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Europium-Doped Ceria Nanocrystals as Nanozyme Fluorescent Probes for Biosensing

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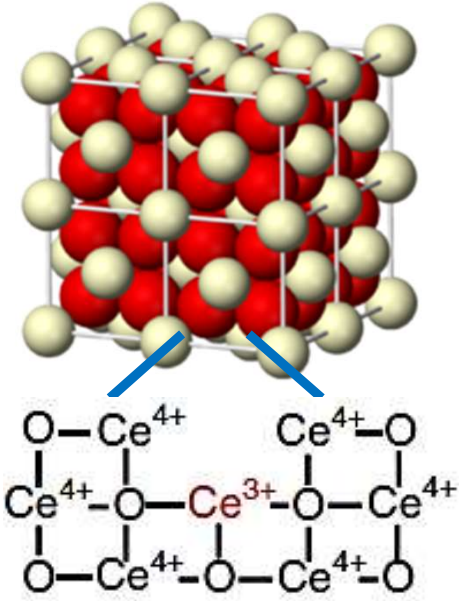
Unique properties of CeO_2 NPs

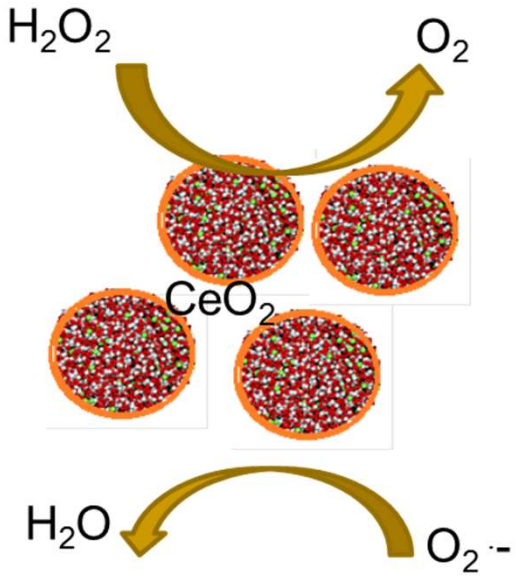
CeO_2 (ceria) NPs, nanoceria

Dual oxidation state



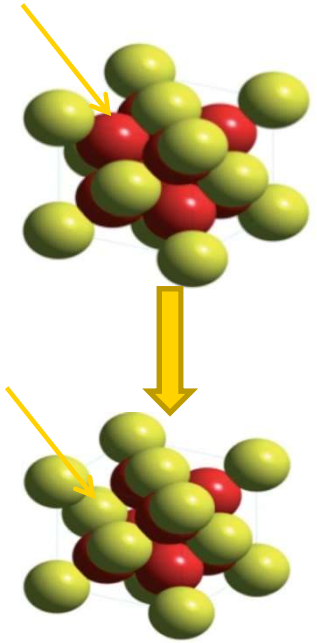
Inter-changeable oxidation states Ce^{3+}/Ce^{4+}
Surface reactivity for ox/red reactions

Recyclable ROS-scavenging activity



Rich surface functionality
Inorganic antioxidant

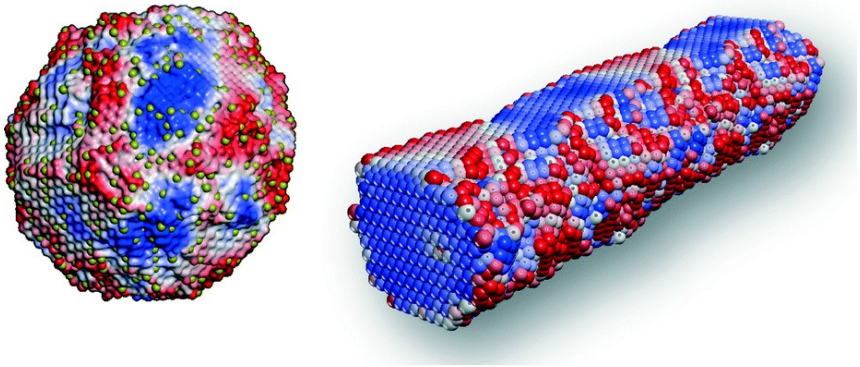
Oxygen vacancy



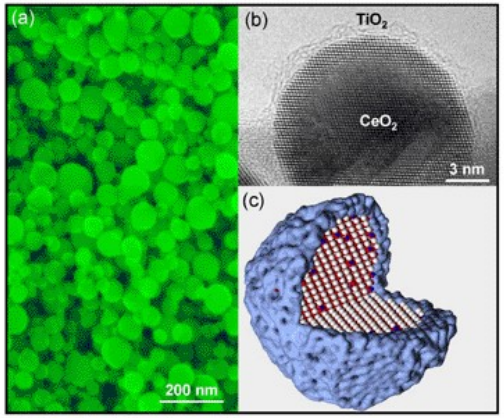
Mobile oxygen under reducing/oxidizing environments
Oxygen release/buffering capacity

- Kwon et. al., *ACS Nano*, **2016**, *10* (2), 2860–2870
- Nelson et. al., *Antioxidants,* **2016**, *5*(2), 15

