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Supporting Material

Title: All-atom models of the membrane-spanning domain of HIV-1 gp41 from Metadynamics

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Supporting Information: All-atom models of the membrane-spanning domain of HIV-1 gp41 from metadynamics

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I. CONVERGENCE OF FREE-ENERGY PROFILES OF GP41 MSD IN PURE WATER

We performed two 120 ns metadynamics simulations starting from two different initial conformations obtained from the 20 ns MD simulation with the MSD solvated in water, (*i*) an α-helical conformation with RMSD_α less than 1 Å and (*ii*) a stable kinked conformation with RMSD_α 6 Å. A repulsive wall with a force constant of 500 kcal/mol was used at 14 Å for the run starting from α-helical conformation and at 12 Å for the run starting from the kinked conformation. The CV profile during the course of the two simulations shows a thorough sampling of the CV space between 0 Å and the upper wall (Fig. S5). After 120 ns of metadynamics calculations the obtained free energy profiles (Fig. S6) from both the runs suggested a stable kinked conformation between 4-6 Å, metastable conformations between 8-10 Å and unstable α-helical conformations between 0-3 Å.

Figure Legends

FIGURE S1 Membrane-peptide models of MSD α-helix with Arg^{694} snorkeling towards exoplasmic head groups (A) and endoplasmic head groups (B). (C) Structural conservation between the two MSD models and the exoplasmic (red) and endoplasmic (blue) snorkeling positions of Arg^{694} after 20 ns of equilibration. The residues with the highest structural conservation are shown in blue and the lowest are shown in red.

FIGURE S2 CV trace during metadynamics calculations for MSD in lipid bilayer with Arg^{694} snorkeling towards the exoplasmic (red) and endoplasmic (green) leaflets as a function of the simulation time

FIGURE S3 RMSD$_\alpha$ if the MSD in pure water with respect to the initial α-helical conformation vs. simulation time during 20 ns of MD

FIGURE S4 Representations of stable kinked conformation (left) and metastable loop conformation of MSD (right) of gp41 MSD in pure water observed in 20 ns MD simulation

FIGURE S5 CV profiles of two 120 ns metadynamics runs with gp41 MSD in pure water starting from a complete α-helical conformation (red) and a kinked conformation (green)

FIGURE S6 Free energy profiles from two metadynamics runs with gp41 MSD solvated in pure water starting from an α-helical conformation (red) and a kinked conformation (green). A repulsive wall of 500 kcal/mol was used at 14 Å for the run starting from an α-helical conformation and at 12 Å for the run starting from the kinked conformation. Both the runs converged to similar free energy profiles after 120 ns suggesting a stable kinked conformation and metastable loop conformations. Average free energy from both the runs is shown in blue.

FIGURE S7 Stable and metastable conformations of gp41 MSD in membrane with Arg^{694} snorkeling towards the exoplasmic and endoplasmic leaflets

FIGURE S8 Arithmetic average of free energy profiles for two 10 ns intervals after filling time 240 ns for the Arg^{694} snorkeling towards the exoplasmic leaflet model

FIGURE S9 Arithmetic average of free energy profiles for two 10 ns intervals after filling time 120 ns for the Arg^{694} snorkeling towards the endoplasmic leaflet model

