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NANONEWS

Tel Aviv University Center for Nanoscience and Nanotechnology

Editors: Dr. Nava Ariel Sternberg and Prof. Koby Scheuer

This issue of Nanonews is dedicated to the memory of Prof. Eshel Ben Jacob (1952-2015), a great scientist and a friend and to the memory of Alex Epstein (1953-2015), our highly professional staff member and a friend.

Prof. Eshel Ben Jacob
(1952-2015)

Alex Epstein
(1953-2015)

About Prof. Ben Jacob, by Prof. Yael Hanein

First and foremost Prof. Eshel Ben Jacob was a physicist.

The starting point of his academic career was solid-state physics, a field that equipped him with tools, insights, and a fearless mindset – all of which he employed in his many scientific endeavors which lasted nearly forty years. His curiosity knew no bounds and over the years he explored more and more scientific fields, from pattern formation in complex systems to understanding the "intelligence" of bacteria. Eshel also studied neuronal systems and gene networks, explored the mysteries of astrocytes, and investigated economic models.

Eshel quickly mastered each field he entered. He built an immense amount of know-how and always combed the available literature for interesting questions and radically new answers. In each of his many explorations, Eshel cooperated with colleagues - the storm of excitement and out-of-the-box thinking Eshel displayed was a stimulating and empowering experience for his peers.

Eshel understood the significance of making science accessible to the public. He appreciated the importance of writing and speaking plainly about complex scientific issues, and accordingly he delivered numerous inspiring lectures to the general public. Despite his expansive scientific workload, Eshel dedicated an immense amount of time and energy to voice the need to support science education in Israel.

Prof. Eshel Ben Jacob was special. His legacy will remain in the vast body of knowledge he generated during his career, and in the friendship and passion to science he shared with so many of his academic peers and the many graduate students he mentored. Eshel will always be remembered for his selfless devotion and boundless passion to people and to science.

Featured article

Metastability in lipid particles exhibits temporally deterministic and controllable behavior

Guy Jacoby, Roy Beck

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Lipid phase-behavior has been the focus of investigation for over five decades due to the lipids, importance as a key constituent in all biological cells. More recently they have been studied as components in bioengineered drug delivery systems[1]. As amphiphilic molecules, lipids are capable of self-assembling into a multitude of diverse functional mesophases, distinguished by their topology and degree of symmetry. A transition between these mesophases can be

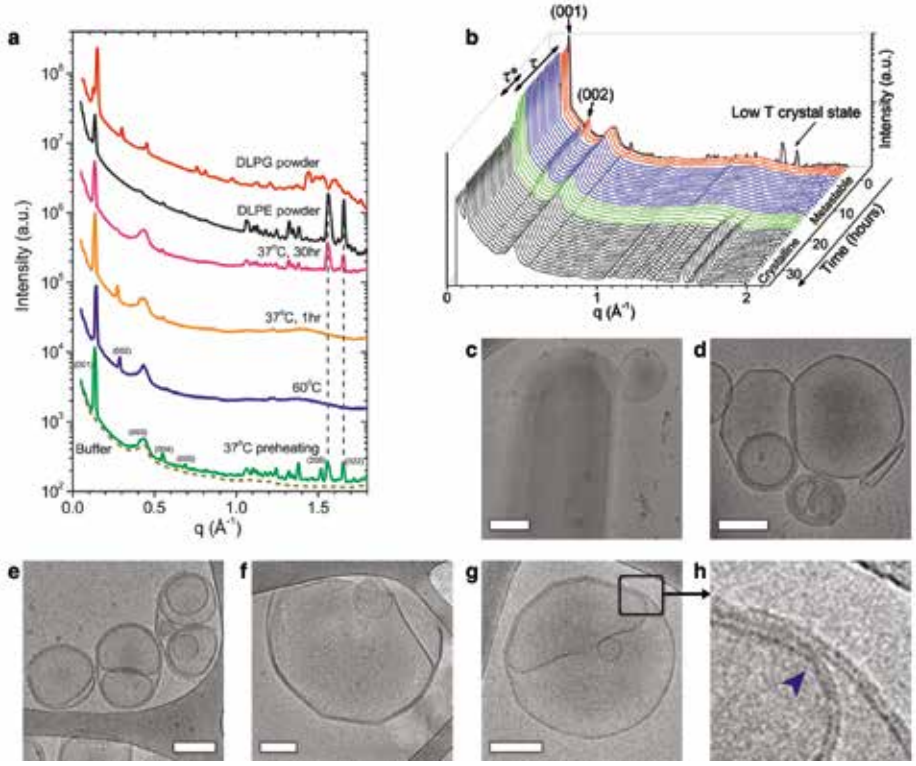

Figure 1: Time-resolved structural analysis of LPs showing delayed crystallization. (**a**) Representative SXS data at different stages of the experiment, compared with DLPE and DLPG powders. Crystalline peaks of the lipid aqueous dispersions match those of pure dry DLPE. (**b**) Initially, at 37 °C (black spectrum), the crystalline state shows wide-angle peaks. When heated to 60 °C (red spectra) the wide-angle peaks disappear with the loss of in-plane lipid order. After cooling back to 37 °C (blue spectra) the Lα phase remains for 16.1 hours and then phase-transitions back into the crystalline state (green spectra). **c-h**, Cryo-TEM images of specimens vitrified at different stages. (**c**) Specimen vitrified from 37 °C prior to heat treatment, showing a large DLPE crystal structure along with uni- and multi-lamellar vesicles. (**d**) Sample vitrified from 37 °C prior to heat treatment showing vesicles with sharp facets. (**e**) Sample vitrified from 60 °C showing large MLVs. (**f**) Sample vitrified from 37 °C 44 hours after cooling. (**g**) Sample of a 90:10 DLPE:DLPG (mole %) vitrified from 37 °C three days after cooling, showing multiple facets on a vesicle. (**h**) High mag of previous micrograph showing the fusion of two membranes (blue arrowhead), separating the crystalline phase (straight facets to the left) from the liquid-crystalline phase (disjoined, curved leaflets to the right).. Unless specified, data are of 95:5 DLPE:DLPG (mole %) dispersions in 150 mM monovalent salt. Scale bar in c corresponds to 200 nm. Scale bars in **d-g** correspond to 100 nm. Adapted from Ref. 4, Jacoby et al., Scientific Reports **5**, 9481 (2015)

induced by changing thermodynamic parameters, such as temperature or pressure, solvent properties or lipid stoichiometry. However, many lipid systems can often display a hysteresis in their phase-transitions, expressed as long-lived metastable states before transitioning to the stable one[2].

