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, helixes 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

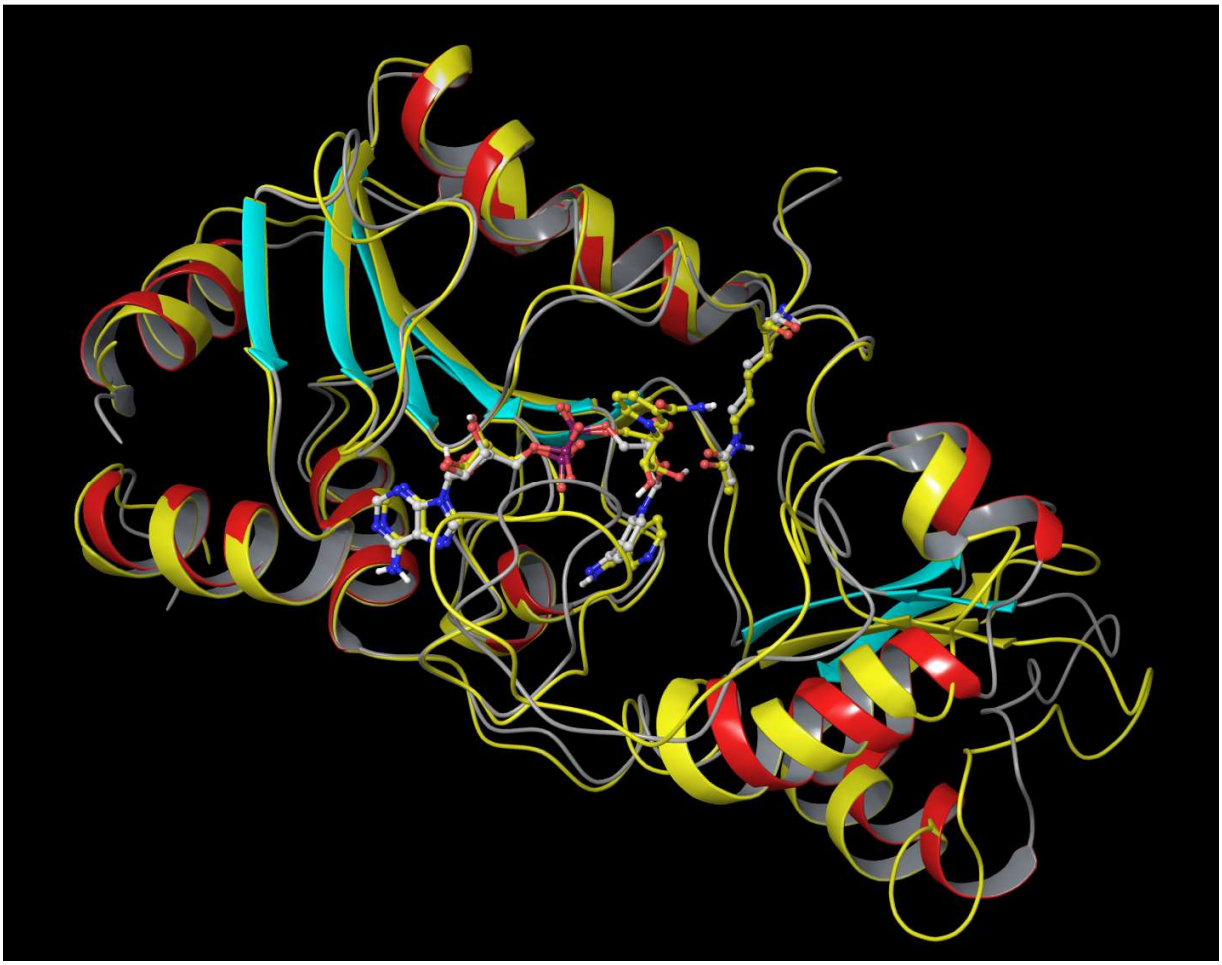


Figure 12: Alignment of complex (Sir2TM/Ac-p53/NAD+/NAM) from MD averaged structure (10 frames from last 10ps) with respect to crystal (pdbID:2H4F) structure. Ribbon representation of crystal structure is colored by secondary structure (sheets in cyan, helixes in red and coils in gray), MD averaged structure 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.

