משרד המדע והטכנולוגיה
Ministry of Science & Technology

MOST Conference

Promoting technological innovations in engineering science

2017

PROGRAM & ABSTRACTS

Sunday June 18, 2017 | 08:30-16:30

Dan Panorama Tel Aviv Hotel

MOST Conference 2017

"Promoting technological innovations in engineering science"

08:30-09:30 Registration

09:30-09:40 **Greetings and Opening Remarks**

Mr. Peretz Vazan, Director General at the Ministry of Science and Technology

09:40-09:50 **The mission of the Ministry of Science and Technology**

Dr. Andrey Broisman, Director of Applied Science and Engineering, Ministry of Science and Technology

09:50-10:30 **The key speech**

Prof. Michael Levitt, Stanford University (Nobel Prize Laureate)

10:30-11:00 Coffee break + Posters

Auditorium 1

Session 1 Biotechnology **Chair:** Prof. Tal Dvir , Tel Aviv University

11:00 **Engineering Organs and Body Parts**

11:20 **Tissue Engineered Heart Construct: Bridging the Gap between Ex and In Vivo Mechanical Effects Towards Clinical Achievements**

11:40 **Converting GsXynB2 from hydrolase to glycosynthase**

12:00 **Hybrid polymer/lipid drug delivery systems for treating oral cancers**

12:20 **Discovery and development of new immunosuppressant by computational and biophysical tools**

12:40 **Analysis of Uterine Peristalsis in Non-Pregnant Mice**

13:00-14:00 Lunch + Posters

Session 2 Bio materials **Chair:** Prof. Daphne Weihs, Technion

14:00 **Investigation of the influences of micro/nano patterning of gel surface on cancer cell interactions**

14:20 **Multifunctional Theranostic Nanoparticles for Alzheimer's Disease**

14:40 **Nanoparticle siRNA with tumor ablation to suppress ablation-induced tumorigenesis**

15:00-15:30 Coffee break + Posters

Session 3 Bio materials **Chair:** Prof. Hadas Mamane, Tel Aviv University

15:30 **How to follow or regulated bi-potential mesenchymal cell fate?**

15:50 **Treatment of hospital wastewater using hybrid MBR-modified AOP technology**

16:10 **Mucoadhesive drug delivery carriers**

Auditorium 2

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13:00-14:00 Lunch + Posters

Session 5 Medical Devices **Chair:** Prof. Michael Margaliot, Tel Aviv University

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Session 6 Medical Devices **Chair:** Prof. Avishay Eyal, Tel Aviv University

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Abstracts

Engineering Organs and Body Parts

Tal Dvir

Director, Laboratory for Tissue Engineering and Regenerative Medicine.
School of Molecular Cell Biology & Biotechnology,
Department of Materials Science and Engineering,
The Center for Nanoscience and Nanotechnology
The Sagol School of Neuroscience
Tel Aviv University. Tel Aviv, 69978, Israel

Abstract

The demographics of the Western world population are shifting towards an increasing elderly population, placing extraordinary demands on our healthcare system. Aging results in failing of different organ, including the heart, brain, spinal cord, etc. In addition, as the number of patient's suffering of cancer increases, there is a growing need for reconstruction surgeries. These shortfalls motivated the development of the tissue engineering concept. In this approach, 3-dimensional (3D) biomaterials serve as extracellular matrix-like scaffolds to the cells, enabling the cells to assemble into effective tissue substitutes, that may restore tissue or organ function. After transplantation the scaffolds either degrade or metabolize, eventually leaving a vital tissue instead of the defected tissue. In this talk I will discuss the recent advancements in the field of tissue engineering. I will describe cutting-edge technologies for engineering functional cardiac, spinal cord and cortical implants, focusing on the design of new biomaterials mimicking the natural microenvironment of tissues, or releasing biofactors to promote physiological processes. In addition, I will discuss the development of patient-specific materials and 3D-printing of personalized and vascularized implants, and even whole organs. Finally, I will show a new direction in tissue engineering, where, micro and nanoelectronics are integrated within engineered tissues to form cyborg tissues and organs.

Tissue Engineered Heart Construct: Bridging the Gap Between Ex and In Vivo Mechanical effects Towards Clinical Achievements

Marcelle Machluf, Biotechnology and Food Engineering, Technion, Haifa Israel

Jacob Bortman, Mechnical Engineering, Ben-Gurion University, Beer-Sheva, Israel

Abstract

The prompt development and clinical implementation of cardiac tissue engineering (CTE) solutions are crucial, considering that cardiovascular diseases and MI in particular continue to be the leading cause of death in the developed world. However, pre-clinical assessment of tissue-engineered constructs in large animal models takes place only after characterizing their biological properties and biocompatibility, *in vitro* and in small animal models, and testing the constructs' mechanical and structural properties *ex-vivo*. The rejection of the construct at that stage of the research spares all the resources invested in it including labor, funding, and most importantly, research time.

Our lab has demonstrated the applicability of decellularized porcine cardiac extracellular matrix (pcECM) for tissue engineering applications, including acellular and recellularized thick myocardial patch as well as cell free and cell incorporated injectable pcECM-based scaffold (Fig. 1). Hence, we recognize the crucial need for platforms enabling a valid prediction of the *in vivo* outcome, particularly the CTE mechanical properties and its suitability for cardiac repair in early stages of the research (Fig. 2). We therefore, developed and currently validating a novel universal *in silico* platform that allow us to to predict the *in vivo* mechanical performance and thus the outcome of the cardiac tissue engineered constructs, based on simple *ex-vivo* measurements. This universal platform developed in collaboration with Prof Bortman, Mechanical Engineering Ben Gurion University should enable the evaluation of patch scaffolds as well as injectable, both synthetic and of natural origin, cell-free and cell-seeded. This research, therefore, develop an *in silic*o predictive tool, which will define the mechanical criteria to be met by developed CTE constructs, will provide comprehensive knowledge regarding the role of scaffold as well as the cellular component in determining the mechanical properties of a construct, and above all, will bridge the gap between *ex* and *in vivo* experimental validation. Such platform will thus reduce significantly the laborious research focused on mechanically unsuitable constructs, and promote and expedite the development of clinically viable solutions, for cardiovascular therapy.

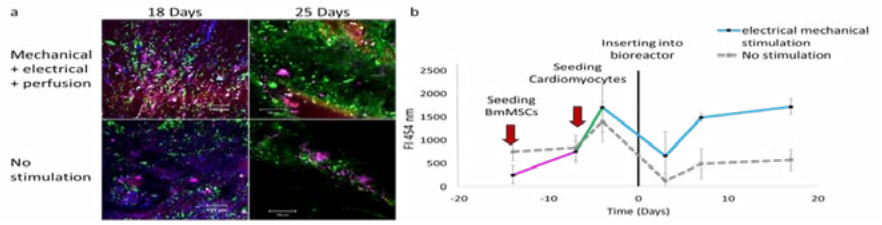


Fig. 1. Co-culturing MSCs and cardiomyocytes on full thickness ECM scaffold. a) Immunofluorescent stains of the cultured scaffold. Blue: Hoechst (nuclei), green: Cellvue Pkh67 (cardiomyocytes), pink: Cellvue claret (hMSCs). Scale bar 100 m. b) Viability of the cells on the scaffold, when cultured using stimulations or without stimulations.

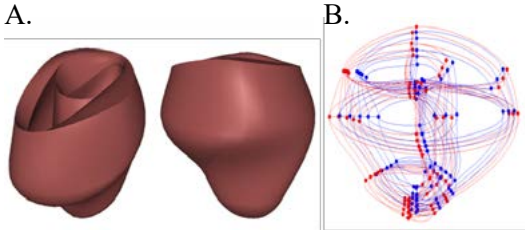


Fig.2 Basic heart model was developed using the finite element code "Continuity. A) Finite element heart model. B) Deformed shape of a loaded heart – FE model results.

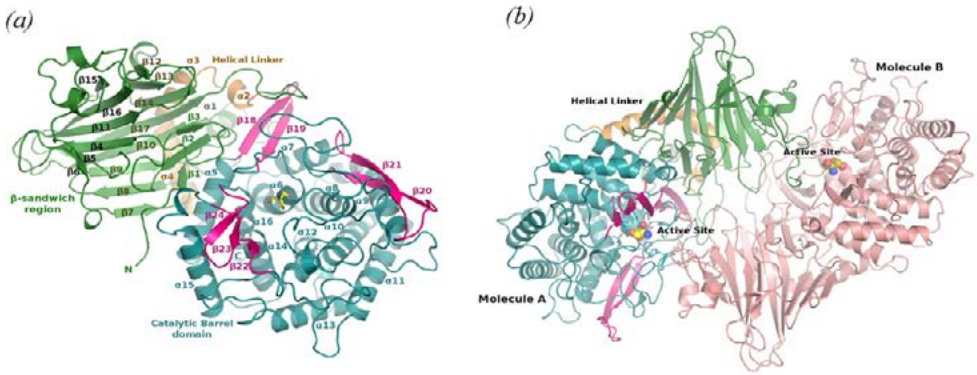
Converting GsXynB2 from hydrolase to glycosynthase

Tomer Cohen[1], Oleg Chmelnik[2], Shifra Lansky[1], Roie Dann[1], Rachel Salama[2], Alon Ben David[2] Yuval Shoham[2] and Gil Shoham[1]

[1]Institute of Chemistry, the Hebrew University of Jerusalem, Jerusalem 91904, Israel
[2]Department of Biotechnology and Food Engineering, Technion, Haifa 32000, Israel

Abstract

Glycosyl hydrolases (GHs) are enzymes that degrade sugar polymers and oligomers, while *glycosynthases* are the reverse enzymes that synthesize sugar oligomers from monomers. The conversion of GHs into glycosynthases has been suggested as a very attractive approach for synthesizing complex carbohydrates by dedicated enzymes. We discovered that *Gs*XynB2, a retaining GH52 b-xylosidase (hydrolase) isolated from the thermophilic bacterium *Geobacillus stearothermophilus,* displays significant glycosynthase ability upon a single mutation of the nucleophile E335 into G335. Moreover, this activity improved 35-fold upon introduction of 10 additional mutations (V29 mutant), obtained through two cycles of directed-evolution experiments. In order to understand the effect of these mutations, we determined the detailed 3D structure of the *Gs*XynB2-V29 mutant, the second structure to be solved from the GH52 family. The *Gs*XynB2 monomer consists of two domains, a catalytic $(\alpha/\alpha)_6$ barrel domain and a β sandwich domain, connected by a helical linker. Two such *Gs*XynB2 monomers interact in a "head-to-tail" fashion to form a biologically functional dimer (see below), as also confirmed by gel-filtration, SAXS and DLS experiments. Xylobiose molecules, the product of catalytic glycosynthesis from XylF monomers, were found trapped in the active sites, confirming efficient glycosynthase activity even in the crystalline state. The *Gs*XynB2-V29 structure enabled structural mapping of the directed-evolution mutations and pointed out the most crucial mutations, thereby providing a structural basis for the enhanced glycosynthase activity of the mutated enzyme. This novel structure-function information, has been recently used for the rational engineering of significantly improved *Gs*XynB2 glycosynthase, so far with a 100-fold catalytic enhancement over the original mutant. These promising results can now be applied for further improvement of the glycosynthetic activity of *Gs*XynB2, as well as the conversion of related GH enzymes into efficient biotechnologically-relevant glycosynthases.

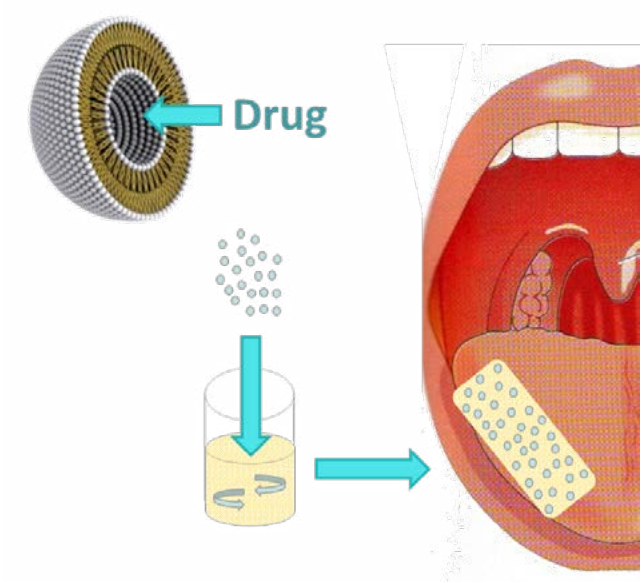


Hybrid polymer/lipid drug delivery systems for treating oral cancers

Mor Goldfeder, Odaya Printz, Jasmine Ghantos,
Imad Abu El Naaj, Havazelet Bianco Peled, Avi Schroeder
Department of Chemical Engineering, Technion – Israel Institute of Technology, Haifa, Israel
Department of Oral and Cranio-maxillofacial Surgery, Poria Medical Center, Tiberius, Israel

Abstract

Oral cancer is the sixth most prevalent cancer worldwide. Specifically, squamous cell carcinoma (SCC) accounts for over 90% of all head and neck cancers, and the overall survival rates are only 40–50%. Over the past decade incidences of oral cancers have risen by 35%, with limited treatment modalities. Administering anti-cancer agents in close proximity to the cancerous lesion has proven clinically effective when dealing with head and neck tumors. To date, no drug delivery system for the controlled administration of anti-cancer agents to the oral cavity exists in the clinic. We are developing a new type of hybrid system, composed of bio-adhesive polymeric matrixes that harbor drug-loaded lipid nanoparticles. The polymeric matrix is engineered to adhere to the oral mucosa for the duration of the drug release, and the nanoparticles are designed to penetrate the tissue and release protein drugs.



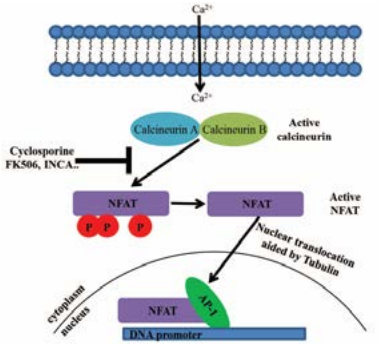
We have shown that most liposomes (200 nm, DMPC:Cholesterol, 60:40) are released from alginate gels within hours, a result which promising for a localized treatment. Furthermore, we loaded the liposomes with model proteins and showed the protein is released from the hybrid system in a more controlled and slower rate than free protein in alginate gel. *In vitro* experiments on oral cancer cells of the tongue were performed in order to screen for both chemo- and biotherapeutic drugs which will be loaded into the liposomes, and the effect of alginate gels on both normal and cancer cells have been examined.

Discovery and development of new immunosuppressant by computational and biophysical tools

Vera Gayder, Miriam Qublan, Olga Romanenko, Elad Cohen, Itai Bloch and Maayan Gal Migal – Galilee research institute, Kyriat Shmona, 11016, Israel

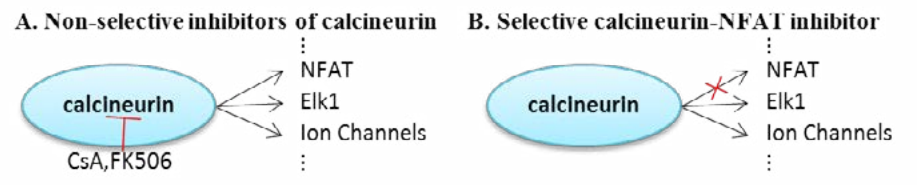
Abstract

The nuclear translocation of the transcription factor Nuclear Factor of Activated T-cells (NFAT) and the interaction of the latter with the protein phosphatase calcineurin are crucial for T-cell activation. In its basal state, NFAT is heavily phosphorylated by various kinases, which keeps NFAT inactive in the cytoplasm. Rising Ca^{+2} levels activate calcineurin, which subsequently dephosphorylates NFAT and initiates its nuclear translocation.



The Calcineurin-NFAT pathway. An increased level of intracellular calcium activates the hetero-dimer phosphatase Calcineurin (Calcineurin A – catalytic domain, Calcineurin B – regulatory domain), which then dephosphorylates NFAT and initiates NFAT nuclear translocation. In the nucleus, NFAT binds to specific promoters with co-factors like AP-1 to induce transcription of immune related genes. Immunosuppressive drugs as well as other small molecules are capable of binding Calcineurin, obscuring its catalytic activity and therefore blocking T-cell activation.

The two most successful calcineurin inhibitors discovered so far, Cyclosporin A (CsA) and Tacrolimus (FK506) are used as transplantation therapies acting by blocking calcineurin catalytic site. Although highly successful, CsA and FK506 have severe side effects as they are interfering with the general enzymatic activity of calcineurin. By the application of virtual screening and biophysical tools small molecules capable of interfering with the calcineurin-NFAT interaction while keeping calcineurin catalytic site free were discovered. These molecules will not indiscriminately block all signaling downstream of calcineurin and hence have the potential for further development of new immunosuppressant.



Non-selective and selective inhibition of calcineurin. (A) Current drugs obscure Calcineurin catalytic site and are non-selective. **(B)** This proposal aims to find a selective calcineurin-NFAT inhibitor.

Analysis of Uterine Peristalsis in Non-Pregnant Mice

David Elad[1], Dan Grisaru[3,4] ,Ariel J. Jaffa[2,4]

[1]Department of Biomedical Engineering, Faculty of Engineering, Tel Aviv University, Department of Obstetrics and Gynecology, [2]Ultrasound Unit in Obstetrics and Gynecology and [3]Gynecological Oncology, Lis Maternity Hospital, Tel Aviv Sourasky Medical Center, [4]Sackler Faculty of Medicine, Tel-Aviv University.

Abstract

Uterine peristalsis in the non-pregnant uterus of mammals is induced by the spontaneous contractions of myometrial smooth muscles. It plays an important role in spacing the blastocysts within the uterus for implantation at optimal sites during the limited time of the "window of implantation". In mice, uterine peristalsis is most likely the major driving mechanism that controls spatial distribution of the embryos along the uterine horns. In this study, we objectively analyzed the dynamic characteristics of uterine peristalsis from video files of non-pregnant mice uteri. The uterine horns were recorded from mice with open abdomen in the supine position by Professors Duan and Ying (Institute of Zoology, CAS). The video clips were decomposed into BMP images of consecutive frames and filtered for noise reduction. Automatic algorithms for edge detection were utilized to determine the external contours of the uterine horns in each frame. Rigid registration of the frames and straightening of the horns' contours along their centerline enabled to explore the spatial time-dependent motility. Similar to our previous work with human uteri, we applied a fast Fourier transform algorithm to the time-dependent curves in order to reveal the frequency spectra for each horn. The results for several non-pregnant mice uteri will be presented.

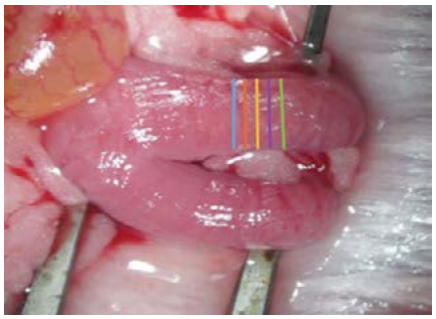


Figure 1: The mouse uterine horns.

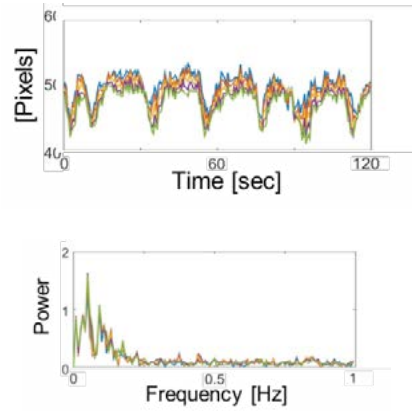


Figure 2: Uterine motility and frequency spectrumm.

Investigation of influences of micro/nano patterning of gel surface on cancer cell interactions

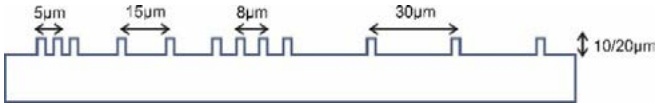
Daphne Weihs

Biomedical Engineering, Technion-Israel Institute of Technology, Haifa 3200003

Abstract

During metastasis, cancer cells migrate away from the primary tumor following routes with different heterogeneous structures, such as blood or lymphatic vessels and collagen fibers. After migrating into a new region, adherent cells interact with encountered topographies in different ways. Microenvironment structure may facilitate or inhibit cancer cell adherence, and is thus highly important to identify. Here, we show how the micro-scale topography of matrix microenvironment affects morphology, adhesion, and alignment of cancer cells as compared to benign cells. We show that our scaffolds are composed of poly(lactic-co-glycolic acid) or PLGA gels generated on top of a Polydimethylsiloxane (PDMS) base with high stiffness (5.5 MPa). The gels are flat (control) or include rectangular cross-section microchannels with varying depths and widths (**Figure 1A**). We compared the interactions of highly metastatic breast cancer cells (MDA-MB-231) and benign breast cells (MCF-10A) on the different substrates. We monitor cells at 3 and 48 hrs after seeding, as measures for, respectively, initial attachment and stable attachment.

We observe that cell morphology, alignment and interactions with the substrate and their neighbors depend on the micropattern scale, and on the cell seeding-density. On channels with a width larger than the cell size (cell diameter is 10-20µm), cells spread randomly for both cell types similar to the control flat surface at all time scales. In contrast, within channels close to the cell size, we observe a time- and cell-density dependence. Three hours after seeding, we observe that both cell types attach to the bottom of the channels, with the benign cells attaching more rapidly. When seeded at high density, 90% of the benign cells exhibited spread, ordered and aligned morphology already after 3 hours (**Figure 1B**). After 48hrs, most cells (and their nuclei) were aligned and attached to the bottom at the edges of the microchannels and metastatic cells stretch out more; cells were also able to cross between the narrowest and lowest profile channels. In the 20um height microchannels both cell types exhibited more cell alignment within the microchannels. Thus, we deduce that both cell types have preferentially migrate towards topographies that can allow them to be in 3D. Tools such as micropatterned substrates and microfluidic devices can reveal preferential features favorable for cancer attachment and dissemination.



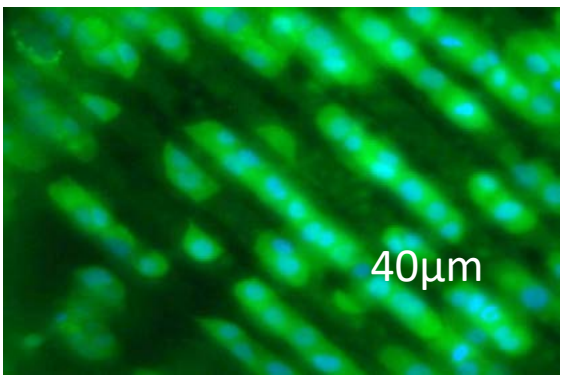


Figure 1. (**A**) PLGA gel with rectangular microchannels. Microchannels had rectangular cross section with widths of 5, 8, 15 or 30µm and depths of 10 or 20 µm (**B**) Benign breast cells (MCF-10A) seeded for 3 hours show preferential attachment to the bottom and side of the channels (20µm depth, 15µm width) and organize in groups. Cell nuclei (blue) are labeled with Hoechst and cytoplasms (green) labeled with Calcein.

Multifunctional Theranostic Nanoparticles for Alzheimer's Disease

Shai Rahimipour[1], Rachela Popovtzer[2] and Dan Frenkel[3]

[1]Department of Chemistry and [2]Faculty of Engineering & The Institute of Nanotechnology and Advanced Materials, Bar-Ilan University, Ramat Gan 5290002, Israel. [3]Department of Neurobiology, Faculty of Life Sciences, Sagol School of Neuroscience, Tel Aviv University, Tel Aviv 6997801, Israel

Abstract

Despite major advances in medicine over the past decade, Alzheimer's disease (AD) remains still an incurable disease, affecting millions of people around the world. Today, around 35.6 million people (0.5% of the global population) are affected by AD and this number is predicted to increase to 65.7 million by 2030 and 115.5 by 2050. AD mainly affects elderly people – the likelihood of developing AD roughly doubles every five years, after age 65. Since the prevalence of AD is expected to rise with the aging of the population, it is crucial to develop new strategies for early diagnosis, effective treatment and accurate follow-up. Very recent clinical trials collectively suggest that the failure to develop therapeutics to treat AD is related to the late diagnostic of the disease that starts far before the appearance of the symptoms.

This study presents the design and development of a new molecular computerized tomography (CT)-based theranostic strategy for early diagnosis and therapy of AD. It is based on blood brain barrier (BBB) permeable gold nanoparticles (GNPs, 30 nm size) that specifically target over-expressed insulin receptors on BBB to cross the barrier, and a novel amyloid β (Aβ) binding cyclic peptide that selectively target soluble Aβ aggregates and inhibits its aggregation and toxicity.

Nanoparticle siRNA with tumor ablation to suppress ablation-induced tumorigenesis

S. Nahum Goldberg

Dept. of Radiology, Hadassah Hebrew University Medical Center, Jerusalem

Abstract

Minimally-invasive, image-guided tumor ablation using radiofrequency (RFA), microwave, and other energy sources is now in widespread clinical use to treat small focal primary and metastatic tumors in the liver, kidney, lung, and other organs. Yet, increasing compelling evidence suggests that focal RFA can stimulate distant tumor growth. Moreover, poorly characterized periablational and distant effects of the procedure that directly influence ablation-stimulated tumor progression remain a substantial, but ever more noted major barrier to clinical efficacy. Thus, strategies to better understand and ultimately modulate local and systemic pro-oncogenic effects of tumor ablation are urgently required to further improve therapeutic effects and, ultimately, clinical outcomes.

In this lecture, we will review the substantial preliminary data elucidating tissue reactions that occur in the zone of non-lethal heating surrounding RF ablation. This includes early transcriptional and secretory activity of hepatocytes and subsequent increased cellular recruitment of neutrophils, macrophages, and activated myofibroblasts. Additionally, we will discuss several key cytokine mediators with probable inter-linked activity (i.e. IL-6, HGF/c-Met, STAT-3, and VEGF) that likely function as the key components of a mechanistic pathway that drives RFA's pro-oncogenic effects. Finally, we will also discuss the development of therapeutic strategies targeting this specific pathway, by suppressing IL-6 or inhibiting c-Met, STAT3, or VEGFR to block hepatic RFA-induced stimulation of distant tumor growth to varying extent, and discuss potential ablation strategies that can potentially minimize this problem including the delivery of siRNA to these cytokines in nanoparticles that preferentially accumulate in the regions in which these cytokines are produced.

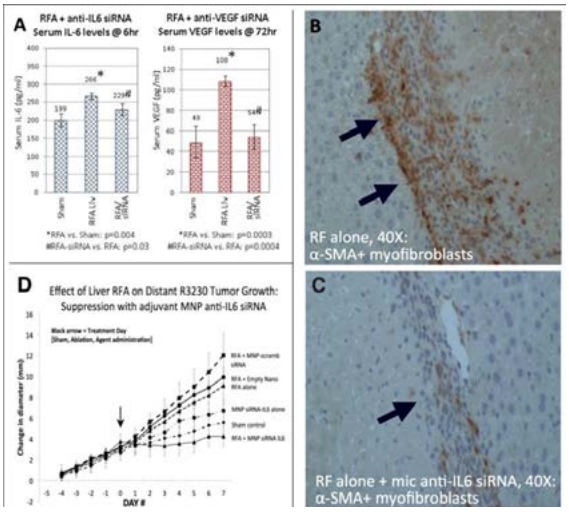


Figure 'Proof-of-concept': Micellar siRNA + hepatic RFA suppresses serum cytokine production, local cell recruitment, and distant tumor growth.

(A) Adjuvant siRNA suppresses cytokine production in early IL-6 (at 6hr) and later VEGF (at 72hr) reactions after hepatic RFA.

(B-C) Adjuvant anti-IL6 siRNA suppresses local α-SMA+ fibroblasts (black arrows) in the periablational rim compared to RFA alone ($p<0.01$).

(D) Adjuvant siRNA suppresses IL-6 mediated systemic effects on distant SC R3230 breast tumor growth after hepatic RF ablation. The growth rate for RF + siRNA-treated tumors is at baseline (or lower) compared to RFA alone ($p<0.01$).

How to follow or regulated bi-potential mesenchymal cell fate?

Dafna Benayahu

Dep. of Cell and Developmental Biology, Sackler Faculty of Medicine, Tel Aviv University

Abstract

Mesenchymal stem cells (MSCs) expressed bi-potential commitment to either adipogenesis or osteoblast fate dependent on cues from the local niche that affect regulation of linage fate. The MSCs are a form of fibroblasts that undergoes morphological changes when cells become adipocytes. We developed tool for live imaging to monitor such changes. The Morphology Mapping Method (MMM) is used for live imaging tracking of cell differentiation. Mesenchymal cells exposed to adipocyte or combined adipocyte/osteoblast differentiation factors and were analyzed for molecular markers to demonstrate the cells' bi-potential fate. The use of MMM allows live imaging to evaluate the level of adipogenesis (LOA) progression and percentage area populated by adipocytes (PAPBA) during the whole culture period. The visualized differentiation progression quantified by MMM monitored at the macro-level of LOA hence evaluated the commitment to a specific lineage. Also method that is based on silica nano-particles (NPs) allow the activation of cells to the fate of differentiation required i.e. into bone forming cells and enhance osteogenesis. The outcome of cells' differentiated into the desire fate in presence of NPs allow us to evaluate the NPs to provide reference for the foundation of the use of cell therapy with NPs that can be translated in biomedical and tissue regeneration for variety of applications . The live-imaging allows quantify the progression into osteoblastic or adipocyte fate to analyze the effects of factors/drug that can shift the balance between lineage. Such method is critical for understanding the pathophysiology related to function of MSCs such osteoporosis and type II Diabetes or in the field of tissue engineering.

