NASA LIFE SCIENCES AND SPACE MEDICINE REQUIREMENTS FOR NANOTECHNOLOGIES

A WHITE PAPER BY THE SL/ADVANCED TECHNOLOGY INTEGRATION GROUP

DON STILWELL, ALYSSA MUELLER, AND TERRI GILBERT
NASA JOHNSON SPACE CENTER

Nanotechnology is one of several enabling technologies for future human missions in the exploration of space. Whether the destination is a long-stay Lunar base or a two and a half year Mars mission, NASA space medicine and life sciences needs are driven by the unique environment in which these missions occur. Hence, it is not surprising that priorities and requirements for nanotechnologies in terrestrial medicine and life sciences research are not identical to those in NASA's human spaceflight programs.

Terrestrial applications are driven by market forces and are geared primarily toward the treatment of diseases endemic to terrestrial environments. There is little likelihood that these terrestrial market forces will drive industry and academia to develop NASA's most critical nanotechnology needs without considerable investment by NASA.

Likewise, the fact that industry or academia develops a technology for terrestrial medicine or research that brings a substantial return on the investment does not guarantee that it will be high on NASA's critical technologies list. For example, the development of a hand-held, non-invasive glucose monitor is a high priority for the management of diabetes in a very large number of patients world-wide, but glucose is only one analyte out of hundreds or thousands that NASA needs to measure in an equally convenient way to guarantee astronaut health and well-being in future space missions. As there is no indication that the space environment produces a particular problem in glucose metabolism that mimics diabetes, NASA's needs might be better met by concentrating its funding on the development of nanotechnologies that are more responsive to the Bioastronautics Critical Path Roadmap (CPR) (see http://criticalpath.jsc.nasa.gov/ for a web-based interface to the CPR).

NASA should perhaps concentrate its efforts on nanotechnologies that promise to provide clinically relevant information about whole spectrums of compounds rather than on single analytes. This is not to say that moderate funding should not be applied to modify technologies that were developed by NASA for other purposes, such as Space Science, and Aeronautics, for potential application in terrestrial medicine, but rather that the bulk of NASA's efforts in space medicine and life sciences nanotechnologies should be specifically focused on the needs identified in the Bioastronautics CPR. This white paper seeks to identify and discuss those needs more specifically as organized by major space medicine and life sciences disciplines or specific technology types.

I. MONITORING AND PREDICTING RADIATION EXPOSURE

The radiation environment of space is far different from that of Earth or from that encountered by X-ray or radiology laboratory workers. Lacking the protective trapping of particles in the Earth's magnetic field and the moderating influences of the Earth's atmosphere, Astronauts in beyond low Earth orbit (LEO) missions will be exposed to a different spectrum of ionizing radiation. Solar Proton Events (SPEs) and Galactic Cosmic Radiation (GCR) can cause death, radiation sickness, as well as increases in cancer or mutagenesis, either acutely or many years after the exposure. Nanotechnology may be employed in developing space-based neutron monitors (spectrometer/dosimeters) which must measure neutron energies to at least 20 MeV in the presence of high levels of protons. Similarly, nanotechnology could be employed in the development of early warning systems for SPEs based on x-ray and gamma ray spectral characteristics of observed solar flares. Small but portable electronic dosimeters, similar in physical size to the badge dosimeters used by radiation workers on Earth, could be based on nanotechnologies that provide both dose and dose-equivalent rates and integrated values for an extremely broad range of particles and energy levels. Such a dosimeter could potentially record counts of the energy, number and types of particles to which an individual astronaut is exposed as recorded in a 3-D nano-structured matrix. Variations in dose can be expected depending on the amount of time each astronaut spends in Intra and Extravehicular activities or within a small radiation shelter. Nanotechnology may also be employed in creating biological radiation sensors, for example, by immobilizing DNA strands or radiation sensitive bacteria on chip surfaces to read individual upsets in genetic or other biological materials.

