Tuning of the photophysical properties of core-shell silica nanoparticles for bio-imaging and photodynamic therapy

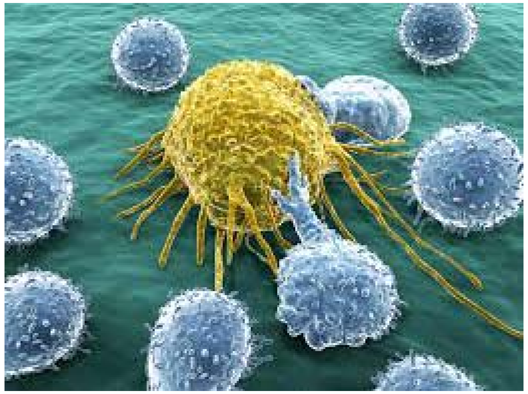
Virginia Martínez

NanoSpain Conf 2017
March 07-10, 2017 – San Sebastian (Spain)
THE LEADING N&N EVENT IN SPAIN

eman ta zabal zazu
UPV EHU
Molecular Spectroscopy Laboratory

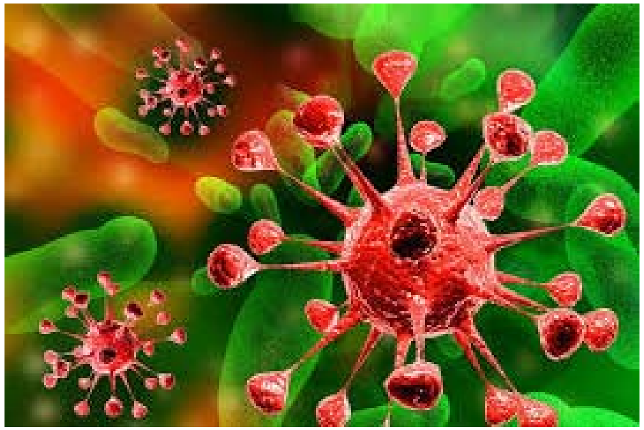
Introduction

Photodynamic therapy (PDT) is a minimally invasive procedure that offers many advantages over traditional cancer treatments

