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Origin of the right-handed twist of β-sheets of poly(LVal) chains

(energy minimization/nonbonded interaction energy/side chain–side chain interaction/side chain–backbone interaction)

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ABSTRACT **The energies of three- and five-chain antiparallel and parallel β-sheets were minimized. Each chain consisted of six L-valine residues with CH_3CO and $NHCH_3$ end groups; the chains were considered to be equivalent, but all dihedral angles of a given chain were allowed to vary independently during energy minimization. The minimum-energy structures had a considerable right-handed twist, as observed in globular proteins. This right-handed twist is due primarily to intrachain nonbonded interactions. Such interactions between the $C^{\gamma 1}H_3$ group of the *i*th residue and the $C^{\gamma 2}H_3$ group of the (*i*+2)th residue of the same chain favor a twist of either handedness over the flat structure. However, many small intrastrand pair-wise interatomic interactions involving the $C^{\gamma 1}H_3$ and $C^{\gamma 2}H_3$ groups, especially the interactions of these groups with the O and amide H atoms of the neighboring peptide groups, make the right-handed twisted structure energetically more favorable than the left-handed one. The intrastrand side-chain torsional energy plays a small additional role in favoring the right-twisted structure over both the flat and the left-twisted structures. The interstrand interactions favor flat structures, but they are not strong enough to overcome the intrastrand interactions that favor the twisted structure; they only decrease somewhat the extent of the right-handed twist of the β-sheets.**

We recently showed that minimum-energy structures of β-sheets consisting of poly(LAla) chains have a right-handed twist (1), as observed in globular proteins (2). As in the case of right-handed α-helices (3), it is the intrastrand nonbonded interaction energy that plays the key role in forcing β-sheets of L-amino acids to adopt a right-handed twist. The nonbonded energy contribution favoring the right-handed twist is the result of many small intrastrand pair-wise interatomic interactions involving the $C^{\beta}H_3$ groups; interstrand nonbonded interactions, also involving the $C^{\beta}H_3$ groups, contribute somewhat, but less so, in influencing the twist.

While these computations on poly(LAla) (1) show the role of the backbone and the $C^{\beta}H_3$ group in producing a right-handed twisted β-sheet, the magnitude of the computed twist is less than that observed in proteins [only a few degrees per two residues (1) compared with observed values in the range of 0° to 60° (4)]. Since β-sheets in proteins contain other residues than alanine, with valine being the most frequently occurring one (5), it was of interest to extend these computations to a β-sheet of poly(LVal) chains. We therefore consider such β-sheets here and gain insight into the role played by the valyl side chain (in addition to the earlier-demonstrated role of the backbone) in producing the right-handed twist.

COMPUTATIONAL METHODS

Computations were carried out on a single polypeptide chain and on parallel and antiparallel three- and five-stranded β-sheets. Each chain had the composition CH_3CO—(L-Val)$_6$—$NHCH_3$. The residue geometry and energy parameters were those of the ECEPP algorithm [empirical conformational energy program for peptides (6)] (see ref. 1 for further computational details).

Generation of β-Sheets. For a β-sheet with equivalent strands, the first chain can be generated by using the ECEPP algorithm, and then all the other chains can be generated by iterative rotational and translational operations on the preceding chain; i.e., the *i*th chain can be generated from the (*i*−1)th chain by the following equation:

$$\mathbf{r}_i = \mathbf{\Omega}\mathbf{r}_{i-1} + \mathbf{T}, \qquad [1]$$

where $\mathbf{r}_i$ and $\mathbf{r}_{i-1}$ are the coordinates of corresponding atoms in the *i*th and (*i*−1)th chains, respectively, $\mathbf{T} = (t_1,t_2,t_3)$ is a translational vector, and $\mathbf{\Omega}$ is the following Euler rotational operator

$$\mathbf{\Omega} = \begin{bmatrix} \cos\alpha\cos\gamma - \sin\alpha\cos\beta\sin\gamma & -\cos\alpha\sin\gamma - \sin\alpha\cos\beta\cos\gamma & \sin\alpha\sin\beta \\ \sin\alpha\cos\gamma + \cos\alpha\cos\beta\sin\gamma & -\sin\alpha\sin\gamma + \cos\alpha\cos\beta\cos\gamma & -\cos\alpha\sin\beta \\ \sin\beta\sin\gamma & \sin\beta\cos\gamma & \cos\beta \end{bmatrix}, \qquad [2]$$

where α, β, and γ are the Euler angles, as defined in ref. 1.

