Alchemical Perturbation Density Functional Theory: Scaling with chemical space

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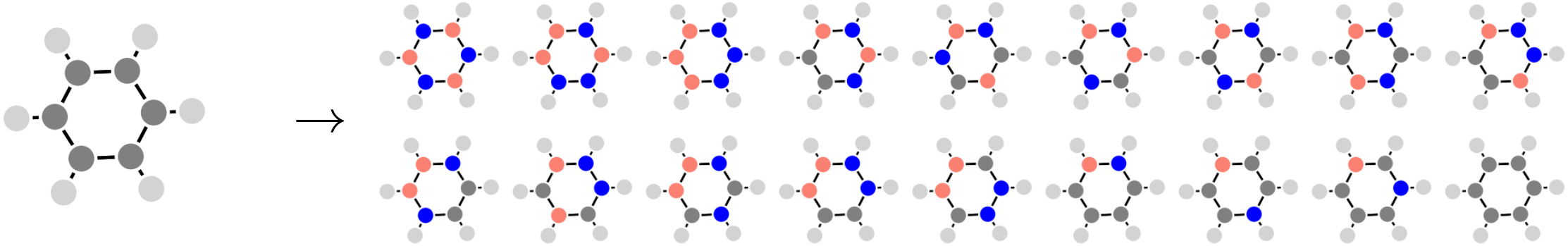
Example

Alchemical Perturbation Density Functional Theory (APDFT)
Uses calculations of *one* molecule to estimate *many* molecules



$$E, \rho, \{\partial^i_\lambda \rho\} \rightarrow \{E_i\}, \{\rho_i\}, \{F_i\}, \{\mu_i\}, \{Q_i\}, \ldots$$

1 system $\rightarrow$ Millions of systems

GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.* **2020** (*arXiv* 1809.01647).

Theory

Interpolate between molecular Hamiltonians

$$\hat{H}(\lambda) \equiv \lambda \hat{H}_\mathrm{t} + (1-\lambda)\hat{H}_\mathrm{r} \qquad \lambda \in [0,1]$$

Taylor expansion around reference molecule

$$E_\mathrm{t} = \sum_{n=0}^{\infty} \frac{1}{n!} \frac{\partial^n}{\partial \lambda^n} \left\langle \psi_\lambda \middle| \hat{H}(\lambda) \middle| \psi_\lambda \right\rangle \Big|_{\lambda=0} = E_\mathrm{r} + \sum_{n=1}^{\infty} \frac{1}{n!} \left. \frac{\partial^n E(\lambda)}{\partial \lambda^n} \right|_{\lambda=0}$$

Hellmann-Feynman theorem

$$\partial_\lambda E = \left\langle \psi_\lambda \middle| \hat{H}_\mathrm{t} - \hat{H}_\mathrm{r} \middle| \psi_\lambda \right\rangle = \Delta E^\mathrm{NN} + \int_\Omega d\mathbf{r} \underbrace{\left(v_\mathrm{t}(\mathbf{r}) - v_\mathrm{r}(\mathbf{r})\right)}_{\equiv \Delta v} \rho_\lambda(\mathbf{r})$$

O. A. von Lilienfeld, *J. Chem. Phys.* 2009.

Theory

Alchemical Perturbation Density Functional Theory (APDFT)

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

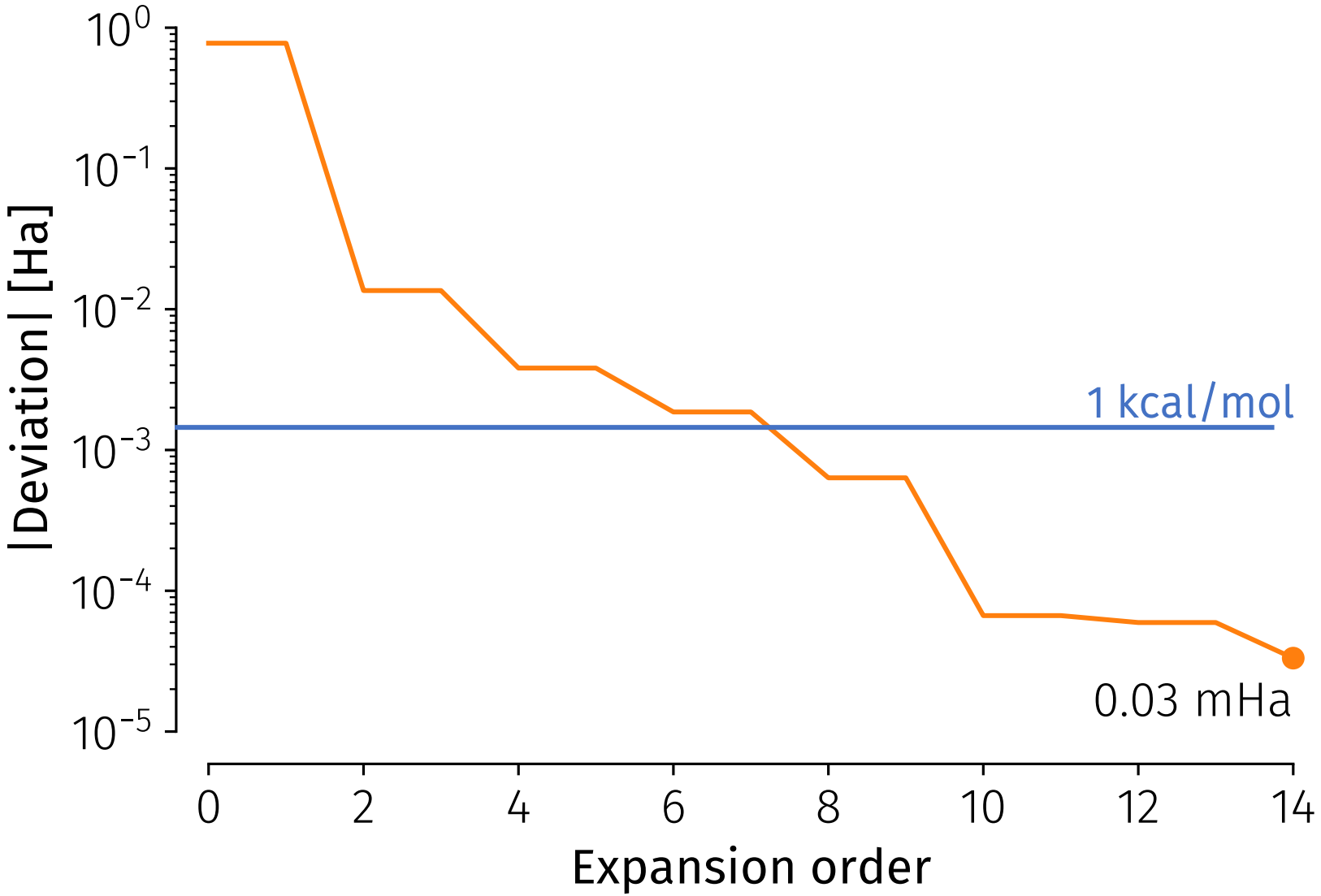
$$\rho_t = \sum_{n=0}^{\infty} \frac{1}{n!} \frac{\partial^n \rho}{\partial \lambda^n}\bigg|_{\lambda=0}$$

- Gives consistent energies, densities, forces, …
- Uses the same derivatives for all predictions
- In practice: truncate after some order *n*

ferchault/APDFT

GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.* **2020** (*arXiv* 1809.01647).

