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Addition/Correction

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Addition to "Specific and Nonspecific Effects of Glycosylation"

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In our 2012 article, we reported atomically detailed simulations of a model octapeptide and related glycopeptides. After that work was published, we realized that those simulations started from configurations with several peptide bonds in a *cis* conformation. Because *cis* conformations are not common in protein systems, we have repeated our simulations, while ensuring that all peptide bonds sample only *trans* conformations. The new simulations yield conclusions very similar to those drawn from the original simulations, although they differ in certain details. As was observed in the experimental studies by Imperiali and co-workers[1−3] and also in our original simulations, our new simulations indicate that glycosylation triggers a conformational switch from an extended ensemble with Asx-turns to a relatively compact ensemble with β-turns. The two most significant differences between the two sets of simulations are the following: (1) Both octapeptide simulations sampled a disordered and relatively extended ensemble. However, the new octapeptide simulation sampled Asx-turns in 12% of conformations, while the original octapeptide simulation sampled Asx-turns in only 2% of conformations. (2) Both glycopeptide simulations sampled a relatively compact ensemble with a metastable native state cluster (NSC) of compact turn conformations. However, the new glycopeptide simulation sampled Type I β-turns in 27% of conformations, with most occurring in the NSC, while the original glycopeptide simulation sampled corresponding β-turns in only 1% of conformations, and the NSC corresponded instead to related turns. Thus, the new simulations are considerably more consistent with the prior experimental observations for the conformational switch from Asx-turns to β-turns upon glycosylation. More importantly, the new simulations remain highly consistent with the major conclusions of our original study and, in particular, with the relative significance of specific and nonspecific effects for driving this conformational switch. Both studies indicate that, although steric crowding by the glycan destabilizes Asx-turns and other extended conformations, nonspecific steric crowding does not significantly stabilize any particular conformation for the short peptide. Instead, both simulation studies indicate that specific glycan−peptide hydrogen bonds and aromatic−glycan stacking interactions contribute to driving this conformational switch. The consistency between the two sets of simulations suggests that these conclusions are quite robust for this peptide system.

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