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Nanoscience in Veterinary Medicine

N.R. Scott
Department of Biological and Environmental Engineering, Cornell University, Ithaca, NY, 14853, USA
E-mail: nrs5@cornell.edu

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ABSTRACT

Nanotechnology, as an enabling technology, has the potential to revolutionize veterinary medicine. Examples of potential applications in animal agriculture and veterinary medicine include disease diagnosis and treatment delivery systems, new tools for molecular and cellular breeding, identity preservation of animal history from birth to a consumer's table, the security of animal food products, major impact on animal nutrition scenarios ranging from the diet to nutrient uptake and utilization, modification of animal waste as expelled from the animal, pathogen detection, and many more. Existing research has demonstrated the feasibility of introducing nanoshells and nanotubes into animals to seek and destroy targeted cells. Thus, building blocks do exist and are expected to be integrated into systems over the next couple of decades on a commercial basis. While it is reasonable to presume that nanobiotechnology industries and unique developments will revolutionize veterinary medicine in the future, there is a huge concern, among some persons and organizations, about food safety and health as well as social and ethical issues which can delay or derail technological advancements.

INTRODUCTION

Nanotechnology, as a new enabling technology, has the potential to revolutionize our agriculture and food systems. Food systems security, disease treatment delivery systems, new tools for molecular and cellular biology, new materials for pathogen detection and protection of the environment are examples of the important links of nanotechnology to the science and engineering of agriculture and food systems (Scott and Chen, 2003). This tool as it develops over the next several decades will have major implications in veterinary and animal science.

What is nanotechnology? The National Nanotechnology Initiative of the U.S. government (National Science and Technology Council, 1999; 2004) describes nanotechnology as: "*research and development (R&D) aimed at understanding and working with - seeing, measuring and manipulating- matter at the atomic, molecular and supramolecular* *levels. This correlates to length scales of roughly 1 to 100 nanometers. At this scale, the physical, chemical and biological properties of materials differ fundamentally and often unexpectedly from those of the corresponding bulk materials.*''

Today in agriculture if an animal becomes infected with disease, it can be days, weeks, or months before presence of the disease is detected by whole-organism symptoms. By that time infection may be widespread and entire herds might need to be destroyed. Nanotechnology operates at the same scale as a virus or a disease-infecting particle, and thus holds the potential for very early detection and eradication. Nanotechnology holds out the possibility that "Smart'' treatment delivery systems could be activated long before macro symptoms appear. For example, a smart treatment delivery system could be a miniature device implanted in an animal that samples saliva or other body fluid on a regular basis. Long before a fever or other symptoms develop, the integrated sensing, monitoring and controlling system could detect the presence of disease and notify the farmer and veterinarian to activate a targeted treatment delivery system. Smart treatment delivery systems are envisioned for animal systems such as drugs, nutrients, probiotics, nutraceuticals and implantable cell bioreactors.

In agriculture and veterinary science, the fundamental life processes are explored through research in molecular and cellular biology. New tools for molecular and cellular biology are needed that are specifically designed for separation, identification and quantification of individual molecules. This is possible with nanoscience and could permit broad advances in veterinary science, such as reproductive science and technology through enzymatic nanobioprocessing, disease prevention and treatment in animals.

WHAT IS NANOTECHNOLOGY?

Nanotechnology is an exciting and rapidly emerging technology allowing us to work, manipulate and create tools, materials and structures at the molecular level, often atom by atom into functional structures having nanometer dimensions. Nature has been performing "Nanotechnological feats'' for millions of years. Through the arrangement of atoms and molecules, biological systems combine wet chemistry and electro-chemistry in a single living system. We are just beginning to understand nanoscale methods used in nature to create self-replicating, self-monitoring, self-controlling and self-repairing tools, materials and structures. "Nano'' usually refers to a size scale between 1 and 100 nanometers (nm). For comparison, the wavelength of visible light is between 400 and 700 nm. A living cell has dimensions of microns (thousands of nanometers). However, the essence of nanotechnology is much more than size because materials behave very different at the nanoscale than in bulk.

