

Figure 11: Alignment of ternary complex (Sir2TM/Ac-p53/NAD+) from MD averaged structure (10 frames from last 10ps) with respect to crystal (pdbID:2H4F) structure. Ribbon representation of crystal structure is colored by secondary structure (sheets in cyan, helices in red and coils in gray), MD averaged structure in lime green color. Carbon atoms in crystal structure are in white, and are in lime green for MD averaged structure. Alignment was made using residues 15-27, 182-242, which forms the stable A binding pocket in Rossmann fold domain (RMSD of backbone of these residues between crystal structure and MD averaged structure is 0.60 Angstrom). RMSD of NAD+ itself (heavy atoms only) after alignment between crystal structure and MD averaged structure is 1.14 Angstrom.

Ac-p53: acetyl- Cellular tumor antigen p53

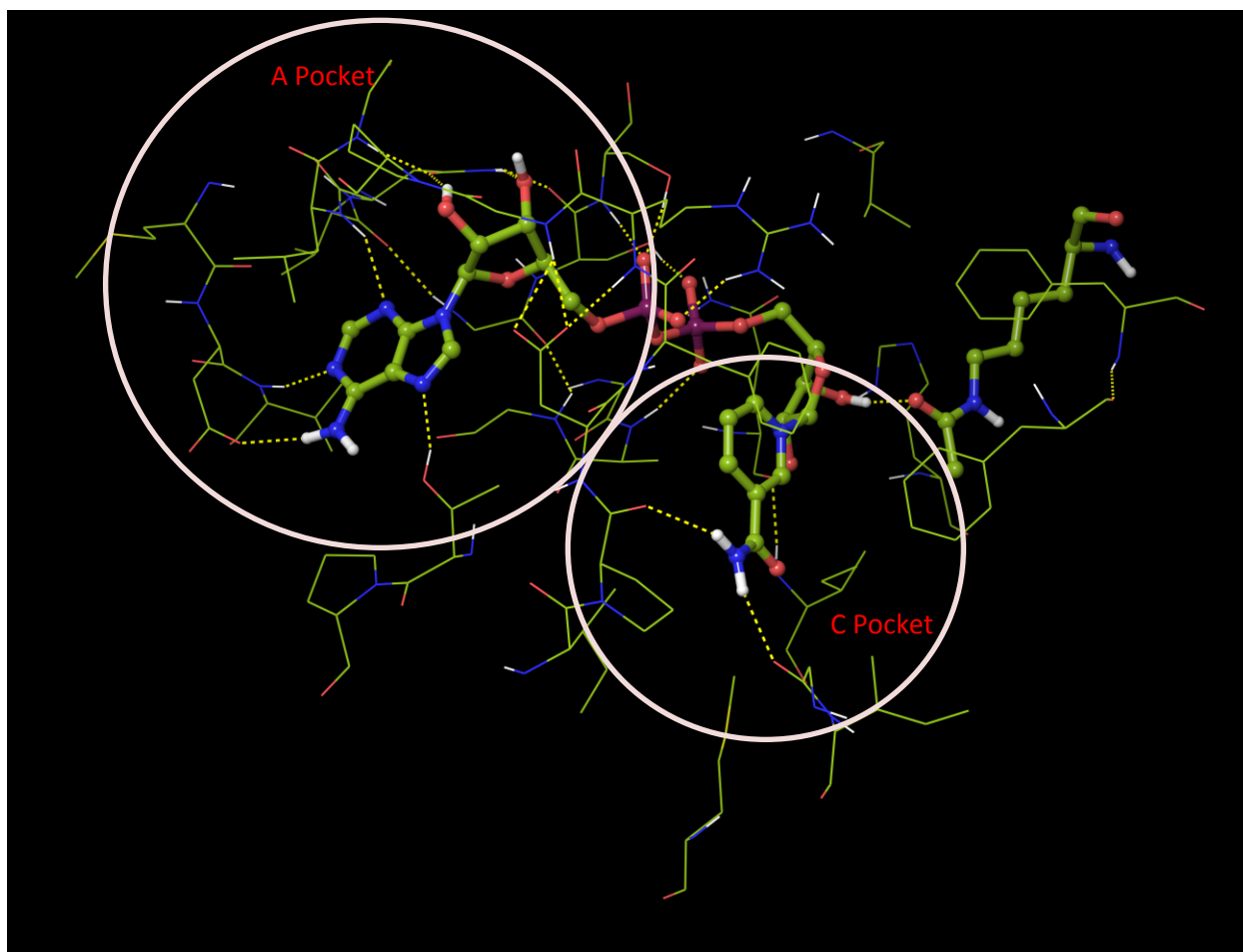


Figure 11a. Observation of A and C pockets from the MD averaged structure over last 10 ps of ternary complex (Sir2TM/Ac-p53/NAD⁺).

