Chapter 13

Emerging BioMEMs Technology

13.1 Introduction ................................................. 414
13.2 Minimally Invasive Surgery ................................. 414
13.3 Point-of-Care Clinical Diagnosis ............................ 415
13.4 Cardiovascular ............................................... 418
  13.4.1 Introduction .......................................... 418
  13.4.2 Pressure and flow measurement ......................... 420
  13.4.3 Cardiac muscle function ................................ 421
  13.4.4 Syncope assessment ................................... 421
13.5 Diabetes .................................................... 422
  13.5.1 Continuous glucose monitoring ......................... 422
  13.5.2 Microdroplet analysis ................................ 423
13.6 Endoscopy .................................................. 424
  13.6.1 Introduction .......................................... 424
  13.6.2 Optical coherence endoscopy .......................... 424
  13.6.3 Micro-optical scanner ................................ 424
13.7 Neurosciences .............................................. 425
  13.7.1 Introduction .......................................... 425
  13.7.2 Probes ............................................... 426
  13.7.3 Nerve regeneration ................................... 427
13.8 Oncology .................................................... 431
  13.8.1 Introduction .......................................... 431
  13.8.2 High-throughput screening ............................ 432
13.9 Ophthalmology .............................................. 432
  13.9.1 Introduction .......................................... 432
  13.9.2 Retinal implants ...................................... 433
13.10 Dermabrasion ............................................... 435
13.11 Tissue Engineering ........................................ 436
  13.11.1 Introduction .......................................... 436
  13.11.2 Cell patterning and bioreactors ....................... 437
13.12 Cell-Based Biosensors ........................................ 437
13.13 Homeland Security ......................................... 438
13.14 Review Questions ........................................... 441
  References .................................................... 442
13.1 Introduction

We are on the threshold of a medical microdevice revolution that will change how we diagnose and treat patients. The promise of bioMEMs is the delivery of sensitive, selective, fast, low-cost, less invasive, and robust methods for diagnosis and pathogen detection. Individualized treatment directed at specific targets and genetic inadequacies will be made, as well as methods of therapy incorporating novel drug delivery devices and other actuator systems.

BioMEMs devices are to the future of medicine as microprocessors were to the computer revolution at the end of the last century, and of no less importance or potential impact. They are the platform upon which the human genome was sequenced in record time, and the basis for research of protein expression in health and disease. Likewise, they are the platform for performing point-of-service diagnostic testing and eventually monitoring evolution of disease in an individual and delivering customized nanomedicine therapy.

Microfluidic-based LOC devices and other μTAS, including DNA and protein microarrays, will be the basis of most if not all diagnostic tools within the next ten years. Transport of samples, reagents, and buffers through microfluidic systems based on electrokinetic and active pumping techniques will be at the heart of these systems. Actuator systems, including environmentally sensitive hydrogels, EAPs, and piezoelectric devices will be used for drug delivery systems, and to fabricate impressive biomimetic systems that imitate smooth and striated muscle function for future artificial muscles, hearts, diaphragms, and limbs.

Treatment-oriented devices will evolve more slowly, largely due to the infancy of the science, the need for confirming clinical studies, overcoming biocompatibility problems, packaging, safety, patent issues, and cost. Nevertheless, they will evolve, including both external and implanted systems.

In the beginning of the book I eluded to a future Physician’s Reference to Biomedical Devices on the desk of every physician, and I hope the intervening chapters have convinced you of this possibility, and excited you into becoming involved in the revolution.

A number of applications have been cited in previous chapters to illustrate the principles and techniques discussed. Now we will look at a few more applications demonstrating integration of these techniques.

13.2 Minimally Invasive Surgery

BioMEMs devices in surgery may improve the functionality of existing surgical tools. They introduce new methodologies, and provide improved feedback or monitoring during procedures. Surgical considerations also include the implanting of probes, stimulators, and other bioMEMs devices such as the Reveal syncope sensor described below. Modification of an existing surgical tool may be advantageous for small companies developing bioMEMs devices, as lengthy clinical trials may be avoided if the modification does not alter the performance of the tool.
Minimally invasive surgery (MIS) is the process of accomplishing a surgical task with the least amount of intrusion, harm, and ultimately cost to the patient. There is typically less postoperative pain, shorter hospital stays, quicker recoveries and less scarring. Among the bioMEMs enhancement areas for MIS are tactile feedback, tissue sensing, and tracking systems [Rebello, 2004].

