Controlling generalization errors for ML-informed molecular discovery

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257th ACS National Meeting, Orlando

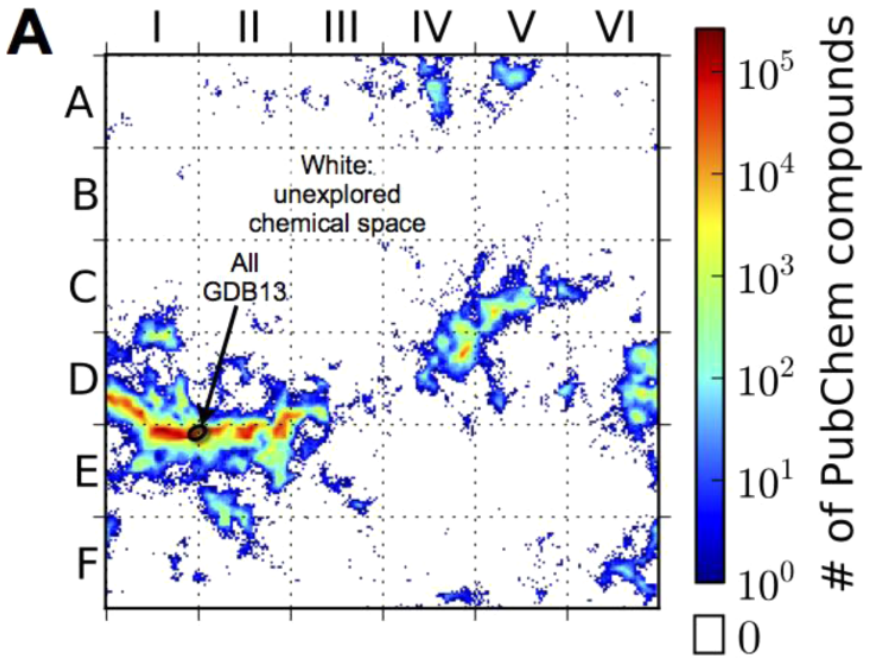
03.31.19

Motivation: chemical discovery

How can we design new materials using computers?

The space of possible chemistries is incredibly vast, with $\mathcal{O}(10^{50})$ small organic molecules.

All potentially undiscovered medicines, catalysts and materials are somewhere, out in this huge space.



Virshup *et al.*, *J. Am. Chem. Soc.*, 135(19): 7296–7303, 2013.

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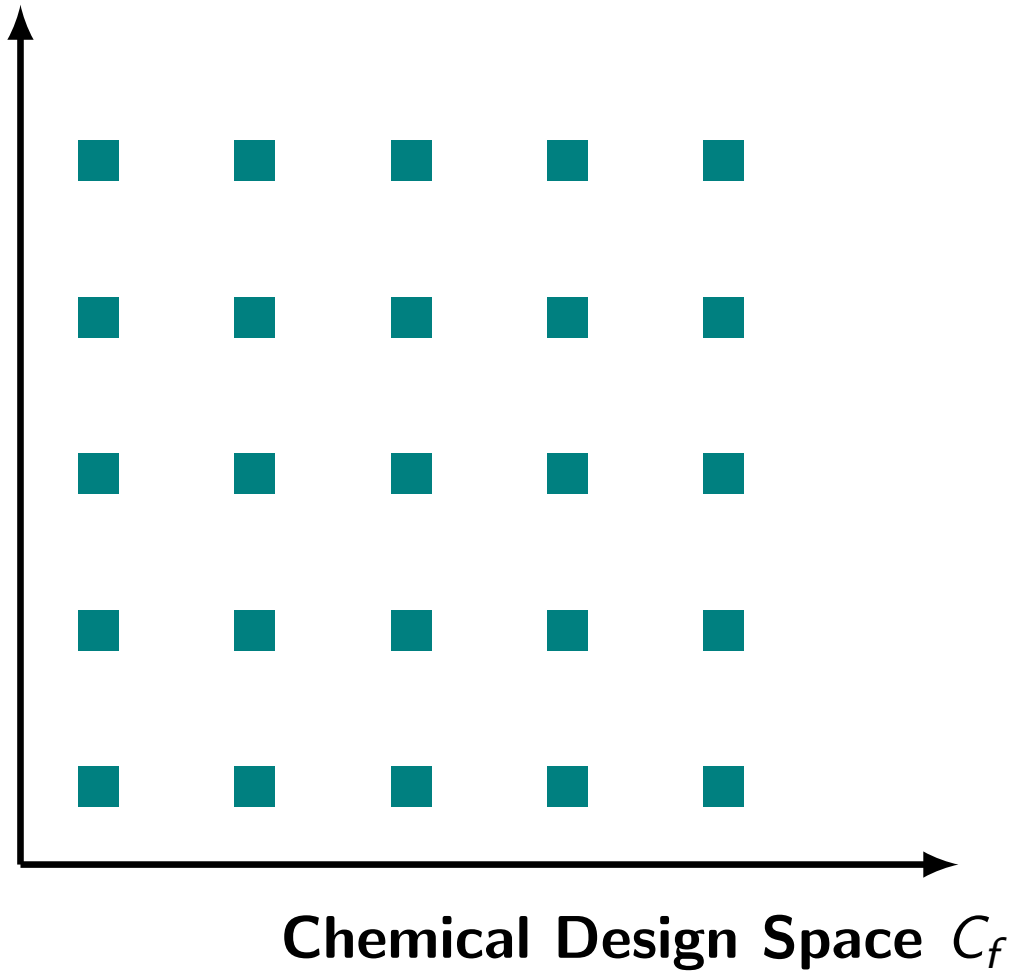

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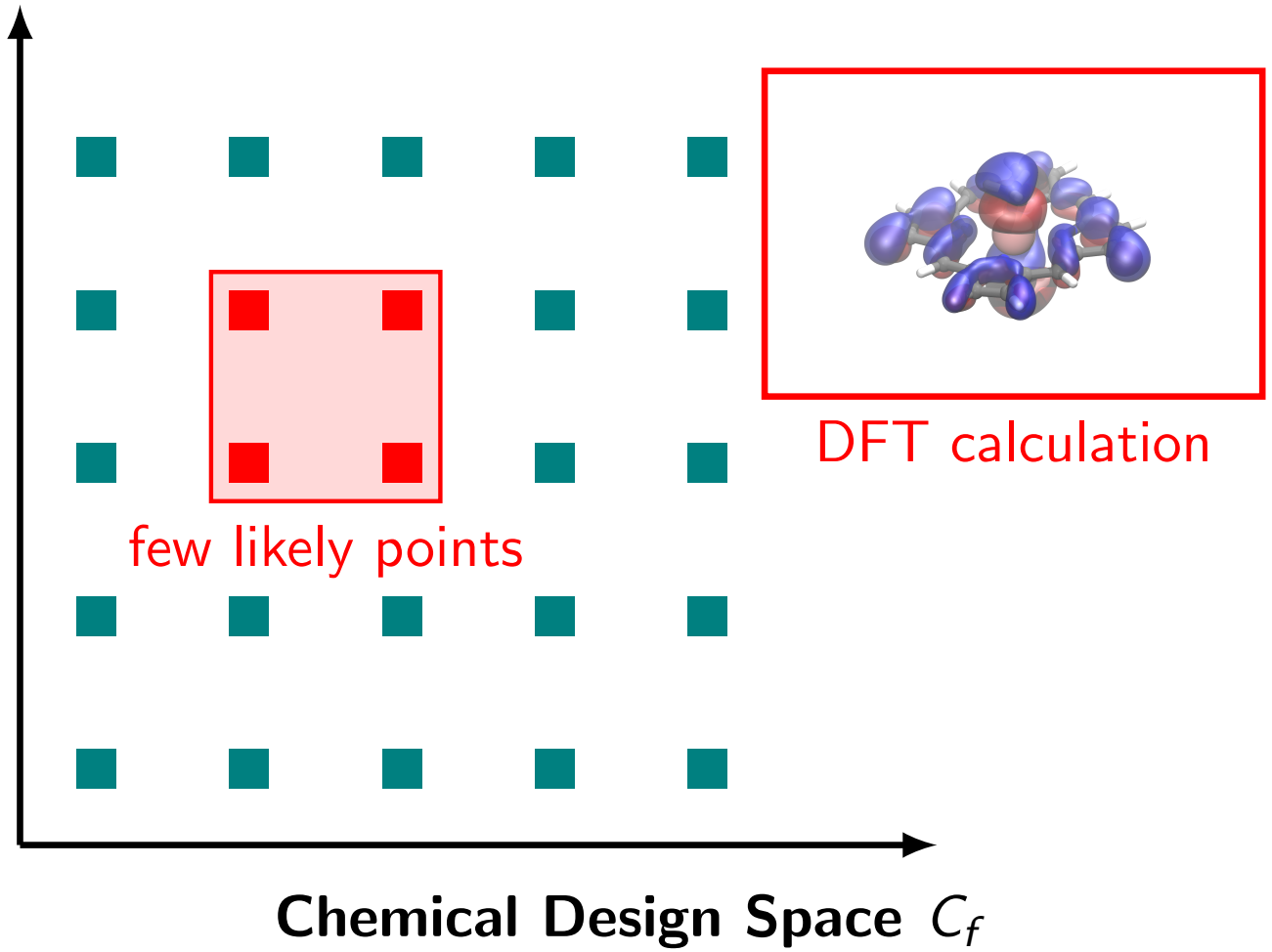

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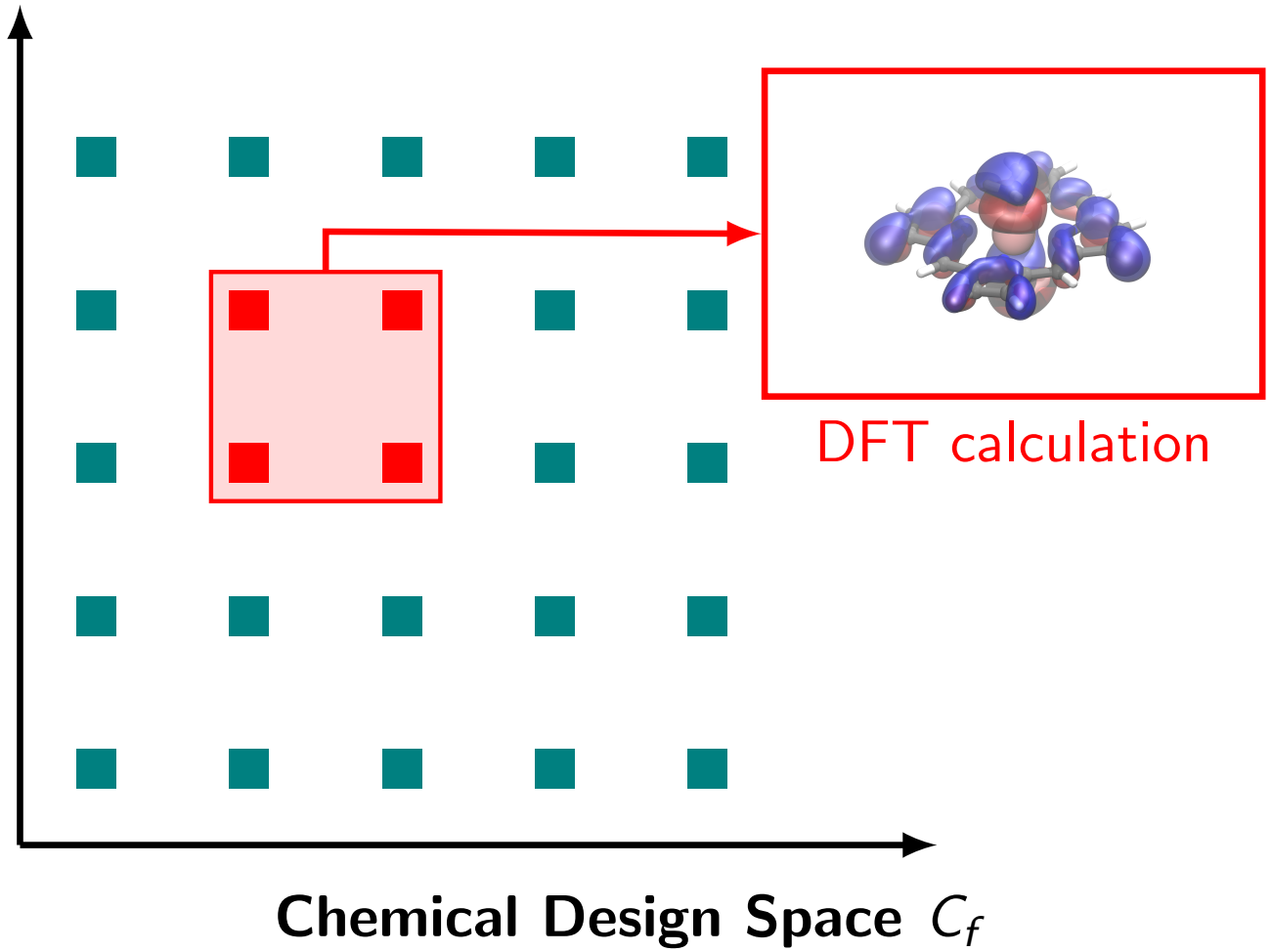

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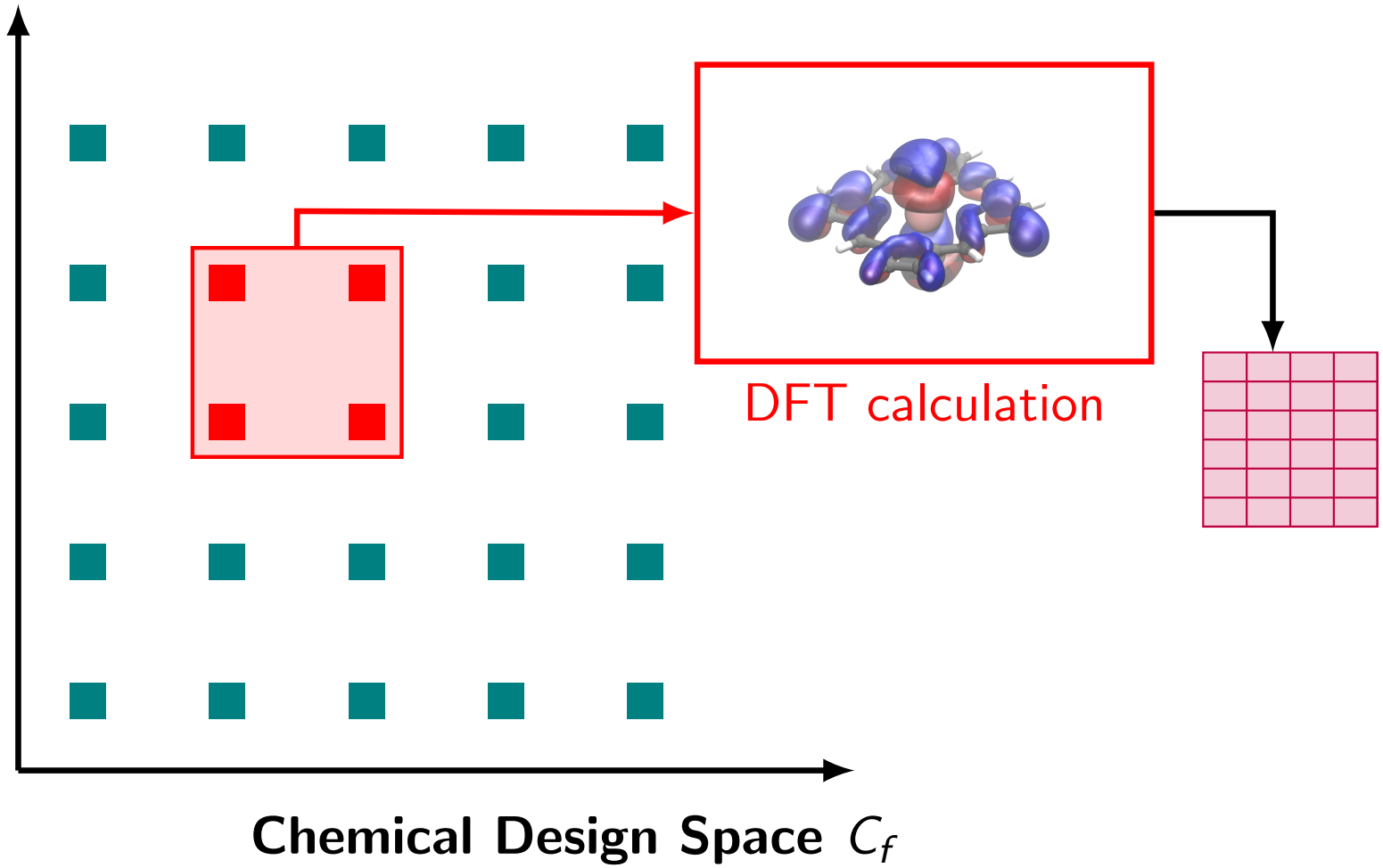

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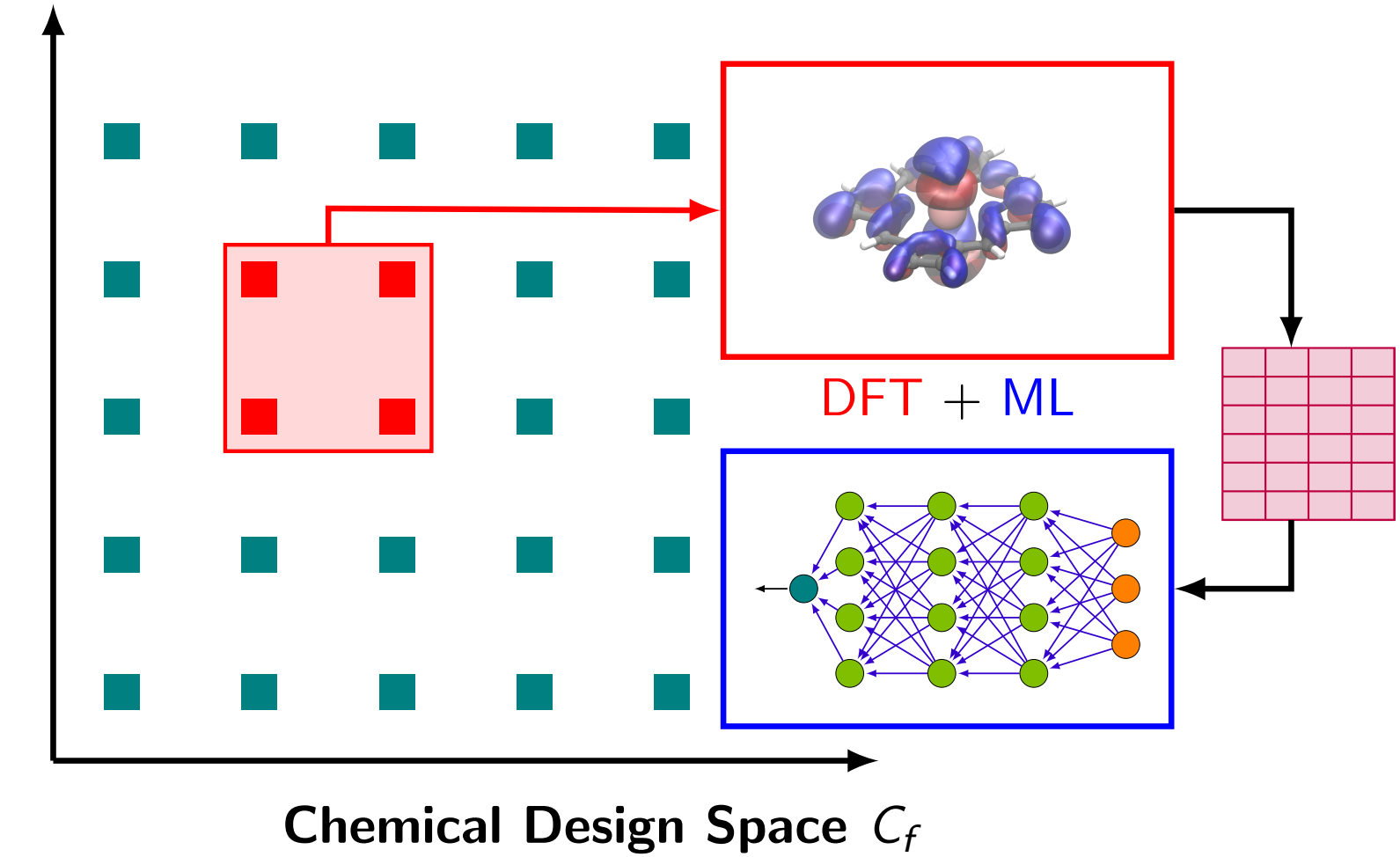

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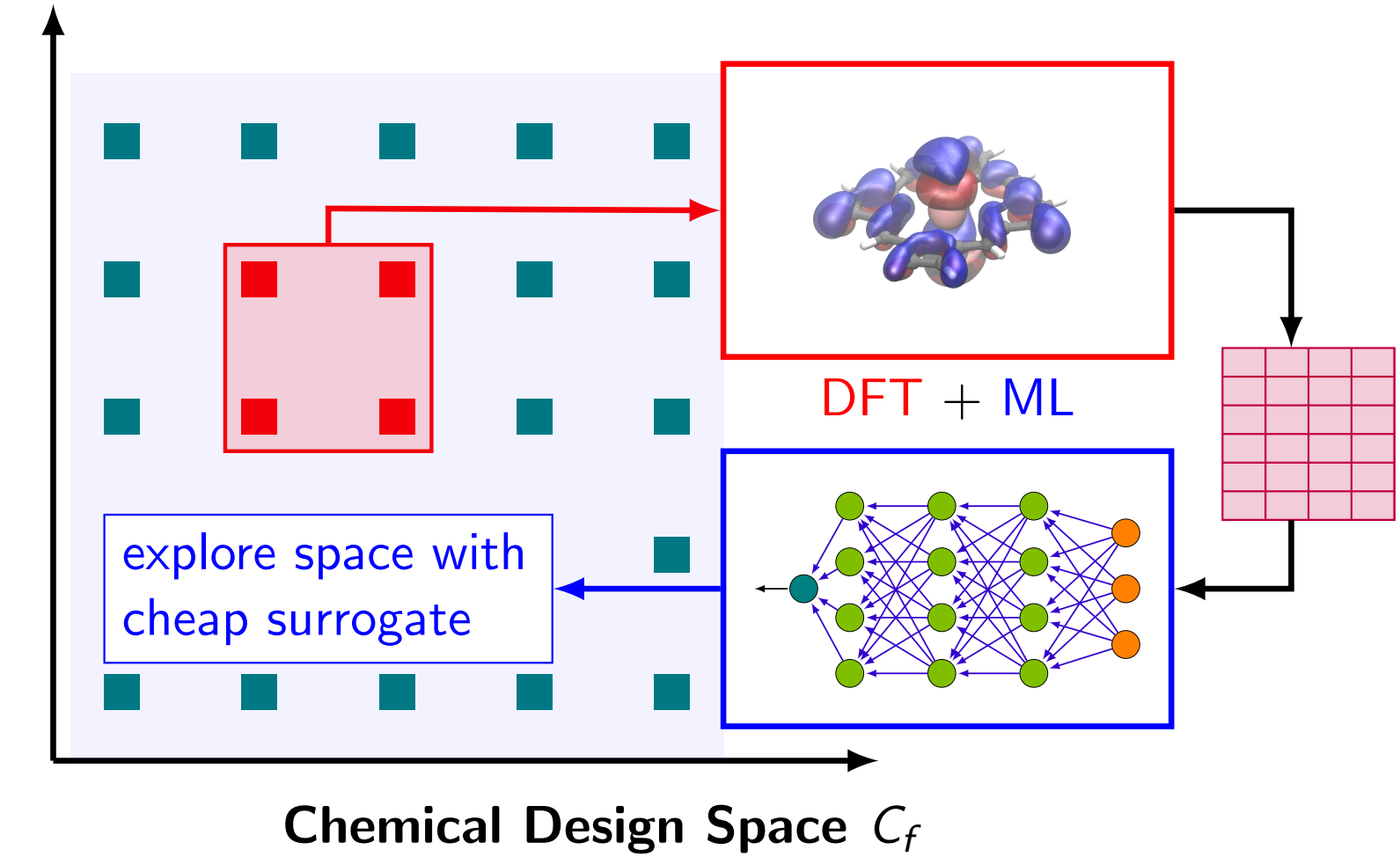

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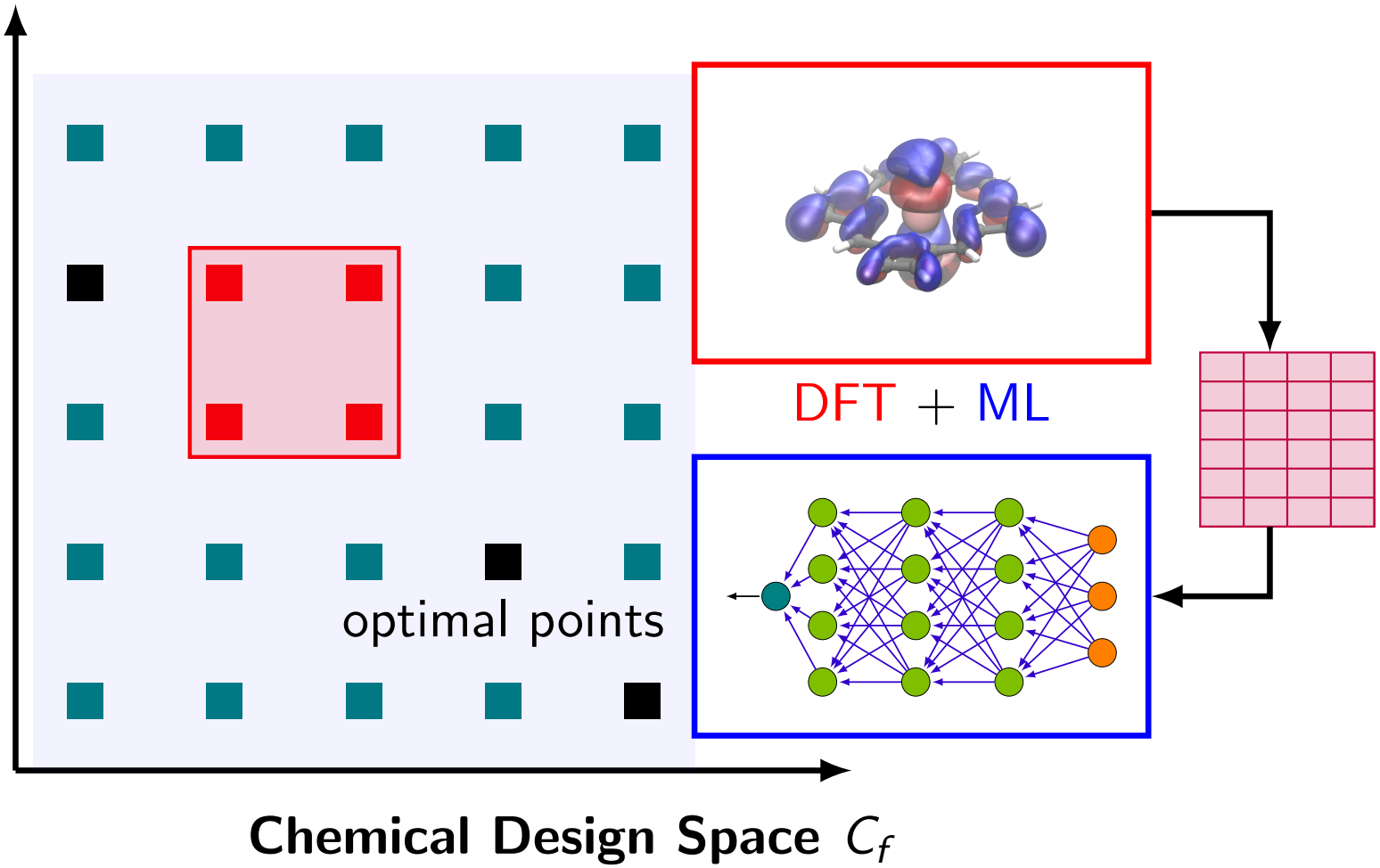

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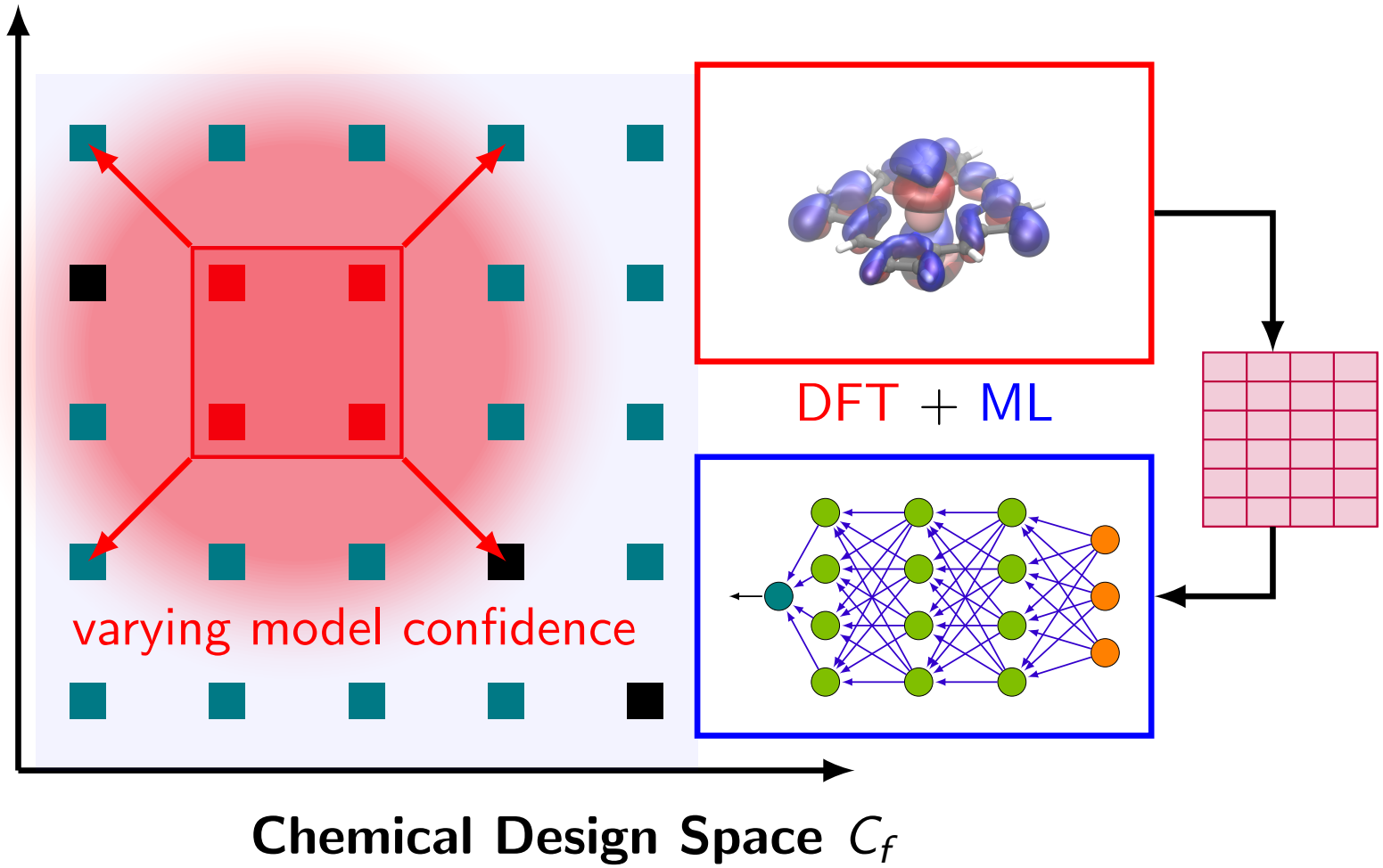
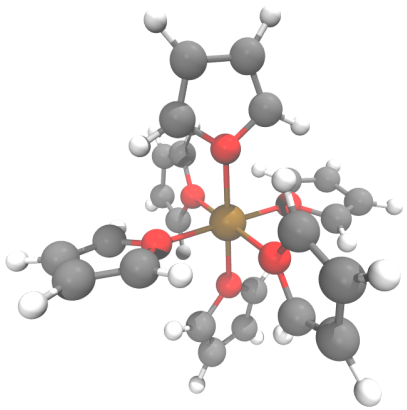
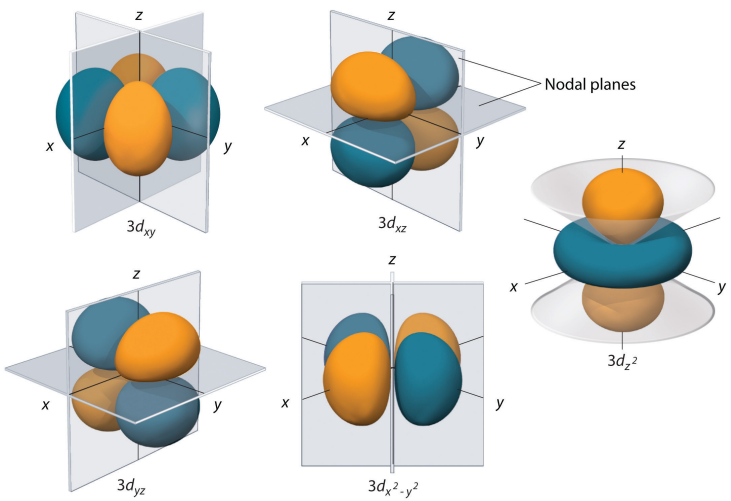


