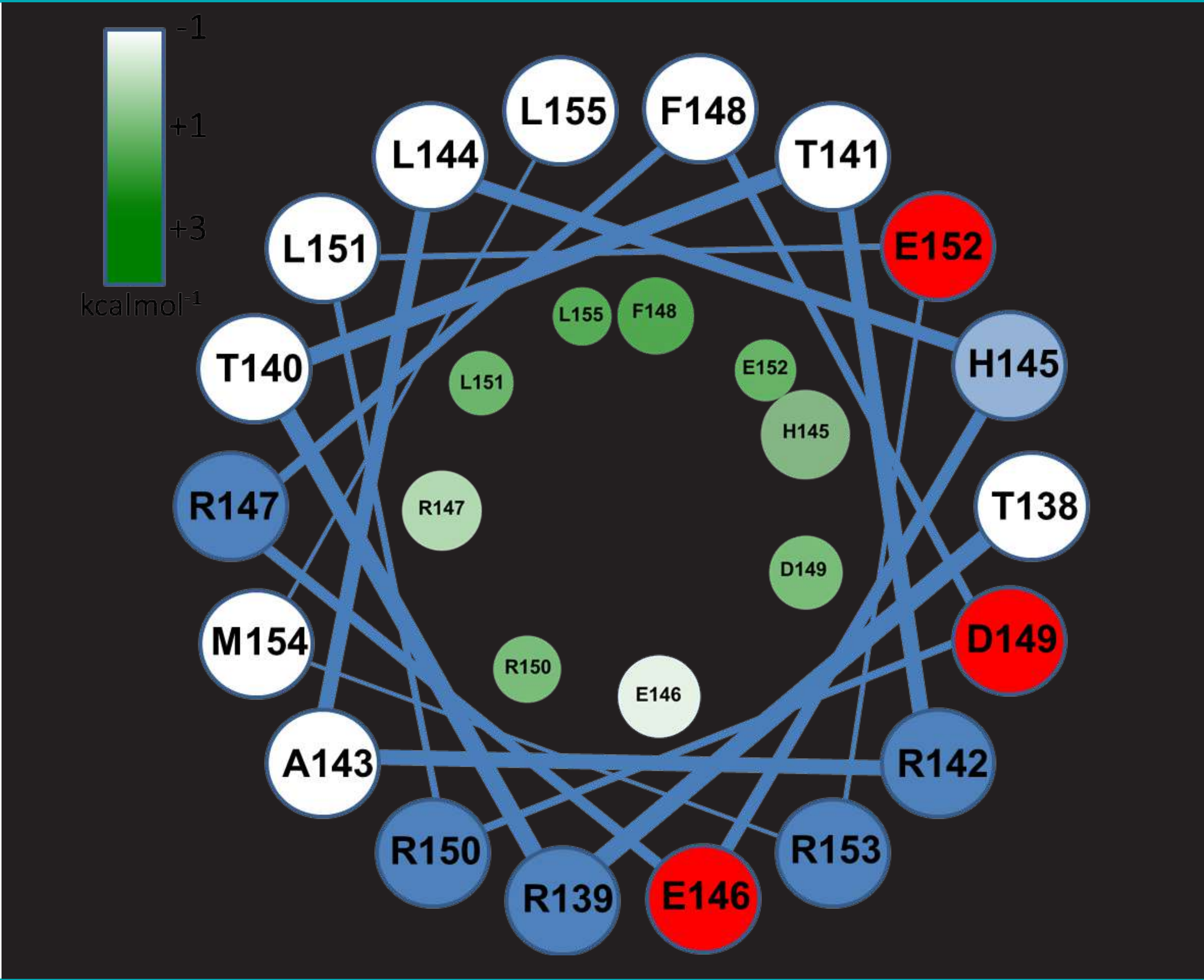
Issue 1 • September 2015 • Tishrei 5776

The Israel Chemist and Engineer

ICE



Joint Publication of

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

The Israel Society of Chemical Engineers
and Chemists (ISCEC)

The Israel Institute of Chemical Engineers
(IIChE: www.iiche.org.il)

Editorial

Scientific Articles

Articles on Education

Article on History of Chemistry

Profiles

Reports

Intellectual Property

Dear Readers,

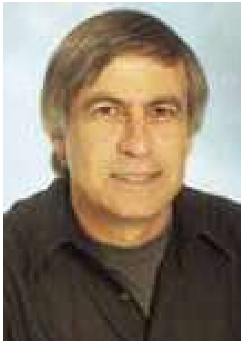
Welcome to the first issue of the Israel Chemist and Engineer (ICE) online magazine. This is a joint venture of the Israel Chemical Society (ICS), the Israel Society of Chemical Engineers and Chemists (ISCEC) at the Association of Engineers and Architects in Israel (AEAI), and the Israel Institute of Chemical Engineers (IIChE). Both Professor Ehud Keinan, the President of the ICS, and Dr Alec Groysman, the Chairman of the ISCEC, have contributed letters in which describe their motivation in setting up the magazine and their vision for the future.

We hope you will find the magazine interesting and will be inspired to contribute to future issues. You will find articles describing state-of-the-art scientific research, as well as articles on how to improve lab courses and chemical engineering education, and some fascinating insights into the history of chemistry. In an effort to reveal the personalities behind the impressive CVs, we include the profiles of six Israeli chemists who were awarded prizes at the ICS meeting in February 2015. Profiles of the other prizewinners will appear in the next issue, planned for January 2016. In addition, there are reports of the ICS meeting, of the Mountain-to-Valley Relay Race in which an enthusiastic ICS contingent participated, and of the newly formed Graduate Student Division of the ICS. Two interesting contributions on Patents are also included.

In future editions, we hope to have profiles of the various chemical industries that contribute to Israel's economy, articles on the various careers open to chemists and chemical engineers in Israel, and a discussion of the future of chemistry education in our high schools which directly impacts recruitment to chemistry and engineering degrees in the universities.

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

Prof. Arlene D. Wilson-Gordon
ICE Editor, Department of Chemistry, Bar-Ilan University



Dear Fellow Chemists and Chemical Engineers,

Chemistry has always been a prominent area of scientific and technological excellence in the State of Israel. The chemical industry has contributed significantly to the national economy, with chemical products forming over 40% of the industrial production and 25% of the country's exports and the chemical R&D standing much higher than the world average. These achievements are remarkable, considering the fact the Israeli chemistry community is quite small with only 6000 chemists, 5000 chemical engineers and 800 teachers.

When we all celebrated in 2004 the first Nobel Prize in Science awarded to Israeli citizens, nobody could predict that in less than a decade the number of Israeli Nobel Prize Laureates in Science would rise to six, or expect that all six would win the Nobel Prize in Chemistry!

The Prizes awarded to Avram Hershko, Aaron Ciechanover, Ada Yonath, Dan Shechtman, Michael Levitt and Arieh Warshel had an enormous impact on the general public. New streets in Israeli cities were named after the Laureates, 4 new stamps were issued by the Israel Philatelic Service in collaboration with the ICS to commemorate the Nobel Prizes, and many young Israelis were attracted to science, and to chemistry in particular.

It is quite symbolic that this year we celebrate the International Year of Light, amazed by how light-based technologies have been promoting sustainable development and solving worldwide challenges. Light is all about chemistry. We use chemical technologies to convert electricity, heat and chemical reactions to light and use it in communication, electronics, materials, photography, medicine and entertainment. All lighting devices, including tungsten and fluorescent lamps, lasers, light-emitting diodes and chemiluminescence, are based on chemistry. Lasers are broadly used in communications, digital technology and for a variety of applications, ranging from precision cutting of metals to medical surgery. Photochemical polymerization produces plastics, dental glues and photo-curing paints. Photodynamic therapy represents a major weapon to fight cancer. Chemistry helps save energy, helps harvest sunlight with solar cells and artificial photosynthesis and helps generate hydrogen, which is the cleanest possible fuel, by catalytic water splitting. All Israeli chemists, chemical engineers and chemistry teachers share the excitement and pride of being members of the Israeli chemistry community.

Since its establishment in 1933, the ICS has been striving to promote the chemical research and development, the chemical industry and chemistry education, as reflected by its diverse membership. It is the time for all chemistry associations to leverage the positive public attitude towards chemistry. Our individual organizations, the Israel Chemical Society (ICS), the Israel Society of Chemical Engineers and Chemists (ISCEC) at the Association of Engineers and Architects in Israel (AEAI) and the Israel Institute of Chemical Engineers (IIChE), all having a long tradition of many years, are strong, reliable and influential. We can influence the general public and government offices even more effectively if we all join forces and coordinate our activities. The ICE Magazine is certainly a very good start of a fruitful collaboration between all chemists and chemical engineers in the State of Israel.

Prof. Ehud Keinan
President, the Israel Chemical Society

Dear Chemical Engineers, Chemists, Teachers of chemistry and all readers who are interested in chemistry,

You are about to explore a new magazine on an exciting subject - chemistry. We are born and live owing to chemical and biochemical reactions. Look around: from the silicon chips in your computer to the water we drink, food we eat, and medicines. Chemical engineers and chemists contribute to the prosperity, comfort, health and well-being we enjoy.

We need energy, raw materials, food, pure water, air, and soil. Chemistry and chemical technology solve all these problems. How efficiently and effectively can we use natural gas (methane) which was found in Israel as a resource for the chemical industry? What are the achievements of chemical science in industry? How can we produce biofuels and energy to save the environment and to produce new drugs? How can we educate creative, knowledgeable, skillful, qualified and fully developed specialists?

About 100 chemical enterprises function in Israel which include basic chemistry, crude oil processing, petrochemistry, pharmaceutical industry, polymeric materials, paints, coatings, food and paper industries. Most of the chemical plants are located in the Haifa Bay area, Ramat Hovav (including Negev region), and near the Dead Sea.

There is an information "explosion" of achievements of chemistry and chemical technology. It is important not to "sink" in the sea of new knowledge and to find exactly what you need. Brilliant chemists and chemical engineers work in Israel.

However, we are facing a lack of highly qualified specialists, able to solve the above mentioned problems. To improve this situation, we should improve education and knowledge transfer. This new magazine is intended to disseminate news in all subjects of chemistry, chemical engineering and education which can be interesting and beautiful, and each person can enjoy and understand more by reading it.

Now we invite you to journey into the wonderful world of chemistry, chemical technology and chemical education.

Dr. Alec Groysman
Chairman, the Israel Society of Chemical Engineers and Chemists at the Association of Engineers and Architects in Israel (AEAI)

New Methodologies and Applications in Electron Spin Resonance - from Wound Healing to Quantum Computing

Aharon Blank
Schulich Faculty of Chemistry, Technion - Israel Institute of Technology, 32000, Haifa, Israel
Email: ab359@tx.technion.ac.il

Abstract: Magnetic resonance (MR) is well-known in the world of chemistry, mainly due to its superb analytical capably to decipher the structure of molecules. This method, which can be applied in connection with either certain nuclei or unpaired electrons, originated from basic physics exploration in the 1940's, and has since expanded to address a variety of applications in diverse fields ranging from chemistry to medicine. However, despite its wide commercial and scientific success, MR still suffers from significant limitations of low sensitivity, coarse spatial resolution in imaging, and high complexity and cost of its system. In this short review, I will describe some of the recent efforts in my lab, aimed at overcoming these limitations, which have resulted in unique experimental capabilities, offering ultra-high sensitivity down to the single electron spin level, as well as sub-micron imaging resolution. These capabilities enable one to address unique applications in materials- and life-sciences, ranging from oxygen measurements in cells to basic experiments in quantum computation. In addition, we are developing other systems that are far less complex and costly than the conventional ones, aimed at specific medical applications. This direction, which is only in its infancy, may lead in the near future to a situation where MR technology can serve as a basis for simple and affordable medical instruments, used by physicians and caregivers at the clinic level.

I. Introduction: the pro and cons of magnetic resonance

Magnetic resonance (MR) is one of the most profound scientific observation methods. MR is concerned mainly with nuclear magnetic resonance (NMR) and electron spin resonance (ESR). It has a broad range of applications from chemical structure determination to medical imaging and basic physics. From a scientific standpoint, MR has been at the center of at least seven Nobel prizes in physics[1; 2; 3; 4], chemistry[5; 6], and medicine[7]. From an industrial standpoint, MR is a multibillion industry aimed primarily at a wide range of medical (magnetic resonance imaging, MRI) and chemical (NMR and ESR spectrometers) applications.

Despite the success of MR methodologies, their application is typically limited by sensitivity (the number of species that can be detected), by their coarse spatial resolution in imaging applications, and by the high cost and complexity of MR technology. Overcoming these barriers will pave the way for transformative developments in the experimental sciences. Our group is trying to address all of these issues, ranging over the whole field of magnetic resonance, although currently we are primarily focusing on methodologies and applications related to electron spin resonance. In this short review of activities, we picked some samples of our work related both to basic methodological developments in ESR, and how they can be applied to practical scientific, technological, and medical applications.

As noted above, the most fundamental limitation of magnetic resonance, including ESR, is the low sensitivity. Let us first remind ourselves what ESR is and the origins of its sensitivity problems.

Aharon Blank is an associate Prof. at the Schulich Faculty of Chemistry, Technion - Israel Institute of Technology. Born in 1972, graduated from the Hebrew University of Jerusalem in 1992 with degrees in mathematics, physics and chemistry; completed his Masters degree at Tel Aviv University in 1997 in electrical engineering - physical electronics under the supervision of Prof. Raphael Kastner and finished his PhD in 2002 at the Hebrew University of Jerusalem in physical chemistry - electron spin resonance (ESR), under the supervision of the late Prof. Haim Levanon. During this time he served 9 years in the IAF as a Scientific Officer and also as a CTO in a medical device company, developing miniature intravascular MRI. Following his PhD he spent 3 years at Cornell University as a postdoc in the group of Prof. Jack Freed (on a Rothschild post-doctoral fellowship), developing the subject of ESR microscopy, and since 2005 he is a faculty member at the Technion. Aharon's main interests today are the development and applications of new methodologies in the field of magnetic resonance. His group works on miniature sensitive ESR resonators, small, self-contained NMR and ESR medical tools, and ESR probes for micro- and nano-imaging.

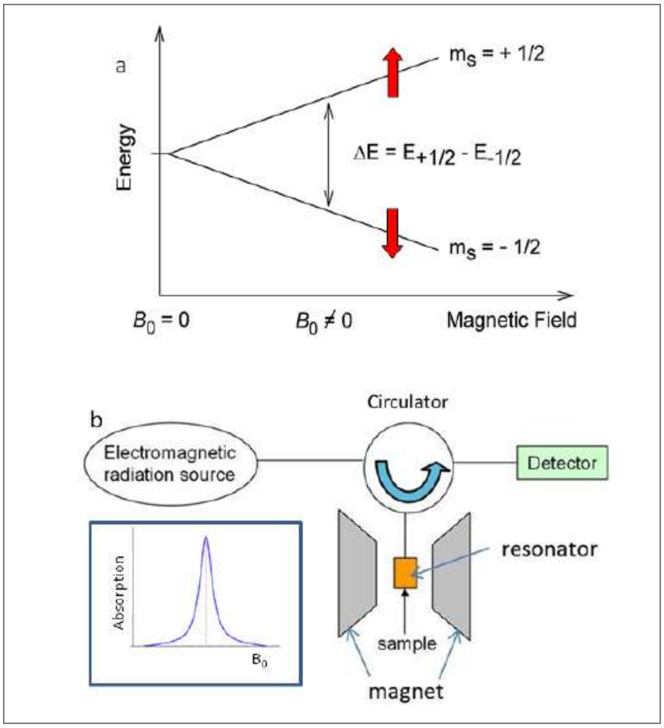


Figure 1: (a) Energy levels of unpaired electron spins as a function of the static magnetic field, showing the so-called Zeeman splitting. **(b)** Simple experimental setup for the detection of unpaired electron spins in a sample. The inset shows the microwave absorption response of the sample as the static field is scanned across the resonance.

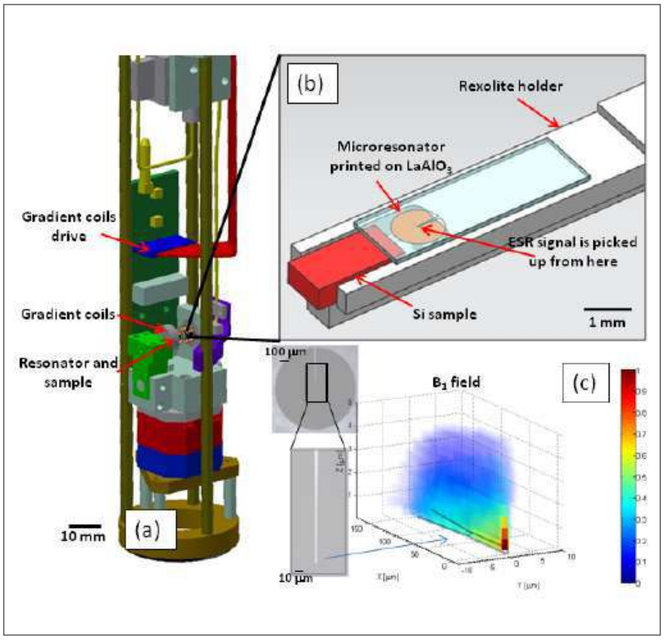


Figure 2: Experimental setup for ultra-high sensitivity and high spatial resolution ESR. (**a**) A drawing of an ESR detection probehead that operates at cryogenic temperatures, showing its main components. **(b)** Zoom-in to the center of the probehead, where a miniature ESR resonator (the "Packman" shaped structure) is located near the sample. **(c)** Microscopic photos of the resonator, showing its details as well as the calculated microwave magnetic field at the center of the resonator, showing that the field is focused in a volume of a few mm3.

