

Bachelor Thesis 2016

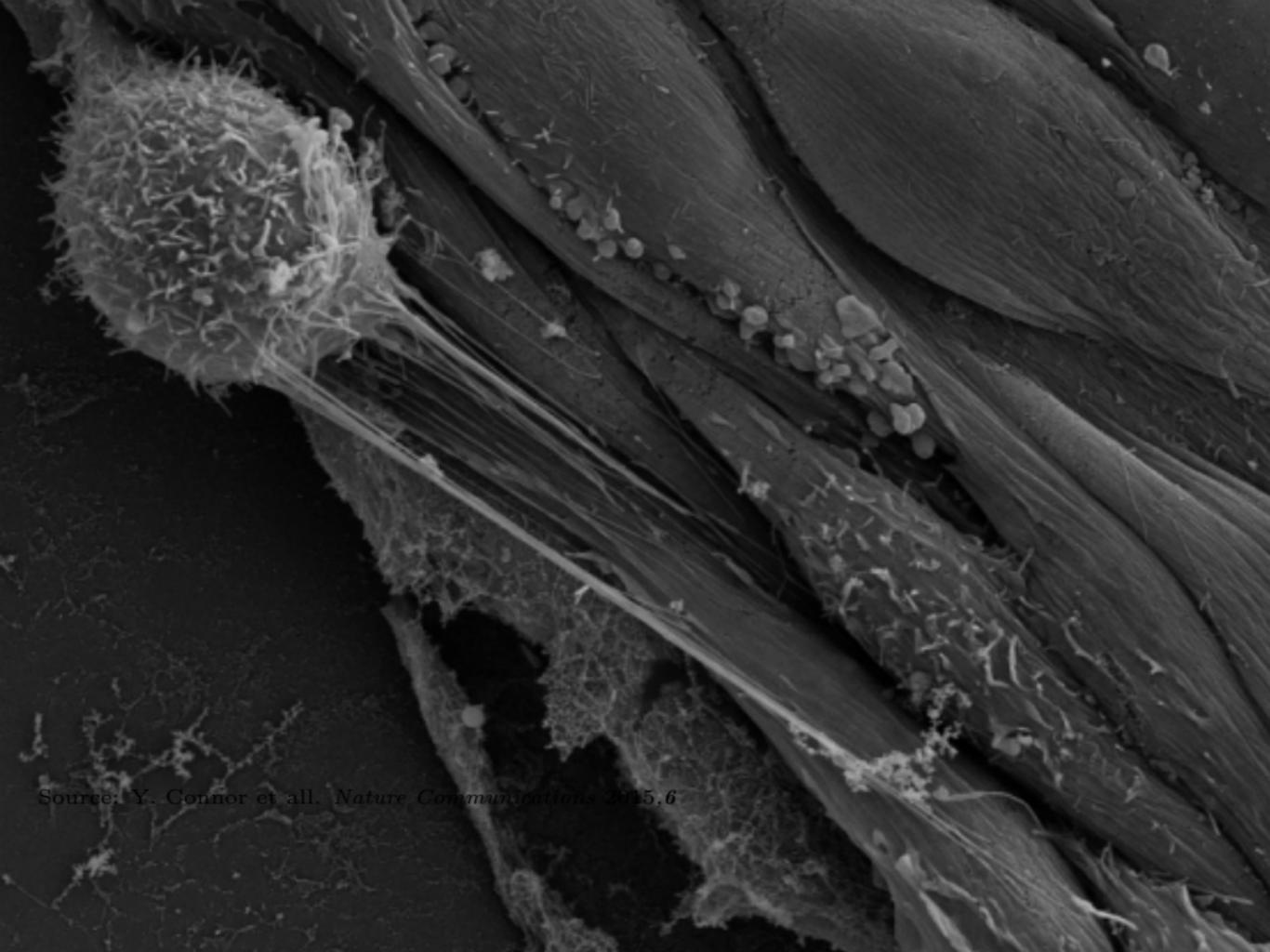
Radiosensitization using gold nanoparticles

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Assistents: Bert De Roo

Mattias Vervaele

Professor: Chris Van Haesendonck

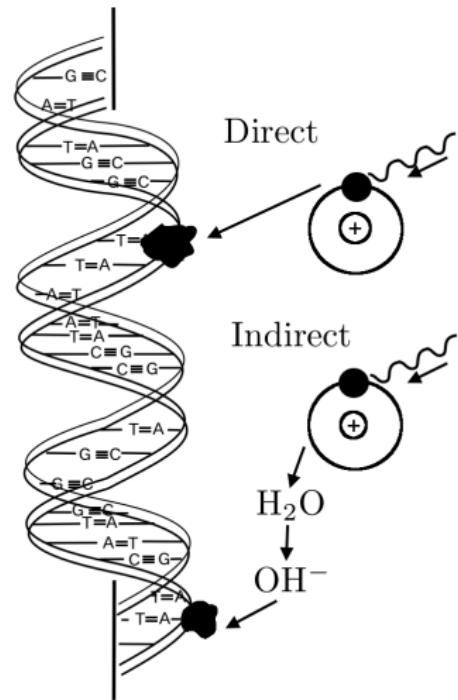


Source: Y. Connor et al., *Nature Communications* 2015, 6

DNA damage using ionizing radiation

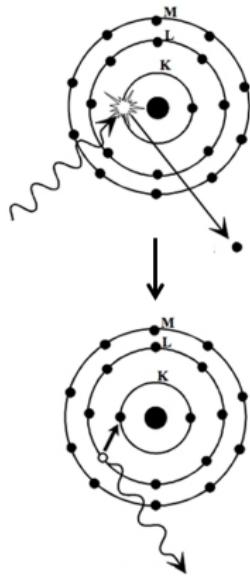
- Chemotherapy
- Surgery
- **Radiation therapy**

