**vpu Transmembrane Peptide Structure Obtained by Site-Specific Fourier Transform Infrared Dichroism and Global Molecular Dynamics Searching**

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**ABSTRACT** The recently developed method of site-directed Fourier transform infrared dichroism for obtaining orientational constraints of oriented polymers is applied here to the transmembrane domain of the vpu protein from the human immunodeficiency virus type 1 (HIV-1). The infrared spectra of the 31-residue-long vpu peptide reconstituted in lipid vesicles reveal a predominantly α-helical structure. The infrared dichroism data of the 13C-labeled peptide yielded a helix tilt $\beta = (6.5 \pm 1.7)°$ from the membrane normal. The rotational pitch angle $\omega$, defined as zero for a residue located in the direction of the helix tilt, is $\omega = (283 \pm 11)°$ for the 13C labels Val13/Val20 and $\omega = (23 \pm 11)°$ for the 13C labels Ala14/Val21. A global molecular dynamics search protocol restraining the helix tilt to the experimental value was performed for oligomers of four, five, and six subunits. From 288 structures for each oligomer, a left-handed pentameric coiled coil was obtained, which best fits the experimental data. The structure reveals a pore occluded by Trp residues at the intracellular end of the transmembrane domain.

**INTRODUCTION**

The structural determination of membrane proteins is still a difficult task for x-ray crystallography and solution NMR methods. The transmembrane domains of ion channels have been approached by molecular modeling (Sansom, 1998; Sansom et al., 1998). In these cases, orientational information combined with a global molecular dynamics (MD) search can be used to obtain a highly reliable structural model (Kukol et al., 1999). Fourier transform infrared (FTIR) spectroscopy has been shown to be a useful tool for secondary structural determination of proteins (Byler and Susi, 1986) and monitoring even subtle conformational changes in bacteriorhodopsin (Torres et al., 1995; Cladera et al., 1996). In this work we have used the recently developed method of site-specific infrared dichroism (Arkin et al., 1997) to obtain the transmembrane helix tilt and the rotation angles of specific residues about the helix axis for the HIV-1 vpu protein.

The 81-residue vpu protein belongs to the auxiliary proteins of the human immunodeficiency virus type 1 (HIV-1) (Cohen et al., 1988; Strebel et al., 1988). It is composed of an N-terminal domain, where residues 1–5 are probably extracellular; a 22-residue segment that spans the membrane; and the cytoplasmic C-terminal domain (Maldarelli et al., 1993). vpu forms homooligomers of at least four subunits, as detected by gel electrophoresis (Maldarelli et al., 1993). The C-terminal cytoplasmic domain is responsible for the degradation of one of the HIV-1 coreceptor molecules, CD4 (Schubert et al., 1996a; Schubert and Strebel, 1994), allowing the env glycoprotein to be transported to the cell surface. The N-terminal domain is responsible for virus particle release (Schubert et al., 1996a), but the molecular basis of these actions is unknown. It has been shown that phosphorylation of the cytoplasmic domain is essential for CD4 degradation, although it is not absolutely required for virus particle release (Friborg et al., 1995; Schubert et al., 1996a; Schubert and Strebel, 1994). Virus particle release is not specific to HIV-1, because vpu is capable of enhancing the particle release of different retroviruses (Gottlinger et al., 1993; Xiao Jian et al., 1992).

The transmembrane domain has been studied independently of the cytoplasmic domain. By analogy with the M2 protein of Influenza A virus (Lamb and Pinto, 1997), it has been suggested that the transmembrane part of vpu may act as an ion channel (Klimkait et al., 1990; Maldarelli et al., 1993; Schubert and Strebel, 1994; Strebel et al., 1989). In fact, ion channel activity for monovalent cations has been observed in Xenopus oocytes and in planar lipid bilayers (Schubert et al., 1996b; Ewart et al., 1996). Recently, however, controversial results have been reported. vpu expression in oocytes reduces basal membrane conductance (Coady et al., 1998), whereas vpu expression in Escherichia coli and eukaryotic COS cells enhances membrane permeability to charged molecules (Gonzales and Carrasco, 1998).

