# Relating Surface Structure to Function in Cell Membrane Penetrating Nanoparticles

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Previous work has shown that the shape and surface structure of nanoparticles plays a key role in their uptake by the cell membrane[1,2]. Despite this, a complete understanding of the structural features that govern uptake remains incomplete. In this study, the effect of spatial distribution of ligands on the nanoparticle surface on vesicle formation was investigated. Coarse grain simulations of the cellular membrane, and of a model nanoparticle were used in the context of an evolutionary algorithm to explore ligand placement. By seeking optimal ligand patterning to enable cell entry across various ligand population sizes, robust nanoparticle designs across a range of binding energies were generated. Designs of the resulting populations were transposed into pairwise ligand distance matrices and used to build networks describing the surface structure. Analysis of these ligand distance networks suggest that arrangements of ligands into low density but connected strings, forming long belts across the particle surface is optimal at low ligand numbers, while at large ligand numbers surface structure plays a less important role. That is, ligands with long lines of ligands perform much better than their evenly spaced counterparts, a novel result which builds upon the models developed in previous studies[1].

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[2] Loverde, S. M., Klein, M. L. & Discher, D. E. Nanoparticle Shape Improves Delivery: Rational Coarse Grain Molecular Dynamics (rCG-MD) of Taxol in Worm-Like PEG-PCL Micelles. *Advanced Materials* **24**, 3823–3830 (2012).