Task ID: 425.023

Project title: Environmental Safety and Health (ESH) Impacts of Emerging Nanoparticles and Byproducts from Semiconductor Manufacturing - Preparation and Characterization of Nanoparticles

Deliverable: Report on the results on the interactions of process contaminates with phase 1 NPs

Background:

Numerous reports published in recent years indicate a growing concern for the potential toxicity of engineered nanomaterials (Balbus et al. 2007; Nel et al. 2006; Handy & Shaw, 2007). Toxicity research is a high priority for the semiconductor industry due to the fact that some nanoparticles (*e.g.* chemo-mechanical planarization (CMP) slurry particles) are currently used in semiconductor manufacturing, and various new nano-sized materials (nanowires, carbon nanotubes, immersion lithography nanoparticles) are being considered for upcoming manufacturing processes. Predicting the potential toxicity of emerging nanoparticles (NPs) will require hypothesis-driven research that elucidates how physicochemical parameters influence toxic effects on biological systems. Of particular concern are NPs of less than 0.1 μm that would escape normal mechanisms of cellular defense (Gwinn & Vallyathan, 2006; Stern & McNeil, 2008). The intrinsic capacity of NPs to penetrate biological tissue may in itself not be the primary cause of toxicity; rather surface properties of NPs may accentuate (or minimize) toxicity. These include high specific surface area, reactive surfaces, and adsorptive surfaces for other toxic chemicals. Contaminants can also accumulate in NPs via nano-capillary condensation (Kelvin effect) in the particle pores. NPs have very high surface curvatures, engendering high surface tensions and energies that might have unique effects on living cells. Reactive radical species can have prolonged lifetimes when sorbed onto NPs. There is a growing consensus that reactive oxygen species (ROS, composed primarily of hydroxyl radicals, hydrogen peroxide and superoxide) are a major contributing factor of NP toxicity (Gwinn & Vallyathan, 2006; Limbach et al., 2007). ROS are normally produced in and around living tissues; however, overproduction can lead to cell toxicity and loss of cell and tissue function.

Objective and key findings:

The goal of this project is to characterize the potential toxicity of current and future NPs and NP-byproducts of SC manufacturing. The information will be used to develop mechanistic hypotheses that will be applied to developing rapid toxicity assessment protocols applicable in

the industrial workplace, as well as to predicting the ESH impacts of NPs based on physicochemical properties. Our hypothesis is that the size and size distribution of nanoparticles intrinsically makes them more adsorptive to external chemicals, and these surface molecules can contribute to the observed toxic effects of NPs on cells.

The objective of this task is to investigate the physicochemical and surface characteristics of Phase 1 NPs relevant to toxicity assessment.

Our results confirmed that contaminant retention by the selected inorganic oxide NPs is compound dependent. The retention affinity of the NPs decreased in the order: CeO_2 > Al_2O_3 > HfO_2. Adsorption on CeO_2 of the test compound considered (H_2O) seems to be due to strong chemisorption. In agreement with literature findings, the retention of contaminants on NPs was shown to be size dependent, as indicated by the increased retention observed for HfO_2 NPs with decreasing particle size. Additional studies were conducted to study the adsorption of a model contaminant, arsenic (arsenate, As(V)), on abrasive CMP nanoparticles. Inorganic arsenic species are expected in CMP effluents from the planarization of silica-gallium/arsenide, a material proposed as an alternative to silica. Alumina and hafnia NPs were found to adsorb considerable amounts of arsenate.