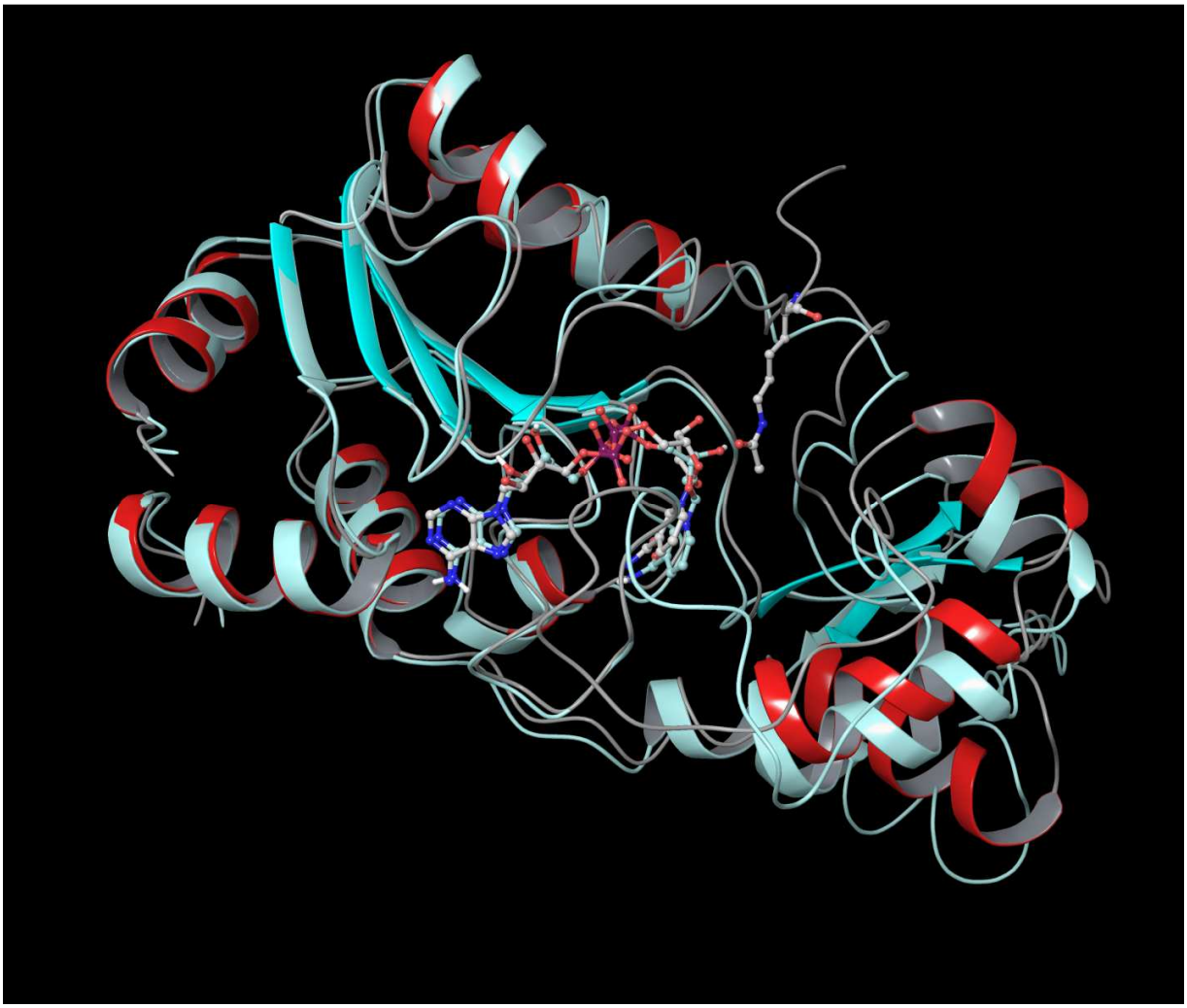


Figure 13: Alignment of binary complex (Sir2TM/ NAD+) from MD averaged structure (10 frames from last 10ps) with respect to crystal (pdbID:2H4F) structure. Ribbon representation of crystal structure is colored by secondary structure (sheets in cyan, helixes in red and coils in gray), MD averaged structure 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.

