Design of Novel Paramagnetic Probes for Studying Molecular Interactions and Mechanisms in Polymer Systems Using EPR Spectroscopy

Polina Ponomareva,[1] Marina Pigaleva[1]

[1] Institute of Chemistry and Biochemistry, Freie Universität Berlin, 14195 Berlin, Germany

polinapon10@zedat.fu-berlin.de

Mucus-like hydrogels are vital biological barriers that serve to shield against pathogens while enabling efficient drug delivery. In this research, electron paramagnetic resonance (EPR) spectroscopy combined with site-directed spin labeling (SDSL) is employed to probe the molecular-level interactions and dynamics within these hydrogels. The study focuses on the design of new approaches to study different mechanisms in polymer hydrogel systems.

As a first step, we investigate soft matter systems based on the synthetic high-molecular-weight sulfated polymers that mimic the rheological properties of mucus and the charge distribution along mucin chains. These polymers can be labeled with a paramagnetic probe to study the formation of multimers and their subsequent degradation upon the addition of dendritic polyglycerol (dPG) thiol particles, which are known to have a mucolytic effect in vitro. We also demonstrate by the EPR spectroscopy that positively charged dPG-amino polymers form complexes with the mucin-mimicking synthetic polymer in solution, which can help to interpret the barrier functions of mucus against viruses. Furthermore, we investigate the gelation kinetics and nanoviscosity of hydrogels by using spin labels attached to polyethylene glycol chains of varying lengths. This approach allows us to explore the dynamics of mucus self-organization with a reporter inside the hydrogel pores and provides insights into functional impairments, such as those observed in cystic fibrosis. Our findings show that the synthetic mucus-like hydrogels significantly hinder the diffusion of spin-labeled molecules, reflecting the dense network and high viscosity typical of gel matrices. These characteristics mirror the properties of native mucus, where solute transport is inherently constrained by the gel structure.

This methodology not only deepens our understanding of particle mobility and interaction mechanisms within hydrogel systems but also lays the groundwork for designing more effective pathogen barriers and drug delivery platforms.