Amino-acid-dependent main-chain torsion-energy terms for protein systems

Yoshitake Sakaé1,2 and Yuko Okamoto2,3,4
1) Department of Theoretical and Computational Molecular Science, Institute for Molecular Science, Okazaki, Aichi 444-8585, Japan
2) Department of Physics, Graduate School of Science, Nagoya University, Nagoya, Aichi 464-8602, Japan
3) Structural Biology Research Center, Graduate School of Science, Nagoya University, Nagoya, Aichi 464-8602, Japan
4) Center for Computational Science, Graduate School of Engineering, Nagoya University, Nagoya, Aichi 464-8603, Japan

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Many commonly used force fields for protein systems such as AMBER, CHARMM, GROMACS, OPLS, and ECEPP have amino-acid-independent force-field parameters of main-chain torsion-energy terms. Here, we propose a new type of amino-acid-dependent torsion-energy terms in the force fields. As an example, we applied this approach to AMBER ff03 force field and determined new amino-acid-dependent parameters for \( \psi \) and \( \psi' \) angles for each amino acid by using our optimization method, which is one of the knowledge-based approach. In order to test the validity of the new force-field parameters, we then performed folding simulations of \( \alpha \)-helical and \( \beta \)-hairpin peptides, using the optimized force field. The results showed that the new force-field parameters gave structures more consistent with the experimental implications than the original AMBER ff03 force field.

I. INTRODUCTION

Computer simulations of protein folding into native structures can be achieved when both of the following two requirements are met: (1) potential energy functions (or, force fields) for the protein systems are sufficiently accurate and (2) sufficiently powerful conformational sampling methods are available. Professor Harold A. Scheraga has been one of the most important pioneers in studies of both of the above requirements. By the developments of the generalized-ensemble algorithms (for reviews, see, e.g., Refs.24–26) and related methods, Requirement (2) seems to be almost fulfilled. In this article, we therefore concentrate our attention on Requirement (1).

There are several well-known all-atom (or united-atom) force fields, such as AMBER6–9, CHARMM10–13, OPLS14,15, GROMOS16,17, GROMACS18,19, and ECEPP20,21. Generally, the force-field parameters are determined based on experimental results for small molecules and theoretical results using quantum chemistry calculations of small peptides such as alanine dipeptide.

In a force field, the potential energy is usually composed of the bond-stretching term, the bond-bending term, the torsion-energy term, and the nonbonded energy term. In these energy terms, it is known that the torsion-energy term is the most problematic. For instance, the ff9422 and ff9923 versions of AMBER differ only in the main-chain torsion-energy parameters. Nevertheless, the secondary-structure-forming tendencies of the two force fields are quite different24,25. Therefore, many researchers have studied this main-chain torsion-energy terms and their force-field parameters. For instance, newer force-field parameters of the main-chain torsion-energy terms about \( \phi \) and \( \psi \) angles have been developed, which are, e.g., AMBER ff99SB24, AMBER ff0325, CHARMM22/CMAP26 and OPLS-AA/L27. The methods of the force-field refinement thus mainly concentrate on the torsion-energy terms. These modifications of the torsion energy are usually based on quantum chemistry calculations28–30 or NMR experimental results13,31.

We have also proposed a new main-chain torsion-energy term, which is represented by a double Fourier series in two variables, the main-chain dihedral angles \( \phi \) and \( \psi \). This expression gives a natural representation of the torsion energy in the Ramachandran space32 in the sense that any two-dimensional energy surface periodic in both \( \phi \) and \( \psi \) can be expanded by the double Fourier series. We can then easily control secondary-structure-forming tendencies by modifying the main-chain torsion-energy surface. We have presented preliminary results for AMBER ff94 and AMBER ff0333,34. Moreover, we have introduced several optimization methods of force-field parameters24–26,35,36. These methods are based on the minimization of some score functions by simulations in the force-field parameter space, where the score functions are derived from the protein coordinate data in the Protein Data Bank (PDB). One of the score functions consists of the sum of the square of the force acting on each atom in the proteins with the structures from the PDB27,28. Other score functions are taken from the root-mean-square deviations between the original PDB structures and the corresponding minimized structures29,30.