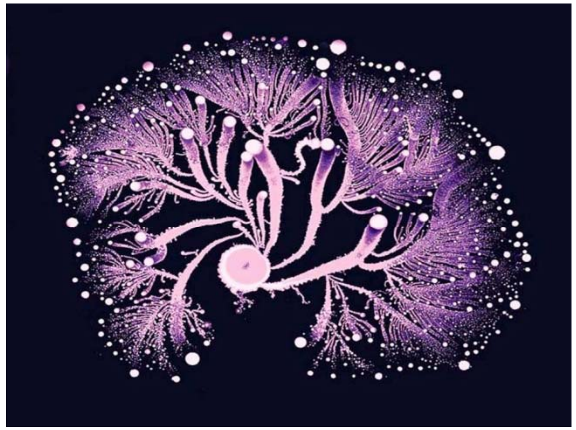


Kill tumor cells

Bacteria



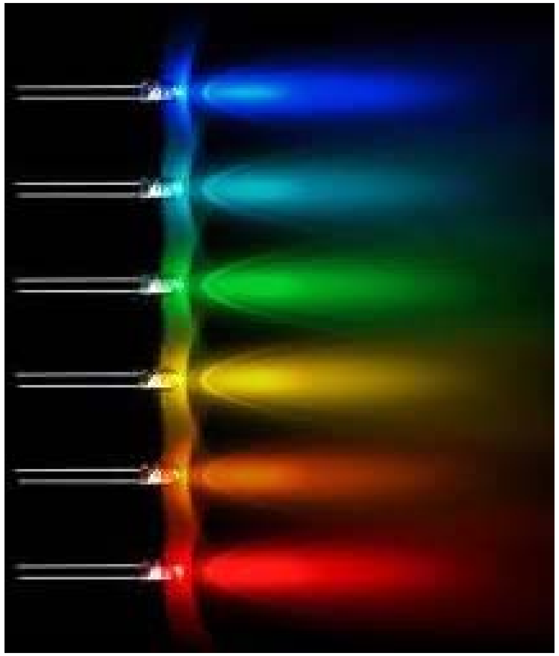
Viruses



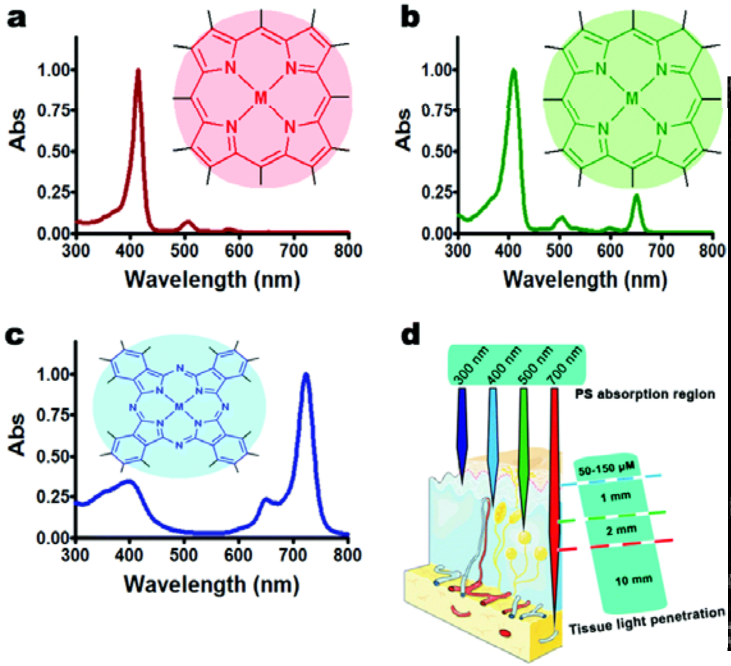
Fungi

Introduction

PDT applications involve three components



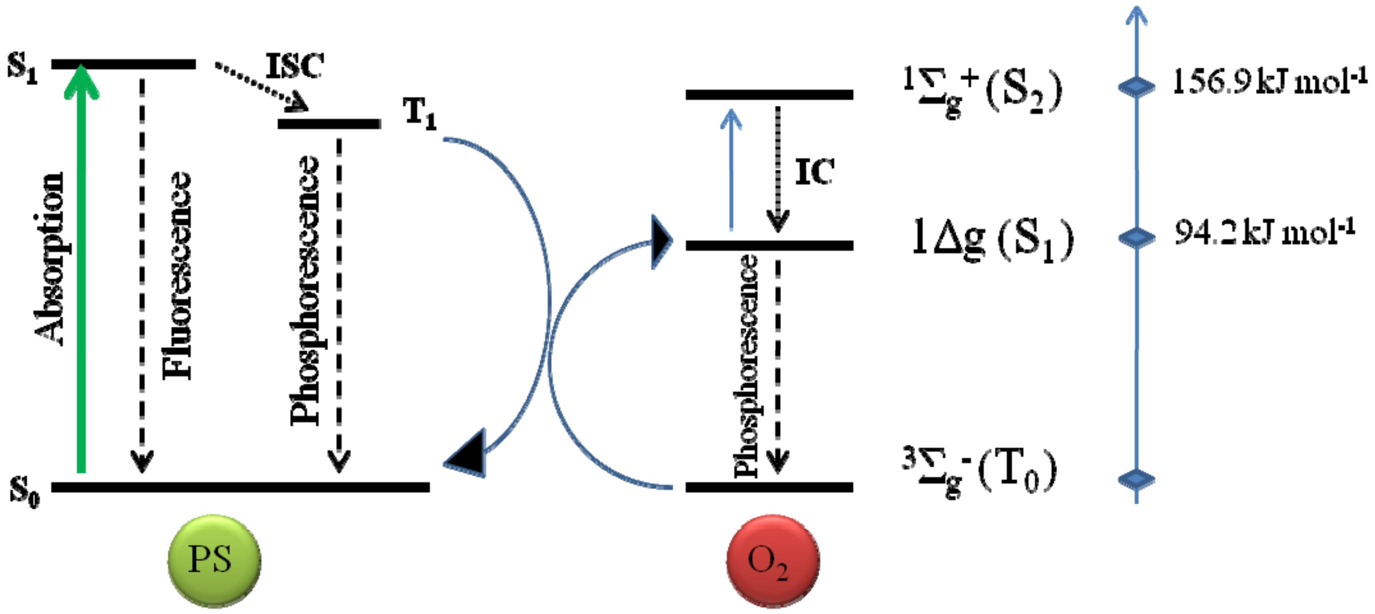
Light

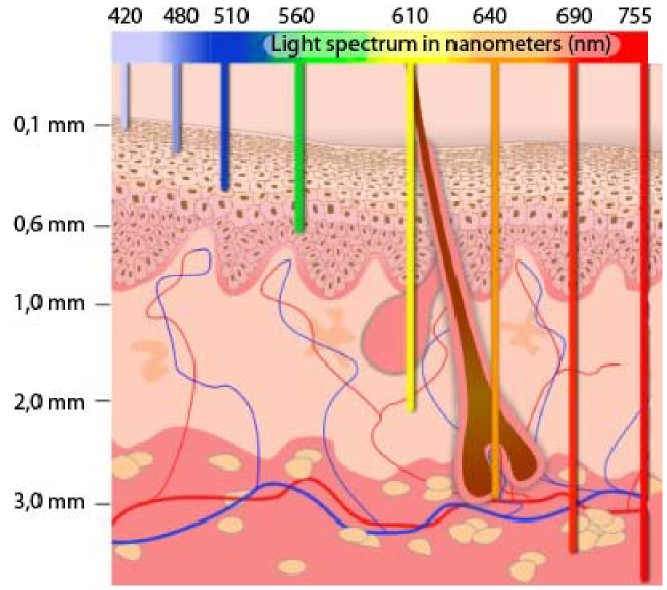


Photosensitizer

Oxygen

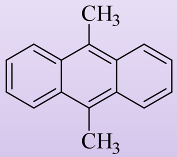
Photosensitizers



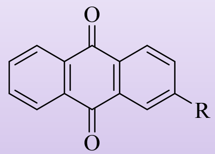


- Low toxicity (dark-conditions)
- Selective accumulation
- High photostability
- High Φ_{Δ} of singlet oxygen production
- High absorption (red region)

photosensitizers

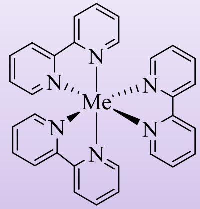


9,10-dimethylanthracene (DMA)



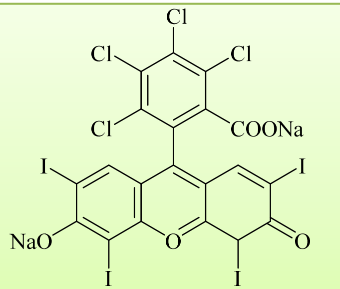
Anthraquinone derivates

Fullerene

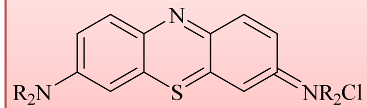


$[Me(bpy)_3]^{2+}$

→ UV absorption ✗



Xanthene dyes:
Rose Bengal



Thiazine dyes:
Methylen Blue $R=CH_3$

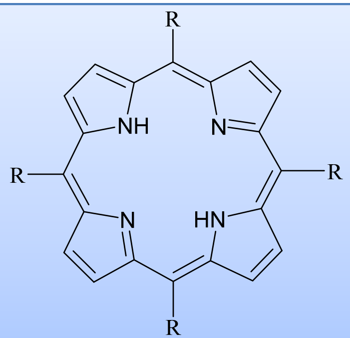
→

Visible absorption ✓

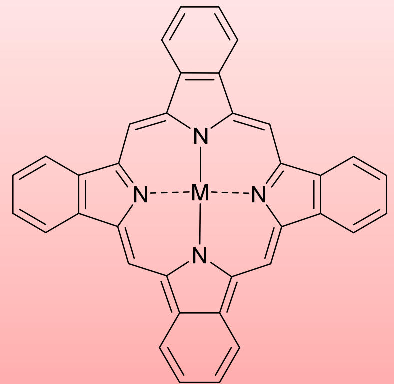
Dye aggregation ✗

Low photostability ✗

Biomedical aplications



Porphyrines



Phtalocyanines

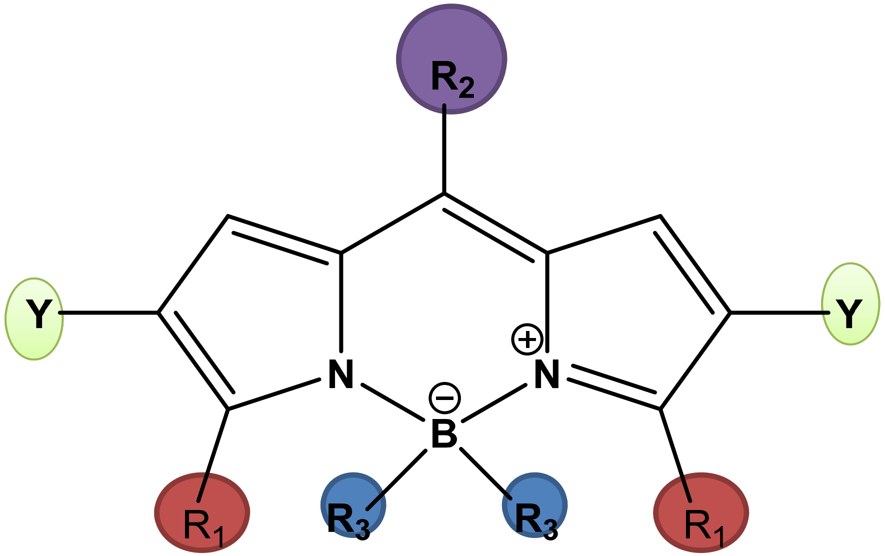
→ Visible absorption ✓

Low absorption coeficient ✗

Low solubility ✗

photosensitizers

New Type of Photosensitizers :
4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY)



