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Determination of Short-Range Potentials for Physics-Based Protein-Structure Prediction

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By integrating *ab initio* energy surfaces of the model terminally-blocked amino-acid residues: glycine, alanine, and proline, we calculated the potentials of mean force corresponding to the bending of the $C^{\alpha} \cdots C^{\alpha} \cdots C^{\alpha}$ virtual-bond angles for the purpose of using them in our united-residue UNRES force field. The potentials for the glycine and alanine residues were found to be bimodal as are the corresponding statistical potentials determined from the Protein Data Bank.

1 Introduction

Local interactions play a very significant role in determining protein structure, because they determine the geometry of secondary-structure elements (e.g., the α-helices and the β-sheets), as well as that of turns and loop regions. Therefore, accurate representation of local-interaction terms in the empirical force fields for physics-based protein-structure prediction is of utmost importance. In this communication, we present the determination of the potentials of mean forces for the bending of the $C^{\alpha} \cdots C^{\alpha} \cdots C^{\alpha}$ virtual-bond angles for the purpose of using them in our united-residue physics-based UNRES force field field[1–4] for protein-structure prediction from *ab initio* energy surfaces of terminally-blocked amino-acid residues, which will replace the statistical potentials determined in our earlier work[2] from PDB statistics.

2 Methods

The model system used to calculate the potentials of mean force corresponding to the bending of virtual-bond angles θ is shown in Figure 1. The neighboring amino-acid residues are included because, from the PDB statistics, it follows[2] that the distribution of virtual-bond angles θ depends on the values of the neighboring virtual-bond dihedral angles γ and, consequently, the bending potentials in UNRES are functions of these angles.

The potentials of mean force of virtual-bond angle bending, $F_{XYZ}(\theta, \gamma_1, \gamma_2)$ (where X, Y, and Z are the types of residue involved; see Figure 1), were computed in this work from the energy maps of terminally-blocked X, Y, and Z residues based on the theory presented in Ref. 5 extended by applying the harmonic approximation to each point of the map of the central residue Y. We used the energy maps of terminally-blocked Gly, Ala,

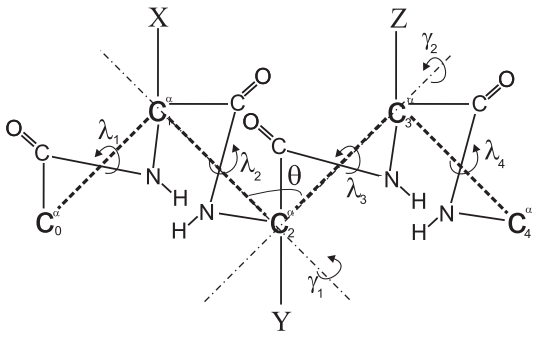

Figure 1. Illustration of a model system for the calculation of the potentials of mean force of the bending of the virtual-bond angles θ. The variables to integrate over are the torsional angles of rotation, $\lambda_1 - \lambda_4$ of the peptide groups about the $C^\alpha \cdots C^\alpha$ virtual-bond axes, while the virtual-bond angle θ and the virtual-bond dihedral angles γ_1 and γ_2 are the primary variables

and Pro calculated in Ref. 5 at the *ab initio* MP2/6-31G** level with the grid of 15°; each point of a map corresponds to a structure minimized in all degrees of freedom except the angles λ. In this work, we computed the Hessian matrices at each point of a map and used them together with minimum-energy values to compute $F_{XYZ}(\theta, \gamma_1, \gamma_2)$. All potentials of mean force were computed at T=298°K.

3 Results and Discussion

The plots of $\overline{F}_Y(\theta)$ (Boltzmann-averaged over the angles γ_1 and γ_2 for X=Gly, Ala, and Pro are shown in Figure 2. In this Figure, the statistical potential $\overline{F}_{Ala}(\theta)$ determined in Ref. 2 is also presented for comparison.

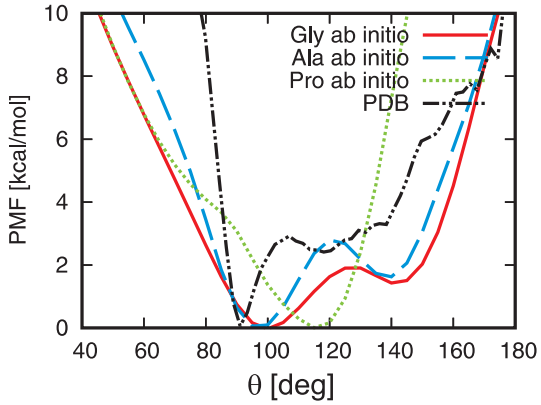

Figure 2. Potentials of mean force of virtual-bond-angle bending Boltzmann-averaged over the virtual-bond-dihedral-angles γ_1 and γ_2 compared with the statistical potential computed from the PDB statistics for Ala-type virtual-bond angles.

It can be seen from Figure 2 that the $\overline{F}_{Gly}(\theta)$ and $\overline{F}_{Ala}(\theta)$ potentials have two minima, one for $\theta = 100^\circ$ and the second one for $\theta = 140^\circ$. Analysis of the complete $F_{XYZ}(\theta, \gamma_1, \gamma_2)$ potentials shows that the first minimum corresponds to the α-helical and the second one to the extended region. This finding agrees with the analysis of the statistical potentials from the PDB[2]. However, the second minimum is not pronounced in the statistical potentials which is caused by the fact that most of the data pertained to α-helical structures. The present potentials are not biased to any organized structure and are, therefore, expected to improve the performance of the UNRES force field.

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