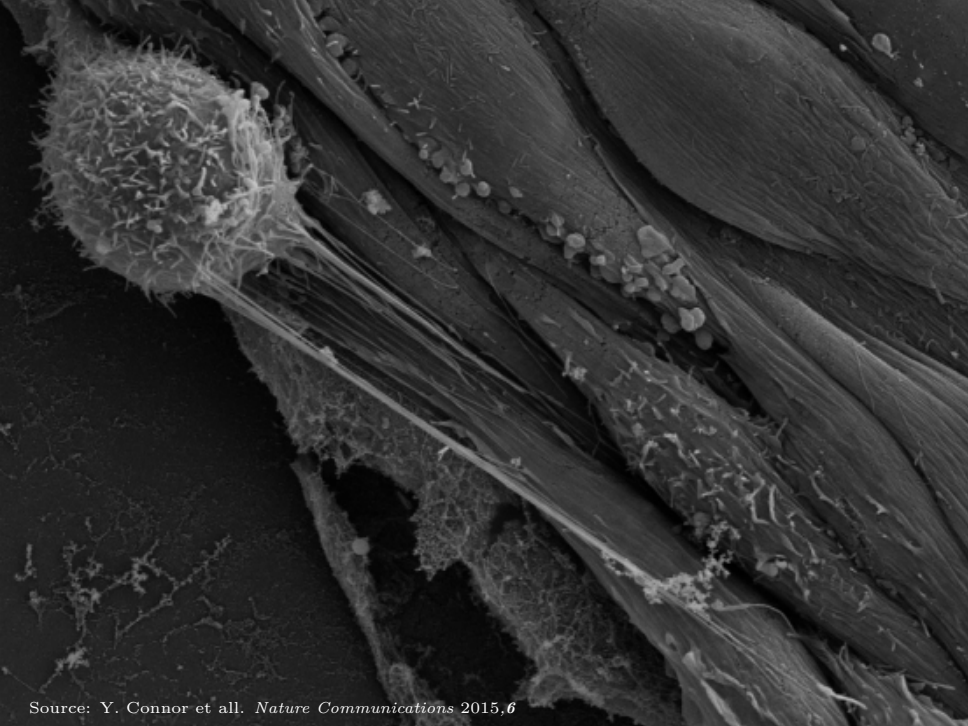


Bachelor Thesis 2016

Radiosensitization using gold nanoparticles

Lies Deceuninck en Hannelore Verhoeven

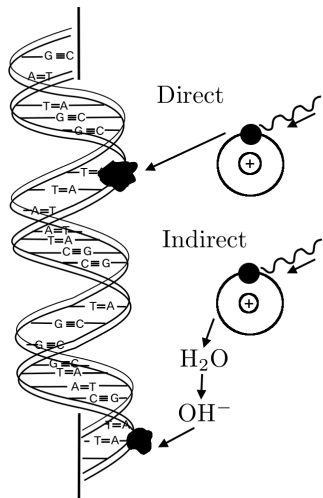
Supervisors: Bert De Roo
Mattias Vervaele
Professor: Jean-Pierre Locquet



DNA damage using ionizing radiation

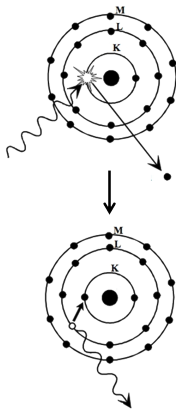
- Chemotherapy
- Surgery
- **Radiation therapy**

Energy \sim MeV

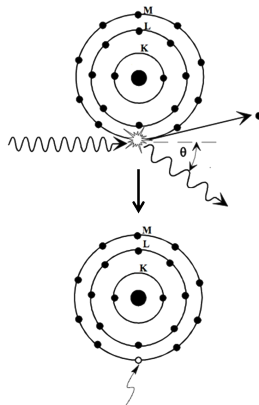


Radiosensitization of cancer cells with gold nanoparticles (GNP) $E \sim \text{keV}$