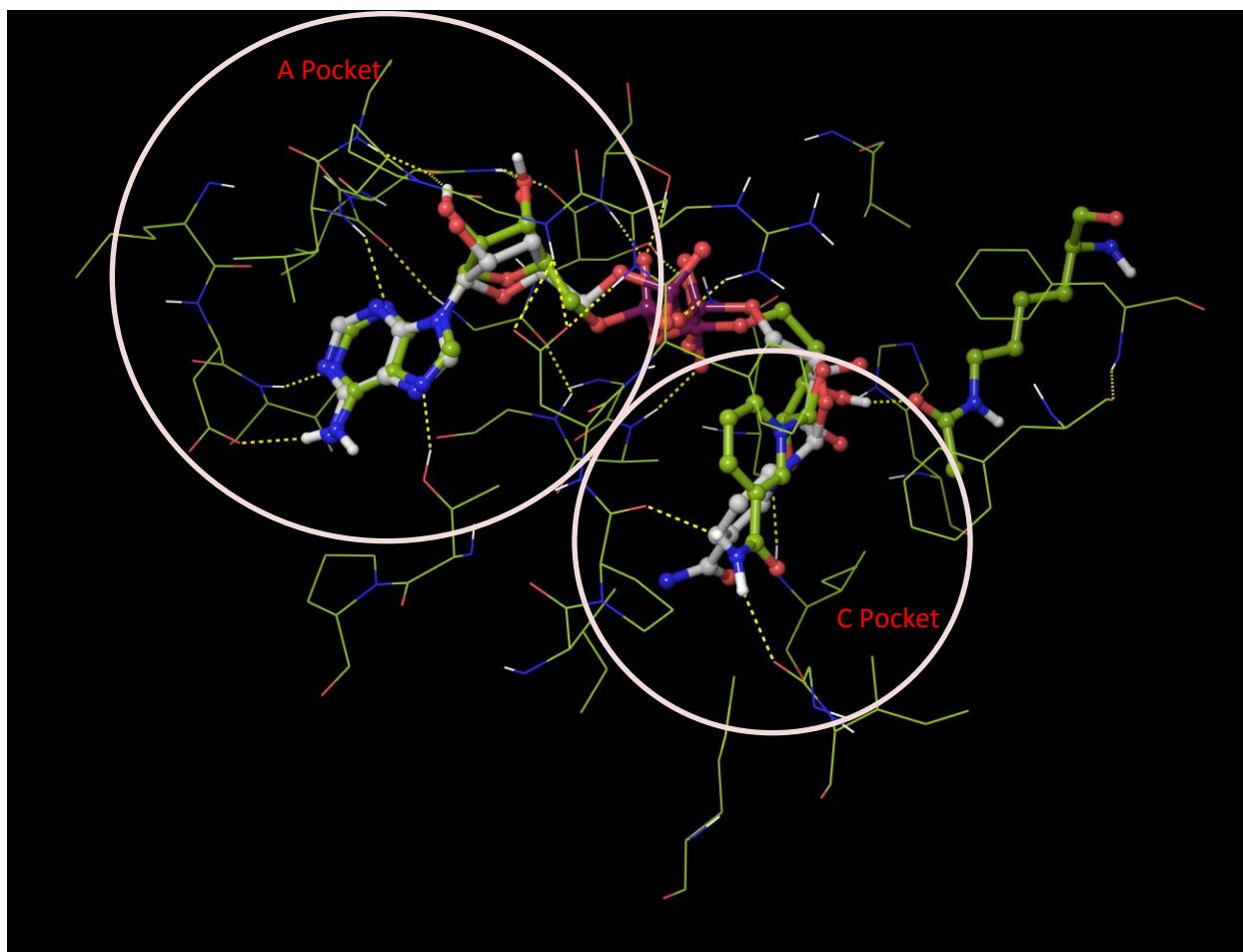


Figure 11b. Observation of A and C pockets from the MD averaged structure over last 10 ps of ternary complex (Sir2TM/Ac-p53/NAD+), reference NAD+ structure (carbon in white) taken from crystal structure 2H4F.