Aside from their charge, electrons also carry the magnetic quantum property of spin. Electrons usually team up in pairs with opposite spins, resulting in a zero net spin. However, in many cases, such as free radical molecules, crystal defects, paramagnetic metal ions, and conduction/mobile electrons, the electrons are unpaired and their spin properties can be measured. Spins can be envisioned as small bar magnets which react strongly to the presence of a large external static magnetic field. Being quantum mechanical creatures, these small magnets can be aligned only at selective angles with respect to the external static field, B_0, i.e. either parallel or anti-parallel to it (Fig. 1a). The energy difference, ΔE, between these two states varies linearly with the strength of the external field ($\Delta E \sim 2\mu_B B_0$, where μ_B is a universal constant termed Bohr magneton), but in any case is quite small, in the range of micro-eV to ~ meV at most, for common static fields in the range of ~0.01-10 Tesla. This is one of the prime reasons why it is so hard to detect the presence of these unpaired spins - hard, but not impossible. In practice, detecting the presence of unpaired electron spins in a given sample can be carried out by employing the typical ESR experimental setup as depicted in Fig. 1b (in a schematic manner). The sample is placed in a static magnetic field and is illuminated by an electromagnetic source whose frequency corresponds to the energy difference between the two spin states (based on the well-known Planck formula $\Delta E = h\nu$, where h is the Planck constant and ν is the radiation frequency). For common magnetic fields, this frequency falls within the microwave (MW) region of the electromagnetic spectrum, with a wavelength of ~few centimeters to a few millimeters. An ESR spectrometer usually scans the magnetic field while keeping the MW frequency fixed, and monitors the reflected vs. incident MW power on the sample (through the detector, Fig. 1b). At specific field points, where the resonance condition is met ($2\mu_B B_0 = h\nu$), the sample absorbs a small amount of the incident MW power and this is manifested as a detectable change in the reflected MW power from the resonator arm (see inset in Fig. 1). This is a sign of the existence of unpaired spins in the sample, with the exact resonance field value for a given MW frequency of excitation used as a spectroscopic marker for characterizing the atomic environment of the unpaired spins. The detection of these changes in the reflected MW power is very difficult when a small number of spins is placed inside the resonator, making ESR far less sensitive than other spectroscopic and analytic techniques, such as fluorescence and mass spectrometry. For example, in the most favorable case of a sample having a narrow ESR spectrum, commercial ESR systems require at least 10^9 spins to achieve a measurable signal during 1 s of acquisition time.

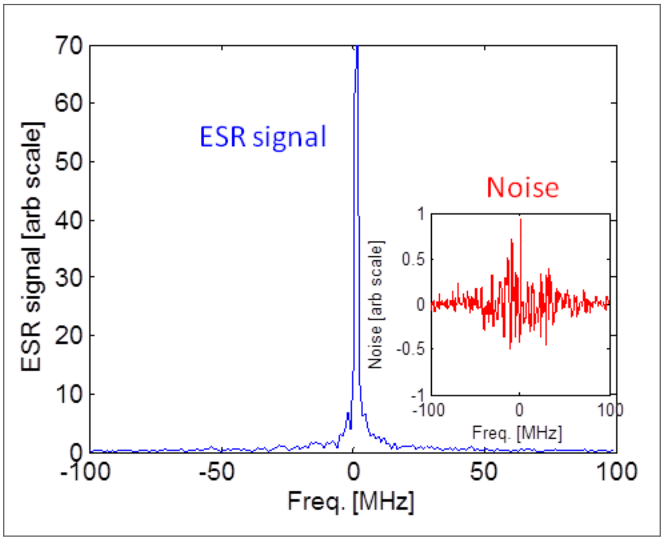


Figure 3: ESR signal and noise in the spectral domain for 28Si:P sample at 10 K, for 1 second of acquisition time[8].

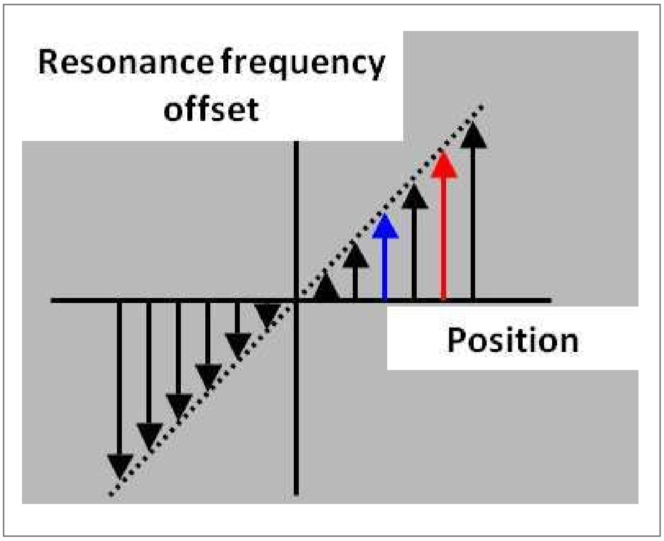


Figure 4: Schematic description of the method for spatial encoding of the sample in magnetic resonance. The resonance frequency of different parts in the sample can be either higher or lower than the resonance frequency of the center of the sample, when a small magnetic field gradient is added to the main static field.

II. Improving the sensitivity

In view of the above, the first challenge that our laboratory had to deal with is to significantly improve the spin sensitivity, aiming at the ultimate sensitivity of a single electron spin. Figure 2 summarizes the approach we took to achieve this goal. It is based on three main pillars. First and foremost, we developed a unique ultra-miniature resonator, which focuses the MW energy to a very small volume, on the mm scale (a highly challenging task since the wavelength of the frequency we work at is ~ 10 mm). This enables us to greatly amplify the response of the MW system to very small changes in the MW properties of a small sample in the resonator (when reaching the resonance condition). The second important point for achieving high sensitivity is that working with such a tiny resonator also enables the use of very low MW power for measuring the sample response, which means that the MW signal coming from the sample can be amplified by very sensitive cryogenic amplifiers that, otherwise, would be damaged by even moderate power MW radiation. This bring us to the last important point in our set up, which includes the use of a cryogenic probehead to enable the measurements at low temperatures where noise level is reduced and also is important for facilitating the use of an ultra-low-noise cryogenic amplifier.

The capabilities of our systems were recently verified by achieving a sensitivity approaching a single electron spin when measuring unpaired spins in phosphorus-doped silicon 28 (^{28}Si:P) wafer (Fig. 3). In this case the sample contained ~ 2×10^6 spins, and analysis of the noise level reveals that a sensitivity of just a single spin can be achieved after a few hours of averaging time[8].

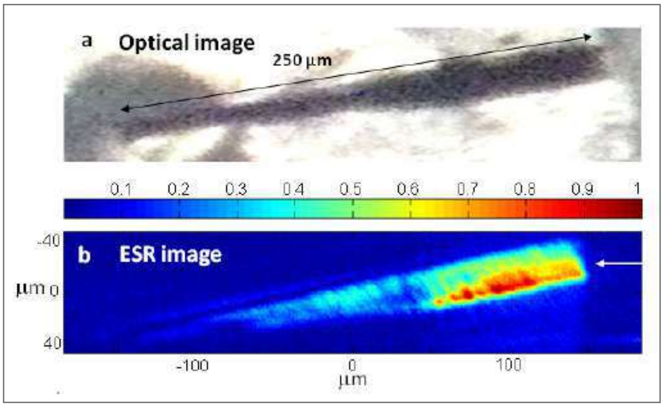


Figure 5: Optical (a) and two-dimensional ESR image (b) of a single paramagnetic Lithium Phthalocyanine crystal. The crystal was positioned with its long axis in the XY plane of the ESR image.

III. Improving the spatial resolution

The second limiting factor for magnetic resonance listed above is the coarse spatial resolution in imaging applications of heterogeneous samples. In order to understand the origins of this limitation, we must first provide a very brief explanation of how magnetic resonance can be used for imaging. The basic idea relies on the linear relation between the resonance frequency and the static field ($\nu = 2\mu_B B_0/h$), as depicted in Fig. 1b. Thus, by placing the sample not in a homogenous static magnetic field, but rather in a field that has a fixed gradient, each position in the sample is encoded by its resonance frequency (Fig. 4). Namely, different parts of the sample exhibit different resonance frequencies, thereby enabling creation of an image of the sample based on the ESR absorption signal at different frequencies.

Based on this explanation, it is evident that the image resolution depends on the strength of the field gradient employed, meaning the larger the gradient the better the resolution will be. However, as the pixels in the image become finer and finer, there are fewer and fewer spins in each pixel, meaning that at some point their number will be smaller than the minimal detectable number of spins of a given setup, resulting in a complete loss of image contrast in favor of noise. The setup shown in Fig. 2 is aimed at addressing both the gradient strength issue, as well as the sensitivity problem, at the same time. On one hand, it greatly improves the spin sensitivity – as explained above. On the other hand, since the resonator is so small, it enables one to employ miniature coils located around the resonator at very close proximity that generate very powerful magnetic field gradients and also can be switched on/off on a fast - nanosecond time scale (which is another important requirement for high resolution imaging in ESR). Figure 5 provides an example of a high-resolution (better than 1 μm) ESR image of a paramagnetic crystal acquired by our measurement system[9].

IV Applications of High Sensitivity / High resolution ESR

The new capabilities described above can be implemented in a variety of scientific and technological applications. For example, in the field of semiconductor devices, high-resolution ESR imaging enables one to observe diffusion and migration phenomena of point defects in amorphous oxides[10]. Amorphous oxides are key ingredients in electronic and optical devices. Such oxides include a variety of point defects that greatly affect their electrical and optical properties. Many of these defects are paramagnetic and, as such, the best tool to identify them and characterize their structure is ESR. However, due to its limited sensitivity and spatial resolution, traditional ESR could not provide information about the defects' migration properties, which are of crucial importance for device fabrication. Ultra-high-resolution imaging modalities such as transmission electron microscope (TEM), as well as theoretical calculations, are severely limited in amorphous media, resulting in a wide knowledge gap in this field. Our ESR microimaging was applied to examine unique samples that are prepared using e-beam irradiation and have well-defined point defect patterns. This provides a capability to unambiguously identify the defects and at the same time track their migration with high spatial resolution, revealing new information about their properties. Figure 6 shows a typical example of ESR imaging results of amorphous

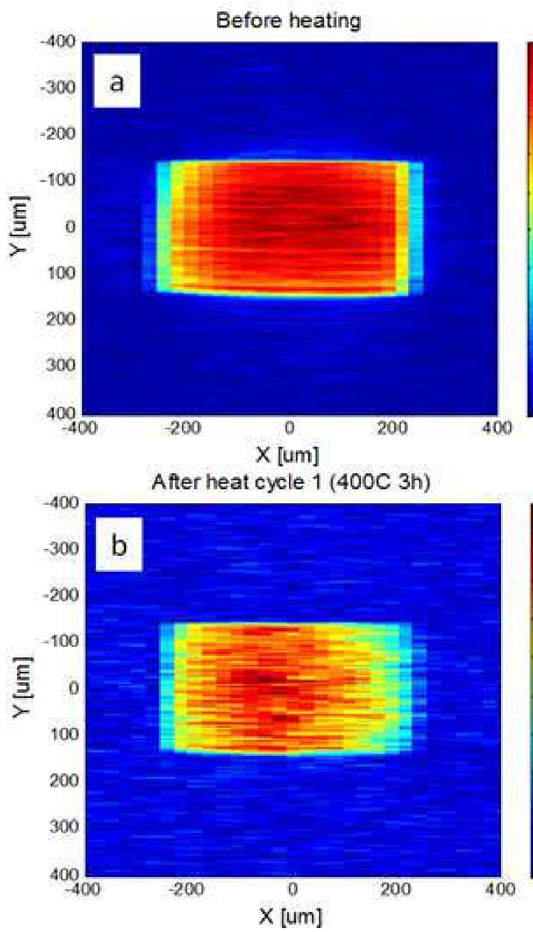


Figure 6: Pulsed ESR 2D images of the irradiated SiO_2 sample before **(a)** and after **(b)** heating cycle at 400 °C for 3 hours. The heat cycle causes some changes in the spatial pattern that can be analyzed to provide information about forces acting on the defects in the SiO_2 and processes they undergo.

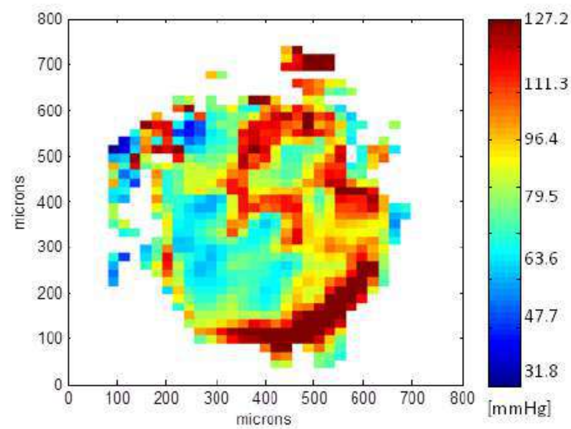


Figure 7: Oxygen map of a spheroid containing LiNc-BuO. The map shows the oxygen concentration in various parts of the spheroid, as derived from their measured spatially-resolved ESR spectrum.

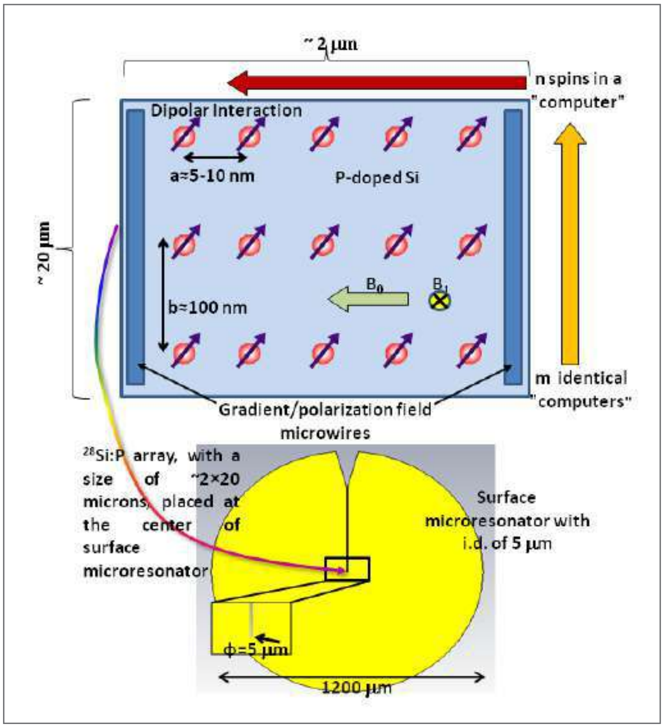


Figure 8: The suggested QC scheme to be used in conjunction with ultra-high sensitivity/high-resolution induction detection[11]. A two-dimensional array of phosphorus atoms is produced inside a pure 28Si single crystal. The crystal is placed upside down on the center of our ultrasensitive surface resonator[16; 17; 18], and operated at cryogenic temperatures. Each phosphorus nucleus in the crystal serves as a logical quantum bit (qubit), while its adjacent electron is the working qubit. The array has two lattice constants: a short one **(a)** that enables electron spins to interact through dipolar couplings along this linear vector (similar to the manner described in ref[19]), and a long one **(b)** that separates many identical copies of the same individual vector computers. Individual spins can be addressed by applying a large magnetic field gradient with DC current into microwires (separating the spins in the frequency domain), and the state of all spins can be read out in parallel via a one-dimensional image along the crystal's x-axis. All parallel identical computer vectors should give the same vector of spin states, thereby increasing the measured signal and also greatly minimizing the need for quantum error correction due to random spin flips, since the measured result averages over ~100-1000 spins per qubit. Information can be swapped between working electron spins and logical nuclear spins through combined radiofrequency (RF) and microwave (MW) pulse sequences, as described in reference[20].

