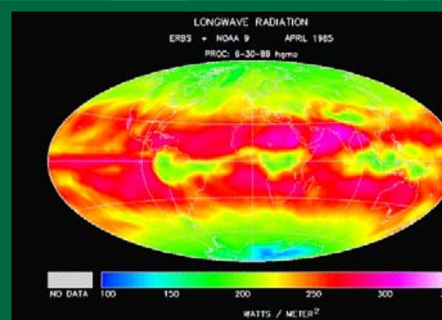
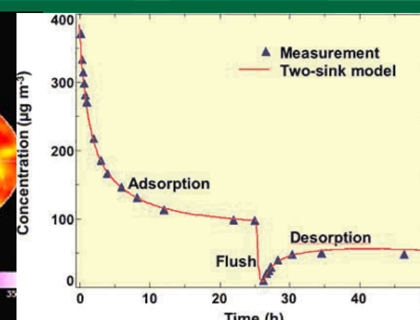
Implications and Drivers: Fate of Nanoparticles in the Atmosphere

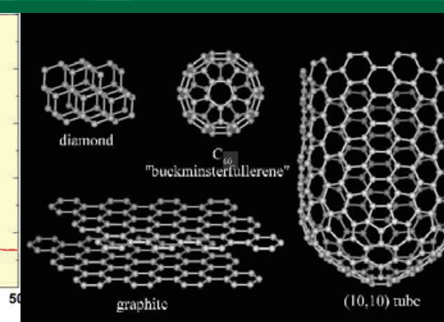
Daniel A. Vallero, Ph.D.

National Exposure Research Laboratory

U.S. Environmental Protection Agency







Nanoparticle Air Monitoring Workshop
Research Triangle Park, NC
March 2, 2009

Office of Research and Development
National Exposure Research Laboratory

Today’s theme: It’s the littlest things that are the most important!

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Some Key Questions

1. **How can/should nanomaterials be characterized physically, chemically and biologically?**
    - What techniques and tools exist, can be modified, or need to be developed for detecting and predicting the hazards of engineered materials?
    - What constitutes a nanoparticle of concern?
        - Engineered? Manufactured? Ultrafine?
        - Carbon, metals, ….?
2. **What is the extent of exposure to the stressor for humans and ecosystems? …. acceptable level of uncertainty of the exposure estimates?**
    - How should we approach nanomaterials exposures in human populations?
3. **Are the exposure concentrations higher or lower than the risk level for the contaminant?**
4. **What physical and chemical properties and processes determine the environmental fate, release, and transport of engineered nanomaterials?**

General Research Objectives

- Determine important physical/chemical/biological properties and processes that may impact exposure.
  - Exposure is likely to be affected by physical and chemical properties that control nanomaterial movement through air, soil, and aquatic ecosystems, and that influence the biological/environmental interface.
- Identification of system parameters that alter the surface characteristics of nanomaterials resulting in their aggregation, chemical reactivity and chemically or biologically mediated electron transfer.
  - Provide the basis for prioritizing potential human exposure and ecosystem exposure pathways that warrant further exploration.
  - Adapt approaches to identify and measure manufactured nanomaterials that may contaminate environmental media.
  - These methods may include electron microscopy, field flow fractionation, chromatography, and bioanalytical methods.

Nano Measurement and Modeling Needs

- Highly varied.
- Emerging sciences:
  - Surface characteristics
  - New concepts for partitioning and other behaviors
  - Definition of nanomaterials (e.g. six nanoparticles of concern
    1. **Cerium oxide**
    2. **TiO_2**
    3. **Carbon?**
  - Modification of existing approaches needed (at least sometimes)
- Food chain (next) might be a good integrating framework for nanomaterials:
  - Plus, it allows HEASD to be a “player” in an ecosystem program (if that is how things remain)

Possible Framework to Link Human and Exposure Analysis for a Nanoparticle (Mangis et al.)

