



Ex Vivo Growth of Bioengineered Ligaments and Other Tissues

Lifelike mechanical loads cause cell cultures to grow into lifelike structures.

Lyndon B. Johnson Space Center, Houston, Texas

A method of growing bioengineered tissues for use in surgical replacement of damaged anterior cruciate ligaments has been invented. An anterior cruciate ligament is one of two ligaments (the other being the posterior cruciate ligament) that cross in the middle of a knee joint and act to prevent the bones in the knee from sliding forward and backward relative to each other. Anterior cruciate liga-

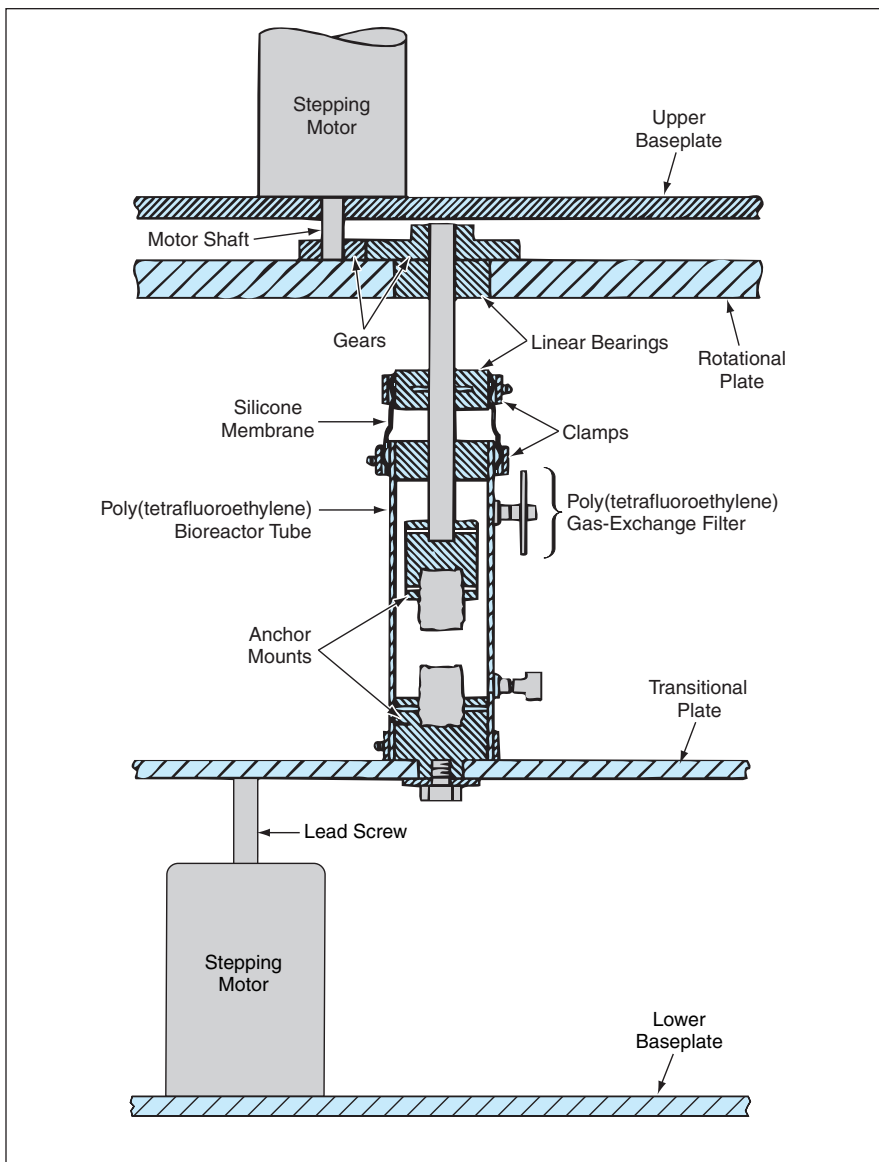
ments are frequently torn in sports injuries and traffic accidents, resulting in pain and severe limitations on mobility. By making it possible to grow replacement anterior cruciate ligaments that structurally and functionally resemble natural ones more closely than do totally synthetic replacements, the method could create new opportunities for full or nearly full restoration of functionality

in injured knees. The method is also adaptable to the growth of bioengineered replacements for other ligaments (e.g., other knee ligaments as well as those in the hands, wrists, and elbows) and to the production of tissues other than ligaments, including cartilage, bones, muscles, and blood vessels.

The method is based on the finding that the histomorphological properties of a bioengineered tissue grown *in vitro* from pluripotent cells within a matrix are affected by the direct application of mechanical force to the matrix during growth generation. This finding provides important new insights into the relationships among mechanical stress, biochemical and cell-immobilization methods, and cell differentiation, and is applicable to the production of the variety of tissues mentioned above. Moreover, this finding can be generalized to nonmechanical (e.g., chemical and electromagnetic) stimuli that are experienced *in vivo* by tissues of interest and, hence, the method can be modified to incorporate such stimuli in the *ex vivo* growth of replacements for the various tissues mentioned above.

In this method, a three-dimensional matrix made of a suitable material is seeded with pluripotent stem cells. The patient's bone-marrow stromal cells are preferably used as the pluripotent cells in this method. Suitable matrix materials are materials to which cells can adhere — for example, collagen type I. The seeded matrix is attached to anchors at opposite ends and then the cells in the matrix are cultured under conditions appropriate for the growth and regeneration of cells. Suitable anchor materials are materials to which the matrix can attach; examples include demineralized bone and Goinopra coral that has been treated to convert its calcium carbonate to calcium phosphate.

