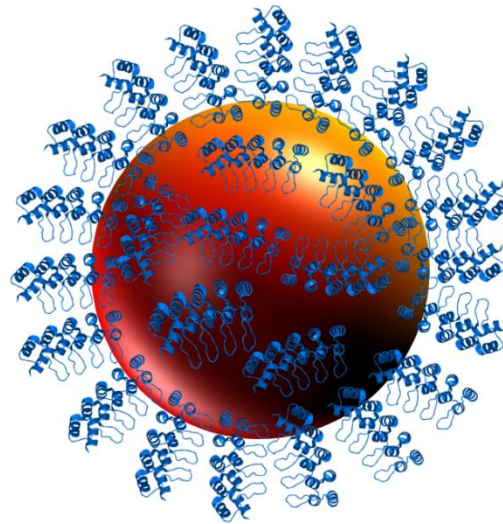


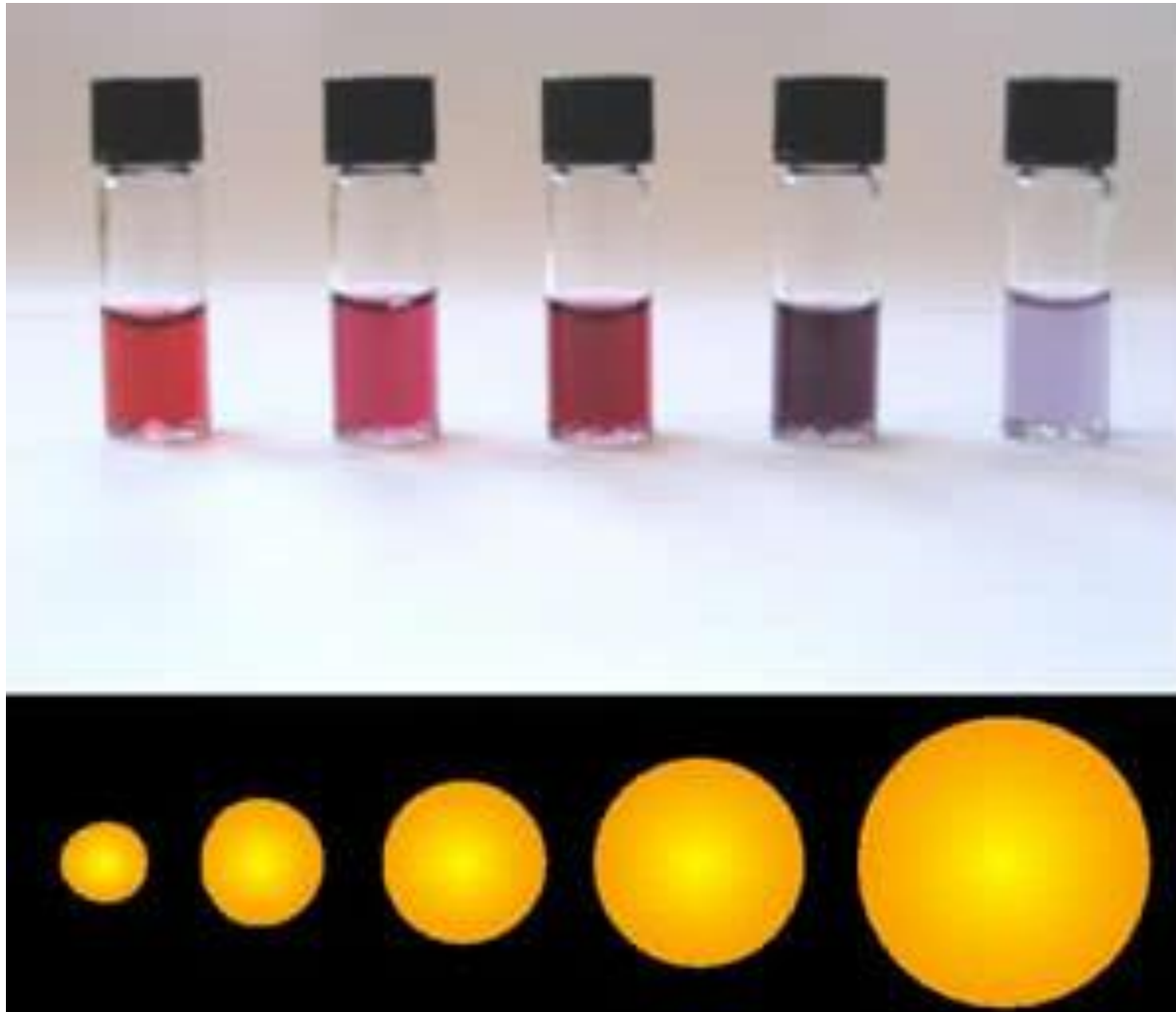
Alexander Kotlyar
Tel Aviv University

Selective Eradication of Cancer Cells by DARPin-Gold Nanoparticle Conjugates

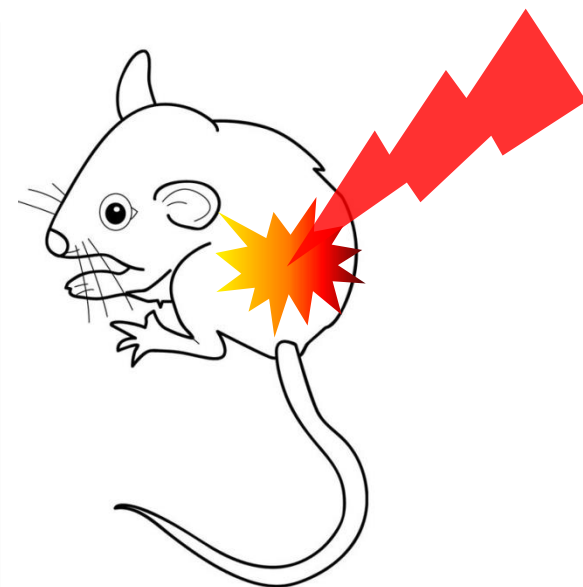
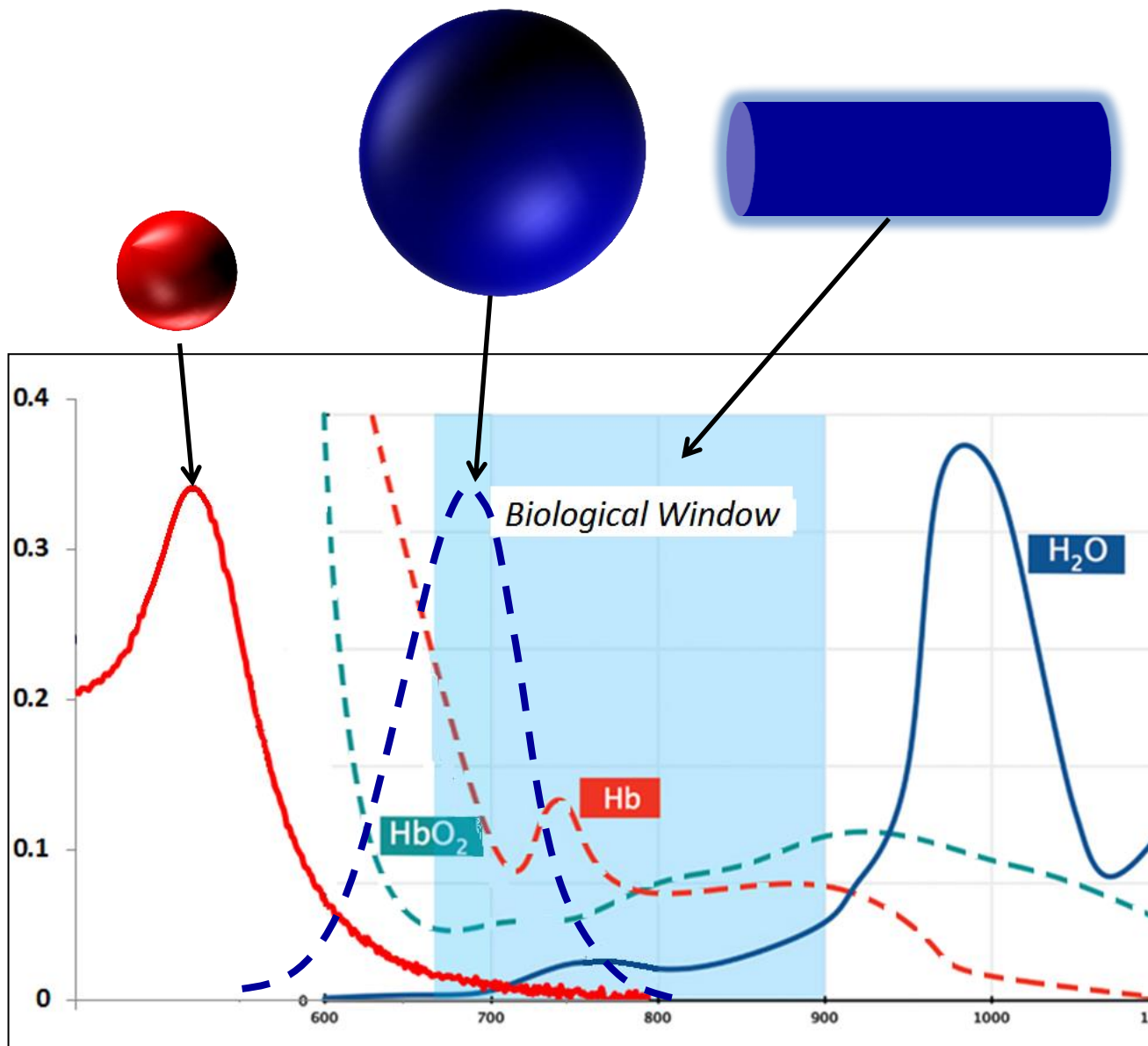


ImagineNano, Bilbao March 13-15, 2018

Gold Nanoparticle

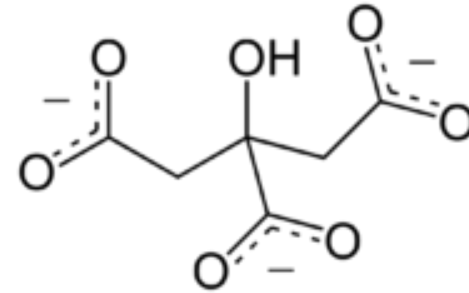
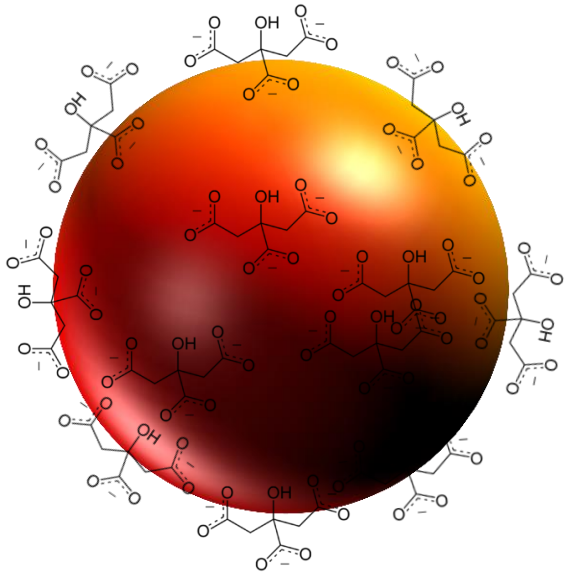


Absorption spectrum of GNPs



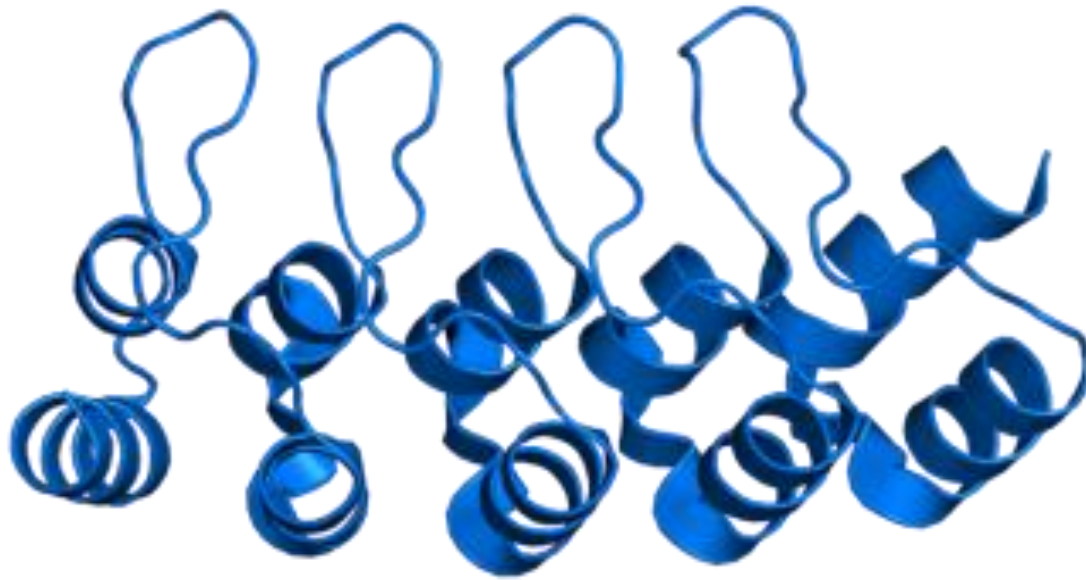
Photothermal therapy (PTT) is a treatment that uses light to destroy cancer cells by heat (hyperthermia)

Stability of gold nanostructures under physiological conditions is low



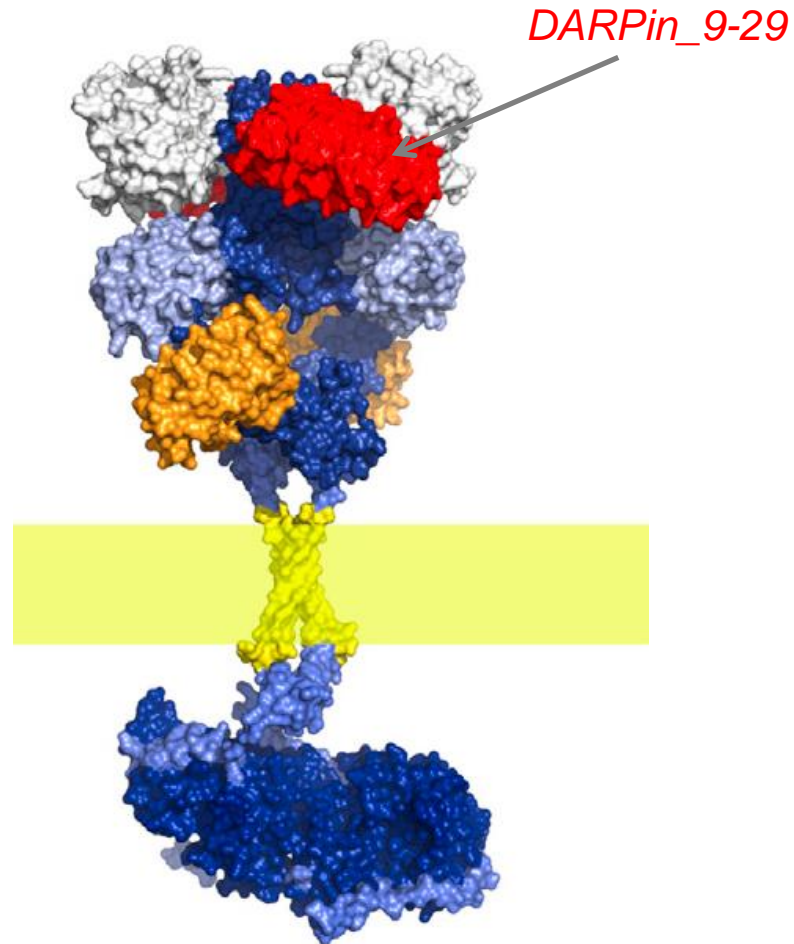
At salt concentrations higher than 20 mM even relatively small particles aggregate

*DARPin*s



DARPin is an acronym for Designed Ankyrin Repeat Proteins. DARPins consist of several (usually 4 or 5) repeat motifs and have a molecular mass of about 14-18 kDa.

High affinity binding of DARPin_9-29 with HER2



Human epidermal growth factor receptor-2
is a target of therapy for breast cancer patients

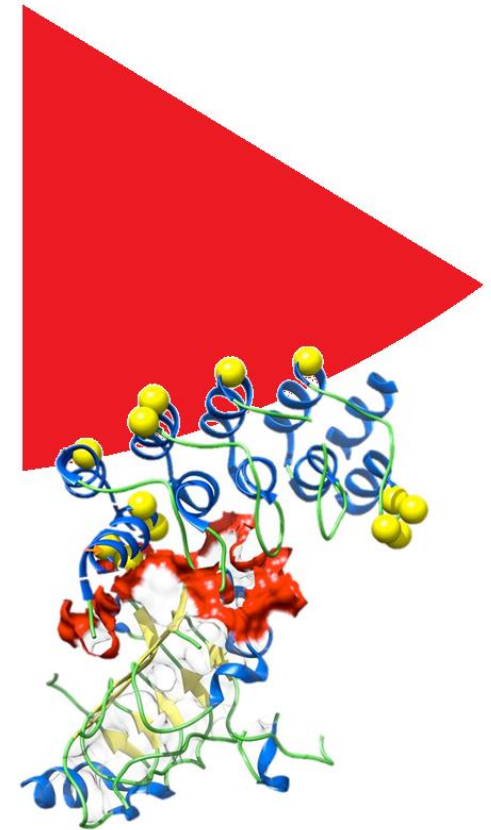
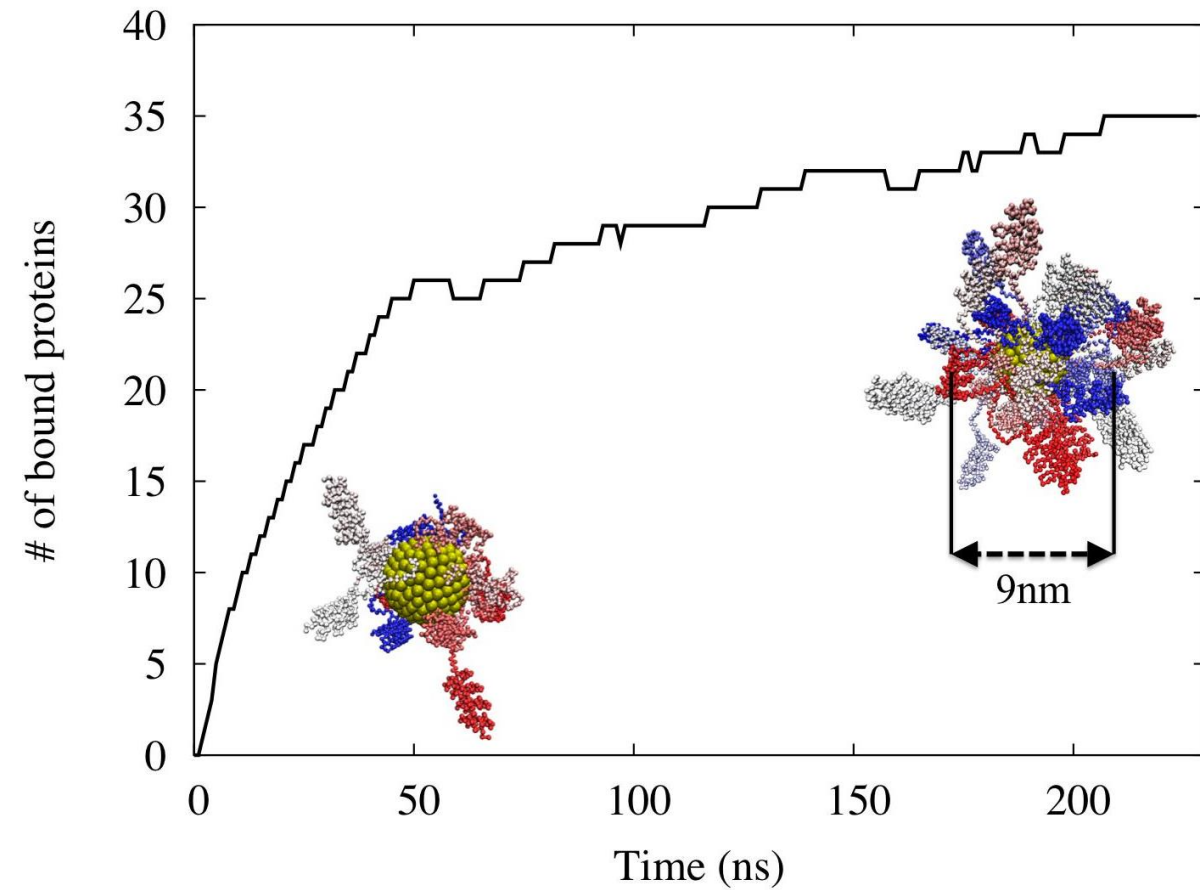
Molecular Dynamic (MD) Simulations of DARPin_9-29 binding to GNPs



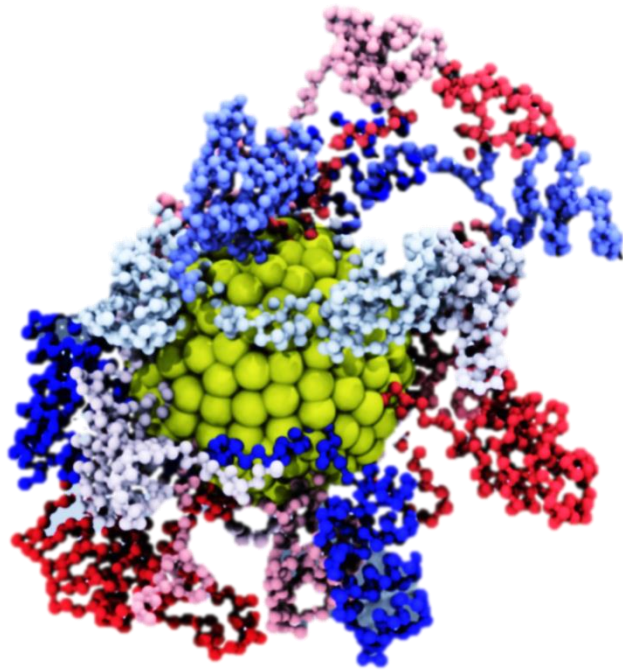
Maria Cristina Menziani



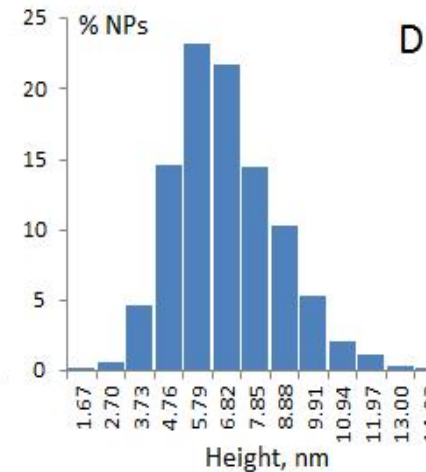
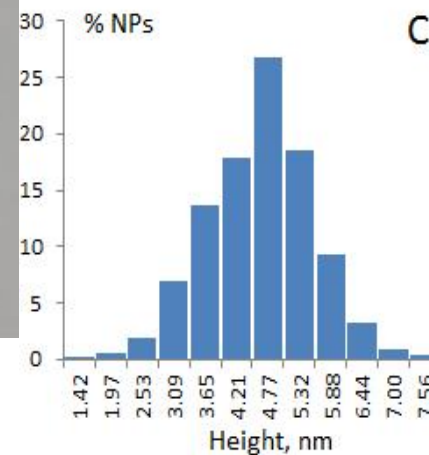
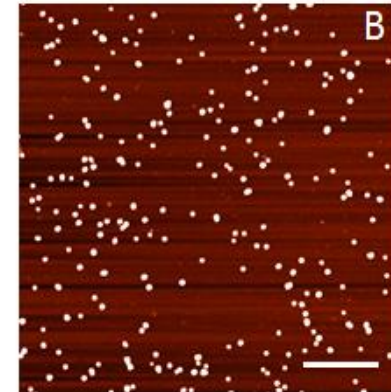
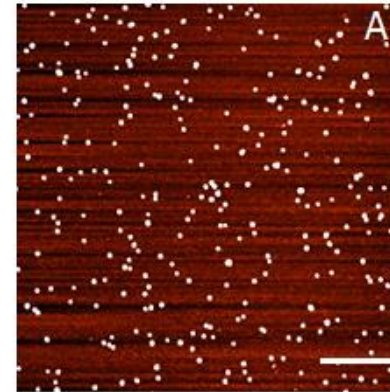
Francesco Tavanti



Stability of GNP-DARPin_{9.29} conjugates

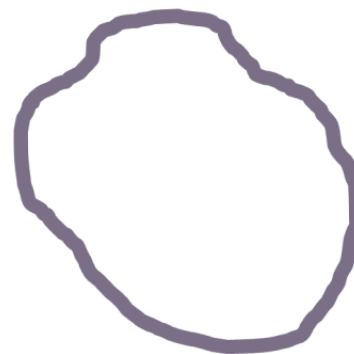
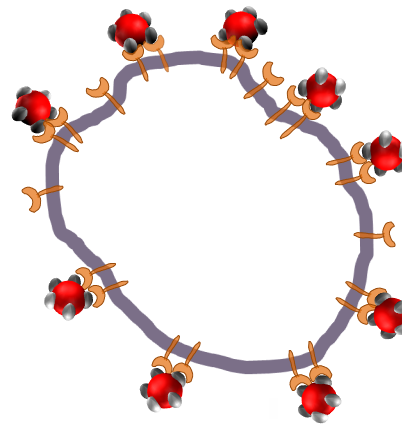
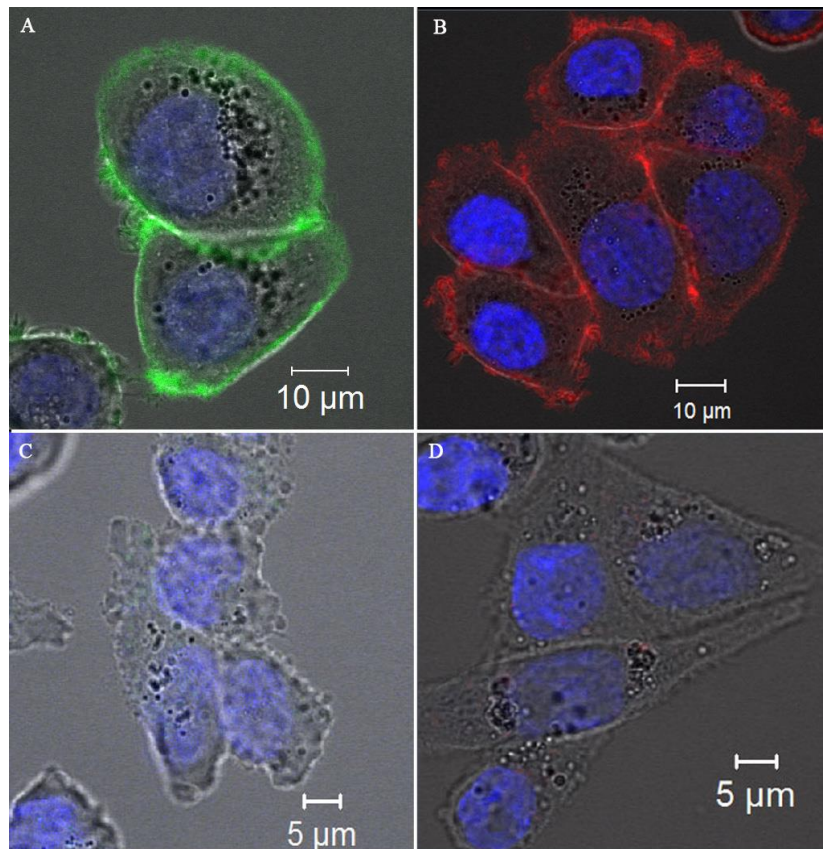


~ 30 DARPin molecules are bound to a GNPs.



The average diameter of citrate-protected GNPs is 4.7 ± 0.5 nm and DARPin-coated GNPs is 6.7 ± 0.6 nm.

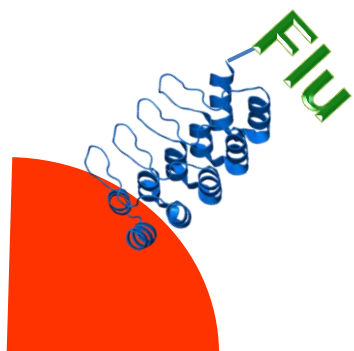
Binding of GNP-DARPin_{9.29} conjugates to the surface of SK-BR-3 cells



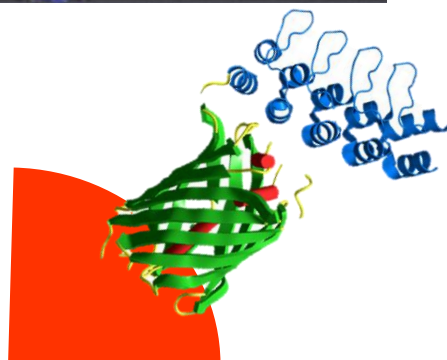
Sergey
Deyev



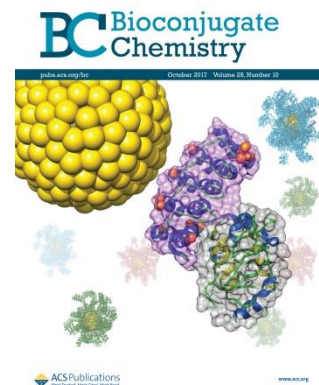
Galina
Proshkina



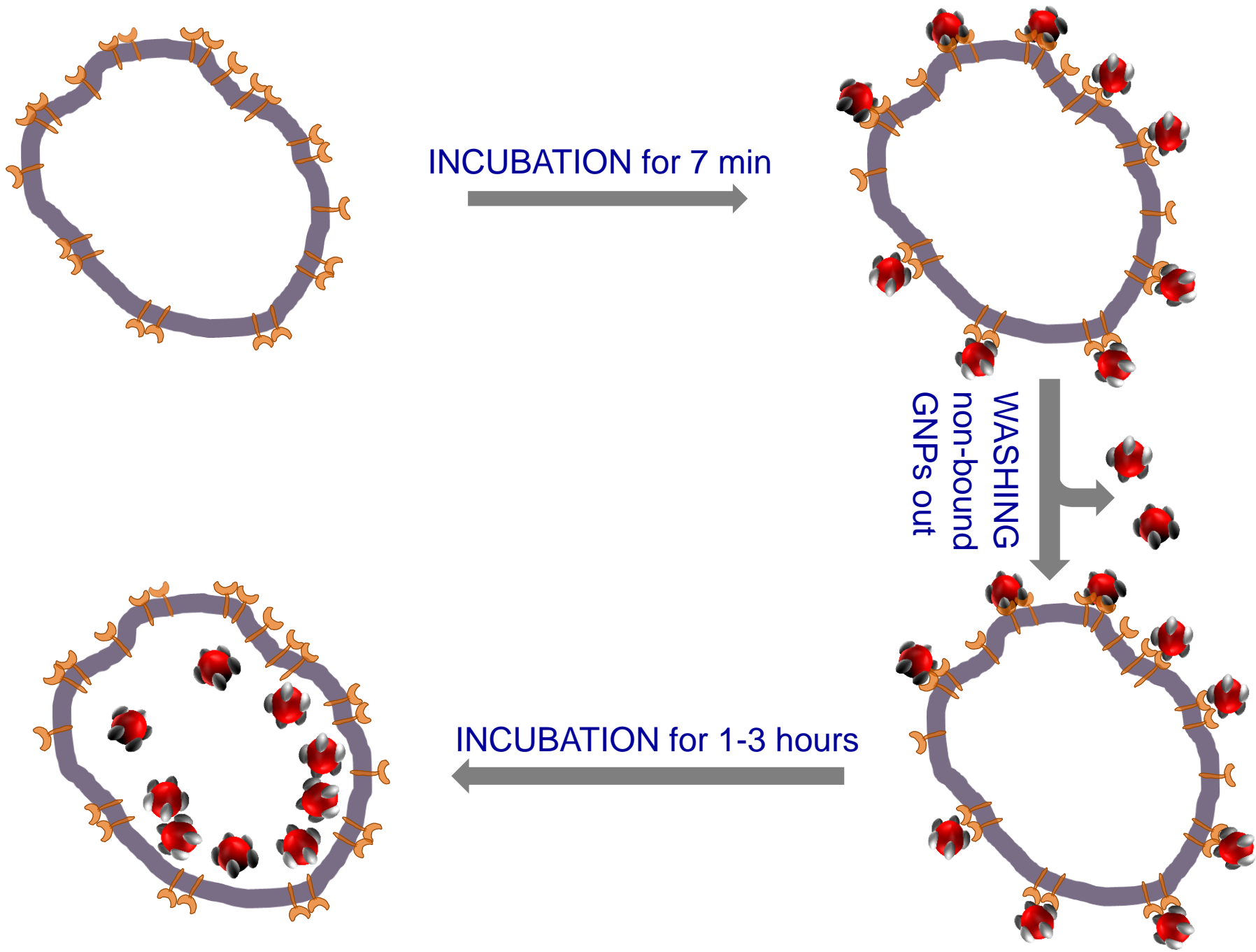
DARPin-Flu



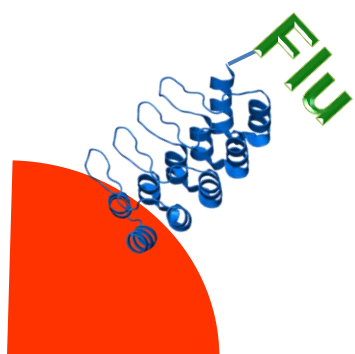
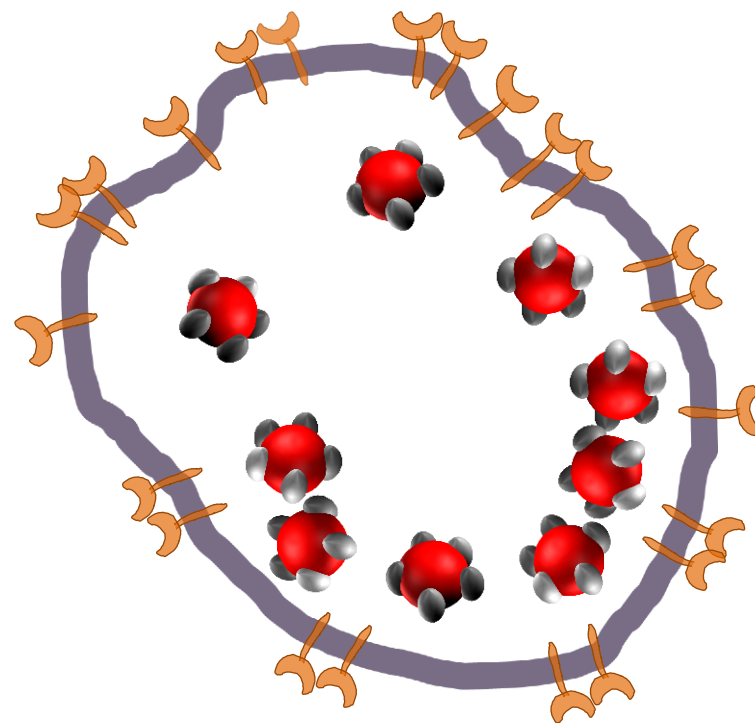
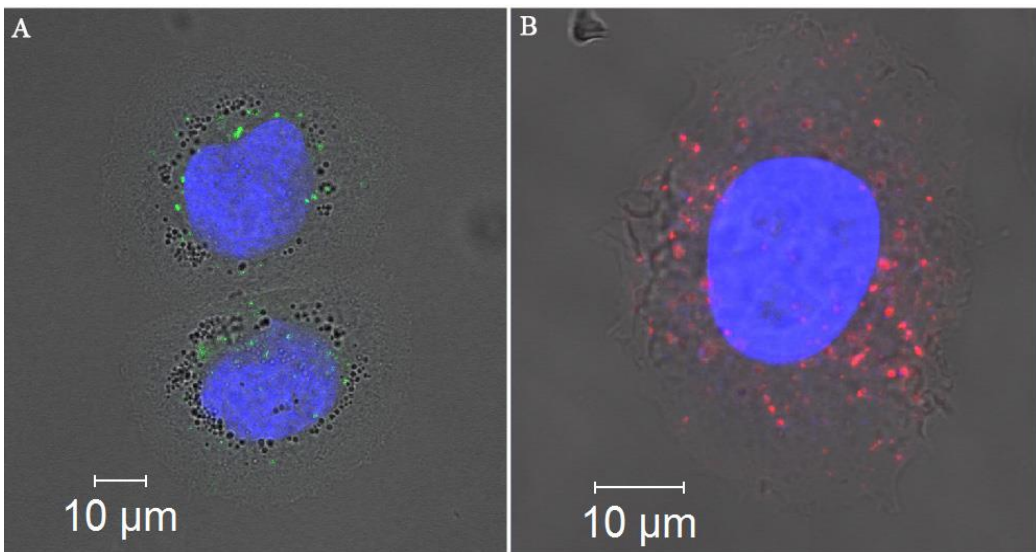
DARPin-mCherry



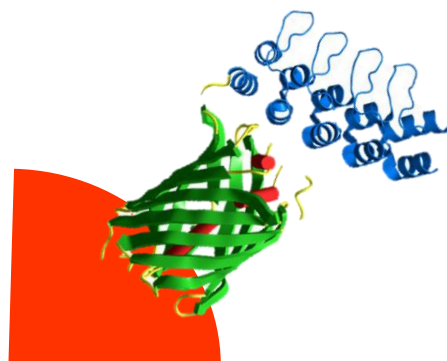
The experiment was conducted as follows...



Internalization of GNP-DARPin_{9.29} conjugates to SK-BR-3 cells

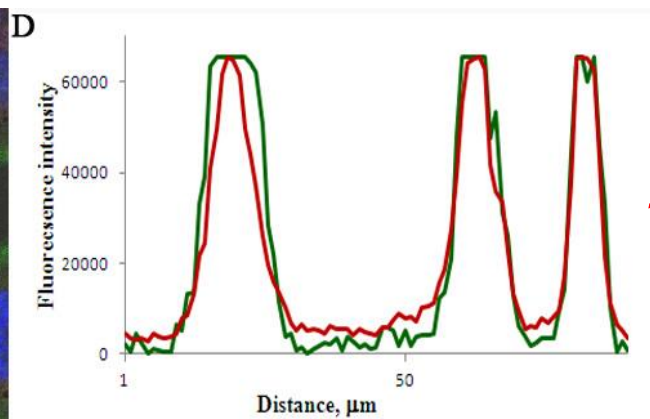
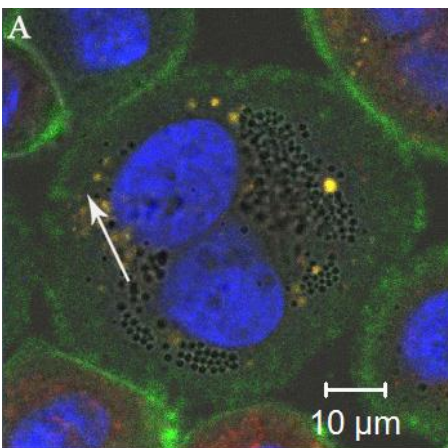


DARPin-Flu

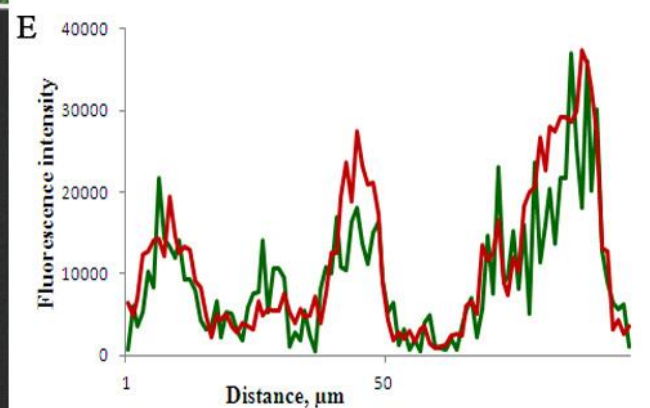
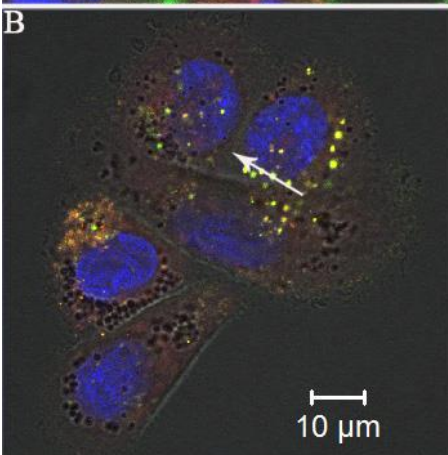
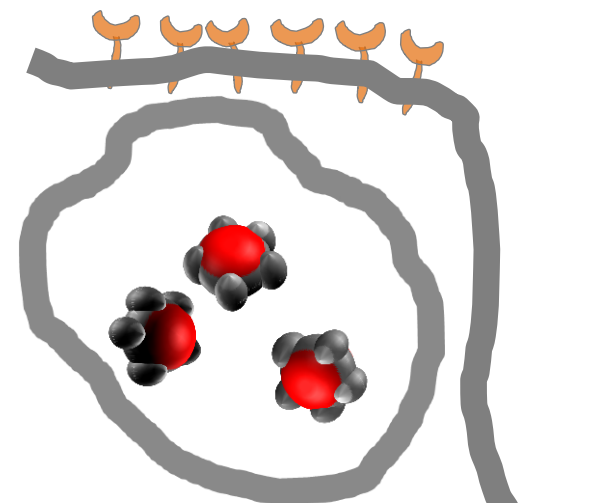


DARPin-mCherry

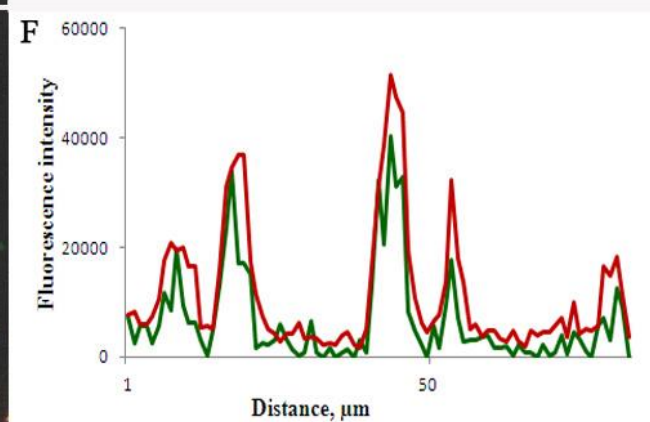
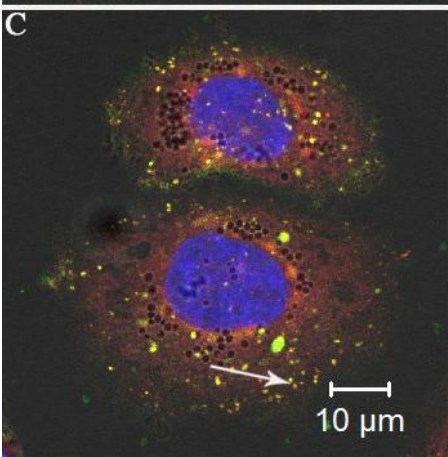
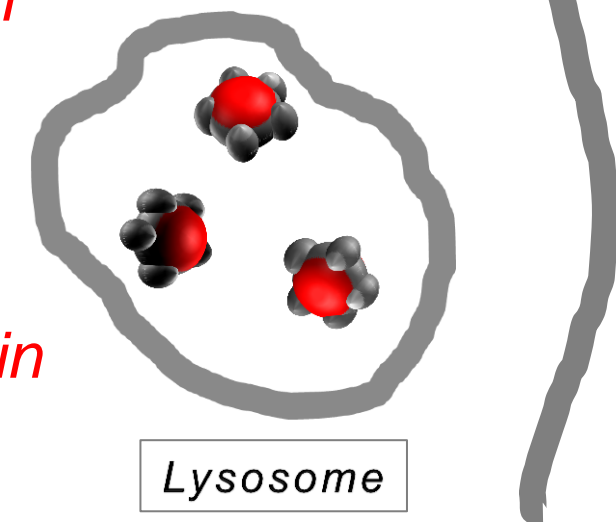
Kinetics of the internalization process



10 min

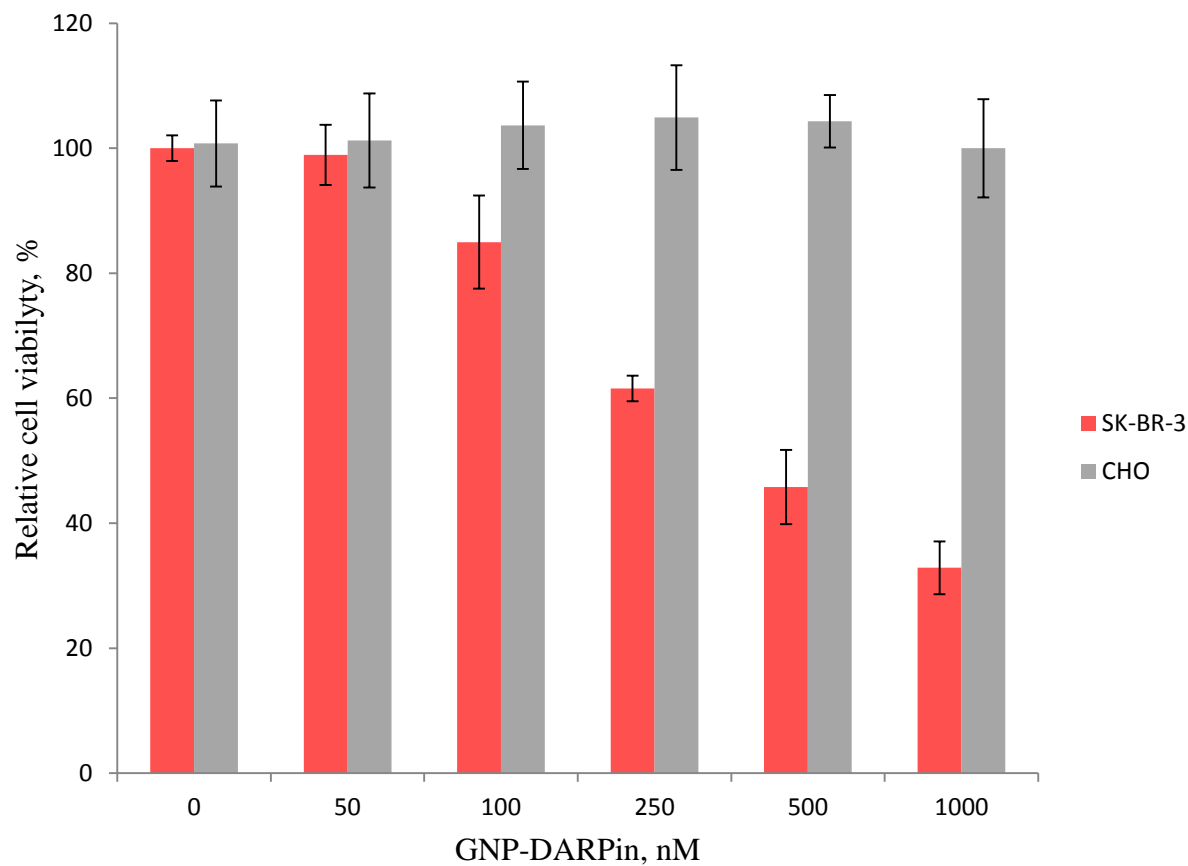
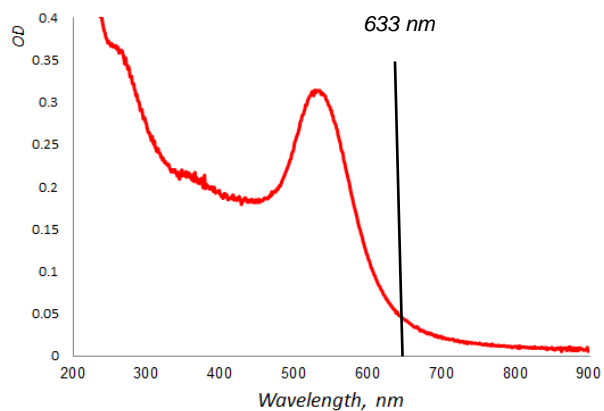


60 min

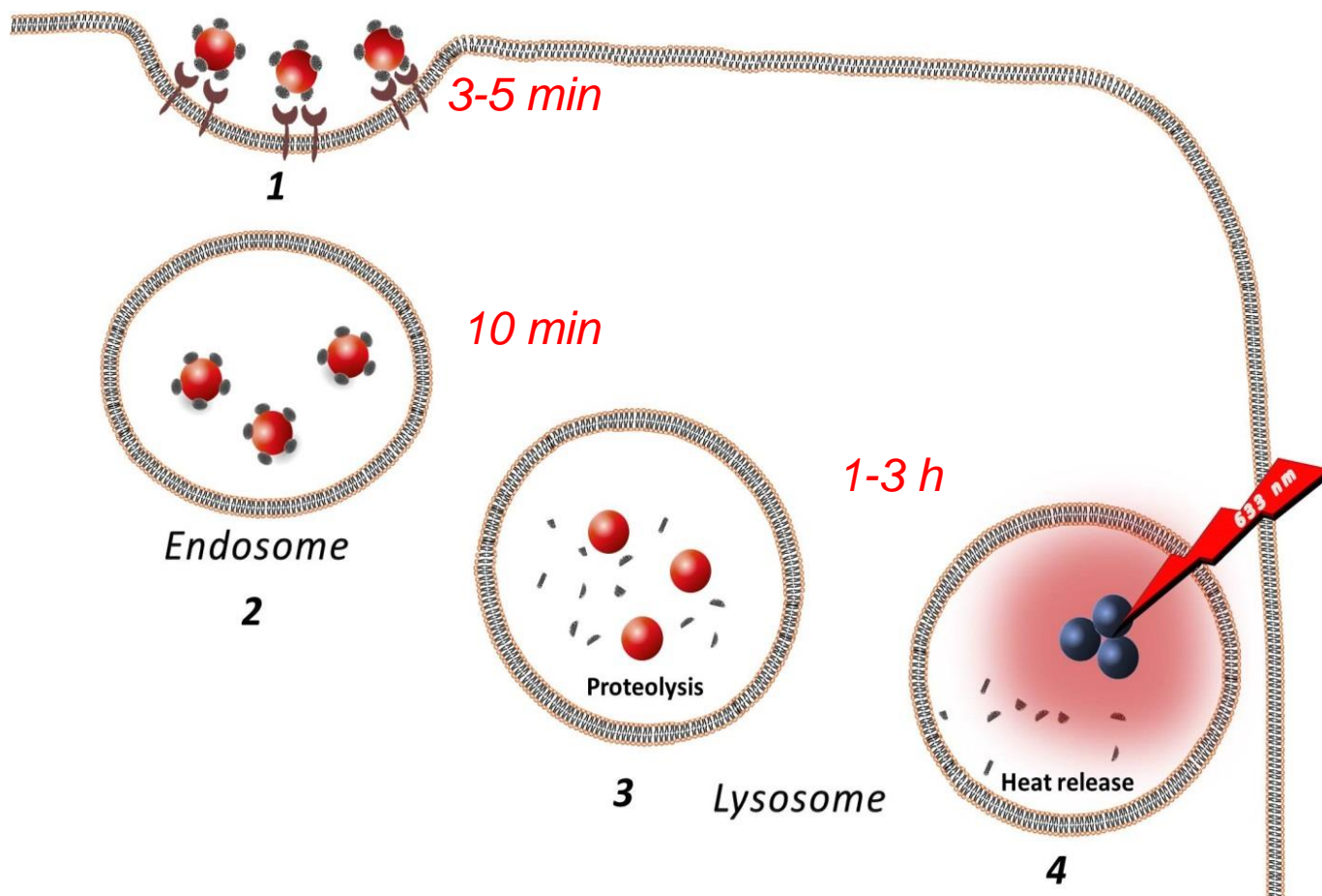


120 min

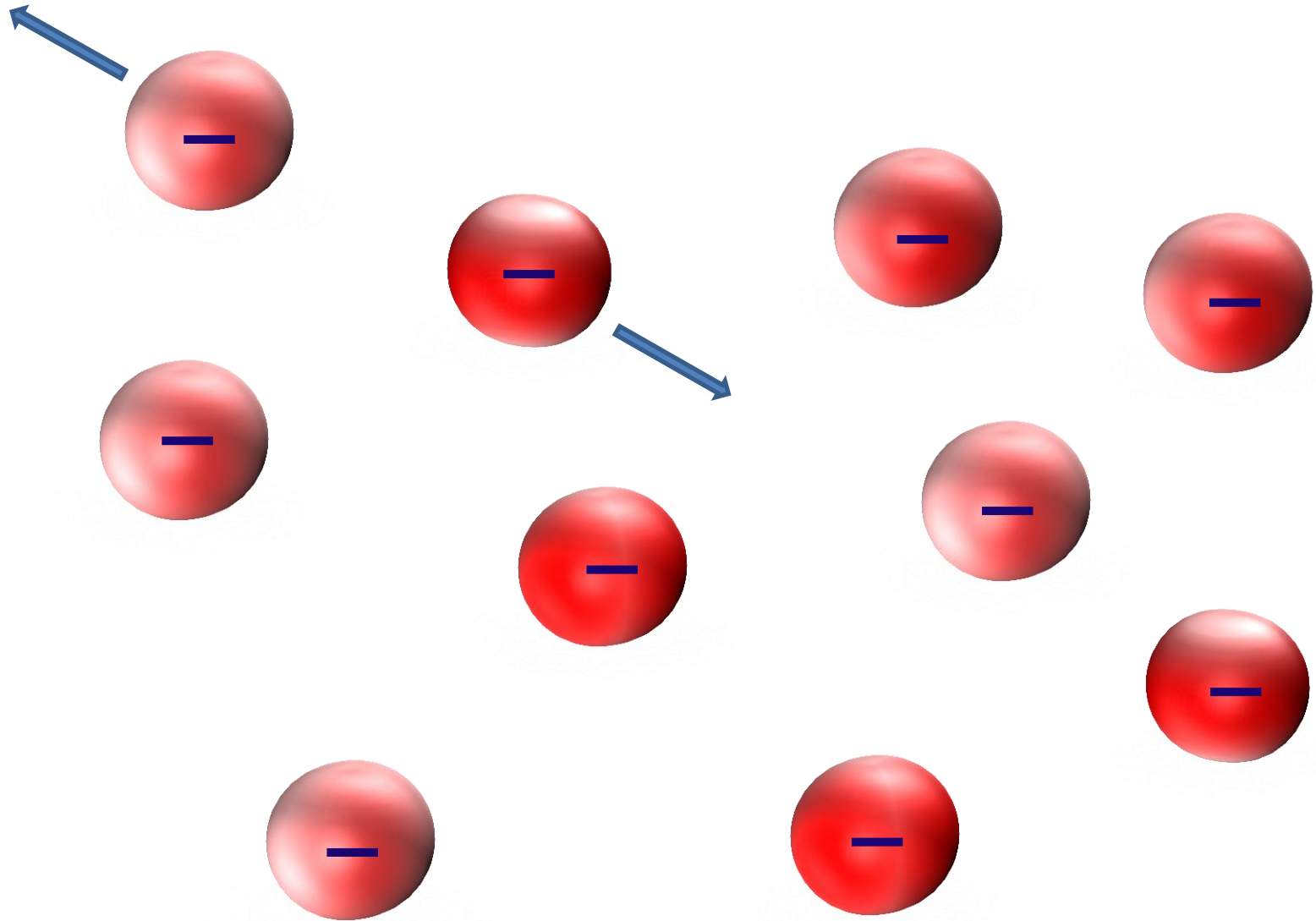
The effect of illumination (at 633 nm) on the viability of DARPin-GNP-treated cells



Tentative mechanism of light-induced elimination of HER2-positive cells

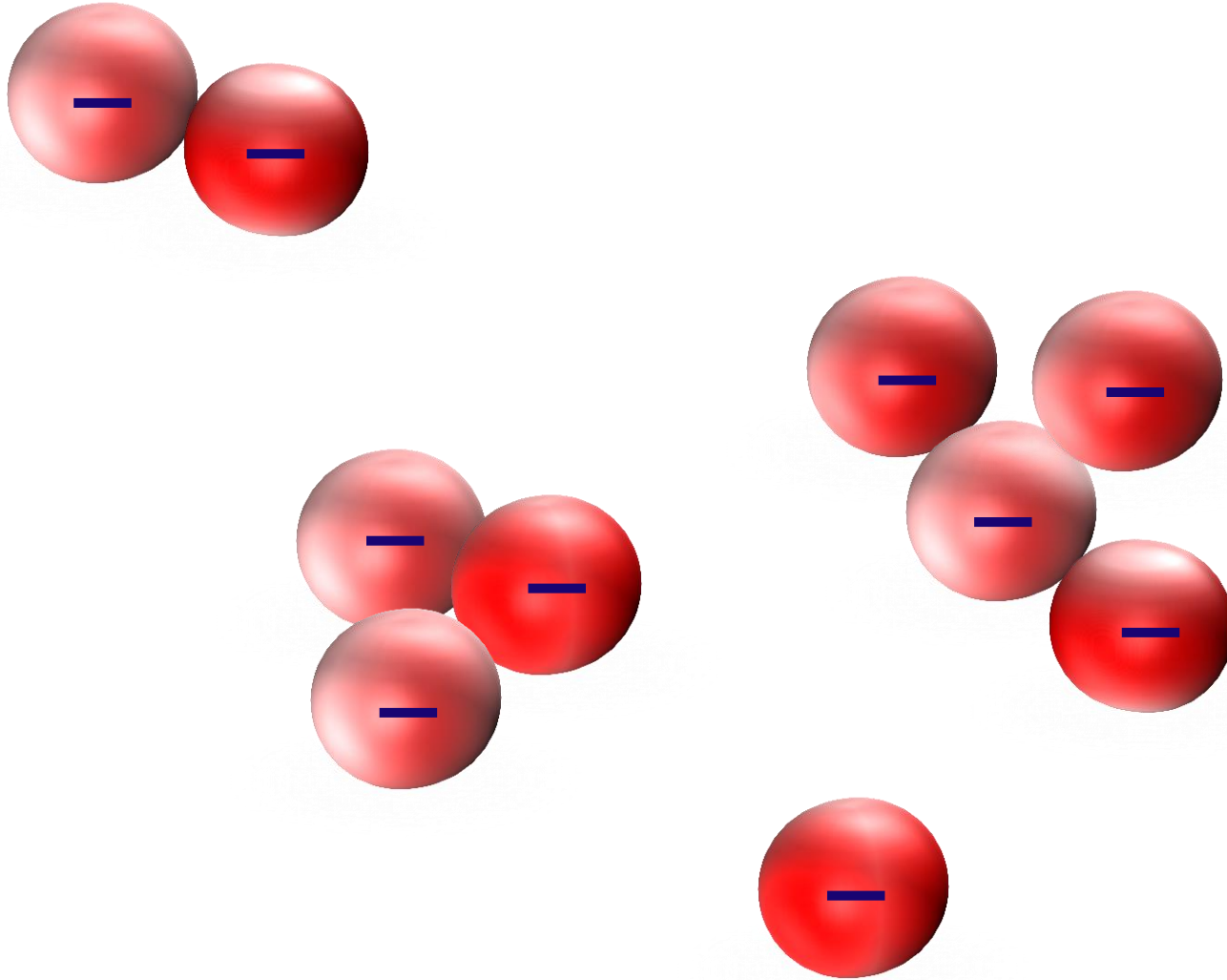


Aggregation of NPs in aqueous solution



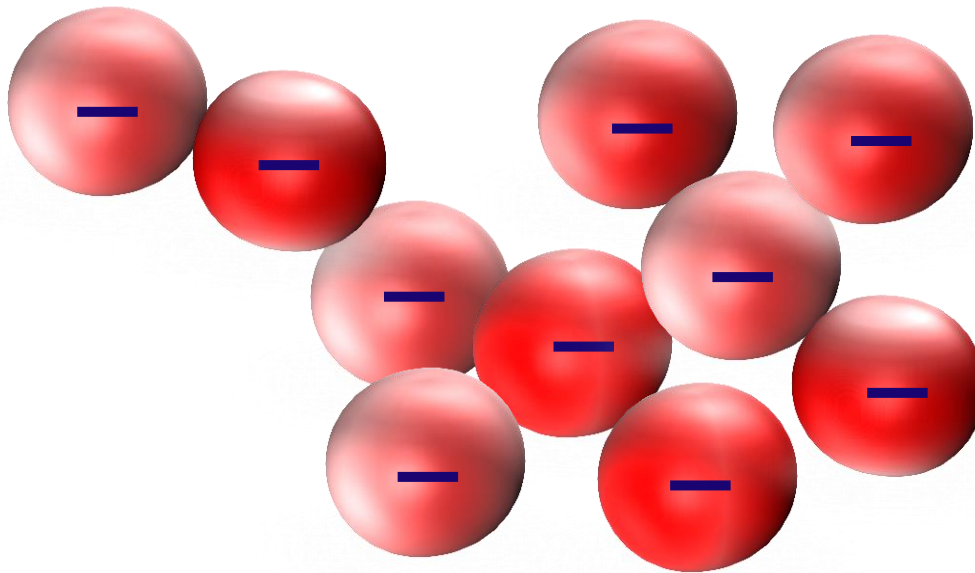
At low ionic strength and neutral conditions

Aggregation of NPs in aqueous solution



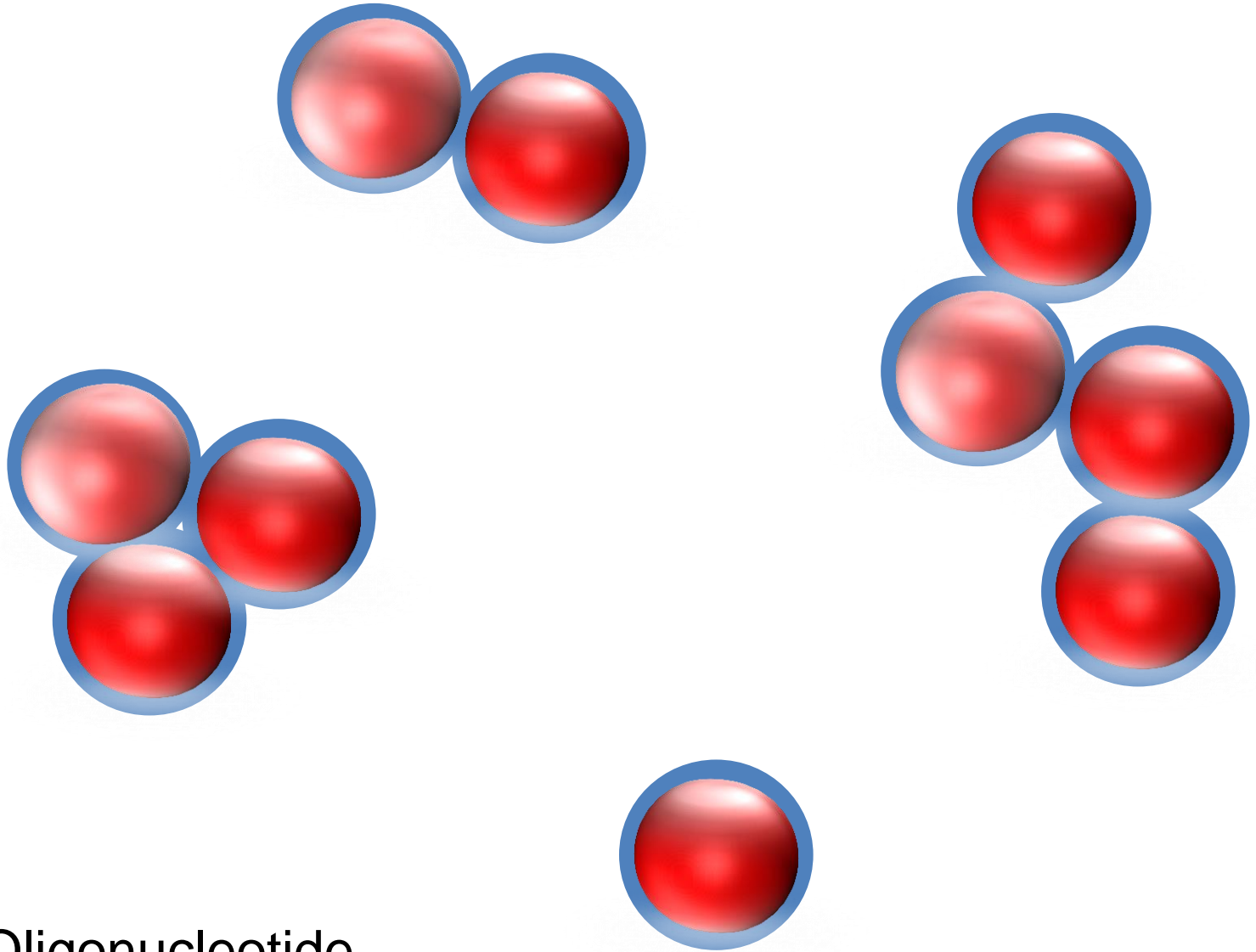
ionic strength is increased or pH is reduced

Aggregation of NPs in aqueous solution



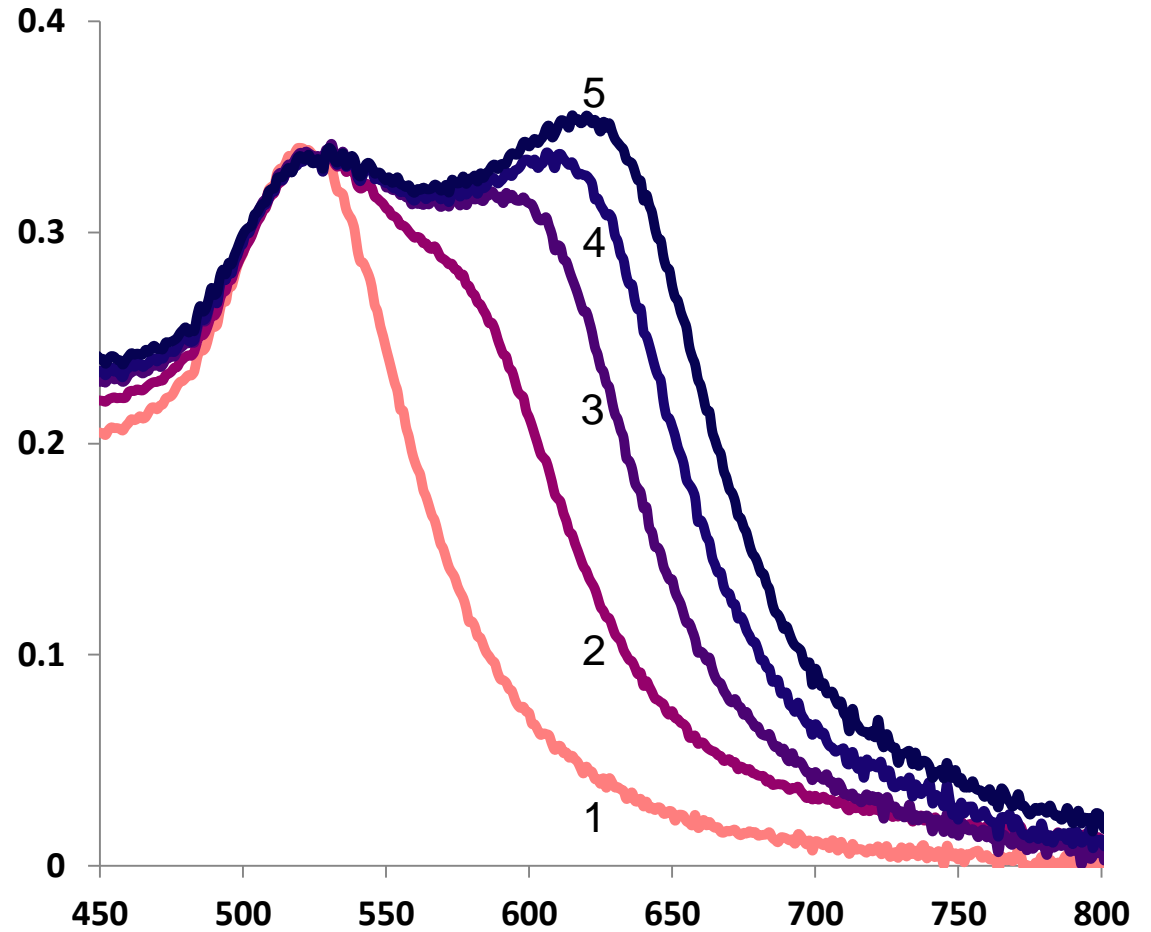
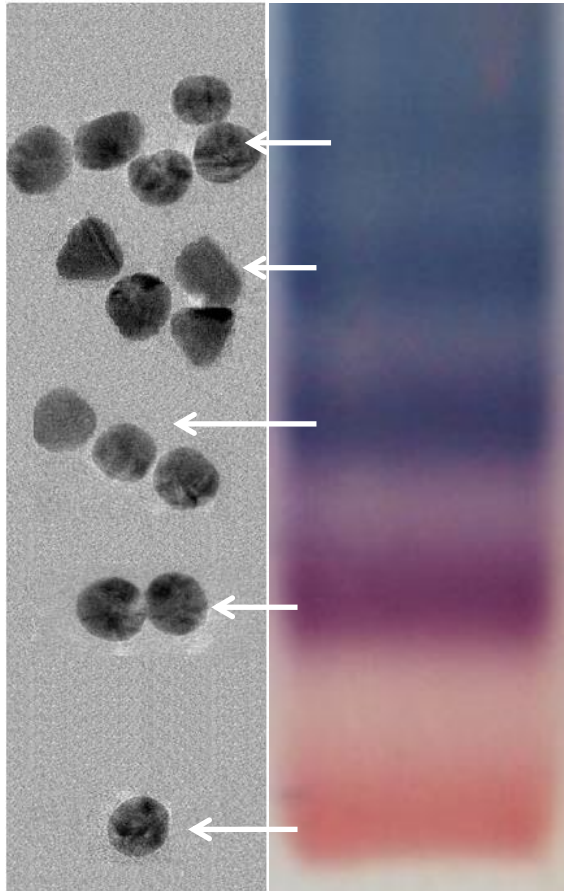
ionic strength is increased or pH is reduced

Aggregation of NPs can be halted

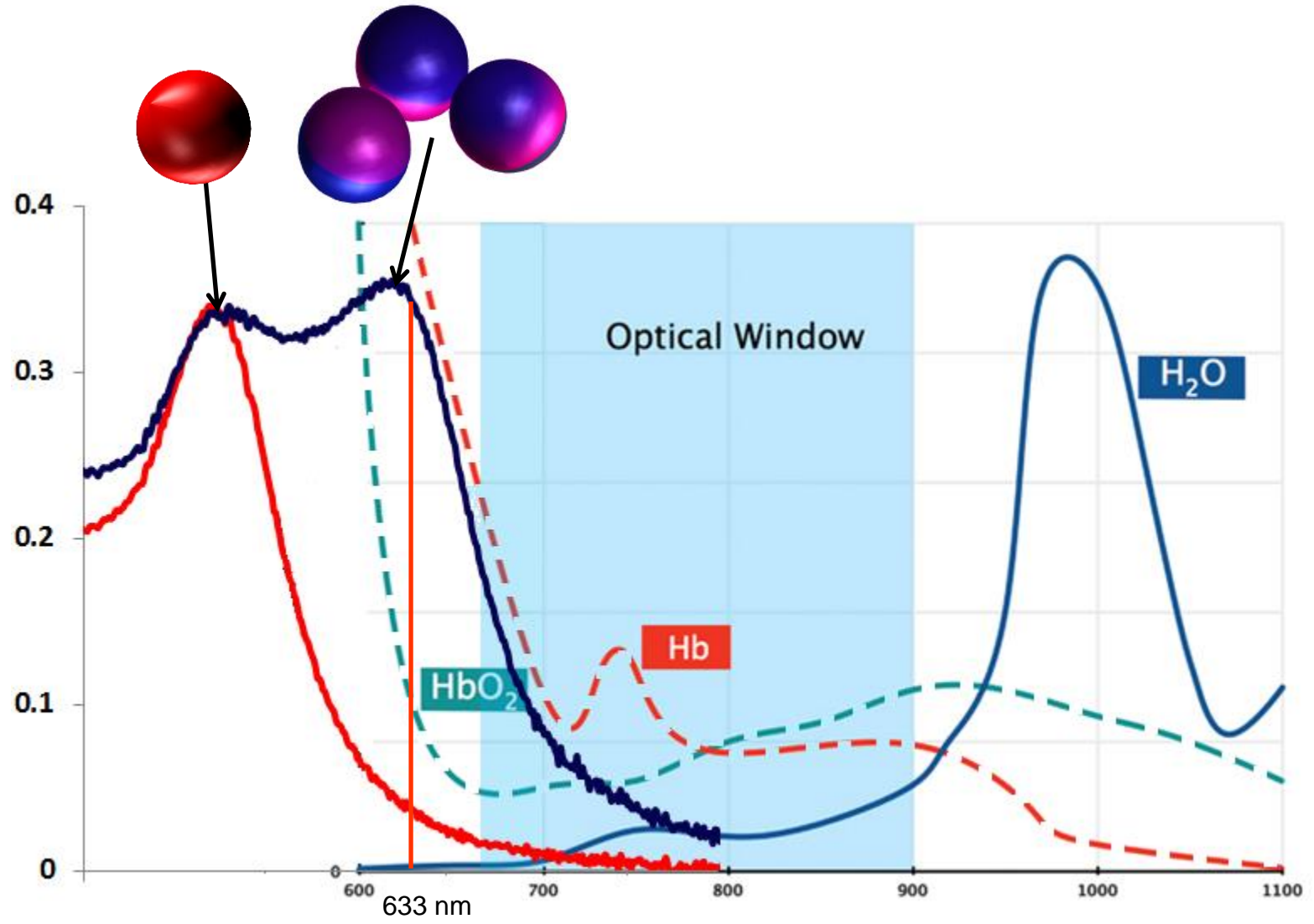


■ = Oligonucleotide
or protein

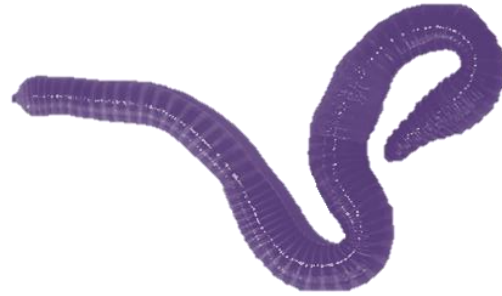
Binding of GNPs to each other results in a red shift of the absorption spectrum



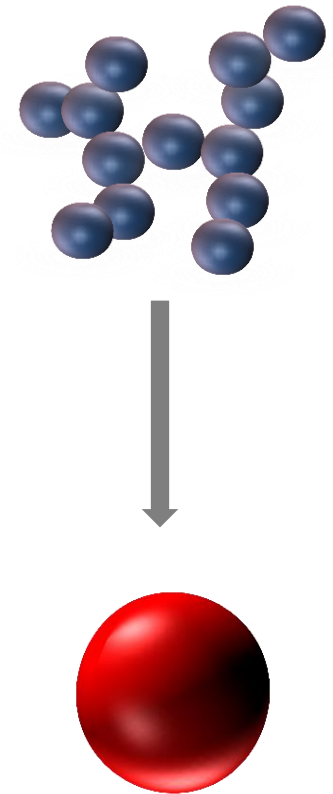
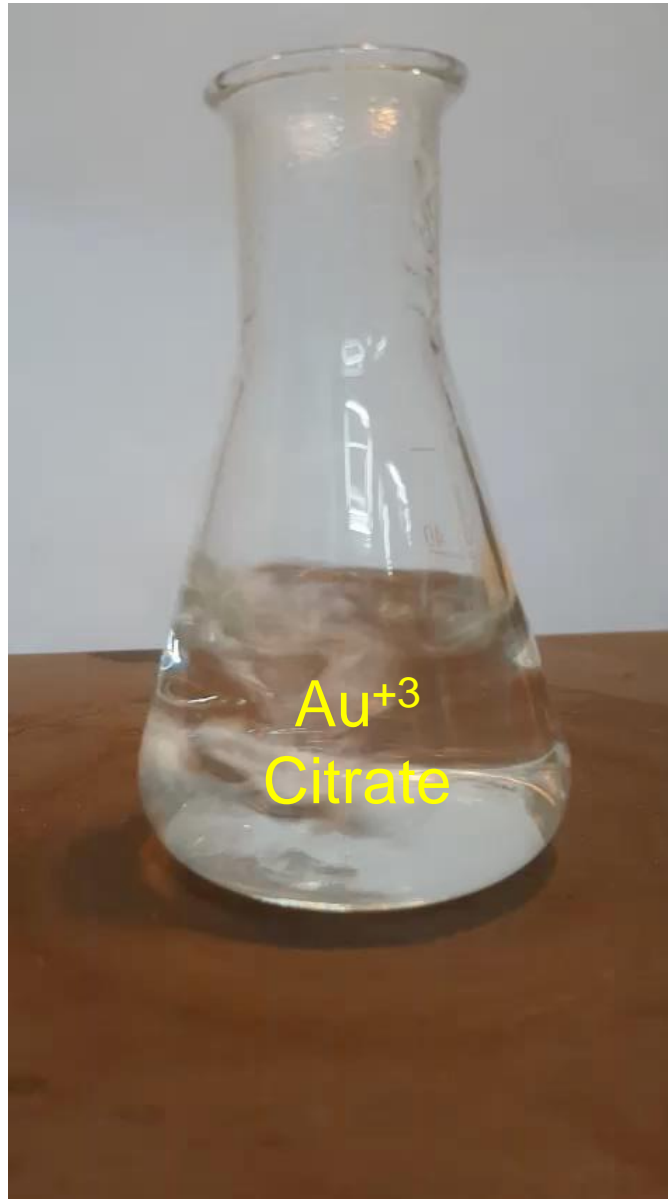
Absorption spectrum of GNPs



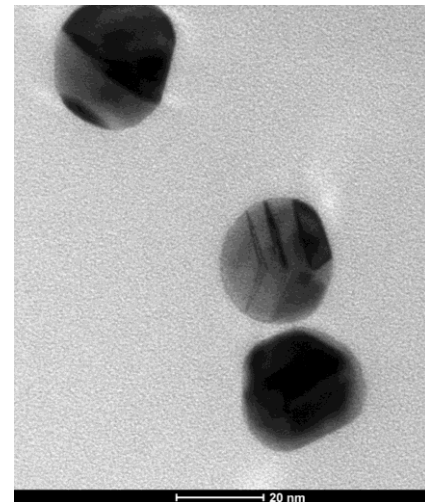
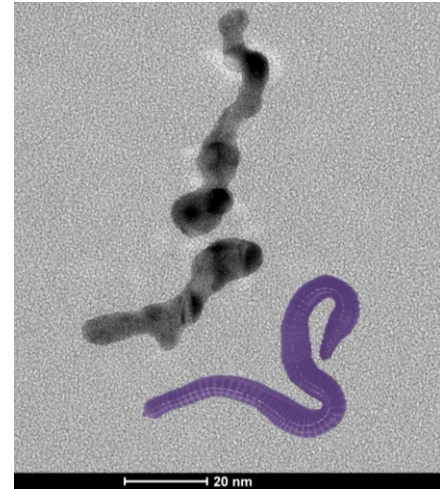
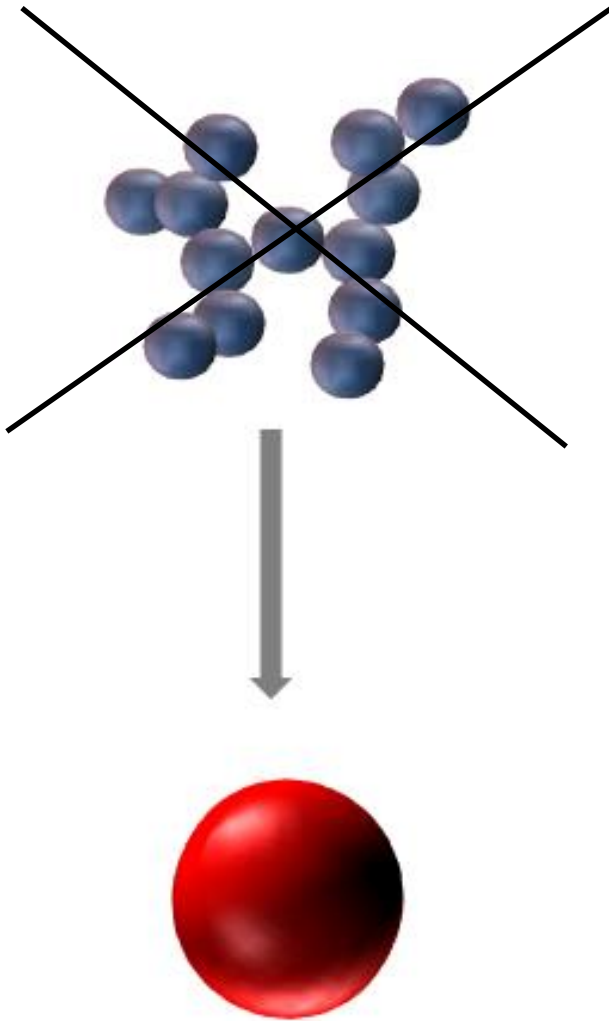
Nanoworms can efficiently kill cancer cells



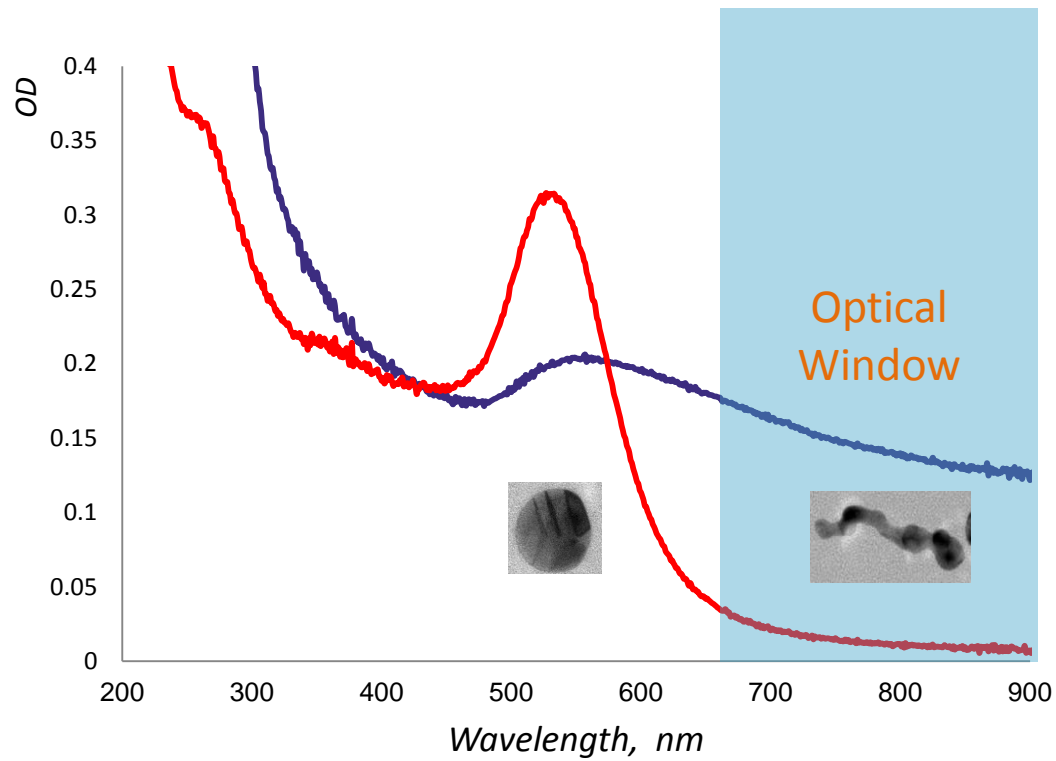
Synthesis of GNPs



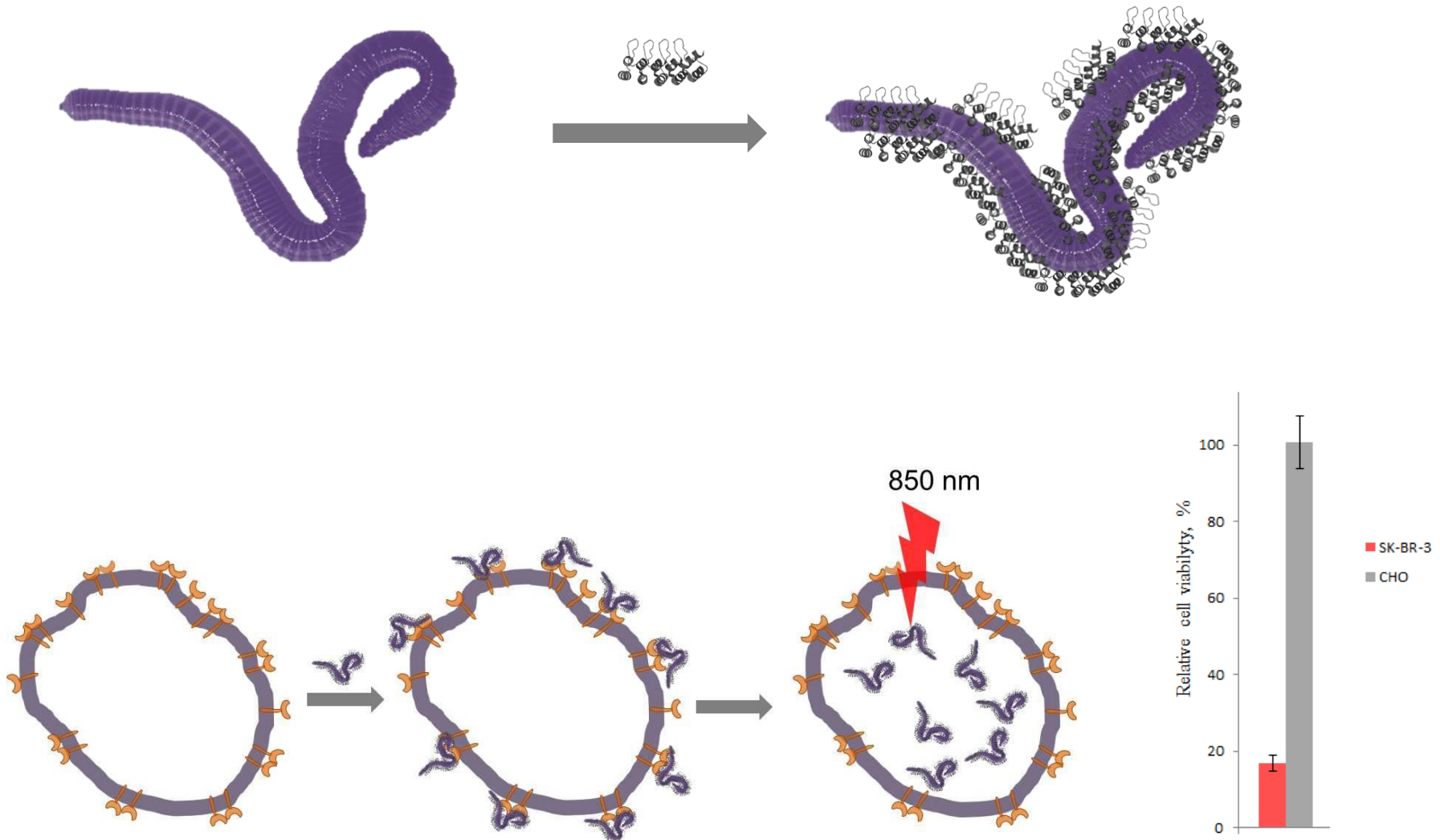
Synthesis of GNPs



Absorption spectrum of gold nanoworms (GNWs)



Treatment with the DARPin –nanoworm conjugates kills cancer cells



THANK YOU FOR YOUR ATTENTION!!!



*Sergey
Deyev*



*Galina
Proshkina*



*Maria
Cristina
Menziani*



*Francesco
Tavanti*



**ISRAEL
SCIENCE
FOUNDATION**