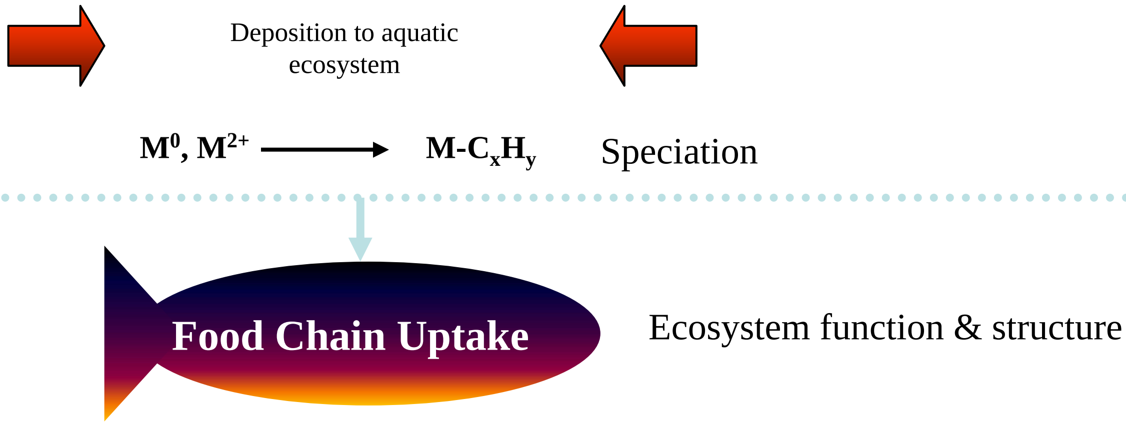
Deposition to aquatic ecosystem

$\mathbf{M^0, M^{2+}} \longrightarrow \mathbf{M\text{-}C_xH_y}$ Speciation

Possible Framework to Link Human and Exposure Analysis for a Nanoparticle

Environmental Measurements & Modeling

Activity and Function Measurements & Modeling



Environmental Measurements & Modeling

Activity and Function Measurements & Modeling

Possible Framework to Link Human and Exposure Analysis for a Nanoparticle

Atmospheric emissions
Natural: Forest fires, volcanoes
Industrial: Power plants

Deposition to aquatic ecosystem

Ground water transport
Natural & industrial sources

$M^0, M^{2+} \longrightarrow M\text{-}C_xH_y$ Speciation

Food Chain Uptake

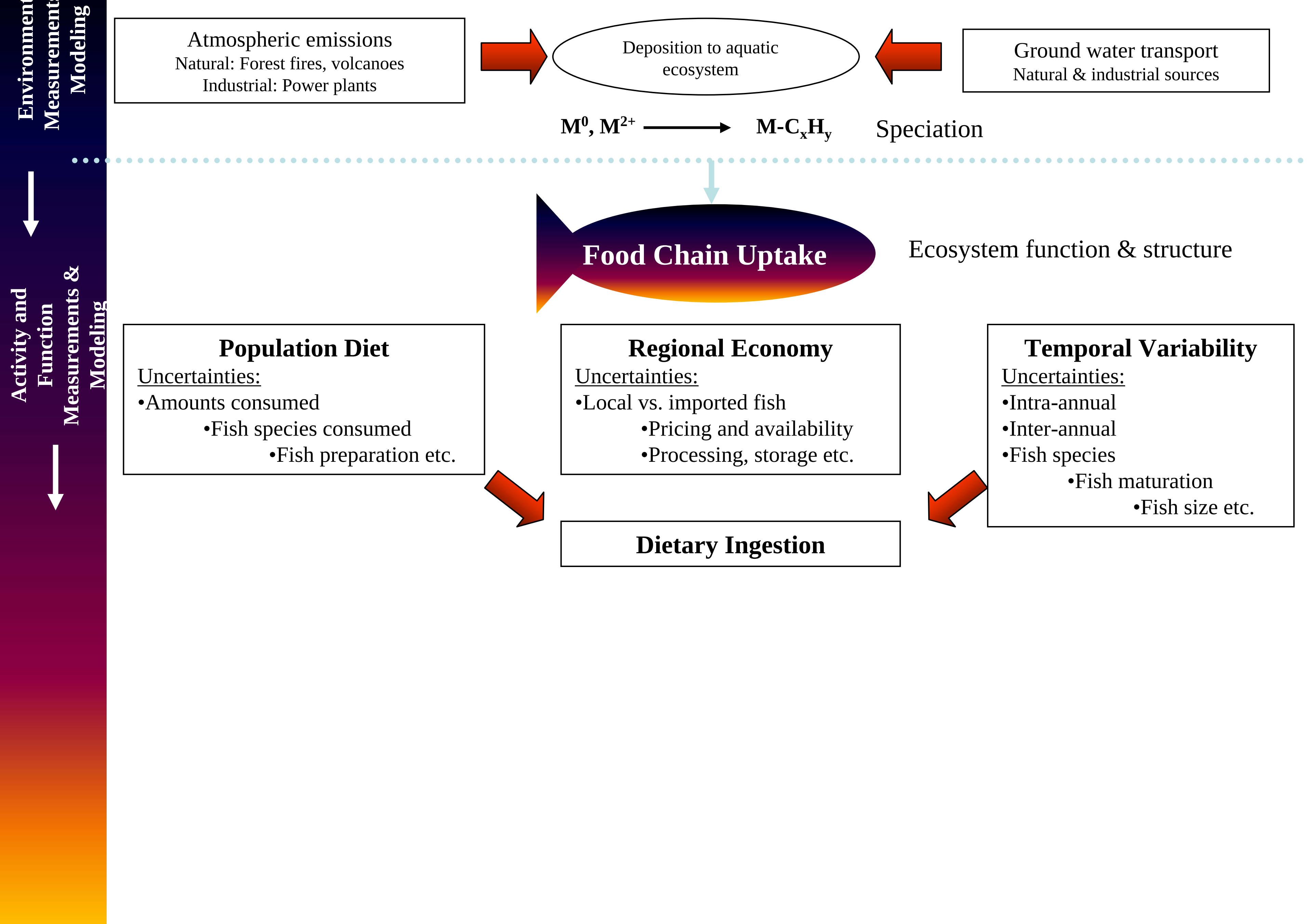
Ecosystem function & structure

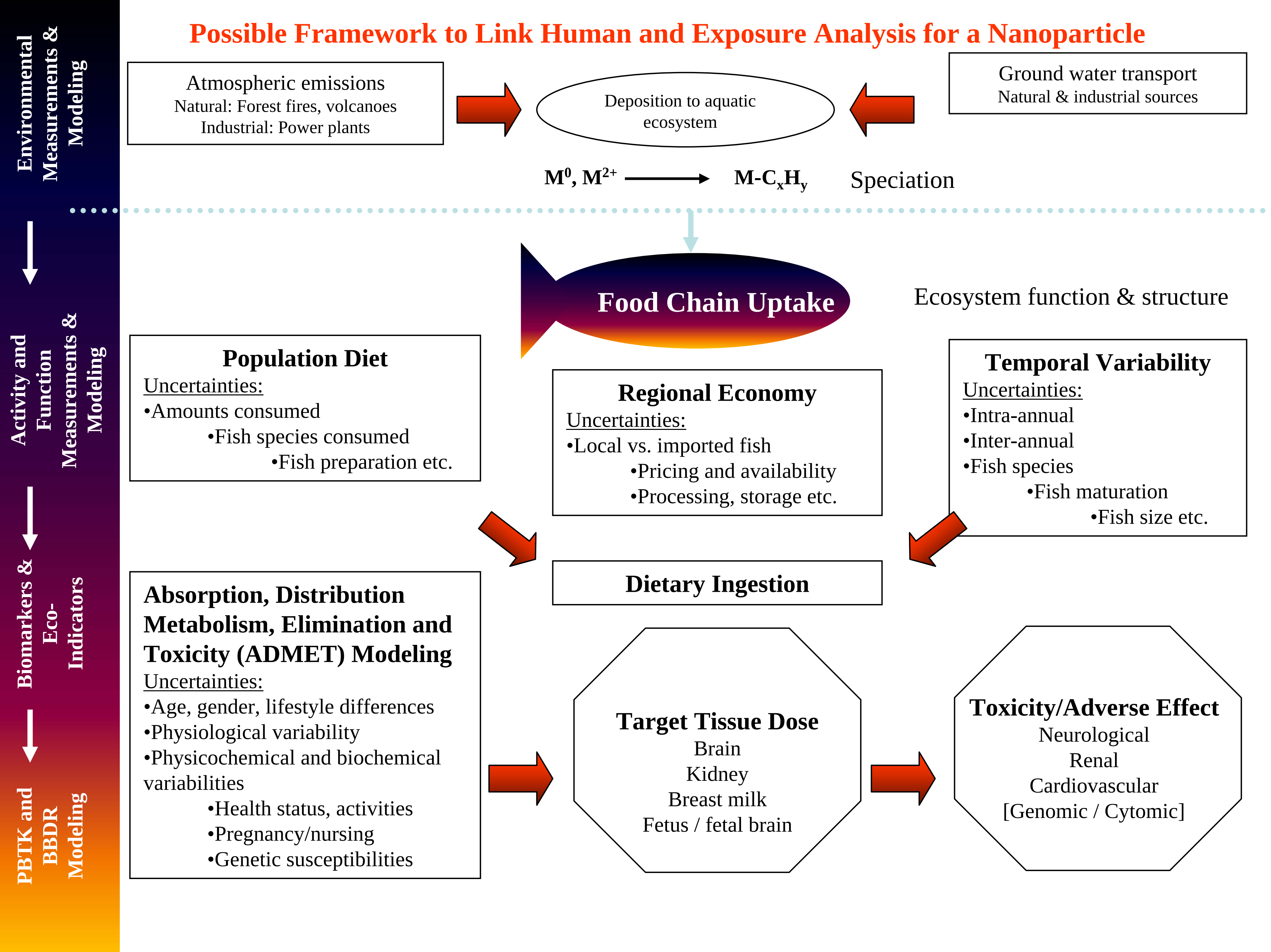
Population Diet
Uncertainties:
- Amounts consumed
- Fish species consumed
- Fish preparation etc.