Photoelectric absorption



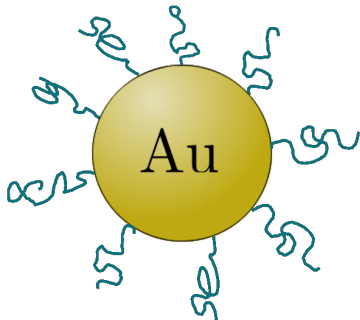
Compton effect



Targeting of the GNP to the tumor

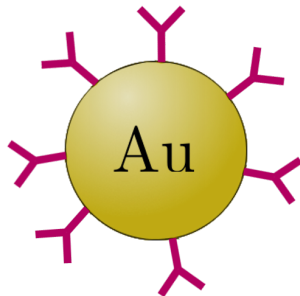
Passive targeting

PEG coating



Active targeting

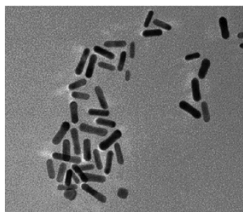
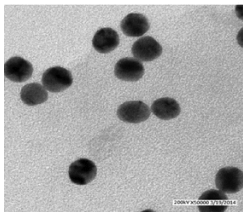
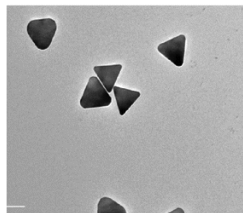
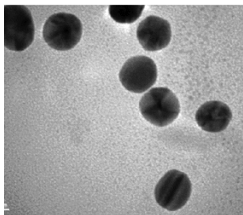
Antibodies



Overview Project

Radiosensitization of DNA using gold nanoparticles

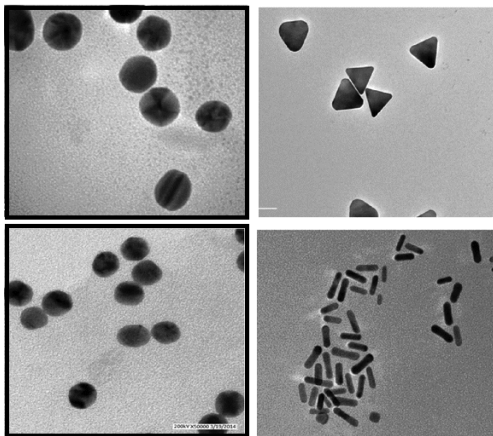
1. Synthesis
2. Characterization
 - a. TEM
 - b. UV-Vis
 - c. DLS
3. Radiosensitization



Overview Project

Radiosensitization of DNA using gold nanoparticles

1. Synthesis
2. Characterization
 - a. TEM
 - b. UV-Vis
 - c. DLS
3. Radiosensitization



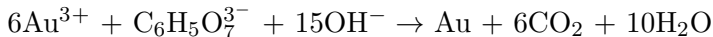
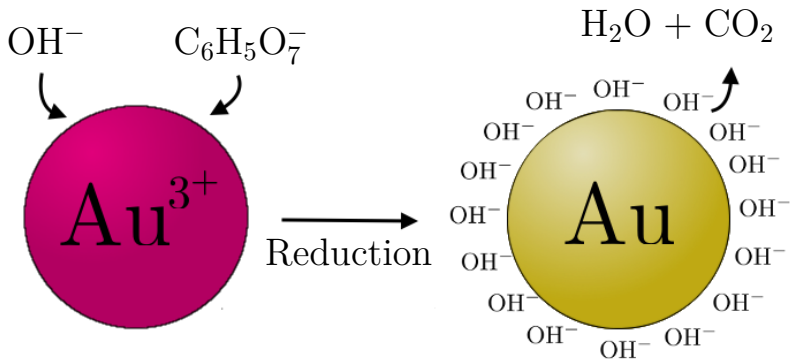
Reduction of gold ions to form GNP