In this article, we propose a new type of the main-chain torsion-energy terms for protein systems, which can have amino-acid-dependent force-field parameters. As an example of this formulation, we applied this approach to the AMBER ff03 force field and determined new amino-acid-dependent main-chain torsion-energy parameters for \( \psi \) (N-Cα-C-N) and \( \psi' \) (Cβ-Cα-C-N) by using our optimization method in Refs.24–26.
In section 2 the details of the new main-chain torsion-energy terms are given. In section 3 the results of applications of the method to AMBER ff03 force field and those of folding simulations of two peptides are presented. Section 4 is devoted to conclusions.

II. METHODS

A. Amino-acid-dependent force-field parameters

The existing force fields for protein systems such as AMBER, CHARMM, and OPLS, etc. use essentially the same functional forms for the potential energy $E_{\text{conf}}$ except for minor differences. The conformational potential energy $E_{\text{conf}}$ can be written as, for instance,

$$E_{\text{conf}} = E_{\text{BL}} + E_{\text{BA}} + E_{\text{torsion}} + E_{\text{nonbond}} . \quad (1)$$

Here, $E_{\text{BL}}$, $E_{\text{BA}}$, $E_{\text{torsion}}$, and $E_{\text{nonbond}}$ represent the bond-stretching term, the bond-bending term, the torsion-energy term, and the nonbonded energy term, respectively. Each force field has similar but slightly different parameter values. For example, the torsion-energy term is usually given by

$$E_{\text{torsion}} = \sum_{\Phi} \sum_{n} V_n \left( \Phi \right) \left\{ 1 + \cos \left[ n \Phi - \gamma_n \left( \Phi \right) \right] \right\} , \quad (2)$$

where the first summation is taken over all dihedral angles $\Phi$ (both in the main chain and in the side chains), $n$ is the number of waves, $\gamma_n$ is the phase, and $V_n$ is the Fourier coefficient. Namely, the energy term $E_{\text{torsion}}$ has $\gamma_n(\Phi)$ and $V_n(\Phi)$ as force-field parameters.

We can further write the torsion-energy term as

$$E_{\text{torsion}} = E_{\text{torsion}}^{(MC)} + E_{\text{torsion}}^{(SC)} , \quad (3)$$

where $E_{\text{torsion}}^{(MC)}$ and $E_{\text{torsion}}^{(SC)}$ are the torsion-energy terms for dihedral angles around main-chain bonds and around side-chain bonds, respectively. Examples of the dihedral angles in $E_{\text{torsion}}^{(MC)}$ are $\phi$ (C-N-C-$\alpha$), $\psi$ (N-C-$\alpha$-C-N), $\phi'$ (C-$\beta$-C-$\alpha$-N-C), $\psi'$ (C-$\beta$-C-$\alpha$-C-N), and $\omega$ (C-$\alpha$-C-N-C-$\alpha$).

The force-field parameters in $E_{\text{torsion}}^{(MC)}$ can readily depend on amino-acid residues. However, those in $E_{\text{torsion}}^{(SC)}$ are usually taken to be independent of amino-acid residues and the common parameter values are used for all the amino-acid residues (except for proline). This is because the amino-acid dependence of the force field is believed to be taken care of by the very existence of side chains. In Table I, we list examples of the parameter values for $\psi$ (N-C-$\alpha$-C-N) and $\psi'$ (C-$\beta$-C-$\alpha$-C-N) in general AMBER force fields.

