m13.o02

The relationship between the molecular structure and the chemical properties: What about the topological analysis of the electron density distribution? An application to hydrogen bonds.

Enrique Espinosa

Université de Bourgogne, LIMSAG-UMR 5633, 9 Av. Alain Savary, 21078 Dijon (France). E-mail: Enrique.Espinosa@u-bourgogne.fr

Keywords: electron density, topological properties of charge distribution, hydrogen bonds

Molecular structure is determined by nuclei positions. From the Hellmann-Feynman theorem we know that the exact ground state electron density distribution $\rho(\mathbf{r})$ depends on the nuclei positions only. Furthermore, the Hohenberg-Kohn theorem states that the total energy of a system can be written in terms of its $\rho(\mathbf{r})$ distribution. In this context, the relationship between the structure of a molecular system and its physical and chemical properties should be reflected by the electron distribution. As far as the molecular structure is the straightforward consequence of interatomic interactions, a correspondence between these interactions and the observed $\rho(\mathbf{r})$ applies. Accordingly, the interatomic interactions described in terms of $\rho(\mathbf{r})$ can be considered as a fundamental subject of study to get insight on the structure-properties relationship, as the former is a conceptual bridge between the latter. The topological analysis of $\rho(\mathbf{r})$ developed by Bader and co-workers [1] is a useful tool for characterizing atomic interactions in internuclear regions. It permits to obtain the molecular space partition into atomic basins that are separated by zero-flux surfaces $S(\mathbf{r})$ of the electron distribution and behave as quantum objects. Along the bond path directions $\rho(\mathbf{r})$ is minimum at the surfaces $S(\mathbf{r})$, where topological bond critical points $\mathbf{r}_{BCP}$ appear and $\rho(\mathbf{r})$ exhibits saddle distributions. Analysis of topological and energetic magnitudes of $\rho(\mathbf{r})$ at $\mathbf{r}_{BCP}$ permits a deep characterization of interactions. Following this description we have analyzed experimental and theoretically calculated energetic properties of hydrogen bonded systems in terms of the $\rho(\mathbf{r})$ distribution at their $\mathbf{r}_{BCP}$'s [2-7].

[1] Bader, R. F. W. (1990). *Atoms in Molecules - a Quantum Theory*, Clarendon Press.
[2] Espinosa, E., Molins, E. & Lecomte, C. (1998), *Chem. Phys. Lett.*, 285, 170-173.
[3] Espinosa, E., Lecomte, C. & Molins, E. (1999), *Chem. Phys. Lett*., 300, 745-748.
[4] Espinosa, E., Souhassou, M., Lachekar, H. & Lecomte, C. (1999), *Acta. Cryst.* B55, 563-572.
[5] Espinosa, E. & Molins, E. (2000), *J. Chem. Phys.,* 113, 5686-5694.
[6] Espinosa, E., Alkorta, I., Rozas, I., Elguero, J. & Molins, E. (2001), *Chem. Phys. Lett.,* 336, 457-461.
[7] Espinosa, E., Alkorta, I., Elguero, J. & Molins, E. (2002), *J. Chem. Phys.,* 117, 5529-5542.

m13.o03

Peptide Plane Flipping Provides an Explanation why Alpha-Sheet is a Likely Conformation for the Amyloid Prefibrillar Intermediate.

James E. Milner-White[a], Steven Hayward[b]

[a]Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK. [b]School of Computing Sciences and School of Biological Sciences, University of East Anglia, Norwich, NR4 7TJ, UK.

Keywords: protein motifs, hydrogen bonds, amyloid

The toxic component of amyloid is not the mature insoluble fibre but a soluble prefibrillar intermediate. It has been proposed[1,2], that alpha-sheet is the key feature of this precursor causing toxicity. The alpha-sheet belongs to a category of protein conformations called nests[3,4] where the main chain parts of successive amino acids residues are enantiomeric (or mirror images). Nests are common peptide motifs and in native proteins 5-8% of all residues are part of such motifs. We show that comparisons of pairs of partly homologous protein three-dimensional structures give rise to many examples where nests and/or short pieces of alpha-sheet interconvert with the beta-sheet conformation via peptide plane flipping. Such flipping is a well-documented[5] phenomenon meaning rotation by about 180° of the CONH atoms with relatively little movement of adjacent atoms. This shows that the alpha-sheet <–> beta-sheet interconversion occurs readily. For longer stretches of beta-strand it is expected to occur via peptide plane flipping of alternate peptide bonds. In whole sheets rows of hydrogen-bonded planes would flip. According to these ideas the first stage in amyloid formation is the assembly of the soluble prefibrillar intermediate consisting of layers of alpha-sheet, while the second stage, occurring via peptide plane flipping, is its interconversion into mature amyloid fibres, composed of layers of beta-sheet.

[1] Armen,R.S., Alonso,D.O.V. & Daggett,V. (2004) *Structure* 12, 1847-1863.
[2] Surridge, C (2004) *Nature* 430, 739; OMS (2004) *Science* 305, 1534.
[3] Watson, J.D. & Milner-White, E.J. (2002) *J. Mol. Biol*. 315, 171-182.
[4] Watson, J.D. & Milner-White, E.J. (2002) *J. Mol. Biol*. 315, 183-191.
[5] Hayward, S. (2001) *Prot. Sci.* 10, 2219-2227.