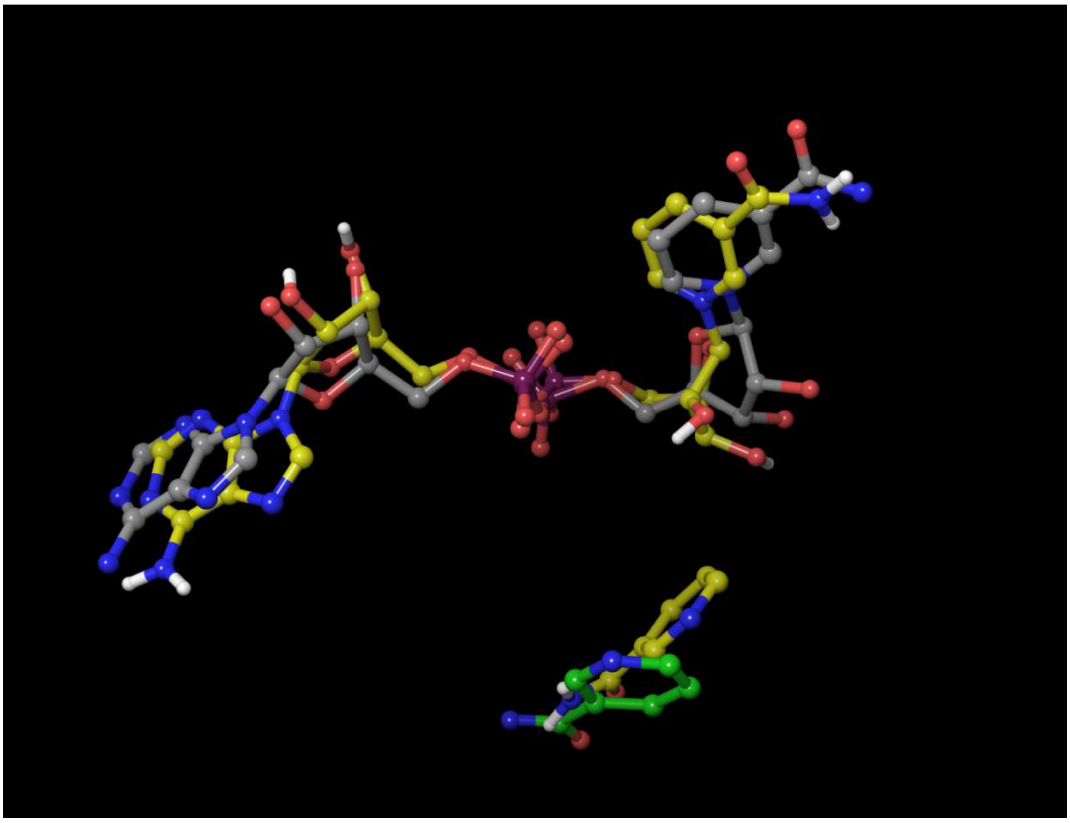
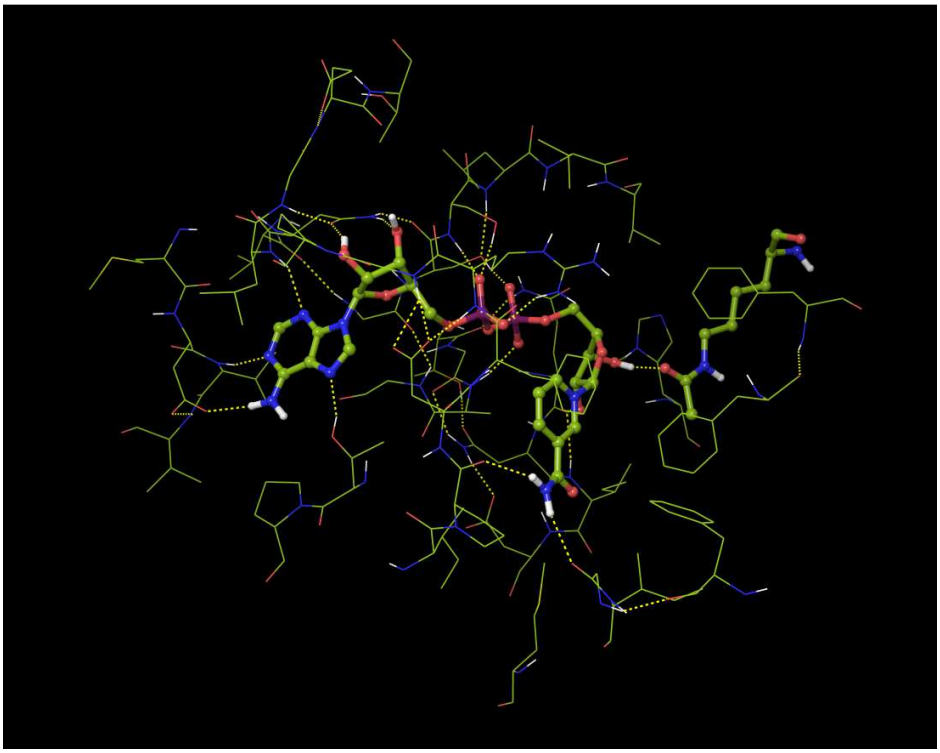
