Scientific Innovation Through Integration

EMSL

SRC Engineering Research Center for Environmentally Benign Semiconductor Manufacturing

Ceria Nanoparticles: Environmental Impacts on Particle Properties and Potential Effects on Biological Systems

D. R. Baer
don.baer@pnnl.gov

P. Munusamy and S. Thevuthasan
EMSL, Pacific Northwest National Laboratory, Richland WA 99352
A. S. Karakoti, S. V. N. T. Kuchibhatla,
Battelle Science and Technology India, Pune, India
S. Seal
Advanced Materials Processing and Analysis Center, Nanoscience Technology Center, Mechanical Materials Aerospace Engineering, University of Central Florida, FL

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Nanomaterials can help solve many important problems

http://www.nisenet.org/catalog/programs/nanotech_consumer_products

There are issues: Increasingly recognized that NP characterization is often inadequate

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Tiny traits cause big headaches

Nanotech medicines held up by lack of particle characterization.
Daniel Cressey

"Characterization is the biggest challenge to this field," Simon Holland, GlaxoSmithKline

"Everybody accepts that as an academic community we haven't been characterizing enough," Kenneth Dawson, University College Dublin

http://www.nature.com/news/2010/100914/full/467264b.html

Nanoparticles designed for medical application

Nano-object Characterization Challenges –
Paper & news article titles suggest problems

- "**The problem with determining atomic structure at the nanoscale**"
  - S. J. L. Billinge and I. Levin, Science (2007).
- "**Common pitfalls in nanotechnology**…,"
  - R. M. Crist, et al. Integr. Biol. (2013).
- "**The characterization bottleneck**,"
  - E. K. Richman and J. E. Hutchison, ACS Nano (2009).
- "**Discriminating the states of matter in metallic nanoparticle transformations: What are we missing**?"
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What is the problem?

Environmental Molecular Sciences Laboratory

EMSL, **a national scientific user facility** at the Pacific Northwest National Laboratory, provides ***integrated experimental and computational resources*** for discovery and technological innovation in the environmental molecular sciences to support the needs of DOE and the nation.

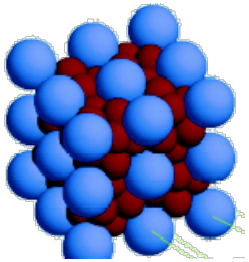
Focus on the environment and energy

What are the issues? What we have learned from many studies

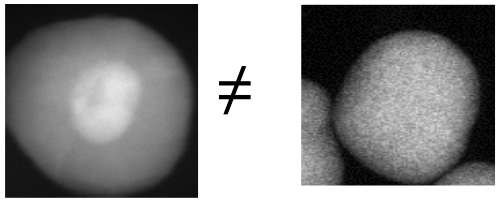
- Focused beneficial and potential negative impacts of three nanoparticles
  - **Iron metal-core oxide-shell** particles to remove environmental contaminants in ground water
  - **Ceria** nanoparticles which have a wide variety of uses
  - **Silver** nanoparticles in wide use in consumer products
- Common **characteristics** that **complicate understanding** and **characterization**
- **Ceria as an example**
  - **Conflicting** Biological impacts
  - **Environmentally** induced **changes** in chemical state
  - **Dynamic**, not static
  - **Synthesis** and **delivery** challenges

Characteristics that complicate understanding and characterization

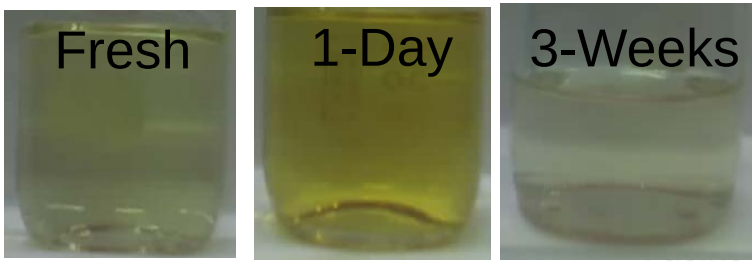
Most atoms are near a surface or interface



Nanoparticles are not created equal



Particles often change as a function of time
Particles are dynamic – not static



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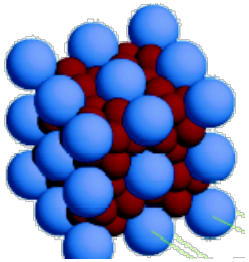

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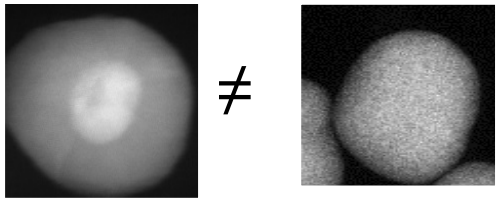
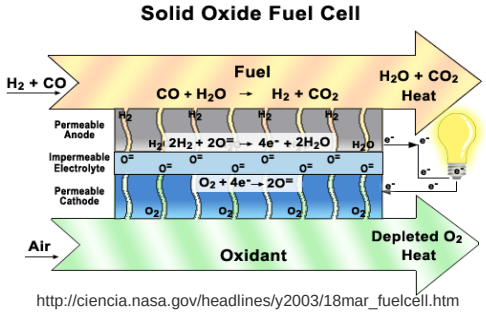


Particles often change as a function of time
Particles are dynamic – not static

An example: Cerium oxide (Ceria, CeO_2) – contradictory behaviors

Solid Oxide Fuel Cells

(Ce 3+ and Ce 4+)

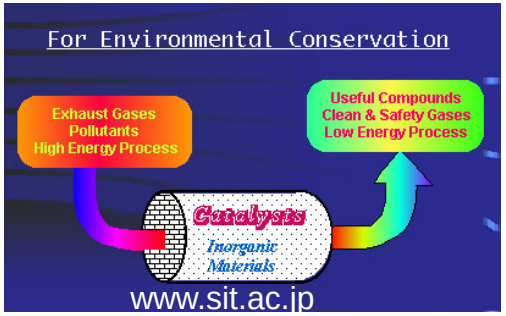


http://ciencia.nasa.gov/headlines/y2003/18mar_fuelcell.htm

Films or powder pellets

Catalysis

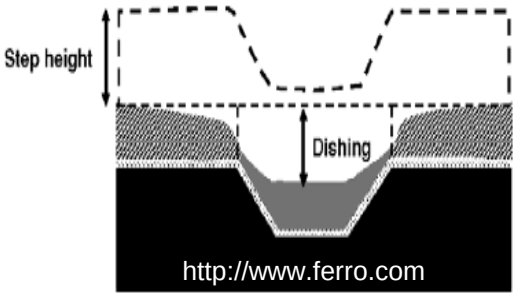
(Ce3+ and Ce4+)



Particles

Microelectronics (CMP)

(Ce3+)



Particles

Bio-medical Applications

(Ce3+ and Ce4+)

Particles

UV-protection Cancer treatment

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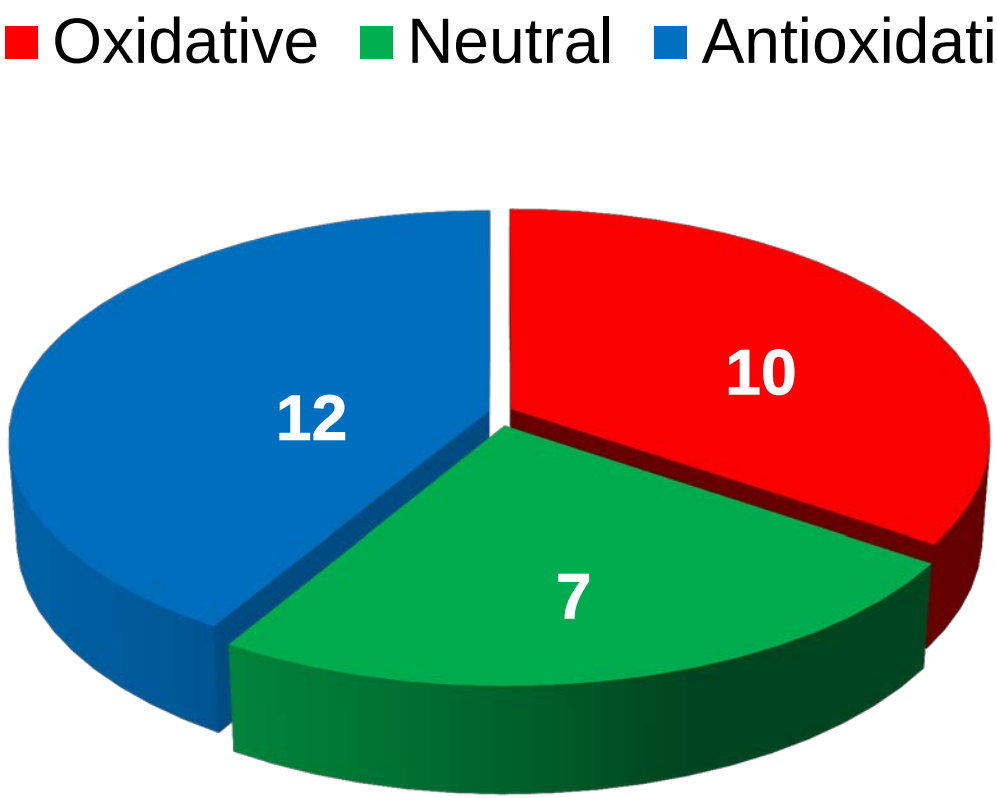
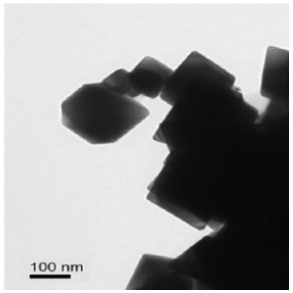
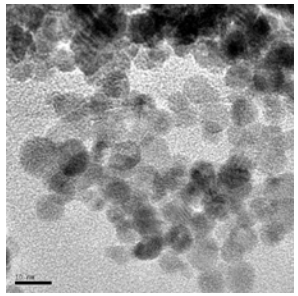
Contradictions in biological impact: Cerium oxide nanoparticles – Antioxidative or oxidative?

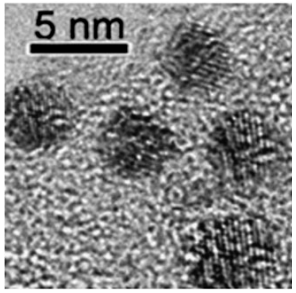


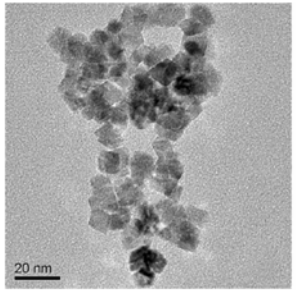
Scattered observations in literature on biological effects of cerium oxide nanoparticles (Dec 2010)

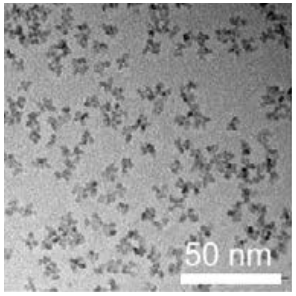
Cerium oxide nanoparticles – What is being tested

