Date: 3/7/2016

Tasks:

1. Mapping the remaining raw data files relevant to the information contained KT documents.

Status: Largely completed, some more data on loop modelling needs to be mapped.

1. Create new B factor plots based on the MD data contained in

 C:\Users\plin\Documents\MD\_works \Flexible\_Loop\_Bfactor\_Summary.xlsx

 Two plots needs to be created.

1. Perform a structure based sequence alignment using PROMALS3D to recreate the figure presented in Pling’s summary document.

The following PDB ids 4I5I, 3ZGV, 4FVT, 3RIY, 3ZG6, 2H59, 1YC2, and 1SZC will be considered for alignment and highlight regions containing the conserved residues critical for catalysis and their mutations.

RC: -- Task 3: is PROMALS3D what Ping used?

If so, please indicate some of the differences between the new alignment/presentation and the old one.

E.g., this might include focusing on a particular region.

RSK: Looking at the image and also digging through the files located in (user: Pling), I do see that Pling has some html result files generated using PROMALS3D. Further looking at the style of the data, I am confident that the alignment output must have been obtained using the PROMALS3D.

Looking at the footnote below that alignment image, I see that the whole point in having the sequence-structure alignment was to highlight residue conservation in the loop region (showing the short helix) and the beta turn region.

However, the image contains the entire sequence space, which looks to be slightly cluttered.

Hence, my suggestion is to use the alignment information provided by PROMALS3D and then filter the aligned region of interest and then proceed to create a sequence logo image to highlight the degree of conservation.

Such a graphic representation would look something like

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*Here, the relative sizes of the letters indicate their frequency in the sequences.*

Alternatively, a simple solution would be to edit the PROMALS3D image and the crop it to focus only on the region of interest.

RC: Let’s prepare drafts of both. I agree that the main purpose was to show sequence conservation in the loop.

Note that Ping might, however, have prepared the graphic as he did because of catalytic residues that were not close to the loop in the primary sequence.

Guan has posted docs/tables to the wiki (you can ask her where) that annotate in detail the catalytic roles of various important residues.

An earlier comp chemist in our group (Eric) had created some such sirtuin sequence logos posted on the wiki in the past.

1. Pymol rendering showing the conformational heterogeneity of the cofactor binding loop (with and without the side chains displayed). The following PDB ids will be used to carry out a structural alignment. (4BVG, 4FVT, 4JSR, and 3GLS).

RC: -- Task 4: Structure alignment from pdbs. Yes, SIRT3 is the priority. I believe there was also a note about Sir2Tm in the Supporting Info. We should bear in mind that using 4 structures might lead to clutter. I believe the priorities were 4BVG and 4FVT? We can consider the others as well possibly for alternate versions of the Fig but with a plan.

RSK: I get your point. I will go ahead and prepare a session file with all four PDB entries. However, for generating image I will use only 4BVG and 4FVT in the display. Since, I will have everything saved in a pymol session file, we can always open the session file and juggle between the PDB entries, as required. A pymol session file will mitigate the need to create a quality rendering each time when required.

RC: Yes, this should work well.

1. A new figure showing the comparison of SIRT3 complexes with cofactor binding loop modeled based on coordinates from ternary and intermediate complexes.

RC: Task 5: This is from MD data, right?

RSK: Yes, that’s right. It’s the MD averaged structure. I have located the pdb file of the MD averaged structure. ***However, the FOOT NOTE for the image provided by Pling in the original summary document says that “the native 4FVT structure after MD is aligned for comparison”. But looking at the image, I see the image to contain only one structure.* This needs to be reconciled. I think that 4FVT\_isoNAM\_v1\_mds\_avg10ps.pdb (native 4FVT simulation average structure) is the structure which Pling is alluding to.**

RC: Note that the figure that Ping made was not the same one we intend to put in the paper. The new figure will use MD average data in place of pdb-based structure alignments to illustrate loop conformational differences. From the reports, you will see that one pdb structure was used as the basis for simulations of two loop conformations (intermediate, ternary); for the second loop conformation, the loop coordinates were substituted from another pdb structure. 4FVT: ternary; 4BVG: intermediate.

For both loop conformations, I believe we have carried out simulations with the ADPR-intermediate and NAM as ligands.

The plan for the figure revision is to align the averaged structures from the simulations with the two different loop conformations.

RC: Also, there were RMSD plots in one Fig, that is later to be merged with either 4 or 5. Are we planning to use the old versions?

RSK: I will have to recreate one so that it match publication quality image standard and for consistency with the other plots. I have appended this item to the task list as item no 8.

1. Recreate new MM/GBSA and MM/PBSA tables similar to the previous PLOS ONE 2014 paper, reporting only binding energy values computed between 2-12 ns time scale. Two such tables need to be created.

RC: Should we list the raw data required for each task under the task?

RSK: Yes, I think that would help in maintaining a good documentation. I have added it as item no 7 to the task list.

1. Add the location/path of the raw data used for completing the assigned task in “Task list1”
2. Replot the two RMSD plots contained in the KT document (manuscript computational section excerpts and task.doc)

You can add my comments and iterate on them in the doc file you posted or directly on the tasks list page.

Should we list the raw data required for each task under the task?

RSK: Yes, I think that would be helpful for documentation purposes. Will add it .

RC: Also, regarding draft captions for the Figures, I believe some were included in the tasks document I posted to dropbox. If some of the planned Figures are missing captions, we can identify them and make caption preparation a task.