

# Luminescence Nanothermometry in Living Cells

**Fiorenzo Vetrone**

Université du Québec, Institut National de la Recherche Scientifique –  
Énergie, Matériaux et Télécommunications, 1650 Boul. Lionel-Boulet,  
Varenes, Québec, Canada, J3X 1S2

**Email: [vetrone@emt.inrs.ca](mailto:vetrone@emt.inrs.ca)**

XIX Escuela Internacional de Verano Nicolás Cabrera, International Summer School on Fluorescent Nanoparticles in Biomedicine, Miraflores de al Sierra, Madrid, Spain, July 16-20, 2012



©2009 UEFA TM

UEFA

**EURO2012**

POLAND-UKRAINE

# La Gazzetta dello Sport

Londra 2012  
-32

Tutto il rosa della vita

**TRE per re**

Ci sei tu? **UNIQIA**

Sottoscrivere la polizza infanzia Uniqia con la polizza vita della Uniqia. Partecipa all'estrazione di 3 TV LED Samsung 32" full HD 3D!

# L'ITALIA CHE VINCE E ANDIAMO!

## Germania a noi due

**EURO2012**  
Dominata l'Inghilterra, colpiti due pali e ai rigori arriva la vittoria (4-2) Giovedì semifinale coi tedeschi

L'abbraccio fra Alessandro Diamanti, 29 anni, e Gigi Buffon, 34 anni, al termine della partita con l'Inghilterra (1-0)

**Editoriale**  
**LA NAZIONALE PIU' BELLA**  
di ANDREA MONTI

La più bella Nazionale dai tempi del Mondiale di Germania cominciata la semifinale di Duro 2012 ai calci di rigore. Avrebbe stanturato di chiudersi prima ma la sofferenza rende ancora più bella la notizia di questa straordinaria "demonstrazione". È un'Italia che vince. Vince col cuore, con classe, con grinta.

L'ARTICOLO A PAGINA 23



**F.1 GP D'EUROPA CHE IMPRESA**

Fernando Alonso, emozionato sul podio

**Capolavoro ALONSO**

Da 11° a primo: trionfo Ferrari a Valencia. E adesso è in fuga Mondiale

**ORA SI PUÒ SOGNARE**

di UMBERTO ZAPPELLONI

Le lacrime di Alonso sono dolci come quelle che ti porta una gioia inattesa, una vittoria neppure sognata. Sono la corrice di un'impresa che produce solo superlativi per Fernando e la sua Ferrari. La gara dipinta sulla pista di Valencia resterà nella storia dei suoi sport.

L'ARTICOLO A PAGINA 94  
ALIEVI: CRIMONESI, PERNA, ORTINOVIS  
DA PAGINA 34 A PAGINA 89

**L'UOMO PARTITA IL COLPO MAGICO**  
**Pirlo e il cucchiaio decisivo**  
«Ha ridato forza a tutti»

GRAZZIANO A PAGINA 10

**L'Allenatore IL C.T. «GRANDE PARTITA»**  
**Prandelli: «Lo meritavamo**  
**Poteva andare solo così»**

ELEFANTE A PAGINA 8

**IL PRESIDENTE A PETRUCCI E ABETE**  
**Il messaggio di Napolitano**  
**«Rivedo Berlino 2006»**

CECCINI A PAGINA 9

**IL ROMPI PALLONE**  
**di GENE GIOCHI**

Massa si giustifica: «Ho accumulato ritardo perché al rifornimento ho anche fatto compilare la carta carburante»

**Intesa POUR HOMME**

**SCHIUMA DA BARBA**  
DERMOPROTETTIVA

**Intesa POUR HOMME**  
AFTER SHAVE ANTIRUGHE

**intesa POUR HOMME**

**LA CERTEZZA DI PIACERE**

# La Gazzetta dello Sport

Londra 2012  
-28

Tutto il rosa della vita

**ORIGINALE**

**DESERTBOOT**

info@sask.it - c.darks.it

## GERMANIA ANCORA BATTUTA (2-1) E ORA LA SPAGNA



**DITISTA** Balotelli innesca il cross di Cassano al 20' p.t. PPP



**DIFORZA** Balotelli scaraventato in rete 12-0 al 95' p.t. RAMELLA



**IN GRUPPO** Di scatti festeggiano con SuperMario INFOPHOTO



**IN PIAZZA** L'entusiasmo dei tifosi davanti ai masticevoli REUTERS

# SIAMO NOI!!!

## Super Balotelli: tutta l'Italia è in festa

**È EUROFINALE**  
Cassano e Montolivo lo ispirano e lui segna due gol da campione. Al 92' il rigore tedesco

**l'Editoriale**  
**E' NATA UNA STELLA**  
di ANDREA MONTI

Finalmente è nata una stella. Eccolo il pianto in mezzo al campo, stufamente come un bronzo di Riace da playstation, il simbolo della nuova Italia: SuperMario Balotelli, il ragazzo dei sogni. Il limite è il cielo, avevamo scelto dopo la prova con l'Inghilterra. Non era retorica, era un giudizio. Ieri la Nazionale lo ha toccato davvero e lo ha dipinto col suo colore: solo azzurro nella notte magica di Varsavia.

L'ARTICOLO A PAGINA 28



L'urco della magia azzurra: Mario Balotelli, 21 anni. Eccolo dopo il secondo gol mentre mette in mostra tutta la sua forza e grinta REUTERS

**GIOIA MARIO**  
**«E' stata la serata più bella della mia vita»**

A PAGINA 6

**PRANDELLI**  
**«Troveremo le forze anche per gli spagnoli»**



Il c.c. Claudio Prandelli, 54 anni ALLE PAGINE 8-9

**IL ROMPI PALLONE**  
**di GENE GIOCHI**

Balotelli con Thiago Silva: «Ha chiesto un incredibile aumento di stipendio, se diventa teorista della Margherita lo accento».

**QUALITÀ AL MIGLIOR PREZZO**

**Esempio ROMA-MILANO in Frecciarossa**

	Standard	Premium	Business	Solitario	Executive
<b>SUPER ECONOMY</b>	9-19-29-39€	39-49€	49-59€		
<b>ECONOMY</b>	49-59€	79€	86€	116€	
<b>BASE</b>	86€	100€	116€	128€	200€

Da oggi biglietti ancora più flessibili e sempre più convenienti

**TRENTITALIA**  
IL MIGLIOR PREZZO

**SUPER ECONOMY, 300.000 posti al mese:** il massimo risparmio!<sup>(1)</sup> - **ECONOMY, 700.000 posti al mese:** convenienza senza rinunciare alla possibilità del cambio prenotazione/biglietto, una sola volta fino alla partenza del treno.<sup>(2)</sup> - **BASE, massima libertà con cambi illimitati gratuiti** fino alla partenza del treno.<sup>(3)</sup> - Informazioni e acquisti on line e presso tutti i canali di vendita. **Trentitalia. La scelta più conveniente che c'è.**

(1) Offerta per treni di categoria Premium. Il livello della prenotazione (Economy, Base) non sono consentiti. (2) Offerta a posti fissi e soggetti a limitazioni. Il cambio prenotazione/biglietto è consentito, a condizione di effettuare il pagamento presso Base, per il stesso tipo di treno e livello di servizio a dispetto di un nuovo biglietto. Il rimborso a l'acquisto di un treno diverso non sono consentiti. (3) L'offerta è riservata ai clienti della categoria Business. Per informazioni e acquisti on line e presso tutti i canali di vendita. [www.trentitalia.com](http://www.trentitalia.com)



# La Gazzetta dello Sport

SEIKO

Londra 2012  
-25  
PARTNER UFFICIALE

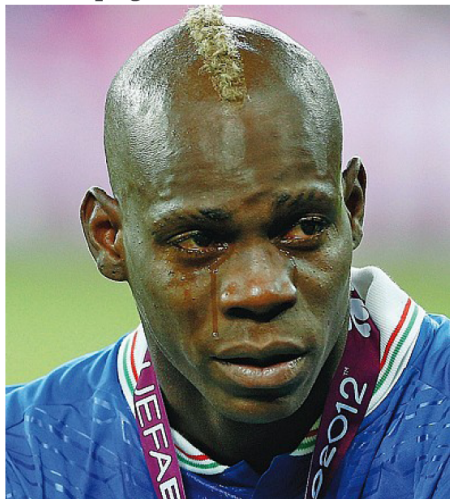
Tutto il rosa della vita



**VINCE LA SPAGNA 4-0: E' CAMPIONE D'EUROPA  
SERATACCIA: GLI AZZURRI ESCONO IN LACRIME**

# COSÌ FA MALE...

Partita chiusa già nel primo tempo: dal 61' siamo rimasti in dieci  
Gli spagnoli dominano e mettono a segno uno storico Triplete

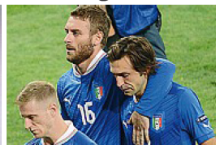


ARCHITTE, BAZZONI, IBANICHI, IBANICHI, BOVOLI, CITO, DE CALD, DIEGO, GRAZIANO, LECARE, MANCHE, RICCI, SCORNICCHI, VELLUZZI, VERNAZZA DA PAG 2 A PAG. 38

**CICLISMO** LO SVIZZERO RESTA LEADER  
Sagan mette sotto cancellara  
Il Tour trova un protagonista  
PASTONESI, SCORNICCHI ALLE PAGINE 46-47

**TENNIS** OGGI TRE ITALIANE IN CAMPO  
Giorgi, sorpresa di Wimbledon  
«Adesso non mi pongo limiti»  
MARTUCCI, BERTOLUCCI A PAGINA 55

**SUPERBIKE** NEL GP DI ARAGONA  
Biaggi-Melanardi: finisce pari  
Tra scintille e pace sul web  
GOZZI A PAGINA 44



**INDISCORSOLABILI**  
Mario Balotelli in lacrime, come il resto dei compagni di squadra. Delusione pura tra i tantissimi tifosi che hanno seguito la partita davanti ai mastrochirri nella piazza d'Italia.



## l'Editoriale GRAZIE LO STESSO

di ANDREA MONTI

*Semplicemente, come si canta allo stadio: grazie ragazzi. Grazie lo stesso. Certo, la lezione è stata severissima. E la valle di lacrime a fine partita lo testimonia. In una finale europea o mondiale non si ricordavano 4 gol di scarto, ma non parliamo di umiliazione. Carone ieri sera ci ha taglietto all'inferno, esauti, malconci, tormentati dai mostruosi diavoli spagnoli che sanno sempre cosa fare col pallone e come punire i peccati altrui.*

L'ARTICOLO A PAGINA 25

## Il Commento SENZA BATTERIA

di LUIGI GARLANDO

*Avevano ancora una lancia di batteria, speravamo di riuscire a fare l'ultima chiamata. E invece nulla. Crollati esauti ai piedi della Spagna, che resta sul trono, splendida regina d'Europa e del mondo. Il 4-0 suona similante, ma non deve rimpicciolare l'orgoglio per il grande torneo giocato dagli azzurri. Anche perché ieri non c'era in campo la vera Italia che, senza la piena salute agonistica, non esiste.*

L'ARTICOLO ALLE PAGINE 2-5

## IL TECNICO «ERAVAMO TROPPO STANCHI» Prandelli: «Grande torneo E il progetto va avanti»

CICCICHIO, ELEFANTE A PAGINA 10

## IL ROMPI PALLONE DI GENE GNOCCHI

*Dopo la deludente prestazione contro la Spagna rivista la quotazione di Balotelli. Moody's l'ha declassato a Forlan.*



# GRAZIE.

Ci avete fatto sognare.  
E il sogno continua.  
Forza Azzurri sempre!



Diamo forza ai tuoi progetti.

