Large-Scale DNA Origami Arrays For Combating Antimicrobial Resistance

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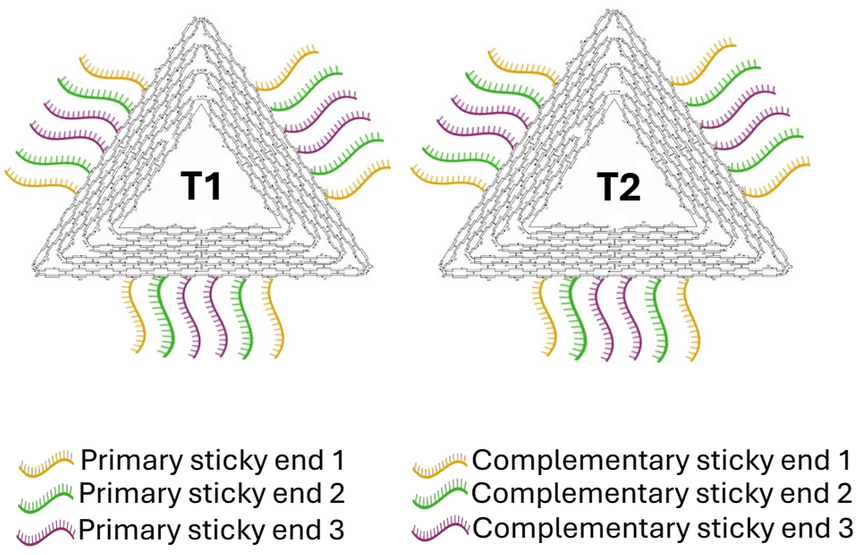
Background and motivation

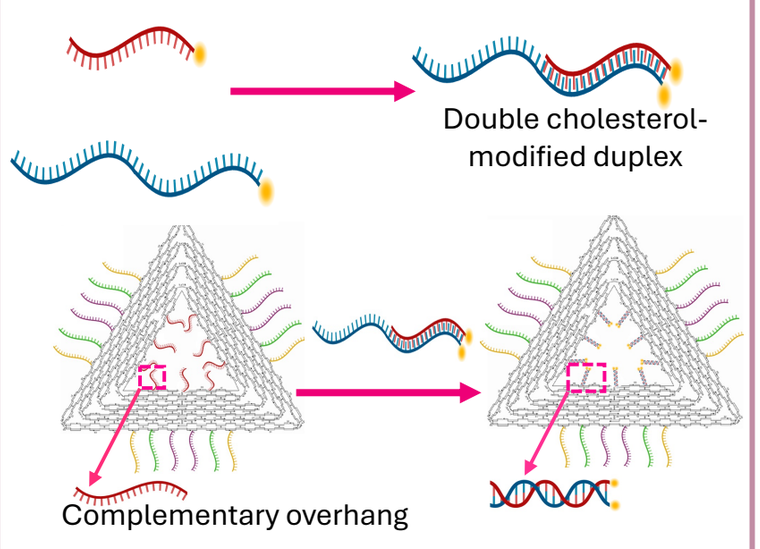
- Antimicrobial resistance is a growing global threat, particularly Gram-negative bacteria due to their outer membrane permeability barrier [1].
- DNA origami nanostructures offer a programmable, biocompatible platform with demonstrated antimicrobial applications [2,3].
- Inspired by neutrophil extracellular traps, this work aims to develop self-assembling DNA origami arrays to physically immobilise the bacteria and deliver antimicrobial peptide.

