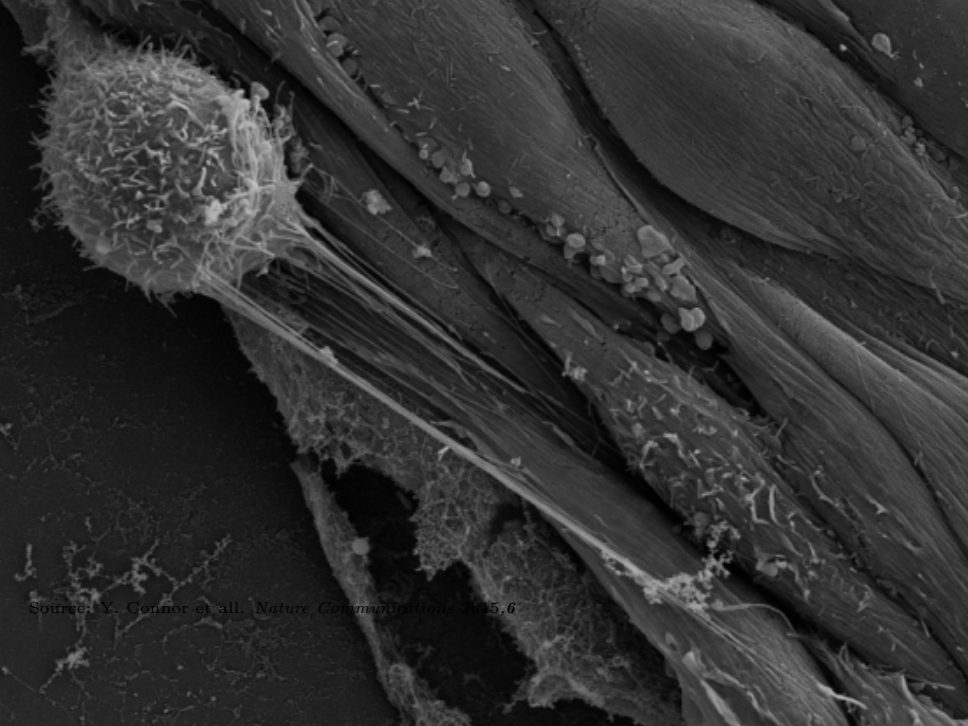


Bachelor Thesis 2016

Radiosensitization using gold nanoparticles

Lies Deceuninck en Hannelore Verhoeven

Assistents: Bert De Roo
Mattias Vervaele
Professor: Chris Van Haesendonck

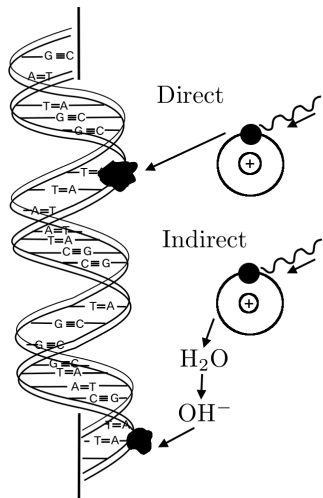


Source: Y. Connor et al. *Nature Communications* 2015,6

DNA damage using ionizing radiation

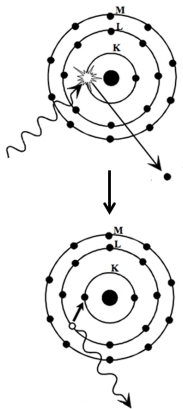
- Chemotherapy
- Surgery
- **Radiation therapy**

Energy \sim MeV

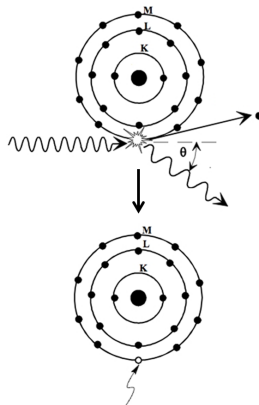


Radiosensitization of cancer cells with gold nanoparticles (GNP) $E \sim \text{keV}$

