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| **Date** | **Task** | **Remark** |
| June 20th | Setting up and calculating MM/GBSA scores from the **1ns** trajectory   1. **Sirt3/INT/NAM - 4FVT rec/loop** 2. **Sirt3/INT/NAM - 4FVT recp/4BVG loop** 3. **Sirt3/2’-OAADPr- 4BVH rec/ loop** 4. **Sirt3/2’-OAADPr- 4BVH recp/3GLS loop** 5. **Sirt3/2’-OAADPr/Ac-cs2 deac-4FVT rec/loop** 6. **Sirt3/2’-OAADPr/ Ac-cs2 deac -4FVT rec/4BVG loop** 7. **4FVT with NAD+/peptide** 8. **4FVT with NAD+/peptide loop from 4BVG** | **STATUS:**  **Trajectories are available for systems**  **A to E**, but for **system F only modelling has been complete.**  \***G and H are now listed in the schedule**  **NB: MM/GBSA and MM/PBSA scores for**  **systems A-E already updated on wiki** |
| June 21st | Setting up Equilibration and 1ns MD simulation for **system F**  Sirt3/2’-OAADPr/deAc-cs2-4FVT rec/4BVG loop  Computing MM/GBSA values from the equilibration and 1 ns simulation trajectory in the evening |  |
| June 22nd | **System G and H**  Modelling 4FVT with NAD+/peptide (Data available from previous PLOS paper)  Modelling 4FVT with NAD+/peptide with loop grafted from 4BVG (**Data available???)** |  |
| June 23nd | Setting up Equilibration and 1ns MD simulation for **system H and rerun the existing MD trajectories for MM/GBSA scores for system G.** | In case if trajectories are available then rerun them for MM/GBSA and MM/PBSA scores |
| June 24th | Computing MM/GBSA values from the equilibration and 1 ns simulation trajectory for systems G and H | Send out the complete report to Dr Raj for his analysis to decide upon which system to be used for the extended 12 ns simulation |
| June 25th  **(WEEKEND)** | Launching the extended simulation for the system pairs decided by Dr.Raj |  |
| June 27-28 th | Miscellaneous task items 1,2  (needs to write a Perl script) | A 12 ns MD simulation will be running in the background |
| June 29-30th | Compute MM-PBSA and MM/GBSA binding energies from the 12ns MD trajectories on the system that will be decided  ---------------------------------------------------  Miscellaneous task items  3,8 and 10  Mostly methodology write-up work |  |
| July 1st | Miscellaneous task items  4 -9 |  |
| July 5th | Miscellaneous task items  4-9  Continued .. |  |
| July 6-7th | Work on side chain validation data  Presenting the data  Miscellaneous task 12 |  |

**The following are the tasks for the paper based on the priority and the time of availability of the data.**

1. Creating probability density distribution plots based on the energies of each frame in the MD simulation. Two version of this figure needs to created (One for continuous data 2-12 ns and the other plot should be for a specified time interval (ie-2-ns window period) . Perl script needs to be written to accomplish this task. Sirt3/INT/NAM complex data available. Sirt3/AADPr product complex data will be computed upon completion of the MD simulation. ( This script is generic so , I listed this task as 1 superseding task 2)
2. Also consider showing a time series plot from t=0 (I believe that a continuous time series plot from t=0 to t= 12ns will require rerunning the trajectories from t= 0 to t=12 ns. We now have continuous data for t=2 to t=12 ns and for specified time intervals (2ns time window). In case if we decide to go by “successive times” as suggested in your earlier comment then we would end up with 6 plots for a single simulation ie, t=0-2, t=2-4, t=4-6 ….)
3. Starting structures for simulations (for SI)
4. Ligand interaction diagrams for Sirt3/INT/NAM complex (data available) the co-products from other systems (Sirt3/AADPr closed and open product complex data not available). Also Sirt3 ternary complex (Sirt3/NAD+/peptide with 4FVT and 4BVG loop)
5. Fig ------Simulated B factor values for Sirt3/2’-OAADPr product complex modeled based on native and closed loop conformation (4BVH). Note Sirt3/INT/NAM Bfac data already completed.
6. Fig ------ Per-residue RMSD values for the cofactor binding loop region calculated with respect to MD averaged structure of Sirt3/2’-OAADPr complex based on open/closed loop conformation. Note Sirt3/INT/NAM rmsd plot already completed.
7. Revise the Table …..MM/GBSA and MM/PBSA conformational energies and binding affinity calculation based on the new simulation results (Sirt3/OADPr closed loop) and sirt3/ternary complex. Also revise the earlier MM/GBSA and MM/PBSA table prepared for Sirt3/INT/NAM as suggested by Dr.Raj because NAM data shows insufficient sampling leading to convergence issue.
8. Time series plot of MM/GBSA and MM/PBSA energies for Sirt3/OAADPr closed/open loop conformation. Also revise the old plot (Sirt3/INT/NAM) with 2 or 3 traces as suggested by Dr.Raj (I guess we can show only 2 traces and not 3 traces).
9. Receptor with INT
10. Receptor with NAM
11. NOT SURE if INT/NAM with receptor can be calculated anyways will give it a try).
12. Identify B factors for any Sir2 simulations available from PL’s data if any to make the plot analogous to that for SIRT3.

(The following will be linked to the MD methodology section)

1. MD simulation method protocol and particular treatment of non-standard residues has to be written.
2. Method for Ligand/NAM placement needs to identified and written for the completeness of supplementary section.
3. Identifying all data on side chain validation carried out by Ping and present the data in a format so as to distinguish sampling/energy errors.
4. Incorporating the references for the computational section and a draft of the methodology has to be written (Will be adapted from the previous PLOS one paper).

Miscellaneous task (less priority)

1. Related structure alignment task: align the PLOS INT/NAM MD average with that from the latest INT/NAM simulation (closed loop), check RMSDs, including that of NAM, acetyl-Lys and rest of ADPR. Note energies cannot be compared since PLOS used 4BVG.
2. Make another version of each of these distribution figures wherein the x axis is RMSD with respect to starting structure. Annotate the location (RMSD) of the MD average structure in each case