Tackling the Gram-Negative Permeability Barrier Through Collaborative Data-Driven Prediction

Philip Gribbon, Fraunhofer ITMP, Schnackenburgallee 114, 22525 Hamburg

The discovery of antibiotics effective against Gram-negative bacteria remains a major challenge, largely due to the limited permeability of the Gram-negative cell envelope. While large-scale screening libraries exist, reliably identifying compounds with a realistic chance of intracellular accumulation remains difficult and costly.

Within the AMR Accelerator project COMBINE, our Scientific Interest Group in Machine Learning is bringing together academic and industry partners to jointly address this challenge by developing predictive models for Gram-negative permeability. Building on previous experimental and computational work contributed by partners (Gadiya et al. 2025, Le Goff et al. 2025, Scalia et al. 2025), our goal is to combine complementary datasets and tools to enable the in silico prioritisation of compounds from large screening libraries that are more likely to succeed as antibiotic candidates.

We are currently establishing a collaborative framework that integrates experimental permeability measurements and relevant proxy data with modern machine learning approaches, ranging from classical algorithms to deep learning. Depending on data availability, models may be trained in a species-specific or cross-species manner to improve generalisability. Initial partners from both academia and industry are already contributing data and expertise, and further participation is actively encouraged.

This contribution introduces the initiative, outlines the data and modeling strategy, and invites additional partners to contribute datasets or tools. By pooling resources across the AMR Accelerator community, we aim to reduce time and cost in early-stage antibiotic discovery and improve our understanding of the determinants of compound uptake in Gram-negative bacteria