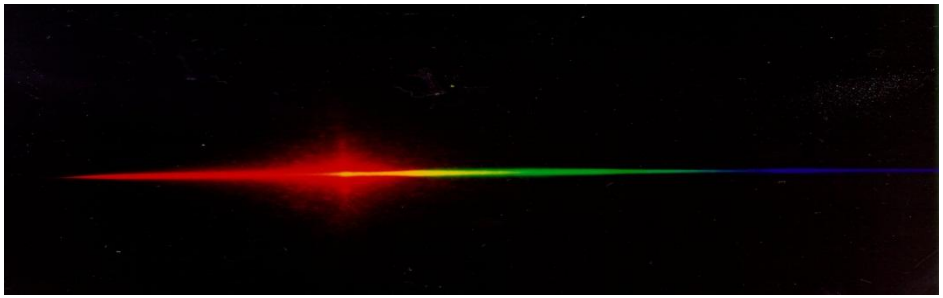
Challenges and Opportunities at the Interface of Nanotechnology and Biomedicine

P.N.Prasad



"Lighting the Way to Technology through Innovation"

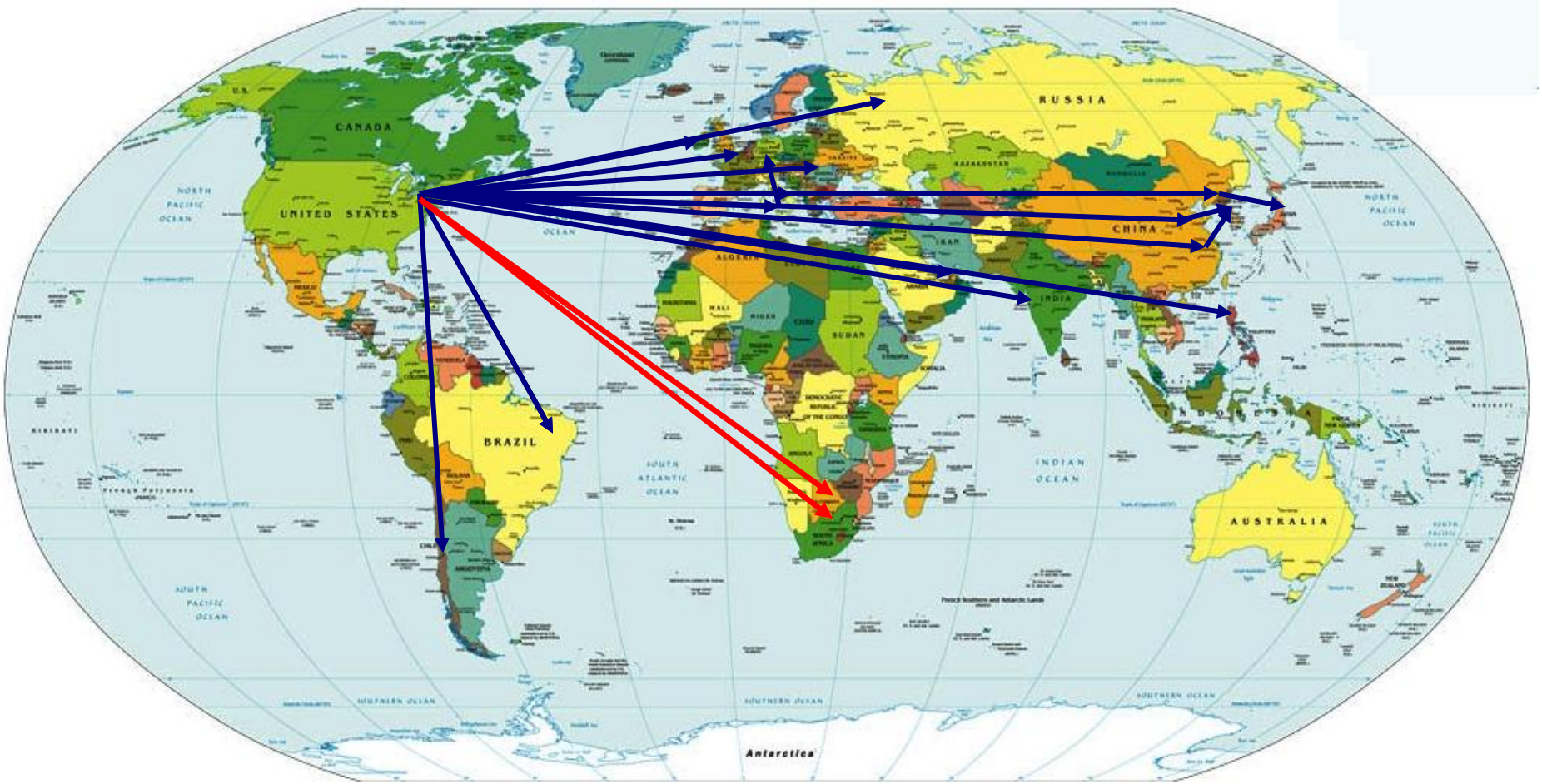
The Institute for Lasers, Photonics and Biophotonics

- Multidisciplinary Frontier Research in Lasers, Photonics and Biophotonics
- Extensive Research Facility ($26 million)
- Education and Training Funded by NSF
- Industrial Collaboration : Co-development, Industrial training, advanced testing
- Technology Transfer : 7 spin off companies *(LPT, ACIS, Hybrid Technologies, NanoBiotix, Nanoaxis, Hangzhou Mingyue Laser Optoelectronics Co and Solexant Inc.)*
- International collaboration : Joint research, Student exchange, Joint workshop

Major Thrust Areas:

- Advanced Nanomaterials with multifunctionalization
- Metamaterials
- Nanophotonics, Nanomagnetics, Nanomedicine
- Nonlinear optics, Multi-photon processes
- Solar energy, portable energy generation
- Multimodal diagnostics and imaging, Light-activated therapy

ILPB Global Collaboration Network



Germany
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Italy
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India
Philippines

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Sweden
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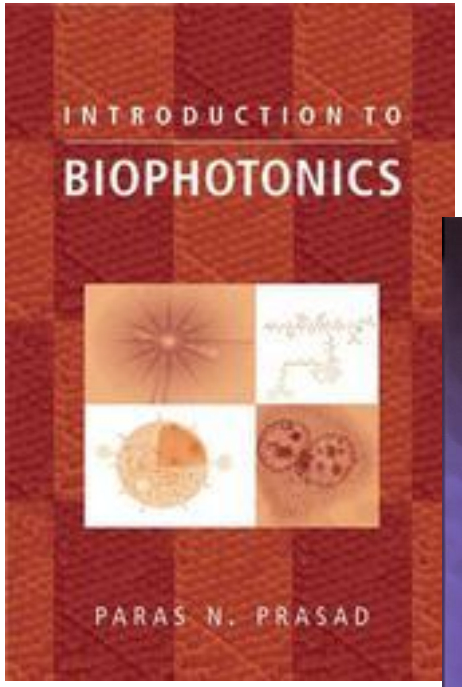
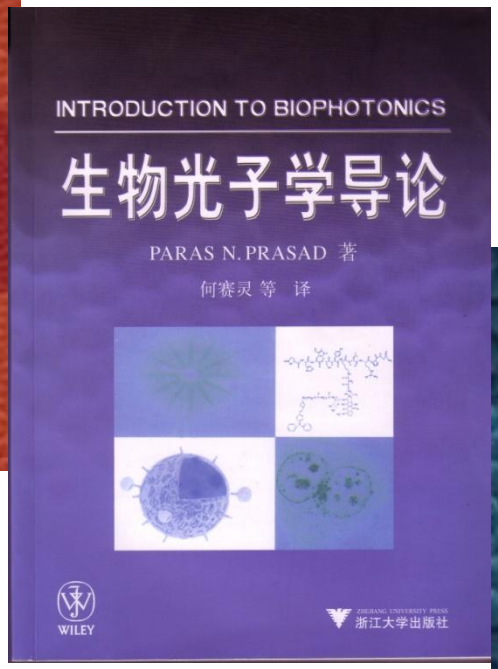

INTRODUCTION TO
BIOPHOTONICS
PARAS N. PRASAD


INTRODUCTION TO BIOPHOTONICS
生物光子学导论
PARAS N. PRASAD 著
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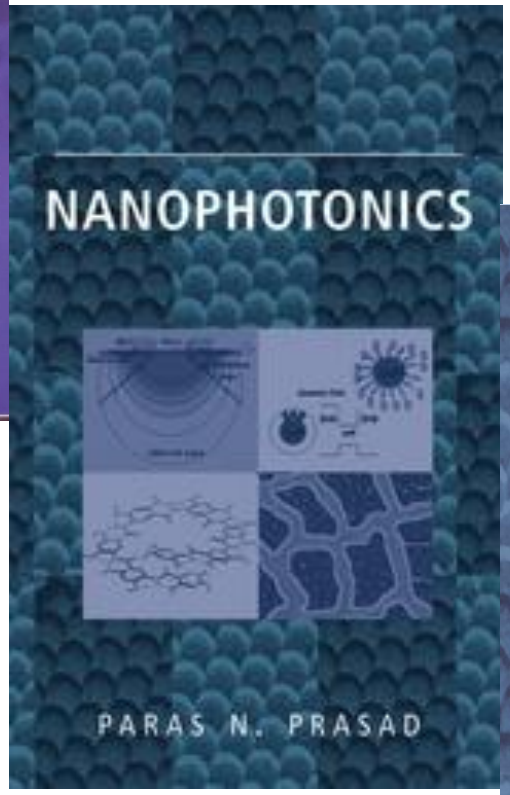
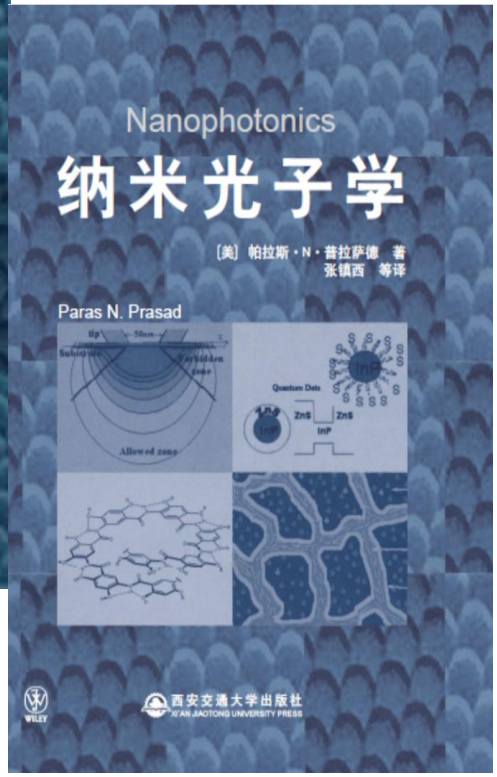

NANOPHOTONICS
PARAS N. PRASAD


Nanophotonics
纳米光子学
[美] 帕拉斯·N·普拉萨德 著
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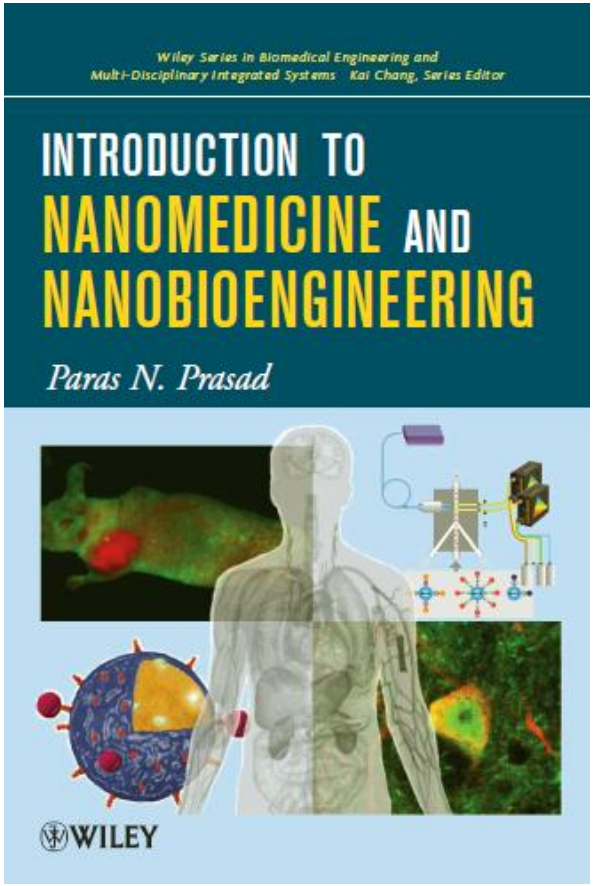
CONTENTS

1. INTRODUCTION
2. THE HUMAN BODY
3. NANOCARRIERS
4. NANOCHEMISTRY OF NANOCARRIERS
5. MULTIFUNCTIONALITIES FOR DIAGNOSTICS AND THERAPY
6. CROSSING THE BIOLOGICAL BARRIERS
7. BIOTARGETING
8. MULTIMODAL BIOMEDICAL IMAGING
9. BIOSENSING
10. HIGH THROUGHPUT MULTIPLEXED DIAGNOSTICS
11. NANOPHARMACOTHERAPY
12. THE HUMAN CIRCULATORY SYSTEM AND THERANOSTICS
13. NANOTECHNOLOGY FOR CANCER
14. GENE THERAPY
15. NANOTECHNOLOGY FOR INFECTIOUS DISEASES
16. REJUVENATION THERAPY
17. STEM CELL BIOTECHNOLOGY
18. TISSUE ENGINEERING
19. NANODERMATOLOGY AND NANOCOSMETICS
20. NANODENTISTRY
21. NANOTOXICITY

"…The first comprehensive and authoritative introduction to Nanomedicine and Nanobioengineering…"

Each chapter ends with highlights and exercises

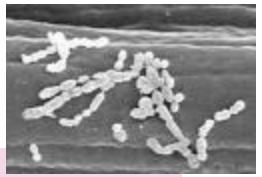


Current and Future Health Care Challenges

Aging

Obesity

Genetic Disorders

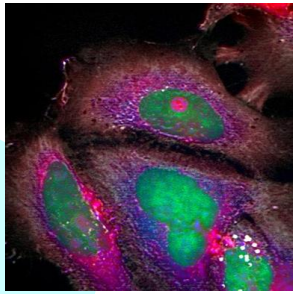


Infectious Diseases

Cancer

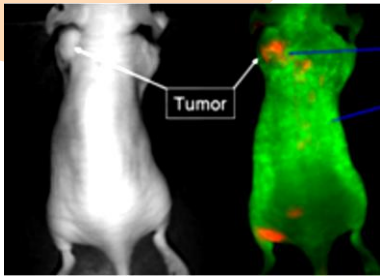
Addictions

Nanomedicine – New Era in Personalized Medicine

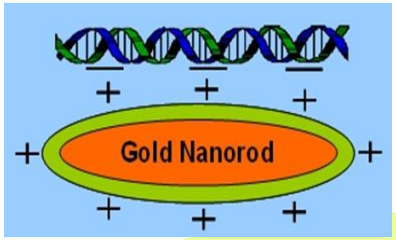


In Vitro **Diagnostics**

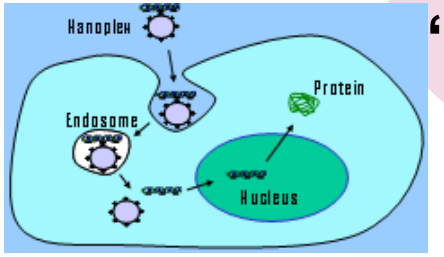
In Vivo **Diagnostics**



NANOMEDICINE Applications



Nanotherapeutics drug/gene delivery



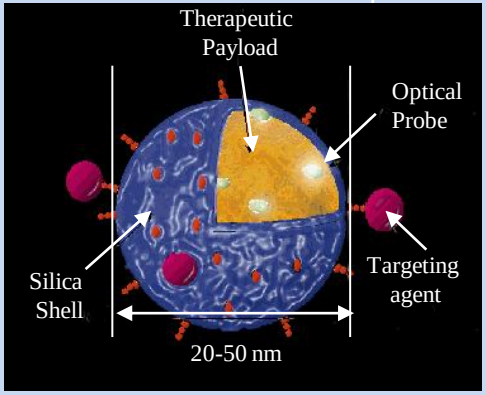
Theranostics: ‘see, treat and see’

NANOMEDICINE

Yesterday's imagination

James Cameron's
"Fantastic Voyage"
(1966)

Today's reality



ILPB Nanoclinics

Patented in 2003, licensed to Nanobiotix (Paris) in 2004

Tomorrow's patient care

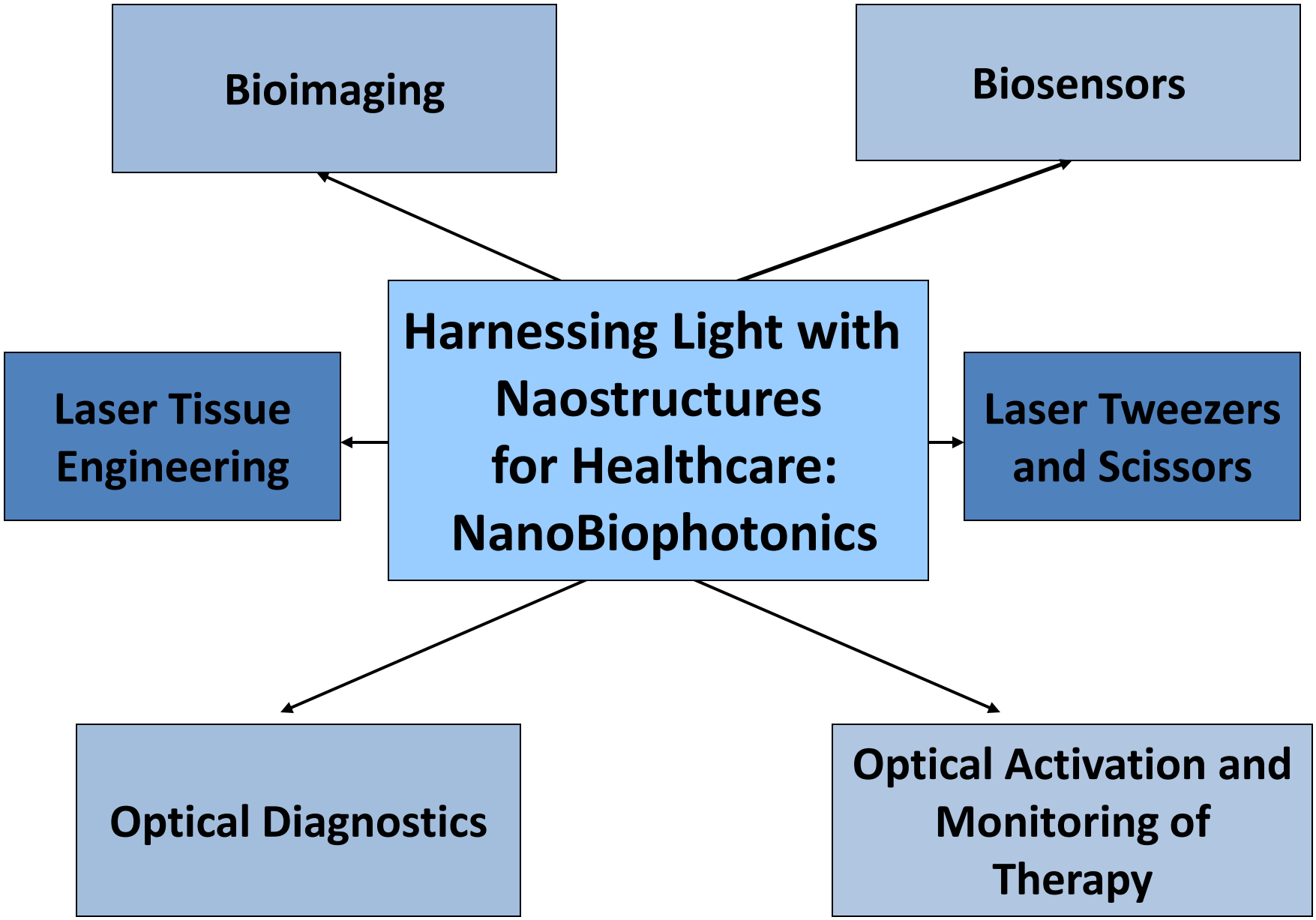
nanoXRay

nanobiotix
Biorevolution_Evolution

Paris, (France)
http://www.nanobiotix.com/

Clinical trial in 2011

Biophotonics and Nanomedicine



BIOPHOTONICS AND NANOMEDICINE

An Interdisciplinary Field

Basic Sciences

Chemistry
Multiscale modeling guided synthesis of Functional Materials and nanoscale building blocks;
Surface modification

Physics
Manipulation of optical , electronic ,magnetic and thermal properties at nanoscale;
Multifunctionality

Biology
Understanding of Biological Processes
Biocompatibility;
Targeting;
Bioelimination

Engineering

Micro/nano Integration

Hardware & Software Control

Biotechnology **Bioinformatics**

Medicine

Diagnostics
In-vitro and *in-vivo;*
Microarray technology

Pharmacology
Disease Modeling;
Pharmacokinetics and Pharmacodynamics

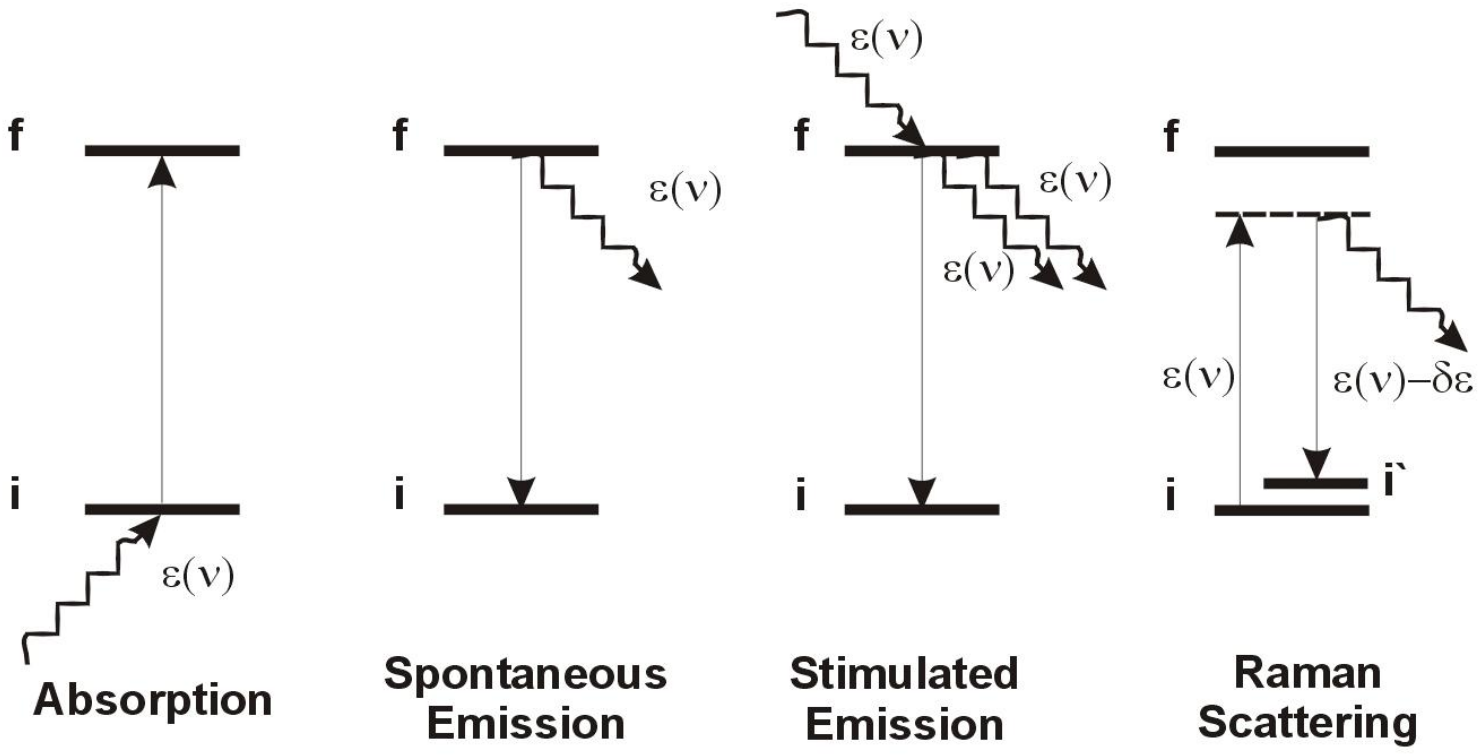
Therapy
Chemotherapy;
Photodynamic Therapy;
Gene Therapy

Toxicity
Chemical toxicity;
Cellular, tissue and organ toxicities;
Immune response

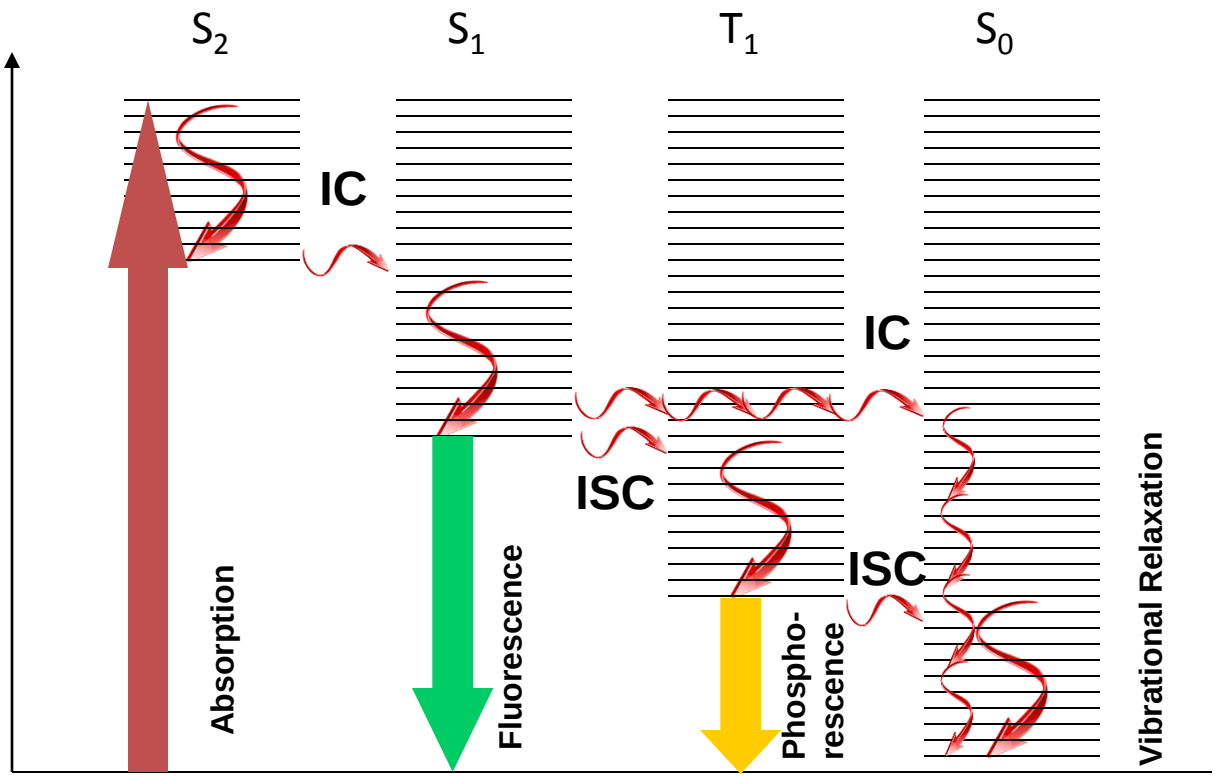
Nanotheranostics
Combined Diagnostics and Therapy;
See, treat and see

