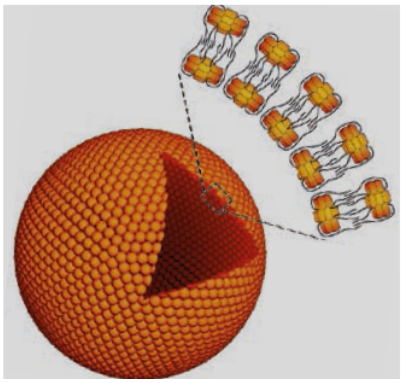
Ilse Katz Institute for Nanoscale Science and Technology
Ben-Gurion University of the Negev

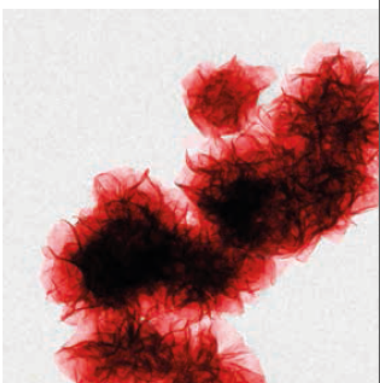
מכון ויצמן למדע
WEIZMANN INSTITUTE OF SCIENCE

Nanoparticles at the Interface Between Biology and the Materials World

July 5-6th, 2015

The David Lopatie Conference Centre
Weizmann Institute of Science, Israel





Sunday

	09:00-09:45	**Registration**
	09:45-10:00	**Welcome and greetings**
Invited	10:00-10:30	**Prof. John B. Matson**, Department of Chemistry, Virginia Tech *Materials for Therapeutic H_2S Delivery*
	10:30-11:00	**Dr. Anna Roig**, Group of Nanoparticles and Nanocomposites. Institut de Ciència de Materials de Barcelona *Albumin-SPIONs: protein surface binding, nanoparticles uptake in cells and fate*
	11:00-11:30	**Prof. Yitzhak Rabin**, Department of Physics, Bar Ilan University *A truly complex fluid: particles with random interactions*
	11:30-12:00	**Coffee**
	12:00-12:30	**Dr. Alexander Vaskevich**, Department of materials & Interfaces, Weizmann Institute of Science *Application of surface "click" reactions to localized plasmon biosensing*
	12:30-13:00	**Dr. Anna Laromaine**, Group of Nanoparticles and Nanocomposites. Institut de Ciència de Materials de Barcelona *Initial evaluation of Iron oxide nanoparticles in C. elegans. A novel strategy to evaluate nanoparticles?*
Invited	13:00-13:30	**Prof. Jinwoo Cheon**, Yonsei University, South Korea *Magnetic nanoparticles: a PRECISION Tool for cell Imaging and activations*
	13:30-14:30	**Lunch**
Invited	14:30-15:00	**Prof. Ehud Landau**, Department of Chemistry, University of Zurich *Concepts and applications of mesoscopic lipidic nanomaterials in biomedicine*
	15:00-15:25	**Mr. Christian Spengler,** Experimental physics, Universität des Saarlandes *Interplay of forces during adhesion & adsorption of biofilm components*
	15:25-15:50	**Ms. Margarita Ritenberg**, Department of Chemistry, Ben Gurion University *Fluorescent amphiphilic carbon dots as a new tool for visualization of Erwinia amylovora exopolysaccharide matrix structure*
	15:50-16:15	**Mr. Vijay Bhooshan Kumar,** Department of Chemistry, Institute of Nanotechnology and Advanced Materials, Bar-Ilan University *Facile one-step sonochemical synthesis of ultrafine and stable fluorescent C-dots for biomedical applications*
	16:15-16:40	**Dr. Santhosh Kotni,** Chemical Physics Department, Weizmann Institute of Science *Towards Strong Coupling of Surface Plasmons and Quantum Dot Excitons*
	16:40-18:00	**Poster session**

Monday

Invited	09:00-09:30	**Dr. Pola Goldberg Oppenheimer**, Department of Chemical Engineering, University of Birmingham *Carbon nanotubes (CNTs) as multiplex surface enhanced Raman scattering (SERS) sensing platforms*
Invited	09:30-10:00	**Prof. Rachel Yerushalmi-Rozen**, Department of Chemical Engineering, Ben Gurion University of the Negev *Nano-structures mediated assembly of small molecules and polymers*
Invited	10:00-10:30	**Prof. Jean-Paul (Moshe) Lellouche**, Department of Chemistry, Bar-Ilan University *Innovative γ -maghemite-polymer hybrid nanocomposites for siRNA/microRNA delivery/gene silencing applications - nanoparticle surface engineering strategies for nanocarrier toxicity control*
	10:30-11:00	**Dr. Roey J. Amir,** Department of Organic Chemistry, Tel Aviv University *Enzyme-responsive micellar nanocarriers*
	11:00-11:25	**Coffee**
Invited	11:25-11:55	**Prof. Esther Segal**, The Department of Biotechnology and Food Engineering, Technion *Mechanism of erosion of nanostructured porous silicon drug carriers in neoplastic tissues*
	11:55-12:20	**Dr. Rahul Kumar Mishra**, Department of Chemistry, Institute of Nanotechnology and Advanced Materials, Bar-Ilan University *New life for an old antibiotic*
	12:20-12:45	**Mr. Nir Waiskopf,** The Alexander Silberman Institute of Life Sciences, The Institute of Chemistry and the Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem. *Semiconductor based nanoparticles in biomedical applications from passive to active functions*
	12:45-13:10	**Mr. Yotam Navon**, Department of Chemical Engineering, Ben Gurion University of the Negev *Thermoresponsive peptide hydrogels*
	13:10-14:00	Lunch
	14:00-14:20	**Dr. Alex Margolin**, Nanomaterials *Science and industry - NanoMaterials perspectives*
	14:20-14:40	**Prof. Oded Shoseyov**, Faculty of Agriculture, Food and Environment , The Hebrew University of Jerusalem *Nano bio mimetics: materials for the future*
	14:40-15:00	**Mr. Amir Naiberg**, Yeda *From basic innovation to products*
Invited	15:00-15:20	**Dr. Jochen Brendt**, Evonik *Inorganic semiconductor layers for display applications: Zinc oxide nanoparticles and other approaches for high mobility thin film transistors*
Invited	15:20-15:40	**Roi Levi,** Department of materials & Interfaces, Weizmann Institute of Science *Electrical and Electromechanical Properties of WS_2 Nanotubes*
	15:40-16:00	**Coffee Break**
Invited	16:00-16:25	**Prof. Mauricio Terrones**, Department of Physics, Department of Chemistry, Department of Materials Science and Engineering and Center for 2-Dimensional & Layered Materials. The Pennsylvania State University & Institute of Carbon Science and Technology, Shinshu University *Two- and three-dimensional carbon materials: from doped graphene to graphene oxide fabrics and nanotube Junctions*
Invited	16:25-16:50	**Prof. Christoph Gadermeier**, Department of Complex matter, Jozef Stefan Institute *Femtosecond exciton and charge dynamics in mono- and few-layer transition metal dichalcogenides*
Invited	16:50-17:15	**Andrés Seral-Ascaso**, School of Chemistry, School of Physics & CRANN Trinity College *General synthesis strategies for layered materials*
Invited	17:15-17:40	**Prof. Veit Wagner**, Department of Physics & Earth Sciences, Jacobs University *Wet-chemical deposition of transition metal dichalcogenides*
	17:40-18:00	**Mr. Oren Meiron**, Department of chemistry, Ben Gurion University *Modifying layered compounds for hydrogen production*
	18:00	**MoWSeS Project meeting**

Materials for Therapeutic H_2S Delivery

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Keywords: *Therapeutic Polymers, Hydrogen Sulfide, Gasotransmitter*

Abstract

We focus on expanding the study and therapeutic use of hydrogen sulfide (H_2S) as a signaling gas. Despite its reputation as a foul-smelling and toxic pollutant, H_2S is a vital biological signaling agent, and it is of interest as a therapeutic, most notably in cardiovascular disease. The majority of biological studies on this gasotransmitter have been carried out with systemically administered small molecule H_2S donors, which have little tissue specificity and the potential for off-target effects. The challenges associated with site specific delivery of gases can be addressed by using functional groups that release H_2S in response to a trigger. We report here on *S*-aroylthiooximes, a functional group that releases H_2S in a controlled manner in response to a cysteine trigger. Furthermore, we have used *S*-aroylthiooximes to develop H_2S-releasing materials, which can offer localized H_2S delivery with tunable kinetics. Our platforms include soluble polymers and nanoparticles as well as peptide-based gels designed to release therapeutically relevant concentrations of H_2S with controllable kinetics. Cell studies show minimal toxicity of these materials and confirm delivery of H_2S to the cell.

Albumin-SPIONs: protein surface binding, nanoparticles uptake in cells and fate

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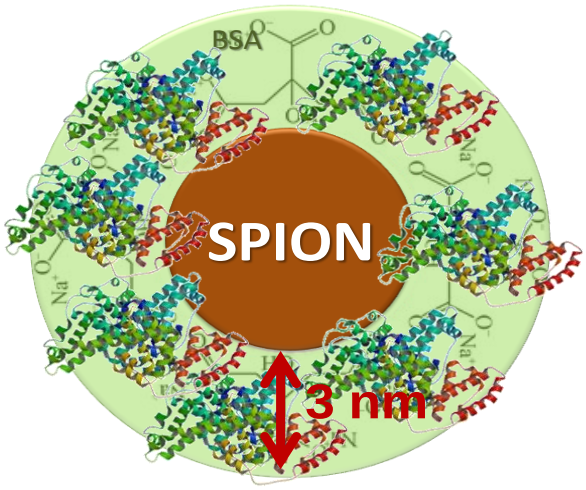
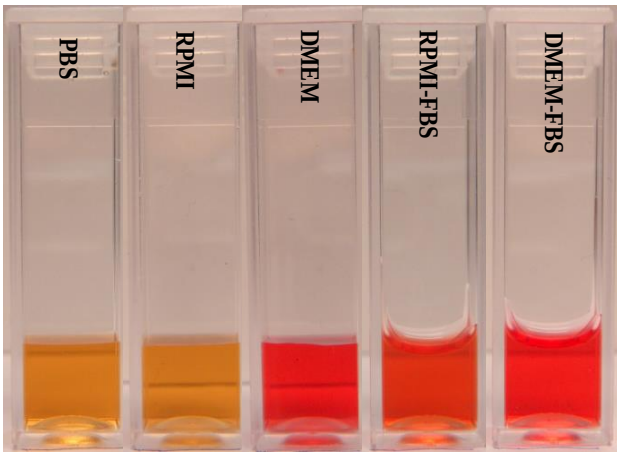
Abstract

Superparamagnetic iron oxide nanoparticles (SPIONs) are demonstrating huge potential in nanomedicine. SPIONs are investigated as MRI contrast agents, in hyperthermia treatment, for drug delivery, targeting therapies, biosensing and magnetic separation. However, the stability of SPIONs in complex biological environments remains a challenge and simple biocompatible surface coatings to stabilize nanoparticles avoiding agglomeration but also enhancing their therapeutical effect and preventing their dissolution are currently being investigated.

