Bachelor Thesis 2016

Radiosensitization using gold nanoparticles

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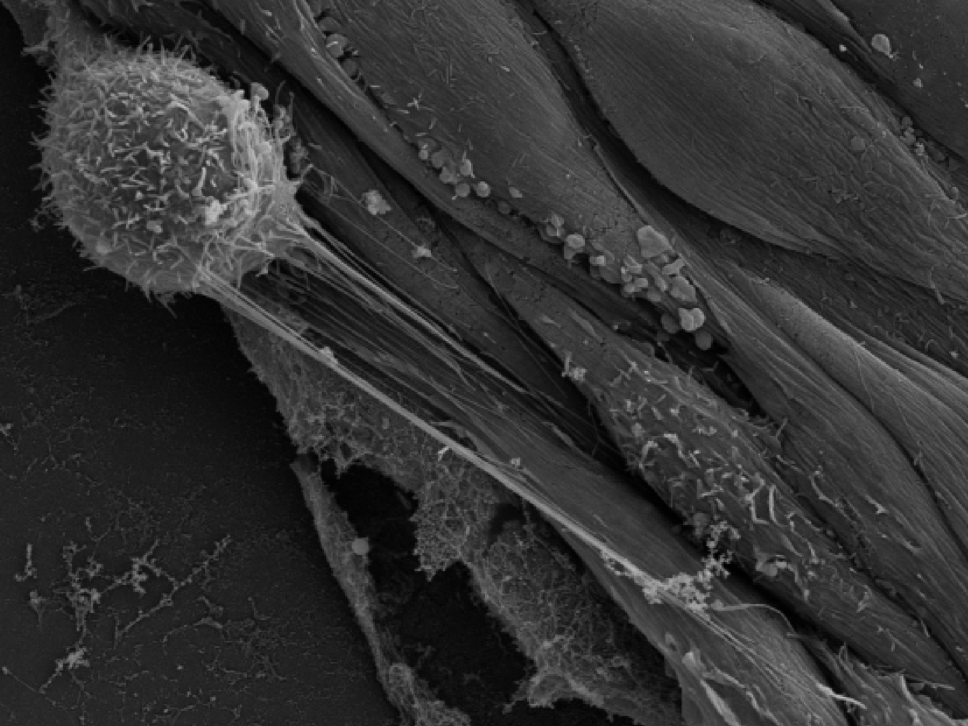
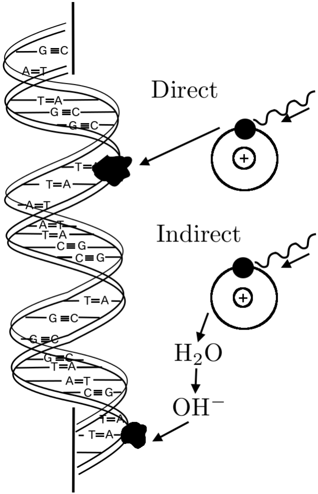
Mattias Vervaele
Professor: Chris Van Haesendonck



DNA damage using ionizing radiation

- Chemotherapy
- Surgery
- **Radiation therapy**

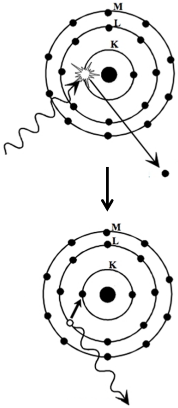
  Energy $\sim$ MeV



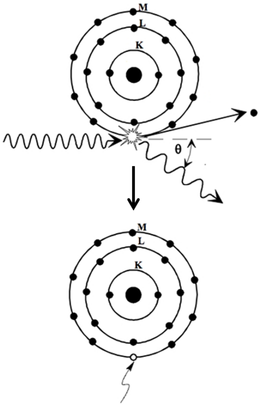
Source: https://chem.kuleuven.be/veiligheid/info/ioniserende-st.htm

