Welcome to the CLU-IN Internet Seminar

Nanotechnology: Implications and Applications

Delivered: October 3, 2011, 1:00 PM - 3:00 PM, EDT (17:00-19:00 GMT)

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- Q&A
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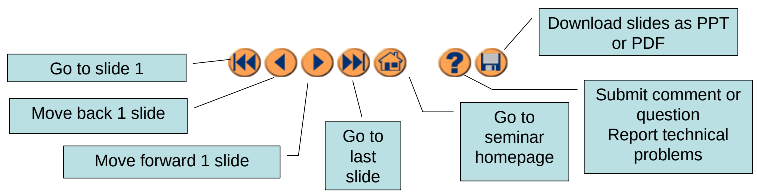

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Although I'm sure that some of you have these rules memorized from previous CLU-IN events, let's run through them quickly for our new participants.

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You should note that throughout the seminar, we will ask for your feedback. You do not need to wait for Q&A breaks to ask questions or provide comments. To submit comments/questions and report technical problems, please use the ? Icon at the top of your screen. You can move forward/backward in the slides by using the single arrow buttons (left moves back 1 slide, right moves advances 1 slide). The double arrowed buttons will take you to 1st and last slides respectively. You may also advance to any slide using the numbered links that appear on the left side of your screen. The button with a house icon will take you back to main seminar page which displays our agenda, speaker information, links to the slides and additional resources. Lastly, the button with a computer disc can be used to download and save today's presentation materials.

With that, please move to slide 3.

Risk of exposure to metal nanoparticles

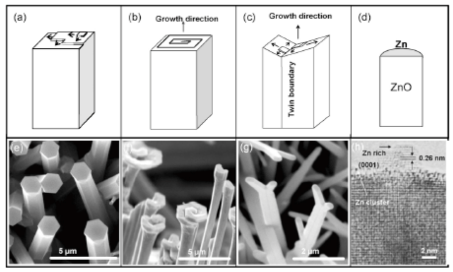
Engineering for toxicology

Ian M. Kennedy
Department of Mechanical and Aerospace Engineering
University of California Davis

Applications of engineered metal oxide nanoparticles

- gas sensors (for example tin oxide)
- platform for biosensors
- solar energy
- cancer therapy via hyperthermia
- MRI contrast agents
- clean up of contaminated water (for example iron)
- catalysts for emission treatment on vehicles
- sunblock
- personal hygiene (nanosilver)

New morphologies



ZINC OXIDE

from Wang et al, Mat. Sci. Eng. 60, p.1 (2008)

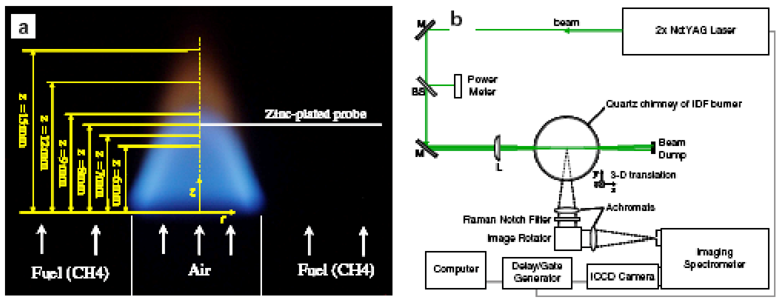
Production of metal oxide nanoparticles

- solution methods
- laser assisted growth
- molecular beam epitaxy
- aerosol methods

furnace

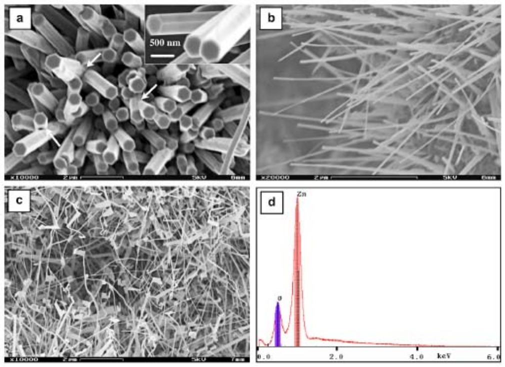
spray pyrolysis

Flame synthesis



ZnO whiskers grown by flame
Xu et al., Chem. Phys. Lett. 449, p. 175 (2007)

ZnO flame synthesis



XU ET AL., CHEM. PHYS. LETT. 449, P. 175 (2007)

Aerosol synthesis offers scalability and high production rates but also possibility of occupational exposures

Risk

Risk = Exposure + Toxicity

Exposure

Occupational and environmental
Inhalation, ingestion and dermal

Fate and Transport in the environment

- Scavenging by other solid materials in water and soil
- Transformation in the environment eg dissolution, change in oxidation state

Toxicity

Uptake and effect

Research areas at UC Davis

- Nanoparticle toxicity with in vitro assays
- Zinc oxide nanoparticle dissolution study
- Mouse nanoparticle translocation
- Nanoparticle stability
- Arsenic remediation using iron oxide nanoparticles

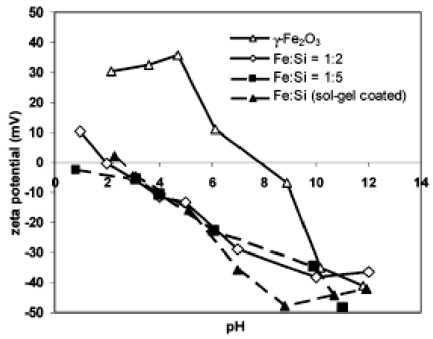
Metal oxides - is composition important?

- surface charge
- pH at isoelectric point

SiO_2	1.7 - 3.5
SnO_2	4 - 5.5
Fe_3O_4	6.5 - 6.8
γ-Fe_2O_3	6.7 - 8
Y_2O_3	7.1 - 9
ZnO	8.7 - 10.3

Metals oxides - is composition important?

- electrostatic attachment of proteins
- Li et al. examined BSA adsorption
- BSA attached via different domains to silica versus iron oxide
- Presents different protein corona to cells



FROM LI ET AL., CHEM. MAT. 18, P. 6403 (2006)

Metal oxides - is composition important?

- Several metal oxide aerosols with similar sizes (40 to 60 nm) and surface area were generated by flame synthesis
- Delivered to human endothelial aortic cells in vitro
- Dose measured by ICP-MS
- Markers of inflammation measured via RT-PCR and proteins via ELISA

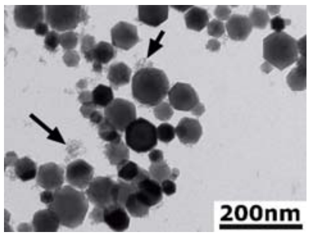
BET Surface areas

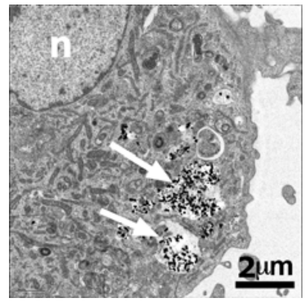
Fe_2O_3 m^2/g	Y_2O_3 m^2/g	ZnO m^2/g
81	41	20

ZnO HAS THE SMALLEST SPECIFIC SURFACE AREA

CERIA HAS ALSO BEEN STUDIED

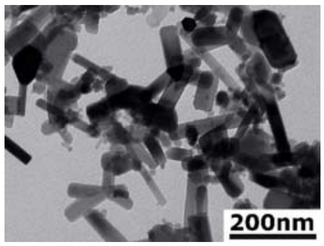
Metal oxides and aortic cells



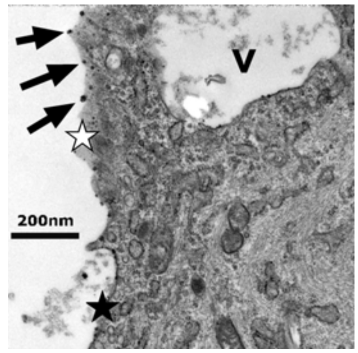


IRON OXIDE

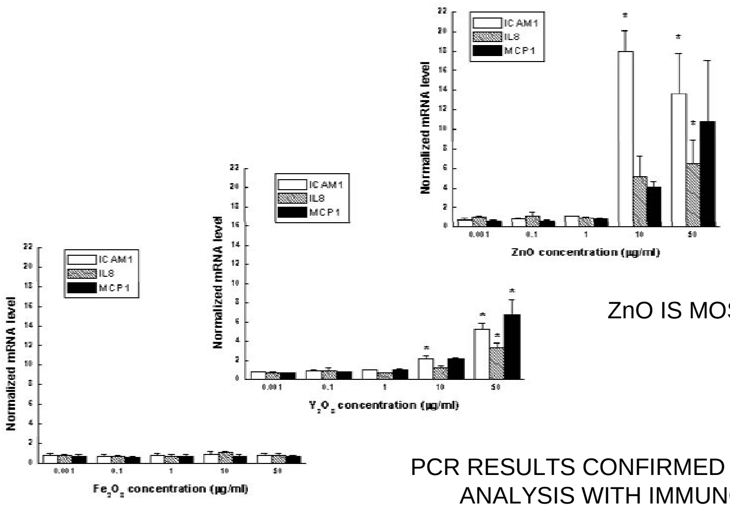
Metal oxides and aortic cells



ZnO



PCR for markers of inflammation



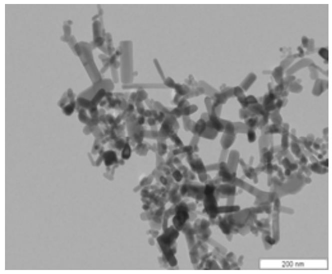
ZnO IS MOST EFFECTIVE

PCR RESULTS CONFIRMED BY PROTEIN ANALYSIS WITH IMMUNOASSAY

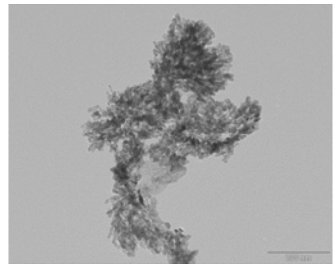
Metal composition

- Nanoscale materials may be more soluble
- Yttrium oxide is slightly basic; ZnO is amphoteric (soluble in acids or bases)
- Particles may be taken up into lysosomes that are acidic
- ZnO was found to be readily dissolved at lysosomal pH
- Nano ceria was minimally effective in inducing inflammation

