S&T

Perspective

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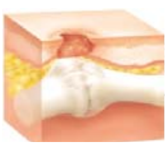
Science and Technology at Strategic Analysis, Inc.

Wound Healing: Present and Future

Enhancing the rate and quality of wound repair is critical to maintaining military functionality both in wartime and during training. Wounds occur from numerous mechanisms including blunt, burn, and penetrating trauma. Regardless of the cause, the repair process prevents blood loss, fights infection, removes devitalized tissue, restores blood flow and forms new tissue. These processes are generally fall into one of three phases: the inflammatory phase including clot formation and influx of immune cells, the proliferative phase consisting of clot resorption and formation of new tissue and vasculature, and finally the remodeling phase consisting of a reduction in cellularity of the wound and scar tissue maturation. The phases are not strongly discrete but represent a continuum of overlapping cellular and systemic processes, all affected by the nutritional, immune and psychological status of the injured individual.



Coordination of wound healing is partly driven by proteins called growth factors, which are secreted by and act on the involved cells. Growth factors stimulate cellular migration and proliferation and the synthesis of extracellular matrix molecules like collagen. Growth factors also attract and activate circulating monocytes and tissue macrophages (and possibly stem cells). Therefore, healing is in part initiated by the early "calling" for action conveyed by these chemical mediators; preclinical studies on the promotion of wound healing by exogenously added peptide growth factors are promising, although hurdles remain to realize their full clinical potential.

Any compromise in meeting the hypermetabolic needs of tissue repair can negatively affect the outcome of tissue repair. The requirement of adequate tissue oxygenation has led to its therapeutic use in the form of hyperbaric O2 therapy and topical delivery via catalytic synthesis of O2 or in the form of oxygenated gels. Another therapeutic strategy is to provide a favorable structural environment for healing to occur, including use of advanced wound dressings that incorporate acellular protein scaffolds alone or with embedded cells or therapeutic genes capable of promoting more rapid and complete healing.

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Data Fusion and Cooperation for Wireless Sensor Networks

Wireless sensor networks can enable many novel applications for homeland security and military operations. Wireless sensor networks represent a real-world example of pervasive computing and offer a powerful new way to interact with and acquire knowledge of the environment.

However, there are a number of challenges in employing a wireless sensor net. The sensors can be subject to severe resource and operational constraints, such as slow processors, small memory sizes, short battery life, low communications bandwidth, short transmission range, and an unreliable network connection. At the same time, the network should have the ability to self-organize, forming clusters of sensor nodes, since wireless sensor networks will often have many nodes and will be deployed in remote environments. This process should be done in a way that optimizes the performance of the sensor network applications. Combined with timeliness requirements for most sensor data and a dynamic network topology, these constraints create an environment unsuitable for many traditional distributed algorithms. Algorithms for wireless sensor networks must have low communication overhead, rely as much as possible on local information, adapt to failures and changes in network conditions, and produce results in a timely fashion. Thus, one must consider the interaction of the self-organization algorithm and the distributed detection processing. The effects of the connectivity of the wireless network and the sensitivity of the sensors on the detection performance also must be studied.

In this research, Strategic Analysis proposes to examine data fusion and sensor cooperation to improve sensor performance. A key performance goal for any sensor is to have a high probability of detection (Pd) and a low probability of false alarm (Pfa). For a wireless, distributed sensor network, we will demonstrate that data fusion and cooperation among sensors can improve system performance.

For more information about sensor networks, please contact Julius Chang at 703-797-4518, jchang@sainc.com.

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www.sainc.com/TechnicalReports/index.htm.

M-CALC IV

A two-day industry meeting on Military and Commercial Applications for Low-cost Cryocoolers (MCALC) was held in San Diego, CA on November 20th and 21st, 2003. The meeting was sponsored by Strategic Analysis, Inc. (www.sainc.com) in cooperation with DARPA, the Army Night Vision Labs (NVESD), and Dr. Martin Nisenoff of Nisenoff and Associates (retired NRL). Attendees included representatives from the U.S. and foreign cooler vendors, users, and integrators, with presentations discussing their cryocooler needs and programs. The continuing objective of this workshop is to perform an industry assessment on the current status of low cost, highly reliable cryocoolers and to estimate the current and perceived needs of the cooled electronic communities. Emphasis is focused on low cost cryocoolers operating in the temperature ranges below 232 K (- 40 C) with attention to the requirements of the user communities on reliability, efficiency, temperature stability, EMI, vibration, audible noise, etc.

During the workshop, Cryocooler vendors and representatives from the user communities (such as IR cameras, cooling of semiconductor devices and chips, cellular base stations, satellite applications, medical applications, and high temperature superconductivity) outlining their projection of cryocoolers needed for present and future generation of equipment. MCALC IV also had additional presentations from some key low-temperature (down to 4K) applications and cryocooler companies. The twenty-three invited speaker presentations included twelve cryocooler manufacturers, ten users, and one discussion of the Cryocooler Database sponsored by the University of Twente of the Netherlands. There was also exhibitor space available for cryocoolers vendors to display their products, brochures and technical data.

The Proceedings from MCALC IV is now available on CD. To view the conference agenda, to find out more information on the MCALC IV Conference, to express interest in MCALC V, to have your name added to the MCALC contact list, or to purchase a Proceedings CD, please visit http://www.sainc.com/MCALC4.

Wound Healing: Present and Future

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Thermal lasers also show promise for wound closure (or "tissue welding"). Laser energy is thought to achieve wound closure by collagen denaturation and cross-linking in addition to stimulating collagen synthesis. New biological solders should improve the ease of use and outcome in terms of wound strength and appearance. Tissue welding also has application for repair of nerve, vascular, microvascular and connective tissue (e.g., tendon) injuries.