Radiosensitization of cancer cells with gold nanoparticles (GNP) E ~ keV

Photoelectric absorption

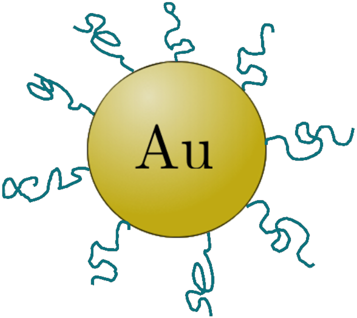


Compton effect

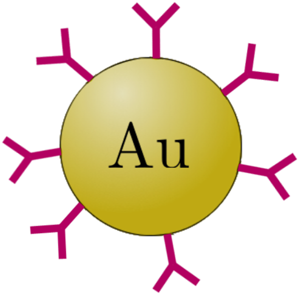


Targeting of the GNP to the tumor

Passive targeting
PEG coating



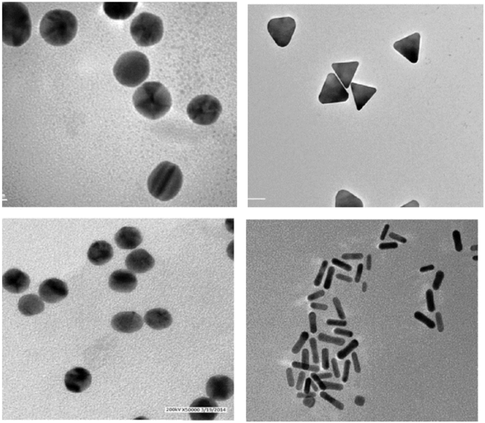
Active targeting
Antibodies



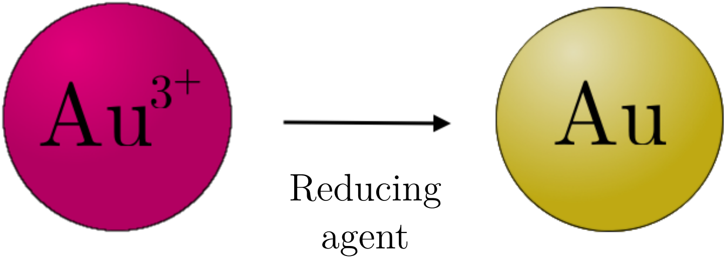
Overview Project

Radiosensitization of cancer cells using gold nanoparticles

1. Synthesis
2. Characterization
3. Radiosensitization

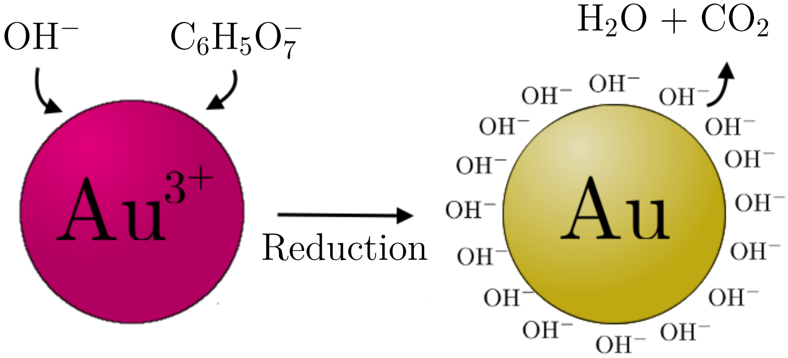


Reduction of gold ions to form GNP



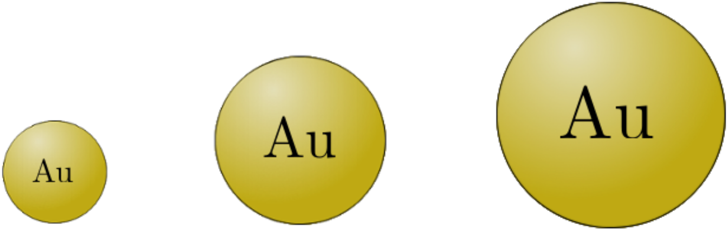
Gold ions: $HAuCl_4$ solution
Reducing agent: $Na_3C_6H_5O_7$