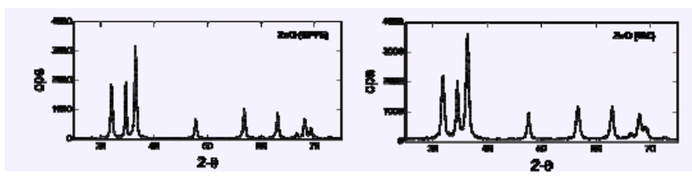
ZnO solubility



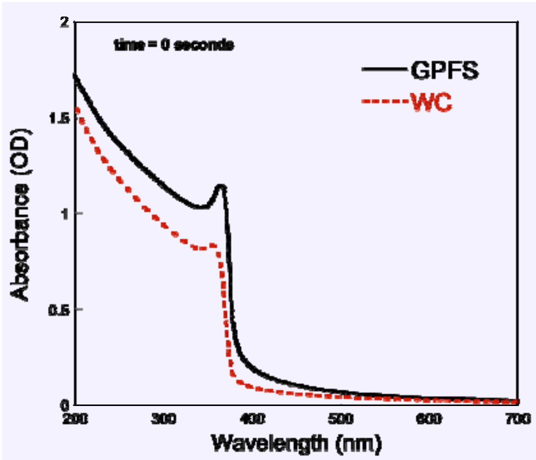
Flame synthesized



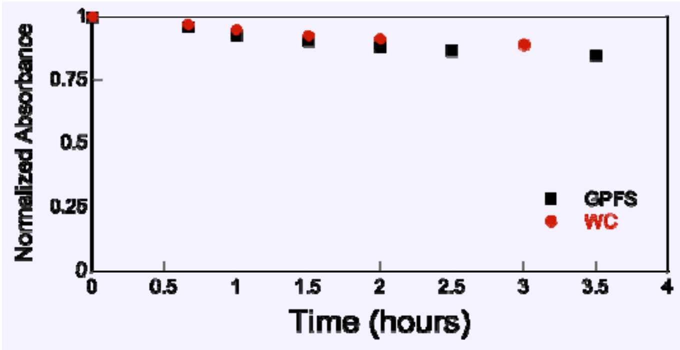
Solution synthesized



Absorbance spectra

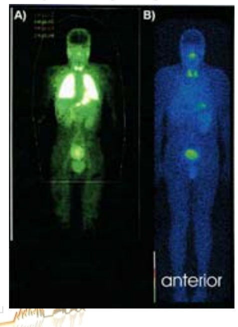


Time course of absorbance

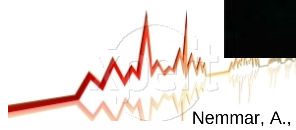


~ 20 % decrease in absorbance for both synthesis methods over a 48 hour period

Translocation studies



- Following deposition, particles may be taken up by cells of the lung or cleared
- They may pass into the cardiovascular system
- Particles can travel along the olfactory nerve to the brain



Nemmar, A., et al. 2002. Passage of inhaled particles into the blood circulation in humans. Circulation 105:411–414.

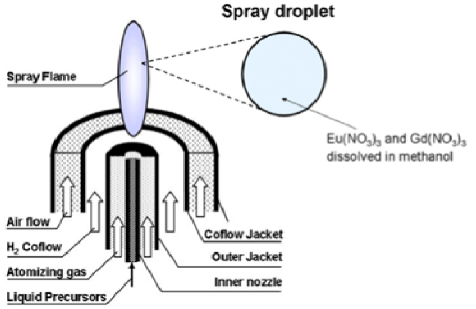
G. OBERDORSTER, Z. SHARP, V. ATUDOREI, A. ELDER, R. GELEIN, W. KREYLING AND C. COX, INHAL. TOX. 16 (2004) 437-445.

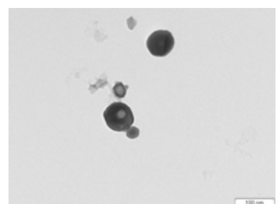
Translocation studies

Goal: determine the fate of inhaled NP in the body

- Previous studies used radioactive tracers
  - Challenging to work with radioactive material
  - Additional toxicity of tracer to cells
- Use Lanthanide NP as tracer
  - Relatively non-toxic
  - Can be used as a fluorescent marker and with ICP-MS
  - Low natural concentrations

Flame synthesis of lanthanide doped metal oxide NP

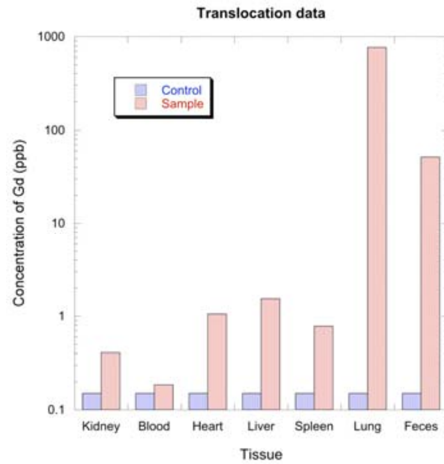




Installation experiment

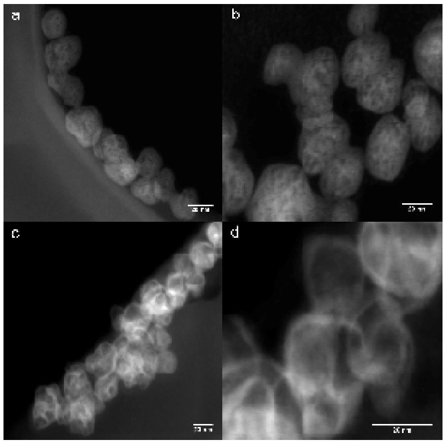
Lung instillation volume = 40 μL
NP concentration = 10mg/mL

- NP solution is instilled in mouse lung
- Mice were necropsied at 24 hr time-point (n=3)
- The harvested tissues are digested in concentrated nitric acid
- The concentration of NP in each tissue is analyzed by ICP-MS



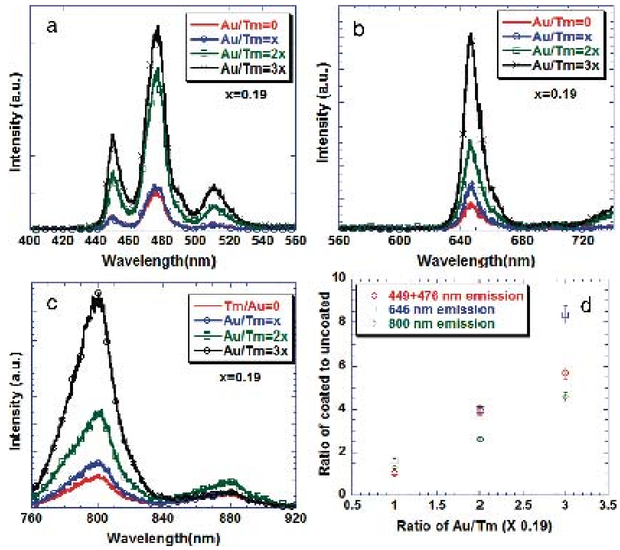
Results demonstrate that most of the particles are still in the lung or pass through the GI tract. Very low concentration of particles translocate to other organs. Mechanism might be different with an inhalation delivery of NPs or the time point before necropsy is extended to allow the transport of particles through the lung

Translocation and imaging with novel core-shell nanoparticles



- Cores of lanthanide-based up-converting phosphor are coated with a thin layer of gold
- The coating enhances the up-converted emission significantly
- Wavelengths are ideal for imaging in tissues

Imaging

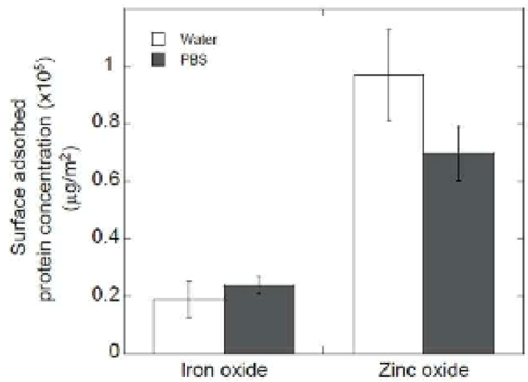


a
Au/Tm=0
Au/Tm=x
Au/Tm=2x
Au/Tm=3x
x=0.19
Intensity (a.u.)
Wavelength(nm)
b
x=0.19
c
Tm/Au=0
d
449+476 nm emission
646 nm emission
800 nm emission
Ratio of coated to uncoated
Ratio of Au/Tm (X 0.19)

