An Orbital-Overlap Complement to Atomic Partial Charge

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Partial Charge and Reactivity

- Atomic partial charges obtained from computed wavefunctions are widely used for interpreting quantum chemistry simulations and chemical reactivities of molecules, solids, surfaces, and nanoparticles
- In many cases partial charge alone gives an incomplete picture of reactivity:[1]
  (1) PhS⁻ is a better nucleophile compared to PhO⁻ in S_N2 reactions with MeI, though PhO⁻ has a more negative charge on the nucleophilic atom
  (2) The carbons of benzene and cyclobutadiene, or those of diamond, graphene, and C_{60}, possess nearly identical partial charges and very different reactivities
  (3) Many nucleophiles attack α,β-unsaturated ketones at the softer β carbon, not at the more positively charged carbonyl carbon
  (4) Halide anions F⁻, Cl⁻, Br⁻ and I⁻ have identical charges but different nucleophilicities
  (5) Carbons in aromatic benzene and anti-aromatic cyclobutadiene have nearly identical partial charges, but different reactivities.

Orbital Overlap Distance $D(\vec{r})$

- The Orbital Overlap Distance $D(\vec{r})$ is constructed from the Orbital Overlap Range Function $EDR(\vec{r}; d)$
- $EDR(\vec{r}; d)$ quantifies the extent to which an electron at point $\vec{r}$ in a calculated wave function overlaps over distance "d"[2-4]

$$EDR(\vec{r}; d) = \int d^3\vec{r}' g_d(\vec{r}, \vec{r}') \gamma(\vec{r}, \vec{r}')$$

$$g_d(\vec{r}, \vec{r}') \equiv \rho^{-1/2}(\vec{r}) \left(\frac{2}{\pi d^2}\right)^{3/4} exp\left(-\frac{|\vec{r} - \vec{r}'|^2}{d^2}\right)$$

$$\langle EDR(d)\rangle = \int d^3\vec{r}' \rho(\vec{r}) EDR(\vec{r}; d)$$

$$D(\vec{r}) = \arg\max_d EDR(\vec{r}; d)$$

- Plots of $D(\vec{r})$ on density isosurfaces complements molecular electrostatic potentials
- The atomic overlap distance D_A, is defined as the average overlap length of electrons assigned to atom A

$$D_A = \int d^3\vec{r} \rho(\vec{r}) D(\vec{r}) w_A(\vec{r})$$

where $w_A(\vec{r})$ is the Hirshfeld weight for atom A.

- D_A complements computed Hirshfeld charges Q_A by measuring the size of orbital lobes that best overlap with the wavefunction around an atom
- Compact, chemically stable atoms tend to have overlap distances smaller than chemically soft, unstable atoms.

Combining Charge and Overlap Distance

- Combining atomic charges (Q_A) and overlap distances (D_A) captures trends in aromaticity, nucleophilicity, allotrope stability, and substituent effects.[1]

System	Q_A (a.u)	D_A (bohr)
S in PhS⁻	-0.561	2.021
O in PhO⁻	-0.825	1.367
F⁻	-1.000	1.237
Cl⁻	-1.000	1.934
Br⁻	-1.000	2.165
I⁻	-1.000	2.476
β-C in Butenone	-0.071	1.302
Carbonyl C in Butenone	0.173	1.183
C in Diamond	-0.003	1.543
C in Graphene	-0.002	1.586
C in C_{60}	0.000	1.603