Formulation of Sheet Twist. The twist of a β-sheet depends on the twist of the constituent chains (1), which, in turn, depends on their helical parameters. It should be noted that the handedness of the twist of the β-sheet (and of its constituent polypeptide chains) is opposite that of the helicity of the polypeptide chains; i.e., chains that have a right-handed twist should be described as left-handed helices and vice versa. A detailed discussion of this point was presented in ref. 1.

For a given set of backbone dihedral angles φ, ψ, and ω, the corresponding helical parameters can be calculated by the following equations (7, 8):

$$\cos\frac{t}{2} =$$

$$0.598\cos[\tfrac{1}{2}(\phi + \psi + \omega)] - 0.270\cos[\tfrac{1}{2}(\phi - \psi + \omega)]$$

$$- 0.216\cos[\tfrac{1}{2}(\phi + \psi - \omega)] - 0.240\cos[\tfrac{1}{2}(\phi - \psi - \omega)] \qquad [3]$$

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$$h\sin\frac{t}{2} =$$

$$2.579\sin[\tfrac{1}{2}(\phi+\psi+\omega)] - 0.337\sin[\tfrac{1}{2}(\phi-\psi+\omega)]$$
$$- 0.358\sin[\tfrac{1}{2}(\phi+\psi-\omega)] + 0.336\sin[\tfrac{1}{2}(\phi-\psi-\omega)] \quad [4]$$

$$n = \frac{360^\circ}{t}, \quad [5]$$

where t and h are the angle of rotation and rise, respectively, per residue and n is the number of residues per turn. The numerical constants in Eqs. 3 and 4 were derived from the geometry of the L-valine residue used in the ECEPP algorithm (6).

For a regular polypeptide chain, the amount of twist per two residues is defined as (1)

$$\delta = 2\left(1 - \frac{180^\circ}{|t|}\right)t = 360^\circ(2 - |n|)\frac{1}{n}. \quad [6]$$

Right twist, flat, and left twist are characterized by $\delta > 0$, $\delta = 0$, and $\delta < 0$, respectively. For an irregular chain, a corresponding average twist can be defined as:

$$\langle\delta\rangle = \frac{2}{\lambda}\sum_{i=1}^{\lambda}\left(1 - \frac{180^\circ}{|t_i|}\right)t_i = \frac{360^\circ}{\lambda}\sum_{i=1}^{\lambda}(2 - |n_i|)\frac{1}{n_i}, \quad [7]$$

where λ is the number of residues per chain and t_i and n_i are computed for each residue i. Eqs. 6 and 7 can be used directly to describe the twist of β-sheets having regular and irregular equivalent chains (1), respectively. A flat β-sheet corresponds to $n = 2$.

Energy Minimization. In the previous energy minimization (1), all of the dihedral angles ω were fixed at 180°. Actually, crystal structure data on proteins indicate that ω may deviate somewhat from 180°. Although such a deviation is generally less than 10°, it will increase or decrease the extent of twist; in some particular conformations, it may even change the direction of the twist. For example, for any fixed (ϕ,ψ) on the line where $n = 2$, when ω changes from negative values through ±180° to positive values, the corresponding regular β-sheet will assume a right-handed twist, a flat, and a left-handed twist, respectively, as shown in Table 1. Therefore, in investigating the twist of β-sheets, it is generally important to allow all of the ω values to vary during energy minimization. For β-sheets with the small alanine side chain (1), however, energy minimization with fixed and variable ω gave essentially the same result.

