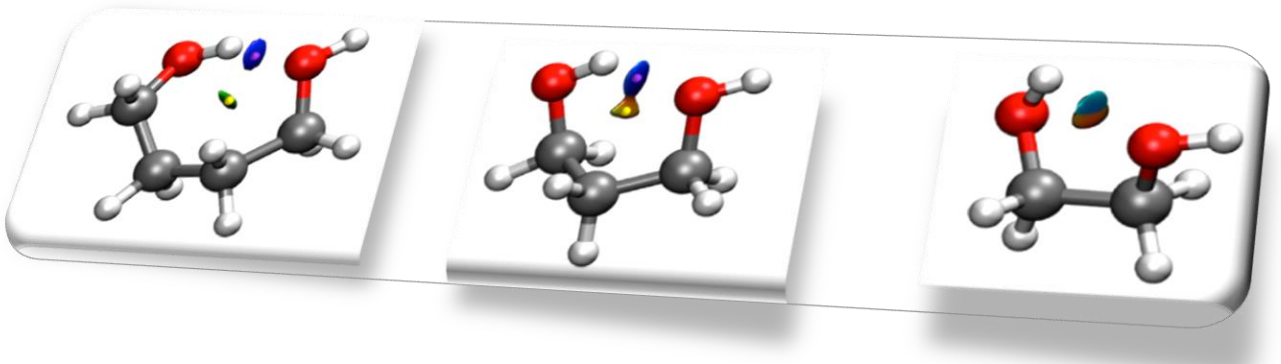
Non covalent interactions

Real space point of view



Julia Contreras García &

Peter Reinhardt

CNRS/Sorbonne Université

Outline

- Why are we still studying NCIs?
- QTAIM (Quantum Theory of Atoms in Molecules)
  - Critical points
  - Integrals
- NCI (Non covalent interaction index)
  - Definition
  - NCI vs AIM
  - Big systems
- Summary

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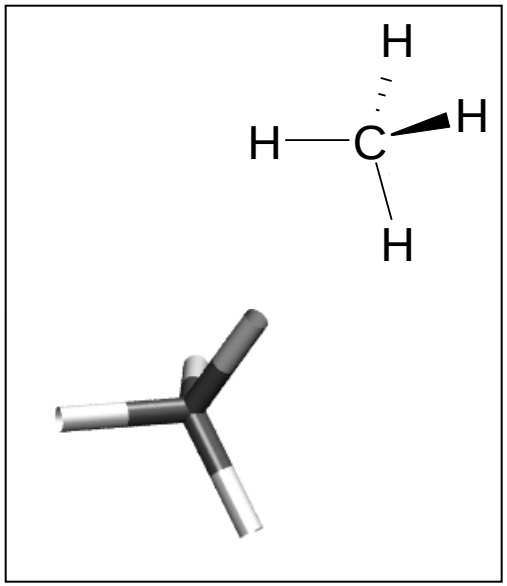
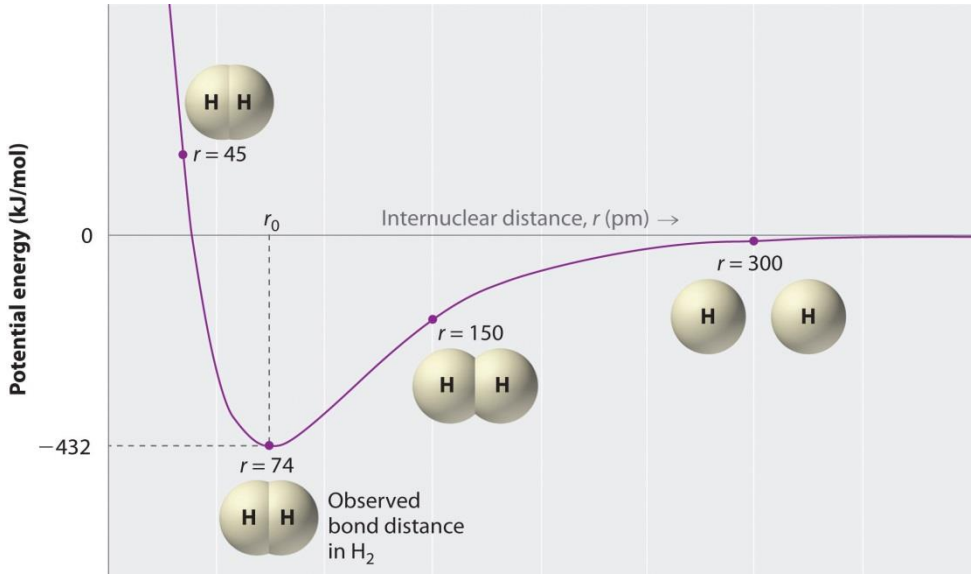
Motivation

Covalent bonds: easy to represent

Why?



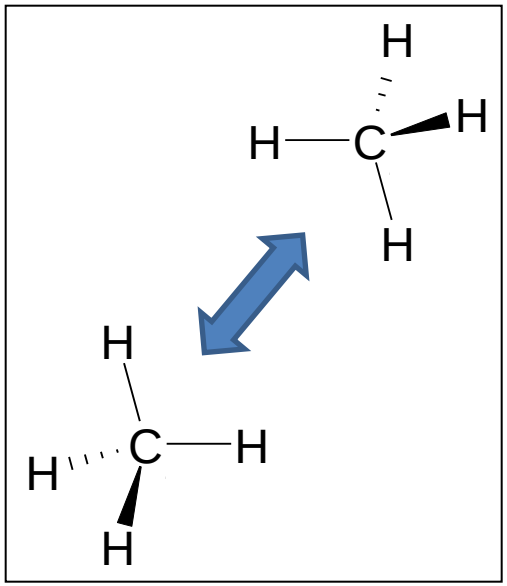


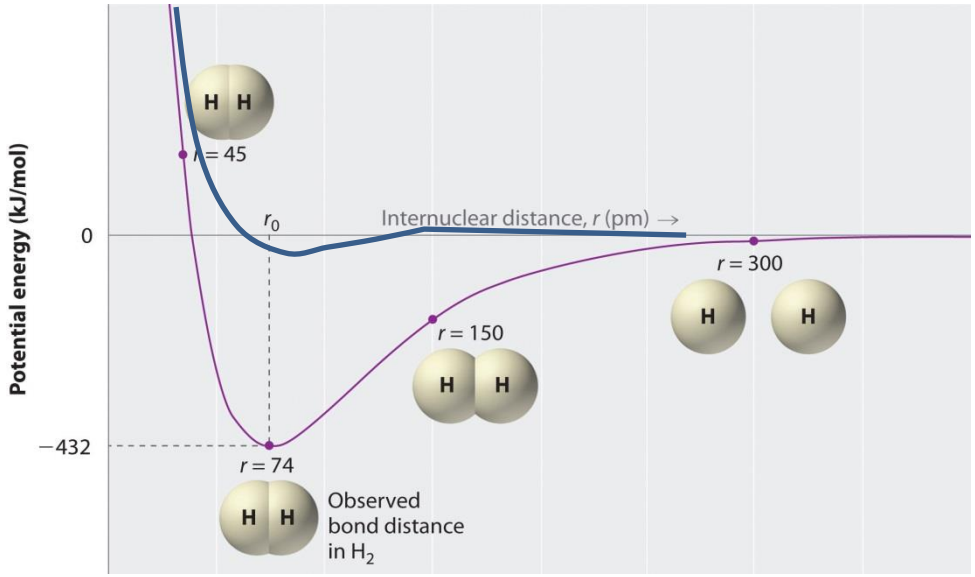
- The binding energy well is very steep
- Easy to parametrize

Motivation

Covalent bonds: easy to represent

Why?



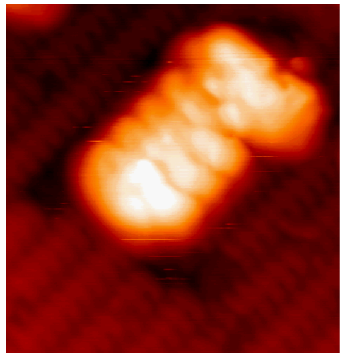


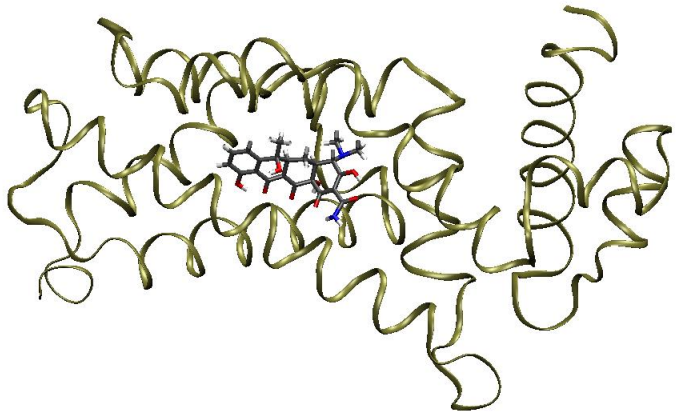
- The binding energy well is shallow (much more non local too!)
  - Less directional
  - Interactions between many atoms…
- This makes it more difficult to detect, calculate, model, add, …

Motivation

Weak interactions are critical for:

- states of matter, water properties, solubility,
- surface chemistry,
- nano-scale and materials chemistry,
- biological chemistry
  - protein folding,
  - ligand-receptor binding,
  - drug interactions





Electron density

- Quantum mechanical information in 3D… electron density!
  - ρ(r) is a fundamental property of any electronic system

$$\rho(\vec{r}) = N \int \ldots \int \left|\Psi(\vec{x}_1, \vec{x}_2, \ldots, \vec{x}_N)\right|^2 ds\, d\vec{x}_2 \ldots \vec{x}_N$$

  - ➢ is experimentally accessible
  - ➢ is defined within the exact many-body theory,
  - ➢ is supported by the Hohenberg−Kohn theorem

Electron density

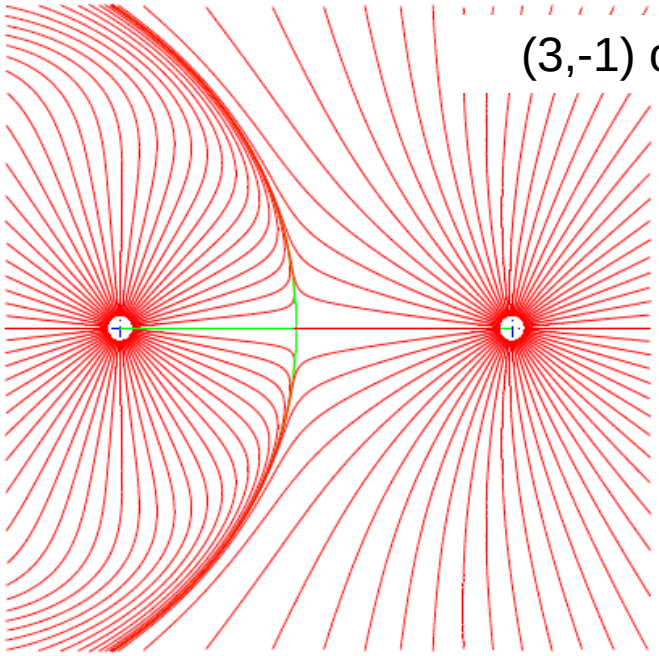
QTAIM: From electronic density to chemical structure

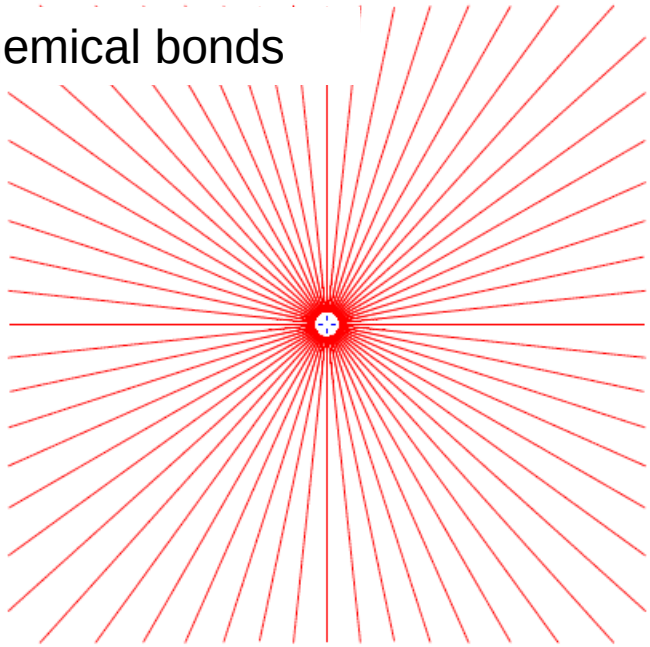
Density

- Maxima = nuclei

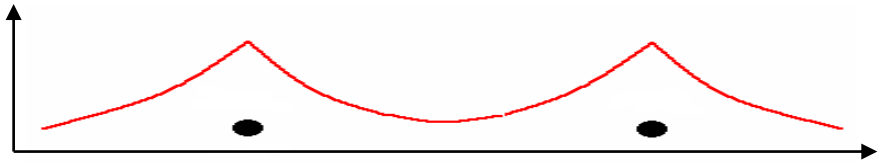
Electron density

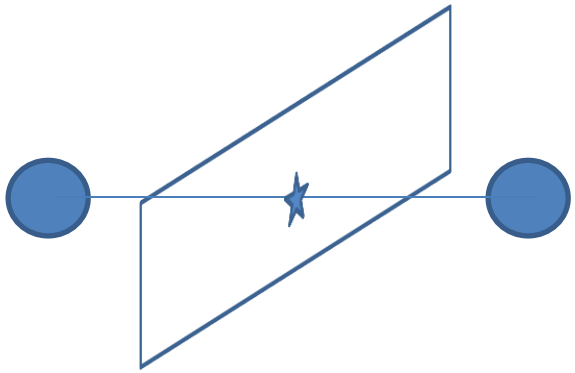
(3,-1) occur at chemical bonds





Plane that contains the nuclei





Electron density

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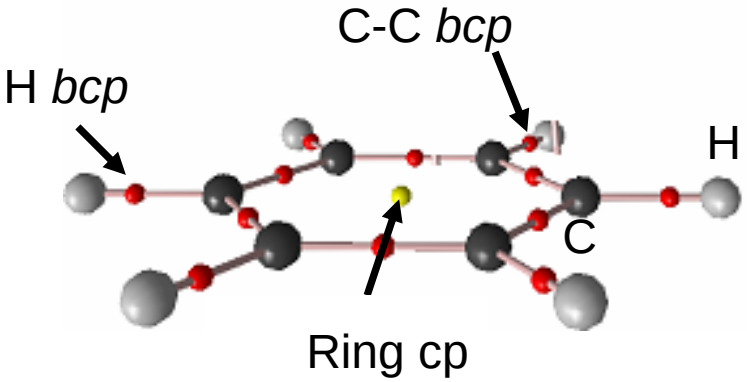
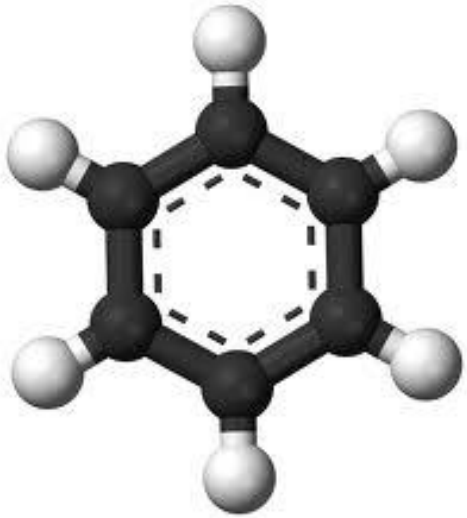


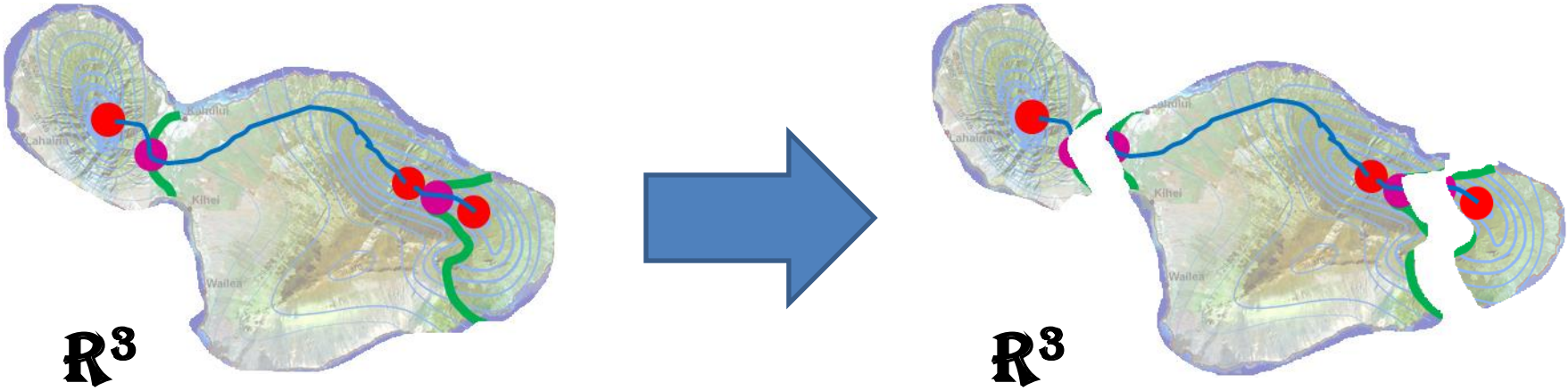


Density → ρ topology → Chemical structure

- Maxima = nuclei
- Bond = 1st order saddle point (*bcp*)

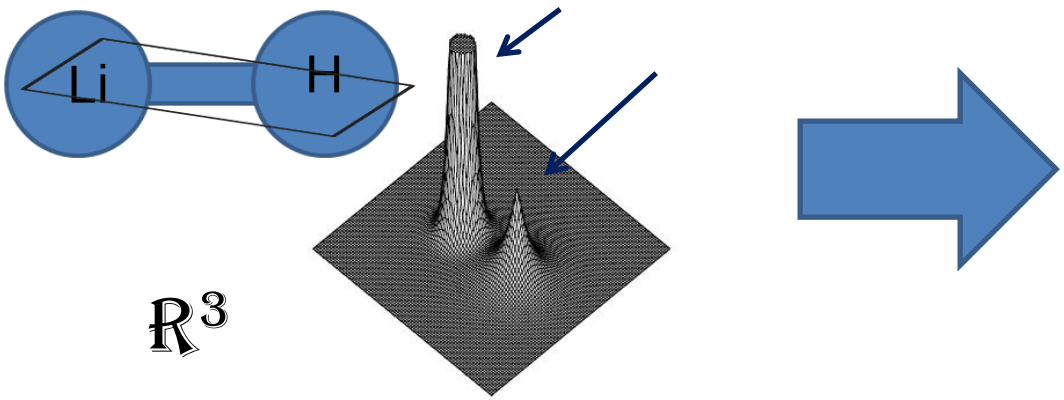
IMPORTANT PROPERTIES

- Each maximum has an associated region of space (basin)
  - Non overlapping
  - They fill up the volume

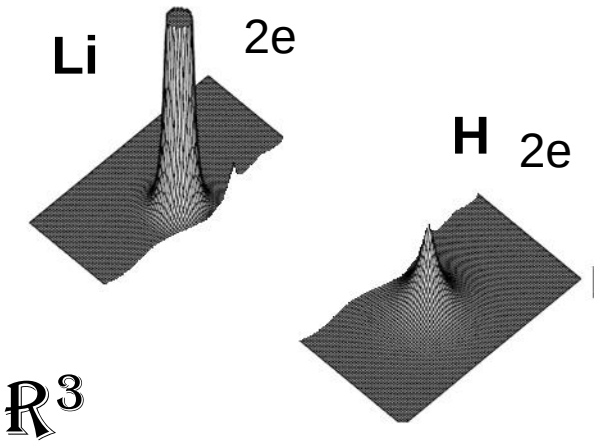


•Electron density

- Each maximum has an associated region of space (basin)
  - Non overlapping
  - They fill up the volume
  - Have a chemical meaning

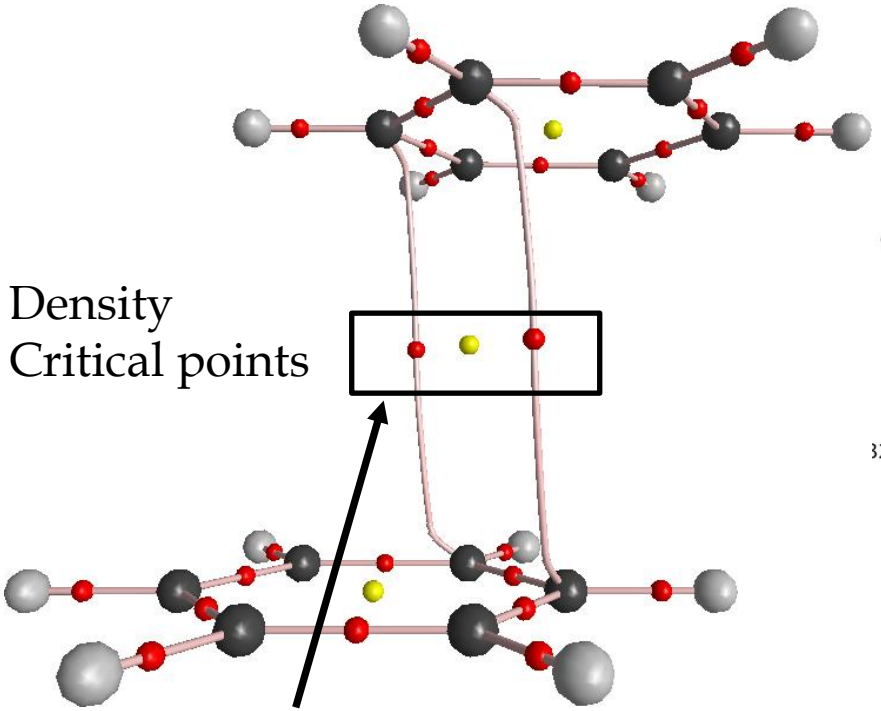


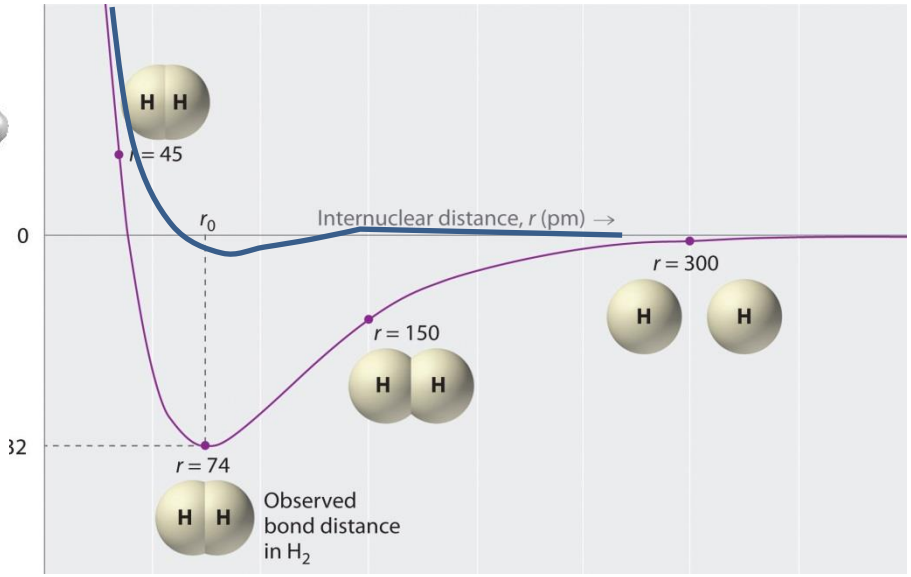
We can integrate properties!



Electron density

The topology of the density alone is not able to provide a satisfactory picture of **weak bonds**





Pair interactions are not well described by critical points

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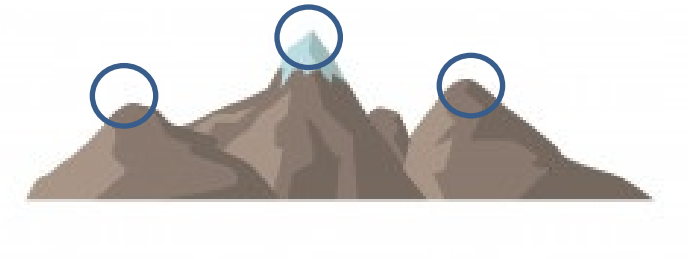
Mathematical description of interactions

Identifying a general shape

Critical point : $\nabla\rho = 0$



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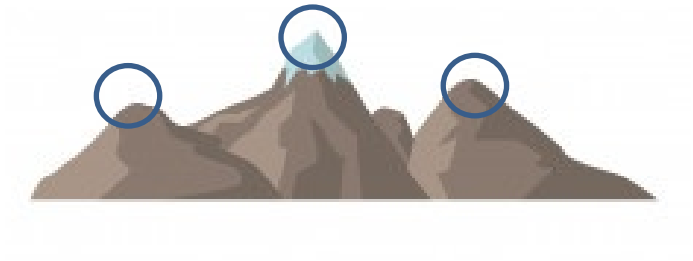
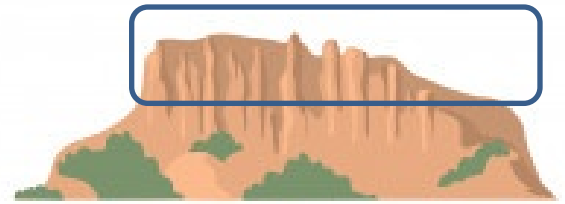


If the profile is flat…

Let's look at the region $\nabla\rho \to 0$



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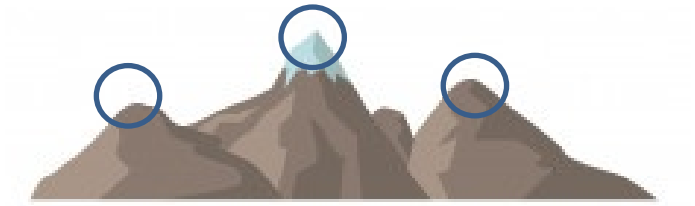

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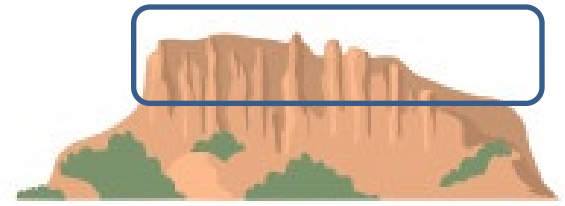
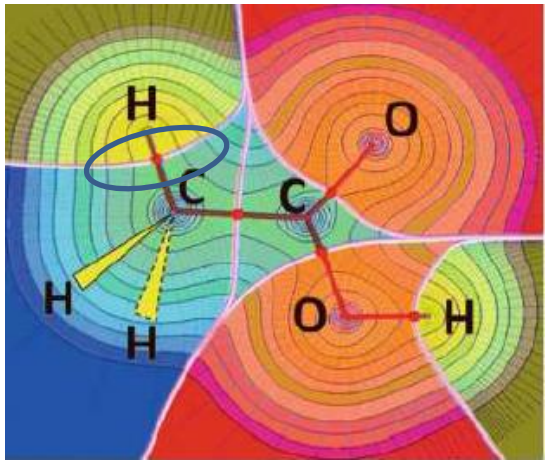


NCI:

analysis of the reduced density gradient at low densities

$$s = \frac{1}{c_s}\frac{|\nabla\rho|}{\rho^{4/3}} \quad \text{with } c_s = 2(3\pi^2)^{1/3}$$



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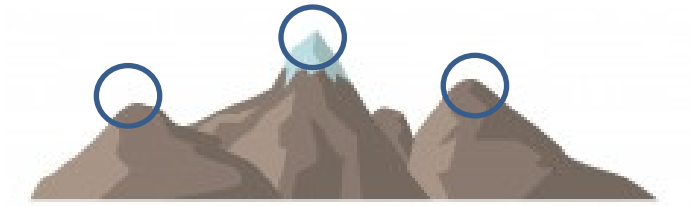

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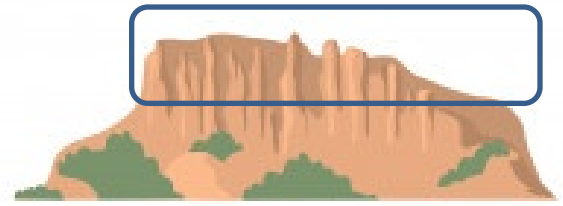

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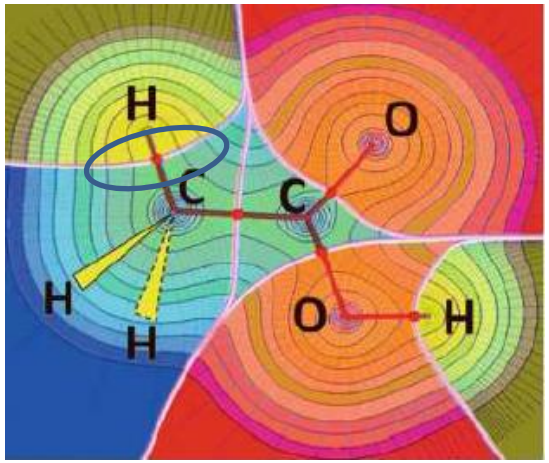
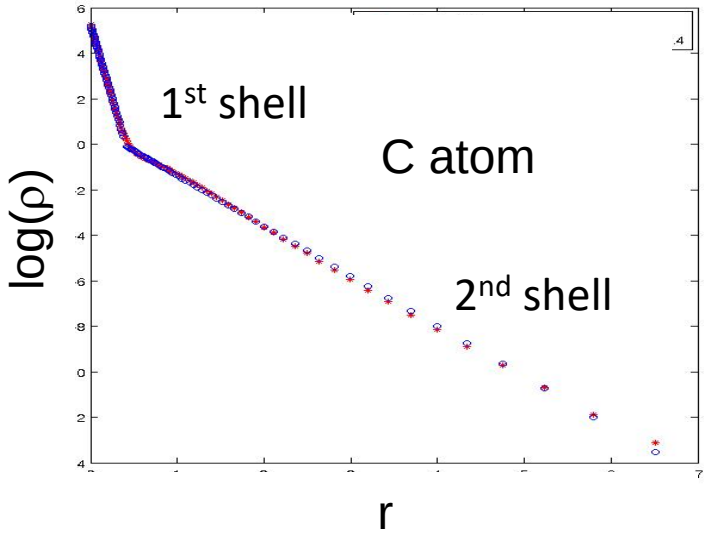


How does it work?