It is theorized that gene therapy, the genetic manipulation of the genome to achieve a therapeutic outcome, could overcome shortcomings encountered with peptide growth factors. The concept of gene therapy for wound healing would involve insertion of a gene for expression by local cells to stimulate/support the healing process. Genes with therapeutic potential include growth factors and components of metabolic pathways for the improvement of energy utilization. It is likely that additional genes will be identified through the Human Genome Project. However, substantial obstacles related to gene delivery and expression exist and are areas of intense research.

Future therapies will undoubtedly be driven by the fields of stem cell and regenerative biology. Regeneration-the true recreation of damaged tissue to its original state-is the gold standard of repair. The ability of certain species (e.g., amphibians) and human tissue (e.g., fetal tissue) to regenerate is well appreciated; development of regenerative therapies will require continued advances in molecular and genomic techniques combined with contributions from the fields of development, embryology and tissue pattern formation. Such therapies will likely involve the use of stem cells, undifferentiated cells capable of producing daughter cells of potentially any tissue type. The working hypothesis is that stem cells would provide daughter cells that contribute to repair. Two important areas of research include learning how to enhance recruitment of stem cells to the site of injury and how to manipulate activation of these cells. Incorporation of recruitment and activation signals into advanced dressings should be an attainable goal once these cues are better understood.

For more information about wound healing, please contact Dr. Jon Mogford at 703-797-4583, jmogford@sainc.com.

Improving Warfighter Information Intake Under Stress

The 2004 Augmented Cognition (AugCog) Principal Investigator meeting entitled "Improving Warfighter Information Intake under Stress with Augmented Cognition", was held from January 5-8 in Orlando, Fl. The goal of AugCog is to improve the human-computer interaction capacity through enhancements to human performance in stressful operational environments. The program recognizes that the tremendous advances in the microcomputer realm have rendered the human the "limiting reaction" for decision making. Inspired technologies look to develop computer systems that adapt to the status and/or capabilities of the involved human.

This meeting focused on mitigating strategies, such as computer recognitionof mental/physical status of the operator, requiring measurement of physiological phenomena in real-time. Mitigation processes focus on information presentation to the human in regards to timing and modality of presentation (e.g., auditory vs. visual). Systems also determine when to abort missions that "overload" a user. Concept Validation Demonstrations by program teams demonstrated such strategies based on operator status, communications management and modality switching. Identification of functional bottlenecks provided foci for model improvement and future directions.

The meeting's main sessions included historical perspectives of the interest in determining user workload, and trying to determine when the brain is "busy". Talks ranged from philosophical perspectives as offered by Dr. Dennis McBride, President of Potomac Institute for Policy Studies, to discussion of understanding how complex situations affect group dynamics as presented by Dr. Peter Merkle of Sandia National Laboratories. Lt. Richard Arnold, PhD, addressed approaches to cognitive state measurement and classifying such states in relation to the task being performed. Such measurements, perhaps filtered for improved selectivity of inputs, should result in actionable meaning provided at the correct tempo. Breakout sessions focused on topics including team mitigation strategies and functional Near Infrared (fNIR) Imaging.

A highlight of the meeting was a presentation by Nobel Laureate Gerald A. Edelman entitled "Neural Darwinism - From Dynamics to Consciousness" Dr. Edelman detailed the inter-relationships among neural plasticity, brain development and consciousness. This overview of his theory regarding the development of the human mind contrasted well with the discussions of complex human-computer interactive systems. AugCog-inspired technologies and methods continue to evolve to incorporate technological advances into applied experimentation and real-world utilization.

For more information about the 2004 Aug Cog meeting, please contact Jon Mogford at 703-797-4583, jmogford @sainc.com.

New Faces at SA

Jon Mogford, PhD: Dr. Mogford joined Strategic Analysis in December 2003 and is working part-time on various projects in DARPA. He obtained his doctoral degree from Texas A&M Health Science Center (Department of Medical Physiology), where he worked on microvascular responses to tissue injury. Most recently he worked in the Wound Healing Research Laboratory at Northwestern University where he coordinated a multi-disciplinary team on a variety of NIH- and pharmaceutical/biotechnology-sponsored projects. This work is focused on the cellular and molecular processes of cutaneous wound healing and scarring; these processes and concepts are applicable to all biological responses to tissue injury. In addition, he has had extensive interaction with industry working with a number of biotechnology/pharmaceutical companies over the last 4 years on wound healing and scarring projects.

New Publications by SA Staff

"Collagen prolyl 4-hydroxylase inhibitor reduces scar elevation in a rabbit ear model of hypertrophic scarring". Wound Repair & Regeneration 2003; 11: 368-372. Kim I and **Mogford JE**, Witschi C, Nafissi M, Mustoe TA.

"Use of Hypoxia-Inducible Factor Signal Transduction Pathway to Measure O2 Levels and Modulate Growth Factor Pathways". Wound Repair & Regeneration 2003; 11(6): 496-503. **Mogford JE**, Roy NK, Cross KJ, Mustoe TA.

"A Novel Murine Model of Cyclical Cutaneous Ischemia-Reperfusion Injury". Journal of Surgical Research 2004; 116(1): 172-180. Reid RR, Sull AC, **Mogford JE**, Roy N, Mustoe TA.

"PDGF-B but not FGF2 plasmid DNA improves survival of ischemic myocutaneous flaps". Archives of Surgery 2004; 139: 142-147. Hijjawi J and **Mogford JE**, Chandler LA, Cross KJ, Said H, Sosnowski BA, Mustoe TA.

"Impact of Aging on Gene Expression in a Rat Model of Ischemic Cutaneous Wound Healing". (Manuscript accepted, Journal of Surgical Research). **Mogford JE**, Sisco M, Robinson AM, Bonomo SR, Zhao Y, Mustoe TA.