

Methotrexate-Loaded Hydrophilic Gold Nanoparticles for Transdermal Delivery

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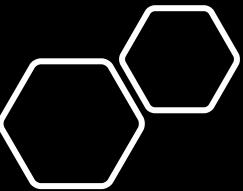
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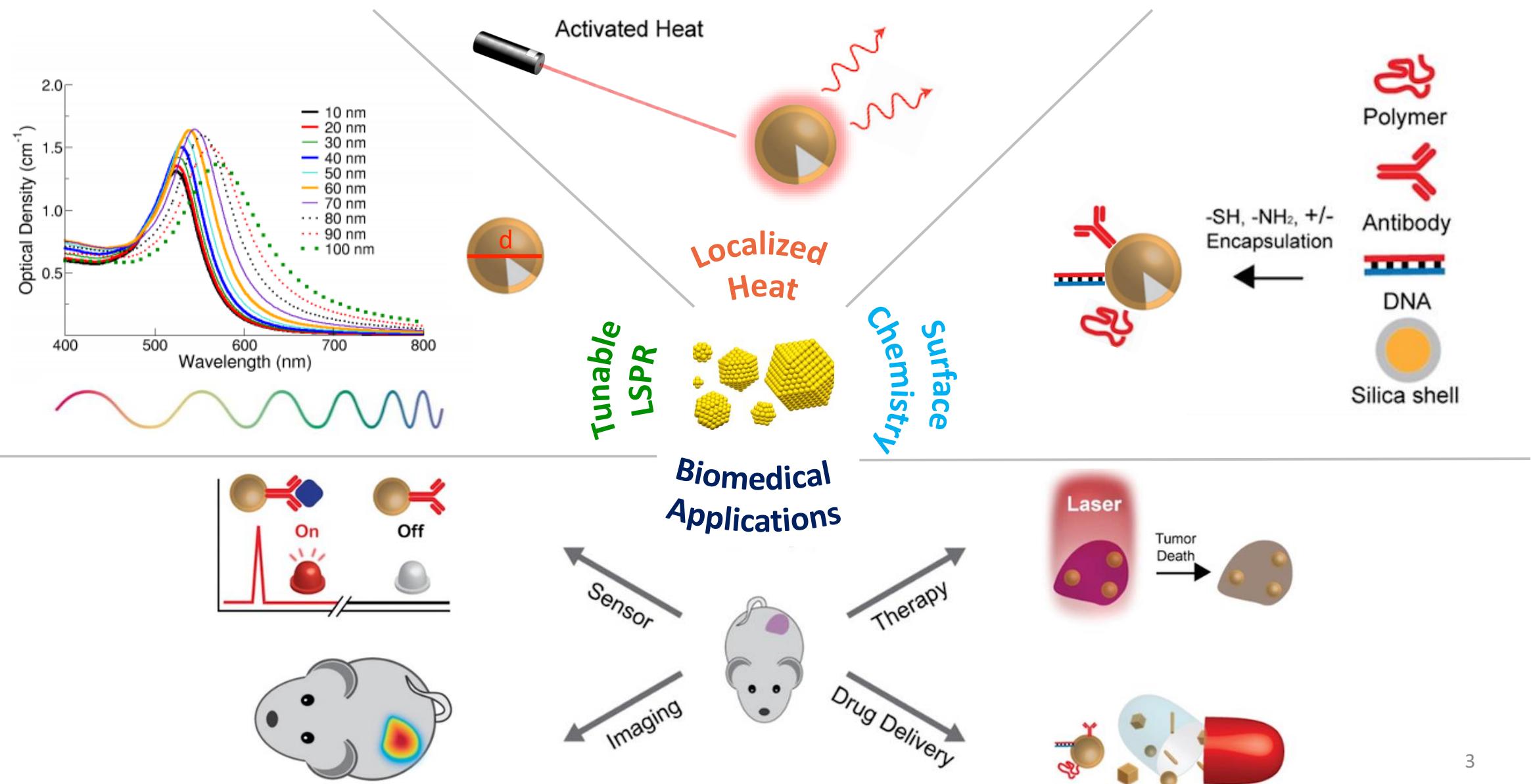
**Nano
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Conference & Exhibition**
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Overview

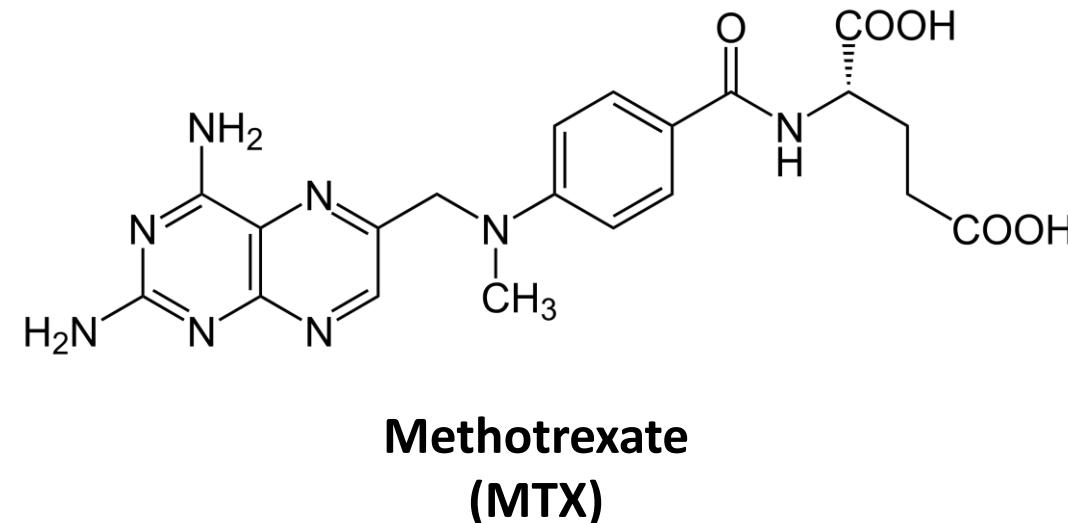
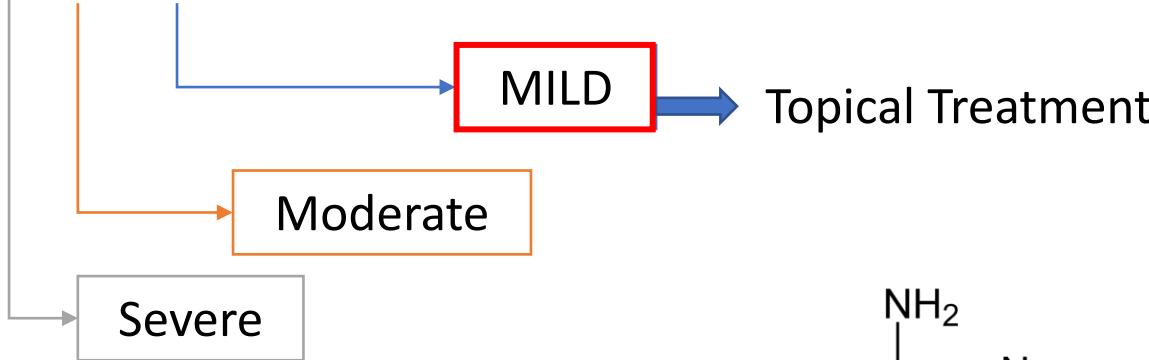
- Gold Nanoparticles: an introduction
- Gold Nanoparticles in Drug Delivery
- Synthesis method
- *in vitro* and *in vivo* studies
- AuNPs and MTX: the interaction
 - UV-Vis, DLS and SAXS
 - HR-TEM and AFM
 - ^1H -NMR and SR-XPS
- Conclusions

