Bachelor Thesis 2016

Radiosensitization using gold nanoparticles

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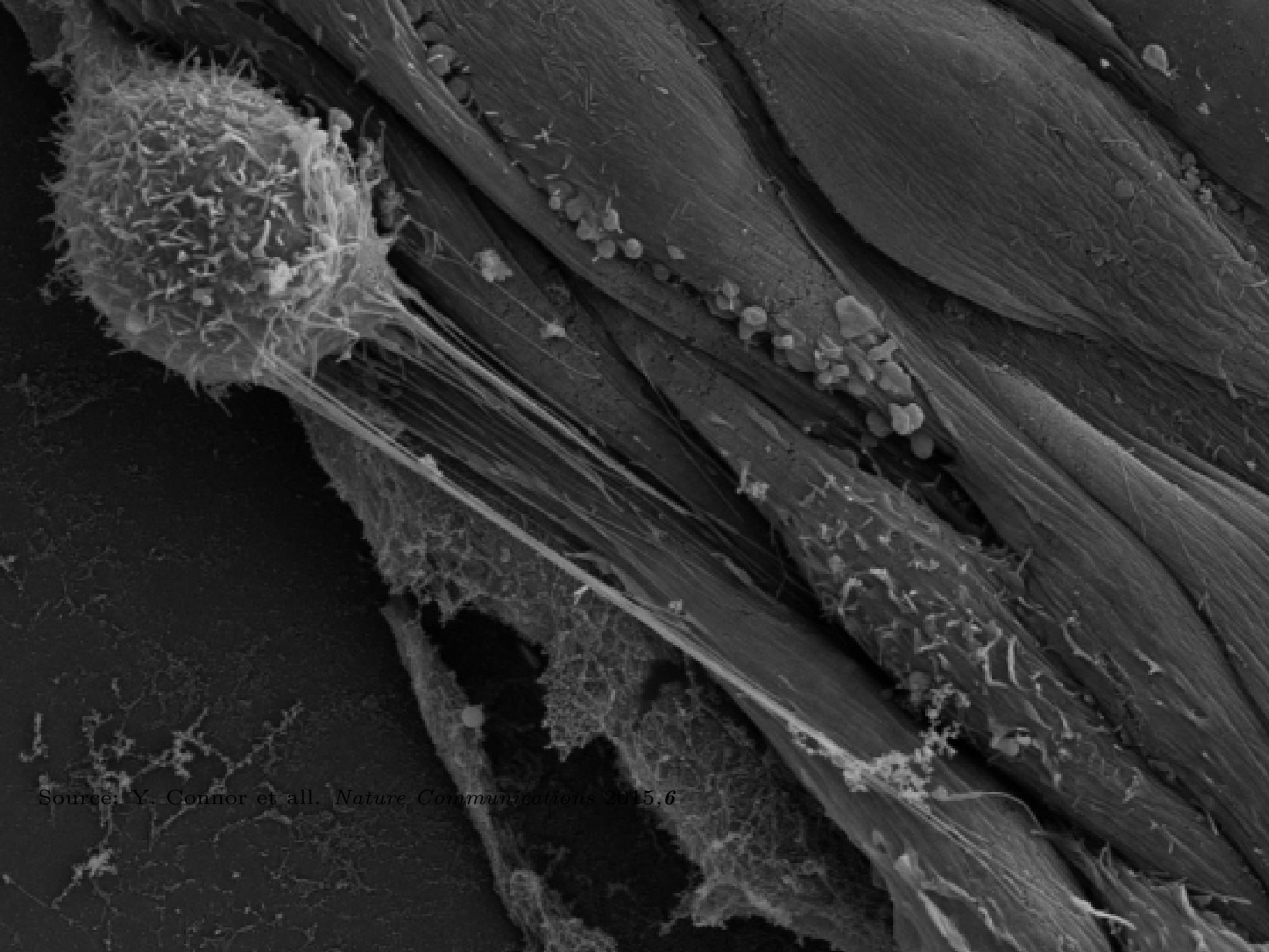
Mattias Vervaele
Professor: Jean-Pierre Locquet

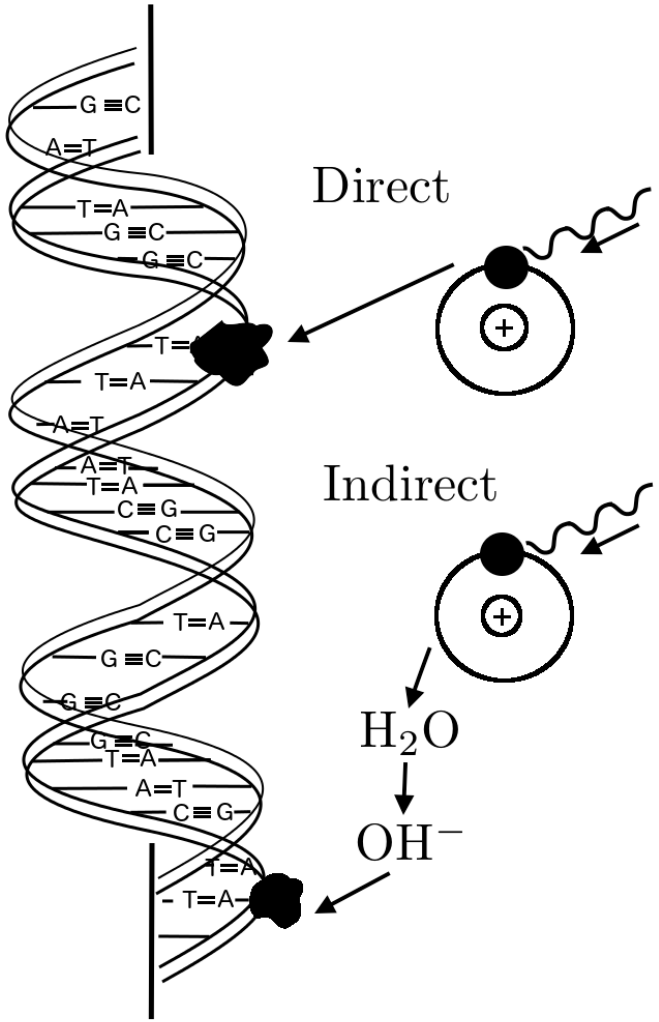


Source: Y. Connor et all. *Nature Communications* 2015,***6***

DNA damage using ionizing radiation

- Chemotherapy
- Surgery
- **Radiation therapy**

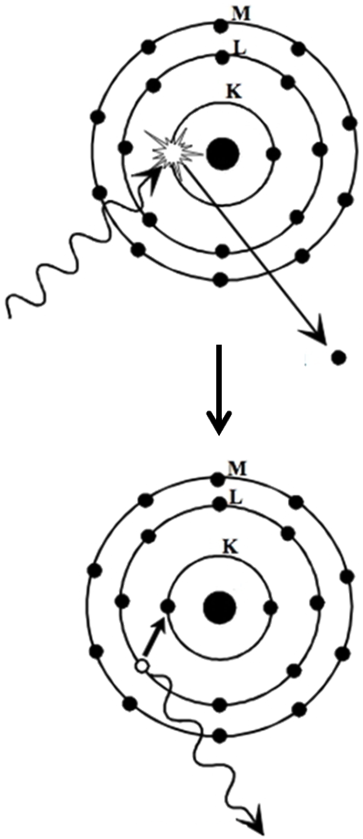
  Energy $\sim$ MeV



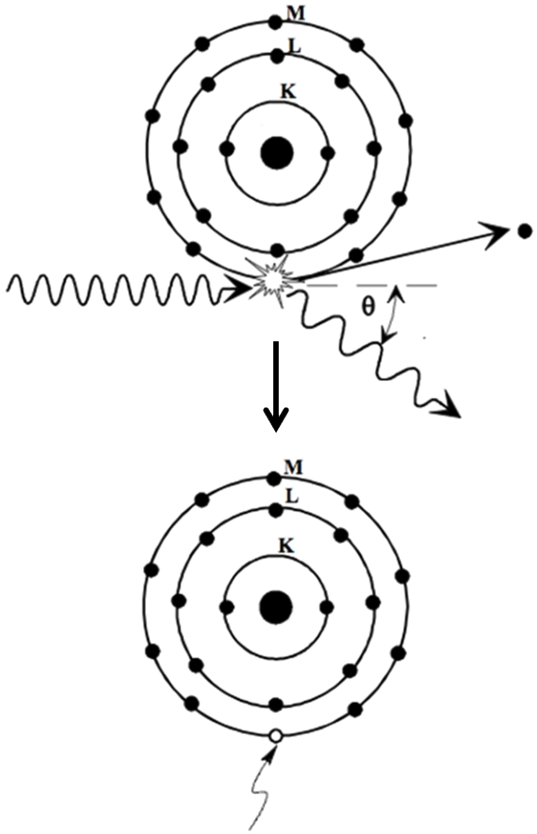
Source: https://chem.kuleuven.be/veiligheid/info/ioniserende-st.html

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

Photoelectric absorption



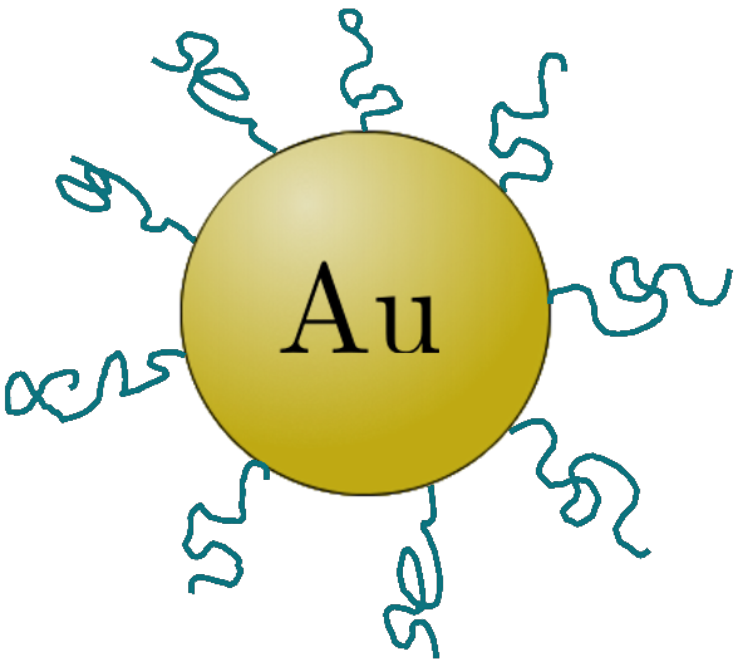
Compton effect



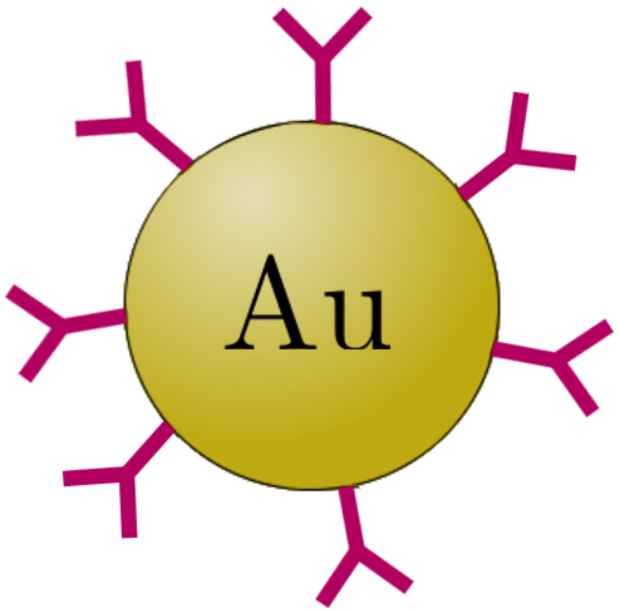
Source: https://en.wikibooks.org/wiki/Basic_Physics_of_Digital_Radiography/The_Patient

