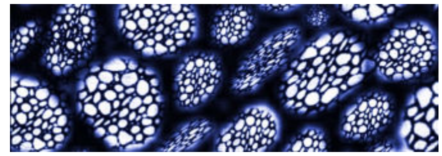

The Interface Between Biomaterials Science and Biotechnology
Medical Device Technology
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Biotechnology has evolved over the years, moving on from crop protection to drug discovery. Similarly, biomaterials science has moved forward from implantable medical device technology to drug and gene delivery and tissue engineering. It was perhaps inevitable that they should eventually meet.

Basic concepts
I am writing this column in Sydney, Australia, at AusBioTech 2006, a forum that facilitates interactions between the scientific and investment communities dealing in biotechnology. It is not surprising, therefore, that I choose to write this particular column on the role of biomaterials in biotechnology. At first sight such a statement may suggest that the article will be extremely short because biomaterials have always been associated with medical technology and not biotechnology. However, these two sectors, as they have expanded and changed direction and emphasis over the years, have started to overlap, and it is interesting to note where materials fit in the new landscape. In writing on this subject, I wish to concentrate on concepts and not semantics, although it does no harm at the outset to explain the nature of the various terms that are being used, sometimes interchangeably and often with confusion.

Biomaterials defined
The term "biomaterials" has been used traditionally and conventionally in the context of materials that are used in medical devices. Specifically, it is used where there is an intention that they have contact with the tissues of the human body, the performance of the materials being defined by the nature of their interactions with those tissues. Biomaterials must be seen within the framework of medical technology or medical engineering, which have been concerned with the use of the principles and practices of technology or engineering in medicine. Biomaterials are not defined as biologically occurring or derived materials.

The essentials of biotechnology
Biotechnology, which clearly sounds similar to medical technology, has conventionally been concerned with an entirely different concept: the use of livings systems to create products for the benefit of human beings. For example, it uses plants, animals and microorganisms or biological processes to produce foods and medicines. The "technology" in biotechnology is all about manipulation of these biological systems. With these concepts in mind, it should be understood that, notwithstanding the similarities between "engineering" and "technology" on the one hand, and between "bio" and "medicine" on the other, medical engineering and biotechnology are

extremely different. The confusion here has not been helped by the introduction of the terms tissue engineering and genetic engineering, as we shall see later.

Before moving on to discuss the tendencies for some parts of medical engineering to overlap with some parts of biotechnology, we should not forget that traditional biotechnology concepts can be used to create biomaterials. The biodegradable polymer polyhydroxybutyric acid is derived by the fermentation of bacteria, which synthesizes this polymer as an energy source, and the polymer can then be used in medical applications. Similarly, in 2005, a team from the Commonwealth Scientific and Industrial Research Organization (wvvw.csiro.au), a government research laboratory in Australia, announced that it had prepared a recombinant protein, pro-resilin. Resilin is an elastic protein found in some insects. It has high strain and energy storage capacities, which provide insects with flight and the jumping ability of fleas. CSIRO cloned a portion of the resilin gene in the insect Drosophila melanogaster and used the bacterium Escherichia coli to express this as a soluble protein, which it then cast and photo-crosslinked as a highly elastic solid that is now under consideration for the fabrication of implantable devices. [1]

Biotechnology is still concerned with its initial major roles in agriculture such as improving crop yields and developing new processes for pest control. Much of this work now involves gene technology. For example, gene silencing techniques are used to control the composition of crops for economic and nutritional purposes, and functional genomic techniques are used to identify the mechanisms by which pests overcome natural plant resistance mechanisms and to subsequently alter the plants to counteract this. However, the developments in these areas have now been accompanied by those involving the understanding of diseases in humans and the discovery of new drugs to combat a wide variety of conditions for which the more conventional pharmaceuticals and vaccines are not appropriate. At the heart of these developments are the techniques for the analysis of deoxyribonucleic acid (DNA) and of gene expression with the so-called "gene- on-a chip" and integrated platforms such as the GeneChip system developed by Affymatrix,[2] which is aimed at the elucidation of the complex biological processes of disease. Biotechnology is now much concerned with the generation of vast genomic data sets. These chips involve microarrays that require sophisticated manufacturing techniques such as photolithography and utilize fairly standard materials such as quartz, which is hardly classed as a biomaterial. Much of what happens in these microarrays occurs at the surface of the quartz wafers, but is essentially material independent. As these techniques develop, it is becoming desirable to interrogate more extensive systems than DNA and single proteins, and biotechnology is beginning to encompass the analysis of cellular behavior. In these situations, the nature of the material as well as its manufactured form is important.[3] [4] I believe that the identification of these materials as biomaterials is extremely appropriate.

Evolving biomaterials

Addressing this issue from the biomaterials/medical engineering perspective, there may be some reluctance to extend the concept of these materials from the implantable medical device to biotechnological assays, but it does have considerable merits. For a long time it has been untenable merely to consider biomaterials as those materials intended to be used for the construction of medical devices. The crucial part of the classical concept of biomaterials is that their performance should be characterized by their interaction with living systems (and preferably human living systems). Thus in itself does not imply that the materials must be within or on those living systems. We have already seen the scope of biomaterials being broadened with their use in drug delivery systems, and as vectors in gene therapy, encapsulating media for cell therapy and, most crucially, scaffolds and matrices in tissue engineering. As this evolution has taken place, there has been an increasing emphasis on the biological properties of biomaterials, rather than on their physical and mechanical properties, which many of my columns have demonstrated. It is now clear that the desirable characteristics of most long-term implantable devices are vested in their inertness, both chemically and biologically. Indeed, in the vast majority of circumstances, biomaterials are, in fact, intended not to interact with biological systems and to deliver their mechanical or physical functionality without doing any harm. With the advent of these newer technologies, the biomaterials are being required to do a little more, in fact, to help stimulate those biological systems in some way. We actually require some tissue engineering scaffolds to help stimulate cells into expressing an extra-cellular matrix, hence regenerating new tissue, and it should be no surprise that totally new paradigms of biomaterials design have been emerging.

All of this has been taking place without much obvious attention, but it is a hugely significant point in biomaterials developments. In classical biomaterials science we have never really understood how biomaterials interact with living systems at a molecular level, but we have not had to. Titanium, polytetrafluoroethylene, platinum and alumina all work well in appropriately chosen systems because they do not interact in any significant or meaningful way with those parts of the body in which we choose to place them. That is now changing with the assistance of regenerative medicine and biotechnology. Many new lessons need to be learnt.

References

1. C.M. Elvin et al.,·"Synthesis and Properties of Crosslinked Recombinant Pro-Resilin," *Nature*, 437, 999-1002, 2005.
2. www.affymatrix.com, accessed 20 November 2006.
3. N. Li et al., "Biology On A Chip: Microfabrication For the Study of the Behavior of Cultured Cells," *Crit. Rev. Biomed. Eng.* 3, 335-73, 2001.
4. W. Senaratne et al., "Self-Assembled Monolayers and Polymer Brushes in Biotechnology," *Biomacromolecules*, 6, 2427-48, 2005.