Project: ***Thinking Big: Structural and Transcriptional Insights into Therapeutic Jumbophages***

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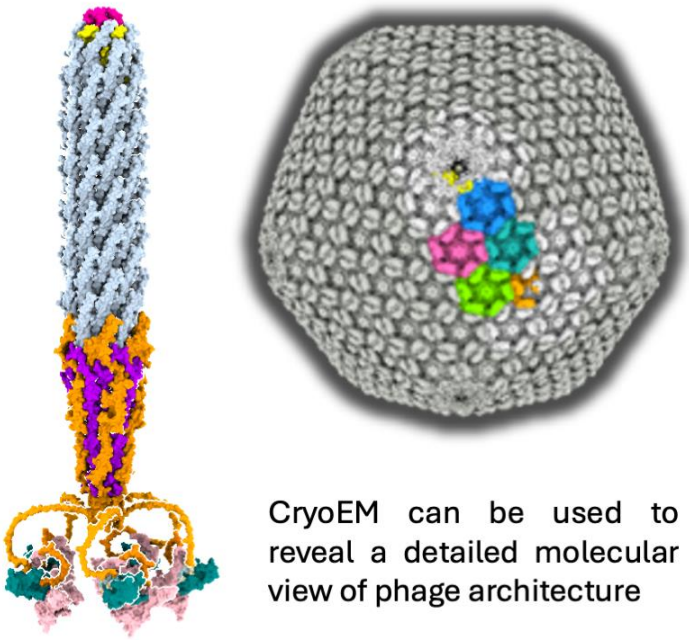
Project:

Antimicrobial resistance (AMR) poses a critical global health challenge, with *Pseudomonas aeruginosa* designated as a WHO priority pathogen. Phage therapy represents a promising alternative to antibiotics, yet bacterial resistance frequently evolves at the phage–receptor interface. Jumbophages, with their large genomes and unique capacity for forming nucleus-like compartments, offer particular therapeutic potential by evading bacterial defences and enabling synthetic biology applications. However, their reliance on host receptors remains a key vulnerability, and the molecular mechanisms underlying phage adaptation and infection efficiency are poorly understood.

This PhD project will investigate the recently isolated jumbophage Sedgewick, housed in the Citizen Phage Library (University of Exeter). Building on preliminary cryoEM structural data and genome annotations, the project will integrate structural biology and transcriptomics to dissect Sedgewick's infection strategy. Key aims include resolving receptor-binding proteins and baseplate architecture, mapping the temporal program of gene regulation, and comparing trained versus untrained phage variants to identify adaptations that broaden host range and overcome resistance. Delivering the first combined structural and transcriptional framework for a therapeutic jumbophage, this work will provide fundamental insights to guide the rational engineering of next-generation phages against AMR pathogens.



CryoEM can be used to reveal a detailed molecular view of phage architecture