Unique surface reactivity

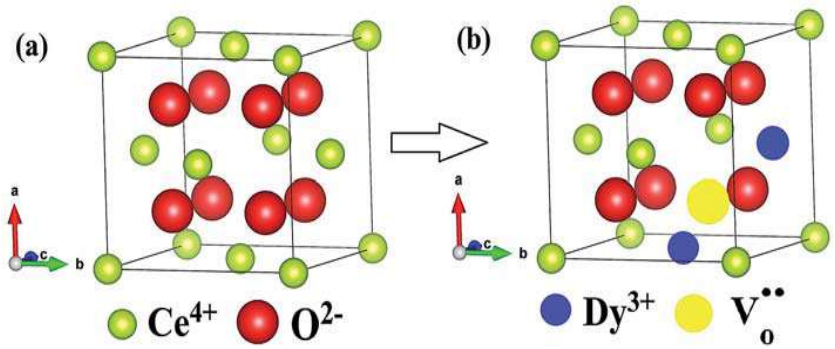


Reactivity hot spots



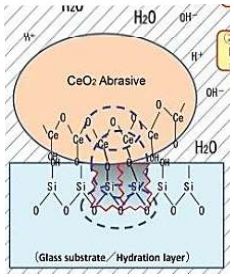
Enhanced properties by doping/surface coatings:

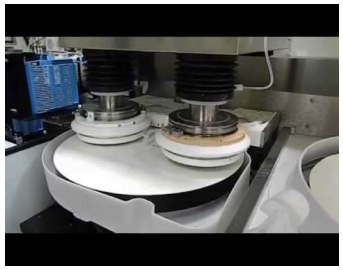
- *Catalysis Pt, Ti*
- *Fluorescence, Eu*
- *Mechanical – coating*
- *Bio-functionalization*



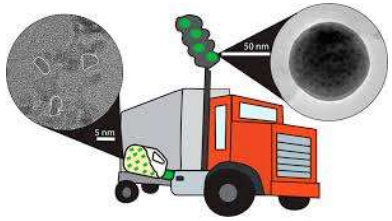
- Sayle et. al., *Nanoscale,* **2013**, *5,* 6063–6073
- Feng et. al., *Science,* **2006**, *312, 1504-1508*

Emerging applications

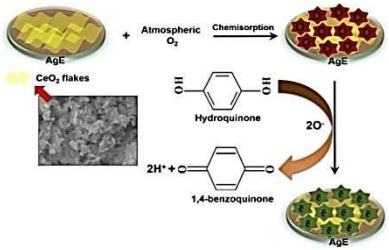


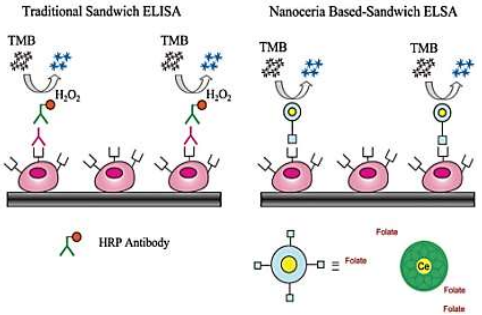


Semiconductors industry



Diesel fuel-borne catalyst (FBC)

