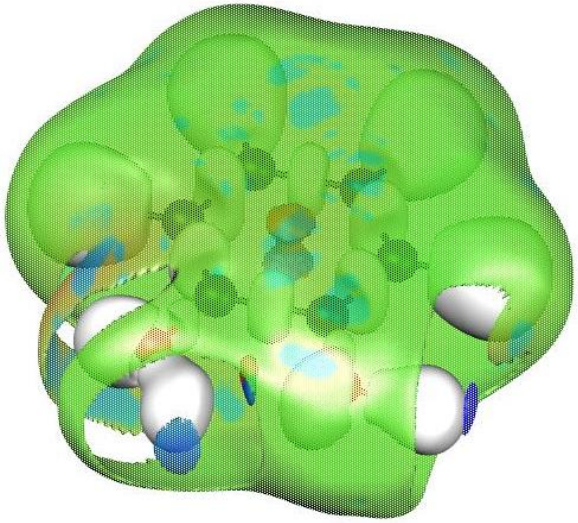
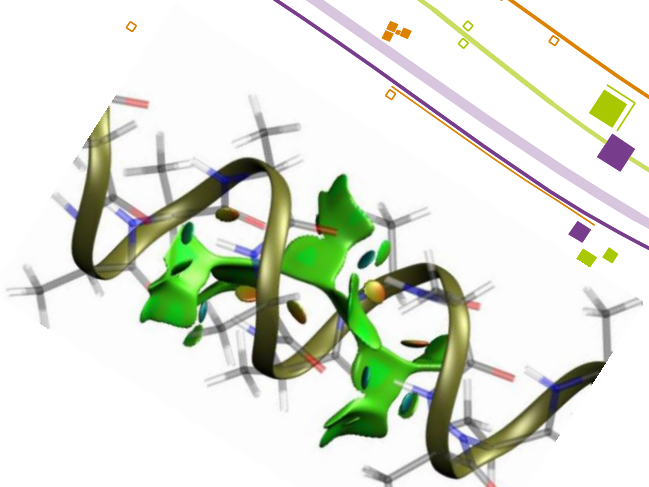
The ELF and NCI analysis

R. Chaudret
J. Contreras-Garcia





Silvi, B.; Savin, A. *Nature* **1994**, *371*, 683.
Piquemal, J. P. *Int. J. Quant. Chem.* **2008**, *108*, 1951.
Johnson, E. R. *J. Am. Chem. Soc.* **2010**, *132*, 6498.
Contreras-Garcia, J. *J. Chem. Theo. Comput.* **2011**. *7*, 625.

IFP Energies nouvelles

Studying chemical bonds

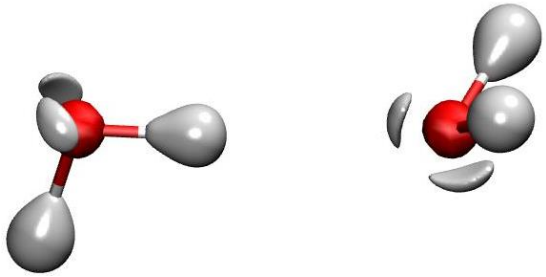
Understanding the stability or reactivity of a system } Main question in chemistry

Strong interaction

(covalent bonds)

Strong density

ELF (Electron Localization Function)

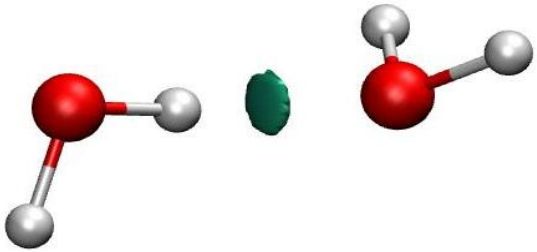


Weak interactions

(van der Waals, hydrogen bonding)

Weak density

NCI (Non-Covalent Interaction)



These 2 approaches are complementary and give access to the whole range of interactions

ELF AND NCI ANALYSIS

- 1- Localizing strong density domains : the ELF analysis
  - The ELF function
  - Topological analysis of the ELF function

- 2- Visualizing weak interactions : the NCI analysis
  - Revealing weak interactions
  - Differentiation between the different interactions type
  - NCI and large systems : the promolecular density

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Definition of the ELF function

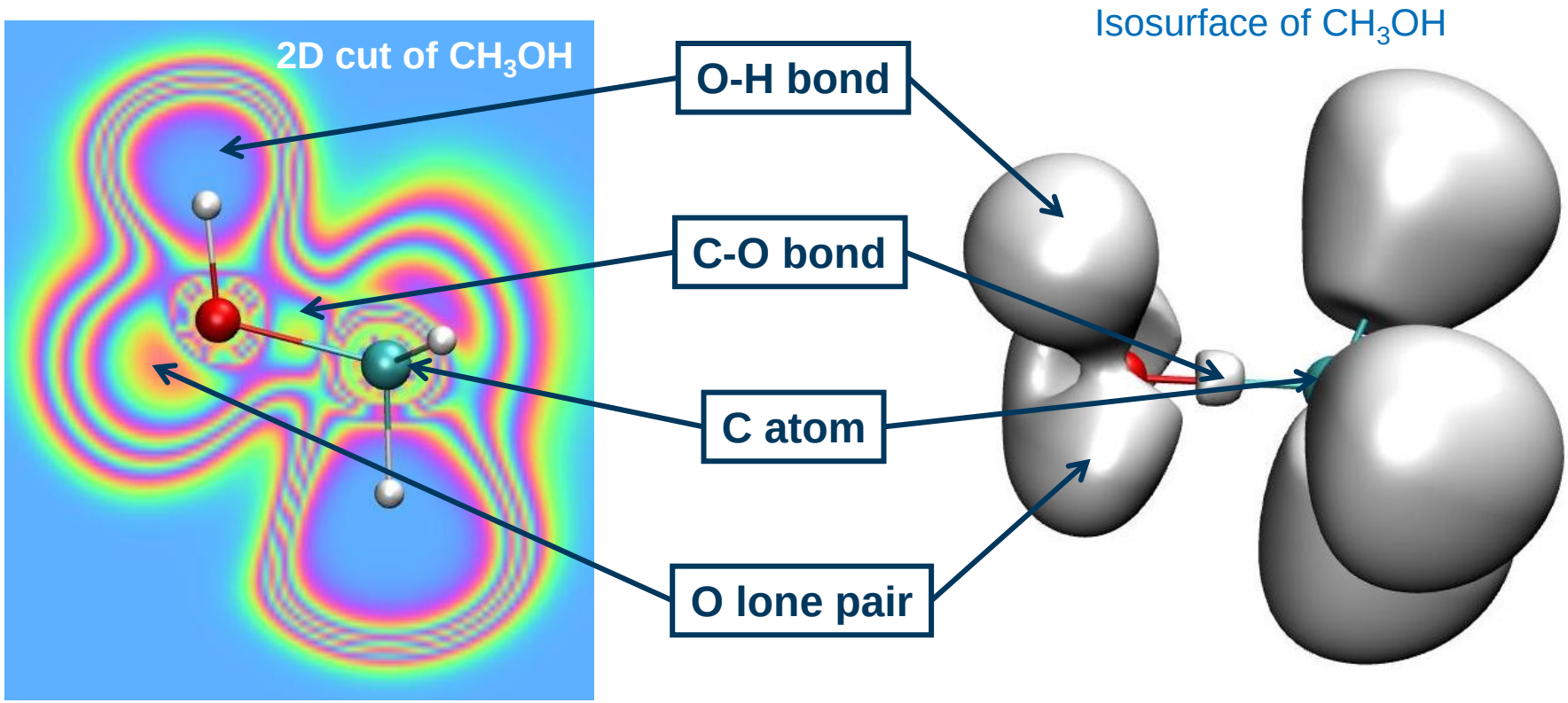
ELF : Electron Localization Fonction

$$\eta(\vec{r})_\pi = \frac{1}{1 + c_\pi(\vec{r})} \quad \text{and} \quad c_\pi(r) = \bar{N}(r)^{-2/3} \frac{\bar{N}_{||}(r)}{\bar{N}_\perp(r)}$$

with
- $\bar{N}_{||}(\vec{r})$ Same spin pairing probability
- $\bar{N}_\perp(\vec{r})$ Opposite spin pairing probability

- Local function → computed on a 3D grid of molecular space
- **0 < ELF < 1**
- Minimum for same spin pair
- Maximum for opposite spin pair

Representation the ELF function



- link with Lewis or VSEPR theory
- **Easy to understand for the chemist**

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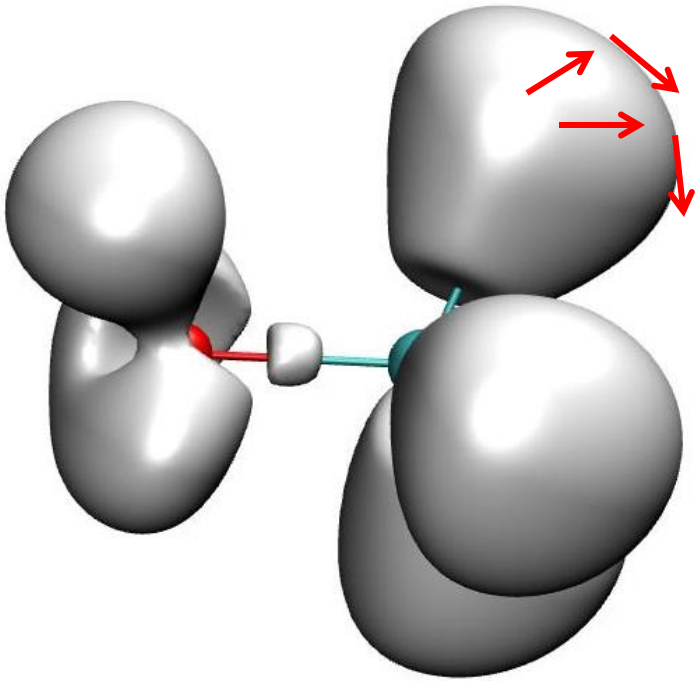
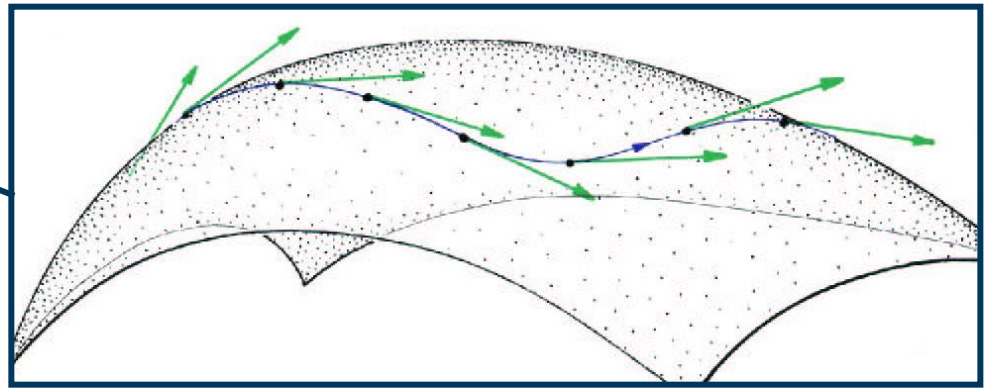
From qualitative to quantitative: Topological analysis of ELF