The classical theory of nucleation and growth, a staple framework for many systems that exhibit first order phase-transitions[3], describes the formation of a stable phase from the bulk of a metastable phase. The energetically favored bulk interactions of the new phase must overcome the unfavored contribution from the interface. In the absence of external perturbations the metastable-to-stable energy barrier can be overcome by spontaneous thermal fluctuations. Therefore, in bulk, nucleation is initiated by an independent stochastic process, resulting in an unpredictable and uncontrollable phase-transition.

Our study focuses on a temperature induced phase-transition in lipid particles, containing a majority of dilauroylphosphatidylethanolamine (DLPE), from a metastable liquid-crystalline (disordered) to a stable crystalline (ordered) phase. In our recent paper, using time-resolved solution x-ray scattering (SXS) and cryogenic transmission electron microscopy (cryo-TEM), we show that the metastable phase lifetime is on the order of tens or hundreds of hours depending on sample parameters[4]. Moreover, we demonstrate that the phase-transition is a collective event, which exhibits a temporally deterministic and controllable behavior, in contrast to the classical nucleation and growth theory.

Lipid membrane crystallization

Studies of DLPE have shown its phase-behavior dependence on thermal history. Whether or not the lipids were preheated above their melting temperature changed the transition pathways in calorimetric and x-ray scattering studies[5-7]. It was also shown that the liquid-crystalline lamellar phase (L_α), which is stable at temperatures above 43°C, becomes metastable upon cool-

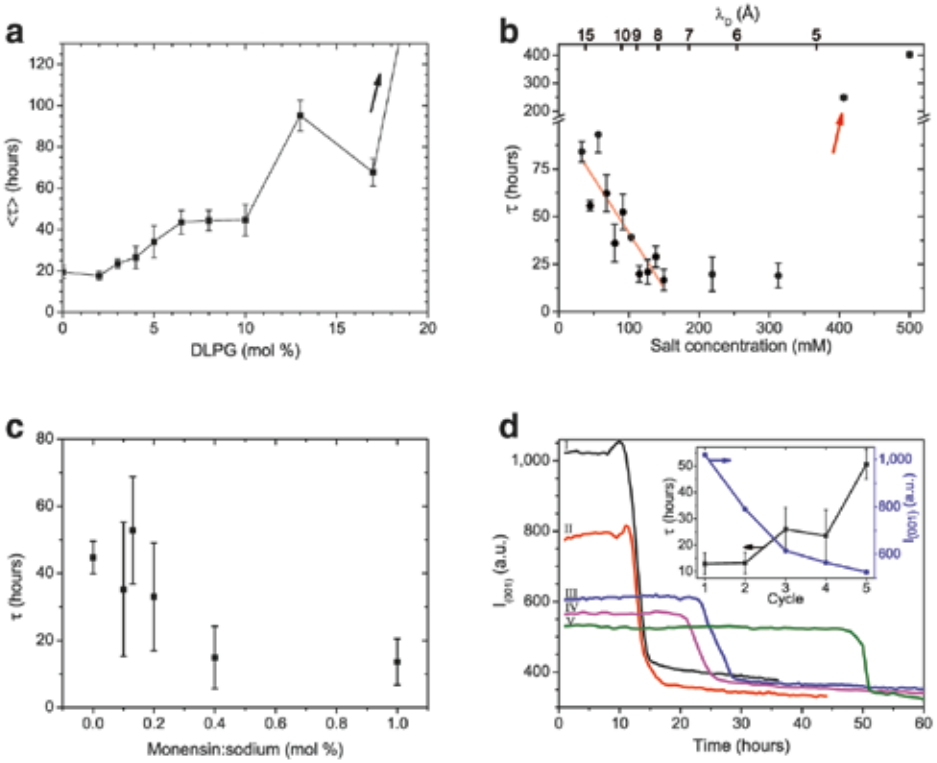

Figure 2: Manipulation of the delay time for crystallization at 37 °C. (**a**) Average delay time increases with the addition of DLPG. Lipid dispersions in buffer containing 150 mM monovalent salt. The last point did not recrystallize in the duration of the experiment (200 hours). (**b**) Non-monotonic effect of salt concentration on the delay time, τ. With the addition of salt, at low concentrations (<150 mM), τ decreases in a linear fashion (red line), while at high concentrations (>300 mM), there is an order of magnitude increase. (**c**) Effect of the monensin ionophore on the delay time. Control sample recrystallized at $\tau = 44.7$ hours. The addition of monensin accelerates recrystallization; sample containing 1mole % monensin:sodium recrystallized with $\tau = 13.6$ hours. Experiments performed on samples containing 90:10 DLPE:DLPG at 150 mM monovalent salt. (**d**) Consecutive heating-cooling cycles display a prolongation of the delay time accompanied by a decrease in the metastable lamellar scattering intensity. The curves represent the intensity of lamellar (001) scattering from the moment the temperature is brought back to 37 °C after heating. Roman numbers indicate the measurement sequence. Inset shows qualitative analysis of the two effects. **b** and **d** represent data of 95:5 DLPE:DLPG (mole %). Error bars represent the average phase transition time <τ*>. Adapted from Ref. 4, Jacoby et al., Scientific Reports **5**, 9481 (2015)

ing to a temperature between 30°C and 43°C. It was further suggested that the DLPE would revert to the low temperature crystalline phase (L_c) spontaneously after an incubation time of several hours. However, these studies did not delve into the dynamics of the metastable-to-stable phase-transition.