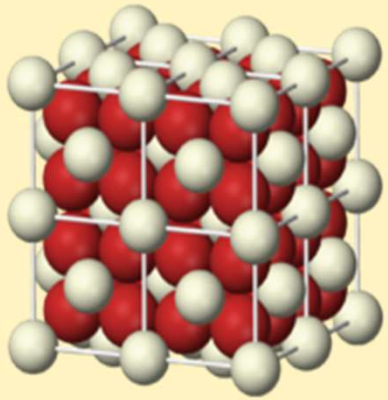




Sensing

Industrial

Biomedical

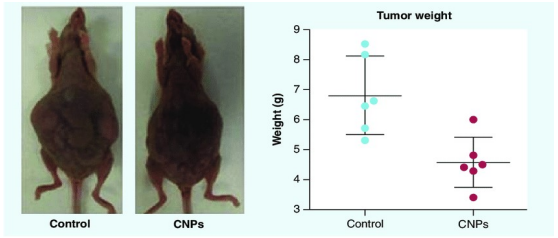


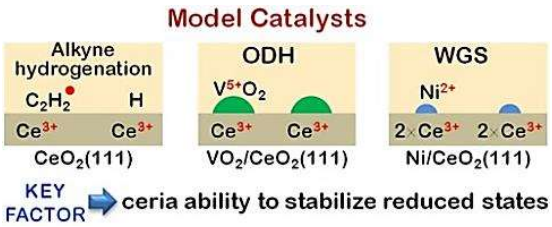
CeO_2-based Materials

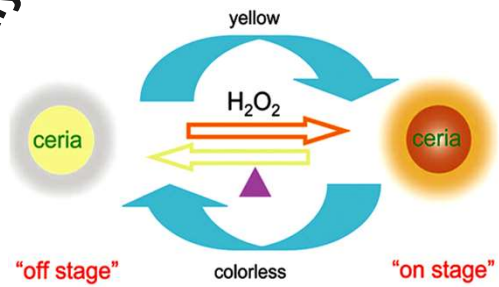
Catalysis

Bioanalytical

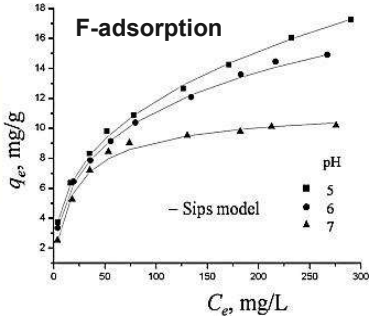
Environmental





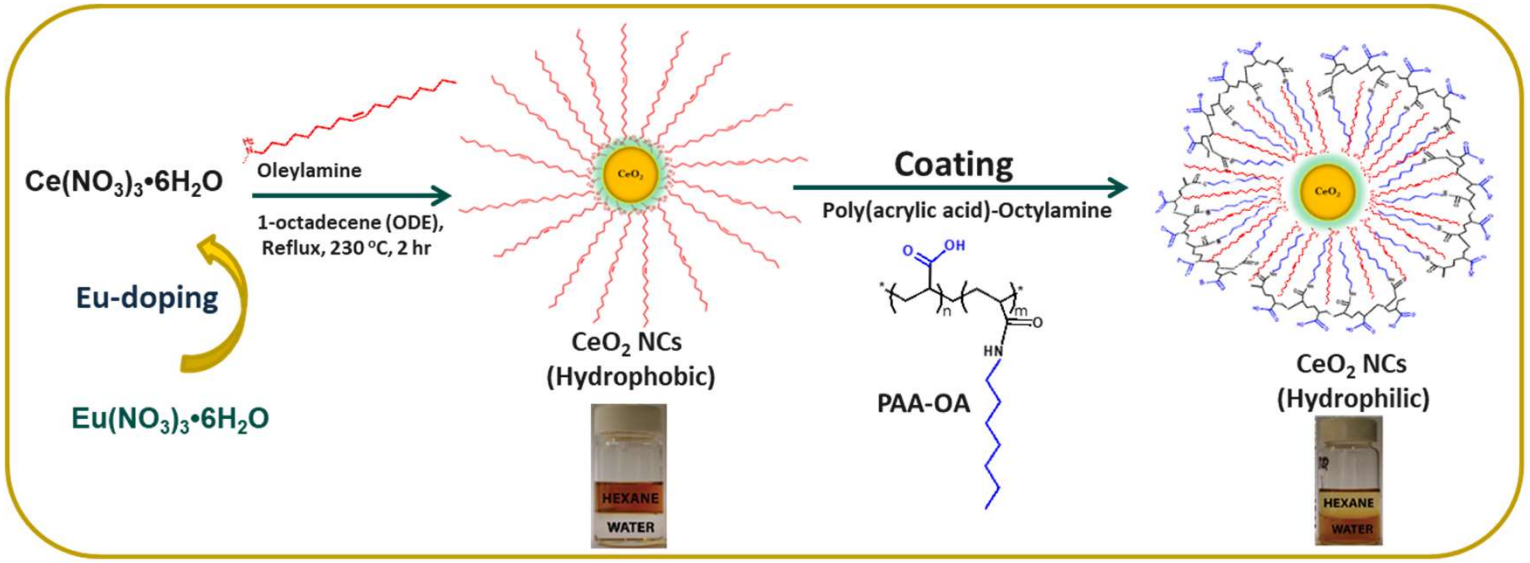


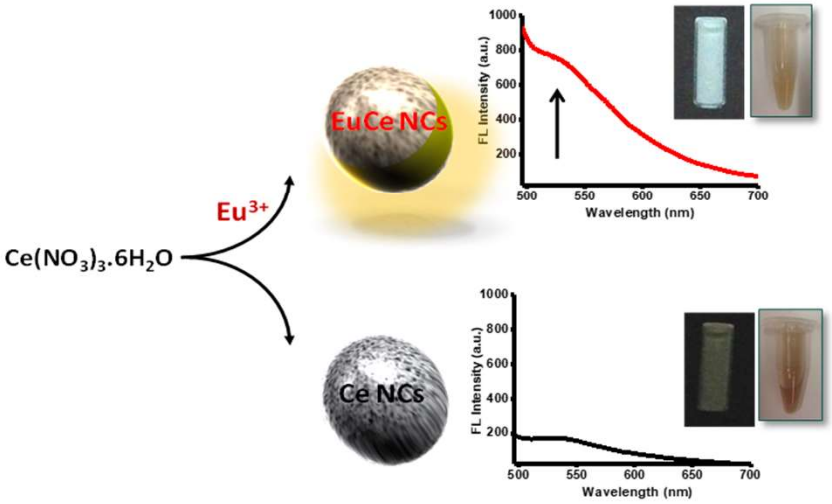
Ce^{4+} – Bone char

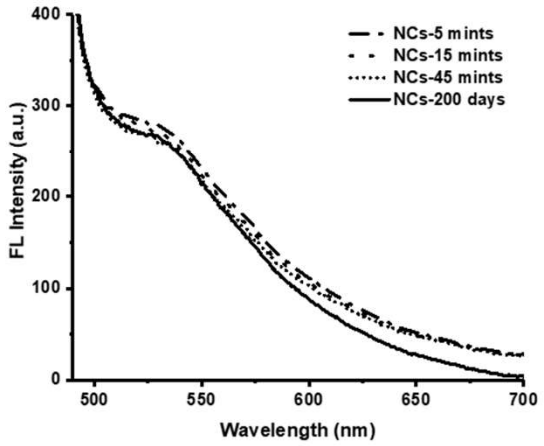


Synthesis of the Eu-doped fluorescence probe

To synthesize and characterize a novel and well-dispersed europium-doped ceria nanocrystals (EuCe NCs) with self-integrated catalytic and fluorescence sensing functions

