Upconversion: Odyssey

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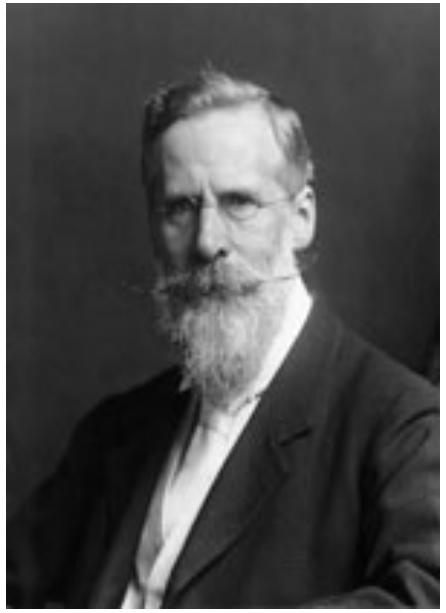


Sir William Crookes (1887)

"These elements perplex us in our researches; they baffle us in our speculations and haunt us in our very dreams. They stretch like an unknown sea before us - mocking, mystifying and murmuring strange revelations and possibilities"

Address to the British Association, 1887

Lanthanum has only one important oxidation state in aqueous solution, the +3 state. With few exceptions, this tells the whole boring story about the other 14 elements.

"*Understanding Chemistry*", *Holden-Day, 1971, p. 862*
G. C. Pimentel & R. D. Sprately,

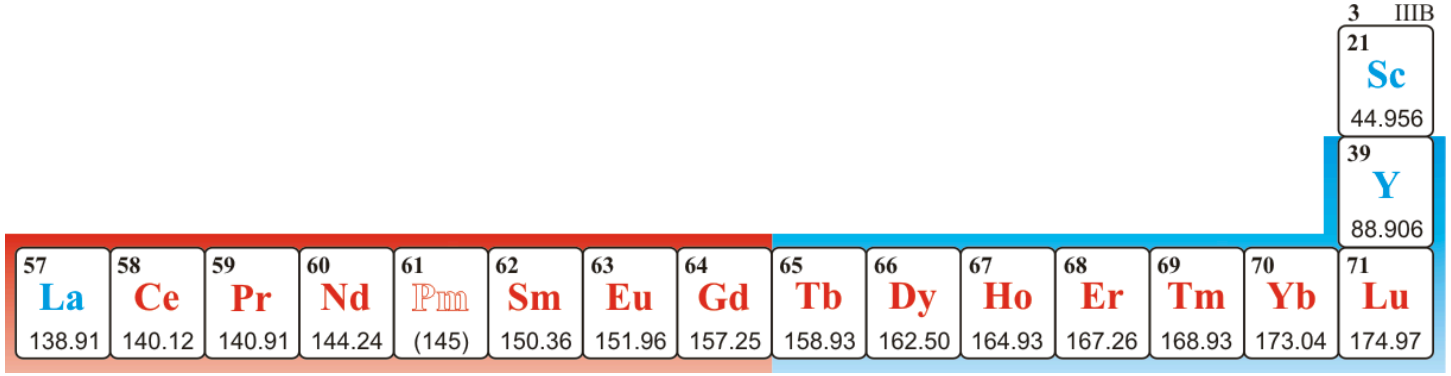
The Lanthanoids (57-71, La-Lu) *'like lanthanum'*

La, Ce, Pr, Nd, Pm, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu

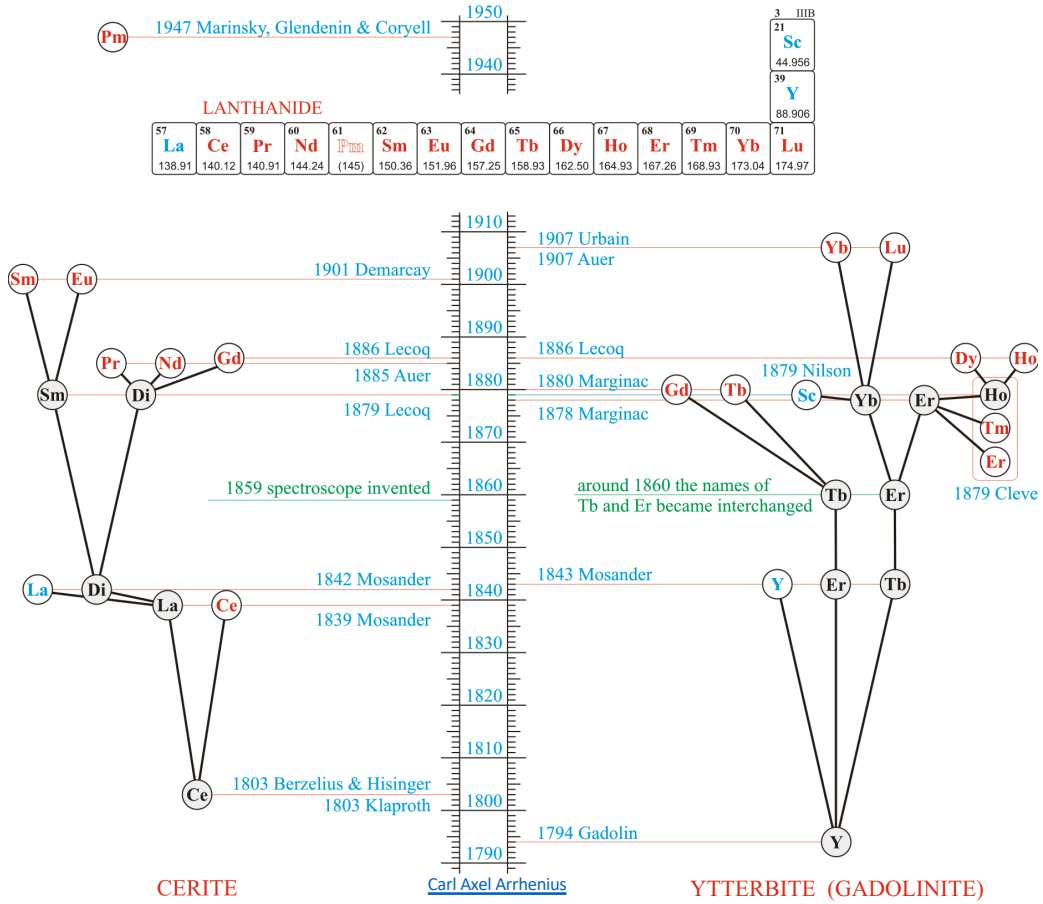
The Lanthanides (58-71,Ce-Lu)

Rare Earths

Sc, Y and the lanthanoids



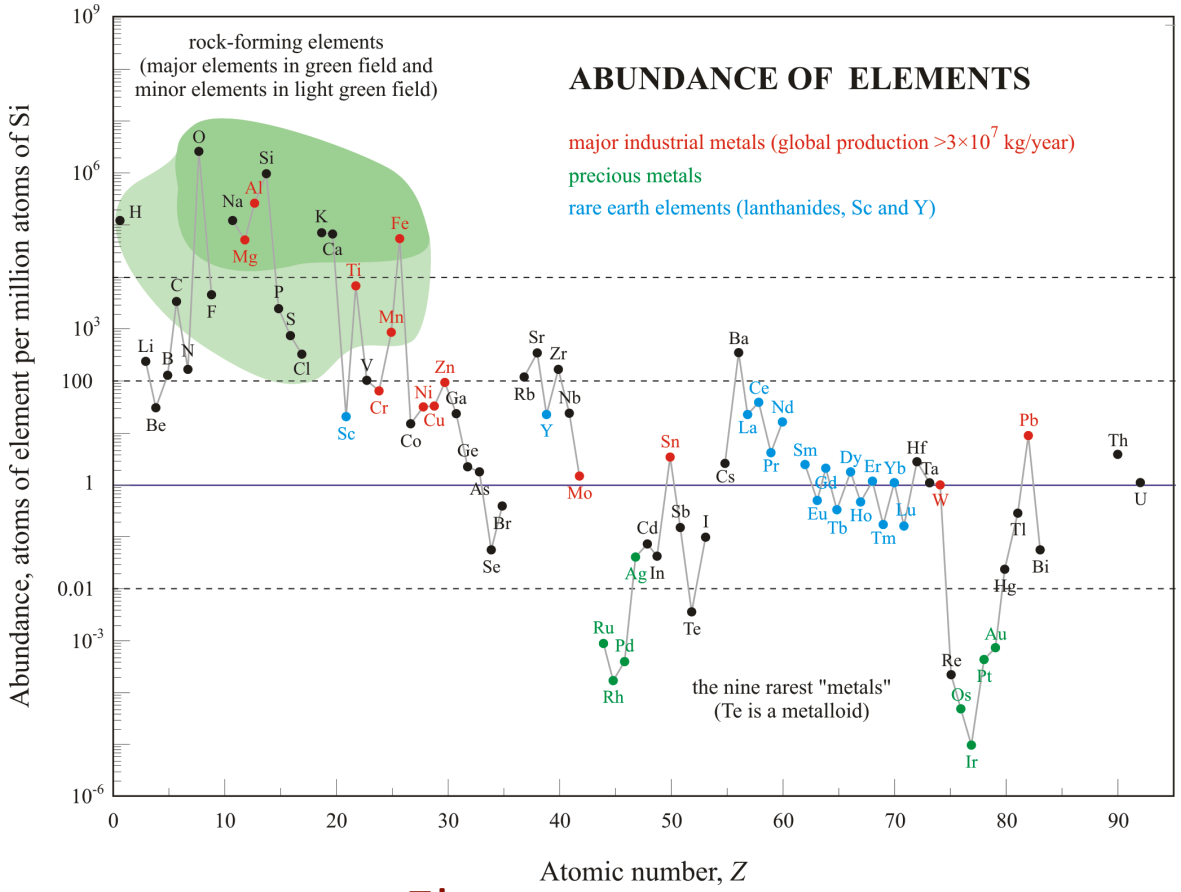
Short History of Rare Earth Elements

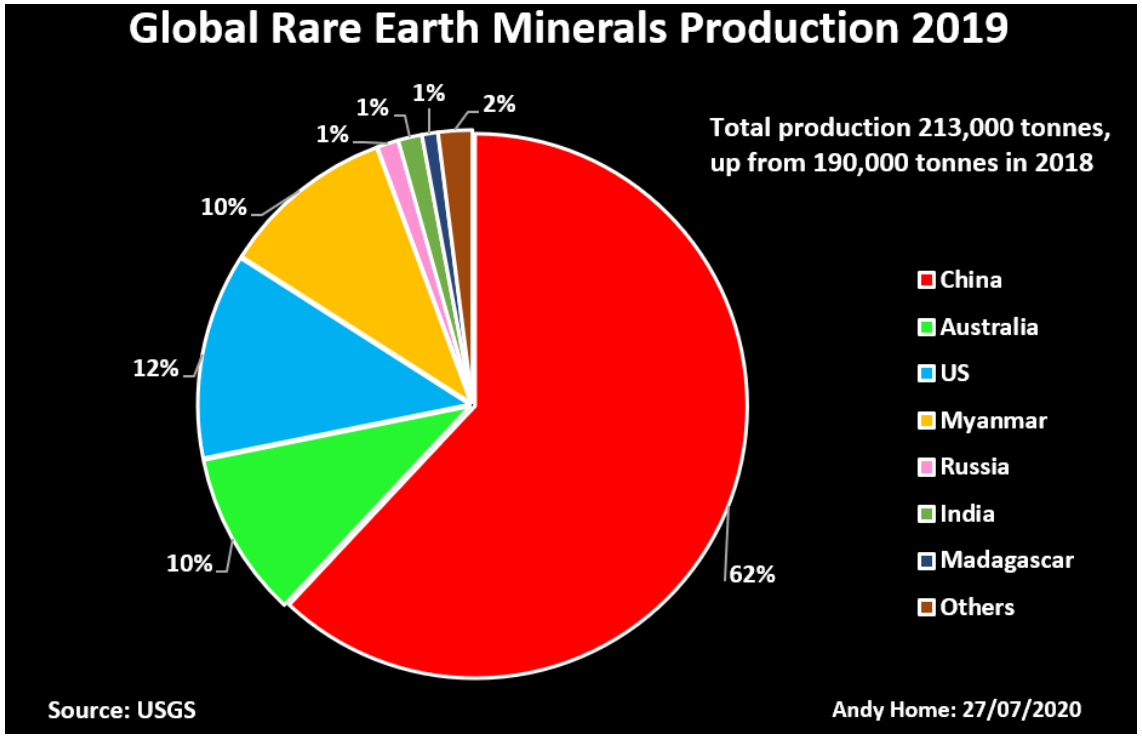


J. Gadolin

L. Wang et al., *Journal of Cleaner Production* , **2017**, *165*, 231.

Abundance of Rare Earth Elements





Element	ppm
La	20
Ce	66
Pr	9.1
Nd	40

Figure courtesy of: Rare Earth Elements (REE)." *EniG. Periodic Table of the Elements*. KTF-Split

Rare Earth Element Commercial Products

Pr Nd Tb Dy	Mobile phones, computer hard drives, cameras
La Ce Pr Nd Dy	Hybrid electric vehicles, high capacity batteries, infrared lasers
La Tb Eu Y	Energy-efficient lightbulbs
La Ce Eu Nd	Glass additives
Nd Sm	Permanent magnets for electric motors
Pm	Portable X-ray devices
Gd	MRI contrast agents
Eu Y Er	Fiber-optic lines and amplifiers

Shapes of f-orbitals

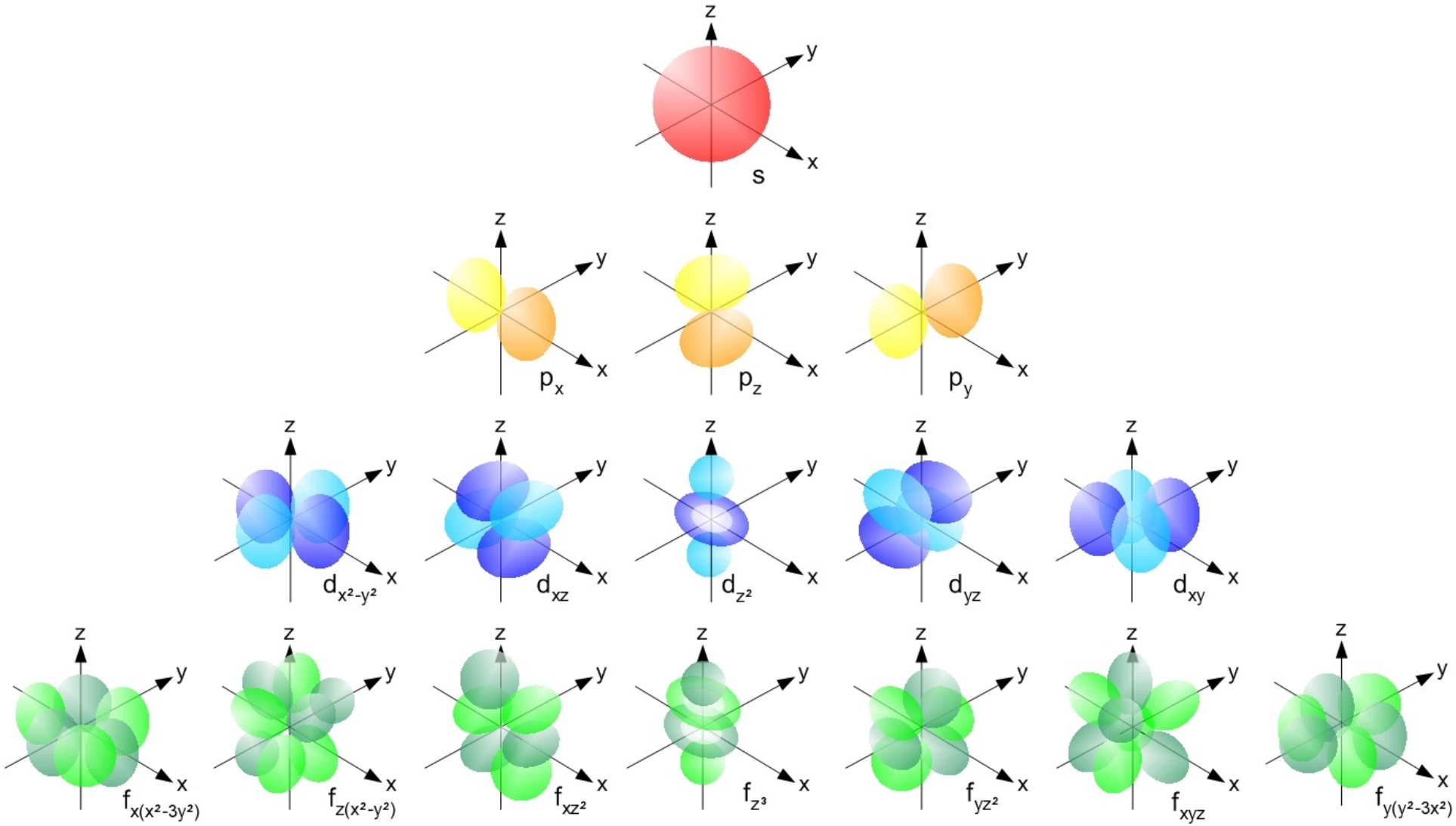
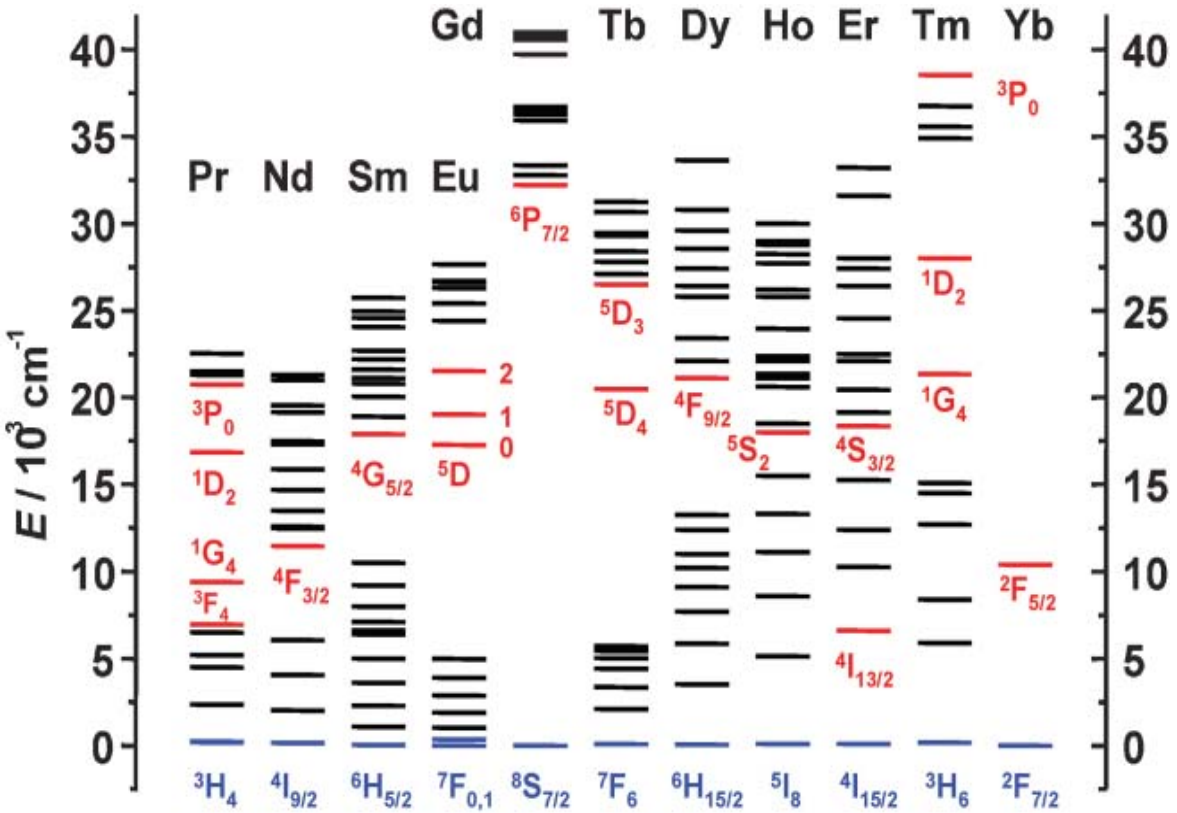
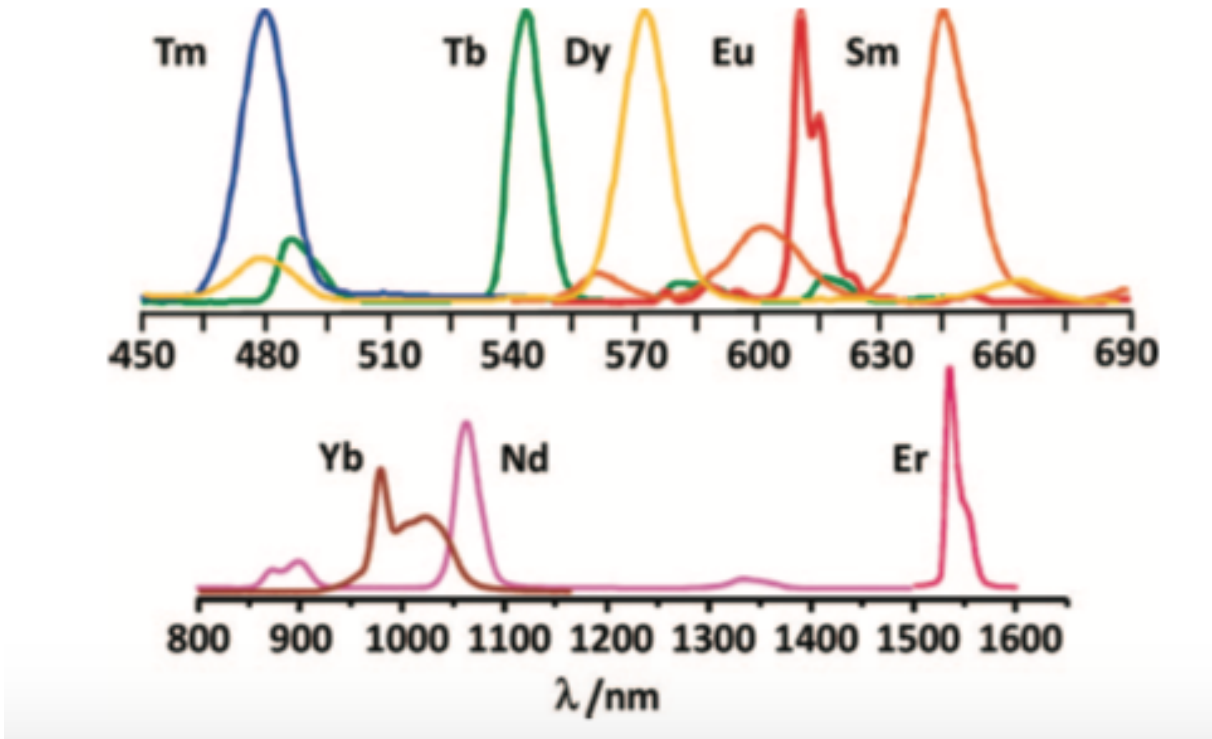


Figure courtesy of : Chemistry LibreTexts

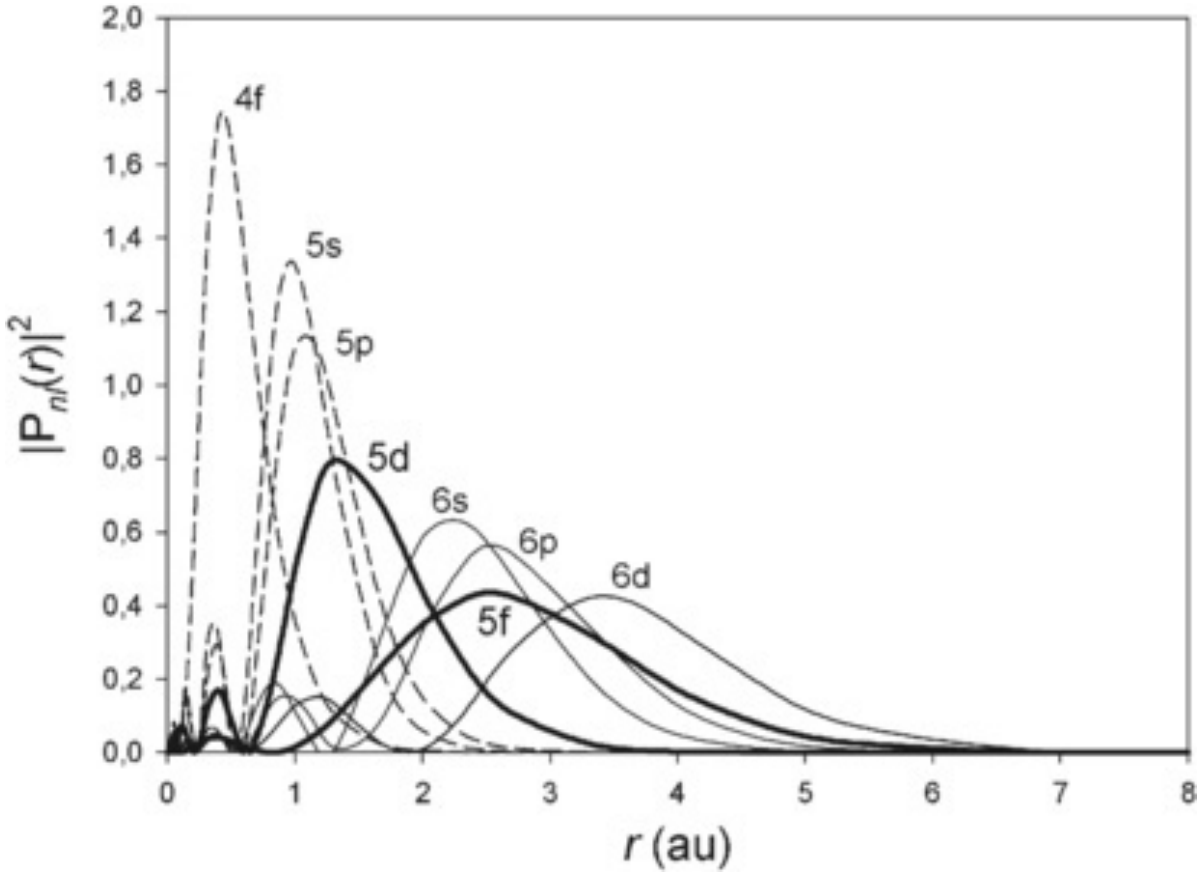
Energy levels of Lanthanides





J.-C. Bunzli., *Chemical Reviews*, **2010**, *110,* 2729.

