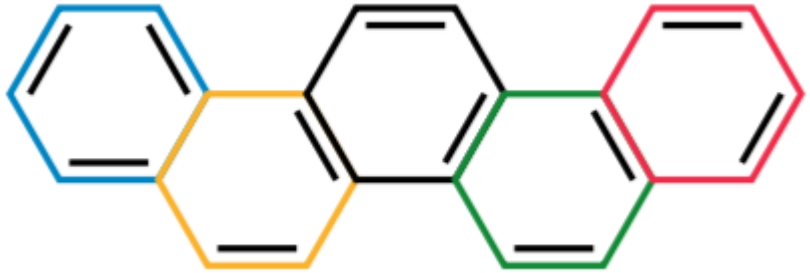
Speed up machine learning



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

Alchemical Enantiomers





x 414 M

Design rules in order of decreasing strength

- Add BN pairs
- Maximize CC bonds
- Substitute sites shared between rings
- Maximize BN bonds
- Avoid N substitutions on rings sharing a larger amount of bonds with other rings
- Balance BN substitutions in each ring

QA: Millions at once!

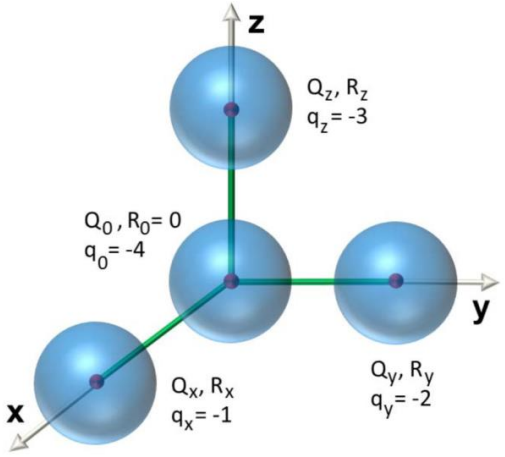
Not a single QM calculation required!

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

PECD Angular Emission

Angular emission

- Expensive to calculate
- Highly coupled degrees of freedom: multidimensional expansion



$$\frac{\mathrm{d}\sigma^{\pm}}{\mathrm{d}\Omega} = \frac{\sigma}{4\pi}\left[1 \pm \beta_1 P_1(\cos\theta) - \frac{1}{2}\beta_2 P_2(\cos\theta)\right]$$

dichroic parameter

anisotropy parameter

Data

- 85 pairs of β_i
- Center: Q_{xyz}=2.5, R_{xyz} = 3, photoelectron = 6 eV

$$\beta_i(\boldsymbol{x}) \simeq \sum_{|\alpha|\leq k} \frac{\partial^{|\alpha|}\beta_i(\mathbf{a})}{\partial x_1^{\alpha_1}\cdots\partial x_n^{\alpha_n}} \frac{(\mathbf{x}-\mathbf{a})^{\alpha}}{\alpha!}$$

GFvR, A Artemyev, B Lagutin, P Demekhin, *J. Chem. Phys.*, 2024.

