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TITLE: Bio-Applications of Giant Magnetoresistance and Tunneling Magnetoresistance Phenomena: In-Flow Magnetic Biomarker Detection

AUTHORS (LAST NAME, FIRST NAME): Torija, Maria A.[1]

INSTITUTIONS (ALL): 1. Advanced Technologies, NVE Corp, Eden Prairie, MN, United States.

ABSTRACT BODY:
Digest Body: Giant Magnetoresistance (GMR) and Tunnel magnetoresistance (TMR) phenomena have found a large number of applications. In some areas, such as data storage, their effect was been revolutionary. Success in medicine has been relatively limited. GMR and TMR materials are a critical component in some implantable and assistive devices, such as cardiac defibrillators and hearing aids. However, after many years of research and development they are just beginning to gain traction for biodetection. Since early 2003, research using these sensors to detect magnetic labelled biomarkers in a double sandwich assay has received moderate academic attention but they are not, for example, in widespread use for point of care applications.

NVE Corporation was an early innovator working with Naval Research Laboratories and other groups to develop sandwich assays and magnetic labels. The first generation of bioparticle detection mainly focused on static detection of trapped analytes. We will use the bead array counter (BARC) system as an example of technological progress and early commercial failure. We will examine the scientific progress this area since BARC and potential future outcomes. Competitive virus or bacteria detection inevitably competes with established optics based technologies enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) for today's rapid test needs. Other issues with state-of-the-art methods include high rate of false negative results (ELISA) and cross contamination (PCR), and the impossibility of target proteins. Magnetic detection can offer improved sensitivity, targeting all types bacteria, viruses, or proteins, and has better integration for miniaturized point of care devices. Commercial success will be driven by advances in two key areas: large engineering investment in parallelization and novel high sensitivity targets for medical applications.

NVE's next generation biosensor offers measurements in flow rather than relying on on-chip binding events. In-flow detection, or the detection of analytes in a channel, presents larger challenges in fluidic and electronic integration but offers speed and simplicity in the bio-functionalization. Magnetic labels and analyte conjugates can be prepared prior to test. This new type of assay depends one single bonding event, particle to biomarker, reducing test times in applications where several particles attach to the same biomarker. This approach also inherently reduces the risks of false negatives. The main disadvantages are the need of partner magnetic components, such as magnetic separators, concentrators, and flux guides.

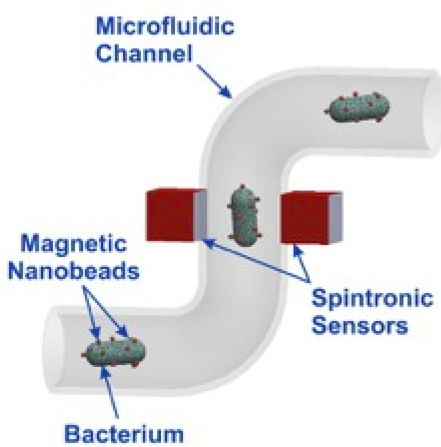
A critical component of success is the biological target. NVE's current development activities focus on *Salmonella,* the most common cause of foodborne illness. The United States Center for Disease Control (CDC) estimates that *Salmonella* causes 19,000 hospitalizations and 380 deaths per year [1]. Many of these cases could be prevented with improved detection. Furthermore, there is growing concern about antibiotic-resistant *Salmonella* strains [2]. Some strains of *Salmonella* may eventually need to be treated as adulterants that are unacceptable in food at any level. The primary roadblock to improved detection is the lack of *in-situ*, high-throughput detection technologies.

NVE's high throughput prototype is a TMR-based lab-on-a-chip sensor for *Salmonella* in a novel through-port configuration for high-volume sample monitoring. The proposed sensor uses a

combination of magnetic nanoparticle (MP) conjugation through DNA aptamers and ultra-sensitive magnetic detection in a single device that can quantitatively analyze a fluid sample for *Salmonella* in just minutes. The novel microfluidic through-port sensor array (fig 1.) allows continuous operation at high flow rates. It also allows sensor arrays to be miniaturized to reduce manufacturing costs without compromising sensitivity or speed. The entire process is compatible with lab-on-a-chip materials and methods so the platform can be easily multiplexed for additional pathogenic bacteria or serotyping. The sensor is significantly faster than qPCR, does not require enrichment, and has a sensitivity of one live *Salmonella* bacteria (i.e., 1 CFU).

Success with this device could open the door for additional targets and applications, validating magnetic detection as superior to currently competitive for technologies for many new uses.

References: 1. https://www.cdc.gov/salmonella/general/
2. Felicita Medalla, Weidong Gu, Barbara E. Mahon, Michael Judd, Jason Folster, Patricia M. Griffin, and Robert M. Hoekstra, "Estimated Incidence of Antimicrobial Drug–Resistant Nontyphoidal Salmonella Infections, United States, 2004–2012" Emerg. Infect Dis. 2017 Jan; 23(1): 29–37.



Pin-hole design of the high through put Salmonella TMR detector.

IMAGE CAPTION:
Pin-hole design of the high through put Salmonella TMR detector.

TABLE TITLE: (No Tables)

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CONTACT (NAME ONLY): Maria Torija