Flexibility Plots for Mucin Runs

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RMSD-based plots

These do a better job validating the simulations than demonstrating flexibility, per se. But, they do a little of that, too.

In each of the plots in this section:

- The plot represents the RMSD values for all simulations referenced to a single input structure as described below.
- The gray backgrounds separate one simulation from another.
- The dark gray background indicates the simulation that was begun from the structure being used as the reference for the RMSD calculations.
- It is important to note that the simulation trajectories were the same. Only the structure used as the reference for calculating the RMSD changes.
- On the X-axis, “Frame Index”, merely indicates the total count of frames processed. There is a loose correlation to simulation time, but the two are not equivalent.
- Y-axes are the same between RMSD classes (backbone or sugar) to simplify comparisons.

Backbone RMSD Comparisons

Eventually, there will/can be plots like these just for the sugar residues.

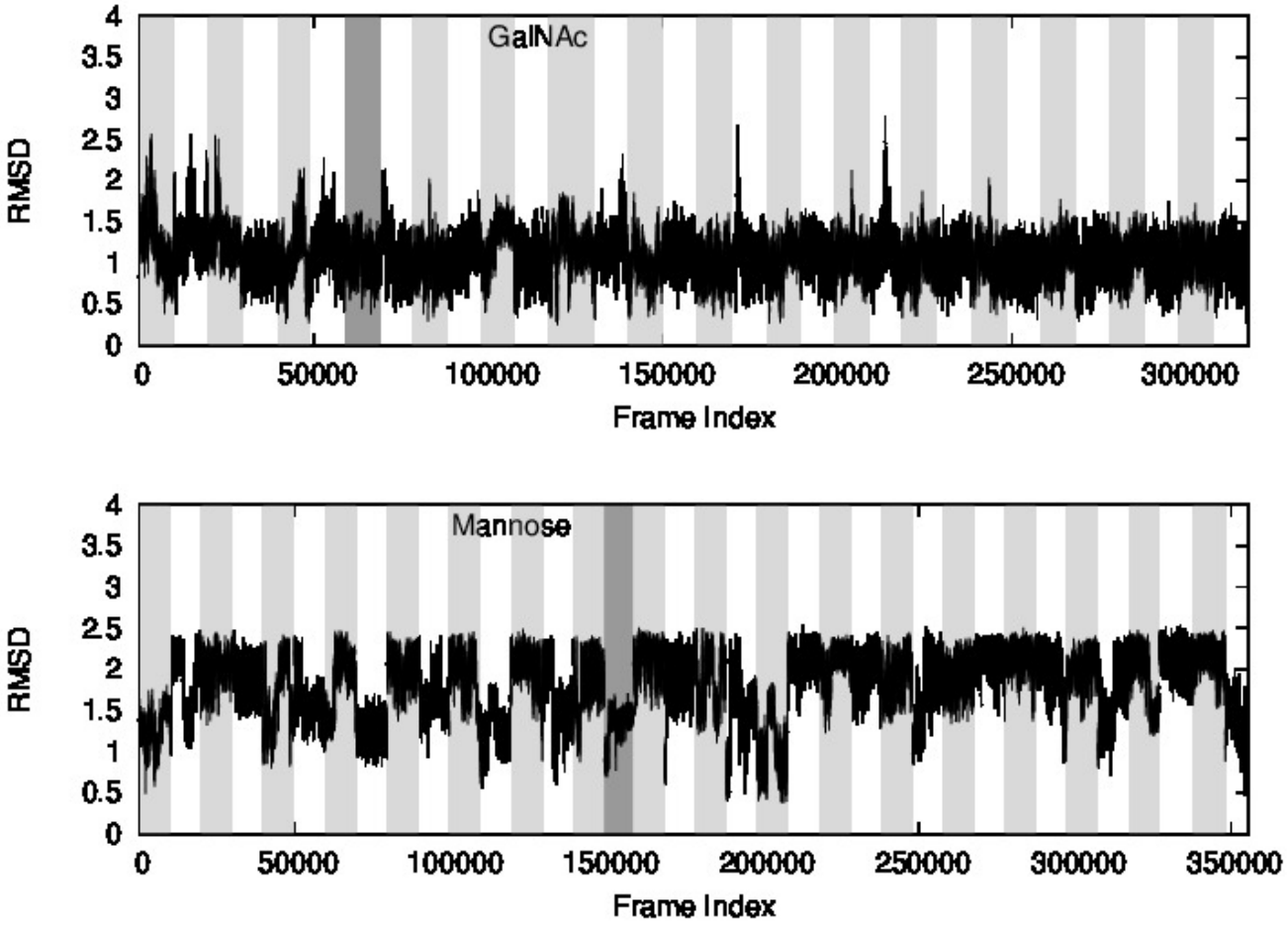
- The RMSD values are for atoms CA, C, O, N & H in the four THR residues.

