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SHORT COMMUNICATIONS

γ-Helix; New-Type Helical Conformation in Proteins Found through Theoretical Analysis on Elastin-Model Polypeptide

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Stable conformations of peptides and proteins are uniquely determined by their primary structures (*i.e.*, amino acid sequences) in a given environment.[1,2] Functions of materials are also uniquely determined by the conformations of molecules constituting materials. So it is very important to construct the mothod to investigate the stable conformations of molecules from their primary structures for recognizing the function of materials in a molecular level. To obtain the solution for the unsolved relation between structure and characteristic elasticity of elastin,[3,4] the molecular force field method, which can make the relative stability of conformations clear as a function of conformational energy, was applied to one of typical Gly, Pro and Val-rich regions of the elastin.

Poly(Val–Pro–Gly–Gly) was selected as a model polypeptide for one of the typical region in elastin such as repeated sequence of Val–Pro–Gly–Gly, Val–Pro–Gly–Val–Gly, and Ala–Pro–Gly–Val–Gly–Val. Stable conformations were searched in whole conformational space of this model polypeptide. Using the energy functions of ECEPP,[5] energy minimizations were carried out by the three-step method.[6,7] This mothod is based on a hypothesis which has been shown for peptide, polypeptide, and protein systems,[2,6-10] That is, a conformational ensemble, which is constructed by many energetically stable conformations, can be primarily given for a molecule within intra-residue interactions. Then, the further range interactions, such as short-, medium-, and long-range ones, change the relative stability of each conformation in the ensemble accompanying the change of dihedral angles of the molecule.

Through three steps of minimizations for Ac–(Val–Pro–Gly–Gly)$_6$–NHMe, 85 helical conformations were finally obtained. Backbone dihedral angles of the lowest-energy conformation in the tetrapeptide repeating unit are (ϕ_{Val}, ψ_{Val}, ϕ_{Pro}, ψ_{Pro}, ϕ_{Gly}, ψ_{Gly}, ϕ_{Gly}, ψ_{Gly})= ($-134°$, $82°$, $-75°$, $92°$, $87°$, $-70°$, $-171°$, $52°$). This lowest-energy conformation forms a new-type helix; γ-helix, originally proposed in this communication. γ-Helix is essentially different from the well-known helices such as α- and β-helices[6,7,11,12] in the following points. That is, the latter helices take spiral structure as a whole, but the former helix does not take such spiral structures. The basic conforma-

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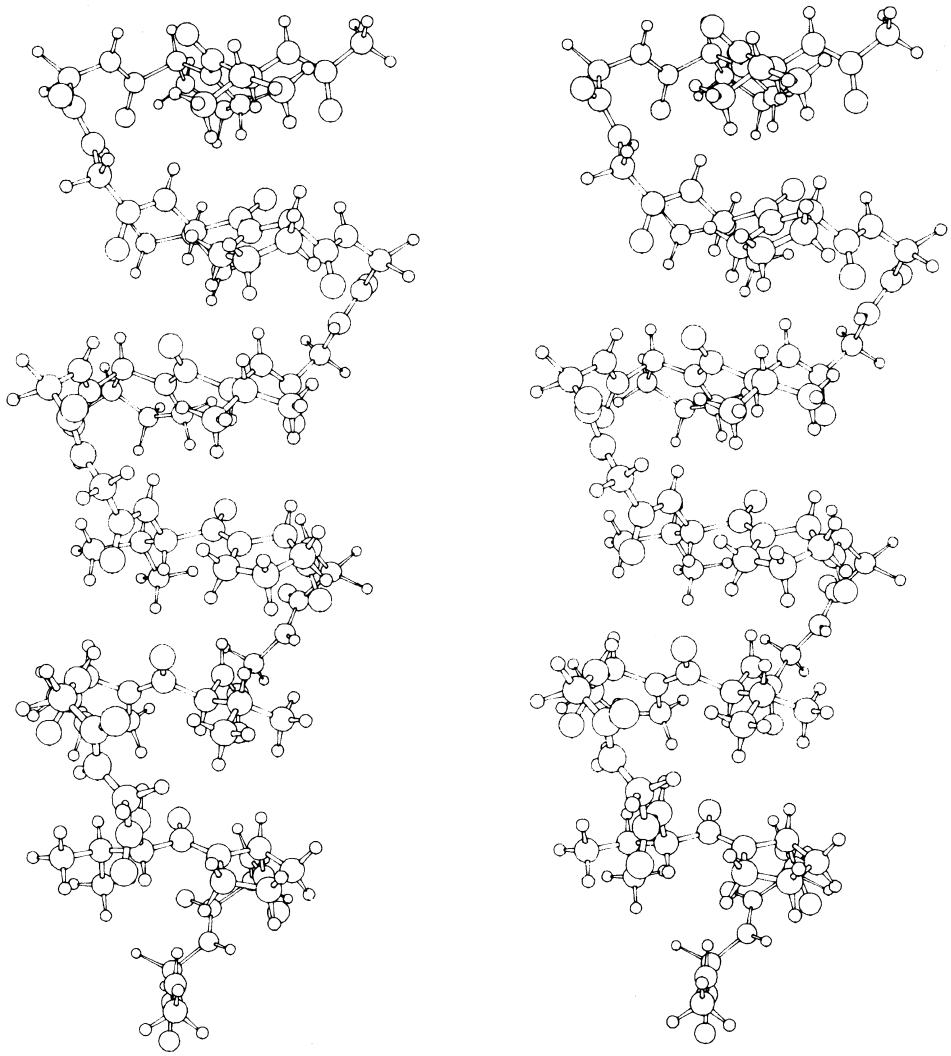

