

## Effect of PEG conjugation on entropy driven self-assembly of coiled coils

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### ABSTRACT

Coiled coil helix bundles are one of the most common protein motifs known, playing significant roles in various mechanobiological processes. The desirable functionalities of  $\alpha$ -helical coiled coils are dependent upon their thermal and structural stability, which can be lost under extreme environmental conditions such as elevated temperatures, pressures, or pH. Recently, conjugation of  $\alpha$ -helices with polymers, particularly poly(ethylene glycol) (PEG), has been utilized to produce environmentally responsive protein-based block copolymers with improved structural and thermal stability. A fundamental question regarding helix-PEG conjugates is how PEG conjugation affects the secondary structure of helices [1] as well as their tertiary structure, which is the mechanism of self-assembly. In particular, the influence of PEG conjugation site on the assembly of helix bundles remains to be fully characterized. In order to address these questions, we perform coarse-grained molecular dynamics simulations of a trimeric coiled coil conjugated with PEG [2]. The effect of conjugation location is studied by covalently attaching the PEG chain either to the end or to the side of each helix in the three-helix assembly. First, we utilize annealing simulations to investigate the melting behavior and thermal stability of the coiled coil with no PEG attached, with side-conjugated PEG, and with end-conjugated PEG. Our simulation predictions for the coiled coil melting temperature are in good agreement with experimental data and show an insignificant difference between the melting temperatures of peptide itself and peptide-PEG conjugates. Next, we study the entropy driven self-assembly patterns of coiled coils with and without PEG by considering various peptide concentrations in the simulation box. Our results show that as the concentration increases, the number of assembled clusters decreases while the aggregation number in each cluster increases. Coiled coils without PEG, with end-conjugated PEG, and with side-conjugated PEG have the smallest number of clusters and the largest aggregation number, in order. These observations confirm that the peptide assembly patterns are affected not only by the presence of PEG chain, but also by the location of PEG conjugation. These findings lay the groundwork for the study of mechanisms underpinning the thermomechanical stability and assembly of coiled coils as well as other helix bundles.

### REFERENCES

- [1] Hamed, E., Xu, T., Keten, S. Poly(ethylene glycol) conjugation stabilizes the secondary structure of  $\alpha$ -helices by reducing peptide solvent accessible surface area. *Biomacromolecules*. 2013, 14, 4053–4060.
- [2] Hamed, E, Ma, D, Keten, S. Effect of PEG conjugation on thermomechanical stability and self-assembly of coiled coil helix bundles (In submission).