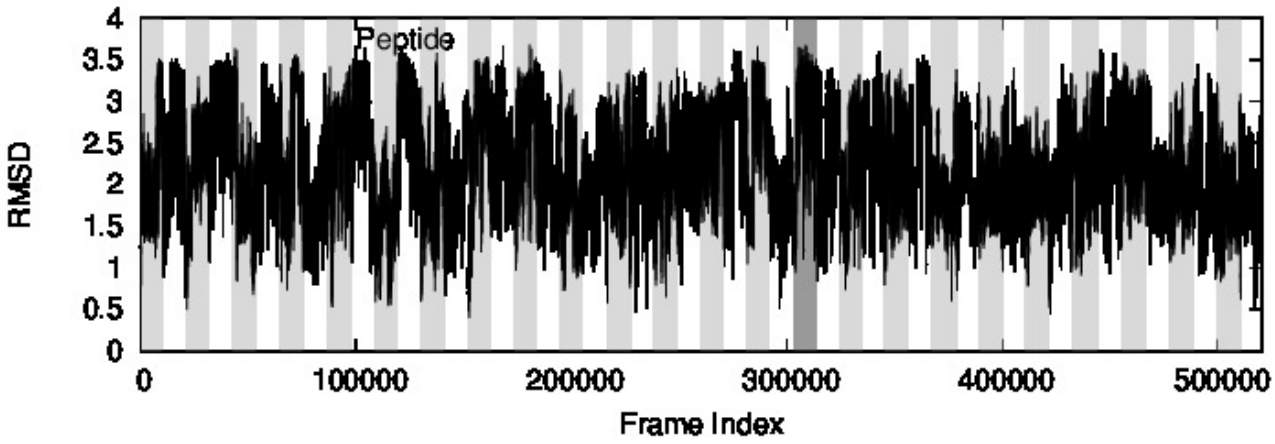
- Using the backbone allows us to also compare to the unglycosylated peptide.

The flexibility of the mannosylated variety compared to the GalNAc-ylated variety is evidenced by the ranges of RMSDs populated as well as by the overall value.

These are the largest backbone RMSDs

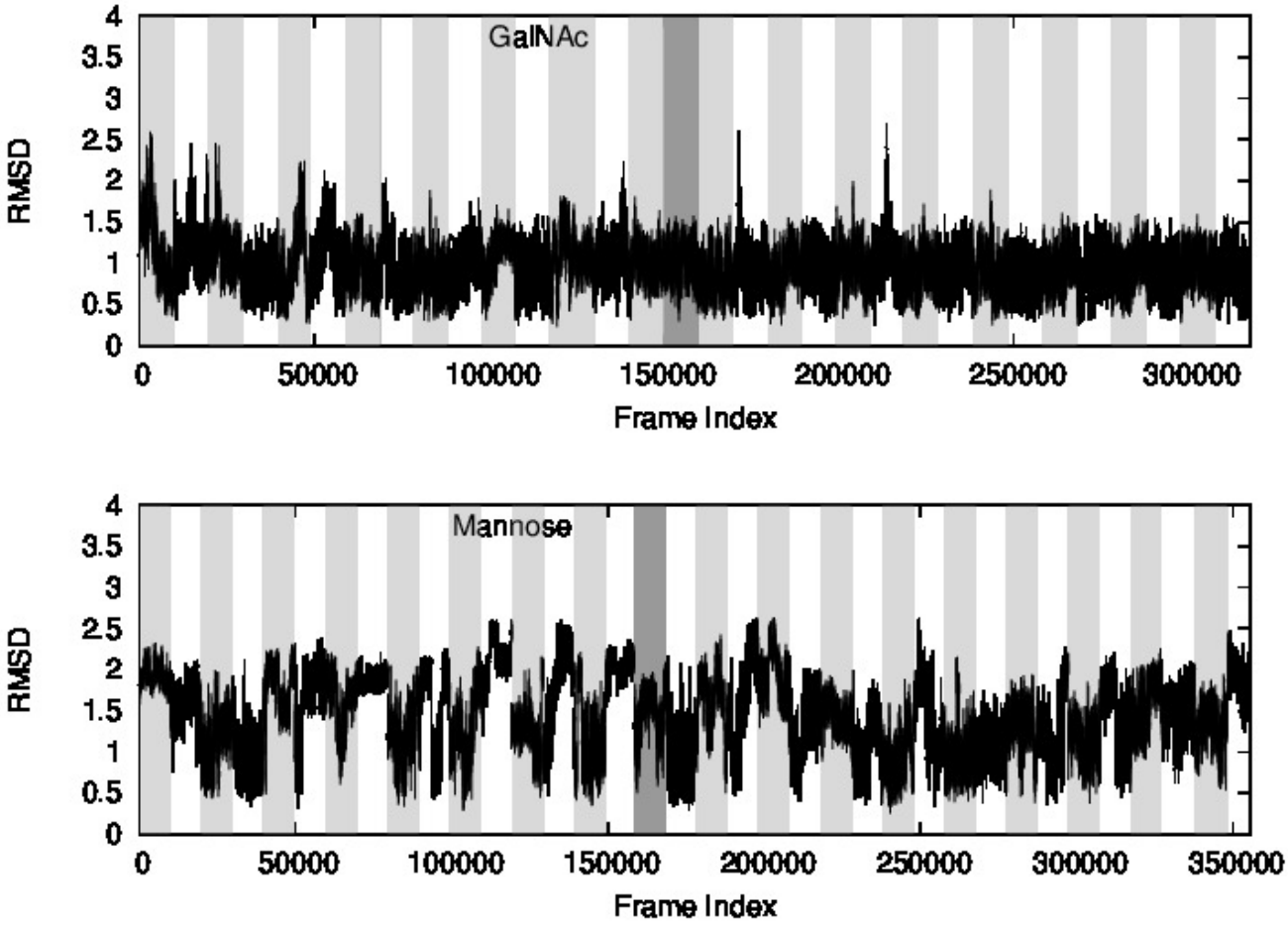
The input structure chosen for these is the one that has the **largest** RMSD, on average, across all simulations. Note that there is a marked difference from GalNAc to Mannose to Peptide.

