Progress Towards Selective End-to-End Coupling in Lecithin Templated Gold Nanorods

By Stephan Hoyer

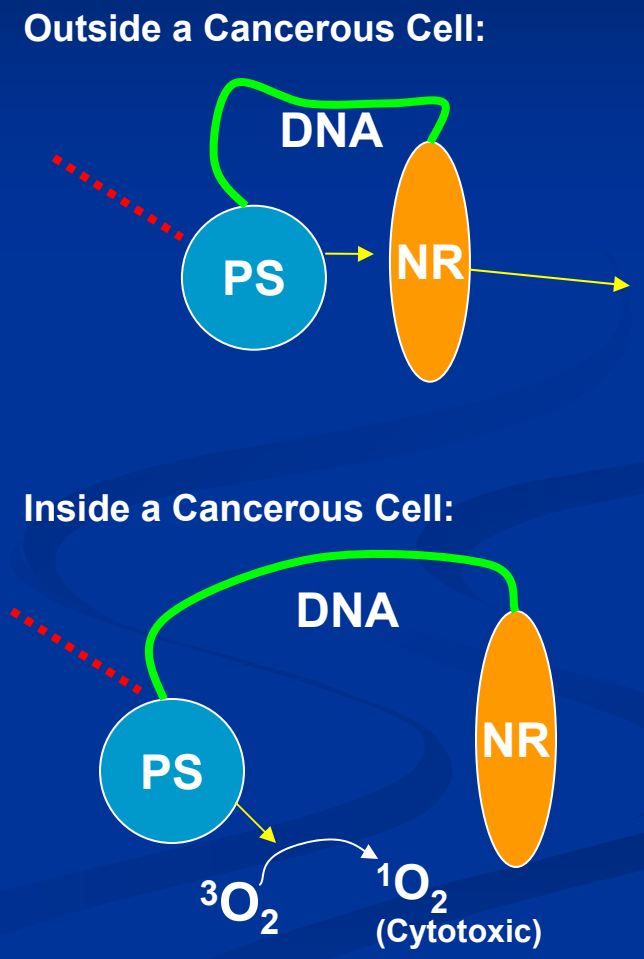
Basics of Photodynamic Therapy (PDT)

- Photosensitive drugs are injected into the body and accumulate preferentially in tumor cells.
- Drug is activated by exposure to laser light at the proper wavelength (around 700nm).
- Activated drug excites nearby normal triplet state oxygen to singlet oxygen.
- Singlet oxygen is highly reactive and kills cells.

Using Metal Nanorods in PDT

Proposed methodology:

- When metal is in close proximity to a photosensitizer (PS), instead of producing singlet oxygen, PS will transfer energy to metal.
- Energy released from the metal is harmless. Hence, nearby metal "turns off" a PS.
- DNA open/close mechanism only moves nanorod (NR) away from PS when in the cancerous cells where the drug needs to be active.



Lecithin Templated Gold Nanorods

- Lecithin is name for a naturally found substance that contains a group of biocompatible phospholipids.
- It serves as a ligand with the gold and may form rod or sphere shaped micelles to template nanoparticles.
- Lecithin provides a biocompatible alternative for templating gold nanorods to the more extensively tested cetyl trimethyl ammonium bromide (CTAB).[1]

[1] "Seeded High Yield Synthesis of Short Au Nanorods in Aqueous Solution." T. K. Sau and C. J. Murphy. *Langmuir*; **20**(15); 6414-6420, 2004.

