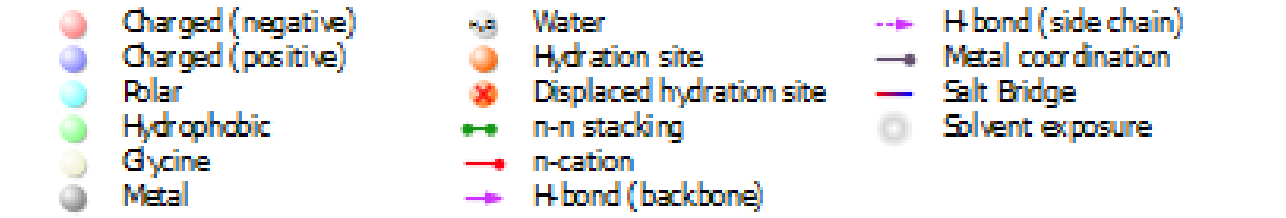
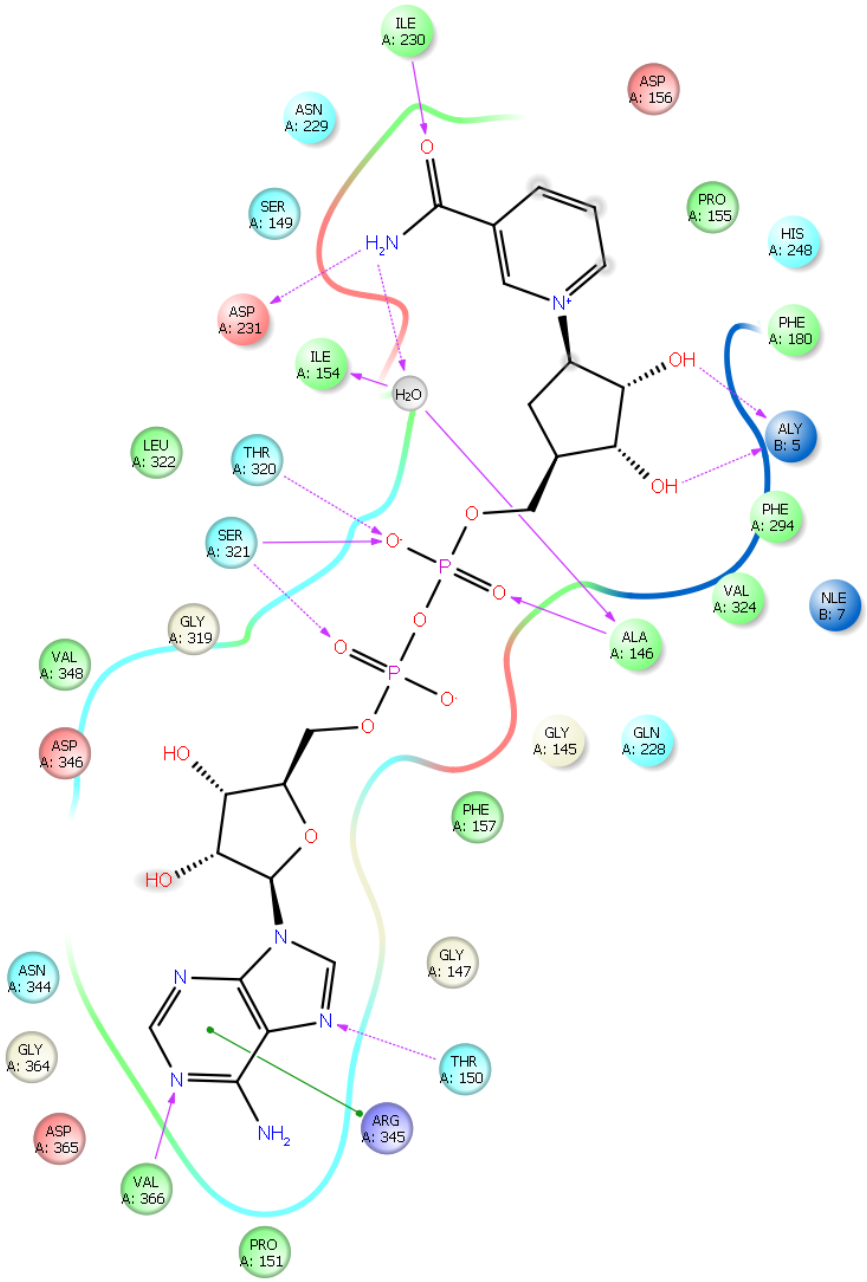
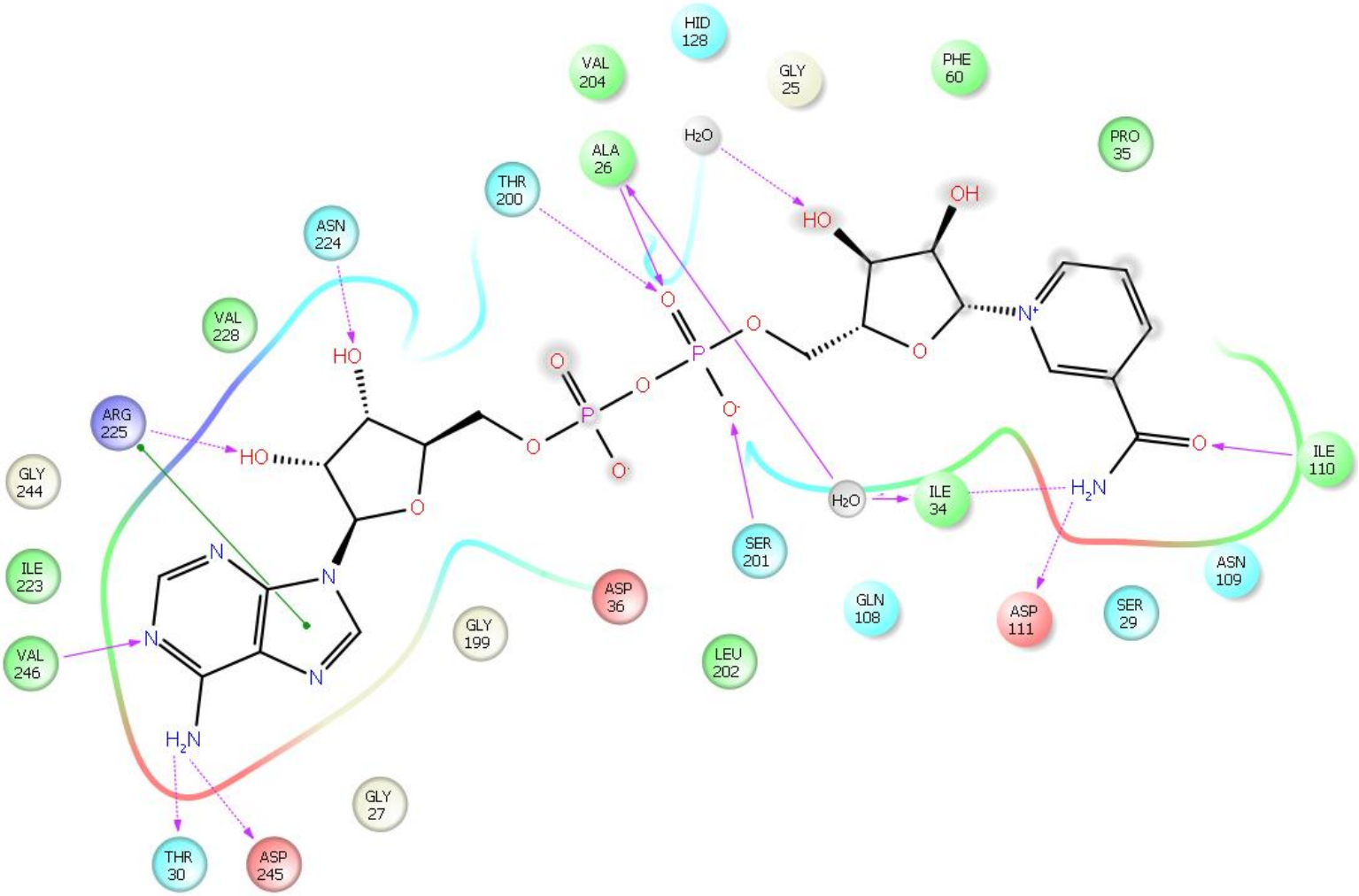
MD Simulations and Structural Analysis of NAD^+ Binding in SIRT3

