The structure of polyglycine in a solvent free environment: A computational study

Fabio Pichierri*

Computational Proteomics Team, Genomic Sciences Center, RIKEN

The conformational behaviour of polyglycine in a solvent free environment has been investigated by means of semiempirical molecular orbital calculations. The results indicate that protonation of the N-terminal end of the peptide decreases the propensity of helix formation by about 80 kcal/mol.

Each one of the twenty natural amino acids possesses a different propensity towards α-helix formation, with glycine at the bottom of the scale. In addition to this, the solvent can either stabilize or destabilize the three-dimensional structure of proteins. For this reason, globular proteins expose their polar residues to the surface whereas hydrophobic residues are kept at the protein interior. It is difficult, however, to disentangle these two issues by limiting experiments to the aqueous environment only.

Experimental and theoretical studies on protein molecules in a solvent free environment may shed some light on how the chemical properties of amino acid residues affect the structural properties of protein molecules.[1,2] In this regard, Kaltashov and Fenselau[1] have shown that the α-helix of melittin is stable in the vacuum. This indicates that the α-helix is an intrinsic structural property of this peptide. More recently, Jarrold and coworkers[2] have performed a series of high resolution ion mobility measurements and molecular dynamics (MD) simulations on both polyglycine and polyalanine peptides. Their results indicated that the protonation of the N-terminal residues of either peptide disrupts the α-helix to yield a globular structure.

Here, we investigate the structure of polyglycine in a solvent free environment by means of quantum chemical SCF-MO–AM1 calculations. The present calculations were performed by employing the parallel version of the Gaussian98 program as implemented on the Fujitsu VPP/700E supercomputer of RIKEN. Since glycine is known to be an α-helix breacker, the present computational results should be somewhat instructive.

As starting geometry we employ the canonical α-helix structure, which was model built with a standard graphical interface. The model peptide herein employed contains 10 glycine residues and it is acylated at its C-terminal end. Hence, there are nine peptide linkages which are progressively numbered from I to IX. The initial structure of this model, shown in Fig. 1, is characterized by six intramolecular N–H::O=C hydrogen bonds with mean H::O distances at about 1.96 Å. A larger model containing 18 glycine residues was employed in a previous computational study which was devoted to the investigation of the elastic properties of the α-helix by means of periodic SCF–LMO–AM1 calculations.[3]

* e-mail address: fabio@gsc.riken.go.jp

The geometry of Gly_{10} was fully relaxed in the gas phase and the optimized structure is shown in Fig. 2. As expected, glycine breaks the α-helical structure and a new pattern of hydrogen bonds is formed. Interestingly, we observe the formation of a pair of bifurcated hydrogen bonds between (I,II) and IV, and between (VI,VII) and IX, respectively. Furthermore, there exists two other hydrogen bonds in the central part of the molecule between residues III–VI and IV–VII. The energy difference between the final and initial geometries corresponds to 75 kcal/mol.

Next, we protonated the N-terminal end of the Gly_{10} peptide and re-optimized the starting model of Fig. 1. The final structure is shown in Fig. 3. As we can see, the peptide wraps around itself so as to solvate the positive charge on the amino-terminal residue. A similar result was observed

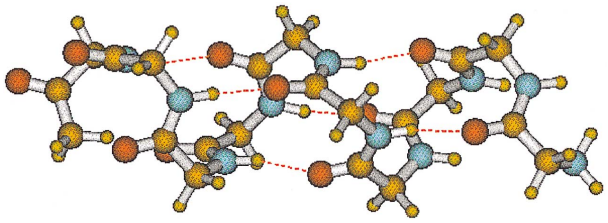

Fig. 1. Structure of the Gly_{10} peptide before geometry optimization. Color code: oxygen (red); nitrogen (blue); carbon (yellow); hydrogen (yellow, small balls).

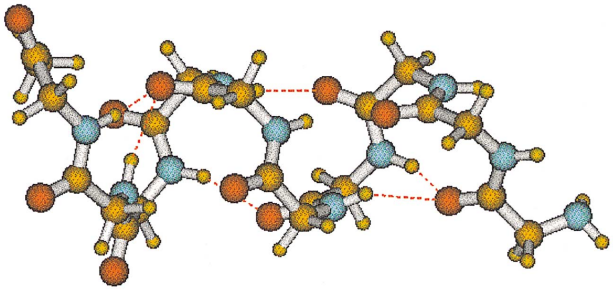

Fig. 2. Optimized structure of the Gly_{10} peptide. Color code: oxygen (red); nitrogen (blue); carbon (yellow); hydrogen (yellow, small balls).

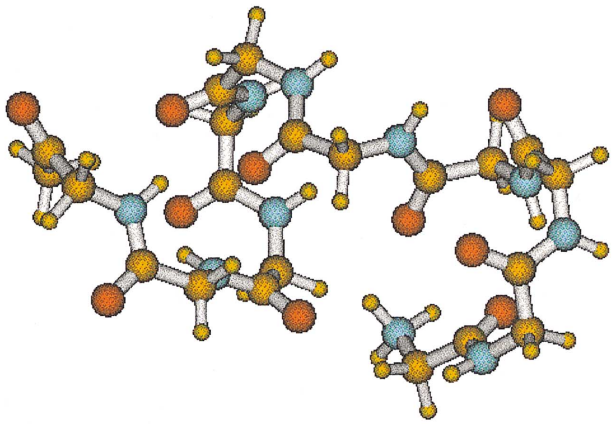

Fig. 3. Optimized structure of the protonated Gly_{10} peptide. Color code: oxygen (red); nitrogen (blue); carbon (yellow); hydrogen (yellow, small balls).

by Jarrold and coworkers[2)] after performing MD simulations in the vacuum. Furthermore, we also notice from Fig. 3 the absence of hydrogen bonds. For the protonated peptide, the energy difference between the final and initial geometry corresponds to 155 kcal/mol. Hence, from the present results, we conclude that protonation of the N-terminal end of the Gly_{10} peptide decreases the propensity of α-helix formation by about 80 kcal/mol.

Our study will continue by extending these quantum chemical calculations to polyalanine peptides and by using implicit solvent models in order to probe the effects of solvent environment on protein structure.

References

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