Model densities

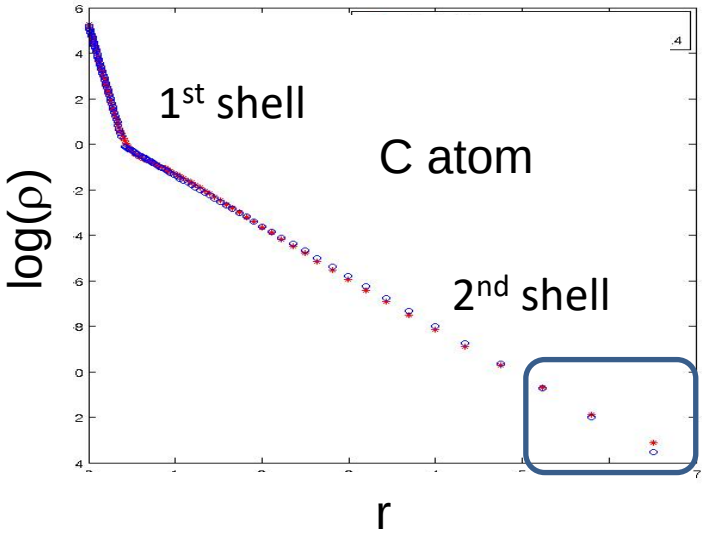


Atoms

•Atomic densities can be mimicked like a sum of $Nshells$ exponentials

$$\rho^{at}(r) = \sum_{i}^{Nshells} c_i e^{-\zeta_i r}$$

Model densities



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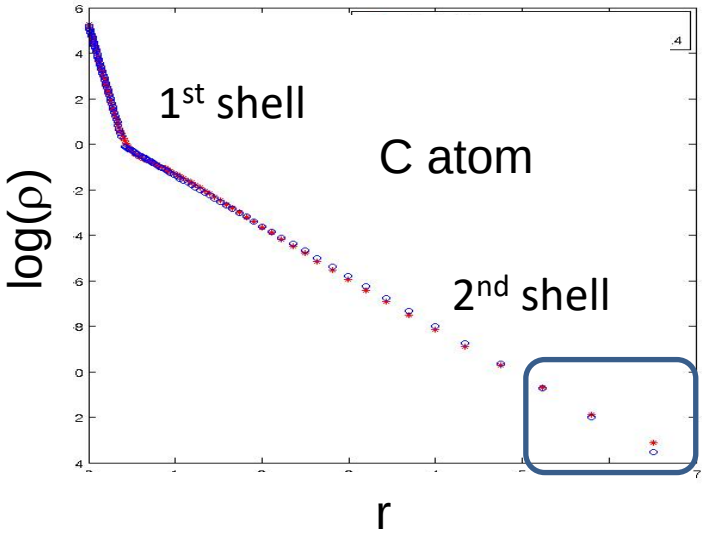

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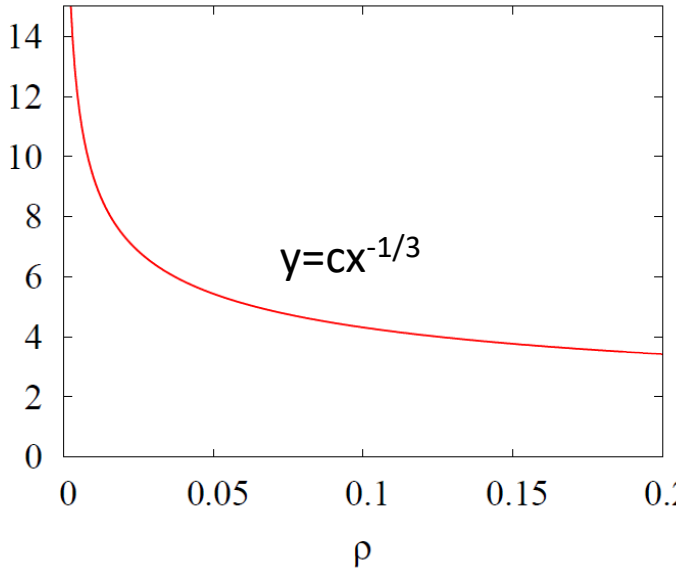

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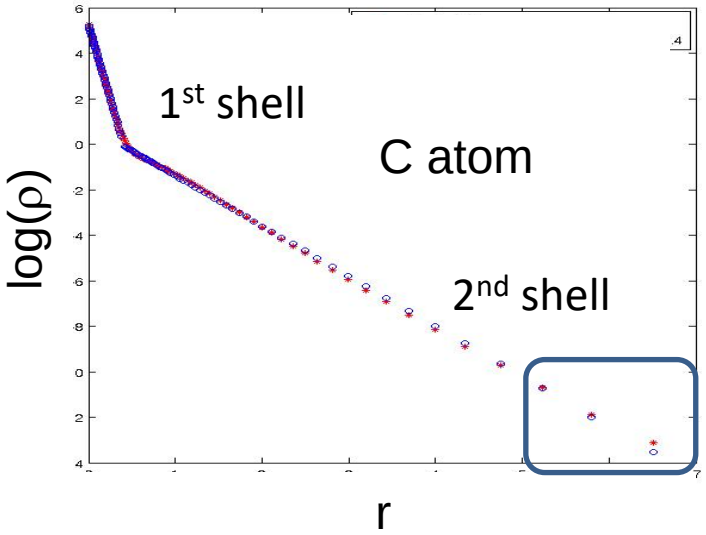

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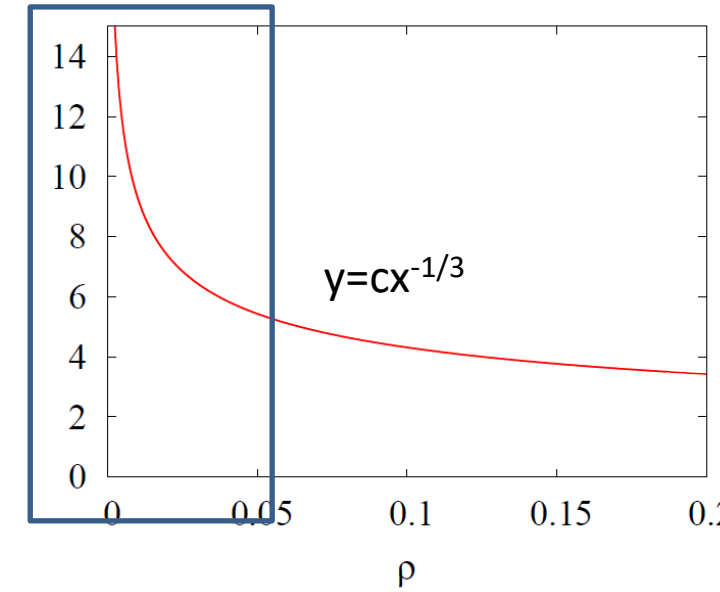
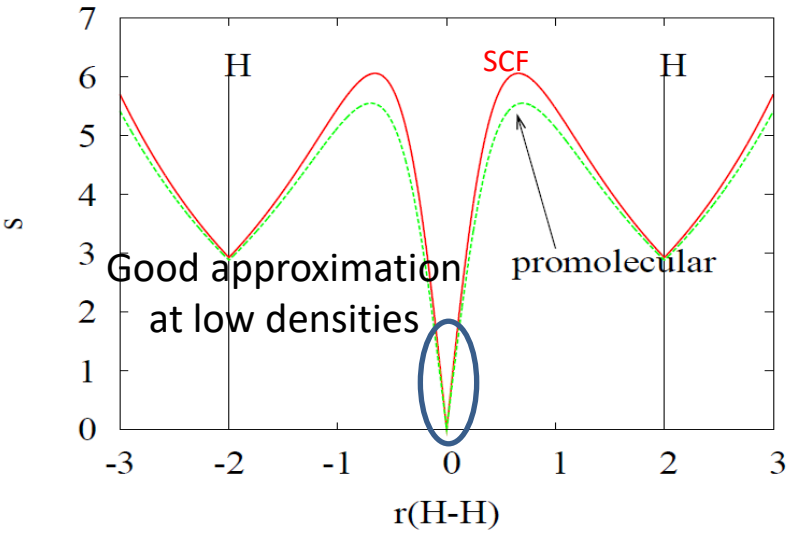
$\lim_{r\to\infty} s(r) = \infty$ (i.e. when $\rho \to 0$)



Interactions



- Promolecular approach $\rho_{molec}(r) = \sum_{j}^{Natoms} \rho_j^{at}(r)$

$$\rho(x,y,z) = \rho_{1s}^{A} + \rho_{1s}^{B} = \left(ce^{-\zeta\sqrt{x^2+y^2+(z-R/2)^2}}\right)^2 + \left(ce^{-\zeta\sqrt{x^2+y^2+(z+R/2)^2}}\right)^2$$

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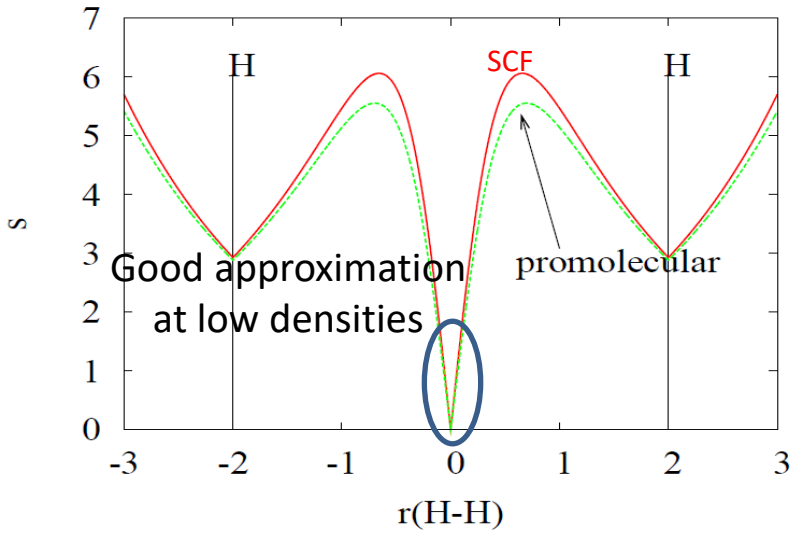

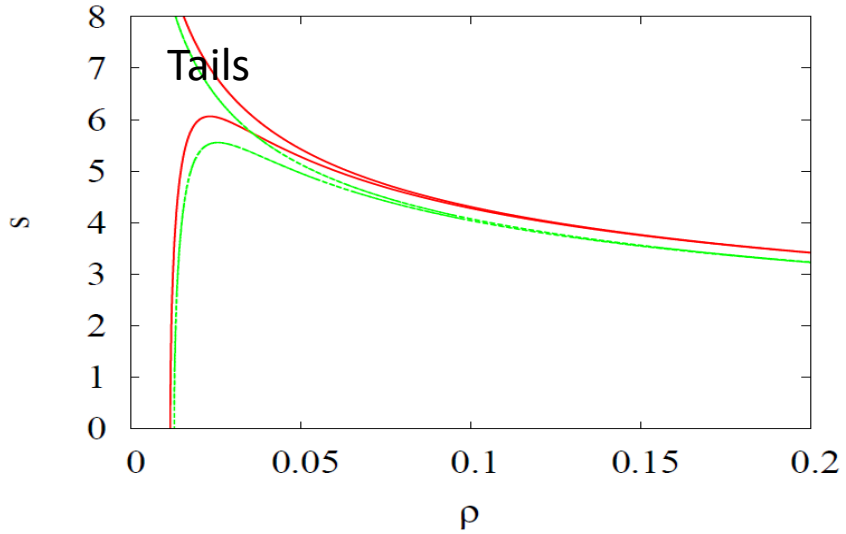

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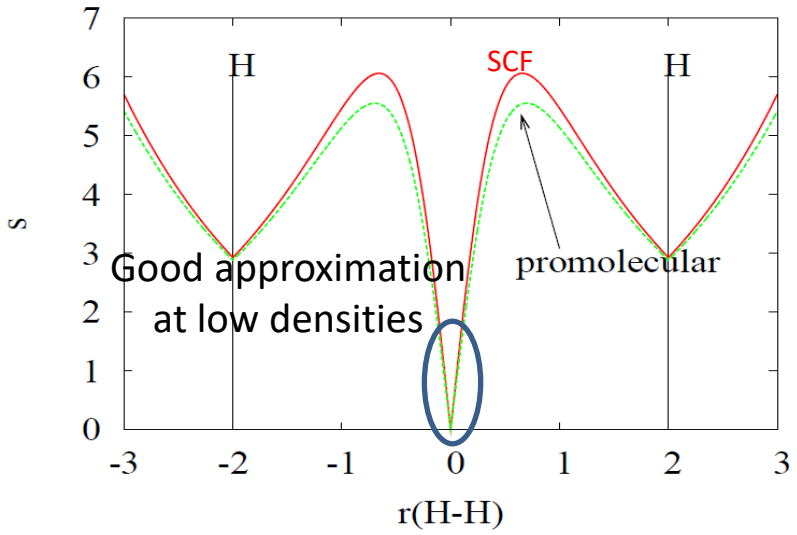

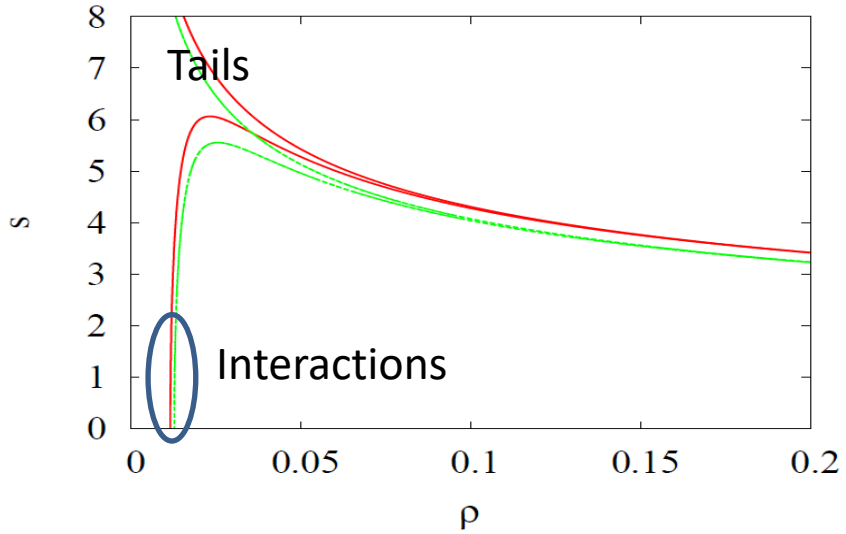

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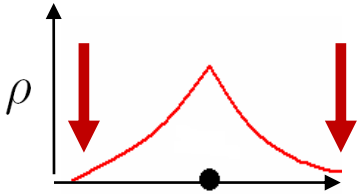
- s →0 in the interactions

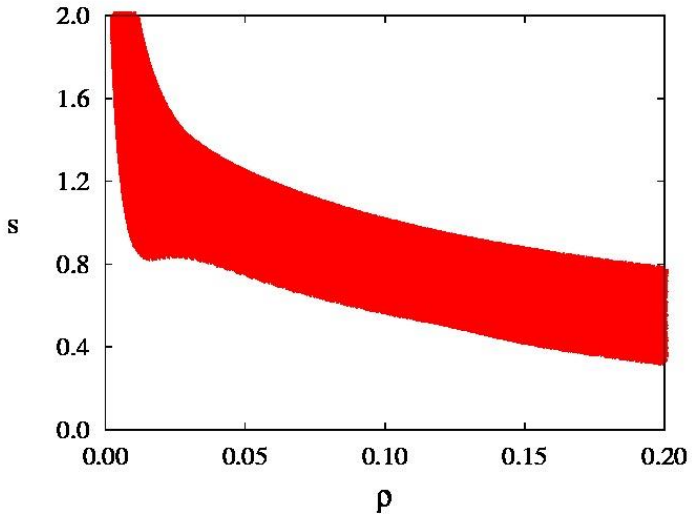
$$\lim_{z\to 0} s(\rho) = \lim_{z\to 0}(e^{R/3}r + O(r^3)) = 0$$

The reduced density gradient

Non-interacting densities



$$s(\rho) \propto \rho^{-1/3} \xrightarrow{\rho \to 0} \infty$$



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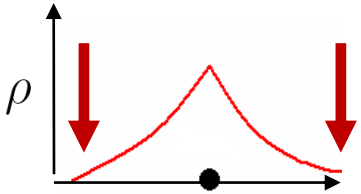

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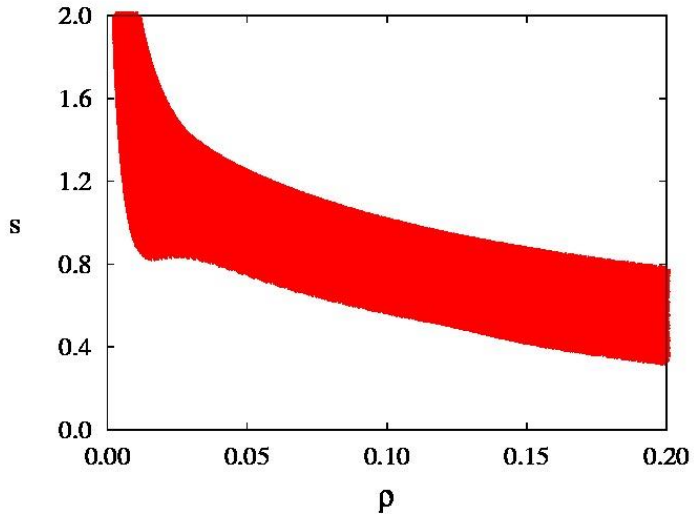
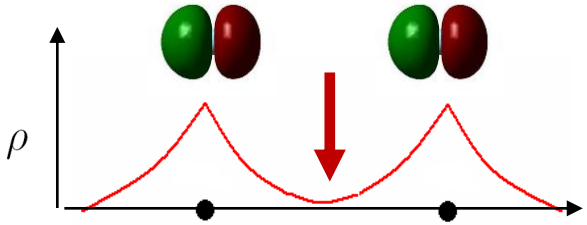
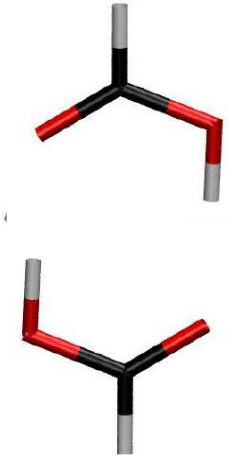
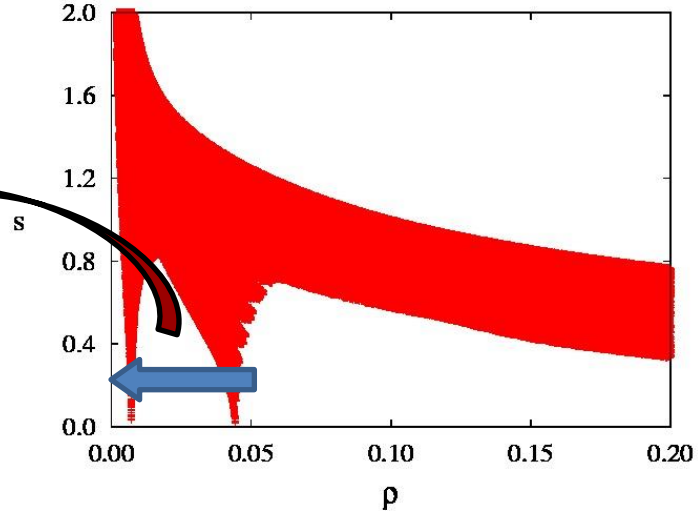


Interacting densities





$$s(\rho) \xrightarrow{r \to 0} e^{R/3} r + O[r]^3 \to 0$$



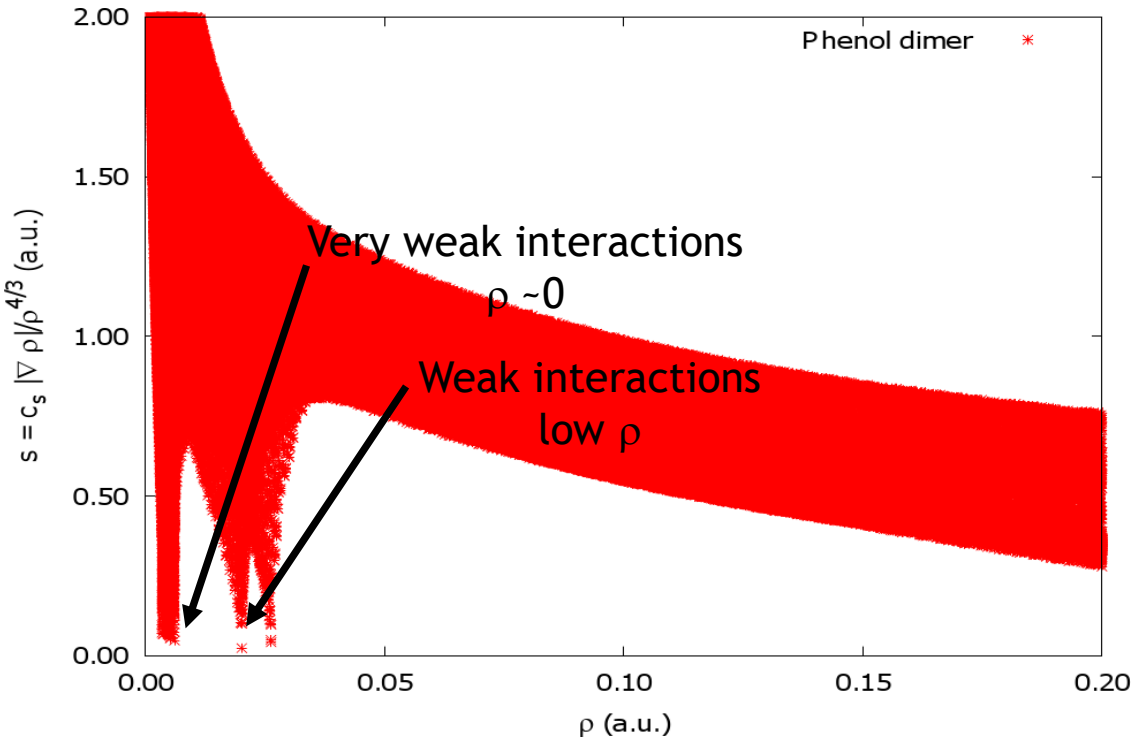
J. Am. Chem. Soc. 132 , 6498 (2010)

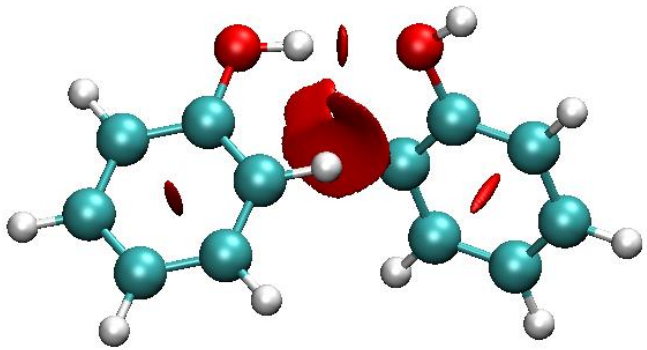
The reduced density gradient

Differentiating interaction types

1

•Density is proportional to the strength of the interaction



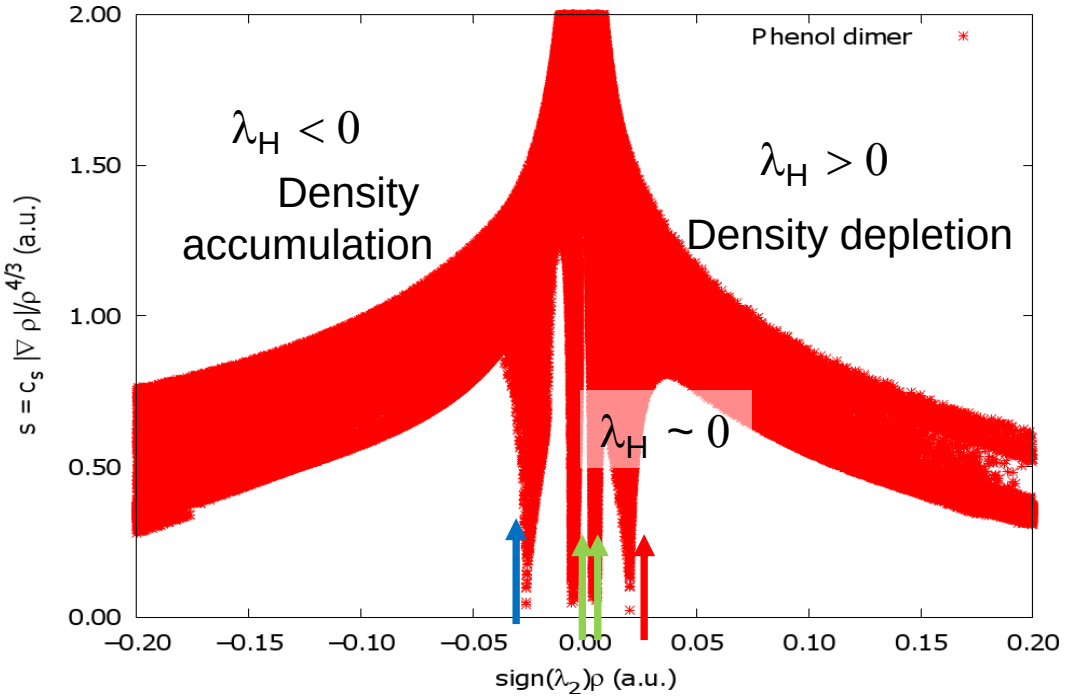


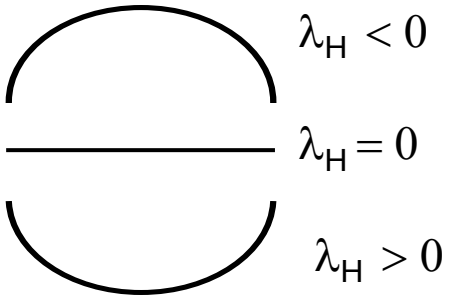
The reduced density gradient

Differentiating interaction types

2

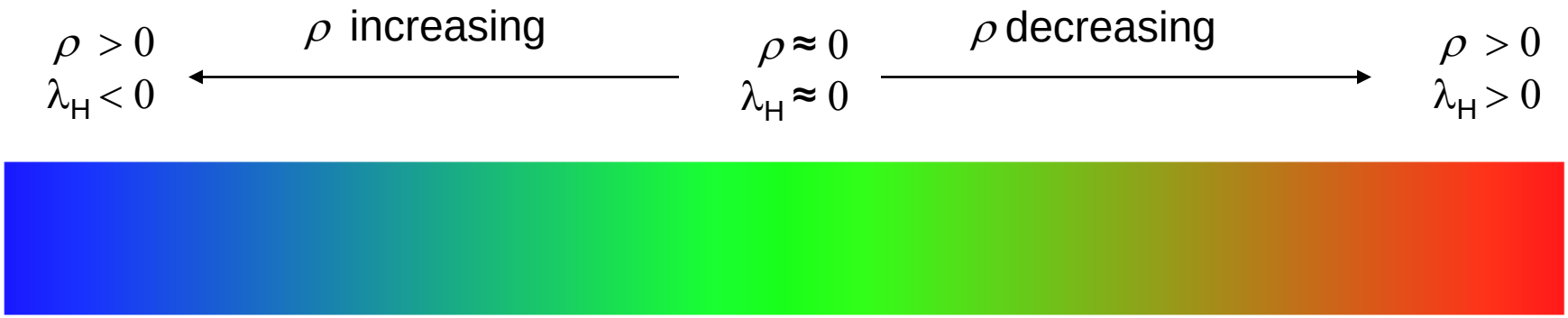
- Bonding interactions →charge accumulation ($\lambda_H < 0$)
- Antibonding interactions → charge depletion ($\lambda_H > 0$)





Interaction types

Different interaction types are represented with different colours



Strong and attractive:

Hydrogen bonds

Very weak:

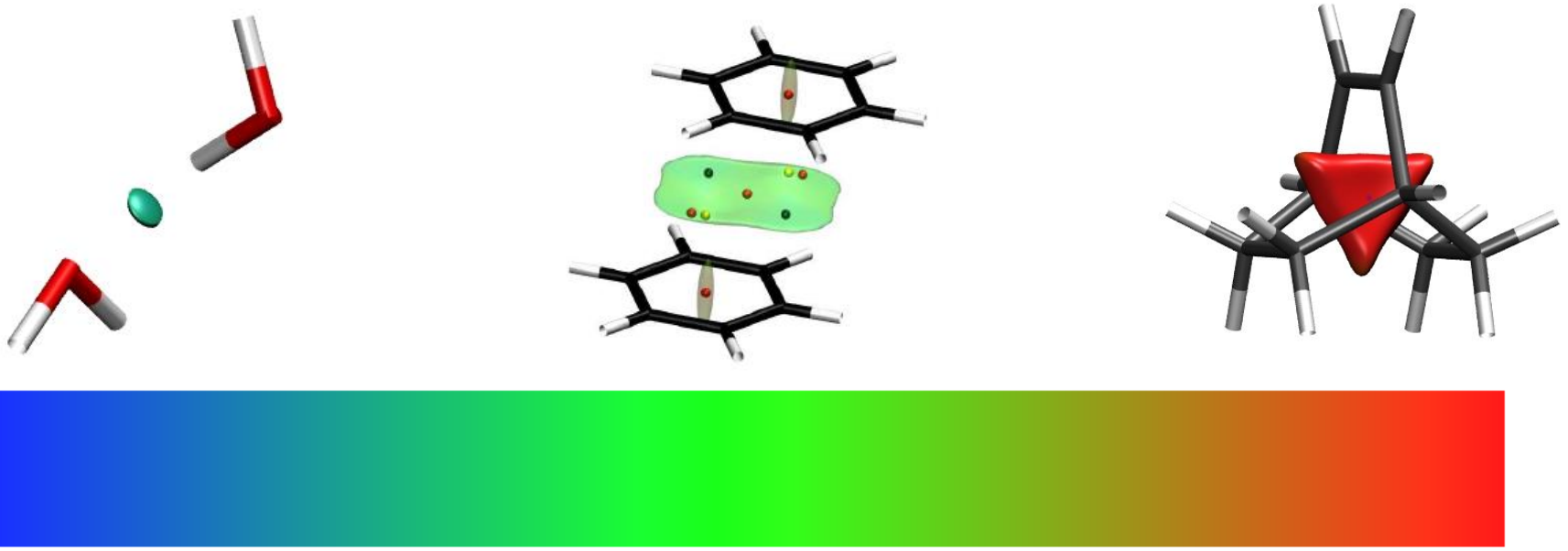
van der Waals

Strong and repulsive:

Steric clashes

J. Am. Chem. Soc. 132 , 6498 (2010)

Interaction types



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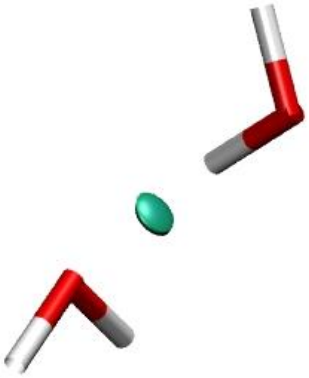
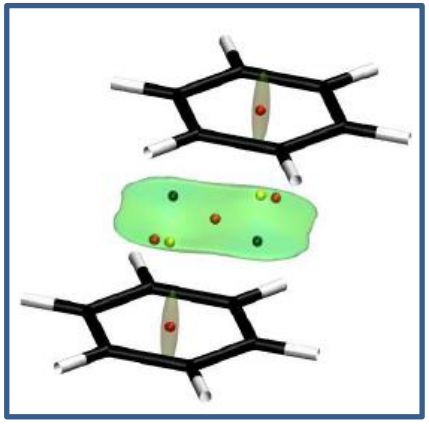
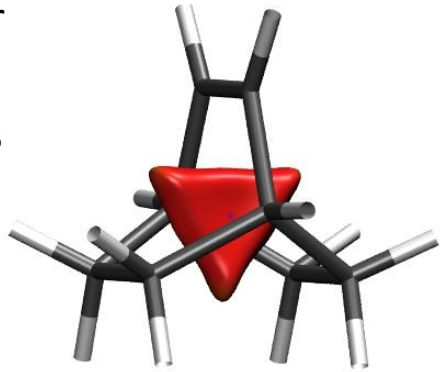
J. Am. Chem. Soc. 132 , 6498 (2010)

Interaction types





Adapted for delocalized interactions



Strong and attractive:

Hydrogen bonds

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van der Waals

Strong and repulsive:

Steric clashes

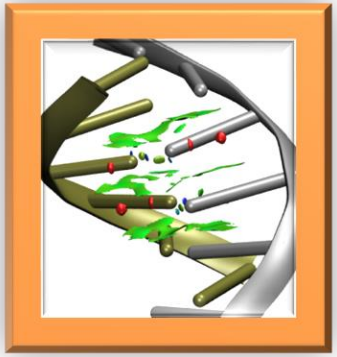
J. Am. Chem. Soc. 132 , 6498 (2010)

The programs

NCIPLOT

NCI for molecules and biomolecules

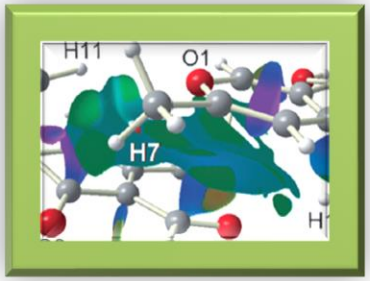
JCTC 7, 625 (2011)



NCIMILANO

NCI for experimental densities

Chem. Eur. J. 18, 15523 (2012)



CRITIC

NCI for solid calculations

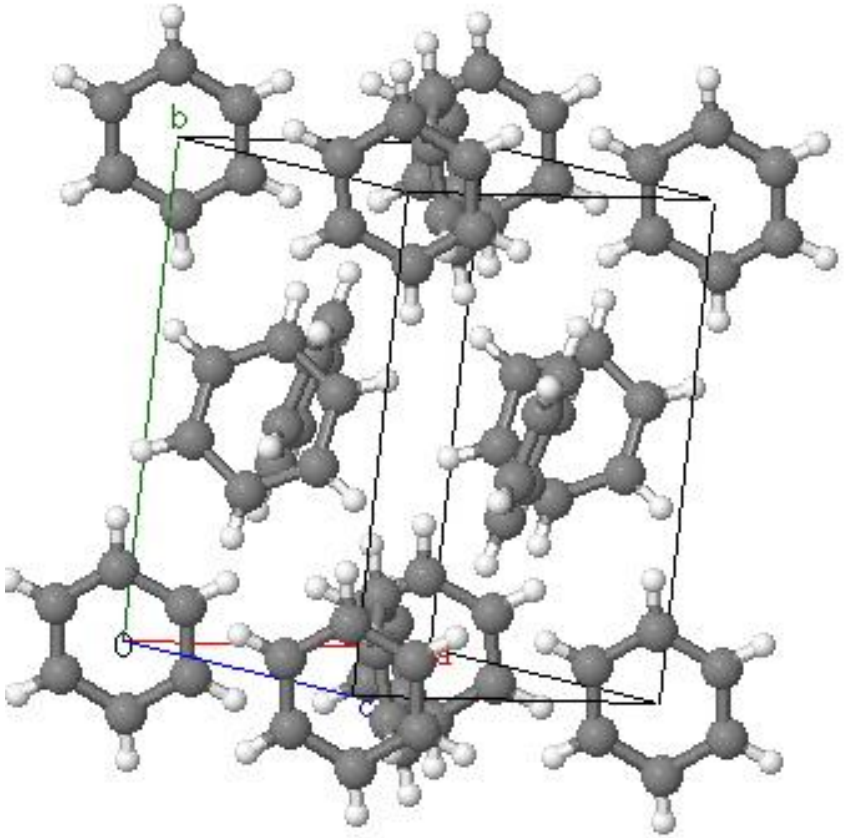
PCCP 14, 12165 (2012)

Outline

- Why are we still studying NCIs?
- QTAIM (Quantum Theory of Atoms in Molecules)
  - Critical points
  - Integrals
- NCI (Non covalent interaction index)
  - Definition
  - NCI vs AIM
  - Big systems
- Summary

NCI vs AIM

Nevertheless, thanks to the shape of the isosurface we can visually collect more information…



Benzene packing maximizes the number of C-H···π and C-H···C contacts.