During the growth process, the matrix is subjected to a combination of tension, compression, torsion, and shear stresses via movement of one or both of the anchors. The figure depicts the combination of (1) a bioreactor tube within which the growth process takes place



The **Anchor Mounts Inside the Bioreactor Tube** are rotated and translated by two stepping-motor-driven mechanisms during growth of a cell culture in a matrix attached to the anchor mounts. The motions impose stresses like those experienced by the cells *in vivo*.

and (2) an apparatus that operates under computer control to generate the required motions. Optimally, the stresses should mimic those to which the anterior cruciate ligament is subjected *in vivo* during normal activity. The bioengineered ligament produced by this method is characterized by a cellular orientation and/or matrix crimp pattern in the direction of the applied mechanical forces, and by the production of collagen type I, collagen type III, and fi-

bronectin proteins along the axis of mechanical loading. Optimally, the ligament thus produced contains fiber bundles arranged in a helical pattern.

This work was done by Gregory Altman, David L. Kaplan, Ivan Martin, and Gordana Vunjak-Novakovic of Massachusetts Institute of Technology for Johnson Space Center.

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:

*Technology Licensing Office
Massachusetts Institute of Technology
Five Cambridge Center, Kendall Square
Room NE25-230
Cambridge, MA 02142-1493
Phone: (617) 253-6966
Fax: (617) 258-6790
E-mail: tlo@mit.edu*

Refer to MSC-23351, volume and number of this NASA Tech Briefs issue, and the page number.

Stroboscopic Goggles for Reduction of Motion Sickness

The view is presented to wearer in snapshots to suppress retinal slip.

Lyndon B. Johnson Space Center, Houston, Texas

A device built around a pair of electronic shutters has been demonstrated to be effective as a prototype of stroboscopic goggles or eyeglasses for preventing or reducing motion sickness. The momentary opening of the shutters helps to suppress a phenomenon that is known in the art as retinal slip and is described more fully below.

While a number of different environmental factors can induce motion sickness, a common factor associated with every known motion environment is sensory confusion or sensory mismatch. Motion sickness is a product of misinformation arriving at a central point in the nervous system from the senses from which one determines one's spatial orientation. When information from the eyes, ears, joints, and pressure receptors are all in agreement as to one's orientation, there is no motion sickness. When one or more sensory input(s) to the

brain is not expected, or conflicts with what is anticipated, the end product is motion sickness.

Normally, an observer's eye moves, compensating for the anticipated effect of motion, in such a manner that the image of an object moving relatively to an observer is held stationary on the retina. In almost every known environment that induces motion sickness, a change in the gain (in the signal-processing sense of "gain") of the vestibular system causes the motion of the eye to fail to hold images stationary on the retina, and the resulting motion of the images is termed retinal slip.

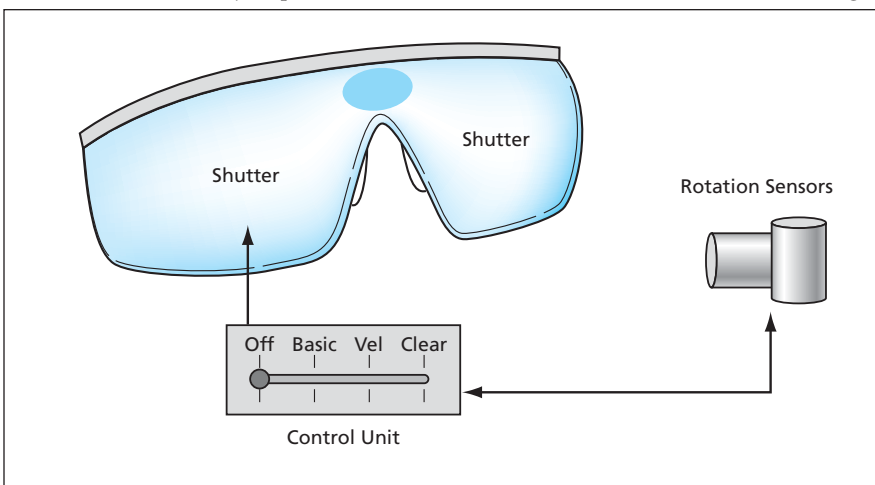
The present concept of stroboscopic goggles or eyeglasses (see figure) is based on the proposition that prevention of retinal slip, and hence, the prevention of sensory mismatch, can be expected to reduce the tendency toward motion sickness. A device according to

this concept helps to prevent retinal slip by providing snapshots of the visual environment through electronic shutters that are brief enough that each snapshot freezes the image on each retina. The exposure time for each snapshot is less than 5 ms. In the event that a higher rate of strobing is necessary for adequate viewing of the changing scene during rapid head movements, the rate of strobing (but not the exposure time) can be controlled in response to the readings of rate-of-rotation sensors attached to the device.

The shutters are compact, fast-acting, low-voltage, low-current liquid-crystal display devices of the polymer-dispersed liquid-crystal type. The shutters are installed in the lens spaces in the goggle or eyeglass frame. Sensors that measure the rates of rotation about the yaw and pitch axis are attached to the frame. Also included is a controller unit that contains a low-frequency oscillator and a switchable driver that receives the rotation-sensor readings. As now envisioned, a user of a production version of the device could select any of at least four basic modes of operation:

- Mode 1: The device would be turned off.
- Mode 2: The shutters would be held transparent, allowing ordinary vision.
- Mode 3: The shutters would open at a standard stroboscopic flash rate of 4 Hz.
- Mode 4: The flash rate would be adjusted according to the sensed rates of rotation. The maximum flash rate would be 40 Hz.

The standard flash rate of 4 Hz was chosen partly on the basis of effectiveness in suppressing motion sickness and



A Pair of Goggles or Eyeglasses contains electronic shutters in place of or in addition to lenses. The shutters can be strobed at either a constant rate or a rate that depends on the rates of yaw and pitch of the wearer's head.