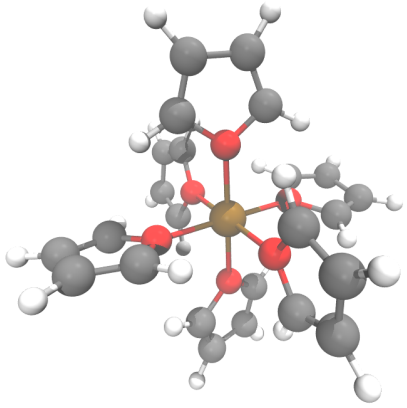
Transition metal complexes

Transition metal complexes



Transition metal complexes

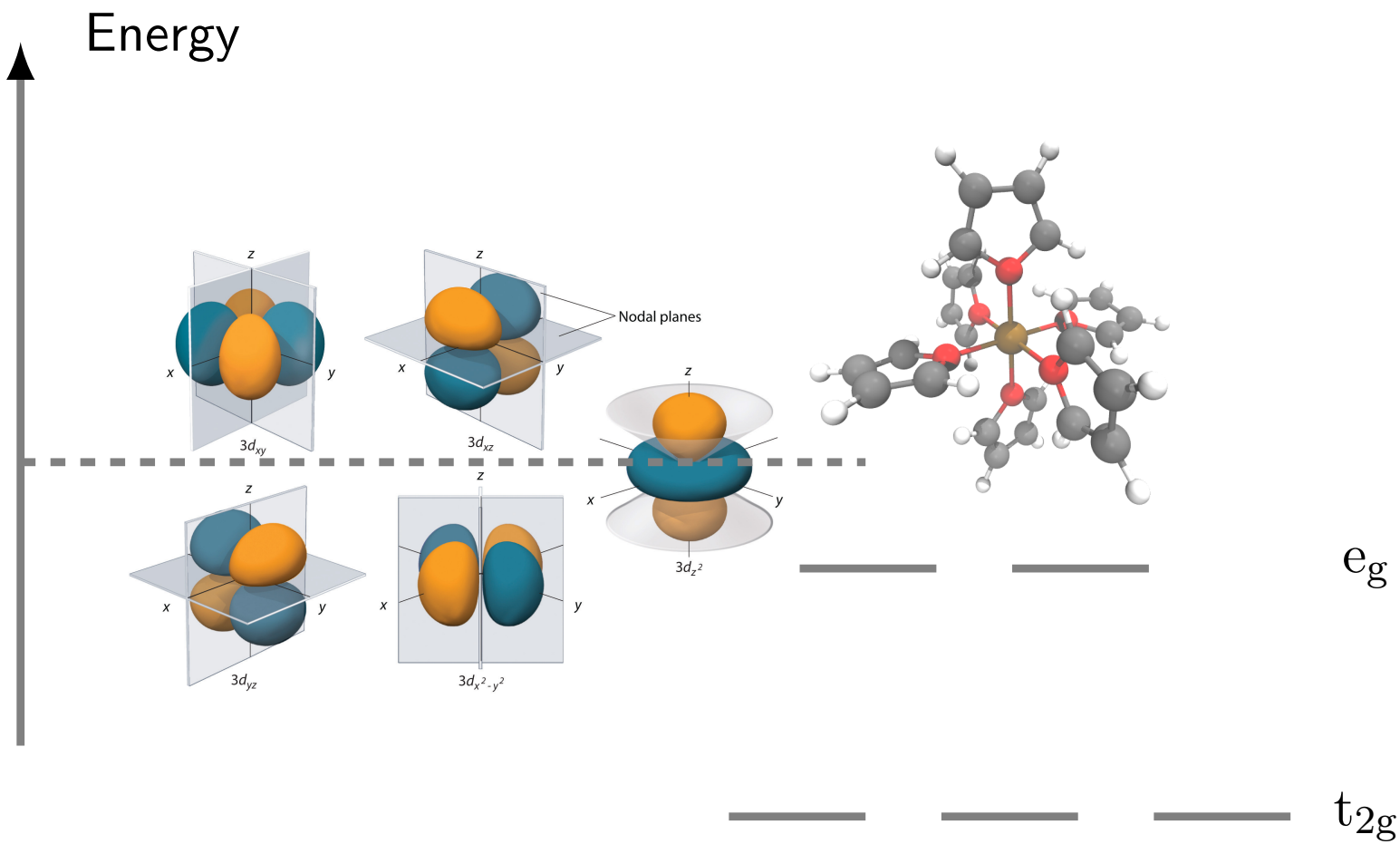




e_g

t_{2g}

Transition metal complexes



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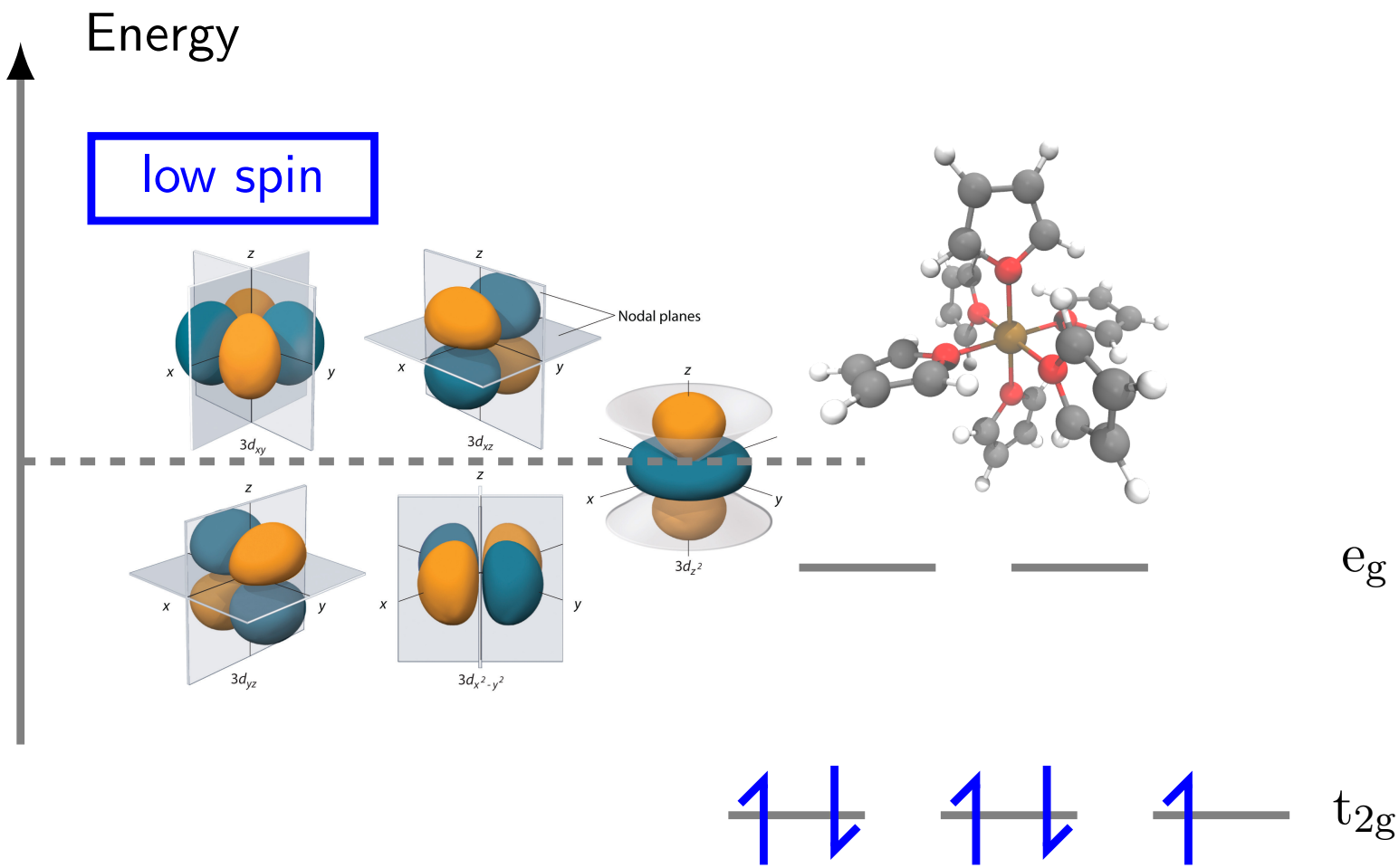

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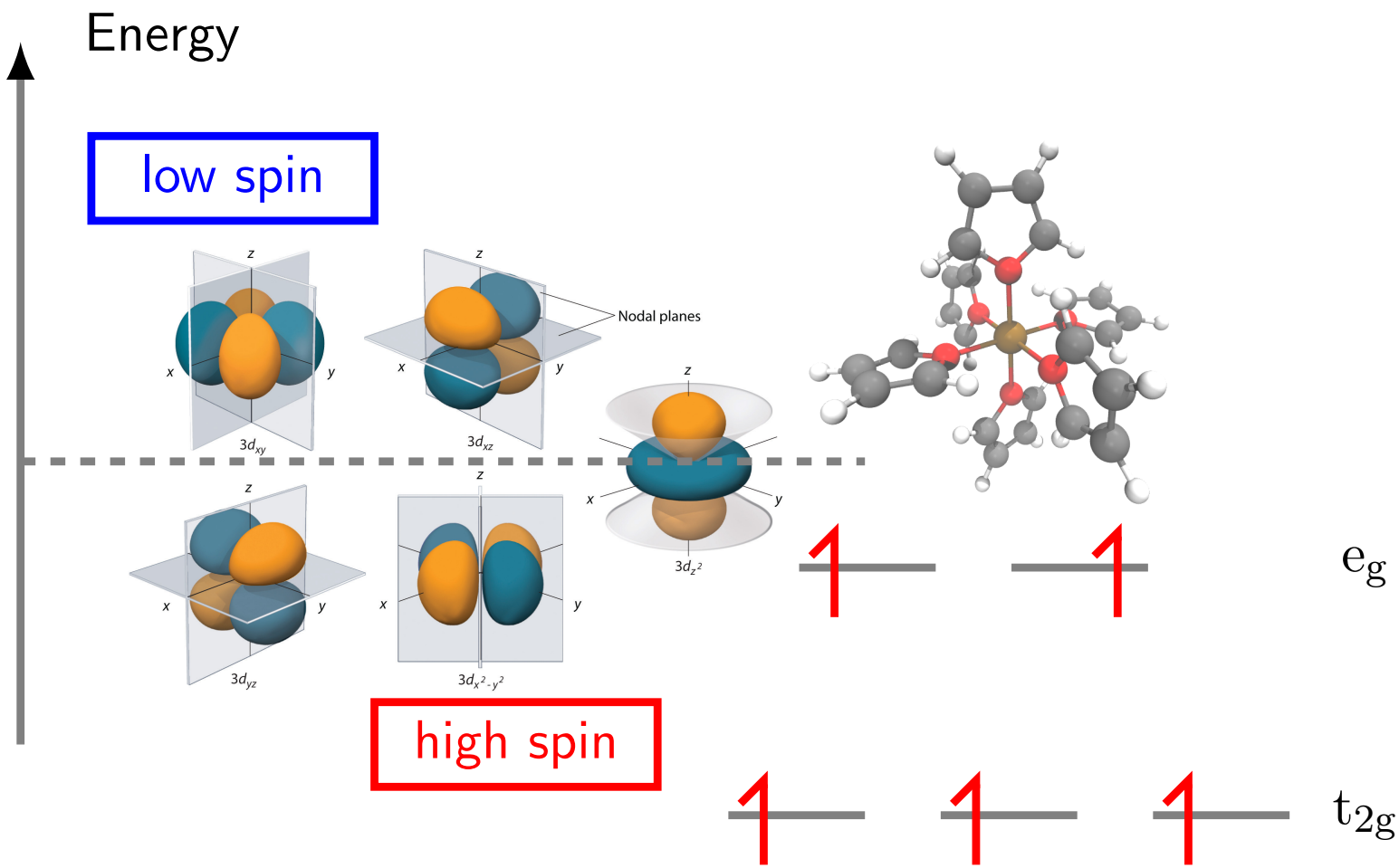

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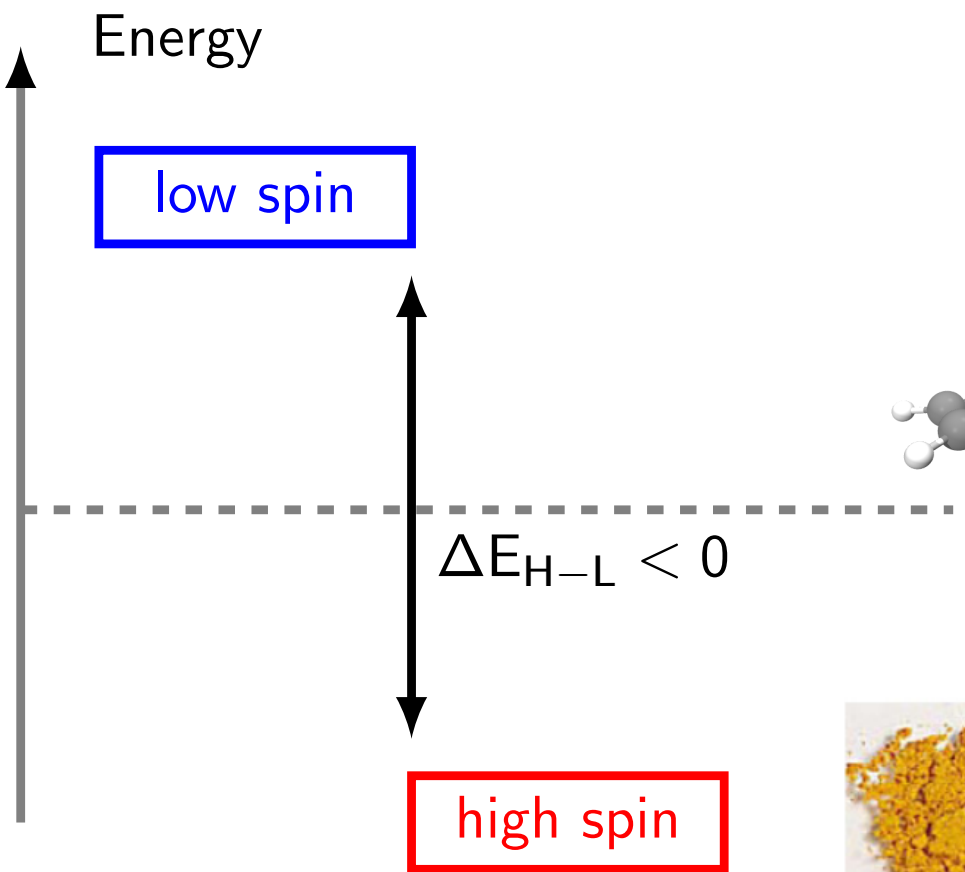

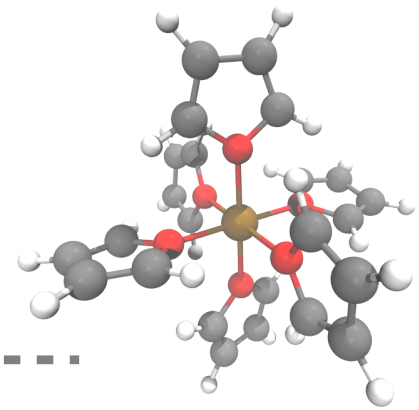

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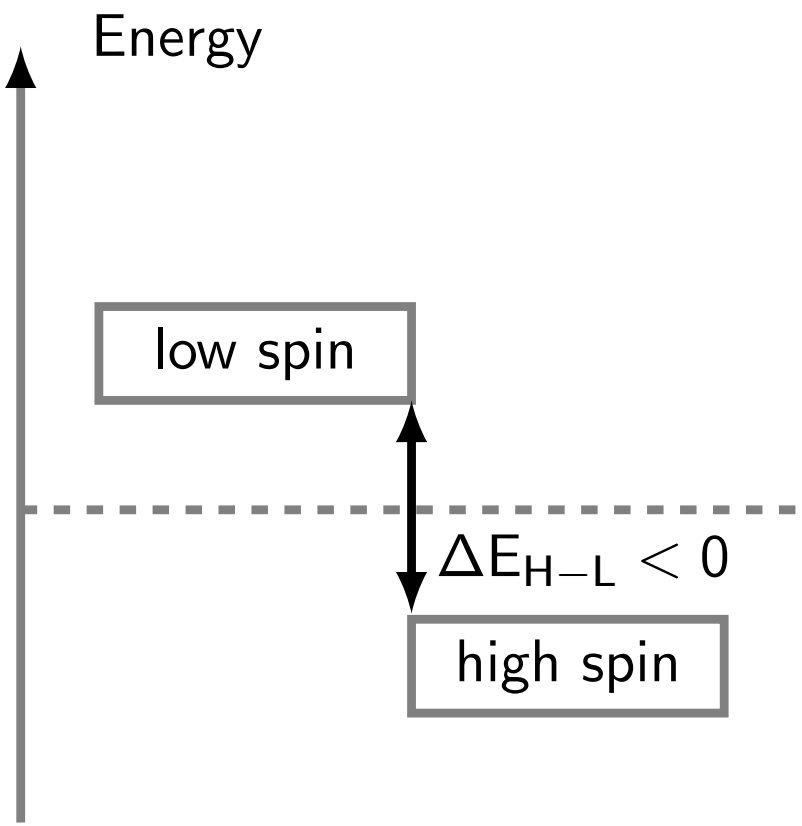

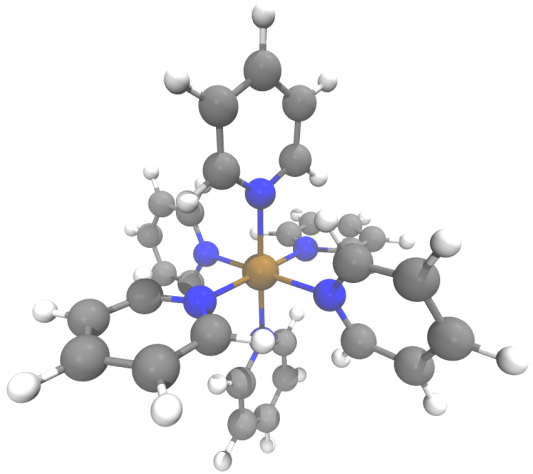

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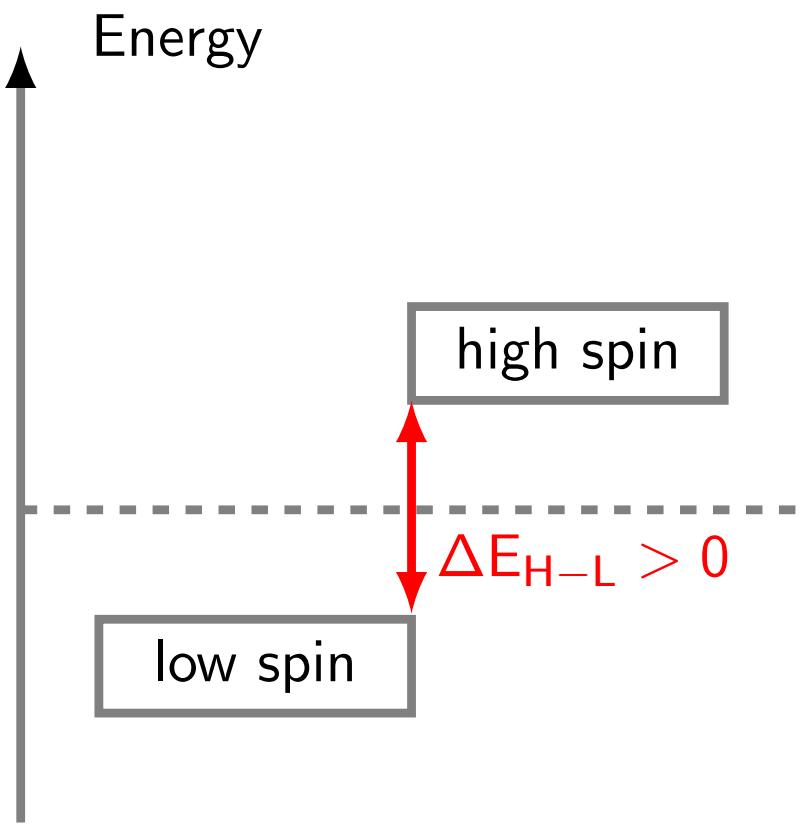

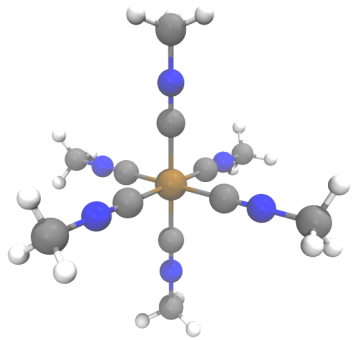

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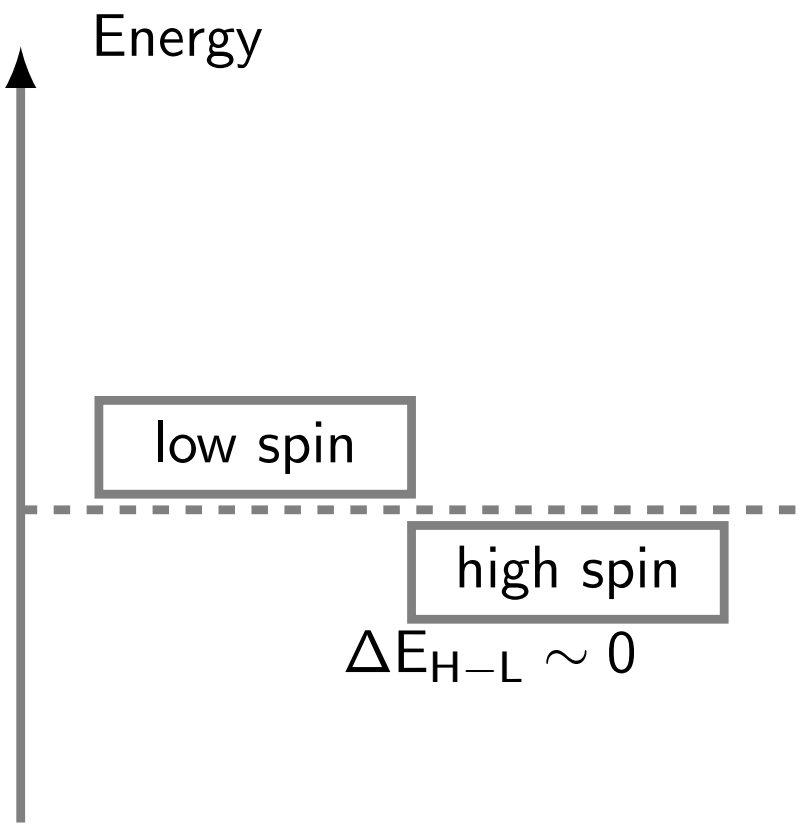

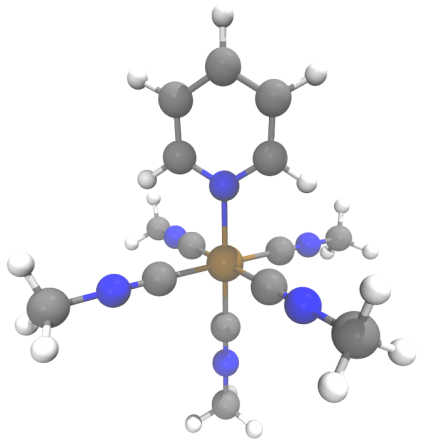

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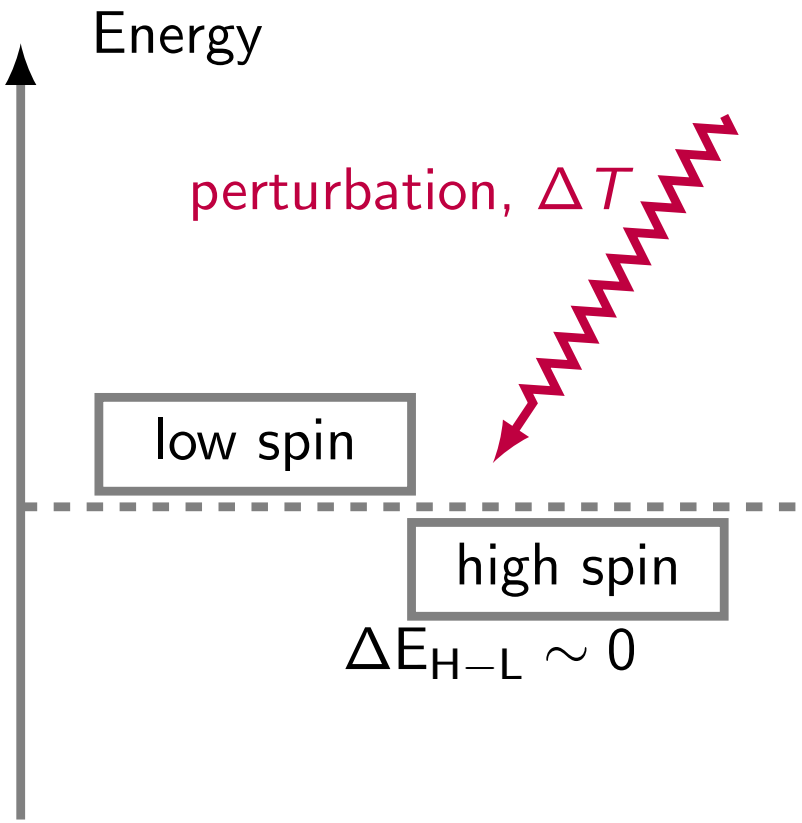

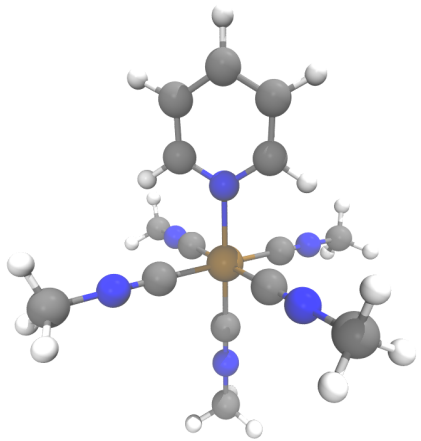

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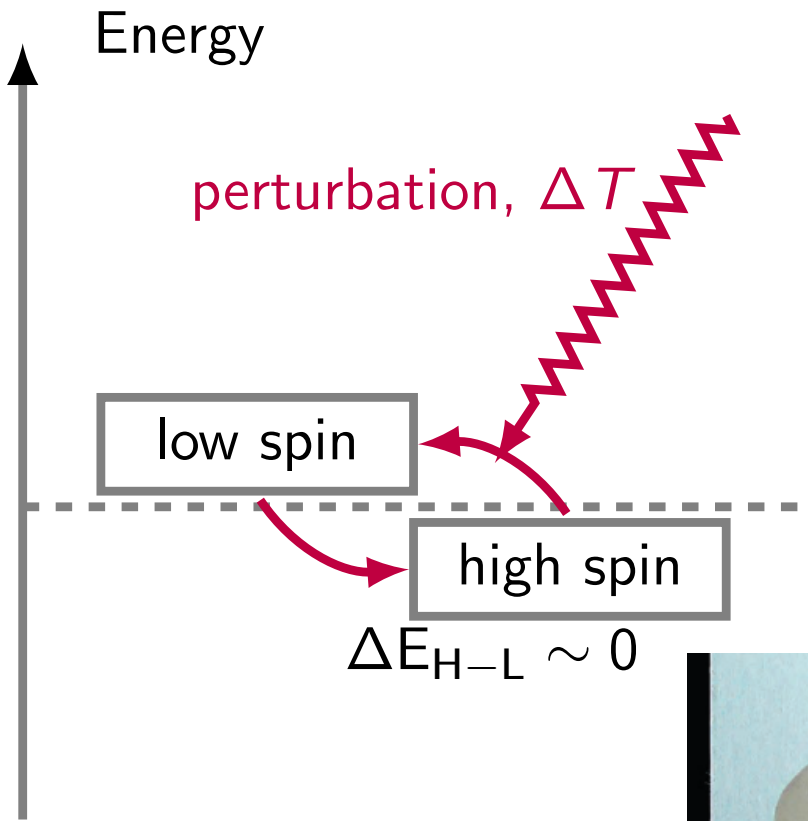

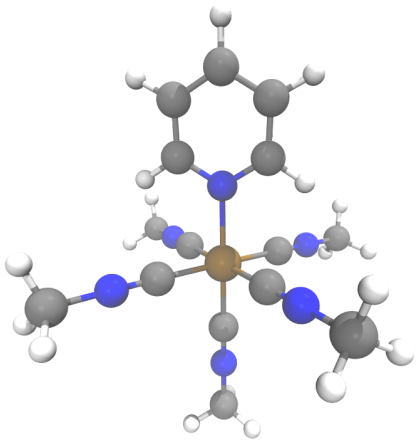

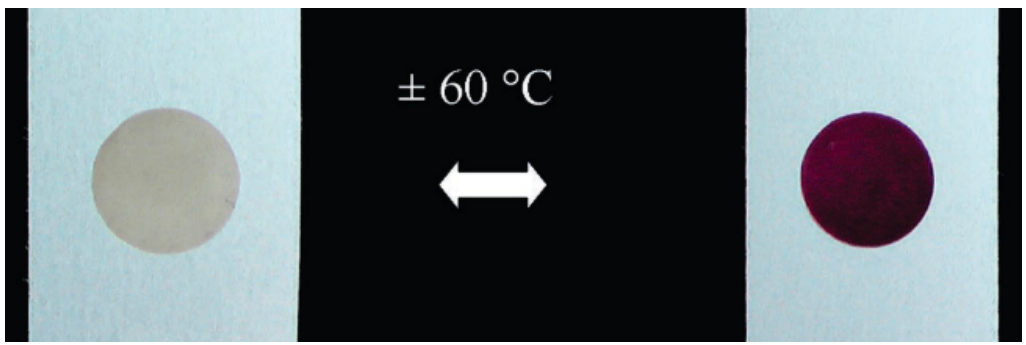

Seredyuk, M *et al.*, *Chem. Mater.*, 18(10):2513–2519, 2006.

