Expert Opinion

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Medical and pharmaceutical nanoengineering conference/ International conference on MEMS, nano and smart systems

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Researchers representing all the northern hemispheric continents gathered for 3 days in Banff, Canada, to hear a wide range of talks on the application of micro- and nanotechnology to drug delivery. Topics included nanotubes, nanoparticles, liposomes, micelles, novel inhaled aerosols, antibody engineering and vaccines. Also featured were talks on the application of micro- and nanotechnology to diagnostics, including microfluidics, as well as biomolecular computing. The conference showcased the first demonstration of preliminary concepts for 'smart particle aerosols', in which nanofabrication methods are used to produce inhaled aerosol particles with 'intelligent' features. The conference provided an excellent forum for cross-fertilisation and discussion between disciplines, with attendees covering a broad range of areas in engineering and the physical and life sciences that are not often found together at a single conference. This breadth of attendees and topics provided a highly stimulating environment. An invitation to next year's conference (24 – 29 July 2005, Banff, Alberta, Canada) was extended, as listed at the conference website [101].

Keywords: drug delivery, nanofabrication, nanoparticles, nanotechnology, respiratory, smart particle aerosols

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1. Medical and pharmaceutical nanoengineering conference

The Medical and pharmaceutical nanoengineering conference (MAPNEC) was held 26 August 2004, as a 1-day symposium within the broader International conference on micro-electro-mechanical systems (MEMS), nano and smart systems (ICMENS). Its purpose was to bring together researchers working in the fledgling field embodied by applications of nanotechnology in pharmaceutics and medicine. A total of 15 papers were presented, giving 20-min talks across 4 sessions. Each presenter also submitted a paper to accompany the oral presentation. These written submissions have been published in the ICMENS conference proceedings, which are available for purchase from the Institute for Electrical and Electronic Engineers [102].

The first session began with an invited talk [1] on the topic of aqueous nanoparticles as carriers of DNA vaccines for pulmonary delivery. Polyepitope DNA was loaded into chitosan nanoparticles (300 – 500 nm in diameter) and delivered to Calu-3 human submucosal gland cells *in vitro*. In addition, endotracheal aerosol delivery was achieved in mice using an aqueous spray (PennCentury, Inc.). The results showed a significantly greater immune response with the nanoparticle DNA delivery than the control groups or intramuscular injection. A related talk in the final afternoon session [2] described the use of gelatine nanoparticles to load double-stranded small interfering RNA oligonucleotides.

The next talk of the first morning session [3] presented a new approach to dry powder aerosol delivery of nanoparticles. This approach uses spray freeze drying of an aqueous nanoparticle suspension containing dissolved lactose to produce micron-sized lactose particles with many nanoparticles embedded within the lactose particle. Dissolution of the lactose following deposition in the lung results in release of the nanoparticles. A related talk in the first afternoon session [4] used this approach as a means to deliver the anticancer compound doxorubicin. The *in vitro* results obtained with lung cancer cell lines showed dramatically improved cytotoxicity with the drug-loaded nanoparticles compared with the controls.

Also presented in the first morning session [5] was a novel method of spray freeze drying that is dramatically quicker than traditional spray freeze drying, as well as being scalable to manufacturing sizes. The versatility of the spray freeze drying was demonstrated by using it to produce both doxorubicin-loaded nanoparticle formulation as well as powders that spontaneously produced ciprofloxacin-containing liposomes (> 80% encapsulation) when reconstituted in a variety of biological and *ex vivo* pulmonary fluids. High fine particle aerosol fractions and low mouth–throat deposition were achieved by the powder aerosol researchers [3-5] by using a novel, proprietary dry powder inhaler.

The second morning session [6] began with a description of a completely new method of generating high aspect ratio aerosol particles using a relatively recent nanofabrication technique called 'glancing angle deposition' (GLAD). The authors produced relatively monodisperse aerosol particles with diameters in the 100-nm range, but having lengths of several µm. The authors' ability to produce submicron diameter aerosol fibres with good control over particle length and diameter makes this technique unique and will find application in research examining fibrous aerosol delivery. Following on from this work, the next speaker [7] presented numerical simulations demonstrating externally activated control over the aspect ratio of fibres in transit in the lung using a high frequency magnetic field. Together, these papers represent the leading edge of a new field, using what we term 'smart particle aerosols' (SPAs), whereby new nanotechnology is used to produce aerosol particles with heretofore unimagined capabilities and 'intelligence'.

The morning sessions continued with Wang *et al.* [5] describing an ordered thin film, made from immobilised purple membrane functions extracted from cultivated *Halobater salinarium*, yielding a photoelectric bacteriorhodopsin transducer.

