Modeling of Ribosomally Synthesized and Post-Translationally Modified Peptides

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Natural products, such as ribosomally synthesized and post-translationally modified peptides (RiPPs), contain novel sidechain conjugations that have not previously been modeled in Rosetta. These sidechain conjugations are intriguing due to their potential to stabilize novel peptide conformations. Lanthipeptides are a class of RiPPs that contain lanthionine rings. The first step of lanthionine ring formation involves dehydration of serine and threonine residues. These dehydrated amino acids are achiral, contain a CA - CB double bond, and serve as a Michael acceptor for enzymatically catalyzed linkage with cysteine. I have implemented support for dehydrated amino acids and lanthionine linkages in Rosetta. For the lanthionine linkages, I utilized the a crosslinker mover implementation to add modeling support. A parallel crosslinker implementation for disulfides performed similarly to the current Rosetta dslf_fa13 disulfide model when evaluated using Rosetta relax. Additionally, I have examined the ability of Rosetta to sample conformations of lanthipeptides with generalized kinematic loop closure based protocols.