## Capturing the Effects of Substituents
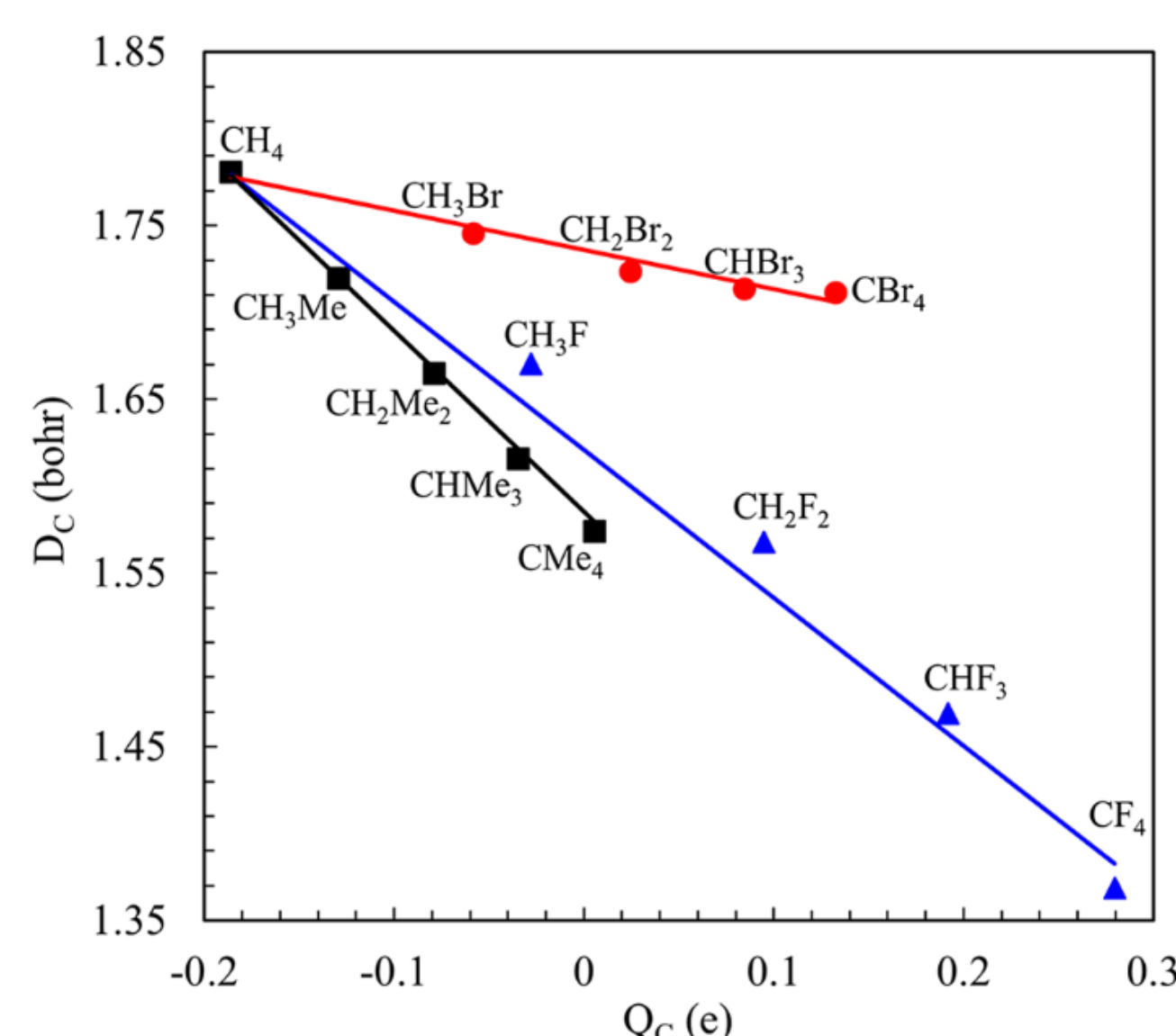
- Calculated in gas phase at B3LYP/6-31+G(d,p) level
- Relation is nearly linear within a substituent class, different substituents have different trends
- More negative Q_C give larger D_C, as only relatively diffuse orbitals are available to hold added electron density
- Binding carbon to large, "*puffy*" bromine atoms makes its orbitals larger, giving a relatively large D_C, whereas compact fluorine atoms makes the carbon orbitals smaller, giving a relatively small D_C.