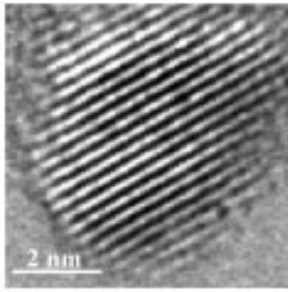


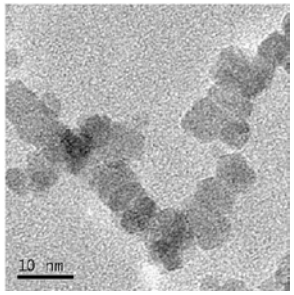


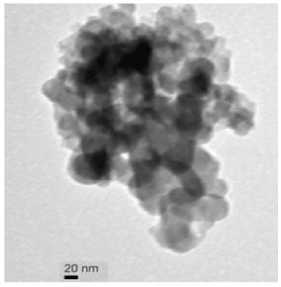


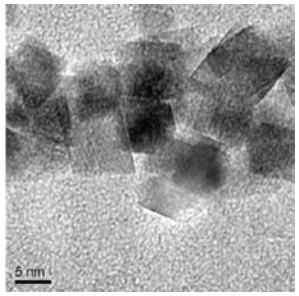


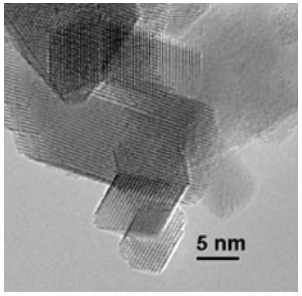


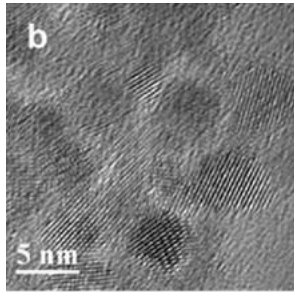












Huge variation in size, shape, crystalline state and agglomeration

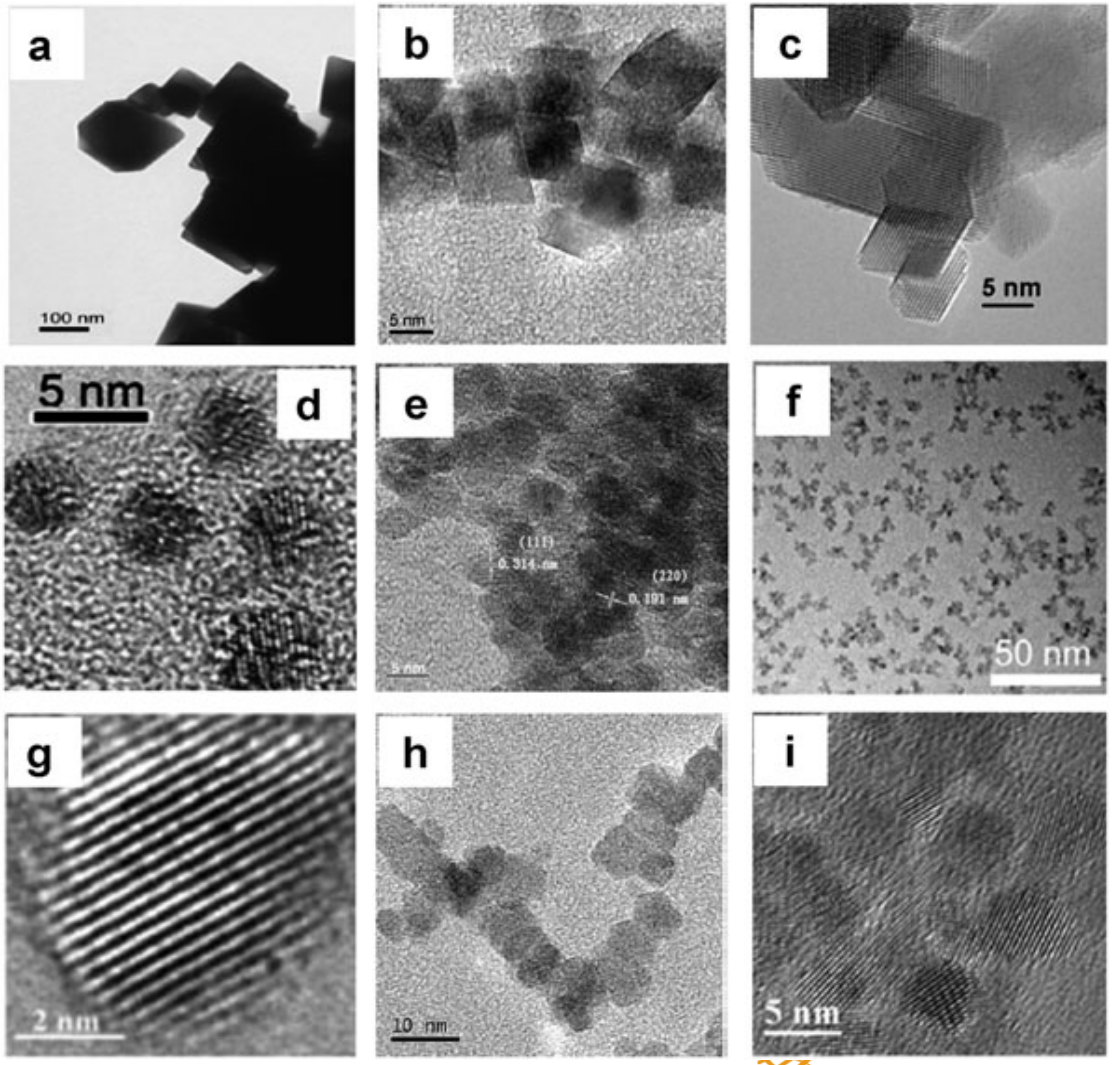
Karakoti et al Surface and Interface Analysis - 2012

Ceria synthesis involved different tempertures

Heated or calcined at high temperature (>300°C)

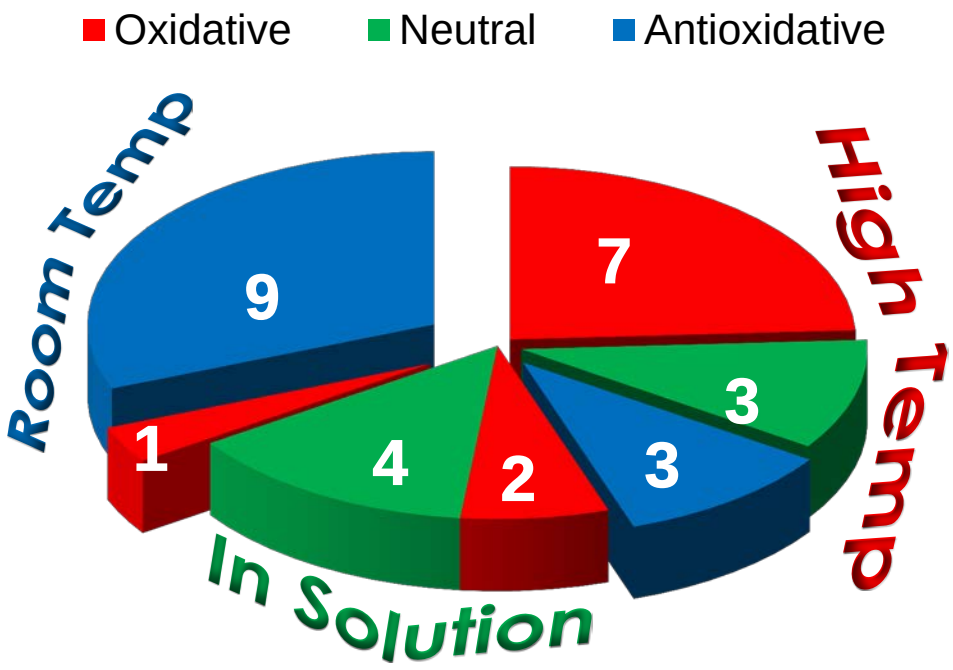
Heated (<100°C) in solution (with or without surfactants)

Room temperature synthesis (with or without surfactants)



Karakoti et al Surface and Interface Analysis - 2012

Cerium oxide nanoparticles – Biological impacts based on synthesis



- Nanoparticles are not created equal
- Lack of control over properties of engineered nanomaterials may lead to varying biological responses
- Only one of the possible reasons not the only possible reason

Karakoti et al Surface and Interface Analysis - 2012

Take home messages

- Synthesis methods, processing conditions and history of nanomaterials have an important impacts on their properties
- Nanomaterials are like chameleons
  - **Nanomaterials are not static entity and often change with conditions**
    - Impacts shelf life and product stability
    - Important for understanding behavior in the environment and biological impacts




Inconsistency chemical and physical properties

- Contradictory reports of **biological impacts** of ceria nanoparticles.
  - Many good anti-oxidant effects
  - Some toxic behaviors reported
- Inconsistent report of physical and chemical Properties
  - Data reported measuring **quantum confinement**
  - Seen in different size ranges (or not seen) by different groups

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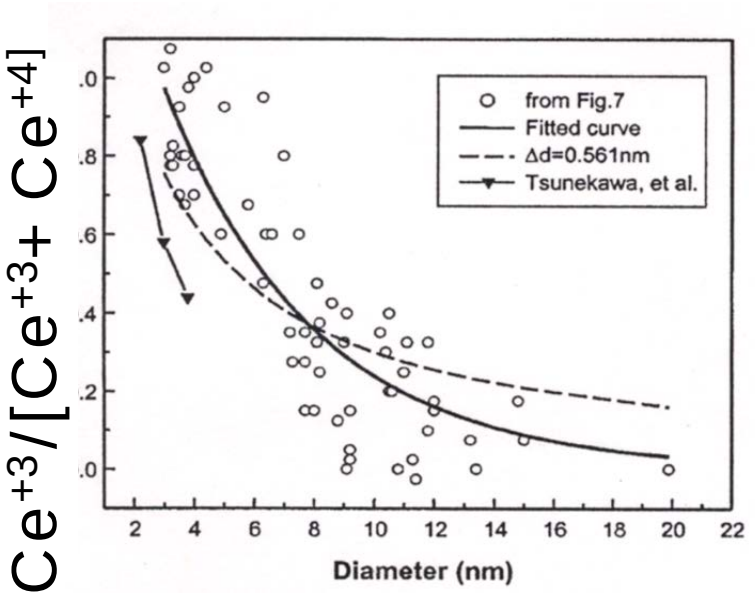
- Inconsistent report of physical and chemical Properties
  - Data reported measuring **quantum confinement**
  - Seen in different size ranges (or not seen) by different groups
- Switching of chemical state important. Can that explain property variations?

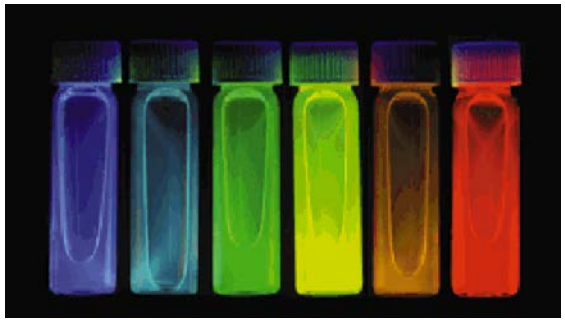
Size and chemical state

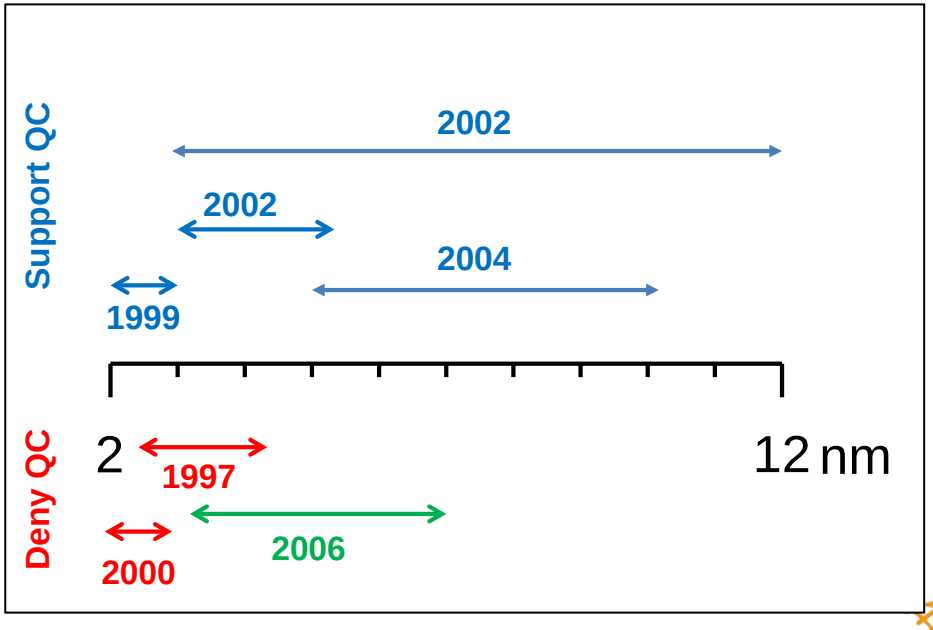


Wu et al. Phys. Rev B 69, 125415, 2004

What causes of differences in observations of quantum confinement?