Photoelectric absorption



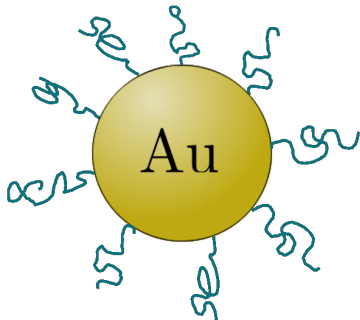
Compton effect



Targeting of the GNP to the tumor

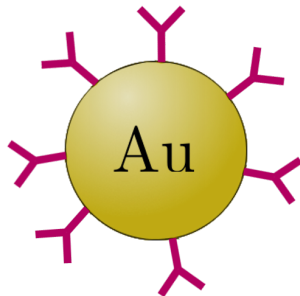
Passive targeting

PEG coating



Active targeting

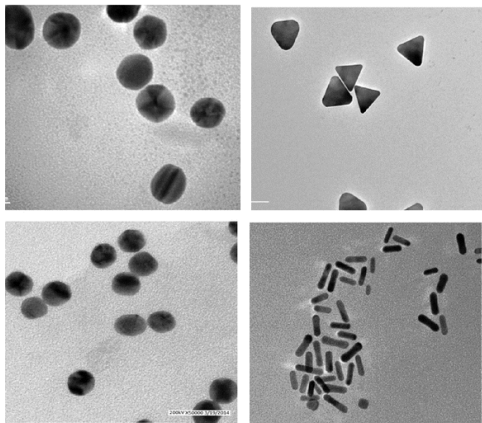
Antibodies



Overview Project

Radiosensitization of DNA using gold nanoparticles

1. Synthesis
2. Characterization
3. Radiosensitization



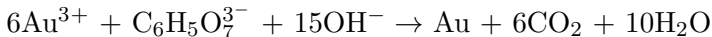
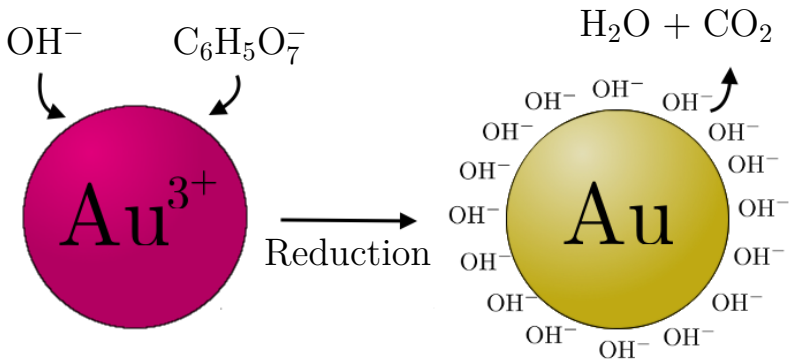
Reduction of gold ions to form GNP



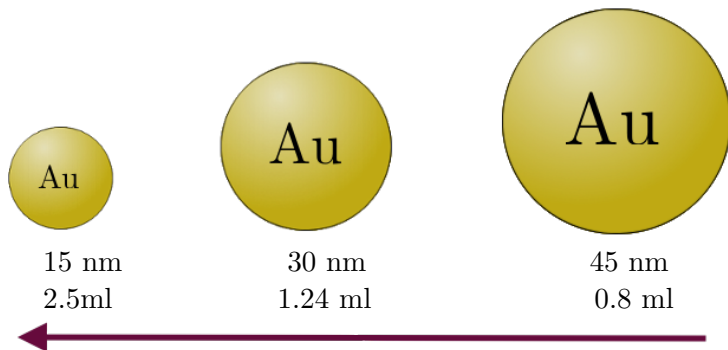
Gold ions: HAuCl_4 solution

Reducing agent: $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7$

Reduction of gold ions to form GNP

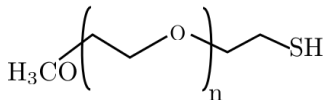
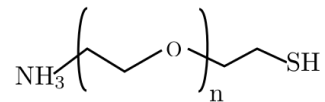
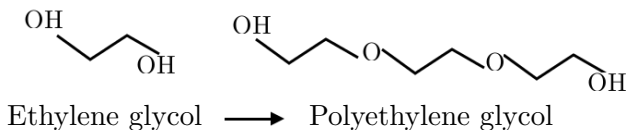