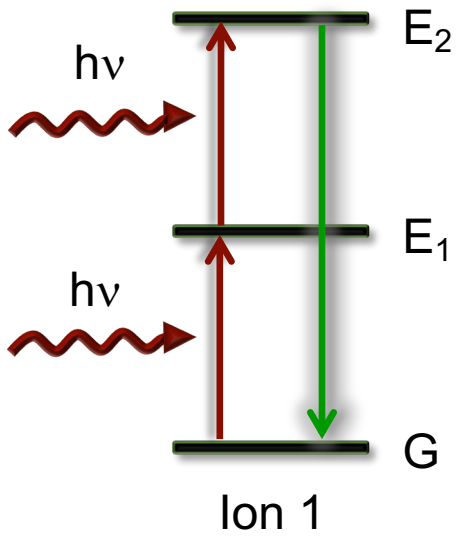
Radial Distribution – f orbital shielding



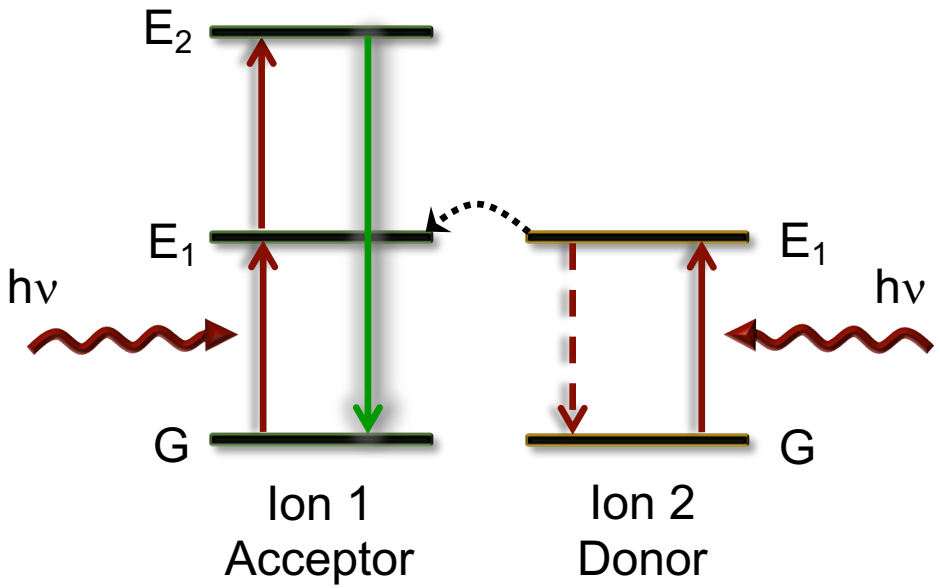
- 4f orbitals highly shielded
  - Minimal effects from the crystal field
- Lanthanides prefer to adopt trivalent configuration (+3 oxidation state)

Anti-Stokes Upconversion Processes

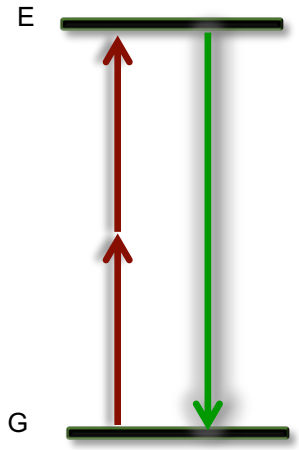
Excited State Absorption



Energy Transfer Upconversion



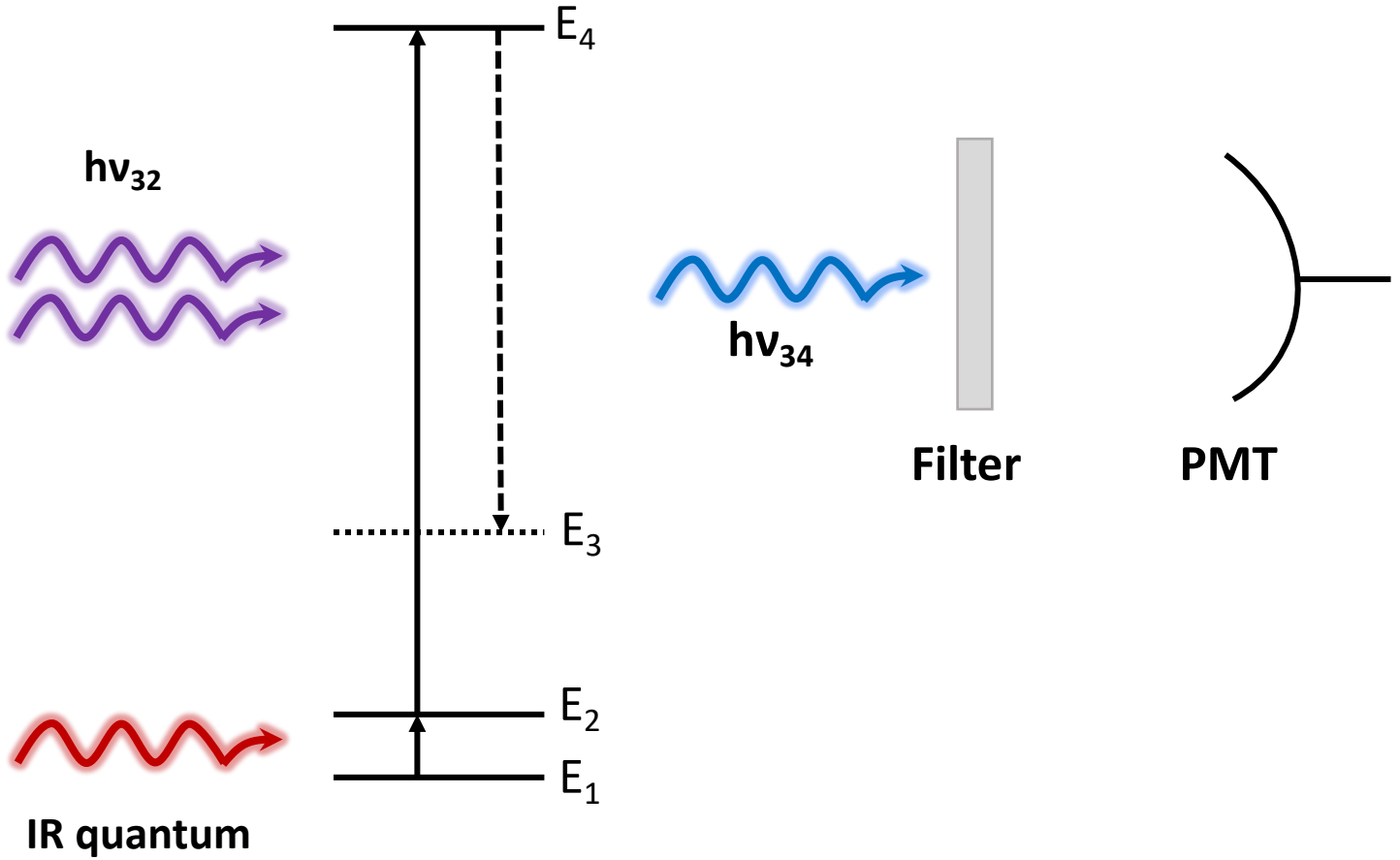
Two-Photon Absorption



Mechanism	Efficiency	Example
Energy Transfer Upconversion	10^{-3}	$NaYF_4$: Yb^{3+}, Er^{3+}
Excited Step Absorption	10^{-5}	SrF_2: Er^{3+}
Second Harmonic Generation	10^{-11}	KH_2PO_4
Two-Photon Absorption	10^{-13}	CaF_2: Eu^{2+}

Upconversion Early Years (1950 – 1960)

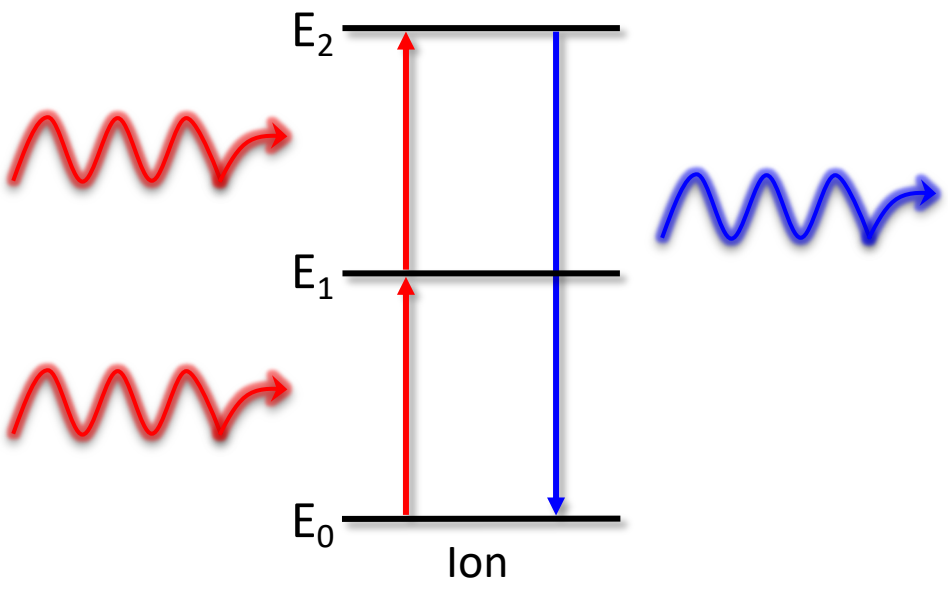
Solid state infrared quantum counters



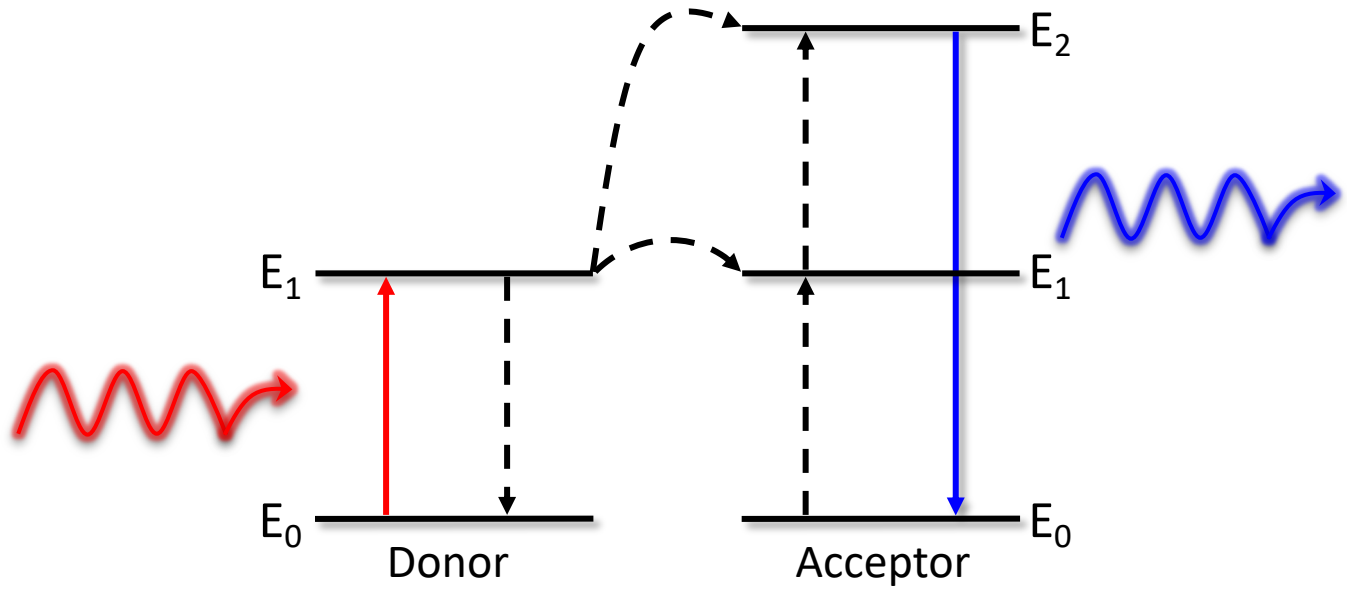
Bloembergen., *Phys. Rev. Lett., 1959, 2, 84*.

Lanthanide Upconverting Nanoparticles

Ground/Excited State Absorption

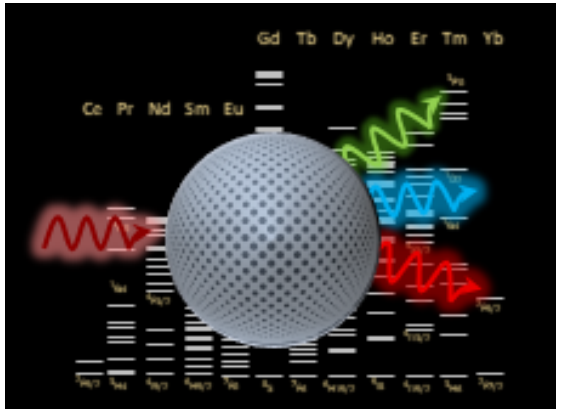


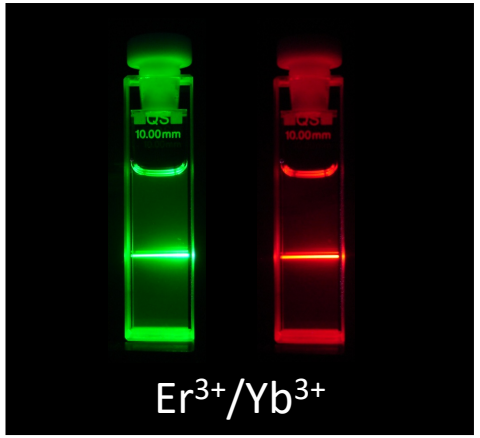
Energy Transfer Upconversion

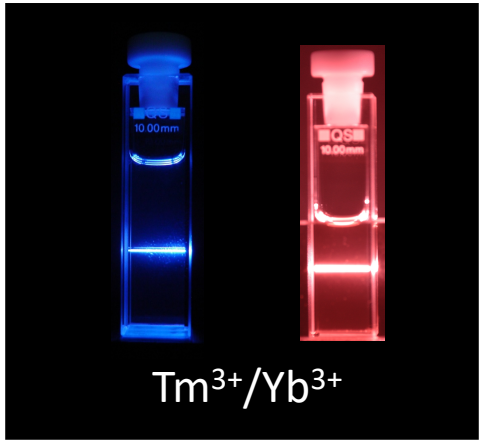


Auzel, F. *J. Lumin.* **1990**, *45* (1), 341–345.

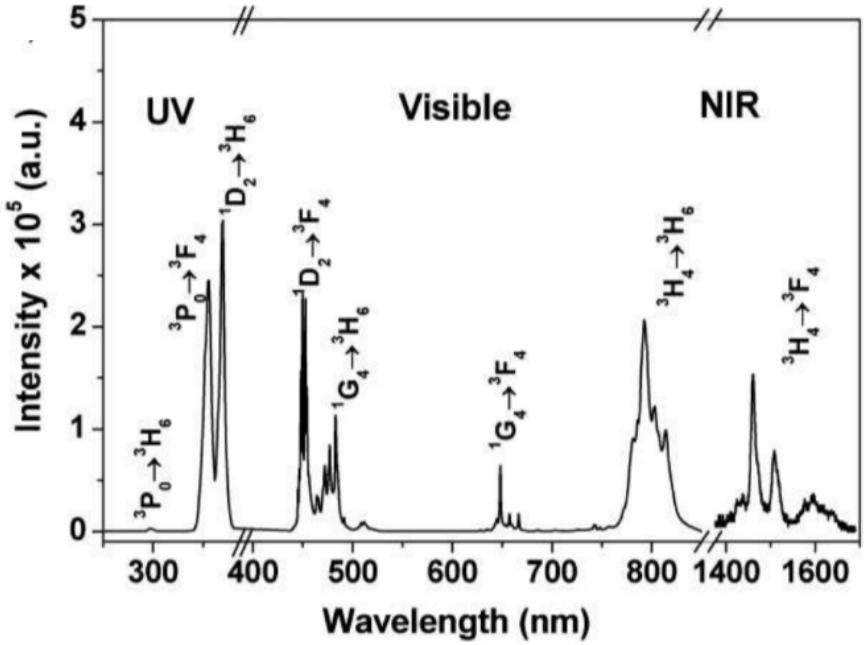
Lanthanide Doped Nanoparticles





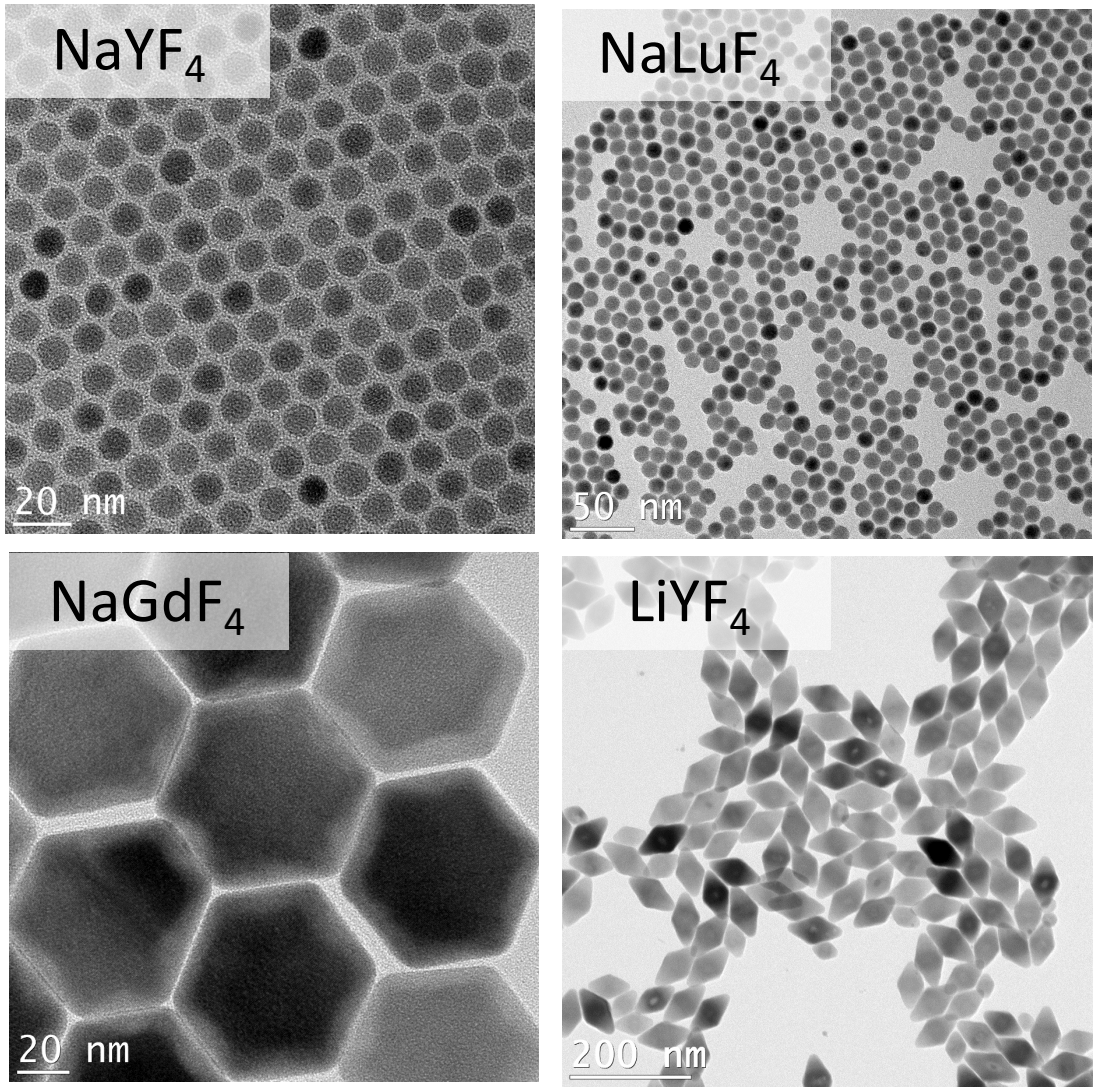


- **Attractive features:**
  - Stability with respect to photobleaching
  - Long photoluminescence lifetime
  - Low toxicity
  - Sharp f-f absorption and emission peaks
  - Flexibility in surface chemistry
  - Small size - optical properties not sensitive to size
  - Emission colour may be tuned
- **More importantly, they can undergo a process known as upconversion**



J. C. Boyer, F. Vetrone, L. A. Cuccia, J. A. Capobianco, *J. Am. Chem. Soc.,* (2006), **128**, 7444-7445.

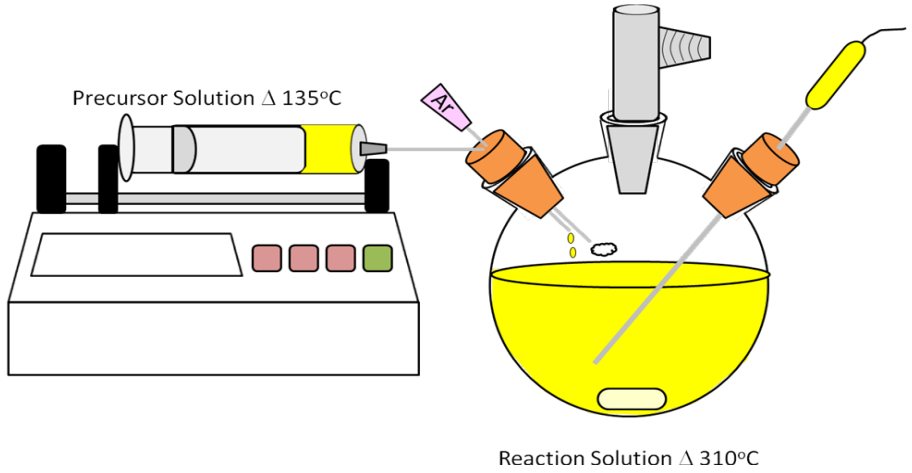
Fluoride Hosts for Upconverting Nanoparticles (UCNPs)



- High upconversion efficiency
- Low phonon energies (<400 cm^{-1})
- High chemical stability
- High radiation stability
- Nanoparticles synthesized by different methods:
  - Thermal decomposition
  - Microwave
  - Co-precipitation
  - Solvothermal

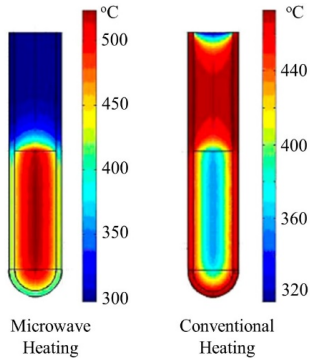
Bottom-Up Nanoparticle Synthesis

Thermal decomposition/Co-precipitation



Solvothermal Synthesis:

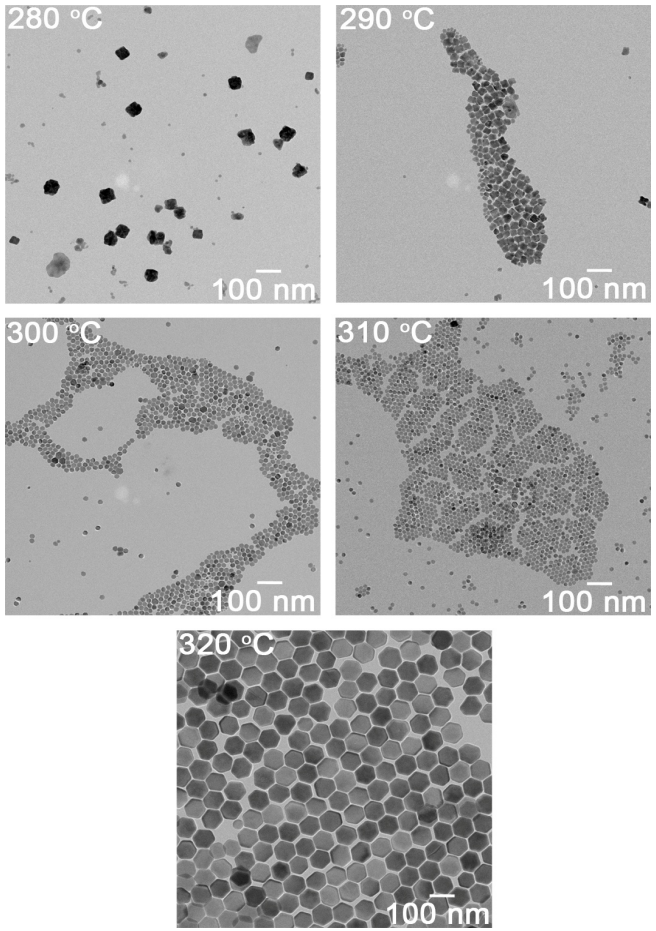
- Varied temperatures
- High pressures

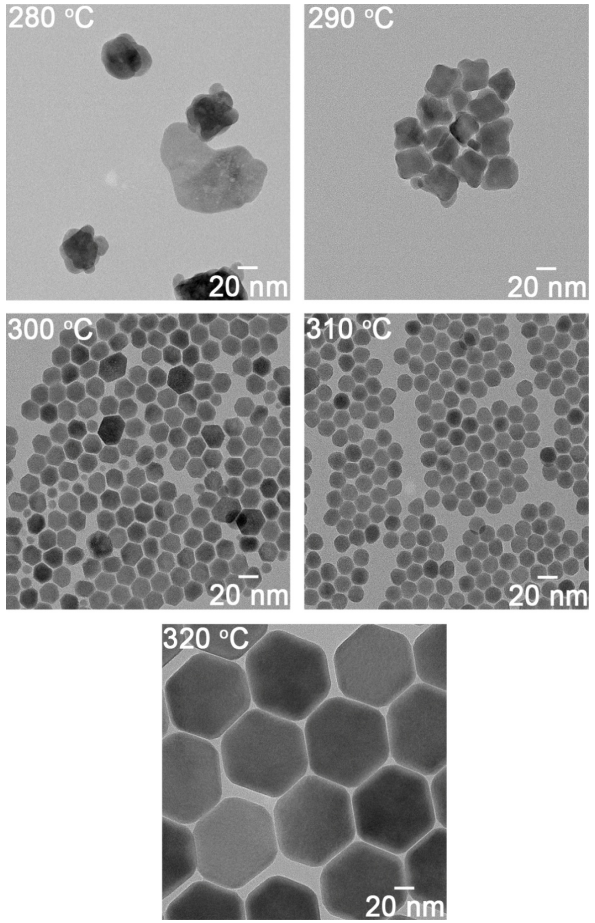


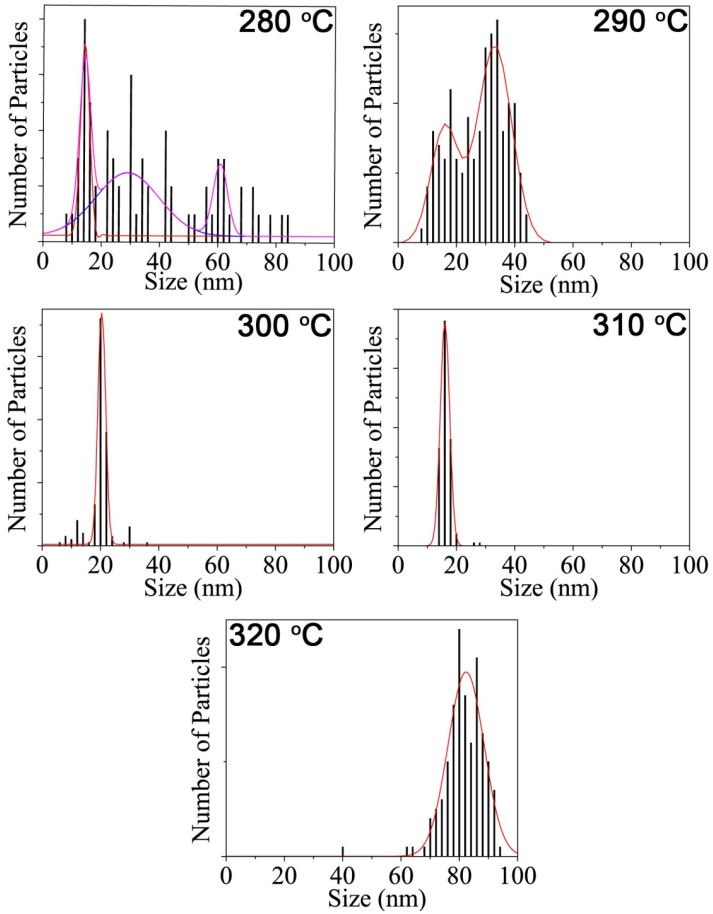
Microwave synthesis:

- Done in minutes
- Uniform temperatures

Temperature and Thermal Decomposition







Reaction Temperature	280 °C	290 °C	300 °C	310 °C	320 °C
Mean Particle Size (nm)	36.4 ± 23.0	26.9 ± 9.3	18.9 ± 4.2	15.4 ± 1.9	80.7 ± 7.2

Atoms at Surface Possess Dangling Bonds

Dangling bonds are orbitals that protrude into space which can be empty or contains a single or pair of valence electrons

