The 18th International Exhibition for Medical Technologies, Pharmaceuticals and Hospital Supplies

26-27 April 2010, David Intercontinental convention center, Tel Aviv

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2010 ISMBE Annual Meeting

Tuesday, April 27 2010, Tel Aviv

Secretariat: E-mail: ismbe@eng.tau.ac.il **מזכירות:**
Department of Biomedical Engineering Fax. 972-3-640-7939 פקס. המחלקה להנדסה ביורפואית
Tel-Aviv University, Tel Aviv 69978, Israel http://www.eng.tau.ac.il/research/ISMBE/ אוניברסיטת תל-אביב, תל אביב 69978

Affiliated to the INTERNATIONAL FEDERATION FOR MEDICAL AND BIOLOGICAL NGINEERING (IFMBE)

ISMBE 2010 Annual Meeting

Tuesday, April 27, 2010, David Intercontinental Hotel, Tel Aviv

Registration	08:30-09:00
Opening	09:00-09:10
Biomedical Engineering Research יו"ר: פרופ' דן אדם, הטכניון	
דר' עידית אברהמי, מכללת אפקה, תל אביב Fluid and structure tango in biomedical research	09:10-09:25
דר' משה ברנד, מרכז אוניברסיטאי אריאל Stents and arteries, war or peace – mechanical aspects	09:25-09:40
דר' דביר ילין, הנדסה ביורפואית, הטכניון Spectrally encoded endoscopy	09:40-09:55
דר' אמיר קרניאל, אוניברסיטת בן-גוריון A turing-like handshake test for motor intelligence	09:55-10:10
פרופ' חיים אזהרי, הנדסה ביורפואית, הטכניון High intensity focused ultrasound – the future surgeon knife	10:10-10:25
Coffee Break	10:25-10:50
Biomedical Industry יו"ר: דר' זהבה בלכמן, מכללת אפקה ודר' קובי ורטמן, Insightec	
יוסי סמולר, מנהל תכנית החממות הטכנולוגיות, לשכת המדען הראשי, משרד התמ"ת תכנית החממות הטכנולוגיות - הפיכת רעיונות טכנולוגיים לחברות הזנק	10:50-11:10
סטיב רודס, מנכ"ל חממת משגב, משגב How to work with an Incubator and what to expect	11:10-11:25
תמיר לויטל, HeadWay , משגב Noninvasive computer controlled device for relief of head and neck pain	11:25-11:40
יאיר מנדלס, Biometrix Medical, ירושלים Converting manual bed side procedures to automated “hands-Off” procedures	11:40-12:00
שלחן עגול: **"תעשיית הביומד והמהנדס הביורפואי".** מנחה: פרופ' דוד אלעד. משתתפים: יוסי סמולר, סטיב רודס, יאיר מנדלס, טובי סיון וקובי ורטמן.	12:00-12:30
Lunch Break – Poster Session (graduate students)	12:30-14:20
ISMBE general assembly meeting	14:20-14:30
יו"ר: פרופ' מיטל זילברמן ופרופ' עמית גפן, אונ' תל אביב **Smart Biomaterials & Cellular Engineering**	
יונתן אלסנר, הנדסה ביורפואית, אוניברסיטת תל-אביב Novel biodegradable wound dressings with controlled release of antibiotics	14:30-14:45
נועה סלומקה, הנדסה ביורפואית, אוניברסיטת תל-אביב Modeling the mechanics of cultured cells	14:45-15:00
דר' דפנה ויס, הנדסה ביורפואית, הטכניון Intracellular micromechanics of living cells	15:00-15:15
דר' אירנה גוטמן, הנדסת חומרים, הטכניון Biomaterials for bone healing	15:15-15:30
יצחק פביאן, Easy-Lap , כפר טרומן Bioresorbable tacks for internal use	15:30-15:45
Closure and Poster Prizes	15:45-16:00

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Abstracts of Lectures

FLUID AND STRUCTURE TANGO IN BIOMEDICAL RESEARCH

Idit Avrahami

The Department of Medical Engineering
AFEKA – Tel Aviv Academic College of Engineering
idita@afeka.ac.il

Problems including time-dependent Fluid-Structure interaction (FSI) and Tissue-Fluid interaction (TFI) are widely found in biological systems and in the design of biomedical devices. These problems are often characterized by unsteadiness, complex geometry, strong coupling and transitional flow. Numerical simulations are a powerful tool for the investigation of the coupled fluid and structure dynamics of such problems, using different approaches. Several parameters such as geometrical complexity, degree of displacement, convergence to steady periodicity, and the system stability may determine the coupling method. In the talk, several numerical studies of biomedical issues will be presented, in order to demonstrate the different coupling approaches.
Among the examples to be presented: flow through non-homogenous coronary artery stenosis, mechanical heart valves, cardiac assist devices, and impedance pumps. In addition to the methodology, the applicative design and hemodynamic aspects of the cases will be discussed, including washout properties and risk for blood clotting. The results obtained from the studies will be compared to experimental analyses.

STENTS AND ARTERIES, WAR OR PEACE – MECHANICAL ASPECTS

Moshe Brand[1], Shmuel Rivkin[2] and Shmuel Einav[3]

[1]Department of Mechanical Engineering and Mechatronics, Ariel University Center
[2]Department of Solid Mechanics, Materials and Systems, Faculty of Engineering, Tel-Aviv University
[3]Department of Biomedical Engineering, Faculty of Engineering, Tel-Aviv University

Approximately 40% of the population in the western world suffers from problems of the blood vessels. Beginning in the mid-80's a medical procedure that did not require opening of the chest cavity was initiated. This treatment, called balloon angioplasty, provides a relatively easy and comfortable solution for the majority of people suffering from blood vessel blocking. For these cases, a balloon is inserted into the artery and inflated in order to widen the narrowed area. While the inflation of the balloon opens the blockage, in most cases restenosis (anew narrowing of the vessel) occurs, since the walls of the blood vessels tend to collapse inwards over time and the blood vessels become constricted again. Therefore, a device is inserted into the narrow area of the blood vessel. This device, called "a stent"**,** has a hollow cylindrical, thin-walled structure, and a spiral or net-like shape. The stent improves the process by preventing severe blockage in the internal space of the artery. The stent keeps the internal space of the artery from decreasing, and for this end it requires a specific geometry and mechanical properties that would enable it to support the walls of the artery. The interaction between the stent and the artery causes the developing of stresses on the walls of the artery that at times creates restenosis.

The goal of this research is to study the mechanical interaction between the stents and the artery. The work necessitated the calculation of the stress developing on the artery's wall. Representation of this stress was performed using a dimensionless variable, when the value of the pressure occurring between stent and artery is normalized relative to a value of average blood pressure. This variable was defined as the "Potential Damage Factor" (DF). For this end – analytic and numeric models were developed. These models enable to calculate the stent to artery stresses, as well as to find their deformation and inter dependence on geometrical parameters and the mechanical properties of the materials.

The way the DF may be calculated for similar cases, applying numeric models will be presented. 2D and 3D numeric models were developed. Comparison between the results supplied by the models for diverse cases showed that a good match exists.