The amount of citrate controls the size

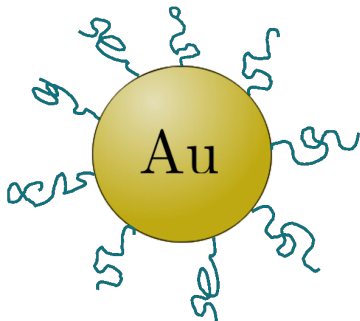


Citrate 1%
100ml HAuCl₄ 0.01%

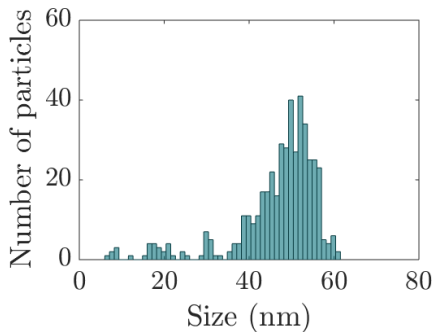
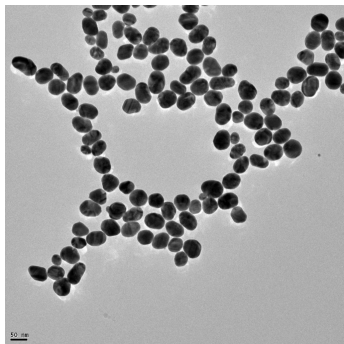
PEG for targeting and stabilization



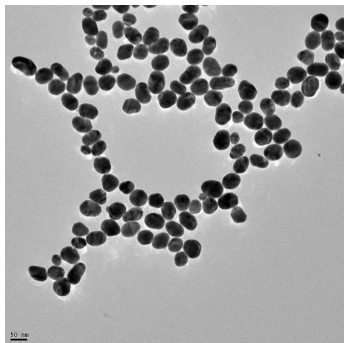
1k, 5k, 10k, 20k



TEM image analysis to determine the core diameter

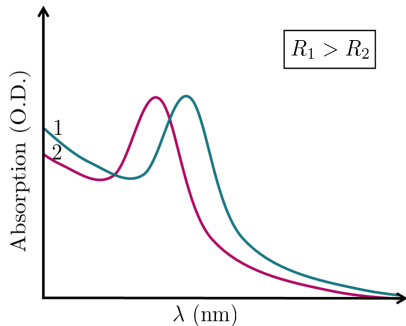
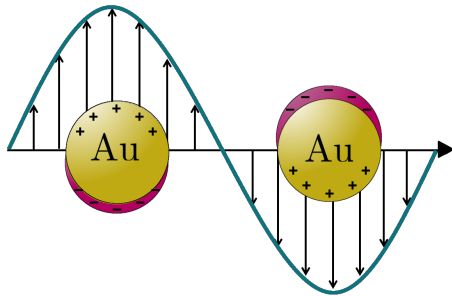


TEM image analysis to determine the core diameter

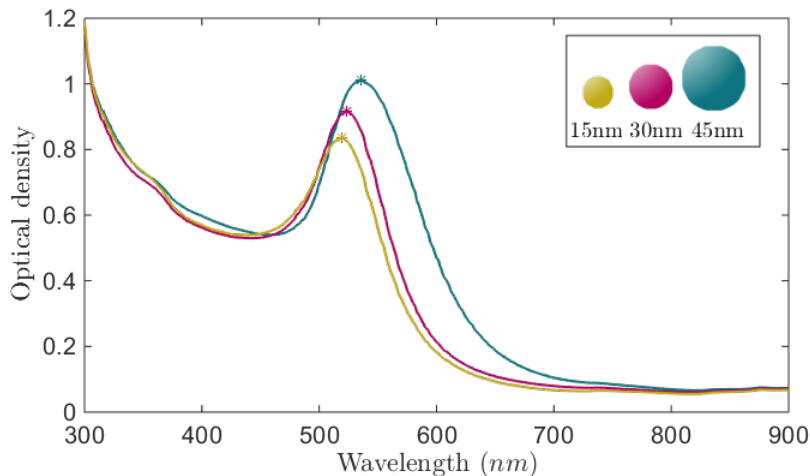


Exp. Size (nm)	Size (nm)
15	12.98 ± 0.23
	2.99 ± 0.16
30	18.29 ± 0.23
45	46.75 ± 0.47