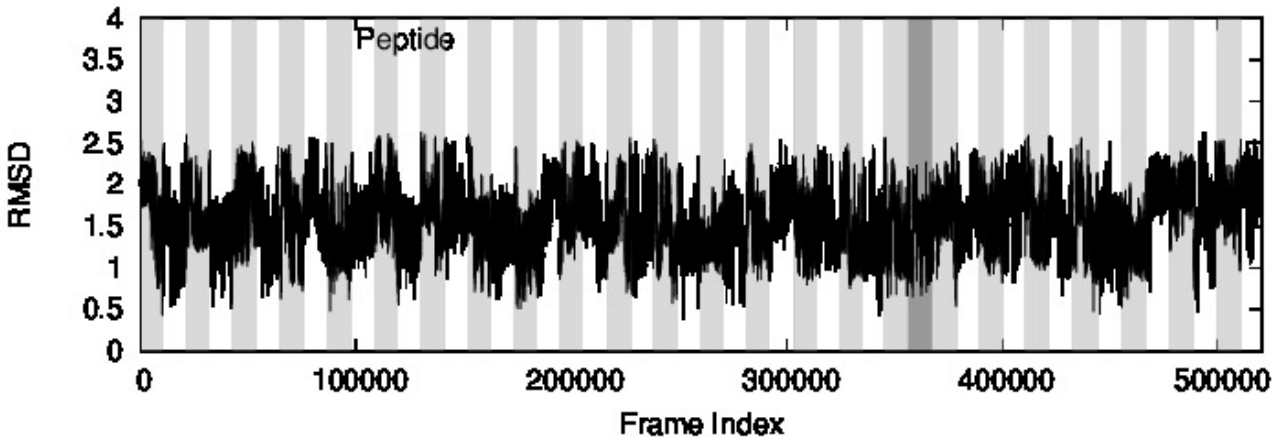




These are the smallest backbone RMSDs

The input structure chosen for these is the one that has the **smallest** RMSD, on average, across all simulations. Note that there is still a marked difference from GalNAc to Mannose, but the difference between Mannose and Peptide is less pronounced.

