



---

## Towards Better Drug Delivery Systems: Theoretical Calculations on the Cationic Ring-opening Polymerization of Poly(2-oxazoline)s

D. Hertsen<sup>1</sup>, H. Goossens<sup>1</sup>, R. Hoogenboom<sup>2</sup>, V. Van Speybroeck<sup>1</sup>

1. Center for Molecular Modeling, Ghent University, Technologiepark 903, 9052 Zwijnaarde, Belgium
2. Supramolecular Chemistry Group, Department of Organic Chemistry, Ghent University, Krijgslaan 281-S4, 9000 Ghent, Belgium

Drug-delivery systems are an essential part of modern day drug design. Therapeutically active compounds are often too unstable to survive the chemically demanding journey between the place of intake and the target site. Therefore, systems have been developed that allow for a smooth passage and at the same time safeguard the valuable properties of the drug. Poly(ethylene glycol) (PEG) has been the gold standard in this field for many years.

Poly(2-oxazoline)s (POX) are biocompatible polymers that are readily synthesized and whose properties can easily be tuned. These polyamides are synthesized by the cationic ring-opening polymerization (CROP) of various types of monomers. Moreover, different properties can be obtained by chemical functionalization of the side chain after the polymerization. Because of their versatility and biocompatibility, POXs are candidate drug-delivery systems and possible alternatives for PEG.

Understanding the factors governing the CROP is a crucial step in the development of POXs as potent drug-delivery systems. Therefore, theoretical calculations were performed on these reactions. At first, only small model systems were considered. The thermodynamic barriers and the polymerization rates for different 2-oxazolines were investigated theoretically and interpreted using molecular descriptors like atomic charges. Afterwards, larger, more realistic systems will be built to take into account the effect of the solvent environment and the role of supramolecular interactions between different chains on the polymerization. Studies on these systems will hopefully contribute to the search for high-molecular POXs with a low polydispersity.

[1] H. Goossens et al. ACS Macro Letters 2013, 8, 651.

[2] K. Kempe et al. Polym. Chem. 2013, 11, 3236

---