Based on dynamic gradient analysis (same as AIM)

Step 1 : Define a gradient field :
ELF(**r**) gradient field





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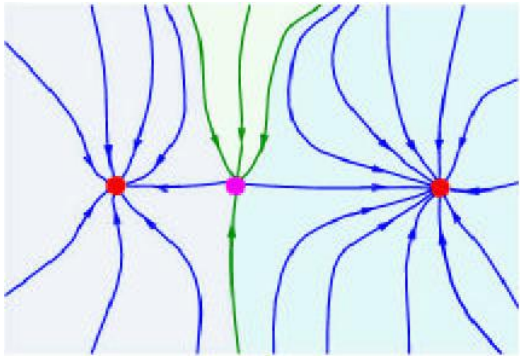
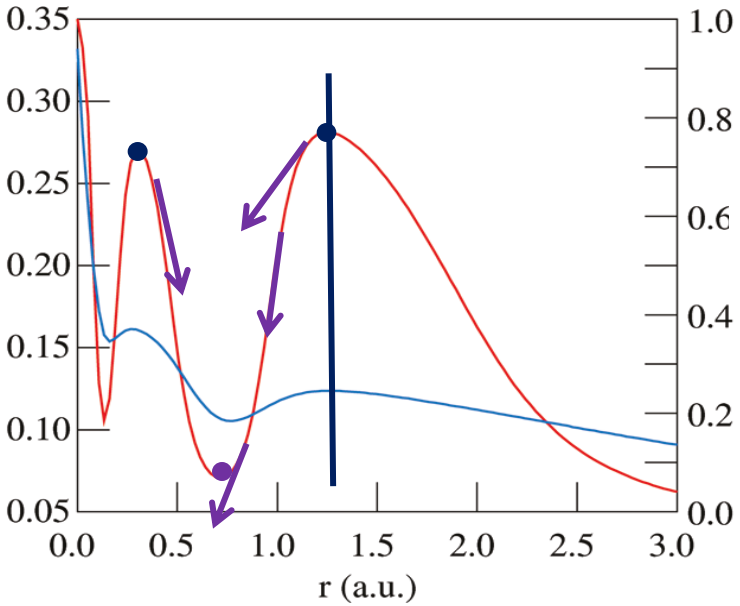
Point of space where the gradient = 0. If this point is a minimum then we will call it an attractor, point of convergence of all the field lines. 0 flux surfaces (field lines don't converge toward any attractor) are called separatrix and are used to divide the chemical space.





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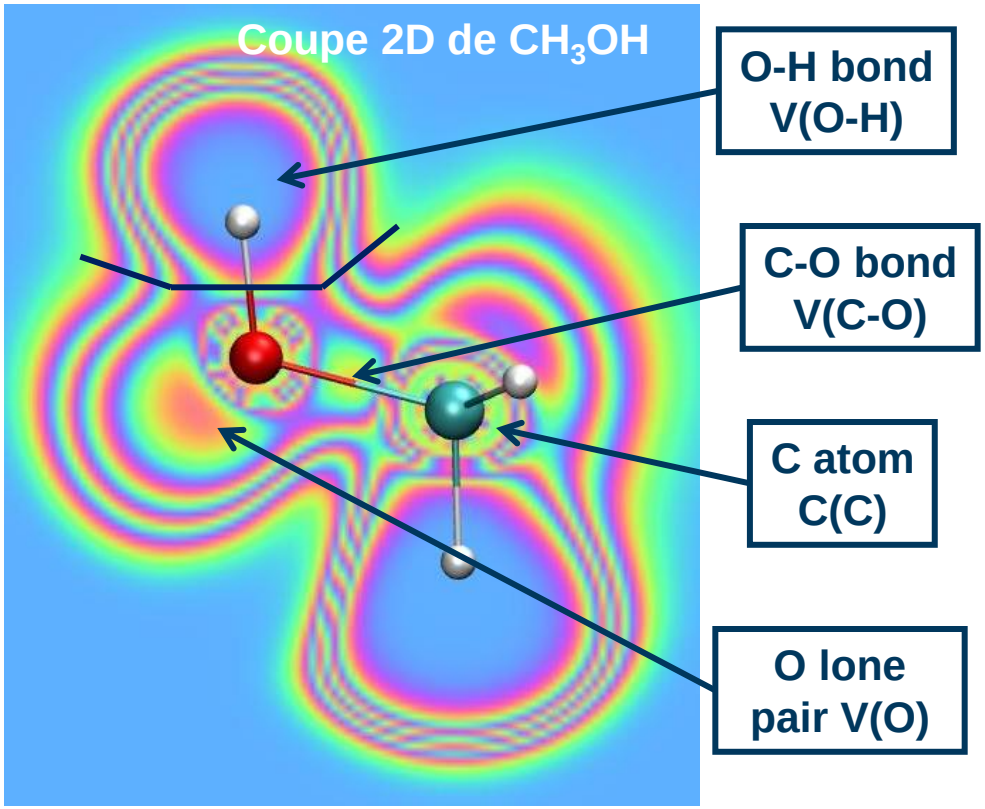
Step 3 : Divide the molecular space into basin having a chemical meaning
Defined depending on the nature of the electrons that characterize them



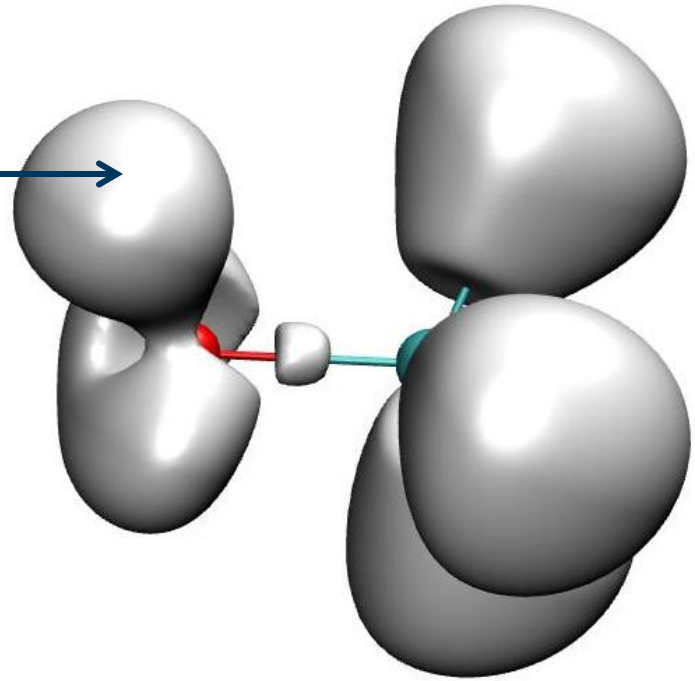
Computation of properties integrated over ELF bassins

$$\vec{r}\,(x, y, z)$$

$$\rho(\vec{r})$$

$$f(\vec{r}) = \left(\frac{\partial \rho(\vec{r})}{\partial N}\right)$$

$$\dots$$



We know the bassin limits (separatrix)

→ We can compute different properties integrated on 1 bassin Ω

$$P(\Omega) = \int_{\Omega} p(\vec{r}) d\tau$$

Properties : Volume, charge, dipole, quadrupole, Fukui functions…

Summary: ELF

- Visualization of the strong pairing regions (bonds, lone pairs, single electron)
- Molecular space divided into basins
- Computation of properties integrated on these basins

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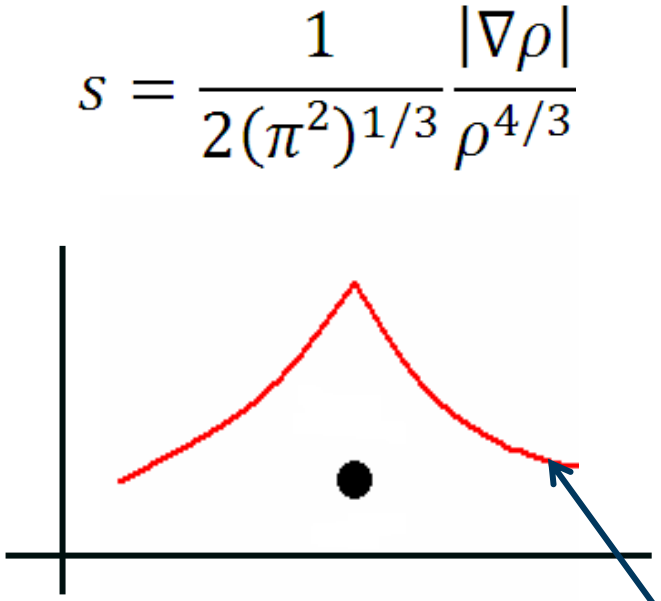
What's NCI ?

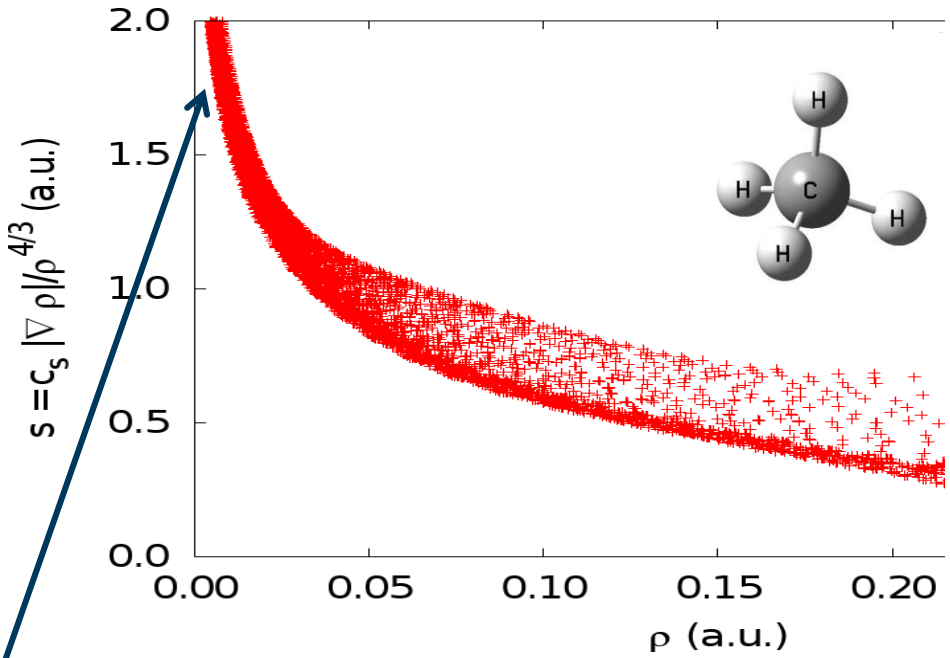
NCI is a method for the visualization of non covalent interactions based on the **analysis of reduced density gradient at low densities**