Energy \sim MeV

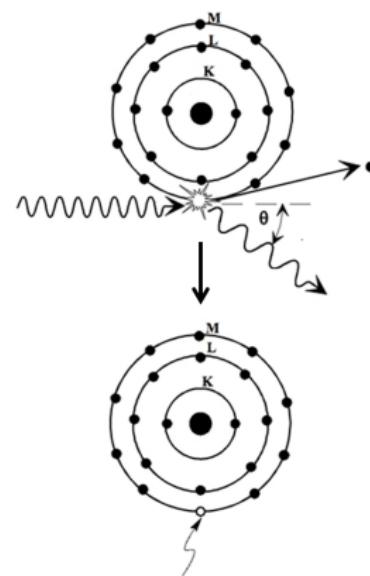


Radiosensitization of cancer cells with gold nanoparticles (GNP) $E \sim \text{keV}$

Photoelectric absorption

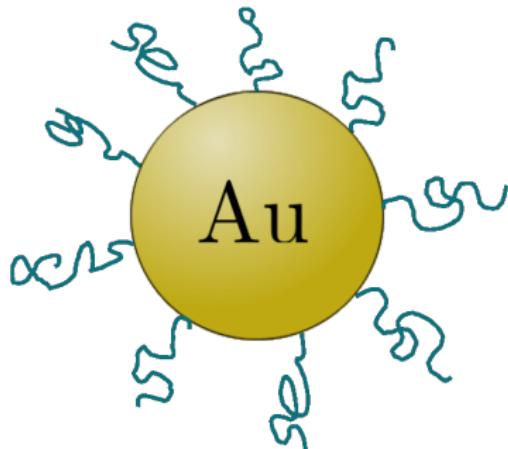


Compton effect

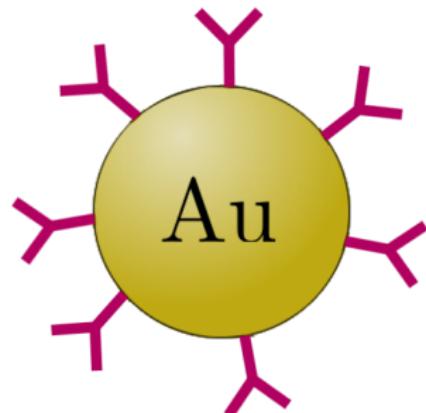


Targeting of the GNP to the tumor

Passive targeting
PEG coating



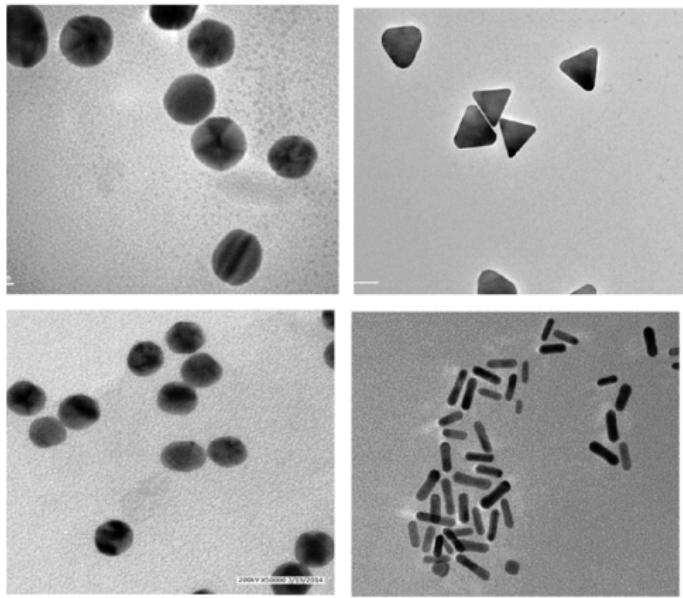
Active targeting
Antibodies



Overview Project