Y = heavy atoms $\longrightarrow$ $^1O_2$

R1 = π-substituents $\longrightarrow$ red abs

R2= graftable groups $\longrightarrow$ surface

R3= solubilized groups $\longrightarrow$ water

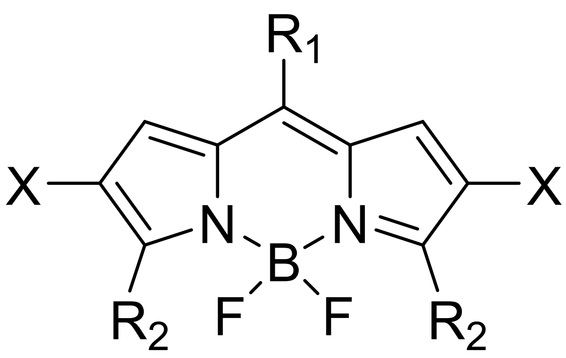
- Very favorable chemical-physical features:

1) High extinction coefficients in the visible
2) Resistance to photobleaching
3) Versatile synthesis

photosensitizers

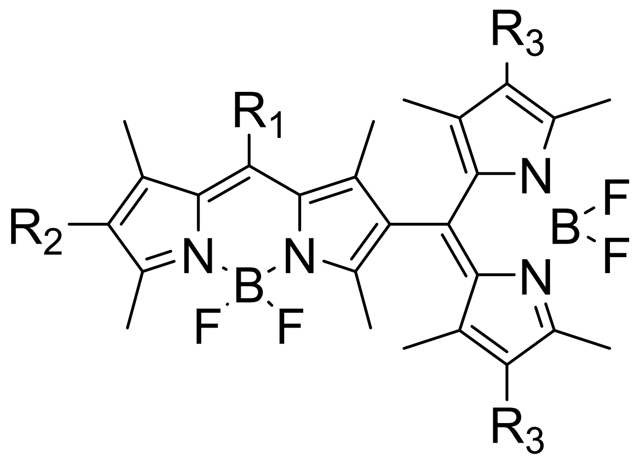
Halogenated BODIPY

blue
green
red



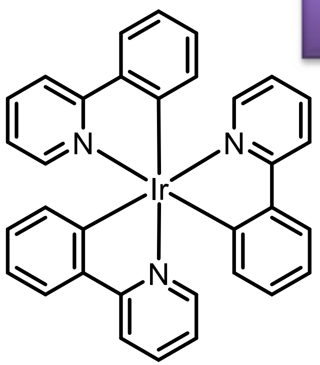
Effect of halogen (X) and the susbtituents (R)
RSC Advances 2016, 6, *41991-41998*

Halogen free: BODIPY dimers

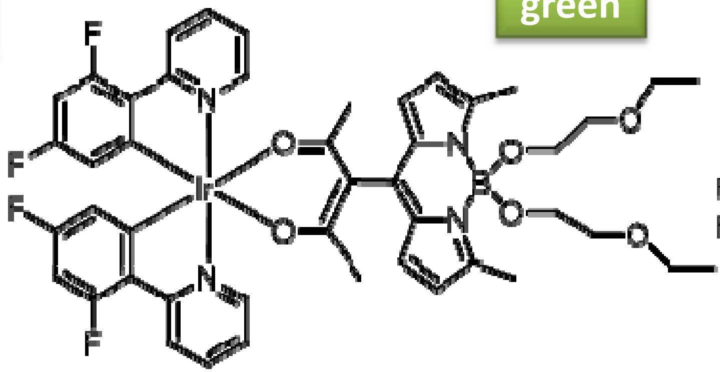


Effect of the solvent and the susbtituents
Chem Eur J 2017 (accepted)

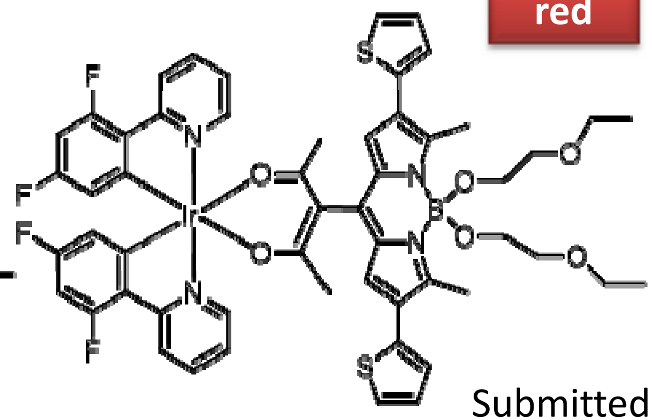
New organometallics:



UV



green

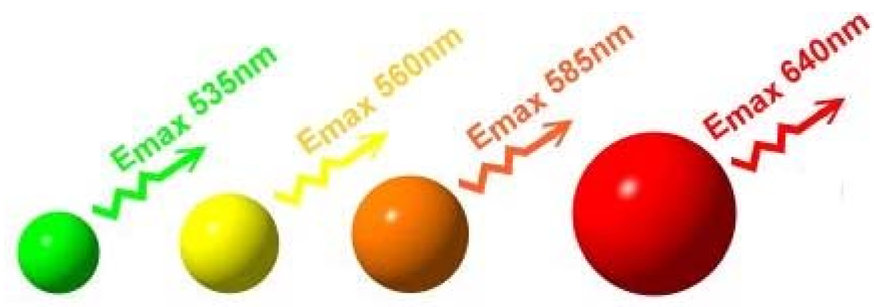


red

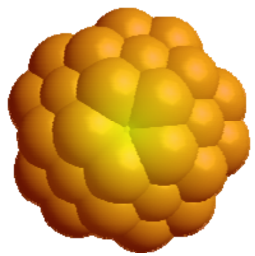
Submitted

Nanocarriers

Nanocarriers for biomedicine:



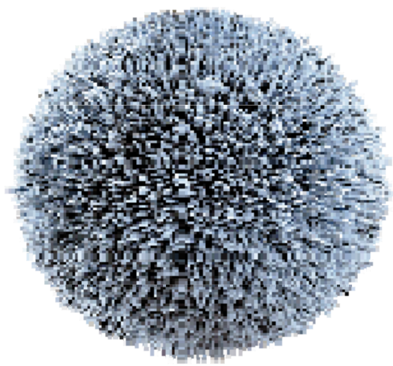
CdSe Quantum Dots drawn to scale



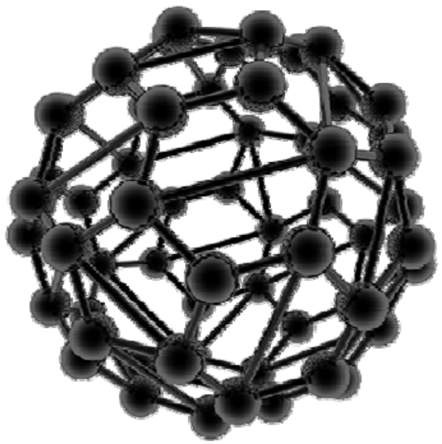
Gold nanoparticle

iron

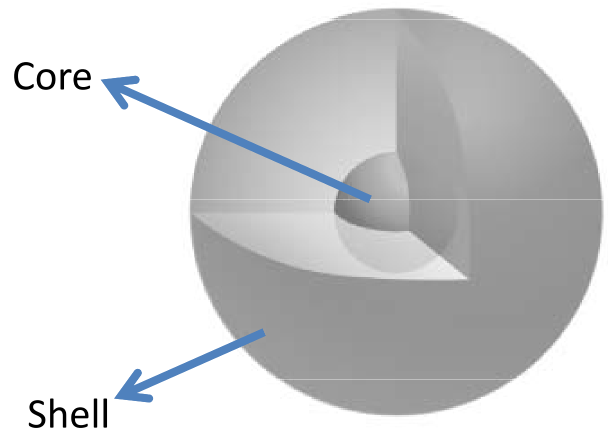
Polymeric



Carbon-NP



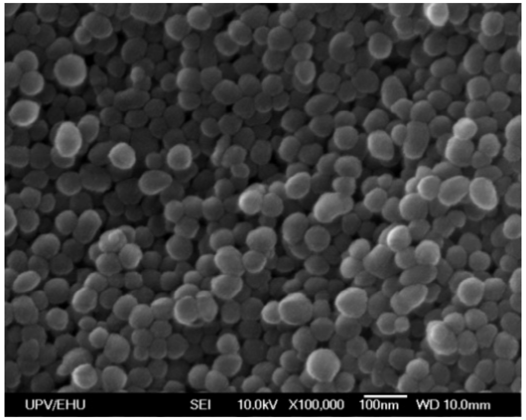
Silica NP

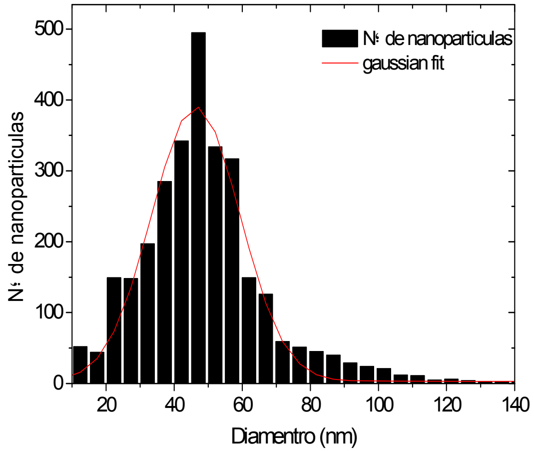


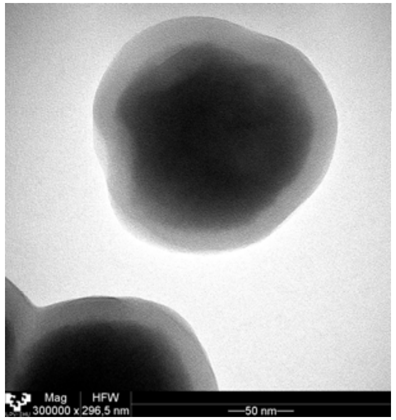
❖ Properties

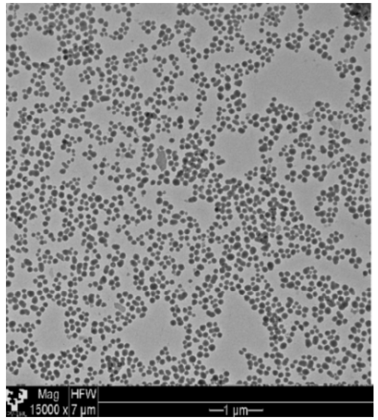
- large surface area (>1000m^2 g^{-1})
- Modifiable size and pore volume (>1cm^3 g^{-1})
- High chemical and thermal stability
- Non toxic and biocompatible
- May have an internal core and an external shell
- Can be grafted with functional groups

NP Characterization



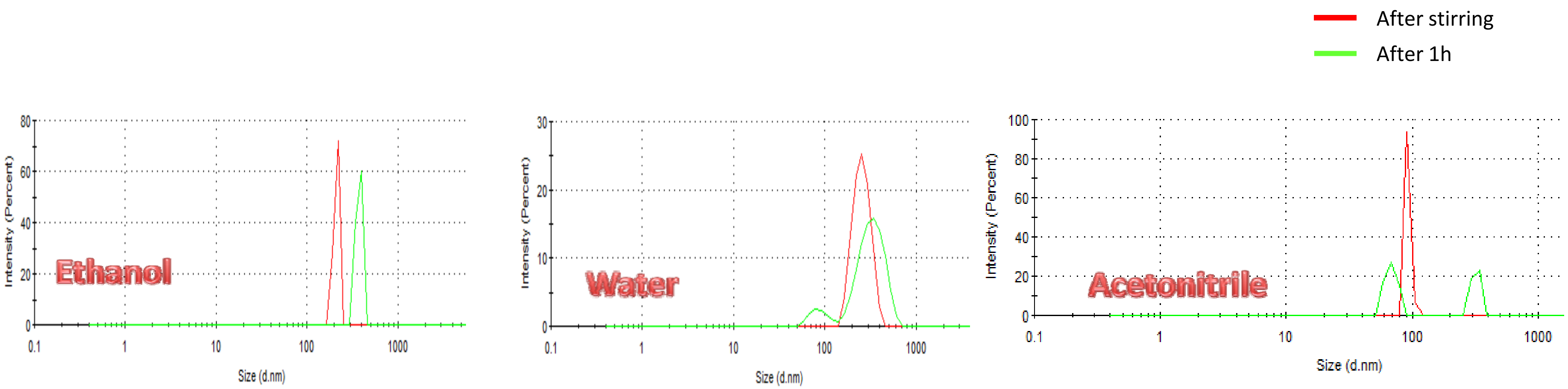






- Spherical and Homogeneus Distribution → **50 ± 15 nm**
- Core-Shell structure
- 4 % of NH_2 on NP surface available for PS grafting
- Well dispersed in polar solvents (DLS)