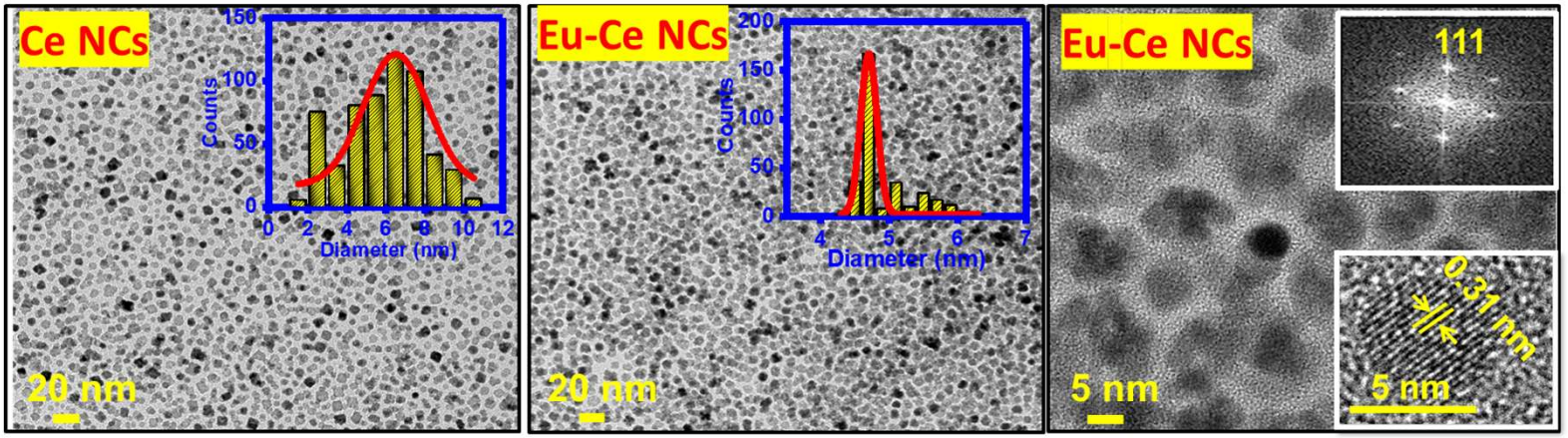




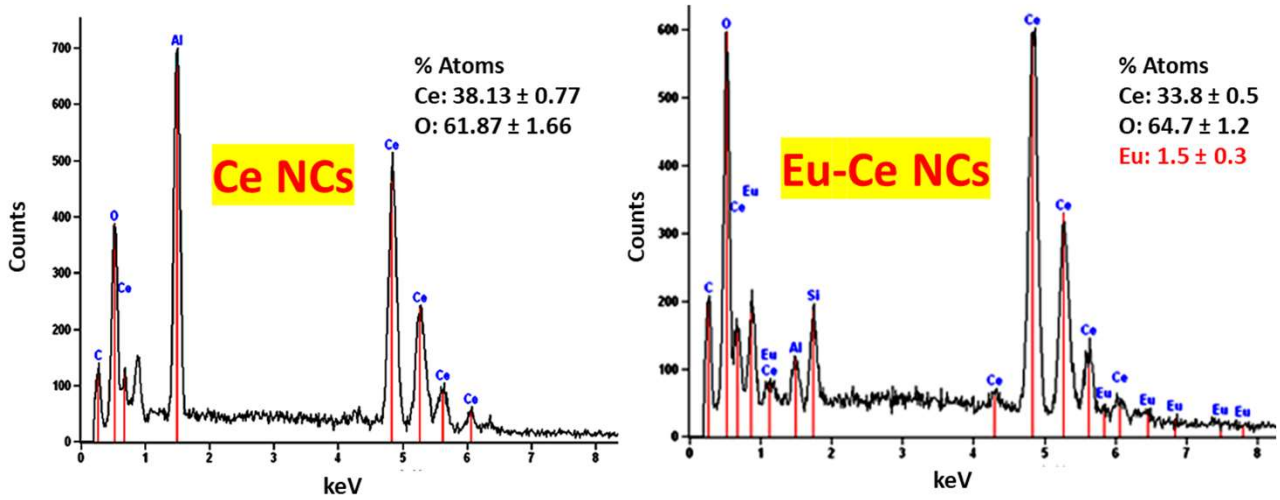


The NCs are stable (in PBS, pH 7.4) over several months

Morphological characterization



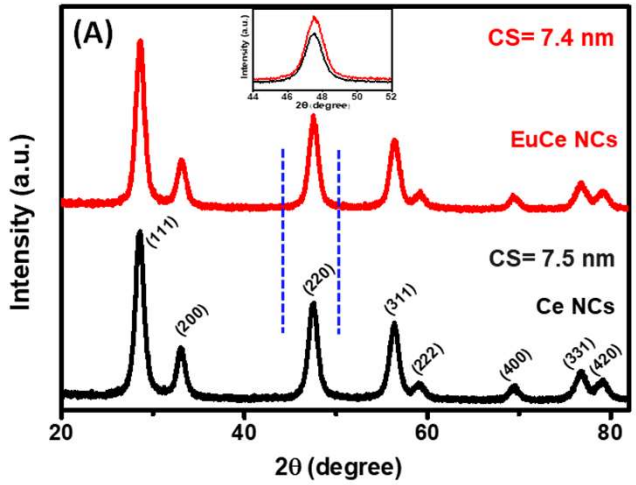
- A highly uniform NCs with average size distribution of 6.5 ± 2 nm.
- Introducing Eu^{3+} into the ceria host resulted in uniform spherical shape NCs with a slightly smaller average size distribution of 4.7 ± 0.1 nm as compared to Ce NCs.
- A diffraction pattern of fcc crystals in the (111) planes.



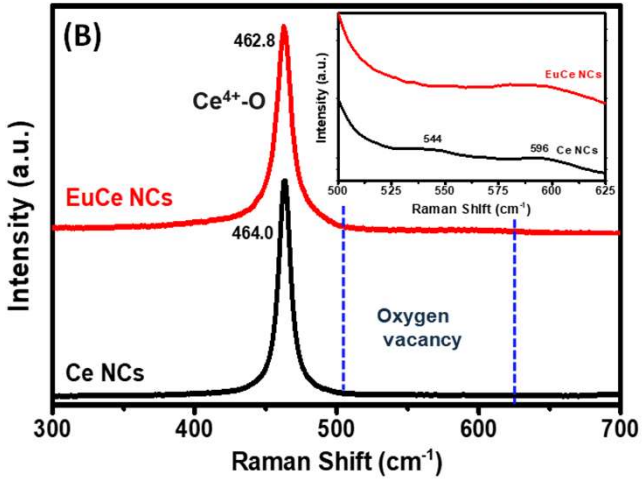
- EDS analysis confirms the presence of Eu atoms in the Eu-Ce NCs.