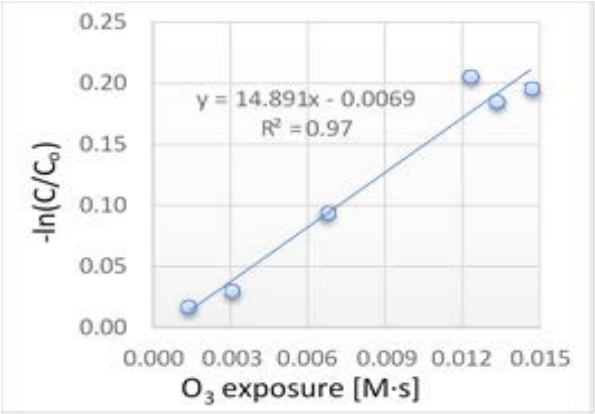
Treatment of hospital wastewater using hybrid MBR-modified AOP technology-a pilot scale project at Tel-HaShomer hospital, Israel

Hadas Mamane

School of Mechanical Engineering, Faculty of Engineering, Tel Aviv University, Tel Aviv 69978, Israel

Abstract

Upstream treatment of hospital wastewater is a relatively new approach that until now has been examined in a limited number of studies. The research findings point on a high potential of the approach in elimination of organic micro/nano-pollutants (OM/NPs) already within the hospital premises. The main bottleneck however is the current stage of optimization of existing treatment technologies for a combined cost-efficient elimination of OMPs. Previous studies explored the potential of biological treatment that was significantly lower than requested treatment goals. Some new studies proposed complementary treatments after bio-treatment including MBR based on either active carbon or ozone based Advanced Oxidation Processes (AOP). This pilot-study proposes, for a first time, a hybrid biological physical treatment based on a combination of membrane bioreactor (MBR) and AOP that is part of the bio-treatment and does not come as a complementary treatment. Pilot experiments are currently being performed at Tel HaShomer hospital including modifications of AOP to achieve a maximal retention of OM/NP combined with a precise pore size modification of MBR membranes. Laboratory scale experiments are being performed with a list of target compounds (Gemcitabine (GEM), Fluorouracil (5-FU), Paclitaxel (TAX), Cyclophosphamide monohydrate (CYP), Doxorubicin (DOX) and hydrochloride Dexamethasone (DEX), examining their reaction with ozone. For example, the figure below presents the removal of CYP vs. ozone exposure. This study is in collaboration with Prof. Avisar.



Mucoadhesive drug delivery carriers

Havazelet Bianco-Peled

Department of Chemical Engineering, Technion – Israel Institute of Technology

Abstract

Mucoadhesion is commonly defined as adhesion events between two materials, at least one of which is a mucosal surface. The mucosa gel layer is a secretion created in specialized epithelial cells lining organs which are exposed to the outer surface of the body yet are not covered with skin. Mucus is composed primarily of water (~95%), but also contains small amounts of salts, lipids, and proteins. The main components responsible for the elastic gel-like structure of the mucus are high molecular weight glycoproteins termed mucins. These molecules can form electrostatic, hydrophobic, sulfide and H-bonding interactions with other substances, a process which potentially leads to mucoadhesion.

Transmucosal drug delivery involves transport of therapeutic agents through the mucosa. This method of delivery offers several potential benefits over oral drug administration including relatively rapid uptake of a drug into the systemic circulation and enhanced bioavailability. Mucoadhesion enhances the performance of transmucosal delivery systems by providing extended residence time of the drug at the site of application.

In my talk I will describe new approaches based on modification of polymers as a way to enhance mucoadhesion. Specifically, Michael type addition reaction is used to covalently attach polymers bearing unsaturated side groups to the mucus. Our studies involved synthesizing of novel biomaterials, and extensive characterization of their properties. We demonstrated a significant improve in adhesion, and lack of toxicity. Applications in the field of oral cancer treatment will be emphasized.

Development of portable and laboratory tools for improving the manual skills and performance of undergraduate dental students

D. Lugassy, Y. Levanon, Y. Kamir, R. Pilo, T. Brosh
Tel Aviv University

Abstract

Dental education involves preclinical and clinical studies. During their initial clinical courses, the students practice handling the basic dentistry tools (such as turbine and drilling bur) by performing basic tooth preparations on plastic teeth. Then, they are challenged by more sophisticated models named 'phantom heads', which is plastic teeth placed in manikins simulating the human head. In this, they are challenged by both performing accurately the instructions and working in un-conventional view point that is, performing tasks indirectly by observing the target tooth via a dental mirror. Aspiring to increase the success rate of the students in these clinical courses we conducted a longitudinal research, using *modified* dexterity tests under conditions of indirect vision used in occupational therapy. The results showed that the O'Connor test under indirect vision is the most compatible way to monitor and predict the manual skills required in pre-clinical year of dentistry. Knowing that, we developed 3-D printed teeth, which simulate the O'Connor test. These teeth were implemented within the 2 jaws of traditional phantom head simulator for home training. The teeth have small drills and the students have to insert fitted pins using tweezers and dental mirrors into these drills (Fig. 1a). This portable kit (Fig. 1b) that can be attached to any table was given to the students for practicing at home and was guided by written instructions starting with easy tasks following by more complicated ones. In order to validate the additional clinical improvement of the students, we compared the manual grades routinely provided in the clinical course between the students who didn't practice with the new portable system to those who practice it at home prior to phantom course for 2 months. The improvement was significant in direct and indirect teeth preparations tasks carried out by drilling as tested in their clinical course. In parallel we developed a computer program running through the Moodle University system that provides the instructions and collecting on-line students' performances. This system will be used during the next academic year.

Fig. 1: a. Metal pins inserted in various directions into 3-D printed tooth. b. The portable phantom head kit.

Biodegradable disposable medical syringes and tubes

Michael Mizrahi and Abraham J. Domb

Institute of Drug Research, School of Pharmacy, Faculty of Medicine
The Hebrew University of Jerusalem
and Azrieli College of Engineering, Jerusalem.

Abstract

Single use medical supplies such as syringes and tubes are made from commodity polymers that are non-degradable and non-recycle. These hazardous waste is either deposited in landfill or incinerated which present an environmental and human high risk upon exposure. It is thus the objective of this work, to develop medical supplies made of hydrolytically degradable polyesters that will be biodegraded and eliminated in water or soil.

The challenge includes: tailor cost effective biodegradable polymeric compositions that are moldable into syringes and meets the medical requirements. We have selected poly(lactic acid) - PLA, as the key polymer for the articles. PLA is considered biocompatible and biodegradable that can be melt molded into devices such as syringes and trays.

PLA and PLA-PCL obtained from bulk producers were injection molded into two types of syringe barrels, thick wall and thin wall syringes. These articles were tested for their mechanical properties compare to similar common hospital syringes. The following mechanical tests were applied: 3-point bending, tensile test, Rockwell hardness tests, injectability, transparency and shear test.

A mold was designed, capable of manufacturing one biodegradable syringe in a single injection molding press action. Several syringes were made out of different biodegradable polymers, and were tested for toxicity and protein adsorption, in order to meet chemical and biological requirements. The stability of the syringes to sterilization by irradiation, ethylene oxide or steam autoclave has also been tested.

The mechanical properties as well as the leachables and protein deposition of the molded PLA based syringes were comparable to the currently used syringes.

PLA syringes prepared by injection molding

This work is supported by a grant from The Ministry of Science and Space

The Impact of Delay Announcements on Hospital Network Coordination and Waiting Times

Galit Yom-Tov, Technion – Israel Institute of Technology

Abstract

We investigate the impact of delay announcements on the coordination within hospital networks using a combination of empirical observations and numerical experiments. We offer empirical evidence which suggests that patients take delay information into account when choosing emergency service providers and that such information can help increase coordination in the network, leading to improvements in performance of the network, as measured by Emergency Department wait times. Our numerical results indicate that the level of coordination that can be achieved is limited by the patients' sensitivity to waiting, the load of the system, the heterogeneity among hospitals, and, importantly, the method hospital use to estimate delays. We show that delay estimators that are based on historical average may cause oscillation in the system and lead to higher average waiting times when patients are sensitive to delay. We provide empirical evidence which suggests that such oscillations occurs in hospital networks in the US.

Joint work with Elad Yom-Tov (Microsoft Research) and Jing Dong (Northwestern University)

Endovascular Electrodes for Electrical Stimulation of Blood Vessels for Vasoconstriction

Yossi Mandel

Faculty of Life Sciences, Optometry Track and Bar Ilan's Institute for Nanotechnology and Advanced Materials, Bar Ilan University. Ramat-Gan, Israel

Abstract

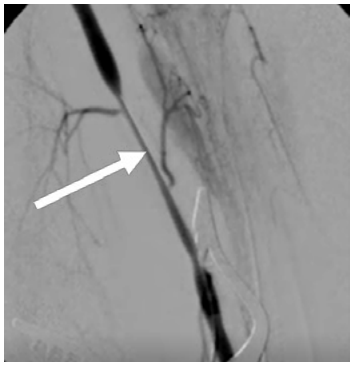
We have recently shown that pulsed electric field applied by extravascular electrodes can elicit robust vasoconstriction. In this study, we present a novel approach for eliciting vasoconstriction by endovascular electrodes, which can be used in cases where external access to the vessel is limited. Using computer simulations, we modeled various geometries of endovascular electrodes and characterized the parameters needed to maximize the induced arterial wall electric field while minimizing endothelial damage.

Based on the optimal parameters obtained by the computer simulation studies we constructed endovascular electrodes with various configurations, such as bipolar or monopolar, as well as pulse parameters which were then further studied in-vivo.

In-vivo experiments with sheep show robust constriction of large blood vessels (such as the carotid artery) in response to electrical pulse activation dependent on pulse duration, pulse amplitude (voltage) and pulse repetition rate. Constriction of up to almost 100 percent could be induced by 1ms, 300-400 V pulses at a pulse repetition rate of 10Hz. Furthermore, bleeding from an induced arterial injury was reduced by up to 3.5 times by electrical activation of the blood vessel.

To investigate whether the applied endovascular treatment resulted in endothelial tissue damage, histological examination was performed which did not reveal any apparent injury.

The results show a promising novel approach for inducing reversible and controlled vasoconstriction in large blood vessels using endovascular pulsed electrical pulses.



Vasoconstriction of a sheep carotid artery (arrow) by pulsed electrical application at 1ms, 300V, and 10 Hz repetition rate.

Investigation of Multimodal Imaging Methods of Nanoparticles for Early Detection of Cancer

Haim Azhari, Or Perlman and Iris S Weitz

Abstract

Multimodal imaging is gaining increased weight in the clinic. This stems from the fact that data acquired from different physical phenomena may provide complementary information and improve the clinical outcome. In this context, nano-sized contrast agents may augment the sensitivity of the imaging modalities used and allow targeted tumor visualization. The aim of the presented research was to explore new methods for multimodal imaging of nanoparticles. The research was comprised of four subprojects:

1*) Copper oxide nanoparticles as a contrast agent for MRI and ultrasound dual-modality imaging*

In this part of the research, we examined the feasibility of increasing image contrast using copper oxide nanoparticles (NPs) under MRI and ultrasound. The proposed NPs were synthesized and characterized as 7nm in diameter, much smaller than the commonly used alternatives. *In-vitro*, *ex-vivo*, and *in-vivo* experiments revealed that the particles are detectable by both ultrasound and MRI. The NPs increase the ultrasonic attenuation coefficient, and shorten the magnetic T1-relaxation coefficient. Hence, it is concluded that copper oxide NPs may potentially find use in the clinic as a dual imaging modality contrast agent.

2) Multimodal ultrasonic computed tomography imaging and MRI of iron oxide nanoparticles

In the second part of the research, we acoustically analyzed the FDA approved iron oxide NPs, currently used for MRI contrast enhancement. The results have shown that iron oxide NPs increase the speed of sound. This property can be utilized for contrast enhancement in ultrasound computed tomography, which is specifically useful for breast cancer detection. Hence, an alternative imaging methodology for this extensively used contrast agent is now feasible, allowing improved certainty in diagnosis using two modalities (MRI-ultrasound). Alternatively, this option can provide a cost effective diagnosis pathway by initially using the inexpensive ultrasound solely, and then in case of uncertainty in the diagnosis, use the expensive MRI. This can potentially save money to the health system.

3) Microwave ablation planning and monitoring using nanoparticle enhanced through-transmission ultrasound

In the third part of the research we explored the feasibility of image-guided microwave ablation monitoring using through-transmission ultrasound. Microwave ablation (MWA) is a minimal invasive therapeutic method, in which a needle-typed antenna is inserted into the target tumor, which is heated until destruction. Imaging is essential for target detection and temperature feedback. Through-transmission ultrasound (TTUS) is a hazardless, cost effective, quantitative imaging method, producing speed of sound (SOS) and attenuation based images. Since SOS is highly sensitive to temperature, TTUS may be useful for ablation monitoring. The purpose of this study was to evaluate a novel image guided MWA method, combining NPs injection under TTUS for therapeutic procedure planning, and SOS-based scanning for temperature feedback and ablation extent analysis. The results indicated that the suggested methodology provide accurate target detection with a 0.6 degrees Celsius temperature resolution.

4) Copper oxide loaded PLGA nanospheres for ultrasound imaging and enhanced tumor ablation hyperthermia

In the fourth part of the research, we embedded 7nm CuO nanoparticles in PLGA nanospheres. The benefits offered by the polymer encapsulation are: controlled drug release, reduction of toxicity and the ability to image and detect the resulting structures using the clinically available B-scan ultrasound as demonstrated by various *in-vitro* and *ex-vivo* experiments. Another clinically important application of the synthesized nanospheres is their potential use for enhanced hyperthermia treatment (designated for tumor destruction). In our experiments, the nanospheres were irradiated *in-vitro* by therapeutic ultrasound. A concentration dependent temperature elevation effect was observed. This may allow a more effective therapeutic procedure.

Ferritin nanocage engineering via magnetotactic bacteria proteins toward in vivo auto-produced MRI contrast agent

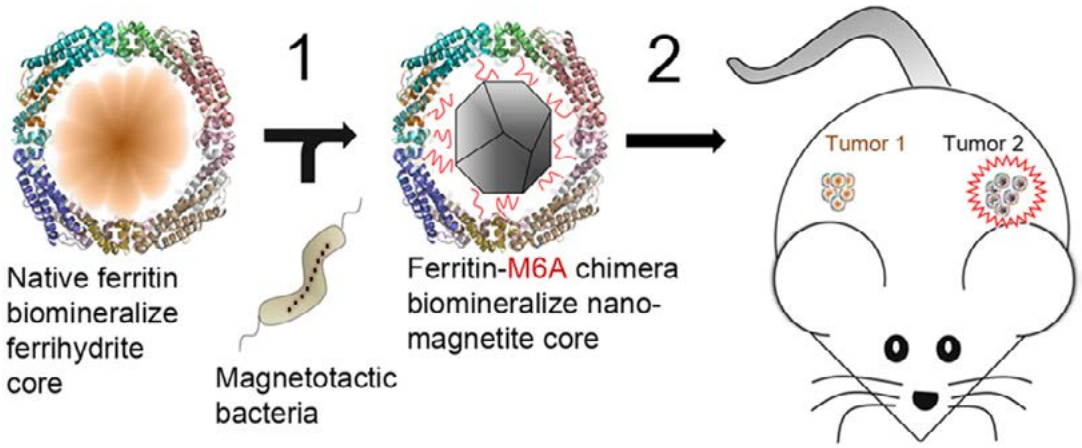
Raz Zarivach[1] and Michal Neeman[2]

[1]Department of Life Sciences, The National Institute for Biotechnology in the Negev and The Ilse Katz Institute for Nanoscale Science and Technology, Ben-Gurion University of the Negev, Beer Sheva, 8410501, Israel.

[2]Department of Biological Regulation, Weizmann Institute of Science, Rehovot 76100 Israel

Abstract

Contrast agents are an important tool for enhancing specific regions or biological targets for MRI imaging. The common contrast agents, as gadolinium complexes and iron oxide nanoparticles, are administrated to the blood stream in order to passively or specifically target the site of interest. Once accumulated at the site of interest, and due to their magnetic properties, these agents enhance the relaxation of water (T1, T2 or T2*) to allow detection by MRI. An alternative approach is to label cells ex vivo using nanoparticles prior to their administration in the framework of cell-based therapy. Yet, the limitation of ex vivo labeling with nanoparticles is, on one hand, the loss of labeling upon cell division and on the other hand, the non-specific contrast generated by particles upon cell death and secondary uptake by phagocytic cells. To overcome these limitations, cells can be genetically engineered to generate their own contrast through the expression of bio-degradable reporter genes that can be detected *in vivo* also in deep tissues. The most popular reporter gene for MRI is the iron binding protein nanocage, ferritin. However, the weak magnetic properties of the ferrihydrite iron core of native ferritin results in low relaxivity and thus low sensitivity for detection. To overcome this limitation, we engineered the ferritin with a superparamagnetic iron oxide core, with magnetosome-associated peptides derived from magnetotactic bacteria. This innovative approach allows ferritins to convert their core into paramagnetic magnetite that has a better MRI contrast. We characterize the ferritin mutants using biophysical, biochemical and cell biology methodologies such as SAXS, TEM, MRI, cellular overexpression, tumor formation and MRI imaging of live mice. Furthermore, the modified ferritin can be used to other future technologies beyond MRI applications including agriculture and human health.



A Generic Platform for Optimized Expression of Bio-Engineered Genes in Micro-Algae

Tamir Tuller

Tel Aviv University

Abstract

The Micro Algae industry is a rapidly growing and fascinating new type of high-tech agricultural industry. Ultimately, microalgae can serve humanity in diverse fields such as food security, food additives, high value products, and energy. Sadly, the entire industry is plagued by lack of efficient high gene expression capabilities. Thus, genetic manipulation aimed for expression of high value products, or efficient energy production (biofuels and hydrogen) are being held till a general platform which allows for high expression will be developed.

In this talk I will describe the generic algorithms we developed for engineering heterologous genes for their efficient expression in micro-algae. Among others, our algorithms combines tools and knowledge from disciplines such as molecular evolution, biophysics, and information theory.

Furthermore, we have already implemented our algorithms on a synthetic fusion protein - Ferredoxin-hydrogenase (Fd-hyd) enzyme in *Chlamydomonas reinhardtii*, demonstrating a significant improvement in comparison to the endogenous variants, and the state of the art design of gene synthesis companies.

When expressed *in vivo*, Fd-hyd catalyzes hydrogen production (an important promising clean energy source) seven times faster than the native enzyme. Thus, the efficient expression of Fd-hyd inalgal may be translated into wide commercialization.

The Ribosome Flow Model: Theory and Applications

Michael Margaliot, School of Elec. Eng.

Tel Aviv University

Abstract

An important stage in the production of proteins from the information encoded in the genes is called translation. During this stage, complex molecular machines, called ribosomes, bind to the mRNA and "read" it in a sequential manner.

In 2011, Reuveni et al. suggested a new nonlinear model for this process called the Ribosome Flow Model (RFM). The RFM can be derived as a mean-field approximation of an important model from non-equilibrium statistical physics called the Totally Asymmetric Simple Exclusion Process (TASEP).

We analyze the RFM using tools from systems and control theory including contraction theory, monotone systems theory, the analytic theory of continued fractions, and convex analysis. We detail several biological implications of the analysis and compare them to known experimental results.

Joint work with Tamir Tuller (Tel Aviv University) and Eduardo D. Sontag (Rutgers University).

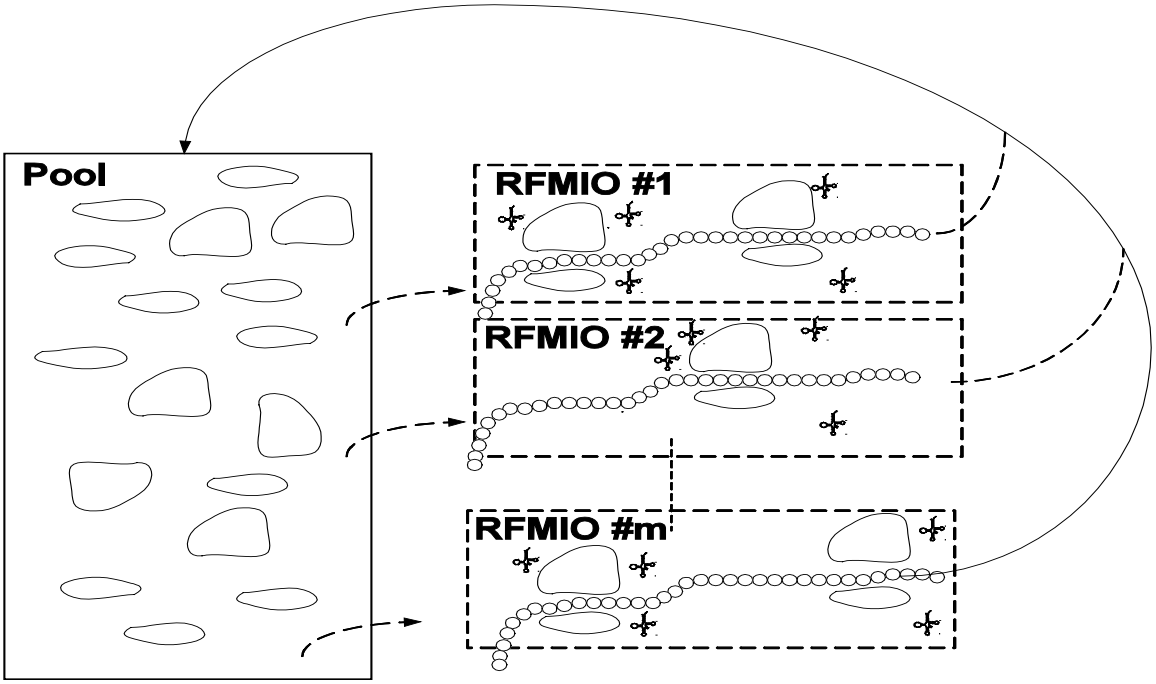


Fig. 1: The *Ribosome Flow Model Network with a Pool* (RFMNP) describes a set of mRNA molecules that are translated in parallel by ribosomes from a finite pool.

Scientific Report "Visible Bioorganic Nanodots", Project 50785

G. Rosenman, T. Ellenbogen, A. Natan

Tel Aviv University

Abstract

1. Nanotechnology of Bioorganic Nanodots (BND), studies of their basic physical and optical properties
Bioorganic Nanodots (BND) self assembled from linear di- and tri- peptides such as FF, FFF, Fmoc-FF (F-phenylalanine amino acid), FW (W-tryptophan amino acid) as well cyclic dipeptides FF and WW have been developed. BND have been fabricated in polar protic and a-protic solvents by using two colloidal technologies of top-down (dissembling process) and bottom up (self-assembling process). *Top-down process* of chemical dissembling is provided by breaking noncovalent bonds, linking elementary building blocks of supramolecular bioinspired nanostructures. *Bottom-up* self-assembly is based on inhibiting the biomolecules self assembly into BND and allows fabrication of dense BND coatings. Discrete BND are homogenous nanoparticles of ~2 nm size, having crystalline structure and containing two peptide molecules.

2. Development of Visible Bioorganic Nanodots (VBND), studies of their basic physical, biological and optical properties
Two methods of fabrication of VBND have been developed. The first method is based on direct conjugation of *green and red fluorescent dyes* to biomolecules followed by their self assembly into VBND. The second method is a new technology which allows transforming the originally non-fluorescent bionanodots into visible VBND by modification of their peptide secondary structure. This novel biophotonic effect of a strong intrinsic blue/green fluorescence is observed due to thermally induced reconformation of original α-helix peptide secondary structure to β-sheets. Such unique optical phenomenon was also exhibited in amyloids fibrils and ascribed to a strong reduction of the energy gap of intermolecular hydrogen bonds of antiparallel β-sheets structure. The visible fluorescent was related to proton transfer from the N- to the C-terminus in these hydrogen bonds. The physical mechanism of the fluorescence found in VBND is differed from inorganic counterpart quantum dots and can potentially lead to a new physics and wide biomedical applications.

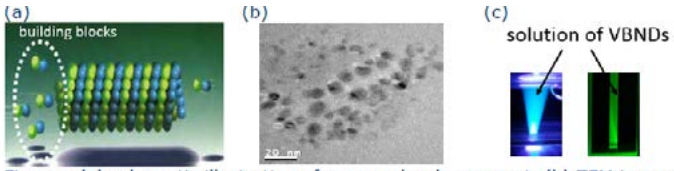


Figure - (a) schematic illustration of supramolecular concept, (b) TEM image of FFF-VBNDs, (b) blue and green fluorescence of VBNDs in ethylene glycol solution.

3. Theoretical explanation for the visible Fluo in BND
The leading hypothesis is that the super-structure, formed by hydrogen bonds, supports Excited State Proton Transfer (ESPT) during the absorption of electro-magnetic wave. This effect is enhanced via molecular aggregation. In order to explore this phenomenon – small peptides, their dimers and the higher ordered structures (trimer, tetramer e.t.c) were analyzed with time dependent density functional theory (TDDFT). We have explored their absorption spectra and emission spectra and its relation to the geometry of the excited states. To this end, we have demonstrated that there are additional peaks that appear in the emission spectra due to the fact that the excited state geometry undergoes ESPT mechanism. This proton transfer can be either inter-molecular or intra-molecular. The results are now being wrapped into publications.

Multiplexing of fiber-optic ultrasound sensors via Optical Frequency Domain Reflectometry (OFDR)

Avishay Eyal, Haniel Gabai and Idan Steinberg

School of Electrical Engineering, Tel Aviv University, Tel Aviv, 6997801, Israel;

Abstract

The field of optical fiber sensors (OFS) is gaining tremendous popularity in recent years. OFS natural immunity to electromagnetic interference, inherent biocompatibility and compactness making them highly attractive for ultrasound sensing. Moreover, their compatibility with photoacoustics can make them useful in situations where traditional piezoelectric probes are inadequate. However, the issue of multiplexing individual OFS into an array remains a challenging and costly task. In this research, we study approaches for multiplexing multiple broadband OFS for ultrasound sensing by exploiting most of the photoreceiver's bandwidth. The design is based on a recently developed system in which all sensing elements are connected to a single interrogator and to a single digitizing circuit (Fig. 1). There are two operation modes: reflection or transmission. Synchronization of the sensor interrogation with the excitation enables very high repetition rates (kHz) making it ideal for applications where imaging of dynamic processes is desired. The laser light is swept linearly and delay differences between the various sensors translate to spectral differences and allow separation of the individual responses of the sensors.

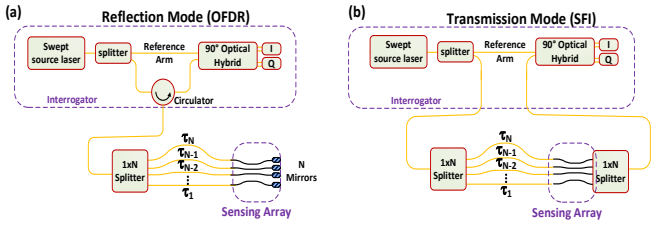


Figure 1. System design. (a) Reflection mode implemented by Optical Frequency Domain Reflectometry (OFDR). (b) Transmission mode uses Swept Frequency Interferometry (SFI). To avoid aliasing, both configurations employs a coherent detection scheme, based on 90° optical hybrid (90° OH) which detects both the In-phase (I) and Quadrature (Q) components of the complex signal.

With the use of a 1MHz ultrasound transducer the sensors were excited with 5 ms tone bursts. The received signals are shown in Fig. 2 with appropriate delays due to different distances from the transducer.

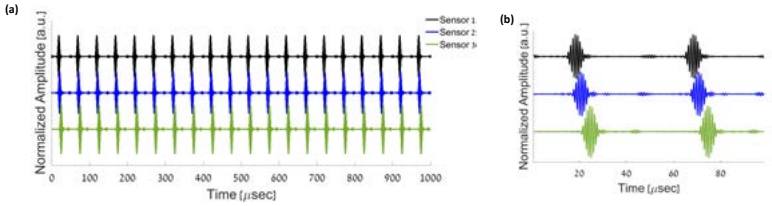


Figure 2. (a) Reconstruction of 20 pulses sequence without averaging. (b) Zoom-in: Temporal delays between the responses corresponds with the array's geometry.

Small, sensitive, portable – towards next-generation arrayed biosensors

Levi A. Gheber

The Avram and Stella Goldstein-Goren Department of Biotechnology Engineering, The Ilse Katz Institute for Meso and Nanoscale Science and Technology
Ben-Gurion University of the Negev, Beer-Sheva, Israel

Abstract

Current micro-array technology produces spots with ~100 µm in diameter and 300 – 400 µm pitch. We show that these dimensions require large, heavy and expensive scanners for readout, rendering these potentially revolutionary tools localized to large institutions. Miniaturization of the spot by several orders of magnitude should, in principle, solve this problem and enable portable arrayed biosensors. Indeed, nano-biolithography techniques have matured over the last decade or so to the point where spots as small as ~20 nm of DNA and/or proteins can be reliably and reproducibly manufactured. However, the dramatic loss in SNR associated with reduction of the spot size (area) presents critical problems, requiring special attention.

We present our latest results in achieving a working antibody chip with sub-µm diameter spots while maintaining high SNR, using the Nano-Fountain Pen (NFP) technique[1-3]. Aided by theoretical modeling and careful examination of binding mechanisms, we show how immobilization surfaces play a crucial role in attaining a good SNR, sensitivity and specificity at these dimensions[4].

For stability and regenerative properties we are studying polymeric detection elements (molecularly imprinted polymers – MIPs)[5], and we show label-free detection (for continuous monitoring) using surface-enhanced Raman spectroscopy (SERS)[6, 7]. Finally on-chip polymer microlenses may provide the required integration of a read-out system[8]. In the particular case of IgG-based sensing we show two oriented immobilization strategies under advanced development in our lab.

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Optical Microfiber Biosensor Enhanced with Photothermal Interferometric Imaging of Plasmonic Nanoparticles

Natan T. Shaked and Pinkie Jacob

Department of Biomedical Engineering, Tel Aviv University, Israel

Yihui Wu, State Key Laboratory of Applied Optics, Changchun Institute of Optics, Fine Mechanics and Physics (CIOMP), Chinese Academy of Sciences, China

Abstract

Sensitive and selective detection of trace amount to target protein and biomolecules is one of the greatest challenges in the field of biosensors. Widely used immunoassays, such as fluorescence detection, are time-consuming, high-cost and tedious procedures. Fiber-optics biosensors are emerging as an alternative immunoassay and provide advantages such as high sensitivity, low cost, and quick response time.

We develop a label-free optical microfiber biosensor for the detection of proteins in solutions, especially cancer biomarkers, in which the sensing principle is based on the detection of the amount and the location of single gold nanoparticles (GNPs) on the microfiber via photothermal phase imaging. The photothermal interferometric imaging system, integrated with evanescent-wave absorption-based biosensor, allows the quantitative detection of small amount of protein traces in liquid samples, with online localization. The use of GNPs for evanescent-wave absorption-based bio-sensing increases the detection sensitivity. In interferometric imaging system, the heat emitted from the GNPs upon illumination changes the local refractive index and thickness of the medium, resulting in enhanced phase contrast that can be detected by interferometric imaging.