SiO_2 piece on which a rectangular pattern of point defects was created by e-beam irradiation. The piece was imaged immediately after preparation and then following a 3h heat cycle at 400ºC. Changes in the image were analyzed to obtain valuable information about atomic level potentials and forces between point defects in SiO_2[10].

Another example, taken from a completely different field, is focused on the use of ESR micro-imaging for mapping oxygen in sub-mm sized tissues. Oxygen (O_2) plays a central role in most living organisms. The concentration of O_2 is important in physiology and pathology. Despite the importance of accurate knowledge of the O_2 levels, there is very limited capability to measure with micron-scale spatial resolution its distribution in millimeter-scale live biological samples. Many of the current oximetric methods, such as oxygen microelectrodes and fluorescence lifetime imaging, are compromised by O_2 consumption, sample destruction, invasiveness, and difficulty of calibration. In the case of biological samples, ESR imaging requires the incorporation of a suitable stable and inert paramagnetic spin probe into the desired object. In our work, we used microcrystals of a paramagnetic spin probe in a new crystallographic packing form (denoted tg-LiNc-BuO). These paramagnetic species interact with the paramagnetic oxygen molecules, causing spectral line broadening that is linearly proportional to the oxygen concentration. This new oximetry microimaging method addresses all the problems mentioned above. It is noninvasive, sensitive to physiological oxygen levels, and easy to calibrate. Furthermore, in principle, it can be used for repetitive measurements without causing cell damage. The tissue model used in this research was spheroids of Human Colorectal carcinoma cell line (HCT-116) with a typical diameter of ~600 microns. Most studies of the microenvironmental O_2 conditions inside such viable spheroids carried out in the past used microelectrodes, which require invasive puncturing of the spheroid and are also not applicable to 3D O_2 imaging. High-resolution 3D oxygen maps could make it possible to evaluate the relationship between morphological and physiological alterations in the spheroids, which would help in understanding the oxygen metabolism in solid tumors and its correlation with the susceptibility of tumors to various oncologic treatments. Figure 7 shows a typical example of an oxygen map measured for one of the spheroids. It indicates that there is more oxygen on the exterior parts than in the inner parts, as one would expect for such tissues. It also shows the significant heterogeneity such spheroids may possess with respect to their oxygen concentration.

A third emerging application of high resolution/high sensitivity ESR comes from the regime of basic physics, where ESR can be used as a basis for a quantum computer[11]. Quantum computing (QC) is a relatively new concept that aims at significantly improving the capability to calculate some types of high complexity problems by making use of unique hardware and algorithms from the regime of quantum physics. Unlike regular computers that make use of binary bits that can be either 0 or 1, QC employs quantum bits that can be either 0, or 1, or in a superposition of states, being both 0 and 1 at the same time, with some probability. The latter situation is of course only possible for a quantum system and thus electron spins, which can exist in this strange superposition of states, were found to be one of the leading candidates to be used as such quantum bits. However, beyond the basic concept, much practical work is still needed. For example, one must enable

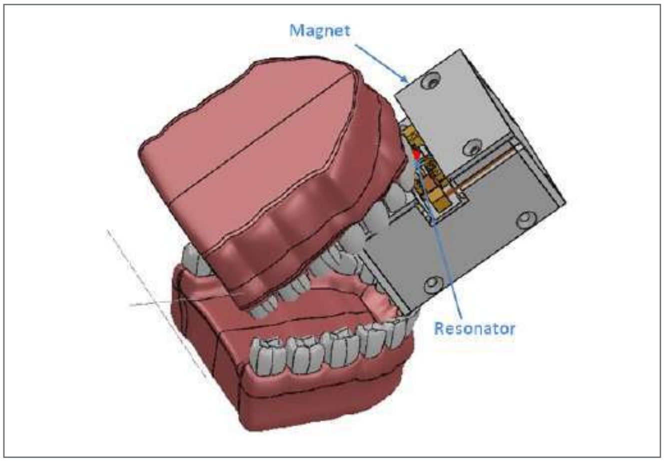


Figure 9: General overview of the compact ESR probehead for ESR measurements of incisor tooth during a projected measurement.

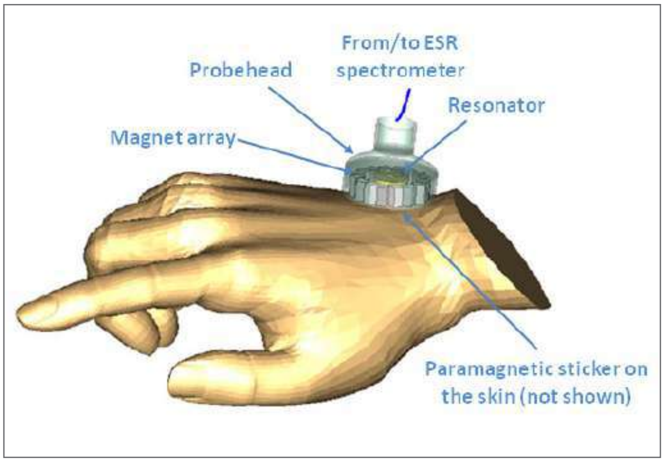


Figure 10: Drawing of the compact skin O_2 ESR probehead, showing the permanent magnet and resonator assembly during a projected in-vivo measurement of skin oxygen level. A special paramagnetic sticker is placed on the skin and the measurement of the relaxation time (T2) of the particles in this sticker provides the oxygen concentration in the skin.

the selective manipulation of these qubits, creating controlled interaction between them to perform calculations, and at the end read out the solution by readout of the state of the electron spins, ideally with single-spin sensitivity and nano-scale spatial resolution. Here is where our high sensitivity/high resolution methodologies come into play in the construction of such unique QC hardware. The basic concept (currently yet only theoretical) is described in Fig. 8[11]. It makes use of an array of multiple identical "computer" vectors of phosphorus-doped silicon where the nuclei serve as logical qubits and the electrons as working qubits. The spins are addressed by a combination of electron spin resonance and nuclear magnetic resonance techniques operating at a field of ~3.3 T and cryogenic temperatures with an ultra-sensitive surface microresonator. Spin initialization to the ground (0) state is invoked by a combination of strong pre-polarization fields and laser pulses. The set of universal quantum gates for this system includes an arbitrary rotation of single qubits and controlled-NOT operation with two qubits. The efficient parallel readout of all the spins in the system is performed by high-sensitivity induction detection of the electron spin resonance signals with one-dimensional imaging.

V. Simple, affordable, and transportable ESR systems

As noted above, the third aspect of magnetic resonance that severely limits its widescale use, is related to the complexity of the systems, their excessive cost and their immobility. Addressing these issues is one of the focal interests of our laboratory, which develops miniature self-contained ESR probes for specific applications, mainly in medicine. However, unlike the cases of sensitivity and resolution improvements, we will not go into the details of the technology behind these devices and simply provide two representative examples that show the scope of our activities in this field.

The first example is a miniature ESR probehead that includes a static field source and a microwave resonator for in-vivo measurement of paramagnetic defects in tooth enamel[12]. These defects are known to be a good marker for quantifying the ionizing radiation dose absorbed in teeth. The probehead has a typical length of just 30 mm and total weight of 220 g. The patient "bites" into the probehead while the measurement procedure is being carried out (Fig. 9). Experimental results with irradiated incisor teeth validated the probehead's sensitivity, being able to detect signals in tooth irradiated by only 2 Gy. Such probe is of importance for fast triage of mass populations that were potentially exposed to ionizing radiation, where a 2 Gy dose serves as a threshold for administrating medical care.

A second example for a compact, simple, and affordable ESR-based measurement system is shown in Fig. 10, which describes a sensor for measuring oxygen content in the skin[13]. Oxygen concentration in the skin is an important clinical indicator for monitoring pathological conditions such as chronic wounds, skin cancer, and peripheral vascular disease. Currently, the only clinically-approved method for acquiring these oxygen levels is based on electrochemical measurements that employ Clarke-type electrodes attached to the skin. This technique has many drawbacks and limitations, making it unattractive for standard medical practice and care. ESR can obtain the oxygen concentration through measurements of the relaxation time (T_2) of paramagnetic species interacting with molecular oxygen and thus provides a possible alternative. However, a traditional ESR setup requires a large homogenous static magnetic field source with a limited gap between the poles and complicated equipment, making it unattractive for clinical use. Our miniature ESR probehead, which is composed of a specially-designed permanent magnet and a small microwave resonator, can be used for these measurements. The small size of the probehead (36 mm diameter cylinder with a height of 24 mm) enables measurements from virtually any part of the skin. Compared to the electrochemical method, this ESR-based approach may provide faster and more accurate readings of oxygen concentration in the skin, making it highly attractive for future clinical use.

VI. Summary and conclusions

The field of magnetic resonance has enjoyed enormous success, but still suffers from some major limitations in terms of sensitivity, imaging resolution, and affordability, which, if solved could boost its impact even further. Our recent work on ESR, which is an indispensable branch of magnetic resonance, has resulted in significant improvement in spin sensitivity (4-6 orders of magnitude) and image resolution (~2 orders of magnitude), as well as showing how compact, simple, and affordable ESR probes can be constructed to address specific applications (mainly in medicine). These new capabilities have already opened the door to unique applications in wide areas of science and technology. Further work along these lines, which include yet additional improvements in sensitivity, image resolution, and simplification of system architectures, are being pursed in our lab. Some of these efforts make use of conventional resonator-based ESR detection approaches, as discussed in this paper, while others look into advanced and alternative techniques such as electrical and optical detection, which may be useful for additional future applications[14; 15].

VII. Acknowledgments

I would like to thank current and past group members that were involved in the construction of our ESR systems and in the application work described in this manuscript: Anton Algin, Yaron Artzi, Ekaterina Dikarov, Dr. Revital Halevy (Herman), Mada Hashem, Shlomo Ish Shalom, Alexander Katchkis, Itai Katz, Sergei Kovel, Michael Levit, Rami Maymon, Michael Nachkovsky, Alon Plattner, Dr. Lazar Shtirberg, Ksenia Sirota, Dr. Yael Talmon, Dr. Ygal Twig, Dr. Nasim Warwar, Helen Wolfson, and Ran Yehiely.

References

[1] I. Rabi, Nuclear magnetic resonance using atomic beam methods (Noble prize lecture, 1944).

[2] F. Bloch, and E.M. Purcell, Nuclear Magnetic Resonance (Noble prize lecture, 1952).

[3] C.H. Townes, N.G. Basov, and A.M. Prokhorov, Maser and laser amplifiers (some of which are based on ESR) (Noble prize lecture, 1964).

[4] N. Bloembergen, and A. Schawlow, The three level maser (Noble prize lecture, 1981).

[5] R.R. Ernst, Development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy (Noble prize lecture, 1991).

[6] K. Wuthrich, Nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution (Noble prize lecture, 2002).

[7] P.C. Lauterbur, and P. Mansfield, Discoveries concerning magnetic resonance imaging (Noble prize lecture, 2003).

[8] Y. Artzi, Y. Twig, and A. Blank, Induction-detection electron spin resonance with spin sensitivity of a few tens of spins. Appl. Phys. Lett. 106 (2015).

[9] L. Shtirberg, Y. Twig, E. Dikarov, R. Halevy, M. Levit, and A. Blank, High-sensitivity Q-band electron spin resonance imaging system with submicron resolution. Rev. Sci. Instrum. 82 (2011) 043708.

[10] E. Dikarov, R. Shklyar, and A. Blank, New Approach for Measuring Migration Properties of Point Defects in Amorphous Oxides. physica status solidi (a). 211 (2014) 2177–2183.

[11] A. Blank, Scheme for a spin-based quantum computer employing induction detection and imaging. Quantum Information Processing 12 (2013) 2993-3006.

[12] H. Wolfson, R. Ahmad, Y. Twig, B. Williams, and A. Blank, A magnetic resonance probehead for evaluating the level of ionizing radiation absorbed in human teeth Health Phys. 108 (2015) 326-35.

[13] H. Wolfson, R. Ahmad, Y. Twig, P. Kuppusamy, and A. Blank, A Miniature Electron Spin Resonance Probehead for Transcutaneous Oxygen Monitoring. Appl Magn Reson 45 (2014) 955-967.

[14] I. Katz, M. Fehr, A. Schnegg, K. Lips, and A. Blank, High Resolution Microimaging with Pulsed Electrically-Detected Magnetic Resonance J. Magn. Reson. 25 (2015) 26–35.

[15] A. Blank, G. Shapiro, R. Fischer, P. London, and D. Gershoni, Optically Detected Magnetic Resonance Imaging. Appl. Phys. Lett. 106 (2015) 034102.

[16] A. Blank, E. Dikarov, R. Shklyar, and Y. Twig, Induction-detection electron spin resonance with sensitivity of 1000 spins: En route to scalable quantum computations. Phys. Lett. A 377 (2013) 1937-1942.

[17] Y. Twig, E. Dikarov, and A. Blank, Cryogenic electron spin resonance microimaging probe. J. Magn. Reson. 218 (2012) 22-29.

[18] Y. Twig, E. Dikarov, W.D. Hutchison, and A. Blank, Note: High sensitivity pulsed electron spin resonance spectroscopy with induction detection. Rev. Sci. Instrum. 82 (2011) 076105.

[19] W. Harneit, C. Meyer, A. Weidinger, D. Suter, and J. Twamley, Architectures for a spin quantum computer based on endohedral fullerenes. Physica Status Solidi B-Basic Research 233 (2002) 453-461.

[20] J.J.L. Morton, A.M. Tyryshkin, R.M. Brown, S. Shankar, B.W. Lovett, A. Ardavan, T. Schenkel, E.E. Haller, J.W. Ager, and S.A. Lyon, Solid-state quantum memory using the 31P nuclear spin. Nature 455 (2008) 1085-1088.

NMR of proteins: Eavesdropping on molecular events

Jordan Chill
Department of Chemistry, Bar Ilan University, Ramat Gan, 52900, Israel
Email: Jordan.chill@biu.ac.il

Abstract: Proteins owe their amazingly diverse and efficient biological activities to their three-dimensional structure and concerted movements of these structural elements. Therefore, understanding biological events on the molecular level requires a structural view of proteins. Nuclear magnetic resonance (NMR) has emerged over the past few decades as a leading method in providing this information, as measureable parameters such as chemical shifts, spin-spin couplings and relaxation rates have been closely correlated to protein structure and dynamics. Using the bacterial potassium channel KcsA as a model system, this article will demonstrate the power of NMR in eavesdropping and reporting on molecular events such as ion conduction, pH-gating and channel-blocking by an inhibitor. Experimental results leading to these molecular conclusions are presented with brief reference to their underlying NMR principles, highlighting the ability of structural NMR methodologies to impact modern biochemical research and drug design.

Protein structure and dynamics

Biological function cannot be imagined without proteins, or polypepetides, polymers composed of the 20 proteogenic α-amino acids. Proteins are responsible for a wide range of cellular tasks and events, including (to name a few) catalysis, recognition, the immune response, transport, cell structure and skeleton, signaling, and neurotransmission. They owe these fascinating capabilities to their three-dimensional structures that create interaction surfaces with unique patterns of charged, polar, and hydrophobic patches. Together, these grant proteins their affinity to ligands and other proteins and ability to perform their function in potent and often highly selective fashion. While structure is not a prerequisite of biological function – indeed, some polypeptides known as intrinsically disordered proteins (IDPs) lack stable structure yet have important biological roles – the two are clearly closely correlated. This accounts for the development of the field of structural biology over the past few decades, emphasizing the structure-function paradigm in understanding proteins and investing extensive research efforts in determining the structure of proteins, typically by X-ray crystallography or by nuclear magnetic resonance (NMR). Also important are protein dynamics, non-random fluctuations in protein structure, which are often at the heart of a biological event; examples of this include the opening/closing of a catalytic site while binding a ligand and conformational changes allowing two proteins two interact. It is clear that a molecular understanding of how proteins fulfill their cellular obligations requires a comprehensive view of protein structure and dynamics.