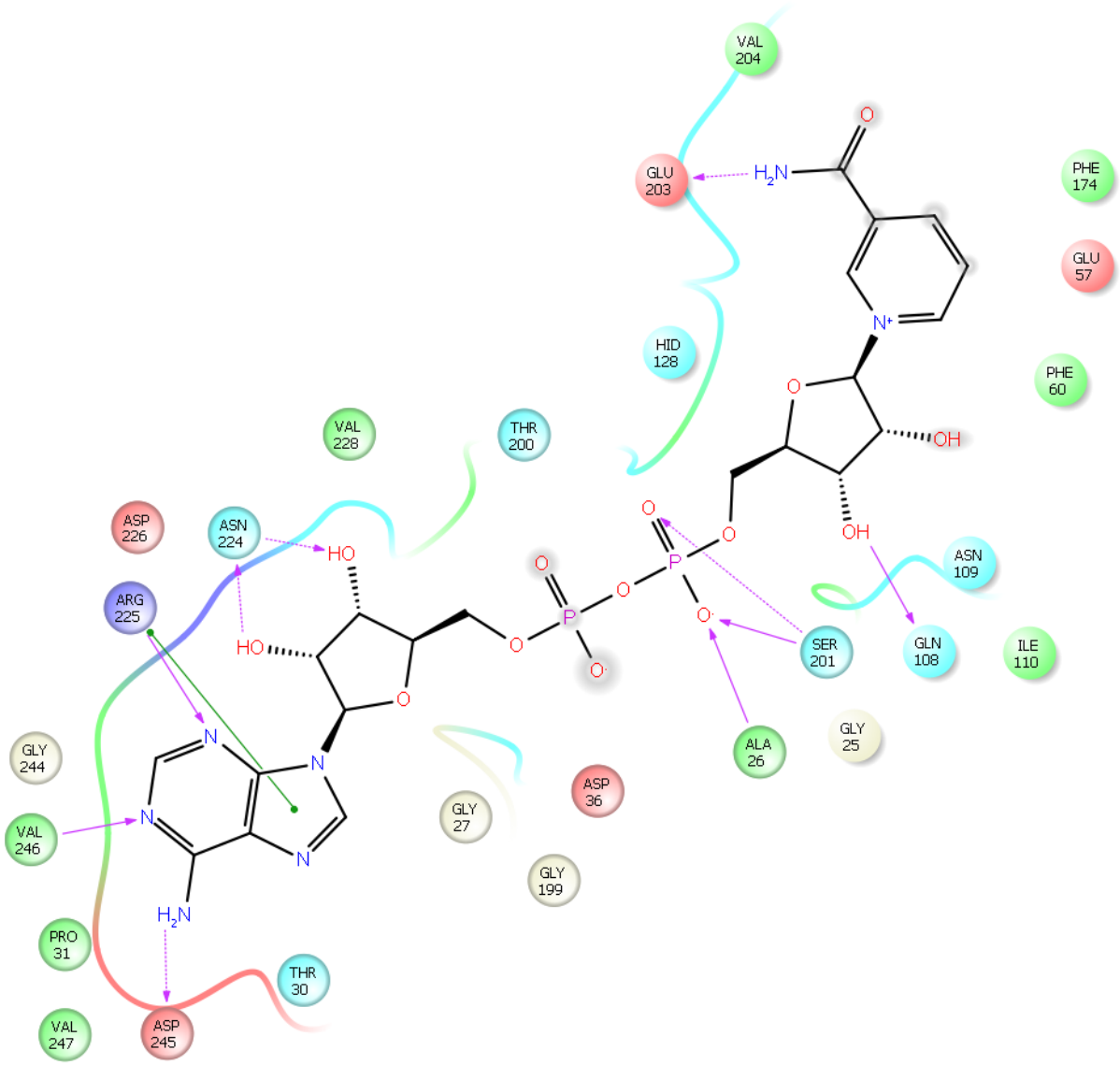




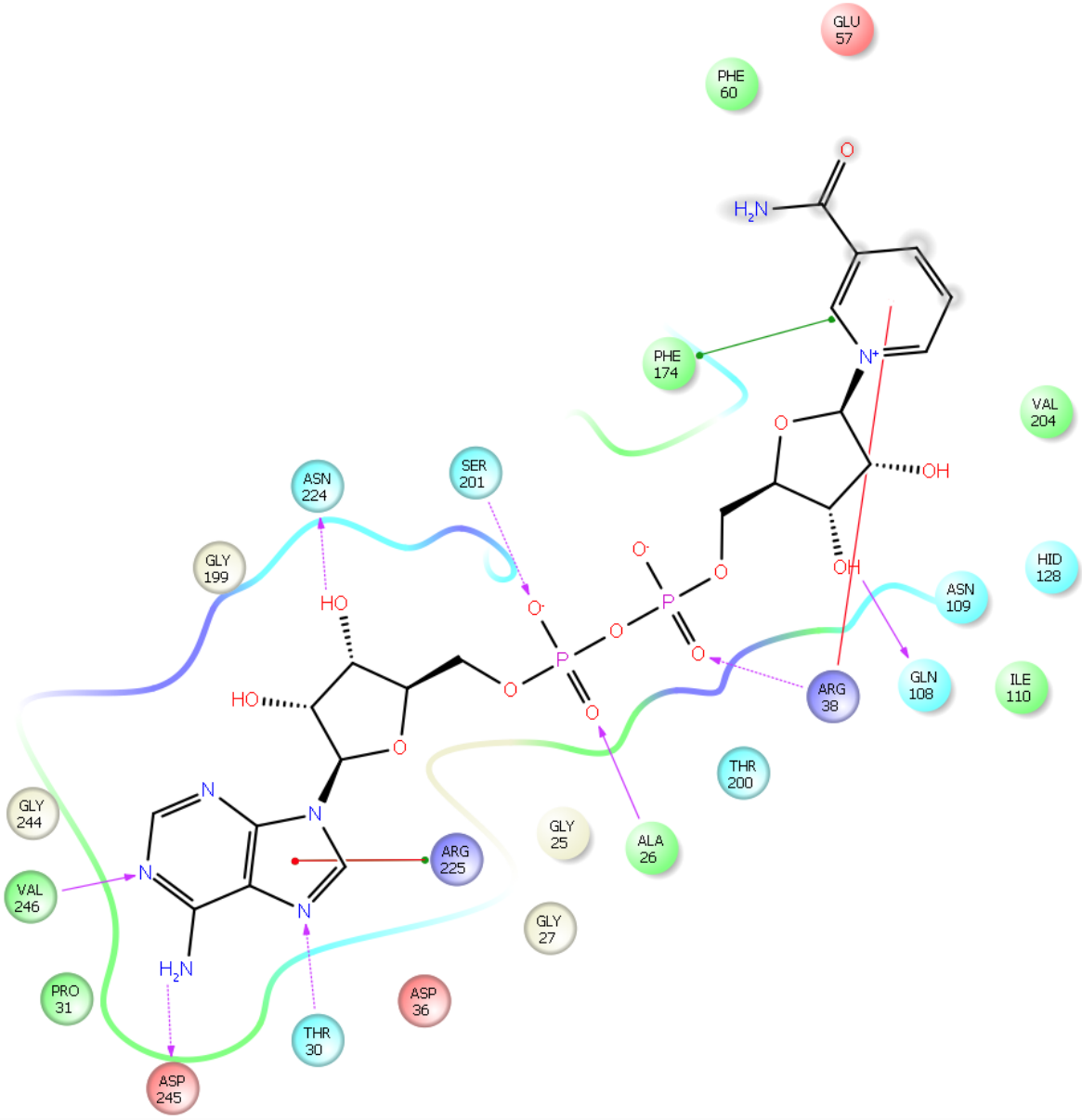
NAD+ with SIRT3 (4FVT): crystal structure