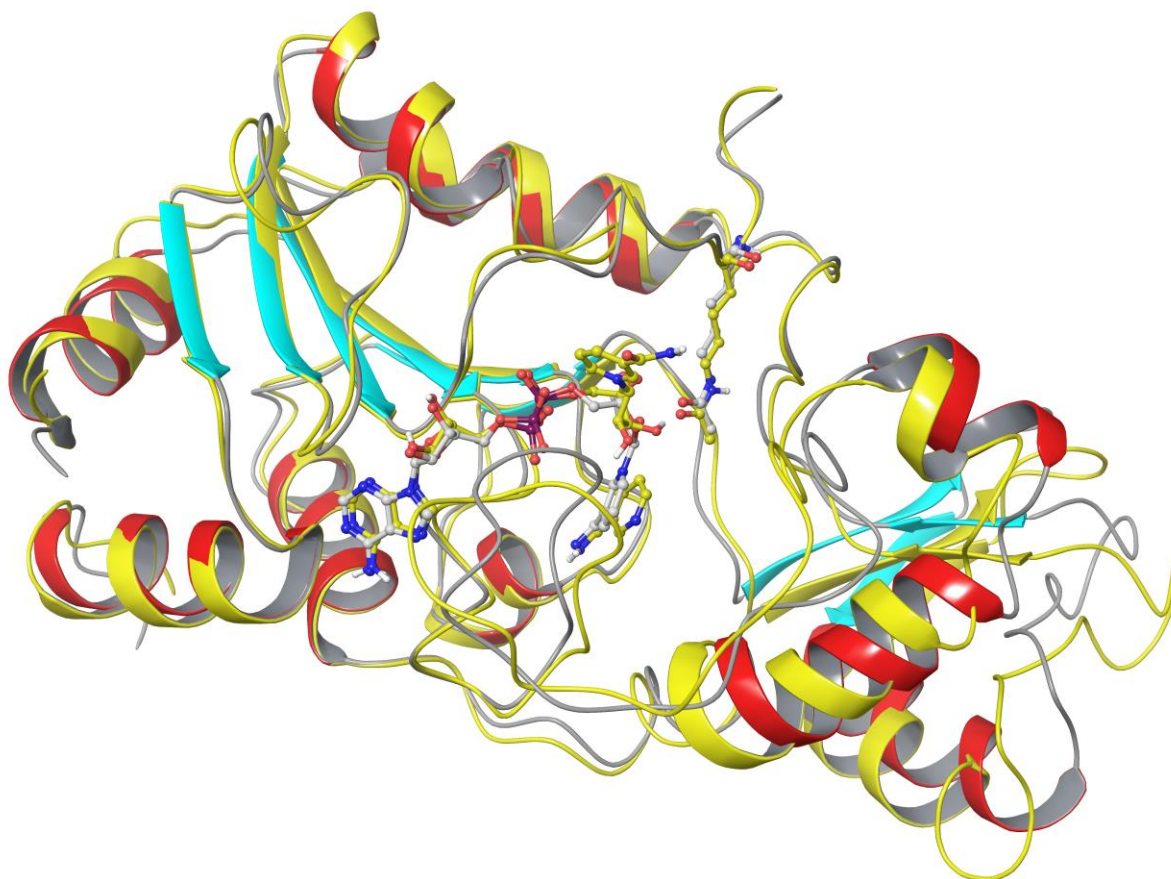


Figure 12: Alignment of complex (Sir2TM/Ac-p53/NAD⁺/NAM) from MD averaged structure (10 frames from last 10ps) with respect to crystal (pdbID:2H4F) structure. Ribbon representation of crystal structure is colored by secondary structure (sheets in cyan, helices in red and coils in gray), MD averaged structure in yellow color. Carbon atoms in crystal structure are in white, and are in yellow for MD averaged structure. Alignment was made using residues 15-27, 182-242, which forms the stable A binding pocket in Rossmann fold domain (RMSD of backbone of these residues between crystal structure and MD averaged structure is 0.83 Angstrom). RMSD of NAD⁺ itself (heavy atoms only) after alignment of MD averaged structure with respect to NAD⁺ from 1YC2:A is 1.11 Angstrom.

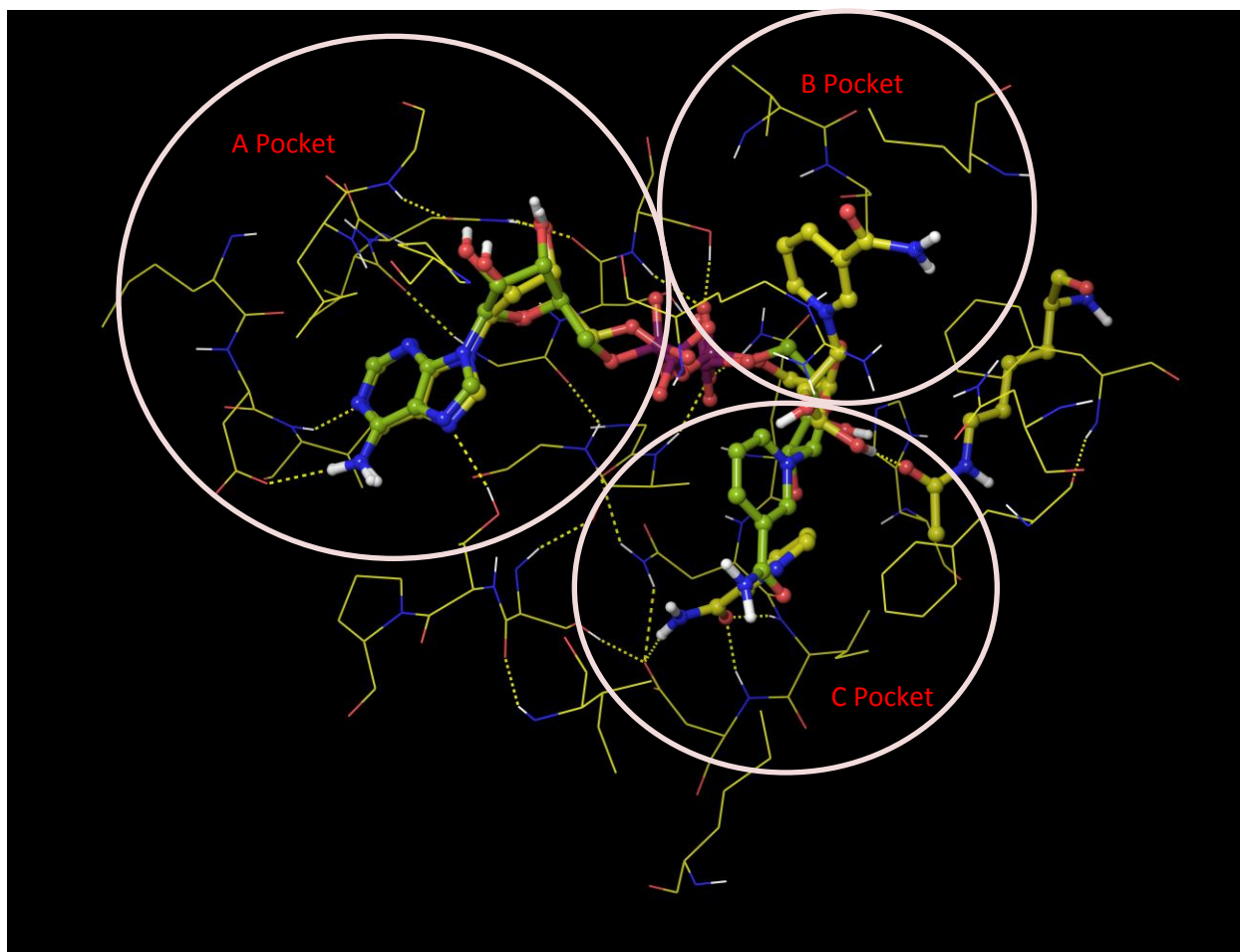


Figure 12b. Observation of A and C pockets from the MD averaged structure over last 10 ps of complex with NAM (Sir2TM/Ac-p53/NAD⁺/NAM), reference NAD⁺ structure (carbon in yellow green) taken from averaged structure over last 10 ps of ternary complex.

