Building a Toolbox for Drug Delivery: Lipid-based Conjugated Polymer Nanoparticles

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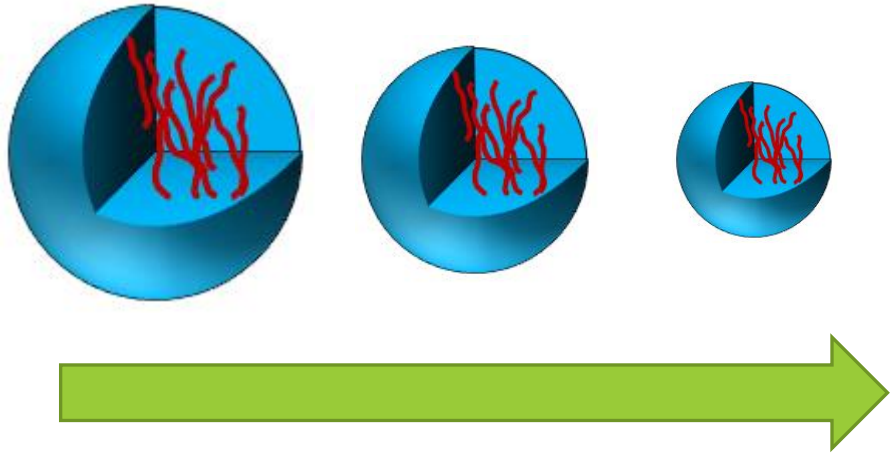


Building a Toolbox for Drug Delivery: Lipid-based Conjugated Polymer Nanoparticles (CPNs)

Presenter: Monika Kojic

Supervisor: Prof. Simon Rondeau-Gagné

Reader: Prof. Tricia Carmichael

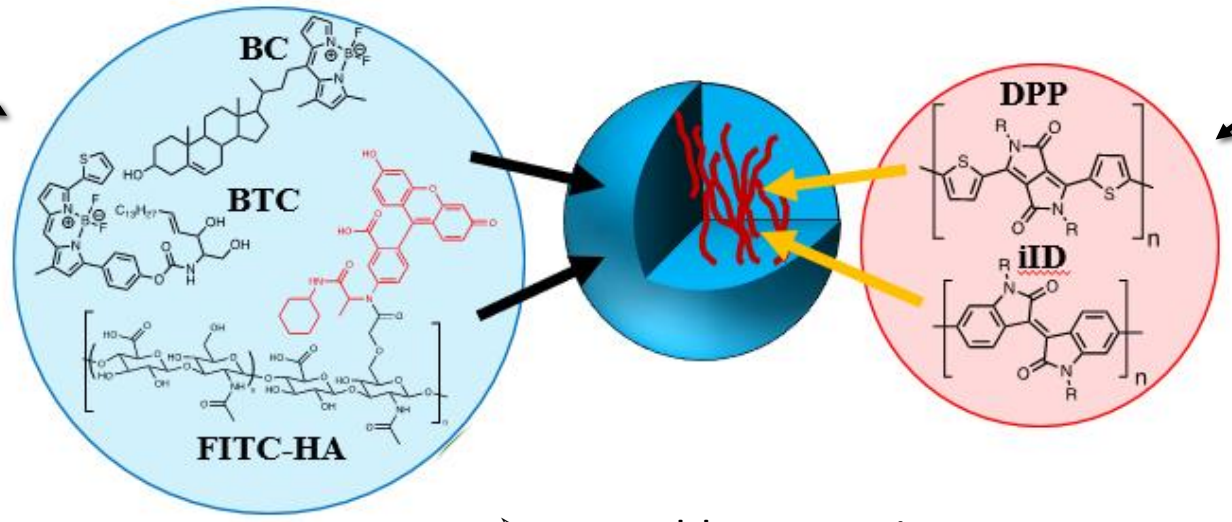
What are Conjugated Polymer Nanoparticles (CPNs) ?

Coating: **Surfactant** (ie. FITC-Hyaluronic acid)[2]

- Amphiphilic
- Conjugated with fluorescent probe

Core: **Polymer** (ie. Diketopyrrolopyrrole (DPP))[2]