Radiosensitization of DNA using gold nanoparticles

1. Synthesis
2. Characterization
3. Radiosensitization



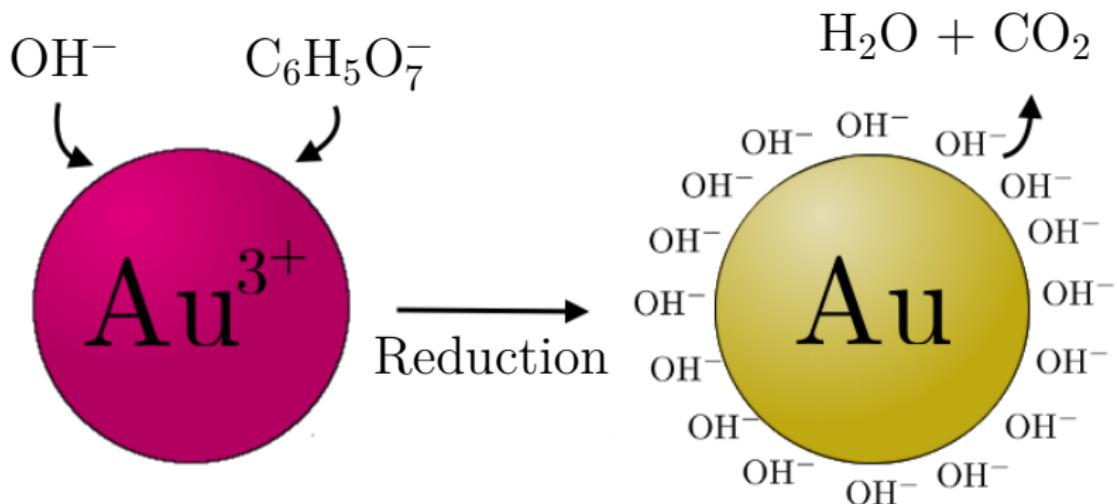
Reduction of gold ions to form GNP



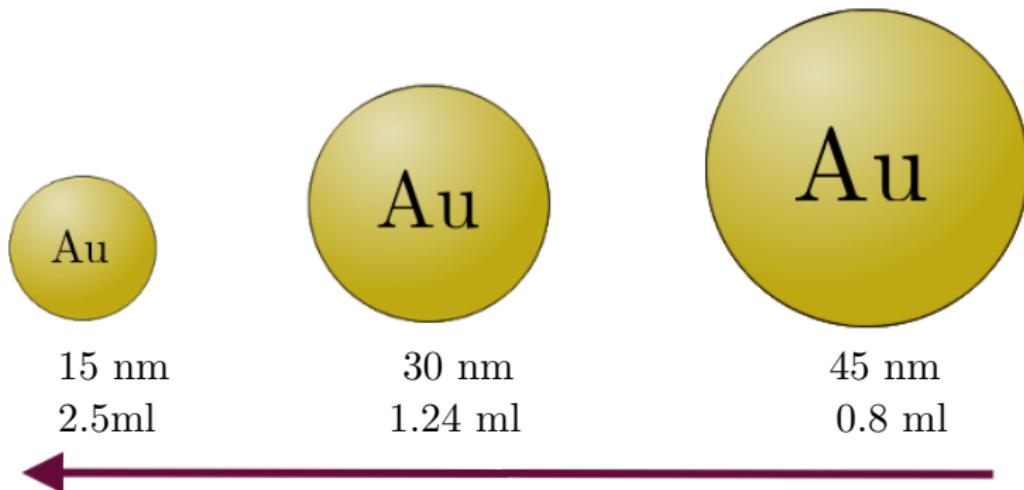
Gold ions: HAuCl₄ solution

Reducing agent: Na₃C₆H₅O₇

Reduction of gold ions to form GNP

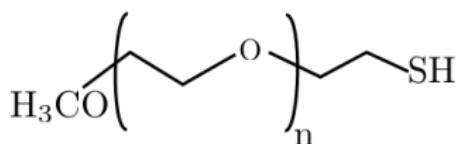
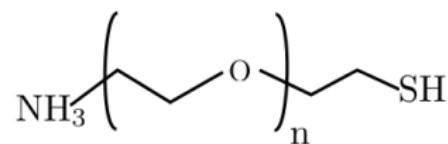
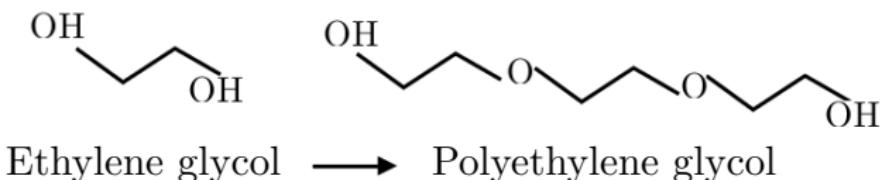