II. SKELETAL INTEGRITY

Considerable data has demonstrated that the average loss of bone mass across astronauts in microgravity, at least during missions of up to one year, is near 1% per month. Whether there is a leveling off of this effect after one year or whether there is a protective effect in partial gravity environments, such as the Lunar 1/6-g or the Martian 3/8-g, is very speculative at this time. Nanotechnology will play an important role in the development of sensors for visualizing bone structure and density in future long duration LEO and beyond LEO missions. Ideally, sensors based on non-ionizing radiation, such as ultrasound, could be used to provide microscopic details of bone structure and density for input to finite element models to derive 3-D visualizations of bone strength and probability of fracture. It may be possible to get measurements of bone strength across all of the bones of the body. Alternatively, a 3-D visualization of bone density and structural strength of just a few bones such as the hip, spine and heel bone could represent the health of all of the bones. If non-ionizing radiation does not provide a solution, nanotechnology can be used to generate sensors and circuits for a compact, lightweight, high-resolution dual energy x-ray absorption (DEXA) instrument for performing bone mineral density (BMD) measurements.

There is a desire, however, to limit the additional radiation that astronauts are subjected to, so such an instrument must result in a finite element model that incorporates both bone morphology and density with minimal radiation exposure. Ideally, any imaging hardware/sensors that are created for measuring bone density for finite element analysis should also be useful for general purpose medical imaging to reduce the overall mass and volume required to guarantee astronaut health. Nanotechnology will also play a key role in developing an automated urine collection system for measurement and analysis of concentrations of Ca++ and many other ionic and non-ionic species in the urine to study calcium metabolism and other markers of bone health. Again, this is related to the general need for monitoring hundreds or thousands of analytes in the urine, blood, saliva, sweat, and interstitial fluid for other purposes.

III. CREW PERFORMANCE

Nanotechnology based sensors will be used to measure physical performance of the astronauts in a variety of situations including exercise. Load cells in the pedals of a cycle ergometer and angle measurements for cycle hubs and many similar devices will automatically monitor astronaut exercise performance, while nanotech dynamometers and other sensors on hip, knee, ankle and other joints will non-invasively monitor the astronaut performance during both exercise and other routine activities and transmit their data wirelessly to transceivers in spacecraft racks. Likewise, nanotech sensors and instrument systems will provide the means to assess lean body mass, aerobic/anaerobic capacity, muscle endurance and strength, thermal regulation, neuromuscular control and other parameters relevant to the exercise and non-exercise performance of individual astronauts. Such advancements would provide early warnings for trends in muscle atrophy and bone deterioration before they become serious and will permit early application of countermeasures as well as a continuous evaluation of their efficacy in individual astronauts.

IV. LABORATORY AND CLINICAL DIAGNOSTICS

Many improvements in laboratory diagnostics for general healthcare and for the treatment of life threatening emergencies will be dependent on nanotechnologies. In terrestrial medicine, automation is frequently used to allow a clinical laboratory technician to do the same test on many samples from many patients at once. In space many thousands of tests must be performed on a single sample from a single subject at once and must be performed in very short order. Laboratory diagnostics, such as are used in hematology, clinical chemistry, pathology, microbiology, and so on, will use nanotechnology to perform simultaneous measurements for hundreds or thousands of substances in urine, blood, saliva, sweat and interstitial fluids. Complex laboratories on a chip will be used to perform cytometry, enzyme-linked immunoassays, and to detect and monitor chemicals, drugs, toxins, blood gases, ionic and non-ionic species.

Some sensors will use complex arrays of biological receptors, enzymes, ligands, DNA, antibodies and other affinity based systems. DNA detectors arrays, for example, currently operate with micron sized active regions and offer the ability to do thousands of measurements individual gene activities. Such arrays will allow hundreds of thousands of human genes to be monitored throughout a mission and will allow the determination of the effects of microgravity on human physiology in ways that are not imagined at present, as well as providing early warning of cancer or other disease states. By determining which genes are activated or inhibited, rack-mounted intelligent medical systems will be able to apply preventative care at the earliest possible point.