- Data reported measuring quantum confinement inconsistent
  - Seen in different size ranges (or not seen) by different groups





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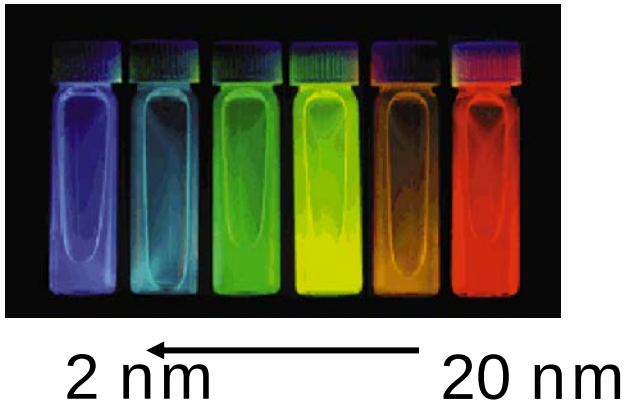
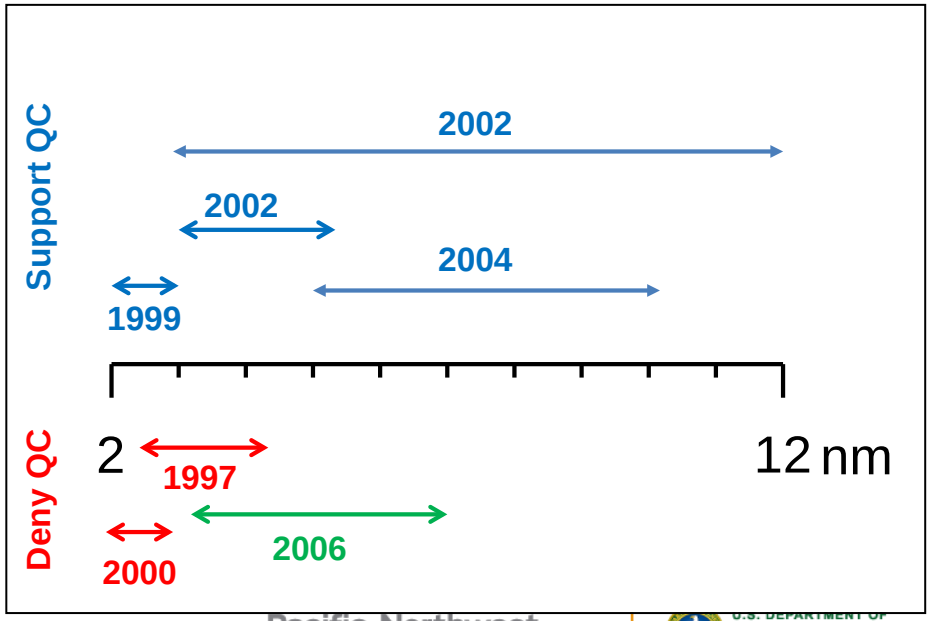


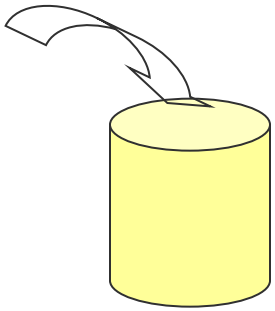
- Quantum confinement identified by measurements of band gap.
- Can we reproduce measurement of changes in band gap as function of size
- Might the BG differences observed be due to chemical state effects rather than quantum confinement?



Formation of Ceria Nanoparticles to study of size dependent oxidation state

$Ce^{3+} + OH^- + ½\ H_2O_2 \rightarrow Ce(OH)_2^{2+}$

$Ce(OH)_2^{2+} + 2\ OH^- \rightarrow Ce(OH)_4 \rightarrow CeO_2.2H_2O$



Particles form quickly when peroxide added salt solution

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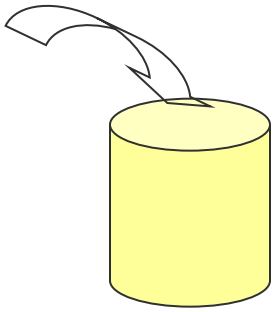
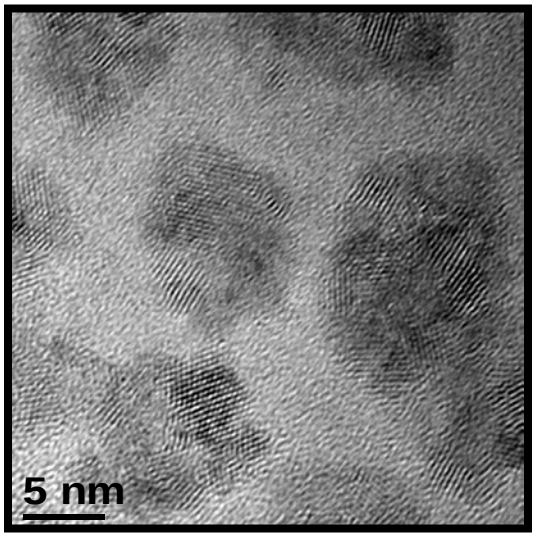


Particles form quickly when peroxide added salt solution

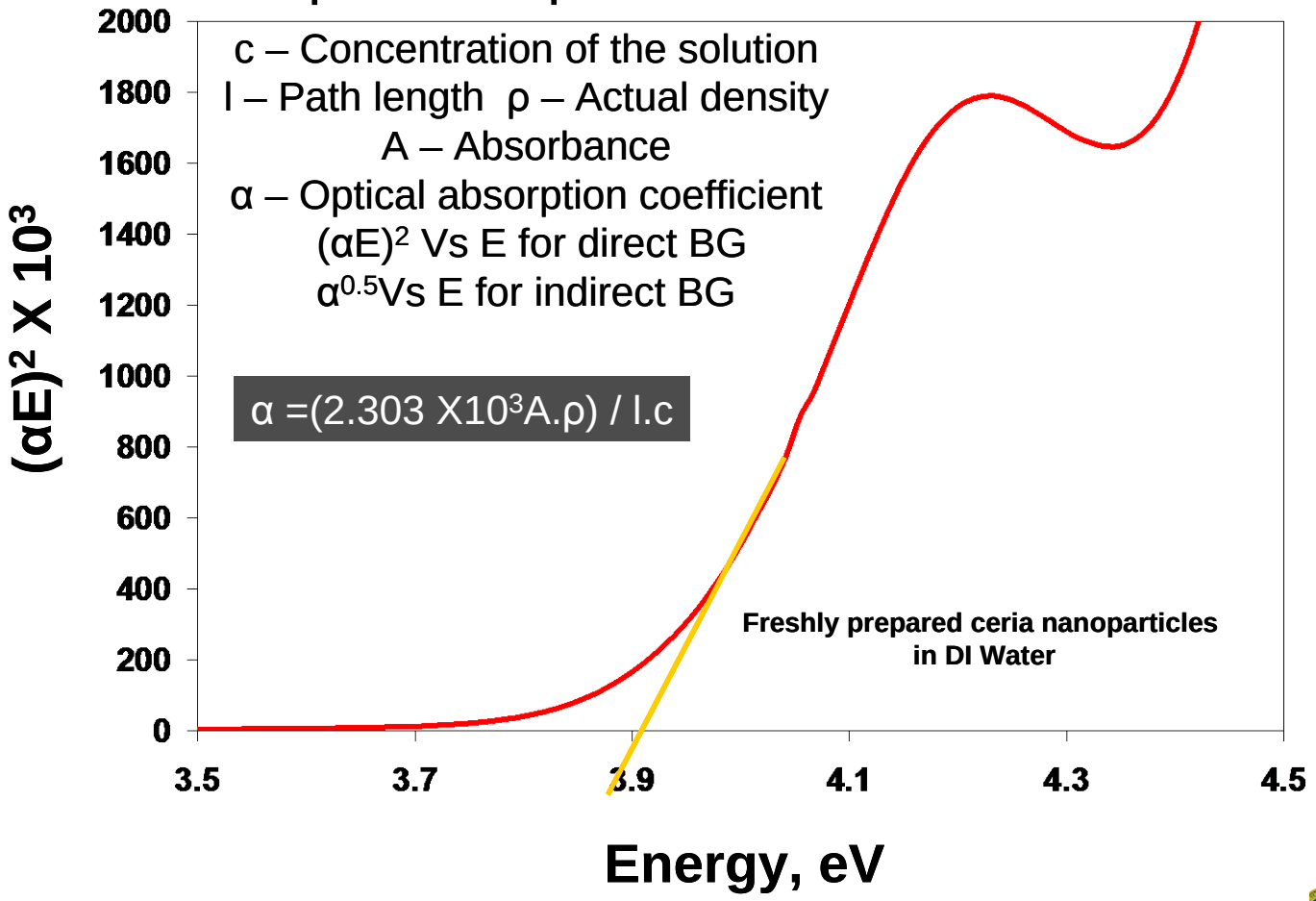
TEM of particles harvested within an hour show 3-5 nm particles in 15-20 nm agglomerates. Particles appear the same to TEM analysis for all conditions to follow



- 15-20nm agglomerates
- No specific morphology

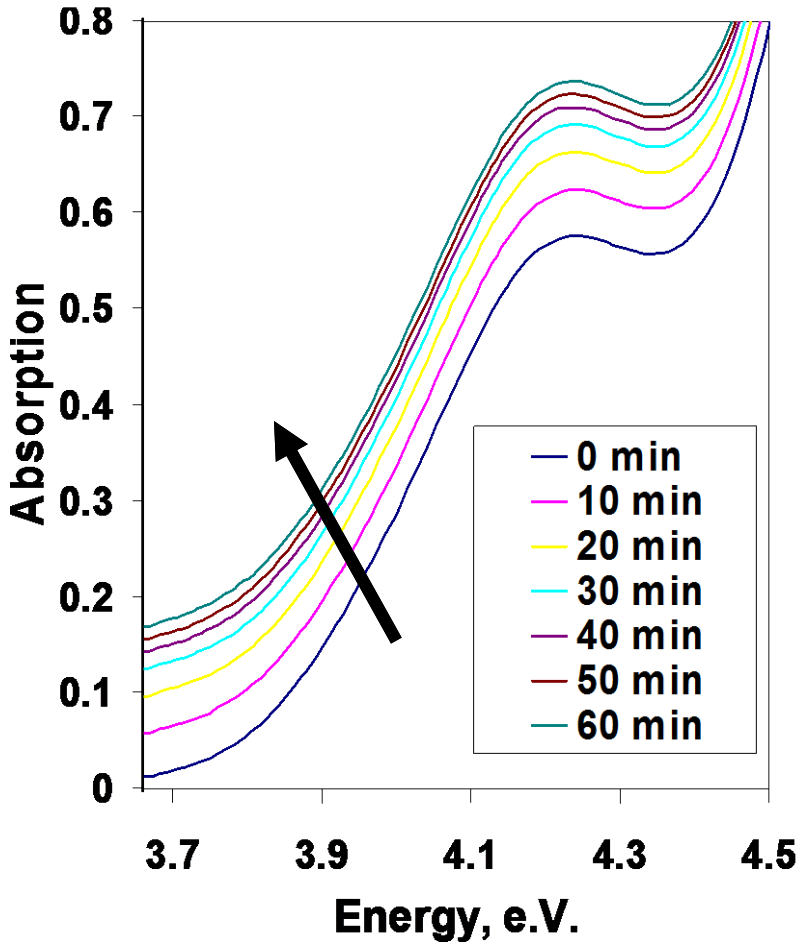
Apparent band gap often determined by optical adsorption

