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Magnetic Properties of Magnetoelectric Nanoparticles With Varying Core-Shell Ratios and Their Effects On In Vitro Neuron Stimulation

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Magnetoelectric nanoparticles (MENPs) convert magnetic fields into localized electric fields, using a core-shell nanostructure based on a magnetostrictive core and piezoelectric shell. These nanoparticles can serve as biocompatible wireless nanotransducers for magnetic-based brain stimulation. We examined the effects of changing the core-to-shell ratio in cobalt ferrite – barium titanate ($CoFe_2O_4$@$BaTiO_3$) MENPs on their magnetic properties, and then we tested their performance in stimulating neurons *in vitro*. The nanoparticles with the highest anisotropy core and lowest core-to-shell ratio were the most effective at activating neurons.

***Index Terms*—Nanoparticles, Magnetic Anisotropy, Magnetoelectric Effects, Neuromodulation**

I. Introduction

Wireless stimulation of neurons is the future of neurophysiological research, as it enables minimally- or non-invasive long-term brain studies without the need for risky implanted devices [1],[2]. Magnetoelectric nanoparticles (MENPs) [3] are an emerging method for advanced neural interfaces. When attached to the neuronal cell membrane, these nanoparticles act as field-controlled electric dipoles which, owing to their magnetoelectric effect, generate a local electric fields across the membrane in response to applied magnetic fields, initiating neuronal firing [4],[5].

The MENP core-shell nanostructure is key to maximizing the magnetoelectric effect and stimulation capability of the nanoparticles. Cobalt-ferrite ($CoFe_2O_4$) core and barium-titanate ($BaTiO_3$) shell MENPs have a well-matched 1:2 ratio in their lattice parameters, promoting the growth of highly crystalline interfaces between the core and the shell. This improves the magnetoelectric effect by efficiently linking the physical deformation of the magnetostrictive $CoFe_2O_4$ core to the piezoelectric $BaTiO_3$ shell. By varying the ratio of $CoFe_2O_4$ and $BaTiO_3$ components we can further tune the magneto-electric response and properties of the particles. Optimizing the magnetoelectric (ME) effect will be critical if MENPs are to replace electrodes in neurostimulation applications.

II. Results

A. MENP magnetic properties

Three different core-shell ratio MENPs were fabricated and measured, labeled E98, E99, and E100, all using the same cores (~20 nm) These nanoparticles had varying core-shell mass ratios of 1:5, 1:7, and 1:9, respectively. The nanoparticles were oriented and fixed to the substrate under a large, aligning magnetic field. They were then measured along the aligned magnetic field axis (parallel ||) and the transverse axis (perpendicular ⊥). With the alignment set from the field emanating from the magnet under the substrate, these orientations are not perfectly defined, with a possible skew angle of 30 degrees.

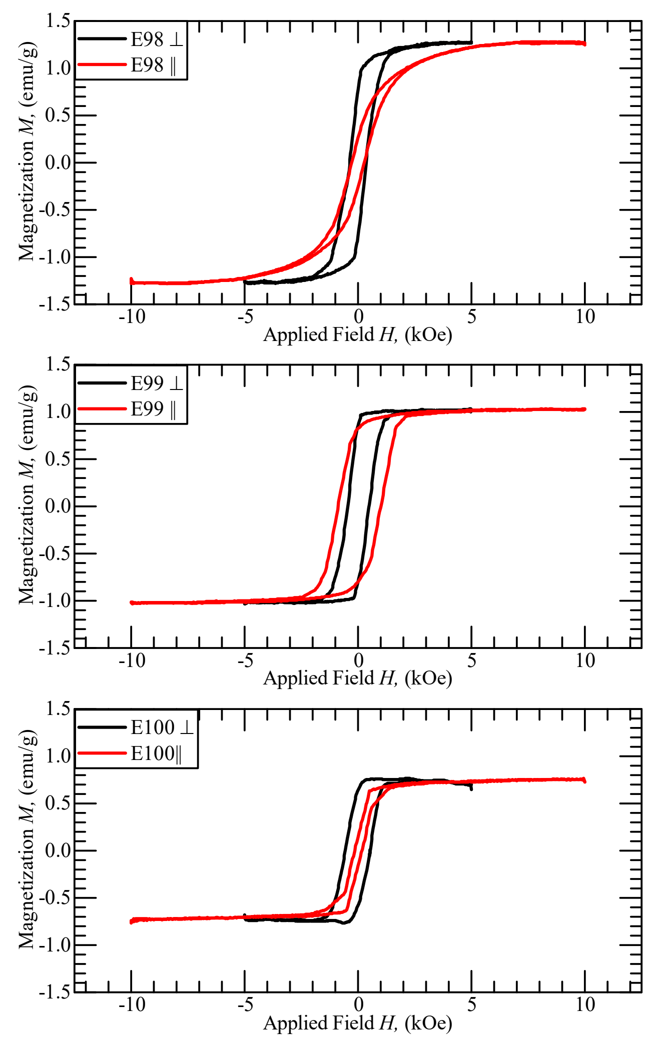

Fig. 1. M-H loops of $CoFe_2O_4$@$BaTiO_3$ MENPS.