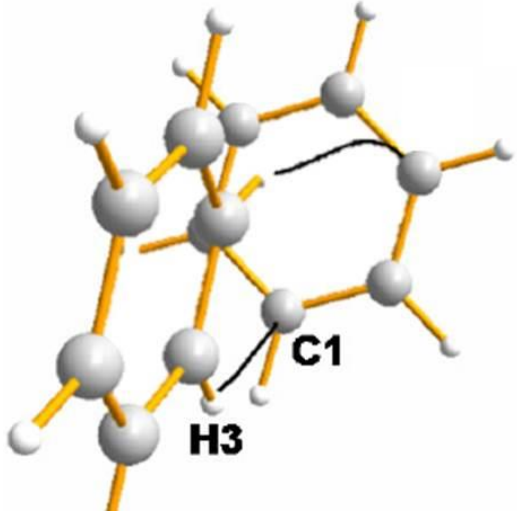
NCI vs AIM

Delocalized interactions

AIM

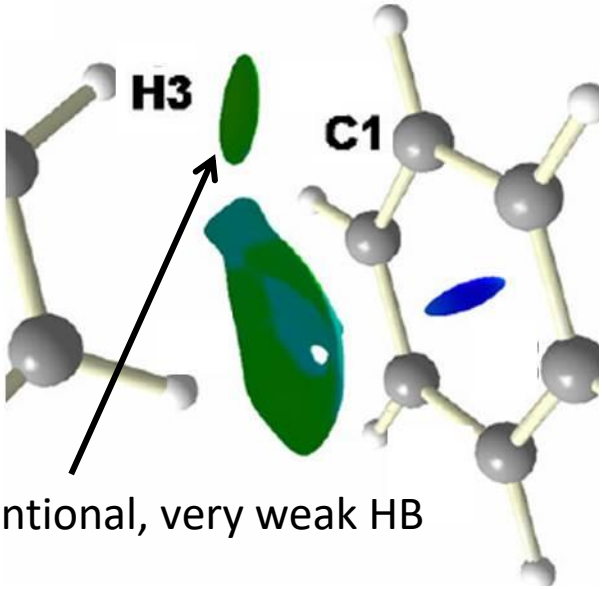
Largely oriented location of H3

Straight BP privileges the interaction of the H with just one single atom of the ring



NCI

Disc-shaped and localized



conventional, very weak HB

NCI and BP pictures nicely match

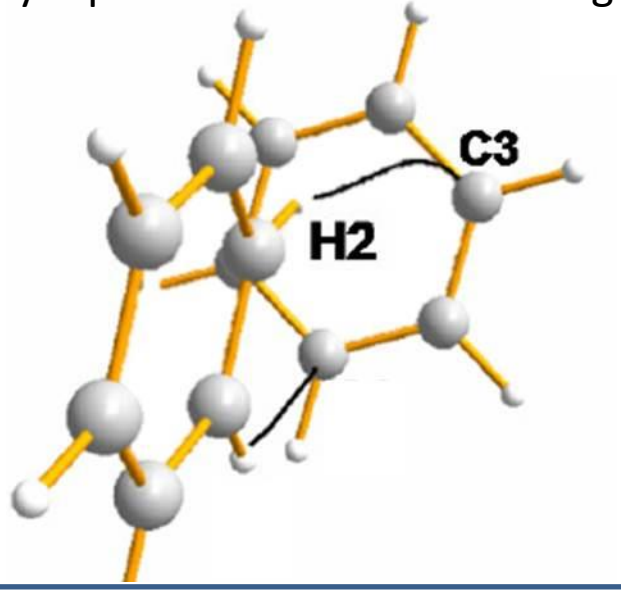
NCI vs AIM

Delocalized interactions

AIM

CH···C interaction significantly bent

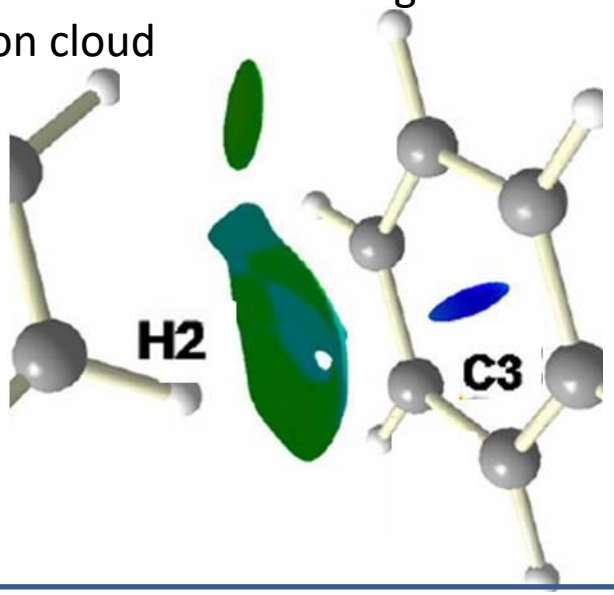
H roughly equidistant to the whole ring



NCI

Large isosurface that covers the ring

C-H···π interaction involving the whole π electron cloud



BP analysis privileges the interaction of the H with just one single atom of the ring

NCI provides a delocalized interaction

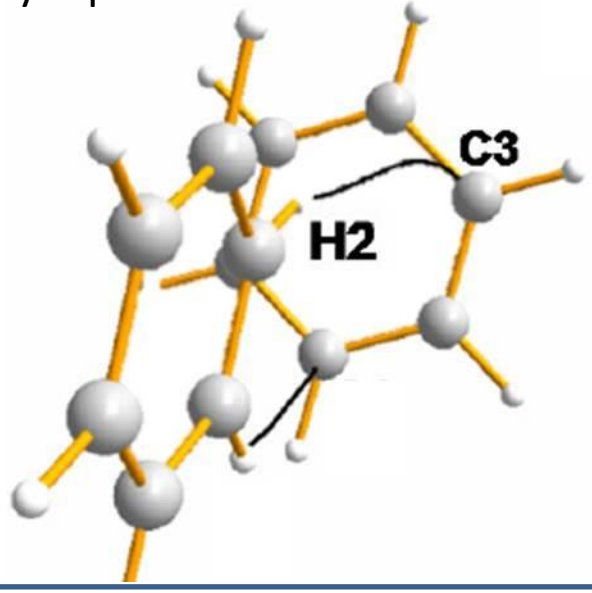
NCI vs AIM

Delocalized interactions

AIM

CH···C interaction significantly bent

H roughly equidistant to the whole ring



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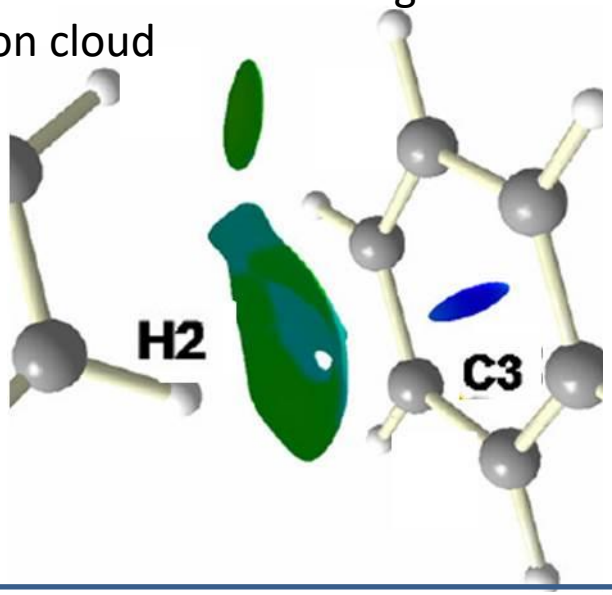
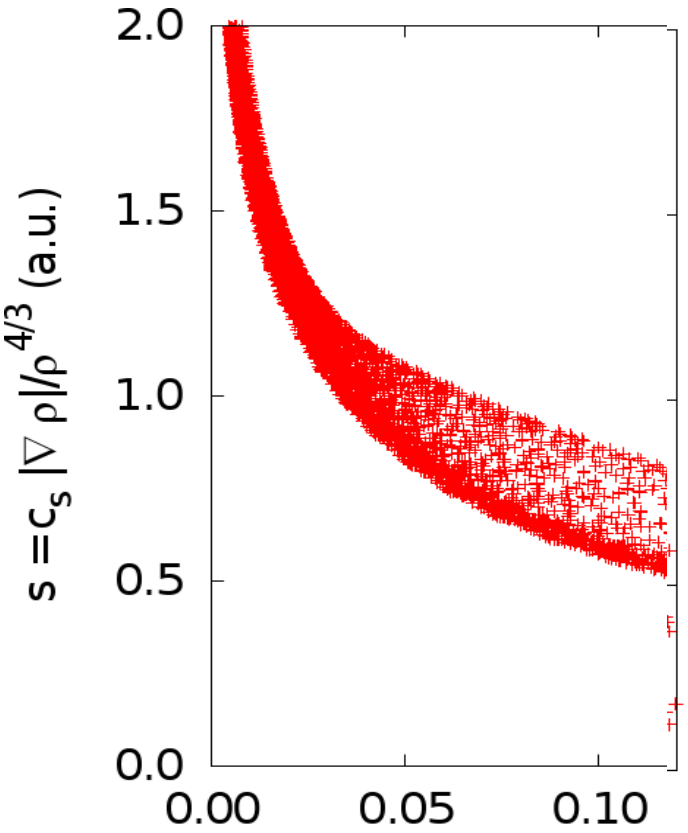
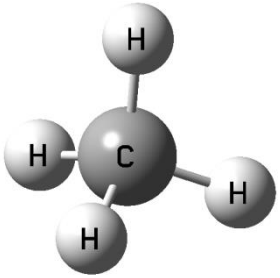


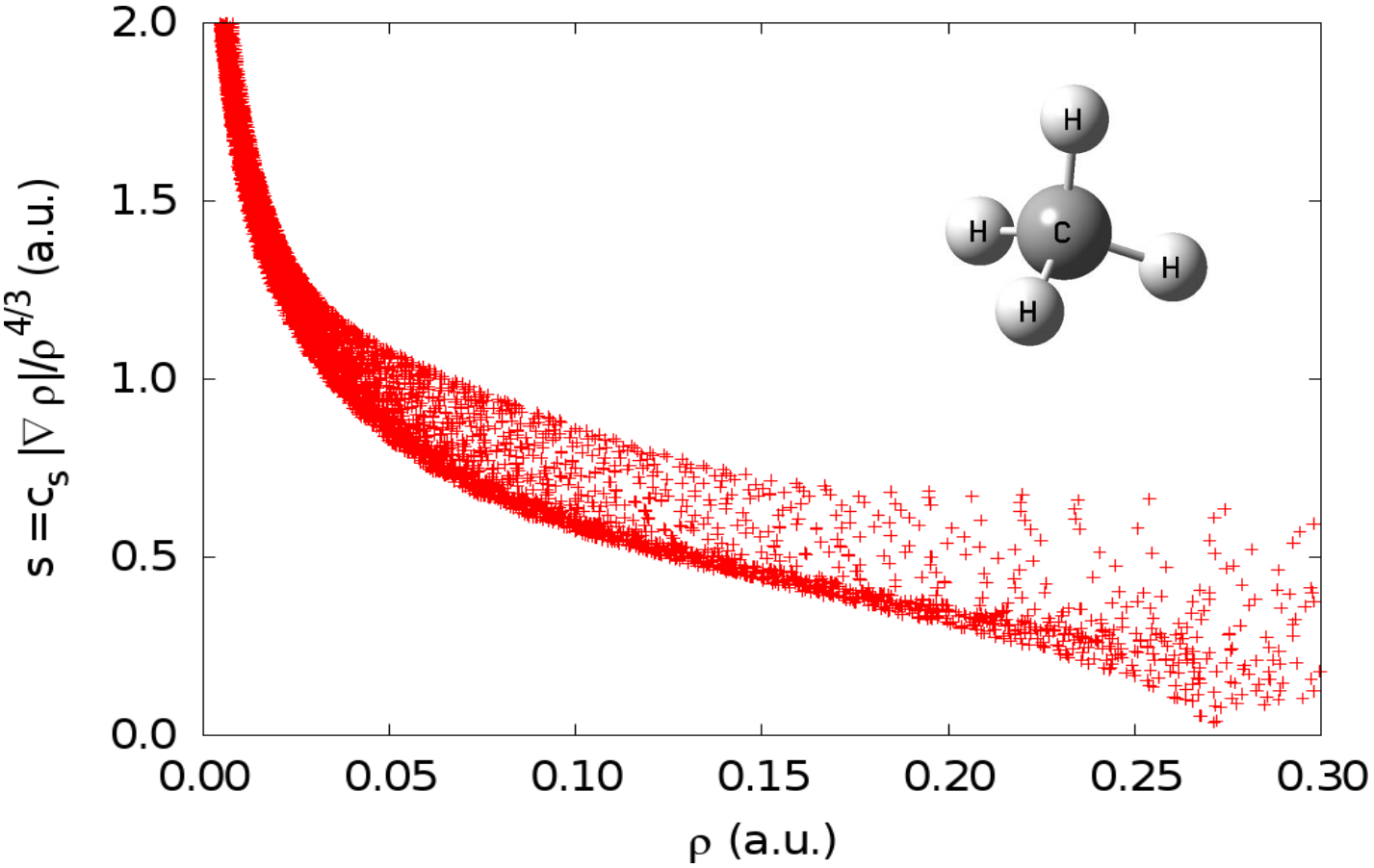
BP analysis privileges the interaction of the H with just one single atom of the ring

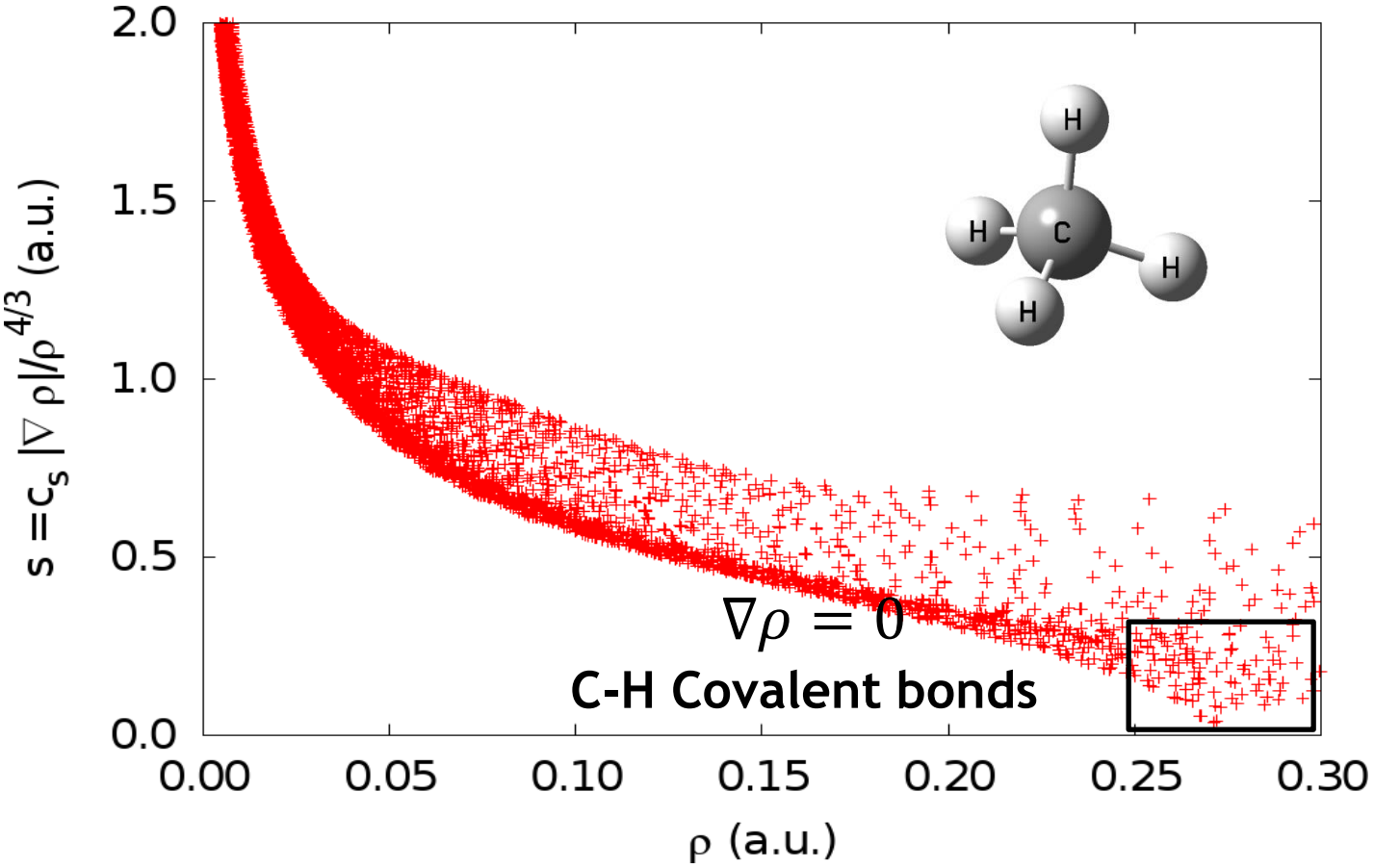
NCI provides a delocalized interaction

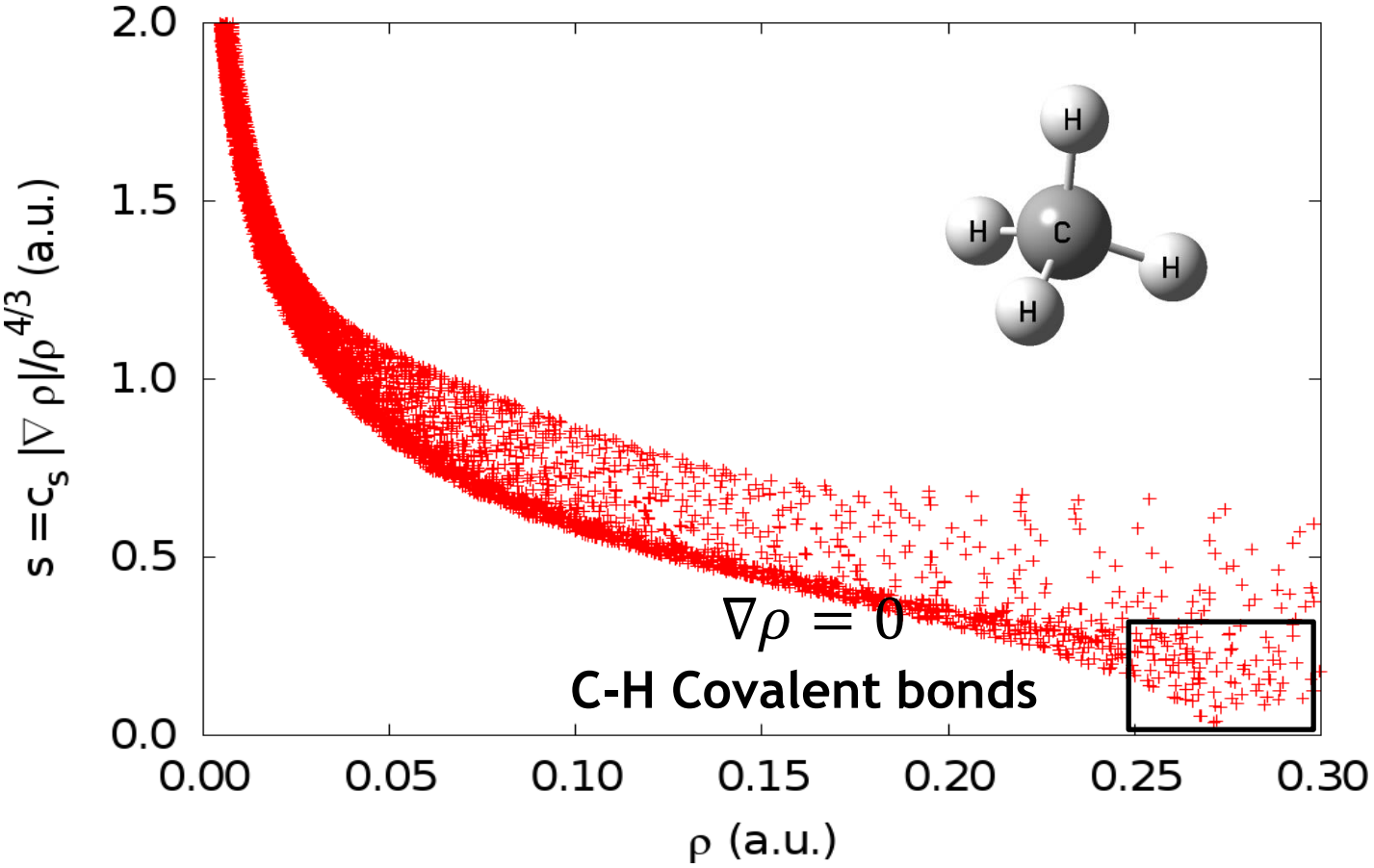
And in strong interactions?


2.0
1.5
1.0
0.5
0.0
0.00
0.05
0.10
s = c_s |∇ ρ|/ρ^4/3 (a.u.)


H
H
C
H
H


2.0
1.5
1.0
0.5
0.0
0.00
0.05
0.10
0.15
0.20
0.25
0.30
s = c_s |∇ ρ|/ρ^4/3 (a.u.)
ρ (a.u.)
H
H
C
H
H

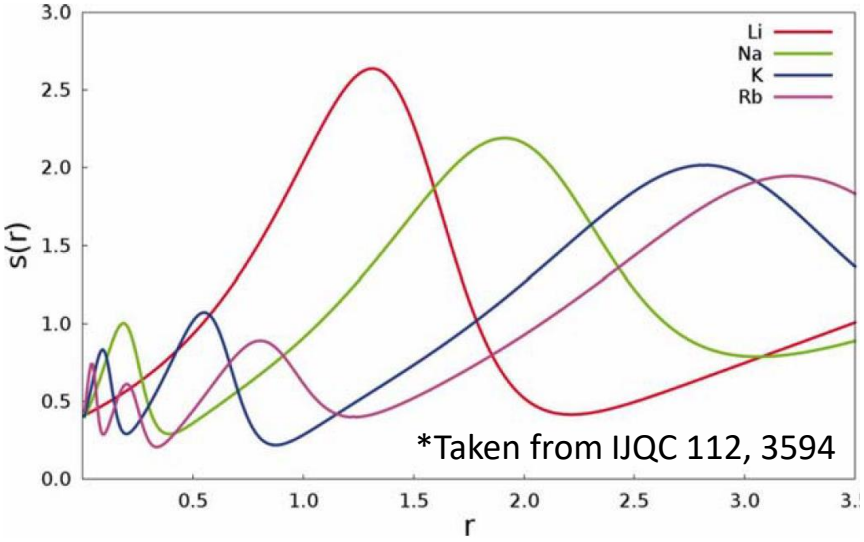

2.0
1.5
1.0
0.5
0.0
0.00
0.05
0.10
0.15
0.20
0.25
0.30
s = c_s |∇ ρ|/ρ^4/3 (a.u.)
ρ (a.u.)
H
H
C
H
H
∇ρ = 0
C-H Covalent bonds



If we keep going to higher densities?

NCI at high densities

- Number of atomic shells are correctly predicted



NCI at high densities

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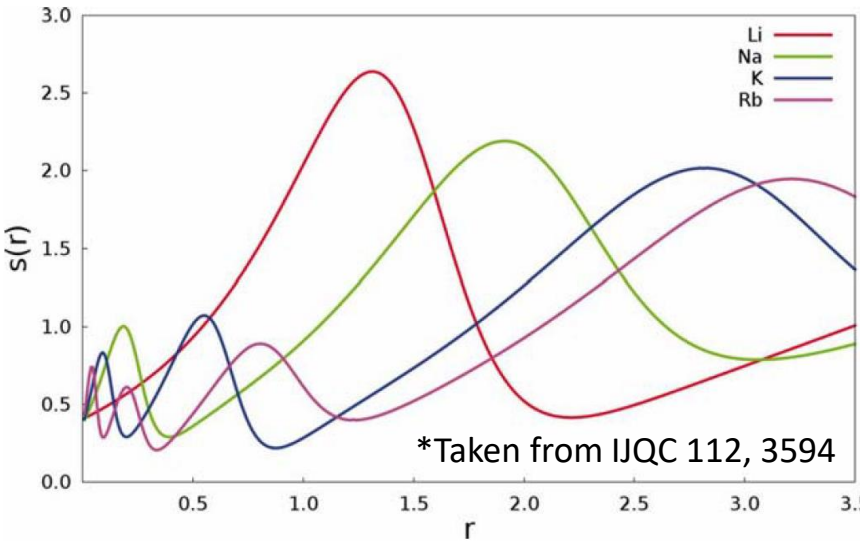
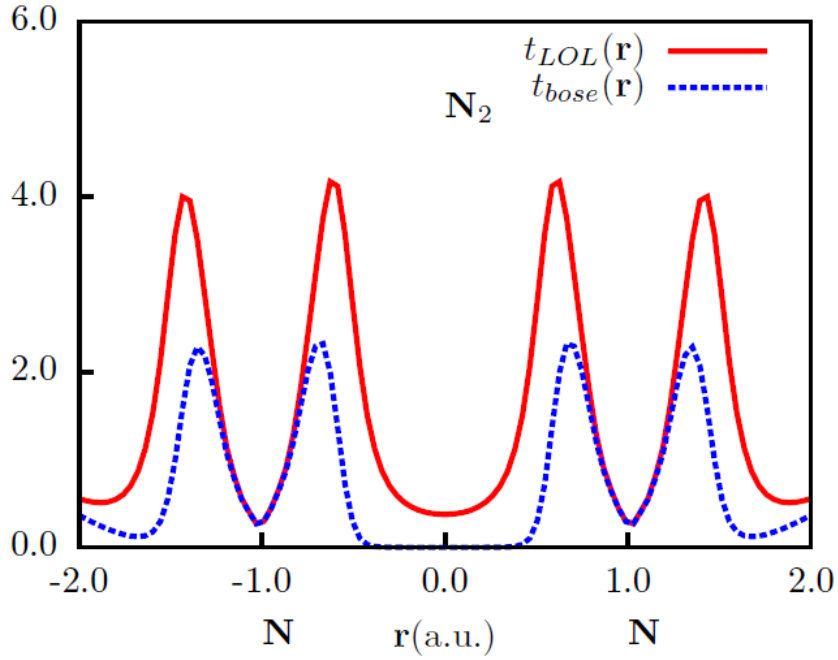


- Lewis pairs



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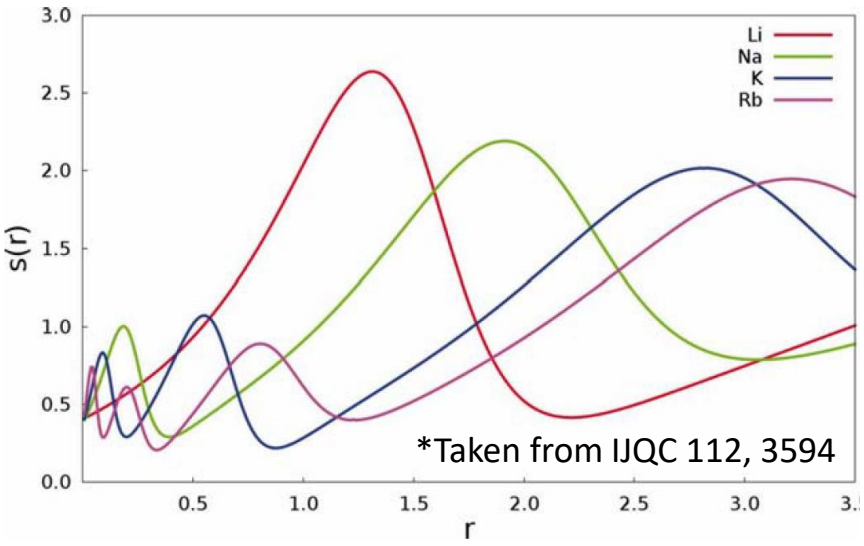
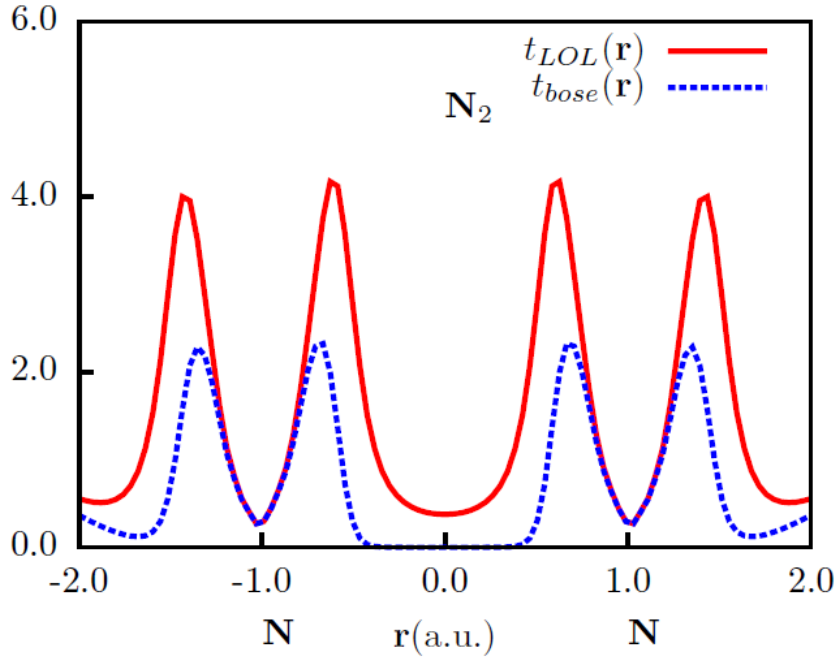


- Lewis pairs



NCI identifies regions of electron localization:

- Shell structure
- Covalent bonds
- Lone pairs

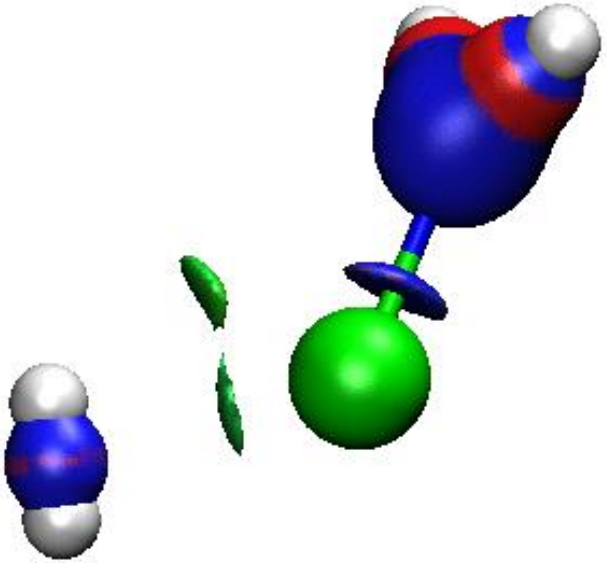
All bonds = Reactivity studies

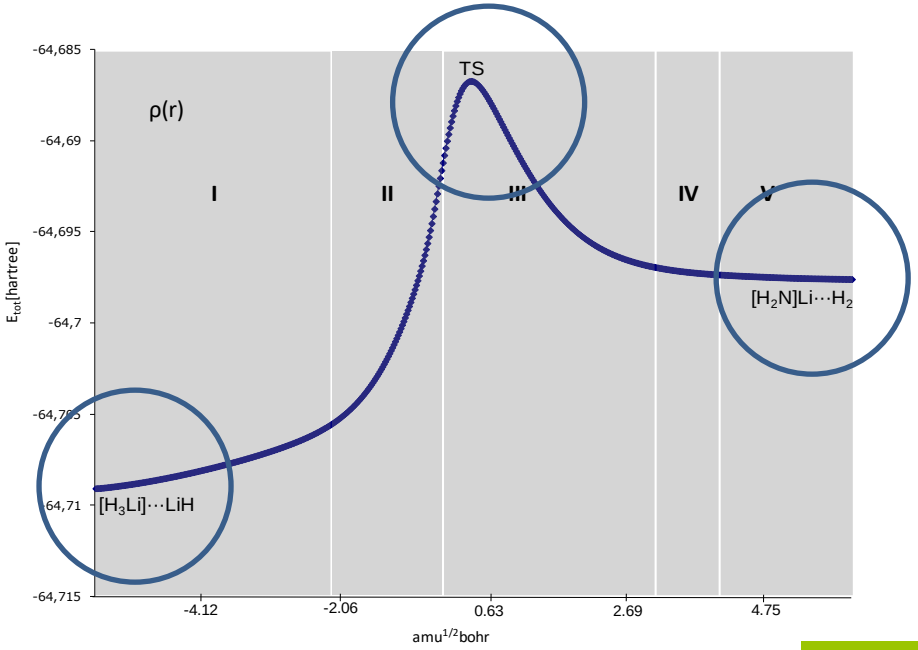
- We can study all interactions types (covalent, ionic, non covalent) on the same ground
- **Ideal for reactivity studies (so we have structure+change!)**

All bonds = Reactivity studies

- We can study all interactions types (covalent, ionic, non covalent) on the same ground
- **Ideal for reactivity studies (so we have structure+change!)**

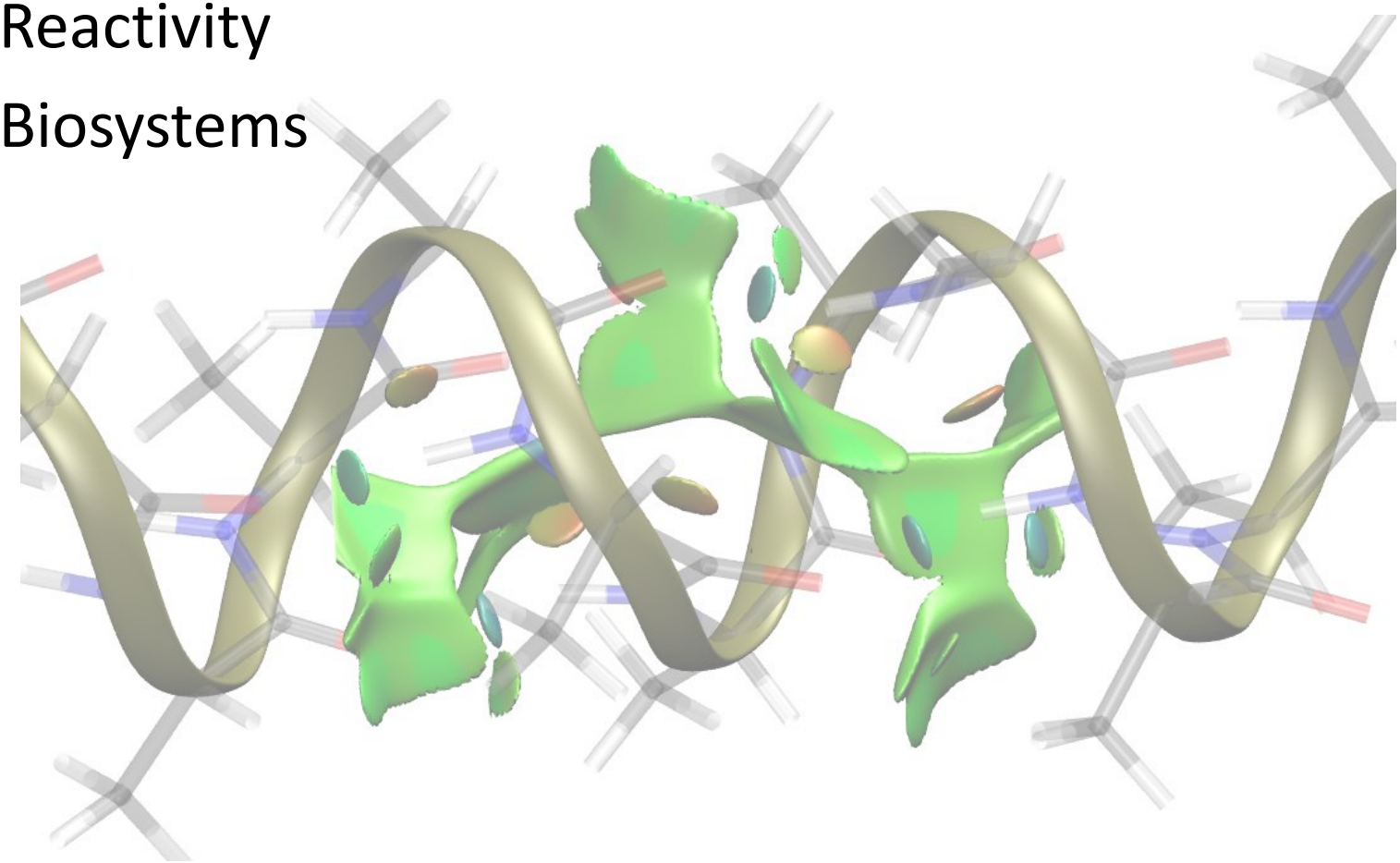
e.g. $LiNH_2 + H_2 \leftrightarrow NH_3 + LiH$





J. Phys. Chem., 118, 1663 (2014)

- Applications to
  - Reactivity
  - Biosystems

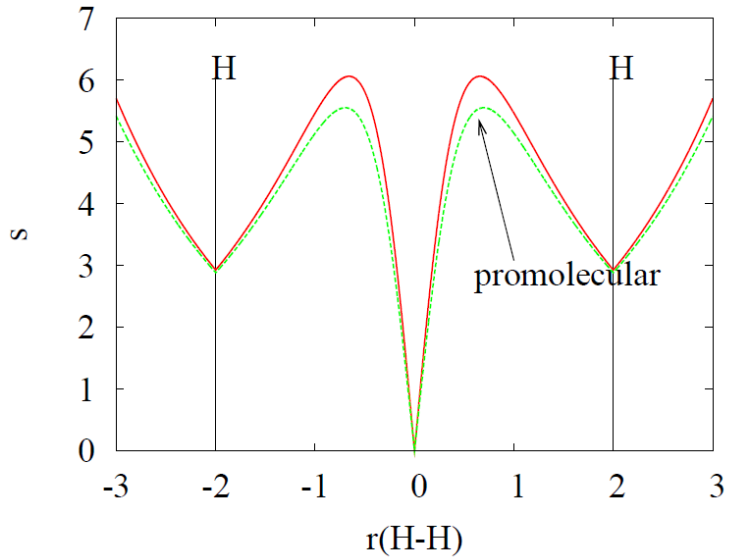


Big systems

•One of the major areas of application of weak interactions are biomolecules

•Wavefunctions are not available

•We can resort to promolecular densities as approximation!