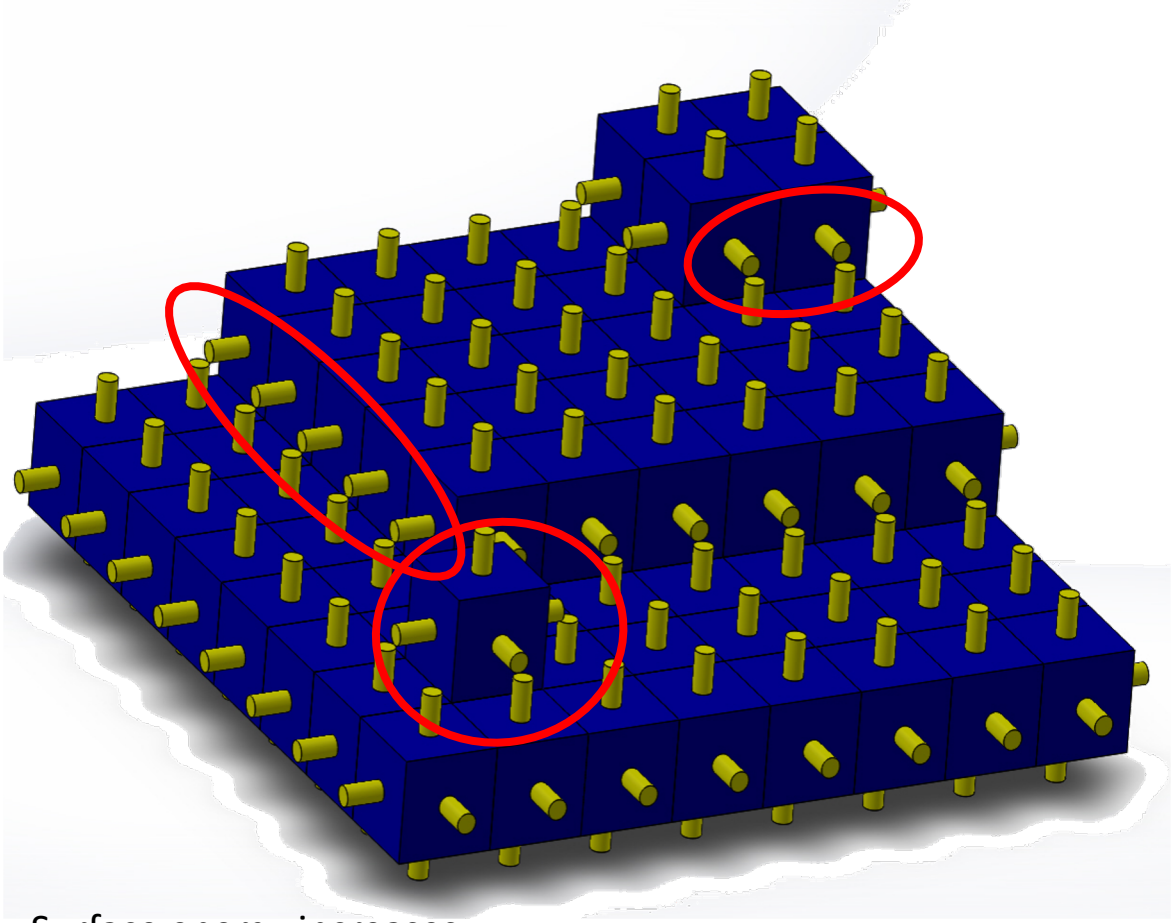
- Unsaturated valence
- Often carry partial charge
- Increase energy of surface

$$\gamma = n_{db}\Phi/2$$

γ = surface energy

Φ = energy of the bond

n_{db} = surface density of dangling bonds

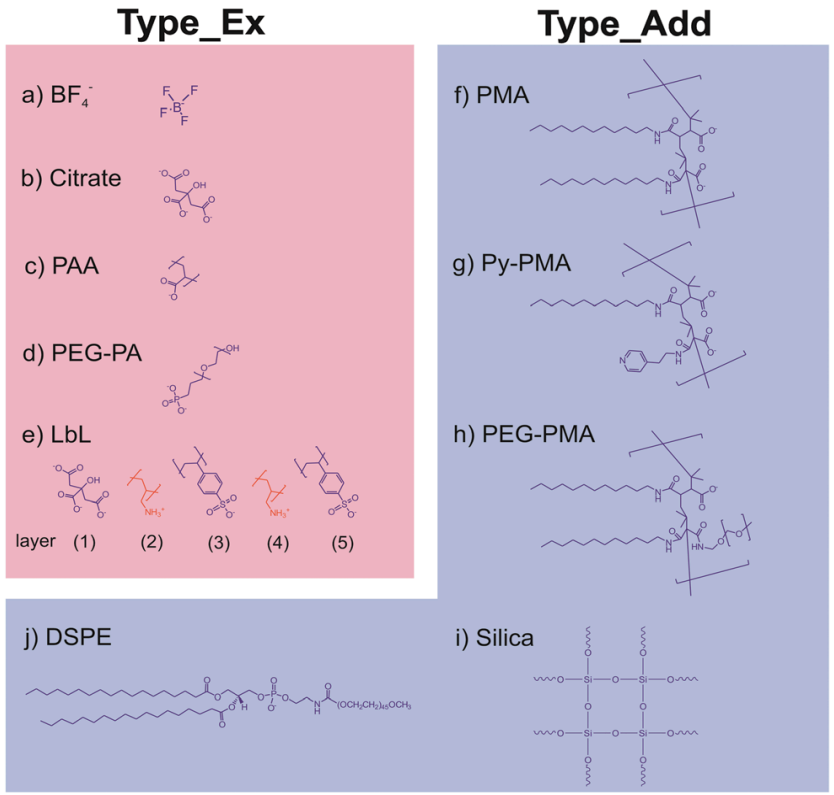


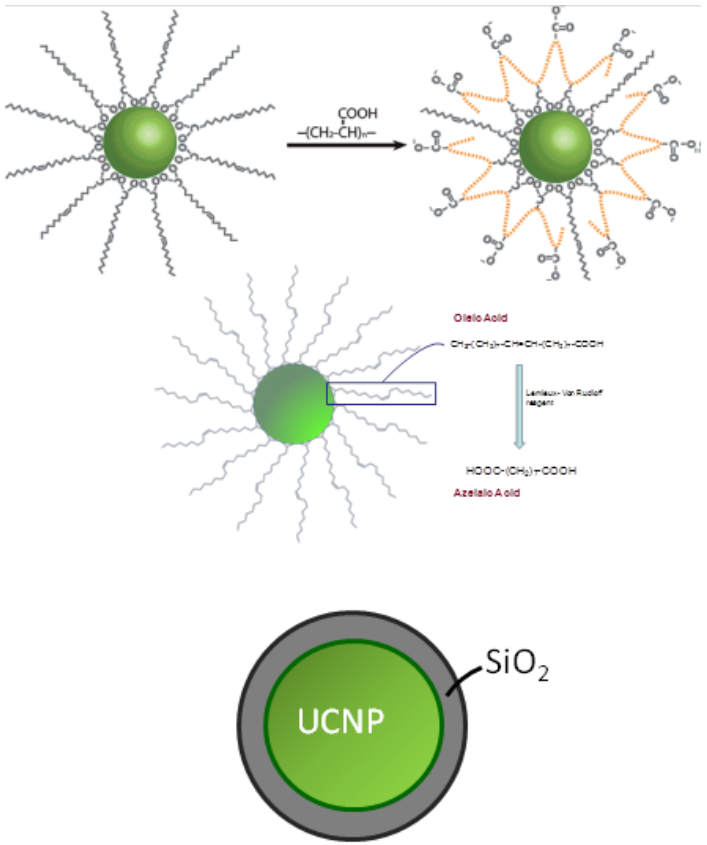
Surface energy increases with density of dangling bonds

Figure courtesy of G. Ozin

The Surface and Dispersibility

- Nanoparticles capped with a surface charge, functional group, other molecule that allows for dispersibility in a specific medium
  - Hydrophilic capping ligands (*e.g.* citrate)
  - Hydrophobic capping ligands (*e.g.* oleate)





Ligand Exchange/ Removal

Can be functionalized to add any ligand which renders it versatile

Oleic Acid Oxidation

Oxidation yields an upconverting nanoparticle coordinated by azelaic acid

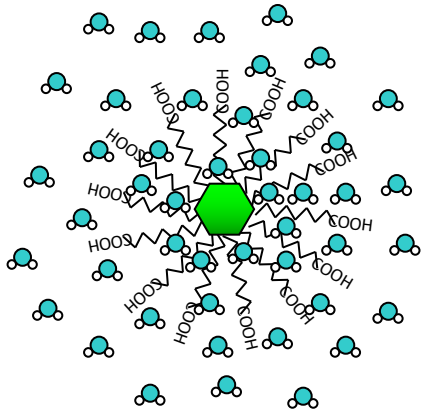
Silica Coating

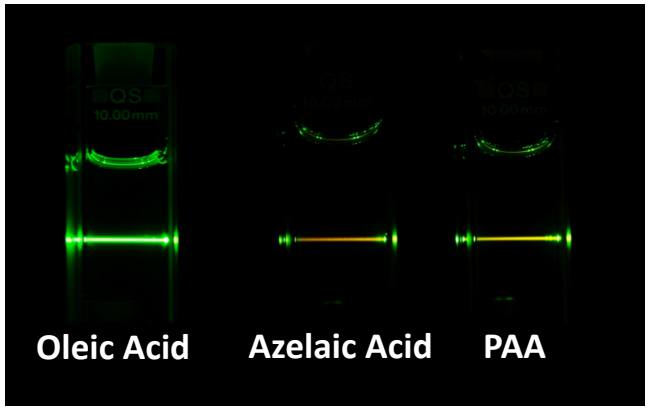
SiO_2 coating can be easily functionalized with different groups or molecules

S.Wilhelm *et al.*, *Nanoscale,* (2015), **7**, 1403-1410

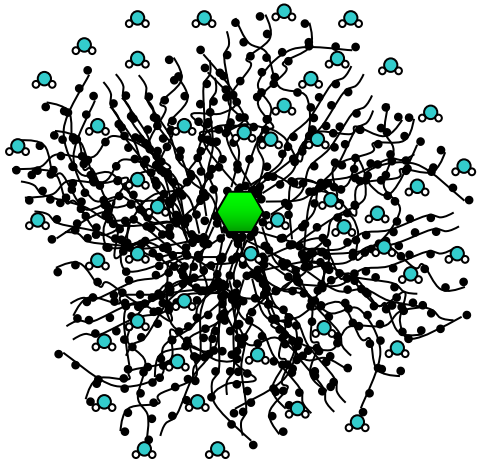
Towards Water Dispersibility

Oxidation



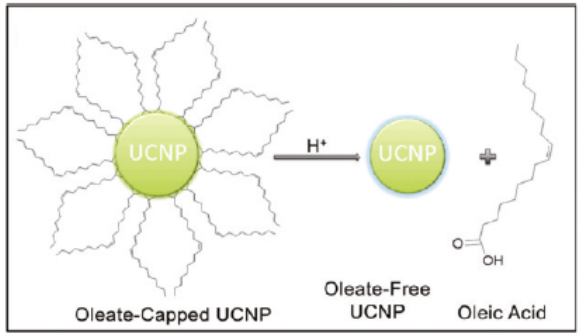


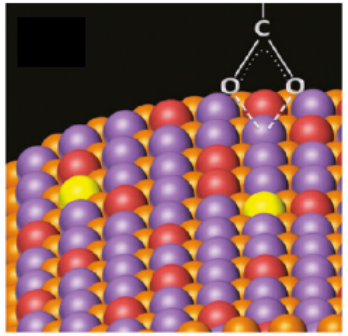
Ligand Exchange

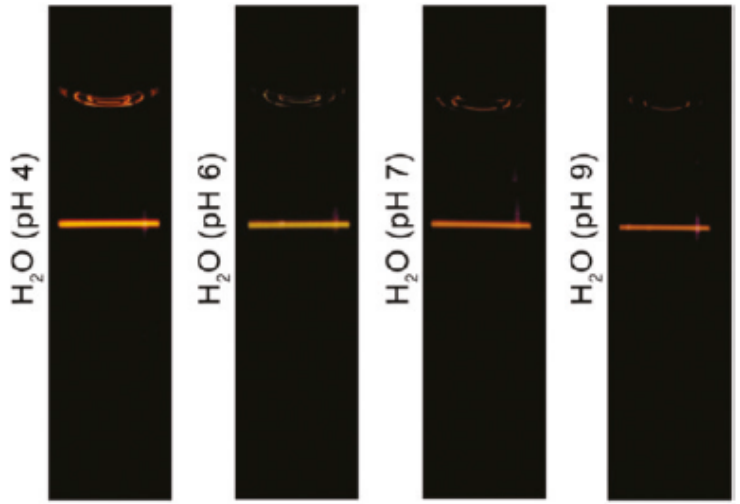


The oleic acid capping ligand was exchanged with a water soluble high MW polymer (PAA M_{wt} 1800)

Ligand Removal





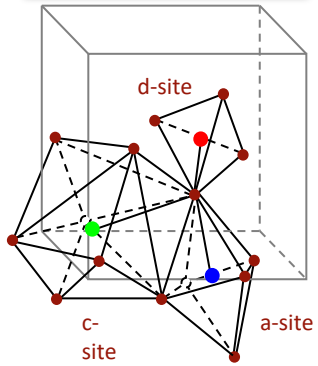


Capobianco, Nano Letters, (2011), 11, 835-840.

Capobianco Lab Timeline

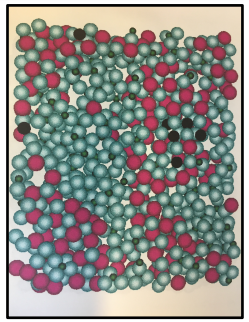
1993-1997 | 1996-2004 | 2000-2008 | 2006-2010 | 2010-2014

Single crystals



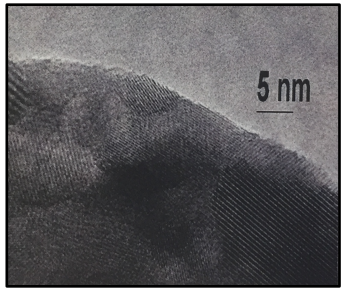
$Gd_3Ga_5O_{12}:Pr^{3+}$

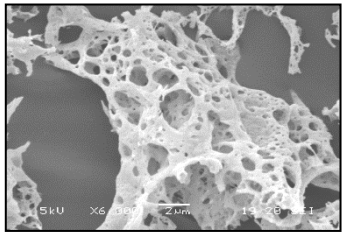
Glasses



$PbO{\cdot}SiO_2:Er^{3+}$

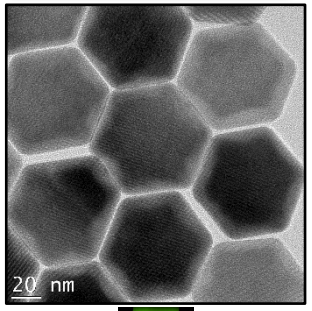
Oxide Nanoparticles



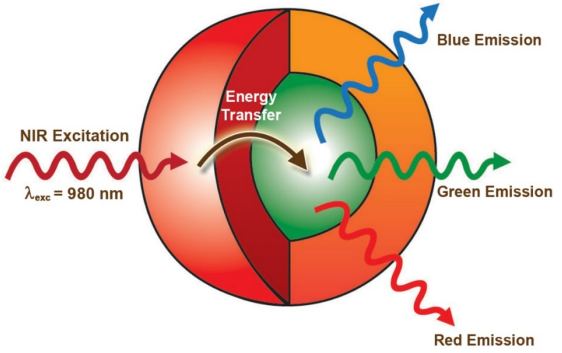


$Y_2O_3:Er^{3+}$

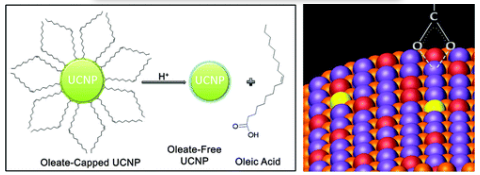
Colloidal

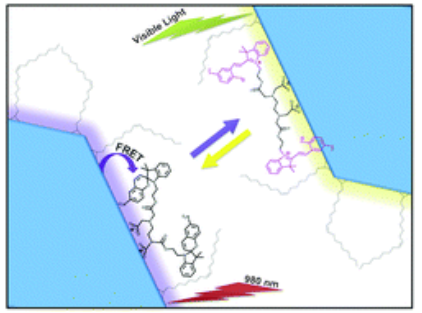


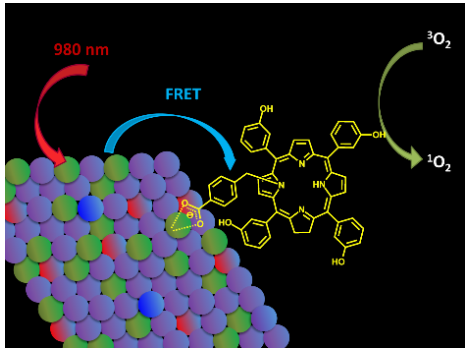
$NaGdF_4:Er^{3+}/Yb^{3+}$



Nanomedicine





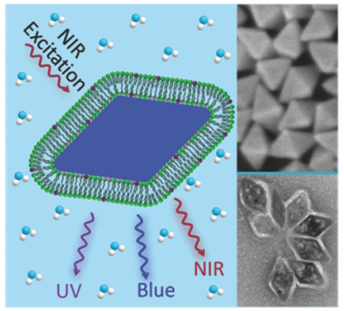


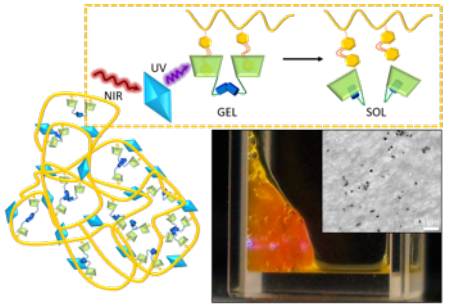
Capobianco Lab Timeline

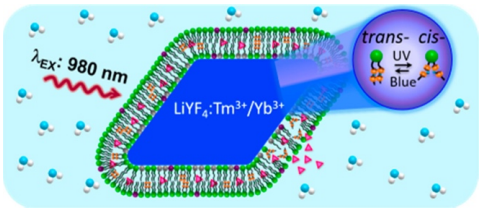
2015-2017

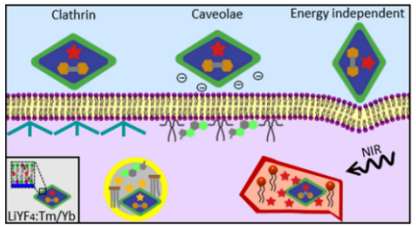
2018 -

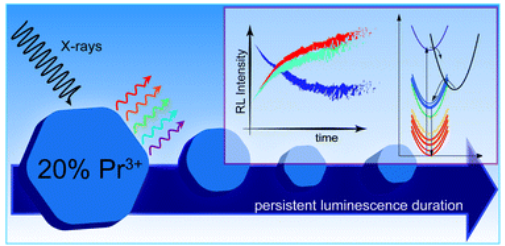
Nanomedicine

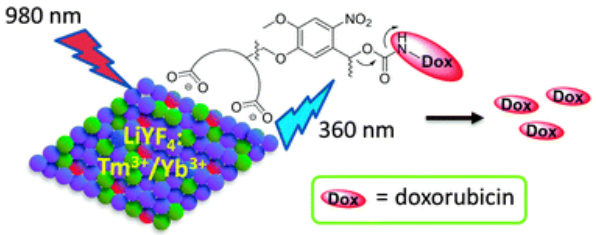


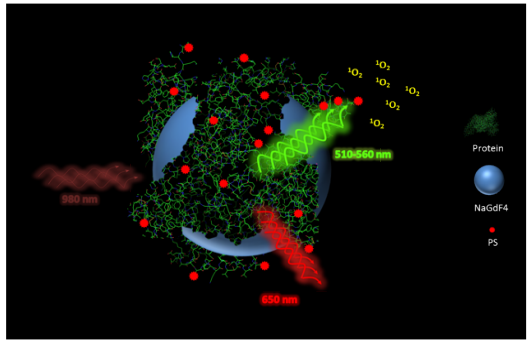


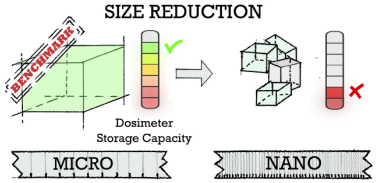


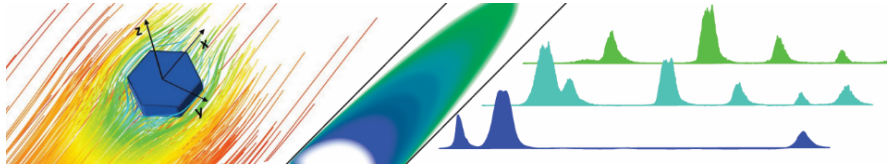


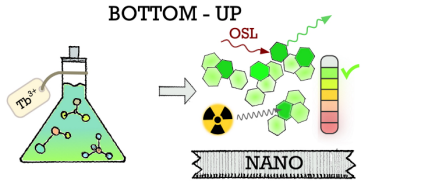


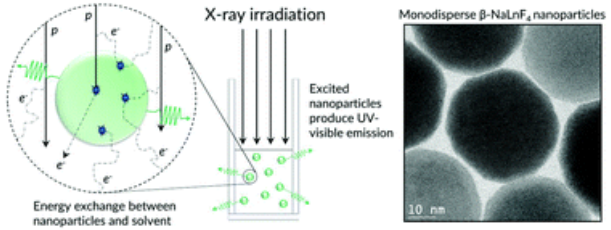


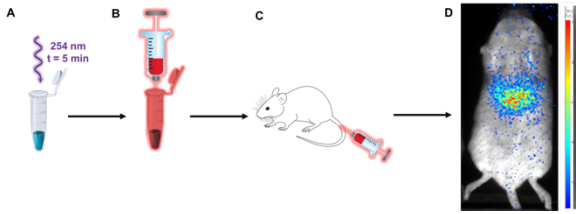


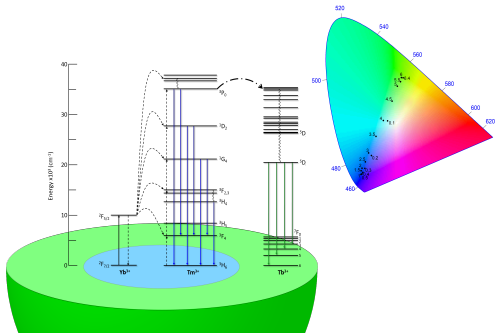


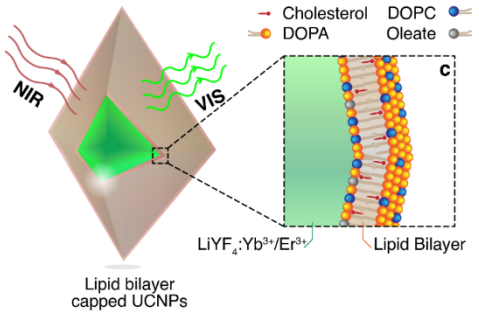


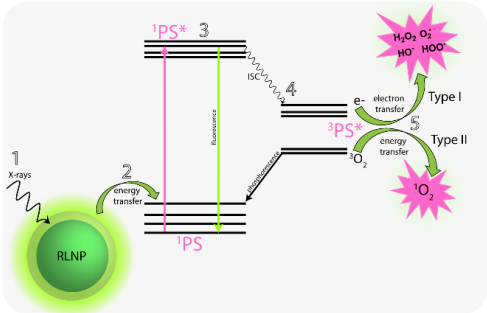






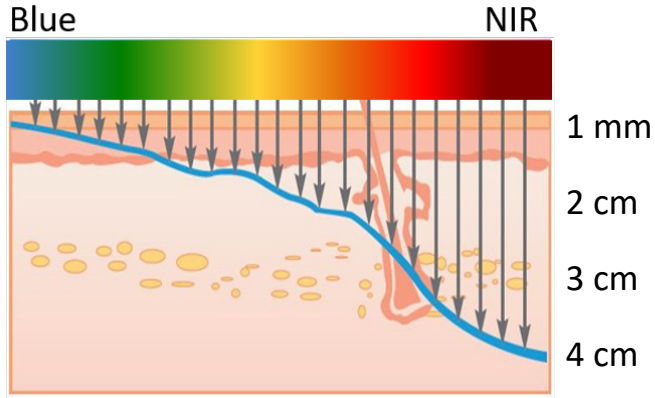


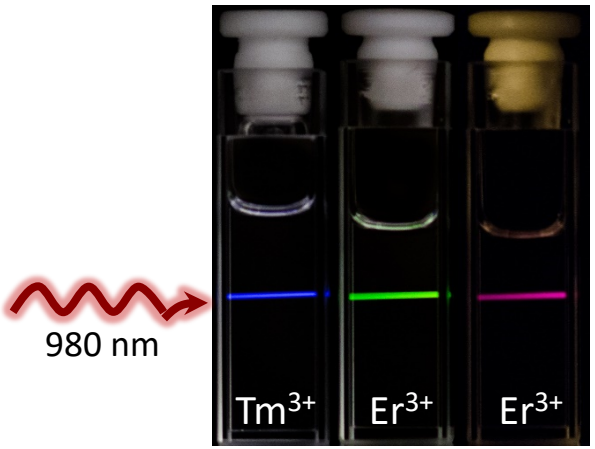




Circumventing the Need for Direct UV Excitation: Lanthanide-Doped Upconverting Nanoparticles

- Anti-Stokes process: UCNPs absorb low energy photons (NIR) and emit high energy photons (UV, Vis, NIR)
- NIR Excitation
  - Reduced scattering
  - Deeper tissue penetration than UV
  - Non-cytotoxic
  - No autofluorescence of tissues
- No photobleaching, photoblinking
- Tunable optical emissions
  - Dopant(s)
  - Concentration