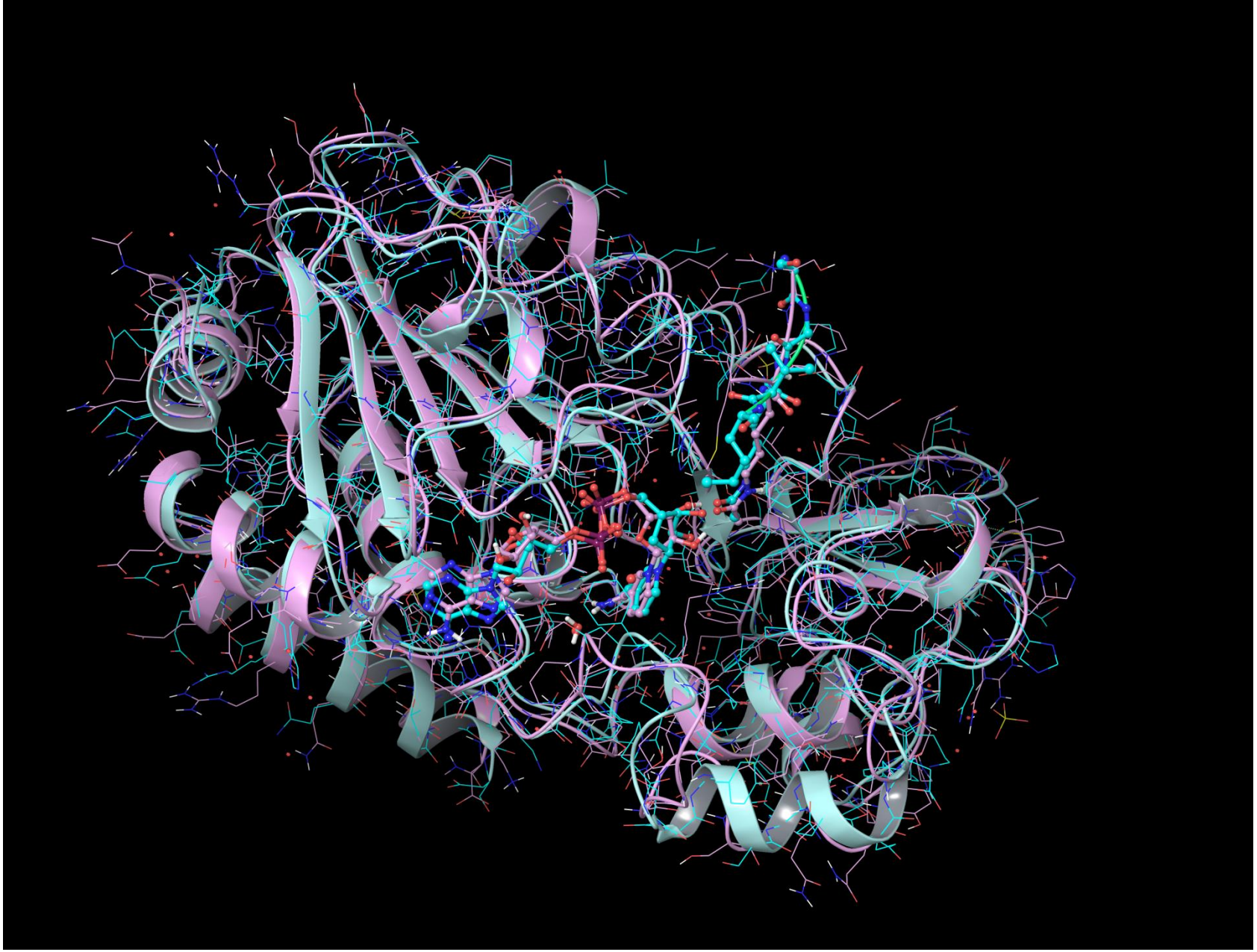
NAD+ with SIRT3: averaged over 10 frames (last 10 ps)
MD simulation of ternary structure (residue number shifted by 120)



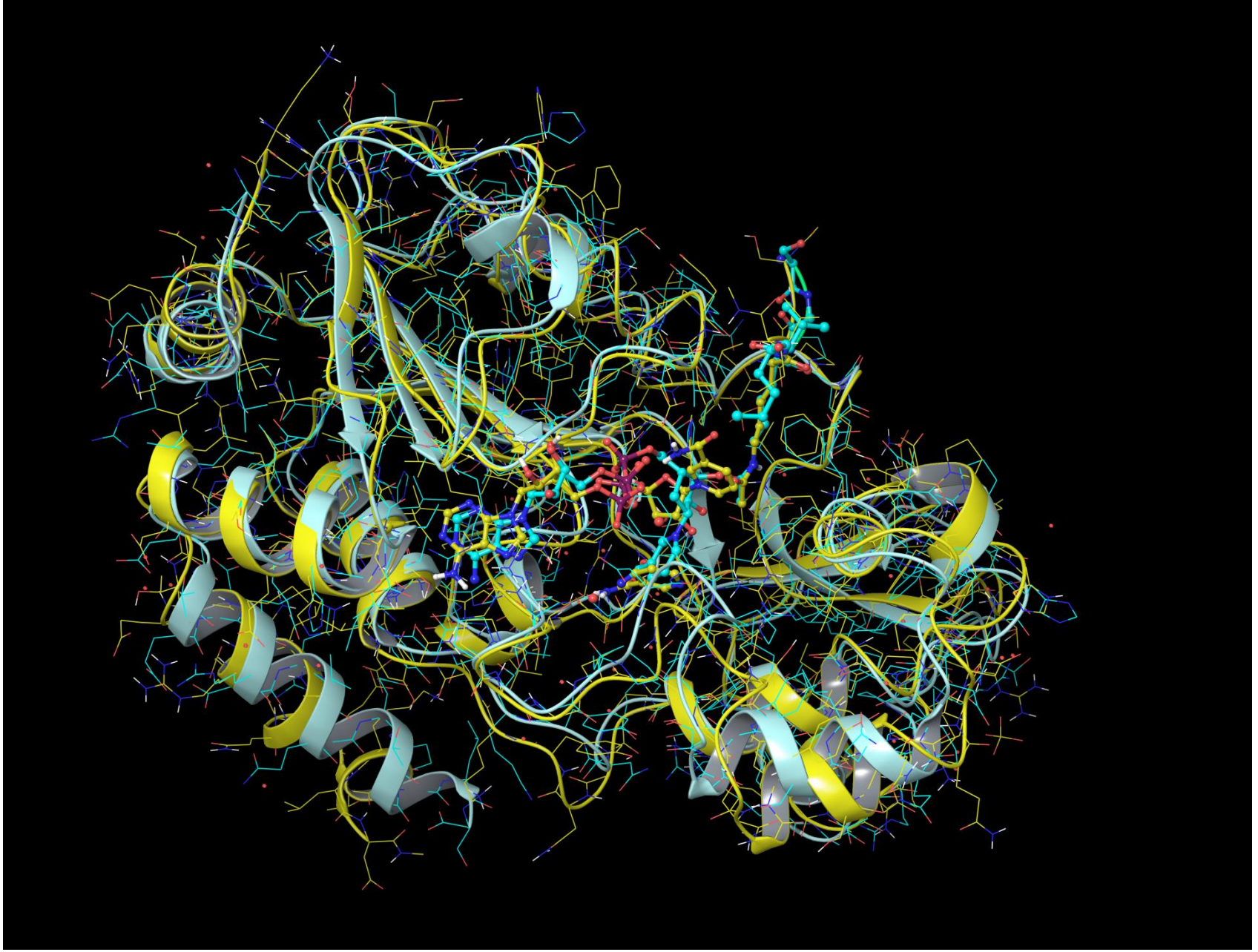
NAD+ with SIRT3: averaged over 10 frames (last 10 ps)
MD simulation of ternary structure + NAM in C pocket



