Polydots: Soft Nanoparticles, at Membrane Interfaces

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Abstract

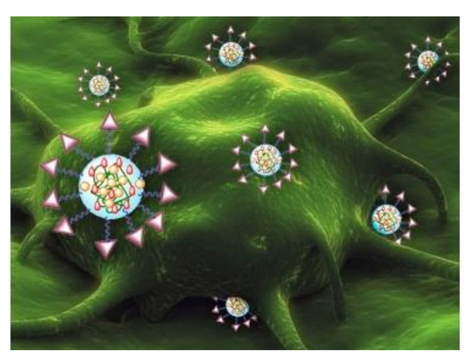
Luminescent polymers confined into long lived polydots form a new class of soft nanoparticles whose emission characteristics are potentially tunable. These polydots are promising targeted drug delivering agents and bio imaging markers. One critical step in the use of any nanoparticle (NP) for medicine is transport across membranes. Its ability to penetrate cells depends on the NPs' surface structure, size, shape and charge as well as membrane characteristics. The soft nature of the polydots provides an edge in comparison to hard NPs. It allows modifications of their interfaces without losing their optical characteristics expressed in shift of emission wave lengths. Here we report the results of an all-atom molecular dynamics simulations of a polydot that consists of a collapsed model polymer, dinonyl poly para phenylene ethynylene (PPE), at the interface of a bilayer composed 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC). Methods of impregnating the membranes with polydots will be discussed following by effects of the polydot on the structure and dynamics of the membranes. In parallel, the effects of the membrane on the polydot will be introduced.

Introduction

Polydots which are made by confining luminescent polymers into nano dimensions are emerging as multifunctional nano scale materials with a potential for therapeutic applications.

❑ **Properties of polydots**

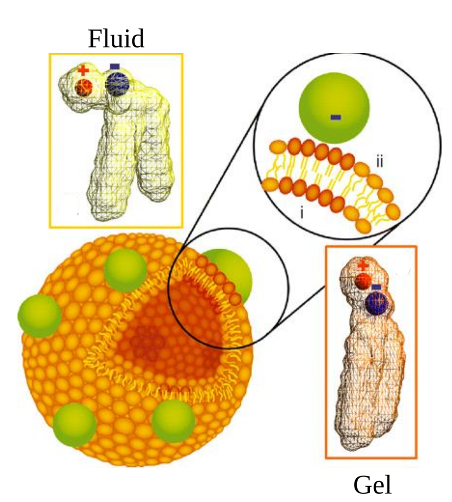
- High luminescence
- Low quenching rates
- Biocompatible
- Tunable
- Less toxic



Soft NPs on the surface of tumor cells[5]

❑ **NP effects on biological membranes**

- Hole formation
- Changing membrane fluidity
- Membrane thinning
- Expanding pre-existing defects



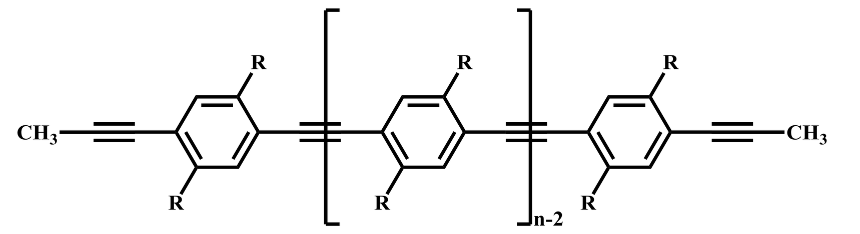
NP effect on membrane fluidity[1]

Goals

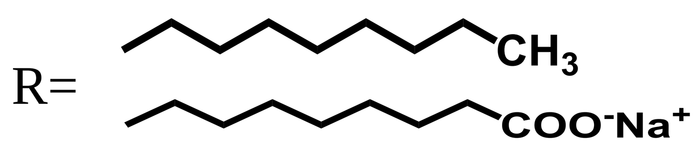
❖ Resolve the changes in structure and dynamics of biological membranes upon introduction of polydots

