Department of Computer Science

Research Name: New Framework for Accurate Indoor Positioning and Navigation

Research Name: Discrete geometry

Research Name: Analyzing HTTPS Encrypted Traffic to Identify User’s Operating System, Browser and Application

Poster#1: Encrypted Video Traffic Meta Data Enrichment

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Poster#36: The Mechanism Of Metal Nanoparticles Catalyzed Water Reduction By Sodium Borohydride: Studied By Isotopic Markers
Department of Computer Science
Research Name: New Framework for Accurate Indoor Positioning and Navigation

Lecturer: Prof. Boaz Ben Moshe

Abstract

Performing a room-level positioning using WLAM and Cellular cells information is a well-known methodology which was suggested and implemented by many researches. In this paper we present a general framework for accurate indoor positioning and navigation which improves the expected accuracy to a sub-meter error rate. The main algorithm is using dominant landmarks such as lights in order to perform object level optic-flow. Moreover, the use of "glowing-markers" allowed us to accurately map relatively complex indoor buildings with compact representation. Such light-map is the basis for our modified particle filter navigation algorithm. The suggested method was implemented and tested on android based mobile devices (such as phones, watches, glass). The implementation is based on low resolution video feed (QV GA-QQV GA) fused with IMU-sensors which combined allowed a robust landmark tracking and navigation in 10-60Hz even on low-end device.
Research Name: Discrete geometry
Lecturer: Dr. Gabriel Nivasch

Abstract

Discrete geometry is the study of combinatorial properties of geometric objects such as points, lines, planes, polygons, etc. In this talk I will describe some problems studied in discrete geometry, including some of my work:

1) How to arrange $n$ points in the plane so that they determine as few distances as possible?

2) Given $n$ points in the plane, consider all the different triangles they determine. Can we make sure no point in the plane is contained in too many triangles? What happens in higher dimensions?

3) Given $n$ line segments that possibly intersect one another, how many intersection points are visible from below?
Research Name: Analyzing HTTPS Encrypted Traffic to Identify User’s Operating System, Browser and Application

Jonathan Muehlstein, Ofir Pele, Amit Dvir, Yehonatan Zion, Maor Bahumi, Itay Kirshenboim, Ran Dubin

Abstract

Desktops and laptops can be maliciously exploited to violate privacy. There are two main types of attack scenarios: active and passive. In this paper, we consider the passive scenario where the adversary does not interact actively with the device, but he is able to eavesdrop on the network traffic of the device from the network side. Most of the internet traffic is encrypted and thus passive attacks are challenging. In this paper, we show that an external attacker can identify the operating system, browser and application of HTTP encrypted traffic (HTTPS). To the best of our knowledge, this is the first work that shows this. We provide a large data set of more than 20000 examples for this task. Additionally, we suggest new features for this task. We run a through a set of experiments, which shows that our classification accuracy is 96.06%.
Abstract

Currently most network traffic is video. It is predicted to increase to 80% by 2020. Recently, video network traffic has started to be encrypted, which enables companies, like ISP and security companies, to collect QoE, personal user information and the video view time signature. Recently, Google changed its game rules and made "YouTube" videos encrypted which also prompted other sites to work over HTTPS.

National security organizations, ISPs and cyber companies have shown an enormous interest in acquiring information on the type of videos that people watch and their quality. However, due to encryption, DPI solutions are no longer viable.

We develop a solution based on machine learning techniques that can identify a video stream in encrypted traffic, identify the video's title and classify the video representation quality.
Poster#2: SLAM Algorithmic and Mathematic Models

Ben Yehuda, Vlad Landa, Boaz Ben Moshe

Abstract

Mapping an indoor area and determine self-position is a well-known problem, therefore we develop a new system for indoor position in tunnels. In order to see the advantages of the new system we experiment within a tunnel, where we record data with the system within a tunnel and checked few paths for collecting the best data. The system includes Lidar which gives us a distance in high bound rate, an optic flow that compare two sequence frames for calculation of the movement and a 6-dof that displays the orientation. All the data is recorded to a file. Then, we operate the mapping algorithm based on live Visual Odometry and integration with ROS platform and we get the following result:

Map

System
Poster#3: Perceptual Color Difference

David Zar, Ofir Pele

Abstract

In this project, our work is to develop a measure of color difference that matches perceptual color difference. For that, we collect information about perceptual color difference by distributing questionnaires, and testing it using existing methods of measuring perceptual color difference. Our main goal is to test and improve a distance proposed by Dr. Ofir Pele and Prof. Michael Werman. Pele and Werman suggested a color difference based on two observations. First, and very important for us, perceptual color differences were designed to be used for very similar colors. Thresholding was proposed to solve the problem for large color differences. So all pairs of colors that are totally different will get the same distance. Pele and Werman showed this does not solve the problem for medium distances. For that, they suggested their method, which is based on color names. The second observation is that when color difference is used for edge detection, many small distances around the just noticeable distance may account in false edges. Their suggestion is to reduce the effect for small perceptual distances.
Abstract

Bladder cancer (BC) is the most frequently occurring urological cancer and accounting for approximately 200,000 new cases worldwide annually. Mathematical models of cancer have been extensively developed with the aim of predicting tumor growth and efficacy of therapeutic. My lecture will be included 3 parts:

In the first part, I will present a multi scale cellular automata (CA) model to study the growth of BC. Based on this multi-scale model of BC development and growth, I investigate cell mutation pathways, simulate numerically BC initiation, and spread, and build in silico environment for testing various therapy strategies, used by the urologists.

In the second part, I will show a modeling study of bladder cancer via pulsed immunotherapy with Bacillus Calmette-Gue´rin (BCG) - an attenuated strain of Mycobacterium bovis (M. bovis). Impulsive differential equations are used for studying periodic BCG instillations (pulsed BCG therapy). The mathematical relationships between schedule (pulsing frequency) and dose (therapy strength) are determined through appropriate mathematical analysis.

The final goal in the talk is to determine the applicable treatment regime that prevent immune system side effects from BCG and enhance tumor destruction. For this, I will use a schematic representation of the BCG-tumor-immune system and by estimation of the different rates which control this system we construct a set of differential equations. The variables of the equation set are...
the number of tumor cells, bacteria cells, immune cells, and cytokines participating in the tumor-immune response. I simulate this model over a clinically relevant range of initial tumor sizes (distribution area) and tumor growth rates (tumor grade) using Matlab software. The using of the indicators from biomarkers are the initial conditions for immune system and tumor characteristics.

This model successfully retrieved previous clinical results for BCG induction treatment and BCG maintenance therapy with 82% complete response rate. I suggest that this flexible and versatile tool will help for physicians to plan new treatment protocols.
Research Name: The wave solutions for the Camassa-Holm and the Degasperis–Procesi equations  
Lecturer: Dr. Alexander Rasin

Abstract

The Camassa-Holm (CH) and the Degasperis–Procesi (DP) equations are by now recognized as archetypes of integrable equations. They have (weak) "peakon" solutions - solitary waves with discontinuous first derivative at their crest - and numerous other types of travelling wave solutions, including solitons (smooth solitary waves), cuspons and various periodic structures. We present the Backlund transformation (BT) for the CH and the DP equations. Unlike for the vast majority of BTs studied in the past, for the CH and the DP equations the transformations act on both the dependent and (one of) the independent variables. As a result of the BTs application we have received the travelling wave solutions, such as soliton and cuspon. We show that the peakon solution can be obtained from soliton as a limiting case. Superposition principles are given for the action of double BTs on the variables of the CH equation. Applications of this superposition principle are presented, specifically we constructed multi-soliton, multi-cuspon and soliton-cuspon solutions.
Research Name: 3D numerical approximation of relativistic particle beams by asymptotic expansion

Anne Le Blanc, Franck Assous

Abstract

We propose a new paraxial model that approximate the coupled time-dependent Vlasov-Maxwell equations. It is derived by introducing a frame which moves along the optical axis at the speed of light, so that the bunch of particles is evolving slowly in this frame. We also introduce a small parameter and use asymptotic expansion techniques to obtain a new paraxial model which is accurate up to fourth order. The simplicity of the formulation allows to use a finite-difference or finite element discretization for the Maxwell equations. Hence, using a particle approximation for the Vlasov equation, a particle-in-cell technique can be easily developed.
Poster#4: ALIT
Sagi Behor, Bar Peretz, Roman Yavich

Abstract

Colorblind people face many difficulties in everyday life that normally sighted people are just not aware of—the easiest thing might be difficult and frustrating. If colorblind people had an instrument that can help them to perceive and recognize the color and hues, their daily basis will be much easier, comfortable and less frustrating. This tool is our app: "ALIT". The app will be adapted for Android's devices. With this app the colorblind aim on an object, and the app will process the image that is received and display the color of the object as a text-output to the user. The app will also read aloud the name of the color, for the user convenient. In order to represent the color in the ideal way we convert the color data from RGB presentation to HSV presentation.