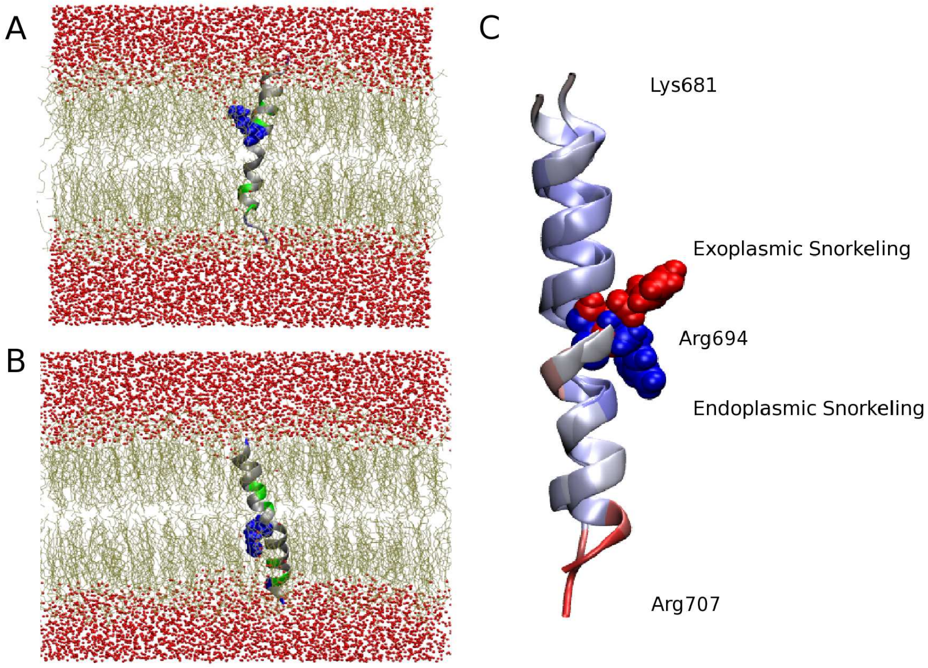

FIGURE 1: Gangupomu and Abrams

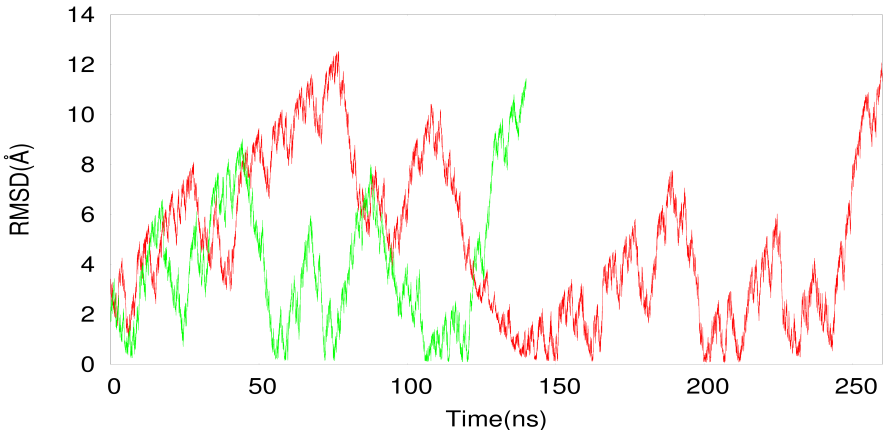

FIGURE 2: Gangupomu and Abrams

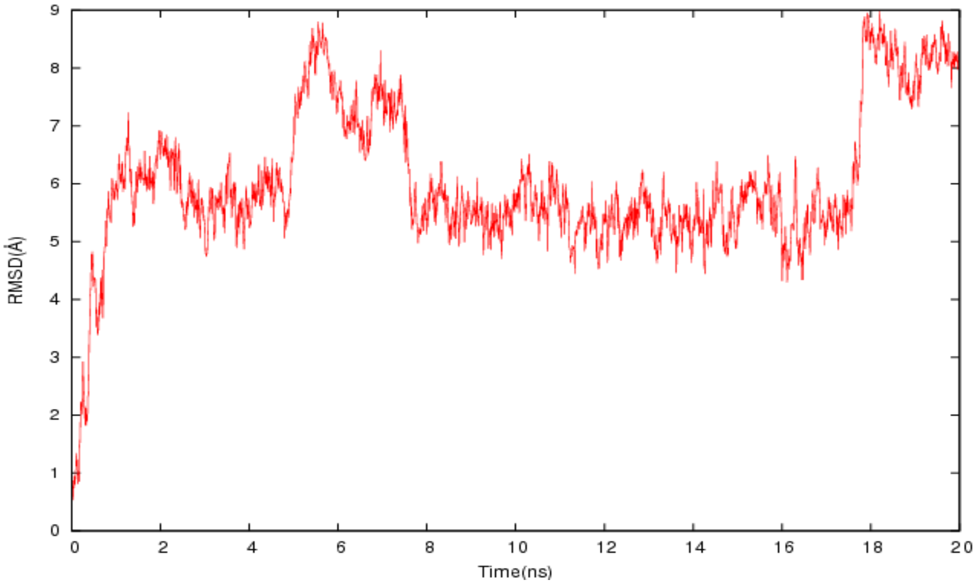

FIGURE 3: Gangupomu and Abrams