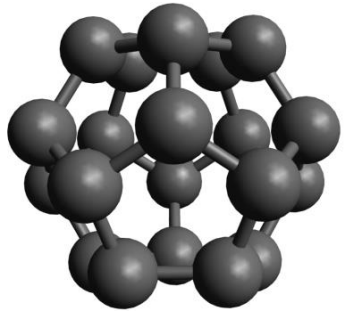
Convergence



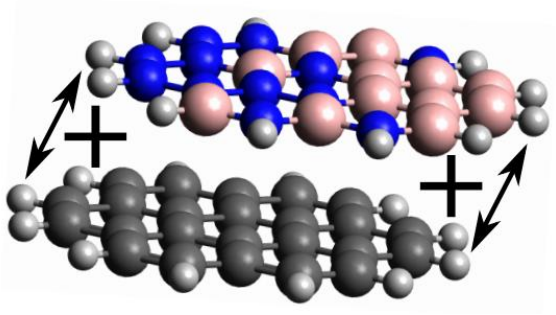
< H_2 to He
HF/def2-TZVP
DiffiQult, algopy

Applications

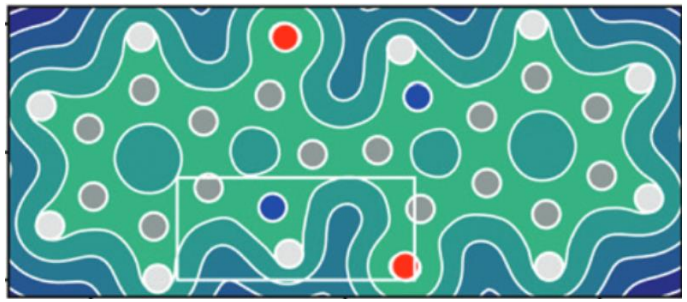
Covalent Energies



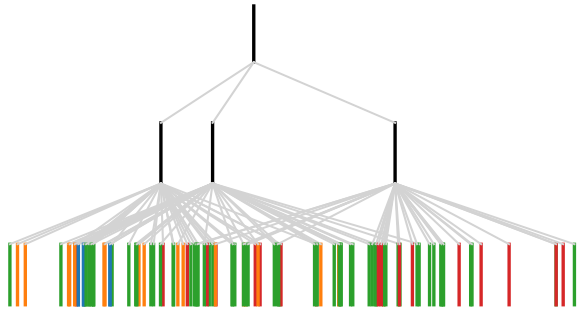
Non-covalent Interactions



Deprotonation Energies



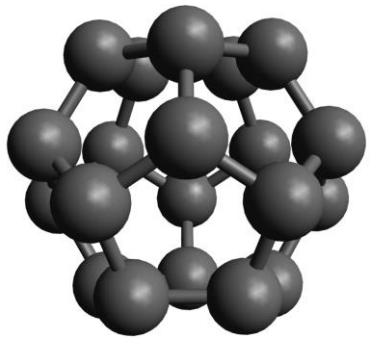
Energy Decomposition



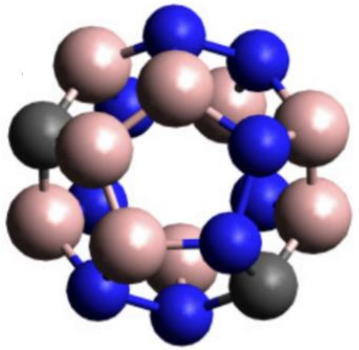
Covalent Energies

- BN-doped C_{20}
- APDFT2: one SCF, one derivative
- Key trick to scale with chemical space:

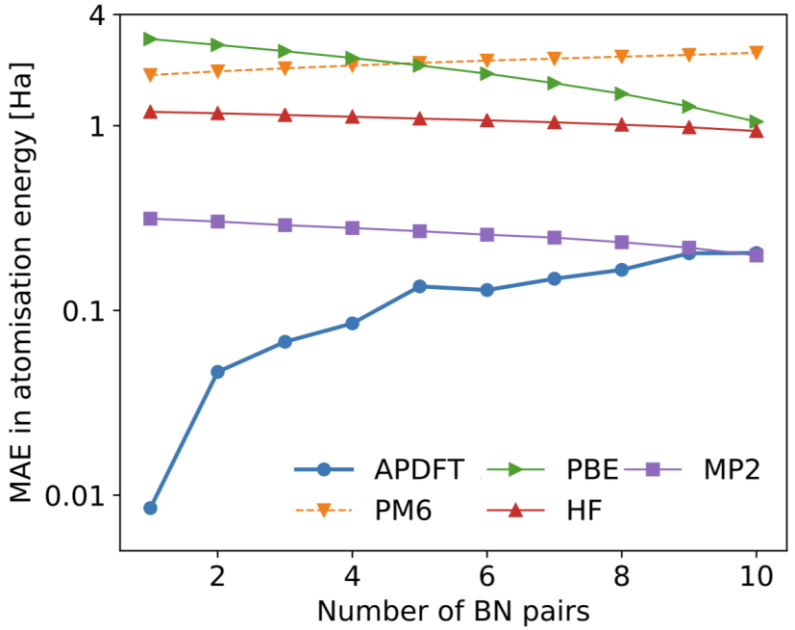
$$\frac{\partial \rho}{\partial \lambda} = \sum_I \frac{\partial \rho}{\partial Z_I} \frac{\partial Z_I}{\partial \lambda}$$

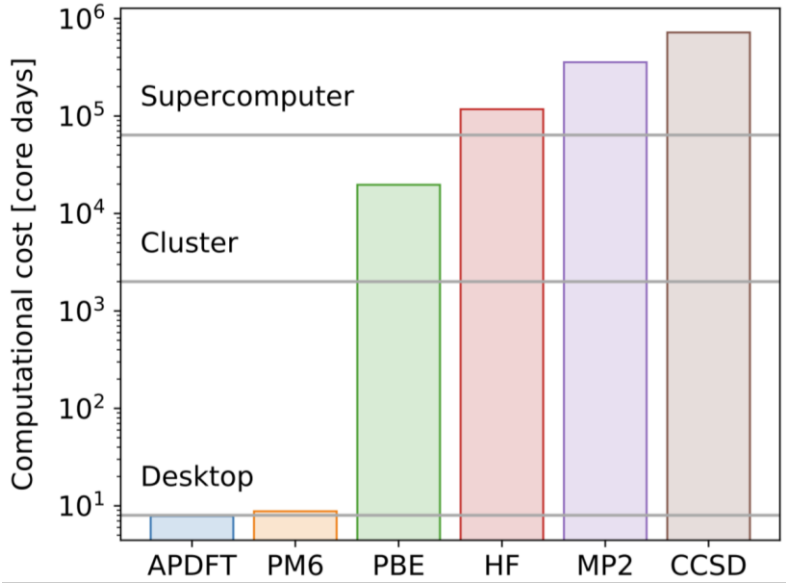


C_{20}



$3.1 \cdot 10^6$ targets



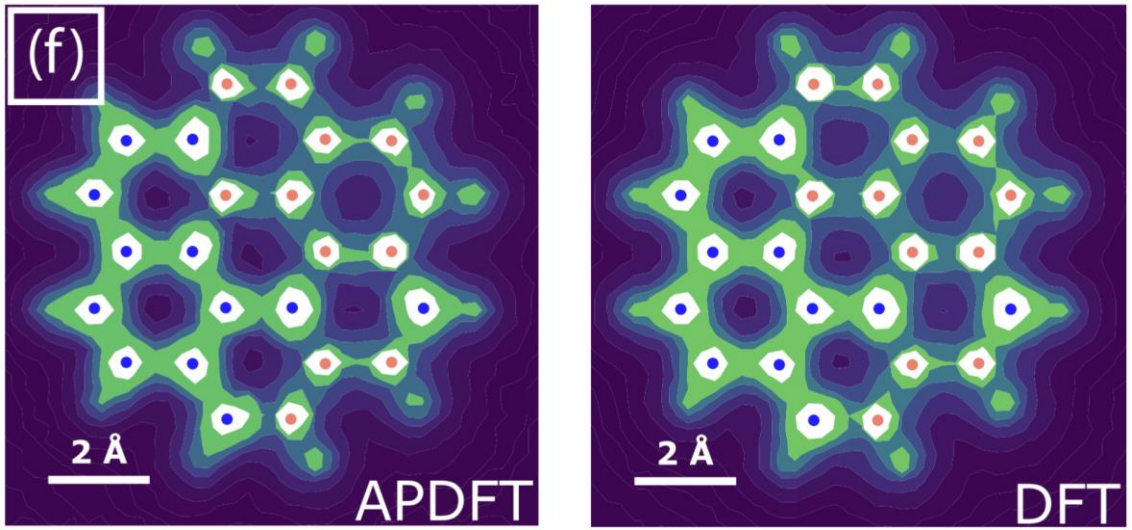


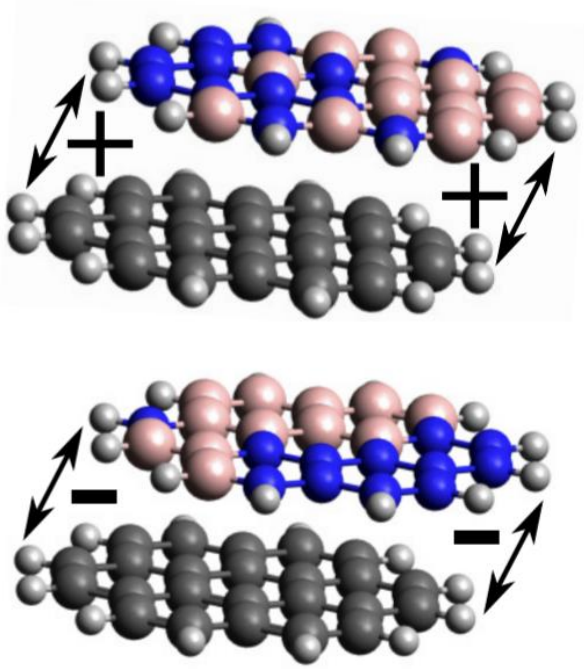
GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.* **2020** (*arXiv* 1809.01647).