Regional Economy
Uncertainties:
- Local vs. imported fish
- Pricing and availability
- Processing, storage etc.

Temporal Variability
Uncertainties:
- Intra-annual
- Inter-annual
- Fish species
- Fish maturation
- Fish size etc.

Possible Framework to Link Human and Exposure Analysis for a Nanoparticle





Possible Framework to Link Human and Exposure Analysis for a Nanoparticle
Environmental Measurements & Modeling
Activity and Function Measurements & Modeling
Biomarkers & Eco-Indicators
PBTK and BBDR Modeling
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M^0, M^{2+} → $M\text{-}C_xH_y$
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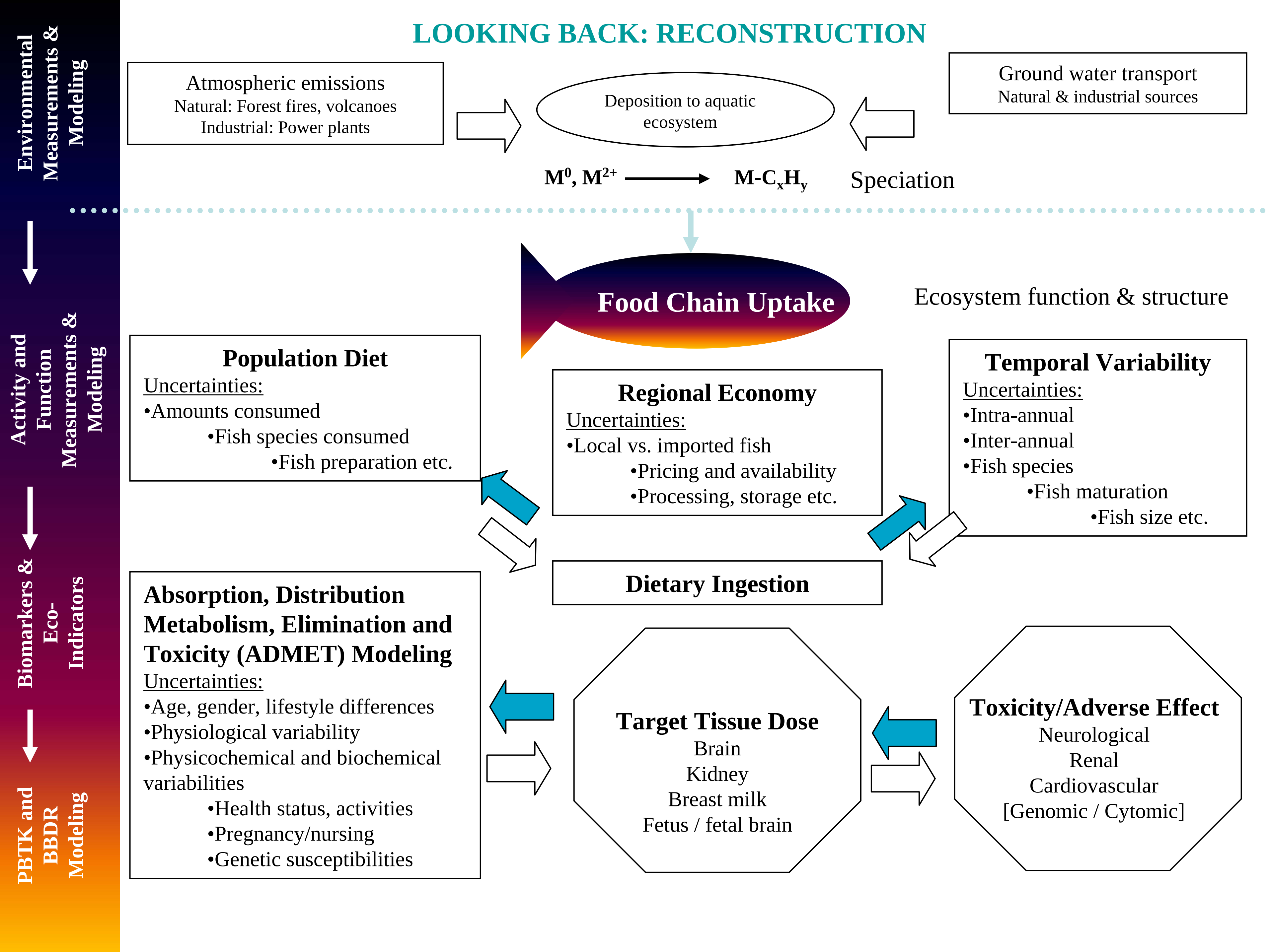
Dietary Ingestion
Absorption, Distribution Metabolism, Elimination and Toxicity (ADMET) Modeling
Uncertainties:
•Age, gender, lifestyle differences
•Physiological variability
•Physicochemical and biochemical variabilities
•Health status, activities
•Pregnancy/nursing
•Genetic susceptibilities
Target Tissue Dose
Brain
Kidney
Breast milk
Fetus / fetal brain
Toxicity/Adverse Effect
Neurological
Renal
Cardiovascular
[Genomic / Cytomic]


LOOKING BACK: RECONSTRUCTION
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Breast milk
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Toxicity/Adverse Effect
Neurological
Renal
Cardiovascular
[Genomic / Cytomic]

Specific Nano-Air Research

1. Airborne nano characterization
2. Atmospheric simulation chamber
3. Human exposures?
4. Atmospheric dispersion

Uncertainty Example: Unexpected Chemical Results

- TiO_2 in water (1 mg/mL) -- Fails to form suspension

- TiO_2 in DMSO (1 mg/mL) -- Forms milky suspension
  - Not very toxic per unit mass **EC50 = 1594 ppm**

- After 5 min sonication
  - Toxicity/unit mass <u>increases</u> **EC50 = 48.2 ppm**

- After 30 min sonication
  - Toxicity/unit mass <u>significantly increases</u> **EC50 = 0.0047 ppm**

- UV exposure also increases toxicity

What is going on here?

- Ultrasound irradiation of TiO_2 in aqueous solution resulted in significant generation of hydroxyl radicals and DMSO was a radical scavenging agent.
  - Shimizu et al. Ultrason. Sonochem. 14 (2007) 184
- TiO_2 photocatalyzes the breakdown of DMSO in water to form Sulfinic, Sulfonic and Sulfuric Acids.
  - Mori eat al. Talanta 70 (2006) 169

$$\mathbf{(CH_3)_2SO} + {}^{\bullet}OH \longrightarrow \mathbf{CH_3S(O)OH} + {}^{\bullet}CH_3$$

$$CH_3S(O)OH + {}^{\bullet}OH \longrightarrow CH_3S(O)(OH)_2 + O_2 \longrightarrow \mathbf{CH_3S(O)_2OH} + HO_2$$

$$CH_3S(O)_2OH + {}^{\bullet}OH \longrightarrow \mathbf{H_2SO_4} + {}^{\bullet}CH_3$$

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Chemistry
Important if true?

