Phase II Grant for the NSEC Center for Affordable Nanoengineering of Polymeric Biomedical Devices (CANPBD)

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Intellectual Merits

The research vision of CANPBD is to revolutionize medical diagnosis and medicine by establishing an affordable multiscale synthesis and fabrication protocol leading to nanofluidic and polymer therapeutic devices for personalized nanomedicine.

An important emphasis of Phase II is to commercialize the developed technologies in close collaboration with end users.

The broader impacts of the activities planned for Phase II are to:

1. commercialize nanoengineered biomedical devices through affordable manufacturing methods and novel design;
2. extend research results from medical/biology applications to functional nanocomposites, water treatment, homeland security, environmental protection, and food industry toxicology;
3. establish new products and new industries to create high-paying jobs;
4. train the 21st century workforce in economically important and critical high-tech fields.

Phase II Automated Cell to Biomolecule Analysis Platforms:

The research plan in Phase II comprises two highly integrated nanofactory assembly (or disassembly) systems identified based on the center's expertise and the needs to develop personalized nanomedicine, CANPBD's long-term goal. These systems not only provide fundamental science and technical challenges in various nanotechnologies that are essential for the development of our targeted biomedical devices, but also interdisciplinary system integration opportunities that require highly integrated team efforts to solve many system level challenges and technical barriers not faced in individual projects. In the following, we briefly describe two nanofactory platforms that are particularly useful for the aforementioned biomedical applications and how relevant CANPBD technologies and scientific studies are applied to their design, fabrication, and bioevaluation.

Automated Cell to Biomolecule Analysis (ACBA)

The ACBA is a specific example providing a process for disassembling cells into their components and analyzing the component profiles. The goal of the ACBA is to transform heterogeneous cell populations harvested *in vivo* and produce (a) homogeneous cell sub-types, (b) intracellular 'spectra' showing characteristic protein, DNA, RNA and miRNA profiles for a given cell type, and (c) label-free detection of critical miRs resulting from the dose-controlled response of individual cells to chemo- and gene therapy. The scientific aim of this nanofactory approach project is to design and test an automated low-cost cell separation to biomolecule analysis system through viable nanotechnologies for the investigation of cancer cell biology and cell response to therapy using miR profiling.

Significant progress has been made on the two core platforms that support the proposed ACBA Nanofactory System. These platforms, whose component stages are schematically illustrated in the Fig. 1 flowchart, are based on two distinct manipulation schemes.

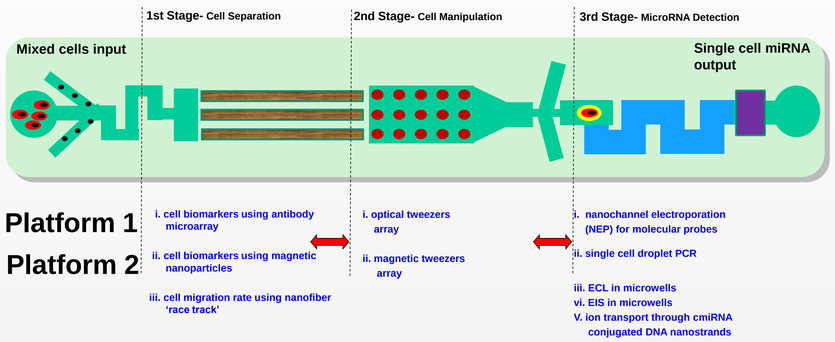

Fig. 1 Schematic flowchart of stages within ACBA platform.

1. Optical Tweezers based ACBA Platform.

Platform 1 integrates optical tweezers based manipulation with a novel DNA combing and imprinting (DCI) process and nanowire electric circuit designs. Fully separated cell populations in a microarray will be transferred by optical tweezers to embedded field line circuitry within the biomolecular analysis/detection stage. These separated cell populations of interest will be treated with dose-controlled drug/gene (e.g. miR) injection using a newly developed 'nanochannel electroporation technique'. This method relies on highly focused and localized electric field strength provided by the presence of nanochannels intersecting the cell surface. The modeling and experimental researchers are working closely to address a number of challenging and relevant micro/nanofluidic phenomena including nanochannel-based cell electroporation

