Lomonosov Moscow State University

SYNTHESIS AND CHARACTERIZATION OF A BIFUNCTIONAL PLATFORM BASED ON MAGNETITE-GOLD NANOPARTICLES FOR THERANOSTICS OF CAN-CER

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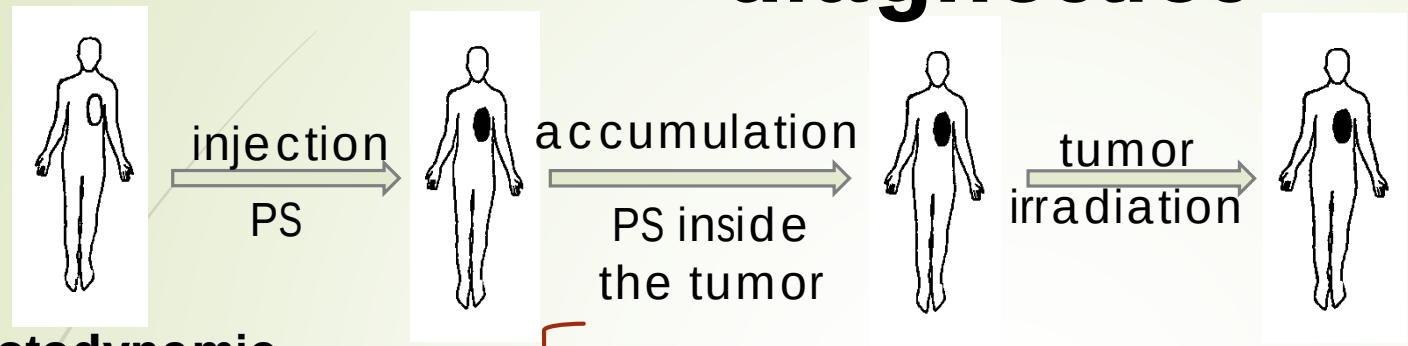
Photodynamic therapy and fluorescence diagnostics

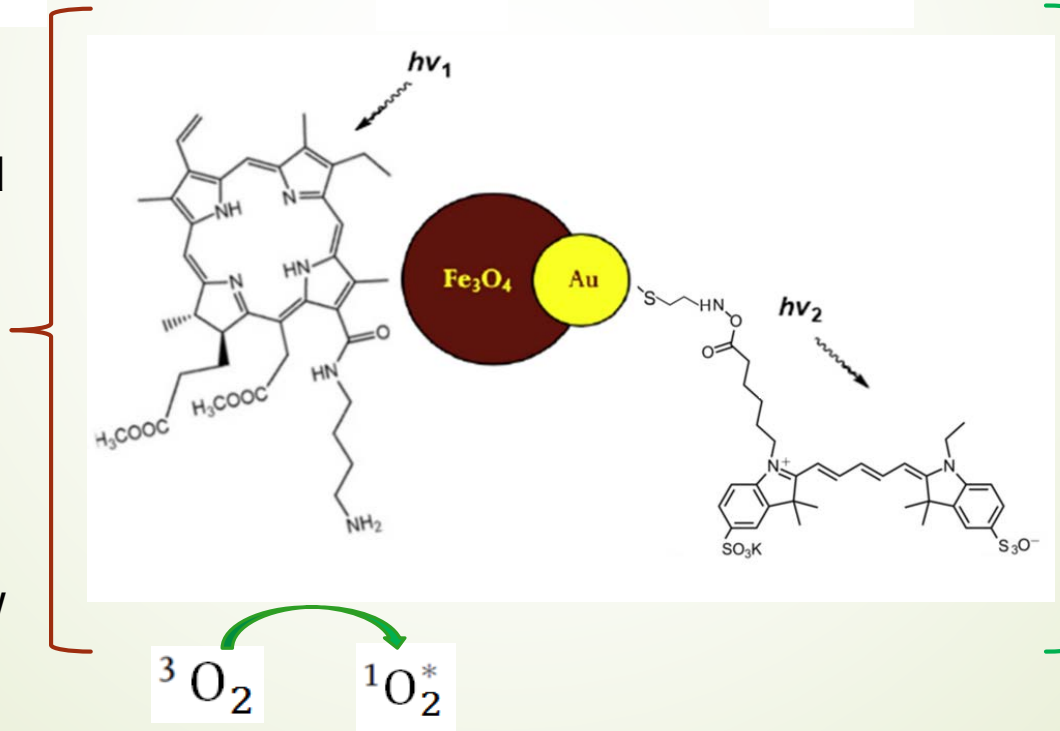


fluorescence diagnostics + photodynamic therapy (theranostics)

photodynamic therapy

-absorption in the near infrared region
-high quantum yield $^1O^*_2$
-low dark toxicity
- quickly excreted from the body