Biomolecular NMR: opportunities and challenges

Nuclear magnetic resonance (NMR) is a spectroscopy based on a fundamental physical property of atoms, nuclear spin. When placed in a magnetic field the quantum properties of spins divide them into two populations separated by an energy difference. Since the width of this gap depends upon molecular and electronic structure, the absorption spectrum under magnetic field (in the radio-wave MHz range) reflects the location of the observed nuclei (www.nobelprize.org/nobel_prizes/physics/laureates/1952/purcell-lecture.pdf). In the case of proteins, the number of observable nuclei (sometimes thousands) precludes their identification by standard methods. Instead, new methodologies have been developed for proteins, notably isotopic labeling, heteronuclear NMR

Jordan Chill received his BSc in Chemistry summa cum laude from Tel Aviv University, and his PhD (with distinction) from the Weizmann Institute under supervision of Prof. Jacob Anglister (Structural Biology). His PhD work was awarded the Ester Helinger Excellence Prize. Chill conducted his post-doctoral studies as an EMBO fellow in the laboratory of Dr. Adriaan Bax at the National Institutes of Health (Bethesda, MD, USA) where he studied the structure and function of the KcsA potassium channel using nuclear magnetic resonance (NMR) methods. Since 2007 Chill heads the Biomolecular NMR group at Bar Ilan University, and in 2014 he was appointed Associate Professor. The Chill group employs sophisticated NMR methods complemented by other biophysical approaches to investigate protein structure, protein-protein interactions, membrane-associated proteins and intrinsically disordered proteins, all in the context of biological function, health and disease.

and multidimensional NMR, which together allow individual nuclei to be assigned to observed frequencies in the spectrum (see[1,2] for additional reading). While this article highlights the abilities of high-resolution NMR recorded in liquid samples, it should be mentioned that proteins may be studied in the solid state. The main difference between the two methods is that high-resolution NMR requires rapid re-orientation of the studied protein (typical self-rotation times of < 50 ns), whereas solid state NMR does not stipulate this requirement but encounters other experimental difficulties beyond the scope of this article[3,4]. A corollary to this is that high-resolution NMR hits against a 'size-frontier', currently ranging in the 50-400 kDa size depending on the desired information, beyond which re-orientation is too slow and quality spectra can no longer be obtained.

At the heart of biomolecular NMR applications to structure biology lies the fact that measureable NMR parameters have been systematically correlated with structural parameters; in other words, NMR measurements can be interpreted in terms of protein structure. This is summarized in Table 1.

A first step towards this implementation of NMR methods is the 'assignment' process, in which the resonance frequencies in the spectrum are identified with the magnetically-active nuclei of the protein, whose primary sequence is typically known[1,14]. Once the assignment is in place the data obtained can be related to a particular atomic distance or dihedral angle, eventually leading to structural information. Briefly summarized, the main advantages of high-resolution NMR over other methods (particularly its methodological nemesis, X-ray crystallography) are: (i) structural information is obtained in solution, the native environment of proteins, rather than in a crystalline state, (ii) protein motions and conformational fluctuations on a wide timescale range can be detected, (iii) NMR is particularly adept at studying high- and low-affinity protein complexes as well as unstructured proteins, often inaccessible to other methods.

The bacterial potassium channel KcsA

In the next few sections I would like to demonstrate the power of NMR in characterizing protein structure, dynamics and function for the well-known bacterial potassium channel KcsA. Thus, a few words of introduction to this extraordinary protein are in order. KcsA, a protein assembly from the soil-residing bacterium Streptomyces lividans, is embedded in the bacterial cell membrane and responsible for cellular K+ influx and efflux. Determination of the KcsA structure by crystallography in 1998[15] revealed several salient features of the channel. Each channel is comprised of four identical subunits arranged around an axis of symmetry, thus forming a pore. The channel has a 'turret' extracellular domain to which channel inhibitors bind, a membrane-spanning domain including the selectivity filter and an extracellular segment. The membrane-embedded region of the channel is highly hydrophobic and is comprised of two long α-helices that span the membrane width (~34 Å) and a shorter helix ('pore' helix) stretching across the membrane. The latter supports the selectivity filter, a sequence of five amino acids Thr-Val-Gly-Tyr-Gly whose carbonyl oxygens protrude into the center of the pore and provide an energetic surrogate for solvation water ligands as they are shed by K+ ions crossing the membrane. This explains why ions larger – and, ironically, also smaller – than K+ fail to enter the pore. Notably, the 5-residue sequence is conserved in all prokaryotic and eukaryotic K+-channels[15]. Figure 1 schematically describes the KcsA channel. The

Table 1: NMR measureables and related parameters of proteins structure and dynamics

NMR measurement	Related to….	Notes
chemical shift	dihedral angle	Correlated to secondary structure via the backbone dihedral angles.[5-7]
scalar coupling	dihedral angle	^{3}J couplings extensively studied (Karplus equations).[8,9]
dipolar coupling	bond orientations	Often detected as "residual" dipolar couplings (i.e. when isotropic tumbling is perturbed) in solution NMR.[10]
Overhauser effect	^{1}H-^{1}H distances	Intensity is proportional to the inverse sixth power of the distance.[1]
relaxation rate	motions (ps to sec)	nuclear relaxation (typically of amide ^{15}N or carbonyl ^{13}C) under different mechanisms reports on different timescales of motion.[11]
paramagnetic relaxation	nucleus-electron distance	Spin-label is tethered to the protein and its effects used to measure intra- or inter-protein distances.[12,13]
proton exchange with solvent	protection factor, protein folding	Signal disappearance due to exchange is related to solvent exposure.[1]

opening and closing of channels is often controlled by a cellular stimulus such as membrane potential ('voltage-gating') or binding of a ligand (i.e. 'nucleotide-gating'), a behavior which will be modulated by an adjacent protein domain. KcsA lacks such a function but is known to open upon exposure to protons ('pH-gating')[16,17].

Case study 1: Structure and function of the channel

As proteins come, KcsA presents a considerable challenge. It is ~68 kDa in molecular weight (four subunits of 17 kDa each) and as a membrane protein must be solubilized in detergent- or lipid-micelle to be viable in aqueous solution, further raising the size of the assembly to 120-170 kDa depending on choice of detergent. On the other hand, two favorable factors in studying KcsA are the four-fold symmetry of the channel, meaning that all four subunits give the same spectrum, and its thermophilic nature, allowing measurements to be conducted at the advantageous temperature of 45-50 °C. Using 3D triple-resonance NMR (correlating three different nuclei, ^{1}H, ^{15}N and ^{13}C) we could determine the resonance frequency of each nucleus in KcsA. An immediate result of this was the identification of secondary structure in the channel, the two transmembrane (TM) helices, the pore helix as well as a helical region in the intracellular C-domain (Figure 2).

To confirm that the channel is stabilized by the detergent (sodiumdodecylsulfate, SDS, known more for its denaturing properties) we followed a K^+-titration by NMR. The spectrum clearly identified residues near the selectivity filter affected by K^+ occupancy, and successfully established the affinity of ions to this site, obtaining a similar value (K_d = 3 mM) to that determined using other methods (Figure 3)[18]. Thus, NMR successfully identified the fold of KcsA and could be used to follow binding of ions in the closed state of the channel. Additional experiments later characterized the interaction of the channel with detergent molecules and its dynamics within the TM domains that contribute to its biological activity[19].

Case study 2: The pH-gating role of the intracellular C-terminal domain

Our focus was next transferred to the C-terminal domain (CTD) of KcsA, a stretch of 40 residues that extend into the bacterial cytoplasm. Due to the relative flexibility of this region it was absent from the original crystal structure. It was shown by various biophysical methods[18,20], and proven in a later crystal structure[21,22], that the CTD adopts a helical conformation, and that the four subunits associate into a helical bundle. However, pH gating in the CTD remained a controversial issue. pH is known to trigger the opening of the turret region and the lower gate, the crossing point of the four TM-helices, but its effect on the CTD was the subject of several studies with contradictory results[23,24].

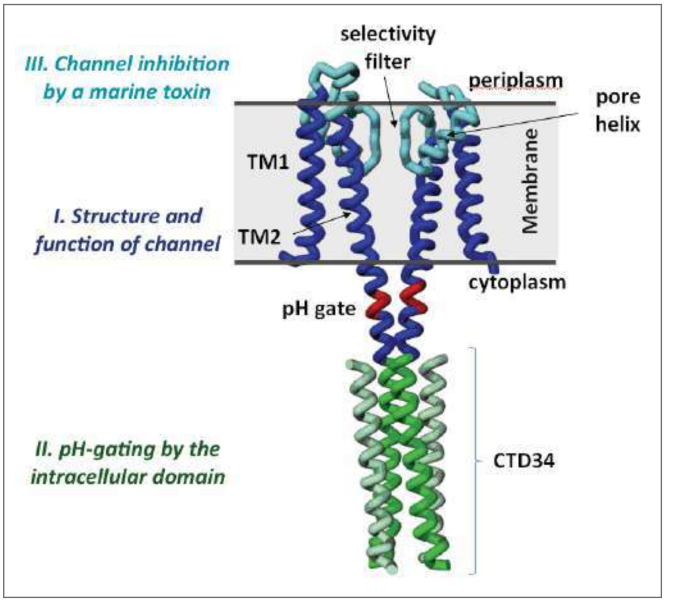


Figure 1: Schematic representation of the KcsA channel. The diagram shows structural features of the channel and highlights the regions discussed in the text. (Adapted from[25].)

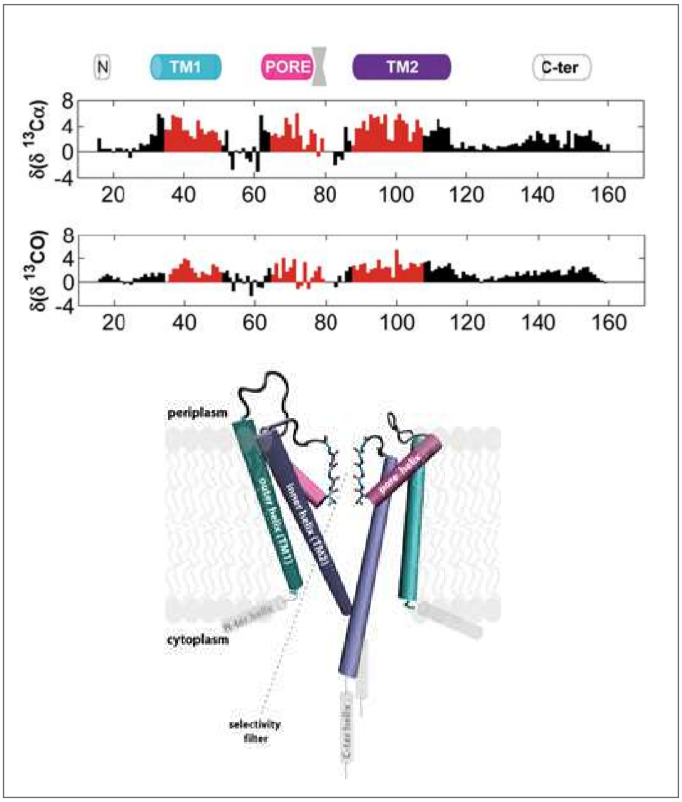


Figure 2: Secondary structure of the KcsA channel. Top, secondary chemical shifts of $^{13}C'$ and $^{13}C\alpha$ nuclei along the KcsA backbone reveal the transmembrane and pore helices and the helical tendency of the cytoplasmic domain. **Bottom**, schematic channel structure with structural elements color-coded. (Adapted from[18].)

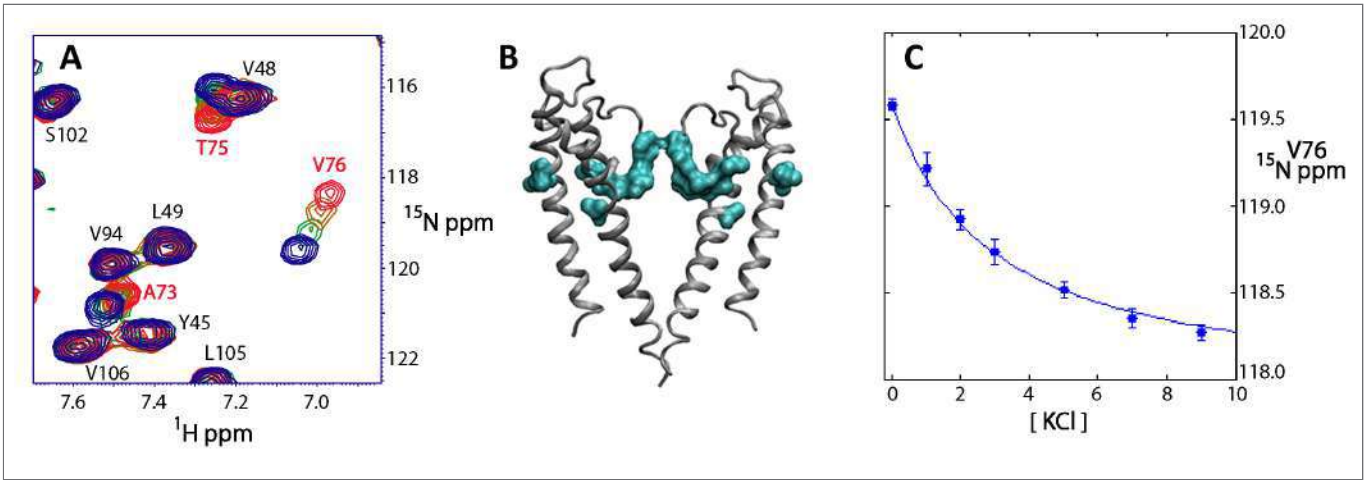


Figure 3: Schematic representation of the KcsA channel. (A) Region of ^{15}N, ^{1}H-TROSY-HSQC spectrum revealing changes induced by titration of KCl. **(B)** Residues affected by K^+-titration are shown, indicating the site occupied by the ion. **(C)** Since the shift in peak position is proportional to occupancy fraction these results were utilized (specifically using residue V76) to determine the binding constant of K^+ to the channel selectivity filter. (Adapted from[18].)

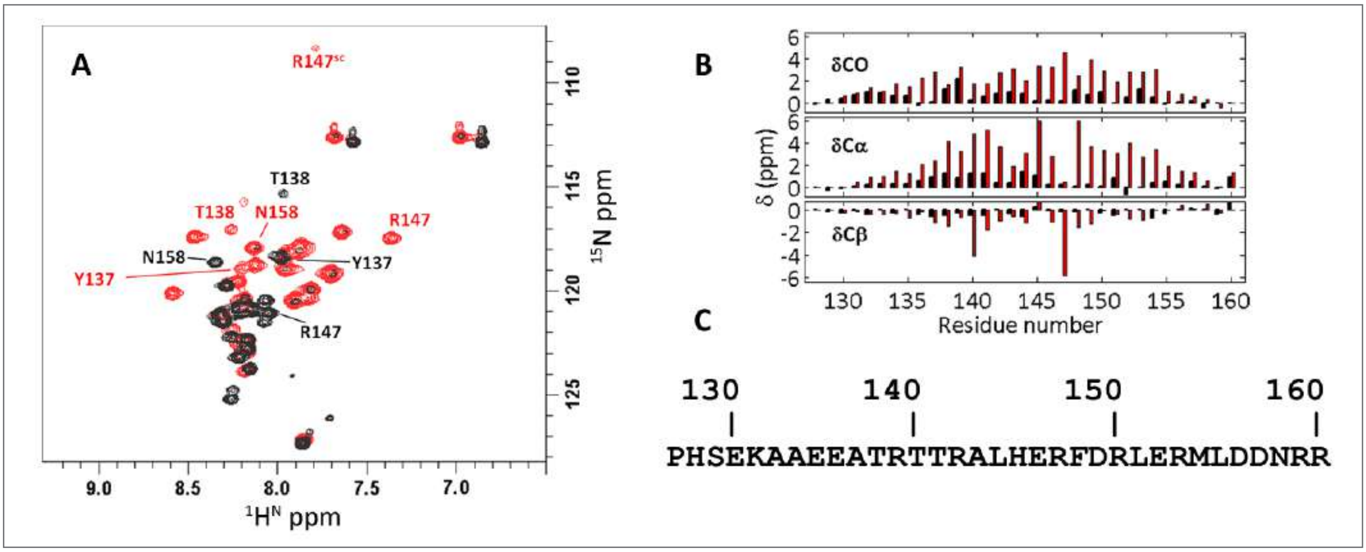


Figure 4: The helical cytoplasmic domain undergoes oligomerization. (A) ^{15}N, ^{1}H-HSQC spectrum of the CTD34 peptide at low (0.2 mM, black) and high (2.7 mM, red) concentration., with key residues labeled. Both spectra were acquired at 298 K on a 700 MHz spectrometer in phosphate buffer (10 mM) and NaCl (20 mM) at pH 7.3. **(B)** Secondary chemical shifts (^{13}C', ^{13}Cα, ^{13}Cβ) of the CTD reveal a helical tendency for the monomer and a well-formed helix for the oligomer. **(C)** Amino acid sequence of the CTD34 peptide. (Adapted from[25].)

To address this question, we prepared an isotopically labeled polypeptide containing the last 34 residues of the CTD (CTD34) and followed its behavior in solution. The 'fingerprint' spectrum of CTD34 (Figure 4), in which the amide ^{1}H,^{15}N pair of each residue affords a single cross-peak, exhibited a concentration-dependent behavior which could only be accounted for by an oligomerization event. Appearances of the spectrum obtained at low and high concentrations suggested an increase in structural 'compactness' in the latter case, and using ^{13}C chemical shifts as described in the previous section we determined that the high-concentration form of CTD34 was strongly helical, but, interestingly, its low-concentration form was partially helical as well. Final verification of the oligomer as a tetramer (as expected for the four-fold symmetrical channel) was not possible by NMR, and was eventually determined using sedimentation equilibrium (SE) (Figure 5)[25]. While it had been known that the cytoplasmic domain contributes to the overall stability of the channel, here was first convincing evidence that it represents an independent tetramerization domain.

