

Hirshfeld methods and Quantum Crystallography

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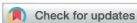
Quantum Crystallography ?

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Quantum crystallography†

Simon Grabowsky,*^a Alessandro Genoni*^{bc} and Hans-Beat Bürgi*^{de}

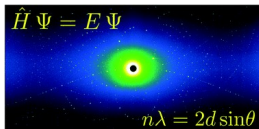
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Approximate wavefunctions can be improved by constraining them to reproduce observations derived from diffraction and scattering experiments. Conversely, charge density models, incorporating electron-density distributions, atomic positions and atomic motion, can be improved by supplementing diffraction experiments with quantum chemically calculated, tailor-made electron densities (form factors). In both cases quantum chemistry and diffraction/scattering experiments are combined into a single, integrated tool. The development of quantum crystallographic research is reviewed. Some results obtained by quantum crystallography illustrate the potential and limitations of this field.

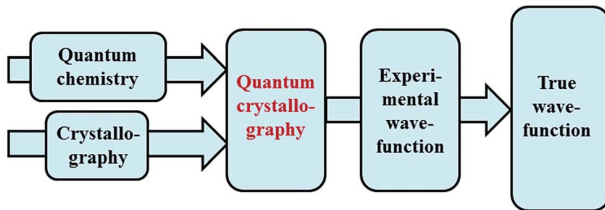


See also: Genoni *et al.*, Quantum Crystallography:

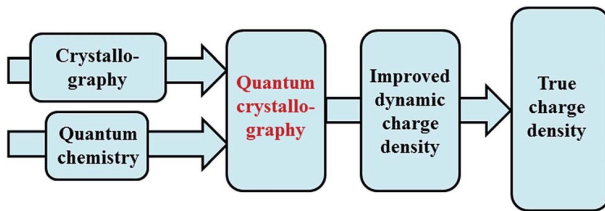
Current developments and future perspectives, *Chem.*

Eur. J., 2018, DOI:10.1002/chem.201705952

QC results and XRD as mutual constraints

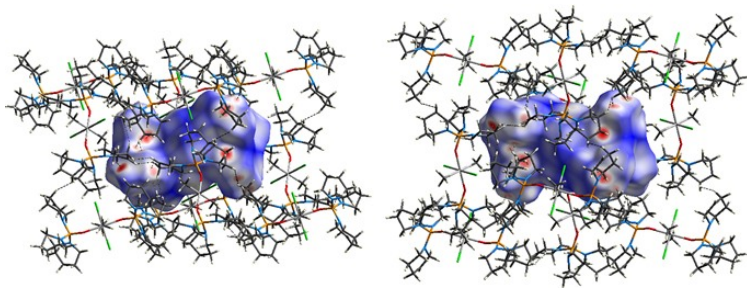


Clinton *et al.* (1969)



Jayatilaka & Dittrich (2008)

Doing more with your diffraction data - I



Tarahhomi & Van der Lee, *in press* (2018)

Doing more with your diffraction data - II

Classical and more advanced structure analyses

- ▶ Classical analysis
 - ▶ atomic positions → *structure*
 - ▶ packing features
 - ▶ interactions by analysis of atom-atom distances
- ▶ Electron density (ground state of the system - Hohenberg-Kohn theorem)
 - ▶ → total energy of the system
 - ▶ → molecular properties such as inter and intramolecular interactions/chemical bonds

$\rho(\mathbf{r})$ is a quantum-mechanical observable!

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From theory to practice

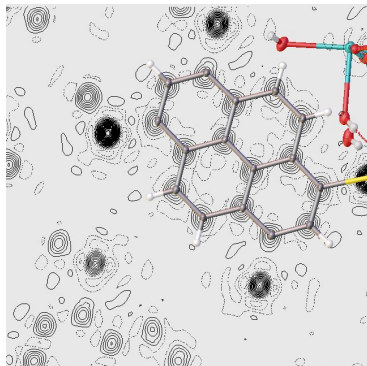
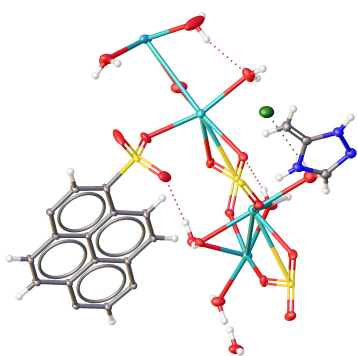
- ▶ Electron density and chemical bonding
- ▶ Experimental and theoretical modelling of electron densities
- ▶ Hirshfeld analysis
 - ▶ Hirshfeld surfaces
 - ▶ Hirshfeld refinement
- ▶ Software
 - ▶ Tonto & CrystalExplorer
 - ▶ Tonto & OLEX2

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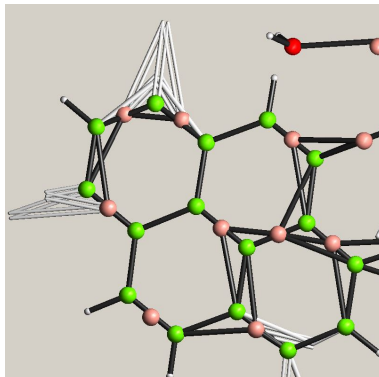
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X-rays interact with electrons



RECIPROCS BAG at Soleil - february 2018 - Zheng, Legrand, Van der Lee *et al.*

Residual density



RECIPROCS BAG at Soleil - february 2018 - Zheng, Legrand, Van der Lee *et al.*

History of electron density and chemical bonding - I

It seems to me that the experimental study of scattered radiation, in particular from light atoms, should get more attention, since along this way it should be possible to determine the arrangement of the electrons in the atoms

P. Debye - Zerstreung von Röntgenstrahlen: Ann. Phys **351**, 809-823 (1915)

An electron may form a part of the shell of two different atoms and cannot be said to belong to either one exclusively

G. N. Lewis - The atoms and the molecule : J. Am. Chem. Soc. **38**, 762-785 (1916)

History of electron density and chemical bonding - II

Pauling (1939) - On the nature of the chemical bond → application to the elucidation of complex substances

