הפקולטה להנדסה ביו- רפואית בטכניון

פרויקט גמר תשע"ד

בשיתוף:

שלום רב,

אנו שמחים להציג בפניכם את תקצירי הפרויקטים של הסטודנטים המסיימים לימודיהם בשנה זו, שנת תשע"ד.

הפרויקט, המבוצע ע"י סטודנטים בשנת הלימודים האחרונה, מהווה את גולת הכותרת של לימודיהם לתואר בהנדסה ביו- רפואית.

במסגרת הפרויקטים מביאים הסטודנטים לידי ביטוי את הידע והכלים שרכשו במהלך השנים בתחומי ההנדסה, המדע והרפואה.

מטרת הפרויקטים, הינה לתת מענה לצרכי הפיתוח והמחקר של חברות העוסקות בתחום ההנדסה הביו- רפואית, תוך עמידה בסטנדרטים המקובלים ובמקביל, לתת ניסיון ואתגר מקצועי לסטודנטים המסיימים ולעודד השתלבותם בתעשייה הביו- רפואית.

לפרויקטים חלק חשוב בעידוד היזמות בקרב הסטודנטים, וחלקם אף מובילים להקמת חברות הזנק ורישום פטנטים.

פרויקטים אלו מהווים נדבך מרכזי בחזון הפקולטה, לחתור לבניית גשר למצוינות ובמה לקשרים ושיתופי פעולה ארוכי טווח בין האקדמיה והחברות המובילות בתעשייה.

ברצוננו להודות לחברת CByond על המעורבות בנושא הפרויקטים, הן בהנחיית מספר פרויקטים בעבר והן בהשתתפות פעילה בימי הצגת הפרויקטים, ועל הקצאת המשאבים לחלוקת פרסים לפרויקטים המצטיינים – תרומה מרשימה ובעלת משמעות רבה.

הפקולטה מאחלת הצלחה לסטודנטים המסיימים, ומקווה לראותם בעתיד נוטלים חלק פעיל בפרויקטים חשובים אלו כמנחים מהתעשייה.

בברכה,

ד"ר אלכס וילנסקי , אחראי קורס פרויקטים

פרופ"ח אמיר לנדסברג , דיקן הפקולטה

In vitro microcirculatory blood flow using microfluidics and velocimetry techniques: role of hematocrit and diameter

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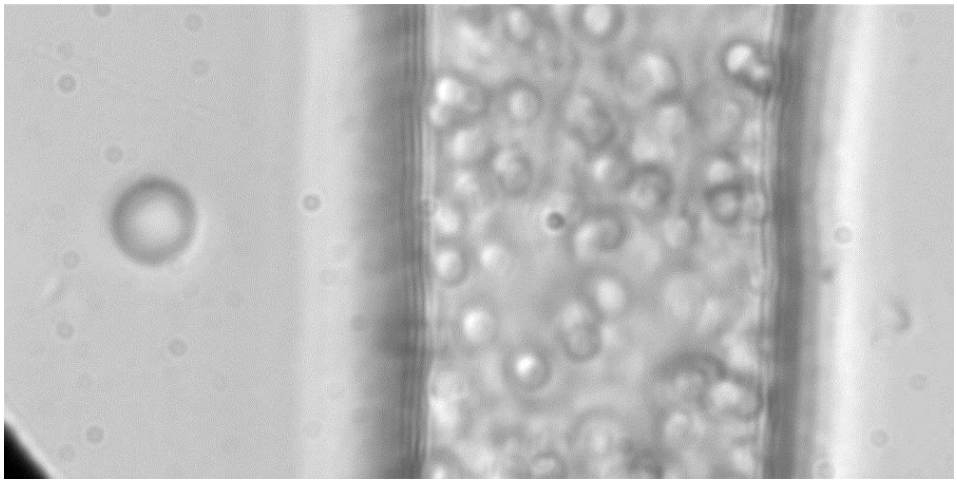
In vitro velocity measurement of blood flow in microchannels has been studied extensively in recent years, presenting velocity profiles and particle tracking mostly for microchannels range >100µm width. However, the influence of channel diameter and hematocrit level on flow was not investigated thoroughly. In this study, we characterize flow pattern in narrow microchannels range~25-100 µm using particle image velocimetry (PIV) technique. Following Farhaeus-Lindqvist effect on blood viscosity, we measure the influence of varying hematocrit levels, 0% (pure water with fluorescent particles) -13%, on flow. Our results, describing pure water flow at different diameters, show a good match to theoretical flow, furthermore we expect to see a plug like flow as we increase hematocrit levels. A better observation on flow characteristics in pre-capillary arterioles may assist with better understanding flow patterns in capillaries. Future work could include mimicking Alveolar Capillary Network (ACN) and further understanding perfusion to the lungs.



Red Blood Cells flowing through a microchannel of 25um width

as viewed in a light microscope enlarged X40

Resonant Femtosecond Pulse Irradiation of Gold Nanorods: Particles Re-shaping and Consequent Damage to targeted Cancerous Cells

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In recent years, resonant laser irradiation of specifically targeted gold nanoparticles has been proposed as an effective therapeutic tool for treating malignant tissues. A wide range of nanoparticles (i.e. spheres, rods, shells, etc.) with either continuous-wave illumination or short-laser pulses (nanosecond to femtosecond range) were used.

In this paper we used 4:1 aspect ratio gold nanorods either in solution or targeted to malignant cells and irradiated them by a single femtosecond pulse at 800 nm using different fluencies and pulse durations. The spectrum of the irradiated particles and their shape were determined, statistical analysis of the particles' shape distribution was established using a dedicated Matlab code and cell death rate was monitored by staining for necrosis.

The results showed that under all irradiation conditions tested, a large percentage of the rods turned into spheres after the first pulse, restricting in-resonance irradiation conditions to one pulse. Cell death rate was found to be inversely proportional to pulse duration, proposing a role for ionization in the mechanism leading to cell death.

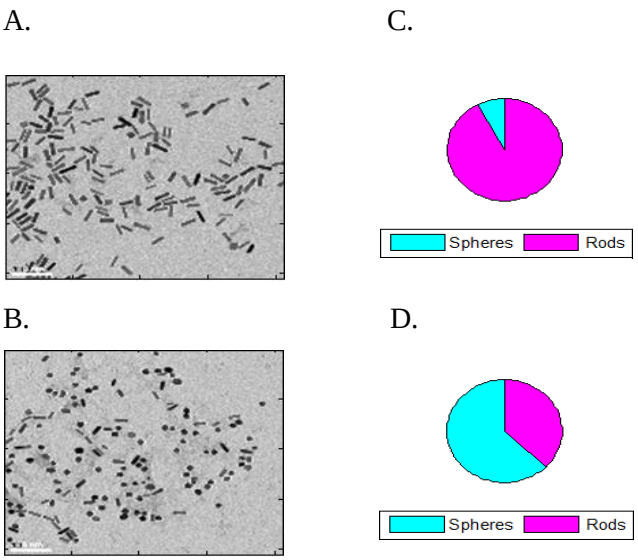

Figure 1: ***TEM images of gold nanoparticles and their corresponding shape distribution diagram.*** A. C. non- irradiated, control nanorods B. D. following 1 pulse irradiation at 800 nm, fluence: 5 mJ/cm^2. Scale bar represents 100 nm.