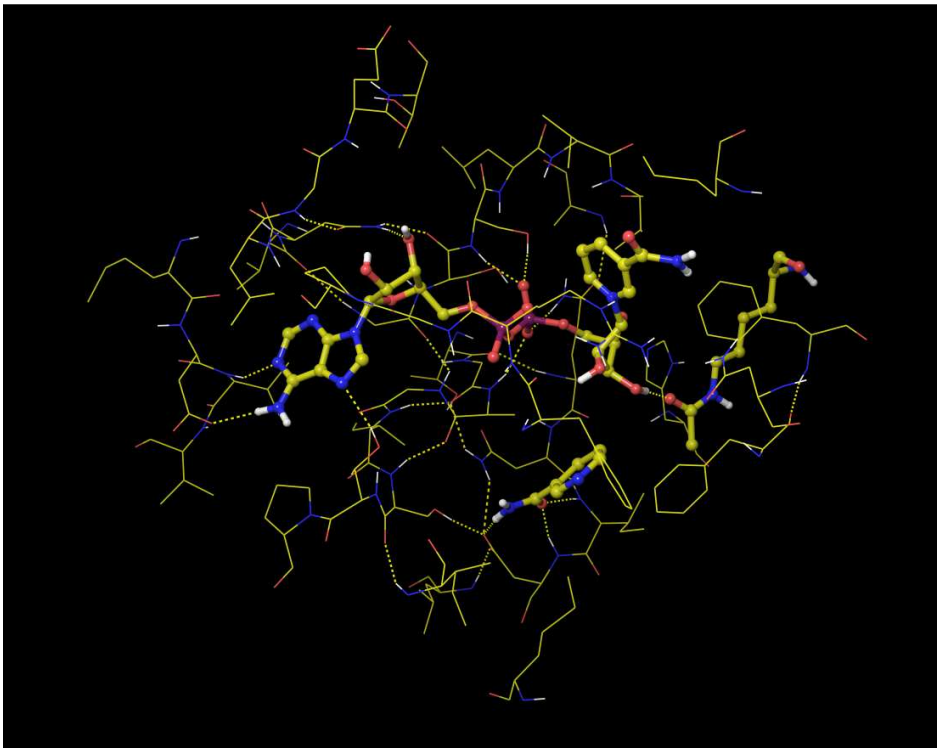


