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The Israel Chemist and Chemical Engineer

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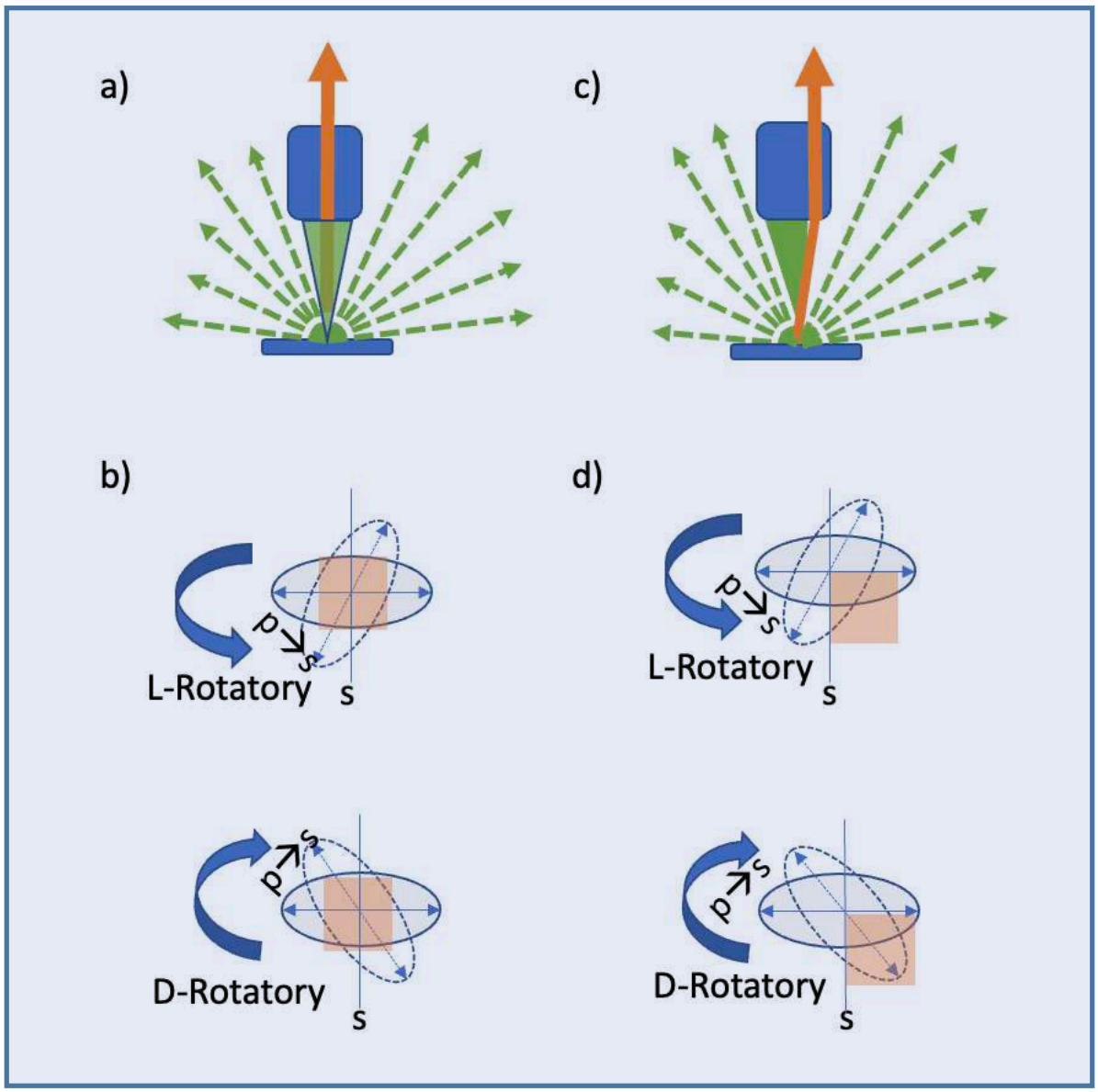

The Israel Chemical Society
(ICS: www.chemistry.org.il)

Editorials

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Front cover: Figure 9 of Aviv et al.'s article that appears in this issue.

Dear Readers,

Welcome to the ninth issue of the Israel Chemist and Engineer (ICE) online magazine, a publication of the Israel Chemical Society (ICS). We hope you will find the magazine interesting and will be inspired to contribute to future issues.

We start with Hagit Aviv, Vinayaka Harshothama Damle and Yaakov Tischler of Bar-Ilan University who contribute an article on their latest research on low-frequency Raman spectroscopy as a versatile technique for material characterization and detection.

Amnon Bar-Shir of the Weizmann Institute (recipient of the 2021 ICS outstanding young scientist prize) contributes a fascinating review of his work on novel molecular architectures for "multicolor" magnetic resonance imaging.

Bob Weintraub continues to inform us about the history of science, this time with a timely article on "César Milstein (1927-2002) and monoclonal antibodies: Father of modern immunology."

Arie Gillon, the founder of Bargal Analytical Instruments, presents a fascinating scientific detective story in which he uses his analytical skills to investigate the origin of a chess set that has been in his family for many years.

I had the pleasure of interviewing Leeor Kronik of the Hebrew University for this issue of the ICE. Leeor is a recipient of the 2021 ICS outstanding scientist prize. His call to educate young scientists in ethical standards is of particular importance.

Prof. Shimon Vega OBM of the Weizmann Institute passed away in 2021. Some of his students and postdocs got together to share their recollections of the time spent in his group and the lasting impression he made on them. The collection was edited by Gil Goobes of Bar-Ilan University and Amir Goldbourt of Tel Aviv University. After the recollections of Shimon's students and postdocs, Yona Siderer, a specialist in the history of science at the Hebrew University, contributes her own appreciation of Shimon's friendship and hospitality.

Mindy Levine of Ariel University, the recipient of the ACS award for encouraging women into careers in the chemical sciences, sponsored by the Camille and Henry Dreyfus Foundation, contributes an article based on her talk at the ACS symposium celebrating her award, "Agency, advocacy, and attention: A tale of encouraging women into careers in the chemical sciences."

If you have suggestions for future editions, comments on the current issue, or would like to contribute an article, please contact me at gordon@biu.ac.il.

Arlene D. Wilson-Gordon
Professor Emerita
Chemistry Department, Bar-Ilan University
ICE Editor

Dear Colleagues,

With the Covid-19 pandemic and its consequences fading away, we are back on track. Skipping the 2021 Annual Meeting of the ICS was painful, but we kept our traditional award ceremony and held it at the Open University campus on July 1, 2021. The 86th ICS Meeting, which took place on September 12–13, 2022, 2.5 years after the 85th Meeting, was a happy gathering of many ICS members, with long-missed in-person networking and exchanging ideas and recent discoveries. Unfortunately, the Chinese delegation we expected to host canceled their arrival due to the pandemic. We all thank the chairpersons of the organizing committee, Profs. Charles Diesendruck and Saar Rahav of the Technion.

We look forward to the 87th Meeting, which will take place on July 4–5, 2023, at the International Convention Center, Jerusalem, as part of the International Chemistry Congress (ChemCon2023). The event, which will include the two-day 87th ICS Meeting, a one-day "Good Carbon" symposium (July 3, 2023), and a three-day international exhibition, reflects a fruitful collaboration between the ICS and the Haaretz/TheMarker Group. The ChemCon2023 will create high interest and synergism among chemists, chemical engineers, businesspeople, venture capitalists, government agencies, startup entrepreneurs, chemical industry leaders, and the public.

The 87th ICS Meeting will include nearly 100 lectures in four parallel sessions, over 300 posters, and various social events. The traditional ICS Prize Ceremony will recognize outstanding scientists, graduate students, teachers, and the prominent green chemical industry. Following our long tradition, we'll host a large delegation from Denmark, consisting of 11 professors including Nobel Prize Laureate Morten P. Meldal, and 20 graduate students from the University of Copenhagen, the Technical University of Denmark, and Aarhus University. The Meeting is organized by a joint team from Ariel University, Tel Aviv University, and the Hebrew University, chaired by Profs. Alex Schechter and Flavio Grynszpan.

The "Good Carbon" Symposium will focus on using compounds of a single carbon atom, such as natural gas and carbon dioxide emissions, as feedstock for the chemical industry. The symposium will highlight the methanol-based economy, methanol-to-olefins (MTO) processes, synthetic fuels, novel fuel cells, and clean energy.

2023 will be my second year as Vice President and President-elect of the International Union of Pure and Applied Chemistry (IUPAC), and in 2024 I'll start my two-year term as the Union's 41st President. In this capacity, I wish to promote the Chemist's Oath as a global initiative, planning to run the first pilot in Israel.

As is the case for the Hippocratic Oath, the Chemist's Oath will have a moral value rather than a legally binding commitment. It will enhance the newly graduated chemist's ethical behavior and professional pride. The following text of 57 words is my proposed draft of the Chemist's Oath. Believing in collective wisdom, I invite you to modify the text while keeping it clear and concise.

'By what I hold most sacred, I solemnly swear to pursue scientific truth and expand knowledge ethically and responsibly. I will promote diversity, equity, inclusivity, and mutual respect for all. As a member of society at large, obligated to all my fellow human beings, I will use my chemical expertise to sustain life and protect the environment.'

With your help, I wish to crystallize the final version and offer it as a pilot among the 2023 chemistry graduates in one or two countries before proposing it through IUPAC to the global community.

Finally, please help develop the ICE magazine under the leadership of Prof. Arlene Wilson-Gordon, and contribute an article to the ICE on any topic you like, including popular science, history of science, report on an event, opinions, etc. Please, don't hesitate to contact Arlene or me on these matters.

Enjoy your reading,

Ehud Keinan

President, the Israel Chemical Society

Low-frequency Raman spectroscopy – a versatile technique for material characterization and detection

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Abstract:

Low-frequency Raman spectroscopy (LFRS) is a branch of vibrational spectroscopy that allows easy interpretationand highly sensitive structural identification of trace amounts of chemicals based on their unique vibrational characteristics. Due to the continuous technical improvement in Raman spectroscopy, advanced development of the device has been achieved and more applications have become possible. This article illustrates the use of LFRS for unique applications such as crystalline phase identification, enantiomeric identification, and enantiomeric separation. We present a general summary of our different research efforts in the field of polarised LFRS. The aim of this article is to highlight potential applications of different types, especially applications developed to characterize organic crystalline materials.

Overview of Raman Spectroscopy

Raman spectroscopy (RS) is an optical means of probing the vibrational modes of materials. The spontaneous Raman effect is a scattering phenomenon where photons, i.e. electromagnetic radiation of a specific wavelength, interact with the analyte i.e. the material under observation in either the ground state or one of the excited rotational-vibrational states. This interaction results in promoting the molecule into a so-called "virtual energy state" for a very short period before an inelastic photon is scattered. The resulting inelastically scattered photon which is "emitted"/"scattered" can be either of higher (anti-Stokes) or lower (Stokes) energy than the incoming photon. The probability of such inelastically scattered photons is much lower than elastically scattered photons, called Rayleigh scattered photons. Upon such interaction, the resulting rotational-vibrational state of the molecule differs from its original state, before interaction with the incoming photon. The difference in energy between the original state and the new state leads to a shift in the emitted photon's frequency, resulting in a Raman shift [1].

RS displays several advantages over other techniques such as infrared spectroscopy. For example, the quality of the signal collected is barely affected by the presence of water, allowing for its use in many applications where infrared analysis is not reliable. A representative case study is the in-situ monitoring of a fermentative process where Raman techniques outperforms any other spectroscopic approach. Nonetheless, Raman analysis in addition to its intrinsic property of lower signal strength compared to fluorescence or absorption, suffers from some difficulties such as the

Hagit Aviv is a researcher at the Department of Chemistry, Bar-Ilan University and a co-founder of the Center for Energy and Sustainability. Until recently, as the lab manager of the Device Spectroscopy Laboratory, Hagit initiated projects and collaborations to develop spectroscopy techniques using Raman spectroscopy, specifically LFRS. Previously, her post-graduate work was centered on the field of polymers, and her doctoral research dissertation focused on synthesis and characterization of iodinated nano- and macro-particles for CT and MRI imaging.

challenge of developing quantitative robust and trustworthy methods of data analysis. However, many methods have been developed for enhancement of these signals over the years by many research groups. These include chemical, surface, and cavity enhancement techniques that were reported by us [2–4]. Furthermore, the presence of highly active Raman species such as carbon particles can mask the presence of other species. Several studies have been devoted to overcoming these drawbacks. Among these different approaches, it is known that polarized Raman spectroscopy provides information on molecular orientation and bond vibrational symmetry, in addition to general chemical identification [5].

In general, in polarized RS the spectra captured are either parallel or perpendicular to the inherent polarization of the excitation laser. However, Raman optical activity deals with the polarization phenomenon differently by observing the evolution of the Raman spectrum at different polarization angles. Polarization measurements provide useful information about molecular shape and the orientation of molecules in ordered materials, such as crystals, polymers, and liquid crystals.

The RS modes at lower wavenumbers (< 200 cm^{-1}) are called low-frequency Raman (LFR) modes and the technique used to analyse this region of the spectrum is called low-frequency Raman spectroscopy (LFRS); the technique is very similar to spontaneous RS. LFRS is possible due to recent development of much sharper optical filters called volume holographic filters (VHFs). These filters facilitate easy observation of wavenumber shifts that are as low as 5 cm^{-1} away from the laser line. The LFR region is rich in information relating to lattice vibrations, crystallinity, symmetry, and inter-molecular acoustic modes, as well as phonon modes [6].

LFRS for identification of crystalline phases in methylammonium lead iodide

Energy conversion from light to electricity has remained a major research area since the discovery of the photo-electric effect. While many materials and technologies have been developed over the years for this purpose, semiconductor-based solar cells have been spearheading the solar cell world due to their considerably higher efficiencies in spite of being expensive. The higher cost of existing technology has led to the expansion of research beyond conventional crystalline semiconductor materials. Organo-inorganic hybrid perovskites (OHPs) have remained promising in these efforts due to their exceptional performance resulting from their intrinsic properties such as high absorption coefficient, tunable band gap, long charge carrier diffusion, low exciton binding energy etc. Methylammonium lead iodide ($MAPbI_3$) is the most widely used perovskite solar cell material. While the performance of the perovskite solar cells (PSCs) is commendable, the stability of OHPs remain questionable due to their high sensitivity to humidity, light, and temperature. The instability affects the crystal structure of the material and leads to degradation of crystal structure [7]. Here, we

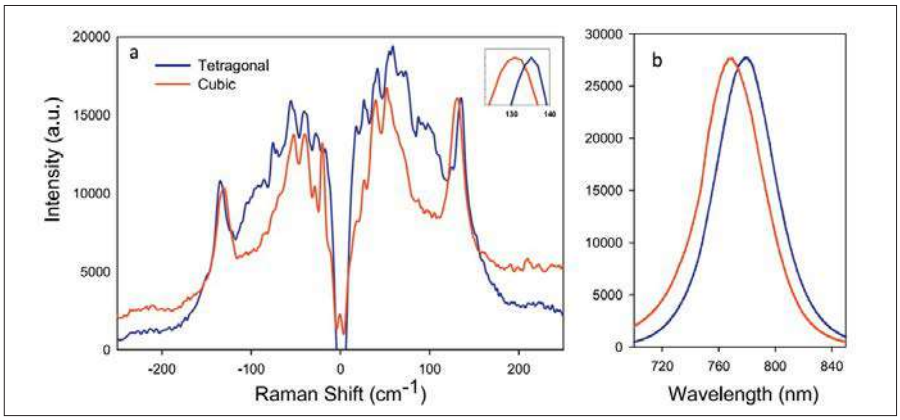

Figure 1. (a) Low-Frequency Raman Spectra and (b) PL spectra of tetragonal and cubic phases of $MAPbI_3$ confirming laser-induced phase transition.[§]

Vinayaka Harshothama Damle is a visiting researcher at the Faculty of Information Technology and Electrical Engineering, University of Oulu. Before that, he was a doctoral researcher at the Institute for Nanotechnology & Advanced Materials, Bar-Ilan University, Israel. He moved to Israel for his PhD after completing his MSc in Physics from National Institute of Technology Karnataka, India and gaining 2 years of industrial experience in various roles parting as an electron microscopy technologist of a research facility. His doctoral research dissertation mainly focused on engineering Raman scattering phenomena to probe light-matter interactions, emphasizing development of spectroscopic techniques for material detection. His research focuses on molecular photonics and spectroscopy, with special emphasis on device spectroscopy, nanometrology, and energy materials.

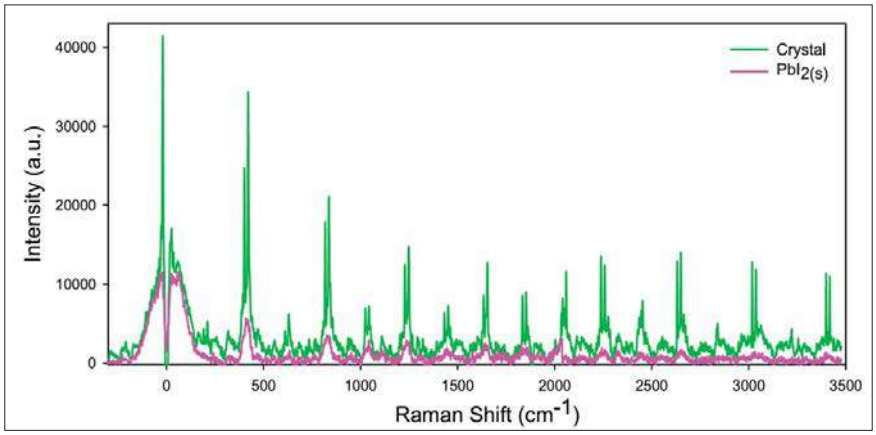

Figure 2. SRS from the resonant vibrational mode when laser power crosses 15 mW (green plot), and RRS obtained from high laser power excitation of PbI2(s) (pink plot).§

§ Figure 1 and Figure 2 are reprinted with permission under © license 5338940298014.

present LFRS as a handy tool to identify and characterize phase transformations within such highly sensitive materials.

Our preliminary work showed that the LFR modes are dependent on the crystallinity of the analyte material. It was observed that even in-situ changes in the material matrix upon laser excitation can successfully be captured with the right optical set-up and laser power. This was observed in examination of $MaPbI_3$ single crystals. It is well-known from the literature that $MAPbI_3$ exhibits different stable crystalline phases at different temperatures. At temperatures below 164 K it is orthorhombic, between 165-330 K tetragonal and at higher temperatures cubic. Additionally, there is a general agreement within the literature on thermally induced phase transitions in $MAPbI_3$ [8]. In one of our earlier works, we presented a photo-induced phase transition [9]. A mere 2-minute excitation of $MAPbI_3$ single crystals in the tetragonal phase with a 532 nm laser above 15 mW power resulted in the formation of cubic phase at ambient conditions and this phase transformation was confirmed using the photoluminescence (PL) shift as shown in Figure 1. Such dynamic phase transitions are hard to capture in conventional crystallographic techniques such as XRD. However, LFRS makes a good candidate for such thermal and photo-induced phase transition observations. When lower laser power can be used for characterizing the former, sufficiently high laser power facilitates both phase transition and detection. In addition to these unique characteristics of phase identification and phase transition detection, the study also revealed some interesting characteristics of the material such as Raman stimulation of iodine vapor signals in addition to stimulated spontaneous Raman signals.

The overlap of the excitation laser with the electronic absorption band of the material results in resonance Raman scattering (RRS). This overlap results in a higher scattering intensity compared to the fundamental spontaneous Raman bands and in many cases leads to appearance of overtone bands [10]. On the other hand, stimulated Raman scattering (SRS) is a third-order nonlinear process that exhibits narrow-line emission from existing Raman shifts. In a regular experimental framework, this process is induced using two synchronized pulsed lasers as single-frequency excitation sources, or a narrowband source synchronized with a broadband source for multiplex excitation [11]. Certain materials under certain specific conditions self-induce SRS when subjected to a high enough laser power, even when the exciting laser is continuous wave (CW). This self-stimulated phenomenon is generally referred to as impulsive stimulated Raman scattering, or cascaded Raman process. Self-induced SRS is extensively investigated for ionic crystals, and it is understood that non-linear Raman gain is governed mainly by large crystal size and ionic radius of the cation; both of which are true for the $MAPbI_3$ crystals used for this study [12]. Figure 2 represents the SRS from the resonant vibrational modes when the excitation laser power exceeds 15 mW.

Yaakov R. Tischler leads the Device Spectroscopy Laboratory (DSL) at Bar-Ilan's Institute for Nanotechnology and Advanced Materials. The lab is focused on studying and tailoring light-matter interactions in nanoscale devices and nanostructured materials. This involves research on microcavity polaritonic devices, organic-based lasers, near-field scanning microscopy, and applied vibrational spectroscopy. One of the main thrusts of DSL is Raman spectroscopy, which includes development of new spectroscopic techniques and applications thereof. Yaakov opened DSL 12.5 years ago and personally holds 13 US Patents. His former students and post-docs have gone on to make an impact in government, academic and high-tech sectors, particularly in the semiconductor and photonics industries as well as in start-ups.

LFRS for differentiation of enantiopure and racemic chiral molecules

Chiral molecules form the basis of biological systems. Their occurrence is universal in the living world. They are present in the form of basic structures such as sugars and proteins and more complex ones such as amino acids, enzymes, and nucleic acids. The left- and right-handed chiral compounds exhibit different physiological effects and biological activities in biotic systems due to their contrasting interactions with proteins and enzymes [13]. It is therefore important to accomplish separation of enantiopure products from their counterparts. While various forms of chiral chromatography are widely used for enantiomeric separation, the identification of enantiopurity is achieved by studying their optical rotation or different forms of circular dichroism. While these studies are simple, they demand the analyte to be in solution form. Although X-ray diffraction, differential scanning calorimetry, inelastic neutron scattering etc. enable identification in the solid form, they are much more complex and expensive [14].

Most of the work on LFR for chiral analysis was conceived together with our colleague Prof. Mastai. In these works, we demonstrated that LFRS can be used for crystal chirality investigations, particularly for distinguishing between racemic and enantiopure organic crystals [15]. Enantiopure chiral crystals are those comprising only one type of chiral crystal among the two possible forms. However, when a crystal contains equal amounts of each enantiomer constituting an enantiomeric pair, it is called a racemate. Most racemic mixtures crystallize as racemic crystals; however, in some cases (5% to 10% in nature), racemic compounds crystallize in a conglomerate form that is a mixture of homochiral crystals. It is known from the literature that racemic crystals are denser than the corresponding enantiopure crystals. This is generally explained by the difference in their hydrogen bonding. In the case of an enantiopure material, crystallization is dictated

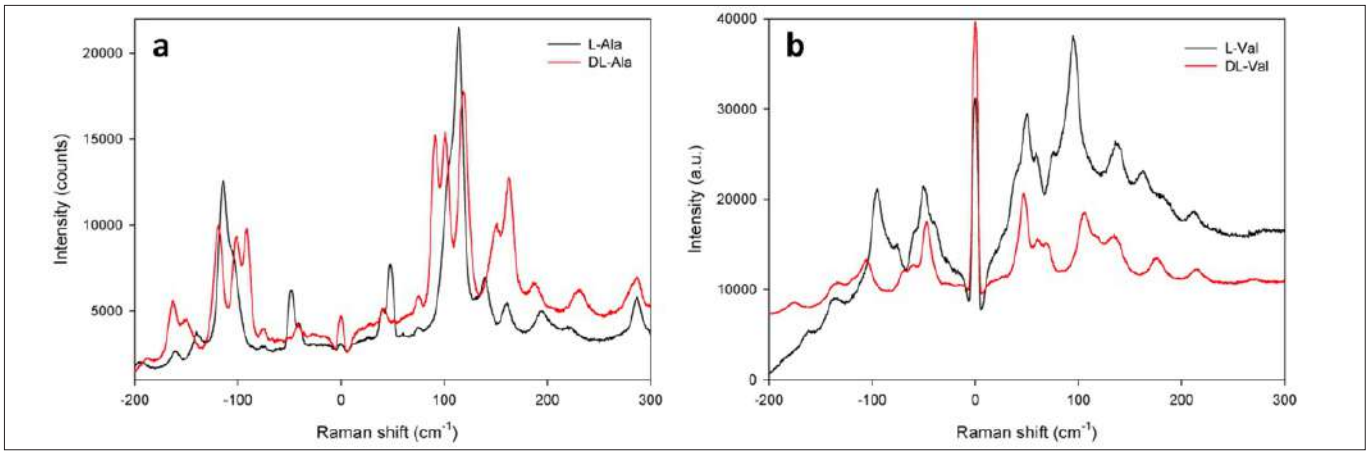

Figure 3. LFR spectra of (a) L-Alanine, DL-Alanine crystals, and (b) L-Valine, DL-Valine crystals‡.

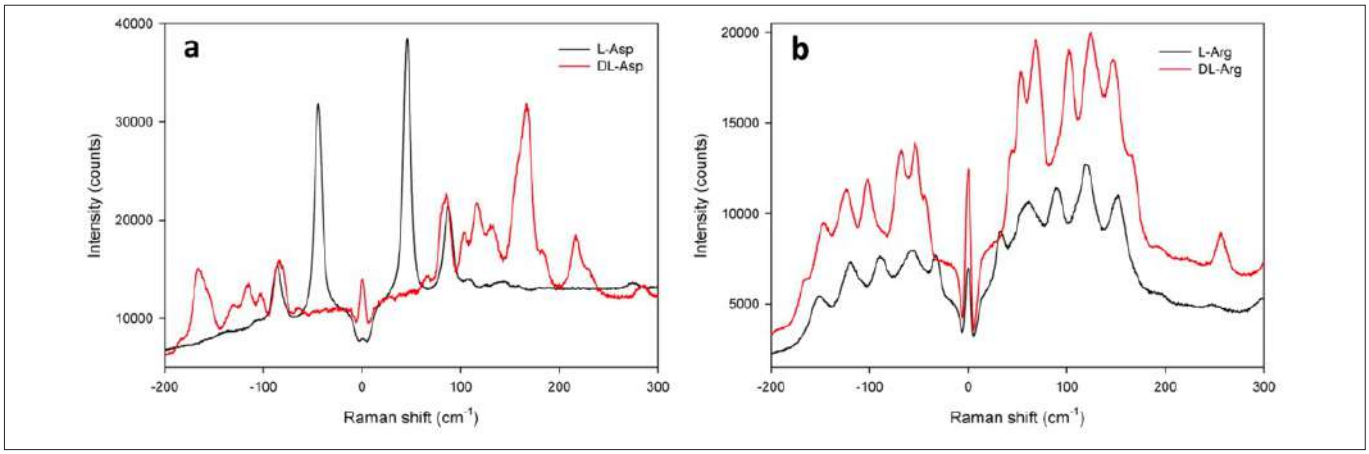

Figure 4. LFR spectra of (a) L-Aspartic acid, DL-Aspartic acid crystals, and (b) L-Arginine, DL-Arginine crystals‡.

‡ *Figure 3 and Figure 4 are reprinted with permission from J. Phys. Chem. A 2017, 121, 7882-7888 ©2017 American Chemical Society.*

by the chirality, and thus the hydrogen bond network is limited, whereas for racemic crystals, there is an extremely large availability of hydrogen bonding modes [16]. Hence the structure is stochastically defined. These considerable differences in the crystalline structure result in differences in the intermolecular interactions of racemic and enantiopure crystals. As a result, distinct vibrational modes exist in enantiopure and racemic crystals that are detectable by LFRS. Some examples of enantiomeric differentiation from their racemic mixtures are presented in Figure 3 and 4. Hence, it is observed that LFRS produces completely different spectra for racemic and enantiopure crystals. Moreover, LFRS offers faster and more sensitive chiral characterization in crystals than currently used methods, enabling facile measurements for microcrystals and detection of defects in chiral crystals. More detailed study can be found elsewhere [15].

Polarization dependence of LFRS in organic single crystals

Crystallization is a very unique phenomenon in pure compounds. Post nucleation, under a conducive environment, crystallization results in formation of highly ordered structures and adaptation of a unique three-dimensional orientation. The crystal structure governs physical and chemical properties in materials [17]. Therefore, it is extremely important to investigate and understand the structure and orientations of intermolecular interactions in crystals.

