# Heterogeneous, multi-layered conjugated polymer nanoparticles for theranostic applications

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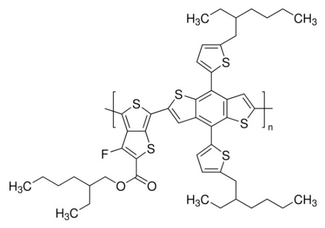
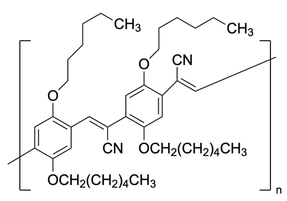
## CONJUGATED POLYMER NANOPARTICLES (CPNs)

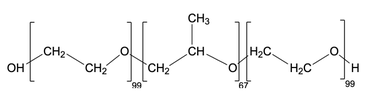
Nanomaterials have seen a wide range of applications including **drug delivery** and **biosensing**[4]. Organic semiconductors in the form of conjugated polymers in particular show remarkable **fluorescent** and **oxygen excitation** capabilities, allowing for **theranostic** (therapeutic and diagnostic) applications.



PTB7-Th



CN-PPV

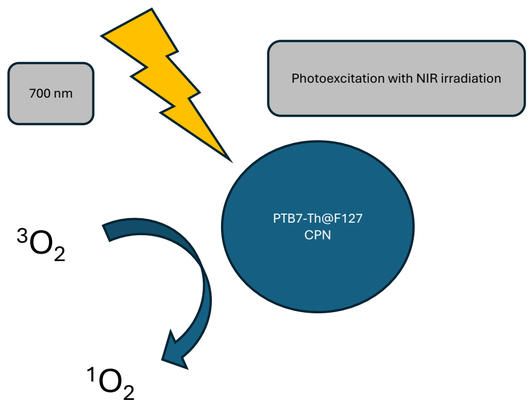


Pluronic F127

Conjugated polymers have characteristic **pi-bond conjugation**, resulting in high optical response in a tunable region, dependent on polymer length. This can be taken advantage of for fluorescent imaging in the **NIR-I and NIR-II** windows, allowing for **diagnostic** capabilities[1,4].

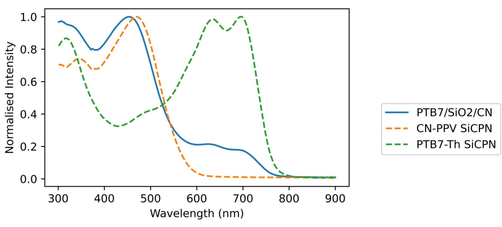
Conjugated polymers are **hydrophobic**; **Pluronic F127** block co-polymer is added to stabilize CPNs in aqueous solution[1].

**Excited** CPNs have a chance to cross from excited **singlet** ($S_1$) to **triplet** ($T_1$) state, allowing them to excite native dioxygen from triplet ground to **singlet excited state**[1,4].



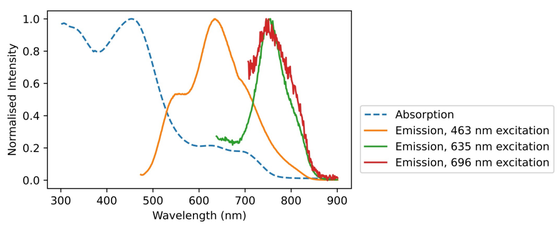

**Singlet oxygen** is highly reactive, causing **oxidative stress** to cells in the vicinity of the particle. It also **deactivates** certain enzymes found on tumour cells, allowing for effective anti-cancer **therapeutic** capabilities[1,3,4].

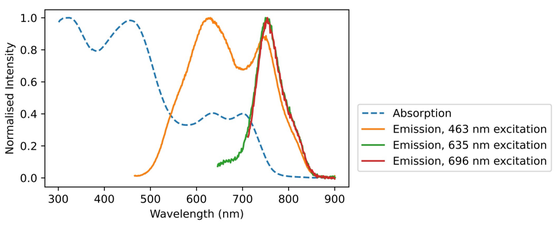
## ABSORPTION AND EMISSION SPECTRA OF HETEROGENEOUS CPNS




Absorption spectra comparison, **heterogeneous** particles vs **single-polymer** particles. PTB7-Th in the core, silica shell, and CN-PPV on top, is denominated as PTB7/$SiO_2$/CN. Spectrum seems to be a linear combination of the two separate polymer absorption spectra.