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

Definition of a weak interaction
1- Molecule alone (no interaction)

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

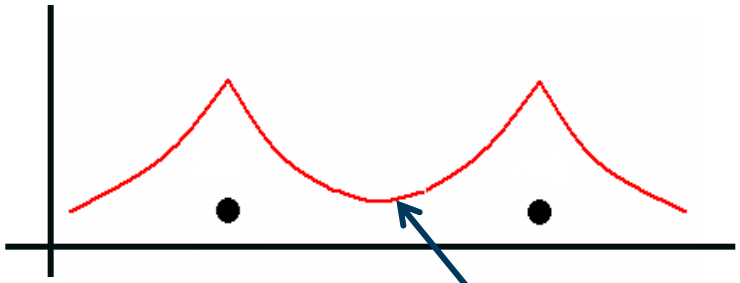


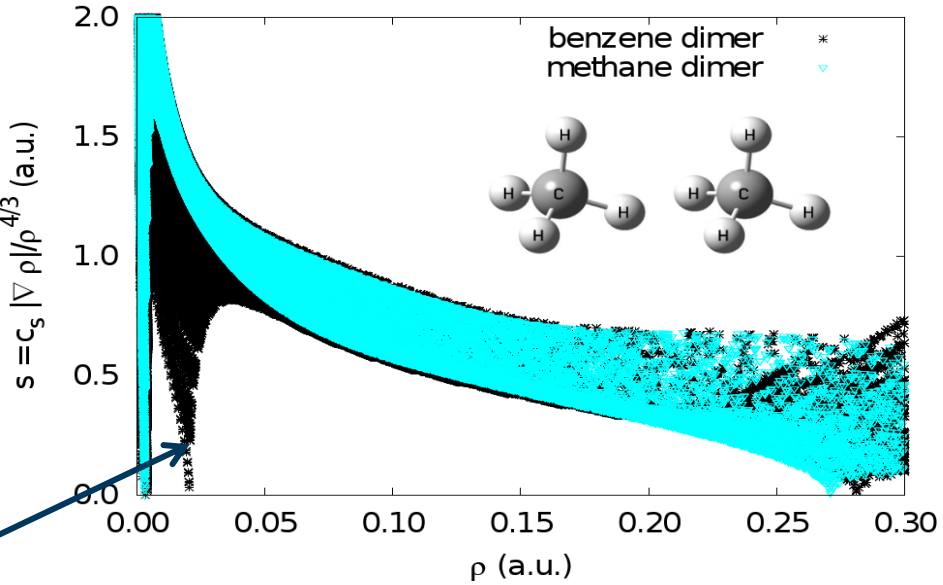


When we get further
ρ→0 and s(ρ)→∞

Definition of a weak interaction
2- Molecules with interactions

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



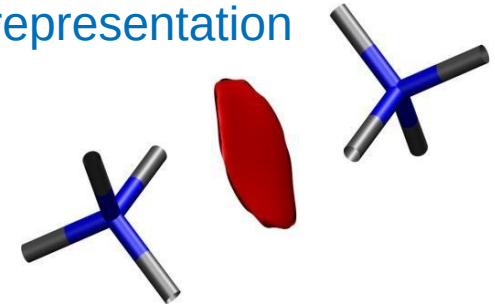


Local minimum with ρ very small and s(ρ) →0

→ Interacting densities

→ **Non covalent interactions**

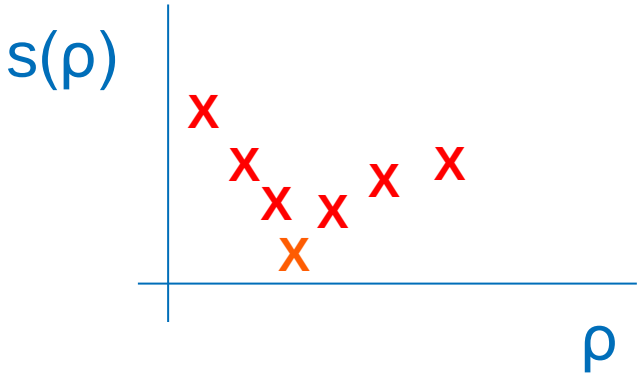
3D representation

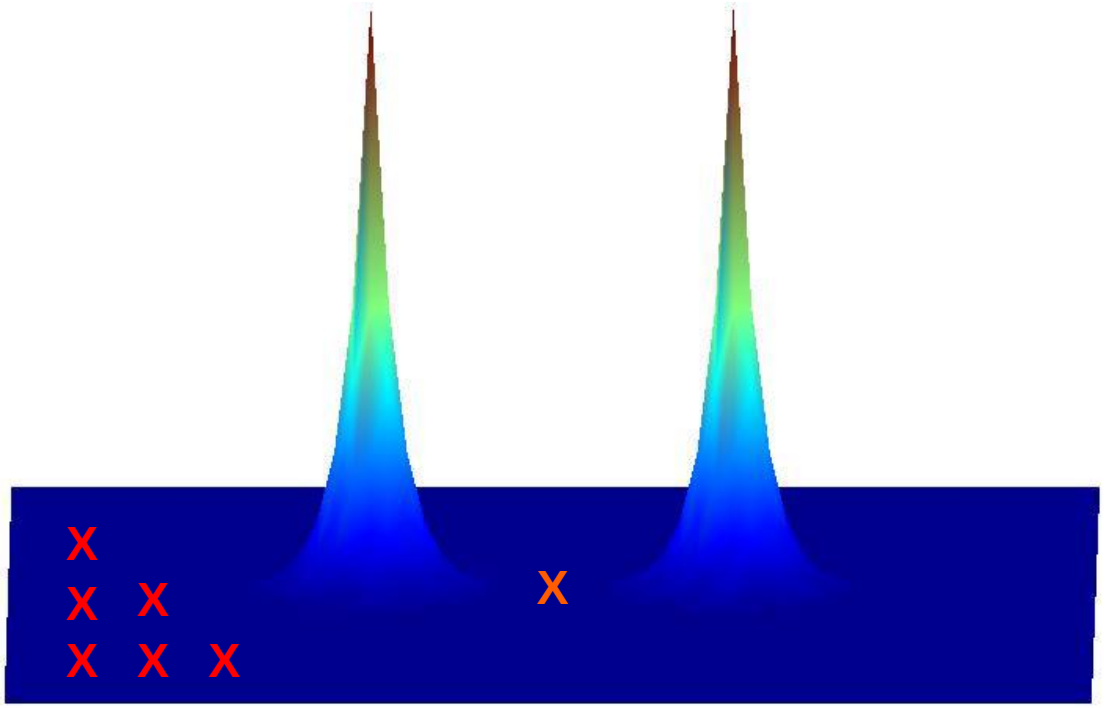


Definition of a weak interaction
2- Molecules with interactions

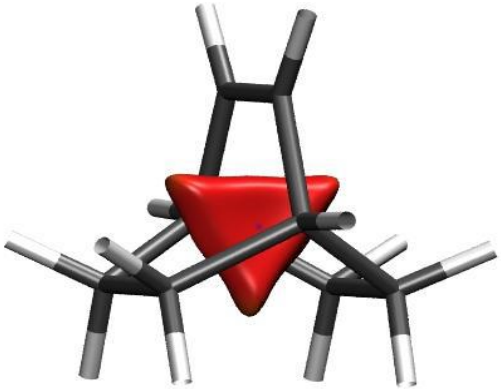
Meaning of the spikes :

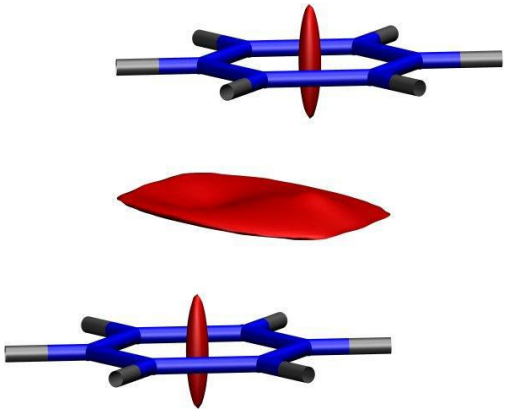
If we go back to the 3D space

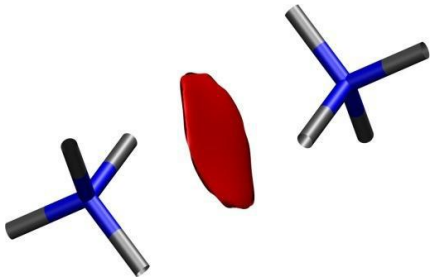


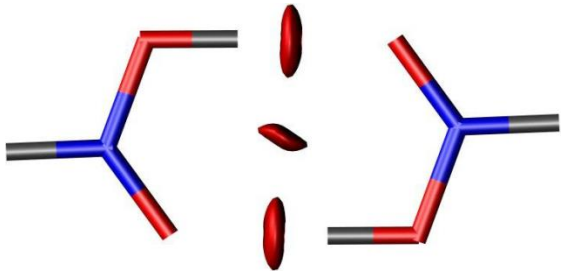


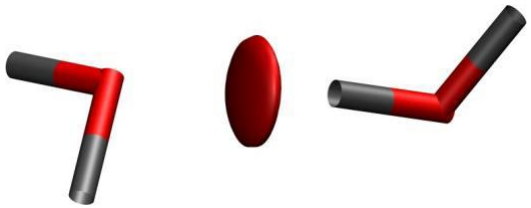
Representation of the non covalent interactions











All the type of interactions have similar representation: so far no distinction based on the strength or the nature (attractive or repulsive)

It is necessary to find other criteria to distinguish between the different interactions types

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Differentiation of the interactions

1- Strength

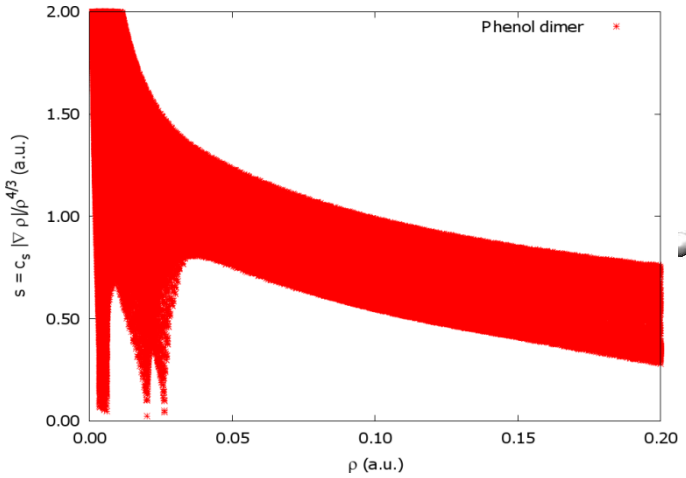
The electronic density is proportional to the strength of the interaction (AIM)