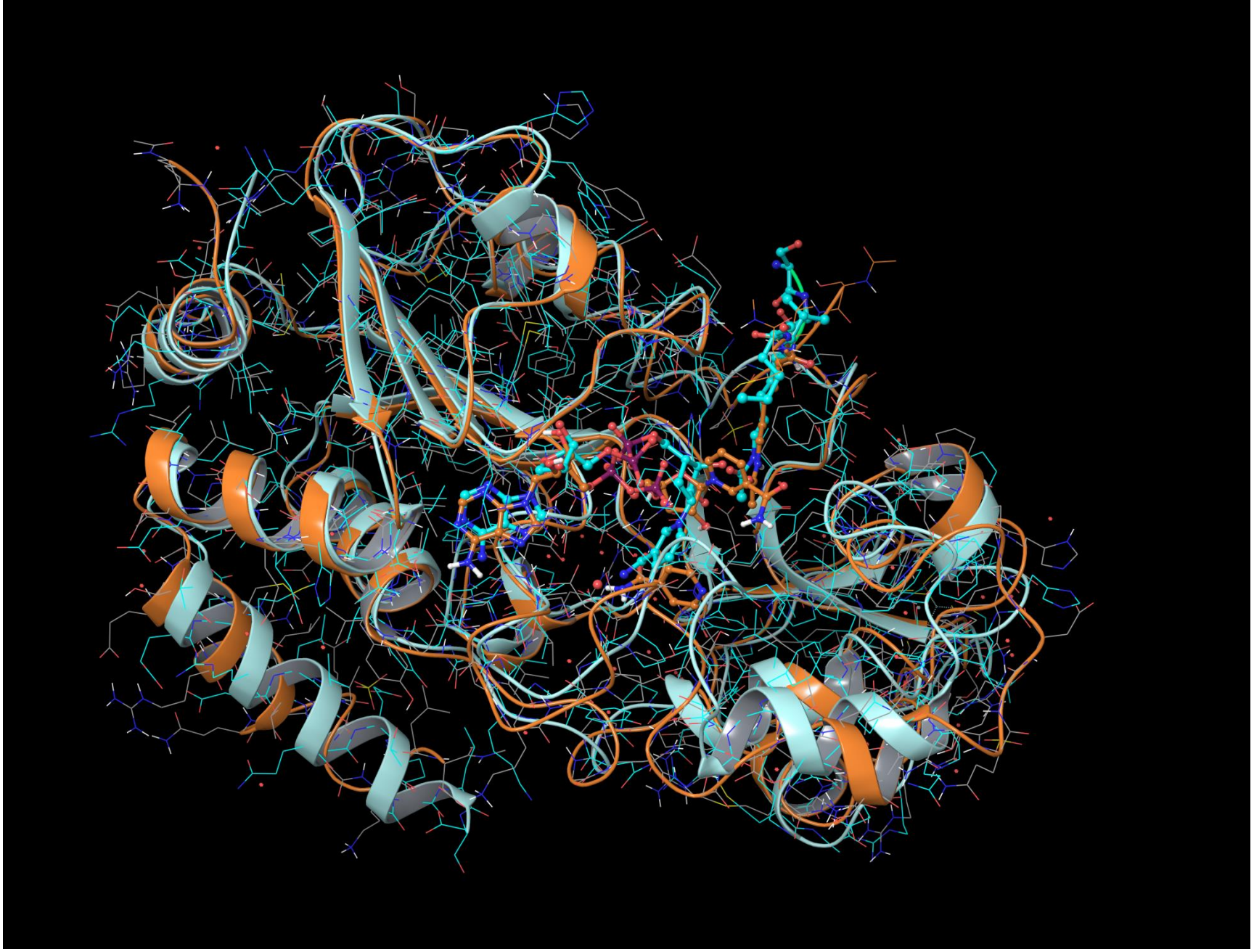
NAD+ with SIRT3: averaged over 10 frames (last 10 ps)
MD simulation of ternary structure + isoNAM in C pocket



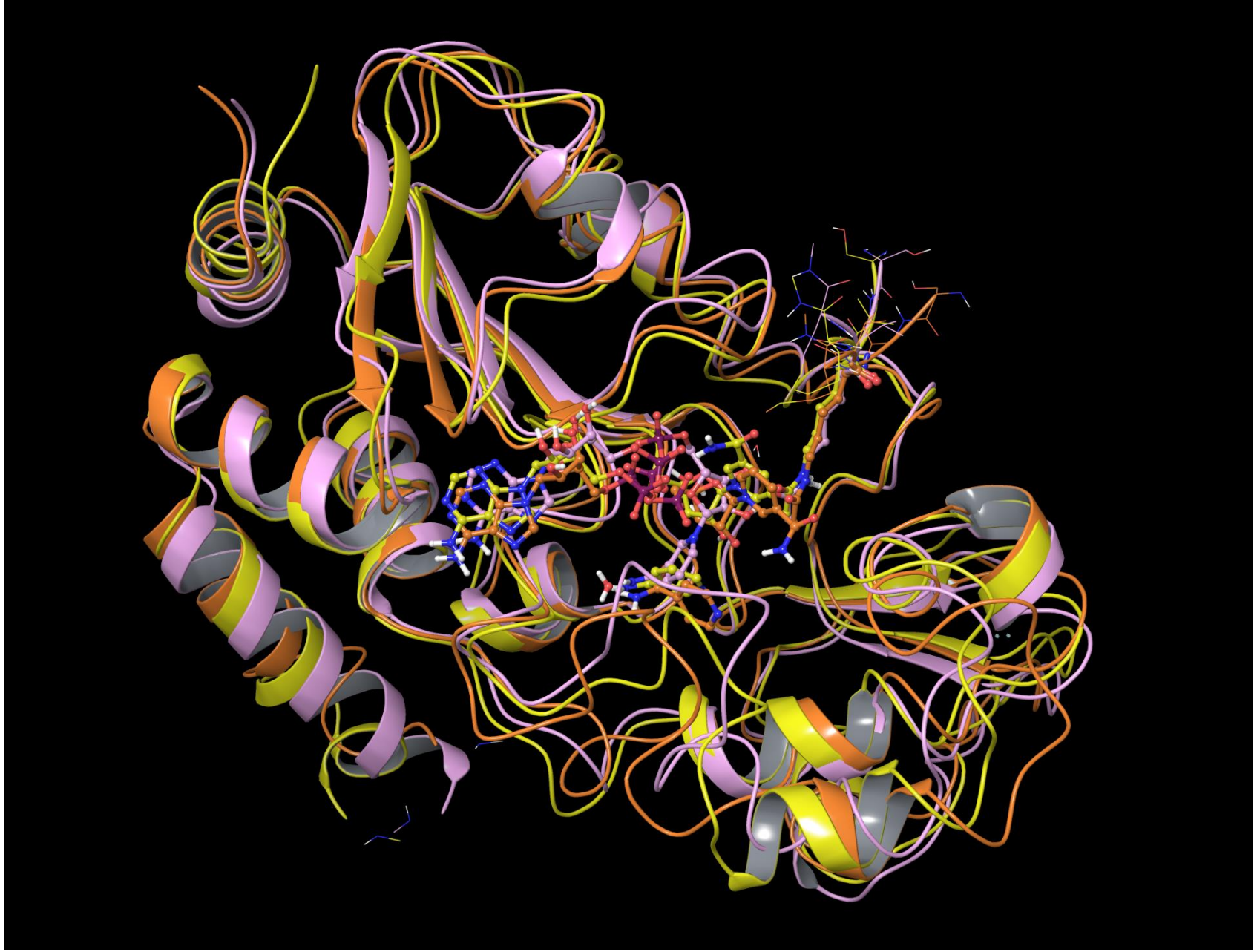
Comparison of MD averaged structure with crystal structure (cyan)
(MD simulation of ternary structure: pink) Protein RMSD: 1.149 Angstrom



