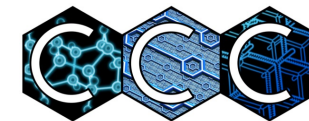


# Substituents Effects on Non-Covalent Interactions Between Aromatic Systems



## Hunter-Sanders model [1]

$\pi$ -system = a positively charged  $\sigma$ -framework sandwiched between two negatively charged  $\pi$ -electron clouds. The interaction is  $\pi$ - $\sigma$  rather than  $\pi$ - $\pi$ . Electrostatic effects determine the geometry, while van der Waals interactions account for the major contribution to the magnitude of the interaction.

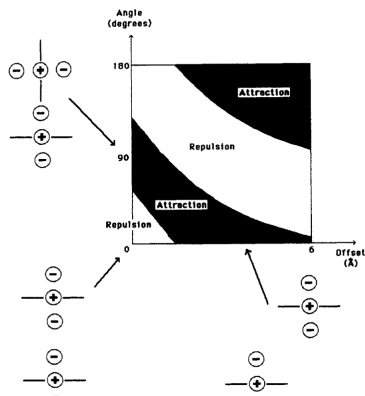


Figure 9. Interaction between two idealized  $\pi$ -atoms as a function of orientation: two attractive geometries and the repulsive face-to-face geometry are illustrated.

[1] Reprinted with permission from JACS 1990, 112, 5525, © 1990 ACS.

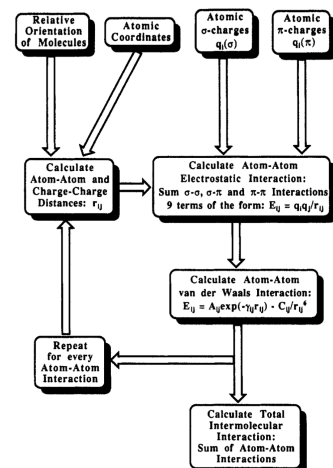


Figure 4. Algorithm used for calculation of  $\pi$ - $\pi$  interaction energies.

## H-S model disproved (Sherrill et al., Wheeler & Houk, Herbert et al. [2])

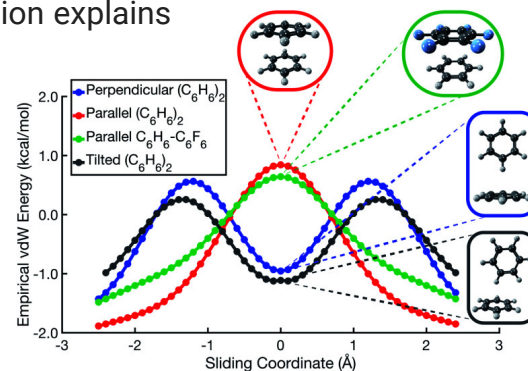
The Hunter-Sanders model is based solely on classical electrostatics and ignores charge penetration. A quantum-mechanical analysis (SAPT) demonstrated that electrostatics has very little influence on the conformational landscape of benzene dimers and cannot explain the slip-stacked arrangement of  $C_6H_6 \cdots C_6F_6$ . This geometry is due to the competition between dispersion and Pauli repulsion. This interpretation explains the persistence of offset  $\pi$ -stacking in large PAHs.

This geometry is due to the competition between dispersion and Pauli repulsion. This interpretation explains the persistence of offset  $\pi$ -stacking in large PAHs.

Classical Electrostatics



Steric Repulsion

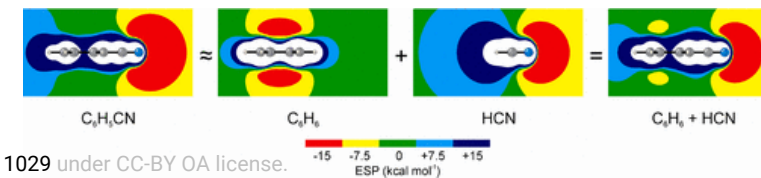


[2] Reprinted from Chem. Sci. 2020, 11, 6758 under CC-BY OA license.

## Substituent effects [3]

$\pi$ -stacking is conventionally expected to be stabilised when one of the rings has an EWG and the other one has an EDG. However, the interaction was shown (a range of DFT and SAPT methods) to arise from local interactions between substituents rather than between the rings.

Substituent-induced changes in the ESP above the center of aryl rings result from through-space effects of substituents rather than changes in the distribution of the  $\pi$ -electron density.



[3] Reprinted from Acc. Chem. Res. 2013, 46, 1029 under CC-BY OA license.

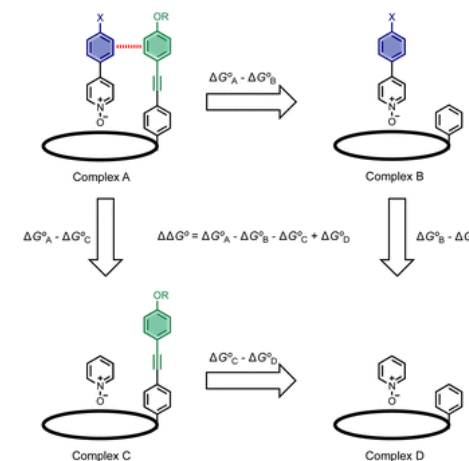
**“the results show that not only is aromaticity unnecessary for  $\pi$ -stacking interactions, but it actually hinders these interactions to some extent”**

## H-S model returns (in water) [4]

Experimental study: isothermal titration calorimetry (ITC).

Addition of substituents to the guest phenyl group stabilises the complex by a factor of 1,000. EWGs increase the strength of the interactions, elucidating the role of electrostatics in stabilising both edge-to-face and stacking interactions.

Substituents effects are enhanced in water because of the entropic contributions associated with the desolvation of substituents.



[4] Reprinted from Chem. Sci. 2023, 14, 6226 under CC-BY OA license.