Figure 1. New helical conformation, γ-helix, proposed as a model conformation for polypeptide having one of the typical amino acid sequence, Val–Pro–Gly–Gly, of elastin.

tional unit of γ-helix takes counterclockwise small local spiral formed by 12 consecutive backbone atoms from carbonyl carbon of Val residue to α-carbon of Val residue in the next Val–Pro–Gly–Gly unit, and also takes double-bend structure at Pro–Gly–Gly portion. each spiral rotates 193 degrees around helical axis in a counterclockwise direction, so consecutive spiral almost locates in the opposite side of helical axis. γ-Helix forms two kinds of characteristic regions along the helical axis. One of them is constituted by hydrophobic residues such as Val and Pro whose α-carbon and side-chain atoms are laterally striped in Figure 2, and another one is hydrophilic regions constituted by polar groups such as N–H and C=O. Figures 1 and 2 also clearly exhibit that two hydrophobic regions are symmetrically situated in the opposite side along the helical axis, and side-chain groups

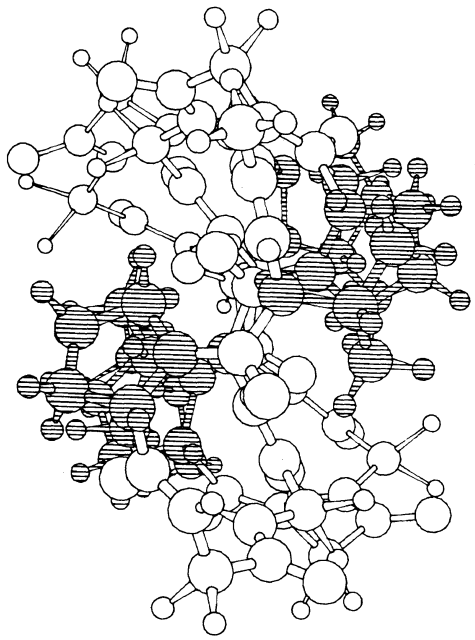

Figure 2. γ-Helix viewed from parallel to the helical axis. Hydrophobic groups are laterally striped. A molecular diagram is shown for four repeating units of tetrapeptide-sequence Val–Pro–Gly–Gly.

of Val and Pro residues are exposed to the outside of helix, and that two hydrophilic regions are also symmetrically situated in the opposite side along the helical axis and carbonyl oxygens of Gly3 residue which are free from intramolecular hydrogen bond are exposed to outside of helix. Such intramoleculally non-hydrogen bonded polar atoms, which are typical in γ-helix, cannot be found in α-helix. These facts indicate that γ-helix is a conformation which effectively interacts with water molecules contained in elastin by forming intermolecular hydrogen bonds and by hydrophobic interactions. Hydrophobic and hydrophilic regions form four stripes which are counterclockwisely twisted along the helical axis. These facts also suggest that above typical regions in γ-helix can form higher-ordered structure of elastin molecule through intermolecular interactions. The results that γ-helix has the hydrogen bonds (Gly4)NH···OC(Pro) and no other types hydrogen bonds corresponding to the experimental results[13] on the temperature dependence of the proton chemical shift of HCO–(Val–Pro–Gly–Gly)$_{35}$–Val–OMe in H_2O from 0°C to 50°C, *i.e.*, Gly4 NH exhibits the lesser temperature dependence, but Val NH and Gly3 NH exhibit the large ones.

Moreover, γ-helix could be converted to other helices which were found in the conformational ensemble of model polypeptide and have more than twice length of γ-helix along helical axis by crossing over the low-energy pass which exist in the 10-dimensional (ϕ, ψ, χ)-space of this system. The distributions of hydrophobic and hydrophilic groups of the extended helix are significantly different from those of γ-helix. That is, the hydrophobic groups are more exposed to the aqueous environments in the extended helix than in γ-helix. These facts indicate that the origin of characteristic elasticity of elastin molecule could be explained by two factors. One is the energetical factor corresponding to the conformational change of polypeptide chain (*i.e.*, the increase in conformational energy by the extension of molecules), and the another is the entropical factor corresponding to the change of spatial arrangement of immanent water molecules in elastin system caused by further exposure of hydrophobic groups along the helical axis (*i.e.*, the decrease in entropy). Above viewpoint on the character of elastin obtained by the theoretical conformational analysis on elastin-model polypeptide corresponds to the previous viewpoints experimentally investigated on elastin.[3,4]

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