Light Scattering Characterization



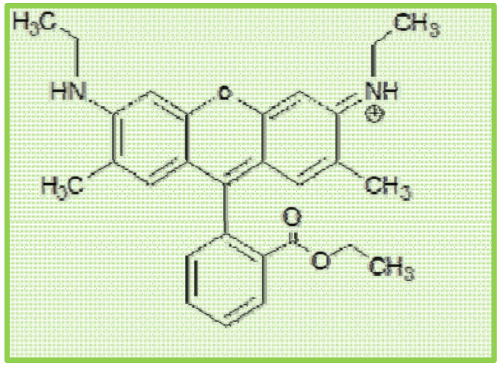
Solvent	Diameter (nm) (t=0 s) stirring	Diameter (nm) (t=1 h) without stirring	
EtOH	212±13	374±26	
water	257±54	90±22 (11%)	336±102 (89%)
ACN	92±3	68±7 (60 %)	321±23 (40%)

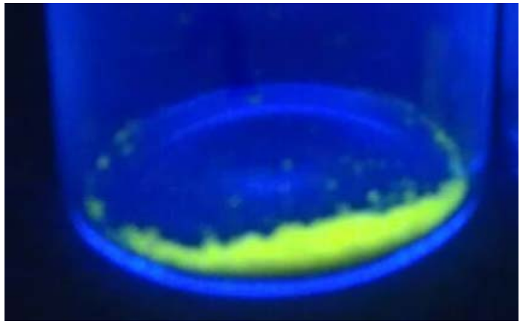
P21

The best solvent for silica NP suspension: ACN

Working in the Core: imaging

Rhodamine 6G

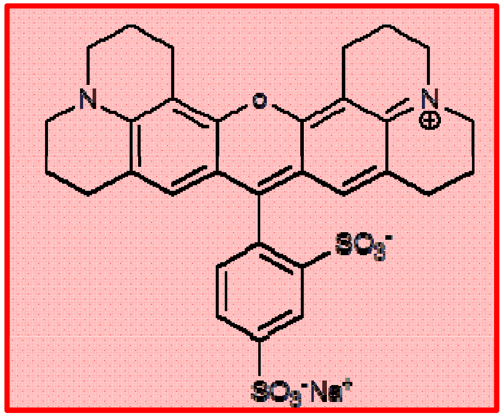


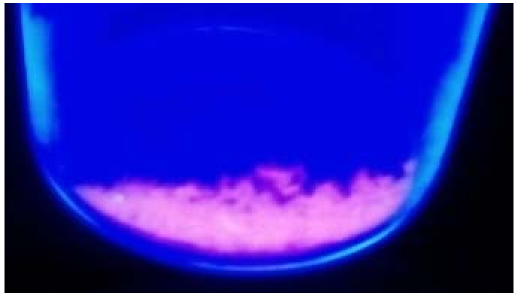


λ_{abs} = 528 nm λ_{fl} = 543 nm

Φ_{fl} 0.30

Rhodamine 640





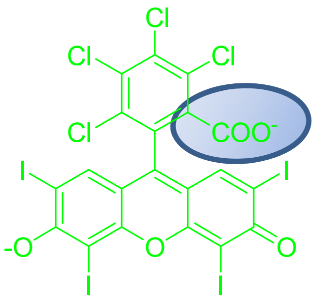
λ_{abs} = 570 nm λ_{fl} = 590 nm

Φ_{fl} 0.52

Universidad del País Vasco Euskal Herriko Unibertsitatea

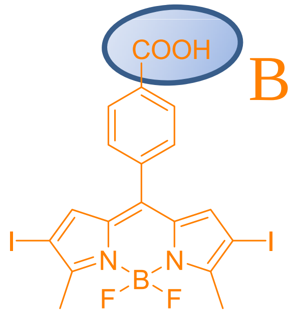
Working on the Shell: therapy

RB



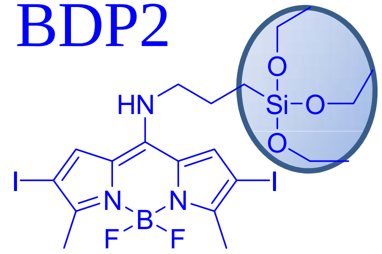
Rose Bengal

BDP1



BODIPY-Ph-COOH

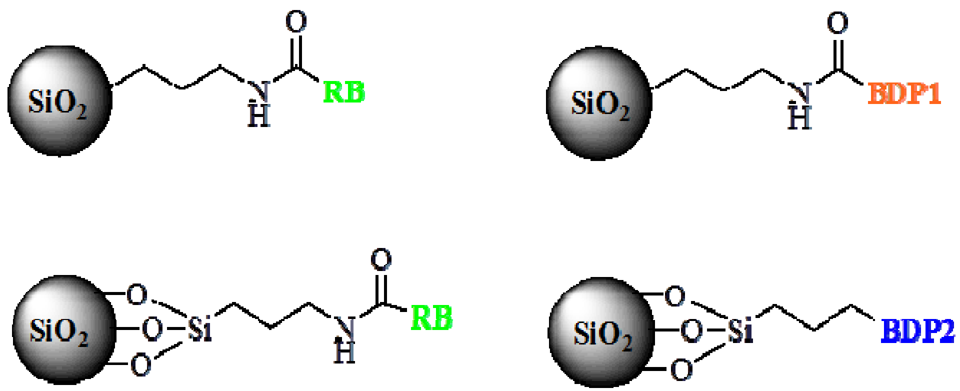
BDP2



BODIPY-Si(OEt)$_3$

➢**RB** and **BDP1** are grafted by Peptide coupling reaction $\longrightarrow$ **Amide** formation