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

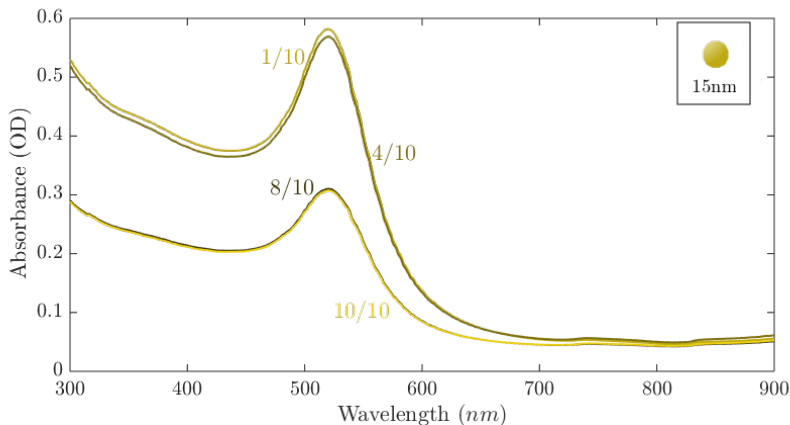


Absorption measurements (UV-Vis) to determine the relative size



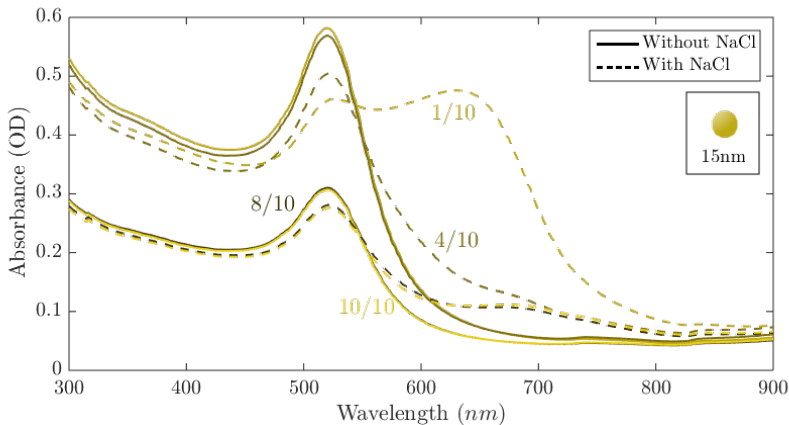
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

1. Add PEG and preform UV-Vis measurement
0.2cm



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

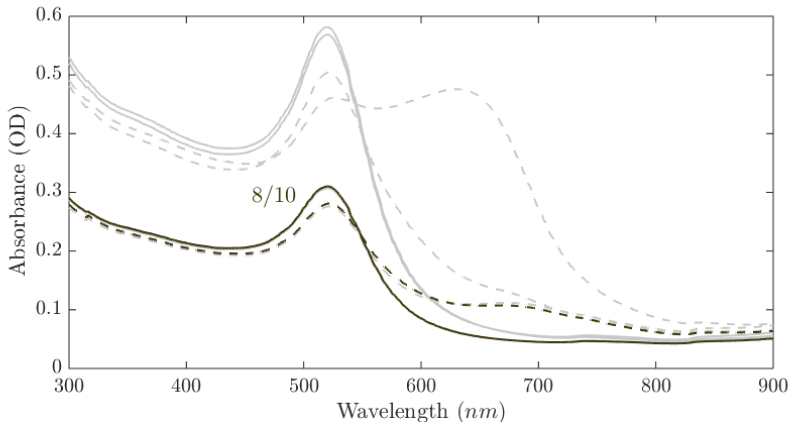
2. Add NaCl and perform UV-Vis measurement