Over the years, many different physical techniques hav e been used to characterize crystalline structures, such as X-ray diffraction (XRD), thermal analysis, and electron diffraction. In general, each face of a single crystal provides detailed structural information. The most common experimental method that allows resolution of individual atoms is single crystal X-ray diffraction (SCXRD) [18]. However, it requires a sufficiently large crystal that is at least partially transparent i.e. in general is bright looking, having clear edges and faces, and is free of inclusions. Another method for characterizing crystals that uses X-rays is near-edge X-ray absorption fine structure, a technique which determines the molecular orientation for non-transparent samples. Raman spectroscopy, with established higher sensitivity than XRD in crystal purity investigations, provides information on both covalent bonds based on intramolecular vibrations and intermolecular interactions [19]. At the same time, intermolecular interactions that result in shear modes, breathing modes, and hydrogen bond stretching modes are lower in energy and are observed in LFRS. The LFR modes are generated by weak interactions including molecular degrees of freedom and shear modes, and are observed in the lower range of LFRS, while vibrational modes that are generated by stronger intermolecular interactions such as hydrogen bonds exhibit larger LFR shifts within the LFRS spectral range. Theoretical and computational efforts have successfully assigned these larger LFR modes to hydrogen bond stretching vibrations using density functional theory (DFT) calculations. Previous studies have used polarized Raman spectroscopy for various applications in material characterization. Polarization dependence in Raman, along with transmission electron microscopy, is used to investigate the crystallographic orientation of dark crystals [20].

Polarization-dependent contrast in the interaction cross section of LFR modes was primarily probed in this study. We observe that investigation of crystal structures is indeed possible by studying vibrational modes obtained from each face of a single crystal using LFRS. Unlike other methods,

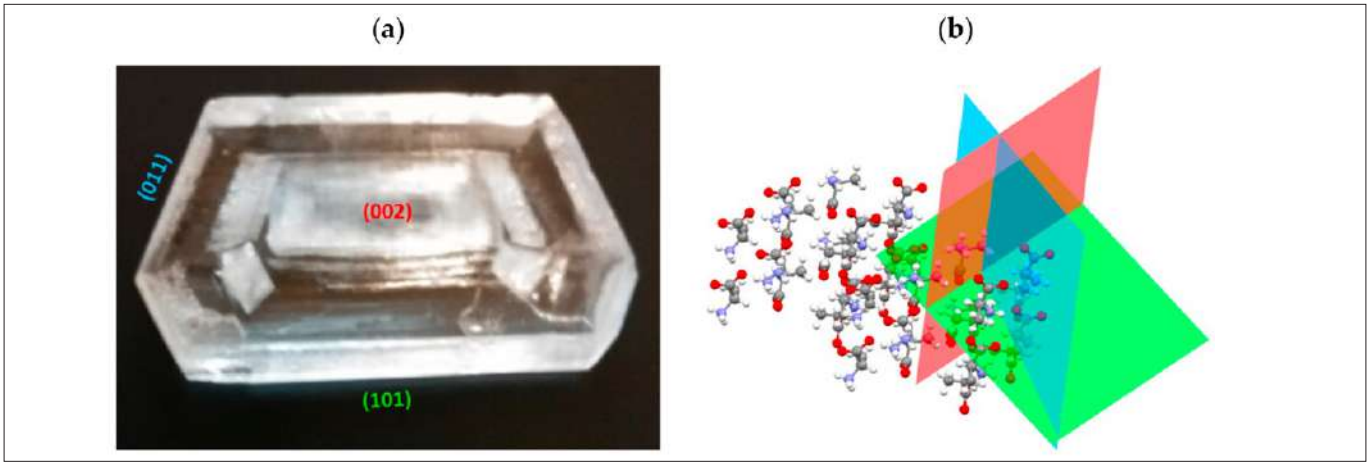

Figure 5. (a) Photo of L-aniline single crystal and measured planes. (b) L-aniline crystal structure constructed using the program "Mercury" along with the measured planes (101), (002), and (011).

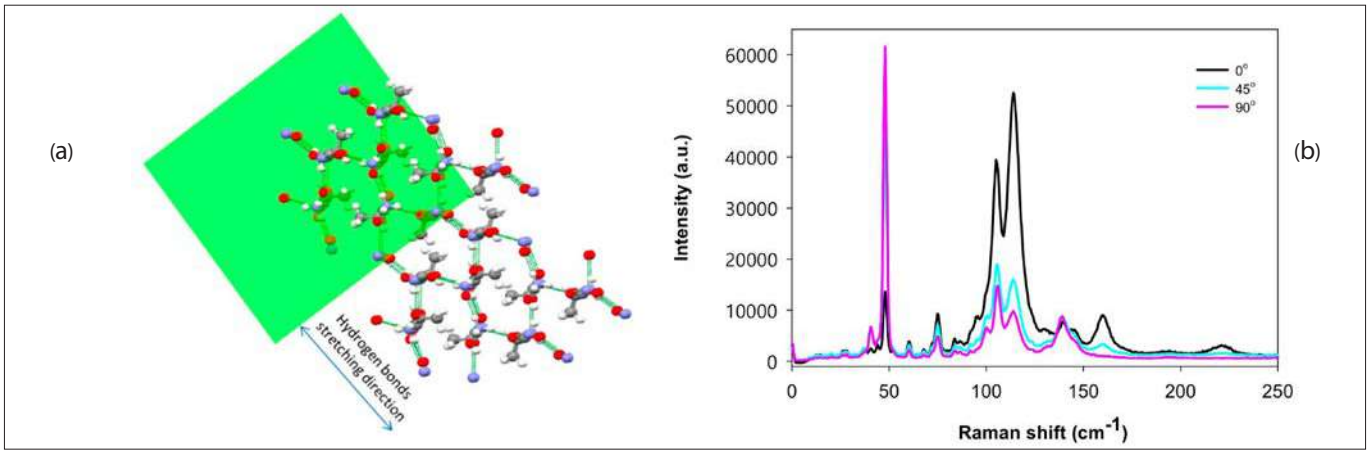

Figure 6. (a) Hydrogen bonds' simulation (dotted lines) in the L-alanine single crystal relative to the (101) plane. (b) LFRS of crystals excited from (101) direction with three different polarization angles.

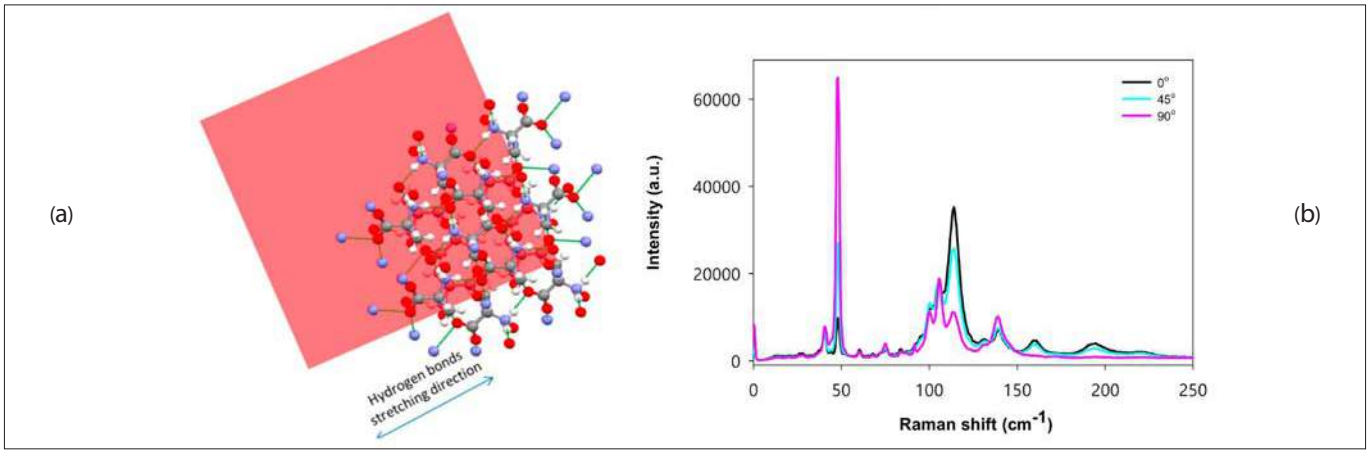

Figure 7. (a) Hydrogen bonds' simulation (dotted lines) in the L-alanine single crystal relative to the (002) plane. (b) LFRS of crystals excited from (002) direction with three different polarization angles.

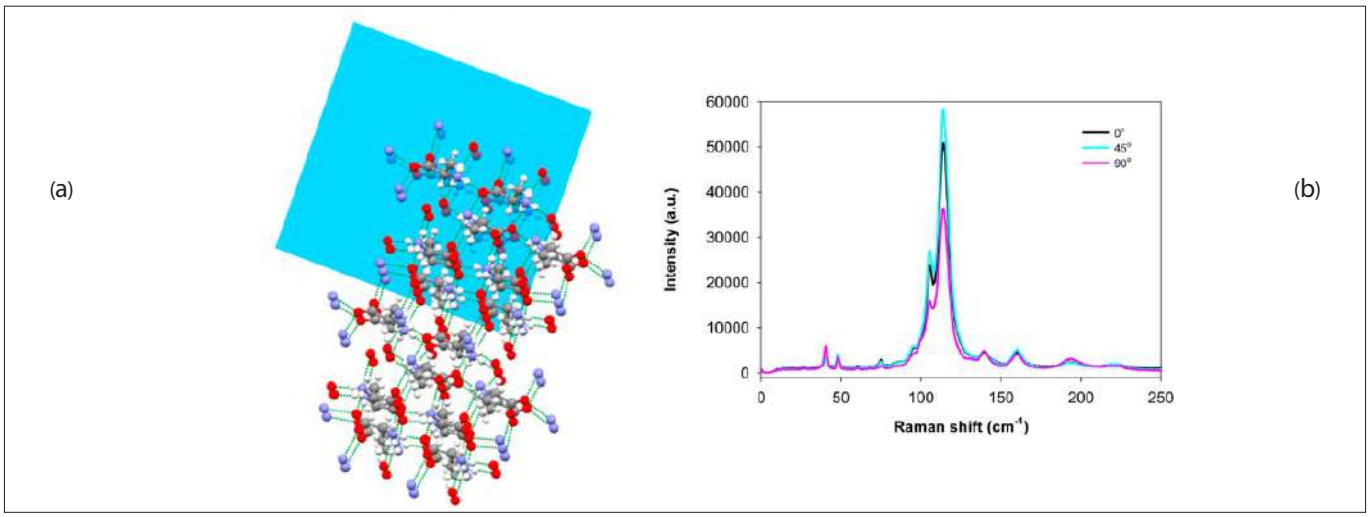

Figure 8. (a) Hydrogen bonds' simulation (dotted lines) in the L-alanine single crystal relative to the (011) plane. (b) LFRS of crystals excited from (011) direction with three different polarization angles.

due to the reflection geometry of the optical set-up, even lack of transparency does not affect the ability to characterize the structural properties of a crystalline material. The only known governing factors for successful characterisation is presence of hydrogen bonds in addition to other low energy modes. The contrast in polarizability of hydrogen bond in the crystal in different directions resulted in characterizability of the structure using LFRS. The variation of polarizability of the hydrogen bonds and resulting spectral contrast is presented in Figures 5–8. A detailed report of this can be found elsewhere [21].

Polarized LFRS for identification of enantiomers

An overview of enantiomers and chirality is presented in earlier sections. Enantiomers being molecules with mirror symmetries have right-handed or left-handed symmetry in their structure. This results in anti-parallel polarizabilities. In other words, when plane-polarized laser excitation along a particular polarization plane is incident on D- and L-enantiomers, the polarizabilities induced in the molecule are opposite to one another [22]. With LFR modes in general being orientation dependent, the LFR interaction cross-section is therefore dependent on the polarization angle of the excitation laser [23]. This counterintuitively results in different scattering cross sections along different polarization directions. Observation of this contrast is impossible in RS systems that have normal angle of incidence.

This work is the realization of a theoretical study of the polarization phenomena with respect to the laser and Raman signal propagation in optically active samples, which was proposed elsewhere [24]. In our work, we engineered an asymmetry into the optical set-up in both excitation and collection geometries and constructed an off-axis excitation collection set-up. In addition to the engineered asymmetry, the excitation and collection geometries were modified to accommodate polarizers to allow capture of orthogonally polarized signals. This resulted in enantio-contrasting interaction cross sections along excitation geometry and enantio-selective LFR spectrum in collection geometry. Figure 9 represents the schematics of asymmetry induced into the optical system by virtue of modification and resulting asymmetrical interaction cross sections and induced contrast into the collection signal. Experimental details can be found elsewhere [25]. The study was the first of its kind for identification of enantiomers in their solid form using LFRS.

For representation purposes, we present the spectra showing enantioselective contrast between enantiomeric pairs in Figure 10. A detailed explanation of the experimental set-up can be found elsewhere.

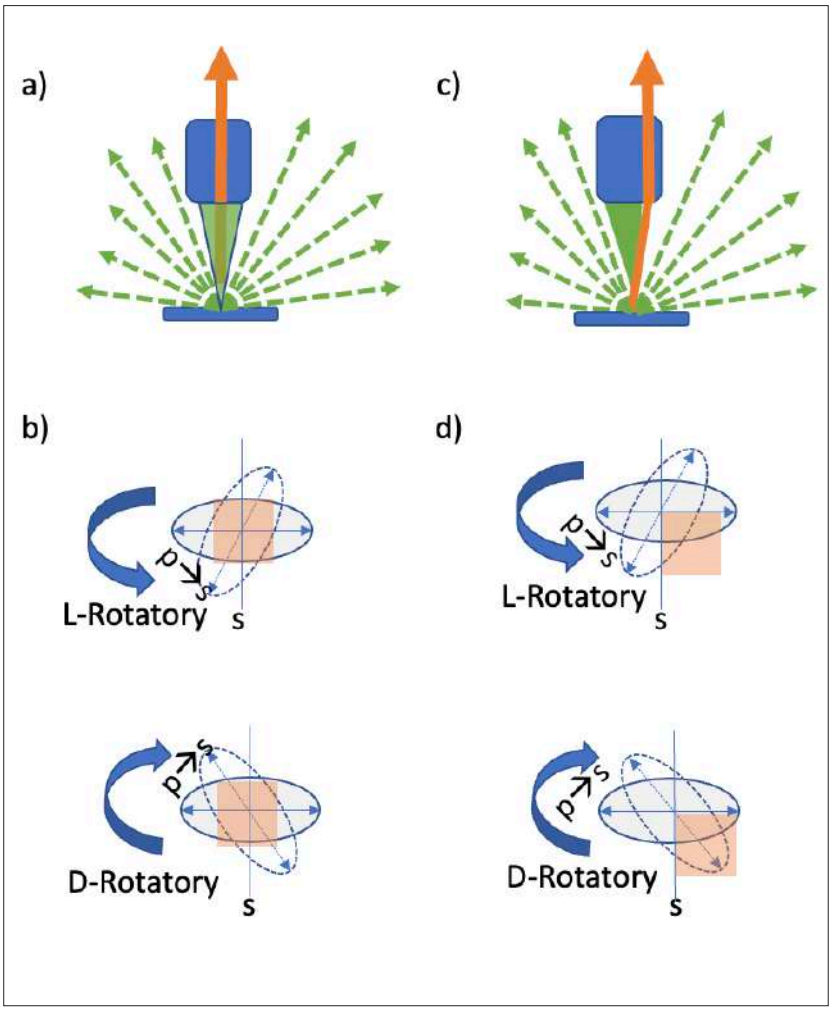

Figure 9. (a) Schematic representation of conventional Raman excitation and collection and (b) its collected focal area. (c) Schematic representation of the modified Raman setup and (d) its collected focal area. The modified Raman collects different intensities from the polarization planes after excitation of optically active materials. The schematics are approximate representations directed to understand the processes. The colored squares are a guide to the eye, representing (a) a symmetric interaction cross section for both D and L enantiomers and (b) relative asymmetric interaction cross section for D and L enantiomers*.

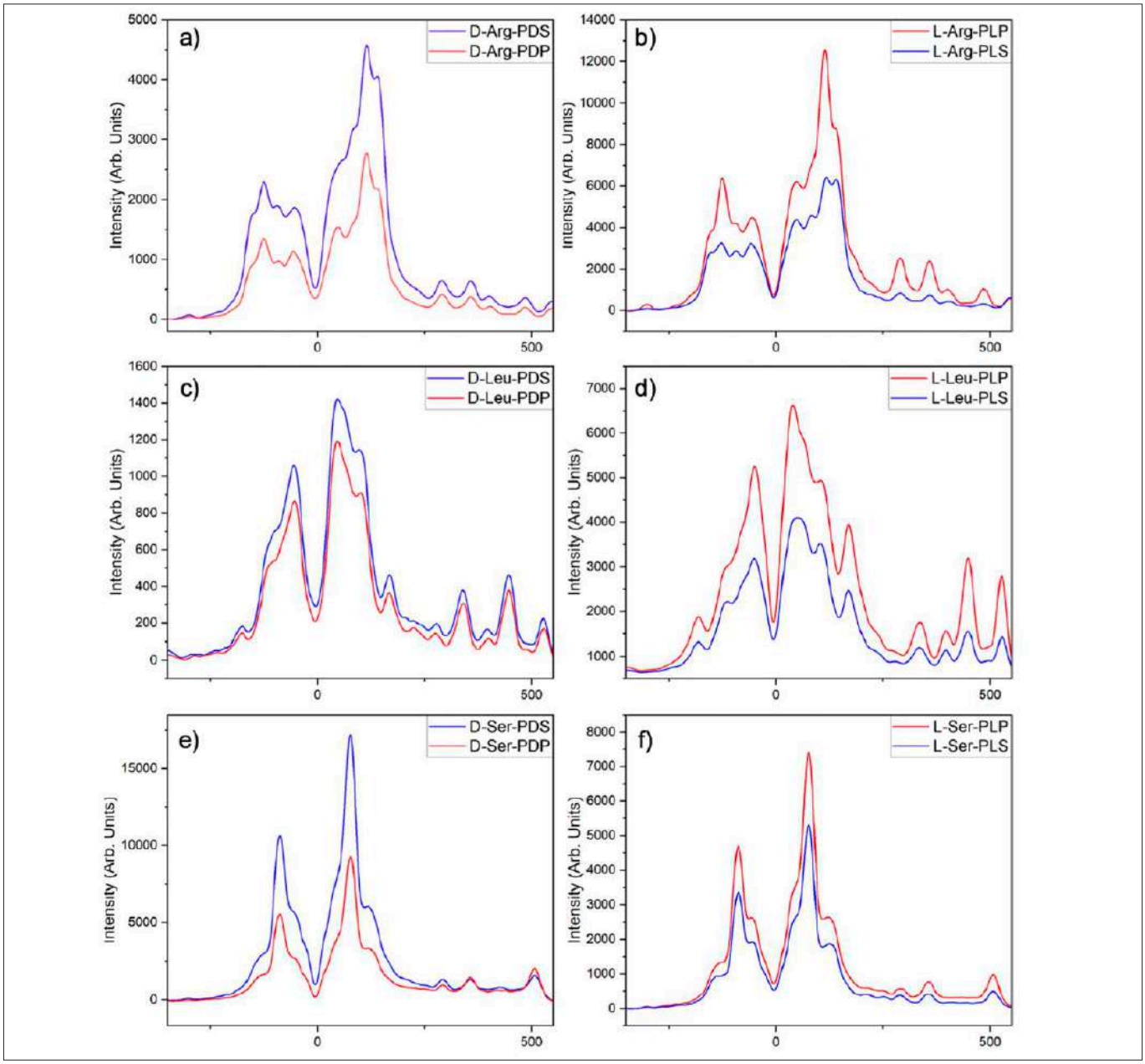

Figure 10. LFR spectra of (a) D-arginine, (b) L-arginine, (c) D-leucine, (d) L-leucine, (e) D-serine, and (f) L-serine. All powders were excited using P-Polarization. Red curves present the signal collected along P-Polarization, and blue curves present the signal collected along S-Polarization*.

* *Figure 9 and Figure 10 are reprinted with permission from Anal. Chem. 2022, 94, 3188−3193 ©2022 American Chemical Society.*

Conclusion

Raman spectroscopy is a well-known powerful analytical tool that has become increasingly important in recent years. More recently, the development of VHFs has led to high impact research in LFRS. The main aim of this article is to summarize unique characterization efforts using LFRS and polarized LFRS, leading to evolution of the technique into a versatile characterisation and material detection tool. In this article, we have summarised four of our distinct research efforts leading to the unique application of LFRS for enantiomeric identification in solid form.

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Novel molecular architectures for "multicolor" magnetic resonance imaging

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Abstract:

Luminescent materials with their rich color palettes have revolutionized the field of bioimaging through the ability to distinguish between spectrally resolved colors and, thus, to map the complexity of biological systems. Yet, advanced solutions to overcome the restricted tissue penetration of light are still needed to allow in vivo mapping of tissue multiplexity in both health and disease. Among the diverse capabilities and many advantages of MRI, the ability to encode specific frequencies of imaging agents and, by that, to allow pseudo-color display of MRI maps, is unique. Here, I summarize our recently developed molecular probes that are capable of generating artificial MR-based colors. To this end, the use of nanofabrication, supramolecular chemistry, and protein engineering approaches to generate novel molecular formulations (inorganic nanocrystals, supramolecular assemblies, and enzyme/substrate pairs) as MRI sensors with unique multicolor display characteristics is reviewed.

1. Introduction

The complexity of biological processes, as well as their tightly controlled regulation, attracts researchers from a wide range of scientific fields. Such multiplexity is apparent in almost every aspect of life, in health and in disease, from enzymatic activity to protein-protein interactions, from metal ion homeostasis to cell function, from gene expression to neuronal activity, or from gene networks to disease onset and therapeutics mechanisms. Although our accumulated knowledge allows us to understand many aspects of these processes, some are still elusive, unknown, or cannot be studied in an intact live organism. In this regard, luminescent sensors (small molecules [1], proteins [2], or nanoformulations [3]) have been the "highlighter pens" of science for decades, since they enable molecules (or cells) of interest to be tagged, enabling mapping of their location, levels, and functions in multiple distinguishable colors. This capability has advanced our ability to reveal the complexity of cellular events, study their tight regulation, and explore a wide range of biological processes concurrently. Perfecting the chemical and optical properties of luminescent materials, in addition to dramatic improvements in microscopy technologies, provide scientists with the ability to visualize multiple biological targets simultaneously within the same imaging frame. However, the light signal source of these materials remains an obstacle when information is desired from the deep tissue of a live subject.

MRI, with its unlimited tissue penetration capabilities and ability to combine information from biological targets with high-resolution anatomical images, has become a valuable imaging technology for molecular and cellular imaging.

Amnon Bar-Shir earned his BSc (2002) and MSc in chemistry from Tel Aviv University (2004, under Michael Gozin), both magna cum laude. His PhD (2009, under Yoram Cohen) focused on advanced diffusion NMR and MRI to study the structure and function of the central nervous system. As a postdoc at the Johns Hopkins University School of Medicine under Assaf Gilad he developed genetically engineered reporters for MRI. In 2014 he joined the Weizmann Institute, where he created new kinds of biosensors with artificial "multicolor" features for MRI applications. His lab uses synthetic chemistry, nanofabrication, and protein engineering to generate novel molecular formulations, such as small molecules, nanocrystals, supramolecular assemblies and proteins, as MRI sensors of high sensitivity, specificity, and orthogonality. He has used these methods for in-vivo molecular and cellular MRI studies for mapping inflammation, multiplexed in-vivo MRI, imaging orthogonal reporter genes, and sensing metal ions. In addition, he used his techniques to study fundamental questions in supramolecular chemistry, including kinetic features of dynamically exchanging molecular systems and control over nanocrystal formation. Amnon's research achievements were recognized recently by the 2019 Krill Prize, and the 2021 ICS Excellent Young Scientist Prize.

Moreover, the versatility of MRI contrast mechanisms [4, 5], and the variability in imaging probe identities (including non-^{1}H tracers), create many possibilities for the design of MRI sensors. One feature that is unique to MRI is that this technique relies on MR properties, which allows, among other advantages, differentiation between molecular entities based on their chemical environment, which is reflected by a characteristic chemical shift. If spectrally resolved, the frequencies of multiple chemical shifts of properly designed molecular probes can be exploited for multiplexed imaging by introducing MRI maps with pseudo-color features [6, 7]. Such pseudo-MRI-colors can be generated using several strategies, including the use of non-^{1}H nuclei, which frequently provide improved spectral resolution, or through magnetization transfer mechanisms that benefit from the high sensitivity of ^{1}H-MRI. In recent years, our lab has focused on the development of novel molecular formulations of a variety of types, as well as on developing methods for pseudo-color *in vivo* MR imaging. I here provide an overview of our recent developments, emphasizing the newly proposed MRI sensors that are based on inorganic nanocrystals (NCs), host-guest systems, and engineered proteins, which have the potential to extend the MRI toolbox with features that have been, thus far, inaccessible.

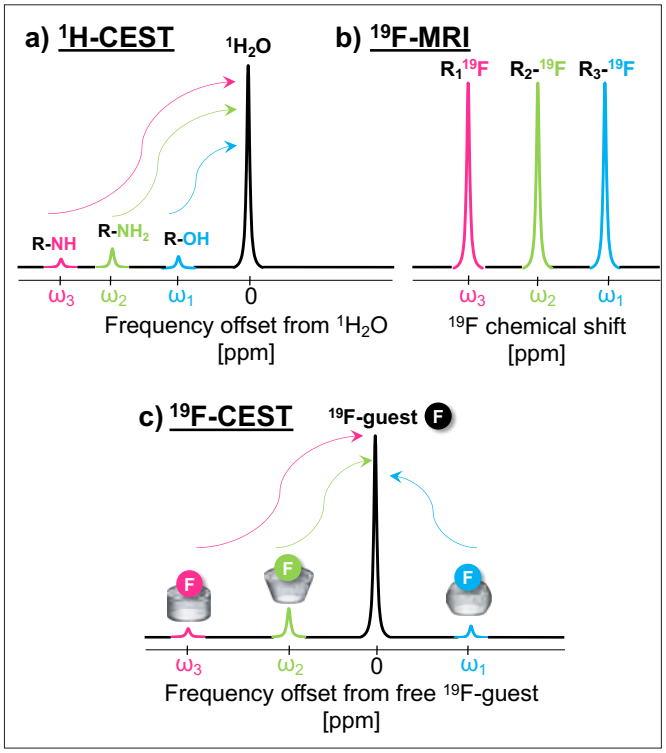

Figure 1. Strategies to generate artificial colors in ^{1}H- and ^{19}F-MRI frameworks. (a) Artificial colors can be generated in CEST-MRI by exploiting the different chemical shift offsets of different exchangeable protons of ^{1}H-CEST agents. (b) In ^{19}F-MRI, artificial colors can be generated by using different ^{19}F-agents based on the difference in the ^{19}F-chemical shifts of their fluorinated content. (c) In the ^{19}F-CEST approach, which is applied on host-guest systems (termed guest exchange saturation transfer, GEST), the same principles used to generate artificial colors in ^{1}H-CEST are used. In this case, the different chemical shift offsets are obtained from the complexation of a ^{19}F-guest with a different molecular host in the solution.

Principles of generating pseudo-colors for MRI

Several strategies have been proposed to generate pseudo-colors for MRI applications. One example is the use of the chemical exchange saturation transfer (CEST) contrast mechanism to produce artificial MRI colors (Figure 1a). By applying a saturation pulse at the specific resonance of an exchangeable proton of a putative CEST agent, it can be "tagged." This tag (manifested by its MR signal nullification) is transferred to the water protons in the surrounding area and leads to ^{1}H-MRI signal reduction as a result of the dynamic exchange process of the "tagged" protons with the water protons. Using multiple CEST agents with exchangeable protons that resonate at different and specific chemical shift offsets ($\Delta\omega$s) from the resonance of the water protons (set at 0.0), artificial MRI colors can be generated, as demonstrated for several applications [6, 8]. The relatively large chemical shift range of fluorinated materials in a ^{19}F-MR framework was also exploited for spectral differentiation between different fabrications and presents this range in a pseudo-color manner (Figure 1b) [7, 9, 10]. Benefitting from the negligible tissue background in ^{19}F-MRI and the ^{19}F-MR signal quantifiability, multicolor ^{19}F-MRI studies provide unique multicolor MRI features that are not accessible to a ^{1}H-CEST-based approach. Combining the two strategies for multicolor MRI, i.e., CEST and ^{19}F-MR to obtain ^{19}F-CEST [11] (Figure 1c), provides a novel MRI platform that can be implemented for applications in which both ^{1}H-CEST and ^{19}F-MRI are not applicable.