Non-covalent Interactions

- BN-doped coronene dimer
- APDFT2: one SCF, 24 derivatives
- SCAN+VV10

$$\rho_t = \sum_{n=0}^{\infty} \frac{1}{n!} \left. \frac{\partial^n \rho}{\partial \lambda^n} \right|_{\lambda=0}$$





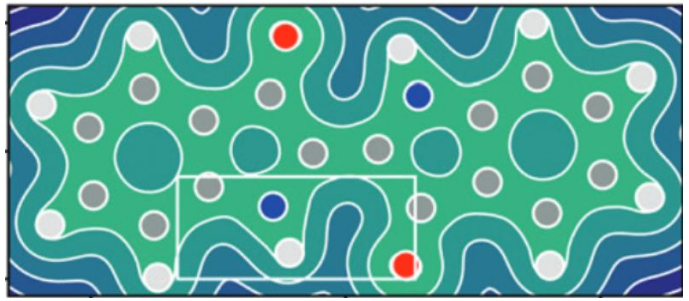
$2.8 \cdot 10^{10}$ targets

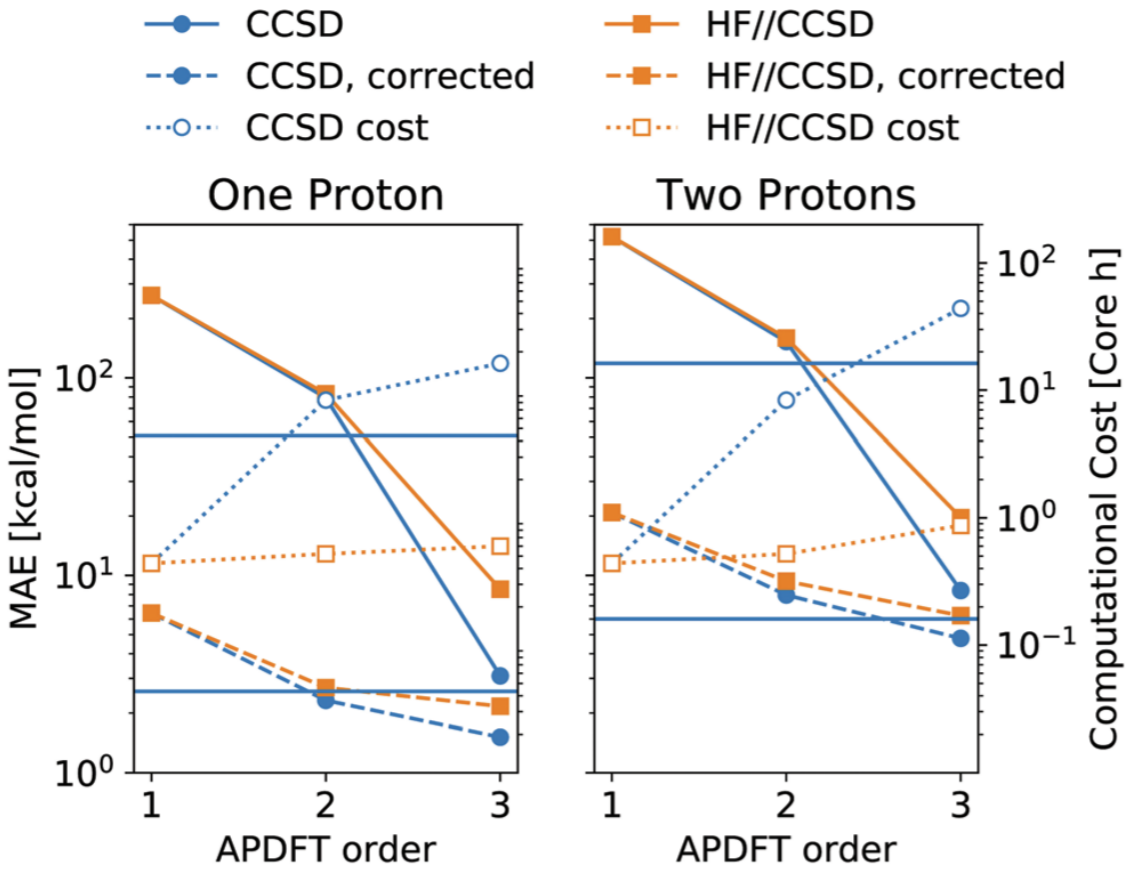
GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.* **2020** (*arXiv* 1809.01647).

Deprotonation Energies

Higher order perturbations evaluated at a lower quality level of theory

$$\Delta E \approx \Delta E_{\mathrm{NN}} + \int \mathrm{d}\mathbf{r} \Delta v \left[\rho^{\mathrm{CCSD}} + \frac{1}{2}\frac{\partial \rho^{\mathrm{HF}}}{\partial \lambda} + \frac{1}{6}\frac{\partial^2 \rho^{\mathrm{HF}}}{\partial \lambda^2} \right]\Bigg|_{\lambda=0}$$

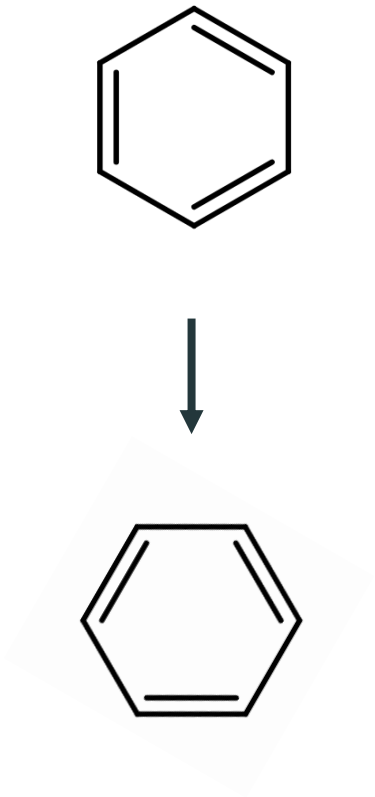




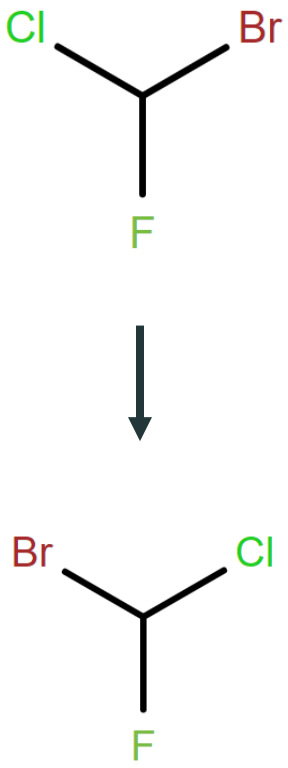
GFvR, O. A. von Lilienfeld, *Phys. Chem. Chem. Phys.* **2020** (*arXiv* 1911.13080).