First, to find the optimized geometry that gives maximum photothermal phase fingerprint, the photothermal phase profiles of GNPs of different geometries were calculated. Our results show that due to their specific geometry, nano-bi-pyramids have higher plasmonic photothermal phase signals than those obtained by nanorods of the same cross-section. Therefore, we have synthesized these specific GNPs. Second, a single-mode optical microfiber was produced by fiber-pulling procedure and was placed and fixed in a fluid cell. Then, to obtain the quantitative phase image of GNPs on the microfiber, an interferometric optical imaging setup was built. The optical system consists of one laser source (532 nm) for photothermal excitation of GNPs, and another source (632.8 nm) for interferometric microscopy. The target protein was tagged with GNPs and immobilized onto the microfiber by bio-functionalization using aminopropyl-trimethoxysilane. The GNPs on the optical microfiber are then imaged using the optical interferometric setup for online sensing of the GNPs location on the fiber, significantly enhancing the imaging and specificity properties of the sensor.

High-Speed Autonomous Robot Navigation in Dynamic Urban Environments

Elon Rimon[1] and Zvi Shiller[2]

[1]Mechanical Engineering, Technion
[2]Mechanical Engineering and Mechatronics, Ariel University

Abstract

Most robot motion planning algorithms, which are based on geometric obstacle avoidance, do not take *dynamic safety concerns* into account and are hence *not suitable* for the emerging challenges of autonomous robot navigation in dynamic urban environments. Furthermore, urban environments pose physical challenges such as bumps, potholes, debris, or fallen trees. In such situations, which are *not* rare, the autonomous vehicle should be capable of safely avoiding static and moving obstacles while negotiating the challenging terrain. The combination of uneven terrain, static and moving obstacles, and the high safety standards expected of autonomous vehicles makes autonomous motion in crowded urban environments a serious challenge.

We have approached this challenge in two steps: 1. Developing a *novel configuration space theory* for high-speed collision free navigation, subject to dynamic safety constraints, and 2. Developing a unified approach to compute the safe velocity limit that accounts for vehicle dynamics, ground irregularities and moving obstacles.

Our earlier work extended the Voronoi diagram to account for safe braking speeds while avoiding cylindrical obstacles. We extended this work by accounting for additional safety constraints such as sliding and tipover, using tools from calculus of variations. The time optimal trajectory was then computed by applying a convex optimization algorithm. This led to the realization that the optimal paths (the projection on the configuration space of the optimal trajectory) are composed of six distinguished path primitives. Along these primitives, the robot must travel while applying its maximal linear and angular accelerations while satisfying state control constraints that involve the robot's speed and its turning radius. This allows for quick computation of a safe high speed trajectory in static environments.

The second part of this research focused on computing the safe velocity limits for motion on uneven terrain that is populated by static and moving obstacles. A unified approach is proposed that maps the dynamic constraints imposed by the uneven terrain to the vehicle's velocity space. This mapping computes the vehicle's velocity limit along a straight line emanating from its current position for some predefined distance. This produces a velocity limit curve, below which the vehicle is ensured not to slide, tipover, or lose contact with the ground. It accounts for the terrain profile along the selected straight line, the location and normals at the contact points between the wheels and ground, and vehicle's dynamics. Repeating this computation radially around the vehicle's current position produces a manifold in the velocity space that bounds the region of safe velocities for motion in all directions. Adding to this representation the mapping of the moving obstacles (vehicles and pedestrians) in the form of their velocity obstacles produces an efficient representation of the safe vehicle's velocities that ensure dynamic stability and collision avoidance with the surrounding vehicles and pedestrians. This algorithm was demonstrated in simulations, and its high speed obstacle avoidance was experimentally tested with a mobile robot developed for this purpose.

Bio Sensory (vision +Sonar) inspired for Robot localization and mapping

Ron Sudar, Yossi Yovel & Hedva Spitzer,*

School of Electrical Engineering, Engineering Faculty; Zoology department, Life Science
Tel Aviv University

Abstract

Animals' brains can "easily" solve the SLAM (Simultaneously Localization and Mapping) problem which is crucial for many robotic applications. To approach the SLAM problem different animals use different dominant sensors and probably also integrate information from multiple sources. This sensory integration can contribute to SLAM and compensate on each other.

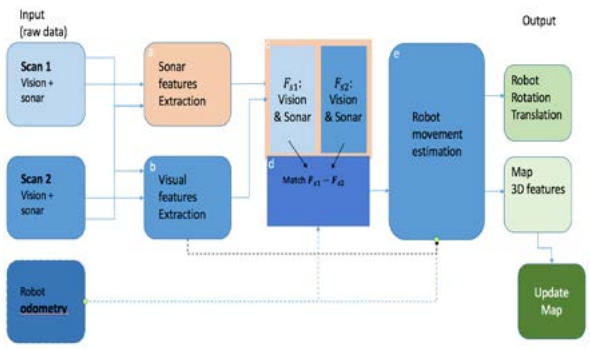
Even though many different statistical approaches have been tested in attempt to solve the SLAM problem in robotics, this problem in general (not limited to specific applications) is still considered an extremely challenging one.

Our aim was to apply several sensors to a robotic platform, which will serve as a prototype for a mammal-like navigating robot and develop biological inspired algorithms to integrate the data, and map the environment with multisensory (vision, Sonar and olfaction).

The aim of our group is to combine sonar depth information with spatial information (XY plane) from the camera. To fuse this information from the two sensors, we utilize two microphones to compute the depth and the orientation of the object (XZ plane) to locate the object in the visual image (see block diagram below).

To achieve our goal a simple computation of the orientation using standard Difference Time of Arrival (DTA) of the acoustic signal from the two ears is not sufficient. To improve the accuracy in the object's orientation, we transmitted a wide-band linear down sweep chirp. We are in the process of developing a novel method that integrates the information from DTA and the decay function of the different frequencies, which is changed according to the object's orientation. We are developing an energy function that combines the above terms. We minimize this function according to the depth (r) and orientation of the object (), such that both terms (DTA and frequencies decay) will be satisfied. We started to perform experimental tests with the robot in order to test the above suggested model. We found already that several free independent parameters of the object play a role in the algorithm ability to evaluate the prediction of the object orientation. Among these parameters are the viscosity, size and etc.

In addition, we planned to integrate an IR camera (in a similar way as the RGB camera), in order to enable the robot "see" during dark illumination conditions. The first stage we choose to adapt our previous algorithm to compress the wide dynamic range of the IR images, in order to enable us to better observe in similar objects as appeared in the light illumination condition.



Development of novel topologies of parallel robots and characterization of their singular configurations

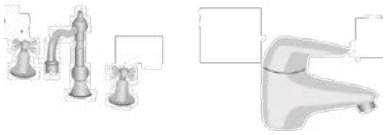
Offer Shai (deceased) & Yoram Reich

School of Mechanical Engineering
Tel Aviv University

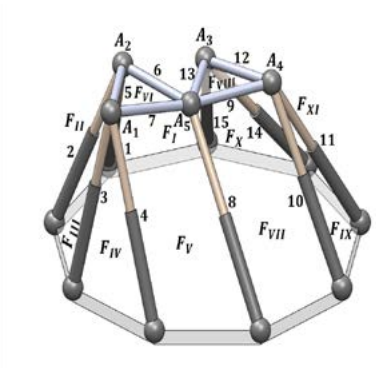
Abstract

Parallel manipulators are stiff and accurate mechanical systems due to their construction, where an end effector, a platform, is manipulated by several simple actuators in parallel. This parallelism also allows minimizing the weight of the robot compared to the weight it carries, thus permitting faster movements. These advantages come with some challenges. The control of these manipulators is more complicated than serial manipulators and they have singular positions that must be avoided to maintain their accuracy or stability.

It is not difficult to determine whether a particular given position of a parallel manipulator is in a singular position. One can analyze the Jacobean matrix of the manipulator to accomplish this. Nevertheless, this is an implicit representation of the singularity that is not effective in determining a trajectory for the manipulator movement. A more effective way is to have an explicit characterization of singularities. In order to understand the difference between these two ways, consider the following faucets where we want to fix the flow and temperature. The left is difficult to control because the control is implicit and the right is easy because the control is explicit.

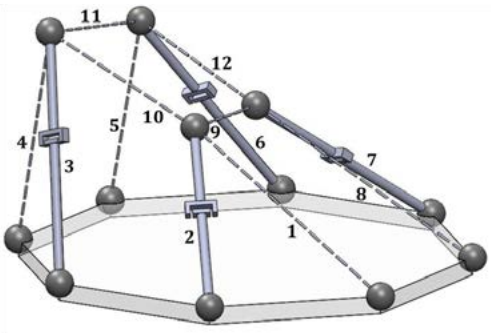


This project aims to develop both new configurations of parallel robots and characterize their singularities in an explicit manner. New manipulators will be developed based on 3D Assur Graphs and a new method for generating all possible Assur Graphs. This allows creating arbitrary complex configurations. We further develop a general approach to find singular positions that also allows characterizing other parallel manipulators, such as 3/6 SP, 3D Tetrad, spatial double Triad, or spatial Pentad. This approach can be applied to other types of manipulators such as tensegrity structures or foldable tensegrity structures.



Spatial double Triad

Foldable Tensegrity structure



Tetrad Tensegrity parallel robot

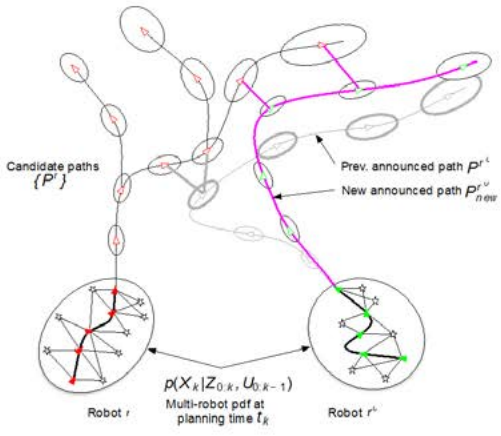
Decentralized Multi-Robot Belief Space Planning in Unknown Environments via Identification and Efficient Re-Evaluation of Impacted Paths

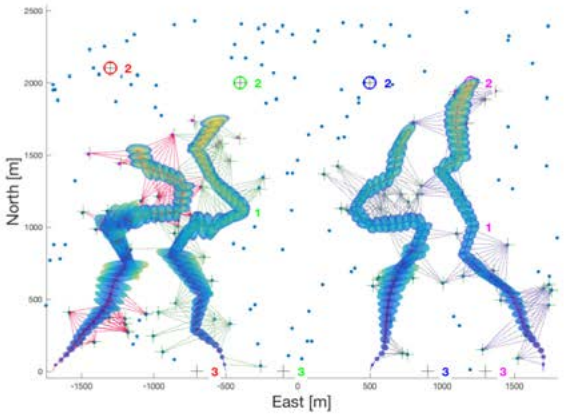
Tal Regev and Vadim Indelman

Technion – Israel Institute of Technology

Abstract

In this research we develop a new approach for decentralized multi-robot belief space planning in high-dimensional state spaces while operating in unknown environments. State of the art approaches often address related problems within a sampling based motion planning paradigm, where robots generate candidate paths and are to choose the best paths according to a given objective function. As exhaustive evaluation of all candidate path combinations from different robots is computationally intractable, a commonly used (sub-optimal) framework is for each robot, at each time epoch, to evaluate its own candidate paths while only considering the best paths announced by other robots. Yet, even this approach can become computationally expensive, especially for high-dimensional state spaces and for numerous candidate paths that need to be evaluated. In particular, upon an update in the announced path from one of the robots, state of the art approaches re-evaluate belief evolution for all candidate paths and do so from scratch. In this work we develop a framework to identify and efficiently update only those paths that are actually impacted as a result of an update in the announced path. Our approach is based on appropriately propagating belief evolution along impacted paths while employing insights from factor graph and incremental smoothing for efficient inference that is required for evaluating the utility of each impacted path. We demonstrate our approach in synthetic realistic simulations.





Our Eyes Beneath The Sea – a Holistic AUV Based Framework for Visual Seafloor Surveys – the Platform

*Yevgeni Gutnik, Tali Treibitz, Groper Morel**

**The Hatter Department of Marine Technologies, Leon H. Charney School of Marine Sciences, University of Haifa, Israel*

Abstract

AUVs are primary used for seabed survey, bathymetric mapping and sub-bottom profiling. Based on this typical use AUVs are designed to sweep large underwater areas at a relatively high speed with efficiency and endurance being of most importance. Hulls of a torpedo shape equipped with fins to control depth and heading provide a balanced solution to most of the requirements derived from this operational profile but this hydrodynamic design requires maintaining a minimal speed, as otherwise steering and depth keeping capabilities are lost. Avoiding collisions at this speed and beyond obliges a significant minimum height above the seabed thus delicate maneuvering and operation at very low speeds are difficult. Luckily those requirements are of a less importance to this type of AUVs. But, a direct consequence of this design is that visual survey performed by this type of vehicles is not ideal in terms of detail, resolution and color. Hovering AUVs are more suitable for imaging tasks, but this is a recent idea with only a few configurations developed thus far. In this context, the SPARUS II AUV (Fig. 1) was found to present an excellent basis platform that following extensive adaptations will provide an optimal vehicle for underwater visual mapping of distinct targets.

With the SPARUS II as the base platform, upgrades and modifications were developed and are incorporated to allow dense imaging scenarios. Accurate attitude control, dynamic positioning and station keeping capabilities are integrated in the existing platform. With the addition of two new lateral cross body high efficiency thrusters to the already existing three thrusters (two longitudinal and one vertical) the upgraded propulsion system will allow uncoupled horizontal motion (surge, sway and yaw) and extremely precise station keeping. Thrusters' allocation is continuously calculated and controlled by the maneuvering control algorithm to ensure optimal maneuvering. To allow the development of the maneuvering controller a dynamic model based on the solution of the 6-DoF equations of motion (x, y, z, roll, pitch yaw) was developed. The hydrodynamic coefficients were calculated based on both numerical and empirical methods and will be validated experimentally. A dedicated thruster model was developed, experimentally calibrated and will be validated in the pool. Finally, a novel pressure resistant stereo-based imaging system to include two cameras (Fig. 2) and high intensity strobe lights is under development and will be integrated in the AUV platform to offer an attractive vehicle for underwater visual mapping and modeling.

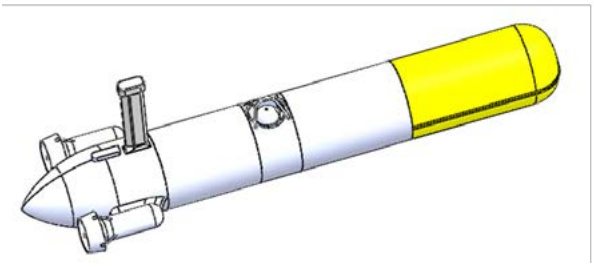


Fig.1: The basic SPARUS II platform prior the modifications

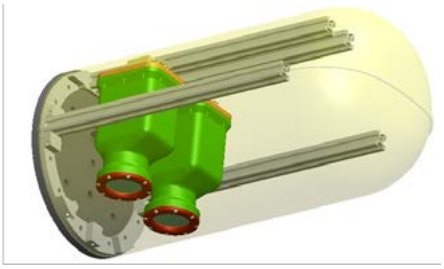


Fig.2: Stereo imagining system

Follow me… Proxemics and responsiveness for following tasks in adaptive assistive robotics

Tal Oron-Gilad[PI], Yael Edan[PI], Idit Shalev[PI], Vardit Fleishman-Serna, Shanee Honig, Dror Katz & Hanan Zeichik

Ben-Gurion University of the Negev

Abstract

Background. Person-following is an important for assistive robotic applications, yet, a non-trivial problem to solve. Successful introduction of assistive robotics into seniors' daily life will depend on user acceptance, satisfaction, and affordability. Robotic platforms should move efficiently and have enough power to carry objects. Since the people they will need to follow vary in their mobility and the context of their walk, the human-robot system must adapt to the context of use and maintain appropriate proxemics and responsiveness. **Aims.** To advance robotic adaptive person following algorithms (APFA) to include concepts from human-human interaction with an aim: a) to improve older users' wellbeing and b) to generate guidelines for future user-attentive robotic assistants, individualized to the special needs of each elder user in the context of use; c) showcase the importance of social concepts for human-robot interaction (HRI) with older users; and d) develop tools and measures to evaluate user satisfaction and identify factors that should be included in future developments of assistive robots. **Progress.** Algorithms for tracking that reduce the number of losses and improve the robot's ability to self-recover in unknown environments have been developed. Five algorithms and two human-following methods were developed and tested in a series of experiments with a mobile robot platform. **User studies**. *The first study* evaluated proxemics preferences and user engagement among elderly users. An explicit preference of the closest following distance was found while standing, whereas an implicit indifference to the following distances and acceleration values were observed while walking. In addition, while performing a secondary task, those who succeeded in it, engaged less with the robot and perceived the robot's behavior differently than the rest. This indicates that user tasks must be accountable in the design of robotic spatial behavior. *The second study* evaluated how people naturally guide the robot and whether gesture vocabulary used for human-human communication can be applied to human-robot interaction using WoZ technique. Simple commands yielded higher consistency among participants regarding their meanings. Voice commands were more frequently used than gestures, though a combination of both was sometimes more dominant for certain commands. When participants were asked to identify predefined commands presented as hand gestures, inconsistency of identification rates for opposite commands was observed. The results of this study could serve as a baseline for future developed commands vocabulary promoting a more natural and intuitive human-robot interaction style.

Wet Power: harnessing energy from evaporation

Yehuda Agnon, Tehnion

Abstract

Dry Power technology is capable of producing low-cost, renewable energy - on a global scale - from an untapped, vast new source: The evaporation of water.

The evaporation of a ton of water can produce well over 25 kWh of mechanical (or electrical) energy. This is more than the hydroelectric power potential (per ton water) of an 8,000m elevation drop. Until recently there was no feasible technology for harnessing the energy of water evaporation. This is the goal of the *Wet Power* invention.

Wet Power is a "spin-off" of thermoacoustics, which is a novel technology in its own right.

Thermoacoustics is currently available for use in the following applications:

1. Thermoacoustic Engines, converting thermal energy into pressure oscillations (intense acoustic energy), which in turn can be converted into electric power.

2. Thermoacoustic Heat-pumps, driven by intense acoustic energy.

The "Wet Power" invention expands the scope of thermoacoustics to new horizons. The invention provides an optimal mechanism and device for producing mechanical power, in the form of pressure oscillations (very intense sound waves). This is done without any moving parts. The energy source for driving these self-sustained oscillations is the pressure change of dry air, induced by the evaporation of water. The pressure oscillations are concurrently converted into electricity.

The projected capital cost is less than $300/kW for small units and much less for large units. *Wet Power* enables mechanical energy conversion without the necessity of a high temperature heat source. This is in sharp contrast to devices currently available in the art which require temperatures as high as 500 degrees Celsius. The Wet Power device can operate at much lower temperatures, offering a substantial advantage in terms of its implementation, with or without coupling to low-temperature heat sources, such as roof-top solar collectors.

Wet Power can also provide heating and cooling, and can be implemented over a very wide range of scales.

The relatively dry air, which is the source of energy, acts as a very large natural reservoir. It collects and stores solar energy from a wide area - and makes it available around the clock, in a concentrated location.

Potential methods proposed in the art for utilizing the energy source described herein, are based on mechanical devices which are complex, bulky and inefficient and require many moving parts.

We'll also mention briefly another invention: Agam-Energy's economic liquid-ring turbine that can drive cars much more efficiently and with extremely little emissions.

Spatial Evolution of an Initially Narrow-Banded Wave Train: Relation to appearance of rogue waves

Lev Shemer

School of Mechanical Engineering, Tel-Aviv University, Tel-Aviv 69978, Israel

Abstract

Results of numerical simulations, coupled with measurements in a wave tank, of the spatial evolution of unidirectional deep gravity wave trains with spectra containing initially only two or three harmonics are presented. Nonlinear evolution of water gravity waves is often related to the temporal Benjamin-Feir instability of Stokes waves. Since in any experimental facility the evolution occurs in space rather than in time, linear spatial rather than temporal stability of monochromatic wave train was studied first in the framework of the spatial version of the Zakharov equation. The analysis allowed establishing the frequencies of the linearly most unstable disturbances and the domain of frequencies where the infinitesimal disturbances grow exponentially with distance. This preliminary analysis provided the background for study of nonlinear spatial evolution of simplest possible wave systems with finite initial amplitudes. Experiments yield results consistent with the numerical simulations.

As long as the frequency spacing between the initial harmonics remains sufficiently large, the effect of the spectral widening is limited, and the evolution at the slow spatial scale is dominated by three major harmonics. For the system consisting of a carrier wave and two sidebands, these harmonics govern the evolution along the whole extent of simulations; while for an initially bi-modal spectrum the governing harmonics have frequencies ω_- and ω_+ present in the initial spectrum, as well as $\omega_+ + \Delta\omega$ that is generated nonlinearly. The modulation pattern of a system that everywhere along the tank contains only three dominant components exhibits nearly perfect spatial Fermi-Pasta-Ulam periodicity. As the initial spectrum becomes narrower and the groups grow longer, new harmonics are generated by nonlinear interactions and the spectrum widens. This process is accompanied by gradual disruption of the regular modulation pattern. The total wave energy is conserved; however, it becomes more uniformly distributed among numerous harmonics. This spatial evolution may be accompanied by a considerable increase in the maximum envelope height; the maximum crest height may exceed the initial values by a factor of two and more. Such an amplification of the height of the steepest wave is similar to that observed in experiments and numerical simulations for a wave train initially corresponding to Peregrine breather (Shemer & Alperovich 2013, Shemer & Ee 2015).

The present study demonstrates that linear approach based in the Benjamin-Feir instability is largely irrelevant to appearance of rogue waves. The nonlinear periodic Fermi-Past-Ulam recurrence was obtained in the present numerical simulations based on the spatial Zakharov equation for initial spectra with two or three harmonics with spacing roughly comparable with that of the most linearly unstable sideband frequency and observed experimentally. However, this periodic or quasi-periodic modulation also is not characterized by an essential wave steepening and thus is not related directly to the rogue waves phenomenon. The deterministic extremely steep waves may evolve from any initially narrow-banded wave train as a result of nonlinear interactions that cause spectral widening and generation of new coherent spectral components.

Modeling and control of near-field acoustically levitated and transported objects

Izhak Bucher

Mechanical Engineering, Technion

Abstract

Near-field acoustic levitation is caused by small amplitude, controlled, ultrasonic oscillations. These vibrations give rise to an elevated average pressure in a thin layer of air and thereby can hold objects of several kg with no mechanical contact. The elevated pressure is generated due to the nonlinearity and viscosity of compressed air residing between the oscillating actuator and a floating flat object, e.g. a silicon wafer. The wafer can be 'held in the air' at controlled heights of 5 to 200 micrometers.

By controlling the vibration patterns of an undelaying structure, the position of the levitated object can be determined in resolution of sub-micrometer.

Clearly, holding an object with no mechanical contact is beneficial for clean room applications, therefore an improved version creates ultrasonic traveling waves that can both levitated, moved and revolved as demonstrated on a silicon wafer in the xyz and theta directions. A physical realization leads to an over-actuated, nonlinear MIMO system that was realized with some success will be shown as a working laboratory implementation.

The seminar will briefly describe the physical background, the mechanics and dynamics of the levitation devices and the employed control and sensing methodologies. Several laboratory experiments will be shown and analyzed and open issues will be laid in front of the control-experts community.

Aluminum-Water Green Propellant for On-Board Propulsion Systems

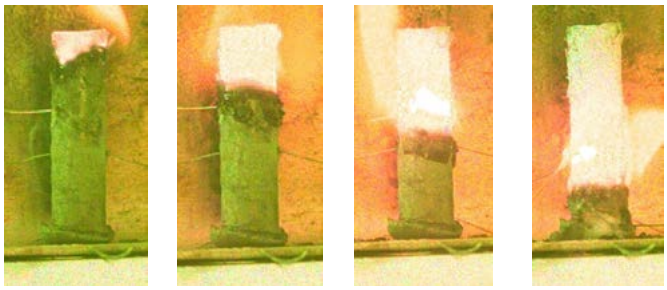
Yinon Yavor and Alon Gany - Faculty of Aerospace Engineering

Technion - Israel Institute of Technology, Haifa, Israel

Abstract

Small satellites require a propulsion system for positioning and attitude control, due to the small drag forces applied by collisions with space dust during the mission. An additional requirement of space vehicles is the ability to de-orbit the satellite into earth's atmosphere, and prevent further accumulation of dangerous space debris. For that purpose, most active propulsion systems thus far use liquid propellants, which require injection systems, in addition to propellant storage tanks and possible cooling systems. Therefore, the development of new solutions has been widely encouraged, among them green propellants, which possess low toxicity, low cost, and performance similar to conventional propellants. Aluminum-water propellant satisfies these conditions, as its combustion products comprise solely from inert aluminum oxide and gaseous hydrogen. Moreover, using a solid rather than liquid propellant diminishes the need for complicated injection systems and storage tanks.

During the research, combustion experiments were conducted at different operating pressures for propellants containing distilled water and three different nanopowders of aluminum: ALEX (uncoated), V-ALEX (Viton coated), and L-ALEX (stearic acid coated). Initial investigation focused on extracting the power-law relation between the propellant burning rate ($\dot{r}$, in mm/s) and the combustion pressure (P_C , in [bar]); the burning rate is considered an important parameter when determining the propellant performance properties.



t=0 [s] **t=9.5 [s]** **t=19.8 [s]** **t=30.9 [s]**

Figure 1: Combustion stages of a burning Al-water propellant ignited at atmospheric pressure

Burning rate experiments (as seen in Fig. 1) were conducted in the pressure range of 1-75 atm, and different trends were identified for the different powder sizes and powder coatings. The burning rate measurements for ALEX propellants showed an increase with pressure, characterized by the power law relation of: $\dot{r} = 2.41 \cdot P_c^{0.35}$, which presents a pressure exponent (n=0.35), as well as burning rate values, which are similar to those of conventional solid propellants. The burning rates of L-ALEX propellants follow the equation: $\dot{r} = 0.862 \cdot P_c^{0.47}$, which actually demonstrates lower burning rates than those obtained for the uncoated powder. The burning rates of V-ALEX propellants were surprisingly characterized by two regimes: A roughly constant ("plateau") burning rate at pressures lower than 18 bar, reaching 4-5 mm/s; and a high-exponent power-law-relation ($\dot{r} = 0.178 \cdot P_c^{0.83}$) starting from 2-3 mm/s at 20 atm.

Static motor has been designed and built, and measurements of chamber pressure and thrust were recorded during the Al-water propellant combustion. Preliminary experiments show that both ALEX and V-ALEX propellants exhibit steady combustion throughout the motor firing, and the data for pressure and thrust are with good agreement with the calculated estimations.

Additive manufacturing of metallic parts with improved physical and mechanical properties for applications under severe conditions

H. Abramovich, Faculty of Aerospace Engineering, Technion, I.I.T., 32000, Haifa, Israel

Abstract

Additive manufacturing (AM), also known as 3-D printing, is a process by which material is deposited layer-by-layer to build a tangible product. The aim of the project[1] is to combine a basic scientific research, materials engineering and applications of materials produced by additive manufacturing with unique properties under severe conditions. The present multidisciplinary project includes the fabrication of 3D-printed parts and improvement of their mechanical and physical properties by post processing treatment (PPT). Understanding the physical metallurgy of the microstructure evolution during fast solidification and cooling rates as well as the effect of PPT on the microstructure and properties of AM parts will play a crucial role in addressing both fundamental and applied problems for current and future 3D printing technologies.

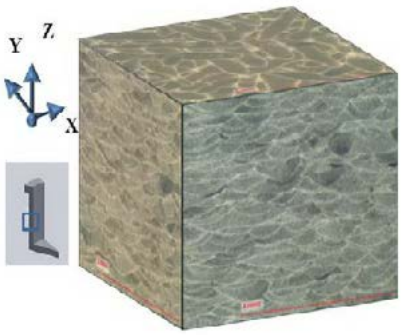
Three groups (BGU, Technion and NRCN) under the coordination of Prof. N. Frage (BGU) are working together on the various aspects of the projects.

The focus of the BGU group activities is on the structure characterization, mechanical and thermal properties of AM-SLM AlSi10Mg and Ti6Al4V materials. The specific micro and macro-structural features as well as types of inherent process defects are under investigation. Weldability of small AM parts by electron beam welding (EBW) will be examined.

The Technion group is responsible for printing and characterization of Ti6Al 4V parts by EBM 3D printer. The NRCN group investigates properties of recycled Al powders, fabrication and characterization of AM Ti6Al4V samples. The effect of the extremely fast solidification of SLM AM parts on their structure is studied by neutron diffraction method. Thermally induced porosity (TIP) formed during heat treatment of AM parts is investigated together with BGU.

EBM ARCAM A2X

EOSINT M 280



AlSi10Mg Microstructure

A novel soil remediation based on a combination of a recycled extraction solution and Liquid-Liquid Critical Solution Mixtures

Zvi Ludmer[1], Roman Goikhman[1], Noam Dolev[1], Amos Ullmann[2], Neima Brauner[2], Zhanna Katz[2,]

[1]Biochemistry, Robert H. Smith Faculty of Agriculture, Food and Environment, Hebrew University, Rehovot, Israel

[2]Environmental Engineering Tel Aviv University, Israel

Abstract

Soil contamination by toxic heavy metals (Cd, Cr, Cu, Pb, Zn etc.) and mutagenic polyaromatic organic compounds (PAH/PCB) is well-recognized worldwide problem that poses a risk to environment and to human health. Existing soil remediation methods are mostly expensive and only moderately efficent in cases of severe contamination. Our developed innovative remediation method based on "Phase Transition Extraction", which has been previously developed by our group, allows removing simultaneously heavy metals and organic contaminants from soils or sludge. The method is based on the use of biodegradable chelators that are dissolved in a mixture of water with ecologically-friendly organic solvents. Such mixture forms one phase under mild heating and separates into two phases upon cooling to room temperature after contact with contaminated media, bearing heavy metal contaminants in mostly water phase, and organic contaminants in mostly organic phase.