Nanofluorides

Fluorine-19 is the second most NMR-sensitive nucleus (after ^{1}H) and is therefore favorable for MR-based studies (NMR and MRI) and fluorinated materials have been proposed as ^{19}F-MR imaging tracers [12], overcoming some of the major drawbacks (i.e., strong background signal, non-quantifiable, challenging in multiplexing, etc.) of paramagnetic contrast agents. Combining this with the fact that ^{19}F-nuclei do not exist in soft biological tissues, the ^{19}F-MR signal of an introduced ^{19}F-tracer can be directly monitored and presented

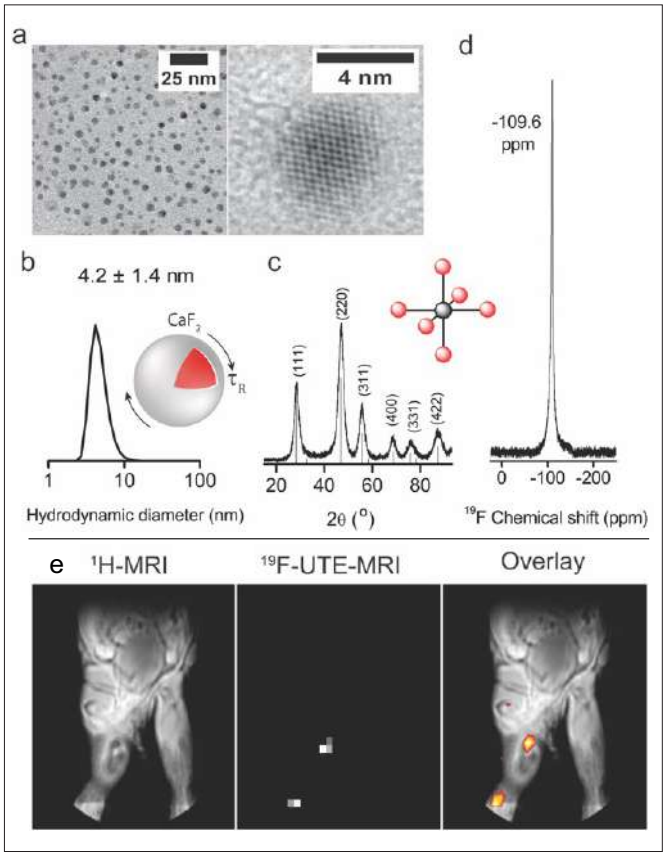

Figure 2. ^{19}F-NMR and ^{19}F-MRI of water-soluble CaF_2 NCs. (a) TEM images. (b) DLS histogram. (c) XRD pattern with schematic of the Ca^{2+} first coordination sphere (red spheres represent ^{19}F-atoms). (d) High-resolution ^{19}F-NMR in water. (e) *In vivo* imaging of PEGylated CaF_2 showing anatomical ^{1}H-MRI of a representative mouse (left) and matched ^{19}F-MRI (middle) shown as a pseudo-color map overlaid on ^{1}H-MRI (right). Modified from reference 15 with permission.

as a quantitative "hot-spot" map over anatomical ^{1}H-MRI. In this regard, perfluorocarbons (PFCs), fluorine-rich materials, have been successfully used in a wide range of ^{19}F-MRI applications [12, 13], including clinical setups [14]. Relying on the relatively large range of their chemical shift appearances in the ^{19}F-NMR spectrum (a few tens of ppm), PFCs have been proposed for multiplexed *in vivo* ^{19}F-MRI [7, 9, 10]. Nevertheless, their introduction as emulsions of a typical 100–200 nm size (i.e., PFC nanoemulsions) and because they are organic formulations, PFC nanoemulsions are not applicable for studies for which ultrasmall (<10 nm) nanoformulations are desired, and they lack the well-established and diverse chemistries of inorganic nanocrystals (NCs). Moreover, they do not cover the whole range of ^{19}F-NMR chemical shifts, which span over almost 200 ppm when using inorganic fluorides (as shown by solid-state NMR).

An inorganic, small-size alternative to PFC nanoemulsions may, therefore, be fluoride-based NCs (M_xF_y, M = metal ion, $F = F^-$), which had not been studied in solutions with high-resolution ^{19}F-NMR and were not used in ^{19}F-MRI until very recently. This is because in NC-based formulations, the restricted mobility of the elements within the crystal frequently results in NMR line-broadening, and high-resolution NMR signals from the core of the NCs' nuclei cannot be obtained using liquid-state NMR experiments. Overcoming such limitations and, thus, successfully performing liquid-state ^{19}F-NMR experiments of M_xF_y in solution, we offered a novel kind of ^{19}F-nanotracers for ^{19}F-MR imaging, which are based, for the first time, on inorganic fluoride NCs, namely nanofluorides [15]. These nanofluorides combine the advantages of inorganic NCs (e.g., small and controllable sizes, dense fluoride content, monodispersity, colloidal stability, surface modifiability, designed as non-spherical materials, etc.) with the merits of ^{19}F-MRI. In addition, the large chemical shifts of nanofluorides, which can span over almost 200 ppm, provide a platform for the development of a series of fluoride-based NCs with different ^{19}F-NMR chemical shifts, which can serve as artificial "multicolor" tracers for multiplexed MRI.

Demonstrating that high-resolution ^{19}F-NMR spectra can be achieved by sufficient averaging of homonuclear dipolar interactions of ^{19}F-nuclear spins within small-size fluoride-containing NCs (i.e., nanofluorides), we showed that CaF_2 NCs can be used as nano-sized molecular tracers for ^{19}F-MRI [15]. First, small, water-dispersed CaF_2 NCs were synthesized and found to be highly crystalline and monodispersed (Figure 2a) with preserved monodispersity in water, as determined by dynamic light scattering (DLS, Figure 2b). The XRD pattern of the synthetic CaF_2 NCs (Figure 2c) features a typical cubic-phase, fluorite-type, fcc structure, where all fluorides are expected to be magnetically equivalent, as reflected by the first coordination sphere scheme (inset, Figure 2c). Indeed, a singlet peak was observed in the high-resolution ^{19}F-NMR spectrum of water-dispersed CaF_2 NCs at -109 ppm (Figure 2d), similar to the frequency obtained for CaF_2 powder with solid-state NMR [16]. Then, the potential of using the proposed CaF_2 NCs as imaging tracers for *in vivo* ^{19}F-MRI was evaluated in a mouse model of inflammation. To this end, polyethylene-glycol (PEG)-coated CaF_2 NCs were injected into a group of inflamed mice. A clear ^{19}F-MRI signal was observed at the region of the popliteal lymph node of NC-injected mice in the same leg as the injection site (Figure 2e) one hour post-injection.

Although their potential to be used *in vivo* was evident, the T_1 relaxation times of nanofluorides are relatively long (>10 sec) [15], which limits signal averaging and, thus, the signal-to-noise ratio (SNR) in ^{19}F-MR images at a given imaging time.

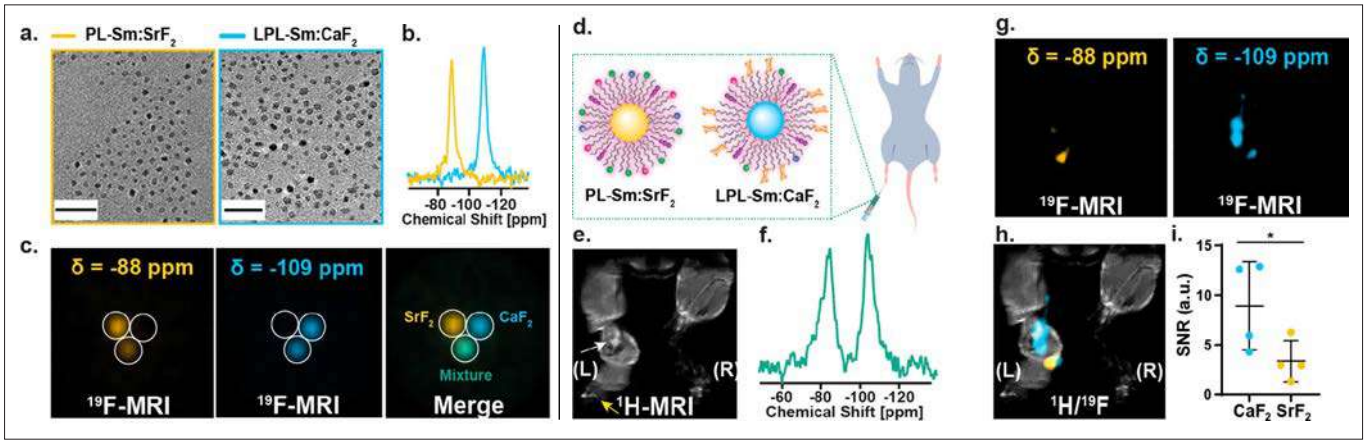

Figure 3. Multicolor ^{19}F-MRI with nanofluorides. (a) TEM images (scale bar: 50 nm) of Sm:SrF_2 and Sm:CaF_2 nanofluorides and (b) their ^{19}F-NMR spectra when dispersed in water. (c) Multicolor ^{19}F-MRI of a phantom containing SrF_2, CaF_2, or a mixture of these. (d) Schematic representation of nonglycosylated PL-Sm:SrF2 and glycosylated LPL-Sm:CaF2 NCs injected as a mixture into the footpad of an inflamed mouse. (e) ^{1}H-MRI of the inflamed mouse; white arrow indicates the inflamed lymph node, and yellow arrow represents the injection site. (f) *In vivo* ^{19}F-NMR spectrum (total injected PL-Sm:SrF_2 and LPL-Sm:CaF_2). (g) ^{19}F-MRI acquired with the center of the frequency offset set at either −88 ppm (left, yellow) or −109 ppm (right, light blue). (h) Representative ^{1}H/^{19}F MRI showing the higher accumulation of LPL-Sm:CaF_2 NCs in the LN. (i) Dot graph presenting the ^{19}F-MRI signal of either PL-Sm:SrF_2 or LPL-Sm:CaF_2 in the lymph node ROI (n = 4, Student's t test, * represents a p value <0.05). Scale bar: 50 nm. Modified with permission from ref. 17
https://pubs.acs.org/doi/10.1021/acsnano.1c01040

To overcome this pitfall, nanofluorides were doped through their fabrication with the paramagnetic dopant Sm^{3+}, which induced a significant paramagnetic relaxation enhancement (PRE) effect. Specifically, the T_1 of nanofluorides was shortened more than 200-fold, from a T_1 of ca. 15 s for non-doped CaF_2 to an ultrashort T_1 of 70 ms for Sm:CaF_2 resulting in an eight-fold enhancement in their ^{19}F-MRI SNR [17]. Then, with the introduction of paramagnetic nanofluorides (with Sm:CaF_2 as a putative example), the ability to classify different types of synthetic nanofluorides and present them in a "multicolor" fashion was also examined. In this regard, the large range of chemical shifts of nanofluorides, which spans from BaF_2 (ca. -10 ppm) to MgF_2 (ca. -200 ppm) [16], provided a platform for the development of a series of fluoride-based NCs with different ^{19}F-NMR chemical shifts. To demonstrate this ability, paramagnetic nanofluorides of the Sm:SrF_2 type were synthesized to have a size and shape similar to Sm:CaF_2 (Figure 3a). Dispersed in water, well-resolved, high-resolution ^{19}F NMR peaks that differed from one another by more than ~20 ppm (Figure 3b) were obtained with the expected characteristic resonances for SrF_2 (-88 ppm) and CaF_2 (-109 ppm). Such relatively large difference in their chemical shifts allowed spatial mapping of the two types of nanofluorides (Sm:CaF_2 vs. Sm:SrF_2) in the same imaging frame, without overlapping signals and without affecting the two detectable ^{19}F-MRI signals (Figure 3c). Specifically, we demonstrated the immune specificity of lactose-phospholipid coated Sm:CaF_2 (i.e., LPL-Sm:CaF_2, namely paramagnetic glyconanofluorides) over phospholipid coated Sm:SrF_2 (i.e., PL-Sm:SrF_2, and thus referred to as non-glycosylated nanofluorides), in real-time, in the same inflamed tissue by presenting their spatial distribution as a multicolor ^{19}F-MRI map (Figure 3d–i).

In addition to the ability to use them as imaging agents for ^{19}F-MRI, in general, and the potential to use them for multicolor MRI applications in particular (Figure 3), we developed a liquid-state NMR approach with which to study the formation pathways of nanofluorides with a conventional NMR setup, without the need to disturb the reaction conditions. Synthesizing nanofluorides under *in situ* NMR conditions, we were able to probe their sub-nm growth over the entire course of their formation, highlighting their controllable growth mechanisms (coalescence vs. classical simple-growth), which resulted in different morphological and functional features [18, 19]. Examining the correlation between the crystallographic features of the nanofluorides and their relaxation properties, we have developed an approach to shorten the T_1 relaxation times of the fluoride content in nanofluorides by 10-fold only by introducing a defect in their crystals. Such an approach for nanocrystalline-defects relaxation enhancement (NDRE) demonstrates that, while avoiding the use of paramagnetic elements and without introducing the PRE-effect to shorten T_1 values, we were able to extensively enhance the longitudinal relaxation rates of small-sized fluoride NCs to improve ^{19}F-MRI performance [20].

Guest exchange saturation transfer (^{19}F-GEST)

The millimolar sensitivity of ^{19}F-probes restricts the implementation of ^{19}F-MRI to study and map biologically relevant low-concentration targets and calls for novel developments. The maturity of the CEST contrast for MRI [21] opened opportunities to indirectly detect low concentrations of solutes, exploiting both dynamic proton exchange processes and magnetization transfer capabilities. The establishment of the CEST approach created opportunities to implement the CEST principles into ^{19}F-MRI [11, 22] as first demonstrated with fluorinated chelates for sensing and mapping of metal ions [23]. This demonstration of ^{19}F-CEST applicability provided a diverse platform for the development of novel strategies for multicolor MRI. For that purpose, and inspired by the hyperCEST [24] methodology (used with hyperpolarized ^{129}Xe gas as the guest), we developed the ^{19}F-GEST (guest exchange saturation transfer) approach [25–27]. Capitalizing on the different chemical environments of the inner cavity of two different macrocyclic hosts that induce different chemical shift offsets (Δω) of a rapidly exchanging complexed ^{19}F-guest (either upfield or downfield relative to the non-complexed agent), we were able to demonstrate the use of a single ^{19}F-agent for dual-color ^{19}F-MRI with micromolar detectability based on GEST (Figure 4a). Analogously to ^{1}H-CEST, the large ^{19}F-MR signal of the free ^{19}F-agent mimics the $^{1}H_2O$ signal and the ^{19}F-agent that is bound to the molecular host resembles the exchangeable proton in ^{1}H-CEST (compare Figures 1a and 1c). The two different chemical shifts obtained for a bound ^{19}F-agent is a result of the diversity of macrocycles that can be used and the saturation transfer capability is a direct benefit of the reversible dynamic interactions of supramolecular host-guest assemblies that allow the amplification of the ^{19}F-MR signals of extremely low concentrations of complexes.

More specifically, the ^{19}F-agent (or ^{19}F-guest) fluroxene is capable of generating significant ^{19}F-GEST contrast in the presence of two different molecular hosts with two opposite Δω values, either downfield, when incorporated into cucurbit[7]uril (CB7, obtaining a fluroxene@CB7 complex), or upfield, when incorporated into octa-acid (OA, obtaining a fluroxene@OA complex) relative to the resonance of unbound fluroxene (Figure 4b). While the GEST effect of fluroxene@OA was at Δω = -1.6 ppm and represented as a green color, the GEST effect of fluroxene@CB7 was obtained at Δω = 2.2 ppm and is represented as magenta in the GEST map (Figure 4c–g). Importantly, the existence of either the host or the guest or their complexes does not affect the ^{19}F-MRI appearance and the ^{19}F-GEST contrast is obtained "on demand" upon the application of the saturation pulse at the Δω of the host-guest complex and can be presented as a dual-colored MRI map (Figure 4e). Note that the ^{19}F-GEST effect can be observed from the intensity of the free ^{19}F-guest at the ^{19}F-NMR spectrum when acquired from a defined voxel using

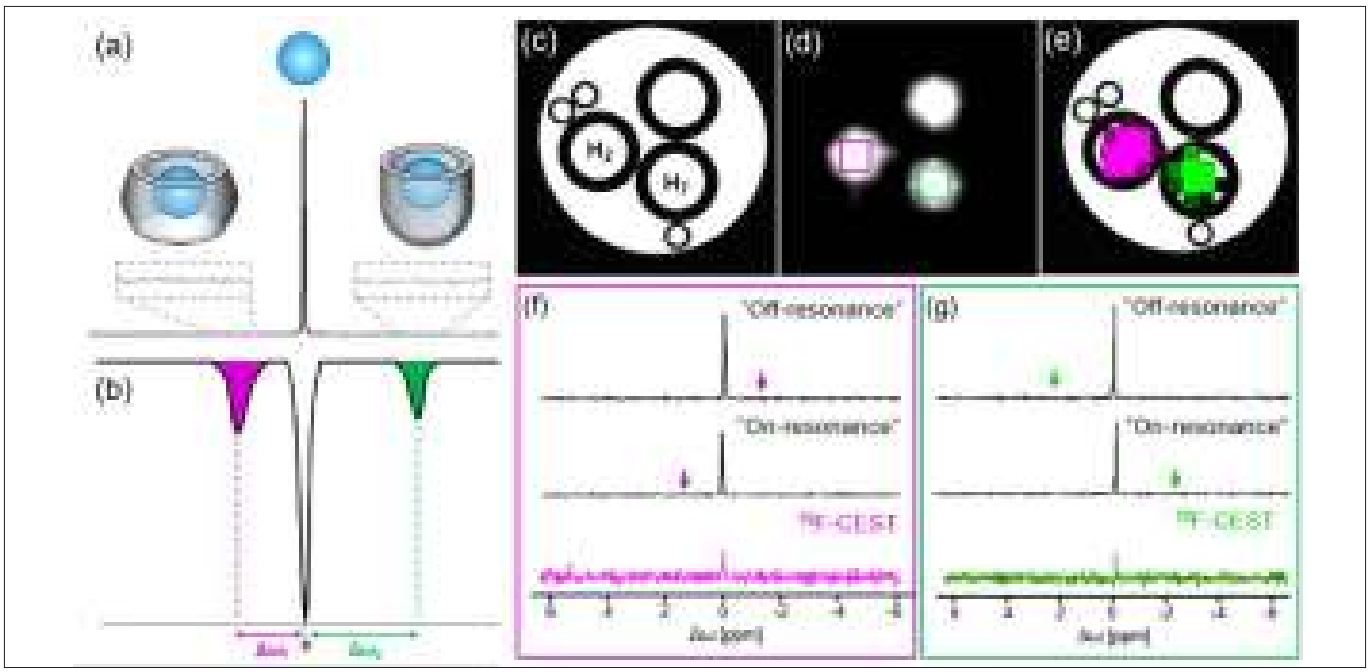

Figure 4. ^{19}F-GEST using host-guest molecular pairs. (a) ^{19}F-NMR spectrum of an aqueous solution of the ^{19}F-guest fluroxene (G, 5 mM) and two molecular hosts (50 μM each), CB7 (H_2) and OA (H_7). (b) Schematic z-spectrum representation of an H-G system depicting the opposite GEST effect of a single guest in the presence of two different molecular hosts. (c) ^{1}H-MRI, (d) ^{19}F-MRI, and (e) ^{19}F-GEST map of 5 mM fluroxene and 5 μM of either H_2 (CB7) or H_7 (OA). (f, g) Localized spectroscopy-GEST data of two voxels, as labeled in d.

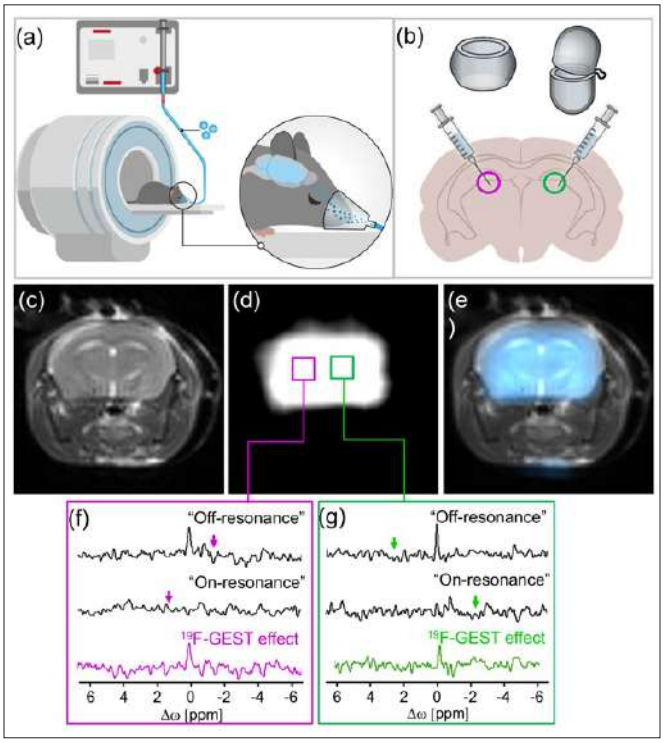

Figure 5. *In vivo* ^{19}F-GEST. (a,b) Schematic illustration of the *in vivo* experimental setup, (c) ^{1}H-MRI, (d) UTE-^{19}F-MRI, and (e) ^{19}F-MRI signal overlaid on the ^{1}H-MRI of a live mouse anesthetized with 4% fluroxene. (f,g) Localized ^{19}F-GEST MRS data.

localized MR spectroscopy (MRS) approaches applied with a pre-saturation pulse at the desired frequencies (Figures 4f,g).

Using a fluorinated anesthetic as an inhalable ^{19}F-guest (i.e., fluroxene), the potential use of ^{19}F-GEST for *in vivo* studies was demonstrated (Figure 5a). To do so, aqueous solutions of either CB7 or OA (in its dimeric form) were delivered intracranially to two opposite hemispheres in the brain of a live mouse (Figure 5b). The examined mouse was then anesthetized with the inhalable ^{19}F-guest fluroxene for the *in vivo* ^{19}F-GEST examination following confirmation of a homogenous distribution of the ^{19}F-guest in the brain with ^{19}F- MRI (Figure 5d–e). *In vivo* localized ^{19}F-GEST MRS (Figures 5f,g) was then performed using two voxels localized at the injection sites of either CB7 (pink square, Figure 5d) or dimeric-OA (green square, Figure 5d) showing the *in vivo* applicability of ^{19}F-GEST through a clear saturation transfer effect observed in the obtained ^{19}F-NMR spectra (Figures 5f and 5g) [28]. This ^{19}F-GEST MR approach offers an alternative strategy with which to detect very low levels of thermally polarized pools of fluorine-19 spins with readily available hardware and may open new avenues for the development of additional molecular architectures for multicolor ^{19}F-MRI, which, so far, has relied on the ability to detect high concentrations of fluorinated pools (Figure 1b).

Despite its potential, even in an *in vivo* setup (Figure 5), the fact that ^{19}F-GEST relies on synthetic organic molecular hosts restricts the values of the Δωs of incorporated fluorinated guests to a few ppm. This limits not only the number of artificial ^{19}F-GEST colors that can be obtained, but also compromises the spectral resolution of ^{19}F-GEST. To overcome this and expand the number of artificial ^{19}F-GEST colors and enhance ^{19}F-GEST spectral resolution, we proposed a paramagnetic GEST (paraGEST) approach for multiplexed imaging based on paramagnetic supramolecular systems. Inspired by paramagnetic CEST (paraCEST) [29] and the potential to induce pseudo contact shifts (PCSs) to exchangeable fluorinated guests, paraGEST was developed. To do so, we synthesized a library of paramagnetic cavitands based on a lanthanide-cradled α-CD (Figure 6a) and identified a putative fluorinated guest (*para*-trifluoromethyl-benzylamine), which adopts the GEST principles and is capable of producing artificial paraGEST MRI colors (Figure 6b). Establishing an approach we termed CODE-HD (COlor Display by Exploiting Host-guest Dynamics), where principles of host-guest binding kinetics with paraCEST and ^{19}F-MRI were combined, we demonstrated a unique approach to generate artificial MRI colors. By inducing PCSs to the chemical shift of dynamically exchanging fluorinated guests in a ^{19}F-NMR framework, which is controlled by the lanthanide element of the paramagnetic host, spectrally resolved artificial colors can be obtained (Figure 6). We demonstrated the versatility of CODE-HD by showing the ability to convert a given color code to another just by replacing the fluorinated guest (and using 3,5-difluorobenzylamine) and enhancing the spectral resolution of the ^{19}F-GEST spectrum as well as enriching the ^{19}F-GEST color palette with additional artificial colors [30]. Such features provide CODE-HD with a convertible color-code capability – a property that is not possible for classical luminescence-based colors or for MRI-based artificial colors.

Proposing GEST ^{19}F-NMR for the study of binding kinetics in a variety of host-guest supramolecular systems, our group demonstrated how this GEST technique, which can be applied using conventional NMR setups, can expand the NMR toolbox currently available to study dynamic host–guest systems in solution without any special expertise or dedicated hardware [31]. Demonstrating the performance of ^{19}F-GEST NMR to study systems composed of cucurbit[n]urils [26, 32], molecular capsules [27], bambusurils [25], cyclodextrins [30], and their mixtures [28] showed its potential to obtain even more artificial MRI colors than those demonstrated above. Nevertheless, although the ^{19}F-GEST MRI provides unique multicolor MRI features that are not applicable in either ^{1}H-CEST MRI or ^{19}F-MRI, it is important to stress that much more effort is needed before GEST and/or paraGEST are implemented for routine use in imaging setups.

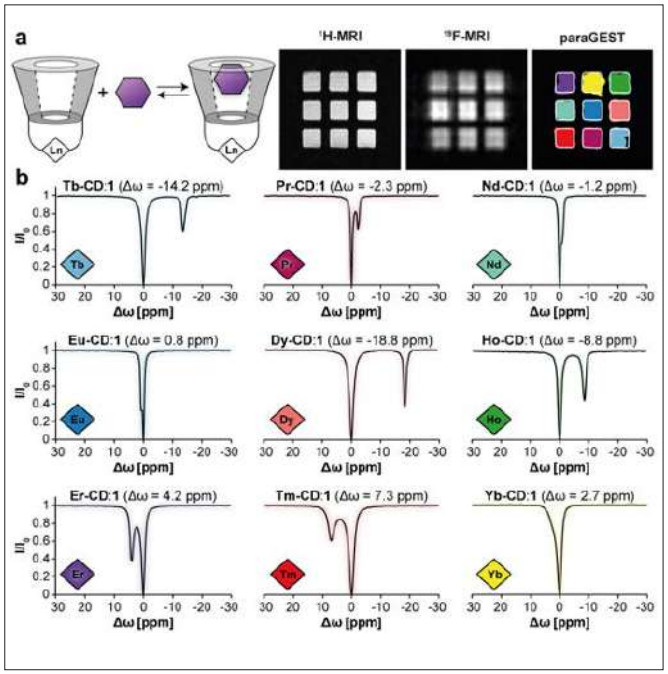

Figure 6. ParaGEST. (a) The dynamic exchange process between a paramagnetic-CD and a fluorinated-guest that allows paraGEST MRI. (b) z-spectra of solutions containing Ln-CD hosts and a ^{19}F-guest. Data were obtained with the fluorinated guest *para*-trifluoromethyl-benzylamine. Modified from Reference 30, which is licensed under a Creative Commons Attribution 4.0 International License http://creativecommons.org/licenses/by/4.0/.