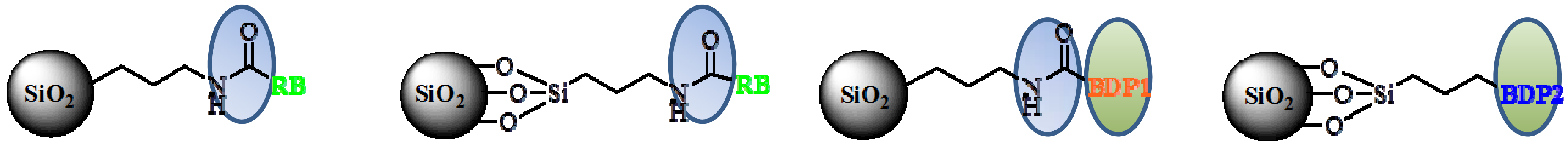
➢**BDP2** is grafted by direct polymerization of the triethoxysilyl derivative



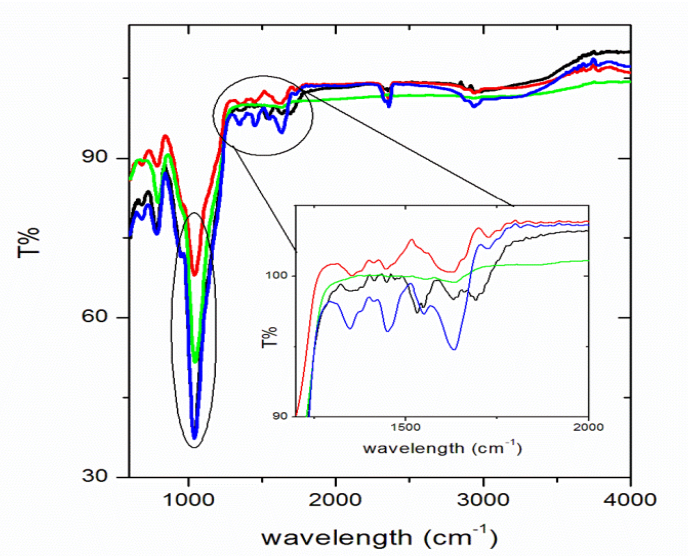
(NH_2-grafting)

(OH-grafting)

Grafting Characterization



IR



The typical IR peaks: 1600 cm^{-1} and 1550 cm^{-1}

XPS

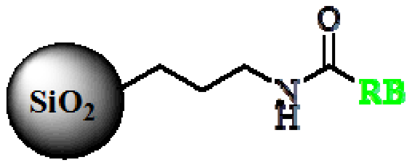
Sample	% At Concentration						
	C	O	N	Si	Cl	F	I
NP	15	52	4.0	26	2.5	-	-
NP-BDP1	22	44	7	22		2.3	2.2
NP-BPD2	23	42	5.1	24	2.4	2.2	1.6

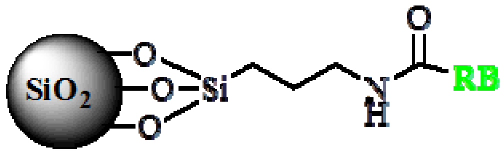
New F and I atoms indicative of BDP molecular structure

Estimation of Grafted PS

Sample	method B (mol/gr)
NP-RB1	3.3×10^{-6}
NP-RB2	4×10^{-6}
NP-BDP1	1.8×10^{-6}
NP-BDP2	5.2×10^{-6}

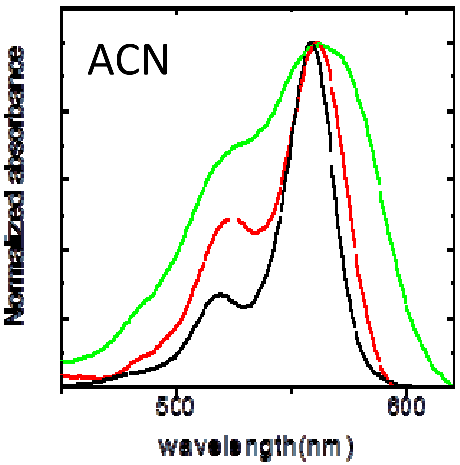
Grafting of Rose Bengal

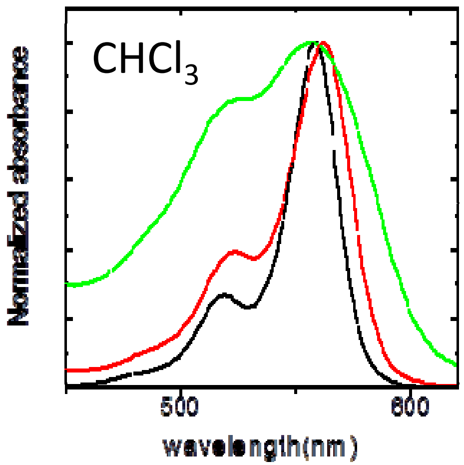




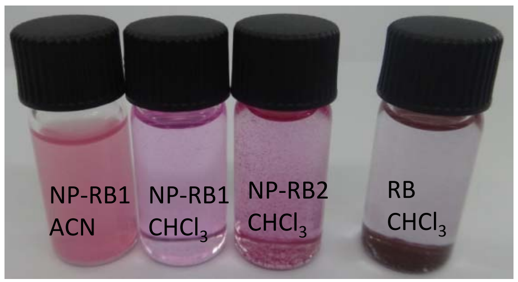
NP-RB1
(NH_2-grafting)

NP-RB2
(OH-grafting)





- Prominent shoulder at 518 nm
  - RB H-type aggregation
  - Interparticle aglomeration
- Less polar solvents
  - NP-RB1 the aggregation is decreased
  - NP-RB2 the aglomerations is still obvious (more OH)



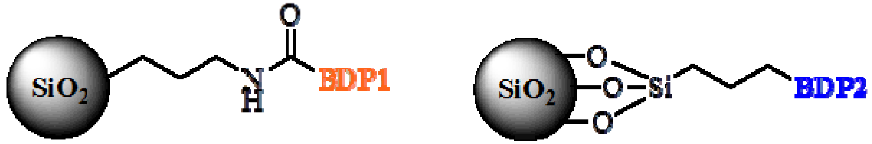
$\Phi_{\Delta CN}$ = 0.10
Φ_{CHCl3}= 0.07