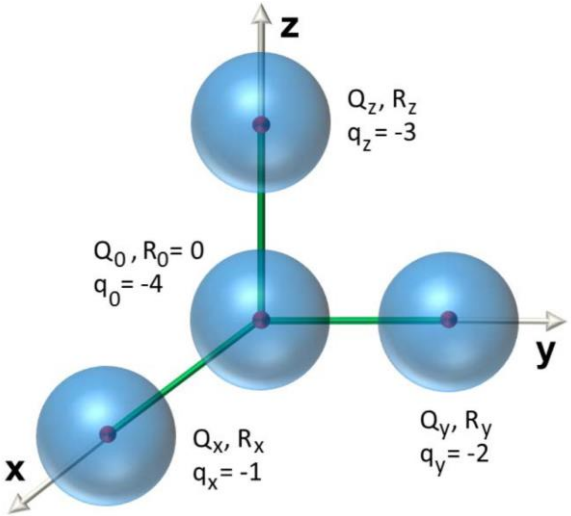
Optimization

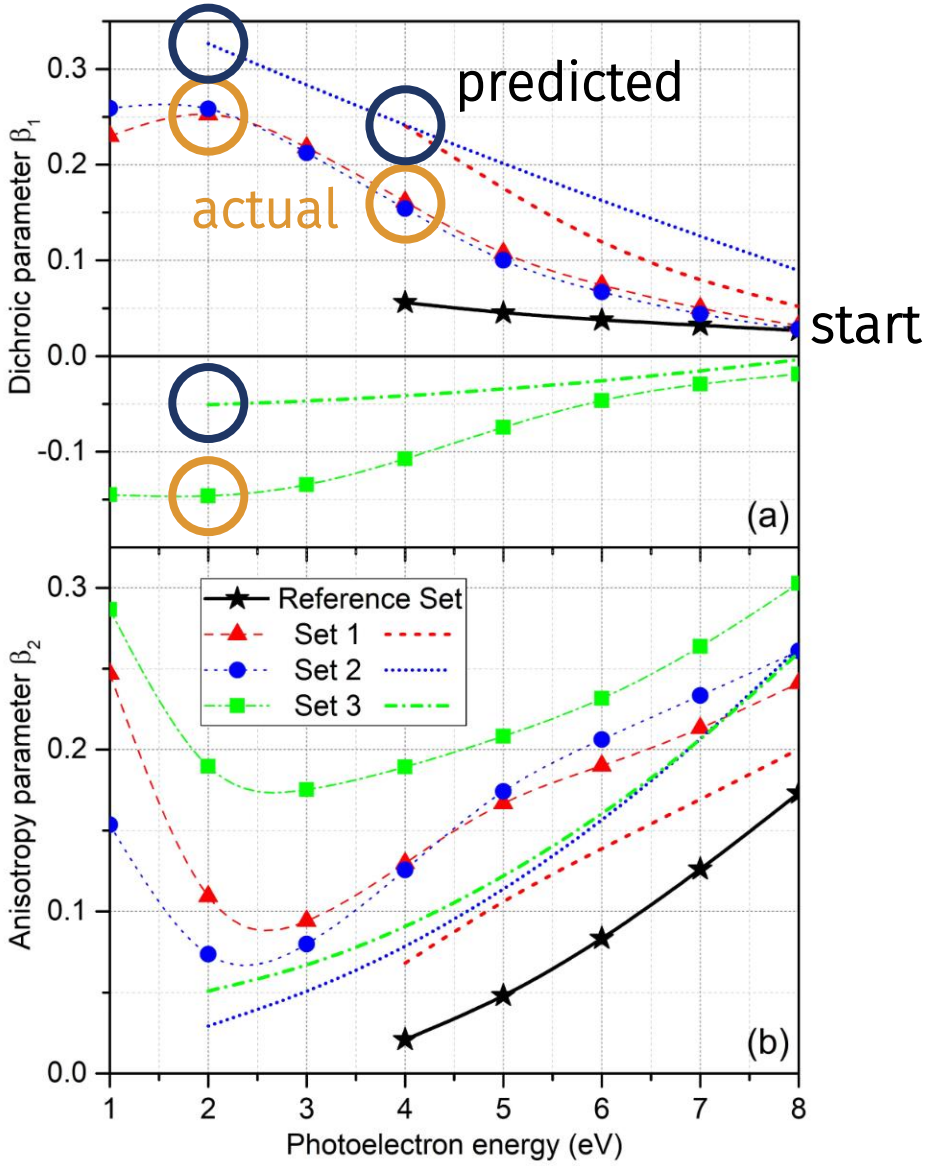
Objective

- Modify **all** Q_i, R_i, photoelectron energy
- Find extremal β_1, predict matching β_2

Results

- max β_1: 5.6% → 25.8%
- Min β_1: 5.6% → -14.7%





GFvR, A Artemyev, B Lagutin, P Demekhin, *J. Chem. Phys.*, 2024.