Genetically engineered reporters for multicolor MRI of gene expression

The revolution of multicolor imaging of multiplex biological systems would not be complete without the development of fluorescent proteins as reporter genes. In this regard, the evolution of the green fluorescent protein (GFP) from its first isolation from the *Aequorea victoria* jellyfish, through the cloning of its gene and its expression as an imageable reporter in cells, to the extension of the fluorescent protein family to a color palette beyond green, has changed science and resulted in the founders being awarded the Nobel prize in chemistry. Realizing the challenges of fluorescent imaging, genetically engineered MRI reporters have been developed as potential alternatives for non-invasive spatial maps of reporter-gene expression [33]. Nevertheless, although extensively developed and demonstrated in multitude animal models, MRI-based reporter-gene signals lack the orthogonal, color-like display capabilities of luminescent reporters. To accomplish multi-color MRI mapping of transgene expression, we aimed to design a set of orthogonal reporter genes that produce multicolor MRI signals that can be spectrally resolved and spatially mapped [34]. To this end, we used a genetically engineered reporter system composed of a reporter gene/reporter probe pair. More specifically, we capitalized on the vast existing knowledge of a genetically engineered reporter system used in nuclear imaging and composed of a deoxyribonucleoside kinase (dNK) as the reporter gene and synthetic imageable deoxyribonucleoside (dN) as the reporter probe [35, 36].

Our MRI reporter system, which we termed GeneREFORM (stands for GENetically Engineered REporters FOR multicolor-MRI), is composed of orthogonal reporter probe/reporter gene pairs of dN/dNK. The dN/dNK system relies on the fact that imageable dN is trapped upon its phosphorylation solely in cells engineered to express the heterologous dNK transgene. For GeneREFORM, the synthetic dNs used as the putative reporter probes were the CEST-MRI detectable pyrrolo-deoxycytidine (pdC), a deoxycytidine analog and 5-methyl-dihydrothymidine (5-MDHT), a thymidine analog. Importantly, pdC and 5-MDHT generate CEST contrast from their -NH protons that resonate at Δω = 6 ppm (-NH of pdC) [37] and Δω = 5 ppm (-NH of 5-MDHT) [38, 39], allowing their use as artificial MRI colors in CEST MRI (Figure 7a,b). With the aid of a structure- and evolution-based protein design method, called PROSS [40], followed by active-site-specific mutagenesis of promiscuous dNKs, namely *Dm*-dNK and HSV1-TK, two highly active and fully orthogonal dNKs were developed and obtained. The *Dm*-dNK_7C (PDB Entry - 6YBH) variant was found to be highly active with regard to its ability to phosphorylate pdC with negligible capability

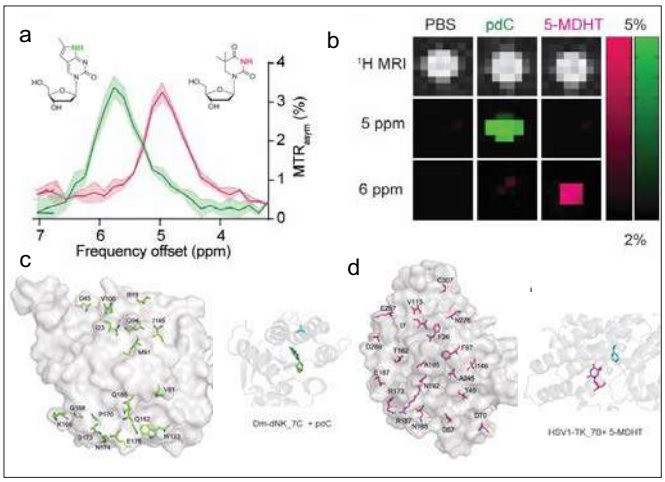

Figure 7. GeneREFORM design. (a) MTR_{asym} plots (i.e., CEST effects representation) of 5-MDHT and pdC emphasizing the negligible level of overlap of CEST peaks. (b) CEST-MRI maps of 5-MDHT, pdC, and PBS solutions obtained at Δω = 5 and 6 ppm. (c) Crystal structure of *Dm*-dNK_7C, presenting its mutations, and inset showing the magnification of the active site with pdC. (d) HSV1-TK_7B structure, presenting its mutations (computational model) and magnification of the active-site vicinity with docked 5-MDHT (right). Modified with permission from Reference 34.

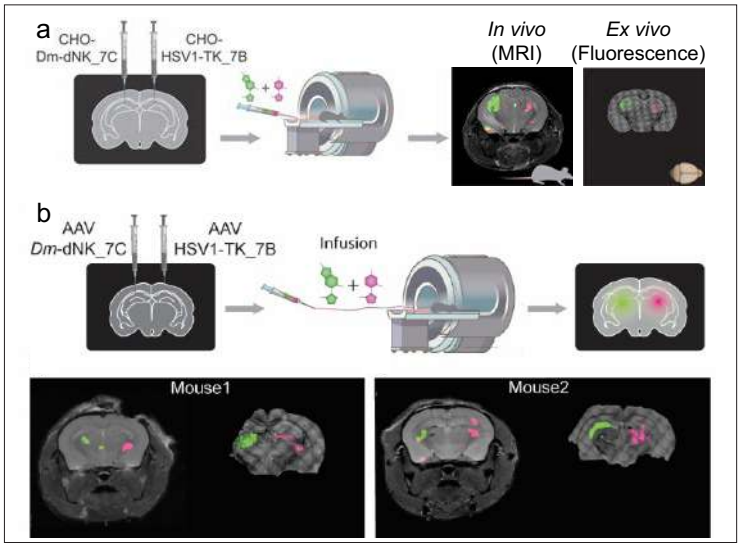

Figure 8. *In vivo* MRI of GeneREFORM. (a) Schematic illustration of the performed *in vivo* study of intracranial injection of transgene-expressing cells, and the CEST maps on an anatomical MR image of the mouse brain. The fluorescent images of a brain cryo-section show the expression of the transgenes. (b) Schematic illustration of the *in vivo* study of intracranial injection of AAV-Dm-dNK_7C and AAV-HSV1-TK_7B in two sets of representative mice showing the CEST maps on an anatomical MR image and the corresponding fluorescent images of a brain cryo-section showing the transgene expression. Modified with permission from Reference 34.

to convert 5-MDHT; and the variant HSV1-TK_7B was confirmed to be a specific dNK for 5-MDHT and not reactive with pdC. Obtaining two highly active and highly orthogonal dN/dNK pairs (pdC/*Dm*-DNK_7C, Figure 7c and 5-MDHT/HSV1-TK_7B, Figure 7d), the molecular components of GeneREFORM were established.

Using these components, we demonstrated the ability to use GeneREFORM to map the simultaneous expression of two different transgenes with MRI in two different animal models. In the first model, tumor cells expressing either of the two transgenes, HSV1-TK_7B or *Dm*-dNK_7C, were inoculated intracranially into the two brain hemispheres of immunodeficient mice. Seven days later, after two contralateral tumors were developed in the brains of this group of mice, a mixture of pdC and 5-MDHT was injected intravenously into the studied subjects. The CEST maps obtained at $\Delta\omega$ = 5 and $\Delta\omega$ = 6 ppm revealed the accumulation of 5-MDHT or pdC in HSV1-TK_7B- or *Dm*-dNK_7C-expressing cells, respectively, as manifested by the pseudo-colored CEST map display (Figure 8a). A similar observation was obtained when the expression of the orthogonal transgenes was mediated by adeno-associated virus (AAV) vectors (Figure 8b). Overall, we showed, for the first time, the development and implementation of a genetically encoded reporter system, GeneREFORM, that is not based on luminescence and enables the mapping of transgene expression in a pseudo-multi-color fashion, noninvasively [34].

Summary and outlook

Using synthetic chemistry, supramolecular chemistry, nanofabrication, and protein engineering approaches to generate various types of novel molecular formulations as MRI sensors with unique features, we demonstrated several strategies with which to obtain artificial MRI colors. Having demonstrated the potential of small-sized inorganic nanofluorides to be used as imaging agents for ^{19}F-MRI applications, and considering the extensive use of inorganic NCs for *in vivo* imaging, we envision that further uses of nanofluorides in additional scenarios are just a matter of time. Moreover, the extensive demonstrations of nanofluorides as ideal matrices for NCs with up-conversion fluorescent properties and demonstrations of the use of nanofluorides for CT imaging show the potential to further develop our fluoride-based NCs as materials for multimodal-imaging, beyond multicolor ^{19}F-MRI. The innovative GEST and paraGEST approaches that we have proposed in which host-guest chemistry is combined with ^{19}F-NMR, CEST, and MRI should be further developed to obtain novel molecular systems for molecular and cellular MRI. While the main challenge in applying GEST-MRI *in vivo* is the need to deliver both the host and the guest to the imaging region, relying on brain-deliverable molecular guests (i.e., fluorinated anesthetics), the potential to modify molecular hosts to recognize biomarkers of neuropathologies (e.g., amyloid-beta plaques in Alzheimer's disease) create opportunities to develop GEST-MRI as a diagnostic tool. Finally, the successful demonstration of the ability to map transgene expression with GeneREFORM, in a pseudo-multi-color fashion, noninvasively, could transform MRI into a powerful tool with capabilities and possibilities that have, to date, been unattainable. GeneREFORM should be further developed to provide additional MRI "colors" and should be applied in developing fields, such as cell-based and gene-based therapies.

In conclusion, there is no doubt that luminescent colors have changed research in the life sciences from the ground up, and, although they are still the obvious choice to illuminate the complexity of biological systems, MRI-based "colors" can extend the available "multicolor" toolbox for scenarios that are not amenable to the use of light. Moreover, and different from other imaging modalities, the information obtained by MRI "colors" can be correlated with other anatomical and physiological parameters that are routinely obtained in MRI studies.

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César Milstein (1927-2002) and monoclonal antibodies: Father of modern Immunology

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Abstract:

"It is not an exaggeration to describe César Milstein's contribution to science and medicine as the most important immunological advance of the century. His discovery of the method to produce monoclonal antibodies reinvented the field of immunology. The ability to make monoclonal antibodies at will in the test tube and in unlimited quantities, to any sort of antigen—whether an interesting chemical, infectious microorganism, cancer or normal cells—opened numerous new and unforeseen avenues for research, many with medical implications" [A. Karpas, American Association of Immunologists]. Milstein was born and raised in Argentina. In 1964, he fled the political upheavals and rising antisemitism to the UK, where he spent almost his entire career. In 1975, Milstein together with his post-doc Georges J. F. Köhler discovered the technique to produce monoclonal antibodies. For this discovery, Milstein shared part of the 1980 Wolf Prize in Medicine and in 1984, he and Köhler shared part of the Nobel Prize in Physiology or Medicine.

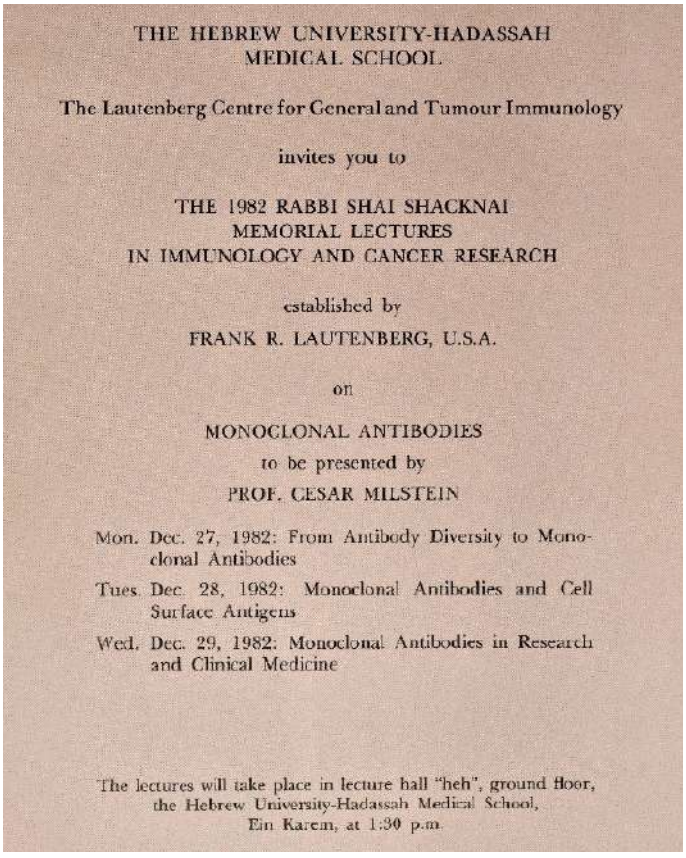
Introduction

The hybridoma technique is a method for producing large numbers of identical antibodies from a single clone of cells or cell line, also called monoclonal antibodies. This represents the most important immunological advance of the last century. Scientists for a long time hoped that it would become possible to produce monoclonal antibodies with predetermined specificities. This dream became a reality in 1975 when César Milstein and his post-doc Georges J. F. Köhler described the hybridoma technique for production of monoclonal antibodies [1]. They immortalized antibody-producing cells by fusing them with tumor cells. The method allows unlimited production of monoclonal antibodies with predetermined specificity. Monoclonal antibodies have opened up completely new fields for theoretical and applied biomedical research and allow precise diagnosis and treatment of disease. These cells are called *hybridomas* – from *hybrid* and *-oma* (meaning tumor) [2]; and since the antibodies obtained from hybridomas are produced by *clones* (meaning identical copy) derived from a *single* lymphocyte, they are called *monoclonal antibodies*. (The term *hybridoma* was coined by Leonard Herzenberg while on sabbatical in Milstein's lab [3].) For work on monoclonal antibodies, Milstein shared part of the 1980 Wolf Prize in Medicine, delivered the 1982 Rabbi Shai Shacknai Memorial Prize Lectures in Immunology and Cancer Research at the Hebrew University of Jerusalem, and Milstein and Köhler shared part of the 1984 Nobel Prize in Physiology or Medicine. Milstein is regarded as the "Father of Modern Immunology," see Figures 1–3 [4-7].

Bob Weintraub was born in Brooklyn, New York and made aliyah in 1975 to Beer Sheva, where he remained. He earned the PhD in Physical Chemistry from MIT and the Diploma in Library Science from the Hebrew University of Jerusalem. He held positions in scientific and technical librarianship in industry, hospital and academic institutions. He is now retired. He has an interest in the history of chemistry.

Figure 1. César Milstein with a spinning culture flask containing monoclonal antibodies growing in a fluid, ca. 1990s. Image courtesy of MRC Laboratory of Molecular Biology.

Figure 2. César Milstein, left, at the award ceremony of the 1980 Wolf Prize in Medicine. Milstein is seen receiving the award from President Yitzhak Navon, Chagall State Hall, The Knesset, Jerusalem. Milstein's father came with him to the ceremony. Milstein: "On that occasion, however, he could not stop himself when I gave my three-minute speech of thanks. This was when I mentioned that I was a typical example of a Jew of the Diaspora, the beneficiary of the determination of the parents that were willing to make all sorts of sacrifices to see their children in higher education. He jumped from his seat, came to the rostrum (the ceremony took place at the Knesset and I received the award from the hands of the President of Israel) and to my great embarrassment gave me a kiss! The audience, however, loved it." [15] Photograph courtesy of the Wolf Foundation.



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to be presented by

PROF. CESAR MILSTEIN

Mon. Dec. 27, 1982: From Antibody Diversity to Monoclonal Antibodies

Tues. Dec. 28, 1982: Monoclonal Antibodies and Cell Surface Antigens

Wed. Dec. 29, 1982: Monoclonal Antibodies in Research and Clinical Medicine

The lectures will take place in lecture hall "heh", ground floor, the Hebrew University-Hadassah Medical School, Ein Karem, at 1:30 p.m.

Figure 3. Invitation from commemorative booklet for the award to César Milstein of the *1982 Rabbi Shai Shacknai Memorial Prize Lectures in Immunology and Cancer Research* delivered at the Hebrew University–Hadassah Medical School, Ein Karem. Three lectures were delivered: From Antibody Diversity to Monoclonal Antibodies; Monoclonal Antibodies and Cell Surface Antigens; and Monoclonal Antibodies in Research and Clinical Medicine. Image courtesy of Cambridge University, Churchill Archives Centre.

César Milstein

César Milstein (1927–2002) was born in Bahía Blanca, Argentina, where he grew up. It was a Jewish family, his father from Ukraine and his maternal grandparents from Lithuania. Argentina at the turn of the last century was a frequent destination for Jewish families escaping antisemitic persecution in Russia. Baron Hirsch founded the Jewish Colonization Association, which sponsored Jewish immigration to Argentina. Milstein's parents spoke Yiddish at home and for several years he attended a Yiddish-speaking school. Milstein started his studies at the National College in Bahía Blanca and in 1952 earned his BS in chemistry from the University of Buenos Aires [8-10].

During his student years, Milstein was active politically and sided with left-wing student movements. He spoke out against the right-wing Juan Perón government. Milstein was popular on campus and in 1951 became president of the student union, which was risky as student leaders were being arrested. At Buenos Aries, Prof. Andrés Stoppani agreed to be Milstein's research advisor for PhD studies in biochemistry. Milstein began his research and was shocked to see, as a result of Peronist policies, how underfunded the research lab was. Stoppani feared that Milstein's political views and history of campaigning against the Peronist education policy would lead him into trouble; further, support was not available to university departments with doubtful loyalties. He advised Milstein to take time off from his studies until the political environment changed. As Milstein had recently married, he and his wife left on honeymoon. They were away for a year, hitchhiking through Europe and Israel, including several months as volunteers on kibbutzim. By 1954, the situation had calmed down, and Milstein started working with Stoppani [11].

Milstein earned his PhD in 1957 from the medical school at Buenos Aires with a thesis on disulphide bonds and thiol groups in dehydrogenases. He then earned a second PhD in 1960 at the Department of Biochemistry at Cambridge University on the mechanism of metal activation of enzyme kinetics and heavy metal activation of phosphoglucomutase. At Cambridge he met the prominent biochemist Fred Sanger, and they formed a lifetime association. A short time after completing his PhD, Milstein returned to Argentina as Head of the Division of Molecular Biology, National Institute of Microbiology, Malbrán Institute, Buenos Aires, where he continued research on projects that he had worked on at Cambridge, and further developed techniques for the study of sequencing and marking the active centers in phosphoglucomutase, phosphoglyceromutase and alkaline E. Coli. It was a time of reform after the Peronist government fell. Soon afterwards, there was the military coup of 1962, which put in another right-wing government. With the coup, persecution began to mount against political dissenters and Jews. Milstein remained at the institute for two years until government political interference in his laboratory became unbearable and he resigned [12].

Milstein recalled the visit of the Minister of Public Health to the institute, "It was during [José María] Guido's administration. …He came to interview us, the rebels, who were writing letters against him, because he had fired the director, and he said to us, 'But you are good kids, brilliant scientists. You don't have a future in this country, why don't you leave? Intellectuals should leave. It's best if they leave as they are all communists and Jews.' " People under Milstein's direction were fired for "ridiculous" reasons. Milstein said, "Either you reinstate them, or I quit." Milstein then returned to Cambridge where he rejoined Sanger at the newly established Medical Research Council Laboratory of Molecular Biology. He remained there for the rest of his career [13].

Myeloma fusions and monoclonal antibodies

The experiment

Neuberger and Askonas: "Research into fusion between different myeloma cell lines was originally initiated out of pure intellectual curiosity. But it was this curiosity-driven research that led to the technology for the derivation of monoclonal antibodies of predefined specificity, a technology with a huge impact on research, therapy, diagnostics and industry." [14]

Milstein, in discussing his early work on monoclonal antibodies, "In 1970, we started experiments using myeloma cells in culture. These are B-cell tumors which secrete tumors with myeloma proteins. These proteins are structurally the same as antibodies, but, since they are made by tumors, they are directed against unknown antigens. The idea was to see if such cells mutated their myeloma proteins as we predicted for antibodies." This experiment required analysis of 7000 individual clones. The results did not explain the expected diversity of antibodies.

"In parallel we also started using myeloma cells in culture to understand why only one of the two chromosomes produced antibody. This is known as allelic exclusion. Only one of the two alleles makes the antibody. The question we set out to investigate was whether fusion of two myeloma cells will produce hybrid cells co-expressing both antibodies or not. … The results showed that hybrid cells were capable of expressing both myeloma proteins and indeed light and heavy chains of both parental cells." [15] The antibody molecule is made up

of four polypeptide chains, two identical light chains and two identical heavy chains, and can be thought of as forming a flexible Y-shaped structure. Antibodies produced by myeloma cells are all identical.

At this time Georges Köhler joined the group as a post-doc. His project was to grow a myeloma cell in culture capable of recognizing an antigen, in order to derive mutants with altered affinity for the antigen. The project was not successful.

Milstein: "[Köhler] started a side project that involved variations on the theme of hybridization of two myeloma cells. The combination of the need of antibody-producing cells in tissue culture, which could not grow, and the experiments with hybrid myelomas, did the trick. Why not try to make the cell we needed? Perhaps we could substitute one myeloma cell for an antibody producing normal B-cell? Normal antibody-producing B cells die very quickly, but perhaps we could immortalize the antibody production by fusion with the myeloma cell line? To our surprise, the experiments were a resounding success from start to finish. Within a short time, we derived cell lines in culture making antibodies against preselected antigen." [15-16]

Preparing cell lines against a pre-selected antigen

The steps in the production of cell lines against a preselected antigen are summarized on the Nobel Prize website for 1984: "Spleen cells are prepared from animals, usually mice, which have been immunized with a selected antigen. These cells are then fused with myeloma cells maintained in culture in the laboratory. The product of this fusion is referred to as a hybridoma. Surprisingly, a hybrid of two cells can survive and also continue to divide. In this particular hybrid the myeloma cells contribute the capacity for survival, whereas the spleen cells direct the synthesis of antibodies with the preselected specificity. By special arrangements it is possible to achieve a multiplication of hybridoma cells but not of isolated myeloma cells. The hybrids obtained are propagated in a highly diluted state so that colonies deriving from single hybrid cells can be isolated. By use of a sensitive method the clones which produce the specific antibodies are identified. A particular hybridoma can then be used for future, unlimited production of a highly specific antibody." [6]

Köhler and Milstein: "We used sheep red blood cells (SRBC) as immunogen (An *immunogen* is a specific type of antigen that is able to elicit an immune response.), which enabled us, after culturing the fused lines, to determine the presence of specific antibody producing cells by a plaque technique. The hybrid cells were cloned in soft agar and clones producing antibody were easily detected by an overlay of SRBC and complement. Individual clones were isolated and shown to retain their phenotype as almost all the clones of the derived purified line are capable of lysing SRBC. The clones were visible to the naked eye." [1]

Successful results

Köhler and Milstein: "Three different experiments were successful in producing a large number of antibody-producing cells. Three weeks after the initial fusion, 33/1,086 clones (3%) were positive by direct plaque assay. The cloning efficiency in the experiment was 50%. In another experiment, however, the proportion of positive clones was considerably lower (about 0.2%). In a third experiment the hybrid population was studied by limiting dilution analysis. From 157 independent hybrids, as many as 15 had anti-SRBC activity. The proportion of positive over negative clones is remarkably high. It is possible that spleen cells which have been triggered during immunization are particularly successful in giving rise to viable hybrids. It remains to be seen whether similar results can be obtained using other antigens. (The technology was soon extended to every conceivable immunogen [7] .)

"The cells used in this study are all of BALB/c (laboratory-bred strain of the house mouse) origin and the hybrid clones can be injected into BALB/c mice to produce solid tumors and serum having anti-SRBC activity. It is possible to hybridise antibody-producing cells from different origins. Such cells can be grown in vitro in massive cultures to provide specific antibody. Such cultures could be valuable for medical and industrial use." [1]

The hybridoma revolution: an offshoot of basic research

Milstein, in the introduction to the 1999 paper called "The hybridoma revolution: an offshoot of basic research," wrote, "The production of monoclonal antibodies against predefined and, even more importantly, novel antigens has had an enormous impact in biology, medicine, and industry. Indeed, the hybridoma technique has been one of the pillars of the biotechnology revolution. Yet, none of the current applications were the goal of the research that made it possible. With hindsight, it may seem obvious that the invention of a method to immortalize cells that produce specific antibodies should have such potential. At the time, however, these most important applications were neither in our minds nor in the minds of biologists or even immunologists. When we stated in the original study that 'Such (monoclonal antibody) cultures could be valuable for medical and industrial use' we were thinking about immunoassays and passive therapy. It was only later that we started to consider seriously other possibilities. The technology was based on methods of somatic cell genetics, which we were using to analyse the origin of

antibody diversity, and arose from a practical need, namely to have an antibody secreting cell line that was suitable for studies of somatic mutation of antibody genes." [3]

Argentina declared 2021 as year of tribute to César Milstein

The President of Argentina declared 2021 as the year of tribute to Milstein. This is in context of the World Health Organization declaration of the role of scientific research as a tool against the Covid-19 pandemic. This marked the 60th anniversary of Milstein's return to Argentina when he was appointed Head of the Department of Molecular Biology of the Carlos Malbrán National Institute of Microbiology.

Declaration: "That the legacy of Dr. César Milstein transcended the borders of the country, and his discovery of monoclonal antibodies set a milestone in the history of medicine and influenced various specialties such as immunology, oncology, biotechnology, as well as the industry.

"As a result of these findings, in recent years it was possible to develop various innovative drugs, such as drugs to prevent transplant rejections, passive immunization for respiratory syncytial virus, therapies for asthma and for immune-mediated diseases such as rheumatoid arthritis, psoriasis and Crohn's disease or hidradenitis suppurativa, and improved survival rates and quality of life for cancer patients.

"Dr. Milstein maintained a deep commitment to science and promoted universal access and availability of knowledge for the benefit of society as a whole, renouncing personal economic benefits and rewards." [17]

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The story of a chess set – a scientific detective story for Holocaust Remembrance Day

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I learned to play chess at the age of five. My father wanted a partner to play with him, and he started to train me as soon as he thought it was possible. We played with an impressive chess set that had survived tens of years and eventually joined my chess set collection (see Figures 1 and 2). At age 14, I started studying chemistry, and soon I was wondering what the figurines were made of. They seemed to be made of plastic but, in the 1950s, the only abundant plastic materials in Czechoslovakia were PVC and Bakelite, polymers substantially different from the half-transparent and layered material of our chess set.

The question remained open for decades, until I realized that an instrument, which we purchased for our demonstration lab in Bargal Analytical Instruments, could easily give me an answer. A Fourier-transform infrared (FTIR) spectrometer

(a)

(b)

Figure 1. (a) The chess set, (b) some of the chess pieces.

Arie Gillon started studying chemistry at the age of 14, at the High School of Chemical Technology in Prague, Czechoslovakia. He completed his academic degrees in organic chemistry at the Technion, under the supervision of Eli Loewenthal, Shlomo Been and Dan Becker. His post-doc mentor was Yitzhak Apeloig. During his DSc studies, he acted as the chairman of the Technion Junior Staff Association. In 1988, he established Bargal Analytical Instruments Ltd., which now has over 40 employees and is one of the major suppliers of scientific instruments in Israel.

with attenuated total reflectance (ATR) diamond accessory (Thermo Nicolet iS5 with iD5) allows a non-destructive measurement of the IR spectra of solids. The software includes a library of reference spectra that can be used to identify compounds. The library includes a large number of polymers, so I thought it should be simple to identify the material from which my chess set is made.

I brought chess pieces of both colors to the lab, and we made several measurements. The result was shocking: the library search determined with the highest probability that the figurines are made of human skin [see Figures 2(a – c)]. The ATR accessory measures a very thin layer, just about 1 micron (one thousandth of a millimeter) thin, so there was the possibility that what we measured was epithelial cells from our fingers. We therefore washed the figurines thoroughly, but the result gave an even higher probability that they were made of human skin.