However, this amino-acid independence of the main-chain torsion-energy terms is not an absolute requirement, because we are representing the entire force field by rather a small number of classical-mechanical terms. In order to reproduce the exact quantum-mechanical contributions, one can introduce amino-acid dependence on any force-field term including the main-chain torsion-energy terms. Hence, we can generalize $E_{\text{torsion}}^{(MC)}$ in Eq. (4) from the expression in Eq. (2) to the following amino-acid-dependent form:

$$E_{\text{torsion}}^{(MC)} = \sum_{k=1}^{20} \sum_{\Phi_{MC}^{(k)}} \sum_{n} V_n \left( \Phi_{MC}^{(k)} \right) \left\{ 1 + \cos \left[ n \Phi_{MC}^{(k)} - \gamma_n \left( \Phi_{MC}^{(k)} \right) \right] \right\} , \quad (4)$$

where $k (= 1, 2, \cdots , 20)$ is the label for the 20 kinds of amino-acid residues and $\Phi_{MC}^{(k)}$ are dihedral angles around the main-chain bonds in the $k$-th amino-acid residue.

B. Optimization method for force-field parameters

In the previous subsection, we have generalized the main-chain torsion-energy term $E_{\text{torsion}}^{(MC)}$ so that its parameters are amino-acid dependent. The question is then how to obtain optimal parameter values for this new main-chain torsion-energy term.

One method is to use the parameter optimization method that was introduced in Refs. 23–25. We first retrieve $N$ native structures (one structure per protein) from PDB. We try to choose proteins from different amino-acid sequence homology as much as possible. If the force-field parameters are of ideal values, then all the chosen native structures are stable without any force acting on each atom in the molecules on the average. Hence, we expect

$$F = 0 , \quad (5)$$

where

$$F = \sum_{m=1}^{N} \sum_{i_m=1}^{N_m} \frac{1}{N_m} \left| \vec{f}_{i_m} \right|^2 , \quad (6)$$

and

$$\vec{f}_{i_m} = - \frac{\partial E_{\text{total}}^{(m)}}{\partial \vec{x}_{i_m}} . \quad (7)$$
Here, $N_m$ is the total number of atoms in molecule $m$, $E_{\text{total}}^{(m)}$ is the total potential energy for molecule $m$, and $f_i$ is the force acting on atom $i$. In reality, $F \neq 0$, and because $F \geq 0$, we can optimize the force-field parameters by minimizing $F$ with respect to these parameters in the main-chain torsion-energy term in Eq. (4). In practice, we perform a minimization simulation in the main-chain torsion-energy force-field parameter space for this minimization.

III. RESULTS AND DISCUSSION

A. An example of the amino-acid-dependent force-field parameter optimizations

We present the results of our optimizations of the force-field parameters $V_{ij}(\Phi_{MC}^{(k)})$ for the main-chain angles $\Phi_{MC}^{(k)} = \psi^{(k)} (N-C_{\alpha}-C-N)$ and $\psi^{(k)} (C_{\beta}-C_{\alpha}-C-N)$ in Eq. (4). We did this for the case of AMBER ff03 force field. We determined these $V_{ij}(\Phi_{MC}^{(k)})$ values for the 19 amino-acid residues except for proline.

At first, we chose 100 PDB files with resolution 2.0 Å or better, with sequence similarity of amino acid 30.0 % or lower, and with less than 200 residues (the average number of residues is 117.0) from PDB-REPRDB.

We then refined these selected 100 structures. Generally, data from X-ray experiments do not have coordinates for hydrogen atoms. Therefore, we have to add hydrogen coordinates. Many protein simulation software packages provide with routines that add hydrogen atoms to the PDB coordinates. We used the AMBER11 program package.

We thus minimized the total potential energy $E_{\text{total}} = E_{\text{conf}} + E_{\text{solv}} + E_{\text{constr}}$ with respect to the coordinates for each proton conformation, where $E_{\text{constr}}$ is the harmonic constraint energy term ($E_{\text{constr}} = \sum_{\text{heavy atom}} K_x (\vec{x} - \vec{x}_0)^2$, and $E_{\text{solv}}$ is the solvation energy term. Here, $K_x$ is the force constant of the restriction and $\vec{x}_0$ are the original coordinate vectors of heavy atoms in PDB. As one can see from $E_{\text{constr}}$, the coordinates of hydrogen atoms will be mainly adjusted, but unnatural heavy-atom coordinates will also be modified. We performed this minimization for all the 100 protein structures separately and obtained 100 refined structures by using $K_x = 100$ (kcal/mol). As for the solvation energy term $E_{\text{solv}}$, we used the GB/SA solvent included in the AMBER program package ($igb = 5$ and $gbsa = 1$).