DFT data

train on $\sim 100 - 2000$ of DFT calculations:

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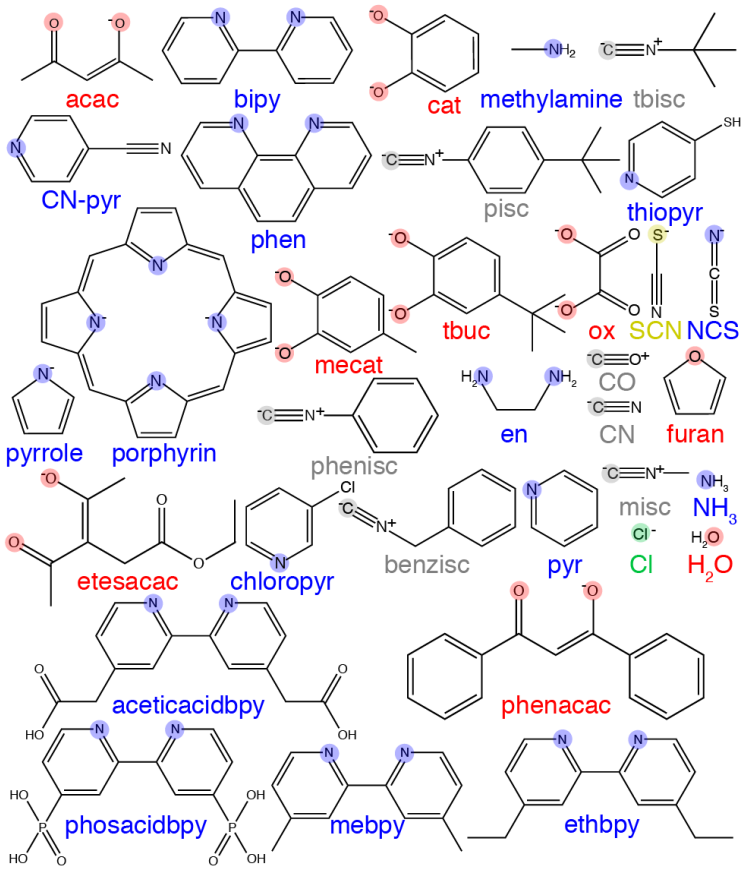

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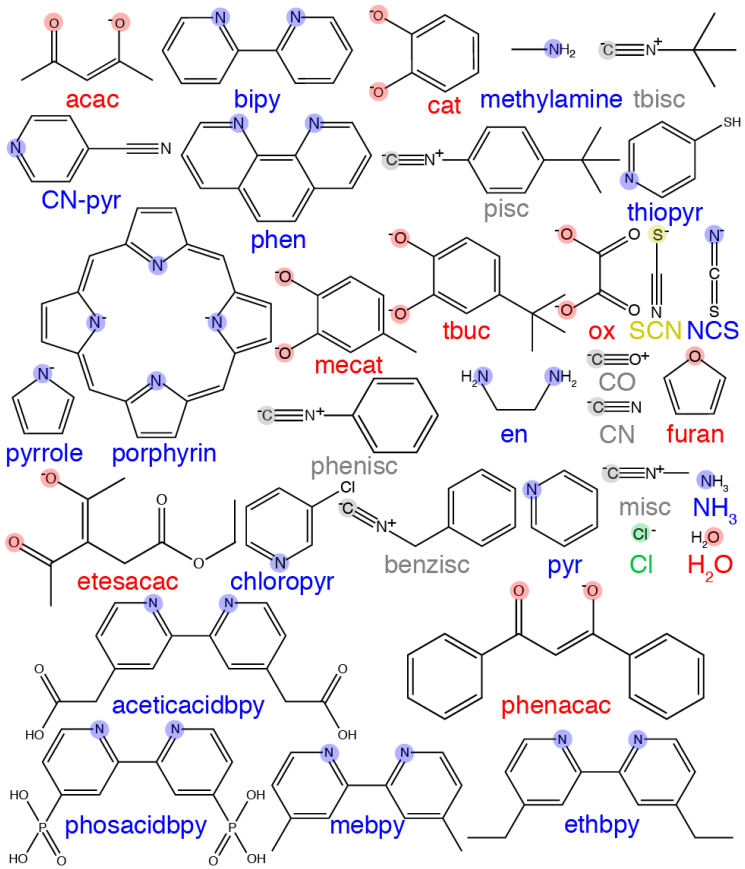

Cr	Mn	Fe	Co

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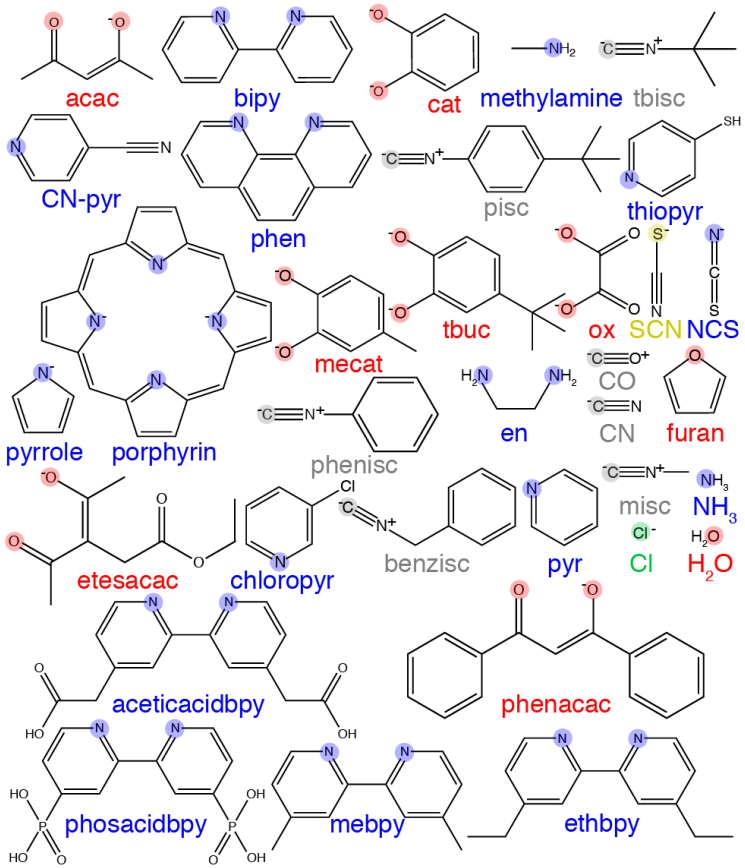

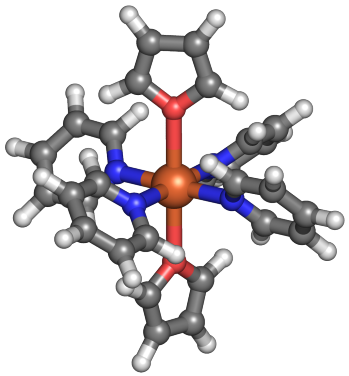

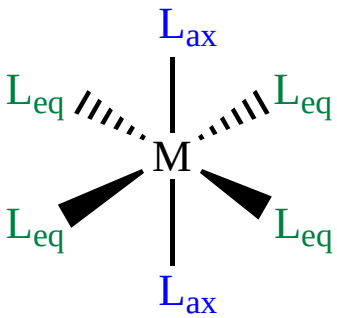

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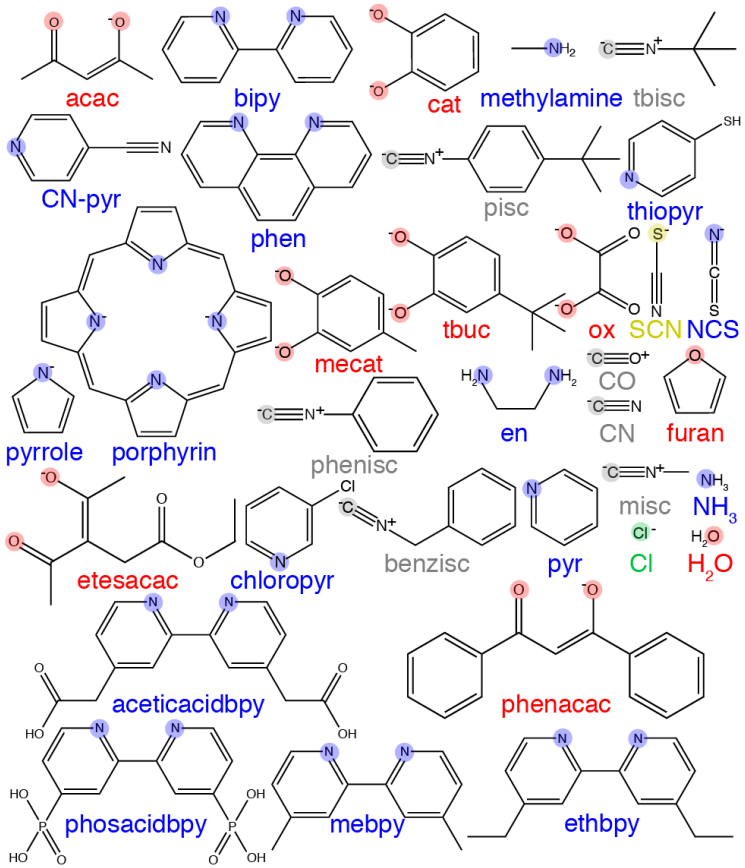

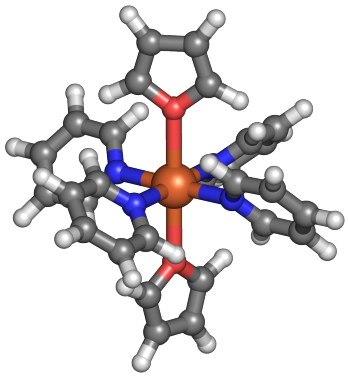

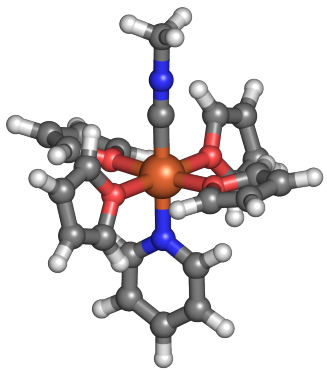

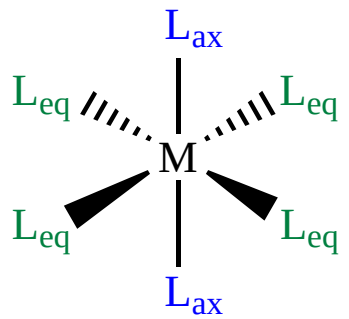

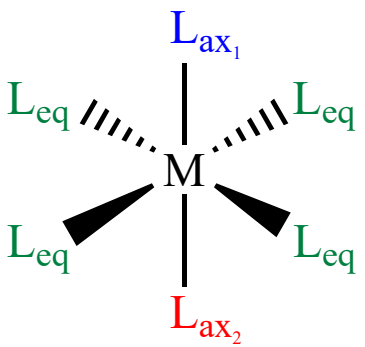

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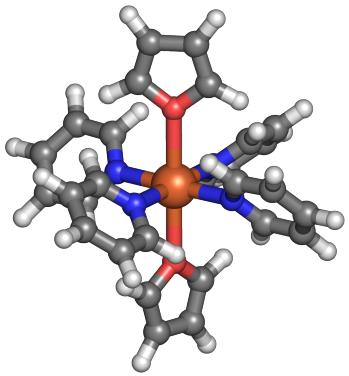
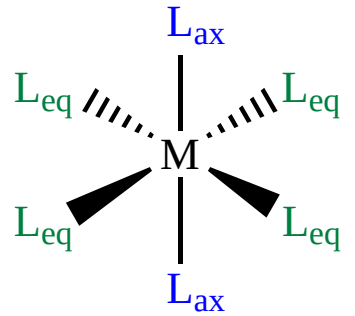
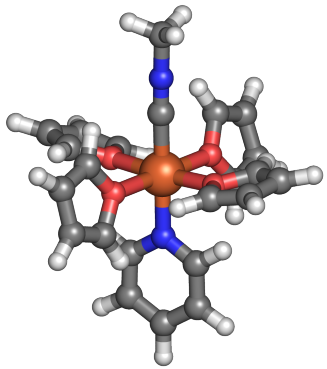
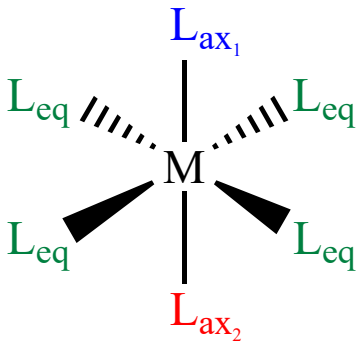
Details:
B3LYP-like DFT
gas phase optimizaton
LANL2DZ/6-31G*
high- and low-spin
M(II)/(III)









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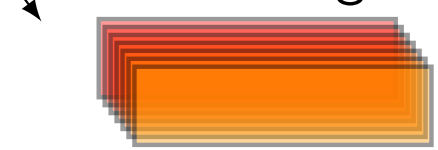
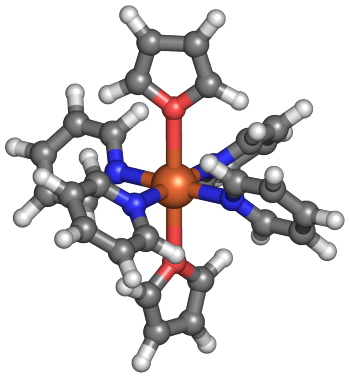
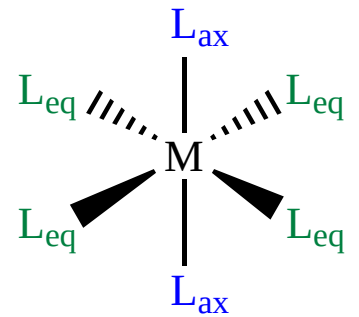
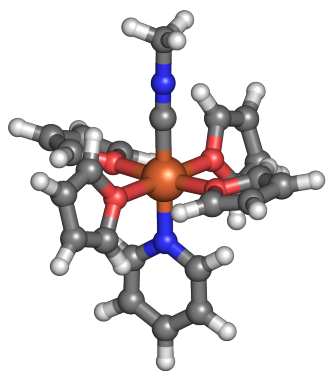
LANL2DZ/6-31G*
high- and low-spin
M(II)/(III)

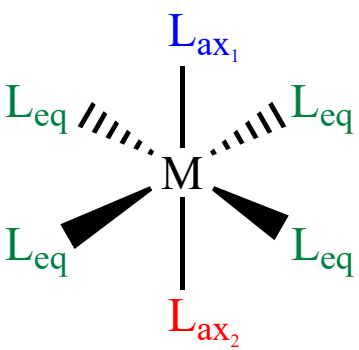
HF exchange varied $0 - 30\%$











Cr	Mn	Fe	Co

Predictive modeling of TM complexes

First attempt using simple features inspired by inorganic chem:

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metal properties

identity

Fe(II)

oxidation state

Predictive modeling of TM complexes

First attempt using simple features inspired by inorganic chem:

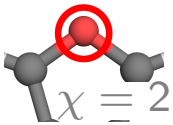
metal properties local ligand properties

identity

Fe(II)

oxidation state

$\chi = 3.44$



$\chi = 2.55$

$\max \Delta\chi$

Predictive modeling of TM complexes

First attempt using simple features inspired by inorganic chem:

metal properties

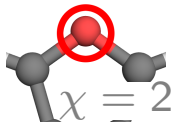
identity

Fe(II)

oxidation state

local ligand properties

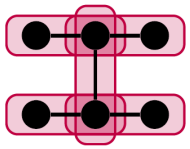
$\chi = 3.44$



$\chi = 2.55$

$\max \Delta\chi$

global properties



Kier index

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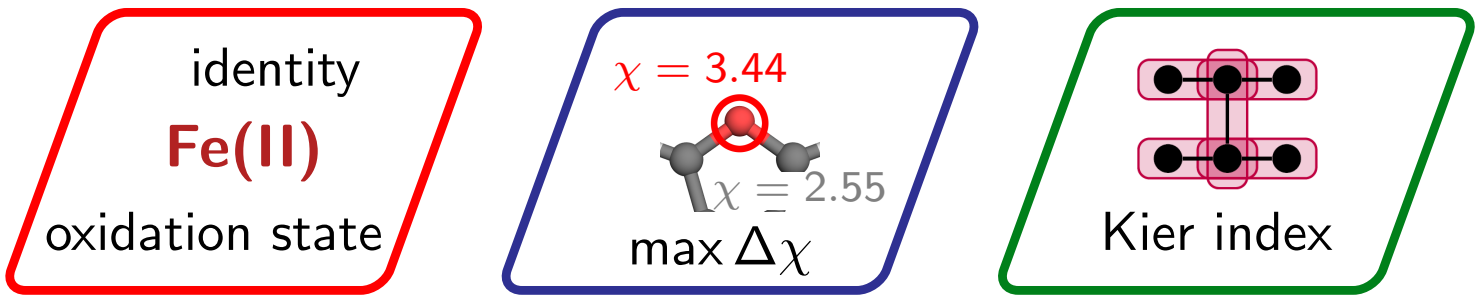

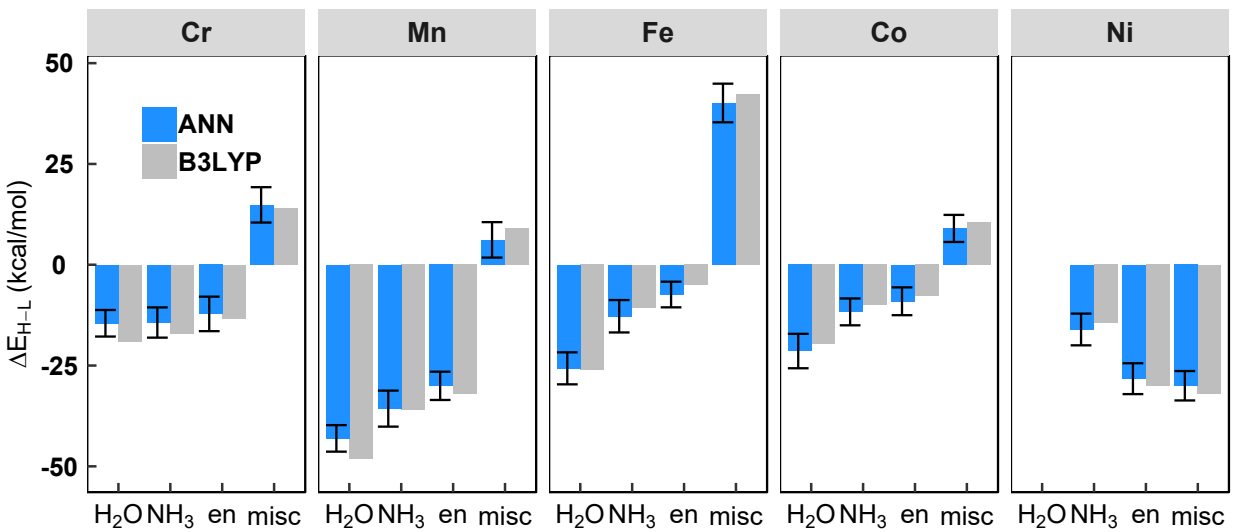

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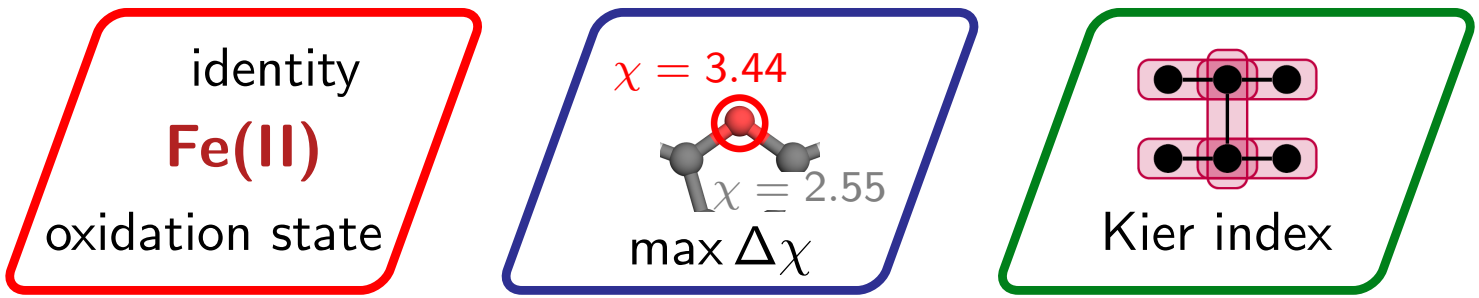

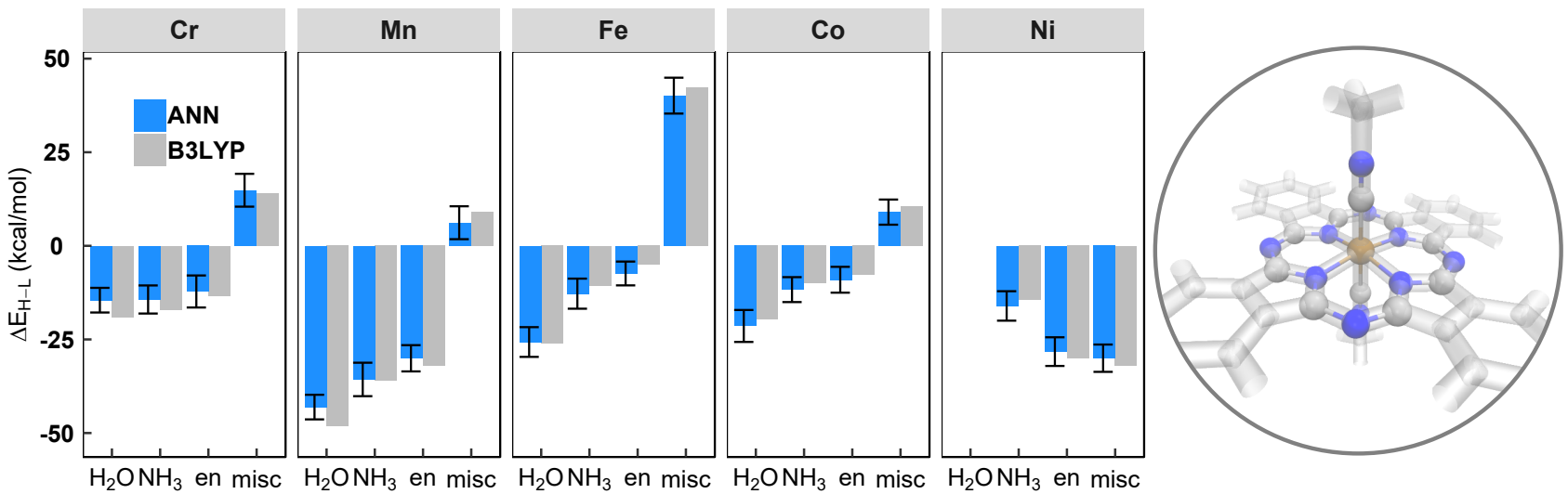

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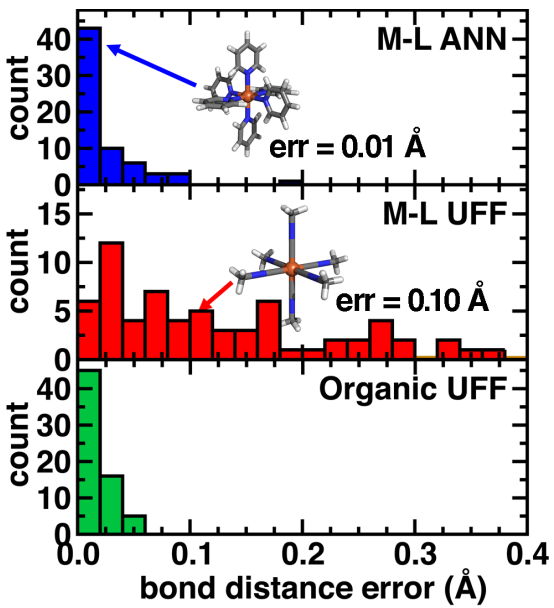

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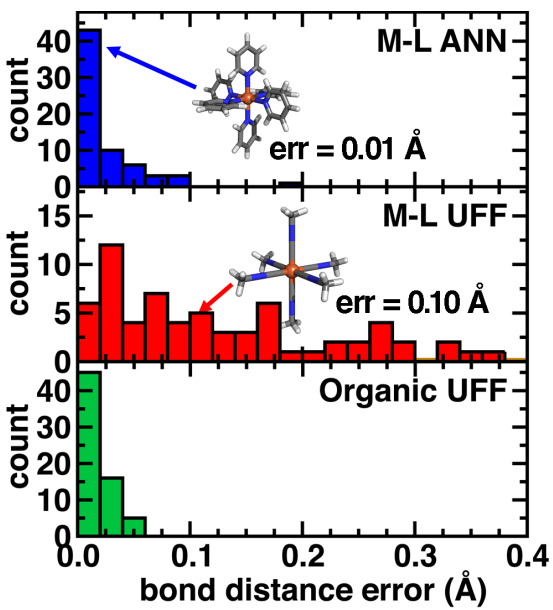
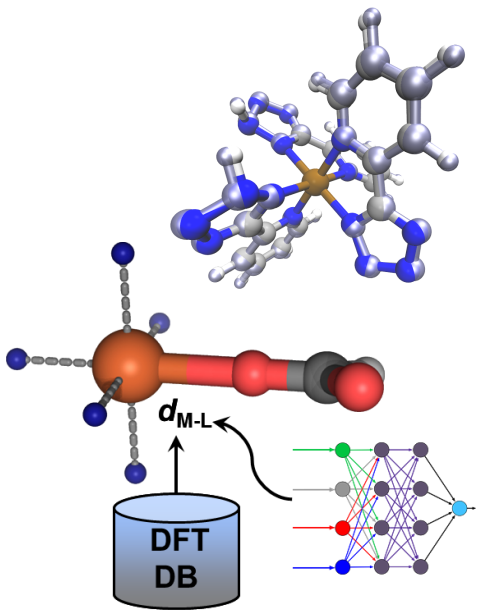


we can predict bond lengths and use this to intialize new calculations



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Model transferability

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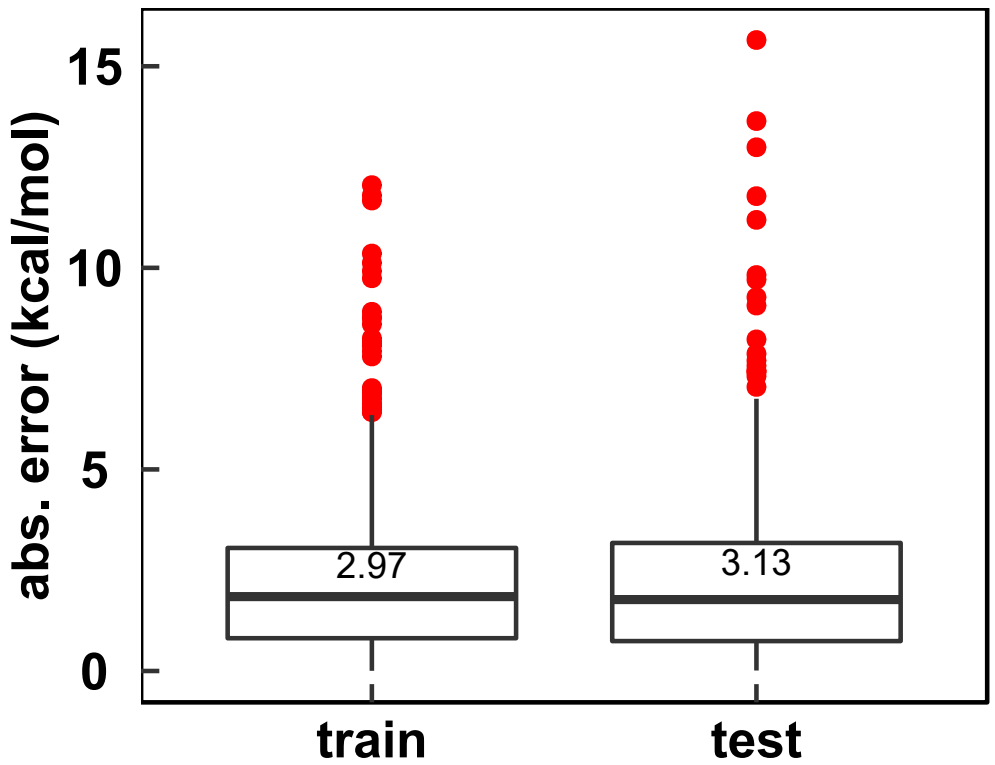

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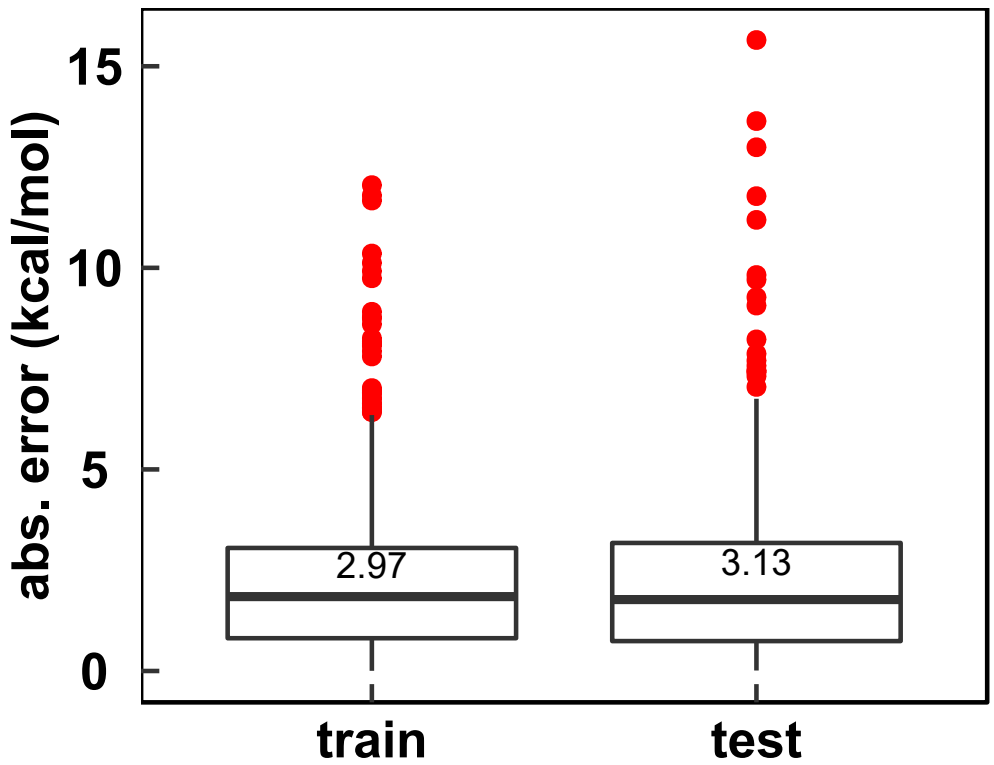

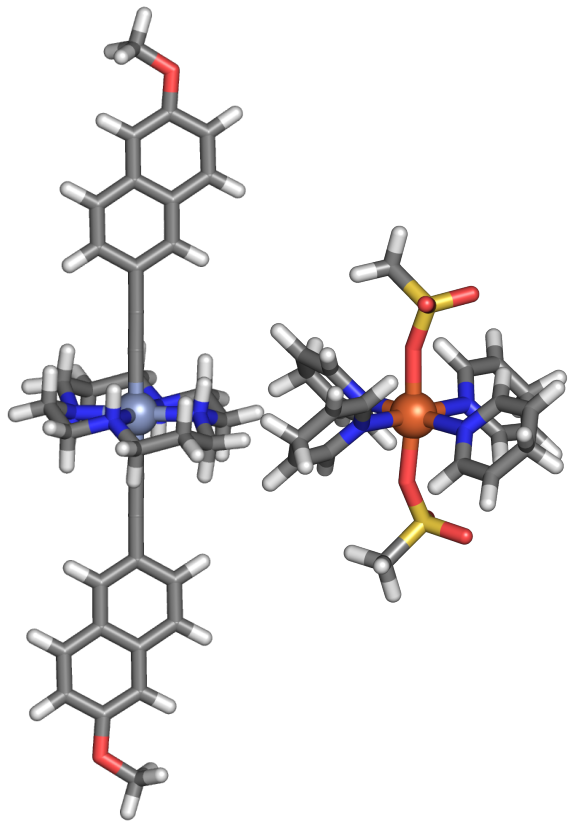

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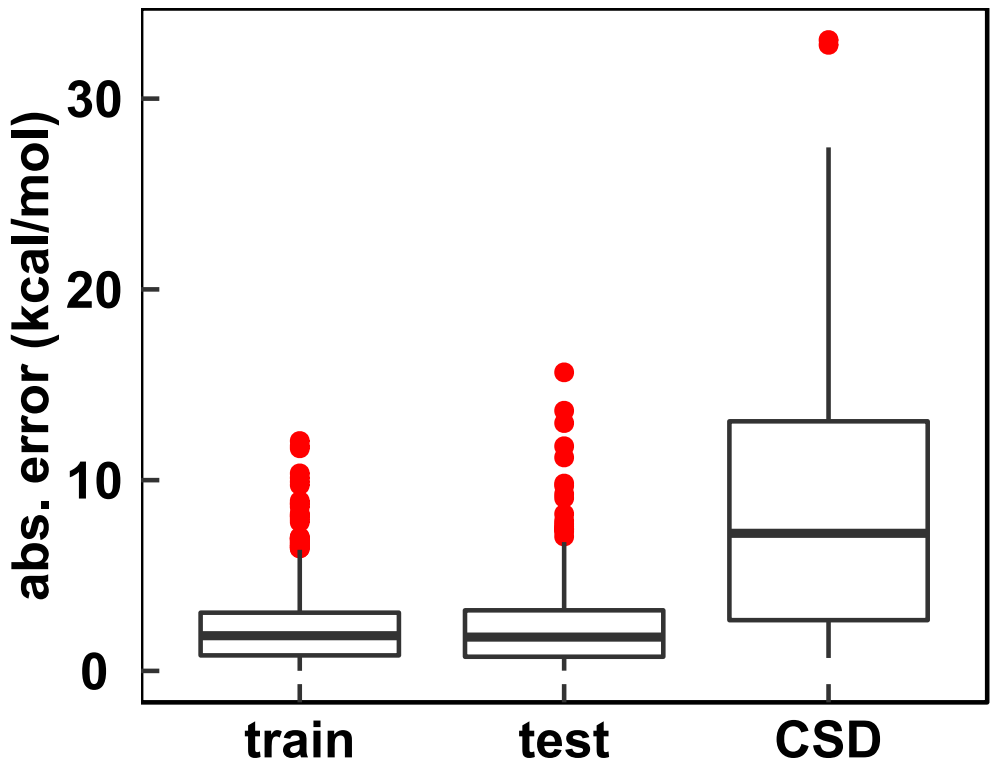

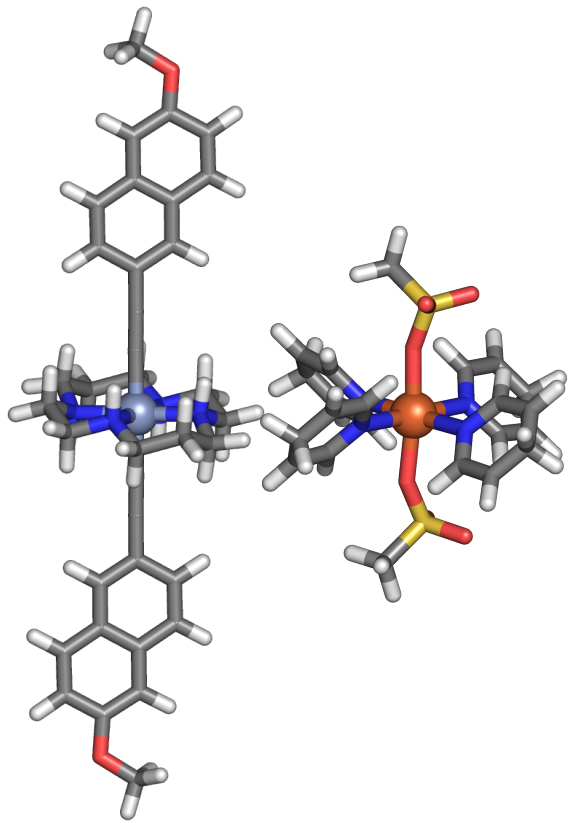

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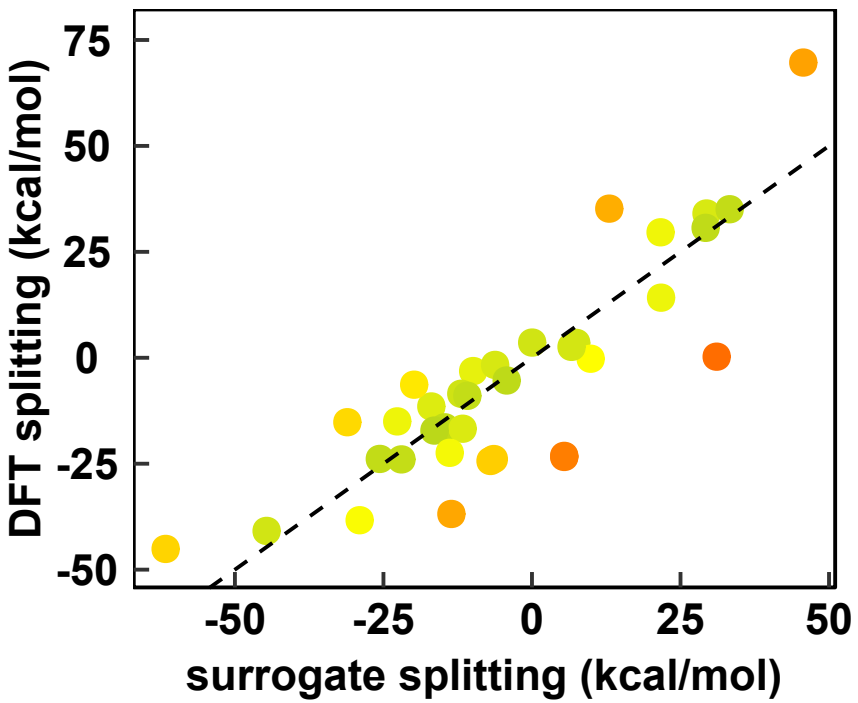