Nanorod Synthesis

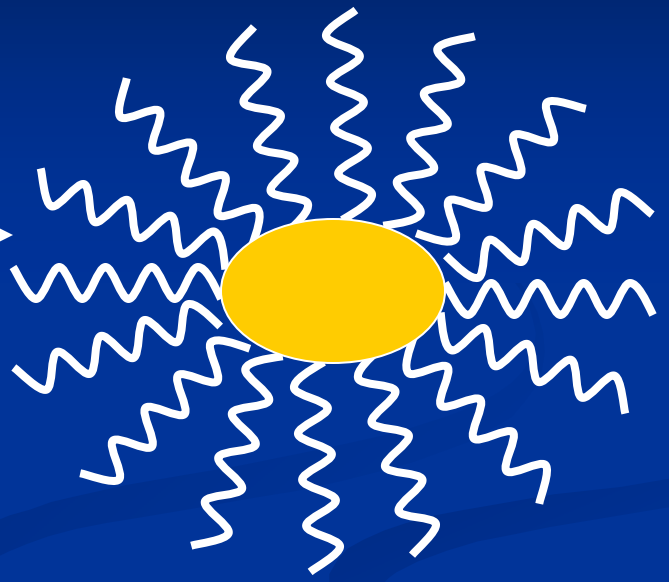
$HAuCl_4$

Lecithin

Mystery Reducing Agent

16 hours (overnight)

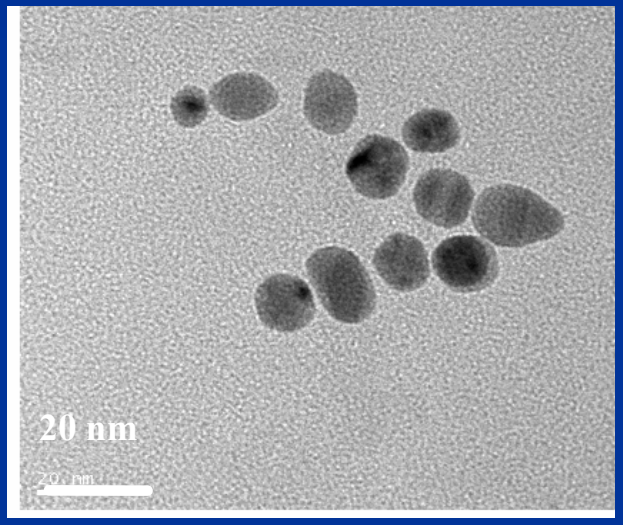
Aqueous



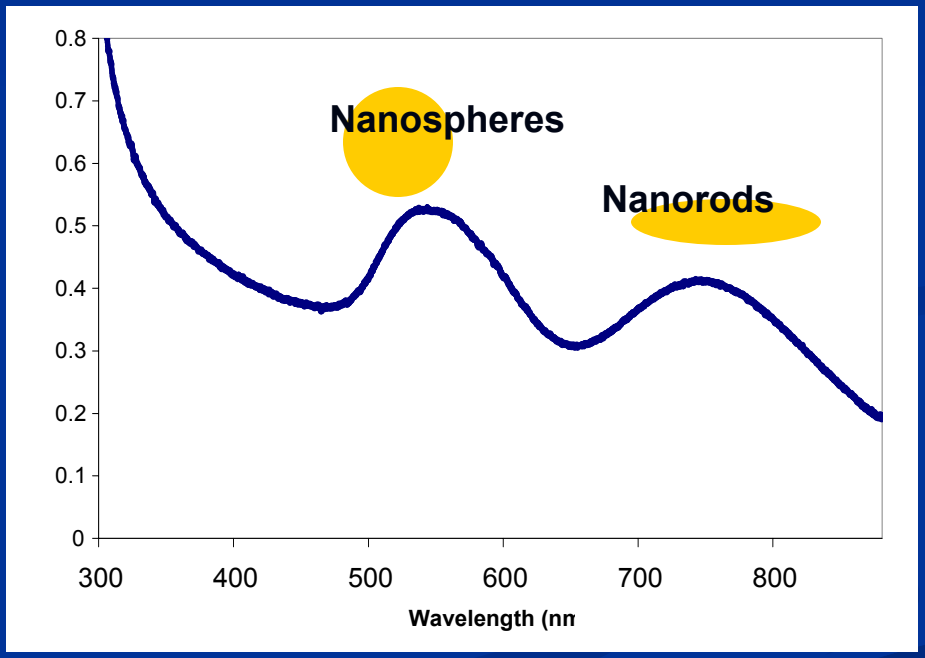
- Some unknown component of lecithin reduces the gold very slowly to enable nanorod formation.
- Lecithin and $HAuCl_4$ were generally in aqueous solution, although a co-solvent could be added to change nanorod properties.