The amount of citrate controls the size

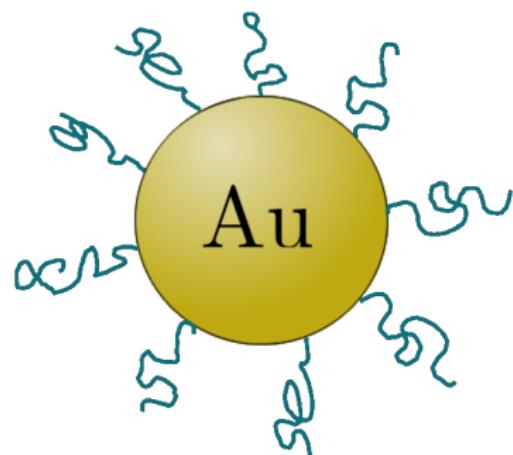


Citrate 1%
100ml HAuCl₄ 0.01%

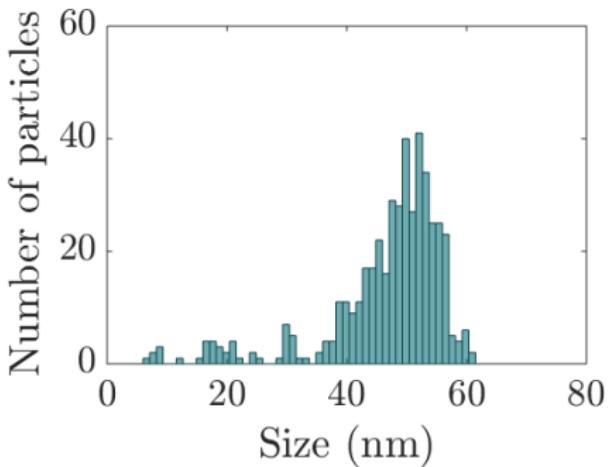
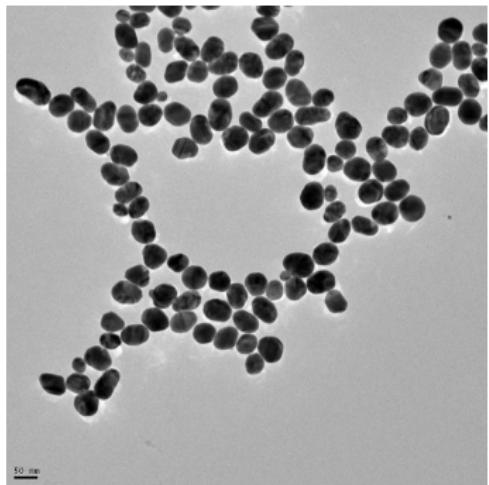
PEG for targeting and stabilization



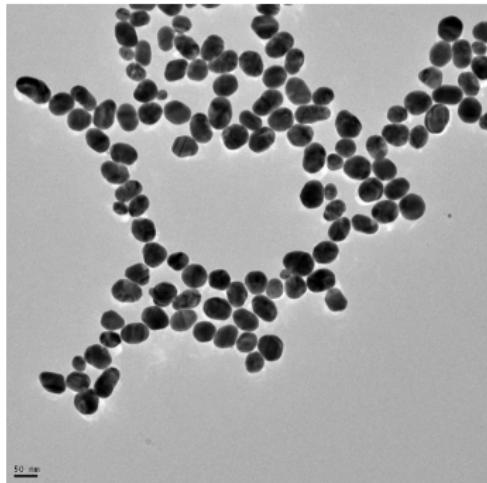
1k, 5k, 10k, 20k



TEM image analysis to determine the core diameter

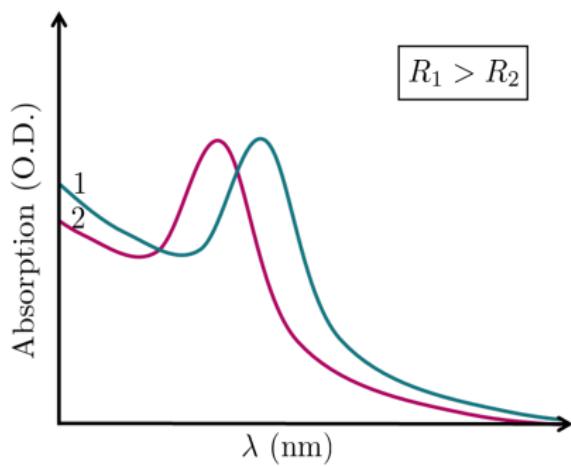
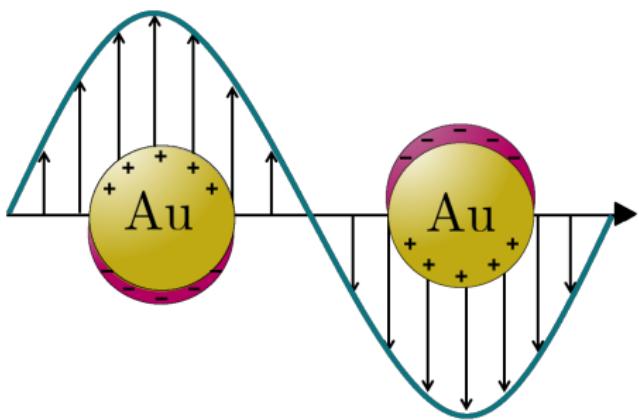