Interactions

Group terms

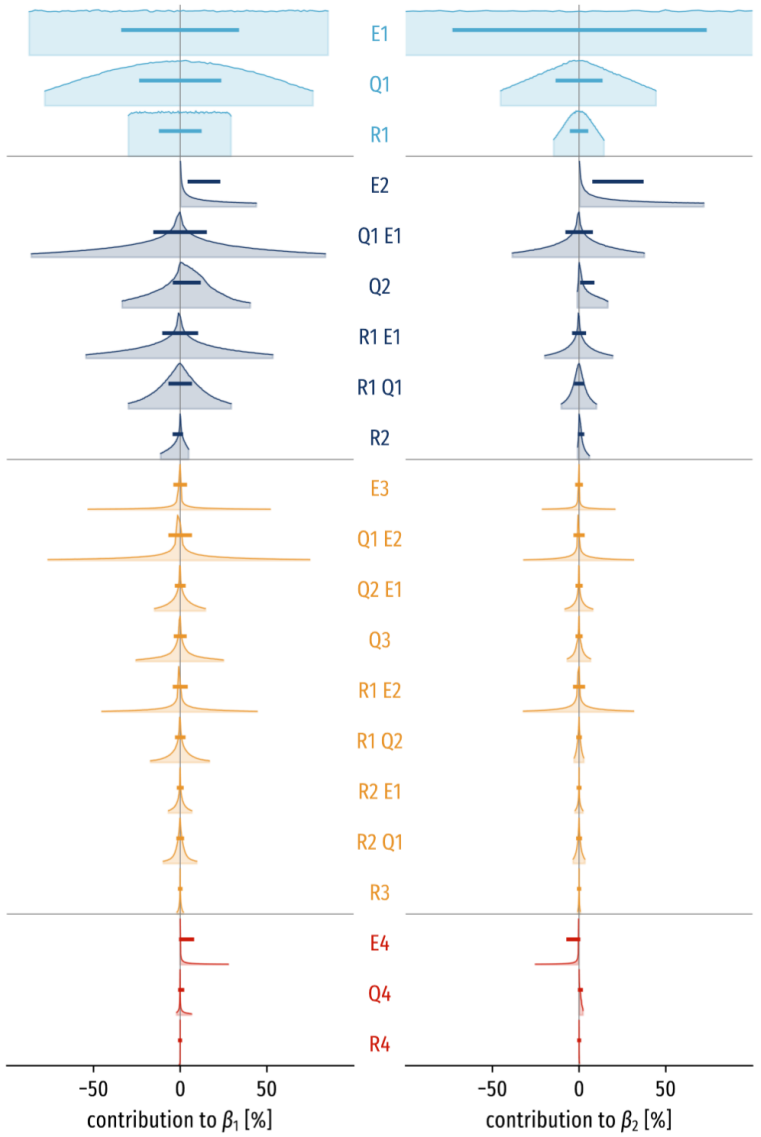
- Q_i: Q
- R_i,: R
- photoelectron energy: E
- Mixed: count groups

$$\frac{\partial \beta_i}{\partial R_x} \qquad \frac{\partial^2 \beta_i}{\partial Q_y^2} \qquad \frac{\partial^2 \beta_i}{\partial R_x Q_y}$$

∈ R1 ∈ Q2 ∈ R1 Q1

Results

- Converges quickly
- Few third order terms contribute
- Almost no spatial-spatial coupling



GFvR, A Artemyev, B Lagutin, P Demekhin, *J. Chem. Phys.*, 2024.