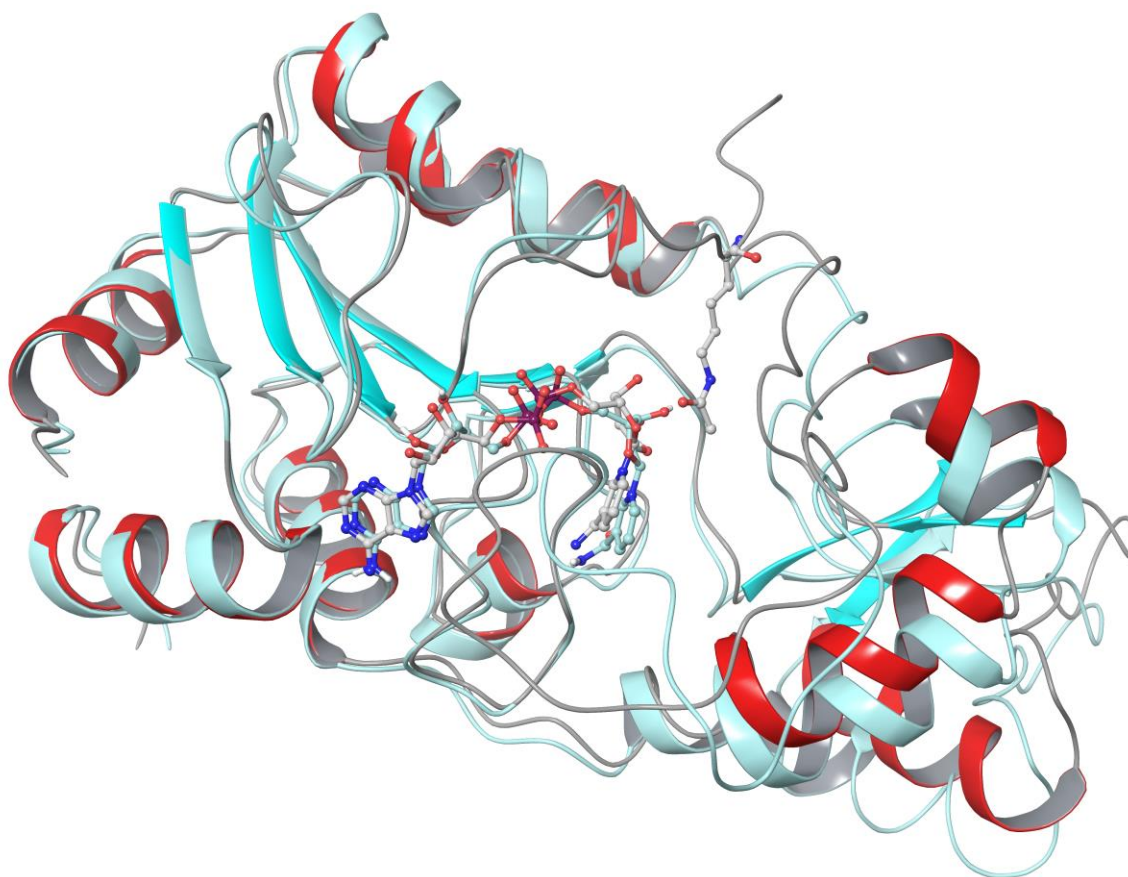


Figure 13: Alignment of binary complex (Sir2TM/ NAD⁺) from MD averaged structure (10 frames from last 10ps) with respect to crystal (pdbID:2H4F) structure. Ribbon representation of crystal structure is colored by secondary structure (sheets in cyan, helices in red and coils in gray), MD averaged structure in light blue color. Carbon atoms in crystal structure are in white, and are in light blue for MD averaged structure. Alignment was made using residues 15-27, 182-242, which forms the stable A binding pocket in Rossmann fold domain (RMSD of backbone of these residues between crystal structure and MD averaged structure is 0.76 Angstrom). RMSD of NAD⁺ itself (heavy atoms only) after alignment of MD averaged structure with respect to NAD⁺ from 1YC2:A is 0.83 Angstrom.