Comprehensive cellular protein analysis (proteomics) and enzyme assays are equally feasible and instructive. A nanotech-based gas chromatograph/mass spectrometer (GC/MS) or similar technologies, such as a nanotech-based MS/MS, will allow the characterization and quantification of multitudes of substances in a single small biological sample. In many cases, sensors will be integrated with on-chip signal processing and data acquisition along with microfluidics and other sample transport and preparation technologies. Systems for sensing biological and inorganic substances of interest in both aqueous and gaseous phases are needed. Technologies such as micro-machined ion-mobility spectrometers, ion trap mass spectrometers, calorimetric spectrometers, microlasers and optics, on-chip separators, optical spectrometers (e.g., UV, visible, and infrared), ultra sensitive acoustic wave detectors, polymerase chain reaction (PCR) gene sequencing instrumentation (including restriction enzyme digestion and PCR amplification) and many others could potentially reside on the same chip or in close proximity allowing minute quantities of sample to provide a wealth of information. The advantages of a laboratory on a chip include device miniaturization for the space and volume restrictions of space travel, lower power consumption, nearly instantaneous response times for near-real time results, conservation of reagents, and ease of operation by non-laboratory personnel, such as astronauts. As with many advances in nanotechnology, the chief difficulty may be in integrating these many different units into functioning systems and interfacing them to the macro real world. This is an area that NASA will need to concentrate on if these technologies are to be useful.

V. MEDICAL MONITORING

A. IMAGING

General purpose medical imaging technologies, such as magnetic resonance or ultrasound imaging may rely on nanotechnologies to keep size down while improving capabilities. Sensors originally designed for astrophysics research might be applied to SPECT, X-ray, thermal or other imaging modalities. Newer, less developed methods such as optical transmission or reflection imaging or other non-ionizing techniques will employ nanotechnologies. Muscle imaging technology to monitor changes in muscle mass, morphology, biochemistry and connective tissue and many other internal organs will take on great importance in addition to other diagnostic uses. Nanotechnology may reduce the size and power consumption while increasing the speed of processors to provide extremely sophisticated image processing and pattern recognition capabilities in all of the equipment mentioned herein.

B. PHYSIOLOGIC MONITORING

Surface sensors for routine physiological monitoring (ECG, EMG, EOG, BP by pulse transit times between separated sensors, pO2 through pulse oximetry, HR, etc.) will employ on-sensor power and wireless telemetry to make them extremely easy to use and apply. Active sensor technologies can reduce or eliminate electrical noise at the skin-electrode interface and permit electrolyte-less (or dry) electrodes to provide artifact free reception. As with essentially all of NASA’s discipline needs, nanotechnology will eventually result in computers that are so small and consume such little power that considerable signal processing and intelligent will be placed at the sensor, greatly amplifying the capabilities of physiological monitoring systems. Other sensors will provide easily implanted, injectable, or ingestible biomedical sensors for routine physiological monitoring. Such sensors might be energized by the ambient electromagnetic fields or by external electromagnetic querying. Many physiological sensors based on nanotechnology could be woven into clothing making donning and doffing of sensors a painless affair. Similar miniature transmitters will enable monitoring of the location and health of many stowable items. The Shuttle-*Mir* program demonstrated that locating items was often more difficult than expected. Tools and other re-usable items were often lost onboard *Mir* necessitating frequent resupplies. If a method similar to the RF tags used in warehouses could be employed, locating lost items and automatically determining their fitness for service could be easily accomplished.

VI. THERAPEUTICS

Therapeutics can benefit from nanotechnology, such as the development of transdermal or injected drug delivery systems or methods of genetic material transvection to cure disease states or to correct, on-the-spot, adverse genetic responses to space flight conditions. Nanotechnology sensors placed at the tips of endoscopic surgical tools could aid in navigating through the body and in repairing tissues. Some sensor tips could be adapted to identify cancerous tissues while others could participate in control loops that would sense the presence of tissues to be avoided when cutting, such as blood vessels, etc. Nano-particles can be coated materials that have an affinity for certain types of cells or organs or that will only release their therapeutic payloads when they come into contact with certain cells, thereby increasing the safety and efficacy of therapeutics while reducing the quantity required to achieve the desired result.

