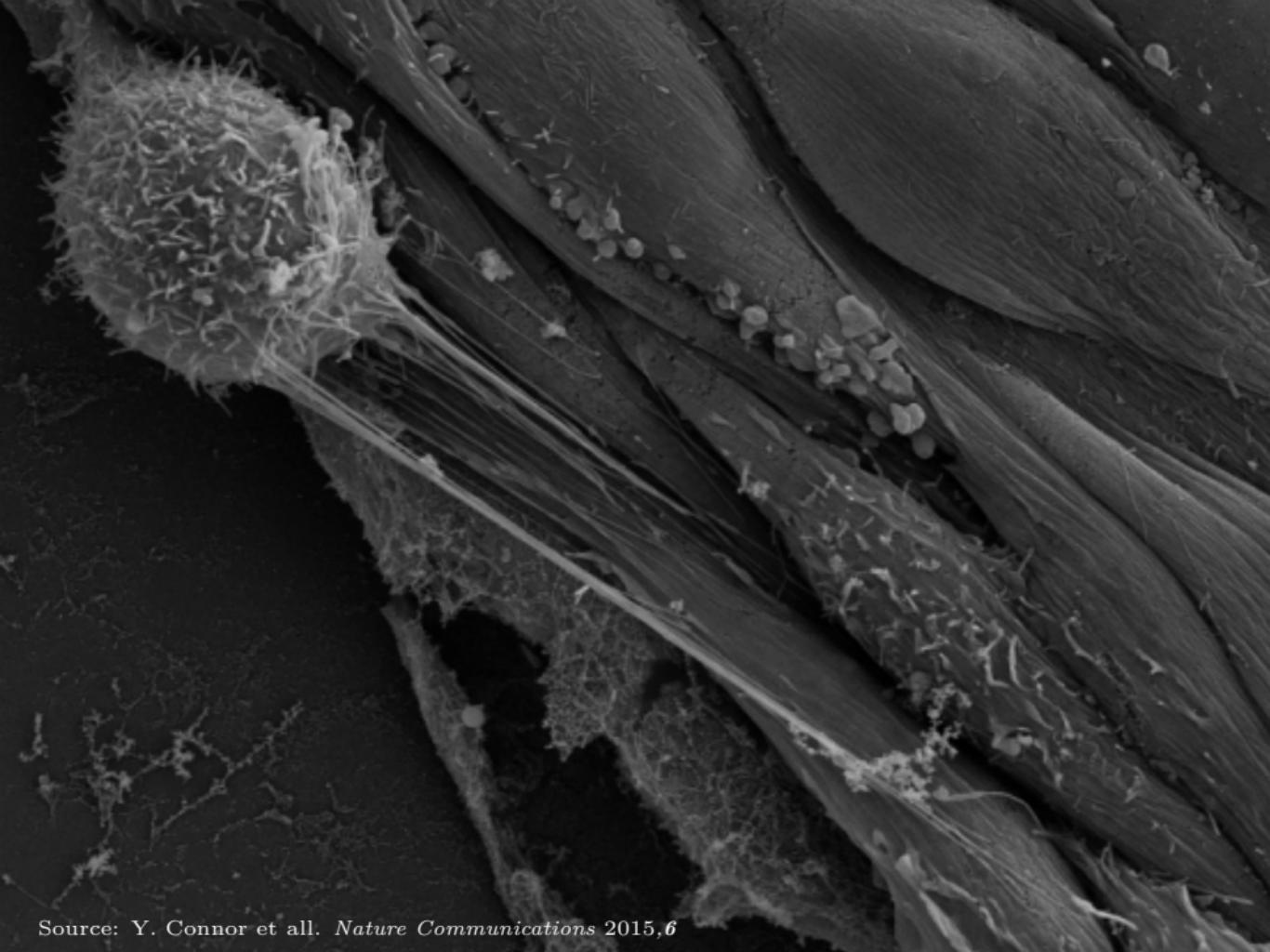


Bachelor Thesis 2016

Radiosensitization using gold nanoparticles

Lies Deceuninck en Hannelore Verhoeven

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

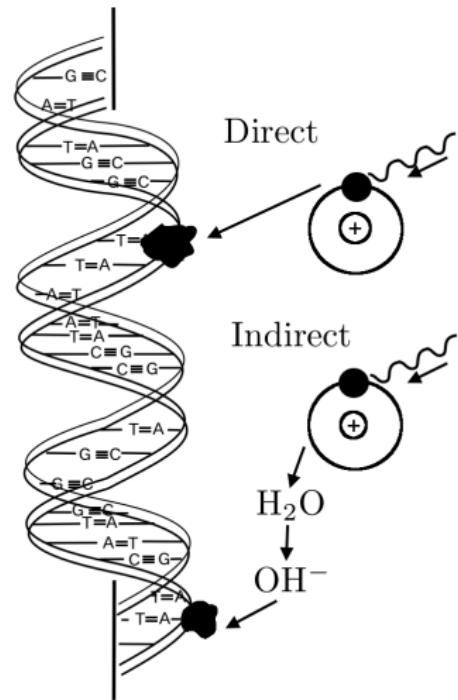


Source: Y. Connor et all. *Nature Communications* 2015, **6**

DNA damage using ionizing radiation

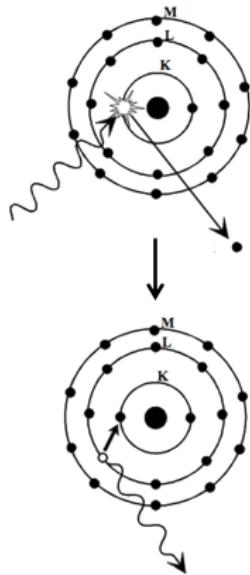
- Chemotherapy
- Surgery
- **Radiation therapy**

Energy \sim MeV

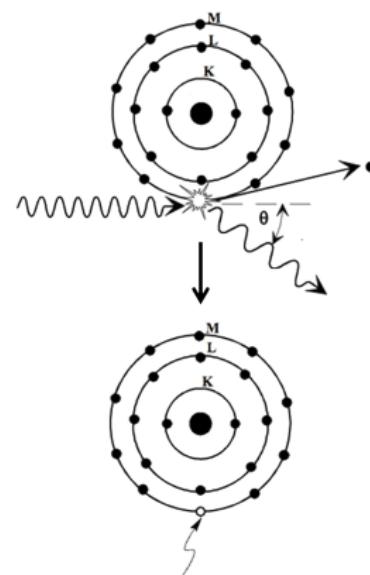


Radiosensitization of cancer cells with gold nanoparticles (GNP) $E \sim \text{keV}$