In HSV the color is presented as a cylinder, with three coordinates: Hue, Saturation and Value. In this presentation we found it easier to represent every color in words that every colorblind can understand. We decided to lose some of the accuracy to make it simpler for the colorblind people. In our current state, the user can open the app, aim on a specific object through the camera and the color values, in HSV presentation, of the object is presented in upper left corner of the screen. In addition, the sight changes its color accordingly to the objects color. Our next milestones is to find the algorithm that converts a color from HSV values to a name. In addition, we will add all the features that we think that will give the user the best experience—flashlight, saving photos and more.
Department of Physics
Abstract

The anticancer effect of millimeter wavelength irradiation on human cells was investigated in past, while the distinct effects were observed, partly contradictory. These effects possibly were connected to different irradiation conditions and type of the examined cells, so future investigations are needed. The human lung cancer is the most aggressive and widely spread type of cancer and new method of treatments are needed.

In this work the effect of low intensity millimeter wavelength (LI-MMW) electromagnetic waves on human lung cancer cells (H1299) was investigated in vitro by swept frequency (75-110 GHz, W-band) with synthesizer, for different exposition times. The effects of irradiation were analyzed by using fluorescent microscope imaging.

The conditions of irradiation were examined and calibrated; the frequency spectra of the reflected and transmitted signals through the medium and the cells were measure and compared. Although, the energy dose energy applied to the cells was lower (0.4-0.8 nJ per cell), the significant morphological changes in the cells were observed.

To conclude, we found the influence of the LI-MMW on the cell size, shapes and the changes in nuclear division that were seen in increased formation of multi-nuclear (polyploidy) cells.
Abstract

Equilibrium of atoms, the A and B coefficients for absorption and emission. Then we move to the description of the properties of black holes like the no-hair theorem, the second law of thermodynamics for black holes and the Hawking radiation. The full quantum properties of black holes are still elusive as we do not have yet a quantum theory of gravity. Following similar steps taken in the early stages of quantum mechanics we obtain the quantization condition for the black holes, the Hawking radiation formula, the A and B coefficients for black holes. Thus, exploring the principles of early quantum mechanics as for atoms, and in complete analogy to atomic physics many of the known properties of black holes are reproduced and some new insights obtained.
Research Name: THz Conductivity of Optimally Doped La$_{2-x}$Ce$_x$CuO$_4$
Superconductors
Jonathan Bechor, Aviv Moshe, Eliav Tubul, Eliyahu Farber

Abstract

THz transmission technique in the Mach Zehnder interferometer arrangement was applied for measurements of the complex transmission function in electron doped La$_{2-x}$Ce$_x$CuO$_4$ thin films. The measurements were carried out in a frequency range of 5 cm$^{-1}$ - 20 cm$^{-1}$. The real part of the conductivity reveals a sub-gap like feature at 7.6 cm$^{-1}$ in a temperature range $T < 15$ K. Above $T_c$ the real part of the conductivity shows a Drude-like behavior in our frequency range. The penetration depth as a function of temperature shows a non $d_x^2 - v^2$ - wave behavior and diverges at $T_c$ once the energy of the mentioned sub-gup is approached.
Poster#5: Competition Between Enhanced Cooper Pairing and Suppressed Phase Coherence in Coupled Aluminum Nanogranins

Nimrod Bachar, Eliyahu Farber, U. S. Pracht, L. Benfatto, G. Deutscher, M. Dressel, M. Scheffler

Abstract

Deterministic enhancement of the superconducting (SC) critical temperature $T_c$ is a long-standing goal in solid-state physics. In a large variety of SC systems, the initial enhancement via tuning of a control parameter is followed by a suppression of $T_c$, shaping a superconducting dome in the phase diagram. This dome was postulated to be shaped by a competition between two energy scales: the superconducting energy gap $\Delta$ and the superfluid phase stiffness $J$ [1]. One of the first evidence for such dome-like phase diagram was shown for granular Al, i.e. thin films composed of nano-scaled grains separated by thin insulating barriers, where grain-coupling acts as control parameter [2].

In this work, we used DC transport measurements and optical THz spectroscopy in order to study the development of $T_c$ and the energy scales $\Delta$ and $J$ as a function of the grain coupling and explain the phase diagram of granular Al [3,4]. Starting from well-coupled grains, $\Delta$ grows as the grains are progressively decoupled, causing the unconventional increase of $T_c$ with sample resistivity. When the grain-coupling is suppressed further, $\Delta$ saturates while the critical temperature $T_c$ decreases, concomitantly with a sharp decline of $J$, delimiting a SC dome in the phase diagram. The crossover to a phase driven SC transition is accompanied by a pseudogap observed in the normal state above $T_c$. Overall, we demonstrate that granular Al is an ideal testbed to understand the interplay between quantum confinement and global superconducting phase coherence due to nano-inhomogeneity.


Nonlocal Electrodynamics in Weyl Semi-Metals

B. Rosenstein, H.C. Kao, M. Lewkowicz

Abstract

Recently synthesized 3D materials with Dirac spectrum exhibit peculiar electric transport qualitatively different from its 2D analogue, graphene. Neglecting impurity scattering, the real part of the conductivity is strongly frequency dependent (linear), while the imaginary part is non-zero (unlike in undoped, clean graphene). The Coulomb interaction between electrons is unscreened as in a dielectric and hence is long range. We demonstrate that the interaction correction renders the electrodynamics nonlocal on a mesoscopic scale. The longitudinal conductivity $\sigma_L$ (related by charge conservation to the electric susceptibility) and the transverse conductivity $\sigma_T$ are different in the long wave length limit and consequently the standard local Ohm's law description does not apply. This leads to several remarkable effects in transport and optical response. We predict a charging effect in DC transport that is a direct signature of the nonlocality. The optical response of the WSM is also sensitive to the nonlocality. In these materials p-polarized light generates bulk plasmons as well as the transversal waves. The propagation inside the WSM is only slightly attenuated. At a specific (material parameter dependent) frequency the two modes coincide, a phenomenon impossible in a local medium. Remarkably, for any frequency there is an incident angle where total absorption occurs, turning the WSM opaque.
Department of Molecular Biology
Abstract

More than 90% of cancer-related mortality is due to metastases rather than primary tumors. Metastasis formation is strongly dependent on the migration capabilities of tumor cells: in order to form metastases tumor cells have to migrate away from the primary tumor into blood vessels and later on out of blood vessels into secondary tissues. Most of our knowledge on tumor cell migration comes from studies on the cytoskeleton, adhesion complexes and signaling molecules, whereas very few studies evaluated the role of the cell nucleus and its major constituent, chromatin, in the migration process.

We were able to show that tumor cell migration is associated with and dependent on global chromatin condensation. Therefore, we anticipated that tumor progression that is dependent on increased cellular migration capabilities should be associated with increased chromatin condensation. Interestingly, in some types of cancer, such as melanoma, the opposite has been reported. In trying to resolve this contradiction, we have found that during growth (“steady-state”) conditions, tumor progression is associated with global chromatin de-condensation that is beneficial for faster proliferation. However, upon induction of migration, in both low- and high-metastatic melanoma cells chromatin undergoes condensation to support the cellular migration capabilities.

Our results reveal that induction of chromatin condensation by migration signals is maintained throughout tumor progression, whereas the organization of chromatin during “steady-state” conditions is altered during tumor progression. Thus, tumor progression is associated with an
increase in chromatin dynamics. This aspect should be taken into consideration when trying to treat cancer with chromatin targeting drugs.
Abstract

The continued evolution of antibacterial resistance threatens to seriously compromise our ability to treat bacterial infections and pose a great public health concern. Therefore study of the molecular mechanisms conferring antibiotic resistance and understanding bacterial virulence traits involved, are crucial in order to control resistance spread and design novel effective therapeutics. Enteric bacteria are natural inhabitants of human and animal gut flora but may become opportunistic pathogens causing various infections. Multiple processes that compel the emergence and spread of antibiotic resistance among enteric bacteria will be discussed including the world-wide spread of successful multi-drug resistant strains, and the inter-species spread of antibiotic resistance-encoding transferrable genetic elements. New antibacterial drugs will also be presented.
Abstract

Approximately 1% of the general population suffers from Intellectual Disability (ID), caused by several environmental, genetic or combined factors. The current study involves analysis of Whole Exome Sequencing (WES) data from pediatric ID patients, for the detection of novel genes and mutations leading to ID, using Mutation Annotator, an automatic data analysis tool developed in our lab.

In the current talk, I will present a novel mutation in the MED25 gene leading to syndromic ID. The syndrome, characterized by eye, brain, cardiac and palatal abnormalities, as well as growth retardation, microcephaly and severe ID, was detected in seven patients from four unrelated families, all originating from the same village. WES analysis identified a homozygous mutation p.(Tyr39Cys) in MED25, believed to be the cause of the syndrome. The protein encoded by MED25 belongs to the Mediator (MED) complex, an evolutionary conserved multi-subunit RNA polymerase II transcriptional regulator complex.