The numeric models were calculated first for an artery defined as consisting of elastic-linear, isotropic material. In recent research works found in the literature, the blocked artery is considered to be a multi layered material with non linear properties. Hence, additional numeric models were formulated, in which the artery is modeled as a two layered material with non linear and hyper elastic properties. Also in this latter case, high agreement was obtained as a result from these models. This agreement enables us to assume that it is feasible to compute the damage factor using a 2D model. Based on this assumption we proceeded to use the 2D model in order to compute the DF for a collection of cases in which a stent is inserted into arteries with varying blocking percentages and with diameter that are also changing. Moreover, we will use the 2D model for computing the DF for stents of various types. This numeric model would provides data to the operating team during the catheterization process and help to arrive at a decision regarding, e.g., what type, size of stent to use which best fit each patient.

FUNCTIONAL, ULTRA-MINIATURE ENDOSCOPY

Dvir Yelin

Department of Biomedical Engineering, Technion – Israeli Institute of Technology,
yelin@bm.technion.ac.ilHaifa 32000, Israel. Email:

Small diameter endoscopes are limited in their ability to provide sufficient image quality and functionality for accurate medical diagnosis. The compact dimensions and excellent light transmission of optical fibers now allow the assembly of miniature, flexible endoscopic probes for clinical applications. Fiber bundle endoscopes are capable of excellent image quality and are being widely used for minimally invasive clinical diagnosis; however, their image quality becomes a limiting factor at sub-millimeter diameters endoscopes. Rapid distal scanning of a beam from a single optical fiber allow high quality endoscopic imaging without the visual artifacts of fiber bundles, but the size of the scanning mechanism make this approach difficult to implement in the smallest endoscopes. A recently introduced approach, termed spectrally encoded endoscopy (SEE), combines high quality imaging and functionality into sub-millimeter single fiber probes by utilizing a miniature lens-grating combination that encodes space with wavelength. Replacing rapid distal scanning with spectral encoding, SEE probes can be made as thin and flexible as the optical fiber itself. Without the need for rapid scanning, spectrally encoded imaging was demonstrated promising for video-rate confocal microscopy, flow cytometry of large quantities of cells, and comprehensive large area micro-endoscopy. Moreover, incorporating the SEE probe into the sample arm of a Michelson interferometer, SEE enables three-dimensional, video-rate imaging with high sensitivity and low signal-to-noise ratio, and is also capable of sub-surface microscopy, blood flow imaging, and mapping acoustic vibrations. Recently, we have shown that SEE is capable of color and fluorescence imaging with only slight modifications to the standard endoscopic probe. With its high image quality and broad feature set, SEE could be useful for various clinical applications that require safe, minimally invasive functional imaging of hard-to-reach locations within the body.

A TURING-LIKE HANDSHAKE TEST FOR MOTOR INTELLIGENCE

Amir Karniel

The Computational Motor Control Laboratory, Department of Biomedical Engineering,
Ben-Gurion University of the Negev, Beer-Sheva, Israel
akarniel@bgu.ac.il

A model is the first step in understanding any natural phenomenon. Reaching an understanding of human intelligence must, by its very nature, be a long-term study, and a yardstick is required to track our progress. The Turing test provides such a measure based on questions and answers to a model and to a person; however, it is binary and limited to the linguistic aspects of intelligence. The ultimate Turing-like test would be to build a robotic device with abilities indistinguishable from those of a human being. The implications of developing such a test cover many aspects of engineering, medicine, life sciences and social sciences. A salient function of the brain is the control of movement, with the human hand being the most sophisticated demonstration of this function. Therefore, we design a Turing-like handshake test, for motor intelligence.

We administer the test through a telerobotic system. Instead of asking the test subject whether the other party is a person or a computer program, we employ a forced-choice method that asks which of two systems is more human-like. By comparing the developed model with a weighted sum of human and passive systems, we construct a psychometric curve and extract a quantitative grade for the developed system in terms of similarity to the human handshake. The test subject is engaged in a task of holding a robotic stick and interacting with another party (human, artificial, or a linear combination of the two). We tested a number of well-known scientific hypotheses with the aim to develop the simulated handshake.

In discussing further development of the Turing-like handshake test, one should also note that the standard Turing test is a perceptual test and recent studies distinguish between perception and action. Future studies should explore three versions of the test in order to accurately assess the nature of human-like handshake: 1. a psychometric test of the perceived similarity; 2. a motor behavior test that will explore the motor reaction of the interrogator which may differ even when he/she states that both movements are similar; 3. an ultimate optimal discriminator which tries to distinguish between human and machine handshakes based on the force and position trajectories.

In this talk I'll describe the Turing like handshake test, our preliminary results and what we can learn from them about the natural properties of human handshake. then I'll discuss the implications and future medical applications, for diagnostic purposes as well as for the design of human like robots to assist the elderly population and the physically disabled.

This study is supported by the Israel Science Foundation (ISF grant number 1018/08). Further information about the studies at the Computational Motor Control Laboratory is available at URL: http://www.bgu.ac.il/~akarniel/

בס"ד

HIGH INTENSITY FOCUSED ULTRASOUND (HIFU): THE FUTURE SURGEON KNIFE

Haim Azhari

Dept. of Biomedical Eng. Technion IIT, Haifa 32000, Israel
Haim@bm.Technion.Ac.IL

High intensity focused ultrasonic (HIFU) offers a tool for non-invasive tissue treatment. With this technique, an ultrasonic transducer, or an array of transducers, located near the body is used to focus a high-energy acoustic beam on the tissue region to be treated (commonly a lesion). The acoustic energy is absorbed by the tissue at the focal point causing a significant temperature elevation resulting in local tissue ablation and or cavitation bubbles which upon their collapse induce tissue destruction. Although the medical application of this technique has already been suggested about sixty years ago, actual clinically approved systems have been introduced only about a decade ago. Image guided HIFU surgery has been recently offered as a non-invasive alternative to conventional lumpectomy and cosmetic applications. Currently, the therapeutic ultrasonic beam is guided mainly by an MRI scanner, which can provide both anatomical images of the organ and a thermal map of the treated area. In his lecture this and alternative guidance methods will be discussed and several applications will be reviewed.

HOW TO WORK WITH AN INCUBATOR AND WHAT TO EXPECT

Steve Rhodes

The Trendlines Group, Misgav Venture Accelerator
The Trendlines Building, Misgav Business Park, M.P. Misgav 20174 Israel
steve@misgav-venture.com

In the past decade, incubators have become a major engine of medical device entrepreneurship in Israel, funding approximately 30 new medical device companies every year. Incubators can provide medtech entrepreneurs with a unique opportunity to receive funding and support that can support the conversion of a good idea into a great company.

Although Government-licensed incubators in Israel have very similar offerings in terms of funding and administrative support, there are significant differences between incubators in terms of the support given in areas such as corporate governance, strategic planning, business development, raising capital, technology support, facilities, and more. Entrepreneurs considering entering an incubator tend to focus on the financial terms of their relationship with the incubator, yet arguably the financial terms are the least important element of the incubator-entrepreneur relationship. The entrepreneur's goal in working with an incubator should be to optimize the chances of success of his enterprise. The often-overlooked elements are those that contribute to the enterprise's potential success.

The entrepreneur should undertake a due diligence process, reviewing the incubator before reaching a decision regarding with which incubator to work. During the review process, the entrepreneur should ask questions of the incubator staff and of other entrepreneurs operating within the incubator aimed at understanding the incubator's success rate, added-value services, and the work environment within the incubator. This process should also help the entrepreneur to understand whether s/he will feel comfortable working with the incubator staff.