Photoelectric absorption

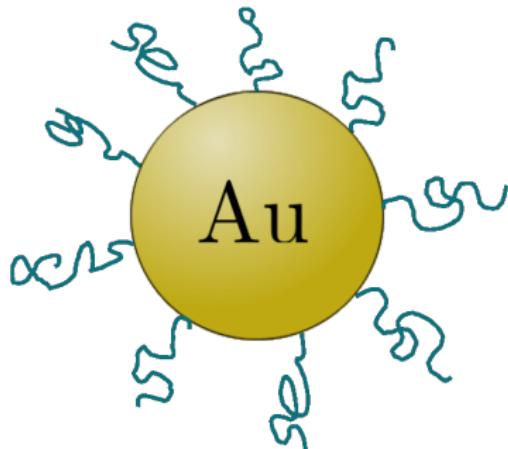


Compton effect

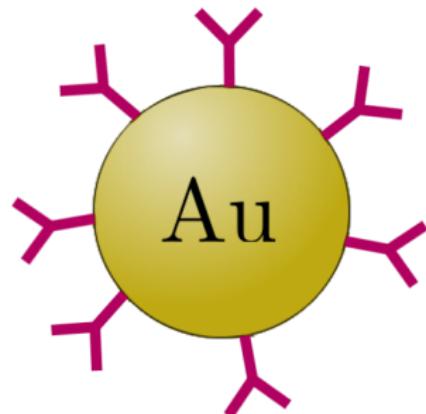


Targeting of the GNP to the tumor

Passive targeting
PEG coating



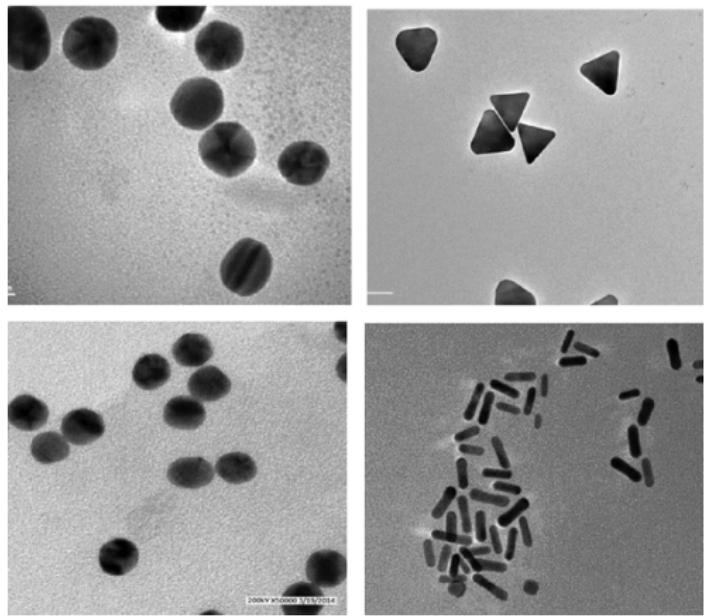
Active targeting
Antibodies



Overview Project

Radiosensitization of DNA using gold nanoparticles

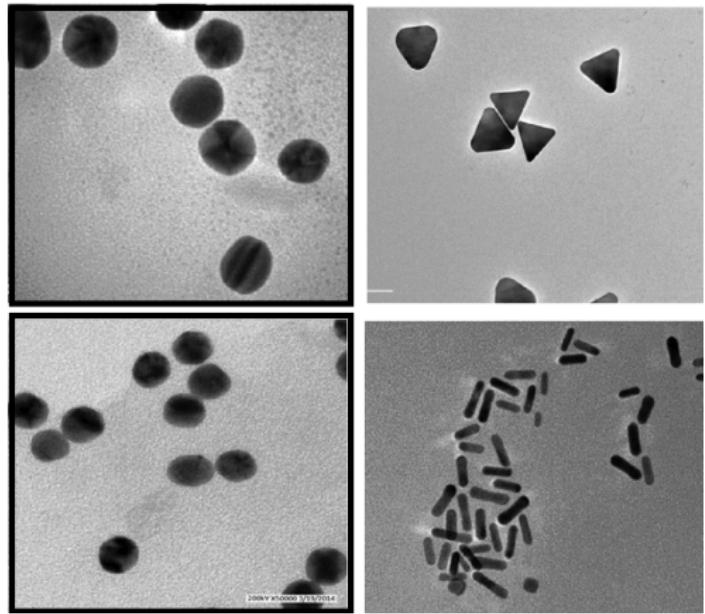
1. Synthesis
2. Characterization
 - a. TEM
 - b. UV-Vis
 - c. DLS
3. Radiosensitization