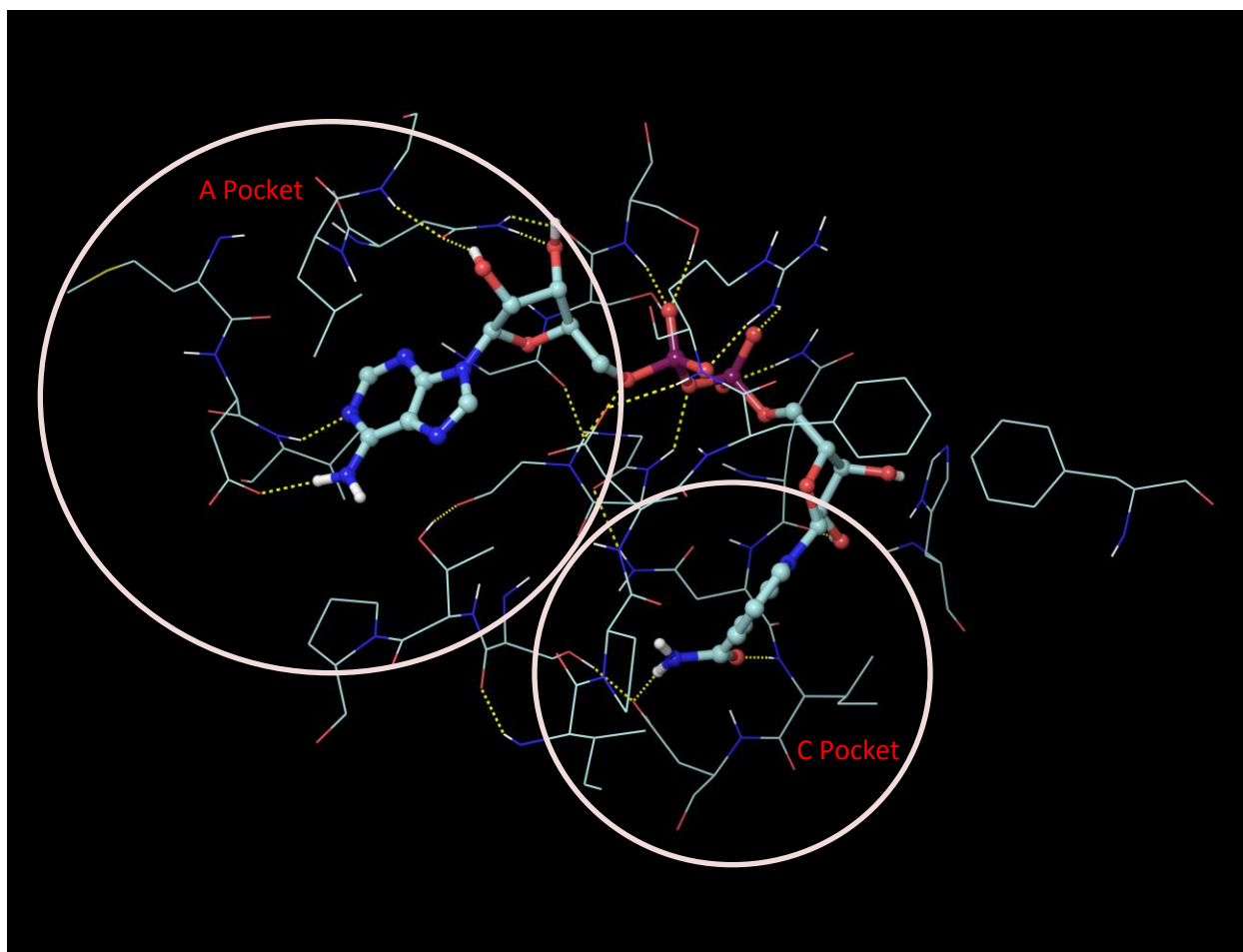


Figure 13a. Observation of A and C pockets from the MD averaged structure over last 10 ps of binary complex (Sir2TM/NAD+).

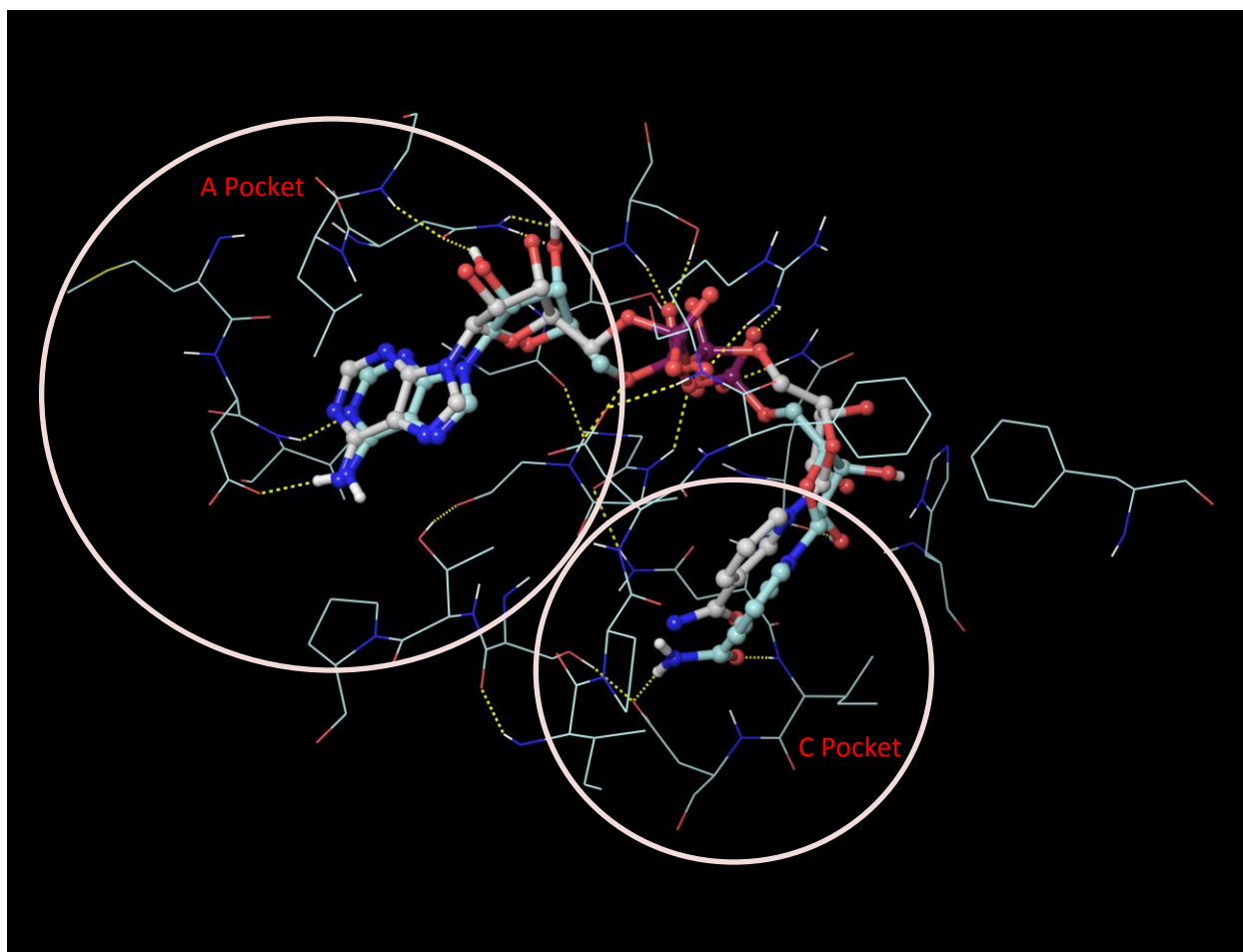


Figure 11b. Observation of A and C pockets from the MD averaged structure over last 10 ps of binary complex (Sir2TM/NAD+), reference NAD+ structure (carbon in white) taken from crystal structure 2H4F.