Figure 2: ***Malignant white blood cells irradiated by 1 pulse at different pulse durations.*** Fluence: 100 mJ/cm^2. Red staining represents necrotic cells.

Physiological Model Based Image Analysis of Doppler Ultrasound Velocity Profiles

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Introduction: In the rapidly growing field of medical technologies, clinical based costume software is of interest. Our present work, which focuses on cardiac functional measurements, attempts to adjust physiological parameters calculated by CircAdapt; a mathematical model of cardiovascular system; using several modes of ultrasound (US) data acquisition.

Methods: The current study uses semi-automatic segmentation method to extract the velocity profile envelope of blood flow through the aorta from US Doppler Mode (Figure1). Afterwards, the spatial mean velocity profile is calculated according to center of mass and compared to the equivalent profile calculated by CircAdapt. The inputs for CircAdapt are adjusted to the subject parameters such as heart rate, aortic area, flow, etc.

Results: Comparison between the measured and calculated profiles ($R^2 = 0.6008$) has demonstrated a resemblance between them (Figure2) which allows us to study the sensitivity of the CircAdapt model to certain physiological parameters.

Conclusions: The mean velocity profile estimated by the CircAdapt model may converge to the actual physiological profile extracted from US Doppler Mode by adapting certain physiological parameters in the model to the subject's parameters. This adjustment will enhance the performance of the mathematical model in comparison to gold standard methods.

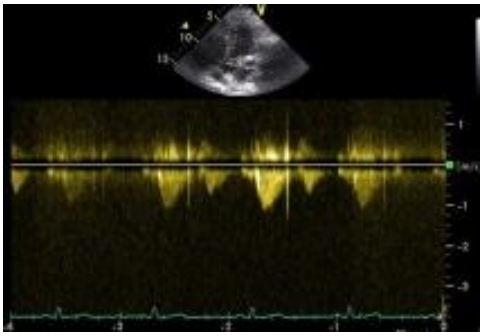

Figure 1. Ultrasound Doppler: blood flow velocity through the aorta as a function of time.

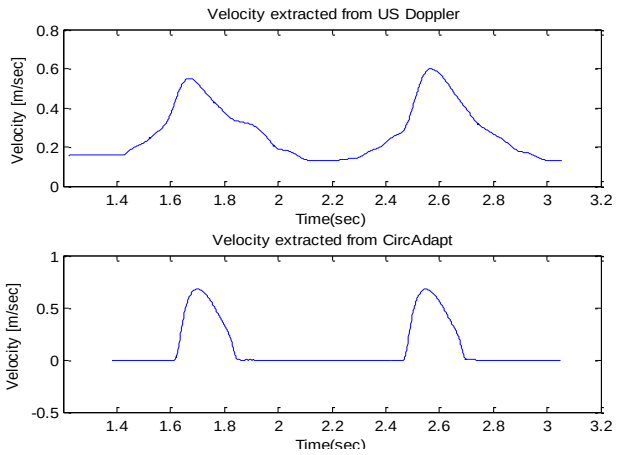

Figure 2. Comparison between Mean Velocity Profiles through the aorta, extracted from US Doppler and the CircAdapt Model

3D Holographic Patterns Generation for Artificial Vision Restoration

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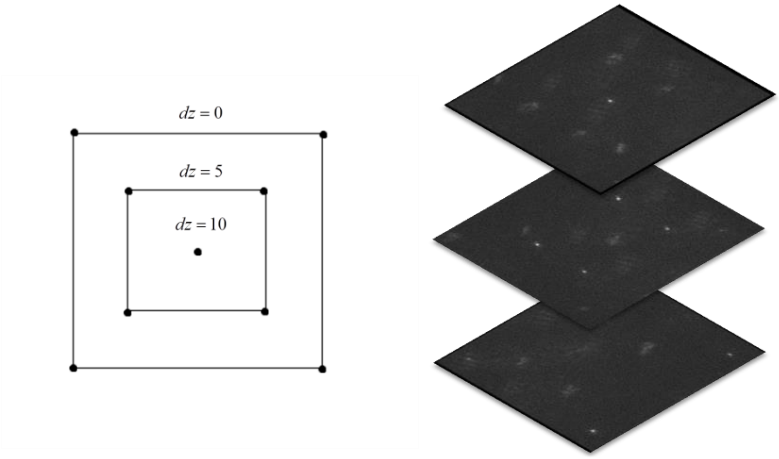
Introduction:
Direct optical stimulation enables precise spatial and temporal control of neuronal activity, and has major implications for medical applications such as retinal prostheses. In our project we designed, implemented and analyzed 2- and 3D holographic patterns in optical setups intended for artificial stimulation of retinal neurons in both isolated and intact blinded retinas.

Methods:
By using a phase-only computer generated holography (CGH) interface based on a spatial light modulator (SLM) it is possible to generate a variety of spatial patterns, and to axially translate holographic spots by adding a parabolic phase to the hologram's analytical expression.

Results:
We developed holographic patterns and analyzed their projections in two different setups used for both *in vitro* and *in vivo* experiments. We created meaningful spatial patterns for experiments intended on extracting significant information from the mouse visual cortex. In addition, axially shifted spots in 3D-generated patterns had similar sizes and shapes (mean FWHM = 8.25 μm).

Conclusions:
Our GUI enables the projection of single-cell resolved holographic patterns in both 2 and 3 dimensions. This will allow remote focusing of 2D patterns onto cells without moving any optical components, and targeting of neurons in 3D layers.



An example of a 3D pattern: A pyramid with 3 planes. $\mathrm{FWHM}(\mathrm{dz}=0)=7.91\mu\mathrm{m}$, $\mathrm{FWHM}(\mathrm{dz}=5)=8.14\mu\mathrm{m}$, $\mathrm{FWHM}(\mathrm{dz}=10)=8.72\mu\mathrm{m}$.