My parents lived before WWII in the small town of Chust in Ruthenia, which is known as the Carpathian Ukraine, at that time Czechoslovakia. Following German occupation of Czechia in 1939, Czechoslovakia was dismembered and Ruthenia with over 100,000 Jews, 14% of the population, was annexed to Hungary. The Hungarian Jews, although persecuted, were saved from the Holocaust until March 1944, when Germany occupied Hungary. My family was transported to Auschwitz on the festival of Shavuot, June 1944. When my parents, among the few that survived, were liberated, they had the choice of returning home to Ruthenia, which was now annexed to the Soviet Union, or remaining in Czechoslovakia. The Jews who decided to stay were relocated to the Sudetes region (north-west Bohemia, near the German border), which was half-empty, after the transfer of more than three million Germans to Germany. My parents were accommodated in an apartment left by Germans, and I was born there. Three years later, when we moved to Prague, my

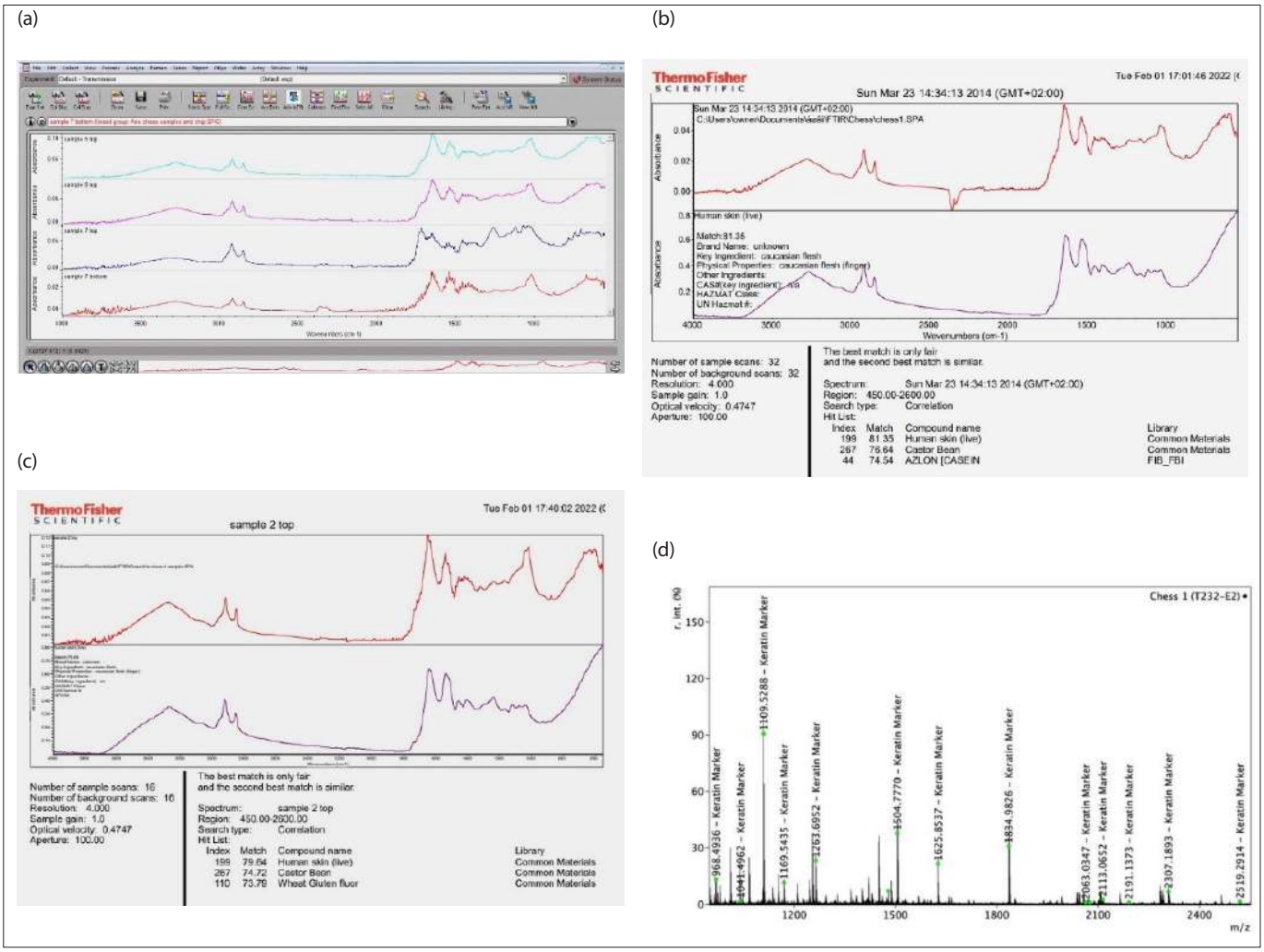

Figure 2. (a) FTIR spectra of several chess pieces, (b,c) typical library search, (d) PMF spectrum with highly conserved keratin ions indicated.

parents again received an apartment in which Germans had lived during the war.

I have no idea whether my father purchased the chess set, or perhaps found it in one of the flats among the gadgets left behind by the Germans. I suppose he found it in one of the flats because, after the war, he could not possibly afford to purchase such an apparently expensive set.

It is known that, during the Holocaust, the Nazis produced artifacts from bodies of Jews they murdered. They made not only soap from human fat, but also "ornamental" objects like lampshades, from human skin. There is no evidence of chess figurines made from human skin, but it could be possible. If so, my chess set should be in Yad Vashem, the Holocaust memorial museum in Jerusalem, and not in my private collection. It became crucial for me to pursue this issue thoroughly.

When identifying compounds by searching a spectral library, it is most advisable not to depend on the computer blindly, but to compare the spectra visually. Inspecting the library spectra revealed that the IR spectra of bovine leather and human skin are almost identical, and that the probability that the chess pieces are made of processed bovine leather is just a few percent lower than that they are made of human skin. The expert opinion of Prof. Stephen Weiner from the Archeology Department of the Weizmann Institute of Science in Rehovot and of Dr. Michael Bradley from Thermo Scientific in Madison, Wisconsin, was that it is impossible to distinguish between human skin and bovine leather by means of IR spectroscopy. They both recommended solving the problem by DNA analysis.

I turned to my friends in the forensic department of the Israeli Police. It was explained to me that the forensic lab in Jerusalem compares human DNAs, but does not have the ability to compare DNA of other species. I was referred to Dr. Gila Bar-Gal (no connection to my company Bargal Analytical Instruments) in the Faculty of Agriculture of the Hebrew University, who deals with the analysis of the origin of DNA. Gila was very responsive. Incidentally, at the same time, she was asked to check a horn smuggled from India, suspected to be ivory, and we could help her by using FTIR/ATR to show that it was a plastic artifact. Gila's staff used a polymerase chain reaction (PCR) replication technique and confirmed that the samples were of human origin.

Gila used her remarkable scientific insight and compared the DNA of the chess pieces with that of her students. It was identical to one of them, indicating that they had contaminated the samples with their fingers. They resampled the chess figurines several times, but did not succeed in producing DNA pure enough to get a meaningful result. In the case of ancient tissues, this is a prevailing problem and Gila's recommendation was to send the samples to a lab specializing in ancient DNA sequencing. Genetic sequencing is done in Israel on modern DNA only, so the samples had to be sent abroad. This did not happen, so the issue was postponed for some time.

Several years later, I saw on TV news a report that included an interview with Prof. Oded Rehavi of the Neurobiology Department in Tel Aviv University, in which it was mentioned that he deals with ancient DNA. Oded referred me to Prof. Christopher Mason of Cornell University, who collaborates with him and whose lab performs the DNA sequencing for him. Chris volunteered to run the DNA analysis of the chess pieces free of charge, but requested samples of bovine and human skin as a reference. There was no problem with bovine skin; I simply cut a piece out of one of my leather belts. Regarding human skin, I turned to my friend Prof. Juri Kopolovic, the head of the Pathology Department of Hadassah Ein Karem Hospital in Jerusalem. Juri explained that it is illegal to supply human samples, but generously offered to provide a piece of his own skin after some minor surgery he planned to undergo.

In the meantime, I asked Chris why he needs references, as the human and bovine DNA sequences are known. Instead of replying, he referred me to a forensic lab in Texas, that specializes in ancient genome sequencing. The manager of the lab ruled out any possibility of performing DNA sequencing on skin that had been treated chemically. End of story; there was no need any more for Juri's altruistic donation of his own skin.

Oded Rehavi mentioned to me that there are works negating the conjecture that the infamous lampshades were made of human skin. A due search led me to Mark Jacobson's book [1]. The book describes a lampshade found in the USA, whose DNA sequencing revealed human origin. Several years later, in repeated testing, human contamination of the sample was detected, and the lampshade was determined as being most probably made of parchment. This was published in 2012 in National Geographic's TV movie Human Lampshade: A Holocaust Mystery.

To my surprise, the program featured Prof. Chris Mason from Cornell with whom I had been in touch, as the scientist who performed both the original and the following corrective analysis. He testified that the correction was facilitated by advanced technology, that had improved between the analyses. Why then was it impossible to perform DNA sequencing of the tanned leather/skin of my chess set, while

Figure 3. Pawn interior.

Figure 4. Vietnamese horn chess figures.

it could be done on parchment, which is virtually the same material? This question remained unanswered.

I continued to search. I found out that the infamous Buchenwald human skin lampshade, which was photographed by the US army when liberating the Buchenwald concentration camp, had disappeared. Another lampshade, claimed to be made of human skin in one of the USA museums, was found to be made of cellulose. The conclusion is that if the Nazis used Jewish corpses as a raw material, this was not a systematic effort but a local initiative.

From Jacobson's book [1], I learned that Yad Vashem, the holocaust museum in Jerusalem, is not allowed to keep human remains, and that holocaust museums in general are not interested in artifacts of this kind, which in their opinion distract public attention from the main issue of the Holocaust to side issues and controversial legends.

The conclusion was that I have to keep the chess set in my possession. What is it made of? This question remained unanswered. But this was not the end of the story.

When I submitted this story to all the people mentioned in it with a request for permission to mention their names, I received updated and interesting information. First, Chris Mason answered that he would be willing to analyze the sample after all, if it would arrive with the requested reference material. Further, Gila Kahila Bar-Gal had advanced in her research and was now able to deal with ancient samples. She sent a detailed report of the work performed on mitochondrial DNA sequencing of the white chess piece, which provided inconclusive results. The DNA quality did not allow the identification of the source reliably, but the results hinted at domestic sheep (Ovis aries), breed Awassi. This breed is in fact abundant in the Middle East but not in Europe, which was supposedly the origin of the chess set. Gila suggested submitting an additional, cleaner sample.

Finally, Steve Weiner turned my attention to an article on zooarchaeology by mass spectrometry (ZooMS) by Matthew Collins [2], professor of Palaeoproteomics in the Department of Archeology in Cambridge University, and also in the University of Copenhagen. This novel method establishes the source of bones found in archeological sites by identifying proteins by means of high-resolution mass spectrometry (MALDI-TOF). I turned to Matthew and he referred me to Dan Kirby from Dan Kirby Analytical Services in Milton, Massachusetts. This is the lab that performs the ZooMS testing, which was in the meantime renamed PMF (peptide mass fingerprint) analysis.

I responded by opening the bottom cover of one of the hollow pieces (Figure 3) and grinding its inner part with a new grindstone fitted on a drill. I divided the resulting powder into three samples. I brought one of them to the Faculty of Agriculture, and sent one to Chris Mason with a sample of human skin that I got from a plastic surgeon. The third I sent to Dan Kirby, who sent me a prompt and surprising report: The PMF spectrum clearly shows that the sample does not include collagen, the protein found in skin and hide, but

keratin, the protein found in hair, feathers, nails, horns and hooves [see Figure 2(d)]. The method used by Dan could not point at a specific animal, except to establish that it was a mammal. From the size of the chess pieces, Dan suggested that their source was either equine or bovine hooves.

From a literature search I learned that hooves are built of several layers and are far from being homogenous, as they seem to be from the outside. Their only use is grounding them to powder for fertilizers and animal feed. However, chess sets made of horns were on sale in the mid-20th century, mainly in the USSR. Today, copies are manufactured in Vietnam from buffalo horns. Among the photos of the Vietnamese products on sale, I found sets similar to mine, but obviously more shiny and not peeling (Figure 4). I informed Dan of this and he promised to repeat the analysis with a method he was currently developing, that would establish the horn origin more precisely. A week later I received the second answer: The existing databases negated equine origin, but still could not distinguish between bovine and ovine origin.

The bottom line is that I can relax. My chess set is almost certainly made of sheep horn.

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Shimon Vega in the eyes of his students and postdocs

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Introduction

Versions of this article were previously published in the Journal of Magnetic Resonance [1] and the Ampere Bulletin [2] and it is reproduced here with permission.

Professor Shimon Vega (1943–2021) (Figure 1) of the Weizmann Institute of Science passed away on November 16, 2021. Shimon established theoretical frameworks to develop and explain solid-state nuclear magnetic resonance (NMR) and dynamic nuclear polarization (DNP) techniques and methodologies. His departure left a profound mark on his many students, postdocs, and colleagues. Shortly after his passing, they assembled spontaneously for an international online meeting to share reflections and memories of their experiences in his lab and how they were affected by them during that period of time, and throughout their scientific careers. These thoughts and feelings are presented here.

Amir Goldbourt received his BSc from Tel-Aviv University. He completed his PhD with Professor Shimon Vega in the Chemical Physics Department of the Weizmann Institute of Science in 2003. Following a post-doctorate with Professor Ann McDermott at Columbia University, he returned to Israel in 2007 and joined Tel Aviv University where he now heads the solid-state NMR group in the School of Chemistry. His research interests are in structural virology, in studying the role of Lithium as a therapeutic agent, and in the development of NMR techniques for quadrupolar spins.

Figure 1. Shimon Vega as a young and older man, and his signature Dutch tulips.

Amir Goldbourt

When I was a PhD student with Shimon, Claude Cohen-Tannoudji visited the Weizmann Institute. Perhaps his most memorable advice was how to pick your supervisor. He said: "Find a person that you like and the science will be great." I thought how lucky I was to choose the right supervisor. I was learning from an amazing scientist but, moreover, a unique human being who always gave you the feeling that you are the most important person in his life at that moment and those that follow. The years 1996–2003 will always be engraved in my memory.

I joined Shimon's lab as I wanted to see in my own eyes how quantum mechanics comes to life in experiments, and magnetic resonance was the right choice for that. Shimon made quantum mechanics real and beautiful. For that reason, although Shimon suggested that I work on ^{2}H NMR (which I did at the beginning), I was asking for more energy levels. Thus, my PhD studies focused on half-integer quadrupolar nuclei. From Shimon's perspective, that only meant that the math is more fun, because he could now diagonalize 4×4 and 6×6 matrices, and he could do it in ease by scribbling transformation operators on the blackboard. But Shimon would make you do it yourself with his endless patience. You would stand in his famous room at the end of the corridor, stand near the blackboard, and try with all your effort to diagonalize Hamiltonians. While you are mixing up Hamiltonians with density matrices, Shimon would work on his computer and occasionally throw insightful remarks, and you would realize that while working on his own affairs, he would still be one-hundred percent focused on your endless struggle and lead you to the correct solution. The greatness of Shimon as a PhD mentor was his ability to make you learn in a gentle and elegant way by guiding you without explicitly solving anything directly. Somehow, he would cause your mind to arrive at the correct answers.

Gil Goobes received his BSc at Tel-Aviv University. He completed his MSc and PhD with Professor Shimon Vega in the Chemical Physics Department of the Weizmann Institute of Science in 2002. Following a post-doctorate with Professors Gary Drobny and Patrick Stayton at the University of Washington, he returned to Israel in 2007 and joined Bar-Ilan University where he is heading the solid-state NMR group in the Department of Chemistry and Institute of Nanotechnology and Advanced Materials. His research interests are in fundamental molecular understanding of biomaterials in Nature and medical applications and advanced materials in energy-related systems.

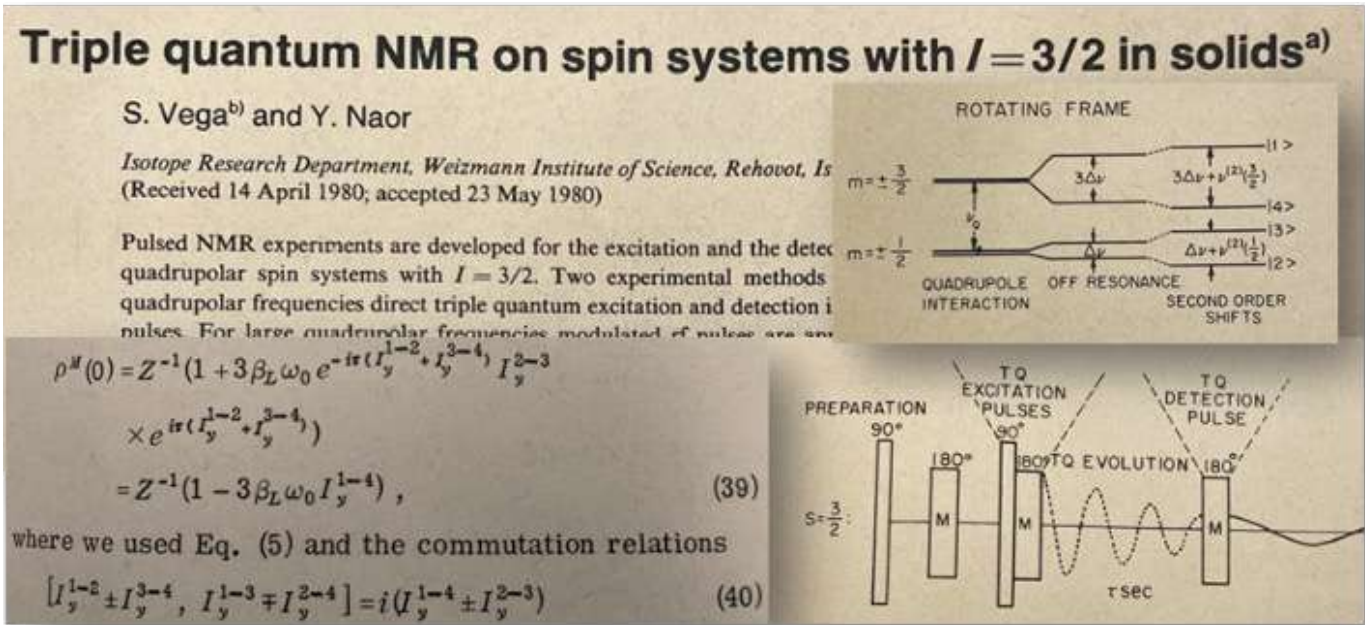

Figure 2. Collage of Vega and Naor paper [3].

Shimon wrote many seminal papers when I was still at elementary school, many of them on multiple-quantum NMR using fictitious spin operators. The most influential paper that goes with me everywhere (I still have the yellowed hard-copy, as authors used to get them by mail from the journal) was on triple-quantum excitation of quadrupolar nuclei [3] (see Figure 2). I still think and feel fictitious spin-half operators, and use these tools to understand problems we encounter in our lab. I feel obliged and enthusiastic to always pursue better ways to perform quadrupolar NMR spectroscopy.

I try to take from Shimon the patience, the quest for every detail, the devotion to scientific truth and integrity, and the devotion to be there for any eager student, be it your own, or someone else's. Like all great artists, Shimon's scientific song and spin art will always be with us.

Gil Goobes

As an undergraduate student, I had a sense that nuclear magnetic resonance was an exciting field, and probably what I will want to carry out my research on. Professor Gil Navon taught a course on magnetic resonance spectroscopy at that time and was running in parallel a graduate level course on the subject – which I, naturally, joined. Before moving to the Weizmann Institute for my graduate degrees, determined to continue with NMR, I asked the teaching assistant in the graduate course, Itamar Ronen, now Professor at the Leiden University Medical Center, who should be contacted in case I am interested in NMR theory, and his immediate response was Shimon Vega!

So, this paved the way to carrying out both my MSc and PhD research with Shimon and turned out to be a judicious and gratifying experience. One aspect of working with Shimon on NMR problem solving is the perpetual test of the depth of dive into the theory that one was willing and capable of taking. You can imagine climbing a winding road to a high snowy peak with a cheerful clear-eyed guide always showing up in front of you, restless, at each curve and turn, never tired and always leaping forward two steps ahead, effortlessly. Mind you, you still had to climb up yourself, whether it was writing down the correction terms for finite-pulse XY-8 REDOR using Floquet theory or working out the analytical expressions for matrix diagonalization of homonuclear-coupled spin Hamiltonians.

One quality of Shimon which may not strike one immediately as typical of him was his openness to new ideas and initiatives. We were allowed the time to program a Matlab code for the REDOR transform (which was already proposed by Karl Mueller at the time) and amused ourselves with possible kernel functions suitable for the other anisotropic interactions. We discussed ways of polarization enhancement and delved into fundamental reasons why an equivalent of stimulated emission population inversion in a MASER in the microwave region was not possible in the radiofrequency region for NMR. However, lengthy digressions from the topic were gently and cleverly discouraged as Shimon was too knowledgeable to allow a complete waste of time. One of the projects, in which I felt that Shimon was caught slightly

surprised with an unanticipated result, was flipping individual proton lines while applying a phase-modulated Lee Goldburg (PMLG) decoupling field, which we were running together with Elena Vinogradov. We tested the crystalline hydrate of histidine with its 10-proton spin system and were trying to record the magnetization transfer between protons after such DANTE-PMLG flip, only to discover that the protons would diffuse fast, too fast when the strengths of all contributing interactions were accounted for. It dawned on us, then, that the sample we used was uniformly ^{13}C labeled and that the homonuclear carbon-carbon couplings would serve as a spin bath that would cause the extra leakage of spin magnetization through the non-negligible ^{1}H–^{13}C couplings. By including CW decoupling on the ^{13}C through the sequence and verifying with a natural abundance histidine sample we could confirm that this was the reason for the faster spin diffusion.

It was the outstanding combination of Shimon's true caring mentorship and sweeping endeavor at solving fundamental research challenges that made the experience of spending time under his tutelage unforgettable. Thank you, Shimon.

Yonatan Hovav

I was a student of Prof. Shimon Vega during my masters and PhD, as well as during a short postdoctoral period, with most of our time together devoted to the study of static solid state DNP. There is much praise to give Shimon as a teacher, a mentor, a scientist, and a person. Below are some glimpses into who he was to me, and I believe to his other students and co-workers as well.

I joined Shimon's group after taking his NMR primer. Something in his enthusiasm and friendliness drew me to him. I did not have a quantum mechanical background, but was fascinated by it, and hoped Shimon would help me understand it better. To join the lab, you had to go through Shimon's fire test (I believe most, if not all, of his students passed it): "Why would you come to my lab?" he would ask, "You will need to work much harder to get the same results as in other labs." And he was right – my MSc period left me confused and with few results, at least in my mind, and yet I stayed for a PhD. It was there that all the hours spent with Shimon and his students sank in, and suddenly things made sense. I ended up spending most of my time writing and playing with quantum mechanical simulations, trying to understand the basic mechanisms of DNP.

Shimon would often say that our task in science is to transfer the knowledge from one generation to the next – starting from the giants of old and building the generation to come – and in his knowledgeable and patient way he acted on it. His door was always open to us, and we could come and ask any question. The main obstacle was finding a time where there wasn't another student in the room already, whether one of his own students or not. Going into his office with a question, he would often take me back several steps to the basics, making sure I built a solid foundation in his patient way. I would then solve my question with him on the board or at the office armed with the new understanding he gave me. He had a way of simplifying the physics – one day he took me on a *gedanken* bus ride to explain perturbation theory. But as time went on, we talked more and more in matrices and Hamiltonians, creating a Vega group shorthand DNP convention. When a hard question came, we would often work on it in parallel.

Shimon would take the research to heart, as well as his student's wellbeing. He would come to see how an experiment was going (spinning on the lab chair in his energetic way), coming to the student office to hear the latest experiment or simulation results, or calling you to his office and saying he didn't sleep at night thinking about the problem at hand. He would help out when needed, learn about what we discovered, and give direction in his gentle way: "If I were you I would do this and that next," he would say. His reactions were often an inverse reflection of my own feelings: when I was excited about some new result, he would cool me down, talking about possible problems or the next steps; and when I was down – he would try to pick me up, pointing to past successes.

Shimon would always have something good to say about everyone. If he disagreed with the theory, he would point to the experiment, and while he worried that a competitor would publish something before us – it always felt we belonged to the same group. While he believed in his way of thought – he tried to connect it to that of others. Before anything else, he would view you as a person, and as such would treat you in his friendly and polite way.

I feel fortunate, thankful, and privileged to have had Shimon as my professor, and to have taken part in his group.

Ilia Kaminker

As perhaps all the others who have passed through Shimon's research group, I shared the same experience of having to convince him to take me in. I spent six years, during my PhD with Daniella Goldfarb, sitting in the student room two doors from Shimon's office. By the time I was looking for a postdoctoral position, we knew each other. I took Shimon's NMR primer, he helped us with theory on one of my papers

with Daniella, and I heard him present many times in various magnetic resonance conferences. Still, when I asked him if I could join his group, he tried, as was his custom, to talk me out of it. Fortunately, I was persistent enough and had the honor and privilege to work with Shimon for two years (2012–2014).

During that time, we worked closely with Shimon's PhD students Daphna Shimon and Yonatan Hovav with constant support from Akiva Feintuch. When I joined the group, the three of us were working on separate projects, all having to do with understanding of DNP. Somehow, after a few months, all the projects had merged, and we realized that we are actually all working together on different aspects of one bigger problem. The combined effort during the remaining year and a half remains a unique scientific experience with the three of us under constant guidance from Shimon, tackling, revealing and slowly understanding a complicated phenomenon.

Another profound influence of Shimon on me was the realization that there are different levels of understanding. All of us sometimes say to ourselves "now I understand it."

Shimon had very strict requirements as to what "understanding" means. Understanding for him had to do with rigorous derivation; it had to be firmly based on the very basics of magnetic resonance and quantum mechanics. He did not believe in hand-waving arguments – they never convinced him. It took me quite some time to adapt myself to Shimon's requirement of "understanding" and I am very grateful to him for this. It has undoubtedly made me a better scientist.

I miss Shimon greatly. After returning to Israel I had many ideas that I was hoping to discuss with him. I wanted to invite him to see my lab – something that, now, will never happen. Rest in peace, Shimon.

Vladimir Ladizhansky

I joined Shimon's group as an MSc student in 1993 on the advice of Professor Yehiam Prior, and had the privilege of spending the next six years in his lab and continuing to learn from him for much longer. My MSc and PhD theses were at the interface of chemistry and physics, focusing on the analysis of II-VI diluted magnetic semiconductors and semiconductor nanoparticles. As Shimon's main interest was in the fundamentals of NMR spectroscopy, most other graduate students and postdocs in the lab worked on various spectroscopic problems (e.g., RFDR, NMR of quadrupolar nuclei, proton spectroscopy). Early in my PhD, I became somewhat dissatisfied with my "outcast" status and asked Shimon to involve me in the spectroscopy projects. At the time, he was working on the theory of cross polarization (CP) and offered me the opportunity to join these efforts. My first assignment was to read and understand an article that Shimon had just published along with another PhD student, David Marks, in which they established a unified view of static and magic-angle spinning CP experiments [4]. The CP paper was one of my first encounters with complex NMR spectroscopy, and it served as an entry to my scientific career. I struggled with that paper back then (and still do now!) as it is quite intense mathematically, but after numerous hours of discussions, working through our disagreements together, and getting through the equations with his guidance, a consistent picture of one of the most important solid-state NMR experiments began to emerge. The CP paper shaped my understanding of dipolar recoupling experiments, and specifically those that involve strongly coupled systems.

Shimon had an amazingly clear and at the same time constantly evolving picture of magnetic resonance and the ability to bring physics to life. His door was always open to students, and interacting with them and mentoring them were among his greatest joys. He valued our opinions and ideas even if they were nonsensical. In many ways, his influence, which was not limited just to science, had a profound impact on my life and future career. We have lost a true scientist and scholar. He will be dearly missed.

Michal Leskes

I got to join Shimon's group pretty randomly. I was a Chemistry undergraduate in my second year at Tel Aviv University, looking for something to do in the summer. I came across the summer program at Weizmann and thought I'd try. I quickly realized I had no idea how to choose a lab for the summer and going through the webpages of researchers at Weizmann didn't help at all, since nothing made sense. I knew I liked spectroscopy, but beyond that I decided to choose based on who was smiling in their photo – and that is how I got to Shimon Vega's group. This was probably the best career move I made… joining Shimon's group for that summer completely determined what kind of research I would do in the next few years and what kind of scientist I aspire to be.