Overview Project

Radiosensitization of DNA using gold nanoparticles

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



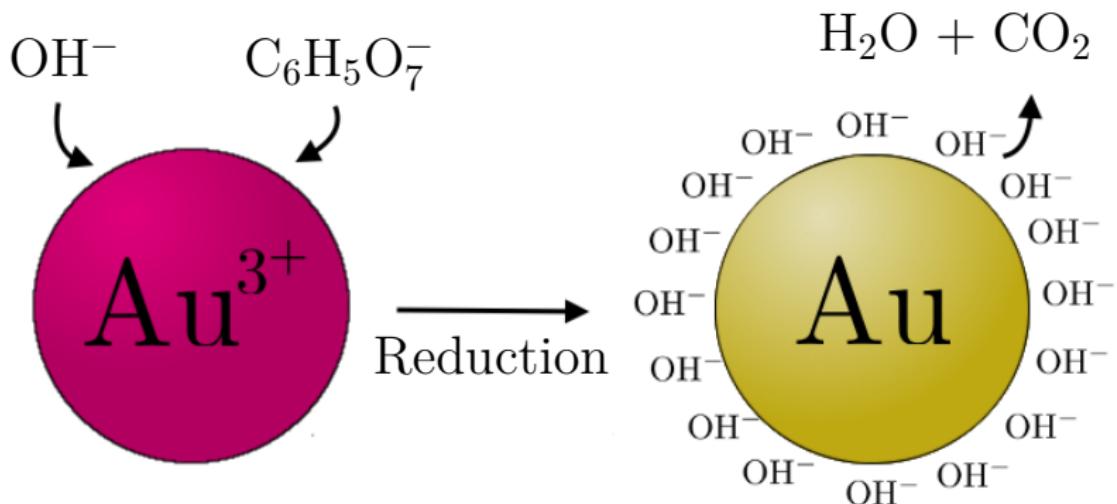
Reduction of gold ions to form GNP



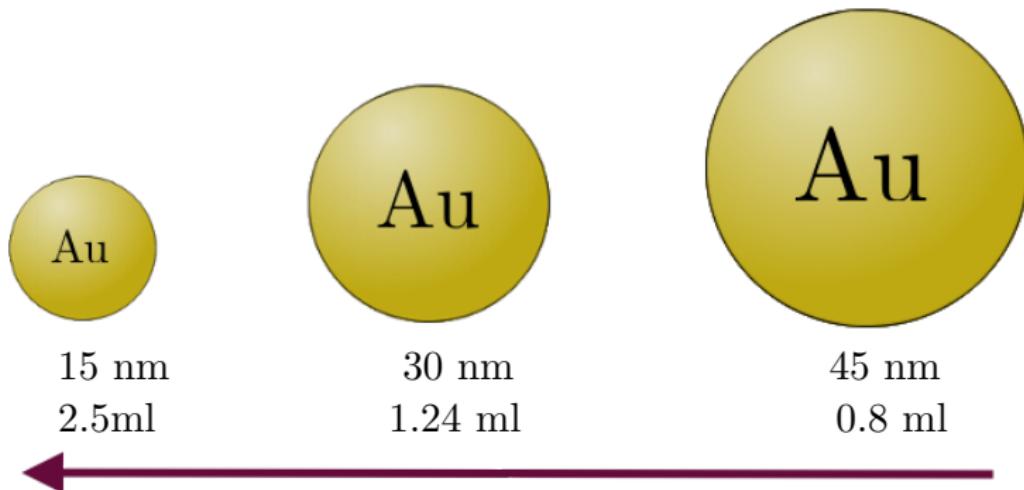
Gold ions: HAuCl₄ solution

Reducing agent: Na₃C₆H₅O₇

Reduction of gold ions to form GNP

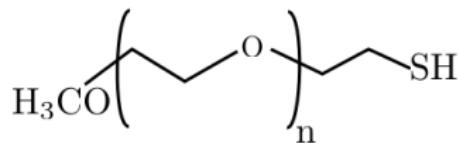
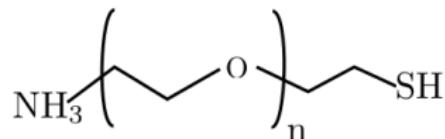
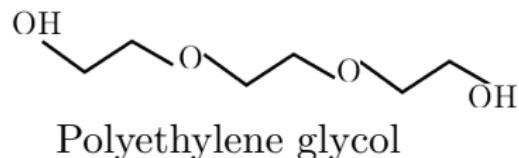


The amount of citrate controls the size

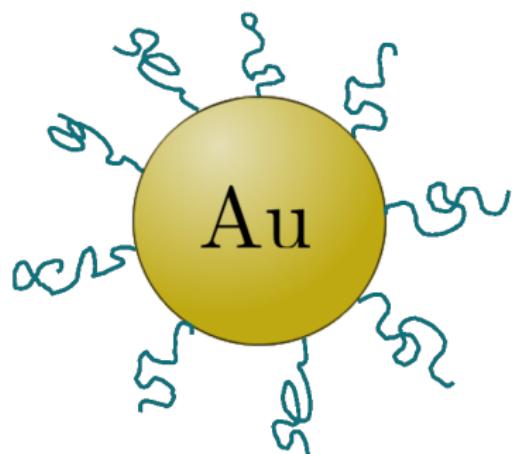


Citrate 1%
100ml HAuCl₄ 0.01%

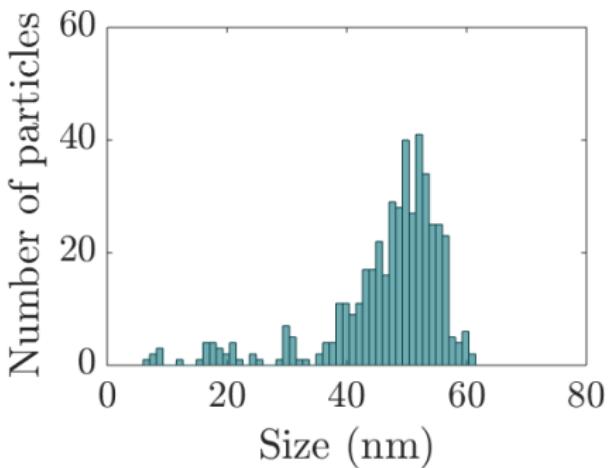
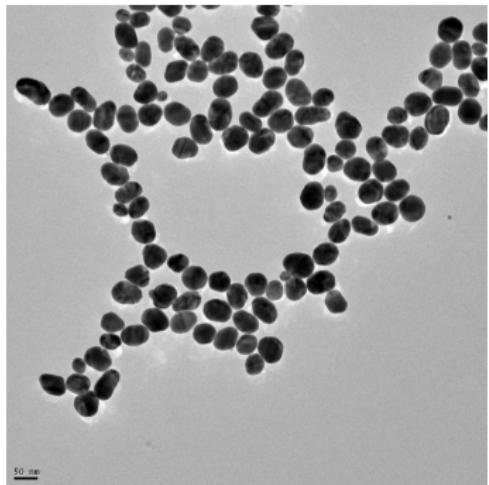
PEG for targeting and stabilization



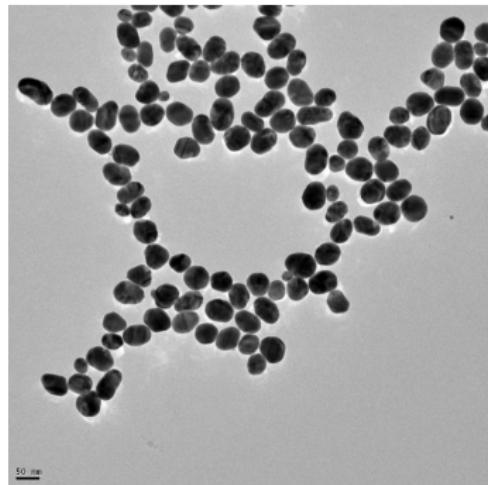
1k, 5k, 10k, 20k



TEM image analysis to determine the core diameter

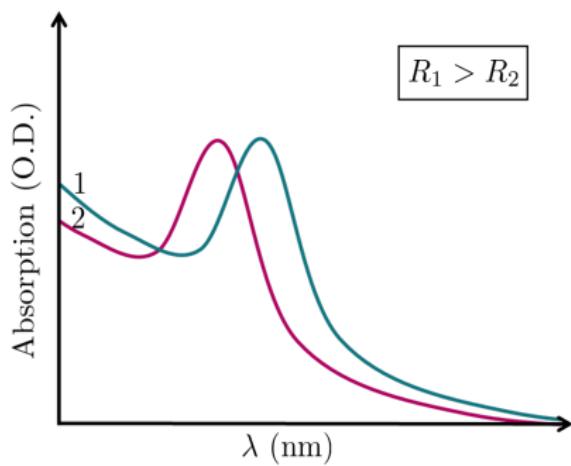
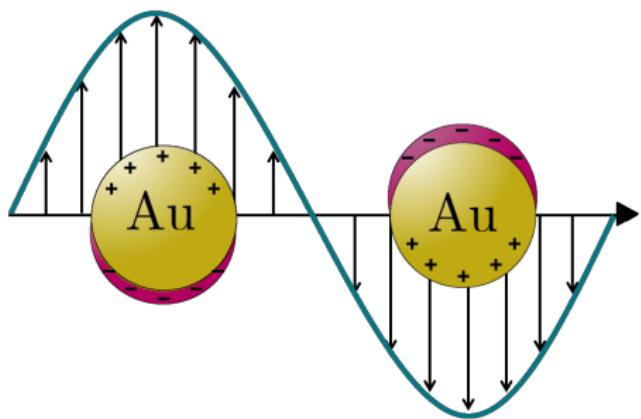