The energy of each β-sheet was calculated with the ECEPP algorithm (6) and minimized by alternating between the two function-optimizer algorithms, MINOP (9) and POWELL (10), until the energy converged to its minimum value. The computational procedure is basically the same as in ref. 1 but more variables are involved here during energy minimization because the constraint of fixed ω (at 180°) (1) is now relaxed and also because there are more dihedral angles in the side chain of valine than in alanine. For example, when minimizing the energy of a β-sheet with equivalent strands, each of which consists of six valine residues, there are 42 variables—namely, ϕ_i, ψ_i, ω_i, χ_i^1, $\chi_i^{2,1}$, $\chi_i^{2,2}$ ($i = 1,2,\ldots,6$), α, β, γ, t_1, t_2, and t_3.

Initial values of the backbone dihedral angles for energy minimization were selected as described earlier (1)—namely, by choosing (ϕ_i,ψ_i) along the line on which $n = 2$ at 10° intervals of ϕ_i, with $\omega_i = 180^\circ$ and $\chi_i^{2,1} = \chi_i^{2,2} = 60^\circ$ ($i = 1,2,\ldots,6$). For each such backbone conformation, all three staggered conformations around the C_i^α—C_i^β bond—i.e., $\chi_i^1 = 180^\circ$, 60°, and −60°, respectively—were used as starting points.

Table 1. Effect of ω on the twist of a regular β-sheet with fixed (ϕ,ψ)

ϕ, deg	ψ, deg	ω, deg	t,* deg	δ,† deg
−153.0‡	151.0‡	−178.0	−178.3	3.4
		±180.0	±180	0
		178.0	178.3	−3.4

* Computed by using Eq. 3.
† Computed by using Eq. 6.
‡ This value of (ϕ,ψ) was chosen because it lies on the $n = 2$ line; i.e., it represents a flat sheet when $\omega = \pm180^\circ$. Any other choice of (ϕ,ψ) on the $n = 2$ line in the β-sheet region results in the analogous conclusion.

RESULTS AND DISCUSSION

The results obtained after energy minimization are given in Tables 2 and 3. All minimum-energy β-sheet conformations starting from $\chi_i^1 = 60^\circ$ or -60° were at least 14 kcal/mol per chain (1 cal = 4.18 J) higher in energy than those starting from $\chi_i^1 = 180^\circ$. They are therefore not listed in Tables 2 and 3. Stereo drawings of the minimum-energy antiparallel and parallel β-sheets with five strands are shown in Fig. 1 *A* and *B*, respectively.

From Tables 2 and 3, the following conclusions can be drawn. (*i*) All of the average twists $\langle\delta\rangle$ are positive, indicating a right-handed twist (also, see Fig. 1). The values of $\langle\delta\rangle$ for the sheet structures are 22–30°, almost 5 to 6 times the values found for poly(LAla) β-sheets (1). (*ii*) The antiparallel sheets are more twisted than the corresponding parallel ones. This means that, in comparison with parallel sheets, antiparallel sheets are more flexible (11, 12) so that a larger twist can be tolerated. (*iii*) The energies given in Table 3 for parallel structures are about 1 kcal/mol per chain lower than those of antiparallel ones, showing that parallel β-sheets of poly(LVal) are lower in energy, in contrast to the situation for β-sheets of poly(LAla) chains (1). These results, concerning the different relative stabilities of parallel

Table 2. Backbone dihedral angles characterizing minimum-energy β-sheets consisting of CH_3CO—(L-Val)$_6$—$NHCH_3$ chains

	Single polypeptide chain			Antiparallel sheet						Parallel sheet					
				Three chains			Five chains			Three chains			Five chains		
i	ϕ	ψ	ω	ϕ	ψ	ω	ϕ	ψ	ω	ϕ	ψ	ω	ϕ	ψ	ω
1	−86.3	100.1	179.7	−90.8	118.5	−174.8	−91.3	120.4	−174.4	−99.4	93.6	−172.8	−100.8	94.1	−172.4
2	−84.0	106.9	179.8	−102.0	105.1	−176.2	−103.6	105.1	−175.9	−99.5	101.6	−175.0	−100.3	101.5	−174.5
3	−83.6	105.2	179.6	−94.8	101.5	−179.5	−95.5	101.7	−179.5	−92.4	99.7	−177.9	−92.9	99.6	−177.4
4	−83.4	105.8	179.9	−87.5	102.3	177.3	−87.5	102.2	177.0	−87.8	101.5	179.7	−88.3	101.4	−179.8
5	−83.5	106.3	179.4	−86.0	106.1	179.8	−86.2	106.4	180.0	−86.9	106.9	−178.6	−87.3	106.9	−178.1
6	−85.5	96.8	178.8	−85.0	93.9	178.9	−85.0	93.6	178.9	−85.5	97.9	179.0	−85.7	98.4	179.1