❖ Determine the conformation and stability of polydots as they pass through membrane

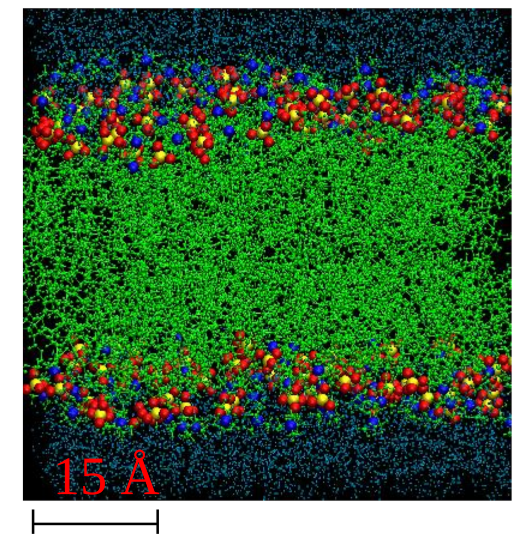
Methodology



*Dialkyl poly p-phenylene ethynylene (**PPE**) (n =120)*



Carboxylate fractions f = 0 and 0.4



DPPC membrane

http://lipidbook.bioch.ox.ac.uk/lipid/show/id/4.html

❑ **Carboxylate groups are possible sites for**

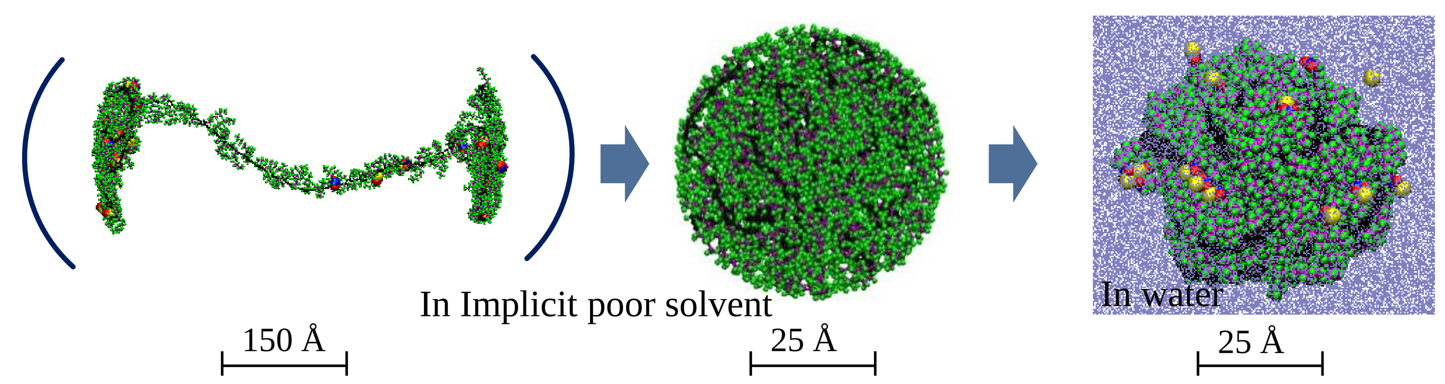
- Tunability
- Sensing
- Chemical diversity for functionalization

❑ Molecules are built with Material Studio, Accelrys Inc.