Methodology

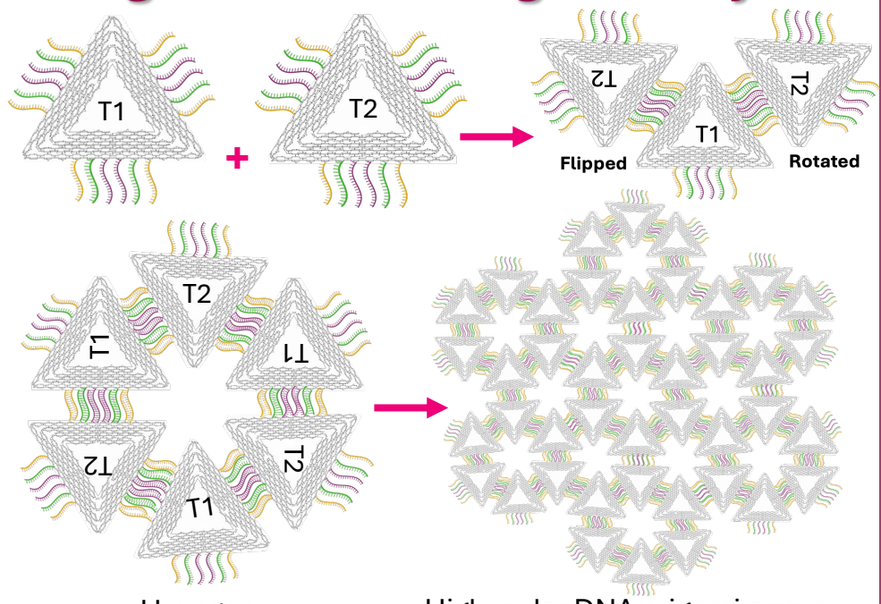
1. Two-tile design with mirrored sticky ends