Symmetries to exploit

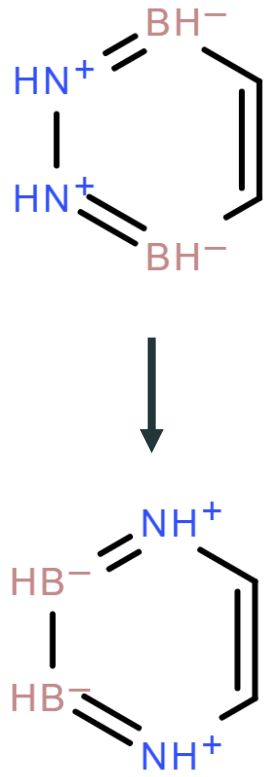
Translation
Exact



Rotation
Exact



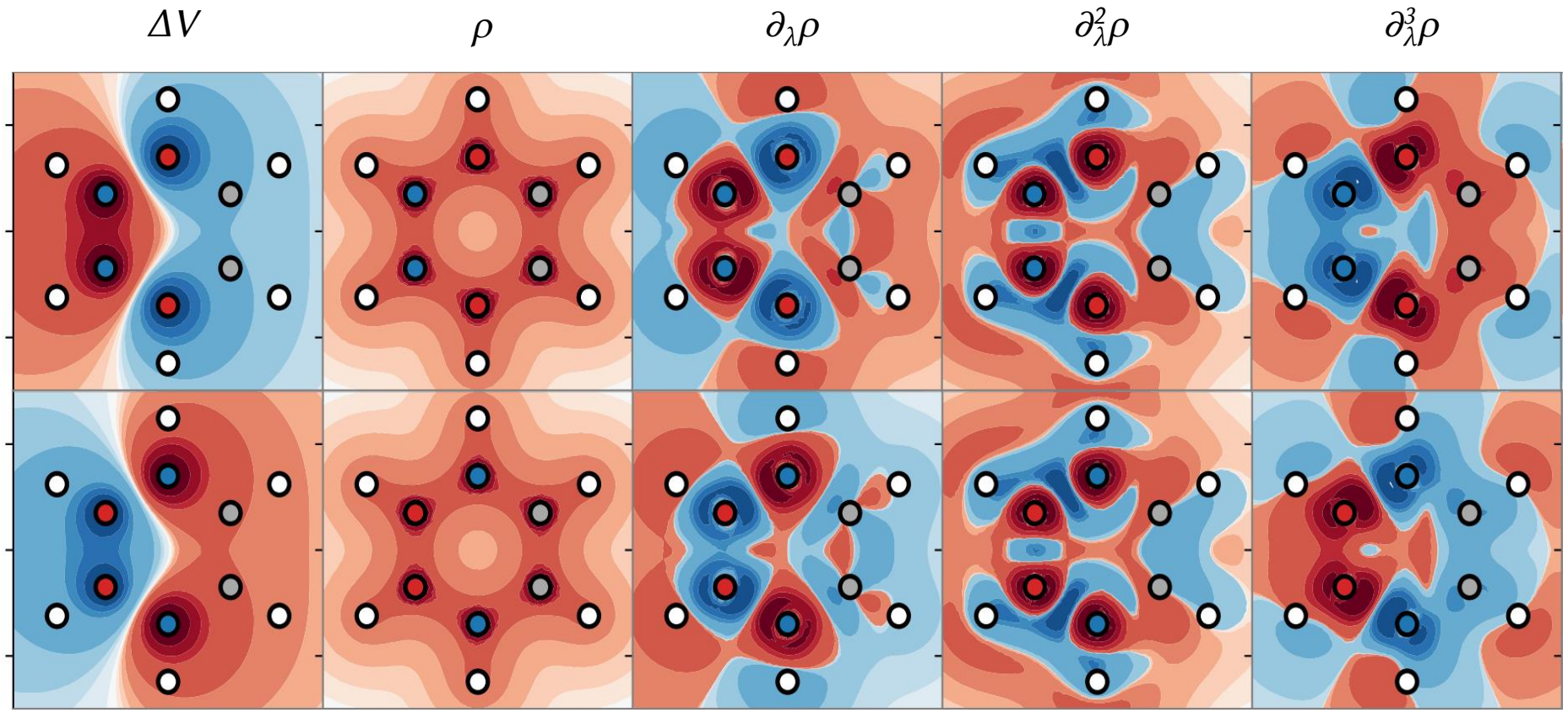
Spatial reflection
Approximate



Alchemical reflection
More approximate

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Theory



< BN-doped benzene
CCSD/def2-TZVP
Gaussian09

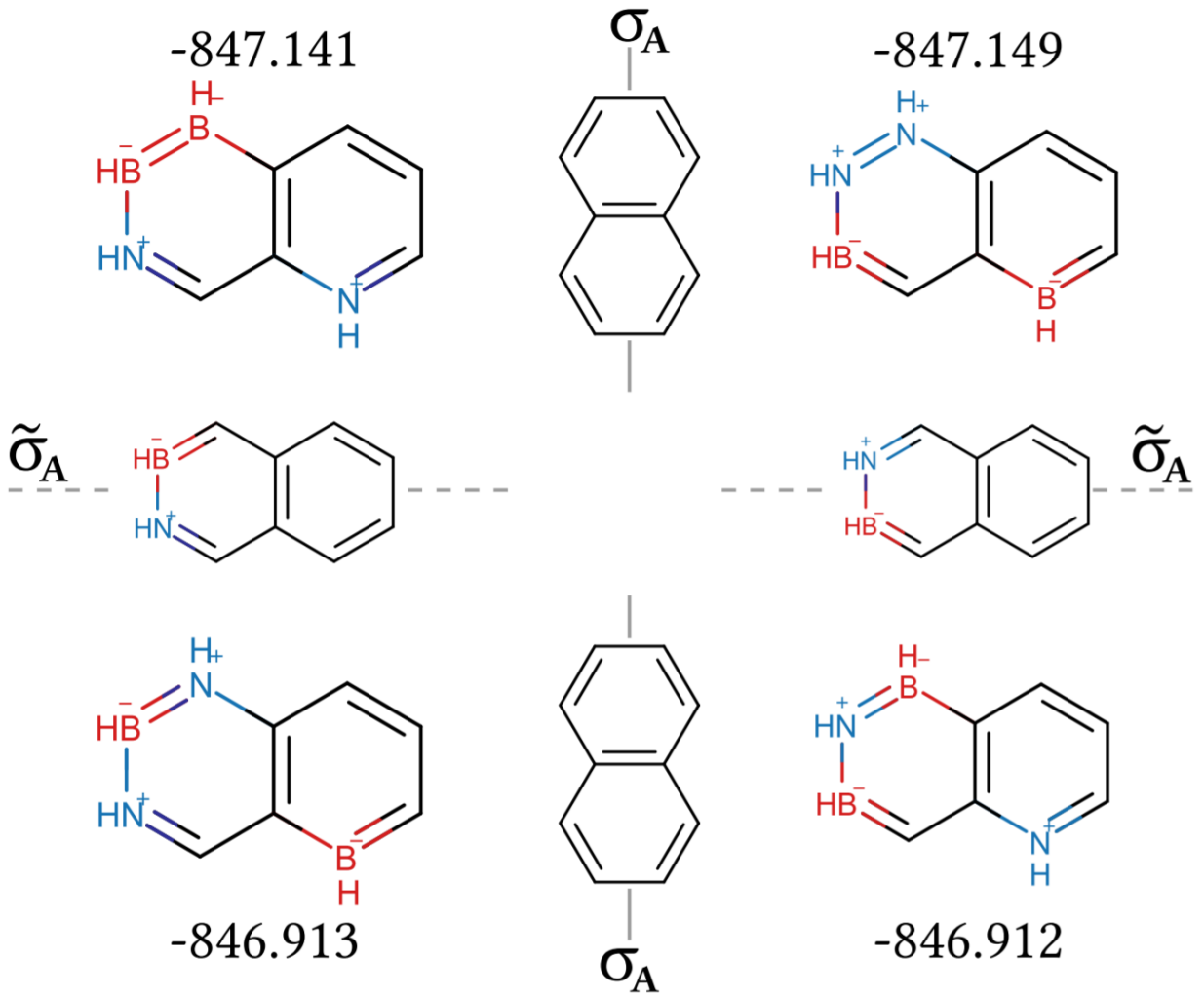
$$E_\mathrm{t} = E_\mathrm{r} + \Delta E^\mathrm{NN} + \int_\Omega d\mathbf{r} \sum_{n=0}^{\infty} \frac{1}{(n+1)!} \Delta v \frac{\partial^n \rho_\lambda(\mathbf{r})}{\partial \lambda^n}\bigg|_{\lambda=0}$$