Reduction of gold ions to form GNP



$$6Au^{3+} + C_6H_5O_7^{3-} + 15OH^- \rightarrow Au + 6CO_2 + 10H_2O$$

The amount of citrate controls the size



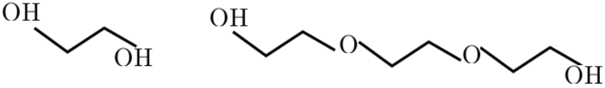
15 nm 30 nm 45 nm

2.5ml 1.24 ml 0.8 ml

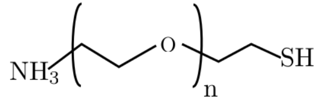
Citrate 1%

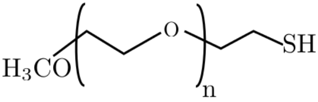
100ml $HAuCl_4$ 0.01%

PEG for targeting and stabilization

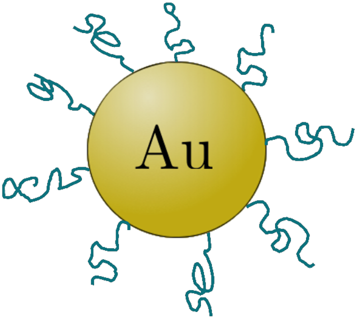


Ethylene glycol → Polyethylene glycol

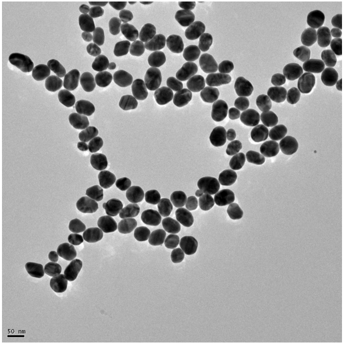


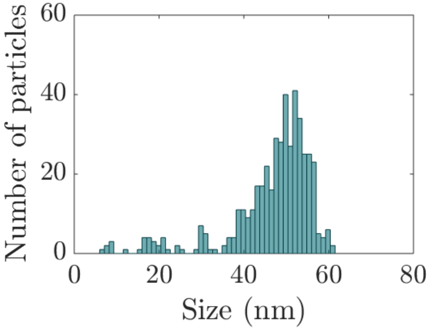


1k, 5k, 10k, 20k

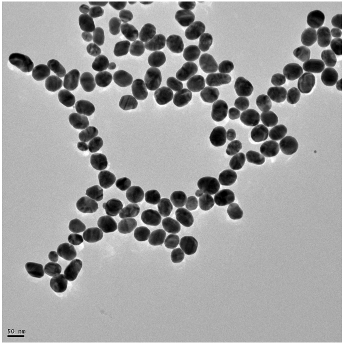


TEM image analysis to determine the core diameter



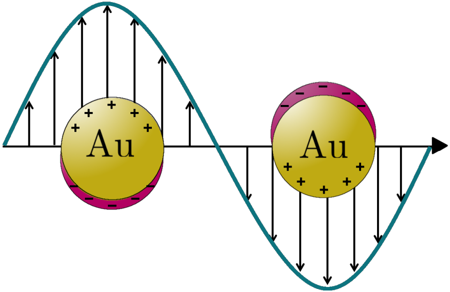


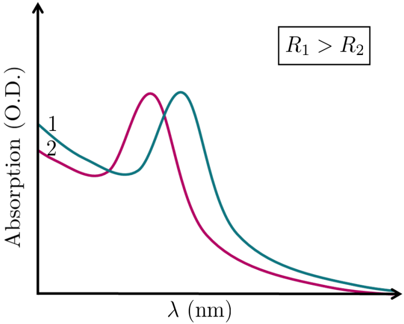
TEM image analysis to determine the core diameter