Big systems

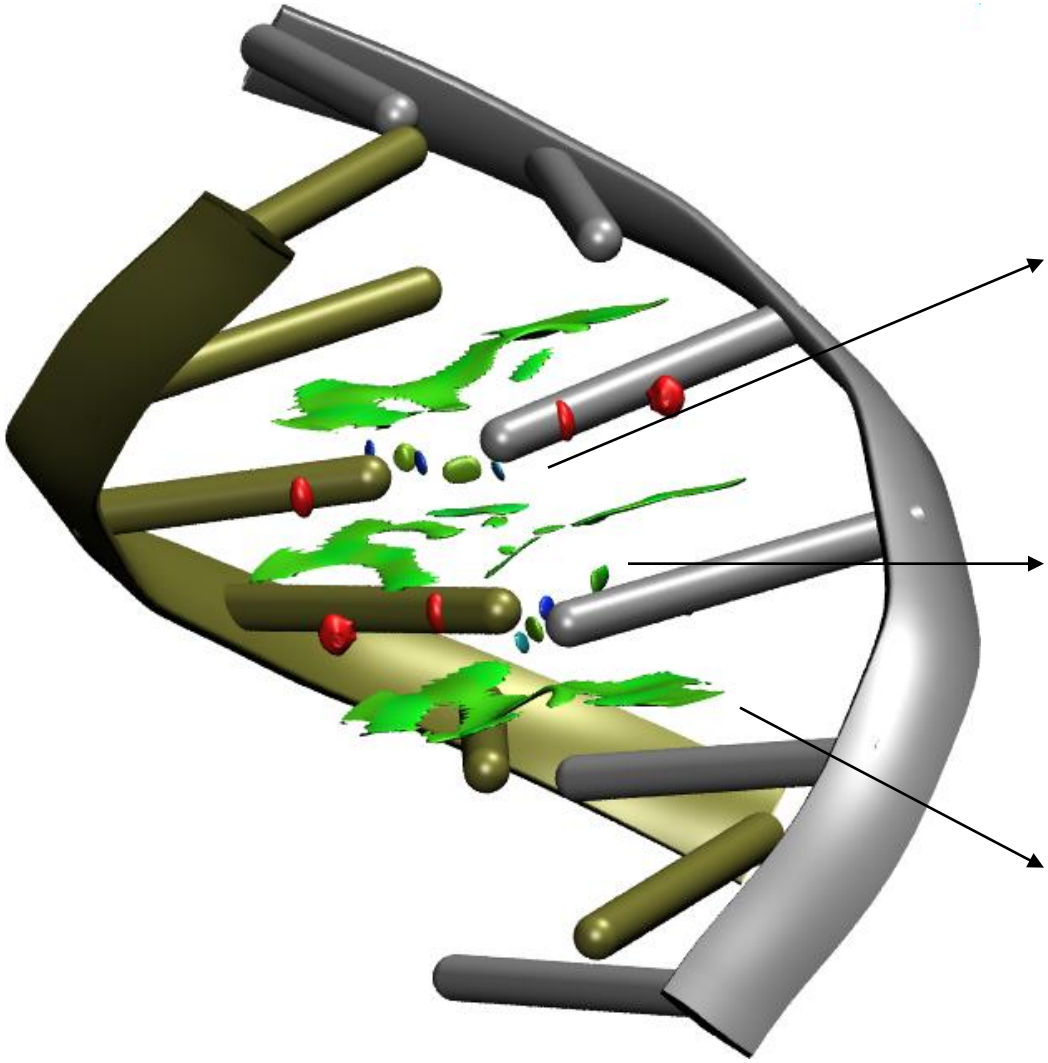
Easy to code internally

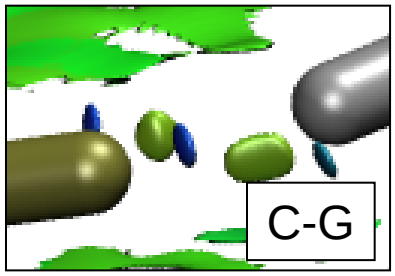
- Sum overs exponentials located on atoms

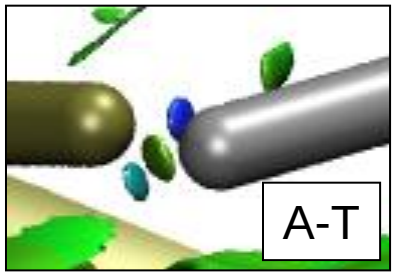
$$\rho_{molec}(r) = \sum_{j}^{Natoms} \sum_{i}^{Nshells} c_{i,j} e^{-\zeta_{i,j} r}$$

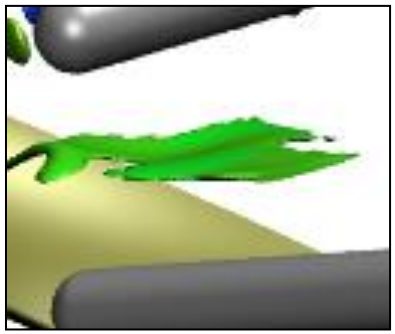
- Parameters ζ_i and c_i for each atom are internally stored in the code
- No need for wavefunction (we need atomic coordinates)
- Sum on a grid (very fast)

Big systems







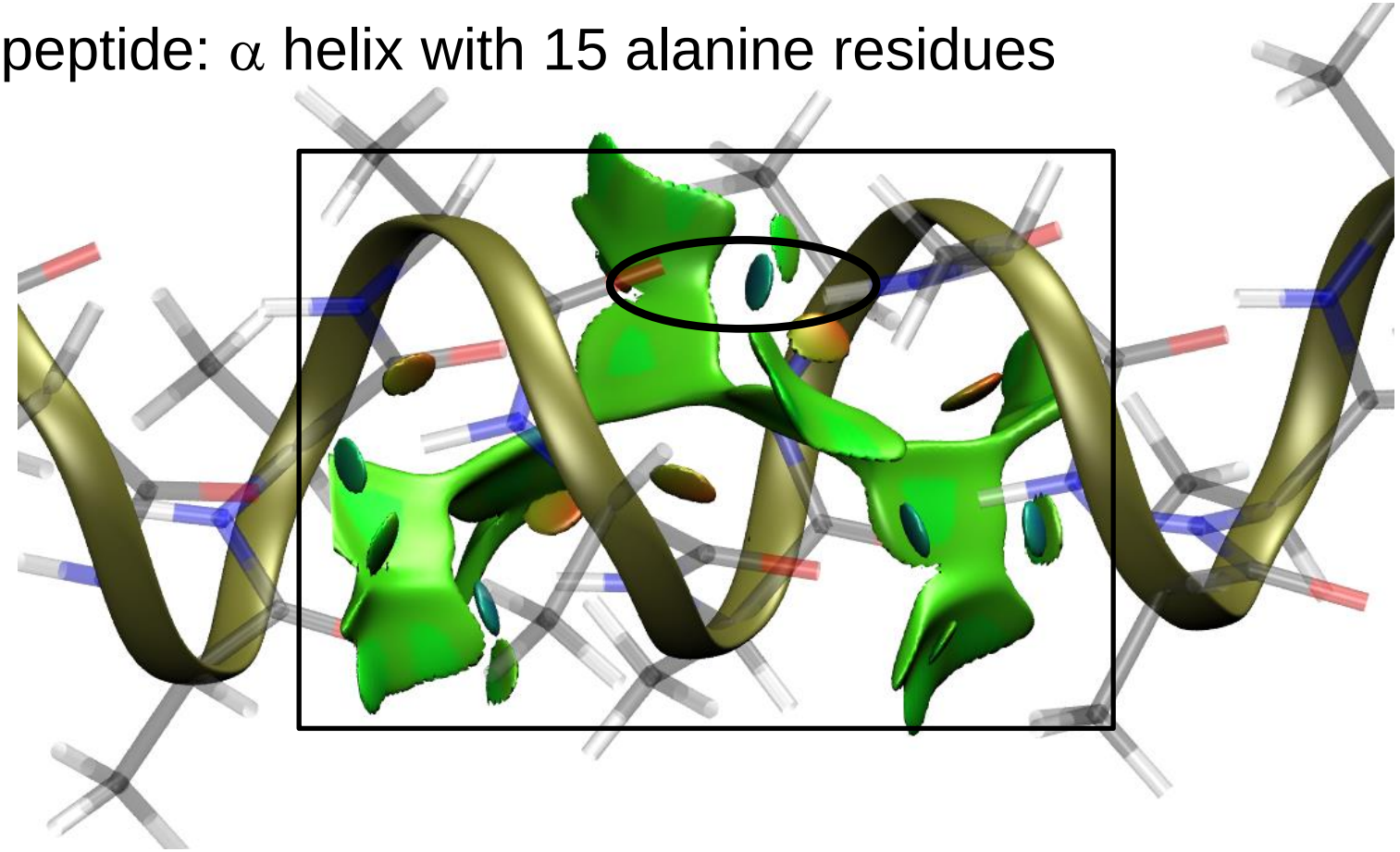


H-bonds between bases

π-stacking

Big systems

Polipeptide: α helix with 15 alanine residues

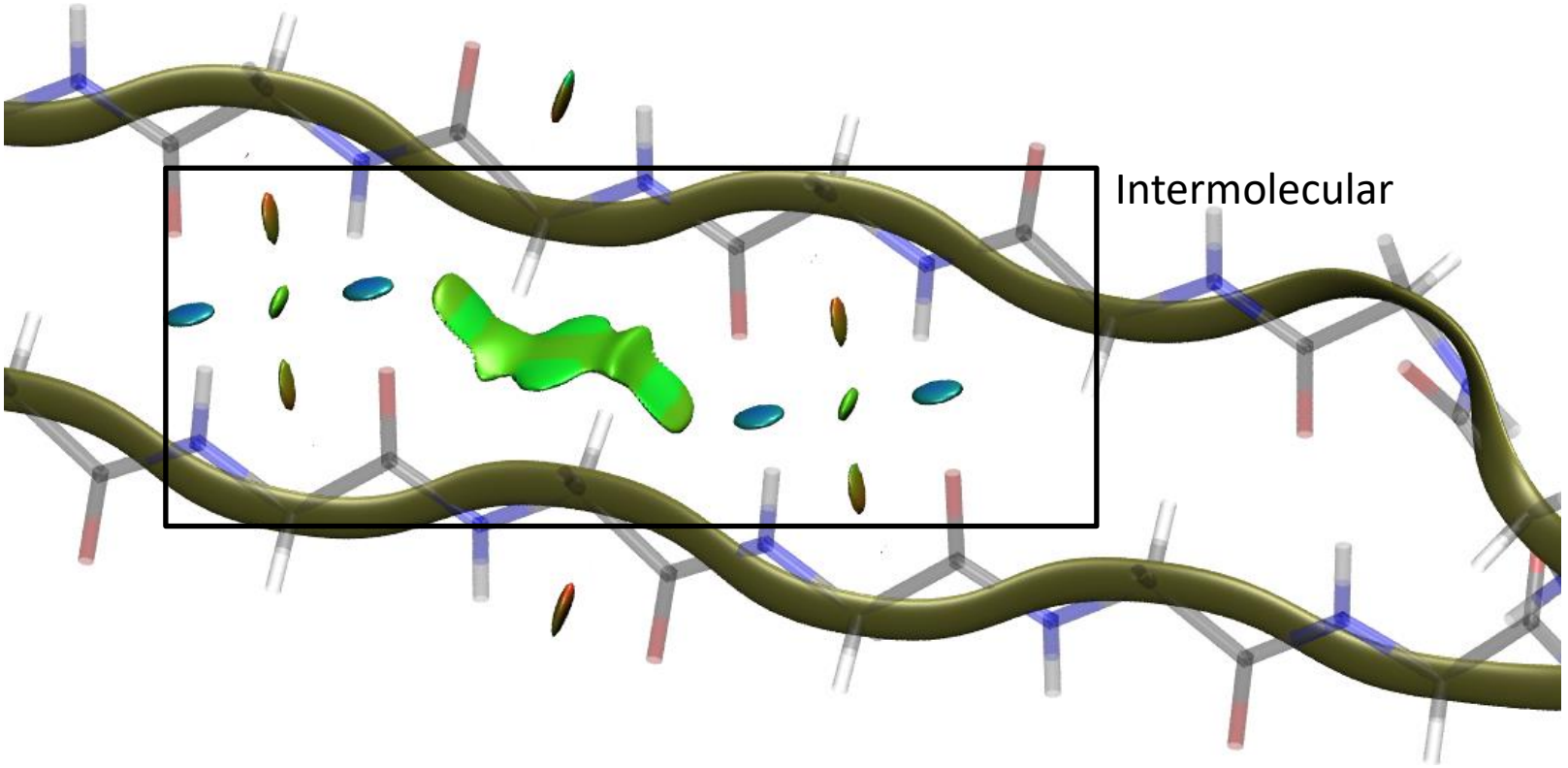


- Hydrogen bonds stabilize the helix
- Big region of van der Waals interaction inside the helix and between methyle lateral chains one step away

Big systems

polypeptide: anti-parallel β-sheet consisting of 17 glycine residues

- HB between C=O and N-H groups in parallel chains
- Van der Waals interactions between CH_2 groups



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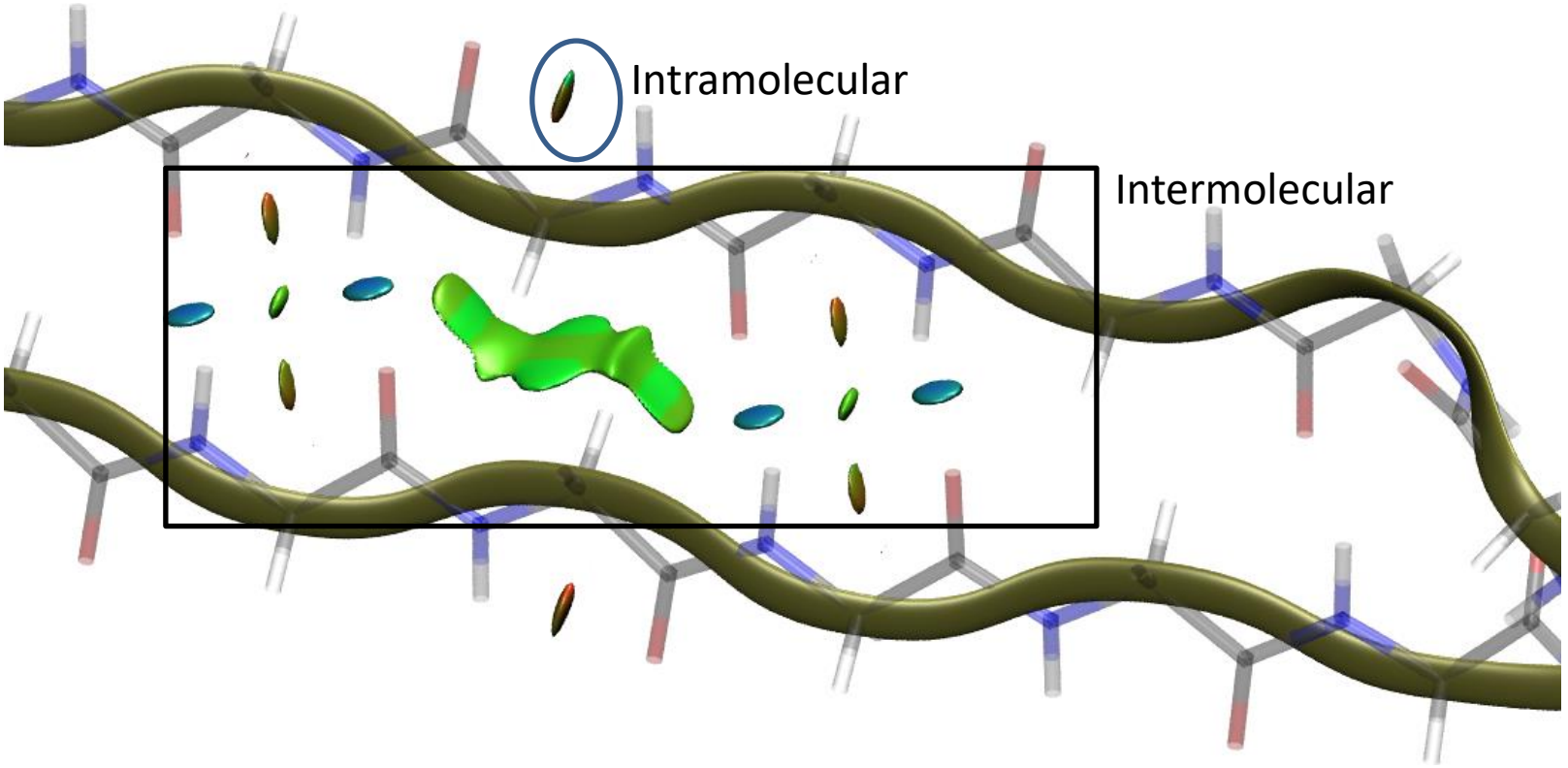

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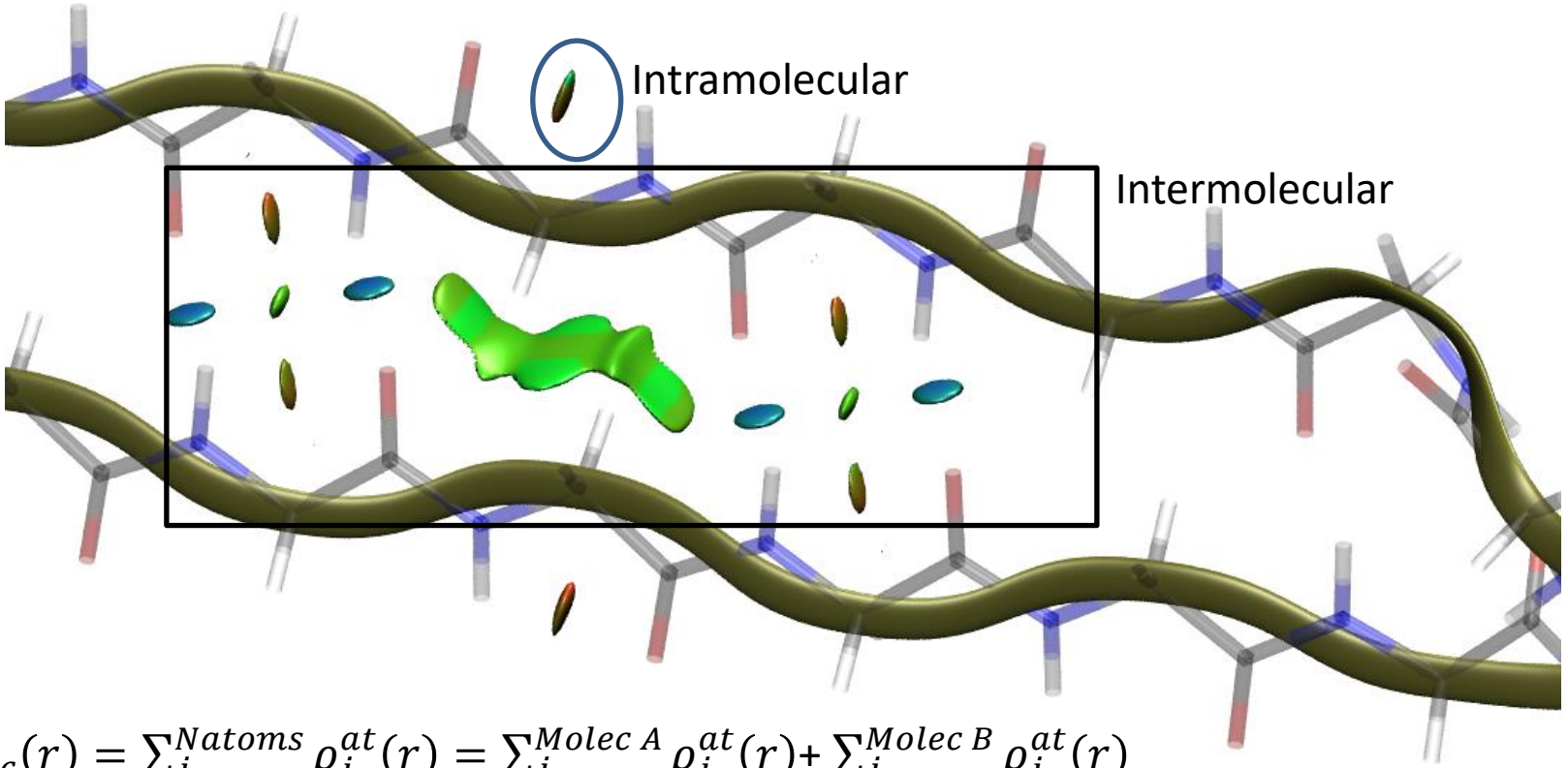


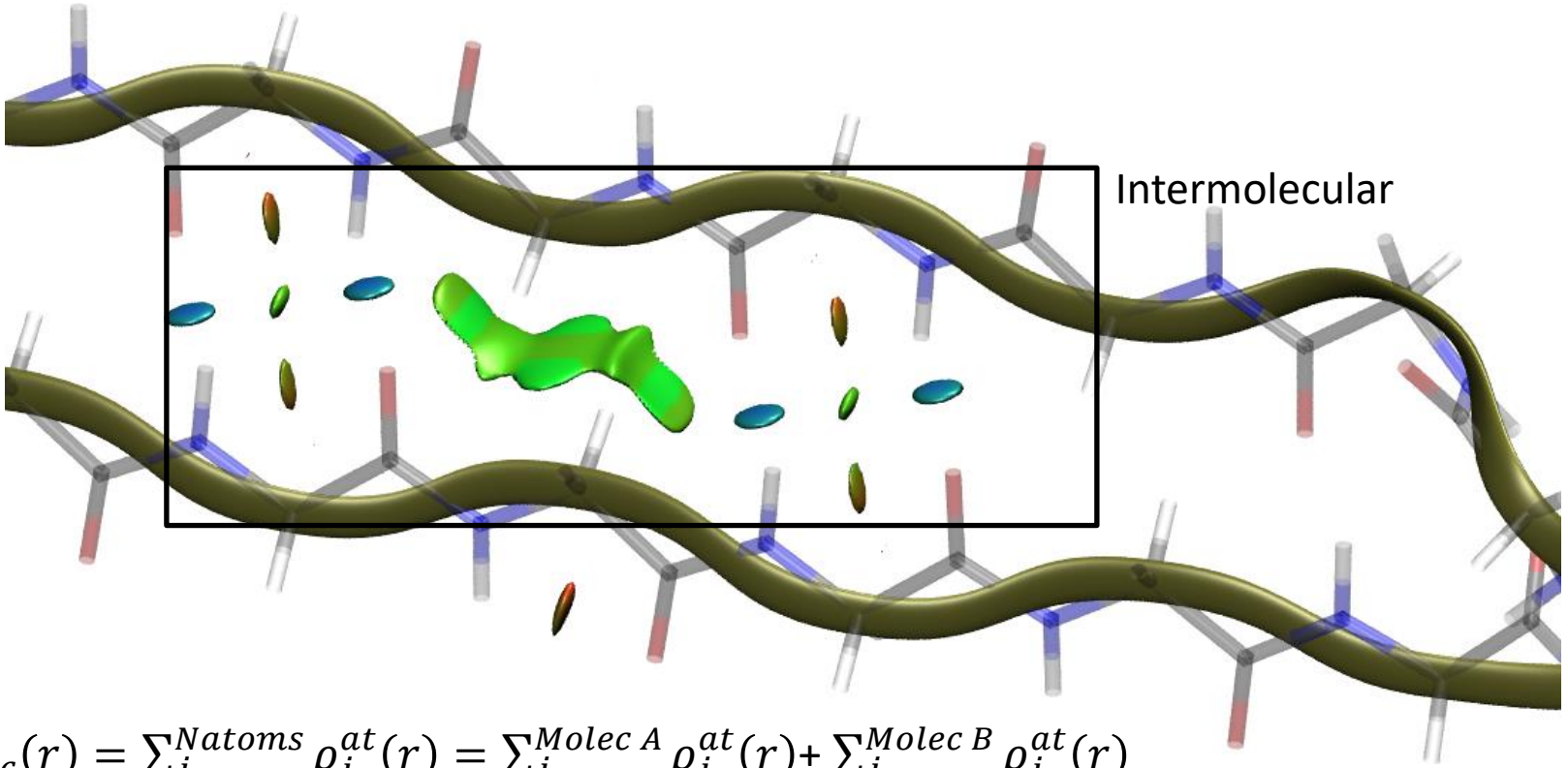
$$\rho_{molec}(r) = \sum_j^{Natoms} \rho_j^{at}(r) = \sum_j^{Molec\ A} \rho_j^{at}(r) + \sum_j^{Molec\ B} \rho_j^{at}(r)$$

- If $\rho_{molec}(r) \approx \sum_j^{Molec\ A} \rho_j^{at}(r)$ ->Intramolecular
- Otherwise -> Intermolecular

Big systems

polypeptide: anti-parallel β-sheet consisting of 17 glycine residues

- HB between C=O and N-H groups in parallel chains
- Van der Waals interactions between CH_2 groups



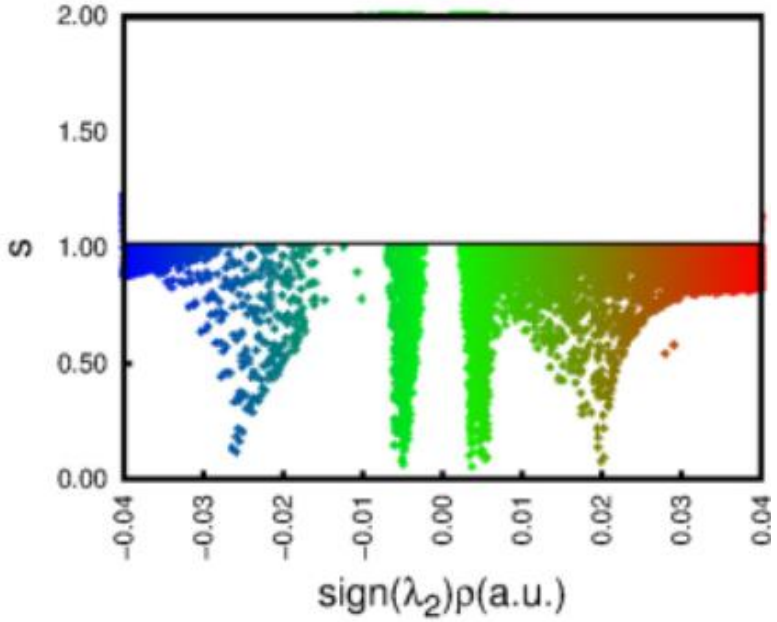
$$\rho_{molec}(r) = \sum_j^{Natoms} \rho_j^{at}(r) = \sum_j^{Molec\ A} \rho_j^{at}(r) + \sum_j^{Molec\ B} \rho_j^{at}(r)$$

- If $\rho_{molec}(r) \approx \sum_j^{Molec\ A} \rho_j^{at}(r)$ ->Intramolecular
- Otherwise -> Intermolecular

Criterion to plot ONLY intermolecular **(important!)**

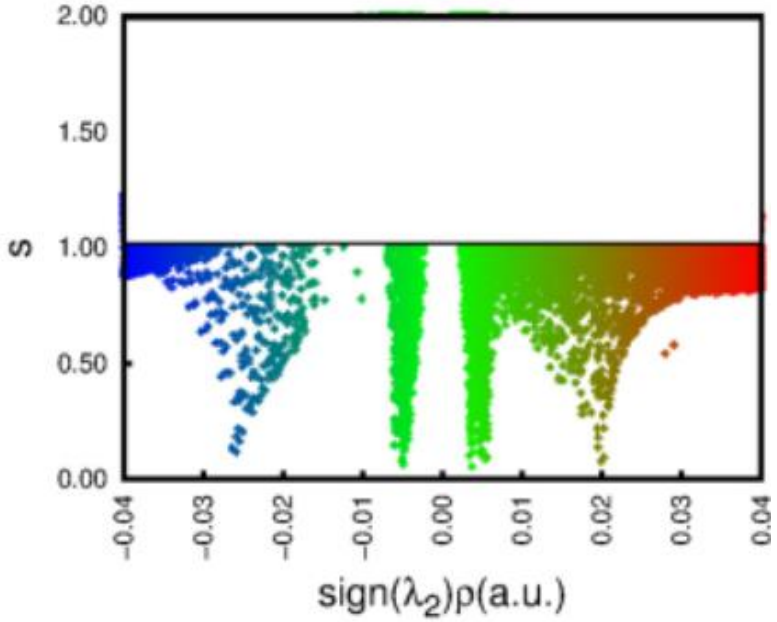
Can we quantify it??

Definition of NCI regions in terms of ρ



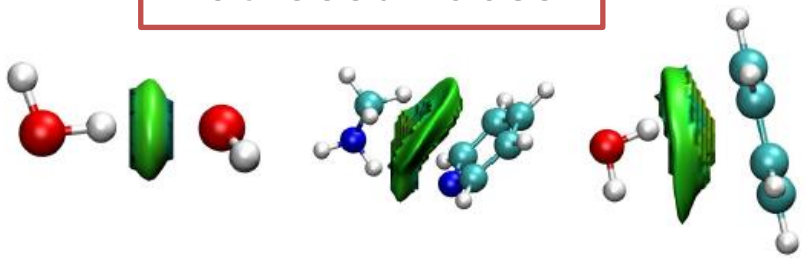
Intermolecular: we identify the regions where density comes from both fragments

Definition of NCI regions in terms of ρ

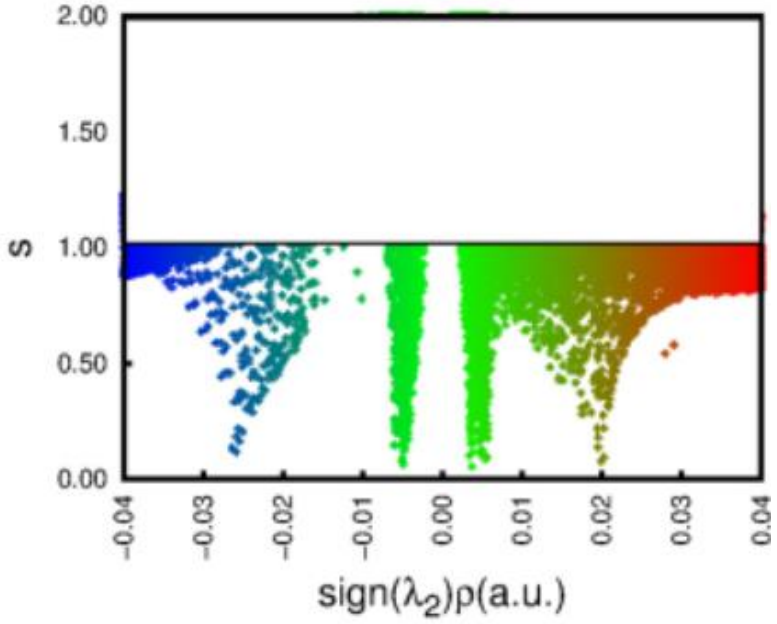


Intermolecular: we identify the regions where density comes from both fragments

Not isosurfaces!



Definition of NCI regions in terms of ρ



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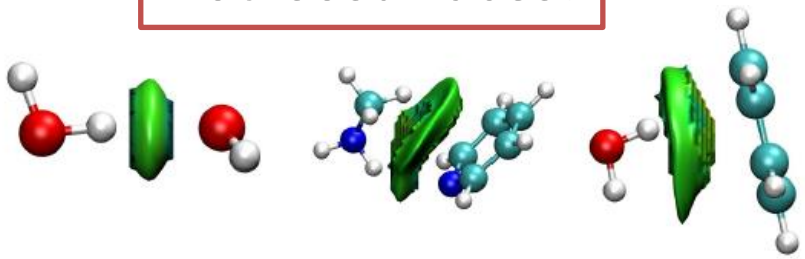
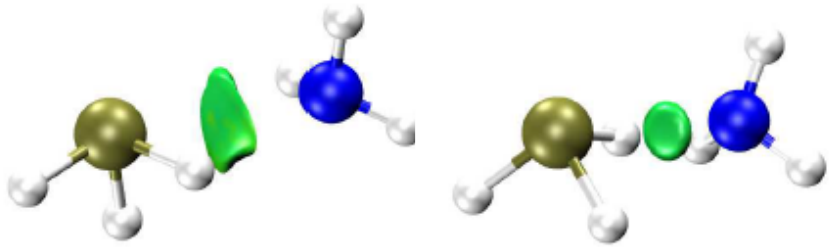


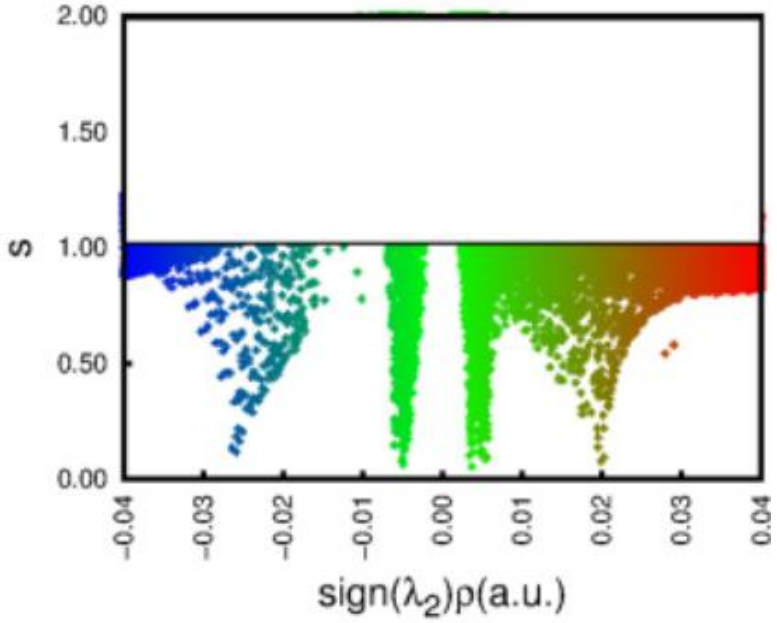
- We can integrate properties

$$q_{NCI} = \int_{\Omega(NCI)} \rho(\vec{r}) d\vec{r}$$



V_{NCI}=26.99 a.u. V_{NCI}=13.77 a.u.