Only in retrospect can I appreciate the dedication of Shimon. I was only a second-year undergraduate student, yet Shimon spent a few hours every day with me, teaching me the basics of NMR in solids. We would talk during the day, and he would give me questions to think about and get back to him for the next day. Taking the train from Tel Aviv to Rehovot and back

every day gave me time to process these lessons. After a month Shimon said I was ready to run the first NMR experiment of $^{1}H–^{29}Si$ CP on mesoporous silica (of course with guidance from Shifi Kababya). By the end of the summer I was running variable temperature $^{13}C–\{^{17}O\}$ REAPDOR experiments that in addition to useful dephasing curves also caused a mini-flood in the NMR room. This was a great summer and I summarized it in a poem to Shimon – "A fun summer it's been, with magnetic resonance and O seventeen. But after all of the time you've put in, I still don't know what is spin!"

I really did not fully appreciate this period in real time, but when I came back to Weizmann as a graduate student I realized what a unique person and teacher Shimon was and chose to join his group for my PhD. With Shimon, and a yearly visit from Madhu, we were working on homonuclear and heteronuclear decoupling using Floquet theory to understand our results. Life was a constant debate between theory and experiment and a feeling of uncertainty and confusion. But what kept me going and kept it all fun was a kind of safety net I felt Shimon provided – I felt that Shimon had it all figured out. That in fact he had this master plan of what we were doing, and perhaps we're missing a minus sign here or factor of two there, but overall he already knows what we will get because he solved it all late at night. I was never alone, any doubt or panic about some basic or complex concept that suddenly did not make any sense could be resolved after talking to Shimon (or after an email from him written at 4 am!). It was also great fun to argue with him about results and to be joyful together when theory perfectly matched the experiment.

Towards the end of my PhD, during my postdoc and then after joining the Weizmann Institute as faculty, I learned that Shimon was also the kindest, most patient listener. It never mattered what he was in the middle of or how stressed he was, he was always happy to take a break and talk about whatever was on my mind, be it the next scientific or personal challenge. It was such a privilege to have my office two floors above his and my NMR lab two floors below his office, making it my first stop coming up from the lab whenever we got a new scientific success or failure. It will take me some time before I don't pause on the second floor of the Perlman building. Shimon, I miss you. Thank you for all that I know and all that I don't know… and now have no one to ask.

Fred Mentink-Vigier

"If you join us, then what will you do after your post-doc?" Shimon started my interview with this question. To be honest, I think the question made me join Daniella Goldfarb and Shimon Vega back in 2012. The question revealed how much he cared about the people he worked with, and this is probably the reason why, up to his illness, we remained close.

The two years I spent at the Weizmann were very stimulating. From the very first days I was exposed to the group discussions about Liouville space, relaxation, and DNP. I was fascinated by the discussion between Akiva Feintuch, Yonatan Hovav, and Shimon but barely understood them. Shimon's office door was always open, and we could come in anytime to bring up a question or discuss the experimental results. Shimon was a fantastic teacher for whom no question is stupid. Instead, he would not only explain in detail, but would reformulate until we really understood. The open door-policy had additional perks. During the discussion someone would come in and contribute or bring another question, expanding the scope of my initial visit.

As a postdoc, Shimon and Akiva gave me the MAS-DNP project due to my coding skills but I barely understood the theory when I started it (of course, Shimon made me familiar with it). One day, I wanted to check the cross-effect simulations and ran them in absence of microwave irradiation. The result was "weird": the nuclear polarization at steady state deviated from thermal equilibrium. I did not believe it and was sure that something was wrong with the code. Shimon had a different stance and we spent four days discussing and running simulations until we understood it. The effect was real. Shimon's attitude taught me to welcome any result that would change my view of the problem.

After two years at the Weizmann Institute, the MAS-DNP simulations officially became my project, one that I still work on. I was afraid I would lose contact with him and rejoiced when my (French) phone plan included unlimited calls to Israel: I could continue talking with Shimon while riding my bike in the morning.

We officially continued to work together until 2017 and we last were in touch for science on a daily basis during spring 2020, when I was deriving the "Landau-Zener" cross-effect evolution operator for strongly coupled electron spins.

Shimon was always modest in his presentations, and clearly was driven by the genuine interest of "understanding" any experimental observations. However, I would dare say that for him, personal relations were the most important aspect in his life. I witnessed it firsthand from his lifelong friendship with Daniella Goldfarb, Lucio Frydman, Zeev Luz and many others. As one may expect, after nine years, our relationship expanded well beyond the professional sphere. We would always begin our discussions with "How is life treating you?" or "How are the kids?" We last met at Euromar 2019 and

it's hard to express how much I'll be missing him. Shimon did his best to promote my work and help me integrate into the NMR community. He made me meet people and talk at conferences, and in that sense, he went beyond the question he asked during my interview: he helped me build my career.

He was conscious of his role as mentor, and I owe Shimon so many things that I hope the reader can measure the respect I, and others, have for him.

P. K. Madhu

Shimon Vega was an exceptionally kind and compassionate person and a scientist *par excellence*. My own association with Shimon as a post-doctoral fellow was from November, 1997, until May, 1999. However, our collaboration continued strongly with our last joint paper on heteronuclear spin decoupling that came out in 2017. We had very regular discussions on NMR and related science, life in general, a bit on politics, culture, and history all along until March 10, 2021, before he was admitted to hospital. Our last discussion was on the possibilities of locking half-integer quadrupole spins, one of his favorite topics, which he shared with his brother Lex. In our conversations in the second week of March 2021, Shimon also shared his pain in losing Prof Konstantin Ivanov (Kostya Ivanov) (who succumbed to Covid19 on March 5, 2021), a friend and colleague of both of us.

Shimon, noted for some of the most insightful research in the area of magnetic resonance, both electron and nuclear magnetic resonance, has influenced professionally and to some extent personally the lives of many of us who have come in contact with him. This could be in the form of graduate students, post-doctoral fellows, colleagues, course students, or listeners to one of his great talks packed with science, wit, and active involvement. His enthusiasm has been often contagious and his understanding deep enough to compel chairmen of his talk sessions to give him enough time after regular sessions to explain to the particular conference audience nuances of his theoretical ideas. These were always done with a deep flair to packed audiences. Shimon was indeed one of those rare combinations of openness to new ideas with deep-rooted knowledge on sound, pen-and-paper principles, rather than pursuing transient fashions. He belonged to that genre with a great willingness to share his knowledge with others and was a restless researcher ready to question the so-called established paradigms. His inquisitiveness had always motivated his colleagues, taking the respective research to even higher levels. Of the many contributions Shimon had made, some to highlight are in the magic-angle spinning experiments in solid-state NMR, breaking the barrier into understanding quadrupole spins, introducing Floquet theory to understanding and developing various experiments and improving resolution and sensitivity of solid-state NMR experiments and, in the last few years, providing insights into the important field of DNP in NMR.

Shimon had fun doing science and was never shy of sharing his ideas and thoughts at any stage of a concept, whether published or not. For him, understanding an idea was important and the only key issue. The rest were all details for the sake of others. He was a great, active, and patient listener who put all at ease and treated others with a child-like innocence and unbridled laughter. I remember various conferences, including the Indian Magnetic Resonance Society meetings to which he came a few times, schools and workshops, and other gatherings where his infectious enthusiasm would positively influence the students and others and even the on-lookers. He did not know that he was a rock star, but he was indeed one in the field of NMR and in science.

The NMR community and I will definitely miss Shimon. It was indeed a privilege to have worked with him, known him a bit, and travelled and interacted with him. The dimensions of the matrices he worked with are most often boundless, and his memories with us also will remain so.

Toda Raba Shimon.

Silvia Pizzanelli

I joined Shimon's lab in 2002–2003 as a postdoc with a fellowship funded by the Center of Excellence on "the origin of ordering and functionality in meso-structured hybrid materials" of the Israel Science Foundation and the Italian National Research Council. During my PhD in Chemistry at Pisa University under the supervision of Carlo Alberto Veracini, I had studied liquid crystals using ^{2}H NMR and often had come across papers by Zeev Luz and Shimon Vega. As I wished to further specialize in solid state NMR, my obvious choice was Shimon's lab. I simply wrote him an e-mail, and he simply answered inviting me to the Weizmann Institute for a first meeting.

My project dealt with the adsorption-desorption kinetics of tetra-alanine at the surface of the pores of an MCM-41 mesoporous material. I spent the first months in preparation of the sample. Since an aqueous solution of the peptide was to be inserted in the pores of MCM-41, I could not use the capillary condensation method, usually employed for the insertion of pure liquids. Therefore, I just added MCM-41 to the solution, but this method was fraught with potential

problems, like incomplete filling, location of the solution in the extra-porous space, or instability of the MCM-41 structure. In this process, Shimon was a continuous source of critical questions and pertinent suggestions, constantly challenging the interpretation of a phenomenon through the experimental evidence. But Shimon was also a man of great humanity. When Saddam Hussein was captured during the second Gulf War, I have a vivid memory of his sense of discomfort as he could not rejoice over the misfortune of any person. Sometimes he shared with me his genuine interest on the people around us, referring either to science or to human relationships. In these small talks, he was sharp and direct, and my personal views were usually in consonance with his, which created a positive and friendly atmosphere. His humbleness still echoes in my mind in the words "there is a whole world out there" that he used to say when he came across some robust and comprehensive study of a subject he had only marginally touched.

After 2003 I chose to go back to Italy and life brought me far from the adsorption project started with Shimon. On the contrary, he went on for another ten years investigating different peptides and porous materials. Today my only regret is that I did not continue collaborating with him, although he gave me the chance to do it by giving me samples and a program for simulating MAS spectra in the presence of a two-site motion.

Ingolf Sack

Shimon was an extraordinary person and outstanding teacher. Perhaps he was the most important teacher for me, with whom I was fortunate to spend a certain period of my life in Israel, at the Weizmann Institute. Shimon had the ability to explain things that loomed only hazily on the horizon of my experimental work in solid-state NMR. This allowed him to predict early on how we would need to design the experiments to accurately determine ^{2}H–^{13}C distances with maximum signal yield. Whether it was the analytic derivation of the Hamiltonian in this specific spin-1 spin-1/2 quantum system, or tensor diagonalization in general, Shimon did this with an ease as if it were small talk. Indeed, working with Shimon had the joy, inspiration and ease of a long conversation among friends in which one learns much about the essentials of science and the meaning of life. I am forever grateful to Shimon for the time I was privileged to spend with him, which had a lasting impact on me beyond the realm of science.

Daphna Shimon

I'm honored to be Prof. Vega's last PhD student. When I joined his group in 2008, the interest in DNP was seeing resurgence, and I had the great privilege of learning NMR and DNP from Shimon, while also learning DNP together. We spent many hours sitting together trying to understand the experimental data I had accumulated, and to figure out how to model the spin physics of DNP when we could only simulate at most 5–6 spins. There were many days when he would come in the morning and tell me that overnight he had thought of another way we could try and simulate the thing we were looking for. This persistence is something that I always associate with Shimon. He would never give up on trying to understand even the smallest experimental feature. The things I will most remember about Shimon are probably the things many others will remember too: how kind he was, how humble, how good a teacher, and how he always knew

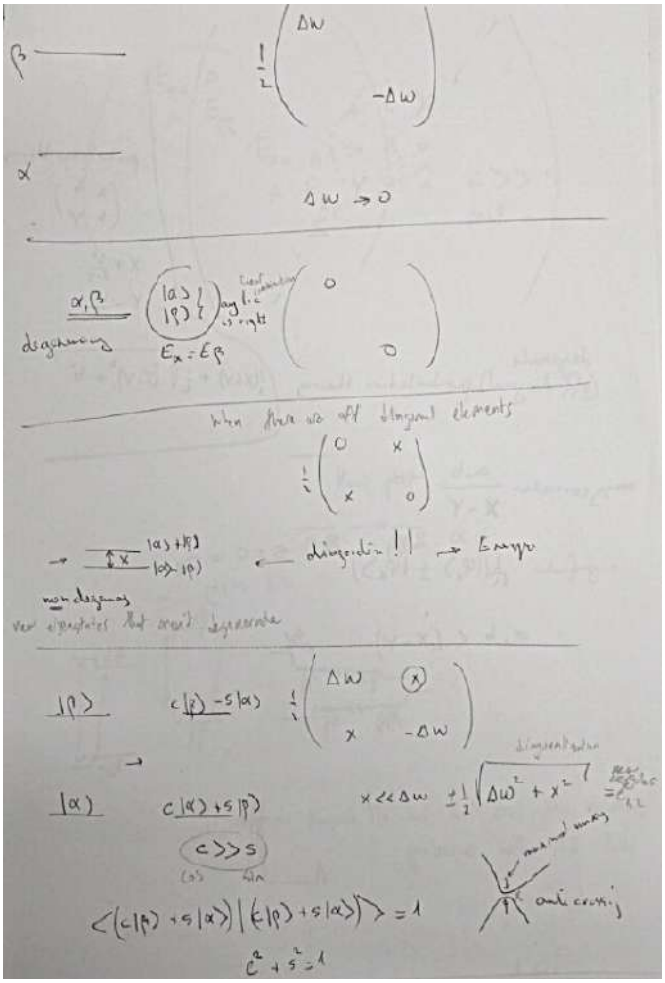

Figure 3. Shimon Vega's handwritten explanation of an off-resonant two-level system.

how to adapt his explanation of a topic to the person he was talking to. At the very beginning of my masters, I was starting to write simulations of DNP, but I did not fully understand what I was doing. One day, I was simulating a small spin system, and he had me look at the energy levels as a function of the off-resonance. He had me zoom all the way in, and then asked me what I saw. He used this exercise to explain anti-crossings and state mixing. That was the day I finally understood the simulations. I kept the piece of paper, which he wrote upside down so I could read it while he was writing, and I still have it to this day. It's a joy to look back and realize how clearly he could explain complicated topics. Part of this paper is shown in Figure 3.

Sunderasan Jayanthi

I was fortunate to be associated with Shimon during my graduate studies at the Indian Institute of Science (IISc) in Bangalore. Thanks are due to Madhu for introducing me to Shimon in 2004. While at the IISc, I had frequent email conversations about NMR with Shimon, and most of the time he responded within 24 hours. He had invested time and patience in answering my NMR-related queries, and those discussions were very helpful for me in my early research, and also throughout my career.

Subsequently, I joined Shimon at the Weizmann Institute as a postdoctoral student in 2010–2013. I was his last postdoctoral student who worked in a solid-state NMR project. During that time, we worked closely with Asher Schmidt and Shifi Kababya, which led us to multiple train journeys to Haifa, starting early morning, utilizing the time during our journey to discuss Floquet theory and deuterium dynamics. The eight-hour computational time for a Floquet Matlab simulation was addressed in one of those train journeys with a lot of equations and, in the following week, we could reduce the computational time to a few minutes. Whenever I was stuck with the underlying theory of deuterium dynamics and adsorption-desorption kinetics of small molecules in mesopores, he reassured me that "we are together in this project, we will understand it soon." That was more than an assurance and I realized only later, when I started my career, that the knowledge I acquired when I was with him was abundant and priceless. Whenever I reached out, he continued his support by all possible means, with no hesitation and no delay, but each time with more energy, enthusiasm and joy. He helped me tremendously in every aspect of my life, be it NMR, career, or personal life.

Shimon was such a wonderful person, a "spring of wisdom" as Asher says, a humble human being and a great scientist. His passing away has left a void impossible to fill. Yet I consider myself privileged and fortunate to have known him. The amount of cheerfulness, knowledge, care, concern, friendliness, and comfort that he has given each one around him, I hope will lead me ahead in my journey. The contagious energy and enthusiasm when he was around is what I would like to carry in his absence. By behaving the 'Shimon way', he taught me how to treat others, how to be humble yet competitive, ambitious but aware of our own limitations, and finally to respect everyone for what they are. I will be missing Shimon, yet Shimon will always be around.

Elena Vinogradov

When I was accepted to the PhD program at the Weizmann Institute I was elated and somewhat surprised. I was not sure what I would study, but I was quite sure it would not be NMR. In fact, during the admission interview I was asked about NMR and I told them, honestly: "I don't know much about it, I am not interested in it and I prefer not to answer any questions about it". Despite my *hutzpah*, I was accepted. And then, I had to take a quantum mechanics course. And I was privileged to meet the best teacher I had ever met and one of the best people I was fortunate to encounter. Shimon's approach to teaching stunned me. He rarely gave a straight answer. He was always asking what we thought. He was actually making sure that we understood. He was always saying that he does not know/remember or only recently understood the answer. It was always "answering a question with a question", but taken to unbelievable levels of scientific curiosity. I was hooked on the discussion. On the opportunity to think. I thought to myself that it would be interesting to do a rotation in his lab. The rest "is history".

My first project was under the supervision of him and Professor Zeev Luz (another giant of NMR). The project failed, but the remnants of the simulation code came useful in the next steps. I was lucky to join Madhu and work on the PMLG experiment. The most challenging and rewarding part was the derivation of the bimodal Floquet theory and its application to describe the combined effects of MAS and periodic RF. We spent countless hours going over the equations, of course with me trying mostly to catch up with what Shimon had already understood. Many times Shimon would come in the morning and say something like "I was thinking about it…" which would start derivations and discussions that ensued for several days. The whiteboard would be covered with formulas, and signs of "do not erase" would be written. Floquet theory described all the experiments beautifully. Not only were we able to explain experimental observations (broadenings at specific spinning frequencies) but also to predict experimental

features, such as the position of the rotary lines. Moving on to less steps and expanding to a windowed version, the scaling factors, the deterioration of efficiency, everything was explained there, by the Floquet theory. To have a theory that correctly predicts experimental outcomes and to be able to confirm it by doing the actual experiment is exactly what science is about.

Shimon was always respectful of others. He was humble and always knew something wise to say (or not to say) in challenging situations. I left solid state NMR and moved to imaging. During all the years after my PhD I would call Shimon often to talk about science and life. He was always interested, even in the projects that had little to do with his own research. When DNP reached *in vivo* imaging we had several interesting discussions about its applications and the future of the technology. After these conversations I always felt enlightened and optimistic about science and life in general.

Without Shimon, the world is darker. Shimon, you are greatly missed.

Yona Siderer

I met Professor Shimon Vega during my doctorate studies at the Weizmann Institute of Science in Rehovot. I was running experiments using an electron spin resonance (ESR) machine under the guidance of Prof. Zeev Luz and Prof. Shmuel Malkin, attempting to understand the mechanism of oxygen evolution in plants.

Many years have passed. In recent years, Shimon helped me a lot translating titles and texts of old scientific books in Dutch. Those books were cited as the sources of books from which Japanese scholars learnt chemistry in the years 1820–1850 and later. There were original books in Dutch and books that were translated into Dutch from European languages – French, English, Swedish, Latin and others. The Dutch language of the end of the 18th century was different from the one of today and sometimes Shimon had difficulty in translating a certain word, saying that it was actually taken from German, but he made efforts to find the best translation of the text.

The spelling of words and names in Dutch also sometimes changed. Shimon found on the internet the cover pages of two different books by the same author, where the spelling of the author's name had changed. This information helped me to refute the claim of a referee, and I could justify my claim that the spelling I wrote was the correct one. I included Shimon Vega's name in the acknowledgements to my article published that year (2021).

When there was a map of the Far East in Latin that I was curious about, Shimon asked one of his students from another country to help in the translation. These are small memories telling a little about Shimon's supportive and friendly personality.

I was well aware of the professional appreciation of Shimon, but beyond the scientific conversation, his good heart and his personal and friendly relations encouraged me to get his assistance. He was also a perfect host. Sometimes I arrived at his office in the afternoon from the nearby library or San-Martin restaurant. Upon my request, Shimon served me coffee in his office or, even, when there was a shortage, went to the students' office in order to get more coffee.

And then he fell sick, his illness lasted many months, we hoped for his recovery, but to no avail. I shall miss him very much.

On January 18, 2022, at MIT, an online tribute symposium "Remembering Shimon Vega" was organized by his long-time friends and colleagues Robert Griffin, Kong Ooi Tan, Daniella Goldfarb and Lucio Frydman. This seminar is available online [5].

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Interview with Prof. Leeor Kronik – recipient of the 2021 ICS outstanding scientist prize

Arlene D. Wilson-Gordon
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Q: Where were you born and where did your parents come from?

A: I was born in Rehovoth. My mother was also born in Rehovoth. Having worked at the Weizmann Institute of Science for a long time, I guess I didn't stray very far… My father was born in Vilnius, Lithuania. His family fled their home when he was a toddler, as the German Army was advancing towards the city. Ultimately he made Aliyah to Israel, on his own, when he was 18.

Q: What and who inspired you to study chemistry?

A: Frankly, I didn't enjoy high school chemistry. I felt that I didn't really understand it. Yes, I could memorize some seemingly arbitrary rules and solve homework problems accordingly. But I couldn't see the logic behind it. In particular I couldn't see the emergence of a complete picture from a small set of axioms, as in math, or from a few postulates, as in physics. In an odd way, that inspired me, because I thought that there has to be more to chemistry and that one day I'll return to it. And I did, but only after a PhD thesis on optoelectronic properties of semiconductors, with Prof. Yoram Shapira at Tel Aviv University. This led me to take a life-long interest in how all properties of matter emerge from the constituent atomic species and their organization in space, which I started pursuing actively as a post-doc with Prof. Jim Chelikowsky at the University of Minnesota. By that time, I had a thorough education in quantum mechanics, which turned out to be the fundamental basis of chemistry that I was missing, and so the road back to chemistry was clear.

Q: Why did you choose your particular field of chemistry?

A: In light of the above, it is no surprise that my field is theoretical and computational chemistry, specifically first principles calculations based mostly on density functional theory. Such calculations allow the prediction of properties of matter based solely on the periodic table and the rules of quantum mechanics, which is what I was looking for all along.

Q: Do you enjoy teaching and interacting with students?

A: Very much so. In fact I was a teacher (I taught mathematics in an evening school and physics in a high school) even before

Arlene Wilson-Gordon was born in Glasgow, Scotland. She completed her BSc (Hons) at Glasgow University and her DPhil at Oxford University under the supervision of Peter Atkins. After a postdoc at the Hebrew University with Raphy Levine, she joined the faculty at the Department of Chemistry, Bar-Ilan University, where she rose to the rank of Professor and in 2015, Professor Emerita. Her research interests lie in the field of theoretical quantum and nonlinear optics. She is the editor of the Israel Chemist and Engineer, an online magazine for all who are interested in chemistry and chemical engineering.

I was a researcher. I still enjoy teaching. And I take great pride in former students who went on to have successful careers of their own in academia or in industry.

Q: What do you consider to be your greatest scientific achievement, so far?

A: My research involves both the development of the theory and its application to problems of interest. On the methodology front, I would say that a significant achievement is my part in the development of methods for accurate prediction of electron and optical spectroscopies from density functional theory, some of which have found wide use. On the applications front, I would say that a significant achievement is a set of true predictions (i.e., made before or in the absence of experiment) of the structure of molecular crystals, and of surprising mechanical, electrical, optical, and even magnetic properties thereof, including the identification of novel mechanisms.

Q: What problems would you like to tackle in the near and far future?

A: On the methodology side, I would like to tackle some of the major computational bottlenecks we face. On the applications side, I would like to expand our efforts in the area of materials for energy and sustainability.

Q: What do you consider to be your greatest contribution to Israeli society?

A: As the third generation to participate in this novel and wondrous project called the State of Israel, my greatest contribution is simply to be a part of this project, and to have my family, my home, and the center of my life in it.

Q: Would you recommend a career in academia to young scientists?

A: Absolutely! An academic career is not for everyone, but if you "caught the bug" of research, namely asking important scientific questions and working tirelessly towards finding at least some answers, an academic career can make a real difference and be very rewarding.

Q: What are the main challenges facing Israeli science?

A: There are many challenges that both Israeli and international science face. Let me mention just one. Much of what we do is supported by the public and depends on earning and maintaining the public's trust and respect. To that end, we need to do a better job at communicating scientific ideas and achievements, including their societal importance and relevance, to the general public, as part of an ongoing dialogue. We should do that without condescension and in a language that is accessible to all, or at least most, people.

Q: If you had a magic wand, what would you change a) in academic life, b) in Israeli society?

A: In Israeli Academia, if I had a magic wand I would mandate a short ethics workshop. In a world of increasing inter-personal collaboration and computer-based experiments and analysis, it is an absolute must to understand what we can and cannot do while engaging in scientific research. This goes for both how we treat data and how we treat each other. Specifically, obviously everybody should be very clear as to glowing-red lines that should not be crossed in data acquisition and manipulation. But in a modern research environment of joint publications, patents, etc., both faculty and students need to be clearly informed as to ethics of joint research.

In Israeli society, I would like to see a stronger fact-based dialogue where we are regularly exposed to, and respect, meaningful points of view that are different from our own.

Q: Do you have any advice for young people embarking on their career?

A: Follow your curiosity, speak your truth, and never compromise your values.

Q: How do you enjoy your free time?

A: Obviously spending time with my family! I also practice Shotokan Karate on a regular basis. I'm a proud member of the Israel Association of Baseball and of "Club 5" – Israel's Classic & Collectors Vehicle Club.

Agency, advocacy, and attention: A tale of encouraging women into careers in the chemical sciences

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Abstract:

The continued and persistent gender gap in the chemical sciences, in which more men than women choose to study chemistry, continue to advanced degrees in chemistry, and ultimately pursue careers in chemistry, is a deeply concerning phenomenon that has the potential to negatively impact scientific progress due to a lack of diversity among scientists. In this article, I summarize the talk that I gave at the national meeting of the American Chemical Society in March 2022 in honor of my receiving the Camille and Henry Dreyfus Award for Encouraging Women into Careers in the Chemical Sciences. This talk focuses briefly on the problem of the gender gap, and much more extensively on ways in which we can address that gender gap and continue to make progress in enhancing diversity.

Introduction

This article is adapted from a talk that I gave at the national meeting of the American Chemical Society, in a symposium celebrating my receiving the Camille and Henry Dreyfus Award for Encouraging Women into Careers in the Chemical Sciences.

One thing that is clear when we talk about women in the chemical sciences, is the fact that despite a significant amount of effort and attention towards addressing issues of gender disparity in the chemical sciences, significant gaps in the percentage of men and women in the chemical sciences still exist. A report published by Linda Wang in *Chemical and Engineering News* in 2016 indicated that although some gains had been made in the percentages of female faculty, particularly in top chemistry departments, the overall percentage of women at all levels of academia remained disappointingly low (percentage of women by rank: 26% of assistant professors; 30% of associate professors; 14% of full professors). At the current rate of improvement, researchers estimate that it will take an additional 136 years to close the gender gap in the chemical sciences.

Associate Professor **Mindy Levine** joined the Department of Chemical Sciences at Ariel University in the Fall of 2019. Prior to that, she was a faculty member at the University of Rhode Island from 2010–2019, first as an Assistant and then as an Associate Professor. Mindy's research focuses on the development of novel, practical chemical sensors, using fluorescence and/or colorimetric changes, with a particular focus on the use of supramolecular, cyclodextrin-based chemistry. Mindy is also a passionate advocate for the promotion of women and girls in science, and was the recipient of the American Chemical Society's National Award for the Encouragement of Women into Careers in the Chemical Sciences. She recently ran Chemistry Camp for Girls in Israel, for 33 girls in grades 5 and 6, and continues to run high-quality programing for girls and young women to support their continued interest in chemistry.

This situation of a lack of women in the chemical sciences tracks with my own experiences, where although I had a significant number of female colleagues at the high school and undergraduate levels (including attending an all-female high school), that number started to drop in graduate school at Columbia University, during my postdoctoral fellowship at MIT, and in my first faculty position as an assistant professor at the University of Rhode Island.

There are several questions we can have around this topic, including what factors cause or at least contribute to this gender gap, but I want to focus more on what we can do about that gap. This question can be broken into two parts, as we can ask both, "What can we do on an institutional level?" and "What can we do as individuals?" that will contribute to addressing this issue.

Before we move to answering those questions, though, I want to clarify that the lack of gender diversity in the chemical sciences is not a "feminist" or "women's" niche issue. It is an issue that affects every person who is invested in successful scientific outcomes, which should be the entire population. This is true because having more diverse scientists means that more, better, and faster progress is highly likely; as the research has shown, increased diversity across all axes and in all disciplines leads to enhanced productivity and to a markedly improved work product. The issue of gender disparity in the chemical sciences is something that should interest all of us, even though my oldest son, who was 10 years old at the time, told me that, "Really you are the only one who cares about these kinds of women's issues. That's because you are a woman. This will not be of interest to anyone else."