- Unexpected synergistic effects
  - TiO_2 not particularly toxic
  - DMSO nontoxic

    + Energy $\longrightarrow$ Very toxic

Characterize/Report

UV effects

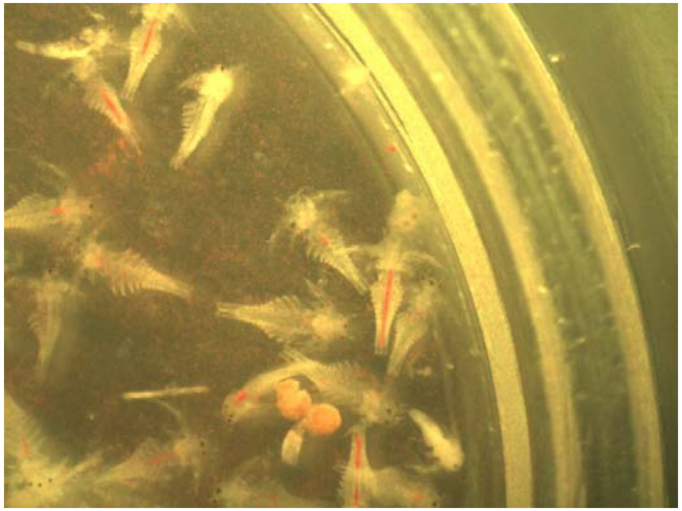
Radical effects

Toxicity effects

Other Chemical candidates

Unexpected Biological Results

Control Exposure

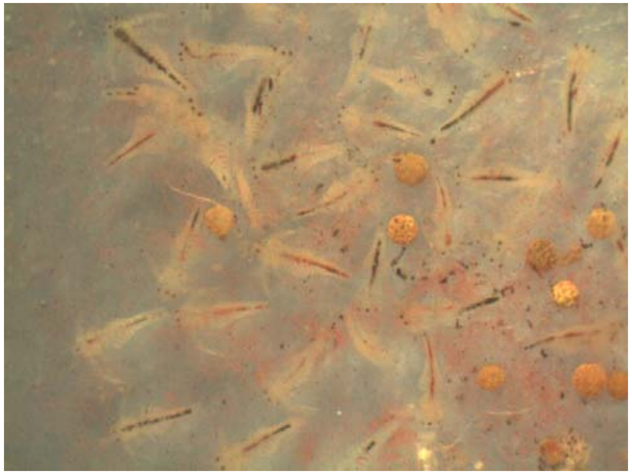


Rapid screening assay based on Thamnocephalus

Rather than showing
typical toxic response
(inhibition of indicator bead uptake)

Organisms concentrate C-70 in digestive track

Exposure to C-70, 60 ppm



Biology: Important if true?

- Unexpected mechanism for bioaccumulation
  - Possible exposure pathway
- Characterize observations
  - Long-term toxic effects
  - Reproductive effects
  - Fullerenes in the digestive track
    - Composition (LC/MS)
    - Aggregation (thin section TEM)

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Participants and Collaborations

- HEASD-LV
  - Kim Rogers
  - Manomita Patra (NRC post-doc)
- UNLV
  - Dave Hatchett Associate Professor, Chemistry Dept, UNLV
- ERD Athens
  - Dermont Bouchard
  - Cissy Ma (post-doc)
- EERD Cincinnati
  - Jim Lazorchak
  - Helen Poynton (ORIS post-doc)

Nano Bioanalysis

- Quantum Dots (QD): Semiconductor Nanostructures
- Unique physiochemical properties due to combination of core composition and quantum-size confinement
- QD Core - a metal and semiconductor particle, smaller than its Bohr radius (1-5 nm)
- QD Shell – hydrophobic but can be functionalized to increase water solubility and biological activity/compatibility
- Cd and Se known to cause acute and chronic toxicities

Bioanalytical Research Issues

- QDs an be conjugated with bioactive moieties (e.g., antibodies, site specific gene and drug delivery)
- QD toxicity depends upon size, charge, shell materials, coatings, and conc.
- Size makes QDs easily transportable through human body (e.g.,burrowing)
- 2012 global market estimate for NMs is $1 trillion
- 1 million workers in US

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Characterization: The NanoDot

- Properties of QDs make them useful but hazardous
- Occupational and non-occupational exposures are not known
- Fate/transport and exposure pathways are not known

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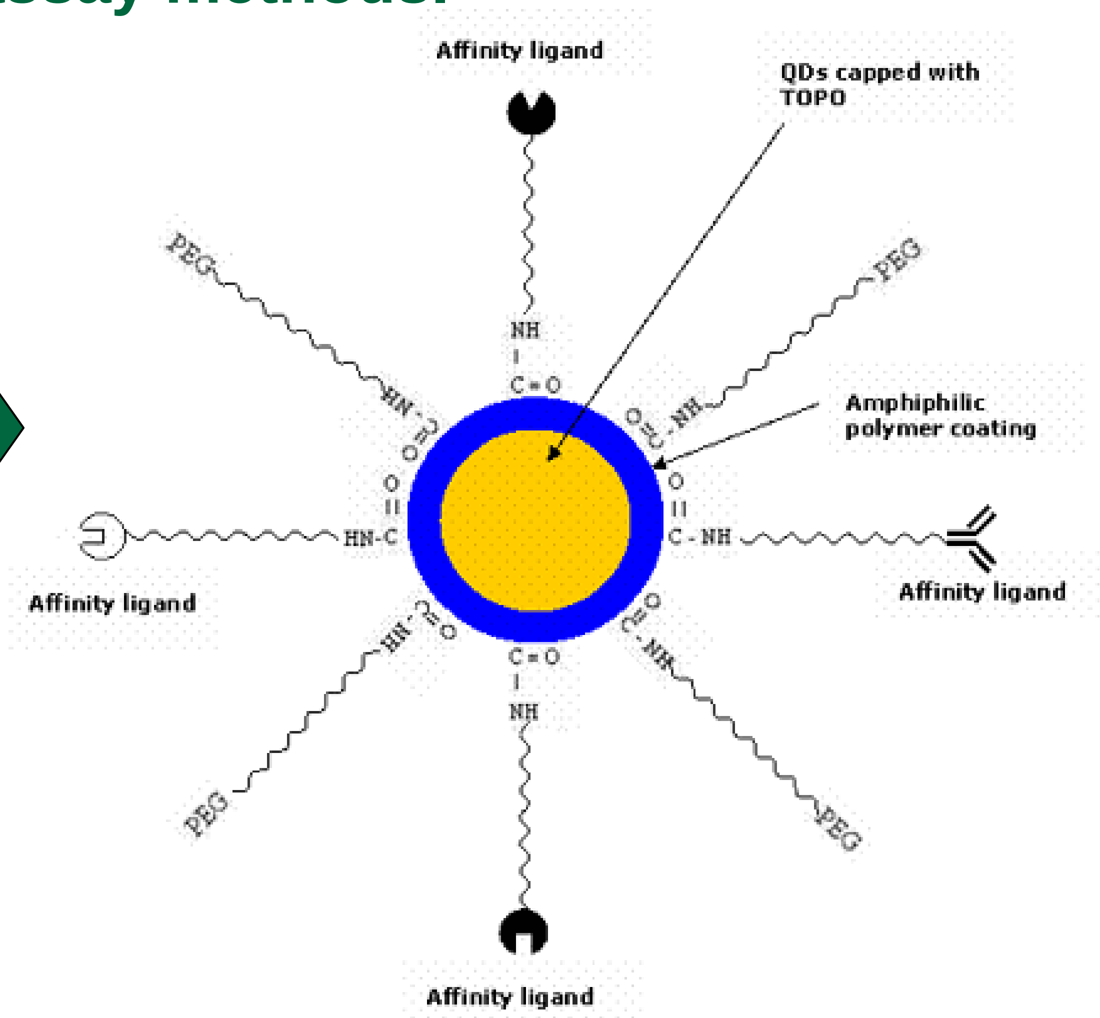
Quantum dots can be conjugated to various affinity ligands (e.g., peptide, antibody, inhibitor, etc) for microarray and immunoassay methods.