LIGHT – MATTER INTERACTIONS FOR BIOPHOTONICS

Linear Light-Matter Interactions

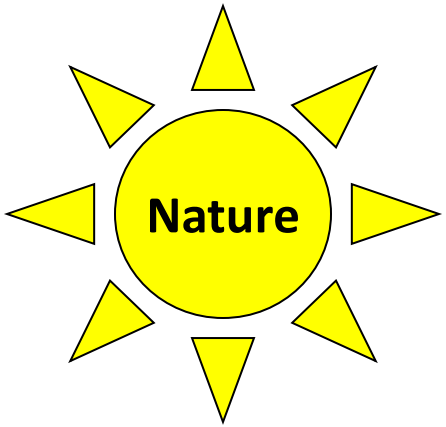


The Jablonski Diagram Describing Possible Fates of Excitation

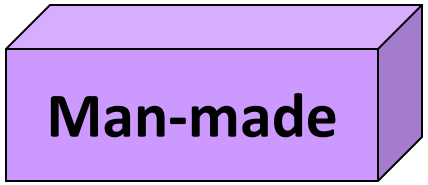


Non-radiative Processes: Energy dissipation through vibrational relaxations

Light activation

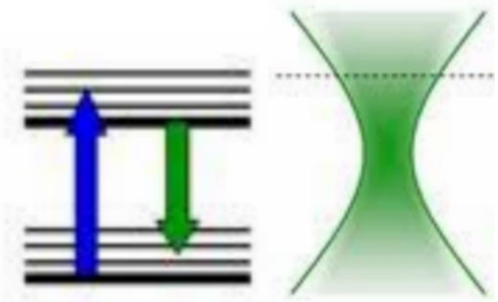


VS

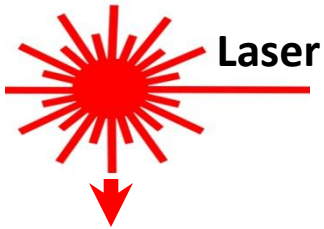


Incoherent

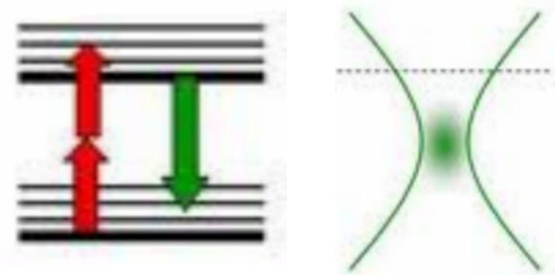
One-photon processes



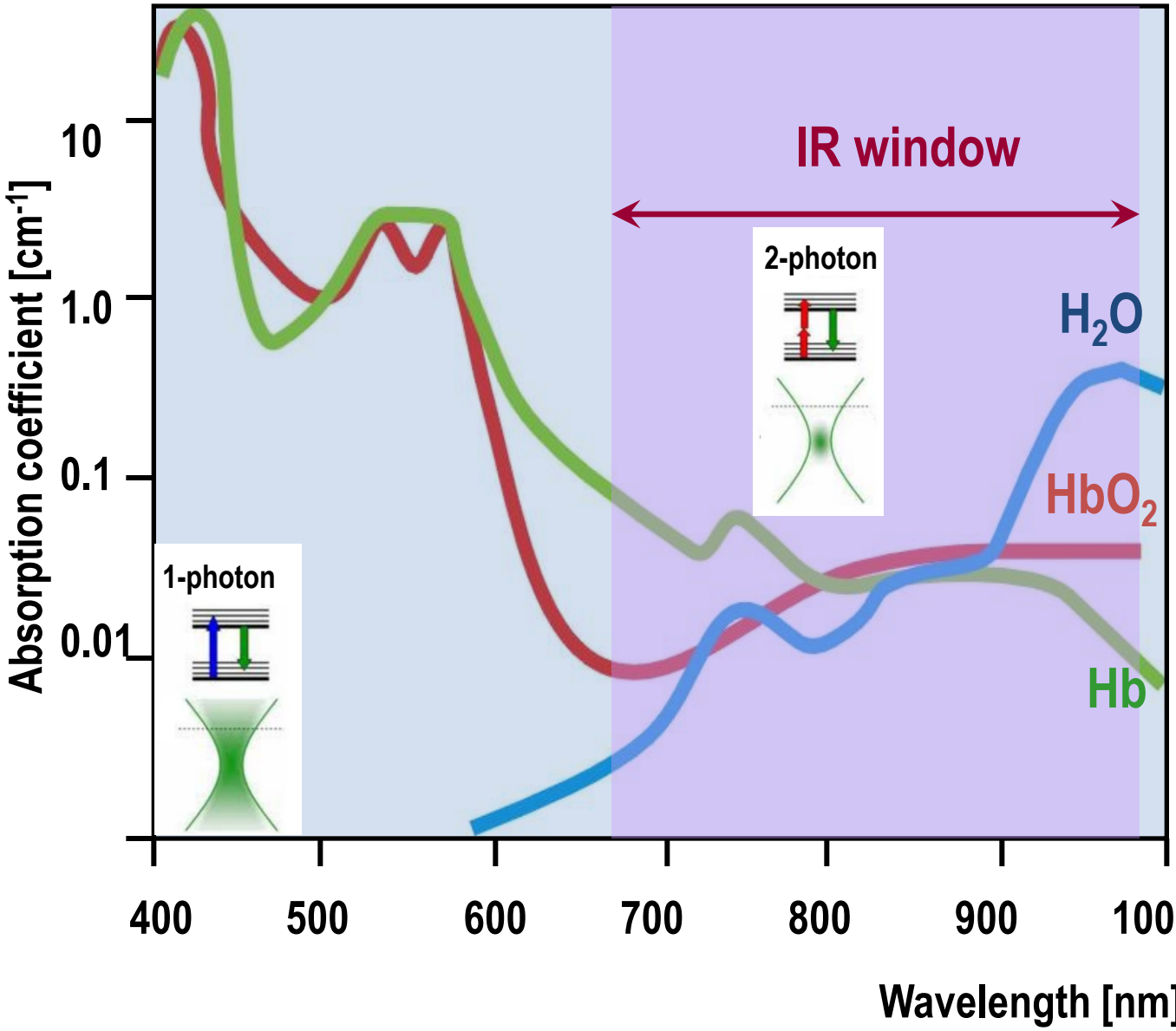
Coherent, intense, ultrashort pulses



Multi-photon processes

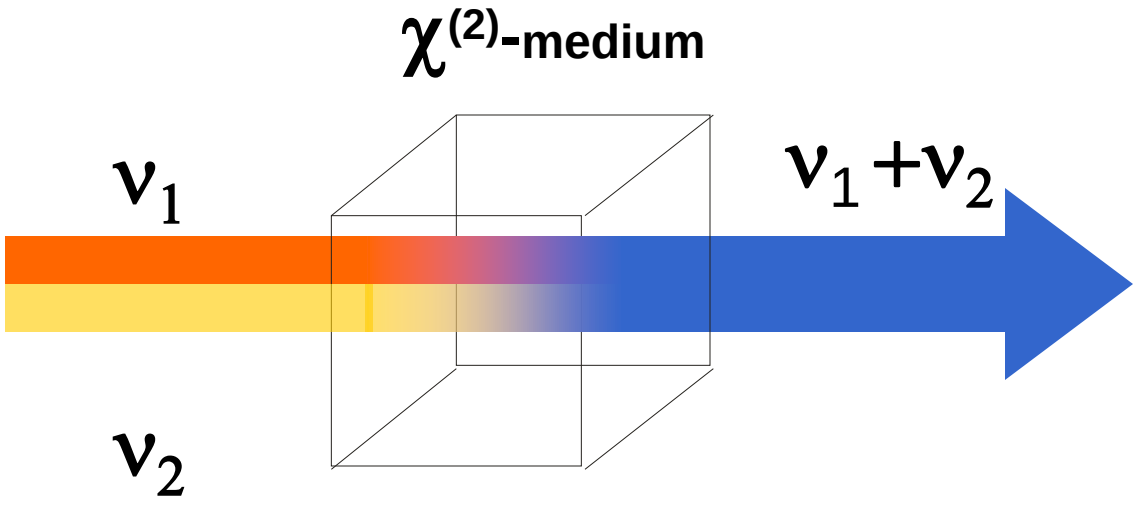


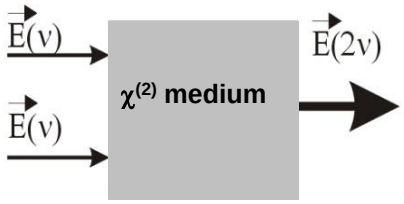
Two-Photon Versus One-Photon Bioimaging



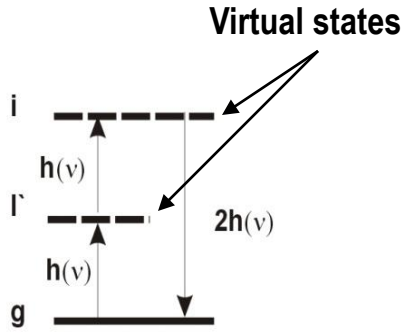
- Low Autofluorescence
- Low Photodamage
- High Tissue Penetration
- 3-D Imaging
- Localized Excitation and Imaging

Frequency Conversion

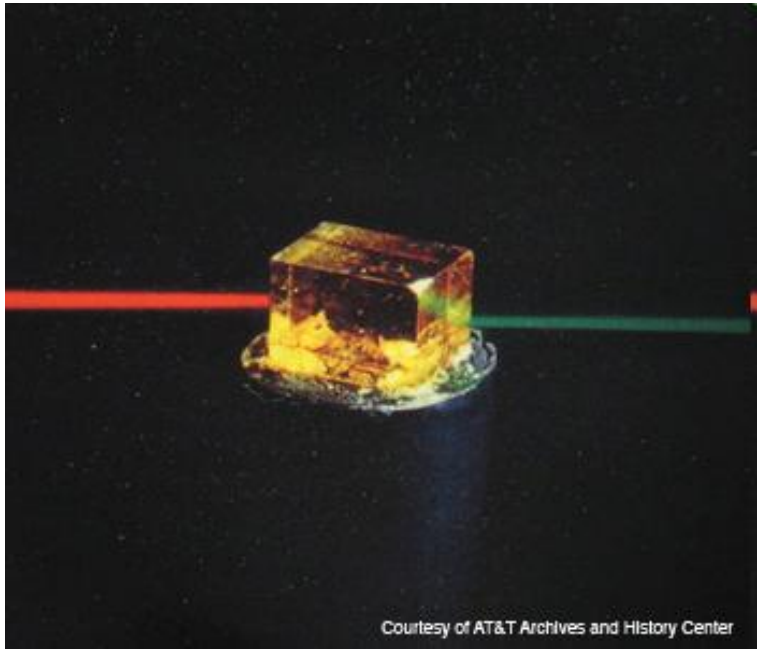




The SHG process



Energy level description



Probes symmetry breaking (cell membrane)

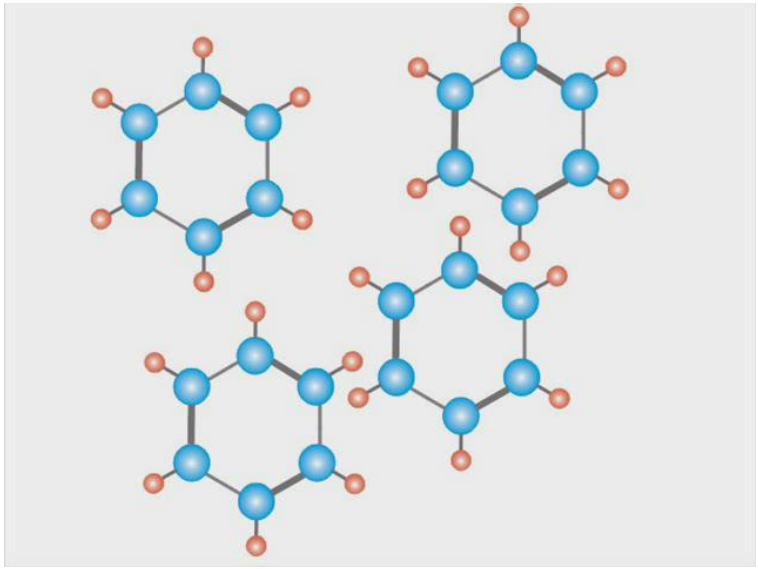
Coherent Anti-Stokes Raman Scattering

$\omega_{vib}=\omega_{pump}-\omega_{Stokes}$

Excitation

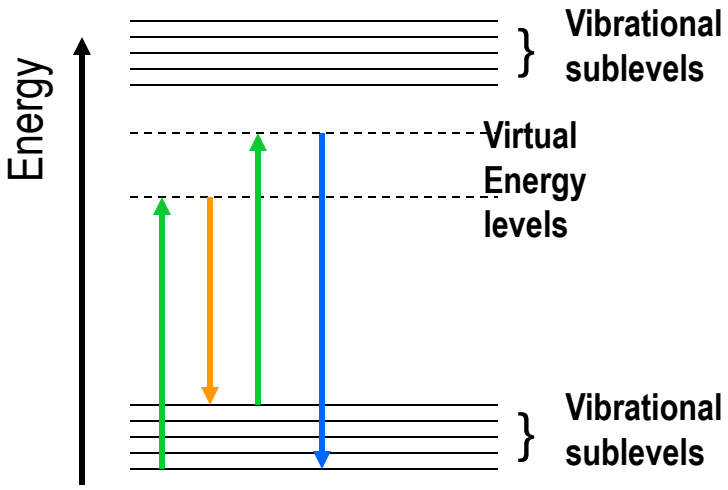
ω_{pum}

ω_{Stokes}

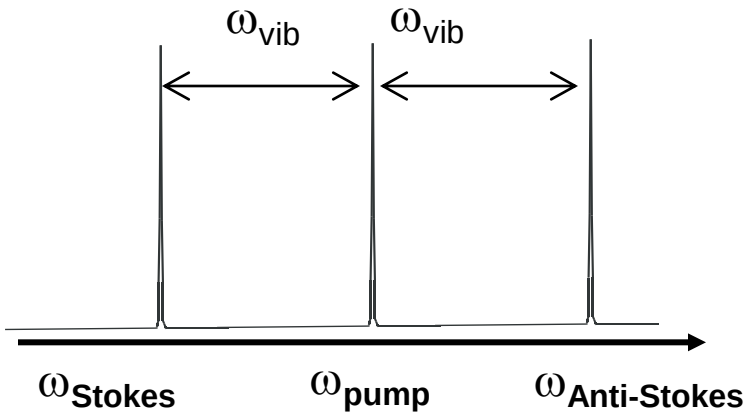


CARS

$\omega_{Anti\text{-}Stokes}$



$\omega_{Anti\text{-}Stokes}=2\omega_{pump}-\omega_{Stokes}$



Spontaneous Raman & CARS

Raman

- Low intensity of signal distributed in 4π spatial angle; therefore not efficient for imaging
- Raman Intensity is linearly depends on molecular concentration; therefore microspectrometry useful for quantitive characterization of local concentration of biomolecules

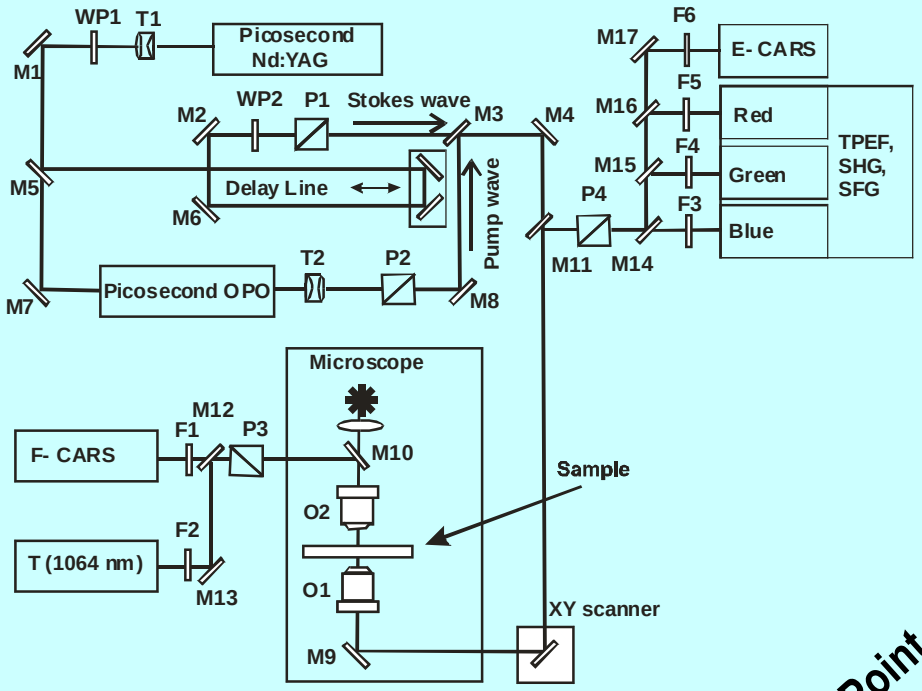
CARS

- High intensity coherent and directional process with accumulation of signal; therefore suitable for imaging
- Non-linear intesity dependence provides high 3D resolution

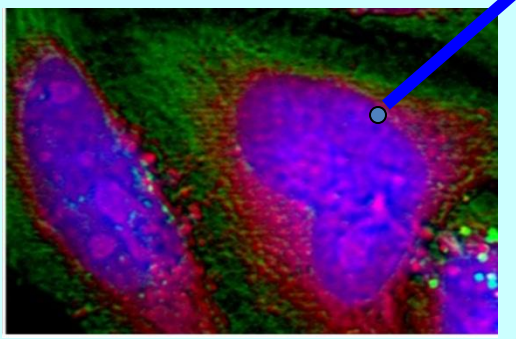
MULTIPLEXED BIOPHOTONICS IMAGING PLATFORM

ILPB Multiplex Biophotonics Platform

Multimodal Nonlinear Imaging Setup

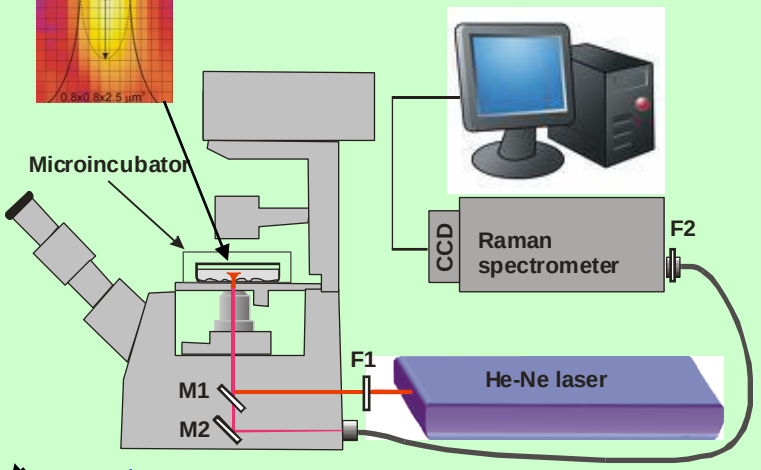


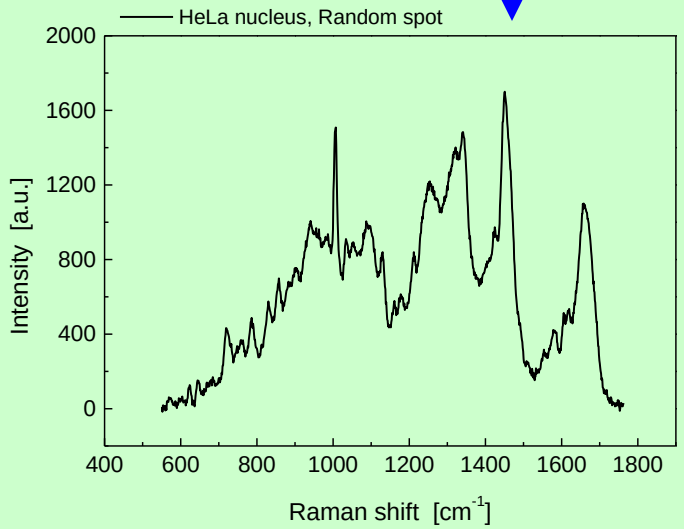
CARS,
2-photon,
SHG,
SFG



Point of interest

Micro-Raman Setup

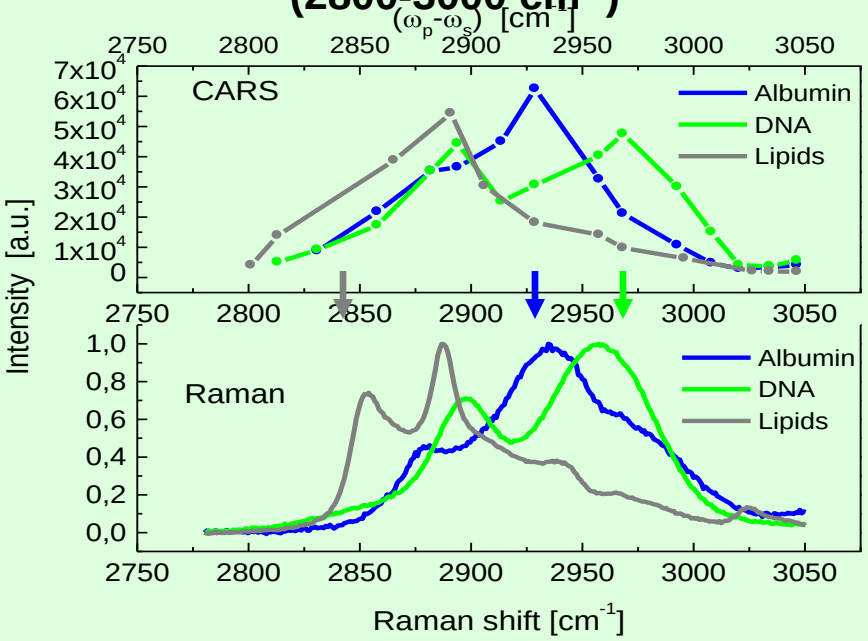




Multimodal CARS/TPEF Imaging

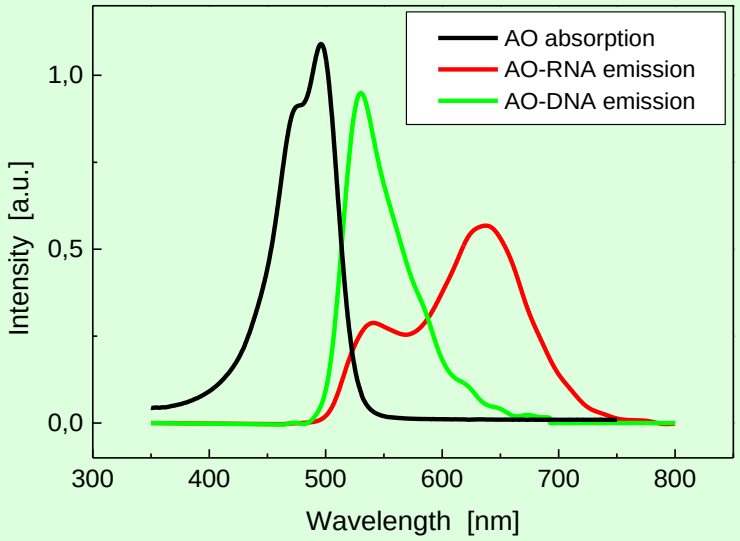
CARS Imaging is one of the most promising technique to observe cellular bio-molecular composition and to investigate its dynamics

Raman and CARS Spectroscopy of Proteins, DNA and Lipids (2800-3000 cm^{-1})

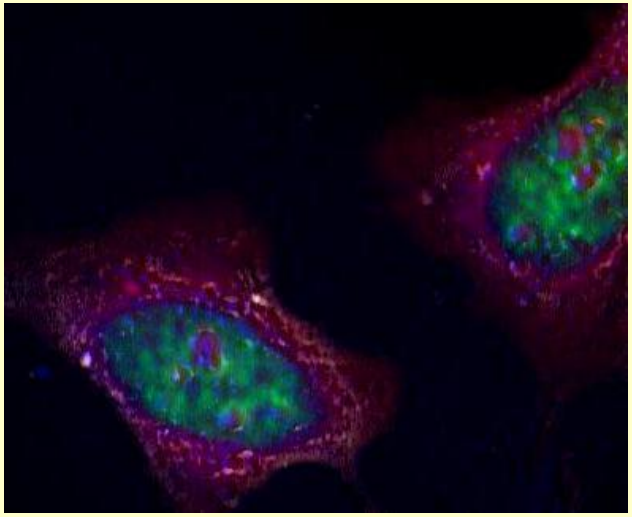


2840, 2930 and 2970 cm^{-1}

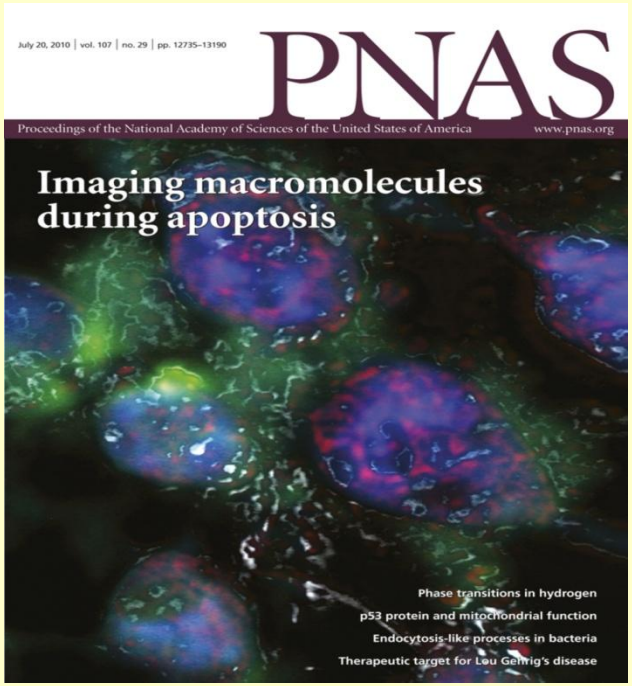
Two-photon excited fluorescence (TPEF) spectroscopy of DNA and RNA labeled with Acridine Orange



Structural Changes in apoptotic HeLa cells



30 min of treatment



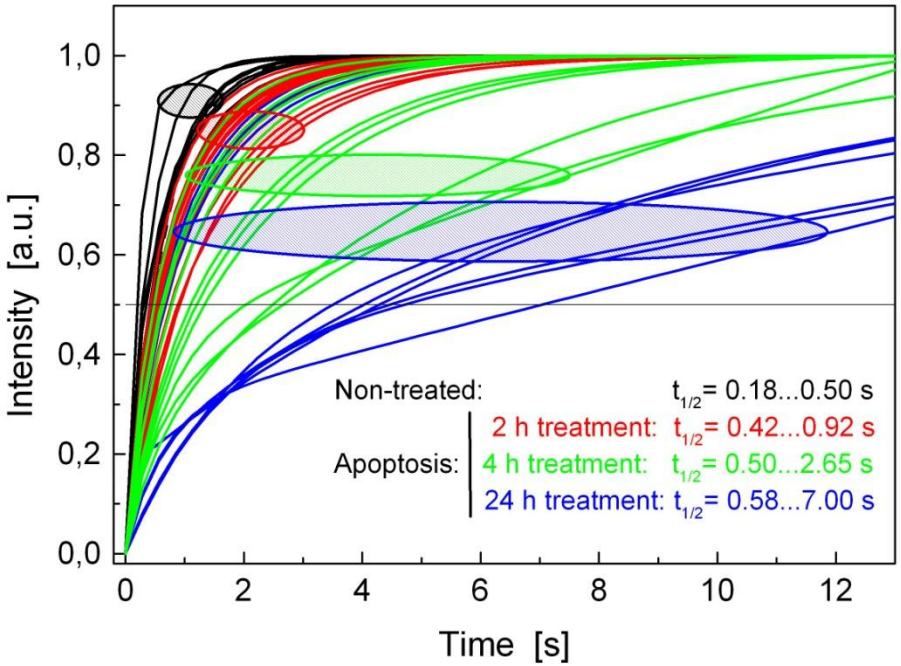
24 h of treatment

Cover page PNAS, 107, 29 (2010)

Multimodal CARS/TPEF imaging

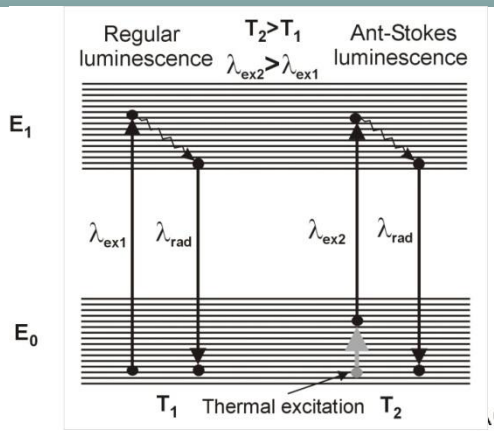
DNA/RNA/Proteins/Lipids

GFP Fluorescence Recovery after Photobleaching (FRAP)

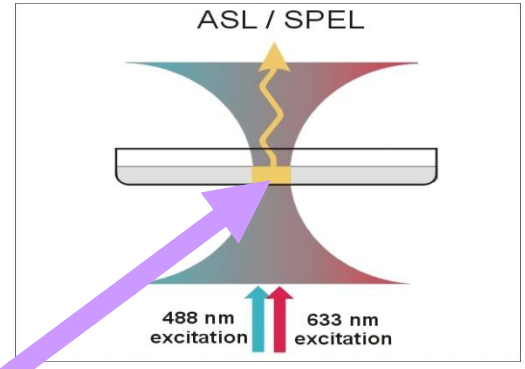


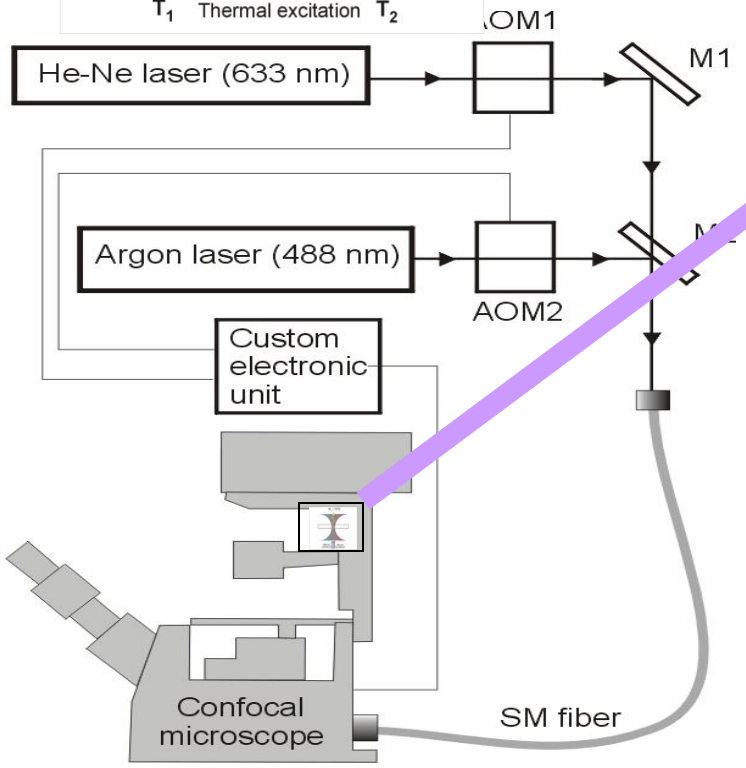
A. Pliss, A. Kuzmin, A. Kachynski and P. Prasad, Proceedings of National Academy of Sciences of the USA, 107(29) 12771 (2010).