Gold nanoparticles: an introduction



Gold nanoparticles in Drug Delivery

Psoriasis → Chronic inflammatory skin condition (2% of population)



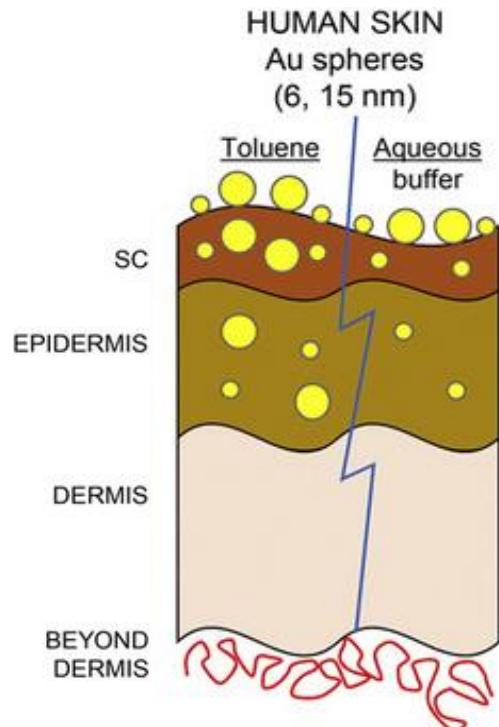
- ✓ Inhibitor of dihydrofolate reductase
- ✓ Decrease inflammation
- ✓ Slowdown keratinocytes hyperproliferation



- ✗ pH dependent low solubility in water
- ✗ Unsatisfactory percutaneous penetration
- ✗ Toxic dose-related side effects

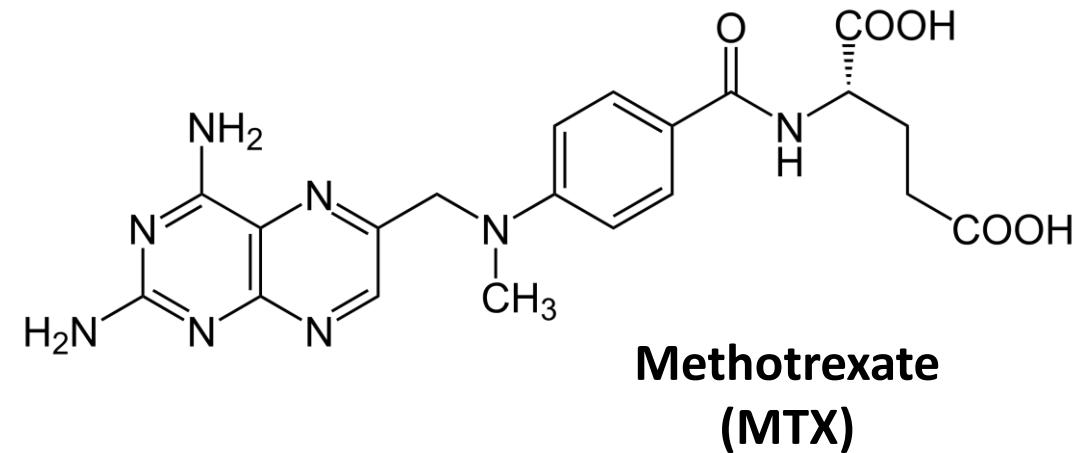
Gold nanoparticles in Drug Delivery

1. How to improve skin penetration?
2. How to reduce side effects of MTX?



Human skin; 6 nm NPs to deeper skin layers.
15 nm NPs in furrows only
(aqueous buffer) & to deeper layers (toluene) [75]

- Nanoparticles in the range 6-15 nm can pass across human skin
- ↑ surface-to-volume ratio ↓ dose



Methotrexate (MTX)