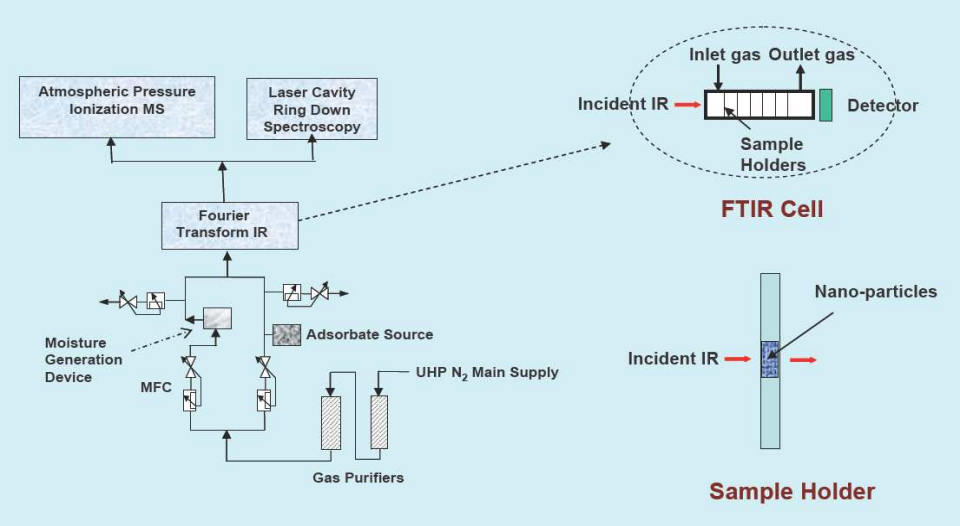
Additional work focusing on the stability of NP dispersions in various biological media commonly utilized in toxicity testing confirmed significant NP aggregation. Polyacrylate dispersants were shown to be effective in minimizing inorganic oxide NP aggregation in biological media at concentrations sufficiently low to avoid biological inhibition.

Furthermore, a process model was developed to describe the adsorption and desorption of contaminants on NPs which includes transport processes as well as rates for simultaneous adsorption and desorption.

Method of Approach

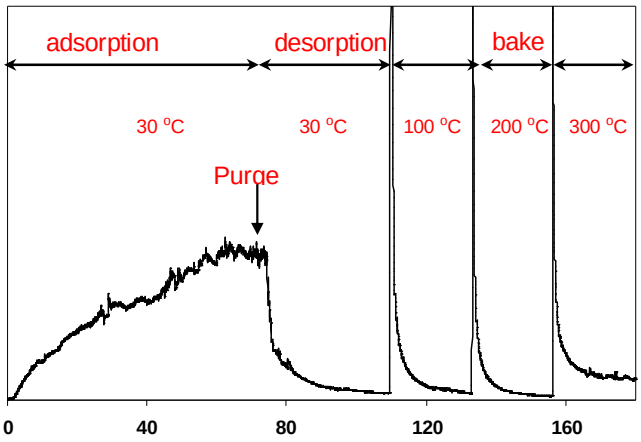
Physical Characterization of Nano-Particles Surfaces:

The experiential set up for the physical characterization is shown in the following figure:



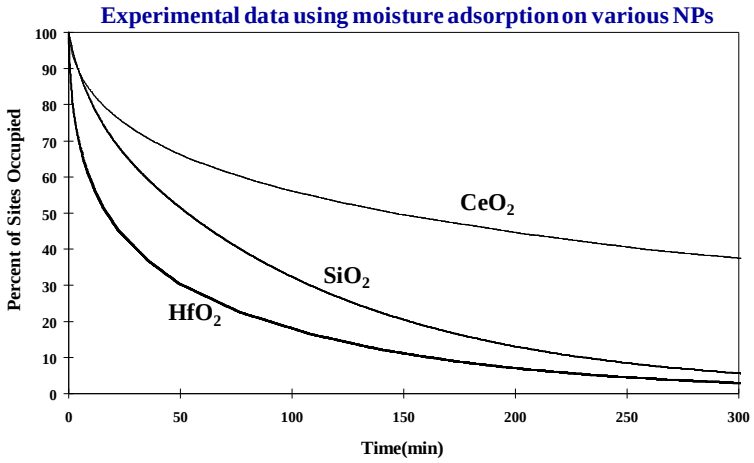
In a typical experiment, the sample is placed in a special cell that we have designed for placing the NPs in the path of the FTIR beam. The output of the FTIR cell is then sent to a mass spectrometer and also to a laser cavity ring-down spectrometer for gas analysis. This allows us to monitor the dynamic of moisture adsorption and desorption from the NP samples both by monitoring the solid sample and also by monitoring the purge gas that carried the desorbed gas out of the cell.

