Reimagine

A New Instron® Way

Tissue Engineering and Regenerative Medicine

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Welcome

Since 1946, Instron® has been dedicated to providing you with comprehensive solutions for your research, quality, and service-life testing requirements. Today, we are Reimagining a New Instron Way by leveraging our innovative technology in partnership with the recent acquisition of Tissue Growth Technologies (TGT) to provide the most comprehensive commercial solution for the Tissue Engineering and Regenerative (TERM) market.

Replacing body parts is one of mankind's earliest aims, as patients and healers have attempted to cope with disabilities. Tissue Engineering & Regenerative Medicine are dedicated to creating new tissue-engineered medical devices that replace and/or enhance tissue function that has been impaired by disease, injury, or age. Instron products are designed to assist this process at every step from characterization of native tissues to cell culture or evaluation of tissue engineered products.

We present the following TERM 2014 Year in Review to help you Reimagine Your New Instron Way in the world of Tissue Engineering and Regenerative Medicine! Sign up for our TechNotes Bio newsletter at go.instron.com/technotesbio to stay current with our cutting-edge solutions.

You might need a new Instron tissue engineering solution if you...

- Do 3D cell culture
- Develop or evaluate scaffold materials
- Use a bioreactor chamber
- Perform mechanical stimulation inside an incubator
- Perfuse media through your sample

INTRODUCING THE INSTRON® BIOREACTORS

Instron® frames are integrated with clean test chambers, submersible fixtures, and biologically compatible materials, and are designed with flexibility to meet these application demands. The temperature-controlled BioBath and submersible pneumatic grips allow for ease of specimen loading and alignment in an accurately controlled fluid environment. This bath was specifically designed for compatibility with our video extensometers, allowing for unparalleled accuracy in strain measurement. Together, the Instron testing system and accessories provide the biologic and mechanical environment necessary to determine tissue engineering benchmarks.

Instron's Bioreactor Series of instruments set the standard for 3D cell culture and tissue engineering research. Available for most construct geometries, these instruments mimic the in vivo mechanical environment with user-controlled loading conditions. The modular design allows for virtually limitless system configurations, ensuring that the bioreactor systems can meet Researchers needs today and in the future. Chambers and grips can also be used on standard Instron frames for seamless transition from cell culture to characterization and evaluation.

Pulsatile Pressure

LumeGen

- Provides physiological flow and pressures
- Current research applications include blood vessel and heart valve tissue engineering