**MARCA**

Lunes 2 de julio de 2012 • 1€

www.marca.com • @marca

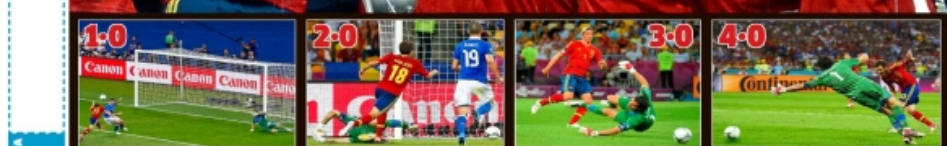
TAG Heuer Carrera Calibre 1887  
IN-HOUSE MANUFACTURED CHRONOGRAPH

LA ROJA SE EXHIBE COMO EL MEJOR EQUIPO DE TODOS LOS TIEMPOS

# ESPAÑA Y NADIE MÁS



La selección tritura a Italia con un fútbol primoroso, gana su tercera Eurocopa y consigue la Triple Corona que nadie logró jamás



1-0 de cabeza a centro de Cesc, abre el marcador 2-0 golazo por la banda y marca a poste de Xavi Xavi deja a Torres solo para batir a Buffon Torres existe a todo, que ama a jugar Torres existe a todo, que ama a jugar

**Torres, Pichichi de la Euro e Iniesta, MVP de la final**

El manchego, máximo favorito para ser Balón de Oro de la Euro

«El Niño»: dos finales, dos goles

LA CAMISETA OFICIAL DE LOS CAMPEONES

HOY CARTILLA GRATIS

**SEAT**

SEAT LEÓN COPA  
AHORA, MUCHO MÁS LEÓN POR MUCHO MENOS.  
**12.400€**  
Y TAMBIÉN POR 109€/MES

SEAT LEÓN COPA SUPEREQUIPADA  
POR **12.400€**  
Y TAMBIÉN POR 109€/MES



## INRS (administration générale)

QUÉBEC

### Centre Eau Terre Environnement

- Hydrologie et gestion intégrée des eaux de surface
- Biogéochimie et problématiques de contamination
- Géodynamique des ressources naturelles et de l'environnement
- Assainissement et décontamination environnementale

### Centre Énergie Matériaux Télécommunications

- Matériaux avancés et photonique ultrarapide
- Télécommunications
- Énergie durable

LAVAL

VARENNES

MONTRÉAL

### Centre Urbanisation Culture Société

- Espace urbain, re compositions territoriales et analyse spatiale
- Diversification des modes de vie
- Pratiques culturelles et institutionnalisation de la culture
- Lien social, famille et générations
- Migrations et dynamiques de population

### Centre INRS – Institut Armand-Frappier

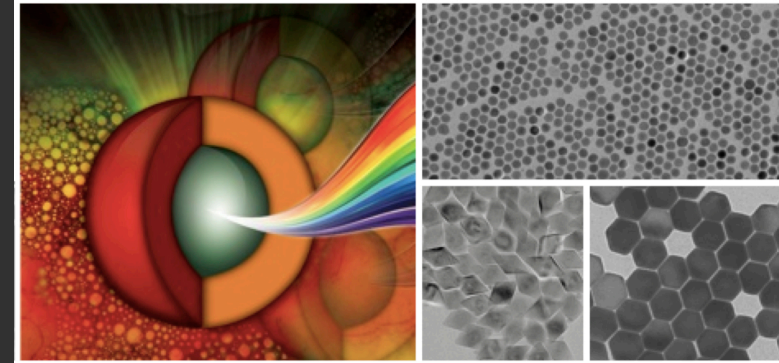
- Immunité, maladies infectieuses et cancer
- Toxicologie et biotechnologie environnementales
- Pharmacochimie moléculaire

# Synthesis

- Novel multiphoton excited nanoparticles
- Novel NIR emitting nanoparticles

# Multifunctional Nanovehicles

- Light sensitized targeted release of bone growth factors (bone regeneration, bone cancer)

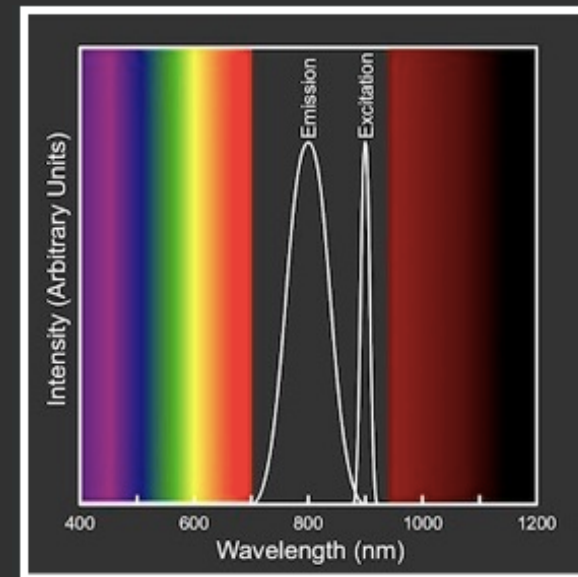


# Biosensing

- Optical barcode sensor arrays
- Ir-Metal NP-Multiphoton Excited NP-DNA complexes



# Nanothermometry



# Nanoscale

[View Online / Journal Homepage / 1](#)  
Dynam

Cite this: *Nanoscale*, 2012, **4**, 4301

[www.rsc.org/nanoscale](http://www.rsc.org/nanoscale)

## REVIEW

### Luminescence nanothermometry†

Daniel Jaque<sup>\*a</sup> and Fiorenzo Vetrone<sup>\*b</sup>

Received 30th March 2012, Accepted 14th May 2012  
DOI: 10.1039/c2nr30764b

The current status of luminescence nanothermometry is reviewed in detail. Based on the main features of luminescence including intensity, bandwidth, bandshape, polarization, spectral shift and lifetime, we initially describe and compare the different classes of luminescence nanothermometry. Subsequently, the various luminescent materials used in each case are discussed and the mechanisms at the origin of the luminescence thermal sensitivity are described. The most important results obtained in this field are summarized and the advantages and disadvantages of these approaches are discussed.

### Minireviews

#### Upconverting Nanoparticles

### Upconverting Nanoparticles for Nanoscale Thermometry

Lorenz H. Fischer, Gregory S. Harms, and Otto S. Wolfbeis\*

*Angew. Chem.*, **50**; 4546 (2011)

## Thermometry at the Nanoscale

Carlos D. S. Brites,<sup>a</sup> Patricia P. Lima,<sup>a</sup> Nuno J. O. Silva,<sup>a</sup> Angel Millán,<sup>b</sup> Vitor S. Amaral,<sup>a</sup>

Fernando Palacio,<sup>\*b</sup> and Luís D. Carlos,<sup>\*a</sup>

DOI: 10.1039/C2NR30663H



## Students and Collaborators



- Prof. José García Solé
- Prof. Daniel Jaque
- Prof. Angeles Juarranz de la Fuente
- Prof. Francisco Sanz-Rodríguez
- Prof. Maria Carmen Iglesias-de la Cruz
- Dr. Emma Martin Rodriguez
- Laura Martin Maestro



- Prof. Adolfo Speghini
- Prof. Marco Bettinelli
- Dr. Fabio Piccinelli
- Dr. Marco Pedroni



- Prof. John A. Capobianco
- Dr. Venkatarmanan Mahalingam
- Dr. Nicoleta Bogdan
- Rafik Naccache



- Prof. Dongling Ma
- Dr. Marta Quintanilla Morales
- Dr. Haiguang Zhao
- Fuqiang Ren
- Yue Huang

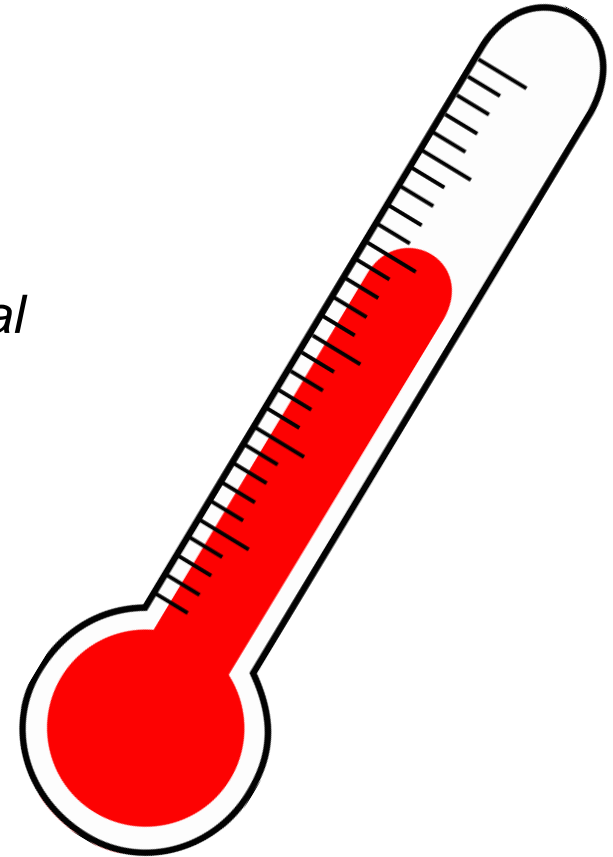
## Nanothermometry

- What is Nanothermometry?

*Nanothermometry aims to extract knowledge of the local temperature of a given system with sub-micrometric spatial resolution*

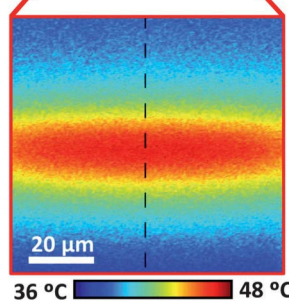
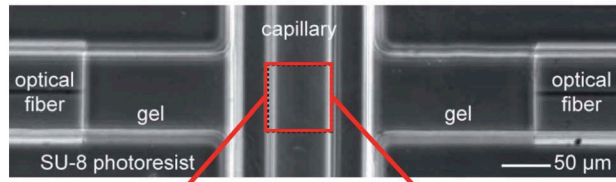
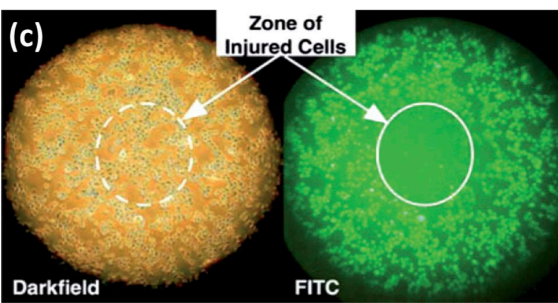
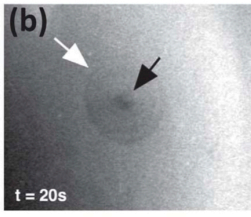
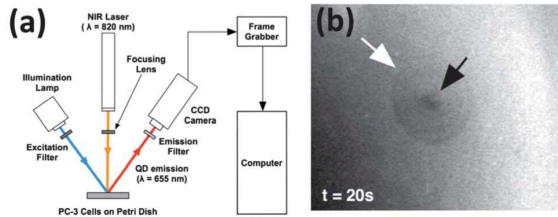
- Why is it Important?

Such knowledge is required for the complete understanding of micrometric and nanostructured systems whose dynamics and performance are strongly determined by temperature

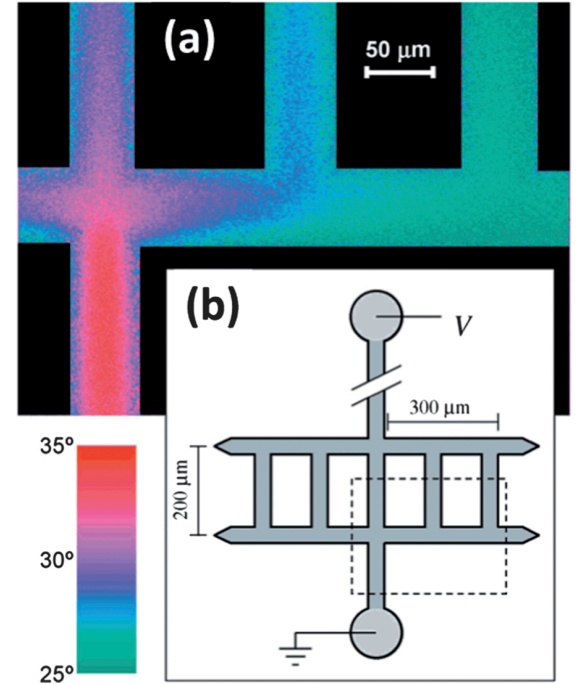


# Uses of Nanothermometry

- Micro/Nano-Electronics
- Integrated Photonic Devices
- Biomedicine



Thermal image of an opto-fluidic device using fluorescent dyes  
N. Ishiwada, S. Fujioka, T. Ueda and T. Yokomori, *Opt. Lett.*, 2011, **36**, 760-762.