CHARACTERIZING HEART RATE VARIABILITY-BREATH RATE VARIABILITY RELATIONSHIP USING FREQUENCY AND TIME-FREQUENCY METHODS IN RATS DURING HIFU PACING

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Head of project: Dan Adam

Under the supervision of: Amit Livneh

Introduction:

Heart rate variability (HRV) is the beat to beat change in heart rate, describing the deviation of the heart rhythm from the average rhythm at a specific time. The phenomenon is well characterized but further study of the interplay with Breath rate variability (BRV) is required, especially in extreme circumstances (long term anaesthesia, high intensity focused ultrasound (HIFU) insonation)

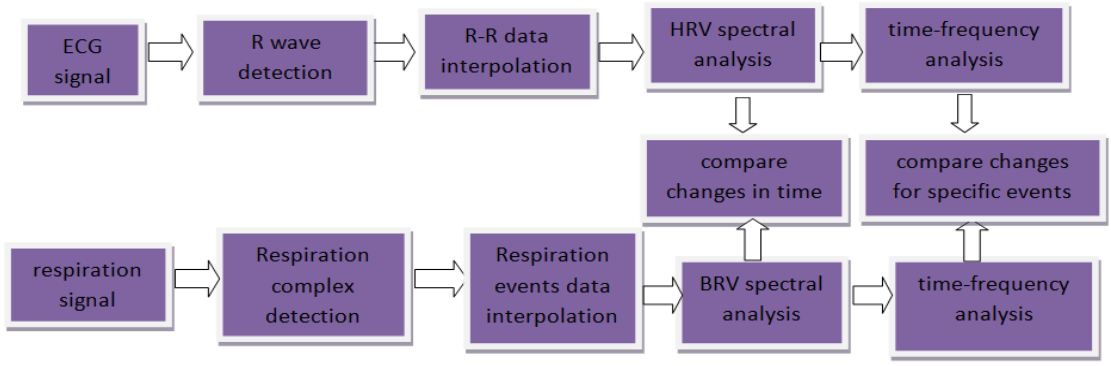
Project objectives:

We study the following questions:

1. Is there a frequency shift in HRV and BRV spectral maps that can be correlated with experiment progression in time (Frequency analysis)
2. Is there a correlation between premature beats occurrence rate to changes in BRV spectral map (Time-Frequency Analysis)
3. Is there a correlation between specific respiration patterns (e.g. frequent gasping) to changes in HRV spectral map (Time-Frequency analysis)

Methods:

ECG and respiration signals were acquired during HIFU pacing experiments in anaesthetized rats. The signals were analysed offline using proprietary Matlab software. ECG R-wave detection algorithms were adapted for rats. HRV power spectrum and spectrogram were acquired by interpolating the R-R interval data and using FFT based spectral analysis. BRV analysis was performed using similar methods. The HRV and BRV temporal spectrums evolution and cross correlation were examined.



Cancer Cell Response to Near-Monochromatic Illumination

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Fluorescence microscopy with near-monochromatic illumination is widely used in biological research, to facilitate in-vitro visualization of intracellular structures.
While this approach is widely used, any detrimental effects of this type of illumination on the cells have not been widely studied. Our goal was to assess the effects exhibited by cells to this kind of illumination. In this work we used high metastatic-potential epithelial breast-cancer seeded on glass coverslips and placed under a fluorescent microscope where they were subjected to various illumination protocols varying parameters such as exposure dynamics, illumination wavelength, and illumination intensity. We observed that these cancer cells change their shape, exhibit membrane protrusions and well attached cells become rounded, in the presence of this kind of illumination and that the nature and magnitude of the response changed as different protocols were used. Our work can serve as a preliminary map for these cell responses, however, future work with other types of cells should be conducted to provide more insight, allowing researchers to eliminate this effect and increase experimental accuracy.

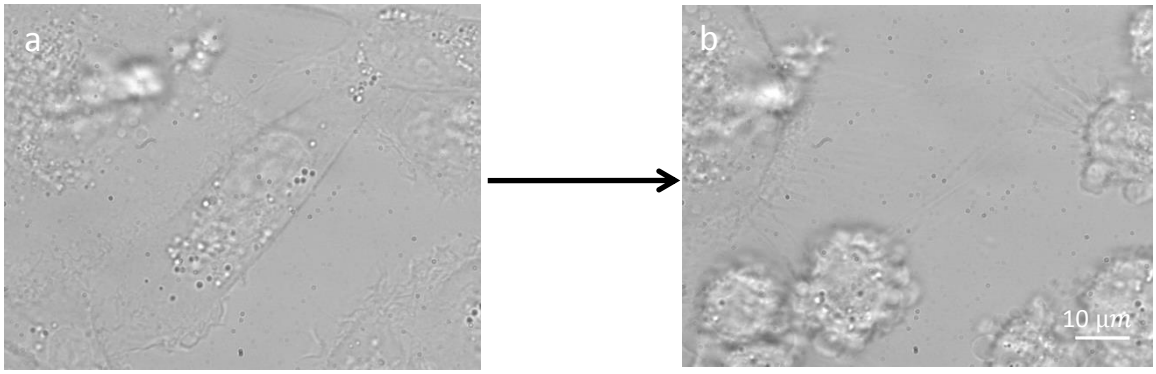

Figure 1: Cells exposed to near-monochromatic illumination. a) Cells before illumination. b) Cells after 7 minutes of continuous exposure to illumination at λ=470-495 nm.

Controlling Collagen-Gel Stiffness and Pore Size through Gelation Conditions

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Metastatic cells have been known to apply forces on a non-degradable, impenetrable gel (PAA). Continued work in the lab includes evaluating if this ability exists in a physiological gel system. In this project, we have used collagen gels with modulated stiffness as the model system, chosen in the stiffness range determined for PAA gels. The gels were prepared by incubation at 37°C at various times. Cross-linking was done using glutaraldehyde (GA), and TRIS buffer was added to stop the cross-linking, as GA was found to be harmful to cells. We used rheometry to evaluate the elastic shear modulus of the gel. Gel stiffness was modulated by modifying gelation process conditions, focusing on gelation time, cross-linker concentration, and cross-linking time. The experiments showed that an increase in cross-linking time, cross-linker concentration, and gelation time will result in a larger elastic shear modulus. We have concluded that the optimal gelation period is 2.5 hours long. In addition, the optimal cross-linking time is 30 minutes and the GA concentration should be 0.4% w/v (weight to volume ratio). Integrating these conditions provides control of gel stiffness, allowing flexible experiment design to simulate a physiological environment.

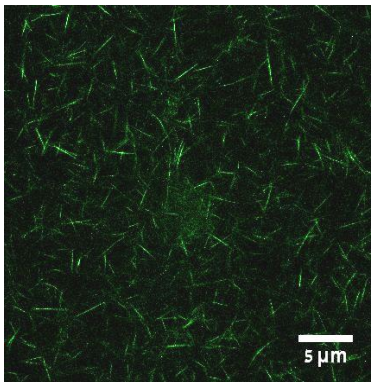

Figure 1: Collagen gel fibers under confocal microscope

Optimization of Strain Measurement on a Capsule in the Colon and Analysis of Strain Signal Obtained from Clinical Trials

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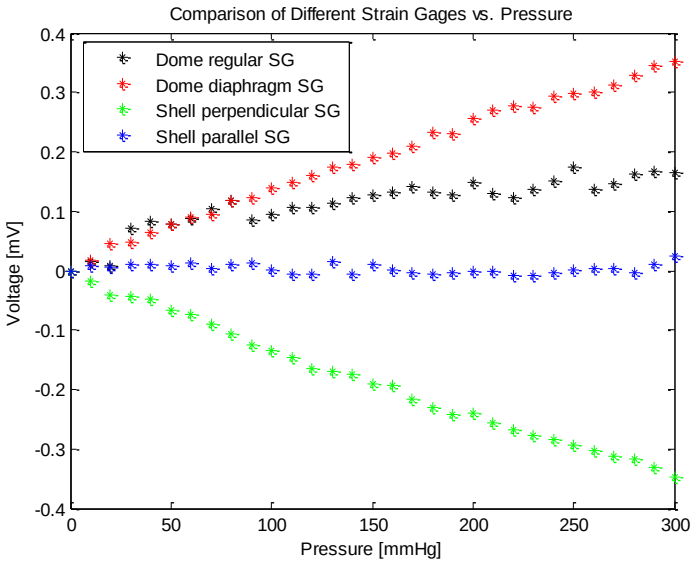
[2] Check-Cap Ltd, Isfiya, Mount Carmel, Israel

Introduction: Check-Cap develops a state of the art technology for colorectal cancer screening, using a swallowable capsule containing an X-ray transmitter. Strain signal, an indication of the pressure in the colon, is expected to be improved when a strain gauge is located in the most sensitive area on the capsule. In addition, information obtained from strain signal analysis will contribute to improve the screening algorithm.