Additionally, the limited shelf life of many pharmaceuticals and weight and storage constraints such as the need for refrigeration, the tendency of some substances to absorb moisture form the air, etc., suggest that a chemical laboratory on a chip might be fruitfully used to make many classes of pharmaceuticals as they are needed from raw materials.

Likewise, bioreactors with genetically modified organisms could potentially be used to generate a plethora of useful substances and nanotechnology could be employed to automatically control the culture medium while extracting and concentrating products by liquid or gas chromatography or other separation methods. It is even possible to use genetically modified organisms to create non-biological enzymes for catalyzing non-biological reactions in the manufacturing process. The manufacture of the precise prescriptions required for a crew each day would potentially save considerable launch mass and in-flight waste due to spoilage. One problem that will affect therapeutics in the space environment is the large differences in response to drugs that are caused by the effects of microgravity or partial gravity on the human body. Nanotechnology may be used in monitoring the actions of drugs and controlling their rate of delivery in response to actual physiological responses in individual crew members. Much discussion of the potential use of nanorobotics for cellular repair and monitoring is in the popular and scientific press and need not be repeated here.

VII. ENVIRONMENTAL MONITORING AND CONTROL

In the enclosed environment of a long-duration spacecraft, the quality of water and air becomes a major issue. Sensors, such as electronic noses and tongues, could be used to detect parts per billion of contaminants before the situation becomes critical. Some devices, such as mass spectrometers, are well suited to determining minute quantities of contaminants in air or water. Some localization of the source of contaminants might be possible if these devices could be made small enough and low power enough to be placed at several locations throughout the spacecraft. Cooperative behavior amongst such sensors could result in wireless intelligent sensor networks that are aware of the time at which each contaminant arises at each sensor and can predict the exact location of the source of contamination.

A variety of methods might be used to detect, count and characterize individual particles such as dust, pollen, microorganisms or spores in both water and air, allowing the on-board computers to know the precise physical, biological, or chemical remedies to apply to bring the counts down to normal. Other environmental parameters of interest are humidity, combustion products, toxic gases, and volatile gases. Many of these same technologies may be employed in measuring respiratory gases to sample the exhaled stream on a breath-to-breath basis.

VIII. CREW TRAINING AND PERFORMANCE

Nanotechnology will be used to improve the virtual or augmented reality (VR/AR) interfaces that astronauts use to do their work or to train for future events such as landings on distant planetary surfaces, aerobraking back into Earth orbit, reviewing surgical procedures or providing just-in-time training and access to technical information during spacecraft system troubleshooting. VR and AR, when combined with nanotech-based body tracking, may serve as the interface to endoscopic surgical tools to allow large gross movements of the body or fine movements of the hand to control fine instruments at the tip of an endoscope, thereby eliminating the tremor that frequently accompanies microsurgical technologies. Nanotechnology may also be employed to produce new methods for providing haptic feedback or other methods of stimulating body sensor mechanisms.

IX. CONCLUSION

There are many other potential uses for nanotechnology that we have not even thought of yet. Those who are interested in developing nanotechnologies for potential use in future human missions are encouraged to work with Space Physiology, Medical Operations and Space Medicine experts at the Johnson Space Center to determine precisely what the NASA needs are and what specifications would be best suited to our needs. There is also considerable knowledge at JSC on NASA safety, reliability and quality assurance requirements for flight instrument design.

The development of flight instruments is not identical to the development of similar instruments in the commercial sector, in part because of the effects of microgravity on instrument function, but also because of other special requirements of the spaceflight environment. It is helpful for technology developers to receive the advice of experienced professionals before setting out to meet NASA needs. In general, Space Physiology, Medical Operations and Space Medicine experts at the Johnson Space Center will be pleased to discuss the unique requirements and issues associated with space flight, because of their great need for these critical technologies in our program.

Don Stillwell
(281) 483-7308
donald.j.stilwell1@jsc.nasa.gov

Alyssa Mueller
(281) 244-5537
smueller@ems.jsc.nasa.gov

Terri Gilbert
(281) 333-0190 ext. 48
tgilbert@futron.com

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