Color coded thermal image of a multi-branched microfluidic circuit  
D. Ross, M. Gaitan and L. E. Locascio, *Anal. Chem.*, 2001, **73**, 4117-4123

## Nanothermometry in Biomedicine

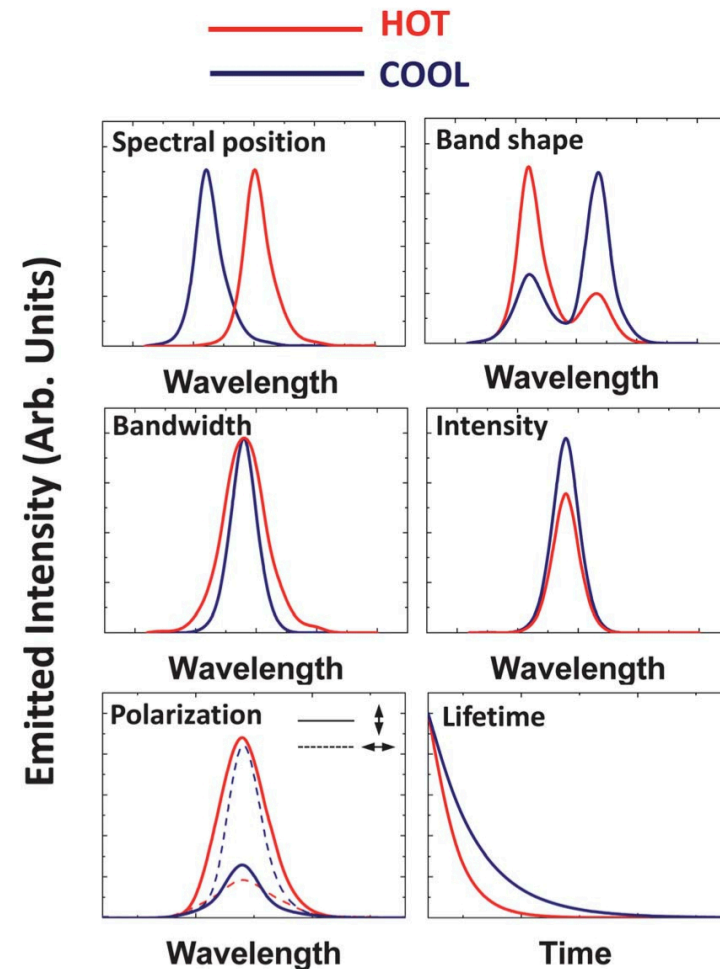
- **Fundamental Interest:** Temperature plays a **crucial** role in most biosystems determining their dynamics and properties
  - Cell division rates (i.e. determines rate of tissue growth)
  - Drastically affects mechanical, structural and optical properties (i.e. leads to denaturation in proteins)
- **Disease Detection:** Vital for the early detection and treatment of many diseases
  - First signatures of any given illness is the appearance of thermal singularities.
  - In cancer, thermal singularity associated with incipient tumors becomes detectable when they reach a size consisting of thousands of cancer cells (i.e. when the tumor size is well below 1 mm)

## Types of Nanothermometers

- Electrical Nanothermometry
- Mechanical Nanothermometry
- Optical Nanothermometry
  - Interferometry
  - Reflection
  - Raman
  - Pyrometric
  - Infrared
  - Fluorescence/Luminescence

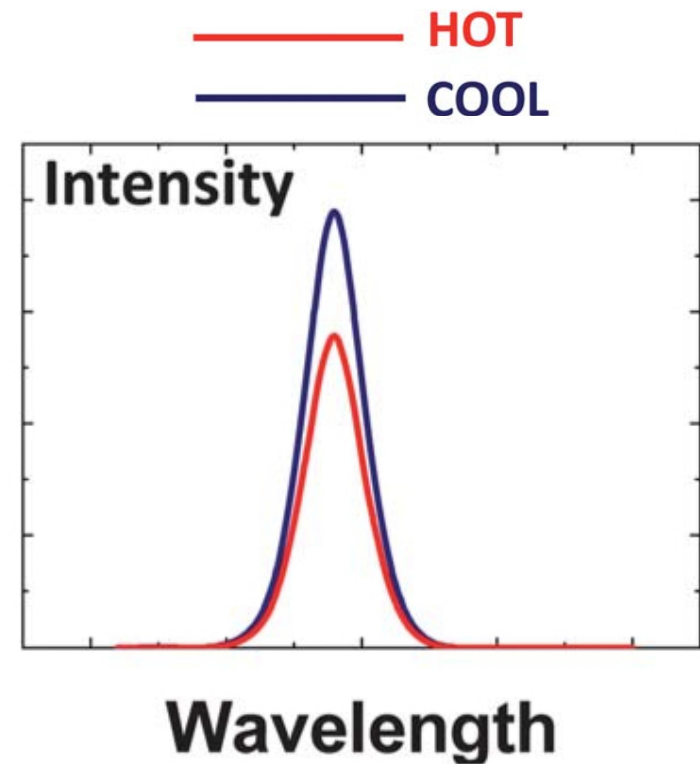
# Different Classes of Luminescence Nanothermometers

- Intensity Luminescence Nanothermometry
- Band-Shape Luminescence Nanothermometry
- Spectral Luminescence Nanothermometry
- Polarization Luminescence Nanothermometry
- Bandwidth Luminescence Nanothermometry
- Lifetime Luminescence Nanothermometry



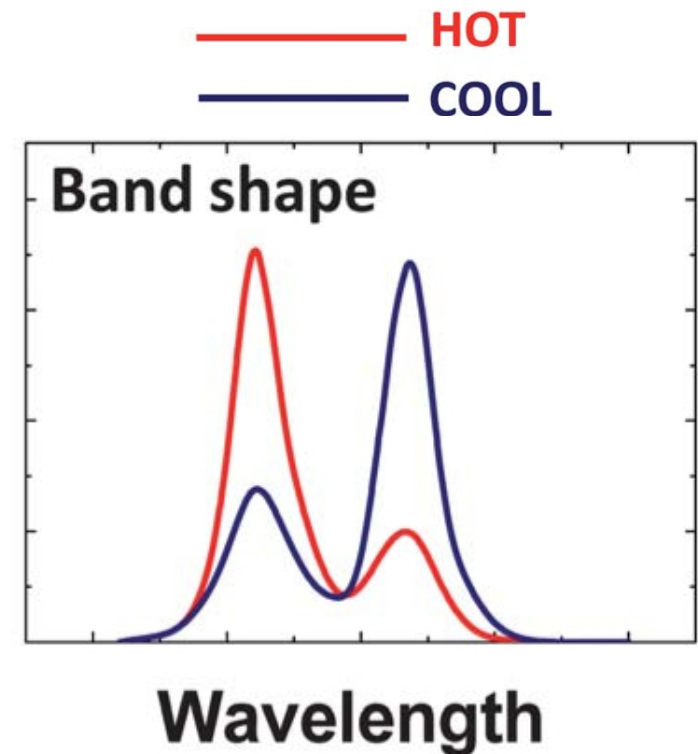
# Intensity Luminescence Nanothermometry

- Thermal sensing is achieved through the analysis of the luminescence intensity
- When temperature changes, there is an overall change in the number of emitted photons per second such that the emission spectrum becomes less (or more) intense
- Generally caused by the thermal activation of luminescence quenching mechanisms and/or increases in the non-radiative decay probabilities



# Band-Shape Luminescence Nanothermometry

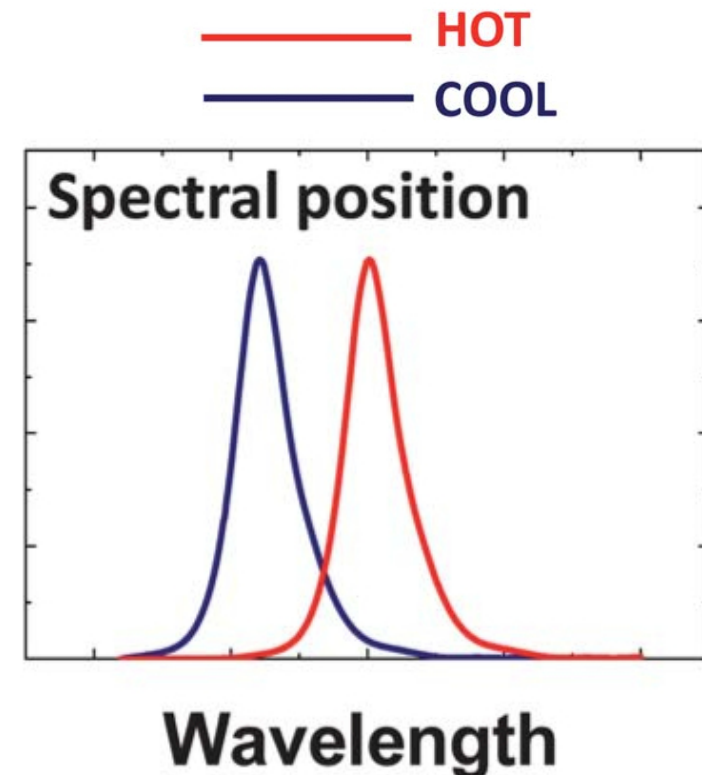
- Refers to the relative intensity between the different spectral lines that make up the luminescence spectrum
- Thermally induced variations in the band-shape usually take place when the electronic states from which emission is generated are very close in energy such that they are thermally coupled
- Often referred to as **radiometric** sensing
- Can be also present in mixed systems, *i.e.* systems containing more than one class of emitting centers





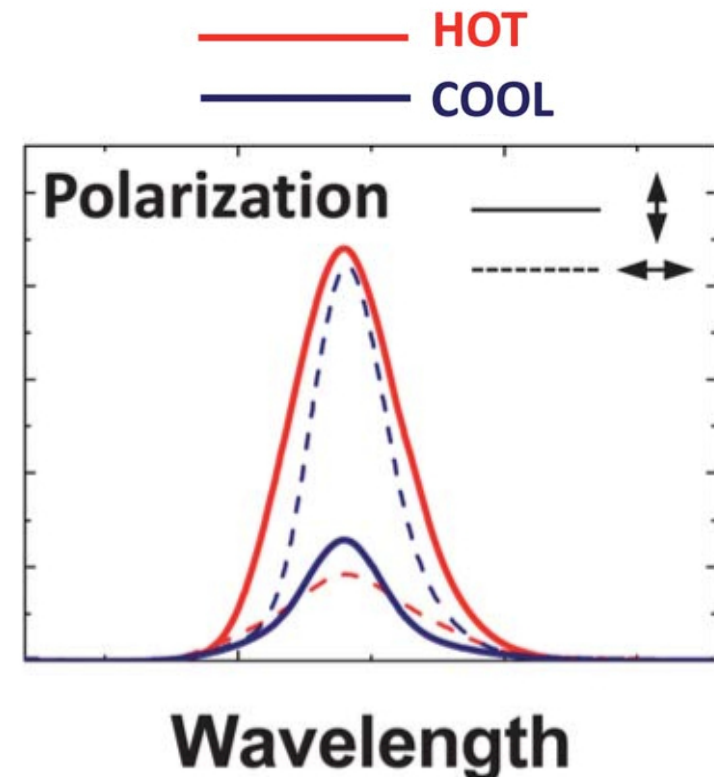
# Spectral Luminescence Nanothermometry

- Based on the analysis of the spectral positions of the emission lines, which are unequivocally determined by the energy separation between the two electronic levels involved in the emission
- This depends on a large variety of temperature dependent parameters of the emitting material including:
  - Refractive index
  - Inter-atomic distances (density)



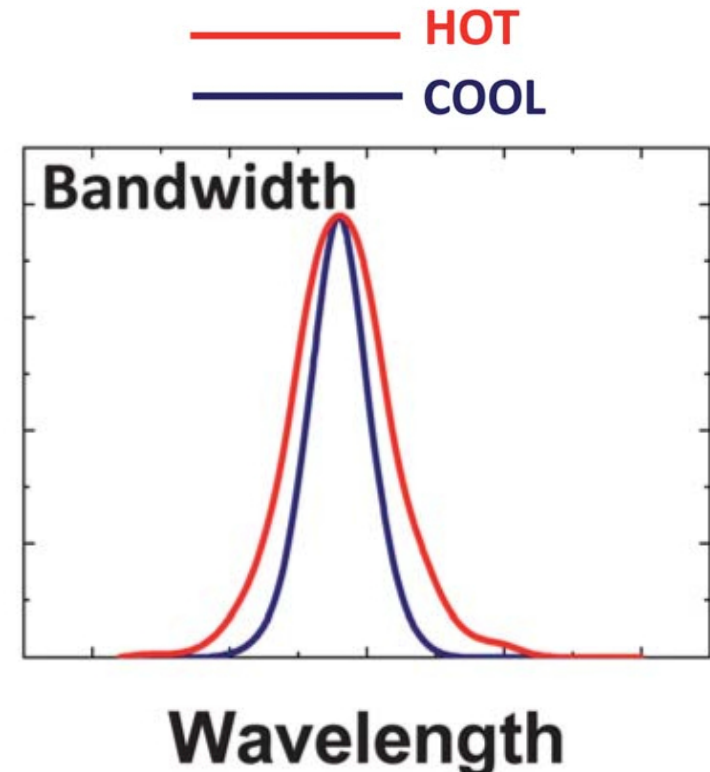
# Polarization Luminescence Nanothermometry