Band-gap value can be obtained from the energy intercept of the plot between αE^2 and E



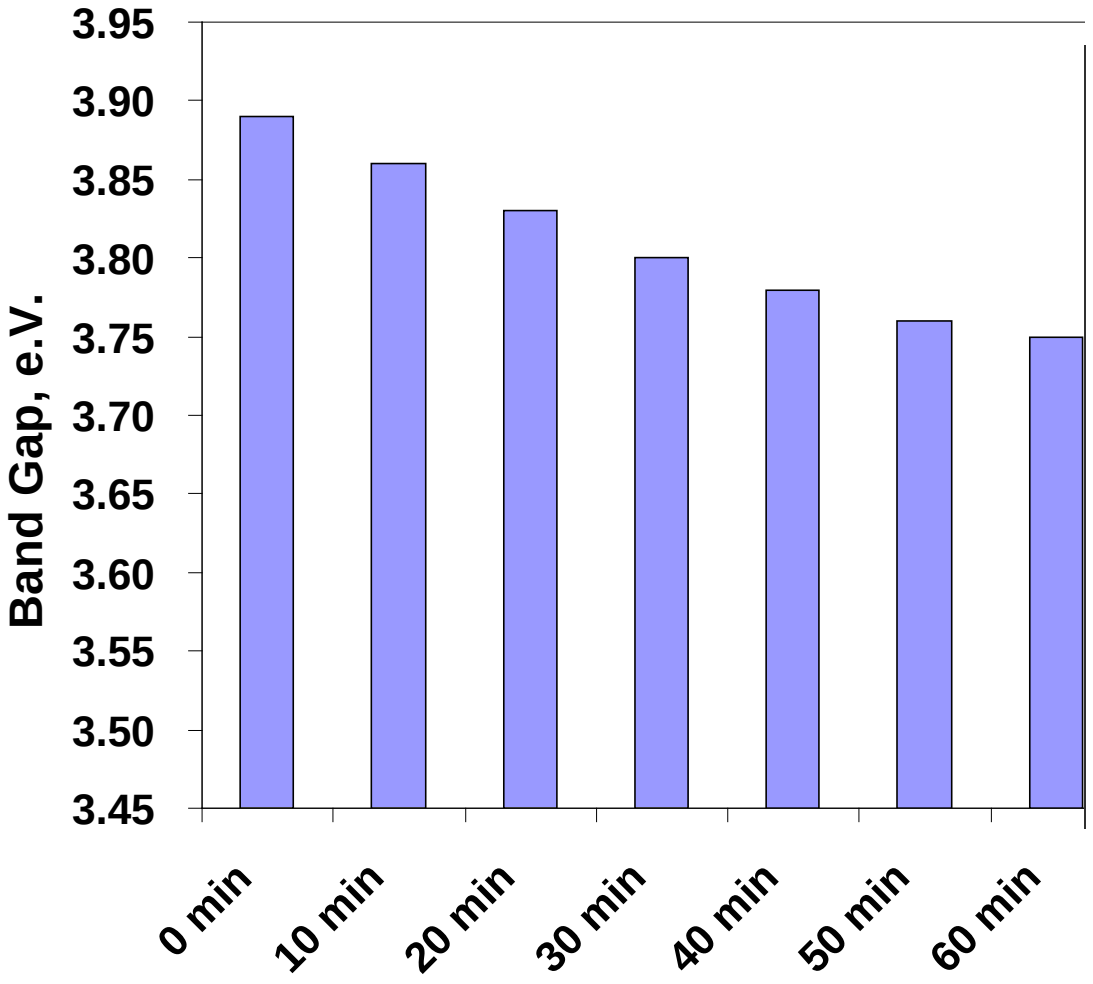
Absorption Data During Nucleation

Absorption Data Collected Soon After Nucleation Appears Consistent with Quantum Confinement



Band gap appears to shrink as particles grow

Bohr radius ~7.0nm



Band gap variation in water based ceria nanoparticles as a function of time

Band gap appears to shrink as particles grow

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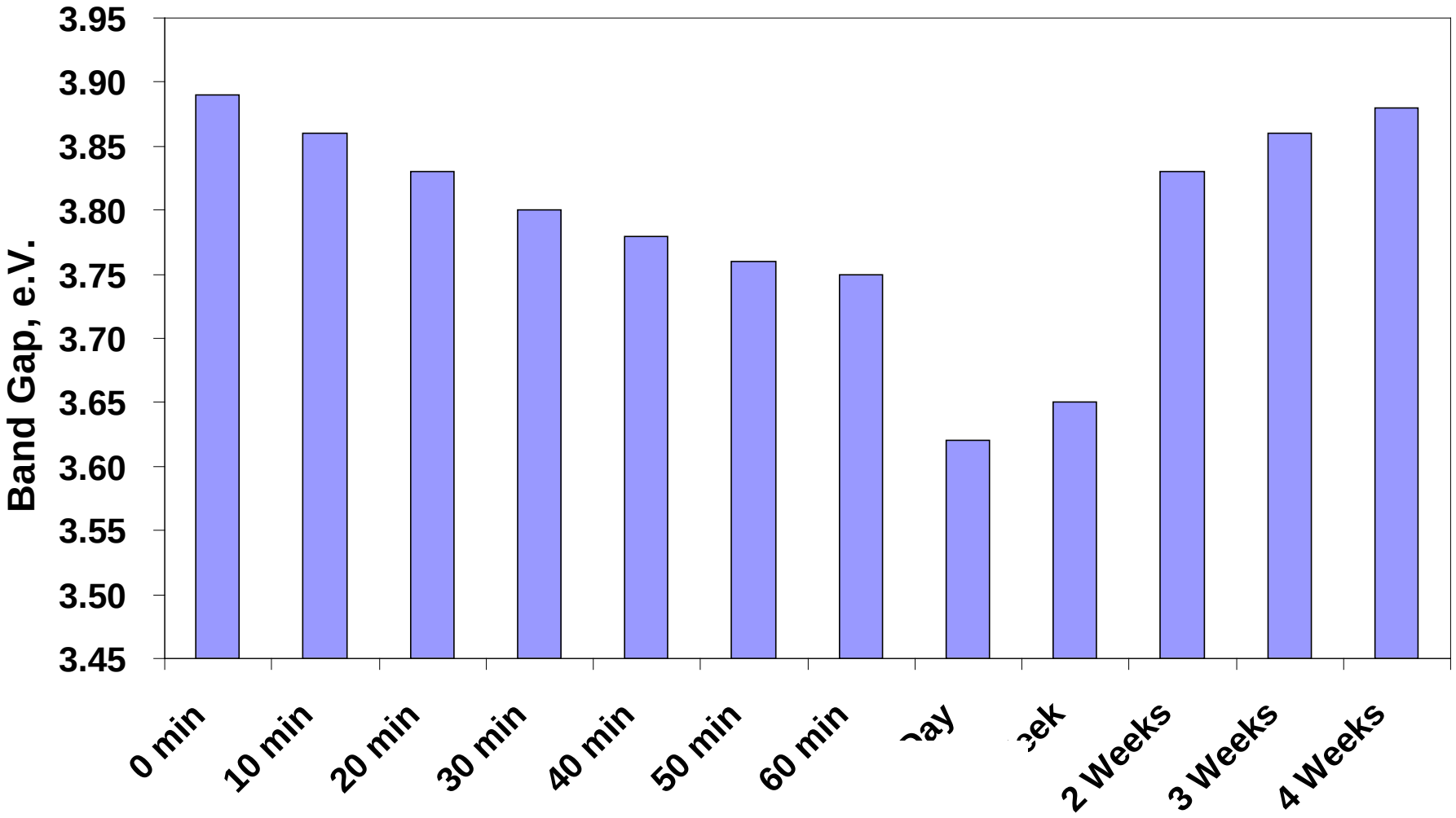

Band gap variation in water based ceria nanoparticles as a function of time

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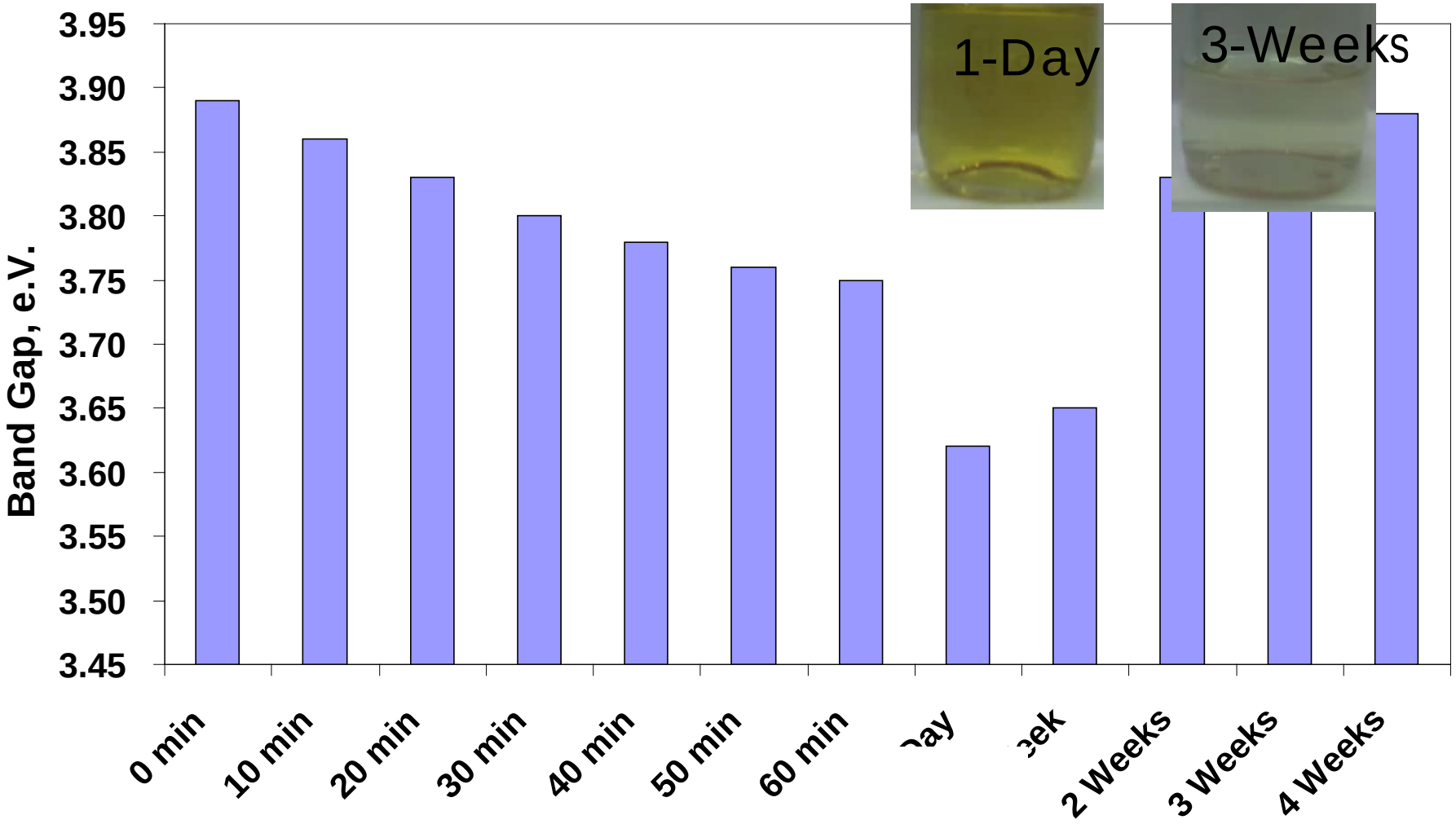
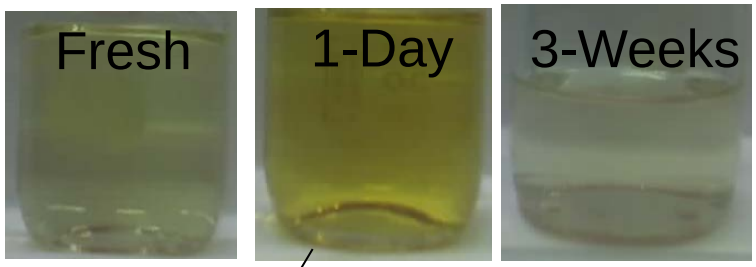
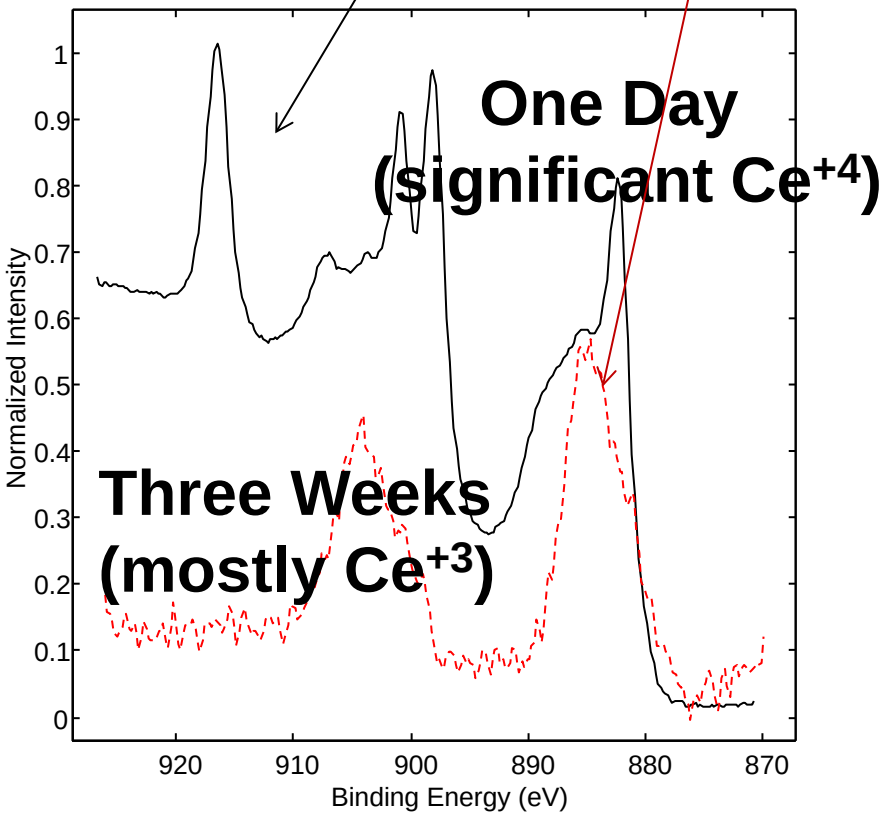