Stability and toxicity

- DLS used to study aggregation kinetics of iron and zinc oxide NPs in water, PBS, and complete cell culture growth medium
- Bovine serum was found to stabilize NPs in growth medium
- Flow had a major impact on reducing aggregation
- Flow also had a major impact on cellular response to zinc oxide – oscillatory flow caused more inflammatory response than static or pulsatile flow

Proteins adsorbed

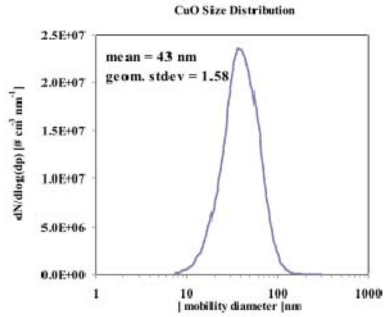


Copper oxide toxicity in duckweed

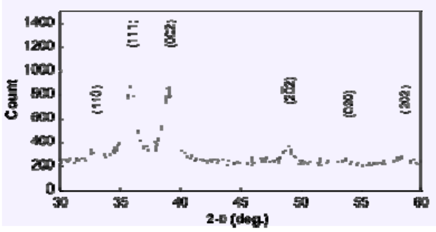
- Duckweed is a common model for aquatic plant toxicity
- CuO nanoparticles synthesized by a flame aerosol route
- Added to plants
- Effect on growth compared to equivalent dose of soluble copper

CuO NP characterization

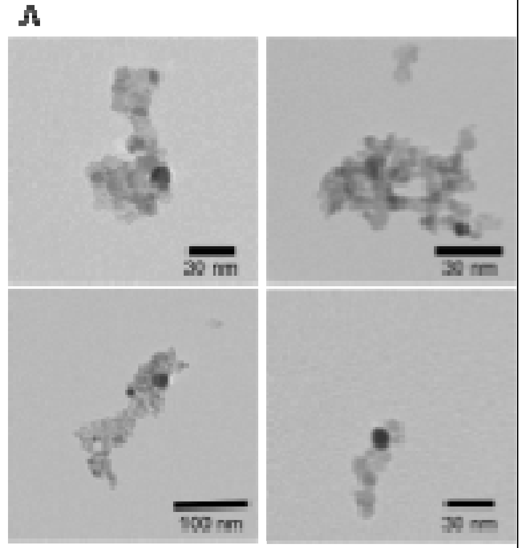
SMPS



XRD

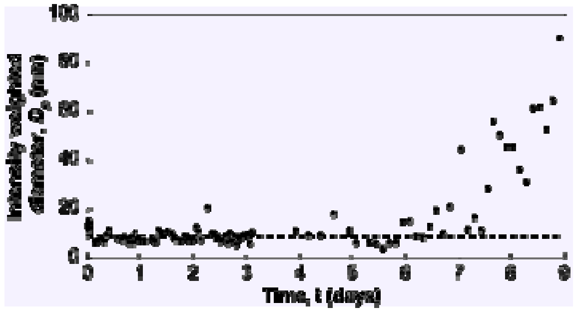


TEM

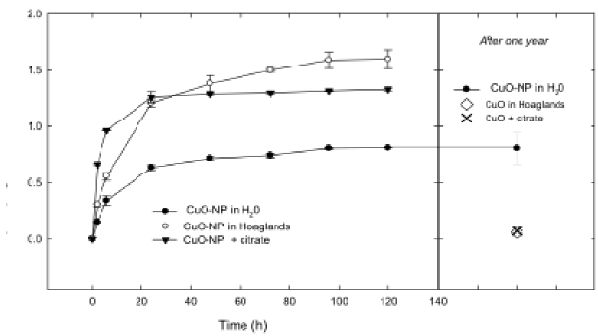


NP stability in plant growth medium

DLS measurements

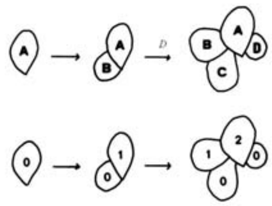


Cu dissolution from 10 ppm initial concentration

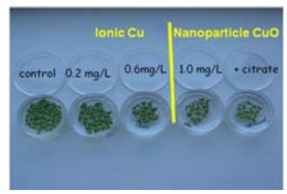


Soluble Cu, µg/L

Duckweed model

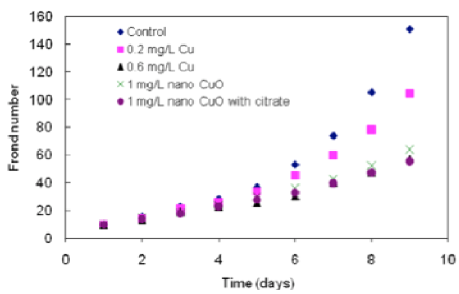


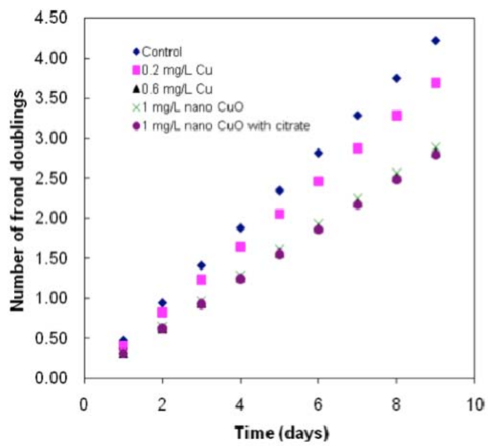
Doubling time for duckweed is known – growth inhibition can be modeled explicitly



Significant decrease in duck weed growth in the case of plants exposed to CuO nanoparticles

Duckweed growth curves





Key results

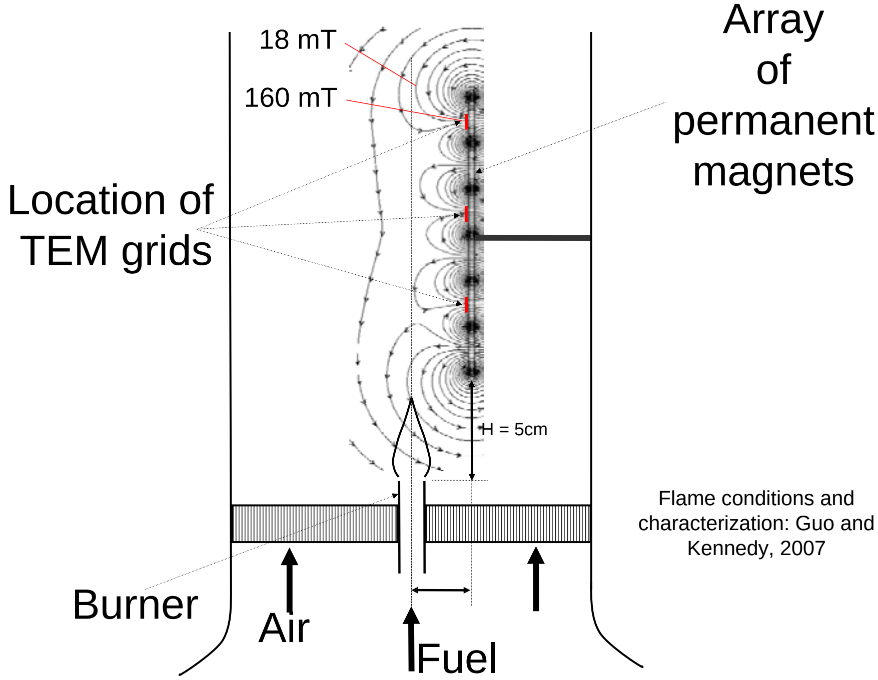
CuO nanoparticles were synthesized in a hydrogen diffusion flame

Cu from NP CuO into duckweed is three times more effective than Cu from soluble copper

The large plant uptake of Cu from NP CuO suspension explains the inhibitory effects on growth and chlorophyll content

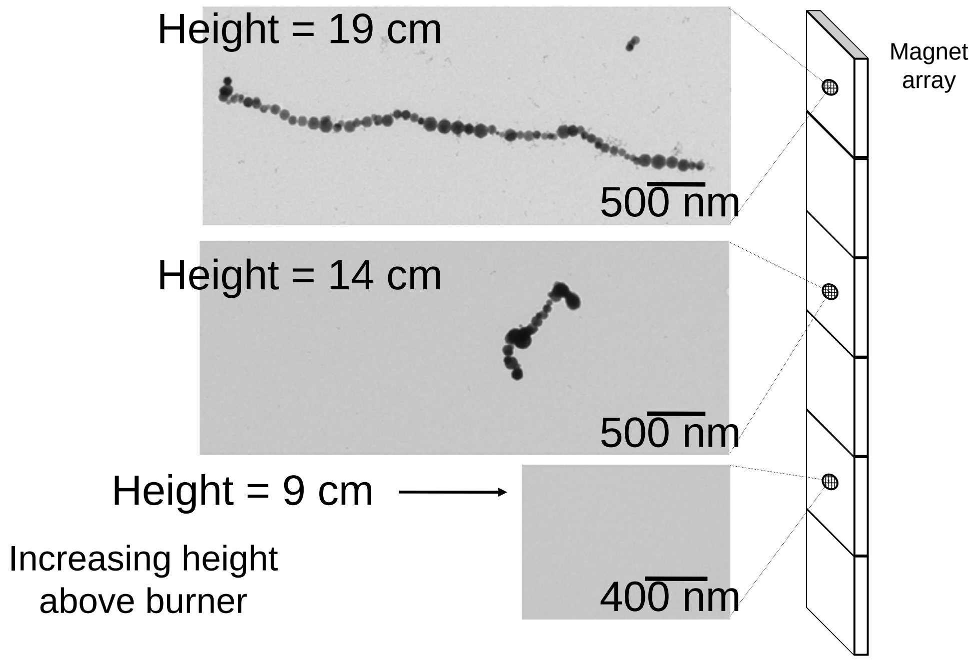
Arsenic remediation using iron oxide NP chains

