|  |  |  |
| --- | --- | --- |
| **Date** | **Task** | **Remark** |
| May 27th | Prepare draft for side chain prediction and refinement which Ping had implemented earlier. Upon review by Dr.Raj the protocol will be implemented for the other model that will be prepared( sirt3/OAADPR complex with an open loop) | High priority |
| June 6-7th | Installing Schrodinger suiteNB: If everything goes fine we could gain a day.The whole schedule would get shifted ahead by a day.Will also look into all previous notes prepared by Ping and Arabinda in this regard.-----------------------------------------------Time will be also used to calculate the MM/PBSA and MM/GBSA binding energies of Sirt3/OAADPr complex with native loop. (Simulation will be complete d during my vacation and I will re-run the trajectories on the very first day after I return from vacation)In NB: An MM/PBSA rerun take s ~ 6 hrs | Since it’s not a license upgrade, installation of the latest version needs to be done from scratch.I believe that the desktop machine will be used as the license server and a gpu node can be added to the node list authorized to access the license file. The second part is bit tricky.I have kept aside two days for this because if any issue pops up during installation I we need help from Schrodinger support team.NB: in the interest of time if any issues arise we will stick with the windows machine to get the side chain job completed quickly |
| 8-9th June | Modelling the Sirt3/AADPr product complex with an open loop conformation in Prime. This task includes side chain prediction, model refinement using Prime and model validation. The protocol employed by Ping would be followed for consistency purpose. |  |
| June 10th | Setting up an MD simulation for the modelled system.I have accommodated this task into a single day schedule (really tight assuming that I will have no issues during structure preparation).Since, I will have prior experience in creating parameters for AADPr, I think it should be easy to replicate here too, because the AADPR is the same. | This includes parametrizing non-standard residues and obtaining QM partial charges followed by minimization and equilibration. |
| June 11th **(WEEKEND)** | Analyzing if the system has equilibrated and then launch the production simulation for the sirt3/AADPr production complex with open loop conformation. | This will be done over the weekend to effectively utilize the weekends for the run time. |
| June 13-15th | Compute MM-PBSA and MM/GBSA binding energies for Sirt3/OAADPr/ deace-peptide complex of the complex with an open loop conformation.------------------------------------------------Compiling a report of the MD work, in particular updating the MM/PBSA table, generating MD based B fac plots, and generating time vs energy plots as done for other Sirt3/INT/NAM complexes contained in the manuscript | A detailed list of miscellaneous task is listed at the end of the document |
| June 16th | Completion of other works related to manuscript draft will be undertaken. It includes writing up the method section ( It has not been touched upon till date)1. Adding references for the supplementary method section.
2. Any other pending work related to manuscript like image editing, formatting reference style etc if any
3. Creating ligand interaction plots
 | A detailed list of miscellaneous task is listed at the end of the document |
| June 17th | Reserve day, to complete any task if behind schedule. |  |

**Miscellaneous task list**

The following are the tasks for the paper.

Fig ------Simulated B factor values for Sirt3/OAADPRr complexes modeled based on native closed conformation (4BVH) and an open loop conformation as see in apo enzyme (3GLS).

Per-residue RMSD values for the cofactor binding loop region calculated with respect to

MD averaged structure of Sirt3/OADPr complex modeled based on an open and closed loop conformation.

Fig Ligand interaction diagrams for the product interacting with open and closed loop conformation and for Sirt3/INT/NAM complex

Table …..MM/GBSA and MM/PBSA conformational energies and binding affinity calculation based on the new simulation results

Time series plot of MM/GBSA and MM/PBSA energies for Sirt3/OAADPr with open and closed loop conformation.

Creating probability density distribution plots based on the energies of each frame in the MD simulation.

SI Fig ------: Plot showing crystallographic B-factor values of the Cα atoms belonging to the co-factor binding loop region of Sirt2 in different states.

Method for Ligand/NAM placement needs to be worked out for the supplementary section

MD simulation method in particular treatment of non-standard residues has to worked out

Working with Alok and Guan in editing the graphic image files.