|  |  |  |
| --- | --- | --- |
| **Date** | **Task** | **Remark** |
| June 7th | Sirt3/AADAPr ( open loop simulation) job submitted  Installation of Schrodinger software done. | This job will be completed by Friday evening.  I will be doing the MM/PBSA scoring on June 11th (Saturday ) |
| June 9th -10th | 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. | Once the modelling job is done the preliminary data form the modelling will be send out to Dr. Raj for his evaluation and approval before subjecting the model for MD simulation |
| June 12th  **(WEEKEND)** | Compute the MM/PBSA energies for  Sirt3/AADPR (closed loop conformation) | Send out the report to Dr.Raj for his analysis |
| June 13th  **(WEEKEND)** | Setting up an MD simulation for the modelled Sirt3/AADPr (open loop conformation) system.  I have accommodated this task into a single day schedule (really tight assuming that I will have no issues during setting up the MD system). Since, I will have prior experience in creating parameters for AADPr, I hope that 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 simulation. |
| June 14th | Analyzing if the system has equilibrated and then launch the production simulation for the sirt3/AADPr production complex with open loop conformation. **( 2 hr task)**  Rest of the time to be used for completing the miscellaneous task based on the order of priority and the availability of data at that time. ( listed at the end of the document) | Miscellaneous task items listed 1 and 2 will be undertaken |
| June 15th | Miscellaneous task items  3, 4,5 |  |
| June 16th | Miscellaneous task items  6,7 ( needs to write a Perl script ) |  |
| June 17th | Miscellaneous task items  8,14,15,16 |  |
| June 18th  **(WEEKEND)** | Compute MM-PBSA and MM/GBSA binding energies for Sirt3/OAADPr/ complex with an open loop conformation.  ------------------------------------------------  Update the MM/PBSA and MMGBSA tables with the new numbers |  |
| June 20th | Miscellaneous task items  9-13 |  |
| June 21 | Reserve day, to complete any miscellaneous task |  |

**Miscellaneous task list based on the priority list prepared by Dr.Raj**

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

1. Fig ------Simulated B factor values for Sirt3/OADPRr complexes modeled based on native closed conformation (4BVH). Note Sirt3/INT/NAM complex already completed.
2. Fig ------ Per-residue RMSD values for the cofactor binding loop region calculated with respect to MD averaged structure of Sirt3/OADPr complex based on closed loop conformation. Note Sirt3/INT/NAM complex already completed.
3. Fig Ligand interaction diagrams for Sirt3/INT/NAM complexes with 4FVT and 4BVG loop. The second figure would be for Sirt3/OADPr with a closed loop conformation (4BVH).
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).
5. Revise the Table …..MM/GBSA and MM/PBSA conformational energies and binding affinity calculation based on the new simulation results (Sirt3/OADPRr closed loop). 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.
6. Time series plot of MM/GBSA and MM/PBSA energies for Sirt3/OAADPRr closed 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).
7. Receptor with INT
8. Receptor with NAM
9. NOT SURE if INT/NAM with receptor can be calculated anyways will give it a try).
10. Creating probability density distribution plots based on the energies of each frame in the MD simulation. (Perl script needs to be written). Sirt3/INT/NAM complex.
11. A similar version of the figure with X axis RMSD and Y axis probability density (**less priority**).
12. Fig ------Simulated B factor values for Sirt3/OADPRr complex modeled based on open and closed conformations (3GLS).
13. Fig ------ Per-residue RMSD values for the cofactor binding loop region calculated with respect to MD averaged structure of Sirt3/OADPr complex based on open loop conformation.
14. Fig Ligand interaction diagrams for Sirt3/OADPr complexes with open and closed loop conformation (4BVH).
15. Creating probability density distribution plots based on the energies of each frame in the MD simulation (Sirt3/OADPr/ open loop conformation)
16. B factors for any Sir2 simulations available from PL’s if so make the corresponding plot analogous to that for SIRT3.
17. Method for Ligand/NAM placement needs to be written for the supplementary section
18. MD simulation method protocol and particular treatment of non-standard residues has to be written. ( This will be linked to the MD methodology section)
19. Starting structures for simulations (for SI)