- Hydrophobic

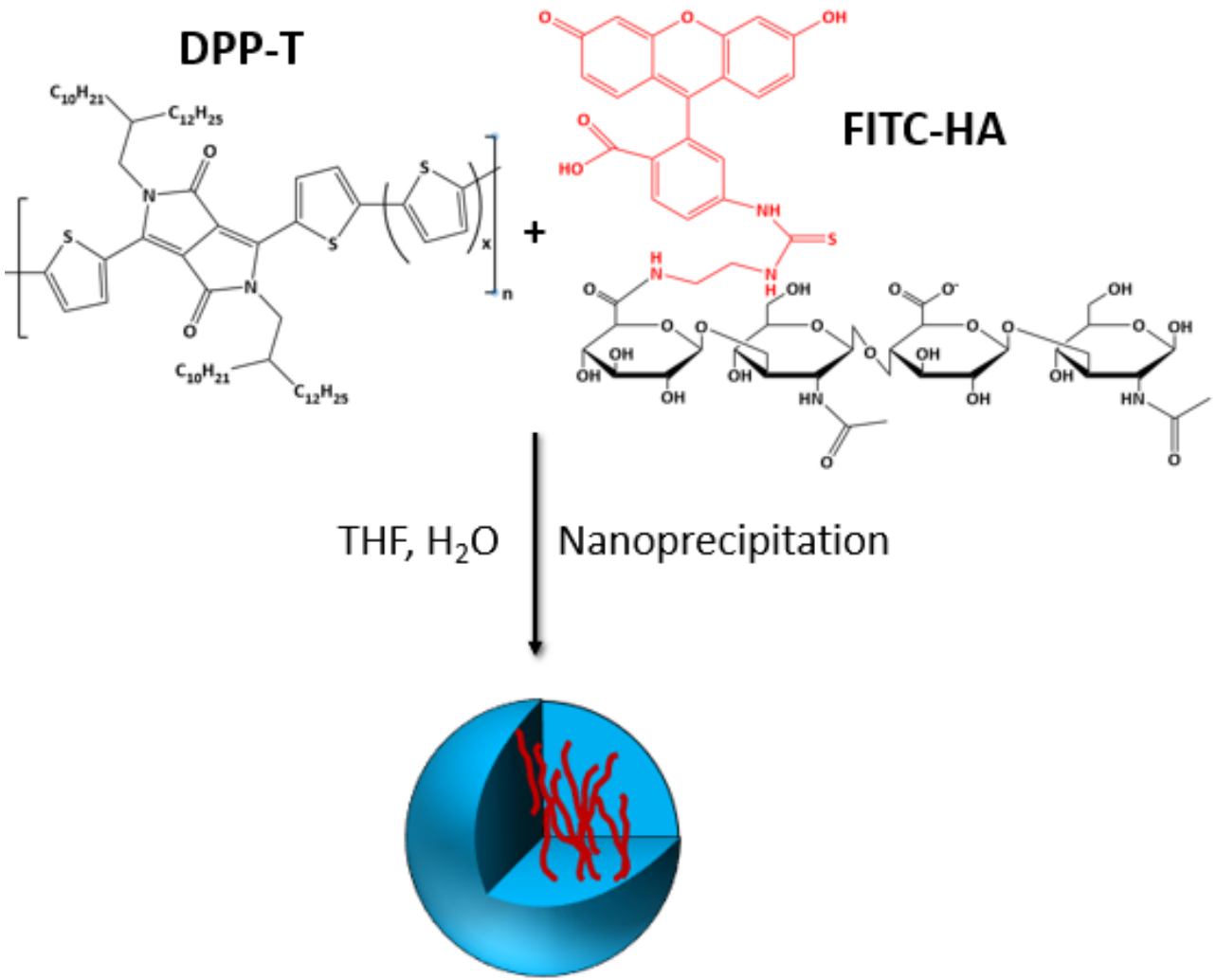


Highly versatile nano-structured materials:[1]

- Tuneable properties
- Versatile synthesis
- Biocompatibility
- Less toxicity

1. Tuncel, D.; Demir, H. V. Conjugated Polymer Nanoparticles. *Nanoscale* **2010**, *2* (4), 484.
2. Langlois, A. et al. Photophysical and Optical Properties of Semiconducting Polymer Nanoparticles Prepared from Hyaluronic Acid and Polysorbate 80. *ACS Omega* **2019**, *4* (27), 22591–22600.

CPNs as Anticancer Therapeutics



- It has been demonstrated that diketopyrrolopyrrole **(DPP)-based CPNs,** using FITC-HA as a surfactant, can **selectively target** CD44+ cells in GBM cell cultures and exhibit **anti-tumourigenic activity.**
- Potential of **CPNs as targeted therapeutics** for stem cell driven **cancers like Glioblastoma (GBM)**

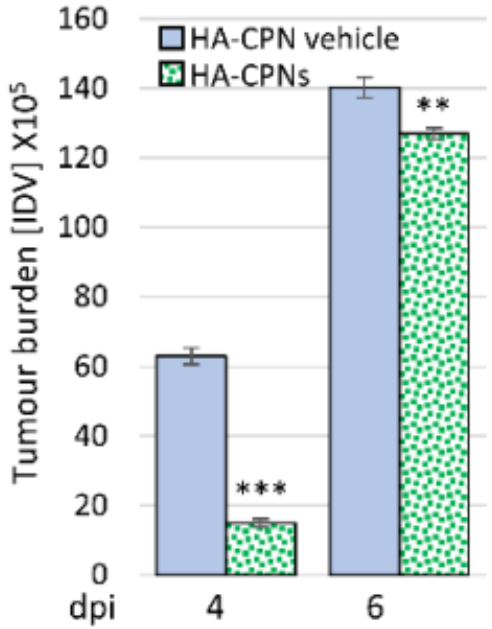


Figure 1:[1] Average tumour burden quantification in PDXs derived from CD44+ HF3035 and HF2303 GBM lines - treated with HA-CPNs vs. HA-CPN vehicle control.