TEM image analysis to determine the core diameter

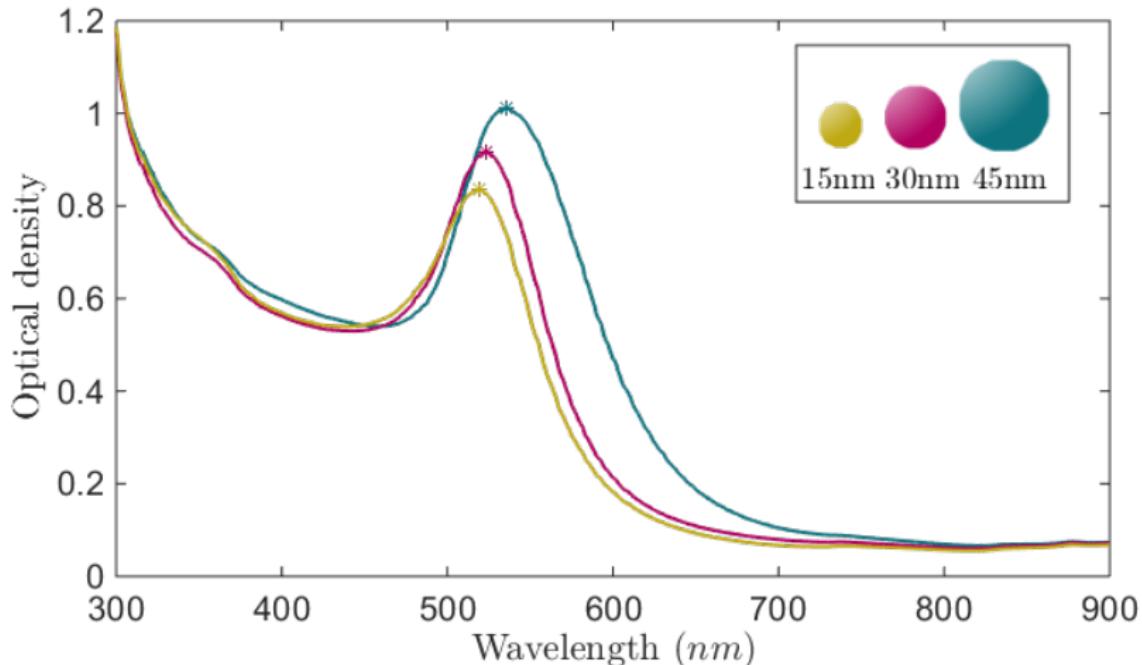


Exp. Size (nm)	Size (nm)
15	12.98 ± 0.23
	2.99 ± 0.16
30	18.29 ± 0.23
45	46.75 ± 0.47

Absorption measurements (UV-Vis) to determine the relative size

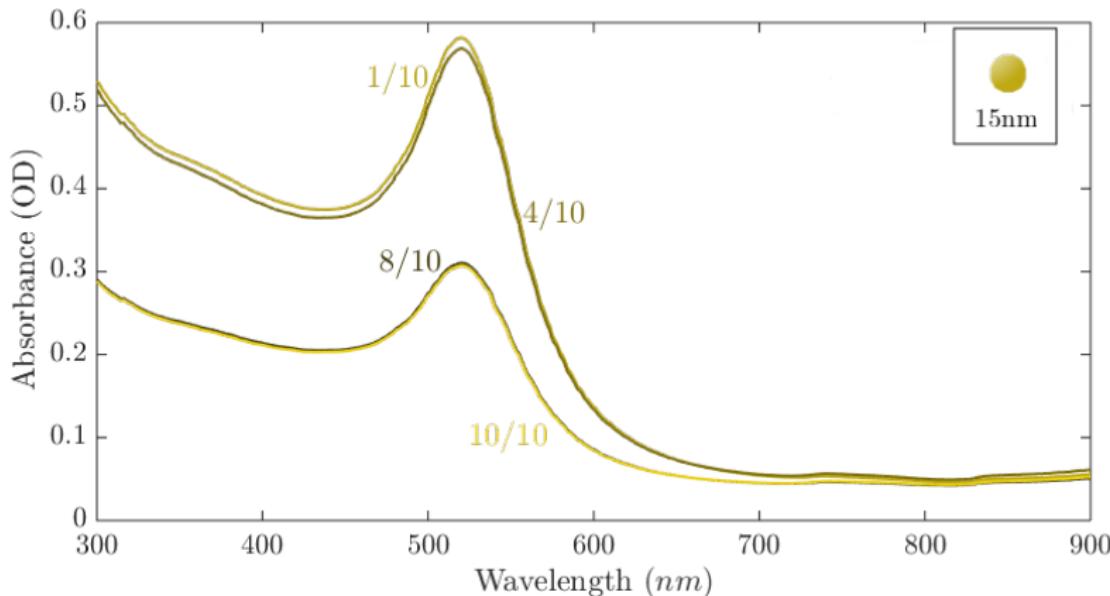


Absorption measurements (UV-Vis) to determine the relative size



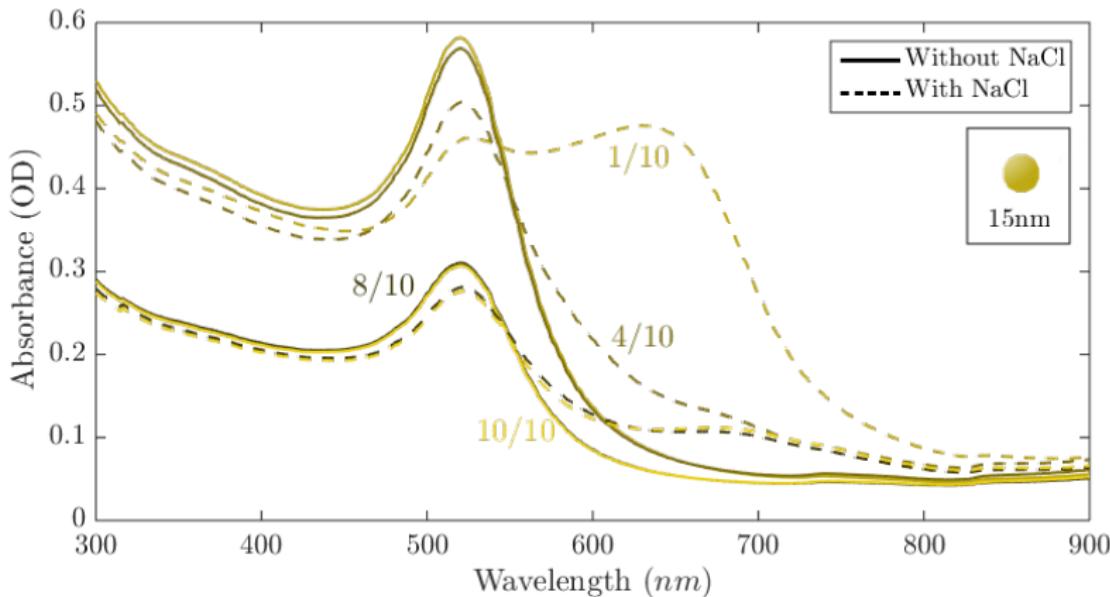
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