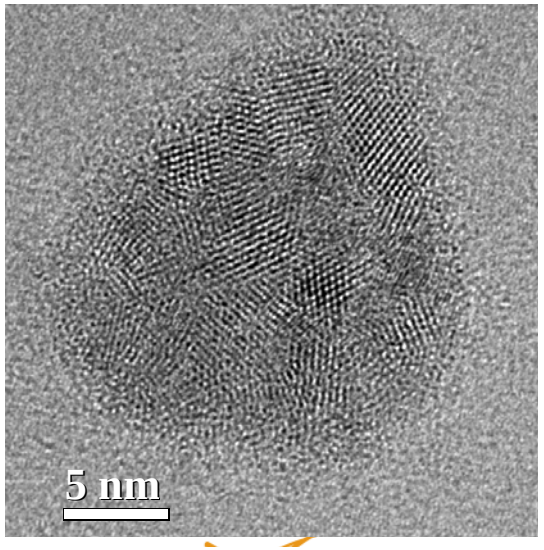
Band gap variation in water based ceria nanoparticles as a function of time

Ceria particles can change chemical state: Time and Environment factors



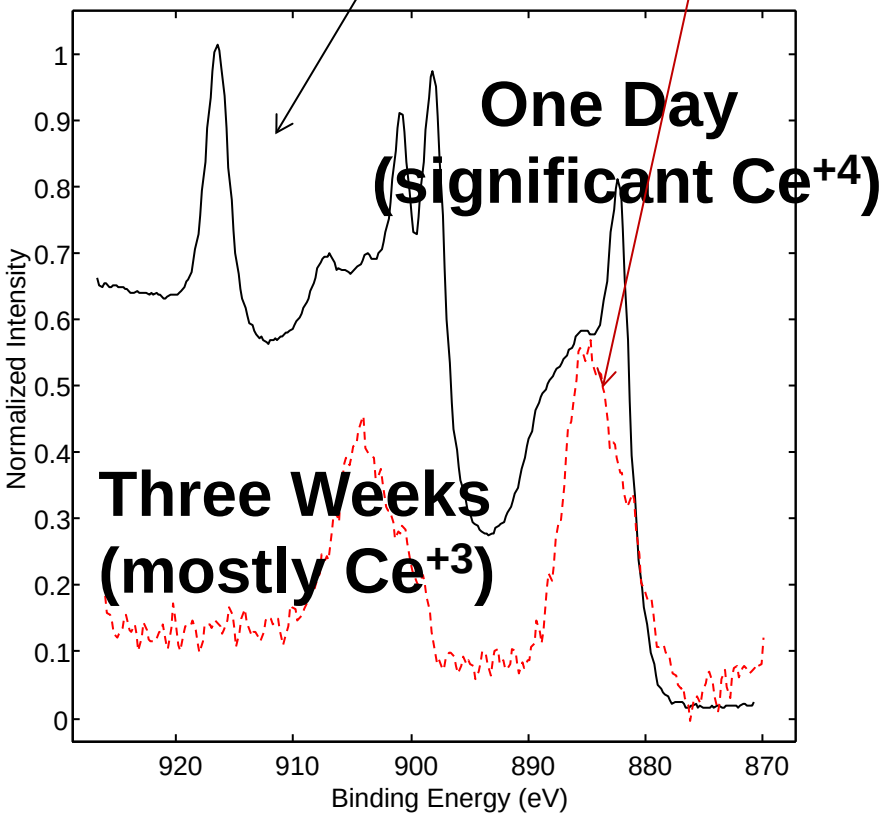


- TEM data at 1 day and 21 days shows 10-20 nm agglomerates made up of 3 to 5 nm particles for most conditions



SVNT Kuchibhatla et al. Journal of Physical Chemistry C 2012

Ceria particles can change chemical state: Time and Environment factors



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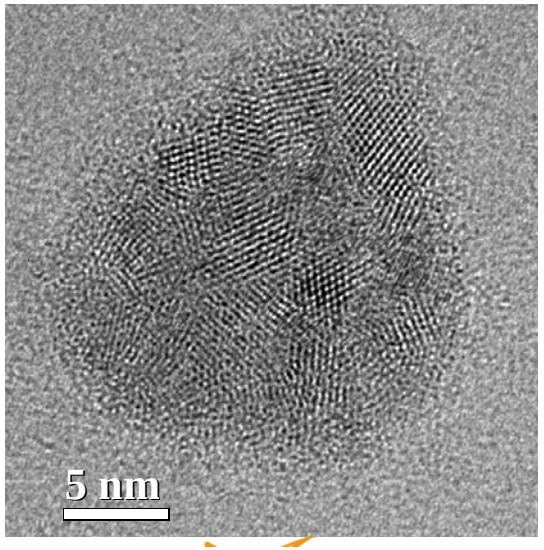
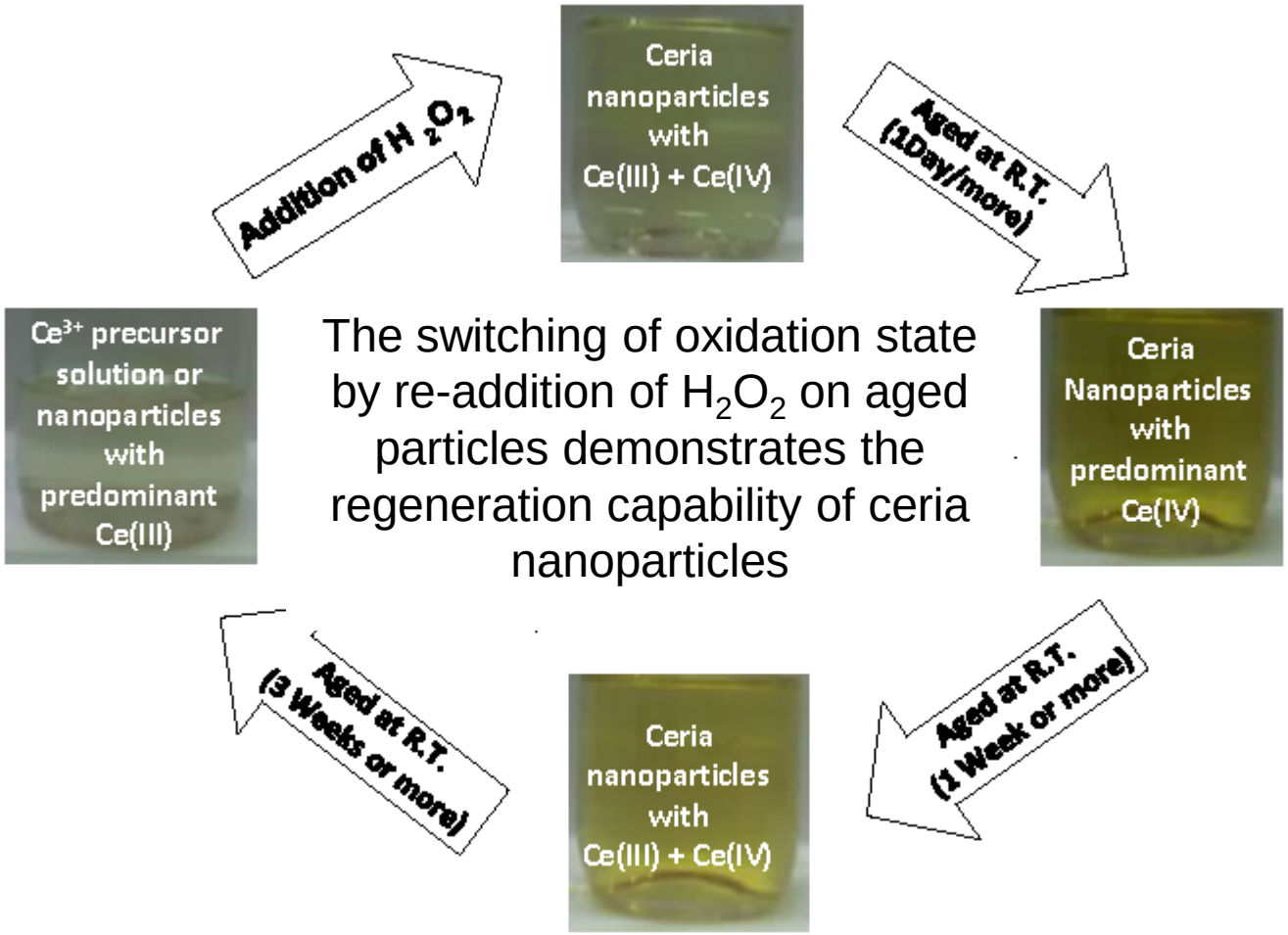