Although seemingly demanding in terms of the potential for the incubator to control the new enterprise, the incubator contract is actually less demanding than venture contracts. A typical agreement provides the incubator with the potential to veto many corporate issues and to control the company's finances; unlike the venture agreement, however, the incubator agreement usually confers ordinary shares on the incubator. The need for veto and control provisions is critical to any investor, and because of the incubator's special relationship with the Office of the Chief Scientist of the Ministry of Industry, Trade, and Labor, many of these provisions are required. The due diligence process should help the entrepreneur understand how often, if ever, these seemingly draconian provisions are actually relied upon.

Once an incubator has funded a new company, the entrepreneur should take maximum advantage of the services and support, formal and informal, that the incubator can provide. The entrepreneur can take a number of simple steps that will ensure that the new company receives the optimal support from the incubator; these include:

- Take full advantage of the incubator's physical facilities;
- Organize a kick-off meeting with the incubator staff to align expectations and to developed a detailed work plan;
- Meet frequently with incubator staff – on both a formal and informal basis;

By making the incubator a full partner in the new company and taking optimal advantage of the services that the incubator has to offer, the entrepreneur can significantly increase the chances of success.

NONINVASIVE COMPUTER CONTROLLED DEVICE FOR RELIEF OF HEAD AND NECK PAIN

Tamir Levital, CEO

Headway Ltd., Misgav Venture Accelerator, M.P. Misgav 20174, Israel
E-mail: tamir@headwaymedical.com

Persistent headaches affect millions of individuals each year. In the United States alone, physicians and outpatient departments recorded over ten million visits in (2002) from patients complaining of persistent headaches. Over five percent of the general population suffers from chronic migraine or tension-type headaches, or medication overuse headaches. Current treatments for head and neck pain have proven ineffective for many patients. Treatments such as medication, invasive procedures, physical therapy and additional methods (exercise and acupuncture) can produce undesirable side effects. As many patients do not respond well to these treatments, there is a clear need for new solutions.

Occiflex consists of a computer controlled, specialized head cradle that is adjusted to the patient's head and neck. Optimized for each individual patient's treatment, the cradle moves the head gently along a predefined three-dimensional course determined by and based on the practitioners' (physicians, physical therapists, and others) preprogrammed treatment movements. Occiflex™, an innovative patent-pending medical device by Headway, has been proven to be an effective treatment for patients suffering from chronic neck pain and headaches. Occiflex is indicated for patients who present with cervicogenic headaches, whiplash, post-trauma, cervical facet-joint disorder, pain from post-spinal surgery, tension-type headaches, medication over-use, migraines and myofascial pain syndrome. Once the adjustment session has been performed, the device will operate in a fully automated mode, allowing the caregiver to attend to other patients.

CONVERTING MANUAL BED SIDE PROCEDURES TO AN AUTOMATED "HANDS-OFF" METHOD

Yair Mendels, CEO

Biometrix LTD
yair@biometrixmedical.com

From the onset of Critical Care Units, an evolution of a multi parametric approach to numerous invasive and noninvasive clinical procedures and technologies has immerged in order to better diagnose, monitor and treat the critically ill patient. Nowadays, the typical ICU bedside is severely crowded with instruments, monitors, cables and fluid lines. Such a complex environment indicates a demand for highly professional costly clinical staff, all in an era of enforcing budgetary restraints.
Furthermore, the vast information flow of I/O data and commands, the endless manual handling of fluid lines, catheters, fluid reservoirs etc. not only increases the risk of potential mistakes and malpractice but increases the risk of cross contamination and catheter related infections.
In this short presentation, two examples will be demonstrated where manually operated bedside procedures have been converted into automatic ones. It is expected that successful implementation of these methods will result in less clinical staff interference and work load, lower risks of human error and due to the "hands off" automatic approach, one can expect a lower risk of cross contamination and infections.

NOVEL ANTIBIOTIC-ELUTING WOUND DRESSINGS WITH CONTROLLED RELEASE OF ANTIBIOTICS

Jonathan Elsner[1], Israela Berdicevsky[2], Adaya Shefy-Peleg[1], Yehuda Ullmann[2,3], Dana Egozi[3] and Meital Zilberman[1]

[1]Department of Biomedical Engineering, Tel-Aviv University, Israel
[2]Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel
[3]Department of Plastic Surgery, Rambam Medical Center, Haifa, Israel
elsner@eng.tau.ac.il

Despite advances in treatment regimens and the best efforts of nurses and doctors, about 70% of all people with severe burns die from related infections. We propose a new biodegradable composite wound dressing that can be loaded with drugs like antibiotics to speed up the healing process. Our new composite dressing material, based on a polyglyconate mesh, coated with a porous Poly-(DL-lactic-*co*-glycolic acid) (PDLGA) matrix, is designed to protect the wound until it is no longer needed, after which it dissolves away by chemical degradation to non-toxic products. The latter was prepared using the freeze-drying of inverted emulsions technique which enables high porosity. This unique composite dressing design is advantageous in that it enables the combining of good mechanical properties with the desired drug release profile and preservation of the drug's activity.

Drug release profiles generally exhibited an initial burst effect accompanied by a decrease in release rates with time over periods ranging from several days to 30 days, depending on the emulsion's formulation. Albumin and Span80 were found to be effective surfactants for stabilization of the inverted emulsions and their incorporation in the aqueous phase resulted in a lower burst release. Higher organic: aqueous phase ratios, polymer content and molecular weights all reduced the burst release of the antibiotics from the wound dressings and prolonged their release due to changes in the porous matrix structure. Changes in the porous matrix structure were also found to be beneficial in fine-tuning water absorbance capacity and vapor permeability (WVTR). We were able to cover a large range of WVTRs, between 480 and 3452 g/m^2/day. The lowest value is similar to that reported for film-type wound-dressings, whereas the highest value is similar to that of foam-type dressings.

The release of antibiotics from our structures resulted in a significant decrease in bacterial viability *in-vitro* and practically no bacteria survived after 2 days when initial bacterial concentration of $1x10^7$CFU/ml was used. Hence, the preparation method did not affect the drug's potency as an antibacterial agent. Furthermore, diffusion tests demonstrated effective bacterial inhibition around the dressing material over two weeks. *In-vivo* tests of the dressing material on second degree burns in guinea-pigs demonstrate better wound contraction and faster healing compared to conventional dressing material. Thus, these unique structures are potentially very useful as burn and ulcer dressings.

MODELING THE MECHANICS OF CULTURED CELLS

Noa Slomka, Amit Gefen

Department of Biomedical Engineering, Faculty of Engineering, Tel Aviv University,
Tel-Aviv 69978, Israel, E-mail: gefen@eng.tau.ac.il

Image-based finite element modeling is presently considered a leading biomechanical research methodology at the organ scale. At the cell scale, confocal microscopy can potentially replace traditionally used imaging methods at the organ scale, e.g. magnetic resonance imaging and computed tomography, to obtain a set of planar images of the cell in order to reconstruct a three-dimensional (3D) model. However, image-based modeling has not yet been employed at a cell-scale for large deformation analyses. Hence, a new modeling methodology, which is capable of performing large deformation analyses of 3D confocal-based cell models, is presented in this study. This methodology is employed for studying cellular strains of cells subjected to compression and stretching, which are typically used in pressure ulcer and deep tissue injury research, selected here as an example application.