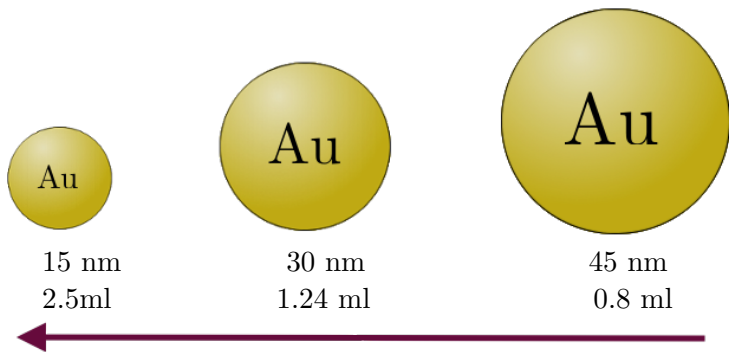
Gold ions: HAuCl_4 solution

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

Reduction of gold ions to form GNP

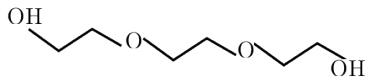


The amount of citrate controls the size

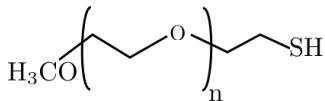
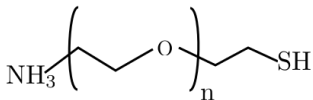


Citrate 1%
100ml HAuCl₄ 0.01%

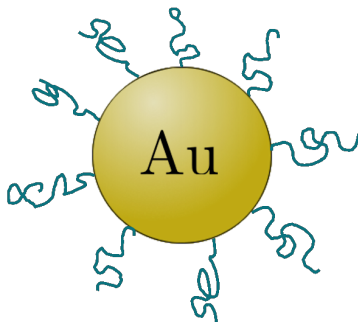
PEG for targeting and stabilization



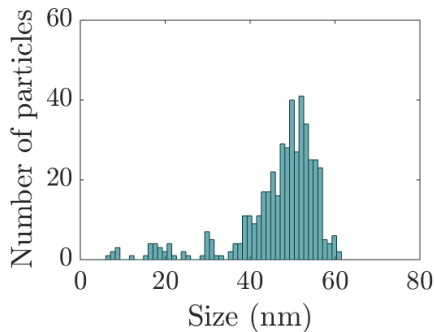
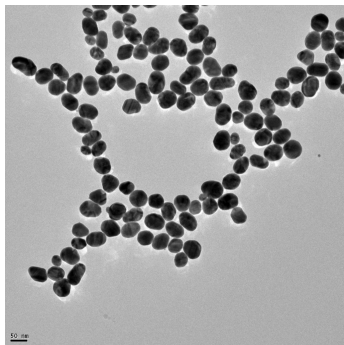
Polyethylene glycol



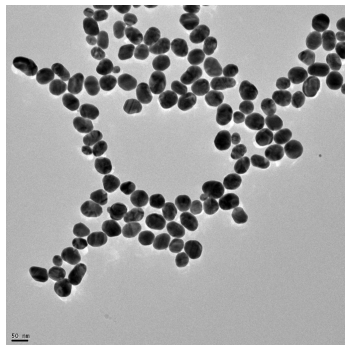
1k, 5k, 10k, 20k



TEM image analysis to determine the core diameter

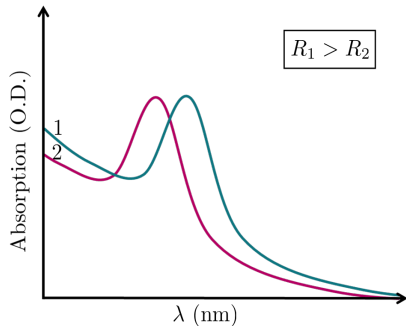
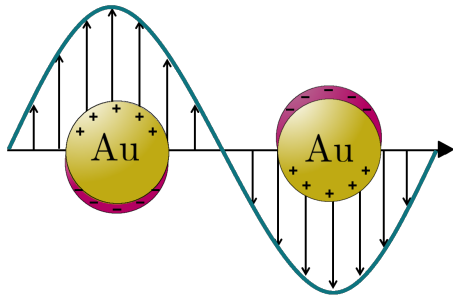