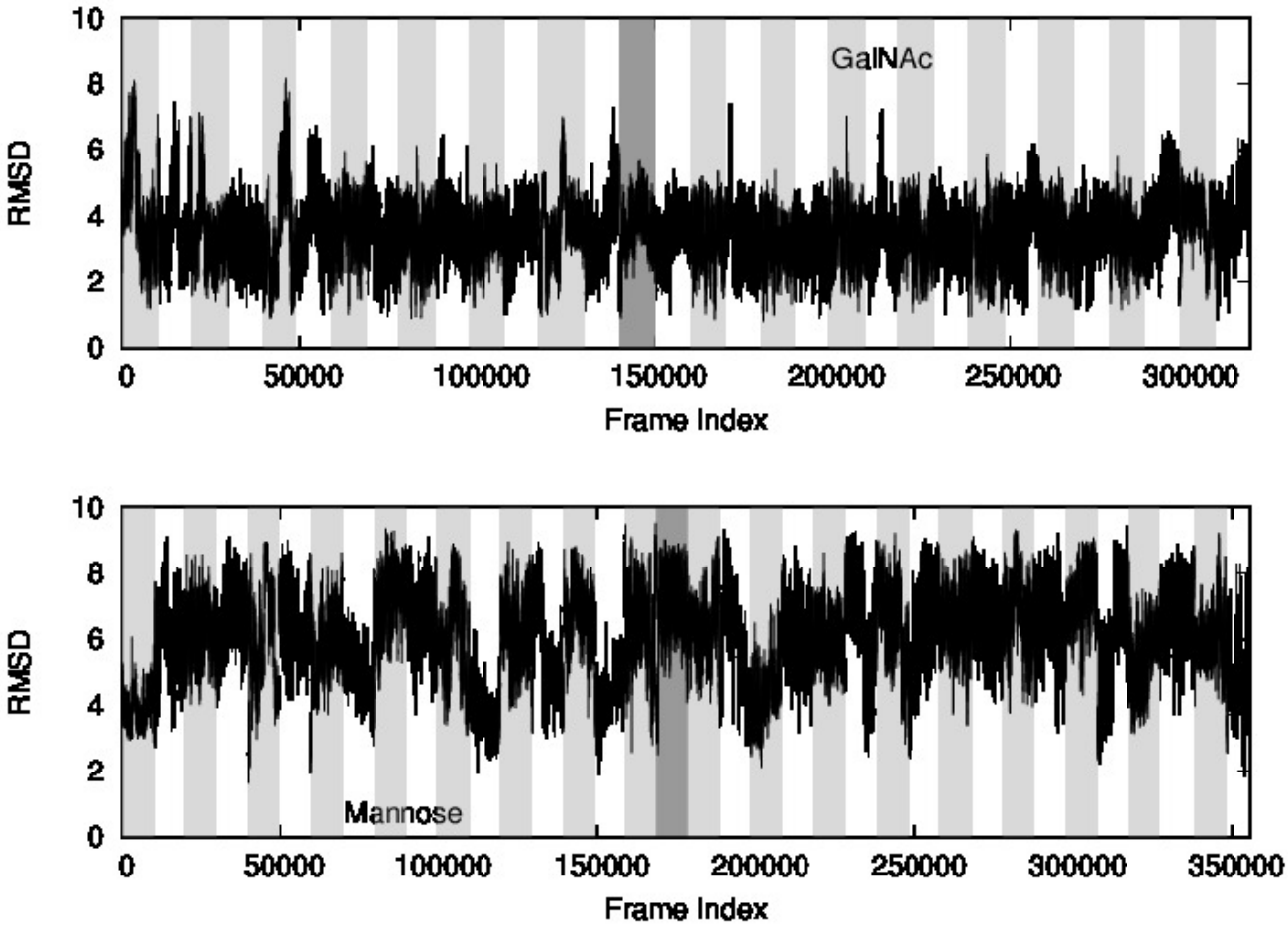




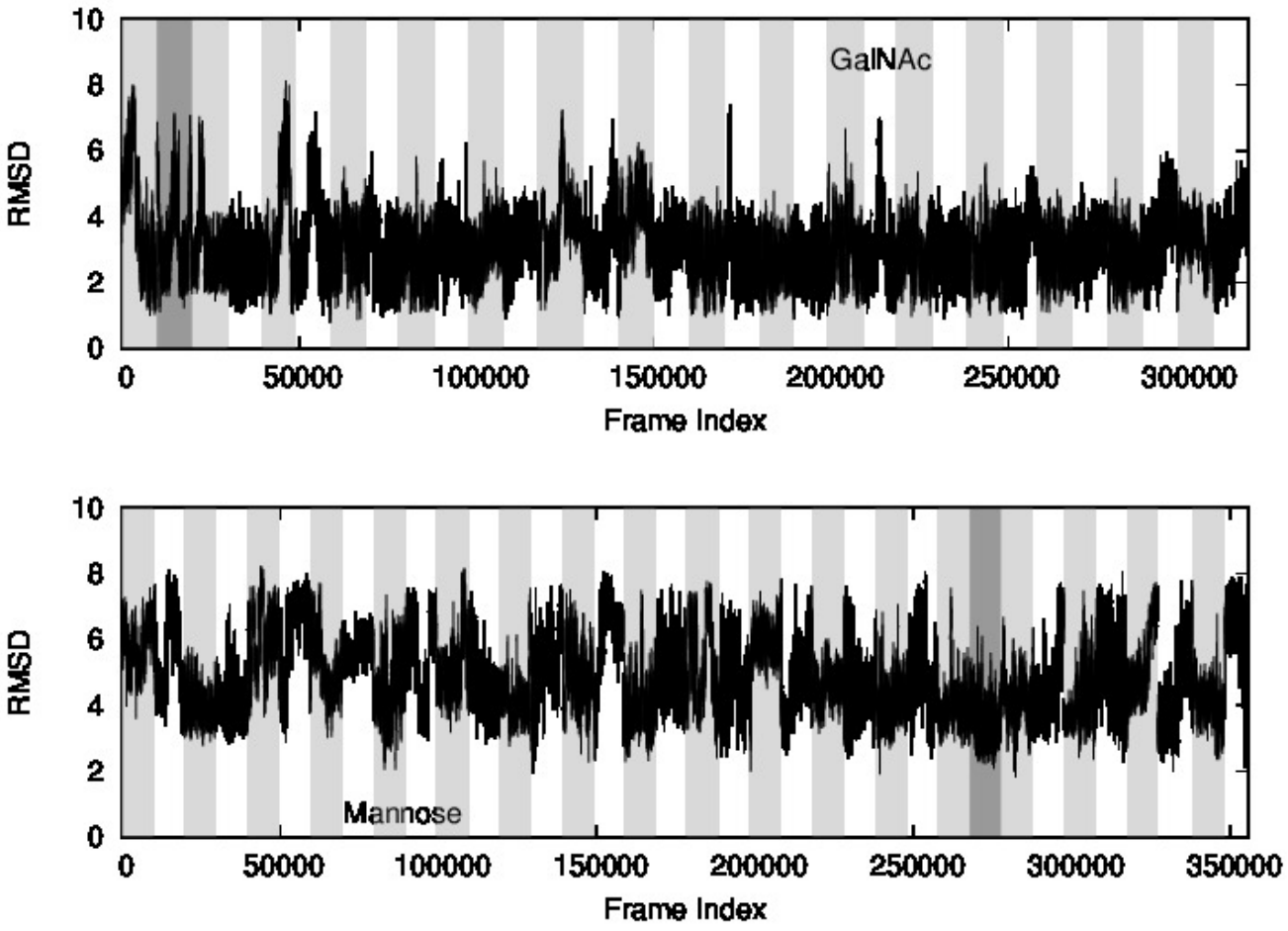
Sugar RMSD Comparisons

These plots are just like the ones before, except these concern the heavy atoms in the glycans. There are no Peptide plots here, because that variant didn't have any sugar atoms.

These are the largest glycan RMSDs