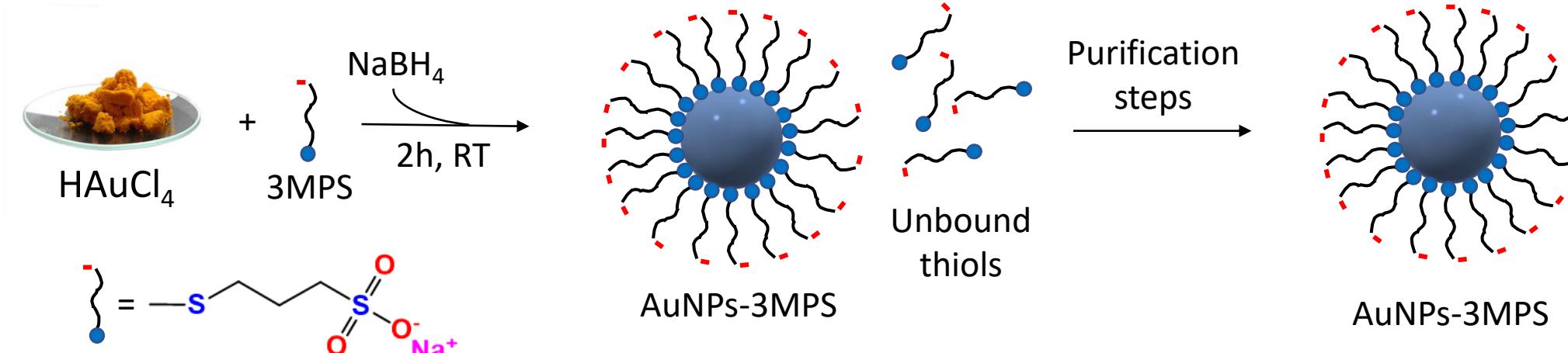
Gold Nanoparticles



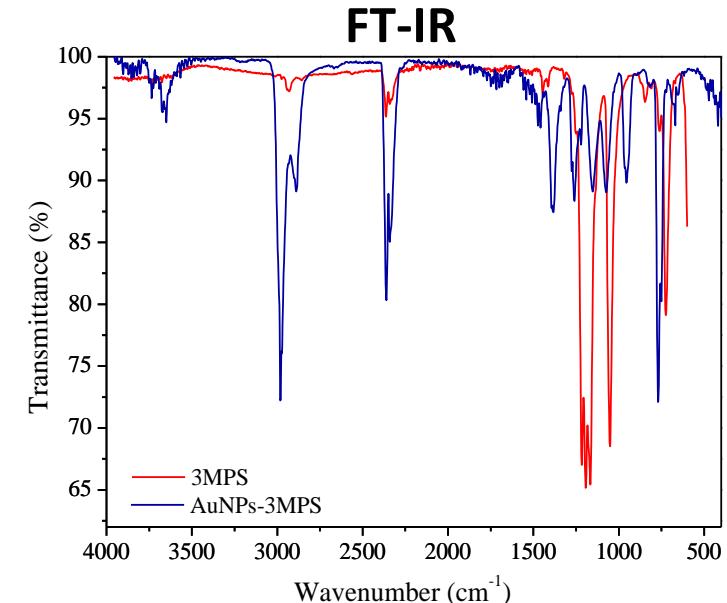
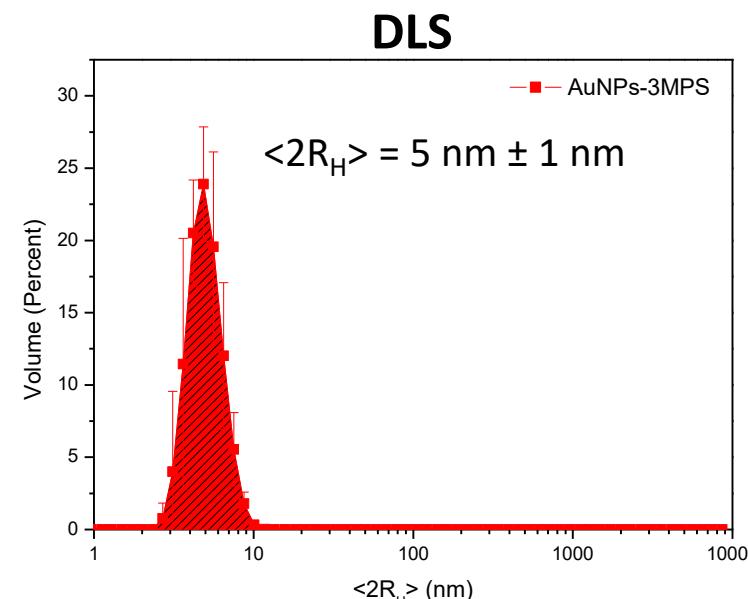
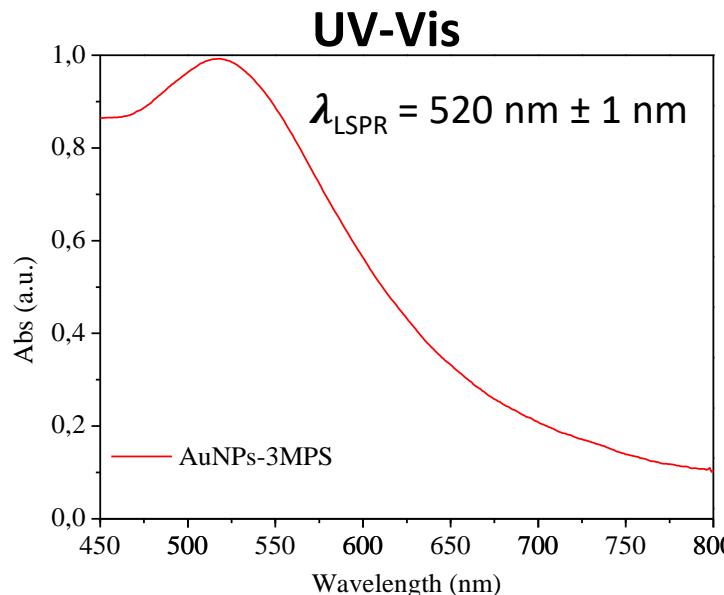
Immobilization of the drug on AuNPs

Synthesis Method

i)

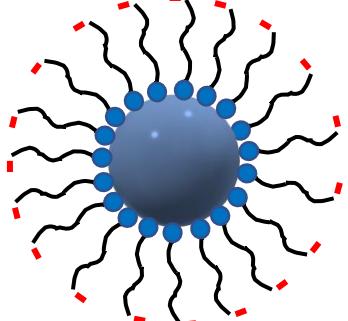


3MPS = Sodium 3-mercaptopropanesulfonate

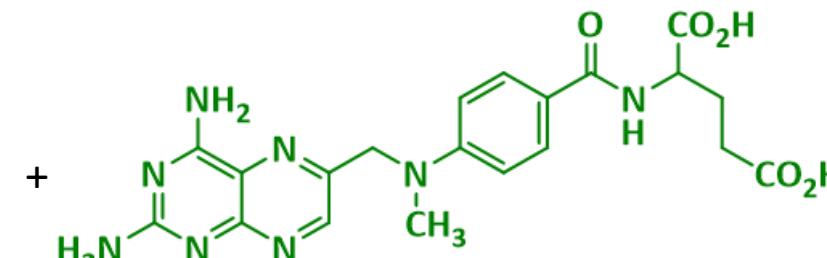


Synthesis Method

ii)