- low values of Stokes shift (low contrast of images)
-low fluorescence intensity (because high quantum yield $^1O^*_2$)



fluorescence diagnostics

-high photostability
-intense fluorescence
- high values of Stokes shift
-diagnostics without concomitant toxicity

Universal Agents Based on Magnetite-Gold Nanoparticles as Systems for Drug Delivery in Tumors

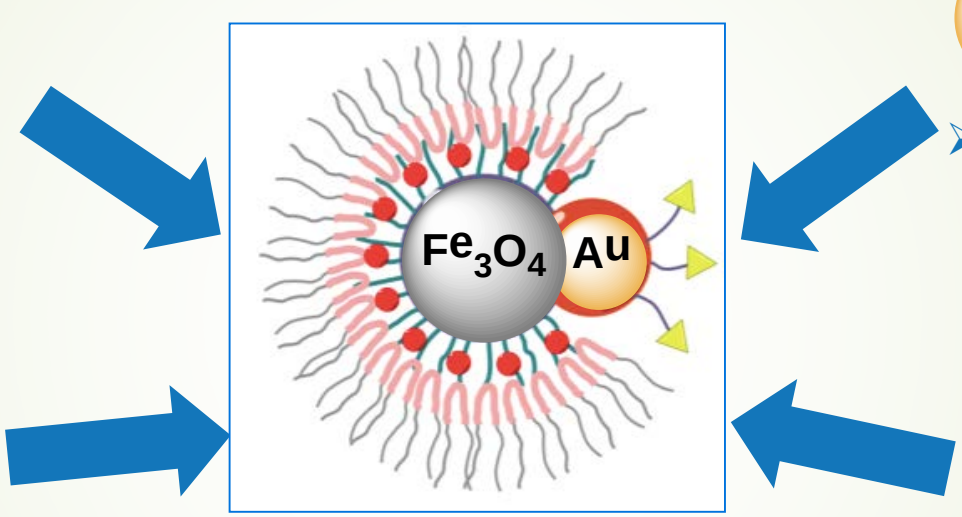
Magnetite

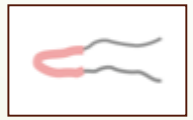
Fe_3O_4

- Contrast in MRI images
- Linkage with the PS and its "magnetic" delivery

Photosensitizer (PS)

Chromophore for photodynamic therapy





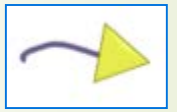
DOPAC (EDC/NHS), PEG

- Stability in physiological environments
- Covalent conjugation

Au

Gold

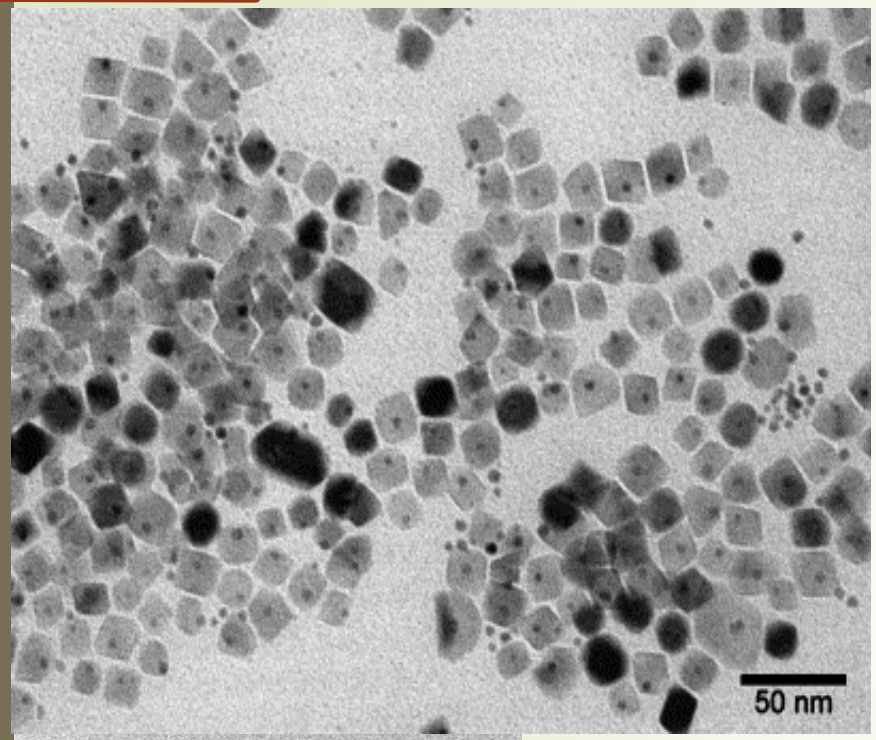
- Covalent bond with FP for fluorescence diagnostics
- Use of hyperthermia