The final talk of the morning described experiments that shed light on the mysteriously negative effect that high humidity has on the behaviour of metered-dose inhalers during mechanical ventilation of intubated patients. In particular, Martin and Finlay [8] detailed convincing data that suggests there is a transient period of particle growth due to water condensation after evaporation of propellant from the particles. These temporarily enlarged particles suffer increased deposition and reduce the efficiency of delivery, compared with the case when dry air is entrained with the propellant droplets.

The afternoon session began with a description of the development of a device for the genetic analysis of cancer cells via portable microfluidics and ended with a brief explanation of kinase (biomolecular) computing.

The final afternoon session included a talk focusing on biodegradable polyrotaxanes used as drug carriers in which a pH-sensitive release of cyclodextrins occurs [9], followed by a description of the use of cyclodextrins in molecular recognition of various amino acids. The day closed with a talk on the use of nonlinear filtering to aid in a numerical simulation of the stochastic behaviour of promyelocytic leukaemia nuclear bodies within a cell nucleus.

2. International conference on MEMS, nano and smart systems

The remaining part of the ICMENS provided a forum for the discussion of new developments, recent progress and innovations in the design and implementation of MEMS, nano, and smart systems-on-chip. It addressed all aspects of design methods of those systems. The emphasis of the presented talks was on the current and future challenges in research and development, in both academia and industry. It emphasised long-term, fundamental research aimed at discovering novel phenomena, processes, and tools; addressing the integration of nano, MEMS and smart systems grand challenges; supporting new interdisciplinary research activities and addressing research and educational activities on the societal implications of advances in nanoscience and nanotechnology. The conference featured 34 regular sessions in addition to the 4 sessions covered by MAPNEC. Of these 34 sessions, 6 covered the 2004 Canada-Japan nanopharmaceutical symposium (CJNPS), whereas 3 sessions were used to present the Symposium on space applications of micro and nano technologies (SSAMNT). Sessions presented in the CJNPS focused on issues related to nanobiomaterials, nanopharmaceutical formulations, antibody engineering and delivery, macromolecular drug delivery and analysis, vaccine delivery and therapeutic challenges. Sessions presented in the SSAMNT covered the use of optical microsensors and micromirrors in space, accelerometers designed for micromanipulators and microsensors applications for aircraft prognostic and health management.

Other topics covered in ICMENS 2004 included: fabrication and application issues in microfluidics, such as nanostructures and microfluidics, discrete and continuous microfluidics, optics and microfluidics. A number of sessions were also dedicated to nanowires and nanotubes, spintronics, smart structures and integrated systems, computational nanoscience, the experimental and theoretical applications of MEMS and nano-electro-mechanical systems (NEMS), novel nanofabrication and characterisation techniques, MEMS modelling, sensors and micro devices, and finally, actuators in bioMEMS and NEMS.

A series of five keynote presentations were given throughout ICMENS 2004. An outstanding talk in this series was given by

C Montemagno on the 'Integrative technology and engineering emergent behaviour into materials and systems'. Montemagno indicated that integrative technologies, the merging of nanotechnology, biotechnology and informatics, offers an opportunity for realising true advances in the manner in which technology interacts with humanity. Using the power of nanotechnology, Montemagno discussed the possibility to manipulate matter in a way that will place molecules where needed, when needed, to perform functions that are required. This can be achieved using the inspiration of biotechnology to select the tools of molecular manufacturing and to provide a baseline understanding of the way nature manipulates matter and information. Montemagno also demonstrated the use of informatics to create a robust framework for transforming the information implied in molecular and larger scale interactions to engineer complex adaptive systems that demonstrate embedded higher-order behaviour. Collectively, these technologies established the basis for integrative technology, a new IT [10]. In this talk, the implementation of integrated technology and its manifestation in the synthesis of a new class of smart materials was also presented. In this example, it was shown that these materials have the potential to emulate much of the functionality associated with living systems, such as the active transport and transformation of matter and information, and the transduction of energy into different forms [10]. The details of the technological demands and the results of efforts associated with the production of these new functional materials were also presented by Montemagno. Other elements of this discussion covered the genetic engineering of active biological molecules into engineering building blocks, the precision assembly of these molecules into a stable, 'active' material, and the capability of embedding intelligent behaviour into the matrix of the assembled matter.

On the spin of electronics, S Parkin presented his views on the recent advances in generating, manipulating and detecting spin-polarised electrons and electrical current, which make possible new classes of spin-based sensor, memory and logic devices. It was shown that a key component of many such devices is the magnetic tunnelling junction (MTJ) – a sandwich of thin layers of metallic ferromagnetic electrodes separated by a tunnelling barrier, which is typically an oxide material only a few atoms thick. The magnitude of the tunnelling current passing through the barrier can be adjusted by varying the relative magnetic orientation of the adjacent ferromagnetic layers. As a result, Parkin demonstrated that MTJs can be used to sense the magnitude of magnetic fields or to store information. By altering the composition and thickness of the MTJ's layers, its properties can be 'magnetically engineered' via phenomena such as exchange bias and oscillatory interlayer coupling to match its properties to a particular use, such as in the ultra-sensitive data-reading elements within magnetic hard-disk drives, or the storage elements in non-volatile magnetic random access memories (MRAMs) [11]. It was indicated that prototypes of cross-point architecture MRAMs using MTJ cells have demonstrated the possibility of a highly attractive high performance, high density non-volatile memory technology.