Atomic Overlap Distance and Aromaticity
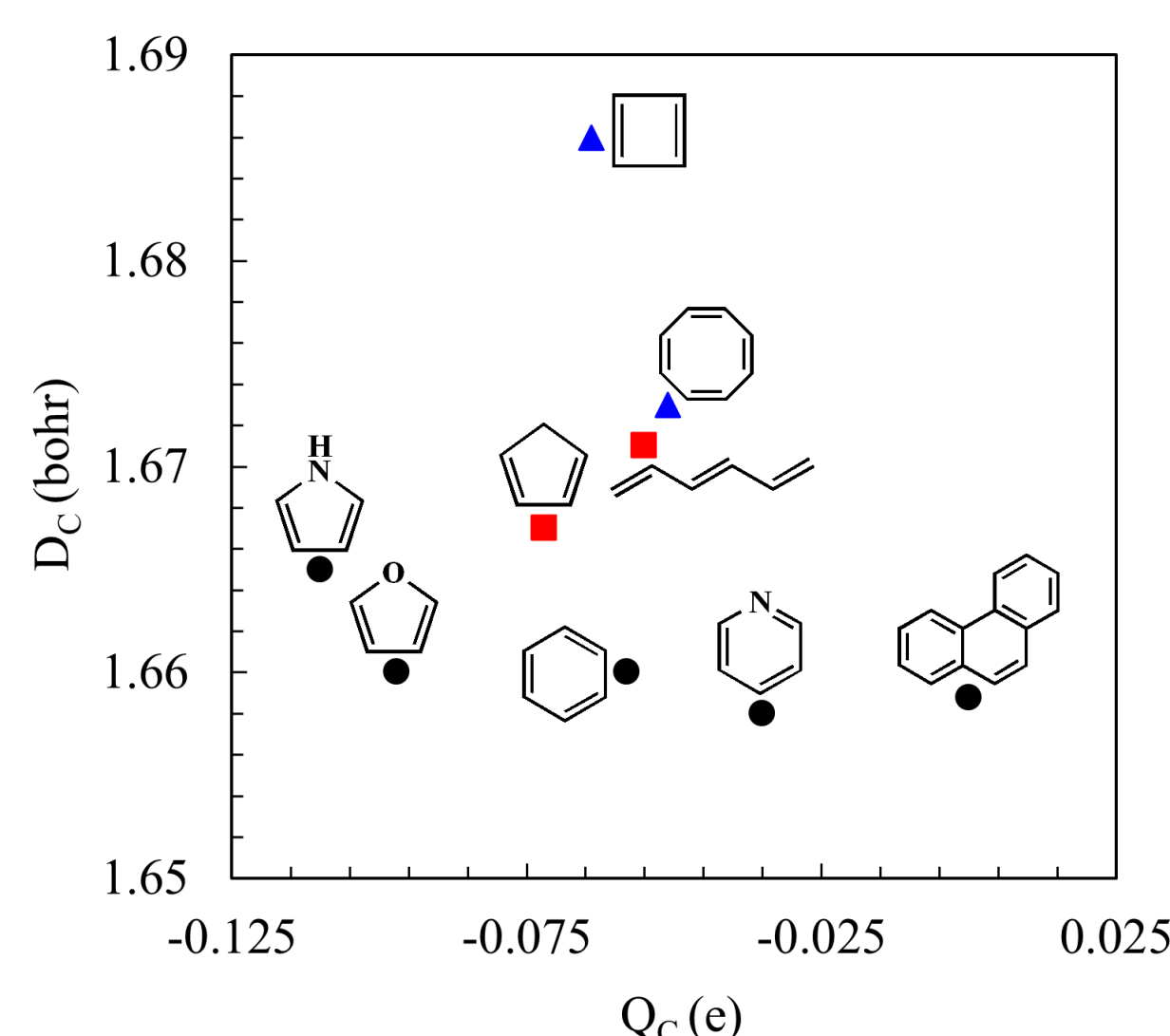
- Aromatic benzene, non-aromatic hexatriene, and anti-aromatic cyclobutadiene have nearly identical Q_C, their computed D_C clearly distinguish the relatively unstable, weakly bound, diffuse carbons of cyclobutadiene.