NP-RB2

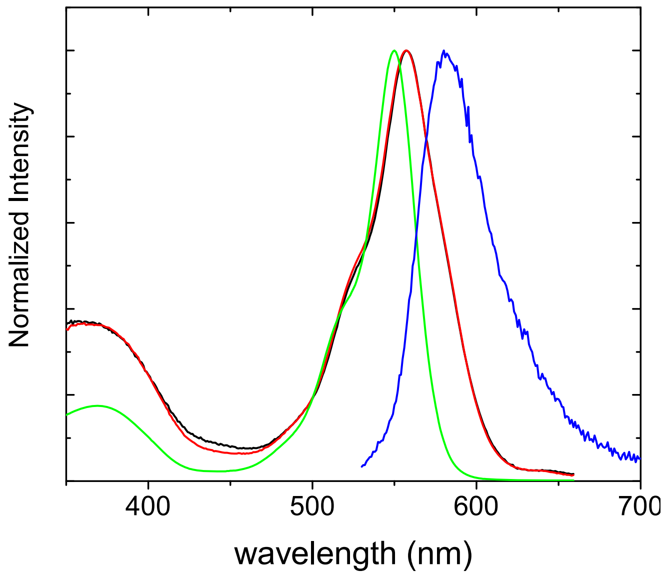
$\Phi_{\Delta CN}$ = 0.14
Φ_{CHCl3}= 0.27

NP-RB1

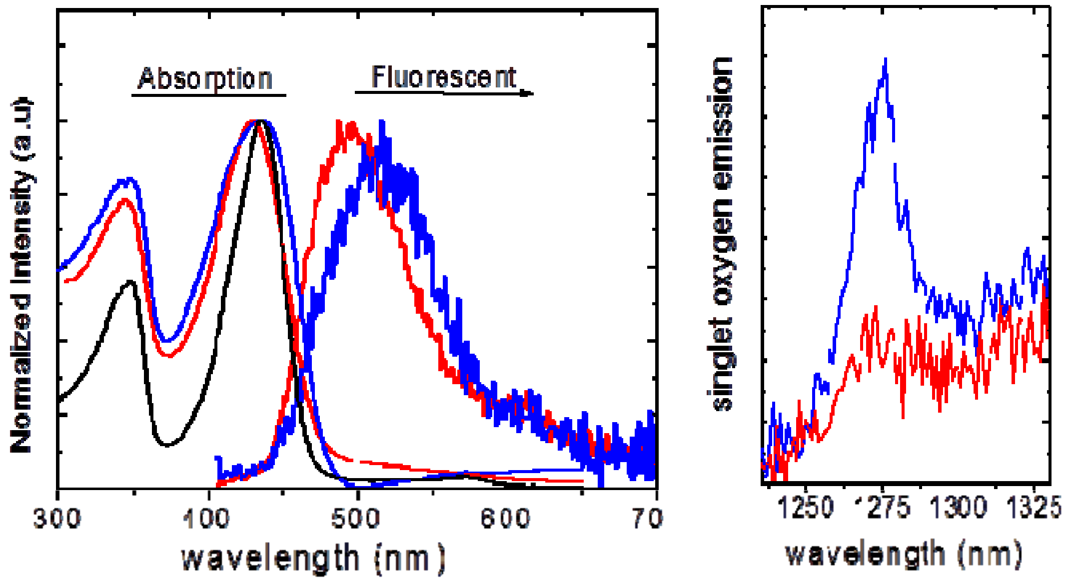
Grafting of new BODIPY



BDP1



BDP2



$\Phi_{\Delta CN} = 0.33$
$\Phi_{CHCl3} = 0.37$

BDP1

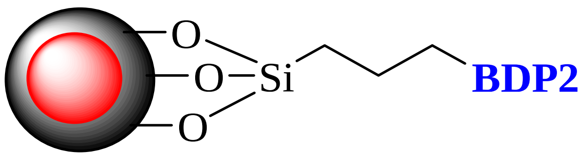
$\Phi_{\Delta CN} = 0.36$
$\Phi_{CHCl3} = 0.38$

BDP2

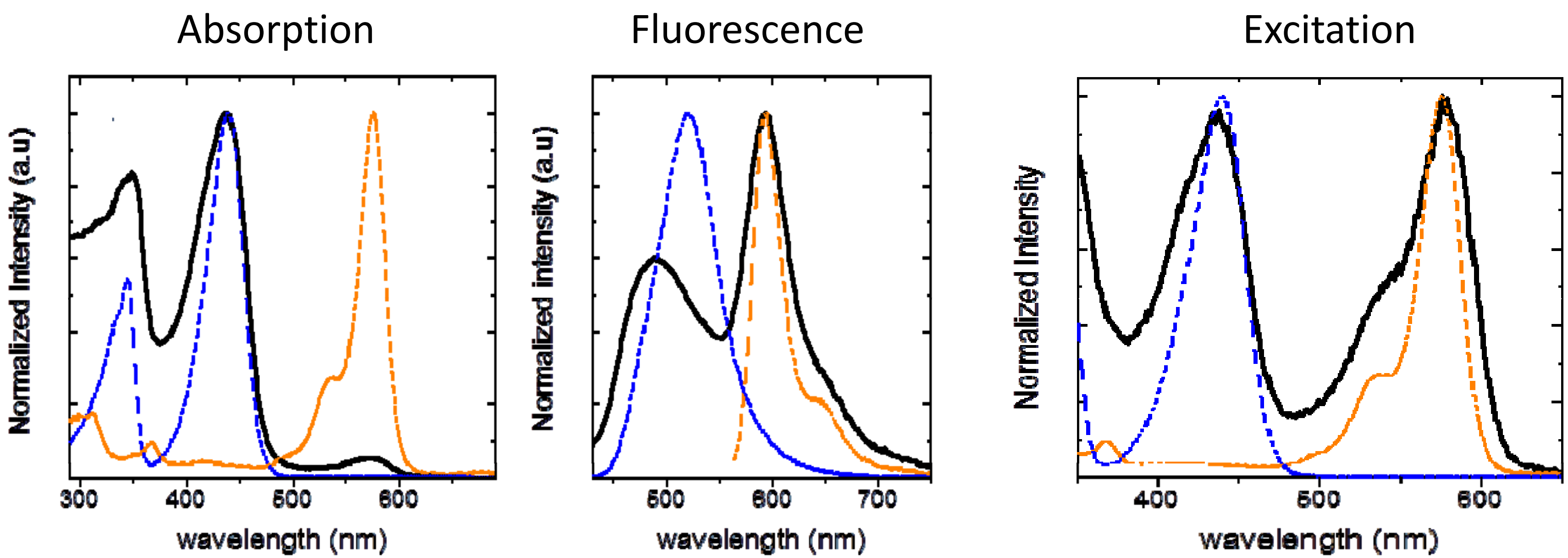
- No evidence of dye aggregation
- Stable suspension in both solvents for NH and OH grafting