The roots of nanotechnology go back to the 1959 talk presented by Nobel Prize winning physicist, Richard Feynman (1961) at a meeting of the American Physical Society titled, "There's plenty of room at the bottom''. Simply put, Feynman's message was that in the future scientists and engineers would be able to build structures from atoms and molecules, from the "bottom up''. A later and important development was the discoveries of Fullerenes, better know as "Buckyballs'' by a group including Nobel Prize winning Richard Smalley. This led to the discovery of tube-like structures of carbon atoms which is basically a rolled up sheet of carbon that has outstanding properties. In the1980's Eric Drexler (Drexler, 1986; Drexler *et al*., 1991) proposed a major new idea that one could create a self-replicating "assembler'', a molecular machine that can be programmed to create "molecular manufacturing'' of molecular structures from simple chemical building blocks.

The science and engineering of nanobiosystems is one of the most exciting and challenging areas of nanotechnology. In an effort to identify opportunities at the interface of biotechnology and nanotechnology, a recent report of the National Nanotechnology Initiative (NNI) Workshop on Nanobiotechnology (Vogel and Baird, 2003) sought to identify fundamental changes that nanoscience and nanotechnology can bring to biology and medicine. The NNI describes nanobiotechnology as the integration of nanotechnology with biology and medicine using the above definition as a starting point. Kahn (2006) provides a very readable and interesting discussion of future directions and applications of nanotechnology.

I would like to suggest we are at an extremely exciting time in the evolution of science and engineering, a time where convergence of major technologies, nanotechnology, biotechnology, information technology and cognitive science is poised to lead to a new agriculture and veterinary science. It is this convergence that will truly be a key to so many of our future advancements, including in veterinary medicine in the broader context. A convergence of nanotechnology and biotechnology to create nanobiotechnology in the first instance is enhanced by the integration of information and cognitive sciences. I call this convergence the "Little BANG'' theory and suggest that it will create the intellectual curiosity and excitement that physicists have ascribed to development of the "Big Bang'' theory. ETC (2004) proposed the acronym BANG to represent:

- Bits- the basic unit in information science
- Atoms- the basic unit for nanotechnology
- Neurons- the basic unit of cognitive science
- Genes- the basic unit in biotechnology.

Others in the science community have also labeled this convergence of these technologies as NBIC for neurons, biotechnology, information science and cognition. Space does not permit a presentation of the specific tools within nanoscience that will be used. Scott (2005) has provided a brief discussion of microfluidics, BioMEMS, nucleic acid engineering, nanosensors, nanotubes, buckballs, dendrimers, quantum dots and nanoshells with a focus on applications in veterinary medicine.

APPLICATIONS IN VETERINARY MEDICINE

ETC (2004) has stated, "Over the next two decades, the impacts of nanoscale convergence on farmers and food will exceed that of farm mechanization or the Green Revolution.'' One area of great agricultural importance is animal management and health. Feneque (2003) and Scott (2005) write that nanotechnology has the potential to significantly affect the way veterinarians will practice veterinary medicine. Food security and safety create a need for new solutions. Enter nanotechnology, where the applications of nanotechnology in medical and agricultural applications are almost mind-boggling. Although much research and major company developments are necessary for nanotechnology to be common place in agriculture there are numerous glimpses of the future in applications for drug delivery, disease diagnosis and treatment, animal nutrition, animal waste management, animal breeding and identity preservation. Some exciting applications are discussed further below.

"Smart'' Drug Delivery: Today, application of antibiotics, probiotics and pharmaceuticals are delivered primarily through feed or injection systems to animals. Delivery of medicines is either provided as "preventative'' treatment, or is provided once the disease organism has multiplied and symptoms are evident. Nanoscale devices are envisioned that will have the capability to detect and treat an infection, nutrient deficiency, or other health problem, long before symptoms are evident at the macro-scale. This type of treatment could be targeted to the area affected. "Smart Delivery Systems'' can possess any combination of the following characteristics: time-controlled, spatially targeted, self-regulated, remotely regulated, preprogrammed, or multifunctional characteristics to avoid biological barriers to successful targeting. Smart delivery systems also can have the capacity to monitor the effects of the delivery of pharmaceuticals, nutraceuticals, nutrients, food supplements, bioactive compounds, probiotics, chemicals and vaccines.

Smart Systems Integration: The nanotechnologies described above will only reach their full potential through integration. Thus, "Smart Systems Integration'' is similar to designing and building the logic of a "nervous system'' that will allow the individual parts to work together. Integration of the nanotechnologies into a working control system (whether remotely controlled or under automatic control) will require electronic communication between several technologies, including the sensing systems, reporting systems, localization systems and control systems.