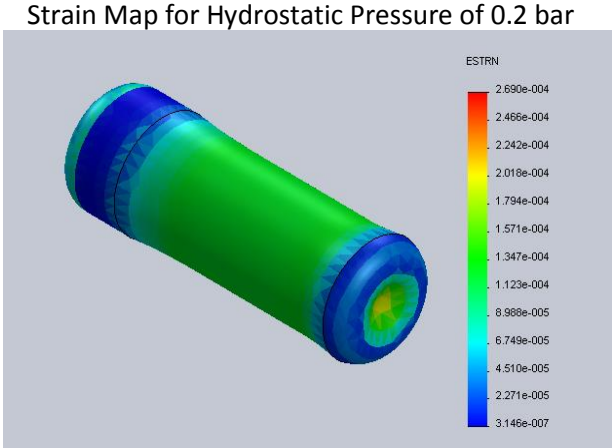
Methods: A SolidWorks® simulation of the hydrostatic pressure applied on the capsule was followed by strain gauge characterization and location on the capsule. Hydrostatic pressure was applied on the capsule using a pressure chamber and Strain signal analysis was done using Matlab®.

Results: The highest sensitivity for strain changes was detected in the center of the dome, and in the shell area in the longitudinal direction. Distinction between different areas of the intestine was hard to obtain by comparison of frequency spectrums, however, an inverse relation was found between average strain amplitude and capsule motility.

Conclusions: For improved strain signal, the ideal locations for strain gauges are on the center of dome and on the shell area in the longitudinal direction. According to the results, frequency spectrum analysis will not contribute to improve the screening algorithm. However, high strain amplitude can indicate the presence of a barrier in the colon, and might be useful for detection of areas suspected to contain polyps.



Strain Map for Hydrostatic Pressure of 0.2 bar



Development of an Asthma Drug release Inhaler Controlled by Respiratory Flow

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[1]Department of Biomedical Engineering, Technion - IIT, Haifa

[2]Rambam Health Care Campus - Hospital, Haifa

[3]Respeer

Asthma is a respiratory disease which affects an increasing proportion of the world population. Since no preventive treatment is well established yet, asthma patients use inhalers, which contains dose of medicines, to prevent or stop asthma attack. Patients often make critical errors while using the inhaler. These errors result in a poor drug delivery, sub-optimum asthma control, and increased inhaler usage.

In this study, we present a novel design of asthma inhaler which attempts to improve the inhaler usage and the treatment efficiency. To that end, we used a Ventolin inhaler, which is a common metered-dose inhaler used for asthma treatment, and attempt to redesign it with SolidWorks to include a mechanical drug release system that is controlled by the patient's inhalation airflow.

To evaluate the operation forces needed to release the drug, we used a force meter. Based on the measured values, we designed two models with different mechanical triggers resulting in the drug release. The first trigger is based on the inhalation airflow pressure, and the second on an airflow turbine.

Comparison between the two models has revealed that the first model require smaller forces to release the drug and provide better performances. Therefore, we have decided to manufacture this model and use it in the future clinical trials.

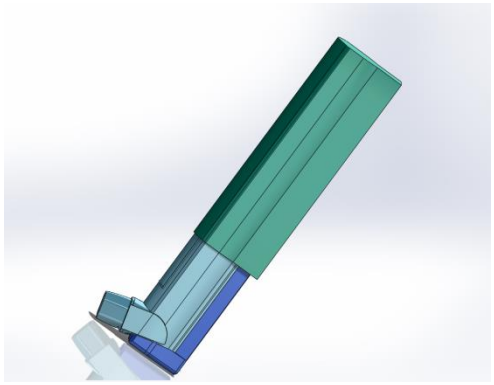

Figure 1 first solution based gate valve & spring

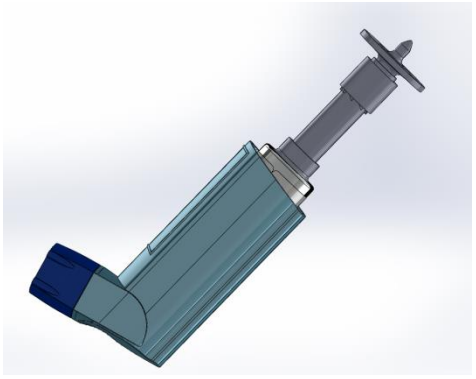

Figure 2 second solution based turbine & spring

Surfactant and Liquid Plug Delivery Using Microfluidic Models of Airways

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[1] Department of Biomedical Engineering, Technion - IIT, Haifa, Israel

Liquid boluses appear in the lungs in two forms: external sources, such as medicine, instilled in the lungs; and internal sources, such as a symptom of a disease or at full expiration in a healthy person. The investigation of liquid plug delivery will aid future research in lung therapy delivery systems, by allowing doctors and nurses to better understand the correlation between dose volume and lung generation penetration. We do this by pushing liquid bolus through small lung airways models at a constant pressure. Our microfluidic lung models are made out of PDMS in a process called softlithography. The liquids used in this study vary in viscosity and surfactant concentration and are pushed at pressures (velocities) that mimic different physiological conditions. We found that a higher degree of shedding occurs in the following three situations: higher speeds, which correlates to a higher Capillary number for a given fluid; tree models of greater asymmetry; and lower surface tension. We conclude that the asymmetric microfluidic model is a useful tool in investigating liquid plug delivery *in vitro*. Future research should involve different surface treatments to the PDMS microfluidic device to better mimic the inner lumen of airways, as PDMS in its natural state is hydrophobic unlike the lungs.

