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Supplementary information for the manuscript titled "Finite temperature string method with umbrella sampling using path collective variables: Application to secondary structure change in a protein"

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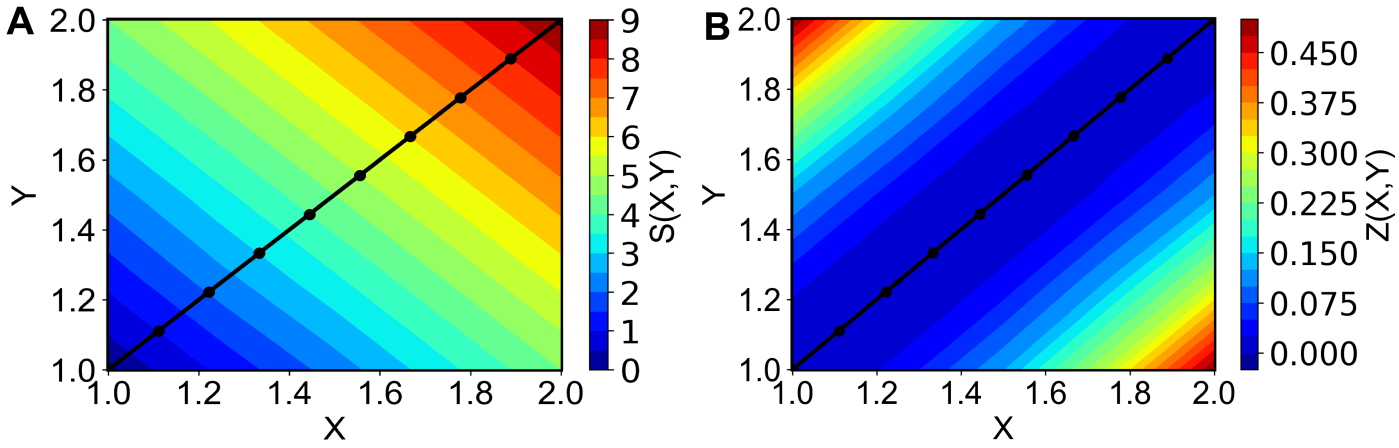

Figure 1: **Path collective variables** Projection of path collective variable (A) S and (B) Z in the 2D Cartesian coordinates system where the reference path is a linear set of ten coordinates.

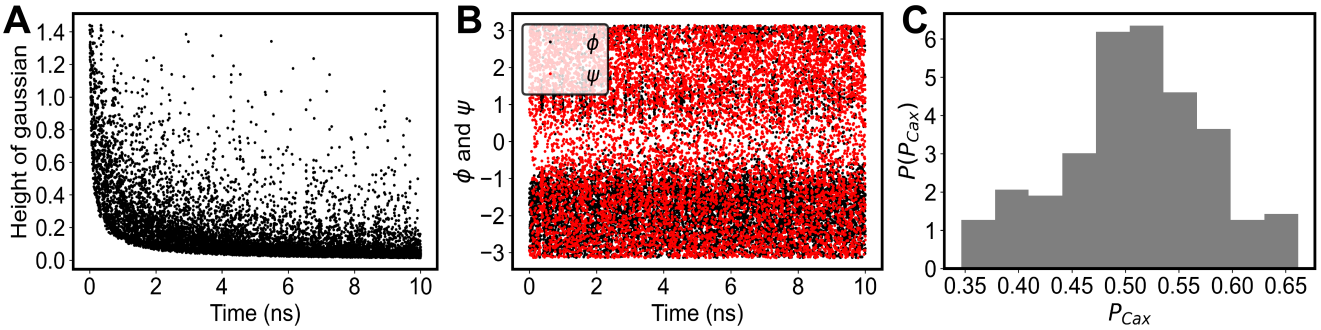

Figure 2: **Alanine-dipeptide** (A) Change in the Gaussian height during metadynamics simulations, (B) ϕ and ψ sampling during metadynamics, and (C) Committor distribution with a committor value peaked at $\frac{1}{2}$.

