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Controllable liposome binding interactions using PEG-mediated DNA nanostructures

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Membrane bilayer structures are vital for compartmentalising cells and their contents within biological systems. Membrane-bound complementary DNA nanostructures are capable of interacting with lipid membranes to shape and span lipid bilayers (Darley *et al.*, 2019). Modified DNA-liposomes have the potential to build interconnected synthetic *ex vivo* systems that can demonstrate dynamic membrane aggregation, communication, and morphological manipulation through DNA mediated interactions like strand displacement and switching (Singh *et al.,* 2021). Dynamic DNA-liposome systems open up broader implications for biophysics and nanomedicine, most notably the targeted delivery of molecular payloads through directed membrane fusion (Löffler, Ries and Vogel, 2020).

An asset of DNA nanotechnology is that it can provide triggerable spatiotemporal control of DNA-liposome interactions. Using a DNA nanostructure conjugated with PEG blocker molecules, we seek to regulate surface binding of liposome vesicles. We designed a cholesterol modified DNA structure with a conjugated PEG molecule on the end to act as the membrane-bound blocker of biotin-streptavidin-biotin mediated surface binding. A single stranded DNA toehold sequence added to the cholesterol-modified strand allows the controllable displacement and release of the PEG-conjugated DNA from the liposome surface. This displacement interaction was observed using an SDS-PAGE gel, and further confirmed using fluorescence microscopy. Once displacement was confirmed, fluorescence microscopy was used to observe how the PEG conjugated DNA nanostructure could block liposome surface binding interactions, and how directed displacement of the PEG blocker could allow for control over the timing of liposome surface binding.

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2. Löffler, P. M. G., Ries, O. & Vogel, S. (2020) 'DNA-Mediated Liposome Fusion Observed by Fluorescence Spectrometry', *Nucleic Acid Detection and Structural Investigations: Methods and Protocols* (eds. Astakhova, K. & Bukhari, S. A.), p. 101–118.
3. Singh, J. K. D., Darley, E., Ridone, P., Gaston, J. P., Abbas, A., Wickham, S. F. J., Baker, M. A. B. (2021) 'Binding of DNA origami to lipids: maximizing yield and switching via strand displacement', *Nucleic Acids Res.* **49**, p. 10835–10850.