These are the smallest glycan RMSDs

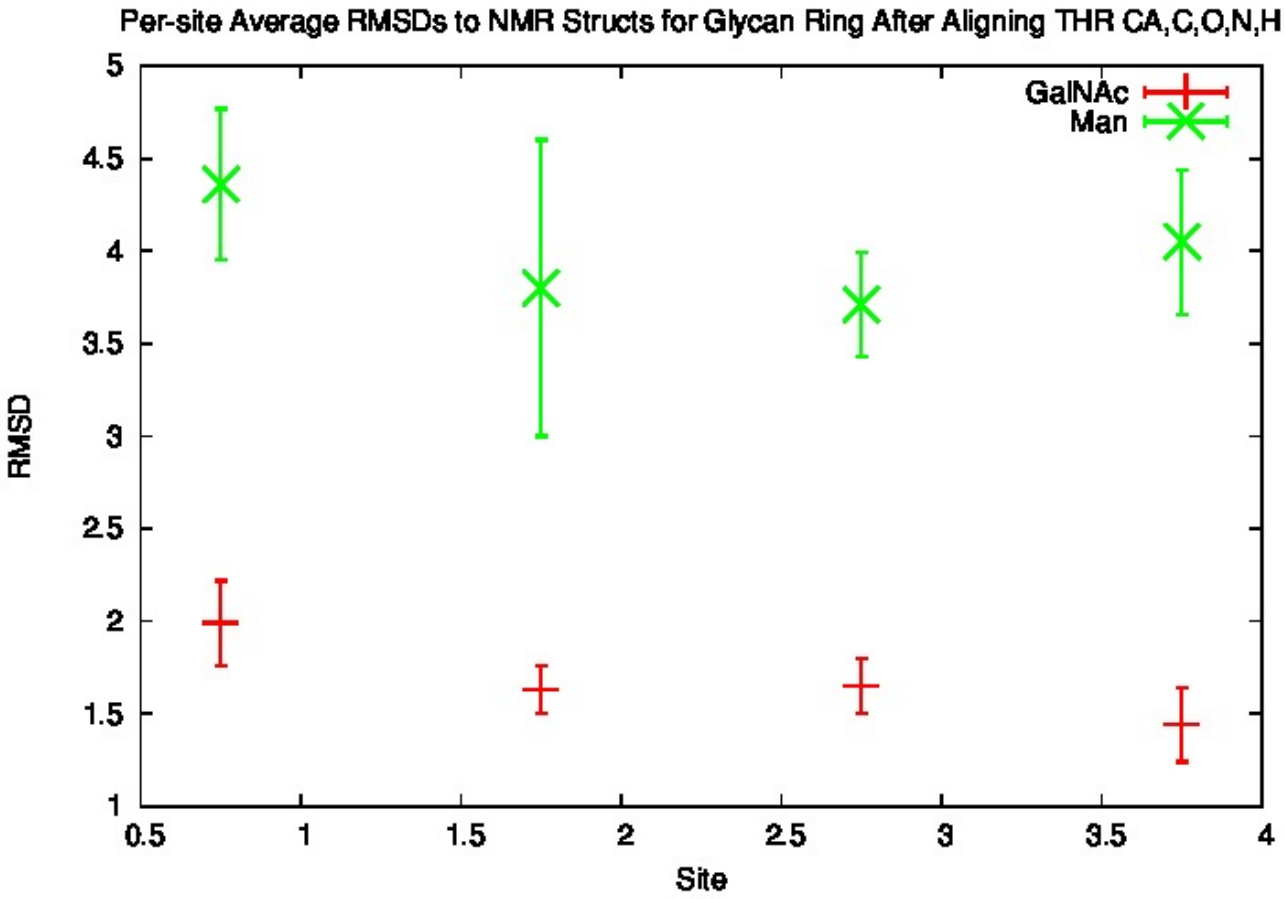


Flexibility of the Individual Glycans

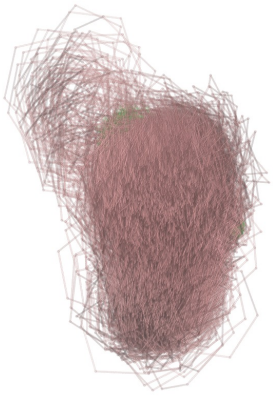
The previous plots concerned the strand as a whole. The following concerns the flexibility of the individual glycans at each site.