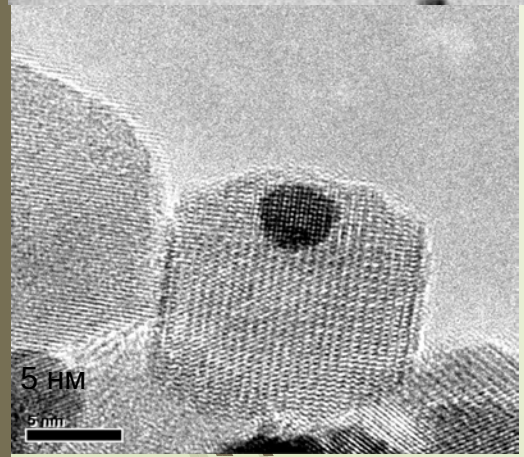


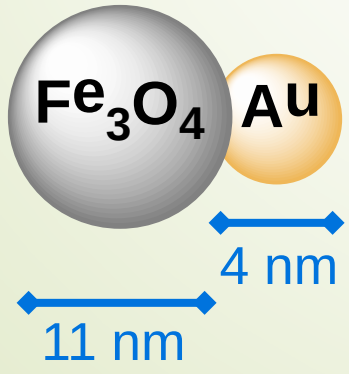
Fluorophore (FP)

Chromophore for fluorescence diagnostics (detection)

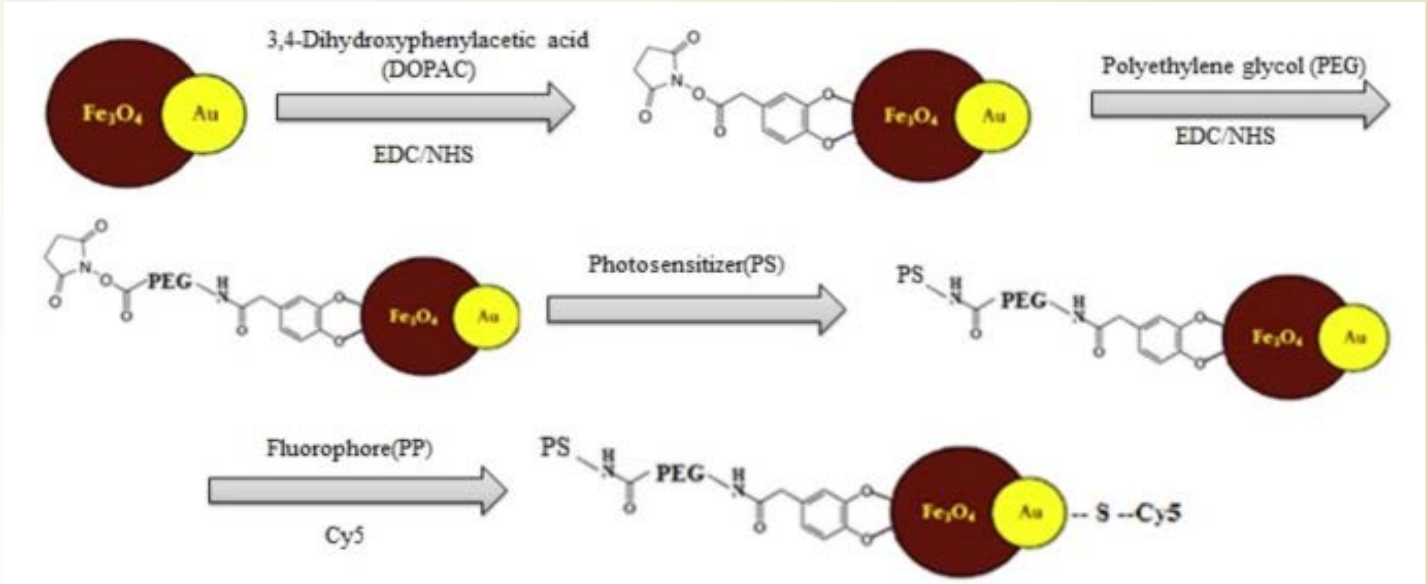
Transmission electron microscopy of the obtained NPs (TEM)