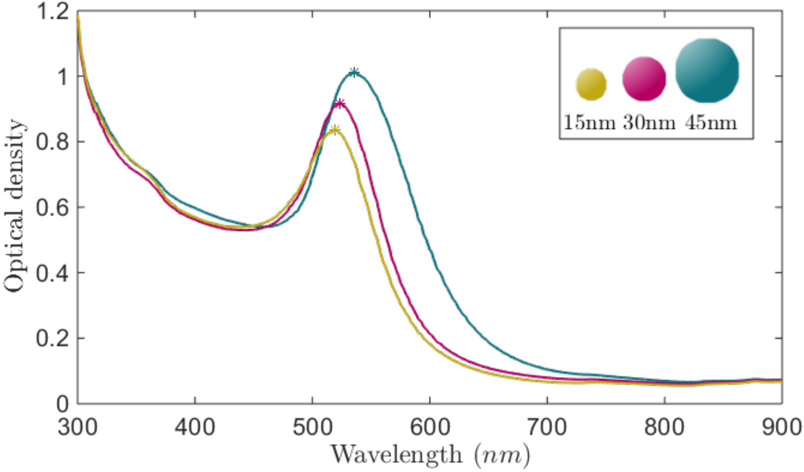
Exp. Size (nm)	Size (nm)
15	12.98 ± 0.23
	2.99 ± 0.16
30	18.29 ± 0.23
45	46.75 ± 0.47

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



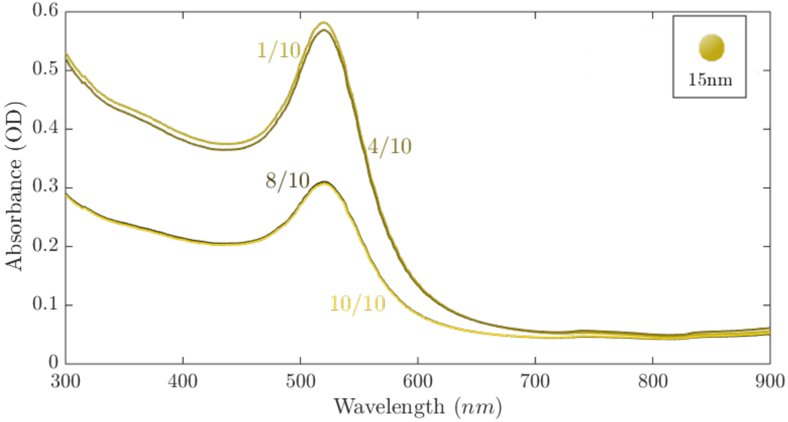


Absorption measurements (UV-Vis) to determine the relative size



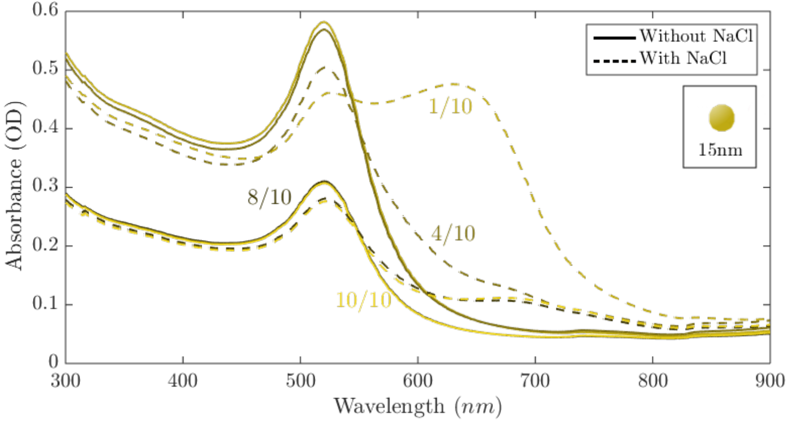
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