Non-trivial Predictions for Nanomaterials
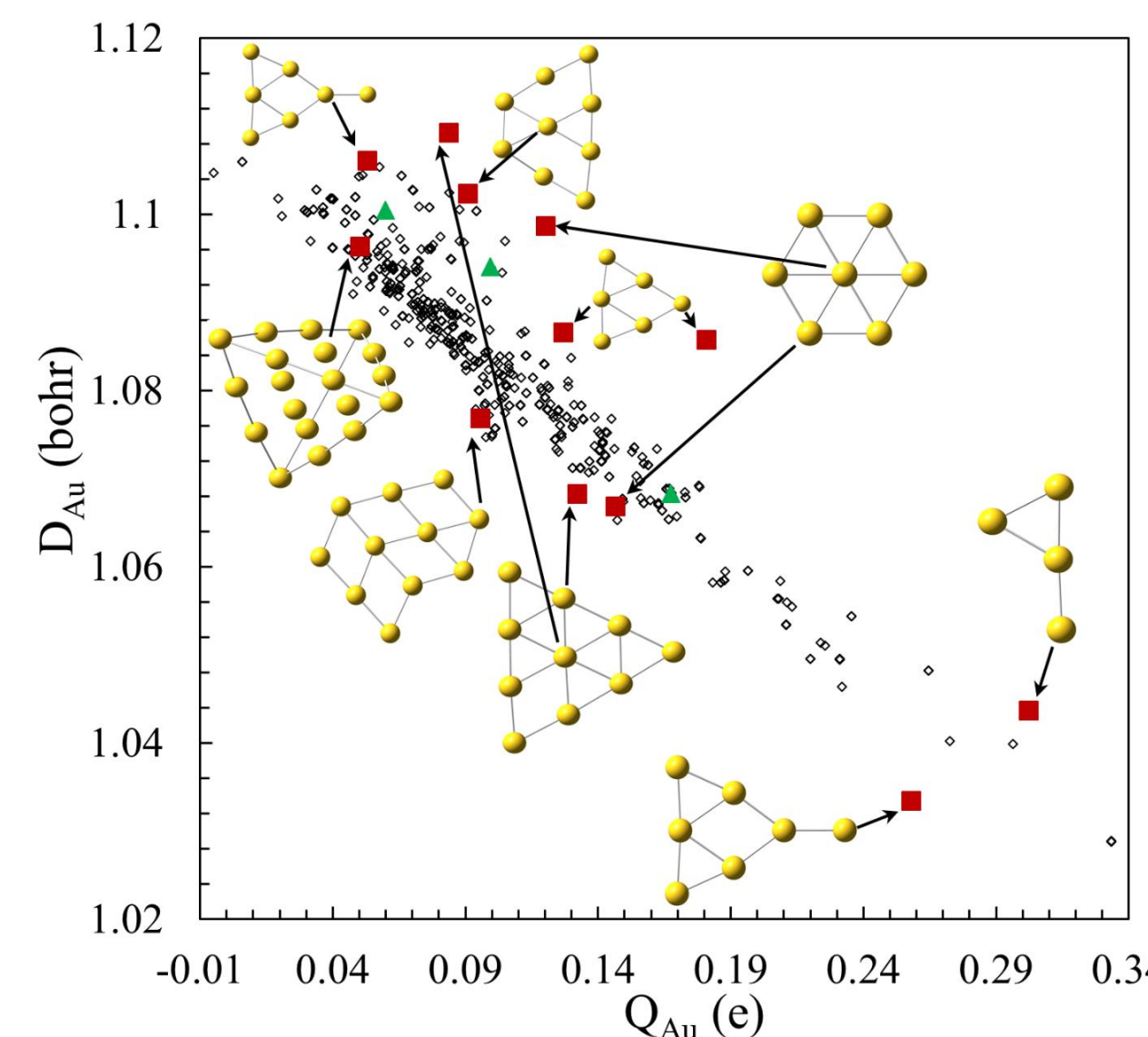
- Calculated in gas phase at PW91/LANL2DZ level
- The outer Au atoms have unusually small D_{Au}, while the central atom has an unusually large D_{au}
- Rationalizes a huge body of experimental and theoretical work on MAu_6 hexagons, in which the central atom is replaced with dopant M.