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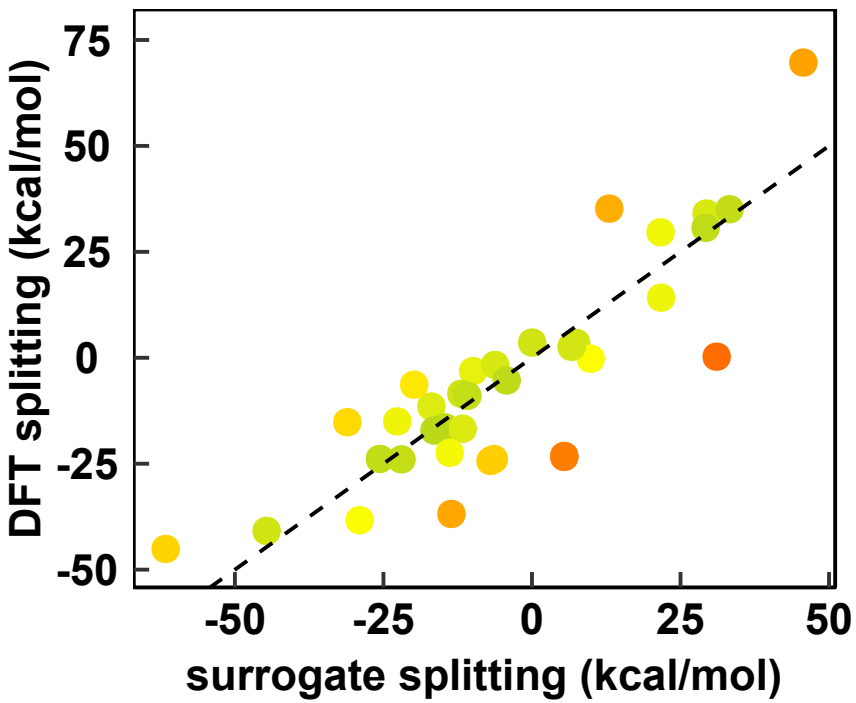

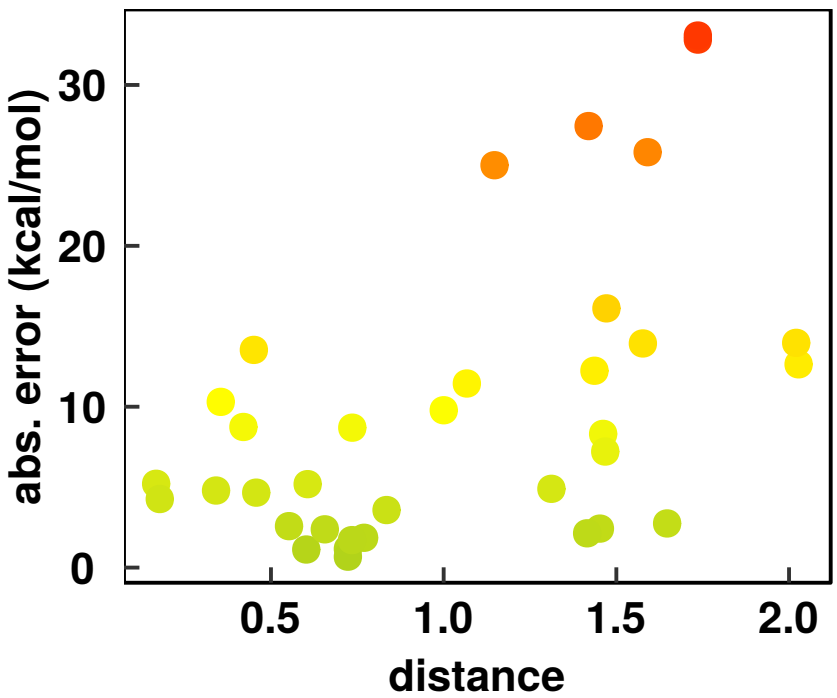

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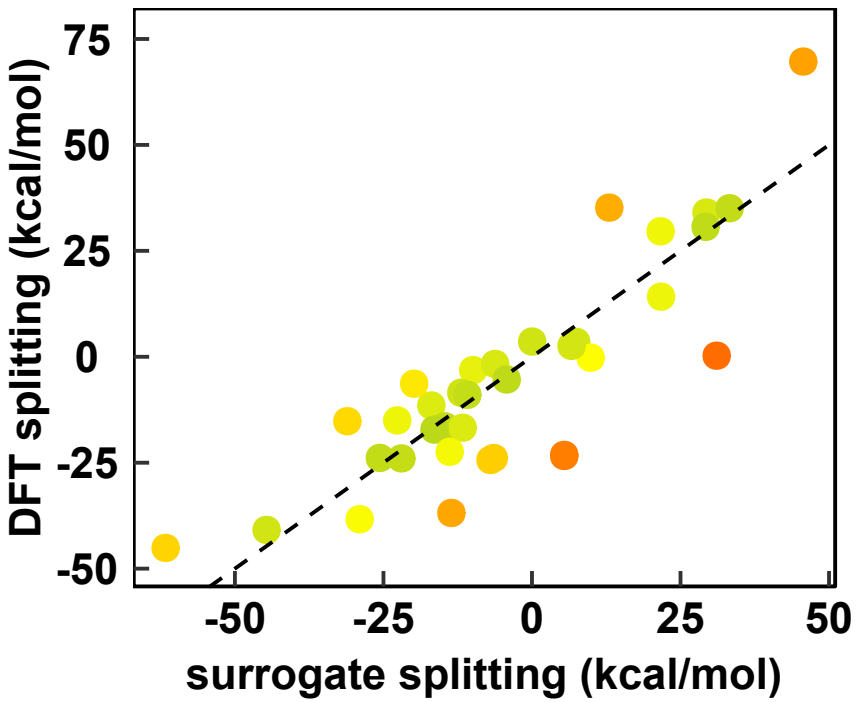
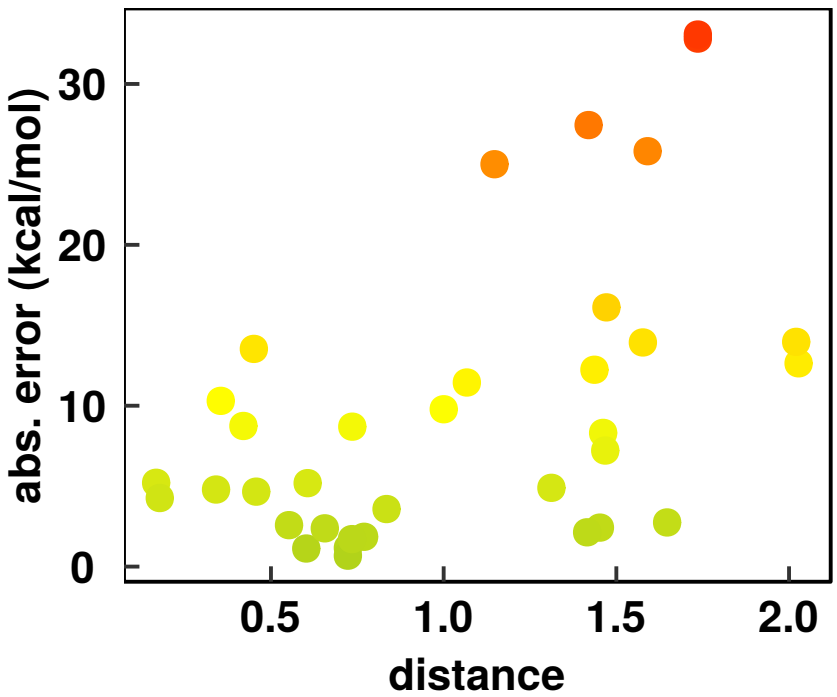


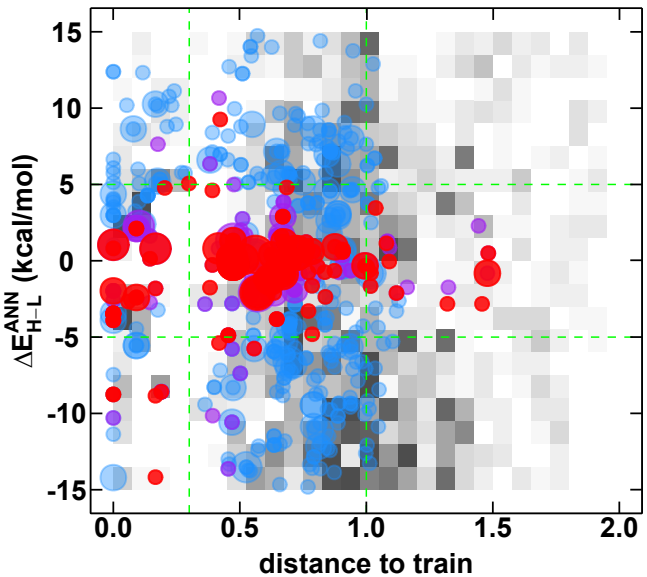


using simple distance worked pretty well!

TM complex discovery with ANNs

Spin splitting design:

We combine ANN predictions and uncertainties using an evolutionary algorithm.
Error control allows 60% of leads to be validated with DFT.[1]



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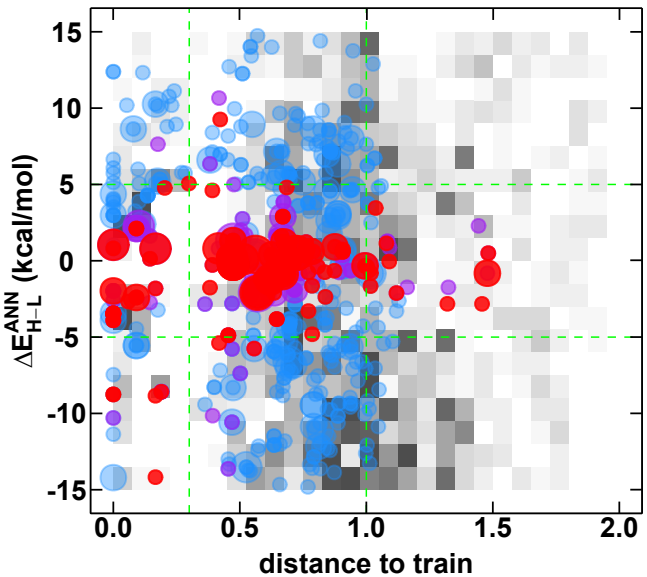
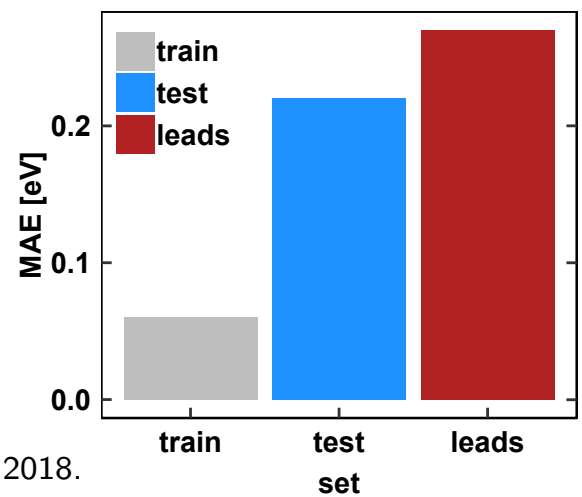


Frontier orbital properties:

This approach also works for frontier orbtial design[2], obtaining average HOMO of 3.98 eV compared to target 4.00 eV.



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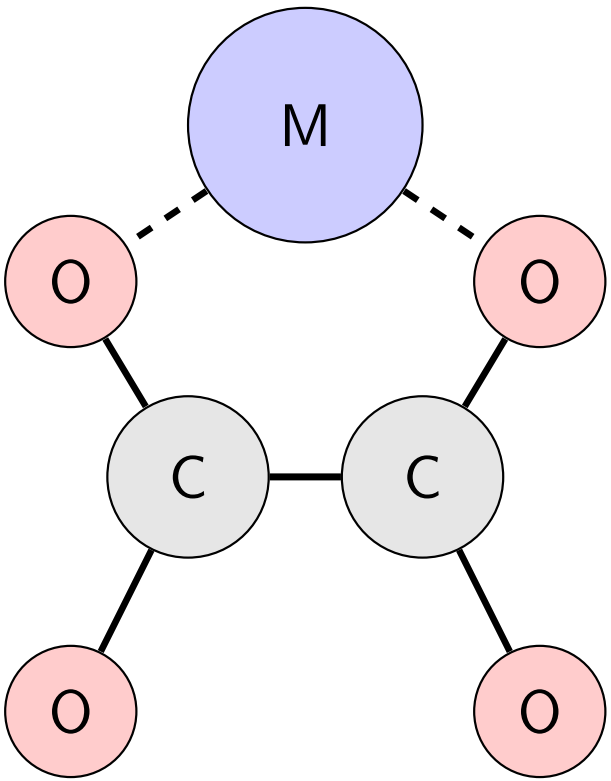

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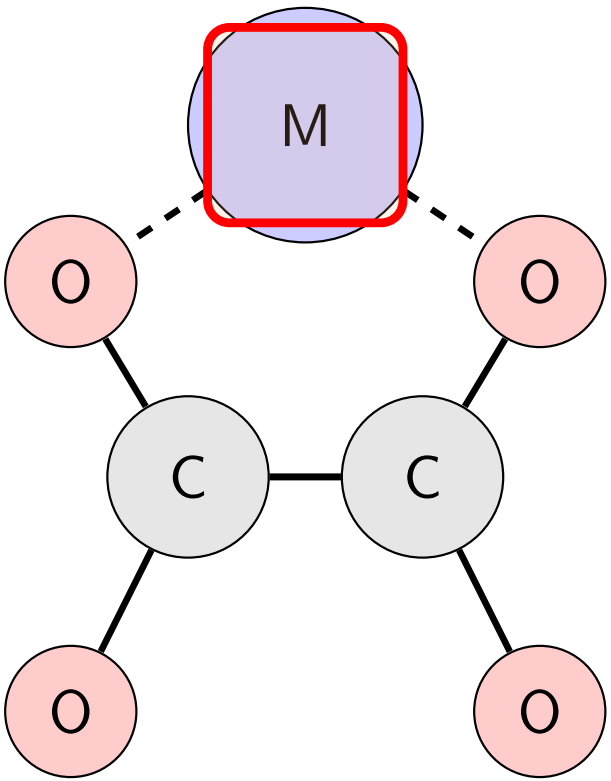

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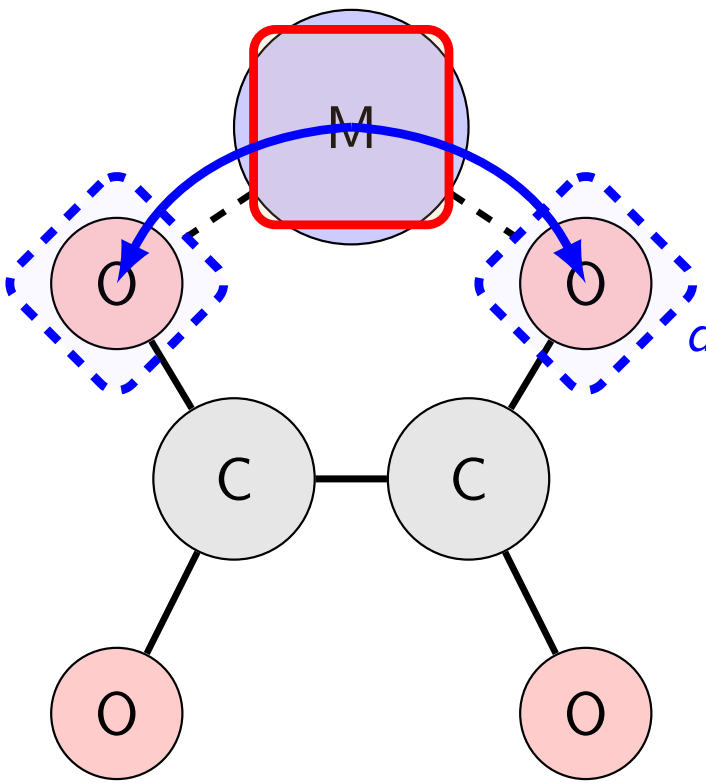

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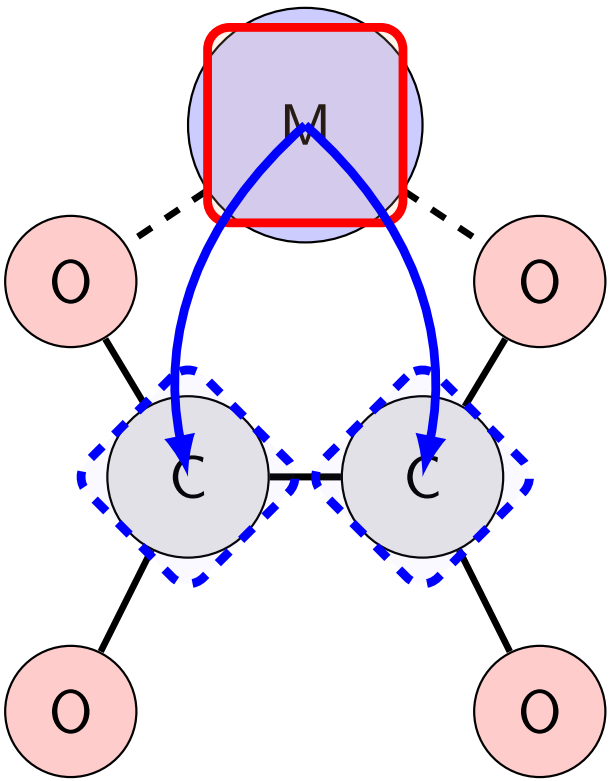

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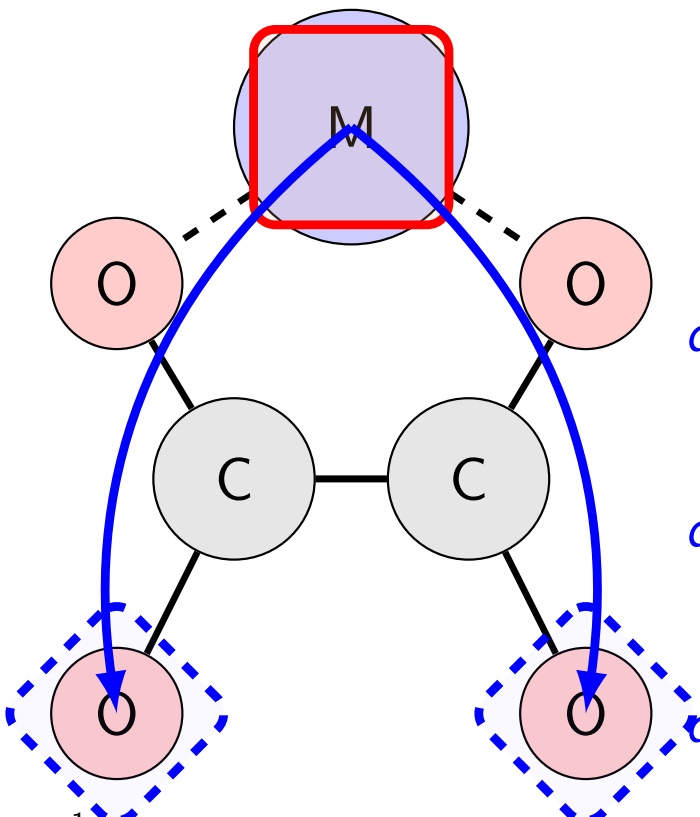

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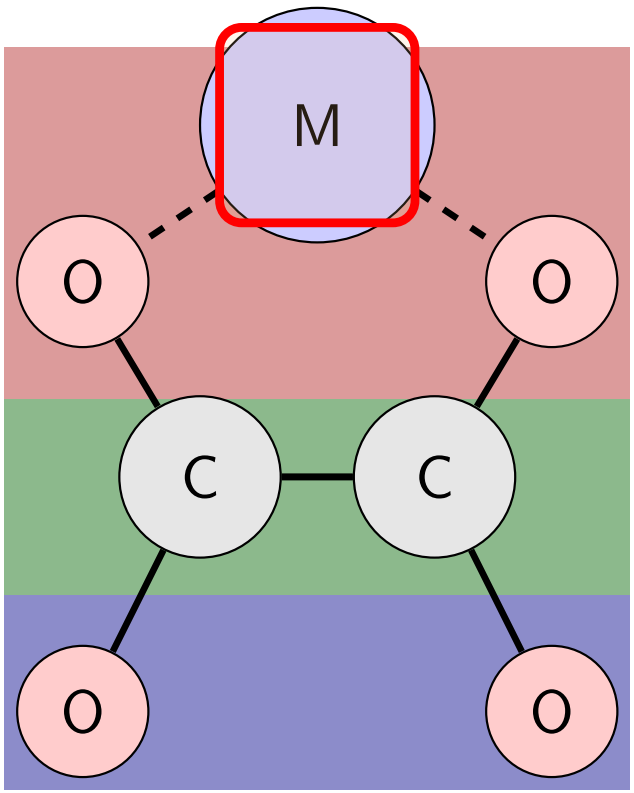

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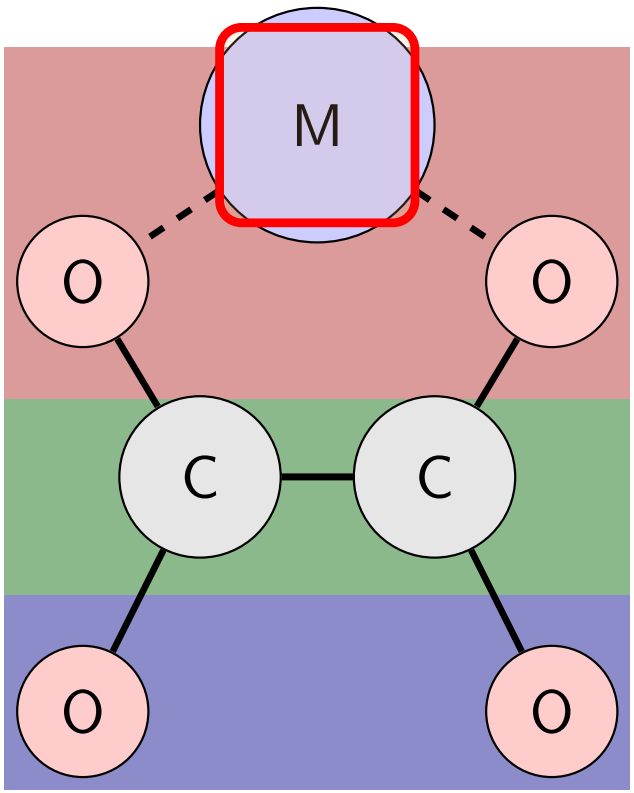

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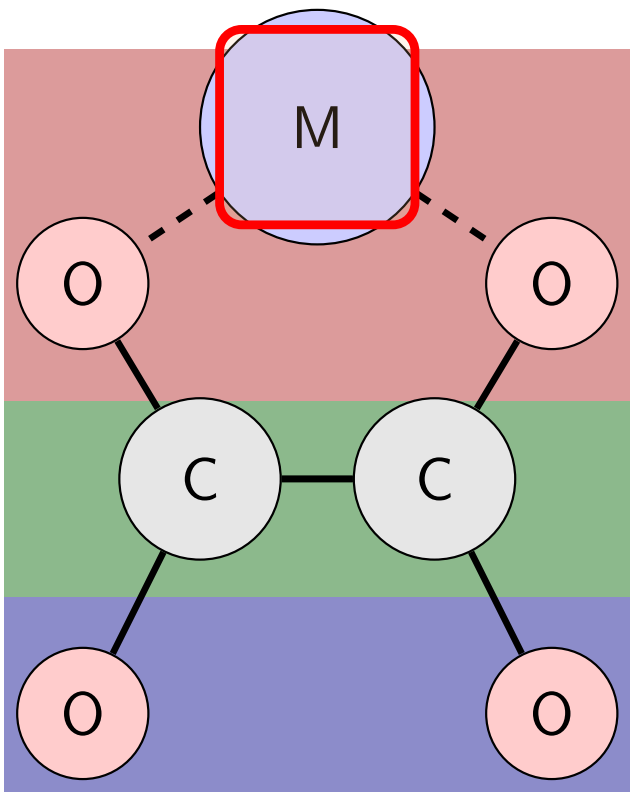

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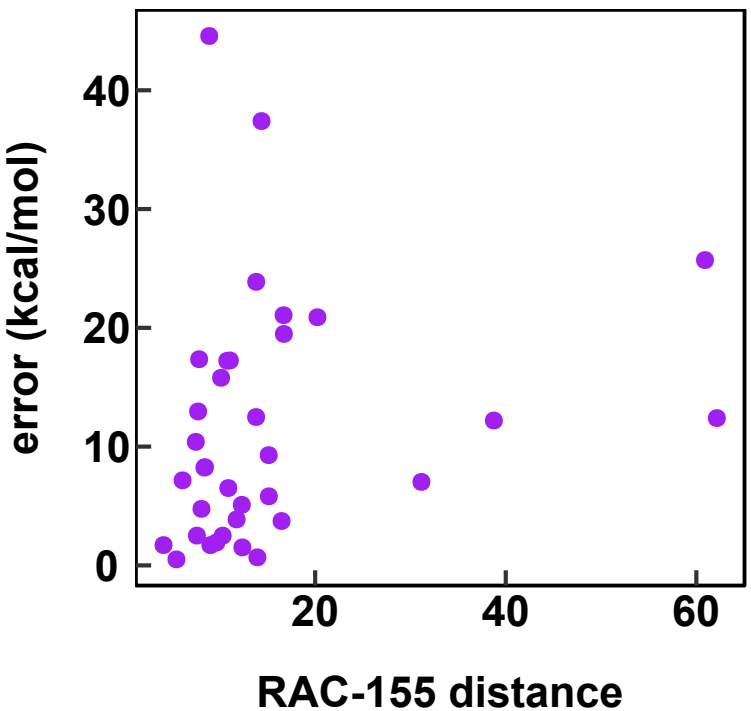

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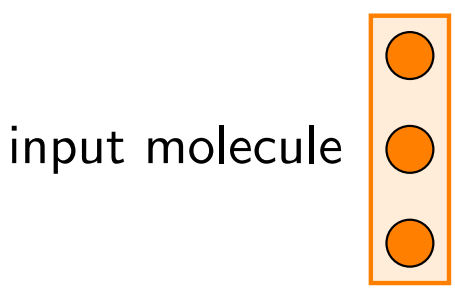

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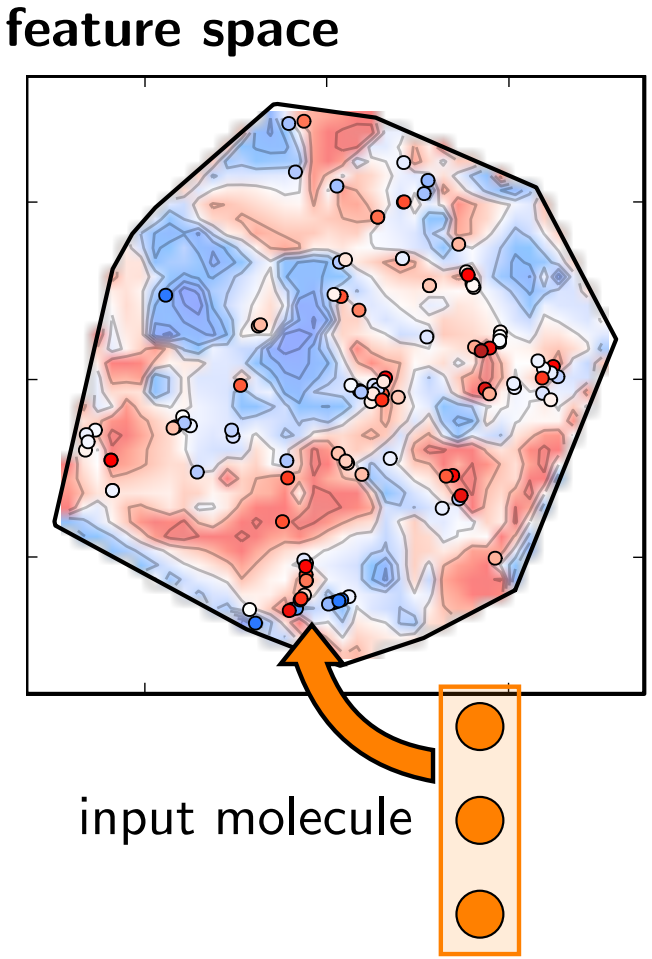

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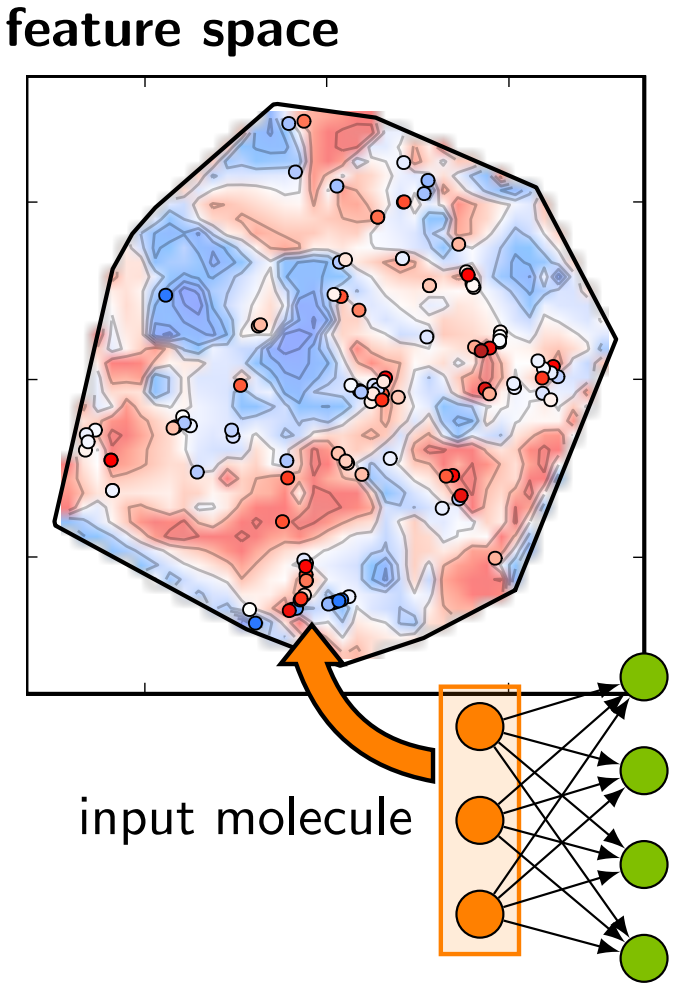

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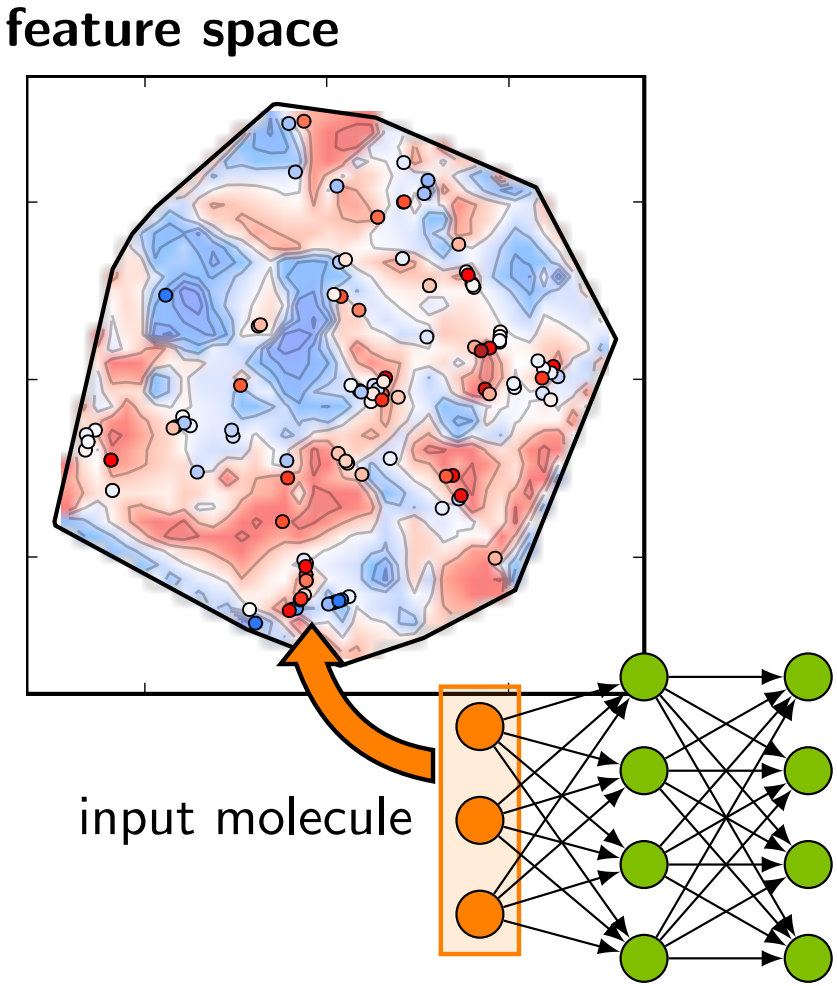