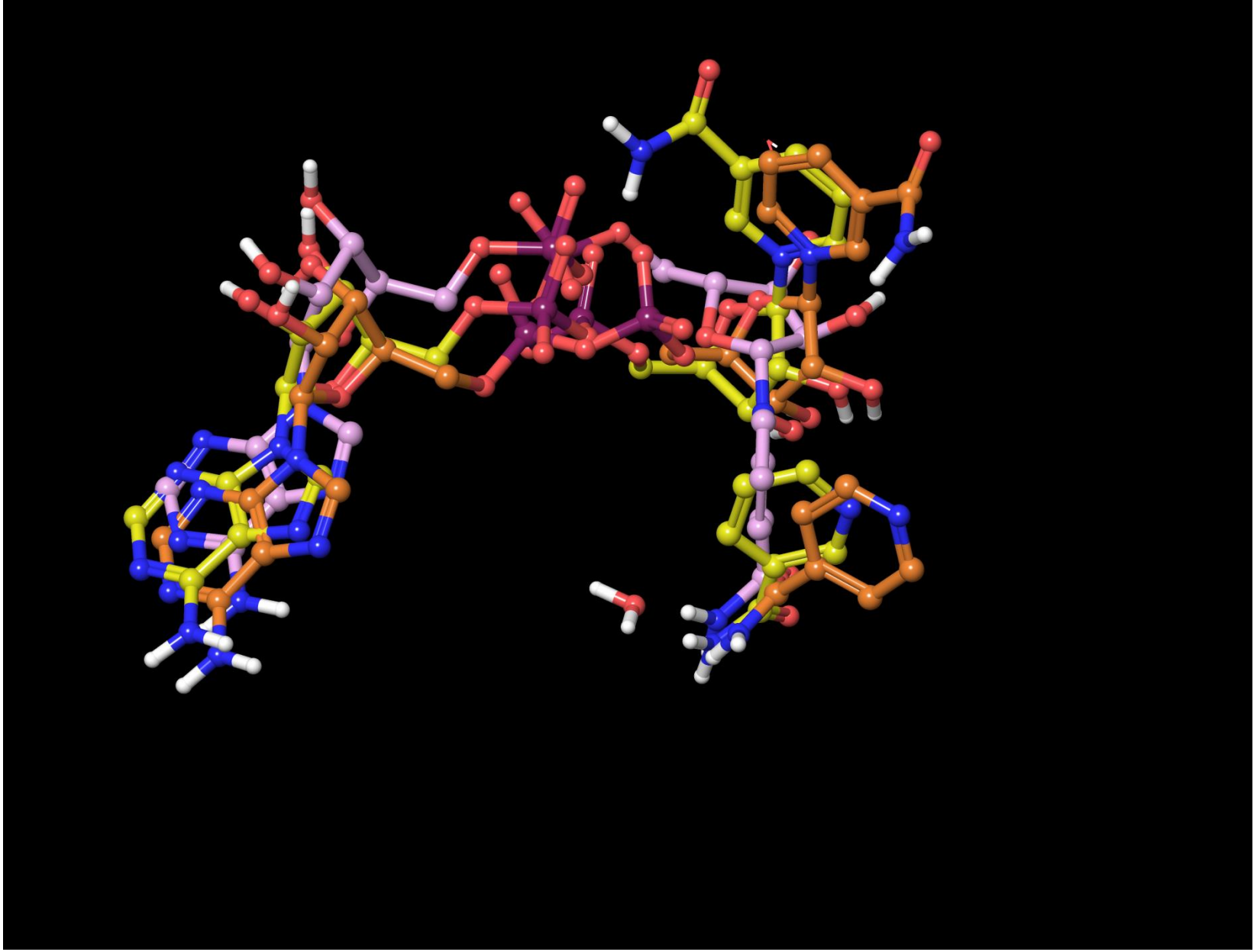
Comparison of MD averaged structure with crystal structure
(MD simulation of ternary structure + NAM: yellow) Protein RMSD: 1.570 Angstrom