Absorption/emission spectra, **heterogeneous particles.**

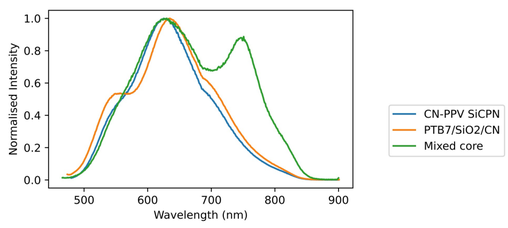


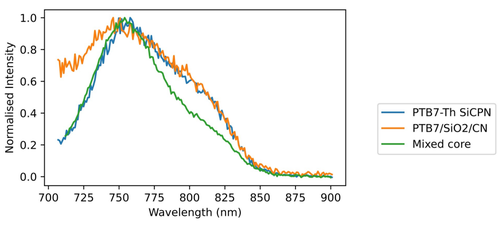




Absorption/emission spectra, **mixed core particles.** PTB7-Th and CN-PPV were mixed in equal parts by weight and synthesis carried out as normal.

## Comparing single-polymer silica-shelled particles to heterogeneous and mixed core particles

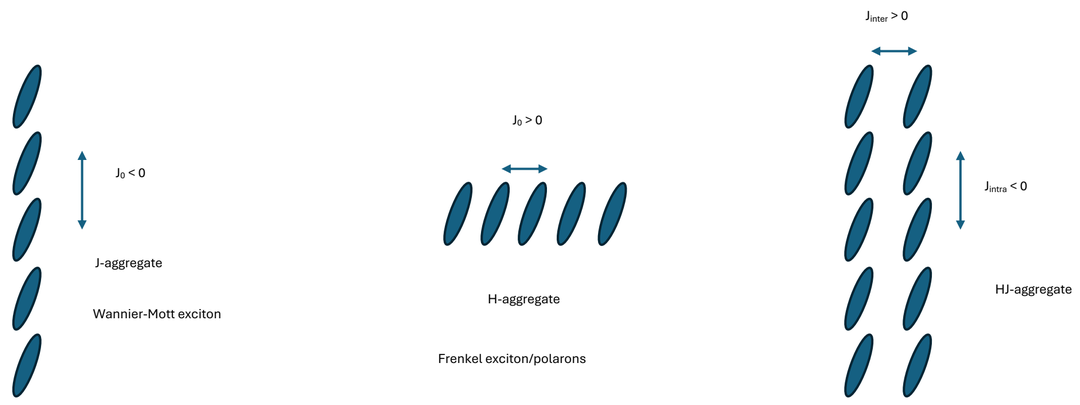
Emission, **463 nm** excitation. Obvious energy funneling **in mixed core particles**. While unknown if a precise core-shell-shell structure has been achieved for the **heterogeneous** SiCPN, the lack of energy funneling between the two polymers suggests they are **separated**.




Emission, **696 nm** excitation, no significant difference between samples. In this case, the polymer excited is PTB7-Th, which is of lower energy and thus is **not** expected to funnel any to the higher-excitation CN-PPV.