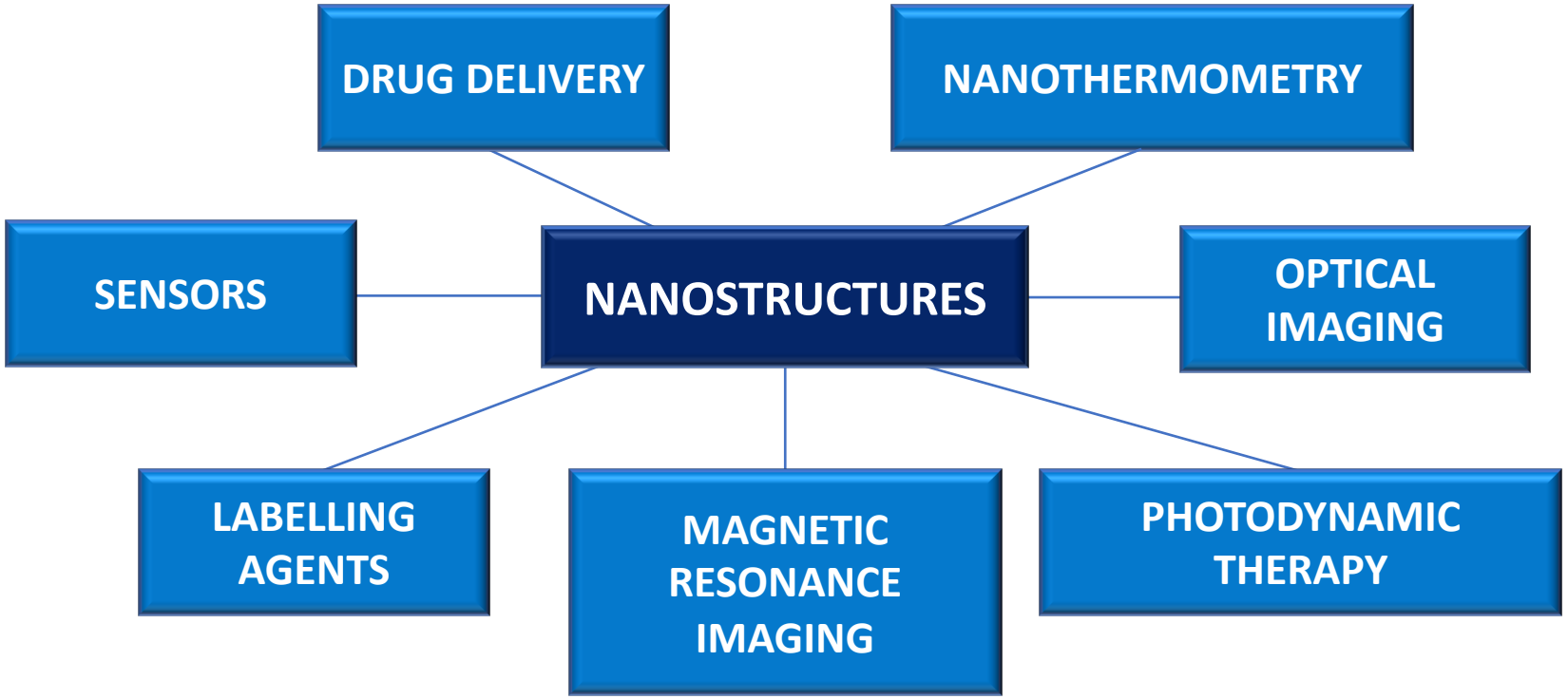




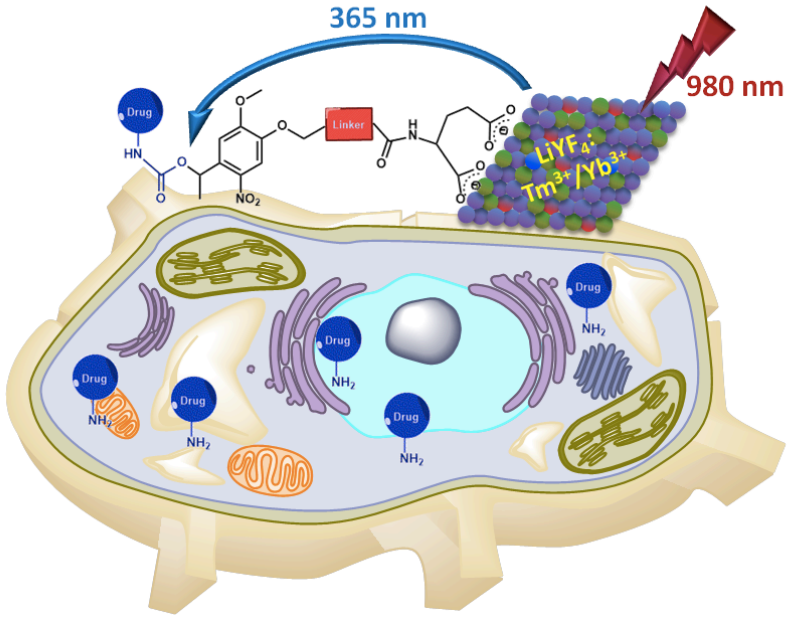
Skin Image taken March 14th 2017: http://www.dermeo.com, Photographs of UCNPs by D.R. Cooper

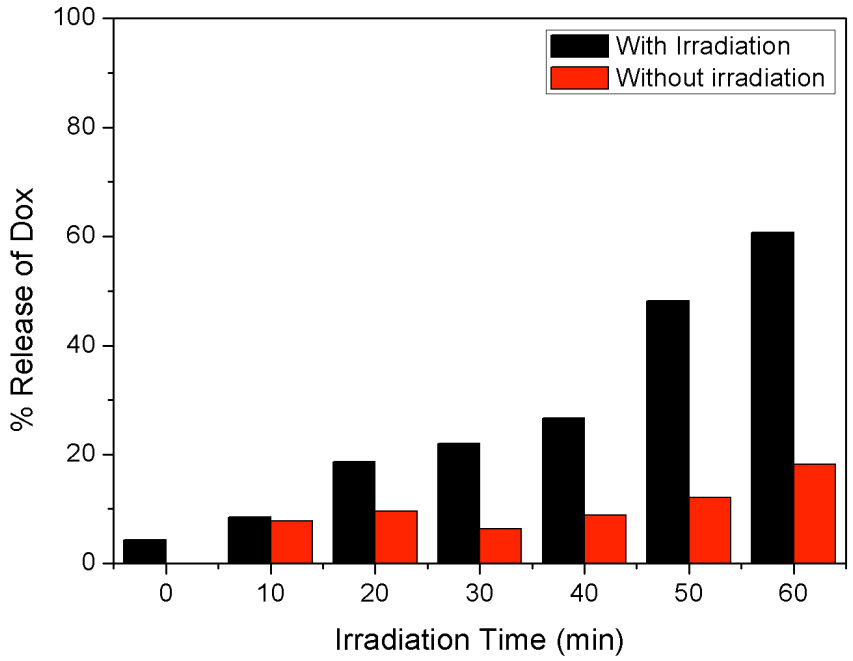
Nanomaterials in Biology

- Biological systems → size of proteins 10 nm approx.
- Allows to probe and modify biological systems



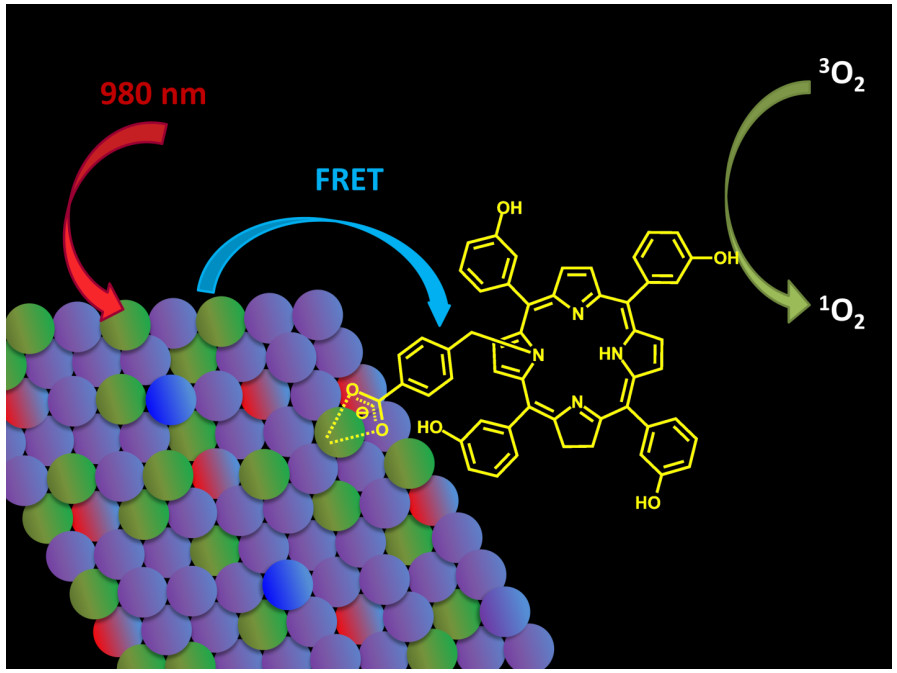
Using Lanthanide-Doped Upconverting Nanoparticles to Release Photocaged Doxorubicin

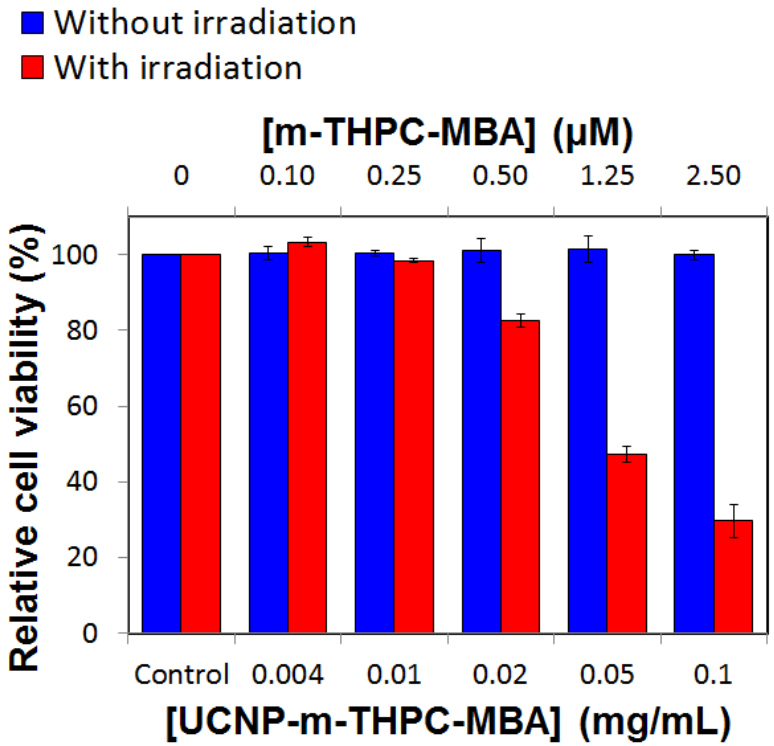




M. M. Dcona, Q. Yu, J. A. Capobianco, M. C. T. Hartman, *Chem.Comm*, 8477-8479 (2015)

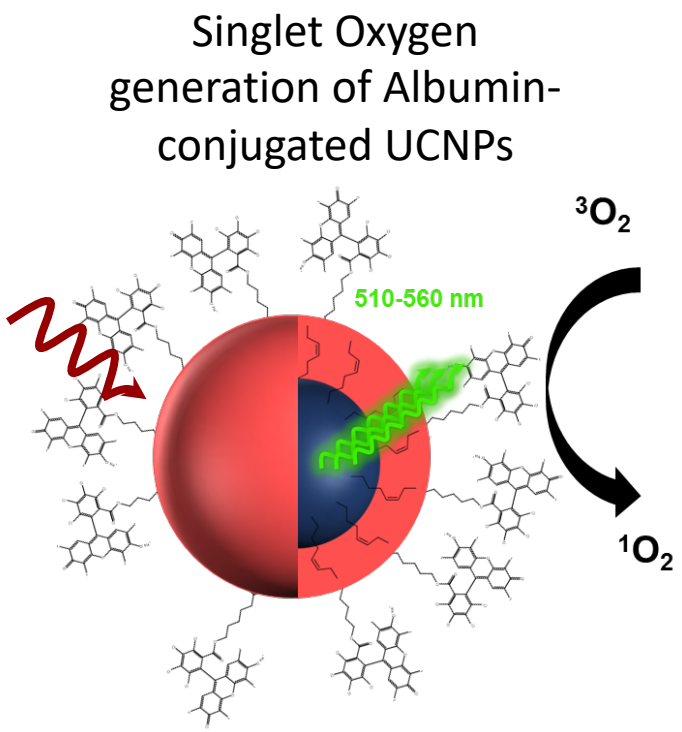
Chemical modification of temoporfin – a second generation photosensitizer activated using upconverting nanoparticles for singlet oxygen generation

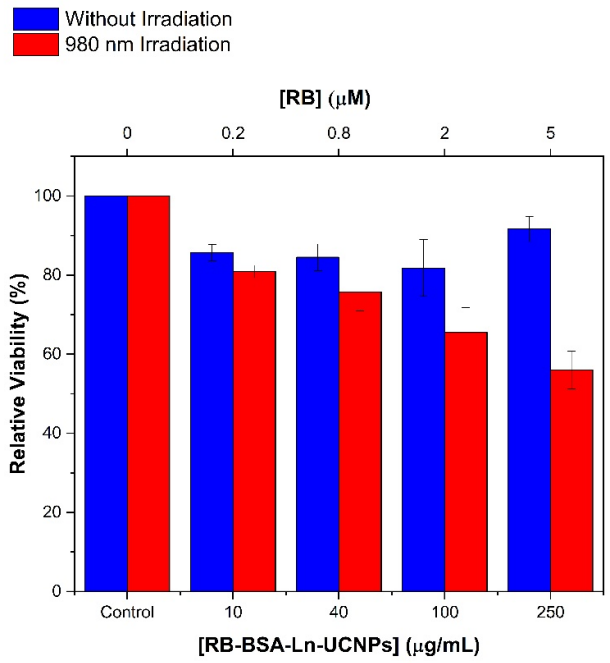


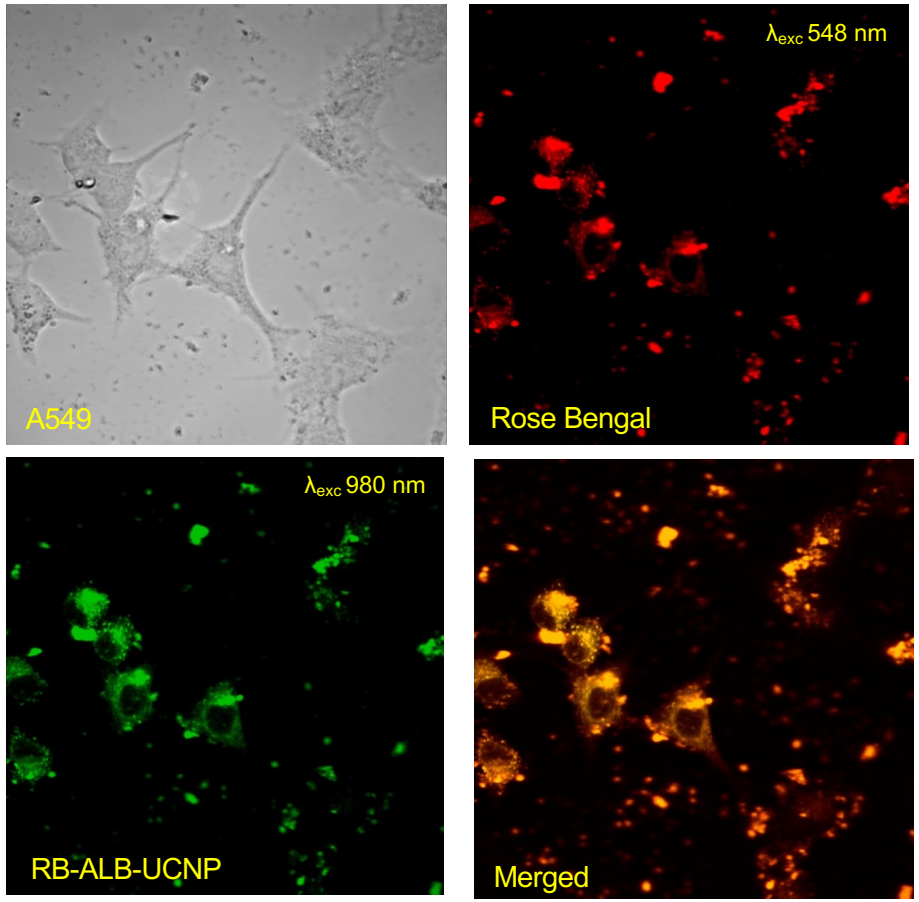


Q. Yu, J. Capobianco, Chem. Commun., 2014, 50, 12150-12153

Dual Activity of Rose Bengal Functionalized to Albumin-Coated Lanthanide-Doped Upconverting Nanoparticles: Targeting and Photodynamic Therapy

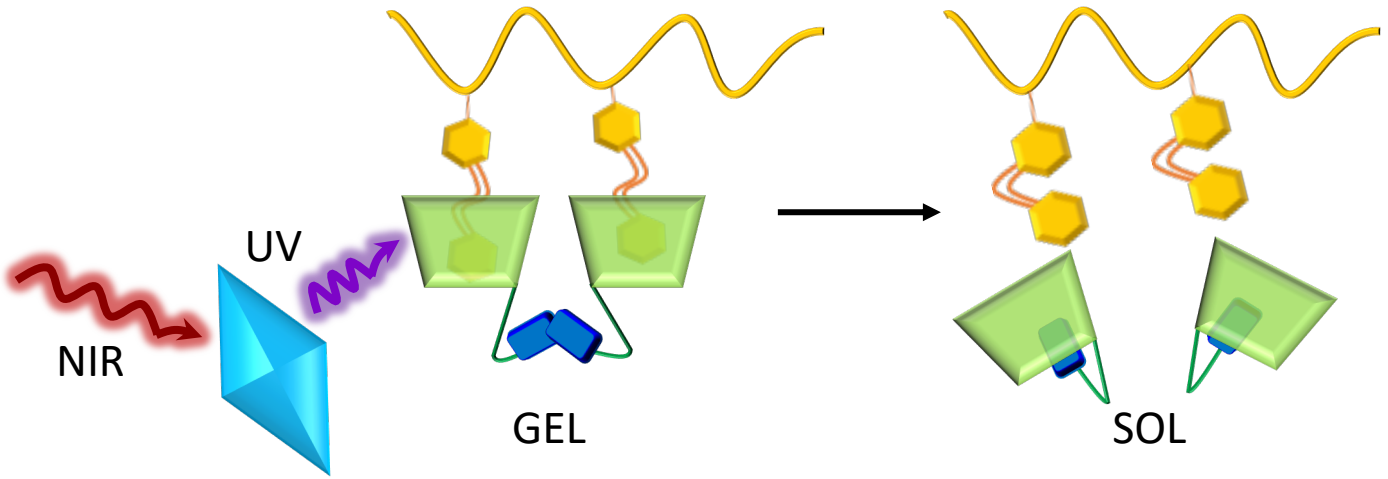


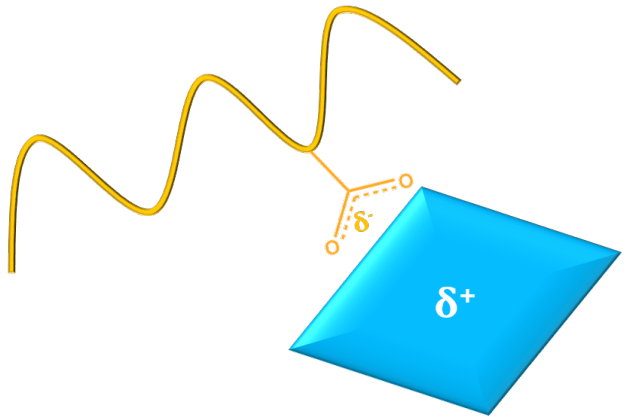




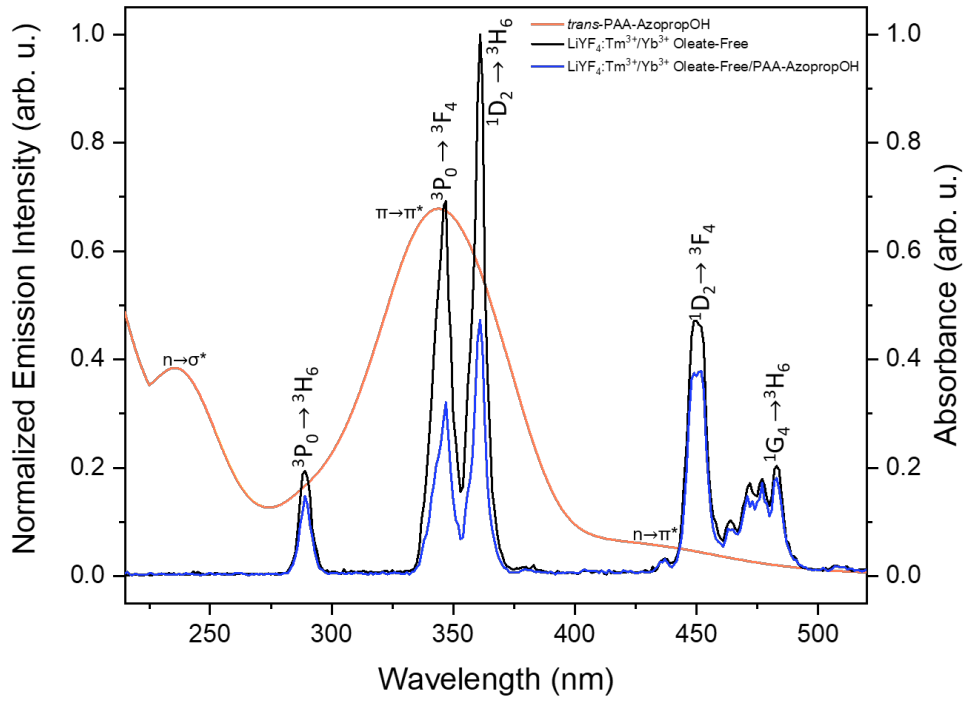
T. Sabri, *et al.,* ACS Appl. Mater. Interfaces 10, 32, 26947-26953

Development of a NIR-Responsive Supramolecular Hydrogel Using $LiYF_4:Tm^{3+}/Yb^{3+}$ Upconverting Nanoparticles





- **Guest-Host interactions** between hydrophobic *trans*-azobenzene and inner hydrophobic cavity of β-CD
- **Hydrophobic interactions** between deoxycholate plugs

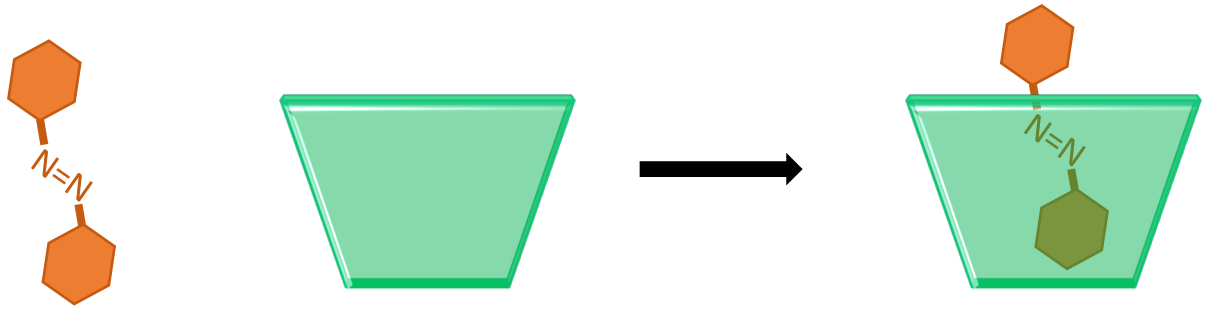


Energy Transfer Efficiency: 53 %

G.A. Mandl *et al., Chem. Commun.,* 2018, DOI: 10.1039/C8CC03101K

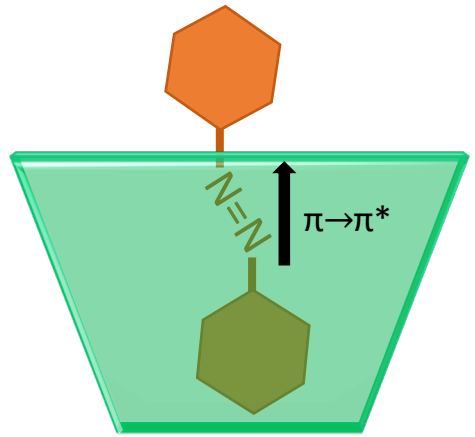
Induced Circular Dichroism

When an achiral guest is placed into a chiral environment, a circular dichroism signal is induced.



Azobenzene (Achiral) | β-Cyclodextrin (Chiral cavity) | Azobenzene-Cyclodextrin inclusion complex

The Azobenzene Case



π→π* ICD > 0

n→π* ICD < 0

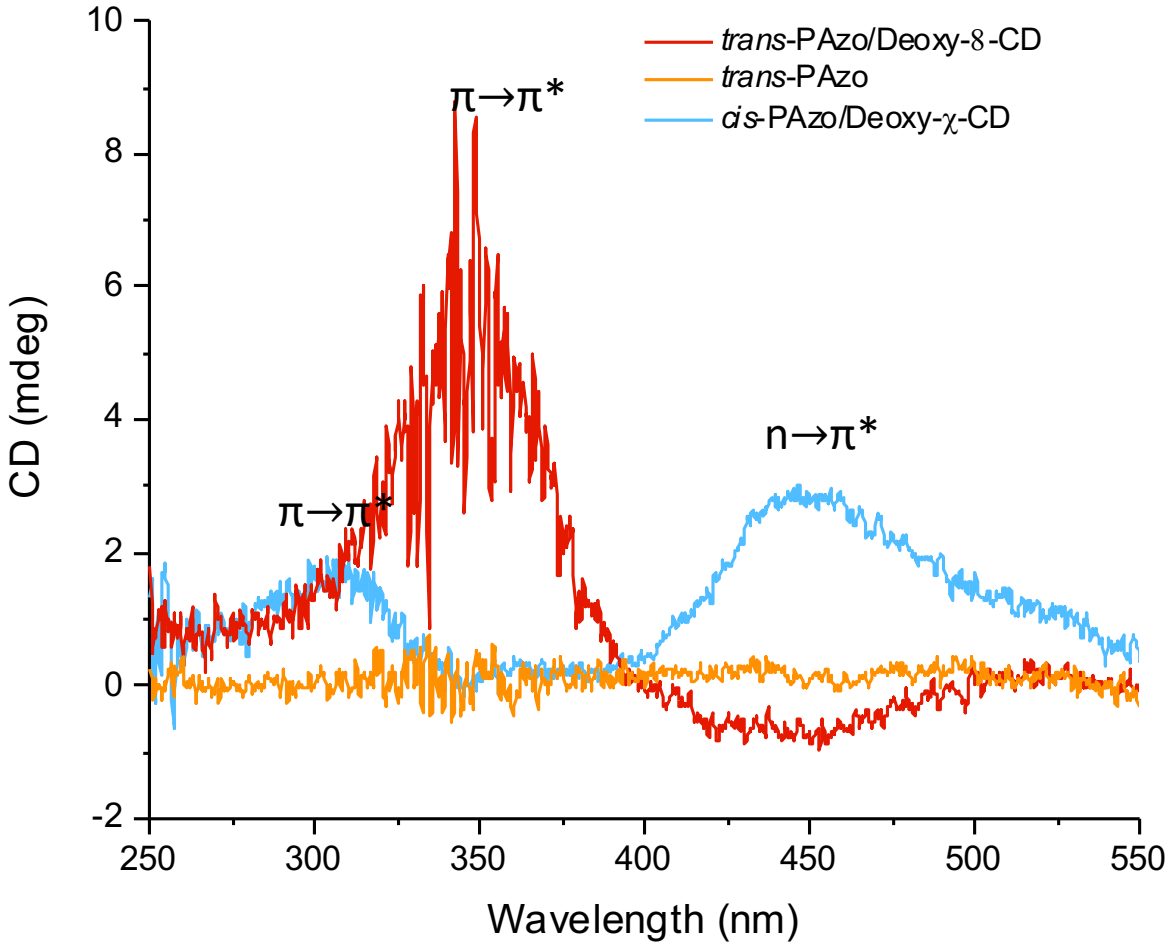
Empirical rules:

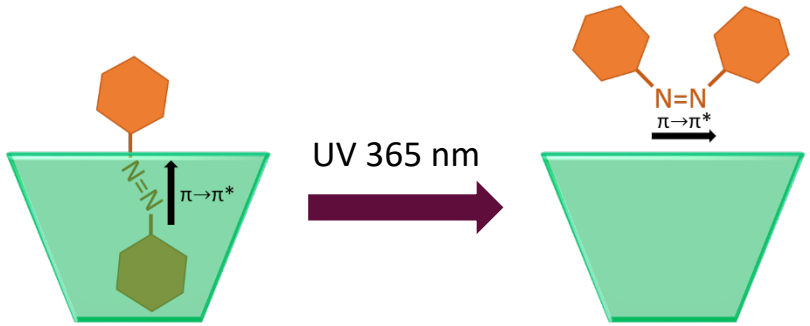
- If the direction of the chromophore absorption transition moment and the main symmetry axis of the CD macrocycle are **parallel**, the ICD signal is **positive**.
- If the absorption transition moment is **perpendicular** to the main axis, the ICD signal is **negative**, and the perpendicular-polarized signal value should be -1/2 in magnitude.
- The ICD signal signs are reversed when the chromophore is located partially outside the CD cavity.