- In anisotropic media, the emitted radiation is generally non-isotropically polarized
- Consequently, the shape and intensity of the emitted radiation are strongly dependent on its polarization
- Exploits the ratio between the luminescence intensities emitted at two orthogonal polarization states



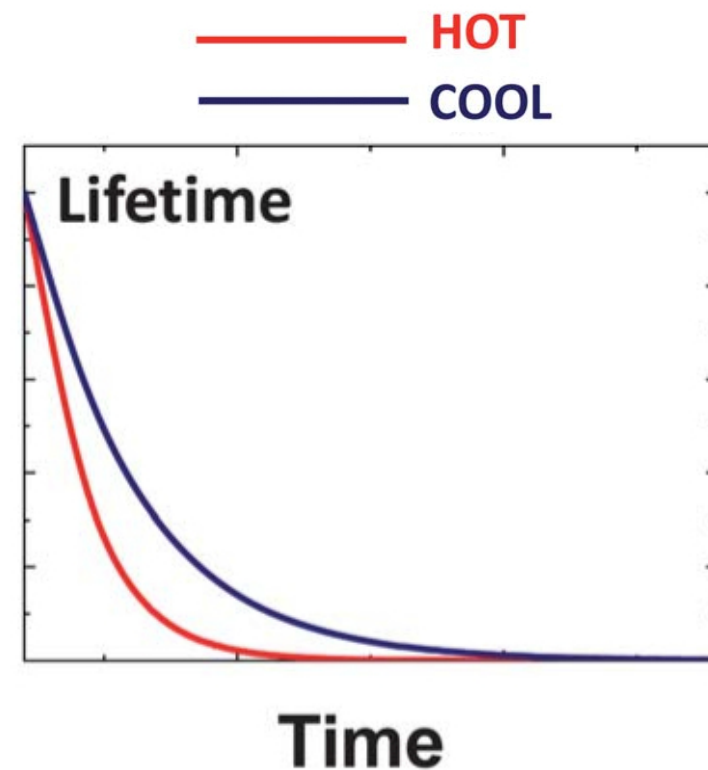
# Bandwidth Luminescence Nanothermometry

- The width of the various emission lines that make up any luminescence spectrum is determined by the properties of the material:
  - Degree of disorder
  - Temperature
- As the temperature of a luminescent material is increased, a corresponding increase in the density of phonons occurs resulting from the spectral contribution of homogeneous line broadening
- Near RT, homogeneous line broadening leads to a linear relationship between bandwidth and temperature



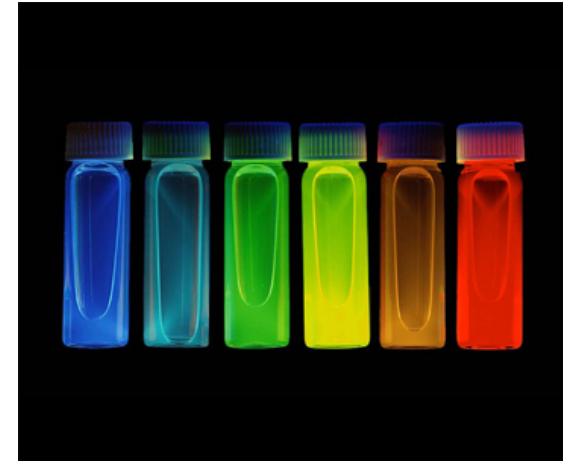
# Lifetime Luminescence Nanothermometry

- Luminescence lifetime,  $\tau_f$ , is defined as the time that the emitted luminescence intensity decays down to  $1/e$  of its initial value after a pulsed excitation
- Indication of the total decay probability of the emitted intensity (this probability is defined as the inverse of the luminescence lifetime)
- Decay probabilities from electronic levels depend on many factors and many of them are related to temperature
  - Phonon assisted energy transfer processes
  - Multiphonon decays



## Luminescent Nanoparticles

- Nanoparticles have demonstrated their significant potential in applications related to both diagnostics and therapeutics.
- Semiconductor quantum dots (QDs) are widely used in many fields
- Most nanoparticles are excited with UV light, which has several limitations
  - Low penetration depths
  - High autofluorescence
  - Potential damage to specimens under study



[http://nanoe.ece.drexel.edu/wiki/index.php/Quantum\\_Dot\\_Challenge](http://nanoe.ece.drexel.edu/wiki/index.php/Quantum_Dot_Challenge)



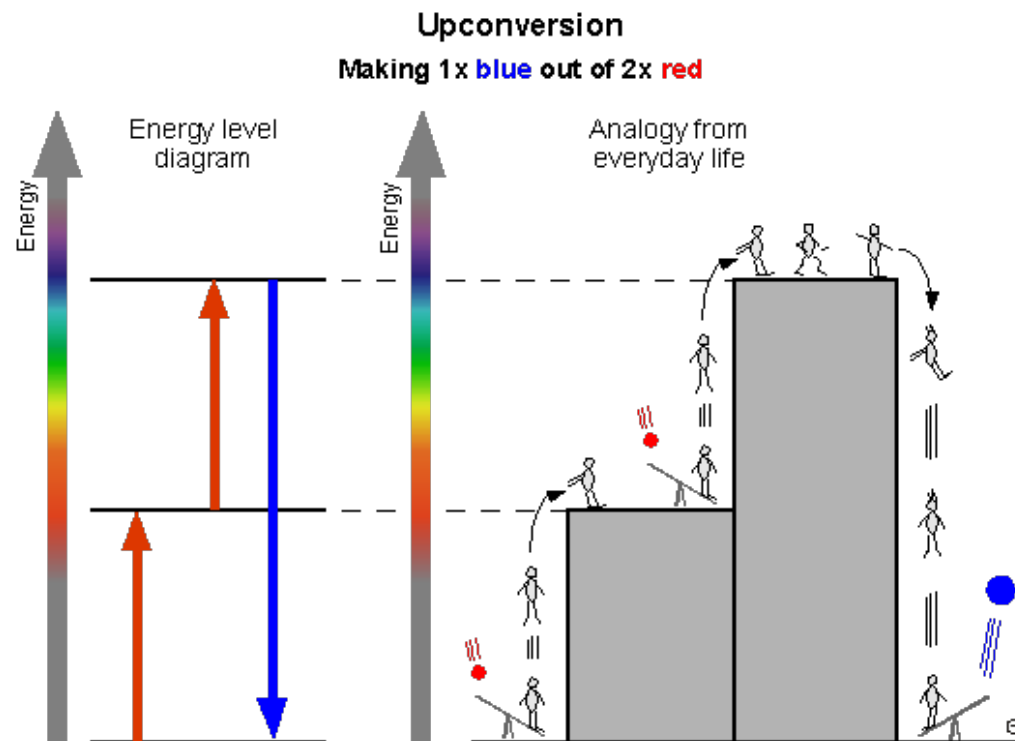
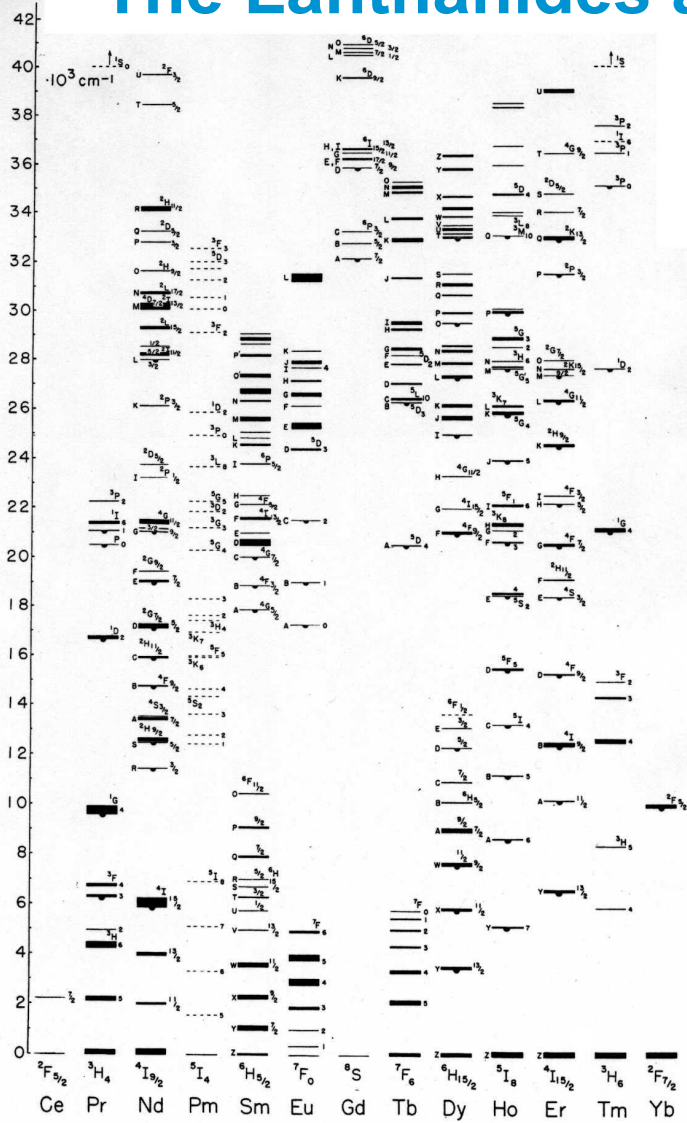
<http://www.immunology.utoronto.ca/FlowCytometry/FlowIntro.htm>

## Multi-Photon Excited Luminescent Nanoparticles

- Multi-photon excited luminescent nanoparticles are finding widespread use in nanomedicine
- Semiconductor quantum dots (QDs), gold nanorods (GNRs) are being used in two-photon imaging applications
- Excitation with NIR light (800-1000 nm):
  - Increases tissue penetration depths
  - Minimizes autofluorescence
  - Does not have negative effects on biological specimens



# The Lanthanides and Upconversion



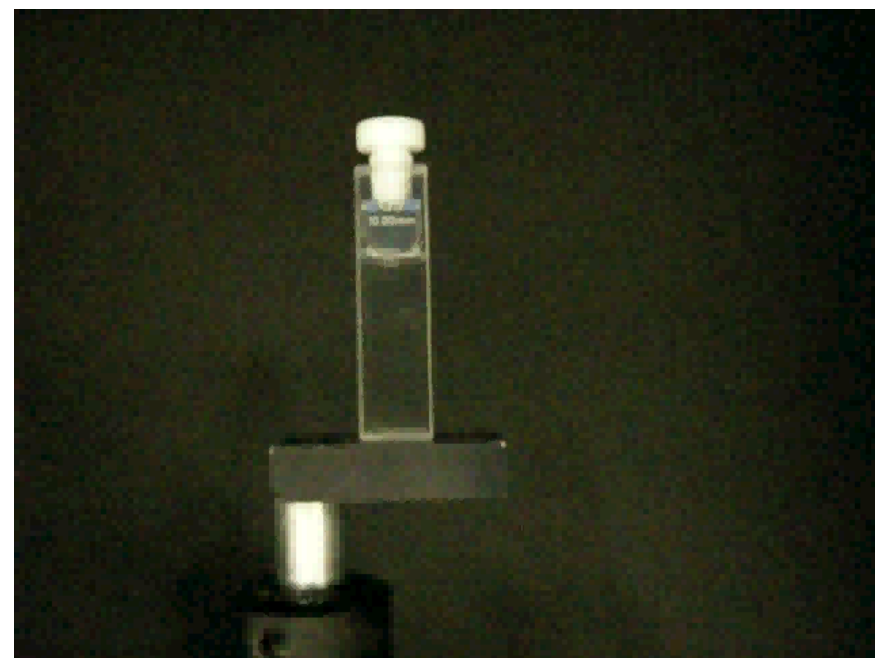
[http://www.dcb-server.unibe.ch/groups/quedel/research/hug\\_upc\\_movie.htm](http://www.dcb-server.unibe.ch/groups/quedel/research/hug_upc_movie.htm)