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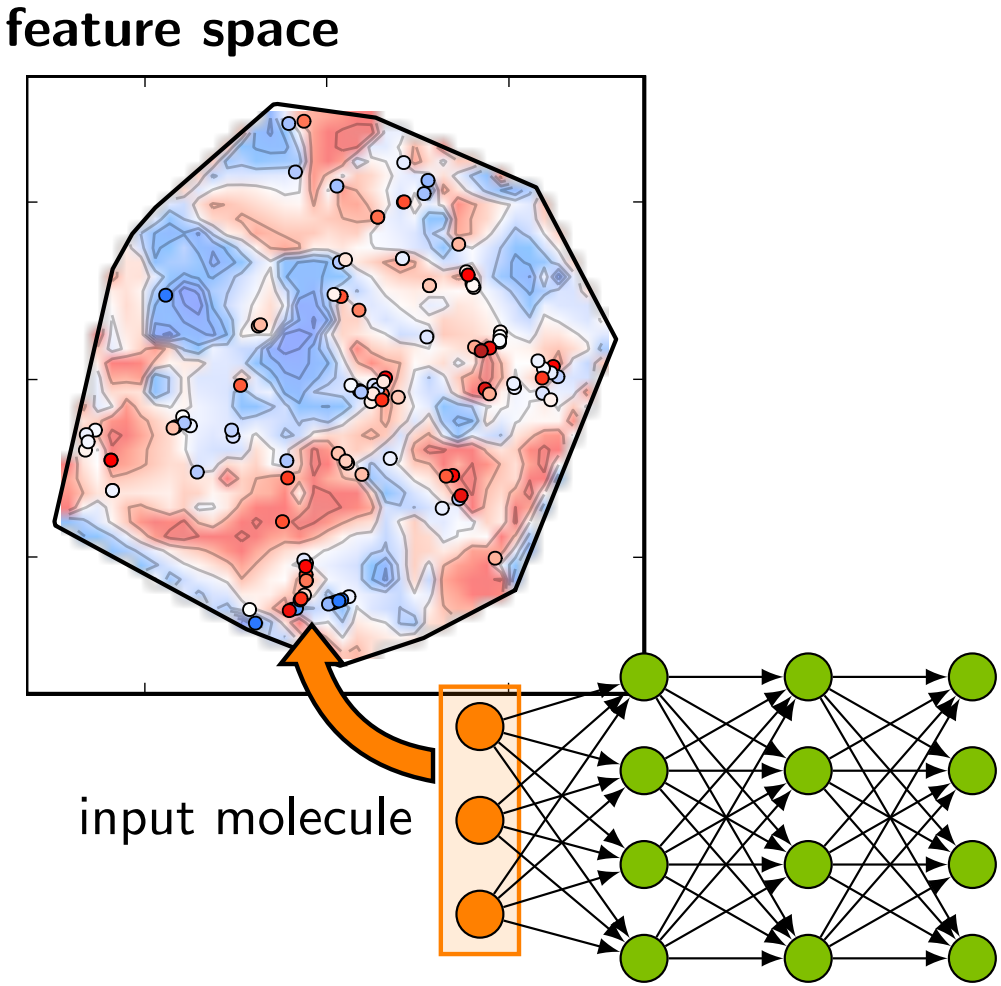

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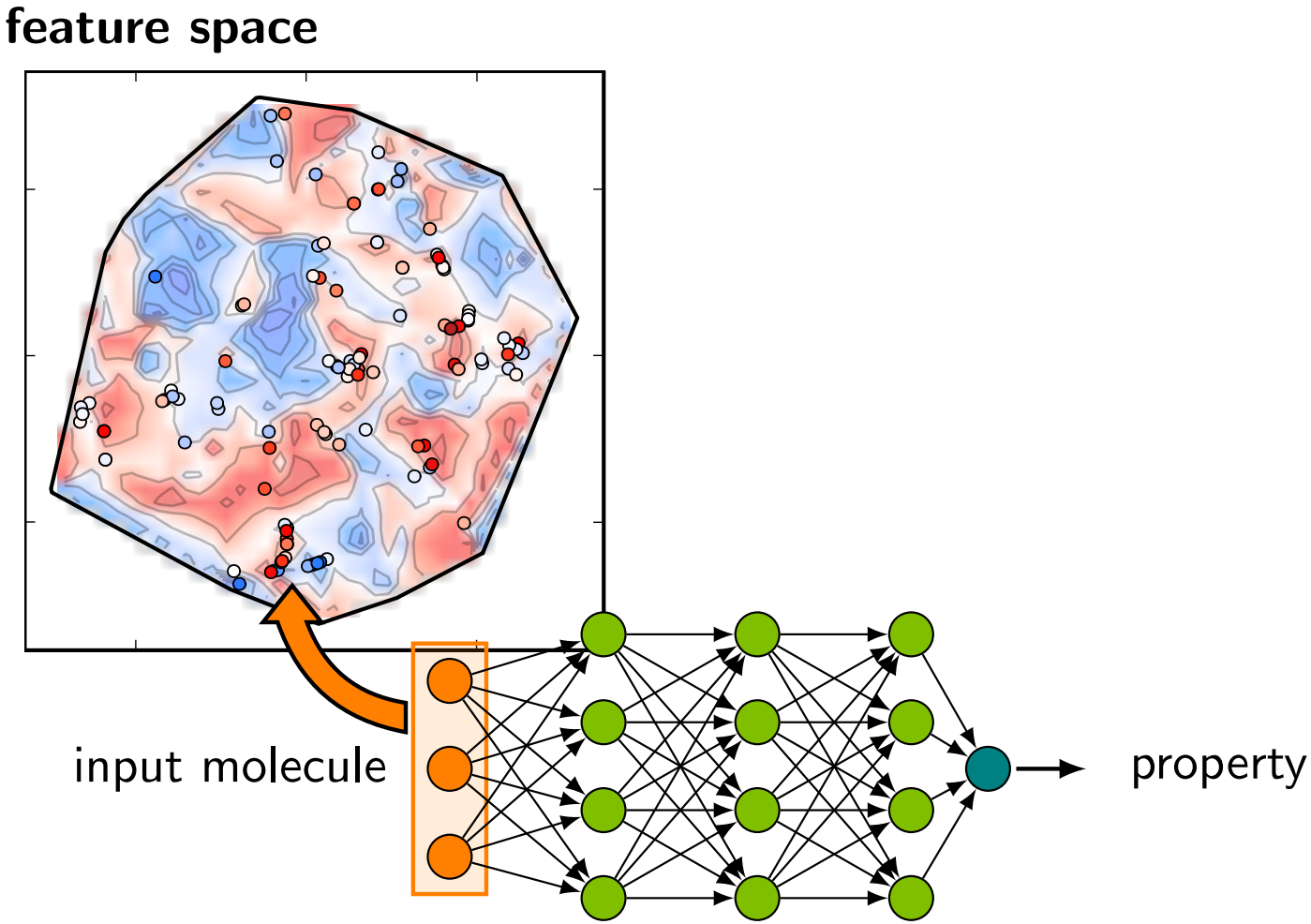

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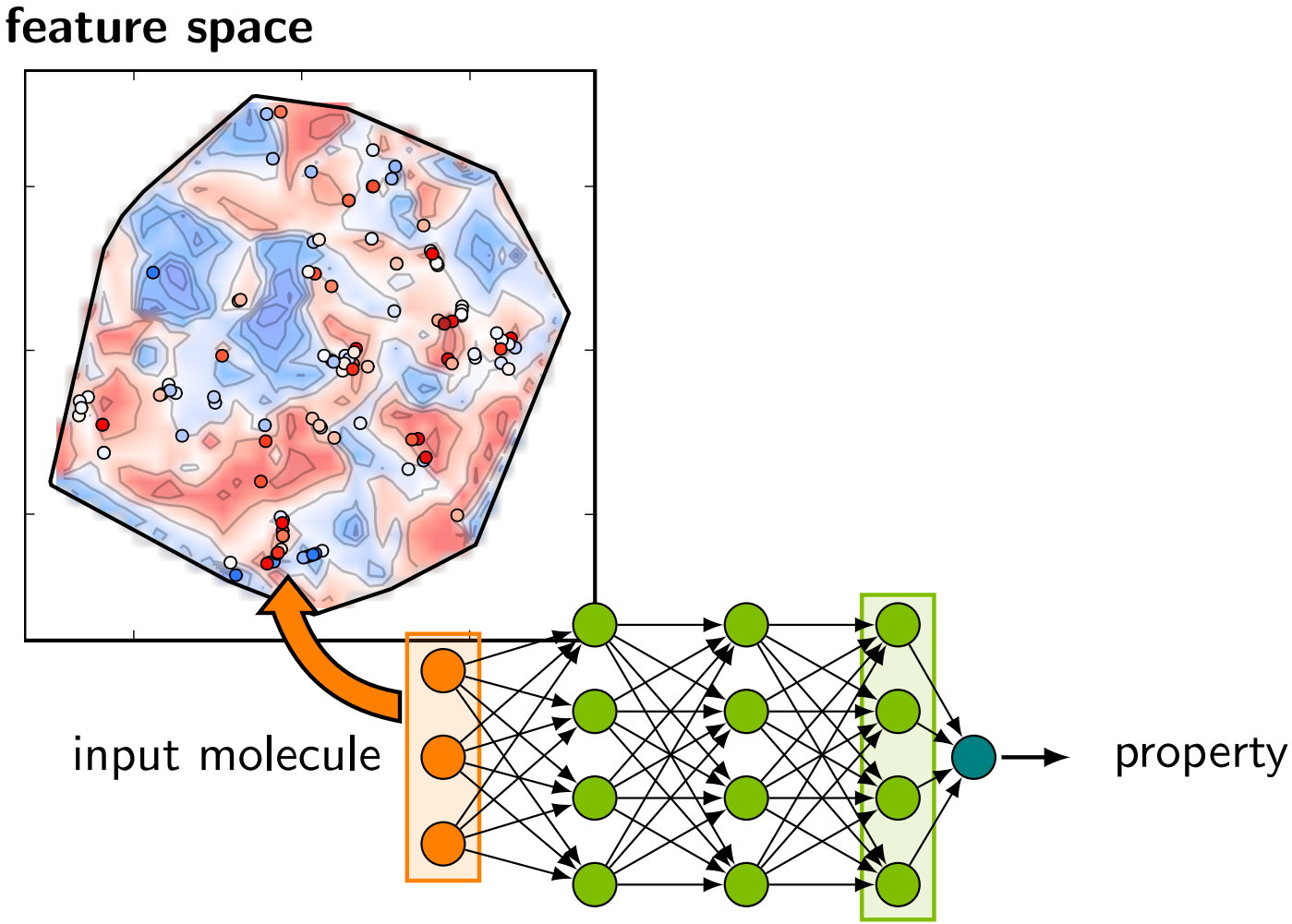

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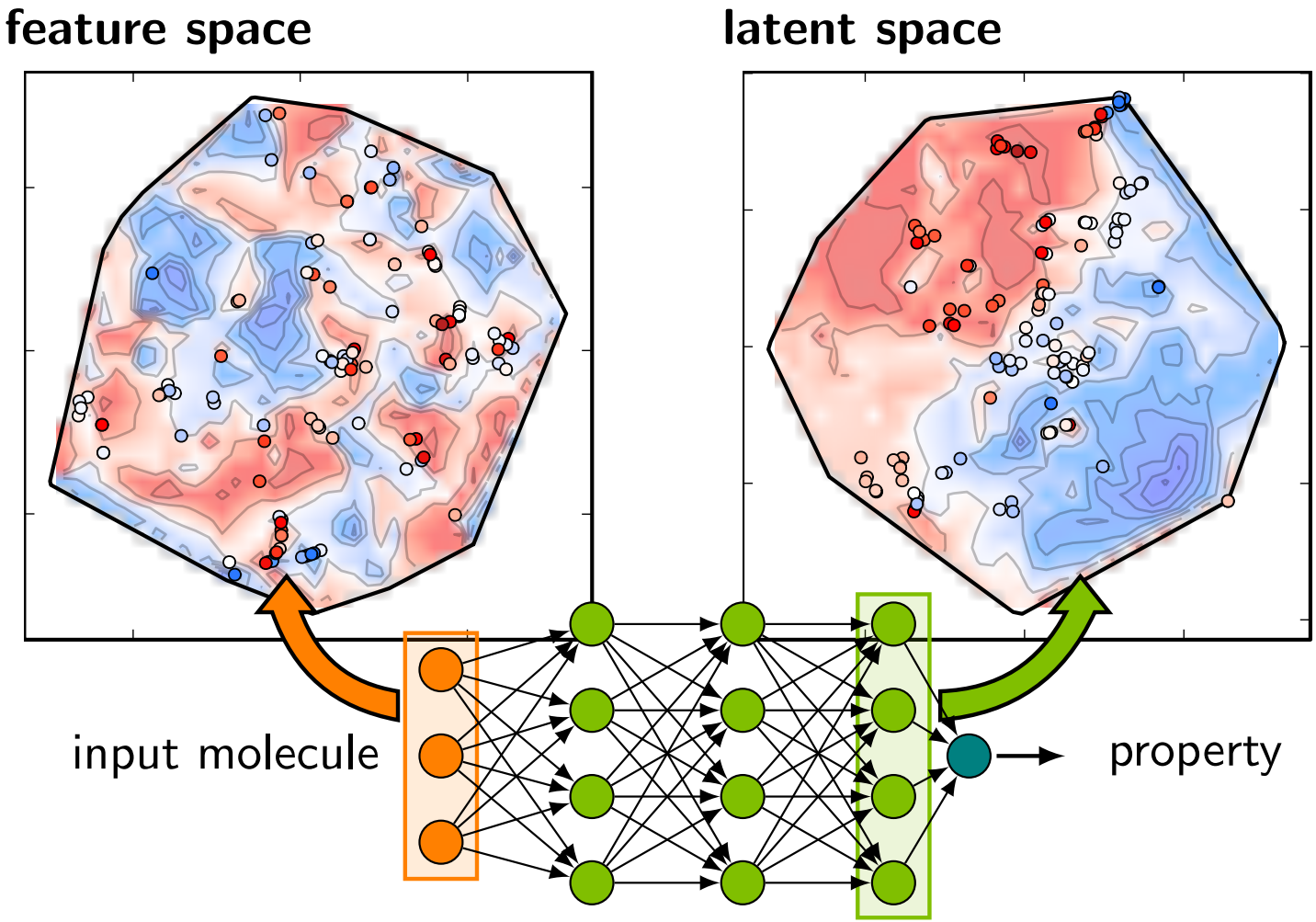

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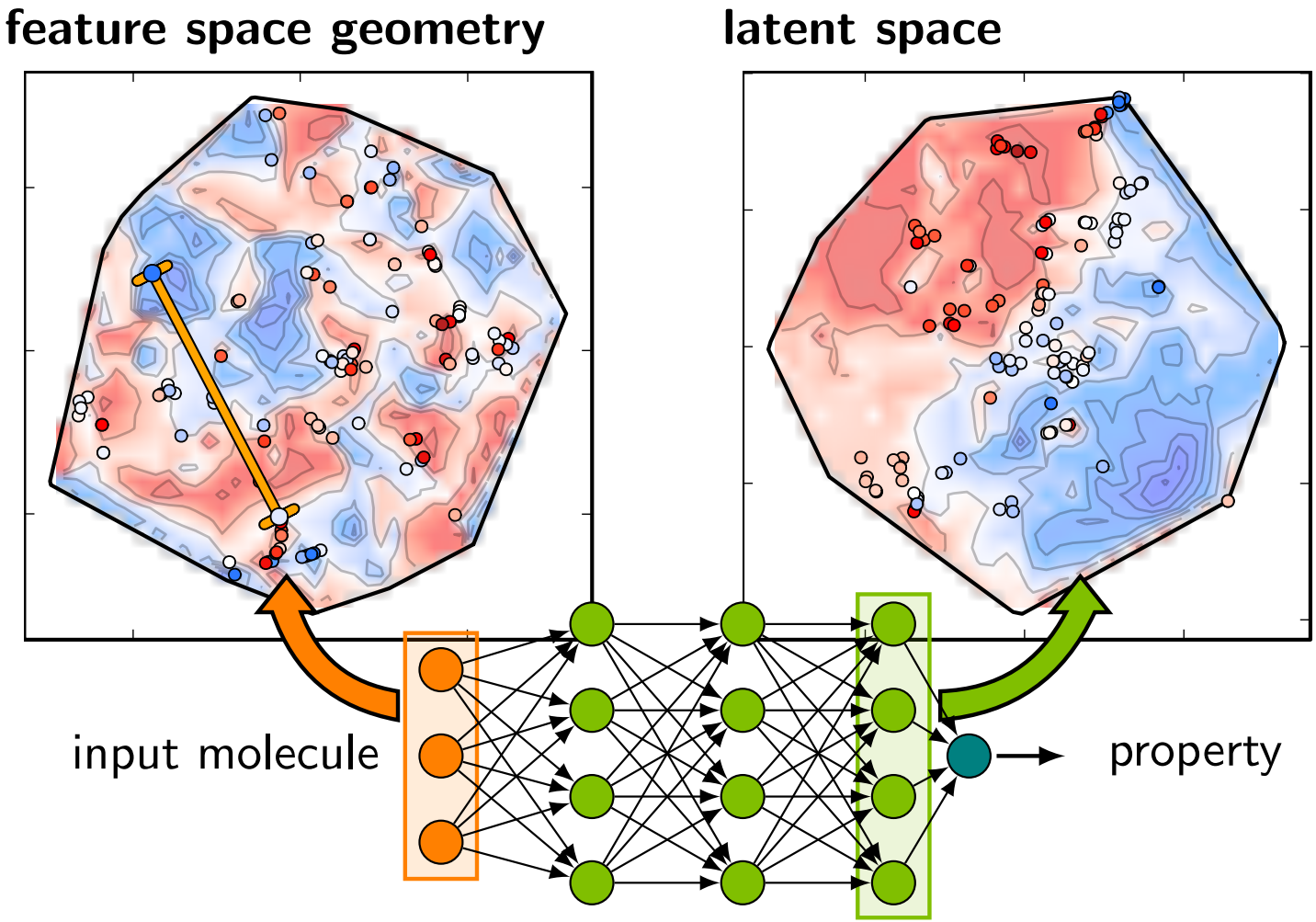

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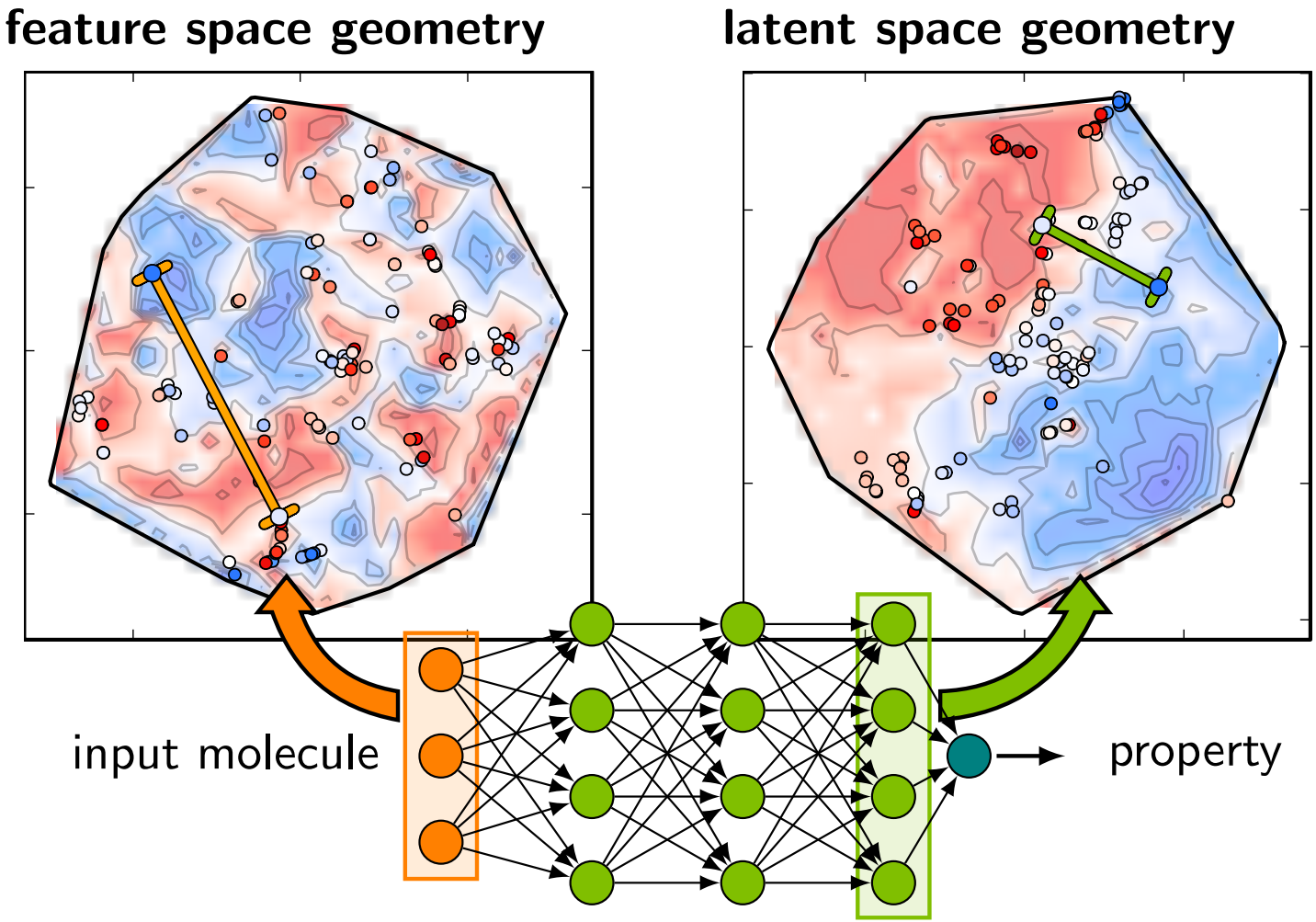

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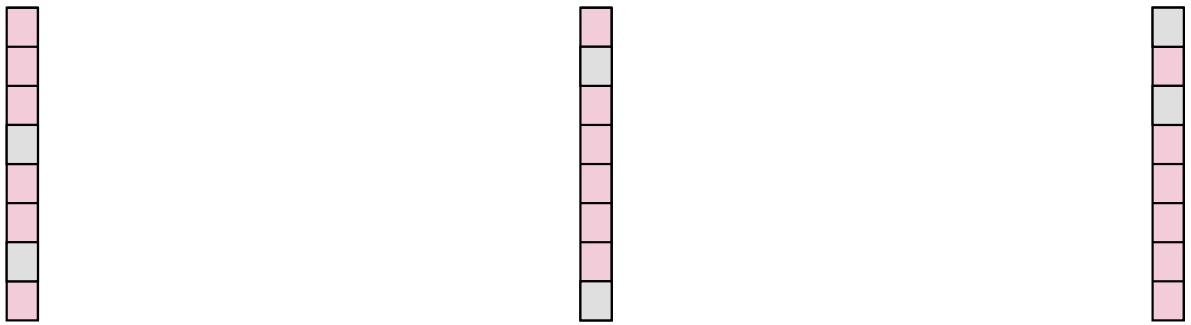

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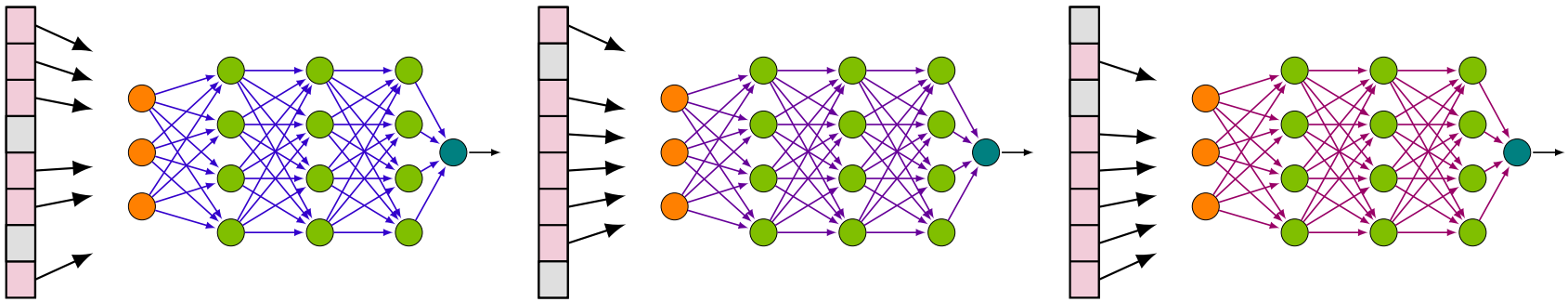

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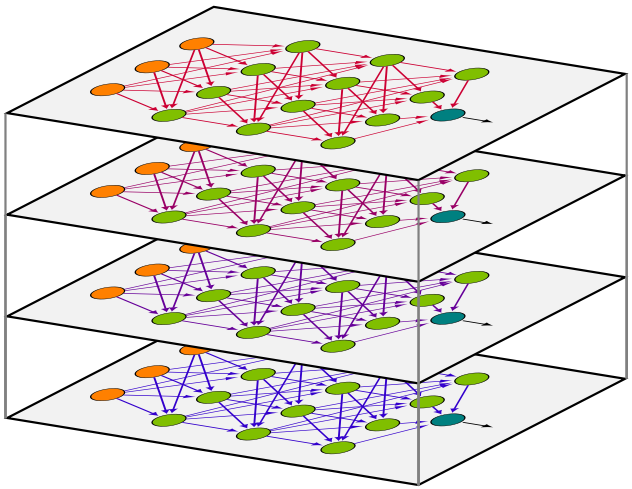

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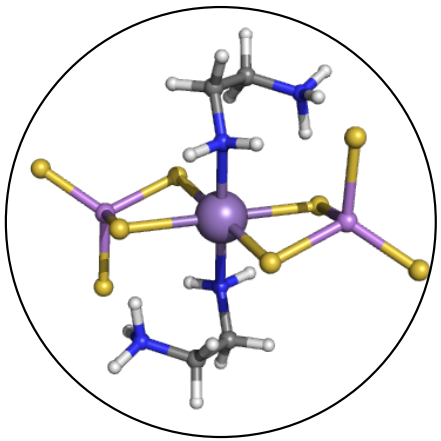

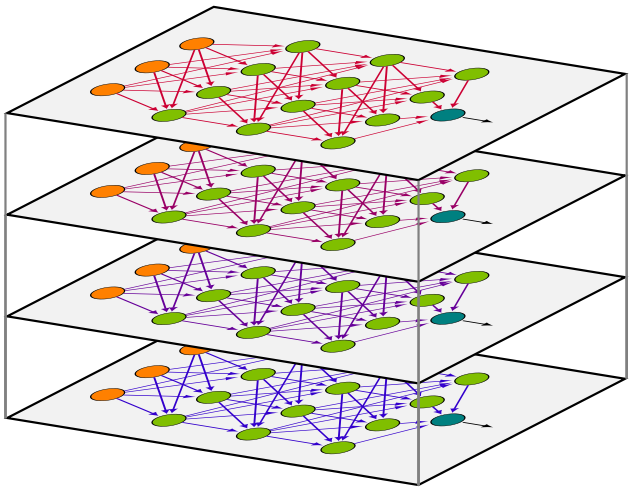

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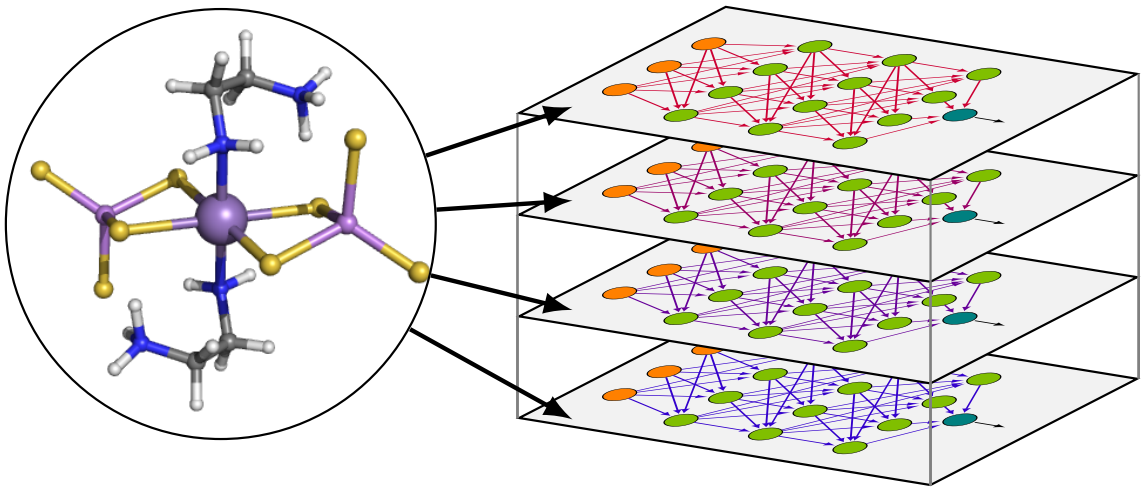

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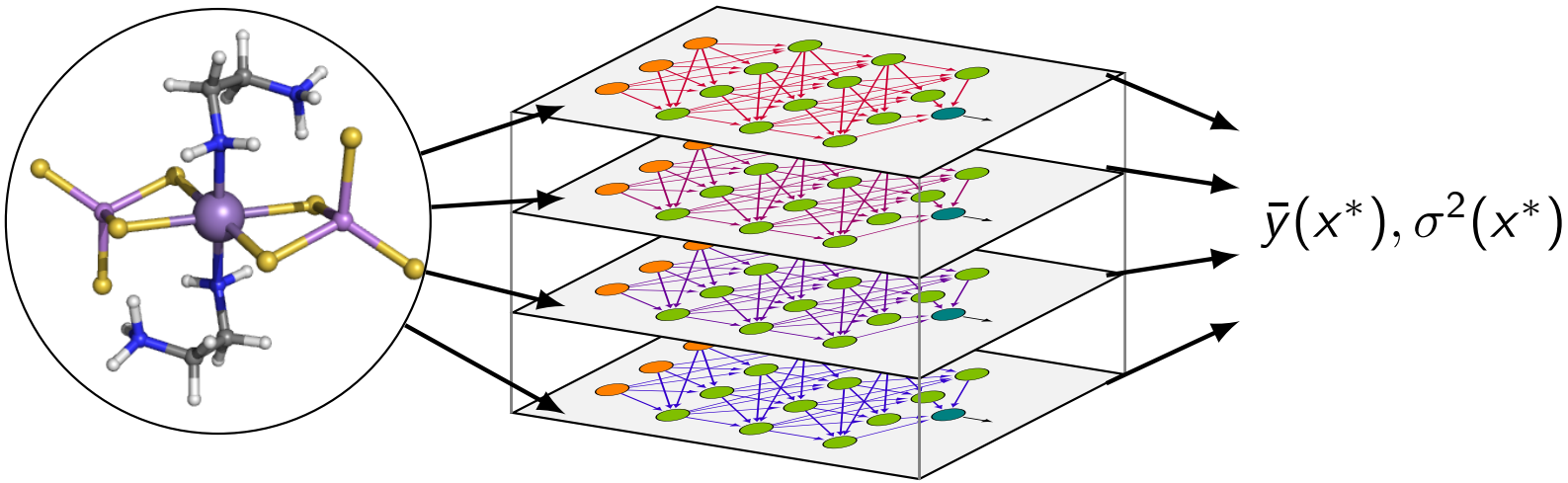

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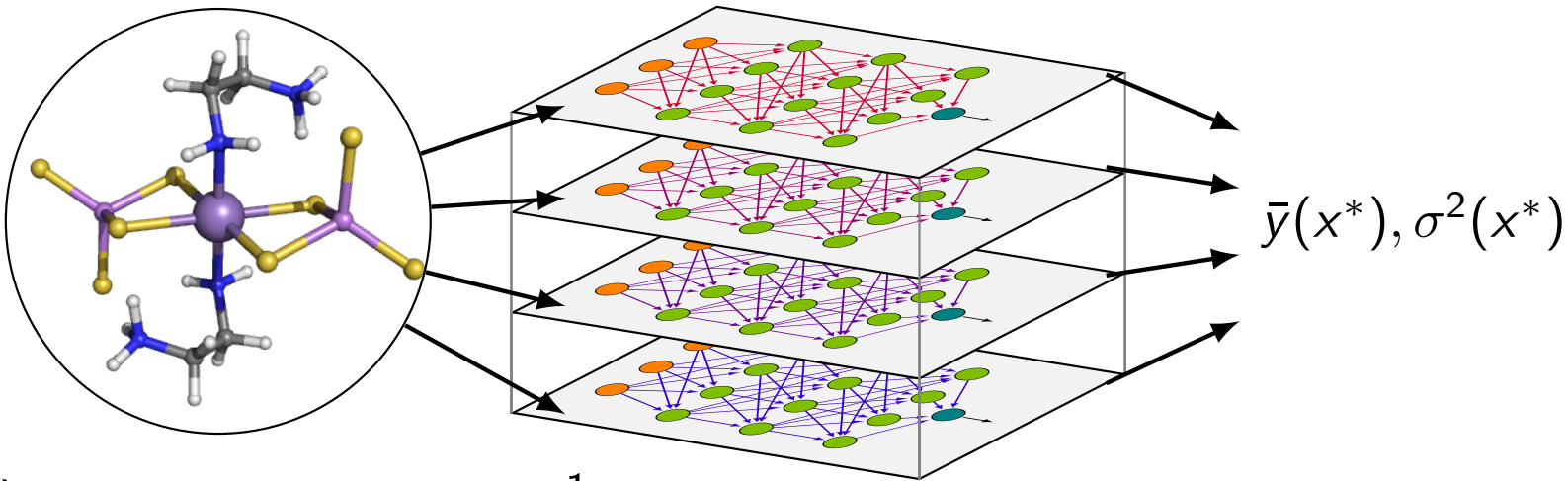

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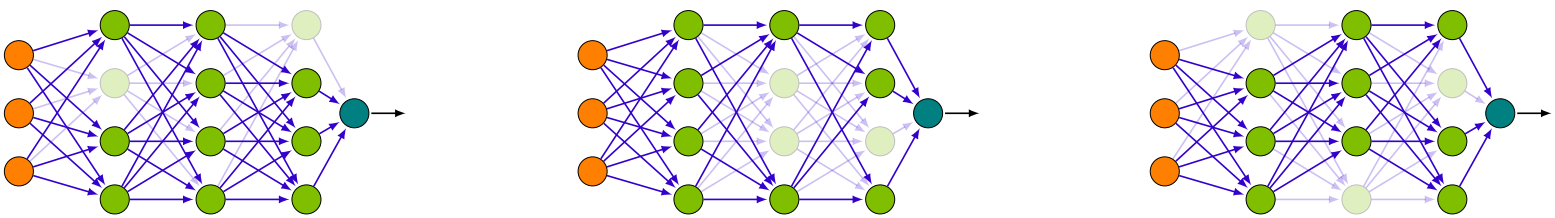

