Predicting the conformational preferences of proteins using a physics-based free energy method

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1 The confinement method produces correct results in control experiments

As a first step, we performed several control experiments to verify that our implementation of the confinement method produces results compatible with previous calculations reported in the literature.

The method has previously been applied to a 16 amino acid residue β-hairpin from protein G, known as BHP[?]. We calculated the free energy difference between two different conformations of the peptide: (1) the native conformation, called bhp1, with a two-stranded β-sheet; and (2) a conformation, called bhp3, which has a three-stranded β-sheet. Analysis of long (4 μs) equilibrium simulations[?,?] shows that bhp1 is the more favorable configuration by 1.8 kcal/mol. Using the confinement method, we obtain a value 1.7 kcal/mol, which is in good agreement with the equilibrium simulations and with previous calculations using the confinement method[?].

[Figure 1 about here.]

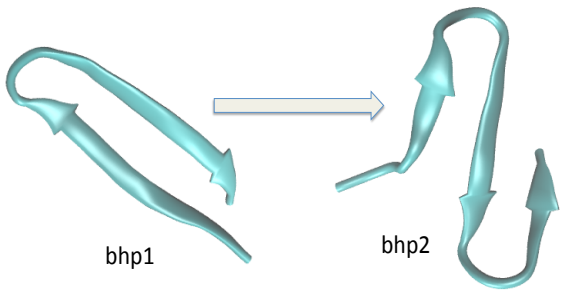

Figure 1: Two conformations from β hairpin from protein G, bhp1 and bhp2. The two stranded β sheet, bhp1 is the native structure and the three stranded β sheet is known as bhp3.