# Upconverting Lanthanide-Doped Luminescent Nanoparticles

- Goal:
  - *Synthesis of new luminescent  $\text{Ln}^{3+}$ -doped nanoparticles and investigate their application to biology, specifically in nanothermometry*
- Requirements:
  - Small size with narrow particle size distribution
  - Monodispersed
  - Water dispersible and/or dispersible in aqueous media
  - Biocompatible
  - Appropriate surface functionalization

## Upconversion of Lanthanide-Doped Nanoparticles



NaYF<sub>4</sub> nanoparticles co-doped with Er<sup>3+</sup> (or Tm<sup>3+</sup>) and Yb<sup>3+</sup> ions

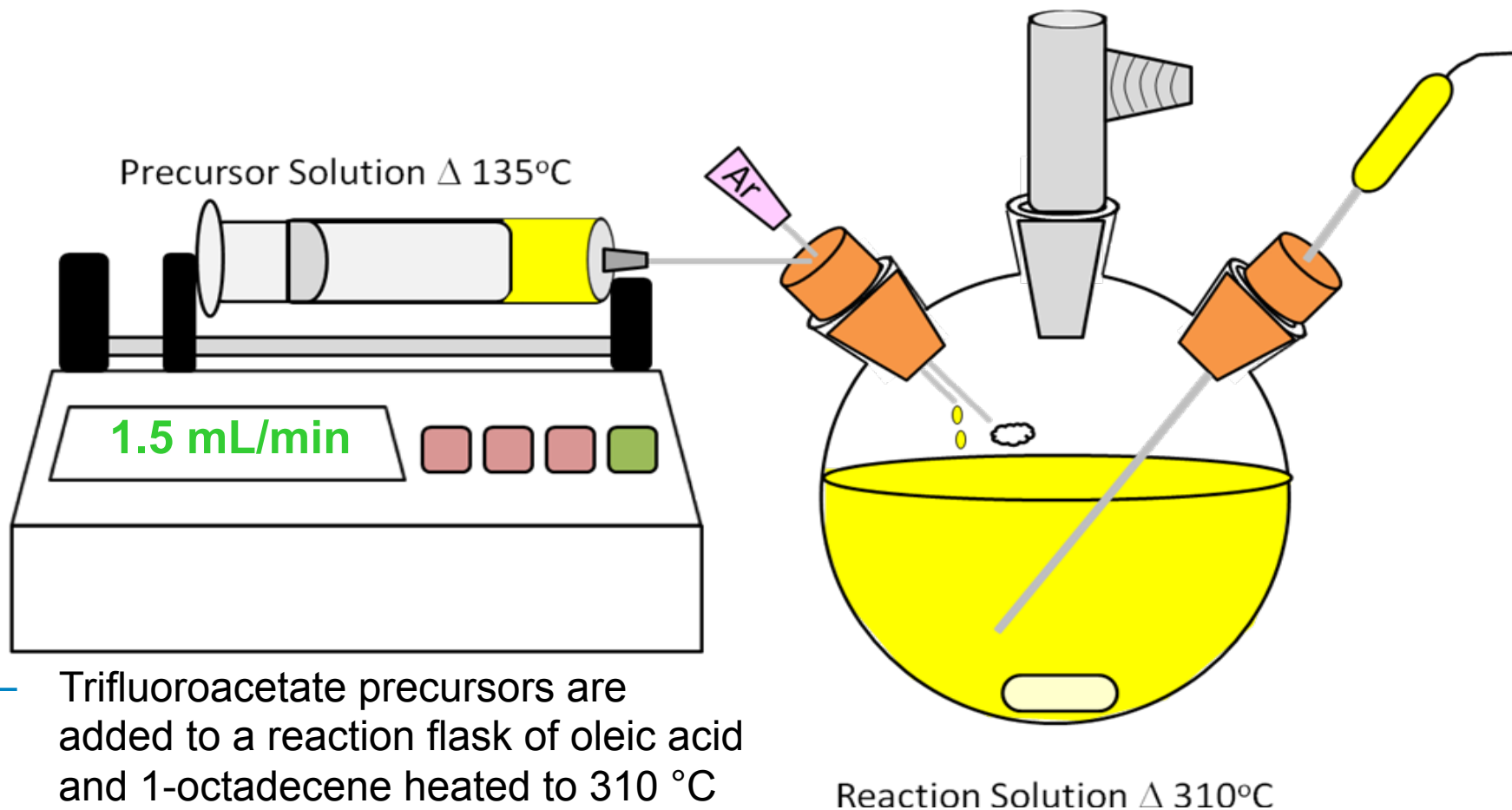
## The Fluorides, Why $MLnF_4$ ( $M = Na, Li$ and $Ln = Y, Gd$ )?

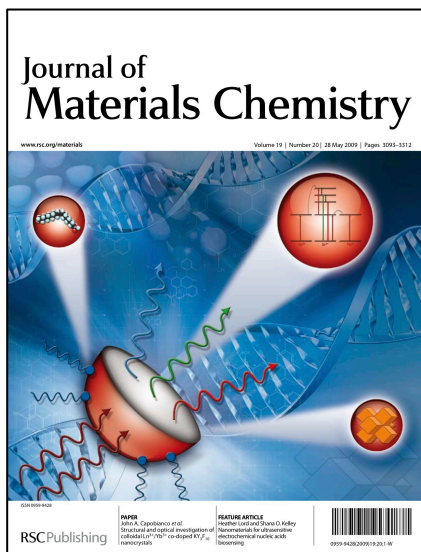
- Fluorides possess highest upconversion efficiencies among bulk materials
- Upconversion reported from colloidal dispersion of various fluoride nanoparticles
- $NaYF_4$
- $NaGdF_4$
- $LiYF_4$
- $BaYF_5$
- $KY_3F_{10}$
- $CaF_2$
- $GdF_3$
- $KGdF_4$

# Synthesis of Fluoride-Based Upconverting $\text{Ln}^{3+}$ -Doped Nanoparticles

- Three main synthesis strategies:
  1. Prepare hydrophobic nanoparticles *via* **thermal decomposition synthesis**
    - Modify the surface for water dispersibility
  2. Directly prepare hydrophilic nanoparticles *via* **solvothermal synthesis**
  3. Rapidly prepare upconverting nanoparticles *via* **microwave-assisted synthesis**

## Thermal Decomposition

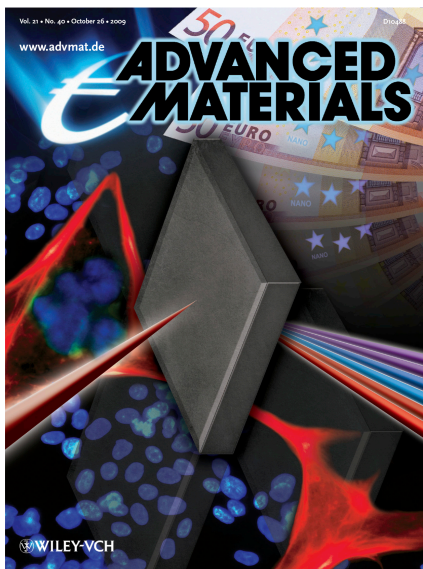




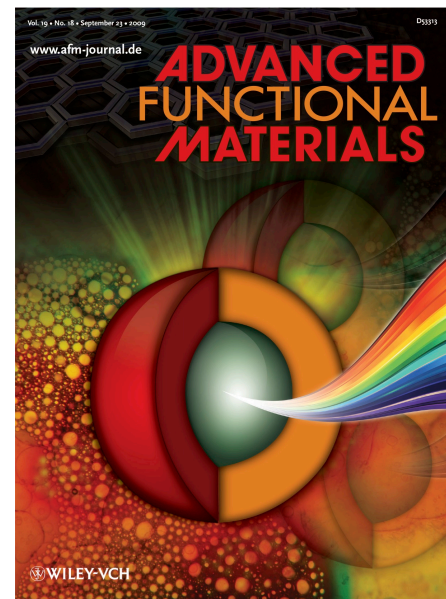
V. Mahalingam, F. Vetrone, R. Naccache, A. Speghini, J. A. Capobianco, *J. Mater. Chem.*, **19**; 3149 (2009)



F. Vetrone, R. Naccache, V. Mahalingam, Christopher G. Morgan, J. A. Capobianco, *Adv. Funct. Mater.*, **19**; 2924 (2009)

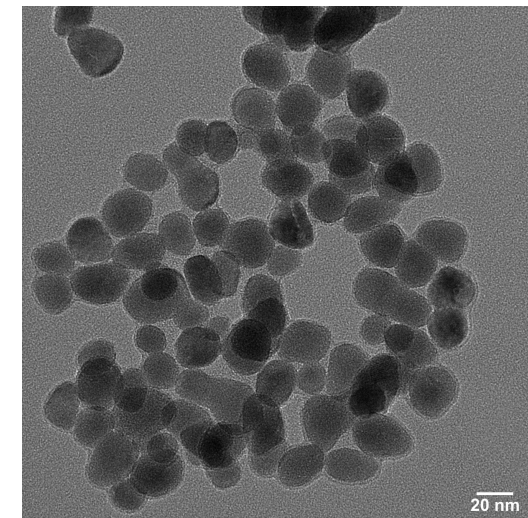


V. Mahalingam, F. Vetrone, R. Naccache, A. Speghini, J. A. Capobianco, *Adv. Mater.*, **21**; 4025 (2009)  
*UV to NIR luminescence, Nature Photonics, Research Highlights*, Volume 3, Page 606, November 2009

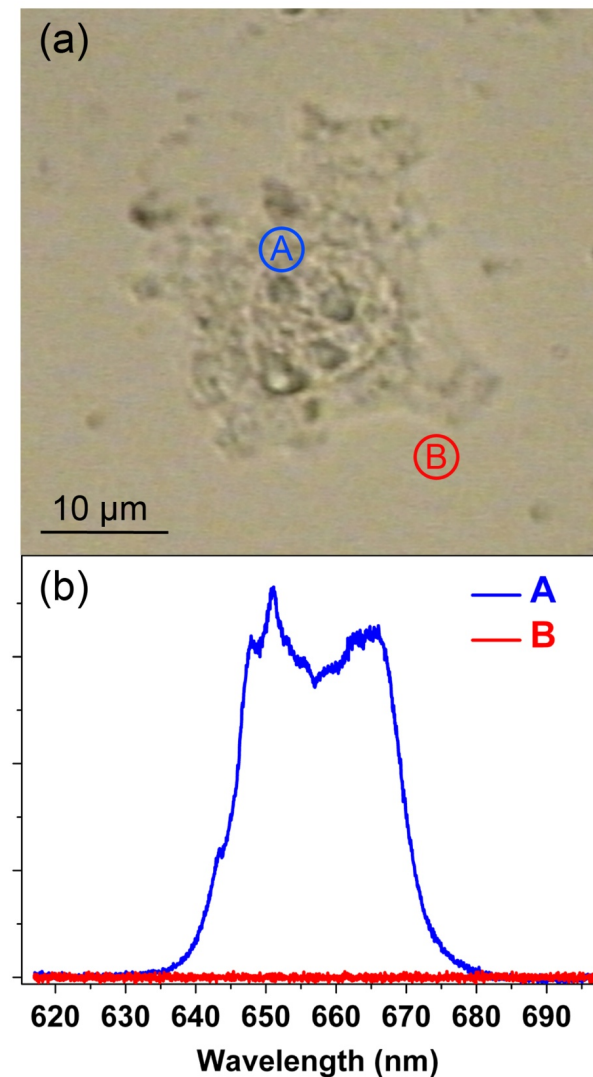
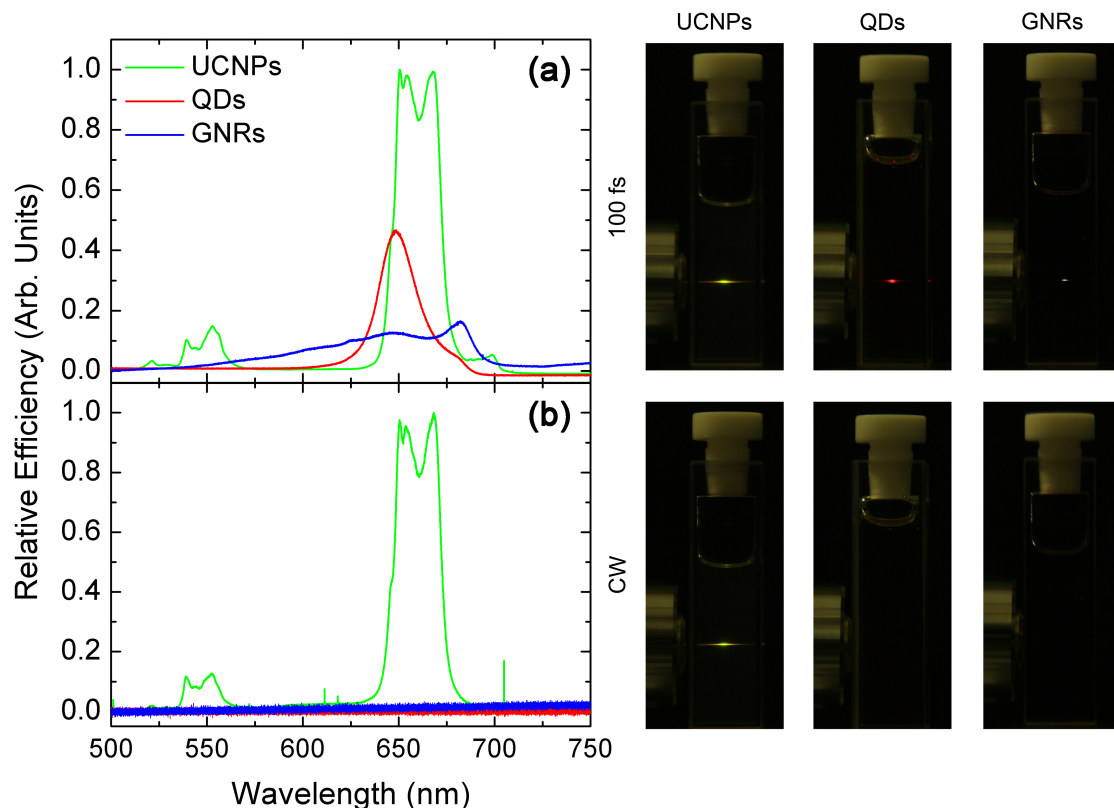