Studying the metastability

Using time-resolved SXS and cryo-TEM we were able to observe and record the phase-transition dynamics and quantitatively extract structural information of the phases and the metastable state and transition lifetimes. This allowed us to qualitatively evaluate the mechanism leading to the metastability. Figure 1 shows the SXS data of an experiment performed to retrieve the aforementioned information. Scattering curves of a sample, initially found in the crystalline state at low temperatures, show long-range correlation peaks of the lamellar structure (small angles) as well as in-plane order of the hydrocarbon chains (wide angles). The same sample is then heated above the melting temperature to 60°C, and the rapid transition to the liquid-crystalline phase is evidenced by the disappearance of the in-plane correlation peaks at wide angles. By cooling to 37°C, the liquid-crystalline L_α phase remains metastable for many hours before reverting back to its initial crystalline state. In addition, cryo-TEM images representative of the different stages of the experiment and the corresponding morphological changes are shown (Figure 1 c-h). The images revealed structural information which supported the scattering data, as well as shed new light on the possible mechanisms of recrystallization.

In order to test the reproducibility of the phenomenon, we performed the aforementioned scattering experiment on 24 samples with the same lipid stoichiometry and at the same conditions (solvent). The delay time to phase-transition has a Gaussian normal distribution, rather than an exponential distribution, which is expected for a stochastic Poisson process. Moreover, analyzing the

SXS data of more than 60 experiments in varying conditions, revealed the robust nature of the phenomenon[4].

The delay time to recrystallization was further studied by changing various parameters of the system, and recording their effect on the metastable phase lifetime. We showed that by changing solvent salinity, lipid stoichiometry, the inclusion of cross-membrane ion-carriers, or performing consecutive phase-transitions we were able to manipulate the delay time (Figure 2). By affecting the interactions of the lipids, water molecules, and ions, we are able to control the metastability lifetime.

Inspiration from ferroelectricity

The time scales of the delay time to phase-transition, and of the phase-transition itself, are orders of magnitude larger than those associated with typical lipid diffusion. Moreover, the data suggest a cooperative and collective crystallization event. These findings led us to search for a suitable model that will consist of these characteristics, and such a model was found in an entirely different field. Delayed nucleation, similar to the one which we have been investigating, was observed and studied theoretically in the paraelectric to ferroelectric phase-transition in barium titanate[8-10]. In an attempt to elucidate this non-classical nucleation and growth phenomenon, the theory included nucleation mediated by long-range interactions. In the studies mentioned, the metastable activation energy-barrier was modeled as time-dependent, which ultimately defined the delay time of the system. The delay time was measured to be six orders of magnitude larger than the expected time-scale, similar to what we observed.

Our findings have presented an accessible system displaying non-classical nucleation and growth, and have opened new avenues for research in metastability and controlled delayed nucleation. Finally, DLPE:DLPG dispersions are currently being studied as components of drug delivery nano-carriers[11-13]. Manipulation of delayed nucleation may ultimately aid in designing novel modalities for entrapment of therapeutic payloads and their controlled release.

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Research news

Nano Structured N-doped TiO_2 Photo-Catalytic Membranes for Water Treatment

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According to the World Health Organization (WHO), over the last 30 years there has been a substantial global shortfall in availability of potable water - primarily arising from population growth, over-exploitation, and industrial contamination and pollution. The introduction of membrane filtration systems in water treatment is rapidly growing, specifically microfiltration systems (MF), with pores in the 0.1-10 µm range, offers quick and selective separation of

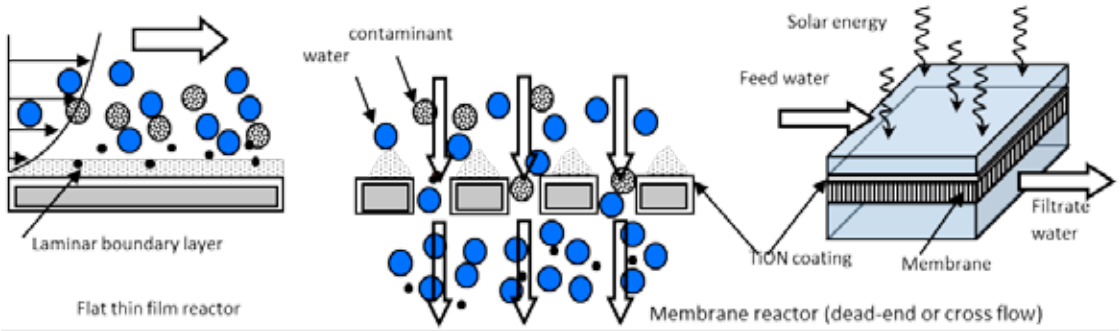

Figure 1: The principle of flat thin film compared to combined filtration and chemical degradation reactors

suspended particles, larger pathogenic micro-organisms while operating at low pressure values. However, a number of contaminants, including micro-pollutants (e.g. pharmaceuticals, pesticides), and pathogenic microorganisms (e.g. small bacteria and viruses), can only be poorly removed from water by MF alone. More effective, low-cost, robust methods to disinfect and decontaminate water are needed, without further stressing the environment or endangering human health by the treatment itself.

The combination of solar energy to activate nano-structured photocatalyst via advanced oxidation process (AOP) is among the most promising emerging water treatment processes and is anticipated to play a crucial role in combination with conventional technologies. Titanium dioxide (TiO_2) is one of the most commonly used materials for photocatalytic applications[1]. In TiO_2 based AOP, a broad spectrum of pollutants are chemically oxidized by the nonselective highly reactive hydroxyl radicals. TiO_2 activation can be achieved by ultraviolet (UV) light ($\lambda < \sim 390$ nm), which results in about 5% spectral overlap between its absorbance and sunlight emission. Hence, modification of the physicochemical and optical properties will allow utilizing a larger fraction of the solar spectrum which is an economic and ecological light source. Doping TiO_2 with non-metal atoms like nitrogen has the potential to significantly improve its activity under UV and visible light[2-4].