1. Lubanska, D. et al. Impairing Proliferation of Glioblastoma Multiforme with CD44 Selective Conjugated Polymer Nanoparticles. ChemRxiv 2021. This content is a preprint and has not been peer-reviewed.

Lipid Nanocarriers in Drug Delivery Systems

Lipid nanostructures as carriers in drug delivery systems offer:

- **Non-toxicity**
- **Biocompatibility**
- **Increased specificity**
- **Increased stability**
- **Simpler synthesis**

Wong et al.

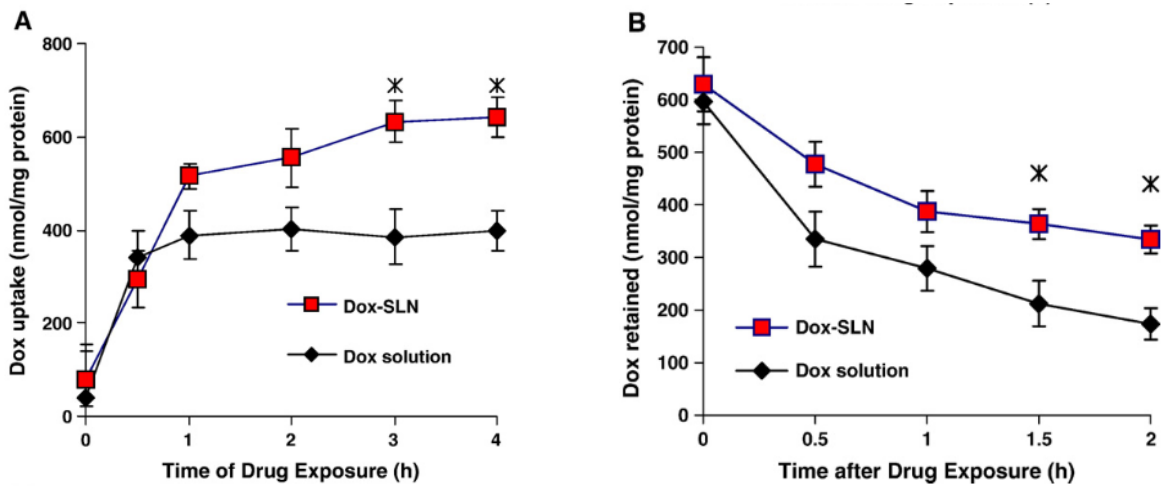


Figure 2:[1] Effect of polymer-lipid nanoparticles containing doxorubicin (Dox) on(A) cellular uptake and (B) cellular retention of Dox by a P-glycoprotein overexpressing murine cancer cell line EMT6/AR1.

Bhalekar et al.

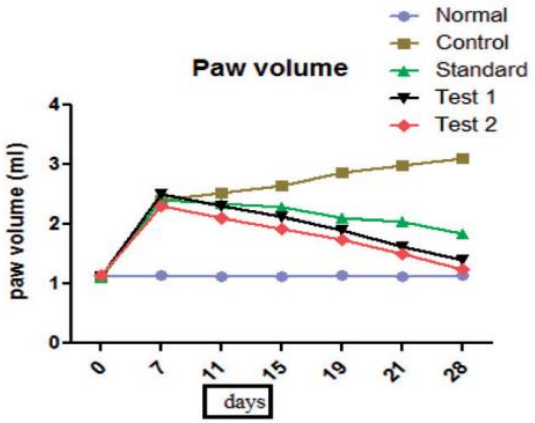


Figure 3:[2] Effect of piperine SLN on paw edema. Test 1: oral piperine SLN dispersion and Test 2: topical piperine SLN gel.

1. Bhalekar, M. R.; Madgulkar, A. R.; Desale, P. S.; Marium, G. Formulation of Piperine Solid Lipid Nanoparticles (SLN) for Treatment of Rheumatoid Arthritis. *Drug Development and Industrial Pharmacy* **2017**, *43* (6), 1003–1010.
2. Wong, H. L.; Bendayan, R.; Rauth, A. M.; Xue, H. Y.; Babakhanian, K.; Wu, X. Y. A Mechanistic Study of Enhanced Doxorubicin Uptake and Retention in Multidrug Resistant Breast Cancer Cells Using a Polymer-Lipid Hybrid Nanoparticle System. *Journal of Pharmacology and Experimental Therapeutics* **2006**, *317* (3), 1372–1381.