## Solvothermal Synthesis

- Synthesize upconverting nanoparticles that can be dispersed directly in water
- No additional step required
- Prepared starting from the metal chlorides and  $\text{NH}_4\text{F}$  and a capping ligand in ethylene glycol
- Ligands (e.g.)
  - Polyethylenimine (PEI) –  $\text{NH}_2$  Groups
  - Poly(sodium 4-styrenesulfonate) – SH Groups
  - Polyacrylic acid –  $\text{COOH}$  Groups



# Two-Photon Optical Imaging

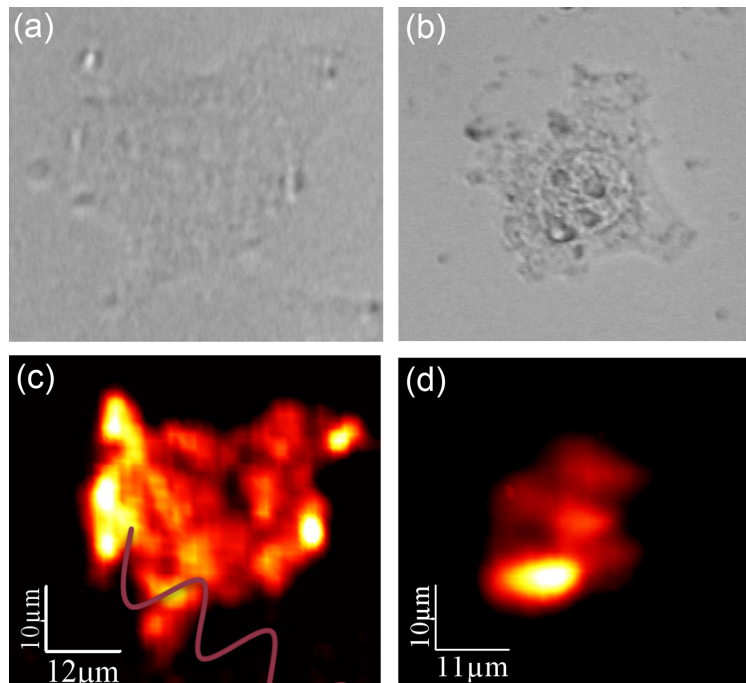


L. Martinez Maestro, E. Martín Rodríguez, F. Vetrone, R. Naccache, H. L. Ramirez, D. Jaque, J. A. Capobianco and J. García Solé, *Opt. Express*, **18**, 23544 (2010)

F. Vetrone, R. Naccache, A. Juarranz de la Fuente, F. Sanz-Rodríguez, A. Blazquez-Castro, E. Martín Rodríguez, D. Jaque, J. García Solé, J. A. Capobianco, *Nanoscale*, **2**, 495 (2010)



# Two-Photon Optical Imaging



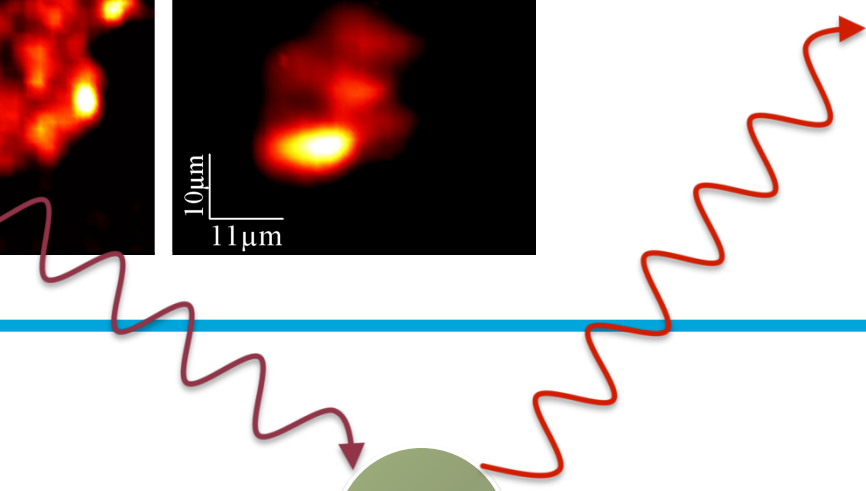
UCNP

UCNP

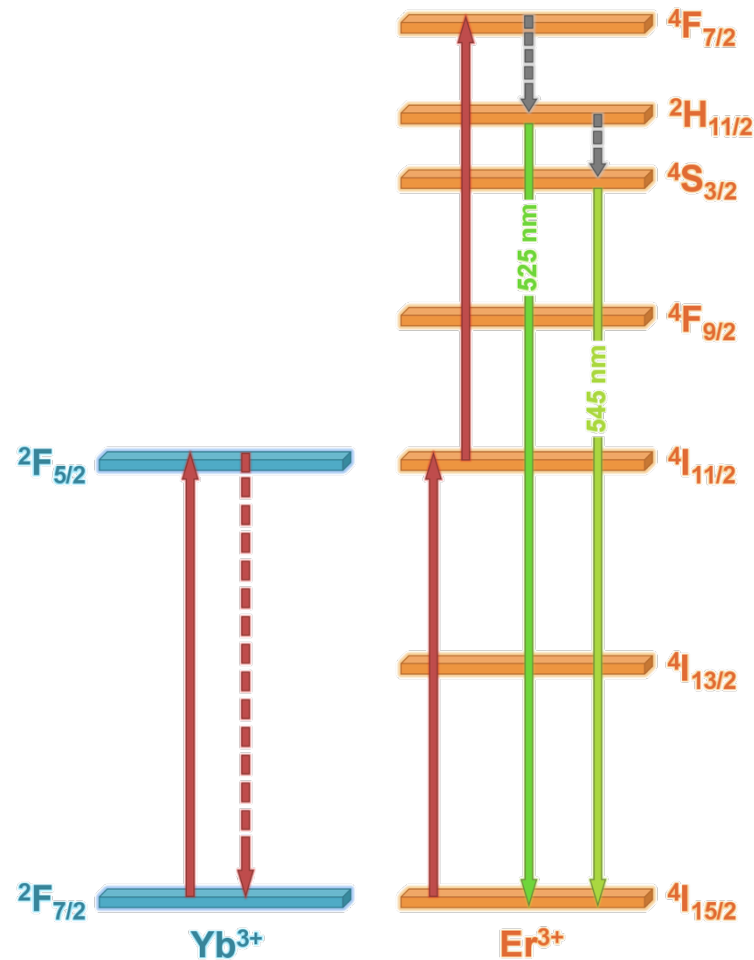
UCNP

UCNP

HeLa Cancer Cell

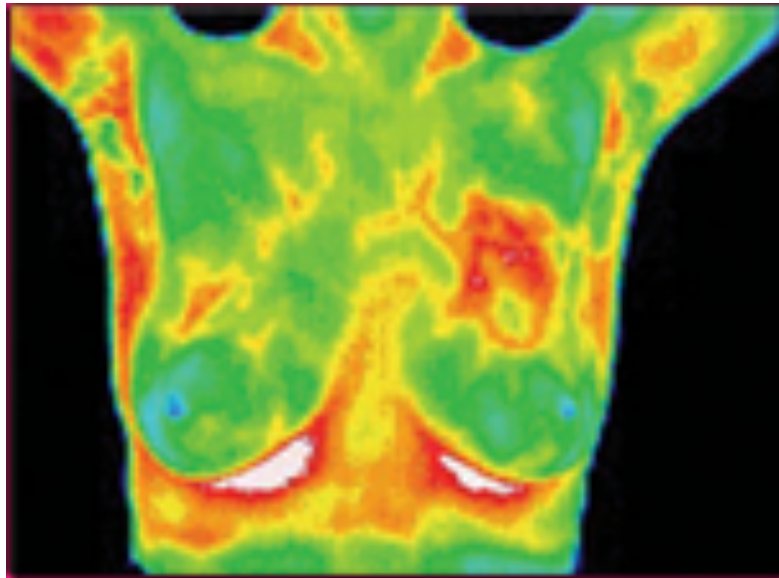


# Er<sup>3+</sup>/Yb<sup>3+</sup> Co-Doped Nanoparticles



## Nanothermometry → Thermal Imaging – Why?

- Tumors are “warmer” because their larger metabolic activity and also because the more intense blood circulation in its surroundings



- Early detection of disease
- Several years before a mammogram

Tumors and other diseases are easily treated with early detection.

90 days: 2 cells

1 year: 16 cells

2 years: 256 cells (the size of grain of rice)

