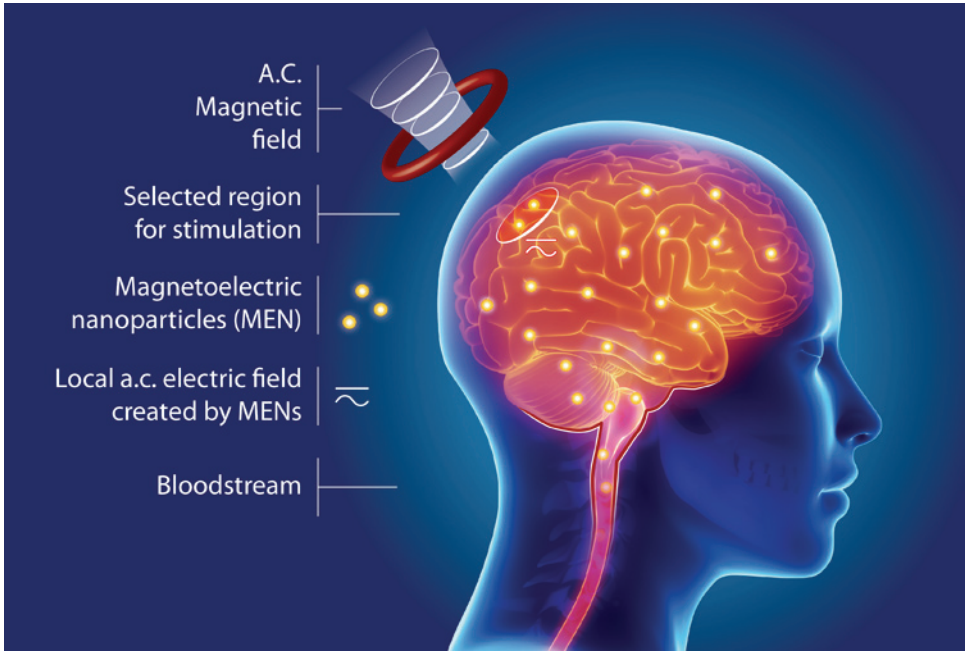
Wireless Deep-Brain Stimulation With Magnetoelectric Nanoparticles

The brain is a complex bio-electric circuit made of billions of neurons that are inter-connected through chemical and electrical synapses. The ability to remotely stimulate selective neurons deep in the brain remains a major challenge. Overcoming it will enable highly personalized "pin-point" treatments for neuro-degenerative diseases such as Parkinson's and Alzheimer's Diseases, Essential Tremor (ET), Epilepsy, and others. Furthermore, by the law of reciprocity, this nanotechnology can pave a way for reverse-brain engineering.

This FIU team has invented and patented a technology (S. Khizroev and M. Nair, "Wireless brain stimulation," U.S. Patent application 13/900,305, filed 05/22/2013, granted 01/26/2016) to answer the above challenge by using a novel class of multifunctional nanoparticles known as magnetoelectric nanoparticles (MENs). Because of MENs capability to couple magnetic and electric fields at the sub-neuronal level, they enable a unique way to combine the advantages of both the high efficacy stimulation by the electric fields and the external-control capability of the magnetic fields. They therefore open a novel pathway to control the brain.



Wireless deep-brain stimulation with Magnetoelectric Nanoparticles administrated into the brain via an IV injection. Image provided by CAKE.

This study, conducted on mice, demonstrated for the first time the feasibility of using MENs as externally controlled "smart" nanoparticles for wireless navigation and selective control of specific functions deep in

the brain. The paper recently published by FIU investigators has been selected in the list of 100 Top Science and Technology Stories of the Year (2016) by *Discover* Magazine (January 2016 issue) [R. Guduru, P. Liang, J. Hong, A. Rodzinski, A. Hadjikhani, J. Horstmyer, E. Levister, and S. Khizroev, "Magnetoelectric spin on stimulating the brain," *Nanomedicine* (London) 10 (13), 2051-2061 (2015)]. On behalf of FIU, the team has put together several multi-million-dollar research proposals on the subject.

This breakthrough study represents an important milestone in deep-brain stimulation because it provides a wireless and non-invasive way to achieve significant results. Current DBS technology is operated at macro-scale and often relies on highly-invasive direct-contact-electrode techniques. Current non-invasive brain stimulation methods include rTMS and tDCS, but in both the depth and locality of focus are strongly limited. FIU's technology, using MENs, overcomes the current technology's roadblocks.

The completed study is a stepping stone towards the development of a precision nanotechnology for simultaneously achieving the following three important functions: 1) stimulation; 2) release of drug(s) and other macromolecule(s), e.g., peptides, RNAs, and others, in selective brain regions via remote control, and; 3) mapping the electric field due to neural activity. Achieving each of these functions would be important milestones on their own. Achieving all these three functions simultaneously may very well present a pathway to next-generation pinpoint treatment of neurological diseases.

In the near-term future, a main end-user product would be an advanced wireless deep-brain stimulation (DBS) technology for treating patients with Parkinson's Disease, Essential Tremor, Alzheimer's Disease, Autism, and other neurological diseases.

Even more far-reaching applications might be envisioned when biodegradable MENs will be developed in the future. This is definitely within reach due to the recent development in the emerging field of carbon based nanotechnology. Potential applications span from the prevention and treatment of neurodegenerative disorders to opening pathways to significantly improving fundamental understandings of the brain and to reverse-engineering the brain.

> **Economic impact**: According to the 2011 technology assessment by experts at California Institute of Technology, the deep-brain stimulation (DBS) market was around $360 million. Conservative projections indicate that the technology can impact the multi-billion-dollar medical and information processing market segments.

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