Bader (1965 - 1990) - Quantum theory of atoms in molecules → chemical bonding based on the topology of electron density distribution

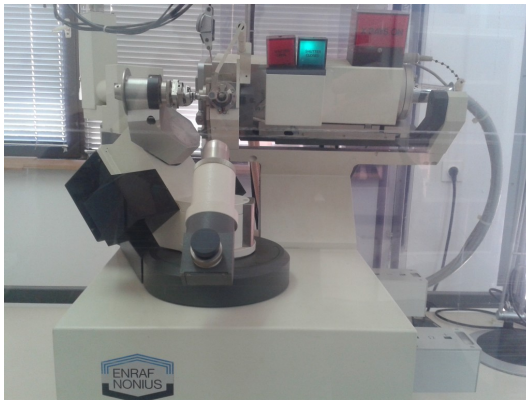
Stewart (1976), Hansen & Coppens (1978) - Extension of refinement techniques to include effects of chemical bonding

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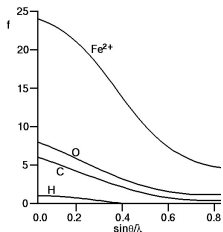
Experimental determination of electron density



The spherical and the aspherical model

$$F(hkl) = \sum_j f_j \exp[2\pi i(hx_j + y_j + z_j)]$$

$$f_j(\mathbf{q}, E) = \int \rho_j(\mathbf{r}) \exp[i\mathbf{q} \cdot \mathbf{r}] d^3r$$



spherical electron distribution →

$$f_j(q, E) = \int \rho_j(r) \exp[iq \cdot r] d^3r$$

IAM: Independent Atom Model

Calculation of spherical atomic scattering factors

Journal of Research of the National Bureau of Standards

Vol. 55, No. 1, July 1955

Research Paper 2604

Data on the Atomic Form Factor: Computation and Survey

Ann T. Nelms and Irwin Oppenheim

This paper presents the results of calculations of atomic form factors, based on tables of electron charge distributions computed from Hartree wave functions, for a wide range of atomic numbers. Computations of the form factors for five elements—carbon, oxygen, iron, arsenic, and mercury—are presented and a method of interpolation for other atoms is indicated. A survey of previous results is given and the relativistic theory of Rayleigh scattering is reviewed. Comparisons of the present results with previous computations and with some sparse experimental data are made.

IAM uses quantum-mechanically calculated atomic scattering factors (*ex-situ*) ··· as does Hirshfeld Atomic Refinement (*in-situ*).

Treatment of the aspherical atomic scattering factors in the multipole model

$$F(\mathbf{q}) = \sum_i^{N_{\text{atoms}}} \sum_j^{N_{\text{sym}}} \left[P_{i,\text{core}} f_{i,\text{core}}(\mathbf{q}) + P_{i,\text{val}} f_{i,\text{val}}(\mathbf{q}, \kappa) + \sum_l^4 \Phi_{il}(\mathbf{q}, \kappa'_l) \sum_{m=-l}^l P_{ilm} Y_{lm}^i(\mathbf{q}/|\mathbf{q}|) \right] e^{i\mathbf{q}\cdot\mathbf{r}_{ij}} \cdot T_i(\mathbf{q})$$

Three contributions: core - spherical valence - aspherical valence electrons; $f_{i,\text{core}}$ and $f_{i,\text{val}}$ are derived from the classical spherical atomic scattering factors $f(q, E)$

To be refined: population parameters P , expansion-contraction parameters κ and κ'

In between the IAM and the multipole model

The different single-crystal refinement methods

- ▶ Independent atom model refinements (SHELXL, CRYSTALS, JANA)
- ▶ Intermediate approaches
 - ▶ Maximum Entropy methods (BAYMEM)
 - ▶ Database transfer (INVARIOM, MOPRO)
 - ▶ Hirshfeld refinement (TONTO)
- ▶ Multipole refinements (XD, MOPRO, JANA)

Quantum-mechanical determination of electron density

Solve the Schrödinger equation

$$\hat{H}\psi = E\psi$$

Two approaches

- ▶ Wave function based *ab initio* → ρ is the square of the absolute value of the wave function
- ▶ Electron density based → density functional treatment

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The Hirshfeld surface

Where are the interactions between molecules located in space?
How is the surface of a molecule defined?

→ Hirshfeld partitioning:

$$w(\mathbf{r}) = \frac{\sum_{i=1}^{N_{\text{molecule}}} \rho_i(\mathbf{r})}{\sum_{i=1}^{N_{\text{crystal}}} \rho_i(\mathbf{r})} = \frac{\rho_{\text{promolecule}}(\mathbf{r})}{\rho_{\text{procrystal}}(\mathbf{r})}$$

where $\rho_i(\mathbf{r})$ is the spherically-averaged atomic electron density function.

$$\text{Hirshfeld surface} \rightarrow w(\mathbf{r}) = 1/2$$

Intermezzo

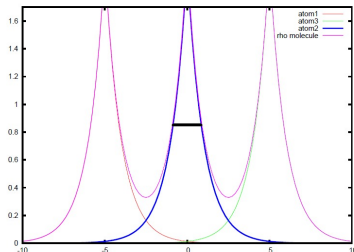
Hirshfeld did not invent the Hirshfeld surface, but he did invent the 'stockholder partitioning scheme' for an atom in a molecule; Spackman generalized the concept to a molecule in a crystal and named it Hirshfeld surface.