Undifferentiated muscle cells (C2C12 myoblasts) were stained with fluorescent staining of actin filaments (FITC-labeled Phalloidin) in order to identify cell morphology, and scanned using a confocal microscope. The resulting z-stack images were utilized to reconstruct a 3D model of the cells geometries, including nucleus, cytoplasm, plasma membrane and cytoskeletal fibers. Cells were subjected to compression and stretching and the magnitude and distribution of the strains in the plasma membrane and the nuclear surface area (NSA) of two cells were studied.

Localized stretches were observed in the plasma membrane and NSA of cells for both loading configurations. We found that global cell deformation larger than ~15% should be applied in cell compression tests in order to induce large tensile strains (>5%) in the plasma membrane and NSA. Correspondingly, we found that tensile strains in the elastic plate substrate in cell stretching experiments should exceed ~3%. Our developed methodology is able to provide magnitudes and distributions of localized cellular strains specific to test setup and cell type, and thus can be utilized to significantly enrich experimental cellular mechanics studies in classic cell loading designs which typically involve large cell deformations. However, this methodology has a broad spectrum of applications in many other fields in the exciting field of cellular mechanics.

INTRACELLULAR MICROMECHANICS OF LIVING CELLS

Daphne Weihs

Faculty of Biomedical Engineering, Technion-Israel Institute of Technology, Haifa 32000

E-mail: daphnew@tx.technion.ac.il

Cell biomechanics and especially intracellular measurements in living cells are of growing interest as they can show cell responses to their environment. In the current talk, we will focus on measurements of intracellular transport-dynamics and structure using internalized sub-micron particles as local probes. Those measurements are minimally invasive, provide quantitative real-time data, and can reveal changes in local structure and mechanics of the cell. We highlight variations between cells of different types and focus on living cells to various physical and chemical treatments. Of specific interest is the different mechanical response of electrically treated breast-cancer cells in a model for their in vivo microenvironment, e.g. the tumor stroma. The approaches described here can be correlated with many other techniques to provide a full and more quantitative picture of cell mechanics.

MATERIALS FOR BONE HEALING

Irena Gotman

Faculty of Materials Engineering, Technion

The use of man-made porous materials as substitutes for conventional bone grafts has been a growing area of research in regenerative medicine. When such bone graft substitutes are placed in bone voids, they act as scaffolds for "in situ tissue engineering" of a new bone. Regardless of the material used, the scaffold should be highly porous with interpenetrating pore structure to allow the transport of body fluids, vascularization, and finally ingrowth of the new bone tissue. The 3-D architecture of the porous foam is also a key element in its mechanical performance whereas cell attachment and biological activity are controlled by the chemistry and morphology of the pore surfaces. In this talk we'll focus on strong open-cell scaffolds made of shape-memory NiTi alloy whose architecture resembles that of cancellous bone. Different chemical and biomimetic modification approaches to the enhancement of bone regenerating capability of Ti alloy scaffolds will be demonstrate

List of Graduate Students Posters

	יו"ר: ד"ר אמיר קרניאל, אונ' בן-גוריון, ד"ר ענת רטנובסקי, מכללת אפקה, פרופ' חיים אזהרי, הטכניון
1	מורן אביב, הנדסה ביורפואית , אונ' תל-אביב **NATURAL-SYNTHETIC MALLEABLE COMPOSITE HYDROGEL HYBRID FOR TISSUE ENGINEERING.**
2	סרגי וייסמן, הנדסה ביורפואית אונ' בן-גוריון **PASSIVE FETAL MONITORING BY ADVANCED SIGNAL PROCESSING METHOD**
3	איתן לוי, הנדסה ביורפואית , אונ' תל-אביב **LATENT SEMANTIC ANALYSIS FOR CASE-BASED DECISION SUPPORT IN THE PEDIATRICS DEVELOPMENTAL DISORDERS DOMAIN**
4	עדי שיינפלד, הנדסת חשמל, אונ' תל-אביב **FLOW MAPPING USING PHOTOACOUSTIC DOPPLER WITH TONE-BURST EXCITATION**
5	לירון אברהם, הנדסה ביורפואית, אונ' תל-אביב **MECHANICAL STIMULATION OF EPITHELIAL OVARIAN CANCER CELLS**
6	אילנה ניסקי, הנדסה ביורפואית, אונ' בו-גוריון **PERCEPTION OF STIFFNESS DURING SIMULATED NEEDLE INSERTION**
7	מיכל שטרן-פרי, הנדסה ביורפואית, אונ' תל-אביב **EXPERIMENTAL MODEL FOR STRESS FRACTURES IN RATS**
8	יעל נדלין-כרמלי, הנדסה ביורפואית, אונ' תל-אביב **ANALYSIS OF MUSCLE ACTIVITY DURING BREASTFEEDING**
9	אמיר קרייצר, הנדסה ביורפואית, אונ' תל-אביב **CONTROLLED RELEASE OF ANTIPROLIFERATIVE DRUGS FROM NOVELBIORESORBABLE STENTCOATING**
10	אמיר קרייצר, הנדסה ביורפואית, אונ' תל-אביב **NANO-STRUCTURED BIORESORBABLE FILMS LOCATED WITH BIOACTIVE AGENTS FOR BIOMEDICAL APPLICATIONS**
11	שרית יניב, הנדסה ביורפואית, אונ' תל-אביב **BIO FLUID ASPECTS OF EMBRYO TRANSFER**
12	לילך ישורון, הנדסה ביורפואית, טכניון **ULTRASONIC IMAGING and MEASUREMENT OF THERMAL PROPERTIES OF TISSUES**
13	נעמה גל, הנדסה ביורפואית, טכניון **EVIDENCE OF STRONG ANOMALOUS DIFFUSION IN LIVING CELLS**
14	יונתן אלסנר, הנדסה ביורפואית, טכניון **PROCESS-STRUCTURE-PROTEIN RELEASE EFFECTS IN ACTIVE SCAFFOLDS FOR TISSUE REGENERATION DERIVED FROM INVERTED EMULSIONS.**

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Abstracts of Posters

NATURAL-SYNTHETIC MALLEABLE COMPOSITE HYDROGEL HYBRID FOR TISSUE ENGINEERING

***Moran Aviv, *Shmuel Einav, **Zvi Nevo and ***Ehud Gazit**

*Department of Biomedical Engineering, Tel-Aviv University, ISRAEL
**Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine, Tel-Aviv University, ISRAEL
***Department of Molecular Microbiology and Biotechnology, Faculty of Life Sciences, Tel-Aviv University, ISRAEL
Email: moranav2@post.tau.ac.il

