SI Table ---:

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| --- | --- | --- | --- |
| **Complex** | **Global heavy atom RMSD** | **Co-factor loop RMSD** | **Substrate RMSD** |
| Sirt3/ADPR complex/NAM modelled from 4FVT (**MD average**)  vs  Sirt3/ADPR complex/NAM modelled from 4FVT but with loop replaced from 4BVG (**MD average**) | 2.2 Å | **5.9Å** | ADPR (0.4Å)  Peptide part  ( 0.9Å)  NAM  (**6.7** Å) |
| 4FVT (ternary complex) – Xtal  vs  Sirt3/ADPR complex/NAM modelled from 4FVT (MD average) | 1.9Å | 3.9Å | ADPR part (0.62Å)  peptide part  ( 0.5Å) |
| 4FVT (ternary complex) – Xtal  vs  Sirt3/ADPR complex/NAM modelled from 4FVT but with loop replaced form 4BVG (MD average) | 1.1Å | 3.7Å | ADPR part (0.3Å)  peptide part  (0.7 Å) |
| 4FVT (ternary complex) – MD average  vs  Sirt3/ADPR complex/NAM modelled from 4FVT (MD average) | 2.27 Å | 3.94 Å | ADPR part (2.00Å)  NAM part (6.77Å)  peptide part  ( 1.74Å) |
| 4FVT (ternary complex) – MD average  vs  Sirt3/ADPR complex/NAM modelled from 4FVT but with loop replaced form 4BVG (MD average) | 1.5 Å | 4.35 Å | ADPR part (1.54Å)  NAM part (1.13Å)  peptide part  ( 2.21Å) |
| 4BVG (native intermediate) Xtal  vs  Sirt3/ADPR complex/NAM modelled from 4FVT (MD average) | 2.0Å | 6.3Å | NAD part (0.65.Å)  peptide part  ( 0.55Å) |
| 4BVG (native intermediate) Xtal  vs  Sirt3/ADPR complex/NAM modelled from 4FVT but with loop replaced form 4BVG (MD average) | 1.0Å | 1.4Å | NAD part (0.4.Å)  peptide part  ( 0.8Å) |
| 4BVG (native intermediate) MD average  vs  Sirt3/ADPR complex/NAM modelled from 4FVT (MD average) | NA | NA | NA |
| 4BVG (native intermediate) MD average  vs  Sirt3/ADPR complex/NAM modelled from 4FVT but with loop replaced form 4BVG (MD average) | NA | NA | NA |
| 4FVT (ternary complex) – Xtal  vs  4FVT (ternary complex) – MD averaged | 1.1Å | 2.2Å | NAD part (0.4Å)  Peptide part  (1 Å) |
| 4FVT (ternary complex) Xtal  vs  Sirt3/ternary complex/with 4BVG loop (native intermediate loop) MD averaged | 1.6Å | 4.0 Å | NAD part (2.4Å)  peptide part  ( 0.44Å) |
| 4BVG (native intermediate) Xtal vs Sirt3/ternary complex/modelled with 4BVG loop (native intermediate loop) MD averaged | 1.63Å | 1.62Å | NAD part (2.84Å)  Peptide part  ( 0.68Å) |
| 4BVG (native intermediate) Xtal  vs  4BVG (native intermediate) MD averaged | 1.6Å | 1.8Å | NAD (0.5Å)  Peptide part  ( 2.6 Å) |
| 4FVT (ternary complex) Xtal vs Sirt3/product complex/with 4FVT loop (native ternary loop) MD averaged | 1.57Å | 3.04 Å | NAD part (2.0Å)  Peptide part  ( 0.93Å) |
| 4FVT (ternary complex) Xtal vs Sirt3/product complex /with 4BVG loop (native intermediate loop) MD averaged | 1.82Å | 3.68Å | NAD part (2.43Å)  Peptide part  ( 0.43Å) |
| 4BVG (intermediate complex) Xtal vs Sirt3/product complex /with 4FVT loop (native ternary loop) MD averaged | 1.81Å | 4.37Å | NAD part (2.54Å)  Peptide part  (1.06 Å) |
| 4BVG (intermediate complex) Xtal vs Sirt3/product complex /with 4BVG loop (native intermediate loop) MD averaged | 1.72Å | 2.14Å | NAD part (1.73Å)  Peptide part  (0.34 Å) |

*\*Note: Only the matching atoms were considered for RMSD calculation.*