Albumin is the most abundant protein in serum and has many important physiological functions in the circulatory system. Moreover, one the first FDA approved nanomedical products (Abraxane®) is a formulation of paclitaxel-albumin nanoparticles where the presence of albumin facilitates the transport of paclitaxel through the endothelial cells enhancing its accumulation in the tumor.

I will show that bovine serum albumin (BSA) stabilizes SPIONs controlling their aggregation and improving their colloidal stability in biological media. Moreover, BSA forms a protein corona around the nanoparticles modifying their initial surface chemistry and providing a new but distinct bio-identity to the nanoparticles when exposed to biological media, cells and organisms. The binding affinity and conformation changes of BSA upon binding to the SPIONs and how cytotoxicity, cellular uptake, distribution and fate of nanoparticles are affected by the protein presence will be reported.





A truly complex fluid: particles with random interactions

Yitzhak Rabin

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We use molecular dynamics simulations to study multicomponent systems in the limiting case where all the particles are different. The particles are assumed to interact via Lennard Jones (LJ) potentials, with identical size parameters but their pair interaction parameters are generated at random from a uniform or from a peaked distribution.

We analyze both the global and the local properties of these systems at temperatures above the freezing transition and find that APD fluids relax into a nonrandom state characterized by clustering of particles according to the values of their pair interaction parameters.

Application of surface "click" reactions to localized plasmon biosensing

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Nanosized metallic structures exhibit an extinction band attributed to localized surface plasmon resonance (LSPR), whose wavelength and intensity are sensitive to changes in the structure and environment of the metal nanostructures. The latter, together with the simplicity of the technique and the use of low-cost equipment, have made LSPR spectroscopy a promising tool for sensitive and affordable label-free optical biosensing. We have used LSPR transducers based on gold nano-island films to demonstrated sensing of specific receptor–analyte interactions, such as antigen-antibody (immunoassay),[1] protein-carbohydrate,[2] and RNA-antibiotic[3] biorecognition.

Formation of a recognition interface (i.e., a receptor layer) on the Au transducer surface is commonly done using sulfur-based tail groups such as thiols,[4] thus immobilizing a self-assembled monolayer (SAM) of the thiolated receptors on the Au surface. While this approach leads to stable recognition layers, it has a major drawback in that it requires thiol-modified receptors. Each prospective receptor has to be modified with a thiol end-group, which may be challenging, as (i) thiolation is a non-trivial chemical manipulation, (ii) thiol-derivatized molecules are usually rather unstable, and (iii) biological receptors are often complex and/or expensive molecules.

Here we present an alternative approach to the preparation of biorecognition interfaces on LSPR transducer surfaces by means of "click" reactions. We use the Cu(I) catalyzed 1,3-cycloaddition reaction between azide and acetylene.[5] The receptors are chemically modified with an acetylene group, which is considerably simpler than thiolation while producing a stable product; the Au surface is derivatized with a simple, commercially-available long-chain thiol azide. The azide-derivatized Au surface is reacted with the acetylene-modified receptors using "click" chemistry, to produce the biorecognition interface on the LSPR transducer.

The above scheme is demonstrated with several acetylene-derivatized compounds. These include a simple molecule (propargylamine), a chromophore (alkyne dansyl), and a biological receptor (arginine propargylamide). In all cases the Au is modified with a SAM of a commercially-available long-chain thiol-azide. The surface "click" reactions are studied using transmission UV-Vis spectroscopy, X-ray photoelectron spectroscopy (XPS), and polarization-modulation infrared reflection-absorption spectroscopy (PM-IRRAS).

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Initial evaluation of Iron oxide nanoparticles in *C. elegans*. A novel strategy to evaluate nanoparticles?

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Keywords: *nanoparticles, C. elegans, iron oxide nanoparticles, BSA*

Abstract

Caenorhabditis elegans (*C. elegans*) is a 1-mm long free-living soil nematode widely used in biomedicine as a model organism. Its key attributes as an experimental system, including its simplicity, transparency, short life cycle, sequenced genome and small body size, together with the ease of cultivation in the lab, make *C. elegans* a promising animal model to evaluate nanoparticles *in vivo*.

We evaluated iron oxide nanoparticles (SPIONs) synthesized in our laboratory, of around 6nm, superparamagnetic coated with citrate (C) as surfactant or with the protein bovine serum albumin (BSA).
SPIONs localized in the intestinal tract of the *C. elegans* and due to the transparency of the animal; we could simply visualize them with an optical microscope. On the other hand, we quantify by magnetometry the amount of SPIONs ingested and the viability of *C. elegans* upon ingestion.

In all cases, the nanoparticles remained superparamagnetic inside the worms. Once the nanoparticles were excreted, the C-SPIONs were found to be partially dissolved inside the alimentary system of *C. elegans*, whereas BSA-SPIONs were not. The BSA coating appears to act as a protective layer and decreases the toxicity of SPIONs, especially at high concentrations.

We argue that this relevant information on the chemistry and toxicity of SPIONs *in vivo* could not be gathered using more classical approaches such as cell culture assays; thus endorsing the potential of *C. elegans* to assess nanomaterials at early stages of their synthetic formulations.

MAGNETIC NANOPARTICLES: A PRECISION TOOL FOR CELL IMAGING AND ACTIVATIONS

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One of the important trends of next-generation biomedical sciences is the development of new tools that can accurately image, identify, and execute desired missions in a selectively programed manner. Nanotechnology is among one of the essential platform tools for targeted imaging, therapy, and simultaneous monitoring of therapeutic efficacy. In this talk, I will discuss magnetic nanoparticles as a core platform material and tool for a variety of functionalities such as sensing, targeting and signaling of cells in a selective and efficient way. Their unique utilizations in highly accurate dual-modal MR imaging, therapeutic hyperthermia of cancer cells, controlled drug/gene delivery, and molecular level cell signaling and cell fate control will be discussed.

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Concepts and Applications of Mesoscopic Lipidic Nanomaterials in Biomedicine

Ehud M. Landau

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Lipidic cubic phases, introduced two decades ago as membraneous matrices for the crystallization of membrane protein, were shown to be extraordinarily successful in membrane structural biology. Because of the unique set of properties of such lipidic materials – they are biocompatible, biodegradable, stable in water or oil, optically transparent, adhesive to hydrophilic as well as hydrophobic surfaces, deformable, loadable, and switchable, one can envisage their application in various areas ranging from cell biology to physiology, biomedicine and materials science. We have expanded the scope of these materials through design and synthesis of novel lipids, and their assembly into biomaterials with controlled functionalities. Structure, dynamics and properties of these biomaterials will be presented, as well as their application in membrane biology, drug release and sequestration, biodevices and molecular recognition.

Interplay of forces during adhesion & adsorption of biofilm components

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The formation of a biofilm begins with the adhesion of proteins and bacteria to a surface. Adhesion, however, is poorly understood in biological systems since many parameters are difficult to control, for instance the conformation of a protein or its enzymatic activity. By a judicious choice of substrates, we are able to discern effects of short- from those of long-range forces. Examples are given for proteins, colloids and bacteria interacting with solid surfaces [1-4]. Adhesion forces can be measured by using an atomic force microscope in force spectroscopy mode. That way, also the effect of fluoride as tooth protection as well as the influence of cell wall macromolecules can be probed by single cell force spectroscopy .

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Fluorescent amphiphilic carbon dots as a new tool for visualization of *Erwinia amylovora* exopolysaccharide matrix structure

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Keywords: *Carbon Dots, Photoluminescence, Biofilm, Plant Pathogen.*

Abstract

Bacterial biofilms development mechanisms have been extensively studied during past several decades. It is been shown that exopolysaccharide matrix (EPS) plays a crucial role in biofilm virulence and also acts as a barrier against host defense systems. For example, in *Erwinia amylovora* which causes fire blight - a serious disease of rosaceous plants - the bacteria pathogenicity mainly depends on its ability to produce exopolysaccharide amylovoran. We show that newly-synthesized amphiphilic photoluminescence carbon dots (CDs) can specifically bind to *Erwinia amylovora* EPS, enabling unprecedented visualization of its structure and growth kinetics. Using the amphiphilic CDs we found, for example, that *Erwinia amylovora* EPS matrix development begins in "seed-like" elongated structures, which subsequently self-assemble into bigger "dendrite-like" structures during longer incubation times. Furthermore, amphiphilic CD-based imaging makes possible real-time analysis of the activity of biofilm inhibitors. In particular, we found that quorum sensing inhibitors directly affect EPS growth and structural features.

Facile One-Step Sonochemical Synthesis of Ultrafine and Stable Fluorescent C-dots for Biomedical Applications

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Keywords: *C-dots, fluorescence, sonochemistry, quantum yield, bioimaging.*

ABSTRACT

This work describes a one-step sonochemical synthesis of carbon dots (C-dots), which is carried out by sonication of polyethylene glycol (PEG-400) for 0.5-3 hour. It demonstrates how various sonication parameters such as sonication time, temperature and amplitude of sonication determine the size and the fluorescence of the C-dots. The produced C-dots are found in the PEG medium and have an average diameter of 2-9 nm, depending on the preparation conditions. The highest quantum yield of emission was ~16%. The synthesized C-dots was used for coating of polythene and finally it was used for bioimaging applications.