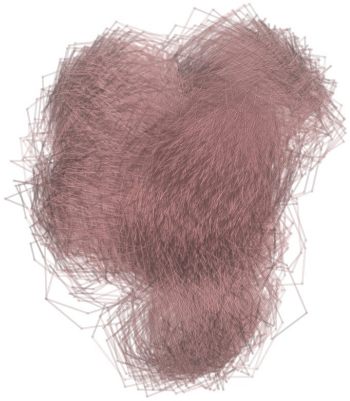
In this section, before an RMSD or other measurement was taken, the atoms CA, C, O, N & H of an individual threonine residue were aligned. Then, the ring atoms of the glycan attached to that threonine are considered. We consider only the ring atoms so that the difference in numbers of atoms between the GalNAc and the Man are not relevant.

This plot shows the average, per-site, RMSD of each glycan's ring atoms after each THR was aligned to the THR in each NMR structure. That is, these RMSDs are compared to the NMR structures. (It would be equally reasonable, and would answer a slightly different question, if the RMSDs were considered only WRT the simulation information).



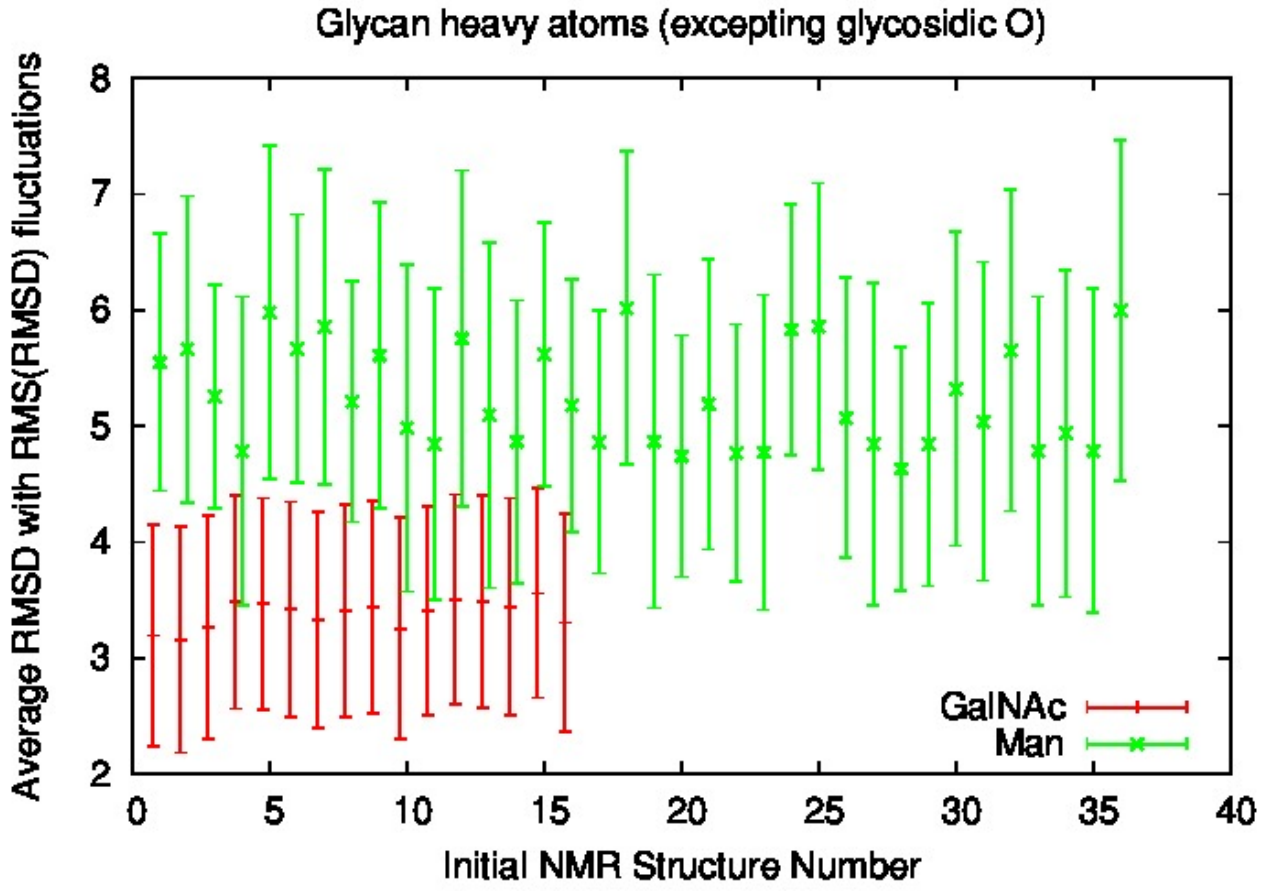
To give an idea what that looks like, we consider just one thr/glycan site, but we consider the trajectories in all simulations. The following represent site 1 in each system. Here, all trajectory frames for all trajectories were aligned, as described above, for the first THR residue. Then, without further changing anything, every 100th frame is shown all at once. The molecules are shown as glass sticks so that places where the color is darkest represent places where the molecules are the most overlaid. Only the glycan ring atoms are shown, and they are pink. The THR residue is shown in green (and is barely visible). The view is from the "glycan" side. To the extent reasonable, the two sets of molecules are oriented so that their THR atoms are in approximately the same positions, and their sizes are equivalent. It is quite obvious that the Man (right) explores far more conformational space than the GalNAc (left).