Tension

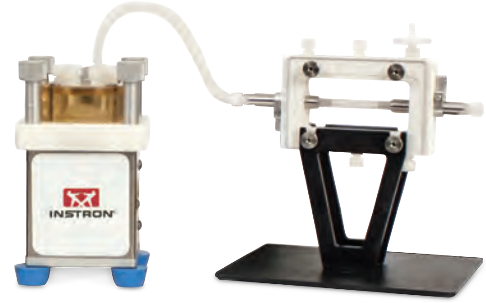
LigaGen

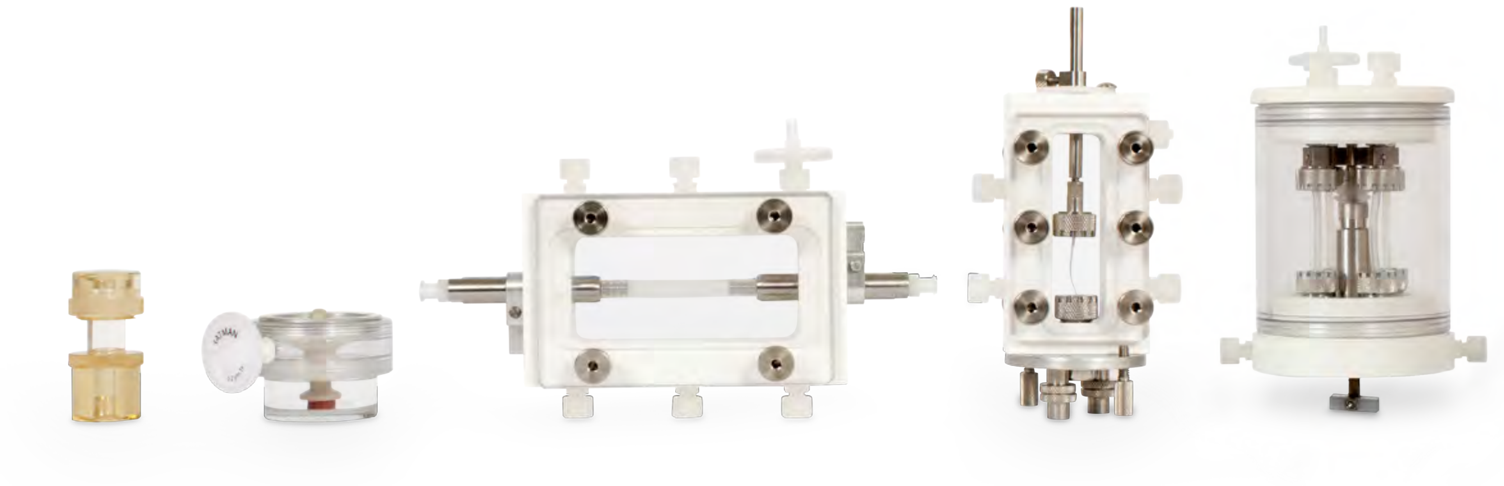
- Provides physiological tension
- Current research applications include ACL tissue engineering, collagen gel stimulation, and human hand tissue engineering

Compression

CartiGen & CartiGen HP

- Provides physiologic compression with either mechanical compression platens or hydrostatic pressure
- Current research applications include cartilage and meniscus tissue engineering, tumor cell investigation, and stem cell differentiation





Instron® Bioreactor Chambers & Grips

Instron bioreactor chambers can now be easily transferred to testing systems using the Bioreactor Adapter Kit. For example, the L30-1 bioreactor chamber can be used on the LigaGen bioreactor system for cell culture and then moved to the ElectroPuls™ E1000 to test the ultimate strength of the engineered tissue.

Bioreactor Chambers accommodate tension for biologic specimens ranging from 10 – 150 mm in length. Bioreactor grips can be used with or without the bioreactor chamber to grab onto biologic specimens ranging from 2 – 10 mm in width. These biologically designed components are rated for use in applications with forces ranging from 0 – 40 N and frequency ranging from 0 – 5 Hz.

Bioreactor Chamber & Grips Design Philosophy – Biology Matters!

Biological Requirement	Instron Solution
Fit the Specimen	• Bioreactor chambers and grips accommodate small specimen sizes and small fluid volumes
Keep it Sterile (Clean)	• Unique seals to accommodate mechanical motion without compromising the sterile barrier • FDA approved silicone o-ring seals • Simple connectors and minimized parts for easy transport and assembly • Bioreactor chambers and grips can be steam sterilized for repeated sterile use

Keep Cells/Tissue Alive	• Bioreactor chambers and grips are FDA Class VI medical grade materials
	    • Fully submersible
	    • Corrosion resistant

Provide a Controlled & Physiologic Environment	• Bioreactor chambers and flow loop components include .2 um filters and gas permeable materials to equilibrate the inside of the chamber with the incubator gas concentrations and temperature • Bioreactor chambers can be used with flow loops to maintain physiological temperature, gas, and nutrients while on a testing frame or housed in a standard benchtop incubator during culture
Accommodate Cell Seeding of 3D Constructs	• Bioreactor chambers include multiple ports to gain access to the constructs throughout cell culture or testing • Removable windows for 360° access to the constructs for installation and cell seeding

Introducing the NEW TE200 and TE200PB Testing Systems

Instron® bioreactors and accessories answer the smallest challenges, the universal testing machines answer the biggest, and the new bioreactor compatible Instron TE200 and TE200PB test instruments cover everything in between. These new systems are small enough to fit in a standard benchtop incubator for all your living system applications and powerful enough to test new combination (tissue + predicate device) medical devices. They also allow researchers to choose the tool that fits their project as opposed to choosing a project to fit their tool. Examples of project modifications to fit the available tools include: changing sample geometries to fit the grips or splitting experiments by environment, a static test with live cell culture, and a dynamic test without cells.