Backbone dihedral angles are given in degrees. After minimization, the side-chain dihedral angles χ_i^1, $\chi_i^{2,1}$, and $\chi_i^{2,2}$ fell within the ranges −176° through ±180° to 176°, 54–60°, and 64–70°, respectively. They are not given here.

Table 3. Parameters characterizing minimum-energy β-sheets consisting of CH_3CO—(L-Val)$_6$—$NHCH_3$ chains

	Single polypeptide chain	Antiparallel sheet		Parallel sheet	
		Three chains	Five chains	Three chains	Five chains
Twist ⟨δ⟩,* deg	37.4	30.0	29.8	22.4	22.1
Euler angle, deg					
α		−101.0	−101.1	115.6	115.5
β		80.3	80.9	14.2	14.2
γ		−59.4	−59.3	−107.7	−107.9
Translational displacement, Å					
t_1		16.6	16.5	0.8	0.8
t_2		1.6	1.7	−4.9	−4.9
t_3		6.6	6.7	−0.8	−0.7
Energy, kcal/mol					
E_{total}†	18.1	−15.3	−51.7	−18.2	−57.5
E_{chain}‡	18.1	19.5	19.7	19.7	19.9
E_{inter}§	0.0	−73.9	−150.2	−77.3	−157.0

* Mean twist per two residues; see Eq. 7.
† Total energy of the β-sheet.
‡ Total intramolecular energy of each constituent chain.
§ Sum of all interchain energies in the β-sheet.

and antiparallel β-sheets of poly(LAla) and poly(LVal), respectively, agree fully with conclusions reached from CD, IR, and Raman spectroscopic measurements on heptapeptides of L-alanine and L-valine (13, 14). Because of the bulkiness of the branched valine side chain, the packing of chains in the parallel β-sheet is energetically more favorable, as indicated below. In the parallel-chain structure, valine side chains with $\chi^1 \approx 180°$ are oriented similarly, so that neighboring side chains on adjacent chains nest compactly against each other (Fig. 1*B*). In the antiparallel structure, however, side chains with $\chi^1 \approx 180°$ are oriented in opposite directions (Fig. 1*A*) so that alternate pairs of adjacent side chains will pack back-to-back, leaving unfilled space, or front-to-front; the latter results in overly close distances between CH_3 groups and hence in repulsive interactions (4, 14). Richardson's (4) empirical conclusions about the preferred orientations of the valine side chains in observed β-sheets are confirmed by these calculations. It is also of interest to point out that our calculated lower energies for parallel β-sheets of poly(LVal) chains account for the fact that the frequency of occurrence of valine residues in parallel β-strands is much higher than that in antiparallel β-strands (5, 15). (*iv*) The twist of a sheet decreases slightly in going from a three-chain to a five-chain structure. This tendency is in agreement with experimental observations (4). The total interchain energies E_{inter} for five-chain structures are slightly less than twice those for the corresponding three-chain structures. The differ-