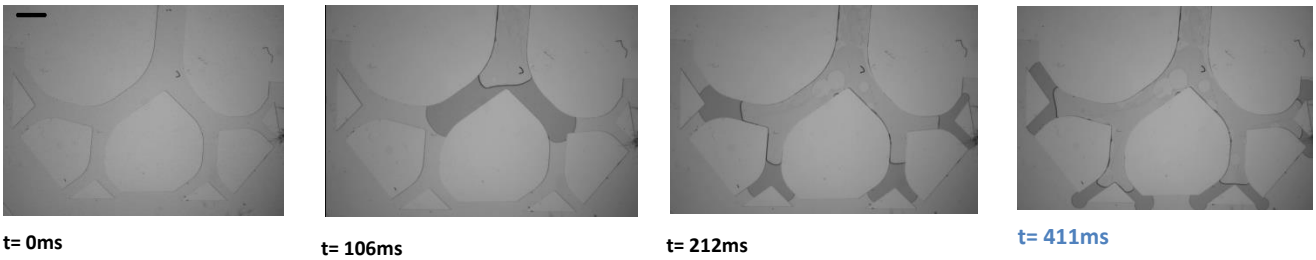

Figure 1: 1% Tween 20 in water bolus propagation through an asymmetric microfluidic device. [scale bar 1600µm]

A Physiology-Based Device Model of Ureteric Stents Fatigue Testing

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[2]Allium Medical Solutions Ltd. Caesarea Industrial Park South, 38900 Israel

Ureteric stents are meant to prevent or treat obstructions of the ureter and to allow urine flow. Nowadays, the mechanical properties of the stents are tested in a non-physiological context. Here, we propose a device model that simulates the physiological peristalsis motion in the ureter, in order to test the mechanical fatigue of the stents.
Based on an analysis of the physiological conditions in the urinary system, and in particular in the ureter, we designed our device model in SolidWorks® (Fig. 1).
The key requirements of our device are to simulate the peristalsis motion by a periodic contraction which propagates in one direction along the ureter and is expressed by a radially symmetrical diameter diminution, while keeping the modeled ureter in its linear form.
Finally, it is concluded that the device should be constructed of: a flexible tube which models the ureter, two pulleys with radial cut which diminish the tube's diameter. The pulley's axis is constrained by a circular path to allow the one-directional contraction motion. In addition, a DC-motor and a set of gears are used to transmit a synchronized motion.

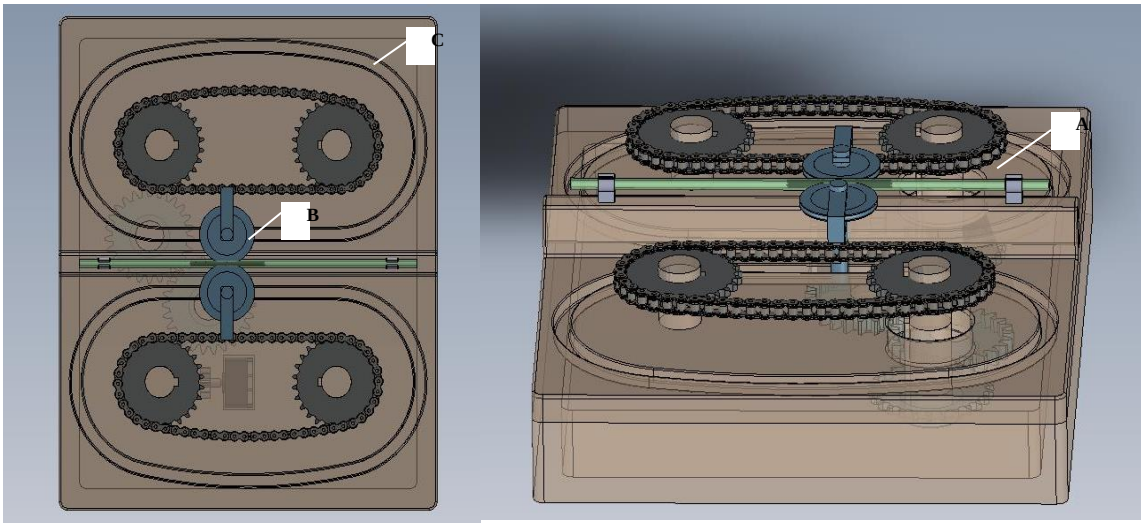

Figure 3 - Testing device model. A - Ureter model tube, B - Contracting pulleys, C - Circular path. (Background - motor and gears)

Stationary Clutter Removal from Echocardiographic Imaging Using the Singular Value Filter

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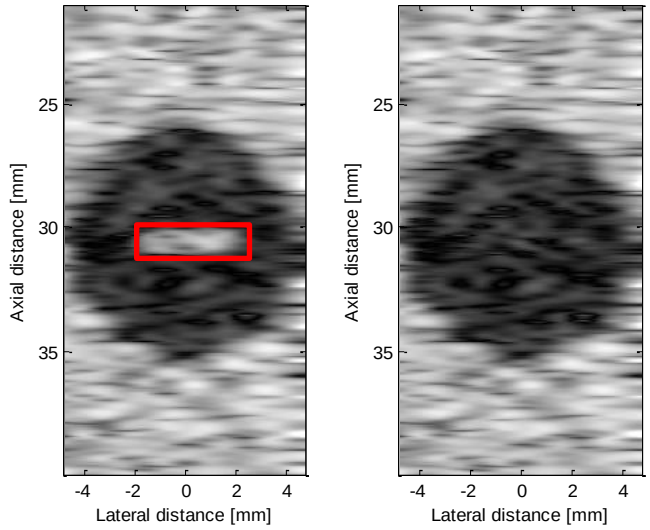
Introduction: Clutter artifacts can degrade image quality by reducing contrast or biasing functional measurements, such as myocardial strain in cardiac imaging. This phenomenon is typically caused by multi-path reverberation or off-axis scattering, and appears as a quasistatic region of echo signal. The singular value filter (SVF) has been presented for principal component analysis (PCA) based signal separation. This approach allows clutter removal from 2D echocardiography cines.

Methods: A software-based simulation was built in FIELD II using MATLAB (MathWorks Inc., Natick, MA). The obtained data was subjected to filtering. Design of SVF is based on the expected source signal model and statistical assumptions. The optimal SVF parameters were chosen by minimizing the MSE between the clutter-free and the clutter filtered images over a pre-determined grid of parameters.

Results: The optimization process reveals that there is a certain set of parameters that is best for SVF clutter removal. In simulated lesion images, SVF provided artifact suppression with an average contrast-to-noise ratio improvement of 1 dB, the images before and after the clutter removal are presented in Figure1.

Conclusions: SVF technique provides sufficient removal of clutter artifact in simulated data, hence it has high potential application in medical imaging for artifact suppression and improved motion estimation.



(a) (b)

Figure 1. Example simulation images: (a) Unfiltered image; the red box indicates

Small footprint spirometry

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1 Department of Biomedical Engineering, Technion - IIT, Haifa, Israel
2 Respeer
3 Rambam Health Care Campus

Introduction:

Spirometer is a device that measures respiration volume and flow. It's a necessary device for many Asthma and lung disease patients. The main goal of the project is to provide a proof of concept for smartphone based spirometry.

