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CEPP

Frontiers
in Research

Frontiers in Research Reviews:

New Frontiers in Biomedical Engineering

INTRODUCTION

The first question that arises in introducing this series is how does biomedical engineering differ from the biomedical sciences, such as physiology and pharmacology, which are perhaps the normal bases of articles in this journal? The origin of the word 'engineer' was ultimately from the Latin *ingenium*, relating to ingenuity or clever invention.[1] The biomedical engineer relies not only on the reductionist approach in the seeking of scientific knowledge, but is also constructionist in assembling systems of understanding and manufacturing clever devices. The articles in this series provide but a small sample of the burgeoning array of ingenious methods that are being developed by engineers in collaboration with biologists to discover, understand and control biomedical processes and the design of devices to measure, image, augment and replace natural processes.

A complexity of the human body, and biology in general, resides in the multiple scales of size and time. The basic unit is the cell, which is typically 1–10 μm, compared with the complete system, a body of dimension of approximately 2 m, or six orders of magnitude greater. Atomic and molecular components of cells are orders of magnitude smaller. Process times can range from nano- and microseconds for electrical impulses and chemical reactions to the ageing process of order 100 years. In addition to the traditional scientific method of reduction to understand individual components of the human body, a systems approach is also required to appreciate interactions and feedback occurring between all the parts. Engineering has a tradition of the systems approach and has had spectacular successes in understanding and designing complex systems, such as aircraft and automobiles. Although biological systems can be even more complex, it is anticipated that a similar approach will be valuable to understand them fully.

This series is focused on the area of biofluids, not a severe restriction given the human body comprises 60–70% fluids, with numerous fluid dynamic processes occurring throughout. A major fluid flow is that of blood circulation, which appears as a common thread throughout the five articles. Highlighted are the contributions of engineering to imaging techniques, supercomputing modelling, coupled fluid/structure systems, cellular dynamics and the design of artificial parts.

A major challenge to communication between biologists and engineers is that of different language. Each discipline has its own vast set of vocabulary and the proclivity, for convenience, often to lapse into the abundant use of acronyms. As far as possible, the articles in this series seek to minimize the use of jargon, or at least use them with some explanation. Breaking down the barriers between the disciplines is an important aim of this series.

Imaging of both form and function is an extremely important area of biomedical research, with many techniques being pursued, such as fluoroscopy,[2] electron microscopy,[3] magnetic resonance imaging,[4] electron paramagnetic resonance imaging,[5] photoacoustic imaging,[6] positron emission tomography,[7] near infrared imaging[8] and ultrasound.[9]

Engineering research has a long history of contribution to imaging in fluid dynamics, with many visualization and measurement techniques developed to understand fluid flow velocity, shear stress and pressure. Fouras *et al.*[10] present three cases where the quantitative method of particle image velocimetry (PIV)[11] can be used to determine the flow and shear stress fields in respiratory, bioreactor and vascular flows. The synchrotron has evolved over a number of decades to become a powerful imaging tool, including for many biomedical applications.[12] Importantly, PIV techniques are being transferred to synchrotron X-ray imaging for measurement at the small scales typical of biomedical research to provide quantitative and dynamic views.[13,14]

The building block of life is the cell. The human body contains many types of cells; in particular, blood cells comprise erythrocytes and leucocytes, the latter being involved in the body's defence. The intersection of mechanical and chemical engineering, with their focus on the effect of mechanical forces and chemical reactions and biology, involving organic responses and transformations, is beautifully illustrated in the article by Simon *et al.*[15] The movement of a particular leucocyte, the neutrophil, from the blood stream to rolling, tethering and adhering to the vessel wall is a complex process. This transport or movement is found to result from the synchrony of mechanical and chemical properties of the neutrophil and endothelial cells in a flow shear microenvironment.

At the next level up in space dimension, the interaction of the vessels with the blood being transported is a subsystem of great importance. Fluid–structure interaction represents a traditional area of engineering research, with varied applications, such as marine structures, heat exchangers, oil/gas risers and aircraft wings. Early models of the flow of blood have assumed rigid vessel walls, which is a reasonable approximation for large arteries, but not for small

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vessels. The paper by Bertram[16] describes the fluid–structure interaction in the vasculature and the engineering tools to simultaneously model solute transport. To understand the action of the mechanosensors and chemosensors at vessel surfaces, it is important to understand the environment within which they operate. The problem of distended vessels is discussed; the analysis of the propagation and reflection of waves can be used to access information on pathological malformations of the system vasculature. Deflation of vessels is also an important problem, relevant to, for example, sleep apnoea. Two-phase flows and surface tension, common in chemical engineering, are important in pulmonary airways because of their liquid lining and are involved in the collapse of conduits, which can limit the flow in the respiratory system.