Towards Strong Coupling of Surface Plasmons and Quantum Dot Excitons

Kotni Santhosh[†], Nir Zohar[†], Ora Bitton[‡]and Gilad Haran[†*]

† Department of Chemical Physics and ‡ Chemical Research Support, Weizmann Institute of Science, Rehovot, Israel.

Abstract:

Due to their ability to confine light into nanometer-sized volumes, plasmonic metal nanostructures have been successfully used for improving the sensitivity of molecular fluorescence and Raman spectroscopies. A current frontier of molecular plasmonics is the investigation of strong coupling of molecular excitations to surface plasmons, which can pave the way to applications such as quantum information processing and single-photon sources. Though some studies on strong coupling between organic molecular aggregates and plasmonic structures have appeared in the literature recently no experiments involving individual quantum emitters have so far been reported. Here we employ semiconductor quantum dots (QDs) as quantum emitters coupled to silver dimer nanoantennas. QDs have several advantages over organic molecules, such as their high photostability. We develop methods based on e-beam lithography to fabricate bowtie-structured dimer nanoantennas and position QDs within their gaps. Antennas with one to several QDs are generated, and the plasmonic properties of every single antenna are characterized by dark-field microspectroscopy. Our results show that the strong coupling regime is indeed achieved even with few QDs within the plasmonic cavity. Polarization-dependent experiments further support the plasmon-exciton strong coupling and also show how important is the hot spot for achieving that regime. Numerical calculations carried out on our systems support the experimental data and suggest that the coupling is much stronger when the QD is located at the edges rather than at the center of the bowtie. Our experiments thus provide a realization of strong light-matter interaction close to the ultimate limit of a single emitter, based on localized surface plasmons and under ambient conditions.

Carbon Nanotubes (CNTs) as Multiplex Surface Enhanced Raman Scattering (SERS) Sensing Platforms

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Keywords: *CNTs, SERS, EHD Patterning, Vertically Aligned Carbon Nanotube Forests (VACNTF).*

Abstract

Medical diagnostics, homeland security and forensics increasingly demand specific analytical technologies for quick point-of-care diagnostics. Raman spectroscopy is a well-known analytical tool, but has very weak signals and hence is unsuitable for trace level analysis. Enhancement *via* localized optical fields on metallic structures[1] generates huge signals in SERS, enabling down to single molecule detection,[2] which can be tuned by manipulation of the sub-micron architectures. Nevertheless, the application of SERS has been inhibited by the irreproducibility and complexity of fabrication routes. The ability to generate straightforward, cost-effective, multiplex-able and addressable SERS substrates with high enhancements is of profound interest for miniaturised sensing devices. Carbon nanotubes (CNTs) have been concurrently, a topic of extensive research[3] however, their applications for plasmonics has been only recently beginning to gain interest. CNTs can provide low-cost, large-active-area patternable substrates which, coupled with appropriate functionalization capable to provide advanced SERS-platforms.

Herein, advanced methods to generate CNT-based SERS active detection platforms will be discussed. First, a novel electrohydrodynamic (EHD) lithographic technique will be introduced for patterning CNT-polymer composites, providing a straightforward, single-step approach for generating high-fidelity sub-micron-sized nanocomposite structures within which anisotropic CNTs are vertically aligned. The created structures are readily fine-tuned, which is an important requirement for optimizing SERS to obtain the highest enhancements with each of the EHD-CNTs individual structural units functioning as an isolated sensor. Further, gold-functionalized VACNTFs are fabricated as SERS micro-platforms. The dependence on the VACNTs' diameters and density play an important role in the Raman signal strength, thus highlighting the importance of structural parameters, previously overlooked in designing and fabricating optimized CNTs-based SERS nanoprobes. VACNTs forests patterned into predesigned pillar structures are further utilized for multiplex detection of bio-analytes. Since CNTs exhibit electrical conductivity and unique adsorption properties, these are further harnessed in the development of novel chemical and bio-sensing platforms.

References

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Nano-structures mediated assembly of small molecules and polymers

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&

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The effect of embedded nano-structures on the self-organization and ordering of a *host media* of self-assembling molecules has been demonstrated in a few systems. Observations accumulated over the last two decades indicate that embedded nano-structures may affect the phase diagram of the host material, shift the onset of micellization, the liquid-liquid phase transition, induce polymer crystallization and more. Rationalization of the observed behaviors indicates that the relevant mechanisms are fundamentally different from those predicted by classical colloidal theories. In my talk I will describe experimental studies of a few examples investigated by us over the last years, where nano-structures induce self-assembly in a surfactant phase, modify the phase diagram of an amphiphilic polymer in an aqueous media, and nucleate the crystallization of conjugated polymers.

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Innovative γ-Maghemite-Polymer Hybrid Nanocomposites for siRNA/microRNA Delivery/Gene Silencing Applications - Nanoparticle Surface Engineering Strategies for Nanocarrier Toxicity Control

Jean-Paul Lellouche,[1*] Liron Limor Israel,[1] Stella Ostrovsky,[1] Katya Buchman-Kapilov,[1] Valeria Lia Yarmiyaev,[1] Emmanuel Lellouche,[2] & Shulamit Michaeli[2]
Nanomaterials Research Center, Institute of Nanotechnology & Advanced Materials, Bar-Ilan University, Ramat-Gan 5290002, Israel ([1]: Department of Chemistry & [2]: Faculty of Life Sciences) - **lellouj@biu.ac.il**

Keywords: *Nanoparticle surface engineering, siRNA and/or microRNA gene delivery & silencing, nanocomposite toxicity mitigation, γ-maghemite nanoparticles*

Abstract

Iron oxide nanoparticles (NPs) have been quite widely used in numerous biotechnology applications (magnetism-driven cell separation, magnetic field-guided drug/gene delivery, non-invasive tissue MRI, anti-cancer hyperthermia). Serious drawbacks dealing with NP fabrication, *i.e.,* both *detrimental NP aggregation* and *controlled NP surface functionalization versatility* including *intrinsic nanocarrier toxicity mitigation are* extremely challenging issues calling for innovative solutions.

Our recent work in the field led to the discovery of a novel method/concept for the (i) aggregation control of ultra-small hydrophilic super-paramagnetic maghemite (γ-Fe_2O_3) NPs and for (ii) its successful use for NP functionalization toward siRNA/microRNA-mediated gene delivery/silencing applications. *This nanofabrication method does not make use of any surface-passivating organic species*. Indeed, the controlled high-power ultrasound-assisted metal Ce(III/IV) cation doping of the surface of 45/50 nm-sized (DLS) maghemite NPs strongly modified the NP surface charge to highly positive values (+41.0 - +53.0 mV range) of ζ potential. Such a $Ce^{3/4+}$ cation-doping process enabled (i) an effective charge control of NP aggregation, (ii) the full NP water compatibility for biological applications, and finally (iii) the development of quite versatile surface engineering chemistries using the known rich $Ce^{3/4+}$ complex *coordination chemistry* for any biomolecule or organic species (PEI polymer for example) binding.

This new NP "*inorganic*" stabilization and surface functionalization approach afforded optimized ultra-small core $Ce^{3/4+}$-doped γ-Fe_2O_3 NPs leading to various hybrid 25kDa *b*-PEI polymer-based decorated nanocomposite carriers (NCs) for siRNA/microRNA *in vitro/in vivo* delivery applications. In addition, effective chemical strategies for nanocarrier toxicity mitigation will be reported based on selected amine function chemical modifications (*N*-amidation, *N*-alkylation, selective amine group oxidation, etc…). Such NC surface modifications lead to quite effective ***in vitro*** *(screening step)****/in-vivo*** end-user applications dealing with safe effective siRNA/microRNA delivery.

Enzyme-responsive micellar nanocarriers

Assaf J. Harnoy, Ido Rosenbaum, Marina Buzhor, Liat Frid, , Merav Segal, Yael Cohen, Gadi Slor, Natalya Weber and Roey J. Amir*
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Keywords: *Block-copolymers, self-assembly, smart materials, Enzyme-responsive, drug delivery.*

Abstract

The rising demand for smart drug delivery systems that can release their molecular cargo only at the target tissue has driven the development of stimuli-responsive micellar nanocarriers. Among the various types of stimuli, such as pH, temperature and light that were utilized to trigger the disassembly of such smart assemblies, enzymes offer great potential due to the often-observed over expression of specific enzymes in various diseases, which potentially could be utilized to trigger the release at the target site. In this talk we will report a highly modular molecular design of amphiphilic block copolymers based on a linear hydrophilic polyethyleneglycol (PEG) and an enzyme-responsive hydrophobic dendron. Taking advantage of accelerated divergent synthetic methodology [1], the PEG-Dendron hybrids were synthesized in high yields through a combination of amidation and tiol-yne reactions. These amphiphilic hybrids self-assembled in water into smart micelles, which could disassemble and release the encapsulated molecular cargo upon enzymatic activation. The high modularity of these PEG-dendron hybrids offers great control over the disassembly rates of the micelles [2] and allowed us to compare two diverse loading approaches: covalent and non-covalent encapsulation [3]. Such enzyme-responsive amphiphilic hybrids could potentially be applied in the future as nanocarriers with adjustable release rates for biomedical delivery applications.

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Mechanism of Erosion of Nanostructured Porous Silicon Drug Carriers in Neoplastic Tissues

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Keywords: *Porous silicon, biodegradation, cancer microenvironment*

Abstract

Local drug delivery systems are increasingly under development as systemic drug administration is associated with detrimental side effects and low drug bioavailability. Nanostructured porous Si (PSi) emerges as a promising platform for drug delivery owing to its high biocompatibility, degradability, high surface area and internal volume available for drug loading. The potential impact of PSi on future healthcare is evident by the current assessment of various PSi devices for medical applications in clinical trials.

Our work focuses on the design and synthesis of PSi matrices as carriers for different antineoplastic drugs, tailoring their nanostructure and surface properties to exhibit a desired release profile. The resulting PSi carriers demonstrate high loading efficacy of different drugs and profound cytotoxicity towards MDA-MB-231 cells *in vitro*. When progressing to *in vivo* models, we revealed that correlation between *in vitro* and *in vivo* behavior of PSi persists only under specific conditions that mimic local oxidative stress manifested by the tumor microenvironment. Under these conditions PSi erosion is enhanced compared to healthy state. Using our model system, we identify determinant factors that modulate material erosion and drug release (doxorubicin is used as a model drug) to begin to unravel the importance of the physiological microenvironment in determining device performance and therapeutic capacity.

