

In the second of a series of four CIMIT Forums devoted to Nanotechnology and Medicine, Mehmet Toner, PhD, MGH spoke on “The Coming Merger of Living Cells and Microdevices”. Microfabricated devices dealing with non-living systems, such as genes-on-a-chip for genetic analysis, or labs-on-a-chip for applications such as PCR, electrophoresis, and flow cytometry, are being merged with living cells to make a new class of devices. MEMS microfabrication builds upon well-established silicon wafer processing methods and photolithographic patterning technology. The implications of placing cells upon MEMS structures include cell growth in homogeneous local environments as well as the ability to perform local measurements of cell physiology in a controlled microenvironment. A number of core technologies, such as microfabrication, surface engineering and microactuators are being applied both to basic science and to medical applications including diagnostics, therapeutics and drug discovery. One example is blood analysis on a chip, which starts with careful blood handling to avoid artifacts, followed by measurements and analysis using bioinformatics. A microfiltration device which excludes red blood cells and separates the flowing white blood cells into subpopulations using an array of functionalized microposts has been developed. A number of schemes to collect cells on locally-modified substrates and then use laser microdissection to remove specific pure cell populations were described. Devices to collect cells in a closed system and controllably lyse specific cell have also been developed. The microfabrication of a tissue engineered liver by controlled deposition of patterns of hepatocytes, which were then activated by co-culture, and its testing in an animal model was discussed.

Lionel C. Kimerling, PhD, MIT spoke on “Disease as a Material Process” and presented a nano-medical road map for materials, processes and applications. Two approaches to nanoprocessing were distinguished; “top-down” processes involves creating nanostructures out of macrostructures while a “bottom-up” approach involves the self-assembly of atoms or molecules into nanostructures. Three examples were given to illustrate the approach. In the pharmaceutical industry, an AIDS drug, Ritonavir, had been on the market for two years when a poorly-soluble polymorph appeared, necessitating withdrawal of the drug. A combinatorial chemistry approach, which applied 2000 conditions and 32 solvents to synthesis of the drug was applied and showed that there were in fact four different structures whose formation conditions were now known. The analysis defined the conditions for reliable formation of the desired structure; however the information was too late to regain the market. The formation of cataracts has been studied and is now known to result from an attractive interaction between lens proteins which leads to aggregation and phase separation. This in turn leads to diminished lens homogeneity and opacity. A similar materials science approach was used to study Alzheimer’s disease, which is characterized by the growth amyloid β plaques. The formation of micelle-like aggregates, which act as nucleation centers for fibrils, was studied and found to be an activated process which is highly temperature dependent. However a direct application to the treatment of Alzheimer’s has yet to be found. Finally, the use of an implantable microchip drug delivery system for BCNU in cancer treatment was described. Cups filled with the drug are sealed by a gold cover whose dissolution can be controlled by an applied voltage. In addition, an immune booster can be introduced separately from BCNU.