In my 1995 Guest Editorial, “Biomaterials in the 21st Century?” (JRRD 1995;32(3):vii–viii), I discussed many of the new devices, organ replacements, prostheses, and orthoses for use in rehabilitation. In concluding that editorial, I introduced what is now considered by almost all biomaterials researchers to be the exciting future of the field, the concept of biomimetics and its associated methodology, tissue engineering (although these terms were not used specifically in the editorial). What I now wish to address in more detail are these two driving forces of biomaterials research in the present and for the future.

Biomimetics has become a key methodology in biomaterials research. In the former editorial, I defined it as, “the development of synthetic materials systems based on information derived from biological systems.” This definition is essentially a paraphrase of the definition I used in “Biomimetic Materials” in the 1994 McGraw-Hill Yearbook of Science and Technology. Although the concept of biomimetics goes back several decades, full importance of using a biomimetics approach in developing new materials became apparent nationally when the NSF sponsored a University/Industry Workshop on Biomolecular Materials, October 1990. International recognition soon followed as evidenced by the Bionic Design International Workshop: Molecular Machine System and Biocrystallization and Adaptive Structure held in Tsukuba, Japan, January 1992. Since then, several journals emphasizing biomimetics have been introduced.

Biomimetic research is directed at developing knowledge of the biological processes, cellular and sub-cellular, that are responsible for the initiation and subsequent growth and development of tissues, organs, or structures with specific properties and functions. Such knowledge could then be applied using modern techniques of cell and molecular biology, genetic engineering, and state-of-the-art technology. This is where tissue engineering comes in. It may be loosely defined as the integration of cellular and molecular biology with materials, mechanical, electrical, and chemical engineering to manipulate and/or reconstruct tissue function and properties. Or as my junior colleague Dr. Ravi V. Bellamkonda (one of the new breed of biomaterials scientists trained in tissue engineering) has so aptly put it, “tissue engineering is an interdisciplinary effort to develop protocols for: structural augmentation, regeneration, or functional replacement of compromised tissues.” This can be achieved by using modern biological and instrumental techniques to organize cells and control their
phenotypical expression to help solve the medical problems created by such compromised tissues. He also has provided a neat, simple diagram that demonstrates the tissue engineering approach for the functional replacement of tissues (Figure 1).

Thus, instead of the traditional concept of biomaterials (i.e., neat, passive, load-bearing, safe), we now wish to develop active "designer" biomaterials by careful design based on structural and chemical modification, by developing templates for cell seeding and selective gene expression, and by developing controlled or evoked response through receptor-mediated interactions. How does all of this impact on the needs of Veterans in specific and the over-all population in general? The answer to this question may be found by simply citing all the areas of research presently underway using tissue engineering to develop biomaterials to replace tissues, organs or structures necessary to maintain or enhance the quality of life, or in some cases to maintain life itself. Examples of tissue engineering have been presented in much greater detail than I can cover here in a short editorial. The importance and range of research in the field is exemplified by an entire section of 16 chapters presented under the title "Tissue Engineering" in the Massive CRC Press/IEEE Press 1995 volume, The Biomedical Engineering Handbook.

Cell-surface interactions are being studied as the adherence of cells to a culture support is necessary in the development of new dermal dressings and other soft tissue replacements. The adsorption of proteins into surfaces is studied as a precursor to developing more effective cardiovascular devices and prostheses or to develop surfaces that encourage bone healing. Understanding the relationship between the states of protein adsorption and cell-protein-surface interactions should lead to the development of blood-compatible materials that last the lifetime rather than determining the lifetime of the recipient of the required cardiovascular prosthesis or device. Critical here is the understanding of the effects of fluid shear stresses on cellular function. How such stresses affect the adhesion of cells to various surfaces is also important. Also blood related is the attempt to reconstitute bone marrow, because of its importance in the development of mature blood cells from immature stem cells. Other research is directed at developing blood substitutes, especially of concern for situations where transfusion is needed in the absence of donor blood. Tissue engineering is being used to develop substitutes that create many functional liver equivalents as an alternative to liver transplants; clearly a profound need, as the number of livers required for transplantation yearly exceeds the number of donors by almost 10-fold.

As with liver transplants, there are insufficient donors for kidney transplants. Thus, the major treatment for the loss of kidney function due to damage or pathology is dialysis, a costly, time- and energy-consuming procedure. Not all dialysis users gain the same degree of health maintenance on dialysis. Here, tissue engineering leading to an implantable composite-synthetic material/biological tissue, the bioartificial kidney, appears to be a significant approach to provide relief for the many dialysis users who are not immediate or suitable candidates for a transplant.

One of the areas of tissue engineering most exciting and relevant to the VA’s Rehab R&D mission is its application in the nervous system. Damage or degeneration of neural tissues can lead to paralysis or disease such as Parkinson’s. Replacement of specific neuroactive molecules could eventually aid in treatment of severe pain, as suffered by cancer patients; Parkinson’s disease; Alzheimer’s disease; and what is known as Lou Gehrig’s disease (amyotrophic lateral sclerosis) among others. Another aspect of the effort in the nervous system is nerve regeneration by tissue reconstruction. The importance of this in injuries or pathology leading to spinal dysfunction

![Figure 1.](image_url)

**Figure 1.**
The dynamics of tissue engineering (after Bellamkonda).
is obvious. Similar techniques could be used in restoration of the optic nerve when damaged. Under ideal circumstances there is even the possibility of the direct fusion of severed axons. These attempts to enhance regeneration and aid in the reconstruction of cut or damaged neural tissues is being researched in both the peripheral and central nervous system. It is also possible to use tissue engineering of neuronal cells to develop biosensors or the bridging of nerves with external electronics in order to control artificial limb prostheses.

Tissue engineering is being used in attempts to cure diabetes by developing implantable materials to release encapsulated pancreatic islet cells within the body rather than the traditional method of injecting insulin on a scheduled basis. Similar studies are developing implantable materials for other immunoprotective devices. Massive losses of dermal tissue due to fire or pathology means disfigurement or, at worst, death. Thus, the development of skin regeneration based on an analog of the extracellular matrix as a template is actively under way. There already is evidence that this technique will create regeneration of the dermis rather than scar tissue in wounds where no regeneration occurs spontaneously. There are studies underway to develop a template for meniscus regeneration. The meniscus in the knee has important functions in knee biomechanics. When torn due to pathology or injury as in many sports, it causes pain and limits knee function. Thus, regeneration of the tissue is to be desired. Other important areas of the musculoskeletal system in which tissue engineering is playing an important role include the repair of skeletal muscles, tendons, ligaments, cartilage, and even bone itself.

This is the exciting and challenging future for biomaterials/biomedical engineering researchers. It will be the “new breed,” who are as well versed in cellular and molecular biology as they are with specialized aspects of materials science and engineering, along with expertise in mechanical or electrical or chemical engineering, who will be at the forefront of this dynamic, society-serving endeavor.

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