For these refined protein structures, we performed the optimization of force-field parameters $V_{ij}(\psi^{(k)})$ of $\psi$ and $\psi'$ angles for AMBER ff03 force field by using the function $F$ in Eq. (4) as the total potential energy function ($E_{\text{total}} = E_{\text{conf}} + E_{\text{solv}}$) for the Monte Carlo simulations in the parameter space. Here, we used AMBER11 for the force calculations in Eq. (4). We have to optimize the 38 ($= 2 \times 19$) parameters simultaneously by the simulations in 38 parameters. However, here, for simplicity, we just optimized two parameters, $V_{ij}(\psi^{(k)})$ and $V_{ij}(\psi'^{(k)})$, for each amino-acid residue $k$ separately, keeping the other $V_{ij}$ values as the original values. In order to obtain the optimal parameters, we performed Monte Carlo simulations of two parameters ($V_{ij}$ of $\psi$ and $\psi'$) for the 19 amino-acid residues except for proline. In Table III, the optimized parameters are listed.

B. Test simulations with two peptides

In order to check the force-field parameters obtained by our optimization method, we performed the folding simulations using two peptides, namely, C-peptide of ribonuclease A and the C-terminal fragment of the B1 domain of streptococcal protein G, which is sometimes referred to as G-peptide.

The C-peptide has 13 residues and its amino-acid sequence is Lys-Glu-Leu-Ala-Ala-Lys$^+$-Phe-Glu-Arg$^+$-Glu-His$^+$-Met. This peptide has been extensively studied by experiments and is known to form an $\alpha$-helix structure. Because the charges at peptide termini are known to affect helix stability, the N and C termini of the peptide was blocked with acetyl and N-methyl groups, respectively.

The G-peptide has 16 residues and its amino-acid sequence is Gly-Glu$^+$-Trp-Thr-Tyr-Asp$^+$-Asp$^+$-Ala-Thr-Lys$^+$-Thr-Phe-Thr-Val-Thr-Glu$^+$. The termini were kept as the usual zwitter ionic states, following the experimental conditions.

For the folding simulations, we used replica-exchange molecular dynamics (REMD). REMD is one of the generalized-ensemble algorithms, and has high conformational sampling efficiency by allowing configurations to heat up and cool down while maintaining proper Boltzmann distributions. We used the AMBER11 program package.

The unit time step was set to 2.0 fs, and the bonds involving hydrogen atoms were constrained by SHAKE algorithm. Each simulation was carried out for 30.0 ns (hence, it consisted of 15,000,000 MD steps) with 16 replicas by using Langevin dynamics. The exchange procedure for each replica were performed every 3,000 MD steps. The temperature was distributed exponentially: 650, 612, 577, 544, 512, 483, 455, 428, 404, 380, 358, 338, 318, 300, 282, and 266 K. As for solvent effects, we used the GB/SA model in the AMBER program package ($igb = 5$ and $gbsa = 1$). The initial conformations for each peptide were fully extended ones for all the replicas. The REMD simulations were performed with different sets of randomly generated initial velocities for each replica.

