Protein mimicry and recognition with foldamers

Ivan Huc
Faculty of Chemistry and Pharmacy, Ludwig-Maximilians-University Munich, Germany
E-mail: ivan.huc@cup.lmu.de

Aromatic oligomers constitute a distinct and promising class of synthetic foldamers – oligomers that adopt stable folded conformations. Single helical structures are, to a large extent, predictable, show unprecedented conformational stability in essentially all solvents, and represent convenient building blocks to elaborate synthetic, very large (protein-sized) folded architectures. Cavities can be designed within such synthetic molecules that enable them to act as artificial receptors and molecular motors. This lecture will give an overview of our current efforts to design and select aromatic foldamers and foldamer-peptide hybrids to recognize protein surfaces.[1-3] It will also highlight the benefits of foldamer macrocyclization to access to otherwise improbable molecular shapes[4-6] and showcase key methodologies, *e.g.* solid phase synthesis, crystallogenesis, and single crystal x-ray diffraction.

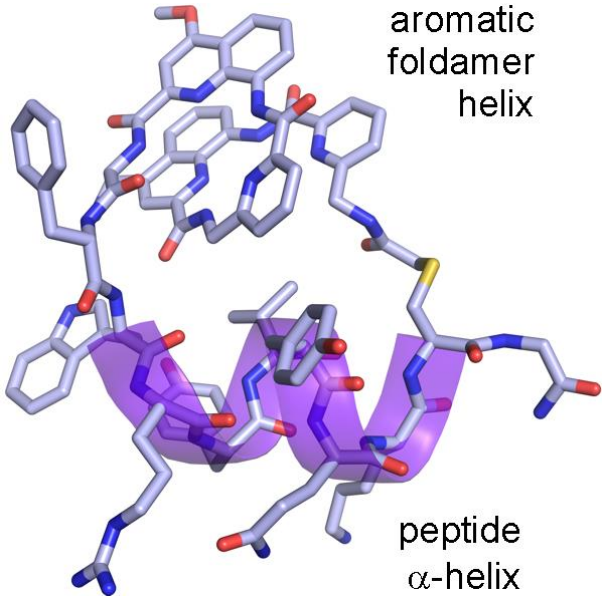

Figure 1. Structure of a foldamer-peptide hybrid in its conformation bound to a protein target.

References

1 J. M. Rogers, S. Kwon, S. J. Dawson, P. K. Mandal, H. Suga, I. Huc., *Nat. Chem.* **2018**, *10*, 405.
2 C. Tsiamantas, S. Kwon, J. M. Rogers, C. Douat, I. Huc, H. Suga, *Angew. Chem. Int. Ed.* **2020**, *59*, 4860.
3 S. Dengler, R. Howard, V. Morozov, C. Tsiamantas, Z. Liu, C. Dobrzanski, V. Pophristic, S. Brameyer, C. Douat, H. Suga, I. Huc, *Angew. Chem. Int. Ed.* **2023**, *62*, e202308408.
4 K. Urushibara, Y. Ferrand, Z. Liu, K. Katagiri, M. Kawahata, E. Morvan, R. D'Elia, V. Pophristic, A. Tanatani, I. Huc, *Chem. Eur. J.* **2021**, *27*, 11205.
5 S. Dengler, P. K. Mandal, L. Allmendinger, C. Douat, I. Huc, *Chem. Sci.* **2021**, *12*, 11004.
6 C. G. Pappas, P. K. Mandal, B. Liu, B. Kauffmann, X. Miao, D. Komáromy, W. Hoffmann, C. Manz, R. Chang, K. Liu, K. Pagel, I. Huc, S. Otto, *Nat. Chem.* **2020**, *12*, 1180.