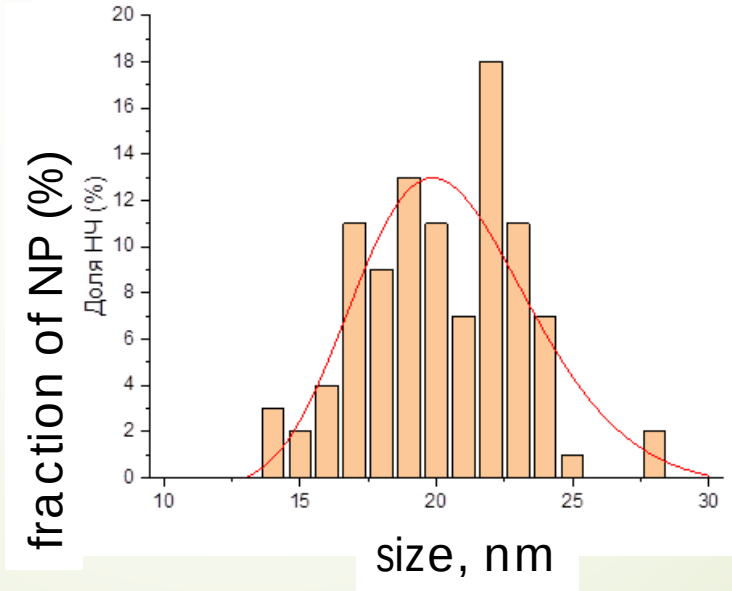


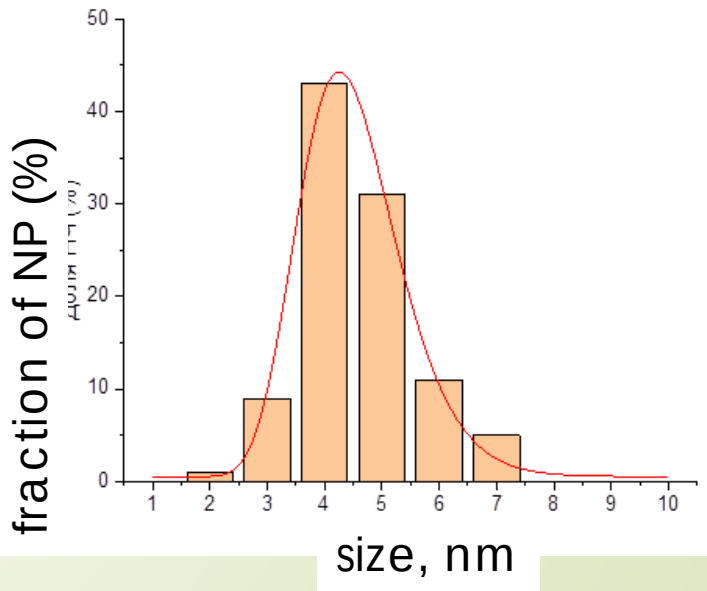




Scheme of synthesis



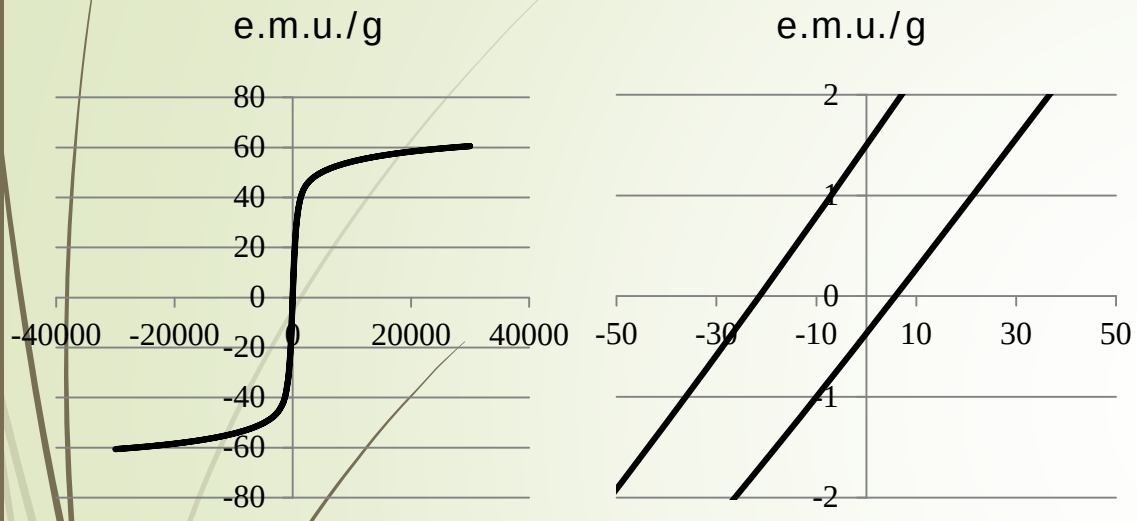




D_{Fe3O4} =11,64±1,51