Disease Diagnosis and Treatment: Imagine the possibility of injecting nanoparticles into an animal and then a day, a week or month later being able to run a light over the animal body to sense a disease or physiological disorder. Effectively, animal information can be obtained from scanning the "nanobarcode'' as the animal passes through a readout system, not unlike an item scanned in today's supermarket. The system will, if necessary, activate disease-killing agents to destroy diseased cells. Researchers at Rice University (Hirsch *et al*., 2006) are doing just this by using nanoshells injected into the animal's bloodstream with targeted agents applied to the nanoshells to seek out and attach to the surface receptors of cancer cells. Illumination of the body with infrared light raises the cell temperature to about 55°C which "burns'' and kills the tumor.Others have been experimenting with "smart'' superparamagnetic nanoparticles. These nanoparticles when injected in the bloodstream target diseased receptor cells. These nanoparticles are made from iron oxides that when subjected to a magnetic field enhances the ability of the nanoparticles to locate diseased cells. At the site of the abnormal cell the nanoparticles emit an attached drug to kill the diseased cells.Quantum dots may also be injected into the bloodstream in animals and they may detect cells that are malfunctioning. Because quantum dots respond to light it may be possible to illuminate the body with light and stimulate the quantum dot to heat up enough to kill the diseased cell. Nucleic acid engineering-based probes and bar-coding methods (Li *et al*., 2005) offer powerful new ways to deliver treatment or prevention of a particular disease. Nanosized, multipurpose sensors are being developed to detect almost everything from physiological parameters (blood pressure, temperature, heart and respiration rates, etc.) to toxic compounds (Kan, 2006). The veterinarian will be able to know the status of every animal's physiological condition and levels of certain compounds. The implantable sensor once swallowed or implanted will continue to send data through out the life of the animal and later after slaughter to track animal products.

Identity Preservation: Identity Preservation (IP) is a system that creates increased value by providing consumers with information about the practices and activities used to produce agricultural, particularly, animal products. Today, through IP it is possible to provide stakeholders and consumers with access to information, records and supplier protocols regarding such information as farm of origin, environmental practices used in production, food safety and security and information regarding animal welfare issues. Each day shipments of livestock and other agricultural products are moved all over the world. Currently, there are financial limitations for the numbers of inspectors that can be employed at critical control points for the safe production, shipment and storage of food and other agricultural products. The keys are biodegradable sensors for a historical record of both physical and biological parameters. The future of the meat industry may well depend on an ability to track the product from birth through growth and through movement from farm to slaughter through processing to packaging and ultimately to the consumer's table. A key will also be the inclusion of results of possible future mandatory mad-cow tests. Of course, a major issue exists with regard to public acceptance of biodegradable nanoparticles in the steak!

Animal Breeding: Management of breeding is an expensive and time-consuming problem for dairy and swine farmers. A proposed solution under study is a nanomaterial (nanotube) implanted under the skin to provide real time measurement of blood estradiol changes. The nanotubes (O'Connell *et al.*, 2002) are used as a means of tracking estrus in animals because the nanotubes have the capacity to bind and detect the estradiol antibody at the time of estrus by near infrared fluorescence. The signal from this sensor will be incorporated as a part of a central monitoring and control system to actuate breeding. The natural follow up would be to have an implanted nanocapsule of semen triggered on demand to fertilize an egg.

ETHICAL ISSUES

Nanotechnology is sure to be a part of the future of veterinary medicine and animal management and health. However, any new technology carries an ethical responsibility for wise application and the recognition that there are potential unforeseen risks that may come with the tremendous positive potential. The action group on erosion technology and concentration (ETC, 2004) has raised significant concerns about the potential negative impact of nanotechnology on agriculture. They argue that there is a need for a wide-ranging debate about nanotechnology and its effect on economics, health and the environment. ETC frames the debate around two areas: 1) health and safety and 2) broader social and ethical issues.

Gordijn (2003) characterizes the optimistic visionary perceptions as utopian dreams and the worst-case scenarios as apocalyptic nightmares. He argues that there is a need for a balanced ethical view and he has offered a six-step method to develop a more balanced view. Nevertheless advances in nanotechnology in the agriculture and food system will likely continue to be a very contentious area for some time because of the concerns of many about the safety and health of food and others who are concerned about the possible implications on the structure of agriculture.

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