► Detectable by Thermal Imaging

3 years: 4,896 cells

4 years: 65,536 cells

5 years: 1,048,576 cells

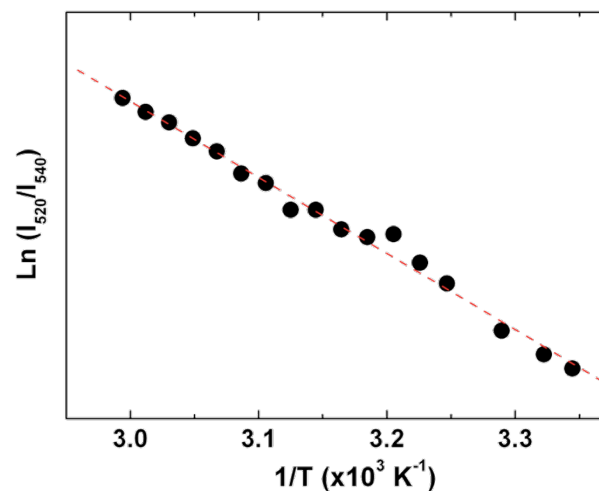
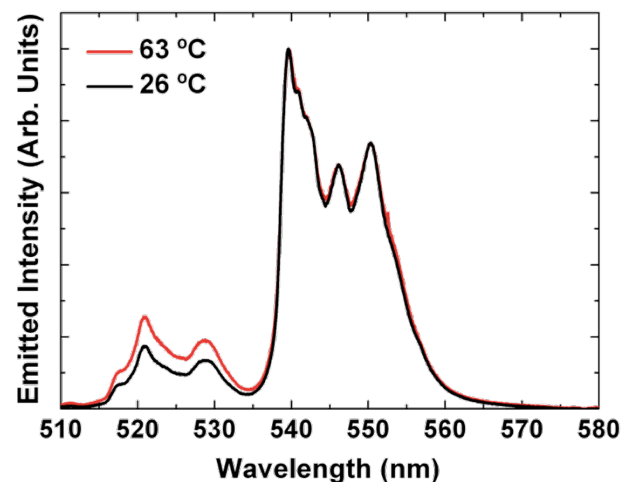
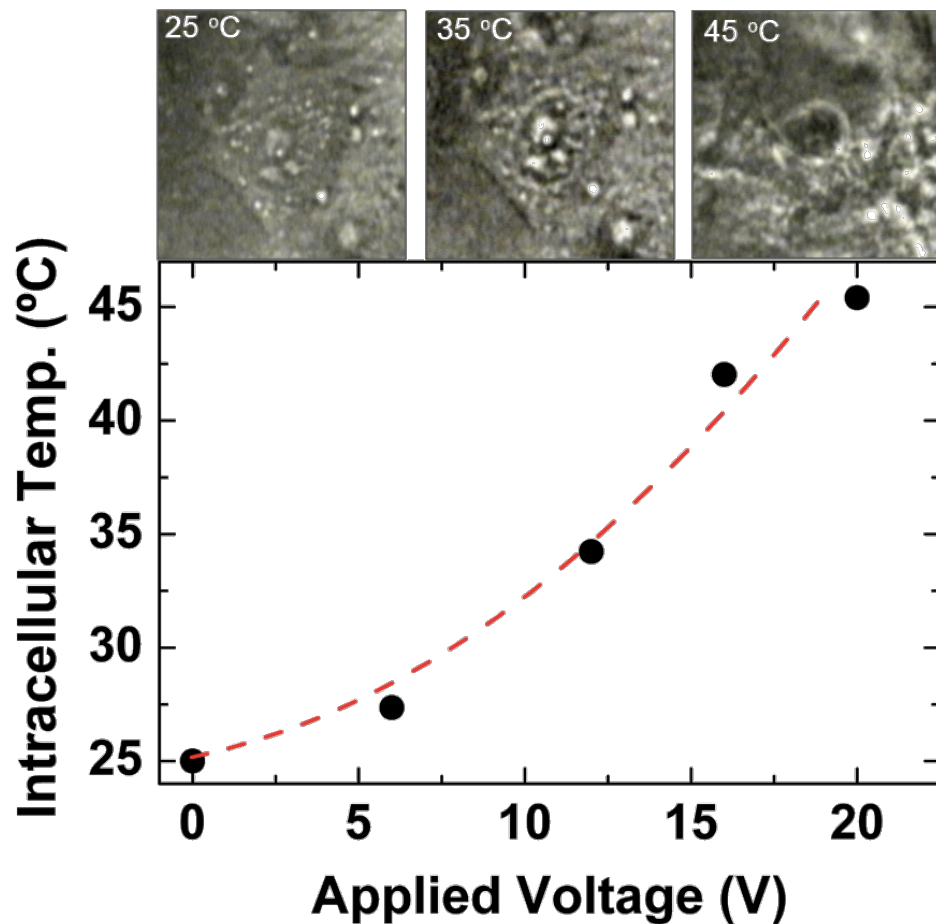
6 years: 16,777,216 cells

7 years: 268,435,456 cells

► Detectable by Mammography

8 years: 4,294,967,296 cells

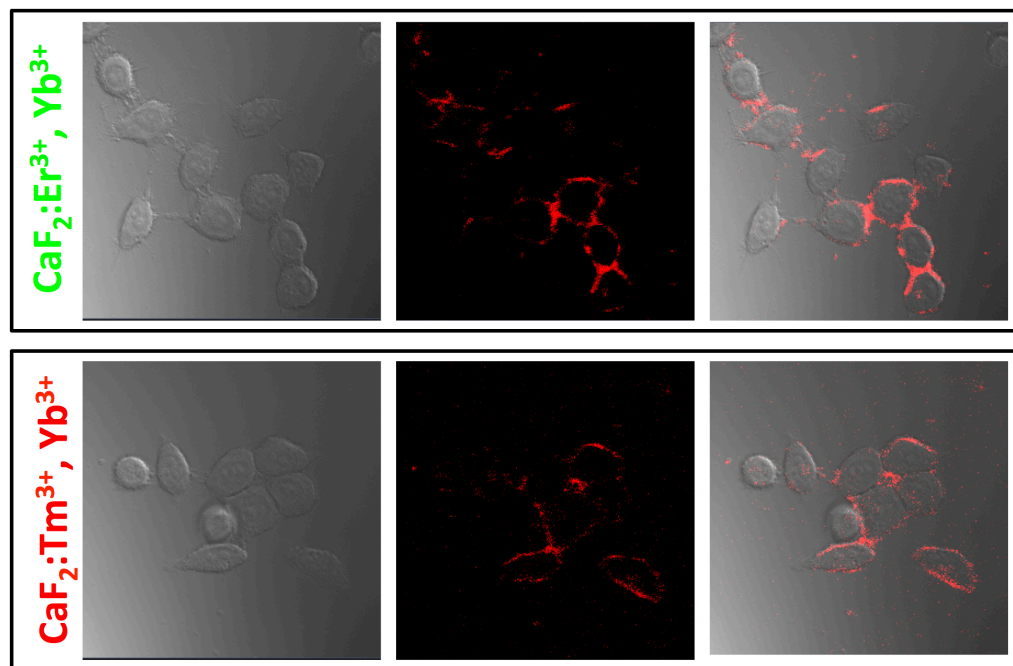
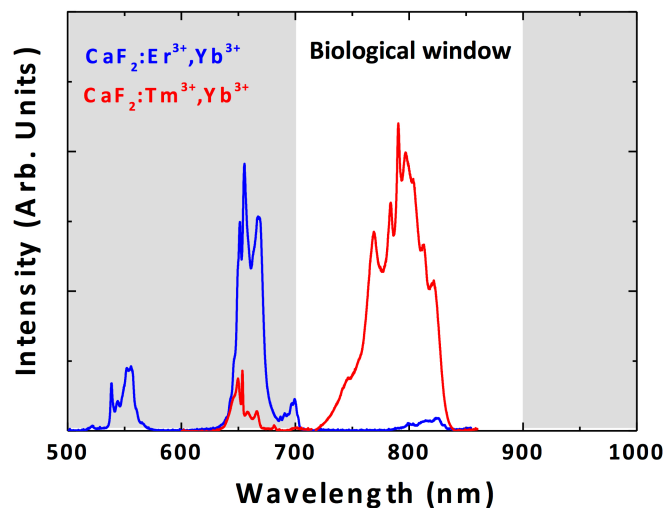
# Nanothermometer



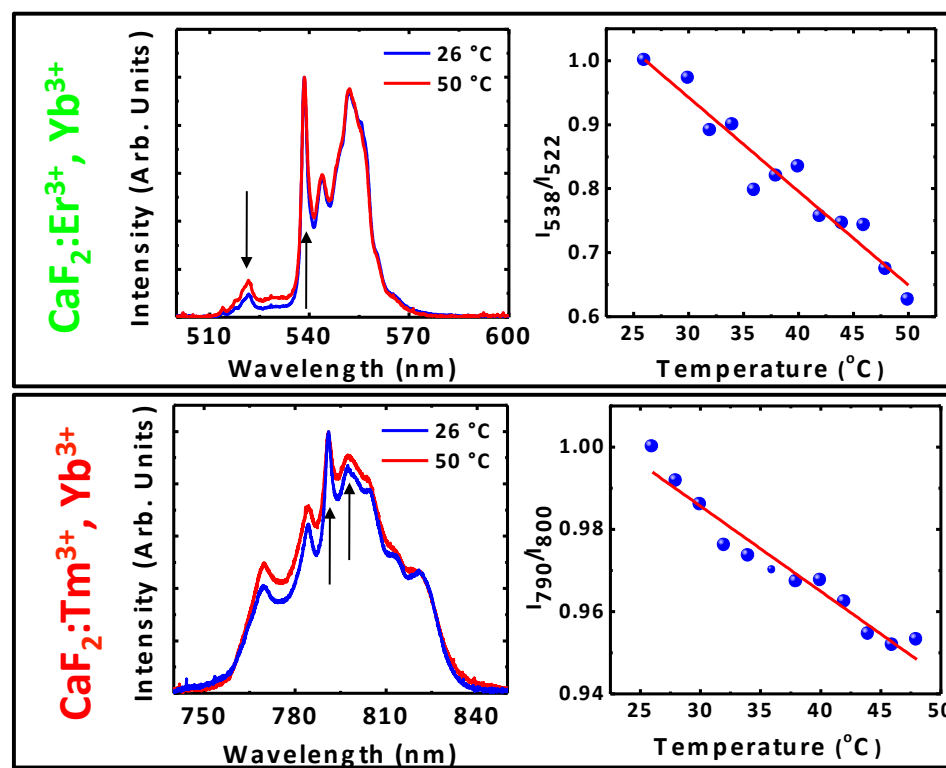
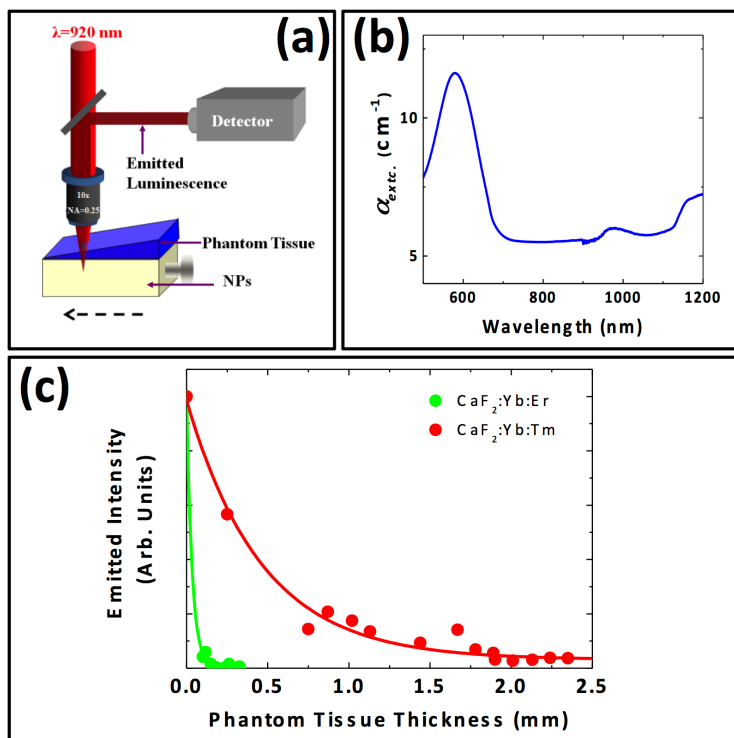
## NIR-NIR Multi-Photon Imaging

- The advantages of NIR excitation light has been previously discussed
- However, an optimal system with **both** excitation and emission wavelengths that lie within the optimal window for tissue penetration would be a powerful tool for future *in vivo* imaging and nanothermometry
- The  $\text{Tm}^{3+}$  ion has a strong emission at 800 nm

# NIR-to-NIR Multi-Photon Imaging with $\text{CaF}_2:\text{Tm}^{3+}$ , $\text{Yb}^{3+}$ Upconverting Nanoparticles



# CaF<sub>2</sub>:Tm<sup>3+</sup>, Yb<sup>3+</sup> Upconverting Nanoparticles: Towards Multi-Modality

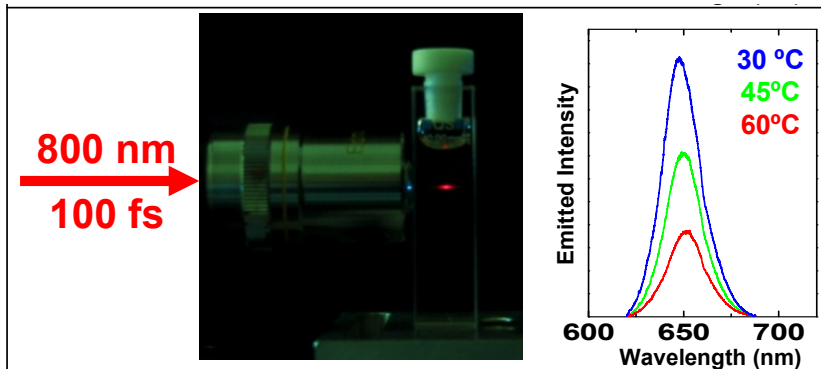


## Quantum Dots as Nanothermometers

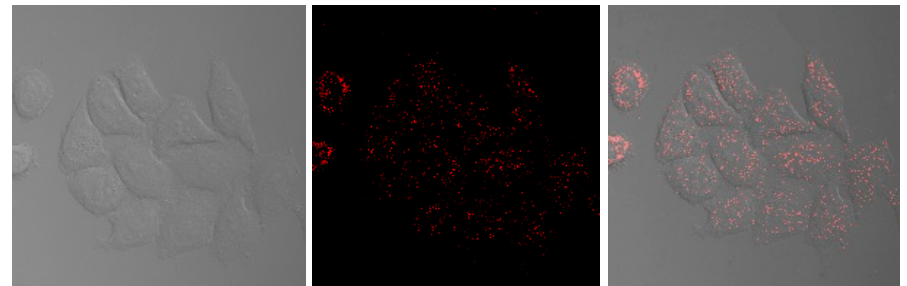
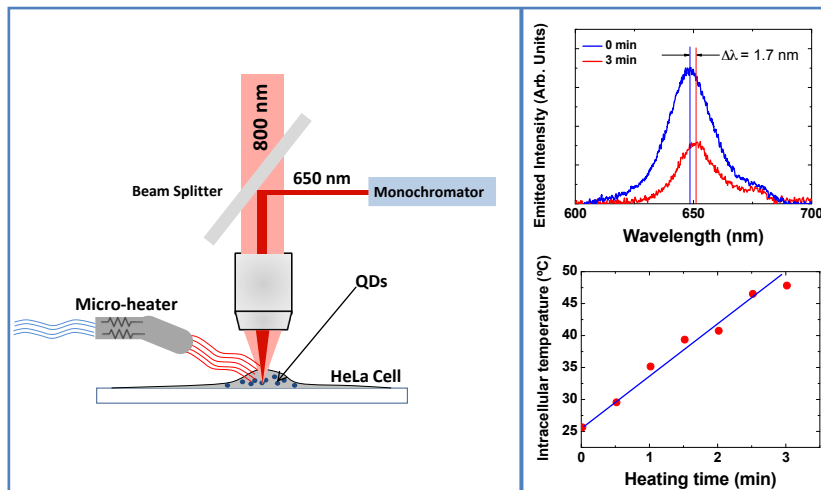
- CdSe/CdS or CdTe
- PbS/PbSe (Chalcolgenides)
- Core/Shell (PbS core/CdS shell)