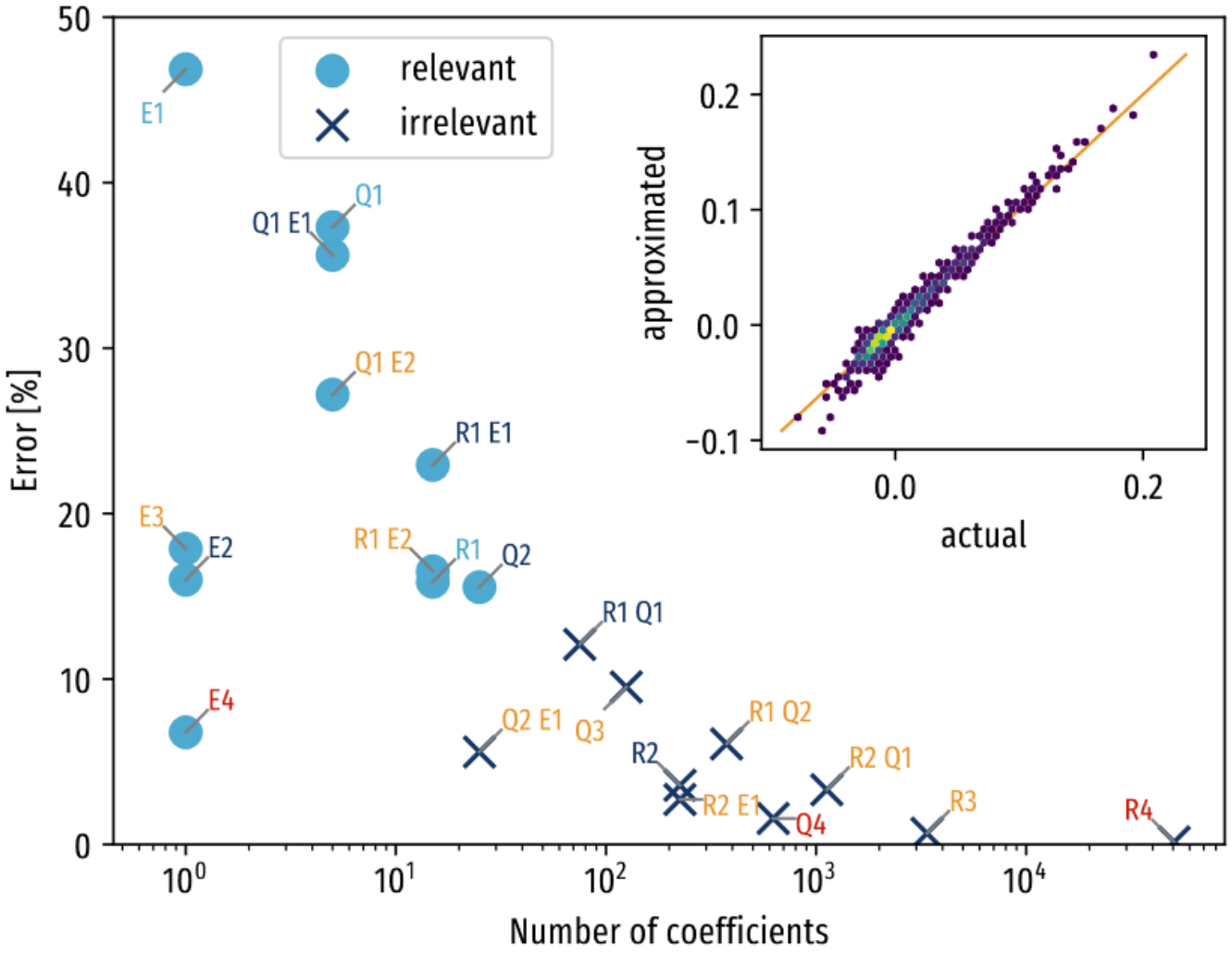
Towards Molecules

Relate to cost

- Expensive terms also irrelevant
- For molecules, subset only
- Allows for efficient stencil design

Estimated speedup

$$\frac{3^N}{N^2 + 12N - 1}$$



GFvR, A Artemyev, B Lagutin, P Demekhin, *J. Chem. Phys.*, 2024.

Limitations

Both energy and density derivatives are hard

- Finite differences — expensive, numerical instabilities
- Hellmann-Feynman — finite order, basis set inaccurate
- Coupled-perturbed — finite order, tedious
- Conceptual DFT — memory hungry, no post-HF
- Automatic differentiation — niche: DiffiQult, quax, dqc, …

ferchault/APDFT ferchault/APHF

aspuru-guzik-group/DiffiQult

CCQC/Quax

diffqc/dqc Alchemy!

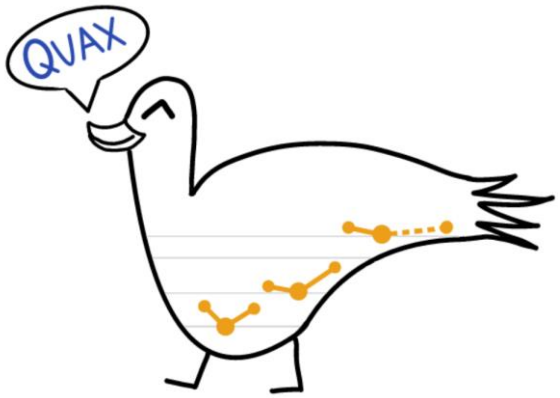
fishjojo/pyscfad

Gaussian basis sets not overly cooperative

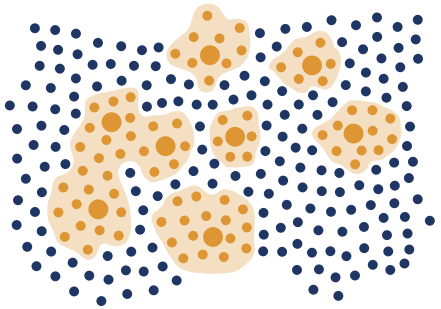
- Elements are discrete, derivatives are not
- Density converges more slowly with basis set quality than energy: Problem for APDFT and AIT
- Unless complete basis set limit: Pulay terms

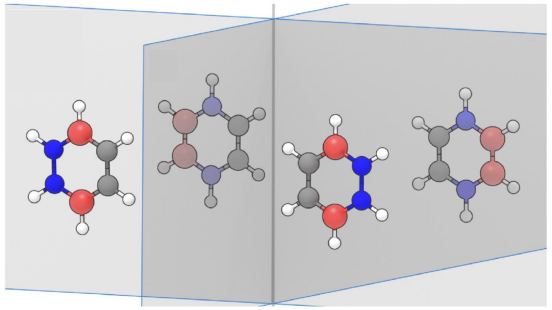
Convergence

- Finite radius
- Not all systems are made equally



Summary





Efficient | Re-use knowledge, no one-by-one

Symmetries | Reducing (“folding”) search space

Physics-driven | Predictive power

Differentiable Chemistry | Arbitrary derivatives of many properties

Closed-Form | Explainable and shows structure

Fast Design | Can assess whole regions at once

Thanks

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Simon Krug
Boris Lagutin
Anatole von Lilienfeld
Alex Maldonado
Michael Sahre

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