New Life for an Old Antibiotic

Rahul Kumar Mishra,[†,‡] Elad Segal,[†,‡] Anat Lipovsky,[†] Michal Natan,[∥] Ehud Banin,[∥] and Aharon Gedanken*[,†,§]

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ABSTRACT

Restoring the antibacterial properties of existing antibiotics is of great concern. Herein, we present, for the first time, the formation and deposition of stable antibiotic nanoparticles (NPs) on graphene oxide (GO) sheets by a facile one-step sonochemical technique. Sonochemically synthesized graphene oxide/tetracycline (GO/TET) composite shows enhanced activity against both sensitive and resistant Staphylococcus aureus (*S. aureus*). The size and deposition of Tetracycline (TET) nanoparticles on GO can be controlled by varying the sonication time. The synthesized NPs ranged from 21 to 180 nm. Moreover, ultrasonic irradiation does not cause any structural and chemical changes to the TET molecule as confirmed by Fourier transform infrared spectroscopy (FTIR). The virtue of $\pi - \pi$ stacking between GO and TET facilitate additionally the coating of TET NPs upon GO. A time dependent release kinetics of TET NPs from GO`s surface is also monitored providing important insights regarding the mechanism of antibacterial activity of GO/TET composites. Our results show that the GO/TET composite is bactericidal in nature, resulting in similar values of minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC). This composite is found to be active against TET resistant *S. aureus* at a concentration four times lower than the pristine TET. The sensitive *S. aureus* follows the same trend showing six times lower MIC values compared to pristine TET. GO shows no activity against both sensitive and resistant *S. aureus* even at a concentration as high as 1 mg/mL, but influences the biocidal activity of GO/TET composite. We propose that the unique structure and composition manifested by GO/TET composites may be further utilized for different formulations of antibiotics with GO. The sonochemical method used in this work can be precisely tailored for the stable deposition of a variety of antibiotics on the GO surface to reduce health risks and increase the spectrum of applications.

Semiconductor Based Nanoparticles in Biomedical Applications

From Passive to Active Functions

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Recent years developments in the synthesis and surface engineering of semiconductor nanocrystals (SCNC) allows to control and tune their properties for diverse applications from printing ink and solar cells to biomedical applications, etc.

From the first proof of concept for the ability to use SCNC for tagging biological molecules, SCNC were developed and used in various biomedical applications, spanning imaging, sensing, delivery and controlled release both *in vitro* and *in vivo.* In all these applications the SCNC are specifically designed not to affect the biological system which limits their potential use.

In this lecture I will present the recent years shift from these initial and traditional biomedical applications to the current research in the field attempting to use SCNC for controlled modulation of the biological system functionalities.

During the talk I will present past and current projects we were working on starting from the tagging of biomolecules for imaging and sensing in vitro and in vivo to the use of SCNC in photodynamic therapy and the pioneered work done in collaboration with the lab of Prof. Hanein from Tel Aviv University in which we have demonstrated for the first time the ability to optically stimulate blind retinas attached to flexible CNT-SCNC films.

The ability to use light excitation of SCNC for modulation of biological systems will hopefully yield better understanding of biological processes, reveal the underlying mechanisms for different diseases and open new venues for developing novel nano-devices for treatment and prevention modalities of diverse diseases.

Thermo-responsive peptide hydrogels

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Developing the ability to change the properties of a material at a specific point in time is important both for a basic understanding of the material's properties and for exploitation of such materials in a variety of biomedical applications, such as sensing, drug delivery, and tissue engineering. The work presented here focuses on developing novel responsive biomaterials by drawing inspiration from natural responsive materials (e.g., muscles), in which small structural changes in a hierarchically organized system are multiplied over several length scales to generate large macroscopic changes. Elastin like-peptides (ELPs) comprised of Xaa-Pro-Gly-Yaa-Gly pentapeptide repeats are artificial biopolymers that exhibit an inverse temperature transition behaviour characterized by a change in the peptide secondary structure; therefore they are ideal building blocks for such dynamic materials.

Here we present a study of a novel class of hydrogels with branched ELPs as cross linkers. Several ELPs, including dendritic and hyperbranched peptides with different chain lengths and generations, were synthesized and characterized to determine their transition temperature in solution, using UV-vis spectroscopy and circular dichroism (CD) spectroscopy. We were able to evaluate the topological effect on the LCST behaviour of the system.

ELPs with physiologically relevant transition temperatures were incorporated as cross-linkers in a synthetic polymer hydrogel, and the gel properties were studied.

"Nano Bio Mimetics: materials for the future"

Oded Shoseyov

The Robert H Smith Institute of Plant Science and genetics. The Faculty of Agriculture, The Hebrew University of Jerusalem.

200 years of modern chemistry introduced into our life a wide range of un-sustainable synthetic materials which carry serious environmental and economic consequences while some of the materials such as certain plastics and ceramics do not perform as we would like.

In contrast, millions of years of evolution created super performing sustainable materials produced by plants, insects and animals. Nano Bio Mimetics is a new field in science and technology that brings together for example the toughness of cellulose nano-fibers from the plant kingdom, the remarkable elasticity and resilience of resilin that enables flees to jump as high as 400 times their height from the insect kingdom, and the adhesion power of super-biological glue of mussels that enable it to bind tightly to different surfaces under water from the marine kingdom. These novel super performing new materials are the materials for the future.

Inorganic semiconductor layers for display applications: Zinc oxide nanoparticles and other approaches for high mobility thin film transistors

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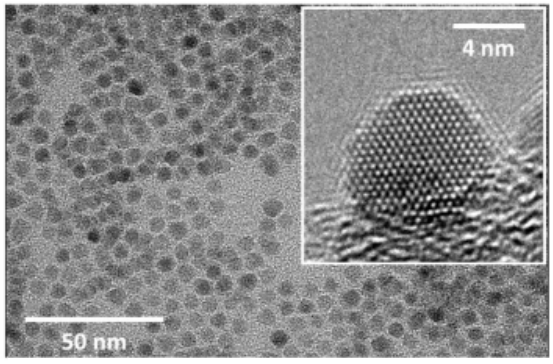
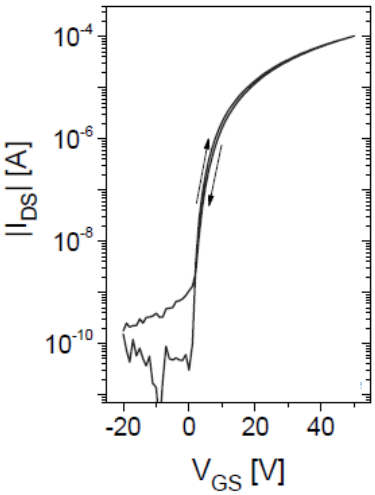
Keywords: *thin film transistor, zinc oxide, nanoparticles, flat panel display*

Abstract

For a long time amorphous silicon was state of the art as semiconducting material in flat panel displays. With increasing display resolution and refresh rate the required electronic properties (specially the charge carrier mobility) reach the limits of amorphous silicon. Thus, since a few years the big players in electronic industry changeover their display production lines from amorphous silicon to new semiconductor materials. As alternative low temperature polycrystalline silicon (LTPS) and oxide semiconductors (e.g. IGZO) are new materials for thin film transistors (TFT) – the heart of each modern flat panel display.



TEM image of zinc oxide nanoparticles used for TFT fabrication



Transfer curve of a TFT processed from zinc oxide nanoparticles

In this work we present the state of the art for zinc oxide layers in TFTs for display applications with a special focus on solution-based deposition techniques like spin coating and slot die coating. Nanoparticles as well as precursor-based approaches are discussed and compared to approved technologies. In order to disperse metal oxide nanoparticles it is necessary to functionalize the surface or to use additives. This necessity is also a great disadvantage since it introduces foreign species into the film. Approaches to remove these impurities afterwards are presented. Furthermore, the interplay of the film morphology and the device characteristics is recognized and described. Besides to the majority of reports describe the use of high annealing temperatures, a chemical approach to improve the film morphology and thereby the performance of the device is introduced.

Electrical and Electromechanical Properties of WS_2 Nanotubes

Roi Levi[a,*], Jonathan Garel[a], David Teich[b], Gotthard Seifert[b], Reshef Tenne[a], Ernesto Joselevich[a]
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Theoretische Chemie, Technische Universität Dresden, Germany

The use of various nanostructures such as nanotubes and 2D sheets in electrical and electromechanical devices is the subject of intensive research in recent years. In particular, the electronic properties of inorganic compounds such as the dichlcogenides sparked the research of their incorporation into nano-electro-mechanical systems (NEMS). WS_2 nanotubes (INT-WS_2) have been shown to exhibit superior mechanical properties and interesting stick-slip mechanical phenomena[1] and thus are a natural candidate for electro-mechanical devices.

We show here that INT-WS_2 possess significant field-effect mobility and surprisingly high current carrying capacity[2]. We further present the first demonstration of a significant torsional electro-mechanical response in pure inorganic nanotubes[3]. The INT-WS_2 exhibited a highly repeatable increase of the conductivity in response to strain and/or torsion. These results are in qualitative agreement with the theoretical calculations presented here for torsion and previous theoretical predictions for strain. The large sensitivity to torsion and tension suggests INT-WS_2 as promising in NEMS such as nano-gyroscopes and accelerometers.