Dipole Moments:
trans: 0 D
cis: 3 D

Francisco Mendicuti and María Jose Gonzalez-Alvarez, Supramolecular Chemistry: Induced Circular Dichroism to Study Host-Guest Geometry. J. Chem. Educ., 2010

Induced Circular Dichroism Studies

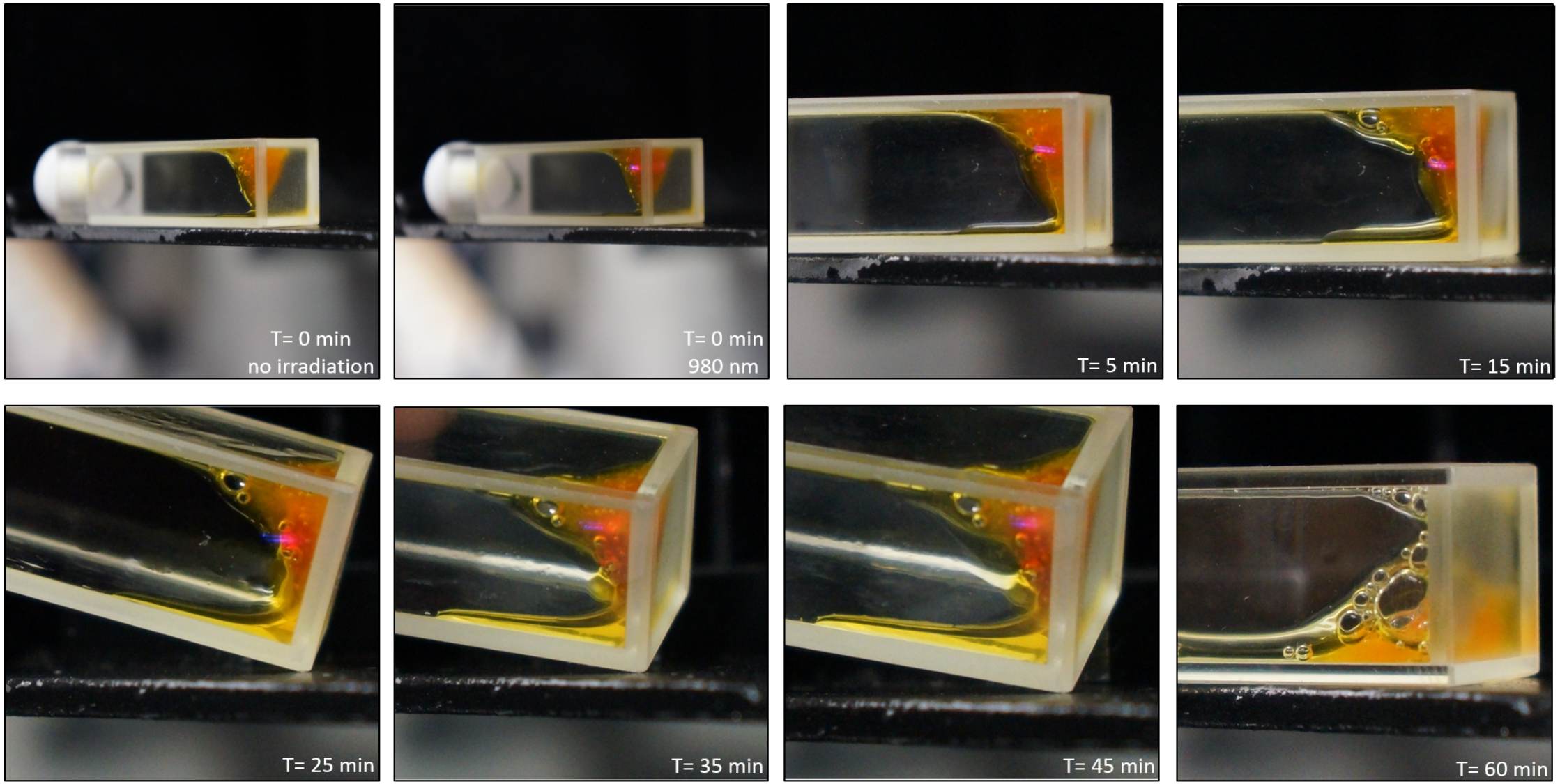




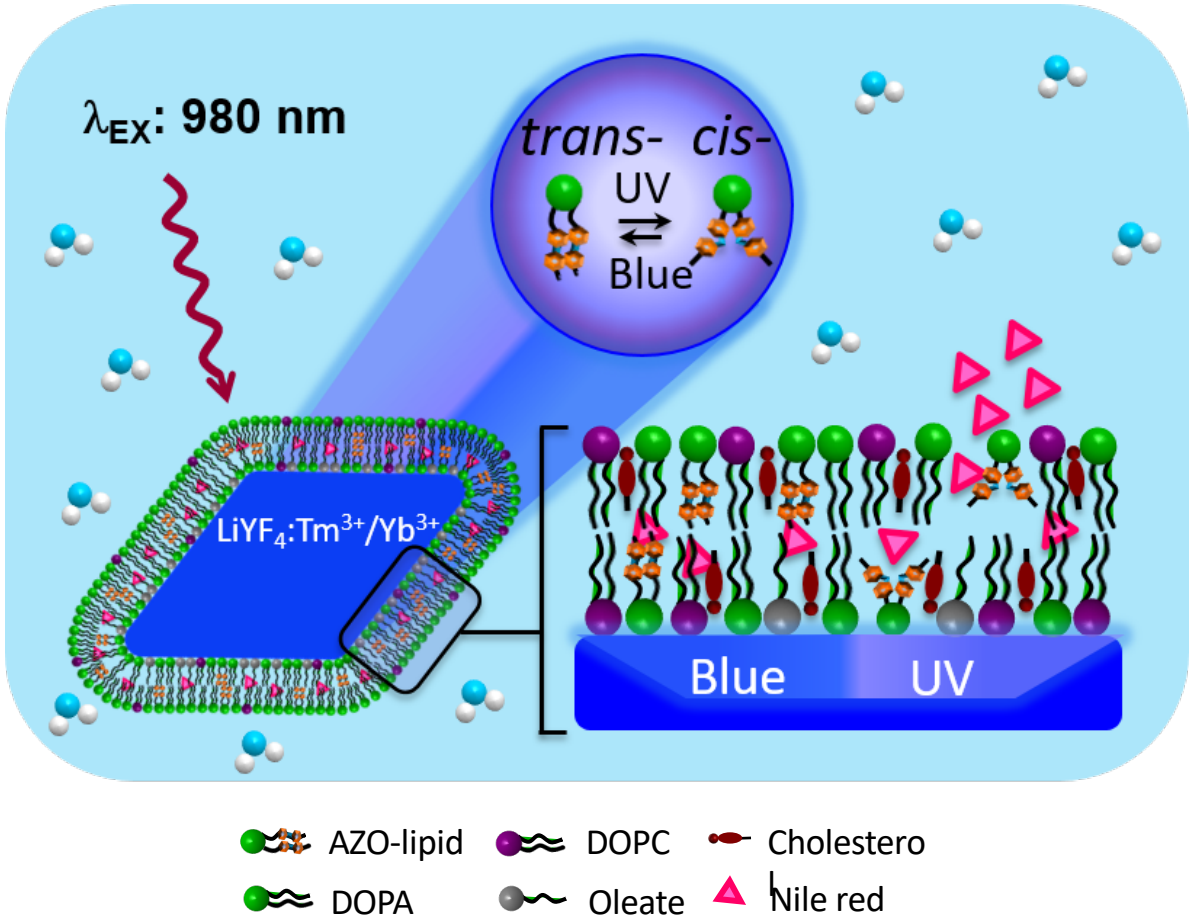
- *cis*- obtained under 365 nm UV irradiation for 5 min

G.A. Mandl *et al., Chem. Commun.,* 2018, DOI: 10.1039/C8CC03101K

NIR Activation of the Hydrogel



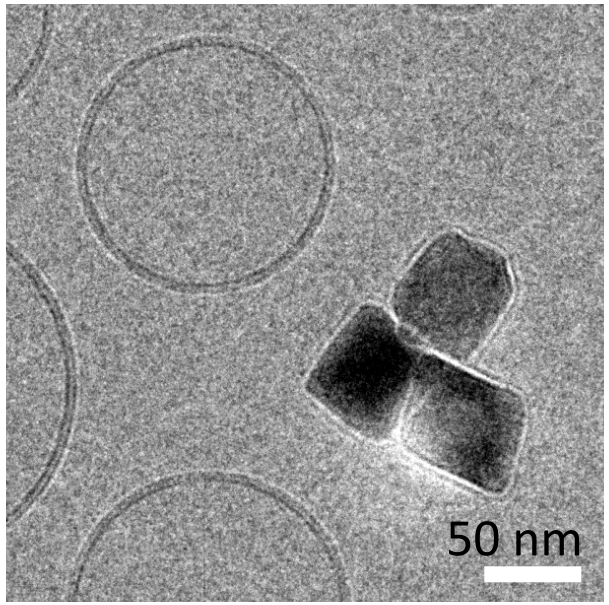
Photoswitchable supported lipid bilayer controlled by $LiYF_4:Tm^{3+}/Yb^{3+}$ UCNPs

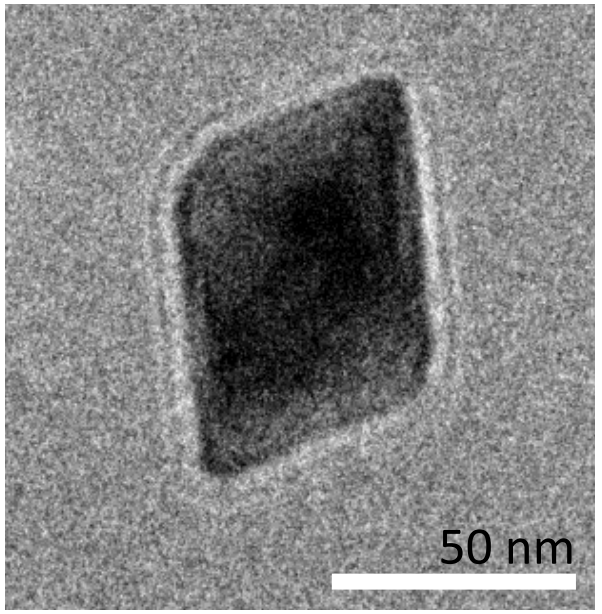


ACS Applied Nano Materials DOI: 10.1021/acsanm.8b01396

Formation of the Supported Lipid Bilayer on $LiYF_4:Tm^{3+}/Yb^{3+}$ UCNPs

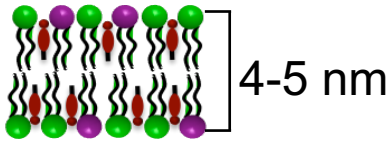
Cryo-TEM





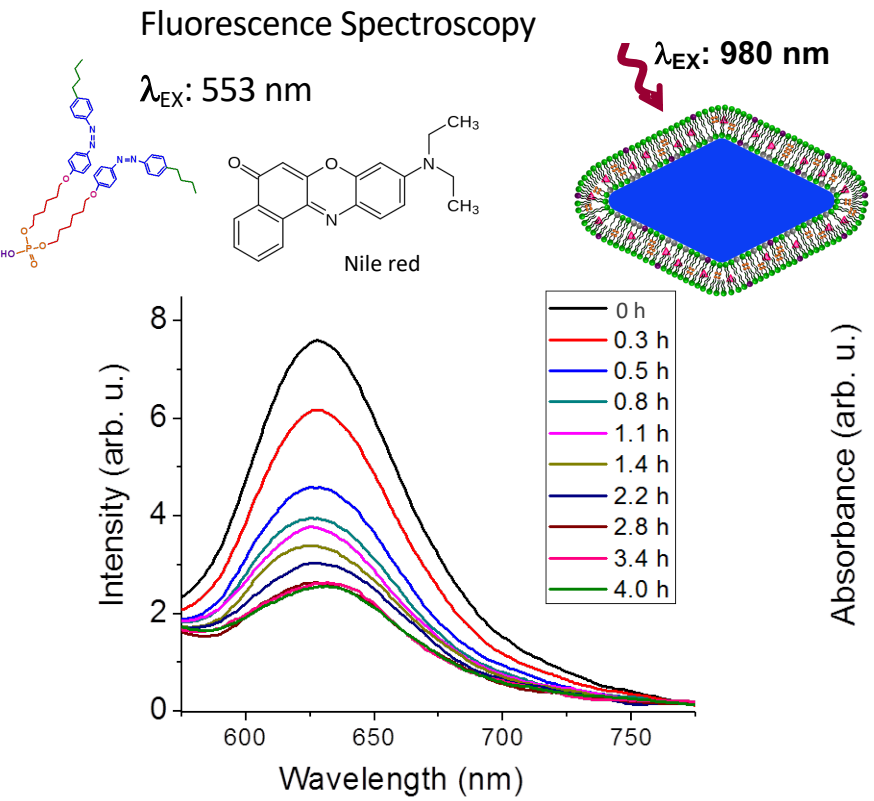
Liposome:
4.0 nm ± 0.4 nm

SLB:
4.4 nm ± 0.4 nm

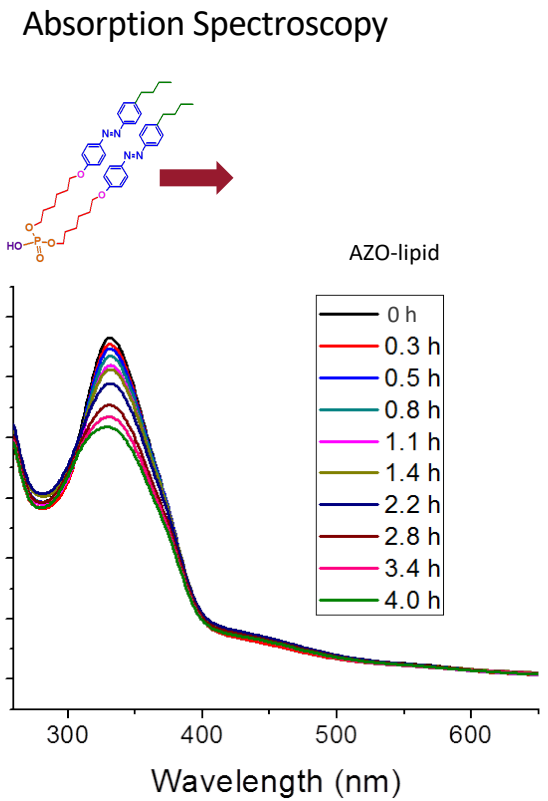


Rojas-Gutierrez P. A., *et al.*, ***Part. Part. Syst. Charact.***, (2016), **33**, 865-870

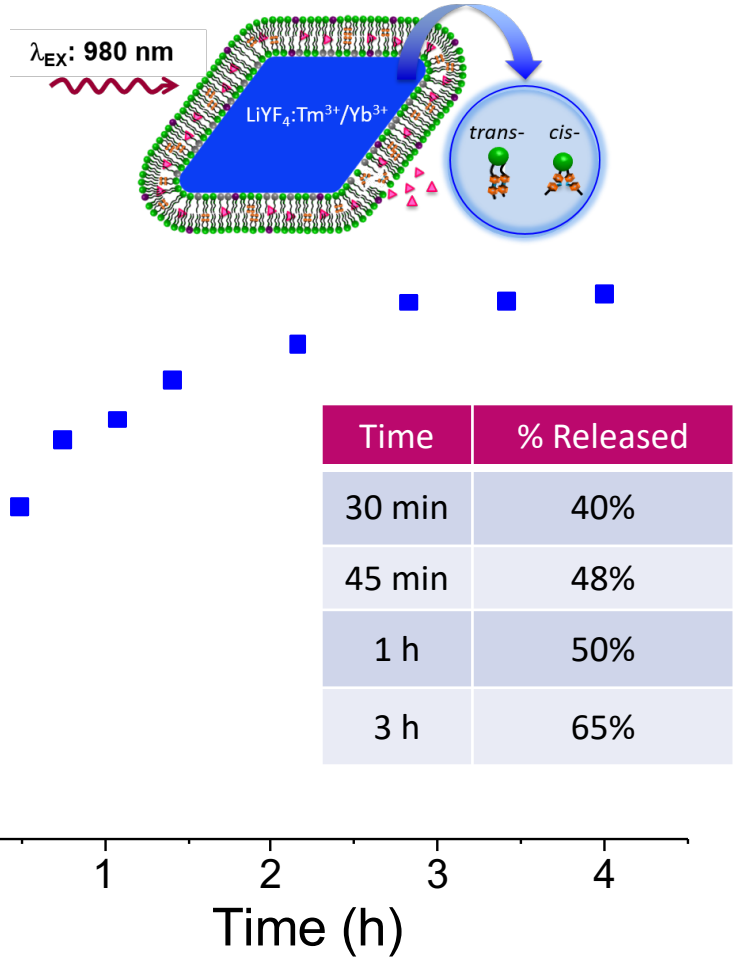
NIR triggered release of Nile Red encapsulated in photoswitchable SLB-$LiYF_4$:Tm^{3+}/Yb^{3+} UCNPs



Nile Red: 9-diethylamino-5H-benzo[α-]phenoxazine-5-one

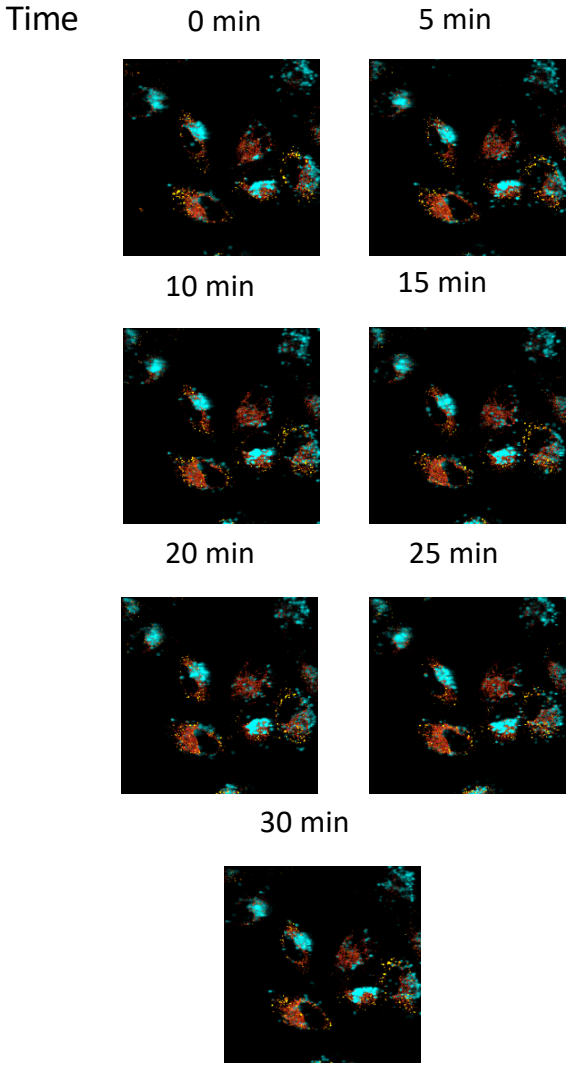


AZO-lipid: Di(6-{[4-(4-butylphenyl)azo]-phenoxy}-hexyl)phosphate

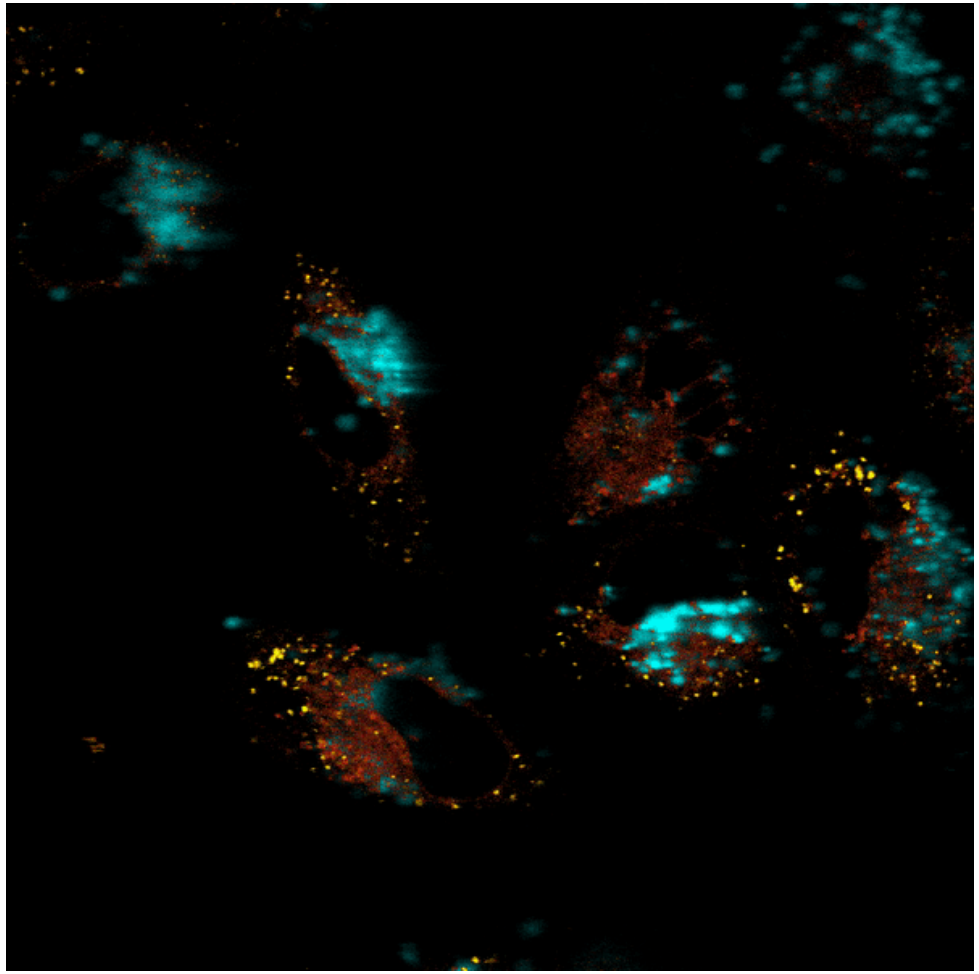


Time	% Released
30 min	40%
45 min	48%
1 h	50%
3 h	65%

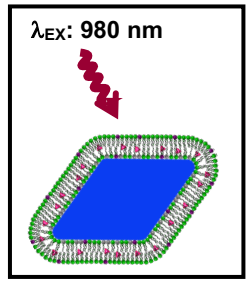
Live lung cancer cells with NR-SLB-$LiYF_4$:Tm^{3+}/Yb^{3+} UCNPs under NIR irradiation as function of time



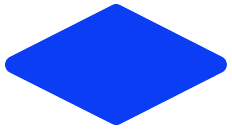
Lambda scan using λ_{ex} 980 nm



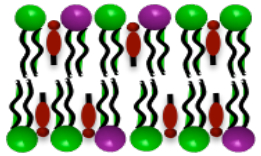
- Cells do not die after 30 minutes of NIR irradiation



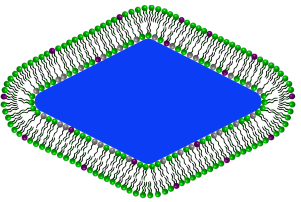
Cytotoxicity of SLB-$LiYF_4$ UCNPs in A549 lung cancer cells



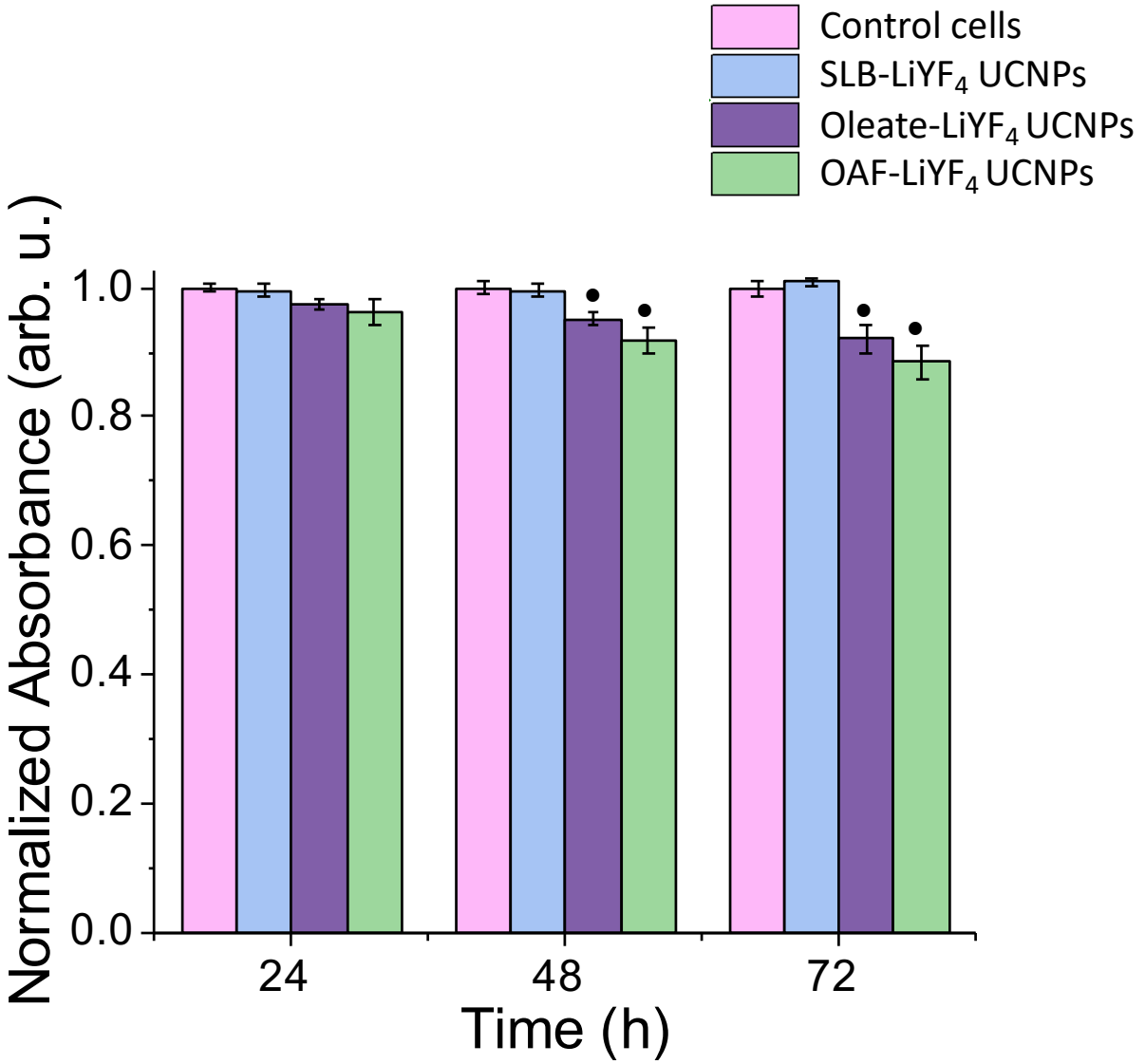
OAF-$LiYF_4$ UCNPs



Oleate-$LiYF_4$ UCNPs



SLB-$LiYF_4$ UCNPs



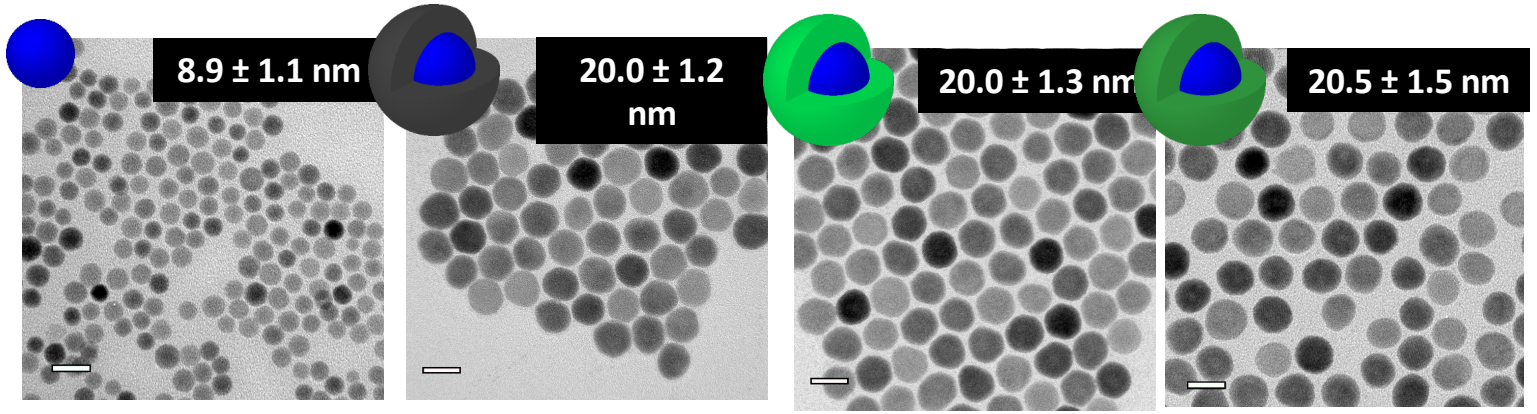
OAF: Oleic acid free

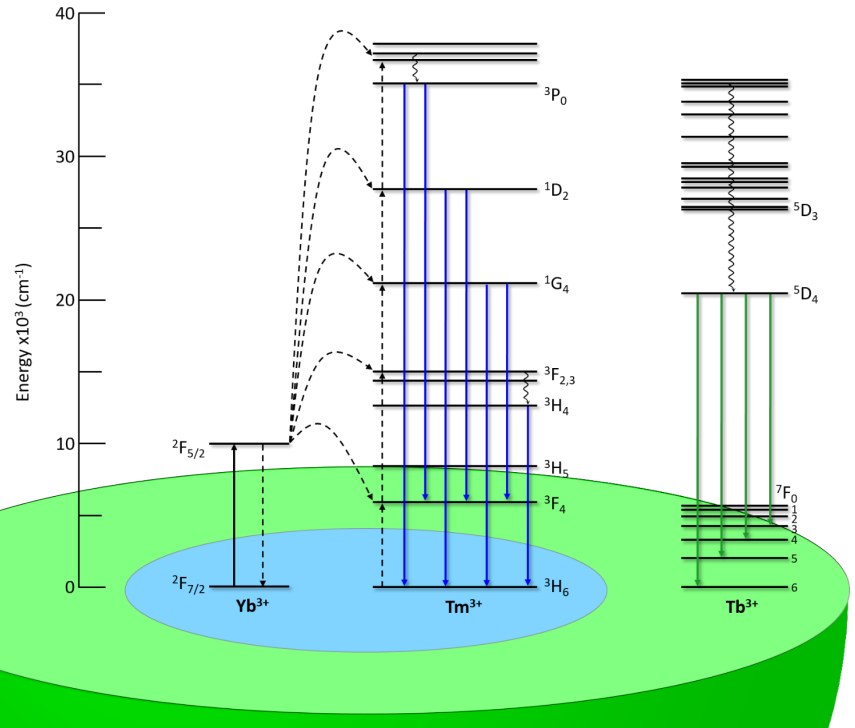
Intrinsic Time-tunable Emissions in Core-Shell Nanoparticle Systems: A Proof of Concept