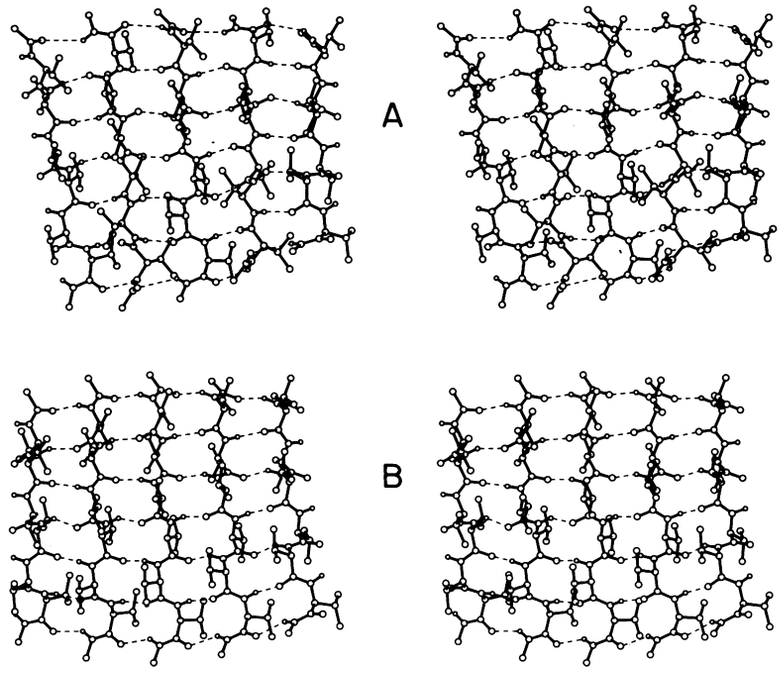

FIG. 1. Stereo drawings of the minimum-energy β-sheets with five CH_3CO—(L-Val)$_6$—$NHCH_3$ chains. (*A*) Antiparallel structure. (*B*) Parallel structure. Hydrogen atoms of the valyl side chains and of the NH_2- and COOH-terminal CH_3 groups have been omitted. Hydrogen bonds between neighboring chains are indicated by broken lines.

ence is about 2.4 kcal/mol and arises mostly from the interaction between nonneighboring chains in the five-chain structures. To some extent, this provides a small added stabilization to the sheets with more chains. (*v*) Considering the values of ω given in Table 2, we find that they range from $-172°$ through $\pm 180°$ to 177°. Furthermore, for the parallel structures, the deviations from $\omega = \pm 180°$ are somewhat larger and negative values of ω occur somewhat more frequently. Such a deviation from planarity of the peptide group in the direction of negative values of ω favors a right-handed twist for the β-sheet, as shown in Table 1. Because there is less flexibility of the hydrogen-bonded structure in parallel β-sheets, greater deformation of the planarity of the peptide group is needed to form a right-handed twist. In this sense, we arrive at the same conclusion as Salemme (16); namely, the deformation from planarity of the peptide group is a result of the twist of the sheet and the energy balance thereof.

Origin of the Right-Handed Twist. We now consider the factors that lead to a right-handed twist of the β-sheets. For this purpose, the minimum-energy results for an extended single chain CH_3CO—(L-Val)$_6$—$NHCH_3$ are also listed in Table 3. We see that the value of the average twist for such a single chain is 37.4°, considerably larger than those of minimum-energy β-sheets composed of the same chains. This indicates that intrachain interactions play the key role in forcing β-sheets of L-amino acid residues to adopt a right-handed twist, while hydrogen bonds between strands of sheets favor flat structures (1).

The next question is "what kind of interactions make the single extended poly(LVal) chain adopt the right-handed twist?" To answer this question, we take the regular single poly(LVal) chain, CH_3CO—(L-Val)$_6$—$NHCH_3$, as a model and compare the following three conformations: (*i*) the right-twisted chain with $\delta = 37°$, (*ii*) the flat chain with $\delta = 0°$, and (*iii*) the left-twisted chain with $\delta = -37°$. These conformations were obtained as follows. These values were fixed: $\omega = 180°$, $\chi^1 = 180°$, $\chi^{2,1} = \chi^{2,2} = 60°$; and the energy of a regular chain was minimized with respect to (ϕ,ψ), leading to structure A with $(\phi,\psi) = (-86.5°, 105.3°)$, located on the right side of the $n = 2$ line (1). Conformations B and C were chosen to have the same value of h but were located on the $n = 2$ line and on its left side, with $(\phi,\psi) = (-97.0°, 92.8°)$ and $(-107.5°, 80.3°)$, respectively. Then, (ϕ,ψ,ω) were kept fixed, and the energies of these three regular chains were minimized with respect to χ^1, $\chi^{2,1}$, and $\chi^{2,2}$, giving the conformations and energies listed in Table 4. Their stereo drawings are shown in Fig. 2 *A*, *B*, and *C*, respectively.