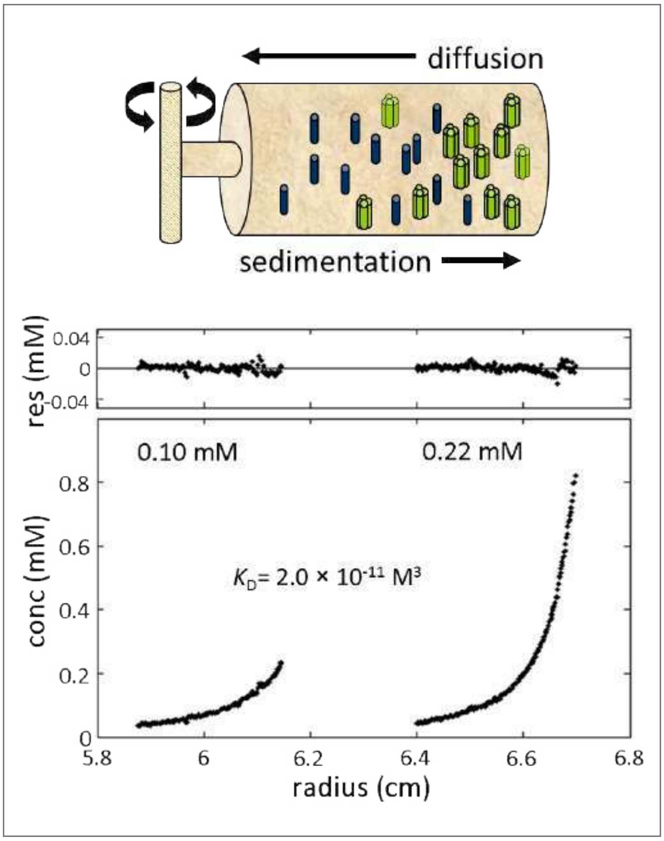


Figure 5: Sedimentation equilibrium determines CTD34 to be a tetramer. Top, schematic representation of the sedimentation equilibrium (SE) experiment for CTD34 which is an interchanging mixture of monomer (blue) and tetramer (green). While sedimentation pushes the more dense proteins away from the axis of rotation, diffusion negates this process. Eventually a steady-state impasse between these two forces is established and protein locations are fixed. Since proteins of different sizes behave differently under this combined force effect, the ensuing gradient of protein concentration can be interpreted in terms of molecular mass (i.e. tetramer concentration is higher away from the axis, monomer concentration is higher close to the axis). **Bottom**, SE curves at two concentrations recorded at identical conditions to NMR experiments and at 40,000 rpm. Fitting of the concentration vs. distance-from-axis curves to the monomer-oligomer model of exchange results in an optimal fit for n=4 (i.e. a tetramer) and a K_d of 2 x 10^{-11} $M^{3,}$ in excellent agreement with NMR results. (Adapted from[25].)

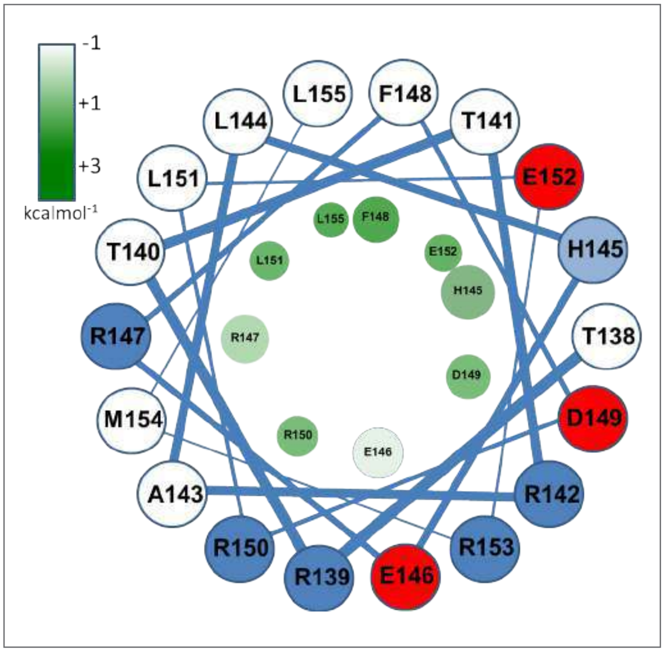


Figure 6: Helical wheel representation of CTD34 with contributions to tetramerization. Residues 138-155 are shown in 'helical wheel' format that emphasizes the spatial location of reach residue. Color coding is blue (red) for positively (negatively) charged, light-blue for H145, and white for hydrophobic residues. The polar face (right-bottom) and hydrophobic face (left-top) of the peptide are evident, as is the unique position of residue R147. The inner circle shows residues mutated to Ala and color-codes their contribution to tetramer stability from high (dark green) to low (light green). Circles representing the residues decrease in size in moving from the N- to the C-terminus of CTD34. (Adapted from[26].)

This experimental platform allowed us to answer two important questions regarding CTD function, (i) which structural elements contribute to tetramer formation, and (ii) is this region of the channel pH-sensitive? Using NMR and SE we measured the stability of 12 CTD peptides mutated to Ala at one position, a method known as alanine-scanning mutagenesis (Figure 6). This approach identified three factors contributing to tetramer stability, here in order of decreasing importance: (i) The strong hydrophobic interaction between residues lining the inner face of the helical bundle (e.g. Phe148, Leu151, Leu155), (ii) electrostatic inter-subunit interactions between charged residues (e.g. Arg147, Asp149, Glu152), (iii) residues contributing to the inherent helicity of CTD34 (e.g. D157, R159, charged residues at the C-terminal end of the helix)[26]. The dominance of the hydrophobic effect is somewhat surprising in light of the emphasis placed on the central electrostatic motif in the crystal structure, yet is perfectly consistent with the modern view of protein folding and its rate-determining forces.

The role of Arg147 is unique in this context; although it is anomalously located on the hydrophobic face of CTD34, its side-chain charge is stabilized by neighboring Asp149 and Glu152 of the adjacent subunit. This is why mutating Arg147 to Ala has only a minor effect upon tetramerization – Ala is a helix-promoting residue that feels quite at home on the hydrophobic face, and the stabilizing side-chains can easily re-orient themselves towards the aqueous environment. In contrast, similarly mutating Asp149 or Glu152 abolishes the tetramer because Arg147 loses its electrostatic underpinning and pays a high energetic penalty for being 'stranded' in the hydrophobic region of the peptide.

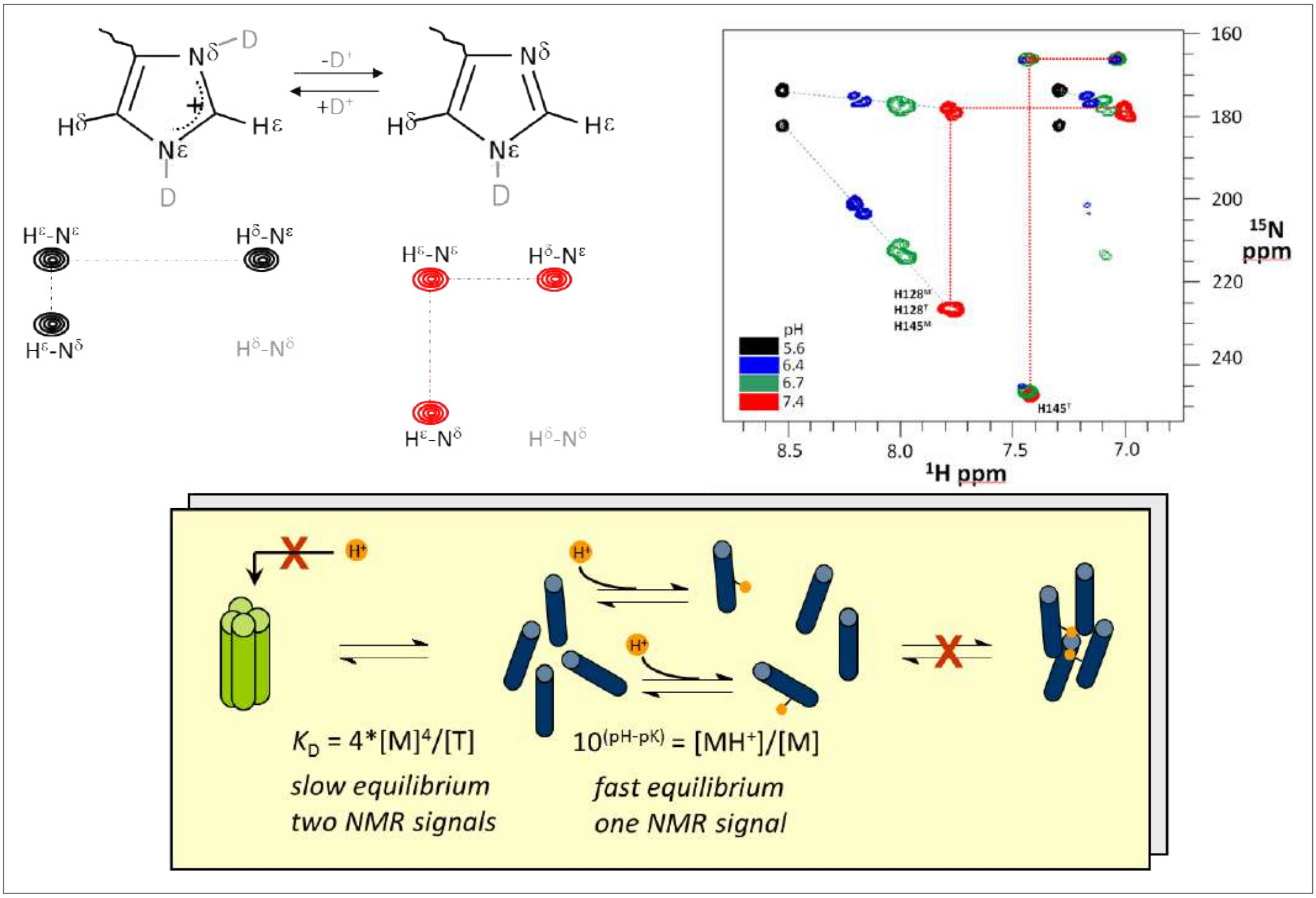


Figure 7: Protonation of His145 is the mechanism for pH-induced dissociation of CTD34. Top left, the imidazole ring and its typical chemical shifts in (un)protonated form. **Top right**, long-range ^{15}N,^{1}H-HMQC spectrum acquired for a 1.2 mM CTD34 sample at various pH values ranging from 7.4 (red) to 5.6 (black). Red dashed lines show the imidazole ring patterns for a pH of 7.4; blue dashed lines indicate the gradual shift of the imidazole rings shifts of His128 (monomer/tetramer) and His145 (monomer) from the $N^{\varepsilon 2}$-H tautomer to the protonated form. **Bottom**, model of pH-induced dissociation is shown. Reversible dissociation of CTD34 is disrupted by protonation of the monomeric form which cannot return to the tetrameric state. (Adapted from[25].)

Finally, the presence of residue His145 in the critical core region of the tetrameric bundle made it a potential source of pH sensitivity, since this is the only residue with an ionizable group with a pKa value in the pH 4-7 range. A long-range heteronuclear NMR correlation experiment was used to follow the protonation state of this residue (Figure 7), and indeed the monomer-to-tetramer shift could be accounted for by protonation on this imidazole ring. Furthermore, this 'pH-effect' was abolished by the His-to-Ala mutation at position 145. These results put to rest the controversy as to the role of the CTD in pH-gating of KcsA[25]. A biological interpretation of this 'pH-switch' is not straightforward; one possible explanation is that a small rise in intracellular proton levels may signal the need for increased efflux of the positively charged potassium to maintain membrane polarization level, and this would be achieved by a subtle change in the CTD. Further light may be shed on this matter by extending our NMR study to full-channel and even cellular levels, and these approaches are currently being explored.

Case study 3: The molecular basis of channel inhibition by a marine toxin

An important aspect of the biochemistry of ion channels is the ability of various natural compounds to inhibit their activity, often by physically occluding the conduction pore. Typically, such toxins are short polypeptides (20-70 amino acids) rigidified by multiple crosslinking disulfide bonds and found in marine lifeforms (sea anemones) as well as in terrestrial ones (scorpions, snakes and spiders). One well known toxin is ShK, found in the Stichodactyla helianthus sea anemone of the Caribbean Sea, which binds to the human voltage-gated Kv1.3 channel at picomolar affinity[27]. The 35-residue ShK has attracted some pharmaceutical research because Kv1.3 is

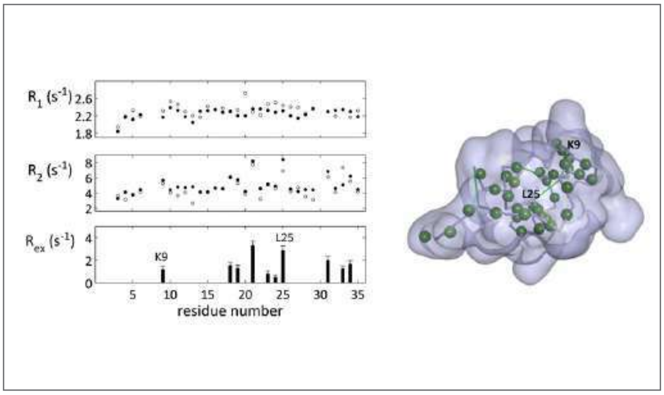


Figure 8: ^{15}N relaxation rates reveal slow motions in the ShK toxin. Left, relaxation rates in the Z-direction (R_1, upper panel), and X-Y direction (R_2, middle panel); data obtained at 700 (600) MHz shown in filled (open) circles. Calculated contribution of slow motions to relaxation (R_{ex}, bottom panel) is shown as bars for relevant residues. Right, the ShK toxin shown as a space-filling surface (grey) and highlighting backbone ^{15}N nuclei. As an example, two of the ^{15}N nuclei affected by slow motions, Lys9 and Leu25, are labeled. (Adapted from[32].)

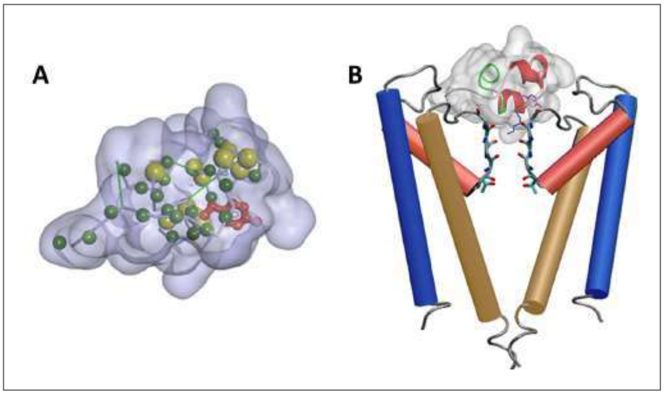


Figure 9: Analysis of relaxation rates suggests a role for a minor conformer in ShK binding to the potassium channel. (A) structure of the ShK toxin highlighting ^{15}N nuclei (green), residues affected by slow motion (yellow) and their proximity to key residue Tyr23 (red). **(B)** ShK fits into the vestibule of the channel (depicted with cylinders for helices and stick-mode for the selectivity filter) by inserting residue Lys22 (blue) into the selectivity filter and interacts with turret residues via residue Tyr23 (magenta). Although the known structure of ShK is shown, it most likely interacts with the channel in a more open conformation for which the structure cannot be determined based on the currently available data. (Adapted from[32].)

prominent in T cells responsible for autoimmune diseases, and blocking it has been shown to reduce symptoms of multiple sclerosis and rheumatoid arthritis. The key here, however, is selectivity: in its current form ShK will also block the Kv1.1 channel, with untenable side-effects upon heart and kidneys. It remains a promising lead compound that could form the basis for blockers with improved potency and selectivity, and clinical trials of ShK-inspired homologs are underway[28]. This underlines the importance of understanding the structural basis for binding of ShK to channels – armed with this information the drug design process can be greatly streamlined.

Recently ShK became available in isotopically labeled form – by bacterial expression rather than chemical synthesis[29] – providing the possibility of characterizing its molecular motions using ^{15}N relaxation measurements, since (without digressing into an elaborate theoretical discussion[11,30,31]) there is a strong relation between polypeptide dynamics and relaxation rates, which are the rates at which the NMR magnetization returns to its equilibrium state in each of the three axes. Polypeptide motions are usually divided into global 'tumbling' motion, typically in the ns range for proteins, and local motions that may be either faster (e.g. sub-ns motions of an amino-acid side-chain) or slower (e.g. ms motions of an entire protein domain) than molecular tumbling. The pattern of relaxation rates observed for a particular amino acid can distinguish between these possibilities and thus shed light on the behavior of the polypeptide chain. ShK exhibited an overall tumbling time of ~2.5 ns, consistent with its molecular size (approximate molecular diameter of 20 Å) but also an increase at several residues in relaxation of magnetization in the X-Y plane typically resulting from slow movements on the ms timescale (Figure 8). More sophisticated relaxation measurements established that the detected movement reflects an exchange equilibrium occurring at ~ 5,000 per second between the known structure of ShK and a minor (less than 0.5%) conformer[32]. Faster relaxation in this case stems from the loss of signal to chemical exchange (e.g. some of the molecules have shifted to the minor form and no longer contribute to signal in the spectral position of the major conformer) rather than the usual release of energy to nearby spins.

