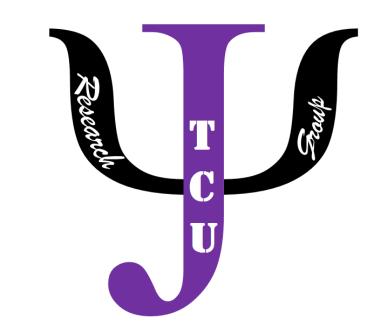


# An Orbital-Overlap Complement to Atomic Partial Charge

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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<sup>-</sup> is a better nucleophile compared to PhO<sup>-</sup> in S<sub>N</sub>2 reactions with MeI, though PhO<sup>-</sup> 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<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup> and l<sup>-</sup> 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" <sup>2-3</sup>

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

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

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

- $D(\vec{r}) = \arg\max_{d} EDR(\vec{r}; d)$
- 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.

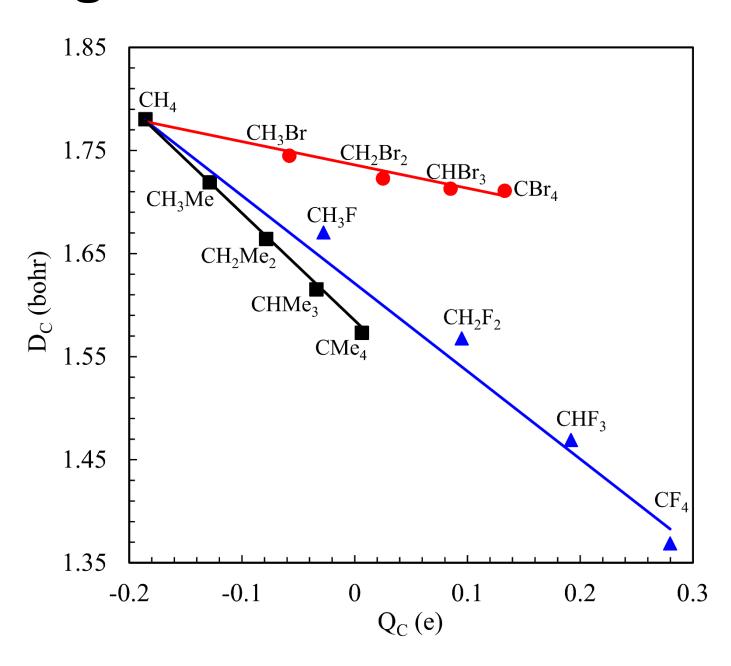
- $D_A$  complements computed Hirshfeld charges  $Q_A$  by measuring the size of orbital lobes that best overlap with the wavefunction around an atom
- Compact, chemically stable atoms tend to have overlap distances smaller than chemically soft, unstable atoms.

## 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.<sup>1</sup>

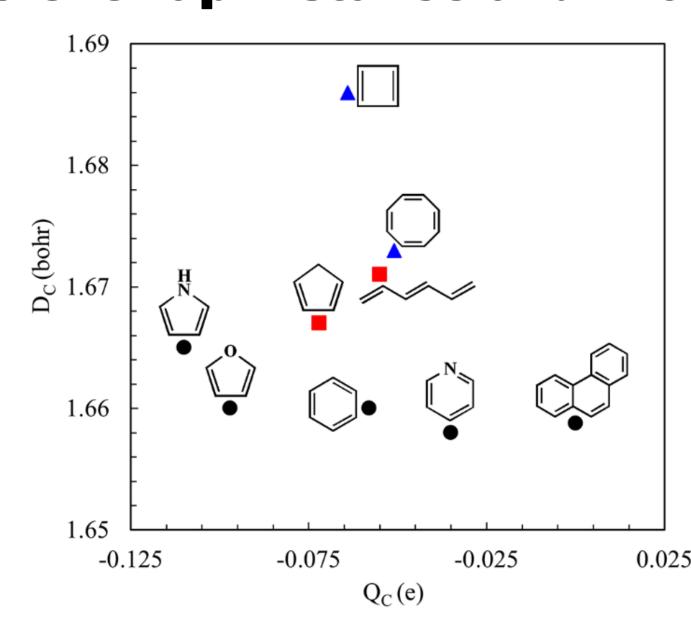
System	<b>Q</b> <sub>A</sub> (a.u)	D <sub>A</sub> (bohr)
S in PhS <sup>-</sup>	-0.561	2.021
O in PhO	-0.825	1.367
F-	-1.000	1.237
CI-	-1.000	1.934
Br-	-1.000	2.165
<b> </b> -	-1.000	2.476
β-C in Butenone	-0.071	1.302
Carbonyl C in Butenone	0.173	1.183
C in Diamond	-0.003	1.543
C in Graphene	-0.002	1.586
C in C <sub>60</sub>	0.000	1.603