TEM image analysis to determine the core diameter

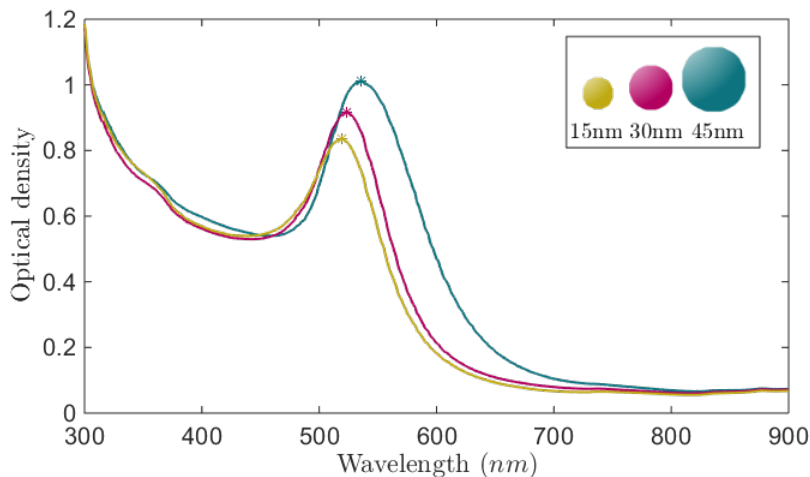


Exp. Size (nm)	Size (nm)
15	12.98 ± 0.23 2.99 ± 0.16
30	18.29 ± 0.23
45	46.75 ± 0.47

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

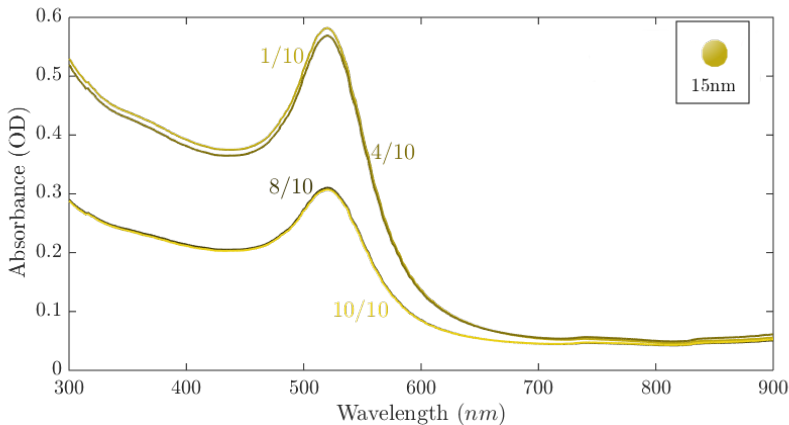


Absorption measurements (UV-Vis) to determine the relative size



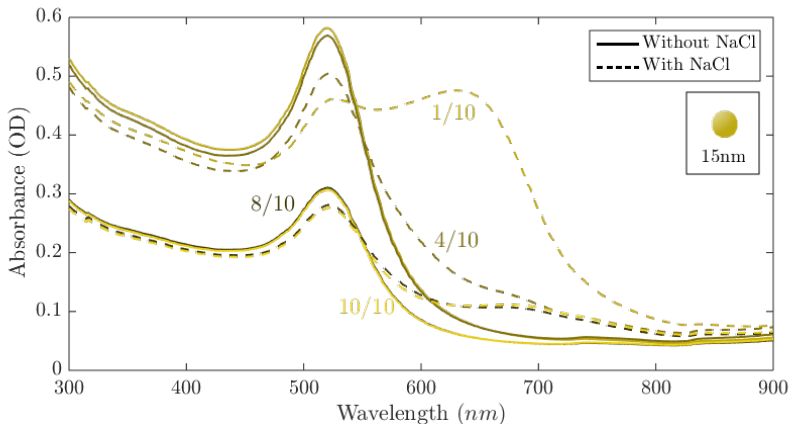
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