The catalyst can be deployed either as a suspension of particles, or a coated flat surface. The suspended particles require separation/recycling from the treated water which is an inconvenient and an expensive process. Alternatively, immobilized thin film reactors are limited by diffusion across the laminar boundary at the film surface in addition to the significantly smaller surface area compared to catalytic powder. Among the various configurations (e.g. fixed-bed, rotating disk, falling film, etc), photocatalytic membranes are of the highest interest to this work (**Figure 1**). In this configuration, the catalyst is embedded in a membrane matrix, thus immobilized, and activated by direct illumination of the membrane. A hybrid system combining both membrane filtration and photocatalysis may gain tremendous popularity because of their multiple functions: 1) decomposition of organic pollutants and biological toxins, 2) inactivation of pathogenic microorganisms, 3) physical separation (turbidity reduction, color), and 4) self-antibiofouling action.

This research is a part of an international collaborative project titled: Nano-structured TiON photo-catalytic membranes for water treatment (NATIOMEM). In this work, a sol-gel method was developed to deposit photocatalytically active thin films of N-doped TiO_2 on porous commercial α-Al_2O_3 ceramic membranes. X-ray diffraction (XRD) results determined that N-doped TiO_2 coating is present on the surface in the form of an anatase phase while X-ray photoelectron spectroscopy (XPS) data provided an estimated surface coverage (~84%). The filtration and photocatalytic activity (PCA) of the membrane found in laboratory experiments was presented, using a versatile laboratory flow cell illuminated by a solar simulator. Utilization of solar irradiation has been optimized by TiO2 modification via nitrogen doping which allowed expending activity to UV-visible light. The PMR was found to be superior (by 90%) to the immobilized flat reactor configuration in photocatalytic oxidation of the environmentally persistent pollutant carbamazepine. The disinfection efficacy of PMR was determined by inactivation of MS2 virus which is considered worst-case scenario in virus removal by traditional membrane filtration due to its unique physico-chemical properties. The PMR achieved > 99.99% removal of the virus, meets the EPA requirement for surface water.

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Nonlinear Crystal with Super-Narrow Response

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Nonlinear crystals convert laser light from one frequency to another. While the nonlinear crystal is usually designed to work at a specific wavelength, it also converts efficiently frequencies which are in the vicinity of that wavelength. When the input laser consists of multiple wavelengths and only a specific designed wavelength is of interest, this wide response must be narrowed so that the unwanted wavelengths would be filtered out.

However, in order to achieve a narrow conversion response, a long crystal is needed, since the spectral width of the efficiency response function of regular nonlinear crystals is inversely proportional to the crystal's length. Unfortunately, longer crystals are more expensive and possess larger footprint. Moreover, the maximum length of most existing crystals is limited to a few centimeters at most.

In our research[1], we show that by appropriate modulation of the nonlinear crystal, the width of the converter can be made as narrow as we like, irrespective of the crystal's actual length. This is achieved by binary modulating the nonlinear coefficient of the crystal with a "super-oscillating" function.

Super oscillating functions are functions that oscillate locally much faster than their highest Fourier component. Fourier transform of a function tells us what are the frequencies (or oscillations) that compound the function. Therefore one might expect that a function which exhibits high frequencies locally, will also show this high frequency in its Fourier transform. In super oscillating functions, however, is not the case, and a locally high frequency is "missing" from the transform. Theoretically, one can use this type of functions to encode Beethoven's 9th symphony in only 1Hz sampling resolution (!), however it is experimentally very difficult due to the very low amplitude of the super oscillations.

This work brings the concept of super oscillations to the nonlinear optics regime for the first time. Figure 1 shows a schematic description of the experiment: a super oscillating crystal, having the same length as the normal periodically poled crystal, exhibits a fast oscillation and two very close zero nodes. These zero nodes can be arbitrarily close, and allow filtering two close wavelengths, by placing them at these points of zero efficiency.

The efficiency of the designed crystal, η, is proportional to:

$$\eta \propto \left(cos\frac{f(\lambda - \lambda_0)}{2} - s \right)^2$$

Where s is between 0 and 1, λ is the input laser wavelength, and λ_0 is the design wavelength. The highest frequency of this function is f (which is proportional to the crystal length), however the function has a small oscillation near λ_0, which can be as small as we'd like it to be by making s close to 1. Figure 2 presents the theory and experimental results for 10mm KTP crystal.

This high resolution nonlinear filter can have applications in optical communication, spectroscopy, quantum information and more.

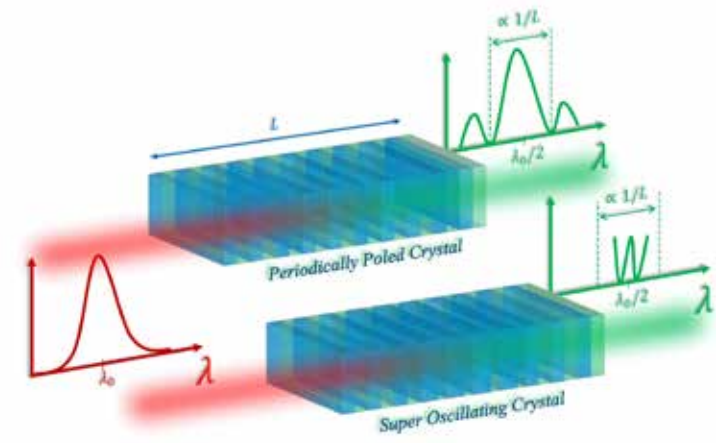

Figure 1. Schematic description of periodically poled and super-oscillating crystal

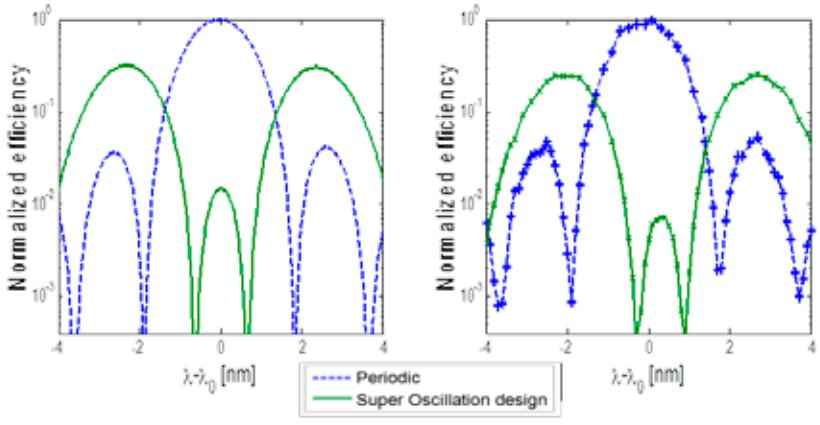

Figure 2. Normalized Efficiency. Simulation (left) and experimental (right) results of normal periodically poled (dashed blue) and super oscillating (solid green) KTP crystals. Both crystals have the same length of 10 mm, but the super oscillating crystal has a spectral width of only 1.1 nm (in green), 69% less than the spectral width of a normal crystal (in blue)