The third keynote talk was given by M Gad-el-Hak on the 'holy grail of microfluidics' and the growth of MEMS and its application in microdevices such as pumps, sensors, actuators, motors, turbines, gears, ducts and valves. This talk underlined the problem that although microdevices often involve mass, momentum and energy transport, the continuum-based Navier-Stokes equations, with either the traditional no-slip or slip-flow boundary conditions, work only for a limited range of Knudsen numbers, above which alternative models must be sought. These include: molecular dynamics simulations (MD); Boltzmann's equation; direct simulation Monte Carlo (DSMC); and other deterministic/probabilistic molecular models [12].

The fourth keynote presentation in the conference was given by P Laibinis on the solution-phase process for generating nanometer-thick coatings with controlled interfacial properties. Laibinis' group is active in developing methods for forming films with controlled architectures on subnanometer dimensions, and in providing insight into the operable structure–property relationships when surfaces can be tailored and defined at this scale.

Approaches for producing such surfaces are described in Laibinis' work to produce antifouling coatings on the inner surfaces of microfluidic devices that are targeted for biological/biomedical applications [13]. Laibinis presented a class of reactive oligo(ethylene glycol)-terminated silane compounds developed by his group that are capable of generating antifouling coatings by this approach that are 1 – 2 nm in thickness, chemically robust, and able to retard protein adsorption.

3. Expert opinion and conclusion

A diverse range of new and interesting drug delivery concepts were presented at this conference by speakers from across the globe, including Japan, Germany, the US and Canada. A number of speakers presented novel aspects of nanoparticle drug delivery for vaccines and anticancer therapy. The use of nanofabrication techniques for producing inhaled aerosol particles was showcased for the first time to the authors' knowledge, thereby ushering in the era of SPAs for inhalation drug delivery. The marriage of nanotechnology and aerosol delivery via SPAs represents a new and exciting frontier for those willing to look to future horizons. The highly interdisciplinary and leading edge nature of the talks presented at this conference made for an extremely stimulating environment and we look forward with anticipation to ICMENS/MAPNEC 2005, to be held 24 – 29 July 2005, Banff, Alberta, Canada.

Bibliography

1. BORCHARD G, BIVAS-BENITA M, JUNGINGER H: Developing and testing of drug carrier systems for pulmonary drug delivery. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):188.
2. ZILLIES J, COESTER C: A new delivery system for double dtranded siRNA oligonucleotides based on gelatin nanoparticles. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):432.
3. ELY L, WANG Z, SHAM J *et al.*: Development of inhalable nanoparticles. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):193.
4. TAO X, CHEN H, WANG Z, FINLAY W, LÖBENBERG R, ROA W: Cytotoxicity of drug-loaded nanoparticles and lipsomes carried by aerosol 'cluster bombs' in lung cancer cells. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):344.
5. WANG Z, LÖBENBERG R, SWEENEY L, WONG J, FINLAY W: Improved drug delivery: spray freeze dried nano-liposomal inhaled aerosols. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):196.
6. GILBERTSON K, FINLAY W, LANGE C, BRETT M, VICK D: Nanofabrication of high aspect ratio aerosol particles for deposition studies in a model human airway. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):268.
7. SHANG Y, FINLAY W, MOUSSA W: Thermally induced fiber deformations using high frequency magnetic field. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):271.
8. MARTIN A, FINLAY W: Effect of humidity on size distributions of MDI particles exiting a mechanical ventilation holding chamber. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):280.
9. ITO A, OOYA T, YUI N: Hydrolyzable polyrotaxanes consisting of beta-cyclodextrins and Pluronic® for drug delivery. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):428.
10. MONTEMAGNO C: Integrative technology engineering emergent behavior into materials and systems. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):2.
11. PARKIN S: The spin on electronics! *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):88.
12. GAD-EL-HAK M: Liquids: the holy grail of microfluidics modeling. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004):332-337.
13. LAIBINIS P: Solution-phase processes for generating nanometer-thick coatings with controlled interfacial properties. *Proceedings of the 2004 International Conference on MEMS, NANO and Smart Systems.* Banff, Canada (2004).

Websites

101. http://www.icmens.org
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102. http://shop.ieee.org/store/
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