Experimental setup



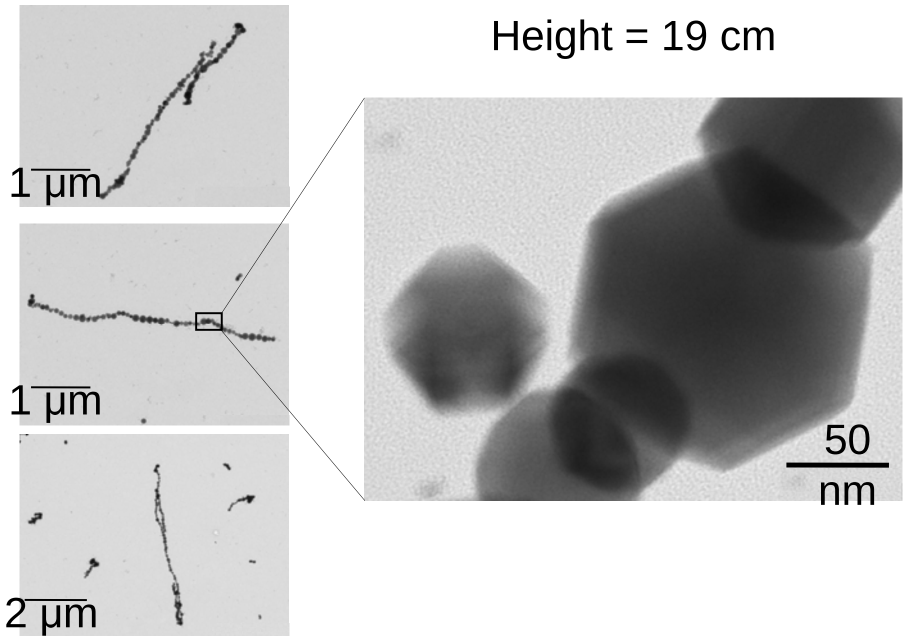
Flame conditions and characterization: Guo and Kennedy, 2007

Particle characterization (TEM) (1)

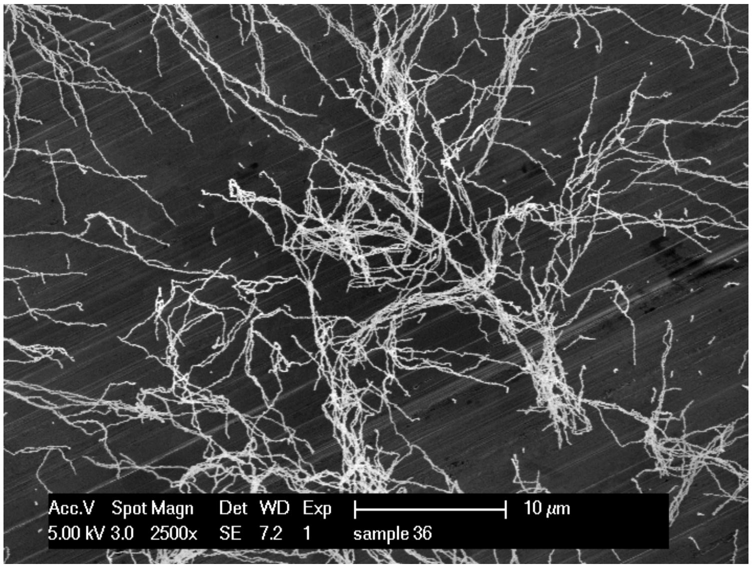


Particle characterization (TEM) (2)

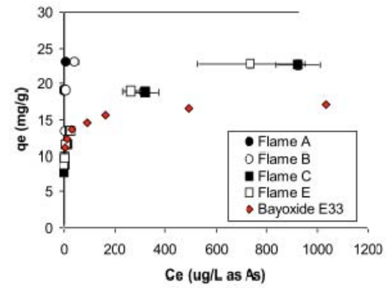
Height = 19 cm

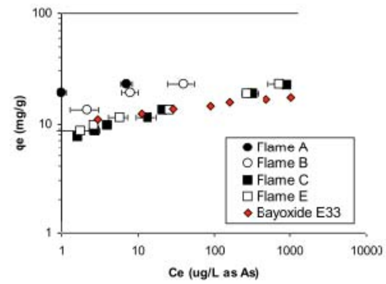


Particle characterization (SEM)

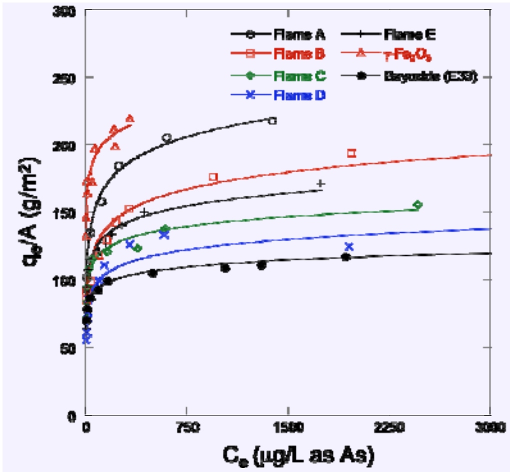


Arsenic adsorption isotherms





As adsorption - surface area normalized



Oxidation state of the Fe plays a role

Nanomaterials as Environmental Sensors

Donald Lucas
Lawrence Berkeley National Laboratory
EPA Web Oct. 3, 2011

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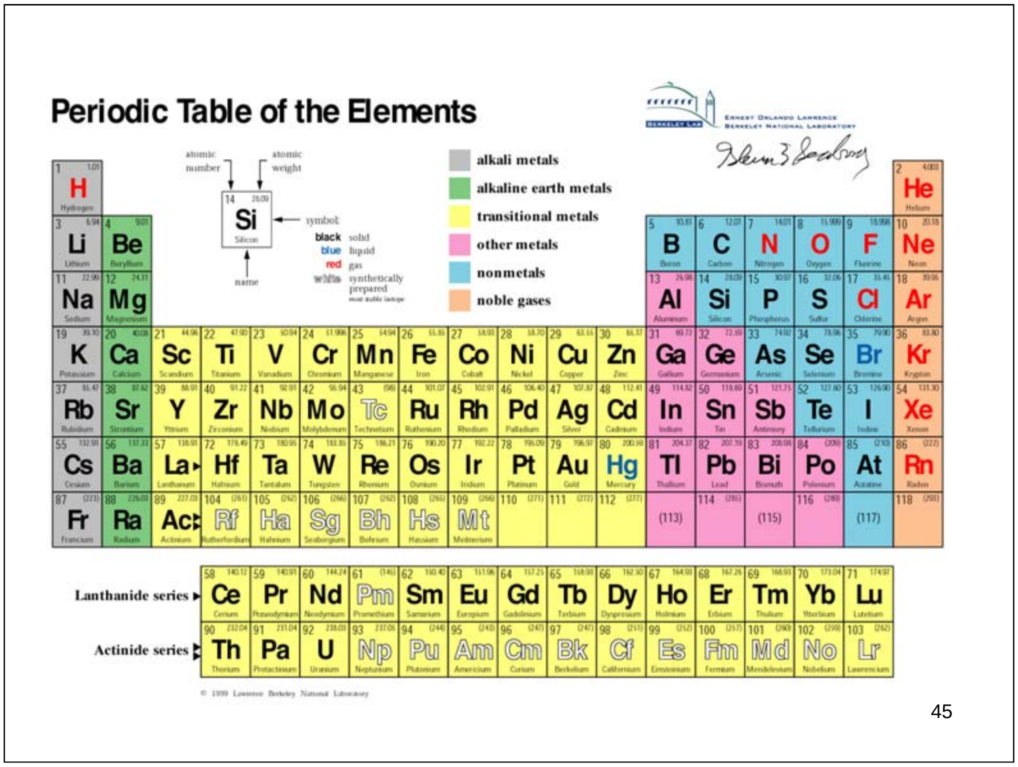


Founded in 1931 by E. O. Lawrence: invented cyclotron and “big science”

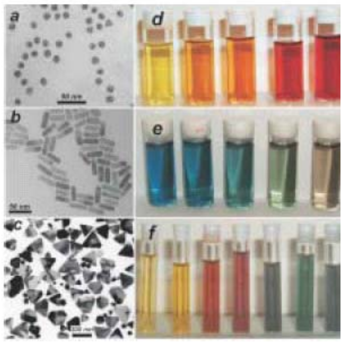
First U.S. National Laboratory
11 Noble Prize Winners (plus 2008 Peace Prize)
16 elements

4,200 employees, 2,500 researchers

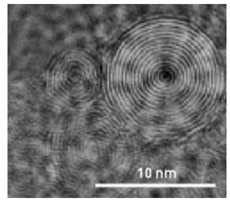
No classified research

Elements discovered by Berkeley Lab physicists include astatine, neptunium, plutonium, curium, americium, berkelium*, californium*, einsteinium, fermium, mendelevium, nobelium, lawrencium*, dubnium, and seaborgium*. Those elements listed with asterisks (*) are named after the Laboratory or some of its principal scientists.