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

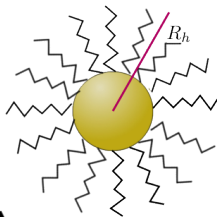
bigger size \rightarrow too little PEG

same size \rightarrow enough PEG



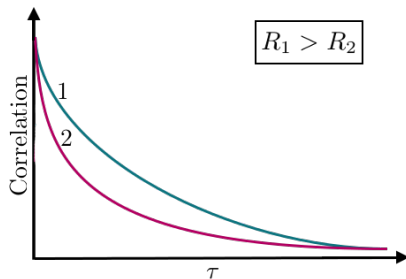
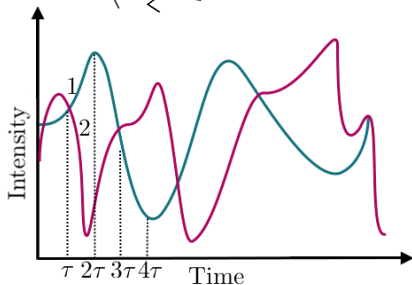
Light scattering experiments to determine the hydrodynamic radius (R_h)

Important for diffusive properties

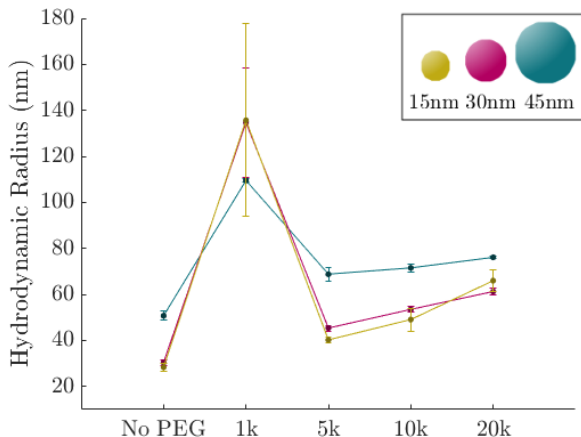


Correlation:

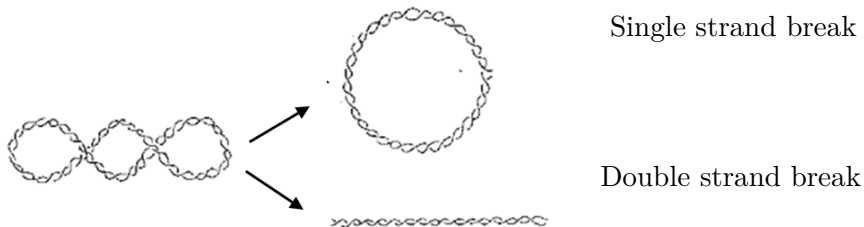
$$g(\tau) = \frac{\langle I(t) \rangle \langle I(t+\tau) \rangle}{\langle I(t) \rangle^2}$$