TEM image analysis to determine the core diameter

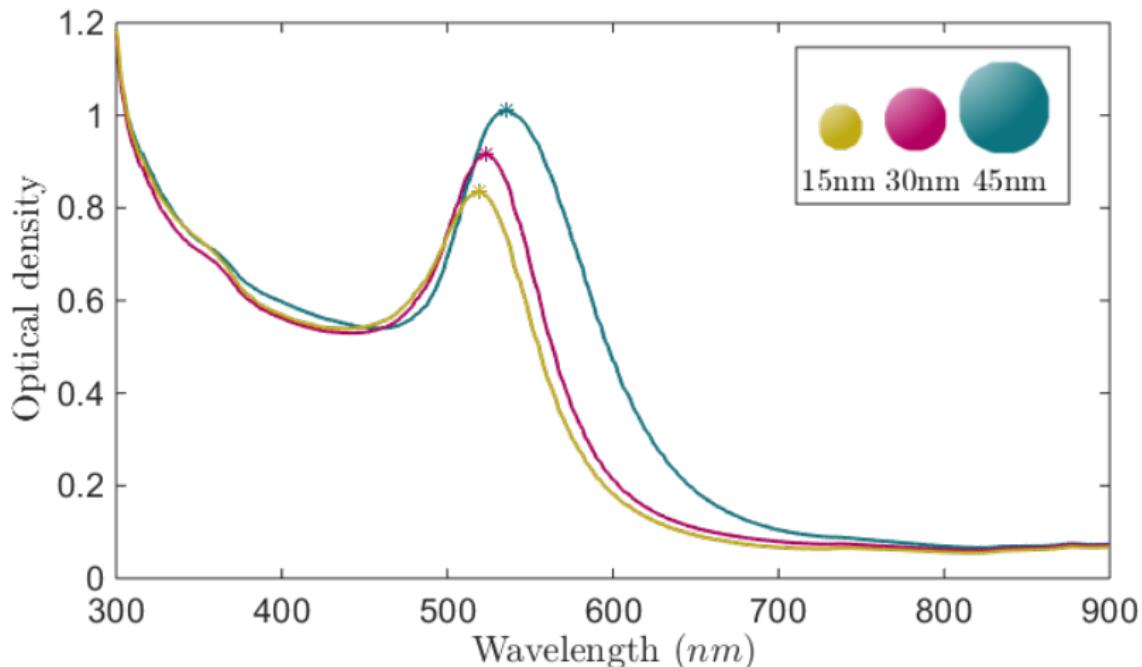


Exp. Size (nm)	Size (nm)
15	12.98 ± 0.23
	2.99 ± 0.16
30	18.29 ± 0.23
45	46.75 ± 0.47

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

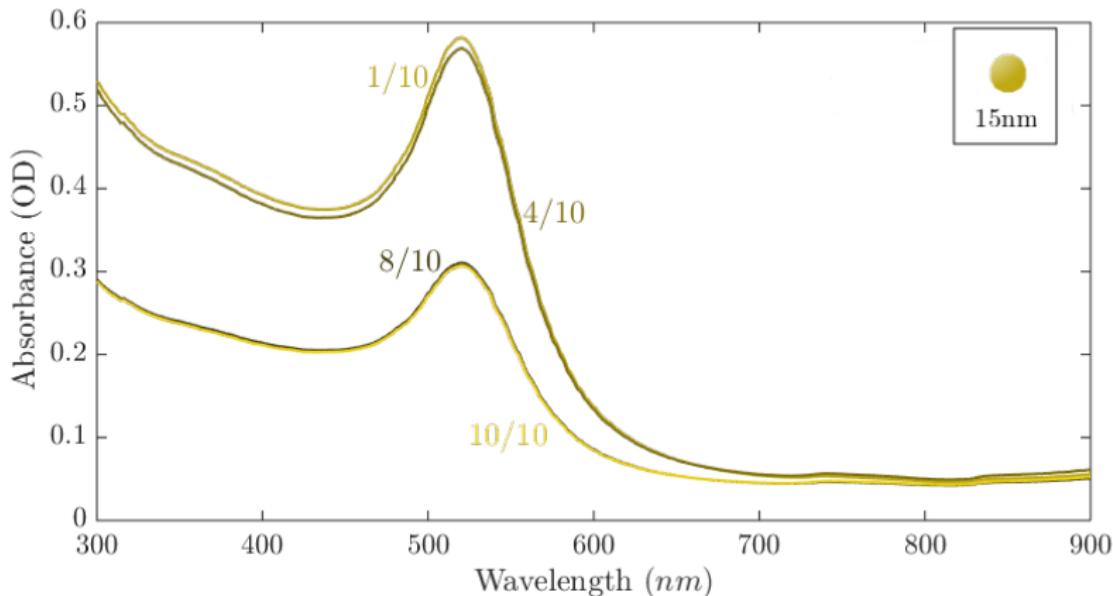


Absorption measurements (UV-Vis) to determine the relative size



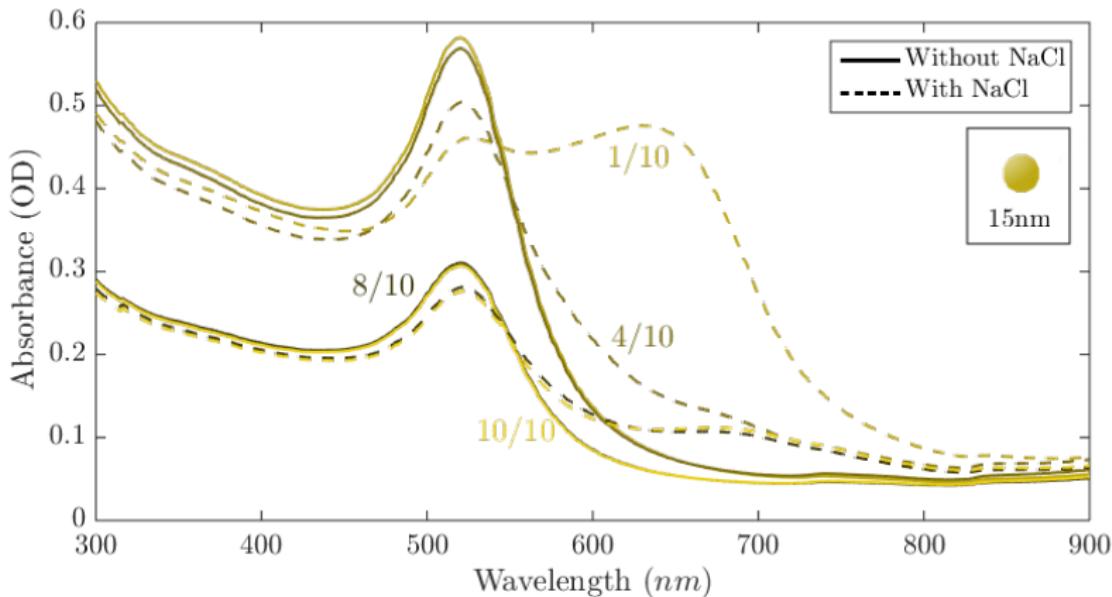
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