The minor conformer is far below the detection level, and therefore cannot be directly observed by NMR. However, it had left us spectral clues to its nature. We observed that all residues affected by the exchange phenomenon were clustered around residue Tyr23, a key residue on the channel-binding surface, whose absence reduces binding affinity by three orders of magnitude. The importance of Tyr23 is somewhat perplexing in view of the fact that it is has little exposure to the solvent (and therefore should not be able to 'feel' the channel') as compared to other residues in this region. Our relaxation results hint that the minor conformer might be less structured (supported by the chemical shift results) and more 'open' so as to expose Tyr23 to channel interactions, as demonstrated in Figure 9. In other words, the channel may recognize the minor conformer only and exert conformational selectivity which would eventually draw the equilibrium towards binding of the entire inhibitor population[32]. Such a mechanism has been proposed in the binding of other toxins and inhibitors[33,34] and so appears highly plausible. This information is clearly of great importance when designing new inhibitors; polypeptides resembling the 'open' minor conformer and stabilized in this more energetic conformation would be expected to bind the channel at higher affinity, providing us with a basic yet effective criterion for inhibitor design.

Summary

In investigating three aspects of potassium channel KcsA structure and dynamics – overall fold, tetramerization and pH sensitivity, and binding of the ShK blocker – we have demonstrated the ability of biomolecular NMR to follow biological processes on the atomic level. Chemical shifts, their titration-induced perturbations, and magnetization relaxation rates were interpreted in terms of molecular structure and motions, providing a real-time view of ongoing events in the behavior of the channel. It is evident that this powerful approach has important implications on how we perceive molecular processes in biological systems, as well as upon the application of this knowledge to the design of more potent and selective protein ligands, leading to structure-based drug design capabilities. The examples brought here are paralleled by others in the study of protein-protein and protein-nucleic acid interactions, intrinsically disordered proteins, aggregation-prone and misfolded proteins, and ultra-large protein assemblies. It is my belief that continuous methodological development will enable NMR to address more complex and challenging systems in the future, allowing it to continue eavesdropping on molecular events and providing us with useful and intriguing secrets of the protein kingdom.

Acknowledgements

The work described here has resulted from the efforts of several students and colleagues of mine. I would like to acknowledge the contributions of John Louis, Frank Delaglio and Ad Bax (NIH, Bethesda, MD, USA) to the earlier part of this work, my graduate students Guy Kamnesky, Inbal Sher and Orel Hirschhorn for the later part of this work, all other group members for support and helpful discussions, and my collaborators, Shih Chieh Chang, Sandeep Chhabra and Raymond Norton (Monash University, Parkville, Australia), Ying Li (University of Louisville, Louisville, KY, USA), Arthur G. Palmer III (Columbia University, New York, NY, USA), and Jingfei Chen and Lishan Yao (Qingdao Institute of Bioenergy and Bioprocess Technology, Qingdao, Shandong, China) for their strong support. I also acknowledge the ongoing assistance of my research associate Hadassa Shaked as well as Eva Meirovitch for ever-helpful insight and comments. I am grateful to all. Research described here was conducted with the support of a long-term EMBO fellowship, an NIH post-doctoral fellowship, the Converging Technologies fund and the Christians for Israel Chair for Medical Research.

References

1. Wuthrich, K. (1986). *NMR of proteins and nucleic acids*.
2. Cavanagh, J., Fairbrother, W. J., Palmer III, A. G., Skelton, N. J. & Rance, M. (2006). *Protein NMR Spectroscopy, Second Edition: Principles and Practice*.
3. Zhou, D. H., Shea, J. J., Nieuwkoop, A. J., Franks, W. T., Wylie, B. J., Mullen, C., Sandoz, D. & Rienstra, C. M. (2007). Solid-state protein-structure determination with proton-detected triple-resonance 3D magic-angle-spinning NMR spectroscopy (2007). *Angew. Chem. Int. Ed. Engl.*, **46(44),** 8380-8383.
4. Weingarth, M. & Baldus, M. (2013). Solid-state NMR-based approaches for supramolecular structure elucidation. *Acc. Chem. Res.* **46**, 2037-2046.
5. Shen, Y. & Bax, A. (2010). SPARTA+: a modest improvment in empirical NMR chemical shift prediction by means of an artificial neural network. *J. Biomol. NMR* **48,** 13-22.
6. Wishart, D. S. & Case, D. A. (2001). Use of chemical shifts in macromolecular structure determination. *Meth. Enz.* **338**, 3-34.
7. Cavalli, A., Salvatella, X., Dobson, C. M. & Vendruscolo, M. (2007). Protein structure determination from NMR chemical shifts. *Proc. Natl. Acad. Sci. USA* **104**, 9615-9620.
8. Karplus, M. (1963). Vicinal proton coupling in nuclear magnetic resonance. *J. Am. Chem. Soc.* **85**, 2870-2871.
9. Bystrov, V. F. (1976). Spin-spin coupling and the conformational states of peptide systems *Prog. NMR Spectroscopy* **10**, 41-82.
10. Bax, A., Kontaxis, G. & Tjandra, N. (2001). Dipolar couplings in macromolecular structure determination. *Meth. Enzymol.* **339**, 127-174.
11. Palmer III, A. G. (2014). Chemical exchange in biomacromolecules: past, present, and future. *J. Magn. Reson.* **241**, 3-17.
12. Battiste, J. L. & Wagner, G. (2000). Utilization of site-directed spin labeling and high-resolution heteronuclear nuclear magnetic resonance for global fold determination of large proteins with limited nuclear overhauser effect data. *Biochemistry* **39**, 5355-5365.
13. Clore, G. M. & Iwahara, J. (2009). Theory, practice, and applications of paramagnetic relaxation enhancement for the characterization of transient low-population states of biological macromolecules and their complexes. *Chem. Rev.* **109**, 4108-4139.
14. Bax, A. & Grzesiek, S. (1993). Methodological advances in protein NMR. *Acc. Chem. Res.* **26**, 131-138.
15. Doyle, D. A., Cabral, J. M., Pfuetzner, R. A., Kuo, A., Gulbis, J. M., Cohen, S. L., Chait, B. T. & Mackinnon, R. (1998). The structure of the potassium channel: molecular basis of K+ conduction and selectivity. *Science* **280**, 69-77.
16. Cuello, L. G., Romero, J. G., Cortes, D. M. & Perozo, E. (1998).

pH-dependent gating in the Streptomyces lividans K^+ channel. *Biochemistry* **37**, 3229-3236.
17. Heginbotham, L., LeMasurier, M., Kolmakova-Partensky, L. & Miller, C. (1999). Single streptomyces lividans K^+ channels functional asymmetries sidedness of proton activation. *J. Gen. Physiol.* **114**, 551-559.
18. Chill, J. H., Louis, J. M., Miller, C. & Bax, A. (2006). NMR study of the tetrameric KcsA potassium channel in detergent micelles. *Prot. Sci.* **15**, 684-698.
19. Chill, J. H., Louis, J. M., Baber, J. L. & Bax, A. (2006). Measurement of ^{15}N relaxation in the detergent-solubilized tetrameric KcsA potassium channel. *J. Biomol. NMR* **36**, 123-136.
20. Cortes, D. M., Cuello, L. G. & Perozo, E. (2001). Molecular architecture of full-length KcsA: role of cytoplasmic domains in ion permeation and activation gating. *J. Gen. Physiol.* **117**, 165-180.
21. Uysal, S., Vasquez, V., Tereshko, V., Esaki, K., Fellouse, F. A., Sidhu, S. S., Koide, S., Perozo, E. & Kossiakoff, A. (2009). Crystal structure of full-length KcsA in its closed conformation. *Proc. Natl. Acad. Sci. USA* **106**, 6644-6649.
22. Uysal, S., Cuello, L. G., Cortes, D. M., Koide, S., Kossiakoff, A. A. & Perozo, E. (2011). Mechanism of activation gating in the full-length KcsA K^+ channel. *Proc. Natl. Acad. Sci. USA* **108**, 11896-11899.
23. Imai, S., Osawa, M., Takeuchi, K. & Shimada, I. (2010). Structural basis underlying the dual gate properties of KcsA. *Proc. Natl. Acad. Sci. USA* **107**, 6216-6221.
24. Pau, V. P., Zhu, Y., Yuchi, Z., Hoang, Q. Q. & Yang, D. S. (2007). Characterization of the C-terminal domain of a potassium channel from Streptomyces lividans (KcsA). *J. Biol. Chem.* **282**, 29163-29169.
25. Kamnesky, G., Shaked, H. & Chill, J. H. (2012). The distal C-terminal region of the KcsA potassium channel is a pH-dependent tetramerization domain. *J. Mol. Biol.* **418**, 237-247.
26. Kamnesky, G., Hirschhorn, O., Shaked, H., Chen, J., Yao, L. & Chill, J. H. (2014). Molecular determinants of tetramerization in the KcsA cytoplasmic domain. *Prot. Sci.* **23**, 1403-1416.
27. Tudor, J. E., Pallaghy, P. K., Pennington, M. W. & Norton, R. S. (1996). Solution structure of ShK toxin, a novel potassium channel inhibitor from a sea anemone. *Nat. Struct. Biol.* **3**, 317-320.
28. Beeton, C. et al, (2006). Kv1.3 channels are a therapeutic target for T cell-mediated autoimmune diseases. *Proc. Natl. Acad. Sci. USA* **103**, 17414-17419.
29. Chang, S. C., Galea, C. A., Leung, E. W., Tajhya, R. B., Beeton, C., Pennington, M. W. & Norton, R. S. (2012). Expression and isotopic labelling of the potassium channel blocker ShK toxin as a thioredoxin fusion protein in bacteria. *Toxicon* **60**, 840-850.
30. Mandel, A. M., Akke, M. & Palmer, A. G. (1995). Backbone dynamics of Escherichia coli ribonuclease HI: correlations with structure and function in an active enzyme. *J. Mol. Biol.* **246**, 144-163.
31. Kay, L. E. (1998). Protein dynamics from NMR. *Biochem. Cell Biol.* **76**, 145-152.
32. Sher, I., Chang, S. C., Li, Y., Chhabra, S., Palmer III, A. G., Norton, R. S. & Chill, J. H. (2014). Conformational flexibility in the binding surface of the potassium channel blocker ShK. *ChemBioChem* **15**, 2402-2410.
33. Ulens, C., Hogg, R. C., Celie, P. H., Bertrand, D., Tsetlin, V., Smit, A. B. & Sixma, T. K. (2006). Structural determinants of selective a-conotoxin binding to a nicotinic acetylcholine receptor homolog AChBP *Proc. Natl. Acad. Sci. USA* **103**, 3615-3620.
34. Camilloni, C., Cavalli, A. & Vendruscolo, M. (2013). Replica-averaged metadynamics. *J. Chem. Theory Comput.* **9**, 5610-5617.

Chemistry by (Mechanical) Force

Charles E. Diesendruck
Schulich Faculty of Chemistry, Technion – Israel Institute of Technology
Email: charles@tx.technion.ac.il

Abstract: Chemical changes caused by mechanical stress (mechanochemistry) is not a new field in materials science. A chapter dedicated to this subject can be found in older polymer physics books. However, only in recent years has mechanochemistry reappeared as a useful methodology in polymer chemistry and even synthetic organic chemistry. In this article, I review the scientific development of this important energy transduction process, that ultimately led to the development of mechanophores, molecules that selectively respond to mechanical stimuli in a productive way. Finally, I describe some recent work on polymer mechanochemistry and new mechanophores that were developed for different applications, such as using mechanochemical changes to study stress distribution in polymers, change reaction mechanisms or develop new mechanoresponsive materials.

Introduction

Several energy sources are used to drive chemical reactions. Commonly, we use heat to bypass high-energy transition states. In photochemistry, we convert low energy molecules to high-energy reactants using photons. In electrochemistry, we use electrical potential to add or remove electrons and induce the chemical change. Even in reactions where simply mixing two reactants at room temperature leads to products, we make use of the chemical potential stored in high-energy reactants to drive the reaction towards lower energy products.

A different approach that requires a bit of imagination is to use mechanical energy. How can we transmit mechanical energy to molecules? Atomic force microscopy (AFM), where we use a very small tip to attach and pull molecules from surfaces (Figure 1), is a possibility[1]. However, carrying out a reaction molecule by molecule does not look very practical if one wants to prepare large amounts of compounds.

As in many other fields of science, we can look to nature to find some ideas of how to use mechanical force to induce a chemical change. One process that comes to mind is the production of petroleum. Over millions of years, organic remains from living beings are converted under high pressure and temperature to this very valuable liquid. However, waiting millions of years for a chemical process is not a practical option.

A second example is how organisms convert physical signals into chemical responses. How do we feel touch? How do we hear by detecting vibrations of air? The body uses numerous approaches to detect these changes in the mechanical environment such as opening or closing of ion channels and changing the conformation of a protein, among others[3]. The chemical meaning of an ion channel opening or closing or of enzymes changing their activity due to change in conformation are examples of mechanochemical transformations: the formation or breaking of chemical bonds, supramolecular and covalent, through the utilization of mechanical force.

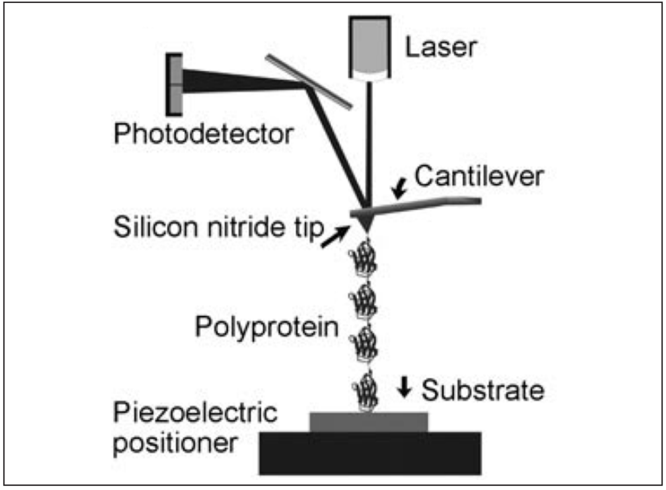


Figure 1: Stretching molecules using atomic-force microscopy[2]. Reproduced from ref. 2. Copyright 2008 Wiley-VCH Verlag GmbH & Co. KGaA.

Charles Diesendruck received his B.Sc. in analytical and environmental chemistry from Ben-Gurion University of the Negev. After serving in the army and working a few years at Chemada Fine Chemicals, he returned to BGU to complete a M.Sc. and a Ph.D. in organometallic chemistry with Prof. N. Gabriel Lemcoff. Diesendruck was a postdoctoral fellow in materials chemistry at the Beckman Institute for Advanced Science and Technology at the University of Illinois at Urbana-Champaign, working at the Autonomous Materials Systems group with Prof. Jeffrey S. Moore. In October 2014, Diesendruck joined the Schulich Faculty of Chemistry at the Technion, doing research in the fields of polymer chemistry and mechanochemistry.

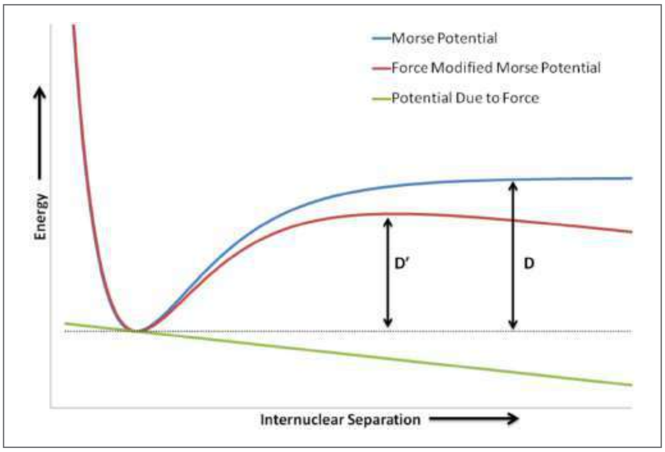


Figure 2: Change in Morse potential due to mechanical potential.

History

While mechanochemistry is not the go-to methodology for today's chemists, it's been in use since the Stone Age[4]. Grinding mixtures with mortar and pestle is at the very beginning of chemistry. Spices were mixed using this methodology, then minerals for the preparation of paints, or plants for the preparation of medicines[5].

