

BOOK REVIEWS

Annual Review of Biomedical Engineering, 2012. Martin Yarmush, James Duncan and Marth Gray (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, California 94303-0139, USA. Vol. 14. 479 pp. Price: US\$ 83.

In the past few decades, various human diseases have triggered incisive research at the interface of engineering and biology/medicine, leading to the new discipline of bioengineering. In the field of materials science, a new class of materials, i.e. biomaterials has increasingly received wider attention. The fast progress of these disciplines has been reflected with the launching of new scientific journals as well as new edited books or textbooks. The impact of ongoing research as well as future research perspectives in this broad area of bioengineering has been aptly documented in this volume. The volume contains 19 chapters, principally covering four major areas: (a) *in vitro/in vivo* diagnostic models for toxicity, cancer and heart attack; (b) various imaging techniques to assess or image diseased organs or tissues and (c) analytical predictive modelling to understand various mechanisms of clinical relevance.

Although various drug delivery methods are being studied widely in the last few decades, understanding of the nanoparticulate drugs with the biological system is lacking at multiple length scales. In the chapter entitled 'The effect of nanoparticle size, shape, and surface chemistry on biological systems', by Albanse *et al.*, an understanding of the interactions between nanoparticles and biological systems is discussed in great detail. Extensive research in the area of nanotechnology enables the availability of nanoparticles with controlled shape and size. In a typical drug delivery system, a nanoparticle is coated with polymers, drugs, fluorophores, peptides, proteins or oligonucleotides, and eventually administered into cell cultures or animal models. The chemistry and configuration of nanoparticle-based drug delivery systems strongly influence their interaction with serum proteins and cell membrane receptors, cellular uptake, gene expression, and toxicity. In particular, various studies correlating the properties of nanomaterials such as size, shape, chemical functionality, surface charge, and composition with biomolecular signalling, biological kinetics, trans-

portation and *in vitro/in vivo* toxicity are critically analysed. The current progress in studies of the interactions of nanomaterials with biological systems using various characterization tools and biochemical assays is mentioned and the chapter closes with a perspective on the long-term implications of these findings.

The chapter 'Tendon healing: repair and regeneration', by Volete *et al.*, reviews the composition and functional properties of healthy tendon and also describes the structural, biological, and mechanical changes during the process of tendon healing. In reference to the biochemical pathways activated during repair, some cutting-edge strategies for the enhancement of tendon healing are discussed.

With the advent of new manufacturing technologies, the fabrication of custom-made biomaterials is being attempted in various research groups. Lantada and Morgado, in the chapter entitled 'Rapid prototyping for biomedical engineering: current capabilities and challenges' discuss a new set of manufacturing technologies to address market requirements for biomaterial fabrication in a customized manner to provide support for research prototypes. Typically, rapid prototyping allows prototypes to be produced in a wide range of materials with remarkable precision in a couple of hours. The authors focus on the main fields of application for rapid prototyping in biomedical engineering and health sciences, as well as on the most remarkable challenges and research trends. The combined use of medical imaging tools, CAD and CAE software, and rapid prototyping technologies enable the cost-effective and time-efficient development of personalized biomedical devices. It is expected that in future, biomimetic porous 3D scaffolds of desired pore architecture will be produced to support structures for cell culture.

In an important chapter, Atheshian and Humphrey explain the evolution and usefulness of continuum mixture models for biological tissue growth and remodelling. Biological processes involve mass exchanges that increase, decrease, or replace materials that constituent cells, tissues, and organs. Given that the type and extent of changes in structural integrity depend on the different constituents involved (e.g. cytoskeletal or extracellular matrix proteins), the continuum theory of mixtures is ideally suited to

model the mechanics of growth and remodelling. Both the illustrative examples as well as some open problems in the fields of modelling soft-tissue growth and remodelling are discussed in this chapter.

Kim *et al.*, in the chapter 'Flexible and stretchable electronics for biointegrated devices', illustrate how the advances made in the field of materials and manufacturing enable the construction of high-quality electronics and optoelectronic-based devices, which can readily integrate with the soft, curvilinear surfaces of the human body. The resulting capabilities create new opportunities for studying disease states, improving surgical procedures, monitoring health/wellness, establishing human-machine interfaces, and performing other functions. In particular, the authors illustrate the usefulness of such devices in terms of their integration with the brain, heart, and skin.

Cheng and Lu discuss the emergence of synthetic biology as an important discipline at the interface of engineering and science. Translating engineering ideas for biological systems, this article also emphasizes the need for changes in the engineering mindset to be applied to biological problems. It also discusses the progress and challenges in synthetic biology and illustrates the areas where synthetic biology may impact biomedical engineering and human health.

In case of myocardial infarction, i.e. 'heart attack', the cardiac tissues are largely damaged. In the context of cardiac diseases, Madsen and Christini discuss how nonlinearities in cardiac electrophysiology influence normal and abnormal rhythms and how bifurcations change the dynamics. In particular, many recent developments in computational modelling at the cellular level that are focused on intracellular calcium dynamics are discussed, particularly in the context of the importance of nonlinearities in calcium dynamics: repolarization alternant and pacemaker cell automaticity.