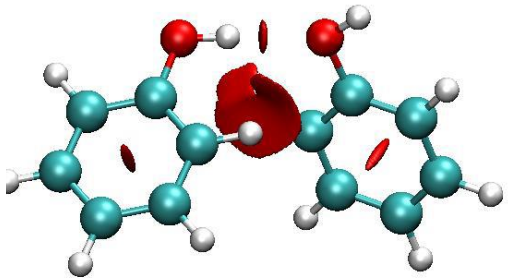
2- Nature

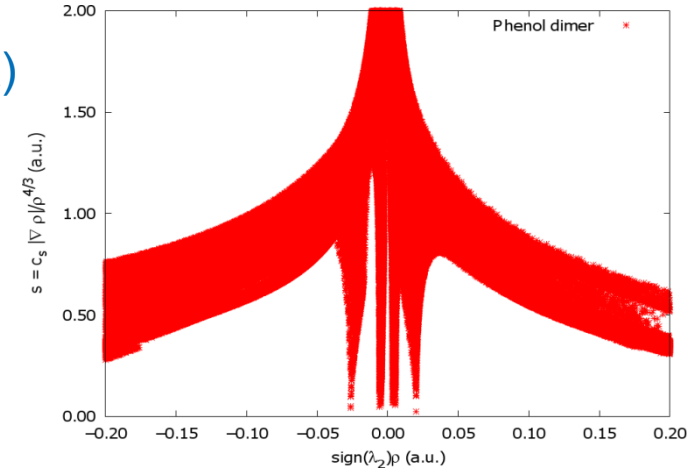
Multiplication by a constant (λ) based on the derivatives

λ < 0 : attractive

λ > 0 : repulsive







?

Differentiation of the interactions

$\rho < 0$
$\lambda < 0$

$\rho \approx 0$
$\lambda \approx 0$

$\rho > 0$
$\lambda > 0$

attraction

repulsion

Hydrogen bond

Vdw interactions

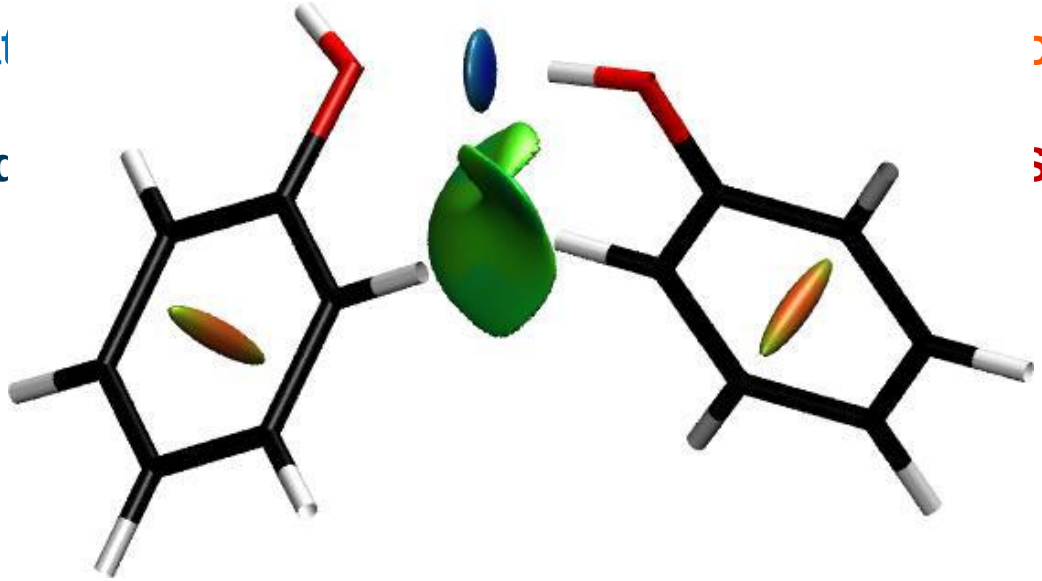
Steric clashes

Differentiation of the interactions

ρ < 0 λ < 0	ρ ≈ 0 λ ≈ 0	ρ > 0 λ > 0

at on

Hydrogen bonc Steric clashes



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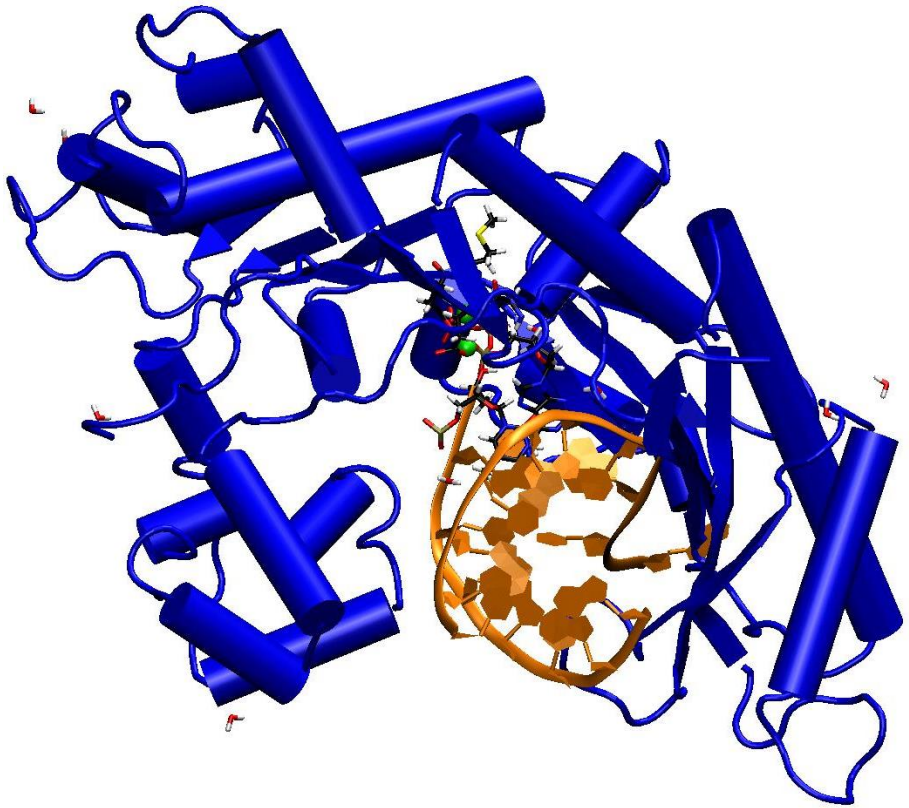
Large systems bring new problems



More than 10000 atoms

→ No more quantum calculation possible

→ No relaxed density

→ Use of an approximate density:

Promolecular density

Promolecular density

Promolecular density

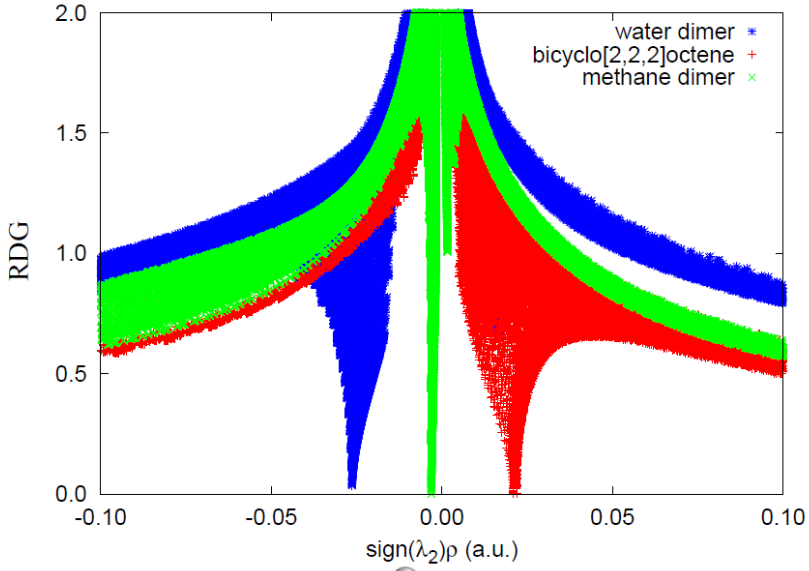
Molecular density ≈ Sum of atomic density parameterized on the isolated atom

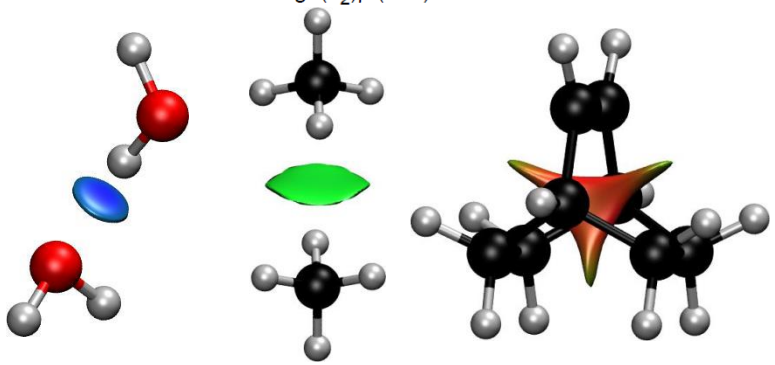
$$\rho^{pro} = \sum_i \rho_i^{at} \qquad \rho_{at} = \sum_j C_j e^{-\frac{\vec{r}}{\zeta_j}}$$