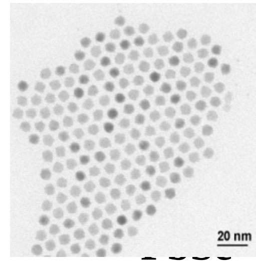
Nanoparticles are everywhere!



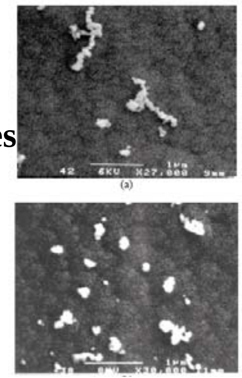
Au and Ag nanoparticles and nanorods



Nano-onions



PbSe



NaCl before and after laser irradiation

Cover Photo: C&E News May 1, 2006

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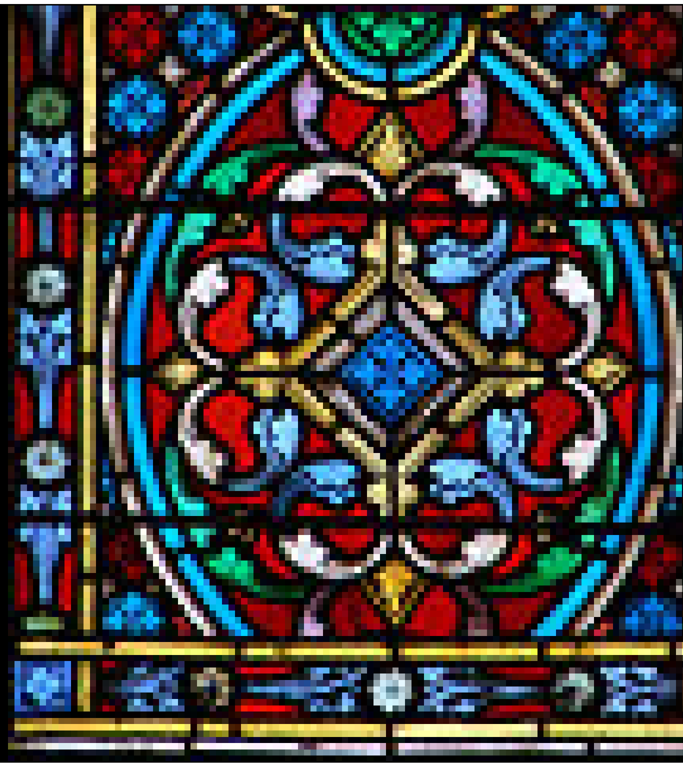


BERKELEY LAB
Nanocrystals
Glass

Firepit in Xuan Wei County, China

Firepit in Hesse Hall, UC Berkeley

Humans have been exposed to nanoparticles for millennia!

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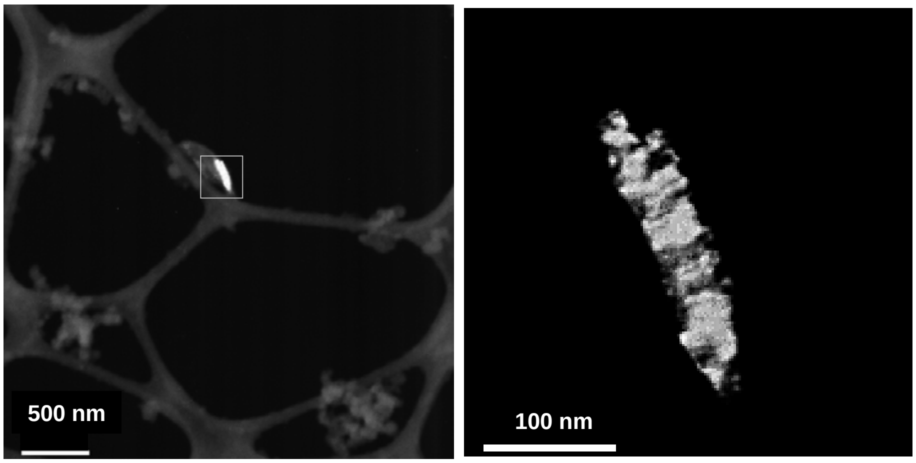
Microfibrous quartz in soot emissions?



Can those fibrous quartz in coal be emitted into air? The answer is positive.
--- Microfibrous quartz crystals were found in the soot particles from the coal linked to the highest lung cancer rate.

Metal detection with engineered nanomaterials

Goals:

- Cheap, reusable, simple method to detect metals in environmental samples (air or water)
- Can we achieve high sensitivity and selectivity with speciation?
- Can we develop something like pH paper for metals such as mercury an arsenic?

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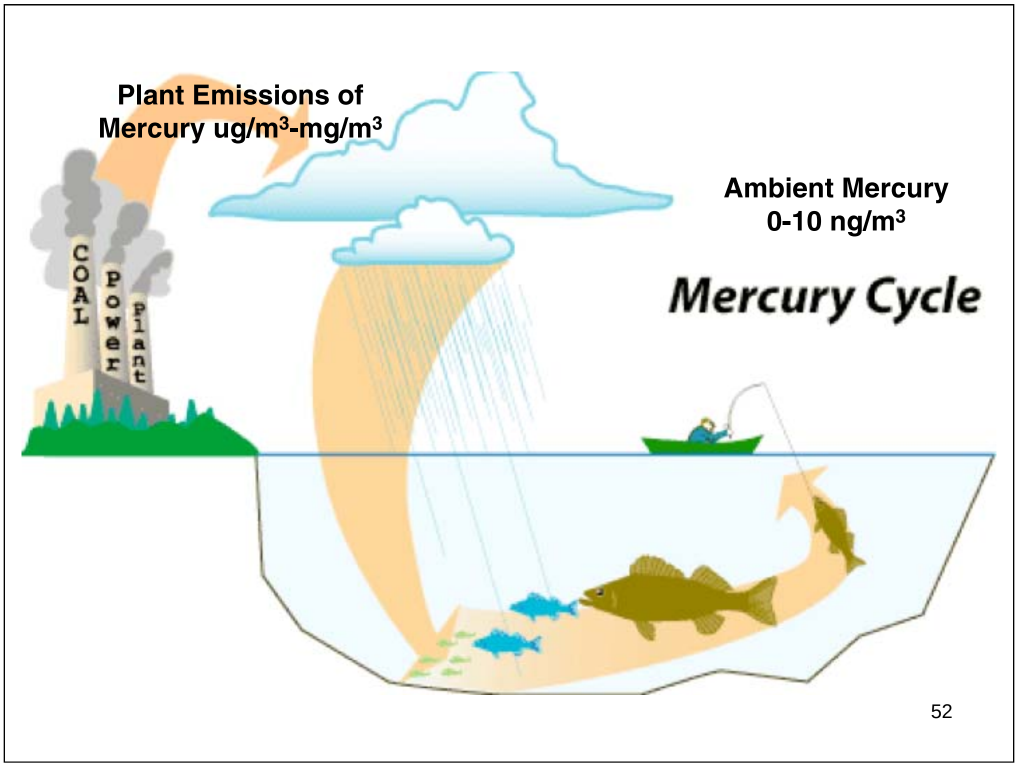
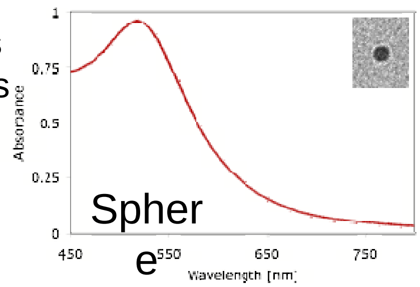
Ammino propyl tri ethoxy silane



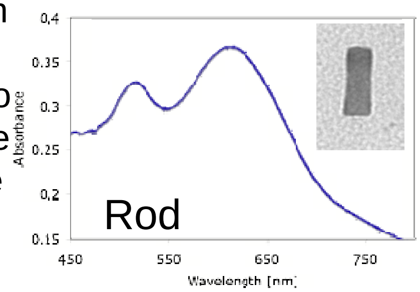
Mercury slide - health effects and such

Nanoparticle color depends on their composition, shape, and size

Metal nanoparticles exhibit vibrant colors depending on their shape, size, and composition.



