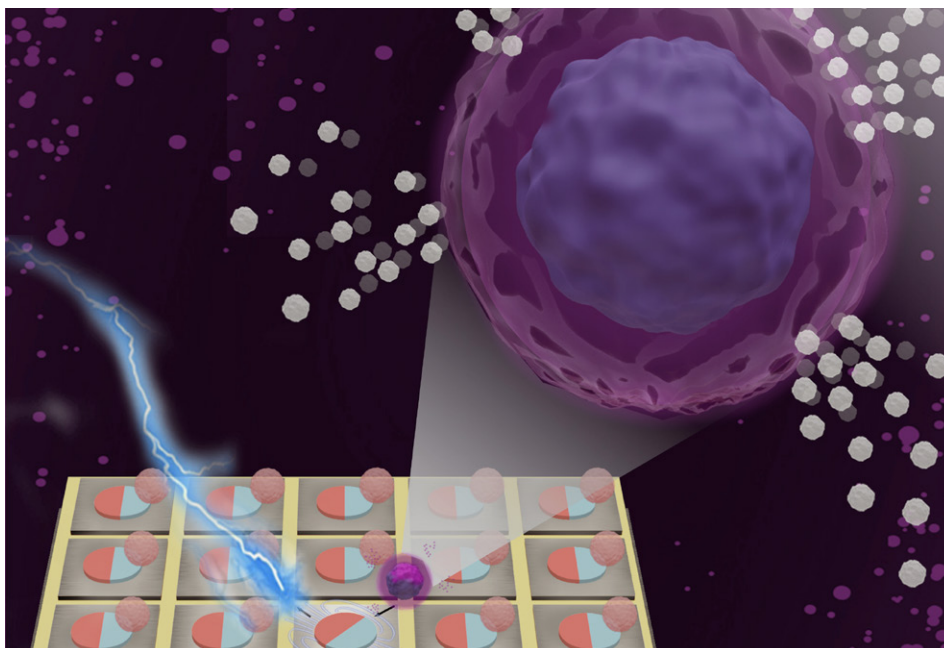
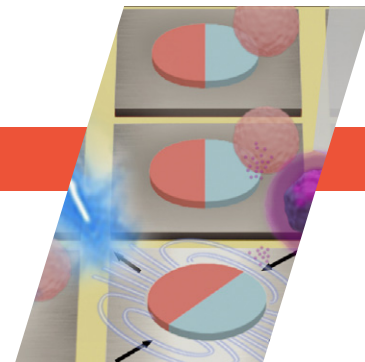


Programmable Micromagnets for Single-Cell Sorting



Cover image depicting a cell being released from a micromagnetic array based on criteria chosen to support cell therapies. In this case, the released cell is shown secreting exosomes and cytokines (white particles) that activate the immune system to target and kill cancer cells.

A need for selective cell-sorting

A promising personalized form of immunotherapy adapts a patient's own T cells to fight certain types of cancer, such as leukemia and lymphoma. The process involves extracting T cells from the patient's blood, re-engineering them to target cancer cells, and sorting them so that only the most effective are reproduced in the quantities needed for treatment.

While high-throughput, bulk sorting can be done by magnetic tagging of cells, so far there has been no way to magnetically capture and release individual cells based on desired characteristics. Here, researchers used the ALS to characterize the properties of magnetic microstructures

with electrically controllable magnetizations and demonstrated their ability to capture and release single cells on demand.

A strain-mediated switch

The researchers created microstructures using Terfenol-D, a metallic compound of terbium, dysprosium, and iron that's highly magnetoelastic (i.e., its magnetization changes when compressed or stretched). Microdisks of Terfenol-D were sputter-deposited onto a substrate material (PMN-PT) that's piezoelectric (i.e., expands or contracts in response to an applied electric field).

In concept, a voltage applied to a particular microdisk would act as a strain-mediated switch for the Terfenol-D magnetic state, allowing the programmed

Scientific Achievement

Researchers using the Advanced Light Source (ALS) demonstrated that electrically induced mechanical strain can control the magnetic state of tiny magnets used to sort biological cells.