- Density stored in NCIPLOT
- Only coordinates needed

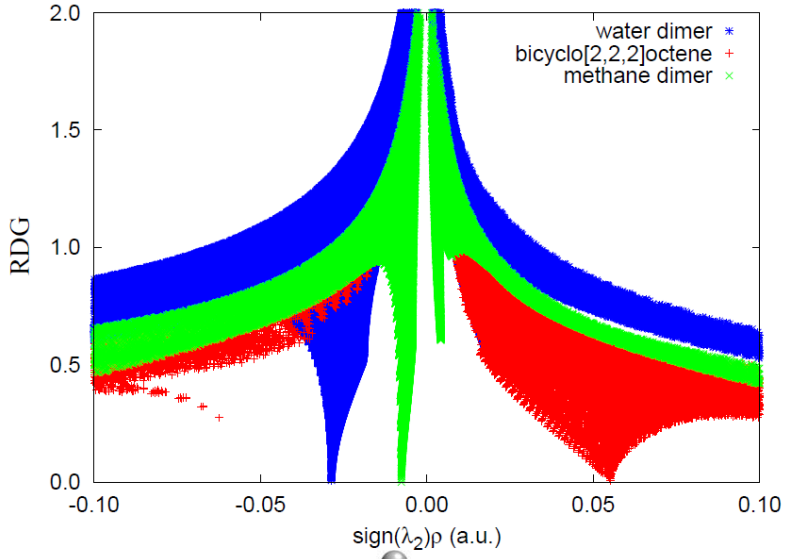
Promolecular density

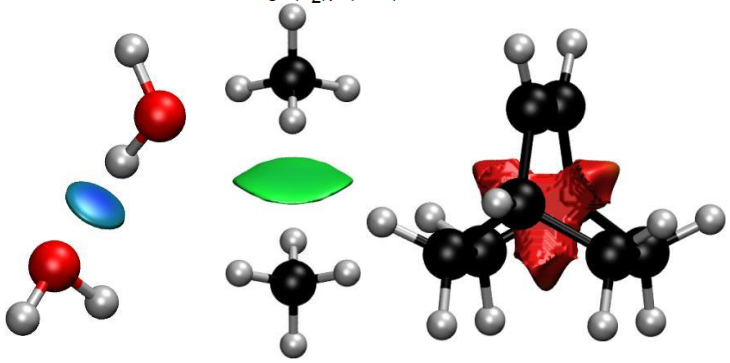
SCF



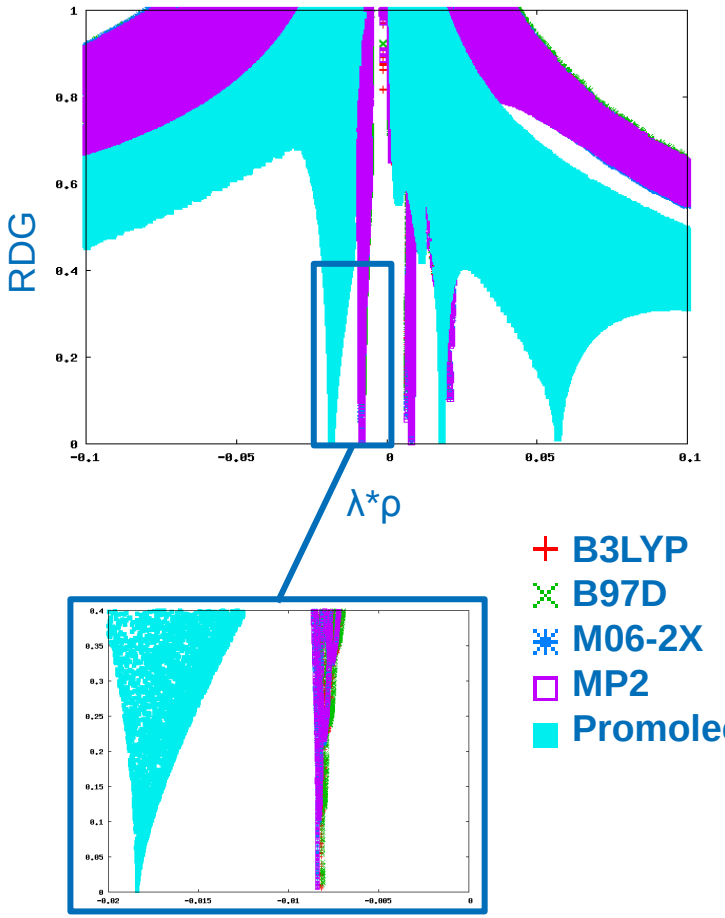


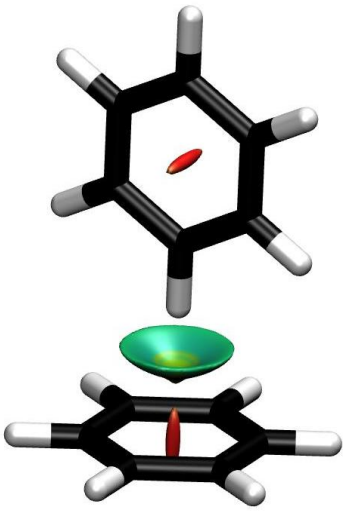
Promolecular



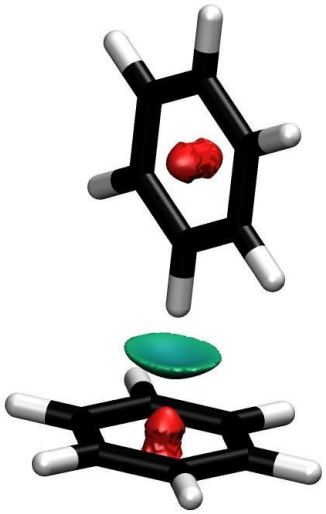


Influence of the level of theory on the NCI analysis





post-HF or DFT density



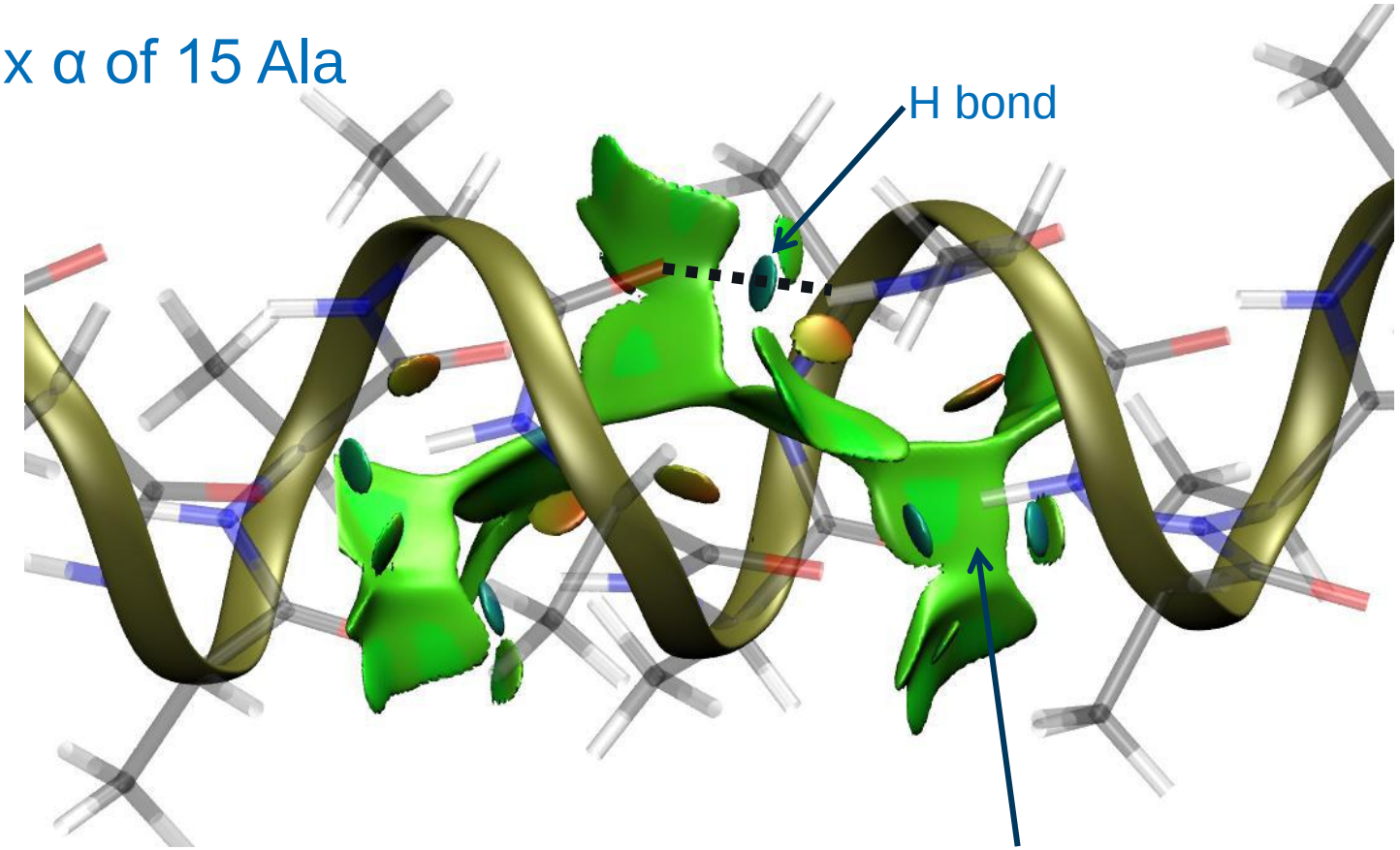
Promolecular densities

For a same geometry:

- NCI DFT/post-HF idem
- NCI promolecular : qualitatively similar

Promolecular density for biological systems

Helix α of 15 Ala



Summary: NCI

- Visualization of the non covalent
- Differenciation of the interaction depending on their nature and their strength
- For large system: use of promolecular density

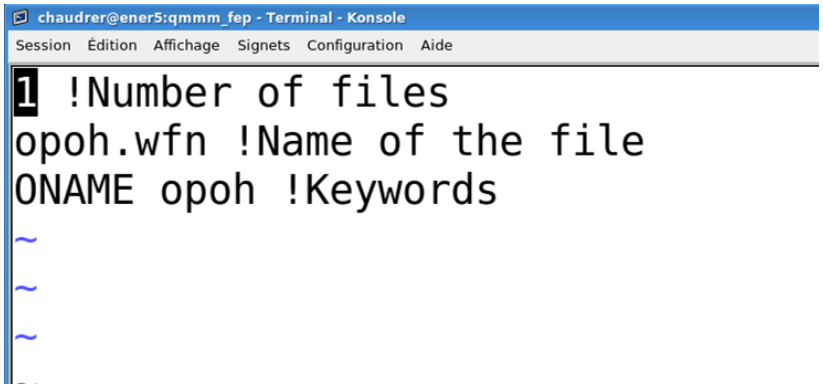
Exercices : ELF and NCI analysis of the catechol

First steps into topological analysis

Silvi, B.; Savin, A. *Nature* **1994**, *371*, 683.
Piquemal, J. P. *Int. J. Quant. Chem.* **2008**, *108*, 1951.
Johnson, E. R. *J. Am. Chem. Soc.* **2010**, *132*, 6498.
Contreras-Garcia, J. *J. Chem. Theo. Comput.* **2011**. *7*, 625.

IFP Energies nouvelles

NCI analysis: Input



- Different type of input: wfn / xyz
- Different possible keywords:
  - ✓ **ONAME** name: ouput files name
  - ✓ **CUTOFF** rho rdg: cutoff general (dat and cube)
  - ✓ **CUTPLOT** rho rdg: cutoff for cube files
  - ✓ **LIGAND** ligand-file-number interaction-cutoff: compute only the interactions within X Å of the ligand.