SVNT Kuchibhatla et al. Journal of Physical Chemistry C 2012

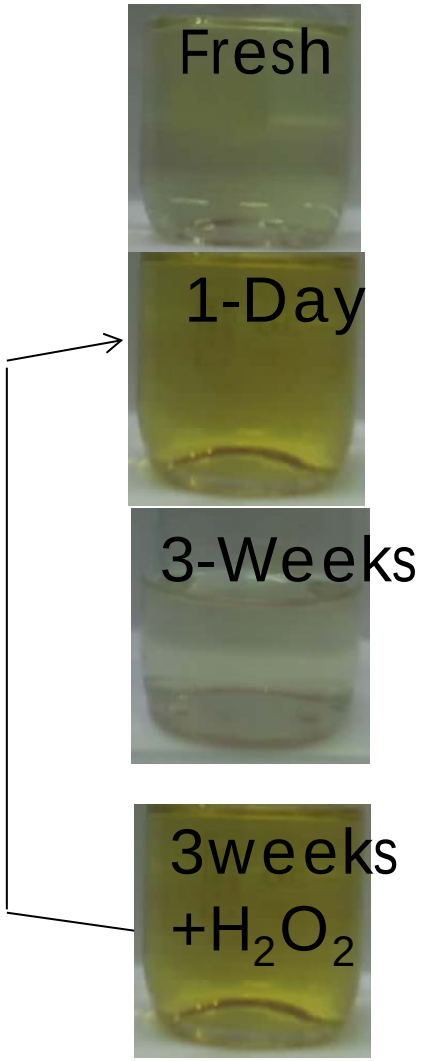
Oxidation reduction cycle for one type of ceria nanoparticle



The switching of oxidation state by re-addition of H_2O_2 on aged particles demonstrates the regeneration capability of ceria nanoparticles

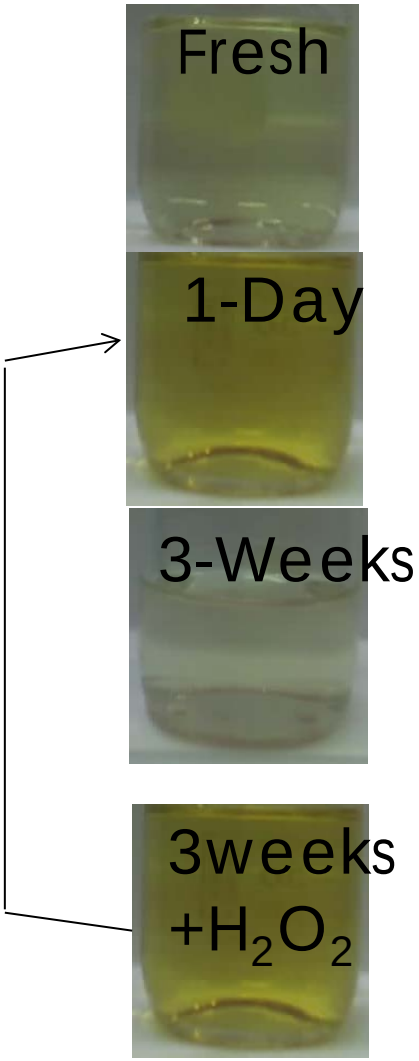
SVNT Kuchibhatla et al. Journal of Physical Chemistry C 2012

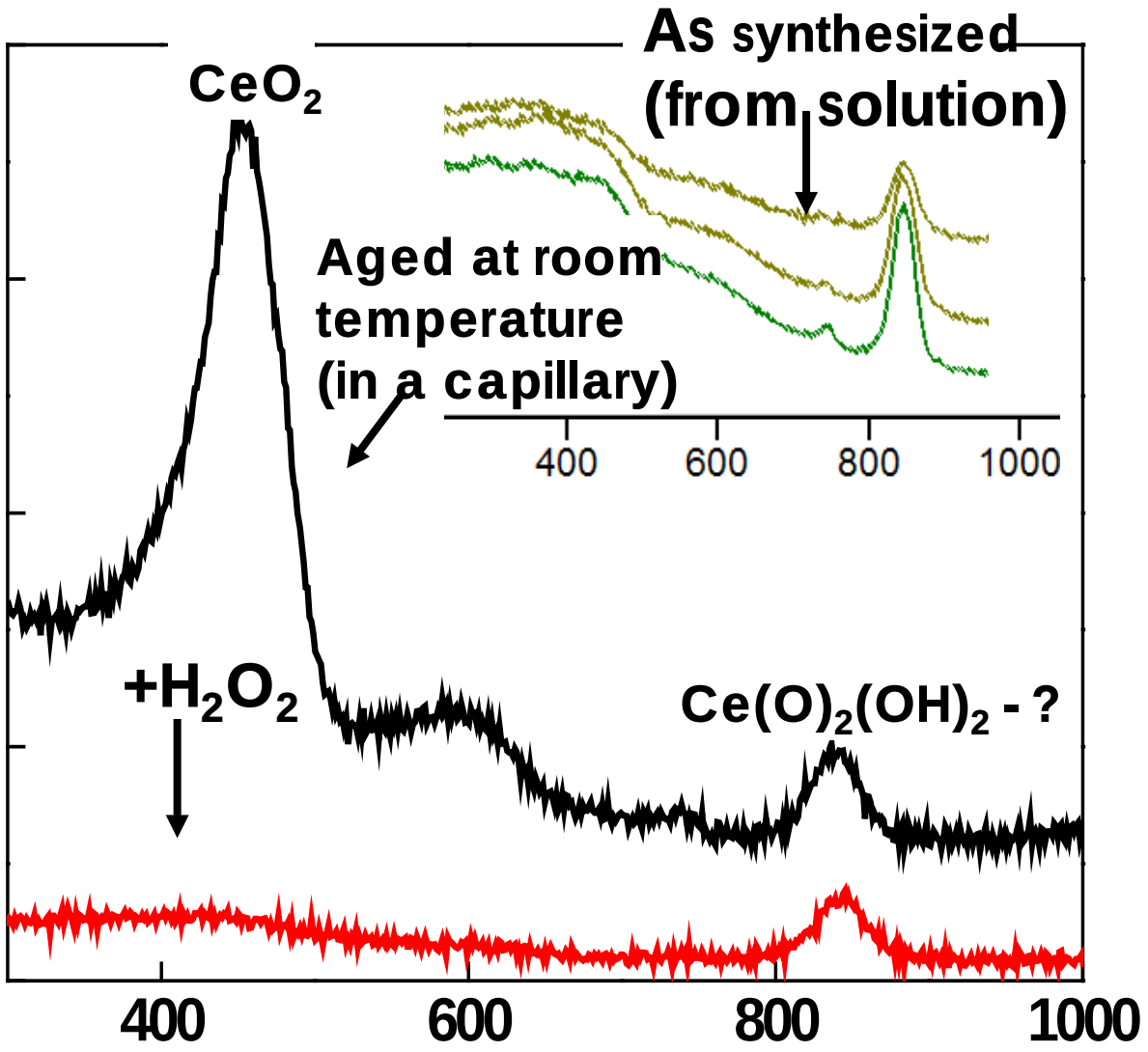
What is happening to the particles in solution?



What is happening to the particles in solution?

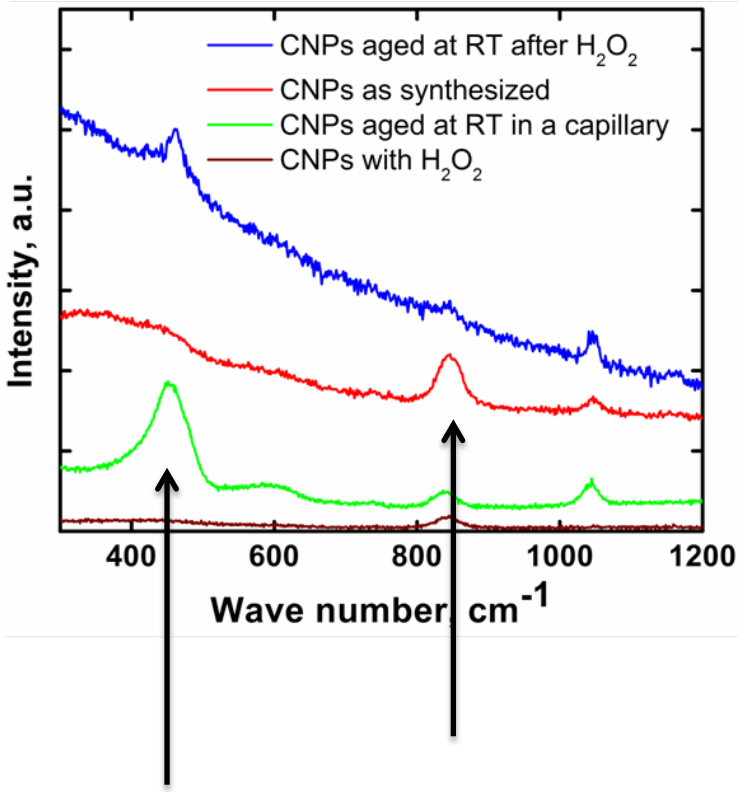
Add Optical Method - In situ Raman





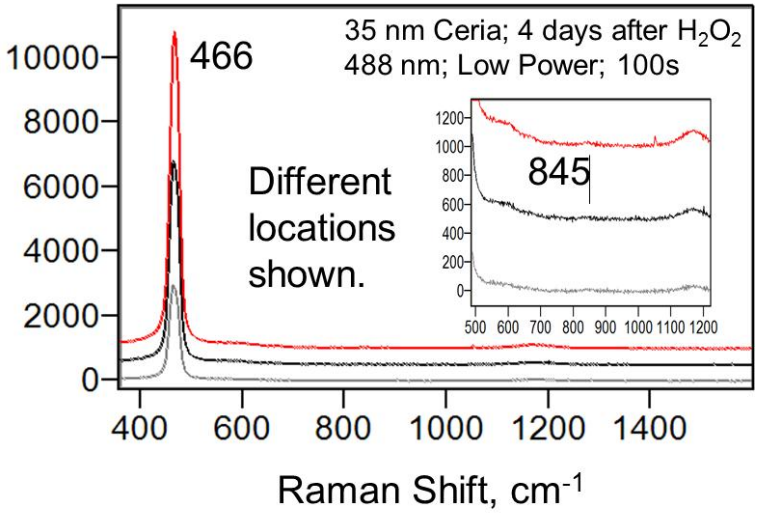
Raman Data: Ceria particles of different sizes

3 nm ceria

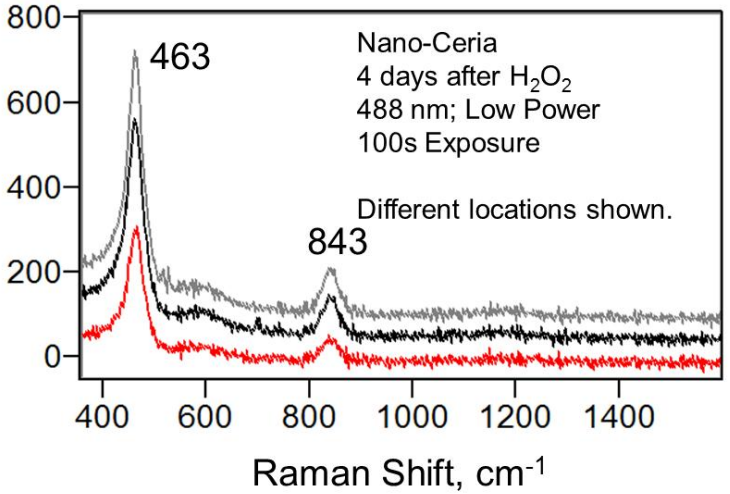


ceria Oxyhydroxide

35 nm ceria



8 nm Ceria



Ceria nanoparticles can do the unexpected ! – *environment again*

- Particles can change oxidation state in solution depending on the oxidizing potential of the solution
- TEM shows the particles to be similar in either chemical state *(may be due to vacuum and/or probe damage)*
- Dynamics light scattering sees particles in solution in either condition
- **However - XRD and laser Raman indicate that the small particles can fundamental switch structures between an oxyhydroxide (when Ce^{+4}) and a defected ceria structure (when Ce^{+3})**