In Fig. 1, $\alpha$-helicity and $\beta$-strandness of two peptides obtained from the REMD simulations are shown. We checked the secondary-structure formations by using the DSSP program, which is based on the formations of the intra-main-chain hydrogen bonds. As is shown in Fig. 1, for the original AMBER ff03 force field, the $\alpha$-helicity is clearly higher than the $\beta$-strandness not only
in C-peptide but also in G-peptide. Namely, the original AMBER ff03 force field clearly favors α-helix and does not favor β-structure. On the other hand, for the optimized force field, in the case of C-peptide, the α-helicity is higher than the β-strandness, and in the case of G-peptide, the β-strandness is higher than the α-helicity. We conclude that these results obtained from the optimized force field are in better agreement with the experimental results in comparison with the original force field. In Fig. 2 310-helicity and π-helicity of two peptides obtained from the REMD simulations are shown. For 310-helicity, there is no large difference for both force fields in C-peptide, and in the case of G-peptide, the value of the optimized force field slightly decreases in comparison with the original force field. π-helicity has almost no value in the both cases of the original and optimized force fields in two peptides.

In Fig. 3 α-helicity and β-strandness as functions of temperature for the two peptides obtained from the REMD simulations are shown. For α-helicity, the values of both force fields decrease gradually from low temperature to high temperature in the case of C-peptide. On the other hand, in the case of G-peptide, there are small peaks at around 300 K and 358 K for the original and optimized force fields, respectively. For β-strandness, in the case of C-peptide, it is almost zero for both force fields. In the case of G-peptide, for the optimized force field, there is clearly a peak around 300 K. In Fig. 4 310-helicity and π-helicity of the two peptides as functions of temperature are shown. For 310-helicity, in the case of both peptides, the values of the optimized force field are lower than the original force field as a whole except around low temperature in C-peptide. For π-helicity, it is almost zero for both force fields in the two peptides.

In Fig. 6 the lowest-energy conformations of C-peptide obtained from the REMD simulations in the case of the original and the optimized force fields are shown. In the case of the original force field, all the conformations have helices. No. 3 has only 310-helix, No. 13 has both α-helix and 310-helix, and the rest of the conformations have only α-helix. In the case of the optimized force field, seven conformations (Nos. 2, 4, 5, 7, 8, 12, and 13) have helices. Nos. 2, 5, 7, 13 have only α-helix, Nos. 4, 12 have only 310-helix, and No. 8 has both α-helix and 310-helix. Additionally, there is one β-bridge structure in No. 10. In Fig. 4 the lowest-energy conformations of G-peptide are shown. In the case of the original force field, all the conformations except for No. 4 have helices. No. 6 has both α-helix and 310-helix, Nos. 5, 7, 11 have only 310-helix, and the rest have only α-helix. In the case of the optimized force field, Nos. 11 and 12 have α-helix, No. 8 has 310-helix, No. 5 has β-bridge, and Nos. 7, 9, 10 have β-strand. These results clearly show that the optimized force field favors helix structure much less than the original force field, and, additionally, in the case of G-peptide, slightly favors β-structure.

IV. CONCLUSIONS

The main-chain torsion-energy terms are the most problematic terms in the force field for protein systems. We therefore concentrate our attention on these terms in order to obtain optimal protein force field. In this article, we proposed amino-acid-dependent main-chain torsion-energy terms in the force field for protein systems. This generalization gives more freedom to the force-field optimization problem. In principle, we can introduce amino-acid dependence on any force-field term. The present work introduced this dependence on even the main-chain torsion-energy terms, which previously had been treated independent of the amino-acid residue type.

As an example of the present general formalism, we modified the AMBER ff03 force field so that the V_ i parameters of the main-chain ψ and χ angles may be amino-acid dependent except for proline (hence, 38 parameters were optimized). Although preliminary because we did not optimize the 38 parameters simultaneously, our optimized parameters already gave structures more consistent with the experimental implications than the original AMBER force field in the folding simulations of two small peptides.

We can easily apply the present formulations to other popular force fields such as AMBER ff99SB, CHARMM22/CMAP, etc. This will be our future work.

