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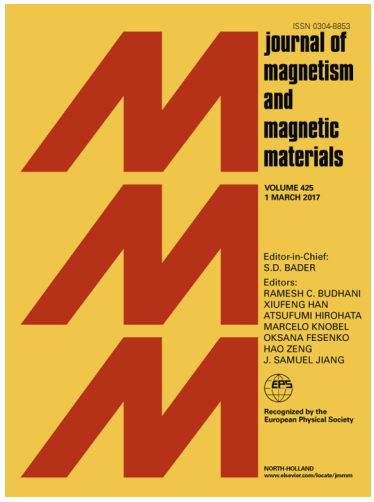

Alignment of Collagen Matrices using Magnetic Nanowires and Magnetic Barcode Readout using First Order Reversal Curves (FORC) (invited)

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ACCEPTED MANUSCRIPT

Alignment of Collagen Matrices using Magnetic Nanowires and Magnetic Barcode Readout using First Order Reversal Curves (FORC) (invited)

Anirudh Sharma[1], Michael D. DiVito[2], Daniel E. Shore[3], Andrew D. Block[1], Katie Pollock[2], Peter Solheid[4], Joshua M. Feinberg[4], Jaime Modiano[5], Cornelius Lam[6], Allison Hubel[2,6], and Bethanie J.H. Stadler[1,3*]

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Collagen matrices are one form of artificial tissue that has applications in biomimetic organs, or tumors, and in fundamental biology. Anatomical organs and tissues are often composed of aligned collagen, and in this study cross-linking nickel magnetic nanowires (MNWs) to collagen allowed a one-step bi-directional alignment of the collagen matrices when processed in a uniform magnetic field. These matrices were analyzed by differential interference contrast (DIC) microscopy, scanning electron microscopy (SEM) and polarized transmittance. The bi-directional alignment was also confirmed by plated, stained arachnoid cells from the blood-brain-barrier (BBB). Arachnoid cells are morphologically sensitive to their extracellular matrix (ECM) environment, and in this study, they were observed to spider out in two distinct directions as predicted by microscopy and transmittance. In fact, MNW-collagen matrices plated with arachnoid-cells are promising for future studies of artificial BBBs. Other cells (here osteosarcoma) have been observed to internalize MNWs, which leads to the possibility of barcoding matrices and cells with distinct signatures, pending a magnetic readout technique. To this aim, mixtures of two different MNW populations were analyzed using first order reversal curves (FORC), and the relative concentrations of the two populations were correctly estimated with negligible error for ratios of 1 : 23 and only 7% error for ratios of 1 : 115. Together, these studies open a path for magnetic identification of artificial tissues where distinct magnetic labels on matrices and in cells combine for a unique fingerprint.

Keywords: Collagen, Magnetic alignment, Blood-brain-barrier, arachnoid cells, Osteosarcoma, Magnetic nanowires, FORC, Nano barcodes

INTRODUCTION

Simultaneous, multiplexed diagnoses using large bioassays or tissue biopsies is possible via magnetic techniques, and much effort has been invested in tuning the magnetic properties of magnetic nanoparticles (MNPs) [1-4]. However, MNPs are recently almost exclusively used for separation (aka enrichment) with multiplexed diagnoses occurring by means other than magnetic signatures, for example by mass spectroscopy [5], photoacoustics [6], nuclear magnetic resonance [7], flow [8], or by moment (measuring the number of MNPs, not the type of MNP). This research has largely been driven by a narrowing focus on the detection of sparse analytes. Indeed, zeptomolar detection limits (10^{-16}) have been achieved [9,10], which could be important in early detection of diseases, such as cancer.

However, there are medical applications for multiplexing that do not require zeptomolar detection. One example is immunotherapy in cancer, where many leukocytes may reach a tumor

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