1. Add PEG and preform UV-Vis measurement

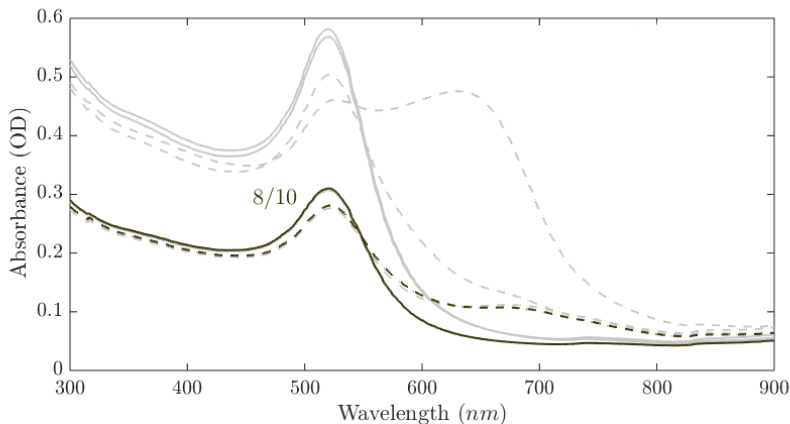


Absorption measurements (UV-Vis) to determine the optimal PEG proportion

2. Add NaCl and perform UV-Vis measurement

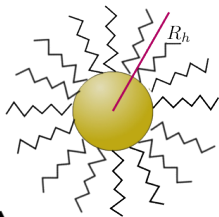


Absorption measurements (UV-Vis) to determine the optimal PEG proportion



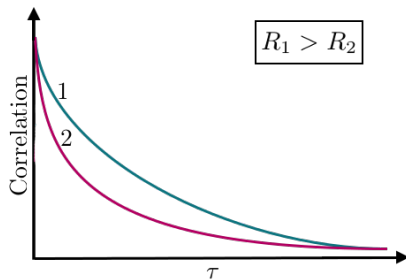
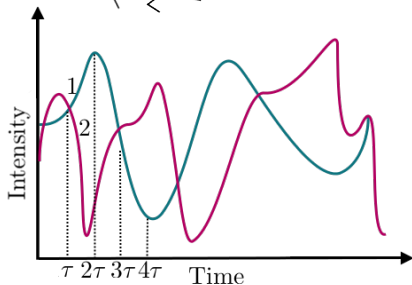
Light scattering experiments to determine the hydrodynamic radius (R_h)

Important for diffusive properties

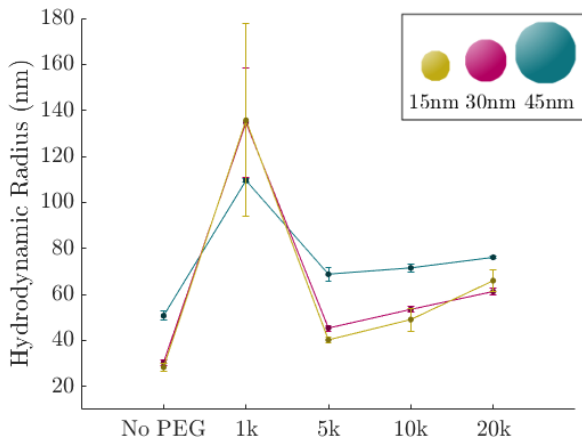


Correlation:

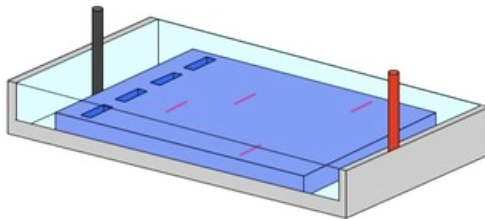
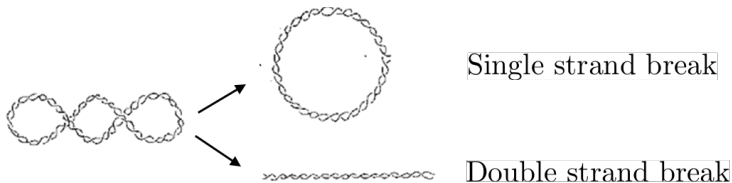
$$g(\tau) = \frac{\langle I(t) \rangle \langle I(t+\tau) \rangle}{\langle I(t) \rangle^2}$$



Hydrodynamic radii for the three different GNP with different functionalizations

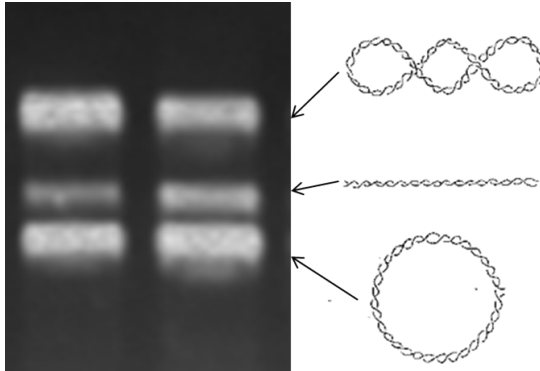


Gel electrophoresis to analyse DNA damage



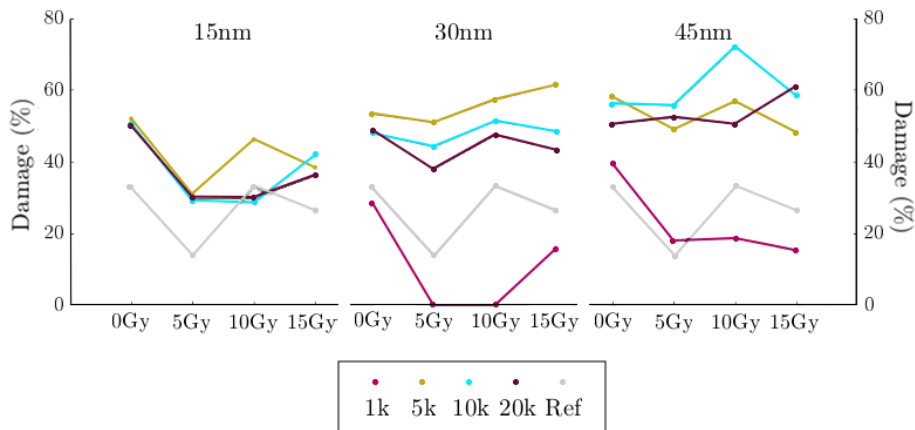
Sources: <https://www.quora.com/Whats-the-difference-between-a-plasmid-and-a-virus>.
<http://www.vce.bioninja.com.au/aos-3-heredity/molecular-biology-technique/dna-profiling.html>

Gel electrophoresis to analyse DNA damage



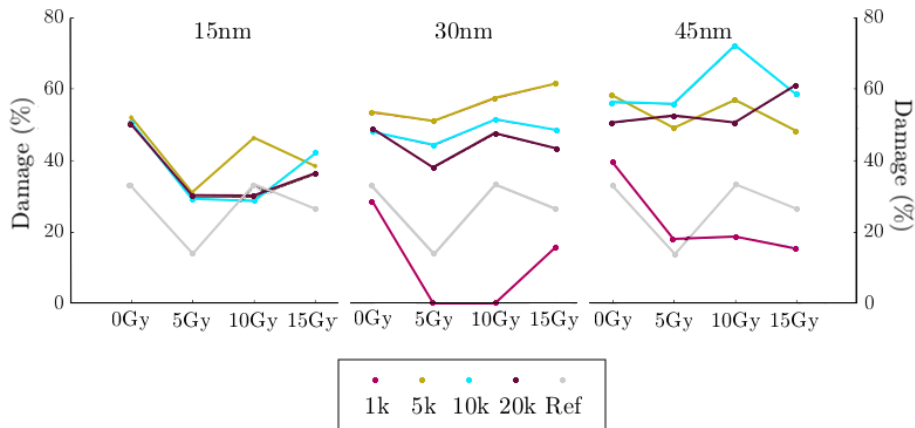
Source: Maunus R et al. Horton JR, Zhang X. Nucleic Acids Research, 34(3):939-948, 2006.

