cific application could be performed, which would then match the characteristics of the antenna with the protein solder and tissue to best effect wound closure. An additional area of interest with potential benefit that remains to be validated is whether microwave energy can effectively kill bacteria in and around the wound. Thus, this may be an efficient method for simultaneously sterilizing and closing wounds.

Using microwave energy to seal wounds has a number of advantages over lasers, which are currently in experimental use in some hospitals. Laser tissue welding is unsuitable for emergency use because its large, bulky equipment cannot be easily moved between operating rooms, let alone relocated to field sites where emergencies often occur. In addition, this approach is highly dependent on the uniformity and thickness of the protein solder as well as the surgeon's skills. In contrast, the use of microwave energy is highly tolerant of the thickness of the protein solder, level of fluids in and around the wound, and other parameters that can adversely affect the outcome of laser welding. However, controlling the depth of penetration of the microwave energy into the wound is critical for achieving effective wound sealing without damaging the adjacent tissue. In addition, microspheres that encapsulate metallic cores could also be incorporated into the protein solder to further control the depth of penetration of the microwave energy.

This work was performed by G. Dickey Arndt, Phong H. Ngo, Chau T. Phan, and Diane Byerly of Johnson Space Center; John Dusl of Jacobs Sverdrup; Marguerite A. Sognier of Universities Space Research Association; and Jim Carl of Advanced Electromagnetics. For further information, contact the JSC Innovation Partnerships Office at (281) 483-3809.

This invention is owned by NASA, and a patent application has been filed. Inquiries concerning nonexclusive or exclusive license for its commercial development should be addressed to the Patent Counsel, Johnson Space Center, (281) 483-1003. Refer to MSC-24238-1.

Principles, Techniques, and Applications of Tissue Microfluidics

This technique can be used in the diagnosis of diseases such as cancer.

NASA's Jet Propulsion Laboratory, Pasadena, California

The principle of tissue microfluidics and its resultant techniques has been applied to cell analysis. Building microfluidics to suit a particular tissue sample would allow the rapid, reliable, inexpensive, highly parallelized, selective extraction of chosen regions of tissue for purposes of further biochemical analysis. Furthermore, the applicability of the techniques ranges beyond the described pathology application. For example, they would also allow the posing and successful answering of new sets of questions in many areas of fundamental research.

The proposed integration of microfluidic techniques and tissue slice samples is called "tissue microfluidics" because it molds the microfluidic architectures in accordance with each particular structure of each specific tissue sample. Thus, microfluidics can be built around the tissues, following the tissue structure, or alternatively, the microfluidics can be adapted to the specific geometry of particular tissues. By contrast, the traditional approach is that microfluidic devices are structured in accordance with engineering considerations, while the biological components in applied devices are forced to comply with these engineering presets.

The proposed principles represent a paradigm shift in microfluidic technology in three important ways:

- Microfluidic devices are to be directly integrated with, onto, or around tissue samples, in contrast to the conventional method of off-chip sample extraction followed by sample insertion in microfluidic devices.
- Architectural and operational principles of microfluidic devices are to be subordinated to suit specific tissue structure and needs, in contrast to the conventional method of building devices according to fluidic function alone and without regard to tissue structure.
- Sample acquisition from tissue is to be performed on-chip and is to be integrated with the diagnostic measurement within the same device, in contrast to the conventional method of off-chip sample prep and subsequent insertion into a diagnostic device. A more advanced form of tissue integration with microfluidics is tissue encapsulation, wherein the sample is completely encapsulated within a microfluidic device, to allow for full surface access.

The immediate applications of these approaches lie with diagnostics of tissue slices and biopsy samples — e.g. for cancer — but the approaches would also be very useful in comparative genomics and other areas of fundamental research involving heterogeneous tissue samples.

The approach advocates and utilizes the bottom-up customization of microfluidic architectures to biosamples, in contrast to the traditional top-down approach of building the architectures first and then putting the biosamples inside. Further, as particular embodiments of the above principle, novel techniques of sub-sample selection and isolation are presented. These techniques would have wide applicability in fundamental research and biomedical diagnostics.

In particular, an *in situ* microfluidic technique of single-cell isolation, or multiple single-cell isolations, is described, and is performed upon tissue sections attached to pathology glass slides. The technique combines the advantages of preserving the architectural integrity of the tissue section while allowing flexibility and precision of cell selection, rapid prototyping, and enhanced sample purity, while benefiting from the experience of the pathologist in the selection process. The result is a system that would allow the rapid and reliable biochemical analysis and diagnosis of pathologic processes with sensitivity extended down to the level of even a single cell, with high levels of confidence in the diagnostic determination.