I want to also be clear that for as much as there is a significant issue of a persistent gender gap in the chemical sciences between men and women, that gap is even more pronounced for other gender minorities, and is also more acute for women who also identify as members of other minority groups, and that the challenges and opportunities for both of those populations are worthy of their own, dedicated talk.

Agency

Coming back to the question of what we can do about the gender gap between men and women, let us focus on what we can do as individuals, using the guiding idea of "agency." Using "agency," defined as "the capacity, condition, or state of acting or of exerting power," as the guiding principle means believing that I as an individual have the power to change a situation, and to exert control over a situation, rather than thinking that the situation exerts control over me.

Under this guiding principle, I have been privileged to be able to lead chemistry camp for middle school girls, initially funded by the Dreyfus Foundation through a Special Grant Program in the Chemical Sciences. Starting in 2013, I led a week-long, full-time, free program for girls in grades 6–8, which provided immersive science experiences, interactions with female scientists, and a positive, supportive environment for girls to experience, experiment, and enjoy science. This program had broad success, received significant media attention, and was able to impact approximately 280 girls (40 girls/year over 7 years). Key results of this program were published in the *Journal of Chemical Education*, and highlights include the moment when a previous participant of the camp returned to act as a mentor for the students. That previous student, who had participated in the program when she was in 7th grade, returned as an undergraduate student studying biology at the University of Rhode Island. When asked why she decided to study science as an undergraduate, she explained that her participation in chemistry camp was the first time she understood that science could be fun, and that the scientific community could be a home for her.

In July 2022, I was thrilled to be able to bring chemistry camp to Israel, again through funding provided by the Dreyfus Foundation, and ran Chemistry Camp for Girls in Israel for 33 girls who had finished grades 5 and 6. I am looking forward to continuing the tradition of Chemistry Camp for Girls, now in its new location.

Other examples of agency, or situations in which I was able to directly impact the situation of gender disparity in the chemical sciences, include Sugar Science Day. This program, built entirely around the chemistry of sugar, was run for high school girls as an integrated outreach component of my funded NSF CAREER grant. Moreover, I also facilitated paid internships for high school girls, in which the participants were selected from the population of those who participated in Sugar Science Day, as well as ACS Project SEED, which provided economically disadvantaged high school students, particularly females, with paid scientific internships. Many of these students co-authored scientific papers based on their work in the lab, attended conferences, and presented the results of their work. A significant fraction of these students went on to study science in college, and to focus on scientific or medical fields for their chosen careers.

This kind of outreach to students at the high school level occurred concurrently with a strong culture of female mentorship in the laboratory, focused particularly on two outstanding former PhD students in my laboratory, Dr. Nicole Serio and Dr. Dana DiScenza, as well as a large number of female undergraduate students.

I am thrilled to be able to continue my efforts to mentor and encourage female students even after my move to Israel in August 2019, including through my participation in the Alpha program for high school girls, as a mentor of undergraduate students in the research laboratory, and as a mentor of a team of undergraduate entrepreneurship students. The entrepreneurship students recently won first prize in a student competition for their ideas focused on the development of a sensor for date rape drugs. I am also thrilled that I have been able to open a new nonprofit organization, WonderLab Israel, where much of my efforts towards educating girls in science will be able to be centralized, formalized, and optimized.

Advocacy

This agency, and work done using "agency" as a guiding principle, has been done concurrently with my work on advocacy, focusing on advocating for the needs of female scientists in a way that will help address the continued gender disparity. In one example, I was part of a group of faculty and staff members who established the Professional Family Travel Fund at the University of Rhode Island, a fund designed to support faculty members in meeting their caregiving and professional responsibilities while traveling. This fund, which was used almost exclusively by female assistant professors, provided supplementary money for these faculty members to travel with an infant and a caregiver for that infant or to provide assistance for an aging parent while the faculty member was traveling.

Attention

A third principle, "attention," refers to the ability to draw attention to injustices, inequity, and unfair situations, particularly by those who have power to highlight injustices against those who lack that power. In one example, I was able to highlight the overwhelmingly male contingent of special delegations that have been brought to meetings of the Israel Chemical Society. In one outcome of this attention, I led a discussion around such gender inequities in the first ever "Power Hour" type discussion at the 2022 Israel Chemical Society Meeting, in September 2022.

Ambition

The fourth "A" that I want to discuss, "ambition," is a little difficult to discuss, because I would like to encourage women to push themselves a little more, to say "yes" when they can, even when it is difficult and even if it comes at a significant expense. When I asked the organizers of an ICS meeting how they ended up with an all-male delegation, they informed that they had asked many women to be part of the delegation, but none of them had said yes. There are many possible "next steps," including asking more women, and addressing issues that make it hard for women to say "yes," but it can also include encouraging women to try to say "yes" a little more often, and to push themselves outside of their comfort zone.

What does it mean to push outside of our comfort zone? I can take a lesson from the times that I take my children bungee jumping, or rock climbing, or rappelling, with a fabulous tour guide who has now been with our family several times. This tour guide, Ariel, tells us very clearly that is OK to be afraid in certain situations, it is normal to be afraid, but that we can do things even when we are afraid. Even more so, every time we do something even though we are afraid, it becomes a little bit easier to do something similar the next time. We can remember that we are able to do hard things, to do things that make us nervous, and to be successful in doing so, and then we can train ourselves to push even a little bit more.

Women can do that in their professional roles too, just as my kids and I can do when we go bungee jumping. We can, and we should, and we will. When we do, we will all benefit.

Conclusion

With tremendous gratitude to my parents, Dr. Jerry and Syma Levine, my three mild-mannered, well-behaved boys, my former research group at the University of Rhode Island, my current research group at Ariel University, and all of my colleagues, both past and present – you have all been invaluable in enabling me to be as successful as I have been. Let's keep making everything possible.

The 86th Annual Meeting of the Israel Chemical Society: September 12–13, 2022, David Intercontinental Hotel, Tel Aviv, Israel

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Introduction

The Annual Meeting of the Israel Chemical Society (ICS) has a long history since its establishment in 1933 and is a well-known event in the scientific landscape of the State of Israel. These colorful gatherings of Israeli chemists usually occur in mid-February, which is the inter-semester break for all Israeli universities. Unfortunately, the Meeting of 2021 fell victim to the global Covid-19 pandemic, forcing a gap of 2.5 years between the 85th Meeting of February 2020 and the 86th Meeting in September 2022.

Following ICS tradition, the chemistry departments of the six major research universities share responsibility for organizing these meetings in a six-year cycle in a constant order: the Hebrew University of Jerusalem, Technion, Tel Aviv University, Bar-Ilan University, Ben-Gurion University of the Negev, and the Weizmann Institute of Science. Thus, looking back at the ICS history of the past two decades, the Technion has taken responsibility for organizing the 68th Meeting (2003), the 74th Meeting (2009), the 80th Meeting (2015), and the 86th Meeting (2022).

Another unique tradition the ICS has followed for more than 25 years is hosting high-profile delegations of distinguished scientists from top academic institutions worldwide to deliver plenary and keynote lectures. This tradition has created outstanding opportunities for many Israeli scientists, particularly graduate students, to interact with world-renowned chemists, thus enhancing the prospects of networking and scientific collaboration. Unfortunately, the large delegation of 10 scientists and 20 graduate students from the Chinese Academy of Sciences and the University of Peking could not participate due to the "zero-Covid policy" of the Chinese authorities and restrictions on international travel.

Nevertheless, it provided an opportunity for a happy gathering of many students and scientists from around Israel, after 2.5 years of restrictions on public meetings, even in the absence of a foreign delegation. Over 600 participants enjoyed a diverse scientific program that included two plenary lectures. The 18 parallel sessions included 18 keynote lectures, 63 invited lectures, and 31 flash talks. The 240 posters were equally distributed between two poster sessions, and four were selected to receive the best poster prizes, announced at the closing ceremony.

The ten sessions of the first day included Organic and Inorganic Chemistry (organized by Sergey Semenov of the Weizmann Institute), Chemical Biology and Biochemistry (organized by Muhammad Jbara of Tel Aviv University), Materials and Devices (organized by Adi Salomon of Bar-Ilan University, Spectroscopy (organized by Aharon Blank of the Technion), Chemical Education (organized by Sharona T. Levy of Haifa University), Organic and Inorganic Chemistry (organized by Graham de Ruiter of the Technion), Chemical Biology and Biochemistry (organized by Noam Adir of the Technion), Industrial and Analytical Chemistry (organized by Amir Mizrahi of the NRCN), Theoretical Chemistry (organized by Uri Peskin), and Energy (organized by Malachi Noked of Bar-Ilan University).

The eight sessions of the second day included Organic Catalysis (organized by Mark Gandelman of the Technion), Polymer & Supramolecular Chemistry (organized by Gabriel Lemcoff of the Ben-Gurion University), Nanochemistry (organized by Lilac Amirav of the Technion), Agricultural and Food Chemistry (organized by Guy Mechrez of the Volcani Institute), Bioorganic Chemistry (organized by Amnon Bar-Shir of the Weizmann Institute), Polymer and Supramolecular Chemistry (organized by Michael Silverstein of the Technion), Electrochemistry (organized by David Eisenberg of the Technion), and Soft Matter and Biophysics (organized by Bat-El Pinchasik of Tel Aviv University.

In addition to the scientific program, the ICS held its traditional General Assembly on the afternoon of the first day,

discussing the past year's activities, plans for the next year, and financial issues. Mr. Shimon Nizrad, the ICS Accountant, provided an overview of the ICS's budget, legal status, and financial goals. A Gender Equality Power-Hour took place on the second day, chaired by Mindy Levine of Ariel University. The prize ceremony, which took place on the evening of the first day, was preceded by a reception and light dinner for all participants.

The event attracted many sponsors, including the Weizmann Institute of Science, Tel Aviv University, Bar-Ilan University, Ben-Gurion University of the Negev, the Hebrew University of Jerusalem, Ariel University, and the Technion.

The experienced team of Diesenhaus-Unitours Incoming Tourism Ltd., staffed by Orit Gilad, Anat Reshef, Tsipi Laxer, and Magali Mizrahi, took responsibility for the actual operation, including all technical aspects, administration, organization of the exhibition, promotion, etc.

The meeting included a commercial exhibition by 17 providers of lab equipment, scientific instrumentation, chemicals, materials, analytical chemistry services, publishing houses, and intellectual property management. Exhibitors included Arad-Ophir Information Specialists Ltd., Bargal Analytical Instruments Ltd., BioAnalytics Ltd., Bruker Scientific Israel Ltd., Holland Moran Ltd., Meshulam Avni & Son Ltd., ILPEN Scientific Equipment & Supplies Ltd., JEOL (UK) Ltd., Labotal Scientific Equipment Ltd., LabSuit Projects Ltd., Mark Technologies Ltd., Mercury Ltd., Dr. Golik Scientific Solutions Ltd., New Technology S.K. Ltd., Rhenium Ltd., Spectro Israel Ltd., and Tzamal D-Chem Laboratories Ltd.

This mix of excellent lectures, colorful poster sessions, exhibitions, and other activities created a vivid atmosphere with vibrant discussions, exchange of information, and social gathering, all reflected by the collage of photographs (Figure 1).

Opening Ceremony

Prof. Saar Rahav, co-chairperson of the organizing committee, opened the meeting and greeted the guests and participants: "Good morning, everyone. On behalf of the other co-chairman Prof. Charles Diesendruck and the organizing committee, I am delighted to welcome you to the 86th meeting of the Israel Chemical Society in Tel Aviv.

It has been a while since the previous meeting. The covid pandemic caused many upheavals. We all remember the lockdowns and their effect on our personal lives and our ability to teach and work on our research. Our academic community showed remarkable resilience in dealing with the changing conditions and found ways to continue our scientific work and adjust to teach remotely. Arguably, the aspect that affected the most was our ability to meet in workshops and conferences. Thankfully, things are much improved now.

The pandemic has affected our ICS meeting as well. We were forced to postpone the meeting, and just when things seemed normal again, a new wave meant we had to postpone it again. Even now, when almost all restrictions are removed, it still affects us. The international delegation we lined up could not come since China still has stringent covid regulations and is practically isolated from the rest of the world.

Despite the difficulties, it is crucially important that we continue our longstanding tradition of ICS meetings. This celebration of Israeli chemistry is a unique opportunity to share our enthusiasm for science and to recognize excellence in research, teaching, and other aspects of academic life. I thank many colleagues who showed flexibility in dealing with the forced changes, in particular the ones who were called to contribute on short notice due to the changing dates of the meeting.

I am delighted to see so many graduate students in the crowd. This meeting allows you to explain your research to other scientists and expose you to different aspects of chemistry. Those who have not experienced hearing a talk detailing some attractive solution to a scientific problem said to themselves, this idea is simply brilliant; I wish I had thought about that. Such gems of science inspire us to keep asking difficult and important questions. And who knows, perhaps a new idea you encounter today will be relevant to your research tomorrow. I therefore warmly encourage you to use this occasion to get to know your colleagues and their work. You may discover new ideas that will inspire your love of science, or you may meet someone to collaborate with in the future.

This meeting could not have happened without the generous support from the seven major Israeli universities and research institutions. We are grateful for their help. I wish you all an illuminating, productive, and inspiring meeting."

Prof. Ehud Keinan, president of the ICS, added his greetings: "Good morning everybody, and welcome to the 86th Meeting of the ICS. First, I would like to thank all the people who made it possible, chairpersons Charles Diesendruck and Saar Rahav and their colleagues from the Technion, including members of the organizing committee and session organizers. Many others deserve our thanks, including all the sponsors, the Diesenhaus-Unitours team, and administrative manager Tali Lidor for taking care of all the small details.

Figure 1. Collage of random photos that reflect the general atmosphere of the 85th ICS Meeting. Photographs by Allon Zaslansky.

It's a pleasure to open this Meeting after a gap of two and a half years. We postponed this Meeting more than once and even considered waiting for another year until February 2023. It is typical for the Israeli community that no matter what the circumstances are, we keep going and continue our annual meetings as usual. As we all know, nothing is standard in Israel, but the past two years have been very unusual in Israel and worldwide. The ICS was established in 1933, and we'll celebrate our 90th anniversary next year. Holding now the 86th Meeting means that the Israeli community of chemists met uninterrupted almost every year over the past nine decades. And we had many reasons to postpone these meetings, including World War II, Israel's War of Independence, and many other upheavals. Thus, skipping the 2021 meeting due to Covid-19 was a rare historical event. We were fortunate to hold the 85th ICS meeting in mid-February 2020 with the Yale delegation, just two weeks before hell broke loose and Covid-19 changed all human activities worldwide.

Although we lost the opportunity to host the Chinese delegation of 30 scientists from China, I'm happy to see the many enthusiastic young people eager to resume the Annual Meeting and meet friends and colleagues from around the country.

I take this opportunity to announce the general plans for the 87th Meeting. The ICS managing Board has decided to hold it on the first week of July, immediately after the end of the academic year, to maximize the number of participants. W will host a large delegation from Denmark, including 10 professors and 20 graduate students from the University of Copenhagen, the Technical University of Denmark, and Aarhus University.

The Meeting will be part of a more significant event named Chemistry Congress, ChemCon 2023, planned for July 3–5, 2023, at the International Convention Center, Jerusalem. We join forces with the Haaretz/TheMarker Group to organize these events because the two organizations share complementary expertise and experience. The Haaretz Group, which is 103 years old, and a bit older than the ICS, will allocate its international content marketing tools to maximize the ChemCon2023 exposure. In contrast, the ICS will ensure a relevant, packed, and well-diversified scientific program.

The ChemCon2023 will include three major components to create synergism and generate high interest among chemists, chemical engineers, businesspeople, government agencies, and the public: A one-day symposium on "The Good Carbon" opportunities, the two-day ICS 87th Annual Meeting, and an unprecedentedly large, three-day international chemistry exhibition.

The "Good Carbon" Symposium will focus on using compounds of a single carbon atom, such as natural gas and carbon dioxide emissions, as feedstock for the chemical industry. The symposium will highlight the methanol-based economy, methanol-to-olefins (MTO) processes, synthetic fuels, novel fuel cells, and clean energy. These topics will create high interest for businesspeople, venture capitalists, government ministries, startup entrepreneurs, chemical industry leaders, and the public.

The ChemCon Exhibition will provide direct access to global chemical research, development, and manufacturing. All aspects of chemistry, including research tools and infrastructure, analytical methods and instrumentation, energy, synthetic fuels, environmental sciences, green energy, nanotechnology, materials science, food science, agriculture, pharmaceuticals, bio-analytics, quantitative measurement of biological molecules, industry and manufacturing, process control, quality assurance and quality control of manufactured products, industrial processes, intellectual property, venture capital companies, and more.

The ChemCon2023 will create synergism between the academic, business, and government communities, generating high interest among chemists, chemical engineers, businesspeople, government agencies, and the public in chemistry opportunities. Take advantage of the opportunity to attend the event.

Thanks again for participating in the 86th ICS Meeting; I wish you an enjoyable, highly fruitful experience!"

Plenary lectures

Leeor Kronik of the Weizmann Institute of Science, the ICS Prize of Excellence winner, lectured on "Predicting materials properties from first principles: A density functional theory journey." He provided some perspectives from his journeys in predicting materials properties from first principles, based on density functional theory. On the one hand, he emphasized the ongoing dialogue between theory and a diverse set of experiments, covering the range of chemical, mechanical, electrical, optical, magnetic, and more. On the other hand, he surveyed highlights from work on developments within density functional theory, especially on orbital-dependent functionals, which have been indispensable to gaining true predictive power.

Stephen Weiner and **Lia Addadi** of the Weizmann Institute of Science, winners of the ICS Gold Medal, lectured jointly on "Biomineralization is chemistry and biology with a history."

They explained that biomineralization is widespread and involves many disciplines in chemistry, biology, materials sciences, optics, environmental and historical sciences. The evolution of mineralized products is well-documented in the fossil record because they are relatively well preserved. Hence, this field has a rich history. Organisms deposit a wide range of organic and inorganic compounds to fulfill disparate functions from defense to structural support, from camouflage to vision. Depending on the functions and the evolutionary pathways, the final phase of the deposited solids may be crystalline or stable amorphous. The basic processes in biomineralization involve the uptake, transport, and deposition of ions in a solid state or concentration of endogenously produced molecules.

In many cases, organisms form a disordered transient phase that subsequently crystallizes. Most of the utilized compounds are sparingly soluble in both extra- and intracellular environments, raising the question of how cells transport and concentrate vast amounts of the materials without compromising their metabolism. Steve and Lia focused on two main subjects. The first addressed ion pathways in biomineralization, with a perspective on the uptake, transport, and deposition of calcium, carbonate, and phosphate. The second was on the structure and function of organic crystals that produce structural colors, are critical components in visual systems, or may be involved in enhancing photosynthesis. They pointed out that biomineralization is an inherently interdisciplinary field that presents many fascinating research questions. This field is essential for understanding challenging questions relevant to diverse disciplines, some of which relate to the many threats our planet is now experiencing.

Keynote lectures

Gonen Ashkenasy of Ben-Gurion University lectured on "Emergence of function in primitive chemical systems out-of-equilibrium."

Micha Fridman of Tel Aviv University spoke about "Guiding antifungal drugs to their target-harboring organelle: Stretching drug delivery to a higher level of resolution."

Moshe Kol of Tel Aviv University lectured on "Poly(lactic acid): New catalysts, materials and processes."

Yaron Paz of the Technion lectured on "Transient FTIR spectroscopy as a tool for studying photocatalytic materials."

Shirly Avargil of the Technion lectured on "Assessing students in a chemistry-based escape room – why and how?"

Roman Dobrovetsky of Tel Aviv University, winner of the ICS Young Investigator Award, lectured on "P with a touch of B."

Amnon Bar-Shir of the Weizmann Institute, winner of the ICS Young Investigator Award, lectured on "Molecular and cellular imaging with MRI: Probes design and applications."

Francesco Ferella of INFN and University of L'Aquila, Italy, spoke about "Performing matrix extraction and characterization of copper cables for LEGEND experiment by high-resolution inductively coupled plasma mass spectrometry."

Gershon Kurizki of the Weizmann Institute of Science spoke about "From open-system to closed-system quantum thermodynamics: Coherent heatronics."

Emanuel Peled of Tel Aviv University, lectured on "High-energy lithium metal batteries."

Ilan Marek of the Technion lectured on "Nucleophilic substitution at quaternary carbon stereocenters."

Yossi Weizmann of the Ben-Gurion University lectured on "Diverse self-assembly structures from nucleic acids and nanoparticles for biological and plasmonic applications."

Efrat Lifshitz of the Technion lectured on "Local and global magnetism in semiconductor nanostructures."

Meital Reches of The Hebrew University spoke about "Biodegradable coatings that resist bacteria, viruses, and fungi."

Assaf Friedler of The Hebrew University spoke about "Peptide inhibitors of protein–protein interactions."

Gabriel Lemcoff of the Ben-Gurion University lectured on "A personal perspective on ring-opening metathesis polymerization."

Michal Leskes of the Weizmann Institute spoke about "Elucidating the structure and function of the electrode-electrolyte interface by new solid state NMR approaches."

Lihi Adler-Abramovich of Tel Aviv University lectured on "Designing new bioinspired 3D nanostructure for biological applications."

The ICS Awards Ceremony

Following ICS tradition, all prizes were awarded at the special ceremony, which took place on September 12 after the open reception. All prize winners signed the traditional ICS poster, Figure 2.

Figure 2. The traditional ICS poster autographed by all 22 prize winners.

The 2021 ICS Prize for an Excellent Graduate Student was awarded to seven excellent students in alphabetical order by the ICS president and a representative of the relevant university:

Ran Attias of Bar-Ilan University carries out his PhD work under Prof. Doron Aurbach. He received his BSc in biotechnology engineering in 2015 from Ben-Gurion University and his MSc in chemistry in 2017 from Bar-Ilan University. His work focuses on interfacial phenomena related to charge-transfer processes on the electrode-electrolyte solution interface during the intercalation process of magnesium ions into metal-oxide and metal-sulfide cathodes. Ran published over 20 research papers, 10 of them as the primary author.

Subhash Garhwal of the Technion received his BSc (Hons) in chemistry (2015) from the University of Delhi and MSc in organic chemistry from the Indian Institute of Science Education and Research, Bhopal (2018) with Dr. Joyanta Choudhury. His PhD work at the Technion with Dr. Graham de Ruiter focuses on the design and synthesis of PCNHCP pincer complexes with first-row transition metals, such as iron and cobalt, to catalyze organic transformations, including hydrogen isotope exchange, alkene isomerization, alkyne hydrofunctionalization, and selective C-H activation of aryl ketones, esters, and amides.

Qais Jaber of Tel-Aviv University carries out his chemical biology research under Prof. Micha Fridman's supervision. He obtained his BSc (2016) and MSc (2018) in Chemistry from Tel-Aviv University with high distinction. His research focuses on developing new antifungal agents and novel molecular tools, such as live-cell fluorescent imaging as probes for deciphering the mode of action of fungal pathogens. He published his results in Angewandte Chemie, ACS Chemical Biology, European Journal of Medicinal Chemistry, ACS Central Science, ChemBioChem, and Genetics.

Efrat Shukrun-Farrell of the Hebrew University works under Prof. Shlomo Magdassi, focused on forming new photopolymerizable pre-ceramic compositions for 3D printing of hybrid and ceramic objects with high geometrical complexity and unique properties. She produced new materials for making organic-silica objects with high silica content at centimeters to micron scale, the first photochemical preparation of low-density ceramic aerogels, and the first 3D printing of ordered-mesoporous silica monoliths.

Ebaston Thankarajan of Ariel University has recently completed his PhD under Professors Gary Gellerman and Leonid Patsenker. He has developed a series of fluorescently monitored targeted drug delivery systems, and activatable photosensitizers for photodynamic therapy of cancer and antimicrobial photodynamic therapy. The ISF supported this work. He continues this line and a new project funded by NOFAR, developing fluorescence-based tools for detecting and identifying pathogenic bacteria.

Ilia Tutunnikov of the Weizmann Institute received his BSc in Chemistry from Tel Aviv University in 2016 and then started his direct track PhD, supervised by Professors Ilya Averbukh and Yehiam Prior. His experimental work focuses on laser control of chiral molecules and echoes in single quantum systems. His theoretical work has led to the first experimental demonstration of the laser-controlled enantioselective orientation in a gaseous medium. He investigated the echo phenomenon in single vibrationally excited molecules and several other single quantum systems. The enantioselective orientation may pave the way to novel analytical and separation techniques. Ilia received the John F. Kennedy Award of the Weizmann Institute for his outstanding PhD research.

Jonathan Tzadikov of the Ben-Gurion University obtained all his degrees from Ben Gurion University, BSc (2016), MSc (2018 cum laude), and PhD under Prof. Menny Shalom. He inserts heteroatoms into carbon networks to fine-tune their electronic, optical, electrochemical, and chemical reactivities. His unprecedented, scalable approach involves molten-state intermediate, using molten precursors, polycyclic aromatic hydrocarbons with various heteroatoms, such as elemental sulfur or ammonia-borane complex. The new materials show promising performance towards electrochemical oxygen evolution reaction (OER), Na-ion, and Li-ion batteries.

The 2021 ICS-Uri Golik Prize for an Excellent Graduate Student was awarded to **Shahar Dery** of the Institute of Chemistry, the Hebrew University of Jerusalem, for elucidating structure-reactivity correlations at the single nanoparticle level, revealing reactivity patterns for oxidation and hydrogenation reactions. Shahar was born in Jerusalem in 1989. Upon completing his military service, he obtained his BSc (2014) and MSc (2016) from the Hebrew University under Prof. Norman Metanis, working on deselenization of selenocysteine. In 2016, he joined the lab of Prof. Elad Gross at the Hebrew University to study catalytic reactions on the nanoscale. His PhD research focuses on elucidating structure-reactivity correlations at the single nanoparticle level using IR nanospectroscopy. By combining specifically-designed model systems and high-spatial-resolution IR measurements, Shahar probed the surface of catalytic nanoparticles following oxidation and hydrogenation reactions. In doing so, invaluable chemical information was obtained, revealing two different reactivity patterns for oxidation and hydrogenation reactions. The fundamental insights gained from his studies may enable

the development of optimized heterogeneous catalysts for the chemical industry. His list of awards includes three Dean's awards for his bachelor's and master's studies and a faculty excellence scholarship for MSc students. Shahar received the Ministry of Energy Scholarship, the Rudin Scholarship, and the Azrieli Fellowship. He won the Prof. Rahamimoff Travel Award for young scientists of the BSF to conduct collaborative research in the lab of Prof. F. Dean Toste at UC Berkeley. He also received the HUJI NANO 2020 award for excellent PhD research. Shahar has published 20 research papers in high-profile journals.