1. Add PEG and preform UV-Vis measurement

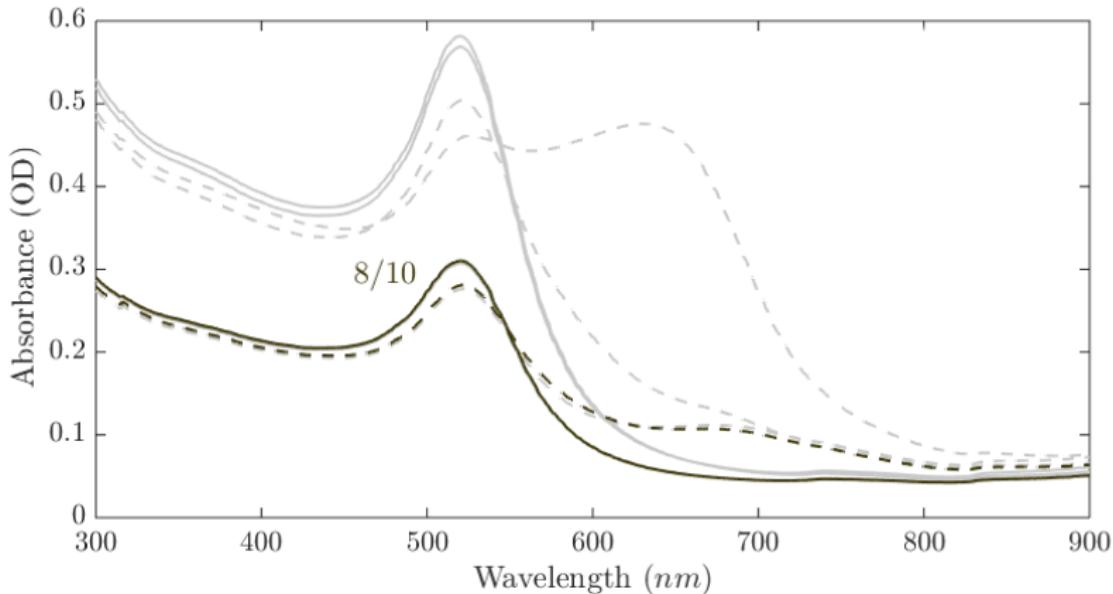


Absorption measurements (UV-Vis) to determine the optimal PEG proportion

2. Add NaCl and preform UV-Vis measurement

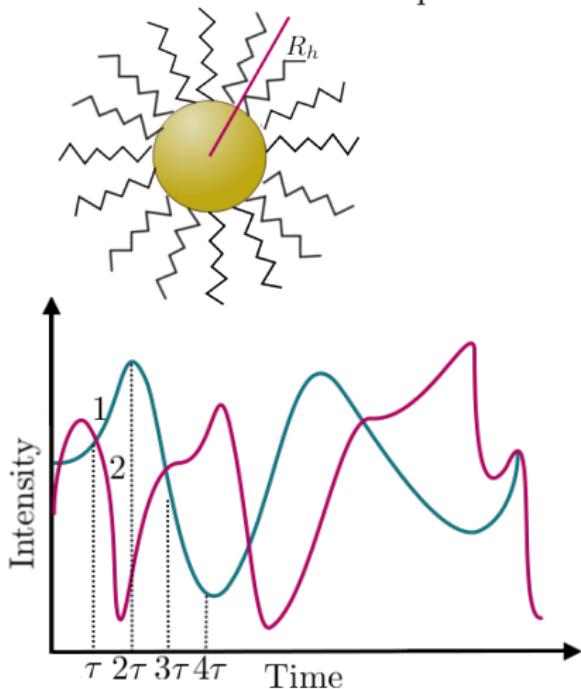


Absorption measurements (UV-Vis) to determine the optimal PEG proportion



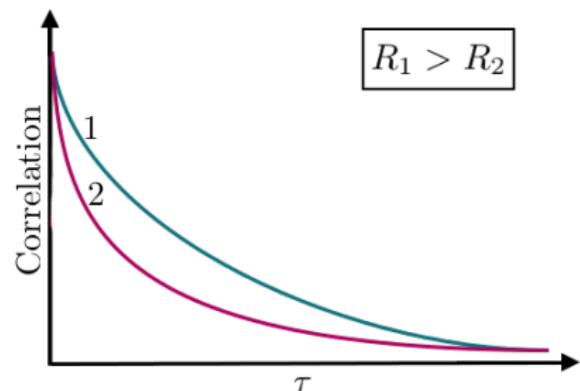
Light scattering experiments to determine the hydrodynamic radius (R_h)

Important for diffusive properties

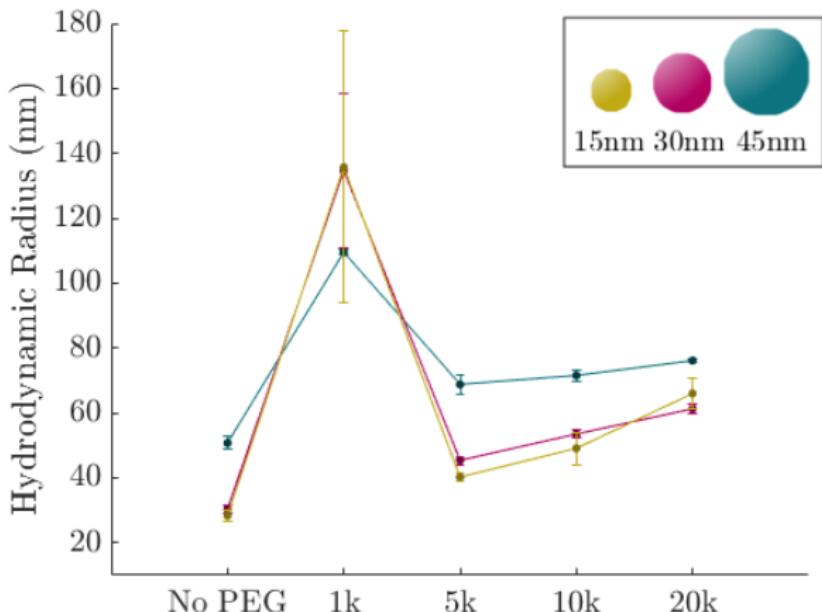


Correlation:

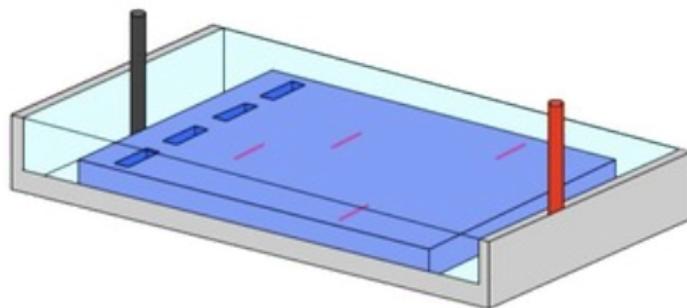
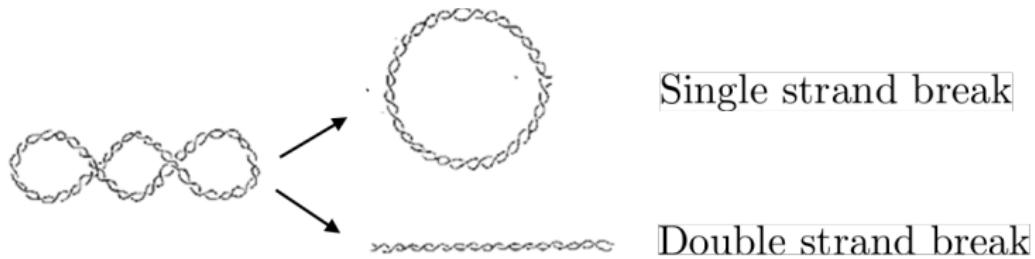
$$g(\tau) = \frac{\langle I(t) \rangle \langle I(t+\tau) \rangle}{\langle I(t) \rangle^2}$$



