Supporting Information: Conformational Discrepancies between Molecular Dynamics Force Fields and Vibrational Spectroscopy in Short Alanine-Based Peptides

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Simulations

As further support of the sensitivity of the VCD signal, Figure S1 also displays simulations of 100% PPII, 100% alpha right-handed helix and 100% beta conformations. Whereas the IR exhibits differences in intensity distribution and band position, the VCD exhibits different significantly different signals for different conformations. The alpha helical conformation exhibits a band shape that will be referred to as a positive couplet, and this couplet can be recognized as the opposite of the PPII signal.

We used the superpositions of two-dimensional Gaussian and plateau functions to describe the conformational distributions reported by Best and Hummer for the force field ff03\(^1\). As shown in Table S1, this yielded practically identical J-coupling constants.

FRET Analysis

Energy transfer efficiencies from the steady-state as well as time-resolved fluorescence measurements were calculated by using eqs. S1 and S-2 and the corresponding \( R_{eff} \) values have been calculated using eq. S-3 for steady-state and eq. S-4 for the time-resolved measurement. Note that a biexponential decay function allowed for satisfactory fitting of all lifetime decay traces (\( \chi^2 < 1.1 \)), such that we have employed average fluorescence lifetimes (\( \tau_{avg} \)), calculated as \( \tau_{avg} = \tau_1 \alpha_1 + \tau_2 \alpha_2 \), in eq. 3; \( \tau_1 \), \( \tau_2 \) are the lifetime components from the biexponential fitting and \( \alpha_1 \) and \( \alpha_2 \) are their corresponding pre–exponential factors.

\[
E = 1 - \frac{F_{DA}}{F_D} \quad \text{(S-1)}
\]

\[
E = 1 - \frac{\tau_{DA}}{\tau_D} \quad \text{(S-2)}
\]

\[
R_{eff} = R_0 \left( \frac{1-E}{E} \right)^{1/6} \quad \text{(S-3)}
\]
\[ R_{\text{eff}} = (1 - F) \left\{ R_0^6 \left( \frac{1}{E_{tr}} - 1 \right) \right\}^{1/6} + FR_{vdw} \quad (S-4) \]

where \( F = E_{ss} - E_{ir} \) and \( R_{vdw} \) was assumed to be 4 Å, according to ref.\(^2\).

Note that, the FRET efficiencies from the time-resolved experiments need to be “corrected” for a static quenching component (\( F \) in eq S-4), which takes into account a small fraction of conformations, which are in contact (with an assumed van-der-Waals distance 4.0 Å) when excitation occurs, and which escape from the time-resolved detection due to immediate quenching by FRET.
Table S1. J-coupling constants calculated by using the superposition of different distribution profiles (two-dimensional Gaussian and plateau) to describe the conformational distribution of a single alanine residue in A5W based on the results of a MD simulation with a modified AMBER force field denoted as ff03*. DFT-based Karplus parameters were used for the calculations.3

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<tr>
<th></th>
<th>Plateau [Hz]</th>
<th>Gaussian [Hz]</th>
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<tbody>
<tr>
<td>$^2J(H^\alpha H^\alpha)$</td>
<td>5.78</td>
<td>5.78</td>
</tr>
<tr>
<td>$^2J(H^\alpha C')$</td>
<td>0.40</td>
<td>0.39</td>
</tr>
<tr>
<td>$^2J(H^\beta C')$</td>
<td>1.38</td>
<td>1.38</td>
</tr>
<tr>
<td>$^3J(H^\alpha C^\beta)$</td>
<td>3.62</td>
<td>3.62</td>
</tr>
<tr>
<td>$^1J(NC^\alpha)$</td>
<td>11.43</td>
<td>11.43</td>
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Figure S1. Simulations of the IR and VCD amide I band profile for a five-residue peptide. The black line reflects 100% PPII (-70°, 145°), the red line 100% alpha helical conformations (-60°, -60°) and the blue line is 100% β-strand (-120°, 120°) for each of the five residues.
Figure S2. Simulations of the amide I’ band profile of the IR and VCD spectrum of a five residue poly-alanine peptide with the red line using a pseudo-Gaussian distribution of PPII coordinates (centered around -70,145) and the black line using a uniform distribution of conformations in the PPII trough of the Ramachandran plot. The black line is barely noticeable because of the close agreement between the simulations.
Figure S3. The conformational distribution for residue 4 of A₅ obtained from MD simulations with a modified AMBER force field denoted as ff03*.¹ The list of coordinates was kindly provided by Dr. Best.
References