DNA damage analysis



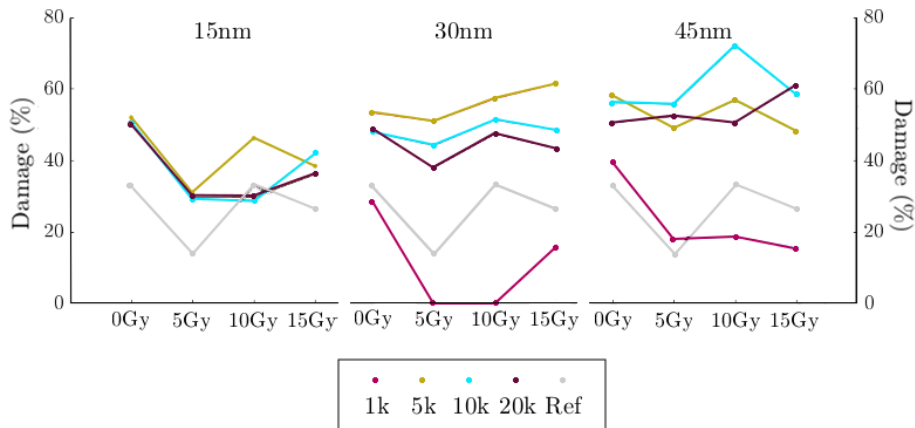
DNA damage analysis

Strange results for 1 k PEG



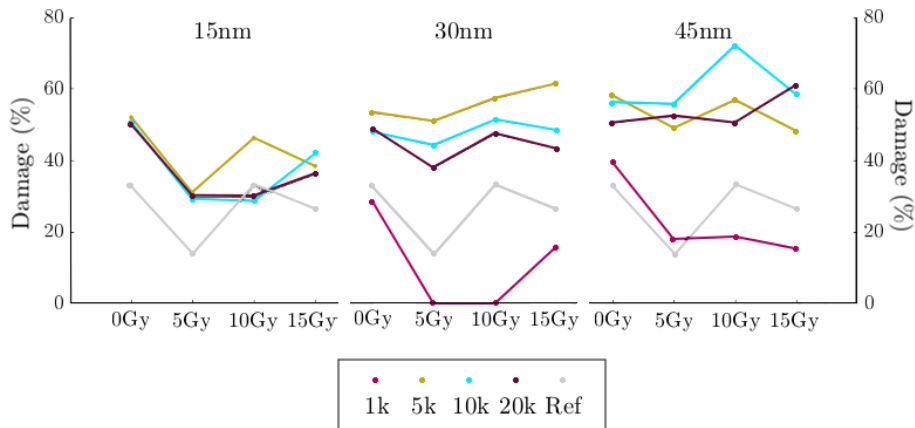
DNA damage analysis

Curves are not rising



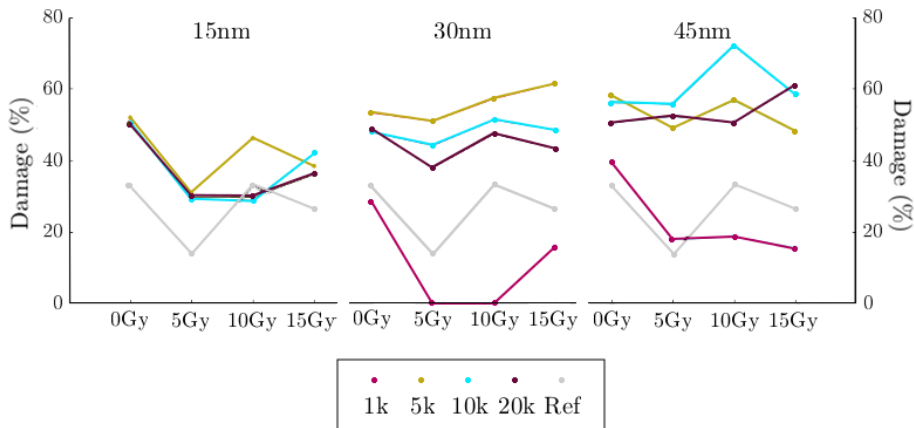
DNA damage analysis

Reference sample has an unexpected form



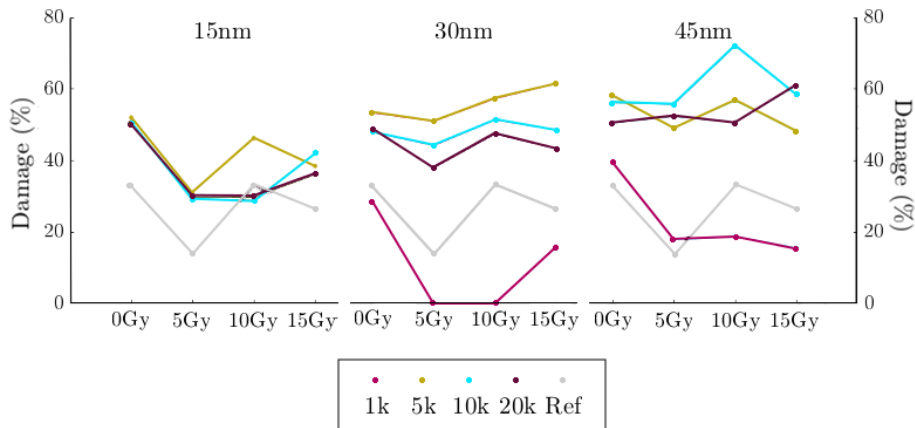
DNA damage analysis

DNA damage at 0 Gy