Significance and Impact

The work lays the foundation for a programmable, single-cell sorting platform to support a wide variety of biotechnology applications, including personalized cancer treatments.

capture and release of cells tagged with magnetic beads, based on complex behaviors or functions (e.g., cell-killing, secretion, motility).

Single-domain configuration

To characterize the magnetic properties of the Terfenol-D microdisks, the researchers used photoemission electron microscopy (PEEM) at ALS Beamline 11.0.1. X-ray magnetic circular dichroism (XMCD) experiments at Beamlines 4.0.2 and 6.3.1 provided supporting element-specific data. The ability to image the in-plane magnetization was crucial to obtaining direct evidence of the effective single-domain magnetic configuration of the Terfenol-D microdisks, even in the absence of an external magnetizing field.

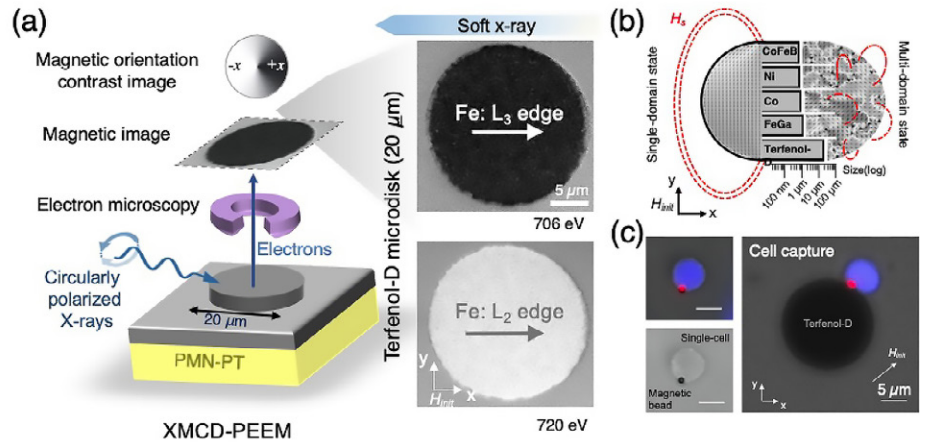
The results showed that the Terfenol-D sustained the single-domain state to a scale comparable to that of a human cell (20 μm), an order of magnitude larger than other commonly studied magnetoelastic micromagnets. A large single domain produces a magnetic field strong enough to firmly capture magnetically tagged cells in microfluidic environments and are much more responsive to strain than multidomain structures.

Proof of concept

To demonstrate how the platform works, the researchers flowed magnetic beads through a microfluidic channel on top of Terfenol-D microstructures, which readily captured the beads. When a voltage was applied to the substrate, induced strains in the substrate caused the Terfenol-D magnetization to rotate, reducing the attractive force between bead and disk. When the fluid drag force exceeded the magnetic force, the bead was released.

The researchers also tested the platform's compatibility with the sorting of T cells based on the secretion of interleukin-2 (IL-2), a signaling molecule that regulates T cell proliferation and differentiation. Over time, magnetically trapped single T cells revealed two distinct sub-populations, differentiated by a fluorescence signal associated with IL-2 accumulation.

In future experiments, the researchers expect to incorporate local surface electrode pads to generate a more diverse regional strain profile in the piezoelectric substrate. For now, these experiments lay the foundation for using large arrays of magnets to capture, observe, and selectively release cells with specific functions that may lead to improved therapeutic performance.



(a) Schematic of the XMCD-PEEM experiment (left) and PEEM images of a Terfenol-D microdisk (right), acquired at the Fe L₃ and L₂ absorption edges, showing the single-domain magnetic configuration at a diameter of 20 μm . (b) Comparison of length scales for single-domain states in different magnetoelastic materials. (c) Bright-field and fluorescence images of a magnetically and fluorescently labeled single cell (purple).

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