Introduction: Development of malleable polymeric nanofibers is of great scientific and technological interest due to their wide-range applications in biomedicine and biotechnology. Particularly, composite nanofibers derived from natural and synthetic polymers, combining the favorable biological properties of the natural polymer and the mechanical strength of the synthetic polymer, represents a major advantageous advancement in tissue engineering and regenerative medicine. Here we present the development and characterization of an innovative natural-synthetic polymeric nanofiber hydrogel hybrid comprised of Hyaluronic acid (HA) and FmocFF. HA, a biodegradable, nonimmunogenic, and biocompatible natural polymer, which represent remarkable viscoelastic properties, is an attractive biomaterial for cells in tissue engineering. FmocFF is a short peptide with a protected group, which can self assembled into nanostructures and form hydrogels in the macrostructure. The hydrogels are characterized by remarkable rigidity and biocompatibility. The design combines the technological advances in biocompatible polymers and nanofibrous matrices with significantly improved mechanical and biological properties as friendliness to cells.
Objectives: (a) Development of well-blended composite hydrogels, combined of a natural polymer, HA, and the self-assembled peptide, FmocFF, either interacting or just intercollating, for tissue engineering applications. (b) Creation of biocompatible hydrogels with good mechanical properties to support cell growth, without using chemical crosslinkers. (c) Characterization of the structural, mechanical and biomechanical properties of the hydrogels.
Methods: Preparation of HA - FmocFF Hybrid Hydrogels by physical mixing. Characterization by: (a) Macro and Micro analysis (TEM, E-SEM); (b) Rheology and Viscosity; (c) Swelling; (d) Vitality assay (AlamarBlue, MTT); (e) Biodegradability of HA.
Conclusions: A malleable homogeneously composite hydrogel hybrid was developed, combining HA, a natural polymer, and the self-assembled peptide, FmocFF. The innovative hydrogel hybrid shows good mechanical properties (e.g. shear stress, viscosity, elasticity) with good biocompatibility and improved adhesion of few kinds of cells. A higher concentration of peptide, the less swelling is attained, the higher density and rigidity of the hydrogel, contributes to slow HA degradation. HA improves the hydrogel hybrid elasticity, and contributes to improved cell adhesion and biocompatibility. FmocFF improves the hydrogel hybrid mechanical features (e.g. shear stress), and slows down the HA degradation (probably due to a lower rate of diffusion of the digesting enzyme).

PASSIVE FETAL MONITORING BY ADVANCED SIGNAL PROCESSING METHOD

Sergey Vaisman, Amir Geva, Gershon Holcberg, Shimrit Yaniv Salem

Ben Gurion University of the Negev, Beer Sheva, Israel.
sergeyv@bgu.ac.ilEmail:

Fetal Heart Rate (FHR) monitoring is one of the most important fetal well being tests done during both antepartum and intrapartum periods of pregnancy. Existing methods for monitoring fetal heart rate are based on Doppler ultrasound. This technique has a number of disadvantages: it is an active method, in which ultrasound energy is transmitted into fetus body; the monitor itself is expensive, and on top of that this method leads to high false positive rate in predicting neurological problems, particularly in pathological cases and in multifetal pregnancies.

Fetal heart rate monitoring by phonocardiography is an appropriate alternative. The idea is to pick up the sounds of the fetal heart from the maternal abdominal surface and to calculate FHR based on the detected cycle time. Being totally passive and having low cost, this method is safe and easy for long and continuous monitoring. There are, however, multiple challenges in implementing the passive method. Being originally week signals, fetal heart sounds are further attenuated and interfered by passing through a complex fetal-maternal environment. These challenges make fetal heart sounds impossible to be detected without applying appropriate signal processing methods. Several approaches for passive fetal monitoring have been proposed, however the researches had difficulties to obtain a reliable result in highly disturbed cases.

In this work, an advanced signal processing method based on adaptive wavelet denoising was developed. The method combines extraction of features specific to fetal heart sounds with their subsequent denoising. As a result, the reconstructed signal is effectively denoised of internal and external interferences and contains mostly S1 and S2 fetal heart sound peaks. By that, the FHR calculation procedure confidence is increased and its dependency on strict timing rules is minimized. The new method is more simple and robust than the ones used in most of the previous studies.

For implementing the method, a measurement system has been designed and built including sensors, analog signal preprocessing unit, and digital signal processing algorithms. 14 records of fetal heart sound signals have been collected from 36-40 weeks pregnant women and FHR has been generated from these records using the developed approach. Results show good compatibility with FHR obtained simultaneously from Doppler ultrasound monitor, also in highly disturbed cases.

LATENT SEMANTIC ANALYSIS FOR CASE-BASED DECISION SUPPORT IN THE PEDIATRICS DEVELOPMENTAL DISORDERS DOMAIN

***Eitan Lavi[a], Yuval Shahar[b], Mitchell Schertz[c], Shmuel Einav[a]**

[a] Biomedical Engineering Department, Tel-Aviv University, Israel,*correspond to: LaVi.eiTan@gmail.com
[b] Medical Informatics Lab ,Department of Information Systems Engineering, Ben Gurion University, Israel
[c] Institute for Child Development ,Kupat Holim Meuhedet, Central Region, Herzeliya, Israel

Abstract and Objective: While 1 in 5 children suffers from Pediatrics Developmental disorders (PDD), PDD specialists are operating in IT darkness; their domain is ontologically and taxonomically ill-defined and no prototypical cases or clinical decision making models are available to assist them. PDD is pressing for Medical Informatics solutions, yet no prior research has been dedicated to developing Decision-Support Systems (DSS) or methodologies for PDD. This ongoing research is being conducted on a real-life case-base from a major PDD clinic in Israel, with the primary objective of constructing a robust Case-Based-Reasoning (CBR) agent to perform CBR retrieval to predict diagnoses of new cases. Heretofore we have implemented and tested the retrieval and reuse modules of the CBR cycle. Ultimately, the significance of such work is in helping to lay the foundations for a CBR system which allows clinicians to objectively utilize the whole of their collective past experience in order to individually produce better decisions in diagnosis and treatment of developmental disorders.

Introduction: PDD refer to any delay in development based on that expected for a given age level or stage of development. These disabilities constitute a substantial impairment and are caused by a myriad of biological and non-biological factors. Currently, PDD has no formal clinical model for decision making, no clear or widely approved taxonomy, no agreed upon names for the different pathological states and not even an agreement as to what exactly are the different pathological states that exist. There is, therefore, also no agreement regarding treatment methods for the various syndromes. Having no robust clinical model to aid him, a PDD specialist relies mainly on his own (available memory of) past experience, signifying the need for a CBR decision-support methodology in this domain.

Methods & Results: Our case base consists of 8022 cases, each holding 182 attributes, 80 of which are free-text (encompassing most of the clinical information). The case base is extremely sparse and noisy; the free-text fields are written by several physicians, often alternating between languages and writing with abbreviations and spelling errors. Further, the prediction task is difficult as each case is assigned a combination of diagnoses (3 in average) from a list of 235 possible morbidities. The developed algorithms are constructed as follows: (a) an import & preprocessing module; (b) a transformation module; (c) a generic multilingual text-mining module; (d) a generic CBR retrieval pre-processor module to construct similarity matrices for all attribute types, including novel NA handling as well as methodologies for robust and generic Latent-Semantic-Analysis (LSA)-based construction of similarity matrices. (e) A novel CBR retrieval & prediction module. Our retrieval-based predictions were tested using a Leave One Out methodology. Typical [mean AUC ROC, mean P Value, mean SAR value] (±STD) obtained by averaging results for 300 test cases, for a specific set of retrieval and reuse methodologies, for K=500, were [0.93±0.095, 0.035±0.0.074, 0.86±0.046] respectively. We believe that CBR approaches can greatly help in building an information structure for PDD.

