Supporting Information for “Molecular Dynamics Simulations Elucidate Oligosaccharide Recognition Pathways by Galectin-3 at Atomic Resolution”

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Description of Supplemental movie:

Movie S1 demonstrates a representative Molecular dynamics simulation trajectory capturing the process of ligand N-acetyllactosamine (LacNAc) binding to Galectin-3 in atomistic resolution.
Figure S1: Time profile of hydrogen bonds between the LacNac and key amino acid residues around binding site. Presence of persistent hydrogen bonds between LacNac and key amino acid residues in the binding pocket is evident beyond the binding event.

Figure S2: RMSD profile of binding pocket of galectin-3 CRD with respect to crystal structure (pdb id: 1KJL). Both representative trajectories indicate no significant change in pocket before or after ligand binding.
Figure S3: The time profile of binding trajectory for LacNAc-derivative.

Figure S4: Network showing the LacNAc-derivative’s binding pathway. Path flux is represented with thickness of arrows and path percentages are indicated. B. Key interactions stabilising the non-native encounter-complex of Galectin-3/LacNAc-derivative.

Figure S5: Network of Trp181 stabilization.
Figure S6: Details of key residue-interactions with LacNAc-derivative in the binding pocket

Contact matrix of ligand with all the amino-acid residues of Galectin-3 : 138 dimensions

Dimensional reduction by tICA : 20 dimensions

Building 500 micro states using k-means clustering algorithm

Computing implied timescales at different lag-times to identify a working lag-time ($\tau$)

Markov state model with kinetic mapping $T(\tau)$ using lag-time $\tau = 10$ns/7.5ns

Coarse graining of 500 micro-states into kinetically relevant macro states

Figure S7: The outline of MSM protocol adopted in the current article. Also shown is the plot of implied time scale as a function of lag-times