Surface Overlap Distance

- Plots of overlap distance $D(\vec{r})$ on molecular surfaces like electron or spin density isosurfaces captures chemical hardness/softness, acid-base interactions, halogen bonding and other σ-hole interactions
- Maximum surface value of $D(\vec{r})$ complements molecular electrostatic potential (ESP)
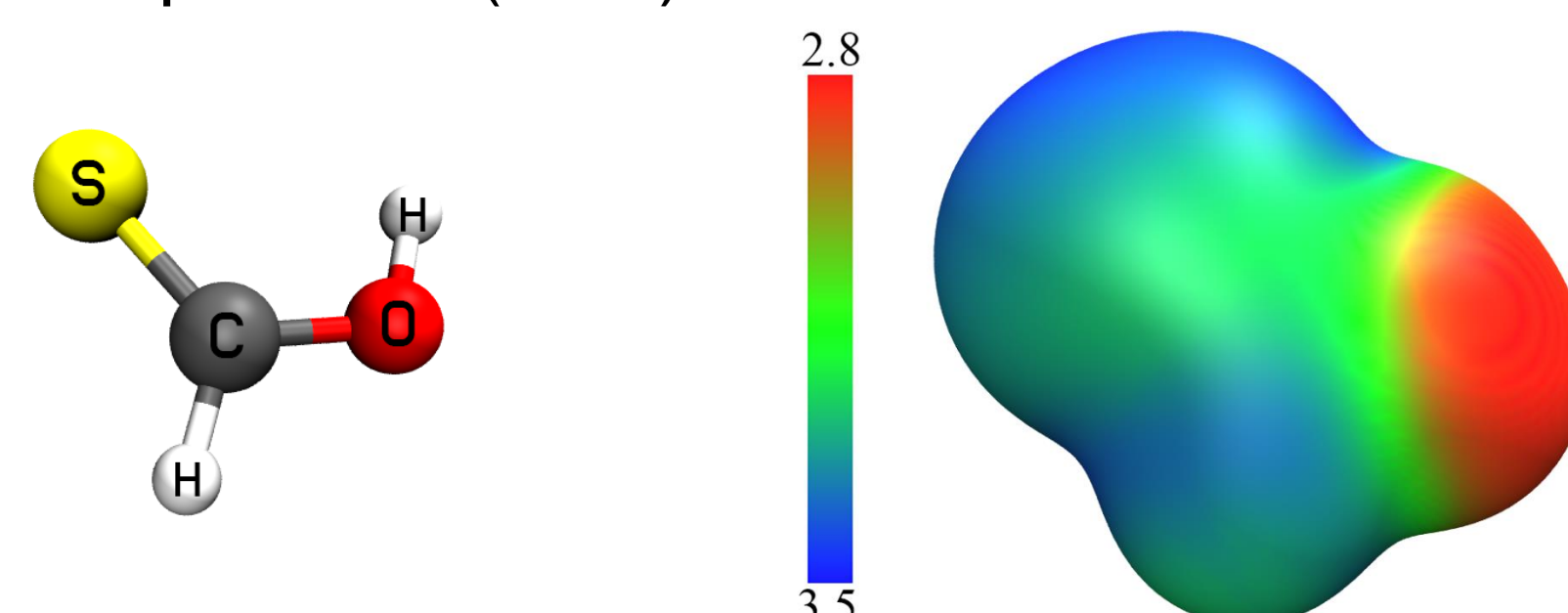
- $D(\vec{r})$ of thioformic acid plotted on 0.001 e/bohr³ electron density surface distinguishes chemically hard oxygen (red) from chemically soft sulfur (blue).