The following graph illustrates a typical experimental procedure. First we expose the sample to a certain challenge level of adsorbent (adsorption). After saturation, we begin the purge process and we desorb to baseline. Then we increase the temperature in steps (Temperature Programmed Desorption) to get more activated compound out. Moisture is used for chemisorptions (activated adsorption), IPA is used for physisorption (easily comes off).



A process model is also developed for this adsorption and desorption on NPs . The model includes transport processes as well as rates for simultaneous adsorption and desorption (details on the poster).

The figure below shows results on the dynamics of moisture desorption from same-size NPs of three oxides. It shows that contamination retention is compound dependent: the retention



is highest for CeO_2 and lowest for SiO_2; adsorption on CeO_2 seems to be strong chemisorptions. CeO_2 and HfO_2 adsorb and hold and contaminants more than SiO_2 does.

Additional studies were conducted to study the adsorption of a model contaminant, arsenic (arsenate, As(V)), on abrasive CMP nanoparticles. Inorganic arsenic species are expected in CMP effluents from the planarization of silica-gallium/arsenide, a material proposed as an alternative to silica. Alumina and hafnia NPs were found to adsorb considerable amounts of arsenate. The adsorptive capacity of these two nano-sized materials is comparable to that of a commercial α-Al_2O_3 developed for application in the removal of arsenic from drinking water, as shown in the Table below. The Freundlich constants K_F *and 1/n* determined for HfO_2 NPs were 3.512 [(mg As g^{-1} Alumina)(mg As $L^{-1})^{-1/n}$] and 0.267, respectively, and the linear regression coefficient, r^2, was 0.911.

Table. Freundlich isotherm model parameters for the adsorption of As(V) onto alumina NPs (our study) and onto activated alumina (cited studies).

	$C_s = K_F\, Ce^{1/n}$			
Initial Concn. Ranges (mg L^{-1})	K_F	$1/n$	R^2	Reference
0-500	27.82	0.21	0.931	This study
0.6-0.7	0.99	1.02	0.985	Sun et al. (2010)
2.6-11.5	0.36	0.27	0.984	Lin (2001)
0-80 (Ce*)	0.13	0.24	0.990	Jang (2002)

* Equilibrium concentration in the aqueous phase determined in the adsorption isotherm experiments.

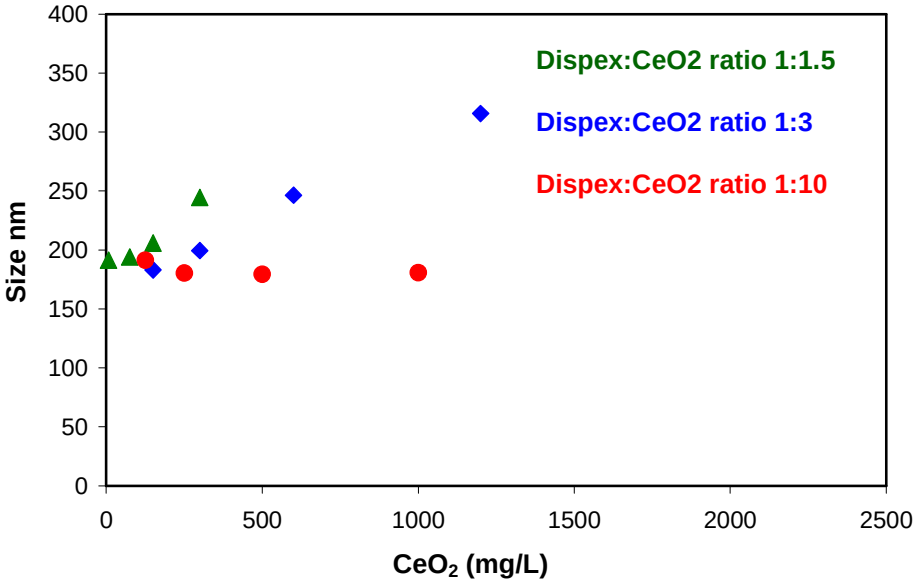
The units of K_F are [(mg As g^{-1} Alumina)(mg As L^{-1})$^{-1/n}$]

Some NPs are capable to enter into cells. Our results suggest that adsorption of contaminants onto the highly activated surfaces of NPs could contribute to the toxic effects reported for some NPs. This hypothesis will be investigated in future research.