Structural characterization

Powder X-ray diffraction (PXRD)

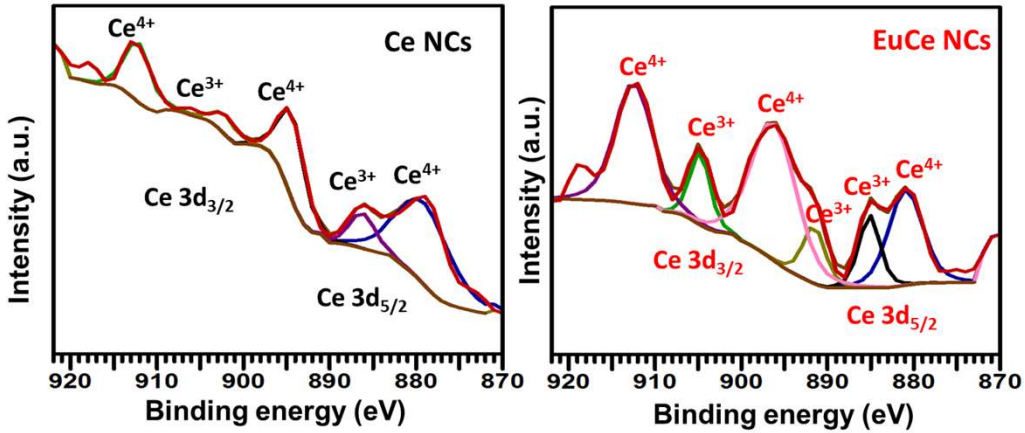


Raman spectroscopy



- Diffraction peaks reveal formation of a face centered cubic (fcc) structure. After incorporation of Eu^{3+} in the ceria lattice the intensity of the diffraction peaks is enhanced.
- Raman spectroscopy analysis demonstrates changes in the vibrational structure caused by doping with Eu^{3+}.

XPS Analysis

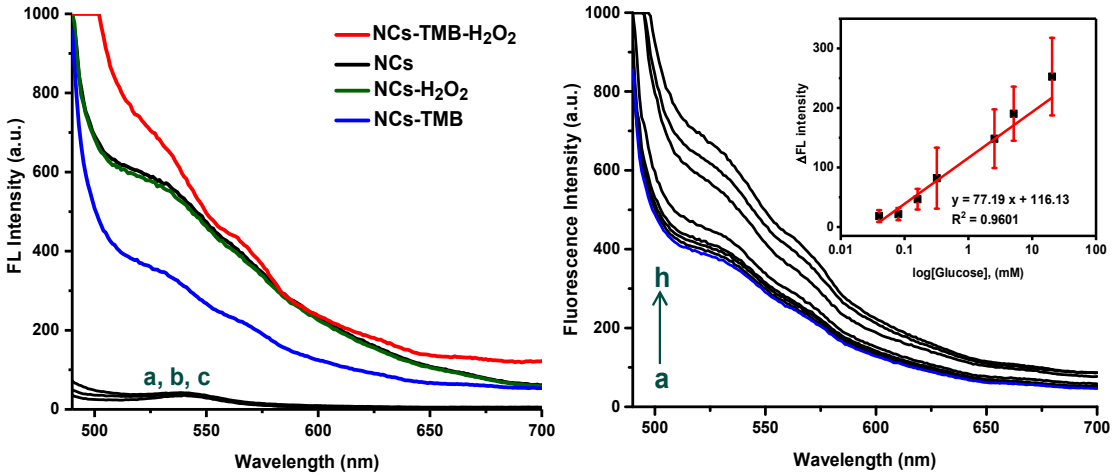


[Ce^{3+}] = Ce NCs: 18.9% EuCe NCs: 29.3%

- All peaks changed significantly suggesting changes in Ce^{3+} concentration due to doping.