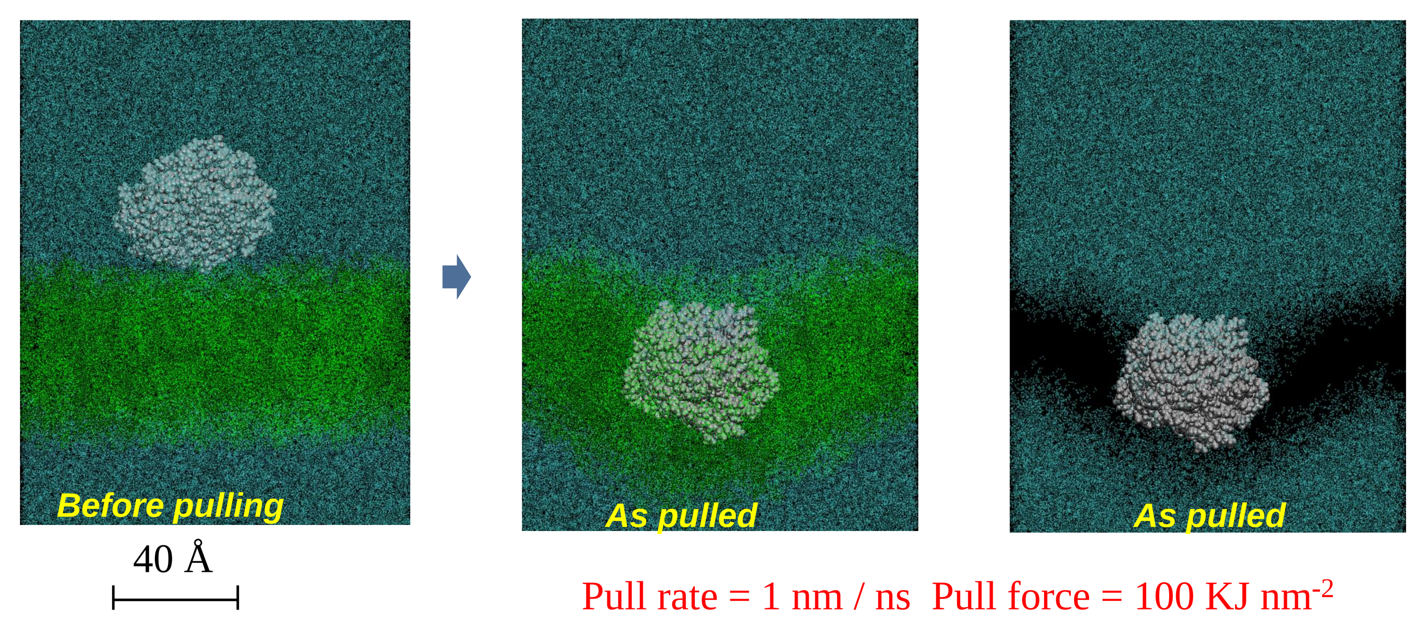
❑ Force fields OPLS-AA with TIP4P/05,[3] CHARMM36 with TIP3P