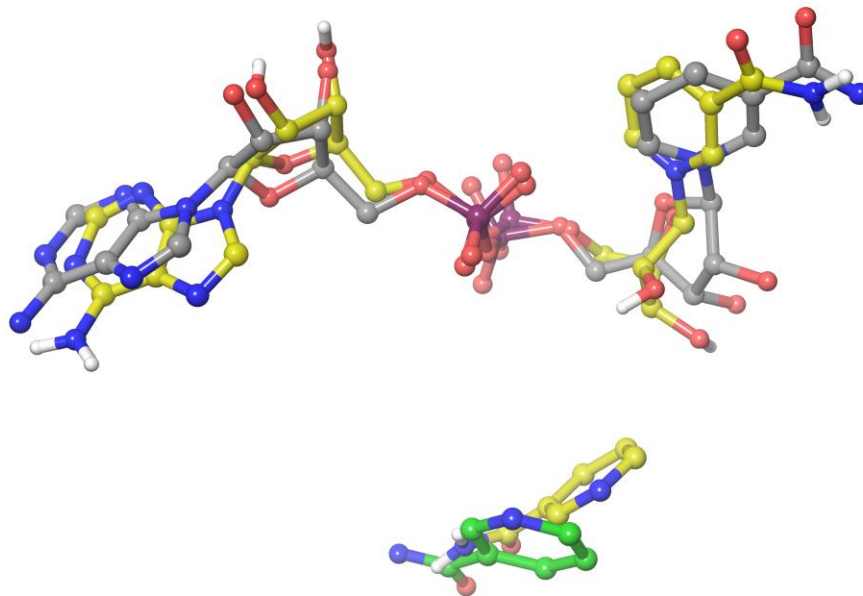
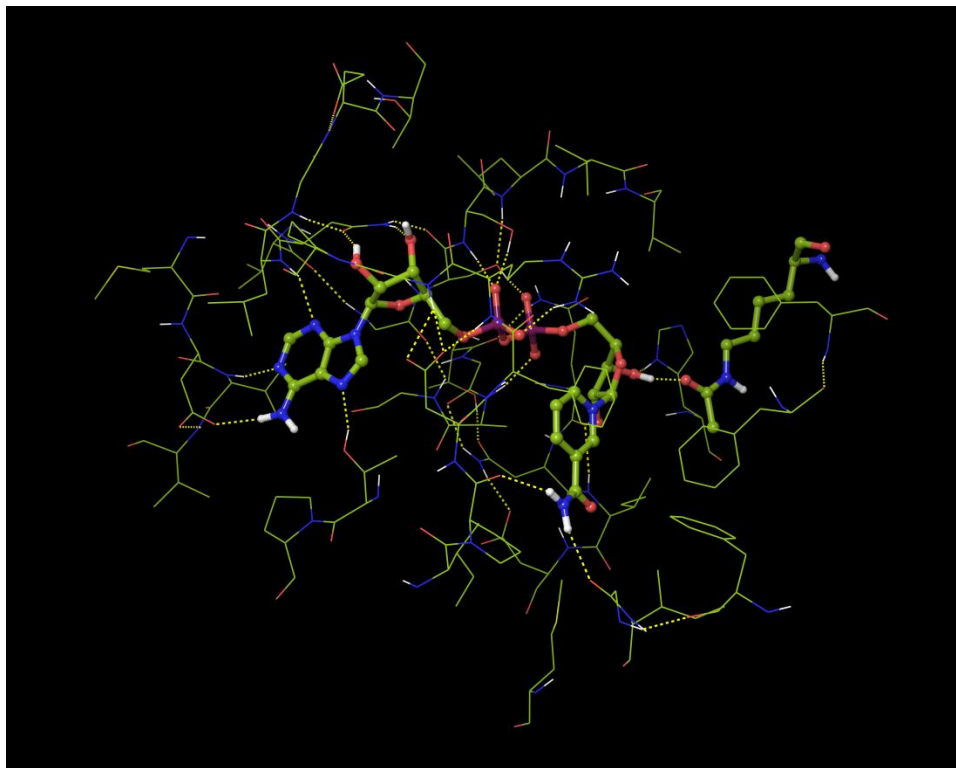
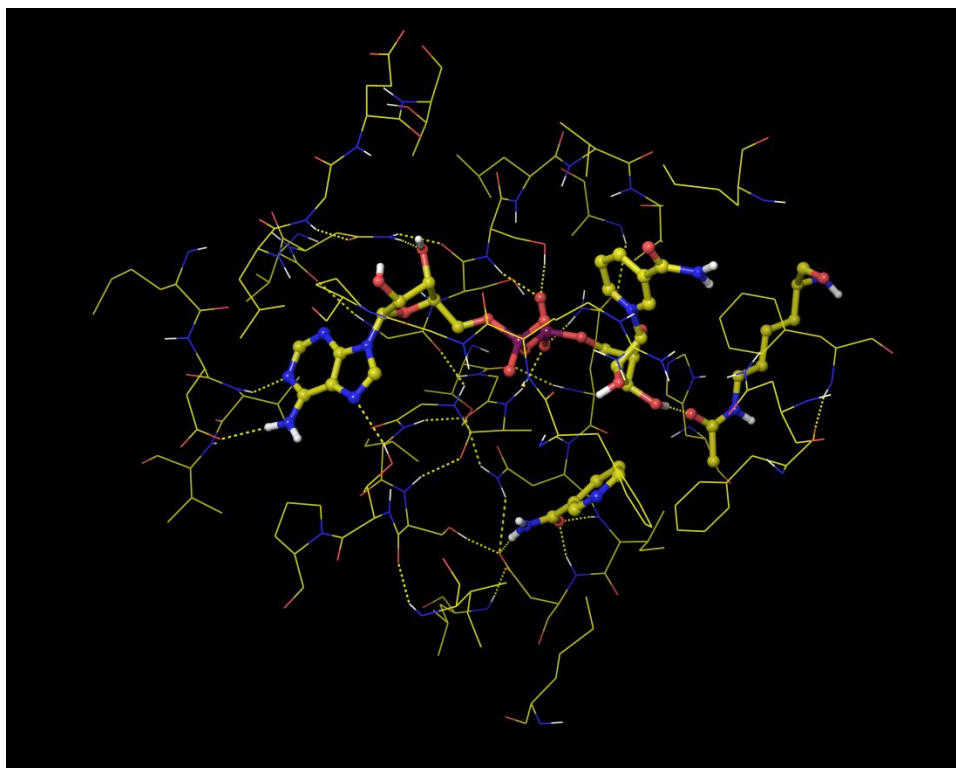


Figure 14: Alignment of NAD⁺ and NAM in complex with NAM (Sir2TM/Ac-p53/NAD⁺/NAM) from MD averaged structures (10 frames from last 10ps, carbon in yellow) with respect to starting structure (NAD⁺ in AB pose and NAM in C pocket taken from 1YC2:A, carbon in grey).