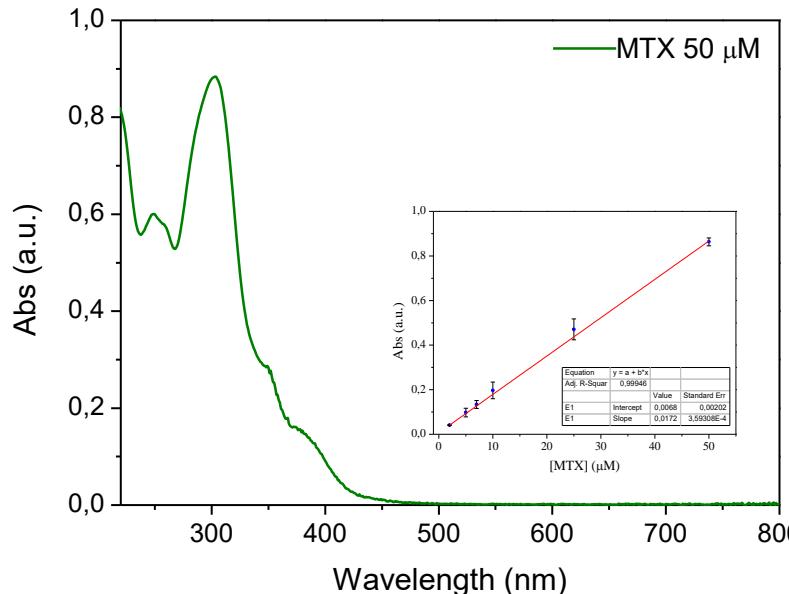


AuNPs-3MPS

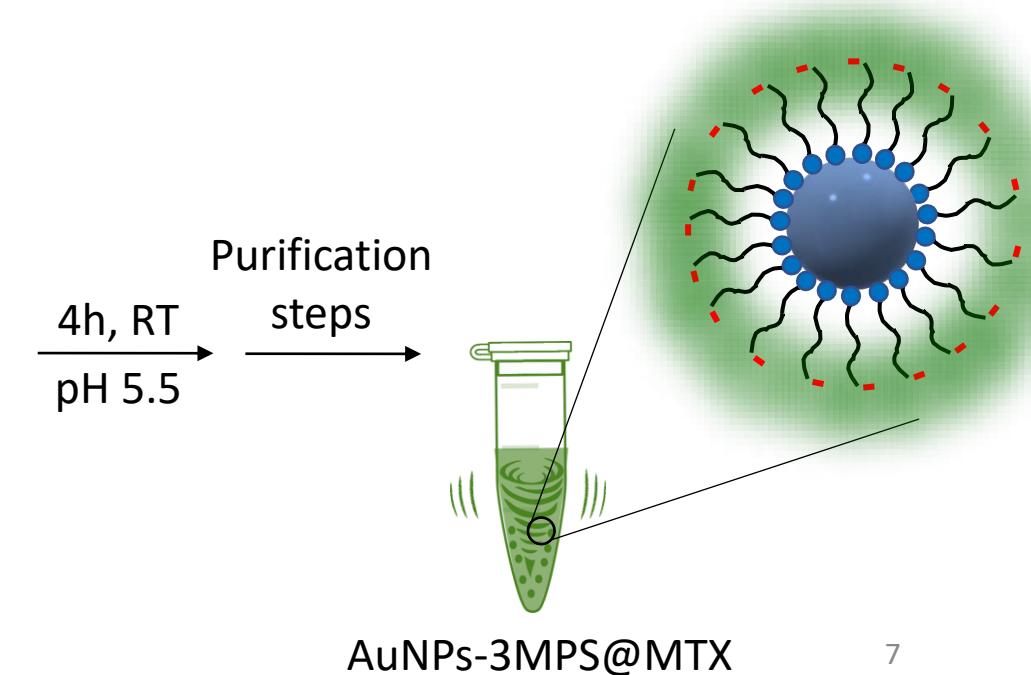


Methotrexate
(MTX)

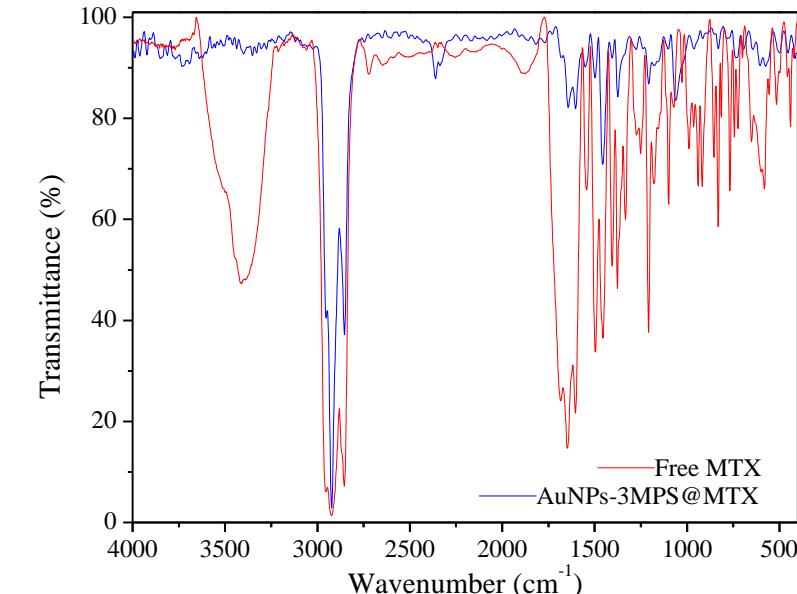
Ratio wt/wt 5 : 1



- %Loading = $80 \pm 5\%$ by interpolation at 302 nm
- $\epsilon_{302\text{nm}} = 19,330 \text{ M}^{-1} \text{ cm}^{-1}$



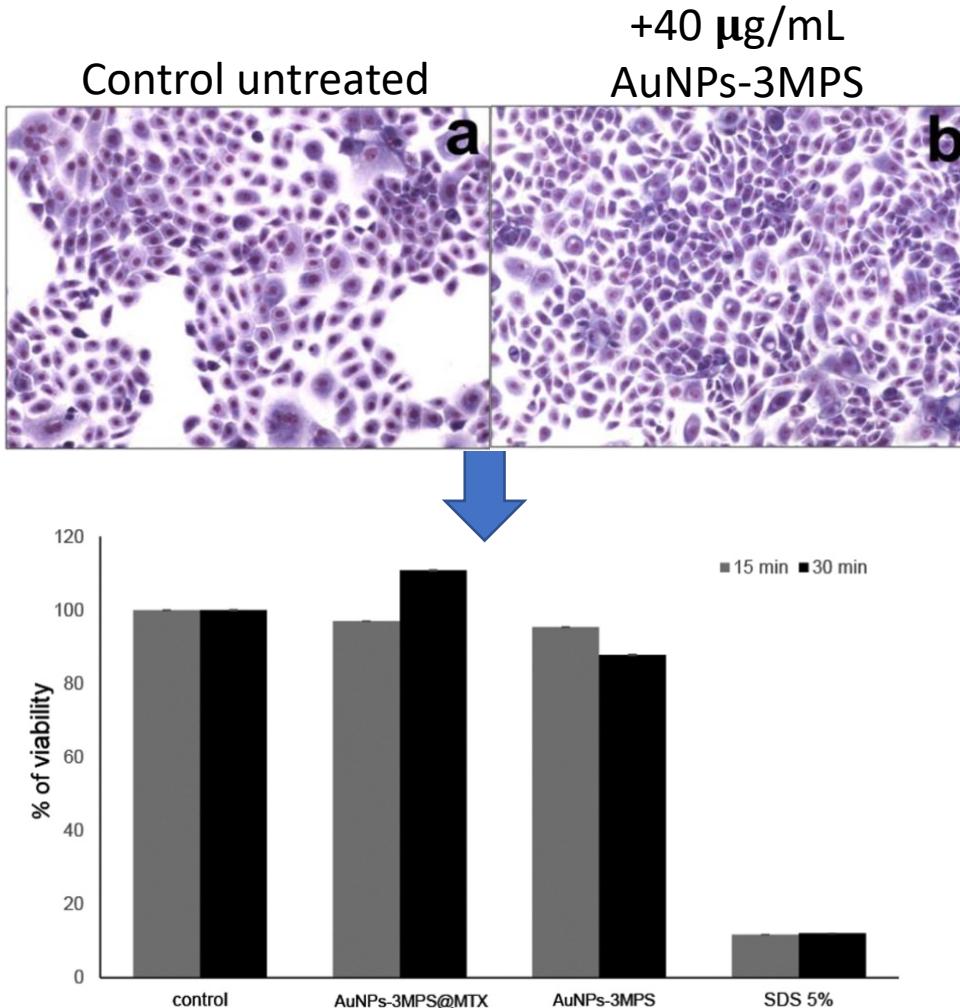
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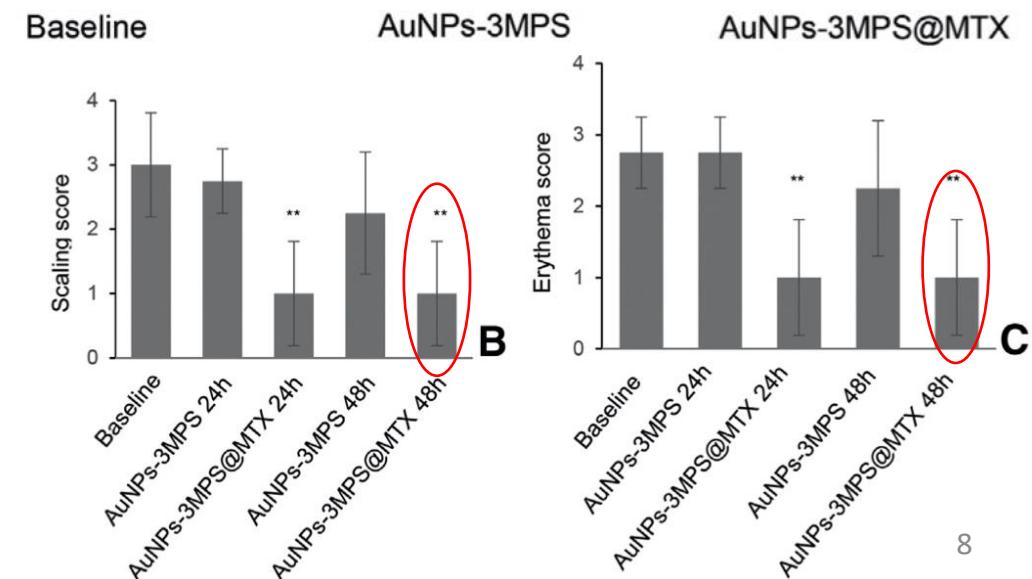
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in vitro and *in vivo* studies

- To assess efficacy in the treatment of psoriatic symptoms of AuNPs-3MPS@MTX
- To exclude toxic conditions of AuNPs-3MPS and AuNPs-3MPS@MTX



FORMULATION: AuNPs-3MPS@MTX + Locobase cream

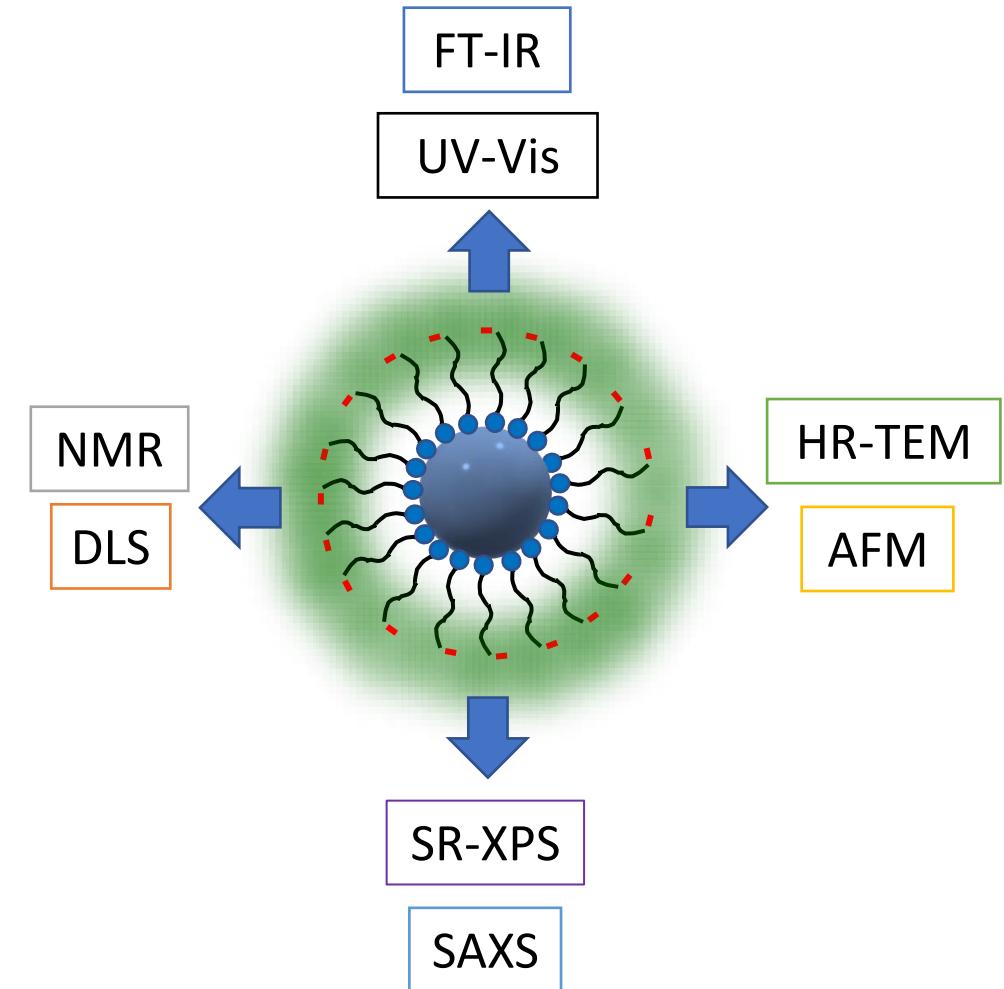


AuNPs and MTX: the interaction

- ✓ Hydrophilic Gold Nanoparticles functionalized with 3MPS thiols
- ✓ Successful loading ($80\pm5\%$) of MTX onto nanoparticles surface
- ✓ Small-sized AuNPs-3MPS@MTX are non-toxic carrier both *in vitro* and *in vivo*
- ✓ AuNPs-3MPS@MTX reduce psoriatic symptoms within 48 hours

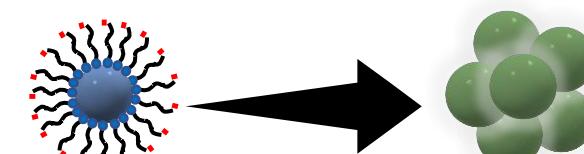
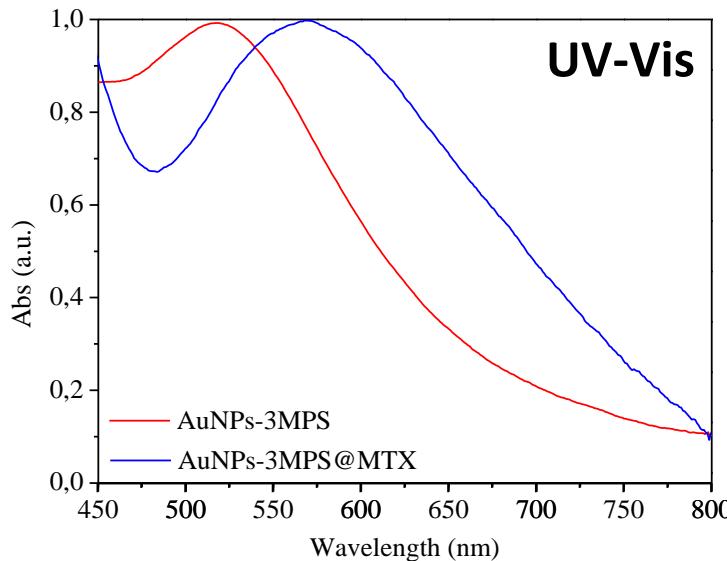
→ How AuNPs and MTX interact with each other?

- Nanoparticle@Drug **physicochemical interactions**

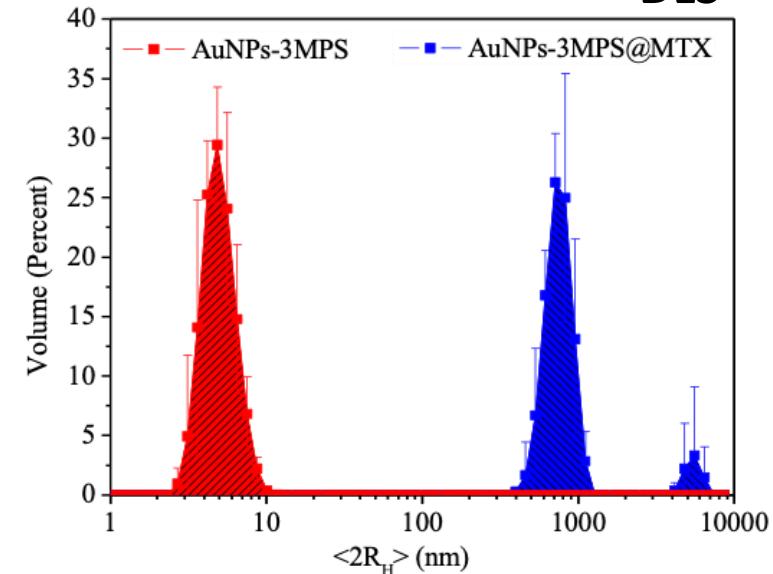


AuNPs and MTX: UV-Vis, DLS and SAXS

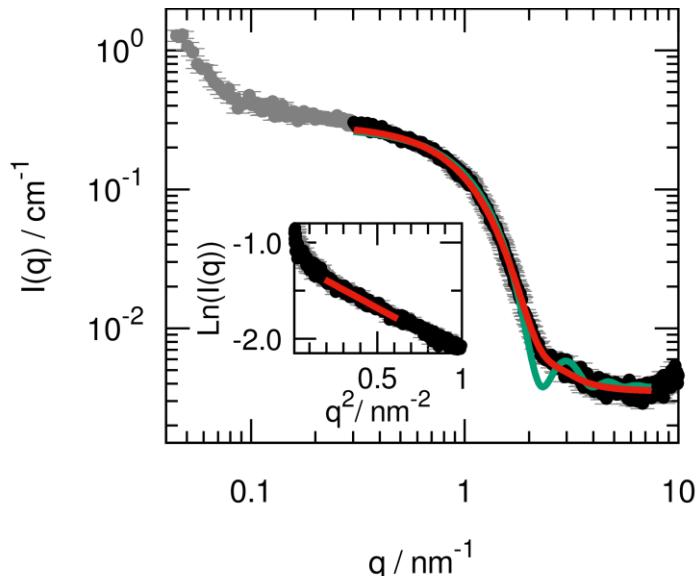
DLS



λ_{LSPR}	520 nm	570 nm
$\langle 2R_H \rangle$	$5 \pm 1 \text{ nm}$	$710 \pm 160 \text{ nm}$

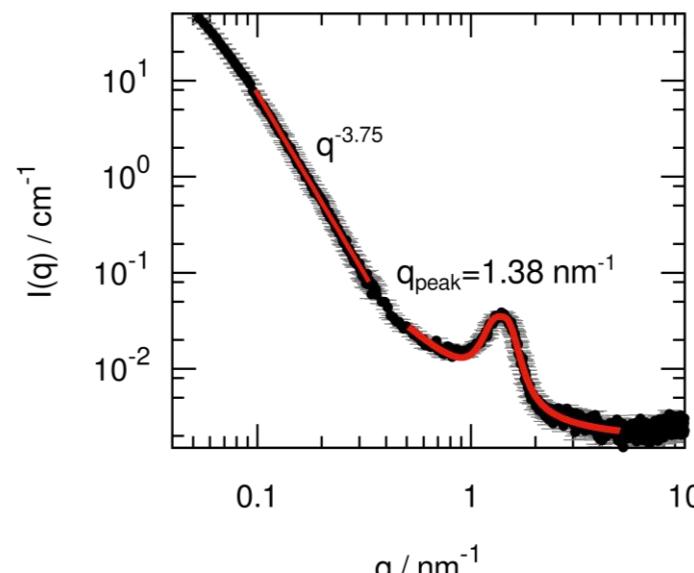
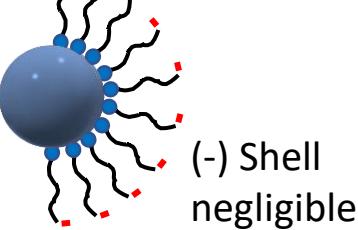


SAXS Fit: Homogeneous sphere + polydispersity of $1.60 \text{ nm} \pm 25\%$ width



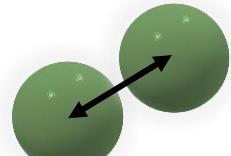
- $R_g = R \cdot \sqrt{0.6} = 1.69 \text{ nm}$