Targeting of the GNP to the tumor

Passive targeting
PEG coating



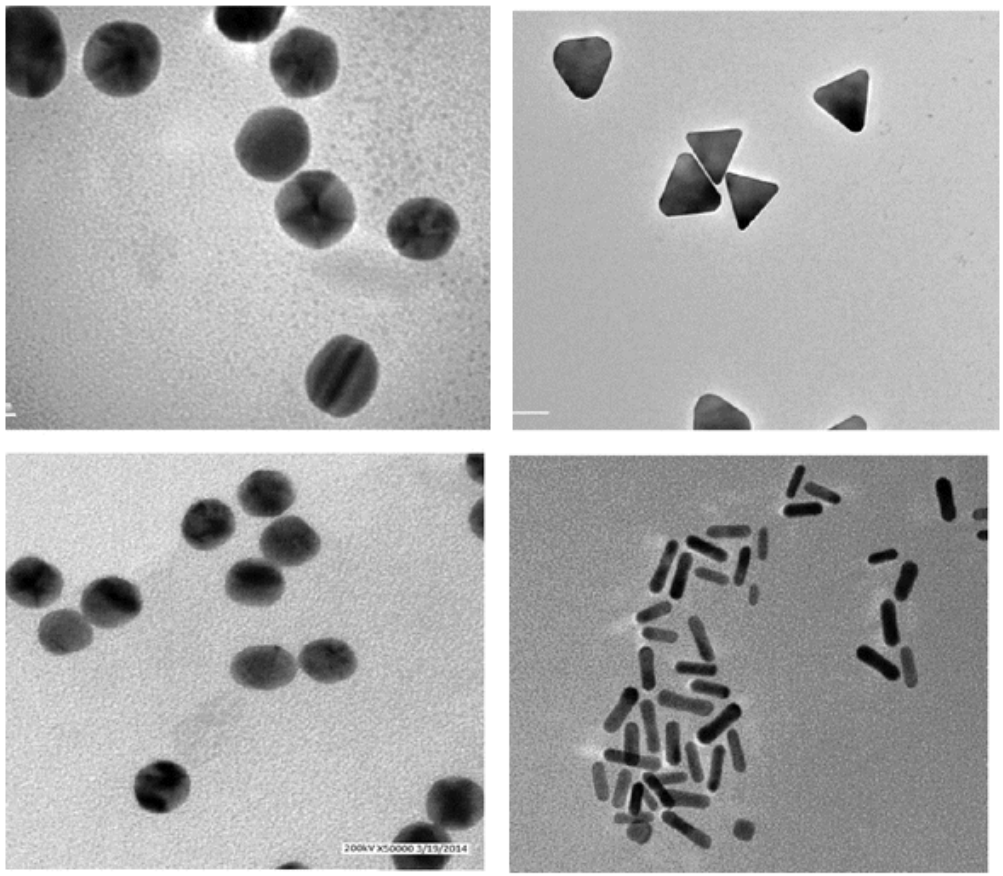
Active targeting
Antibodies



Overview Project

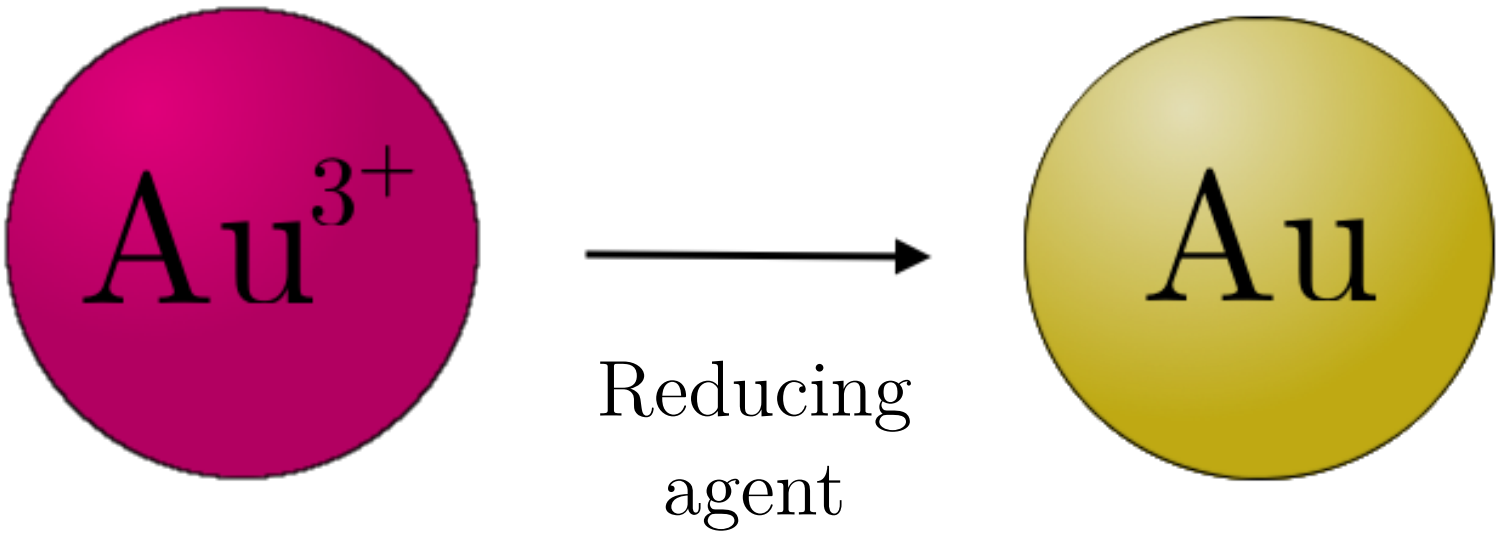
Radiosensitization of DNA using gold nanoparticles

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



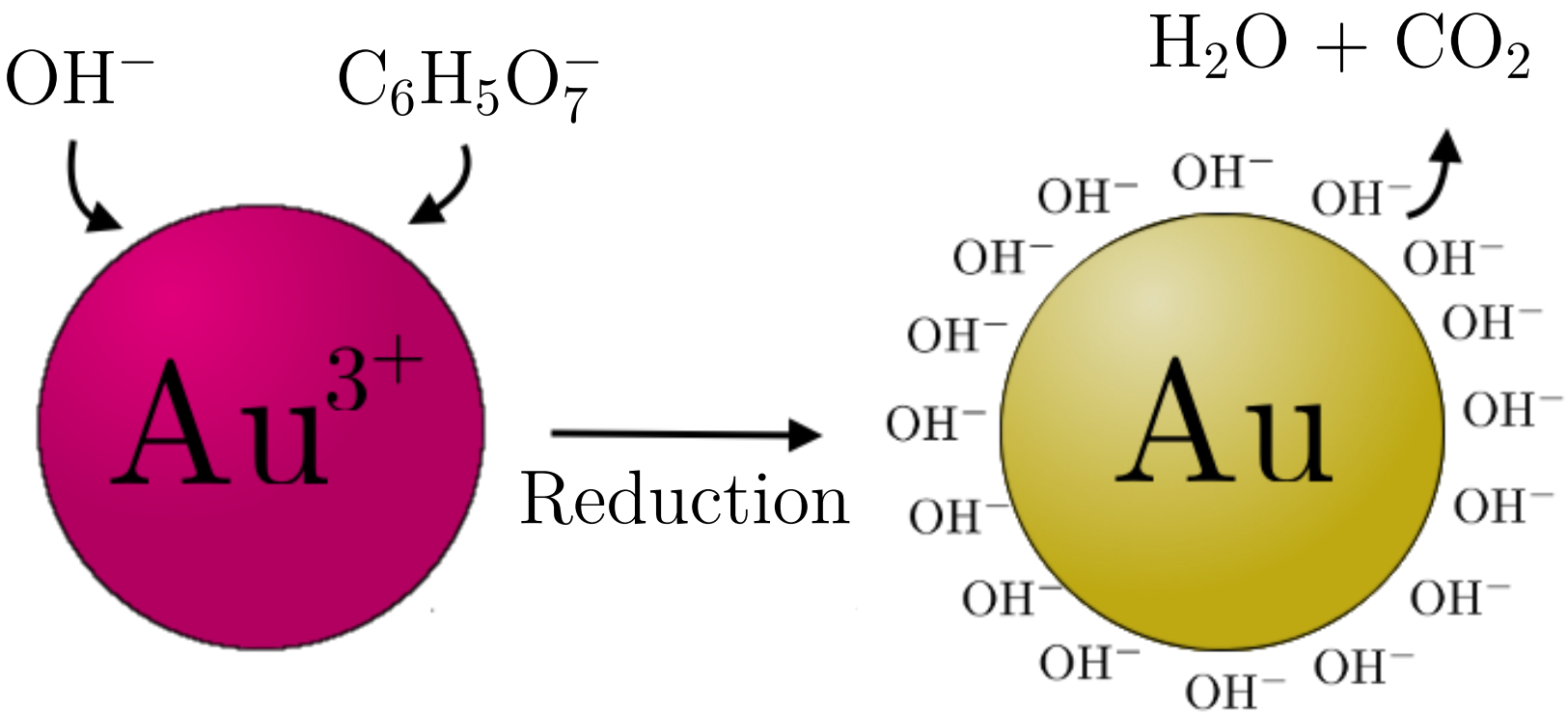
Source: A. Chaudhary et all. *Phys. Chem. Chem. Phys., 2014* ***16***