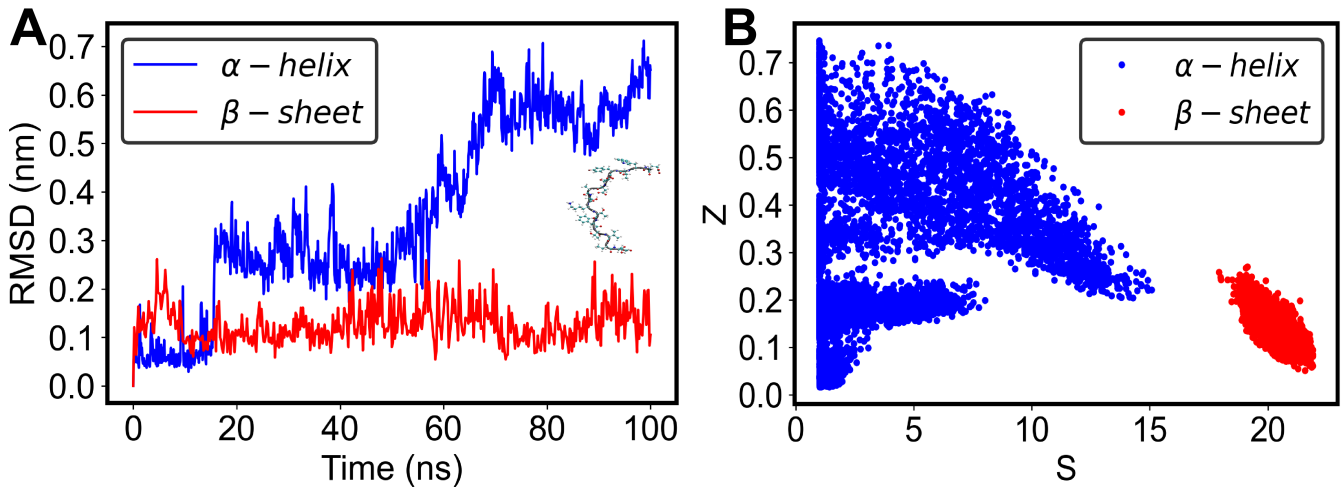

Figure 3: **G-protein unbiased simulations** (A) RMSD from the unbiased simulations of α-helix and β-hairpin structures. α-helix is completely unfolded after 60 ns of simulation. Inset illustrates the final structure of the α-helix at the end of the simulation. (B) S and Z sampling in unbiased simulations of α-helix and β-hairpin states.