The Hirshfeld atom

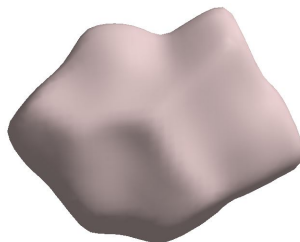
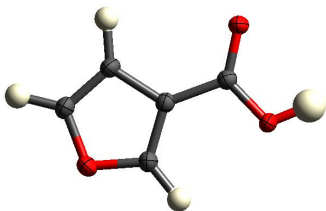
$$w_i(\mathbf{r}) = \frac{\rho_i(\mathbf{r})}{\sum_{i=1}^{N_{\text{molecule}}} \rho_i(\mathbf{r})} = \frac{\rho_i(\mathbf{r})}{\rho_{\text{promolecule}}}$$

where $\rho_i(\mathbf{r})$ is the spherically-averaged atomic electron density function. $w_i(\mathbf{r})$ defines the relative share of atom i to the total promolecule density at \mathbf{r} .

Hirshfeld atom $\rightarrow w_2(\mathbf{r}) = 1/2$

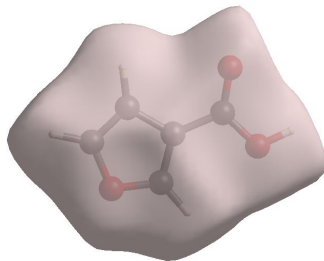


The Hirshfeld surface visualized



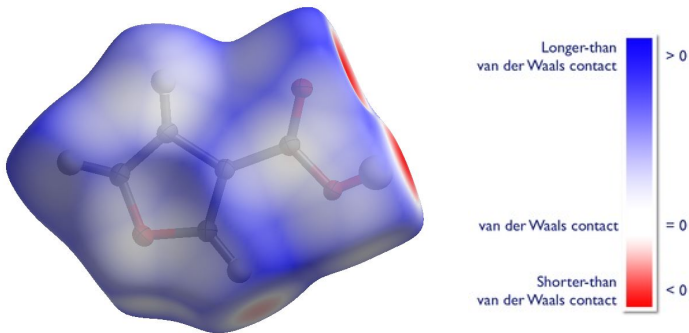
Not very interesting

The Hirshfeld surface visualized - transparency



Nice but mapping a property on the surface is more interesting!

Mapping properties on the Hirshfeld surface



Mapped with the d_{norm} property

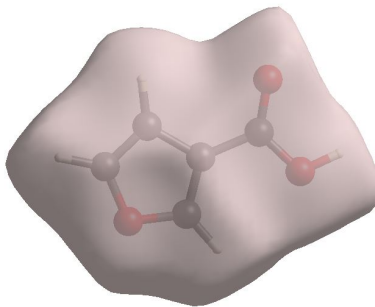
d_i , d_e and d_{norm}

Definitions

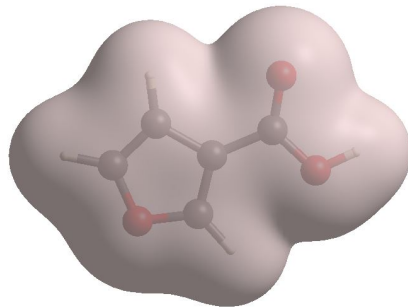
- ▶ d_i : distance from the surface to the nearest nucleus internal to the surface
- ▶ d_e : distance from the surface to the nearest nucleus external to the surface
- ▶ d_{norm} : normalized contact distance

$$d_{\text{norm}} = \frac{d_i - r_i^{\text{vdW}}}{r_i^{\text{vdW}}} + \frac{d_e - r_e^{\text{vdW}}}{r_e^{\text{vdW}}}$$

Hirshfeld surface versus Promolecule surface



isosurface at 0.5

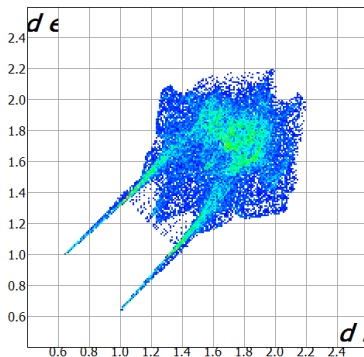


isosurface at 0.002 a.u.

Promolecule surface is rather a surface in the gaz state

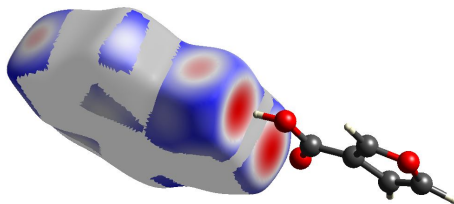
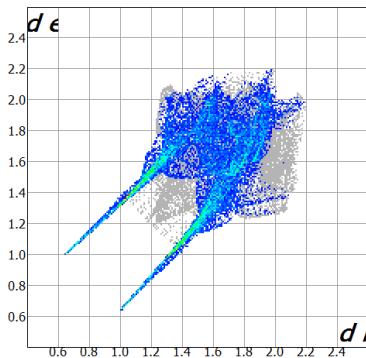
Fingerprint plots

Each (d_i, d_e) pair on the Hirshfeld surface is taken and plotted in a 2D plot, where the color indicates the frequency (number) of (d_i, d_e) pairs found: white = no pairs; increasing pair frequency from blue to red.



isosurface at 0.5

Decomposed fingerprint plots



Contribution of O...H interactions: 46.5 %.

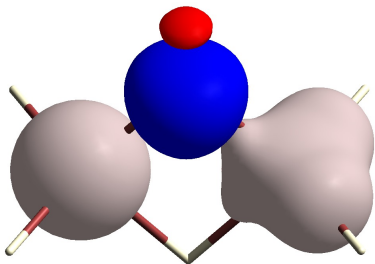
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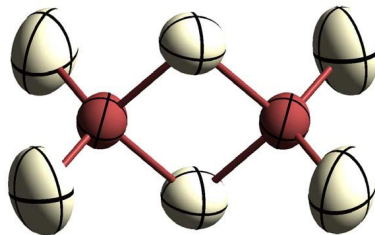
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Hirshfeld refinements

Using tailor-made aspherical atomic electron densities, which are extracted from a crystal-field embedded quantum-chemical electron density using Hirshfeld's scheme



Diborane (B_2H_6); left - IAM
B-atom; right - Hirshfeld B-atom;
blue and red - deformation
Hirshfeld density for bridging H



Result of HAR: 50% probability
level

Hirshfeld Atomic Refinement - I

Step 1 - creating initial density - ED cycle

1. calculate QM initial density from IAM positions
2. divide QM density in Hirshfeld atoms
3. calculate charges and moments of these Hirshfeld atoms
4. calculate electric crystal field
5. calculate new QM density
6. go to 2 until convergence in molecular energy

Hirshfeld Atomic Refinement - II

Step 2 - structure refinement - HAR cycle

1. Fourier transform the Hirshfeld atoms in order to obtain non-spherical atomic scattering factors
2. perform a structure refinement
3. go to 2 until convergence

Then alternate ED cycle and HAR cycle until complete convergence

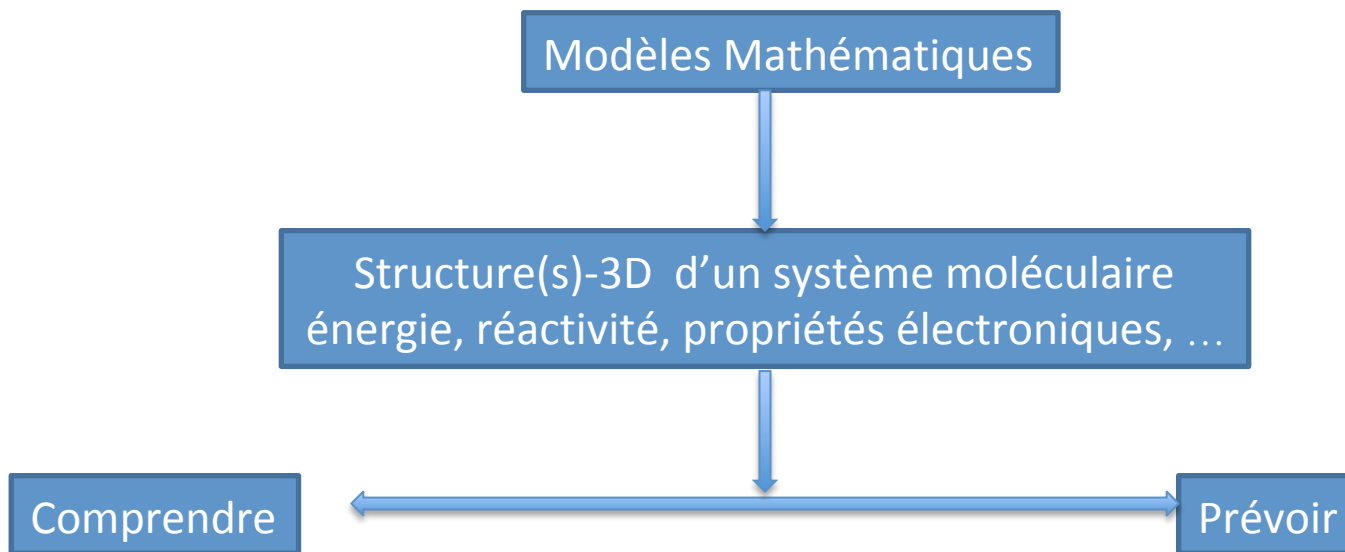
Note: the spherical atomic scattering factors used in IAM refinements have been obtained by theoretical calculations ... Thus 'Hirshfeld' refinement is a natural extension of 'IAM' refinement.

Quantum-mechanical electron density calculations

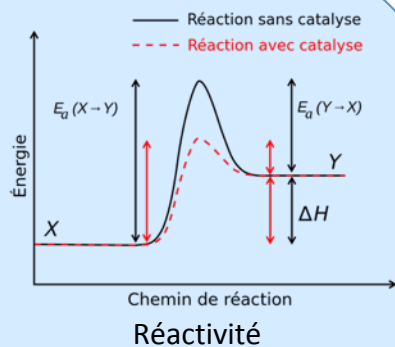
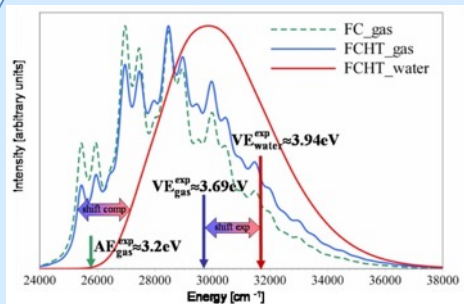
Details

- ▶ Hartree-Fock (rhf) and Kohn-Sham (rks/BLYP) density functional theory
- ▶ wavefunction is calculated self-consistently (SCF)
- ▶ possibility of inclusion of cluster of charges and dipoles during the SCF calculation in order to account for the crystal environment
- ▶ def2-SVP or cc-pVDZ Gaussian basis sets perform well, no need for more elaborate sets

Modélisation moléculaire?



Méthodes Quantiques

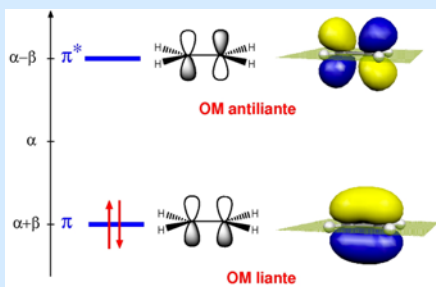
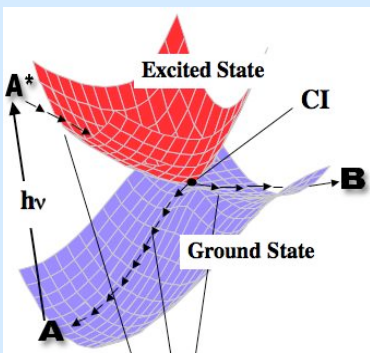


Spectroscopie

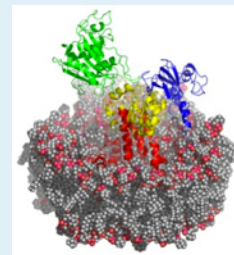
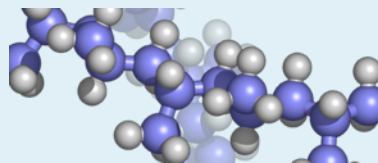
Photochimie

Méthodes Semi-empiriques

Méthodes *ab initio*
et DFT



Méthodes Classiques



Propriétés
Structurales

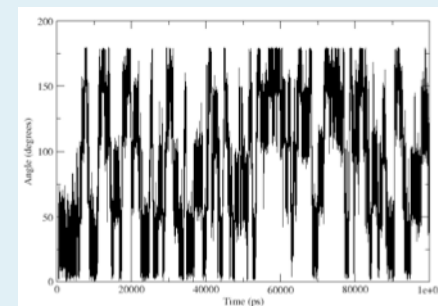
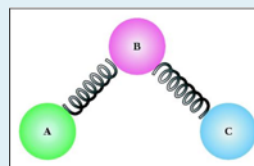
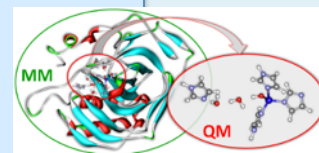
Polymères
Macromolécules
Matériaux

Biochimie
Biologie

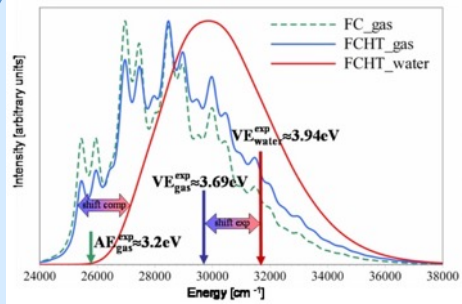
Mesoscale

Mécanique
Moléculaire / Dynamique
Moléculaire

QM/MM

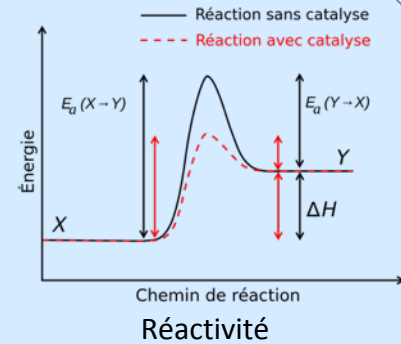


Quantum methods



Photochimie

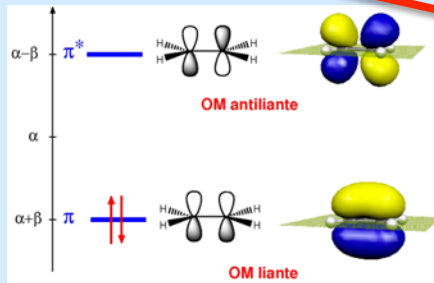
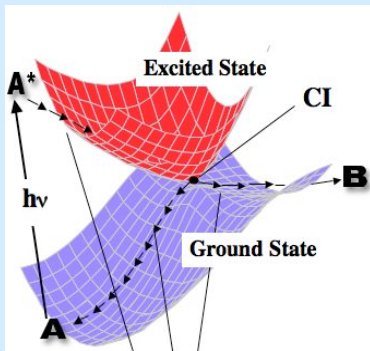
Spectroscopie



Méthodes Semi-empiriques

Méthodes *ab initio*
et DFT

Méthodes
Multiréférences



$$\hat{H}\Psi = E\Psi$$

Déterminant simple

$$|\Psi_e(n)\rangle = \frac{1}{\sqrt{n!}} |\varphi_1 \varphi_2 \varphi_3 \dots \varphi_n\rangle$$

Electrons de valence, solvant, ...



AM1
PM3
...

Déterminant simple

$$|\Psi_e(n)\rangle = \frac{1}{\sqrt{n!}} |\varphi_1 \varphi_2 \varphi_3 \dots \varphi_n\rangle$$

Tous les électrons, solvant, ...



6-31G(d)
6-311++(3df,3pd)
B3LYP
M08
...

Déterminants multiples

$$\Psi_e = C_0 \Psi_0 + \sum_{ra} C_a^r \Psi_a^r + \sum_{a<b} \sum_{r<s} C_{ab}^{rs} \Psi_{ab}^{rs} + \dots$$

Tous les électrons, (solvant), ...



CI
CASSCF
CC
...

L'équation de Schrödinger

$$\hat{H}\Psi = E\Psi$$

Associe la fonction d'onde ψ à l'énergie E du système par l'opérateur Hamiltonien \mathbf{H}

- Fonction d'onde = orbitales atomiques (moléculaires), mouvement des électrons dans le champs d'un ou plusieurs protons constituant les noyaux.
- $\hat{H} = \hat{T}_N + \hat{T}_e + \hat{V}_{eN} + \hat{V}_{ee} + \hat{V}_{NN} + V_{ext}$ T termes cinétiques, V termes coulombiens
- solution exacte seulement pour l'atome d'hydrogène !

$$\left[\frac{-\hbar^2}{2\pi m_e} \left(\frac{\partial^2}{\partial x_e^2} + \frac{\partial^2}{\partial y_e^2} + \frac{\partial^2}{\partial z_e^2} \right) - \frac{\hbar^2}{2M_N} \left(\frac{\partial^2}{\partial x_N^2} + \frac{\partial^2}{\partial y_N^2} + \frac{\partial^2}{\partial z_N^2} \right) \right] \varphi(x_e, y_e, z_e, x_N, y_N, z_N) + V(x_e, y_e, z_e, x_N, y_N, z_N) = E \cdot \varphi(x_e, y_e, z_e, x_N, y_N, z_N)$$



Approximations

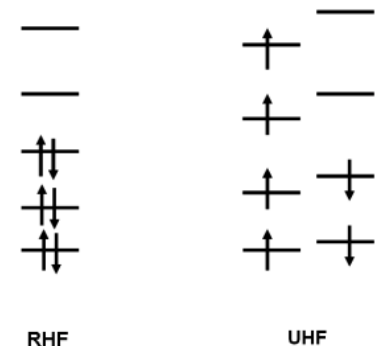
L'équation de Schrödinger

$$\hat{H}\Psi = E\Psi$$

- $\hat{H} = \hat{T}_N + \hat{T}_e + \hat{V}_{eN} + \hat{V}_{ee} + \hat{V}_{NN} + \cancel{V_{ext}}$
- Approximation de Born-Oppenheimer : traite uniquement le cas des électrons en considérant les noyaux fixes dans l'espace (justifié par la différence de masse 1880 plus faible)
 - ☞ $H = T_e + V_{eN} + V_{ee} + V_{NN}$ et considérant V_{NN} constant (noyaux fixes), $H = H_e + V_{NN}$
 - ☞ et corollaire : la fonction d'onde totale peut-être approchée par le produit des solutions mono-électroniques : $\psi_{totale} = \psi(1) \cdot \psi(2) \dots \psi(n)$
- À partir de là plusieurs méthodes pour calculer l'énergie du système

Méthodes ab initio

- Principe d'exclusion de Pauli : 2 électrons ne peuvent pas se trouver simultanément dans le même état quantique -> introduction d'une fonction pour les propriétés de spin : χ = spinorbitale
 - La fonction d'onde ψ s'écrit sous la forme d'un déterminant de Slater $\Psi = 1/\sqrt{n!} \det |\chi_1 \chi_2 \dots \chi_n|$
 - Le nouvel opérateur prenant en compte ces spinorbitales = opérateur de Fock et équations d'Hartree-Fock
 - Méthodes ab initio (ou HF, **Hartree-Fock**) : toutes les intégrales sont calculées
- Pour les systèmes à couche fermée, simplification RHF (**Restricted Hartree-Fock**) : contributions identiques des 2 électrons de même couche, de spins opposés
- Radicaux : UHF (Unrestricted Hartree-Fock)
- Problème méthode HF : corrélation électronique pas prise en compte
 - méthodes post-HF : CI, CASSCF...



Méthodes DFT

- Autre méthode moins couteuse pour prendre en compte effets de corrélations électroniques : la DFT
- Thomas et Fermi, Hohenberg et Kohn : dans son état fondamental l'énergie d'un système est complètement déterminée par une fonctionnelle de sa densité électronique $\rho(r)$
 - ☞ (Une) variable principale : gain sur le temps de calcul
 - ☞ Problème : forme mathématique de la fonctionnelle inconnue !
- Développement de méthodes par **Kohn et Sham**

Méthodes semi-empiriques

- Hartree-Fock simplifié : e^- internes négligés, e^- de valence représentés par une base minimale, paramètres empiriques pour certaines intégrales...
- Méthodes AM1, PM3, SAM1... non utilisées par HART

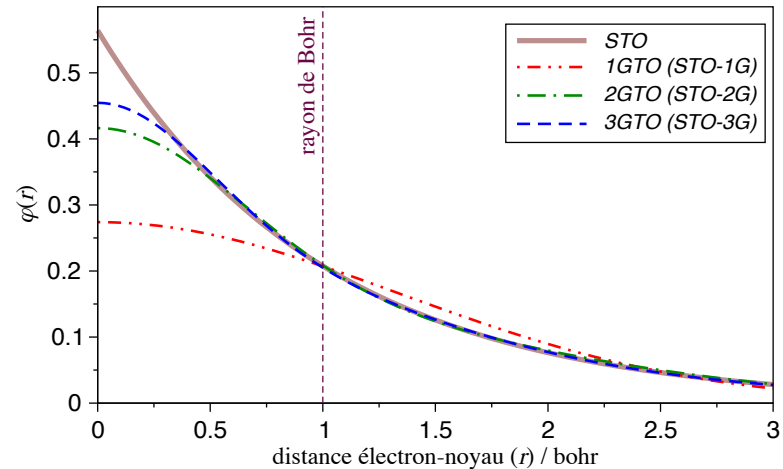
Fonction d'onde, orbitales atomiques et moléculaires

Fonctions de base, ou jeu de bases (basis set)

Orbitales moléculaires = combinaison linéaire des orbitales atomiques

Orbitales atomiques

- Orbitales de type Slater (Slater-type Orbital : **STO**)
 - précises à $r \approx 0$ ou très loin
 - intégrales bi-électroniques à 3-4 centres analytiquement impossible
- Orbitales Gaussiennes (Gaussian-type Orbital : GTO)
 - intégrations plus facile
 - maniement plus simple (produit de gaussienne = gaussienne)
 - moins précises à $r \approx 0$
 - majoritairement utilisées



Combinaison de plusieurs primitives = représentation des orbitales atomiques : fonctions de base

Exemples

STO-3G : 3 primitives gaussiennes sont utilisées pour décrire une orbitale de type Slater

3-21G, 4-31G, 6-311G... : bases à valence splittée

- ex. 4-311G : 4 primitives gaussiennes pour les e^- de cœur, 3 orbitales de valence (3, 1, 1 : triple zéta) représentées respectivement par 3, 1 et 1 gaussiennes

cc-pVDZ, cc-pVTZ... : cc-p = correlation-consistent polarized, V = valence orbitals only, D T Q... = valences splittées double, triple, quadruple zéta

def2SVP, def2TZVP, def2TZPP : nouvelle définition (def2) des bases d'Ahlich et al., valence splittée (simple, double... n zéta), polarisation (P) mais pas diffusion

Parfois ajouts de fonctions nécessaires (si non intégrées à la fonction de base)

- fonction de polarisation (modification de la densité électronique autour du noyau)
notée par *, ex. 6-31G*

- fonction diffuse (modification de la densité électronique à longue distance du noyau, ex. atomes chargés ou radicalaires), notée +, ex. 6-31+G

Attention : plus les fonctions de base sont complexes plus le calcul est long : en Hartree-Fock le temps de calcul est proportionnel à N^4 , N étant le nombre de primitives présentes dans la base

| Basis Set | Applies to | Polarization Functions | Diffuse Functions |
|-----------------|-----------------------|------------------------|---|
| 3-21G | H-Xe | | + |
| 6-21G | H-Cl | * or ** | |
| 4-31G | H-Ne | * or ** | |
| 6-31G | H-Kr | through (3df,3pd) | +,++ |
| 6-311G | H-Kr | through (3df,3pd) | +,++ |
| D95 | H-Cl except Na and Mg | through (3df,3pd) | +,++ |
| D95V | H-Ne | (d) or (d,p) | +,++ |
| SHC | H-Cl | * | |
| CEP-4G | H-Rn | * (Li-Ar only) | |
| CEP-31G | H-Rn | * (Li-Ar only) | |
| CEP-121G | H-Rn | * (Li-Ar only) | |
| LanL2MB | H-La, Hf-Bi | | |
| LanL2DZ | H, Li-La, Hf-Bi | | |
| SDD, SDDAll | all but Fr and Ra | | |
| cc-pVDZ | H-Ar, Ca-Kr | included in definition | added via AUG- prefix (H-Ar, Sc-Kr) |
| cc-pVTZ | H-Ar, Ca-Kr | included in definition | added via AUG- prefix (H-Ar, Sc-Kr) |
| cc-pVQZ | H-Ar, Ca-Kr | included in definition | added via AUG- prefix(H-Ar, Sc-Kr) |
| cc-pV5Z | H-Ar, Ca-Kr | included in definition | added via AUG- prefix (H-Na, Al-Ar Sc-Kr) |
| cc-pV6Z | H, B-Ne | included in definition | added via AUG- prefix (H, B-O) |
| SV | H-Kr | | |
| SVP | H-Kr | included in definition | |
| TZV and TZVP | H-Kr | included in definition | |
| QZVP and Def2 | H-La, Hf-Rn | included in definition | |
| Midix | H, C-F, S-Cl, I, Br | included in definition | |
| EPR-II, EPR-III | H, B, C, N, O, F | included in definition | |
| UGBS | H-Lr | UGBS(1,2,3)P | +,++,2+,2++ |
| MTSmall | H-Ar | | |
| DGDZVP | H-Xe | | |
| DGDZVP2 | H-F, Al-Ar, Sc-Zn | | |
| DGTZVP | H, C-F, Al-Ar | | |
| CBSB7 | H-Kr | included in definition | +,++ |

Mais en pratique métaux de transition mal (ou non) traités par HART, idem éléments lourds (Br = erreur)

STO-3G and 3-21G accept a * suffix, but this does not actually add any polarization functions.

Serveur Lame HP Proliant BL460c : 388 cœurs de calcul, procs. Intel Xeon

Centre Régional de Compétences en Modélisation Moléculaire, Aix-Marseille université

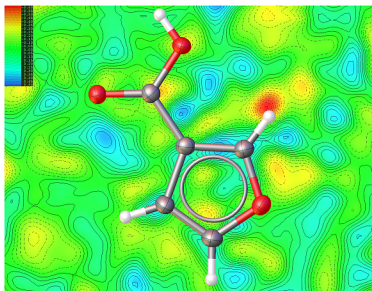


Ecryst377 (C5 H4 O3)

| RHF | Base | 1 processeur | 4 processeurs | 8 processeurs | 16 processeurs | diffusion (n proc) | (cluster et nbr. proc) |
|-----|------------|--------------|---------------|---------------|----------------|--------------------|--------------------------|
| | STO-3G | 2,6 | | | | | |
| | cc-pVDZ | 8,6 | | | | | |
| | cc-pVTZ | 50 | 13 | | | | |
| | cc-pVQZ | >6h | | | 36,4 | | |
| | def2-SVP | 5 | | | | | |
| | def2-TZVP | 32 | 10,6 | | | | |
| | def2-TZVPP | 42,5 | | | | | |
| RKS | cc-pVTZ | | | 29 | | | 40,5 (cluster 8, 8 proc) |
| | def2-SVP | | | 5,4 | | | |
| | def2-TZVP | | | 20,3 | | | |

Temps processeur (min.)

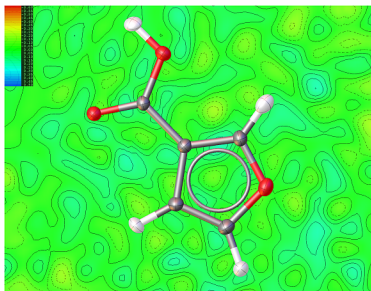
Example - ecryst377



IAM Refinement

$$R_1 = 0.0409; \Delta\rho_{\min} = -0.611;$$

$$\Delta\rho_{\max} = 0.496$$



Hirshfeld Atomic Refinement

$$R_1 = 0.0343; \Delta\rho_{\min} = -0.282;$$

$$\Delta\rho_{\max} = 0.239$$

Isocontour levels from -0.6 to $0.5 \text{ e}\text{\AA}^{-3}$ in steps of $0.05 \text{ e}\text{\AA}^{-3}$ (red negative; blue positive)

HAR QM calculations: *Hartree-Fock*; spinorbital: *restricted*; basis set: *def2-SVP*

Experimental data resolution (according to Dauter - *Acta Cryst.* **D55**, 1703-1717, 1999): 0.77 \AA

Benefits of Hirshfeld Atomic Refinement

- ▶ free refinement of hydrogen positions possible → hydrogens at neutron positions
- ▶ free refinement of hydrogen isotropic or anisotropic ADP's possible
- ▶ but (ecryst377):
 - ▶ classical refinement: $N_{\text{par}} = 78$; $N_{\text{ref}}(I > 2\sigma(I)) = 836$
 - ▶ Hirshfeld refinement: $N_{\text{par}} = 109$; $N_{\text{ref}}(I > 2\sigma(I)) = 836$
- ▶ ADP's of all atoms become 'neutron' like
- ▶ modeling of density 'inside' chemical bonds

Validation of Hirshfeld Atomic Refinement results

Criteria

- ▶ do not use CheckCif !
- ▶ are R -factors lower?
- ▶ is there less residual electron density?
- ▶ are hydrogens at neutron positions?
- ▶ hydrogen ADP's: Hirshfeld rigid body test
 - ▶ *the relative vibrational motion of a pair of bonded atoms has an effectively vanishing component in the direction of the bond*
 - ▶ $|z_{AB}^2(A) - z_{BA}^2(B)| < 5\sigma$
 - ▶ use platon: calc TMA 40 12 HINCL

PLATON listing file

Rigid-Body Model Libration Corrections for Bond Distances and "Hirshfeld Rigid-Bond" Test (Acta Cryst., 1976, A32, 239-244)

| Bond | | Bond Distance | Components of the Correction | | | | Vibration Along the Interatomic Bond | | | Angle with Lib. Axes | | | |
|---------|---------|---------------|------------------------------|---------|---------|---------|--------------------------------------|-----------|------------|----------------------|--------|--------|--------|
| Atom(I) | Atom(J) | Obsd | Calcd | Del(L) | Del(M) | Del(N) | I to J | J to I | Difference | Sqrt(Diff) | L(1) | L(2) | L(3) |
| O(1) | - C(1) | 1.3138(14) | 1.3201 | -0.0017 | 0.0061 | 0.0005 | 0.0131(5) | 0.0140(7) | 0.0009(9) | 0.0300 | 108.52 | 31.58 | 65.40 |
| O(1) | - H(1) | 1.036(17) | 1.0379 | 0.0024 | -0.0001 | -0.0003 | 0.0177(5) | 0.037(14) | 0.019(14) | 0.1378 | 6.77 | 91.56 | 96.35 |
| O(2) | - C(1) | 1.2307(14) | 1.2357 | -0.0011 | -0.0051 | -0.0001 | 0.0143(5) | 0.0120(7) | 0.0023(8) | 0.0480 | 127.48 | 137.82 | 106.51 |
| O(3) | - C(3) | 1.3512(16) | 1.3548 | 0.0031 | -0.0022 | -0.0004 | 0.0179(5) | 0.0169(7) | 0.0010(9) | 0.0316 | 22.23 | 107.87 | 102.77 |
| O(3) | - C(4) | 1.3736(15) | 1.3804 | -0.0005 | 0.0069 | 0 | 0.0210(5) | 0.0197(7) | 0.0013(9) | 0.0361 | 85.85 | 21.72 | 68.73 |
| C(1) | - C(2) | 1.4611(15) | 1.4644 | -0.0034 | 0.0004 | 0.0004 | 0.0141(7) | 0.0129(6) | 0.0012(9) | 0.0346 | 172.63 | 86.78 | 83.40 |
| C(2) | - C(3) | 1.3670(16) | 1.3722 | -0.0015 | -0.0053 | 0.0002 | 0.0140(6) | 0.0134(7) | 0.0006(10) | 0.0245 | 131.51 | 135.66 | 102.81 |
| C(2) | - C(5) | 1.4396(16) | 1.4457 | -0.0024 | 0.0059 | 0.0003 | 0.0138(6) | 0.0140(7) | 0.0002(9) | 0.0141 | 121.69 | 39.81 | 68.53 |
| C(3) | - H(3) | 1.039(17) | 1.0437 | 0.0008 | -0.0051 | -0.0002 | 0.0146(7) | 0.071(12) | 0.056(12) | 0.2366 | 85.05 | 156.39 | 112.94 |
| C(4) | - C(5) | 1.3595(18) | 1.3629 | 0.0027 | 0.0022 | -0.0003 | 0.0155(7) | 0.0155(7) | 0.0000(10) | 0 | 16.85 | 73.21 | 88.60 |
| C(4) | - H(4) | 1.089(16) | 1.0923 | -0.0024 | 0.0025 | 0.0003 | 0.0143(7) | 0.036(11) | 0.022(11) | 0.1483 | 149.13 | 63.77 | 74.88 |
| C(5) | - H(5) | 1.100(12) | 1.1056 | 0.0003 | 0.0052 | -0.0001 | 0.0157(7) | 0.028(11) | 0.012(11) | 0.1095 | 69.07 | 28.07 | 72.09 |

Limitations of Hirshfeld Atomic Refinement

Limitations

- ▶ Computational cost - 3 hours and 16 processors for 20 atoms - scales with N up to $N^{2.5}$
- ▶ Molecular wavefunctions are used, so coordination polymers or inorganic structures not feasible
- ▶ Supramolecular features not well reproduced (polarization...)
- ▶ Hirshfeld partitioning not unique
- ▶ Disorder can not be treated, nor aperiodicity
- ▶ Only isolated molecules, no extended polymeric-like structures

Hirshfeld Atomic Refinement vs Multipole modelling

What is better ?

- ▶ Multipole modelling uses the experimental density
- ▶ Hirshfeld Atomic Refinement uses a calculated density
- ▶ Anisotropic refinement of hydrogens (nearly) not possible with multipole modelling
- ▶ ADP's hydrogens from HAR and neutron refinements comparable

Will Hirshfeld Atomic Refinement replace IAM refinement and even multipole refinement?

Contents

From theory to practice

- ▶ Electron density and chemical bonding
- ▶ Experimental and theoretical modelling of electron densities
- ▶ Hirshfeld analysis
 - ▶ Hirshfeld surfaces
 - ▶ Hirshfeld refinement
- ▶ **Software**
 - ▶ Tonto & CrystalExplorer
 - ▶ Tonto & OLEX2

Tonto, CrystalExplorer & OLEX2

Tonto characteristics

- ▶ For quantum chemistry and quantum crystallography
- ▶ Free under the LGPL license
- ▶ Coded in Fortran, interfaced using the Foo scripting language
- ▶ Hartree-Fock and DFT calculations
- ▶ Backend for
 - ▶ CrystalExplorer (GUI)
 - ▶ OLEX2 - interfaces to the Hirshfeld Atomic Refinement part of TONTO

Time for the demos !