(a)



(b)

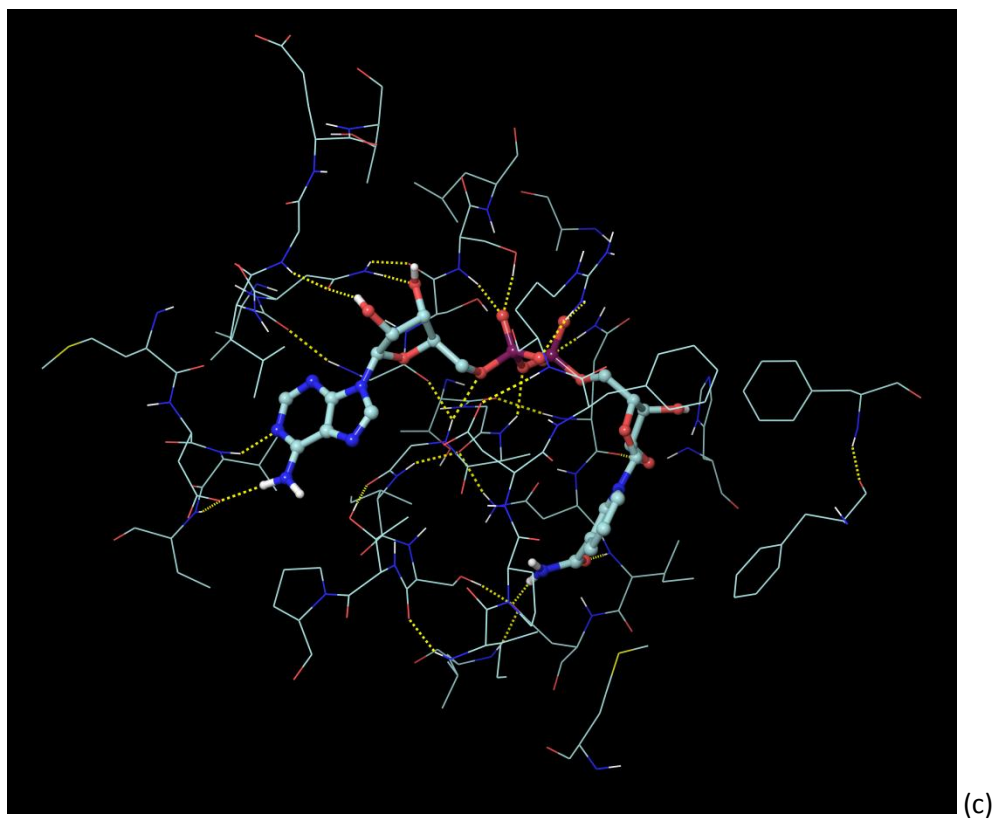
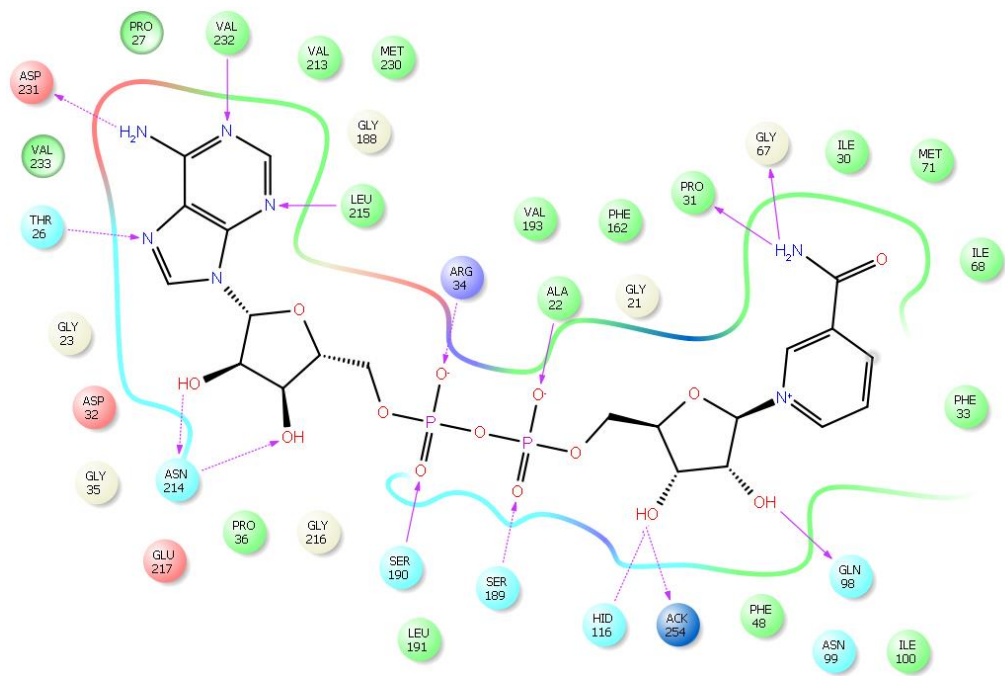
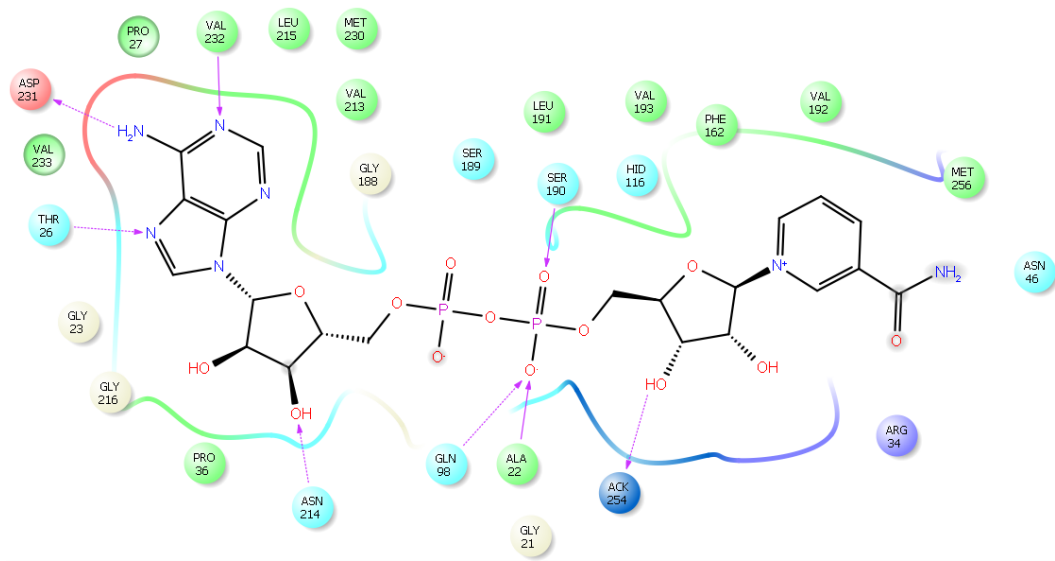