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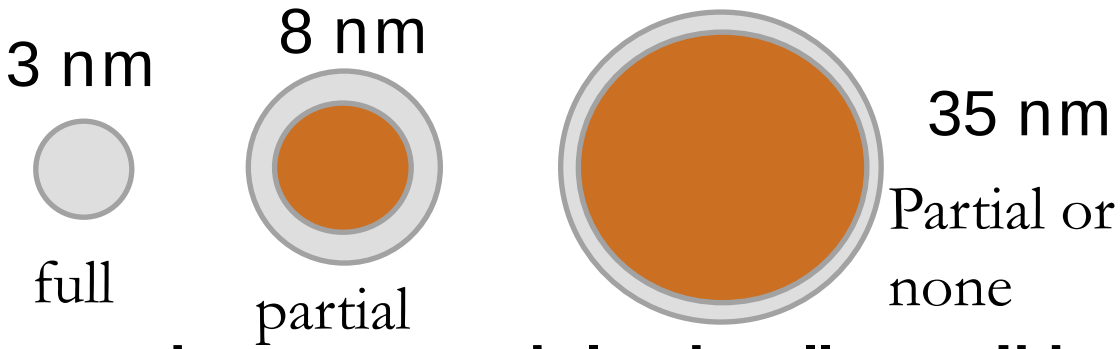
- **However - XRD and laser Raman indicate that the small particles can fundamental switch structures between an oxyhydroxide (when Ce^{+4}) and a defected ceria structure (when Ce^{+3})**
- Small particles switch completely; larger partially or not at all

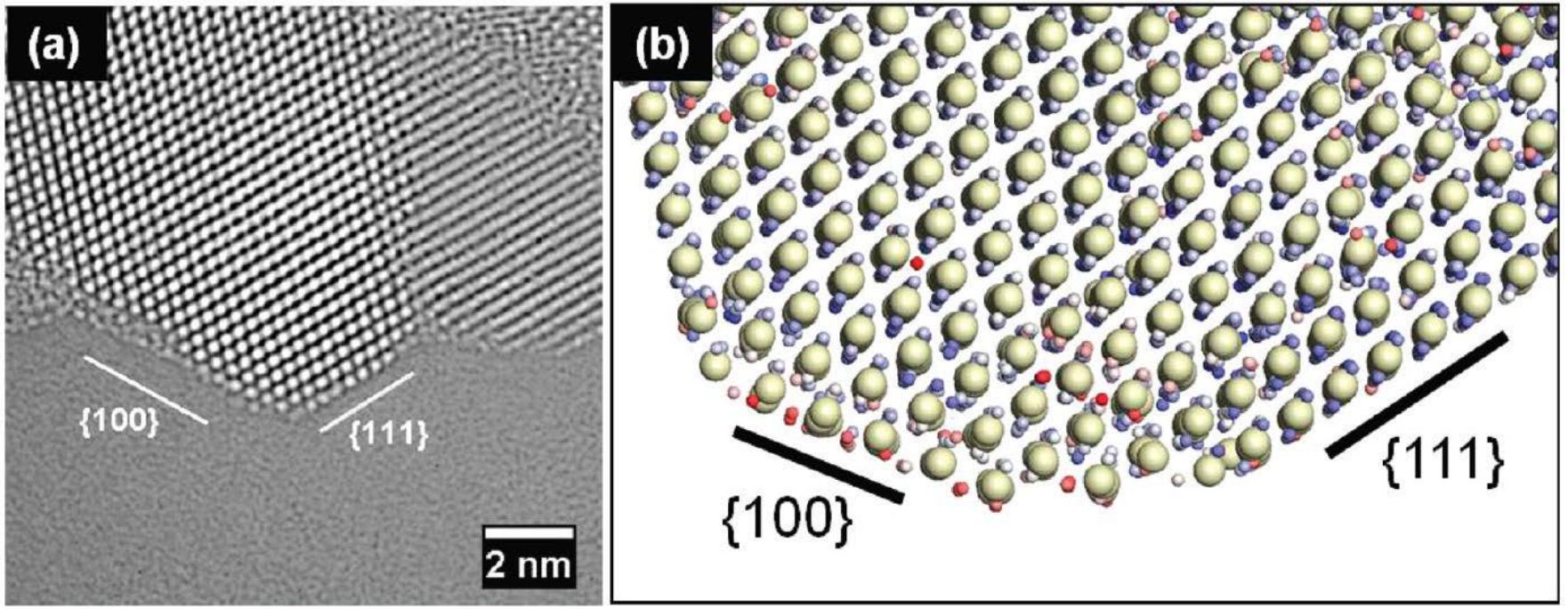


- **Are they ceria nanoparticles in all conditions? Do they remain nanoparticles?**

What are the issues? What we have learned from many studies

- Focused beneficial and potential negative impacts of three nanoparticles
  - **Iron metal-core oxide-shell** particles to remove environmental contaminants in ground water
  - **Ceria** nanoparticles which have a wide variety of uses
  - **Silver** nanoparticles in wide use in consumer products
- Common **characteristics** that **complicate understanding** and **characterization**
- **Ceria as an example**
  - **Conflicting** Biological impacts
  - **Environmentally** induced **changes** in chemical state
  - **Dynamic**, not static
  - **Synthesis** and **delivery** challenges

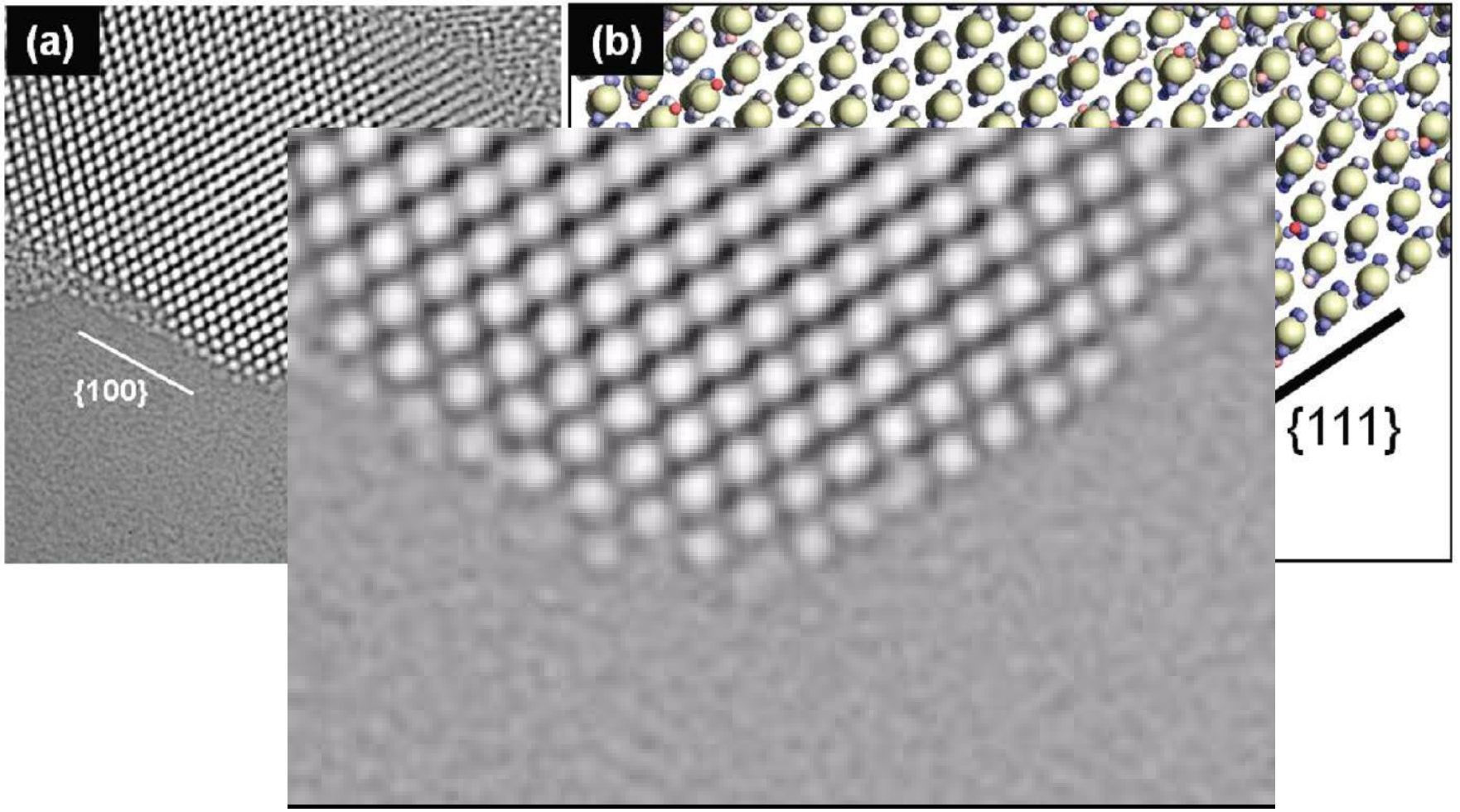
We think of surfaces as static



Electron microscopy observations of ceria nanoparticle

BHATTA ET AL. ACS Nano VOL. 6 ’ NO. 1 ’ 421–430 ’ 2012
www.acsnano.org

We think of surfaces and objects as static: They are not! Think dynamics, motion and change



BHATTA ET AL. ACS Nano VOL. 6 ' NO. 1 ' 421–430 ' 2012
www.acsnano.org
Can find movie on website as supplemental material

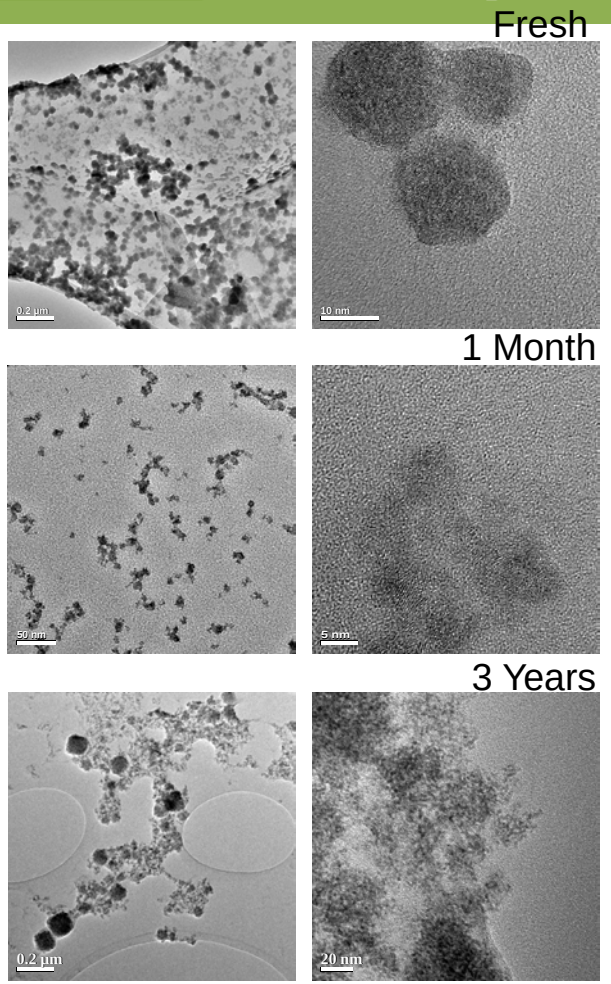
Challenges in Delivering Particles for Biological Studies

- Precursors – Cerium nitrate hexahydrate (99% and 99.999% Sigma Aldrich) and hydrogen peroxide (30% w/v) (Sigma Aldrich)
- Aged at room temperature in lab conditions
- TEM and UV-Visible spectrophotometry as a function of aging
- Oxidation state changes from 4+ to 3+ over time