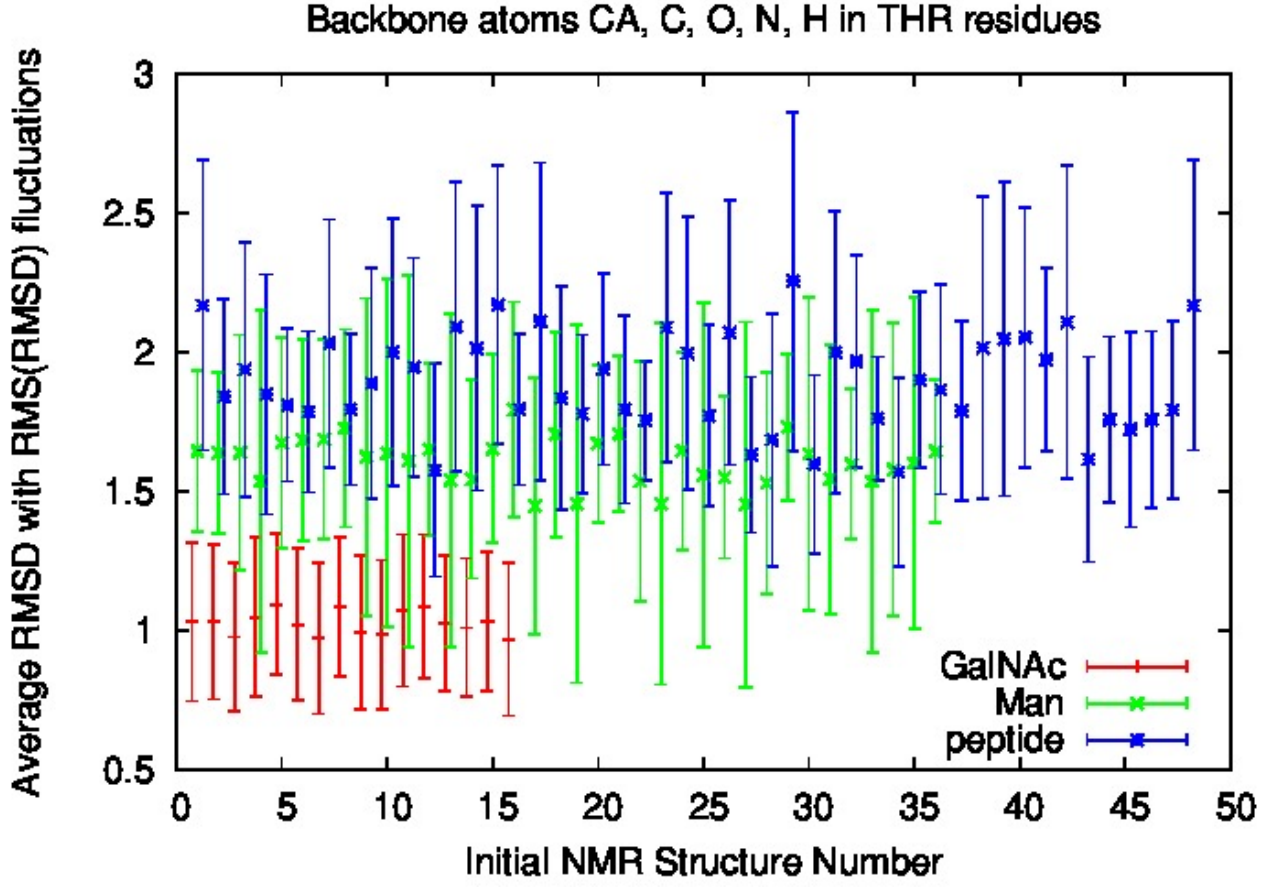




Relevant Validation RMSD Plots

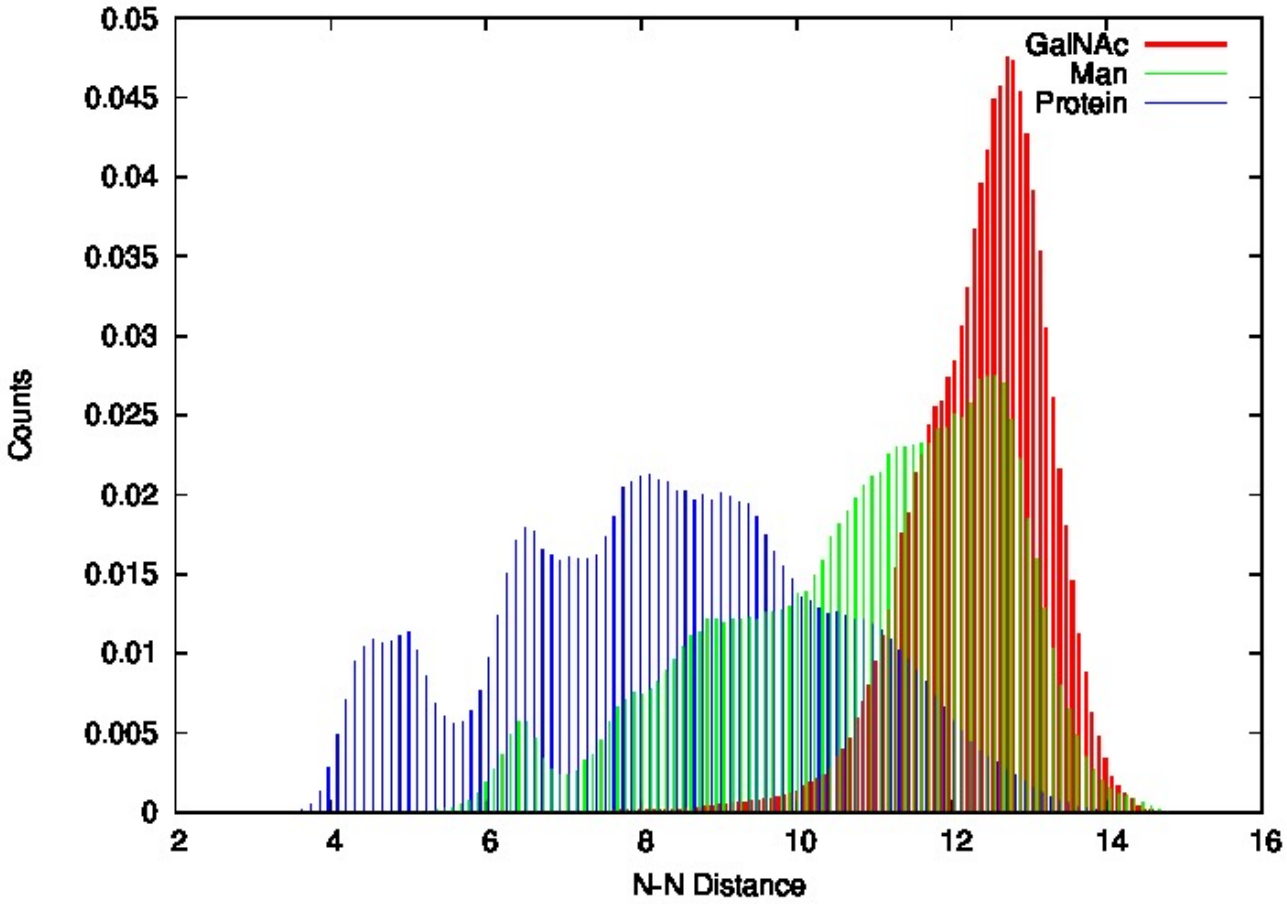
These really fall more under validation than flexibility, and they are discussed more in that post. In each, though, it is pretty obvious that the GalNAc is the least flexible.


Glycan heavy atoms (excepting glycosidic O)
Average RMSD with RMS(RMSD) fluctuations
Initial NMR Structure Number
GalNAc
Man
0
5
10
15
20
25
30
35
40
2
3
4
5
6
7
8


Backbone atoms CA, C, O, N, H in THR residues
Average RMSD with RMS(RMSD) fluctuations
Initial NMR Structure Number
GalNAc
Man
peptide
0
5
10
15
20
25
30
35
40
45
50
0.5
1
1.5
2
2.5
3

Distance-based plots

One of the simplest ways to illustrate the difference in flexibility between the three variants is to measure the length of the peptide chain. Here, we choose to measure the distance between the backbone N atoms that flank the four THR residues: that is, the N's on either side of the set of 4. The distance is in Angstroms. These are normalized counts, so represent the fraction found at each distance. The total numbers of counts are: GalNAc: 317740; Mannose: 355643; Peptide: 520408. These counts represent all simulations.



Note that there is a very obvious progression toward greater flexibility as: GalNAc < Man < Peptide. It is also worth noting that the GalNAc preferentially keeps the backbone as extended as possible. The Man has some effect in that regard, but the backbone of a mannosylated system populates states that are far more compact than those apparently possible if the derivative is a GalNAc. The unglycosylated peptide, of course, is the most flexible of the three.