Research highlights

Micro- and nanosystems meet biology: artificial life on a chip

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Abstract

We highlight recent reviews and reports on the use of micro and nanosystems to solve biological problems. The matching length scale allows micro- and nanotechnology to create tools for engineering biological systems at molecular and cellular levels. Simple microdevices such as reactors, microchannels and concentration generators with features on the order of micrometers make the implementation of artificial life on a chip possible. These new tools allow for the investigation of complex gene expression dynamics and tissue or organ-level physiology. The next step will be the use of these tools as models for both health and disease for drug discovery.

Micro- and nanoscale tools for cellular- and molecular-level manipulation

Micro- and nanotechnologies have been emerged as the driving force in various areas of modern science and technology. While micro technology is mainly based on the top-down machining approach, nanotechnology relies on the bottom-up synthesis and self-assembly. Systems with components size smaller than 100 nanometers are considered as nanosystems. Systems with larger structures up to less than one millimeter are microsystems. The capability to artificially create structures in this length scale opens up new phenomena and functionalities because things behave differently as expected with our intuition for the human scale of meters. The basic scaling law, the square-cube law, indicates that surface-based phenomena become more significant than volume-based phenomena as the size decreases.

Let take examples from biology to illustrate the different size scales. Complex molecules such as proteins have a size ranging from few to ten of nanometers. A more complex system such as a virus is about one hundred nanometers in size. Living systems such as bacteria have sizes ranging from one hundred nanometers to one micrometers. Cells, the building block of complex organisms in plant and animal kingdoms, are several micrometers in size. Interestingly, these size scales of biological systems match the size scale of micro- and nanosystems [1]. Thus, micro- and nanotechnology can create tools that can construct and manipulate biological systems at the molecular and cellular levels, Figure 1.

Figure 1. Scale of biological systems with corresponding technologies and engineered systems. Figure adapted from [1] with permission.

Molecular-level manipulation

At the molecular level, Bar-Ziv's group from Weizmann Institute recently reported microractors for the synthesis of protein with the help of DNA templates assembled using photolithography [2]. The microractors were fabricated in silicon using well established etching processes. The microreactors with 50-micron diameter represent artificial cells that are capable of metabolism, programmable protein synthesis and communication. The surface of the reactor is coated with double-stranded DNA using chemical photolithography. Reactants and products were transported by molecular diffusion across microchannels measuring 1 to 3 micrometers by 20 micrometers in cross section. Diffusive transport is well controlled through the channel length ranging from 50 to 300 micrometers. These microchannels represent the simplest form of a concentration gradient generator, a useful tool for biological research in microscale [3]. Through the length of the microchannel, the diffusion time or the effective protein lifetime can be controlled allowing the detailed study of gene expression dynamics. Interconnected reactors establish the communication. Complex dynamics of activator and repressor is controlled through the diffusion length, resulting in a spatiotemporal oscillating pattern of gene expression. Besides the gene expression study, an interesting technical solution reported in this work is the use of magnets for bonding the glass cover slide to the silicon chip. A ring magnet embedded in PDMS also works as a self-sealing removable fluidic interconnects which suit well to low-pressure applications.

Cellular-level manipulation

At the cellular level, microtechnology allows for the implementation of microfluidic cell culture devices. These devices contain living cells that can simulate tissue-level and even organ-level physiology. Bhatia and Ingber recently published an excellent review on microfluidic organs-on-chips [4], an emerging area where micro and nanosystems will have a significant impact for the understanding of biological processes, the discovery and the development of new drugs. Similar to the concept of microreactors for gene expression discussed above, an organs-on-chips device provides culture chambers that are continuously perfused. These devices allow the integration of sensors, and provide easy access to conventional microscopy. Thus, real-time monitoring and imaging of biological processes are possible in this platform. Another advantage of organs-on-chips devices is the precise control of a wide range of system parameters such as mechanical strain (Figure 2) [5] that would allow systematic parametric study of physiological phenomena. Recently, basic mechanisms of a wide range of organs including liver, kidney, intestine, lung, and heart have been modelled and studied on the chip. By connecting compartments representing different organs of the body, the study of adsorption, distribution, metabolism, elimination and toxicity (ADMET) of drugs can be carried out in vitro, without the need of animal models.

Figure 2. Cell stretching device for modelling gut and lung: (a) Device concept; (b) operation modes; (c) an array of 15 cell stretching units. Figures adapted from [5] with permission.

The above examples of how biological systems are engineered at molecular and cellular levels illustrate the potential impact of micro- and nanosystems on biology. Micro- and nanotechnology will be transformative for many areas of biology from basic research to commercial applications. Combined with person-specific cells, personalised health and disease models on a chip will be possible, and the vision of personalised medicine will be the reality in the near future. With possible commercial applications for the wellness industry, micro- and nanosystems for biology will have impact beyond the treatment of diseases.

References

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