Methods:

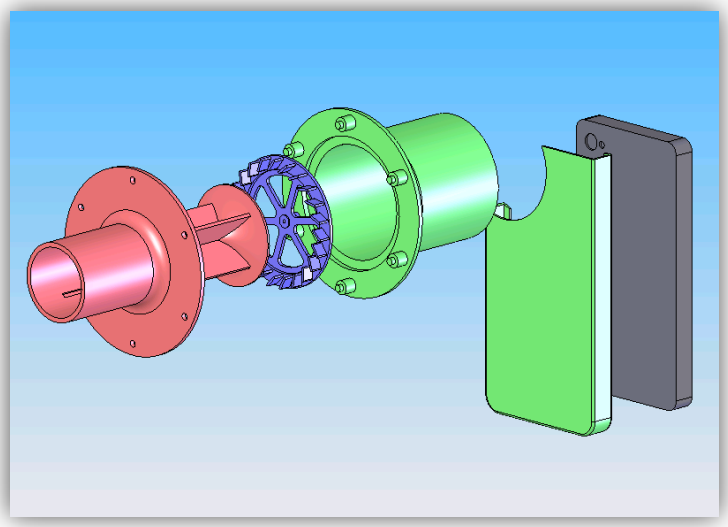
An electric circuit that measures RPM of a turbine was built to enable several methods of RPM measurement using different turbine designs. In addition smartphone mounted turbine designs were manufactured using 3D printing.

Results:

The project's RPM measurement circuit results were tested in comparison to an industrial Tachometer and showed correlation between the two systems.

Conclusions:

The project included both electric circuit design and mechanical design of a device for 3D printing. The results of the project have demonstrated the feasibility of smartphone based spirometry using smartphone sensors.



The 3D spirometer model connected to the smartphone

Breast Imaging Using Through- Transmission Ultrasound and Contrast Agent

Roby Akav, Fatima Bibar, Haim Azhari and Alex Vilensky

Department of Biomedical Engineering, Technion- IIT, Haifa, Israel

Breast cancer is the most common malignant disease in women. Early detection is essential for improving survival rate. X-Ray mammography is associated with ionizing radiation and has limitations especially for women with dense breast. The aim of this project was to investigate a new ultrasonic method for breast imaging.

The method is based on acquisition of acoustic projections using computerized through transmission before and after injection of a contrast agent (CA). Then, comparing the resulting changes by investigating the following parameters: amplitude, time shift, cross-correlation, coherence, pulse-inversion analysis. Data was obtained from a tube phantom and from 6 women.

In the phantom study all parameters have shown significant changes ($p<0.05$ using non-paired t-test), stemming from the CA. Changes were also observed in the suited group of women. However, they were inconsistent and correlated moderately with mammographic references.

Our phantom studies suggest that the combination of through-transmission ultrasound measurement and a contrast agent doping may potentially offer a novel method for breast screening. However, the clinical utility in women was not yet proven. Further study is still needed.

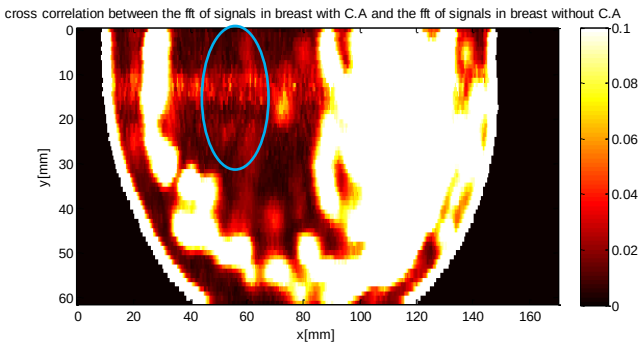


Figure 4: A breast image created from cross correlation between the fourier transform of filtered signals before and after the injection of contrast agent. The marked area is the tumor area according to mammography scan.

A Novel Method for Chronic Single Cell Analysis

Using Microfluidic Devices

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Current microfluidic devices offer incomplete solutions for adherent single cell analysis. Existing methods for single adherent cell analysis can support cell culturing for only 48 hours or less due to an inability to deliver nutrients to the cells while maintaining chemical isolation between microenvironments. This inability dramatically hinders research on diseases such as cancer, where single adherent cells play an important role in the development of the disease. We prepared and used a silicone based organic polymer to manufacture droplet based microfluidic devices from a silicon wafer. We seeded the devices with human fibroblast (HNDF) cells and then implemented a method for medium renewal using a PET membrane. Our successful implementation of the membrane within a dual layered microfluidic device allowed us to visualize diffusion to the cellular microenvironments. Using this technology, medium renewal to single adherent cellular microenvironments can be made possible, thus prolonging assay durations and bringing new capabilities for single cell analysis research.

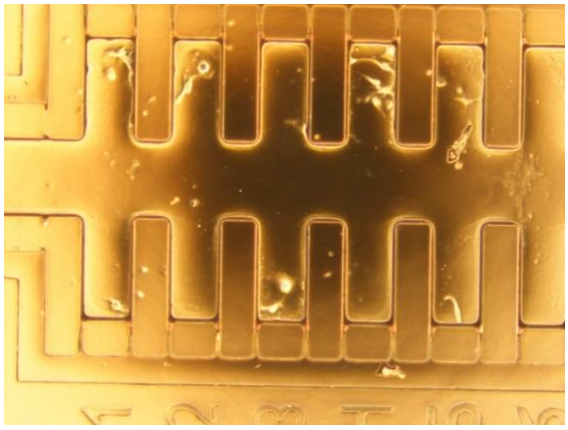

Figure 1: Cells suspended in a droplet based microfluidic device.

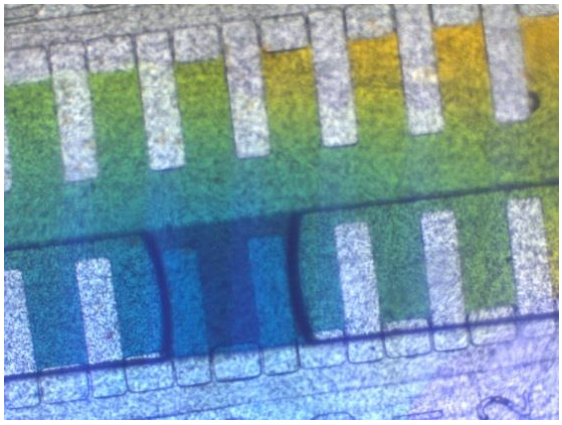

Figure 2: Visualizing diffusion between the upper and lower layers through the "sandwiched" PET membrane.

In-Vitro Microfluidic Models Of Pulmonary Airways To Investigate Surfactant Secretion In Pulmonary Epithelial Cells Subjected To Shear Stress

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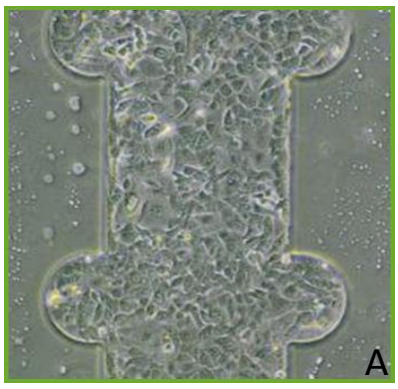
Fetal breath movements induce pressure on pulmonary epithelial cells (EC) and cause fluid motion during embryonic development. Such flows subject shear stress upon EC causing mechanical stimulation, along with distension, on a mosaic of cells lining alveolar walls, including type II ECs, the surfactant secreting cells, within the alveolar spaces. As surfactant plays an important role, including the prevention of lung tissue from collapsing, it is of high importance to understand the effect of mechanical stimulation and particularly the effect of shear stress on surfactant. Therefore, the purpose of our project is to investigate and quantify surfactant secretion as a function of the shear stress subjected on the EC.