Choosing the Right Fit for Your Bio Applications

	TE40	TE200	TE200PB	5942/5943	E1000
Compatible with Live Cell Culture*	●	●			
Compatible with Bioreactor Chambers	●	●	●	●	●
High-Elongation Tests		◐	◐	●	◐
High-Frequency Tests	●				●
Fatigue Tests	◐	◐	◐		●
Creep/Relaxation Tests	●	●	●	●	●

* Fits in an incubator

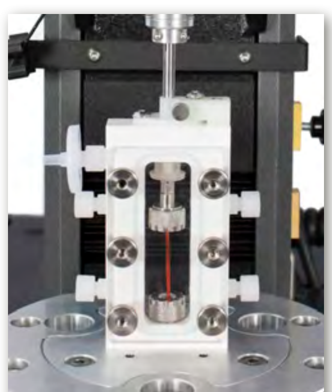
● Fully Capable ◐ Partially Capable

What do agriculture, food production, and medical devices have in common? They are all part of the increasing Biotechnology industry that uses living systems and organisms to make their products. Living systems include everything from single cells, to tissues, to whole organisms, to entire communities.

Products designed using living systems or for living systems, require evaluation and testing in a manner that mimics the living systems environment. However, the variation in application, system, and product development for this industry means that not all living system instrumentation is equal. The biotechnology industry needs a tool box of solutions.

TE40 & L30-1 Bioreactor Chamber

TE200 & L30-1 Bioreactor Chamber



5942 & L30-1 Bioreactor Chamber

E1000 & L150-1 Bioreactor Chamber

PRODUCT DEVELOPMENT LIFE CYCLE FOR MEDICAL DEVICES

Component Selection & Testing

Do you know which material is best suited for your stent application?

Instron® Electromechanical Testing Systems can measure material properties, such as elongation and load, in tension, compression, or simple cyclic.

Prototype Design Testing

Do you know how your medical device behaves in vivo?

Instron bioreactors mimic physiologic environments on the benchtop.

Durability Testing

Do you know if your medical device will last 10 years in a patient?

Instron ElectroPuls™ simulates 10 years of wear in 45 days.

Packaging

Do you know if your device will be delivered safely?

Instron machines are extensively used in quality control to ensure sterile packaging that is easy to open in the OR.

APPLICATION CHALLENGES

Hydrogels are Hard to Hold

Jiggly, water-soluble monomers are excellent candidates for cell culture, stem cell differentiation, cancer cell research, wound healing, drug delivery, tissue engineering, and medical device development. And, just like all new materials, it must be well characterized in order to trust results and develop new products. But we all know that gripping a jello-like substance is a challenge.

Dr. John H. Brekke – a pioneer in the fields of tissue engineering and regenerative medicine – established BRTI Life Sciences in 2003. His mission is to create matrix technologies for biomedical researchers that are "biologically relevant, defined, tissue-like, translational, and free from chemical or UV crosslinking reagents". As a result of his mission, the firm has developed a unique, biomimetic hydrogel intended as a three-dimensional environment for study of stem cells and their therapeutic applications. Cell-Mate3D, a biomimetic 3D cell culture matrix, is designed to support and enhance cell culture assays. The materials are carefully chosen and processed to create an ideal microenvironment for your cells.

