

Supporting Information

Looking Back, Moving Forward: Lipid Nanoparticles as a Promising Frontier in Gene Delivery

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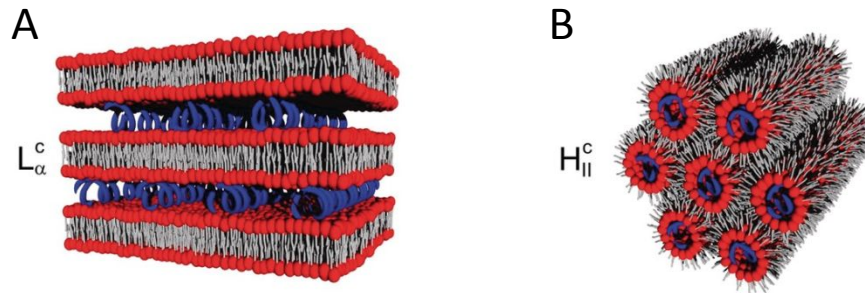


Figure S1. Synchrotron Small Angle X-ray Scattering (SAXS) has unveiled that the most prevalent nanostructure within lipoplexes is the lamellar phase (depicted in panel A). This lamellar structure comprises a stack of lipid bilayers with interleaved monolayers of DNA rods aligned in parallel. In specific lipoplex compositions, the DNA rods are inserted into the aqueous channels of an inverted hexagonal lipid framework (panel B). The symmetry of this configuration matches that of the inverse hexagonal H_{II} phase found in pure lipids without DNA. Because the lipid chain packing in the H_{II} phase is constrained, the diameter of the water channels is only slightly larger than that of the DNA rods. Powerful electrostatic attractions occur between the phosphate charges on the DNA surface and the positively charged head-groups in the surrounding lipids, leading to a minimal separation between the lipid and DNA surfaces, typically within the range of one to two water molecule diameters. Reprinted from Tresset, G. The multiple faces of self-assembled lipidic systems. *PMC Biophys* 2, 3 (2009). <https://doi.org/10.1186/1757-5036-2-3>.