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Atomic-resolution structure of the intact M13 filamentous bacteriophage virus by magic-angle spinning NMR: a quadrupled hydrophobic/aromatic binding epitope

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Filamentous bacteriophages are viruses that infect bacteria via the tip of the pilus protein assembly. They replicate using the cell machinery and leave the cell intact after their release. Filamentous phages are primarily composed of thousands of copies of a single short coat protein, about 50-amino-acid long, that wrap a circular single-stranded DNA. The lengths of such phages are in the order of one micrometer and their diameter is a few nanometers long. Since such viruses cannot be crystallized and are not amenable to solution NMR studies due to their large molecular weight, in the order of tens of MegaDaltons, we employed magic-angle spinning (MAS) solid-state nuclear magnetic resonance (ssNMR) in order to study the structure of the M13 bacteriophage. Using MAS it is possible to obtain high-resolution spectra that report on the chemical shifts of all carbon and nitrogen atoms in the virus provided that an intact phage sample has been prepared by infecting host cells, which were grown in a medium that contains ^{13}C and ^{15}N labelled precursors such as glucose, glycerol, and ammonium chloride[1]. By employing multi-dimensional MAS ssNMR experiments that recouple the dipolar interaction between atoms close in space (up to ~7.5Å) we can obtain pair-wise approximate distance information. The distances, as well as the chemical shift frequencies, are further used as constrains for the mutual calculation of the secondary, tertiary, and quaternary fold of the virus[2]. For this calculation, we used the fold-and-dock protocol of the software CS-Rosetta[3], in collaboration with N. Sgourakis (currently at UC Santa Cruz) and D. Baker from the University of Washington in Seattle. The resulting structure, appearing under PDB entry 2MJZ, shows that the one-micron-long virus consists of a 7.04 nm diameter. It is composed of pentamers of the coat protein subunit (information which was available from fiber diffraction data) that are related to each other by a translation of 16.6 Å and a rotation of 36.4°, that is, they have a close to perfect C_5S_2 symmetry. Each subunit has a slightly bent and rigid α-helical structure with a short flexible N-terminus that adopts a type-II β-turn structure. The structure is stabilized by a repeating hydrophobic-aromatic binding epitope that is located at the interface between the subunits. A close examination of the structure shows that each subunit participates in four such hydrophobic "locks" that spiral along the entire phage, thereby "locking" the structure and providing the unusually high stability for the virus. Further ssNMR experiments that probed the DNA-coat protein contact interface[4] verified the correct orientation of the capsid and showed that it involves interactions between the positively charged lysine residues and the negatively charged DNA phosphates.

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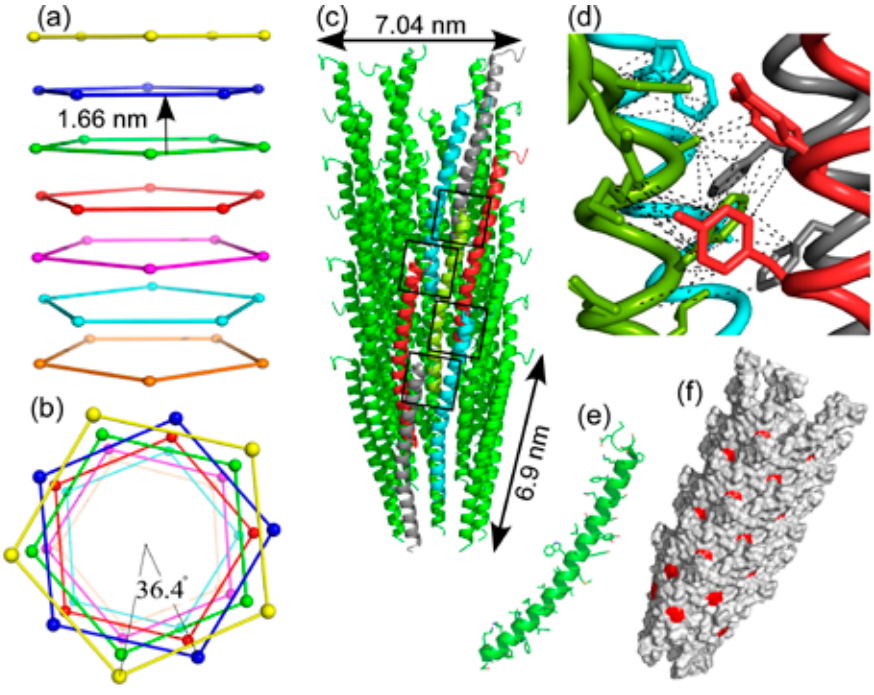

Figure 1: (a) Symmetry of the pentamers, side view. Each subunit is represented by the location of the proline-6 backbone nitrogen atom. (b) Top view of the pentamers. (c) Cartoon view of 35 subunits of the viral capsid, approximately 1 percent of its lentgh; boxes indicate the location of the four hydrophobic/aromatic pockets within the light-green colored subunit. (d) A close view of the sidechain packing – expansion of the top hydrophobic pocket showing aromatic sidechains. (e) The structure of a single subunit. (f) A surface plot of the viral capsid with the tryptophan residue colored in red demonstrating how the hydrophobic pocket spirals along the capsid.