DNA from 204 control individuals of the same ethnic origin were tested for MED25 mutation by restriction analysis, none of whom carried the mutation. In contrast, 80 inhabitants of the affected patients' village revealed a carrier rate of 8.7%, suggesting this variation to be a founder mutation.

The above case report demonstrates the utility of a fast and user-friendly workflow for WES data analysis to accelerate the diagnostic procedure and should significantly improve genetic counseling.
Poster#6: Insulin Sensitivity is Improved by the Beduin Medicinal Plant, Sarcopoterium Spinosum

K. Rozenberg, Skalka Nir, S.R. Sampson and Z. Kerem, Tovit Rosenzweig

Abstract

Sarcopoterium spinosum (Thorny burnet) is an abundant plant in Israel, used by Beduin medicinal practitioners for the treatment of diabetes. The aim of this study was to clarify its mechanism of action in the treatment of type 2 diabetes (T2D).

In-vivo studies were performed on KK-Ay (spontaneously developing T2D) and high fat diet-fed mice given the extract for 6 and 9 weeks respectively. Glucose and insulin tolerance tests were performed, and the activation of insulin signaling pathway in soleus muscle and liver was followed. Mechanisms of action were investigated in L6 myotubes and 3T3-L1 adipocytes using Western blot analysis and glucose uptake assay.

S.spinposum extract improved glucose tolerance and insulin sensitivity in treated mice, KK-Ay mice being more sensitive for the treatment. S.spinposum extract increased glucose uptake in 3T3-L1 adipocytes. An additive effect was found between S.spinposum and insulin. Using specific inhibitors we showed that while inhibition of PI3K did not affect S.spinposum-dependent glucose uptake, inhibition of AKT completely abrogated this effect, suggesting that S.spinposum activates AKT via PI3K independent mechanism. This unique mechanism of action was confirmed using Western blot analysis, showing that in contrast to insulin action, neither ser473 nor thr308 was phosphorylated by S.spinposum. However, translocation of PKB from the cytoplasm to the membrane and the nucleus
was detected. In addition, events downstream of AKT activation—GSK3β, FOXO and PRAS40 phosphorylation, and GLUT4 translocation—were increased by the extract. AMPK is not involved in the effects of S.spinosum.

We propose that the active ingredients in S.spinosum activate PKB by a unique mechanism which is independent of ser473 and thr308 phosphorylation. Identifying the active molecules and clarifying its mechanism of action may lead to the development of new agents for the treatment of insulin resistance.
Poster#7: N-Acetyl-Cysteine (NAC) Supplementation Improves Insulin Sensitivity: a Personalized Recommendation is Required

Alona Falach, Lital Argaev-Frenkel, Hava Rozenfeld, Moria Chetboun, Sanford R Sampson, Tovit Rosenzweig

Abstract

Meta analyses conclude that antioxidant (AOX) supplementations have no beneficial effects on the prevalence of type 2 diabetes (T2D). These disappointing results conflict with most in-vitro and in-vivo studies showing interference with oxidative stress and benefits of AOXs on insulin sensitivity and β-cell function. Recently, the role of reactive oxygen species in a large number of physiological functions, including transmission of insulin signaling, was demonstrated. We suggest that while AOXs are beneficial for reduction of oxidative stress, inappropriate intake of AOX, either at lower or higher than the optimal dose, impairs the effectiveness of treatment. The aim of this study is to clarify the dose-response effects of the AOX N-acetyl-cysteine supplementation on the progression of T2D.

Methods: Experiments were conducted on KK-Ay mice, given NAC at different concentrations (200-1800 mg/kg/day) for 6 weeks. Glucose and insulin tolerance tests were performed and plasma insulin, total antioxidant capacity (TAC) and lipid peroxidation were measured. Insulin signaling pathway was followed in soleus muscle and pancreas was stained by H&E.

Results: Although lipid peroxidation was reduced and TAC elevated in all concentrations used, glucose intolerance was not corrected in the 200 mg/kg/day treated mice. While 600, 1200 and 1800 mg/kg/day NAC were all found to improve glucose tolerance, only the 1200 mg/kg/day treatment increased insulin sensitivity as indicated by improved insulin tolerance test, reduced plasma insulin
and improved transmission of insulin signaling in soleus muscle and liver of treated mice. Islet hypertrophy was also corrected only in the 1200 mg/kg/day treated animals.

Conclusion: The inconsistency in the literature regarding AOXs and prevention of diabetes may result from the lack of clear guidelines for effective doses. Thus, there is a need to identify certain biomarkers for the target oxidative state that should be maintained in order to obtain optimal outcomes.
Nonalcoholic fatty liver disease (NAFLD) is the hepatic manifestation of the metabolic syndrome (MS). The benefits of moderate wine consumption on various components of the MS are well established. However, as alcohol consumption is related to the progression of liver diseases, it is not recommended for NAFLD patients.

Aim: To investigate the potential benefits of red wines, containing different polyphenol levels, and pomace on hepatic health and glucose tolerance in high-fat diet (HFD)-fed mice.

Methods: HFD-fed mice were supplemented by 0.1 or 1 ml/day red wine, prepared according to different protocols of maceration: short (SM), regular (RM) or long maceration (LM). Other groups were supplemented with non-alcoholic wine, equivalent doses of ethanol, or pomace (50 mg/day). The different supplements were given for 11 weeks. Glucose and insulin tolerance tests were performed, serum insulin was measured and hepatic triglyceride content was analyzed using biochemical and histological methods.

Results: No adverse effects on TG accumulation and hepatic histology were detected in all test groups. While SM-wine had an adverse effect on glucose disposal, LM-wine improved glucose tolerance, insulin sensitivity and hepatic steatosis. Both alcoholic and non-alcoholic components of
the wine contribute to its beneficial effects. Pomace improved all parameters measured; body weight gain, glucose tolerance, insulin sensitivity, hepatic TG content and histology.

Conclusion: Maceration time has a major effect on the beneficial properties of wine. Pomace, the main waste product of wine industry, might be used as a supplement with beneficial health outcomes, without the concerns regarding adverse effects of alcohol.
Poster#9: Subgrouping of pediatric medulloblastoma using an integrated analysis of MicroRNA-mRNA expression profile

S. Gershman, S. Michowiz, H. Toledano, O. Barinfeld, A. Pinchasov, N. Goldenberg-Cohen, Mali Salmon-Divon

Abstract

Medulloblastoma (MB), the commonest malignant brain tumor of childhood, is divided into four tumor subgroups representing distinct clinical, biological and molecular entities. Subsequently, treatment should be designed according to the specific subgroup. MicroRNAs (miRNAs) are involved in carcinogenesis and tumor progression by regulating post-transcriptional gene expression. However, the miRNA-mRNA regulatory network in MB is far from being fully understood. The aim of the study is to identify novel miRNA subgroup biomarkers and their target mRNAs for rapid, specific and cost effective diagnosis by analyzing integrated mRNA-miRNA transcriptome sequencing from tumors. With this aim, integrated whole transcriptome mRNA and miRNA expression analysis was performed on primary tumor samples collected from 10 MB patients. 867 mature miRNAs were identified in at least a single MB sample, of them 462 were common to all 4 subgroups. 25 (2.5%) of all expressed miRNAs appeared to be significantly differentially expressed between the medulloblastoma subtypes (FDR<0.1). Namely, upregulation of hsa-miR-224-5p and hsa-miR-449c-5p was found exclusively among WNT, while downregulation of hsa-miR-135b-5p characterized SHH. Among groups 3 and 4, hsa-miR-20a-5p was upregulated or downregulated, respectively. RNA-seq from the same tumor samples identified 500 genes that vary between the four subtypes (q value <0.05), among which 69 (13.8%) have anti-correlated miRNA-mRNA interactions with the 25 detected miRNA biomarkers. The predicted mRNAs targets of these miRNAs are associated with
different signaling pathways, known to have a role in MB biology. Our study demonstrates that miRNAs are readily detectible and are highly specific to distinct MB subgroups. Understanding the involvement of miRNAs and their targets in MB related signaling pathways may improve diagnosis and advance the development of targeted treatment for MB.
Poster#10: Utilizing the Benford law for unravelling tissue specificity

Deepak Karthik, Gil Stelzer, Sivan Gershonov, Danny Baranes, Mali Salmon-Divon

Abstract

The reduction in sequencing costs has led to an unprecedented trove of gene expression data from diverse biological systems. Subsequently, principles from other disciplines such as the Benford law, which can be properly judged only in data-rich systems, can now be examined on this high-throughput transcriptomic information. The Benford law states that in numerical data, the proportion of numbers beginning in any given digit is not uniform but rather skewed, with 1 being the most common digit and 9 the rarest. Here we demonstrate that digital gene expression data has a Benford-like distribution when observing an entire gene set. This phenomenon was conserved in a wide range of biological tissues and developmental conditions. However, when obedience to the Benford law is calculated for individual expressed genes across thousands of cells, genes that best and least adhere to the law are enriched with tissue specific or cell maintenance descriptors, respectively. Surprisingly, a positive correlation was found between the obedience a gene exhibits to the Benford law and its expression level, despite the former being calculated solely according to first digit frequency while totally ignoring the expression value itself. These results demonstrate the applicability and potential predictability of the Benford law for gleaning biological insight from simple count data.
Poster#11: Epithelial-Cell Adhesion And Invasion Of Extended-Spectrum Beta Lactamase-Producing Extra Intestinal Escherichia Coli Isolates Reveal St131 Superiority

Kira Kondratyeva, Ayala Wollman, Gabi Gerlitz, Shiri Navon-Venezia

Abstract

Multidrug-resistant ESBL-producing extraintestinal Escherichia coli (MDR ExPEC) is reaching endemic occurrence worldwide due to the clonal expansion of sequence type (ST) 131 lineage. This clone colonize various hosts including animals, birds, and humans and is the major cause for urinary tract infections in human both in hospitals and in the community. The endemic nature of this clone is not fully understood. We aimed to compare the adhesion and invasion capabilities of various multidrug resistant (MDR) ExPEC lineages to human epithelial cells in order to examine the superior gut-colonization potential of this clone.