- **More information in NCI-manual.pdf in document folder**

NCI analysis: running simulation

1- (already done bu don’t forget to set up the NCI environment)

Ex: setenv NCIPLOT_HOME /home/irsrvhome1/R07/chaudrer/programmes/nciplot

(Needed to find the promolecular densities stored)

2- Run NCI : **nciplot NCI.inp >NCI.out**

NCI analysis: Output files

NCI.out :

1. Opening
2. If promolecular : look for the atomic densities
3. Display the input information (keywords)
4. Display the parameters for the calculation
   - Coordinates of the starting point of the grid
   - Coordinates of the ending point of the grid
   - Step (x, y, z)
   - Number of steps (x, y, z)
5. Display the name of the other output files

NCI analysis: Output files

NCI.dat:

Contains all the values of ρ and s(ρ) (to plot the 2D graph)

To plot NCI.dat with gnuplot:

1. Open gnuplot
2. Enter: plot “NCI.dat”
3. The 2D graph should appear

NCI analysis: Output files

NCI-*.cube

NCI.vmd

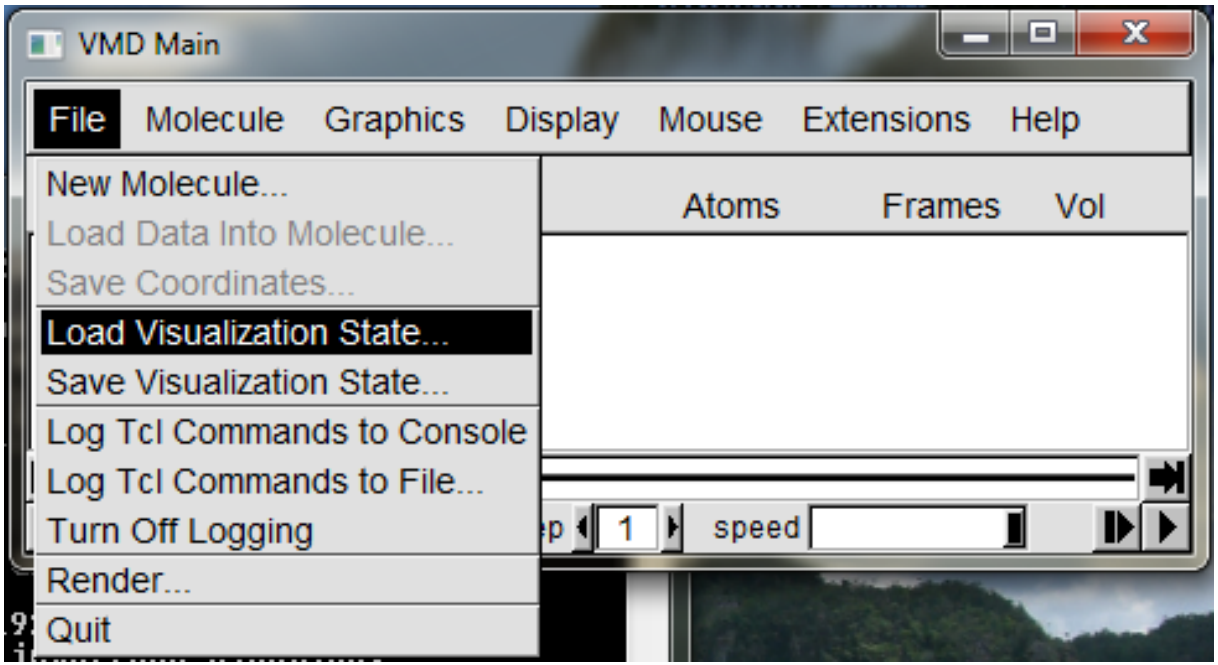
Use vmd to analyse

Basic use of VMD

vmd-tutorial.pdf in the documents

Basic use of VMD: open file

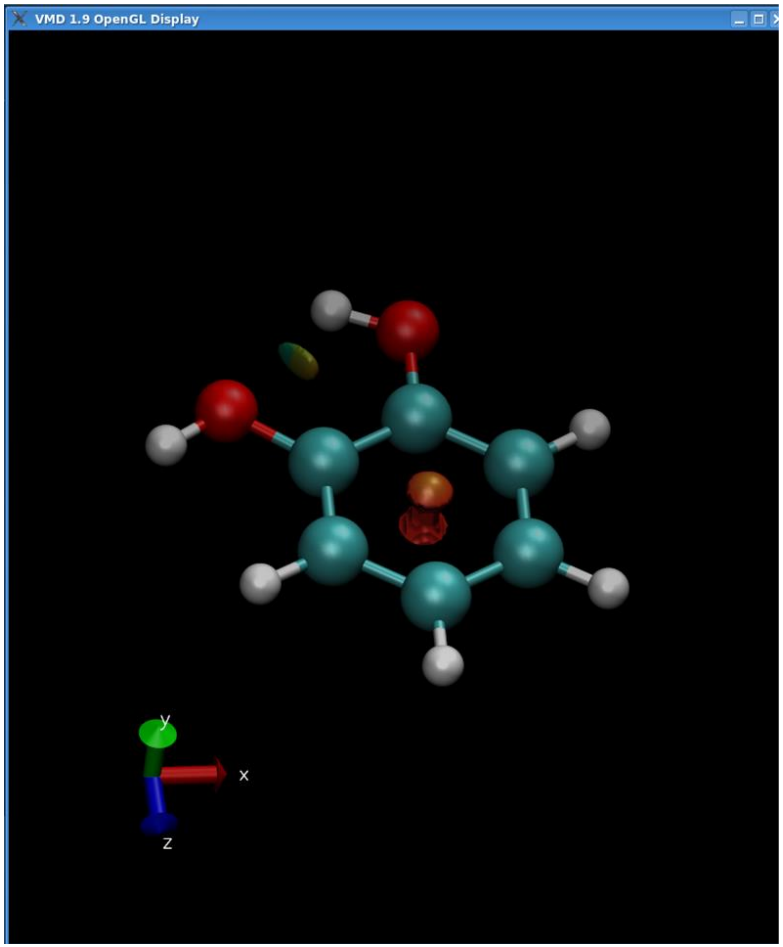
1. Open VMD : vmd
2. File > Load Visualisation State



3. Select NCI.vmd
4. Open

vmd –e NCI.vmd

Basic use of VMD



Basic use of VMD: Graphics > Representation

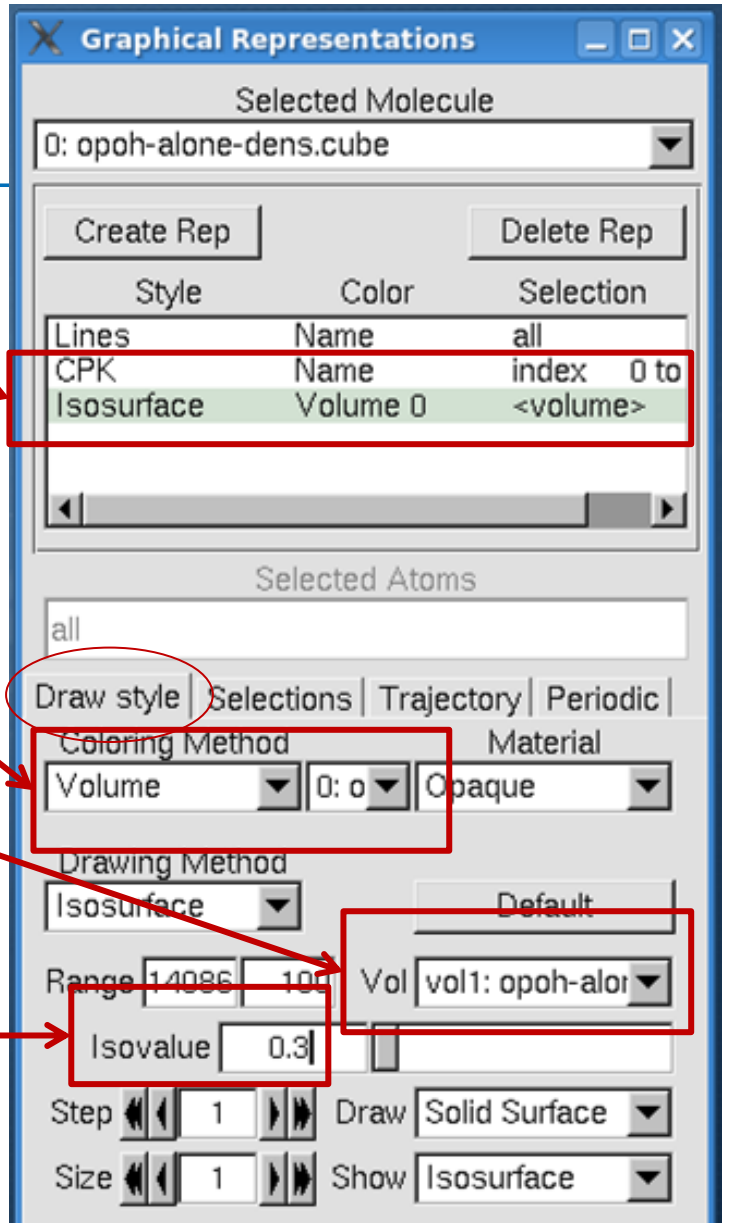
Selected representation:

represent the isosurface

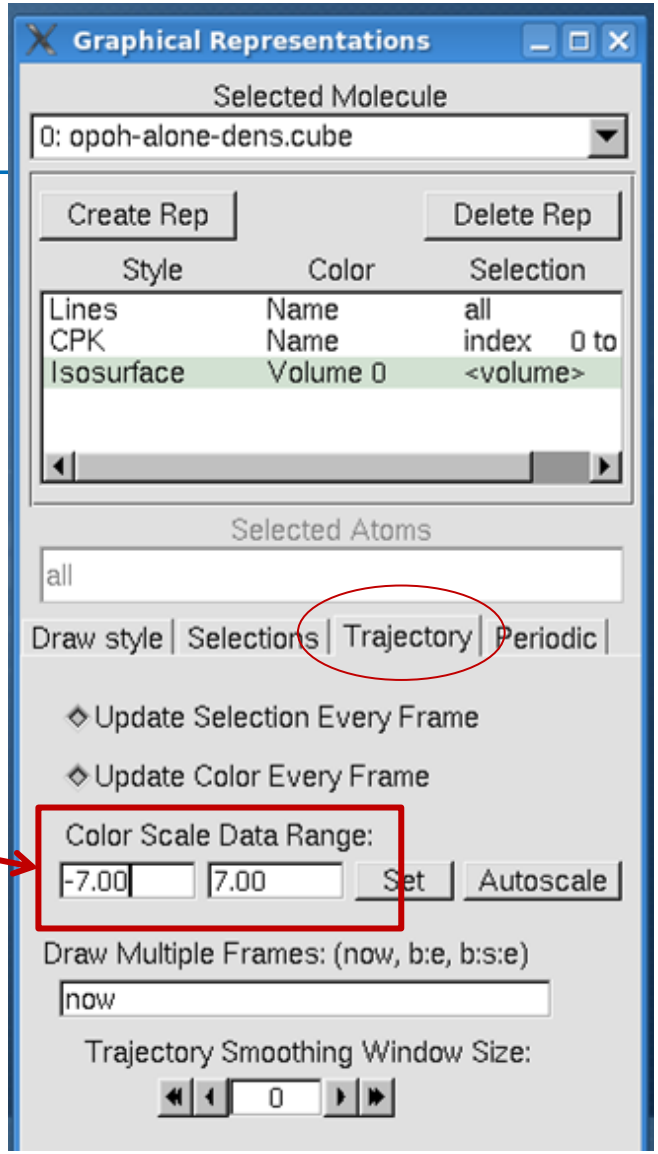
The isosurfaces are colored depending on the cube selected