Capturing Trends in HSAB


Geometry   MESP (a.u) $D(\vec{r})$ (bohr)
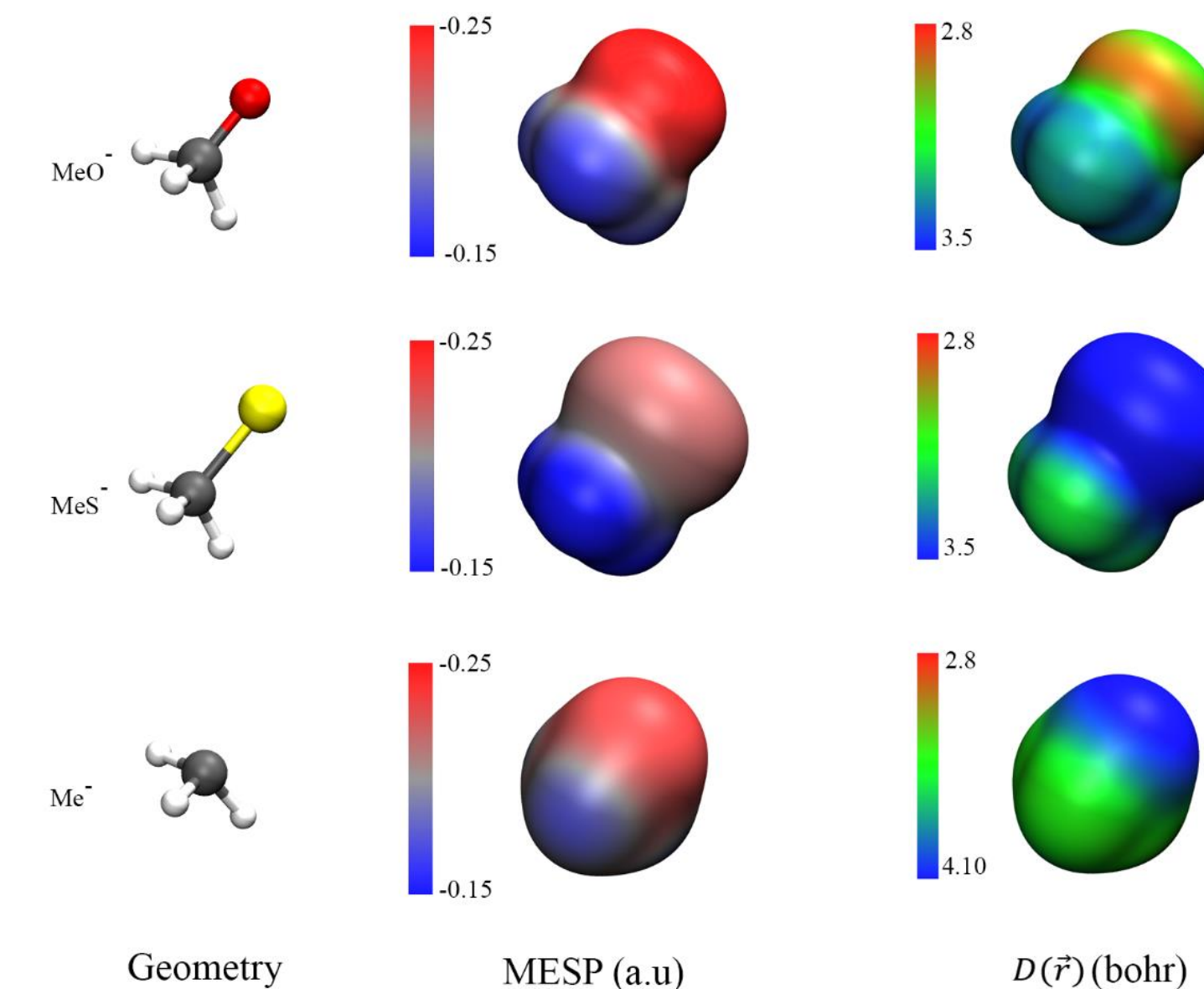
- Plotted on 0.001 e/bohr³ electron density surface[5]
- H⁺ being a hard and strong acid prefers MeO⁻ (small $D(\vec{r})$) over MeS⁻ (large $D(\vec{r})$) whereas Au⁺ which is a soft weak acid shows opposite behavior.

Lewis Base	ESP (a.u)	$D(\vec{r})$ (bohr)	Interaction Energy (kcal/mol)	
			H⁺	Au⁺
MeO⁻	-0.256	3.081	394	427
MeS⁻	-0.214	3.683	365	433
Me⁻	-0.231	4.238	429	481