The method of site-specific infrared dichroism (Arkin et al., 1997) combined with a global MD search has recently yielded a structure for the tetrameric influenza M2-H⁺ channel that is not only in accordance with NMR data, but is also consistent with results obtained by the use of mutagenesis that are available in the literature (e.g., Holsinger et al., 1994). Because the oligomerization number of vpu is not known, we extend the method, first by undertaking the MD search for different oligomerization states, as the orientational data are independent of the helix oligomerization. Second, we introduce two 13C-labeled residues, instead of one, in the same peptide, to enhance the signal-to-noise ratio. Third, we modify the search by releasing the con-
strait of the rotation angles and selecting the correct model from the pool of structures by subsequent analysis of the geometry. This extension is necessary because the low tilt of the vpu helices does not create substantial energy differences between models with different rotation angles for a specific residue.

The combined spectroscopic and molecular modeling approach yields in this case a single pentameric structure, which answers the question of vpu oligomerization and gives a detailed molecular structure of the transmembrane domain of the protein.

**MATERIALS AND METHODS**

**Peptide purification and reconstitution**

Synthetic peptides corresponding to the N-terminal domain of the HIV-1 vpu sequence found in different isolates (BH10, HXB3, MCK) (OWL composite database, version 30.02, 1998) were made by standard solid-phase F-moc chemistry, cleaved from the resin with trifluoroacetic acid, and lyophilized. The sequences corresponding to residues 1–31 are 1) MQPIQIAIVALVV 13C1-AILAIVV 13C1-VWSIVIIEYRK and 2) MQPIQIAIVALVV 13C1-AILAIVV 13C1-VWSIVIIEYRK, each with two carbonyl 13C amino acids (Cambridge Isotopes Laboratories, Andover, MA) at positions Val5, Val15 and at positions Ala6, Val21, respectively. After the lyophilized peptides were dissolved in 2 ml of trifluoroacetic acid (final concentration ~5 mg/ml), they were injected into a 20-ml Jupiter SC4-300 Å column (Phenomenex, Cheshire, England) equilibrated with 95% H2O, 2% (v/v) acetonitrile, and 3% (v/v) 2-propanol. Peptide elution was achieved with a linear gradient to a final solvent composition of 5% H2O, 20% trifluoroethanol, 28% acetonitrile, and 47% 2-propanol (BioRad Sprint; Perceptive Biosystems, Cambridge, MA). All solvents contained 0.1% (v/v) trifluoroacetic acid. Peptide-containing fractions were checked by mass spectrometry, and the pooled fractions were lyophilized and dissolved in a solution of 5% (v/v) β-octylglycopyranoside (Melford Laboratories, Ipswich, England) and 12.5 mg/ml dimyristoylphosphocholine (Sigma). After 24 h of dialysis in water, 6 h of dialysis in 10 mM phosphate K2HPO4 - KH2PO4 buffer (pH 7.0) was performed.

**Infrared spectroscopy**

FTIR spectra were recorded on a Nicolet Magna 560 spectrometer (Madison, WI) equipped with a high-sensitivity liquid nitrogen-cooled MCT/A detector. Attenuated total reflection (ATR) spectra were measured with a 25-reflection ATR accessory from Graseby Specac (Kent, England) and a wire grid polarizer (0.25 mm; Graseby Specac). Two hundred microliters of sample (~2.5 mg/ml protein and 12.5 mg/ml lipid) were dried onto a trapezoidal Ge internal reflection element (50° × 20 mm) under a stream of nitrogen. After the instrument was extensively purged with dry nitrogen, 1000 interferograms were averaged for every sample and processed with 1-point zero filling Happ-Genzel apodization.

Fourier self-deconvolution (FSD) (Kauppinen et al., 1982) was applied to the spectra in the amide I region to separate the overlapping 12C and the site-specific 13C amide I peaks. The enhancement corrected for the natural abundance of 13C by the equation

\[ \frac{R_{\text{corr}}}{R_{\text{site}}} = \frac{R_{\text{helix}}}{R_{\text{helix}} + r(R_{\text{helix}} - R_{\text{site}})} \],

where \( R_{\text{helix}} \) and \( R_{\text{site}} \) are dichroic ratios for the helix (12C) and the site-specific (13C) amide I mode, respectively, and \( r = 0.091 \) denotes the fraction of randomized 13C in the 22-residue transmembrane part, considering the 1% natural abundance of 13C. For transmission spectra, 50 μl of sample was dried on a CaF2 window of 15 mm diameter. D2O exchange was performed by incubating the sample for 2 h in 99% D2O before drying. To monitor the D2O exchange, the amide II band between 1525 cm^-1 and 1570 cm^-1 was integrated, and the area \( A_l \) was divided by the total amide I area \( (y = A_l/A) \) to account for differences in protein concentration. The amount of D2O exchange was then calculated by dividing the corrected amide II area in D2O \((y_{D2O})\) by \( y_{H2O} \).