The objectives of this study included optimization of the process conditions, and upscaling to the pilot scale towards developing a protocol for industrially feasible new soil remediation technology.

Thus, a pilot facility was designed and constructed at the Faculty of Agriculture in Rehovot. The pilot facility includes multifunctional reactor that serves for both soil remediation process and recovery of the organic solvents using distillation.

Two approaches were examined for soil remediation. First, a single step process that simultaneously extracts both organic and inorganic contaminates. Second, two stages process that involves extraction of organic contaminants using biodegradable organic solvents, followed by removal of heavy metals using water solution of biodegradable chelators. *Two approaches were compared and the results will be reported in the presentation.*

To optimize cost and feasibility of the entire process, the recovery-reuse cycles for solvents and chelators were tested and developed.

We believe that the entire developed, upscaled and optimized technology will be ultimately successfully applied in industrial soil remediation worldwide.


Posters

1- In vivo neuroimaging of exosomes using gold nanoparticles

Oshra Betzer[a,b*], Nisim Perets[c*], Ariel Angel[c], Menachem Motiei[a], Gal Yadid[b,d], Daniel Offen[c] and Rachela Popovtzer[a**]

[a]Faculty of Engineering and the Institute of Nanotechnology & Advanced Materials Bar-Ilan University
[b]The Leslie and Susan Gonda Multidisciplinary Brain Research Center, Bar-Ilan Universityc. [c]Felsenstein Medical Research Center, Sackler Faculty of Medicine, Tel Aviv University
[d]Everard and Mina Goodman Faculty of Life Sciences, Bar-Ilan University

Exosomes, extracellular vesicles that participate in cell-to-cell communication, are emerging as effective therapeutic tools which offer a promising solution for the treatment of various pathologies that conventional medicine cannot cure effectively. Exosomes possess an intrinsic ability to cross biological barriers, enabling bypassing of the blood-brain barrier (BBB) and transport into the brain. However, to elucidate the trafficking and communication mechanisms of exosomes, especially for brain disorders, and to promote their therapeutic application, a better understanding of the *in vivo* bio-distribution and pharmacokinetics of exogenously administered exosomes is needed. Herein, we established a new neuroimaging method for *in-vivo* tracking of exosomes within the brain, based on gold nanoparticle (GNP) labeling and computed tomography (CT) imaging. GNPs were found to be directly up-taken by exosomes via an active mechanism, rather than indirectly, via parent cells. Optimal parameters were determined for labeling and neuroimaging, including size and administration route. Our technique enabled tracking of the homing of intranasaly-administered, GNP-labeled exosomes to the lesion area in a mouse model of focal ischemia. This novel technique for *in-vivo* neuroimaging of exosomes within the brain can serve as a general platform for implementation in various theranostic applications.

2- Differentiating Between Cancer and Inflammation: A Novel Metabolic-Based Method for Functional CT Imaging

Tamar Dreifuss,[a] Menachem Motiei,[a] Oshra Betzer,[a,b] Galith Abourbeh,[c] Eyal Mishani,[c] and Rachela Popovtzer[a]

[a]Faculty of Engineering and the Institutes of Nanotechnology & Advanced Materials, Bar-Ilan University
[b]Gonda brain research center, Bar-Ilan University
[c]Cyclotron-Radiochemistry-MicroPET Unit, Hadassah-Hebrew University Hospital

One of the main limitations of the highly used cancer imaging technique, PET-CT, is its inability to distinguish between cancerous lesions and post treatment inflammatory conditions. The reason for this lack of specificity is that [^{18}F]FDG-PET is based on increased glucose metabolic activity, which characterizes both cancerous tissues and inflammatory cells. To overcome this limitation, we developed a nanoparticle-based approach, utilizing glucose-functionalized gold nanoparticles as a metabolically targeted CT contrast agent. Based on previous knowledge that newly formed blood vessels in growing tumors differ from those in inflammation, we hypothesized that the proposed technique may provide the ability to differentiate tumors from non-malignant metabolically active processes. Indeed, our approach has demonstrated, by both CT and quantitative measurements, specific tumor targeting and distinction between cancer and inflammation, in a combined tumor-inflammation mouse model. By contrast, FDG-PET/CT scans showed no visible nor quantitative differentiation between the two. In conclusion, our new concept of functional CT imaging overcomes the main drawbacks of the currently used FDG-PET and provides a new set of capabilities in cancer detection, staging and follow-up. This novel technology can be applicable to a wide range of cancers which exhibit high metabolic profiles.

3- Gold Nanoparticles for Non-invasive Cell Tracking

Rinat Meir

Bar-Ilan University

Cell-based therapy is the transplantation of living cells for the treatment of diseases and injuries. Such therapy offers a promising solution for the treatment of various pathologies that conventional medicine cannot cure effectively, thus encouraging future medical breakthroughs. For instance, cancer-fighting T cells may be injected in the course of cancer immunotherapy, and stem cells may treat neurodegenerative diseases, heart disease, muscular dystrophy and diabetes. A major obstacle in the advancement and implementation of cell therapy is the challenge of no-invasively tracking transplanted cells in the body. *In vivo* cell tracking could elucidate essential knowledge regarding mechanisms underlying the success or failure of therapy. An optimal solution for the challenge of cell tracking does not yet exist hence the need for an accurate imaging technique. We developed a novel methodology for longitudinal and quantitative *in vivo* cell tracking, based on the combination of CT as an imaging modality and gold nanoparticles as labeling agents. We were able to show that uniting the superior visualization abilities of classical CT with state-of-the-art nanotechnology is the key for high-resolution cell tracking. In the future, this technology has the potential to be applied clinically and to serve as an early warning system for patients after cell transplantation.

4- Protein Engineering of 2-Hydroxybiphenyl-3-Monooxygenase for Structure-Function Studies

Almog Bregman-Cohen, Ayelet Fishman

Department of Biotechnology and Food Engineering, Technion-Israel Institute of Technology, Haifa 3200003, Israel

2-Hydroxybiphenyl 3-monooxygenase (HbpA) from *Pseudomonas azelaica* is an NADH-dependent flavoprotein, that catalyzes the first step in the degradation pathway of 2-hydroxybiphenyl. The crystal structure of the enzyme with bound substrate has been recently reported by us. In order to study structure-function implications and the ability of HbpA to produce antioxidants and chiral sulfoxides, several hundreds of variants with mutations in the active site were generated and characterized. It was found that residues N205, R242 and P320 are involved in enabling the movement of the FAD cofactor, which in turn influenced HbpA activity. Residues D222 and M223 seem to be involved in NADH entrance or binding in the active site since most variants that were characterized resulted in a decrease of specific activity and affinity. The exceptions were D222N which significantly increased its affinity towards NADH, and M223Q that increased NADH oxidation by 1.3-fold. Variant W225A led to a 14-fold decrease in specific activity while W225Y showed elevated specific activity, indicating on involvement of W225 in the catalytic reaction. While most variants that were generated for residue M321 lost their activity, variants M321L, M321F and M321V exhibited improvement in hydroxylation efficiency. Interestingly, variant M321A, which was less active than WT by 1.4-fold on the natural substrate, demonstrated altered regiospecificity by oxidizing for the first time 3-hydroxybiphenyl to 3,4-dihydroxybiphenyl. These results suggest that M321 is crucial for proper orientation of the substrate in the active site pocket. The new insights will be utilized for tailoring biocatalysts with improved activity and selectivity towards various antioxidants and chiral sulfoxides.

5- Engineering food texture using enzymatic crosslinking

Sivan Isaschar-Ovdat

Department of Biotechnology and Food Engineering, Technion – Israel Institute of Technology, Israel

One of the challenges food professionals face is the need to manufacture nutritious foods that also offer pleasurable textures and experiences. Soy proteins have become popular due to their health benefits and availability and are used as dairy and meat replacements. The goal of this study was to investigate the effect of tyrosinase crosslinking on soy protein-based emulsions and gels as well as the underlying mechanism behind the enzyme's crosslinking activity using peptides derived from glycinin. First, tyrosinase from *Bacillus megaterium* (TyrBm) was used to induce crosslinking bonds in glycinin and optimal conditions were found. Crosslinked glycinin was used to fabricate o/w emulsions that were studied for their physical stability, particle size and shear viscosity. A two-fold reduction in creaming velocity and a similar increase in viscosity was obtained when TyrBm treatment was applied after homogenization. Overall, the crosslinked glycinin formed a more stable emulsion with a gel-like structure. Second, heat-induced soy glycinin gels were evaluated for their rheological behavior and texture properties. TyrBm-crosslinked glycinin gels possessed a 330-fold higher storage modulus (G') and a 2-fold increase in hardness and gumminess compared to the non-crosslinked control. SEM imaging linked these macroscopic phenomena to a 3-fold increase in pore diameter. In addition, a reduced sugar and fat soy-based chocolate pudding was fabricated using TyrBm. The crosslinked soy based pudding exhibited higher hardness than the non-crosslinked pudding. A tasting panel reported a significant positive correlation (p-value<0.05) between the crosslinked soy pudding and measures of "stable" and "firm" texture. These results confirm that TyrBm-crosslinking of soy proteins can affect the product texture, not only in a pure protein system but also in a complex food matrix. The enzymatic crosslinking led to improved texture and can potentially be used to fabricate food products with lower amount of fat, protein or stabilizers.

6 - Combining Prefrontal Transcranial Magnetic Stimulation with Electroencephalography to Identify ADHD and its Severity

Aviad Hadar

Ben-Gurion University of the Negev

Background: The current diagnosis for attention-deficit-hyperactivity-disorder (ADHD) is based on subjective examination and clinician's impression. Development of objective procedures is critical for prognostic assessment, reduction of error in diagnosis and further understanding of the pathophysiology of the disease. Here we explored a novel diagnostic tool for the assessment of ADHD severity based on neural markers registered from a pathophysiologically-relevant brain region.

Methods: Neural activity of 41 healthy and 34 ADHD adults was recorded using Electroencephalography (EEG) during 2 experimental protocols: (1) a session of Transcranial Magnetic Stimulation (TMS) over the right prefrontal cortex, and (2) while performing a Stop Signal task. ADHD severity was measured by standardized psychiatric assessment.

Results: Early TMS-evoked potentials (TEP) and N2 and P3 ERP components in the Stop Signal task were found to be significantly reduced in ADHD as compared with matched controls. Significant correlations were found between these components and ADHD severity. Backward stepwise regression analysis revealed that the combination of P3 amplitude in unsuccessful stopping trials and Early TEP was optimal and highly predictive ($R=0.61$) of ADHD severity.

Limitations: No stimulation control site was employed. In addition, control subjects were not diagnosed by a psychiatrist to assure their self-report of absence of psychiatric diagnosis of ADHD.

Conclusion: Electrophysiological abnormalities were detected to construct a robust predictive model of ADHD severity. These findings further implicate the right PFC in the pathophysiology of ADHD. By capitalizing on the neural signature of these abnormalities, this combined model can be utilized for the assessment of response to treatment and eventually for individualization of therapy.

7- Personalized Nutrition by Prediction of Glycemic Responses

David Zeavi

Weizmann Institute of Science

Elevated postprandial blood glucose levels constitute a global epidemic and a major risk factor for prediabetes and type II diabetes, but existing dietary methods for controlling them have limited efficacy. Here, we continuously monitored week-long glucose levels in an 800-person cohort, measured responses to 46,898 meals, and found high variability in the response to identical meals, suggesting that universal dietary recommendations may have limited utility. We devised a machine-learning algorithm that integrates blood parameters, dietary habits, anthropometrics, physical activity, and gut microbiota measured in this cohort and showed that it accurately predicts personalized postprandial glycemic response to real-life meals. We validated these predictions in an independent 100-person cohort. Finally, a blinded randomized controlled dietary intervention based on this algorithm resulted in significantly lower postprandial responses and consistent alterations to gut microbiota configuration. Together, our results suggest that personalized diets may successfully modify elevated postprandial blood glucose and its metabolic consequences.

8- Miniature spectral and polarimetric liquid crystal based systems and their applications

Maroan Abo-lil

Ben-Gurion University of the Negev

Liquid crystal (LC) is a special kind of mesophase material. Its electro-optical properties grant it a significant presence in wide display devices. In addition, designing and integrating novel LC devices (LCD) in various non-display photonic applications is a recent emerging field. The main advantage of integrating LCDs is the ability of modulation light without using mechanical rotations low voltages.

In this research, we are focusing on polarimetric and multi spectral imaging systems based LC devices and their applications. Since Polarimetric imaging system is based on extracting the difference in polarizing properties between the target and backscatter light, it is a significant candidate for imaging through turbid mediums and conditions such as imaging through rain, haze and turbid water.

Multi spectral imaging system has a strong ability to distinguish the differences in the spectrum of transmitted or reflected light in addition to the spatial resolution. Imaging system with this property can be useful for precise food quality or detecting diseases of plants, trees and fruits. Further, A compact Spectro-polarimetric imaging system based LC devices has a high potential in many applications such as biomedical, agriculture and food quality systems. The research involves developing and integrating LC devices for spectral and polarization control, optical design and image processing. These proposed developments are supposed to improve the captured images quality and contrast.

9- Short Term Plasticity of Short Plasticity: Stimulus Specific Adaptation to Temporal Gaps

Bishara Awwad and Israel Nelken

Dept. of Neurobiology and the Edmund and Lily Safra Center for Brain Sciences, Hebrew University, Jerusalem,Israel.

The detection of short gaps in a continuous stimulus is important for a number of auditory tasks. We studied the coding of gaps in auditory cortex using an oddball paradigm. The stimuli consisted of either 200 ms long broadband noise bursts or broadband noise bursts with a short gap (~10 ms), starting 100 ms after stimulus onset. The evoked response to a gap consists of two components (P1 and P2), representing the responses evoked by the onset of the stimulus followed by the responses evoked by the trailing edge of the gap. The well-studied forward masking in auditory cortex is reflected by the finding that generally, the P2 response is smaller than the P1 response, so that the P2/P1 ratio is typically smaller than 1. When the gap stimuli were rare within a sequence of continuous noise bursts (gap deviant), the P2/P1 ratio was greater than when the gap stimuli were common (gap standard). Moreover, in many neurons, when the gap was long (20ms), the P2/P1 was greater than 1, reversing the ubiquitous finding of forward masking. To study the mechanism that underlies the difference between the responses to standard and deviant gaps, we conducted current clamp recordings using intracellular sharp electrode. Recording the responses while injecting different currents to the neuron allowed us to extract the total conductance of the cell as well as the reversal potential of the stimulus-driven currents as a function of time during the sensory response. Our results suggest that when gaps are deviant, the P2 response shows a change in excitatory-inhibitory balance, with excitation becoming more prominent, than when gaps are standard, accounting for the larger response to deviant gaps. This finding shows that short-term context modifies not only response sizes, but also short-term plasticity mechanisms.

10- GLUT4 translocation test for organic extracts of *Rosmarinus officinalis* L., Lamiaceae: in vitro evaluations of their anti-diabetic activity and cytotoxicity

Sleman Kadan[1,2], Hilal Zaid[2] and Yoel Sasson[1]

[1]Casali Center for Applied Chemistry, Institute of Chemistry, The Hebrew University of Jerusalem, Givat Ram, Jerusalem 91904, Israel.
[2]Qasemi Research Center- Al-Qasemi Academy, P.O Box 124, Baqa El-Gharbia 30100, Israel.

Introduction

Rosemary (*Rosmarinus officinalis* L., Lamiaceae) is a woody perennial herb, native to the Mediterranean region, but is now cultivated all over the world as an ornamental and aromatic plant. The leaves of rosemary are commonly used for flavoring foods as a condiment, but this plant has also been widely used for different medicinal purposes, such as, anticancer, antidiabetic, anti-inflammatory and antinociceptive, antioxidant.

Diabetes is a metabolic disease usually caused by a combination of hereditary and environmental factors, which result in hyperglycemia and other classical symptoms, especially polyuria, polydipsia and polyphagia. Eventually, hyperglycemia leads to serious damage in blood vessels.

The aim of this study was to evaluate the role of glucose transporter-4 (GLUT4) in the anti-diabetic effects of the aerial parts of Rosemary methanol, hexane and cichloromethane.

Materials and Methods

The air-dried aerial parts of *Rosmarinus officinalis* L. were ground, 10 g of the powder were then packed in the thimble of the Soxhlet apparatus and were extracted with 150 ml methanol (MeOH), dichloromethane (DCM) or hexane, and then refluxed for 24 hours to give a dark green extract.

The extracts anti-diabetic activity was examined by measuring the relative amount of GLUT4 translocation to the plasma membrane in the presence and absence of insulin. L6 muscle cells, stably expressing myc-tagged GLUT4, were utilized. These cells have been repeatedly shown to display insulin regulated GLUT4 traffic. L6 myoblasts were pre-treated with increasing concentrations of Rosemary extracts for 20h, followed by 3h serum-deprivation and insulin stimulation for 20 min and then GLUT4myc levels at the plasma membrane was determined. Toxicity of the extracts was determend by MTT and LDH leakage assays.

Results and Discussion

Cytotoxic and anti-diabetic properties of the extracts were evaluated using L6-GLUT4myc muscle cells stably expressing myc epitope at the exofacial loop (GLUT4). No cytoxic effects were observed in treated cells up to 0.25 mg/ml extract as measured with MTT and LDH-leakage assays. GLUT4 translocation to the plasma membrane was elevated by 2.5 and 5.5 folds (-/+ insulin) after treatment with Rosemary extracts for 20 h.

11- Head-Mounted Projection system for visual stimulation and cortical recordings as a novel method for studying natural and artificial vision in behaving animals

Tamar Arnes-Arad

Bar-Ilan University

Purpose: Accurately assessing natural and artificial visual function performance in awake and behaving animals is of great importance for studying various retinal diseases and treatments. Here we present the development of a novel customized head-mounted projection system integrated with electrodes for recording visual evoked potentials (VEP) in response to natural and artificial stimulus for assessing visual functions in awake and behaving animals.

Methods: We devised and customized a Digital Mirror Device (DMD) based head-mounted system, to project high quality images at visible and near IR light onto the rat retina and performed computer simulations to characterize and optimize the optical properties of the system. The design included a periscope like system to relay the DMD projected image onto the rat retina, and fitted onto the rat skull using a customized head plate and adaptor.

VEPs were recorded using electrodes implanted into the visual cortex and embedded into the mounting head plate. VEPs induced by flashes with varying pulse durations (ranging from 0.25msec to 8msec), varying frequency (ranging from 1Hz to 32Hz) and varying contrast levels projected by the head mounted projector were investigated in both anesthetized and awake animals.

Results: The system enabled the projection of images with MTF values higher than 0.85, with optimal image quality obtained at a 1mm pupil diameter, with a retinal image diameter of 3mm corresponding to 45 degrees visual field in the rat. Robust VEP signals were recorded in response to images projected at various contrast and light intensity. The VEP amplitude decreased as a function of temporal frequency reaching the noise limit for frequencies higher than 32Hz and increased as a function of stimuli duration, reaching a plateau at pulses longer than 10ms. Similarly, a decrease in VEP amplitude for decreasing contrast was also observed, reaching the noise level at 6% contrast**.**

Conclusions: Our results demonstrate the feasibility of investigating visual function performance in rats using a novel head-mounted projection system. This system may prove to be a vital tool in studying natural and artificial vision in awake and behaving animals, and for the evaluation of various treatments or other interventions, such as training for the studying of visual cortex plasticity.

12- Focal Electroretinogram and Visual Evoked Potential in Rats

Adi Gross

Bar-Ilan University

Purpose: Measurements of focal retinal function is helpful in evaluation localized retinal malfunction and in assessing intervention efficiency in treatment modalities such as retinal prostheses, genetic therapy or stem cell transplantation. In this work we characterized the focal Electroretinogram (fERG) and Visual Evoked Potential (fVEP) in response to a photopic localized visual stimulus projected on pigmented rat retina.

Methods: fERGs and fVEPs signals were recorded in Long-Evans anesthetized rats in response to visual stimulus consisted of LED flashes relayed through circular apertures which are incorporated into a fundus camera (Micron IV, Phoenix Research Lab) optical path. Stimuli with varying irradiances, repetition rates, and spot diameters ranging from 0.5 to 3.0 mm were investigated at various background illumination. VEP signals were recorded using screws electrodes implanted over the primary visual cortex and ERG signals were recorded using a corneal contact electrode.

Results: The fERG b-wave amplitude increased with light intensity reaching a plateau at 4*103cds/m2, and decreased with increasing stimuli repetition rate and increasing background illumination. The fVEP amplitude (N1P2) demonstrated a similar trend, however, a plateau was observed at a lower stimuli luminance (1*103cds/m2) suggesting a smaller cortical dynamic range as compared to the retina. fERG and fVEP b-wave amplitude increased with stimuli spot size reaching a plateau at smaller spot size for high intensity illumination levels, suggesting a contribution of the scatter effect. The b-wave latency decreased with increasing stimuli luminance, reaching a minimum at luminance levels above 10cds/m2. The photopic stimuli elicited a robust photopic negative response (PhNR) with increasing amplitude and latency for increasing stimuli irradiance and spot size.

Conclusions: The effect of various retinal focal stimuli parameters on fERG and fVEP signals in normal pigmented rats show characteristic responses. A robust PhNR component was found and characterized. Evidences for a scatter effect were found at high irradiance stimuli, which could be reduced by addition of background illumination. In addition, our results demonstrate the larger retinal dynamic range as compared to the cortical dynamic range under photopic conditions. This study can serve as a basis for evaluating localized retinal function as an important research tool for investigating retinal diseases in rodents.

13- Multimodal *In-vivo* High Resolution Imaging of Gold Nanoparticle Labeled Photoreceptor Precursors

Yoav Chemla (1), Oshra Betzer (2), Amos Markus (1), Astar Shamul (1), Menachem Motiei (2), Nairouz Farah (1), Rachela Popovtzer (2), Yossi Mandel (1)

(1) Faculty of life Sciences, Optometry Track and Bar-Ilan Institute for nanotechnology and Advanced Materials (BINA), Bar-Ilan University, Ramat-Gan, Israel
(2) Faculty of Engineering and the Institute of Nanotechnology and Advanced Materials, Bar-Ilan University, Ramat Gan

Purpose: Imaging of transplanted cells in the retina is an important research area and a valuable clinical tool. The use of gold nanoparticles (GNPs) for imaging and drug carrying was recently introduced for various purposes and applications. In this study, we investigated the use of GNPs as a potential novel imaging modality for ocular cell therapy in a rat model.

Methods: GFP-expressing human embryonic cells (hESC) were differentiated into photoreceptor precursors (PRPs) in a 24 days protocol, recently optimized at our lab. Twenty nm diameter GNPs conjugated to a PEG7 (*Polyethylene glycol)* linker and coated with glucose, were synthesized and characterized using transmission electron microscopy (TEM), dynamic light scattering (DLS) and ultraviolet-visible (UV-vis) spectroscopy. PRPs, and a cancer cell line (MeWo expressing GFP) uptake of the GNPs was verified using TEM and dark field microscopy. The toxic effect of the GNPs on the cells was evaluated by cell morphology and MTT cell viability and proliferation assay. The GNPs-labelled cells were transplanted into the sub-retinal space of the rats and monitored *in-vivo* using a rodent fundus camera, equipped with fluorescence (GFP tracking) and Optical Coherence Tomography imaging OCT capabilities for retinal structure visualization (Phoenix Research Laboratory, Micron IV). In addition, the GNP-labeled cells were imaged *in-vivo* using a micro-CT scanner (Skyscan 1176, Bruker, Belgium).

Results: The PRPs marker cone-rod Homeobox (CRX) revealed that hESC were efficiently differentiated into PRPs (approximately 80% yield). TEM and dark field microscopy demonstrated the successful uptake of the GNPs by the cells. Results revealed no toxic effect of GNPs on the cells. Cell migration was visualized by CT imaging of the labelled cells. The fluorescent cells were further visualized by a fluorescence fundus camera revealing no fluorescence quenching effect caused by the GNPs.

Conclusions: GNPs cell labeling has low toxicity and could be imaged by CT following transplantation to the rat retina. This method of cell labeling with GNPs offers a valuable tool for molecular imaging in retinal cell therapy and diagnostics.

14- Alginate mediated maleimide modified PEG for enhanced mucoadhesion

Yarden Shtenberg, Mor Goldfeder, Avi Schroeder, Havazelet Bianco-Peled

Technion-Israel Institute of Technology

The effective delivery of pharmaceutical agents to mucous-coated tissues is an unmet technological challenge. In this study we describe a new mucoadhesive delivery system composed of alginate (Alg) grafted with a unique functional end-group (maleimide) modified polyethylene glycol (PEG). Maleimide moieties are known for their ability of creating covalent bonds in biological systems via a Michael addition with thiol residues of proteins. Moreover, maleimide consists of two carbonyl groups, which produce hydrogen bonding with the mucus glycoproteins. In the present work, we synthesized a novel polymer (Alg-PEG-maleimide), verified formation of the desired product through Nuclear Magnetic Resonance (NMR) and Fourier Transform Infrared Spectroscopy (FTIR), confirmed biocompatibility, and evaluated the adhesive properties by several methods including tensile study, rotating cylinder and rheology. The novel polymer system demonstrates enhanced mucoadhesion properties with respect to natural and thiol-modified polymers and similar drug release properties.

15- Biological Computing Using Fluorescence Lifetime Imaging Measurements

Eran Barnoy, Dror Fixler, Rachela Popovtzer

Faculty of Engineering & The Institute of Nanotechnology and Advanced Materials, Bar-Ilan University, Ramat-Gan, Israel.

Using responsive conjugation and activatable probes, it is possible to make a system that reacts fluorescently in a manner corresponding to specific triggers or environments. A combination of several biological triggers can be viewed as biological computing.

In the current research, we explored the effects of a combination of biologically meaningful inputs on a fluorescent nano-system using fluorescence lifetime imaging microscopy (FLIM) to demonstrate different logic operations. Gold nanoparticles (GNPs), known for their strong influence on nearby fluorophores, were functionalized using a cleavable peptide, and were then conjugated to fluorescein or fluorescein diacetate (FDA). Connection to GNPs was severed by adding the enzyme caspase-3, and FDA was activated by increasing pH.

FLIM results revealed a FLT of 3ns and FI of under 2000AU for fluorescein conjugated to GNPs, and subsequent exposure to caspase raised the FLT to 4ns and FI to over 10000AU. In FDA samples, particles with FDA exhibited an FLT of 1ns and intensity of 100AU. Incubation with caspase raised the FLT to 3ns and FI to 2000AU. Raising surrounding pH increased the FLT to 3.7ns and FI to 2500AU. Meanwhile, a combination of caspase and raised pH recovered a FLT of 4ns and FI of 3500AU.

Using controlled chemical reactions and the sensitive FLIM modality, we have demonstrated initial, intermediary, and final steps in a system consisting of combined enzyme activation and change in pH. Through both FI and FLT, we are able to differentiate between logic situations of YES, NOT, AND, OR, NOR, and XOR gates from this simple-to-manufacture and biologically relevant probing system.

16- Computational modeling and systems biology of mRNA translation and its evolution

Renana Sabi

Tel Aviv University

mRNA translation is a key process in all living organisms in which the information encoded in the DNA is converted into proteins. Translation proceeds in three steps: initiation, elongation and termination; its regulation has a great impact on cellular development and may occur at each stage of this process. For example, during elongation, certain peptide sequences within the newly synthesized protein may interact with the ribosome and stall the translation process.

The goal of my research is to enable the development of biotechnological approaches for gene expression engineering by comprehensively analyzing experimental measurements of active ribosomes during the cell cycle of the baker's yeast.

Most of the studies on translational regulation are focused on ribosome stalling caused by individual amino acids, are performed in small-scale of refer to the translation process as a whole. In this research, we suggest for the first time multidimensional large-scale computational approaches for detecting dozens of short peptides that can stall ribosomes, studying the unique regulation at the initiation and elongation phases of translation, and using this information for gene expression engineering purposes.

Our findings will throw light on protein evolution and mRNA translation and open the door to various biomedical, medical and biotechnological applications such as gene expression/protein modeling and engineering.

17- PEAR: PEriodic and ApeRiodic signal separation for fast fMRI

Lior Weizman[1], Karla Miller[1], Yonina C. Eldar[1], Mark Chiew[1]

[1] Department of EE, Technion, Haifa, Israel
[2] FMRIB Centre, University of Oxford, Oxford, United Kingdom

Undersampling of functional MRI (fMRI) data leads to increased temporal resolution, as it allows shorter acquisition time per frame. High quality reconstruction of fMRI data from undersampled measurements requires proper modeling of the fMRI data. Recent publications suggest that the fMRI signal is a superposition of periodic and aperiodic signals. In this paper we develop an fMRI reconstruction approach based on this modeling. The fMRI data is assumed to be composed of two components: a component that holds a sum of periodic signals which is sparse in the temporal Fourier domain and an component that holds the remaining imaging information (consisting of the background and aperiodic signals) which has low rank. Data reconstruction is done by solving a constrained problem that enforces a fixed, moderate rank on one of the components, and a limited number of temporal frequencies on the other. Our approach is coined PEAR - PEriodic and ApeRiodic signal separation for fast fMRI. Experimental results are based on fMRI reconstruction using realistic timecourses. Evaluation was performed both quantitatively and visually versus ground truth. Results demonstrate PEAR's improvement in estimating the realistic timecourses versus state-of-the-art approaches at acceleration ratio of R=16.6.

18- Analysis and modeling of the sleep-microarchitecture to elucidate healthy and pathological sleep-wake patterns

Hila Dvir, Shlomo Havlin, Ronny Bartsch

Department of Physics, Bar-Ilan University, Ramat Gan

In addition to the regular circadian sleep-wake pattern, humans and animals often exhibit brief awakenings from sleep (arousals), lasting from seconds to minutes, which appear random in time and occur throughout the entire sleep period. Arousals are traditionally viewed as random disruptions of sleep caused by external stimuli or as involved in the pathophysiology of sleep disorders. However, we have recently discovered that brief arousals exhibit temporal organization characterized by a power-law probability distribution for their durations, while sleep-stage durations exhibit exponential behavior. Such complex scale-invariant organization of the arousals makes it unlikely that they are merely a linear response to random external stimuli or that they are primarily associated with sleep pathology, as we observe this behavior under healthy conditions.