## **Capturing the Effects of Substituents**



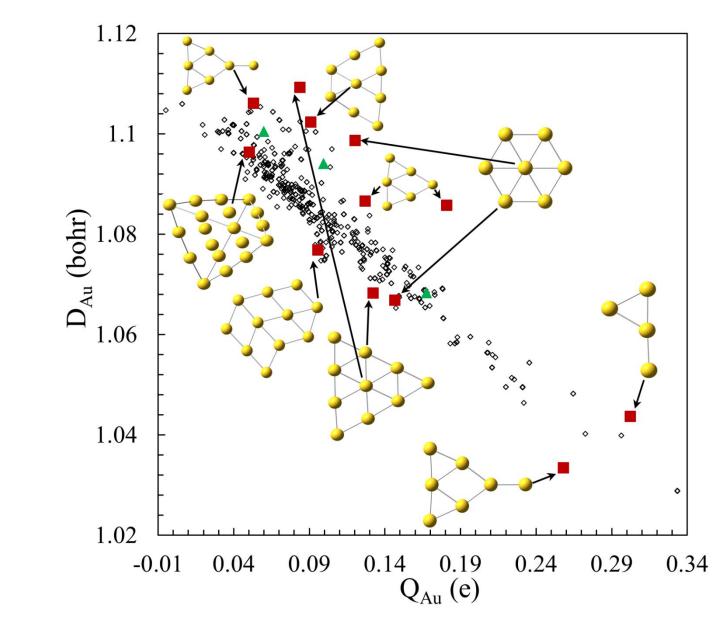
- Calculated in gas phase at B3LYP/6-31+G(d,p) level
- Relation is nearly linear within a substituent class, different substituents have different trends
- More negative  $Q_{\mathbb{C}}$  give larger  $D_{\mathbb{C}}$ , as only relatively diffuse orbitals are available to hold added electron density
- Binding carbon to large, "puffy" bromine atoms makes its orbitals larger, giving a relatively large  $D_{\rm C}$ , whereas compact fluorine atoms makes the carbon orbitals smaller, giving a relatively small  $D_{\rm C}$ .

## **Atomic Overlap Distance and Aromaticity**



• Aromatic benzene, non-aromatic hexatriene, and anti-aromatic cyclobutadiene have nearly identical  $Q_{\rm C}$ , their computed  $D_{\rm C}$  clearly distinguish the relatively unstable, weakly bound, diffuse carbons of cyclobutadiene.

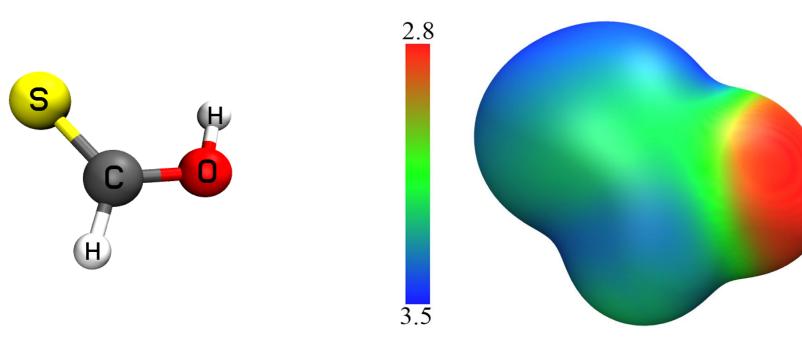
#### **Non-trivial Predictions for Nanomaterials**



- Calculated in gas phase at PW91/LANL2DZ level
- The outer Au atoms have unusually small  $D_{\rm Au}$ , while the central atom has an unusually large  $D_{\rm Au}$
- Rationalizes a huge body of experimental and theoretical work on MAu<sub>6</sub> hexagons, in which the central atom is replaced with dopant M.