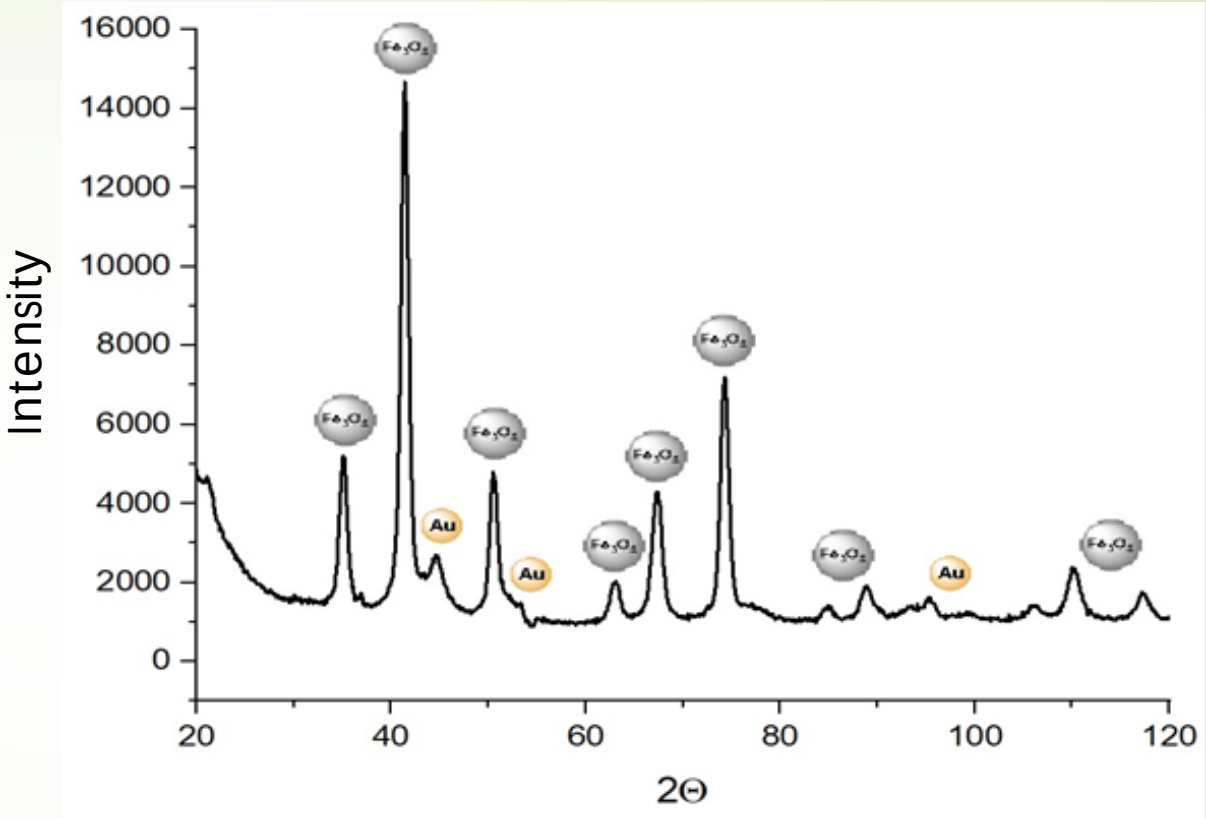
D_{Au} = 4,52±0,83

Magnetic properties



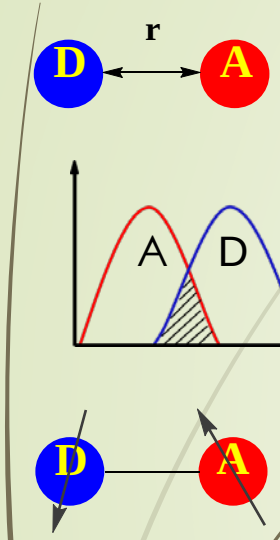
	NP Fe_3O_4-Au	magnetite	maghemite
M_S	62.3	70-80	40

X-ray phase analysis of NPs (XRD)