Time	Zeta potential (mV)	Size by DLS (primary) (nm)	pH
Fresh	35 ± 7	15-25	2.9
1 month	35 ± 7	30-45	3.5
2 months	35± 7	30-45	3.6
6 months	35± 7	70-100	3.8

Summary of various samples

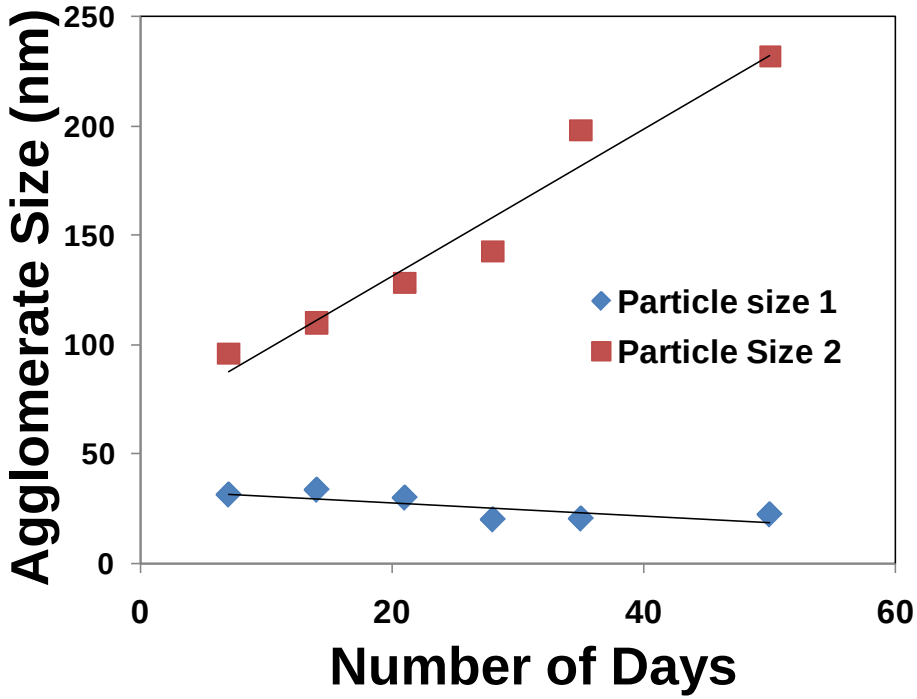
Particles relatively stable ~ year



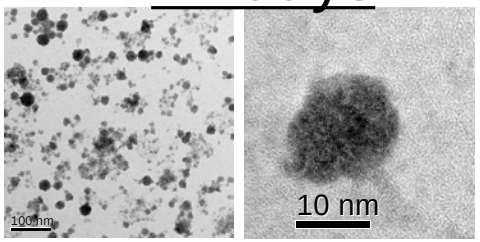
Samples sent back for TEM analysis by collaborator Prof. James McGinnis

Room Temperature Synthesis of Nanoceria – Repeated at EMSL

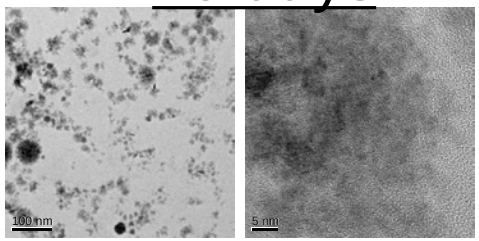
Time (Days)	Zeta Potential	Counts Kcps (DLS)	pH
1	30.5	217	3.5
7	40.7	221	3.6
14	29.43	122	3.85
28	4.73	27	5.0
35	Inconsistent	13.6	5.0
50	Inconsistent	4.2	5.0
54	Inconsistent	No Scattering	



14 days



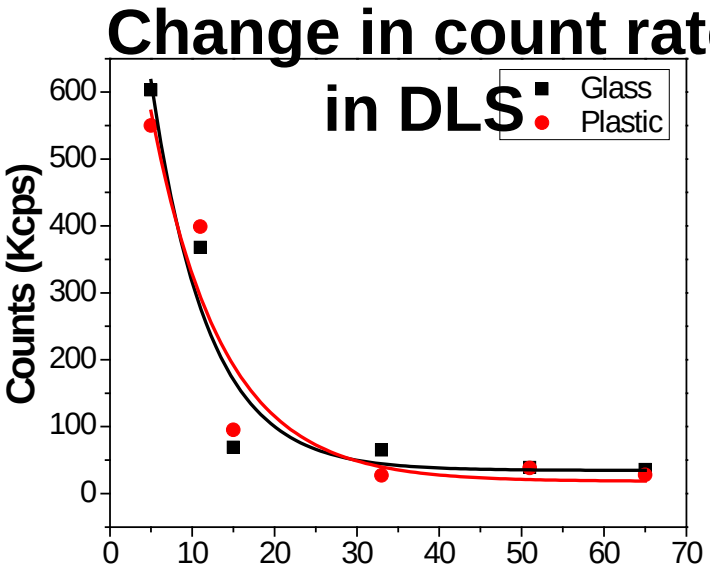
28 days



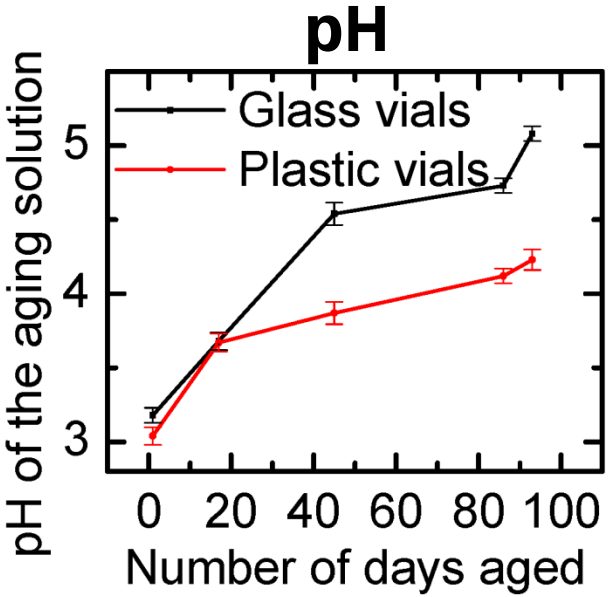
- No particles observed on TEM grids
- Nanoparticles ionized back in solution

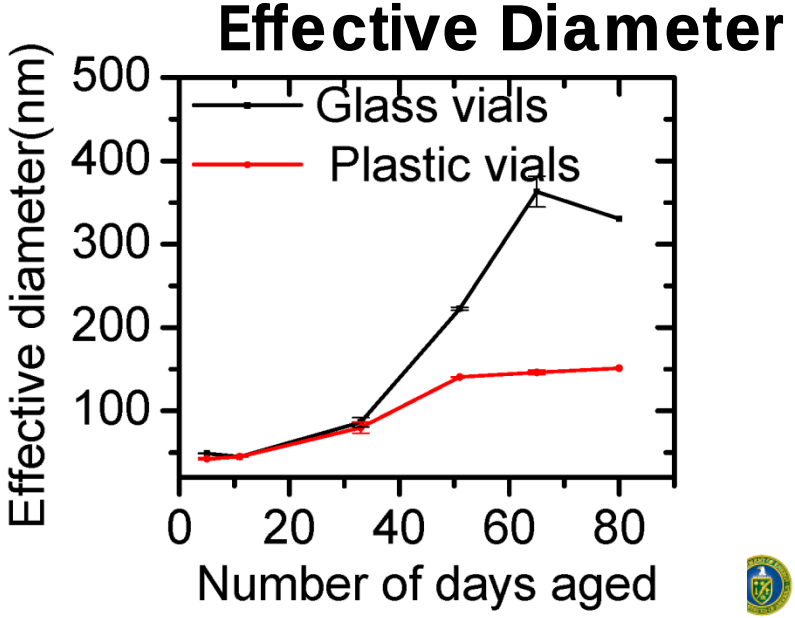
Particles disappear ~ month

What is different – Glass and Plastic Containers, Water, Chemical Batch



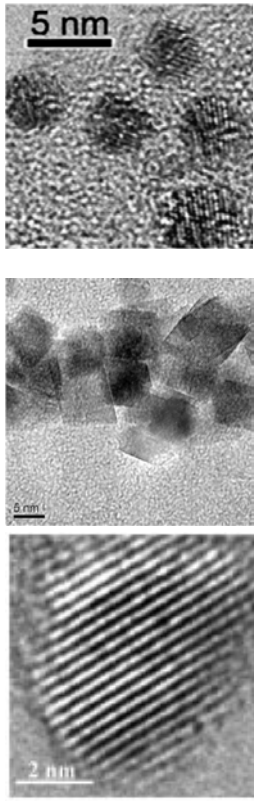
- Changing the container changed the rate of change of pH of the reaction
- The count rate indicated that the dissolution of nanoparticles occurs at the same rate





What have we learned about ceria nanoparticles?

- **Biological outcomes** can depend on synthesis method and processing history
- **Chemical state** of ceria nanoparticles is dependent on particle size, time and the environment
- XRD and laser Raman indicate that small particles are not always ceria in solution but can **switch between an oxyhydroxide** (when Ce^{+4}) and **ceria structure** (when Ce^{+3})
- Only partial or no changes occurring for larger particles
- The same people using the same process can get **different results when "minor" variable are changed**



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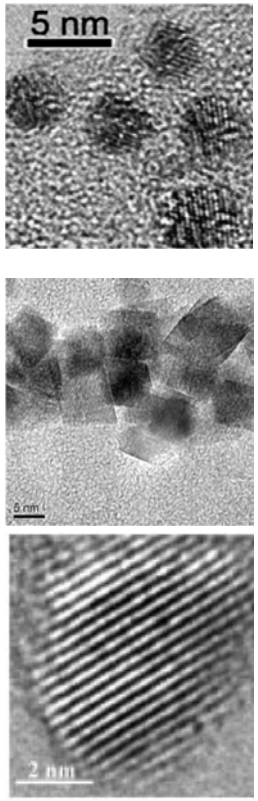
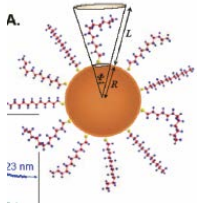
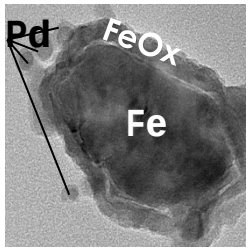


Time and Environment Matter - Synthesis differences *and* ***time/environmental changes*** *can* impact biological and environmental studies - need to be recorded and reported

There are more general lessons

- Nano "object" characterization is ***more important, more challenging, more interesting*** than expected
- ***Synthesis differences*** *and* ***time/environmental changes*** *can* impact technological, biological and environmental studies, shelf life, product stability
- ***Challenges*** **–**
  - **Are the particles really what we think they are?**
    - **How much and what types of characterization is needed?**
    - **Is contamination present on the surface?**
  - **History makes a difference?**
    - **How have they been made and processed?**
    - **What is the shelf life? How long can they be stored?**
    - **How fast do they change in the working environment?**
  - **Particles are dynamic! How quickly do they transform/change in the environment of interest?**





What we have learned?

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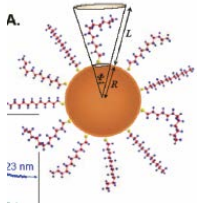

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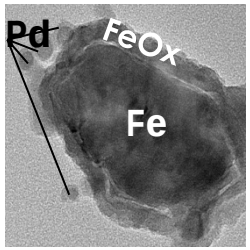

  - **Particles are dynamic! How quickly do they transform/change in the environment of interest?**
  - **Changes are an opportunity as well as a challenge**

Acknowledgements

- Research was performed at the W.R. Wiley Environmental Molecular Sciences Laboratory (EMSL), a national scientific user facility at the Pacific Northwest National Laboratory (PNNL) sponsored by the USDOE-BER (www.EMSL.PNNL.gov)
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