Project Details	
Project Code	IIAR27Ba Matlock
Title	Turning up the volume: plasmid copy number and gene duplications as drivers of antimicrobial resistance evolution
Research Theme	Infection, Immunity & Antimicrobial Resistance
Project Type	Wet lab
Summary	Plasmids are important drivers of antimicrobial resistance (AMR), complicating infections and causing outbreaks. Plasmids frequently alter their structure by duplicating genes, and they can dynamically adjust their copy number. This project investigates whether these phenomena act as evolutionary drivers for AMR, “turning up the volume” on gene dosage to accelerate adaptation and innovation. Combining large-scale genomic surveillance data from hospital bloodstream infections with experimental evolution, you will characterise how pathogens use plasmid flexibility to survive. This work will reshape our understanding of superbug evolution and improve how we track dangerous resistance genes globally.
Description	**Background** Plasmids are major drivers of bacterial evolution because they mediate horizontal gene transfer and disseminate adaptive traits such as antimicrobial resistance (AMR) and virulence. Plasmids frequently undergo recombination, enabling them to acquire and duplicate genetic material, including AMR genes. In addition, plasmids often occur at multiple copies per bacterial cell, altering gene dosage and influencing both resistance phenotypes and the evolutionary trajectory of AMR genes. Although plasmids are commonly implicated in human infection, the evolutionary consequences of AMR gene duplication remain poorly understood. Duplicated loci may represent transient products of recombination that are rapidly lost, or they may be maintained, providing increased resistance, or opportunities for functional divergence. Resolving these alternatives is important for understanding plasmid adaptation and for improving genomic surveillance of clinically important AMR determinants. This project will be one of the first to use the NEKSUS dataset, a population-based genomic surveillance collection comprising more than 3,000 Escherichia coli and Klebsiella bloodstream infection isolates collected from nine UK hospitals during 2023–2024. Unlike many existing collections, NEKSUS systematically sampled all bloodstream infections rather than selectively sequencing resistant isolates, thereby providing an unbiased view of plasmid and AMR gene diversity in clinical populations. Hybrid Illumina–Nanopore sequencing has generated high-quality assemblies that permit detailed characterisation of plasmids and AMR gene context. By integrating comparative genomics, evolutionary modelling, and experimental evolution, this project will determine how variation in AMR gene dosage influences plasmid evolution. **Key research question** How does AMR gene dosage drive the evolution of plasmid-borne antimicrobial resistance? **Specific objectives**

	1. Develop a bioinformatic framework to identify and characterise multi-copy/duplicated AMR loci in clinical bacterial populations. The student will receive training in reproducible bioinformatics and scientific software development by building a Nextflow workflow to systematically characterise AMR loci across the NEKSUS collection. The workflow will identify AMR genes and their genomic context; distinguish chromosomal and plasmid-borne loci; identify duplicated AMR genes and estimate relative copy number using assembly structure and sequencing coverage; characterise plasmid population structure using cutting-edge pangenomic and plasmid comparative methods. This objective will generate the first population-scale map of AMR gene duplication and copy number within a systematically sampled bloodstream infection collection. 2. Quantify the evolutionary dynamics of AMR gene duplication The student will train in cutting-edge phylogenetics as they investigate AMR gene duplication across bacterial and plasmid lineages. Comparative phylogenetic approaches will be applied to selected high-prevalence AMR genes and plasmid groups to estimate rates of gene duplication, loss, and horizontal transfer, while accounting for host and plasmid population structure. This objective will identify the evolutionary contexts in which AMR gene duplication is most likely to persist. 3. Identify the genomic factors associated with AMR gene diversification in plasmids The student will train in data science for genomic data as they test whether multi-copy/duplicated AMR genes show evidence of altered evolutionary trajectories compared with single-copy genes. Comparative analyses will evaluate whether duplication is associated with increased sequence diversification. Factors including plasmid mobility, plasmid copy number, host lineage, and genomic context will be evaluated as predictors of diversification. This objective will establish whether gene duplication facilitates evolutionary innovation in plasmid-borne AMR genes. 4. Experimentally validate the evolutionary consequences of duplicated/multi-copy AMR genes Here, the student will train in experimental evolution. Plasmids carrying single-copy and duplicated AMR genes, at varying plasmid copy number, will be selected for experimental evolution under contrasting antibiotic selection regimes. This experiment will characterise the evolutionary trajectory of the AMR genes, and determine whether laboratory evolution recapitulates patterns observed in the clinical population. By integrating comparative genomics, evolutionary modelling, and experimental evolution, the student will develop expertise across computational and laboratory approaches while determining how variation in AMR gene dosage influences plasmid evolution. **Expected outcomes** This project will provide a mechanistic understanding of how plasmids drive AMR gene evolution in clinically important pathogens. The work will generate novel computational tools for genomic surveillance, and establish whether duplicated resistance loci represent transient genomic accidents or important substrates for long-term adaptation. Such

	knowledge will improve our ability to predict the emergence and persistence of clinically important resistance determinants. **Student ownership and project direction** The project is designed to be highly flexible and student-led. During the first year, the student will identify focal resistance mechanisms, plasmid families and/or bacterial lineages emerging from the NEKSUS analyses and will shape the downstream comparative and experimental work around this biological system. As the project develops, the direction of the computational analyses can be adjusted. For example, the student may be interested in formal software development as opposed to developing research code, or might be interested in using machine learning approaches instead of traditional statistical frameworks. The student will also be encouraged to develop independent research questions arising from the project, creating opportunities for first-author publications beyond the core objectives.
Can be completed part time?	Yes
Supervisory Team	
Lead Supervisor	
Name	Dr William Matlock
Affiliation	Bath
College/Faculty	Centre for Evolution
Department/School	Department of Life Sciences
Email Address	wtm35@bath.ac.uk
Co-Supervisor 1	
Name	Professor Tiffany Taylor
Affiliation	Bath
College/Faculty	Centre for Evolution
Department/School	Department of Life Sciences
Co-Supervisor 2	
Name	Dr Sion Bayliss
Affiliation	Bristol
College/Faculty	Bristol Veterinary School
Department/School	Bristol Veterinary School
Co-Supervisor 3	
Name	Dr Catherine Tooke
Affiliation	Bath
College/Faculty	Centre for Evolution
Department/School	Department of Life Sciences