Key Objectives:

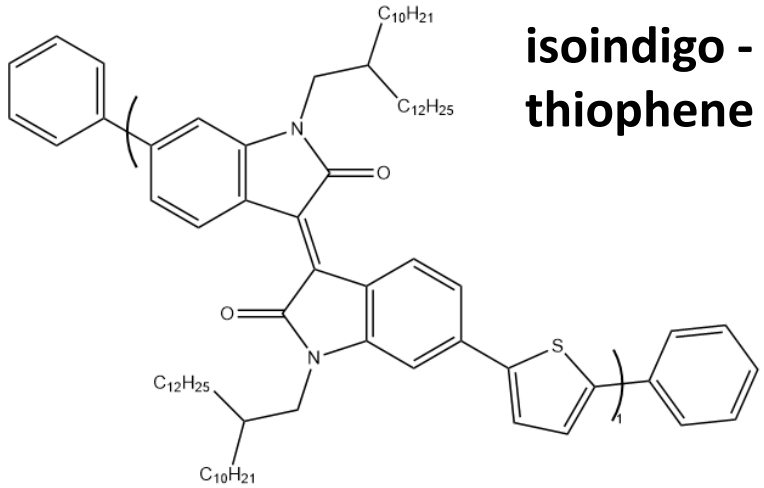
Our primary goals are:

1. To successfully synthesize and characterize a lipid-based CPN system

2. To investigate the potential effects of lipid structure on the properties of the resultant CPNs

3. To evaluate the effectiveness of the lipid-based CPN system as a nanocarrier in drug delivery systems

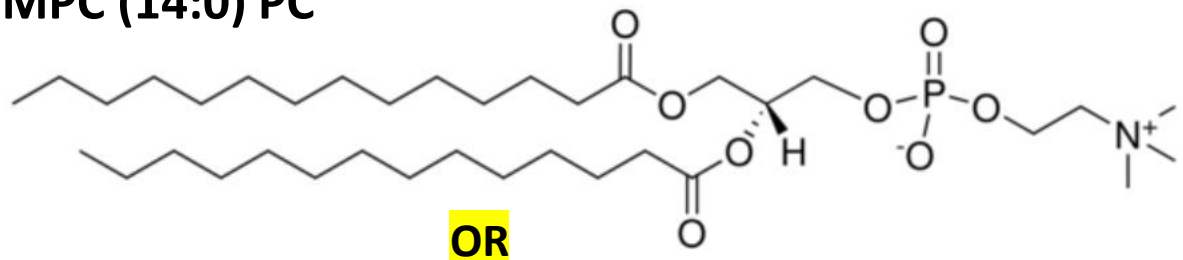
Synthesis of Lipid-coated CPNs



isoindigo - thiophene

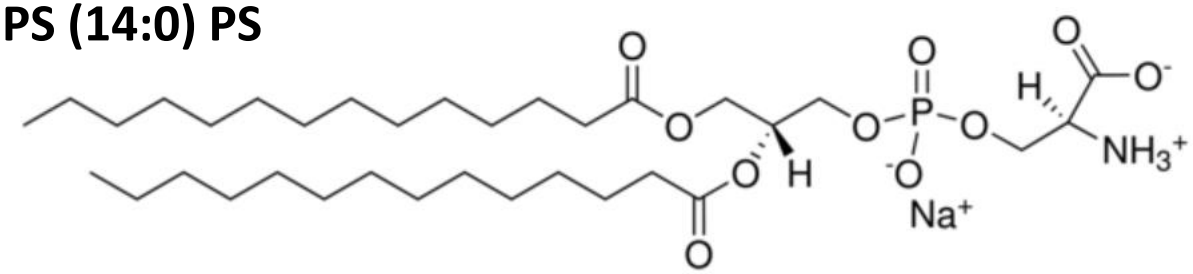
+

DMPC (14:0) PC



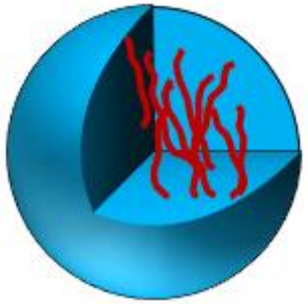
OR

DMPS (14:0) PS



Nanoprecipitation

THF, H_2O



- Nanoprecipitation method was used
- Synthesis was repeated using the 16-C chain form of the two lipids: DPPC (16:0) and DPPS (16:0)