A higher level again in the study of blood flow is the modelling of the vascular system. The power of supercomputing, which has allowed engineers to undertake complete predictions of the flow field around jet aircraft, is now being harnessed with the aim of full-scale simulations of the virtual physiological human. The article by Grinberg *et al.*[17] shows remarkable simulations of the macrovascular network with three-dimensional predictions of blood flow through many connected arteries. The prospect of adding the mesovascular and microvascular networks to complete the system is discussed, with the anticipation that this will be achievable in the next 5 years. A variety of pathologies, such as cardiovascular diseases, and other aspects of medical treatment, such as drug delivery, are expected to be simulated through the growing power of supercomputing.

In addition to assembling system models, the biomedical engineer seeks to construct medical devices and artificial parts. The engineering approach has been used by Dasi *et al.*[18] in the bringing together of engineering tools of imaging, computational modelling and measurement to determine the influence of mechanical forces on cells, leading to the design and manufacture of artificial heart valves. The successful design of these valves is found to require non-physiological blood flow patterns to be understood, as well as the effect of high shearing of blood cells and platelets in the flow.

If biologists reading these articles reflect on the range of engineering techniques that are available, engineers are excited by the biological applications and each group is motivated to develop collaborative links with the other to progress understanding in biomedicine, then the series will have achieved its purpose.

REFERENCES

1. Random House. *Webster's Unabridged Dictionary*. Random House, New York. 2006.
2. Ntziachristos V. Fluorescence molecular imaging. *Annu. Rev. Biomed. Eng*. 2006; **8**: 1–33.
3. Torrealba F, Carrasco MA. A review on electron microscopy and neurotransmitter systems. *Brain Res. Rev*. 2004; **47**: 5–17.
4. Zhang H, Make JH, Prince MR. 3D contrast-enhance MR angiography. *J. Magn. Reson. Imaging* 2007; **25**: 13–25.
5. Hyde JS, Eaton GR, Eaton SS. EPR at work. *Concepts Magn. Reson. A* 2006; **28A**: 1–100.
6. Xu M, Wang LH. Photoacoustic imaging in biomedicine. *Rev. Sci. Instrum*. 2006; **77**: 041101:1–22 (doi:10.1063/1.2195024).
7. Muehllehner G, Karp JS. Positron emission tomography. *Phys. Med. Biol*. 2006; **51**: R117–37.
8. Wolf M, Ferrari M, Quaresima V. Progress of near-infrared spectroscopy and topography for brain and muscle clinical applications. *J. Biomed. Opt*. 2007; **12**: 1–14.
9. Dalecki D. Mechanical bioeffects of ultrasound. *Annu. Rev. Biomed. Eng*. 2004; **6**: 229–48.
10. Fouras A, Dusting J, Sheridan J, Kawahashi M, Hirahara H, Hourigan K. Engineering imaging: Using particle image velocimetry to see physiology in a new light. *Clin. Exp. Pharmacol. Physiol*. 2009; **36**: 238–47.
11. Adrian RJ. Twenty years of particle image velocimetry. *Exp. Fluids* 2005; **39**: 159–69.
12. Margaritondo G. The evolution of a dedicated synchrotron light source. *Phys. Today* 2008; **May**: 37–43.
13. Lee SJ, Kim GB. X-ray particle image velocimetry for measuring quantitative flow information inside opaque objects. *J. App. Phys*. 2003; **94**: 3620–3.
14. Fouras A, Kitchen MJ, Dubsky S, Lewis RA, Hooper SB, Hourigan K. The past, present and future of X-ray technology for *in vivo* imaging of function and form. *J. Appl. Phys*. 2009 (in press).
15. Simon SI, Sarantos MR, Green CE, Schaff UY. Leucocyte recruitment under fluid shear: Mechanical and molecular regulation within the inflammatory synapse. *Clin. Exp. Pharmacol. Physiol*. 2009; **36**: 217–24.
16. Bertram CD. Fluid flow in distensible vessels. *Clin. Exp. Pharmacol. Physiol*. 2009; **36**: 206–16.
17. Grinberg L, Anor T, Madsen JR, Yakhot A, Karniadakis GE. Large-scale simulation of the human arterial tree. *Clin. Exp. Pharmacol. Physiol*. 2009; **36**: 194–205.
18. Dasi LP, Simon HA, Sucosky P, Yoganathan AP. Fluid mechanics of artificial heart valves. *Clin. Exp. Pharmacol. Physiol*. 2009; **36**: 225–37.

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