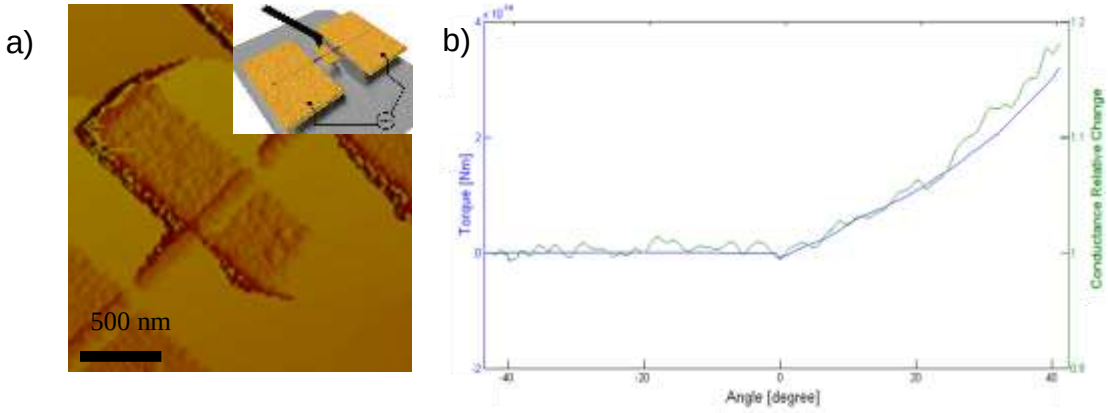

Figure 1 - (a) Atomic force microscope image (AFM) of a WS_2 nanotube-based torsional nano-electro-mechanical system (NEMS). Inset - Schematics of the INT-WS_2-NEMS and the AFM tip used to perform the torsion. (b) INT-WS_2-NEMS electrical response to torsion - change in conductivity as a function of the torsion angle.

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Two- and Three-Dimensional Carbon Materials: From Doped Graphene to Graphene Oxide Fabrics and Nanotube Junctions

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Keywords: *Graphene, Nanotubes, sensors, toxicity, doping.*

Abstract

This talk will discuss the synthesis of large-area, high-quality monolayers of nitrogen-, silicon- and boron-doped graphene sheets on Cu foils using ambient-pressure chemical vapor deposition (AP-CVD). Scanning tunneling microscopy (STM) and spectroscopy (STS) reveal that the defects in the doped graphene samples arrange in different geometrical configurations exhibiting different electronic and magnetic properties. Interestingly, these doped layers could be used as efficient molecular sensors and electronic devices. In addition, the synthesis of hybrid carbon materials consisting of sandwich layers of graphene layers and carbon nanotubes by a self-assembly route will be discussed. These films are energetically stable and could well find important applications as field emission sources, catalytic supports, gas adsorption materials and super capacitors.

We will describe the synthesis of carbon nanotubes and nanotube networks using different dopants during chemical vapor deposition. In particular, the effects of sulfur, boron and nitrogen will be discussed. For example, sulfur induces the formation of pentagons and heptagons, whereas boron aids the growth of heptagonal carbon rings, and nitrogen promotes the formation of pentagonal cusps. It will be demonstrated that it is indeed possible to assemble/grow carbon nanotube networks if a careful control of dopants is achieved during chemical vapor deposition (CVD) growth. High resolution electron energy loss spectroscopy (HR-EELS) studies on these nanotube materials will be presented, and the locations of boron, sulfur and nitrogen within nanotubes will also be shown. First principles theoretical calculations on nanotubes containing pentagon, hexagons and heptagons in the presence of these dopants will be discussed. Recent experiments on the synthesis of large area super-tough smart carbon textiles, capacitors, catalysts and more. We will also discuss the citotoxicity and applications as molecular sensors of these doped nanocarbons.

Femtosecond Exciton and Charge Dynamics in Mono- and Few-layer Transition Metal Dichalcogenides

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Keywords: *2d materials, femtosecond spectroscopy, excitons, charge photogeneration.*

Abstract

Despite their high exciton binding energy, mono- and few-layer semiconducting transition metal dichalcogenides (TMDs) show a strong photovoltaic effect and potential for high sensitivity photodetectors. Both these functionalities require efficient charge carrier photogeneration, either via direct excitation of mobile carriers or via exciton dissociation. We use continuous wave photomodulation and femtosecond pump-probe spectroscopy to identify the spectral features of photogenerated charges in an ensemble of few-layer MoS_2 and WS_2 dispersed in a transparent polymer and trace the dynamics of photogeneration and relaxation of both charges and excitons. We find that the primary photoexcitations are excitons which dissociate efficiently with a characteristic time several hundred fs. In WS_2, thanks to the larger separation of the two main excitonics resonances, we can also resolve the inter-band relaxation of photogenerated carriers. For few-layer MoS_2 blended into a suitable organic semiconductor, we show efficient charge separation, making such blend particularly attractive for photovoltaics. While the yield of exciton dissociation into charges is close to unity in the few-layer case, in monolayers it is considerably lower, due to the higher exciton binding energy. We show that the exciton dissociation in monolayer MoS_2 can be enhanced via applying an electric field.

According to our findings, few-layer TMDs display a behavior which is intermediate between conventional semiconductors on the one hand, and high exciton binding energy materials, such as organic semiconductors, carbon nanotubes, and single-layer TMDs on the other. High efficiency photodetectors and photovoltaic elements based on monolayers require additional measures to achieve efficient exciton dissociation, such as a strong built-in field using appropriate electrode materials, engineering a p-n junction, or a heterojunction device. In few-layers, which have the added benefit of absorbing a larger fraction of the incident light, such measures should not be necessary and simpler, more scalable device structures could be used.

General Synthesis Strategies for Layered Materials

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Trinity College Dublin, Ireland

The challenge of obtaining new materials with optimum properties for electronic and optical applications has located the bidimensional materials as the focus of an important research activity.

Following the first production of graphene, different families of layered materials have been explored as potential candidates for the preparation of self-standing 2D structures. Exfoliation of bulk layered compounds has been widely studied and is a suitable approach for this goal.

Recently, the great compositional diversity of layered materials was pointed out, unfortunately only some of them are commercially available. Thus, having the adequate techniques to produce the bulk layered material is crucial when studying novel materials. In this session, a general overview on the synthesis strategies for the preparation of layered materials will be presented and discussed.

Wet-chemical deposition of transition metal dichalcogenides

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Keywords: *TMDC, MoS2, exfoliation, wet-chemical deposition*

Abstract

Nanoscale materials offer the advantage of high surface to volume ratio, which allows to tune their properties to specific values different than those given by bulk properties. Here, atomically thin 2D materials represent an extreme case. Like graphene, transition metal dichalcogenides (TMDC) form perfectly ordered, layered 2D materials. Cheap deposition methods are required for wide-spread applications of this material class. Here, wet-chemical methods offer the advantage of scalability towards large production volumes.

Two wet-chemical deposition methods for Sulfur-based TMDCs are compared, i.e. exfoliation from bulk materials and chemical synthesis from liquid precursor materials. The targeted application of the materials is to use them as active semiconducting layer in an electronic device.

It is found, that exfoliation allows for successful and reproducible deposition with a 2D-flake size limited to below 1 µm. Additional measures to improve the flake-to-flake contact are required and several approaches are discussed. The chemical synthesis approach uses Ammonium tetrathiomolybdate (ATTM) dissolved in water as precursor solution. The material can be flexibly deposited e.g. by a dip-coating process. This approach requires a post-growth annealing step of 350 °C or beyond to finalize the formation of TMDC. The latter approach allows for much larger 2D-flake sizes exceeding 150 µm, which avoids additional flake-to-flake contact requirements in electronic applications.

Modifying layered compounds for hydrogen production

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**Coresponding author: barsadan@bgu.ac.il*

Abstract: Layered transition metal dichalcogenides (TMDs) gained much attention in recent years. First principle calculations showed that doping and alloying of TMDs can be used in order to modify their electronic and magnetic properties. To date, TMDs alloying is primeraly performed at high temperature, solid state reactions, such as chemical vapor deposition (CVD) or chemical vapor transport (CVT). We have used a low temperature, controllable colloidal synthesis for producing alloyed TMDs, specifically $Mo(S_xSe_{1-x})_2$. Flower like, edge oriented nanostructures were synthesized with varying alloy degrees. The Materials were analyzed using TEM, XRD, UV-Vis and ICP-MS spectroscopy. ICP-MS analysis of the $Mo(S_xSe_{1-x})_2$ alloys showed that increasing the selenium content in the reaction decreases x in the alloy. XRD and UV-Vis spectra results suggests the formation of a homogeneous solid solution rather than two separate phases of MoS_2 and $MoSe_2$. Tunable bandgap was achieved as a function of alloying degree, as measured by UV-Vis. The particles were analyzed for photocatalytical hydrogen evolution reaction using a solar simulating system. We have demonstrated the synthesis of improved edge oriented alloys using simple colloidal technique. By controlling the alloying degrees, the electronic properties of the TMDs can be optimized for a variety of applications such as photo catalysis, optoelectronics, transistors and many others.

Keywords: alloying, hydrogen evolution reaction, MoS_2, $MoSe_2$, $Mo(S_xSe_{1-x})_2$, TMDs, TMDs alloy, transition metal dichalcogenides.