**Data analysis**

The data were analyzed according to the theory of site-specific dichroism presented in detail elsewhere (Arkin et al., 1997), with the extensions described in Kukol et al. (1999). Briefly, the measured dichroism, the absorption ratio \( \beta \), between parallel and perpendicular polarized light \( \beta = A_l/A_\perp \), of a particular transition dipole moment is a function of its spatial orientation. For the amide I mode of an α-helical protein the geometric relation between the transition dipole moment (mainly the C=O bond) and the helix is known from fiber diffraction studies (Tsutobi, 1962). Therefore, by measuring the orientation of the amide I transition dipole one can determine the helix tilt angle \( \beta \) and the rotational pitch angle \( \omega \) of the specific dipole moment about the helix axis. The rotational pitch angle \( \omega \) is arbitrarily defined as 0° when the transition dipole moment, the helix director, and the \( z \) axis all reside in a single plane. Thus, measuring the site-specific dichroism \( R_{\text{site}} \) of the 13C amide I mode at a particular label and the helix dichroism \( R_{\text{helix}} \) allows calculation of the helix tilt \( \beta \) and the rotational pitch angle \( \omega \) of a particular label, as detailed by Arkin et al. (1997), if measurements from two samples with labels at different \( \omega \) are analyzed together. Note that the difference in \( \omega \) between two consecutive residues is assumed to be 100°, as in a standard α-helix. To enhance the 13C amide I mode intensity we extend the formerly presented method by introducing two labels at positions \( i \) and \( i + 7 \). These two labels have approximately the same rotational pitch angle \( \omega_i \). To enhance the 13C site was performed by incubating the sample for 2 h in 99% D2O before drying.

**Molecular modeling**

A global search with respect to rotation about the helix axis, assuming multimeric symmetry, was carried out as described in detail elsewhere (Adams et al., 1995). In brief, all calculations were performed with the parallel processing version of the Crystallography and NMR System (CNS Version 0.3) (Brunger et al., 1998). We have used the OPLS parameter set with a united atom topology, which explicitly represents the polar hydrogen and aromatic side-chain atoms (Jorgensen and Tirado-Rives, 1988). All calculations were carried out in vacuo with the initial coordinates of a canonical α-helix (3.6 residues per turn). Symmetric tetramers, pentamers, and hexamers \((n = 4, 5, 6)\) were generated from the sequence IAIVALV-VAIIIAIVVWSIVII by replicating the helix and rotating it by 360/\( n \) around the center of the multimer. The transmembrane sequence was predicted on the basis of hydrophy analysis. An initial crossing angle of 25° for left-handed and −25° for right-handed structures was introduced by rotating the long helix axis with respect to the long bundle axis. The symmetrical search was carried out by applying a rotation to all helices simultaneously between \( \varphi = 0° \) and \( \varphi = 360° \) in 10° steps. Four trials were carried out for each starting structure, using different initial random atom velocities in each case at both right- and left-handed crossing angles, yielding 36 × 4 × 2 = 288 structures. Each structure was subjected to a simulated annealing and energy minimization protocol. Clusters of similar structures were defined such that the root mean square deviation (RMSD) of the coordinates between two structures within a cluster was not larger than 1.0 Å; a cluster was formed by a minimum of 10 structures. For each
cluster an average structure was calculated, energy minimized, and then subjected to the same simulated annealing protocol as used in the systematic search.

Orientation refinement

To take into account the results obtained from the site-directed dichroism analysis, we have incorporated a new orientation refinement energy term in all molecular dynamics and energy minimization calculations:

\[ E = k_{dichro}(\theta - \theta_0)^2 \]  

where \( \theta \) represents the actual angle and \( \theta_0 \) the target angle. The overall weight constant \( k_{dichro} \) for these orientational constraints was chosen to be \( k_{dichro} = 800 \text{ kcal/rad}^2 \), determined empirically by selecting the minimum value necessary to obtain an identical outcome from MD protocols with different constants. According to the experimental data, two different kinds of restraints can be applied (see Fig. 1):

1. A helix tilt restraint is applied by defining a vector connecting every \( C_{\alpha} \) of residue \( i \) and \( C_{\alpha} \) of residue \( i + 7 \). The angle between these vectors and the \( z \) axis is then set to the value obtained for the helix tilt (the angle \( \beta \)).