Which, if any of these functional groups is important to air?



Characterization of Nanomaterials

- Properties that are relevant to the potential toxicity and transformation and fate of nanomaterials in the environment include
    1. **particle size**
    2. **morphology**
    3. **surface area**
    4. **chemical composition**
    5. **tendency to aggregate.**
- High-resolution microscopy is a critical tool in characterizing these properties.

Objectives for the Atmospheric Chamber Study

1. Explore how different types of nanomaterials could potentially interact with simulated atmosphere mixtures (organic/inorganic gases and aerosols)

2. Examine how atmospheric interactions affect structure and/or chemistry of nanoparticles, which may influence their health effects and ultimate environmental fate

Atmospheric Characterization Research

Broader questions that need to be answered:

1. How does the presence of engineered NPs alter aerosol production and gas-phase chemistry in the atmosphere?
2. How do atmospheric interactions affect size, structure, chemistry of NPs, and how do these properties affect transport, fate, and potential toxicity of NPs?
3. What properties are most relevant to the transport, fate, and toxicity of NPs in air, and how can we best measure them?

Atmospheric Characterization Research

Some specific research questions:

1. Is NP aggregation a consequence of how NPs are sampled? What method of sampling (e.g., active vs. passive) best preserves the natural state of aggregation in the environment?
2. How do engineered NPs change (size, shape, composition) with age in the atmosphere? To what extent do aged NPs attach to natural airborne particles in the atmosphere such as coarse-mode dust (crustal and urban) and diesel soot?
3. Can size, shape, and elemental composition be used to distinguish engineered NPs from natural airborne particles?

Comprehensive Research Is Possible

- Two environmentally relevant NMs (TiO_2 and CeO_2)
- Can combine **chamber experiments** with **sampling methods development** and **physicochemical characterization** to address the research questions.
  - (ICP-MS, combined with
  - High-resolution microscopy)

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Smog Chamber Capabilities

- Generate simulated atmospheric mixtures consisting of gas- and particle-phase photochemical products from the irradiation of one or more parent hydrocarbons

- Maintain consistent chemical composition for periods of up to several days

- Deliver up to 20 L min^{-1} of effluent to auxiliary exposure chamber for nanomaterial experiments

- Monitor changes in the chemistry of the simulated mixtures (hydrocarbon, ozone, NO_x, SO_2 concentrations) using existing monitoring equipment

Overview: Titanium Dioxide

- Photocatalytic compound activated by UV irradiation of 360 nm or less

$$TiO_2 + UV_{\lambda<360\ nm} \rightarrow TiO_2 + h^+ + e^-$$

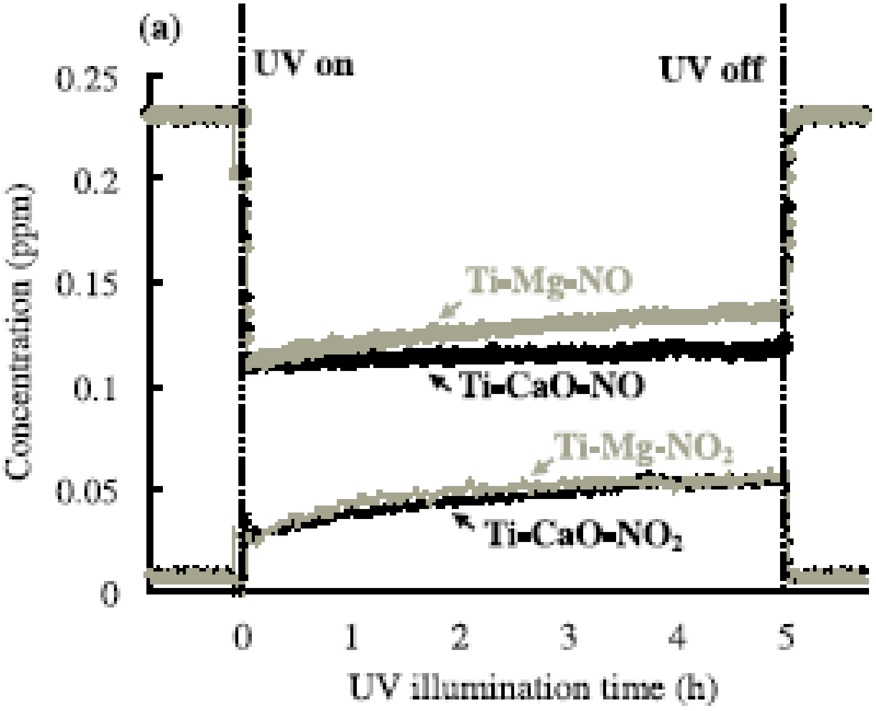
$$R\text{-}OH_{(s)} + h^+ \rightarrow R^+_{(s)} + OH\bullet_{(ads)}$$

$$O_{2\ (ads)} + e^- \rightarrow O_2^-\ _{(ads)}$$

- Usually consists of ~ 30 nm particles coated on supporting materials
- Used for self-cleaning outdoor surfaces
- Tested for NOx abatement

Relevance of Titanium Dioxide to Atmospheric Chemistry

- Uptake and conversion of NOx compounds to NO_3^-
- Uptake and oxidation (often complete oxidation) of many types of VOCs in single-component experiments
- Oxidation of surface-deposited non-volatile organics, including oils and soot (sometimes with release of volatile products)