These techniques would allow the extraction of cells and cell nuclei chosen for their potentially pathologic origin,

e.g. cancer. The chief advantages of the proposed methods are their speed, ease, reliability, and capacity to select individual cells from a tissue slice population with a higher degree of purity and specificity. The result is the extracted DNA can be biochemically analyzed with a higher degree of diagnostic accuracy, as the isolated sub-sample would not be diluted by unwanted material from the ambient tissue. In comparison to other techniques, the proposed methods would combine high specificity with high speed.

This work was done by Lawrence A. Wade of Caltech and Emil P. Kartalov, Darryl Shibata, and Clive Taylor of the University of Southern California for NASA's Jet Propulsion Laboratory. Further information is contained in a TSP (see page 1).

In accordance with Public Law 96-517, the contractor has elected to retain title to this invention. Inquiries concerning rights for its commercial use should be addressed to:

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Refer to NPO-47561, volume and number of this NASA Tech Briefs *issue, and the page number.*

Robotic Scaffolds for Tissue Engineering and Organ Growth

Biocompatible and biodegradable smart scaffolds could reconfigure their shape and size to accommodate organ development.

NASA's Jet Propulsion Laboratory, Pasadena, California

The aim of tissue engineering (TE) is to restore tissue and organ functions with minimal host rejection. TE is seen as a future solution to solve the crisis of donor organs for transplant, which faces a shortage expected only to increase in the future. In this innovation, a flexible and configurable scaffold has been conceived that mechanically stresses cells that are seeded on it, stimulating them to increased growth.

The influence of mechanical stress/loading on cell growth has been observed on all forms of cells. For example, for cartilages, studies in animals, tissue explants, and engineered tissue scaffolds have all shown that cartilage cells (chondrocytes) modify their extracellular matrix in response to loading. The chondrocyte EMC production response to dynamics of the physical environment (*in vivo* cartilage development) illustrates a clear benefit (better growth) when stressed. It has been shown that static and dynamic compression regulates PRG4 biosynthesis by cartilage explants.

Mechanical tissue stimulation is beneficial and (flexible) scaffolds with movable components, which are able to induce mechanical stimulation, offer advantages over the fixed, rigid scaffold design. In addition to improved cell growth from physical/mechanical stimulation, additional benefits include the ability to increase in size while preserving shape, or changing shape.

By making scaffolds flexible, allowing relative movement between their components, adding sensing (e.g., for detecting response of cells to drug release and to mechanical actions), building controls for drug release and movement, and building even simple algorithms for mapping sensing to action, these structures can actually be made into biocompatible and biodegradable robots. Treating them as robots is a perspective shift that may offer advantages in the design and exploitation of these structures of the future.

This work was done by Adrian Stoica of Caltech for NASA's Jet Propulsion Laboratory. For more information, contact iaoffice@jpl.nasa.gov.

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Stress-Driven Selection of Novel Phenotypes

A methodology allows the experimental design of novel peptides and RNAs that have desired properties.

Lyndon B. Johnson Space Center, Houston, Texas

A process has been developed that can confer novel properties, such as metal resistance, to a host bacterium. This same process can also be used to produce RNAs and peptides that have novel properties, such as the ability to bind particular compounds. It is inherent in the method that the peptide or RNA will behave as expected in the target organism. Plasmid-born mini-gene libraries coding for either a population of combinatorial peptides or stable, artificial RNAs carrying random inserts are produced. These libraries, which have no bias towards any biological function, are used to transform the organism of interest and to serve as an initial source of genetic variation for stress-driven evolution.

The transformed bacteria are propagated under selective pressure in order to obtain variants with the desired properties. The process is highly distinct from *in vitro* methods because the variants are selected in the context of the cell while it is experiencing stress. Hence, the selected peptide or RNA will, by definition, work as expected in the target cell as the cell adapts to its presence during the selection process. Once the novel gene, which produces the sought phenotype, is obtained, it can be transferred to the main genome to increase the genetic stability in the organism. Alternatively, the cell line can be used to produce novel RNAs or peptides with selectable properties in large quantity for separate purposes. The system allows for easy, large-scale purification of the RNAs or peptide products.