1. Add PEG and preform UV-Vis measurement
O.2cm



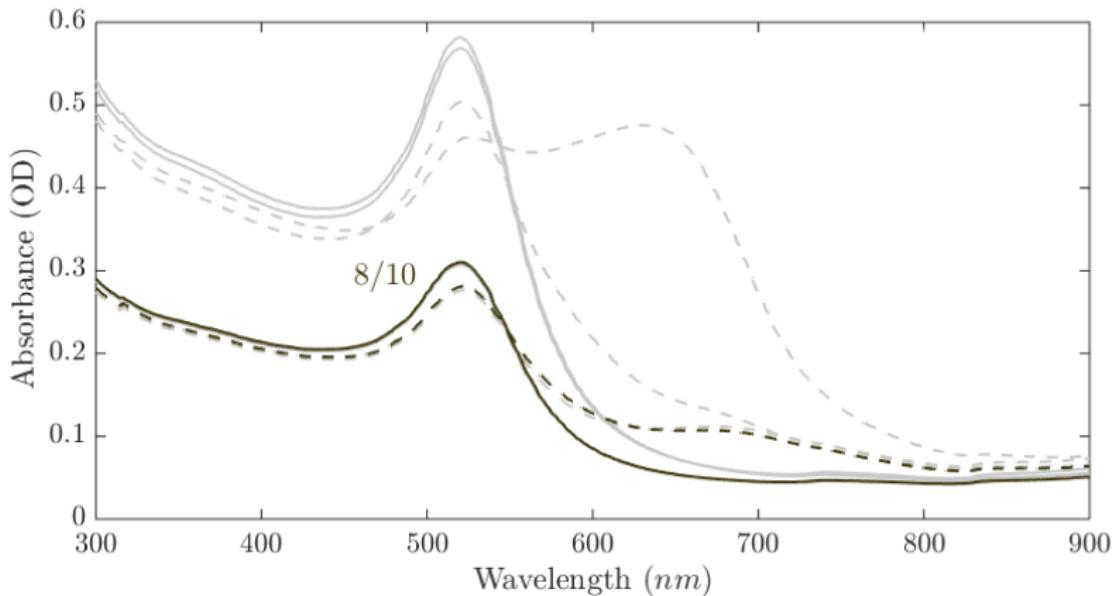
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

2. Add NaCl and preform UV-Vis measurement



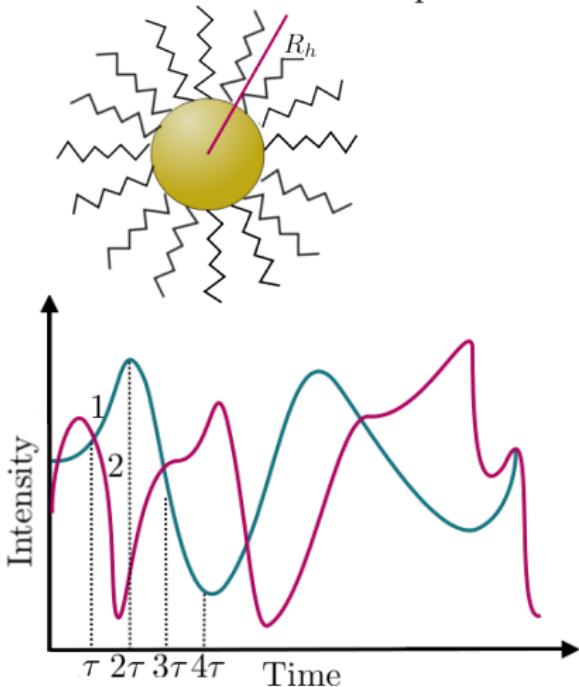
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

bigger size → too little PEG
same size → enough PEG



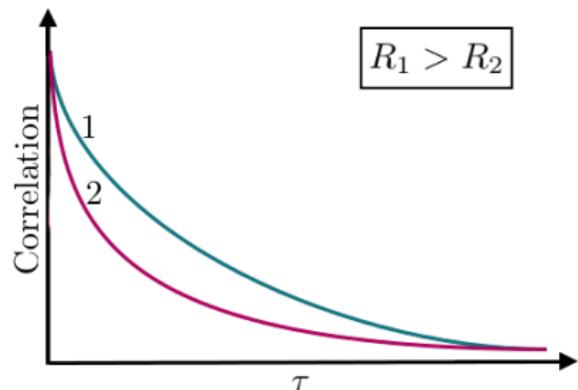
Light scattering experiments to determine the hydrodynamic radius (R_h)