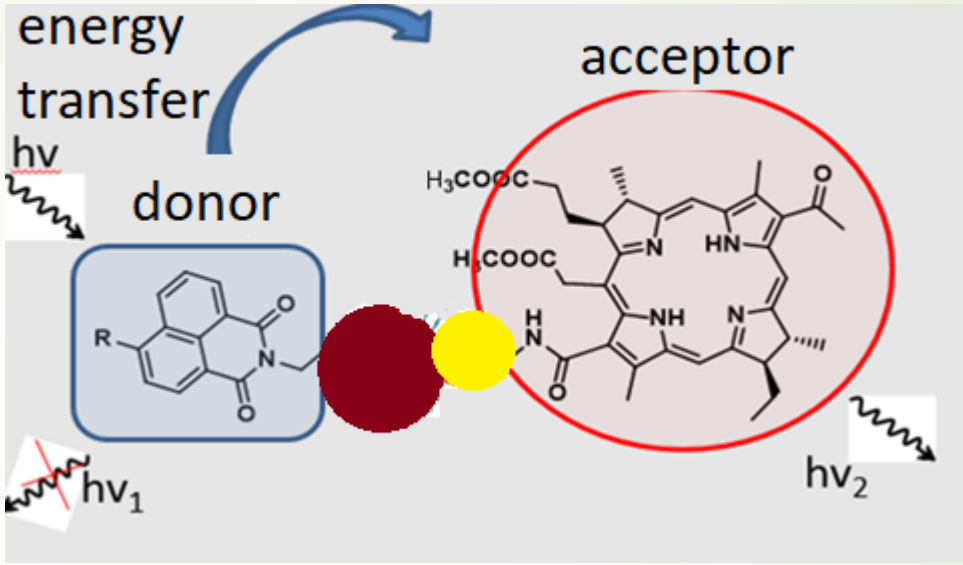


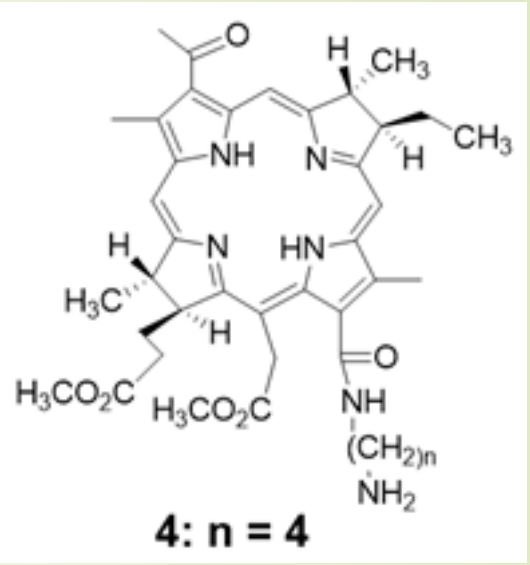
TEM			XRD					
d, nm		particle shape	volume fraction, %		crystallite size, nm		lattice parameter, nm	
Fe_3O_4	Au		Fe_3O_4	Au	Fe_3O_4	Au	Fe_3O_4	Au
11±1,5	4±1	spherical	99,3±2,0	0,7±0,5	12±2,0	5±1,0	0,8387 ±0,0004	0,4064 ±0,0004

Factors that determine the efficiency of energy transfer



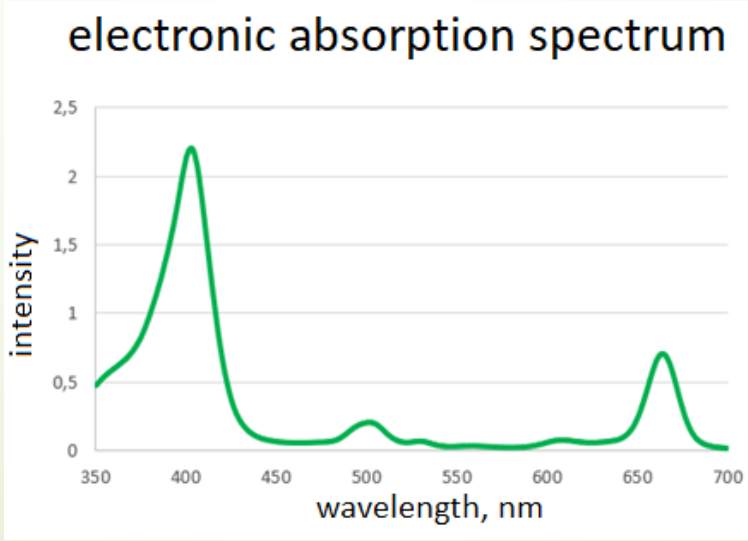
1. **Distance between donor and acceptor**
2. **Overlap integral fluorescence spectra D and absorption A**
3. **Mutual orientation m fluorophores**