Figure 3. Photos from the Award Ceremony of the 86th ICS Meeting. First row from left: Excellent Graduate Students award to Ran Attias of Bar-Ilan University (with David Zitoun and EK), Subhash Garhwal of the Technion (with Noam Adir and EK), Qais Jaber of Tel-Aviv University (with Moshe Kol and EK), Efrat Shukrun-Farrell of the Hebrew University (with Mattan Hurevich and EK). Second row: Ebaston

Thankarajan of Ariel University (with Alex Szpilman and EK), Ilia Tutunnikov of the Weizmann Institute (with Reshef Tenne and EK), and Jonathan Tzadikov of the Ben-Gurion University (with Menny Shalom and EK). The Golik Prize to Shahar Dery of the Hebrew University (in his absence to Efrat Shukrun-Farrell with Uri Golik, Eran Golik, and EK). Third row: the Tenne Prize to Menny Shalom (with Reshef Tenne and EK), the Adama Prize for Technological Innovation to Raz Jelinek of Ben-Gurion University (in his absence to Michael Meijler, Itsik Bar-Nahum, Chief Chemist of R&D at Adama and EK), the Amir Shahar Prize for Excellence in Administrative Management to Sarah Amzallag of the Weizmann Institute (with Dani Shahar, Reshef Tenne and EK), the Dalia Cheshnovsky Prize for Excellence in Chemistry Teaching to Edna Friedman of the Horev Ulpana in Jerusalem and the Tehilla-Evelina de Rothschild Secondary School (with Dani Shahar, Ori Cheshnovsky, Dorit Taitelbaum and EK), Fourth row: the Dalia Cheshnovsky Prize for Excellence in Chemistry Teaching to Orit Weinstock from the Har-Tuv high school (with Dani Shahar, Ori Cheshnovsky, Dorit Taitelbaum and EK), the Itan Peled Prize for Excellent Chemistry Project to Tahel Amzaleg from Ort Kramim, Karmiel (with Dorit Taitelbaum, Nehama Peled, Michael Peled, chemistry teacher Mirit Kramer, and EK), the Itan Peled Prize to Avishag Samara from the Gymnasia Realit, Rishon Lezion (with Dorit Taitelbaum, Nehama Peled, Michael Peled, and EK), the Green Chemical Industry Prize to OR Recycling Park awarded to Nadav Ziv (with Alex Szpilman and EK). Fifth row: the Honorable Member of the ICS to Shimon Shatzmiller of Ariel University (with Alex Szpilman and EK), the ICS Gold Medal to Lia Addadi and Steve Weiner of the Weizmann Institute, the ICS Prize of Excellence to Leeor Kronik of the Weizmann Institute. Sixth row: the ICS Excellent Young Scientist Prize to Amnon Bar-Shir of the Weizmann Institute, the ICS Excellent Young Scientist Prize to Roman Dobrovetsky of Tel Aviv University. Seventh row: the best poster awards. Photographs by Allon Zaslansky.

The 2021 Tenne Family Prize in memory of Lea Tenne for Nanoscale Sciences was awarded to **Prof. Menny Shalom** of the Ben-Gurion University of the Negev for developing synthetic methodologies of carbon nitride-like materials and using them for photoelectrochemical cells and other energy-related applications. Menny was born in 1979 in Tel Aviv, Israel. He received his BSc in Chemistry in 2007 from Bar-Ilan University, followed by MSc and PhD under Arie Zaban at the same University, researching quantum-dot sensitized solar cells. As a Minerva fellow for his postdoc, he then joined Prof. Markus Antonietti at the Max Planck Institute of Colloids and Interfaces (MPI), Germany. In 2013–2016 he was a group leader in MPI and, since the end of 2016, he has become an Associate Professor at the Ben-Gurion University of the Negev. His group synthesizes new materials for energy conversion applications, mainly photo-electrochemical cells and electrocatalysts. Menny's group has published more than 50 papers in excellent journals. His list of awards includes the Wolf Foundation Award for an Excellent MSc student (2009), Wolf Foundation Award for Excellent PhD students (2012), ICS prize for an Outstanding PhD student (2012), Israel Vacuum Society Award (2018), Toronto Prize for Excellence in Research (2018), ICS Excellent Young Scientist Prize (2020) and an ERC starting grant (2019).

Menny's research focuses on several fundamental and applied scientific topics ranging from new synthetic methodologies for 2D metal-free materials, sustainable solar-to-fuel conversion, and the development of new materials and concepts for clean fuel production, e.g., hydrogen, by using photo-electrochemical cells (PEC) and electrocatalysts. His group aims at understanding the structure-property relationships of novel materials. For instance, they rationally design synthetic processes, investigate reaction mechanisms. They study the properties of synthetic metal-free materials, which contain only carbon, nitrogen, phosphorus, sulfur, and boron (CNXs, X = P, S, or B). They employ these materials for photocatalytic and photo-electrochemical reactions. Alternatively, they use them for ceramics based on transition metals as electrocatalysts or co-catalysts in PECs.

Menny's research impacts renewable and sustainable energy production by studying the modes of action of photoactive materials and their behavior. Prof. Shalom's group has tackled the issue of manipulating the materials' final properties by the

rational selection of monomers, building blocks, solvents, reaction conditions, etc. His group has utilized polymeric carbon nitrides and their derivatives as photocatalysts and active material in photoanodes in photo-electrochemical cells. They have developed methods to manipulate the growth of carbon nitride layers on transparent conductive substrates by an intelligent design of the monomers, thus overcoming a crucial bottleneck in the area. They also overcame problems of insufficient light-harvesting, slow water oxidation kinetics, and instability of the photoactive layer. As a result, they achieved state-of-the-art carbon nitride-based PEC cells with efficient, long-term oxygen and hydrogen production.

The 2021 ICS-Adama Prize for Technological Innovation was awarded to **Prof. Raz Jelinek** of the Ben-Gurion University of the Negev for implementing conjugated chromatic polymers as color sensors, and for using carbon quantum dots and nanoscale gold assemblies for biological imaging, and electro-optic devices. Raz Jelinek was born in Beer Sheva, Israel (1964), obtained his BSc (summa cum laude, 1988) from the Hebrew University, and PhD (1988–1993) from the University of California, Berkeley, under Alexander Pines, working on "Double Rotation NMR Studies of Zeolites and Aluminophosphate Molecular Sieves." After postdoc research (1993–1996) at the University of Pennsylvania, he joined the Department of Chemistry at Ben-Gurion University. From 2005 to 2007 he served as the Department Chairman, and currently, he is Vice-President and Dean for Research & Development of BGU. He is the incumbent of the Carole and Barry Kaye Chair in Applied Science, has published over 220 research papers (h-index 49), 15 patents, and 6 books.

Raz is a world leader in the field of conjugated chromatic polymers, such as polydiacetylenes, which his group has implemented as color sensors for water pollutants, volatile organic compounds, proteins, and other biological molecules, as well as mechanical sensing of soft polymers. He is also a leader in the rapidly expanding carbon quantum dots (C-dots) field. He has demonstrated their utilization as biological and chemical sensors, cell imaging agents, bacterial detection, and membrane interactions screening biomolecules. In addition, Raz has worked on self-assembled organized nanoscale gold assemblies, and patented technology was implemented for fabricating various electro-optic devices, including transparent electrodes, antennas, supercapacitors, and physiological pressure sensors. His recent technology allows identifying therapeutic molecules in probiotic fermented microbiota, exhibiting remarkable anti-inflammatory properties. The technology has been translated to a startup company, which has raised a $3.5M investment from a prominent VC fund. Another technology employing C-dot-based capacitive e-nose for contactless bacterial detection through their volatile metabolites constitutes the basis for another startup company in the process of fundraising.

Raz has been awarded numerous grants focused on his applied science work, including three Kamin projects on transparent electrode technology, porous Au/graphene oxide systems for supercapacitor applications and a new electronic nose technology. His Ministry of Energy grant focuses on energy storage in server farms. A Nofar project focuses on polydiacetylene-based water pollution sensing, a Magnet project on pharmaceutical screening, a BARD grant on polydiacetylene-based detection of bacteria in agricultural products, and a Horizon 2020 grant on gas sensing of hazardous materials in containers.

The 2021 ICS-Shahar Prize for the Excellent Administrative Assistant was awarded to **Ms. Sarah Amzallag**, personal assistant to the Dean of the Faculty of Chemistry, the Weizmann Institute of Science. She will receive the prize for her remarkable professional and creative management, work ethics, human relations, and outstanding organizational skills manifested by voluntarily expanding her contributions beyond the formally expected. The prize is in memory of the late Amir Shahar, contributed by Bioanalytics Ltd.

Sarah was born in 1973 in Zurich to a German mother and half Italian/Swiss father. She finished high school in Bern, Switzerland (1994) and started her academic studies in Sociology and History at the University of Zurich. In 1996, Sarah made aliya to Israel and obtained her BA in Sociology and Political Sciences from the Hebrew University of Jerusalem. She worked as an assistant to the deputy VP of the Department of International Relations in the Israel Museum in Jerusalem. She also translated various freelance texts from German to English/Hebrew and vice versa (1999–2022). Following a short period as a marketing secretary at AccuBeat Ltd., Sarah worked for the JDC Israel – The Joint (2003), first as assistant to the Delegations' Unit in the Department of International Relations, later at the Archive of the organization for microfilms research, and finally as the personal assistant to the Head of Relations in India and Donors in Europe. From 2006-2010 Sarah and her family moved to Zurich for five years, where she served as the personal assistant to the Head of the Institute of Pathology, University Hospital Zurich. In 2011, the family (3 children) moved back to Israel, settled in Givat Brenner, and she started working at the Weizmann Institute, first as the secretary of the Department of Structural Biology, and since 2014 as the Administrative Assistant of the Dean of the Faculty of Chemistry.

The departmental head, previous and current Deans, all claim that she actually works as a director of the office, a personal

advisor, and a consultant rather than an administrative assistant. Sarah has revolutionized the work of the Dean's office, dealing with a significant number of topics. In addition to all her duties as an executive assistant to the Dean, she has constantly sought new tasks to take upon herself beyond the formal job description, such as building new websites, introducing an online ordering system for departmental equipment, and dealing with construction planning. As the coordinator of the Faculty Promotions Committee, she developed a computerized tool to follow the complex process of appointments and promotions and obtain valuable statistics. She is also guiding the construction process of the new building for the Faculty of Chemistry. In 2017, Sarah received the Faculty of Chemistry's outstanding employee award.

The 2021 ICS-Dalia Cheshnovsky Prize for excellence in teaching was awarded to two teachers. **Ms. Edna Friedman** from Horev Ulpana in Jerusalem and the Tehilla-Evelina de Rothschild Secondary School, received the prize for her many years of achievements as a high-school chemistry teacher, as an instructor of chemistry teachers in the Jerusalem district, and as a national leader, for implementing diverse and innovative teaching methods, and for educating many generations of students to love chemistry and good citizenship. **Ms. Orit Weinstock** of the Har-Tuv High School received the prize for her many years of achievements as a teacher and coordinator of the chemistry program, as a guide for the chemistry teachers in the southern district and at the national level, for developing innovative teaching methods, and for making chemistry one of the most popular programs at Har-Tuv School.

The 2021 ICS-Peled Prize for outstanding high-school projects was awarded to **Avishag Samara** from the Gymnasia Realit, Rishon Lezion, and **Tahel Amzaleg** from Ort Kramim, Karmiel. Avishag won the prize for her research on the effect of a point mutation on the thermodynamic properties of dihydrofolate reductase. Her supervisor was Dr. Ilia Korobko of the Weizmann Institute of Science. Tahel won the prize for her research on the use of polymers for the development of a mobile artificial kidney. Her supervisor was Prof. Moris Eisen of the Schulich Faculty of Chemistry at the Technion. The ICS-Peled Prize is awarded yearly in memory of Itan Peled who died in the 1995 Arad disaster.

The 2022 ICS Prize for the Green Chemical Industry was awarded to **Daniel Unger** (CEO) and **David Reiner** (Operation Officer) of OR Recycling Park for applying advanced technologies to convert organic wastes into valuable agricultural products, including composts, organo-mineral fertilizers, broiler beddings, and biochar growing substrates. OR Recycling Park, located in the Jordan Valley, is a working model of circular production between five collaborating companies. The park demonstrates a circular economy with zero waste, with every byproduct of one plant becoming a resource for others.

Compost Or receives about half a million tons of organic materials, such as municipal biosolids and agricultural waste, annually. The company recycles organic wastes into a rich, reviving soil conditioner using composting technology that was optimized over the past 20 years. The composting technology produces valuable fertilizers for Israeli farmers and prevents environmentally harmful alternatives, such as incineration, which releases greenhouse gases, or landfills, which contaminate soil and groundwater. Compost Or's research team has collaborated with agricultural R&D over the years. It is the only compost manufacturer in Israel that tests the quality of its product by growing crops in an R&D greenhouse. Compost Or has set up a facility for contaminated soil bio-remediation within the OR Recycling Park. They receive truckloads of soil contaminated with organic pollutants, such as fuels and oils, and decontaminate such soils using biological remediation technologies. For example, the team has recently developed an innovative method to purify soils contaminated by explosive materials.

Fertilo allows farmers and gardeners a way to nourish soils with valuable nutrients while building a living and healthy soil. Their flagship product, Cuftior™, is a concentrated slow-release organo-mineral fertilization pellet. It allows precision fertilization close to the plant's roots. Fertilo's R&D team developed Cuftior™ pellets in cooperation with the Institute for Desert Research, Ben-Gurion University, Israel. Fertilo uses nutrient-rich biosolids mixed with shredded green wood waste, making Cuftior™ a preferred choice for cultivating fields and gardens.

Ecologz aims to provide a national-scale solution to the polluting agricultural fires that adversely affect the general population. They also help Israeli poultry farmers raise healthy broilers without antibiotics. The Ecologz team met both challenges with their SecuriPad™, a biosecurity bedding for poultry farming. The company uses local raw materials from agricultural plantations or forest trimmings. Thus, polluted piles of plant trimmings undergo cleaning and screening stages, followed by compressing and steam sterilization. The product, SecuriPad, offers excellent absorption and evaporation capability, preventing pathogen development and poultry infections.

Earth Biochar develops and manufactures charcoal-like materials using anaerobic pyrolysis. CompoChar™ is a soilless growing medium with excellent water-holding capacity and drainage balance, an internal nutrient reservoir that makes

it a ready-to-use growing medium. CompoChar™ is produced from local, renewable organic raw materials. The company is also developing a set of activated carbon for chemical adsorption.

The 2021 Honorable Member of the ICS was awarded to **Prof. Shimon Shatzmiller** of Ariel University for his extensive contributions to academic research in organic synthesis, national security through extended military service, and chemical industry research and development.

Shimon Shatzmiller (Shatzi) was born in 1942 in Nesher, Israel. From 1960–1964, he studied chemistry at the Technion as part of the academic military reserve program. Following graduation with honors, he served in the IDF (1964–1967). Immediately after being accepted to the MSc program at the Technion, he was called up back to the army for the Six-Day War, serving as an artillery officer on the Syrian front. After the war, he married Shoshana Meirovich, with whom he has three children, Ronit, Noa, and Yonatan. Following his MSc with Prof. Eli Loewenthal, he continued in the same group, researching gibberellic acid synthesis. In 1971, he joined the group of Prof. Albert Eschenmoser at ETH, Zurich, as a postdoctoral fellow. When the Yom Kippur War broke out in October 1973, Shimon returned to Israel to fight as an artillery officer on the Syrian front. In the same year, he accepted a lecturer position at Tel Aviv University. His group developed synthetic methodologies involving chloro-nitrones, and unique carbonyl intermediates, such as 2-acetyl cations and nitrogen derivatives of carbonyl compounds. They discovered amidation reactions with minimal racemization, which yielded antibiotic pentapeptides. Many of his students became independent scientists in the Israeli pharmaceutical industry.

Shimon was a visiting professor at the University of Heidelberg and the Max Planck Society, collaborating with Prof. Richard Neidlein on pharmaceutical chemistry, and at the Africans University, Johannesburg. From 1984–1990, on a sabbatical leave and multiple visits to DuPont's molecular biology lab in Wilmington, Delaware, he worked with Dr. Pat Confalone on drug synthesis, leading to new syntheses of the Losartan for the treatment of hypertension and Sustiva for the treatments of Aids. From 1990–1996, Shimon joined IMI–TAMI, the research campus of Israel Chemicals Ltd (ICL), as a Research Director and Head of the organic division, continuing his university position. He introduced new projects and products, such as fire retardants for plastics, collaborating with Bromine Compounds Ltd. He also established the Novotide division in collaboration with Teva Pharmaceuticals for developing therapeutic peptides. In 1995, after many years of service as an Artillery officer, he was discharged with the rank of reserve brigadier general (Tat-Aluf). In 1998, when the College of Judea and Samaria in Ariel (now Ariel University) opened the Department of Chemical Sciences, Shimon was appointed as its first Chair. He took early retirement from Tel Aviv University for that mission, raised funds, obtained scientific equipment, and recruited faculty and graduate students. He established a collaboration program with scientists from Bar-University for joint guidance of graduate students at Ariel. Shimon served as the ICS President from 1993-1996. For Shatzi's profile in Issue 6 of the ICE magazine, see https://www.chemistry.org.il/resources/ice/ .

The 2021 ICS Gold Medal was awarded to **Prof. Lia Addadi** and **Prof. Steve Weiner** of the Department of Chemical and Structural Biology at the Weizmann Institute of Science, for their joint research on biomineralization, for discovering phenomenal properties of mineralized biological materials, and inspiring scientists worldwide in material science, biomedicine, and climate engineering.

Lia Addadi was born in Padova, Italy (1950), and obtained an MSc in Chemistry from Padova University. She immigrated to Israel in 1973 and received her PhD from the Weizmann Institute (1979) under Prof. Meir Lahav, working on solid-state organic chemistry, stereochemistry, and chiral crystals. Following a postdoc at Harvard University with Prof. Jeremy R. Knowles, Lia joined the Weizmann Institute, studying biomineralization with Steve Weiner since 1983. In collaboration with Meir Lahav and Leslie Leiserowitz, she studied the relations between crystal structure, crystal morphology, and molecular chirality. She has demonstrated that antibodies can selectively recognize crystals and nowadays studies the formation of cholesterol crystals in atherosclerosis, the leading cause of heart attack and stroke. Lia served as the WIS Dean of Chemistry (2001–2004) and Dean of the Feinberg Graduate School (2008–2013). Her long list of awards includes the 1989 ICS Young Scientist prize, the 1996 NIDR prize, the 1998 Prelog medal in Stereochemistry, the 2006 Kolthoff prize, the 2007 Spiers Medal of the RSC, the 2009 ICS Prize of Excellence, the 2011 Gregori Aminoff Prize, and 2018 Honorary Doctorate from ETH. In 2017, she was elected Foreign Associate of the U.S. National Academy of Sciences, and in 2019 she became a Foreign Associate to the American Philosophical Society. She has published about 300 research papers with nearly 40,000 citations and h-index of 95.

Steve Weiner was born in Pretoria, South Africa (1948). He obtained his BSc in chemistry and geology from the University of Cape Town, MSc in oceanography from the Hebrew University (1972), and PhD from CalTech (1977) under Profs. Heinz Lowenstam and Lee Hood, working on mollusk shell formation. He joined the Weizmann Institute in 1977. His book, "On Biomineralization," coauthored with

Heinz Lowenstam (1989), represents an essential reference in the field. In addition to the joint research with Lia Addadi, he has investigated the hierarchical structure of bone. Since 1985, he has developed a new approach in archaeological science, studying archaeological records that are invisible to the naked eye. His book on this approach, "Microarchaeology," was published in 2010. His list of prizes includes the 1980 Samuel Jaroslavsky Prize, the 1984 Ernst D. Bergmann Prize for Chemistry, the 2010 ICS Prize of Excellence, the 2011 Aminoff Prize of the Royal Swedish Academy of Sciences, and the 2013 Pomerance Award for Scientific Contributions to Archaeology from the Archaeological Institute of America. He has published over 350 research papers with 65,000 citations and h-index of 123.

For almost 40 years, Lia and Steve have collaborated on biomineralization, and their work has a broad spectrum of implications. For example, the amount of biogenic minerals produced is so large that it affects the amounts of atmospheric CO_2 absorbed into the oceans. Mineralized biological materials inspire materials scientists, and the importance of this field for medicine is enormous. A significant challenge in this field was identifying common underlying mechanisms used by organisms in forming their minerals. Lia and Steve discovered that many mineralizing organisms do not precipitate their minerals directly out of a saturated solution but first produce a transient, unstable precursor phase. This mechanism has proved to be an overall paradigm-changing strategy. They have resolved other basic phenomena, such as the counterintuitive occlusion of macromolecules inside crystals. They also understood the pathways that ions take from their uptake, concentration in vesicles within cells, and then extrusion into the extracellular space. They have also pioneered how organisms manipulate light by using organic crystals to produce structural colors and vision. With 160 joint papers and several joint prizes, Weiner and Addadi are considered worldwide leaders of the biomineralization field. Many of their students and postdocs have continued research in major academic centers in Israel and abroad. Israel has become a world center of biomineralization with 14 active research groups in Israeli universities.

The 2021 ICS Prize of Excellence was awarded to **Prof. Leeor Kronik** of the Department of Molecular Chemistry and Materials Science, Weizmann Institute of Science, for his pioneering contributions to the development of density functional theory (DFT) and its application to a wide range of contemporary issues in chemistry and materials science. was born in 1970 in Rehovot, Israel. He obtained his BSc in Electrical Engineering (1991) from Tel Aviv University and PhD in Physical Electronics (1996) under the supervision of Prof. Yoram Shapira. Following postdoctoral research at the University of Minnesota with Prof. James R. Chelikowsky (1999–2002), he joined the Department of Materials and Interfaces at the Weizmann Institute. In 2012 he became a Full Professor, and since 2019, he has held the Aryeh and Mintzi Katzman Professorial Chair. For nine years (2012–2021), he served as the Department Chair and is presently the director of the Tom and Mary Beck Center for Advanced and Intelligent Materials.

Through the development of novel orbital-dependent density functional approaches, Prof. Kronik's research has extended the predictive reach of DFT into a various electron and optical spectroscopy scenarios previously believed to be outside its realm, including the quantitative prediction of fundamental and optical gaps, as well as charge transfer excitations, in both molecular and solid-state systems. He has also contributed significantly to the development of methods for large-scale DFT calculations based on real-space approaches. Using these and other tools, in recent years, Leeor has contributed significantly to our understanding of a broad range of topics, including the electronic structure of metal-organic complexes, dynamic disorder processes in halide perovskites, structure and properties of biogenic and bio-inspired molecular crystals, collective effects at molecular electronic and spintronic junctions, and more. With over 250 publications in high-profile journals, including Science, Nature Comm., Nature Materials, Adv. Mater., J. Phys. Chem. Lett., Nano Lett., Angew. Chem., Phys. Rev. B, J. Phys. Chem., JACS, and PNAS, Kronik was cited over 21,000 times with an h-index of 74.

Prof. Kronik was a member of the Young Israel Academy and is a Fellow of the American Physical Society. He has received the Krill Prize of the Wolf Foundation (2006), the ICS Prize for the Outstanding Young Scientist (2010), the Israel Vacuum Society Award (2018), and the Helen and Martin Kimmel award (2021).

The 2021 ICS Excellent Young Scientist Prize was awarded to **Dr. Amnon Bar-Shir** of the Department of Molecular Chemistry and Materials Science, the Weizmann Institute of Science for developing small molecules, nanocrystals, supramolecular assemblies, and proteins, as sensitive and selective sensors for MRI applications; and **Prof. Roman Dobrovetsky** of the School of Chemistry, Tel Aviv University for developing novel concepts in the chemistry of main-group elements, and preparing molecules containing boron, phosphorus, and zinc with unique structures and catalytic properties.

Amnon Bar-Shir was born in Kibbutz Ramat HaKovesh, Israel, in 1975, earned his BSc (2002) and MSc in chemistry from Tel Aviv University (2004, under Michael Gozin), both magna cum laude. His PhD (2009, under Yoram

Cohen) focused on advanced diffusion NMR and MRI to study the structure and function of the central nervous system. As a postdoc at the Johns Hopkins University School of Medicine under Assaf Gilad and Jeff Bulte, he developed genetically engineered reporters for MRI. In 2014 he joined the Weizmann Institute, where he created new kinds of biosensors with artificial "multicolor" features for MRI applications. His lab uses synthetic chemistry, nanofabrication, and protein engineering to generate novel molecular formulations, such as small molecules, nanocrystals, supramolecular assemblies and proteins, as MRI sensors of high sensitivity, specificity, and orthogonality. He has used these methods for in-vivo molecular and cellular MRI studies for mapping inflammation, multiplexed in-vivo MRI, imaging orthogonal reporter genes, and sensing metal ions. In addition, he used his techniques to study fundamental questions in supramolecular chemistry, including kinetic features of dynamically exchanging molecular systems and control over nanocrystals' formation. Dr. Bar-Shir won multiple research grants, including the ERC, two individual ISF grants, BSF, Minerva, and the Israel Precision Medicine Program (IPMP) of the ISF. He was recognized by the 2009 ICS Prize for graduate students, the 2019 Krill Prize, the 2014 NIH Pathway to Independence Award, and the International Society for Magnetic Resonance in Medicine (ISMRM) 2014 Junior Fellowship.

Roman Dobrovetsky was born in Tashkent, Uzbekistan in 1979, and moved to Israel with his family in 1991. After his military service (1998–2002), he obtained his BSc in Chemistry (2005) from the Technion. His PhD research (2005–2011, under Yitzhak Apeloig) focused on developing alpha-functionalized silyl anions. As a postdoc at the University of Toronto under Doug Stephan, he studied frustrated Lewis pairs and Lewis-acid catalysis. In 2015, he joined the School of Chemistry at Tel Aviv University and, in 2020, became an Associate Professor. His fields of interest include main group compounds, focusing on boron, phosphorus, and zinc-based compounds and their chemistry with small molecules. His group developed a diverse research program, including transition metal-free catalysis, geometrically distorted main group centers, stable main group radicals, and the chemistry of boron-cluster-based substituents. His group demonstrated the first geometrically constrained phosphenium cation and its ambiphilic nature. They developed highly selective air-stable Zn-based hydroelementation catalysts. They showed that ortho-carborane substituents could stabilize radicals attached to their carbon atom and used this property to synthesize the first persistent 19-electron molybdenum metalloradical. Utilizing the ability of ortho-carboranes to withdraw electrons into their cage structure, thus forcing geometrical changes on the ligands' structure, they developed the electrochemical tweezers concept. Roman was selected for the Young Investigator Workshop 2018 in Oxford, which recognizes the most promising European organic chemists under the age of 40.

Closing ceremony

Prof. Charles Diesendruck greeted the audience: "Good afternoon, and many thanks to all the survivors for staying until the end of the meeting. As happy as I was in opening the conference yesterday, I'm even more delighted to close it today. It's been a long process that took two and half years and, in my opinion, went quite smoothly and successfully. We had over 600 participants at the conference, with 115 lectures and over 240 posters presented. This has been a major accomplishment, remembering that the meeting was postponed three times and is not occurring at our typical time. I am very happy to pass the heavy hat to the organizers of the 87th ICS meeting, which will take place in early July next year in Jerusalem.

Before announcing the best poster awards, I'd like to thank the organizers and chairs again, from the Technion and outside the Technion, who helped us organize the conference. I thank the speakers and poster presenters for creating fascinating scientific discussions. I want to thank the Diesenhaus team for all their help, especially Tsipi Laxer, who worked directly with us these past months to restructure the conference and be in touch with the speakers. Finally, I want to thank the ICS President, Prof. Ehud Keinan, who wanted very much to be here, but, as you heard, is recovering from Covid. I appreciate his efforts to participate in the first day and prize ceremony. I wish him good health so that he continues representing the ICS in the highly demanding M2V relay race next year.

Finally, I am happy to reach the much-expected poster awards. We have four awards this year, not in order of preference, and I'll call the awardees alphabetically. It is always hard to select four posters out of 240, but Saar and I were not part of the committee. I cannot name the committee members, but we thank them for their efforts.

See you next year in Jerusalem!"

Chairpersons Charles Diesendruck and Saar Rahav announced the four best Poster prizes, all sponsored by BioAnalytics Ltd., and awarded them to the winners:

"Targeting proteins "hot spots" using structured and disordered chimeric peptide inhibitors" was presented by Guy Mayer of the Hebrew University of Jerusalem, who carried out the work with Zohar Shpilt, Hadar Kowalski, Edit Y. Tshuva, and Assaf Friedler.

"A camouflage reflector in the eyes of decapod crustaceans larvae" was presented by Keshet Shavit of the Departments of Chemistry and Life Science at the Ben-Gurion University of the Negev, who carried out the work with Avital Wagner, Bracha Viviana Farstey, Alexander Upcher, Amir Sagi, Venkata Jayasurya Yallapragada, and Benjamin Alexander Palmer.

"Catalytic and photocatalytic formation of nucleobases and nucleotides from pre-biotic substances" was presented by Shoval Gilboa of the Department of Chemical Engineering at the Technion, who carried out the work with Douaa Satel, and Yaron Paz.

"A Matter of Charge: Electrostatically tuned co-assembly of amphiphilic peptides" was presented by Elad Arad of the Departments of Chemistry and the Ilse Katz Institute for Nanoscale Science and Technology at Ben-Gurion University, who carried out the work with Topaz Levi, Ziv Azoulay, Raz Jelinek, and Hanna Rapaport.

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