Hydrodynamic radii for the three different GNP with different functionalizations

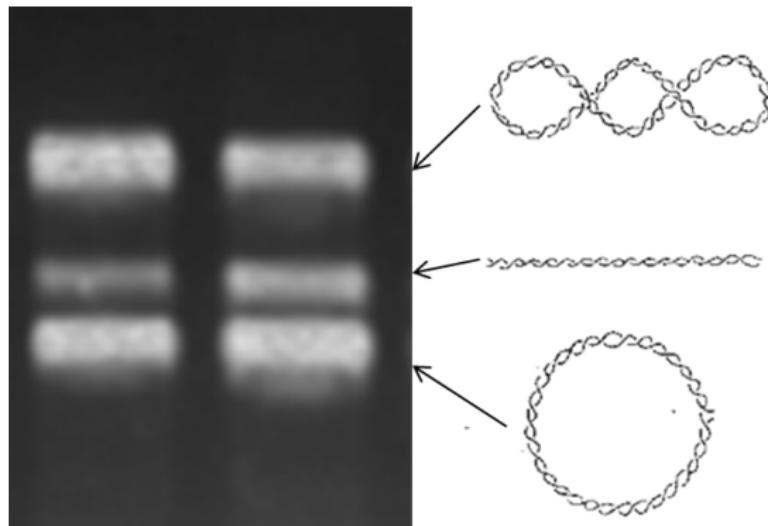


Gel electrophoresis to analyse DNA damage



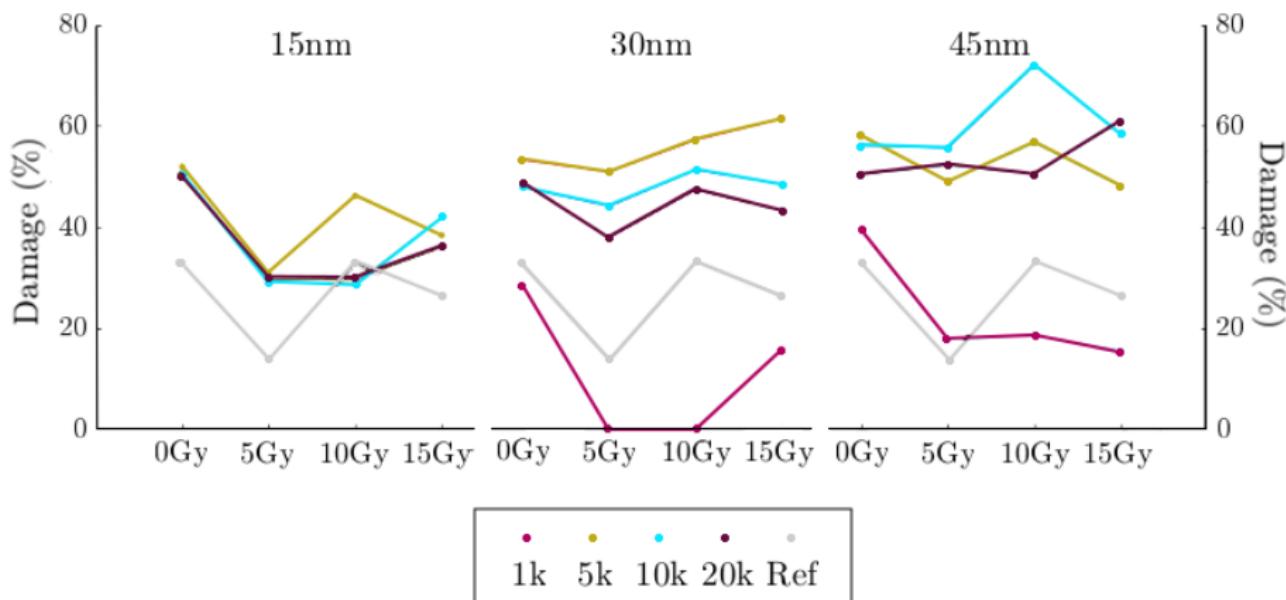
Sources: <https://www.quora.com/Whats-the-difference-between-a-plasmid-and-a-virus>.
<http://www.vce.bioninja.com.au/aos-3-heredity/molecular-biology-technique/dna-profiling.html>

Gel electrophoresis to analyse DNA damage



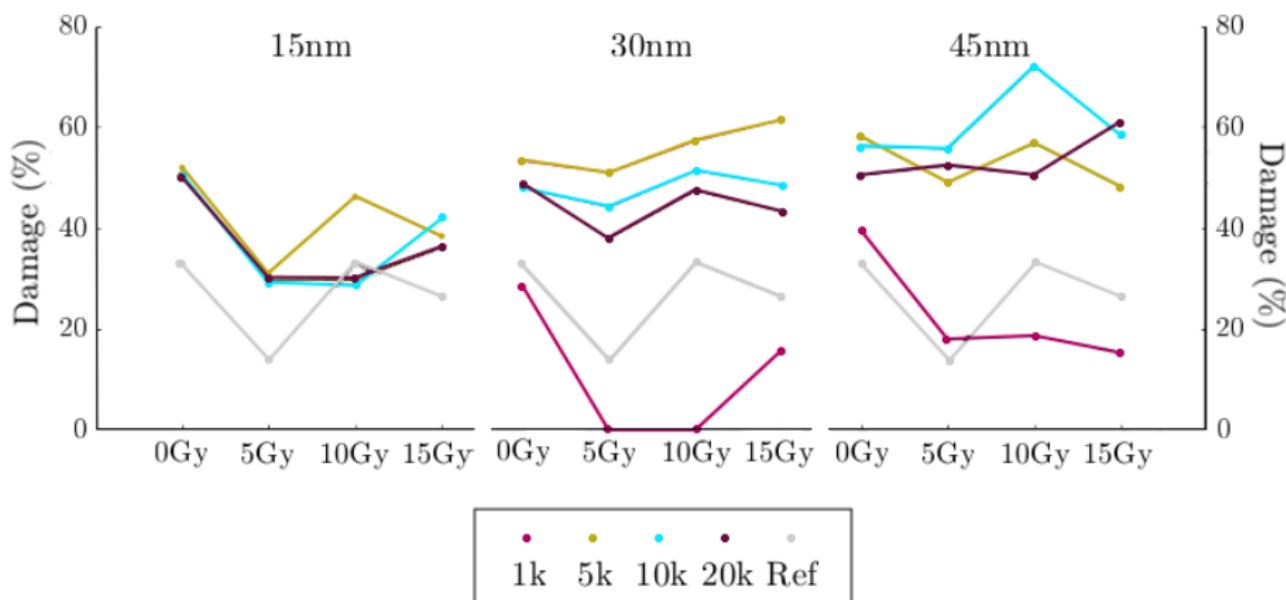
Source: Maunus R et al. Horton JR, Zhang X. Nucleic Acids Research, 34(3):939-948, 2006.