Targeting and Modulation of Cardiac Macrophages for Cardiac Repair

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Heart failure (HF) is a major cause of hospitalization and death, with a steady rise as life expectancy increases. Unlike skeletal muscle, adult cardiac muscle lacks significant regenerative potential. Uncontrolled activation of pro-inflammatory macrophages after myocardial infarction (MI) accelerates adverse left ventricular (LV) remodeling, heart failure, and death.

Ironoxide nanoparticles (IONP) and small iron complexes, such as hemin, have shown potential in modulating the pro-inflammatory M1 macrophages, switching them into the reparative M2 macrophages. Administering these iron compounds in their free form is prone, however, to the well-known deficiencies of treatment with free drugs, especially lack of targeting, that too often result in poor therapeutic responses, poor safety, and treatment failures.

To address this challenge, we formulated the iron compounds in a special type of liposomes that have hyaluronan bound covalently to their surface (denoted HA-LP). Hyaluronan is the natural ligand of the CD44 receptors harbored by membranes of inflammatory cells, endowing HA-LP with the ability to bind with high affinity to the macrophage membrane and to perform there as a slow-release drug depot facilitating and enhancing drug entry into the cell.

Hemin is known to exert its anti-inflammatory activity in macrophages by being both an inducer and a substrate of the intracellular enzyme heme-oxygenase 1 (HO-1). *In vitro* and for the same hemin dose, hemin/HA-LP was significantly better than free hemin, in HO-1 induction and in anti-inflammatory activity.

Active *in vivo* targeting is manifested by preferential accumulation of the therapeutic system at the target, with little or no accumulation elsewhere. To that end, we prepared red-fluorescing HA-LP and IONP-encapsulating HA-LP, that were administered IV to MI mice and pigs, one and three days post MI, respectively. Active targeting was, indeed, achieved in the infarcted heart, in both MI animal models (Figure 1). Lungs, liver, spleen and kidneys of the MI animals were liposome-free (data not shown).

For evaluation of therapeutic responses MI mice were treated one day after the MI by IV administration of: (1) liposomal hemin (HA-LP) (2) drug-free liposomes (HA-LP) (3) free hemin and (4) saline. Hemin dose (free or liposomal) was 2 mg/kg body and the HA-LP dose (drug-free or hemin-loaded) was 50 mg lipid/kg body. Left ventricle (LV) remodeling and function were assessed by echocardiography before, and one week or 30 days after, treatment.

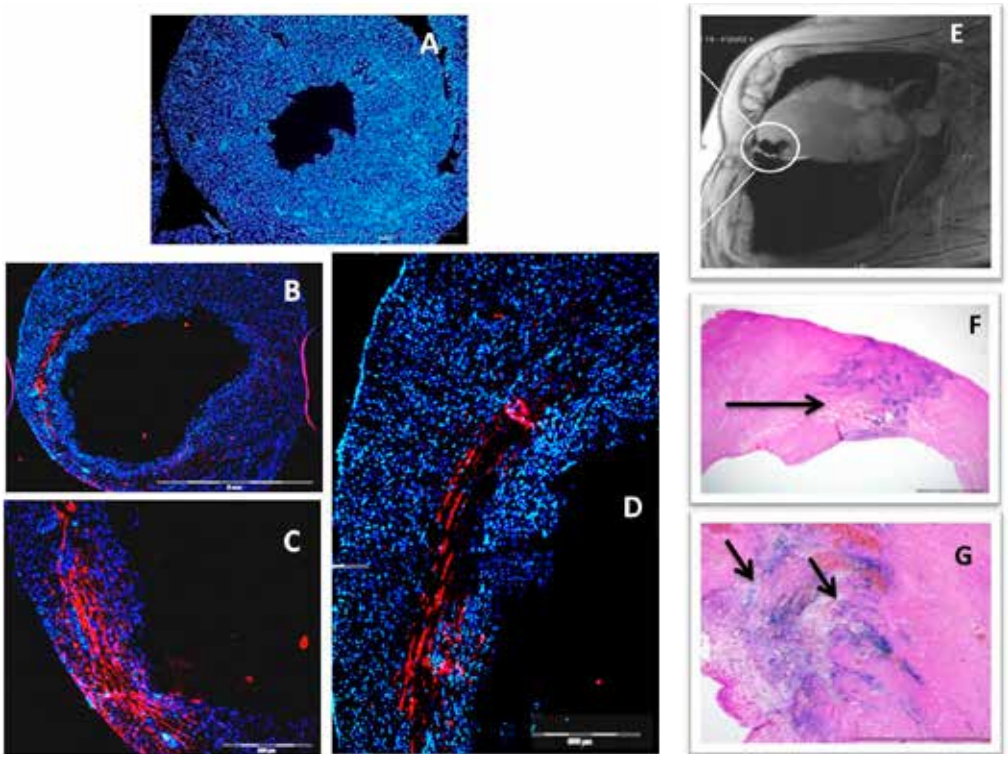


Figure 1: Infarct Macrophage Targeting with HA-LP in mice (A-D) and pigs (E-G) with Myocardial Infarction (MI). **A-D** are images showing active *in vivo* targeting of HA-LP containing the fluorescent lipid tag rhodamine-PE in MI mice. Red indicates the targeted liposomes (HA-LP) and blue is DAPI staining. **Figure 1A** is the normal heart of sham mice**. Figures 1B** is the infarcted heart, **Figures 1C and 1D** are higher magnifications of regions within the infarct heart. **E-G** are images showing active *in vivo* targeting of HA-LP encapsulating an MRI contrast agent iron oxide nanoparticles, to infarcted heart of pig. **Figure 1E** is an MRI image of the pig's heart, **Figures 1F** and **2G** are histological images of the infracted heart of **Figure 1E,** with the liposomes' presence in the heart being identified by arrows marking the liposomes' zone.