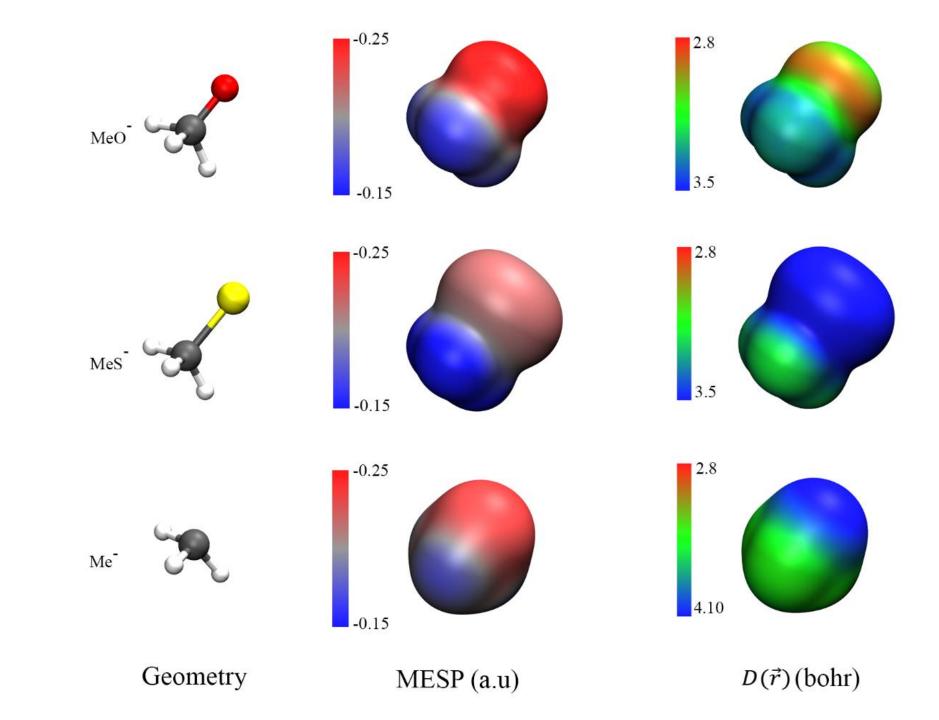
## Surface Overlap Distance

- 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  $\sigma$ -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



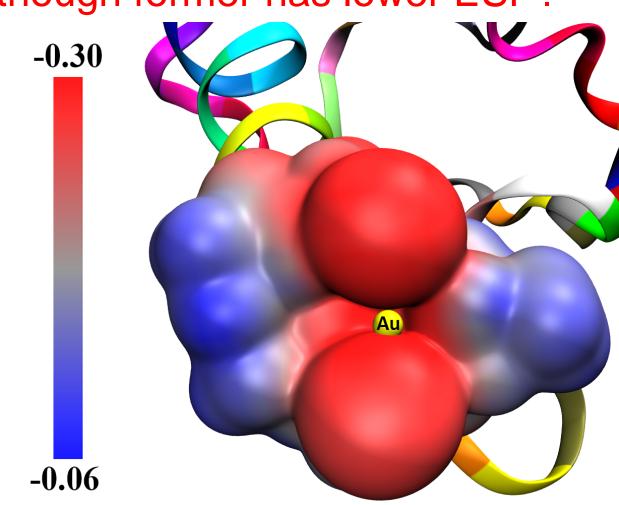
Plotted on 0.001 e/bohr<sup>3</sup> electron density surface<sup>4</sup>

• H<sup>+</sup> being a hard and strong acid prefers MeO<sup>-</sup> (small  $D(\vec{r})$ ) over MeS<sup>-</sup> (large  $D(\vec{r})$ ) whereas Au<sup>+</sup> which is a soft weak acid shows opposite behavior.

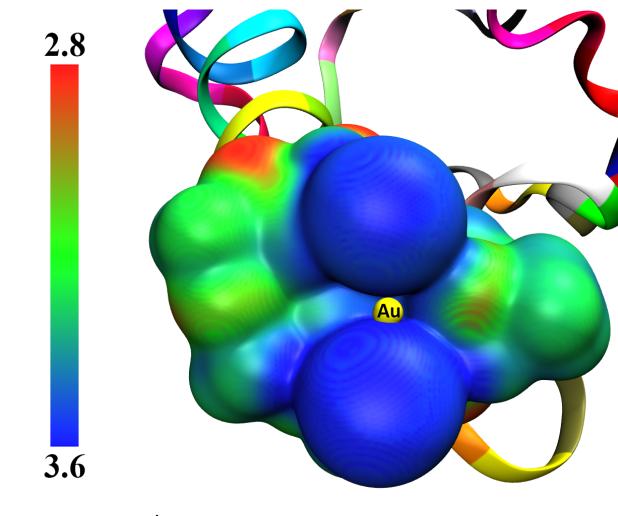
Lewis	ESP	$D(\overrightarrow{r})$	Interaction Energy (kcal/mol)	
Base	(a.u)	(bohr)	H+	Au+
MeO-	-0.256	3.081	394	427
MeS <sup>-</sup>	-0.214	3.683	365	433
Me⁻	-0.231	4.238	429	481

#### Selectivity in Protein-Ligand Interactions

• Why gold-specific protein GolB, shows higher selectivity for Au<sup>+</sup> over Cu<sup>+</sup> though former has lower ESP?



• ESP of Au<sup>+</sup> binding pocket plotted on 0.001 e/bohr<sup>3</sup> electron density surface calculated at ONIOM(ωB97X-D/6-311g(d,p):AMBER) level<sup>4</sup>



- Overlap distance  $D(\vec{r})$  plotted on 0.001 e/bohr<sup>3</sup> 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<sup>+</sup> (ESP=0.304 au,  $D(\vec{r})$ =1.789 bohr) is more positive compared to Au<sup>+</sup> (ESP=0.270 au,  $D(\vec{r})$ =2.030 bohr) but small  $D(\vec{r})$  makes it a hard Lewis acid compared to Au<sup>+</sup> which is a preferred candidate for this binding site.

## Availability

- Multiwfn (<a href="http://sobereva.com/multiwfn/">http://sobereva.com/multiwfn/</a>)
- Gaussian 16 (<a href="http://gaussian.com/gaussian16/">http://gaussian.com/gaussian16/</a>)
- NCIplot (<a href="https://github.com/aoterodelaroza/nciplot">https://github.com/aoterodelaroza/nciplot</a>)

## Acknowledgment

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## References

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- 4. Mehmood, A. et al. Submitted.