Definition of NCI regions in terms of ρ



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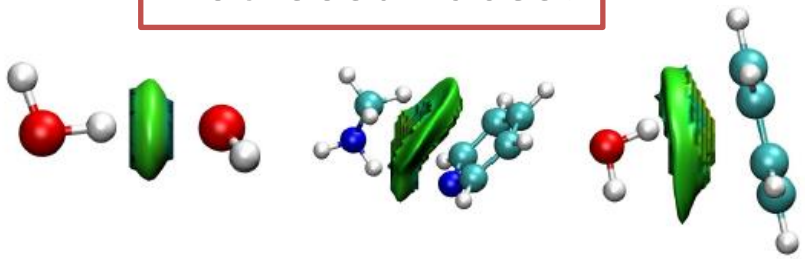

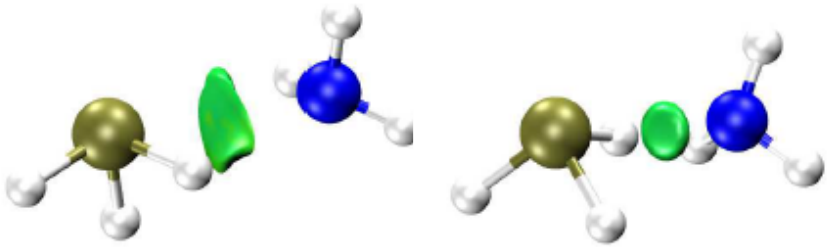

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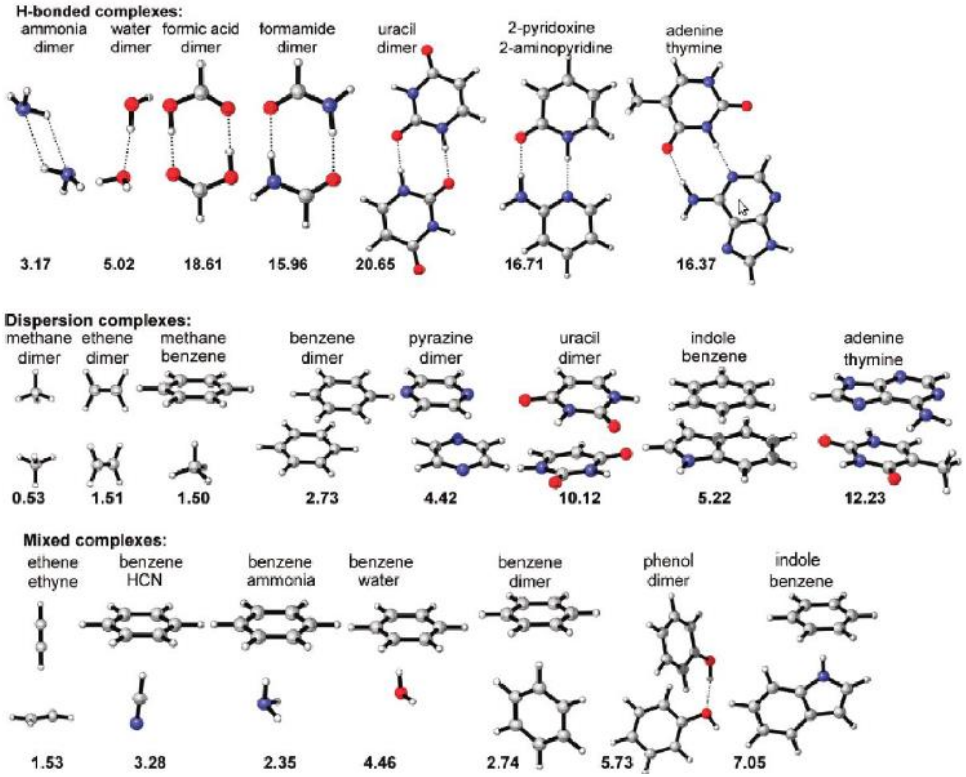
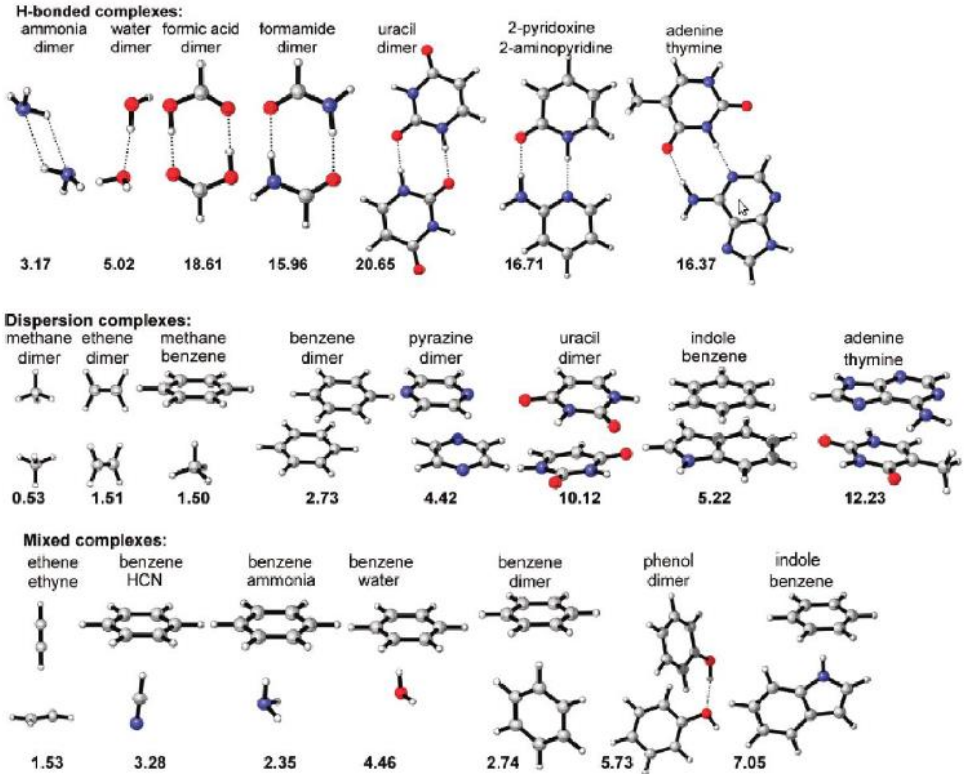
How does it relate to energetics?

S22 benchmark set integration



Method	DFT ε(%)
PBE	54
PBED	17
B3LYPD	16

S22 benchmark set integration



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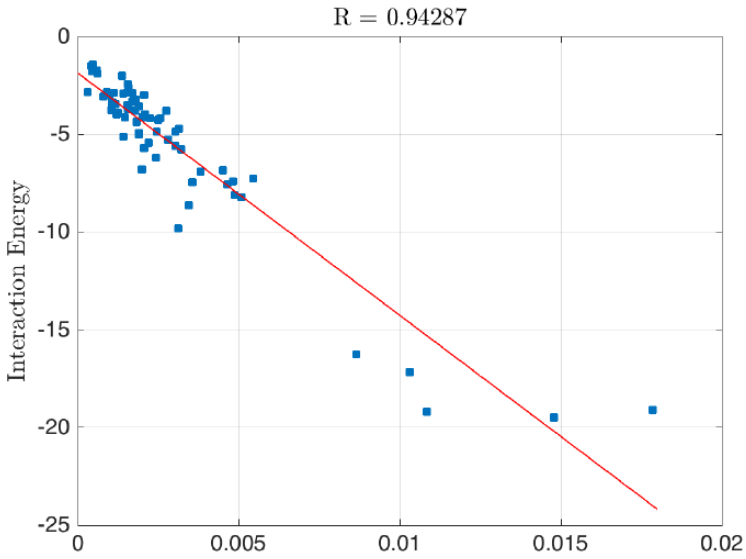

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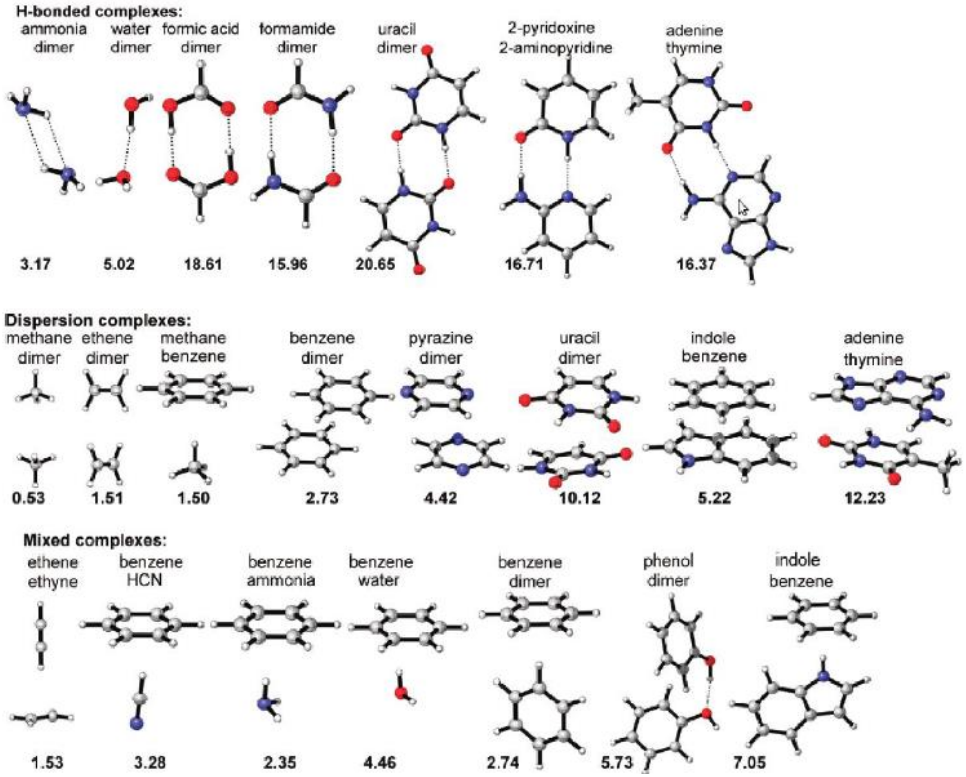

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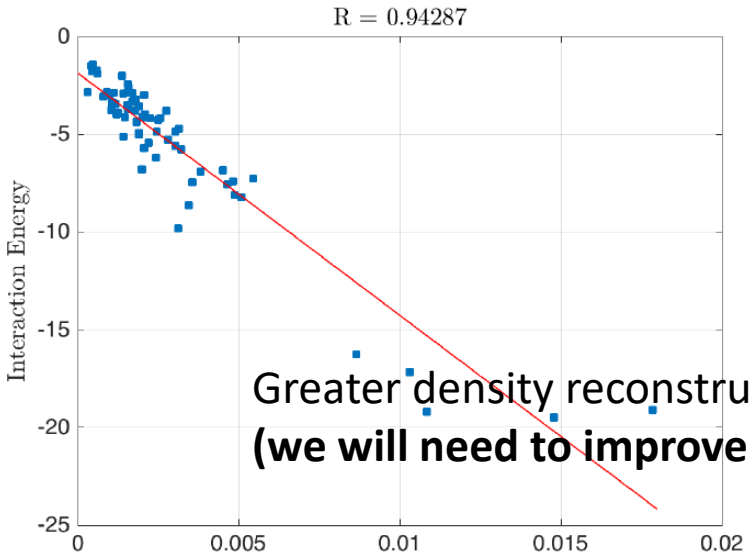
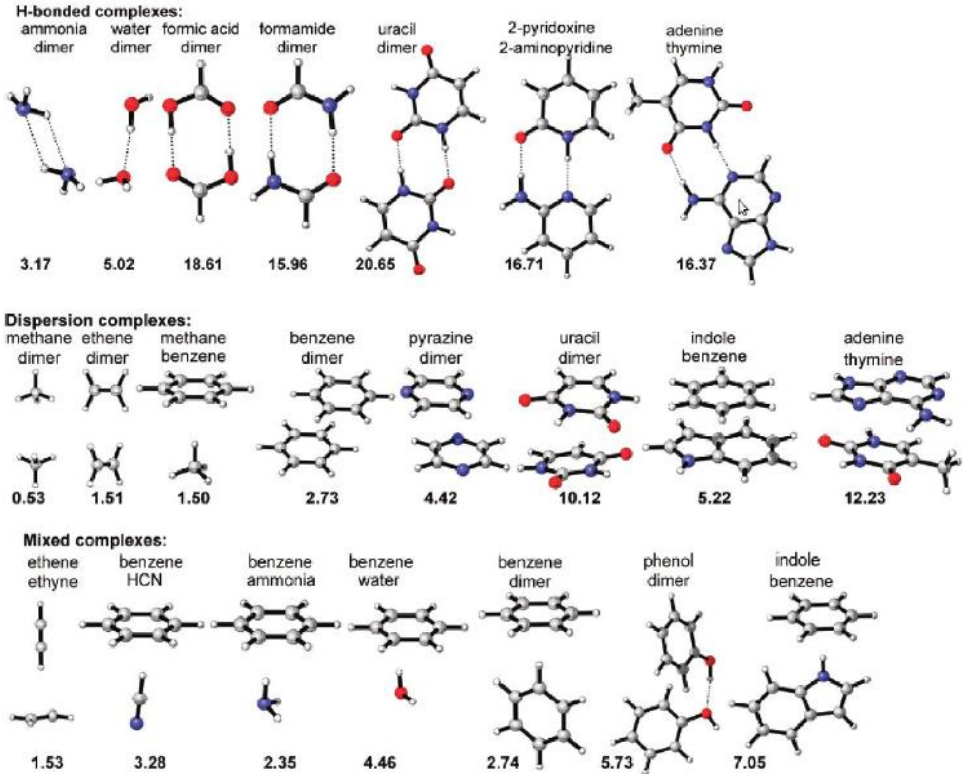


Greater density reconstruction
(we will need to improve this)

S22 benchmark set integration



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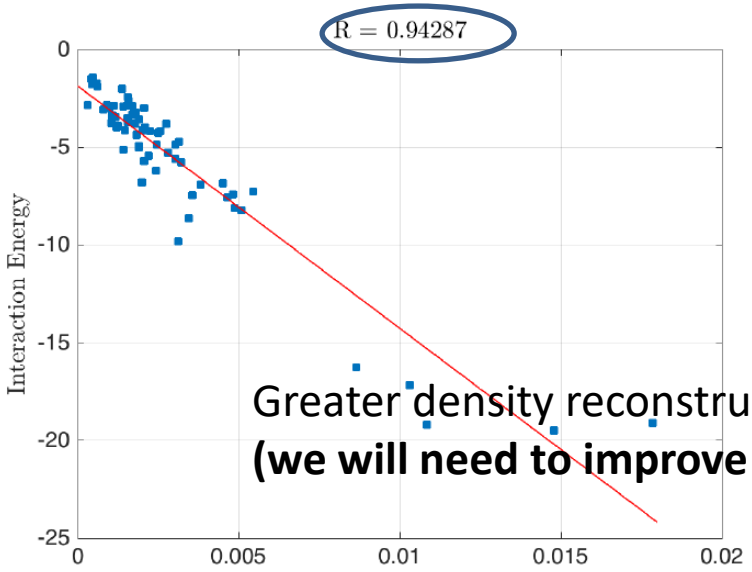
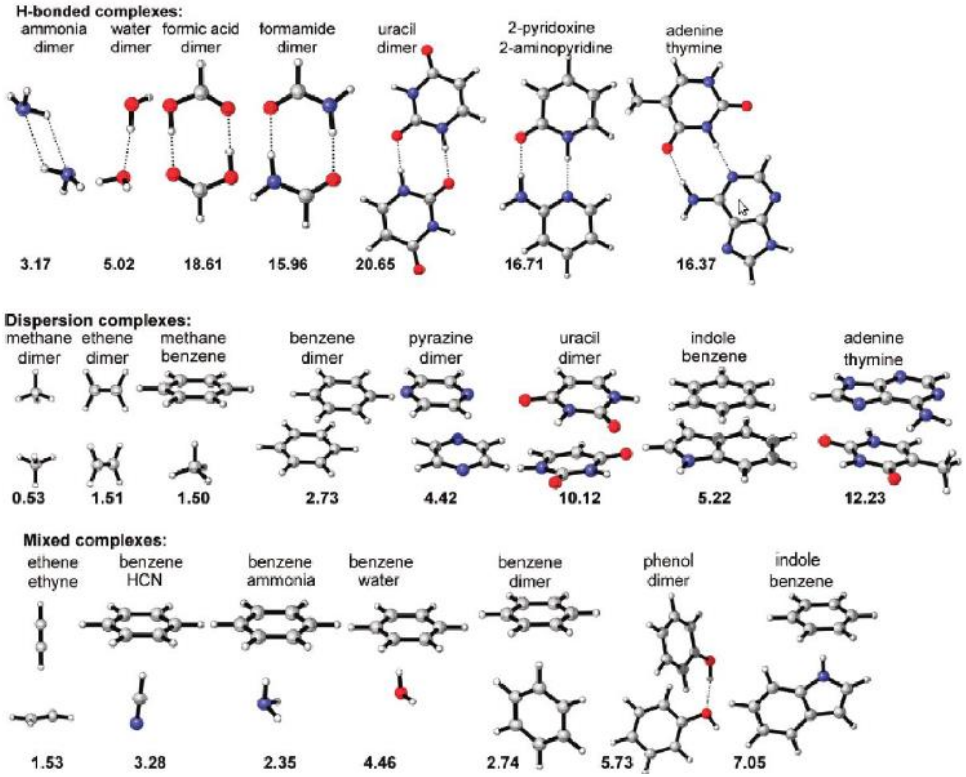


Integration from promolecular density correlates good enough with energetics

Greater density reconstruction **(we will need to improve this)**

S22 benchmark set integration



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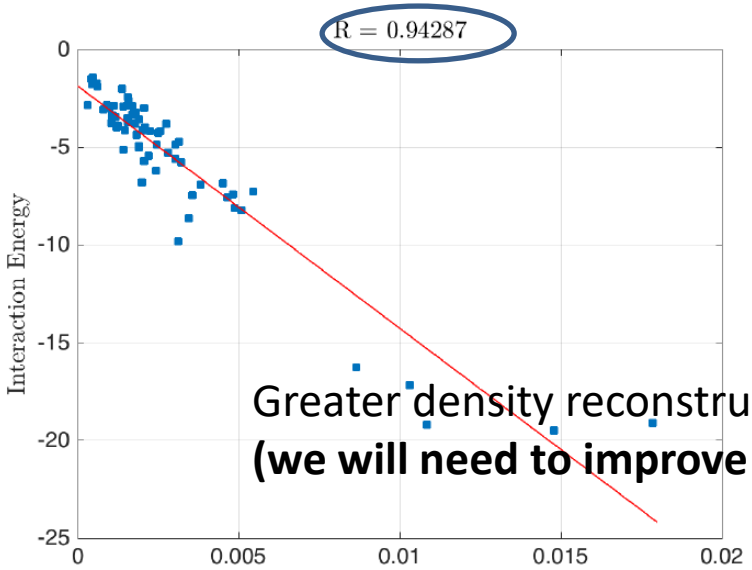
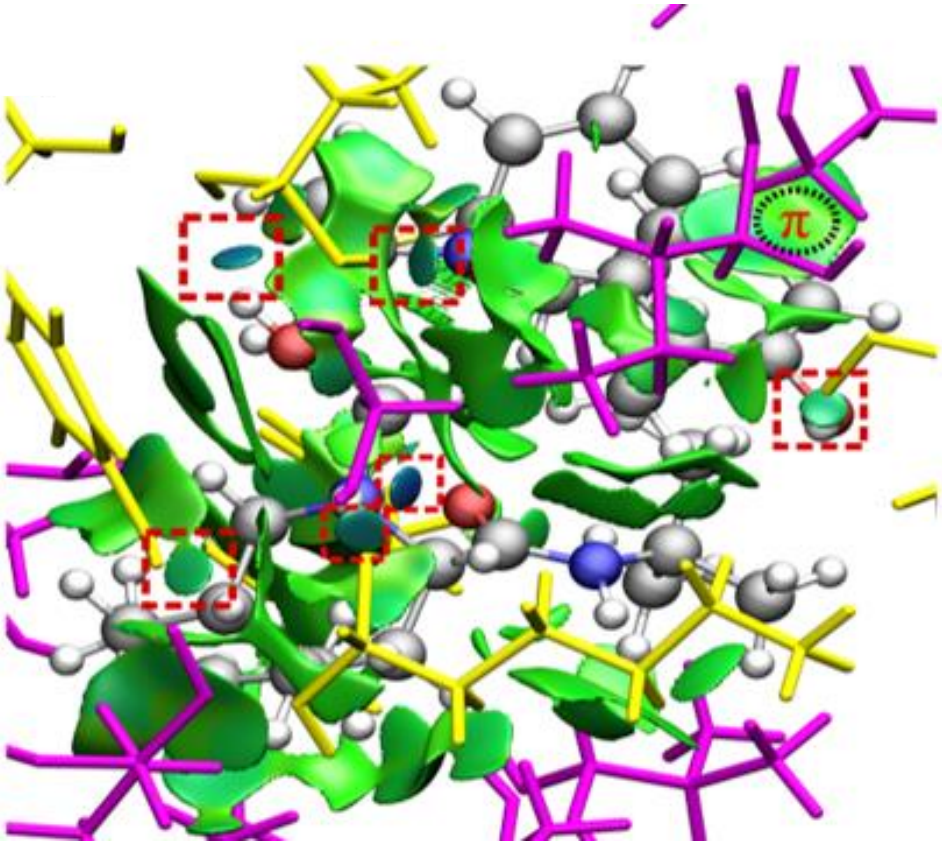
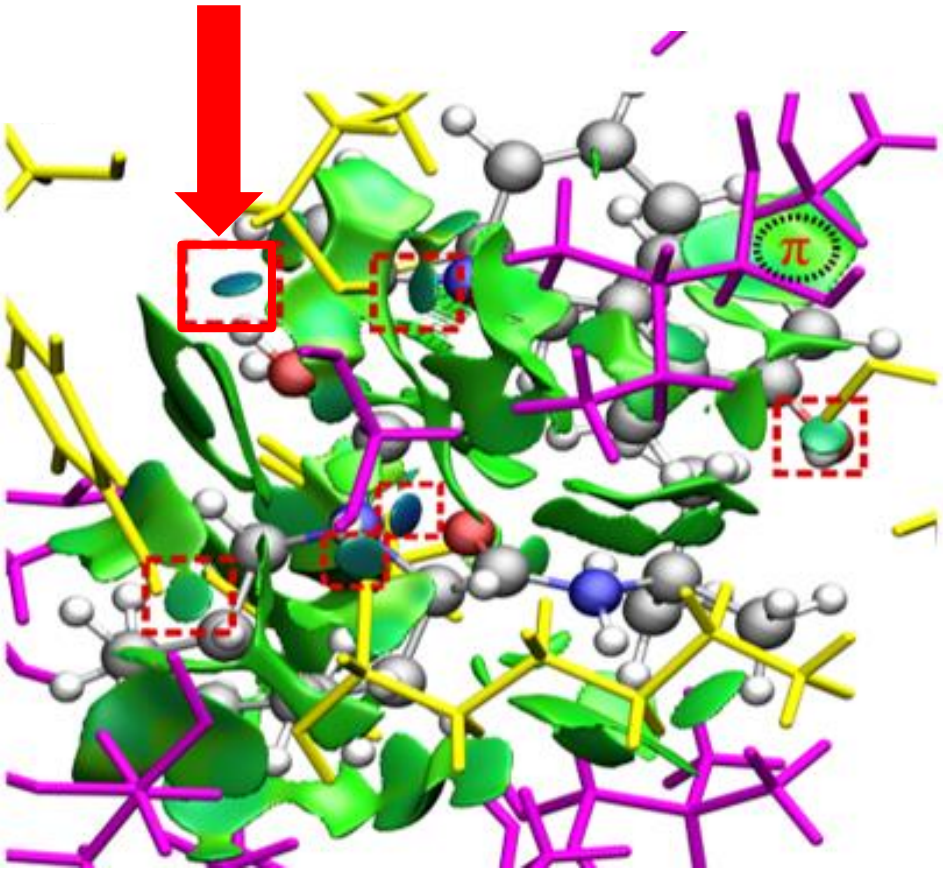


Greater density reconstruction **(we will need to improve this)**

what if we have a complex system?

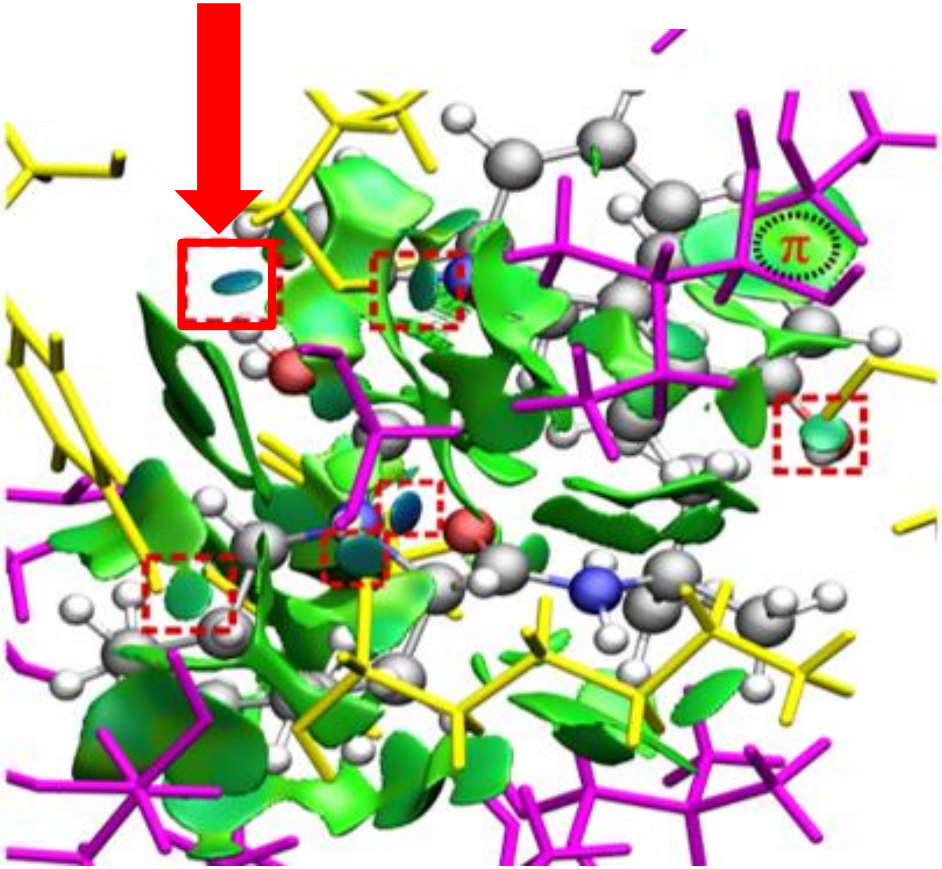


- Imagine we have a ligand in its active site with several HBs



- Imagine we have a ligand in its active site with several HBs
- But only one specific HB which determines the interaction
- The integral **is for all HBs**

$$q_{NCI} = \int_{\Omega(NCI)} \rho(\vec{r})d\vec{r}$$



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$$q_{NCI} = \int_{\Omega(NCI)} \rho(\vec{r})d\vec{r}$$

We need integrals by pieces

Can we quantify it??

- Direct and ML approach

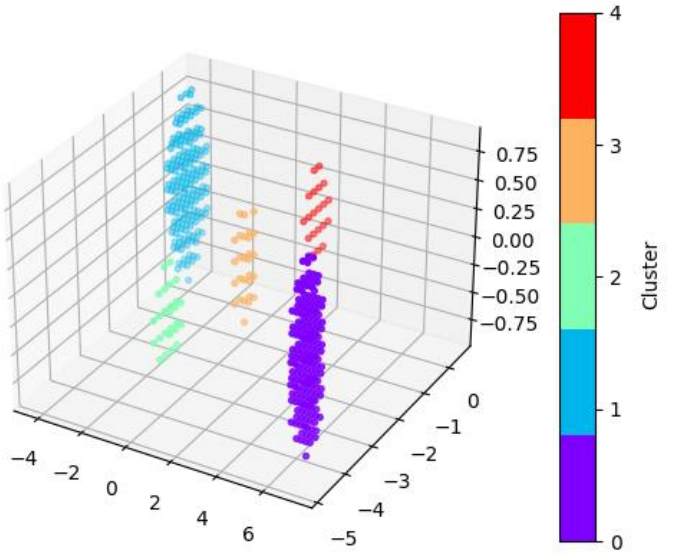
Local integrals

- NCIcluster
- Application to macrocycles

NCIcluster

NCICLUSTER

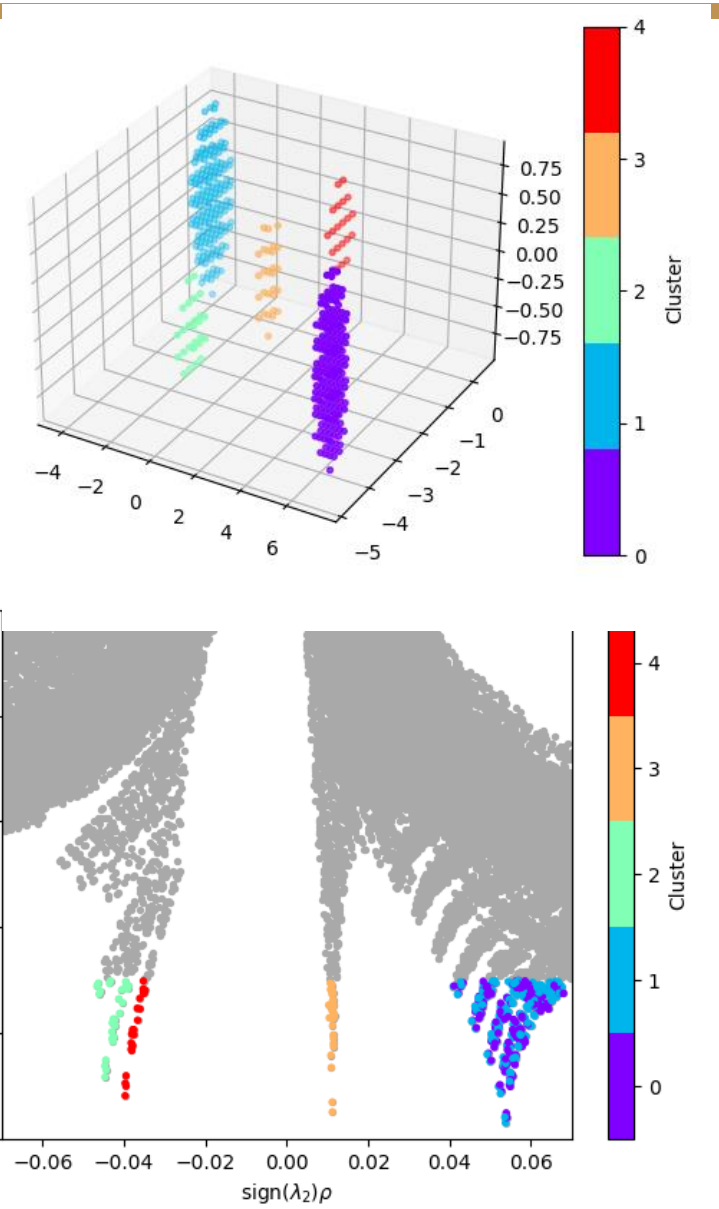
- A machine learning procedure which takes into account the spatial positions of the points inside the isosurfaces as well as the value of sign(λ_2).