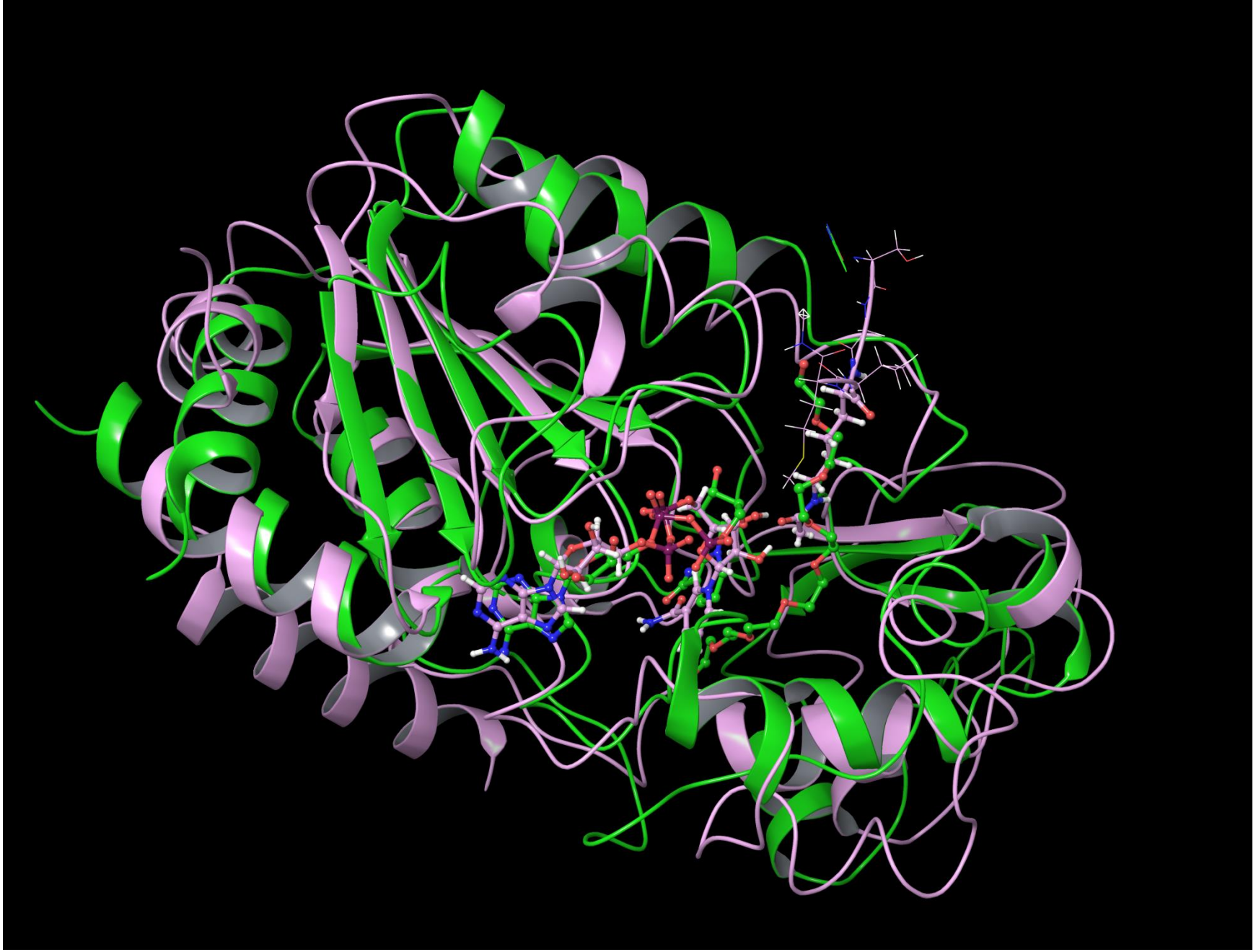
Comparison of MD averaged structure with crystal structure
(MD simulation of ternary structure + NAM: orange) Protein RMSD: 2.090 Angstrom



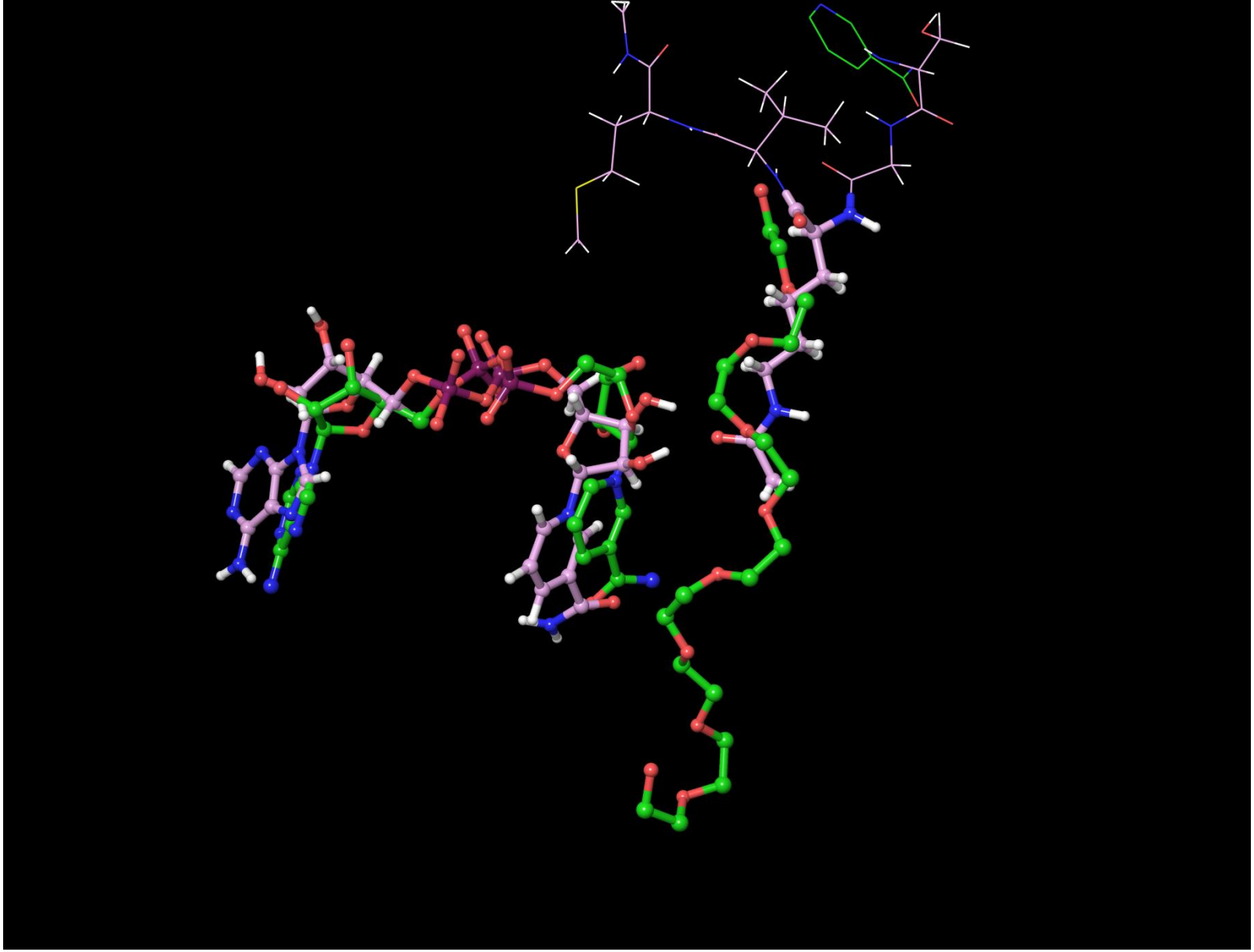
Comparison of MD averaged structures from 3 MD simulations of
ternary structure (pink), ternary structure + NAM (yellow) and ternary structure + isoNAM (orange)