Hydrodynamic radii for the three different GNP with different functionalizations

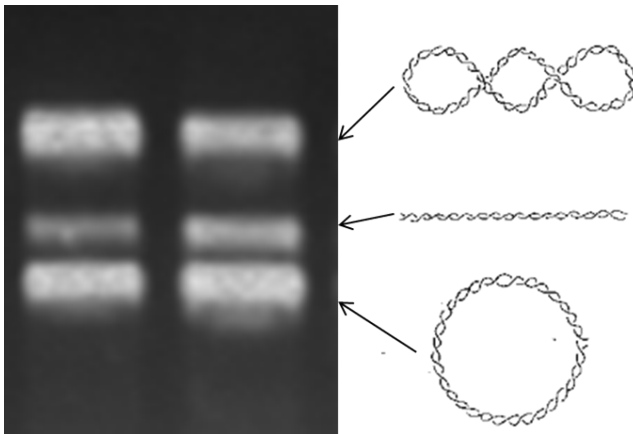


Gel electrophoresis to analyse DNA damage



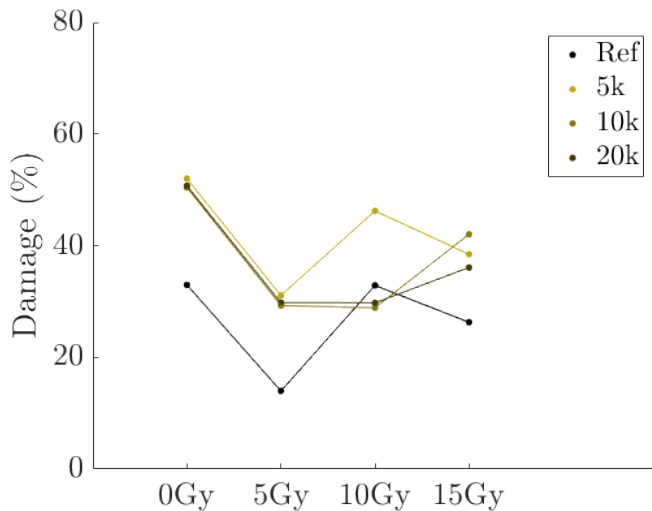
Source: <https://www.quora.com/Whats-the-difference-between-a-plasmid-and-a-virus>.

Gel electrophoresis to analyse DNA damage

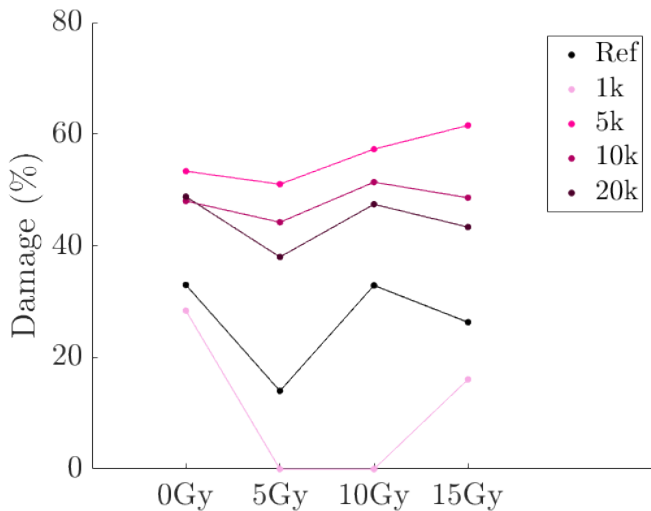


Source: Maunus R et al. Horton JR, Zhang X. Nucleic Acids Research, 34(3):939–948, 2006.

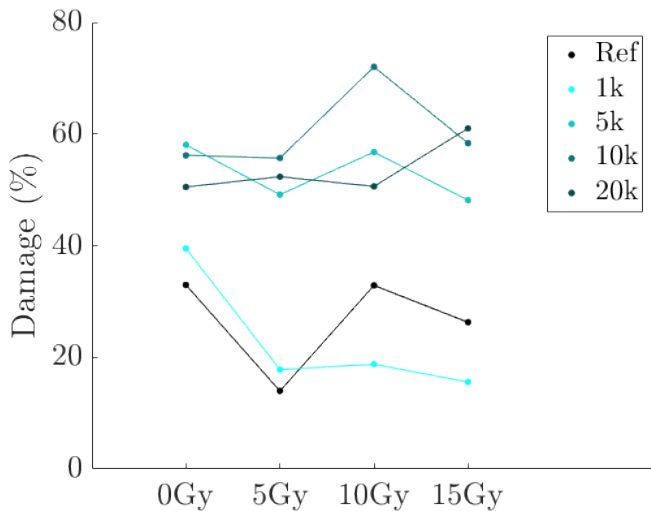
DNA damage analysis for 15nm GNP



DNA damage analysis for 30nm GNP

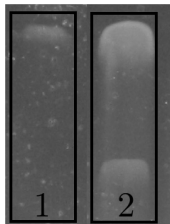


DNA damage analysis for 45nm GNP



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 \rightarrow more DNA damage
- Larger GNP \rightarrow more DNA damage



Conclusion

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

⇒ Radiosensitization effect observed