Dynamic Light Scattering (DLS) Data: Size and Aggregation of CPNs

Lipid	Polymer	Temp. of Nanoprecipitated (°C)	Temp. of DLS (°C)	Z-Average (nm)	PDI
DMPC (14:0) Zwitterionic	**Isoindigo-T-C10C12**	**0** °C	25 C	117.40	0.087
			37 C	118.63	0.088
DPPC (16:0) Zwitterionic	**Isoindigo-T-C10C12**	**0** °C	25 C	178.22	0.196
			37 C	186.40	0.187
DMPS (14:0) Charged	**Isoindigo-T-C10C12**	**0** °C	25 C	92.96	0.115
			37 C	93.38	0.127
DPPS (16:0) Charged	**Isoindigo-T-C10C12**	**0** °C	25 C	80.36	0.138
			37 C	80.94	0.139

Figure 4: DLS data for lipid CPNs at room temperature (25°C) and physiological temperature (37°C).

- All within 80-190 nm range
- Stable under physiological temperature

Transmission Electron Microscopy (TEM) Data: Morphology of CPNs

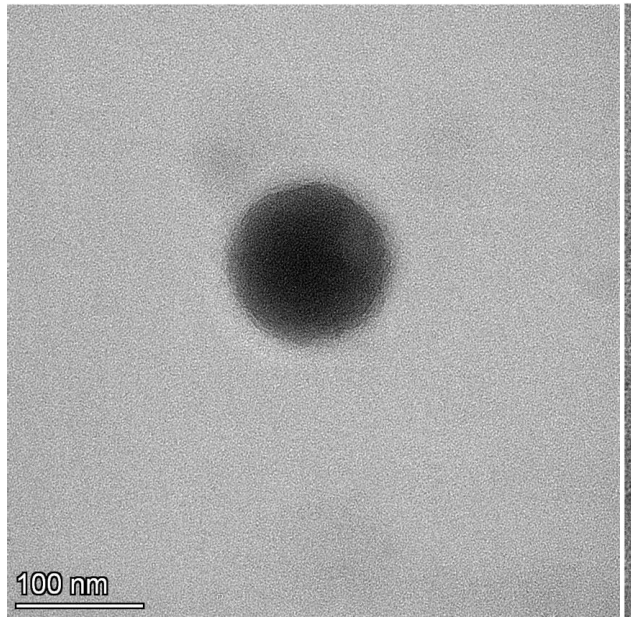


Figure 5: TEM image of DMPC (14:0) CPNs.

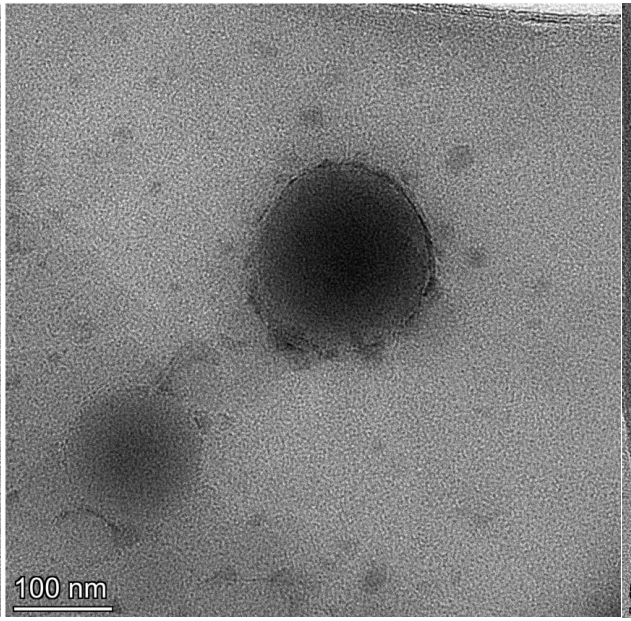


Figure 6: TEM image of DMPS (14:0) CPNs.

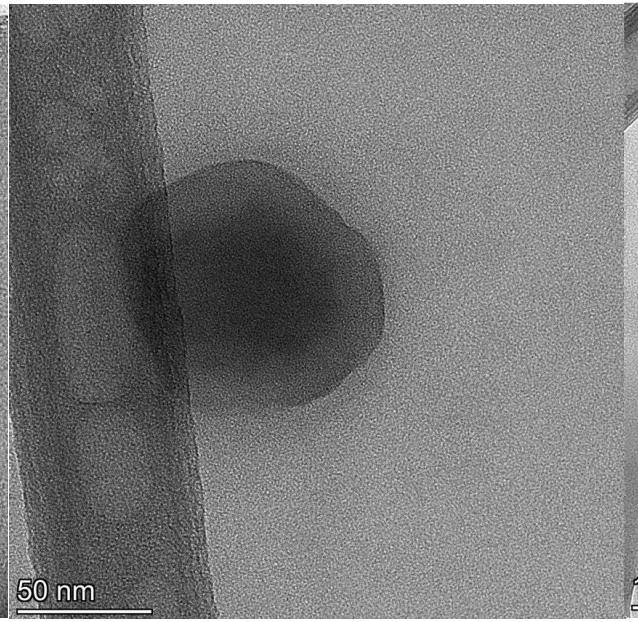


Figure 7: TEM image of DPPC (16:0) CPNs.