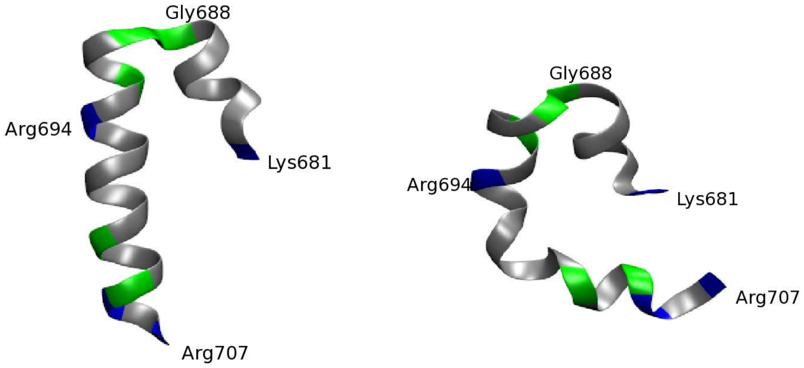

FIGURE 4: Gangupomu and Abrams

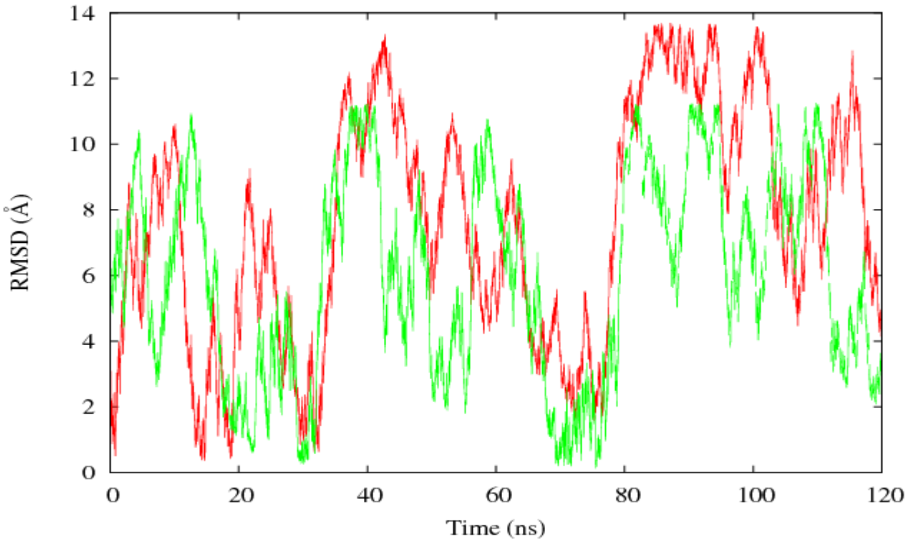

FIGURE 5: Gangupomu and Abrams

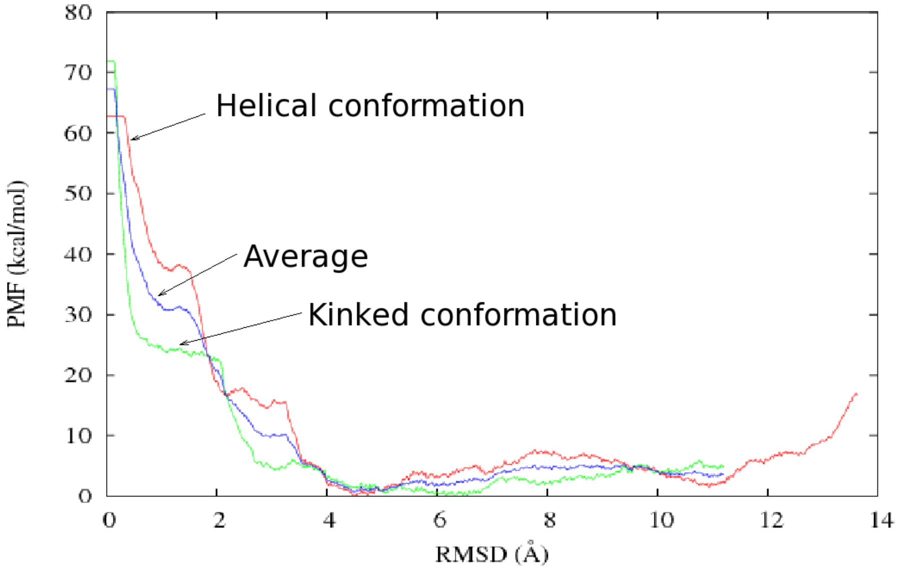

FIGURE 6: Gangupomu and Abrams