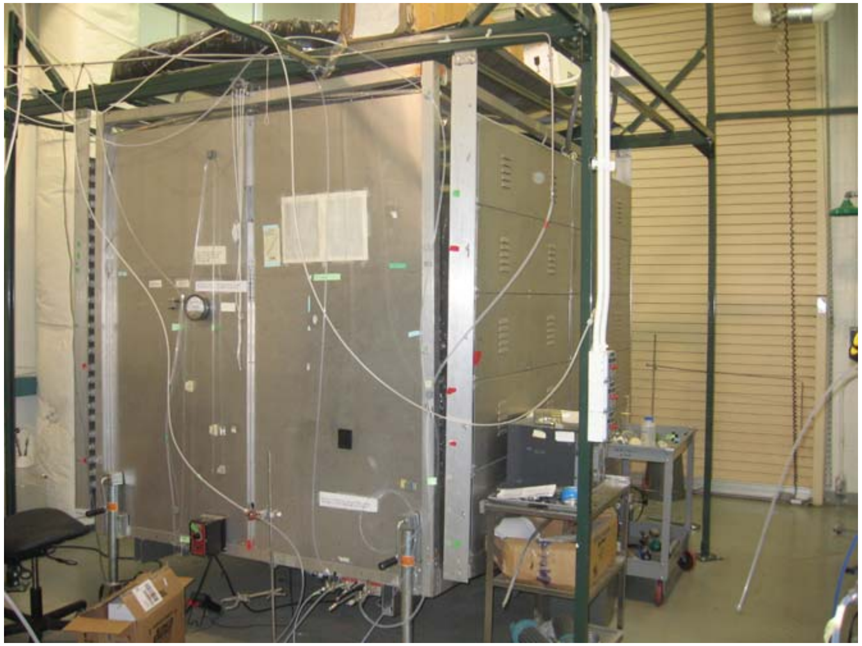


Outstanding Issues: Titanium Dioxide

- Competitive uptake and reaction of VOCs under atmospheric conditions (multiple compounds, variable humidity)
  - Formation of air toxics (particularly formaldehyde, acetaldehyde)
  - Formation of condensable products or SOA precursors
- Wash-out of surface-bound reaction products (nitric acid, organic compounds)
- Reaction of other atmospheric species (SO_2, NH_3)

Proposed Experiments: Cerium Oxide

- Inject exhaust from undoped or cerium oxide-doped Diesel fuel into photochemical reaction chamber
- Measure chemical composition of gas-phase and particle-phase exhaust components
- Irradiate mixture and monitor secondary gas-phase chemistry and SOA formation
- Analyze fate of cerium oxide particles from the doped fuel samples
- Data to be provided to AMD, OTAQ, NERML




BALDOR
DIESEL
DG3E
3000W

Proposed Experiments: Titanium Dioxide

- Auxiliary irradiation chamber added to main photochemical reaction chamber
- Immobilized titanium dioxide samples to be exposed to HC, NOx, and/or photochemical reaction products (gases and SOA)
- Monitor changes in gas-phase chemical composition
- Analyze liquid extracts of titanium dioxide samples for surface-bound intermediates and products

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A few words about human PBTK modeling

- A worthy goal: Provide data and exposure-dose models on the human health and environmental effects of nanomaterials exposure
- A possible approach: Scenario-based exposure-to-dose models allow for the integration of biologically relevant data independent of the data source.

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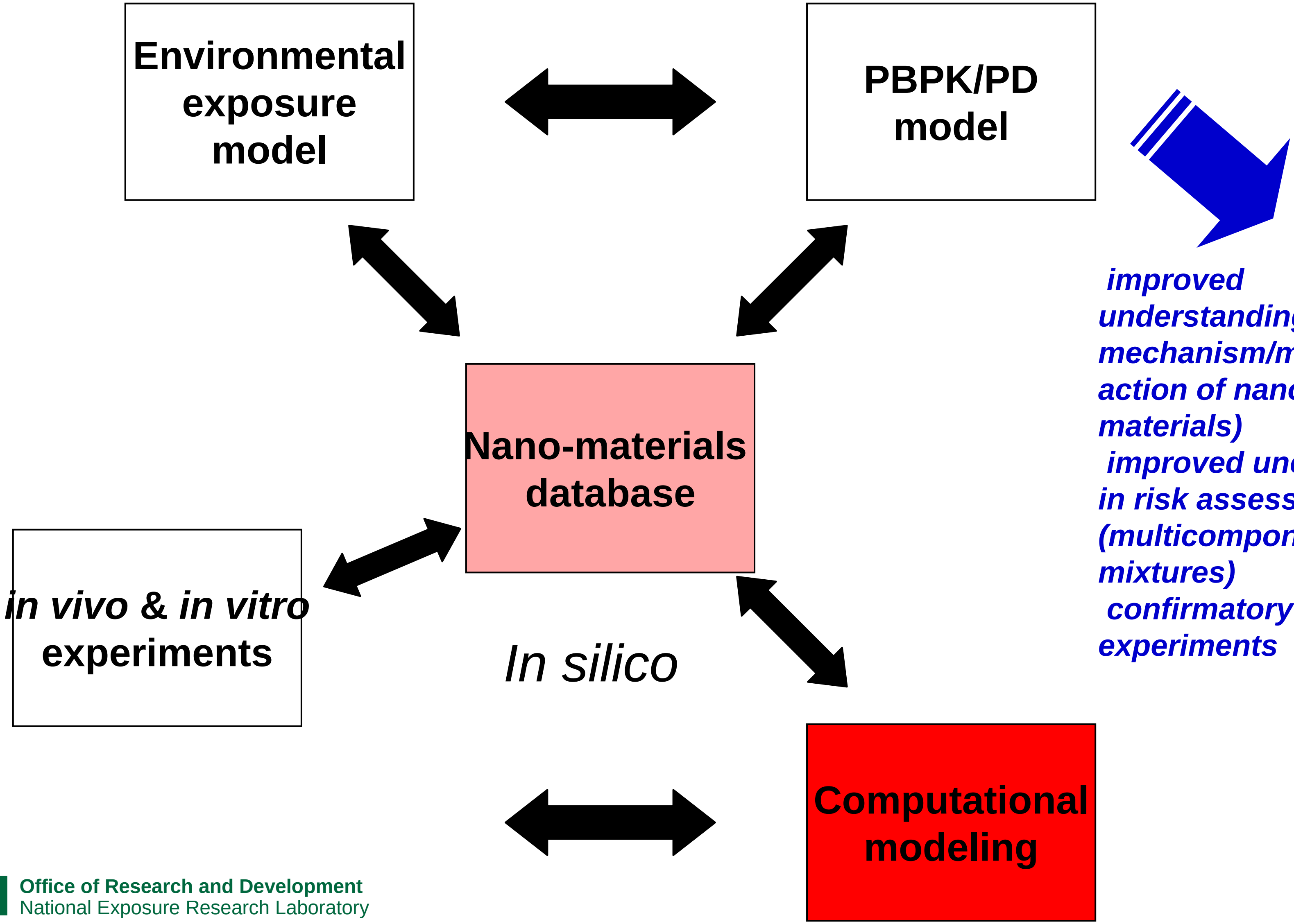
Overall Schema



improved understanding of mechanism/mode of action of nano-materials)
improved uncertainties in risk assessments (multicomponent mixtures)
confirmatory experiments