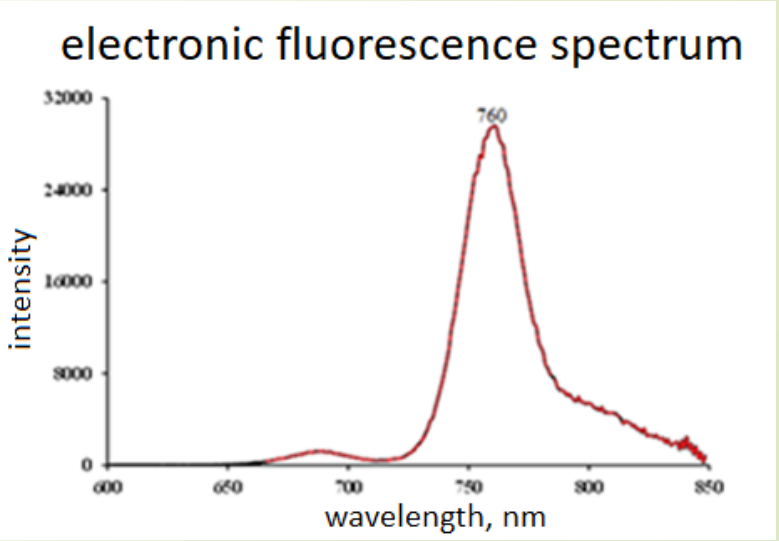




photosensitizer	φO_2^1
PS (n=4)	0.79

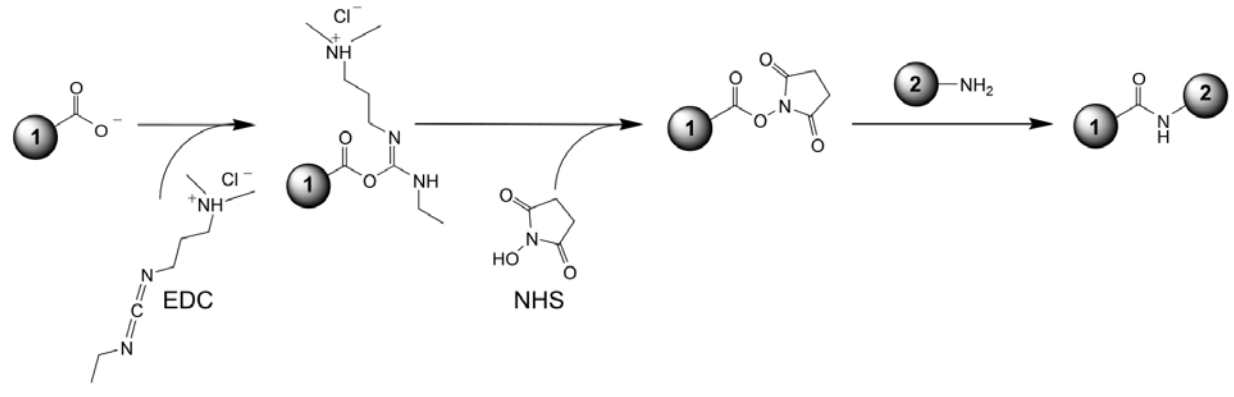
Forster radius (R_0) 14,64 Å

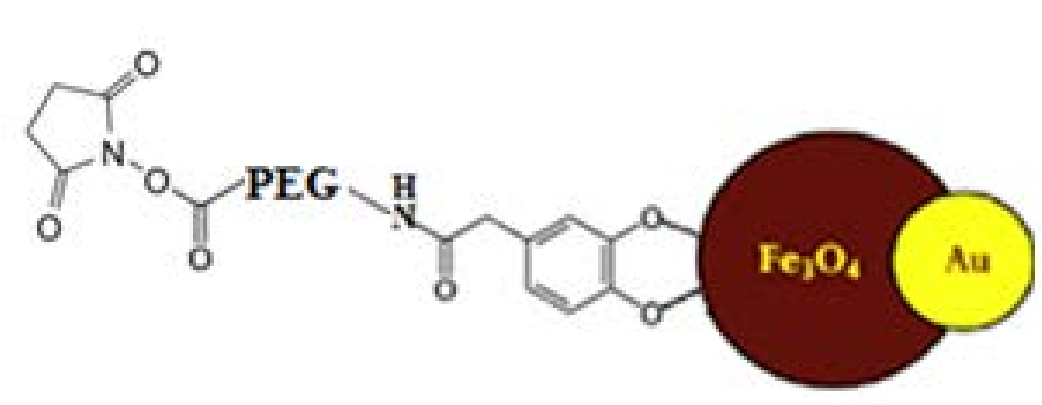




DOPAC/PEG coating

EDC/NHS activation (1-DOPAC, 2 –PEG)



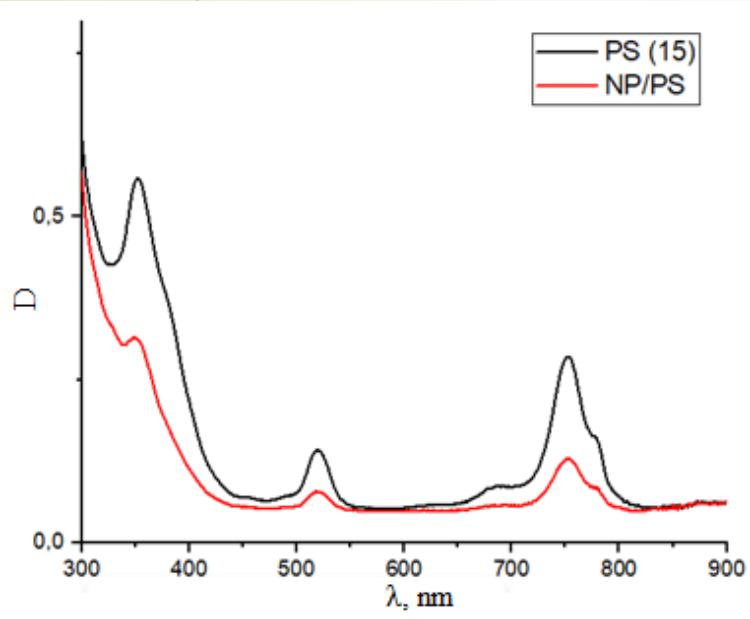


Dynamic light scattering (DLS)