Reduction of gold ions to form GNP



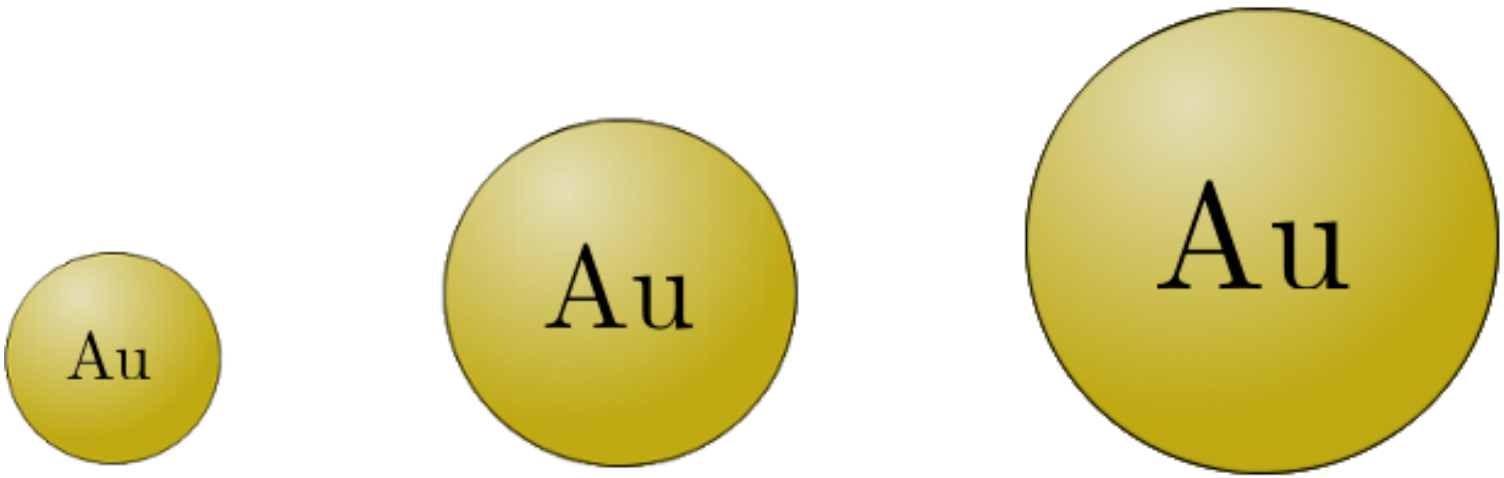
Gold ions: $HAuCl_4$ solution
Reducing agent: $Na_3C_6H_5O_7$

Reduction of gold ions to form GNP



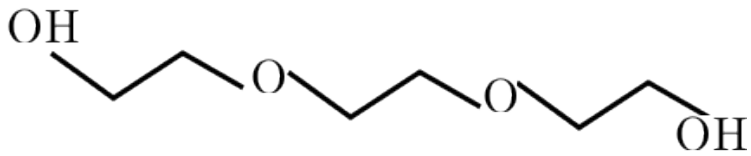
$$6Au^{3+} + C_6H_5O_7^{3-} + 15OH^- \rightarrow Au + 6CO_2 + 10H_2O$$