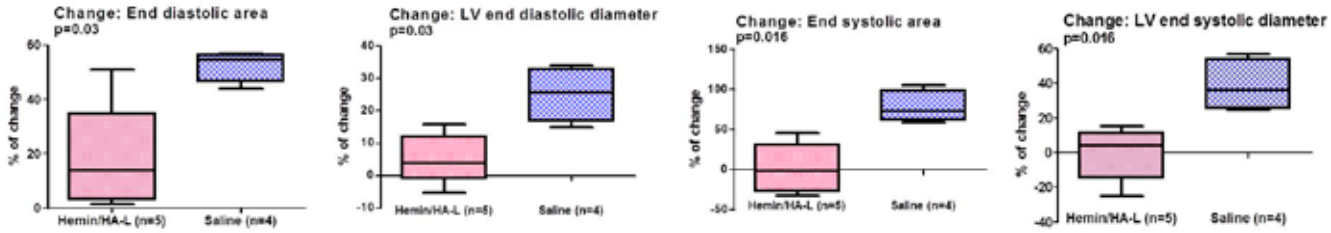


Figure 2: Hemin/HA-LP reduced left ventricle (LV) dilatation in mice 7 days after MI. The MI mice were given a single IV injection of saline or of hemin/HA-LP (2 mg/kg body hemin and 50 mg/kg body lipid) one day post MI, and the therapeutic effect was measured 6 days post treatment (7 days post MI).

Hemin/HA-LP outperformed free hemin generating a significant increase in the M2/M1 ratio for both peritoneal and heart macrophages. Significantly, compared to the untreated control group (mice receiving saline) a single treatment of MI mice with hemin/HA-LP significantly reduced LV dilatation (Figure 2), improved LV function and attenuated LV remodeling, via HO-1 induction. Treatments with equi-doses of free hemin or drug-free HA-LP were similar to the saline control.

In summary, hemin in the macrophage-targeted liposomes is a novel strategy for treatment of MI patients, switching macrophages into an anti-inflammatory phenotype, elevating active HO-1 expression and improving cardiac remodeling and dysfunction.

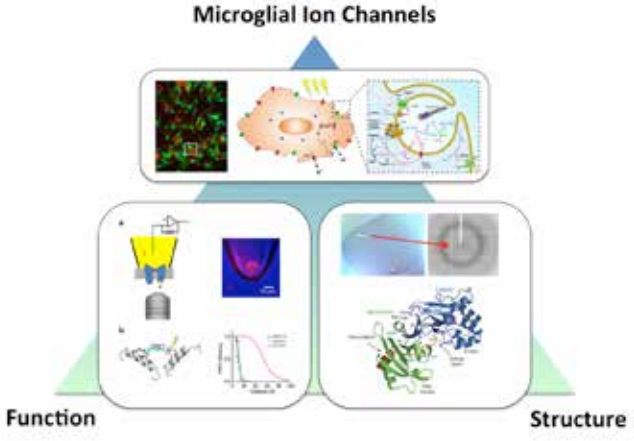
New researchers in the Center

Dr. Yoni Haitin

Dr. Yoni Haitin obtained his PhD in 2010 from the Sackler School of Medicine of Tel Aviv University for his research titled 'Inter-subunit interactions and assembly of the cardiac IKS channel complex: relevance to channel functions and pathophysiology', under the guidance of Prof. Bernard Attali. During that time he used electrophysiology and fluorescence to track the conformational changes associated with IKS potassium channel complex gating, and elucidated its extensive modulation by the auxiliary KCNE1 subunits. He also investigated the molecular mechanism by which naturally occurring mutations hinder IKS function and lead to the development of long QT syndrome, a life threatening form of cardiac arrhythmia.

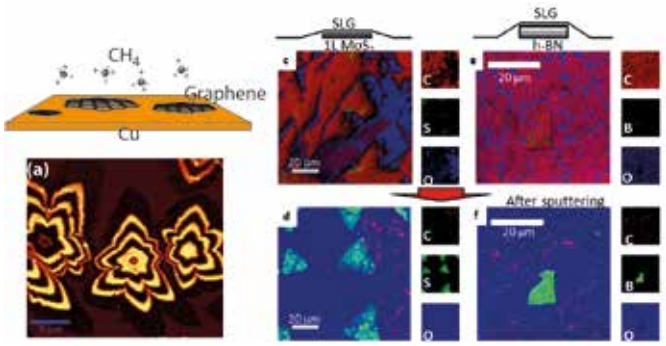
For his postdoctoral studies, Dr. Haitin moved to Seattle and joined the lab of Prof. William N. Zagotta at the Department of Physiology and Biophysics of the University of Washington, first as a Howard Hughes Medical Institute fellow and later as a Human Frontier Science Program long-term postdoctoral fellow. During that time he studied structural and functional aspects of KCNH channel regulation by their intracellular domains using X-ray crystallography and advanced biochemical and electrophysiological approaches. In April 2015 Dr. Haitin joined the department of Physiology and Pharmacology at Tel Aviv University.

The Haitin group focuses on the utmost basic molecular and structural aspects of the emerging roles ion channels play in microglia, the resident immune cells of the brain. Using a combined multidisciplinary approach, which includes novel fluorescence methods to monitor structural dynamics in functioning channels, X-ray crystallography and electrophysiology, his lab aims to understand the molecular mechanisms governing anion channels regulation and, in turn, elucidates how these channels contribute to microglial activity. He is also interested in developing new tools for tracking ion channel distributions in intact cells, and studying the ways they participate in shaping the immune response. Dr. Haitin is a member of the I-CORE Program for Integrated Structural Cell Biology.



Dr. Ariel Ismach

Dr. Ariel Ismach received his B.Sc. from the Ben-Gurion University in Materials Engineering. Then he moved to the Weizmann institute of science where he obtained his M.Sc. and Ph.D. under the supervision of Prof. Ernesto Joselevich from the dept. of materials and interfaces. He received the Ph.D. student prize from the ICS in 2008 for developing novel approaches for the guided growth of carbon nanotubes. In 2009 he joined the group of Prof. Jeff Bokor at the University of California at Berkeley as a postdoctoral researcher where he worked on nanomaterials-based electronic devices. In 2011 he joined the group of Prof. Rodney Ruoff at the University of Texas at Austin as a senior postdoctoral researcher to study the growth of graphene, hexagonal boron nitride (h-BN) and other "beyond graphene" atomic-crystals. He joined the department of material science and engineering at Tel Aviv University in October 2014 to establish the 2D materials lab. His group focuses on the study of growth mechanism of atomic-crystals, specifically, transition metal dichalcogenides (TMDs), with the aim to control their structure and chemical composition and thus their physical properties. Ismach's group will explore how the microstructure of 2D materials (phase, number of layers, stacking order, ad-layers, chemical composition, etc.) affects their electronic and optical properties. In addition, his group will explore new methodologies to tune the electronic properties (band-gap, doping, etc.) by using chemical functionalization schemes and tunable strains.