Cube file whose isosurfaces will be plotted

RDG cutoff to represent the isosurface



Basic use of VMD: Graphics > Representation



Color range

Basic use of VMD: Graphics > Color

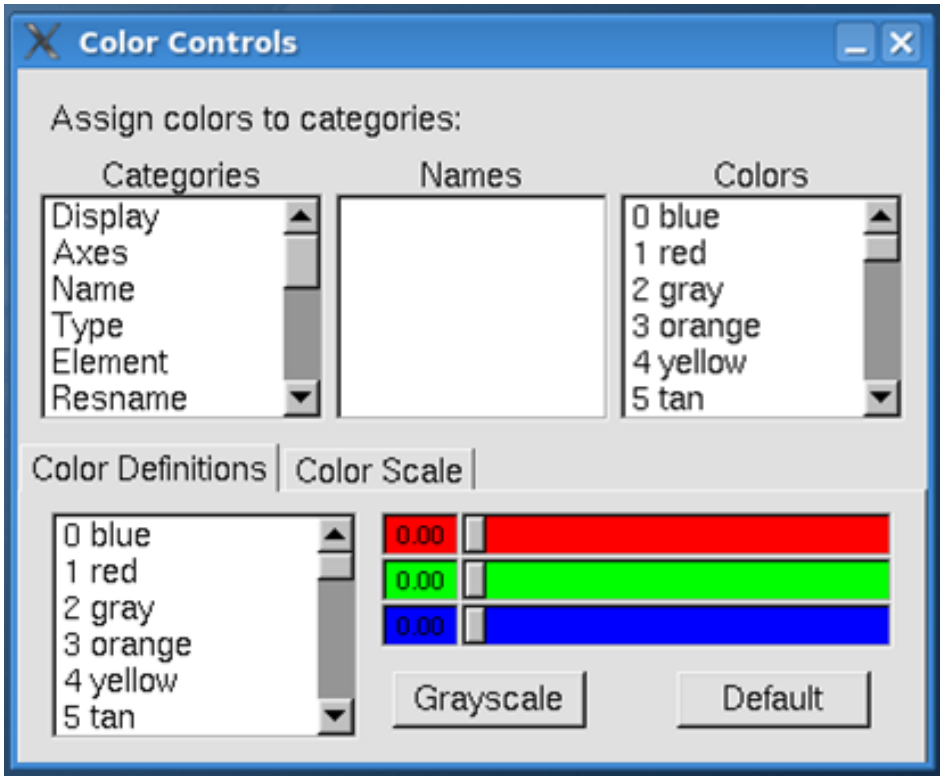
- **Display > Background > White**

→ Set the background white

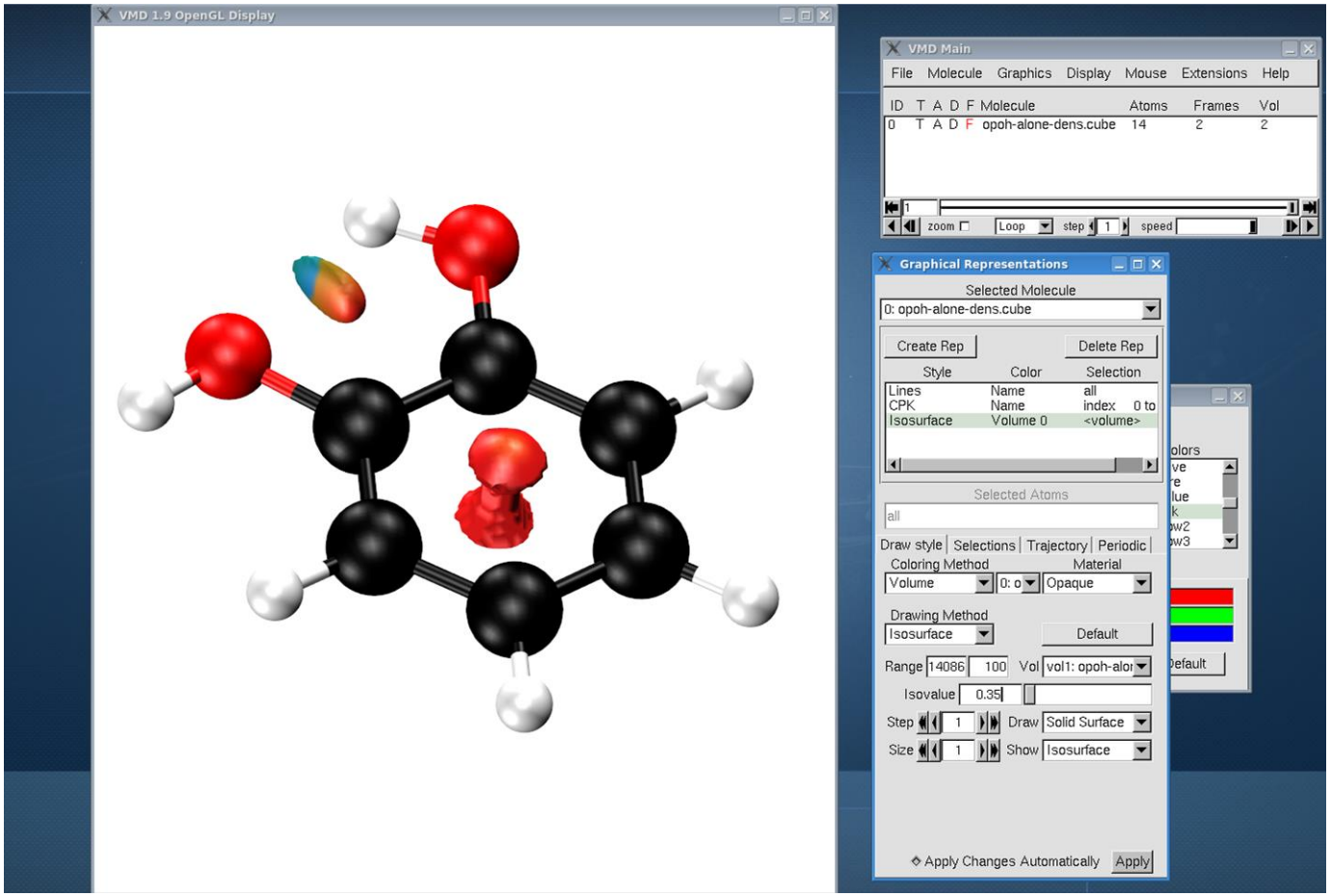
- **Name > C > Black**

→ Set the Carbon atoms black

- **Color Scale** : change the color scale of the interactions (here blue < green < red)

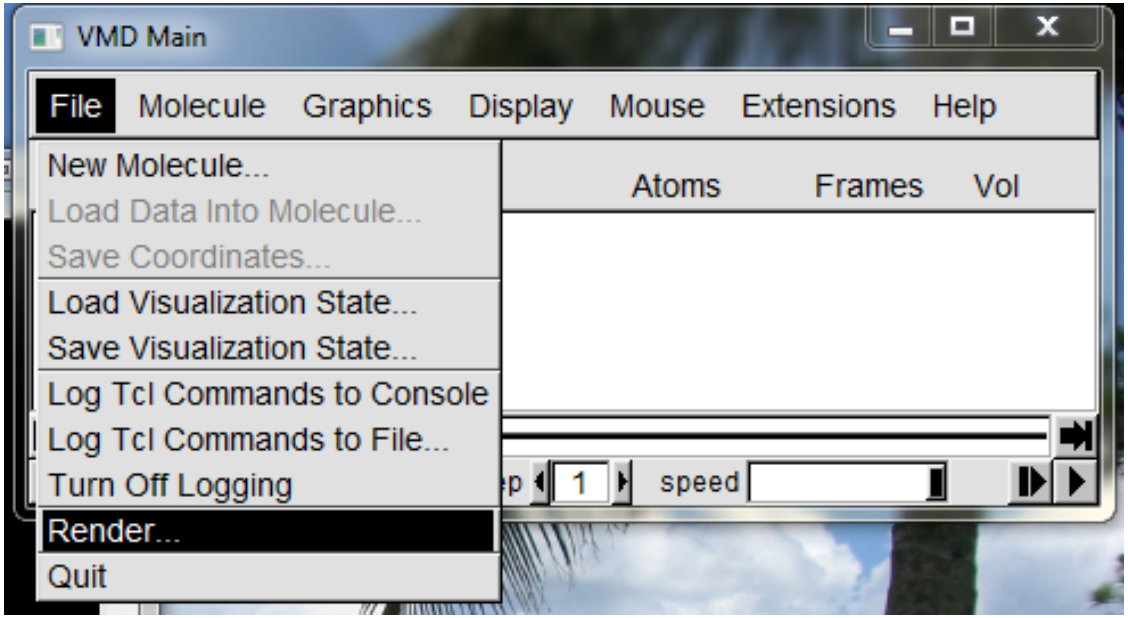


Basic use of VMD



Basic use of VMD: Rendering

Print an image:



Select the rendering mode you prefer (snapshot for exemple)
Give a file name (NCI.tga for exemple)
Click on “Start Rendering”

Exercice 1

1. Run promolecular and wfn NCI analysis for catechol and comment the results. What is unexpected?
2. Associate every spike in the 2D plot to molecular interactions using gnuplot and VMD for both promolecular and wfn.

   What are the differences?

   What is similar?
3. Select a cutoff so that only the cycle tension disappear in VMD but not in the 2D plot for the promolecular case.

   Is it possible to do so for the wfn case?