A collection of 14 MDR community-onset bloodstream isolates were included, 7 belonged to ST131 lineage and 7- NonST131 isolates. Isolates were characterized for antibiotic resistance genes, and adhesion-associated genes. Adhesion and invasion were assessed with human Caco-2 cells. Statistical comparison between groups of ST131 and NonST131 isolates was analyzed using Non-parametric Mann-Whitney test. Fluorescence microscopy visualization using anti-LPS E. coli antisera supported quantitative results.

All ST131 isolates belonged to the virulent phylogenetic group B2 while NonST131 isolates belonged to phylogenetic groups D (5/7), A and B2 (both 1/7). All isolates carried CTX-M-group beta lactamases and showed different adhesins gene content. The average adhesion level of ExPEC to

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Caco-2 cells varied significantly (8.9±2.6% to 25.4±2.8%), with ST131 isolates showing a significantly higher adherence rate compared to NonST131 lineages (17.09±5% versus 13.06±4.41%, respectively, p<0.05). Alongside with adhesion, ST131 isolates showed a more pronounced invasion rates into Caco-2 cells (0.4±0.26% versus 0.16±0.15%, p=0.015). Fluorescence microscopy visualization using anti-LPS antisera supported the cell culture quantitative results.

ST131 ExPEC isolates showed a significant superiority in adhesion and invasion to human Caco-2 epithelial cells compared to other ExPEC genetic lineages suggesting a possible advantage of ST131 in gut-colonization together with an enhanced invasion capabilities. These findings may contribute to our understanding of the high worldwide occurrence and dissemination of this clone.
Poster#12: Assessing the link between the gut microbiome and behavior using a mouse model of dominance and submissiveness

O. Agranyoni, O. Koren, Shiri Navon-Venezia

Abstract

Recent studies have demonstrated that commensal, probiotic, and pathogenic bacteria in the gastrointestinal tract can activate central nervous system (CNS) signaling systems, possibly through neural, endocrine and immune pathways, thus influencing brain function and behavior. This emerging concept of the microbiome–gut–brain axis suggests modulation of the gut microbiome as a potential novel therapeutic strategy for CNS disorders. In our laboratory, we selectively bred mice with strong features of dominance (Dom) and submissiveness (Sub) that represent opposite poles of the behavioral spectrum. We hypothesized that Dom and Sub mice with opposing behavioral phenotypes may possess differential gut microbiomes and that modulation of their gut microbiome may alter their behavior.

Using 16S rRNA gene sequencing, we found Dom and Sub mice's gut microbiome to be comprised of significantly different ratios between bacterial phyla, attributed mainly to bacteroidetes and firmicutes. Changes in the abundances of these phyla have been shown to alter the host organism's nutrient metabolism and to compromise protection against pathogenic phyla. At the same time, the gut microbiome of WT mice, which represent a heterogeneous population displaying a mixed behavioral profile, was found to include bacteroidetes and firmicutes bacteria at a ratio approximately the average between that of Dom and Sub mice.
Dom and Sub mice may be used for further investigation of the effects of the gut microbiome upon behavior. Targeted modulation of the microbiome may induce behavioral changes, leading to a better understanding of the role of the microbiome–gut–brain axis upon behavior.
Poster#13: Novel synthetic cyclic integrin-binding peptide ALOS4: Antitumor activity in animal melanoma models

Shiri Yacobovich, Michael Kirby, Elimelech Nesher, Oryan Agranyoni, Boris Redko, Katerina Gurova, Igor Koman, Osnat Ashur Fabian, Albert Pinhasov

Abstract

Integrins are a family of cellular membrane receptors that involved in wide variety of physiological functioning, including cell division and interactions, as well as intracellular signaling. They are essential for cellular morphology maintenance and motility, as well as cell cycle regulation. Integrins are involved in various pathological conditions, including cancer, infection, thrombosis and autoimmune disorders. In cancer, they contribute to proliferation, survival, differentiation, invasion and metastasis, which have made them a therapeutic target for many cancer types. The integrin αvβ3 has been the focus of intensive research because of its major role in several distinct processes, particularly angiogenesis and tumor metastasis. Metastasis is still the most attributed factor for mortality among cancer patients, due to its resistance to conventional treatments. Integrin αvβ3 expression is markedly upregulated in transformed cells such as melanoma, lung cancer, glioblastoma, prostate cancer and others. In our laboratory we discovered a novel cyclic peptide named ALOS4 consisting of nine amino acids that binds with high affinity to integrins αvβ3 and αvβ5.

In several cell-lines ALOS4 inhibits proliferation and significantly inhibit migration of cancer cells. In animals models of malignant melanoma ALOS4 significantly reduced lung tumor growth and dramatically extended animals life span. Furthermore, no toxicity effects were observed. In a subcutaneous melanoma mice model, ALOS4 has shown a significant reduction in tumor volume and
also an extension in mice's life span. These results suggest that ALOS4 has a potential anti-cancer activity. Ongoing experiments are exploring the mechanism of action of this peptide, which could lead to the development of a novel treatment for cancer metastasis.
Poster#14: Prenatal stress can build, prenatal stress can break: inherited dominance or submissiveness predicts adaptive or maladaptive HPA axis programming

Moshe Gross, Hava Romi, Lena Gilimovich, Albert Pinhasov

Abstract

Gestation is a critical period during which the fetus is highly sensitive to maternal glucocorticoids, whose elevated levels alter programming of the offspring’s Hypothalamus Pituitary Adrenal (HPA) axis. Maladaptive programming of the HPA axis in utero may be involved in anxiety and depressive disorders in adulthood. However, there is high variability in the stress response: while most stress-exposed individuals display resilience, the remainder may develop anxiety- or depressive-like behavior. We reported previously the development of two distinct strains displaying resilience or vulnerability to stress by selective breeding according to mice’s social dominance (Dom) or submissiveness (Sub mice).

Pregnant dams were exposed to Prenatal Restraint Stress (PNS, for 1 hr on PND 13, 16, 17), leading to sharply contrasting alterations in Dom and Sub offspring’s stress coping styles as adults. Offspring born to stressed Dom dams displayed enhanced exploratory behavior in the Elevated Plus Maze, and heightened dominance in the Dominant-Submissive Relationship (DSR) food competition test, suggesting anxiolytic effects of prenatal stress among Dom mice. In marked contrast, stressed Sub offspring remained immobile in the Forced Swim test three times longer than their naïve Sub counterparts, alongside impaired performance in the DSR test.
In order to evaluate the effects of PNS upon mice’s HPA axis regulation, we measured adult offspring’s serum corticosterone levels, which were significantly elevated only among Sub mice born to stressed dams. Given the complementary roles of the hippocampus and amygdale in HPA axis regulation, we measured Glucocorticoid Receptor (GR) levels of Dom and Sub offspring born to PNS dams. PNS markedly elevated hippocampal GR mRNA and protein levels among Dom mice, while lowering Subs’ GR levels. However, PNS demonstrated opposite effects in the amygdale: Sub mice born to stressed dams demonstrated significantly heightened amygdale GR immunoreactivity, suggesting heightened sensitivity to glucocorticoids in the amygdale of Sub mice, alongside more efficient priming of hippocampal negative feedback upon the HPA axis in Doms. Further study of the dimodal effects of PNS upon limbic GR expression will elucidate the functional role of brain region-specific prenatal programming of the GR in resilience or vulnerability to stress.
Formation of diploid cells in budding yeast calls a mating process. It occurs when two haploid cells with opposite phenotypes "a" and "alpha" grow up in an asymmetric fashion to each other and fused. This process is activated by "a" and "alpha “pheromone factors that are expressed and secreted by haploid cells. The mechanism of "alpha “pheromone (MFA1/2) synthesis occurs through an ER -Golgi pathway by alpha haploid cells. "Alpha” pheromone is transported and secreted from the cell by secretory vesicles. Recently we discover that pheromone "a"(MFA1/2) expression dependent on mechanism of mRNA localization. mRNA is delivered to a mating projections (shmoo), locally translated and secreted from the a cells. In this work we found regulatory factors ofMFA1/2 mRNA localization and expression. We show that actin cytoskeleton and ER play an important role in this process. The malfunction of one of regulatory factor affected "a" factor expression, progression of mating process and lead to mating sterility in yeast.
Poster#16: Virally-induced overexpression of Synapsin IIb in the hippocampus alters social behavior in mice