❑ Molecular dynamics simulation code-LAMMPS,[4] GROMACS 4.6.2

Polydot Preparation



Results - Introducing Polydot into Membrane

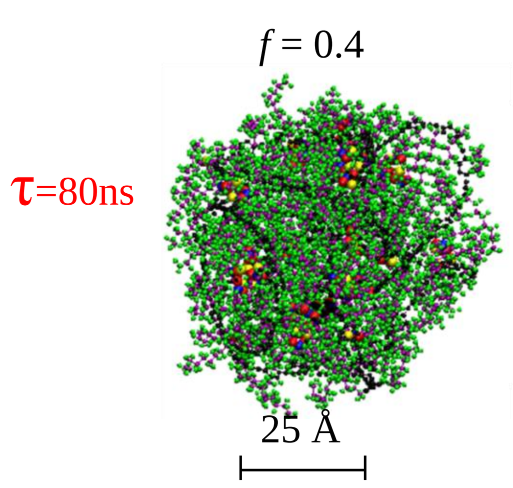


Pull rate = 1 nm / ns Pull force = 100 KJ nm^{-2}

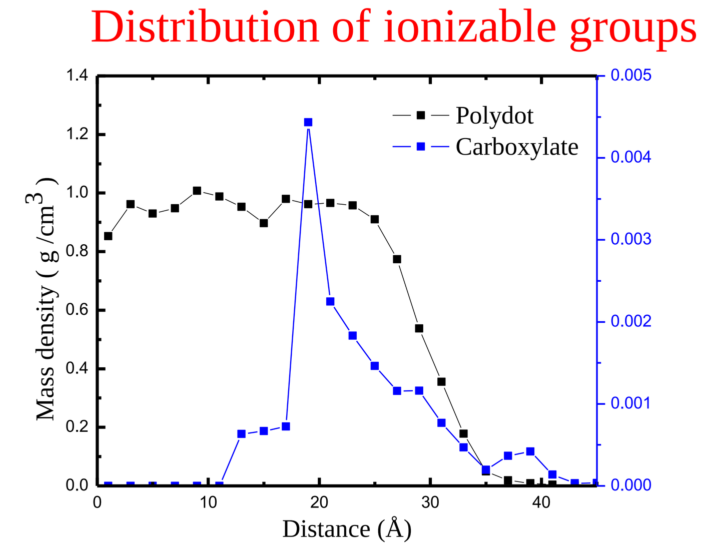
❖ Introduction of polydot deforms the membrane structure