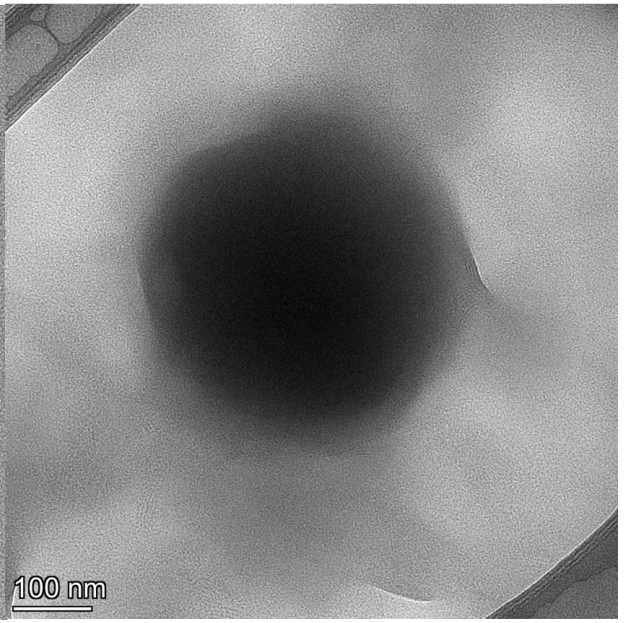


Figure 8: TEM image of DPPS (16:0) CPNs.

