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

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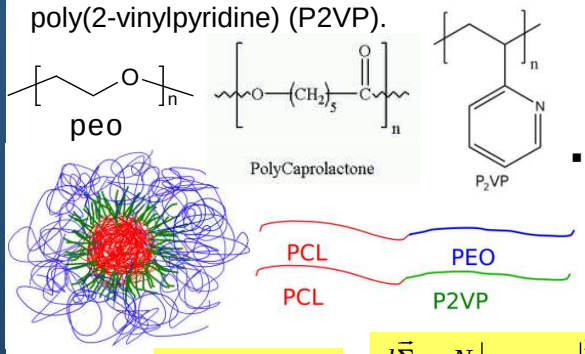
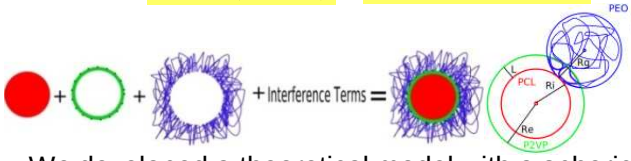
Introduction

- The aim of the project is the preparation of micellar nanocarriers made of biocompatibles copolymers and their structural analysis by Small Angle Neutron Scattering (SANS). These micelles could be used in drug delivery applications to fight cancer[1].
- 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[2].
  The pH in the neighborhood of the tumoral cells is lower than in the healthy cells[3]. We incorporated a pH-sensitive sequence of poly(2-vinylpyridine) (P2VP).



Model

$$\frac{d\vec{\Sigma}}{d\vec{\Omega}} = \frac{N}{V}\left|\sum_i b_i e^{i\vec{q}\vec{r}_i}\right|^2 \qquad \frac{d\vec{\Sigma}}{d\vec{\Omega}} = \frac{N}{V}\left|\sum_i b_i e^{i\vec{q}\vec{r}_i}\right|^2$$



- 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, Rg.
- 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.*

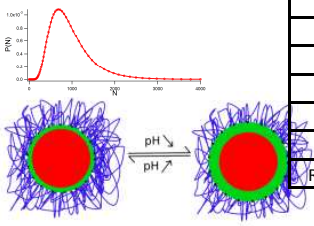
Experimental

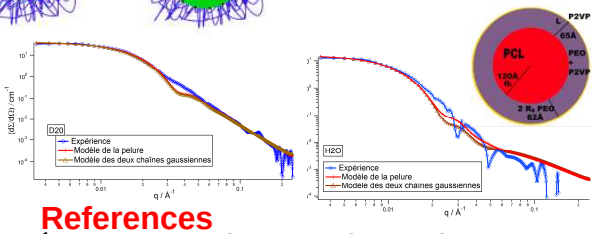
- We prepared PCL_{65}-b-$P2VP_{31}$ / PCL_{65}-b-PEO_{114} and PCL_{32}-b-$P2VP_{52}$ / PCL_{36}-b-PEO_{114} 50:50 mixtures of diblocks copolymers. PCL was synthesized according to litterature[4] and we obtain the PCL_{65}-TEMPO[5]. We copolymerized the P2VP like described in litterature[6].
- SANS experiments performed on the small angle scattering spectrometer (reactor PACE at Saclay, France).λ = 12 Å at 4,7m and 5 Å at 1,5 m – Δλ/λ = 0,1.
- The copolymers were dissolved in DMF then dialyzed again H_2O or D_2O.
- Data recorded at T = 20°C and 70°C (below and above the T_m of PCL).

Results

- The aggregation number (and the core radius) do not change when pH varies. The size of the P_2VP shell does not change either upon pH variation, contrarily to previous work. This could be linked to the short length of the P_2VP block, appears as an essential parameter.
- The PEO gyration radius decreases by about 15% when pH increases from 2 to 10. The P_2VP acts like a stake for the PEO.

	Acidic	Neutral	Basic
N_{max}	680	641	680
R_i	120	118	120
L	65	46	52
Φ	0,083	0,129	0,115
$R_{g,PEO}$	31	29	26
S	0,48	0,53	0,46
$R_{tot} = R_i + 2\,R_{g,PEO}$	183	177	172





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