

# POLY(2-OXAZOLINE)S: FROM FUNDAMENTAL RESEARCH TO APPLICATIONS

Richard Hoogenboom

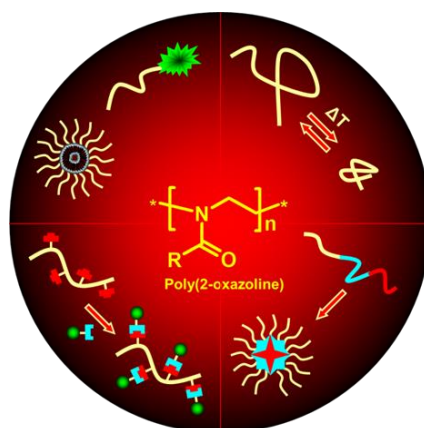
Supramolecular Chemistry Group, Centre of Macromolecular Chemistry, Department of Organic and Macromolecular Chemistry, Ghent University, Krijgslaan 281-S4, 9000 Ghent, Belgium [richard.hoogenboom@ugent.be](mailto:richard.hoogenboom@ugent.be)

## ABSTRACT

The living cationic ring-opening polymerization of 2-oxazolines has been studied in great detail since its discovery in 1966. The versatility of this polymerization method allows copolymerization of a variety of 2-oxazoline monomers to give a range of tunable polymer properties that enable, for example, hydrophilic, hydrophobic, fluorophilic, as well as hard and soft materials. Moreover, the chemical versatility allows orthogonal end-group and side-chain modification of the polymers. However, this class of polymers was almost forgotten in the 1980s and 1990s because of the long reaction times and limited application possibilities. In the new millennium, a revival of poly(2-oxazoline)s has arisen because of their potential use as biomaterials and thermoresponsive materials, as well as the easy access to defined amphiphilic structures for (hierarchical) self-assembly (see Figure).[1-3]

Recent developments from our research group that illustrate the potential of poly(2-oxazoline)s for drug delivery applications will be discussed in this lecture, ranging from fundamental studies on expanding the monomer scope [4,5] and the preparation of defined high-molar mass polymers [6] up to the use of such polymers as pharmaceutical excipients for oral tablets [7], as micellar carriers for drug delivery [5] as well as the preparation of various side-chain functionalized polymers as building blocks for polymer therapeutics[8]. All together, we aim to develop poly(2-oxazoline)s as biomaterials by providing in depth studies on the basic questions, such as biocompatibility and renal clearance as well as by providing proof of concept for use of poly(2-oxazoline)s for various specific applications.

*Disclaimer: Prof. Hoogenboom is co-founder of Avroxa BVBA that commercializes poly(2-oxazoline)s under the tradename Ultraxa®*



**Graphical Abstract.** Structure of poly(2-oxazoline) in the middle surrounded by its use as thermoresponsive polymer, self-assembly, polymer-drug conjugates and coupling of poly(2-oxazoline)s to liposomes and proteins.

## REFERENCES

- [1] R. Hoogenboom, *Angew. Chem. Int. Ed.* 2009, 48, 7978.
- [2] O. Sedlacek, B. D. Monnery, S. K. Filippov, R. Hoogenboom, M. Hruby, *Macromol. Rapid Commun.* 2012, 33, 1648-1662.
- [3] R. Luxenhofer, Y. Han, A. Schultz, J. Tong, Z. He, Kabanov, R. Jordan, *Macromol. Rapid Commun.* 2012, 33, 1613-1631.
- [4] B. Verbraeken, J. Hullaert, J. Van Guyse, K. Van Hecke, J. Winne, R. Hoogenboom, *J. Am. Chem. Soc.* 2018, 140, 17404-17408.
- [5] O. Sedlacek, K. Lava, B. Verbraeken, S. Kasmir, B. G. De Geest, R. Hoogenboom, *J. Am. Chem. Soc.* 2019, 141, 9617.
- [6] B. D. Monnery, V. V. Jerca, O. Sedlacek, B. Verbraeken, R. Cavill, R. Hoogenboom Defined High Molar Mass Poly(2-Oxazoline)s. *Angew Chem. Int. Ed.* 2018, 57, 15400.
- [7] L. Wyffels, R. Hoogenboom, S. Staelens, et al. *J. Controlled Release* 2016, 235, 63.
- [8] O. Sedlacek, B. Monnery, R. Hoogenboom, M. Hruby, et al. *Biomaterials* 2017, 146, 1-12.