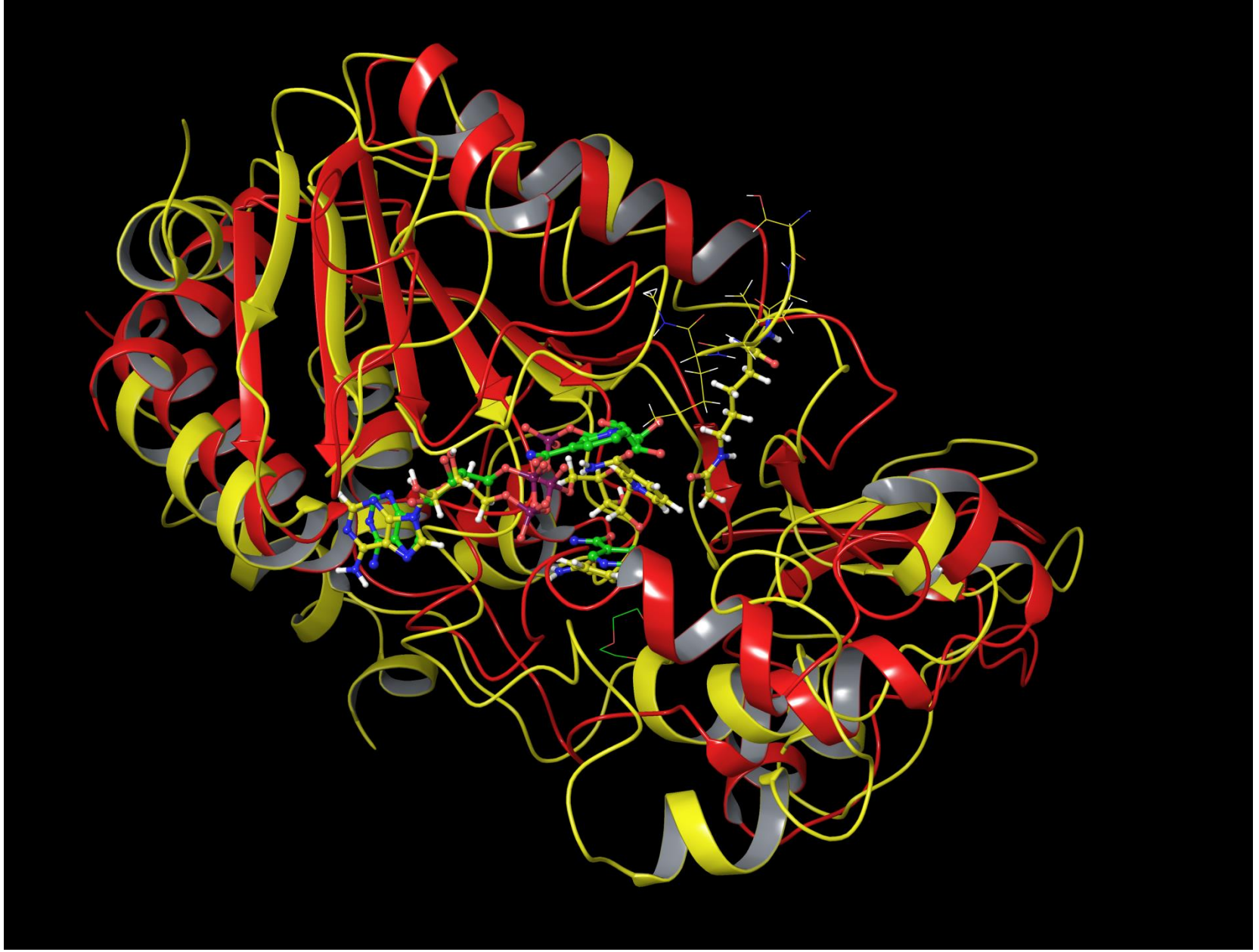
NAD+ of averaged structure from MD simulations
ternary structure (pink), ternary structure + NAM (yellow) and ternary structure + isoNAM (orange)



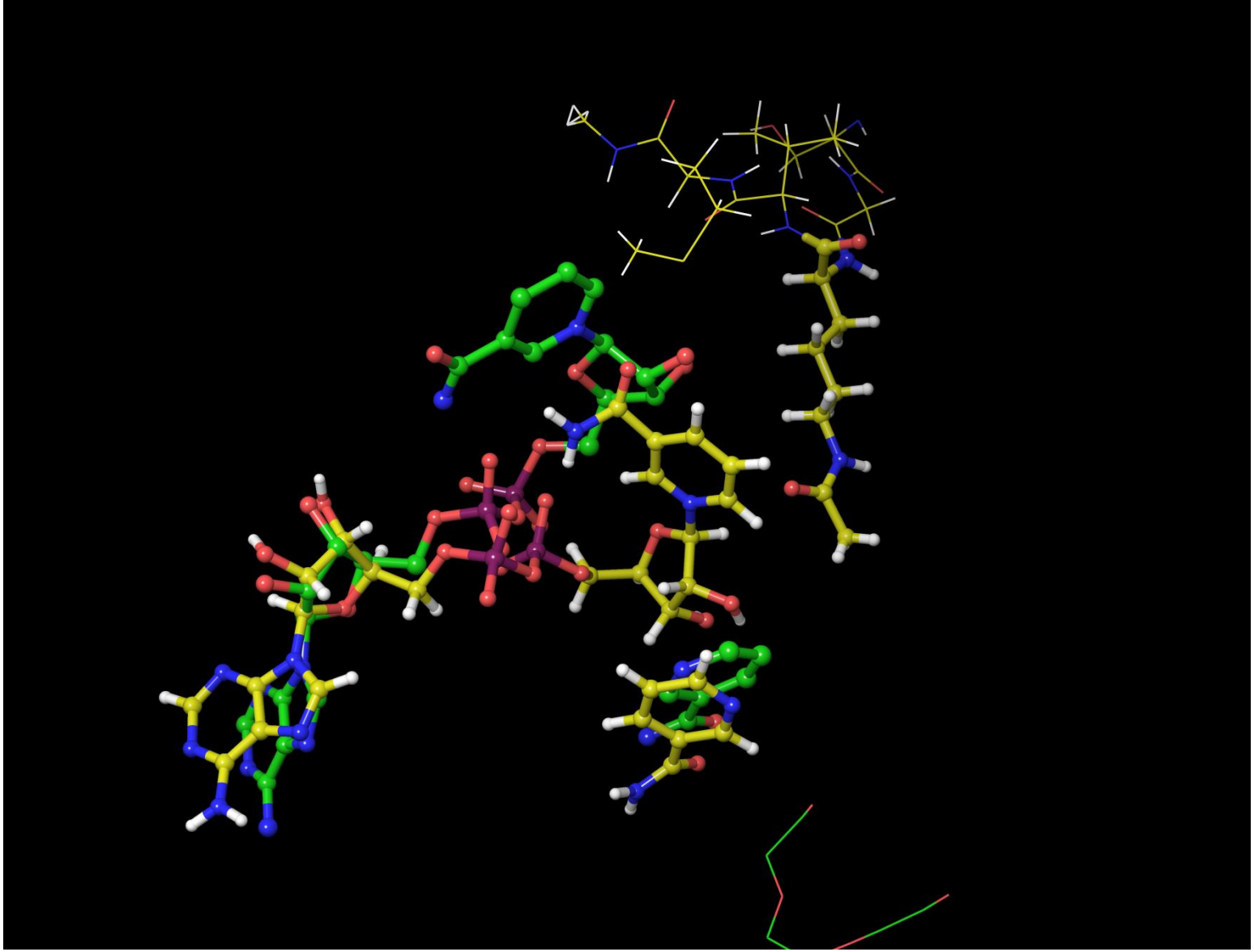
Comparison of MD averaged structure with Sir2Af2 crystal structure (1YC2:B green)
(MD simulation of ternary structure: pink)