2. The four site-specific dichroism restraints are applied by setting the target angles \( \theta \) between the corresponding \(^{13}\text{C}==\text{O} \) bonds of Val\(^{13}\), Val\(^{20}\), Ala\(^{14}\), and Val\(^{13}\) and the \( z \) axis to that obtained from the experiment. These angles are a function of the helix tilt \( \beta \), the rotational pitch angle \( \omega \) (Arkin et al., 1997), and the angle between the transition dipole moment and the helix director, which is known from fiber diffraction studies (Tsuboi, 1962) to be 39° and is \( \alpha = 180° - 39° = 141° \), according to our definition:

\[ \theta = 180° - \arccos(\cos \alpha \cos \beta - \sin \alpha \cos \omega \sin \beta) - 17° \]  

Interaction energy

The average interaction energy per residue gives the nonbonded interaction energy of a particular residue on one helix monomer with all other residues on all other helices.

RESULTS AND DISCUSSION

Secondary structure and membrane incorporation

Transmission FTIR spectra of the amide I and amide II regions of the \( \text{vpu} \) peptide reconstituted in lipid vesicles are shown in Fig. 2. From the dominant amide I intensity centered at 1655 cm\(^{-1} \) with a half-maximum peak width of 18 cm\(^{-1} \) (in H\(_2\)O), it can be concluded that the peptide is mostly \( \alpha \)-helical (Braiman and Rothschild, 1988). The peak centered at 1615 cm\(^{-1} \) arises from the \(^{13}\text{C} \)-labeled amino acids (Tadesse et al., 1991). Other contributions arise from the extramembranous part of the peptide, which contains 29% of the total amino acids.

The measurement of the amount of deuterium exchange after a period of 2 h, obtained by integration of the amide II area between 1525 cm\(^{-1} \) and 1555 cm\(^{-1} \) (see Fig. 2), gives a 46 ± 7% exchange, more than is expected from the 29% extramembranous portion. The results did not change after 6 h of incubation. Thus in addition to the extramembranous part, (24 ± 10)% of the transmembrane amide protons exchange with D\(_2\)O. This corresponds to 5 ± 2 amino acid residues that are accessible from the solution. This result can be discussed in terms of the question of ion channel formation by \( \text{vpu} \) (see below).

FIGURE 1  Schematic diagram of the orientational restraints employed during the molecular dynamics and energy minimization calculations. The helix tilt was restrained to the angle \( \beta \) by defining a vector between every \( C_{\alpha} \) of residue \( i \) and \( C_{\alpha} \) of residue \( i + 7 \), shown as lines. The \( \text{C}==\text{O} \) bonds of the labeled residue pair Val\(^{13}\), Val\(^{20}\) and the residue pair Ala\(^{14}\), Val\(^{13}\) are also shown.

FIGURE 2  Transmission FTIR spectra of the amide I and amide II area of the Val\(^{13}\)/Val\(^{20}\) labeled \( \text{vpu} \) peptide in H\(_2\)O (—), after 2 h of incubation in D\(_2\)O (— — —), and after 6 h of incubation in D\(_2\)O (· · · · · · ). The intensity is normalized to the amide I peak maximum.
Transmembrane orientation

It can be seen that the double-labeled $^{13}$C samples result in a clearly observable amide I $^{13}$C intensity, even without Fourier self-deconvolution (Fig. 3). The helix- and site-specific dichroisms (Table 1) obtained from the ATR spectra, as shown in Fig. 3, are similar. The quantitative analysis of the dichroism proceeds by combining each measurement of a sample with the label in position Val$_{13}$/Val$_{20}$ and each measurement with the label in position Ala$_{14}$/Val$_{21}$, yielding 30 different pairwise results. The final average of the helix tilt is $\beta = (6.5 \pm 1.7)°$, and the rotational pitch angle is $\omega = (283 \pm 11)°$ for Val$_{13}$/Val$_{20}$. From these values the angle between the C=O bond and the $z$ axis can be calculated with Eq. 3. The angles are $21°$ and $16°$ for Val$_{13}$/Val$_{20}$ and Ala$_{14}$/Val$_{21}$, respectively.