This unique coexistence of both scale-invariant and exponential processes as an output of a single sleep regulatory mechanism has not been observed in other integrated physiological systems under neural regulation prior to our discovery. This coexistence resembles the dynamical features of certain physical systems out of equilibrium exhibiting self-organized criticality (SOC), where "quiet" periods following an exponential law are interrupted by recurring "active" periods having scale-invariant power-law characteristics for their size and duration; and where triggering of frequent active periods over a broad range of time scales is an essential component in the self-organization of the system, needed to maintain its critical state.

We propose a novel model to simulate and to explain this sleep phenomenon, based on the concept of SOC, to investigate non-equilibrium features in sleep dynamics, where specific neuronal groups and signaling pathways, nonlinear neuronal feedback interactions and network topologies lead to emergent scale-invariant organization at the system level. Novel markers of sleep dynamics derived from this new modeling will capture very different aspects of sleep regulation as compared to traditional measures, and thus, have the potential to improve current diagnosis and treatment of sleep disorders.

19- Magnetic control of drug carriers and cells for applying local therapeutics

Michal Marcus

Bar-Ilan University

The ability to manipulate and direct drug carriers and cells towards specific sites is of great importance in the field of biomedicine, with many potential implications in therapeutics and in the development of bio-chip devices. A recent and innovative approach to achieve site specific targeting is by incorporating magnetic nanoparticles (MNPs) within drug carriers and cells, enabling the magnetic complex to be remotely-guided by external magnetic field gradients. In our study, we develop magnetic drug carriers for the delivery of active molecules to desired locations and use pre-designed magnetic fields setups to direct the magnetic complexes towards specific target sites. We synthesize magnetic complexes by conjugating iron oxide nanoparticles to proteins. Specifically, we conjugate NGF protein to MNPs to spatially control the differentiation of PC12 cells. In addition, we magnetize cells via MNPs and control their migration and distribution by magnetic hot spots. Cells are incubated with MNPs and turn sensitive to magnetic stimulation with no cytotoxic effect. Using magnetic micro-patterned substrates, we locate MNPs-loaded cells at specific sites, promote cellular growth and affect growth orientation. Our research presents a new concept of directing biological elements to specific areas of interest. This methodology may greatly contribute to the fields of drug and cell therapy as they both deal with the challenge of directing drugs or engineered cells to the site of damage in order to improve treatment efficiency while minimizing side effects.

20- Monitoring Imbalance of Excitation and Inhibition in Epilepsy Patients and Applications to Seizure Prediction using a Portable EEG System

Oshrit Arviv[1], Itzik Mashiach[2], Abraham Goldstein[3, 1], Oren Shriki[4, 5,6]

[1]The Leslie and Susan Gonda (Goldschmied) Multidisciplinary Brain Research Center, Bar-Ilan University, Ramat Gan, Israel
[2] Ovela Technologies, Kfar-Yona, Israel
[3] Department of Psychology, Bar-Ilan University, Ramat Gan, Israel
[4] Department of Cognitive and Brain Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel
[5] The Inter-Faculty School for Brain Sciences, Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Beer-Sheva, Israel
[6] Department of Computer Science, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Epilepsy, a chronic neurological disorder which affects approximately 1% of the world population, is associated with an imbalance of excitation and inhibition in the brain. However, there are currently no available methods to probe the excitation-inhibition balance (EIB) in humans and it is still unclear how an imbalance gives rise to epileptic seizures. Recently, we developed and applied both known and new EIB metrics to brain activity recording from epilepsy patients as well as healthy control subjects. These metrics are based on ideas from the theories of criticality and complexity in neural systems and enable a quantitative assessment of the deviations from healthy brain dynamics. Currently, we explore clinical applications of these metrics, in particular for monitoring the effectiveness of treatments, and predicting in real-time the occurrence of seizures. We use machine learning approaches to construct automatic real-time predictors of inter-ictal and seizure activity based on the EIB metrics. The use of such non-linear metrics, which carry meaningful information about network dynamics, is expected to provide better prediction compared to naïve approaches that rely directly on the raw brain activity or on simple features. The goal is to translate all this into a product: a practical portable EEG system to be used by epilepsy patients on a daily basis.

21- Development of a Novel P53 Based Drug Delivery System forTreatment of Bone Cancer, Osteosarcoma

Mor Goldfeder[1], Hodaya Prinz[1], Sivan Arber[1], Janna Shainsky[1], Lisa M. Abegglen[2], Joshua D. Schiffman[2], Avi Schroeder[1]

[1]Department of Chemical Engineering, Technion-Israel Institute of Technology, Haifa, Israel
[2] Huntsman Cancer Institute, University of Utah, Salt Lake City, UT,USA

Osteosarcoma is the most common malignant bone cancer in children and adolescents however there has been little therapeutic progress for the past 30 years. TP53, a crucial tumor suppressor, is one of the most common genes altered in pediatric osteosarcoma. Due to its role in preventing cancer in mammals, P53 is one of the most studied tumor-suppressor proteins. Elephants have very low cancer occurrence, and it has been discovered that compared to humans they have 20-fold more copies of TP53. We are developing a new class of precision medicines, Elephant-P53 (Ep53) protein-loaded nanoparticles that target cancer cells and trigger TP53-mediated apoptosis in response to DNA damage. Our study is the first to characterize the therapeutic potential of Ep53 variants in osteosarcoma. Transfection of plasmids carrying the genes for ancestral Ep53 and Ep53-r9 results in significant cell death and increased apoptosis. Furthermore we have produced and purified both ancestral Ep53 and Ep53-r9 in a bacterial expression system. Purified proteins were loaded onto liposomal nanoparticles and delivered to osteosarcoma cell lines. The delivery of the protein was imaged using confocal microscope and a significant decrease in cell viability was observed in cells to which Ep53-r9 nanoparticles were added.

22- NMR Investigations of the Structure and Dynamics of New KcsA inhibitors

Netanel Mendelman

Bar-Ilan University

Peptide neurotoxins that inhibit ion channels are commonly used for research and as therapeutic agents. KcsA is considered a model K^+ channel as much is known about its structure, selectivity and gating properties. Hui1 and HmK are two toxins that were isolated from a phase-display library, as exhibited nanomilar affinity to KcsA, This library is based on the scaffold of ShK, a sea-anemone toxin that inhibits the Kv voltage gated K^+ channels. ShK fails to bind KcsA, Hui1 is only selective to KcsA, and HmK can also bind to the Kv channel [1].

Both Hui1 and HmK structures were resolved using 2D NMR spectroscopy. Although their structures and that of ShK are closely related, the electrostatic maps of the three toxins present several differences, especially at the domain which is further from the toxins binding site. This led us to postulate that the selectivity property of the toxins is governed by the electrostatic surfaces.

Initial measurements of binding between Hui1 and KcsA were already accomplished using nanodiscs as membrane mimic environment for KcsA. Perturbations to chemical shifts of only amino acids located in the binding zone in Hui1 NMR spectra, induced by KcsA binding, indicated that a complex had been obtained. NMR relaxation measurements of each residue in Hui1 revealed that amino acids in the binding site experince an exchange property that might enable Hui1 to bind KcsA in a different manner than is known for other toxins. This exchange property was also seen in ShK residues involved in the binding to its Kv channel [2].

This study show the preleminarry steps thowrds obtining a toxin-channel complex structure.

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23- In-Vitro Microfluidic Models of Alveolar Capillary Microcirculation

Hagit Stauber[1], Dan Waisman[2,3], Netanel Korin[1] and Josué Sznitman

[1]Department of Biomedical Engineering, Technion – Israel Institute of Technology, 3200003 Haifa, Israel
[2]Department of Neonatology, Carmel Medical Center, 3436212 Haifa, Israel
[3]Faculty of Medicine, Technion – Israel Institute of Technology, 3200003 Haifa, Israel

The pulmonary capillary networks (PCN) embody organ-specific microvasculatures, where blood vessels form dense meshes that maximize the surface area available for gas exchange in the lungs. With characteristic capillary lengths and diameters similar to the size of red blood cells (RBCs), seminal descriptions coined the term "sheet flow" nearly half a century ago to differentiate PCNs from the usual notion of Poiseuille flow in long straight tubes. Here, we revisit in true-scale experiments the original "sheet flow" model and devise for the first time biomimetic microfluidic platforms of organ-specific PCN structures perfused with RBC suspensions at varying hematocrit, including physiological levels. By implementing RBC tracking velocimetry, our measurements reveal a wide range of heterogonous RBC pathways that coexist synchronously within the PCN; a phenomenon that persists across the broad range of pressure drops and capillary segment sizes investigated. Interestingly, in spite of the intrinsic complexity of the PCN structure and the heterogeneity in RBC dynamics observed at the microscale, the macroscale bulk flow rate versus pressure drop relationship retains its linearity, where the hydrodynamic resistance of the PCN is to a first order captured by the characteristic capillary segment size. In the footsteps of classic works in scaled-up capillary network models, our in vitro platforms help revisit the question of the relative viscosity of blood across confined capillary networks. To the best of our knowledge, our efforts constitute a first, yet significant, step in exploring systematically the transport dynamics of blood in morphologically-inspired capillary networks of the lungs.

24- The autism-mutated ADNP is a stress risk factor: Protection with the regulatory neuropeptide PACAP

Sragovich S.[1] and Gozes I.[1]

[1]The Lily and Avraham Gildor Chair for the Investigation of Growth Factors, Dr. Diana and Zelman Elton (Elbaum) Laboratory for Molecular Neuroendocrinology, Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine, Sagol School of Neuroscience and Adams Super Center for Brain Studies, Tel Aviv University, Tel Aviv, Israel.

Activity-dependent neuroprotective protein (ADNP), discovered and first characterized in the laboratory of Prof. Illana Gozes as vital for mammalian brain formation, was found to be one of the leading genes mutated *de novo* causing an autistic syndrome. Additionally, a unique mouse model of Adnp-haploinsufficiency was developed in the laboratory, with mice encompassing cognitive and social deficiencies. ADNP is regulated by vasoactive intestinal peptide (VIP), as well as pituitary adenylate cyclase-activating peptide (PACAP), which change its content toward neuroprotection. In this respect, PACAP was identified as a sexual divergent master regulator of stress response. Interestingly, the PACAP-regulated ADNP was also found to be sexually dimorphic.

Children with autism may be at increased risk for both encountering stressful events and developing subsequent sequelae. Therefore, we sought to determine the impact of the Adnp genotype and the efficacy of PACAP pre-treatment in our unique mouse model when subjected to stressful conditions, focusing on gender differences. For this purpose, mice were pre-treated twice daily with PACAP for one month, followed by a 48-hour period of solitude in a clean cage under constant bright illumination (stressful conditions). Anxiety levels were tested using the elevated plus maze, and complemented by cognition and social activity tests. Our results revealed that different behavioral impairments displayed in stress-challenged $Adnp^{+/-}$ mice were normalized to the $Adnp^{+/+}$ phenotype by PACAP treatment. Interestingly, significant sex differences were observed with $Adnp^{+/-}$ males more susceptible to stress in the object and social recognition tests.

Our findings suggest a correlation between ADNP levels and stress. Thus, low ADNP transcript expression level may indicate a worse response to stressful events, which can be successfully ameliorated by PACAP treatment. Altogether, this could establish ADNP as a possible biomarker, identifying autistic individuals who are prone to suffer from stress, toward the development of future gender-specific therapies.

Support: Gildor Chair (IG), Elton Lab (IG), AMN Foundation (IG), ISF (IG), MAFAT (IG)

Abstract oral and poster presentation were delivered at the Israeli Society for Neuroscience annual meeting, Eilat, Israel, December 2016.

25- Sexual divergence in activity-dependent neuroprotective protein (ADNP): the brain is not the same

Hacohen-Kleiman Gal, Barnea Anat and Gozes Illana

Tel Aviv University

Autism is a serious neurological-disorder, in growing prevalence affecting millions of children worldwide (5:1 in boys vs. girls). Etiology/drugs treatment for social/vocal communications deficits are still relatively unknown. Activity-dependent neuroprotective protein (ADNP, discovered by Prof. Gozes) is highly expressed in male vs. female brain in humans, mouse (hippocampus) and songbirds[1, 2]. In children, ADNP mutations cause intellectual/motor and speech delays/disabilities[3, 4]. In mice, Adnp knockout is lethal, while Adnp-deficiency (Adnp+/-; model developed by Prof. Gozes) causes sex-dependent autistic-related characteristics[1, 5], including alterations in vocalizations (unpublished). Interestingly, Adnp+/- male mice exhibit higher expression of autism-related genes, while females show higher expression of Alzheimer's-related genes. In turn, treatments with ADNP-snippet peptides protect the phenotype in both sexes. In the zebra finch (*Taeniopygia guttata*) songbird brain, ADNP expression is sexually dichotomous/age-dependent[2]. Only the males sing, fitting to highest ADNP expression found in young male cerebrum, comprising the song system. Similarly, in the domestic canary (*Serinus canaria*), ADNP expression was also found mostly expressed in the male cerebrum, corresponding with the male's sole ability of singing (unpublished). Now, we aim to study potential language-related explanation for sexually dependent ADNP expression in songbird brain, asking, will ADNP-mutated songbirds develop similar speech-delays as ADNP-mutated children and will ADNP-based treatment be beneficial for this circuitry? We hope to help yield the first drug treatment for speech disabilities/autism, adjusted for global use of afflicted men and women.

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26- Mitochondrial Function Profile in Response to Antipsychotics as a Guideline for Personalized Medicine for Patients Suffering from a Psychotic Illness

Odeya Damri[1, 2], Tamara Ifraimov[1, 2], Carmit Marom[2], Vladislava Gurman[2], Joseph Levine[2], Yuly Bersudsky[2], Dorit Ben-Shachar[3], Galila Agam[1, 2]

[1]Department of Clinical Biochemistry and Pharmacology and [2]Psychiatry Research Unit, Faculty of Health Sciences, Ben-Gurion University of the Negev and [2]Mental Health Center, Beer-Sheva, Israel; [3]Lab of Psychobiology, Department of Psychiatry, The Ruth and Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology and Rambam Health Care Campus, Haifa, Israel

Schizophrenia and bipolar disorder (BPD) are the major mental illnesses within the psychotic spectrum. Their worldwide prevalence is of about 1% each in the adult population. They are accompanied by changes in behavioral, emotional and cognitive impairment which disrupt the course of life of the probands and their families. Patients are treated pharmacologically with a variety of antipsychotics/mood-stabilizers. The choice of the medication for a given patient is by 'trial and error', some patients do not respond and in some - the response is only partial. Therefore, patients and their families undergo long-lasting suffering till relief is achieved, the patients receive unnecessary treatment, and an economic toll is prevailed upon the patient, the family and the society.

The involvement of mitochondrial impairment in schizophrenia and BPD is well established. Similarly, antipsychotic drugs and mood stabilizers have been repeatedly shown to affect a variety of mitochondrial functions, components and morphology.

We aim to find out whether the response of a certain mitochondrial parameters' profile to antipsychotics/mood stabilizers assessed in patients' fresh blood lymphocytes in vitro may predict the optimal drug to treat a given patient (personalized medicine).

Our results of the in vitro effect of six drugs (including typical and a-typical antipsychotics and mood stabilizers) on an array of mitochondrial parameters (related to respiration, autophagy, apoptosis, and mitochondrial network dynamics) of healthy subjects' lymphocytes indicate a different fingerprint of the various drugs. This raises the possibility that responding and non-responding BPD and schizophrenia patients to a given drug will present a different signature, a finding expected to provide both pathophysiological and applicative implication.

27- Identification of the genetic and epigenetic markers of stress susceptibility

Moshe Gross

Ariel University

Background: Failure to adjust to psychological stress is implicated in anxiety and depressive disorders, which are a leading cause of disability. Particularly, gestation is a critical period during which the fetus is highly sensitive to maternal glucocorticoids, whose elevated levels may cause maladaptive epigenetic programming of the Hypothalamus Pituitary Adrenal (HPA) axis *in utero*. To investigate the genetic and epigenetic mechanisms responsible for resilience or vulnerability to stress, we make use of two selectively bred mice strains: Dominant (Dom) and Submissive (Sub) mice, whose behavioral phenotype predicts their respectively adaptive or maladaptive responses to Prenatal Restraint Stress (PRS).

Results: Our molecular and immunohistochemical findings demonstrate that PRS exposure led to elevated hippocampal expression of the Glucocorticoid Receptor (GR) among offspring born to Dom PRS pregnancies, while lowering GR levels of their Sub counterparts. In contrast, the heightened GR immunoreactivity found among Sub PRS mice in the amygdala suggest dimodal, brain region-specific prenatal epigenetic programming of glucocorticoid sensitivity. Investigation of the upstream causal factors of resilience or vulnerability to PRS found highly significant differences in both placental weight between Dom and Sub, as well as inverse changes in placental GR expression among the two strains in response to PRS. Pharmacological validation experiments with the synthetic glucocorticoid dexamethasone revealed severe alterations in serotonin metabolism among glucocorticoid-exposed Sub mice, pointing to a molecular substrate of heightened stress sensitivity.

In order to identify the genetic basis of the adaptive or maladaptive stress response, we conducted Whole Genome Sequencing (WGS) of representative Dom and Sub mice, whose preliminary analysis yielded nearly one million single nucleotide polymorphisms (SNPs) differentiating between strains, which are distributed within approximately 3,000 distinct protein-coding sequences. Subsequent gene ontology analysis using bioinformatic tools identified SNPs in functionally relevant genes interacting directly with the GR, and integrative analysis of transcriptomic microarray data selected 24 genes possessing Glucocorticoid Response Elements (GREs) within their promoters, which were found to be differentially expressed between Dom and Sub mice following mild stress exposure.

Outlook: Candidate genetic variations will be further screened for their conservation between mice and human psychiatric cohorts, followed by their validation to pinpoint the specific polymorphisms responsible for resilience and vulnerability to stress. Such biomarkers will enable the development of clinical tools for the identification of individuals vulnerable to stress, enabling the prevention, diagnosis and possibly for treatment of stress-induced disorders.

28- A novel detection method of metastatic cells in the cerebrospinal fluid of pediatric population with medulloblastoma using fluorescence lifetime imaging microscopy

Sivan Gershanov[1], Helen Toledano[2], Shalom Michowiz[3], Gilad Yahav[4], Orit Barinfeld[5], Avraham Hirshberg[6], Mali Salmon-Divon[1], Dror Fixler[4], Nitza Goldenberg-Cohen[5].

[1]Ariel University, Molecular Biology, Ariel, Israel; [2] Bnai Zion Medical Center, Ophthalmology, Haifa, Israel; [3]Schneider Children's Medical Center of Israel, Pediatric Neurosurgery, Petach Tikva, Israel; [4]Bar Ilan University, Faculty of Engineering and Institute of Nanotechnology and Advanced Materials, Ramat Gan, Israel; [5]Tel Aviv University, The Krieger Eye Research Laboratory- Felsenstein Medical Research Center- Sakcler school of medicine, Tel Aviv, Israel; [6]Tel Aviv University, Oral Pathology and Oral Medicine- Maurice and Gabriela Goldschleger School of Dental Medicine, Tel Aviv, Israel.

In pediatric brain tumors, dissemination of malignant cells within the central nervous system confers poor prognosis and determines treatment intensity, but is often undetectable by imaging or cytology. This study describes the use of fluorescence lifetime imaging microscopy (FLIM), a novel diagnostic tool, for detection of metastatic spread. The study group included 15 children with medulloblastoma and 2 with atypical teratoid/ rhabdoid tumor. Cells extracted from the tumor and the cerebrospinal fluid (CSF) 2 weeks postoperatively and repeatedly during chemo/radiotherapy were subjected to nuclear staining followed by fluorescence lifetime (FLT) measurement and cytological study. Control CSF samples were collected from patients with infectious/ inflammatory disease attending the same hospital. Median FLT was prolonged in tumor cells (4.27±0.28ns; P<2.2*10-16) and CSF metastatic cells obtained before chemo/radiotherapy (6.28±0.22ns; P<2.2*10-16); normal in inflammatory control cells (2.6±0.04ns) and cells from children without metastasis before chemo/ radiotherapy (2.62±0.23ns; P=0.858) and following treatment (2.62±0.21ns; P=0.053); and short in CSF metastatic cells obtained after chemo/radiotherapy (2.40±0.2ns; P<2.2*10-16). FLIM is a simple test that can potentially identify CSF spread of brain tumors. FLT changes in accordance with treatment, with significant prolonged median values in tumors and metastases. More accurate detection of metastatic cells may guide personalized treatment and improve the therapeutic outcome.

29- Early Detection of Preeclampsia Using Circulating Small non-coding RNA

Liron Yoffe, Avital Gilam, Orly Yaron, Argyro Syngelaki, Kypros Nicolaides, Moshe Hod and Noam Shomron

Tel Aviv University

Preeclampsia is one of the most dangerous pregnancy complications, and the leading cause of maternal and perinatal mortality and morbidity. Although the clinical symptoms appear late, its origin is early, and hence detection is feasible already at the first trimester. The lack of an early diagnostic marker prevents an effective early intervention treatment. In the current study, we investigated the abundance of circulating small ncRNAs in the plasma of pregnant women in their first trimester (weeks 11-14), seeking transcripts that best separate the preeclampsia samples from those of healthy pregnant women. To this end, we performed small ncRNAs Next-Generation Sequencing (NGS) of 75 preeclampsia and control samples, and identified 25 transcripts that were significantly differentially expressed between preeclampsia and the control groups. Furthermore, we utilized the differentially expressed transcripts and created a pipeline for a supervised classification of preeclampsia. Our pipeline generates a logistic regression model using a 5-fold cross validation on numerous random partitions into training and blind test sets. Using this classification procedure, we achieved an average AUC value of 0.86. These findings indicate, for the first time, the predictive value of circulating small ncRNAs in the first trimester, and lay the foundation for producing a novel early non-invasive diagnostic tool for preeclampsia, which could serve as an effective intervention, and consequently, reduce the life-threatening risk for both the mother and fetus.

30- Revealing and locating degenerative retinal disease-associated genes in the Israeli population

Shirel Weiss[1,2], Nitza Goldenberg-Cohen[1,4]

(1)The Krieger Eye Research Laboratory, Felsenstein Medical Research Center and (2)Sackler School of Medicine, Tel Aviv University, (3) Ophthalmology department, Bnai Zion Medical Center, Haifa, Israel

Background: As the genes involved in various aspects of blindness are revealed, there is increasing interest in the clinical arena to implement this knowledge in clinical practice and enable genetic treatment.

We offer here to characterize mutation carries in families with retinal dystrophies with the vision of personal medicine in the future.

The aim of this study is to find new point mutations and short indels in known genes as well as new genes involved in retinal degeneration.

Methods: Mutation analysis for retinal degeneration was performed in various methods starting with target capture, and moving forward to next generation sequencing, MLPA and the use of advanced bioinformatic tools.

Results: Recruited were 68 families over the last two years. Analysis was made for 10 families in the first year, and 23 in the second year. Of those, 16 were diagnosed for their mutations. Known mutation in known genes were found in 11/16 families, new mutations in known genes in 5 and analysis of new possible genes are currently under investigation in 19 families. Possible new mutation in known genes (2), and possible new genes involved in retinal degeneration (4)

Conclusion: The clinical-research collaboration and the national project of multi-center study yielded high number of families recruited for this study. In 16 families (30%) mutations were detected and the families were further referred for genetic consultation. Other families are now being analyzed, targeting novel mutations and new genes involved in retinal degeneration, using various advanced methods. The new technologies available may enable breakthrough in the understanding of degenerative retinal disease in the near future.

31- Mutant p53 modulates the signal of hepatocyte growth factor (HGF) to confer cancer cells with drug resistance

Yan Stein, Adi Jacob, Naomi Goldfinger, Ravid Straussman and Varda Rotter

Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel

Drug resistance is a major obstacle in cancer therapy. Recently, a co-cultivation screen identified a major role of the microenvironment in promoting drug resistance in various solid tumors. *TP53*, which encodes the tumor suppressor protein p53, is the most commonly mutated gene in cancer. Mutant p53 is a well-known contributor to drug resistance in cancer. However, its role in the context of tumor-stroma interaction has not been thoroughly studied yet. In this study, we performed a cytokine screen, to identify potential secreted molecules which endow the cancer cells with drug resistance in a mutant p53-dependent manner. We established isogenic lung cancer sub-lines, harboring different mutant p53 levels. After treating these sub-lines with the epithelial growth factor receptor (EGFR) inhibitor gefitinib and a cytokine library, we identified several potential cytokines which confer the mutant p53 expressing sub-line with enhanced resistance compared to mutant p53-knocked down sub-line. Remarkably, the most significant factor endowing drug resistance in a mutant p53-dependent manner was hepatocyte growth factor (HGF), which was previously shown to be a major contributor to innate resistance to RAF inhibitors. We further show that mutant p53 can indeed enhance the signal of both phosphorylated MET and phosphorylated ERK, a downstream effector of the HGF/c-MET pathway. Intriguingly, we further observed increased levels of MET receptor in the media of cells knocked-down for mutant p53, which could account for attenuation of MET "shedding" by mutant p53. In all, we demonstrate a novel mechanism for mutant p53-mediated drug resistance, which is not solely dependent on cell-autonomous factors, but rather on a synergistic effect between mutant p53 and secreted HGF. In a broad sense, we demonstrate here how a cancer cell determinant can manipulate a stromal signal for the tumor's benefit.

32- Cell-Specific Computational Modeling of the PIM Pathway in Acute Myeloid Leukemia

Dana Zilberbosh

Tel Aviv University

Personalized therapy is a major goal of modern oncology, as patient responses vary greatly even within a histologically defined cancer subtype. This is especially true in acute myeloid leukemia (AML), which exhibits striking heterogeneity in molecular segmentation. When calibrated to cell-specific data, executable network models can reveal subtle differences in signaling that help explain differences in drug response. Furthermore, they can suggest drug combinations to increase efficacy and combat acquired resistance. Here, we experimentally tested dynamic proteomic changes and phenotypic responses in diverse AML cell lines treated with pan-PIM kinase inhibitor and fms-related tyrosine kinase 3 (FLT3) inhibitor as single agents and in combination. We constructed cell-specific executable models of the signaling axis, connecting genetic aberrations in FLT3, tyrosine kinase 2 (TYK2), platelet-derived growth factor receptor alpha (PDGFRA), and fibroblast growth factor receptor 1 (FGFR1) to cell proliferation and apoptosis via the PIM and PI3K kinases. The models capture key differences in signaling that later enabled them to accurately predict the unique proteomic changes and phenotypic responses of each cell line. Furthermore, using cell-specific models, we tailored combination therapies to individual cell lines and successfully validated their efficacy experimentally. Specifically, we showed that cells mildly responsive to PIM inhibition exhibited increased sensitivity in combination with PIK3CA inhibition. We also used the model to infer the origin of PIM resistance engineered through prolonged drug treatment of MOLM16 cell lines and successfully validated experimentally our prediction that this resistance can be overcome with AKT1/2 inhibition.

33- Human genetics is not the major determinant of gut microbiota composition

Daphna Rothschild*, Omer Weissbrod*, Elad Barkan, Adina Weinberger, Tali Avnit-Sagi, Maya Lotan-Pompan, Noa Kosower, Eran Segal

****Co-authors***

The gut microbiome is associated with many human health parameters, and few bacterial taxa were recently found to be heritable. However, the overall association between the genome and microbiome composition has not been previously explored. We genotyped a cohort of 696 healthy Israeli individuals with a diverse genetic background and a relatively common environment, and demonstrate that there is no statistically significant association between the microbiome and genetic ancestry, single nucleotide polymorphisms (SNPs), or the entire genome. We define the term "biome-effect" to quantify the overall association between the microbiome and phenotypes after accounting for genetic effects, and find significant biome-effect levels for body mass index (BMI), blood glucose levels, high-density lipoprotein (HDL) cholesterol levels and waist circumference. We further demonstrate that the combination of host genetics and the microbiome substantially improves prediction power for these phenotypes, compared to models that utilize only host genetics or the microbiome. Our results indicate that the microbiome composition is dominantly shaped by environmental factors rather than host genetics, and that both factors are independently associated with many phenotypes of interest.

34- Amyloidogenic Properties Of SAA Associated With Systemic Amyloidosis And Its Inhibition As A Therapeutic Strategy

Esraa Haj, Ehud Gazit and Daniel Segal

Department of Molecular Microbiology and Biotechnology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel, 69978

Amyloid A (AA) amyloidosis is a complication of chronic inflammatory conditions. The causative aggregation-prone protein, serum amyloid A (SAA) is produced in the liver and accumulates predominantly in the spleen, kidney and liver. SAA is an apolipoprotein, implicated in cholesterol transport and HDL metabolism, yet its precise function in normal physiology remains unclear. In response to inflammatory cytokines SAA concentration in the serum can be elevated up to 1000 times. It becomes clinically overt mainly when renal damage occurs, manifesting either as proteinuria, nephrotic syndrome, or derangement in renal function. No disease-modifying therapy for AA amyloidosis exists. Current treatments focus on the underlying inflammatory disease by using anti-cytokines and anti-TNF.

Various strategies are currently being assessed for preventing the formation of amyloid fibrils and oligomers. One therapeutic strategy involves the use of small aromatic molecules to inhibit assembly of amyloidogenic proteins. Thus, we are assessing the capability of small molecules, available in our lab, to inhibit the aggregation of SAA.

Furthermore, we are interested in gaining insights regarding structural determinants and residues necessary for the self-assembly of SAA into toxic amyloids using a rationally designed peptide microarray. In applying this approach we designed overlapping peptide library and substitution peptide library . Currently we are calibrating the system to be able to incubate the soluble SAA with the peptides printed on the microarray to track the regions within SAA capable of self-assembly.This work should yield important insights into key molecular events leading to AA amyloidosis and may provide lead compounds for its treatment.

35- Study the roles of Rad18 ubiquitin Ligase in DNA replication and repair

Muhammad Natour and Amir Aharoni

Life science, Ben Gurion University of the Negev

Ubiquitination is an important eukaryotic mechanism of protein regulation. The process of ubiquitination involves conjugating an ubiquitin moiety to a target protein via the activity of three different types of enzymes; E1, E2 and E3. E1 activates the ubiquitin moiety and E2 transfers the activated ubiquitn to the target protein via E3 ubiquitn ligase. E3-ubiquitn ligases must interact with the target proteins to enable ubiquitin conjugation. Rad18 is an E3-ubiquitin ligase involved in the monoubiquitination of PCNA as a response to DNA damage during replication, which promotes the replacement of the normal replicative polymerases by Y- family Translession synthesis (TLS) polymerases. It is well known that Rad18 interacts with several proteins, but PCNA is its only known ubiquitination target. We have used a genome-wide PCA screen to reveal novel Rad18 interacting proteins and we will examine whether these proteins are also Rad18 ubiquitination targets by using biochemical assays. Once novel ubiquitination targets are identified, we aim to study the functional implications of Rad18-dependent ubiquitination on these proteins.