Nanorod Analysis

TEM



UV/Vis Spectrophotometer



UV/Vis by Bahareh Habibi. TEM by Bahareh Habibi and Chunfei Li.

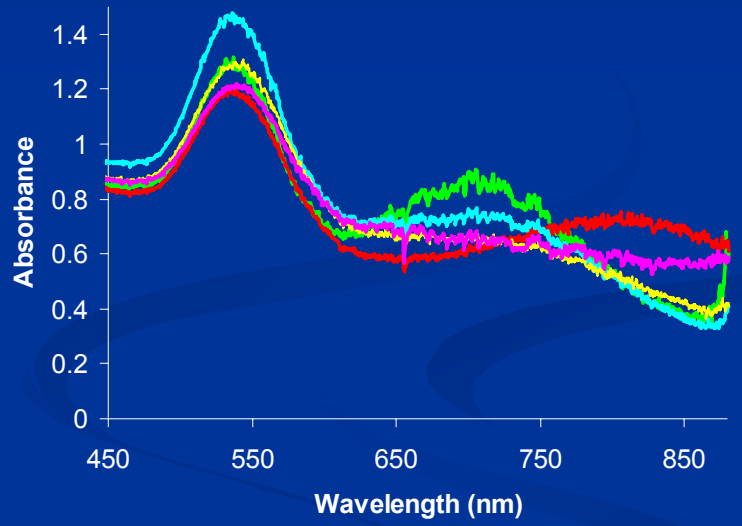
Tuning Gold-Lecithin Nanoparticles

- Only a tight range of concentrations produces nanorods instead of nanospheres.
- Nanorods are desirable because a plasmon resonance at about 700nm works well for applications that use red light such as PDT. This range is significant because it is the wavelength at which light travels best through the body.
- High yield of rod shaped particles over spheres is ideal.

Reproducibility

- A central difficulty quickly appeared with reproducing production of particles under the same conditions.
- Results are only always consistent when made from the same batch of lecithin solution and kept in the same water bath for temperature control.
- Even within the same batches, there was random error in absorbance intensity up to ±10%.

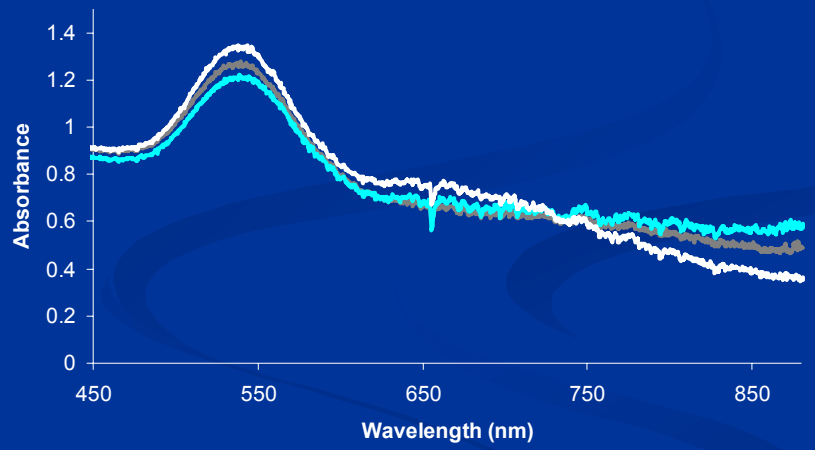
Same procedure (in theory):



Possible Error Solutions

- Lecithin does not appear especially homogeneous in the jar, but even experiments with darker and lighter lecithin sample were still relatively consistent.
- An attempt to change the position of the reaction in the phase diagram to a more stable point by forming nanorods at 35° with 1% n-heptane as a co-solvent also did not yield better consistency.