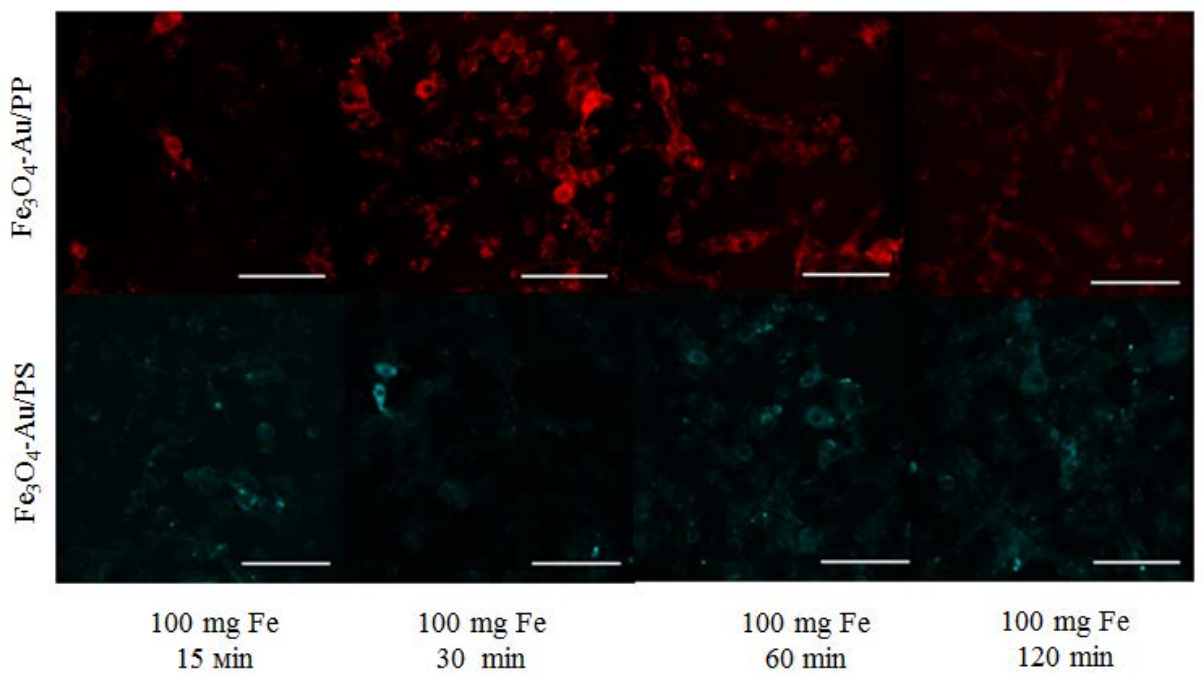
	Fe_3O_4-Au/ DOPAC	Fe_3O_4-Au/ DOPAC/PEG	Fe_3O_4-Au/ DOPAC/PEG/PS	Fe_3O_4-Au/ DOPAC/PEG/FP	Fe_3O_4-Au/ DOPAC/PEG/PS/FP
Size	23,36	24,47	25,76	26,01	25,99
PDI	0,239	0,233	0,329	0,275	0,299

Systems Research Fe_3O_4-Au/PS and Fe_3O_4-Au/FP

absorption spectra Fe_3O_4-Au/PS



In vitro studies on colon cancer cells (CT26)



Conclusions

- The method of combined thermal decomposition of iron pentacarbonyl and hydrogen tetrachloroaurate makes it possible to obtain hybrid magnetite-gold NPs of size Fe_3O_4 10.8±1.5 nm and Au 4.4±0.8 nm, stabilized with oleic acid;
- The FRET-pair PS/FP (PS, n=4/Cy5) was selected and the optical properties were studied;
- Modification of DOPAC and PEG NPs followed by activation of EDC/NHS makes it possible to efficiently attach a PS to the magnetic surface of NPs in a two-phase system (water–DMSO);
- The use of a disulfide derivative of FP makes it possible to provide covalent conjugation with the gold surface;
- It was shown that the systems Fe_3O_4-Au/PS and Fe_3O_4-Au/FP are able to be internalized by CT26 colon cancer cells with the preservation of optical properties.

Future plans

For further research, it is planned to conduct experiments and calculate:
- fluorescence quantum yields of PS and FP;
- by the method of chemical traps, the generation of singlet oxygen for the selected PS according to the formula;
- efficiency of energy transfer by the FRET mechanism according to the formula. It is also planned to further study and characterize the Fe_3O_4-Au/DOPAC/PEG/PS/FP system and Fe_3O_4-Au/DOPAC/PEG/PS and Fe_3O_4-Au/DOPAC/PEG/FP conjugates in vivo.

Thank you for attention!

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