We cultured alveolar epithelial cells (A549 cell line) on an *In-Vitro* model of fetal lungs: a microfluidic chip with anatomically inspired geometry on a 1-to-1 scale. We exposed the cells to constant perfusion of culture media, mimicking flow induced pon the EC *in utero* at three different flow rates: 1, 5 and 10 ul/min. The cells were then stained with fluorescent marker for lamellar bodies (LB), characteristic organelles of surfactant secreting cells. The fluorescently dyed elements were observed under the microscope determining production of surfactant within type II EC, as a result of shear stresses exerted on the cellular layer.

We calculated the relative area of the fluorescently dyed phospholipids to the entire cell area by comparing photos taken using phase contrast and fluorescent microscopy using ImageJ photo analyzer. Calculation of the mean changes in the relative areas and standard deviation of the collected data showed no significant difference between the surfactant secretion before and after 40 min. of exposure to shear stress or between the different flow rates.

During our study we successfully cultured ECs in complex microchannels and were able to stimulate efficient surfactant secretion. Previous studies[1] have shown a correlation between the surfactant secretion and sheer stress subjection upon cells exposed to high flow rates. Our study showed that under low shear stress there were insignificant differences between the flow rates observed both before and after 40 min. of flow.



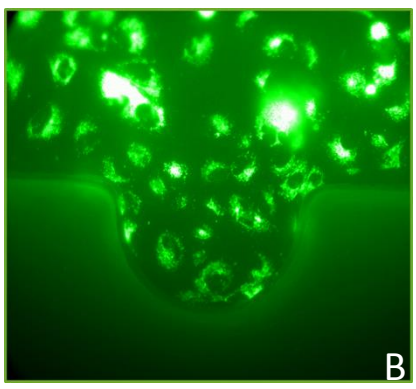


Fig A. confluent ECs in a microfluidic channel with anatomically inspired geometry.

Fig. B ECs stained with Quinacrine observed under a fluorescent microscope

[1] Mahto S.K, Tenenbaum-Katan J, Greenblum A, Rothen-Rutishauser B, Sznitman J. Microfluidic shear stress-regulated surfactant secretion in alveolar epithelial type II cells in vitro American Journal of Physiology - Lung Cellular and Molecular Physiology. 2014.

Improving Electromagnetic Tracking System by Developing an Algorithm for Filtering Interferences Induced by Metallic Objects

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Introduction: Check Cap Ltd. is developing a capsule for colorectal cancer screening, which includes an electromagnetic (EM) tracking system. Once swallowed, the capsule is intended to enable the patient to maintain his daily routine. However, metallic objects in the vicinity of the patient may interfere with the EM tracking system. Our goal is to filter these interferences.

Methods: A model of Check Cap's ELS3 tracking system, including an EM transmitting unit and an EM receiving unit, was used to simulate interferences induced by metallic objects. Data analysis and algorithm implementation were performed using MATLAB and LabVIEW software.

Results: Simulated interferences created by moderate and rapid movement of metals in the vicinity of the tracking system were detected and filtered successfully, both when transient and when becoming stationary. Very slow metal movement interference is ignored by the algorithm.

Conclusions: A filtering algorithm was developed and tested using clinical data and the simulated interferences. This algorithm may provide a solution for real time detection and filtration of common metallic interferences. Clinical studies of algorithm effectiveness under metallic interferences are required for further development and validation.

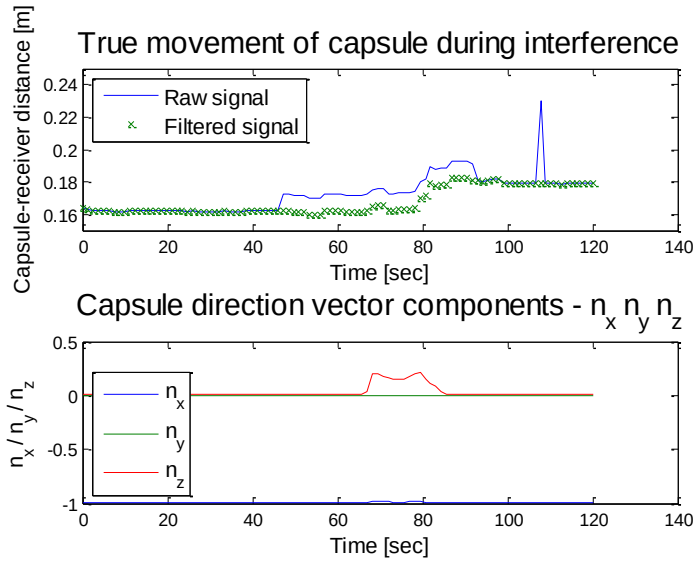

Figure 1: The algorithm performance during a simulated interference. The rapid interference is detected, capsule begins motion as orientation changes while the interference is in progress and true capsule motion is detected.

Development of a Diagnostic Tool for the Characterization of White Blood Cells Using Spectrally Encoded Flow Cytometry

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Abstract:

Measuring patient's blood composition is often the first step in clinical diagnosis, providing quantitative information on cell concentration and morphology. Abnormal amounts of white blood cells (WBC's) can indicate the origin of the disease, as viral diseases typically characterized by elevated amount of lymphocytes in the peripheral blood while bacterial diseases characterized by increasing amount of neutrophils. Using diffractive optics and a high numerical aperture objective lens, spectrally encoded flow cytometry (SEFC) provides confocal images of unlabeled blood cells flowing in small capillaries in patients. Our goal is to establish a diagnostic tool that identifies and characterizes different WBC's from images acquired by SEFC. Using our *in vitro* bench-top SEFC system, we have acquired images of diluted blood samples from human volunteers and developed a specialized algorithm that differentiate between lymphocytes and neutrophils based on their intensity ratio, maximum intensity and different morphology. Using this algorithm, we were able to count lymphocytes and neutrophils percentages in heterogenic blood samples with a high level of certainty. In addition to providing differential blood count, our algorithm could be useful for noninvasive evaluation of the immune system responses to infections and provides accurate determination of different hematological conditions for real-time, effective patient diagnosis.