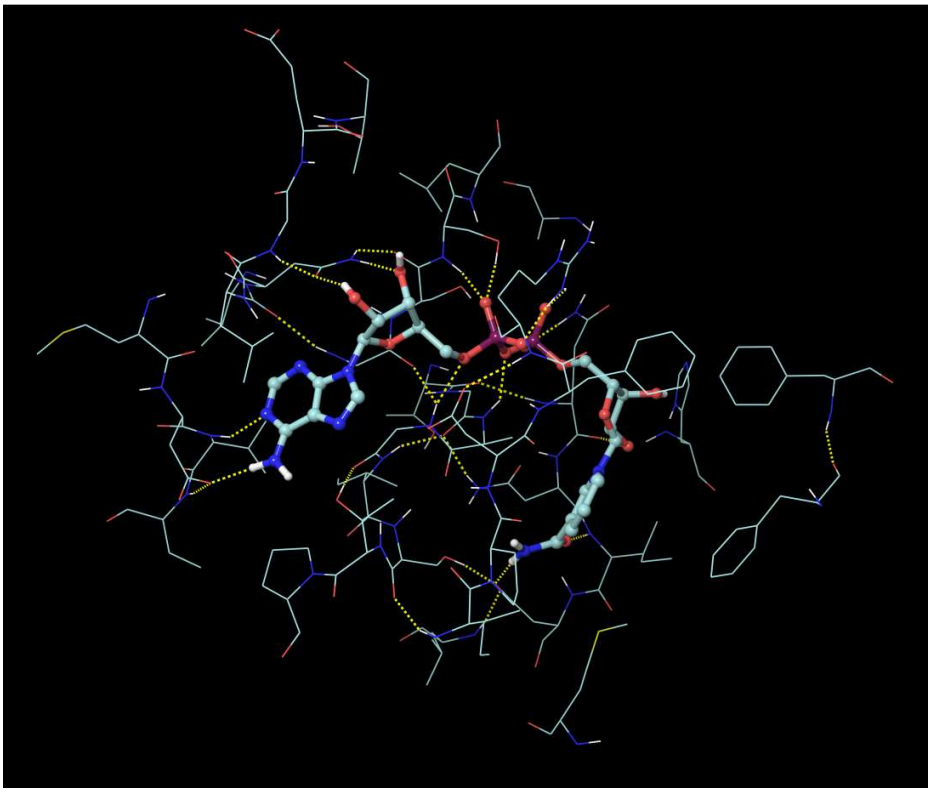
Figure 14: Alignment of NAD+ and NAM in complex with NAM (Sir2TM/Ac-p53/NAD+/NAM) from MD averaged structures (10 frames from last 10ps, carbon in yellow) with respect to starting structure (NAD+ in AB pose and NAM in C pocket taken from 1YC2:A, carbon in grey).



(a)