Dispersion of NPs in biological media utilized for toxicity testing is very challenging (Sager et al. 200; Schulze et al. 2008). Our results confirmed that the CeO_2 nanoparticles (average particle size determined by TEM= 20 nm) underwent very significant aggregation in two media commonly used in toxicity tests with human cells, Mitochondrial Toxicity Test (MTT) medium and Hank's Buffered Salt Solution (HBSS).

Testing the impact of material size on toxicity will require effective dispersion of the NP in the aqueous media. This project will investigate various methods to functionalize NP surfaces using biocompatible ligands in order to promote the stability of NP dispersions and prevent aggregation. Initial studies will consider surface modification by poly-acrylates, thiol-terminated polyethylene glycols (PEGs), and amino acids such as lysine. Preliminary results confirm that polyacrylates (Dixpex) are very effective in minimizing NP aggregation in biological media at concentrations which are sufficiently low to avoid biological inhibition. Lysine was also an

effective dispersant in tests with HfO_2. The figure below shows the impact of adding various polyacrylate dosages on the average particle size of nano-sized ceria. A poly-acrylate to ceria dosage of 1:10 was found optimal to minimize NP aggregation.



REFERENCES

1. **Balbus et al.** 2007. Meeting report: Hazard assessment for nanoparticles - Report from an interdisciplinary workshop. Environ. Health Perspec. **115:**1654-1659.

2. **Gerhardt et al.** 1993. Review of impact of heavy-metals on stream invertebrates with special emphasis on acid conditions. Water Air Soil Pollut. **66**(3-4):289-314**.**

3. **Gwinn et al.** 2006. Nanoparticles: Health effects - Pros and cons. Environ. Health Perspec. **114:**1818-1825.

4. **Handy & Shaw.** 2007. Toxic effects of nanoparticles and nanomaterials: Implications for public health, risk assessment and the public perception of nanotechnology. Health Risk Soc. **9:**125-144.

5. **Jang, M., Shin, E.W. and Park, J.K.** (2002) Removal of arsenic using mesoporous silicate media impregnated metal oxides nano-particles. WEFTEC.

6. **Limbach et al.** 2007. Exposure of engineered nanoparticles to human lung epithelial cells: Influence of chemical composition and catalytic activity on oxidative stress. Environ. Sci. Technol. **41:**4158-4163.

7. **Lin, T.F. and Wu, J.K**. (2001) Adsorption of arsenite and arsenate within activated alumina grains: Equilibrium and kinetics. Water Res. 35(8), 2049-2057.

8. **Nel et al.** 2006. Toxic potential of materials at the nanolevel. Science **311**(5761): 622-627.

9. **Roesijadi, G.** Metallothioneins in metal regulation and toxicity in aquatic animals. 1992. Aquatic Toxicol. **22**(2):81-114.

10. **Sager et al.** 2007. Improved method to disperse nanoparticles for in vitro and in vivo investigation of toxicity. Nanotoxicol. **1**(2):118-129.

11. **Schulze et al.,** Not ready to use - overcoming pitfalls when dispersing nanoparticles in physiological media. Nanotoxicology, 2008. **2**(2): p. 51-U17.

12. **Stern & McNeil.** 2008. Nanotechnology safety concerns revisited. Toxicol. Sci. **101:**4-21.

13. **Sun, W.**, Sierra-Alvarez, R. and Field, J. A. The Role of Denitrification on Arsenite Oxidation and Arsenic Mobility in an Anoxic Sediment Column Model with Activated Alumina. (Under review).