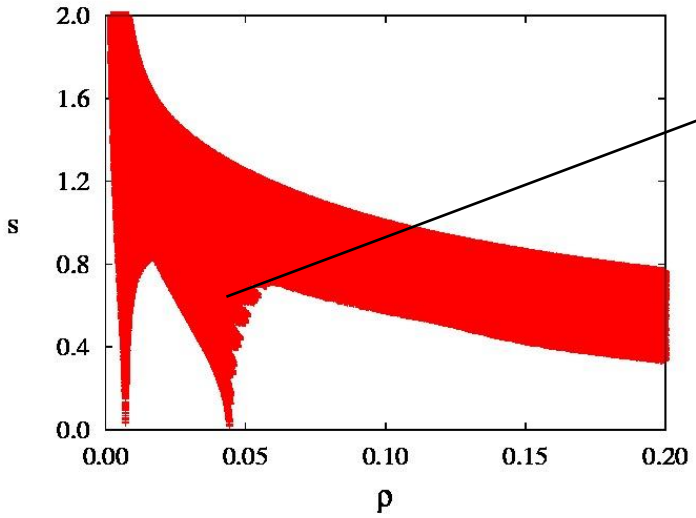
NCIcluster

NCICLUSTER

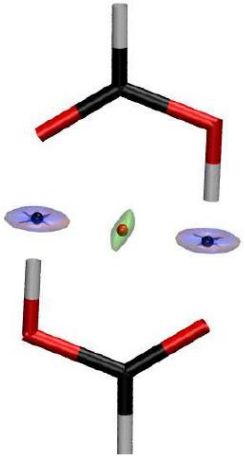
- A machine learning procedure which takes into account the spatial positions of the points inside the isosurfaces as well as the value of sign(λ_2).
- It enables to disentangle the effect of the different non-covalent interactions



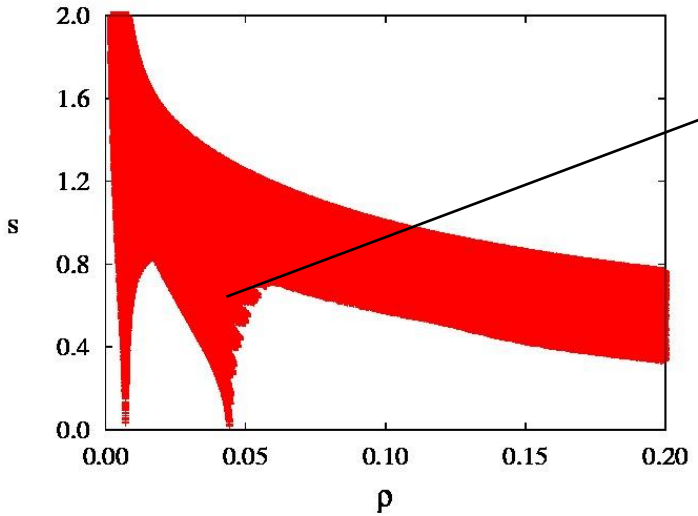
NCIcluster



This peak comes from two different interactions, so we cannot analyze them separately



NCIcluster



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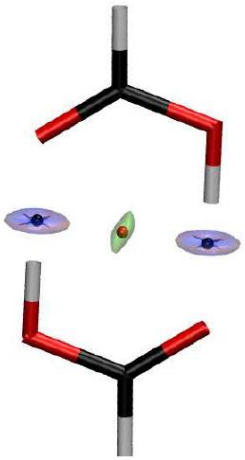
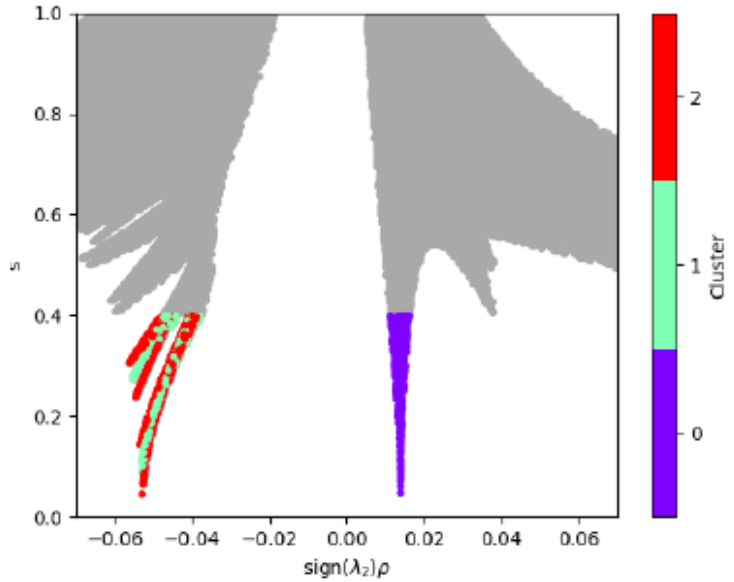
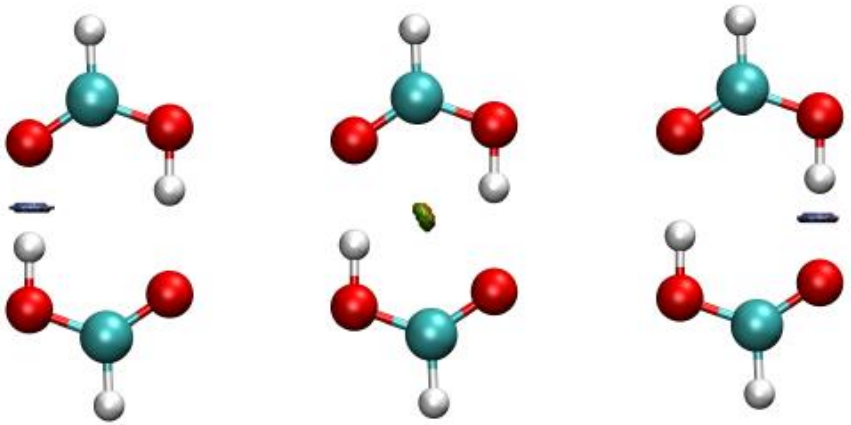


- With NCICLUSTER



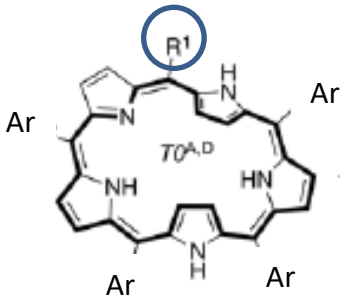

```
ncicluster.py input_names -n 3
```



NCIcluster

We want to focus on a specific interaction

R_1=H, Ar



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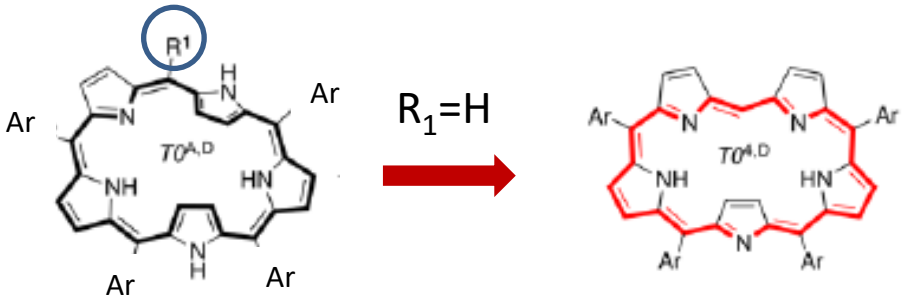

Can be isolated

NCIcluster

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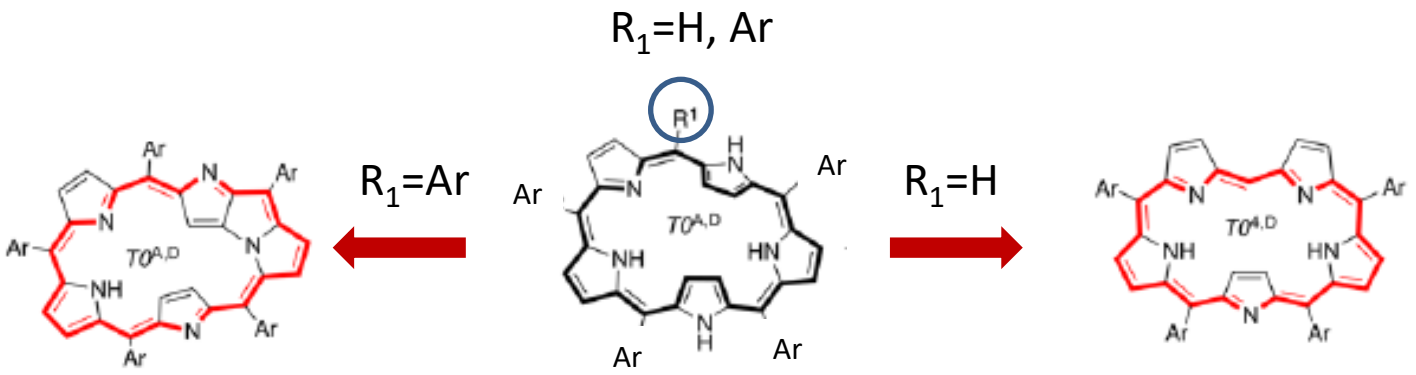
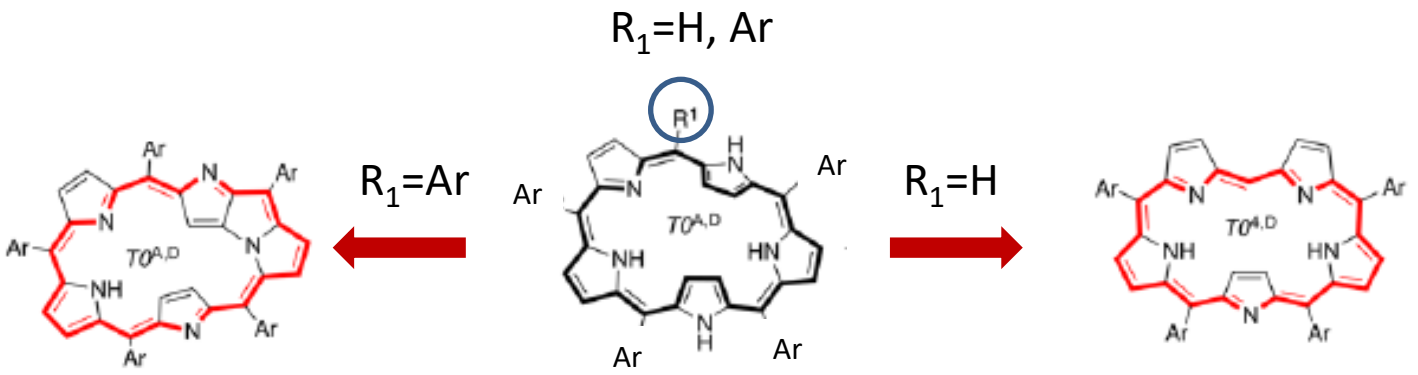


prone to undergo an N-fusion reaction

Can be isolated

NCIcluster

We want to focus on a specific interaction



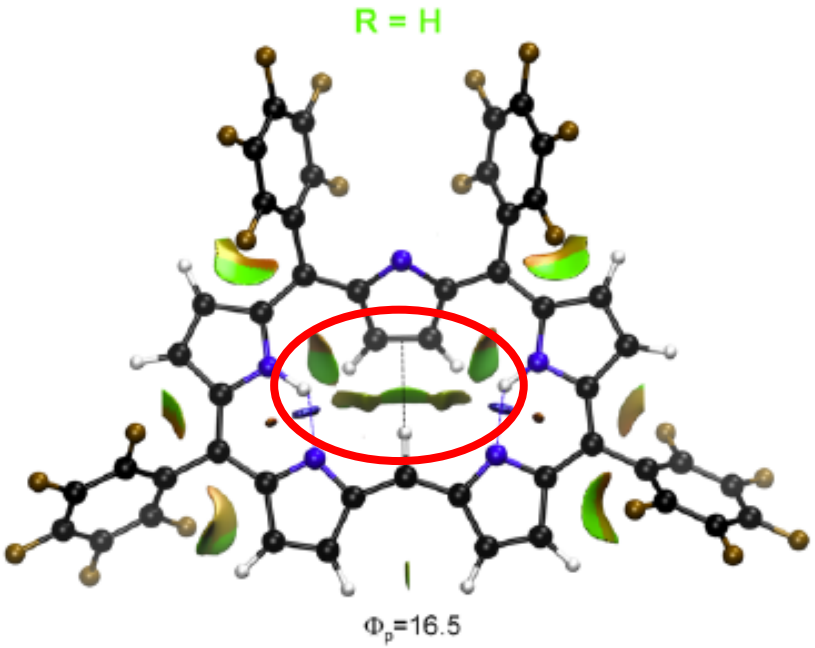
prone to undergo an N-fusion reaction

Can be isolated

This is due to an important conformational change

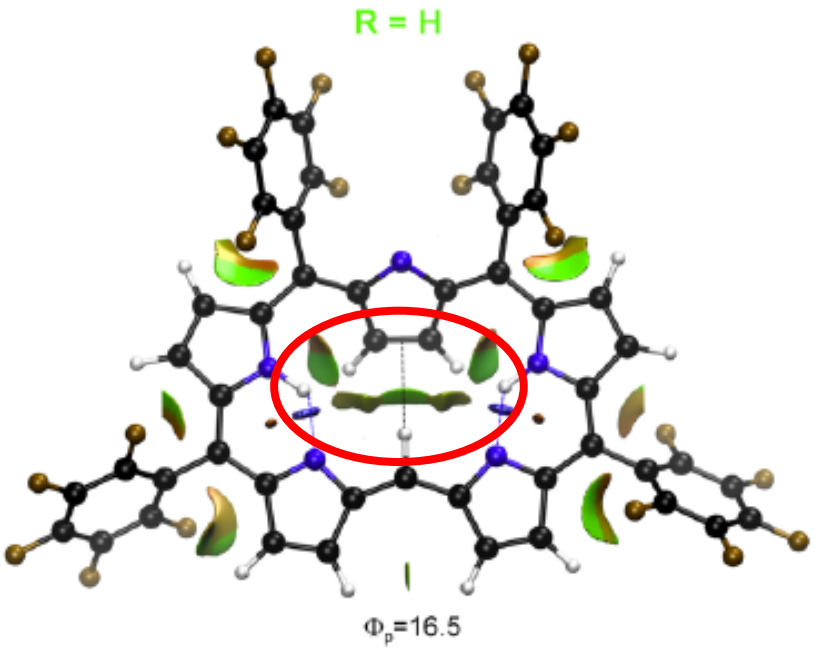
NCIcluster

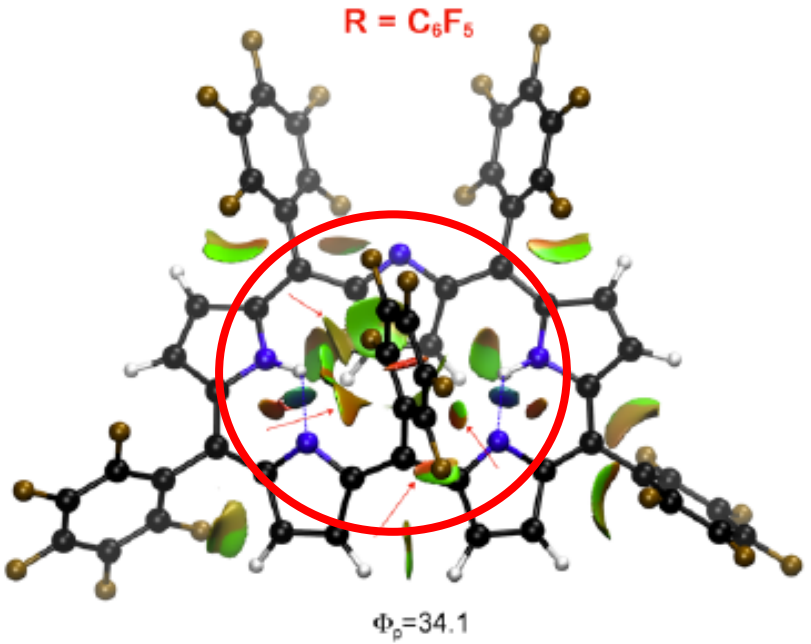
- R_1=H is triangular with a CH-π interaction



NCIcluster

- R_1=H is triangular with a CH-π interaction
- R_1=Ar is puckered





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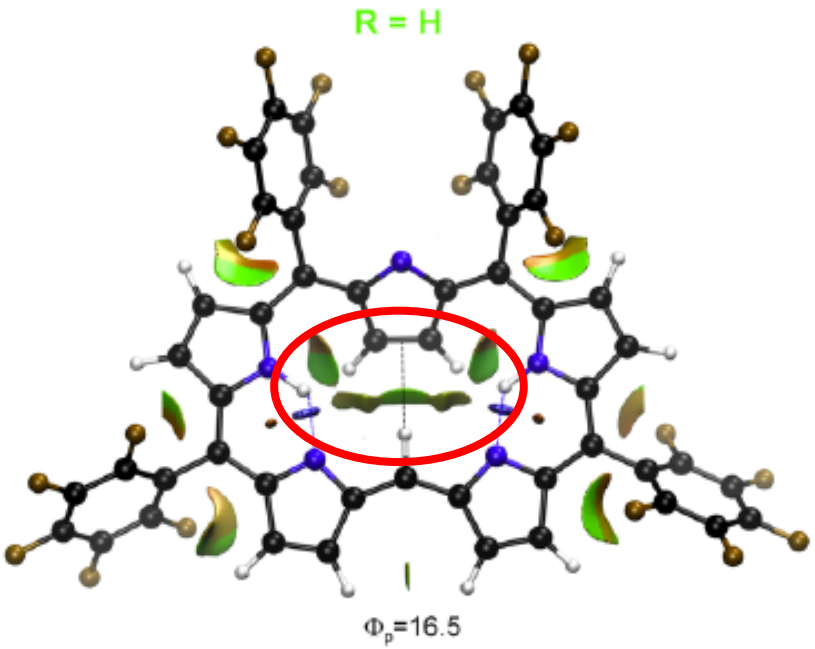
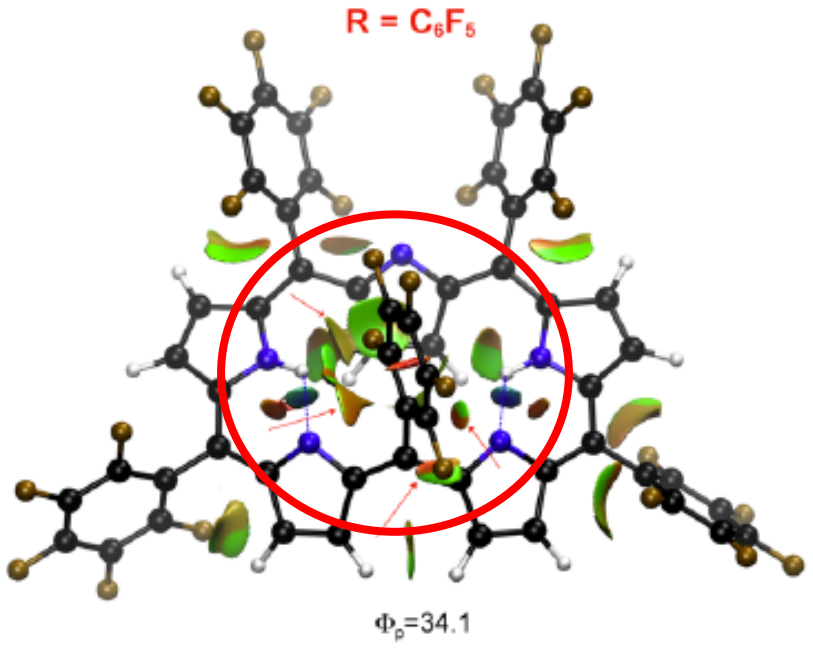
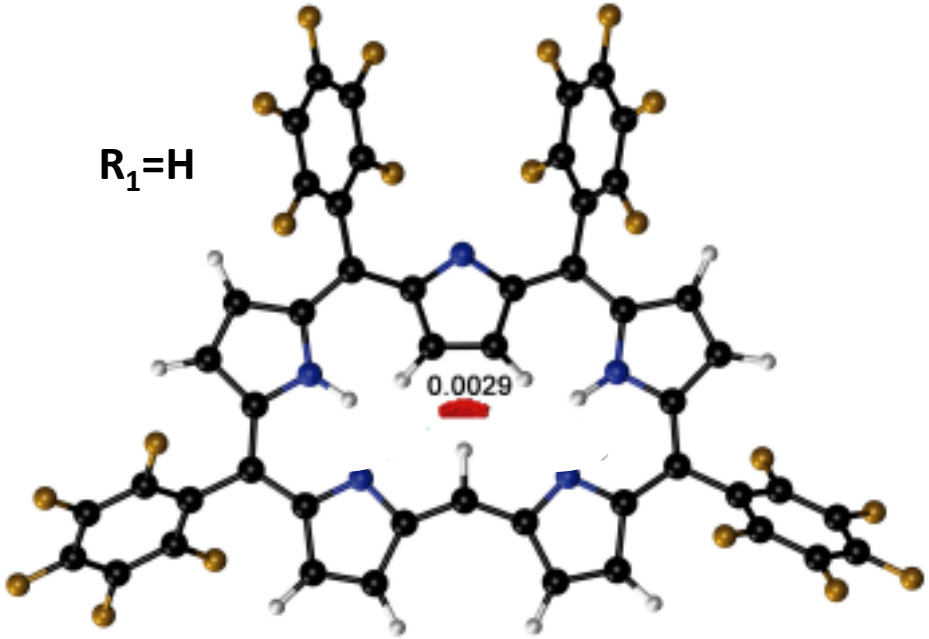


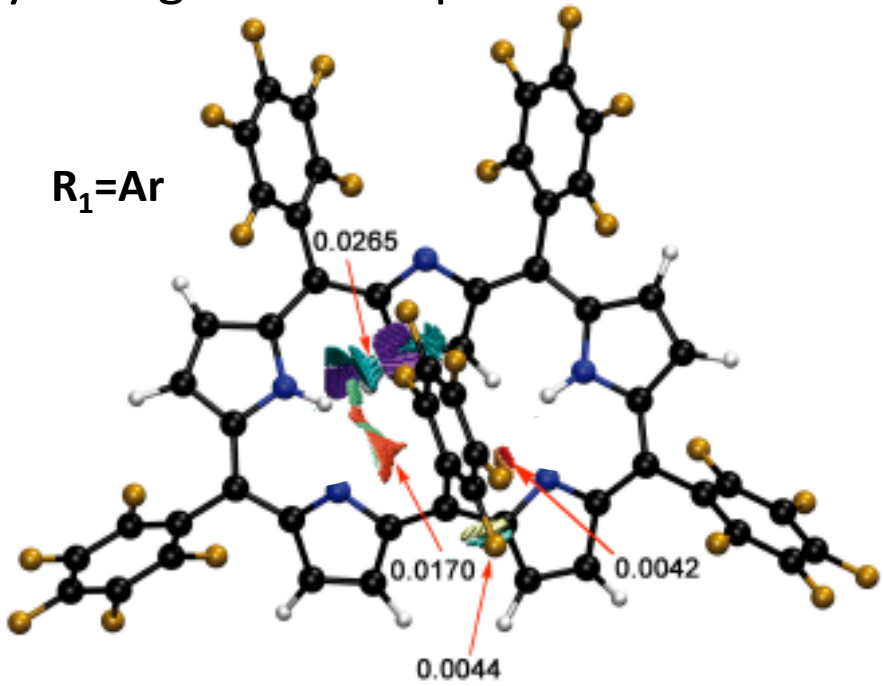


- These interactions are localized, the overall integral is useless!

NCIcluster

Integration of the relevant NCI regions allows quantitatively tracing the conformational stability back to the density changes in real space.

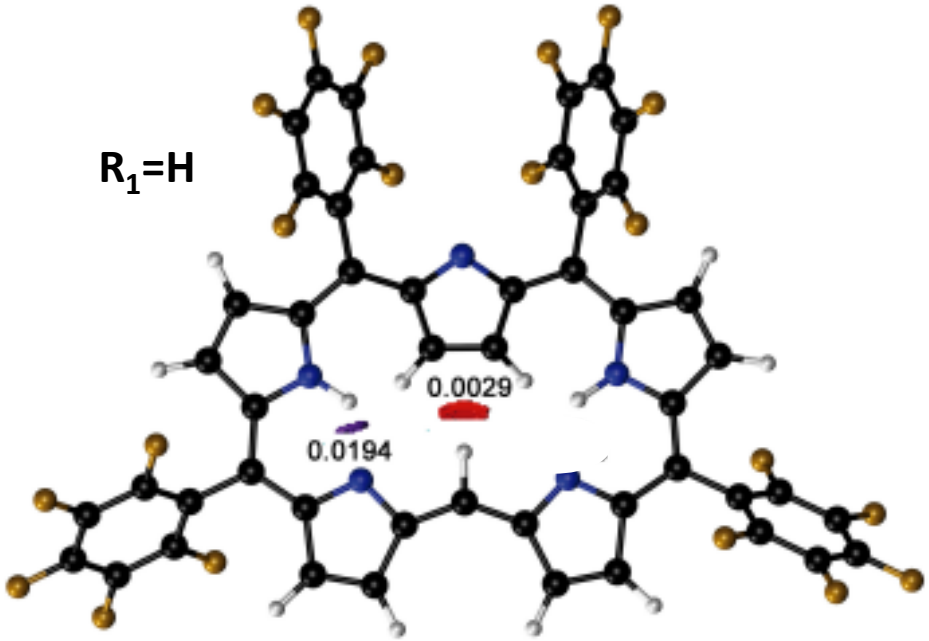


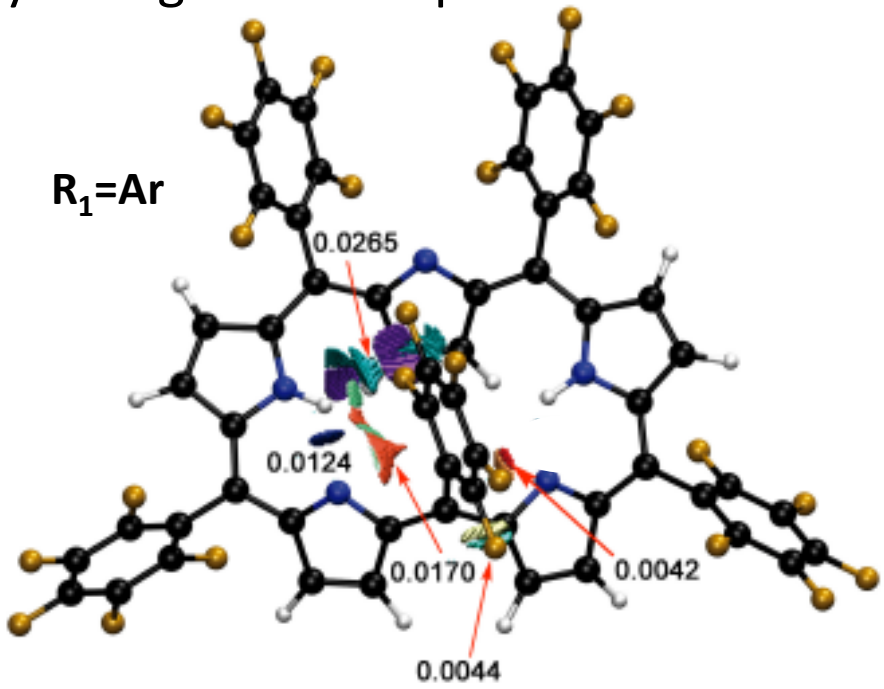


Interaction	R_1=H		R_1=Ar
Sterics	0.0029	Steric repulsion increases	0.0521

NCIcluster

Integration of the relevant NCI regions allows quantitatively tracing the conformational stability back to the density changes in real space.





Interaction	R_1=H		R_1=Ar
Sterics	0.0029	Steric repulsion increases	0.0521
HB1	0.0194		0.0124

NCIcluster

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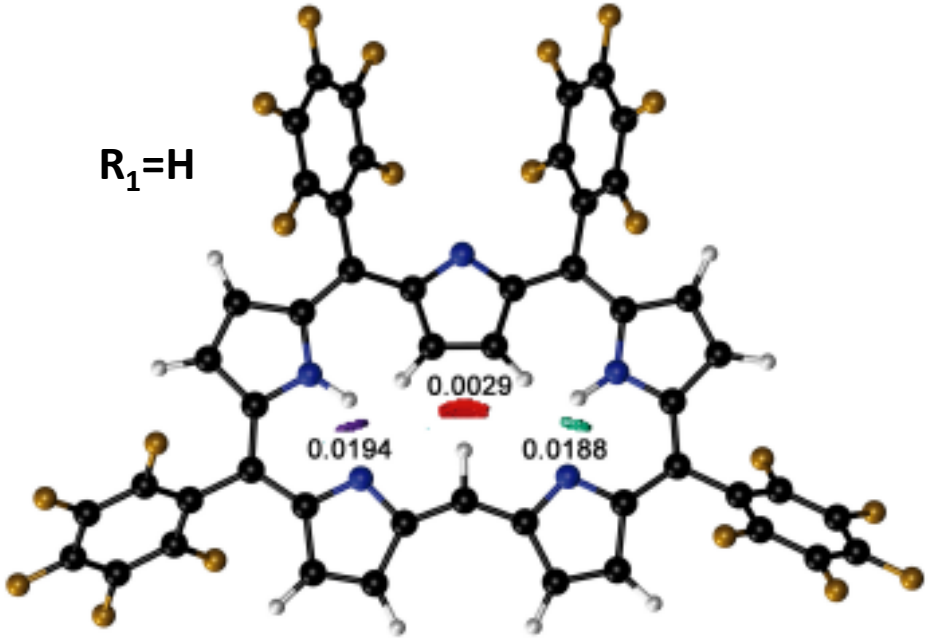
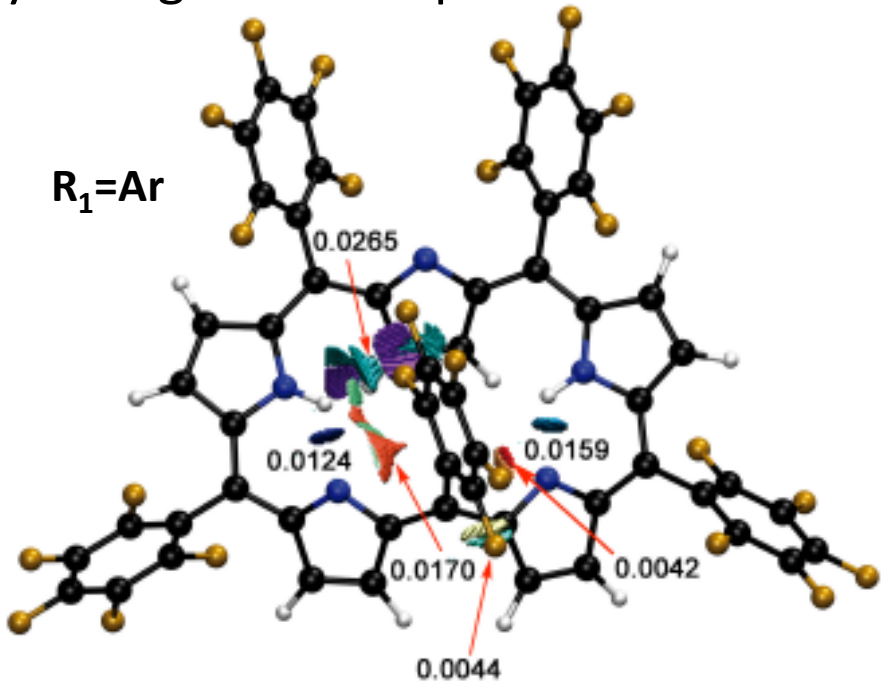
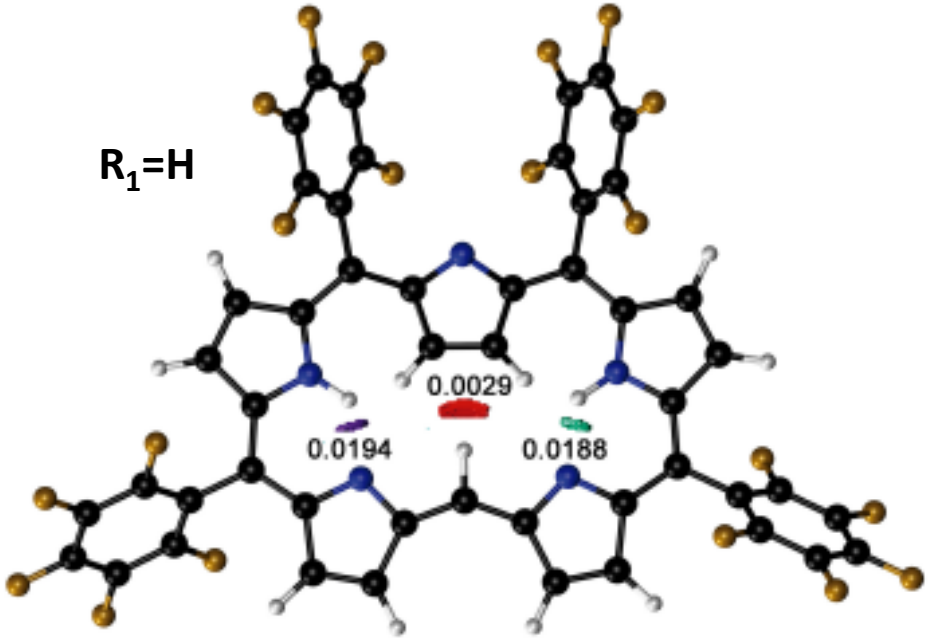


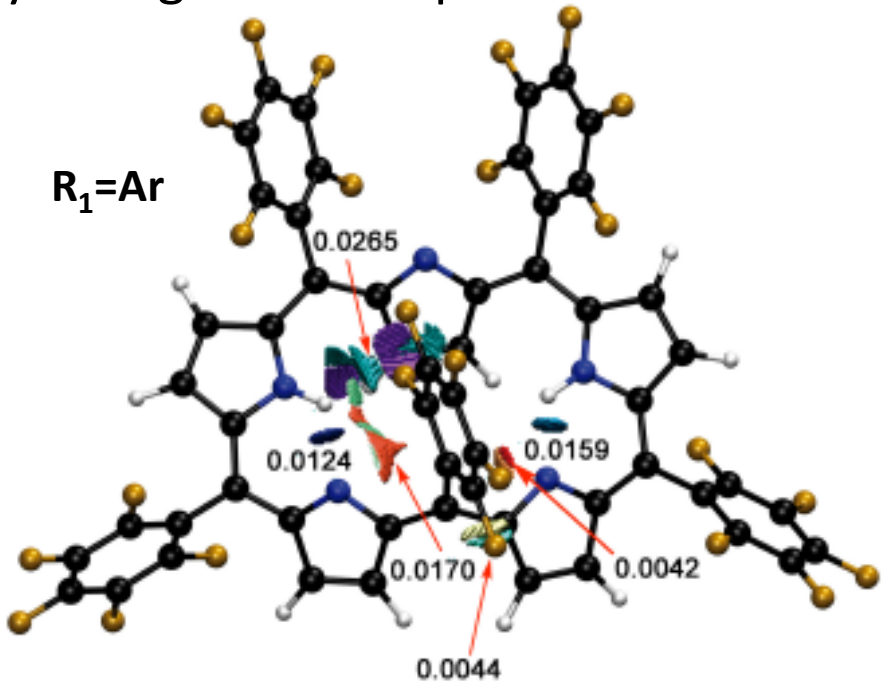


Interaction	R_1=H		R_1=Ar
Sterics	0.0029	Steric repulsion increases	0.0521
HB1	0.0194		0.0124
HB2	0.0188		0.0159

NCIcluster

Integration of the relevant NCI regions allows quantitatively tracing the conformational stability back to the density changes in real space.

