TUESDAY PLENARY

Single Particle Analysis All the Way up to the Stratosphere Daniel Murphy, National Oceanic and Atmospheric Administration (NOAA), Boulder, CO

At NOAA, we have been studying the composition of single atmospheric particles with a laser ionization mass spectrometer for almost 10 years. Such mass spectrometry provides tremendous sensitivity and statistical significance. It is also a very general technique that can measure almost anything present in particles from, organics to mineral dust. For this talk, I will focus on two topics where single particle analysis provides information not available from bulk analyses. The first topic is the stratosphere. There, we can distinguish particles that were formed below, within, and above the stratosphere. That information has implications as diverse as the rate at which organics are oxidized in atmospheric particles to the flux of meteors hitting the earth. The second topic is the nucleation of ice crystals in the atmosphere. There are large differences in composition between particles that are good at nucleating ice and those that are not. The ice nuclei also contain a wide variety of chemical compounds, so the problem is a good match to the capabilities of a mass spectrometer. We were able to confirm some known properties of ice nucleation, such as that mineral dust particles can be excellent ice nuclei. We also found some new properties, such as the effect of organics on particles that aren't such good ice nuclei. Besides the science, I'll show a few pictures of what it is like to put such an instrument on airplanes.

WEDNESDAY PLENARY

Inhaled Insulin and the Marvelous New Innovations in Aerosol Medicines, John Patton, Nektar Therapeutics, San Carlos, CA

In contrast to 10 years ago when the only inhaled medicines were for asthma, inhaled products are now being developed for virtually all types of lung disease (lung disease is among the top 3 killers of humans world wide) and also for the systemic delivery of small and large molecules.

After more than 15 years of development, the first inhaled insulin, Exubera, was approved for marketing in January 2006 in both Europe and the US. In addition to the first non-injectable insulin and the first inhaled systemic drug to be approved in 40 years, Exubera represents a number of technical achievements. It contains the first room temperature stable insulin formulation, the first amorphous insulin formulation, the first spray dried aerosol product, the first unit dose blister powder packaging system, the first fine powder filling system and the first inhalation device as reliable as injections. The development of the product was prolonged by safety concerns (immunogenicity and lung function effects) which were eventually overcome by extensive long term data. Now numerous companies are working on their own inhaled insulins.

The past 15-20 years have seen a large number of innovations in the science and engineering of aerosol medicines. In the area of dry powders, with the use of special safe excipients, particle engineering technology is now to the point where almost any therapeutic molecule can be formulated into a dispersible, stable powder which can be used in small breath-activated devices. In addition, with the new highly dispersible powders, the mass of drug that can be inhaled into the lungs in one breath, has increased from 100s of micrograms (ugs) to >30 milligrams (mgs), which now enables the delivery of anti-infectives in a few breaths as compared to 20-30 minute nebulizer regiments. Spray drying has now become the method of choice for controlling the size, shape and solid state of small inhalable powders (1-3 microns).

Among the liquid delivery systems the vibrating mesh is proving to be an important advance in the generation of "soft mist" aqueous aerosols. In contrast to the older inefficient jet nebulizers which require large amounts of compressed air, the vibrating mesh can generate low velocity high efficiency aerosols essentially air free. This enables anti-infectives to be delivered to ventilated patients who are at high risk for pneumonia without having to interrupt the ventilator breathing settings.

Other innovations include the development of combination products which contain two drugs in the same powder and solution formulations in the metered dose inhaler systems (MDIs, the traditional small asthma inhalers) where ethanol is used to solubilize drugs in the hydrofluoroalkane (HFA) propellants. Finally, the immunoglobulin receptor in the airways has been shown to actively and efficiently shuttle potent therapeutic proteins (i.e. interferons, erthropoietin) into the systemic circulation from the airways via large molecular weight, immunoglobulin fragment – therapeutic protein conjugates.