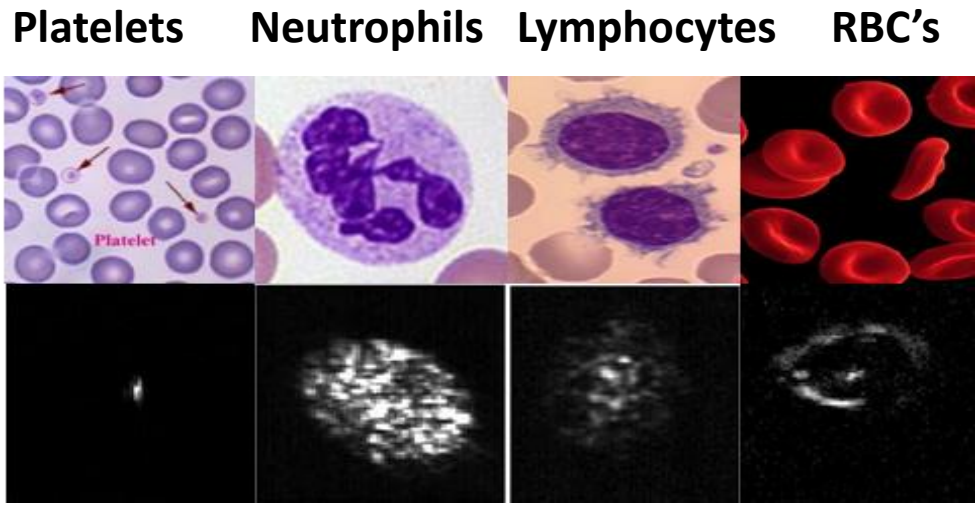

Figure 1: Illustrated images of different blood components that can be detected in SEFC images. Known images of RBC's, lymphocytes, neutrophils and platelets (above) in comparison to SEFC images of the same blood components (below)

Detection of Respiratory Obstruction in Premature Infants During High Frequency Oscillatory Ventilation (HFOV)

Nadir Cohen[1], Chen Torfstein[1], Jimy Pesin[1], Dan Waisman[1,2], Amir Landesberg[1]

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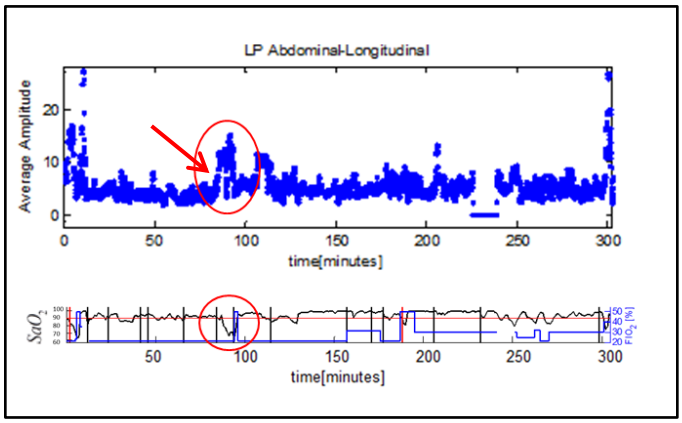
[2] Department of Neonatology, Carmel Medical Center, Israel

Introduction: Currently, no method exists to monitor spontaneous-breathing of an infant during high frequency oscillatory ventilation. The purpose of this research is to find a method for detecting obstructive events earlier than is currently possible using available clinical monitoring techniques.

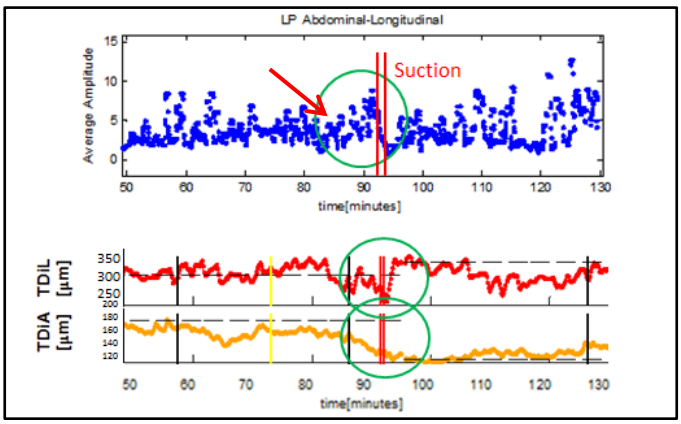
Methods: Acceleration measurements were obtained from sensors attached to the chest and abdomen. The data was filtered into low and high frequency bands. The average amplitude was calculated from moving 30 seconds windows. At least 80% increase in amplitude from baseline was used to indicate an event.

Results: An increase in the average amplitude was observed prior to suction, which was followed by a decrease in the amplitude. Moreover, a correlation between a decrease in the oxygen saturation and an increase in the average amplitude was seen.

Conclusions: Based on the results, spontaneous breathing can successfully be observed during high frequency ventilation. Amplitude changes from spontaneous breathing may be utilized as way to alert the Neonatologist of an obstruction slightly earlier than changes in oxygen saturation.



Decrease in O2 saturation causes an increase in the average amplitude



Average amplitude increases before the suction and decreases after it.
Tidal volume decreases before the suction.

Single Compartment Lung Simulation

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Introduction: Many methods are used to ventilate patients with different pathologies. New ventilation modes emerge constantly, and there is a need to compare their quality to the golden standard in an efficient and economical way. In order to accomplish this goal, we have created an in silico model of the lung.

Methods: Once a physical and mathematical model was established, a modular simulation was developed using MatLab's Simulink. In order to assess the validity of the model, a comparison was made between computed and measured results.

Results: The model generated pressure and flow curves, which were compared to curves measured in a mechanical lung. As seen in Fig. 1, the computed results closely relate (flow $R^2 = 0.93$, pressure $R^2 = 0.7043$) to the measured signal formed using a mechanical lung.

Conclusions: The in silico model suggested in this project excellently mimics the behavior of the golden standard mechanical model used in the development of ventilation methods.

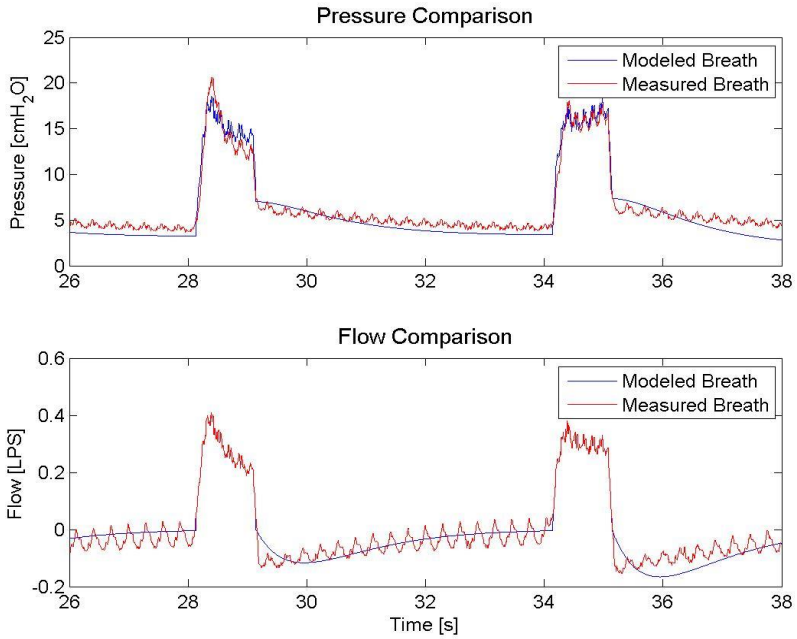

Figure 5: A comparison between a breath generated by a mechanical model and using our simulation.