The uptake and internalization of nano- and microparticles by living cells is crucial in many drug delivery processes. Understanding of elemental steps constituting this process is of great importance. The project aims at elaboration of methods of preparation of polymer prolate spheroidal particles loaded with biologically active compounds or fluorescent probes. They will be used for studies enabling deep understanding of elemental steps of particle adsorption and penetration of thin films (flat and liposomal membranes) modeling membranes of living cells. The particles should be (bio)degradable and allow controlled release of embedded bioactive compounds.

The project will include systematic investigations of fabrication of spheroidal microparticles composed of aliphatic polyesters, polycarbonates and relevant copolymers commonly used for biomedical applications. The particles will be "pure" (from polymer only) or loaded with fluorescent labels (e.g. Nile Red or fluorescein) and/or with Simvastatin (drug used for treatment of inflammation of endothelium of blood vessels). The first step will consist of preparation of nano- and microspheres with controlled diameters and narrow diameter distribution. Two methods will be used for preparation of spherical particles; (i) direct synthesis by dispersion homo and copolymerization of corresponding cyclic monomers (lactides, glycolide, cyclic carbonates) and (ii) from pre-synthesized polymers dissolved in organic solvents, emulsified in water containing emulsion stabilizer (e.g. poly(vinyl alcohol) - PVA) and subsequent evaporation of organic solvent ("oil-in-water" (O/W) emulsification solvent evaporation method).

The particles will be loaded with e.g. Simvastatin or fluorescent probes, during either synthesis or fabrication of spherical particles from pre-synthesized polymers. In the second step the strips will be casted from spherical particles suspended in water solution of PVA. The dry strips will be stretched at elevated temperature, leading to stretching of embedded particles. Dissolution of PVA matrix will yield spheroidal nano- and microparticles with aspect ratio (ratio of long to short axis) up to 10. When required, the last step of particle preparation will consist of their functionalization by labeling with moieties containing anionic (carboxylic) or cationogenic (amino groups), which might be converted to cationic groups by quaternization. The particles will be characterized by determination of their size, size distribution, aspect ratio and zeta-potential.

Rate of particles degradation and release of entrapped compounds will be investigated as a function of particle composition and shape. The above-described particles will be used for studies of their adsorption on flat surfaces coated with lipid layer (electrically neutral and containing anionic or cationic groups). Liposomes – the simplest models of living cells will be prepared from these classes of lipids. Their thickness and structure will be observed by ellipsometry and AFM. Adsorption of spheroidal particles onto the lipid-coated flat surfaces will be monitored by SEM and fluorescence spectroscopy. Process of particles adsorption on liposomes and their internalization will be monitored by Cryo-TEM, fluorescence microscopy and microcalorimetric titration. Similar methods will be used also in the case of studies involving living cell cultures. The knowledge acquired during realization of the project will be important for future design of more efficient drug carriers, which should improve medical treatment in the range of anticancer drugs and anti-artherosclerosis.