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Patton J S, Byron, P.R. Nature Reviews/Drug Discovery 6:67 (2007)
Weers J, et al. Exp. Opin. Drug Delivery (in press) (2007)

THURSDAY PLENARY

The Devil is in the Details: On the Role of Molecular Structure in Secondary Organic Aerosol Chemistry. Paul Ziemann, University of California, Riverside, CA

Measurements indicate that a significant fraction of the mass of atmospheric aerosol particles is organic matter, the majority of which consists of oxidized compounds that are the products of gas-to-particle conversion (secondary organic aerosol, SOA). The chemical and physical processes involved in the formation of SOA are complex and can include reactions of volatile organic compounds (VOCs) with various atmospheric oxidants (primarily O_3, and OH and NO_3 radicals), as well as surface and condensed-phase reactions, homogeneous nucleation, and gas-particle partitioning. It should come as no surprise that understanding and accurately modeling these processes is a major challenge that has not yet been achieved. In this talk, I will focus specifically on the impact of VOC molecular structure on SOA chemistry. Using examples from laboratory studies, I will demonstrate some of the ways in which changes in structure can alter SOA products and yields (which in turn can affect particle properties such as hygroscopicity, CCN activity, light scattering and absorption, and toxicity), and suggest explanations for these effects based on current understanding of chemical reaction mechanisms.

FRIDAY PLENARY

CNN, Clusters, Nanoparticles and Nucleation: Connecting the Dots, M. Samy El-Shall, Virginia Commonwealth University, Richmond, VA

Nucleation is one of the most ubiquitous and important phenomena in science and technology. It plays a central role in the formation of clusters, nanoparticles and crystal growth. In spite of the fundamental and applied interest in nucleation, the nucleus for condensation remains one of the most elusive entities known in chemical physics, and has never been observed directly. Only the consequences of its presence, e.g. droplet formation, precipitation, etc. are observed. For example, in vapor phase nucleation studies, the nucleation rate is often obtained by measuring the rate of production of macroscopic liquid droplets from the vapor phase.

A perspective of this important phenomenon will be addressed with particular emphasis on ion-induced nucleation. The application of Resonant Enhanced Multiphoton Ionization (REMPI) in supersaturated vapors to selectively generate specific ions of interest and study their nucleation behaviors will be discussed. The REMPI nucleation method has tremendous amplification and detection capabilities that can provide valuable and novel analytical tools for the identification of trace components in the vapor phase. Other examples of nucleation-based processes dealing with the formation and properties of molecular clusters and cluster ions, vapor phase synthesis of nanoparticles and polymer nanocomposites, and the condensation of supersaturated vapors on nanoparticles are discussed.

The study of gas phase clusters provides information on how the properties of matter evolve as the size of a material system ranges from molecular to macroscopic dimensions. Detailed information on the structures and conformational changes of molecular and cluster ions can be obtained using the mass-selected ion mobility technique. The mobility measurements provide structural information on the ionized clusters and oligomers on the basis of their collision cross-sections, which depend on the geometric shapes of the ions. The application of ion mobility to investigate the polymerization of ionized acetylene clusters and the formation of Polycyclic Aromatic Hydrocarbons (PAHs) will be discussed. The cluster reactions of small molecules provide novel mechanisms for the formation of large PAH and complex molecular ions.

The application of the laser vaporization controlled condensation (LVCC) technique coupled with a differential mobility analyzer (DMA) to synthesize size-selected semiconductor, metal and intermetallic nanoparticles from the vapor phase will be addressed. The assembly of nanoparticles in the vapor phase into filaments and fibers in the presence of an electric field will be discussed. Enormous electrostatic interaction due to dipole forces is observed between nanoparticles to form chain filaments, and between the chains to form tree-like assemblies. The filaments display stretch and contraction properties depending on the strength of the applied field. These observations have significant implications to the ductility and the plastic behavior of the materials formed from consolidated nanoparticle assemblies.

Finally, a new technique to study the condensation of supersaturated vapors on nanoparticles under well-defined conditions of vapor supersaturation, temperature and carrier gas pressure will be presented. The nanoparticles can be activated to act as condensation nuclei at supersaturations significantly lower than those required for homogeneous nucleation. The question of the *sign effect* in the condensation of supersaturated vapors on charged nanoparticles will be addressed.

This presentation seeks to connect the fields of gas phase clusters, nucleation and nanoparticles and place the integrated fields in context with the aerosol formation mechanisms, properties and applications.