Working on Core-Shell

Different excitation wavelength for imaging and PDT: NP/R640-BPD2



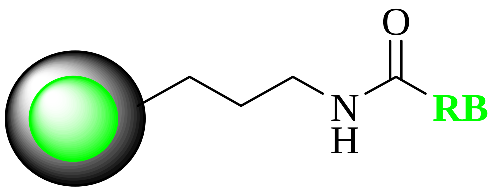
NP/R640-BDP2



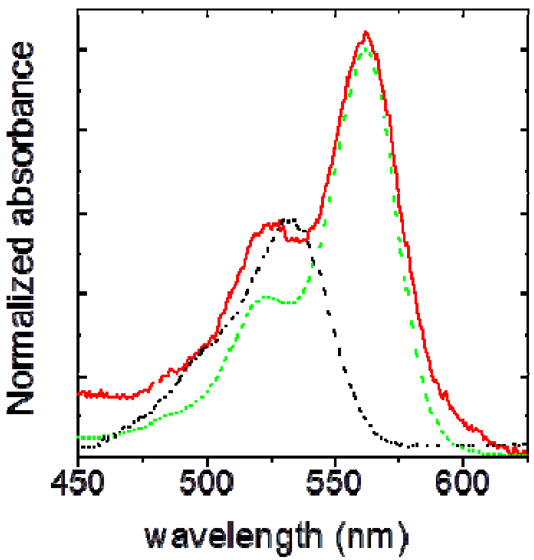
FRET process between dyes → Negligible Singlet Oxygen

Working on Core-Shell

Same excitation wavelength for imaging and PDT: R640-BDP1 and R6G-RB1



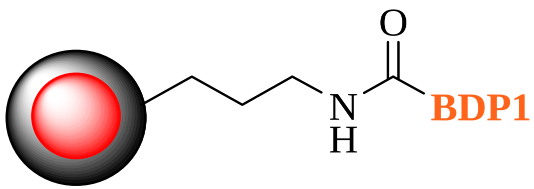
NP/R6G-RB1



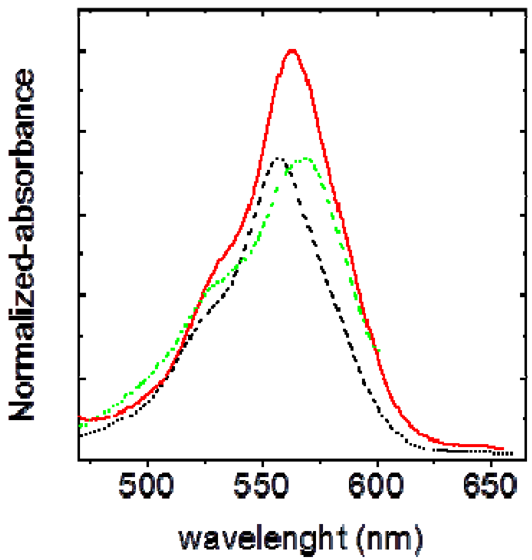
λ_{abs} = 561 nm, λ_{fl} 580 nm

Φ_{Δ} 0.25

Φ_{fl} 0.20



NP/R640-BDP1

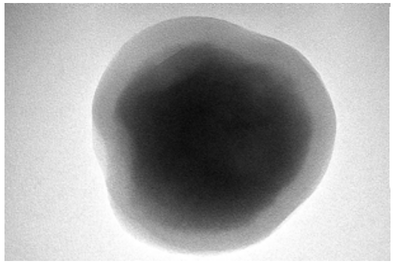


λ_{abs} = 564 nm λ_{fl} = 583 nm

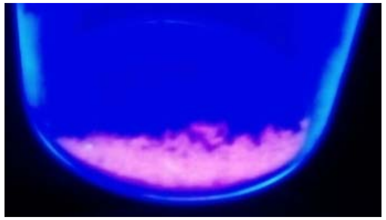
Φ_{Δ} 0.16

Φ_{fl} 0.10

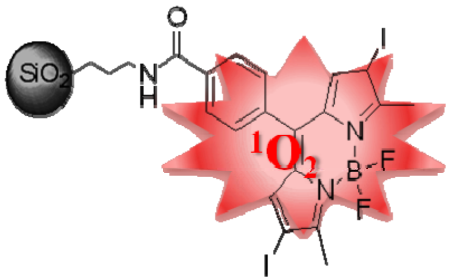
Conclusions



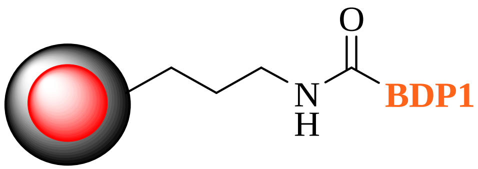
➢ Spherical core-shell silica NPs of 50 nm with amine groups at the external are synthesized



➢ NP for biomaging are obtained by the encapsulation of fluorescent rhodamines in the core (Φfl ≥ 0.3), which allowed their tracking by fluorescence microscopy



➢ NP with good singlet oxygen production for the implementation in Photodynamic treatments are obtained by grafting PS at the external surface. BODIPYs as photosensitizers may offer a good alternative to commercial RB.



➢ NP with dual functionality are obtained by the proper choice of the dyes with opposite photophysical properties.

➢ **Undergoing work:** improve the stability of the NP suspensions in water for *in vitro* phototoxicity experiments (**poster 21**)

Awcknolegements

Collaborations:

Dr. Nerea Epelde-Elezcano

Ruth Prieto-Montero

Prof. Iñigo López-Arbeloa,

Prof. Ross Brown

Prof. Sylvie Lacombe

Alejandro Prieto-Castañeda

Prof. María J. Ortiz

Prof. Eduardo Peña-Cabrera

José L. Belmonte-Vázquez

Funding:

GOBIERNO DE ESPAÑA
MINISTERIO DE CIENCIA E INNOVACIÓN

EUSKO JAURLARITZA
GOBIERNO VASCO

eman ta zabal zazu
Universidad del País Vasco
Euskal Herriko Unibertsitatea

Awcknolegements

Collaborations:

Dr. Nerea Epelde-Elezcano

Ruth Prieto-Montero

Prof. Iñigo López-Arbeloa,

Prof. Ross Brown

Prof. Sylvie Lacombe

Alejandro Prieto-Castañeda

Prof. María J. Ortiz

Prof. Eduardo Peña-Cabrera

José L. Belmonte-Vázquez

THANK YOU FOR YOUR ATTENTION

Funding:

GOBIERNO DE ESPAÑA MINISTERIO DE CIENCIA E INNOVACIÓN

EUSKO JAURLARITZA GOBIERNO VASCO

eman ta zabal zazu

Universidad del País Vasco Euskal Herriko Unibertsitatea

Tuning of the photophysical properties of core-shell silica nanoparticles for bio-imaging and photodynamic therapy

Virginia Martínez

NanoSpain Conf 2017
March 07-10, 2017 – San Sebastian (Spain)
THE LEADING N&N EVENT IN SPAIN

eman ta zabal zazu
UPV EHU
Molecular Spectroscopy Laboratory