From Table 4, we see that all of the electrostatic energies are almost the same, but the nonbonded energy for the right-twisted chain with $\delta = 37°$ is about 4 kcal/mol lower than that of the left-twisted chain with $\delta = -37°$ and about 9 kcal/mol lower than that of the flat structure with $\delta = 0°$. The energy of the flat structure is so high because the distance between the $C^{\gamma 1}$ atom of the *i*th residue and the $C^{\gamma 2}$ atom of the $(i+2)$th residue is too small (see Fig. 2*B*), about 3.5 Å as shown in Table 4, and thus falls into the repulsive range (6). The distances between some of their attached H atoms are even shorter; e.g., the shortest one is only 2.2 Å. As a result, the nonbonded interaction between these two groups, $C^{\gamma 1}H_3$ and $C^{\gamma 2}H_3$, will contribute a nonbonded repulsion energy of about 1.4 kcal/mol. But, in the twisted structures (see Fig. 2 *A* and *C*), the distance between the two C^{γ} atoms increases to about 4.1 Å and the corresponding repulsive energy decreases rapidly, almost to zero. On comparing the two twisted structures, however, the energy preference of the right-twisted one over the left-twisted one is a result of the balance of many small interatomic nonbonded interactions involving the $C^{\gamma 1}H_3$ and $C^{\gamma 2}H_3$ groups, especially the interactions of $C^{\gamma 1}H_3$ and $C^{\gamma 2}H_3$ groups with the O and amide H atoms of the neighboring peptide groups. No individual pairwise interaction can be singled out as making a large contribution to determine the *direction* of twist; this conforms to the observations by von Heijne and Blomberg (17) that "inter- and intra-strand nearest-neighbor interactions of a rather unspecific character are responsible for the main stabilizing forces in the β-sheet."

The torsional energy of the right-twisted chain is about 0.4 kcal/mol lower than that of the left-twisted chain and about 3 kcal/mol lower than that of the flat structure. This is because the side-chain dihedral angles in the right-twisted chain deviate to a lesser extent from the values ($\pm 180°$, 60°, $-60°$) in comparison with both the left-twisted and the flat structure, as shown in Table 4.

Backbone Dihedral Angles in the Strongly Twisted β-Sheets of Poly(LVal) Chains. The minimum-energy β-sheet conformations obtained by starting from $\chi^1 = 60°$ and $-60°$ have backbone dihedral angles near $(\phi,\psi) \approx (-150°, 145°)$ and $(-134°, 150°)$, respectively. Although these values of (ϕ,ψ) are close to those defined for flat β-sheets (18), the energies of poly(LVal) β-sheets with these conformations are very high, as mentioned above. Therefore, they are not stable structures.

On the other hand, the stable structures obtained by energy minimization starting from $\chi^1 = 180°$ have dihedral angles near $(\phi,\psi) \approx (-90°, 105°)$. This indicates that strongly right-twisted β-sheets with β-branched residues, such as valine, can exist with backbone dihedral angles that lie in the large low-energy region of the upper left quadrant of the (ϕ,ψ) map but far from the β-sheet conformations usually considered. These findings account for the fact that observed values of (ϕ,ψ) in β-sheets are distributed over a wide range (see, e.g., figure 7 of ref. 4

Table 4. Parameters characterizing the assigned right-twisted, flat, and left-twisted structures of the regular single chain CH_3CO—(L-Val)$_6$—$NHCH_3$

	Right twisted	Flat	Left twisted
Twist (δ),* deg	37.0	0	−37.0
Dihedral angles,† deg			
ϕ	−86.5	−97.0	−107.5
ψ	105.3	92.8	80.3
χ^1	177.8	171.5	−175.4
$\chi^{2,1}$	56.1	45.7	57.8
$\chi^{2,2}$	65.3	52.2	67.5
Energy, kcal/mol			
E_{TOT}‡	18.3	30.5	23.4
E_{ES}§	26.3	26.2	26.6
E_{NB}¶	−8.5	0.7	−4.2
E_{TOR}‖	0.5	3.6	0.9
Distance between some critical atoms, Å			
$d_{C^{\gamma 1}\cdots C^{\gamma 2}}$**	4.1	3.5	4.1
$d_{H^{\gamma 1}\cdots H^{\gamma 2}}$††	2.6	2.2	2.7

