

POTENTIAL DEPARTMENT OF DEFENSE (DOD) APPLICATIONS OF MAGNETIC CARRIERS

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ABSTRACT: Novel developments in biocompatible magnetic carrier and magnetic sensor technologies will likely have a pervasive, enabling impact on many areas of biotechnology. It is likely that the development of these technologies could also significantly impact the development of a number of future DoD mission capabilities in biological warfare defense, personnel monitoring, and diagnostic and therapeutic treatments for military personnel. It is believed that magnetics is particularly suited to address many DoD requirements in that it offers the promise of a portable, robust, and highly sensitive transduction mechanism for monitoring and controlling biological activity at all levels. This presentation will discuss some of the perceived future military uses of biotechnology and will also speculate on how future investments in bio-magnetics might greatly enable the transition of many exciting developments in biotechnology out of the laboratory and into the hands of the military.

Living cells and tissues exhibit an extraordinary range of functionalities including highly selective biochemical sensing (even in chemically noisy environments), protein synthesis, information processing, and color change. Recent developments in biotechnology offer the promise of exploiting these functionalities for sensing, diagnostic, therapeutic, and other DoD and commercial applications. However, exploitation of these functionalities in devices that can be taken out of a laboratory environment will require the development of biochemical signal transduction mechanisms that are robust, portable, and highly reliable in noisy environments. A transduction mechanism based on a bio-magnetic interface would meet these requirements and offers solutions to outstanding technical issues that continue to keep many innovative developments in biotechnology from being fielded for DoD use. Some specific examples of expected DoD payoff areas include: 1) rapid, robust, hand-held bio-detection devices with multi-analyte capability, high sensitivity (on par with current reagent based PCR and ELISA techniques), and minimal sample preparation requirements; 2) portable, magnetics based micro total analysis (μ TAS) or "lab on a chip" diagnostic

devices; 3) novel, magnetically targeted therapeutics for attacking infected cells and tissues without harmful side effects to surrounding healthy cells and tissues; and 4) new capabilities for initiating and monitoring intracellular functions such as apoptosis, mitosis, protein expression, and color change.

The realization of biomagnetics as a portable, robust transduction mechanism for monitoring and/or initiating biological activity will require research and development in several core areas. These core areas include the following: 1) novel, biocompatible ferrofluids, or magnetic "tags", with superior magnetic properties that are capable of attaching to a wide range of single biomolecules and cells with a high degree of specificity; 2) novel, biocompatible, high sensitivity magnetic sensors capable of detecting single magnetic nanoparticles with diameters ranging from $< 100\text{nm}$ to $> 1\ \mu\text{m}$; and 3) high density magnetic field gradient architectures that are biocompatible and capable of manipulating single magnetic nanoparticles, attached to single biomolecules or cells, with nanoscale precision.

Biological applications of today's commercially available magnetic beads are primarily aimed at bio-separations and image contrast agents. These applications do not require high moment particles or a high degree of uniformity in the particles' magnetic properties. A new class of biocompatible magnetic particles with superior magnetic and physical properties would enable many new applications. For example, the ability to selectively attach a well defined magnetic moment to a single bio molecule or cell could enable a high sensitivity, *quantitative* bio detection mechanism. However, this would require an order of magnitude increase in the magnetic moment of the beads as well as a high degree of uniformity in particle size and moment. This is a tremendous research challenge. Today's beads are primarily ferrite-based due largely to the fact that ferrites are easily stabilized in fluid solutions. The disadvantage of ferrites is their relatively small magnetic moment as compared to ferromagnetic materials such as pure iron, iron cobalt, etc. Developing the surface chemistries to stabilize and functionalize ferromagnetic particles

(as opposed to ferrites) for biological applications is one of the technical hurdles that will require additional research investment. Another technical challenge will be control of the uniformity of magnetic moment between particles. This will likely require controlling compositional and size distribution of magnetic particles to better than 5%. The development of stable, bio-functionalized, highly uniform ferromagnetic particles will require considerable future research investment in order to realize new applications such as quantitative biodetection.

In addition to developing superior magnetic beads or carriers, many future applications will require better magnetic sensors that are biocompatible and capable of detecting and quantifying magnetically tagged bio-molecules and cells. Today's state-of-the-art GMR sensors can easily detect micron size or larger ferrite beads. However, extending the sensitivity of magnetic sensors down into the nanoscale range will be non trivial since for a given magnetic material each order of magnitude reduction in particle diameter results in three orders of magnitude reduction in particle moment. The development of next generation magnetic sensors for biological applications is another area that will require considerable research investment.

Finally, some of the most intriguing and futuristic applications of magnetics in biotechnology involve the use of magnetic forces to control and monitor biological activity at the cellular and sub-cellular level. In addition to requiring novel magnetic particles and sensors, realization of these capabilities will require the development of high-density magnetic field gradient architectures that are capable of generating sufficient forces to manipulate multiple magnetic nanoparticles with nanoscale precision. Once again, developing these high density, high precision, magnetic "tweezers" will require a significant research effort in order to enable a biomagnetics transduction mechanism capable of monitoring and initiating a wide range of biological activity in cells.