Selectivity in Protein–Ligand Interactions

- Why gold-specific protein GolB, shows higher selectivity for Au⁺ over Cu⁺ though former has lower ESP?
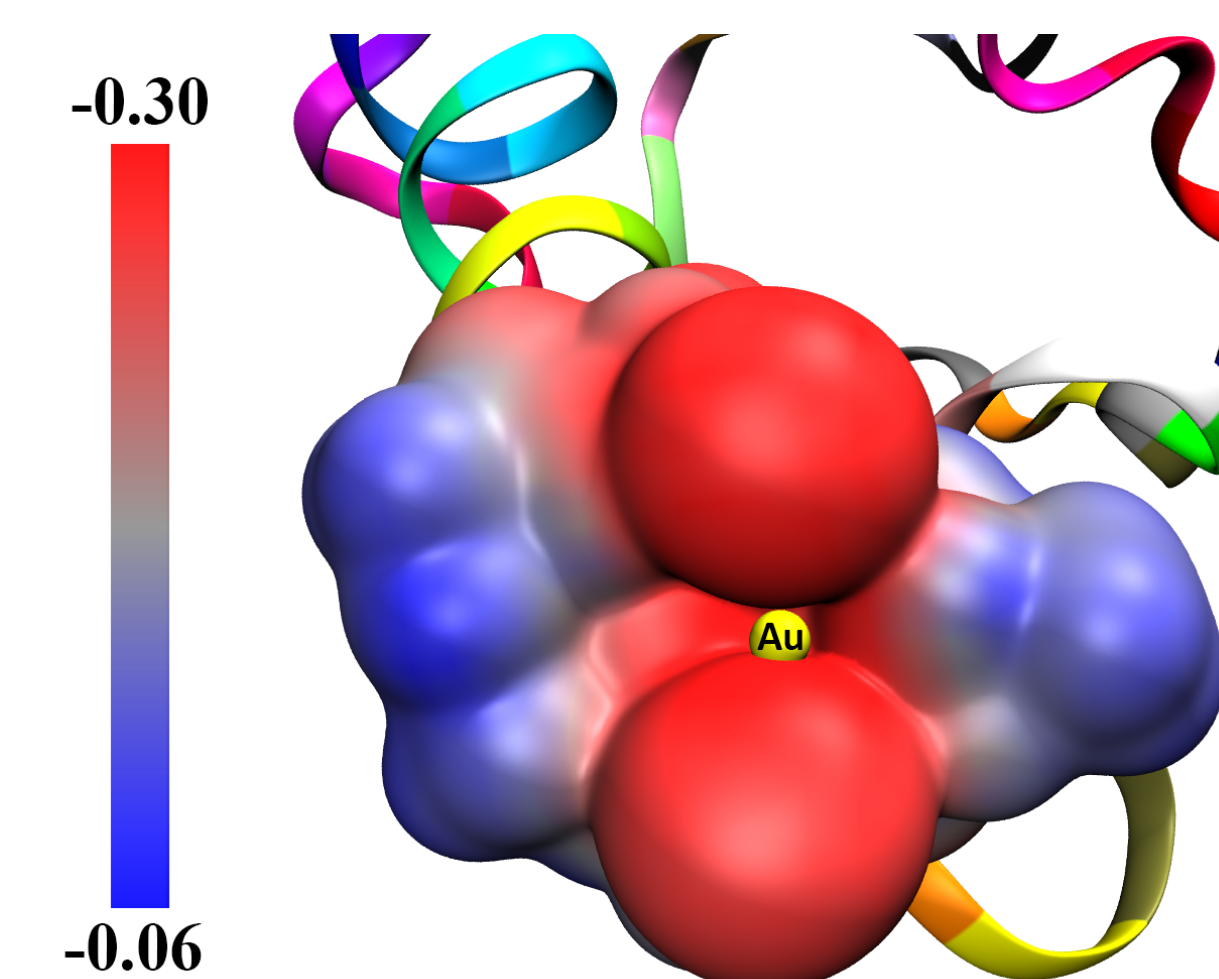
- ESP of Au⁺ binding pocket plotted on 0.001 e/bohr³ electron density surface calculated at ONIOM(ωB97X-D/6-311g(d,p):AMBER) level[5]
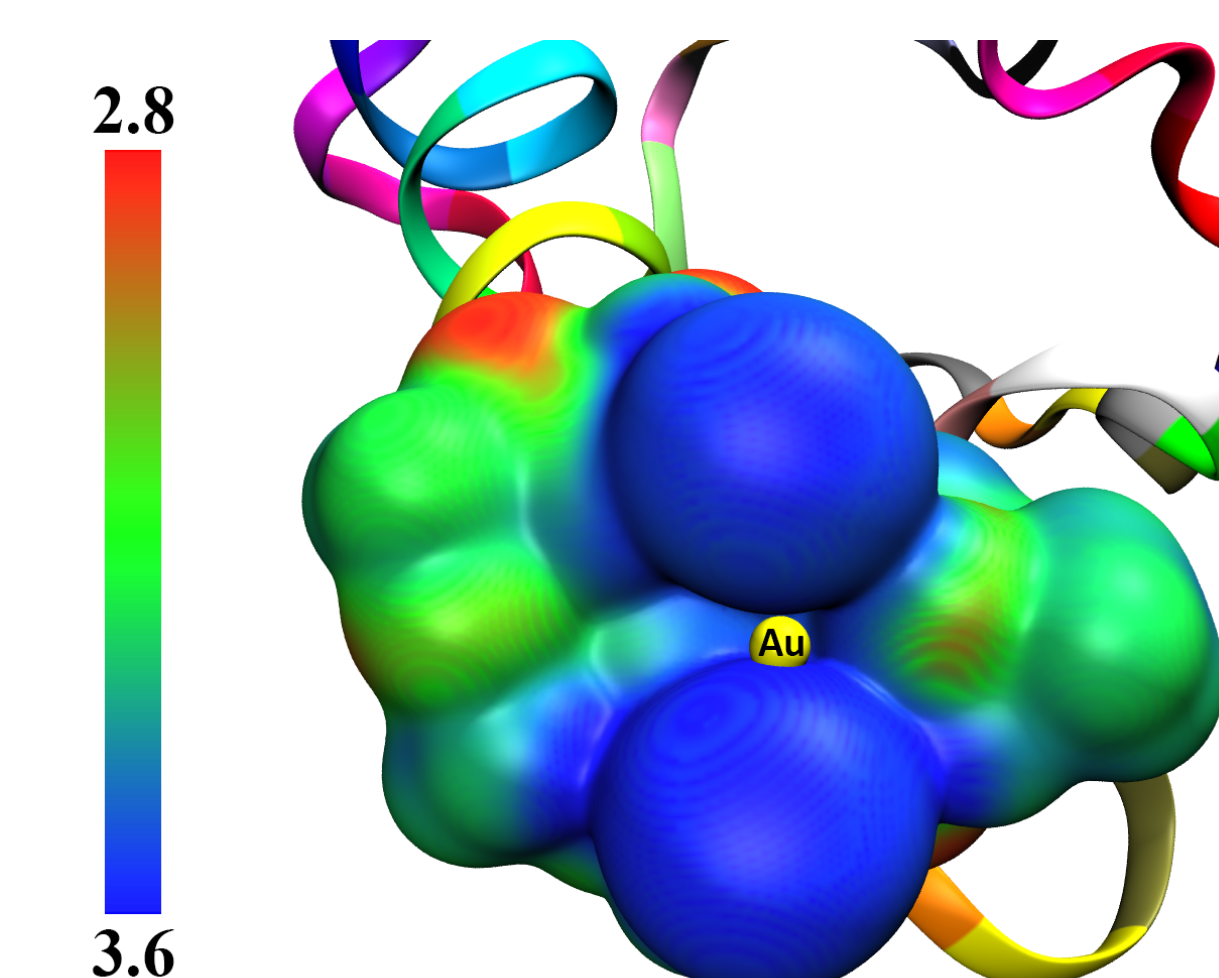
- Overlap distance $D(\vec{r})$ plotted on 0.001 e/bohr³ electron density surface calculated at the same level of theory
- The gold-binding site (ESP=-0.293 au, $D(\vec{r})$=3.692 bohr) is anionic, and has a large overlap distance
- Though Cu⁺ (ESP=0.304 au, $D(\vec{r})$=1.789 bohr) is more positive compared to Au⁺ (ESP=0.270 au, $D(\vec{r})$=2.030 bohr) but small $D(\vec{r})$ makes it a hard Lewis acid compared to Au⁺ which is a preferred candidate for this binding site.

References

1. A. Mehmood and B. G. Janesko, *Angew. Chem. Int. Ed.* 2017, 56, 6878–6881.
2. B. G. Janesko et al., *J. Chem. Phys.*, 2014, 141, 144104.
3. B. G. Janesko et al., *Phys. Chem. Chem. Phys.*, 2015, 28, 18305-17.
4. B. G. Janesko et al., *J. Chem. Theory Comput.*, 2016, 12,79–91.
5. Unpublished results