DNA damage analysis

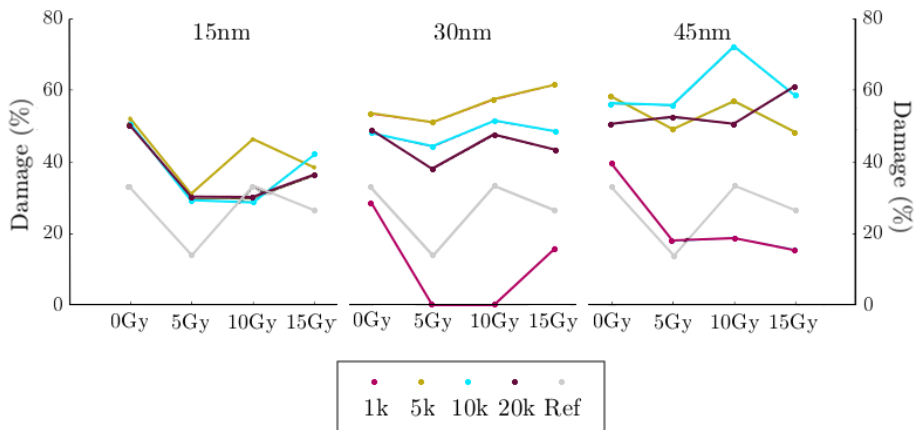
Radiosensitization effect is present



DNA damage analysis

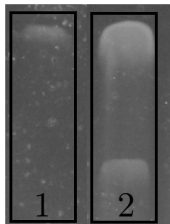
Smaller PEG \rightarrow more DNA damage

Larger GNP \rightarrow more DNA damage



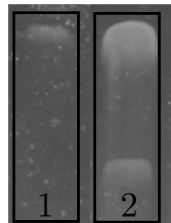
Conclusion DNA damage analysis

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

⇒ Radiosensitization effect observed