* Twist per two residues; see Eq. 6.
† ω was fixed at 180° to compare these conformations at the same value of h, the rise per residue.
‡ Total energy of the single chain.
§ Total electrostatic energy of the single chain.
¶ Total nonbonded energy of the single chain.
‖ Total torsional energy of the single chain.
** Distance between the $C^{\gamma 1}$ atom of the *i*th residue and the $C^{\gamma 2}$ atom of the $(i+2)$th residue.
†† Shortest distance between the hydrogen atoms attached to the $C^{\gamma 1}$ atom of the *i*th residue and the $C^{\gamma 2}$ atom of the $(i+2)$th residue.

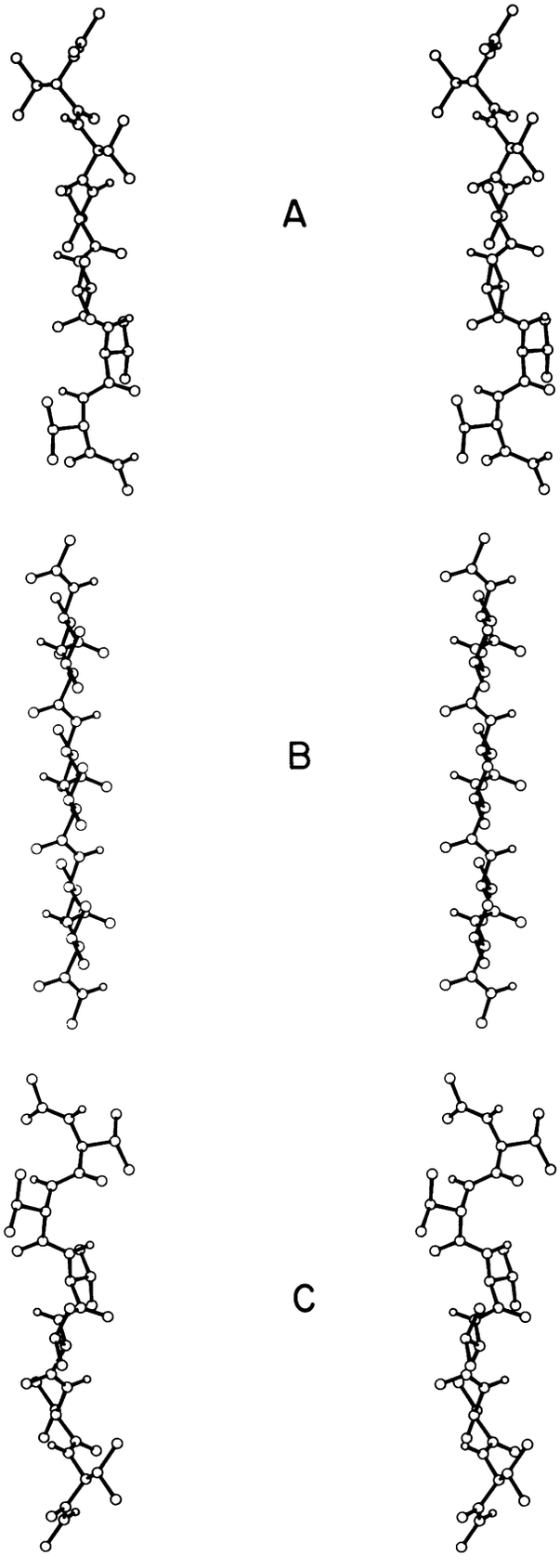

FIG. 2. Stereo drawings of the regular single CH_3CO—(L-Val)$_6$—$NHCH_3$ chain in three corresponding states. (*A*) Right-handed twist with $\delta = 37°$ ($\phi = -86.5°$, $\psi = 105.3°$). (*B*) Flat structure with $\delta = 0°$ ($\phi = -97.0°$, $\psi = 92.8°$). (*C*) Left-handed twist with $\delta = -37°$ ($\phi = -107.5°$, $\psi = 80.3°$). Hydrogen atoms are omitted as in Fig. 1.

and figure 4 of ref. 19) while maintaining a hydrogen-bonded structure.