From Stone Age to modern times, grinding remained a commonly used methodology, and therefore it's hard to associate a specific scientist with its discovery or definition. For example, Faraday reduced silver chloride by grinding it with metals such as zinc, tin, iron, or copper in the 1820s[6]. However, the first systematic studies on mechanochemistry were carried out by Spring[7] and Carey Lea[8] separately in the 1880s, who looked at how different parameters (pressure, for example) affected these inorganic transformations.

Staudinger carried out the first studies of covalent mechanochemistry of macromolecules in the 1930s[9]. After a long struggle to have the idea of covalent macromolecules accepted by the academic community[10] as opposed to polymers being aggregates of smaller molecules, Staudinger published a work that would make a good argument for the defenders of the aggregate theory. Staudinger ball-milled high molecular weight polystyrene, and observed the reduction of its molecular weight as a function of milling time, up to a limit of ca. 11 kDa. Staudinger proposed that mechanical force was able to break covalent bonds, leading to polymers with reduced molecular weight.

Staudinger's fundamental discovery had important technological significance. Given that several properties of materials depend on the molecular weight of the polymer chains, Staudinger's studies explained at the molecular level why materials lose their function under mechanical stress. Indeed, in the next 50 years, mechanochemistry became an important topic in materials science and engineering, with new polymers and materials being tested for their mechanochemical stability. Only in the 1980s, did mechanochemistry reappear as a useful methodology in polymer chemistry, with Encinas' seminal work in which she demonstrated that mechanochemical bond scission events could be selective if weak bonds were incorporated into the main chain of a polymer[11]. This discovery led to the creation of the mechanophore concept, a chemical functional group that reacts selectively under mechanical stress[12].

Uses of Polymer Mechanochemistry

Encinas' work led to renewed interest in the science behind mechanochemistry. Several groups started studying how force is transmitted in different polymers, and the mechanism of selective mechanochemical reactions. Furthermore, different scenarios were developed where the use of mechanochemistry was very beneficial.

The first interesting use of mechanochemistry is changing the energy plane of a chemical reaction. When mechanical potential is included in a chemical reaction, the reaction thermodynamic space is changed due to the directionality of the applied force. The simplest example of this is covalent bond scission. When a σ bond is mechanically stressed, a potential field is added to the Morse-potential between two atoms, reducing not only the transition state, but also stabilizing the disconnected products (Figure 2)[13]. This remarkable effect has been used in the past to develop new organic transformations, such as making thermally forbidden pericyclic reactions the main mechanism at room temperature[29].

The second use is in the field of materials, where mechanoresponsive materials can be designed utilizing mechanochemical bond scission reactions. This allows us not only to study the distribution of force in stressed materials, but also to change the chemistry of the matrix as a function of stress applied[12].

Stress during swelling of polymeric materials

Mechanophores that change their absorbance or become fluorescent after a mechanical signal have been used to study the distribution of forces in stressed materials. Examples include torsional rheometry[14], tensile testing[15] and compression[16]. The most commonly used mechanophore for these studies is spiropyran (SP), which isomerizes to merocyanine by mechanical activation, yielding a strong red color and fluorescence (Figure 3)[17].

Recently, we used SP to study mechanical stress in the chains of cross-linked poly(methyl methacrylate) (PMMA) during swelling[18]. Polymer swelling is an important process with a wide range of applications in sealants, gels, etc. The driving force for swelling has been well studied and is described by the Flory–Rehner theory[19]. However, there is no model that defines

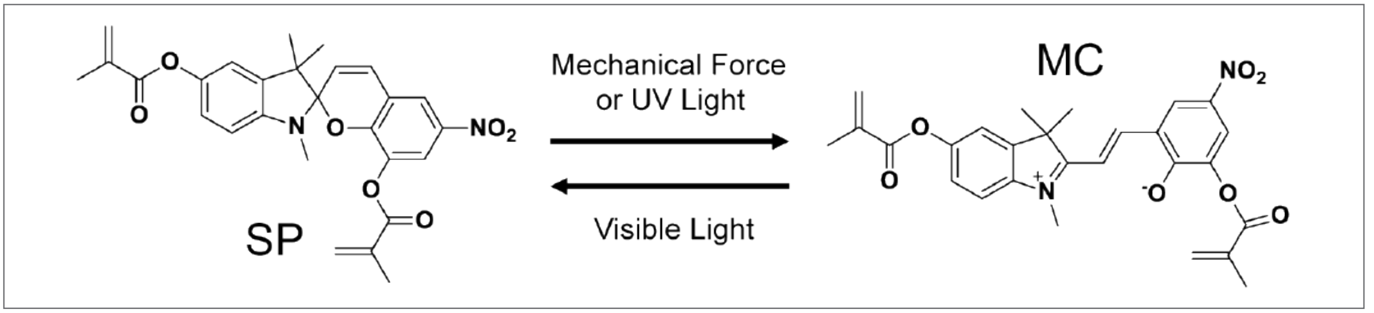


Figure 3: Spiropyran isomerization to merocyanine.

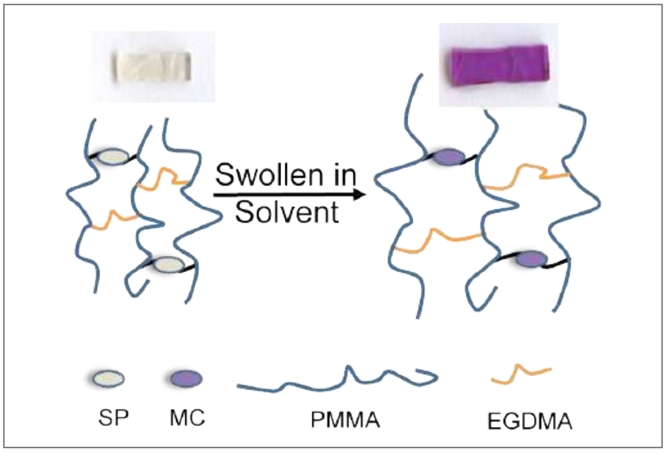


Figure 4: Observing forces during swelling of a SP-containing cross-linked PMMA.

the stress levels created on the polymer chains as they stretch to accommodate the solvent molecules.

We prepared PMMA cross-linked by ethylene glycol dimethacryalte and a small amount of spiropyran dimethacrylate. Measurable pieces of this material were swollen in different solvents and swelling was determined by increase in mass, while mechanochemical activation of SP was measured by fluorescent microscopy. Interestingly, in very good solvents such as chloroform, swelling was very fast and could not be monitored. Moreover, in UV-Vis, we observed a shift in the chemical absorbance of the merocyanine, indicating that its polar environment was changing. Therefore, activation in good solvents could not be compared to other solvents once mechanochemical activation is not the only effect on the fluorescent probe.

In medium-good solvents, such as DMF, acetonitrile and acetone, where no shift in the merocyanine was detected during swelling, we observed that swelling and increase in fluorescence correlated directly. This observation indicates that, during swelling, chains are stretched and enough force to cause SP isomerization is created (Figure 4). Bad solvents such as MeOH and water do not swell the polymer and do not produce any increase in fluorescence. Our studies demonstrated that SP is a useful tool to probe into the stress produced at the molecular level by swelling. We are currently running a systematic study changing cross-link density and comparing swelling to mechanochemical activation in order to develop a model that describes the amount of stress produced during swelling.

Mechanochemical depolymerization

Bone tissue is a mechanoresponsive material which is constantly being removed and deposited in a process called bone remodeling. This mechanically controlled change in the tissue is responsible for healing of fractures and micro-damages in the bones[20].

To mimic this behavior and develop a hard material capable of remodeling, we need to create a material capable of undergoing mechanochemically driven polymerization and depolymerization. Mechanochemical polymerization is a well-known process – most polymers break homolitically to macroradicals, which initiate polymerization in the presence of a monomer[21]. However, while mechanochemistry leads to a slow reduction of the molecular weight, as shown by Staudinger, there is a physical limit to this process below which we cannot accumulate enough force to induce a covalent bond scission, meaning that mechanochemical depolymerization to monomers is unviable.

To address this problem, we turned to low ceiling-temperature (Tc) polymers. Polymers with low Tc can be kinetically trapped at low temperatures with end-caps, providing stable materials above their Tc. A common example is poly(o-phthalaldehyde) (PPA), which has a Tc of -40°C and has been used extensively in photolithography[22].

Our hypothesis was that low Tc polymers could undergo complete mechanochemical depolymerzation back to monomers, if broken above their Tc[23]. The mechanism would be a regular mechanochemical scission to two chains with about half the molecular weight. The two half-chains are now only capped on one end, and should therefore undergo depolymerization from middle to ends (Figure 5). However, polyaldehydes only polymerize or depolymerize ionically, and therefore homolytic bond scission should not lead to depolymerization.

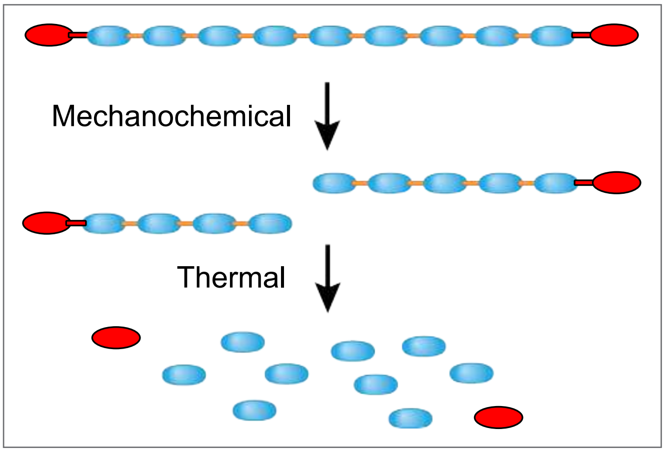


Figure 5: Mechanochemical depolymerization of low Tc polymers (blue – monomer, red – end-cap).

PPA is a polyacetal where the main chain is made exclusively of C-O bonds. The homolytic bond scission would therefore lead to an unstable oxygen radical, while heterolytic bond scission leads to an unstable carbocation. However, the carbocation is benzylic, which may stabilize a heterolytic scission pathway.

High Mw PPA was prepared and stressed under solvodynamic shear using ultrasonication. Samples were taken at different sonication times and tested by gel-permeation chromatography (GPC). With sonication time, the polymer concentration decreased, while the peak of small molecules (monomers) increased. Controls were prepared to assure that the depolymerization was mechanochemical and not due to other effects. First, a poly(methyl acrylate) (PMA) of similar molecular weight was tested. PMA has a much higher Tc, and therefore should only undergo typical mechanochemistry, i.e., scission into smaller chains. Indeed, by comparing the integration of the peaks in the GPC, we observed no change in polymer concentration. Finally, low Mw PPA (40 kDa) was tested. This polymer presents the same chemical composition as the high Mw PPA, but, due to its smaller size, is unable to undergo mechanochemical bond scission. Indeed, in this case no change in the chromatogram was observed during ultrasonication.

Interestingly, we were able to take the mixture after sonication containing solvent, PPA and monomer, cool it below Tc, and induce repolymerization of the monomer by adding an initiator and capping reagent, demonstrating the full circle of polymerization and depolymerization.

A mechanochemical approach to high Tg self-healing materials

As described above, mechanochemistry leads to bond scission in solid materials, which in turn leads to a decline of their mechanical properties. In a self-healing material, new bonds are made to replace those that were cleaved[30]. In this sense, materials made with reversible covalent and supramolecular chemistry work quite well – with several examples of rubbery and glassy materials being made with self-healing capabilities[24]. Some rubbery materials self-heal autonomously, that is without the need of any energy addition[25]. However, in glassy materials, the chains do not move with respect to each other and the functionalities cannot reconnect to make new bonds.

To solve this problem, we proposed the mechanochemical production of a reagent that is not connected to the polymer network. An acid molecule can diffuse in the glassy material, reach different functionalities, and catalyze a bond-forming reaction[26]. The required acid-catalyzed bond-forming chemistry has been known for many years and is in use in photolithography[27]. An example is the acid-catalyzed ring-opening of epoxides, in which few acid molecules can create numerous bonds.

However, the production of acid by mechanochemistry is not trivial. In mechanochemistry, bonds are typically stretched, while in the simplest acid producing reaction, elimination, the bonds are shortened. To solve this problem, we decided to develop a mechanochemical reaction in which the product would be prone to undergo thermal elimination at room temperature. In this case, the acid production is thermal, not mechanochemical, but the elimination can only occur after the mechanochemical reaction is over.

The Craig group had previously demonstrated that gem-dichlorocyclopropanes undergo mechanochemical electrocyclic ring-opening to 2,3-dichloroalkenes[28]. Interestingly, gem-dichlorocyclopropanes as well as 2,3-dichloralkenes, when heated, undergo thermal elimination, producing HCl and a 1,3-diene. If we reduce the energy of the elimination product, we may decrease the thermal transition state, allowing for room-temperature elimination.

To this goal, we prepared dichlorocyclopropanated indenes that were used as cross-linkers in the bulk polymerization of methyl acrylate. These cross-links undergo mechanochemical reaction similarly to the ones shown by the Craig group; however, the product of the reaction is a dichlorocyclohexadiene, which upon elimination produces HCl and chloronaphthalene (Figure 6). The addition of aromatization as a driving force was enough to induce elimination at room temperature. Indeed, this cross-linked PMA, after compression, produced significant amounts of HCl, which was detected using pH indicators. Furthermore, the amount of activation increased with increasing pressure. Finally, the 2-chloronaphtalene was also detected using Raman spectroscopy, demonstrating that the reaction followed the proposed pathway.

Perspective

The fact that mechanical force can drive scission of covalent bonds has been known for over 80 year. However, the use of this methodology to create new chemical reactions or develop

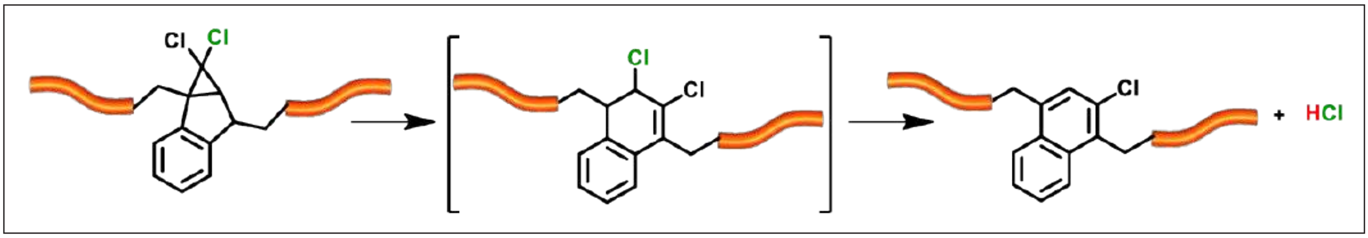


Figure 6: Mechanochemical electrocyclic ring-opening of gem-dichlorocyclopropanated indene followed by thermal elimination to 2-chloronaphtanele and HCl.

smart mechanoresponsive materials is still at the beginning. Mechanical force, contrary to heat or light, is directional, and, therefore, affects the direction of a chemical reaction in different ways according to the angle between the applied force and the reactive bond. In this article, we have described a few examples of how this methodology was used to study polymer physics, and develop new mechanoresponsive materials and new chemical reactions. In our new research group at the Technion, we are looking at novel ways of using polymer architecture to direct mechanical force at the molecular level and developing new materials that better withstand mechanical stress.

Acknowledgments

The author is thankful to Profs. Jeffrey S. Moore, Scott R. White, Nancy R. Sottos and Paul V. Braun from the University of Illinois at Urbana-Champaign for three fantastic post-doc years of meaningful and most productive research. In addition, the author thanks the American Technion Society for a Women's Division Career Advancement Chair.