36- Metals as dual-function matrices for sustained release of drugs

Barak Menagen[(a)], Rami Pedahzur[(b)] and David Avnir[(a)]

[(a)] Institute of Chemistry and the Center for Nanoscience and Nanotechnology, the Hebrew University of Jerusalem, and [(b)] Department of Environmental Quality , Hadassah Academic College, Jerusalem

Sustained release of drugs is a major, well developed field of biomaterials; hundreds of drug-holding matrices are known. The main families of materials used for that purpose have been organic matrices such as polymers and inorganic matrices such as SiO_2, ZnO and TiO_2. It comes as a surprise that the third major family of materials – elemental metals – has not been used as a 3D drug releasing matrix. In our research we have developed methods for the entrapment of various drugs and bioactive compounds within silver and platinum. Generally, the entrapment process involves a carefully developed procedure for reducing the metal cation in the presence of the dissolved drug, which results in the entrapment of the drug inside the bulk of aggregated metal.

The motivation to entrap bioactive materials within silver has been to create dual-functional composites for wound treatment, that is, control of microbial contamination, emanating from the antimicrobial activity of silver, and providing at the same time pain relief capabilities due to the entrapped pain killers. We focused on three main groups of analgesics which are used topically to reduce pain: The non-steroidal anti-inflammatory drugs (NSAID), the opioids, and the local anesthetic (LA) drugs. We have successfully entrapped ibuprofen and naproxen (two NSAIDs), tramadol (an opioid) and bupivacaine (an LA) within silver, resulting in drug@Ag composites. Upon exposure of the resulting composites to water, controlled release of the drugs from the composite occurs while silver ions are released from the bulk metal and create an antiseptic activity, the efficacy of which was proven against *Pseudomonas aeruginosa*.

Platinum was selected as an additional matrix mainly due to its low toxicity towards mammalian cells, which promotes its wide use for a variety of implant applications. The new composites therefore can be used as a matrix for sustained release of drugs needed after implantation, such as for post-operative infection control, for pain management and for anticoagulation activity. Successful entrapments of two types of NSAID's - ibuprofen and naproxen, of an antibacterial agent – chlorohexidine, and of antibiotics - were achieved.

37- The tumor secretome – a new avenue in personalized cancer therapy

Oded Sendler

Weizmann Institute of Science

Recent advances in cancer research and DNA sequencing enable, more than ever before, better tailoring of treatment according to the tumor specific genetic makeup. However, the observed response is far from being complete due to immediate, innate resistance. Unlike acquired resistance, innate resistance is mainly due to non-genetic mechanisms such as secreted factors in the tumor microenvironment (TME) – the tumor secretome.

We hypothesize that in order to optimize patient-specific anti-cancer treatment, the tumor-specific secretome should be taken into account. Specifically, we suggest novel combination treatments that target the cancer cells as well as TME-specific secreted factors that can modulate the response to the anti-cancer drugs. To uncover resistance-related TME factors, we first profiled the effect of 321 secreted factors on the resistance of 60 cancer cell lines towards 30 commonly used anti-cancer drugs. Twenty factors were found to potentially confer drug resistance in specific cancer types. Moreover, we demonstrated that the expression level of these factors in the TME greatly vary between patients, making the case for patient's TME specific treatments. Next, we demonstrated the advantage of TME-based combinatorial treatments in both *in vitro* cancer-stroma co-culture systems, as well as in mice xenograft *ex vivo* tumors from multiple tissue types. Our findings, thus, indicate that targeting TME secreted factors, in combination with anti-cancer drugs, is necessary for optimizing cancer therapy.

38- Molecular approaches for enhancing lipid biosynthesis in microalgae

Moran Topf, Yael Kinel-Tahan, Yaron Yehoshua, Zvy Dubinsky, and Orit Shaul

The Mina and Everard Goodman Faculty of Life Sciences, Bar Ilan University, Ramat Gan, Israel

With the depletion of fossil fuel reserves and the harmful environmental consequences of their utilization, biofuels have become one of the most promising renewable energy sources. Algae can be an ideal source of biofuels. These photosynthetic organisms use solar energy, water, and CO_2 to reproduce and build storage molecules such as carbohydrates and lipids. Microalgae have high photosynthetic yield and rapid growth rate. Their CO_2 fixation rate and lipid production per unit area are 1-2 orders of magnitude higher then those of terrestrial plants. However, currently the production of algal biofuel is still not economically competitive with fossil fuels.

To deal with the problem, we chose to explore molecular mechanisms to control and enhance lipid biosynthesis in microalgal cells. We are testing the potential of novel approaches for increasing triacylglycerol (TAG) content in microalgae and modify their TAG composition. We found a specific promoter, translational enhancer, selectable marker, and stable transformation method suitable our selected microalga, the oleaginous microalga *Chlorella vulgaris* (*C. vulgaris*). We are overexpressing in *C. vulgaris* key enzymes of the TAG biosynthesis pathway. We will determine the impact of these modifications on the growth rate and TAG content of the microalgae. We will also determine the impact on fatty acid profile and lipid chemical and physical properties.

39- Hybrid Bio-Photo-Electro-Chemical Cells for Solar Water Splitting

Dan Kallmann

Technion-Israel Institute of Technology

Photoelectrochemical water splitting uses solar power to decompose water to hydrogen and oxygen. Here we show how the photocatalytic activity of thylakoid membranes leads to overall water splitting in a bio-photo-electro-chemical (BPEC) cell via a simple process. Thylakoids extracted from spinach are introduced into a BPEC cell containing buffer solution with ferricyanide. Upon solar-simulated illumination, water oxidation takes place and electrons are shuttled by the ferri/ferrocyanide redox couple from the thylakoids to a transparent electrode serving as the anode, yielding a photocurrent density of 0.5 mA cm^{-2}. Hydrogen evolution occurs at the cathode at a bias as low as 0.8 V. A tandem cell comprising the BPEC cell and a Si photovoltaic module achieves overall water splitting with solar to hydrogen efficiency of 0.3%. These results demonstrate the promise of combining natural photosynthetic membranes and man-made photovoltaic cells in order to convert solar power into hydrogen fuel.

40- Cryogenic-Temperature Electron Microscopy Imaging of Extracellular Vesicles Shedding

Na'ama Koifman, Idan Biran, Anat Aharon, Benjamin Brenner, Yeshayahu Talmon

Technion-Israel Institute of Technology

Cryogenic scanning electron microscopy (cryo-SEM) is a unique imaging technique, by which cells can be imaged at a high resolution avoiding the addition of fixatives or contrast agents. Cryo-SEM is highly advantageous for imaging shedding cell membranes, which remain unaltered during specimen preparation, thus generating a more accurate and reliable morphological analysis. Moreover, cryogenic temperature electron microscopy is still not widely used for the study of EVs, although it is optimal for the investigation of those systems.

The human leukemia monocytic cell line (THP1) is known to shed EVs under various stimulations. We study the effect of stimulation by exposure to the endotoxin lipopolysaccharide (LPS) or by starvation on THP1.

Unstimulated and stimulated cells were thermally fixed by high-pressure freezing, and imaged by cryo-SEM. EVs isolated from unstimulated and stimulated cells were imaged by cryogenic transmission electron microscopy (cryo-TEM). We also characterized the isolated EVs by nanoparticle tracking analysis (NTA).

Cryo-SEM images show blebbing of cells stimulated by LPS, which is in good agreement with previously suggested models. Micrographs show extensive membrane blebbing, as round, vesicular invaginations. Cells that underwent a 48-hour starvation stimulation exhibited a different morphology, including elongated membrane protrusions and shrunken membrane and nucleus. EV morphologies were shown to be highly heterogenous in size and nanostructure. EVs isolated from cells undergoing starvation were fewer and larger than EVs isolated from LPS-stimulated cells.

Cryo-SEM provides a high magnification view of cells undergoing shedding, revealing the size and morphology of the EVs prior to their release from the cell. Cryo-TEM of the isolated EVs complemented by NTA provides a statistical and morphological characterization of the EVs after their release. Although both starvation and endotoxin-exposure are common stimulations types, they most probably lead to a different cellular response, resulting in differences in size and concentration of the isolated EVs.

41- A longitudinal study of multiple sclerosis using quantitative MRI

Berman S.[1], Petrou P.[2], Kassis I.[2], Raz N.[2], Ben-Hur T[2], Levin N[2]., Karussis D.[2], Mezer A. [1]

[1]*Edmond and Lily Safra Center for Brain Science, The Hebrew University of Jerusalem.*
[2]*Neurology Department, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.*

The brain's white matter tissue consists of myelinated axons and glial cells, and occupies almost half of the brain's volume (Fields, 2008). The axons form fibers that connect cortical regions which form networks necessary for cognitive functions (Moeller, Willmes & Klein, 2015), normal development and aging (Nagy, Westerberg & Klingberg, 2004; Yeatman, Wandell & Mezer, 2014). When the white matter is damaged, the outcome could be destructive (Fields, 2008; Compston & Coles, 2008). Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system, in which myelin is attacked, changing white-matter structure and leaving lesions (scars, sclerosis). Magnetic resonance imaging (MRI) is the most sensitive technique for detecting multiple sclerosis lesions and quantifying their evolution over time. Yet, the variability in the clinical presentation of MS may still result in misdiagnosis, unnecessary referrals and misleading information to the patient, and more quantitative measurements are necessary.

Ongoing developments in quantitative MRI (qMRI) provide in vivo measurements of the white matter microstructure, and physical quantities. Thus, unlike the 'picture-like' images that are produced with anatomical - weighted MRI that are often used in the clinic, qMRI generates brain maps that describe the tissue properties as well as the instrumental biases (Alexander et al., 2011). qMRI therefore enables meaningful measurements between brain regions, between individuals and across time and sites.

In this study, we use data from ongoing stem-cell therapy clinical trials, of primary progressive MS patients. The trials, which began on December 2015, and are expected to be completed by December 2017, are held under the supervision of Prof. Karussis, Head of Hadassah's MS center. For the current study, we analyze the data of 20 subjects, each with at least two separate MRI scans, taken several months apart. The MRI protocols are designed to evaluate changes in the total volume of lesions in the brain and the degree of atrophy. In addition, quantitative data is acquired, specifically diffusion MRI, which enables tracking the white-matter fibers, and anatomical scans from which we map several qMRI parameters (i.e. T1, the longitudinal relaxation time, and proton density). I evaluate the qMRI parameters within and outside of white matter lesions, over the different scans, and with comparison to behavioral parameters assessed by neurologists.

Such unique data from well-controlled clinical trials (in terms of drug treatment and patient selection), including scans at multiple time points, will be fundamental to our efforts to apply and test our technologies in real, ongoing clinical research. This will enable us,to test our ability to track dynamical white matter changes in progressive MS patients, and to quantify therapeutic outcomes.

42- The effect of nuclear structural proteins on chromatin dynamics measured by advanced live imaging methods

Anat Vivante, Irena Bronshtein, and Yuval Garini

Physics Department & Nanotechnology Institute, Bar Ilan University, Ramat Gan, Israel

In eukaryotic cells, tens of thousands of genes are packed in the small volume of the nucleus. The genome itself is organized in chromosomes that occupy specific volumes referred to as chromosome territories. This organization is preserved throughout the cell cycle, even though there are no sub-compartments in the nucleus itself. This organization, which is still not fully understood, is crucial for a large number of cellular functions such as gene regulation, DNA breakage repair and error-free cell division.

The nuclear structure is strongly related to the dynamic properties. Hence, the dynamics of the nucleus content is fundamental for understanding its appropriate function. Understanding the mechanisms that are responsible for maintaining chromosomes within their territories and the role of specific proteins is extremely important.

We use live imaging methods to characterize the dynamic properties of the chromatin and its organization in living cells. More specifically, we use single particle tracking of different genomic regions, and implement Continuous Photobleaching (CP) measurements which provide crucial information on the mobility and binding properties of the proteins.

Through these methods, we analyze the effect of specific nuclear proteins on chromatin dynamics. Finally, we suggest a model of chromatin organization and develop a new type of diagram for mapping and analyzing the regulating networks of chromatin organization.

43- RNAi delivery utilizing quaternized starch based complexes *in vitro* and *in vivo*

Elise Lewis

Ben-Gurion University of the Negev

RNAi therapeutics is a powerful tool for treating gene-causing diseases such as cancer, by utilizing sequence-specific siRNA for gene regulation. Currently, siRNA is examined in a variety of clinical trials and found efficient; however there is still a lack of a delivery platform to target it to the site of interest in the patient's body. Our goal is to establish and characterize a delivery platform, combining efficiency and safety issues. This study focuses on natural polysaccharide, starch, as a delivery carrier due to its biodegradability and biocompatibility, therefore attractive candidate for safe drug delivery. We demonstrated that quaternized starch (Q-starch) undergoes self-assembly formation of Q-starch/siRNA complexes at N/P ratio 2 (molar ratio of polymer amine groups to nucleic acid phosphate groups) and presented efficient gene silencing *in vitro* in ovarian adenocarcinoma cancer cells. In this study, we present our most significant findings in *in vitro* cell model and in *in vivo* mouse model bearing tumors. We explore the complexes' cellular delivery pathway *in vitro* and elucidated the rate limiting step at the cellular level using light-microscopy and biophysical approaches. In addition, we investigated the biodistribution of the complexes and found that siRNA loading by Q-starch is beneficial by means of reducing the clearance of siRNA from the body (increasing the circulatory half-life) and inducing tumor uptake. Interestingly we find that the complexes show high and significant accumulation of siRNA at the lungs which might indicate the application of these complexes for lung malignancies.

44- Horizontal Transfer of the *Salmonella* Infantis Resistance-Virulence

Plasmid pESI to the Gut Microbiota of Warm-Blooded Hosts

Gili Aviv [1, 2,3], Galia Rahav [1, 3], and Ohad Gal-Mor [1, 2,3]

[1]The Infectious Diseases Research Laboratory, Sheba Medical Center, Tel-Hashomer, Israel;
[2]Department of clinical microbiology and immunology, [3]Sackler Faculty of Medicine, Tel Aviv University, Israel

Salmonella enterica serovar Infantis is one of the prevalent salmonellae worldwide. Recently, we showed that the emergence of *S.* Infantis in Israel was facilitated by the acquisition of a unique megaplasmid (pESI) conferring multidrug resistance and increased virulence phenotypes. Here we elucidate the ecology, transmission properties, and regulation of pESI. We show that despite its large size (~280 kb), pESI does not impose a significant metabolic burden *in vitro* and that it has been recently fixed in the domestic *S.* Infantis population. pESI conjugation and the transcription of its pilus (*pil*) genes are inhibited at the ambient temperature (27°C) and by>1% bile but increased under temperatures of 37 to 41°C, oxidative stress, moderate osmolarity, and the microaerobic conditions characterizing the intestinal environment of warm-blooded animals. The pESI encoded protein TraB and the oxygen homeostasis regulator Fnr were identified as transcriptional regulators of pESI conjugation. Using the mouse model, we show that following *S.* Infantis infection, pESI can be horizontally transferred to the gut microbiota, including to commensal *Escherichia coli* strains. Possible transfer, but not persistence, of pESI was also observed into Gram-positive mouse microbiota species, especially *Lactobacillus reuteri*. Moreover, pESI was demonstrated to further disseminate from gut microbiota to *S. enterica* serovar Typhimurium, in the context of gastrointestinal infection. These findings exhibit the ability of a selfish clinically relevant megaplasmid to distribute to and from the microbiota and suggest an overlooked role of the microbiota as a reservoir of mobile genetic elements and intermediator in the spread of resistance and virulence genes between commensals and pathogenic bacteria.

45- Complex I impairments in schizophrenia; a complex story

O. Bergman[1], R. Karry[1], J. Milhem[1], D. Ben-Shachar[1].

[1]Rambam Medical Center Department of Psychiatry and the B. Rappaport Faculty of Medicine- Technion, Laboratory of Psychobiology, Haifa, Israel.

Background: Mitochondrial respiratory chain impairments including complex I (CoI) have been observed in mental disorders including schizophrenia (SZ). Abnormal assembly of CoI 44 subunits into the holoenzyme has been reported in patients with CoI deficiencies, often associated with encephalopathies and psychotic symptoms. Our group has previously shown alterations in the mRNA and protein level of CoI nuclear encoded subunits NDUFV1, NDUFV2 and NDUFS1 both in the brain and periphery of SZ patients. Interestingly these labile subunits (i.e newly imported subunits interchange existing ones in the holo-complex), are probably located at the interaction site with dopamine (DA). Given these findings, we hypothesize that defects in holo-CoI assembly can play a crucial role in mitochondrial dysfunctions observed in SZ.

Methods: Epstein-Barr virus transformed lymphocytes from SZ patients (n=9) and healthy subjects (n=9) were used. Cell lines were assessed for respiration through different respiratory chain complexes. Subsequently, mitochondria were isolated, purified on a percol gradient and solubilized with digitonin. Samples were studied for CoI protein level and in-gel CoI enzymatic activity by BN- and CN-PAGE. CoI synthesis rate was assessed by ^{35}S-methionine pulse-chase with cyclohexamide. Mitochondrial import of ^{35}S-methionine-NDUFV2 following its in-vitro transcription/translation was studied. mRNA poly(A) tail-length distribution of NDUFV2 and NDUFA9 (non-labile subunit) was examined by the Affimetrix poly-A assay kit. Finally, mitochondrial NDUFV2, NDUFV1and NDUFS1 protein folding was analyzed by the CHAPS increased concentrations assay.

Results: A significant reduction (23±0.46%, P<0.001) in CoI-driven respiration rates and a higher inhibition by DA (24%±8.7 vs. 12.5%5.4, P<0.001) were observed in SZ-derived cell lines compared to controls. No change was observed in complexes II- and III-driven respiration. Similar to our previous findings in mitochondrial homogenates, CoI in-gel activity was significantly decreased in patients (25.1±1.4 vs. 18±1.4 OD/mg protein/hr, P=0.008) with no change in its levels. Immunoblotting of specific subunits in the holoenzyme showed no change in their protein levels. However, the coefficient of variance of the labile subunits, but not of the other subunits, was significantly lower in patients, suggesting less flexibility. Synthesis rates of CoI was also significantly lower in patients (0.8±0.1 vs. 2.3±0.6, P=0.01). Import of patient-derived NDUFV2 protein into healthy mitochondria was significantly lower than that of control NDUFV2. Concurrently, import of both patient and control proteins into SZ-derived mitochondria was lower than into healthy mitochondria, yet import of patient NDUFV2 was lower than that of control. These results suggest both protein and mitochondria contribute to the impaired import in patients. Analysis of NDUFV2, but not of NDUFA9, mRNA from SZ patients showed altered poly-A tail length distribution, potentially affecting its metabolism and stability. Finally, our data show that mitochondrial NDUFV2 protein folding, but not that of NDUFV1 and NDUFS1, is altered in patients.

Conclusion: These results support impaired import and assembly of CoI labile subunits, specifically NDUFV2, associated with reduced mRNA and protein levels of several subunits, CoI activity and mitochondrial respiration. Our findings can potentially contribute to the understanding of mitochondrial dysfunction in SZ and suggests CoI, or individual subunits, as a novel target for intervention in SZ.

46- Tumor suppressor crosstalk: Hippo and p53

Noa Furth[1], Noa Bossel[2], Yael Aylon[1], Eytan Domany[2] and Moshe Oren[1]

[1]Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot 76100, Israel
[2]Department of Physics of Complex Systems, Weizmann Institute of Science, Rehovot 76100, Israel

Introduction: Proper cellular response to internal and environmental challenges requires profound interactions between components of different signaling pathways. Specifically, deregulation of the wiring between different tumor suppressor pathways may lead to neoplastic transformation or enable tumor progression and metastasis. The Hippo signaling pathway represses the activity of two transcriptional co-activators, YAP and TAZ; both of which can promote various features of tumorigenic transformation. The p53 pathway is a well-studied signaling pathway that can induce a variety of changes in cell fate, most notably induction of cell cycle arrest and apoptosis. Lately, also pro-survival effects of p53 are being increasingly appreciated. Previous studies from our lab demonstrated multiple interactions between the Hippo kinase LATS2 and p53 in response to different types of stress as well as in stem cell differentiation.

Results and Discussion: Using mass spectrometry combined with global transcriptome analysis, we recently found that silencing of the Hippo pathway tumor suppressor kinases LATS1 and LATS2 (=LATS) in non-transformed mammary epithelial cells (MCF10A) alters p53 toward a state resembling cancer-associated p53 mutants and endows it with an ability to promote cell migration. This coincides with reduced p53 phosphorylation and increased association with the p52 NF-κB subunit. Moreover, we also provide evidence that upon silencing of LATS, p53 augments the activity of the Hippo effectors YAP and TAZ, suggesting an additional p53-mediated mechanism by which LATS restrict YAP/TAZ activity. Notably, LATS kinases are frequently downregulated in various types of cancer. This, may elicit broader signaling alterations than appreciated till now, extending beyond the canonical Hippo pathway and involving also p53.

Conclusions: Our findings suggest that such oncogenic alterations may convert p53 into a state that bears functional resemblance to classical cancer-associated mutant p53. This reduces the pressure to mutate the *TP53* gene and allows some tumors retain a genetically wild type p53 gene.

47- Clock control by polyamine levels through a mechanism that declines with age

Ziv Zwighaft

Weizmann Institute of Science

Polyamines are essential polycations present in all living cells. Polyamine levels are maintained from the diet and de-novo synthesis, and their decline with age is associated with various pathologies. Here we found that polyamine levels oscillate in a daily manner. Both clock- and feeding-dependent mechanisms regulate the daily accumulation of key enzymes in polyamine biosynthesis through rhythmic binding of BMAL1:CLOCK to conserved DNA elements. In turn, polyamines control the circadian period in cultured cells and animals by regulating the interaction between the core clock repressors PER2 and CRY1. Importantly, we show that the decline in polyamine levels with age in mice is associated with a longer circadian period that can be reversed upon polyamine supplementation in the diet. Our findings suggest a cross talk between circadian clocks and polyamines biosynthesis that participate in circadian control, and open new possibilities for nutritional interventions against the decay in clock's function with age.

Highlights

*Diurnal regulation of polyamine biosynthesis by circadian clock and feeding.

*Polyamine levels regulate the circadian period in cultured cells and mice.

*Polyamines modulate the interaction between the core clock proteins PER2 and CRY1.

*Lengthening of the circadian period with age can be reversed by polyamines.

48- Biologically controlled morphology and twinning in guanine crystals

Anna Hirsch, Ben Palmer, Nadav Elad, Dvir Gur, Lia Addadi, Leslie Leiserowitz, and Leeor Kronik

Weizmann Institute of Science

Guanine crystals are widely used in nature as components of multilayer reflectors. Organisms control the size, morphology, and arrangement of these crystals, to obtain a variety of optical "devices" [1]. The reflection systems found in the lens of the scallop eye and in the copepod cuticle are unique in that the multilayered reflectors are tiled together to form a contiguous packed array. In the former, square crystals are tiled to form a reflecting mirror. In the latter, hexagonal crystals are closely packed to produce brilliant colors. Based on electron diffraction, morphology considerations, and density functional theory, these crystals were shown to possess similar monoclinic crystal symmetry, which we have previously identified as different from that of synthetic anhydrous guanine [2]. However, the crystals are different in that multiple twinning about the {012} and the {011} crystallographic planes results in square and hexagonal morphology, respectively. This is a unique example where controlled twinning is used as a strategy to form a morphology with higher symmetry than that of the underlying crystal, allowing for tilling that facilitates optical functionality.

[1] Gur et al., Adv. Mat. (2016)
[2] Hirsch et al., Chem. Mat. 27, 8289 (2015)

49- Characterization of Cholesterol Crystal nucleation and Growth from Biological Membranes in Macrophage Foam Cells

Neta Varsano[a], Tali Dadosh[b], Sergey Kapishnikov[d], Eva Pereiro[e], Eyal Shimoni [b], Xueting Jinf, Howard S. Kruth[f], Leslie Leiserowitz[c] and Lia Addadi[a]*

(a) Department of Structural Biology, (b) Department of Chemical Research Support, (c) Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot, Israel. (d) Soft Matter and Functional Materials, Helmholtz Zentrum Berlin, Germany (e) ALBA Synchrotron Light Source, MISTRAL Beamline– Experiments Division, Barcelona, Spain (f) Experimental Atherosclerosis Section, National Institutes of Health, Bethesda, Maryland

Atherosclerosis, the major precursor of cardiovascular disease, is characterized by the deposition of excessive cholesterol in the arterial intima.[1] Atherosclerotic plaques build up in arteries in a slow process that initiates with uptake of LDL particles by macrophage cells, leading to deposition of cholesterol monohydrate crystals and cell death.[1] Precipitation of cholesterol crystals is a crucial part of the pathological progression.[2]

We suggested that the initial step in atherosclerosis development may be from cholesterol domains segregating in cell membranes and serving as nucleation sites for the formation of 3-dimensional (3D) cholesterol crystals.[3,4] To verify whether this process can be relevant to in vivo processes, we have developed a high resolution correlative method combining cryo-soft X-ray tomography (cryo-SXT) and stochastic optical reconstruction microscopy (STORM)).[5] The approach provides 3D information on large cellular volumes at 70 nm resolution.[5] Cryo-SXT morphologically identifies and localizes aggregations of carbon-rich materials, while STORM identifies specific markers on the desired epitopes, enabling colocalization between the identified objects and the cellular environment. Using a specific antibody (MAB 58B1) which labels cholesterol crystals,[6] we identify and image crystals at a very early stage (200-400 nm) on the cell plasma membrane and in intracellular locations. This technique can in principle be applied to other biological samples where specific molecular identification is required in conjunction with high resolution 3D-imaging.

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50- The SND proteins constitute an alternative targeting route to the endoplasmic reticulum

Naama Aviram, Tslil Ast, Elizabeth A. costa, Eric c. Arakel, Silvia G. chuartzman, Calvin H. Jan, Sarah Haßdenteufel, Johanna dudek, Martin Jung, Stefan Schorr, Richard Zimmermann, Blanche Schwappach, Jonathan S. Weissman & Maya Schuldiner

In eukaryotes, up to one-third of cellular proteins are targeted to the endoplasmic reticulum, where they undergo folding, processing, sorting and trafficking to subsequent endomembrane compartments. Targeting to the endoplasmic reticulum has been shown to occur co-translationally by the signal recognition particle (SRP) pathway or post-translationally by the mammalian transmembrane recognition complex of 40 kDa (TRC40) and homologous yeast guided entry of tail-anchored proteins (GET) pathways. Despite the range of proteins that can be catered for by these two pathways, many proteins are still known to be independent of both SRP and GET, so there seems to be a critical need for an additional dedicated pathway for endoplasmic reticulum relay. We set out to uncover additional targeting proteins using unbiased high-content screening approaches. To this end, we performed a systematic visual screen using the yeast *Saccharomyces cerevisiae*, and uncovered three uncharacterized proteins whose loss affected targeting. We suggest that these proteins work together and demonstrate that they function in parallel with SRP and GET to target a broad range of substrates to the endoplasmic reticulum. The three proteins, which we name Snd1, Snd2 and Snd3 (for SRP-independent targeting), can synthetically compensate for the loss of both the SRP and GET pathways, and act as a backup targeting system. This explains why it has previously been difficult to demonstrate complete loss of targeting for some substrates. Our discovery thus puts in place an essential piece of the endoplasmic reticulum targeting puzzle, highlighting how the targeting apparatus of the eukaryotic cell is robust, interlinked and flexible.

51- Local Communication Circuits Of Colonic Macrophages

B. Bernshtein, M. Gross, C. Curato1, E. David and S. Jung

Weizmann Institute of Science, Department of immunology

Intestinal macrophages reside in the connective tissue underlying the gut epithelium, which separates them from the diverse microbiota populating the gut lumen. This complex and dynamic environment necessitates intimate and precise inter-cellular communication. Unlike other tissue macrophages, gut macrophages are constantly replenished from monocytes, most likely recruited by tonic low-grade inflammatory stimuli.

We established a murine colitis model based on a macrophage-restricted Interleukin 10 receptor (IL10R) deficiency. IL10R-deficient gut macrophages are pro-inflammatory, causing severe colitis that resembles the pathology of children carrying IL10R mutations.

To investigate how macrophage dysregulation affects the epithelium, we performed RNAseq of small and large intestinal epithelial cells of mice harboring mutant macrophages. Colonic epithelial cells readily respond to pro-inflammatory macrophages by up-regulation of anti-microbial peptide secretion. Moreover, we established that the microbiota plays a pivotal role in initiation of the inflammatory process in our mice, since antibiotics treatment rescues the animals from colitis.

To further dissect the specific communication modules between macrophages and epithelial cells, we take advantage of a combined cell ablation and reconstitution strategy developed in our lab that allows us to seed intestinal tissue with macrophages of distinct genotype. Engraftment of mice ablated of mononuclear phagocytes with IL10R-deficient and sufficient monocytes, enables us to monitor monocyte differentiation and their interactions with their close environment.

52-The Effect of Antimicrobial Peptides on Biofilm Formation and Degradation

Li-av Segev-Zarko[1], Ron Saar-Dover[1], Vlad Brumfeld[2], Maria Luisa Mangoni[3] and Yechiel Shai[1]

[1]Department of Biological Chemistry, [2]Department of Chemical Research Support, Weizmann Institute of Science Rehovot, 76100 Israel, [3]Department of Biochemical Sciences, La Sapienza University, Via degli Apuli, 9-00185 Rome, Italy.