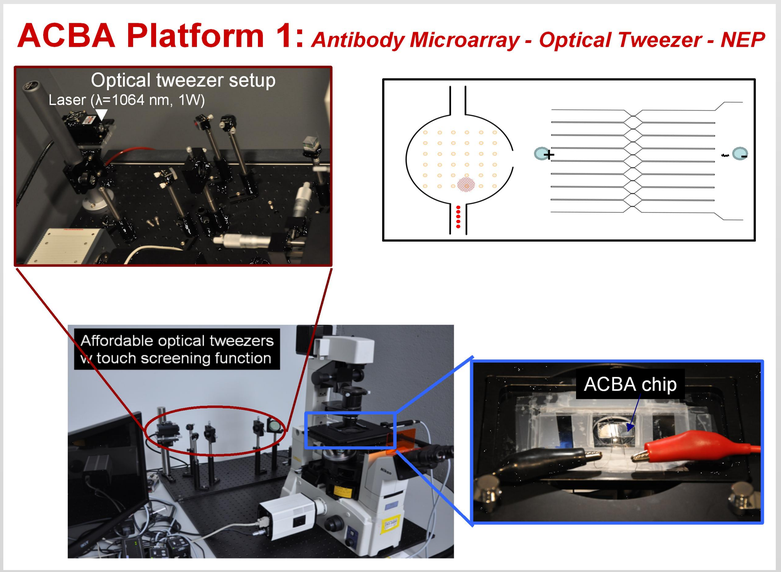

Fig. 2 Layout of optical tweezers manipulation stage of Platform 1. Schematic sketch illustrates concept of nanoelectroporation

2. Magnetic Tweezers based ACBA Platform

Directed, controllable and simultaneous manipulation of large numbers of individual cells is central to the success of ACBA platform 2. We have developed a *new* approach, based on microscopic programmable magnetic traps imprinted on a surface, to apply directed forces on fluid-borne labeled cells. The advantages of this approach are:

(A) Platform's two dimensionality eases: (1) lithographic creation of traps with nanoscale precision, (2) creation of large (10^5 traps/cm^2) trapping densities, (3) real-time microscope viewing, (4) programmable control over trajectory of cells, (5) ready integration into micro-fluidic devices.

(B) Miniature, biocompatible and low cost platform can be developed as "lab-on-chip" units to facilitate standardized biological experiments with small volumes of cell samples.

(C) Dynamic control of these forces offers more precise selection, and thus understanding, of individual cell properties than data-averaging a population of cells.

Figure 3 shows an example of two magnetic tweeezers that rely on zigzag and discrete magnetic bits imprinted on a silicon surface. Magnetically labeled cells are attracted to the vertices of the wires or periphery of disks to be manipulated by weak external magnetic fields. Fig. 4 illustrates separation of cells within a channel using magnetic disks.

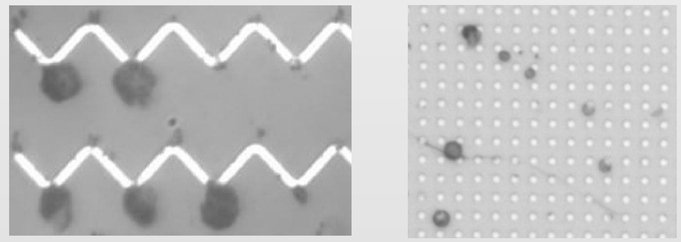

Fig. 3: Cell manipulation schemes of zig-zage wire (left) and disk (right) based magnetic tweezers that underlie ACBA Platform 2.

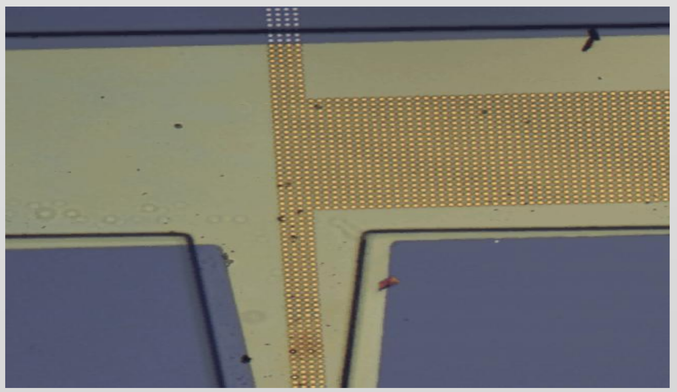

Fig. 4 Platform 2: Cell sorting within microfluidic channel based on remotely controlled magnetic tweezers

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