For example, fiberoptic instruments and small tools may be used to remove a gallbladder through small holes in the abdomen rather than the traditional open incision. Recovery time is markedly improved, and ultimately the risk is lessened (in the hands of a surgeon experienced with the procedure, and with proper choice of technique). The downside is less visualization and “hands-on” mobilization of organs, and some increased risk of bleeding or other complication that may require ultimately converting to an open procedure. MIS accounts for 40% of procedures, and is projected to increase to 80% in the next 15 years [Rebello, 2004].

13.3 Point-of-Care Clinical Diagnosis

Combining microfluidic devices, detection schemes, and microarray devices is the natural evolution for µTAS systems. Advantages of integrated chips include low sample/reagent volume, rapid analysis time, less sample wastage, cost effectiveness, and potential for disposability. Microfluidic systems may be active or passive devices. Advantages of a passive system include no need for a power system, ease of integration, continuity in substrate material, rapid prototyping, low cost, and use without active control. Passive microfluidic components, including valves, mixers (including diffusion), filters, and membranes, were discussed in Chapter 5. Active systems require a reliable power source (typically battery power for hand-held systems) and control electronics. Another consideration for an integrated system is choosing the best substrate, including silicon, glass, or polymer materials.

A disposable smart plastic fluidic biochip for clinical diagnosis is shown in Fig. 13.1. This cartridge-like device and supporting electronics is quite novel in its level of integration. Figure 13.2 shows schematically the passive microfluidic manipulation system based on the structurally programmable microfluidic system (sPROMs) technology developed by Ahn et al. (2004). The novelty of this device is that it allows for a preprogrammed set of microfluidic sequencing with only an on-chip pressure source. The integration of an air-bursting detonator is the fluid-driving source, eliminating the need for active microfluidic pumps. An integrated biosensor array is included for simultaneous detection of multiple clinically relevant parameters. The biochip is inserted into the analyzer unit, where the microfluidic sequencing is initiated by a trigger signal from an electronic controller. After the sample solution (blood) is delivered to the biosensor array, the electrochemical detection circuitry on the analyzer is used to determine the concentrations of the various analytes.

COC was used for the substrate. A custom designed Ni molding block was produced by microfabrication. A rapid thermal process of injection molding was used. The surface of the Ni mold was heated with IR radiation to the same temperature as the injected polymer, which minimizes heat transfer on injection and allows for better flow into the mold detail (Fig. 13.3).
In this device microfluidic manipulations are carried out in a *preprogrammed sequence* without the need for an external control signal. Figure 13.4 shows schematically the integrated dispenser. The reservoir is filled and fluid dispensed in a precise manner through a tree of microchannels (1–7). Flow is controlled with microvalves (R₁–R₆) and channel geometries.

The passive microvalve operates on the principle that when an abrupt change in width is effected across a microchannel fabricated on a hydrophobic substrate, a substantial pressure would be needed to push the fluid across the

**Figure 13.1** Assembled biochip with sPROMs-based microfluidic control system and air-bursting detonators for fluid driving. [Reprinted with permission from Ahn et al. (2004), copyright IEEE.]

**Figure 13.2** Schematic illustration of multianalyte detection disposable biochip cartridge. The biochip incorporates on-chip power sources for passive microfluidic manipulation and a biosensor array for blood analysis. [Reprinted with permission from Ahn et al. (2004), copyright IEEE.]
The pressure required to move the fluid into the channel before the passive valve is expressed by the Hagen-Poiseuille equation for a rectangular channel:

\[ \Delta P_1 = \frac{12L\mu \cdot Q}{wh^3}, \]

where

- \( L \) is the length of the channel,
- \( \mu \) is the viscosity of the fluid,
- \( Q \) is the flow rate,
- \( w \) is the width of the channel, and
- \( h \) is the height of the microchannel.

The pressure required to overcome the passive valve (to overcome surface energy of the narrow channel derived from the higher surface-area-to-volume

\[ \]