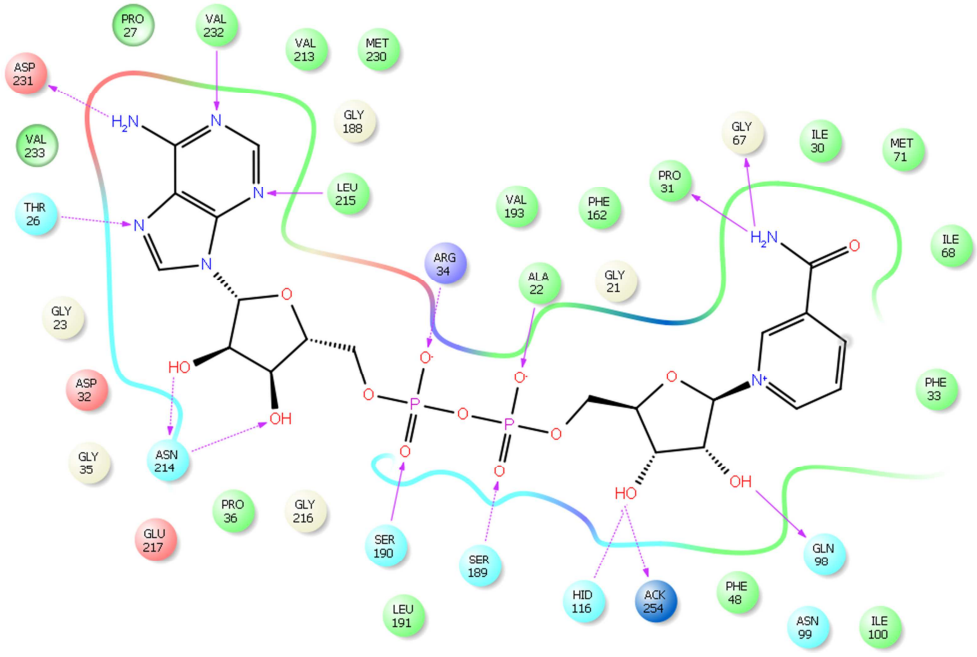


(b)



(c)

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+).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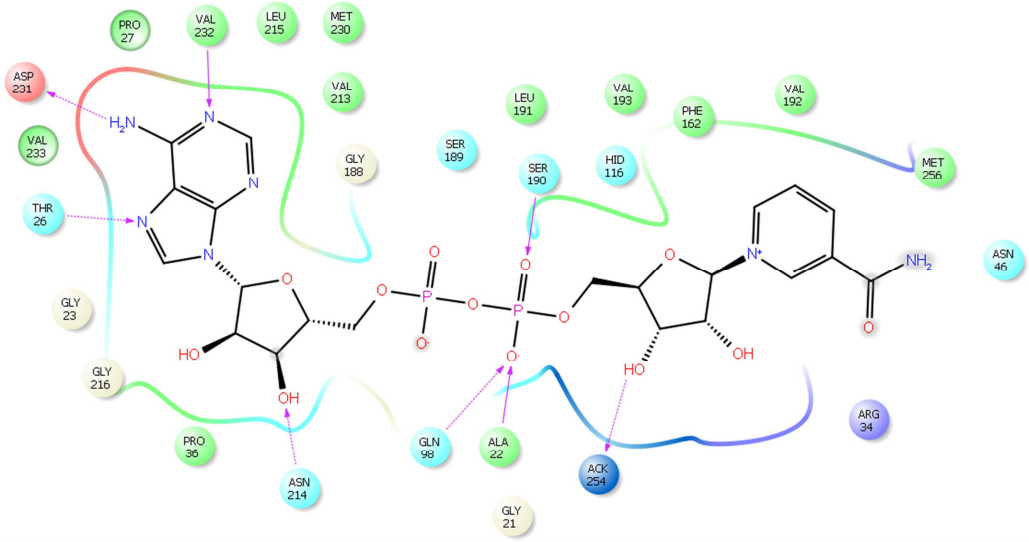
VAL 232
VAL 213
MET 230
ASP 231
GLY 188
VAL 233
LEU 215
THR 26
VAL 193
PHE 162
GLY 67
ILE 30
MET 71
PRO 31
ILE 68
ARG 34
ALA 22
GLY 21
GLY 23
ASP 32
PHE 33
GLY 35
ASN 214
PRO 36
GLY 216
GLU 217
SER 190
SER 189
HID 116
ACK 254
PHE 48
GLN 98
LEU 191
ASN 99
ILE 100

(a)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VAL 232
LEU 215
MET 230
ASP 231
VAL 213
LEU 191
VAL 193
VAL 192
PHE 162
VAL 233
GLY 188
SER 189
HID 116
SER 190
MET 256
THR 26
ASN 46
GLY 23
GLY 216
ARG 34
PRO 36
GLN 98
ALA 22
ACK 254
ASN 214
GLY 21