Bioanalytical applications

❖ Detection of H_2O_2, Glucose, and Lactate



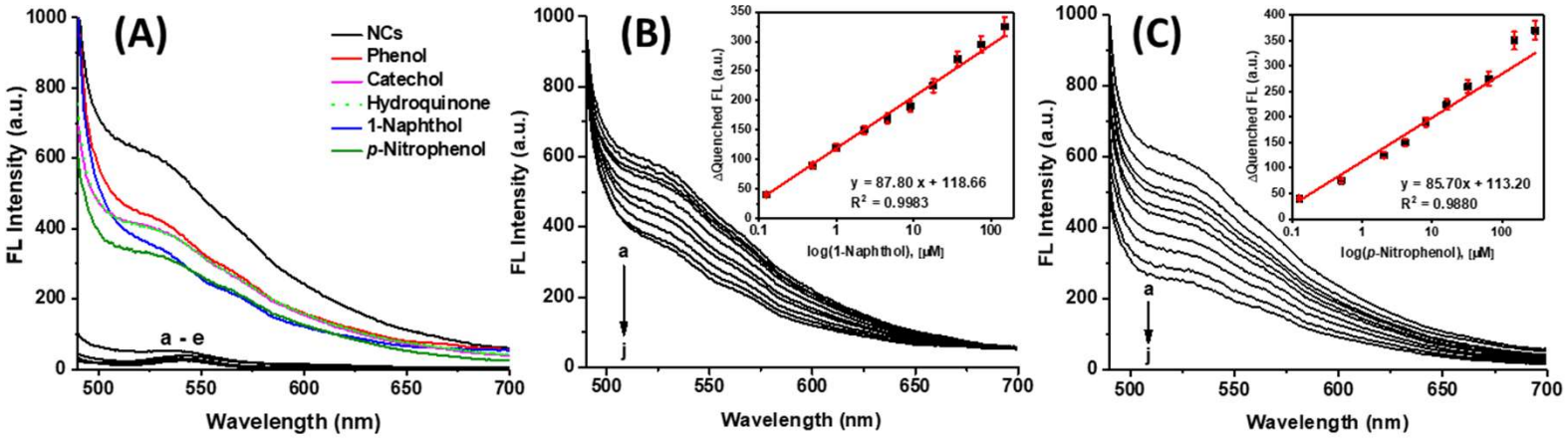
Glucose+ GOx + O_2 + H_2O → gluconic acid + H_2O_2

$2CeO_2 + H_2O_2 \rightarrow Ce_2O_3 + O_2 + H_2O$

- ❑ The range of 0.04−20.48 mM
- ❑ LOD of 175 μM

- ❑ Upon addition of TMB to EuCe NCs, the FL intensity decreased. After addition of H_2O_2, the FL response was significantly enhanced and recovered, which suggests a catalytic effect of the NCs.