ELF input file

To run a complete ELF analysis there are 4 different steps using 3 programms:

1. Compute ELF and AIM fonction on every point of a grid

   Use top_grid or grid09

2. Decompose the ELF volume

   Use top_bas or bas09

3. Decompose the AIM volume

   Use top_bas or bas09

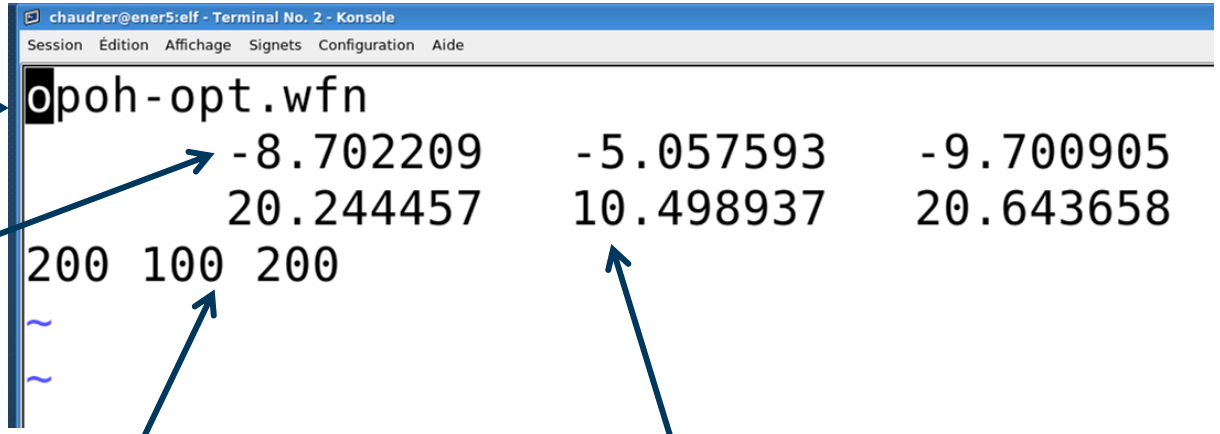
Can be interverted

4. Integrate different properties

   Use top_pop, top_chem or pop09

Here the name of the .wfn and the title within the wfn should be similar

Grid09 input file (can also be done interactively)



Name of the .wfn file to consider

Coordinate of the lowest corner of the grid (given by the programm)

Number of points

Size of each edge of the grid (given by the progamm)

The output are sbf files that can be transformed into cube files :

sbf_to_cube

Bas09 input for ELF (can also be done interactively)

Selection between elf or rho

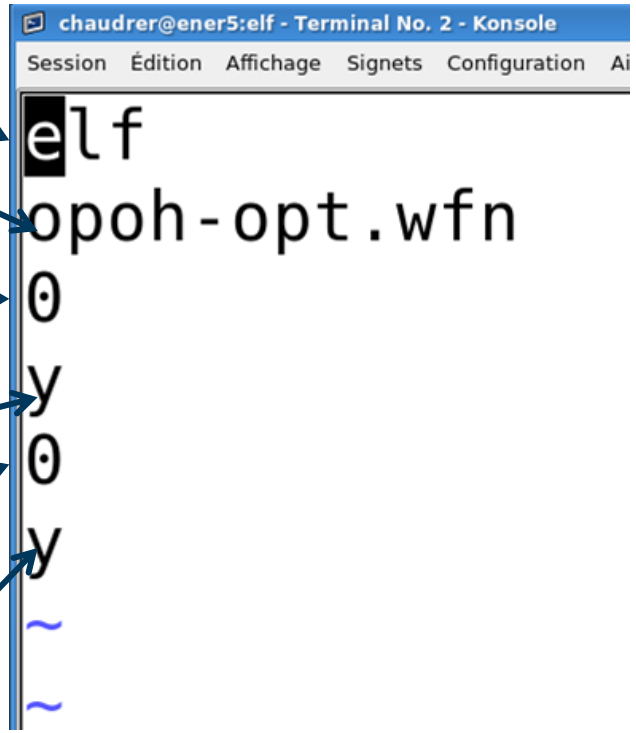
Name of the wfn file (same as precedent)

Accuracy desired
(0=very high, 1=high, 2=medium)

Find external core shell attractors

Search mode
(0=automatic)

Assign grid point to decompose the volume into bassins



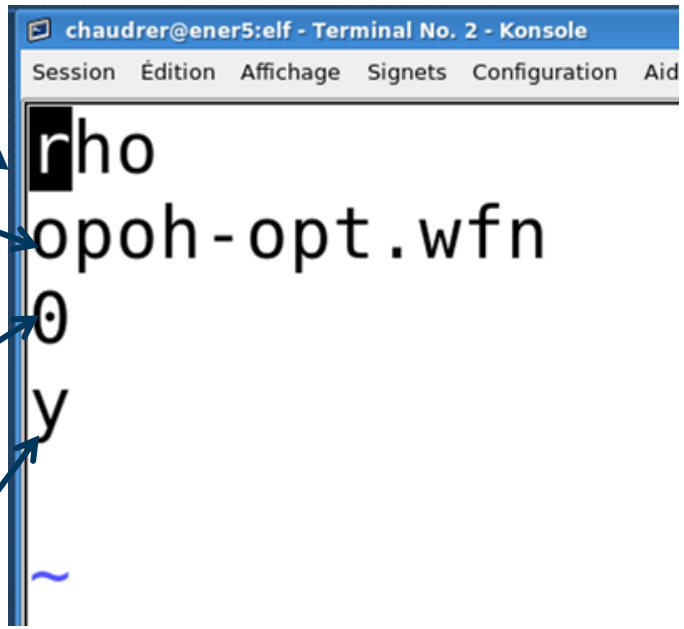
Bas09 input for density

Selection between elf or rho

Name of the wfn file (same as precedent)

Accuracy desired
(0=very high, 1=high, 2=medium)

Assign grid point to decompose
the volume into bassins

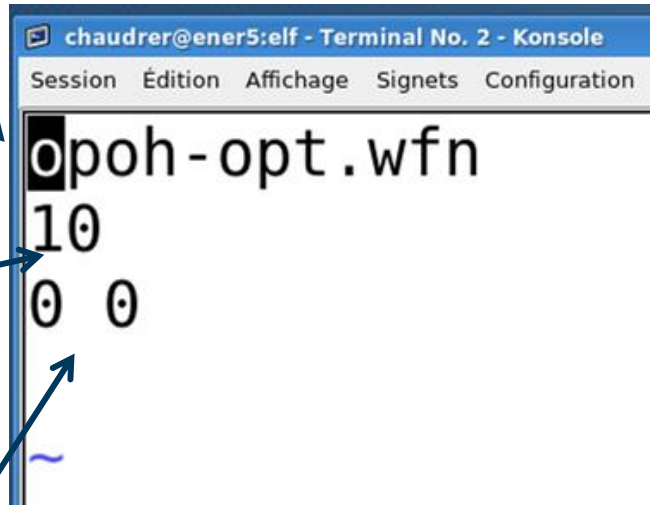


Pop09 input file

Name of the wfn file (same as precedent)

Threshold for integration
(10 = most precise)

Number of ELF and AIM basins considered
(0 0 = all)



Exercice 2

1. Copy phenol files from hydrogen
2. Run ELF analysis of catechol and represent using VMD
3. Represent ELF and NCI analysis on the same vmd windows
4. Compare the lone pairs/O-H bonds (population, volume, shape…) of both hydroxyl groups. How does that compare with NCI results? What would we expect for its interaction with solvent?
5. Comment the nature of the C-O bonds.

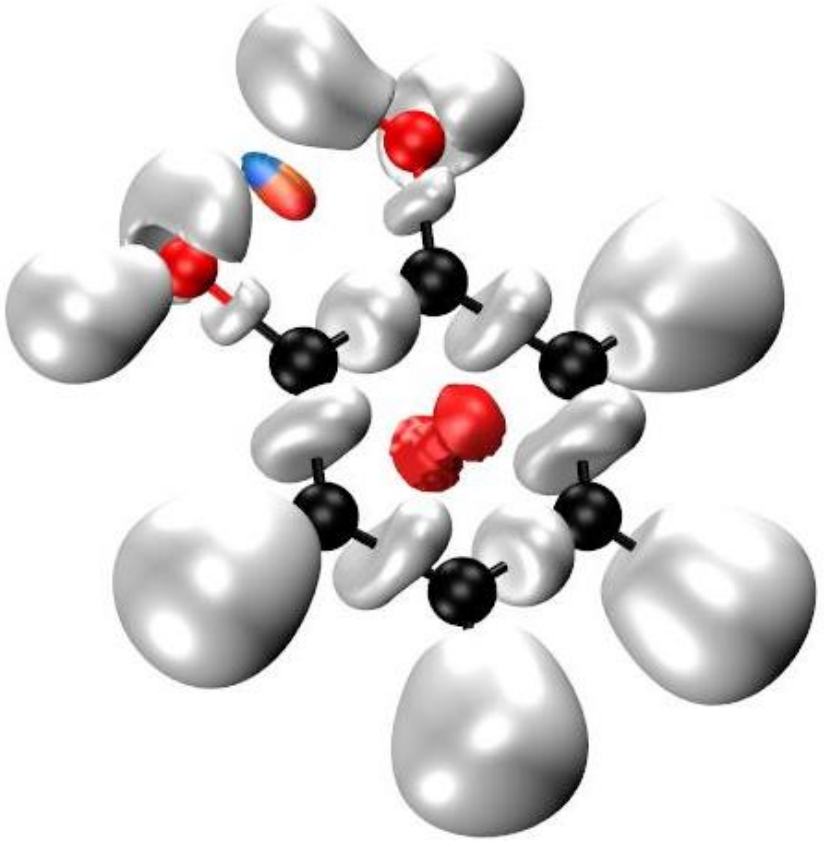
Grid09 output

Grid09 output files are .sbf files

Use **sbf_to_cube**

Visualize cube file with vmd:

File > New Molecule…



Bas09 output for ELF calculations

1. Attractor (ELF or density) x,y,z coordinates
2. Time spent for the calculation
3. Distance of each (valence) attractor from nuclei (ELF only)
4. Angle between attractors (ELF only)

} AIM: only atomic attractors

Pop09 output file

First ELF then AIM

1. Integrated properties for all basins: **volume, population**, pαβ, pαα, pββ, …
2. **Orbital contribution for all basins**
3. **Atomic contribution for all basins** (ELF only)
4. α spin covariance matrix and its correlation coefficients
5. Total covariance matrix and its correlation coefficients

ELF/NCI for reaction mechanism: Running the calculations

- Need the different wfn files from the reaction coordinate
- Run several small scripts to get the calculation automatized
- ATTENTION: For ELF prepare the grid input so that it includes all the atoms of all the structures (get a larger grid)
- Modify the “general” input files
- Run scripts: sh make_elf.sh (do all the ELF calculations)

  sh make_nci.sh (do all the NCI calculations)
- Creation of several new folders to store out, dat, sbf and cube files

ELF/NCI for reaction mechanism: Obtaining the films

- copy result/elf_nci_visualization.pl and result/example-input-vmd-file in cube
- modify input file :
  - NAME name: put the wfn names (NAME-[number].wfn
  - GEOM n1 n2 n3: [number] going from n1 to n2 by step of n3
  - REPRESENTATION [CPK/line/licorice]: VMD representation
  - ELF n: ELF cutoff = n
  - NCI n1 n2 n3: density cutoff = n1, density ranking from n2 to n3
  - set viewpoint…: use vmd to get the desired view of the system
- ./elf_nci_visualization.pl input output vmd-surface-output (vmd-attractor output)
- run vmd to get the tga files: vmd –e vmd-surface-output
- copy, modify and run result/tga2gifanim

Exercice 3

1. Perform the ELF/NCI scripts.

2. Obtain the film with your selected cutoffs, color range and view.

3. Look at the different ELF output. What is the evolution of the populations of the different important basins? Does that correspond to the NCI analysis evolution?

Congrats!

You finished