DNA damage analysis



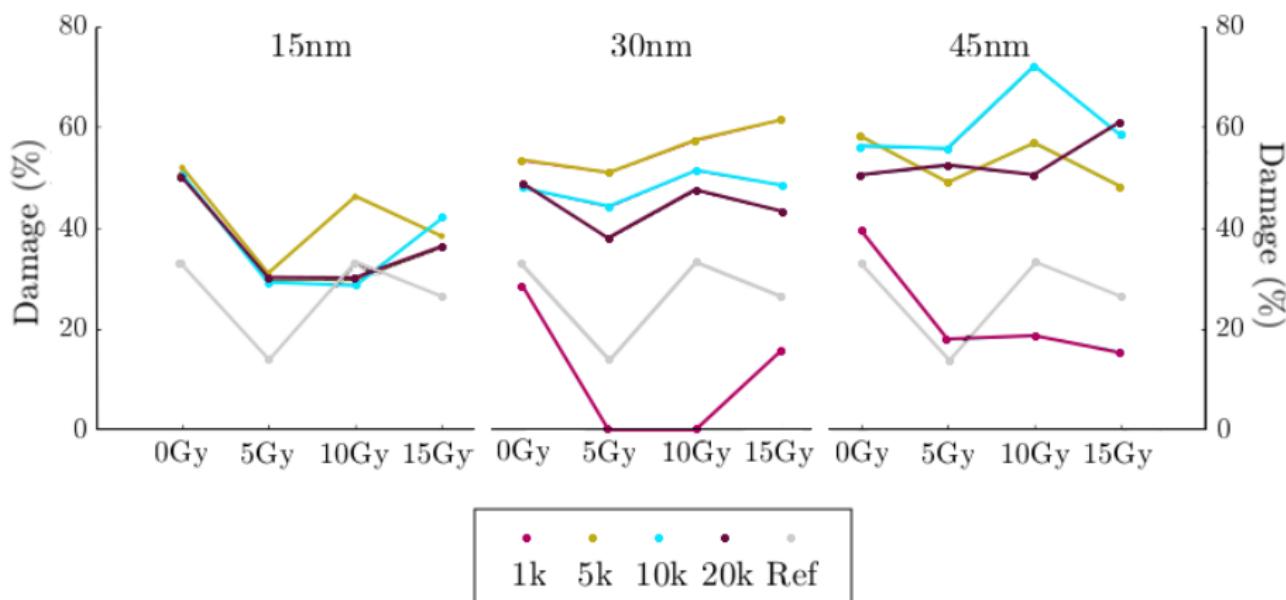
DNA damage analysis

Strange results for 1 k PEG



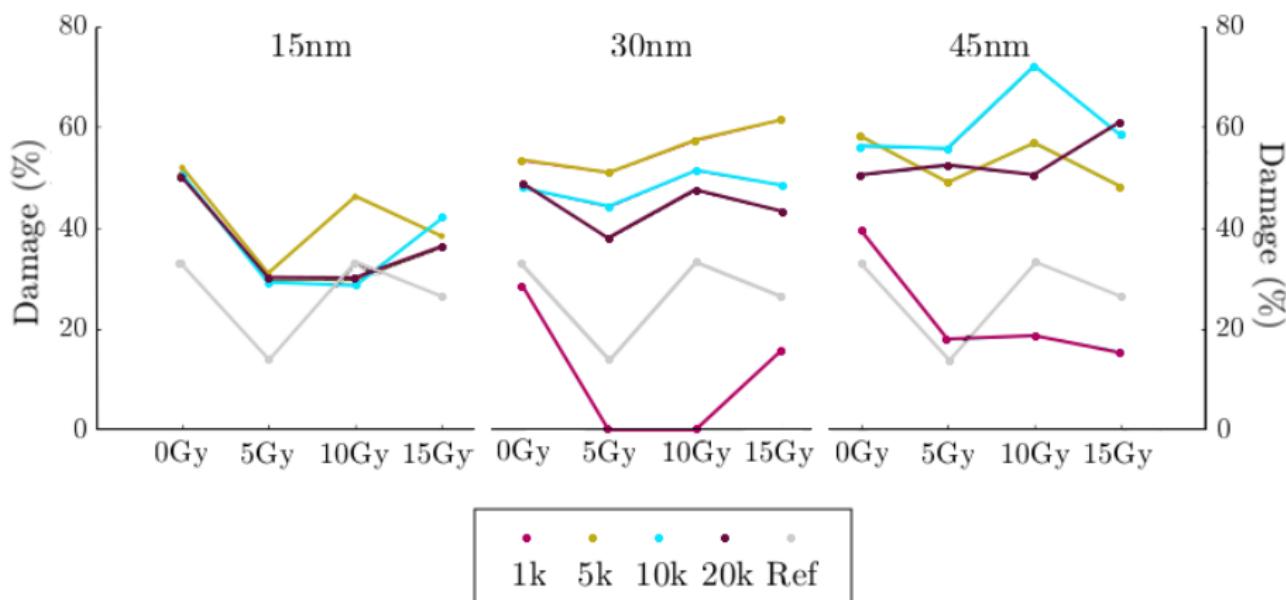
DNA damage analysis

Curves are not rising



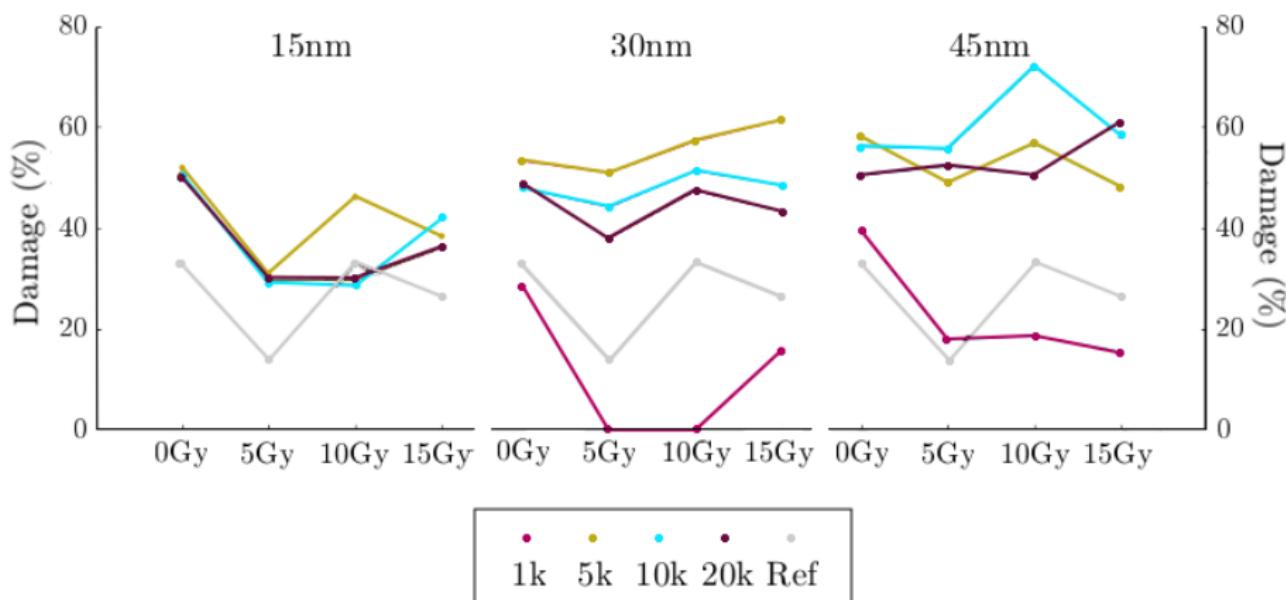
DNA damage analysis

Reference sample has an unexpected form



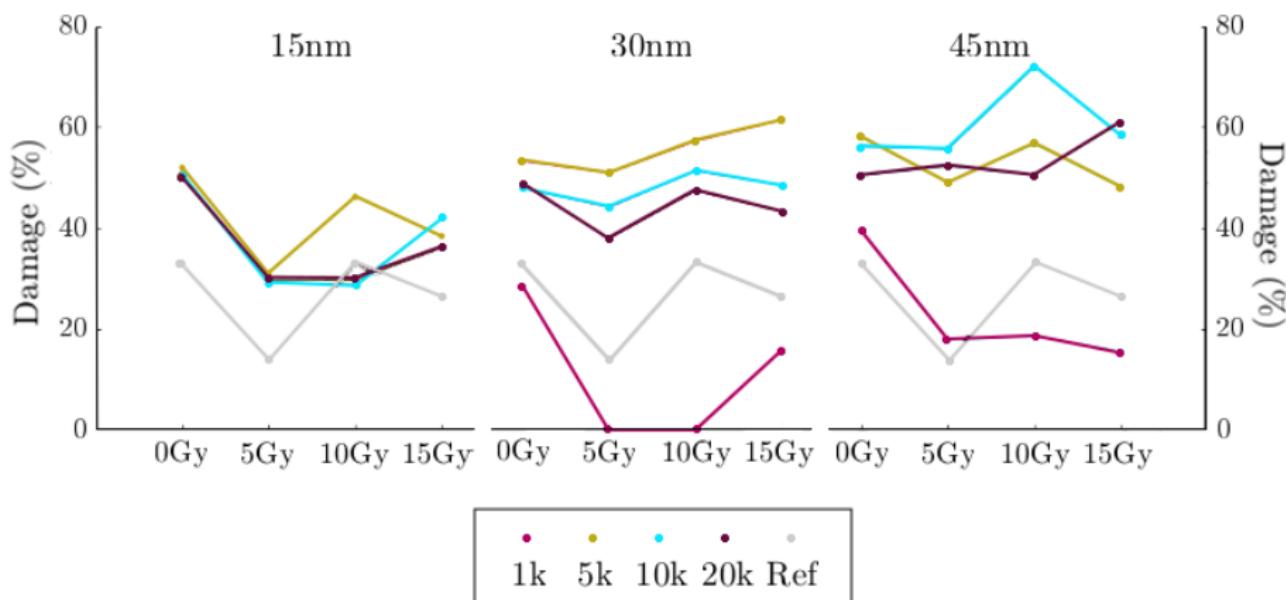
DNA damage analysis

DNA damage at 0 Gy



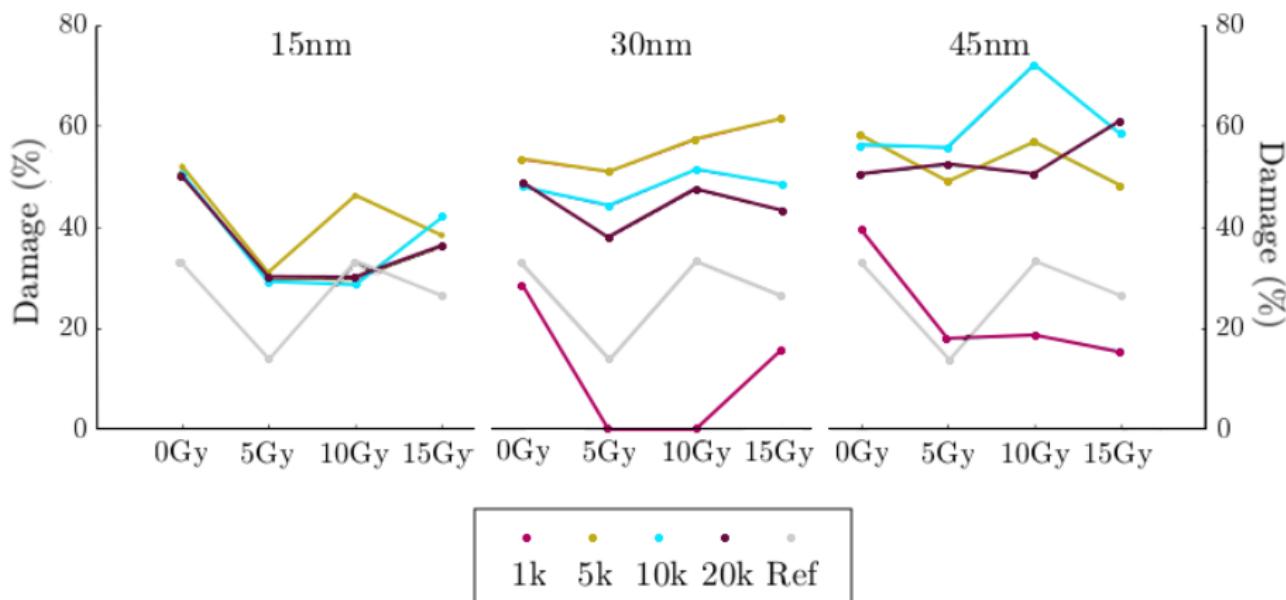
DNA damage analysis

Radiosensitization effect is present



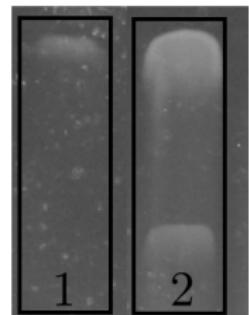
DNA damage analysis

Smaller PEG → more DNA damage
Larger GNP → more DNA damage



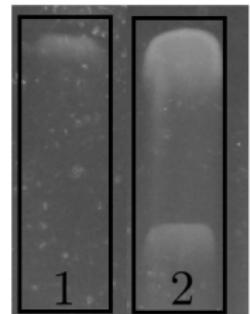
Conclusion DNA damage analysis

- 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 → more DNA damage
- Larger GNP → 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 → more DNA damage
- Larger GNP → more DNA damage



Conclusion

- Functionalization 1k PEG strange behavior
 - Best results with...
 - ...5k functionalization
 - ...largest particles (45 nm)
- ⇒ Radiosensitization effect observed