UV-Vis Spectra: Absorbance of CPNs

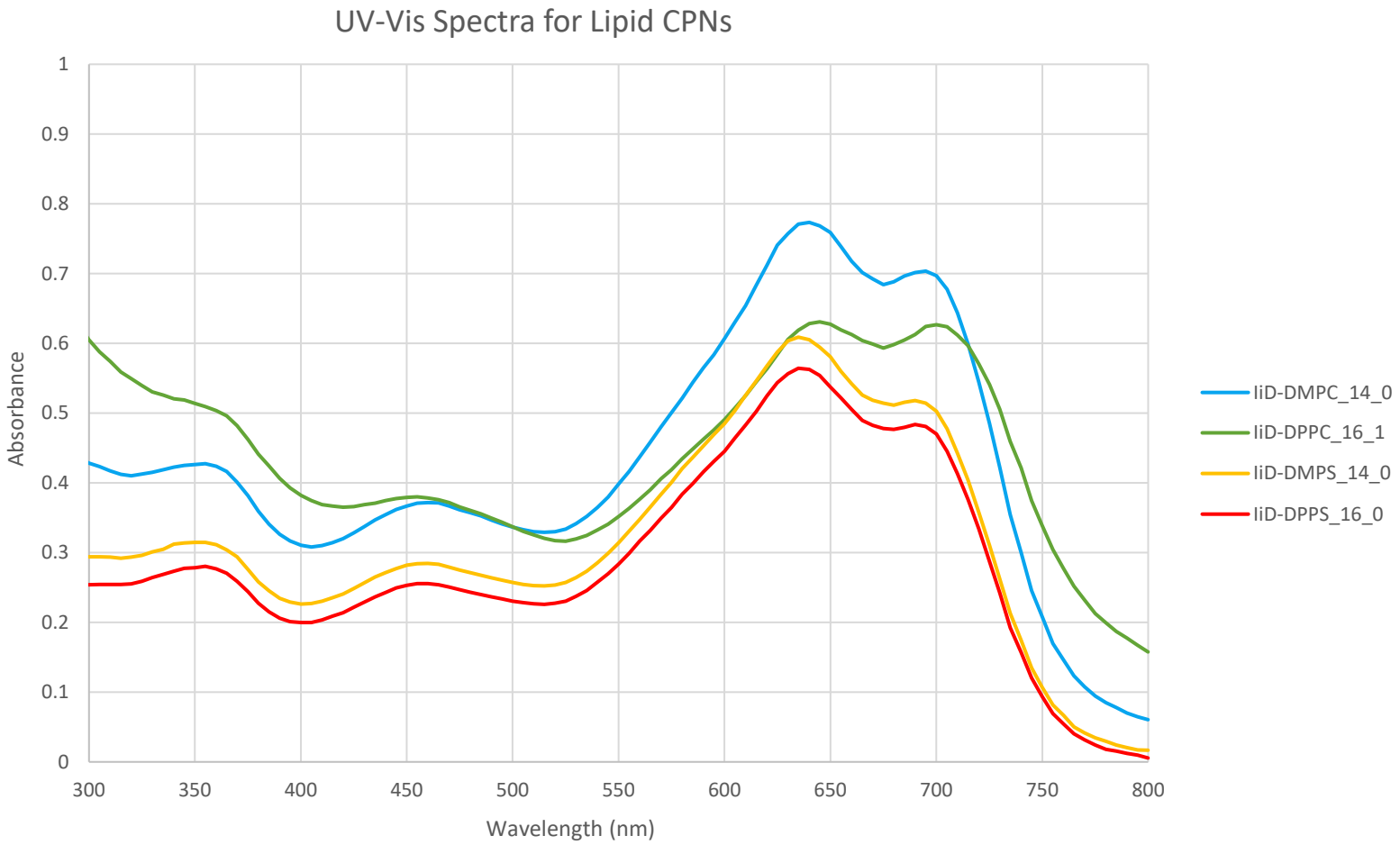


Figure 9: UV-Vis Absorption Spectra of lipid CPNs.

Fluorescence Data: Fluorescence Emission of CPNs

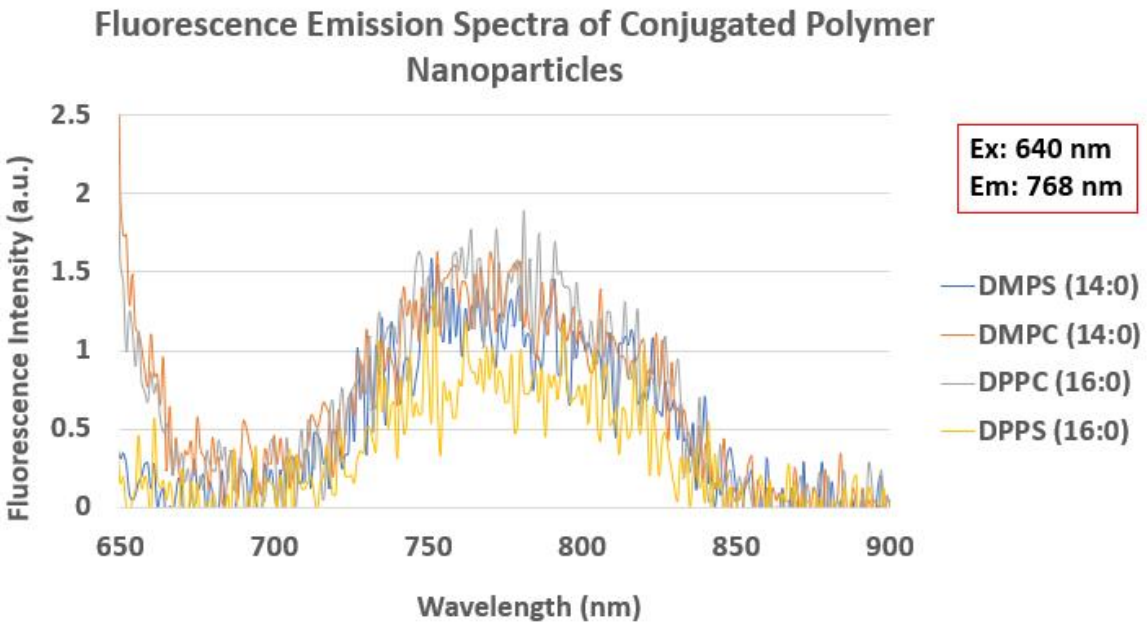


Figure 10: Fluorescence Spectra of lipid CPNs at excitation wavelength of 640 nm.