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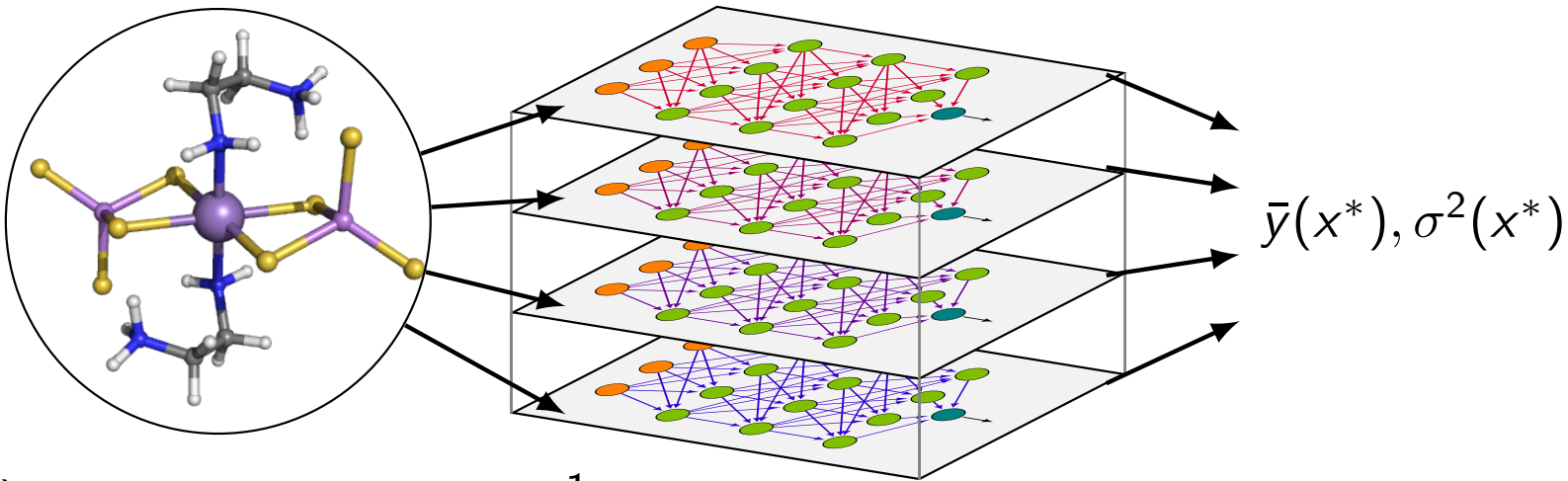

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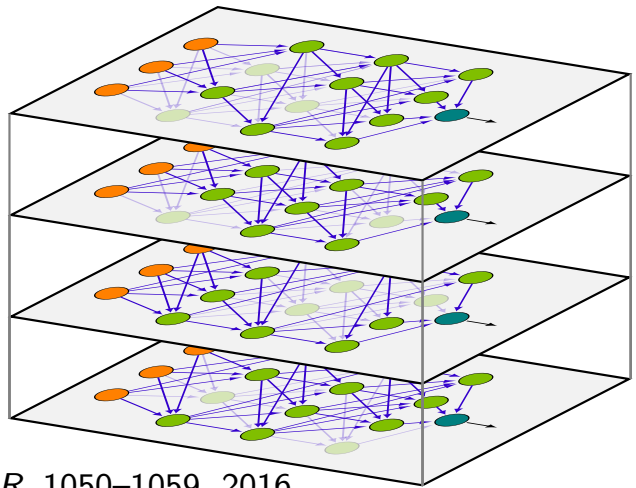

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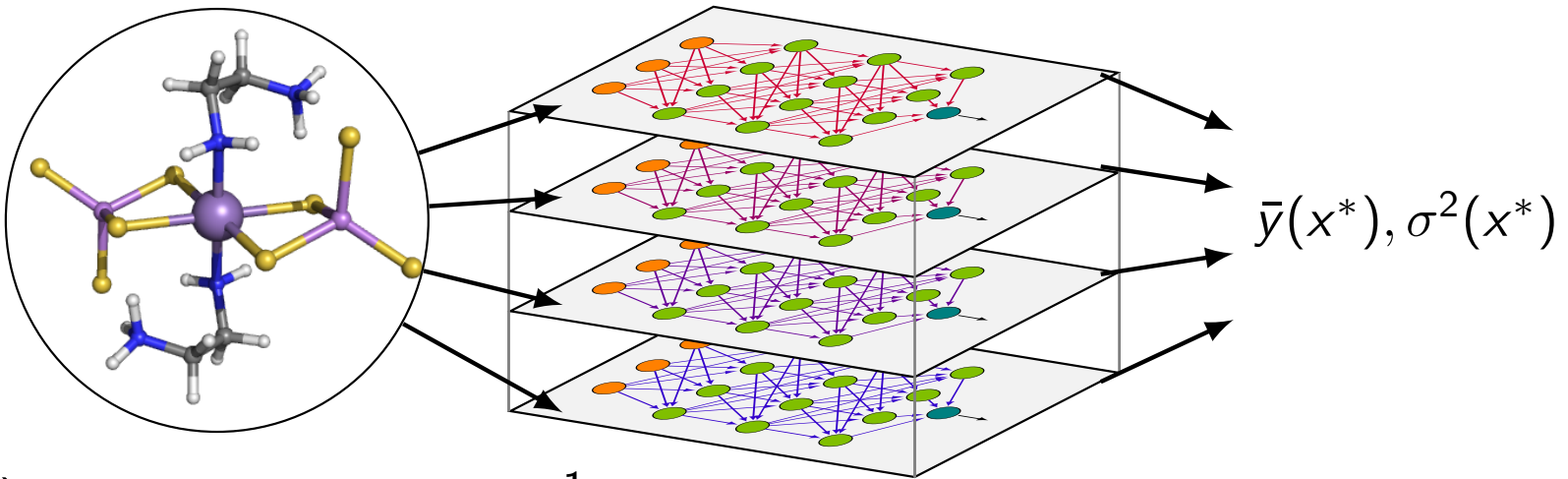

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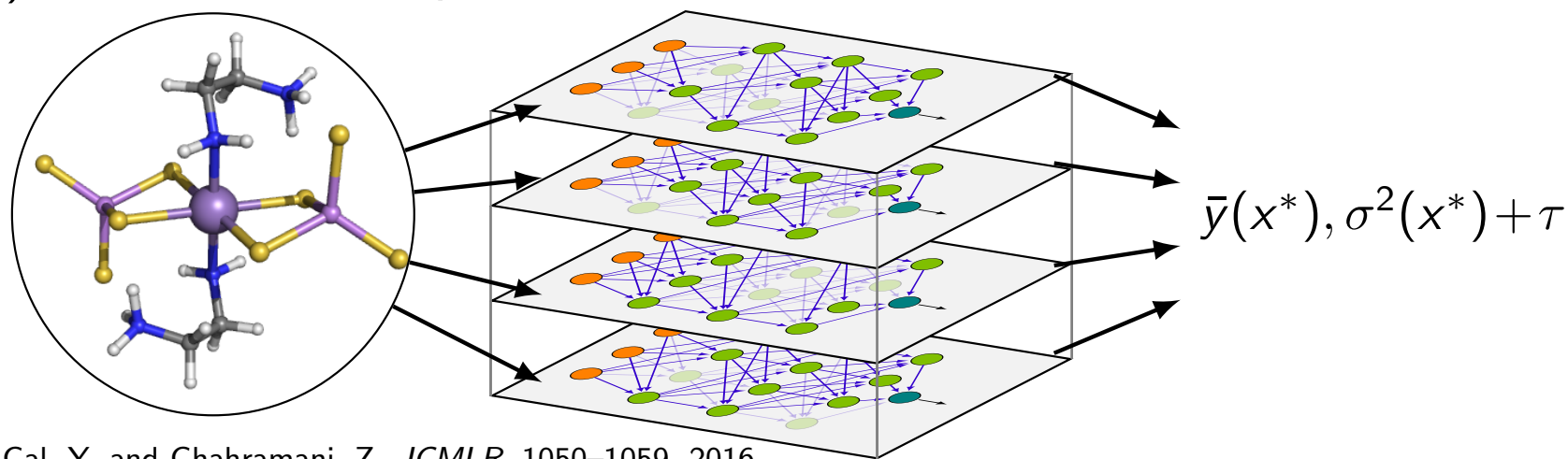

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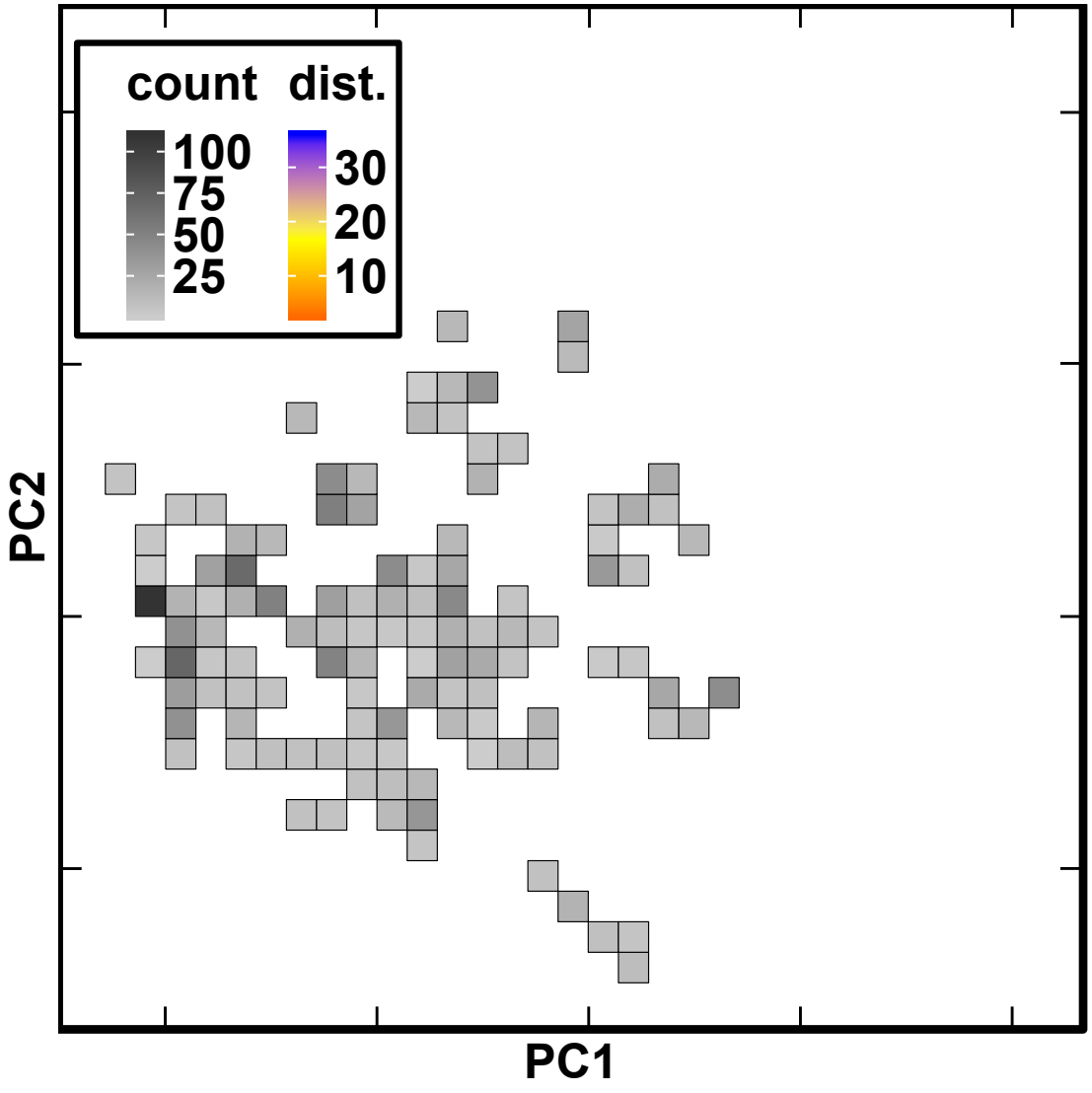

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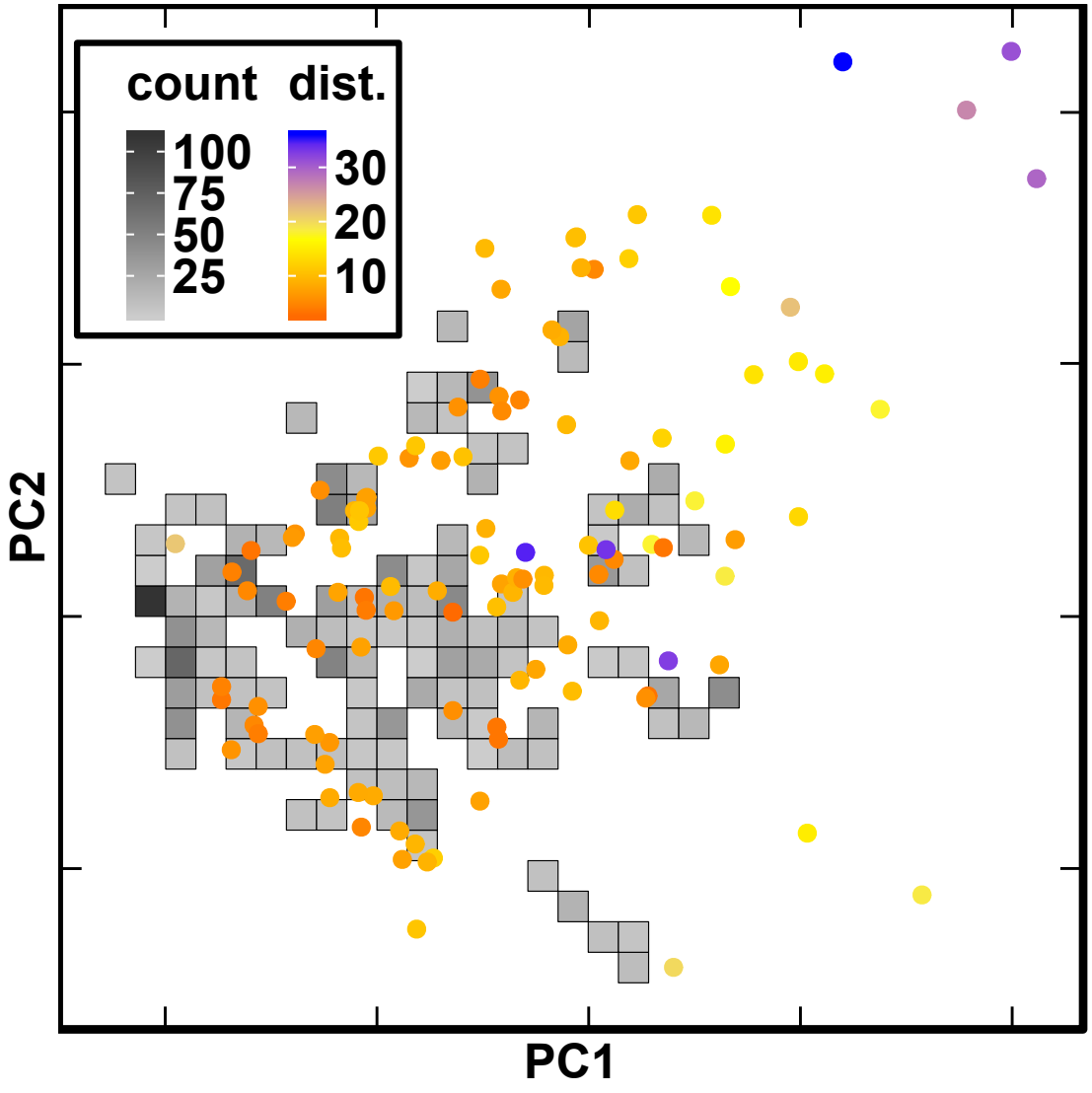

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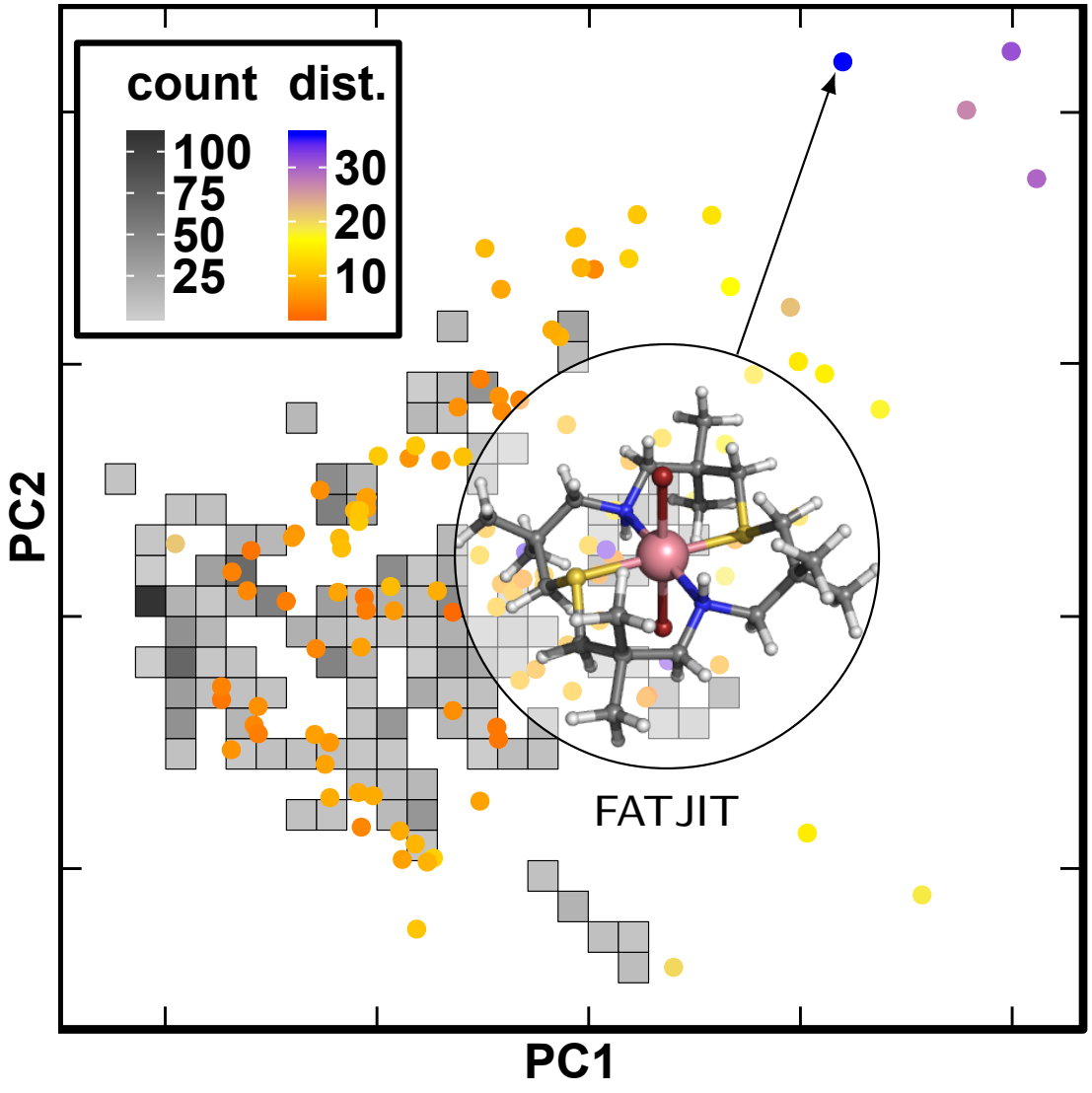

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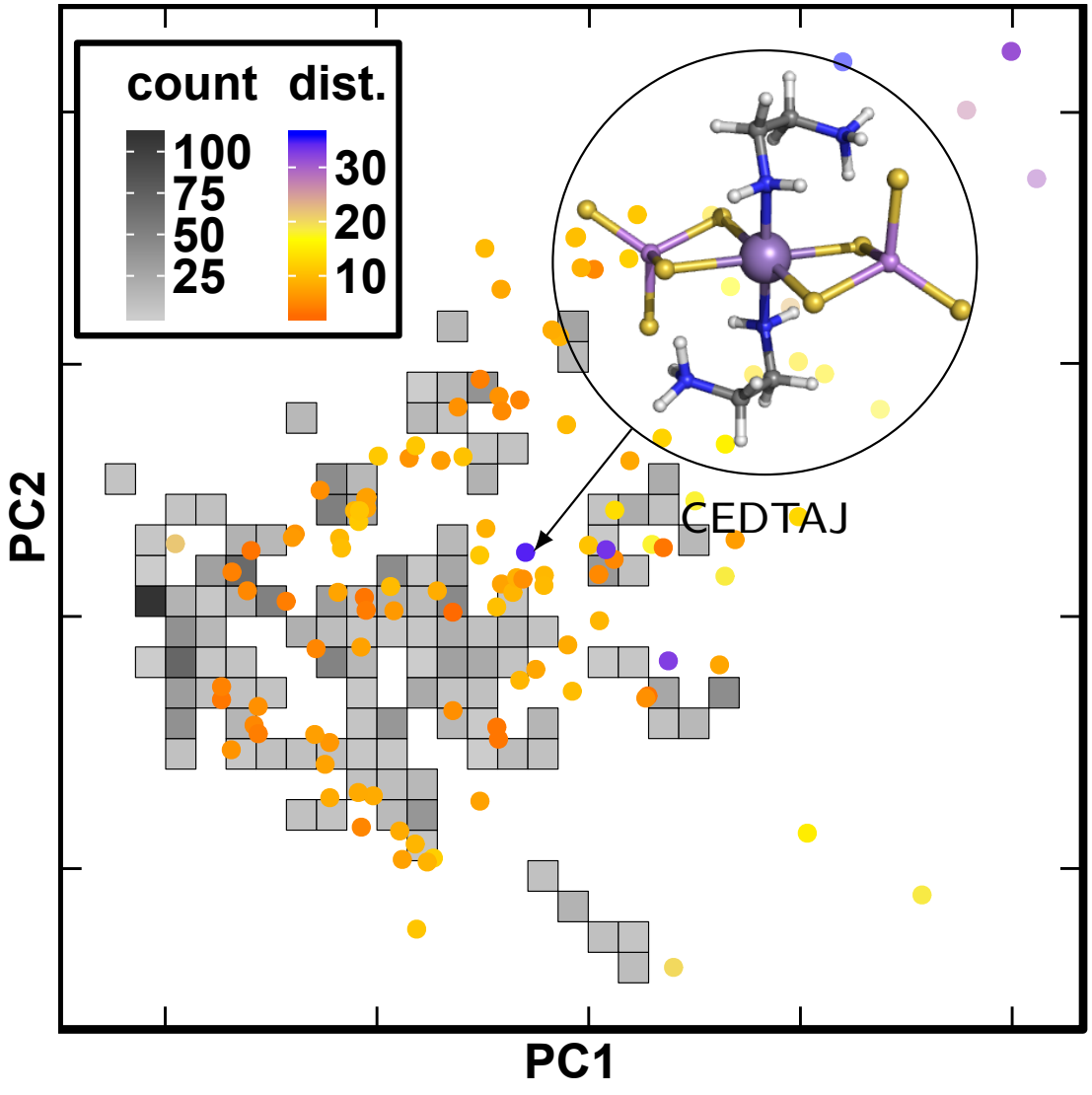

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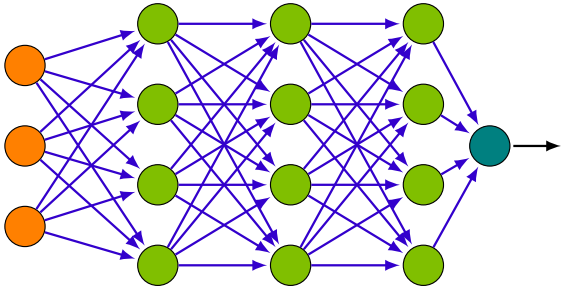

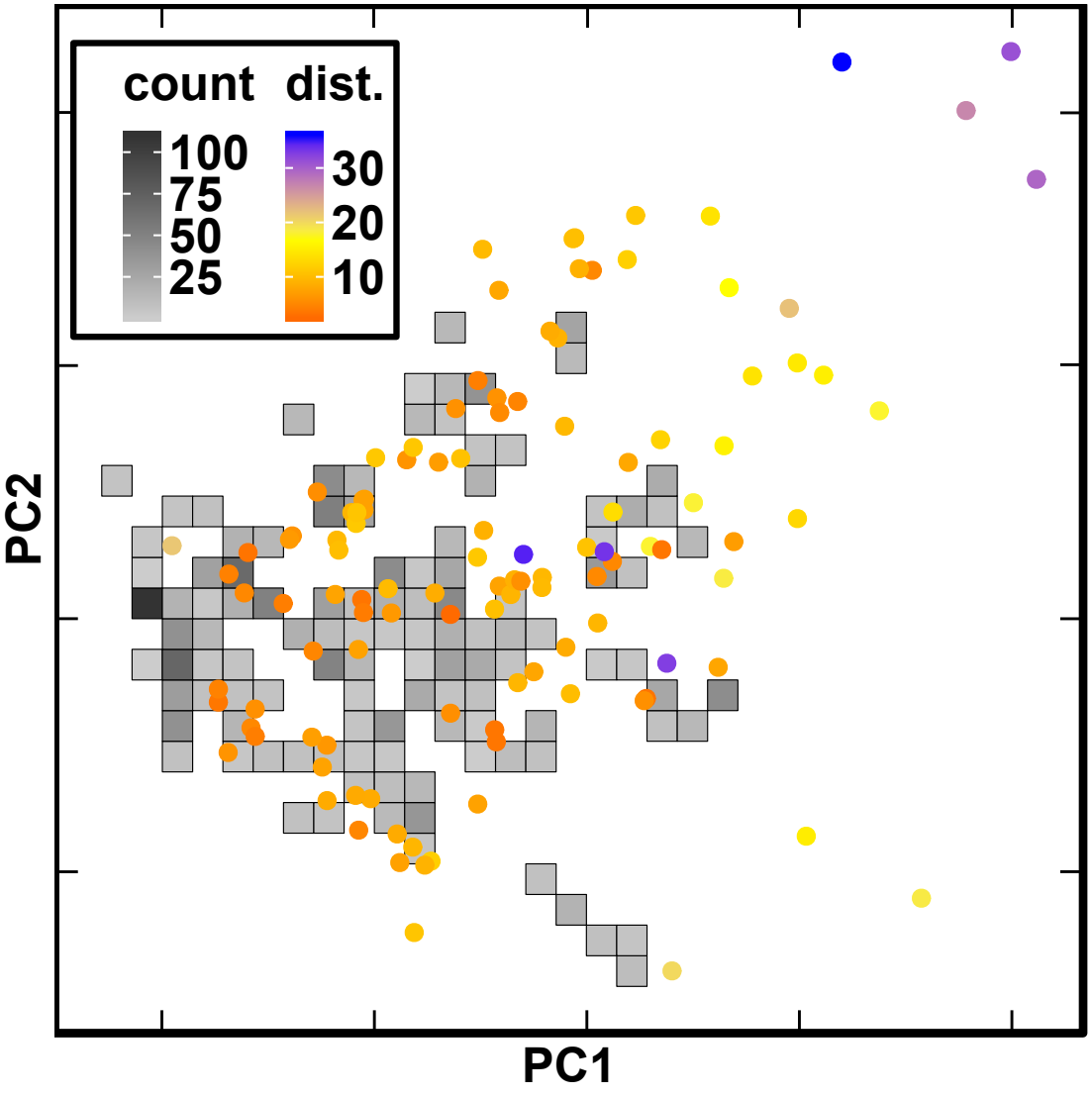

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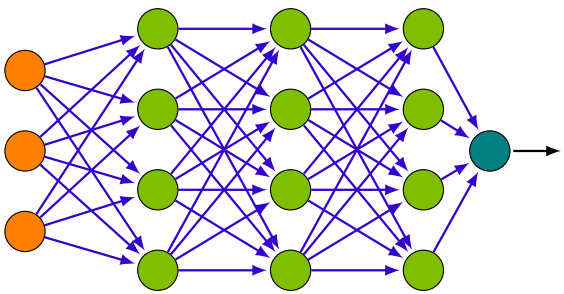

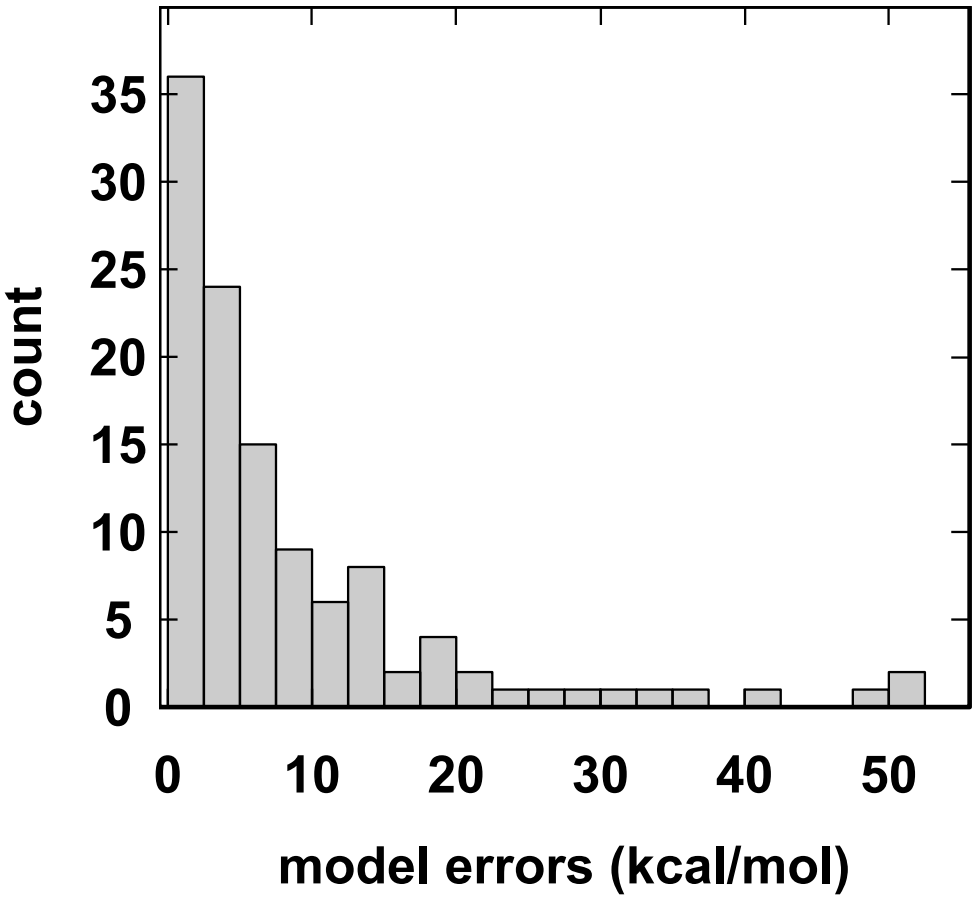

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Key questions:

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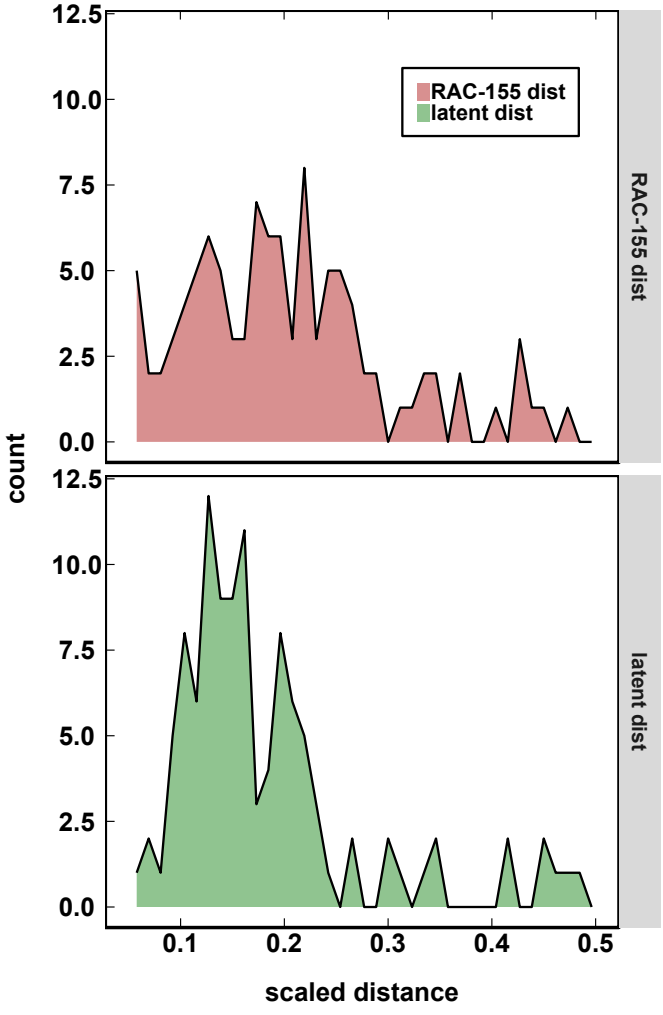