1. Add PEG and preform UV-Vis measurement



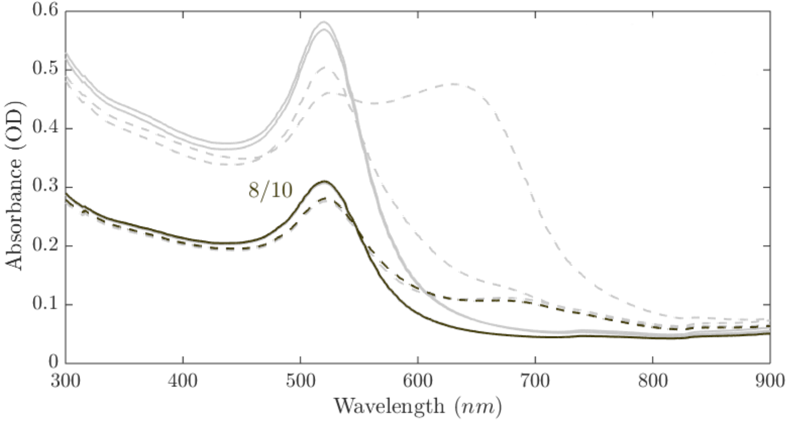
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

2. Add NaCl and preform UV-Vis measurement



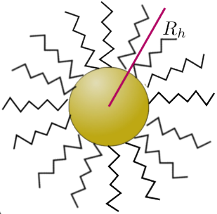
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

bigger size → too little PEG
same size → enough PEG



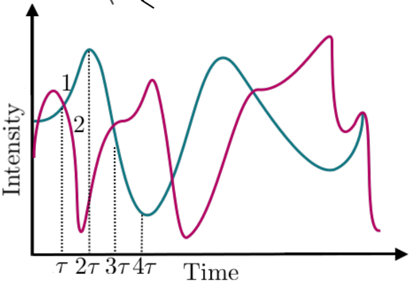
Light scattering experiments to determine the hydrodynamic radius (R_h)

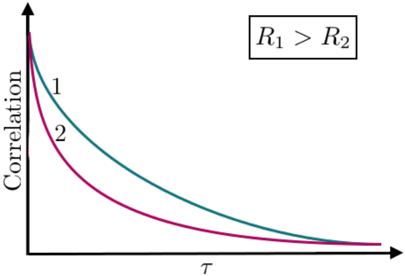
Important for diffusive properties



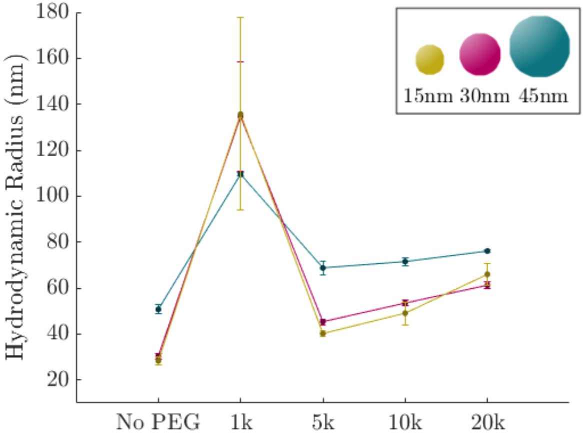
Correlation:

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

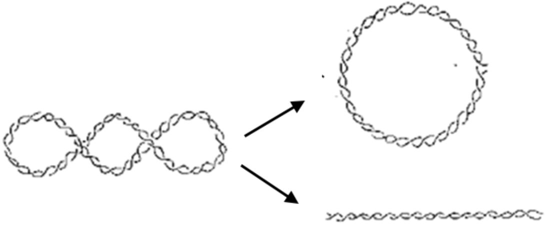




Hydrodynamic radii for the three different GNP with different functionalizations



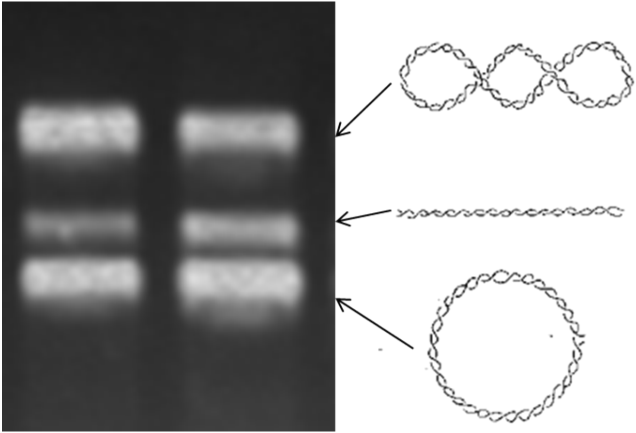
Gel electrophoresis to analyse DNA damage