Collective oscillation of conduction electrons give rise to the localized surface plasmon resonance (LSPR) peaks



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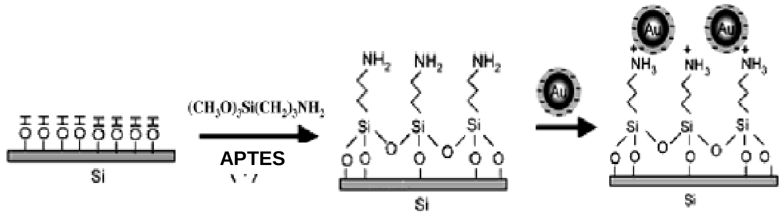
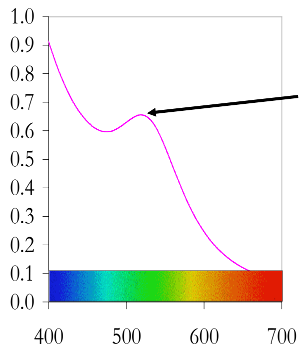
Mercury detector using gold nanospheres

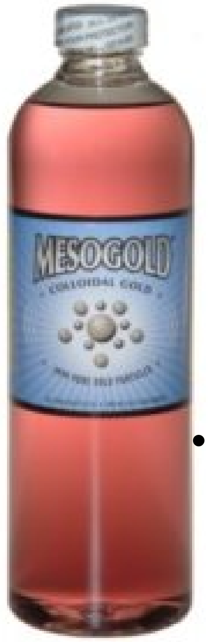




Surface plasmon resonance shifts when Hg bonds to isolated gold nanoparticles. A few Hg atoms in nanoparticle produces measureable shift

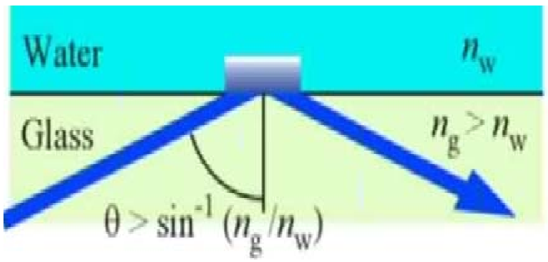
Ammino propyl tri ethoxy silane

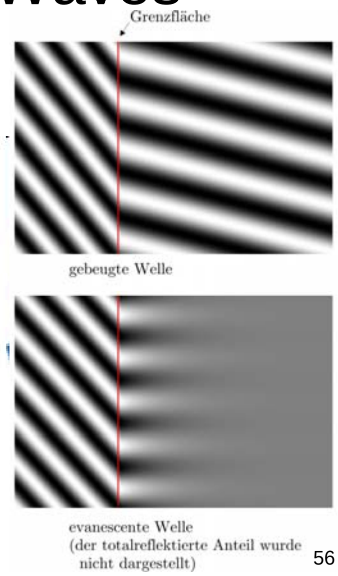
Over-the-counter Colloidal Gold Solution



Claims:
- 3.2 nm gold particles
- Non-toxic to humans
- 1 Tablespoon dose recommended, but power users can take 6-8!

Evanescent Waves





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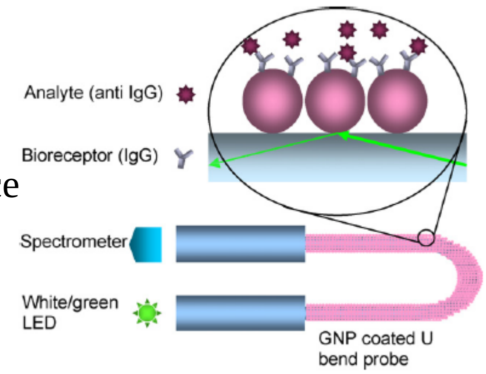
Evanescent Sensors

- Biological sensor
- Detects change in refractive index
- Dependent on surface treatment

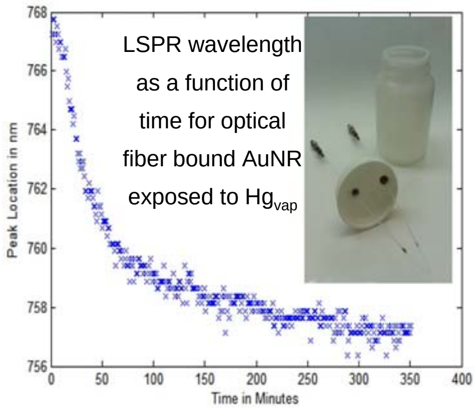


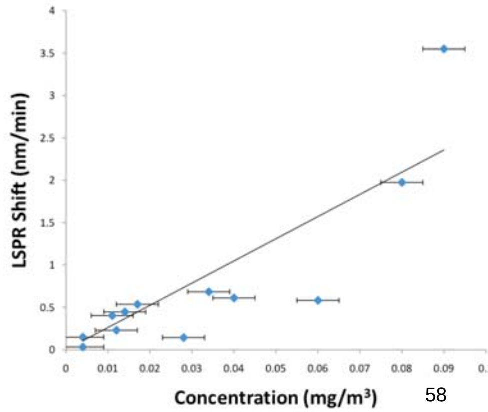
Scheme 1. Optical set-up and sensing scheme used for experiments with U-bent fiber optic probe.

V.V.R Sai, T. Kundu, S. Murkerji 2009 in Biosensors and Bioelectronics

Optical-fiber/gold nanorod Hg sensing in action

Films of gold nanoparticles exposed to mercury vapor show LSPR peak wavelength shifts of up to 20 nm and can be tracked with 0.2 nm wavelength and msec time resolution



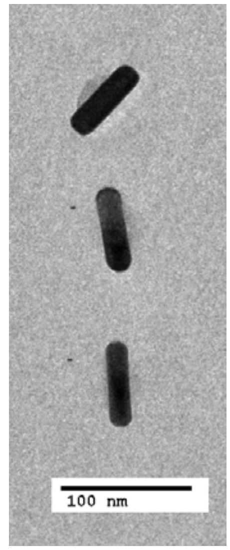


Single gold nanorod Hg_{vapor} adsorption and detection

Individual particle studies have a number of advantages:

- Isolated AuNR LSPR depends on shape, size, environment and composition, but film LSPR also depends on the relative position of the particles

- Investigation of distinct shape and size effects can be executed in parallel



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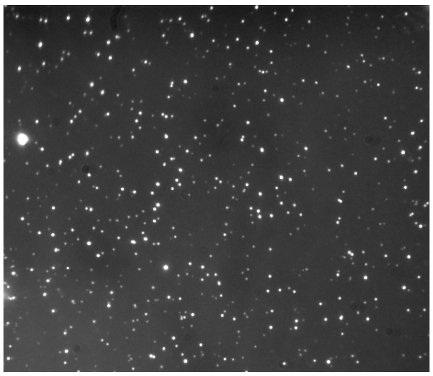
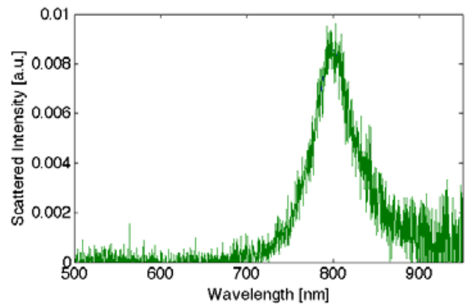
Optical characterization of single gold nanorods (AuNR)

Dark field image



Single AuNR scattered spectrum



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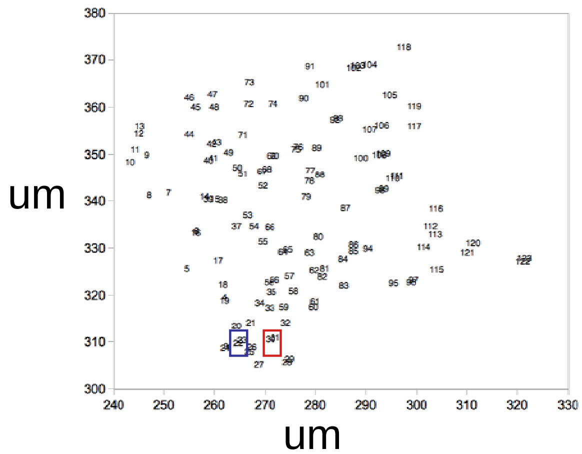
Scale bar on df map, single image just as good , or a series where you show image, circle spot and then show spec

Imaging and mapping gold nanorods with electron microscopy

Each image taken in the transmission electron microscope records the stage location



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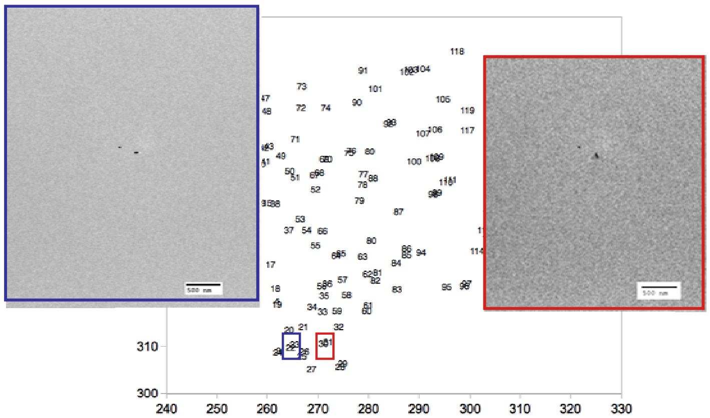
Imaging and mapping gold nanorods

Scanning at 4kx magnification to locate AuNRs



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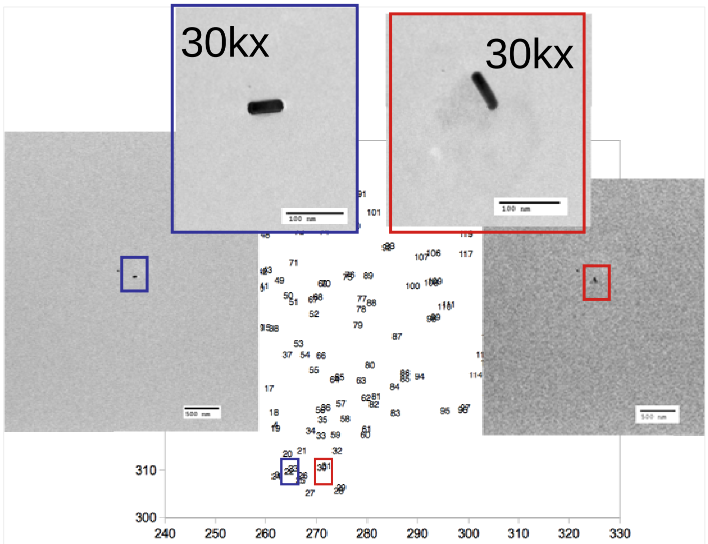
Imaging and mapping gold nanorods