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TABLE I. Torsion-energy parameters \( (V_n, \sigma_n) \) for the main-chain dihedral angles \( \psi \) and \( \psi' \) in Eq. (2) for the original AMBER ff94, ff96, ff99, ff99SB, and ff03 force fields. The values are common among the amino-acid residues for each force field. Only the parameters for non-zero \( V_n \) are listed.

| Force field | \( \psi \) (N-C\( _{\alpha} \)-C-N) | \( \psi' \) (C\( _{\beta} \)-C\( _{\alpha} \)-C-N) |
|-------------|------------------|------------------|
|             | \( n \)          | \( V_n/2 \)      | \( \sigma_n \) | \( n \) | \( V_n/2 \) | \( \sigma_n \) |
| ff94        | 1                | 0.75             | \( \pi \)     | 2     | 0.07    | 0       |
|             | 2                | 1.35             | \( \pi \)     | 4     | 0.10    | 0       |
|             | 4                | 0.40             | \( \pi \)     |        |         |         |
| ff96        | 1                | 0.85             | 0             | 2     | 0.07    | 0       |
|             | 2                | 0.30             | \( \pi \)     | 4     | 0.10    | 0       |
| ff99        | 1                | 1.70             | \( \pi \)     | 2     | 0.07    | 0       |
|             | 2                | 2.00             | \( \pi \)     | 4     | 0.10    | 0       |
| ff99SB      | 1                | 0.45             | \( \pi \)     | 1     | 0.20    | 0       |
|             | 2                | 1.58             | \( \pi \)     | 2     | 0.20    | 0       |
|             | 3                | 0.55             | \( \pi \)     | 3     | 0.40    | 0       |
| ff03        | 1                | 0.6839           | \( \pi \)     | 1     | 0.7784  | \( \pi \) |
|             | 2                | 1.4337           | \( \pi \)     | 2     | 0.0657  | \( \pi \) |
|             | 3                | 0.4615           | \( \pi \)     | 3     | 0.0560  | 0       |
TABLE II. 100 proteins used in the optimization of force-field parameters.

| Fold | PDB ID | Chain | PDB ID | Chain | PDB ID | Chain | PDB ID | Chain |
|------|--------|-------|--------|-------|--------|-------|--------|-------|
| all α | 1DLW  | A     | 1N1J   | B     | 1U84   | A     | 1IBR   | A     |
|       | 1TX4   | A     | 1V54   | D     | 1SK7   | A     | 1TQG   | A     |
|       | 1NV4   | B     | 1DVO   | A     | 1HFE   | S     | 1J0P   | A     |
|       | 1Y02   | A     | 1HYJ   | B     | 1H2T   | A     | 1G8E   | A     |
|       | 1VKE   | C     | 1FS1   | A     | 1D9C   | A     | 1AIL   | A     |
|       | 1QSZ   | A     | 1T8K   | D     | 1OR7   | C     | 1NG6   | A     |
|       | 1C75   | A     | 2LIS   | A     | 1NH2   | B     | 1Q2H   | A     |

| all β | 1XAK   | A     | 1T2W   | A     | 1GMU   | C1-70 | 1AYO   | A     |
|       | 1PK6   | A     | 1OF5   | B     | 1BEH   | A     | 1J08   | A     |
|       | 1UXZ   | A     | 1UB4   | C     | 1LGP   | A     | 1CQY   | A     |
|       | 1PM4   | A     | 1O8U   | A     | 1V76   | A     | 1R6J   | A     |
|       | 1O8A   | D     | 1IFG   | A     |        |       |        |       |

| α/β   | 1ID0   | A     | 1U7P   | A     | 1JKE   | C     | 1MXI   | A     |
|       | 1LY1   | A     | 1NRZ   | A     | 1M5   | A     | 1VC1   | A     |
|       | 1OGD   | A     | 1IIB   | A     | 1PYO   | D     | 1MUG   | A     |
|       | 1H75   | A     | 1K66   | A     | 1COZ   | A     | 1D40   | A     |

| α + β | 1VCC   | A     | 1PP0   | B     | 1PZ4   | A     | 1TU1   | A     |
|       | 1Q2Y   | A     | 1M4J   | A     | 1N9L   | A     | 1LQV   | B     |
|       | 1A3A   | A     | 1K2E   | A     | 1TT8   | A     | 1HUF   | A     |
|       | 1SX7   | A     | 1CYO   | A     | 1ID0   | A     | 1UCD   | A     |
|       | 1F66   | B     | 1KPF   | A     | 1BYR   | A     | 1Y60   | D     |
|       | 1SEI   | A     | 1RL6   | A     | 1WM3   | A     | 1FTH   | A     |
|       | 1APY   | B     | 1N13   | E     | 1LTS   | C     | 1UGI   | A     |
|       | 1MWP   | A     | 1PCF   | A     | 1HR    | B     | 1H6H   | A     |