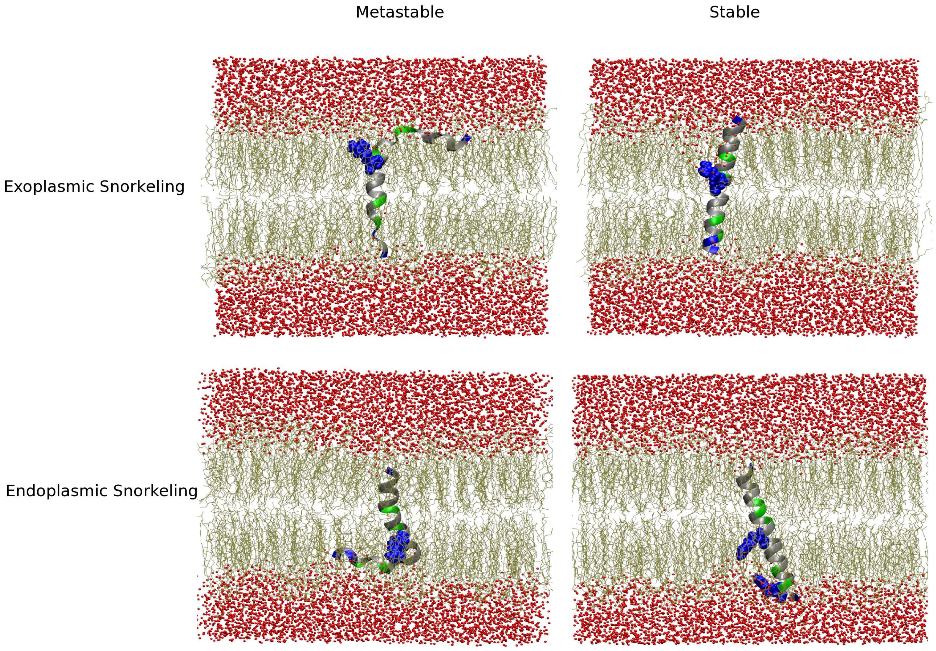

FIGURE 7: Gangupomu and Abrams

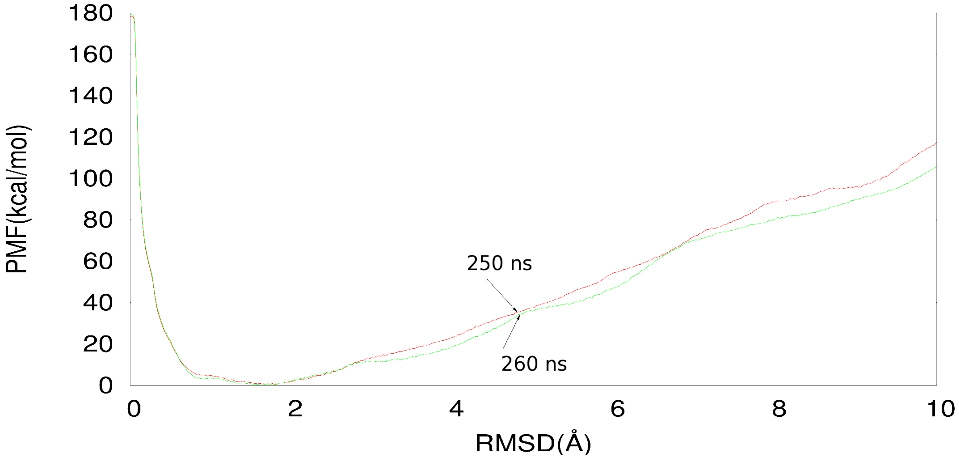

FIGURE 8: Gangupomu and Abrams

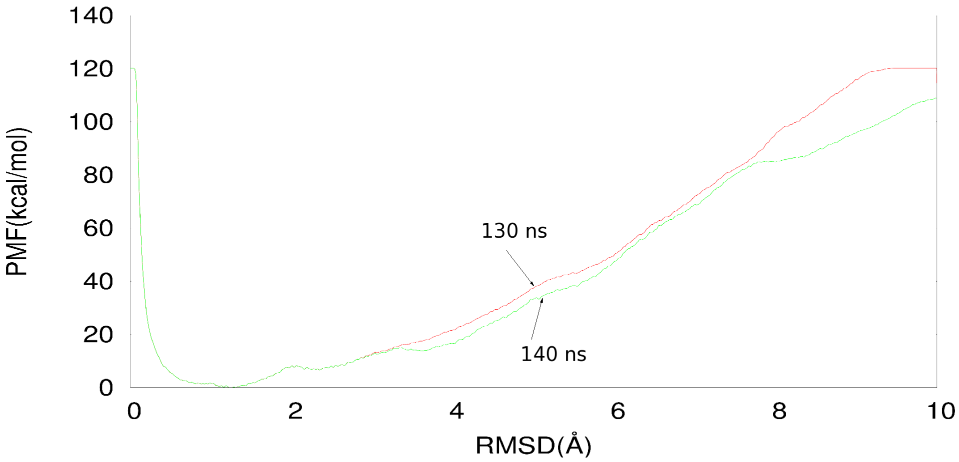

FIGURE 9: Gangupomu and Abrams