Important for diffusive properties

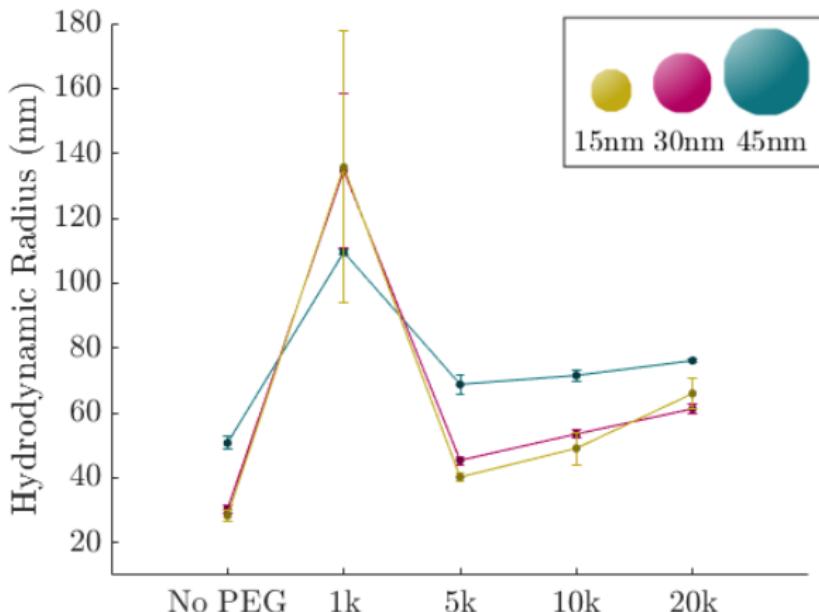


Correlation:

$$g(\tau) = \frac{\langle I(t) \rangle \langle I(t+\tau) \rangle}{\langle I(t) \rangle^2}$$



Hydrodynamic radii for the three different GNP with different functionalizations



Gel electrophoresis to analyse DNA damage

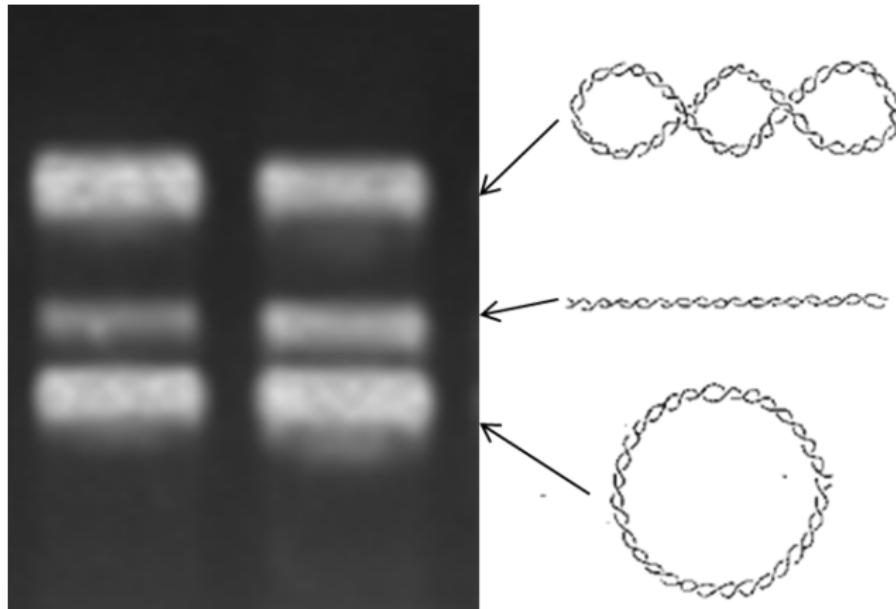


Single strand break

Double strand break

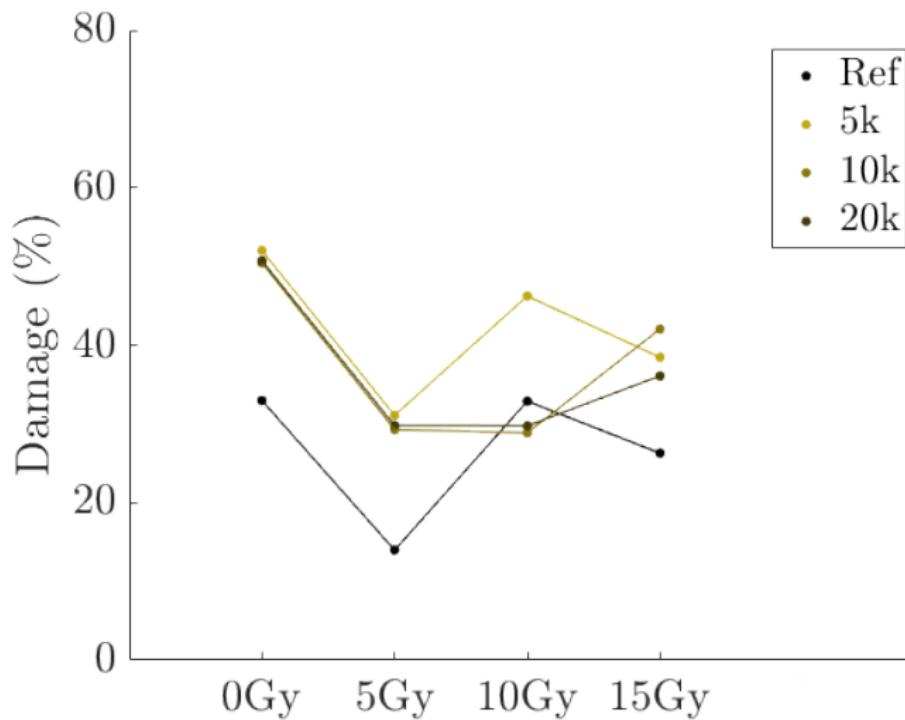
Source: <https://www.quora.com/Whats-the-difference-between-a-plasmid-and-a-virus>.