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Ben-Gurion University of the Negev

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Nanoparticles at the Interface Between Biology and the Materials World

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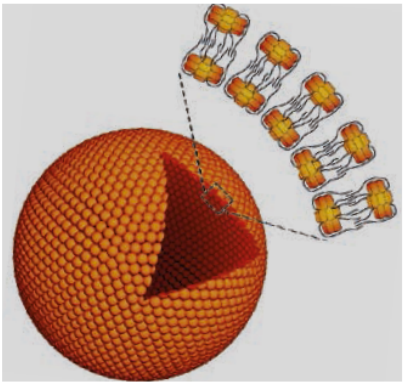

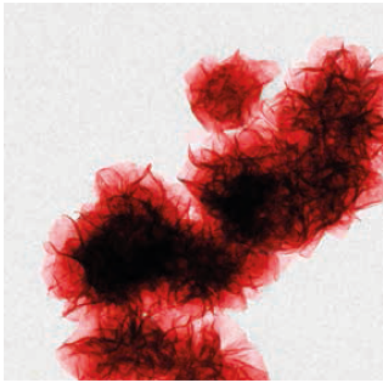

Poster session

P1 **Membrane Interaction of Vesicles Loaded with Fluorescent Carbon Nanoparticles**
Susanta Kumar Bhunia, Raz Jelinek
Department of Chemistry and Ilse Katz Institute for Nanotechnology, Ben-Gurion University of the Negev, Beer Sheva, Israel

P2 **Investigating the transfection cellular path of modified pectic galactan/plasmid DNA complexes in vitro**
N. Buaron, R. Chintacunta, R. Goldbart, T. Traitel, H. Brem and J. Kost
Department of Chemical Engineering, Ben-Gurion University of the Negev, Beer Sheva, Israel

P3 **Membrane - Carbon Dots Interactions Characterization**
Gil Choona, Raz Jelinek
Department of Chemistry and Ilse Katz Institute for Nanotechnology, Ben-Gurion University of the Negev, Beer Sheva, Israel

P4 **Template-induced Au microstructure at the air/water interface**
Hao Jiang, Raz Jelinek
Department of Chemistry and Ilse Katz Institute for Nanotechnology, Ben-Gurion University of the Negev, Beer Sheva, Israel

P5 **Ligand assisted fluorescence enhancement in colloidal 2D CdS_xSe_{1-x} nanosheets synthesized through precursor reactivity control at low temperature**
Pradipta Sankar Maiti, Lothar Houben and Maya Bar-Sadan
Department of Chemistry, Ben-Gurion University of the Negev, Beer Sheva, Israel

P6 **Elucidating the Interactions among Aβ42, Toxicity Inhibitors, and Lipid Membranes and their Biological Significance**
R.Malishev, S.Nandi, S.Kolusheva, Y.Levi-Kalisman, F.G. Klärner, T.Schrader, G.Bitan, R. Jelinek
Department of Chemistry and Ilse Katz Institute for Nanotechnology, Ben-Gurion University of the Negev, Beer Sheva, Israel

P7 **Carbon Dots for Visualization of Membrane Processes and Detection of Bacteria**
Sukhendu Nandi, Raz Jelinek
Department of Chemistry and Ilse Katz Institute for Nanotechnology, Ben-Gurion University of the Negev, Beer Sheva, Israel

P8 **Designing efficient bimetallic photocatalysts for hydrogen production**
Eran Aronovich, Philip Kalisman, Shai Mangel, Lothar Houben, Lilac Amirav, Maya Bar-Sadan
Department of Chemistry, Ben-Gurion University of the Negev, Beer Sheva, Israel

P9 **Self-assembly graft copolymers for the development of novel mucoadhesive polymeric micelles**
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Laboratory of Pharmaceutical Nanomaterials Science, Department of Materials Science and Engineering, Technion-Israel Institute of Technology, Haifa, Israel

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

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Membrane Interaction of Vesicles Loaded with Fluorescent Carbon Nanoparticles

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Keywords: *Fluorescent carbon nanoparticles • vesicles • membrane active compounds • membrane interaction.*

Abstract

Fluorescent carbon nanoparticles got enormous research interest in recent years due to its high optical properties, low cytotoxicity, excellent biocompatibility and low cost. These nanoparticles are more eco-friendly than toxic fluorescent semiconductor nanoparticles. It becomes challenging if such fluorescent carbon nanoparticles can be conjugated with lipids and such type of system can be used for biological applications instead of conventional fluorescent lipids.

Here we have prepared biocompatible amphiphilic carbon nanoparticles by reported method. Lipid has been conjugated with these carbon nanoparticles to form fluorescent lipid. Fluorescent giant and small unilamellar vesicles have been formed from this fluorescent lipid. Giant vesicles shape can be changed by adding different membrane active compounds which interact with the membrane and resulting distortion of spherical membrane surface and significantly deformed vesicle morphology. Fluorescence small vesicles are too small that are not observed under confocal microscope. We have seen emission spectra and spectroscopic change by adding the membrane active compounds.

Another most important experiment, fluorescence recovery after photobleaching (FRAP) can be done by using such fluorescent carbon nanoparticles conjugated lipids compared to very cost effective conventional fluorescent lipids. It can be done by forming solid supported membrane.

The new approach is simple, robust and can be readily utilized for vesicles formation and different significant experiments.

Investigating the transfection cellular path of modified pectic galactan/plasmid DNA complexes *in vitro*

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Keywords: *gene therapy, glioma, non-viral carriers, pectin and cell specificity.*

Abstract

Brain tumors represent one of the most malignant forms of human cancers, where the most common and aggressive is the glioma. We explored a novel gene therapy approach based on natural polysaccharides for targeted delivery to cancerous cells. Galectin-3 is a cell protein that carries an active carbohydrate recognition domain (CRD) for β-galactoside sugars that is highly expressed in a variety of cancer cells, such as glioma. Since the natural polysaccharide pectin has galactose-rich side chains (galactans), it can be utilized as a carrier for delivering genes to glioma cells in a targeted manner, based on the highly specific carbohydrate interaction between galactan and galectin-3 receptors on the cell membrane. Moreover, pectin has been proven to be effective in inhibiting or blocking cancer cell aggregation, adhesion, and metastasis. Since pectin is a natural polysaccharide, it carries further advantages as a gene delivery carrier over the currently available synthetic ones, such as biodegradability, biocompatibility, low immunogenicity, and minimal cytotoxicity.

Modified pectin-based carrier was synthesized and explored. Q-galactan was prepared by modifying quaternary ammonium groups ($Q=N+(CH_3)_3$) on pectic galactan. Q-galactan was successfully synthesized and characterized. A globular condensed complexation with plasmid DNA was clearly observed. Q-galactan was found to form complexes with size ranging from 80 nm to 120 nm, which is suitable for internalization to the cell through endocytosis. The complexes were successfully proven to be non-toxic to C6 rat glioma cells line. Investigation of cellular uptake and cellular path indicated the complexes were able to penetrate the cell membrane and approach the nucleus within 24 hours. Cellular uptake of ~75% was observed at the best conditions. This investigation demonstrates that Q-galactan is a potential carrier for gene therapy. Further studies are required in order to investigate the intracellular barriers for establishing an efficient gene delivery system.

Membrane - Carbon Dots Interactions Characterization

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Keywords: *Carbon Dots •Amine Carbon Dots• bilayer membrane • nanoparticles•*

Carbon dots are quasi crystal nanoparticles with a diameter smaller than 10 nanometers with fluorescence properties. In a work that was done in our group graphite crystal, which is a core of carbon dots, was coated with hydrocarbon chains, forming an amphiphilic structure. In order to create positively charged carbon dots (CDs), the carboxylic groups were substituted with amine groups, to form positively charged amine modified carbon dots (ACDs). So in this study, we wanted to investigate the interactions of these types of carbon dots to a bilayer membrane. Our research goal is to characterize amphiphilic carbon dots & positively charged amine carbon dots interaction with three types of bilayer membrane and to develop a nontoxic microscopy imaging tool.

Template-induced Au microstructure at the air/water interface

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Keywords: *Langmuir monolayers • diacetylene films • octadecyl-melamine • surfactant templates • conductivity.*

Abstract

Langmuir monolayers constitute a powerful platform for self-assembly and organization of amhiphilic molecules. Controlling the structural features of condensed domains formed within Langmuir monolayers, however, is a challenging task. We demonstrate formation of remarkably diverse condensed microstructures in binary monolayers comprising a surfactant (octadecyl-melamine) and diacetylene monomer. Specifically, we show that the mole ratio between the two constituents and composition of the aqueous subphase – specifically pH and dissolved metal ions – dramatically modulated the shapes and dimensions of microstructures formed at the air/water interface. The self-assembled microstructures could be transferred from the water surface onto solid substrates, and subsequently further served as templates for gold coating, yielding electrically-conductive microwires.

Meanwhile, we have also demonstrated a simple strategy for the generation of extremely long (up to several centimeters), horizontally-aligned gold micro-wires, produced through a surfactant monolayer template deposited from gold thiocyanate [$Au(SCN)^{4-}$] aqueous solution. Specifically, we show that the surfactant, octadecyl-maleimide (OM), spontaneously forms oriented micro-wires at the air/water interface, which constitute a template for deposition of metallic gold through binding and crystallization of the soluble gold complex. The Au micro-wires can be subsequently transferred onto solid substrates, and following plasma treatment and gold enhancement exhibit excellent conductivity even at electrode spacings of several centimeters. Importantly, the micro-wire alignment determines the direction of electrical current, demonstrating that long-range ordering of the micro-wires can be accomplished, significantly affecting the physical properties of the system. The new approach is simple, robust, and can be readily exploited for bottom-up fabrication of micro-wire assemblies and transparent conductive electrodes.

Ligand assisted fluorescence enhancement in colloidal 2D CdS_xSe_{1-x} nanosheets synthesized through precursor reactivity control at low temperature

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Keywords: *colloidal synthesis, 2D nanostructures, alloyed semiconductors, , fluorescence enhancement*

Abstract

Two-dimensional (2D) semiconductor cadmium chalcogenide nanostructures have attracted a lot of interest recently due their appealing combination of properties: physical properties close to the quantum wells and chemical properties similar to the colloidal quantum dots. These structures can be prepared colloidally with controlled aspect ratio and uniform thickness. Optoelectronic properties of these atomically thin 2D sheets mostly depend on their thickness. On the other hand, alloying these semiconductors can also provide us additional degree of freedom which can be used to tune their properties by varying their composition. These alloyed semiconductors can open new possibilities in band gap engineering and as well as developing tunable emitters.

Here, we produced ultrathin 2D CdSxSe1-x nanosheets at low temperature by controlling the precursor reactivity. We show despite using the same composition, degree of alloying is highly sensitive to the temperature. We also show how their optoelectronic tuning by molecular modification of the highly active surfaces. Structural, compositional and optical characterizations are presented using TEM, EDAX, powder X-diffraction (PXRD), UV-visible absorption and fluorescence spectroscopy.