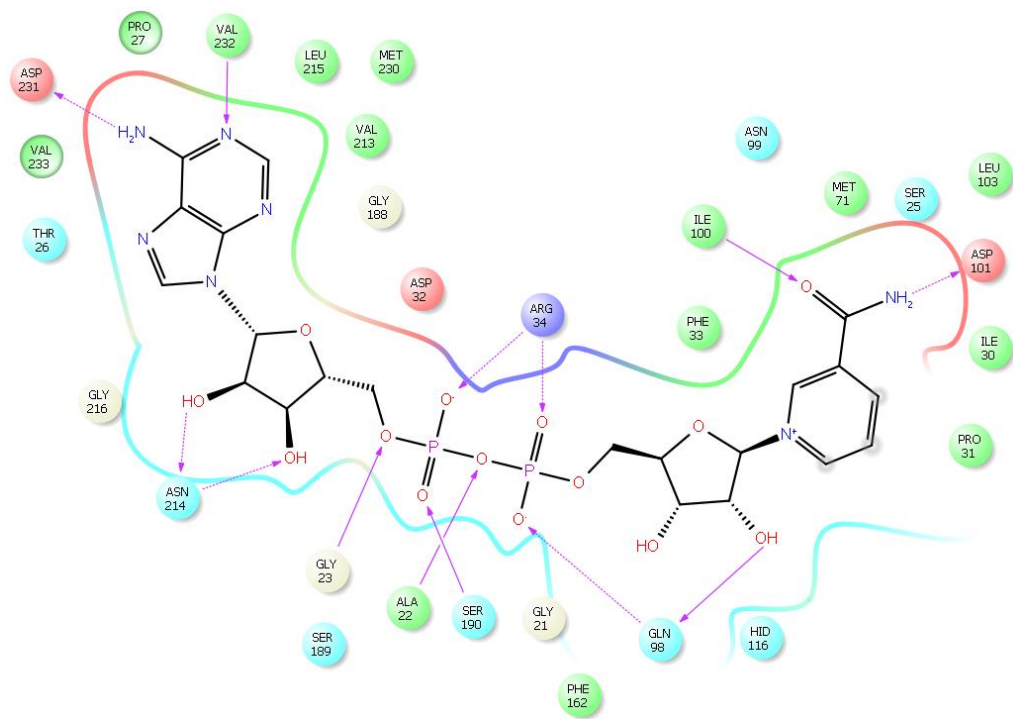
Figure 15. Binding of NAD⁺ and NAM in (a) ternary complex (Sir2TM/Ac-p53/NAD⁺); (b) complex with NAM (Sir2TM/Ac-p53/NAD⁺/NAM); (c) binary complex (Sir2TM/NAD⁺).



(a)



(b)



(c)

Figure 16. Sir2TM-NAD⁺ interaction diagrams of MD averaged structures (10 frames from last 10ps) (a) ternary complex (Sir2TM/Ac-p53/NAD⁺); (b) complex with NAM; (c) binary complex of Sir2TM/NAD⁺.

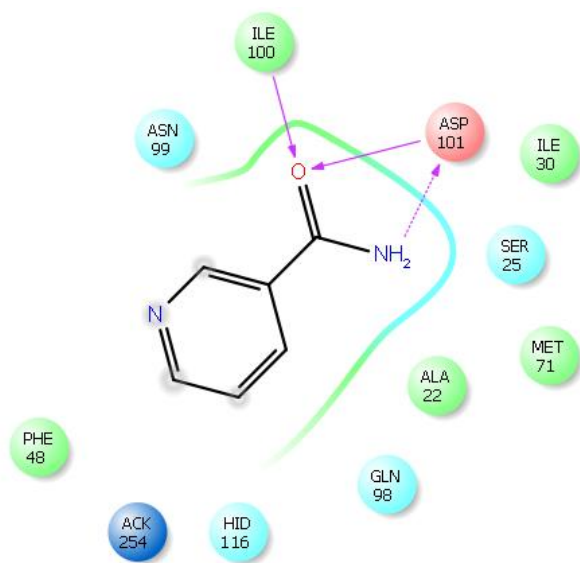


Figure 17. Sir2TM-NAM interaction diagrams of MD averaged structures (10 frames from last 10ps) of complex with NAM.