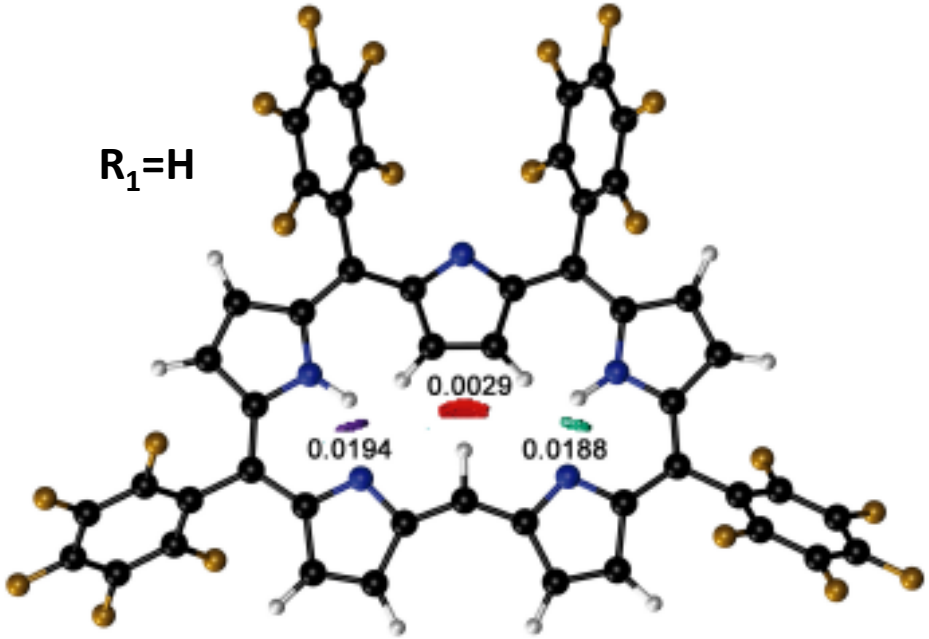


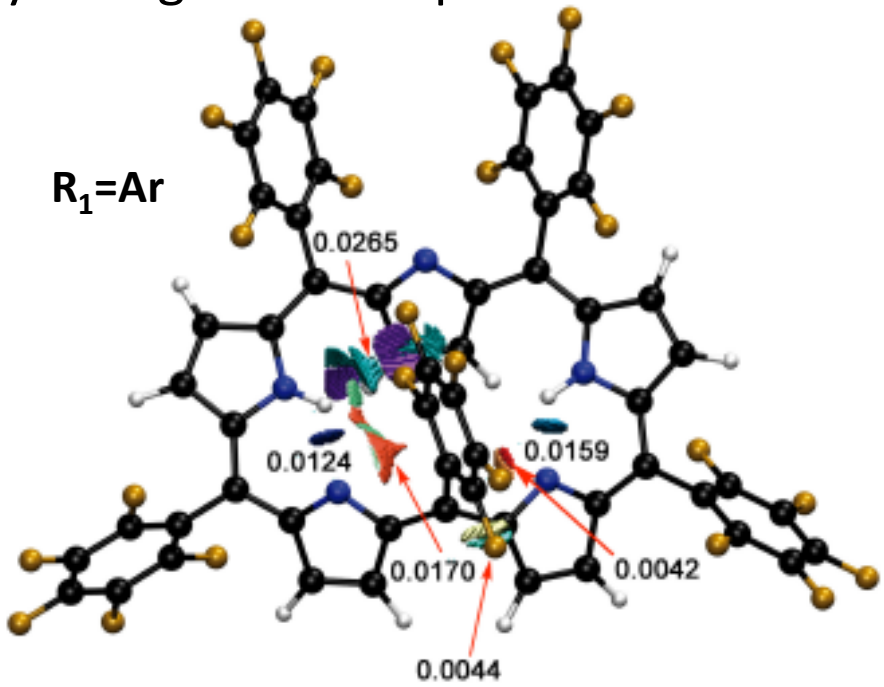


Interaction	R_1=H		R_1=Ar
Sterics	0.0029	Steric repulsion increases	0.0521
HB1 HB2	0.0194 0.0188	Intramolecular HBs are weakened	0.0124 0.0159

NCIcluster

Integration of the relevant NCI regions allows quantitatively tracing the conformational stability back to the density changes in real space.



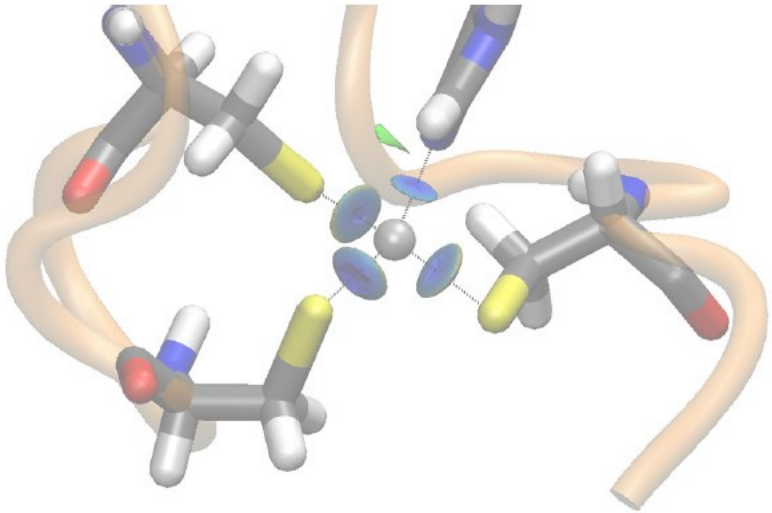


Interaction	R_1=H		R_1=Ar
Sterics	0.0029	Steric repulsion increases	0.0521
HB1	0.0194	These effects would have balanced !	0.0124
HB2	0.0188	Intramolecular HBs are weakened	0.0159

Developments in big systems

Big systems need new developments…

- Better: ELMOs
- Faster: adaptative grids…MDs
- Easier: NCIweb



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- Canonical or localized orbitals have small tails outside the localization region

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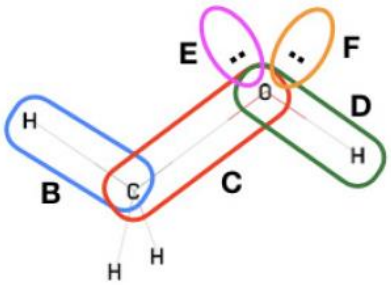
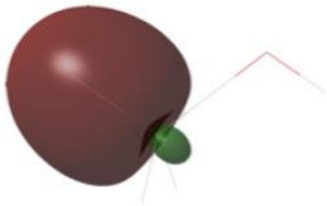
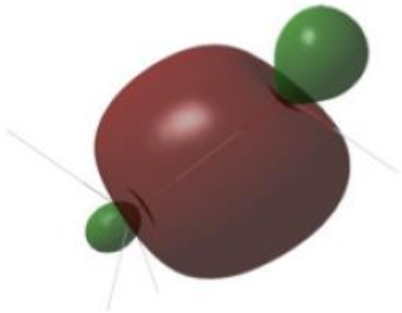
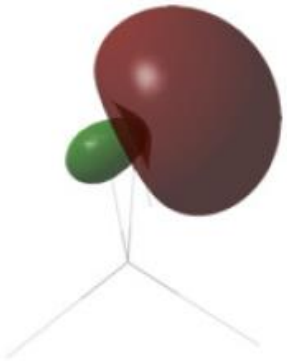




C-H bond

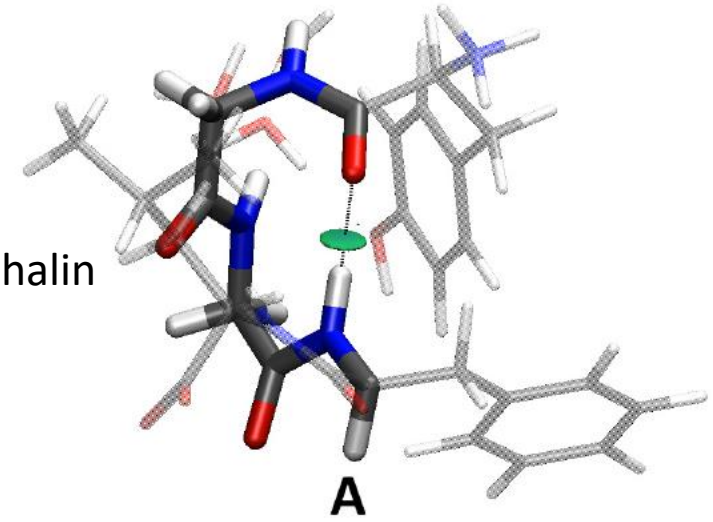


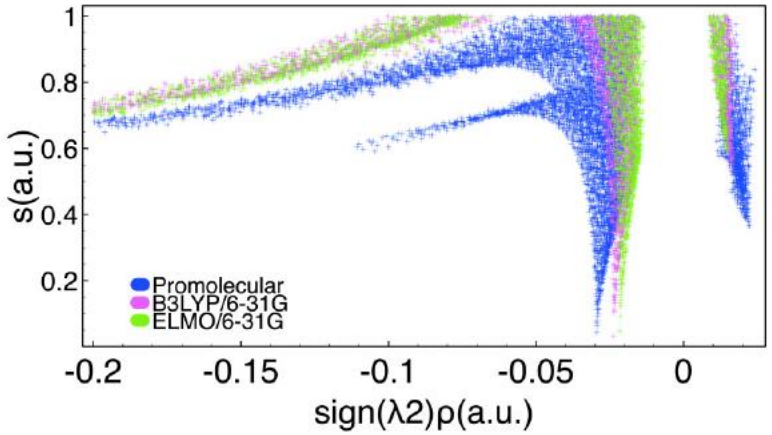
C-C bond



Lone Pair

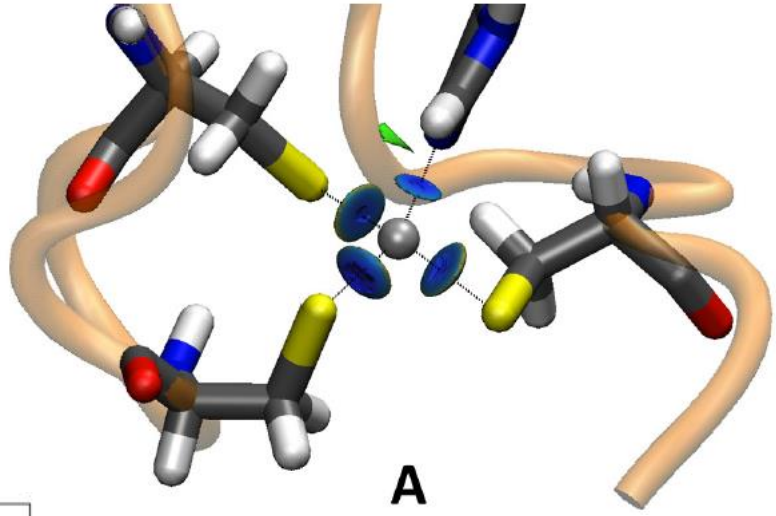
Hydrogen bond in Leu-enkephalin

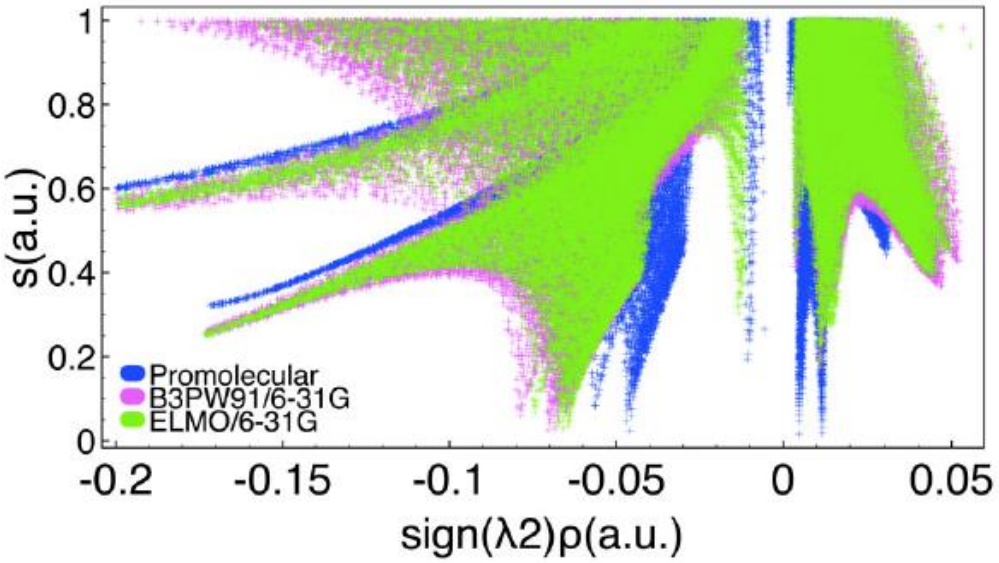




ELMOs are able to reproduce SCF densities more accurately

Especially hard case due to the strong interactions with a charged center





HIV Zinc fingerlike domain
Interactions with the metallic center, Zn^{2+}, and 3 Cys and 1 His

- ELMO results outperform promolecular densities and provides correct answers even in the hardest cases

	Leu-enkephalin	HIV Zn domain
Promolecular	00h 00’ 02’’	00h 00’ 02’’
DFT/6-31G	00h 31’ 31’’	04h 46’ 50’’
DFT/cc-PVDZ	01h 55’ 34’’	51h 36’ 05’’

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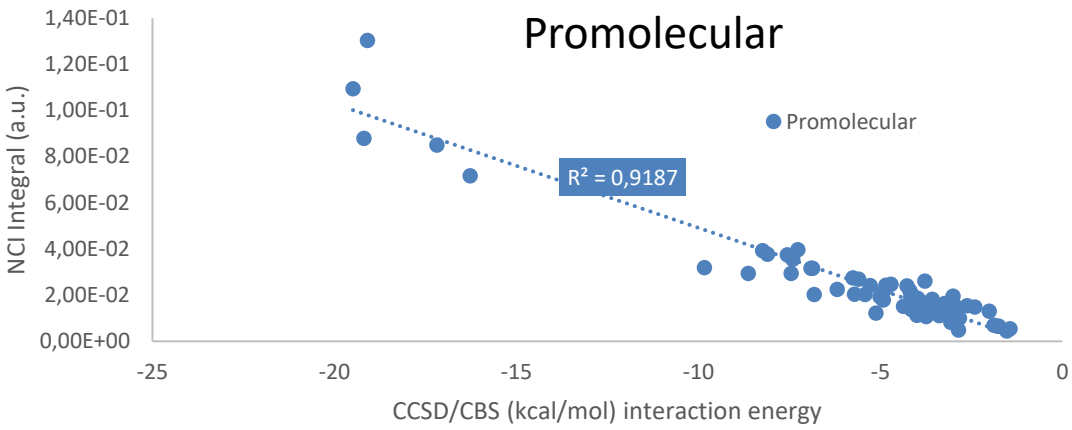
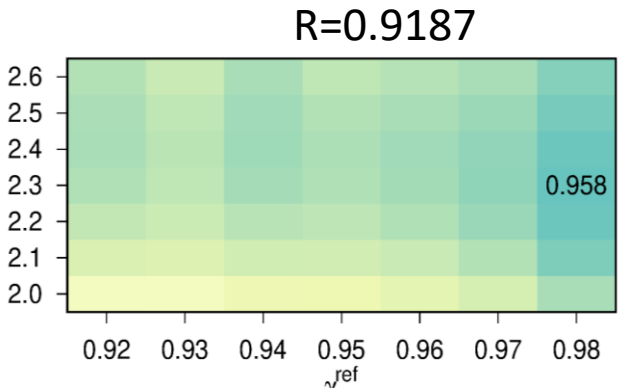
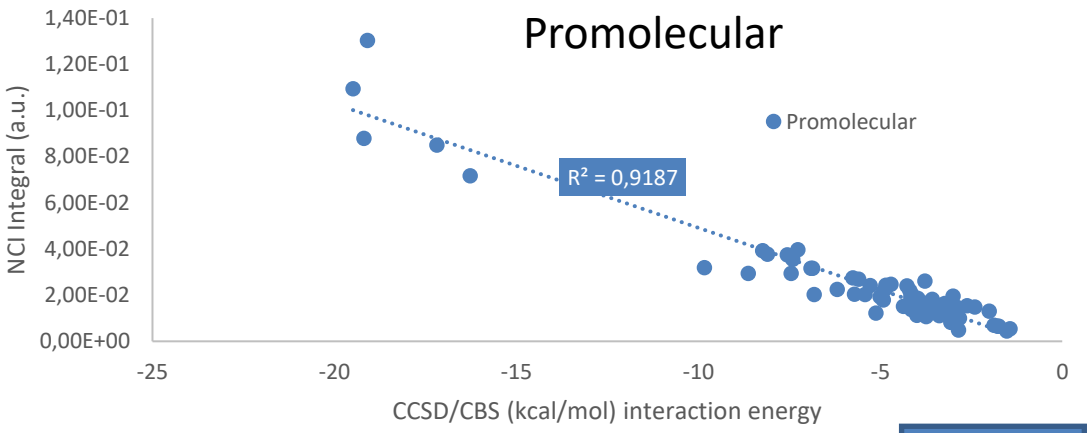
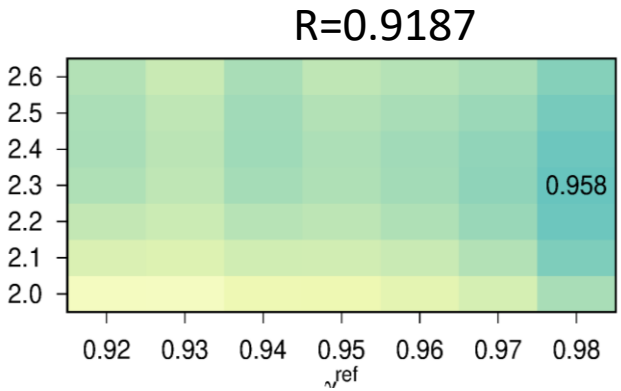
DFT/6-31G	00h 31’ 31’’	04h 46’ 50’’
DFT/cc-PVDZ	01h 55’ 34’’	51h 36’ 05’’
ELMO/6-31G	00h 00’ 04’’	00h 08’ 16’’
ELMO&cc-pVDZ	00h 00’ 06’’	00h 12’ 41’

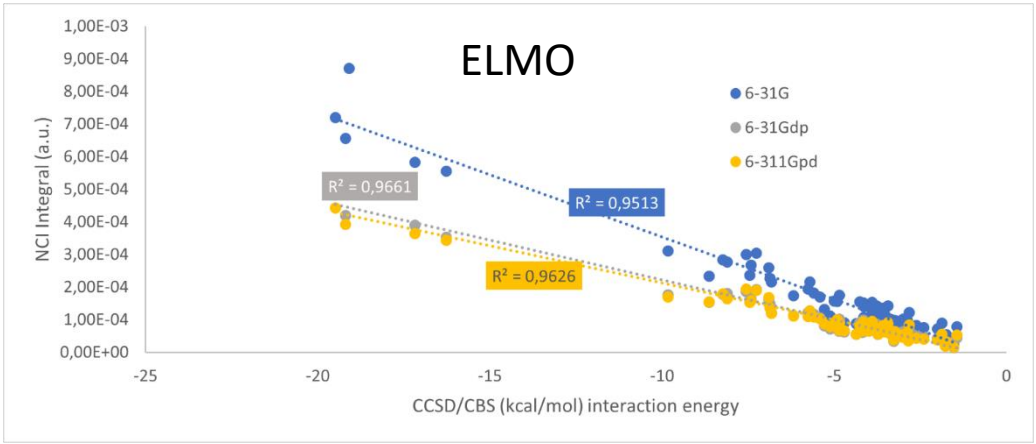
- Similar global computing times Gaussian(+ELMO)+NCIPLOT

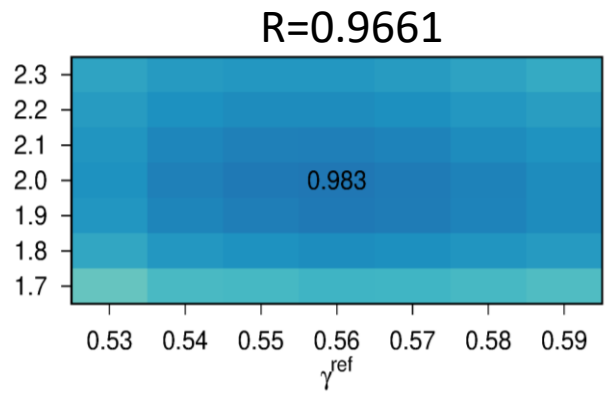

Promolecular
NCI Integral (a.u.)
1,40E-01
1,20E-01
1,00E-01
8,00E-02
6,00E-02
4,00E-02
2,00E-02
0,00E+00
-25
-20
-15
-10
-5
0
CCSD/CBS (kcal/mol) interaction energy
Promolecular
R² = 0,9187


R=0.9187
2.6
2.5
2.4
2.3
2.2
2.1
2.0
0.958
0.92
0.93
0.94
0.95
0.96
0.97
0.98
ref







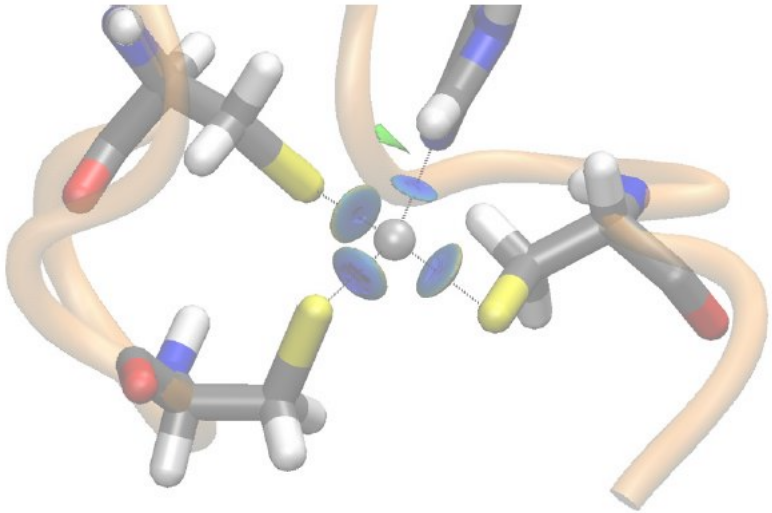


- Energetic estimation is improved

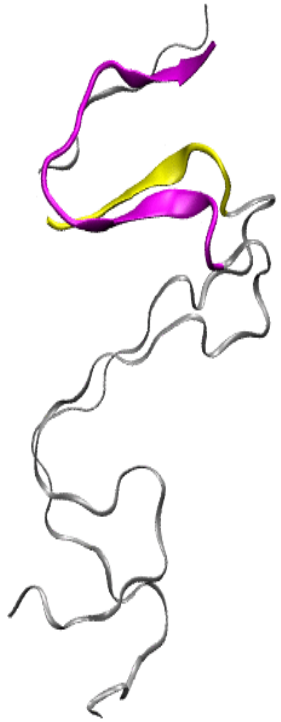
Developments in big systems

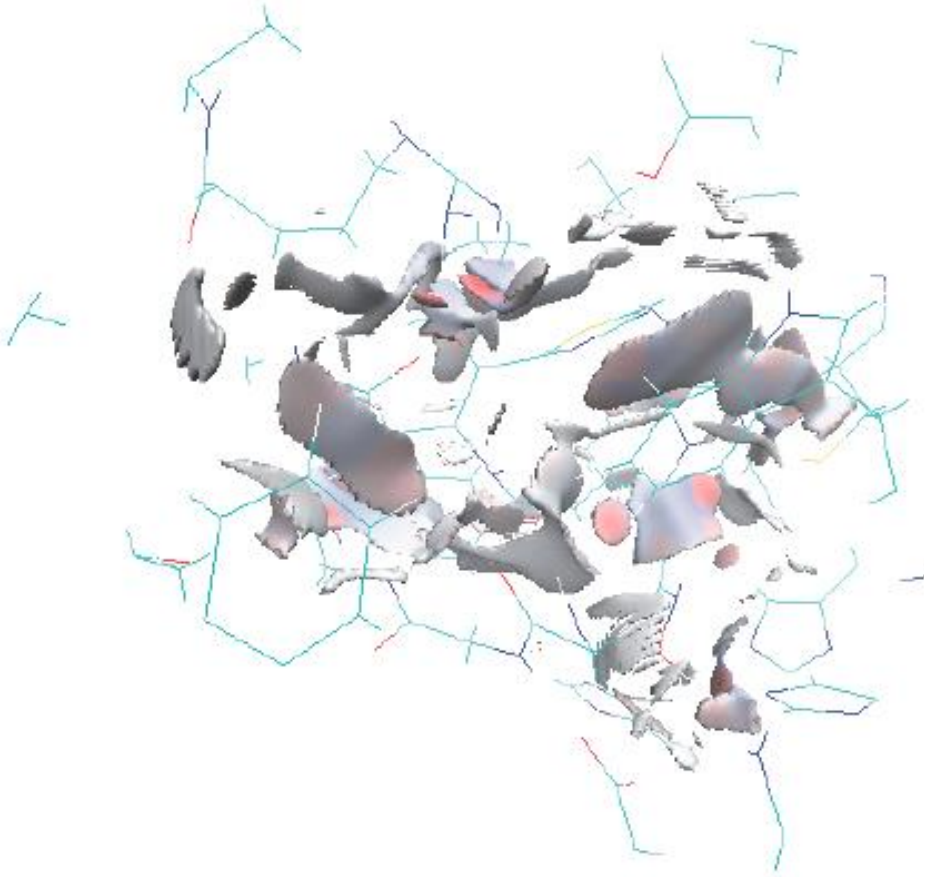
Big systems need new developments…

- Better: ELMOs
- Faster: adaptative grids…MDs
- Easier: NCIweb



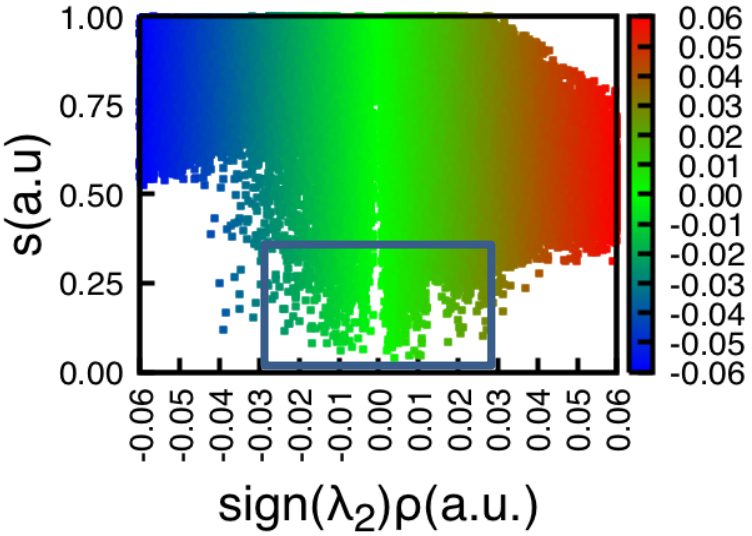
However, still too expensive for dynamical analyses…



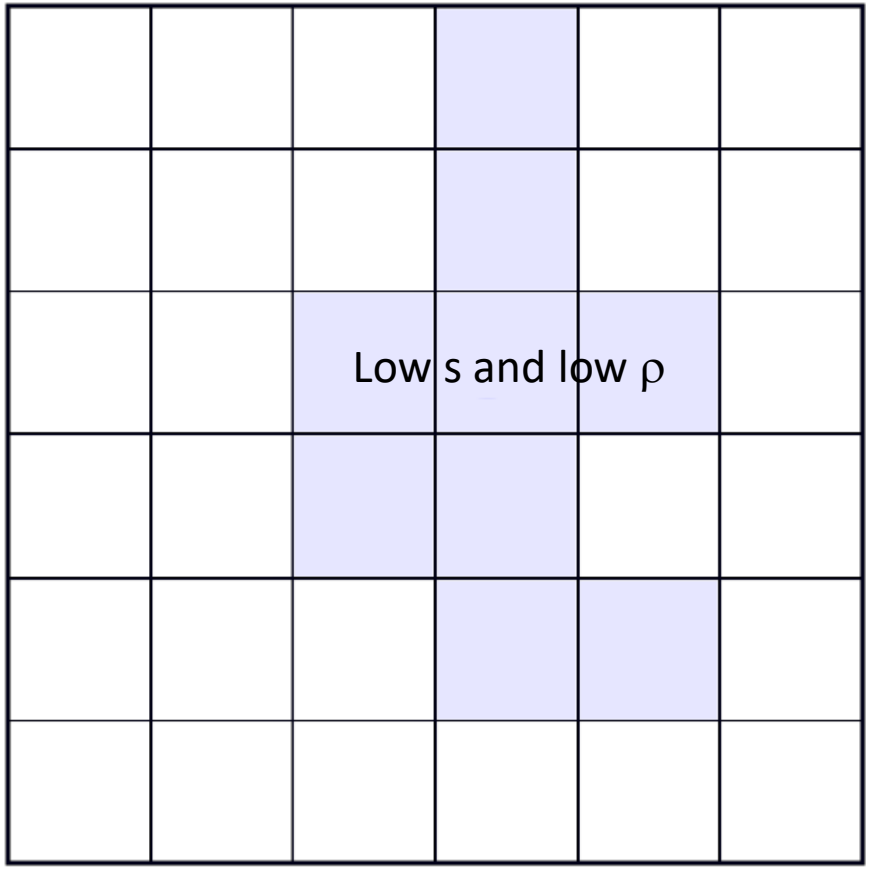


The density and the RDG values are computed at all the boxes

Only a very small percentage of grid points have low r and low s



1ACB (2289 atoms)



- We start with a very coarse grid (4 times the common one)

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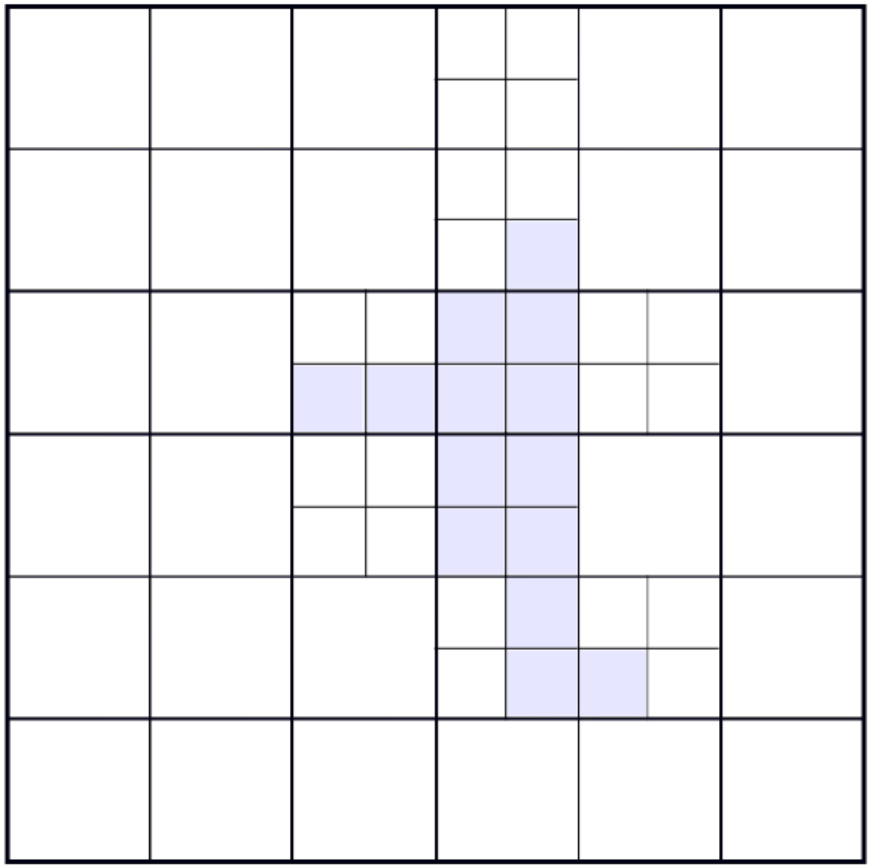

- We start with a very coarse grid (4 times the common one)
- Subdivide in the interesting region several times

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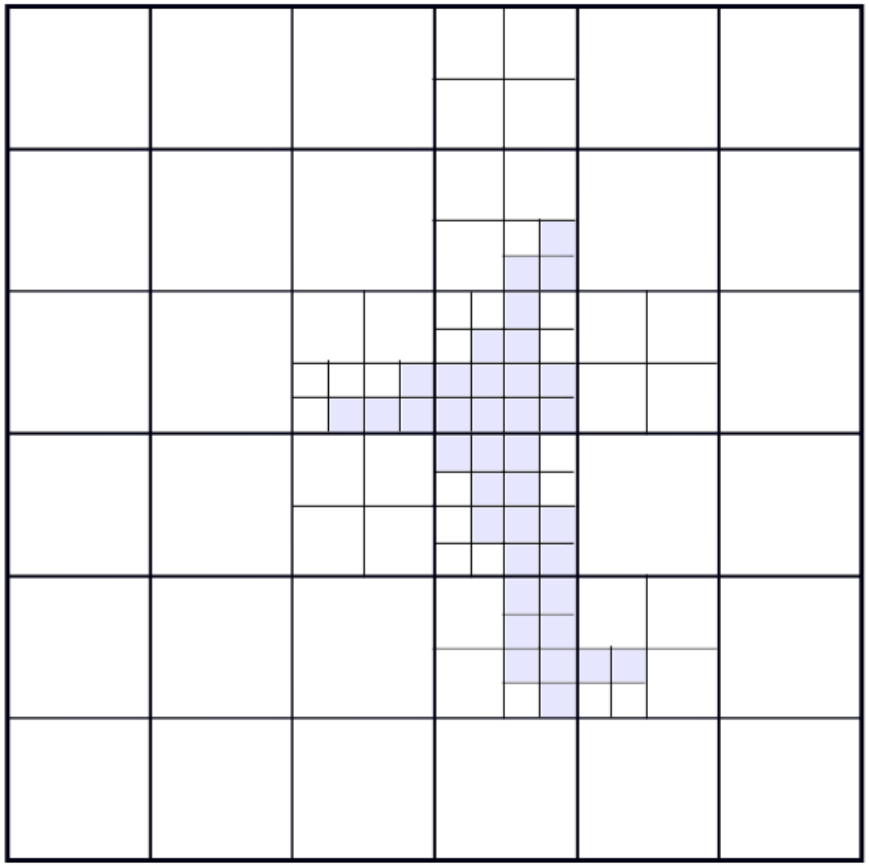