Maryia Bairachnaya, Moshe Gross, Tatiana Tikhonov, Igor Koman, Elimelech Nesher, Michael Kirby, Anton Sheinin, Izhak Michaelevski, Alexandra Stavskey, Daniel Gitler, Albert Pinhasov

Abstract

By selective breeding based on mouse behavior in the Dominant-Submissive Relationship (DSR) food competition test, we developed two distinct mouse line derivatives from the Sabra strain (Wild Type) demonstrating dominance (Dom) or submissiveness (Sub). Using qRT-PCR and Western Blot analysis, we found the Synapsin IIb isoform (Syn IIb) of the SYN2 gene to be constitutively upregulated in the hippocampus and striatum of newborn, juvenile and adult Sub mice, relative to Dom and Wild Type. Furthermore, mating, parturition, as well as antidepressant treatment all reduced the natively-elevated levels of Syn IIb in Sub mice while concomitantly reducing their submissive behavior. Thus, we hypothesized that virally-induced overexpression of exogenously-applied Syn IIb would reduce the innate dominance observed in Dom mice.

Since Dom and Sub mice exhibit significant differences in short- and long-term synaptic plasticity in the CA3 region of the hippocampus, an hSyn:EGFP-Syn-IIb AAV2 vector was constructed to induce expression of EGFP-tagged Syn IIb in neurons after stereotaxic delivery to CA3. Four weeks following viral injection, Dom mice treated with the Syn IIb vector demonstrated significantly increased submissive behavior in the DSR-test, in comparison with vehicle-injected Dom counterparts. Immunohistochemical analysis of hippocampi revealed significantly increased Syn IIb levels in the
CA3 region as well as in CA1 and Dentate Gyrus of virally-injected mice. Thus, our study suggests Syn IIb to be a causal agent in the regulation of some neuronal pathways responsible for social interaction. Further study will evaluate the mechanisms by which elevated expression of Syn IIb in the hippocampus induces submissive behavior.
Poster#17: FACT as a target for cancer treatment

K. Gurova, E. Nesher, A. Safina, Sh. Elbaz, T. Kardashian, Igor Koman

Abstract

One of the major obstacles of current anti-cancer research is finding a way to effectively kill tumor-initiating cells, or so called cancer stem cells (CSC). Targets specific for CSC are needed for execution of this task. Chromatin remodeling remodeling complex FACT (Facilitates Chromatin Transcription) is a histone chaperone consisting of two subunits, Suppressor of Ty 16 (SPT16) and Structure Specific Recognition Protein 1 (SSRP1). As a chromatin remodeler, FACT is involved in binding and destabilization of nucleosomes for RNA polymerase passage, as well as protecting them from falling apart. FACT is critically important for CSC survival. We found that the presence of FACT subunits directly correlates with poor differentiation status, high probability of metastasis and low overall survival as well as the presence CSC markers. Therefore, tumors with high frequency of FACT-positive cells are likely to have a high proportion of CSC. Importantly, tumor cells that express FACT, but not normal cells, cannot tolerate inhibition of FACT expression. Modulation of FACT levels, up or down, results in induction or suppression of CSC properties of transformed cells, respectively. We previously showed that small molecules (curaxins) with broad anti-cancer activity indirectly inhibit FACT. In particular, curaxins induced molecular changes in tumor cells that were consistent with its established mechanism of action: depletion of soluble FACT from the nucleoplasm, activation of p53 (in those cells with a functional p53 pathway), and accumulation of inactive NF-κB in nuclei. We also found that function and level of FACT depends on the interaction of the two FACT subunits with their own mRNAs. Therefore, elimination of binding of any of these components makes this complex very
unstable and easily degradable. Moreover, interference with FACT subunits binding to each other using genetic tools is toxic for tumor cells. The important feature of curaxins is that, in contrast to existing anti-cancer agents, they are more toxic to CSC than to the bulk tumor cell population and normal stem cells. These data suggest that FACT is a promising target in CSC.
Poster#18: CircosVCF – Circos Visualization of Whole-Genome Sequence Variations Stored in VCF Files

D. Levy, E. Drori, M. Salmon-Divon

Abstract

Visualization of whole-genome sequence variations in a meaningful manner is needed to assist researchers in gaining new insights into the underlying data, especially when it comes in the context of whole genome comparisons.

One way of visualize complex genomic information in high-throughput manner is by using the attractive circos plots. However, generating circos visualization of whole genome variation information is a challenging task, which requires computational skills.

CircosVCF is a web based visualization tool of genome-wide variant data described in VCF files using circos plots. The provided visualization capabilities, gives a broad overview of the genomic relationship between genomes, as well as allowing focusing on specific SNP regions. The user friendly interface of CircosVCF supports for an interactive design of the circles in the plot, as well as integration of additional information such as experimental data or annotations. CircosVCF was implemented in JavaScript and is freely available at http://www.ariel.ac.il/research/fbl/software
Department of Chemical Sciences
Abstract

The Fenton like reactions are of key importance in advanced oxidation processes, AOPs, and in biology. Their mechanism was in debate for many years: the question being whether the active intermediates formed are hydroxyl radicals or $L_{m-1}M^{n+2}=O$ complexes. It is now accepted that usually the mechanism involves two steps:

1. $M^nL_m + H_2O_2 \leftrightarrow L_{m-1}M^n(O_2H)/L_{m-2}M^n(H_2O_2)$
   
   $L^{-} \rightarrow M^{n+1}L_m + \cdot OH + OH^-$

2. $L_{m-1}M^n(H_2O_2) \rightarrow L_{m-1}M^{n+2}=O + H_2O$
   
   $RH \rightarrow M^{n+1}L_m + R \cdot + H_2O + OH^-$

It was also shown that at least for $M = Fe$, in the presence of excess $H_2O_2$, the following reaction is of major importance:

3. $(H_2O)_2Fe(OOH)^{2+} + Fe(H_2O)_6^{2+} \rightarrow ((H_2O)_3Fe^{IV}=O + Fe(H_2O)_6^{3+})/(2Fe(H_2O)_6^{3+} + \cdot OH)$

Recent results point out that the reactions:

4. $(H_2O)_{6+1}M^n(OOH)(H_2O_2) \rightarrow (H_2O)_{6+1}M^n(OOH)(OOH)_{1/2}(OH) + OH$

5. $(H_2O)_{6+1}M^n(OOH)(H_2O_2) \rightarrow (H_2O)_{6+1}M^{n+1}(OOH)(OOH)_{1/2}(OH) + OH$

are the source of the ROS when reaction (2) is endothermic. Furthermore in the presence of $HCO_3^-$ /$CO_3^{2-}$, which is present in AOPs and in biology, the reactions:

6. $LM^n(CO_3)(H_2O)_n + H_2O_2 \leftrightarrow LM^n(CO_3)(H_2O)_{n-2}(OOH)$

7. $LM^n(CO_3)(H_2O)_{n-1}(OH) \leftrightarrow LM^n(CO_3)(H_2O)_{n-1}$

8. $LM^n(CO_3)(H_2O)_{n-1} \rightarrow LM^{n-1}(OH)(H_2O)_n + CO_3^-$

9. $LM^n(CO_3)(H_2O)_{n-2}(OH) + H_2O_2 \leftrightarrow LM^n(CO_3)(H_2O)_{n-2}(OOH) + H^+$

10. $LM^n(CO_3)(H_2O)_{n-2}(OOH) \rightarrow LM^n(OH)^{2+}(OOH)(H_2O)_{n-2} + CO_3^-$
have to be considered. This means that in these systems carbonate anion radicals are the major reactive species.
Abstract

Metal complexes, particularly those of transition metals, are utilized as catalysts for a myriad of applications in countless natural and man-made systems, from the active sites of bacterial enzymes to the industrial-scale manufacturing of plastics. Our research involves the design, synthesis and characterization of various metal complexes, and focuses on two main avenues of metal-complex-based catalysis, both of which are related to environmentally-important issues. One research direction involves the utilization of urea, an abundant waste material, as an alternative source of fuel and chemicals. We are developing nickel complexes bearing phenol-based ligands as potential catalysts for the electrochemical oxidation of urea. Active complexes will be incorporated into fuel cells that will generate electricity from this waste material. The second main research direction involves the development of metal-complex-based catalysts for the efficient decomposition of toxic organophosphate contaminants, such as pesticides and warfare agents. A combinatorial approach will be employed for catalyst identification, based on a library of phage-displayed peptides that will be scanned for organophosphate hydrolysis in the presence of various transition metal cations. Catalyst screening and isolation will be aided by activity-based probes, which are currently being designed and synthesized. These and other aspects of our research will be outlined in the presentation.
Research Name: Polarity Reversal in Organic Synthesis

Shimon Maksymenko, Shlomy Aravaa, Jayprakash Kumara, Peter Fristrupb, Mark A. Ironc, Alex M. Szpilman

Abstract

Nature has determined the roles of chemical reagents in organic synthesis as either electrophiles or nucleophiles. Umpolung or Polarity Reversal is a powerful concept that allows these roles to be switched thereby enabling a much larger array of methods to assemble complex organic molecules.