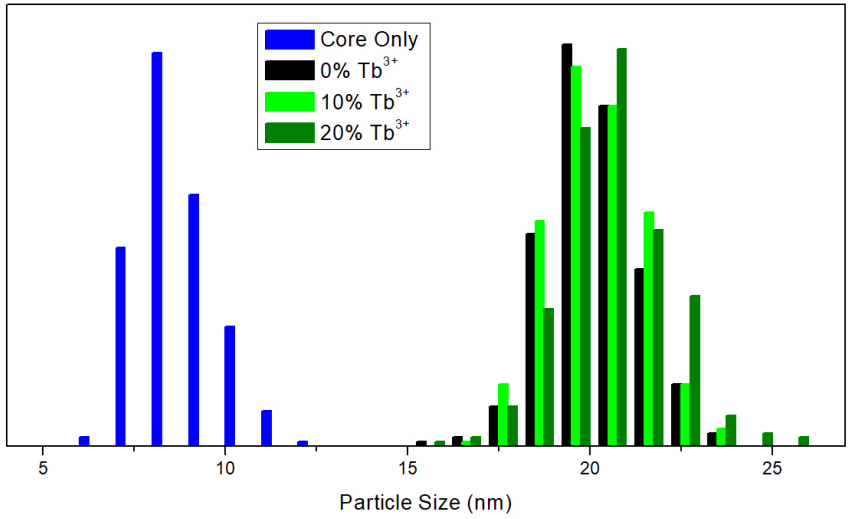
$NaGdF_4$: 49% Yb^{3+}, 1% Tm^{3+}/$NaGdF_4$

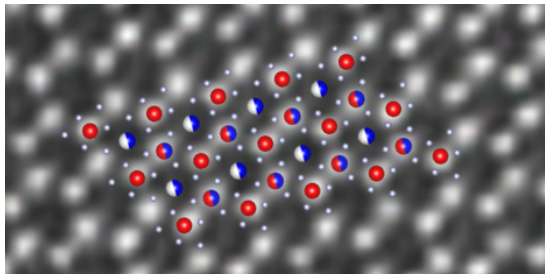
$NaGdF_4$: 49% Yb^{3+}, 1% Tm^{3+}/$NaGdF_4$: **10% Tb^{3+}**

$NaGdF_4$: 49% Yb^{3+}, 1% Tm^{3+}/$NaGdF_4$: **20% Tb^{3+}**





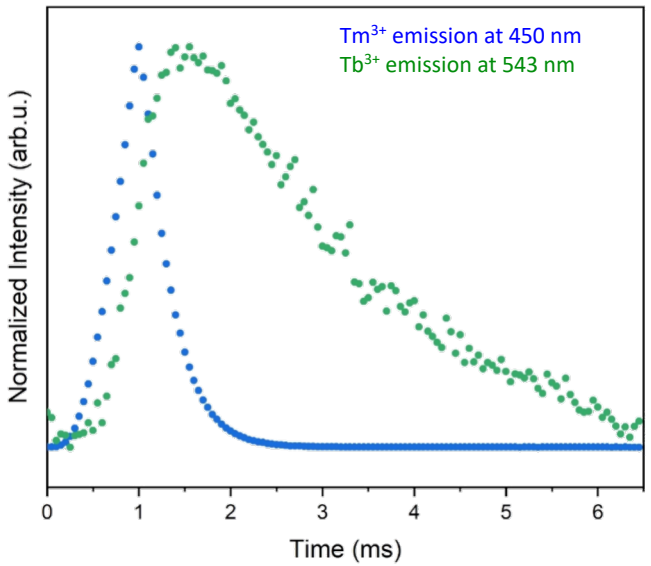


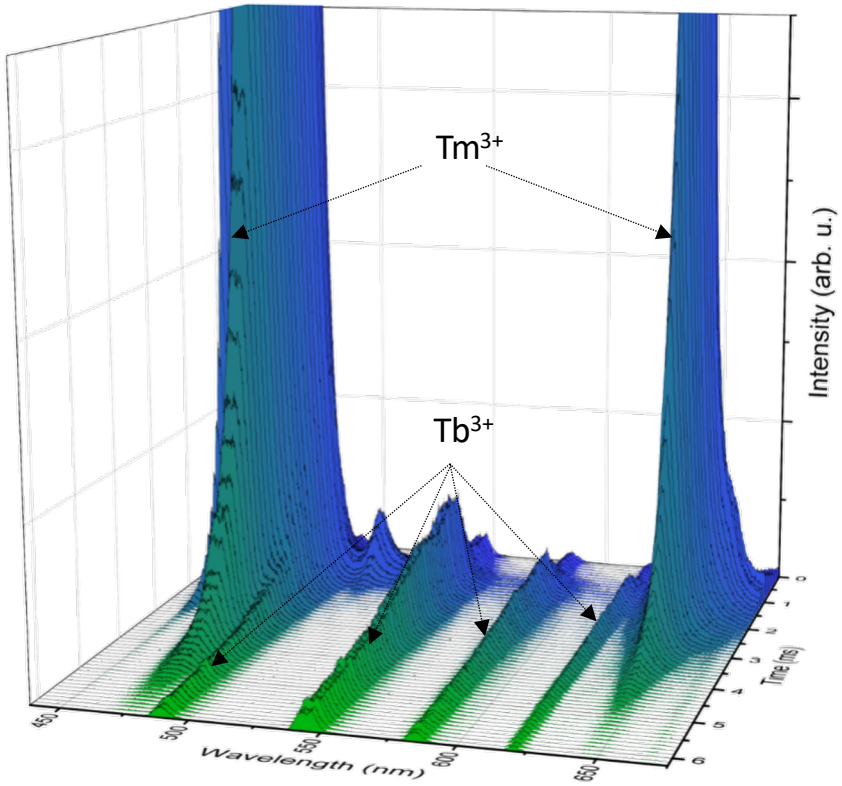


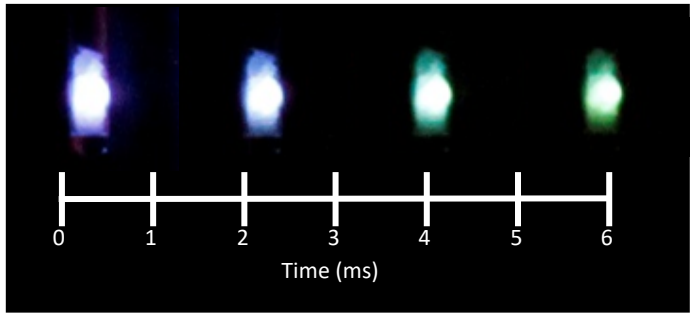
G. Tessitore, S. L. Maurizio, T. Sabri, J. A. Capobianco, *Angew. Chem. Int. Ed.* **2019**, *58*, 9742.

Time-Tunable Emissions

- Different ions have different excited state lifetimes.
  - Tm^{3+}: µs
  - Tb^{3+}: ms
- Plotting emission spectrum after excitation has ceased exhibits this difference in luminescence decay.
- Utilizing this intrinsic property of the luminescent ions as a color-tuning mechanism.



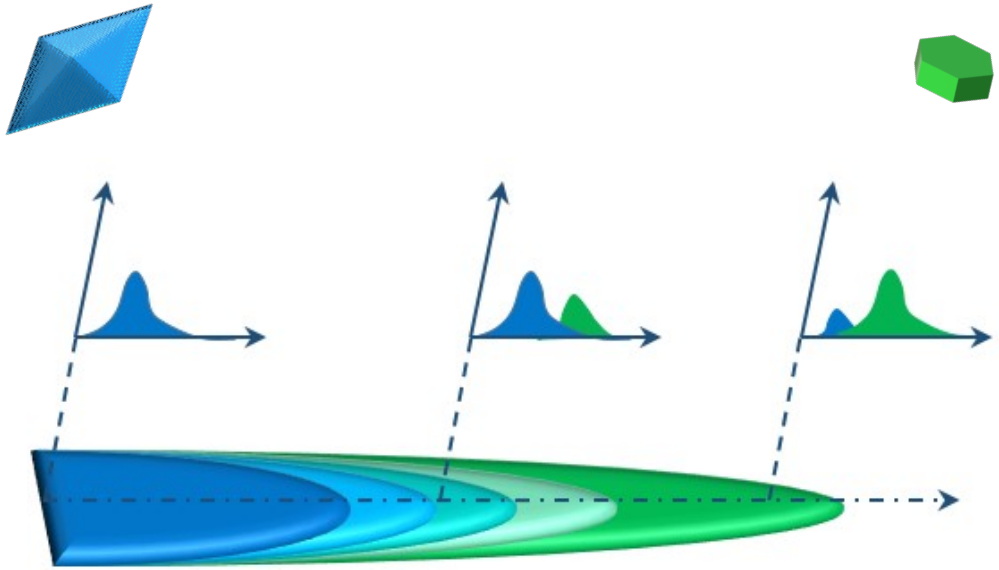




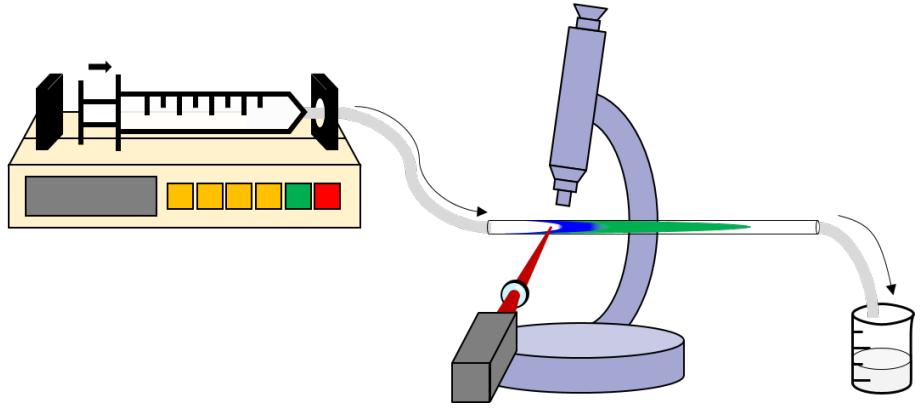
G. Tessitore, S. L. Maurizio, T. Sabri, J. A. Capobianco, *Angew. Chem. Int. Ed.* **2019**, *58*, 9742.

Nanoparticle Flow: Experimental

Systems with multiple emissions with a known difference in rise times



Upconverting Nanoparticles



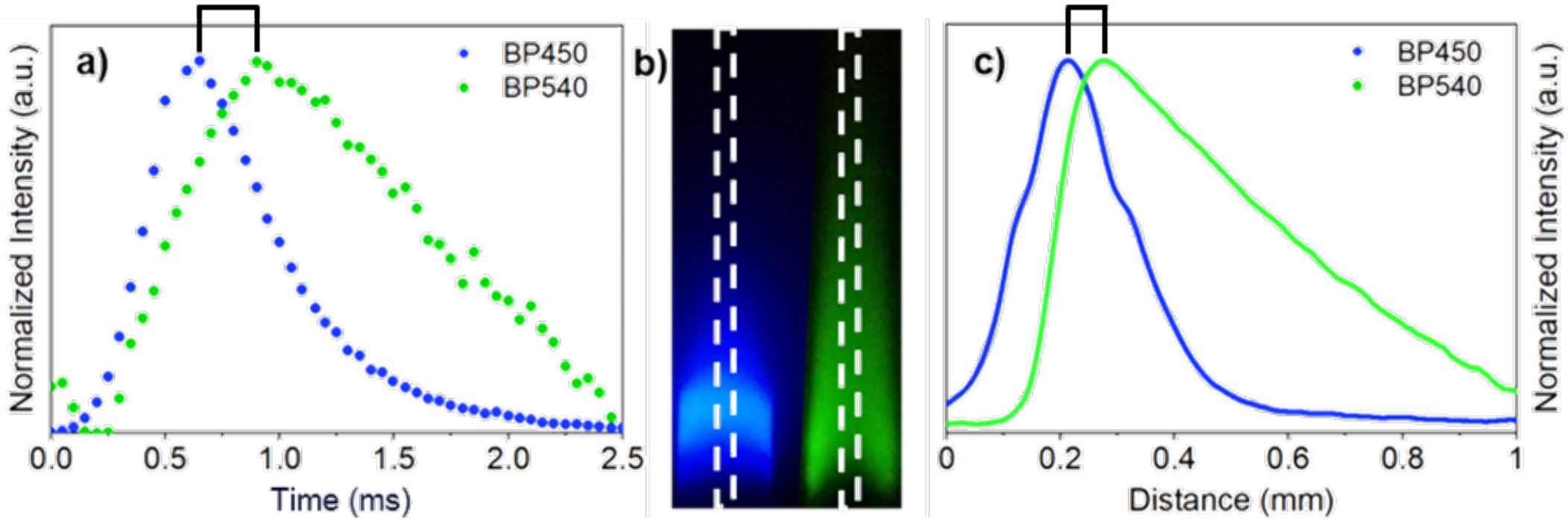
S.L. Maurizio, G. Tessitore, G.A. Mandl, J.A. Capobianco, *Nanoscale Adv.* **1**, 2019, 4492-4500.
G. Tessitore, S.L. Maurizio, T. Sabri, J.A. Capobianco, *Angew. Chem., Int. Ed.* **58**, 2019, 9742-9751.

Multiemission Particle Velocimetry

Blue/Green Bandpass Filter

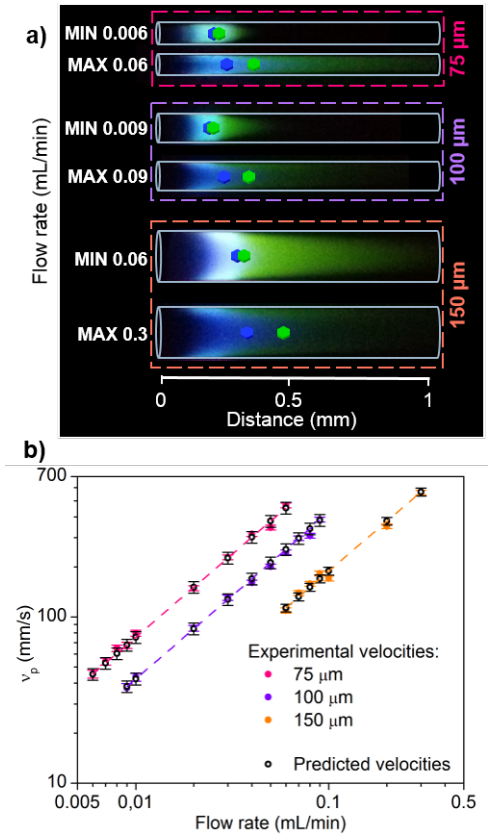
Sequential Emissions
Known Time Interval

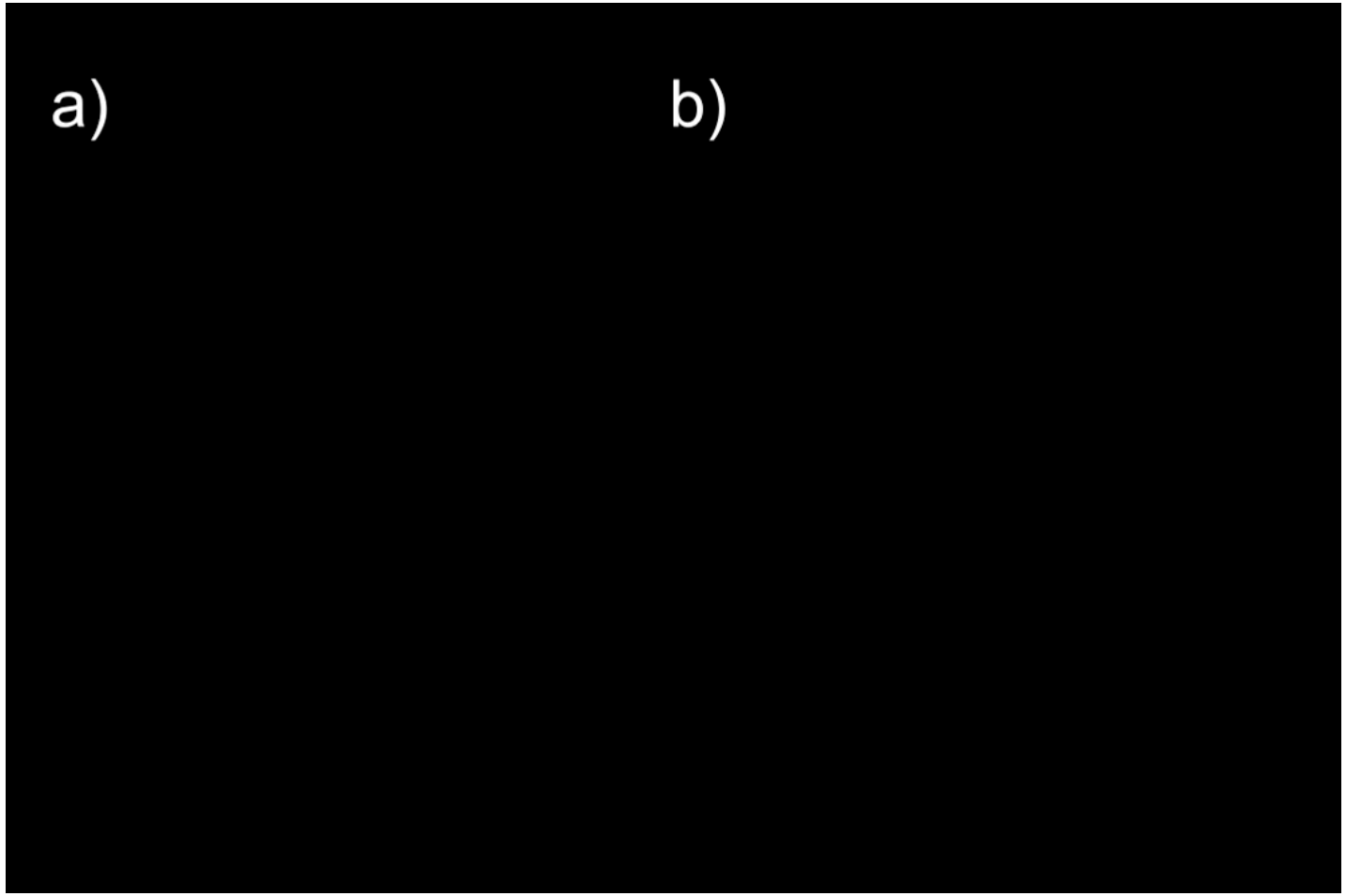
Sequential Emissions
Measured Distance



G. Tessitore, S.L. Maurizio, T. Sabri, C.D. Skinner, J.A. Capobianco, *Adv. Mater.* **32**, 2020, 2002266.

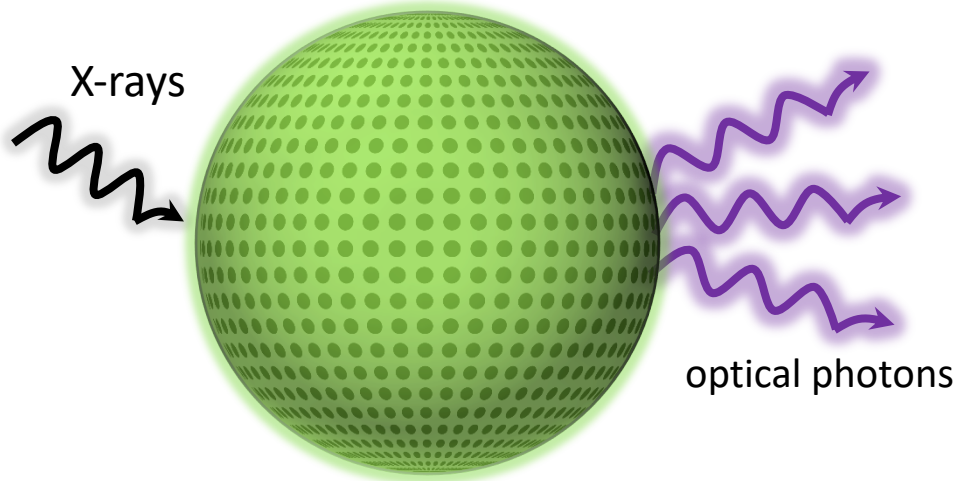
Multiemission Particle Velocimetry Blue/Green Bandpass Filter

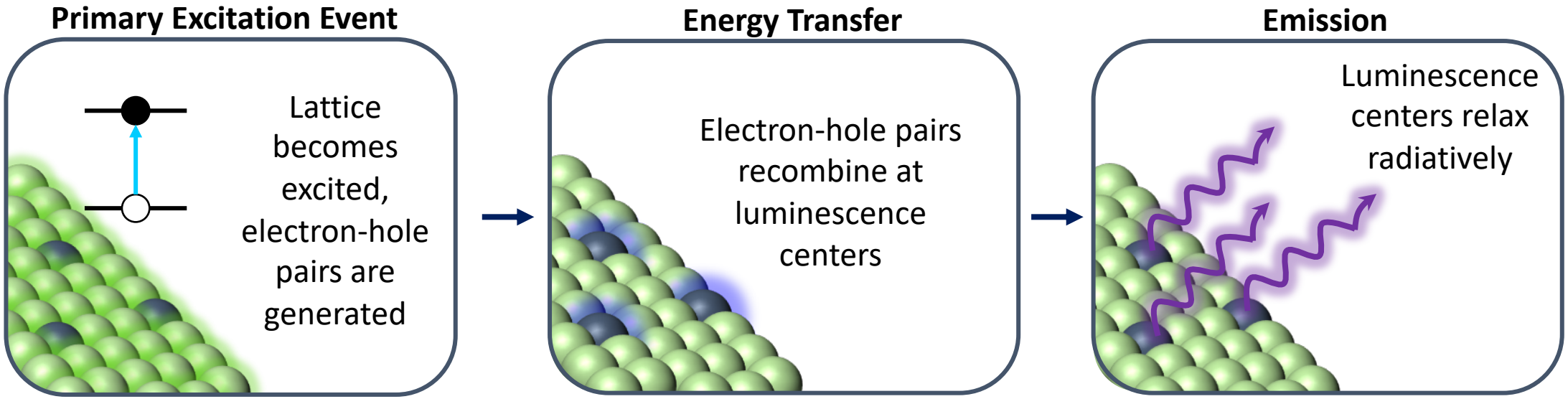




- **Simple**: No calibration required
- **Inexpensive**: No need for specific (and costly) lasers and detectors
- **Flexible**: Each part can be substituted with an equivalent
- **Accurate**: The experimental error is lower than 5%