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Alchemical symmetry

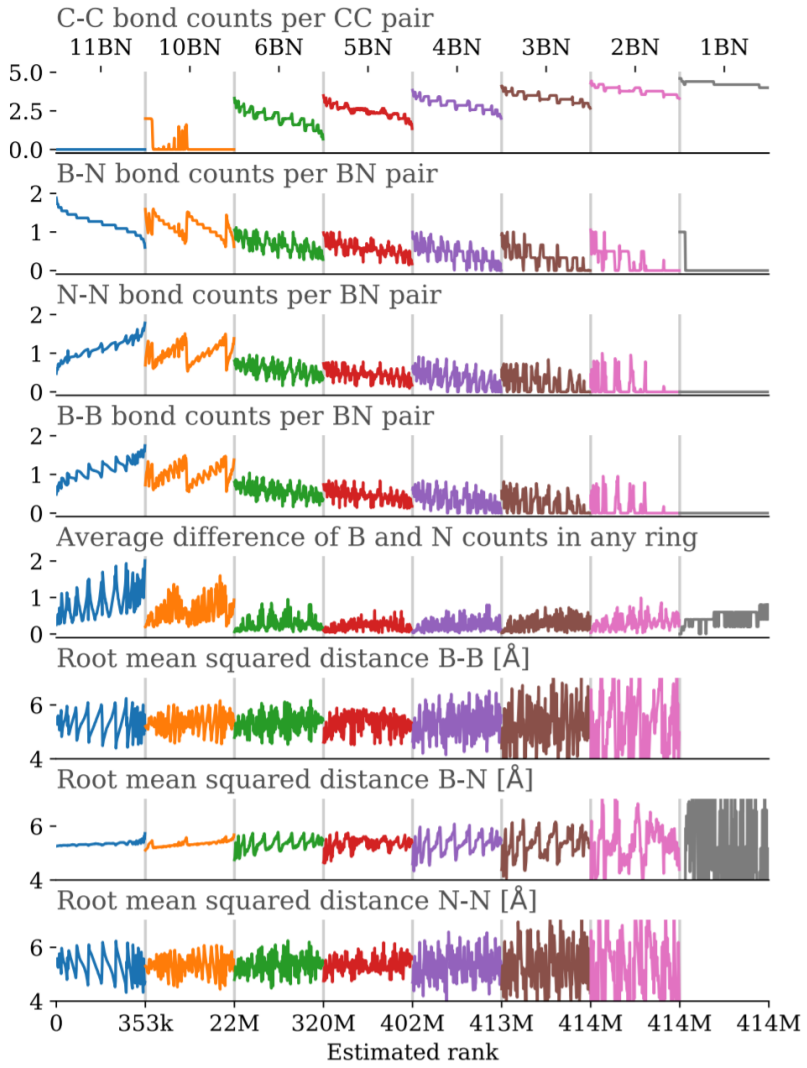
(Approximate) alchemical enantiomers are
- two spatially non-superimposable,
- alchemically coupled,
- and iso-electronic compounds with the same formal charge,
- where each transmutating atom is assigned to exactly one subset within each of which averaging of nuclear charges results in (*nearly) identical* chemical environments.

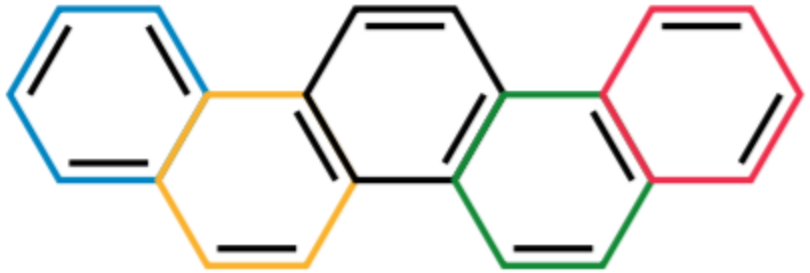
BN-doped naphthalene >
CCSD/cc-pVDZ
Molpro



GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Ranking





x 414 M

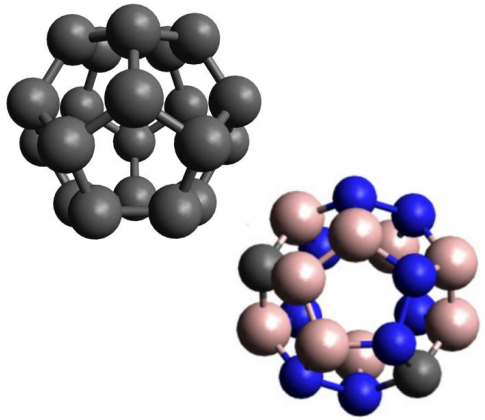
Design rules in order of **decreasing strength**

- 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

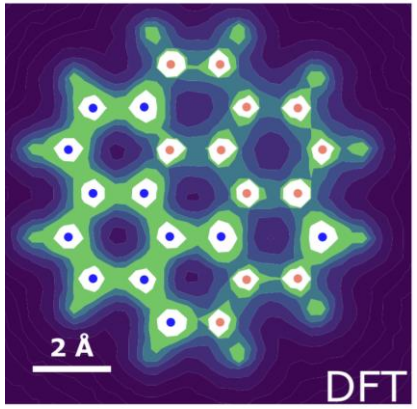
Not a single QM calculation required!

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

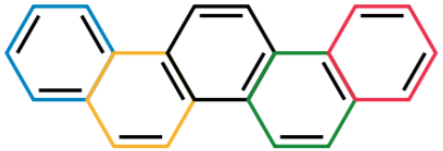
Summary



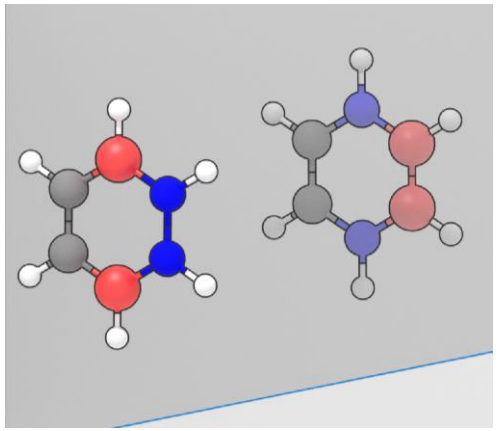
Perturbation can be more accurate than direct enumeration.



Perturbed densities and energies.



Combinatorial scaling with size of system.



Alchemical enantiomers constitute a new symmetry.

APDFT | GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.* **2020** (*arXiv* 1809.01647)

Alchemical enantiomers | GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Mixed derivatives | GFvR, O. A. von Lilienfeld, *Phys. Chem. Chem. Phys.* **2020** (*arXiv* 1911.13080)

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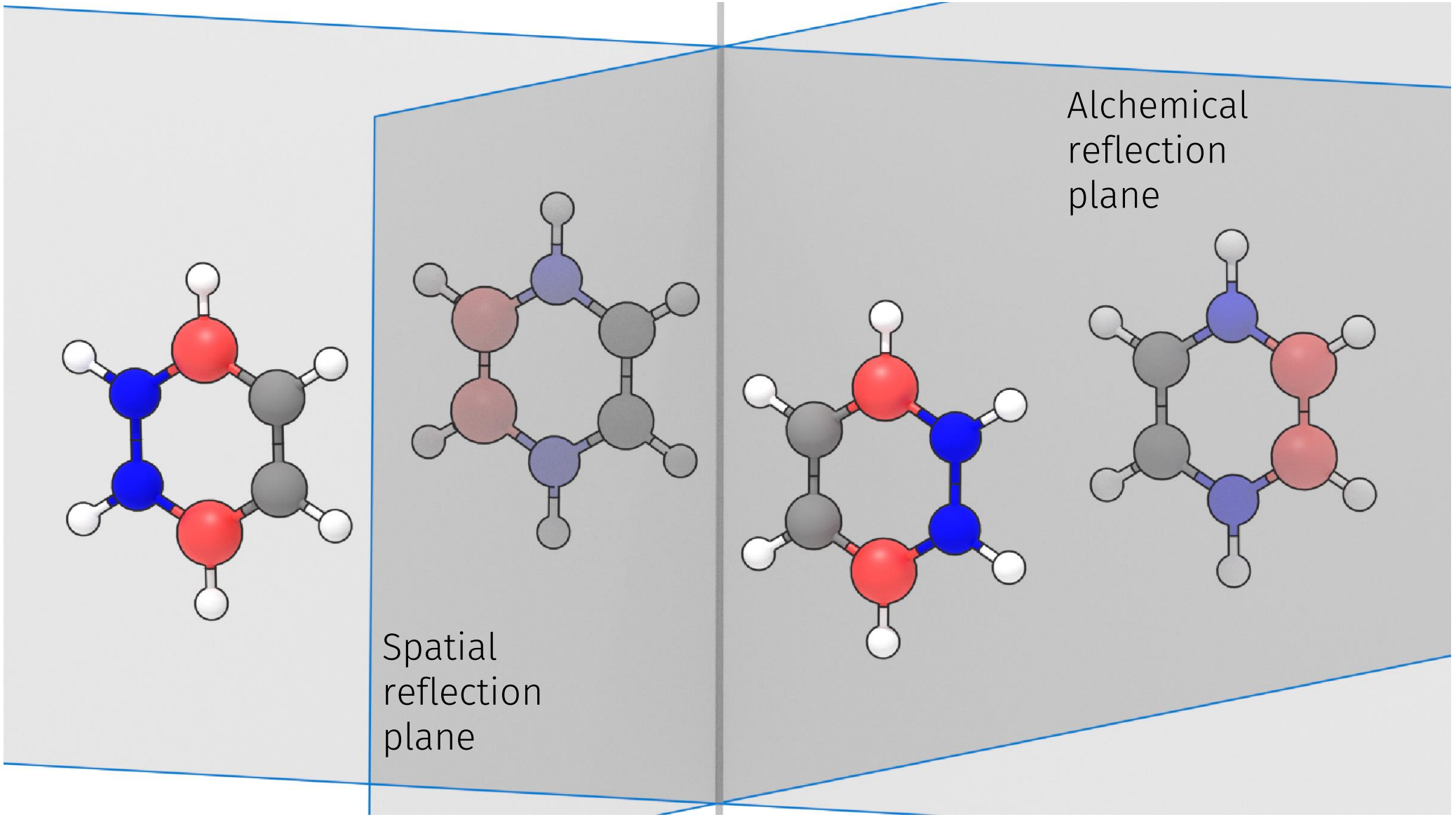
Introduction