Human/Eco Reconstruction Problem: Unbiased Measures of Nanomaterial Characteristics

- Size
- Shape/geometry
- Charge
- Reactivity
- Purity
- Electronic and photonic properties
- Composition
- Functionalization
- Agglomeration state
- Manufacturing process
- Assembly
- Allowed diversity

Nanoparticle Respiratory Deposition Modeling

- Where do the particles distribute in the respiratory tract?
  - **in the naso-pharyngeal, tracheo-bronchial and alveolar regions?**

- Can we anticipate deposition through modeling?
  - CIIT's **MPPD model** (Hamner)
  - Coupled to Current PBPK infrastructure (**ERDEM**)

- Can we improve on these models?
  - Predict surface property effects
  - Predict particle morphology effects
  - Formulate better understanding of repsiratory deposition / absorption and clearance

Nanoparticle Respiratory Deposition Modeling

Supports both human and Eco (e.g. sentinel species) fate and transport

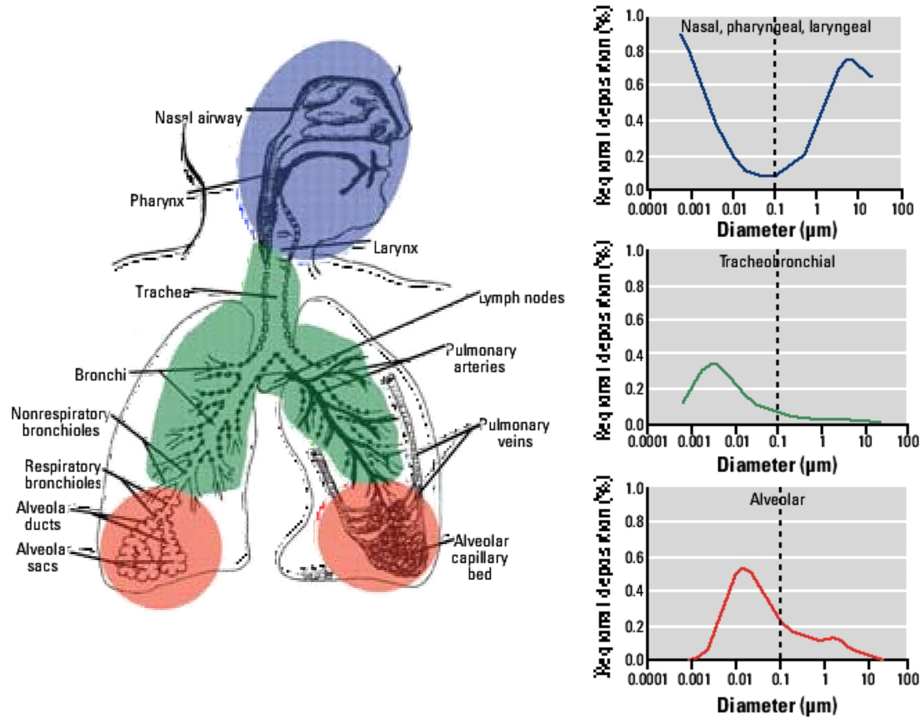
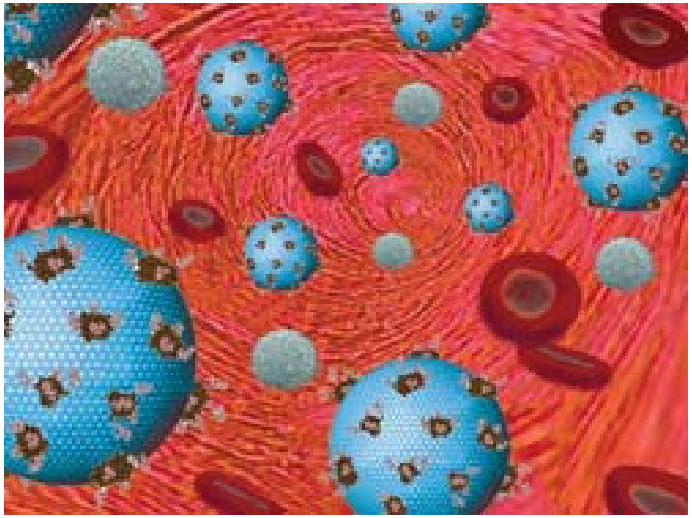


Figure 8. Predicted fractional deposition of inhaled particles in the nasopharyngeal, tracheobronchial, and alveolar region of the human respiratory tract during nose breathing. Based on data from the International Commission on Radiological Protection (1994). Drawing courtesy of J. Harkema.

- Both ICRP and MPPD model can express fractional deposition and clearance as a function of particle size (mean surface area) <u>but not discrete morphologies densities and surface modifications</u>
- **We can** introduce these adjustable parameters!