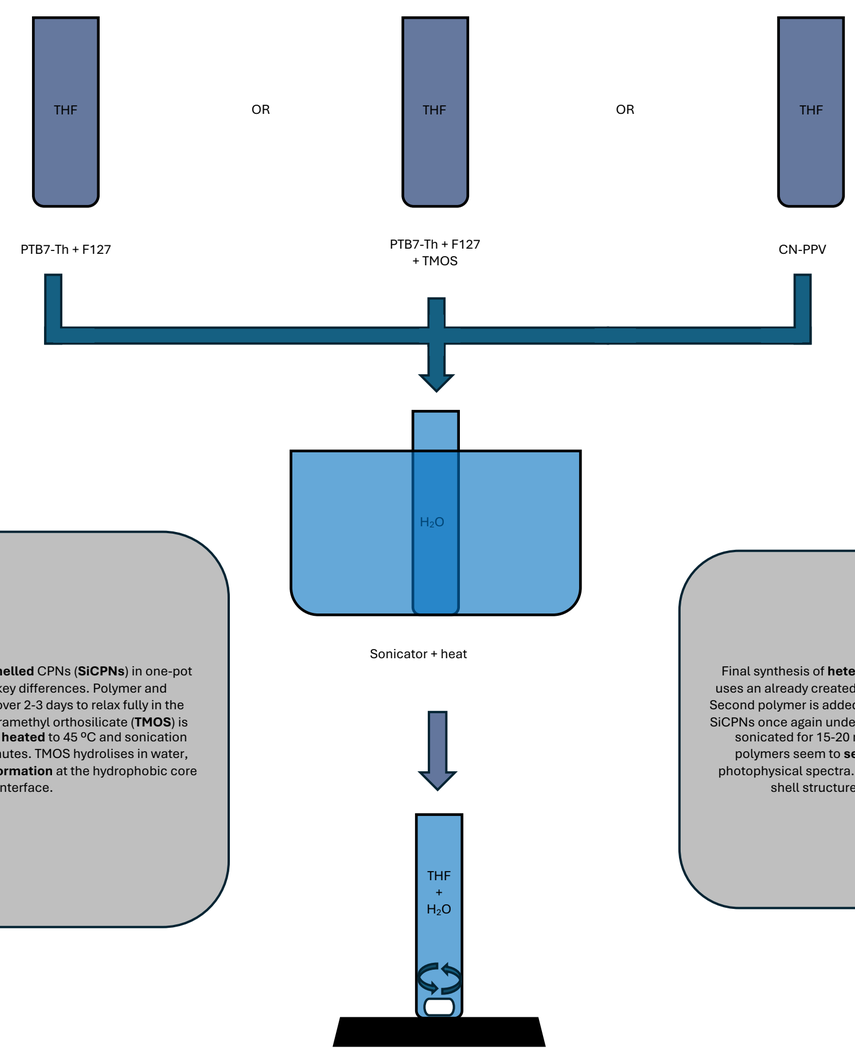
## POLYMER AGGREGATION MODES




Different aggregation states cause spectral shifts; H-aggregation is characterized by a blue shift in absorption, and vice versa for J-aggregates. Polymers aggregate in cores in a combination of these modes, called HJ-aggregation[2]. Aggregation between separate polymer chains result in larger changes in the spectral signatures than self-coiling and self-aggregation[2].

## SYNTHESIS OF CPNs

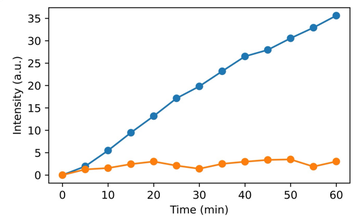
**CPN** synthesis via nanoprecipitation. Polymer and copolymer are dissolved in tetrahydrofuran (THF) and added to water under sonication. Ultrasonication provides agitation necessary for particle formation and is continued for 5-10 minutes. The mixture is then left to stir over a few days to evaporate the toxic THF.



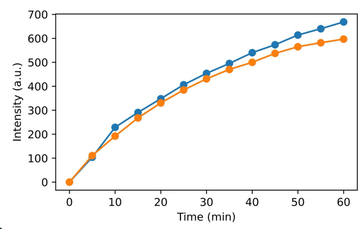

The creation of **$SiO_2$ – shelled** CPNs (**SiCPNs**) in one-pot reaction has some key differences. Polymer and copolymer are stirred over 2-3 days to relax fully in the solvent, after which tetramethyl orthosilicate (**TMOS**) is added. All mixtures are **heated** to 45 ºC and sonication continues for 15-20 minutes. TMOS hydrolises in water, resulting in **silica shell formation** at the hydrophobic core interface.

Final synthesis of **heterogeneous** CPNs, which uses an already created sample batch of SiCPNs. Second polymer is added to an aqueous solution of SiCPNs once again under 45 ºC heating. Solution is sonicated for 15-20 minutes as before. The polymers seem to **separate**, as seen in the photophysical spectra. Whether this is in a core-shell structure is unknown yet.

## CONCLUSIONS AND FUTURE WORK




Singlet oxygen production over one hour




This work has shown that the photophysical **separation** of conjugated polymers in complex, **heterogeneous** nanoparticles is possible, as evidenced by the differences in the emission spectra. While all CPNs thus far have been effective at exciting oxygen, the combination of a **purely NIR-II fluorescent** polymer and an **oxygen exciting** polymer would result in an efficient **theranostic agent**.

Addition of a silica shell seems to **quench** singlet oxygen production in the case of CN-PPV but **does not** have the same effect in the case of PTB7-Th CPNs. Further investigation needs to be conducted on the effects silica shells and layering polymers have on reactive oxygen species production.

## REFERENCES

1. Zhao, M., *et al*, "Theranostic Near-Infrared-Active Conjugated Polymer Nanoparticles", ACS Nano **2021** 15 (5), 8790-8802
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3. Bauer, G., "The Antitumor Effect of Singlet Oxygen", Anticancer Research 36: 5649-5664 (2016)
4. Gao, D., *et al,* "Recent Advances in Conjugated Polymer Nanoparticles for NIR-II Imaging and Therapy", ACS Appl. Polym. Mater. **2020**, 2, 4241-4257