Anti-Stokes Fluorescence Confocal Microscopy
(Temperature Mapping)

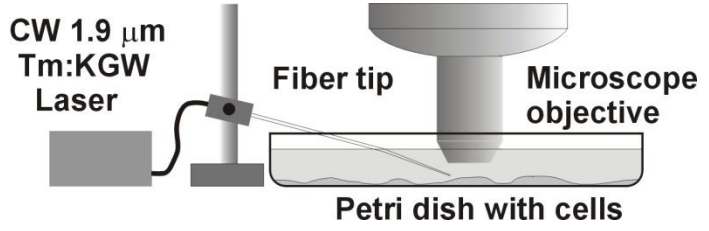


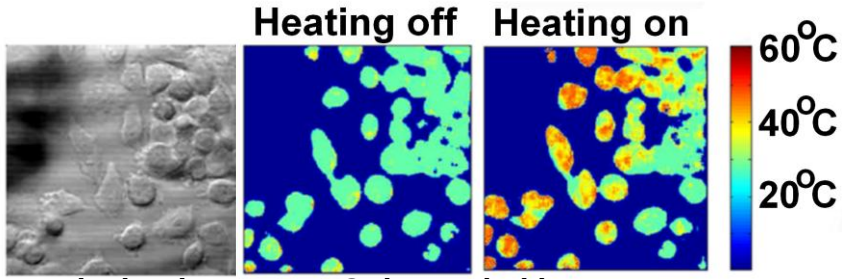
$$I \sim \exp\left(\frac{kT}{E_0}\right)$$





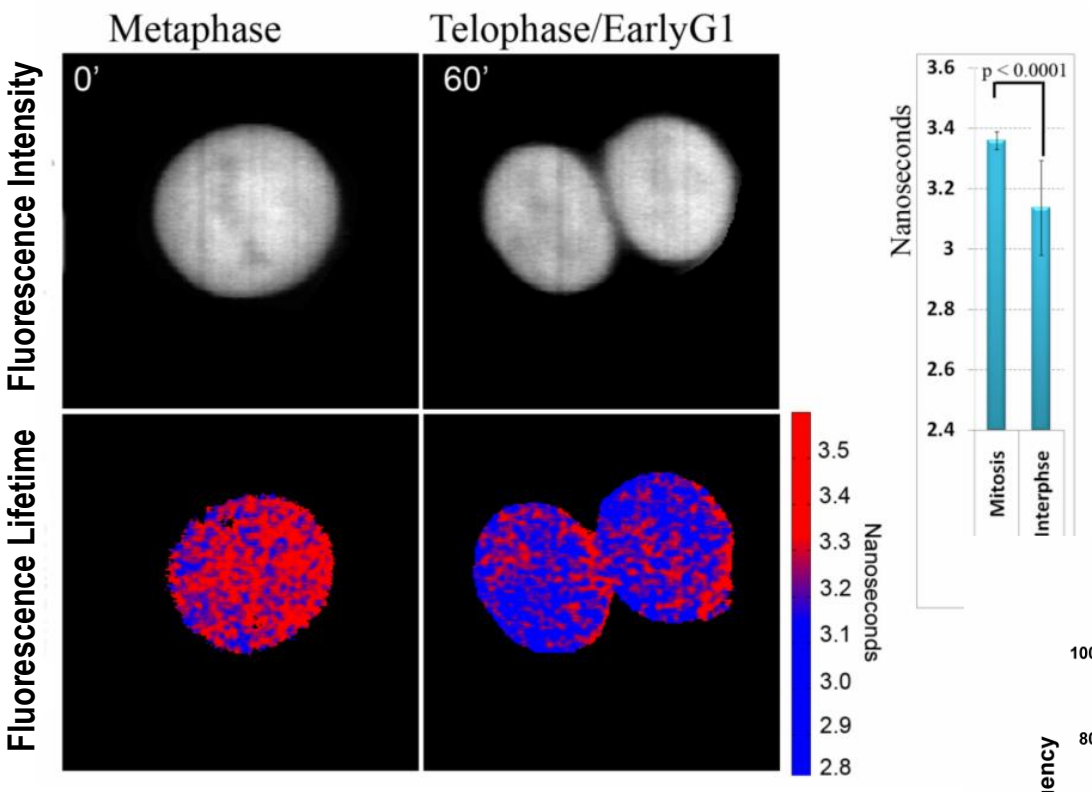
Experimental setup for heating live cells under microscope objective

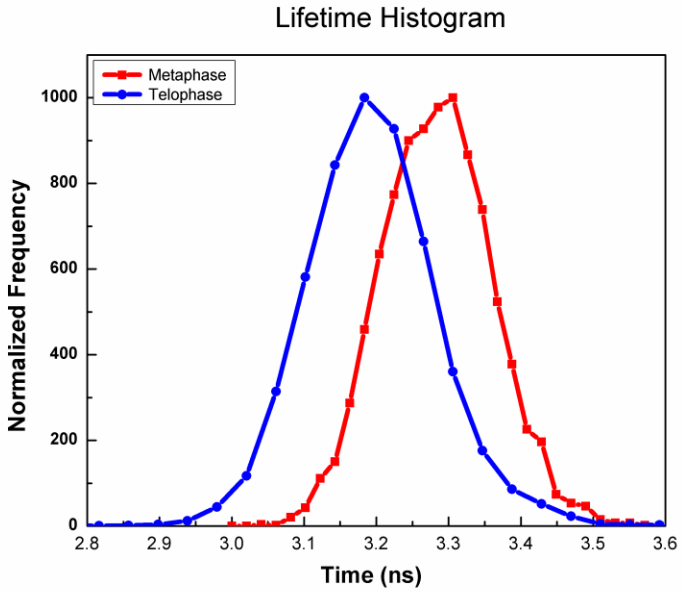




A.V.Kachynski, A.N.Kuzmin, H.Pudavar, and P.N.Prasad, Appl. Phys. Lett. 87 (2005) 023901

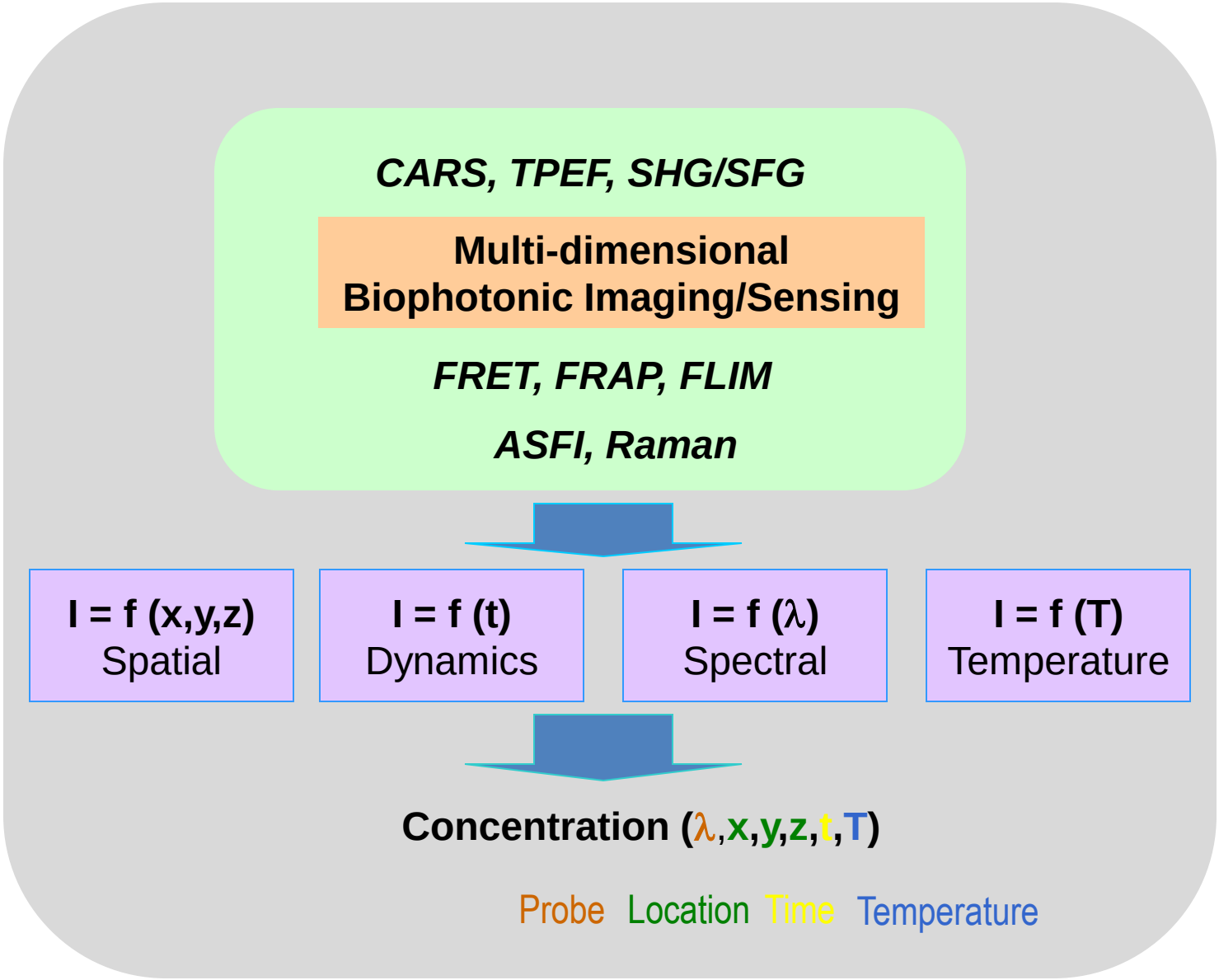
Fluorescence lifetime Imaging



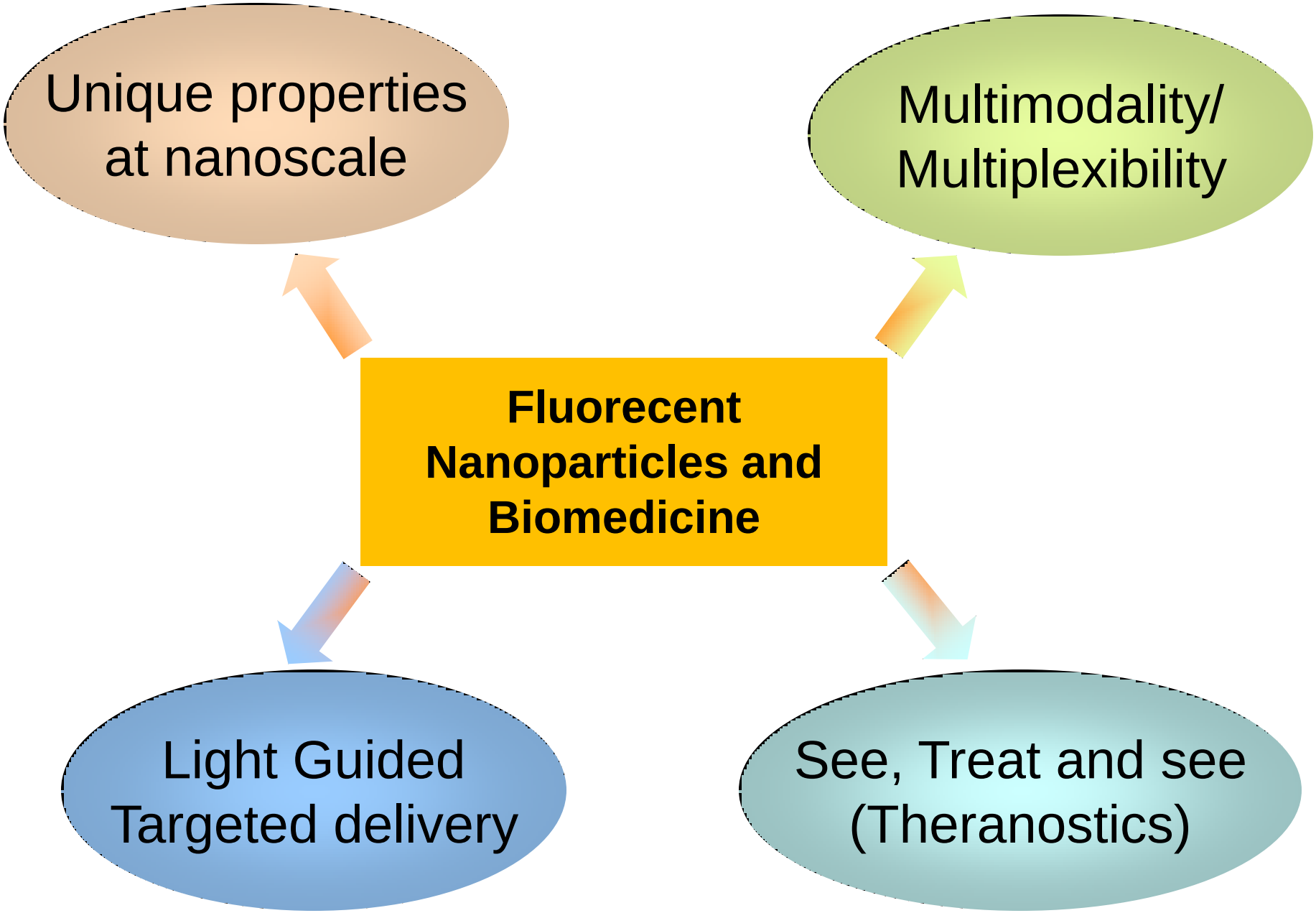


Fluorescence Lifetime of tdTomato Fluorescent Protein in HeLa cells shortens during cell division

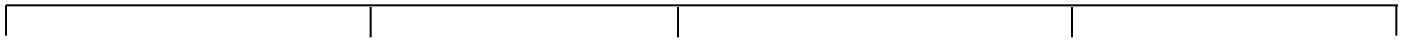
A.Pliss, P.N.Prasad et al. submitted to ACS Chemical Biology


CARS, TPEF, SHG/SFG
Multi-dimensional
Biophotonic Imaging/Sensing
FRET, FRAP, FLIM
ASFI, Raman
I = f (x,y,z)
Spatial
I = f (t)
Dynamics
I = f (λ)
Spectral
I = f (T)
Temperature
Concentration (λ,x,y,z,t,T)
Probe
Location
Time
Temperature

NANOEMITTERS FOR BIOMEDICINE


Unique properties at nanoscale
Multimodality/ Multiplexibility
Fluorecent Nanoparticles and Biomedicine
Light Guided Targeted delivery
See, Treat and see (Theranostics)

Multifunctionality of Nanostructures



Optical

- Imaging
- Sensing
- Light-activated therapy

Magnetic

- MRI
- Sensing
- Magnetic separation

Thermal

- Thermal mapping
- Thermal activation
- Photothermal activation
- Magnetic therapy

Radioactive

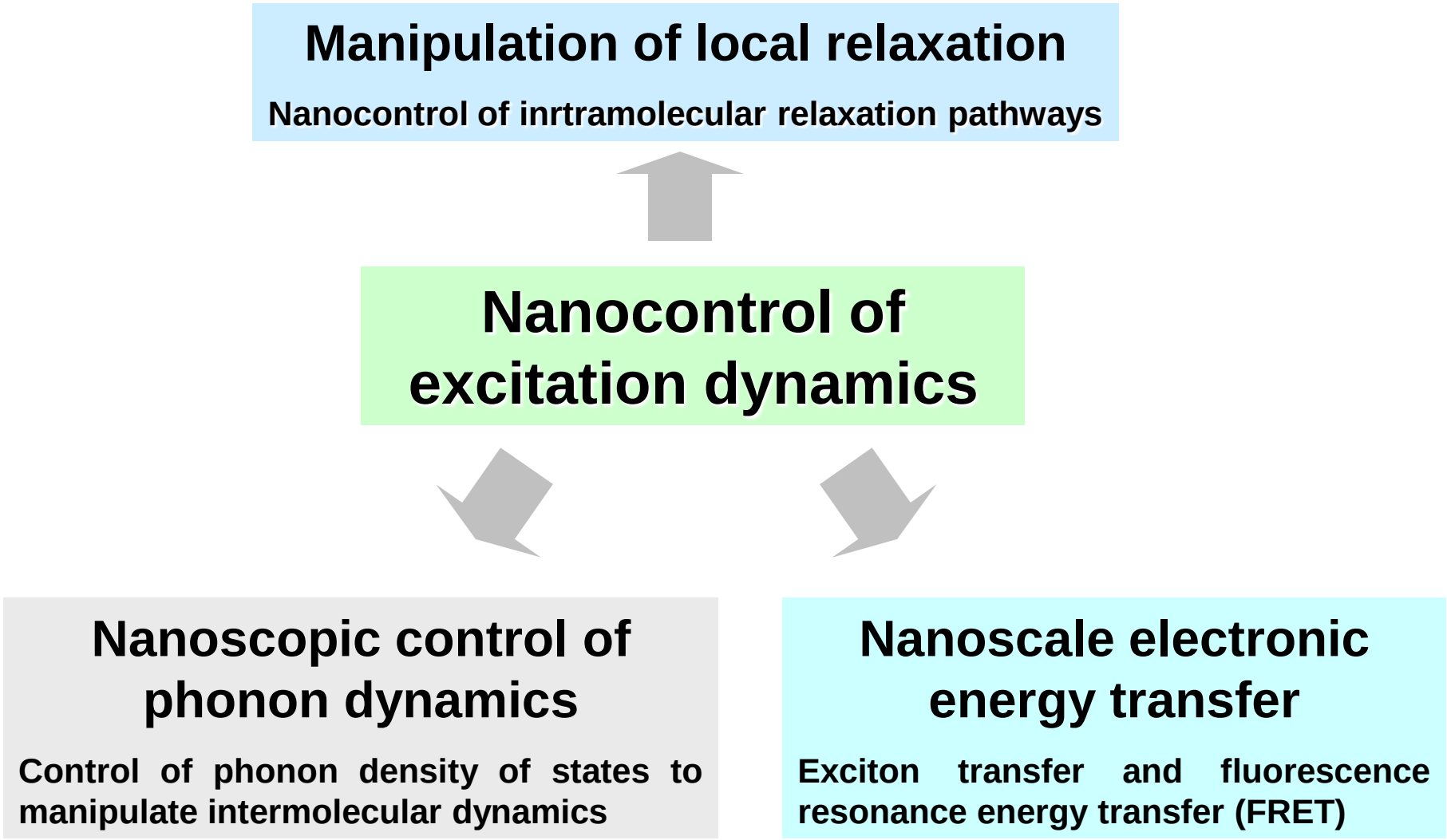
- Radio imaging
- PET
- Neutron capture therapy

Biological

- Targeting
- Enzymatic release

Challenges for Fluorescent Nanoparticles

- **High One- or Two- photon Excitation Efficiency (Absorption Cross-section)**
- **High Emission Efficiency (Quantum yield)**
- **Photostability**
- **Emission in the Near IR spectral range for imaging of deep tissues/ *in vivo* imaging**
- **Multifunctionality**
- **Dispersability in Aqueous Medium with No Significant Reduction of Emission Efficiency**
- **High Cellular Uptake for Cellular Imaging**
- **Biocompatibility and Biodegradability**
- **Nontoxicity**

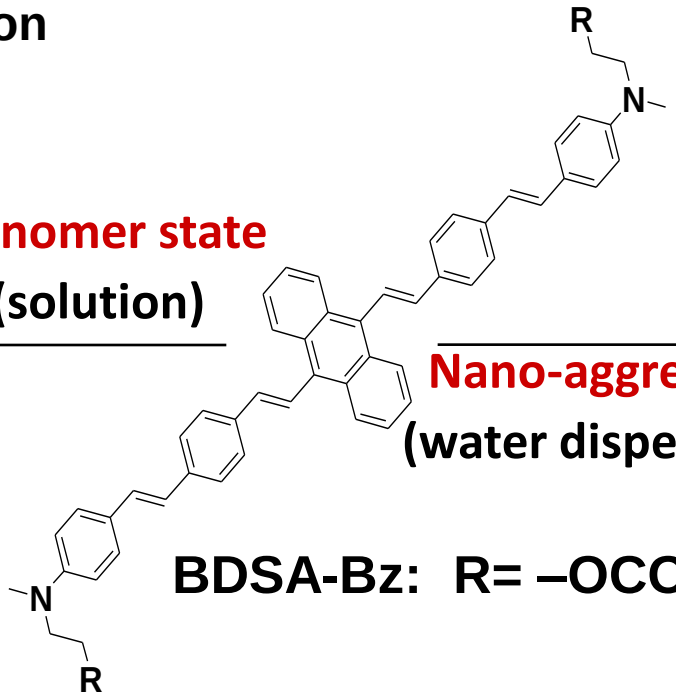

Manipulation of local relaxation
Nanocontrol of inrtramolecular relaxation pathways
Nanocontrol of excitation dynamics
Nanoscopic control of phonon dynamics
Control of phonon density of states to manipulate intermolecular dynamics
Nanoscale electronic energy transfer
Exciton transfer and fluorescence resonance energy transfer (FRET)

Two-photon excitable aggregation enhanced nanoemitters

Weak two-photon fluorescence

monomer state

(solution)

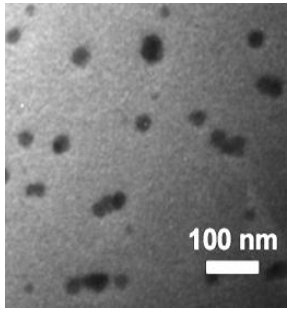


Nano-aggregate

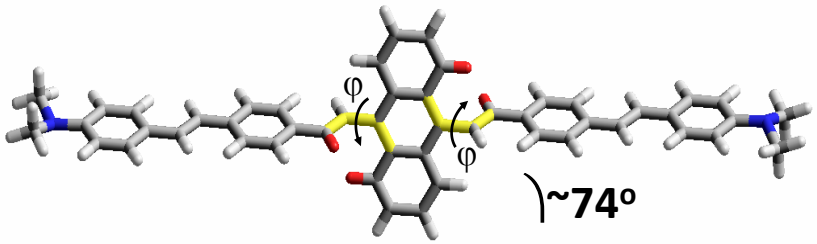
(water dispersion)

BDSA-Bz: R= –OCOPh

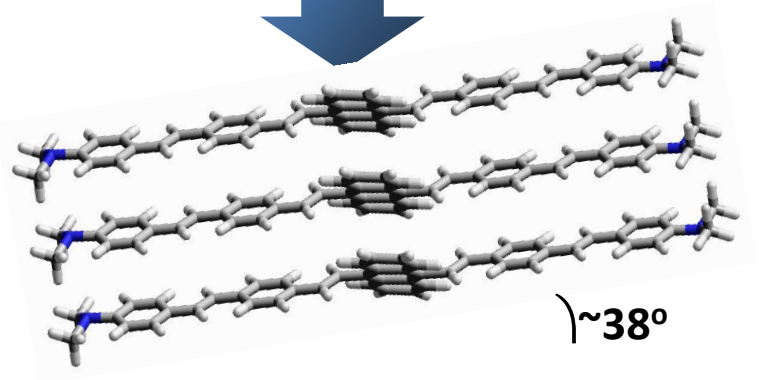
Enhanced two-photon fluorescence



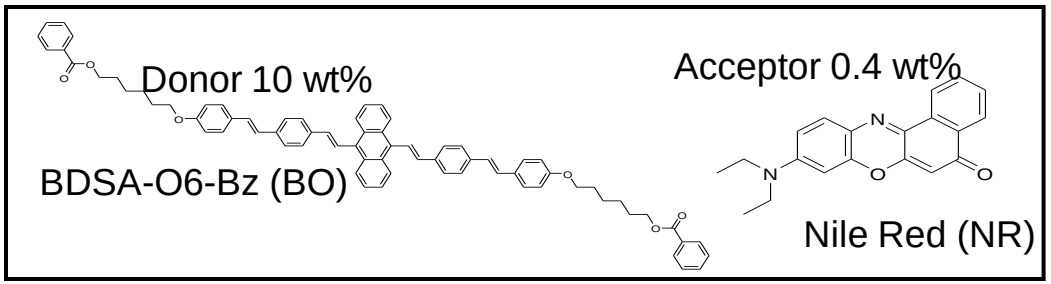
distortion by internal steric hindrance

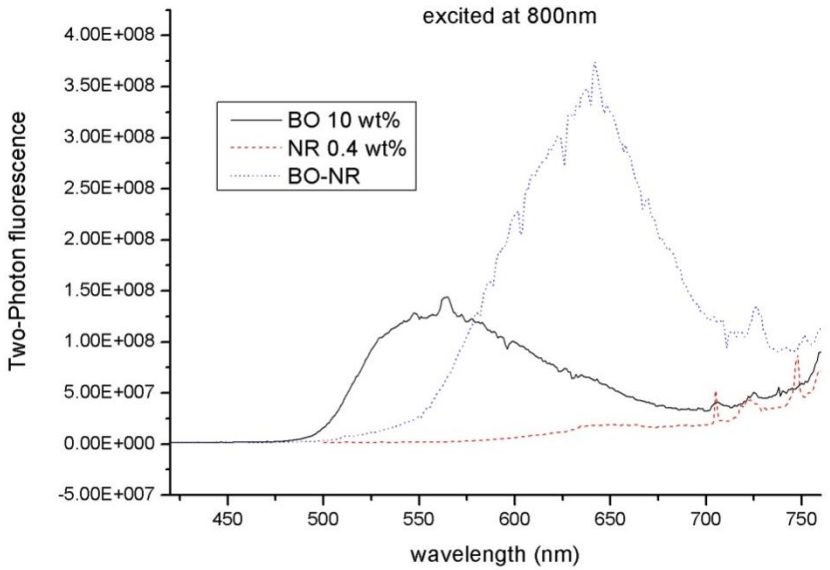


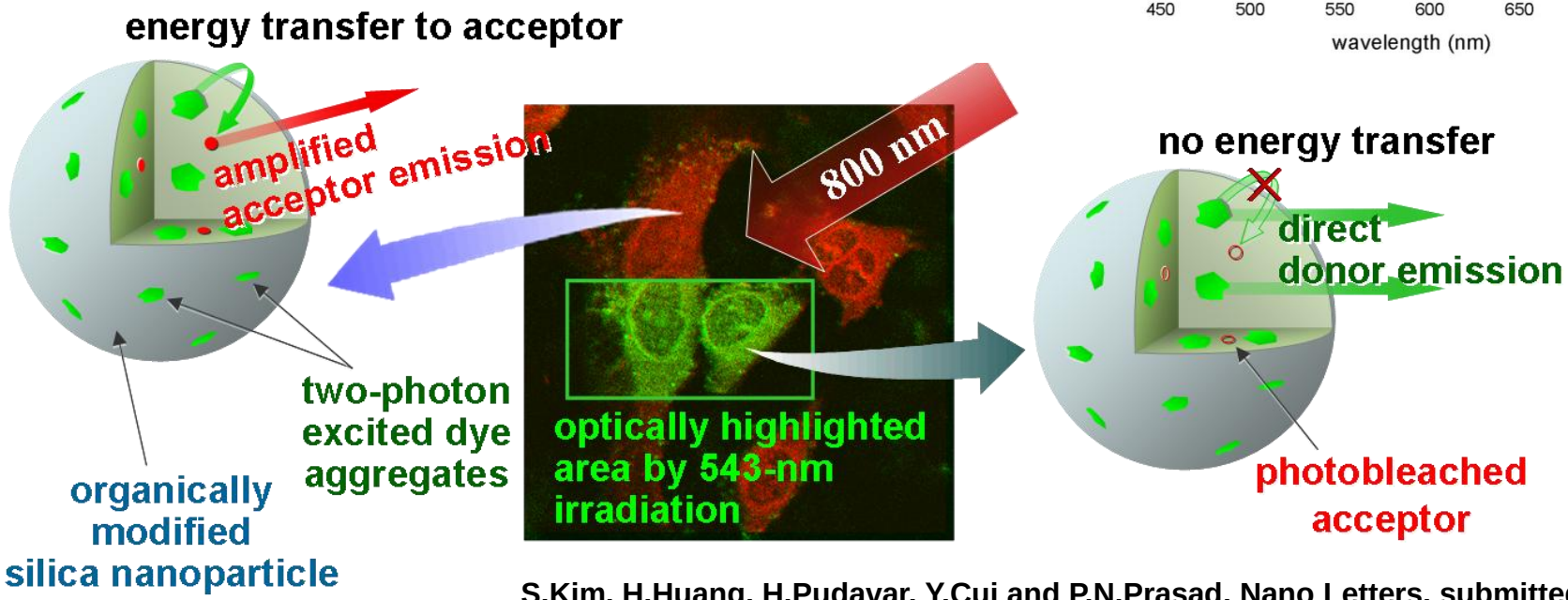
loose stacking by partial planarization



Optical highlighting of cells using FRET based nanoprobes



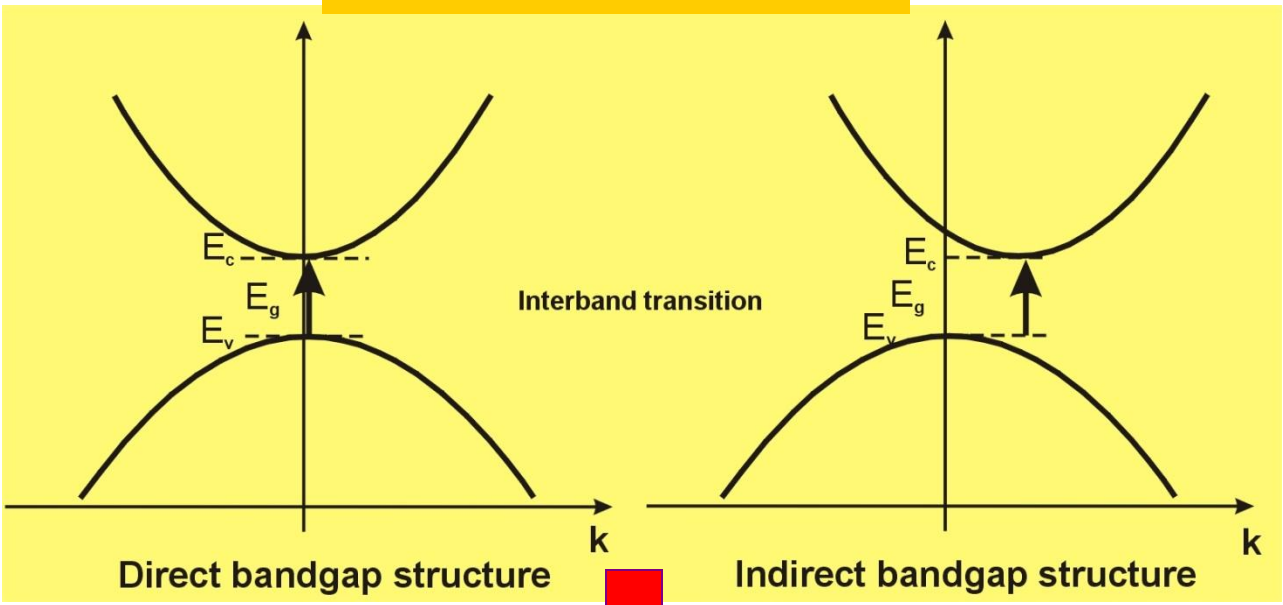




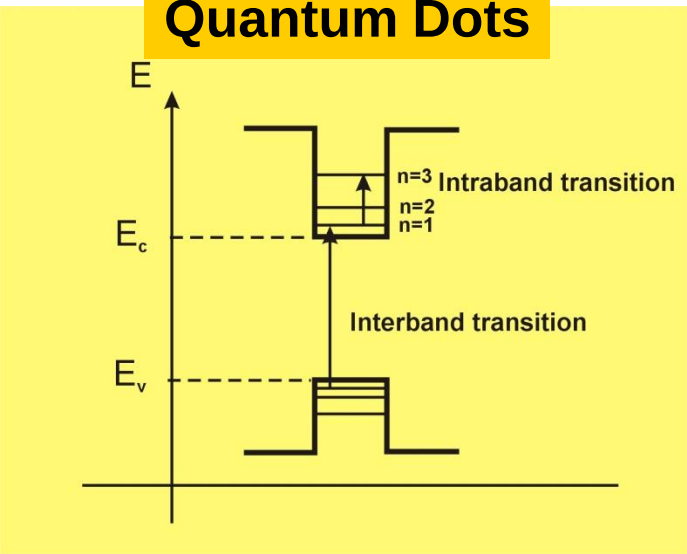
S.Kim, H.Huang, H.Pudavar, Y.Cui and P.N.Prasad, Nano Letters, submitted

Quantum-Confined Structures

Bulk Semiconductors



Quantum Dots



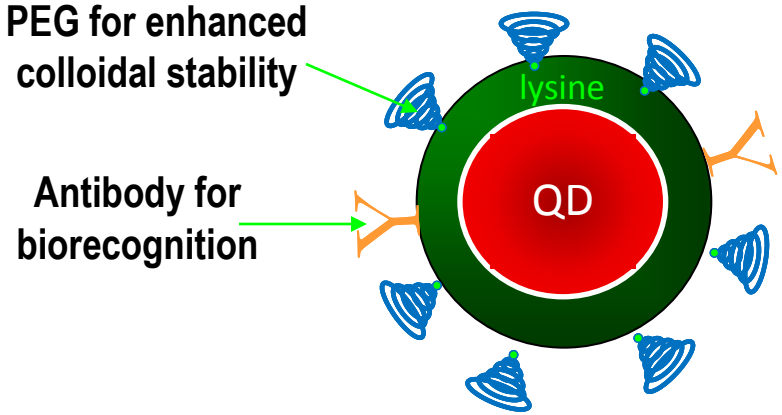
Quantum Dots/Rods: New generation Diagnostic probes

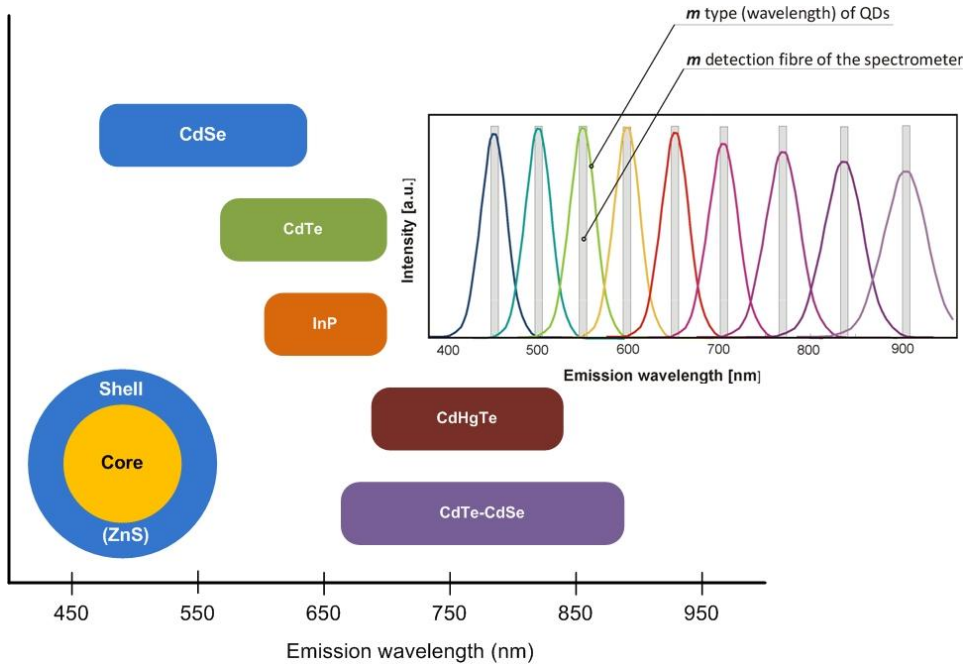
- Semiconductor nanoparticles with unique, tunable optical properties
- Highly photostable
- Narrow, symmetric emission spectra
- Ease of bioconjugation
- Ability for multiplexed analysis