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E98 nanoparticles required the highest applied magnetic field (>7,000 Oe) to reach saturation in the parallel orientation. E99 and E100 had a 20% and 40% decrease, respectively, in saturation magnetization compared to E98. In all cases, remanence of the parallel direction was always lower than that of the perpendicular direction, and of the three, E99 maintained the highest remanence in both directions, with only a 3.5% difference. Coercivity of E99 in the parallel direction yielded the highest value at 945 Oe but had a significant difference between the orientations with a decrease of 50% to 470 Oe in the perpendicular direction. E98 only had a 29% difference in coercivity and increased from parallel to perpendicular instead. E100 also showed a significant increase in coercivity going from parallel (166 Oe) to perpendicular (548 Oe), with almost a factor of three difference in coercivity.

From the M-H loops, E98 was the most anisotropic and had the most consistent coercivity. In contrast, E99 and E100 were relatively isotropic but had noticeably varying coercivity values, with E100 having the smallest coercivity.

TABLE I
NANOPARTICLE MAGNETIC PROPERTIES

Particle and Orientation	Coercivity (Oe)	Remanence (emu/g)	Saturation (emu/g)
E98 1:5 Ratio			
Perpendicular	356.57	0.77	1.28
Parallel	275.46	0.27	
E99 1:7 Ratio			
Perpendicular	470.15	0.86	1.03
Parallel	945.19	0.83	
E100 1:9 Ratio			
Perpendicular	547.68	0.64	0.77
Parallel	166.36	0.14	

B. Neuron Stimulation

We cultured primary hippocampal cells of E18 Sprague Dawley rats for experimentation. Cells were loaded with Cal-520 to generate fluorescent images and coated with 10ug of MENPs. After recording baseline activity, we applied a bipolar square wave in ten 1 second pulses every other second with the electromagnet to activate the particles. Nanoparticles E98 were efficient at stimulating the neuron, generating four major firing events as well as continual activity after the stimulation period had ended. E99 and E100 only had one major firing event during the stimulation period and sporadic post stimulation activity.

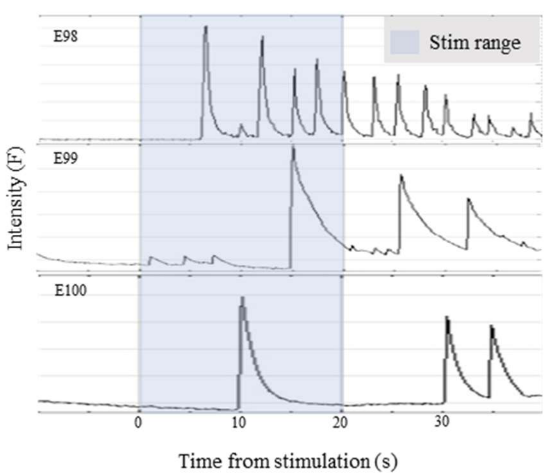

Fig. 2. Fluorescent response from neurons exposed to three separate types of CoFe2O4@BaTiO3 MENPs. The highlighted region represents the period of applied magnetic stimulation field.

III. DISCUSSION

Looking at the M-H loops of the nanoparticles alone, E98 MENPs exhibit the most unique behavior, demonstrating the highest anisotropy of the three types and saturating the slowest. In turn, the highest anisotropy correlates with the highest ME effect, because both the anisotropy and the ME effect are defined by the spin-orbit coupling. At the same time, E98 also showed the highest efficacy of neuronal stimulation, which can be explained by their high ME effect and the fact that the applied magnetic field (1000 Oe) was significantly higher than the coercivity of these nanoparticles. In contrast, the worst performing nanoparticles in terms of stimulation, E100, had the smallest anisotropy and thus the smallest ME effect. In summary, this study shows a correlation between the magnetic properties of MENPs and the wireless neural modulation capability. Particularly, the stimulation efficacy strongly depended on the ratio of the applied field to the coercivity of the nanoparticles, thus indicating the possibility to use a MENP as an On/Off switch for local stimulation. In the future, with improved control over the magnetic field, this approach can one day lead to a high-resolution, wireless neural interface.

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