## Influence of polymer structure and properties on protein-polymer microbubble parameters.

Tatyana M. Estifeeva1, Roman A. Barmin1, Polina G. Rudakovskaya1, Anna M. Nechaeva2, Le-Deygen M. Irina3, Dmitry A. Gorin1

1Center for Photonic Science and Engineering, Skolkovo Institute of Science and Technology, Nobel str. 3, 121205 Moscow, Russia

2Department of Biomaterials, Dmitry Mendeleev University of Chemical Technology of Russia, Miusskaya sq. 9, 125047 Moscow, Russia

3Laboratory of Chemical Design of Bionanomaterials, Department of Chemical Enzymology, Faculty of Chemistry, Lomonosov Moscow State University, Leninskie Gory, 1, building 11B, 119991 Moscow, Russia

## Abstract

Opportunities for improving the efficiency of the optical and biophotonic properties of materials based on microbubbles arise from the ability to vary their parameters by modifying the structural properties of polymeric components. In this work we consider the relationship between the structure of a polymer (N-vinyl-2-pyrrolidone with acrylic acid (P(VP-AA)), its physicochemical properties and the properties of complexes and materials based on this polymer (protein-polymer microbubbles).

For the preparation of protein-polymer microbubbles, we studied a series of copolymers of N-vinyl-2-pyrrolidone with different end mercaptan groups (octodecylmercaptan and octylmercaptan) and molecular weights ranging from 3.5 kDa to 15 kDa. The colloidal properties and specific interaction with the BSA globule of the copolymers had a significant effect on the size, stability, polydispersity and acoustic response of the microbubbles, which is critical for their use in biophotonics as bimodal contrast agents.

Our study confirms that the desired physicochemical properties of protein-polymer microbubbles can be tuned by manipulating the copolymer structures. Using liquid infrared spectroscopy to analyse our complexes and microbubbles, we have tracked changes in the structure of the BSA globule upon addition of the copolymer, resulting in an average increase in the number of beta structures of between 40% and 50%. When microbubbles are formed, the structure of the protein changes again, leading to a decrease in the proportion of beta structures to 45%. We found a difference in the ultrasonic response of microbubbles between the copolymer with octylmercaptan and octodecylmercaptan at similar concentrations. It was also found that a 5:1 mass ratio of protein to copolymer was most effective in maximising the ultrasonic response in the phantom. Tuning these parameters could improve the application of microbubbles in areas such as optical imaging, targeted delivery and controlled release of bioactive particles, and ultrasound diagnostics.

In conclusion, this study deepens our understanding of the relationship between polymer science and biophysics and paves the way for the development of optical and biophotonic applications using protein-polymer microbubbles.