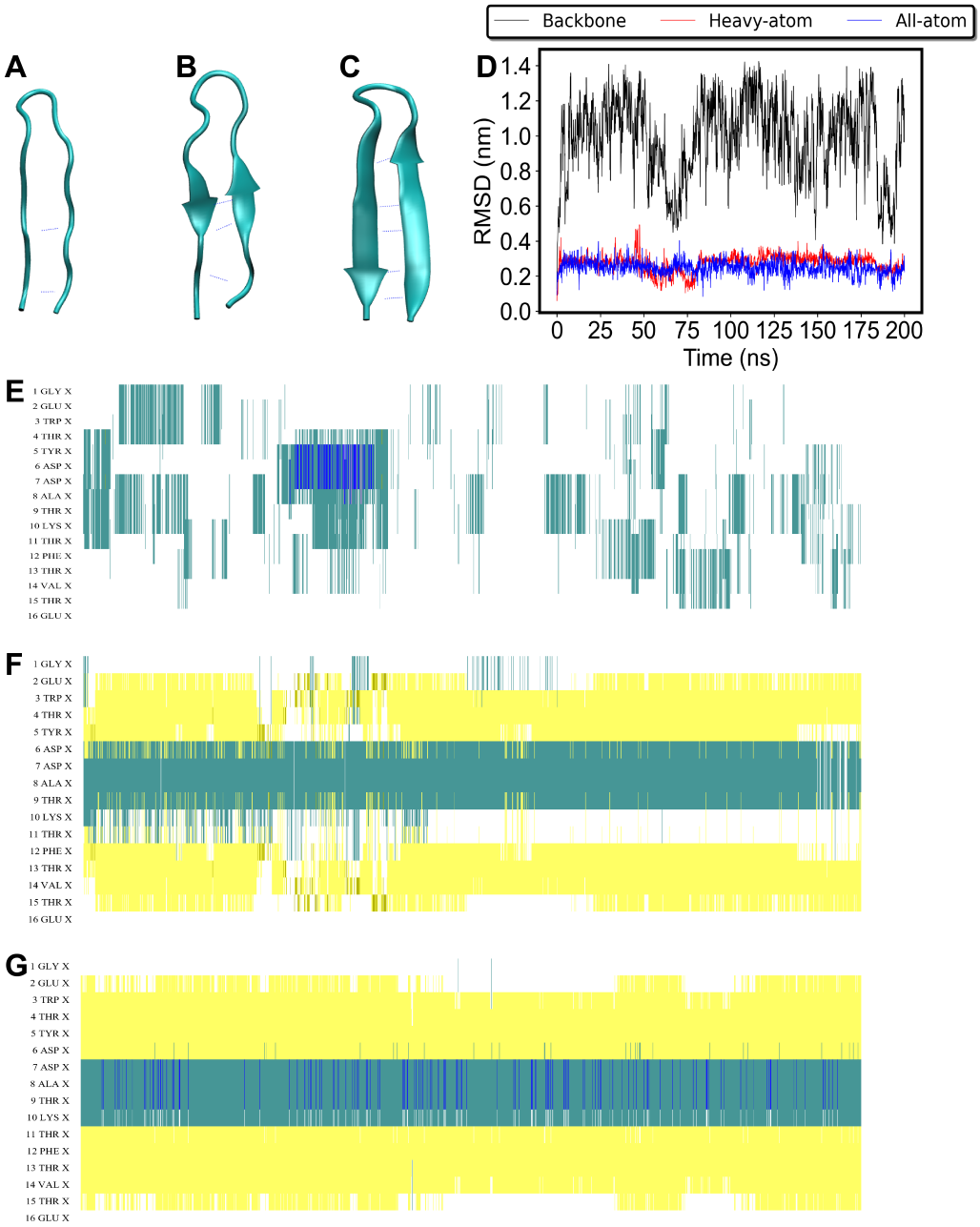

Figure 4: **G-protein pulling simulations** Unbiased simulation of the β-hairpin obtained from the pulling simulations from α-helix to β-hairpin in S and Z space with 22 reference states for the reference state having (A) backbone atom information in the reference path, final pulled state (S, Z = 21.99, 0.011) has 2 Hbonds, (B) heavy atom information in the reference path, final pulled state (S, Z = 21.93, 0.021) has 3 Hbonds, and (C) all atom information in the reference path, final pulled state (S, Z = 21.99, 0.013) has 5 Hbonds. (D) RMSD of the unbiased simulations of the final pulled β-hairpin state indicates that only the backbone atom information in the reference path is insufficient to form a stable β-hairpin. Changes in the secondary structure with time from unbiased simulation for (E) backbone atom information, (F) heavy atom information, and (F) all atom information in the reference path, indicate that including the all atom information in the reference path stabilizes the β-hairpin to the greatest extent.

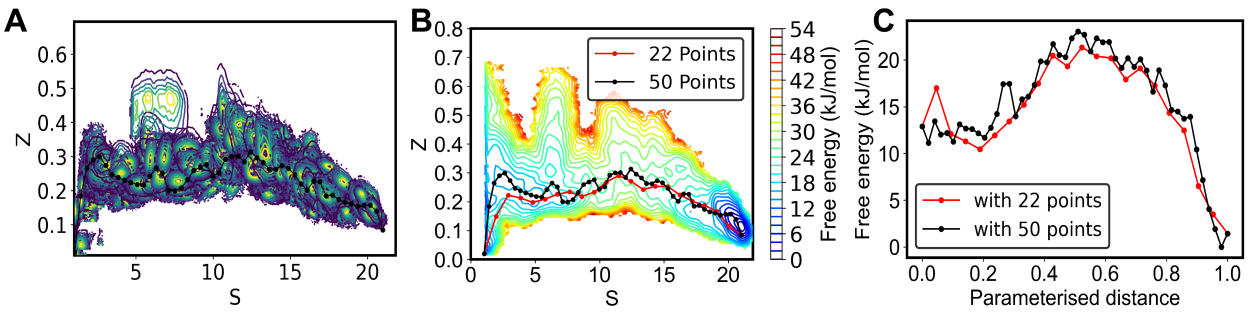

Figure 5: **G-protein free energy estimation** (A) 2D contour maps plotted using the simulation data during the string evolution and the final sampling on the converged path. The contours are plotted for the 80 percentage of the distribution to ensure at least 20 percent of the overlap. (D) Location of the converged string defined by 22 and 50 points. (E) Free energy profile along the 22 point string and 50 point string. Free energy barrier is 21.35 kJ/mol for 22 points string, and 23.03 kJ/mol for 50 points string. The difference is within $\sim k_B T$.