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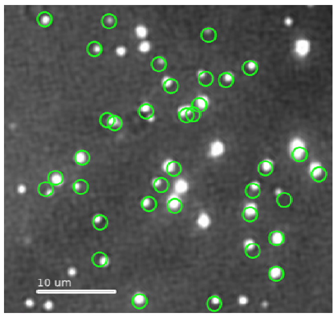
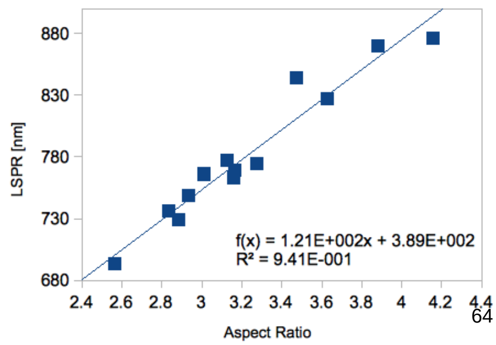
Combining electron microscope and optical data

- TEM stage map points (rings) coincide with the bright spots in the dark field image
- Plot of LSPR dependence on aspect ratio supports the accuracy of this method





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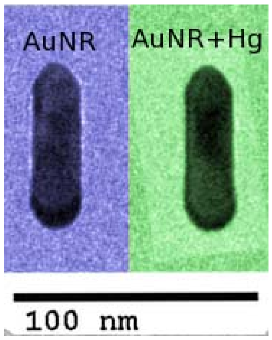
Transmission electron microscopy of saturated amalgam nanorods



After exposure to 116 ug/m^3 of mercury vapor the LSPR peak of this particle shifted 3.5 nm

TEM imaging shows no significant shape or size change to the particles

Elemental analysis with energy dispersive x-ray spectroscopy (EDX) finds the composition to be x_{Hg} = 1.5 %

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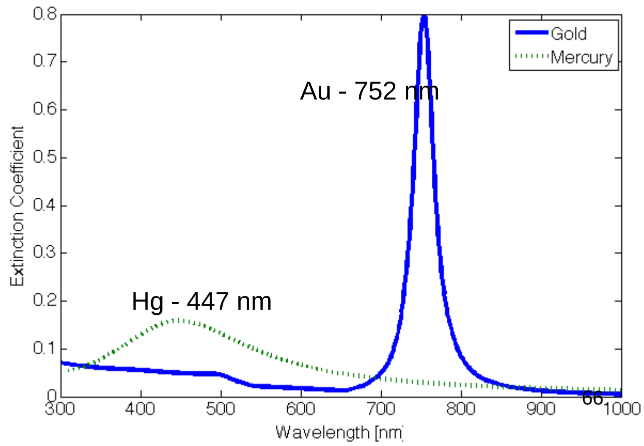
Amalgam nanorod LSPR model

LSPR peak wavelength of alloy nanoparticles depends linearly on mole fraction (S. Link et al. 1999)

Gans theory predicts the extinction coefficient of a nanorod whose environment, shape, size, and dielectric function are known

For a 62 nm long, 20 nm diameter rod, our model predicts a composition of 1% Hg, 99% Au for a 3 nm shift



Significance of gold nanorod based mercury sensing

- Individual gold nanorods have been shown to detect mercury at 10 ug_{Hg}/m^3_{air} (stack emission levels)
- Shifts of 3 nm correspond 4 attograms (4 x 10^{-18}g) of adsorbed mercury
- Nanoparticle surfaces collect mercury as well as bulk gold
- Spheres can be regenerated by gentle heating

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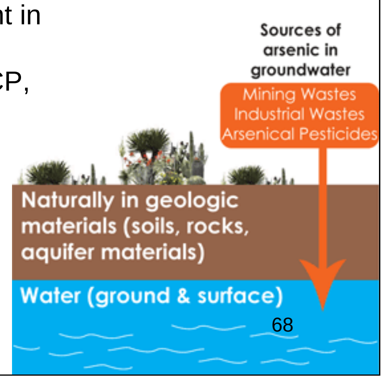
Sensing of arsenic using engineered silver nanoparticles

- As contaminated groundwater: Bangladesh (20 - 50 million affected), India, Thailand, Taiwan, China, USA.
- Side effects: skin, lung, urinary bladder, and kidney cancers
- > 150 ppb: significant increases in cancer mortality
- 10 ppb : WHO guidelines for max. As content in groundwater
- Current detection: Lab-based analyses – ICP, MS, HPLC-MS (<10 ppb)

- What is needed:
  - **- On-site detection**
  - **- Availability in developing countries**

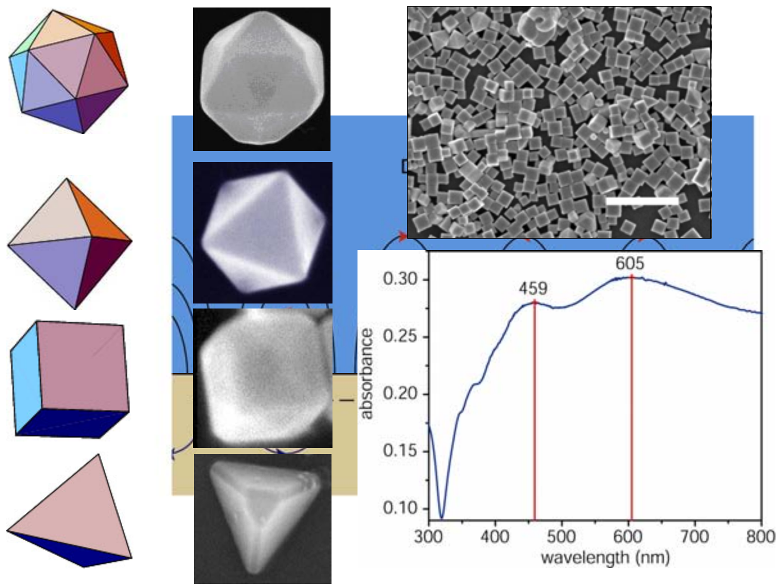


Dr. Oz accused of fear-mongering on apple juice (Arsenic in juice!)

Thursday, September 15, 2011 (AP)
By MARILYNN MARCHIONE,
AP Medical Writer

Arsenic in apple juice! Fed to babies! And it probably came from China! Television's Dr. Mehmet Oz is under fire from the FDA and others for sounding what they say is a false alarm about the dangers of apple juice.

Arsenic detection: shape-dependent plasmon resonances



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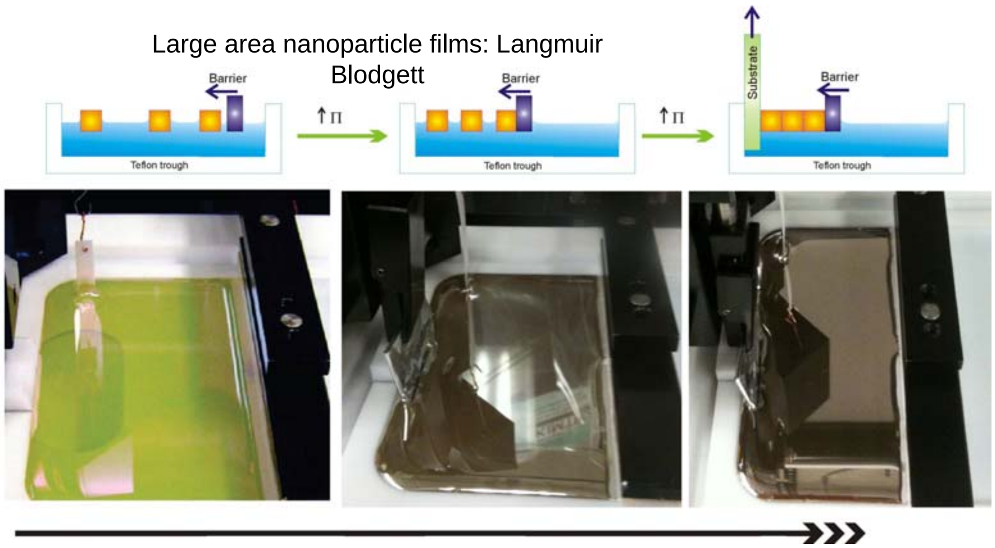
F. Kim et al. *Angew. Chem. Int. Ed.* 2004,43, 3673.

