Polypeptides: from proteins to new approaches in polymer synthesis

Colin Bonduelle

University of Bordeaux, CNRS, Bordeaux INP. LCPO (Laboratoire de Chimie des Polymères Organiques)
ENSMAC, 16 avenue Pey Berland, F-33600, Pessac, France

colin.bonduelle@u-bordeaux.fr

Proteins are natural building blocks that possess many features still unrivaled by their synthetic counterparts, including chemical diversity, hierarchical structure, specific chemical modification, and programmed system dynamics. Combined with their potential for metabolism in living systems (biodegradation, etc.), these properties make proteins highly attractive for designing the polymers of tomorrow. While significant advances have been achieved in genetic engineering, a major remaining challenge is optimizing large-scale protein production (extraction, recombinant protein, etc.). Interestingly, the most economical and efficient route to polypeptides is a chemical approach: the ring-opening polymerization (ROP) of amino acid *N*-carboxyanhydride (NCA) monomers (Figure 1).[1]

Compared to proteins, peptidic polymers are much simpler macromolecules in which amino acids are statistically repeated. However, these polypeptides combine advantageous features of synthetic polymers (solubility, processability, rubber elasticity, etc.) with those of natural proteins (secondary structure, functionality, biocompatibility, etc.).[2] Recent progress in this field has been impressive, and this talk will illustrate: 1) how the secondary structure of polypeptide guide the design of advanced materials,[3] 2) how aqueous ROP of NCA monomers can be extended to a PISA process,[4] and 3) how polymerization of NCAs can afford simplified analogues of natural proteins.[5]

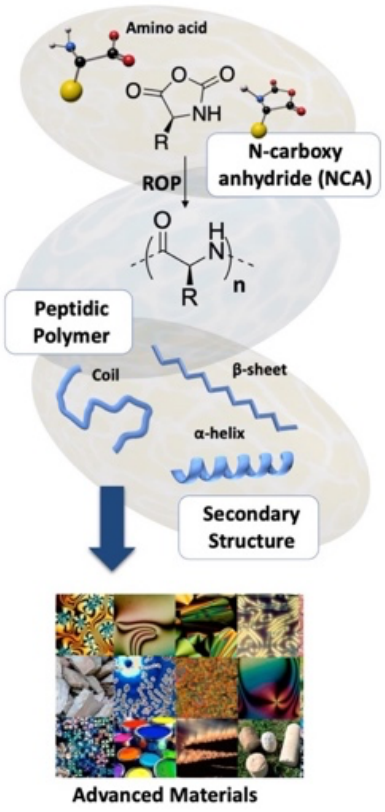

Figure 1. *Peptidic polymers are ideal analogues of proteins to design advanced materials.*

References

[1] J. Cheng et al., *Chem. Soc. Rev.* **2017**, 46, 6570; [2] G.G. Qiao et al., *Chem. Soc. Rev.* **2020**, 49, 4737; [3] a) *Polym. Chem.* **2018**, 9, 4100; b) *Biomacromolecules* **2018**, 19, 4068; c) *Nature Commun.* **2020**, 11, 2051; d) *ACS Appl. Polym. Mat.* **2024**, 6, 15, 8733; e) *Biomacromolecules* **2024**, 25, 3033; [4] a) *Angew. Chem. Int. Ed.* **2020**, 59, 622; b) *Polym. Chem.* **2021**, 12, 6242; c) *Macromol. Commun.* **2024**, 2400079; d) *Macromolecules* **2025**, 58, 13, 6466; [5] a) *Biomacromolecules* **2021**, 22, 57; b) *J. Am. Chem. Soc.* **2021**, 143, 3697; c) *Polym. Chem.* **2022**, 13, 600; d) *Angew. Chem. Int. Ed.* **2022**, 61, e202209530; e) *Prog. Polym. Sci.* **2023**, 147, 101752; f) *J. Am. Chem. Soc.* **2025**, 147, 28, 24213.

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