CONCLUSION

The right-handed twist observed for both antiparallel and parallel β-sheets in proteins can be accounted for in terms of interatomic energies. It is the intrachain nonbonded interaction energy that plays the key role in forcing β-sheets of L-amino acid residues to adopt a right-handed twist. This conclusion differs from that of Raghavendra and Sasisekharan (20), who suggested that the observed twist results from interchain interactions. However, their model consisted of a pair of antiparallel β-strands, each of which had only one L-alanine residue with CH_3CO and $NHCH_3$ end groups. It is unlikely that such short chains can serve as a model for the twist of a β-sheet because of the large influence of the end groups (1). In addition, as pointed out by Lotz *et al.* (21), "the validity [of the calculations in ref. 20] might be questioned, since not even linear, but actually colinear NH· · ·OC hydrogen bonds have been considered, which is a situation seldom encountered in practice."

Finally, because our results are independent of environmental effects in globular proteins (to which the twist might have been attributed), these energy-minimized right-twisted β-sheets should also be expected to occur in fibrous proteins. This has indeed been observed recently by Lotz *et al.* (21).

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1. Chou, K. C., Pottle, M., Némethy, G., Ueda, Y. & Scheraga, H. A. *J. Mol. Biol.*, in press.
2. Chothia, C. (1973) *J. Mol. Biol.* **75,** 295–302.
3. Ooi, T., Scott, R. A., Vanderkooi, G. & Scheraga, H. A. (1967) *J. Chem. Phys.* **46,** 4410–4426.
4. Richardson, J. S. (1981) *Adv. Protein Chem.* **34,** 167–339.
5. Lifson, S. & Sander, C. (1979) *Nature (London)* **282,** 109–111.
6. Momany, F. A., McGuire, R. F., Burgess, A. W. & Scheraga, H. A. (1975) *J. Phys. Chem.* **79,** 2361–2381.
7. Sugeta, H. & Miyazawa, T. (1967) *Biopolymers* **5,** 673–679.
8. Fraser, R. D. B. & MacRae, T. P. (1973) *Conformation in Fibrous Proteins* (Academic, New York), pp. 134–135.
9. Dennis, J. E. & Mei, H. H. W. (1975) *Technical Report No. 75-246, Department of Computer Sciences* (Cornell Univ., Ithaca, NY).
10. Powell, M. J. D. (1964) *Comput. J.* **7,** 155–162.
11. Salemme, F. R. & Weatherford, D. W. (1981) *J. Mol. Biol.* **146,** 101–117.
12. Salemme, F. R. & Weatherford, D. W. (1981) *J. Mol. Biol.* **146,** 119–141.
13. Balcerski, J. S., Pysh, E. S., Bonora, G. M. & Toniolo, C. (1976) *J. Am. Chem. Soc.* **98,** 3470–3473.
14. Toniolo, C. & Palumbo, M. (1977) *Biopolymers* **16,** 219–224.
15. Toniolo, C. (1978) *Macromolecules* **11,** 437–438.
16. Salemme, F. R. (1981) *J. Mol. Biol.* **146,** 143–156.
17. von Heijne, G. & Blomberg, C. (1978) *Biopolymers* **17,** 2033–2037.
18. Pauling, L. & Corey, R. B. (1953) *Proc. Natl. Acad. Sci. USA* **39,** 253–256.
19. Némethy, G. & Scheraga, H. A. (1977) *Q. Rev. Biophys.* **10,** 239–352.
20. Raghavendra, K. & Sasisekharan, V. (1979) *Int. J. Pept. Protein Res.* **14,** 326–338.
21. Lotz, B., Gonthier-Vassal, A., Brack, A. & Magoshi, J. (1982) *J. Mol. Biol.* **156,** 345–357.