Size and composition tunable emission

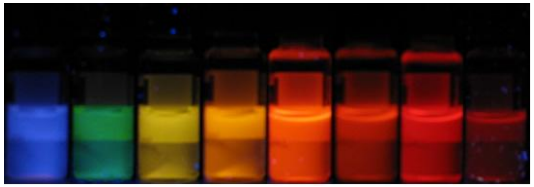
Applications

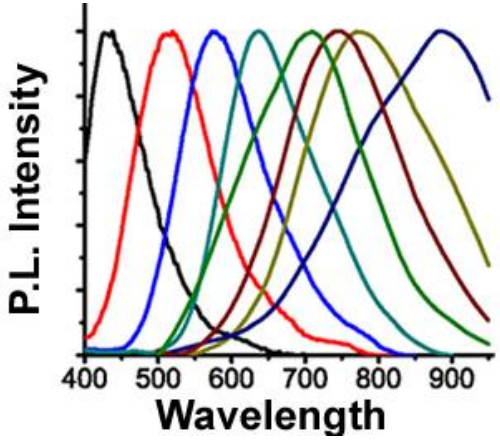
- In vitro Imaging
- In-vitro Diagnostics
- Targeted Drug delivery
- Theranostics





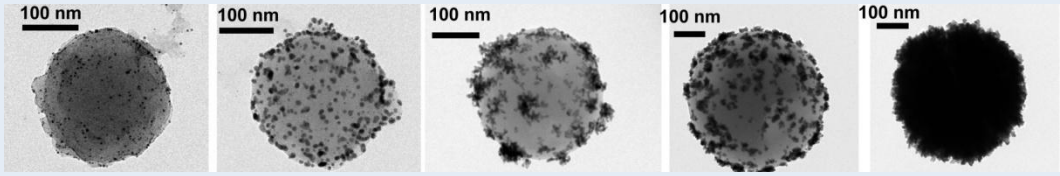
NanoSi is Highly luminescent, while the bulk form is not



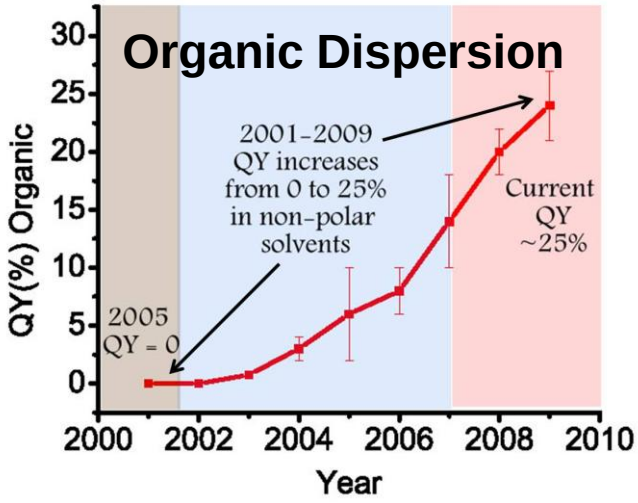


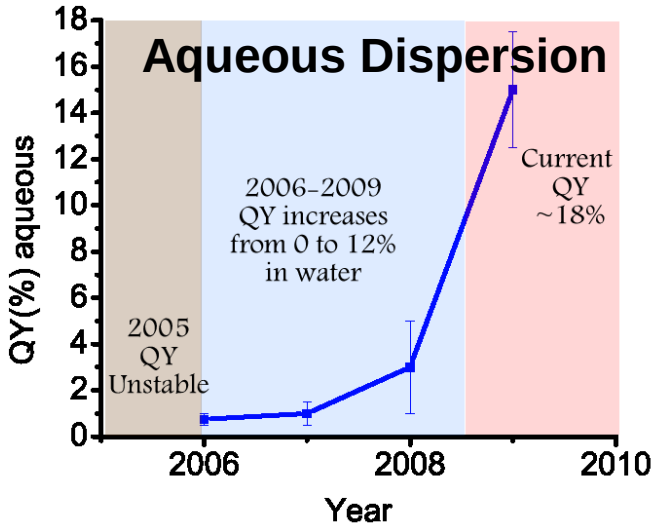
Our contribution:

- Unique proprietary synthesis method
- PL spanning the visible spectrum
- Steadily increasing QY
- Flexible surface modification and encapsulation
- Plasmonically-coupled Si QDs



Plasmonically-coupled Si QDs

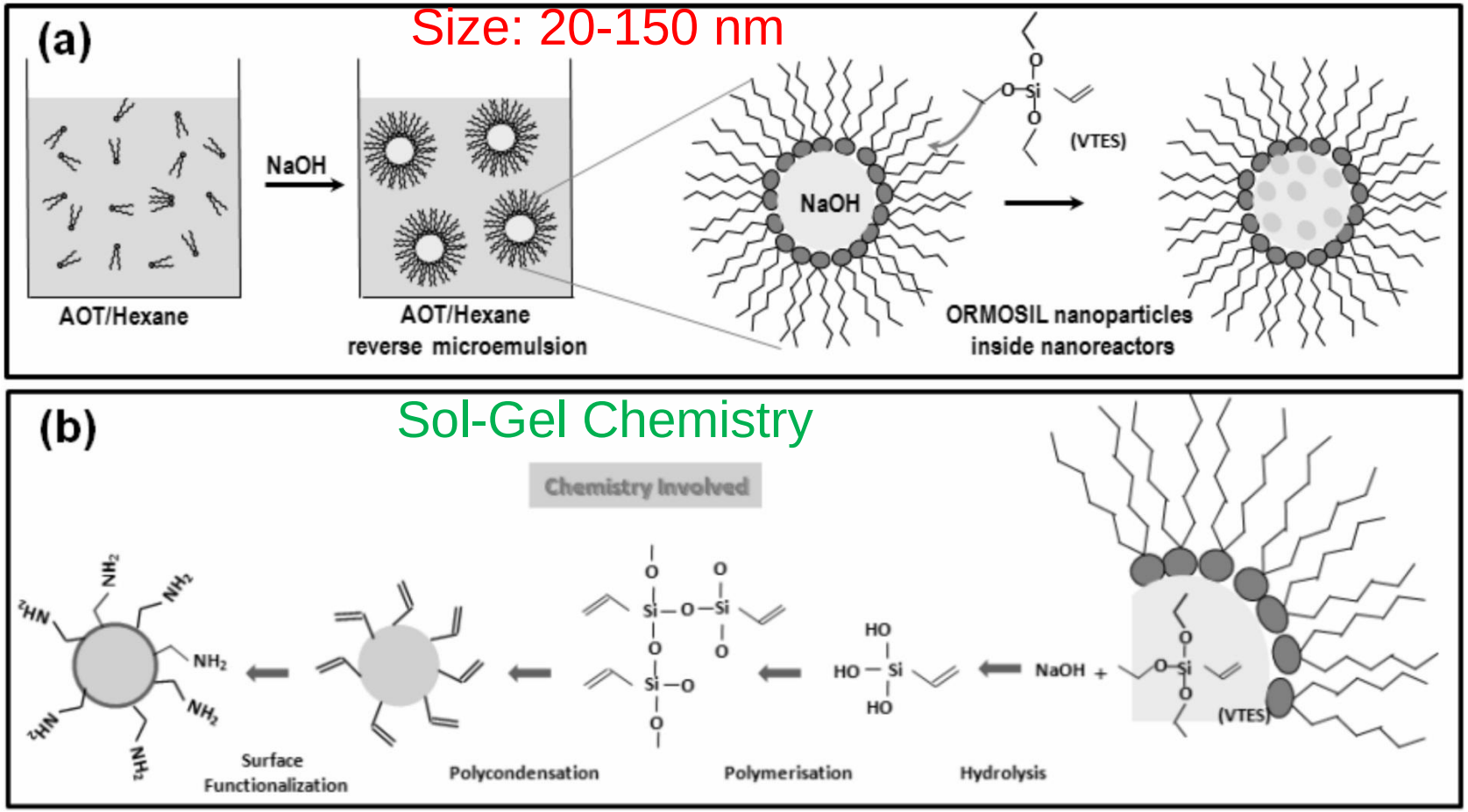




NANOCHEMISTRY FOR NANOEMITTERS

Nanochemistry :Synthesis of nanoparticle

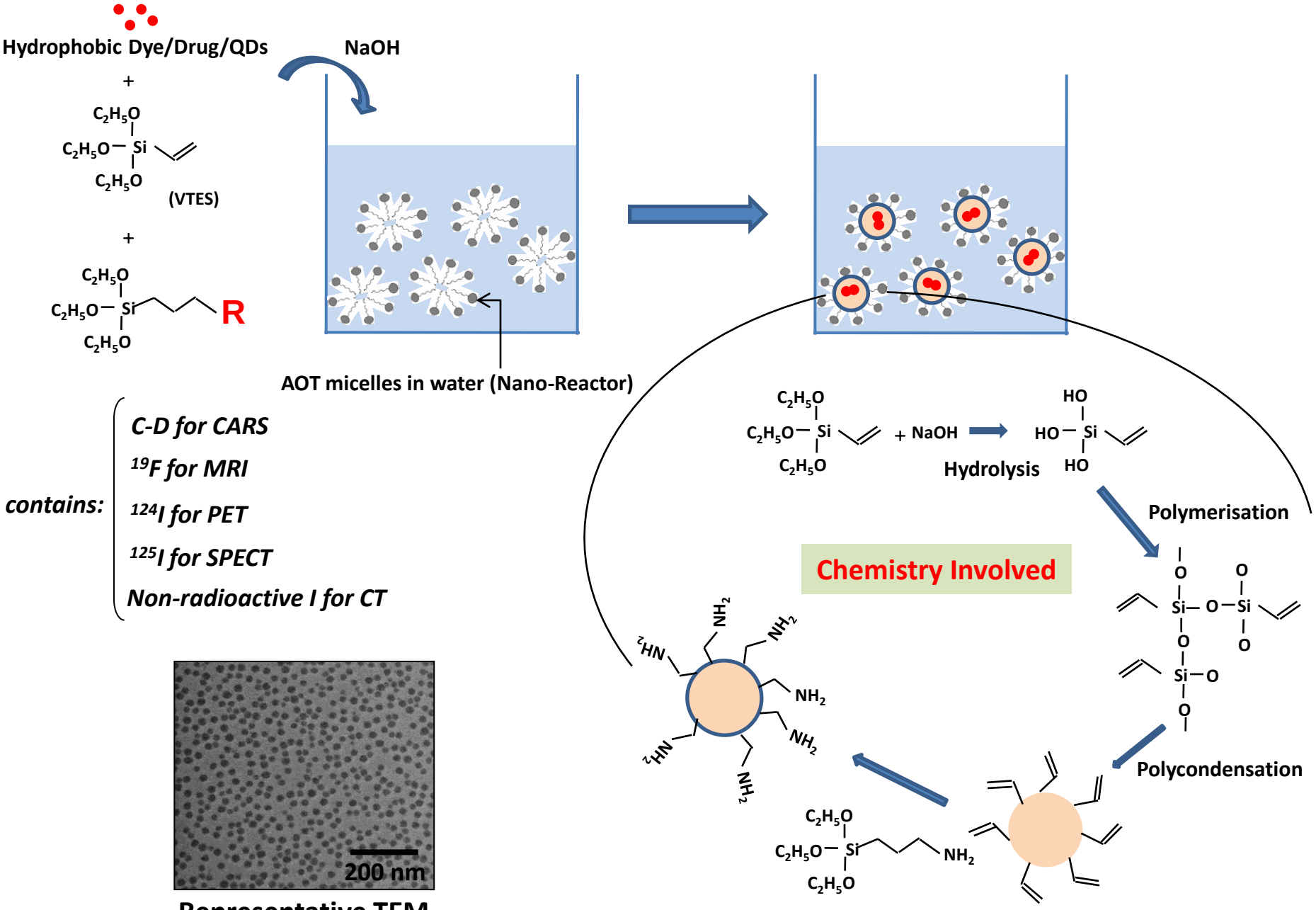
Organically Modified Silica (ORMOSIL) nanoparticles



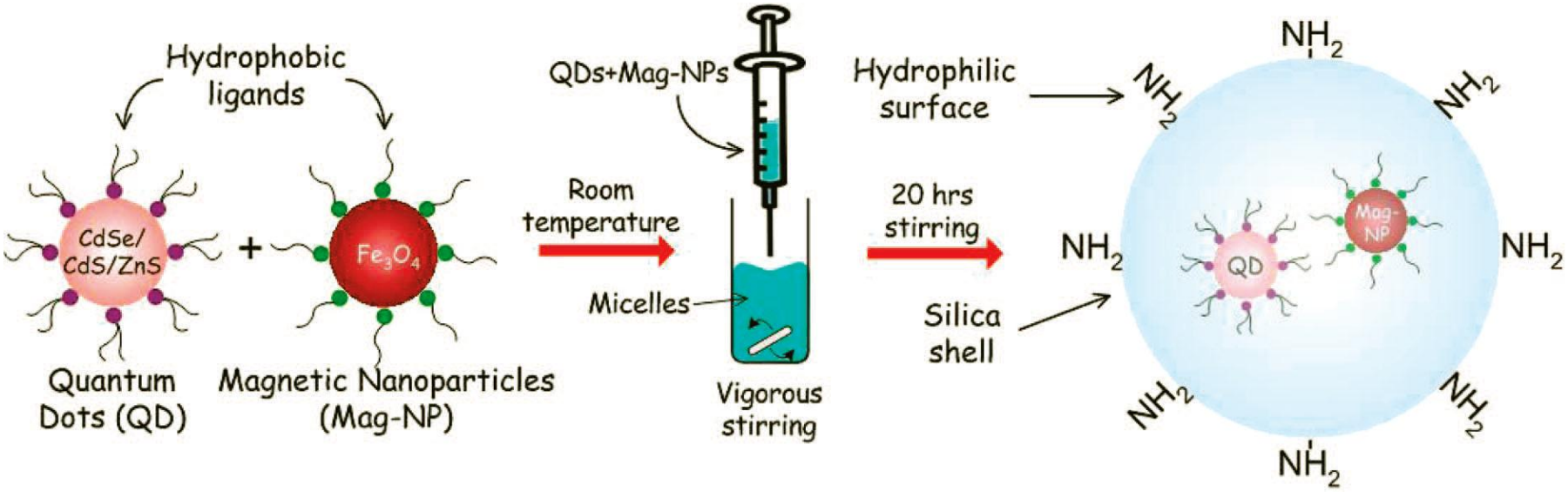
(a) Schematic presentation of synthesis of ORMOSIL nanoparticles using AOT/Hexane reverse microemulsion system

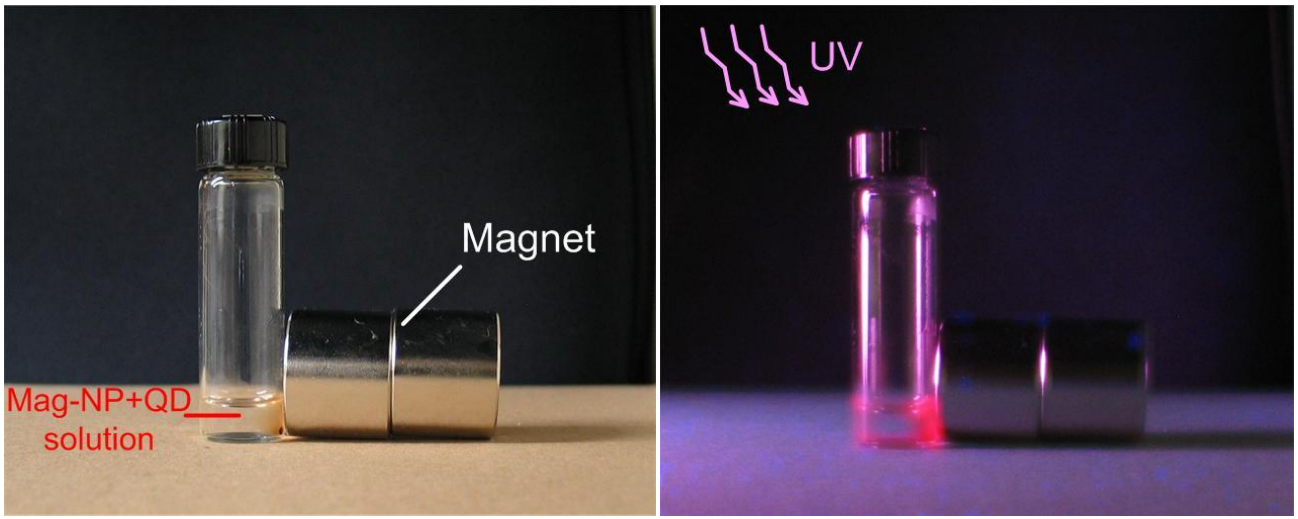
(b) Involved chemistry

Multifunctional (theranostics) ORMOSIL nanoparticle



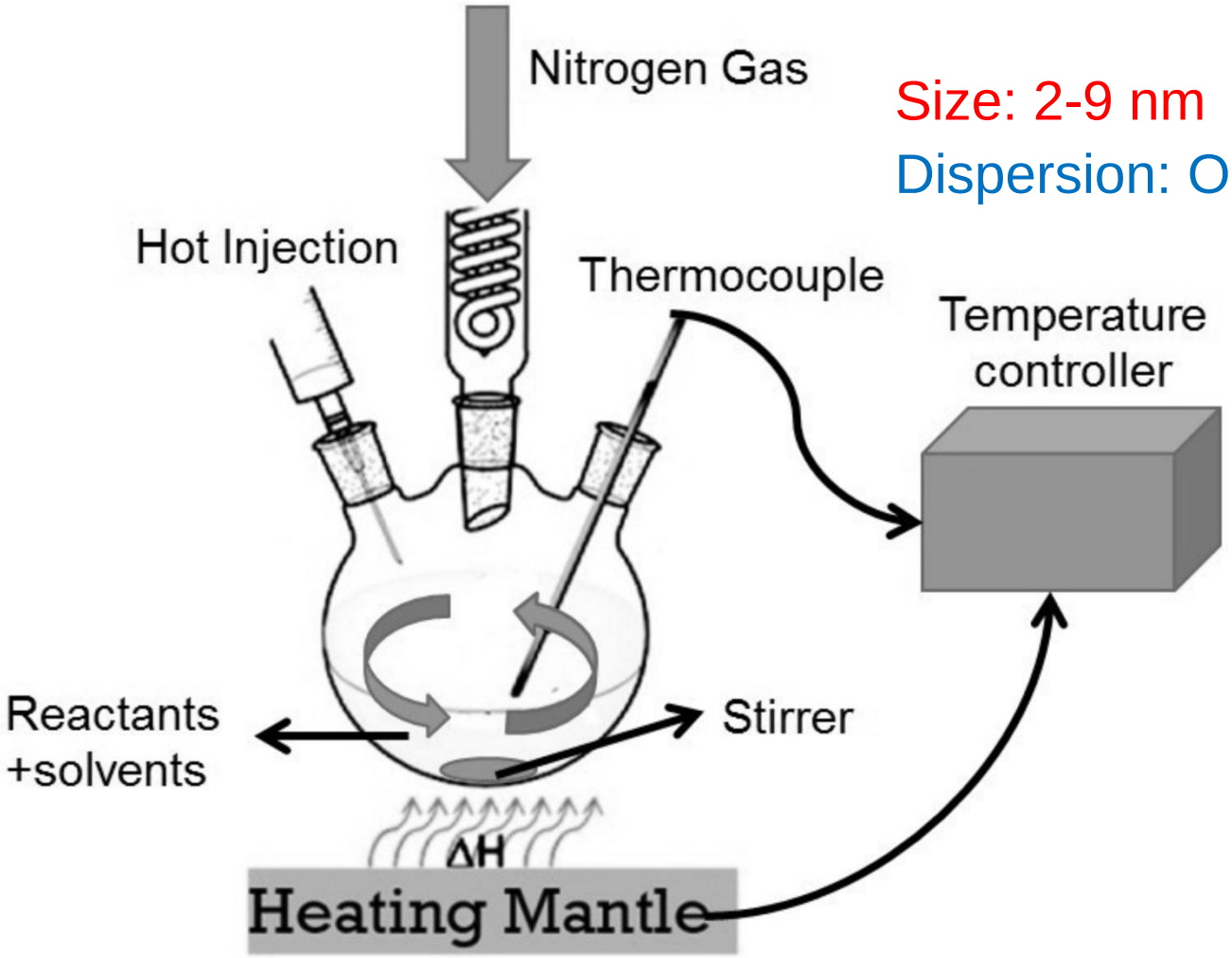
Multimodal (two imaging modalities) ORMOSIL nanoparticle





Prasad et al. J. Phys. Chem. C **112**, 7972-7977 (2008).

Hot Colloidal Synthesis of Semiconductor Nanocrystals



Size: 2-9 nm

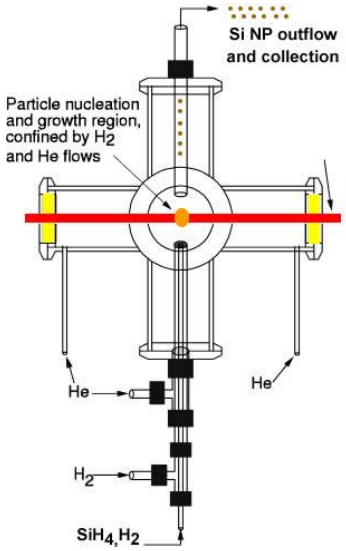
Dispersion: Organic solvent

Courtesy of Y. Li and M.T. Swihart

Gas Phase Synthesis of Silicon (Si) Nanocrystals

(Combination of Bottom Up and Top Down Approaches)

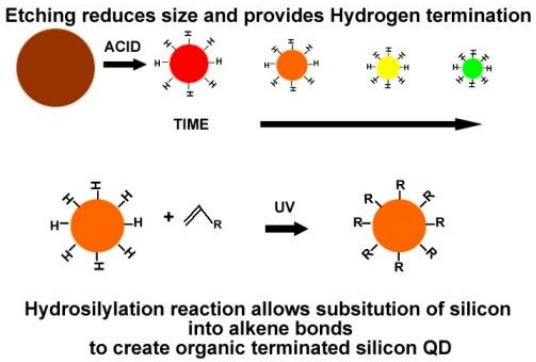
— Bottom-up →



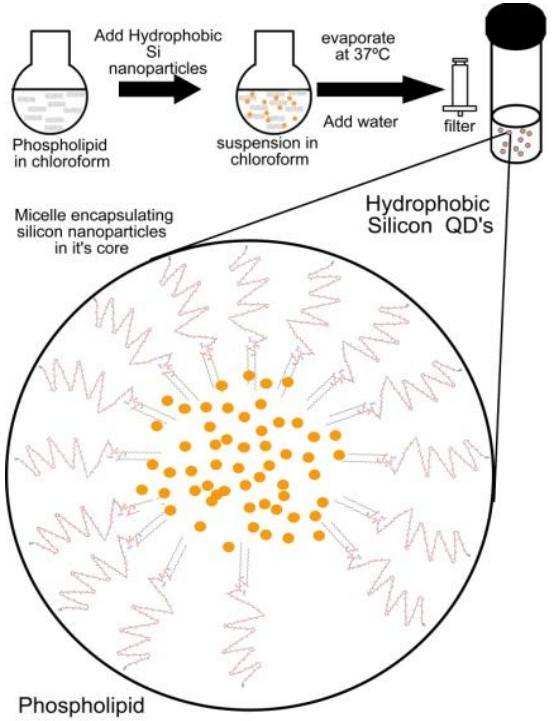
(a) laser pyrolysis

(b) etching

Top-down



(c) hydrosilylation



(d) micelle encapsulation

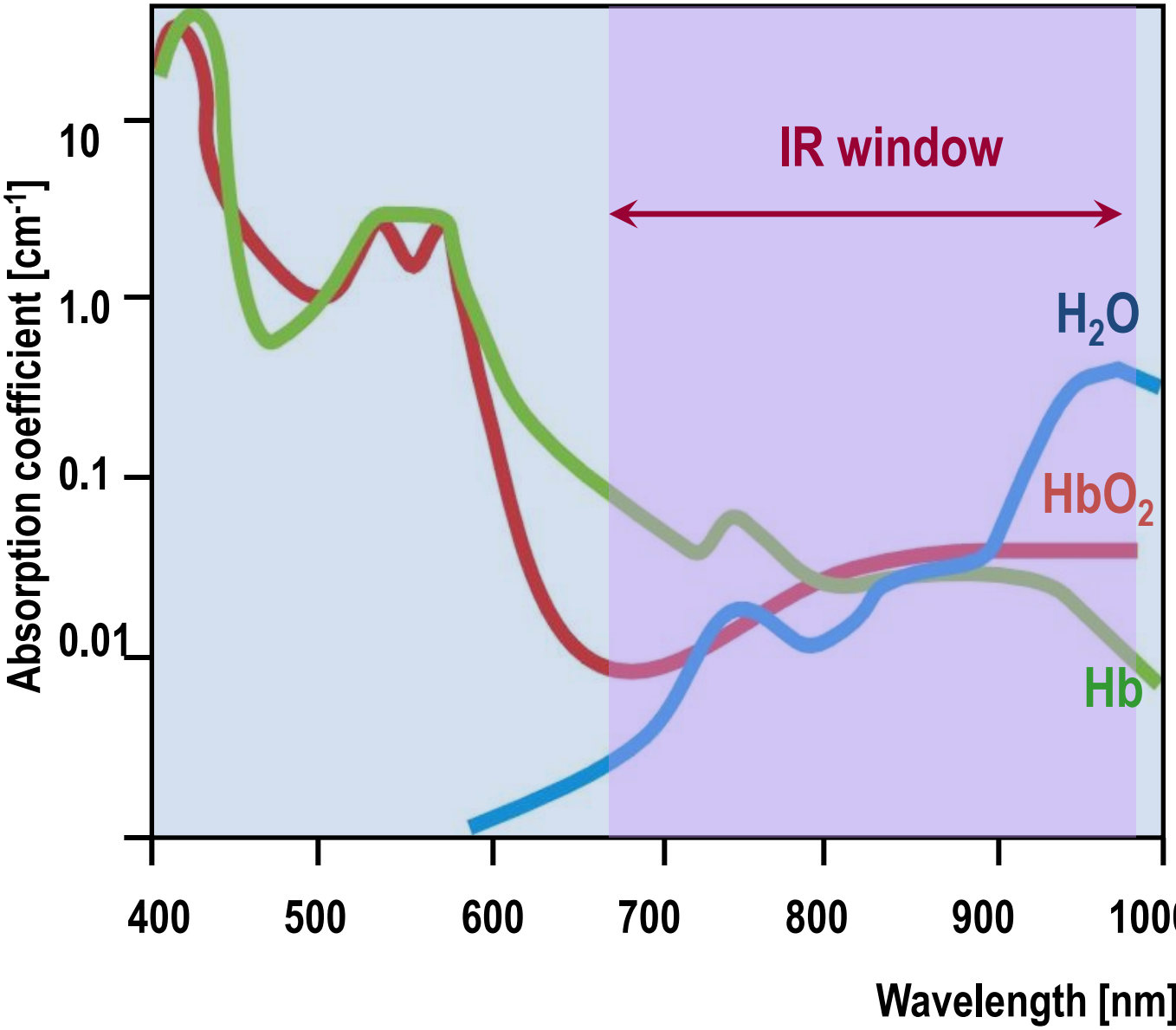
Size: 4-9 nm

Dispersion: Organic solvents — Surface modifications → Aqueous

Prasad et al. ACS Nano, **2011**, *5* (1), pp 413–423

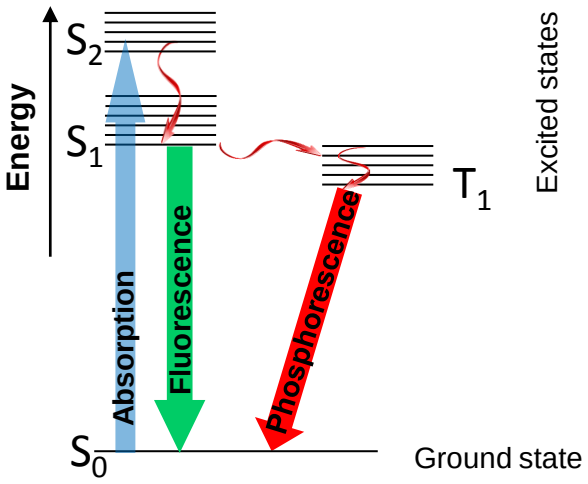
NEAR IR NANOEMITTERS

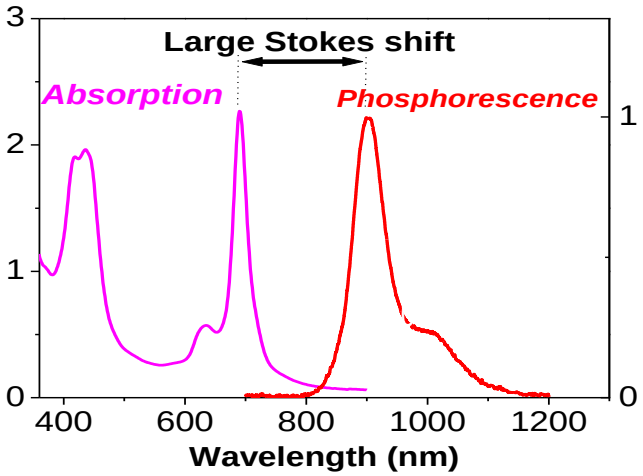
Near IR Nanoemitters for Bioimaging



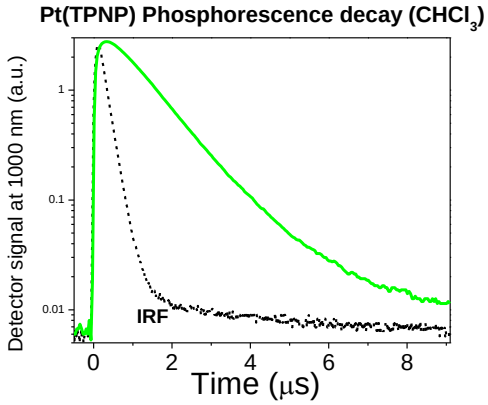
- Low Autofluorescence
- Low Photodamage
- High Tissue Penetration