Molecular model of the vpu transmembrane domain

Assuming tetrameric, pentameric, and hexameric oligomerization, 288 structures have been calculated for each oligomerization state by incrementing the helix rotation parameter $\phi$ in steps of $10°$. Three different search protocols were used: 1) no experimental restraints were applied, 2) the helix tilt restraint was applied, 3) both helix tilt restraint and site-specific rotational restraints were applied. Upon the application of both restraints, no final cluster of structures could be found, based on the criteria of maximum number of structures forming a cluster and lowest energy of the average structure (data not shown). We have therefore performed the same search protocol without constraining the angle between the C=O bond and the $z$ axis. Because this angle is a function of both the helix tilt $\beta$ and the rotational pitch angle $\omega$, removing this constraint generates structures, where the rotational pitch angle is not fixed at the experimental value. The parameters of the average cluster structures after energy minimization are given in Table 2. Inspection of the rotational pitch angles in Table 2 shows that pentamer structure 7 with $\omega_{\text{Val}_{13}} = 316°$ has the rotational pitch angle closest to the experimental value, $\omega = (283 \pm 11)°$. Comparison of the energy of this structure, $E = -182$ kcal/mol$^{-1}$, with the other pentamer structures shows that it is also among the lowest energy structures. But only the experimentally determined pitch angle is used to choose this structure as a model of the vpu transmembrane domain.

Fig. 4 shows the structure of the vpu transmembrane domain. It is notable that the residue Trp$_{22}$ is pointing into the channel lumen, thus occluding the pore, as can be seen in Fig. 5. The only hydrophilic residue, Ser$_{23}$, is pointing outward to the lipid phase, whereby the hydroxyl group is hydrogen-bonded to the carbonyl backbone atoms. Fig. 5 reveals that the pore is accessible up to Trp$_{22}$. The average interaction energy per residue is shown in Fig. 6. The periodicity of the maxima in this graph represents the periodicity of the helix, whereby Trp$_{22}$ contributes most to the interaction energy.

Biological implications

The assumption that vpu forms ion channels is controversially discussed in the literature. In fact there is experimental evidence that low-level expression of vpu reduces membrane conductance in Xenopus oocytes (Coady et al., 1998). In the same study it is questioned that conventional oocyte expression studies are the appropriate method for addressing the formation of ion channels by vpu, because the amount of vpu mRNA (46 ng) often used is lethal within 2 days (Coady et al., 1998). However, conductance measurements in artificial lipid bilayers can be used to show the formation of ion channels. The single-channel traces of Schubert et al. (1996b), from planar bilayers, are clearly indicative of ion channel formation. But it remains unclear why the authors apparently introduced a Gln$^2$-Glu$^2$ muta-
tion in the synthetic vpu peptide that is not found in naturally occurring viral strains. The negative charge of deprotonated carboxylic acids may have a significant impact on ion channel function, even if they are located outside the membrane (e.g., Kukol and Neumann, 1998). The single-channel traces of Ewart et al. (1996) obtained with the wild-type vpu peptide are very noisy, and the conductance varies between 14 and 280 pS. Conductance measurements in lipid bilayers are sensitive to artifacts caused by aggregates of hydrophobic peptides (Tosteson et al., 1988), as pointed out by Coady et al. (1998). This could not be completely ruled out by looking at the data of Ewart et al. (1996). Our results provide some support for the ion channel hypothesis. Although the presented structure has a pore occluded by Trp residues, the deuterium exchange experiments, shown in Fig. 2, indicated that at least part of the transmembrane domain (5 ± 2 amino acid residues) is water accessible. This is compatible with the presence of a partially open pore like the one seen in Fig. 5. In this structure 16 amino acid residues are water accessible, as seen from the extracellular side. Thus the given structure may represent the closed conformation of an ion channel.

### Limitations of the constrained MD search and site-directed infrared dichroism

The method of site-directed infrared dichroism has been applied to the Influenza M2 peptide (Kukol et al., 1999). In that instance it was possible, by introducing both the helix tilt and the rotational constraint, to obtain a unique model based on the criteria of lowest cluster energy and maximum

### Table 1 Helix dichroism $\beta_{\text{helix}}$ and site-specific dichroism $\beta_{\text{site}}$ and lipid asymmetric stretching modes $\beta_{\text{lipid}}$ for the two vpu peptides as noted

<table>
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<th>Peptide</th>
<th>$\beta_{\text{helix}}$</th>
<th>$\beta_{\text{site}}$</th>
<th>$\beta_{\text{lipid}}$</th>
<th>$\beta$</th>
<th>$\omega$</th>
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<td>Val$^{13}$/Val$^{20}$</td>
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Also shown are the calculated lipid order parameters $\beta_{\text{lipid}} = (3\cos^2\beta - 1)/2$ (Braiman and Rothschild, 1988), the helix tilt angle $\theta$, and the rotational pitch angle $\omega$ about the helix axis.