Nanoparticle Circulatory Deposition Modeling

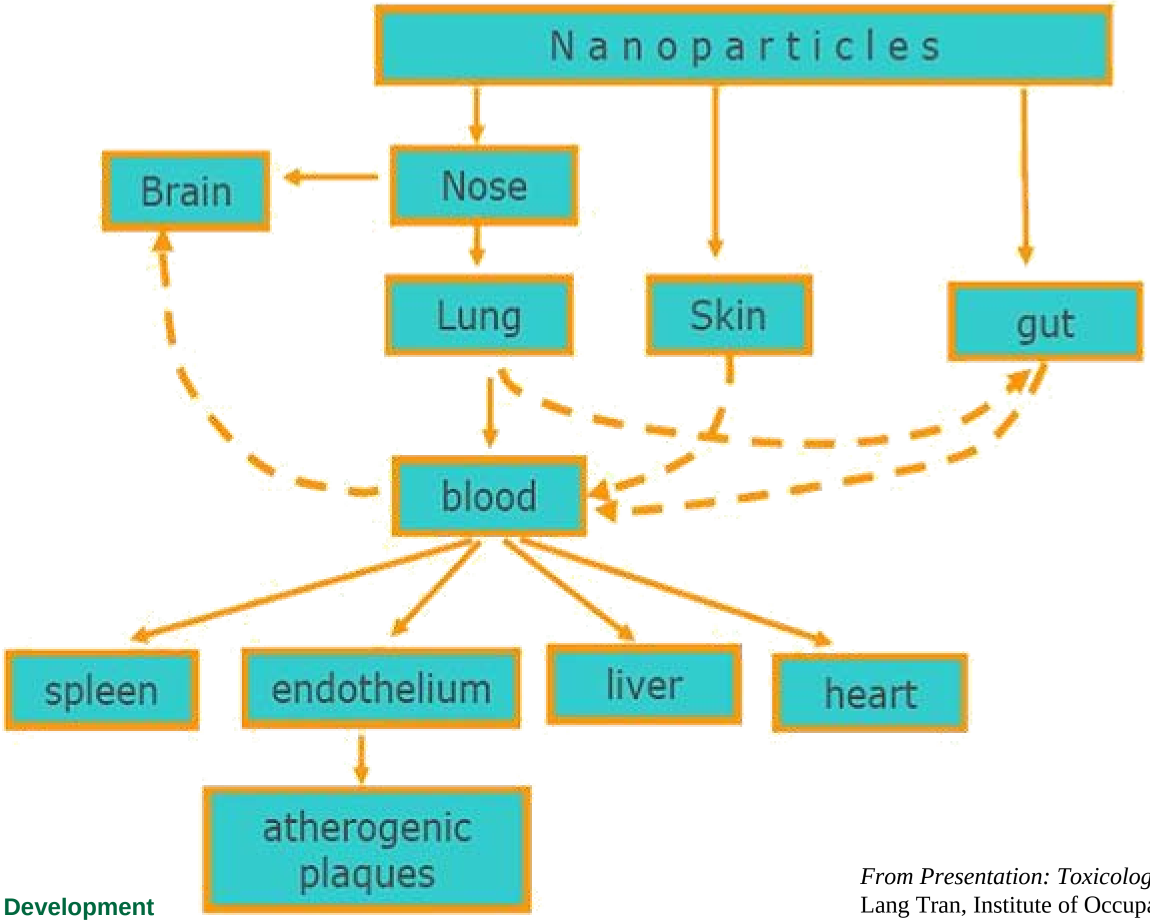


http://radio.weblogs.com/0105910/images/nanoparticles.jpg

- **Where do the particles distribute in the circulatory system / reticuloendothelial system and can we model this?**
- **Can we improve on our understanding of circulatory distribution of nanoparticles?**

FROM EXPOSURE TO INTERNAL DOSE

Hypothetical toxicokinetics of nanoparticles



From Presentation: Toxicological/Health Effects
Lang Tran, Institute of Occupational Medicine
http://www.uc.edu/NOEHS/conference_program.asp

Computational Tools

- Because they are based on organismal biology, these computational models can use experimental data produced from virtually any level of biological investigation, from the molecular dynamic interactions to whole organism responses to exposure. Thus, they can:
  - ✓ tie to exposure reconstruction
  - ✓ link human and ecosystem biomonitoring.

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Thus, the implications are….

- Atmosphere needs more attention from the nano research community.
- Exposure is a good platform to study nanoparticles, including our characterization and chamber capabilities.
- Measurements will support models and vice versa.
- There is a good chance that in the next year we can begin to provide useful information to OTAQ, OAQPS and other air clients.

Fate and Transport of Engineered Nanomaterials in the Atmosphere:

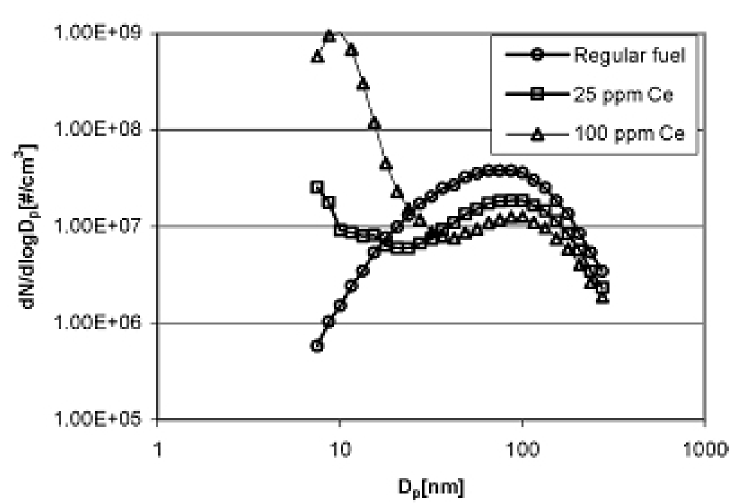
Garnet Erdakos & Prakash Bhave, NERL Atmospheric Modeling Division

Case Study: Investigate the potential effects of nanoparticulate CeO_2 diesel fuel additive on the spatial and temporal distributions of various atmospheric pollutants and deposition loadings.

Fate and Transport of Engineered Nanomaterials in the Atmosphere

Case Study: **Investigate the potential effects of nanoparticulate CeO_2 diesel fuel additive on the spatial and temporal distributions of various atmospheric pollutants and deposition loadings.**

Sample Available Data Overview: Additized Diesel Emissions



size and number distributions

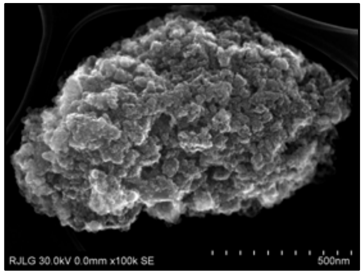
	Percentage Change in Emissions (%)					
Reference	HC	CO	NO_x	PM	TEQ	CeO_2
SwRI	33	8	3	similar		
Farfaletti	4.2	4.2	- 0.8	1.3	- 39	
Park				- 8		~ 300
Cerulean	- 15	- 10	0	- 20		

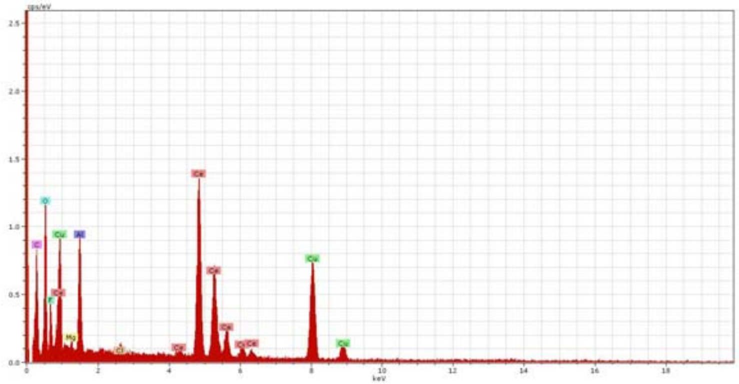
Data Needs: Emissions (particle size distribution, particle number concentration, particle morphology, co-pollutant concentrations); Fuel consumption; CeO_2 characteristics (emissions rates, deposition rates, chemical reactivity, solubility)

- **Expected Impact:** Characterize source-to-ambient step for NM in the exposure-research framework; Guide the prioritization of future resources targeted at characterizing atmospheric NM properties

Caveat!

- These projects (which includes fuel characterization, chamber studies, and methods and filters analyses) are contingent upon FY 09 funds
  - –None received to date….





Disclaimer

Although this work was reviewed by EPA and approved for presentation, but does not necessarily reflect U.S. EPA policy.

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