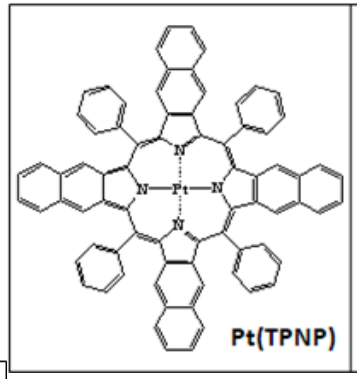
NEAR-INFRARED PHOSPHORESCENCE FOR BIOIMAGING



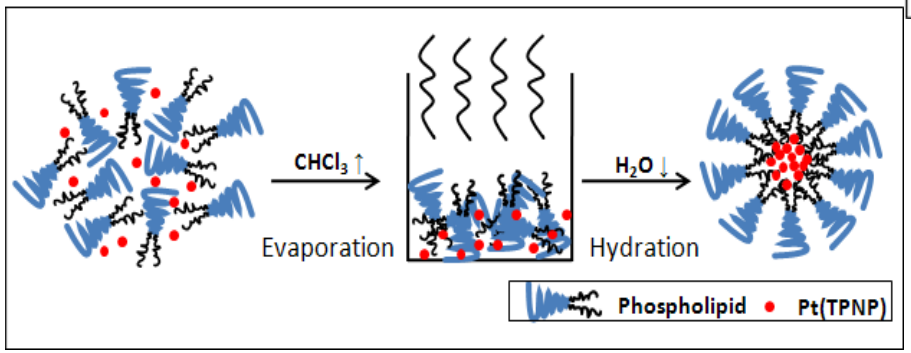


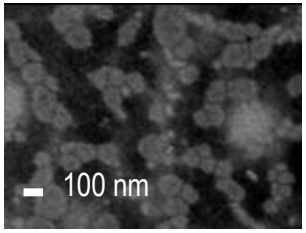
Possibility of Time-Gated Imaging

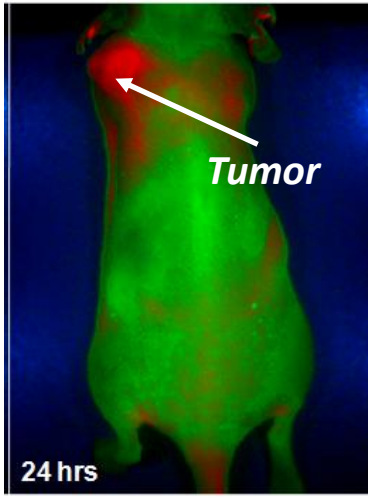




Pt(TPNP) in phospholipid nanomicelles





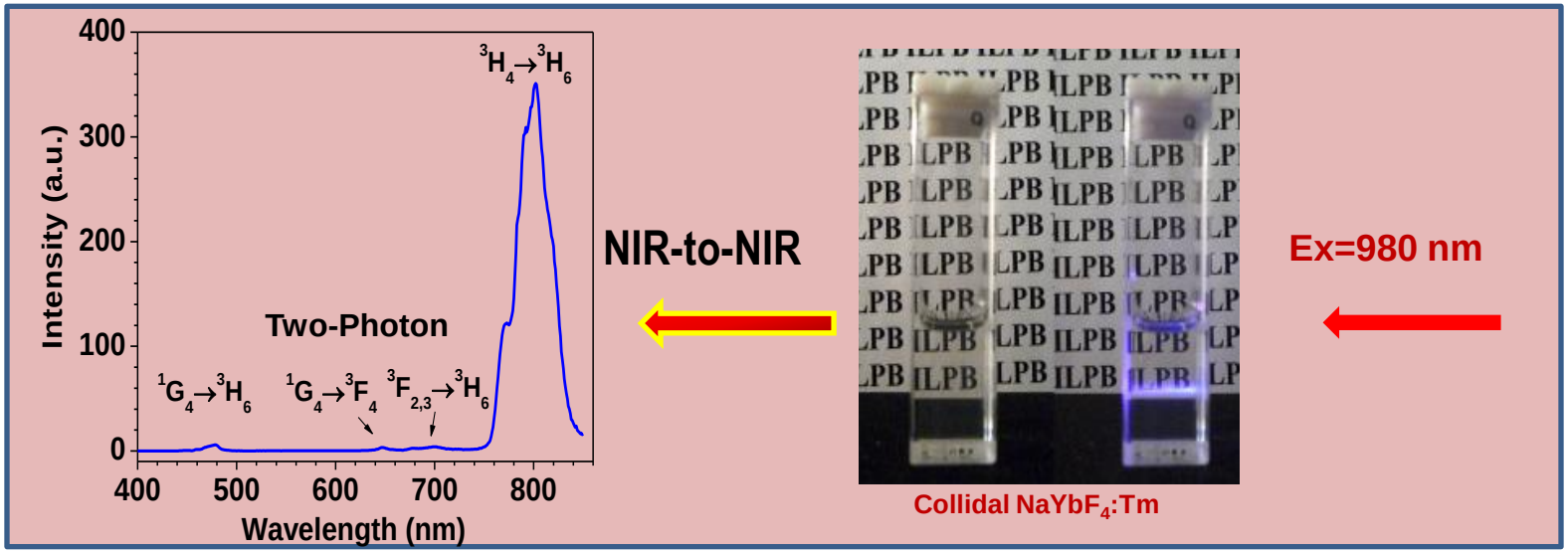


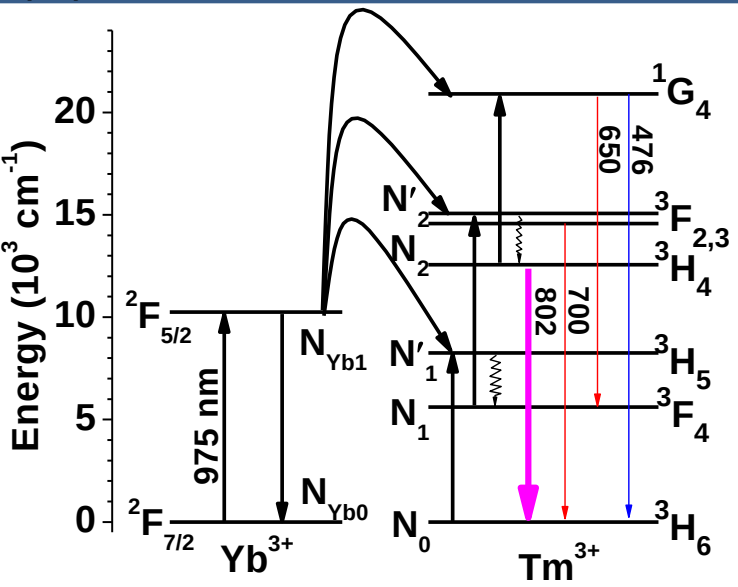
Preferential localization of Pt(TPNP)/ DSPE-PEG/PC in tumors

Collaboration with USC (Prof. M.E.Thompson)

R.Kumar et al, ACS Appl.Mat.2009, 1, 1474

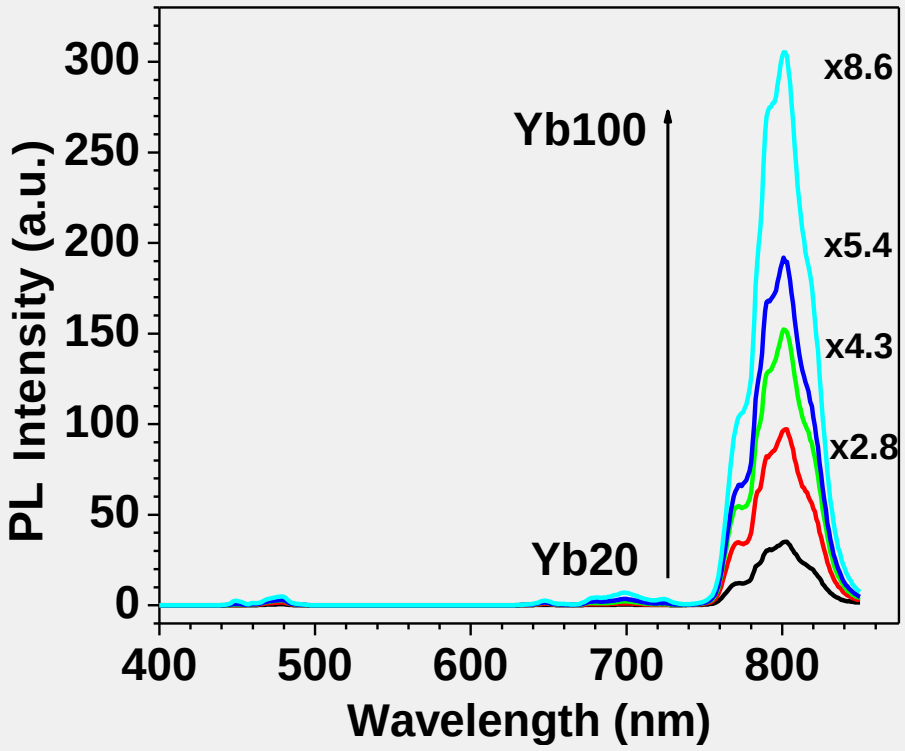
Rare-Earth Doped Upconversion Nanocrystals with NIR-to-NIR Photoluminescence



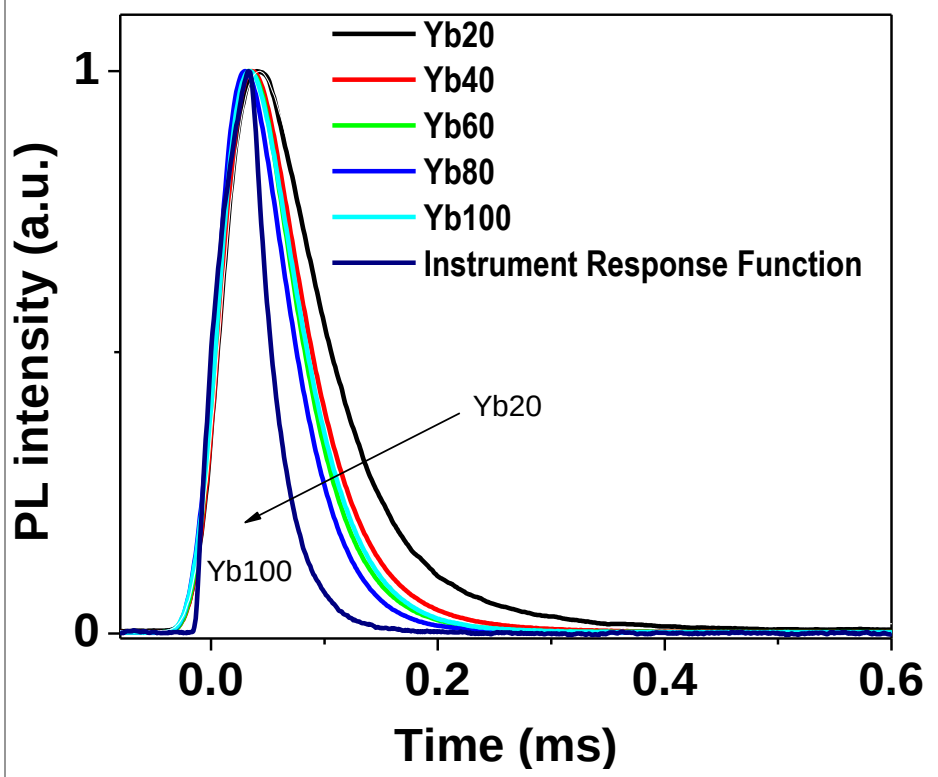


Nanoscale control of energy transfer excitation dynamics

Enhanced NIR-to-NIR upconversion PL in cubic $NaYF_4:Yb^{3+}/Tm^{3+}$ nanocrystals by optimizing Yb^{3+} concentration



Quantum yield is increased by 9 times with the increase of Yb^{3+}



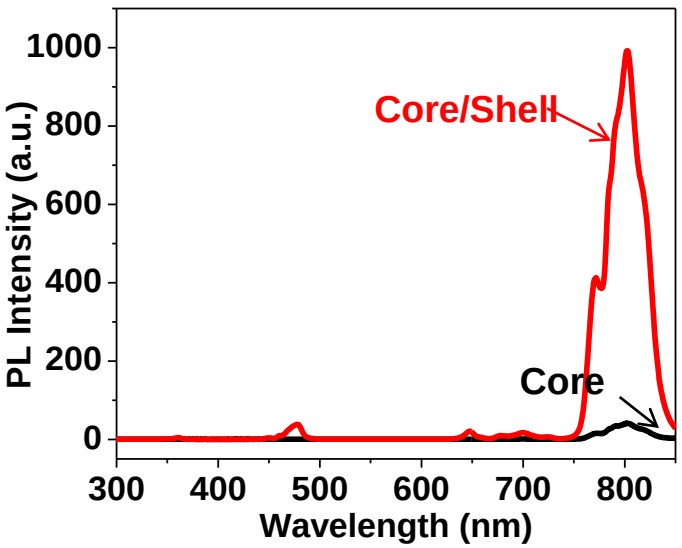
Lifetime of PL of Yb^{3+} at 1050 nm is shortened with the increase of Yb^{3+}

Chen, G., Ohulchanskyy, T.Y., Prasad, P.N et al ACS Nano 4(6), 3163 (2010)

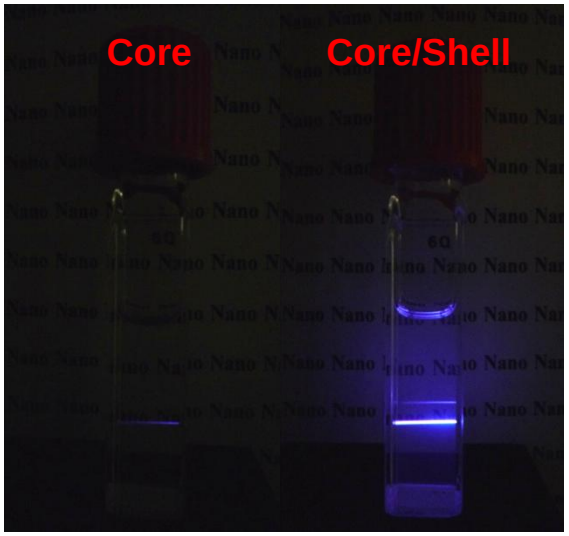
Nanocontrol of surface induced nonradiative processes

Enhancement of NIR-to-NIR upconversion PL in cubic $NaYbF_4:Tm^{3+}$ / CaF_2 core/shell nanocrystals

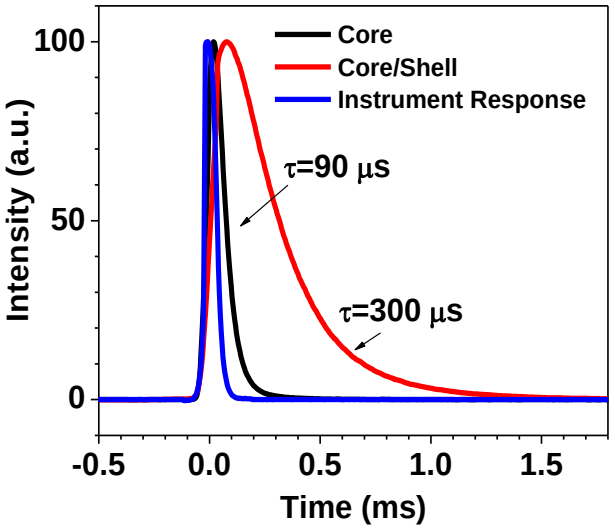
35 Times Enhancement



Ex=0.3 *W/cm²*



PL Decay at 800 nm

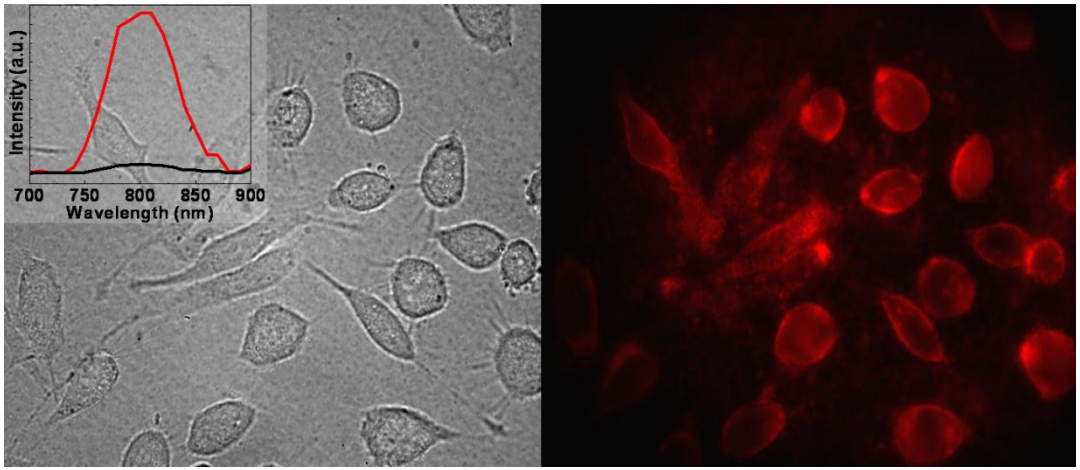


Quantum yield in 30 nm sized cubic core/shell nanoparticles reaches 0.6% (the highest up to date at low power excitation)

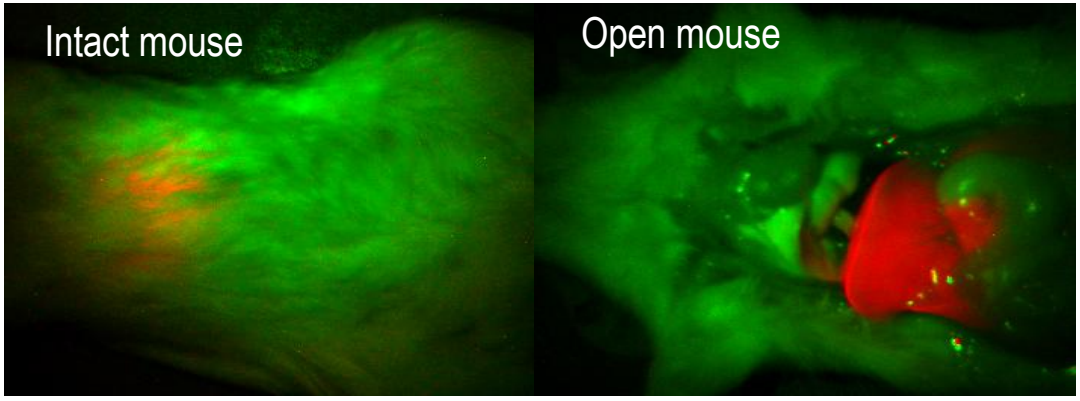
Prasad et al., submitted, 2012

In vitro and *In vivo* Bioimaging Using IR to IR Up-Conversion

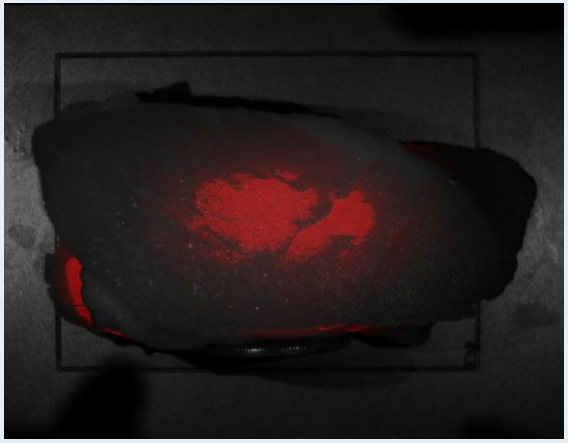
***In vitro* imaging of Panc 1 cells**

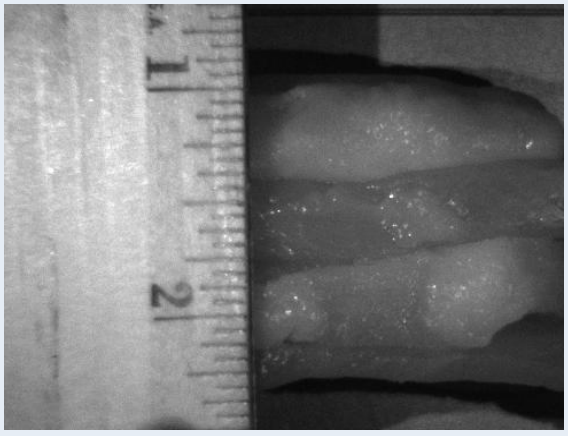


***In-vivo* whole body images of mouse**



How deep the IR-to-IR upconversion emisson of nanophosphors can be seen through biological tissues?





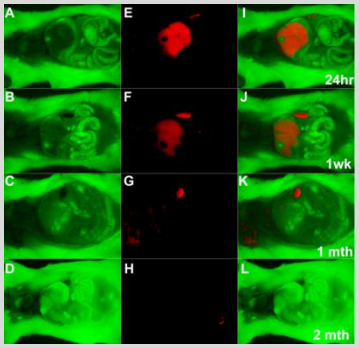
Nyk et al, Nano Letters 8, 3834 (2008)

SILICON: Abundant and Non-toxic

Sand is a natural source of silicon,

There is an abundant supply

Light Emission from silicon
is a useful property for healthcare



380mg/kg of silicon injected intravenously into mice is processed by the liver

It shows no signs of toxicity and clears after 2 months

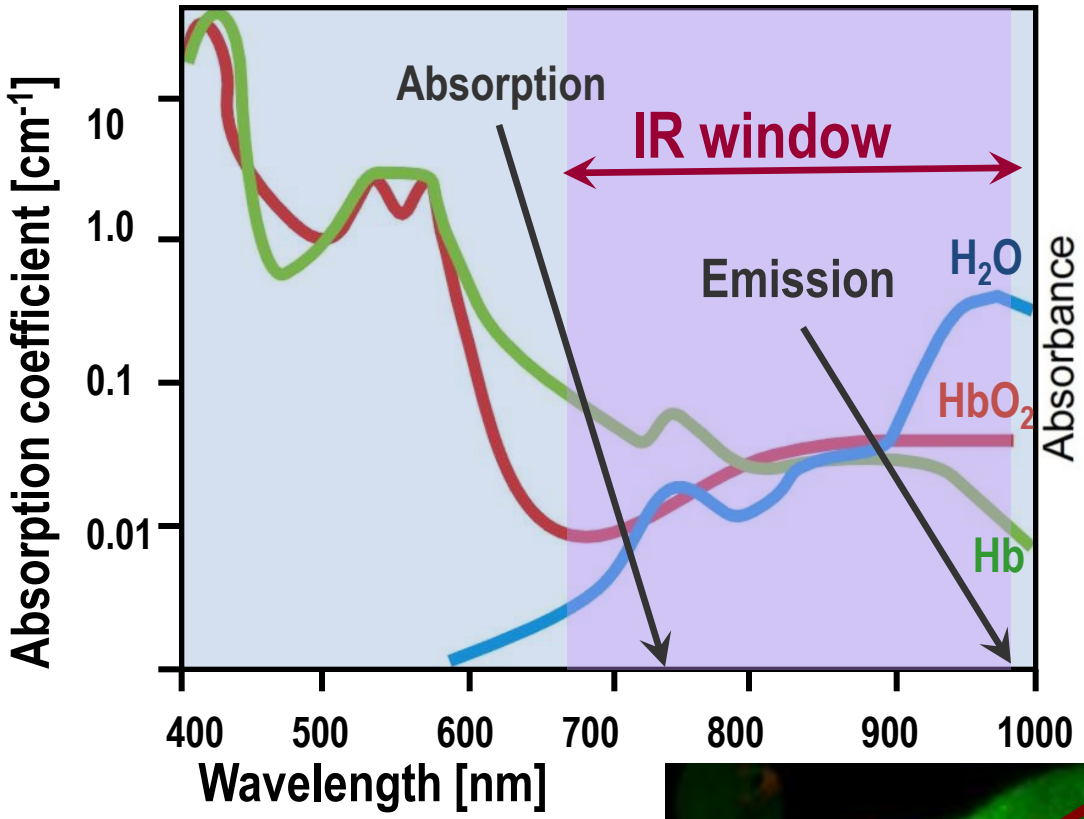
Non-toxic by intravenous injection

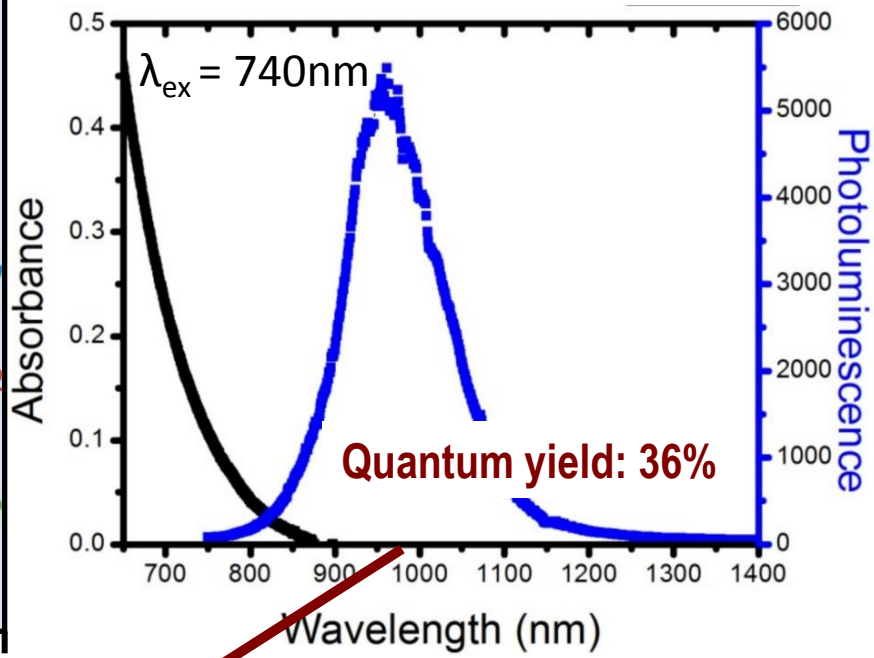
Essential trace element responsible for bone development

Ability to readily degrade by the body

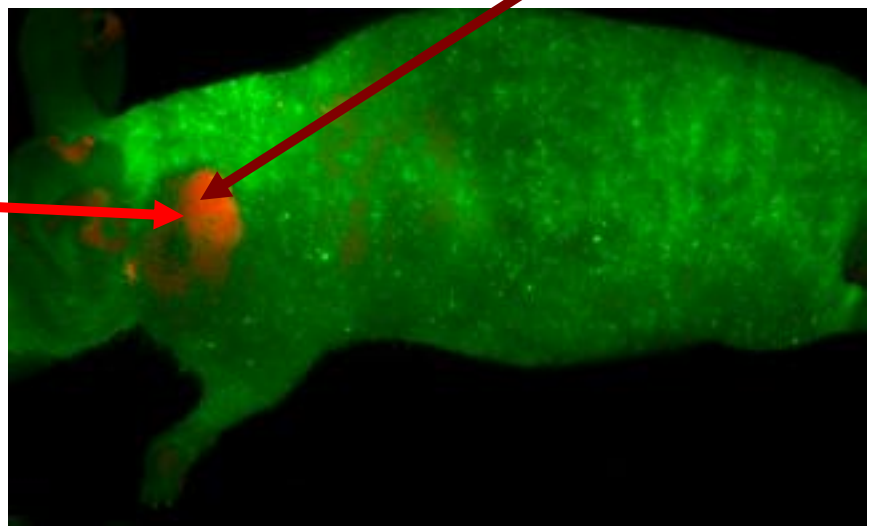
No negative effects on enviro[illegible]nt, 100% recyclable

Near Infrared Emitting Si Quantum Dots



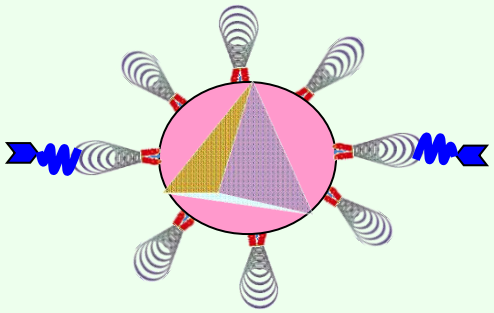


Tumor Targeting



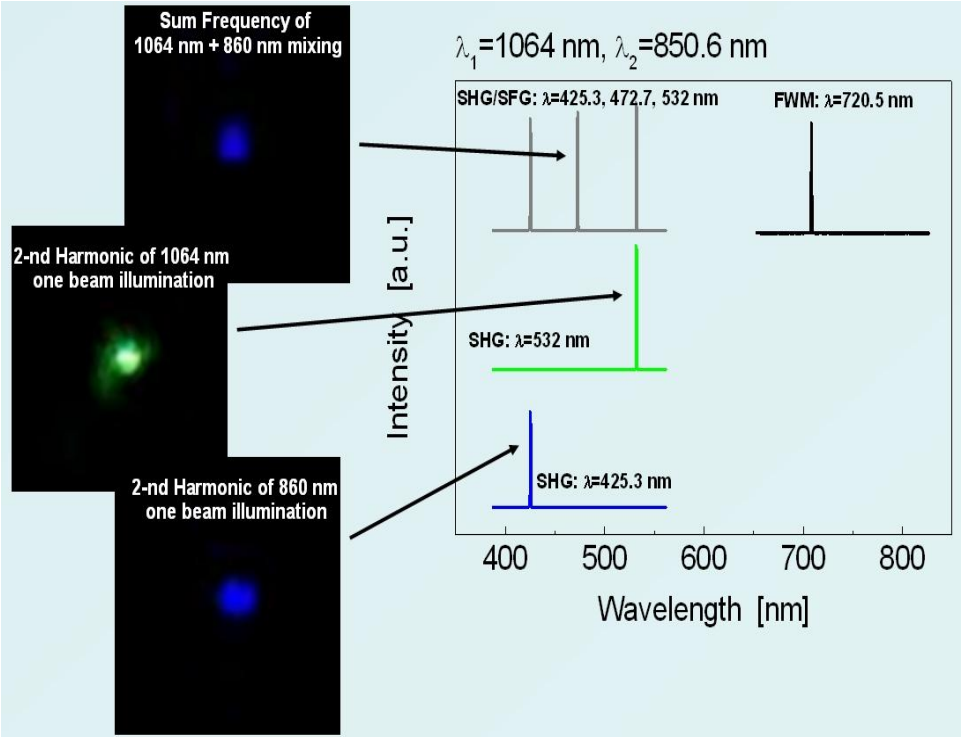
MULTIMODAL IMAGING

ZnO nanoprisms for multimodal nonlinear optical imaging

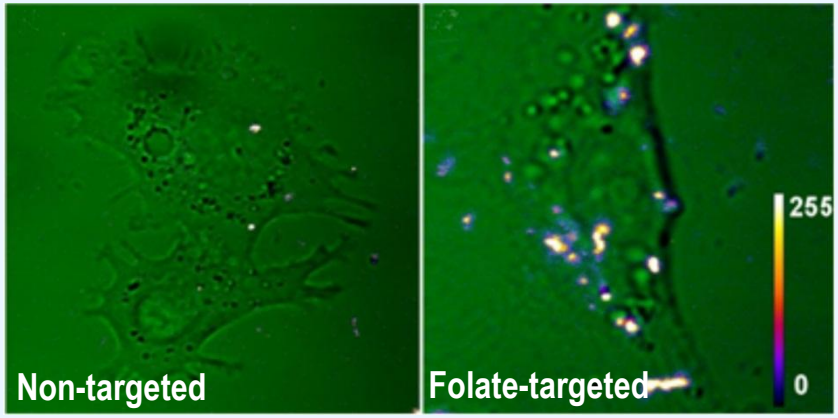


Phospholipid micelle encapsulated and folate targeted

- Wide gape II-VI type semiconductor material
- Hexagonal wurtzite type of structure is a non-centrosymmetric
  => non-zero 2nd order susceptibility
- Highly biocompatible (UV-blocker in sun-screen gel)