Theory

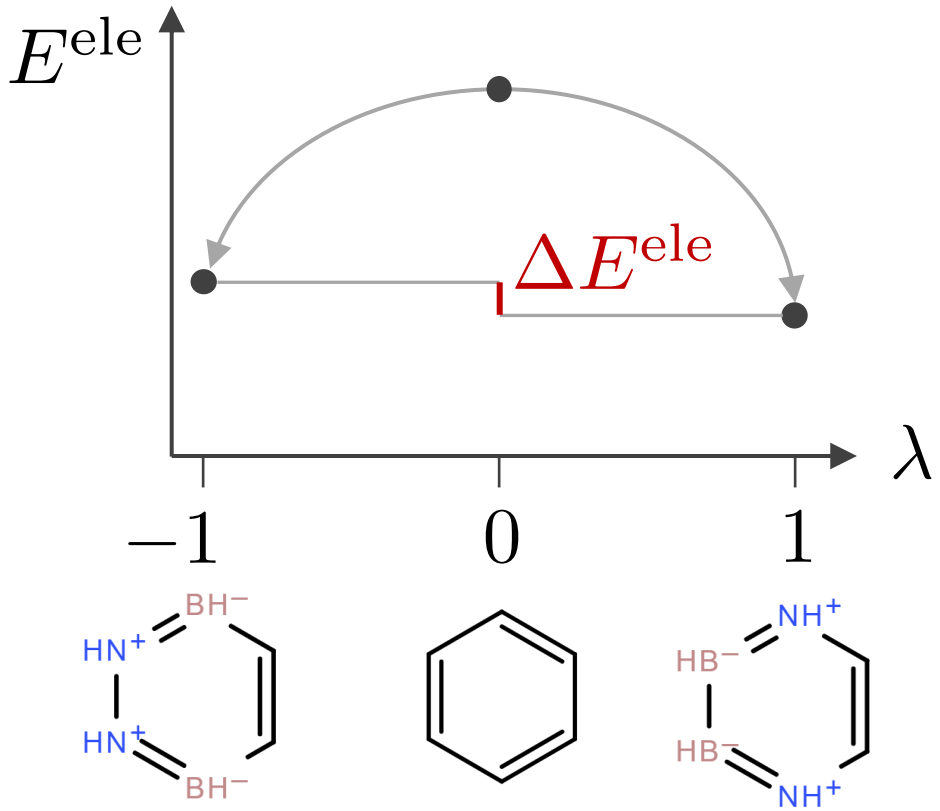
$$\Delta E_{ij}^{\mathrm{ele}} = E_0 - E_0 + \int_\Omega d\mathbf{r} \sum_{n=0}^{\infty} \frac{\Delta v_i}{(n+1)!} \left[\frac{\partial^n \rho}{\partial \lambda_i^n} + \frac{\partial^n \rho}{\partial \lambda_j^n} \right]$$

$$\Delta E_{(0)}^{\mathrm{ele}} = E_0 - E_0 = 0$$

$$\Delta E_{(1)}^{\mathrm{ele}} = 2 \int_\Omega \Delta v \rho = \int_\Omega e \cdot o = 0$$

$$\Delta E_{(2)}^{\mathrm{ele}} = \int_\Omega \Delta v \left[\frac{\partial \rho}{\partial \lambda_i} + \frac{\partial \rho}{\partial \lambda_j} \right]$$

$$= \int_\Omega \Delta v \left[\sum_I \frac{\partial \rho}{\partial Z_I} \frac{\partial Z_I}{\partial \lambda_i} + \frac{\partial \rho}{\partial Z_I} \frac{\partial Z_I}{\partial \lambda_j} \right] = 0$$

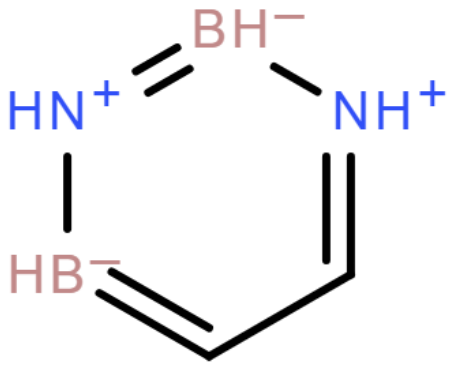


GFvR, O. A. von Lilienfeld, *Science Adv.* 2021 (arXiv 2008.02784).

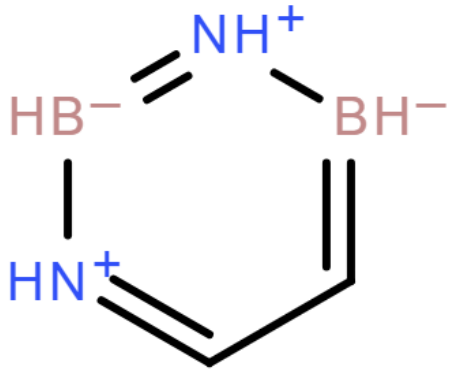
Definition

Alchemical enantiomers are

- two spatially non-superimposable,
- alchemically coupled,
- and iso-electronic compounds with the same formal charge,
- where each transmutating atom is assigned to exactly one subset within each of which averaging of nuclear charges results in identical chemical environments.



These are no alchemical enantiomers!



GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

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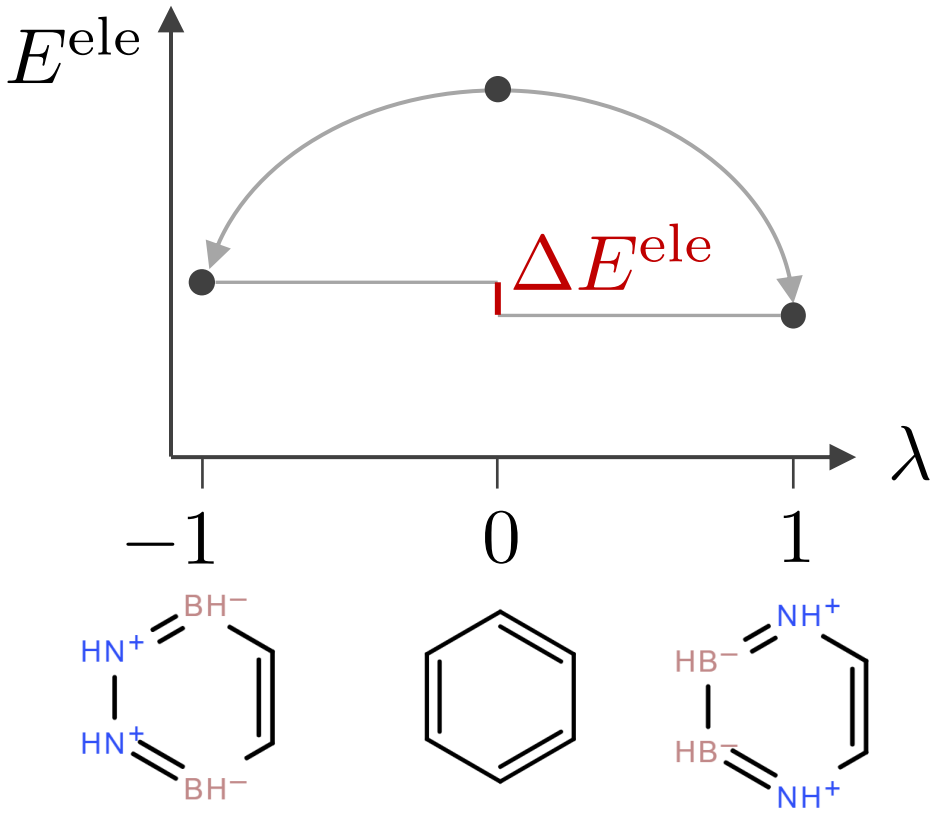