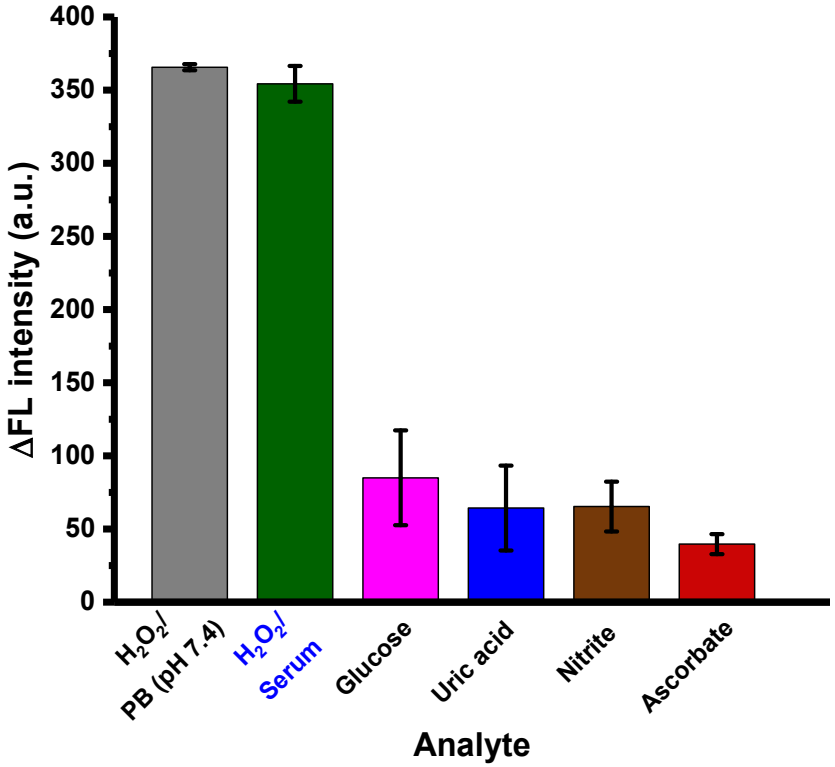
❖ Detection of Phosphatase Activity

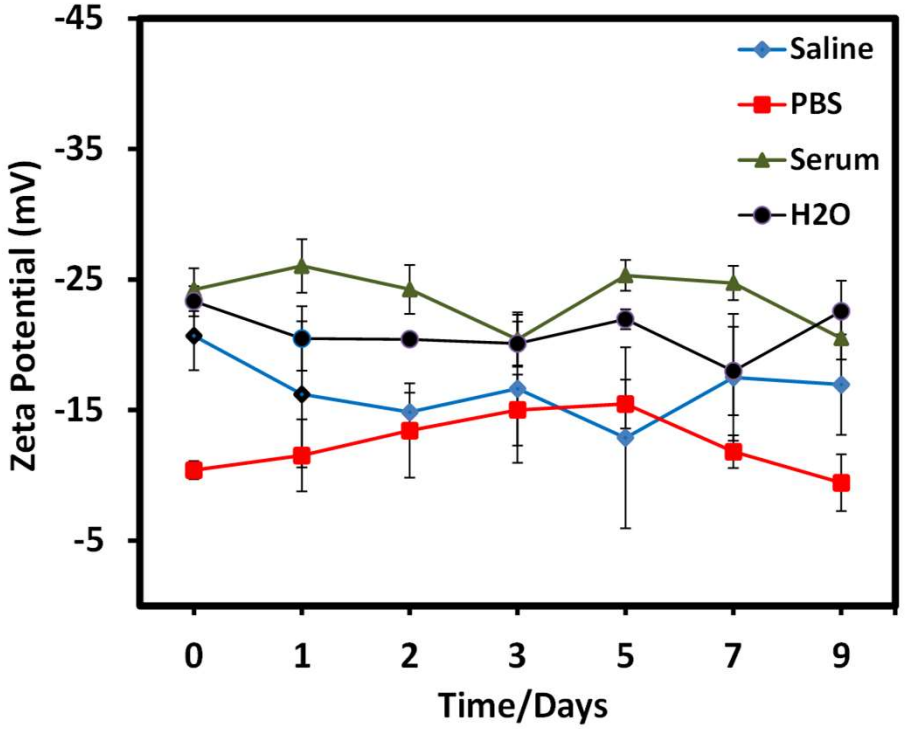


- ❑ The EuCe NCs have also provided an excellent platform for measuring phosphatase activity.
- ❑ The detection mechanism is based on the FL quenching of EuCe NCs by the hydrolysis products of phosphatase.

Selectivity & stability of the probe

❖ **Determination of H_2O_2 in Serum Samples and Selectivity Study**



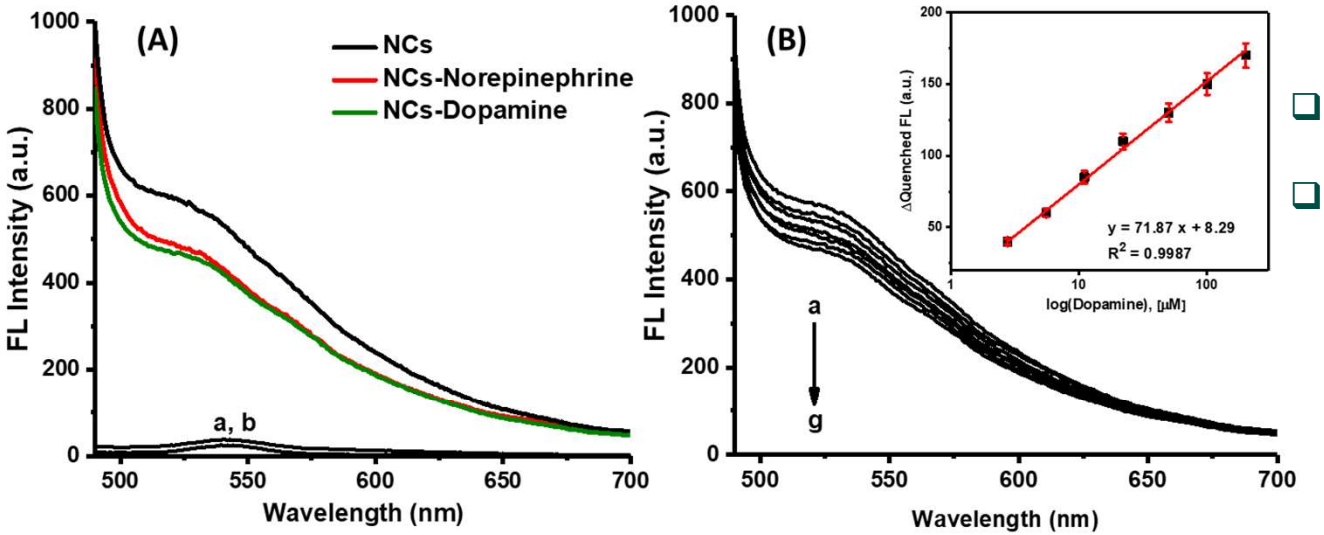


- ❑ The probe works well in a more complex sample (human serum)
- ❑ None of these species produced a significant fluorescent response