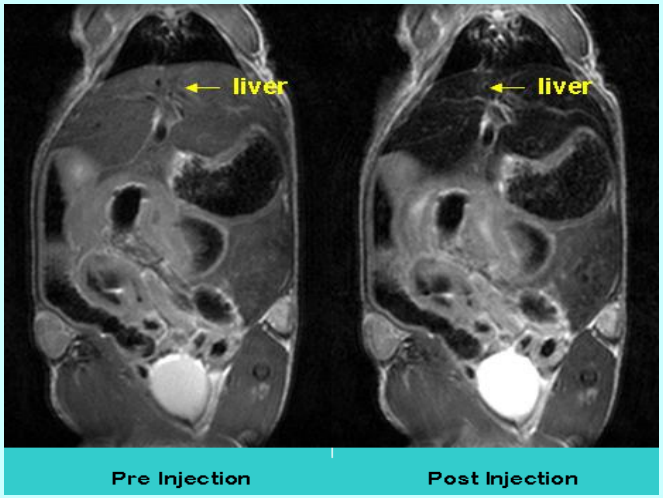
SFG signal recorded from KB cells treated with ZnO nanoparticles

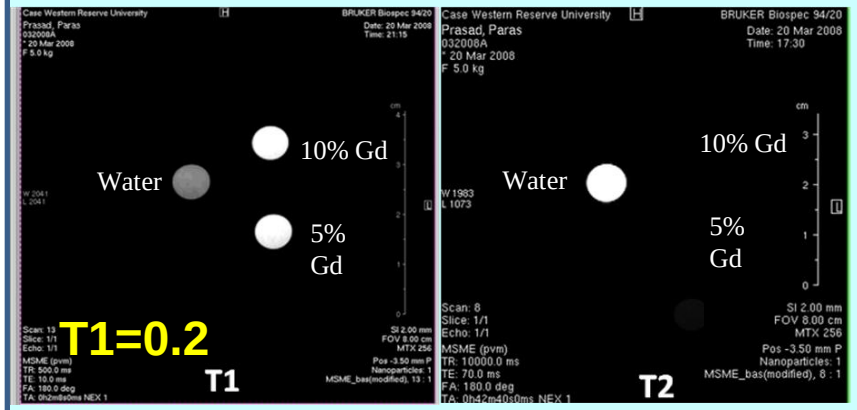


A.V. Kachynski et al, J Phys Chem, 112 10721 (2008)

Upconversion Nanocrystals for Optical and MRI bimodal Imaging

Gd-doped $NaYF_4$:Gd/Yb/Tm Nanoparticles

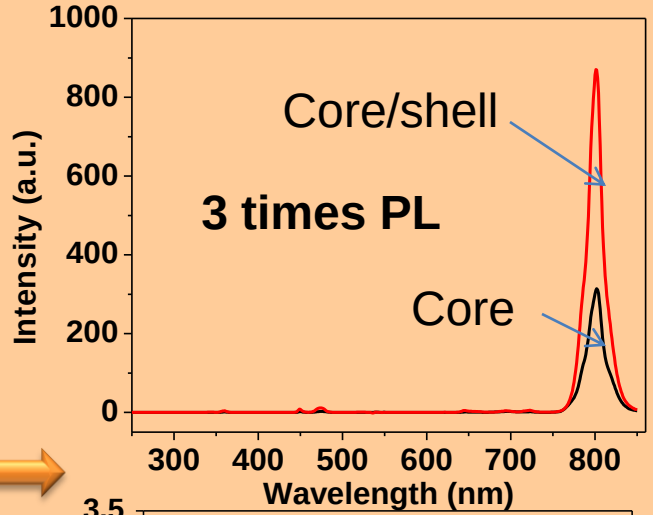


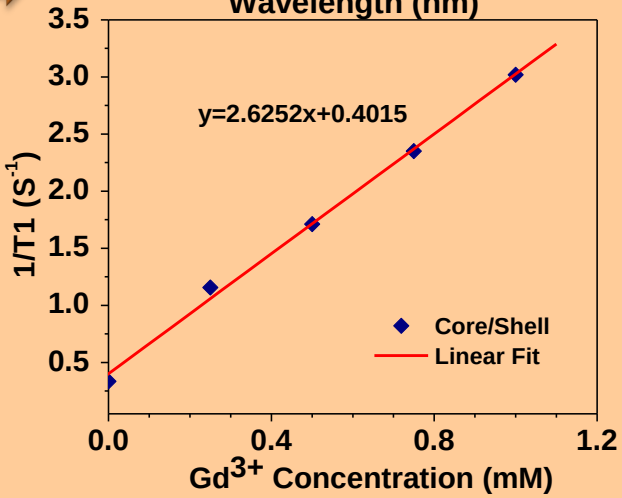


T1 and T2 weighted images of $NaYF_4$ doped with different concentrations of Gd^{+3}

P. Prasad *et al, Adv. Func. Mater. 19, 853(2009)*

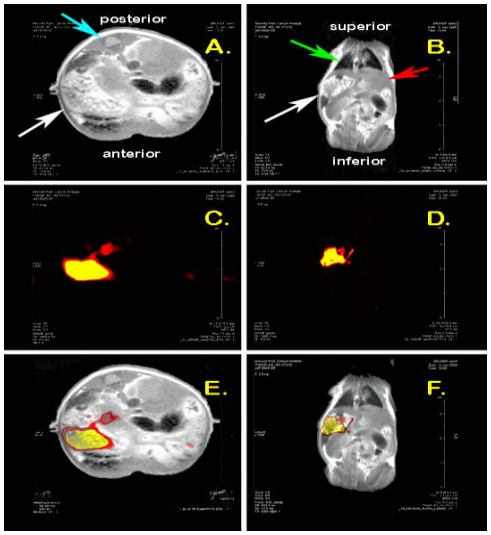
$NaYbF_4$:Yb/Tm/$NaGdF_4$ Core/Shell NPs





T1=2.62, 10 times increase

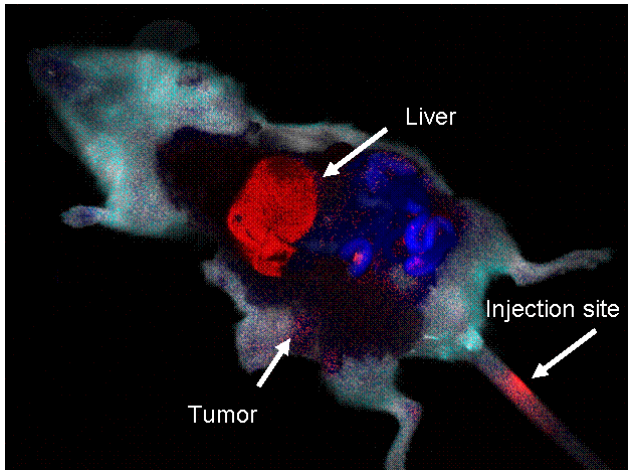
P. Prasad *et al, Nanoscale, 3, 2003 (2011)*



^{19}F-ORMOSIL

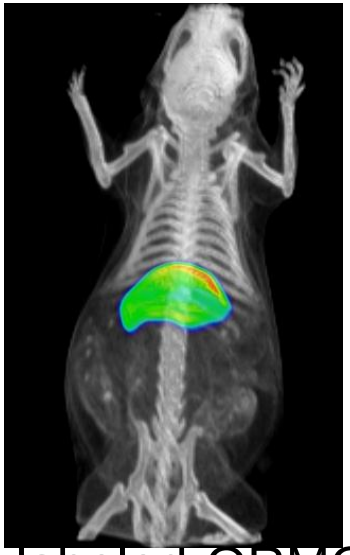
MRI

Optical



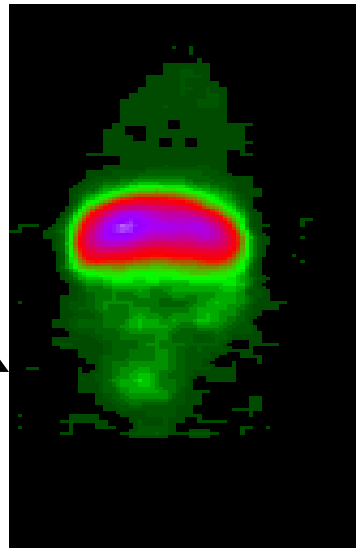
Fluorophore-ORMOSIL

Multimodal *In Vivo* Imaging using ORMOSIL-based Nanoclinic Platform



CT/SPECT

PET



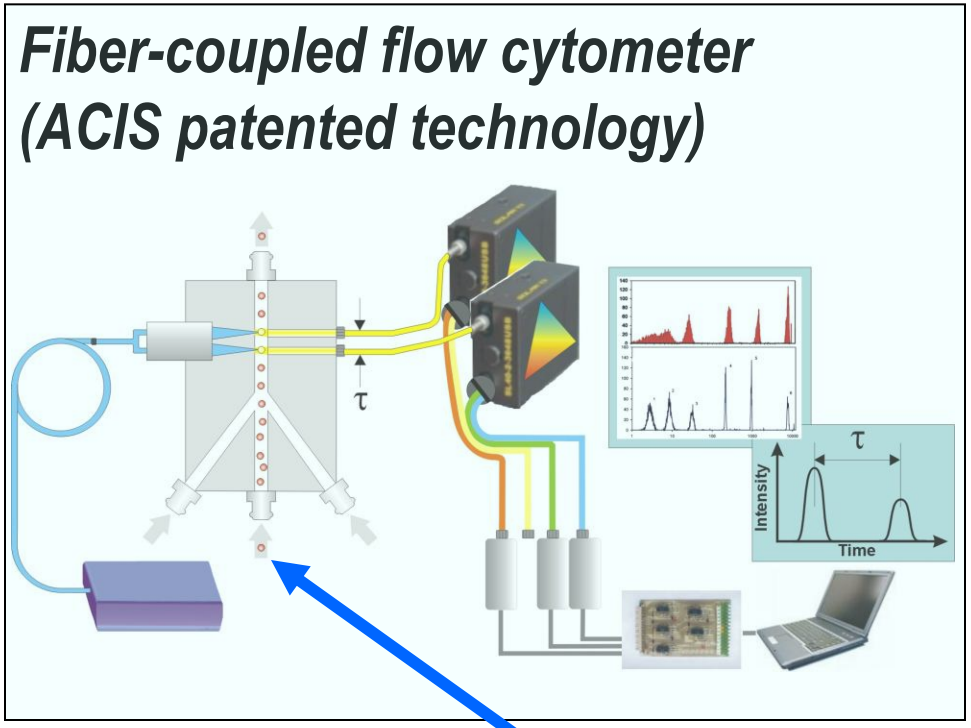
^{125}I labeled-ORMOSIL

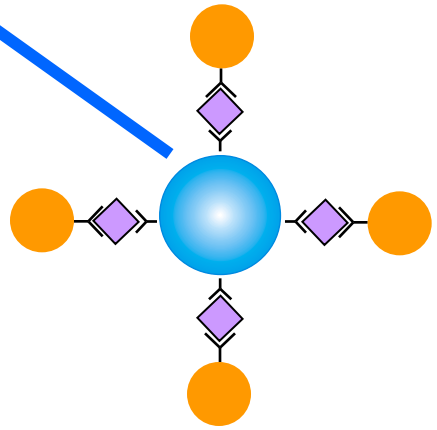
^{124}I labeled-ORMOSIL

HIGH THROUGHPUT FLOW DIAGNOSTICS

High throughput flow diagnostics

Fiber-coupled flow cytometer (ACIS patented technology)

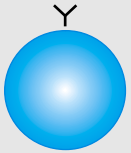




Microbead assay

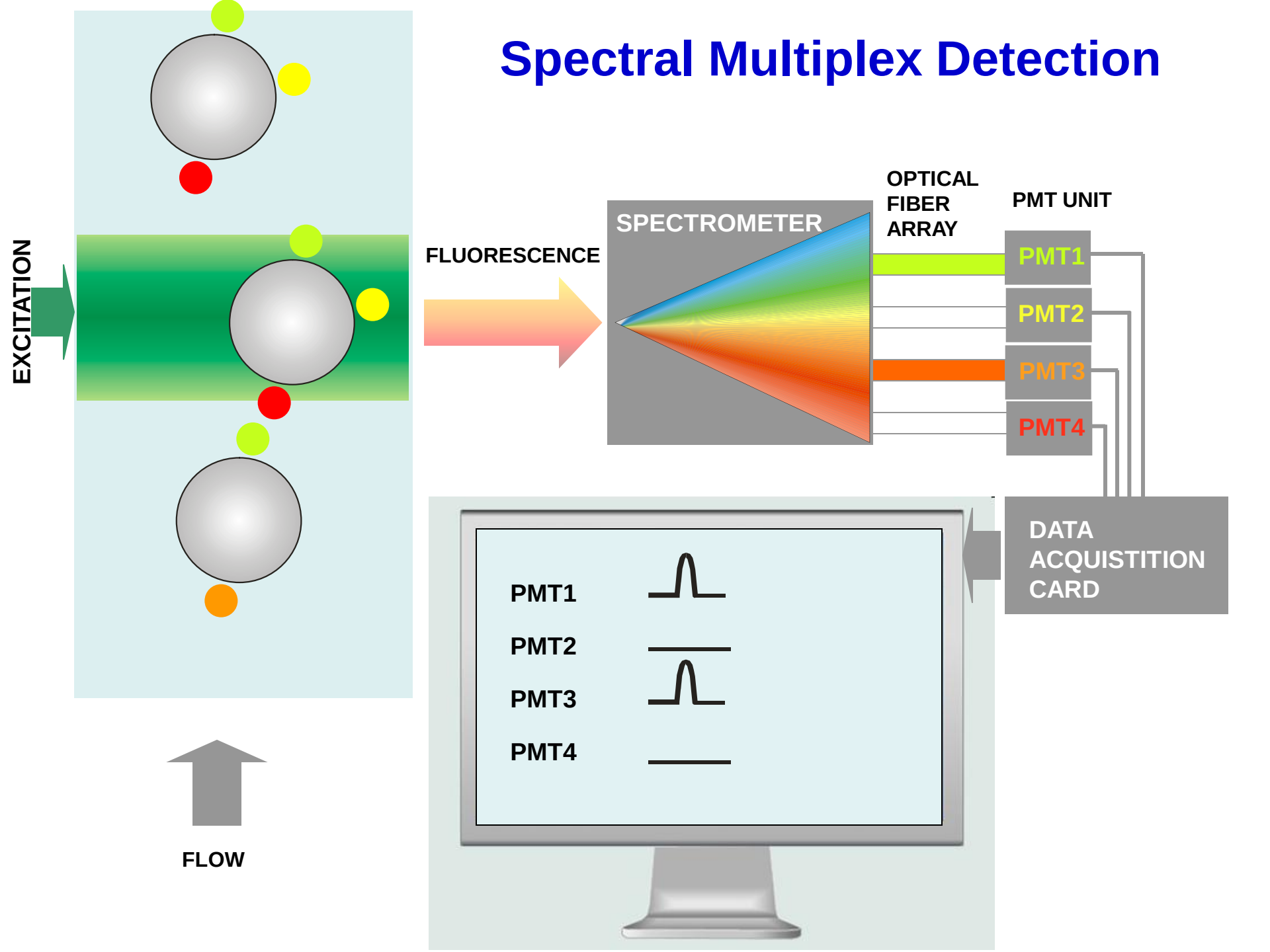
Quantum Dot color coded antibodies

Analytes (disease expression of soluble protein in blood/saliva)

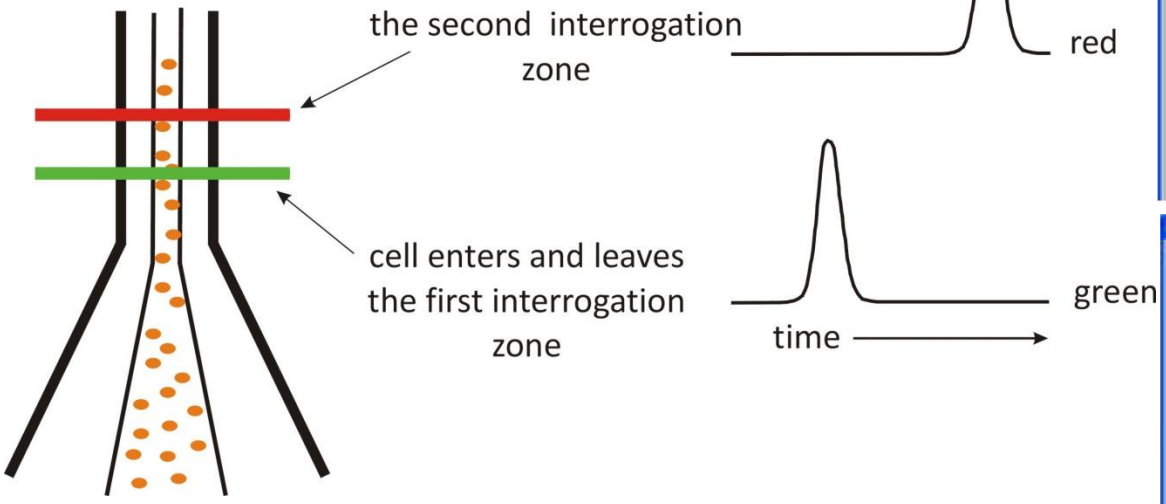


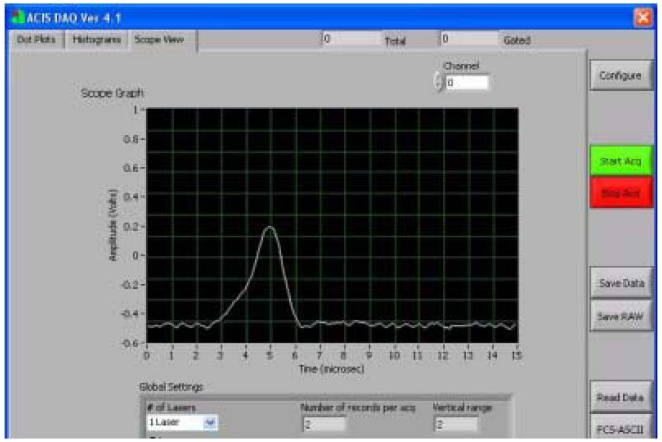
Polystyrene beads conjugated capture antibodies

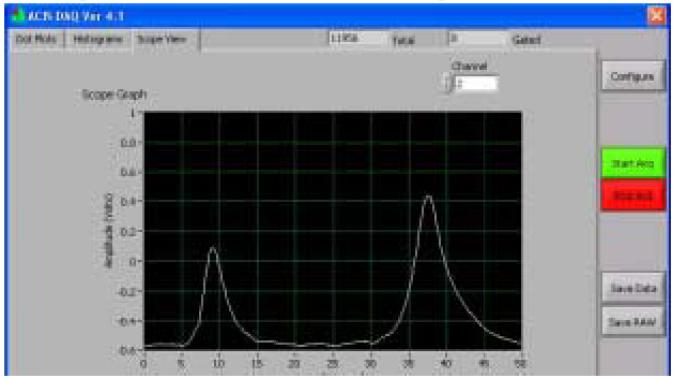
Spectral Multiplex Detection



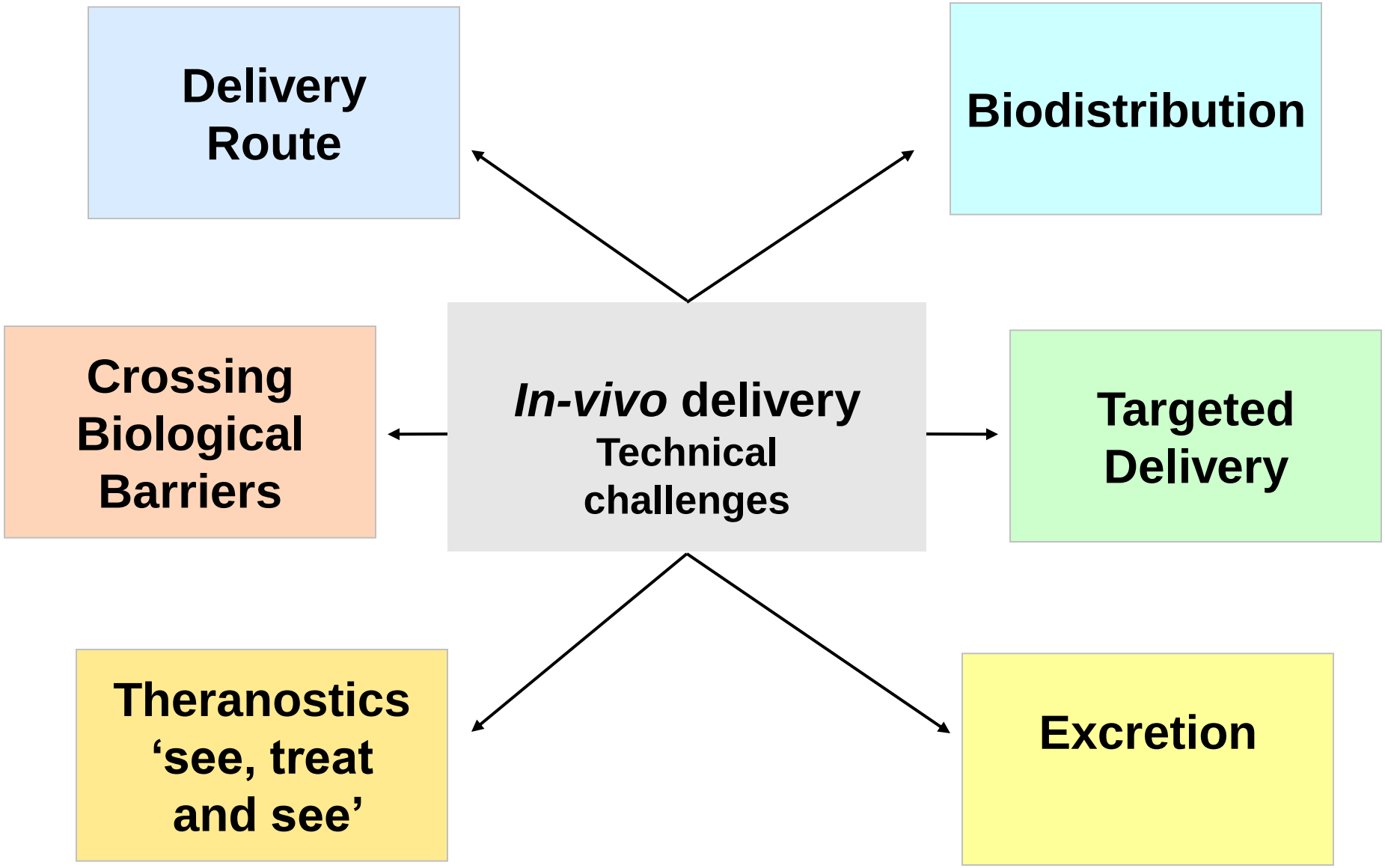
Time Multiplex Detection



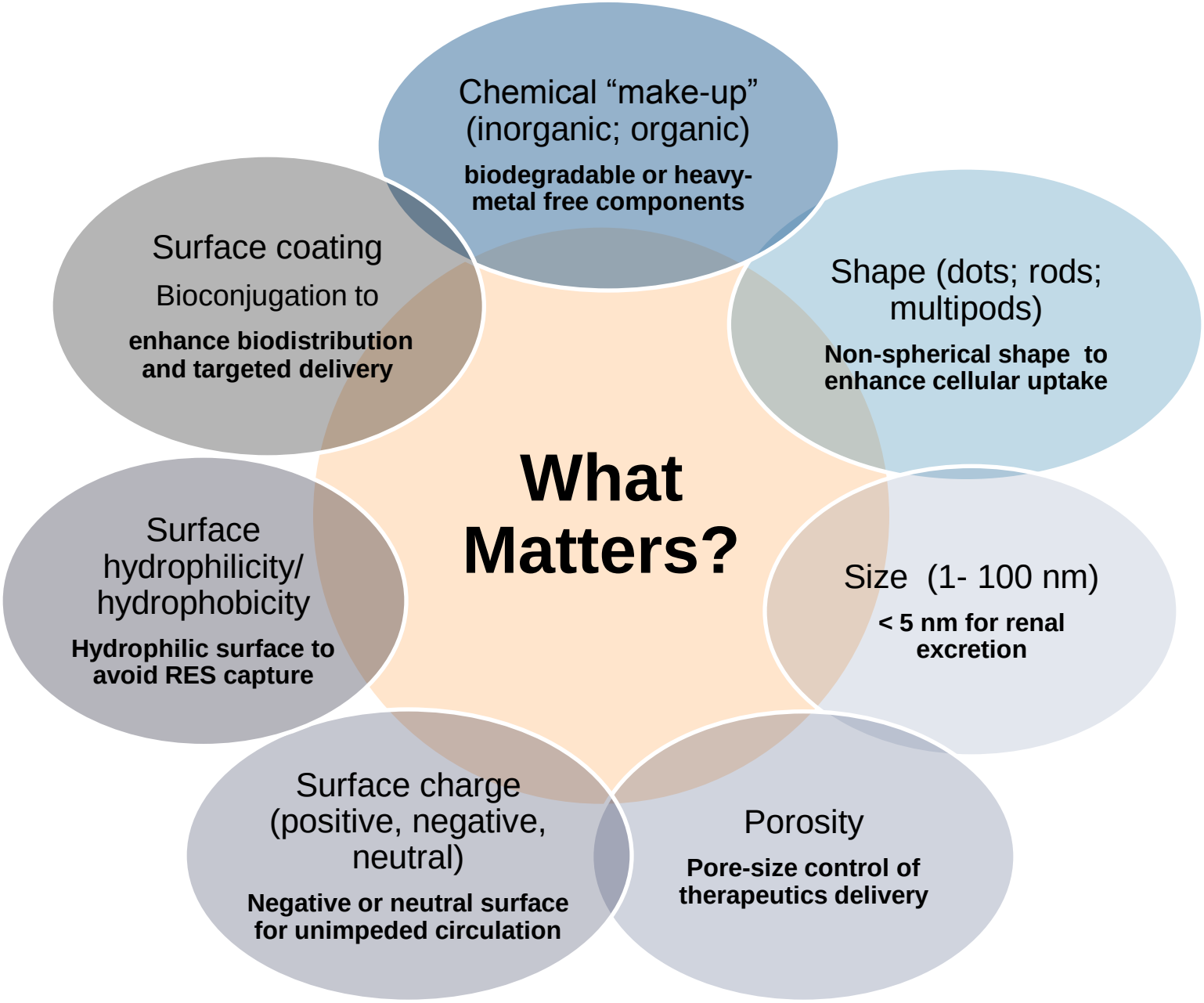




IN VIVO DELIVERY

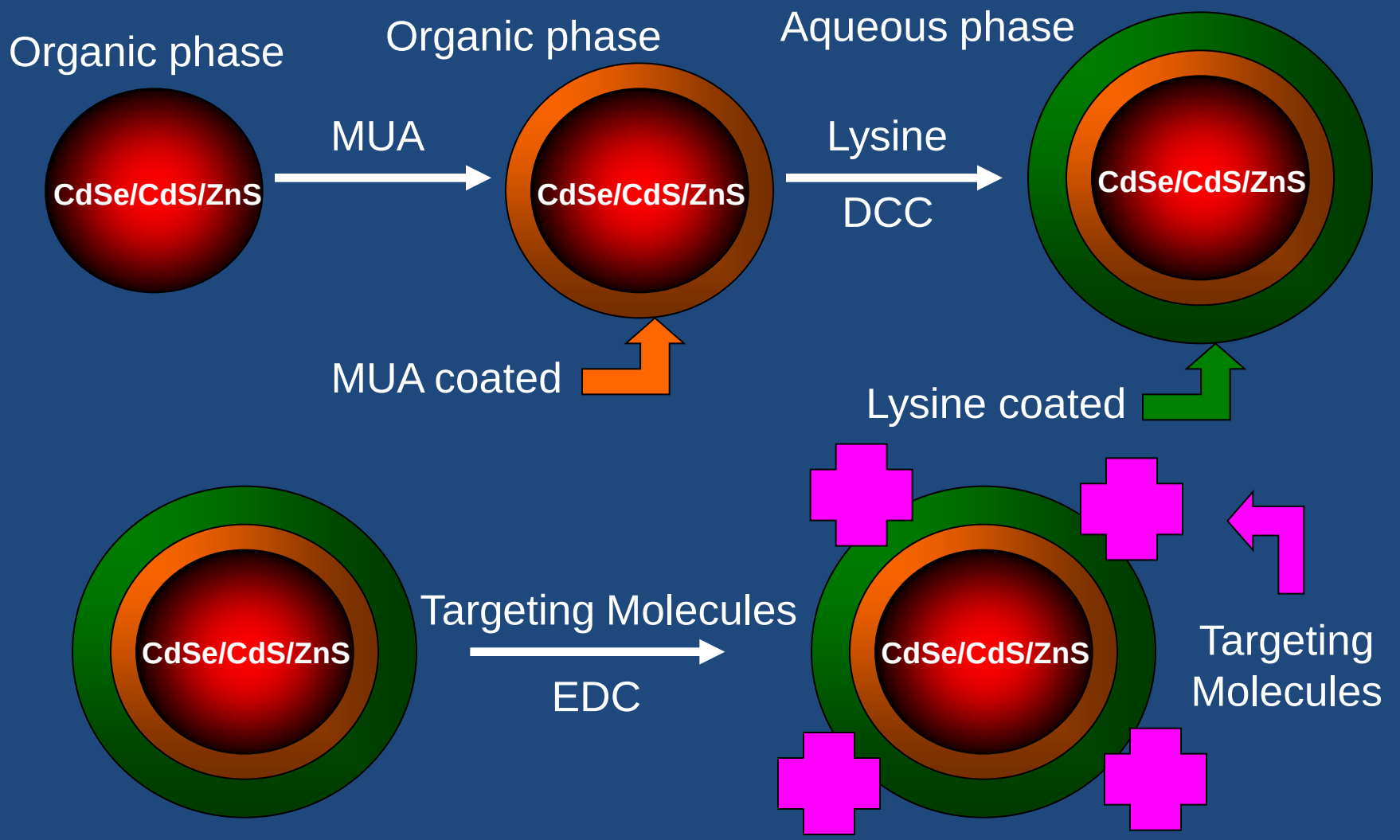

Delivery Route
Biodistribution
Crossing Biological Barriers
In-vivo delivery
Technical challenges
Targeted Delivery
Theranostics ‘see, treat and see’
Excretion