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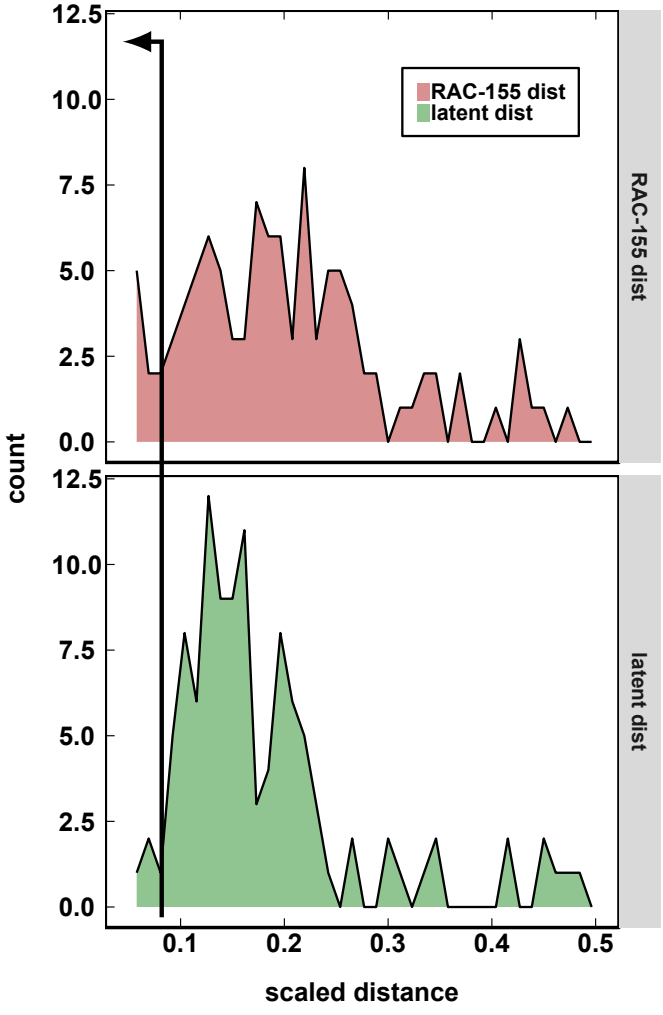

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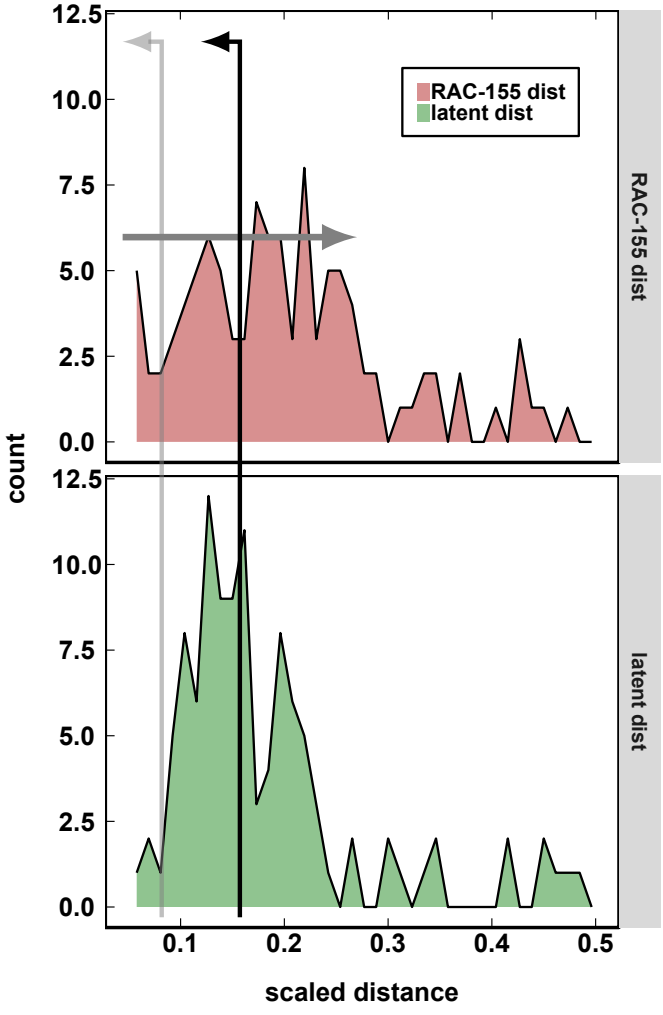

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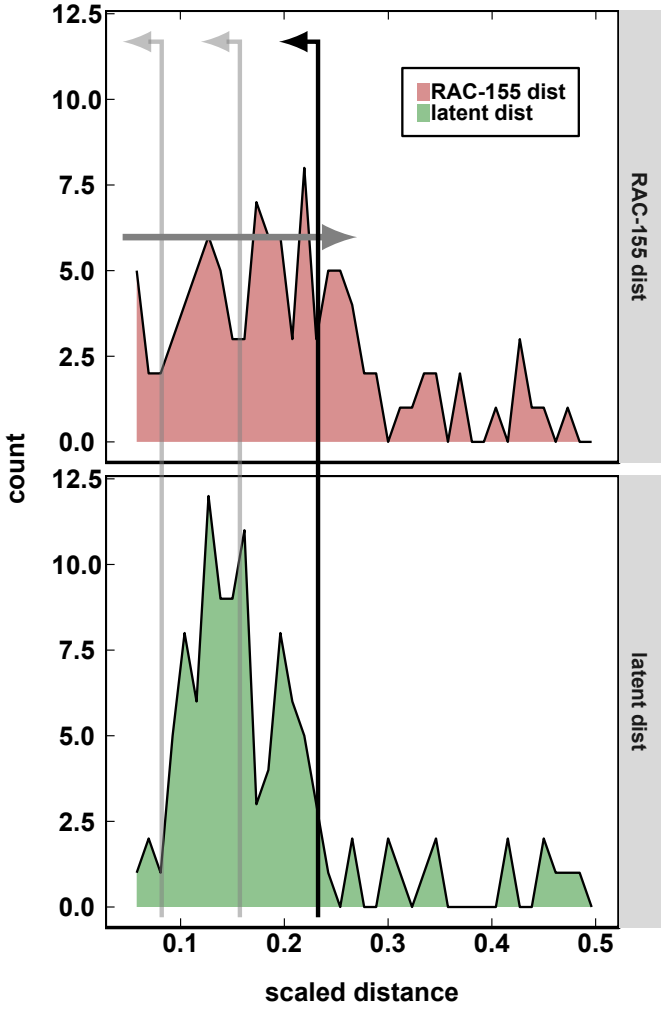

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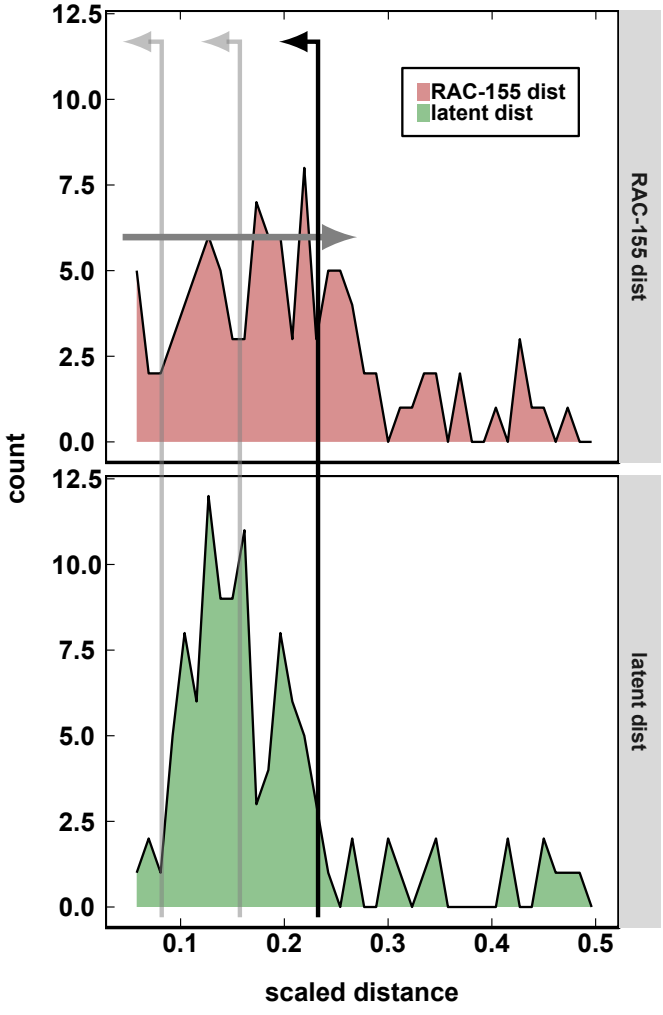

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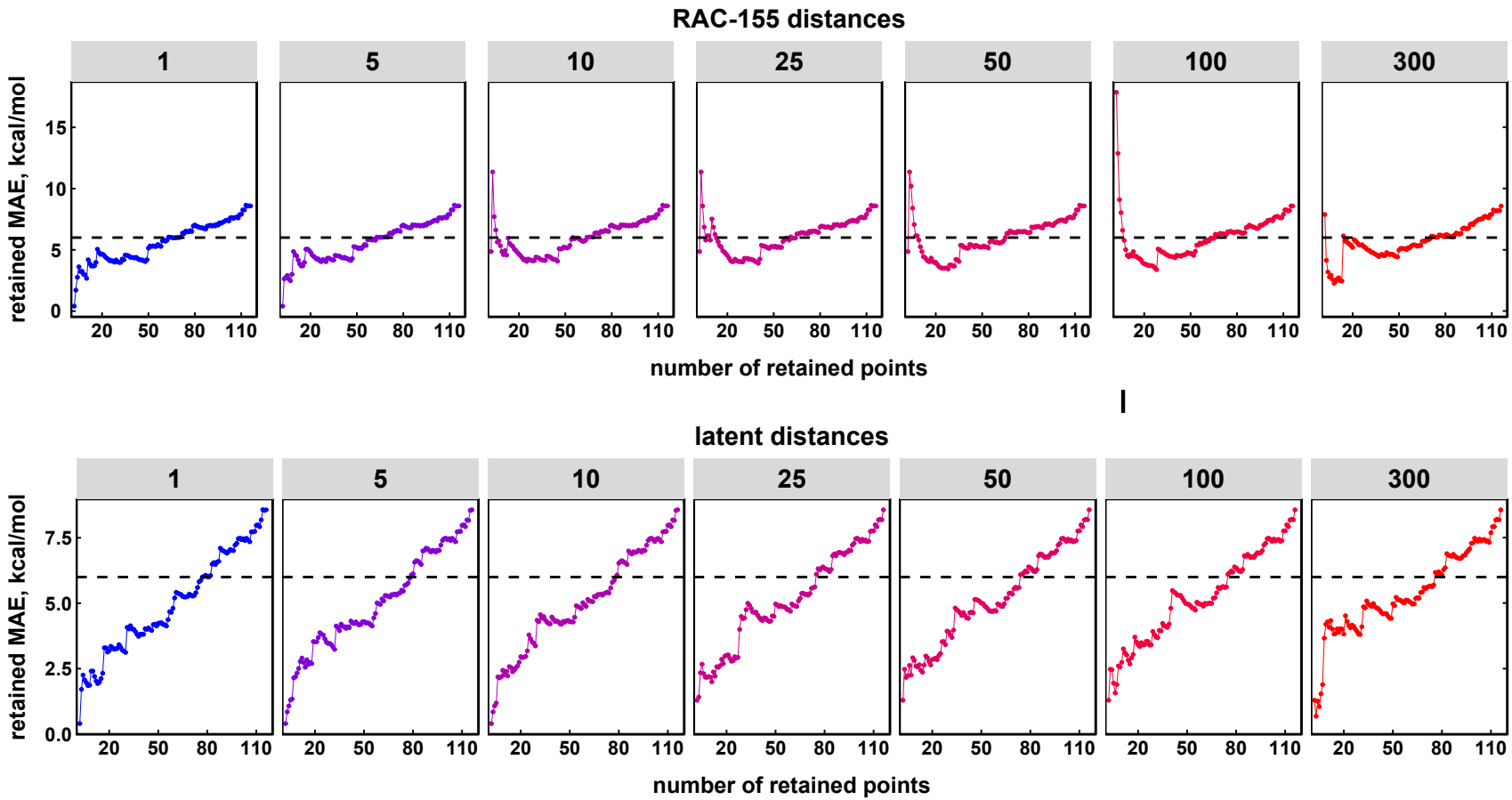
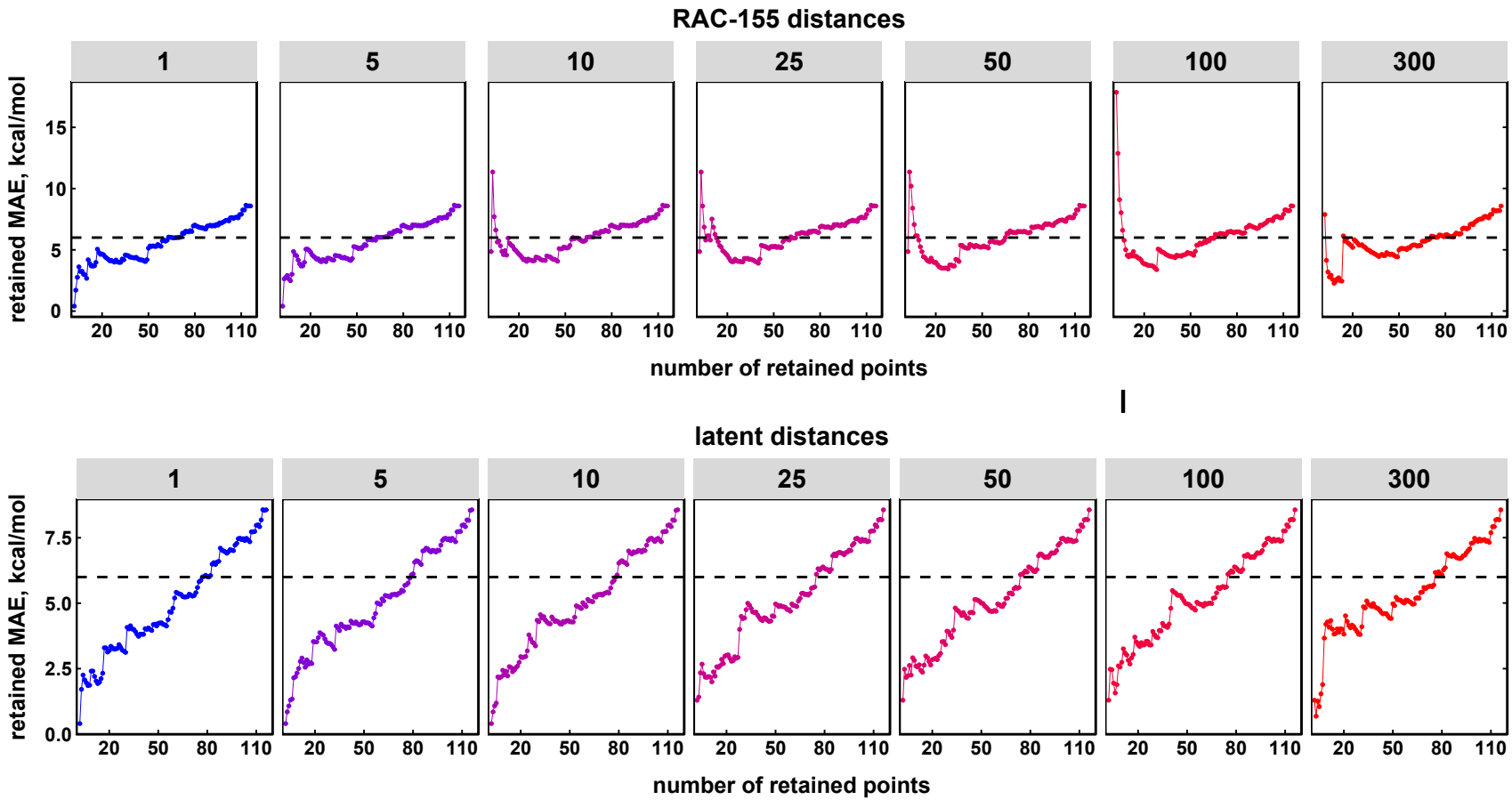


Which distance to measure

We choose to average over 10 neighbors, insensitive to this choice



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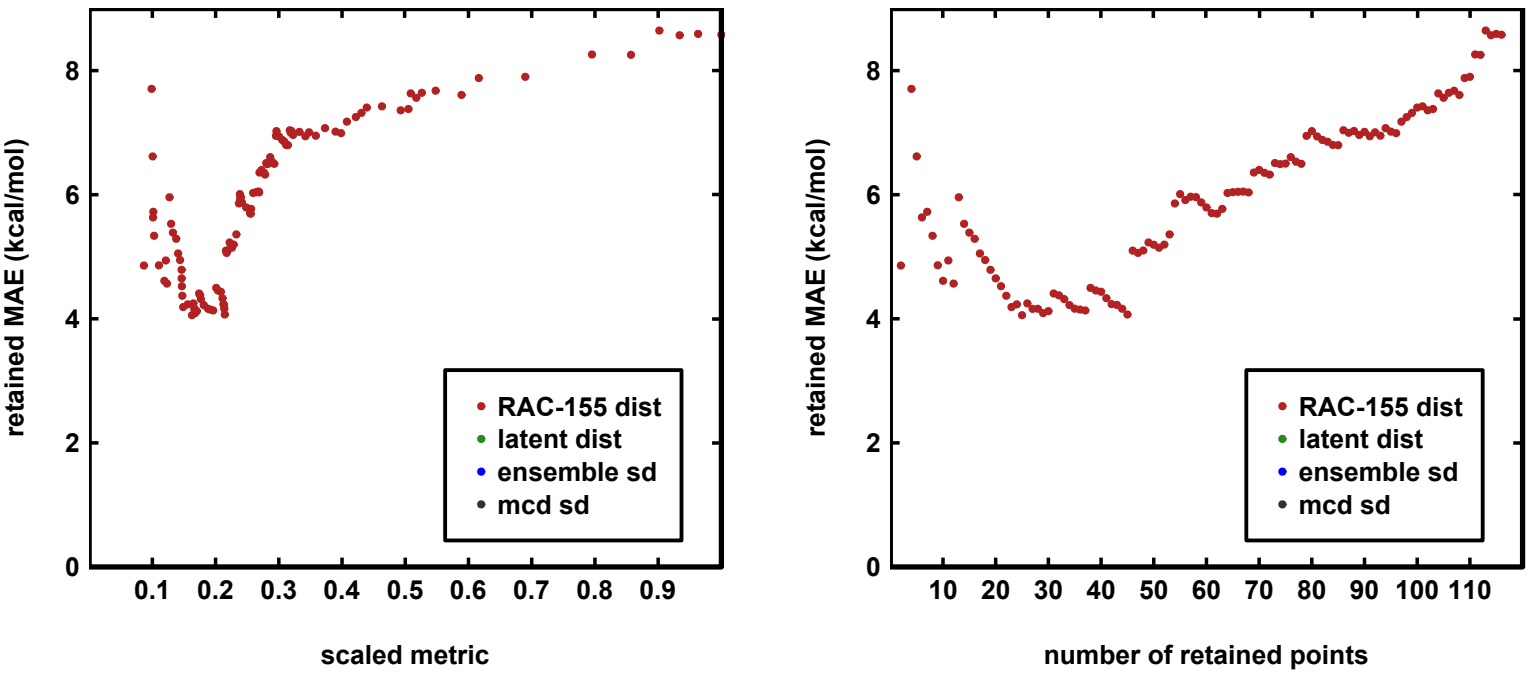

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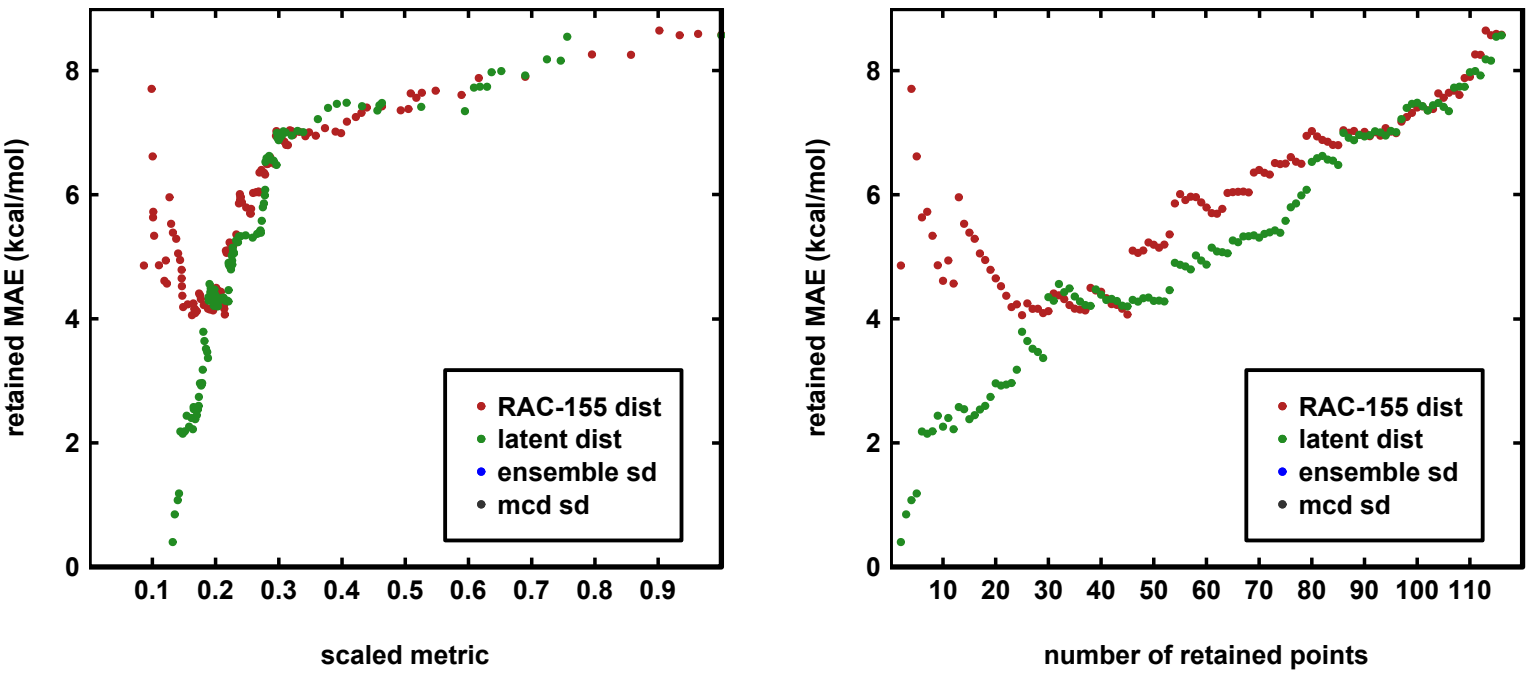

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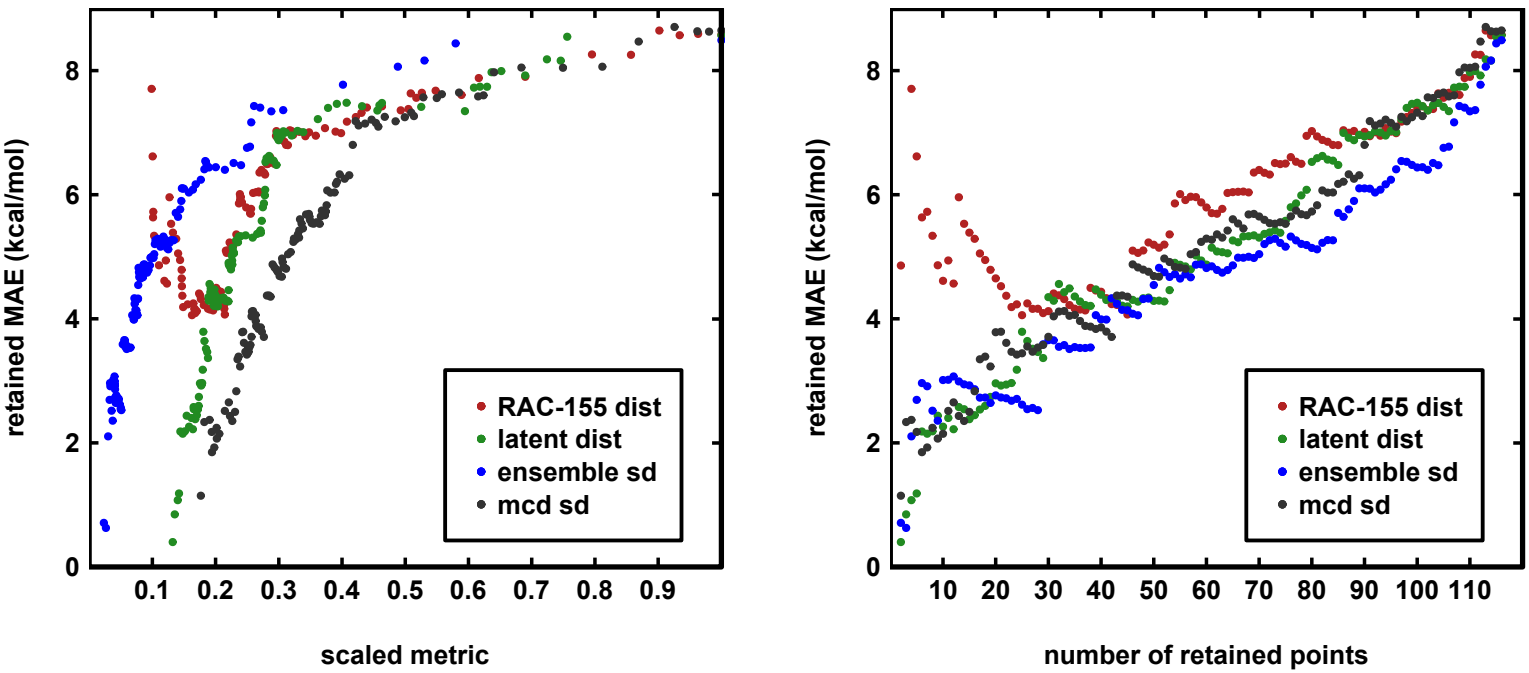

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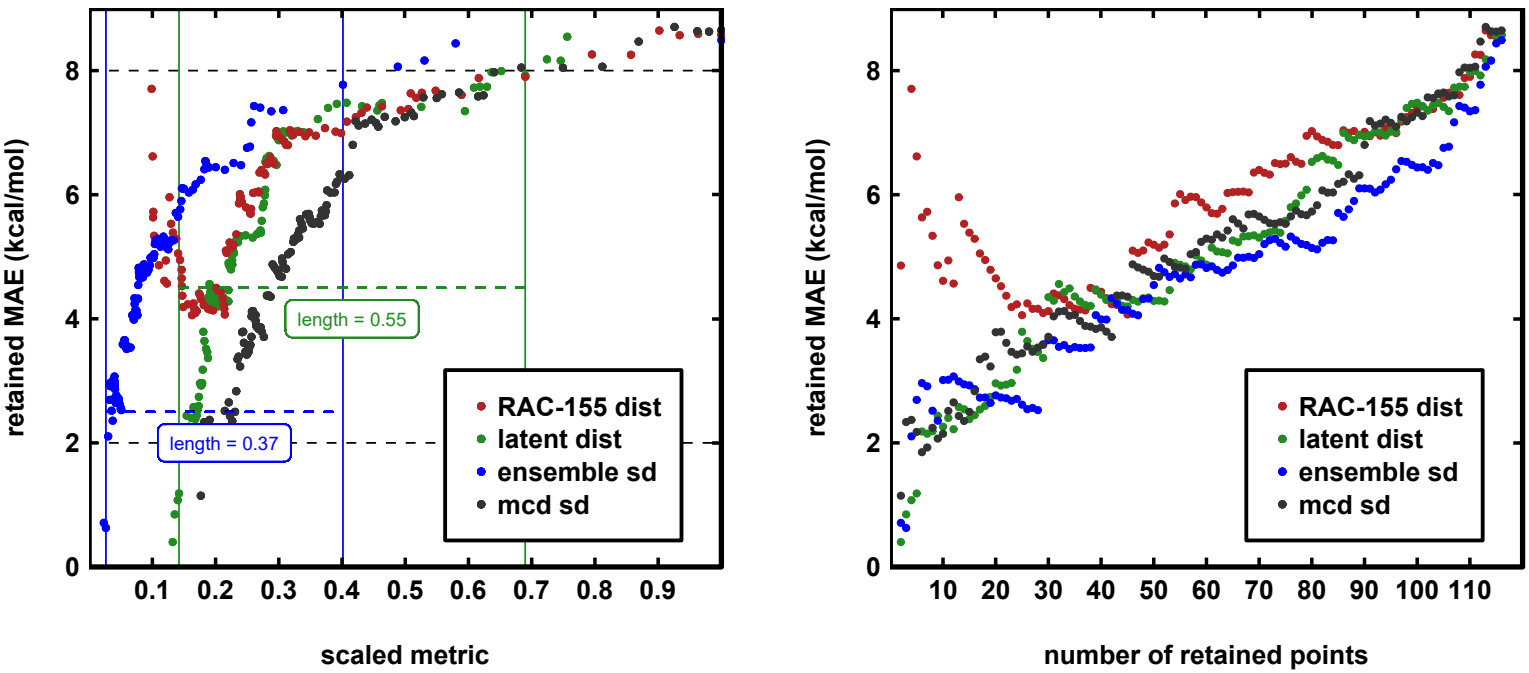

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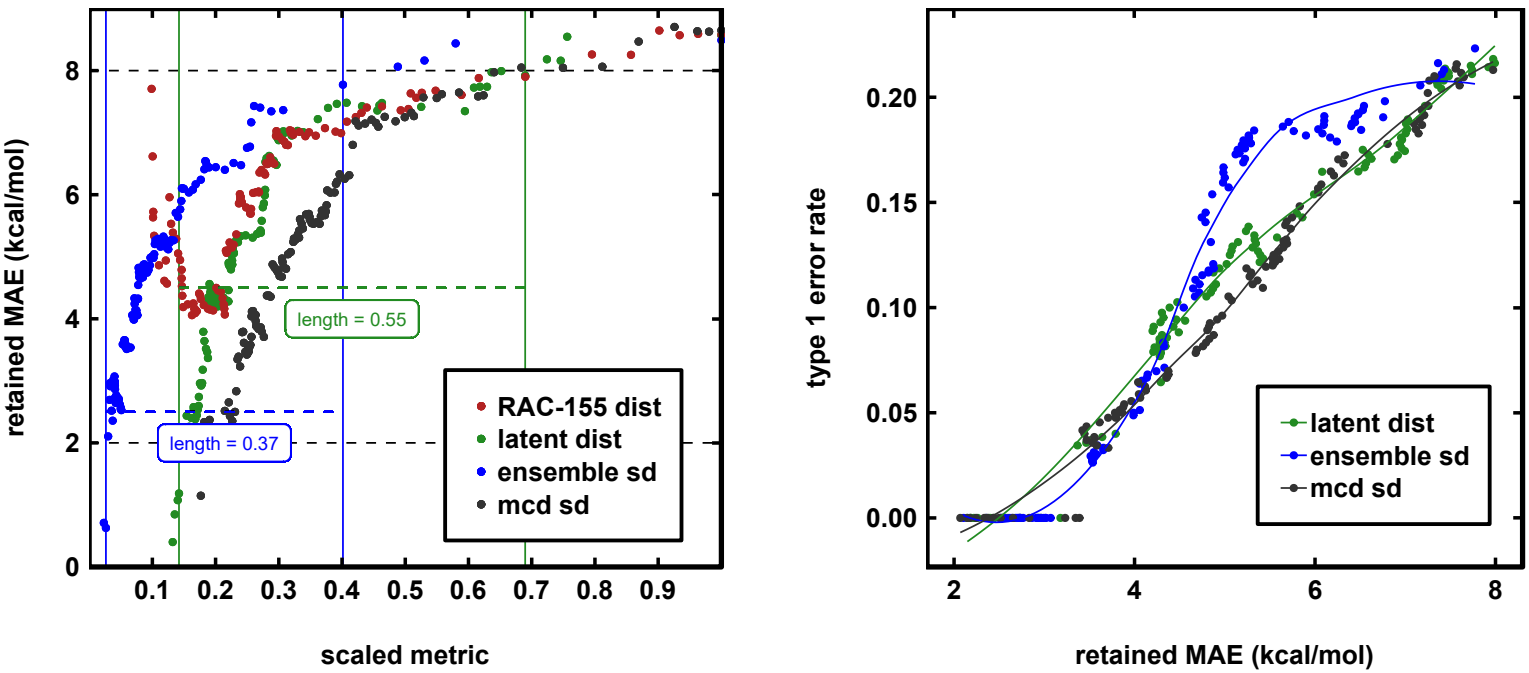

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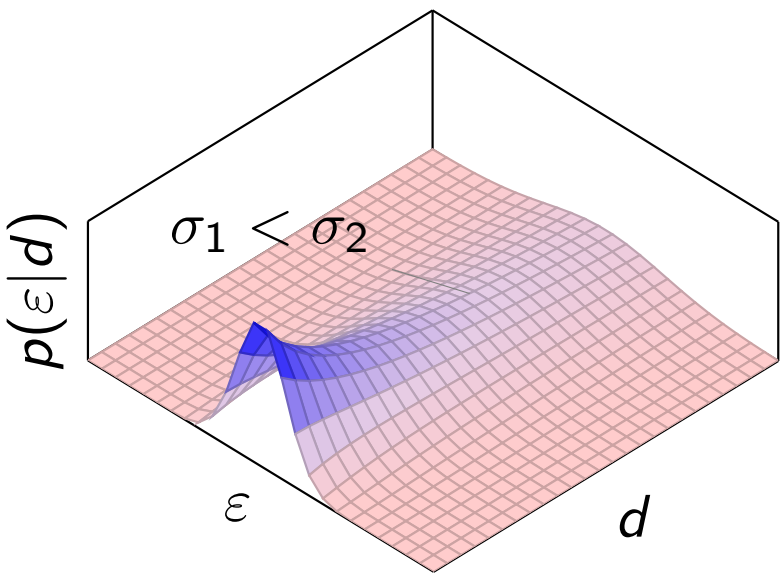

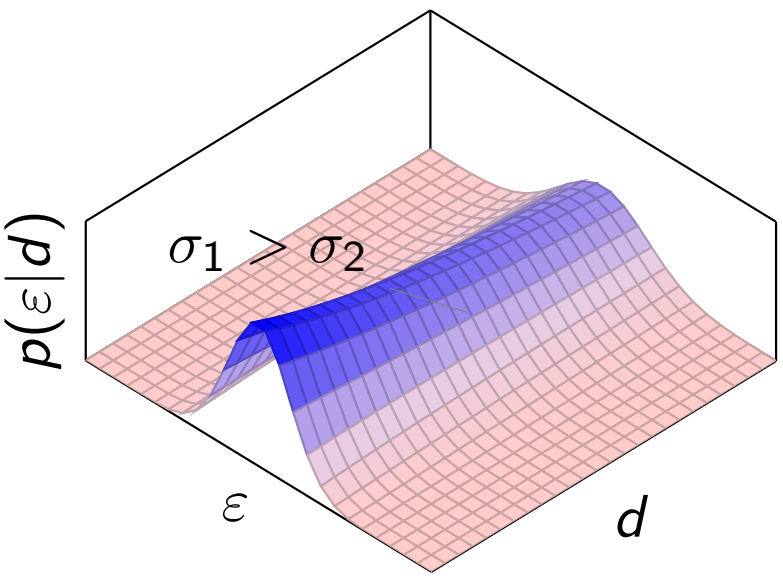

How do these distributions compare?