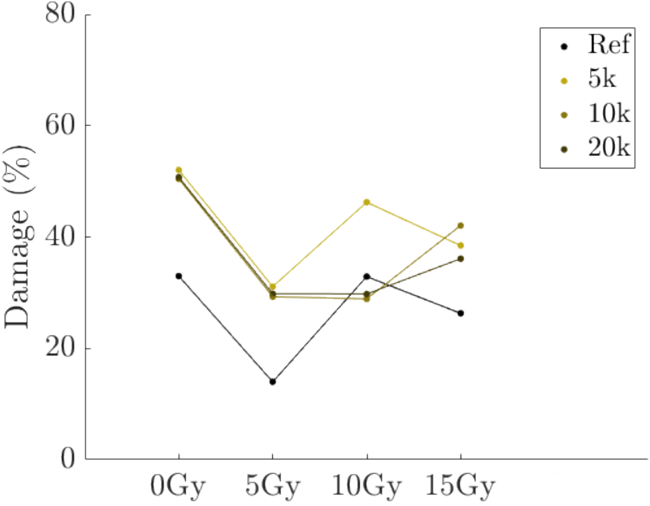
Single strand break

Double strand break

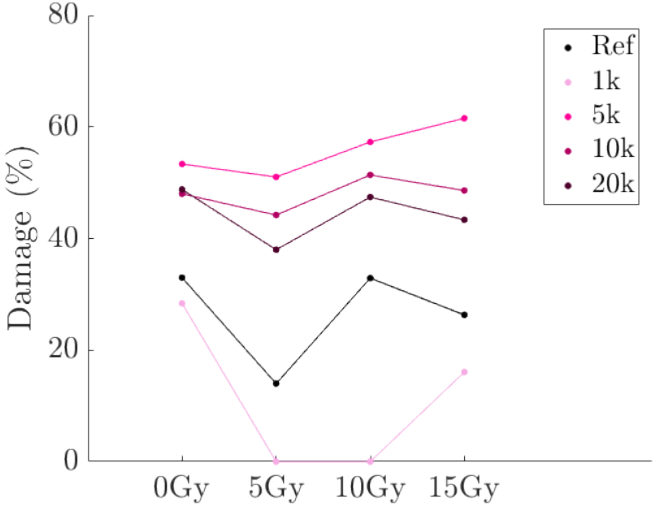
Gel electrophoresis to analyse DNA damage



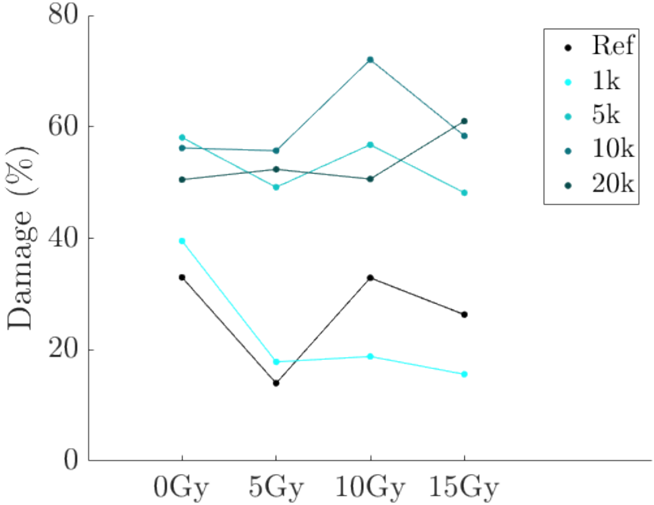
DNA damage analysis for 15nm GNP



DNA damage analysis for 30nm GNP

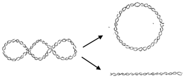


DNA damage analysis for 45nm GNP



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