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- Adaptative grid: 4-2-1

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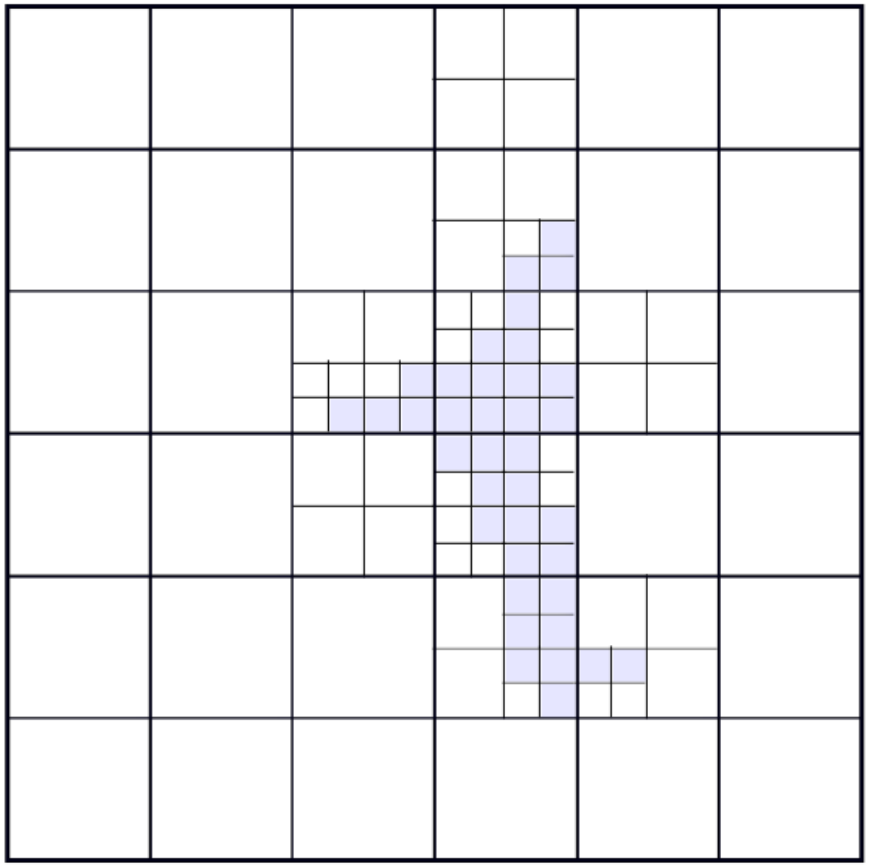
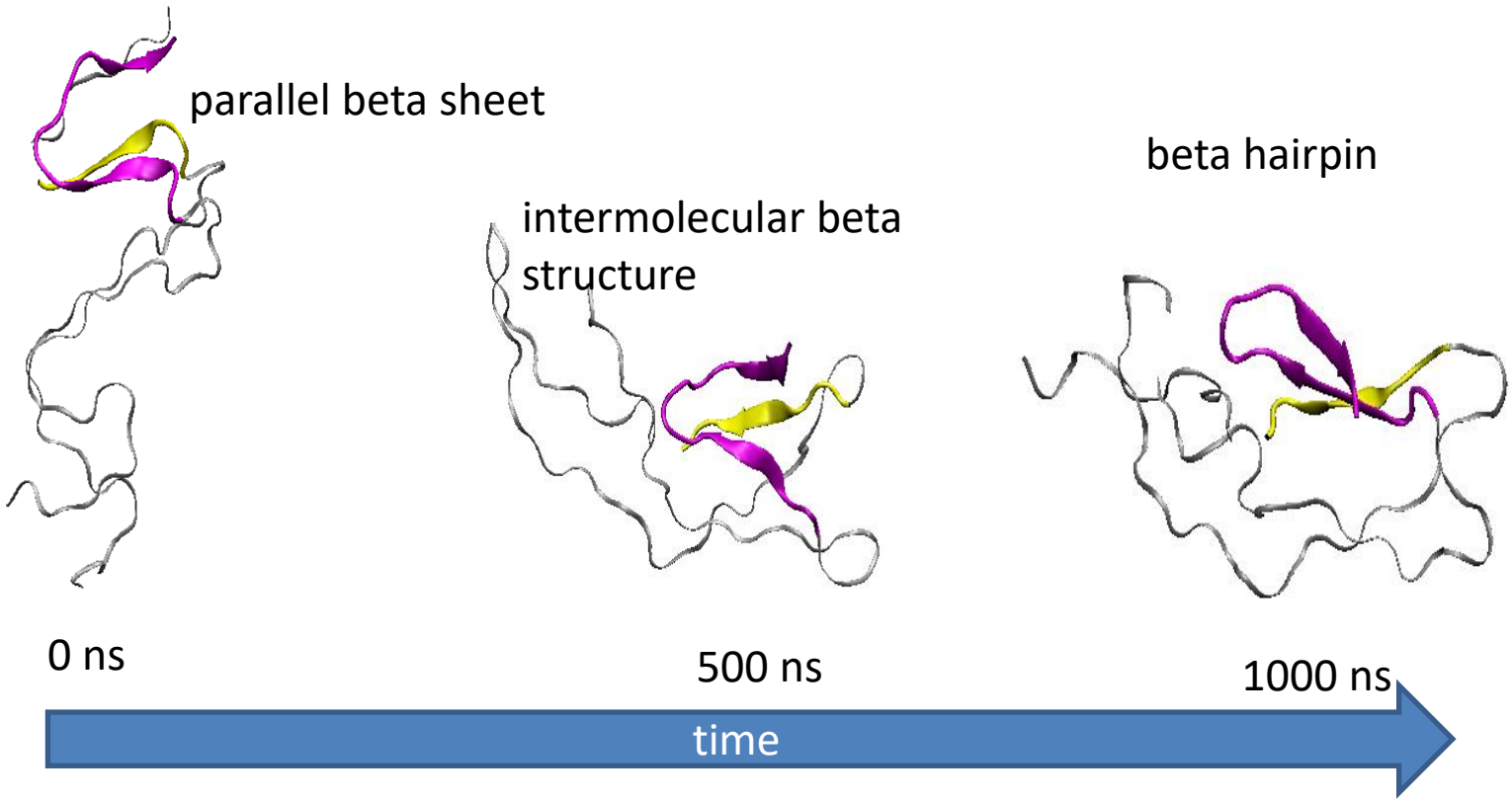


- We start with a very coarse grid (4 times the common one)
- Subdivide in the interesting region several times
- Adaptative grid: 4-2-1

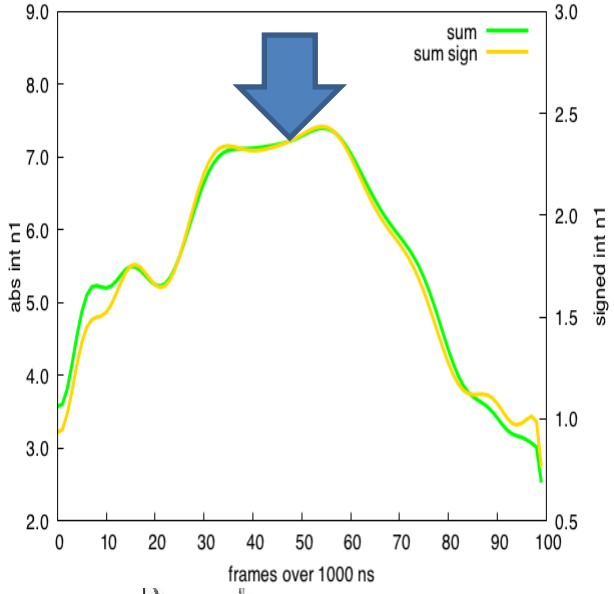
	Old	**New**
t_ρ	260.35	7.36
t_{tot}	267.87	14.84

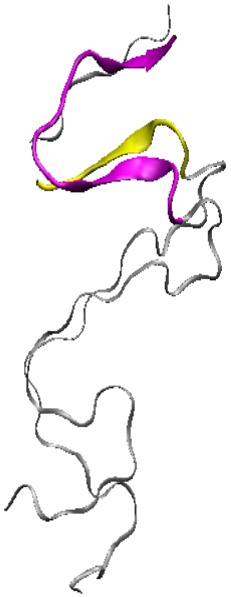


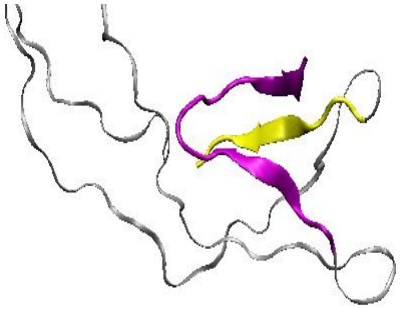
- Dimer of the Aβ42 extracted from the fibril structure
- The initial structure of the fibril folds along the MD due to water exposition

We can track conformational changes along the trajectory.

Intermolecular NCI

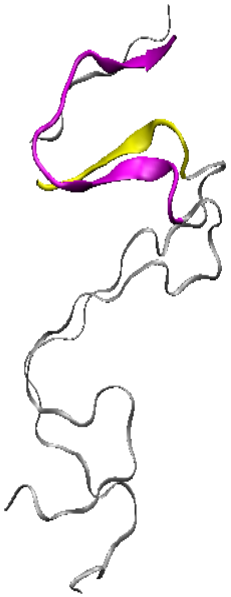




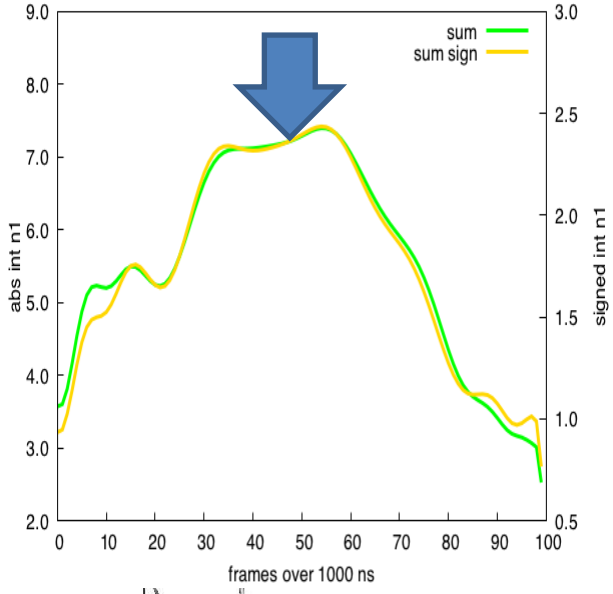


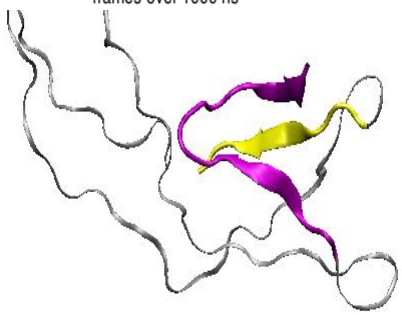
Maximization of intermolecular contacts at 500 ns

We can track conformational changes along the trajectory.



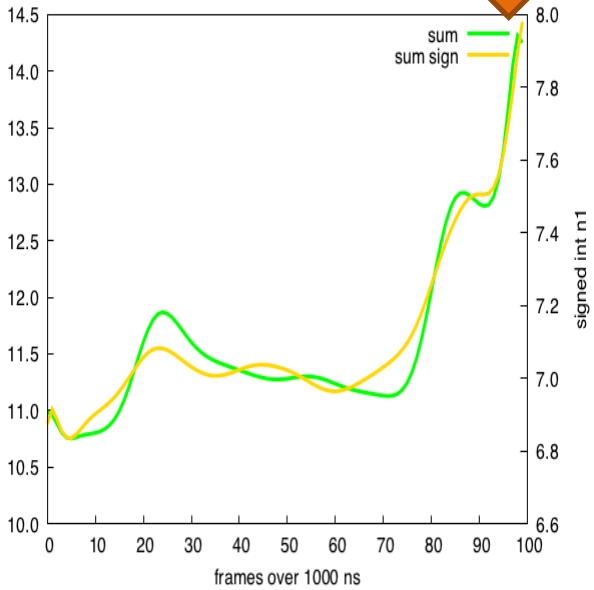
Intermolecular NCI

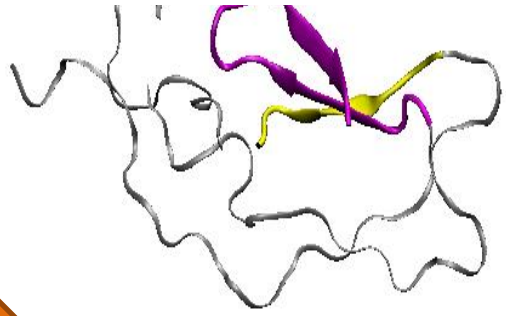




Maximization of intermolecular contacts at 500 ns

Intramolecular NCI





Maximization of intramolecular contacts at 1000 ns

Developments in big systems

Big systems need new developments…

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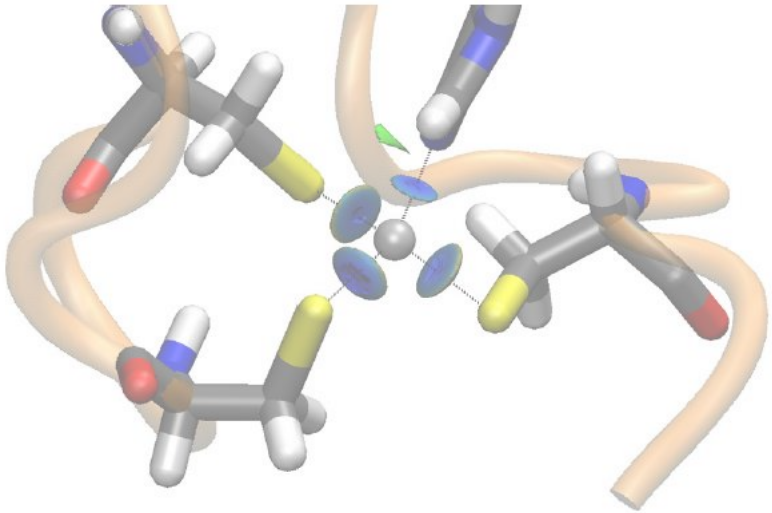
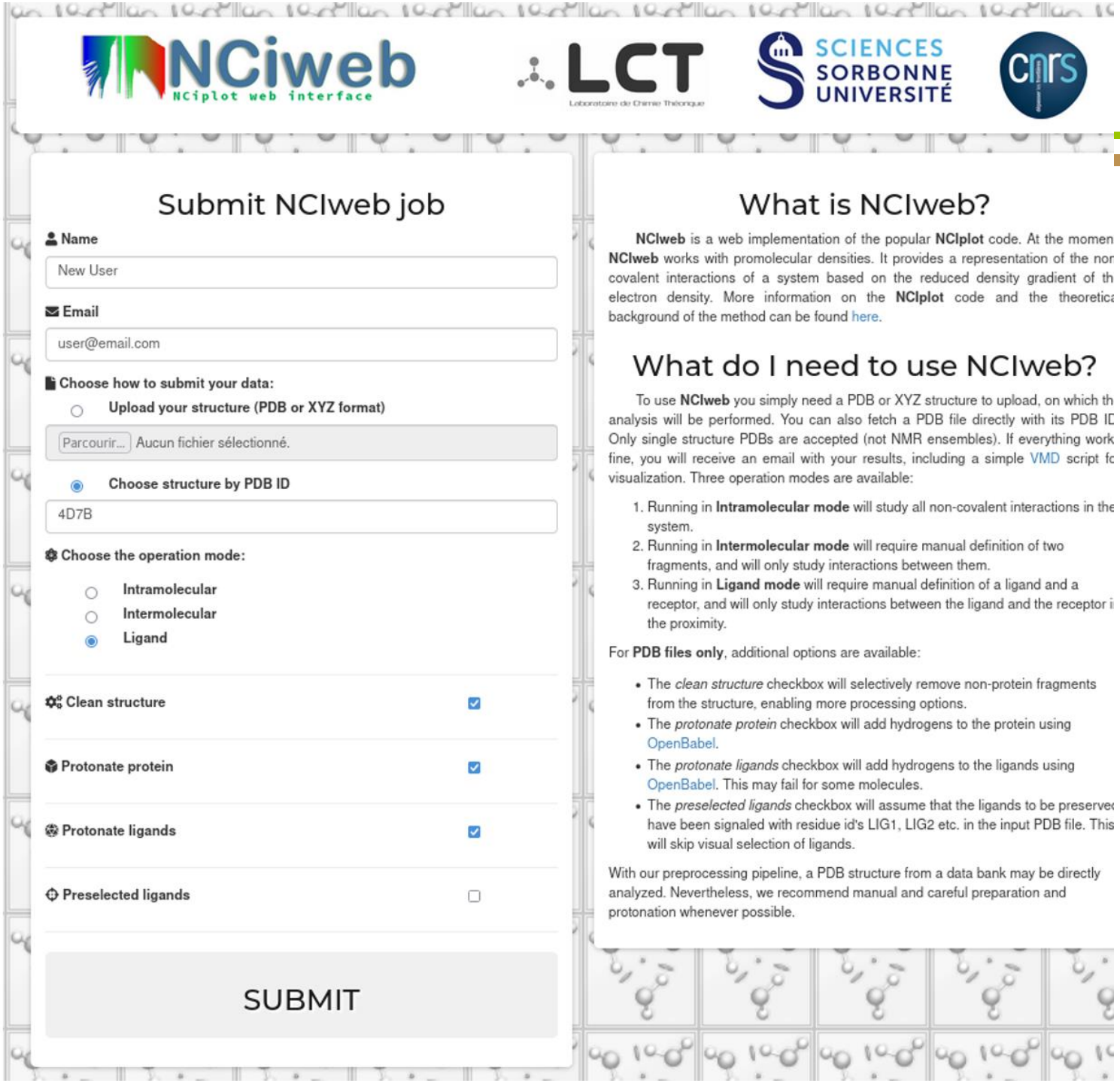
- Easier: NCIweb



NCI online:

https://nciweb.dsi.upmc.fr/index.php


NCIweb
NCIplot web interface
LCT
Laboratoire de Chimie Théorique
SCIENCES
SORBONNE
UNIVERSITÉ
cnrs
Submit NCIweb job
Name
New User
Email
user@email.com
Choose how to submit your data:
Upload your structure (PDB or XYZ format)
Parcourir...
Aucun fichier sélectionné.
Choose structure by PDB ID
4D7B
Choose the operation mode:
Intramolecular
Intermolecular
Ligand
Clean structure
Protonate protein
Protonate ligands
Preselected ligands
SUBMIT
What is NCIweb?
NCIweb is a web implementation of the popular NCIplot code. At the momen
NCIweb works with promolecular densities. It provides a representation of the nor
covalent interactions of a system based on the reduced density gradient of th
electron density. More information on the NCIplot code and the theoretica
background of the method can be found here.
What do I need to use NCIweb?
To use NCIweb you simply need a PDB or XYZ structure to upload, on which th
analysis will be performed. You can also fetch a PDB file directly with its PDB ID
Only single structure PDBs are accepted (not NMR ensembles). If everything work
fine, you will receive an email with your results, including a simple VMD script fo
visualization. Three operation modes are available:
1. Running in Intramolecular mode will study all non-covalent interactions in the
system.
2. Running in Intermolecular mode will require manual definition of two
fragments, and will only study interactions between them.
3. Running in Ligand mode will require manual definition of a ligand and a
receptor, and will only study interactions between the ligand and the receptor i
the proximity.
For PDB files only, additional options are available:
• The clean structure checkbox will selectively remove non-protein fragments
from the structure, enabling more processing options.
• The protonate protein checkbox will add hydrogens to the protein using
OpenBabel.
• The protonate ligands checkbox will add hydrogens to the ligands using
OpenBabel. This may fail for some molecules.
• The preselected ligands checkbox will assume that the ligands to be preserve
have been signaled with residue id's LIG1, LIG2 etc. in the input PDB file. This
will skip visual selection of ligands.
With our preprocessing pipeline, a PDB structure from a data bank may be directly
analyzed. Nevertheless, we recommend manual and careful preparation and
protonation whenever possible.

NCiweb
NCiplot web interface

LCT
Laboratoire de Chimie Théorique

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cnrs

Remember to carefully check the protonation of ligands!

Success! Help us clean your file

A total of **2** ligands were found. By default, **no ligands will be preserved**. Do you want to select which ligands to preserve?

YES

Preserve ligand TCW, number undefined from chain A1126 ? ☑ 👁

Preserve ligand TCW, number undefined from chain B1126 ? ☐ 👁

A total of **2** chains were found. By default, **all** chains will be considered. Do you want to select which chains to preserve?

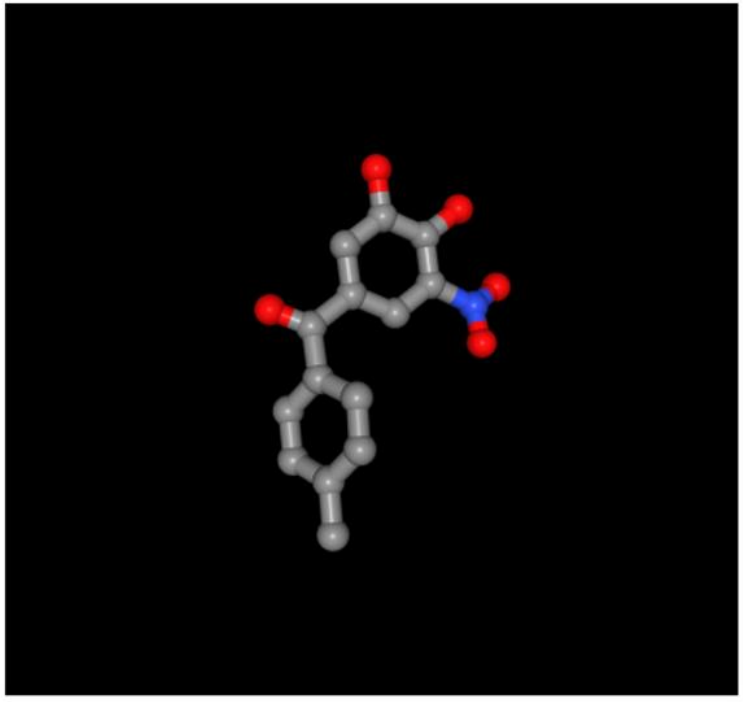
NO

A total of **28** residues with multiple orientations were found. By default, the **first** orientation will be considered. Do you want to select which orientations to choose?

NO

VALIDATE

Visualize your system



Toggle spin! | Toggle rock! | White background

Add Ball & Stick | Add Licorice | Download image

Visualize current selection

NCiweb
NCiplot web interface

LCT
Laboratoire de Chimie Théorique

SCIENCES SORBONNE UNIVERSITÉ

cnrs

Remember to carefully check the protonation of ligands!

Target ligand definition

A total of **1** ligands have been selected. **Define your target ligand using the checkboxes below.** Only interactions between the target and the rest of the system will be studied.

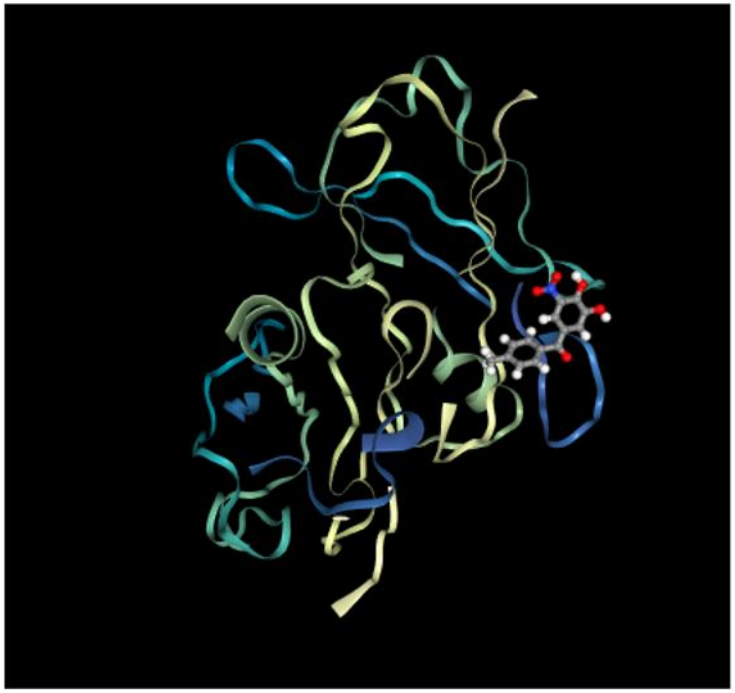
At least **one** ligand needs to be defined.

A **ligand** has been selected! **Ready!** | **Target?**

Ligand TCW, number undefined from chain A1126. 

APPLY

Visualize your system



Toggle spin!	Toggle rock!	White background
Add Ball & Stick	Add Licorice	Download image

Visualize current selection

NCIweb
NCIplot web interface

LCT Laboratoire de Chimie Théorique

SCIENCES SORBONNE UNIVERSITÉ

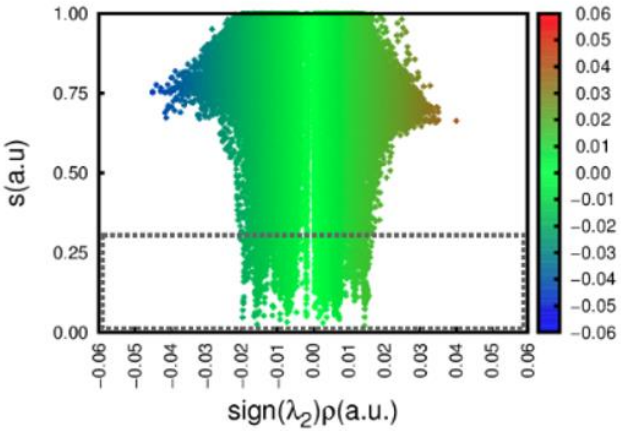
cnrs

NCIPlot Results

job id : **63727bfc62f87**

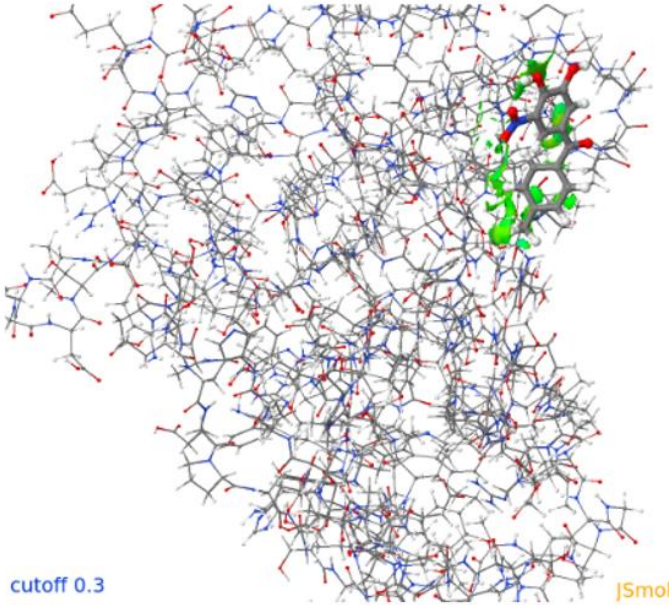
date : 14-11-2022

NCI LOG OUT



TGZ Download 2.27 MB

NCI isosurfaces



cutoff value - 0.3 +

fragment 1 : show atoms ☑ | *show labels* ☐ | *b&s sizes* - +

fragment 2 : show atoms ☑ | *show labels* ☐ | *b&s sizes* - +

For comments or requests contact us!

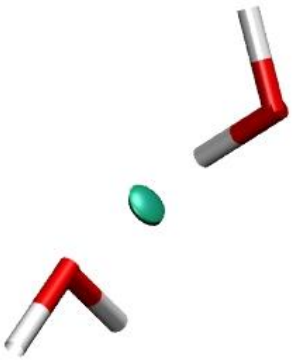
Last modified: November 15 2022

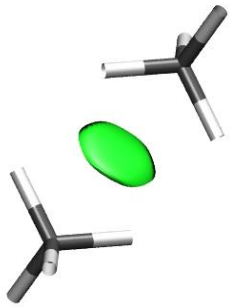
Summary

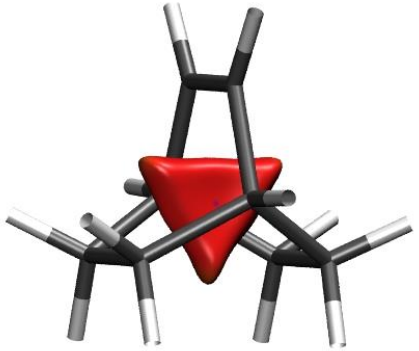
•Non-covalent interactions have a unique signature and their presence can be revealed solely from the electron density.

• This approach provides a rapid and rich representation of van der Waals interactions, hydrogen-bonds, and steric repulsion.

• It is applicable to a wide range of systems: small/large, organic/inorganic, solids, etc.

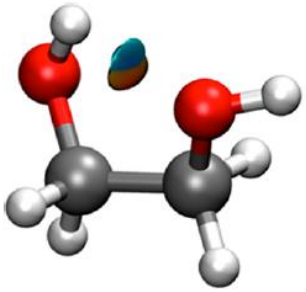




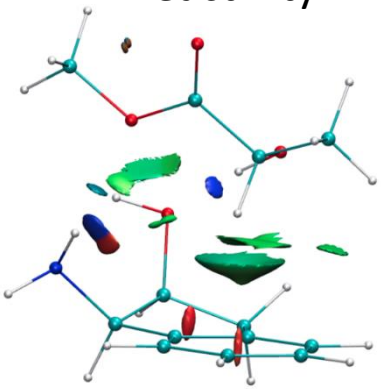


Summary

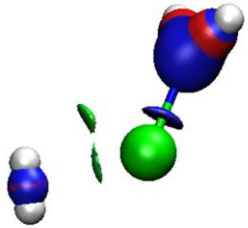
Very weak interactions



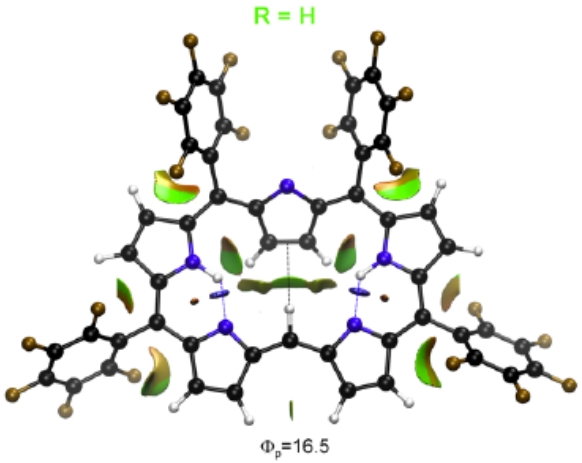
Reactivity



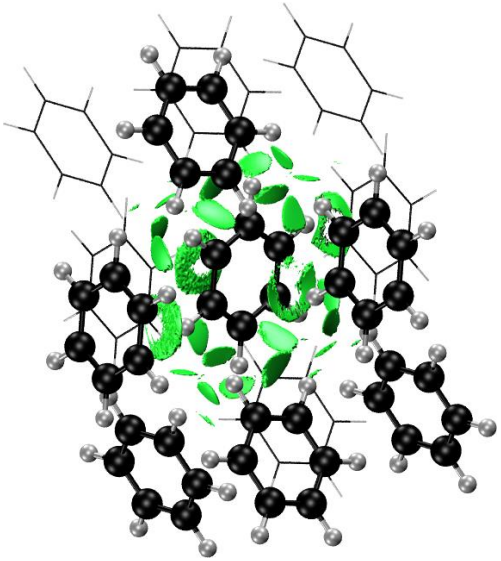
Mechanistic studies



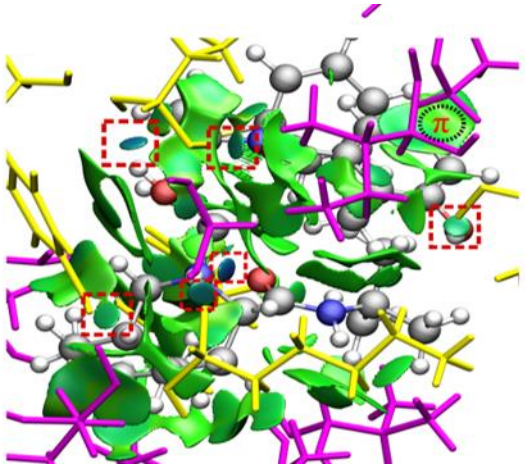
Conformational studies



Packing



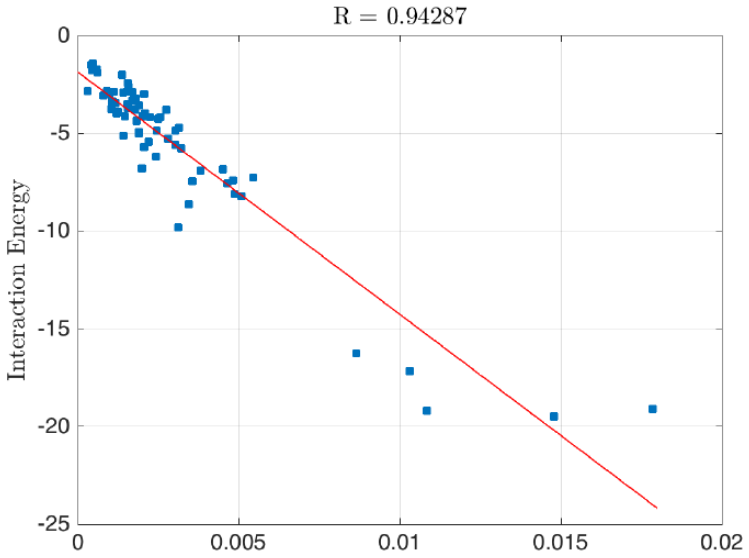
Drug design

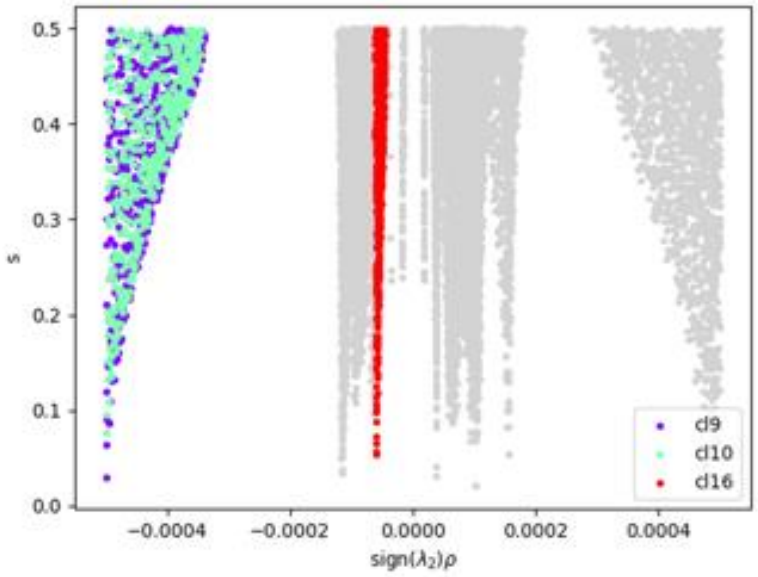


Summary

Developments in quantification

- We can integrate NCI surfaces to obtain insight on energetics
- Integrals can be done by NCI pieces (NCICluster) in order to have a local insight

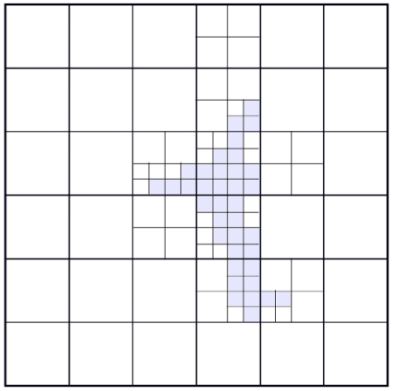


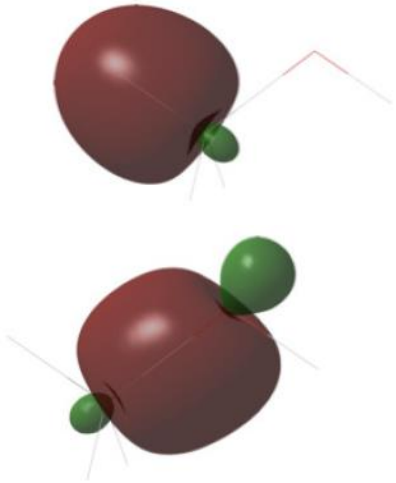


Summary

Developments in big systems

- Faster: adaptative grid
- Better: ELMOs
- Easier: NCIweb





NCiweb
NCiplot web interface

R.A Boto

T. Woller

R. Laplaza

F. Peccati

B. Landeros

D. Ramírez

J. Munárriz

E. Desmedt

D. Arias

T. Novoa

Thank you for your attention!

R.A Boto

T. Woller

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D. Ramírez

J. Munárriz

E. Desmedt

D. Arias

T. Novoa