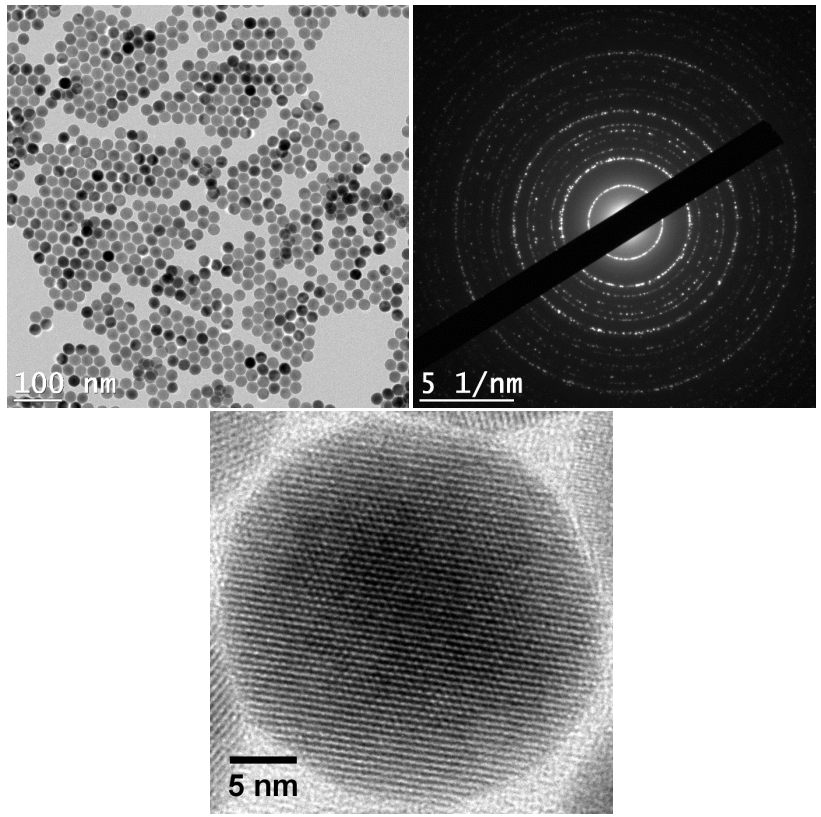
Radioluminescence

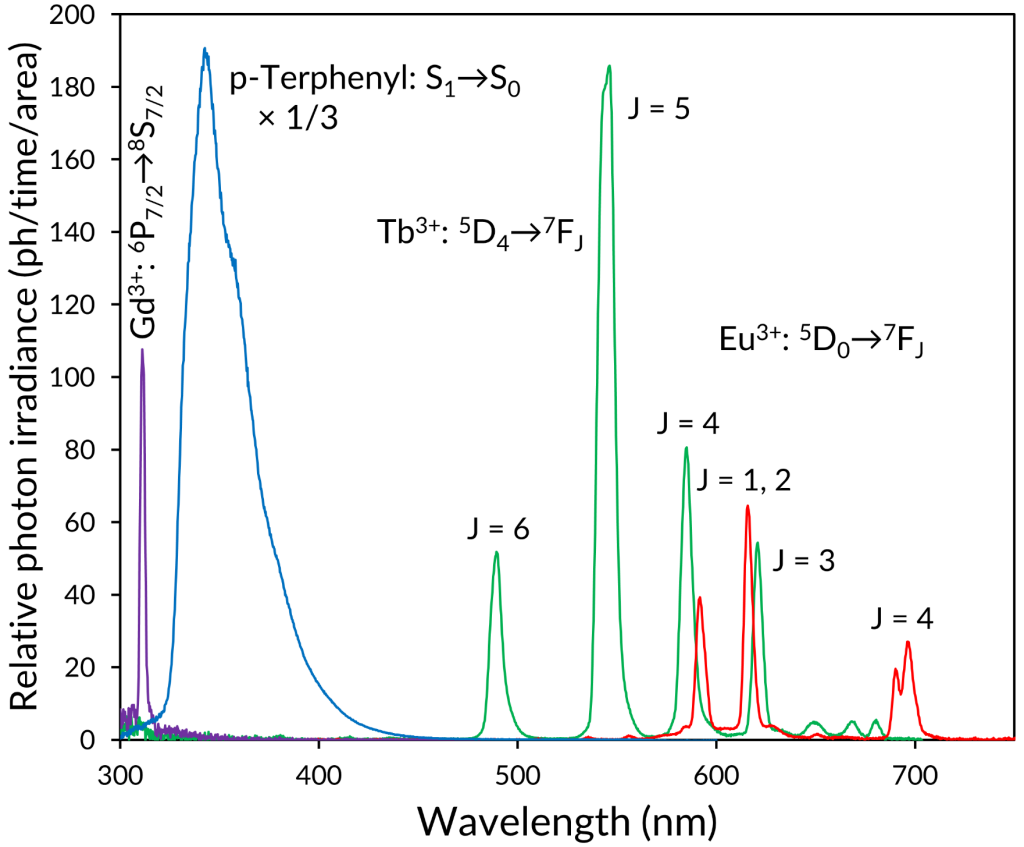




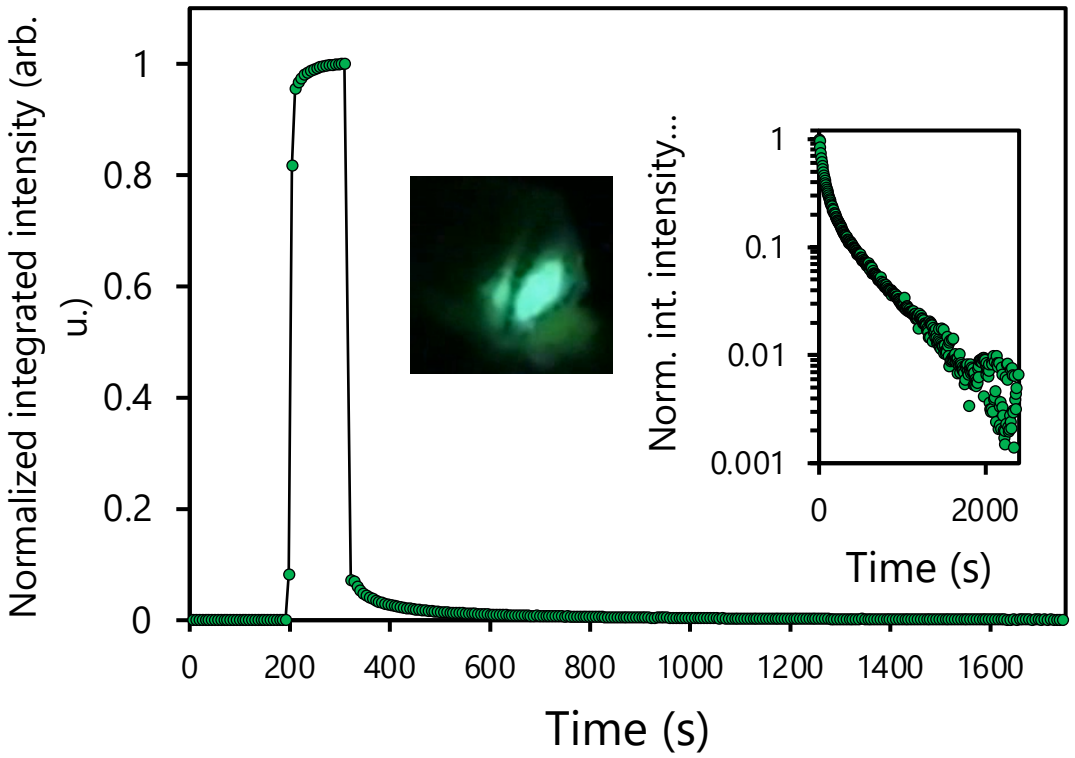
Radioluminescence of novel NPs

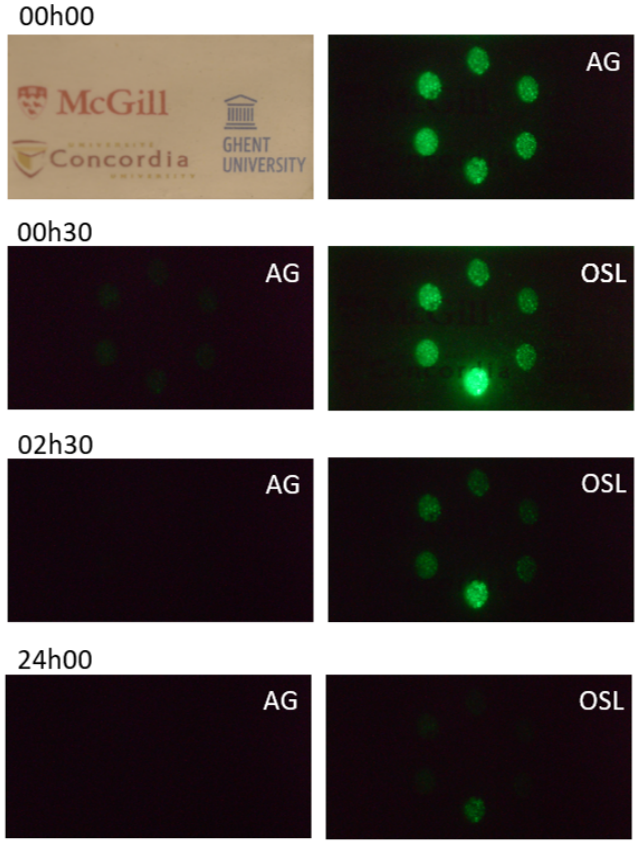
$Na(Gd,Lu)F_4$:Tb



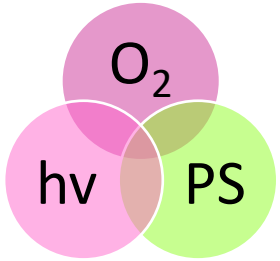


Properties of $Na(Gd,Lu)F_4$:Tb

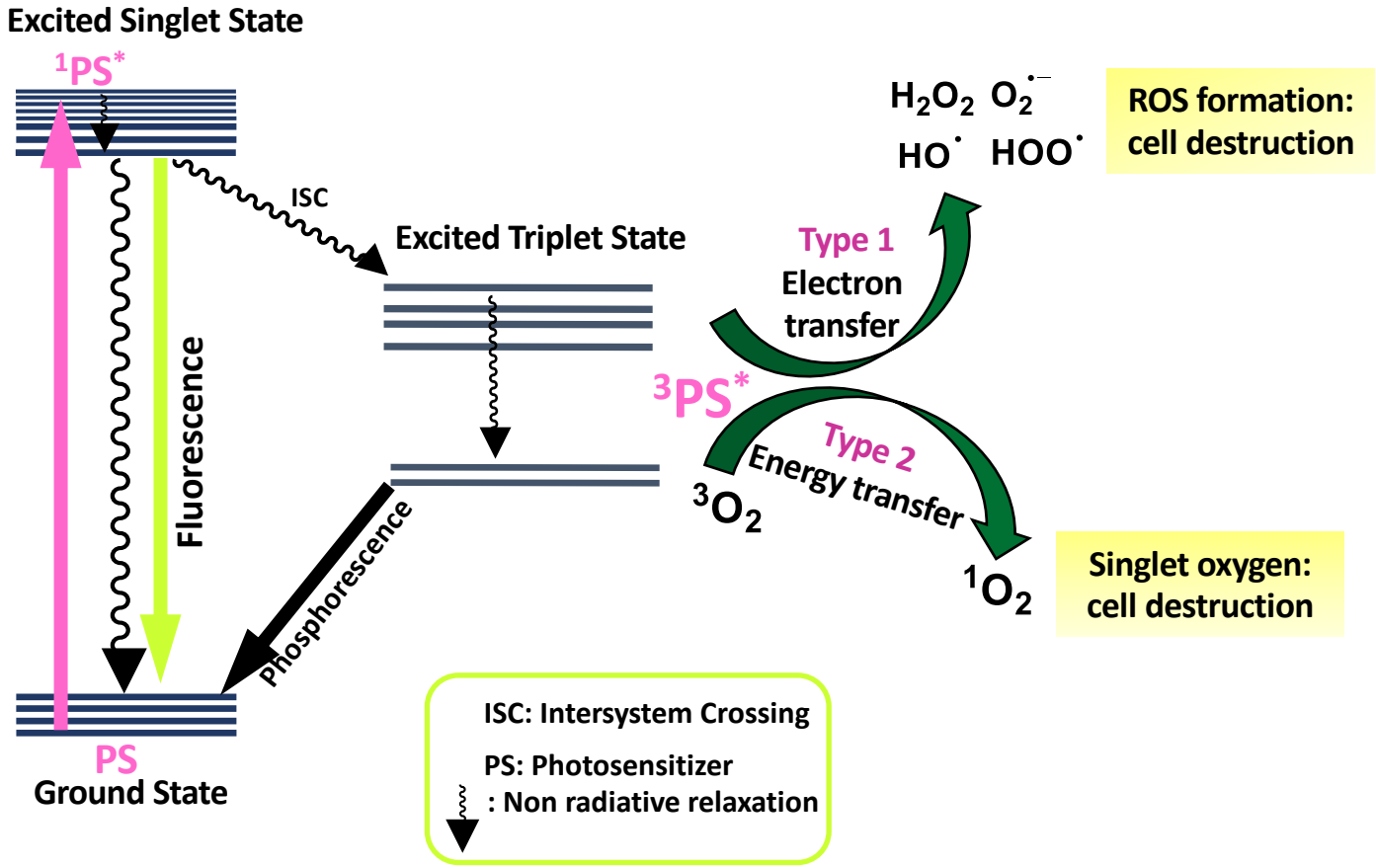




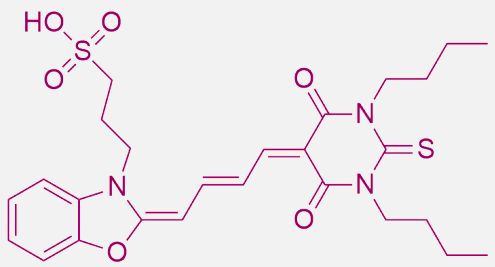
High charge storage capacity and bright optically-stimulated luminescence



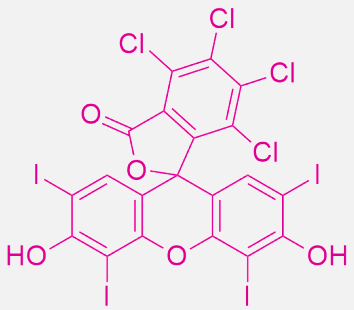
Photodynamic Therapy Mechanism



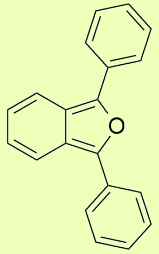
Project Overview



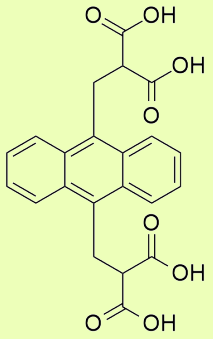
Merocyanine 540



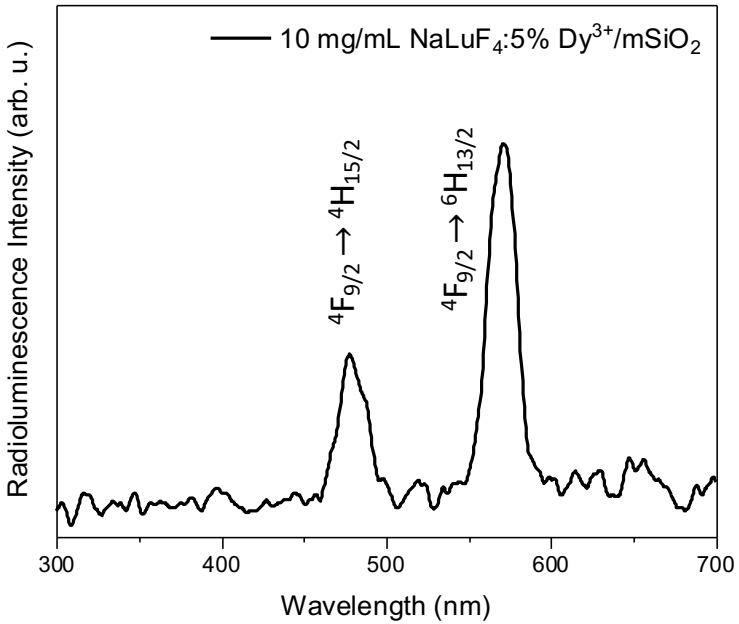
Rose Bengal



DPBF

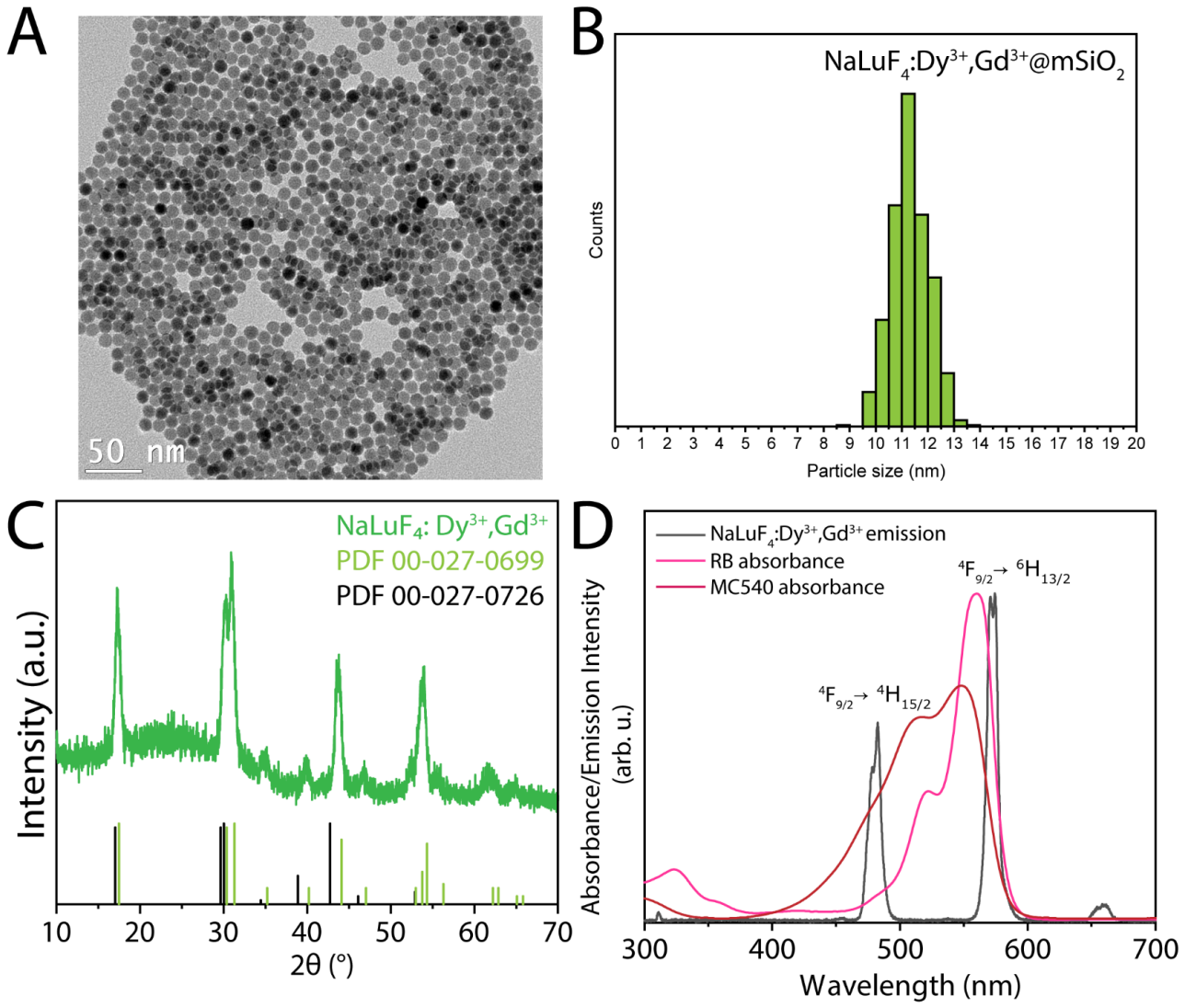


ABDA

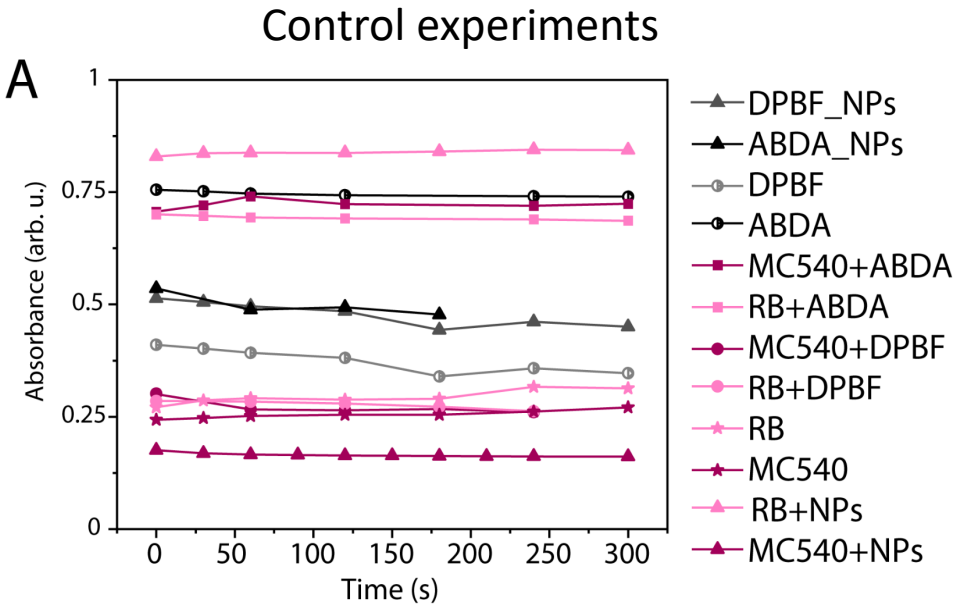


Study the production of reactive oxygen species (ROS) from Dy^{3+} **radioluminescent** nanoparticles using different probes

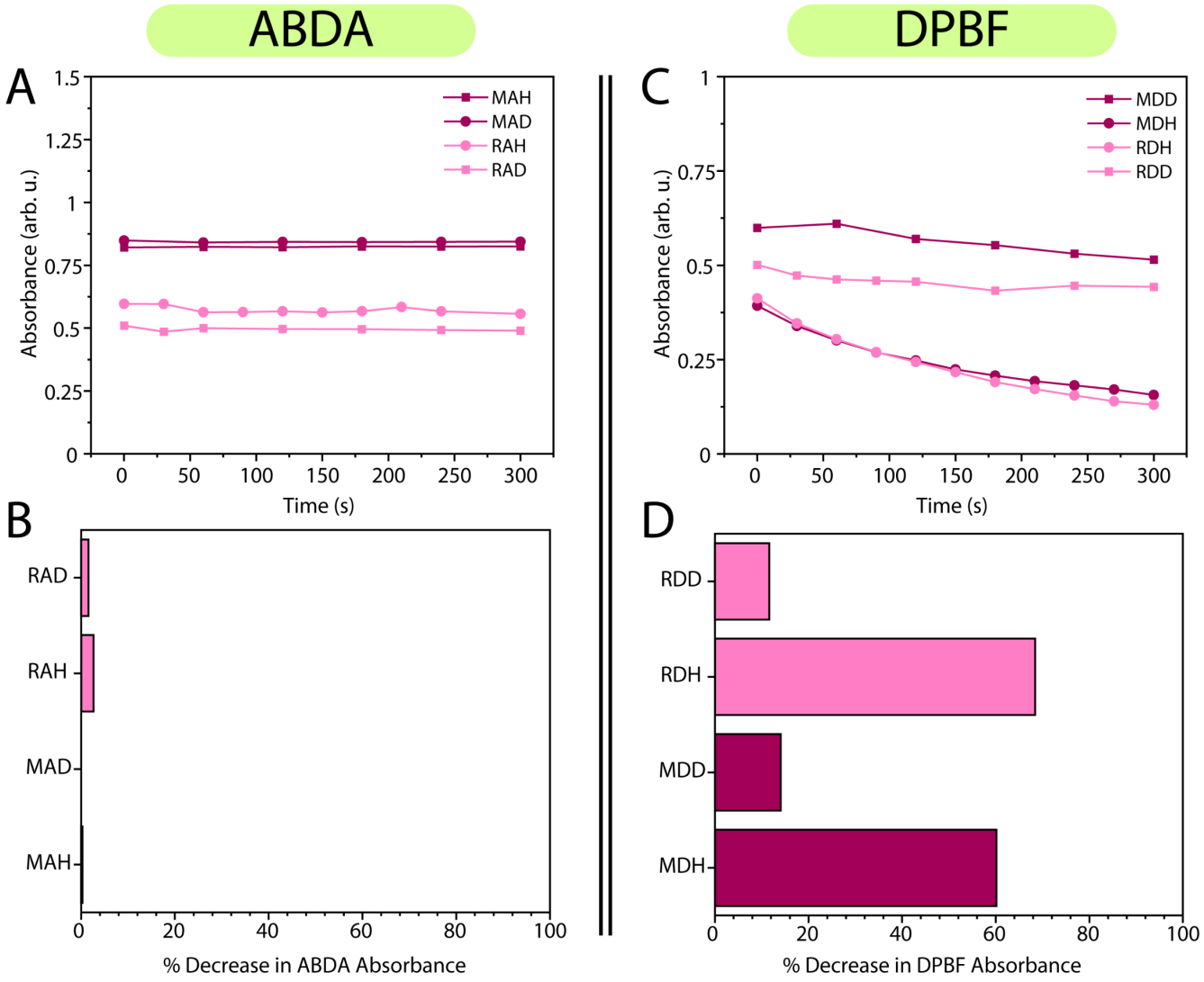
Overlap of Dy^{3+} emissions and RB and MC540 absorptions



