

# pH-sensitive micellar systems for controlled drug delivery: synthesis and structural characterization by small-angle neutron scattering

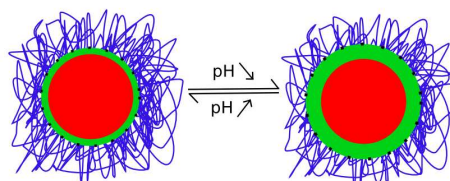
Arnaud Joset<sup>1,2</sup>, Christine Jérôme<sup>2</sup>, Annie Brulet<sup>3</sup>, Bernard Leyh<sup>1</sup>

*Dynamics Laboratory, University of Liège, B-4000 SART-TILMAN, Belgium*

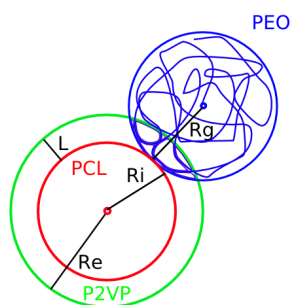
<sup>2</sup>*Center for Education and Research on Macromolecules, University of Liège, B-4000 SART-TILMAN, Belgium*

<sup>3</sup>*Laboratoire Léon Brillouin, (CNRS-CEA), CEA Saclay, 91191 Gif sur Yvette*

The aim of the project is the preparation of micellar nanocarriers made of biocompatible copolymers and their structural analysis by Small Angle Neutron Scattering (SANS). These micelles could be used in drug delivery applications to fight cancer<sup>1</sup>. The hydrophobic polycaprolactone (PCL) core is intended to incorporate the drug. The corona of hydrophilic polyethylene oxide (PEO) stabilizes the nanocarriers with respect to the plasma proteins. The pH in the neighborhood of the tumoral cells is lower than in the healthy cells. We incorporated a pH-sensitive sequence of poly(2-vinylpyridine) (P2VP). As a result, these micelles are expected to deliver their drug near the cancerous cells without affecting the healthy cells. When the pH is acidic, the P2VP is protonated and the chains are repulsive. The micellar size is then larger than in basic pH, when the P2VP is precipitated on the PCL core.



**Figure 1 Mixed micellas. The shell size increases when the P2VP is protonated at low pH values.**



**Figure 2 The core of PCL is spherical, hydrophobic. The thickness of the peel is L and the PEO chains are supposed gaussian.**

We prepared PCL<sub>65</sub>-b-P2VP<sub>31</sub> / PCL<sub>65</sub>-b-PEO<sub>114</sub> and PCL<sub>32</sub>-b-P2VP<sub>52</sub> / PCL<sub>36</sub>-b-PEO<sub>114</sub> 50:50 mixtures of diblocks copolymers. The resulting mixed micelles are analyzed by SANS. We developed a theoretical model with a spherical water-free PCL core. The PEO corona is described as consisting of gaussian chains with a thickness estimated as twice the chain gyration radius, R<sub>g</sub>. We propose two alternatives for handling the P2VP zone. The P2VP molecules are either assumed to be Gaussian chains or they fill a shell of thickness L with possible water penetration. The fitting of the models to the experimental scattering cross sections leads to important structural parameters like the aggregation number, the core radius, the gyration radius and the thickness of the P2VP shell.

## References

<sup>1</sup> Kwon G.S.; Okano T. *Advanced Drug Delivery Reviews*, 21, 2, 1996, 107-116(10)