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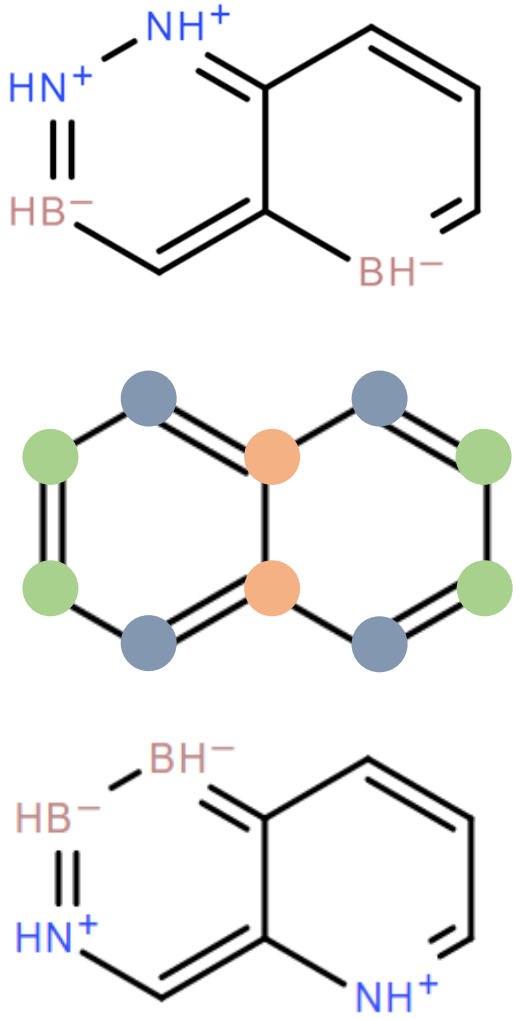
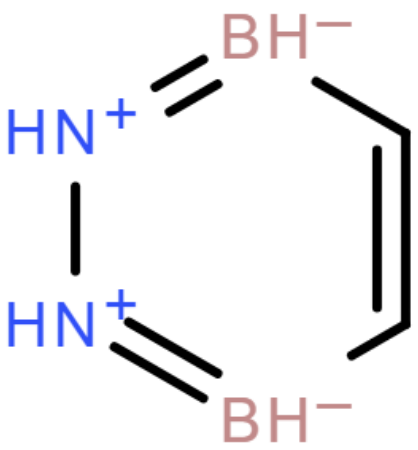
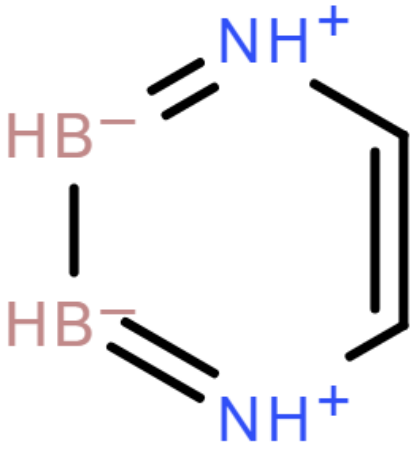


GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Consequences



CC
2BC
2BN
NN



CC
2NC
2BN
BB

Consecutive Elements

Q R S

B C N

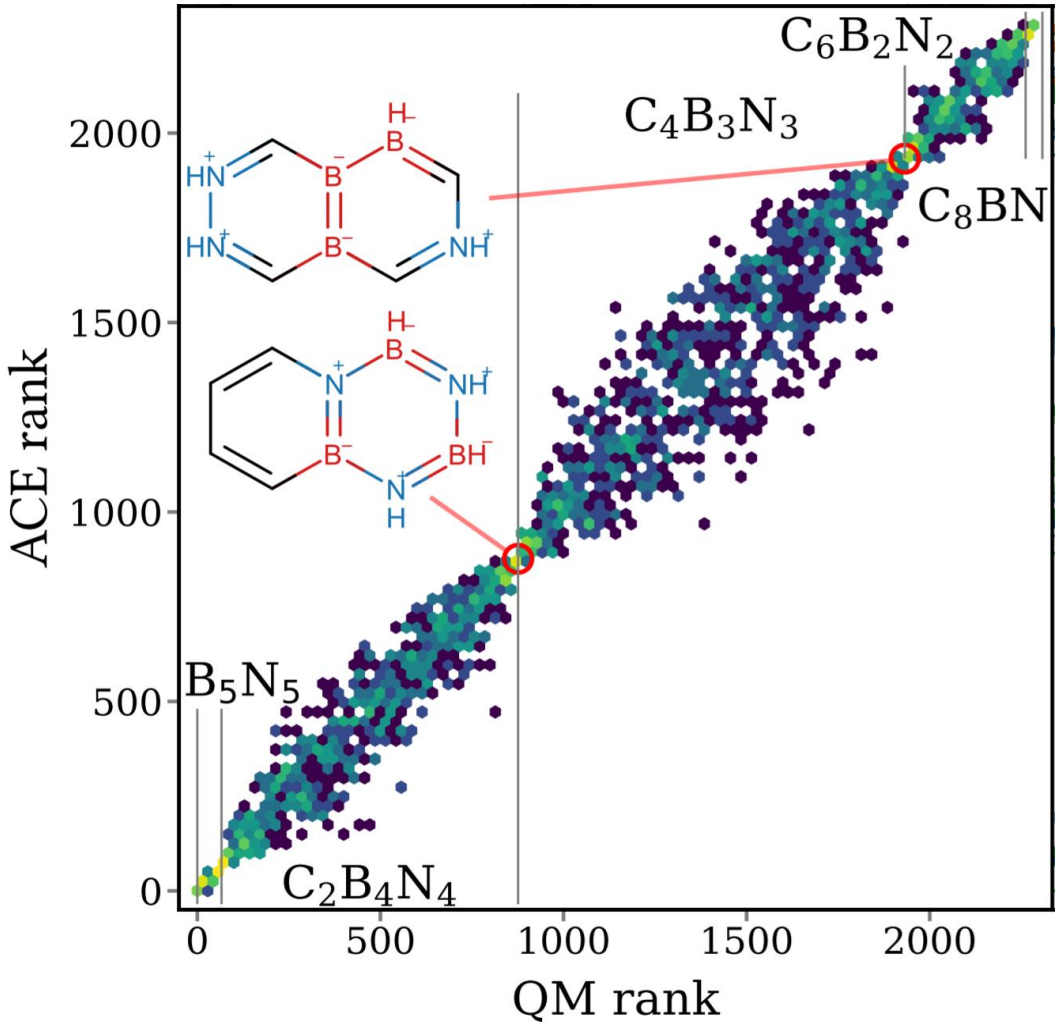
$$E_{\mathrm{QR}} \simeq E_{\mathrm{SR}} + 0.5(E_{\mathrm{QQ}} - E_{\mathrm{SS}})$$

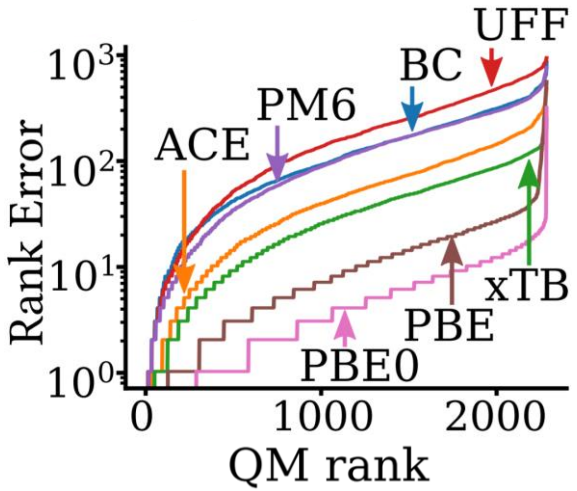
Other skeletons and all substitution patterns