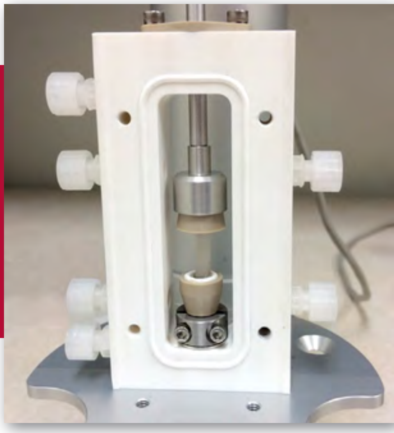
In a recent collaboration with Dr. John Brekke, we have had the opportunity to create a new zero-clamp grip compatible with our bioreactor chamber and frames for tension characterization and stimulation of hydrogels. This instrumentation and mechanical environment allows for Dr. Brekke to test and tune the stiffness of their product. Tissue-like stiffness mimics the in vivo extracellular environment and resulting mechanical signals influence cell behavior and differentiation potential. BRTI plans to supply Cell-Mate3D in a variety of stiffness's, from which customers will be able to choose the correct micro-environment for their specific research.

Severe Organ Shortage

There are 124,010 people waiting for a lifesaving organ transplant. Every 10 minutes someone is added to the national transplant list, and every day 21 people die while waiting for a transplant. This year alone*, 19,426 transplants have been performed from 9,512 donors.

In October, the National Organ Transplant Act turned 30. This Act established the framework for the U.S. organ transplant system and has served as a model for developing other transplant networks worldwide. While technology has changed significantly since the 1980s, the need is exactly the same: to provide healthy organs to patients whose bodies are no longer able to sustain normal function. The demand for donors is increasing; however, due to various social changes, the number of donors is decreasing, resulting in a severe donor organ shortage.

Tissue Engineering & Regenerative Medicine research may have an alternate solution. Decellularization – the process by which all of the cells are removed from a piece of tissue or organ – leaves behind a sterile blueprint for organ regeneration. These tissues and organs seem to provide an ideal transplantable scaffold with all the necessary ultrastructure and signaling cues for cell attachment, differentiation, vascularization, and function. This technology, like anything else, needs assistance translating from academic bench top research into a commercially scalable product. Instron® decellularization chambers are enabling this transition. These chambers are designed to maintain a sterile seal while accommodating pressure and perfusion of multiple solutions for complete decellularization. They can be integrated with our GrowthWorks control hardware and software for automated control or used with a simple perfusion pump, depending on the application.



Hydrogels

Organ Decellularization

3D Cell Culture

Once an organ has been successfully decellularized it can be recellularized (or populated) with the recipient's cells and transplanted in the same way as donor organs. Using the patient's own cells to populate the organ signals the patient's body to recognize and accept the new organ. This process overcomes the donor shortage and need for harsh immunosuppression.

*Data is from January – August 2014

What is Happening in the 3rd Dimension?

3D cell culture is becoming mainstream. Multiple disciplines have determined that animal cells require the biophysical and biochemical cues with in an extracellular matrix to behave and/or differentiate in to truly physiologically realistic functions. However, tools for monitoring or characterizing the cellular mechanical environment are limited to 2D views.

In June, we partnered with an expert in 3D strain mapping, LaVision, along with researchers in Canada and Singapore with 3D strain characterization requirements for their research. Within 24 hours, the team assembled our first 3D digital image correlation system for biological applications.

The Sample

The tissues of interest were bladder and the aortic arch. We mimicked the physiological forces with a pressure bioreactor that dynamically stimulated the tissue from one side with pressurized media.

The Method

Digital image correlation tracks the movement of naturally occurring or applied surface pattern during the test. This is done by analyzing the displacement pattern within discretized subsets of the whole image. The pattern is tracked with a stereoscopic multi camera for full 3D and surface measurements.

The Pattern

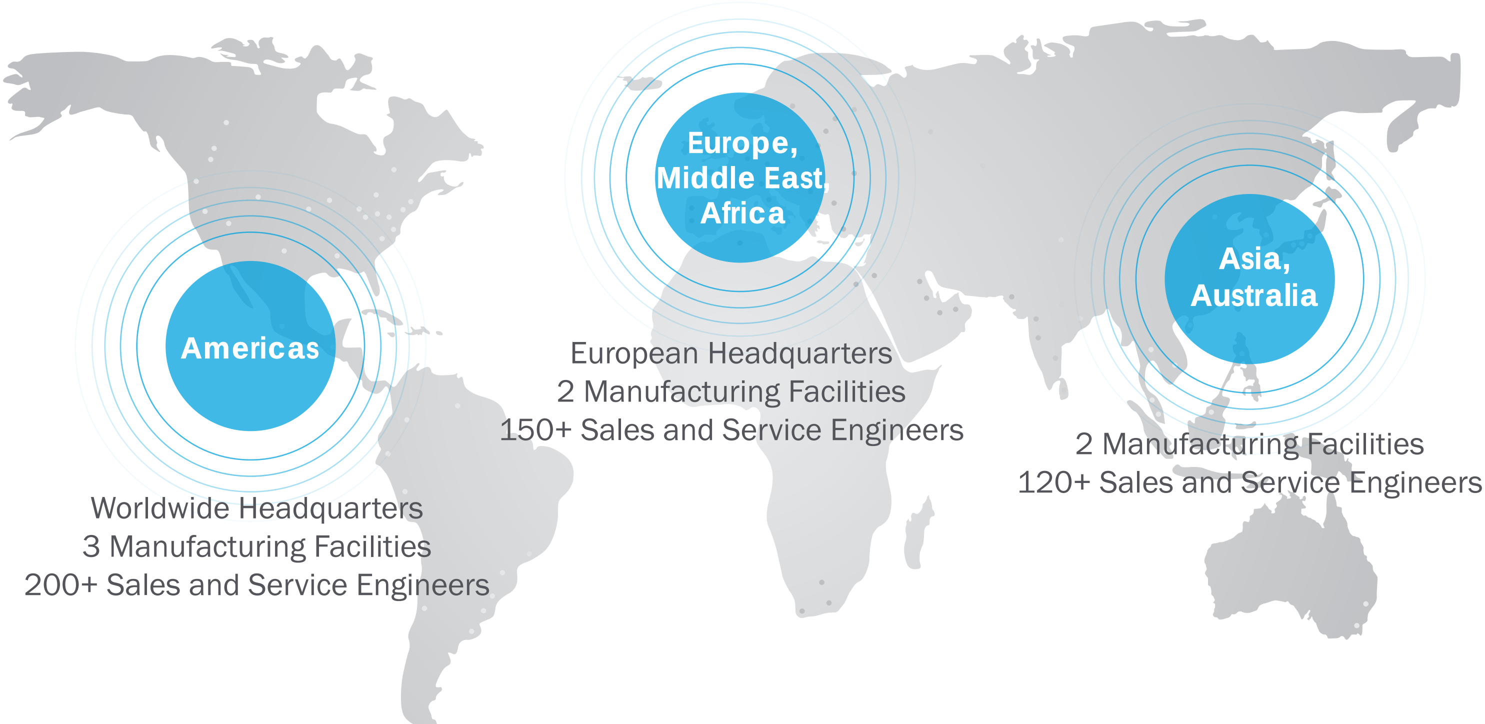
Standard methods of painting or speckling the sample were not appropriate for the live cellular tissue. So, we incorporated a standard biological tracking method by labelling the surface of the tissue with fluorescent beads. When excited by a laser, these particles fluoresce and the pattern could be tracked by the camera and analyzed by the software.

The Results

Our team was able to successfully capture a dynamic 3D strain map of bladder tissue subjected to physiologic forces. This was an experimental protocol that demonstrated the feasibility and necessity of characterizing 3D environments. Currently, our engineering team is evaluating methods to integrate 3D mapping with our standard products. If you are interested in incorporating 3D DIC into your research program, please contact us to discuss how we can provide you with solutions.

Global Support that is Local to You

Operating with 25 offices in 18 countries and with more than 1200 employees, we have a global infrastructure that is local to you, and remain committed to advancing material and component testing techniques.



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