The amount of citrate controls the size

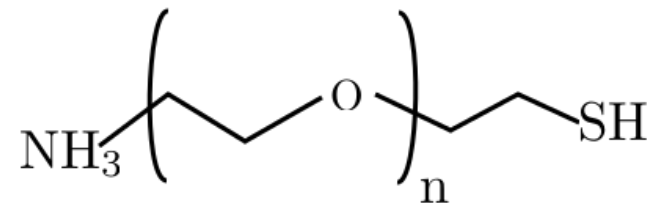


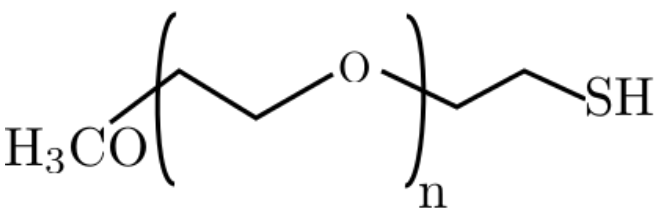
Citrate 1%
100ml $HAuCl_4$ 0.01%

PEG for targeting and stabilization

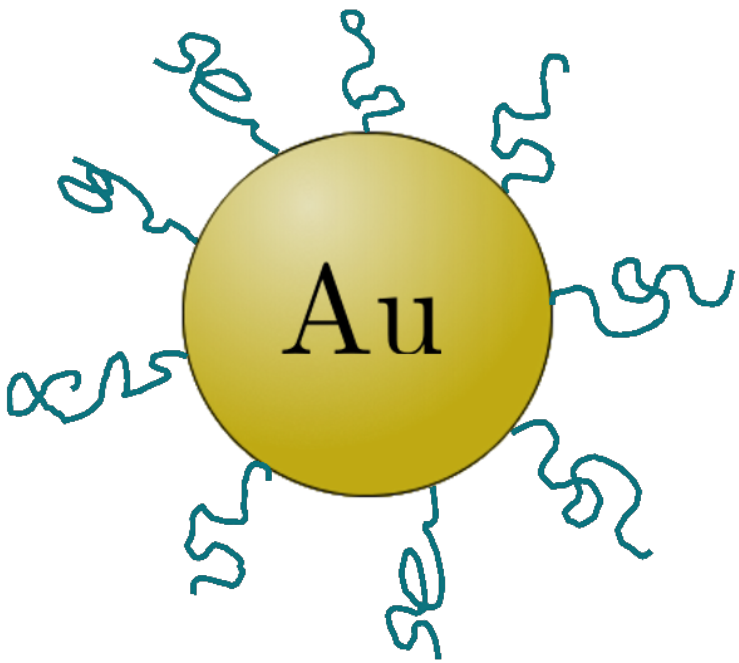


Polyethylene glycol

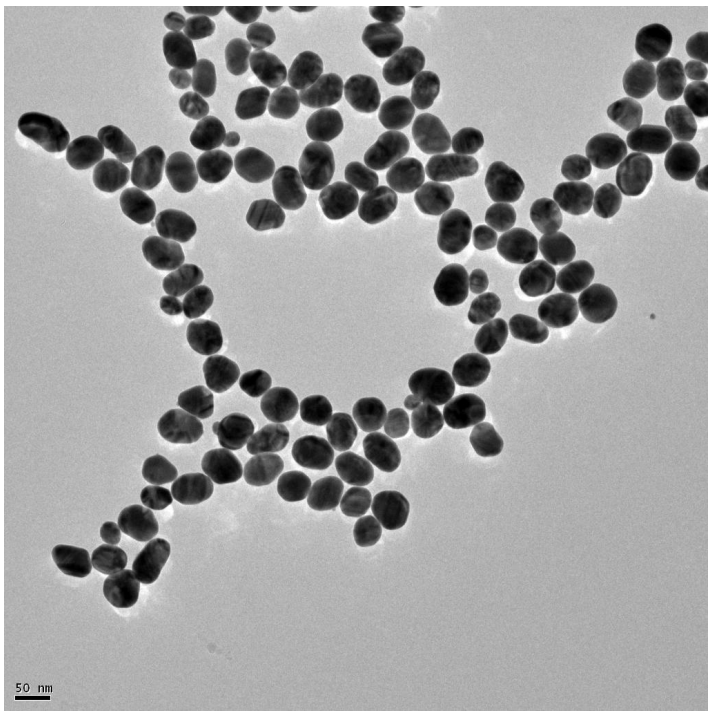


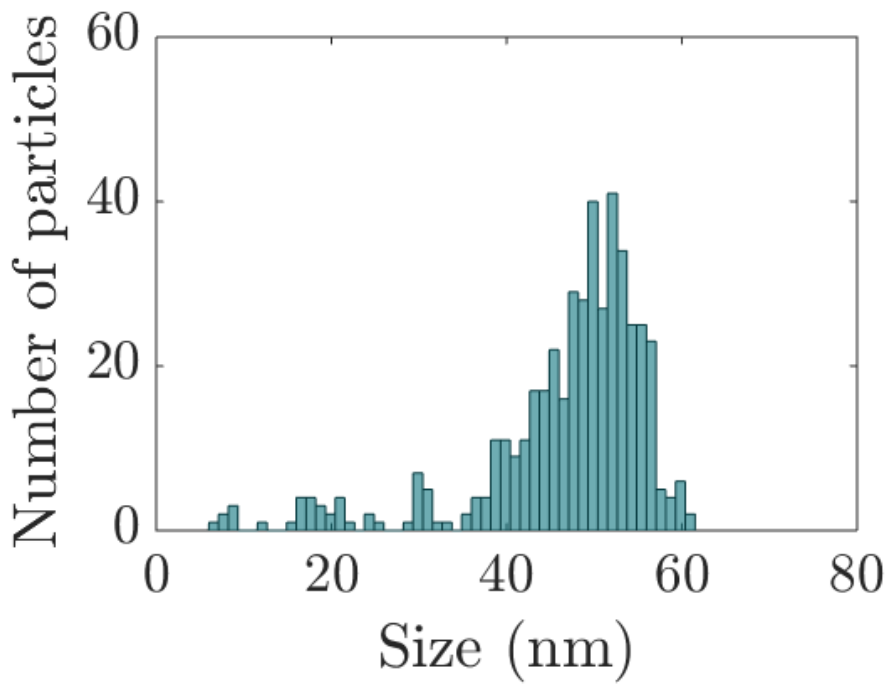


1k, 5k, 10k, 20k

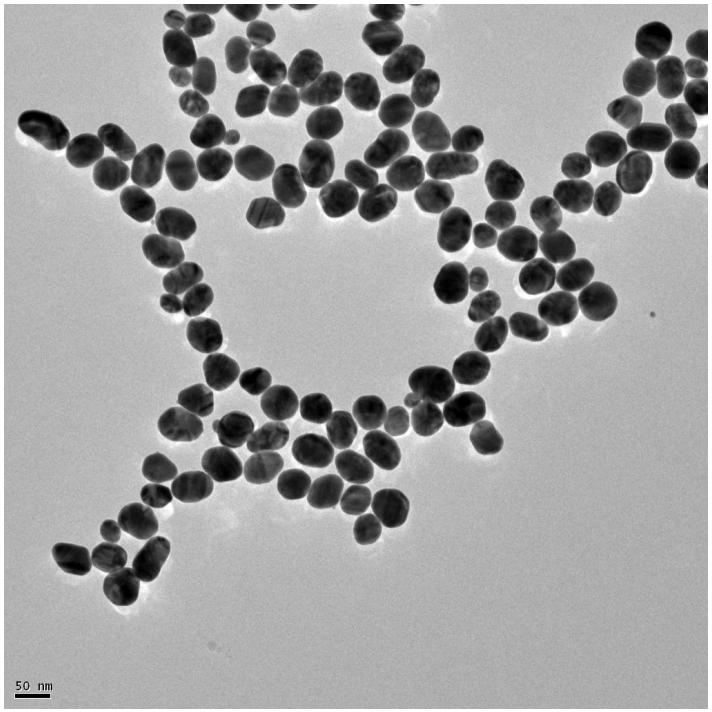


TEM image analysis to determine the core diameter



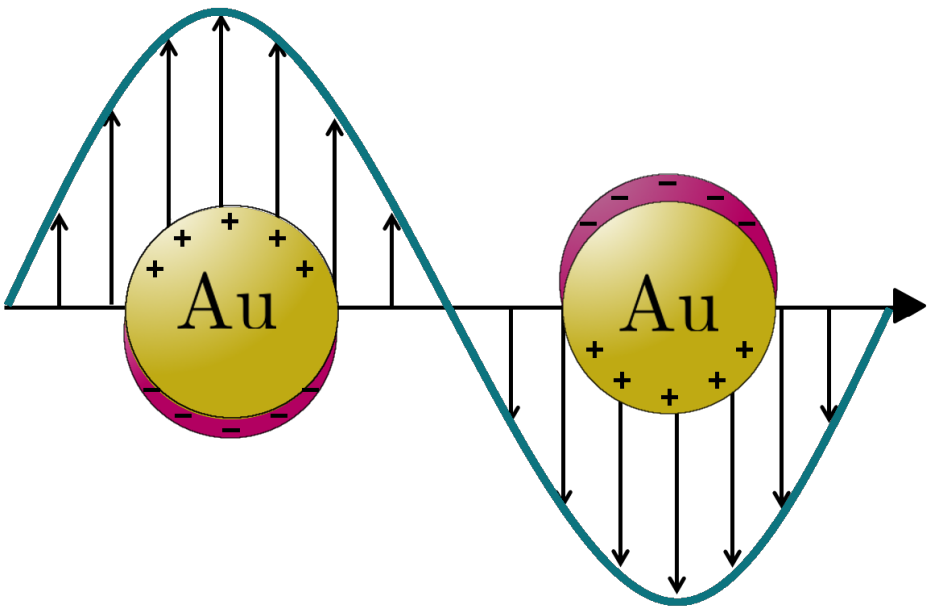


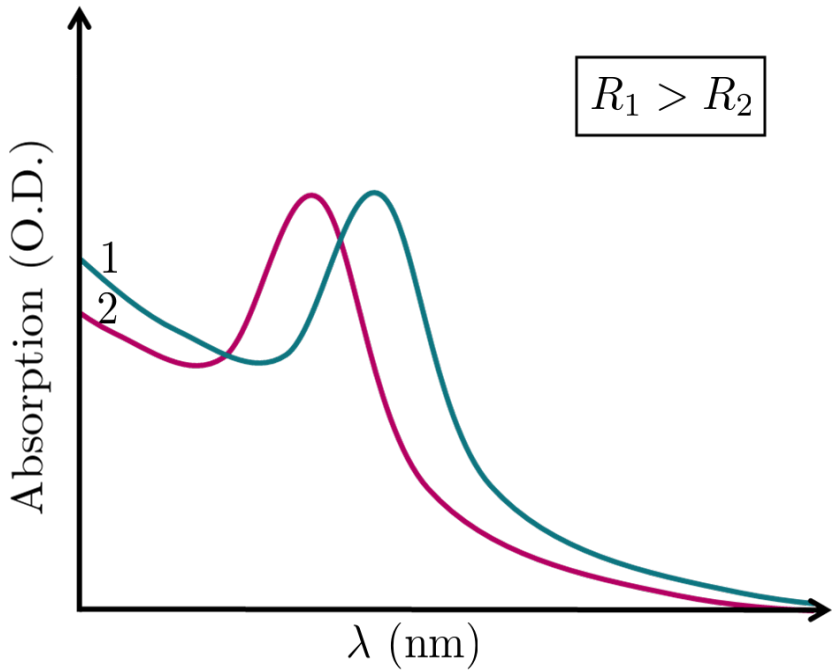
TEM image analysis to determine the core diameter



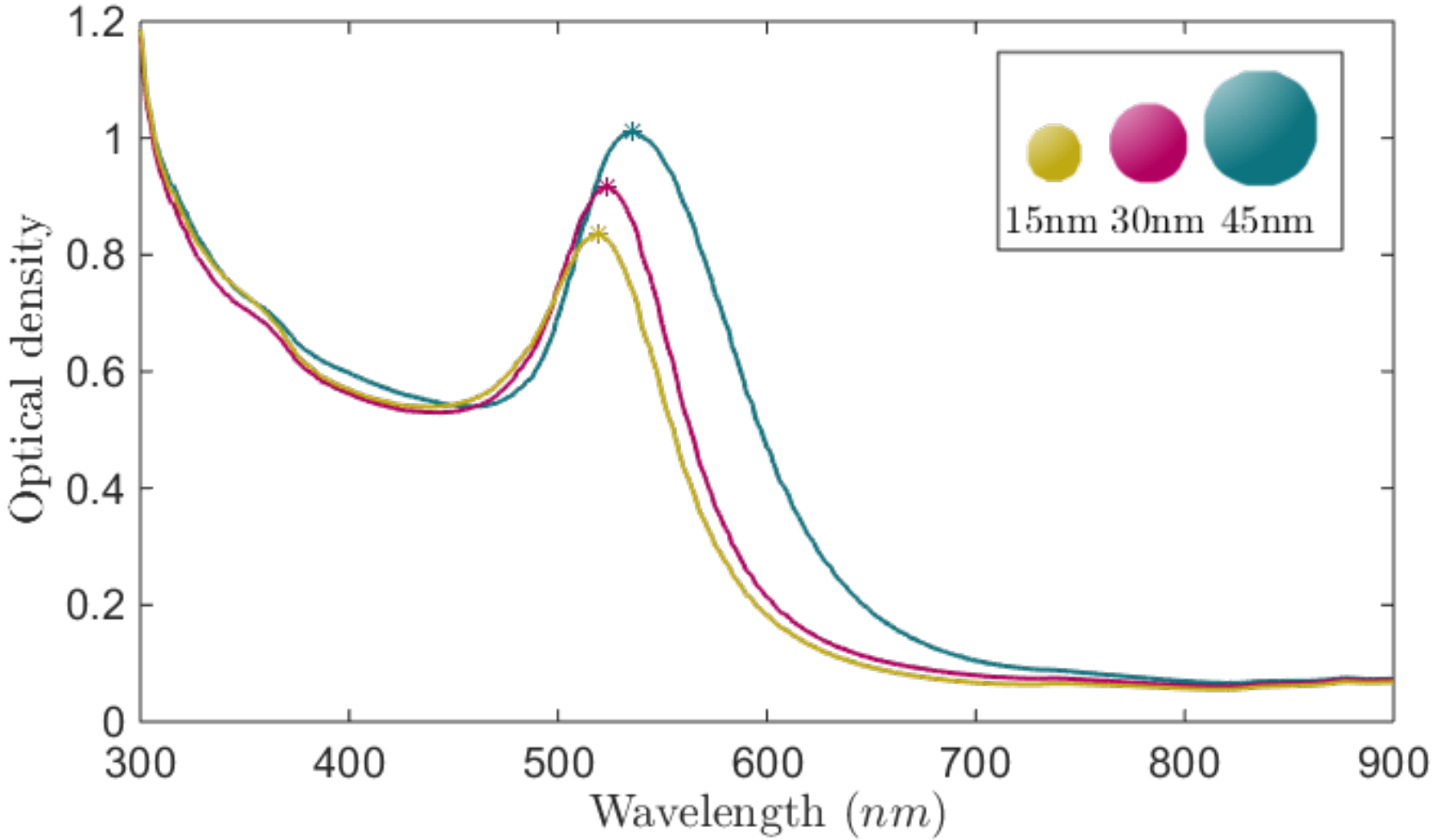
Exp. Size (nm)	Size (nm)
15	12.98 ± 0.23
	2.99 ± 0.16
30	18.29 ± 0.23
45	46.75 ± 0.47