Tailoring of Nanoparticle Platform

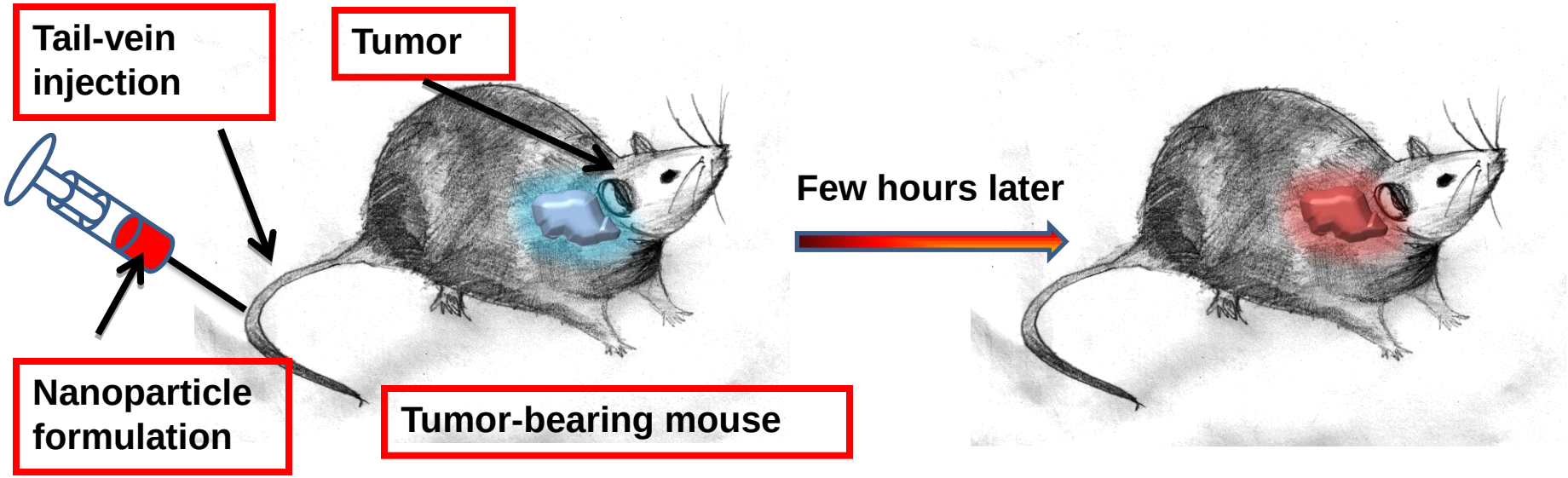


Surface functionalization of nanoparticles

Bioconjugation of Q-dot

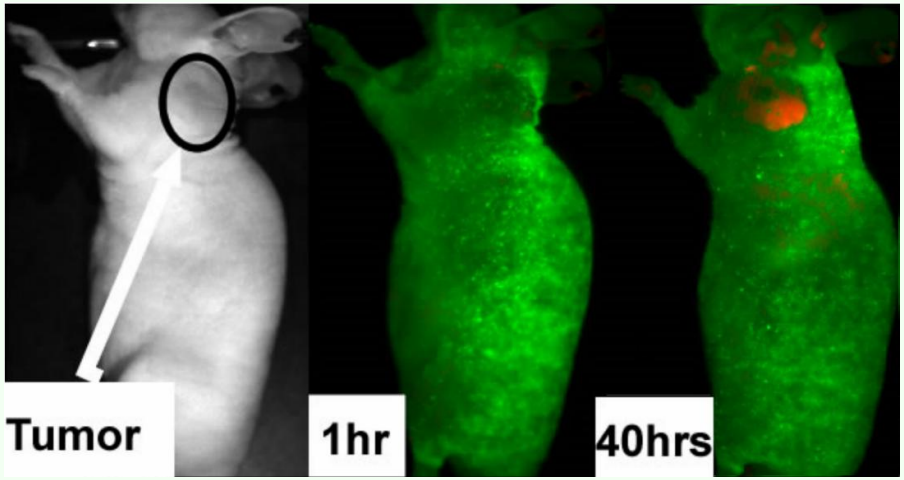


Biocompatible Nano-Silicon for Cancer Targeting in Live animals



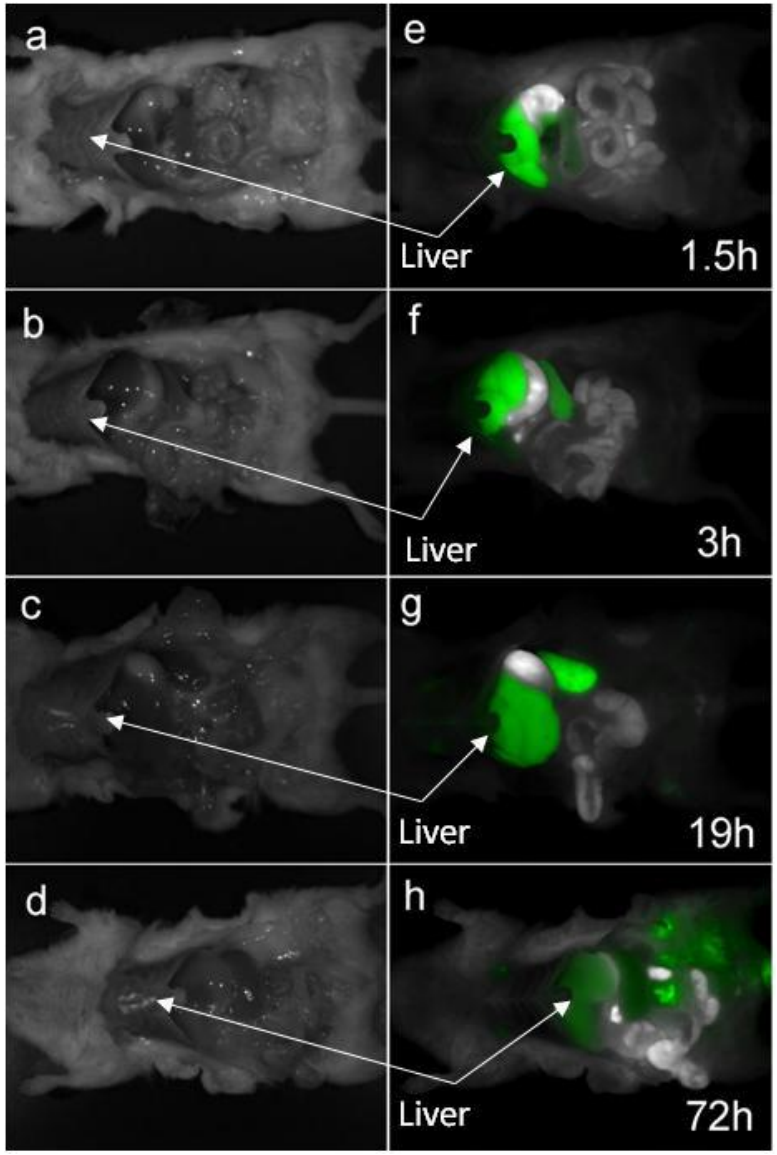
Maestro imaging system

Tumor targeting with nano-silicon



Erogbogbo, Prasad et al. *ACS Nano* 5, 413 (2011).

Excretion of lysine-coated QD



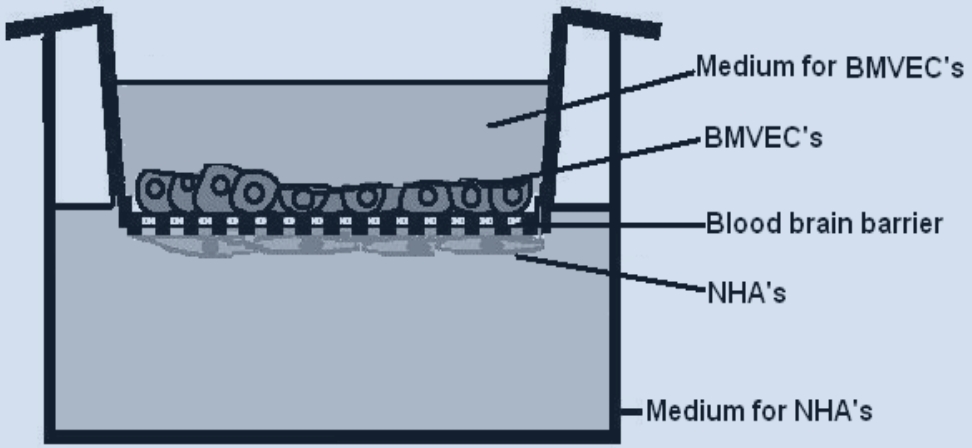
Time dependent liver clearance of lysine-coated QDs

Left: Transmission; Right: Overlay with fluorescence

Prasad et al. Small (2009), 5(17), 1997-2004.

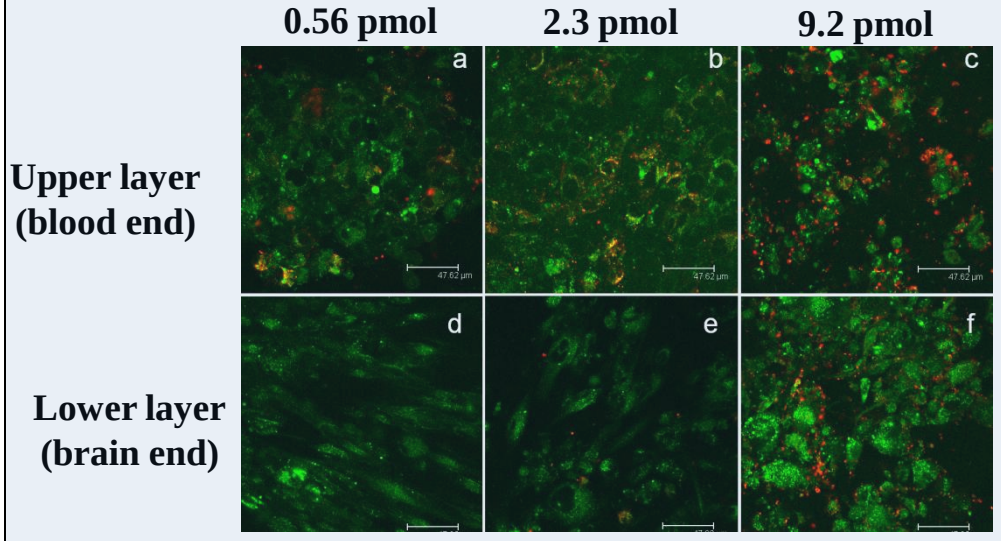
Transferrin (Tf) modified QR for crossing BBB

In-vitro models of biological barriers



BMVECs: Brain microvasculature endothelial cells
NHAs: Normal human astrocytes

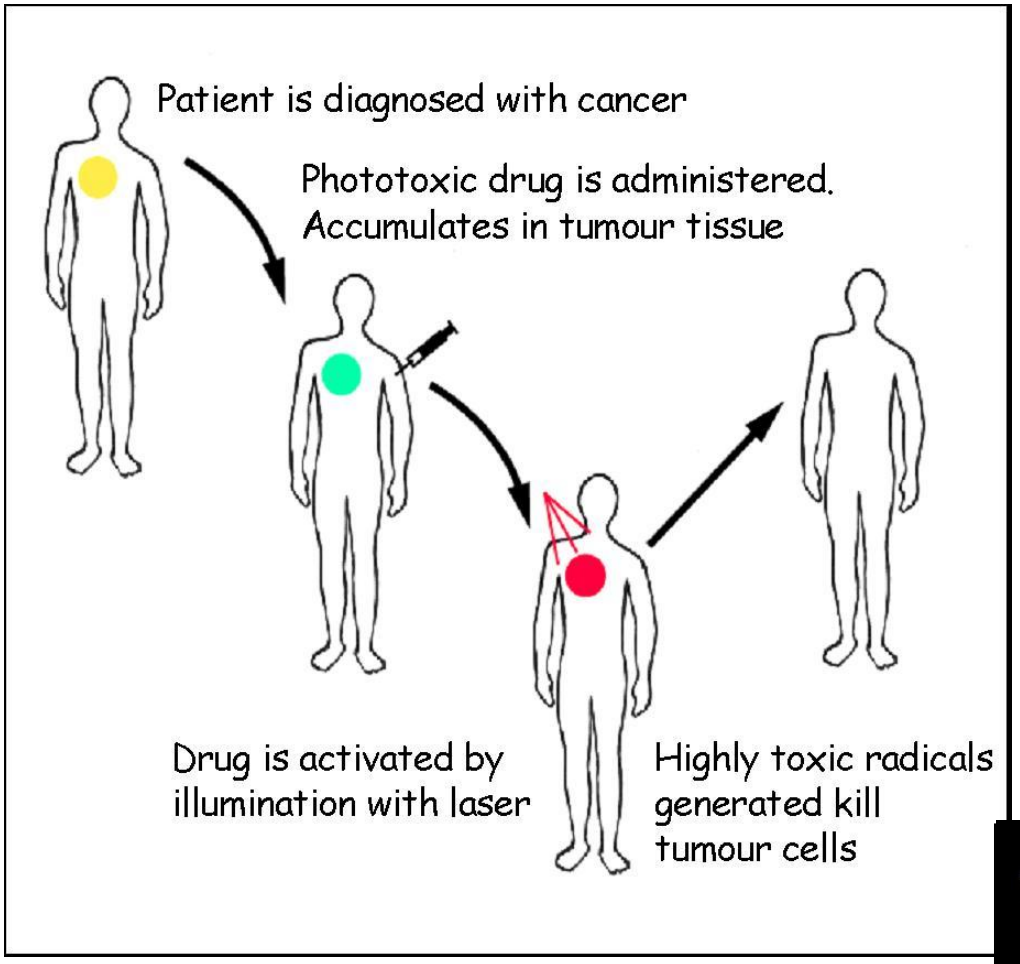
Targeted QRs for *in vitro* Transport Across Blood Brain Barrier

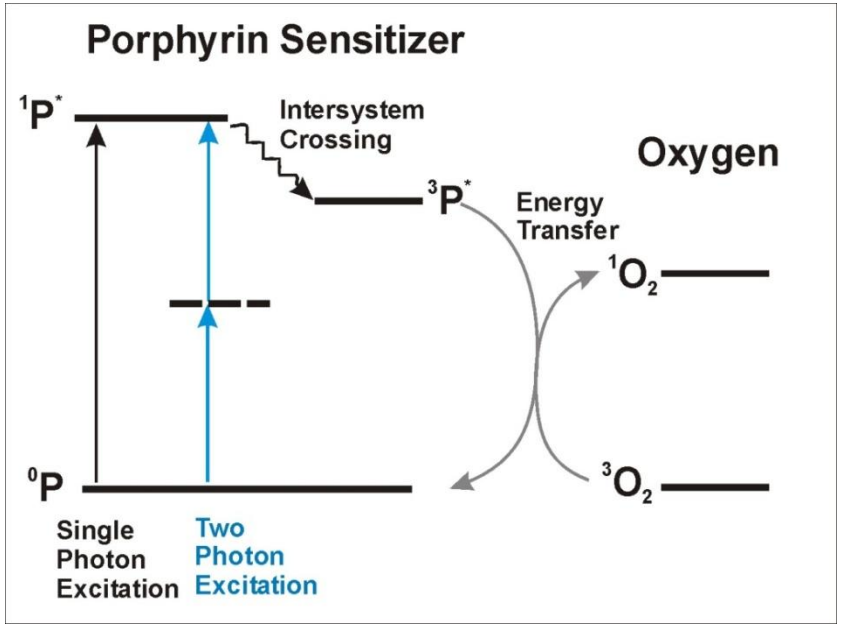


Prasad et al. Bioconjugate Chem., **2008**, *19* (6), pp 1179–1185

LIGHT ACTIVATED AND GUIDED NANOTHERAPY

Photodynamic Therapy



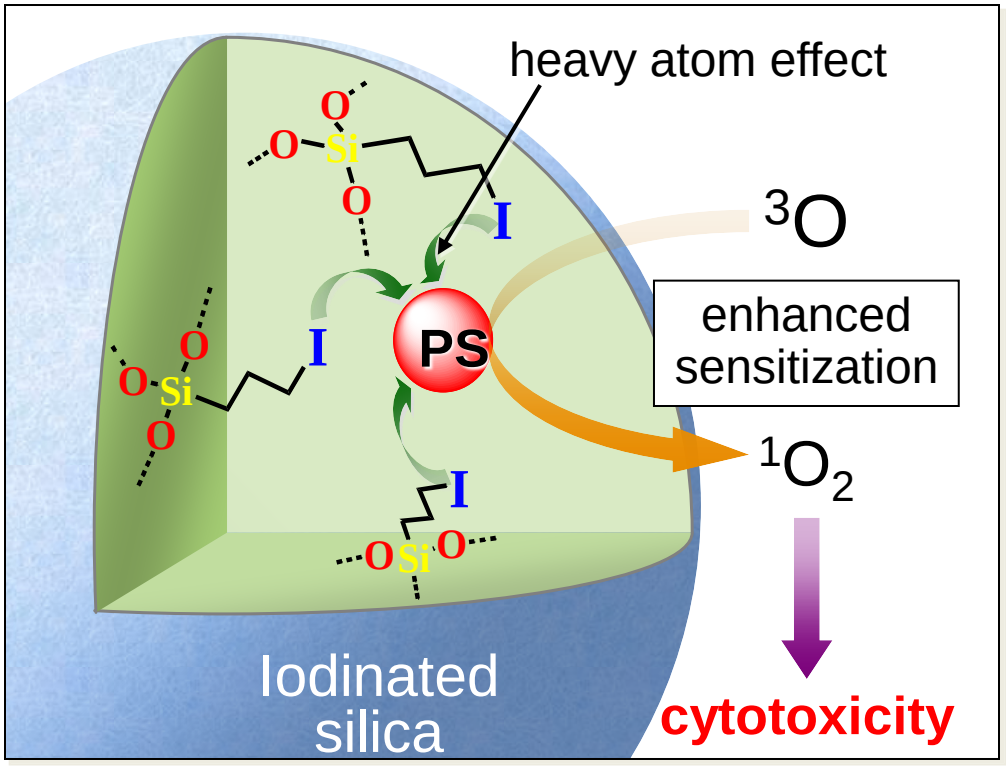


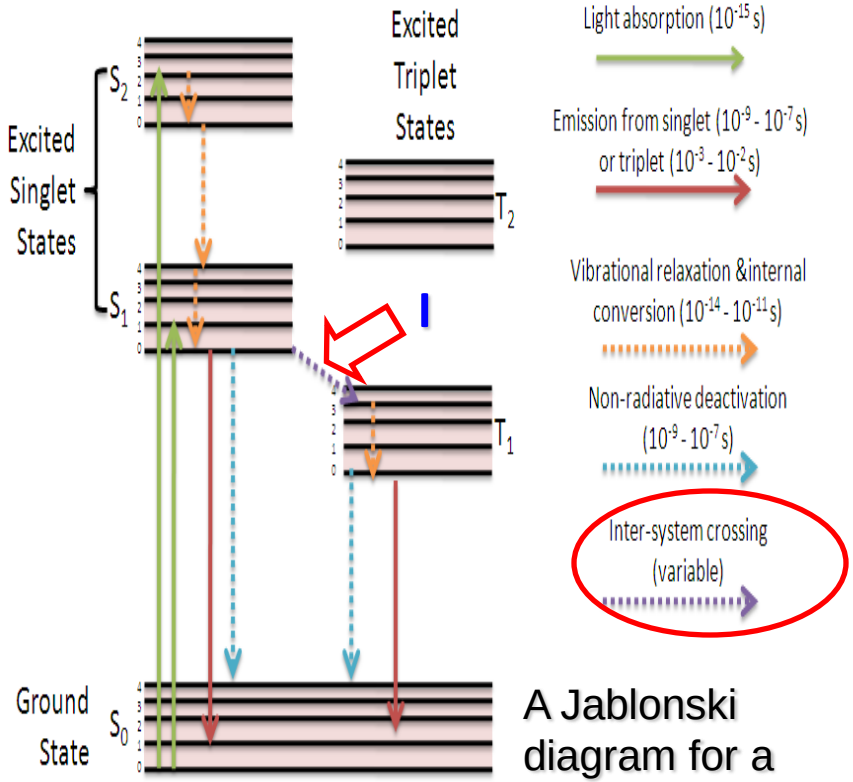
Nanocarrier delivery

Pioneered at Roswell Park

Collaboration with Roswell Park (Dr. R. Pandey)

ORMOSIL Nanoparticles with Intraparticle Heavy-Atom Effect to Enhance Intersystem Crossing

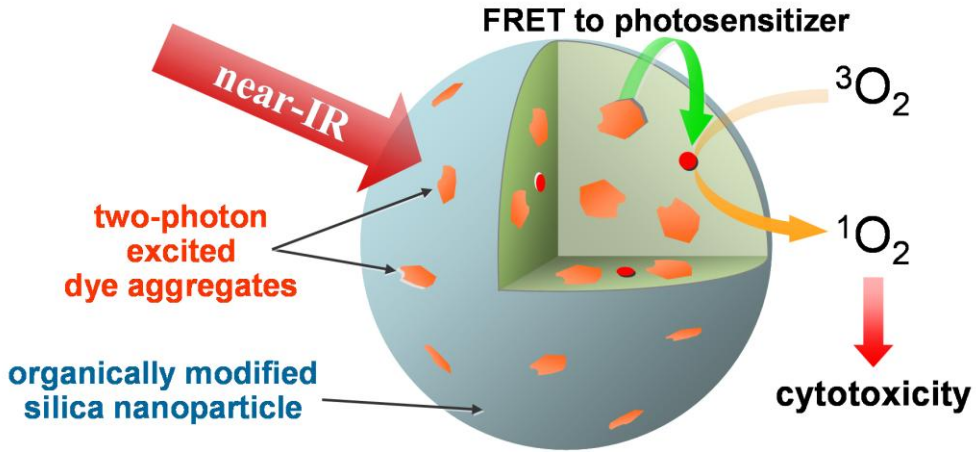


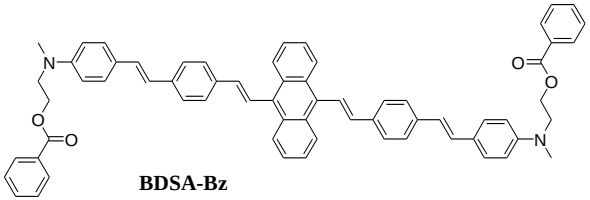


A Jablonski diagram for a molecule of photosensitiser (PS).

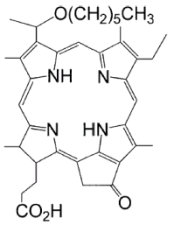
S.Kim, P.N.Prasad et al, J. Phys. Chem.C 2009, 113 (29), 12641

ORMOSIL Nanoparticles Coencapsulating Photosensitizing Drug and Fluorescent Dye Aggregates for Two-Photon Activated PDT

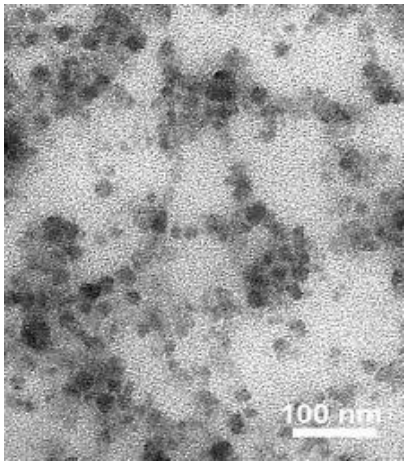




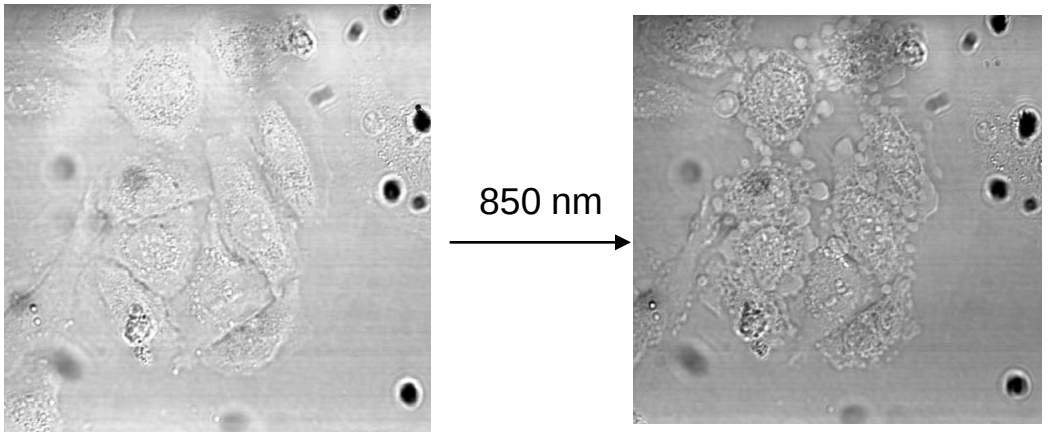
TPA Donor



Singlet Oxygen generating **Acceptor (HPPH)**



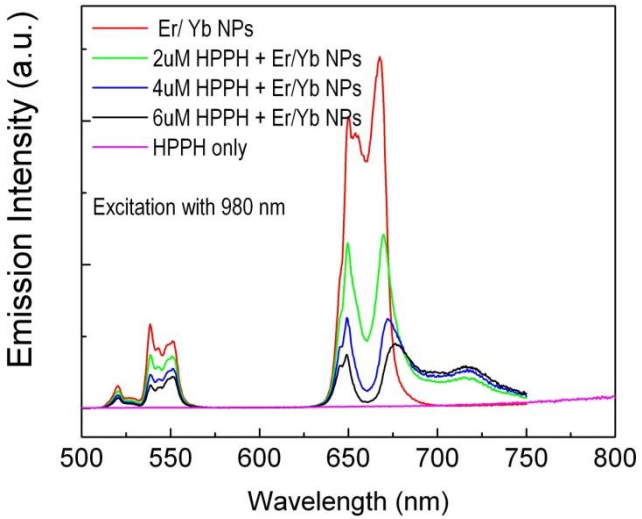
ORMOSIL nanoparticles entrapping HPPH/BDSA



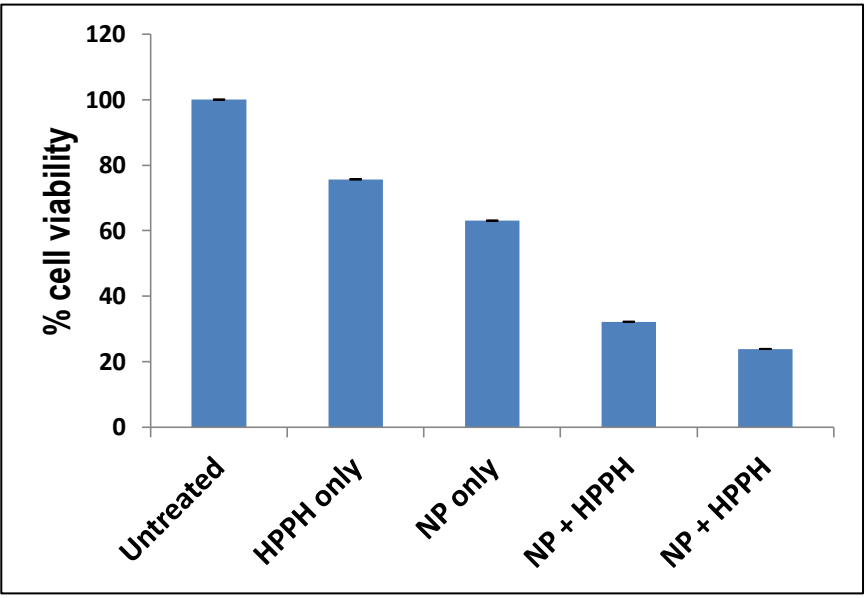
Cells treated with ORMOSIL-HPPH/BDSA nanoparticles before and after excitation at 850 nm

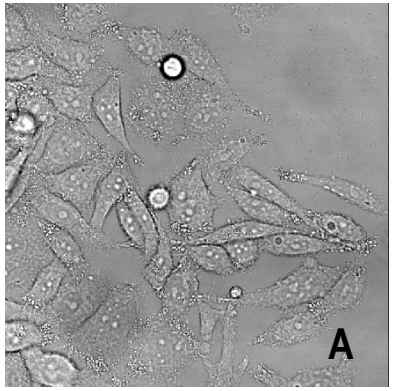
S. Kim, et al., J. Am. Chem. Soc. (2007) , 129(9); 2669-2675

Upconversion photodynamic therapy with ormosil nanoparticles co-entrapping the upconverting nanophosphors and PDT drug

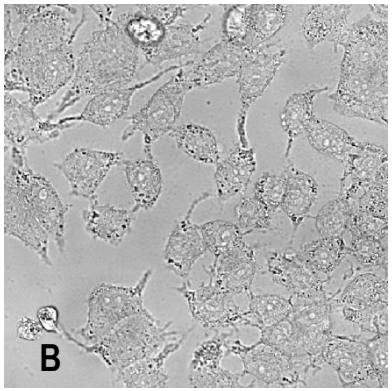


Energy transfer between Yb/Er nanophosphors and photosensitizer (HPPH) co-entrapped within ormosil nanoparticles

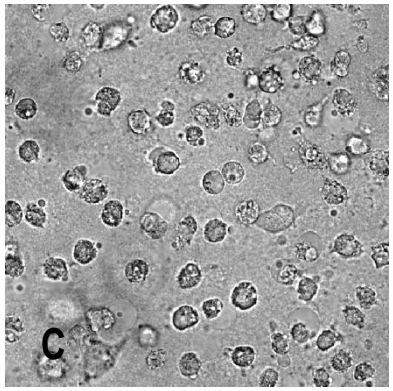




NP only



HPPH only



HPPH + NP

Panc-1 cells treated with ormosil nanoparticles entrapping the upconverting Yb/Er nanophosphors (A), HPPH (B) and co-entrapping both the upconverting Yb/Er nanophosphors and HPPH (C).

.