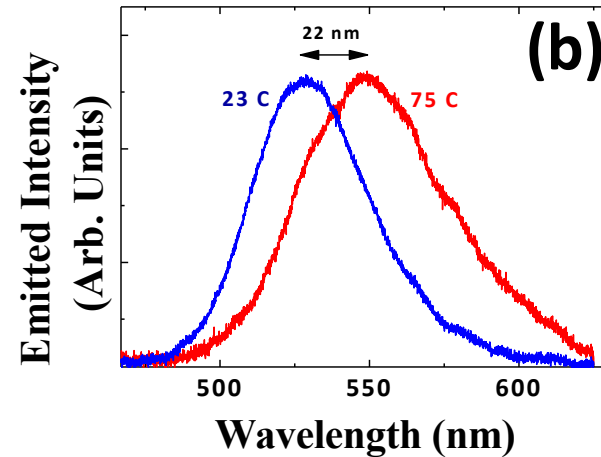
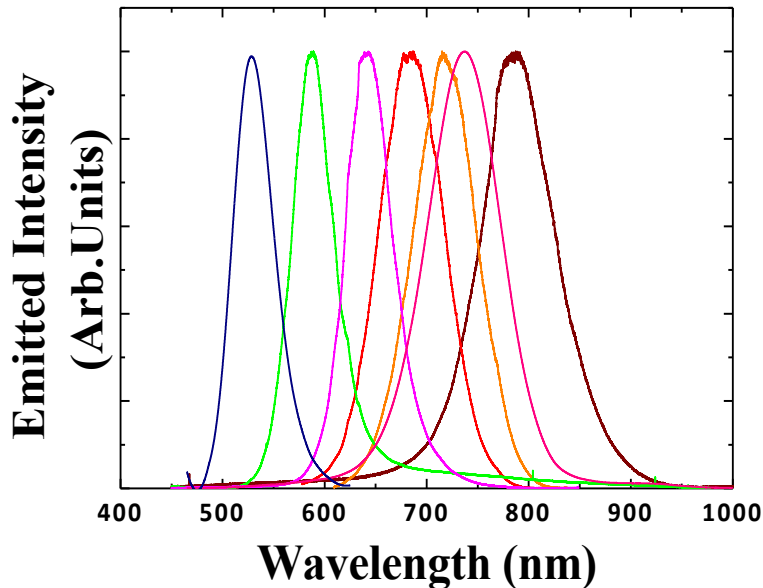
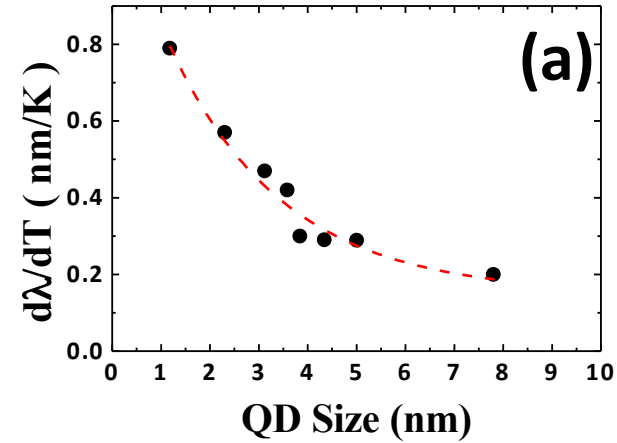
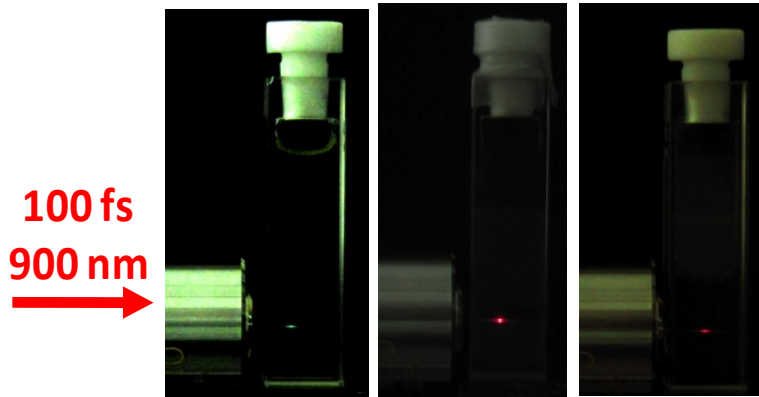
# QD Nanothermometers (CdSe)



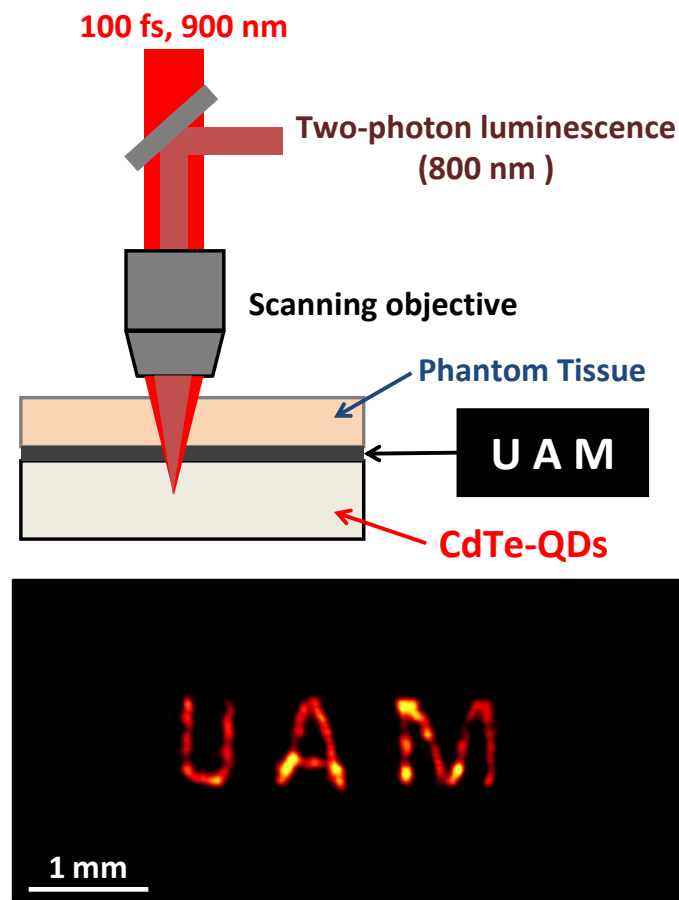
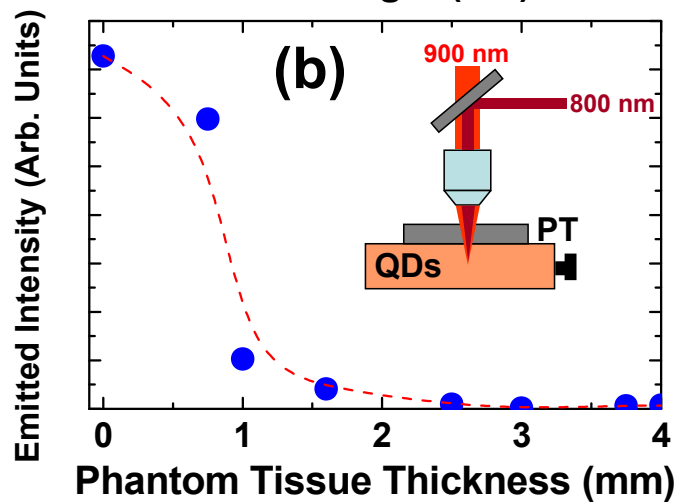
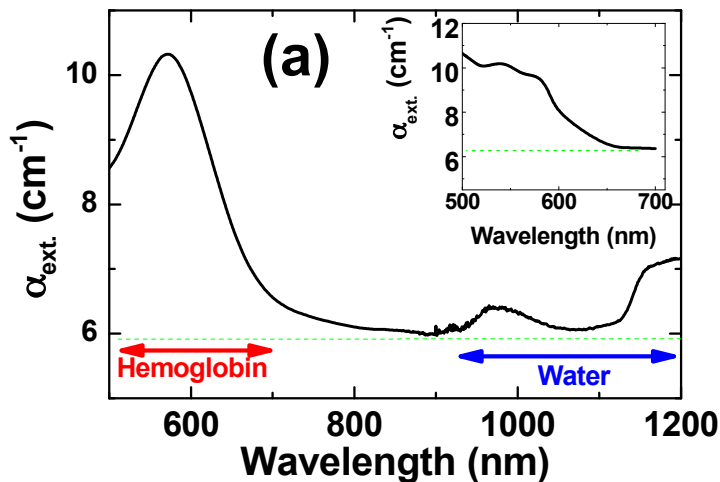
- The two-photon excited emission of CdSe QDs show a double dependence of temperature
  - Red shift of the emission
  - Decrease in intensity



# QD Nanothermometers (CdTe)



# NIR-to-NIR Multi-Photon Imaging with CdTe QDs



## Conclusions

- Multiphoton excited nanoparticles, (i) lanthanide-doped nanoparticles and (ii) semiconductor quantum dots are capable of (up)converting near-infrared light to higher energies.
- Can be synthesized by various techniques
  - Thermal decomposition (requires subsequent surface modification)
  - One-step solvothermal synthesis
  - Microwave-assisted synthesis
- Can be used in various biological applications
  - Biosensing
  - Two-photon optical imaging
  - Nanothermometry

## Acknowledgments



Canadian Institute for  
Photonic Innovations

***Développement  
économique, Innovation  
et Exportation***

**Québec** 



Natural Sciences and Engineering  
Research Council of Canada

***Fonds de recherche  
sur la nature  
et les technologies***

**Québec** 



Canada Foundation  
for Innovation

Fondation canadienne  
pour l'innovation

# INRS

Université d'avant-garde



SE =

$$\frac{1}{n_2 - p_2 - q_2}$$

$$\frac{dQ \text{ carbonus} / dt}{N \times Q / A \text{-prey}} \times 100$$

206 pb/207 pm

Weight (mass/length)

Exotherm

kDa

116-  
66-  
45-  
31-  
21.5-  
14.5-  
6.5-

1 2 3 4 5 6 7 8 9 10 11 12

$u(t)$

$u(s)$

$u(t)$

100as

100fs

(A)  $\epsilon < 0$

(B)  $\epsilon = 0$

(C)  $\epsilon > 0$

$[Cd] - [Cd^{2+}] = 1.0 \text{ nmol/L}$

...ncorporalités. L'espace occupe a.  
...logique des mutations sociales, économique  
de la société québécoise. L'espace s'inscrit  
...l'action publique et des rapports sociaux.  
...ant à comprendre

1961-1978

1946-1960

Avant-garde