PHOTOACOUSTIC DOPPLER WITH TONE-BURST FLOW MAPPING USING EXCITATION

Adi Sheinfeld, Sharon Gilead and Avishay Eyal

School of electrical Engineering, Tel-Aviv University, Ramat Aviv, Tel-Aviv, 69978, Israel
adishein@post.tau.ac.il

A new approach for time-resolved characterization of flow, using tone-burst excitation and the photoacoustic Doppler effect, is proposed and demonstrated. The photoacoustic (PA) technique is based on measuring the acoustical wave generated by absorption of modulated light in a tested sample. This technique combines advantages of high contrast and functional information obtained from optical excitation along with high spatial resolution and weak scattering which characterize ultrasound detection. PA Doppler measurement of flow is based on the Doppler shift induced by moving absorbers, which in the case of blood flow are the red blood cells. In our setup, tone-burst modulation, which is typical to the common technique of ultrasound Doppler, was applied to the optical excitation beam using the unique flexibility of external modulation. It was achieved via modulating the output of a CW tunable laser source by an electro-optic modulator, electronically driven by an arbitrary waveform generator. The detection was performed using an immersion ultrasonic transducer at central frequency of 1MHz. Time-gated spectral analysis performed on the recorded acoustic signals yielded two-dimensional maps of the Doppler shift vs. axial position of a flow of absorbing particles. The detected velocities extended over a wide range from few mm/sec up to 200mm/sec. Using this technique a flow of a suspension of micron-scale carbon particles in a C-flex tube was measured with spatial resolution of 4.5mm and spectral resolution of 1Hz. Use of shorter wavelength and higher modulation frequency, which are currently under study, would facilitate a higher penetration depth and better temporal/spatial resolution.

MECHANICAL STIMULATION OF EPITHELIAL OVARIAN CANCER CELLS

Liron Avraham[1], Uri Zaretsky[1], David Elad[1], Yoel Kloog[2], Ariel Jaffa[3], Dan Grisaru[3]

[1]Department of Biomedical Engineering, Faculty of Engineering Tel Aviv University,
[2]Department of Neurobiochemistry, Faculty of Life Sciences, Tel Aviv University
[3]Lis Maternity Hospital, Tel Aviv Sourasky Medical Center & Sackler Faculty of Medicine, Tel Aviv University, E-mail: elad@eng.tau.ac.il

The development of epithelial ovarian cancer (EOC) begins at the surface of the ovary and grows into the organ. The ovary surface is exposed to peritoneal fluid pressures and shear forces due to continuous peristaltic motions of the gastro-intestinal system, creating a mechanical micro-environment for the cells on the ovary surface. Tumor growth and spreading are associated with increased expression of molecules that are involved in mechanical activity of cells. We hypothesize that mechanical stimuli affect the biological behavior of surface EOC cells, through changes in cellular mechanisms such as proliferation, adhesion and migration. The objective of this study is to explore changes in inter- and intra-cellular signal pathways which mediate these cellular mechanisms. EOC cells from cell lines OC-238 and OVCAR-3 were seeded in plastic flasks, and after 2-3 days were cultured on a denuded amniotic membrane in special wells. Once the cultured layer of EOC cells was ready for flow experiments, the wells were disassembled into sub-units and the well bottoms were mounted in a flow chamber. We conducted steady fluid flow experiments in which we applied wall shear stresses (WSS) of 0.24 dyne/cm^2 to 5 dyne/cm^2 on top of the cultured EOC cells in the flow chamber. The well bottoms were disassembled after termination of the mechanical stimuli in order to conduct biological tests such as immunohistochemical staining of actin and β-tubulin cytoskeletal components and proliferation assays. The results showed that after the mechanical stimulation the cell nucleus takes up less space and the β-tubulin fibers occupy a larger part of the cell cytoplasm. In some of the cells, an elongation of the cells was also observed as the shear stress increases. Detachment of the cells from each other was observed in cells subjected to stimuli of WSS in comparison to the unstressed cells in the control cultures that were packed tightly. We also noticed that proliferation rate increases as shear stress increases, and decreases as time increases. In conclusion, mechanical stimuli influence the cellular morphology and intracellular structure in ovarian cancer cell lines.

PERCEPTION OF STIFFNESS DURING SIMULATED NEEDLE INSERTION

Ilana Nisky[1], Assaf Pressman[1,2], Carla M. Pugh[3], Ferdinando A. Mussa-Ivaldi[2], Amir Karniel[1]

[1] Biomedical Engineering, Ben Gurion University of the Negev, Beer-Sheva 84105, Israel, {nisky, pressman, akarniel}@bgu.ac.il

[2] Sensory Motor Performance Program, Rehabilitation Institute of Chicago, 345E. Superior Street, Chicago IL, sandro@northwestern.edu

[3] Feinberg School of Medicine, Northwestern University, 201 E Huron St, Chicago, IL cpugh@nmh.org

Telesurgery can substantially improve patient care as well as surgical training by providing global access to surgical specialists. In telesurgery the surgeon determines the motion of a remote slave robot by moving a master robot and sensing the forces reflected from the slave to the master. Telesurgery requires transmission of information from a distance, and therefore delay is unavoidable. In the last few years, we have studied the effect of delay on perception of stiffness in linear spring like fields and on action in contact with them.

Here we developed a new protocol to probe the effect on perception and action in the same experiment testing the effect of delay on a nonlinear environment which simulates needle insertion into soft tissue. This task is characterised by transition between a rigid nonlinear boundary area and an internal soft tissue. We employed simulated telesurgery and focused on a simple teleoperation architecture which includes only delay and gains in the transmission channel in order to highlight the effects of delay without additional control considerations

We found that a nonlinear boundary region causes both psychometric and motor overestimation of stiffness, and that delay causes motor but not psychometric underestimation of the stiffness of this nonlinear soft tissue. We show that by changing the teleoperation channel gain it is possible to reduce and even cancel the motor effect of delay. In addition we will show kinematic analysis of movements around the point of transition between the boundary and the soft tissue with and without delay and discuss possible implications for understanting the control strategies around boundaries.

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EXPERIMENTAL MODEL FOR STRESS FRACTURES IN RATS

Stern-Perry M.[1] ,Gefen A.[1,*], Shabshin N.[2,3] Epstein Y.[2,4]

[1]Department of Biomedical Engineering, [2]Sackler Faculty of Medicine, [3]Division of Diagnostic Imaging,
[4]Heller Institute of Medical Research, Sheba Medical Center, Tel Aviv University.
* E-mail: gefen@eng.tau.ac.il

Background: A stress fracture (SF) is a partial or complete fracture of a bone resulting from its inability to withstand sub-threshold repeated stresses. It is a common injury in athletes, dancers and military recruits. To this *in vivo* models and finite element (FE) models simulating physiological aspects related to SFs are limited.
Objective: To develop a well-controlled, combined animal *in vivo* model and computer model, which will enable the investigation of various aspects related to SFs; specifically, estimating the relationship between internal strain/stress distributions and external loading.
Methods: 3D FE model: MRI axial scans of all shin tissues (hind-limb) of a 170g male rat were loaded into parallel planes and contours of all tissues were manually drawn per each slice; then, they were lofted into 3D bodies. This 3D model was imported to an FE solver and loaded with a force of 3.4N on the distal part of the tibia, for calculation of strains/stress distributions. *In vivo* study: Anaesthetized animals were subjected to a daily "training regime" that consisted of repetitive mechanical load of physiological significance (30 min/d, x3d/week, 1-2Hz), which was applied to their heels with a specially designed electrical piston. The peak load was about 6N.
Results: Overall, strains were found to peak between the mid and the third part of the proximal tibia. Peak tensile and compression strains and stresses were within the upper physiological range (~3000 micro-strain). Variations in the shear modulus of the muscle tissue had a negligible effect on both strain and stress distributions in the bone. Effects of variations in the elastic modulus of bone tissue on the peak strains and stresses were more substantial than that of the muscle tissue; the most significant effect was on the peak stress due to changes in the elastic modulus of the bone tissue.
Conclusions: In this study, a FE model that enables to study the 3D internal strain/stress distributions, has been developed. The FE model was found to be a useful tool for estimating strains and stresses during limb loading, which imitates walking movements. This is the first study in which a 3D FE model is combined with an animal SF model. This combined model allows investigation of various aspects of SFs. Future work will include simulation of several mechanical and physiological factors leading to the formation of SFs.

