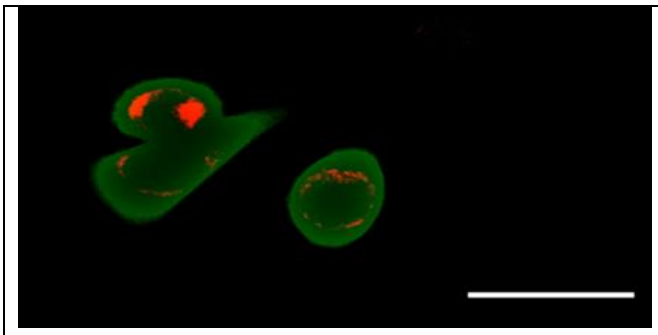
Nanoplastics in living cells. **Robert Holyst**

Industry produces plastics at a rate of 300 million tons per year. Most of them eventually end up in the water and, due to minimal biological degradation, mechanically wear out until reaching a state of plastic nanoparticles (nanoplastics) of sizes 1-100 nm. These nanoparticles penetrate whole organisms and accumulate inside cells, crowding them. We postulate that this crowding impairs diffusive transport in living cells. Impaired transport negatively affects all biochemical processes inside cells. However, we do not know how significant is the impairment of transport. This project will resolve the issue.

Irrespective of nanoparticle cellular uptake pathway, they start to be sorted, translocated and degraded by lysosomes –cell's digestive system. However, digestion of organic nanoparticles is rare, their accumulation in lysosomes is the major fate. The accumulation causes dramatic increase in the size and quantity of lysosomes inside the cell. Enlarged lysosomes are more sensitive to breakage, resulting in the loss of their membrane integrity and release of all the content (i.e. both lysosomal digestive enzymes and accumulated nanoparticles) to the cytoplasm. The cytoplasmic presence of digestive enzymes may initiate slow cell death. Furthermore, the release of nanoparticles due to lysosomal disruption may enhance crowding effects and alter the viscosity of cytoplasm. Any differences in the cytoplasmic viscosity will affect biomolecule mobility, thereby changing the rate constants of all biochemical reactions. Additionally, the active intracellular transport is slowed down. My group already demonstrated that only 4-fold increase of the ambient nanoviscosity stops motion of motor protein kinesin-1.



We exposed HeLa cells expressing GFP (green colour) to polystyrene nanoparticles of radius 25 nm (red spots) for three hours. The concentration of the nanoparticles in the medium was 100 μg/ml (0.1 μM). Morphological changes of cells, caused by accumulated nanoparticles (red) inside cells are visible. Scale bar 30 μm. (Preliminary results)

Therefore the development of the method to study impaired transport in cells, caused by accumulated nanoparticles is the main **objective of this project**. Additionally we will study the uptake and removal kinetics of nanoparticles to and from cells in a wide range of times, and concentrations and sizes of nanoparticles. This analysis will be an important element in the plastic pollution control. We have a long-term research record in physical chemistry of biological systems to ensure necessary tools for this project implementation.

Our project will provide information vitally needed by the World Health Organization (WHO) https://www.who.int/water_sanitation_health/publications/microplastics-in-drinking-water/en/ to assess the risk (at the cellular level) of water contamination by plastic nanoparticles in a wide range of their concentrations. This project is timely, as also explained by the Editorial Material, "Nanoplastic should be better understood" published in Nature Nanotechnology (April 2019).