Origin of Proteolytic Stability of Peptide-Brush Polymers as Globular Proteomimetics

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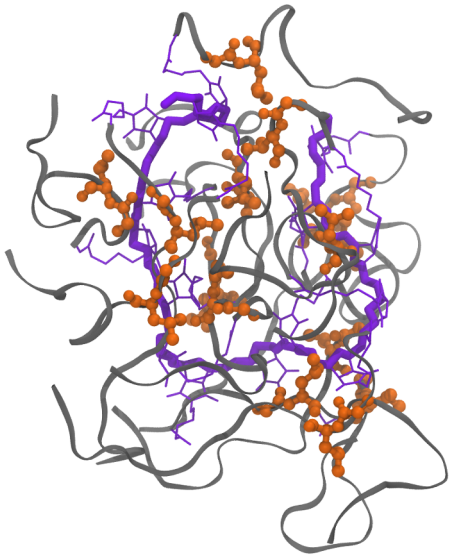
Peptide brush polymers (PBPs), wherein every side-chain of the polymers are peptidic, represent a new class of proteomimetics. In collaboration with Prof. Gianneschi, we found that PBPs display globular morphology, and their proteolytic stability was found to be associated with the hydrophobicity of PBP backbones.

The stability of therapeutic peptides again protease degradation has long been a big challenge for therapeutic drug design. By combining experiments and multiscale simulations, we found that PBPs with a higher hydrophobic backbone display a promising proteolytic stability. Atomistic simulations revealed that a higher hydrophobicity of PBP backbones lead to a more compacted globular morphology of PBPs. The compacted structures consequently protect peptides from the exposure to protease, evidenced by protease-peptide interactions. Impressively, the structure (PBP backbone hydrophobicity) – property (proteolytic stability) relationship holds true for other peptides, suggesting a general feature of PBPs. It thus demonstrates a new means in fine-tuning the stability of therapeutic peptides, which is essential for therapeutic peptide delivery.



Globular morphology of peptide-brush polymers

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