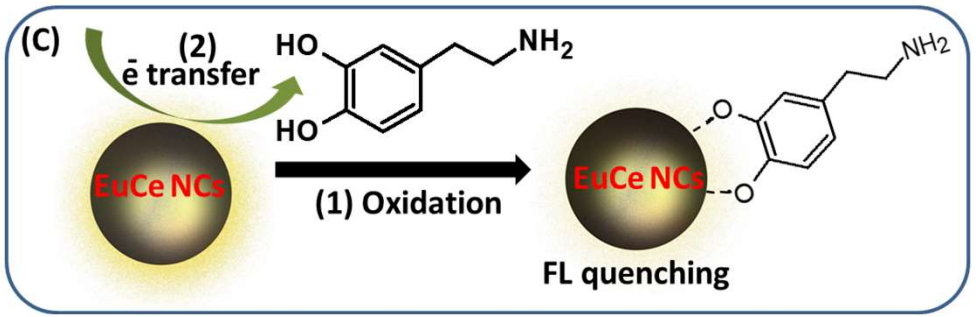
Comparison with the literature

❖ Detection of Neurotransmitters (NTs)

- ❑ The sensing capabilities of this method were further extended to the detection of catecholamine.
- ❑ Using the oxidase like properties of the EuCe NCs to induce in situ oxidation and measurement of NTs.



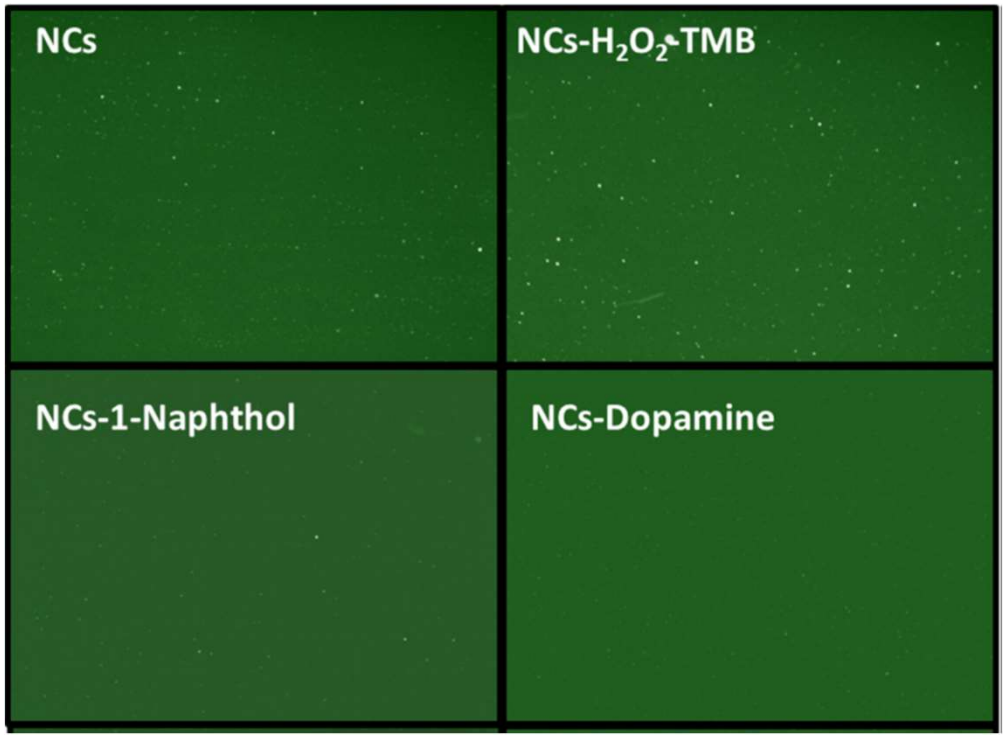
- ❑ Linear range of 2.75−200 μM for dopamine.
- ❑ LOD : 1.0 μM



- ❑ Ceria NPs induce oxidation of the catechol ring in catechol-containing NTs, followed by surface binding of the reactive intermediates

Fluorescence Imaging

The fluorescence images of EuCe NCs in the presence of H_2O_2, 1-naphthol, and dopamine



Fluorescence microscopy images. λex = 466 nm. Magnification of the objective is 63X; the size of the particle has an average of 4.7 ± 0.1 nm.

- The fluorescent intensity of EuCe NCs + TMB + H_2O_2 assay was enhanced, while that of EuCe NCs-1-naphthol and EuCe NCs-dopamine was quenched when compared to EuCe NCs alone.
- This correlates well and confirms the fluorescence spectroscopy data.
- These results are promising and suggest that these EuCe NCs have potential as an imaging probe for diagnostics, and therapeutic applications

Conclusion

- This study described a convenient methodology for the synthesis of highly stable, uniform, water dispersed, and strongly fluorescent lanthanide-doped EuCe NCs.

- The EuCe NCs have an average size of ~5 nm and exhibit excellent fluorescence emission characteristics and stability for several months under different buffer and pH conditions.

- The fabricated new fluorescent Eu-doped CeO_2 NPs was demonstrated with imaging and sensing capabilities for applications in the bioanalytical/sensing & biomedical field.

- We expect the promising potential of this material to open new ways to design nanobiosensors for bioimaging and biocatalytic applications.

Acknowledgments

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