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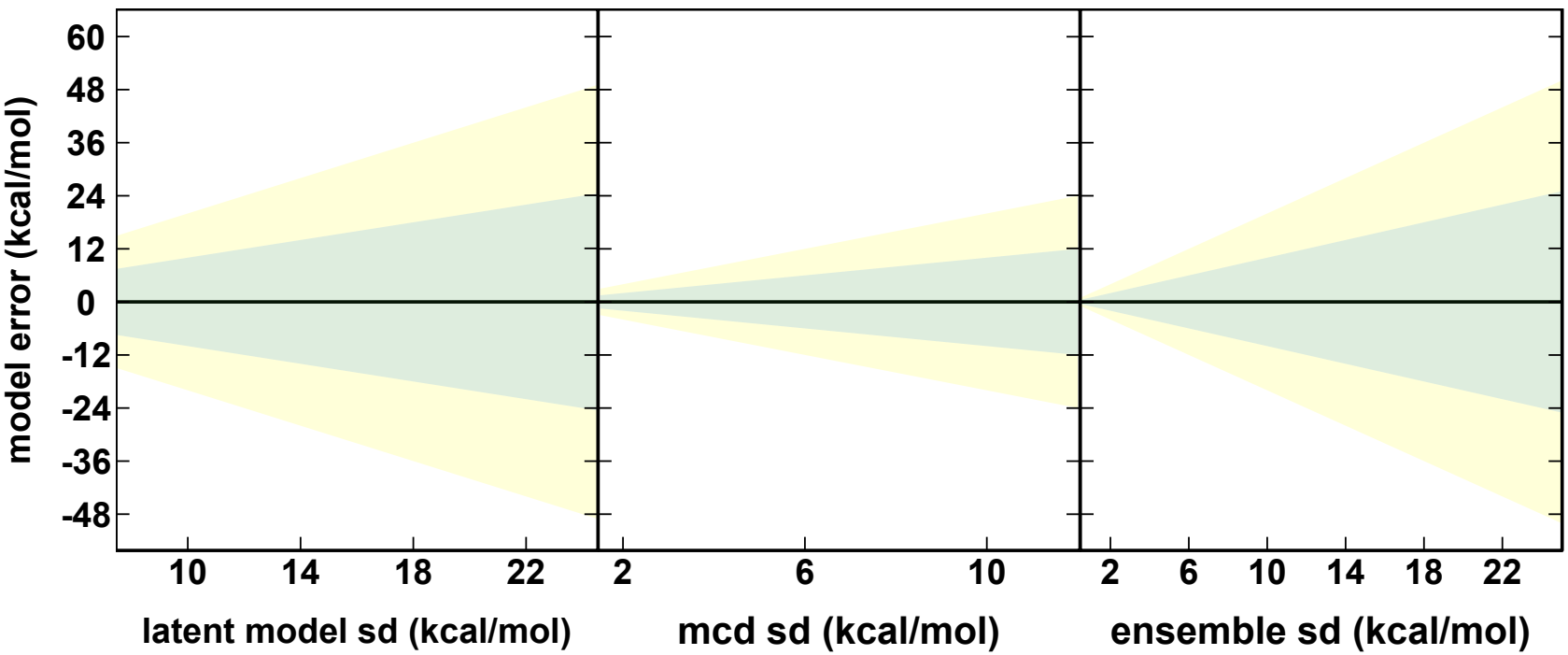

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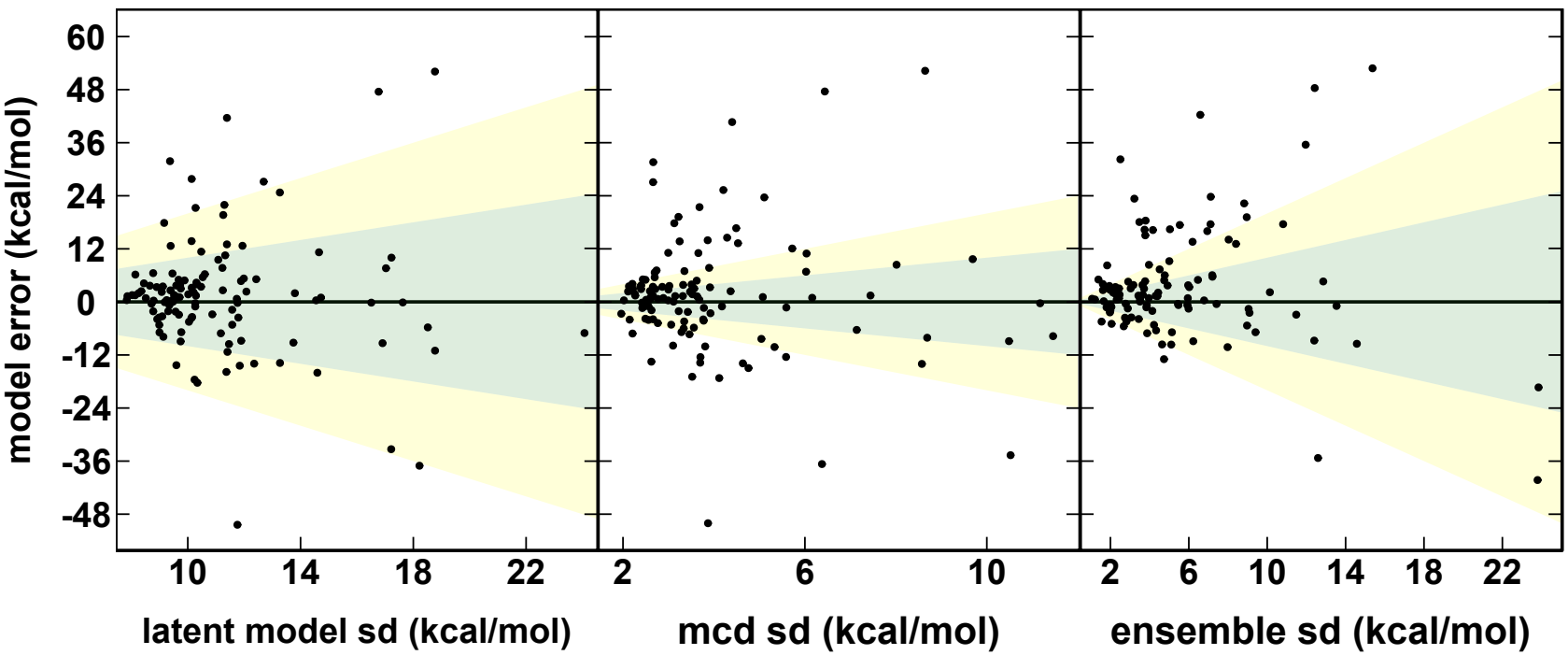

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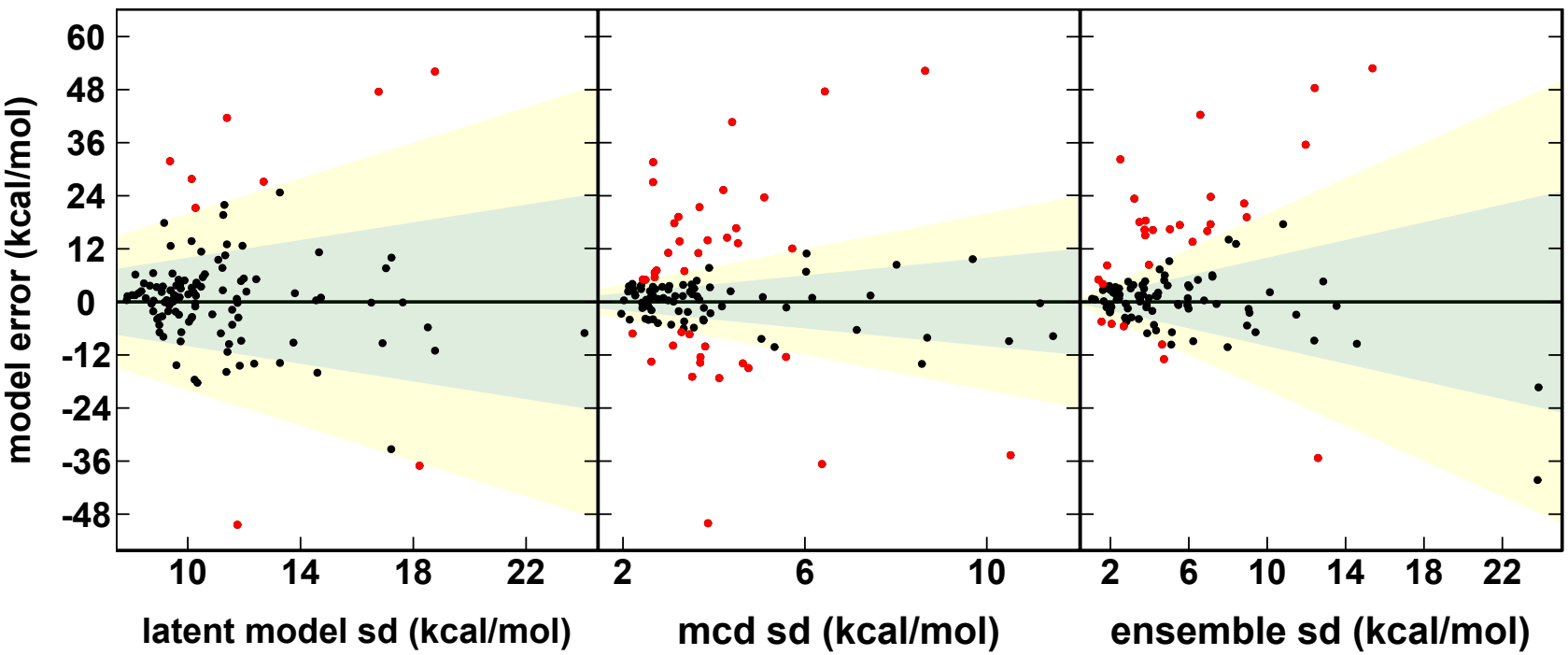

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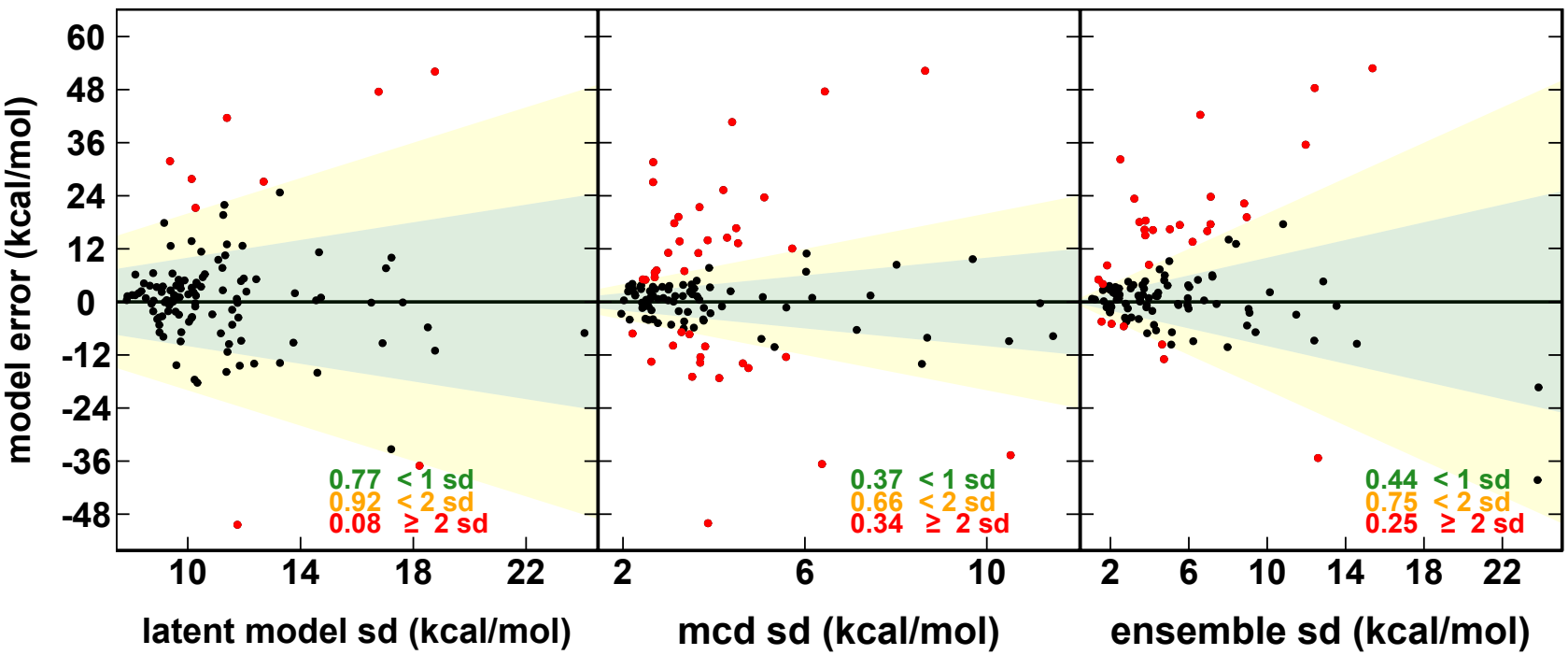

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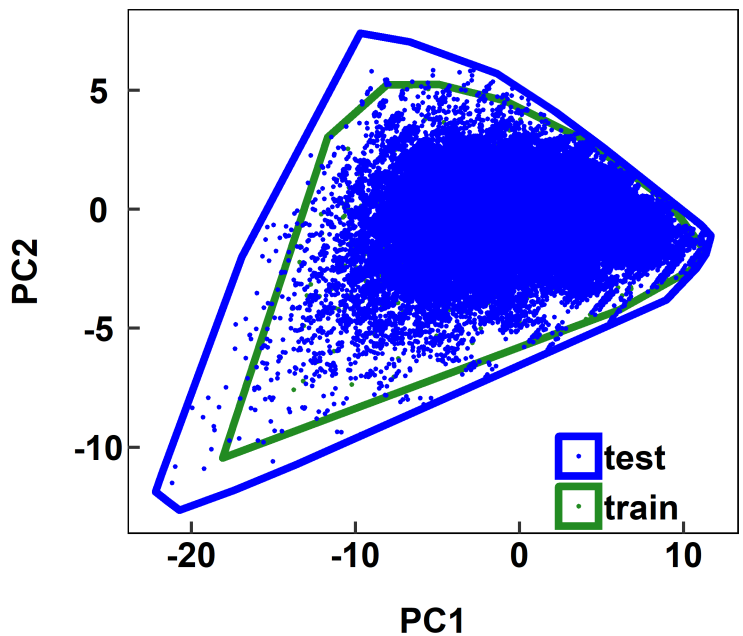

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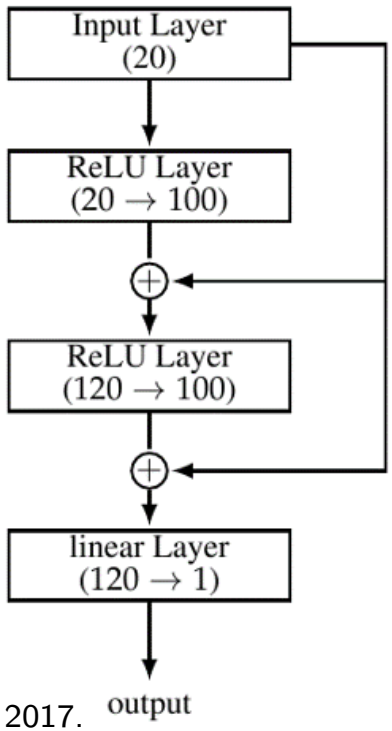

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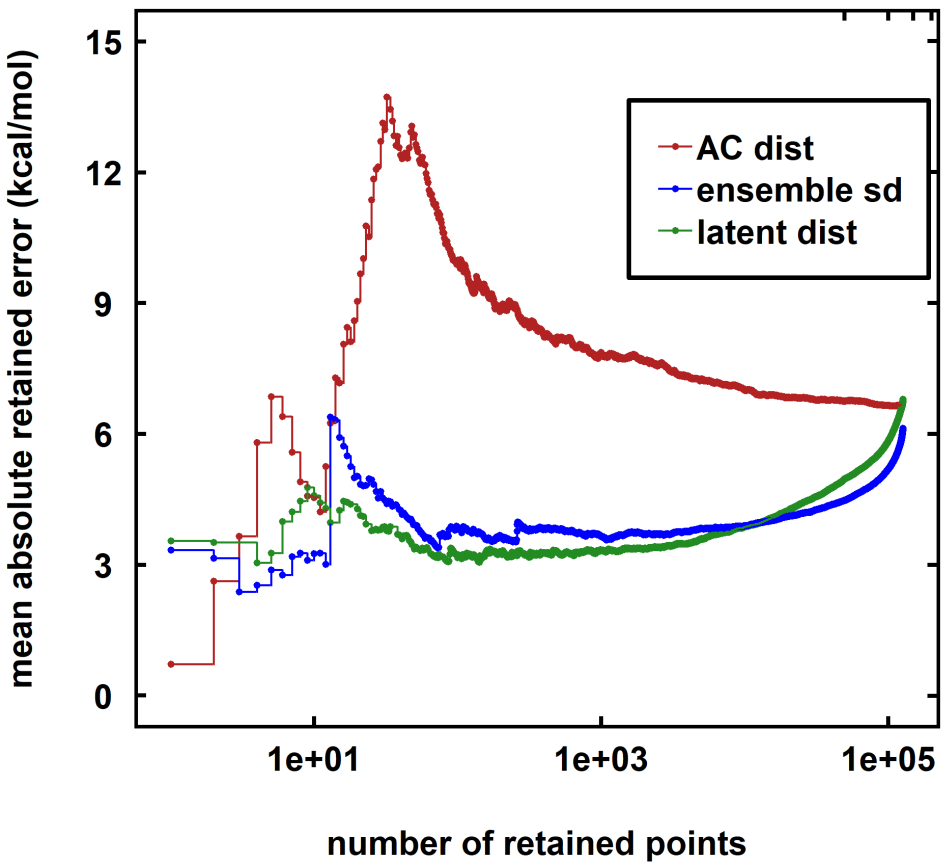

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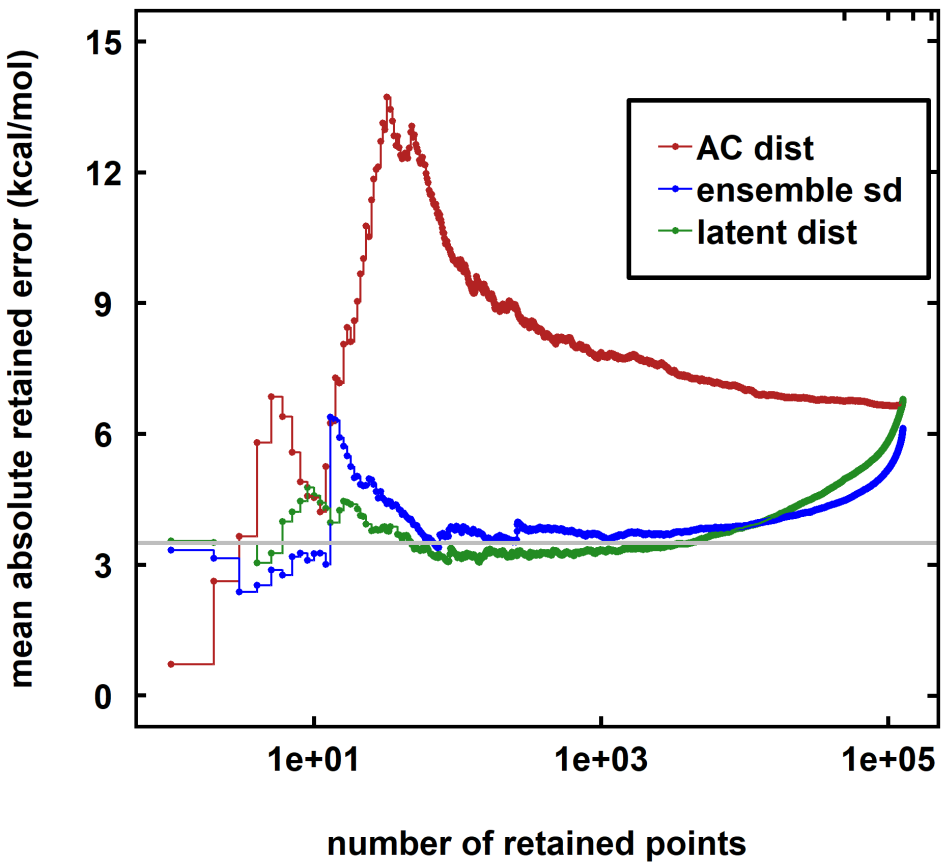

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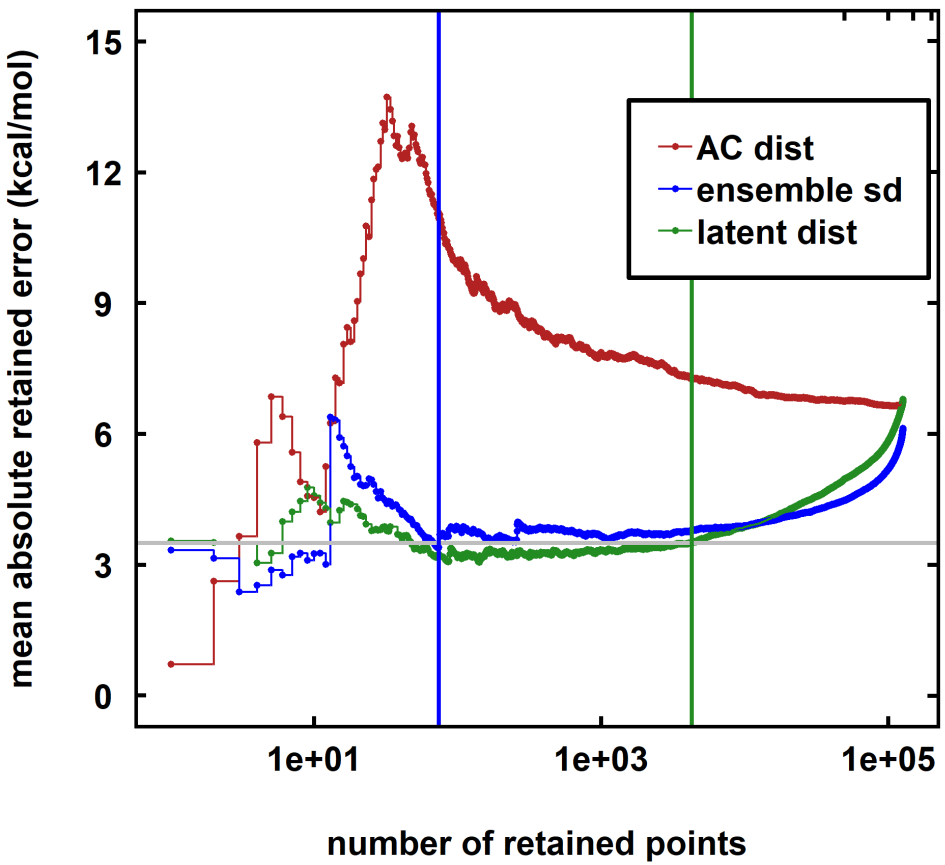
Similar error control can be obtained for this organic data[1]:



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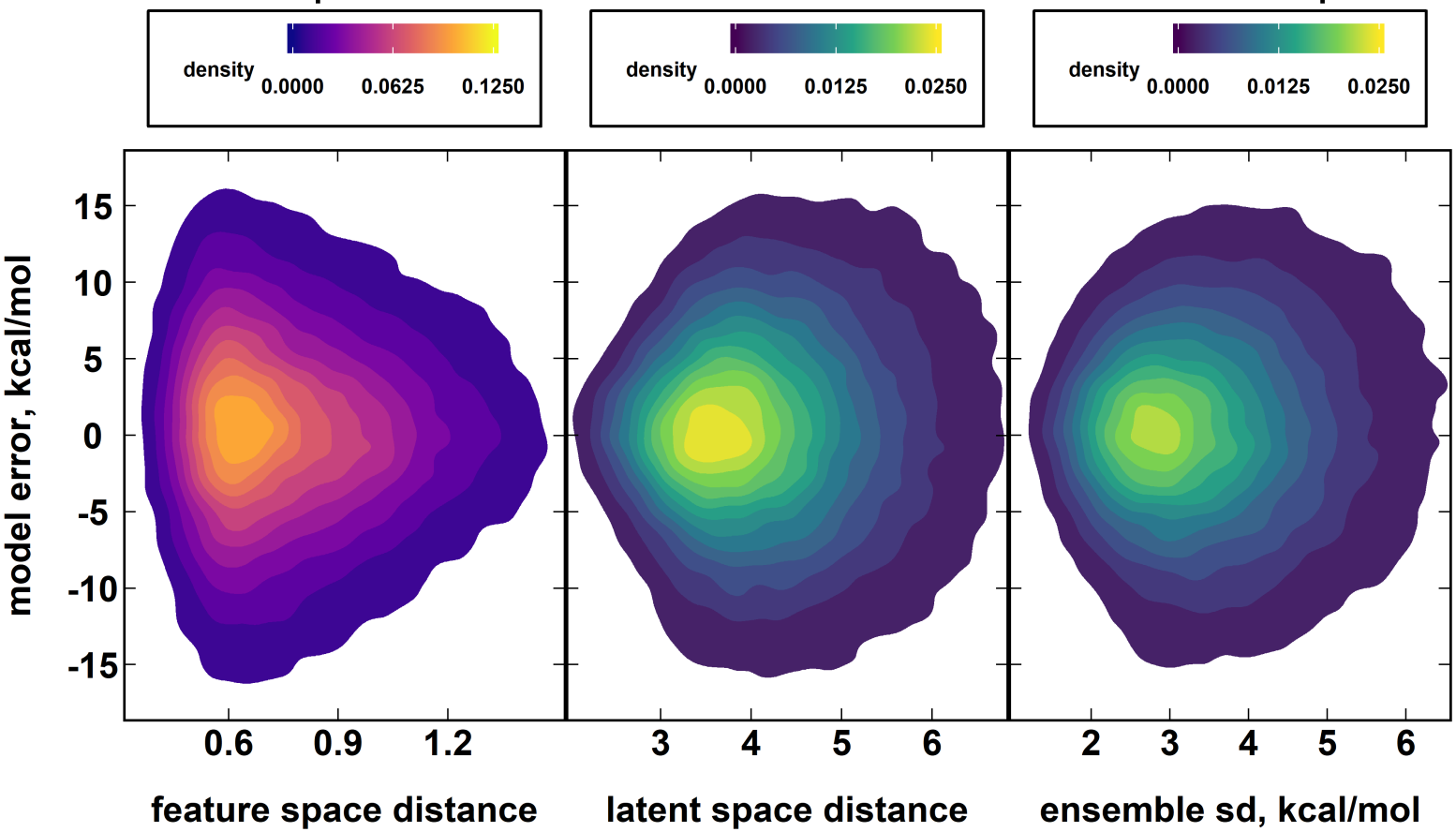

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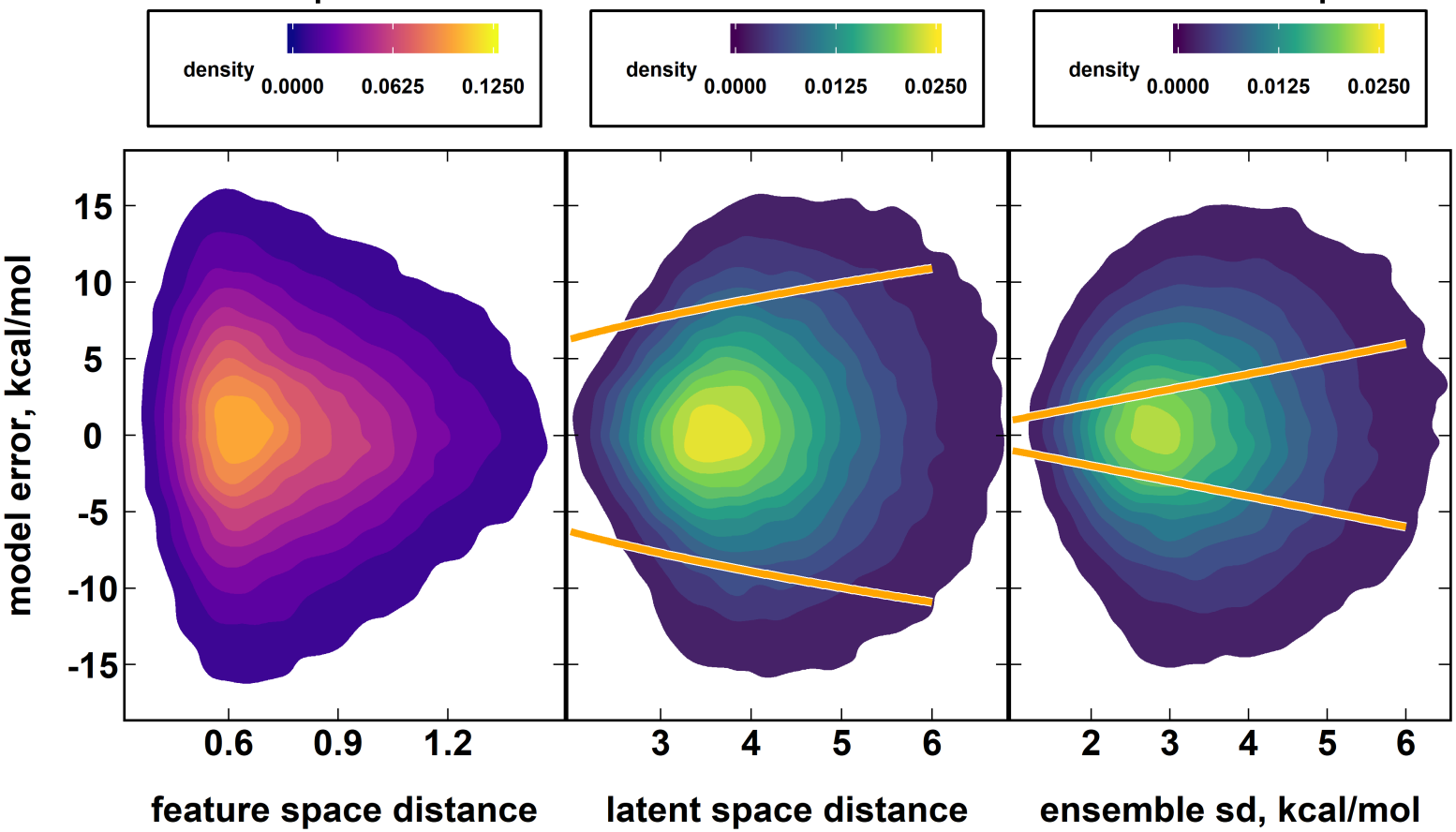
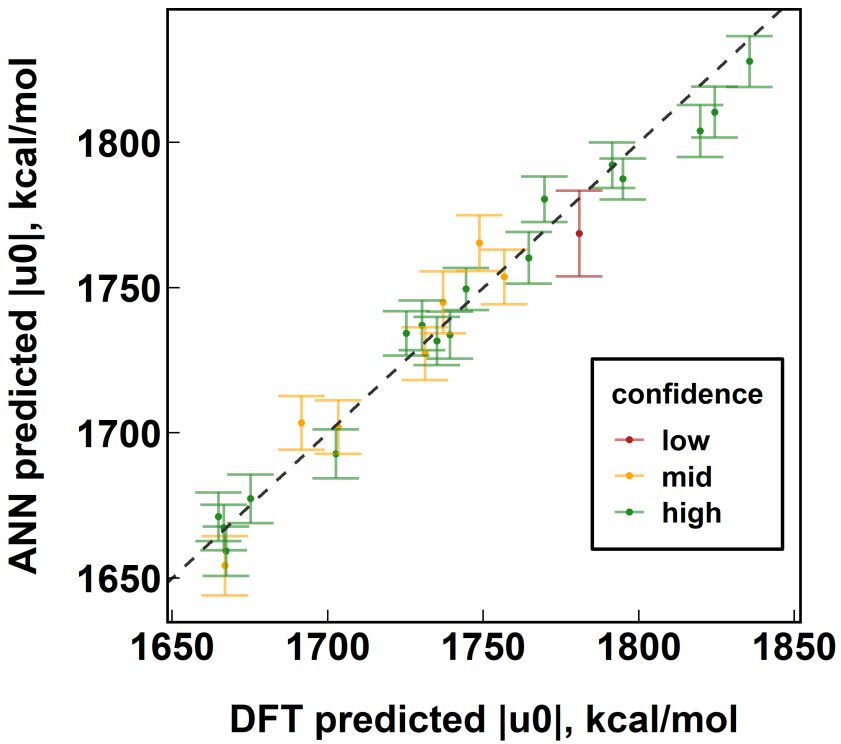


[1]: Janet, J.P., *et al.*, ChemRxiv, 10.26434/chemrxiv.7900277.v1

Summary

- The latent space provides substantially better results compared to raw feature space
- Out-of-sample errors can be controlled
- This method can provide useful errorbars on predictions and recover near-normal error quartiles



Acknowledgments

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