TABLE III. Optimized $V_1/2$ parameters for the main-chain dihedral angles $\psi$ and $\psi'$ for the 19 amino-acid residues (except for proline) in Eq. (4). The rest of the parameters are taken to be the same as in the original ff03 force field (see Table I). The original amino-acid-independent values are also listed for reference.

|ψ(\text{N-Cα-C-N}) | ψ'(\text{Cβ-Cα-C-N}) |
|-------------------|----------------------|
| original ff03     | 0.6839               | 0.7784               |
| Ala               | 0.122                | 0.150                |
| Arg               | 0.409                | 0.200                |
| Asn               | −0.074               | −0.162               |
| Asp               | −0.137               | 0.182                |
| Cys               | 0.361                | 0.089                |
| Gln               | 0.144                | −0.024               |
| Glu               | 0.180                | 0.152                |
| Gly               | 0.258                | −−                  |
| His               | 0.020                | 0.237                |
| Ile               | 0.643                | 0.194                |
| Leu               | 0.382                | 0.257                |
| Lys               | 0.222                | 0.042                |
| Met               | 0.141                | 0.346                |
| Phe               | −0.010               | 0.553                |
| Ser               | −0.248               | 0.475                |
| Thr               | 0.512                | 0.328                |
| Trp               | 0.027                | 0.477                |
| Tyr               | 0.082                | 0.652                |
| Val               | 0.142                | 0.590                |
FIG. 1. $\alpha$-helicity (a-1) and $\beta$-strandness (a-2) of C-peptide and $\alpha$-helicity (b-1) and $\beta$-strandness (b-2) of G-peptide as functions of the residue number at 300 K. These values were obtained from the REMD simulations. Normal and dotted curves stand for the optimized and the original AMBER ff03 force fields, respectively.

FIG. 2. $3_{10}$-helicity (a-1) and $\pi$-helicity (a-2) of C-peptide and $3_{10}$-helicity (b-1) and $\pi$-helicity (b-2) of G-peptide as functions of the residue number at 300 K. These values were obtained from the REMD simulations. Normal and dotted curves stand for the optimized and the original AMBER ff03 force fields, respectively.
FIG. 3. \(\alpha\)-helicity (a-1) and \(\beta\)-strandness (a-2) of C-peptide and \(\alpha\)-helicity (b-1) and \(\beta\)-strandness (b-2) of G-peptide as functions of temperature. These values were obtained from the REMD simulations. Normal and dotted curves stand for the optimized and the original AMBER ff03 force fields, respectively.

FIG. 4. \(3_{10}\)-helicity (a-1) and \(\pi\)-helicity (a-2) of C-peptide and \(3_{10}\)-helicity (b-1) and \(\pi\)-helicity (b-2) of G-peptide as functions of temperature. These values were obtained from the REMD simulations. Normal and dotted curves stand for the optimized and the original AMBER ff03 force fields, respectively.
FIG. 5. Lowest-energy conformations of C-peptide obtained for each replica from the REMD simulations. (a) and (b) are the results of the original AMBER ff03 and the optimized force fields, respectively. The conformations are ordered in the increasing order of energy. The figures were created with DS Visualizer.

FIG. 6. Lowest-energy conformations of G-peptide obtained for each replica from the REMD simulations. (a) and (b) are the results of the original AMBER ff03 and the optimized force fields, respectively. The conformations are ordered in the increasing order of energy. The figures were created with DS Visualizer.