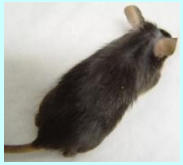
All cells were irradiated with 980 nm

Visible phototoxic action under excitation with 980 nm

R.Kumar, T.Y.Ohulchanskyy, P.N.Prasad, unpublished

Huntingtons Disease

Generation of mouse model using gene insertion



Lung Injury

Increase gene expression after injury to prevent secondary bacteria infection

Drug Addiction

Gene silencing of signaling cascade involved in addiction process

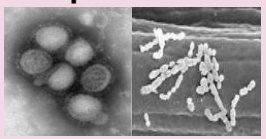
Chronic Pain

Gene silencing of neuron signaling pathways involved in chronic pain

Gene Therapy using ORMOSIL and GNR Nanoparticles

Infectious Disease

Gene silencing to modulate primary influenza infection and secondary bacteria pneumonia



Obesity

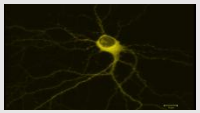
Modulation of energy intake using gene silencing

Asthma

Gene silencing of enzymes causing lung remodeling

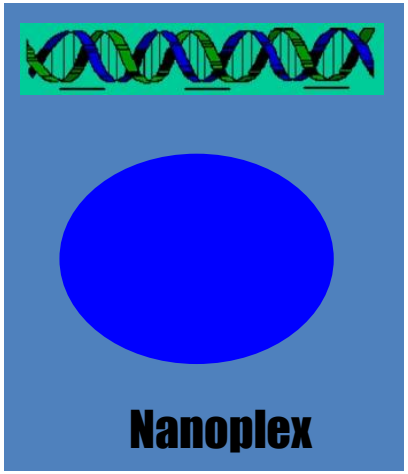
Stroke

Stimulation of neuron repair/replacement (neurogenesis) using gene upregulation

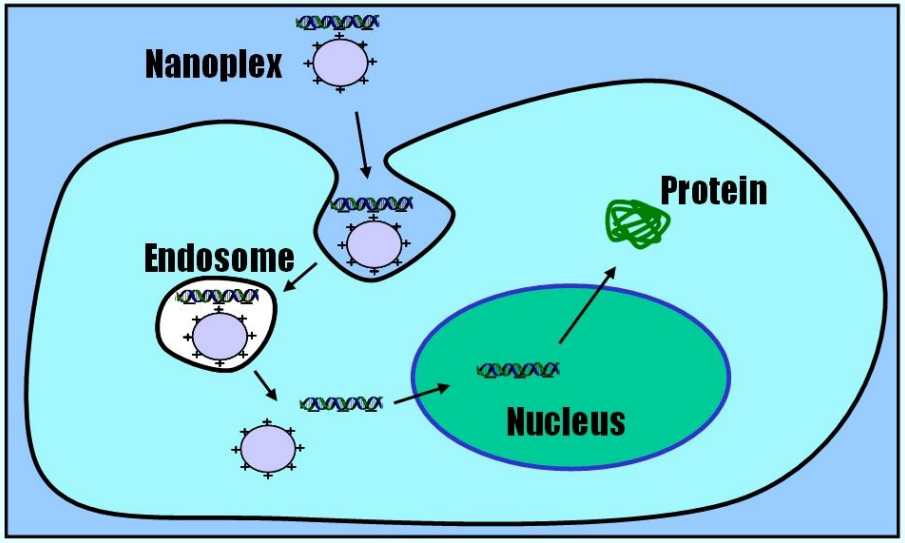


Gene delivery using nanoparticles

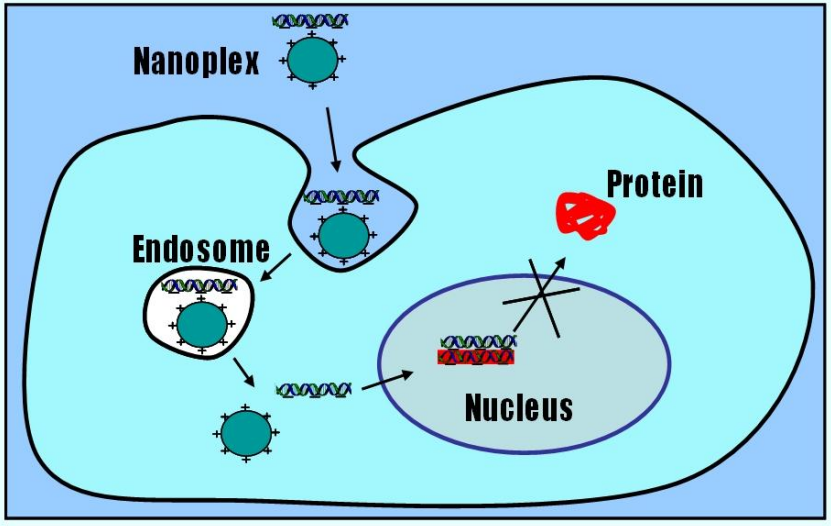
- **Electrostatic gene condensation**
- **Efficient cellular entry**
- **Non-toxicity**
- **High gene expression/silencing**



Gene Augmentation e.g. CFTR gene in Cystic Fibrosis



Gene Silencing e.g. Oncogene in Cancer



Nano-Biophotonics and Gene Delivery

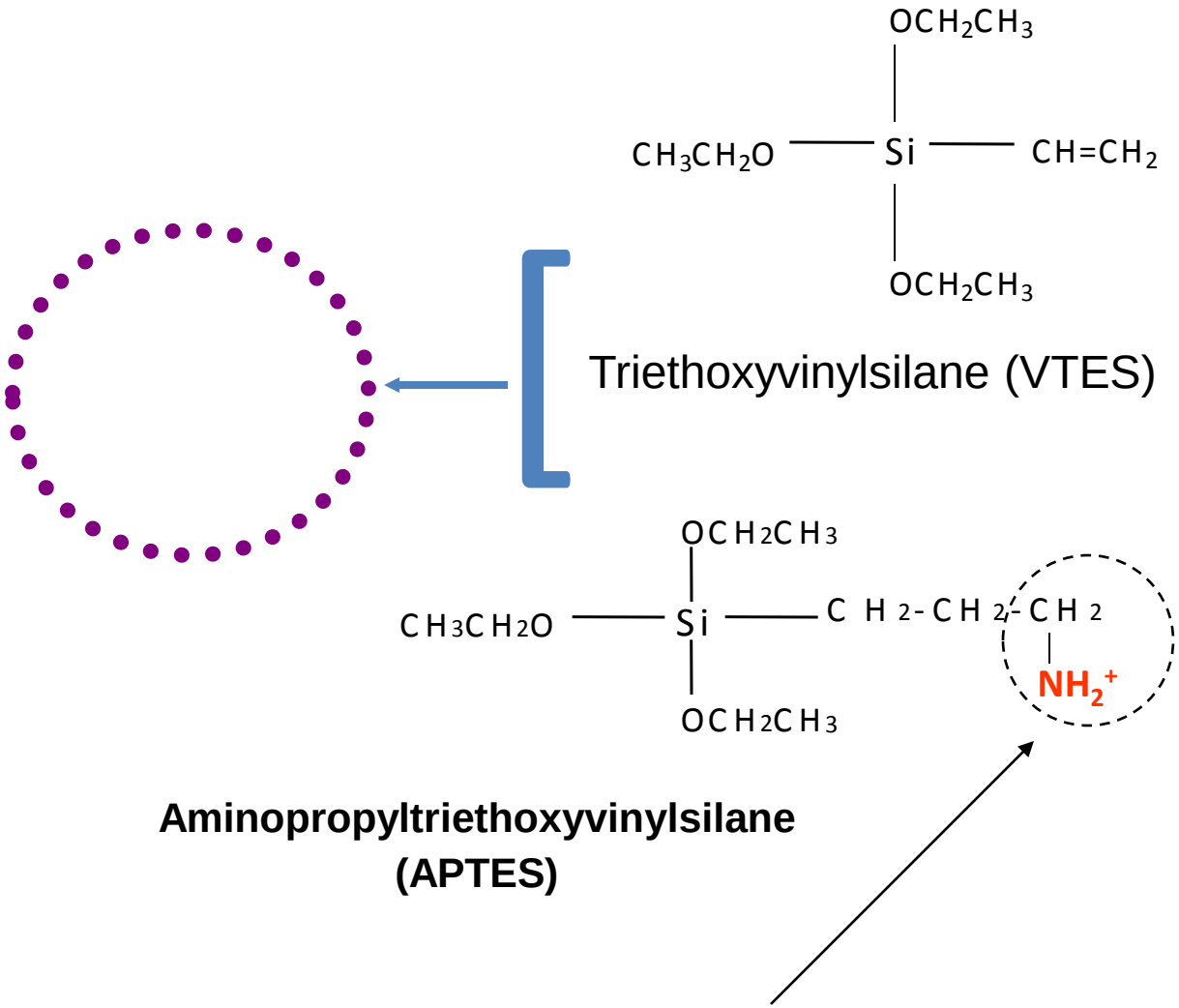
Optical Monitoring of Nanoparticles Carrying genetic payload (Binding, protection from enzymatic degradation, biodistribution)

Light activated and optically monitored release of genetic materials

Optical probing of localization in the nucleus

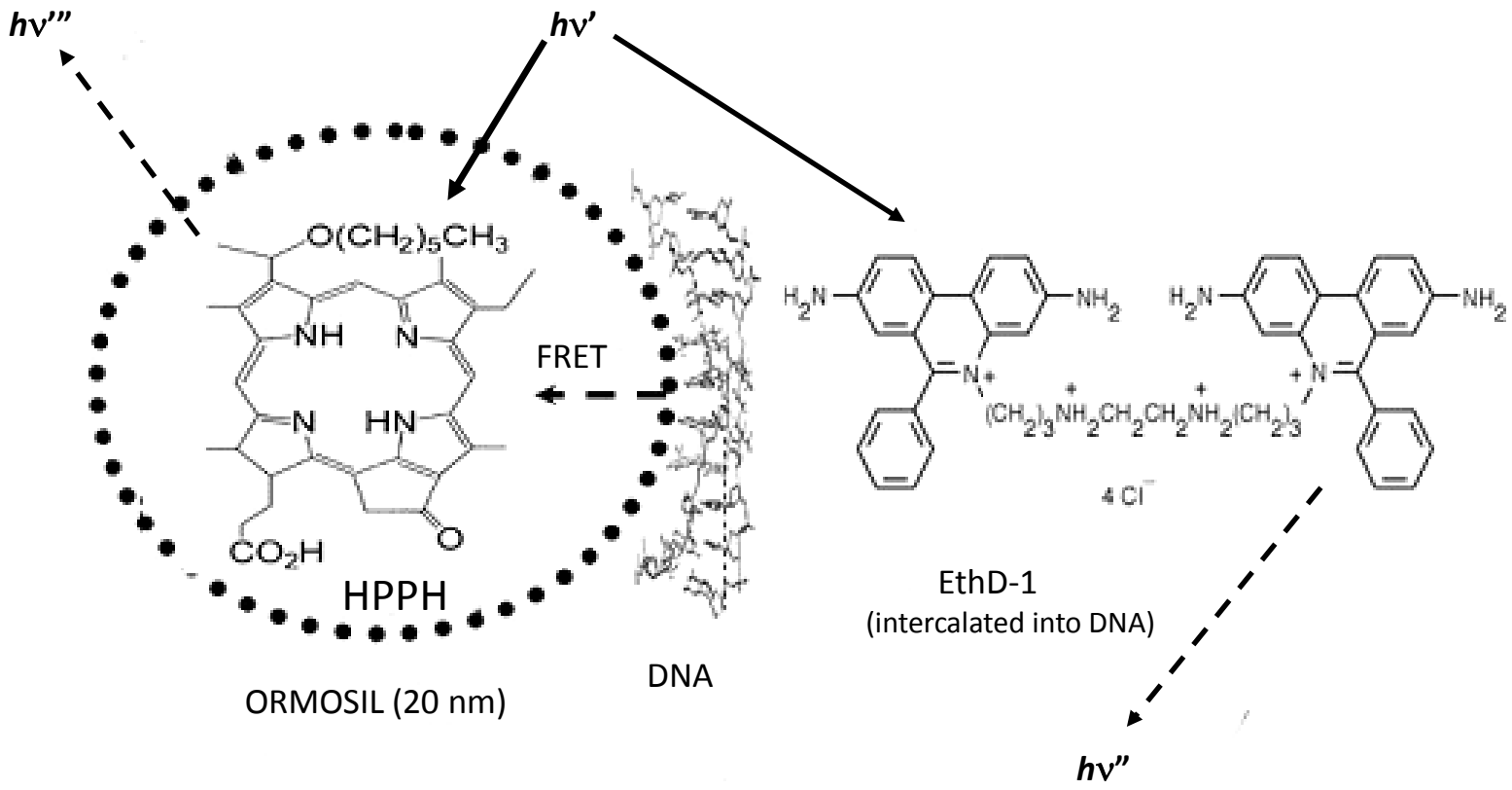
Optical sensing of gene expression using a fluorescent protein vector

Organically modified silica (ORMOSIL) cationic nanoparticles as DNA carriers for gene therapy



Optically Trackable ORMOSIL

Nanoparticles for Gene Delivery



I. Roy, T. Y. Ohulchanskyy, D. J. Bharali, H. E. Pudavar, R. A. Mistretta, N. Kaur, and P. N. Prasad. *PNAS*, 102 (2): 279 (2005).

Can We Live for 1,000 Years ?

Yesterday's imagination

Fountain of youth and longevity

Today's Innovations

Nanomedicine defining the path to Rejuvenation Therapy

Tomorrow's patient care

Health , Wellness and Longevity

Nanomedicine for Rejuvenation Therapy

Free radical removal

Heavy metal removal

Neurological repair

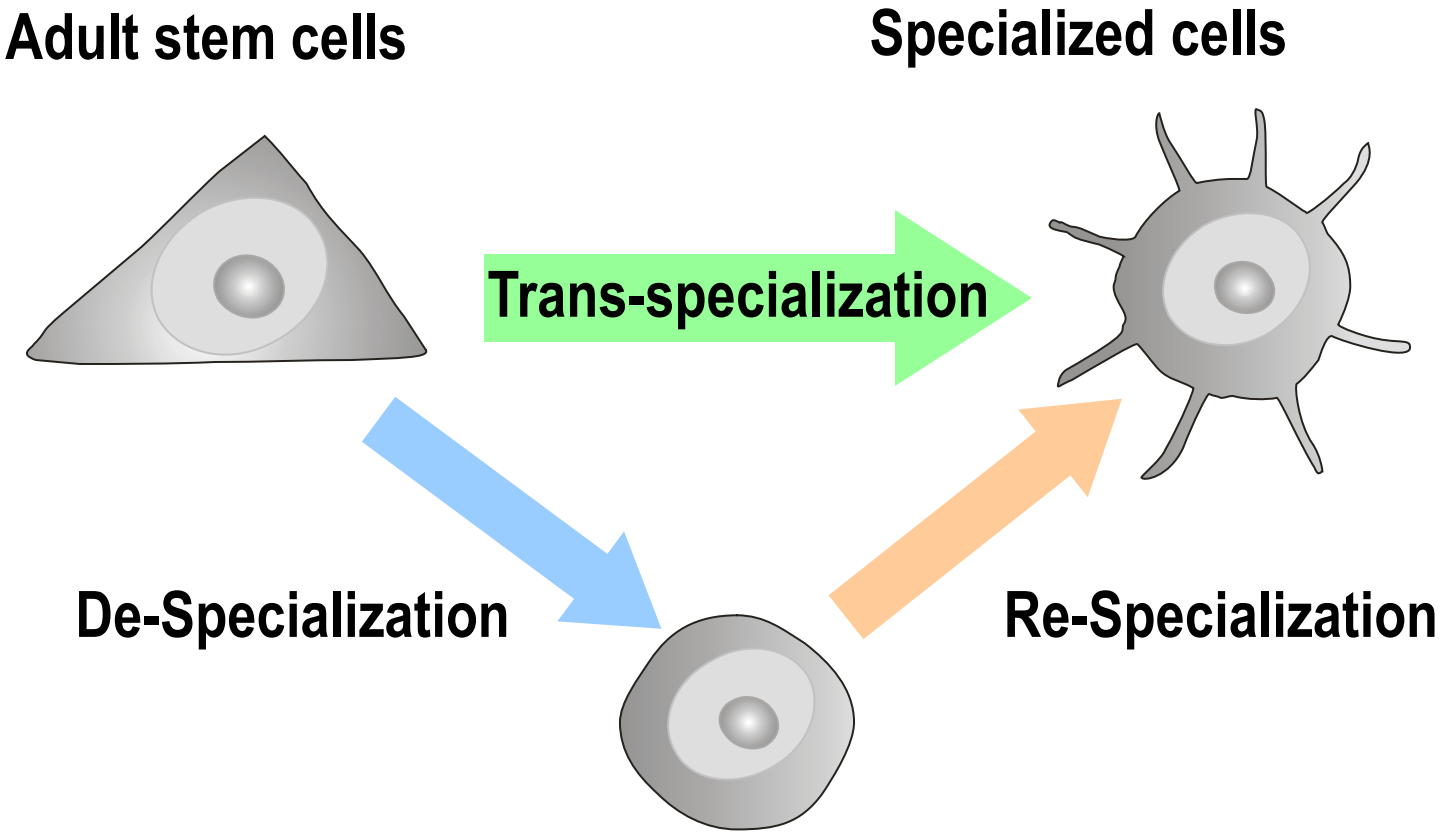
Rejuvenation Therapy

Growth hormone therapy

Stem cell therapy

Tissue engineering and organ printing

Stem cell Nanotechnology

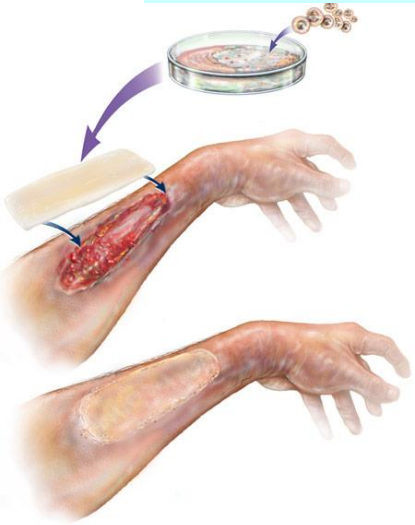


Collaboration: Prof. Jian Feng,
Physiology & Biophysics
University at Buffalo

Nanotechnology based Tissue Engineering

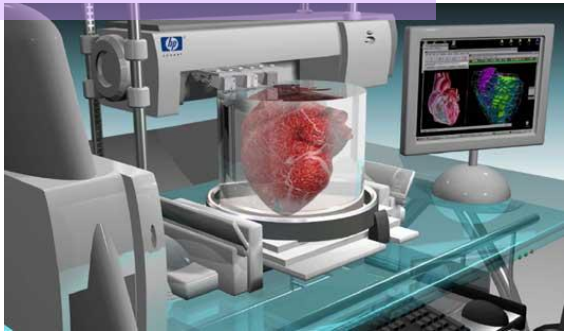
Tissue regeneration

Assembling and Differentiation of Cells on a Biodegradable Scaffold



Organ/tissue printing

Printing of 3-D Assembly of Cells in a Gel Matrix to Generate Tissue Structures and Organs



Tissue nanoengineering

Tissue bonding

Repair of a Tissue Fracture or Tear by Welding or Soldering

Non-human primate nanotoxicity studies

Blood chemistry, behavioral and histological studies indicated no toxicity

Ye, L., Yong, K.-T., Liud, L., Roy, I., Hu, R., Zhu, J., Cai, H., Law, W.-C., Liu, J., Wang, K., Liu, J., Liu, Y., Hu, Y., Zhang, X., Swihart, M.T., and Prasad, P.N. *Nature Nanotechnology* 7, (2012).

Opportunities

- **Photostable , Biodegradable , nontoxic and water dispersible Near IR Nanoemitters with high quantum yield**
- **Optical funtionalities coupled with other funtionalities**
- **Multidimensional and functional imaging, combining biosensing**
- **MEMS/NEMS, micro/nano fabrication, integrated optics for minituarization**
- **Nanoemitter based Microarray technology**
- **Nanoparticle tracking and photoactivation for Gene delivery, Stemcell biotechnology and Tissue Engineering**
- **Light activated and light guided therapy**

Acknowledgements

UB team

- Prof. P. Knight, MD
- Prof. S. Schwartz, MD
- Prof. M. Swihart
- Prof. E. Morse
- Prof. K. Tramposch
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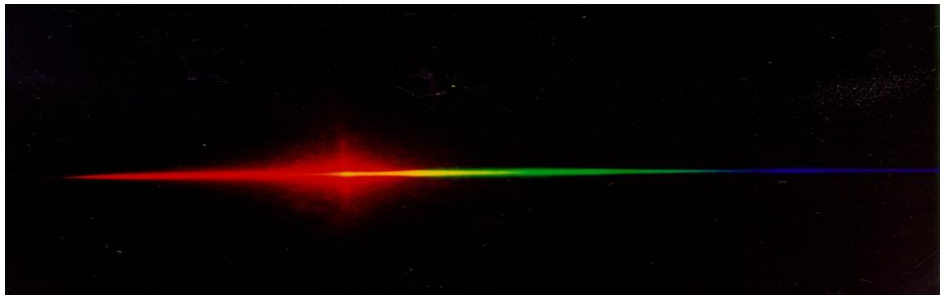
- Dr. T. Ohulchanskyy
- Dr. A. Kachynski
- Dr. A. Kuzmin
- Dr. A. Pliss
- Dr. A. Baev
- Dr. F. Erogbogbo
- Dr. W.C. Law
- Dr. W.J. Kim
- Dr. A.Kopwitthaya

Outside Collaborators

- Prof. R. Pandey
- Dr. P. Wallace
- Dr. U. Sinha, MD
- Dr. R. Masood
- Dr. A. Maitra, MD
- Prof. A. Gomes
- Prof. J. Qu

AFSOR
National Cancer Institute
National Science Foundation
AFRL
OISHEI FOUNDATION

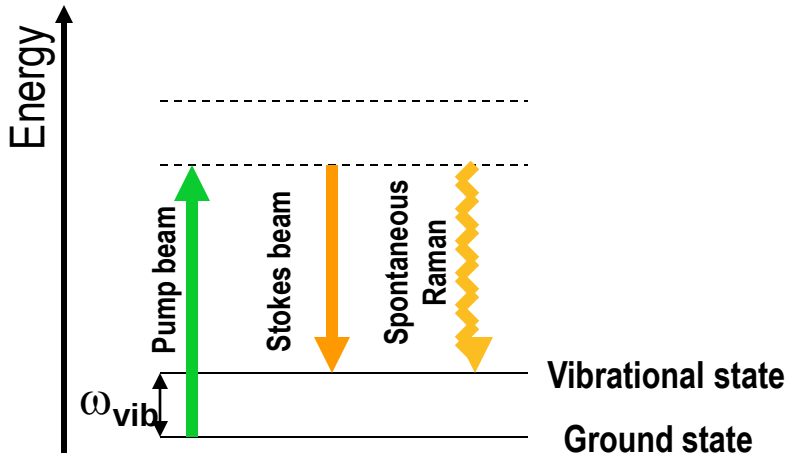
“Lighting the Way to Technology through Innovation”

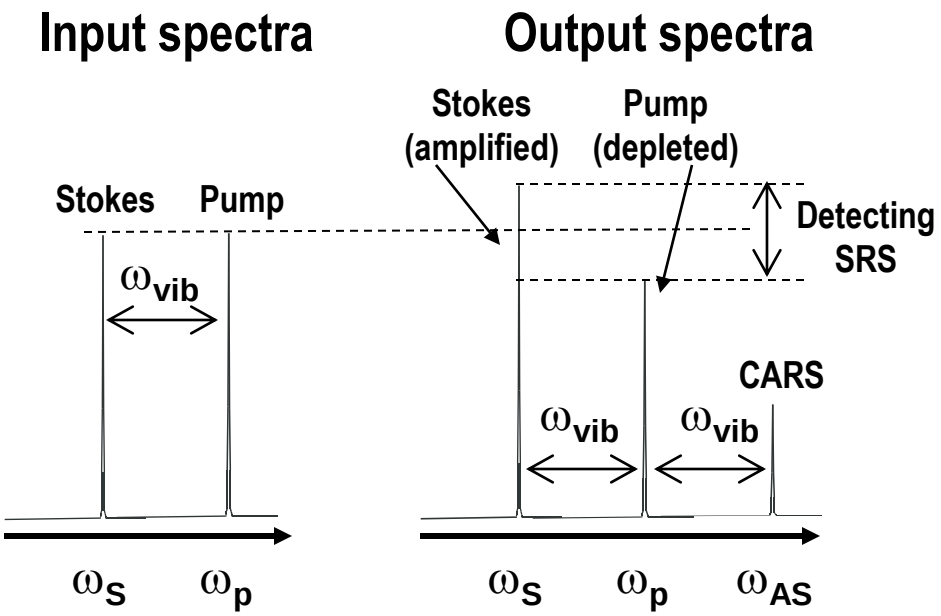


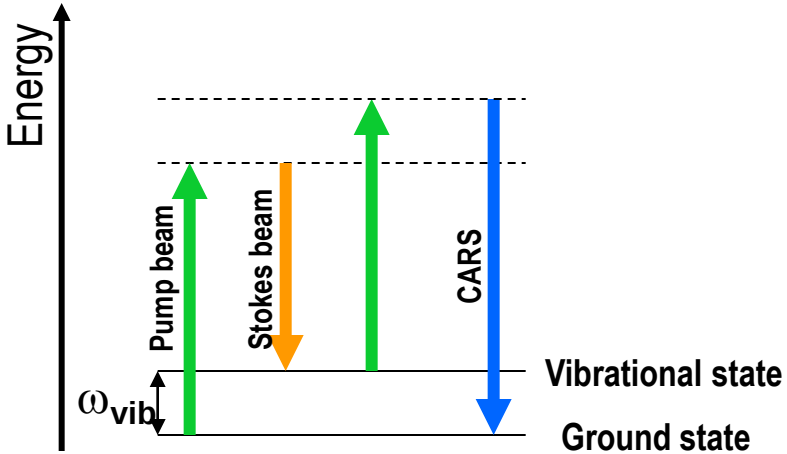
Thank you!

P.N.Prasad

Stimulated Raman vs CARS



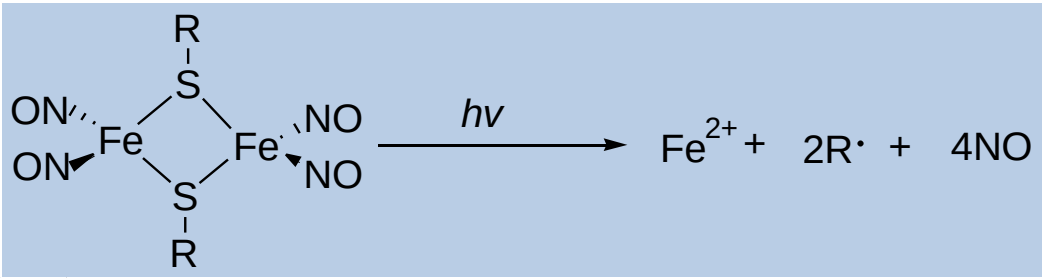


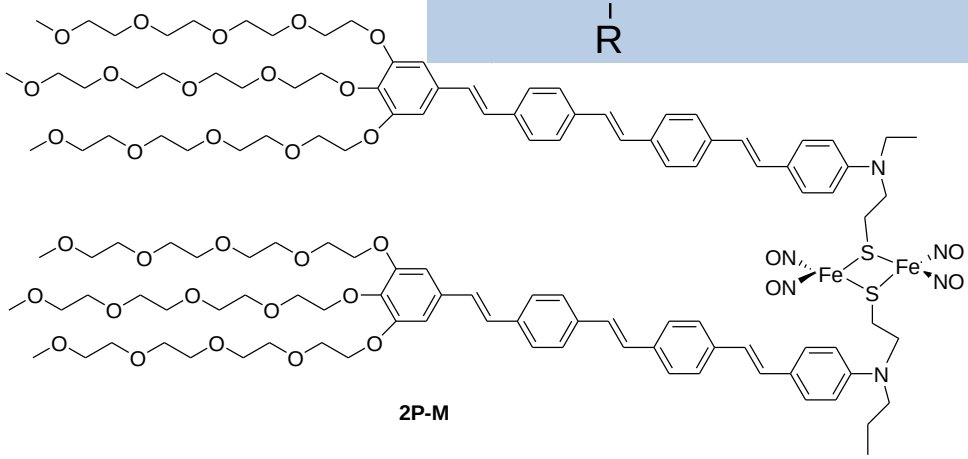


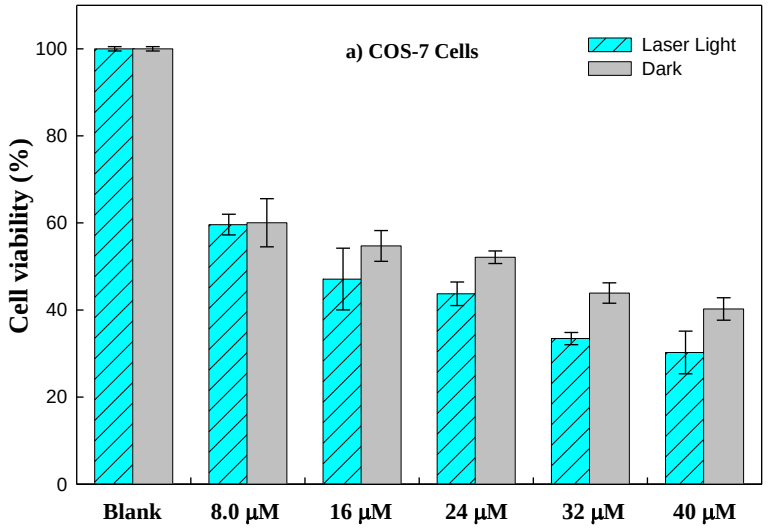
Background, which has to be removed for adequate bioimaging:

- CARS: non-resonant signal of four-wave interaction
- SRS: Stokes wave used to form SRS

Different approach: water soluble two-photon absorbing nitrosyl complex for light activated therapy through nitric oxide release







Percentage of cell survival of Cos-7 cells, after treatment with 2P-M and subsequent irradiation with 775 nm laser light for 5 minutes (with reference to untreated cells under dark as having 100 % survival).

Q. Zheng, A. Bonoiu, T. Y. Ohulchanskyy, G. S. He and P. N. Prasad, Mol. Pharmaceutics, 5 (3), 389–398 (2008)

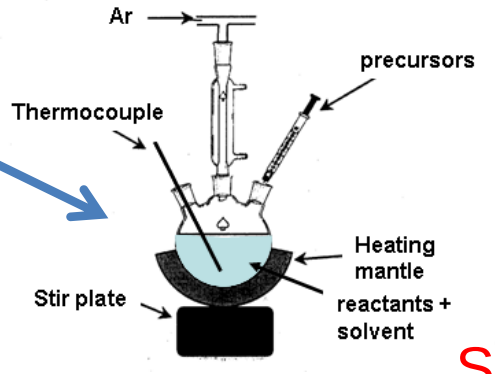
Synthesis of Up-conversion Nanocrystals

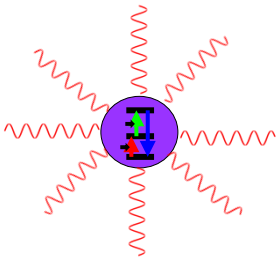
$Ln(CF_3COOH)_3 + M(CF_3COOH)_3$

Thermolysis

Oleic Acid
Coordinating ligand

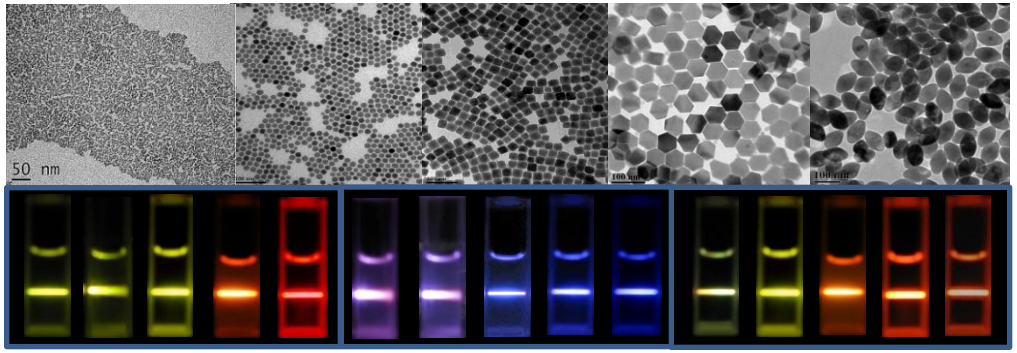
$MLnF_4$ Nanoparticles
(M=Li, Na, K)





Size: 5-20 nm

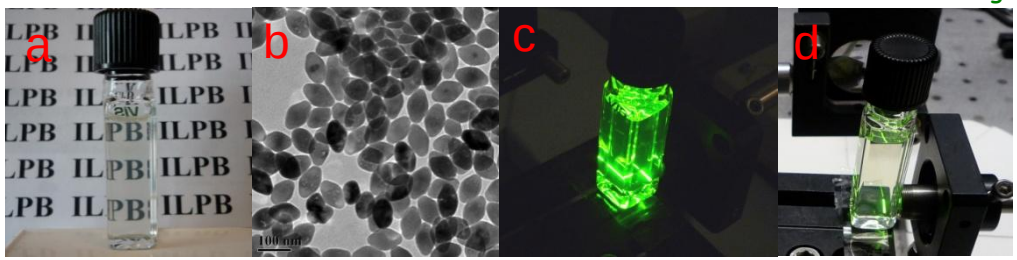
Dispersion: Organic solvents



Controlled synthesis of fluoride upconversion nanocrystals with a wide range of 3-100 nm through controlling the growth Dynamics

Tuning Color Output using
different Lanthanide Ions and Ion-Ion Interactions

980 nm Excitation
Yb3+ sensitizing



Er3+ sensitizing
1490 nm Excitation

Harvesting Different NIR Light Using different Lanthanide Ions

Prasad et al. ACS Nano, **2012**, *6* (4), pp 2969–2977