Umpolung of enolates mediated by hypervalent iodine reagents has shown itself to be the method of choice for functionalizing of carbonyl compounds. This is amply illustrated by numerous papers describing halogenations, oxygenations, aminations, and many other applications.[1] Recently we reported the use of this concept in C-C bond forming reactions.[2,3] These reactions are widely believed to proceed through iodo(III)-enolates.[1] However due to their high reactivity they are difficult to characterize and they have consequently been researched mainly through computational studies.[2,4]
We have now characterized the iodo(III)-enolates generated from acetophenone by React-IR and NMR. A particular point of discussion in the community and a scientific challenge was to determine whether the hypervalent iodine is attached to the O of the enolate or to the C of its keto-form. The application of the iodo(III)enolates in C-C bond forming synthetic reactions, including in reactions that lead to the formation of quaternary carbons, will be discussed.[5]


Poster#19: Corrosion behaviour of MRI 230D and AZ91D magnesium alloys with Plasma Electrolytic Oxidation treatment

Barbara T. Kazanski, Alex Lugovskoy, Michael Zinigrad

Abstract

The applicability of Plasma Electrolytic Oxidation treatment for the corrosion protection of high-pressure die-cast AZ91D and high-pressure die-cast creep resistant MRI 230D magnesium alloys in 3.0 wt% NaCl aqueous solution and corrosion behavior of these alloys was studied in this work by several electrochemical and non-electrochemical techniques. Plasma electrolytic oxidation (PEO) of an MRI 230D and AZ91D alloys was accomplished in a silicate-base electrolyte with KF addition using an AC power source. The corrosion process of both alloys before and after PEO treatment was evaluated by open circuit potential (OCP) measurements, electrochemical impedance spectroscopy (EIS), linear polarization tests, linear sweep voltammetry (Tafel extrapolation) and chemical methods: mass loss and hydrogen evolution. Corrosion rates for each method were calculated and compared and the morphology of corroded surface studied. According to the tests results, the corrosion of both alloys is localized so that corrosion pits are developed on a specimen surfaces. Corrosion rates measured by different methods are all on the order of magnitude of 0.25 – 3.7 mm / year. The protection of both alloys by the PEO decreases the rate of corrosion and shifts the corrosion potential to a more noble value. However, the effect that PEO process has on corrosion resistance of MRI 230D magnesium alloy is not always unambiguous. An attempt to explain the influence of the PEO process on the corrosion behaviour of the MRI 230D alloy is presented. The localized character of corrosion causes some deviations in the results obtained even by the same method and deviations of corrosion rates are observed for all the methods. SEM and light
microscope observation of corroded specimens demonstrated the localized character of corrosion as well, at least at the initial stages.

Typical EIS Nyquist plots for MRI 230D in 3% NaCl
Poster#20: Consolidation of (Ti,Al)N nano powder by Spark Plasma sintering (SPS)
Maya Radune, Sergei Kalabukhov, Strul Moisa, N. Fragie, Michael Zinigrad

Abstract

The present study is focused on the fabrication of bulk materials from (Ti,Al)N nano powders by SPS apparatus. The supersaturated (Ti,Al)N solid solutions with various fraction of AlN was prepared by high energy ball milling (HEBM). SPS consolidation was conducted at 1400°C for 10min with heating rate 50deg/min. All the specimens have a relative density (RD) close to 100%, while the RD of pure TiN was only 97.9%. The maximum mechanical properties (hardness of 1830HV, Young modulus of 416GPa and fracture toughness $K_{IC}$ of 13.44MPa·m$^{0.5}$) we obtained for the specimens with 20%mol of AlN, which display submicron microstructure. These properties are significantly higher than that for SPS-processed pure TiN samples (hardness 1520HV, Young modulus of 385GPa and fracture toughness $K_{IC}$ 3.94 MPa·m$^{0.5}$). The consolidation mechanism of nano powder of the supersaturated (Ti,Al)N solid solution will be discussed.
Poster#21: Bio-Labile Peptidyl Delivery Systems Towards Sequential Drug Release

Elena Ragozin, Gary Gellerman

Abstract

Compact carriers for peptidyl delivery systems (PDSs) loaded with various drugs were synthesized using a simple and convenient solid phase organic synthesis (SPOS) strategy, including semi-orthogonal functional group protection schemes. Each attachment point of the compact carrier can thus be bound to an anticancer agent through a biodegradable covalent link. Chemo- and bio-stability experiments of a model peptidyl platform loaded with three different drugs revealed pH and liver homogenate (metabolic) dependent sequential release behavior. The versatility of this approach will serve to expedite the preparation of PDS libraries. This approach may prove useful for applications suitable for personalized medicine where multiple drug delivery is required in a sequential and controlled fashion.
Using peptides as carriers is one of the most powerful techniques in drug delivery. In cancer, this field is extensively investigated while focusing on targeting the integrin family receptors, which are essentially important for the angiogenic and metastatic processes. The avb3 integrin is highly expressed on many tumor cells and can be effectively targeted by an RGD tripeptidic sequence [1a-b, 2]. Many publications were presented in the last few decades regarding RGD containing peptides which were used as selective carriers of biological active agents to cancer cells.

Herein we present the syntheses, stability profiles and biological evaluation of different peptide-drug conjugates [3-4] with a focus on systems which are based on the RGD recognizing moiety [5-6].


3 - Gilad Y, Firer MA, Rozovsky A, Ragozin E, Redko B, Albeck A and Gellerman G; "Switch off/switch on" regulation of drug cytotoxicity by conjugation to a cell targeting peptide. EJMC 85 (2014) 139-146

4 - G. Gellerman, S. Baskin, L. Galia, Y. Gilad and M. A. Firer; Drug resistance to chlorambucil in murine B-cell leukemic cells is overcome by its conjugation to a targeting peptide. Anti-Cancer Drugs 2013, 24:112-119.

5 - Gilad Y., Weintraub S., Albeck A. and Gellerman G; Synthesis of novel protected Na(w-Drug) amino acid building units and their incorporation in peptide drug conjugates. Submitted

6 - Gilad Y., Noy E., Senderowitz H., Albeck A., Firer MA and Gellerman G; Computational, drug release and biological evaluation of three new anti-cancer cyclic RGD peptide conjugates. Submitted
Abstract

Multiply loaded four new RGD peptide-anticancer agents conjugates were synthesized in order to evaluate their biological activities comparatively with their monomeric analogs. Drug release profiles in different mediums of these new conjugates also were evaluated. The cyclic RGDFK penta-peptide was selected as a targeting moiety due to its high affinity and selectivity to αvβ3 integrin receptor, which is commonly overexpressed in different cancerous cells. The cyclic peptide core was split through the side chain of its Lys by coupling of a sixth AA - either Lys or Ser - to the primary amine, resulting two functional sites which enabled the loading of two equivalents of therapeutics onto a single targeting warhead.

Coupling of 2 eq. of CLB or CPT to Lys splitter resulted in homo-dimeric conjugates 1a&1b respectively, with identical attachment sites for each of the two drugs. The homodimeric conjugate 1c, with two different chemical functionalities for each chemotherapeutic, was resulted by splitting
the core peptide with Ser and consequent loading of the amine and the hydroxyl of Ser with 2 eq. of CLB. The heterodimeric conjugate 1d of CLB and CPT was synthesized by loading each one of the primary amines of the splitting Lys with two different drugs - CLB and CPT. The excess of the drugs loaded on the targeting device reflected in their therapeutic efficacy towards the targeted cancer cells, while their functional versatility was resulted in a variability of their drug release profiles.
Poster#24: "Switch off/switch on" regulation of drug cytotoxicity by conjugation to a cell targeting peptide

Y. Gilad, A. Rozovsky, E. Ragozin, B. Redko, A. Albeck, M.A. Firer, Gary Gellerman

Abstract

Targeted delivery of chemotherapeutic agents is one of the most important and challenging issues in modern chemotherapy. Targeted drug delivery using peptides with the capability of recognizing unique/over-expressed receptors on a cancer cell surface, is a powerful and much inquired technique (1). The conjugation of a number of anti-cancer therapeutics to one targeting peptide, through amino acid platforms, is an opportunity for an efficient and economical utilization of a limited amount of these receptors. In addition, such conjugation can create a multi pro-drug system, in which drugs’ toxicity is reduced. Therefore, a 'second chance' is given to candidates that failed advanced biological trials due to their over-potency.