### Table 2 Parameters of averaged structures obtained from the global search protocol, whereby only the helix tilt is constrained

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<th>No. of structures</th>
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<td>140°</td>
<td>20°</td>
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</table>

The energy ($E$) of each structure, number of structures considered for the average, helix crossing angle $\Omega$, helix rotation parameter $\phi$, and rotational pitch angles $\omega_{\text{val}}$, $\omega_{\text{Ala}}$ are given. The angles are averages over all helices of a structure. Dashes denote cases in which $\omega$ shows large variations between individual helices (more than 60°) and the average could not be determined.
number of structures converging to a single cluster. In our case, the unclear discrimination among the different structures according to the criteria of lowest energy and highest number of substructures forming a cluster is a result of the inherent low tilt angle $\beta$ of the examined system. One of the experimental energy refinement terms employed during the

FIGURE 4  Ribbon diagrams of the vpu transmembrane structure, shown from the N-terminus from Ile$^6$ to Ile$^{27}$ (top) and from the side (bottom). The residues Trp$^{22}$ and Ser$^{23}$ are shown in a ball-and-stick display. The figure was created with Molscript (Kraulis, 1991).

FIGURE 5  Slices of the vpu transmembrane structure. From top to bottom: Ile$^6$-Val$^{12}$, Val$^{12}$-Ile$^{17}$, Ile$^{17}$-Trp$^{22}$, and Trp$^{22}$-Ile$^{27}$. The figure was created with Molscript (Kraulis, 1991).
MD simulation is dependent on the angle $\theta$ between the C=O bond and the $z$ axis, which is a function of the helix tilt $\beta$ and rotational pitch angle $\omega$ of the specific residue. Thus inserting Eq. 3 into Eq. 2, one obtains

$$E = k_{\text{dichro}}((180^\circ - \arccos(\cos \alpha \cos \beta \\
- \sin \alpha \cos \omega \sin \beta) - 17^\circ - \theta_0)^2$$

(4)

This gives the refinement energy as a function of $\omega$ and $\beta$. By plotting Eq. 4 (Fig. 7) for different helix tilt angles $\beta$, it becomes apparent that the energetic discrimination among $\omega$ values is low at a tilt angle of $\beta = 6.5^\circ$ compared to $\beta = 31^\circ$, as obtained from the Influenza M2 peptide (Kukol et al., 1999).

Furthermore, the method of site-directed dichroism is limited to determining $\omega$ at low helix tilt angles. If the helix tilt angle is zero, the site-specific dichroism is equal to the helix dichroism and the rotational pitch angle $\omega$ cannot be obtained. This becomes apparent in Fig. 8, where the site-specific dichroism is plotted as a function of $\omega$ and the helix tilt $\beta$. The difference in the site-specific dichroism is at maximum for different $\omega$ when the helix is tilted by $45^\circ$. In our case $\omega$ has been obtained from the averaging of 30 different results. This allows the determination of $\omega$ to a reasonable accuracy and the subsequent selection of structures that correspond to the experimentally derived angle.

The same limitations also apply to orientational constraints derived from solid-state NMR spectroscopy, which have been recently obtained for the Influenza M2 peptide (Kovacs and Cross, 1997).

CONCLUSIONS

It has been shown that the transmembrane part of the HIV-1 vpu peptide forms an $\alpha$-helical structure in a lipid environment, where the helices are tilted by $\beta = (6.5 \pm 1.7)^\circ$ and the rotational pitch angle of Val$^{13}$ is $\omega = (283 \pm 11)^\circ$. A molecular modeling approach including the experimental data gave a pentameric structure of the vpu peptide, although the oligomerization state was not known a priori. This structure forms the basis for further investigations by biophysical techniques.

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REFERENCES

Kukol and Arkin

HIV-1 vpu Transmembrane Peptide Structure