- $R_g/R_H = 0.69$

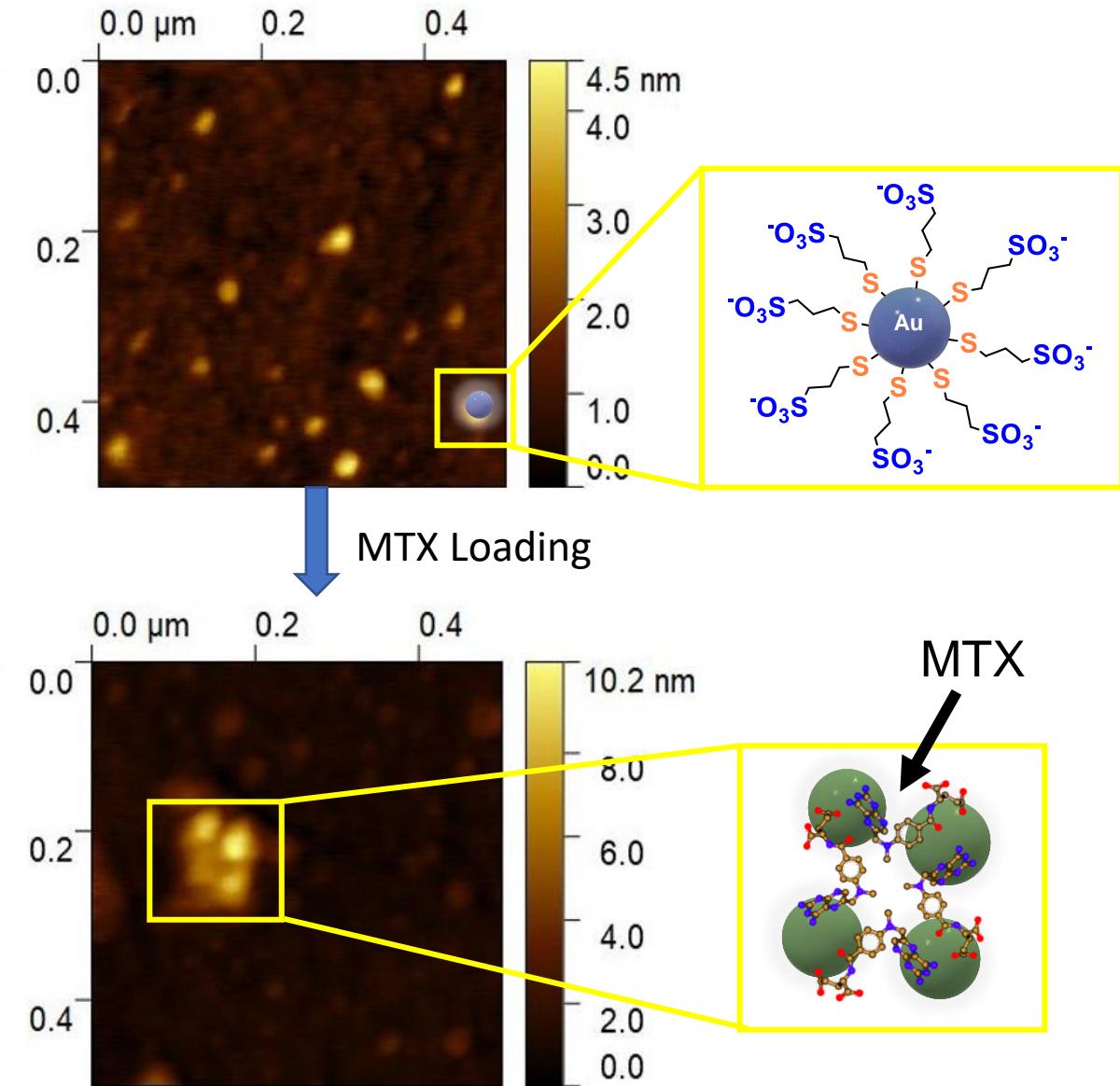
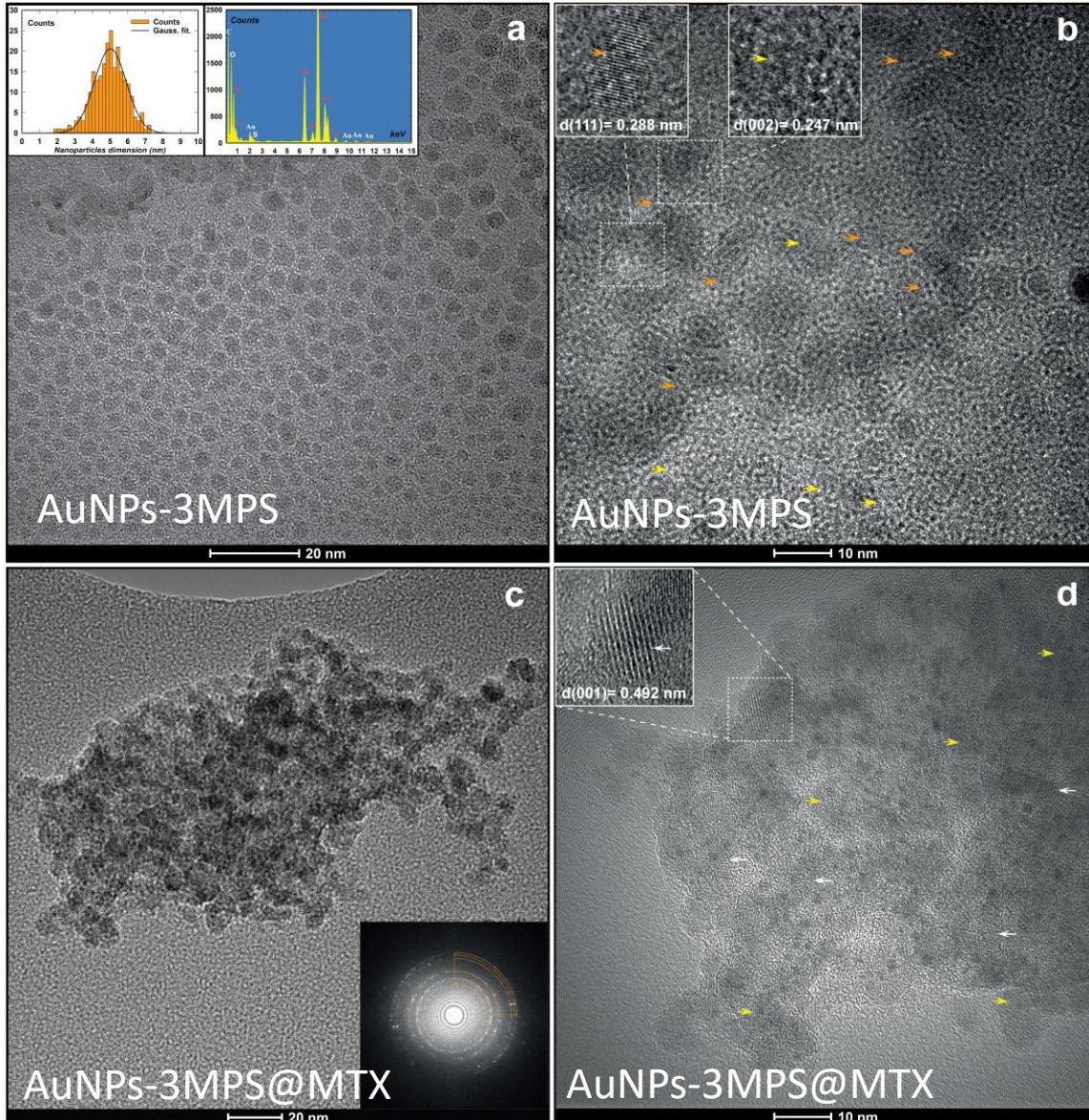