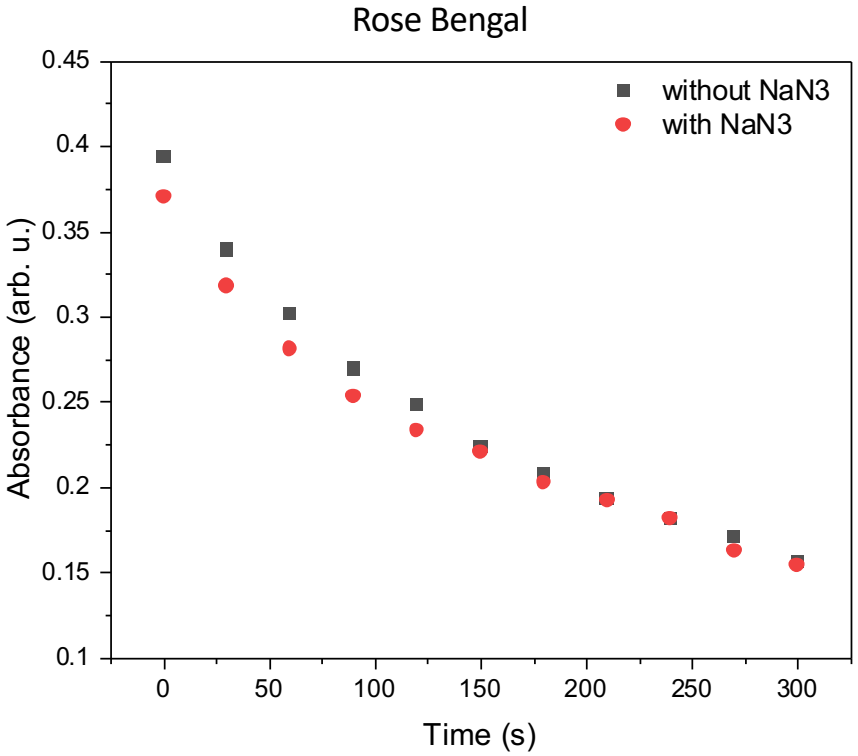
ROS Production under X-rays

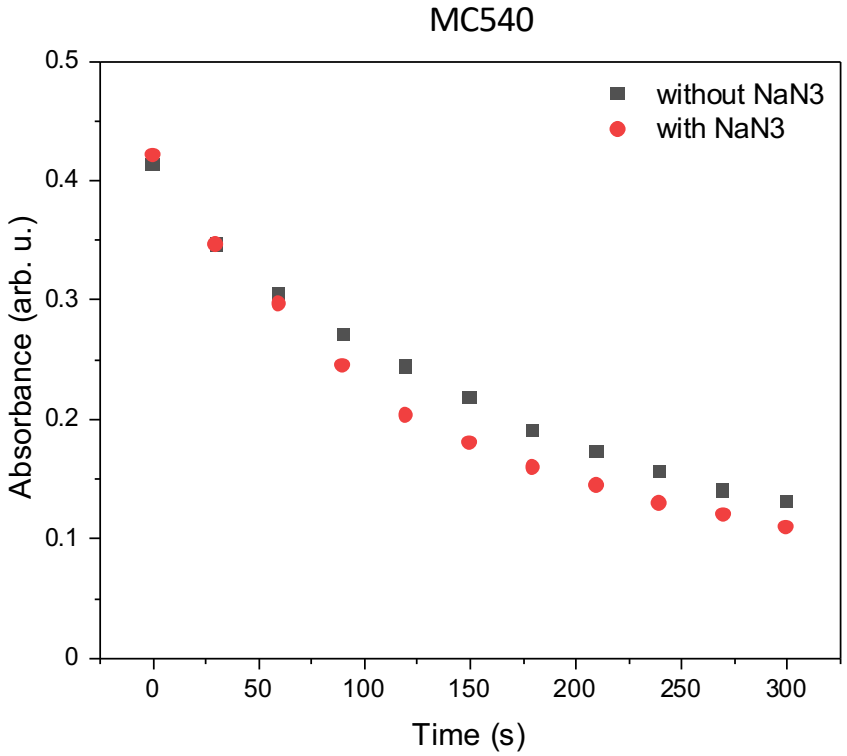


Little to no ABDA decrease = no appreciable singlet oxygen production



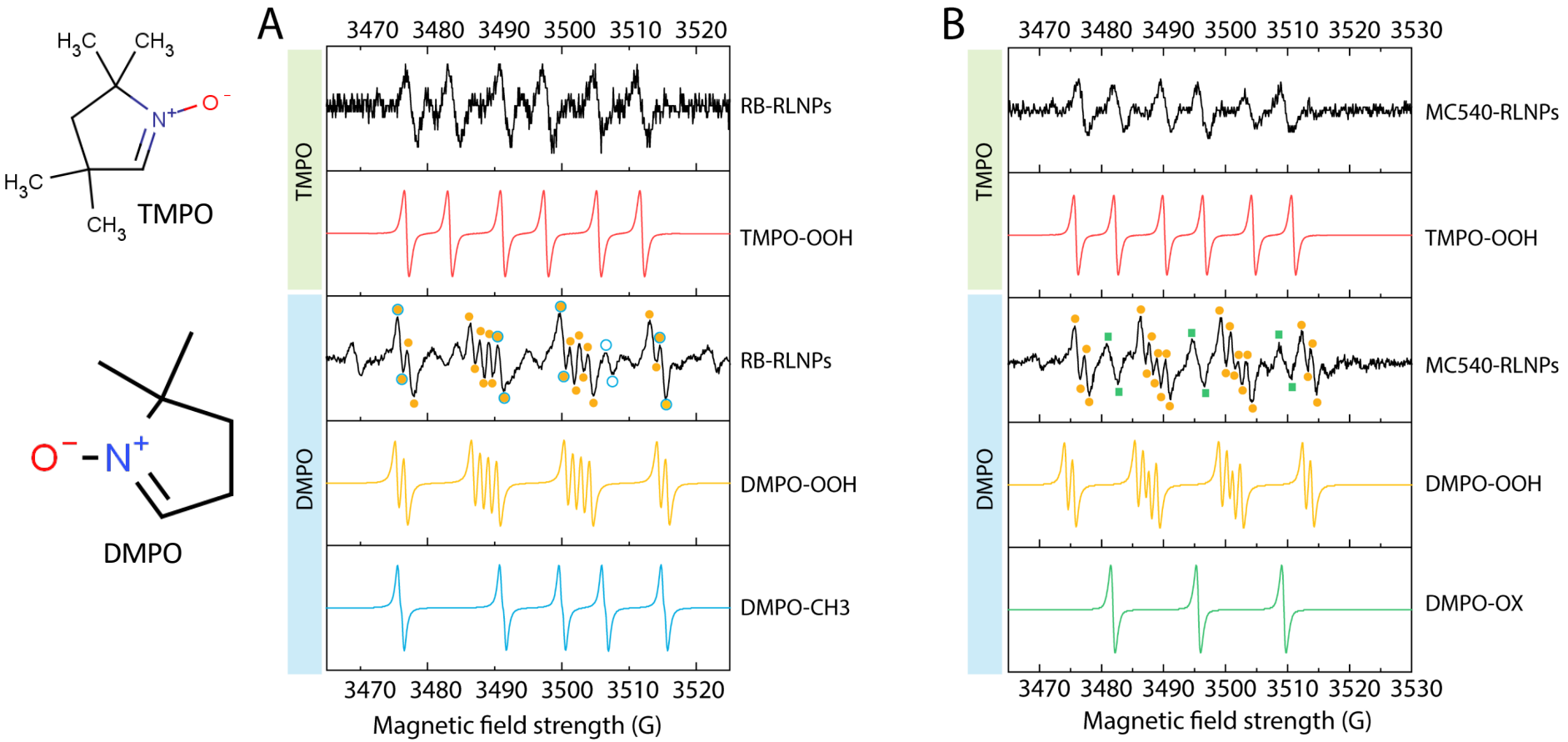
Sodium Azide Assay





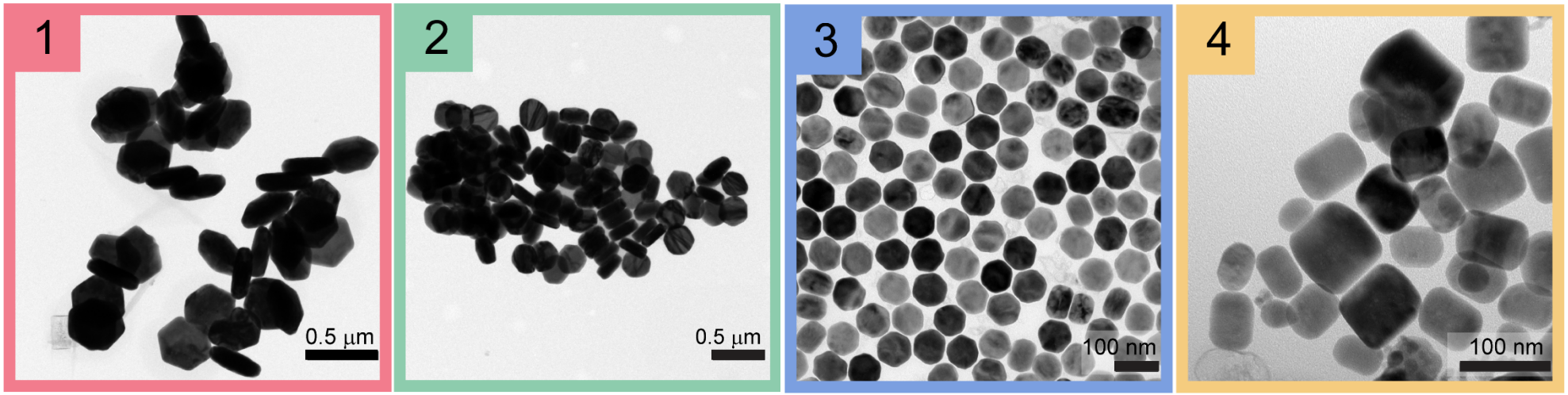
NaN_3 is a singlet oxygen quencher – confirms singlet oxygen is **not** the main ROS produced in either case

EPR – Identifying ROS products

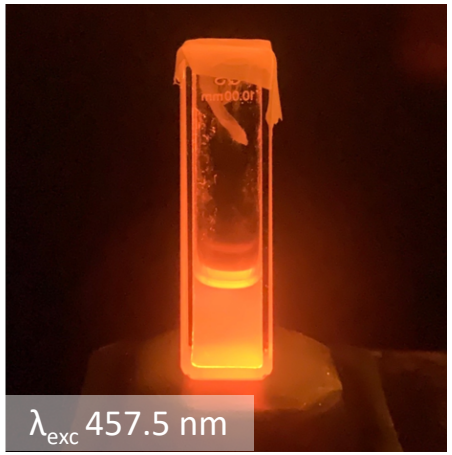


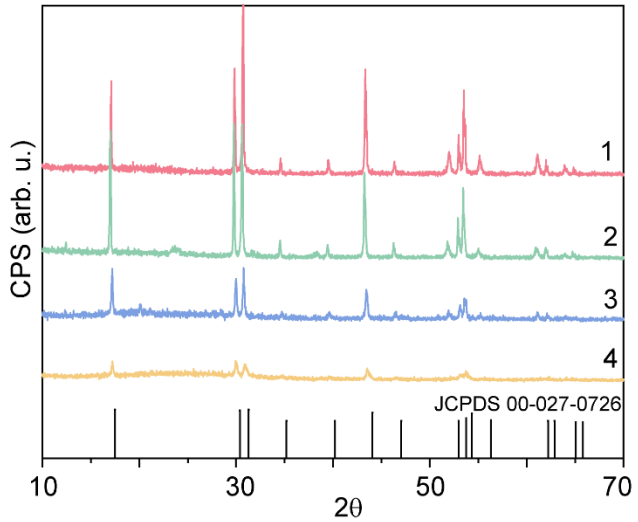
- Superoxide anion ($O_2^{\bullet -}$) and hydroxyl ($OH^{\bullet -}$) radicals are the main species produced

$NaLuF_4$:20% Pr^{3+} Characterization



ICP-MS	
Sample	Av. % Pr^{3+}
1	20.90
2	21.71
3	18.90
4	19.94





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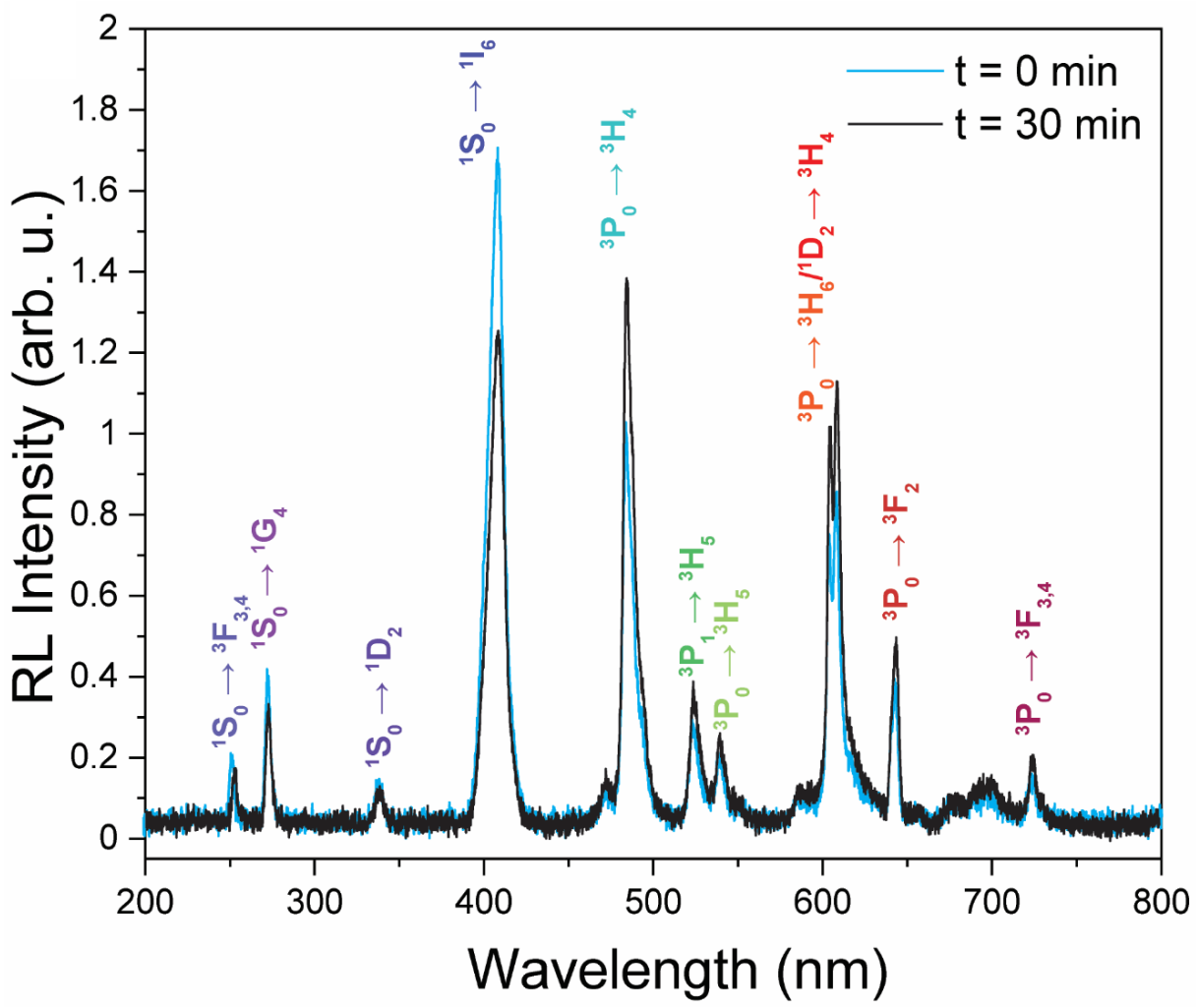
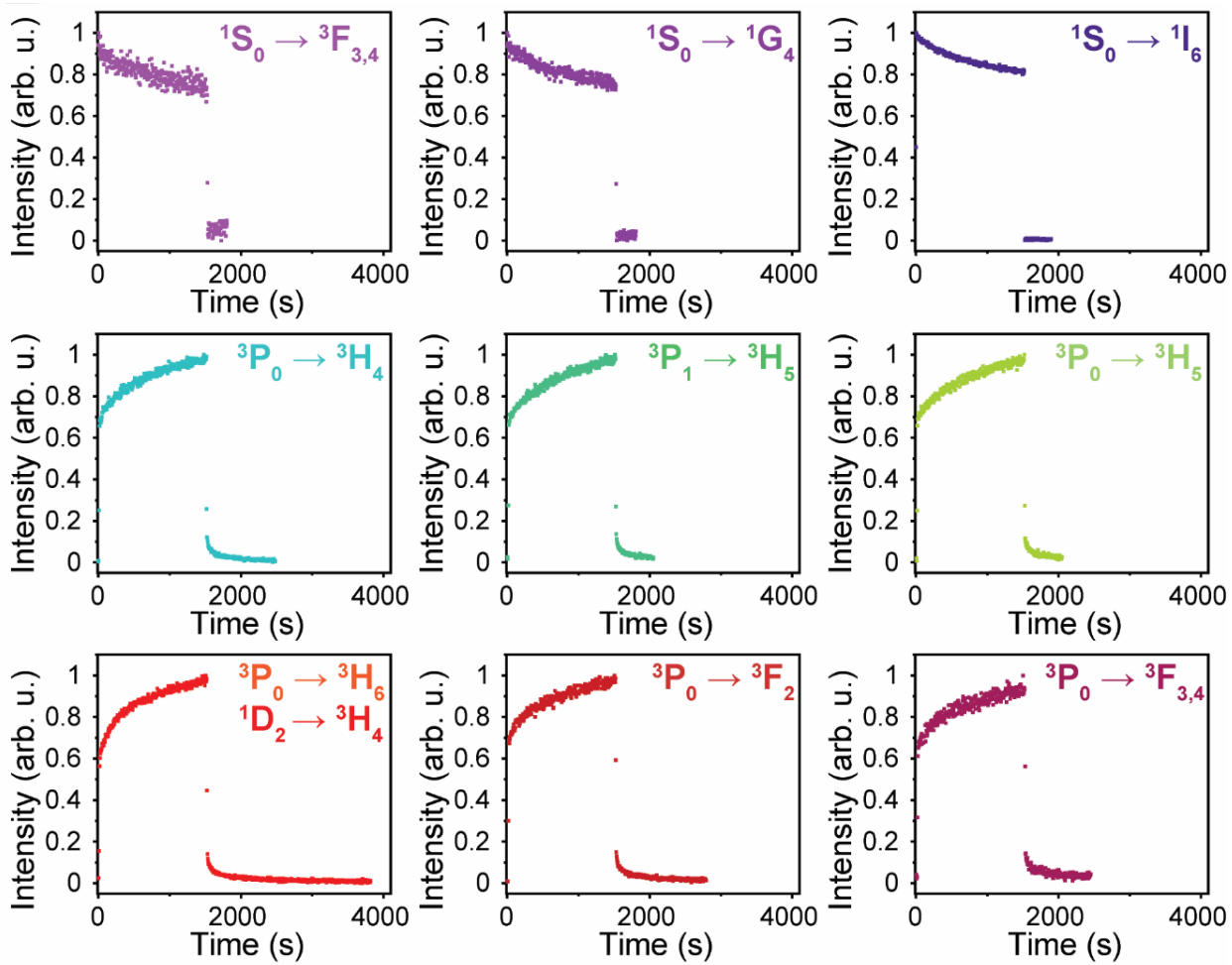
Radioluminescence spectroscopy





50 kVp, 80 µA
unfiltered beam

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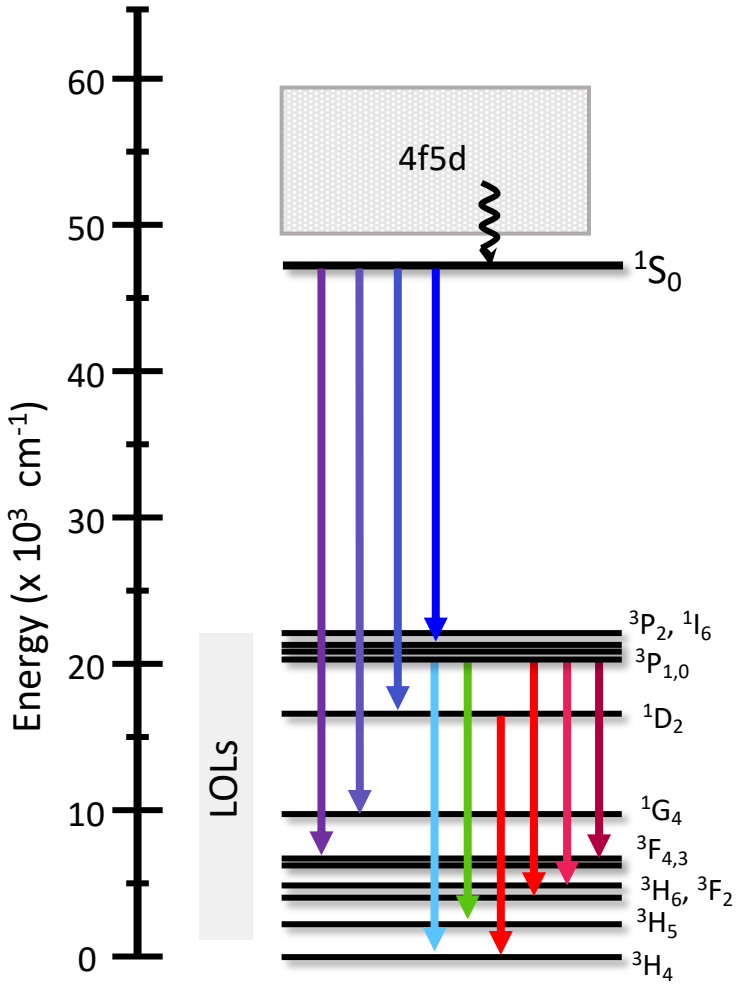
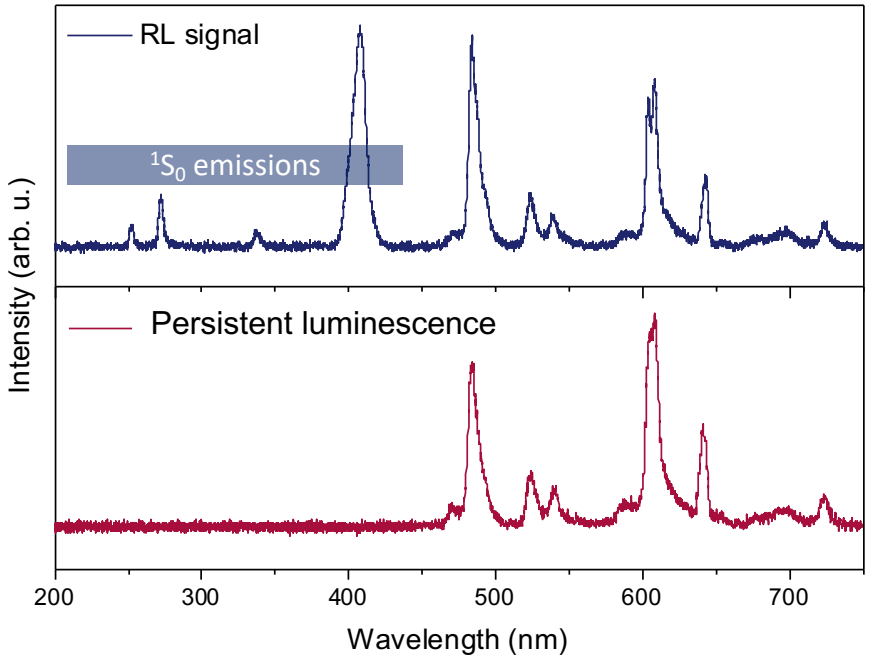
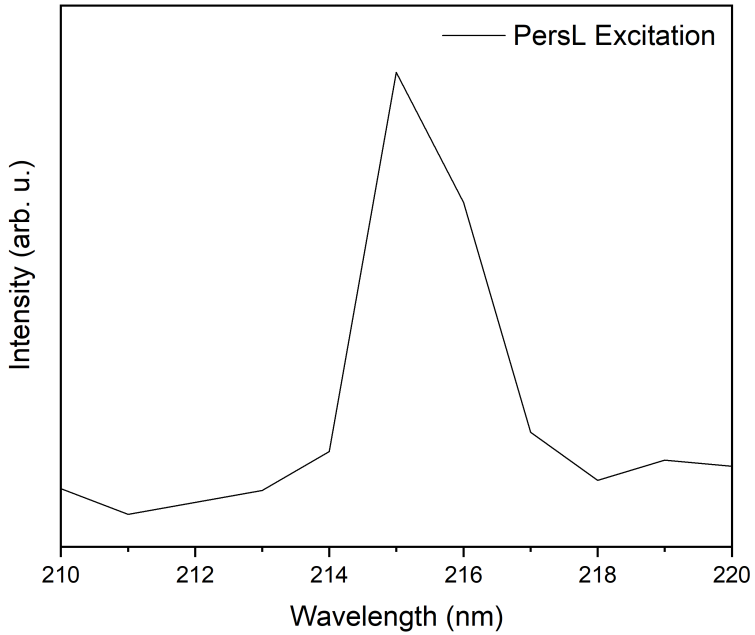
Persistent luminescence spectroscopy







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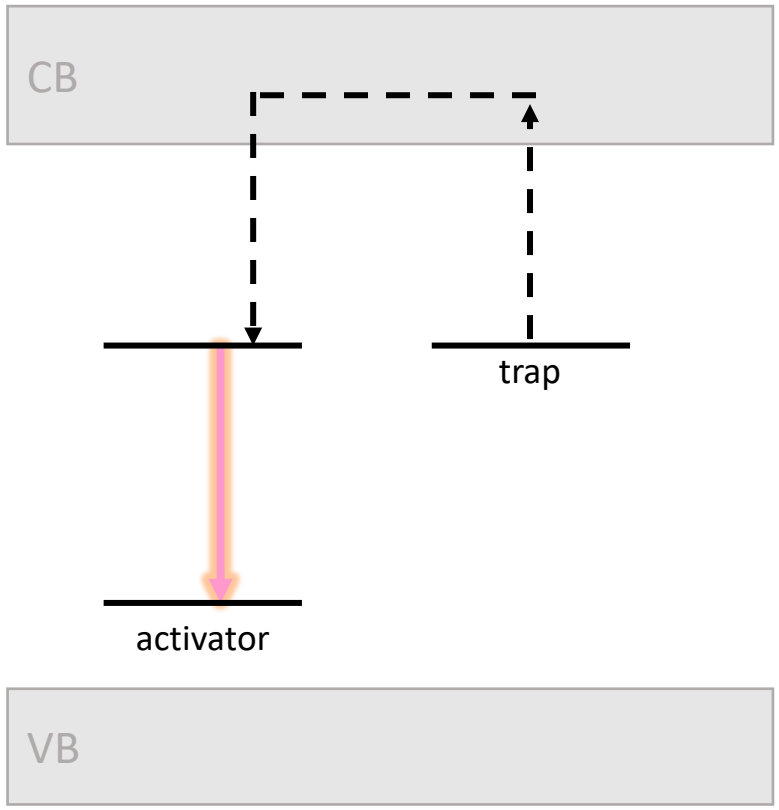
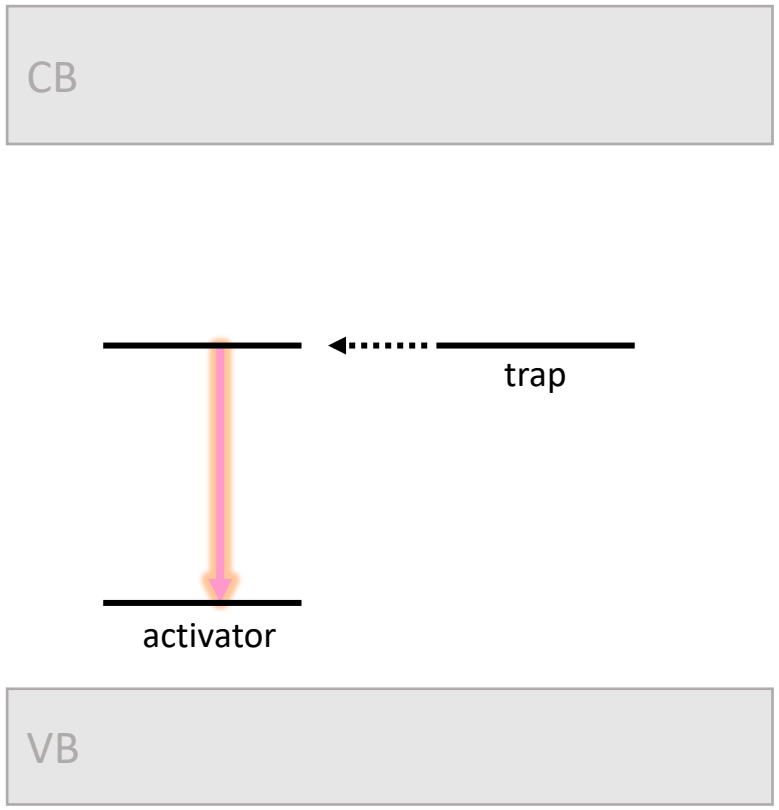
Persistent Luminescence

The continued emission of photons after excitation has ceased

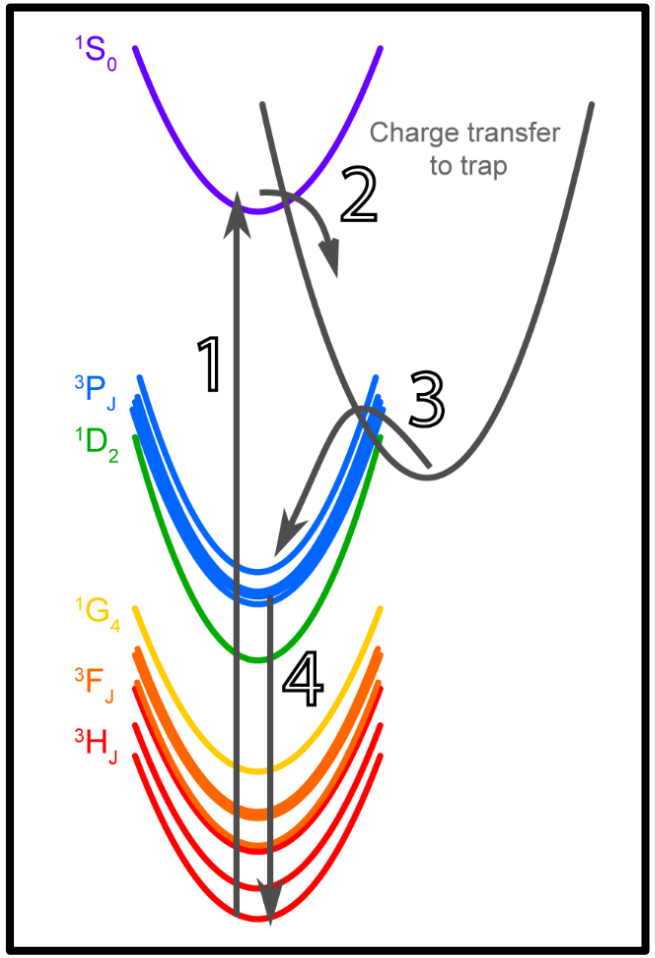
Global (de-)trapping



Local (de-)trapping



The local (de-)trapping mechanism



$NaLuF_4$ band gap: 13.8 ± 0.9 eV

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deltoides


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