

## **“New Insight into the Mechanism of Action of Antibiotic Peptides - The Role of the Electric Double Layer”**

Sławomir Sęk

In an era where antibiotic resistance is soaring, the hunt for new, effective treatments is more pressing than ever. Antibiotic resistance is a formidable global health challenge, worsened by the slow pace of new antibiotic development and increased antibiotic use during the COVID-19 pandemic. Traditional antibiotics are losing their battle against resistant bacteria, creating an urgent need for innovative solutions. Enter antimicrobial peptides (AMPs), potent defense molecules, which offer a promising alternative to conventional antibiotics. These small molecules disrupt bacterial membranes, leading to cell death, and are effective against a broad spectrum of pathogens.

AMPs typically work by forming pores in bacterial membranes or destabilizing them. However, their exact mechanisms can vary, and many aspects of how they work remain mysterious. This project aims to shed light on these mechanisms, focusing on the role of the electrical double layer (EDL) and the polyelectrolytic properties of bacterial cell walls, factors that have not been considered in this context so far. The EDL forms at the boundary between a bacterial cell's membrane and the surrounding liquid. It consists of layers that affect local ionic concentrations, which might be crucial for how AMPs change shape and gather together to attack bacteria. Additionally, the complex structure of bacterial cell walls, rich in components like teichoic acids and lipopolysaccharides (LPS), may help AMPs aggregate, enhancing their ability to kill bacteria.

Understanding these interactions could be key to developing AMPs that effectively target and breach bacterial defenses. The research will explore whether the EDL helps AMPs gather and transform into their active forms and how the polyelectrolytic nature of bacterial cell walls influences AMP behavior. This innovative approach considers factors previously overlooked, aiming to enhance AMP efficacy against superbugs.

This project is vital as antibiotic resistance threatens modern medicine, complicating treatments and making infections harder to manage. Without new strategies, AMR could cause millions of deaths annually and drastically impact the global economy. By investigating how AMPs behave in various environments and their interactions with bacterial membranes, this research could pave the way for new, effective antimicrobial strategies. The project will use advanced instrumental techniques to study these interactions. These will include electrochemical approach combined with spectroscopy and microscopy. The outcomes could revolutionize the development of new antimicrobial agents, offering a robust response to the growing threat of antibiotic resistance and expanding the therapeutic potential of AMPs in medicine and biotechnology.