2. Functionalisation with double cholesterol

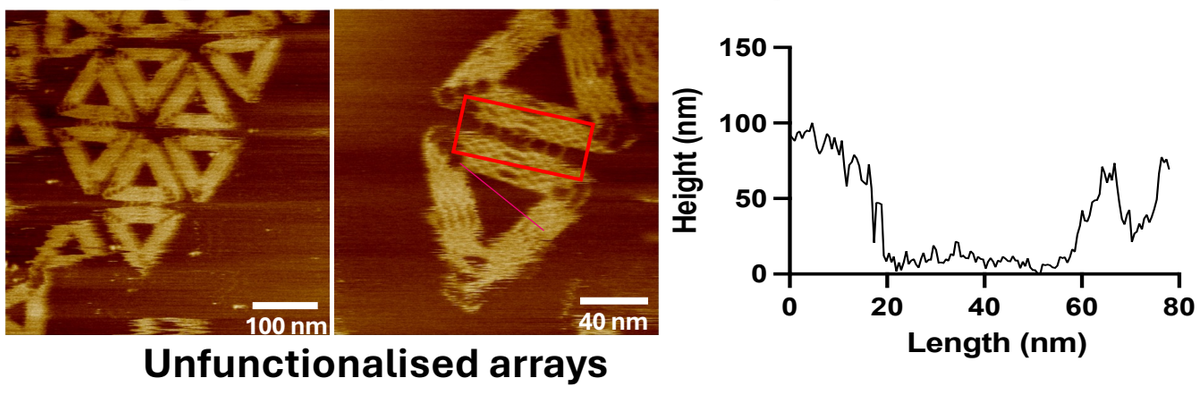


3. Self-assembly of T1 and T2 into high-order DNA origami arrays

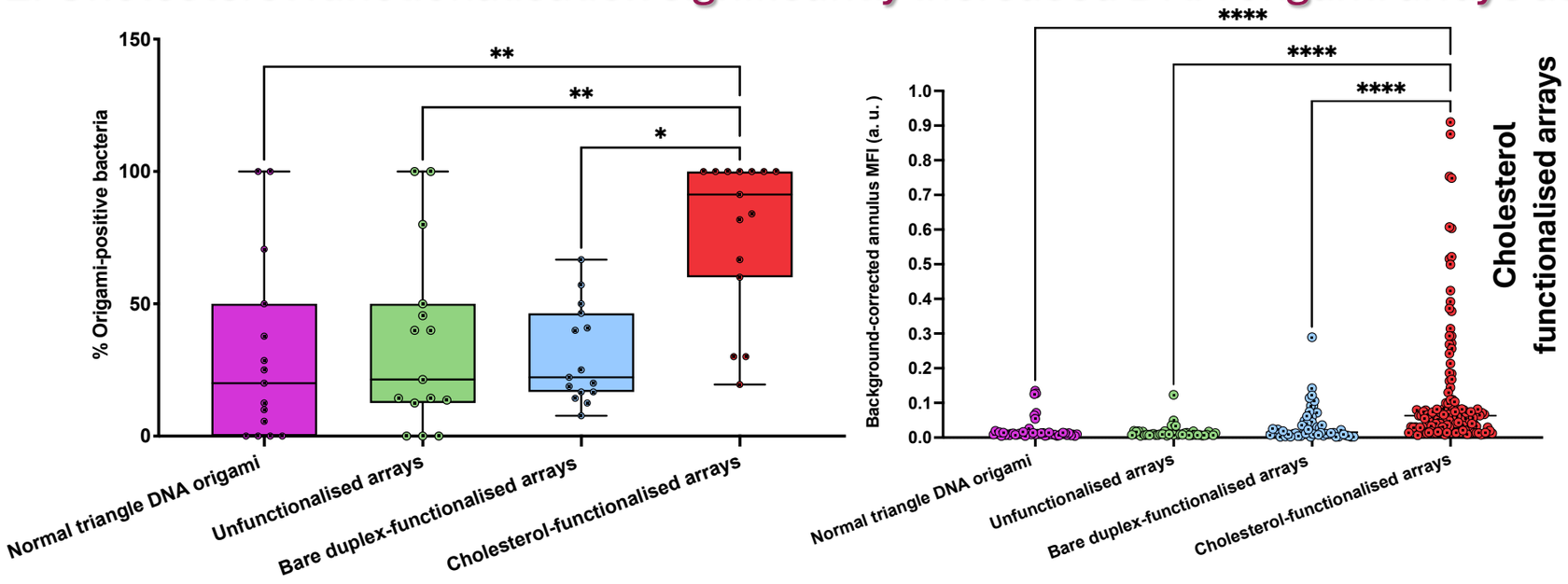


Results

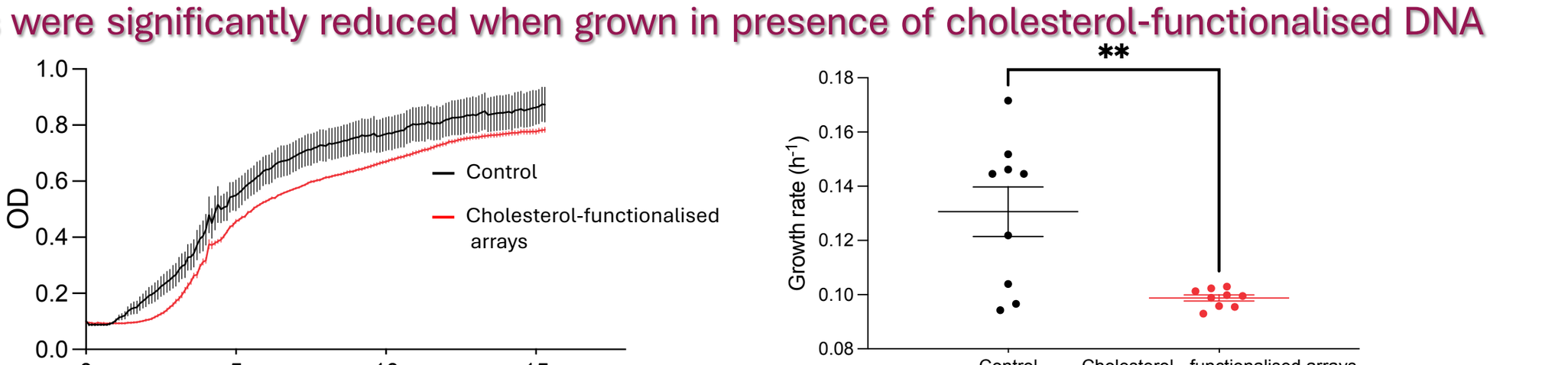
1. DNA origami arrays are successfully functionalised with cholesterol moieties, appearing as bright blobs.



2. Cholesterol functionalisation significantly increased DNA origami arrays association with *E. coli*.



3. *E. coli* growth rates were significantly reduced when grown in presence of cholesterol-functionalised DNA origami arrays.



Future directions

1. Flow cytometry and SEM to characterise arrays-bacteria interaction.
2. pH-triggered antimicrobial peptide functionalisation via i-motif release mechanism.
3. Testing against clinically relevant Gram-negative bacteria.

References

[1] Almarwani, Bashiyar et al., Synergistic Ciprofloxacin-RWn Peptide Therapy Overcomes Drug Resistance in Gram-Negative Bacteria. *ACS Omega* **10**, 35698–35705 (2025).

[2] Mela, Ioanna et al., DNA Nanostructures for Targeted Antimicrobial Delivery. *Angewandte Chemie - International Edition* **59**, 12698–12702 (2020).

[3] Bennett, Isabel D et al., Lipidated DNA Nanostructures Target and Rupture Bacterial Membranes. *Small* **20**, e2207585 (2024).