O-28.4 Short talk

Structural characterization of aerolysin in a membrane-like environment

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Pore-forming toxins (PFTs) are key virulence factors of various pathogenic bacteria and have gained significant attention for their potential applications as biosensors. They are secreted in a soluble form and only upon membrane binding they oligomerize into transmembrane pores. Aerolysin, a β-(PFT), emerged as a powerful tool for nanopore sensing due to its narrow and charged pore lumen which allows the detection of diverse molecules. We recently published the first high-resolution cryo-EM structure of aerolysin in several membrane mimics including copolymer nanodiscs. Using this membrane-like environment allowed the identification of lipids surrounding the pore and to determine its correct position in the membrane. Moreover, the structure revealed key interactions necessary for membrane anchoring and allowed to better understand the pore formation mechanism. Notably, we were also able to identify four constriction rings in the pore lumen which are highly relevant for nanopore sensing. The high-resolution structures will allow for more precise modeling and engineering of aerolysin in the future. As a next step, we aim to discover currently unknown PFTs that could allow new sensing application. By searching the AlphaFold database we identified several promising candidates that we are currently characterizing biophysically and in in the nanopore setup.