The introduction of microfluidic tools has revolutionized the study of vascular physiology as such tools can simulate physiologically relevant culture models. In this context, Wong *et al.* mention the advantages of small dimensions and laminar flow inherent in the microenvironment with fine spatial and temporal resolution. Importantly, the potential advantages of microfluids in terms of the

following aspects are discussed: (a) investigation of hemodynamics on a capillary length scale; (b) the modulation of fluid streams over vascular cells; (c) angiogenesis induced by the exposure of vascular cells to well-defined gradients in growth factors or pressure, and (d) the growth of microvascular network in biomaterials.

Gould discusses the usefulness of optical nanoscopy as a new characterization tool to yield a resolving power that is fundamentally diffraction-unlimited. This tool exploits the photophysical properties of fluorescent probe molecules. The author reviews the basic principles of diffraction-unlimited microscopy and how these principles influence the selection of available algorithms for data analysis.

Bacterial infection has been a perennial problem in the context of implantable biomedical devices. In this context, De Geyster *et al.* review the effectiveness of nanothermal plasma sterilization for living and nonliving surfaces. The concept of inactivation of bacteria by nonthermal plasmas (so-called plasma sterilization) is being exploited in this technique. In addition to the inactivation of bacteria on nonliving surfaces, the article also focuses on the sterilization of living surfaces, such as animal and human tissues. Specific examples to illustrate the effectiveness in case of *Pseudomonas aeruginosa*, exposed to an atmospheric-pressure glow dielectric barrier discharge in a helium/air mixture are provided. Whereas vacuum-based plasma sterilization is a well-established technique, the use of atmospheric-pressure cold plasmas to inactivate bacteria appears to be relatively recent. Although the bactericidal effect of atmospheric pressure is undisputed, most of the mechanisms of action are still unknown and require more in-depth studies.

The chapter entitled 'Regulation of cell behaviour and tissue patterning by bioelectrical signals: challenges and opportunities for biomedical engineering' discusses the molecular-level understanding of regulatory mechanisms to achieve control over cell behaviour and pattern formation. Bioelectrical signals

encoded in spatiotemporal changes of the transmembrane potential (V_{mem}) control proliferation, migration and differentiation. Moreover, endogenous bioelectrical gradients serve as instructive cues mediating anatomical polarity and other organ-level aspects of morphogenesis. It has been categorically mentioned that the membrane voltage is a key parameter in regulating cell properties. Cells that are highly plastic (able to proliferate rapidly, undifferentiated) tend to be depolarized. Importantly, V_{mem} is not simply a reflection of cell state, but an instructive parameter. Artificial depolarization can confer neoplastic-like properties on somatic cells and prevent stem-cell differentiation, whereas artificial hyperpolarization can induce differentiation and suppress proliferation. It is reported that cell and tissue properties can be localized within a multidimensional physiological state space containing a number of orthogonal dimensions indicating membrane voltage, intracellular pH, K^+ content, nuclear potential, Cl^- content, surface charge, etc.

It is well recognized now that rapid deformation of brain tissue in response to head impact or acceleration can lead to numerous pathological changes, both immediate and delayed. Some of the emerging imaging technologies and recent imaging studies provide important data for these purposes. The chapter entitled 'Quantitative imaging methods for the development and validation of brain biomechanics models' describes some of these techniques and data with an emphasis on magnetic resonance imaging approaches. In combination, these imaging tools promise to extend our understanding of brain biomechanics and improve our ability to study TBI *in silico*.

Mechanotransduction may alter cell physiology by stimulating conventional biochemical signalling paths via ion channel activation or activation of other membrane-bound receptors. In the chapter entitled 'Mechanical regulation of nuclear structure and function', the current state of knowledge relating the nuclear architecture and the transfer of mechanical forces to the nucleus medi-

ated by the cycloskeleton is reviewed. Mechanically, the nucleus is composed of two major structures, the lamina and the nucleoplasm within it. Both structures exhibit power-law rheology under creep loading, i.e. no single time constant dominates the response. Moreover, remodelling of the nucleus induces alterations in nuclear stiffness, which may be associated with cell differentiation. These phenomena are discussed in relation to the potential influence of nuclear architecture-mediated mechano-regulation of transcription and cell fate. It is also mentioned that the cells exhibit viscoelastic material properties that are determined by their cytoskeletal organization, which in turn is influenced by external stimuli. For example, osmotic loading stimulated calcium signalling in chondrocytes, which, in turn, triggered disassembly of the actin cortex and a reduction in cell stiffness. Conversely, endothelial cells exposed to shear stress increased actin organization and stiffness. As the tools for studying intracellular biomechanics improve, the connection between physical stresses, nuclear architecture, and gene activity is becoming more apparent. It has been categorically mentioned in this chapter that our increased understanding of this connection would open up the possibility of a new realm of cell signalling pathways comprising biophysical as well as biochemical events.

The book is appropriately indexed. Like the earlier issue (Vol. 13 by the same editors), I strongly believe that this book would be an asset to the institutions as well as researchers in the field of medical biotechnology, bioengineering, biomaterials and nanobiotechnology, clinicians and biologists. This book will leave an impact in the area of medical research and in the emerging area of bioengineering.

BIKRAMJIT BASU

*Materials Research Centre,
Indian Institute of Science,
Bangalore 560 012, India
e-mail: bikram@mrc.iisc.ernet.in*