- More such rules
- No violations

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Ranking



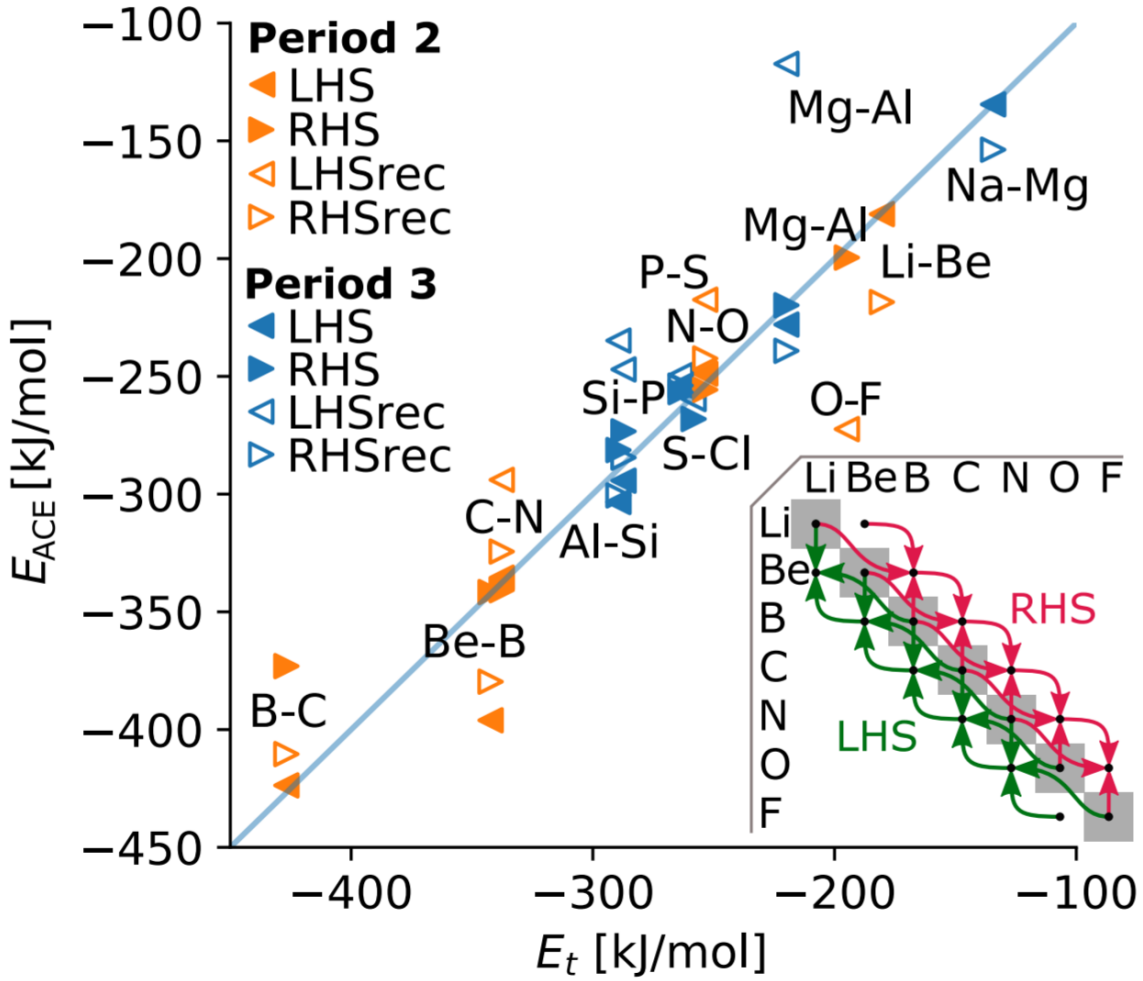


- BN-doped naphthalene
  CCSD/cc-pVDZ
  Molpro/MRCC/xTB-GFN2/mopac/OpenBabel

- BN-doped naphthalene
  CCSD/cc-pVDZ
  Molpro/MRCC

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Consequences



Mean absolute error

Direct:	~10 kJ/mol
Chained:	~22 kJ/mol

- **Bond dissociation**
  G3//B3LYP
  Literature

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

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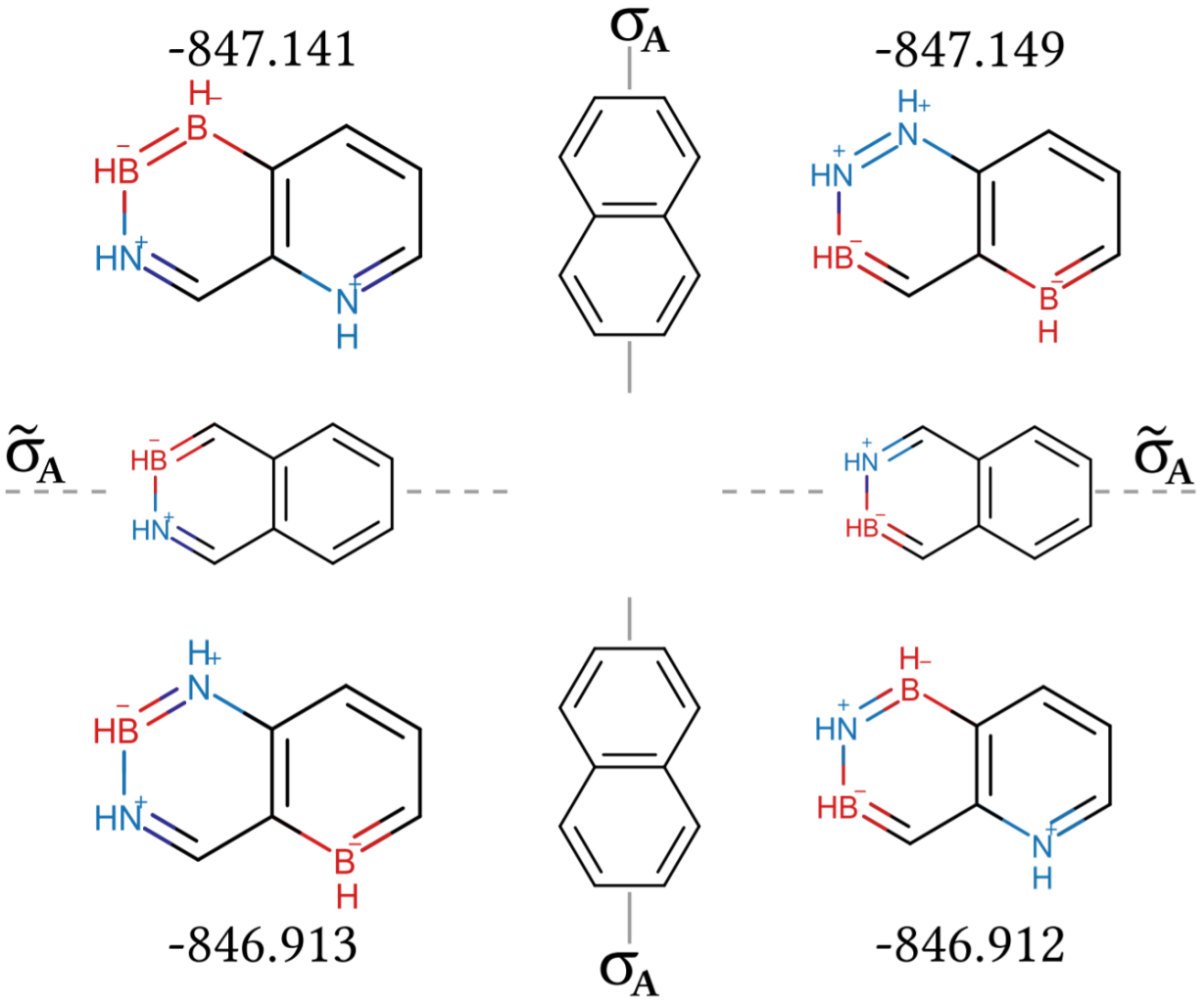
CCSD/cc-pVDZ
Molpro



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