ANALYSIS OF MUSCLE ACTIVITY DURING BREASTFEEDING

[1]Yael Nadlin Carmeli, [2]Anat Ratnovsky, [3]Shaul Dollberg, [3]Dror Mandel, [1]Uri Zaretsky, [1]David Elad

[1]Department of Biomedical Engineering, Faculty of Engineering, Tel Aviv University,
[2]Department of Medical Engineering, Afeka College of Engineering,
[3]Department of Neonatology, Lis Maternity Hospitals, Tel Aviv Sourasky Medical Center.

Breastfeeding is increasingly prevalent worldwide due to the growing awareness and education concerning its advantages, which lie not only in the infant's nutrition, but also in the feeding process that contributes to proper development of the facial muscles and their preparation for future tasks of chewing and speaking. Although the components of breast milk have been studied repeatedly, the physical mechanisms involved in breastfeeding, along with the coordination of suckle, swallow and breathe are still controversial. The aim of this study was to examine the relative roles of the Mylohyoideus (i.e., the submental group which is involved in jaw movement), the Orbicularis Oris (which is involved in mouth movement) and the Sternocleidomastoid (inspiratory accessory group involved in creation of mouth negative pressure) in the feeding process. Simultaneous electromyography (EMG) of these muscle groups was not previously performed, and thus, they were chosen in this study in order to estimate the role of the inspiratory muscles in comparison with that of facial movement and swallowing muscles. Signals of surface EMG were obtained from eight neonates at a mean age of 2.500±1.414 days with a mean weight of 3209±450 g. The acquired signals were processed off-line. The computed normalized mean RMS values were 0.363±0.201, 0.247±0.095 and 0.214±0.082 for the Mylohyoideus, the Orbicularis Oris and the Sternocleidomastoid, respectively. These results suggest that the jaw movement is the primary motion during breastfeeding, while involvement of the inspiratory muscles which generate negative pressures in the mouth is relatively small. These results support and complement previous findings.

CONTROLLED RELEASE OF ANTIPROLIFERATIVE DRUGS FROM NOVEL BIORESORBABLE STENT COATINGS

Amir Kraitzer*, Yoel Kloog and Meital Zilberman***

*Department of Biomedical Engineering, Faculty of Engineering,
**Department of Neurobiochemistry, Faculty of Life Sciences
Tel-Aviv University, Tel-Aviv 69978, ISRAEL

Drug-eluting stents (DES) significantly reduce the incidence of in-stent restenosis, which was once considered a major adverse outcome of percutanous coronary stent implantation. Localized release of antiproliferative drugs interferes with the pathological proliferation of vascular smooth muscle cells which is the main cause of in-stent restenosis. Farnesylthiosalicylate (FTS, Salirasib) is a new rather specific nontoxic drug which was recently developed at the Tel-Aviv University. It is considered an important target for cancer therapy as well as for therapy of other proliferation diseases, including restenosis. Drug- eluting bioresorbable stent coatings were developed and studied. The porous poly (DL-lactic - co - glycolic acid) (PDLGA) matrices loaded with either Farnesylthiosalicylate (FTS) or paclitaxel, were prepared using freeze drying of inverted emulsion technique. The investigation of the new coating was carried out using core/shell fiber structure. The effect of the emulsion's formulation and process kinetics during fabrication on the drug release profile was studied in light of the shell's morphology and its degradation profile. Our results show that the coating's porous structure contained round-shaped pores, usually within the 2.9-6.4 μm range, with a porosity in the range of 67-85%. The pores were partially interconnected by smaller inner pores. The most important parameter affecting release in this system is the copolymer composition. An increase in the glycolic acid content of the PDLGA copolymer enhanced the release rate of both drugs. Also, the FTS release from our highly porous coatings is faster and different from that of paclitaxel. Paclitaxel is more hydrophobic than FTS and creates more interactions with the host polyesters. Therefore, paclitaxel's diffusion through the host polymer is much slower and all changes in formulation parameters affect its release profile mainly after 10 weeks of degradation. The process was found to affect the drug-release profile via two routes: (1) Direct, through water uptake and swelling of the structure, leading to a higher burst release. Degradation of the host polymer affects the drug release rate at a later stage. (2) Indirect effect of the microstructure on the release profile, which occurs via an emulsion stability mechanism.

NANO-STRUCTURED BIORESORBABLE FILMS LOADED WITH BIOACTIVE AGENTS FOR BIOMEDICAL APPLICATIONS

Adi Rachelson, Amir Kraitzer and Meital Zilberman

Department of Biomedical Engineering, Tel-Aviv University, Tel-Aviv 69978, ISRAEL

Controlled drug delivery offers numerous advantages compared to conventional dosage forms given as a systemic treatment, in particular: improved efficacy, reduced toxicity and improved patient compliance and convenience. Several of the most investigated biodegradable systems have been based on emulsions. The use of emulsions for such systems is attractive since parameters such as polymer content, organic to aqueous phase ratio and homogenization rate can be varied to design and tailor the release profiles.

In the present study we developed and studied highly porous nano-structured drug eluting systems loaded with various drugs. The porous films were prepared using the inverted emulsion freeze drying technique. This method is unique not only in enabling to achieve a continuous structure (as opposed to microsphere powders which are obtained using a double emulsion) but also in having the ability to preserve the emulsion's original microstructure. The main goal of this study was to determine the effect of nano-structuring, whether by addition of effective surfactants or by altering kinetic parameters, on the release profiles of hydrophilic and hydrophobic drugs from the nano-structured films. 50/50 poly(DL-lactic-co-glycolic acid) was used as the host polymer of the emulsion's continuous phase. Paclitaxel and Farnesylthiosalicylate (FTS) served as the hydrophobic drugs and were incorporated into the emulsion's organic phase, whereas mafenide acetate and ceftazidime hydrate served as the hydrophilic drugs and were incorporated into the emulsion's aqueous phase. All specimens obtained were highly porous (70%-90%) and included partially interconnected pores. The parameters which had the most significant effect in reducing pore size were the copolymer ratio and the homogenization rate. Bovine serum albumin (BSA) and horseradish peroxidase (HRP) were found to be the most effective surface active agents which, together with a high homogenization rate, yielded homogeneously distributed nano-sized pores (440-600 nm and 730-775nm for systems loaded with hydrophobic and hydrophilic drugs, respectively.Most drug release profiles exhibited an initial burst release, accompanied by a decrease in release rate with time, as typical for diffusion-controlled systems. Nano-structuring had a significant effect on the release profiles of hydrophobic drugs from the bioresorbable films. In this case smaller pore sizes resulted in higher burst effects and higher release rates, due to an increase in the surface area for diffusion. Systems containing hydrophilic drugs were less affected by nanostructuring, most likely due to the fact that these drugs have very high release kinetics in an aqueous medium. Understanding the relationships between processing, microstructure and the resulting controlled release behavior will enable to engineer new implants and to adapt them to a wide variety of biomedical applications.