The increasing number of multidrug resistant bacteria to available antibiotics is a growing problem worldwide. One major strategy for resistance and an important reason for failure of therapy in the clinic is biofilm formation. To cope with unfavorable surroundings many bacteria live as biofilms, sessile micro-colonies adherent to surfaces that secrete an extracellular polymeric substance. An attractive alternative to conventional antibiotics are antimicrobial peptides (AMPs), innate immune system molecules. By designing and synthesizing a series of model peptides that share the same amino acids composition but differ in their biophysical properties, we investigated how different steps of biofilm formation are affected by the AMP's properties. We used Pseudomonas aeruginosa, an opportunistic Gram-negative bacteria, which is a leading cause of severe pulmonary infections in cystic fibrosis patients and medical device contamination. Our work demonstrates that the peptides combat biofilm at different stages of its formation and maintenance: (1) killing bacteria at their planktonic stage (2) preventing bacterial adhesion to biomaterials and (3) degrading pre-formed biofilm. Specifically, we showed that treatment with bactericidal peptides at non-inhibitory concentrations resulted in decreased bacterial attachment to polystyrene and reduced biofilm growth. In addition, degradation of established biofilms by bactericidal and non- bactericidal peptides occurs either by killing of embedded bacteria or detachment of live ones. Finally, as a general trend, substitution of L-to-D amino acids improves the peptide's activity against each stage in the biofilm life cycle. We suggest that reduced bacterial adhesion to surfaces and decreased biofilm growth is due to the peptide's ability to coat either the biomaterial surface or the bacteria itself. Our work sheds light on the mechanism of biofilm inhibition and degradation and how the bacteria responds to its changing environment.

53-Autism-associated changes in the representation of social information in prefrontal circuits

Dana Rubi Levy, Tal Tamir, Maya Kaufman, Aharon Weissbrod, Elad Schneidman and Ofer Yizhar

Weizmann Institute of Science

Deficits in social behavior are among the primary symptoms of autism spectrum disorder (ASD). Although little is known regarding the circuit alterations that might give rise to this complex phenotype, evidence from both human patients and animal models suggests that dysfunctions of the prefrontal cortex (PFC) might play a dominant role in ASD pathophysiology. However, a major gap still exists in understanding the role of this region in social processing. More specifically, it is unclear how the PFC encodes social information, and how changes in these representations might correlate with impaired behavioral response. To address these questions, we utilized a custom-built behavioral apparatus and recorded unit activity in the ventromedial PFC of behaving male mice presented with precisely-timed social and non-social odor cues. We found distinct representation for social stimuli in the vmPFC, such that a large proportion of recorded units (40%) responded exclusively to male or female odors over a repertoire of non-social cues. Cue-responsive units also showed greater response magnitude to social odors than to non-social stimuli. In Caspr2 knockout mice, a well established genetic model of autism, these patterns were significantly altered, such that vmPFC units showed decreased specificity to social odors as well as blunted stimulus-evoked response dynamics. Taken together, our results identify specific representations for salient social stimuli in the mouse vmPFC and indicate altered processing of social information in a genetic model of autism.

54- A Mechanistic Link between Olfaction and Autism Spectrum Disorder

Liron Rozenkrantz[1], Ditza Zachor[2], Iris Heller[1], Anton Plotkin[1], Aharon Weissbrod[1], Kobi Snitz[1], Lavi Secundo[1] and Noam Sobel[1]

[1]Weizmann Institute of Science, Department of Neurobiology, Rehovot, Israel
[2]Asaf Harofeh Medical Center, Autism Center, Zerifin, Israel

A single mechanism underlying the diverse impairments in autism remains unidentified. An emerging theory suggests that internal action models (IAMs), brain templates for sensory-motor coordination, are a common theme in autism spectrum disorder (ASD). However, whether impaired IAMs occur across sensory systems and how they relate to the major phenotype of ASD, namely impaired social communication, remains unclear. Olfaction relies on an IAM known as the sniff-response, where sniff magnitude is automatically modulated to account for odor valence. To test the failed IAM theory in olfaction, we precisely measured the non-verbal non-task-dependent sniff response concurrent with pleasant and unpleasant odors in 36 children—18 with ASD and 18 matched typically developing (TD) controls. We found that whereas TD children generated a typical adult-like sniff response within 305 ms of odor onset, ASD children had a profoundly altered sniff response, sniffing equally regardless of odor valance. This difference persisted despite equal reported odor perception and allowed for 81% correct ASD classification based on the sniff response alone (binomial, $p < 0.001$). Moreover, increasingly aberrant sniffing was associated with increasingly severe ASD ($r = 0.75$, $p < 0.001$), specifically with social ($r = 0.72$, $p < 0.001$), but not motor ($r < 0.38$, $p > 0.18$), impairment. These results uncover a novel language-free task-free ASD marker implying a mechanistic link between the underpinnings of olfaction and ASD and directly linking an impaired IAM with impaired social abilities.

Autistic children display an altered sniff response than that of typically-developed children.

The averaged normalized sniff trace (A, B) and sniff parameters (C) of typically-developed children (TD, A) and autistic children (ASD, B) in response to pleasant (blue) versus unpleasant (red) odors. In upper panel black dotted line depicts p values, green horizontal line marks 0.05 significance level. (D) Correlation of sniff response parameters with autism severity scores (ADOS).

55- Direct Injection Internal Combustion Engine with Waste Heat Recovery Through Methanol Steam Reforming

Arnon Poran, Leonid Tartakovsky

Mechanical Engineering Faculty, Technion

Internal Combustion Engines (ICEs) are major contributors to the global emissions and are also responsible for a substantial part of the world's oil consumption. Two ways of mitigating these problems are increasing the ICEs' efficiency and using low carbon intensity alternative fuels. We use both of these strategies by developing a high-efficiency methanol based propulsion system. The efficiency increase is achieved by using the exhaust gasses' energy to promote methanol steam reforming endothermic reactions and produce hydrogen reach gas mixture (reformate). The reformate's advantages are higher heating value, better combustion properties and it is also less polluting compared to the base fuel, methanol. But, when hydrogen-rich reformate is introduced to the engine through fumigation it can lead to pre-ignition, backfire and reduced maximal power. We suggested solving these problems by direct-injection of the reformate into the engine's cylinder. Using a newly developed ICE-reformer computer model, we have shown that it is not energetically efficient to compress the reformate after the reforming process to enable direct-injection into the cylinder. Because compression of low specific volume liquid consumes less power than compression of high specific volume gas, we suggested performing the reforming reactions under high pressure and introduced a new concept called high-pressure thermochemical recuperation. A direct-injection ICE operated by premade reformate from compressed gas vessels was designed and built in our lab. Engine feeding with reforming products showed 18%-39% increase in indicated efficiency and reduction of 91-94%, 90-96%, 85-97%, 10-25% in NO_x, CO, HC and CO_2 emissions, respectively, compared with gasoline in a wide power range. The combined direct-injection ICE fed through methanol steam reforming system was designed and built and we have succeeded to achieve a steady-state operation of the complete system.

56- Leveraging Internal Viscous Flow to Extend the Capabilities of Beam-Shaped Soft-Robotic Actuators

Yoav Matia, Tsah Elimelech & Amir D. Gat

Faculty of Mechanical Engineering, Technion - Israel Institute of Technology, Haifa, Israel 3200003

Elastic deformation of beam-shaped structures due to embedded fluidic networks is mainly studied in the context of soft-actuators and soft-robotic applications. Currently, the effects of viscosity are not examined in such configurations. In this work we introduce an internal viscous flow and present the extended range of actuation modes enabled by viscosity. We analyze the interaction between elastic deflection of a slender beam and viscous flow in a long serpentine channel, embedded within the beam. The embedded network is positioned asymmetrically with regard to the neutral plane, and thus pressure within the channel creates a local moment deforming the beam. Under assumptions of creeping flow and small deflections, we obtain a fourth-order integro-differential equation governing the time-dependent deflection field. This relation enables the design of complex time-varying deformation patterns of beams with embedded fluidic networks. Leveraging viscosity allows to extend the capabilities of beam-shaped actuators, such as creation of inertia-like standing and moving wave solutions in configurations with negligible inertia and limiting deformation to a small section of the actuator. The results are illustrated experimentally.

57- Dual frequency parametric excitation of a nonlinear multi degree-of-freedom amplifier

Amit Dolev

Technion-Israel Institute of Technology

Virtual topology modification of a multi degree-of-freedom (MDOF), nonlinear, mechanical resonator is introduced as a mean to increase its ability to detect external forces, therefore increase its sensitivity to different inputs. The mechanical resonator is parametrically excited (pumped) by a dual frequency signal, and used as an amplifier of weak and low frequency signals. Efficient amplification is achieved by exploiting the amplifier's natural resonances via a pump signal and a nonlinear feedback applied by controlled electromechanical actuators. The proposed device's topology is controlled in-situ by a microprocessor, hence allows increasing the compliance at desired frequencies with respect to various inputs. Higher compliance is used to enhance the amplifier sensitivity and the ability to amplify signals buried in noise. An experimental rig shows the importance of experimental calibration and system identification to fully calibrate the theory. The experimental results were compared to numerical simulations and analytical solution with favorable agreement with the theory.

58- Novel Biocomposite Materials and Constructs Based on Unique Collagen Fibers for Soft Tissue Bio-Mimetics

Mirit Sharabi[1], Dafna Benayahu[2] and Rami Haj-Ali[1]

[1] The Fleischman Faculty of Engineering, Tel Aviv University, Israel
[2] Sackler School of Medicine, Tel Aviv University, Israel

Soft tissues can be idealized as fiber-reinforced composite materials. From a mechanical point of view, collagen fibers are the main load bearing constituent of the tissue. As such, they are responsible for its stiffness and strength.

The growing need in soft tissue substitutes led to massive efforts to produce new materials that can replace damaged native tissue. Although biological compatibility is an important property of these biomaterials, mechanical biocompatibility is as crucial aspect that often does not get enough attention.

The objectives of the present work were to create a new type of biocomposite materials and constructs. To that end, biomimetics principles were applied by using the shape and structure of native soft tissues. Hence, ultra-long collagen fibers extracted from soft coral were combined with alginate-based hydrogel matrix having different fiber fractions and orientations. The proposed material combinations allowed tailor-designed and hyperelastic mechanical behavior similar to native tissues, e.g. cornea, blood vessels and annulus fibrosus. The new materials and constructs were fabricated and mechanically tested alongside with predictive finite-element (FE) material and structural models that can help in the design of complicated bio-composite constructs. This research enhanced our understanding to the structure-function behavior and the influence of the isolated bio-composite components on the overall mechanical behavior. These new materials and constructs with a combination of numerical simulations have a great potential to create the next-generation of tailor-designed biomaterials for soft issue substitutes.

59- Methodologies for Reduction of Airfoil Aerodynamic Noise

Michael Weidenfeld, Avshalom Manela, Eran Arad

Technion-Israel Institute of Technology

Airfoil noise is a dominant noise component in the acoustic signature of a wide variety of aerodynamic systems, ranging from airplane lift devices, through engine fans and wind turbines, to apping micro-air-vehicles. In line with current interest in reducing noise pollution from aeromachines, we study means to suppress airfoil noise. Making use of biomimetic observations based on the quiet ight of owls, we analyze the separate and combined effects of airfoil elasticity, porosity and material non-homogeneity, on the acoustic signature of an otherwise rigid, impermeable and homogeneous wing. Focusing on low Mach and high Reynolds number ow, the near field is studied using potential thin-airfoil theory formulation, and serves as an effective \compact source term" in an acoustic analogy to obtain the radiated acoustic far-field. Results rationalize porosity's role in airfoil noise attenuation, that is by producing an acoustic dipole opposing direct motion sound. The effects of surface elasticity and mass non-homogeneity are studied by varying the airfoil thickness along the chord. Results indicate significant noise reduction through a phase-shifting mechanism between the motion and wake dipoles, and provide insight into the compromise between aerodynamic efficiency and noise reduction.

60- Wavelength Demultiplexer Operating over Mode Division Multiplexed Signals on Rectangular Fiber

Miri Blau and Dan M. Marom

Applied Physics Department, The Hebrew University, Jerusalem 91904, Israel

We introduce a wavelength demultiplexer operating with multimode waveguides of rectangular geometry matching rectangular fibers. This eliminates the spatial-spectral mixing at output waveguide coupling. Performance is stretched between the need to separate wavelengths and modes.

We propose a multimode waveguide grating router (WGR) design with rectangular waveguides constrained to be single mode in one direction (width, defined in lithography) and multi-moded in height. This waveguide configuration matches the mode structure of rectangular core fibers, and allows for direct interface to this SDM fiber variant and realization of an SDM demultiplexer. By dispersing the signals in the WGR plane, where the mode structure is single mode, the coupling to the demultiplexed output waveguides is devoid of spatial structure which can lead to ill- shaped passbands and modal crosstalk. However, due to different mode propagation constants within the WGR, modal dependency still arises. We analyze this form of WGR demultiplexer, establish its performance bounds, and suggest realizations to make it feasible as a wavelength demultiplexer.

The existence of multiple modes (which should be routed together) leads to mode-dependent-spatial-shifts and as an outcome, to a significant reduction in resolution in standard WGR devices. We propose adjusting the FSR to overlap diffraction orders and generate noncontinuous demultiplexing. For example, for a waveguide supporting 3 spatial modes, if we increase the FSR to obtain two overlapping diffraction orders on the output plane, we can couple the light of the spectral channels using both diffraction orders. This way we don't use neighboring spectral channels and eliminate spectral and mode mixing.

Our solution, based on noncontinous demultiplexing, can lead the way to SDM-WDM devices on chip.

61- Graphene pn Junctions Achieved by Soft Doping with PSBMA

Hadas Alon

Bar-Ilan University

Graphene is one of the most fascinating and promising electronic materials known. While its atomic thickness is a significant advantage in many respects, this unique structure presents a challenge in controlling its charge carrier concentration. In this work, we demonstrate a viable strategy for achieving substantial control over the charge carrier in graphene. Our strategy is based on a PSBMA polymer, which exhibits charge transfer with graphene. The polymer can be patterned by e-beam lithography to enable selectivity of the doping area. This conceptually simple and versatile approach will be applied to build devices such as photodetectors and transistors.

62- Coin age metals-silicon composite for lithium ion battery

Y. Miroshnikov and D. Zitoun

Bar Ilan University, Department of Chemistry and Bar Ilan Institute of Nanotechnology and Advanced Materials (BINA), Ramat Gan 52900, Israel

Today, a great deal of attention is concentrated on silicon (Si) as future anode material for Li-ion batteries, mainly due to its highest known theoretical capacity. However, Si-based anodes face significant challenges such as large volume expansion upon lithium insertion, which can result in electrode fracture and loss of electrical contact. Therefore, free standing silicon as an anode material is still insufficient for the practical use in Li-ion batteries. One of the recently explored routes toward overcoming these issues is Si based nanostructured composites.[1] Furthermore, in order to better understand the mechanisms of the Silicon anode evolution upon lithium intercalation during battery cycling, real time measurements are required.

Surface-enhanced Raman spectroscopy (SERS) is a technique that enhances Raman scattering by molecules adsorbed on rough metal surfaces or by nanostructures, allowing the detection of single molecules. Moreover, coin age metals (Cu, Ag, and Au) are known to be Raman active and allow the SERS effect to take place.[2]

In this research, several coin age metals decorated silicon composites are prepared by a galvanic displacement reaction. We have found that the as prepared materials are electrochemically active and can be suitable to perform as anodes in Li-ion batteries. Moreover, the incorporation of coin aged metals grants silicon surface optical properties. Consequently, by using a specially designed Raman cell,[3] it is possible to follow the processes in silicon- coin age metal based battery trough an *in situ* surface enhanced Raman measurements.

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63- A Table-Top Laser-Based Particle Accelerator

Tal Queller

Weizmann Institute of Science

State-of-the-art high-power laser systems are used to routinely generate extreme energy densities and focused light intensities. During the interaction of these laser pulses with matter a plasma is generated that can both sustain and support huge electric fields. These can be used as a novel type of accelerator structure for electrons and ions. In order to accelerate ions the laser pulse is focused onto a small volume of gas at critical density, which is quickly transformed into a plasma, having a density that is just high enough that the laser pulse cannot enter. A series of electromagnetic processes enables positively charged ions to be accelerated away from the target region. For this purpose, a novel supersonic nozzle and a fast valve have been designed and characterized. The results are presented in this poster. This nozzle creates a supersonic gas flow with the suitable parameters (density distribution) needed for ion acceleration. An accelerator implementing this method could fit into a medium sized laboratory, and still achieve acceleration which with standard accelerators would demand the use of acceleration tubes up to a million times larger in linear size. One of the envisaged applications of such mono-energetic proton pulses which are the product of this accelerator lies in medical radiation therapy of tumors. In this scheme, proton or carbon ion beams are planned to be used to treat deep-sited tumors. Although the critical density is yet to be achieved, a big step towards the goal has been made in the last year, and the promising results are presented below.

64- Searching for beyond standard model physics using trapped radioactive neon isotopes.

Ben Ohayon

The Hebrew University of Jerusalem

Where can we search for new physics? One may probe higher and higher collision energies, by using particle accelerators such as the LHC, investigate background radiation from the big bang using state of the art satellites, or conduct low-energy, high precision experiments, which is the framework of this work. Our system comprises of an atom trap utilizing magnetic fields and powerful lasers to suspend neon isotopes in vacuum and under 1mK. Through a collaboration with the SARAF accelerator facility in the Soreq Nuclear Research Center, we demonstrated production of radioactive neon isotopes by bombarding cooking-salt with neutrons emanating from a lithium-uoride target. We plan to move our trap setup to a new state-of-the-art lab above the SARAF beamline, trap radioactive neon isotope, and investigate their decay products with high precision. Our planned measurement is sensitive to unknown force carriers in nature, such as right-handed weak bosons, and exotic particles, such as those predicted by supersymmetric theories.

65- Mechanism for irradiation induced creep in nano-crystalline dilute alloys

Noya Firman Dimanstein, Yinon Ashkenazy

Racah Institute of Physics, Hebrew University of Jerusalem

One of the main factors limiting the lifetime of materials is deformation due to creep. This failure mechanism is especially important when the material is exposed to radiation and creep is enhanced [1]. While the mechanism controlling creep varies, Irradiation induced creep is controlled by interactions of dislocations with point defects, that are at super- saturation due to the irradiation. A prominent approach for reducing irradiation induce creep in structural materials is the integration of precipitates within the microstructure of the material. The matrix-precipitate interface traps point defects, and thus prevents point defect-dislocation interaction. Along these lines, it was suggested to employ nanocrystalline alloys as radiation resistant material, where small grain size prevents dislocation reactions and the high availability of interfaces serve to trap point defects.

However, it was shown that grain boundary related relaxation due to point defect interactions at the nanocrystalline alloys grain boundary does lead to significant creep rates [2, 3]. We use molecular dynamics simulation to follow nano-crystalline Cu-V and Cu-Nb response to the insertion of point defects into material's grain boundaries. The variation in observed dynamics and its correlation with simulated creep rates serve to identify the creep controlling mechanism. We show that although significant a-thermal relaxation is evident all through the grain boundary, displacements due to stair-rod dislocations are unique in that they show strong correlation with observed variation in creep rates. These structures are shown to concentrate at triple line and quad junctions.

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66- Exciting Localized Surface Plasmons via Extended Ones using Grating Coupling for Ultrahigh Optical Field Enhancement

***Mohammad Abutoama*[*1], *Shuzhou Li*[2], *and Ibrahim Abdulhalim*[1]**

[1]*Department of Electro-Optic Engineering and The Ilse Katz Institute for Nanoscale Science and Technology, Ben Gurion University of the Negev, Beer Sheva 84105, Israel*
[2]*School of Materials Science and Engineering, Nanyang Technological University, Singapore, 639798*

Metal nanoparticles over metal film configuration, is under wide investigation during the last few years [1]. In this configuration a strong electromagnetic field is generated at the gap between the nanoparticles and the metal film. One more interesting configuration of combining metal nanoparticles with metal film is the one proposed by our group [2,3] in which an optimized design was shown for the excitation of the Localized Surface Plasmons (LSPs) through the Extended Surface Plasmons (ESPs) that propagate at the surface of the metal film in the Kretschmann−Raether configuration. This configuration exhibited an additional enhancement of the electromagnetic field in comparison to the conventional metal nanoparticles over metal film configuration and demonstrated experimentally using SEF and SERS. In [3] a squared array of gold NPs on a silver film is used and the excitation has been done using ESPs of the K-R configuration and not from free space. The generated ESPs at the surface of the metallic film then hit the NPs and under the appropriate matching condition excite the LSPs; thus generating intense EM fields at the gap between the NPs and the metallic film [3]. Note that in this work the inter-particle distance of the NPs was taken into consideration to allow achieving the highest enhancement factor. The use of grating instead of prism coupling scheme has several advantages such as: (i) working at normal incidence, (ii) building a compact planar structure that can be integrated with other systems, (iii) creation of multiple resonances which correspond to the different diffraction orders. The existence of both the diffraction grating and the nanoparticles allows the excitation of both surface waves, the ESPs and the LSPs respectively. The coupling between them at the interface shows high local density of the electromagnetic field; thus it can be used to enhance spectroscopic signals and efficiency of optoelectronic devices as well as for biosensing and energy harvesting applications.

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67- A Split-Source Multi-Section High Voltage Power Supply for X-Ray

Liran Katzir

Tel Aviv University, Faculty of Engineering

A high voltage power supply for x-ray applications is proposed. In the proposed topology, a *dc* input of 150 V-400 V is switched at high frequency (100 kHz) to generate multi-phase quasi-sinusoidal voltages. Each phase is then fed to a Half-Wave Cockcroft-Walton voltage multiplier section through an isolation transformer and the multiplier section outputs feed the load. The proposed topology boosts the voltage by two mechanisms: voltage multiplication and a transformer-like mechanism attained by the plurality of the isolated sections.

The proposed split-source multi-section topology attains up to *m* times higher voltage gain and ripple mitigation (*m* being the splitting degree). Simulation and experimental results support the effectiveness of the proposed topology. For instance, in one of the experiments, the load voltage was increased from 2.8 kV to 6.4 kV by applying a split-source three-section topology.

68- Compressive hyperspectral imager for remote sensing

Yaniv Oiknine, Isaac August, and Adrian Stern

Department of Electro-Optical Engineering, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Recently, we presented a new compressive spectroscopy method employing a liquid crystal (LC) phase retarder as a tunable filter. This principle was used for spectral imaging, demonstrating the possibility of reconstructing gigapixel spatio-spectral image cubes from spectral scanning shots numbering an order of magnitude less than what would be required using conventional systems. Here we present a new technique that uses the same method but replaces the LC with a Fabry-Perot (FP) resonator in order to modulate the light. In the first phase, we demonstrated the technique's performance as a compressive sensing spectrometer. Ultimately we hope to demonstrate compressive hyperspectral imaging that can be applied for remote sensing tasks.

69- Isomerization of Isolated Retinal Chromophore

Lihi Mosvat

Bar-Ilan University

One of the main challenges of modern science is to measure structure and structural changes (isomerization) of biological molecules. Recent developments in the field of ion mobility spectroscopy allow us to isolate specific structures of a given molecule, and experimentally determine the relative energies of different isomers and the energy barrier for isomerizations in the gas phase.

One of the most fascinating isomerization in nature is that of the Retinal Protonated Schiff-base (RPSB) chromophore. The isomerization of this molecule after photon absorption is the first step in every known form of animal vision and has intriguing properties: it is very efficient, specific and ultrafast (occurs in less than 200 fs). In order to understand what makes the RPSB isomerization so unique, we measured the energy barrier for each isomerization channel, with ion mobility spectroscopy method, and compare them to RPSB derivatives.

We observe that the barrier height for isomerization is much smaller than within the protein. We find that small changes to the structure of the chromophore have a great effect on its ground-state energetics, and in particular that the methyl group in the C13 position plays a crucial role.

70- High spatial resolution, dynamic and distributed fiber-optic strain sensing based on phasorial Brillouin dynamic gratings reflectometry

A. Bergman[a] and M. Tur[b]

[a]Faculty of Engineering, Bar Ilan University, Ramat Gan 5290002, Israel
[b]School of Electrical Engineering, Tel-Aviv University, Tel-Aviv 6997801, Israel

We demonstrate a novel distributed fiber sensing technique with a record broadband sensitivity of 10nε/√Hz at a sampling rate of 1MHz. A standing acoustic wave is generated by all-optical excitation of two simultaneously counter-propagating Brillouin dynamic gratings. A dual-tone readout probe pulse is used for the distributed measurement of strain-induced nonlinear phase-shifts of the acoustic wave. The phase is demodulated in electrical domain from the beat note of the reflected probe following the hardware-simpler direct detection. The measurement of 5kHz strain vibrations with a spatial resolution of 20cm (limited only by the 0.5ns switching time of our SOA) is reported.

71- Charge Distribution in Nano-Scale Grains of Magnesium Aluminate Spinel

Mahdi Halabi[1], Amit kohn[2], Vladimir Ezersky[1] and Shmuel Hayun[1]

[1]Department of Materials Engineering, Ben-Gurion University of the Negev, P.O.Box 653, Beer-Sheva 84105, Israel
[2]Department of Materials Science and Engineering, Tel Aviv University, Ramat Aviv, Tel Aviv 6997801, Israel

Charge distribution in magnesium aluminate spinel (MAS) results in the formation of a space-charge region that plays a critical role in assigning functional properties. Significant theoretical advances explaining this phenomenon have been accomplished, even though quantitative experimental support from nano-scale granular MAS is only indirect. In this work [1], the electrostatic potential distribution in nano-scale grains of nonstoichiometric MAS (MgO·0.95Al2O3 and MgO·1.07Al2O3) was measured by off-axis electron holography (OAEH) and compared to the distribution of cations and defects in this material as measured by electron energy-loss spectroscopy (EELS). In this manner, we studied the roles of composition, grain size, and applied electric field (EF) on the formation of a space-charge region. We quantitatively demonstrated that regardless of grain size, the vicinity of MgO·0.95Al2O3 grain boundaries presented an excess of Mg^{+2} cations, whereas the vicinity of MgO·1.07Al2O3 grain boundaries included an excess of Al^{+3} cations. The degree of structural disorder (i.e., the inversion parameter, i) indicated that as-synthesized MAS were significantly disordered (i between 0.37 and 0.41), with values decreasing toward equilibrium ordering values following annealing (i between 0.27 and 0.31). The application of an external ~150 V/cm EF during annealing further enhanced lattice ordering (i between 0.16 and 0.19). Such variations in the distribution of cations and defects should determine the space-charged potential (SCP). However, using these measurements to calculate the SCP was not possible due to the wide range of values reported for formation energies of defects (0.82–8.78 eV). Consequently, we correlated local ionic ordering with electrostatic potential in nonstoichiometric MAS. The magnitudes of the SCP in both MgO·0.95Al2O3 and MgO·1.07Al2O3 decreased following annealing from -3.4 ± 0.3 V and 2.0 ± 0.2 V to -2.0 ± 0.2 V and 1.6 ± 0.1 V, respectively.

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72- Thin film metal reservoirs as growth inhibitor/enhancers to modulate the height of carbon nanotubes forests

E. Shawat Avraham, L. Shani, V. Mor, O. Girshevitz, A. Westover, C.L. Pint, and G.D. Nessim

Ben-Gurion University of the Negev

Two years ago, we pioneered the concept of thin film reservoir where we describe how we doubled the height of carbon nanotube (CNT) forests by using a thin film reservoir of iron positioned below the alumina underlayer.[1] We are now submitting a new paper where we show how, by using a copper/silver thin film as a reservoir, we can inhibit CNT growth for the areas positioned above.[2] Using this technique, we show how we pattern the thin film reservoir (using lithography and lift-off) to then replicate this pattern on the CNT forest above.

We also present our most recent development where we use a molybdenum thin film reservoir to further enhance CNT growth, up to 4X (manuscript in preparation). What is most remarkable, and different compared to the iron reservoir mentioned above, is that by varying the thickness of the Mo film, we can modulate the CNT height and grow taller CNTs with thicker Mo layers.

By patterning the reservoir, we show how we can grow patterned CNT carpets with varying heights, all from the same catalyst layer. We will discuss the complex mechanisms based on diffusion from the reservoir to the surface and how the reservoir material interacts with the catalyst material to either inhibit or enhance CNT growth. We believe these findings are significant as they provide a simple way to locally control CNT growth on the third dimension (height) with lithographic precision.

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73- Hybrid Effects in Fracture Toughness of Polymeric Nanocomposites

Nadya Lerman[1], Xiao Hu[2] and Gad Marom[1]*

[1]Casali Institute of applied Chemistry, The Hebrew University of Jerusalem, Israel
[2]School of Materials Science & Engineering, Nanyang Technological University, Singapore

Composite materials contain a continuous (matrix) and dispersed (reinforcement) phases imparting enhanced mechanical properties relative to the matrix alone. Nanometer-scaled reinforcements may improve the polymer mechanical behavior.

A positive hybrid effect, stemming from the contribution of multiple dispersed elements can lead to a great improvement in fracture toughness. This research deals with hybrid effects and synergistic interactions. Understanding these effects may lead to better control of the mechanical properties and better performance of the nanocomposites, for example in applications such as ballistic shielding and structural materials.

First, we modified polyvinyl butyral (PVB), which finds use in films for armored glass. Improving its fracture toughness may increase the glass ballistic resistance. By using nanoclays and carbon nanotubes (CNTs), we achieved a positive hybrid effect in the fracture toughness. It was correlated with the finding that the fracture surface of the hybrid film exhibited the highest roughness according to the profilometer results. The effect may be explained by different mechanisms that act to improve the fracture toughness, such as crack front bowing and pull-out.

Currently, we are testing the fracture toughness of composites comprised from isotactic polypropylene (iPP pure and iPP-maleic anhydride copolymer) with GnP (graphite nanoplatelets) and VGCF (vapor grown carbon fiber), and with nanoclays and SiO_2. These composites contain nanoparticles of similar or identical chemical composition but different geometries, and also nanoparticles of the same geometry but different chemical compositions.

74- Towards improving bioethanol production: *Clostridium thermocellum* cellulolytic system as a model for efficient lignocellulosic biomass conversion

Shahar Yoav, Robert H. Smith

Department of Plant Pathology and Microbiology, Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem, Rehovot,76100, Israel

Development of sustainable renewable alternative energy resources for replacing currently used transportation fossil fuel is an important challenge. Second- generation bioethanol, produced from lignocellulosic waste, is a promising alternative energy source. The production process involves three major steps, namely (A) pretreatment of the lignocellulosic biomass, (B) enzymatic hydrolysis of the biomass into fermentable sugars, and (C) alcoholic fermentation. Despite its applicative nature, the high costs of cellulolytic enzyme production (used for the hydrolysis step) is a bottleneck in the process, rendering bioethanol production economically unfavorable. In order to overcome this hurdle, an efficient cellulolytic enzyme cocktail must be developed. *Clostridium thermocellum* is one of the best known cellulose-degrading bacteria. Its cellulolytic machinery, called cellulosome, is a multi-protein complex containing up to several dozen catalytic subunits as well as structural proteins. The composition of the cellulosomal proteins is known to change in response to the carbon source of the medium. In other words, *C. thermocellum* senses the biomass in the medium and assembles a tailored cellulosome preparation. Here, with the aim of assembling an efficient cellulolytic enzymatic cocktail, six different cellulosome preparations (grown on glucose, cellobiose, microcrystalline cellulose, and three industrially relevant pretreated lignocellulosic biomasses) were investigated. Surprisingly, microcrystalline cellulose- and glucose-derived cellulosomes were consistently equal or superior in their capacity to deconstruct both pure cellulose and lignocellulosic biomasses, and therefore should be used as a model for assembly of efficient cellulolytic cocktails.

75- Photocatalytic Reactive Oxygen Species Formation by Semiconductor−Metal Hybrid Nanoparticles. Toward Light-Induced Modulation of Biological Processes

Yuval Ben-Shahar[1], Nir Waiskopf[1,2], Inbal Carmel[1], Gilli Moshitzky[2], Hermona Soreq[2], Uri Banin[1]

[1]The Institute of Chemistry & The Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem, Jerusalem, Israel
[2]Department of Biological Chemistry and the Edmond and Lily Safra Center of Brain Science, The Hebrew University of Jerusalem, Jerusalem, Israel

Semiconductor−metal hybrid nanoparticles manifest efficient light-induced spatial charge separation at the semiconductor−metal interface, as demonstrated by their use for hydrogen generation via water splitting. Here, we pioneer a study of their functionality as efficient photocatalysts for the formation of reactive oxygen species. We observed enhanced photocatalytic activity forming hydrogen peroxide, superoxide, and hydroxyl radicals upon light excitation, which was significantly larger than that of the semiconductor nanocrystals, attributed to the charge separation and the catalytic function of the metal tip. We used this photocatalytic functionality for modulating the enzymatic activity of horseradish peroxidase as a model system, demonstrating the potential use of hybrid nanoparticles as active agents for controlling biological processes through illumination. The capability to produce reactive oxygen species by illumination on-demand enhances the available peroxidasebased tools for research and opens the path for studying biological processes at high spatiotemporal resolution, laying the foundation for developing novel therapeutic approaches.

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76- Developing New Copper Inks for 2D and 3D Objects by Using Self-Reducing Precursors

Yitzchak (Isaac) Rosen and Shlomo Magdassi

Institute of Chemistry, Casali Center for Applied Chemistry, The Hebrew University of Jerusalem

Fabrication of electronic devices by printing conductive interconnections on plastic substrates is of growing interest. Therefore, several approaches for the sintering of metallic nanoparticles (NP), mainly silver were recently developed. However, the high cost of silver limits commercial use and therefore inks with low cost metals, such as copper, are required. Inks containing copper NPs suffer from stability problems, as the NPs are quickly oxidized, and so lose their conductivity. Therefore, there is an unmet need for a stable copper ink with a low sintering temperature.

Our research is based on using a dispersion ink that contains sub-micron copper salt particles, which are stable to oxidation. Upon heating this ink, after printing, thermal decomposition occurs, the organic matter is converted to volatile species while reducing the copper ions, thus forming a conductive Cu° pattern. Two approaches were investigated to induce decomposition of copper formate patterns, by Intense Pulsed Light[1], and by hot pressing[2]. In the first approache, we found that applying pressure in addition to heat improved the obtained conductivity significantly. This was done by using a hot press, a process that does not require an inert environment, and can be performed with instrumentation already used in the printed circuit boards (PCB) industry. By this method, a printed sample on FR4 or Polyimide was heated under high pressure for 10-30 minutes, resulting in patterns with 20% of bulk copper conductivity and a line height of 10 microns. This is an excellent improvement compared to conductivity of only 1% obtained by only heating the sample without pressure. In addition, a new method[3], Reactive Transfer Printing (RTP) was discovered, based on transfer of copper formate patterns to a second substrate, yielding excellent pattern morphology and conductivity. This method can be used as a non-contact printing method and is very promising also for plastic and 3D electronics. Future work is aimed at using copper precursors to fabricate a new type of copper particle ink. The outcome of the research may have a significant impact on the field of printed electronics in general and in particular on the emerging Israeli industry in this field.

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77- New inks for 3D printing of hybrid and glass structures

Ido Cooperstein and Shlomo Magdassi

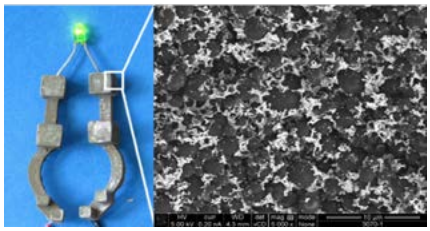
Casali Center for Applied Chemistry, Institute of Chemistry and Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem, Jerusalem, Israel

Three-dimensional (3D) printing is a highly efficient tool, which enables the formation of complex structures that are impossible to fabricate by traditional processes. Currently the main research in this area is focused on the printing technologies, improving the printing speed and the mechanical properties of the printed structures.

In this research, we focus on developing new 3D printable materials that are composed of organic-inorganic hybrid inks. Such hybrid inks enable fabrication of 3D structures with various properties, such as electrical conductivity, high thermal stability, high mechanical strength, and optical transparency.

The ink formulations developed in this work divides into two main approaches:

(1) Formation of 3D conductive objects by impregnating porous organic structures with conductive materials, resulting in electrical conductors embedded within the pores. (2) Formation of opaque or transparent ceramic structures, with excellent heat stability, by new inks composed of ceramic precursors.



Images of printed electric circuit (A) Image of the porous structure after inserting Ag nano particles (B) UHR-SEM image of the printed structure

Image of 3d printing transparent fused silica glass

78- Utilizing combinatorial materials science to discover new metal oxides

Hannah Noa Barad, David A. Keller, Kevin J. Rietwyk, Adam Ginsburg, Maayan Priel, Ilya Grinberg, Assaf Y. Anderson, and Arie Zaban

Department of Chemistry and Center for Nanotechnology and Advanced Materials, Bar Ilan University, Ramat Gan, 5290002

All-oxide photovoltaic devices are an emerging type of solar cells, due to their low-cost, high abundance, and easy fabrication methods. These characteristics allow the metal oxides to be potential absorbers as well as electron/hole conductors in solar cells. Perovskite metal-oxide structures have recently been studied as absorbers for solar cells since the perovskite structure has shown interesting characteristics, which allow, in part, better charge transport in photovoltaic devices. As such, development of new metal oxides, with lower bandgaps as absorbers for solar cells, is important.

In this work, combinatorial material science was used, to new metal oxide solar cell structures. The solar cells were synthesized in a combinatorial library by sequential cycles of pulsed laser deposition (PLD) using targets various targets, which are semiconductors. The combinatorial libraries were fully characterized by x-ray diffraction (XRD) and energy dispersive x-ray spectroscopy (EDS) to detect the materials and phases. I-V measurements showed photovoltaic behavior with high performance for these types of materials. The new solar cell library shows promising improvements for metal oxides in photovoltaic devices.

79- Formation and application of metallic inks for flexible electronics

Yousef Farraj, Shlomo Magdassi

Casali Center for Applied Chemistry, Institute of Chemistry and Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

The fabrication of electrical circuit boards by printing conductive inks has gained much interest in the last decade. Among the printing techniques, inkjet printing has many advantages over screen and gravure, as it does not require contact with the substrate and therefore enables printings on 2D, 2.5D and 3D structures. In today's practice, silver is the most commonly used metal due to its high conductivity and stability under ambient conditions. Therefore, here we present the utilization of a novel roll-to-roll sintering method based on electron beam exposure enabling high throughput of highly conductive inkjet printed silver ink.[1] In addition, since silver is very expensive, we also aim at replacing it with copper, which has a similar conductivity, and is about a hundred times cheaper. However, copper tends to undergo oxidation at ambient conditions, and therefore loses its conductivity. To overcome this problem, we present two approaches for obtaining oxidation-stable copper inks: by formation of a soluble copper complexes which is thermodynamically stable,[2-4] and by the formation of a copper-silver core-shell microparticles. [5, 6] The first ink undergoes decomposition and self-reduction, to yield copper nanoparticles either thermally (below 150 °C), or by plasma treatment at temperatures below 70 °C, which is suitable for plastics electronics including 3D printed objects. In the second approach, an oxidation-stable ink was formed, yielding high conductivity upon thermal treatment, in presence of various carboxylic acids.

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80- Magnetic chiral periodic mesoporous organosilica (PMO) nanoreactors: Design, preparation and applications in asymmetric catalysis

Suheir Omar and Raed Abu-Reziq*

Institute of Chemistry, Casali Center of Applied Chemistry and Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem

Periodic mesoporous organosilica nanoparticles were synthesized in a sol-gel process under mild conditions. Their preparation was mediated by hydrolysis and condensation of bridged organo-alkoxysilane precursor compounds, $(OR')_3Si\text{-}R\text{-}Si(OR')_3$, in the presence of a structure directing agent which assisted the creation of uniform pores and structures. In our project, we succeeded to synthesize and characterize different chiral bridged-silane ligands that were utilized for the preparation of multiple chiral PMO NPs systems. We aimed to synthesize pure chiral PMO NPs that were composed merely of chiral bridged monomers. The preparation of these systems was accomplished by applying different surfactants and ligands who afforded monodispersed chiral PMO NPs consisted of 100% bridged-silane precursor. Moreover, the major advancement in our research was the success – and for the first time- in preparing magnetic chiral PMO NPs. These nanoparticles were synthesized by a co-polymerization of 1,1'-((1R,2R)-1,2-diphenylethane-1,2-diyl)bis(3-(3-(triethoxysilyl) propyl)urea) chiral monomer by an o/w emulsion process, to give magnetic chiral PMO NPs with magnetite NPs in their cores. The incorporation of these PMO NPs with metal NPs such as ruthenium, rhodium and palladium can afford a highly attractable system for many catalytic processes. The potential application of these nanoreactors will be demonstrated in asymmetric transformations.

81- Development of Catalytic Microreactors by Non-aqueous Microencapsulation Method

Ahmad Zarour and Raed Abu-Reziq

Institute of Chemistry, Casali Center of Applied Chemistry and Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem

Despite the greater selectivity and reactivity in homogeneous catalysis compared to heterogeneous catalysis, processes performed by heterogeneous catalysis are more desirable, owing to facile recovery and low costs. The latent monumental potential in the bridging of both types of catalysis has encouraged the development of numerous methods for heterogenization of homogeneous catalysts. As a valuable emerging term, the homogeneous-heterogeneous principle is regarded as the best possible conjunction of both catalytic routes, where green processes with low economic cost and highly desired efficiency can be manifested.

Recently, we developed a new heterogenization method based on non-aqueous microencapsulation.. In this method, the catalyst is encapsulated within silica or polyurea microcapsules by applying either non-aqueous sol-gel processes or interfacial polymerization principles. Both preceded by the preparation of oil-in-oil (O/O) emulsion by dispersing a polar organic phase such as polyethylene glycol (PEG) in a non-polar organic solvent containing a proper surfactant. The catalyst is dissolved in the polyethylene glycol phase. At the end of this process, microreactors of silica or polyurea containing in the core a solubilized catalyst are obtained. The characterization of these microreactors and their catalytic activity in different organic transformations will be presented.

82- “Hybridization between Nano Cavities for Polarimetric Color Sorter at the Sub-Micron Scale”

Elad Segal [a], Adam Weissman [a], David Gachet [b], and Adi Salomon [a*]

[a] Department of Chemistry, Institute of Nanotechnology and Advanced Materials, Bar-Ilan University, Ramat-Gan 52900, Israel.
[b] Attolight AG, EPFL Innovation Park, Building D, 1015 Lausanne, Switzerland.

Color generation is commonly pigmentation-related and is spatially limited to tens of microns, two orders of magnitude above the diffraction limit. Colors can also be generated with interference devices such as photonic crystals and subwavelength plasmonic structures. The latter are suggested as a potential to reach the diffraction limit resolution using advanced fabrication techniques. By controlling a wide span of energies and optical features (colors), we can exploit and engineer sensing devices for ultra-low concentrations. Furthermore, light can be efficiently manipulated by such plasmonic structures followed by polarization. Hence, one can control the simultaneous tuning of the generated frequencies. We exploit the plasmonic-hybridization of nano cavities milled in metallic films, which are excited by propagating surface plasmons, to induce coupling between them. Following hybridization, new states are formed, in analogy to molecular orbitals. The polarization state of the incoming optical field modifies the charge distribution around the cavities, thus, one can actively achieve the whole energy landscape of the optical range. The properties of these devices are unique and related to the interactions between the neighboring cavities. We present a thorough study of the modes which give rise to the enhanced mutual coupling between these cavities.

83- Design and development of antibacterial self-assembling peptide nano-structures and composite materials

Lee Schneider

Tel Aviv University

The development of novel antimicrobial therapeutics is one of the most significant challenges of the 21st century. The recent identification of common structural and mechanistic characteristics shared by antimicrobial and amyloidogenic peptides provides a new paradigm for the development of a novel class of antibacterial agents. In this study, we set out to decipher the functional link between these two entities and are designing self-assembling antimicrobial peptide nano-structures based on their nano-structure forming and membrane interacting capabilities, as well as various biochemical and biophysical attributes. We have identified promising candidates with significant antimicrobial capabilities that cause substantial disruption to bacterial membrane morphology and membrane permeation and depolarization, but are not hemolytic or cytotoxic to eukaryotic cells. In light of the growing necessity of the development of antibacterial materials for biomedicinal applications, we are currently developing engineered tissue scaffolds with intrinsic antimicrobial capabilities by incorporating the peptide nano-structures with various polymers. We are continuing to develop these antimicrobial peptide nano-structures, and plan to integrate them into additional scaffolds, wound dressings and medical device relevant polymers in order to develop antibacterial composite materials. Our unique and interdisciplinary approach provides the foundation for a new approach to antimicrobial drug design and material engineering.

84- External Littelman Paths

Ola Amara-Omari

Bar-Ilan University

The symmetric group Sn has always been an important and be loved mathematical object. The representation theory of Sn has developed in many areas in mathmatics and in the last sixteen years for that matter in physics being the most important of the reaction groups. Every infinite group, for example is a subgroup of symmetric group. There is a connection between the representation theory of Sn with Lie algebras theory categorification, and the study of the group algebras over a field of infinite correspondence of Sn has expand to include the study of Hecke algebras, and also the cy-clotomic Hecke algebras Hd , when the group algebra has a deformation to Hecke algebras. The symmetric group is simplest example of important class of groups appearing in the theory of Lie algebras under the name of "Weyl groups ". some of these other Weyl groups also have a Hecke algebra theory. A ne Lie algebras of type A and their highest weight representations organized as a Kashiwara crystal are important in physics. The basis elements of a highest weight representation with highest weight correspond to irreducible modules in certain block algebras of cyclotomic Hecke algebras of weight. We have three combinatorial representations for the basis elements: as regular multipartitions, as Littelmann paths which are piece-wise linear paths in weight space, and as canonical basis elements which are elements in a structure called Fock space. In our research we are trying to consider the relationship among these three combinatorial representations. Our first results concern external vertices of the Kashiwara crystal in the rank 2 case. We find a direct, non-recursive method to go from the multipartitions to the Littelmann paths.

85- Crustal deformation near the tectonically-active Carmel- Gilboa Fault System and Dead Sea Fault in northern Israel

Dembo, N.[1,2], Granot, R[1]., Hamiel, Y.[2]

[1]Department of Geological and Environmental Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel
[2]Geological Survey of Israel, 30 Malkhe Israel St., 95501, Jerusalem, Israel

In Israel, tectonically-active faults are known to pose a seismic threat to major population centers, industrial facilities, critical infrastructures, and other lifeline structures. Consequently, it is imperative to map active faults and to characterize the deformation caused by their activity. Tectonic activity and crustal deformation in Israel is mainly related to two deformation zones: (1) The Dead Sea Fault (DSF), and (2) The Carmel-Gilboa Fault System. Here we examine the temporal and spatial distribution of rotational crustal deformation near these two major active fault zones. First, we construct a 3-D elastic dislocation slip model to simulate the surface deformation around the faults. The modeling is constrained by GPS measurements, seismic data and structural mapping of active faults. Next, we performed a detailed paleomagnetic investigation of Neogene-Pleistocene basalts surrounding segments of the faults that extend along the Jordan Valley, Yizrael Valley and between the Sea of Galilee and the Hula Valley. Finally, rotations from the mechanical modeling are compared against finite rotations determined based on primary magnetic remanence directions from 29 Neogenic basaltic sites near the Carmel and Gilboa faults and 27 sites near the northern DSF. Paleomagnetic results indicate significant (>20º) rotations near the edges of fault segments and within a right step-over between two prominent segments of the DSF: the Jordan Gorge section and the Hula East Boundary Fault. These results are in general agreement with the rotations obtained from the mechanical models, both revealing localized zones of anomalous rotations that provide constraints on the structural, mechanical and kinematic behavior of the faults. The results from this research bring important new insights on the timing, magnitude and style of deformation near major faults and present a new method that can be used for locating fault activity and slip rates.

86- Diophantine Approximations and the Connection to Dynamical Systems

Nattalie Tamam

Tel Aviv University

The field of Diophantine approximations deals with the approximation of irrational elements (numbers, vectors, matrices etc.) by rational elements, measured by the approximation error with respect to the size of the denominator. It is a central problem in Number Theory and has a long history and many applications. The field of dynamical systems deals with actions of functions on sets, such as movements of particles. Starting with an element of the set, one can apply the given function on it repeatedly to get a trajectory, as the movements of a specific particle over time. In recent decades, great progress was made by relating Diophantine properties to the behavior of trajectories in certain dynamical systems. For example, the set of elements, which have an exceptionally good rational approximation correspond to divergent trajectories. Sometimes there is a simple explanation for the divergence of trajectories, in a similar way a rational number has an exceptionally good rational approximation. Such trajectories are called obvious. Our work concerns with a classification for the existence of non-obvious divergent trajectories under a particular set of actions (closed cones).

87- Extending the Multi-Mode Resource-Constrained Project Scheduling Problem by Including Value Considerations

Naomi Salem Baluka

Technion-Israel Institute of Technology

The current trend in modern project management methodologies is to maximize project values. We suggest a quantitative model that balances time, cost and value. It generates detailed project plans, which are feasible with respect to time, cost and resource-constraints, and considers interactions between technical performance, time and cost. Such interactions, which existing project management models typically ignore, or project managers deal with intuitively, are important for increasing projects' values. The model, which extends the multi-mode resource-constrained project scheduling problem by including value, generates an efficient frontier that includes the best project plans for varying project costs. Since this model belongs to the NP-hard class, we develop specialized genetic algorithms for solving large problems. We provide illustrative examples to demonstrate the suggested approach.

88- Techno-Economic Evaluation of Hybrid Steam Generation by CHP and Electric Steam Generator

Nir Keren, Matan Shnaiderman

Department of Management, Bar-Ilan University, Ramat-Gan 5290002, Israel

Factories, hospitals, and similar organizations require electricity and steam for site operation. Time-of-use electricity rates and flat price for natural gas (NG) are common utility rates. By utilizing the hourly difference between the variable electricity rates and the flat NG price, an optimal operational strategy for decreasing steam generation costs is proposed. This operation is based on configuration of onsite steam and electricity generation by integrating an electric steam generator (ESG) powered by electricity and cogeneration (CHP) driven by NG. Consequently, the demand for electricity and steam can be supplied by three sources: CHP only, CHP and ESG, or ESG and central power plant. This approach reduces the risks associated with volatile energy prices and allows backup and continuity of energy supply by alternating two steam and electricity sources. The aim of this work is to evaluate the profitability of the CHP-ESG configuration for lowering steam generation expenses. Analytical and numerical solutions for the operation and setup phases of CHP-ESG are presented. Additionally, a cost comparison between the conversion of a conventional Mazut boiler to NG and CHP-ESG is demonstrated. Results suggest that the proposed integration of the CHP-ESG with appropriate operational methodology could save up to 46% in costs.

89- Social patterns and spatial codes in Arab towns in Israel

Maisa Totry Fakhoury

Ben-Gurion University of the Negev

This research analyzes the urban order and development of Arab towns in Israel by following the spontaneous emergence of abstract planning codes and principles, influenced by changing social, political and cultural dynamics. Based on a morphological analysis of 77 towns in northern and central Israel, and an in-depth investigation conducted in the city of Sakhnin, in the central Galilee, the research reveals a repeated three-ring structure, corresponding to three socio-political periods. It offers a detailed examination of the links between social values and spatial conduct, thus enabling us to follow how slight changes in social and economic circumstances affect planning principles. In addition, the research analyzes the performance of hierarchic, socially affiliated public spaces existing in traditional neighborhoods and of public spaces that belong to all, strictly divided from the private places, as part of the newer neighborhoods. This analysis provides a comparison between the global-south's point of view on public urban areas and the western- oriented look.

90- Imaging shallow voids using VSP data acquisition

Navon H., Reshef M.

Department of Earth Science, Tel Aviv University, Tel Aviv 69978, Israel

Cavities and voids in the shallow subsurface are posing a security and safety threat. Therefore, identifying and imaging these voids in the shallow complex subsurface has been a subject to many geophysical studies, yet a solution was not found. Of all the geophysical techniques, seismic methods have demonstrated the most success up to date in detecting and imaging the objects. However, conventional surface seismic surveys (SSP) have yet to achieve consistent success in detecting those objects and creating a clear image. SSP is located on the ground and therefore is highly sensitive to ambient noise and the signal from the target can be completely masked by the surface waves. In order to overcome these difficulties subsurface configurations such VSP (Vertical Seismic Profiling) can be applied. This configuration provides the advantages of recording both upgoing and downgoing wavefields, with higher frequency content and better resolution. In addition, VSP configuration enables converting time to depth, map the events to their correct location and retrieve more accurately seismic properties such as *Vp* and *Vs*.

The main aim of this research is to construct a subsurface operation in order to enable the illumination of small anomalous bodies, such as voids and karst, buried in the shallow complex subsurface. In order to achieve the main aim different VSP data sets acquired from an experimental site, using different subsurface geometries and different types of geophones (such as 3 components geophones) were processed. Examining these data sets enabled to produce a reliable velocity model, a better differentiation between the different wave types and preforming the migration process on the different arrivals, including the converted waves. Preliminary results show a rather focused and clear result and indicate a phenomenon of prism wave arrival.

91- Transport characteristics of the pharmaceutical oxaliplatin in natural soil

N. Goykhman, I. Dror and B. Berkowitz

Department of Earth and Planetary Sciences, Weizmann Institute of Science, Rehovot 7610001, Israel

Pharmaceuticals have been reported for over forty years to reach natural water and soil resources. The presence of pharmaceuticals in the environment raises concerns regarding their impact on ecosystems and human health, in spite of their minute environmental concentrations. Therefore, better understanding of transport and fate of pharmaceuticals in the subsurface could improve predictions of their environmental impact and facilitate the design of remediation efforts.

Here we discuss the transport of oxaliplatin ($C_8H_{12}N_2O_4Pt$) through packed, saturated soil columns, under controlled and environmentally relevant redox conditions. Oxaliplatin is a commonly used chemotherapeutic agent that has been detected in hospital effluents [1].

A similar breakthrough pattern of oxaliplatin was found for oxic, nitrate reducing and strong biologically reducing conditions, in columns of loamy, sandy soil. In sand, a significant difference in transport patterns was observed between oxic and chemically reducing conditions. Under all redox conditions, oxaliplatin elution was found to be faster as the ionic strength of the oxaliplatin solution decreases. The results indicate that redox conditions in soil are a less significant factor than expected, while chemical composition of oxaliplatin solutions and soil composition are the leading factors affecting oxaliplatin mobility and fate in the subsurface.

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92- Regenerable stimuli responsive PVP-clay graft composites for the removal of emerging water pollutants from water

Ido Gardi*, Yael G. Mishael

Dept. Soil and Water Sci., The Faculty of Agri., Food and Environ., The Hebrew University of Jerusalem, P.O. Box 12, Rehovot 7610001, Israel

In recent years, many studies have reported the development of polymer-clay composite sorbents for specific and high pollutant removal. High affinity of the pollutants to these sorbents frequently causes regeneration and reuse to be extremely challenging, due to irreversible binding and/or due to polymer loss during regeneration. In the current study, we aimed to develop new regenerable polymer-clay sorbents based on covalently grafted poly vinylpyridine (PVP) to montmorillonite for the removal of three water pollutant classes; inorganic anions (selenate and arsenate), organic anions (methyl blue, eosin bluish and sulfamethoxazole) and non-ionic organic molecules (atrazine). The sorbents were prepared in four stages, characterized by zeta potential, XRD, FTIR, TGA and XPS measurements. 1. Acid activating of the clay 2. Covalently grafting 3-aminopropyltriethoxysilane (ATPES) to the clay 3. Surface initiation with 2-bromoisobutyryl bromide and 4. Surface initiated atom transfer radical polymerization (SI-ATRP) of PVP. PVP grafted chains extend or collapse upon pH decrease and increase, respectively, due to gaining or losing monomer charge. The colloidal size of the new composite can reversibly shrink to nearly a quarter of its original size, upon pH change from 2.5 to 10. At this pH range, sorbent affinity towards water-soluble pollutants drastically changed due to changes in zeta potential and polymer conformation. The affinity of the pollutants to the grafted composite in batch was mainly driven by electrostatic attraction with composite capacity for anions reaching 350 mmol/Kg while thier capacity towards un-charged molecules reached 3 mmol/Kg. Organic anions, which can form both electrostatic and hydrophobic interactions, had even higher affinity to the composite than the oxyanions. Removal of 5 mg/L atrazine in the filter columns presented highly reversible binding with almost full pollutant recovery. The pH change triggered a rapid stimuli release of atrazine from the column. Regeneration cycles did not compromise the filter capacity over three cycles. These results suggest a proof of concept for an efficient “in-column” pH triggered sorbent regeneration.

93- Flow instabilities and vortices by the sea bottom

Gali Hendin

Tel Aviv University

Understanding the flow in the nearshore region is of great importance to many fields of coastal and marine engineering. In particular, the flow near the sea bottom is important, because of its immense impact on sediment transport. When designing marine structures, it is essential to calculate changes in sediment transport due to the structure and provide sustainable design adequate to the flow and wave regime in the designated area. This results in a reduction of maintenance costs (dredging) and beach erosion. Currently, the flow over the sea bottom is not well understood due to physical and mathematical complexity. Analytical models normally assumed two dimensional flow, ignoring the inherent three dimensional nature of the real flow. Nevertheless, in other fields, such as aeronautic engineering, it is shown that three dimensional flow phenomena can significantly alter the flow regime. Görtler vortices are an example of three dimensional flow that emerge from lateral instabilities of the two dimensional problem. Such vortices can tremendously affect the flow conditions and the amount of suspended sediments. The proposed work aims to study the fundamental characteristics of the flow near the sea bottom, investigate conditions for lateral instabilities, and evaluate the characteristics of the resulting Görtler vortices.

94- Cellulose-coated oil-in-water emulsions: from molecular solutions to encapsulated droplets

Sofia Napso, Dmitry Rein, Rafail Khalfin, Yachin Cohen

Department of Chemical Engineering, Technion – Israel Institute of Technology, Technion City, Haifa 3200003, Israel

Cellulose is the most abundant renewable material in nature, yet only a minute fraction of its annual natural production is utilized as a raw material for fabrication of synthetic products, or biofuel. Its processing requires harsh solvents or procedures considered to be detrimental to the environment and are increasingly regulated. Cellulose solutions in an ionic-liquid and its binary mixture with a polar organic co-solvent are of significant interest and have been studied extensively in the last decade, mostly by rheological measurements. However, the solution structure of cellulose in these solvents is not fully resolved. In this work, the structure and thermodynamic properties of cellulose solutions in mixtures of an ionic liquid and a polar organic solvent were studied by small-angle x-ray scattering. These measurements indicate that cellulose molecules are dissolved essentially as individual chains without any significant aggregation, and that these solvents can be considered as "good" solvents for cellulose. Furthermore, the dissolved cellulose chains readily form a unique encapsulation coating in oil-in-water or water-in-oil emulsions by mixing water, oil and cellulose solution in an ionic liquid. A more practical alternative is to form a hydrogel from the cellulose/ionic liquid solution by coagulation with water and applying it to homogenized oil/water mixtures. Structural information on the emulsion particles and the nature of the cellulose coating itself, was obtained using cryogenic electron microscopy and fluorescence microscopy imaging, and their size was analyzed by light scattering. The structure of the coating shell is relevant for specific applications such as controlled release of functional hydrophobic compounds, encapsulated phase-change materials for thermal control in textiles or insulation, and cellulose enzymatic hydrolysis for alternative fuel production from biomass.

95- Self-immolative Chemiluminescent Polymers

Samer Gnaim and Doron Shabat

School of Chemistry, Raymond and Beverly Sackler Faculty of Exact Sciences, Tel Aviv 69978, Israel

Molecular probes based on 3-hydroxyphenyl-1,2-dioxetane chemiluminescence light emission are widely used for various sensing and diagnostic applications (e.g., DNA, enzymatic and chemical probes). Amplification of molecular signals is an important task for the development of sensitive diagnostic probes in the field of chemical sensing. Recently, various approaches have been introduced to increase the signal-to-noise ratio of chemiluminescent light emission as a molecular signal.

This work describes the design and synthesis of a new class of self-immolative chemiluminescent polymers constructed of four complementary components: *i*) chemically stable 1,2-dioxatene analog incorporated an adamantyl group (bulky substituent), *ii*) protected 4-hydroxybenzyl alcohol substituent (self-immolative monomeric linker), *iii*) a chemical or biological responsive group (e.g., silyl protecting group), and *iv*) the monomers are linked together via carbonate linkage.

Our results show that a single cleavage event of the protecting group on the phenol results in the formation of a quinone derivative of 1,2-dioxetane, which undergoes a rapid 1,6-elimination to release the leaving group on the benzyl alcohol. A nucleophilic attack on the benzylic-methide position initiates a chemically initiated electron-exchange luminescence (CIEEL) process affording methyl benzoate and light emission.

Using this new class of chemiluminescent polymers introduce the ability to design a novel stimuli responsive chemilumnescent polymers as an amplification systems.