Elucidating the Interactions among Aβ42, Toxicity Inhibitors, and Lipid Membranes and their Biological Significance

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Keywords: *Alzheimer's disease; membrane; amyloid β-protein (Aβ); polyphenol; molecular tweezer;*

Abstract

Although the precise molecular factors linking amyloid β-protein (Aβ) to Alzheimer's disease (AD) have not been deciphered, interaction of Aβ with cellular membranes has an important role in the disease. However, most therapeutic strategies targeting Aβ have focused on interfering with Aβ self-assembly rather than with its membrane interactions. Here, we studied the impact of three toxicity inhibitors on membrane interactions of Aβ42, the longer form of Aβ, which is associated most strongly with AD. The inhibitors included the four-residue C-terminal fragment Aβ(39–42), the polyphenol (–) epigallocatechin-3-gallate (EGCG), and the lysine-specific molecular tweezer, CLR01, all of which previously were shown to disrupt different steps in Aβ42 self-assembly. Biophysical experiments revealed that incubation of Aβ42 with each of the three modulators affected membrane interactions in a distinct manner. Interestingly, EGCG and CLR01 were found to have significant interaction with membranes themselves. However, membrane bilayer disruption was reduced in the presence of Aβ42, suggesting that the compounds interact preferentially with Aβ42 rather than with the membranes. Importantly, our study reveals that even though the three tested compounds affect Aβ42 assembly differently, membrane interactions were significantly inhibited upon incubation of each compound with Aβ42, suggesting that preventing the interaction of Aβ42 with the membrane contributes substantially to inhibition of its toxicity by each compound. The data suggest that interference with membrane interactions is an important factor in the effect of Aβ42 toxicity inhibitors and should be taken into account in potential therapeutic strategies, in addition to disruption or remodeling of amyloid assembly.

Carbon Dots for Visualization of Membrane Processes and Detection of Bacteria

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Keywords*: Carbon dots, FRET, membrane, amyloid beta, bacteria sensing and detection*

Abstract

Carbon dots (CDs) being a member of carbon nanostructure family have attracted considerable interest in recent years because of their excellent photoluminescence properties which make them useful for bio sensing and imaging applications.[1]
We have developed a novel bottom-up approach for the syntheses of CDs by simple carbonisation process starting from 6-*O*-acylated fatty acid esters of glucose as carbon precursor. The as-synthesised CDs were useful for labelling of membranes and multicolour real time visualisation of membrane processes by fluorescence microscopy in the presence of amyloid beta, one of the prominent toxic factors related to Alzheimer disease. Besides this, because of the emission of CDs in a broad range of spectrum, it was employed as donor in FRET process when they are attached on membranes in presence of variety of acceptors having significant difference in their emission maxima.[2]
The as-synthesised CDs were employed for bacterial sensing and detection. We have observed significant strain-dependent differences in *spectral shifts* and *peak intensities* when CDs are attached to the cell of different bacterial stains due to the distinct membrane compositions and molecular organization of the bacterial species tested, which affect both the affinity of the amphiphilic CDs to the cell membranes, and the environment of the bound nanoparticles.[3]

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Designing efficient bimetallic photocatalysts for hydrogen production

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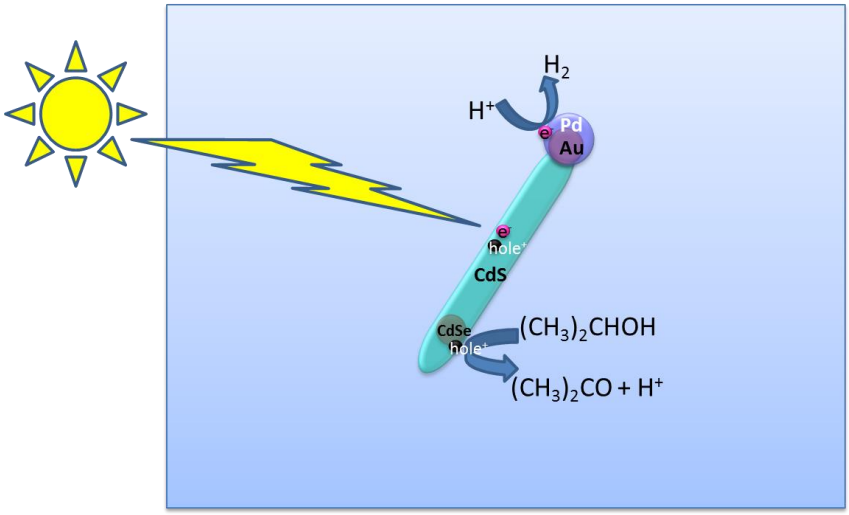
The search for alternative clean and renewable energy source is a major pressing issue. One promising direction is the use of semiconductor nanoparticles as photocatalysts which absorb the solar radiation and produce hydrogen from water. Upon radiation, excited electrons and holes are created. They then migrate to the surface and react with the aqueous solution. Efficient photocatalysts should maintain charge separation of the holes and electrons and contain different sites for oxidation and reduction. Usually a small metallic particle is deposited on the semiconductor which acts as an electron sink and a reduction site for protons.



Hybrid core-shell structures such as CdS@CdSe increase the charge separation and reduce the particle dissolution by confining the holes to the core and leaving the electrons delocalized over the entire structure. A bi-metallic co-catalyst composed of metals such as gold and palladium should improve the photocatalytic activity of the system. Such bimetallic particles possess the ability to attract electrons from the semiconductor and discharge them into the aqueous solution more efficiently then each of the metals on their own. Here we use the CdSe@CdS-Au\Pd system as a case study to explore the effect of the inner structure of the bimetallic tip on the photocatalytic performance. In addition we study the dynamic processes which occur during photocatalysis. For this aim we used high resolution energy dispersive spectroscopy (EDS) for the system characterization and an online GC equipped setup for the long duration photocatalytic hydrogen evolution measurements.

Self-assembly graft copolymers for the development of novel mucoadhesive polymeric micelles

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Keywords: Polymeric micelles; mucoadhessiveness; mucosal drug delivery.

Poor aqueous solubility of drugs is one of the most challenging drawbacks in pharmaceutical product development. Approximately 50-70% of the approved active pharmaceutical ingredients and new chemical entities in the pipeline share this property that in the case of the former reduce oral bioavailability, while in the latter jeopardize their chances to reach advanced preclinical and clinical trials, and eventually the market. Different nanotechnology platforms have been developed to improve the biological performance of poorly-water soluble drugs. Polymeric micelles, self-assembly nanostructures generated by spontaneous arrangement of amphiphilic copolymers blocks above the critical micellar concentration, have emerged as one of the most versatile ones owing to the high diversity of hydrophilic and hydrophobic blocks and the chemical flexibility to tailor the amphiphile architecture (1). Polymeric micelles have been mainly exploited for the intravenous administration of antitumorals. Conversely, two main drawbacks constrain their application by mucosal routes (e.g., oral): weak interaction with mucus and inability to sustain the release of the encapsulated payload over time. Aiming to extend the application of this nanotechnology platform, our research focuses on the design of mucoadhesive polymeric micelles with improved features for the delivery of drugs by different mucosal routes (2). In this context, the production and full physicochemical characterization of a novel type of mucoadhesive polymeric micelles and a new method to evaluate mucoadhesiveness *in vitro* will be reported.

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Topical Therapy with Q-Starch/miRNA Complexes and Ultrasound for Psoriasis Treatment

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Keywords: ***Psoriasis , RNAi therapy , Ultrasound, Starch***

Psoriasis is a chronic inflammatory skin disease that affects millions of people, yet is still without a cure. In recent years, it was discovered that micro-RNAs (miRNAs) have an important role in post-transcriptional gene expression regulation and more than a hundred miRNAs are expressed in the skin. One of these miRNAs was suggested by Lerman et al[1]. as an attractive therapeutic molecule for psoriasis. Although miRNA offers therapeutic potential for treating psoriasis, delivering it topically to the target cells can be challenging. There are several barriers to topical delivery of RNAi: 1. The barrier properties of the top layer of the epidermis (stratum corneum); 2. Naked miRNA/siRNA is unstable *in vivo* due to enzymatic degradation and immunological responses; 3. The efficiency of RNAi that does reach the target cells is further limited by poor cellular uptake. To overcome these obstacles and allow topical delivery of miRNA to skin cells, we suggested the use of ultrasound (US) as a means to enhance biological membrane and skin permeability[2], and quaternized starch (Q-starch) as an miRNA delivery carrier. *In vitro* experiments demonstrated the ability of Q-starch/RNAi complexes to enter human keratinocyte HaCaT cells. *In vitro* and *in vivo* experiments on human skin verified the ability of US application to enhance the transport of the complexes through the stratum corneum into the epidermis. *In vivo* experiments on SCID mice, transplanted with human psoriatic skin, verified the ability of US and modified starch carrier to enhance miRNA transdermal delivery, as well as cell entrance and subsequent decrease in the expression of the miRNA target protein, suggesting that the miRNA is biochemically active.

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Modified starch based carrier for targeting therapeutic plasmidDNA to the nucleus

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Gene therapy is a novel clinical strategy whereby exogenous genetic material is introduced into human cells for the treatment of hereditary or acquired disorders[1]. The main objective of gene therapy is the development of efficient, non-toxic gene carriers that can condense and deliver foreign genetic materials into specific cell types, such as cancerous cells. Non-viral carriers have advantages over viral carriers, since they have low toxicity and induce low immune response; however, their major disadvantage is their relatively low gene expression. In this study, starch, a natural polysaccharide was modified into cationic starch (Q-starch) and was used as a pDNA carrier, due to its biodegradability, biocompatibility, low immunogenicity and minimal cytotoxicity. The objective of this work is improving the modified starch based carrier system[2] in order to maximize its transport efficiency to the nuclear surrounding; for that purpose, the Q-starch surface was grafted with polyethylene glycol (PEG)-Thiol, which will be attached to nuclear localization signal (NLS) peptide. The complex formed based on electrostatic interactions should theoretically lead to appreciable enhancement of active transport of the complex, and consequently gene delivery, to the nucleus[3]. Complexation of Q-starch-PEG-thiol with pDNA was confirmed by gel electrophoresis. Results showed that complexes are formed above N/P=2 similar to Q-starch/pDNA complexes, N/P is the molar ratio between positively charged polymer amine groups to negatively charged nucleic acid phosphate groups.

Complexes, at different N/P ratios, radius, surface charge and morphology were evaluated by Dynamic Light Scattering, Zeta Potential, Atomic Force Microscopy, and Cryo TEM. Results showed spherical nanoparticles that with the increase of the N/P ratio their average surface charge increases, while the radius decreases. The attachment of PEG-thiol to Q-starch, led to the formation of larger complexes with lower charge.