BIO FLUID ASPECTS OF EMBRYO TRANSFER IN A CLOSED UTERINE CAVITY

Sarit Yaniv[1], Ariel Jaffa[2], David Elad[1]

[1]Department of Biomedical Engineering, Faculty of Engineering, Tel Aviv University
[2]Department of Obstetrics and Gynecology, Lis Maternity Hospital, Tel Aviv Medical Center

In natural conception, an ovum is discharged during ovulation and enters into the nearby uterine tube. The ovum may meet the spermatozoa at the ampulla where fertilization may occur. Within three days after a successful fertilization, the embryo enters the uterine cavity and is transported with the uterine fluid for another 3 to 4 days until it is implanted at the fundus, which is the upper part of the uterus. Unlike sperm, the embryo does not have a self –propelling mechanism, and thus, it is most likely passively transported by the intrauterine fluid to its final site of implantation within the uterine wall. The pattern of intrauterine fluid motions are also important factor in extracorporeal fertilization where embryo transfer (ET) is the last manual stage during which the embryo is placed in the uterine cavity by a catheter. In spite of the continuously increasing number of assisted reproductive technologies (ART) cycles due to clinical innovations and technological advancement, the average implantation rates per ART cycle are still under 30% and significantly lower as the subject's age advances. Failure at the embryo transfer stage may be due to poor embryo quality, lack of uterine receptivity, or the transfer technique itself. Nevertheless, after the ET procedure is completed the embryos are conveyed in the uterus for another 2–4 days, as in natural conception, until they are implanted in the endometrium. Thus, intrauterine fluid flow patterns have an important role in all cases of human reproduction.

The main objective of this research was to explore the intrauterine pre-implantation transport of the embryos during and post the ET procedure. Computer simulations were conducted in the sagittal cross section of the uterus in order to investigate the velocity patterns within the uterine cavity, as well as pre-implantation transport of embryos for both natural conception and post-ET, and for a variety of independent parameters (e.g., catheter location, synchronization with channel wall, speed of injection, uterine wall amplitude). We started with the 2D model with open ends into which we inserted the catheter. Then, we moved to a more advanced models with a closed fundal end.

Analysis of the results showed that the fluid flow field and the transport characteristics of peristaltic flow in a closed uteruss are strongly affected by the uterus fundal end. The embryos are most likely to circulate in small loops around their initial location. The transport is also controlled by uterine contraction, as well as by the symmetry, amplitude and frequency of the uterine wall. The results clearly demonstrated that the synchronization between the onset of injection and uterine wall is strongly affected by the embryos location. When the uterine wall movement is in an outward direction, the embryos do not propagate toward the fundus and stay at the vicinity of the catheter. The position of the catheter in the uterine cavity is also an important parameter. Placement of the catheter tip close (≤10mm) to the uterine fundus induces reflux flows that may drive the embryos towards the cervix. This study explores the transport pattern of embryos and the corresponding implications on the success of implantation. It provides predictions of possible patterns of intra-uterine embryo transport while allowing investigation of affecting factors such as uterine physiology and the ET methodology. Finding the optimal value of these set of parameters may help raise the rate of success.

ULTRASONIC IMAGING AND MEASUREMENT OF THERMAL PROPERTIES OF TISSUES

Lilach Yeshurun, Haim Azhari

Faculty of Biomedical Engineering, Technion-Israel Institute of Technology, Haifa, Israel

Introduction: Medical imaging plays a major role in the clinic. Current imaging modalities map different properties of tissues. However, very little attention was given to the thermal properties of the tissue (e.g. thermal conductivity K, and the specific heat constant C). Image-guided HIFU surgery has been recently offered as a non-invasive alternative to conventional lumpectomy in several organs. A lot of research has been done regarding temperature imaging for the purpose of image guided surgery by MRI. MRI has a lot of disadvantages so an alternative which will be cost-effective, radiation-free, and less-restrictive system for thermal monitoring will be useful. Objectives: Utilize through transmission ultrasound for non-invasive mapping of the thermal tissue properties, and assess the potential application of this system for breast imaging and image guided HIFU treatment of the breast. Methods: A HIFU system was used to heat a phantom. During the heating and cooling processes acoustic projections were acquired (the projection is acquired from only one angle). The focus temperature was measured during the experiments directly by thermocouple. The acquired data was processed into TOF images and average speed of sound values. From that, the spatially speed of sound values in the slice were found. From these values it is possible to discover the changes of temperature in the slice over cooling time and the thermal constants. Phantom results and future steps: We succeeded to achieve the spatial speed of sound in the slice of phantom (made of agar) over time. After integration of the data, we generated a graph that matches temperature and speed of sound. From these results we can calculate the spatial temperature changes in the slice over time and the thermal constants. We plan to do the same process to different kinds of tissues and due to the promising results in agar we hope to succeed in tissues as well.

EVIDENCE OF STRONG ANOMALOUS DIFFUSION IN LIVING CELLS

Naama Gal and Daphne Weihs

Faculty of Biomedical Engineering, Technion-Israel Institute of Technology, Haifa, Israel

We evaluated the transport of polymeric particles internalized into living cancer cells. The mean square displacement demonstrates superdiffusion with a scaling exponent of 1.25. Scaling exponents of a range of displacement moments are bi-linear with moment order, exhibiting slopes of 0.6 and 0.8. Thus, we present first experimental evidence of strong anomalous diffusion. Bi-linearity indicates that particle motion is composed of subdiffusive regimes separated by active, yet non-ballistic, flights. We discuss the results in terms of particle interactions with their microenvironment.

PROCESS-STRUCTURE-PROTEIN RELEASE EFFECTS IN ACTIVE SCAFFOLDS FOR TISSUE REGENERATION DERIVED FROM INVERTED EMULSIONS

Orly Grinberg, Jonathan Elsner , Itzhak Binderman and Meital Zilberman

Department of Biomedical Engineering, Faculty of Engineering, Tel-Aviv University
meitalz@eng.tau.ac.il

Tissue regeneration involves the preparation of polymeric structures that serve as degradable scaffolding for bioactive molecules or cells as well as the study of their structure and properties. The main obstacle to successful drug or protein incorporation and delivery from degradable scaffolds is the inactivation of bioactive molecules by exposure to high temperatures or harsh chemical environments. In the present study we developed and studied novel bioresorbable film structures loaded with bioactive agents. Their high porosity is designed to enable tissue growth into the scaffold. The scaffolds were prepared using the freeze drying of inverted emulsions technique, which enabled to incorporate very sensitive bioactive molecules without affecting their activity. Our study focused on the effect of the emulsion's formulation on the porous shell structure and on the resulting cumulative protein release from the composite fibers for 28 days. Poly(DL-lactic-co-glycolic acid) was used as host polymer and horseradish peroxidase (HRP) was used as the protein source. The release profiles usually exhibited an initial burst effect, accompanied by a decrease in release rate with time, as is typical for diffusion-controlled systems. The Polymer initial molecular weight and the HRP content exhibited significant effects on both the scaffold microstructure and the HRP release profile from the scaffold, whereas the copolymer composition, the emulsion's organic:aqueous phase ratio and the polymer content only affected these characteristics in certain cases. We have investigated the effect of this film composed of PDLGA and HRP on cell adhesion and growth of human fibroblasts in culture. We have observed that cells adhered and grew with characteristics of fibroblasts on the film.