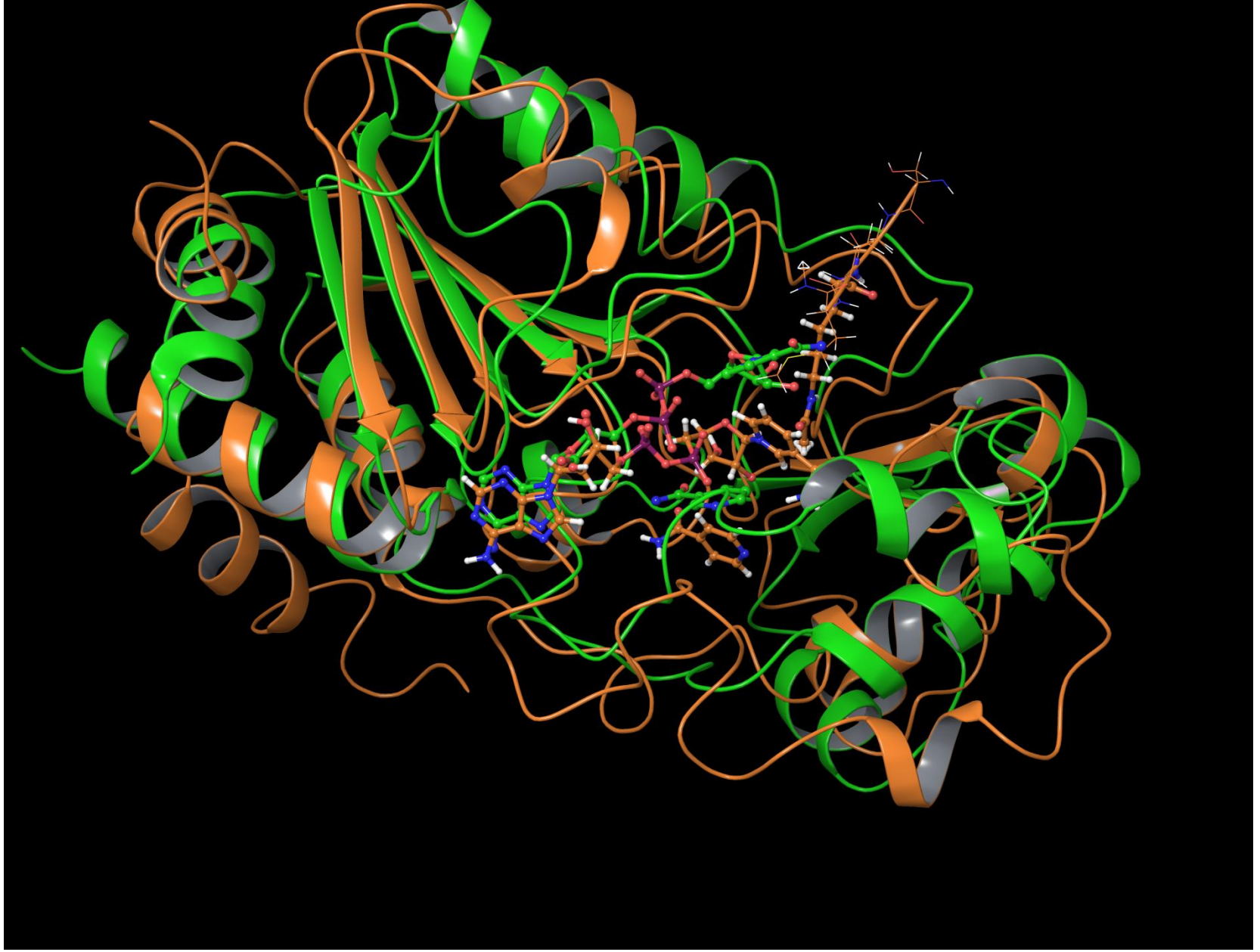
Comparison of MD averaged structure with Sir2Af2 crystal structure (1YC2:B green)
(MD simulation of ternary structure: pink)
The nicotinamide moiety binds somewhat differently without peptide substrate (1YC2:B)



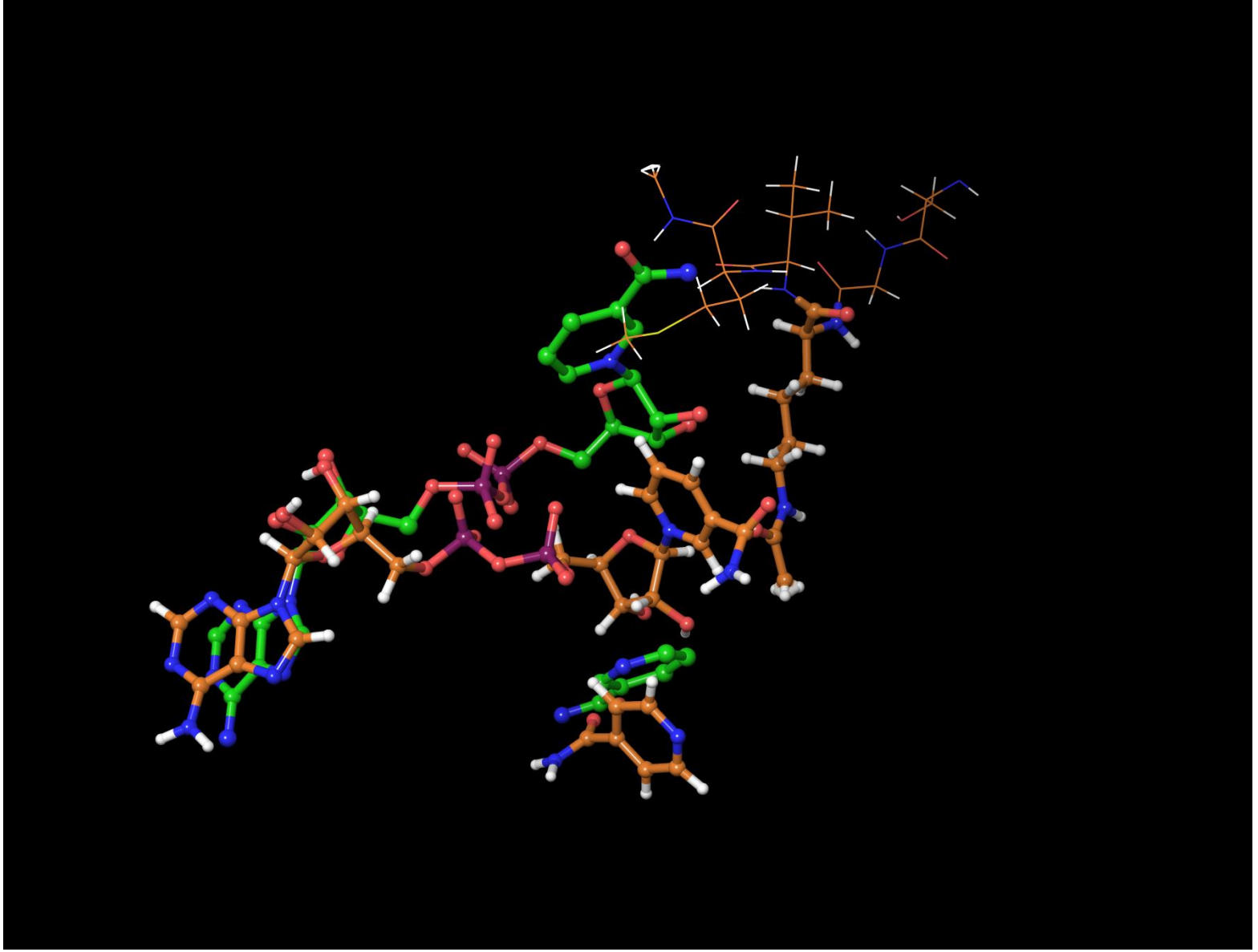
Comparison of MD averaged structure with Sir2Af2 crystal structure (1YC2:D red)
(MD simulation of ternary structure + NAM: yellow)



Comparison of MD averaged structure with Sir2Af2 crystal structure (1YC2:D green)
(MD simulation of ternary structure + NAM: yellow)
The ribose that connects nicotinamide moiety interacts more with SIRT3 (and maybe due to the peptide substrate), resulting more interactions between nicotinamide moiety with SIRT3 as well.



Comparison of MD averaged structure with Sir2Af2 crystal structure (1YC2:A green)
(MD simulation of ternary structure + isoNAM: orange)



Comparison of MD averaged structure with Sir2Af2 crystal structure (1YC2:A green)
(MD simulation of ternary structure + isoNAM: orange)
Again, the ribose that connects nicotinamide moiety interacts more with SIRT3 (and maybe due to the peptide substrate), resulting more interactions between nicotinamide moiety with SIRT3 as well.