New faces at the Center

Yoav Benjamin

Yoav Benjamin joined MNCF staff in March 2015 after 15 years of working for Intel electronics, Numonix, and Micron in Qiryat Gat. Yoav has extensive experience maintaining clean room equipment of various process types, mainly vacuum systems. Yoav has joined MNCF to be the equipment engineer in charge of the Nano clean room and glove box lab. Yoav holds a B.A. degree in Management and industrial control, specializing in DB systems, an AA Electrical technical engineer degree, and a qualified electrician degree as well.

Atomic Layer Deposition – Beneq, INC.

New equipment at the center

Atomic Layer Deposition (ALD) is a thin film growth technique based on self-limited CVD gas-solid chemical reactions. ALD technique enables the growth of precisely controlled ultra-thin films for various applications on nanometer and atomic scales, with highly conformal coating over high aspect ratio topographies. The principle of ALD has been discovered in parallel in 1960 in Russia and in 1970 in Finland but is mostly attributed to Dr. Tuomo Suntola from Finland. The first application utilizing the ALD (as ALE - atomic layer epitaxy) was a pilot production of displays in 1983 which successfully resulted in an installation of large information boards at Helsinki-Vantaa airport. ALD allows for the deposition of high quality films, pin-hole and particle free, with excellent repeatability. The system may consist of a remote plasma source to enrich the precursor chemistries selection and enhance film quality. Having a remote

plasma source added to the system facilitates enables lower temperature and water free depositions, as well as surface treatments to the substrate. ALD can be applied in several advanced applications such as: Nano-electronics, High-k gate oxides, High aspect ratio diffusion barriers for Cu interconnects, Passivation layers for OLEDs and polymers, Passivation of crystal silicon solar cells, Microfluidic and MEMS, Nanoporous structures, and Organic Semiconductors. Numerous materials can be deposited using ALD, those include: Oxides such as Al_2O_3 HfO_2, HfSiO, La_2O_3, SiO_2, STO, Ta_2O_5, TiO_2, and ZnO, Nitrides such as AlN, HfN, SiNx, TaN, TiN, and high quality thin layers of metals such as: Cu, Pt, Ru, W. After a long process of evaluating seven ALD systems, it was decided to purchase the TFC200 ALD system from Beneq. This system will be located in the MNCF Nano clean room and will be operated by MNCF staff.

Prizes and Awards

- Prof. Rimona Margalit and Prof. Dan Peer have won the Untold News Award, Inventions from Israel that might change the world, by the Untold News organization, NYC. The award was given for their development in cancer treatment.
- Roy Shiloh, from the research group of Prof. Adi Arie, has won the David and Paulina Trozkey Graduate Degree Excellence Award.
- Prof. Ehud Gazit was awarded the Kadar Family Award for Excellence in research at TAU.
- Prof. Oded Hod has won the Rector's Award for excellence in teaching.
- Prof. Meital Zilberman has won the first place Innovation Award of the Journal of Wound Care (JWC), which recognizes every year innovation and excellence in research and practice in all aspects of the wound care field. The award was given in the JWC 2015 awards ceremony in London, March 2015.
- Itai Epstein, from the research group of Prof. Adi Arie, has won the Weinstein PhD Studies Award for Excellence in Signal Processing, Nadav Levanon prize, Tel Aviv University, the SPIE Newport Research Excellence Travel Award – Photonics West 2015, and the Ministry of Science and Technology International Conferences Scholarship for Excelling PhD Students – Tel Aviv University, 2014.
- Prof. Abraham Nitzan has won the Israel Chemical Society Medal

News & events

- The Fred Chaoul 10th Annual workshop was held in Ha'Goshrim resort hotel during 15-17 of February 2015. The key note speaker was Prof. Miles Padget from the University of Glasgow who gave a talk titled: "Shaping Light for Imaging and Sensing"
- Tel Aviv University and Tsinghua University XIN Center conducted the International Winter School on Nano-Photonics during February 1-5, 2015 at Tel Aviv University. Participants came from TAU, Tsinghua University as well as other Israeli and International Universities attended. The distinguished speakers list included: Prof. Nader Engheta from the University of Pennsylvania, Prof. John Pendry from the Imperial College in London, Prof. Joseph Zyss from ENS Cachan in France, and Prof. Misha Sumetsky from Aston University in the UK. Some of the topics which were covered were transformation optics, meta-materials & meta-surfaces, nano-antennas and plasmonics, quantum dots, beam shaping and nano-imaging.
- An industry day was held on June 18th featuring technological talks given by MNCF staff, as well as a guest lecture by Ziv Hermon, the CEO of Nanoair cooling, whose prototyping is done in MNCF facilities.
- The Marian Gertner Institue for Medical Nanosystems together with the FTA and the Nanocenter hosted the New Horizons in Nanomedicine featuring Prof. Peter Senter from Seattle Genetics, Prof. Jeffery Karp from Harvard Medical School, Prof. Twan Lammers from Aachen University, and Prof. Yanjon Zhao from Tianjin University. The event took place in 24-25 June at TAU.
- The next Xin Innovation Forum is being held this month between the 15-16th of October, 2015, in Beijing with extensive participation from both Tel Aviv Unviersity and Tsinghua University.
- The next NanoIsrael conference will be hosted by Tel Aviv university and will be held on the 22-23rd of February, 2016, in Smolarz Auditorium. Early registration deadline is November 1st, 2015. More information can be found on the conference website.

The Fred Chaoul 10th Annual Nano Workshop

Tel Aviv University Center for Nanoscience & Nanotechnology
Powering Innovation

Hagoshrim Hotel, February 15-17, 2015

http://nano.tau.ac.il