- Peak at 1.38 nm^{-1}

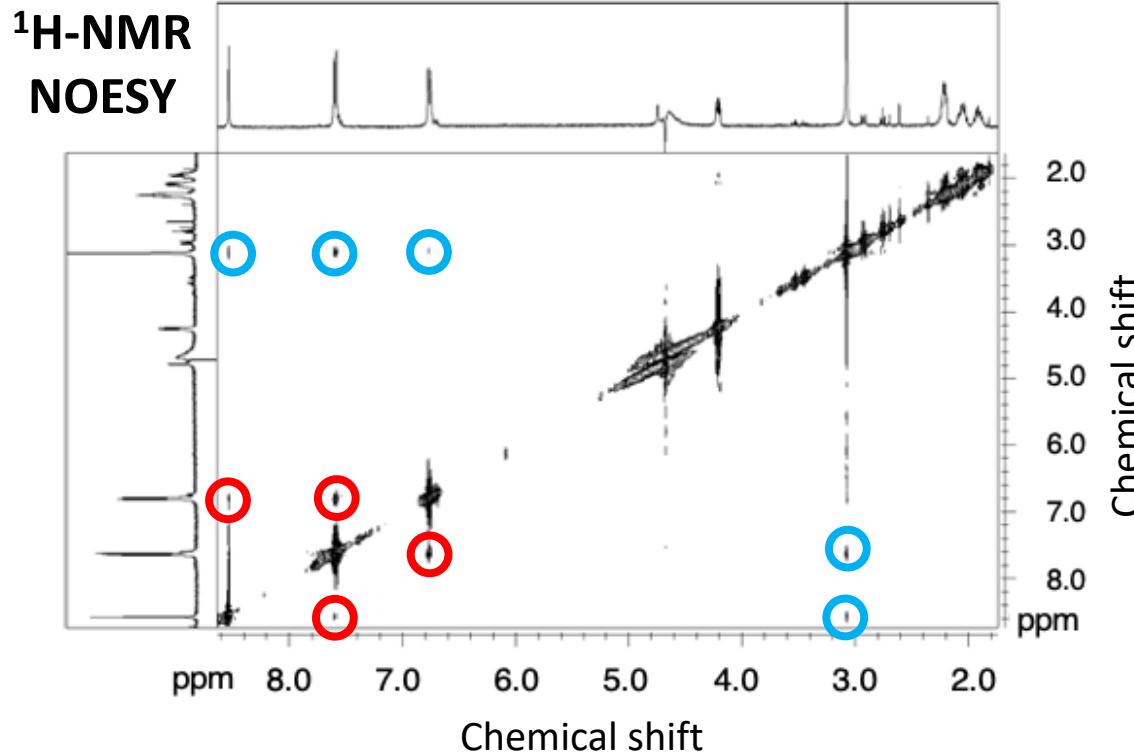
- $d_{\text{AuNPs}} = 4.55 \text{ nm}$



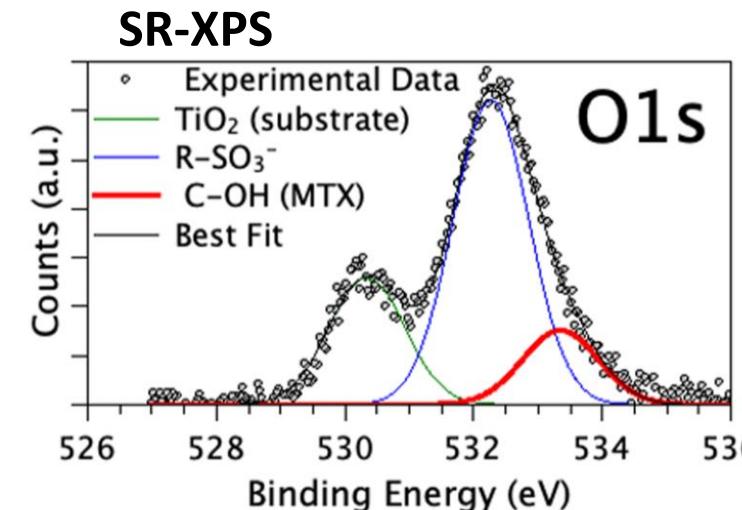
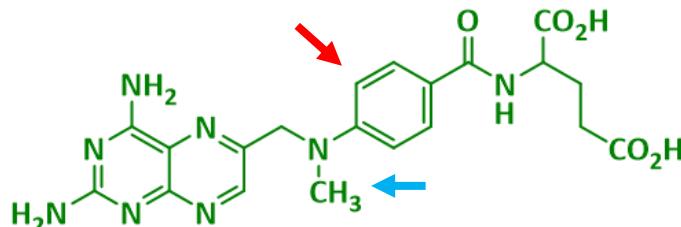
AuNPs and MTX: HR-TEM and AFM



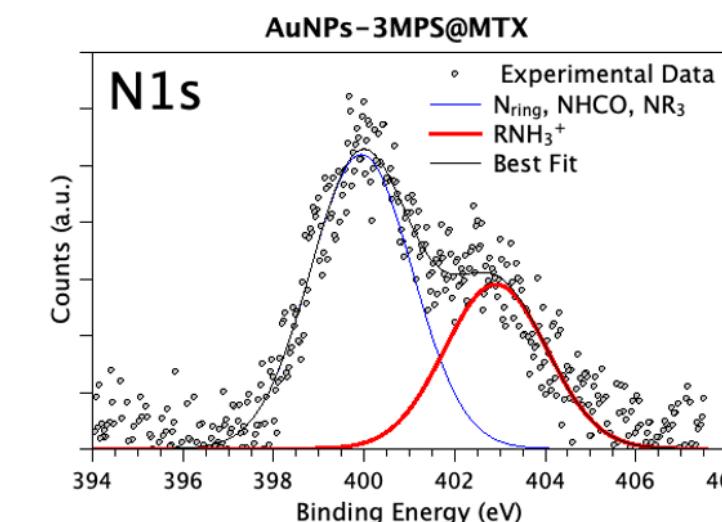
AuNPs and MTX: ^1H -NMR and SR-XPS



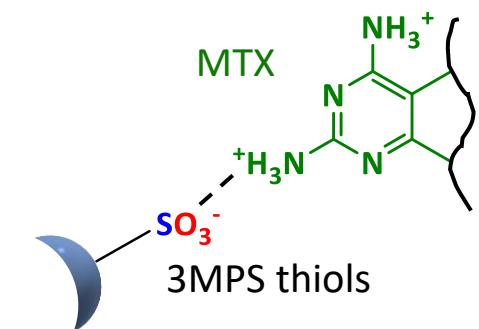
→ Spatial correlation among **aromatic protons** and between **aromatic protons** and **$-\text{CH}_3$** of MTX

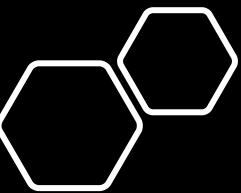


- Effective loading of MTX → peak related to $-\text{OH}$ groups of MTX



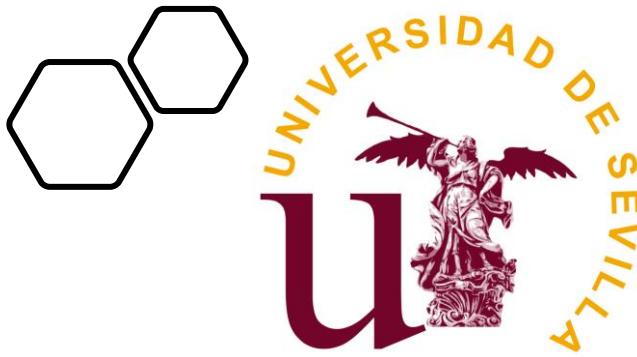
- Signal at 401.6 eV BE associated with RNH_3^+ of MTX





Conclusions

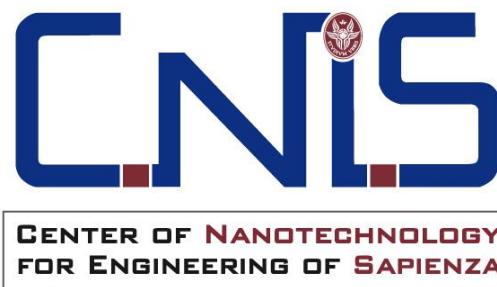
- AuNPs-3MPS and MTX interaction can be categorized into electrostatic binding: NMR and SR-XPS
- Isolated AuNPs showed a tendency to aggregation after addition of MTX: UV-Vis, DLS, AFM and HR-TEM
- MTX interacting electrostatically leads to a formation of large clusters with densely packed arrangement of AuNPs-3MPS@MTX: HR-TEM and SAXS
- The aggregation behavior do not interfere with biological activity



Elettra Sincrotrone Trieste



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- Dr. Igor Píš
- Dr. Francesca A. Scaramuzzo
- Dr. Fabio Sciubba
- Dr. Alessandra Del Giudice

...THANK YOU!

→ See also the poster PS.12 on NanoInnovation website!