We previously have shown a facile synthesis of an anticancer agent - bis-9-anilinoacridine - peptidyle conjugates using Fmoc SPOS (2). Here we show a synthesis of more sophisticated Bi-nuclei amino acid scaffolds, their farther conjugation to a targeting peptide and finally in-vitro tests of these conjugates: This report demonstrates that murine B-cell leukemic cells, previously resistant to a chemotherapeutic chlorambucil, can be made sensitive to that drug so long as it is conjugated to a targeting peptide (3). Another result which is shown therein, is that the linkage of chemotherapeutics to a platform [DNA alkylation agent CLB and Topo I inhibitor camptothecin (CAMP) were linked to Lys] and subsequent conjugation of this platform to the carrier peptide, gains
"switch off/switch on" capabilities specifically activating this "cocktail" of drugs in murine leukemic cells which are expressing antibodies to the carrier (4).


Boris Redko, Elena Ragozin, Bazylevich Andreii, Tuchinsky Helena, Albeck Amnon, Shekhter Zahavi Talia, Oron-Herman Mor, Kostenich Genady, Gary Gellerman

Abstract

Peptide conjugates containing somatostatin (SST) cyclic analogs as a targeting moiety are able to deliver chemotherapeutic agents specifically to cancer cells expressing SST receptors (SSTRs), and hence increasing their local efficacy while limiting the peripheral toxicity. Here, we report on the synthesis and biochemical characterization of new SSTR-specific anticancer peptide conjugates, with different anticancer payloads acting through different oncogenic mechanisms to evaluate their biological activities and to provide a comparative study of their drug release profiles. The SSTR2-specific backbone cyclic peptide 3207-86 was chosen for the synthesis of a variety of novel anticancer drug conjugates with a broad drug release capabilities. The N-terminus of 3207-86 was equipped with GABA to generate free amino group available for the conjugation of chlorambucil, Camptothecin (CPT), Combretastatin 4A, ABT-751, and Amonafide through the formation of various biodegradable bonds. The chemo- and biostability/drug release of all the synthetic compounds was investigated at various pHs and in the presence of mouse liver homogenate, respectively. Their selective cytotoxic effect was evaluated on several human cancer cell lines that overexpress SSTR2. Compared with the free drugs, our peptide–drug conjugates exhibited considerable cytotoxic effect on cancer cell lines versus low SSTR2-expressed human embryonic kidney cells. Functional versatility of the conjugates was reflected in the variability of their drug release profiles, whereas the
conserved sequence of a selective binding to the SSTR2 likely preserved their binding to the receptor and consequently their favorable toxicity toward targeted cancer cells.
Poster#26: Ru-Co-Se Novel Pt-free Catalysts for Oxygen Reduction in Fuel Cells and Metal Air Batteries

Hanan Teller, Shmuel Rosenfeld, Alex Schechter

Abstract

Oxygen reduction reaction (ORR) plays a key role in electrochemical energy conversion systems, in particular, in fuel cell and metal-air batteries cathodes. Platinum is considered the state of the art catalyst for ORR in acidic fuel cells. However, high cost and long term stability shortcomings stimulate the quest for alternative materials. Ru chalcogenides and more specifically RuSe compounds were investigated in the past, demonstrating high ORR activity and high tolerance towards methanol contamination, which is crucial in direct methanol fuel cells (DMFC).

In order to further decrease the Ru content and enhance the ORR rate, we synthesized Ru-Co-Se materials with several Ru to Co molar ratios, applying different synthetic routes. The materials were characterized by XRD, Raman, EDS, and their ORR catalytic activity and kinetic parameters were determined by rotating disk ring electrode (RRDE). It was found that Ru3CoSe2 shows comparable electroactivity with Ru2Se, which has the highest activity known so far (figure 1). The performance of these catalysts was also measured at pH=7 in order to determine their electroactivity as a potential cathode material for bio fuel cells.
Figure 1. Current vs. Potential curves obtained from RDE measurements of oxygen reduction reaction on Ru₂Se and Ru₃CoSe₂ (0.5M H₂SO₄, scan rate = 2mV/sec, 1800 rpm).
Abstract

Electron exchange columns are analogous to ion exchange columns and comprise entrapment of a strong redox reagent that performs oxidation/reduction cycles with the substrate passing through the columns. Such columns are reversible in nature and are more advantageous as the entrapped redox reagent do not contaminate the products. The electron exchange columns reported so far were designed for oxidation processes and have significant drawbacks, such as relatively small redox reagents that result in leaching, and some organic ligands are more procumbent to redox sensitivity and decomposed with time.1-2 Therefore in order to overcome these drawbacks, a redox active polyoxometalate was entrapped in silica sol-gel matrices for electron exchange column applications. Polyoxometalates (POMs) are the most suitable candidates for this purpose having the ability to accept/release several electrons without decomposing and changing their structure and moreover are expected to have stability for many redox cycles.3 The properties of the columns strongly depend on the composition of the precursors used to prepare the matrices.4 The columns exhibit good reversibility and are the first reducing electron exchange columns ever prepared.
References:


Poster #28: Electro Catalytic Activity of Nickel Nanoparticles Deposited On High Surface Area Tin Dendritic Supports Toward Urea Oxidation

Srikanth Kolagatla, Palaniappan Subramanian, Alex Schechter

Abstract

Urea is a cheap and widely available commodity, which is non-toxic, stable, and therefore easy to transport and store. This is a promising material which can be used as a hydrogen carrier either directly or as a source of ammonia. Electrolysis of urea that directly converts urea to hydrogen through electrochemical oxidation with an inexpensive nickel catalyst is been studied extensively because, the nickel catalysts showed both higher current densities and lower oxidation potentials for the electro-oxidation of urea than those of the noble metal catalysts. However, there exist a large over potential between the theoretical oxidation potential (-0.4 V Vs SHE) and observed oxidation potential (0.45 V Vs. SHE) using nickel catalyst in electro-oxidation of urea. Nanostructured metal particle has been widely used as catalyst support to exploit the high surface area of these materials. In this context, herein we report the electro synthesis of tin dendritic structures generated from electroreduction of SnCl2 in presence of sodium citrate as support for nickel nanoparticles. Nickel nanoparticles electrodeposited on Sn dendritic structures were characterized using SEM, XRD and ICP measurements. Cyclic voltammetry was used to evaluate the catalytic activity of Ni nanoparticles on tin dendritic supports. In addition, in-situ surface enhanced Raman spectroscopic experiment was performed to understand the potential dependence of nickel hydroxide catalyst obtained in the presence of urea.
Poster#29: Carbon Supported nickel manganese spinel oxide electrodes: Are they good at catalyzing the oxidation of glycine in alkaline solutions?
Roopathy Mohan, Palaniappan Subramanian, P.Sivakumar, Aharon Gedanken, Alex Schechter

Abstract

Protein is a kind of important organic matter and commonly found in organic wastewaters, such as domestic wastewater and food processing wastewater. As minimum units of protein, amino acids widely exist in wastewater and may cause carbon and nitrogen pollutions. Glycine is the simplest of amino acids, thus it serves as an important model compound in biophysics and biochemistry of proteins. Electrochemical oxidation of glycine, owing to the poor kinetics, is found to be efficient only in the presence of suitable electrocatalyst such as metallic nickel or carbon supported nickel oxide particles. Herein we have explored the possibilities of using a bimetallic catalyst based on nickel and manganese oxide towards enhancing the electrochemical oxidation activity of glycine. Three different composition of Nickel manganese oxide spinel material namely NiMn$_2$O$_4$, Ni$_{1.5}$Mn$_{1.5}$O$_4$ and MnNi$_2$O$_4$ was synthesized by a simple template-free hydrothermal route followed by a thermal treatment in air at 800°C. The structural properties of these materials were evaluated by XRD analysis and the catalysts morphology was characterized by SEM and EDS. The electrochemical properties was assessed by cyclic voltammetric studies which reveals that the as prepared spinel nickel manganese oxide materials displayed enhanced oxidation current density and lower anodic onset potetnial towards glycine oxidation in alkaline solution than the corresponding single oxides (NiO and Mn$_2$O$_3$).
Poster#30: Chemical Modifications of the Bimane Flourophore

Partha J. Das, Omer Goldstein, Daniel Schneiderman, Flavio Grynszpan, Michael Firer

Abstract

The use of small molecule fluorescent probes in chemical biology is particularly desirable as they minimize the perturbations and limit the toxic interference with biological functions.1 In this context syn-bimanes (such as 1) are some of the most compact fluorescent labels available for biochemical labeling applications. To accomplish that task monobromo-bimane (mBBr, 2) undergoes facile nucleophilic substitutions mainly by reacting thiols. This has been widely used to detect glutathione in living cells under physiological conditions.2,3 We expanded the scope of bimane derivatization by synthesizing a keto-bimane derivative (3) that can react selectively with nucleophilic amines via a protonated Schiff base.

The syn-bimane scaffold is characterized by a typical $\lambda_{ex}= 356$ nm and $\lambda_{em}= 485$ nm (in MeOH).

