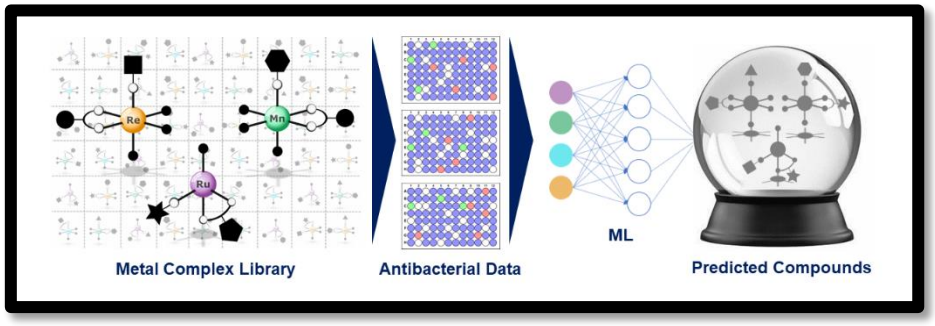
Combining Combinatorial Synthesis and Machine Learning for the Discovery of Novel Metalloantibiotics

Dr. Angelo Frei
Department of Chemistry, University of York, York, United Kingdom

Antimicrobial resistance (AMR) is already causing over 1 million deaths each year. With the clinical pipeline for novel antibiotics with new modes of actions very sparse, this number is expected to further increase in the coming years. As conventional approaches to bacterial infections are failing to provide novel and effective drugs, alternative treatment modalities need to be considered. Over the last decade, metal-based compounds (metalloantibiotics), have emerged as potential new classes of antimicrobial agents.

In this talk I highlight the promise of transition metal complexes as antimicrobial agents and how we employ modular synthesis, automation and machine learning to systematically explore this vast chemical space for promising compounds. This includes our recent training of machine learning models able to increase the hit-rate for Gram-positive active ruthenium metalloantibiotics by a factor of 5x and very new work to expand high-throughput modular metal complex synthesis to novel ligand scaffolds.



Short Biography

Dr. Angelo Frei is a Lecturer in Inorganic Chemistry at the University of York (UK). He studied Chemistry and Biochemistry at the University of Zurich, where he did his Master Thesis with Prof. Gilles Gasser working on ruthenium polypyridyl complexes as photosensitizers for photodynamic therapy. He got his PhD in 2018 with Prof. Roger Alberto on the development of multifunctional cyclopentadiene ligands for theranostic applications. For his first postdoc he was awarded a Swiss National Science Foundation Early.Postdoc Mobility Fellowship to join the group of Prof. Mark Blaskovich at the University of Queensland in Australia. There he started investigating metal complexes as potential antimicrobial agents. In 2020 he joined the group of Prof. Nicholas Long at Imperial College in London to work on novel radioimaging agents for cancer and bacterial infections before being awarded a SNSF *Ambizione* Fellowship at the University of Bern in 2022. Since 2025 he is a Lecturer at the Department of Chemistry at the University of York.
His research interests involve leveraging cutting-edge approaches in modular synthesis, automation and machine learning towards the systematic exploration of the transition metal chemical space for compounds with promising (biological) properties such as metalloantibiotics