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Functional Gold Nanofibers Fabricated through Self-Assembly on Peptide Templates

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Keywords: *Au nanofibers, peptide β-sheets, Au thiocyanate, peptide templates, transparent conductive electrodes*

Abstract

The use of biological materials as templates for functional molecular assemblies is an active research field at the interface between chemistry, biology, and materials science. There is a growing interest in development of "bottom-up" routes for the construction of metal surface patterns and nanostructures on biological templates in the forms of fibers, tubes, sheets, and other aggregates. We present a new "template-directed" bottom-up method for forming Au nanofibers through incubation of β-sheet peptide films in an aqueous solution of $Au(SCN)_4^{1-}$. The peptide domains, assembled upon isothermal compression at the air/water interface, serves as planar scaffolds for Au nanofiber formation. The gold deposition utilizes spontaneous crystallization and reduction of water-soluble $Au(SCN)_4^{1-}$ upon anchoring to surface-displayed amine moieties. A short amphiphilic peptide Pro-Lys-$(Phe-Lys)_5$-Pro (denoted as P_{FK}-5), which forms a β-sheet monolayer while compressed at air/water interface was used for the experiments. The crucial role of the P_{FK}-5 peptide is the display of amino groups employed for binding of the negatively-charged Au(III) complex, which subsequently undergoes crystallization and reduction into metallic Au(0). An interlinked network of crystalline Au nanofibers is readily formed upon incubation of the Au(III) thiocyanate complex with the peptide monolayers. The resultant films were optically transparent, enabled electrical conductivity, and displayed pronounced surface enhanced Raman spectroscopy (SERS) activity. This strategy for obtaining interconnected Au fibers obviates the need for inclusion of reducing agents in the reaction mixture and pre-formation of Au nanoparticle building blocks, making the approach a promising avenue for construction of nano-structured films exhibiting practical applications.

A GRAPHIC USER INTERFACE FOR SCANNING PROBE MICROSCOPE (SPM) FORCE RECONSTRUCTION

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Keywords: *nanometric resolution, SPM force measurement.*

Abstract

SPM (aka AFM) is a common analytical tool to measure hard and soft matter surface topography with nanometer resolution and forces down to the picoNewton. In an effort to streamline the rendering of forces from the microscope voltage vs time raw data, we developed a GUI based on a new solution to the equations that describe the bending motion of the SPM cantilever in the time domain without going to frequency space. The approach presented here introduces a novel boundary condition which takes experimental signals as input. This provides clarity to force reconstruction methods. This presentation considers the cantilever sensor as a filter, with explicit response, allowing SPM experimentalists to convert measured voltage traces to force vs separation curves. Also, based on the algorithm a simple recipe is presented to determine when the simple harmonic oscillator can be safely used for processing the SPM data or if the full theory is necessary. We will show a full solution (KCB) of the Euler-Bernoulli equation that describes the dynamics of the cantilever. This is done by discretizing the problem in space s and time t, and implementing the new boundary conditions that connect the bending of the cantilever to the experimentally measured voltage. We explicitly show the steps required to go from the experimental $V(t)$ to the desired $F(s)$. We apply the KCB method to establish the limits of the simple harmonic oscillator algorithm. We find that the proper algorithm to use can be decided in advance by simply analyzing the SPM measured voltage. All this information is encapsulated in a java GUI for easy of use. We will bring the GUI to the conference to let the audience play with it.

J. Mehlman and F.R. Zypman, Scanning Probe Microscope Force Reconstruction Algorithm via Time-Domain Analysis of Cantilever Bending Motion, J. Adv. Microsc. Res. 9, 268-274 (2014)

Uptake study of Q-starch based siRNA complexes in human ovarian cancer cells

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Keywords: *Quaternized starch, Polysaccharide, Small interfering RNA, Drug delivery, Self-assembly complexes*

Abstract

RNAi therapeutics is a powerful tool for treating diseases by sequence-specific targeting of genes using siRNA. The remaining challenge before widespread clinical use is developing an efficient and safe carrier that will allow overcoming siRNA delivery barriers1. In our previous study, we addressed this issue by developing and characterizing modified potato starch based delivery platform for siRNA as a biodegradable and biocompatible polysaccharide2.

Our therapeutic target is a human ovarian adenocarcinoma cell line, NCI-ADR/Res (NAR), which develops resistance to chemotherapy treatment caused by overexpression of P-glycoprotein (P-gp). Therefore, RNAi induced gene silencing of P-gp is used. We demonstrated that modified 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 that an efficient gene silencing (50% reduction at the protein level) was accomplished after 72 hours of incubation with the complexes.

By identifying the barriers (cell uptake, endosomal escape and decomplexation), and the rate limiting step of the complexes' transport, we will be able to overcome them and thus improve the delivery efficiency. Therefore, our goal is to study the kinetics and mechanism of the complexes' pathway by following each step in the transport mechanism starting from the cell uptake stage, using light microscopy, biophysical approaches.

We demonstrated that the uptake into NAR cells is facilitated by Q-starch since co-localization of siRNA and Q-starch (fluorescently labeled) was visualized. In addition, we present qualitative (confocal microscopy) and quantitative (Imagestream flow cytometry) kinetic uptake study of fluorescently labeled complexes into NAR cells over a 24 hours study. A significant uptake into the cells is observed, indicating that this stage is probably not a significant barrier during the 72 hours gene silencing study. Moreover, we present data indicative of endocytosis mediated uptake of complexes.

Fluids with random interactions: Pair-interaction ordering and particle dynamics

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Keywords: multi-component fluid, molecular dynamics simulation, pair-interaction ordering, particle dynamics

Abstract

We use molecular dynamics simulations in 2D to study multi-component systems in the limiting case where all the particles are different (APD). The particles are assumed to interact via Lennard-Jones (LJ) potentials, with identical size parameters but their pair interaction parameters are generated at random from a uniform (U) or from a peaked (GM) distribution. We analyze both the global and the local properties of these systems at temperatures above the freezing transition and find that APD fluids relax into a non-random state characterized by clustering of particles according to the values of their pair interaction parameters (particle-identity ordering). We also analyze single particle trajectories to study the dynamics of the particles. It is observed that the U system behaves like that of a pure one-component LJ fluid, while the dynamics is different for GM system.

Development and characterization of targeted delivery system based on PI3P and modified starch to overcome insulin resistance

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Insulin resistance is a physiological condition in which cells fail to respond to the normal actions of the hormone insulin leading to high glucose blood level. It has been suggested that in case of obesity Phosphoinositol 3 phosphate (PI3P), a minor component of cellular membranes that regulates biological processes, can help overcoming hepatic insulin resistance.

A major obstacle in delivering exogenous PI3P into cells is overcoming its negative charge (derived from the phosphate groups on the inositol ring) that cause an electrostatic repulsion with the negative surface charged cell membrane. In this work, a positively charged modified starch is proposed as a PI3P carrier in order to overcome this obstacle.

Starch is a natural polysaccharide that is considered advantageous for drug delivery due to its biodegradability, biocompatibility and minimal cytotoxicity. In this study, potato starch was modified into cationic starch (Q-Starch) with the quaternizing agent 3-chloro-2-hydroxypropyltrimethyl ammonium chloride (CHMAC). The positively charged quaternized ammonium groups on the modified starch and the negatively charged PI3P interact electrostatically, allowing for complexes formation.

Q-Starch/PI3P nanoparticles radius and surface charge were evaluated by Dynamic Light Scattering and Zeta Potential at different N/P ratios (Molar ratio of Q-Starch nitrogen groups (N) to PI3P phosphate groups (P)). Preliminary results of *in-vitro* experiments, evaluated by confocal microscopy and ImageStream^X of HEK-293 cells treated with Q-Starch/PI3P complexes, show intra-cellular uptake of Q-starch/PI3P complexes.

Protein loaded PLGA nanoparticles as drug delivery system

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Over the past few decades, there has been considerable interest in developing biodegradable nanoparticles (NPs) as effective drug delivery devices. Poly lactic-co-glycolic acid (PLGA) is a biodegradable and biocompatible FDA approved copolymer, which is known as a vehicle for controlled delivery of drugs[1]. A wide range of proteins have been recognized as a novel generation of drugs, mainly due to their highly specific activity. However, there are several problems associated with therapeutic trials of protein drugs. Among them are the short *in vivo* half-lives and the side effects attributable to the multiple and high-dose injections. The encapsulation of these therapeutic proteins in PLGA nanoparticles has arisen as a promising alternative to overcome these problems[2].

The objective of this study is examining the effect of molecular weight and copolymer composition on the NPs properties, the drug loading level and the protein release kinetics. Thyroglobulin (TG) (Mw 670 kDa), a protein model, was incorporated in PLGA NPs through a modified double emulsion W/O/W solvent evaporation procedure. Two types of 50:50 PLGA copolymer with different Mw were used while preparing the NPs. The size of the NPs was obtained using dynamic light scattering (DLS), surface morphology and shape were investigated by scanning electron microscopy (SEM) and surface charge of the NPs was determined by Zeta potential. The amount of TG loaded was determined by mass balance calculations and spectroscopy. TG was encapsulated successfully in the PLGA NPs resulting in high encapsulation percentage. *In vitro* TG release kinetics experiments from the PLGA NPs found that the Mw of PLGA influence the release rates of the protein.

1. Kumari *et al*, Colloids and Surfaces B: Biointerfaces 75.1 (2010): 1-18.
2. Kinetics. Danhier *et al*, J.Controlled Release, (2012): 161, 2, 505-522.

Thermo-responsive Hydrogels Crosslinked by Branched Peptides

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Elastin is one of the most abundant extracellular matrix proteins. Comprised of the Xaa-Pro-Gly-Yaa-Gly penta-peptide repeats, elastin-like peptides (ELPs) have been found to show lower critical solution temperature (LCST) behavior. We synthesized branched ELPs with the sequence (GLPGL)n, Including peptide dendrimers with different chain length and generations, as well as hyperbranched peptides. We were able to evaluate the topological effect on the LCST behavior. The peptides were further used to crosslink reversible addition-fragmentation chain-transfer (RAFT)-based polymers. Sodium cyanoborohydride reduced the imine, which was formed between the peptide amine and aldehyde from the polymer to secondary amine, leading to a stable hydrogel.