Most bimane derivatives fluoresce at the same emission range except for derivative including fused aromatic rings. A new attempt has been made for the modification of the bimane fluorophore, and thus its fluorescent properties, merely by exchanging an O atom for an S atom (as in 4) while keeping the size of the fluorescent probe. Our preliminary results indicate that instead of affecting the $\lambda_{em}$, bimane 4 presents a red shifted $\lambda_{ex}$ and an unexpected zero Stokes shift.
Synthetic approaches and observed properties of the chemically modified bimanes will be presented.

References:


Poster#31: The Synthesis of Metallic β-Sn Nanostructures for Use as a Novel Pt Catalyst Support and Evaluation of Their Activity toward Methanol Electrooxidation

Olga Krichevski, Hanan Teller, Palaniappan Subramanian, Alex Schechter

Abstract

This study offers a unique insight into the use of high surface area metallic tin as support material for platinum catalysts for fuel cell application. We have synthesized high surface area metallic β-tin nanostructures (TNSs) in aqueous solutions by novel one-pot process and used it as a platinum catalyst support in methanol electrooxidation reaction. Rigorous study of parameters controlling the size and shape of TNSs was performed, including selected surfactant molecules at various concentrations, tin salts, and the addition of sodium citrate. Rod-shaped particles with a 50-nm diameter and 500-nm length were obtained from solutions of selected surfactant in concentrations of 1–20 mM by sodium borohydride reduction. These particles had a β-Sn crystalline core with a main lattice plane of (101) and were covered by a 4-nm oxide shell. A maximal surface area of 170 m² g⁻¹ was measured from a sample prepared by using low concentration of sodium dodecyl sulfate (SDS) (1 mM). This sample is composed of nanorods and nano semi-spherical shape tin particles. Addition of sodium citrate, which acts as a Sn2+ ion ligand, yields longer rods. Electrochemical oxidation of methanol on platinum catalyst, supported on metallic Sn nanostructure, exhibits a high activity, which is comparable to commercial carbon-supported platinum catalysts. In situ surface-enhanced Raman (SER), emphasizing the role of surface oxides on the methanol oxidation activity, further studied methanol oxidation on Pt/TNS, Pt/C, and Pt-Sn alloy catalyst.
Poster#32: Catalytic Decomposition of Hazardous Organophosphate Agents  
Ankana Roy, Partha J. Das, Flavio Grynszpan, Michael Montag, Michael Firer

Abstract

Organophosphates are organic esters of phosphoric acid, which are widely used for various industrial and household applications, e.g., as pesticides, plasticizers, flame retardants and solvents. Some organophosphates are also employed as chemical warfare agents. Those compounds that are utilized as pesticides or warfare agents are highly toxic, and may also be environmentally persistent. Their toxicity stems from potent inhibition of the enzyme acetylcholinesterase, which is crucial for the regulation of neural activity.

The adverse effects of organophosphate toxins on human health and the environment necessitate efficient decontamination strategies. This may be carried out by physical means (e.g., adsorption, flushing) or by chemical decomposition to more benign products. The latter is often done by hydrolysis, either stoichiometrically (e.g., alkaline solutions) or catalytically (e.g., enzymes, transition metal complexes). Contemporary examples of inorganic catalysts for organophosphate hydrolysis include polyoxoniobates, zirconium-based metal-organic frameworks, and zinc-based complexes.

We have recently begun efforts to develop new metal-complex-based catalysts for the decomposition of organophosphates, focusing on hydrolytic cleavage of P=O bonds. A combinatorial approach has been chosen for catalyst identification, based on a library of phage-displayed peptides that will be scanned for hydrolytic activity in the presence of various transition metal cations. Catalyst screening and isolation will be aided by activity-based probes (e.g., fluorescent tags), which
are currently being designed and synthesized. Herein, we shall outline our general strategy for catalyst development, including some preliminary results pertaining to the synthesis of organophosphate toxin surrogates.
Fuel cells are electrochemical devices which convert chemical energy to electrical energy in a much more efficient and clean manner compared combustion engines. Typically, these devices utilize pure hydrogen and air that reacts on Pt based catalyst in the anode and the cathode respectively. Nevertheless, the cost of Pt and its poisoning by CO in the ppm level in hydrogen prevents their commercialization market. Highly dispersed very thin layers of Pt on metallic Sn is being studied in our group. This approach may provide high utilization of Pt as well co-catalysis of adsorbed CO removal from Pt surface via a well-known Pt-Sn bi-functionality mechanism\textsuperscript{1,2}.

PtSn alloys and their CO adsorption have been reported before. However, this research deals with tin coated by Pt and not with an alloy. The effect of various number of Pt(111) slabs on a well-defined core of Sn was studied. The effect of Pt layer number on the adsorption energy of CO was studied in comparison to the adsorption energy of CO over pure Pt.

The approach in this research was mainly computational. The calculations have been carried out using the Vienna Ab initio Simulation Program (VASP) using periodic boundaries, PAW PBE pseudopotentials and default cut off energies were used. According to the computational result, the coated Pt on a tin core changes the adsorption energy of CO on selected sites and geometrical configurations. Correlation between the number of Pt slabs and the adsorb CO adoption energy was found. Reducing the adsorption energy was demonstrated on a single atomic layer slab.

Poster#34: Nickel Complexes as Potential Catalysts for Urea Conversion

Kalaiyarasi Rajavelu, Alex Schechter, Michael Montag

Abstract

In order to meet the growing global demands for energy in the age of environmental awareness, alternative clean energy sources must be explored. Hydrogen gas is such a source of energy, with water being the only byproduct in its energy conversion process. Urea electrolysis is a promising new technology that has the capacity to produce high-purity hydrogen from sustainable sources, such as wastewater. Urea is a highly attractive hydrogen carrier, because it is abundant, stable, non-toxic and non-flammable, and can be stored and transported conveniently, since it is solid under ambient conditions. Nickel metal and nickel oxides have been studied extensively as electrocatalysts for urea conversion, providing relatively high current densities and low overpotentials of oxidation to CO₂ and N₂. Moreover, nickel is intimately involved in urea hydrolysis within the active site of the enzyme urease, and this has inspired chemists to mimic the naturally-occurring bimetallic core of this enzyme. Simplified synthetic bimetallic model systems have been studied as part of the effort to probe the enzymatic mechanism, as well as examine other reactivity patterns. To the best of our knowledge, no molecular nickel-based system has thus far been reported to promote the electrochemical conversion of urea. Herein, we present the synthesis and characterization of nickel complexes of phenol-based binucleating ligands. These are intended to mimic the active nickel-oxide surfaces previously shown to promote urea conversion, with the aim of developing catalysts for urea electrooxidation.
Poster#35: Ru-Co-Se Novel Pt-free Catalysts for Oxygen Reduction in Fuel Cells and Metal Air Batteries

Hanan Teller, Shmuel Rosenfeld, Alex Schechter

Abstract

Oxygen reduction reaction (ORR) plays a key role in electrochemical energy conversion systems, in particular, in fuel cell and metal-air batteries cathodes. Platinum is considered the stat of the art catalyst for ORR in acidic fuel cells. However high cost and long term stability shortcomings stimulate the quest for alternative materials. Ru chalcogenides and more specifically RuSe compounds were investigated in the past demonstrated high ORR activity of as well as high tolerance towards methanol contamination, which is crucial in direct methanol fuel cells (DMFC).

In order to further decrease the Ru content and enhance the ORR rate we synthesized Ru-Co-Se materials with several Ru to Co molar ratios, applying different synthetic routs. The materials were characterized by XRD, Raman, EDS and their ORR catalytic activity and kinetic parameters were determined by rotating disk ring electrode (RRDE). It was found that Ru3CoSe2 shows a comparable electroactivity with Ru2Se which has the highest activity known so far (figure 1). The performance of these catalysts was also measured at pH=7 in order to determine their electroactivity as a potential cathode material for bio fuel cells.
Figure 1. Current vs. Potential curves obtained from RDE measurements of oxygen reduction reaction on Ru$_2$Se and Ru$_3$CoSe$_2$ (0.5M H$_2$SO$_4$, scan rate = 2mV/sec, 1800 rpm).
Poster#36: The Mechanism Of Metal Nanoparticles Catalyzed Water Reduction By Sodium Borohydride: Studied By Isotopic Markers

Alina Sermiagin, Tomer Zidki

Abstract

Nanocatalysts and in particular metal nanocatalysts are one of the most exciting subfields emerged from the nanoscience. Nanoparticles (NPs) are known for their remarkable catalytic abilities and they are extensively investigated due to their properties. Furthermore, water reduction is a reaction vastly studied. There are many studies engaged in the catalytic water reduction by sodium borohydride but the mechanism of these reactions is still unknown.

We are investigating the catalytic water reduction by metal NPs catalysts (silver: Ag-NPs, gold: Au-NPs and platinum: Pt-NPs) using sodium borodeuteride (NaBD4) as an isotopic marker. We monitored the reactions using mass-spectrometry (MS) by following the masses at 2, 3 and 4 amu corresponding to H2, HD and D2, respectively. From the ratios between these products one can conclude about the reduction mechanism.

The reported results indicate that: