s2.m2.p3.la **Prediction of charge density and energy in polypeptides. transferability and beyond.** C. Delafosse, P.J. Becker. *Laboratoire SPMS, CNRS and Ecole Centrale Paris, Grande Voie des Vignes, 92295 CHATENAY MALABRY Cedex France carole@sem.ecp.fr*
Keywords: charge spin densities.

Charge distribution plays a dominant role in conformational studies on molecules or solids. Conformational analysis relies on the minimization of empirical potential energy functions which imply a large number of parameters. A major part of conformational energy is of coulombic origin, and thus totally controlled by the charge density. Since the calculation of this density is computationally very expensive for large systems, most programs use a 'naive' approach, simulating the density by a set of point charges and dipoles adjusted from quantum calculations on small molecules, and therefore transferable within a large set of molecule environment : this often constitutes a poor approximation to the problem, leading to biased results concerning the effective conformation of the system.

A simple method is introduced to predict the electron density in large molecules. A molecule is decomposed into subsystems, the density of which can be considered as additive with a controlled accuracy. This method is based on the Hirshfeld's partitioning scheme, which is very general and independent on any basis set. For a complex molecule we predict a model density built upon fragments that are transferred from simpler systems. The method is compared with Mezey's approach. A significant difference arises when transferability is considered and our approach is not sensitive to basis set problems.

Conformational energies of the complex system are then predicted from the model density, using a density functional scheme, and are compared with ab-initio results. The prediction of the variations of coulombic and kinetic energies requires a very high numerical accuracy (relative accuracy better than 10^{-7} !). The errors introduced by the computational calculations should thus be smaller than this threshold, which constitute a sensitive problem : for several years, many research teams have been working on improving the numerical convergence.

When estimating energy changes associated with a variation of conformation, it turns out that the hypothesis of total transferability is too crude. The density of a fragment is not totally transferable between different conformations. The non-transferable part is very weak compared with the density itself, and would hardly be detected by X Ray diffraction experiments, however it has been shown that this non-transferable contribution to the density plays a dominant role in the energies variations.

For polypeptides, we have found no general way to modelise the deviation of the predicted density with respect to relevant structural parameters. Nevertheless, it appears that the non-transferable density of a given fragment in a molecule can be transferred from a smaller molecule with a similar environment, in the same conformation. Let's assume a torsion around a given bond. Non transferability affects only the neighbors of that bond. The correction of the density can be estimated from a simple analog involving this bond and its immediate environment. The first model of additive fragment densities for a large system is significantly improved by introducing the non-transferable contributions calculated from smaller molecules.

While using the corrected density, the predicted variations of energies now agree with ab-initio calculations with a satisfying accuracy. One can thus predict the conformational energy of a large system by using this reliable model of corrected densities, at a reasonable computational cost.

s2.m2.p4.la **3_{10} helix octapeptide electrostatic potential obtained from transferred experimental electric moments. Comparison to *ab-initio* SCF theoretical calculations.** N. Bouhmaida[§†], N.E. Ghermani[†], C. Jelsch[†], C. Lecomte[†], M.-M. Rohmer[‡], M. Bénard[‡]. [‡]*Laboratoire de Chimie Quantique, CNRS – Université Louis Pasteur 4, rue Blaise Pascal 67000 Strasbourg, France.* [†]*Laboratoire de Cristallographie et Modélisation des Matériaux Minéraux et Biologiques, LCM³B, UPRES A CNRS 7036, Université Henri Poincaré, Nancy 1, Faculté des Sciences, Boulevard des Aiguillettes, BP 239, 54506 Vandoeuvre-lès-Nancy Cedex, France.* [§]*Laboratoire des Sciences des Matériaux, LSM, Université Cadi Ayyad, Faculté des Sciences Semlalia, Boulevard Prince Moulay Abdallah, BP S15, 40000 Marrakech, Morocco.*
Keywords: electrostatic potential, electric moment, tranferable properties.

Electrostatic interactions are essential in macromolecular chemistry, especially for proteins where they are involved in most biochemical processes. Since the electrostatic potential is directly related to the interaction energy, we present in this work, a new way to calculate this property of such molecular systems. In most current calculations, the molecular electrostatic potential is the sum of atomic charges and electric moments contributions. Alternatively, we propose to generate the electrostatic potential using molecular fragment electric moments rather than atomic quantities. The concept of the transferability of such physical properties is fundamental in this approach. Moreover, the fragment electric moments reproduce optimally the experimental electrostatic potential.

Atomic moments are first derived from the fit of the electrostatic potential obtained from the high resolution X-ray experiment on small peptide molecules. The electric fragment moments are then analytically expressed using the Legendre polynomials translation method of Hobson. There after, the electrostatic potential is calculated according to the Buckingham expansion of electric fragment moment contributions.

This method is applied to several small molecules and the average moments of similar fragments are transferred on a 3_{10} helix octapeptide to generate its electrostatic potential. The choice of the fragments is based on both geometrical and peptidic (main chain and side chain) nomenclature considerations. These fragments are also selected to be rigid to avoid distortions of the molecular geometry and subsequently of the electron density.

The electric fragment moments obtained potential is compared to other electrostatic potential calculation methods. A quantitative agreement is observed in the comparison between the obtained electrostatic potential and those computed from a*b-initio* theoretical calculations, from the atomic point charges of AMBER molecular modelling dictionary or directly from the experimental electron density.