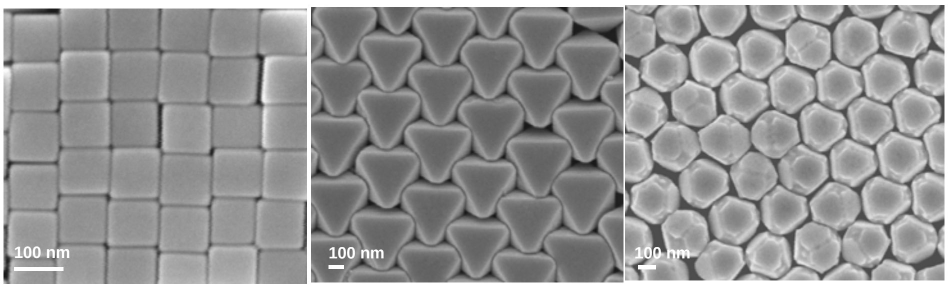
Arsenic (As) Sensing by Ag nanoparticle films

Large area nanoparticle films: Langmuir Blodgett



Increase in pressure

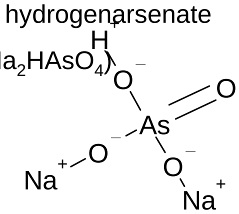
Various LB Ag nanoparticle films

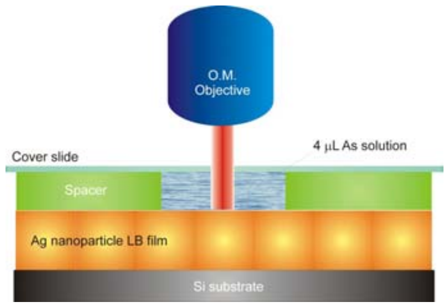


Cube Octahedra Mildly etched nanoparticle

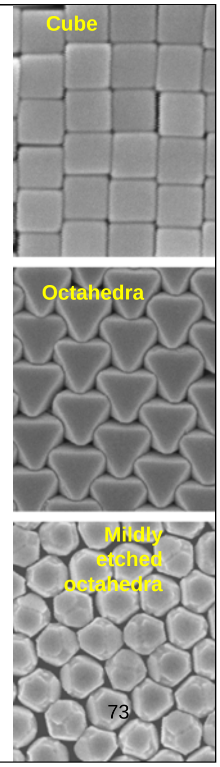
Arsenic Sensing by Surface Enhanced Raman Spectroscopy (SERS)

Probe molecule: Sodium hydrogenarsenate heptahydrate (Na_2HAsO_4)

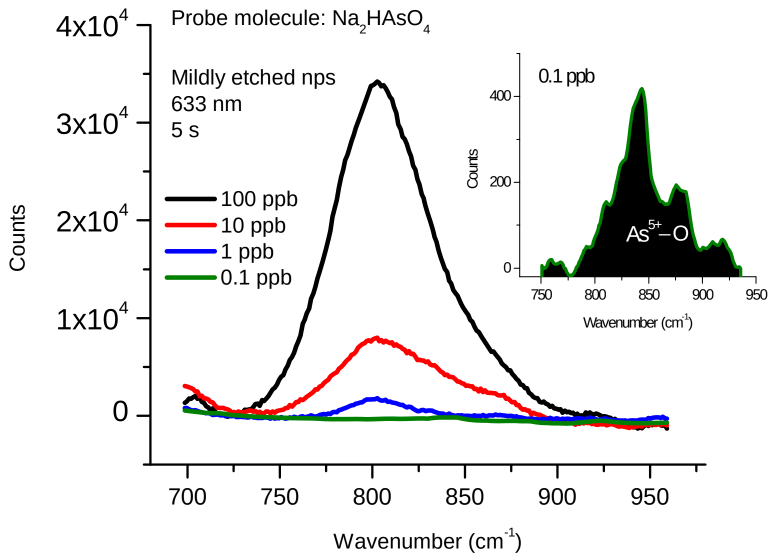




Target concentration		# molecules per laser beam volume	# molecules per volume
100 ppb	500 pM	5.50E+05	1.13E+12
10 ppb	50 pM	5.50E+04	1.13E+11
1 ppb	5 pM	5.50E+03	1.13E+10
0.1 ppb	0.5 pM	550	1.13E+09



Arsenic species sensing



Valley of death – lots of research, not many products!

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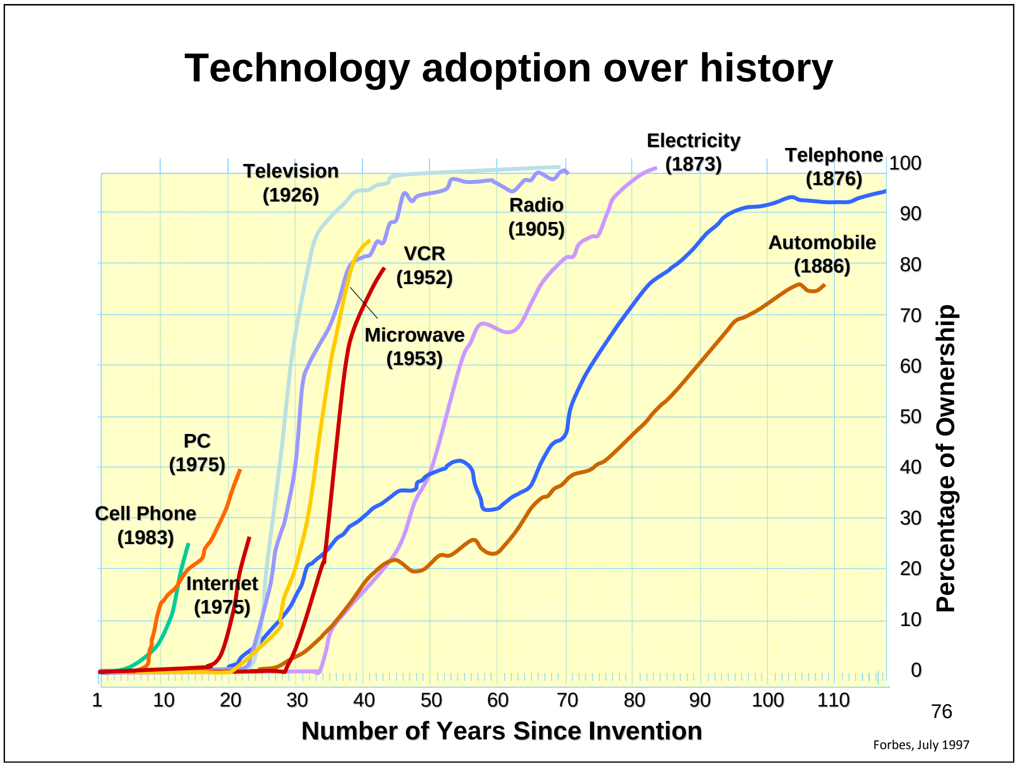
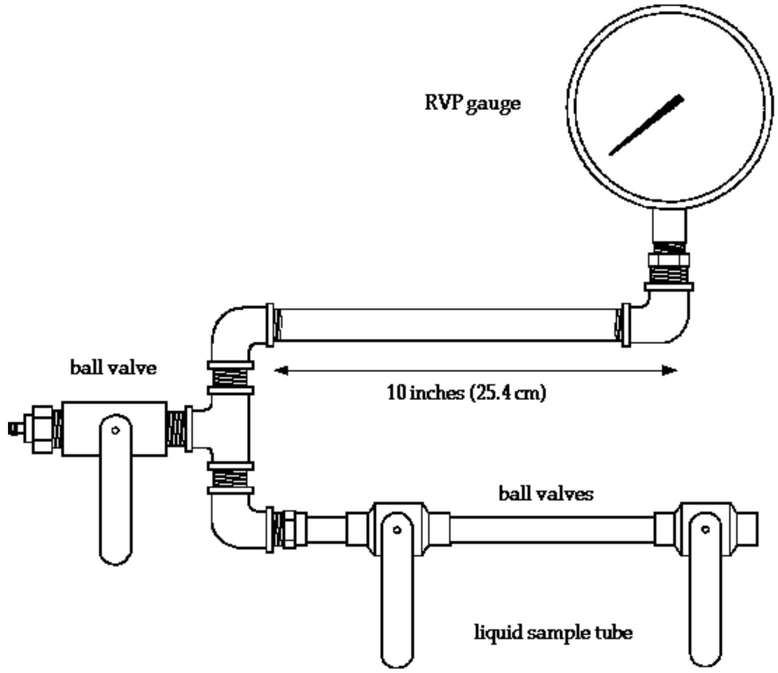

Technology adoption over history
Television (1926)
Radio (1905)
Electricity (1873)
Telephone (1876)
VCR (1952)
Microwave (1953)
Automobile (1886)
PC (1975)
Cell Phone (1983)
Internet (1975)
Percentage of Ownership
0
10
20
30
40
50
60
70
80
90
100
1
10
20
30
40
50
60
70
80
90
100
110
Number of Years Since Invention
Forbes, July 1997

Heavy oil storage tanks: Measuring emissions of hydrocarbons

- LBNL staff scientists worked with industry and regulators
- New sampling methods developed, tested, and approved for use by industry and EPA
- Emissions much lower than previous estimates: industry avoided unneeded pollution control equipment; regulators have better emission inventories


RVP gauge
ball valve
10 inches (25.4 cm)
ball valves
liquid sample tube

Making a successful widget

You need to have a market (think medical and consumer goods, not emissions monitors)

It can take a long time and lots of money for patents, product development, and marketing

Research scientists may not make the best choice for moving forward (researchers want to do more research!)

Basic research grants normally don't cover development costs

Thanks!

- Cathy Koshland and Bob Sawyer
- Peidong Yang and Xing Yi Ling
- Linwei Tian, Amara Holder, and Regine Goth-Goldstein
- Jeff Crosby, Jay James, and David Littlejohn
- NIEHS, Wood-Calvert Chair in Engineering, NCI, WSPA, and DOE

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Resources & Feedback

- To view a complete list of resources for this seminar, please visit the **Additional Resources**
- Please complete the **Feedback Form** to help ensure events like this are offered in the future

Need confirmation of your participation today?

Fill out the feedback form and check box for confirmation email.

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