❖ Water is pulled along with polydot into the membrane

Results – Polydot in Water



Distribution of ionizable groups

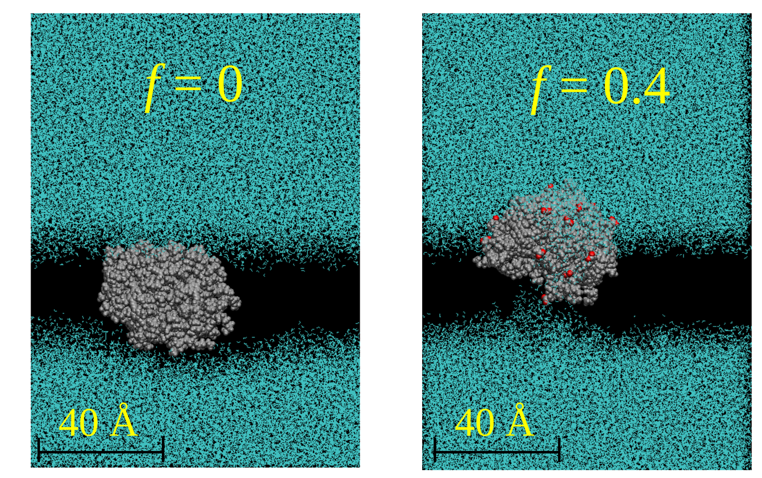


❖ Polydots remain collapsed

❖ Some of the carboxylate groups reside at polydot water interface

Results - Polydot Membrane Complex

40 ns After Releasing the Polydot



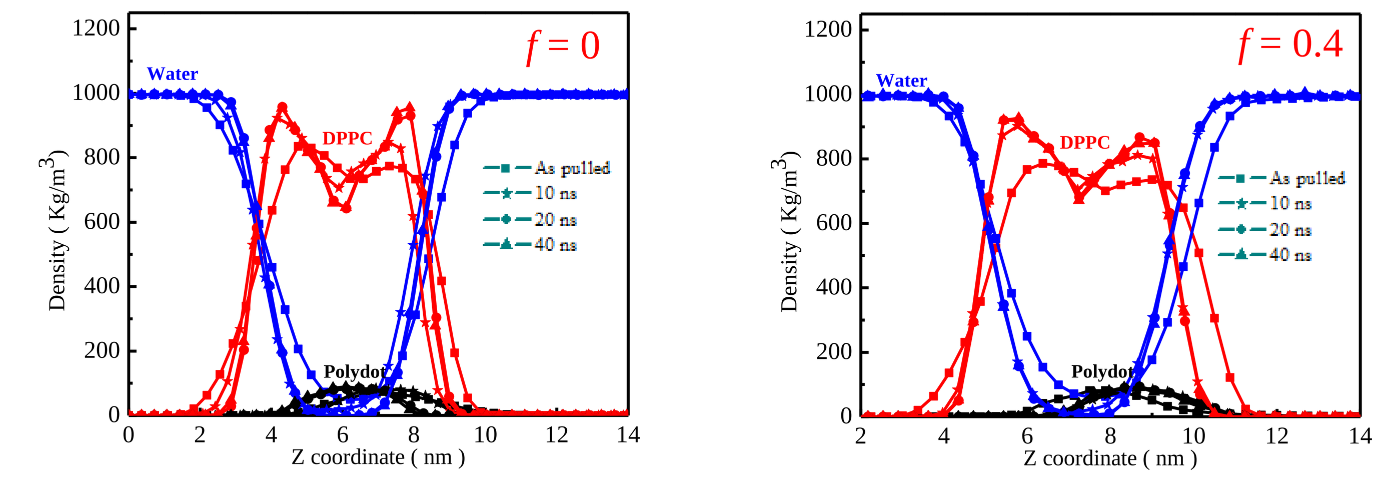
❖ f =0 Polydot

- Resides in membrane

❖ f =0.4 Polydot

- Resides closer to upper leaf

Density Profiles



❖ Water expelled out from membrane interior

❖ DPPC density is not affected

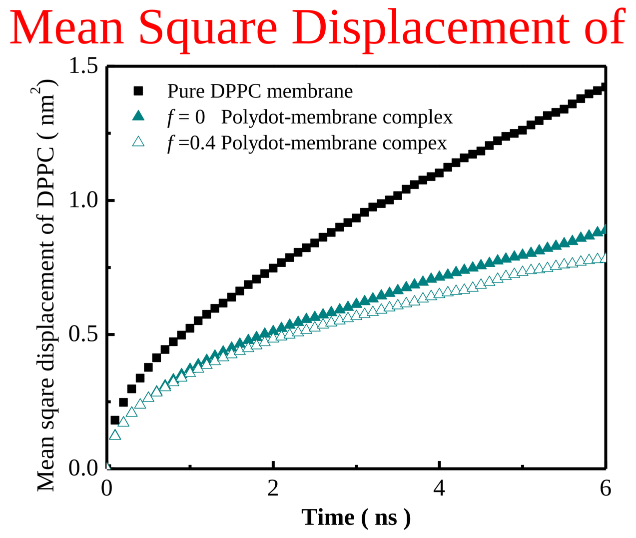
❖ Polydot settles between two leaves

❖ Some water remain inside the membrane

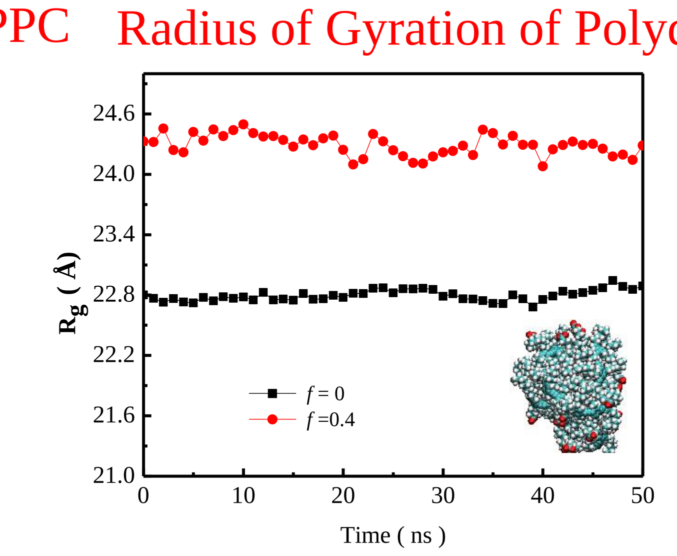
❖ DPPC density is affected

❖ Polydot migrates towards upper leaf

Mean Square Displacement of DPPC



Radius of Gyration of Polydots



❖ Introduction of polydots results in slower dynamics of DPPC molecules

❖ Polydot dimensions are not affected

Summary

❖ f = 0 *and* f = 0.4 Polydots

- Affect membrane structure and dynamics

❖ f =0 Polydot

- Stays in between two DPPC leaves
- No water associated with the polydot remain inside the membrane

❖ f =0.4 Polydot

- Stays closer to upper DPPC leaf
- Water is associated with the polydot remain inside the membrane

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References

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[5]*http://newsoffice.mit.edu/2010/nanoparticle-chemotherapy-1005*