(b)

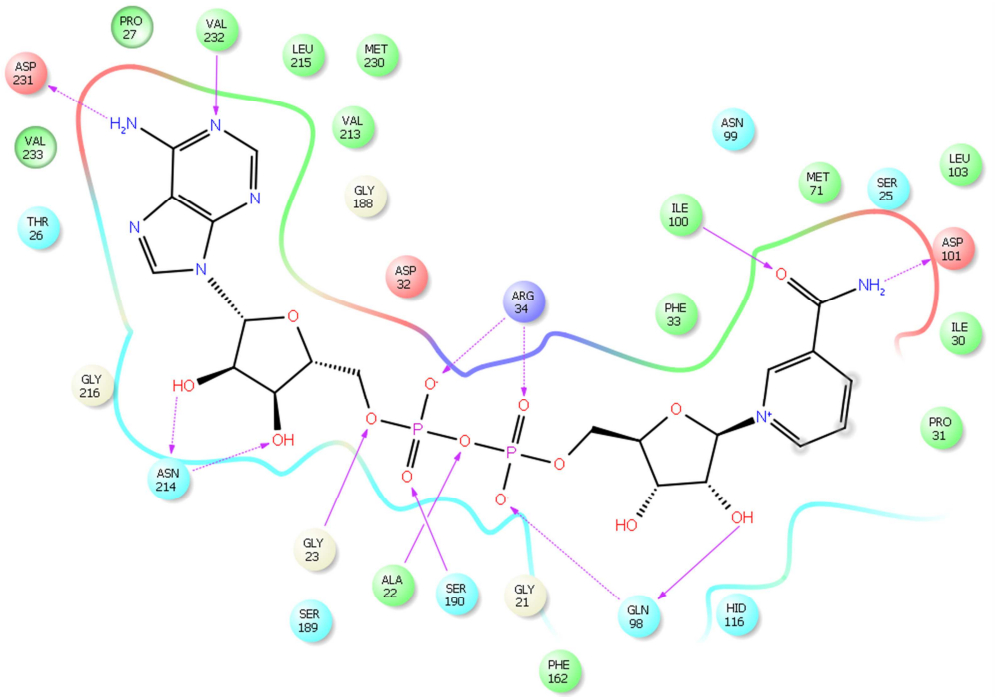

Figure 16. Sir2TM-NAD+ interaction diagrams of MD averaged structures (10 frames from last 10ps) (a) ternary complex (Sir2TM/Ac-p53/NAD+); (b) complex with NAM; (c) binary complex of Sir2TM/NAD+.

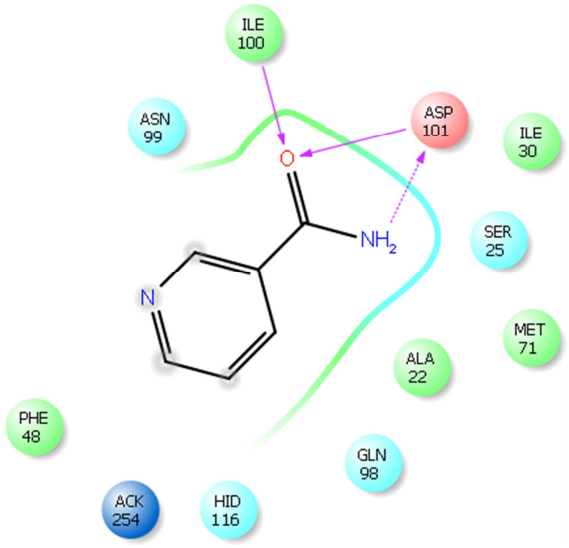

Figure 17. Sir2TM-NAM interaction diagrams of MD averaged structures (10 frames from last 10ps) of complex with NAM.