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



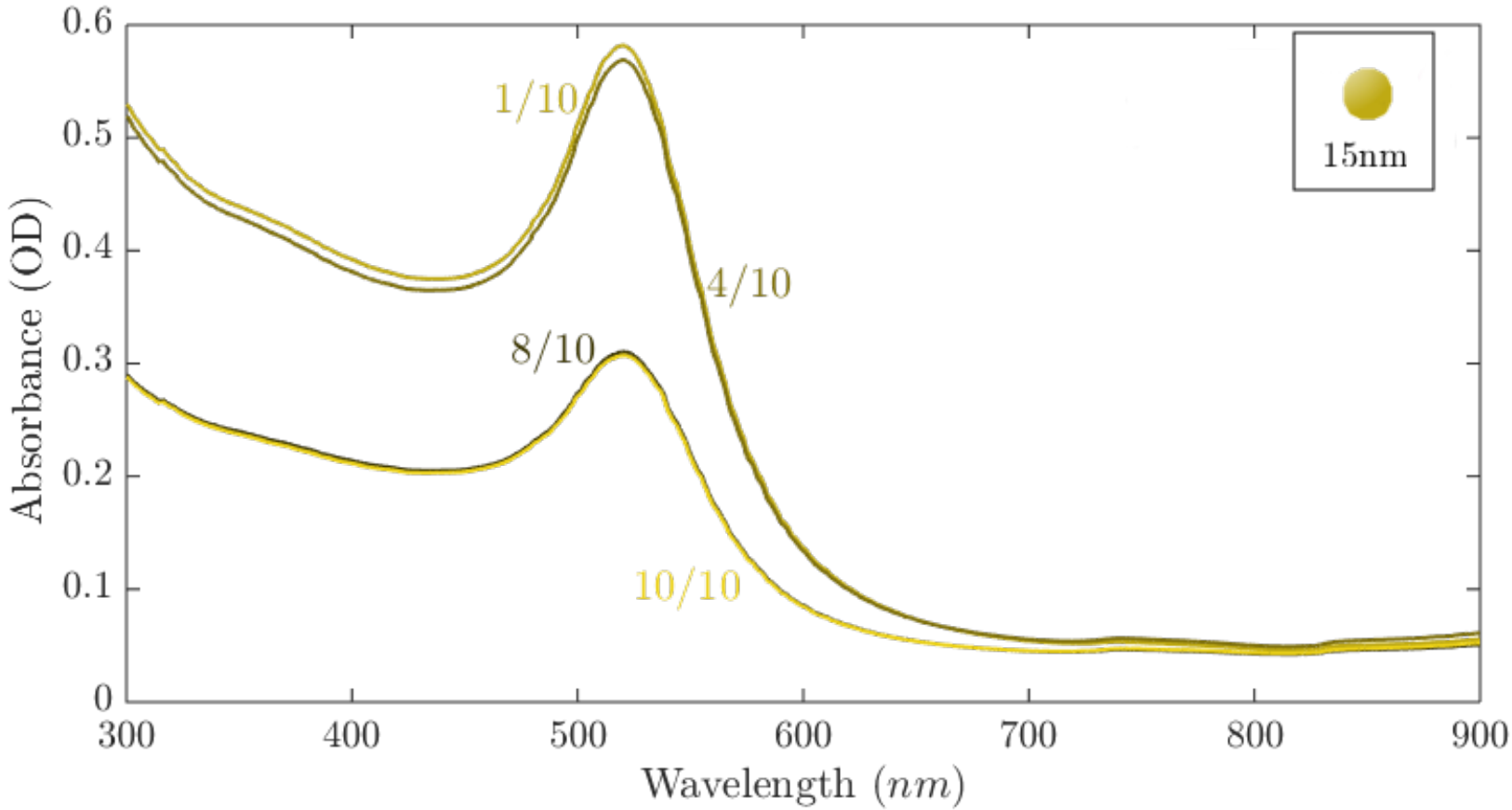


Absorption measurements (UV-Vis) to determine the relative size



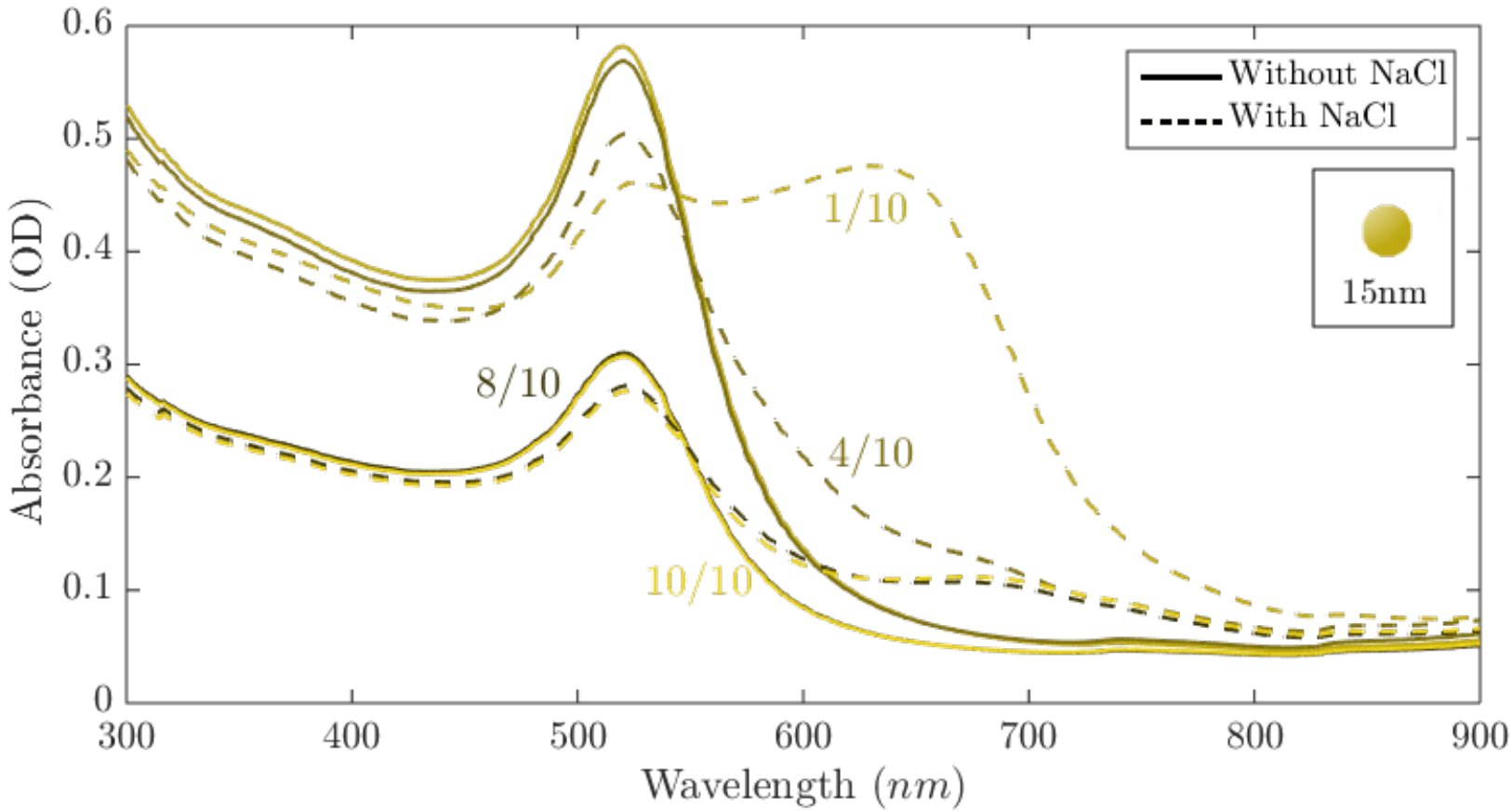
Absorption measurements (UV-Vis) to determine the optimal PEG proportion

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

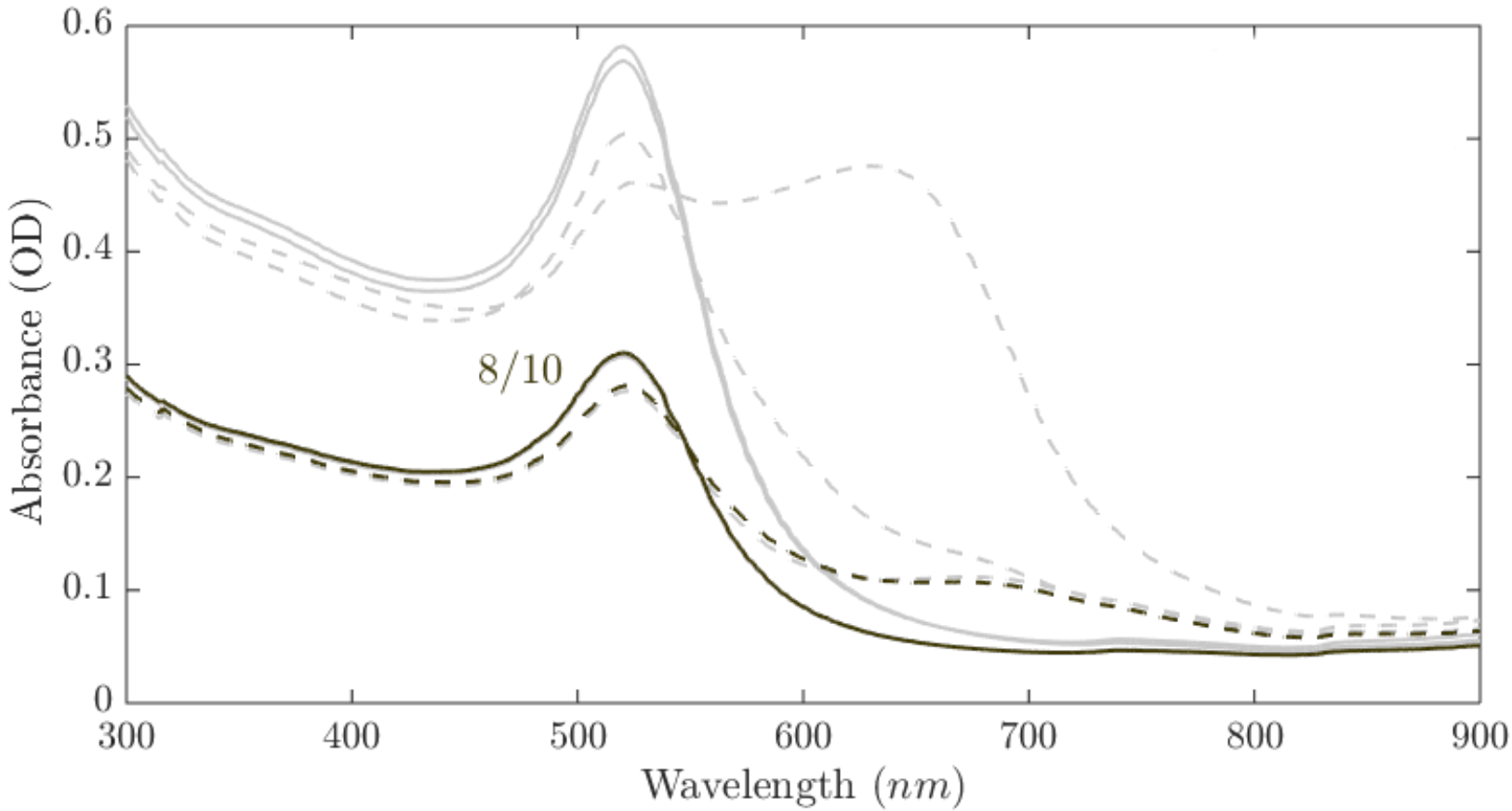


Absorption measurements (UV-Vis) to determine the optimal PEG proportion

2. Add NaCl and preform UV-Vis measurement

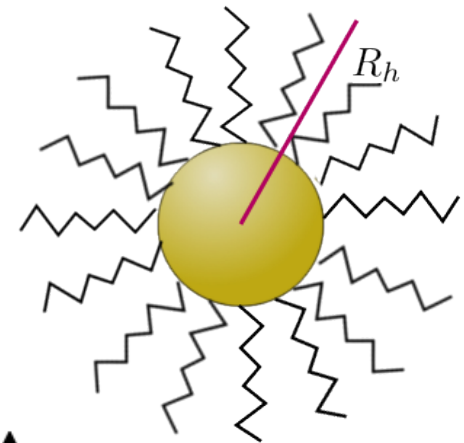


Absorption measurements (UV-Vis) to determine the optimal PEG proportion



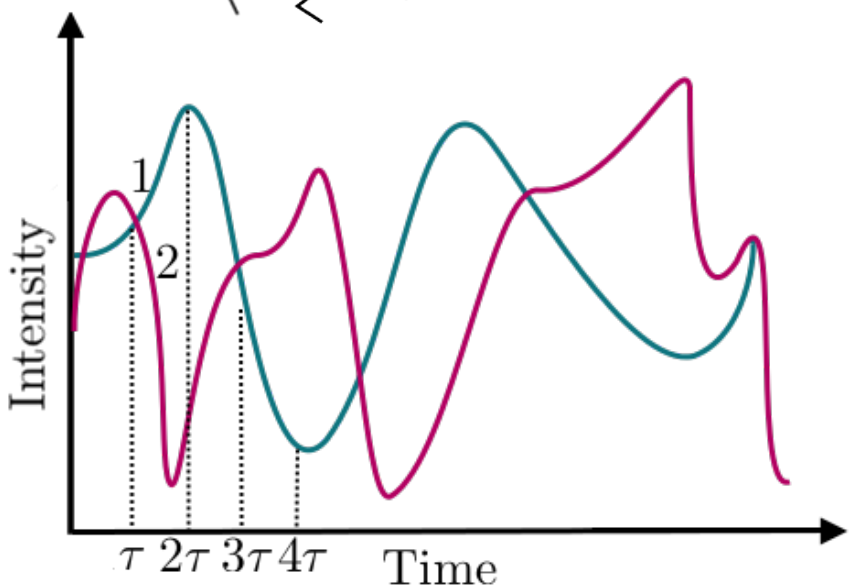
Light scattering experiments to determine the hydrodynamic radius (R_h)

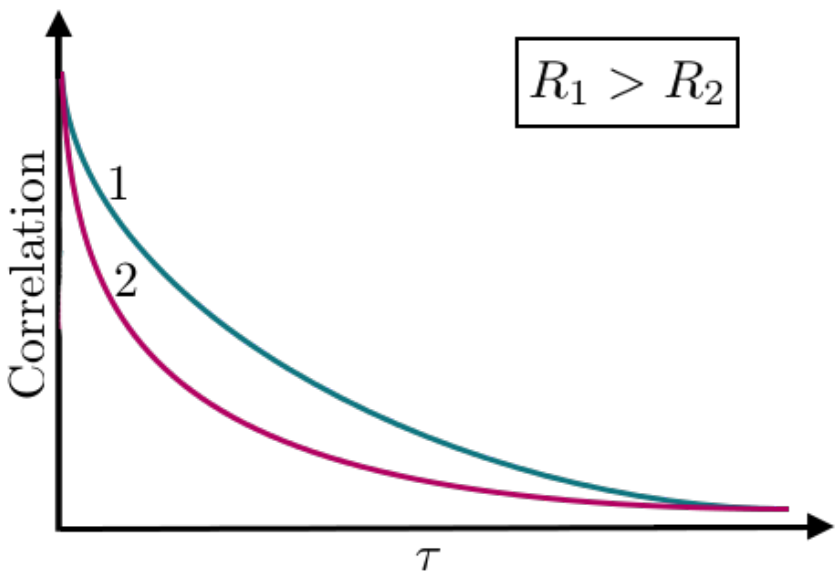
Important for diffusive properties



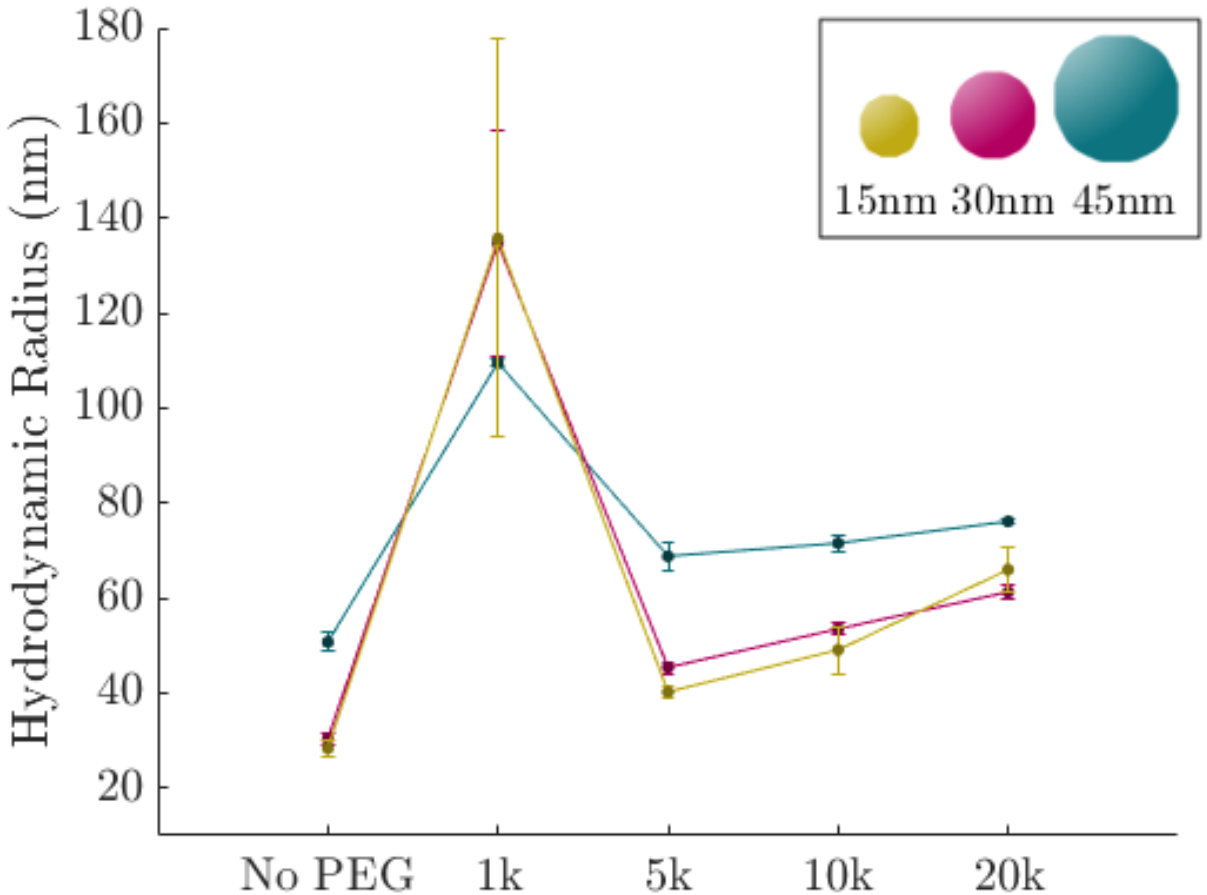
Correlation:

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

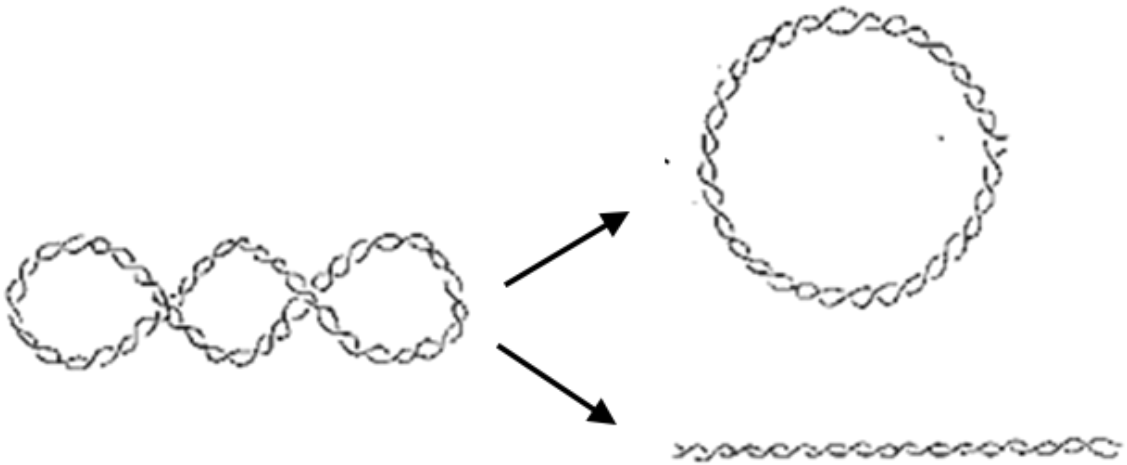




Hydrodynamic radii for the three different GNP with different functionalizations



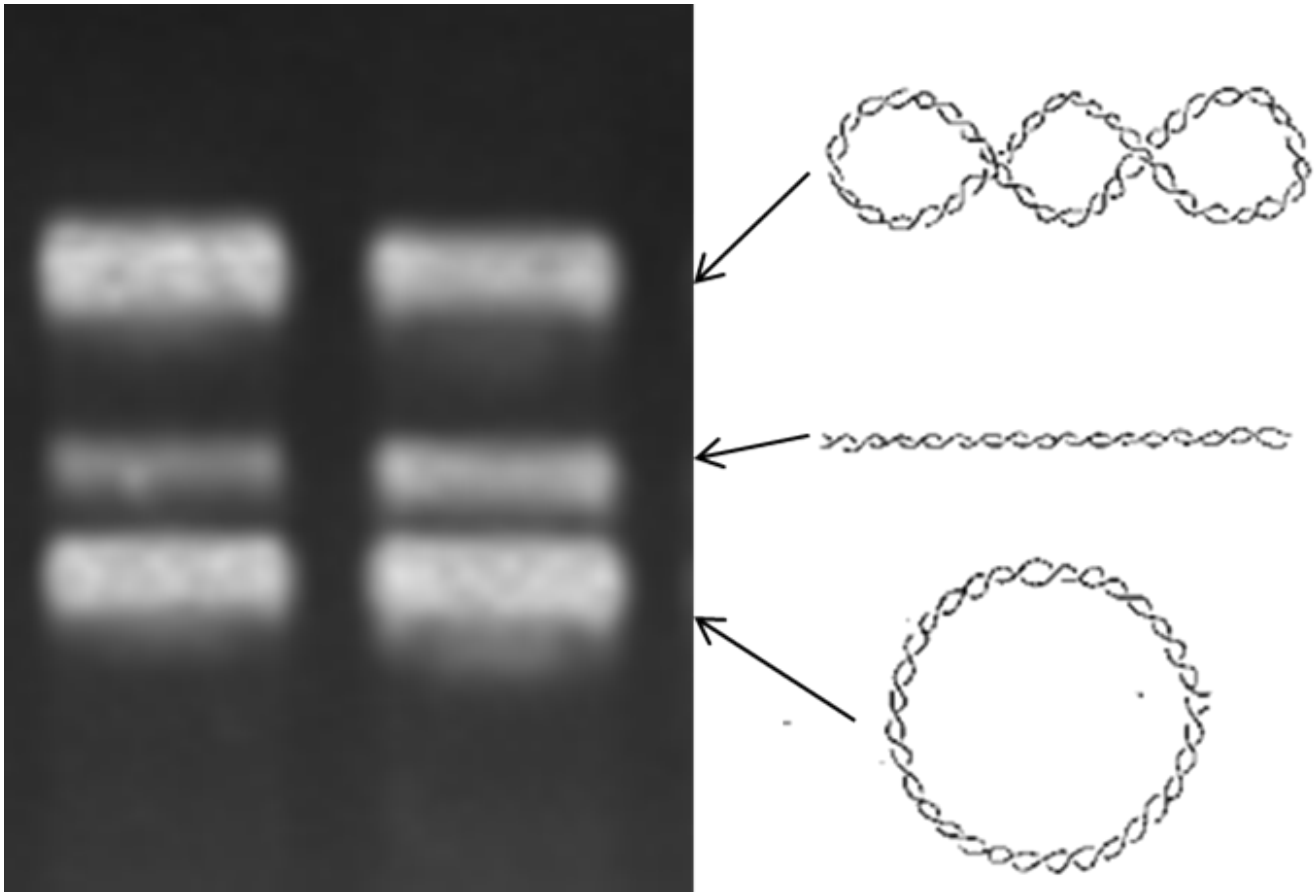
Gel electrophoresis to analyse DNA damage



Single strand break

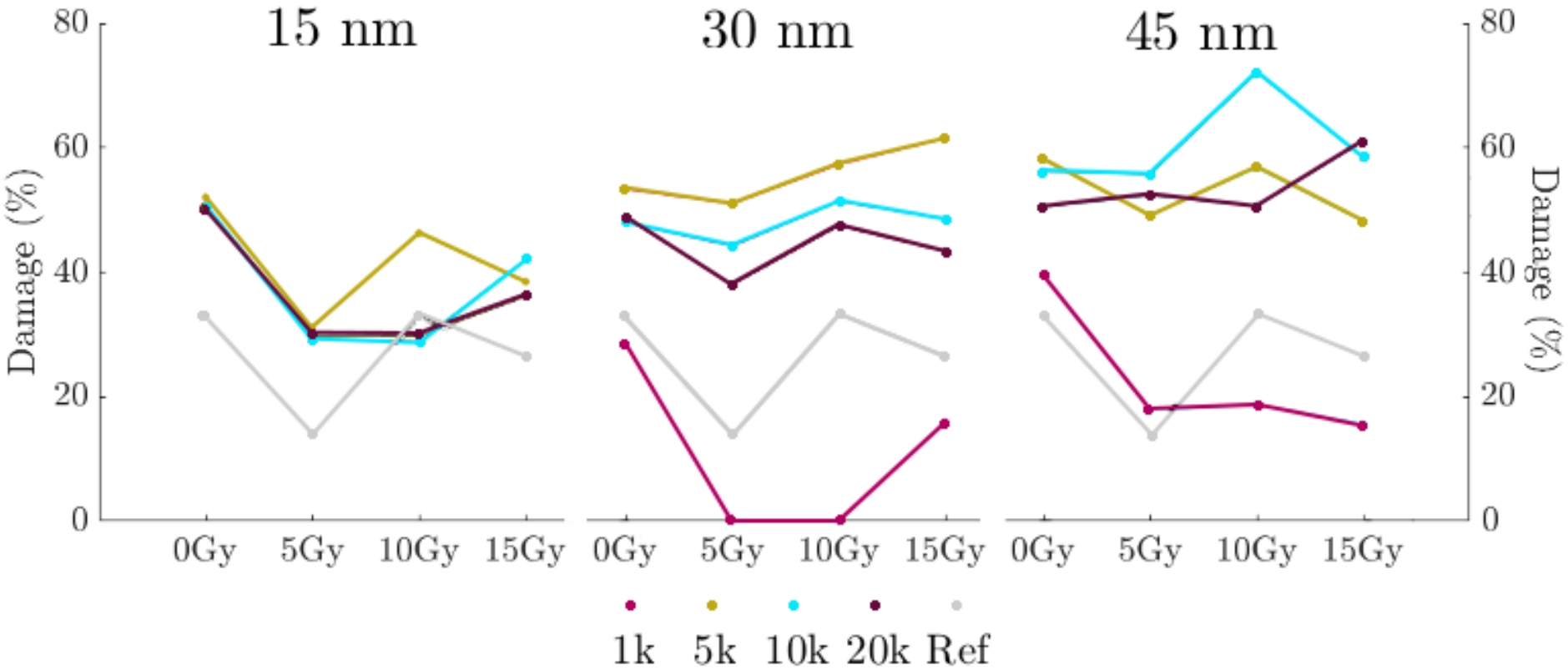
Double strand break

Gel electrophoresis to analyse DNA damage



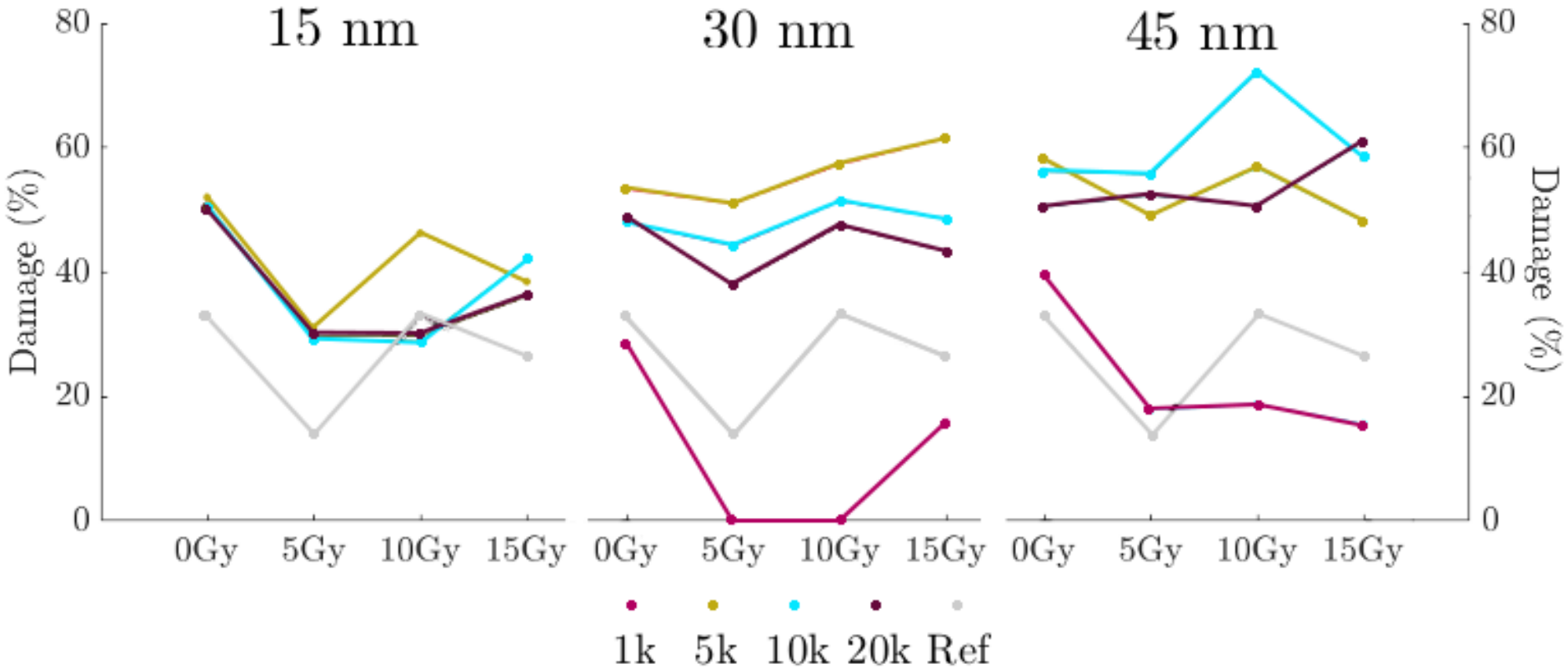
Source: Maunus R et al. Horton JR, Zhang X. Nucleic Acids Research, 34(3):939âĂŞ948, 2006.

DNA damage analysis



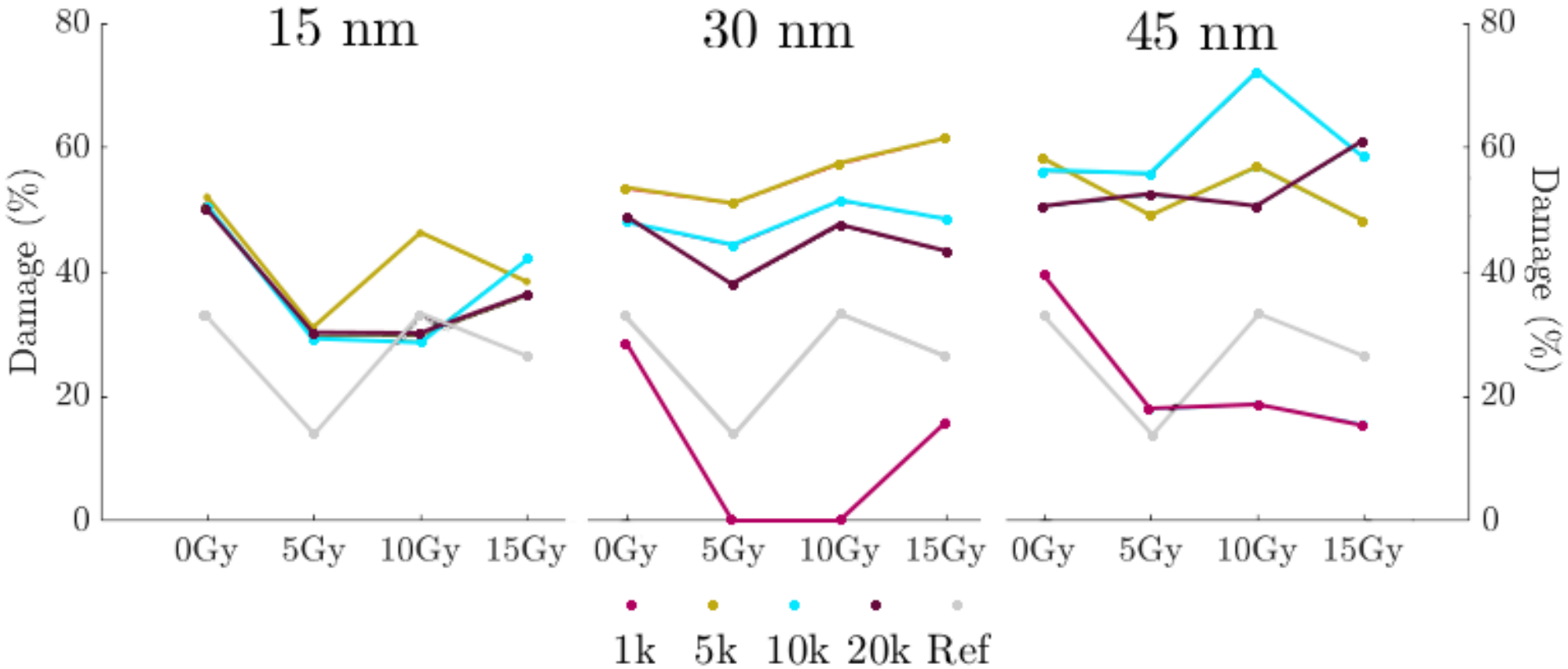
DNA damage analysis

Strange results for 1 k PEG



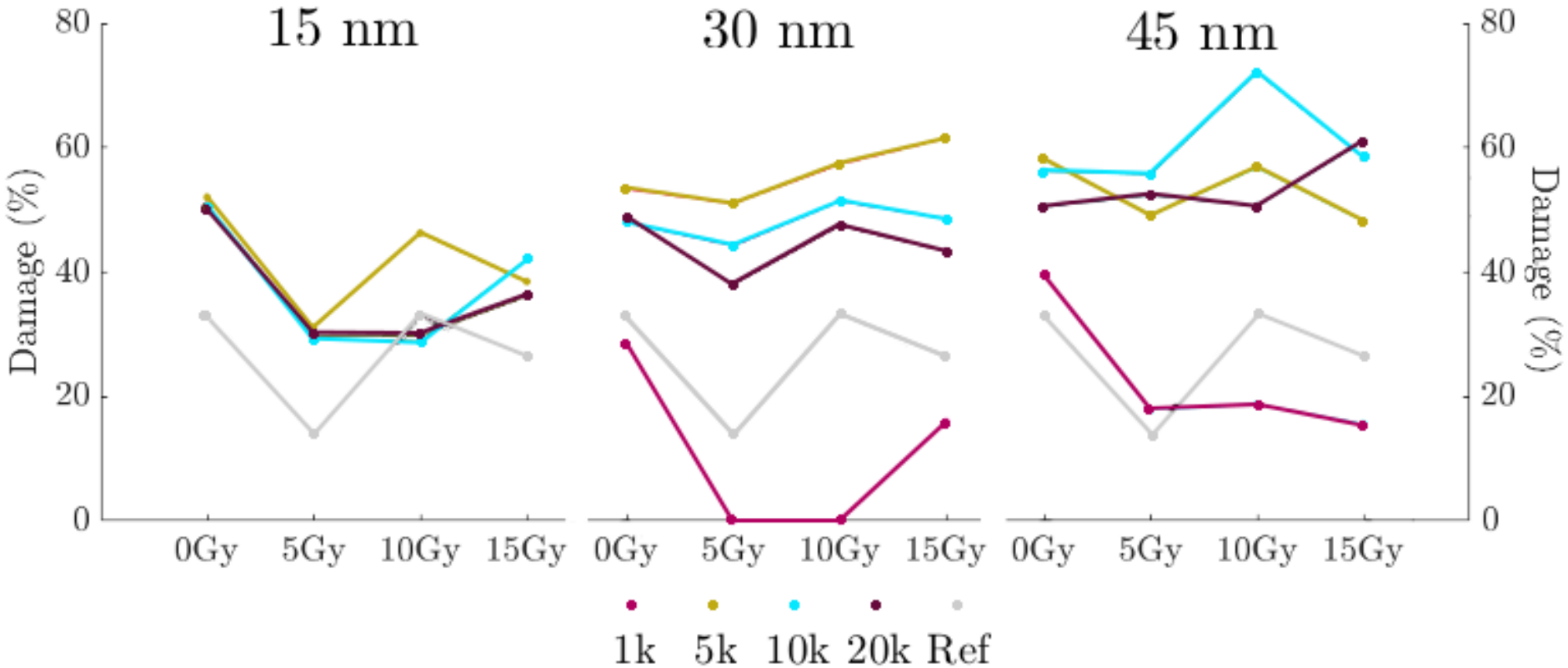
DNA damage analysis

Curves are not rising



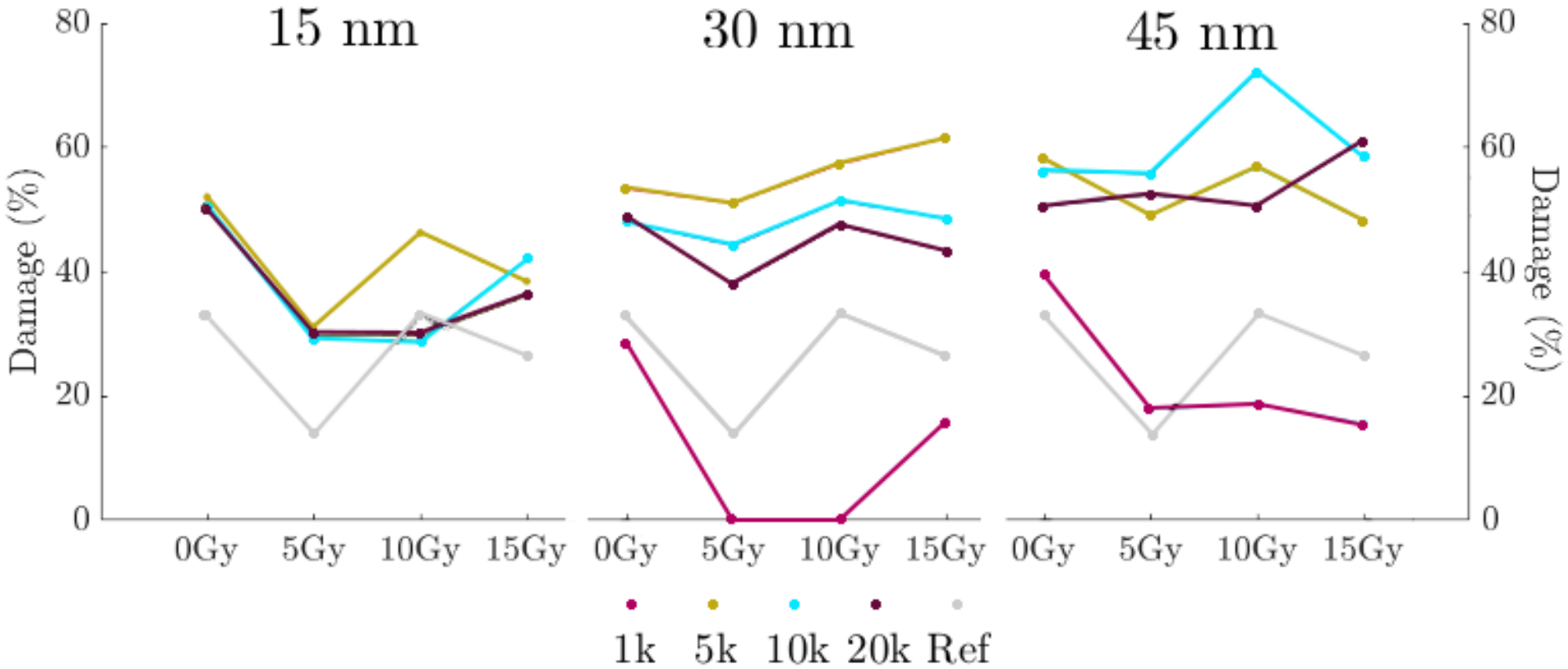
DNA damage analysis

Reference sample has an unexpected form



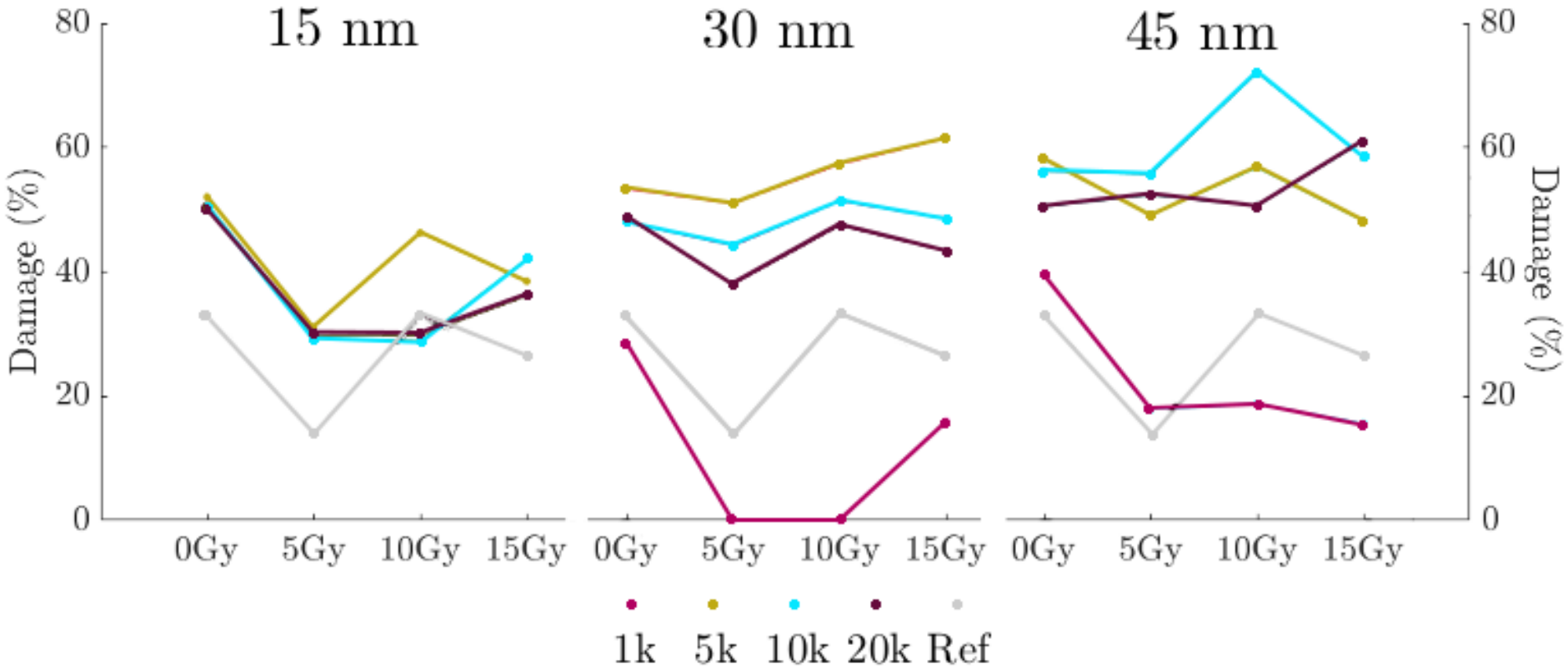
DNA damage analysis

DNA damage at 0 Gy



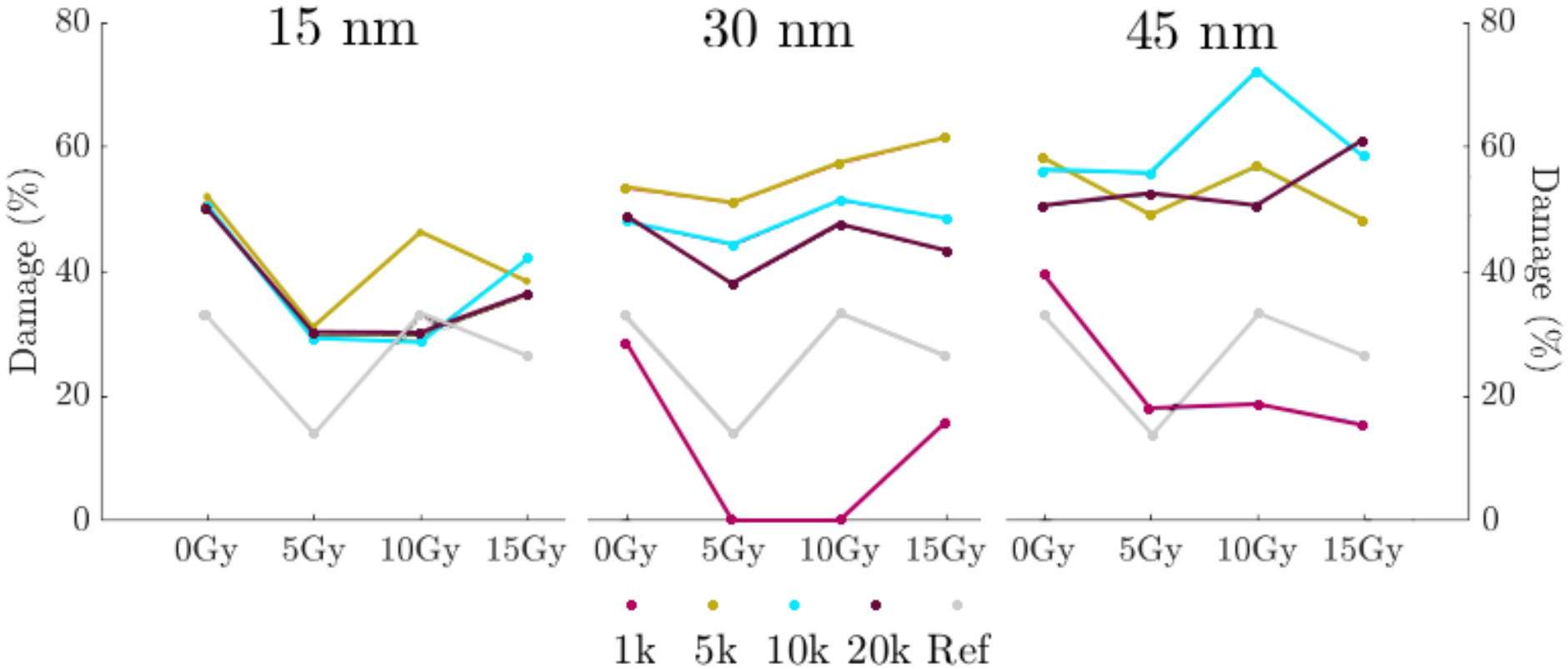
DNA damage analysis

Radiosensitization effect is present



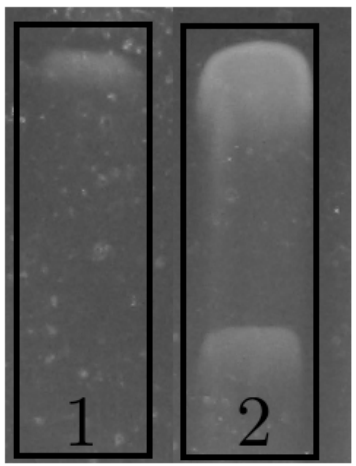
DNA damage analysis

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

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

$\Rightarrow$ Radiosensitization effect observed