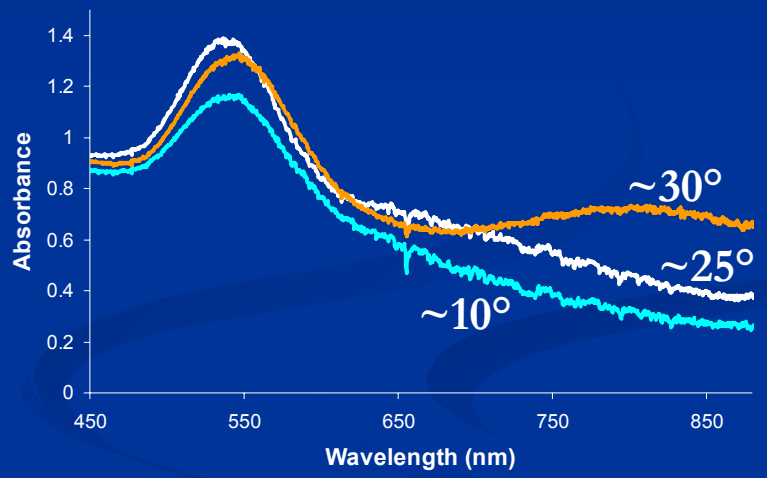
Light, dark and mixed samples of lecithin are too close together to make clear distinctions:



Variation in Temperature

- Anecdotal evidence suggests that nanorod production at higher temperatures (above 25°C) more consistently produces more rod shaped particles but variation is not particularly clear.
- When the nanorod solution was kept cool in the refrigerator, *exclusively* nanospheres were formed.

Results from one trial:



Dealing with Error

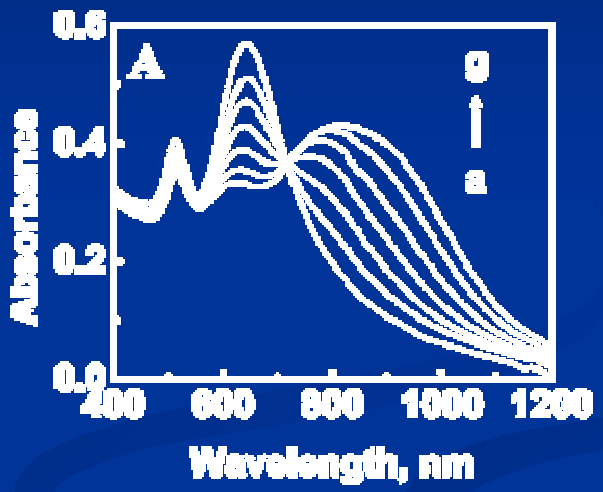
- Variation in co-solvents and temperature changed nanorod formation but did not solve reproducibility issues.
- Remaining sources of error:
  - Unstable temperatures in the water bath. Temperatures varied at times up to ±4°C from the target temperature.
  - Something we missed?
- Apparently CTAB templated nanorod production is really inconsistent, too.

Linking Gold Nanorods

- Selective end-to-end linking between gold nanorods will demonstrate the feasibility of connecting nanorods to the DNA that connects to the rest of the drug.
- Results with CTAB gold nanorods suggest added 11-mercaptoundecanoic acid will selectively attached to ends of nanorods and form chains through hydrogen bonding.

Attempts at adding MUA

- Successful longitudinal linking should result in a third, higher wavelength peak.
- MUA is not soluble in water, which added some complications.
- No change in UV/Vis spectrum was observed in any of my trials done with a wide range of concentrations.



What successful end-to-end linking should look like. Note that the starting nanorods were more pure than mine.

"Uniaxial Plasmon Coupling through Longitudinal Self-Assembly of Gold Nanorods." K. George Thomas, Said Barazzouk, Binil Itty Ipe, S. T. Shibu Joseph, and Prashant V. Kamat. *J. Phys. Chem. B,* **108** (35), 13066-13068, 2004.

Conclusions

- Lecithin templated gold nanorods were produced under procedures previously developed in this lab, but:
  - Low reproducibility
  - Low purity (rod over spherical shaped particles)
- Initial attempts at reproducing end-to-end linking following the paper by Kamat, et. Al. were unsuccessful, but there are other avenues for exploration, as well.

Further Work

- Towards developing reproducible nanorod production:
  - Identify mystery reducing agent.
  - Test nanorod formation at even higher temperatures.
- More attempts (and alternate procedures) for end-to-end linking of nanorods, preferably with purer starting materials.

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