Gel electrophoresis to analyse DNA damage

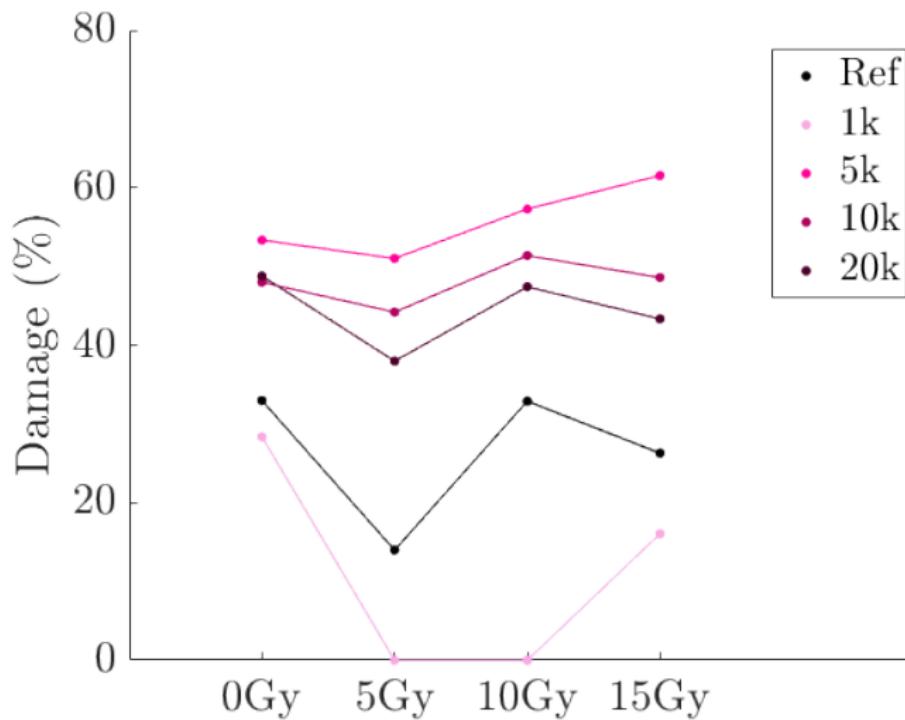


Source: Maunus R et al. Horton JR, Zhang X. Nucleic Acids Research, 34(3):939–948, 2006.

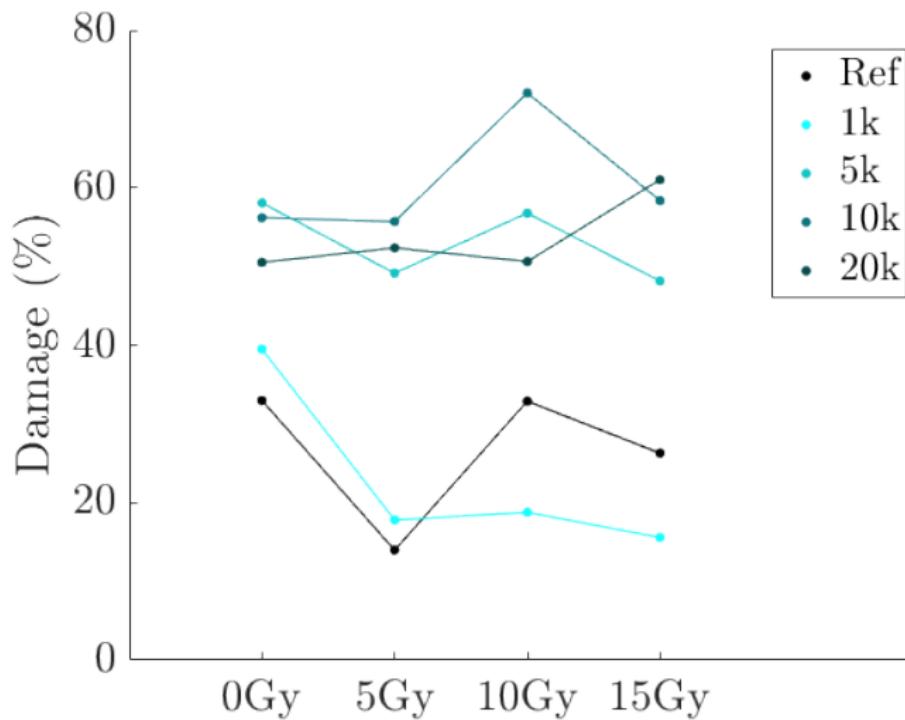
DNA damage analysis for 15nm GNP



DNA damage analysis for 30nm GNP

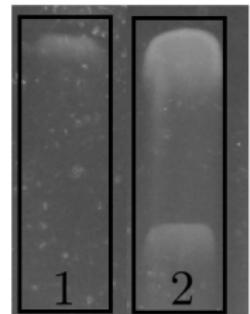


DNA damage analysis for 45nm GNP



Conclusion DNA damage analysis

- Strange results for 1 k PEG
- Curves are not rising (except 30 nm GNP)
- Reference sample has strange form
- DNA damage at 0 Gy
- Radiosensitization effect
- Smaller PEG → more DNA damage
- Larger GNP → more DNA damage



Conclusion

- Functionalization 1k strange behavior
- Best results with...
 - ...5k functionalization
 - ...largest particles (45 nm)

⇒ Radiosensitization effect observed