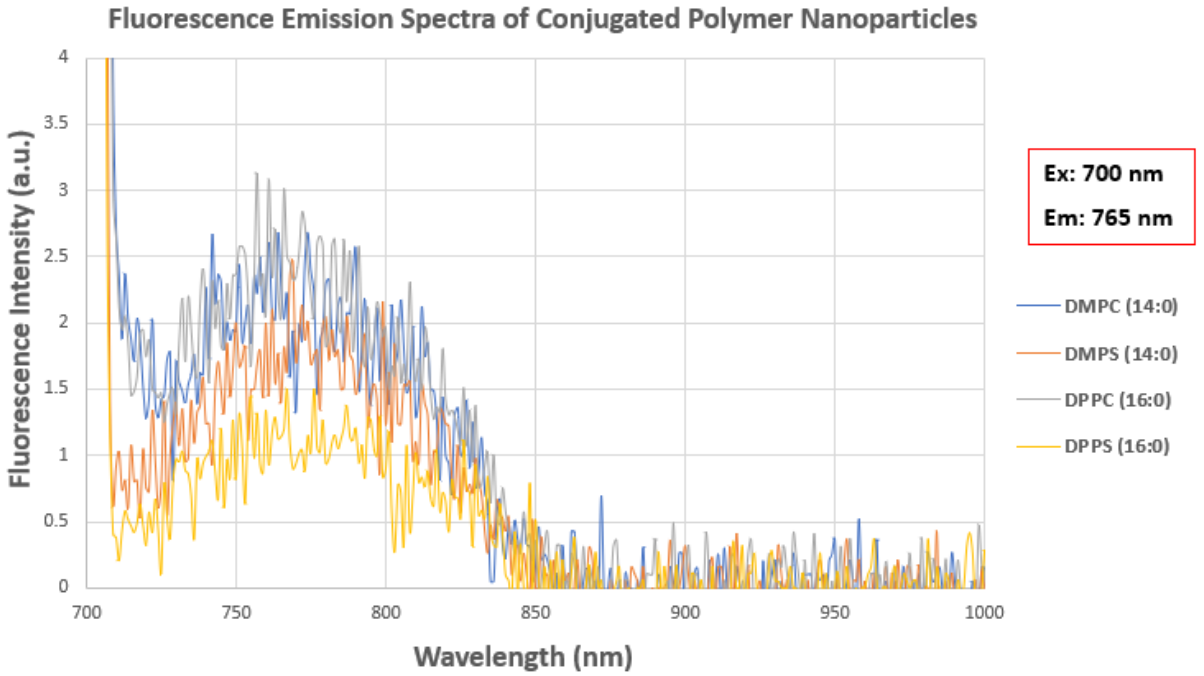
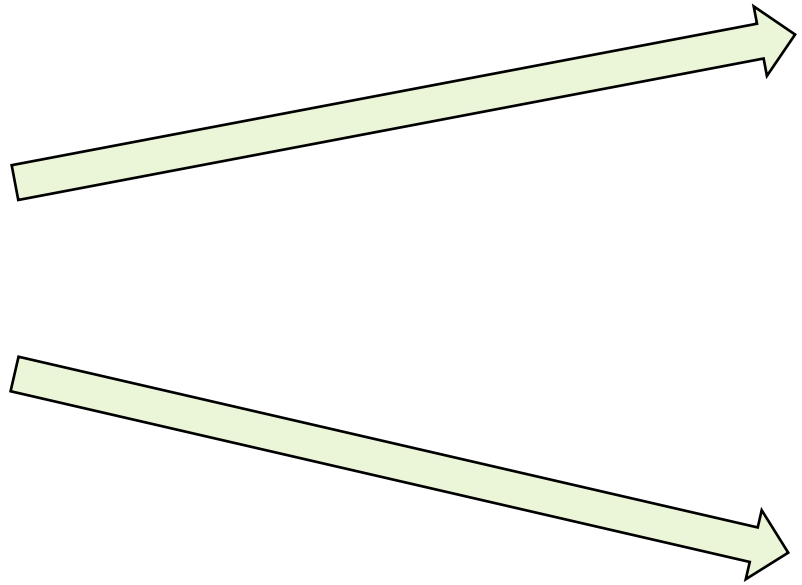


Figure 11: Fluorescence Spectra of lipid CPNs at excitation wavelength of 700 nm.

Future Work

Goals:



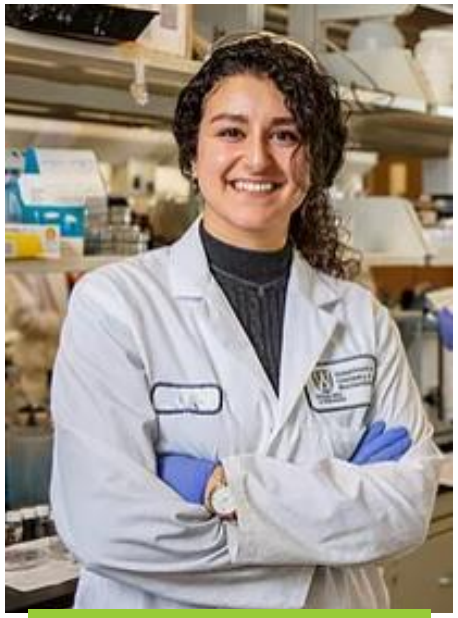
Testing other lipids:

- ❑ Test other lipids (selected based on literature) as surfactants in the CPN system
- ❑ Compare the permeabilities of the lipids in physiological conditions

Optimize CPN system for drug delivery:

- ❑ Conjugate selected drugs onto the CPNs and evaluate effectiveness as nanocarrier for drug delivery
- ❑ Identify biological targets of these lipids

Acknowledgments



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