References

1. Liang, J.; Fernández, J.M. *ACS Nano*, **2009**, 3 (7), 1628–1645.
2. Dougan, L.; Ainavarapu, S. R. K.; Genchev, G.; Lu, H.; Fernandez, J. M. *ChemPhysChem* **2008**, 9, 2836–2847.
3. Vogel, V. *Annu. Rev. Biophys. Biomol. Struct.* **2006**, 35, 459–88.
4. A. J. Lynch and C. A. Rowland, "The History of Grinding", Society of Mining, Metallurgy and Exploration, Inc., Littleton, CO, **2005**.
5. Takacs, L. *Chem. Soc. Rev.* **2013**, 42, 7649-7659.
6. Faraday, M. *Q. J. Sci., Lit., Arts* **1820**, 8, 374.
7. Spring, W. *Bull. Acad. R. Med. Belg.* **1880**, 49(2), 323.
8. Lea, M. C. *Am. J. Sci.* **1892**, 43(3), 527.
9. Staudinger, H.; Heuer, W. *Ber. Dtsch. Chem. Ges.* **1934**, 67, 1159–1164.
10. H. Morawetz, "Polymers—The Origins and Growth of a Science". Wiley-Interscience, New York, **1985**, 86-98.
11. Encinas, M. V.; Lissi, E.; Sarasúa, M.; Gargallo, L.; Radic, D. *J. Polym. Sci. Polym. Lett. Ed.* **1980**, 18, 757.
12. Caruso, M.M.; Davis, D.A.; Shen, Q.; Odom, S.A.; Sottos, N.R.; White, S. R.; Moore, J.S. *Chem. Rev.* **2009**, 109, 5755–5798.
13. Kauzmann, W.; Eyring, H. *J. Am. Chem. Soc.* **1940**, 62, 3113–3125.
14. Kingsbury, C.M.; May, P.A.; Douglas, D.A.; White, S.R.; Moore, J.S. and Sottos, N.R. *J. Mater. Chem.* **2011**, 21, 8381-8388.
15. Beiermann, B.A.; Davis, D.A.; Kramer, S.L.B.; Moore, J.S.; Sottos, N.R.; White, S.R. *J. Mater. Chem.* **2011**, 21, 8443-8447.
16. Davis, D. A.; Hamilton, A.; Yang, J.; Cremar, L. D.; Van Gough, D.; Potisek, S. L.; Ong, M. T.; Braun, P. V.; Martínez, T. J.; White, S. R.; Moore, J. S.; Sottos, N. R. *Nature* **2009**, 459, 68-72.
17. Potisek, S. L.; Davis, D. A.; Sottos, N. R.; White, S. R.; Moore, J. S. *J. Am. Chem. Soc.* **2007**, 129, 13808-13809.
18. Lee, C.K.; Diesendruck, C.E.; Lu, E.; Pickett, A.N.; May, P.A.; Moore, J.S.; Braun, P.V. *Macromolecules*, **2014**, 47, 2690-2694.
19. Flory, P. J.; Rehner, J. *J. Chem. Phys.* **1943**, 11, 521.
20. Fratzl, P.; Gupta, H. S.; Paschalis, E. P.; Roschger, P. *J. Mater. Chem.* **2004**, 14, 2115–2123.
21. Popa, M.; Daranga, M.; Riess, G. *Eur. Polym. J.* **2002**, 38, 407–412.
22. Suda, M.; Hata, M.; Nishida, R.; Oikawa, S. *J. Polym. Sci. A* **1997**, 35, 77–89.
23. Diesendruck, C.E.; Peterson, G.I.; Kulik, H.J.; Kaitz, J.A.; Mar, B.D.; May, P.A.; White, S.R.; Martinez, T.J.: Boydston, A.J.; Moore, J.S. *Nat. Chem.*, **2014**, 6, 623-628.
24. C.E. Diesendruck; J.S. Moore, "Self-Healing Polymers: From Principles to Applications" (Ed. W. Binder), **2013**, 191-211, Weinheim, Germany, Wiley-VCH.
25. Cordier, P.; Tournilhac, F.; Soulie-Ziakovic, C.; Leibler, L. *Nature* **451**, 977-980.
26. Diesendruck, C.E.; Steinberg, B.D.; Sugai, N.; Silberstein, M.N.; Sottos, N.R.; White, S.R.; Braun, P.V.; Moore, J.S. *J. Am. Chem. Soc.* **2012**, 134, 12446-12449.
27. Lee, S. M.; Frechet, J. M. J. *Macromolecules* **1994**, 27, 5160.
28. Lenhardt, J. M.; Black, A. L.; Craig, S. L. *J. Am. Chem. Soc.* **2009**, 131, 10818.
29 Hickenboth, C. R.; Moore, J. S.; White, S. R.; Sottos, N. R.; Baudry, J.; Wilson, S. R. "Biasing Reaction Pathways with Mechanical Force," *Nature*, **2007**, 446, 423-427
30 Diesendruck, C.E.; Sottos, N.R.; Moore, J.S.; White, S.R. "Biomimetic Self-Healing", *Angew. Chem. Int. Ed.*, **2015**, DOI: 10.1002/anie.201500484

Sesquiterpenoides - the holy fragrance ingredients

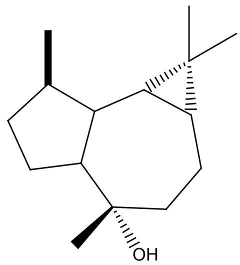
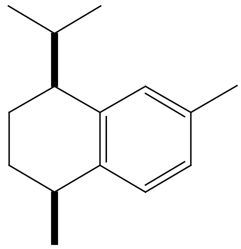
Michael Zviely* and Arcadi Boix-Camps**

Incense is an aromatic substance which is obtained from certain resinous trees and largely employed for purposes of religious worship. The word is also used to signify the smoke or perfume arising from incense when burned.

In ancient times, incense was furnished by two trees, viz. the *Boswellia* sacra of Arabia Felix, and the *Boswellia papyrifera* of India. Mention is made of it in the Bible: "Why do I need the Frankincense that comes from Sheba, and the good cane from a distant country? Your burnt offerings are not acceptable, and your sacrifices are not pleasant to Me",[1] and "Spikenard and Saffron, Calamus and Cinnamon, with all Frankincense trees, Myrrh and Aloes, with all the chief spices".[2] It was procured from the bark much as gum is obtained at present. To enhance the fragrance and produce a thicker smoke various foreign elements were added. These ingredients generally numbered four, but sometimes as many as thirteen, and the task of blending them in due proportion was assigned under the old-law ordinances to particular families.

One important group of fragrance ingredients are found in incense of different origins – sesquiterpene related molecules. Sesquiterpenes are a class of terpenes that consist of three isoprene units and have the molecular formula $C_{15}H_{24}$. Sesquiterpenes may be acyclic or contain rings, including many unique combinations. Biochemical modifications such as oxidation or rearrangement produce the related sesquiterpenoids. Sesquiterpenes are found naturally in plants and insects.

Frankincense is the gum or resin of the *Boswellia Serrata* tree, used for making perfume and incense. The Hebrew word for it is lavonah לבונה, which means "white," referring to the gum's color. The essential oil of frankincense is produced by steam distillation of the tree resin. The oil's chemical components are 75% monoterpenes, sesquiterpenes, monoterpenols, sesquiterpenols, and ketones. It has a good balsamic and sweet fragrance. Some Frankincense characteristic sesquiterpenoids are shown below:

Name of Ingredient	Structure	Organoleptic Characteristics
d-Viridiflorol		Sweet, green, herbal, fruity, tropical, minty
1S-cis-Calamenene		Herbal, spicy

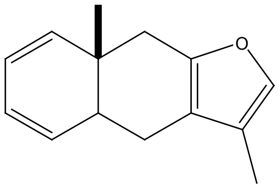
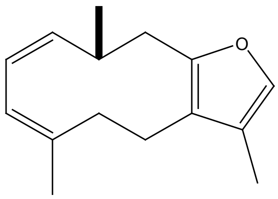
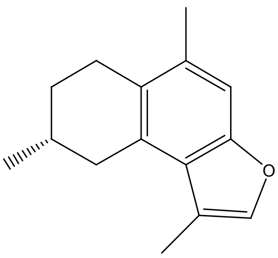
Michael Zviely completed his Ph.D. and Post-Doc at the Hebrew University. He then headed a research group for TAMI (ICL) for almost ten years, and then spent eleven years as Global VP for Research, Development and Science of Frutarom Ltd. After that, he worked three years in China as the CTO for Research and Development of O'Laughlin Industries Ltd. (Shanghai), a company specializing in aroma chemicals - flavor and fragrance ingredients, botanical extracts, cooling agents and UV sunscreen ingredients, followed by a period as VP for Research and Development of Virdia Inc. (HCL CleanTech Ltd.) in Israel and in the USA, on lignocellulose originated bio-materials. In parallel, he held a visiting professorship at Jiangnan University in China for five years. Today Dr. Zviely is a consultant on technology and strategy of specialty chemicals (fragrance and flavor ingredients).

Arcadi Boix-Camps began his career as a perfumer at Firmenich, the 2nd biggest fragrance and flavor company, and for the last 23 years he is the president and master perfumer of Auram International Co., Ltd., a modern company enjoying a world respected technology active in high level creative fragrances both for functional and fine toiletries, sweet flavors and savory flavors. Auram is also top supplier of agarwood oils from different origins being the largest producer in the world and produces its own essential oils mostly used in house to make specialties. Arcadi is an author of many publications on perfumery and wrote several books, e.g. "Perfumery Techniques in Evolution" providing a constructive and open analysis of new perfumery materials and a profound knowledge in the use of perfumery materials in both new and traditional formulas.

* CIC; mzviely@cathay-israel-chemistry.com

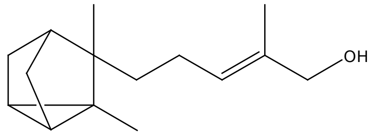
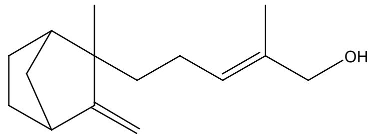
** Auram International Co., Ltd.; www.auraminternational.com; aboix@auraminternational.com

Myrrh comes from a small thorny tree. *Commiphora myrrha*, is the most species rich genus of flowering plants in the frankincense and myrrh family, *Burseraceae* was cultivated in ancient times in the Arabian Peninsula. The grower made a small cut in the bark, where the resin would leak out. It was then collected and stored for about three months until it hardened into fragrant globules. Myrrh was used raw or crushed and mixed with oil to make a perfume. Myrrh oil is steam distilled directly from the myrrh resin. Its aroma is woody, earthy and a bit balsamic. Myrrh is occasionally used as flavoring agents. Somalia and Ethiopia are by far the largest producers of Myrrh.[3] Some Myrrh characteristic sesquiterpenoids are shown below:

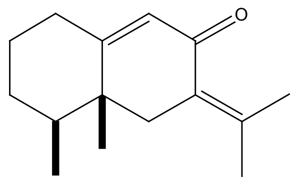
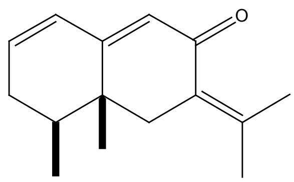
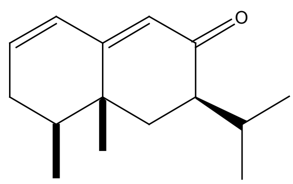
Name of Ingredient	Structure	Organoleptic Characteristics
Furanoedusma-1,3-diene		Typical myrrh, balsamic, woody, musty
Lindestrene		Typical myrrh, balsamic, woody, musty
Dihydropyro-curzerenone		A resinous myrrh odor, best represents the odor of myrrh by itself

One of the oldest incense materials, Sandalwood, has been in use for at least 4,000 years. The sandal tree, botanically known as *Santalum album* belongs to the family *Santalaceae*. The sandal tree grows almost exclusively in the forests of Karnataka, followed by Tamil Nadu, Kerala and Andhra Pradesh, Timor Islands of Indonesia etc. The Sandalwood appears in the Bible as one of the Temple building materials – *Almog* אלמוג: "Also Hiram's ships that delivered gold from Ophir, brought from Ophir a huge quantity of Almog-wood and precious stones".[4]

Sandalwood oil mainly consists of a number of closely related sesquiterpenoids. α-Santalol and β-santalol amount to more than 90% of the oil, β-santalol being the most important character impact compound. Some Sandalwood characteristic sesquiterpenoides are shown in the following table;

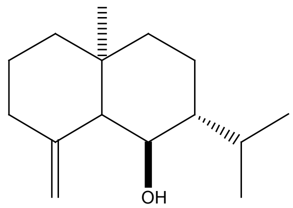
Name of Ingredient	Structure	Organoleptic Characteristics
α-Santalol		A relatively weak, slightly woody odor reminiscent of α-cedrene[5]
β-Santalol		Typical sandalwood odor, with powerful woody, milky and urinous tonalities[6]

Agarwood is the resinous heartwood of the *Aquilaria* tree, a genus belonging taxonomically to the *Thymelaeaceae*. The essential oil is a highly demanded ingredient in fine perfumery for its warm, unique balsamic notes with sandalwood–ambergris tonalities.[7] In this review[7] Regula Neff describes a group of sesquiterpenoides with warm, woody characteristic odor,[8a] which are the heart constituents of agarwood volatiles, some of them are shown below:

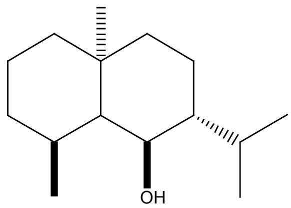
Name of Ingredient	Structure	Organoleptic Characteristics
4S,5R-Dihydro-karanone		Strong woody, slightly camphoraceous, fumigating note, remarkable, intense, woody[8a,b]
4S,5R-Karanone		Woody, amber-like, elegant[8a,c]
Eremophila-9,11-dien-8-one		Sweet, woody, like dihydrokaranone, important oriental, fumigating character[9]

Bursera graveolens is a deciduous tree of the *Burseraceae* family that is distributed from Mexico to Peru. Its woody material has a strong characteristic spicy, sweet and balsamic odor, and is used as incense in churches where it is called "Palo Santo". Palo Santo oil was used during the time of the Incas for its reputed spiritual purifying properties. Many members of the *Burseraceae* family produce a strong fragrance, demonstrated by the use of resin of plants from the Boswellia genus historically as a prominent raw material in the production of frankincense, and the usage of the resin of *Commiphora molmol* and closely related species as myrrh.[10]

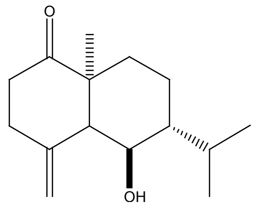
The following four sesquiterpenoids were isolated from *Burseragra veolens*:



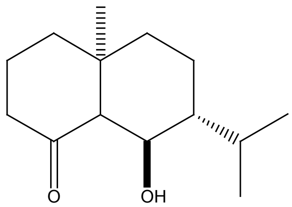
(-)-Juneol



Dihydrojuneol



6β-Hydroxy-4(15)-eudesmen-1-one



6β-Hydroxy-eudesman-4-one

All four have a characteristic weak sweet, woody and herbal odor.

The sesquiterpenoid molecules described above are a part of this important F&F natural ingredients, e.g. valencene,[11] nootkatone,[12] α- and β-vetivones and khusimone[13] discussed elsewhere.

There seems to be a relation between sesquiterpenoids and essential oils used for religious ceremonies. In the former short review discussing sesquiterpenoids, naming them the holy fragrance ingredients, we presented Frankincense, Myrrh, Sandalwood, Agarwood and Palo Santo.[a]

In this part, several different Agarwood oils and ingredients will be discussed more deeply, mostly their sesquiterpenoid aroma molecules. The Agarwood species studied herein are *Aquillaria Agallocha, A. Crassna, A. Baillonii, A. Beccariana, A. Malaccencis, A. Microcarpa, A. Subintegra, A. Banaensis, A. Rugosa and A. Yunnanensis.*

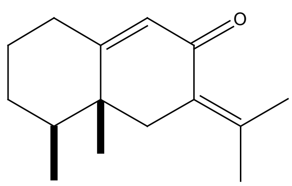
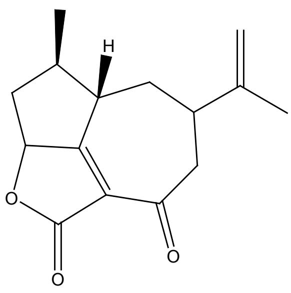
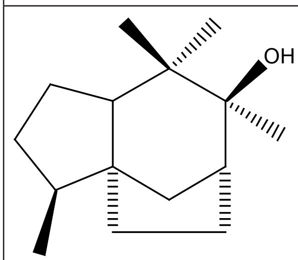
These agarwood oils smell extremely different on their top notes, namely coriaceous, animal, fecal, fruity, extremely leathery (being the most leathery those coming from Papua New Guinea and Indonesia's Irian Jaya regions, which are called Jayapura and Mereke), cheesy, phenolic but when evaporating in the skin after 7 to 8 hours, all of them change to create the most noble, extraordinary, unexpected, surprising, amazing and astonishing woody note that has existed in the world. All of these oils converge-whatever the quality - to the same precious woody note. Studies have been done to understand the reason why and the answer seems mostly to derive amongst the important sesquiterpenoids described herein.

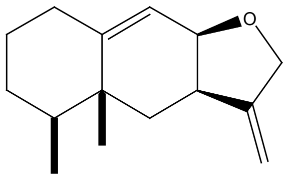
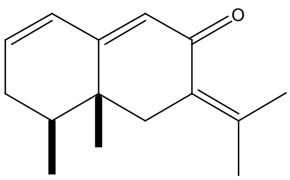
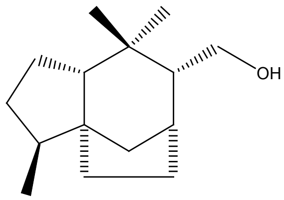
The dry down became all the same. Many of the molecules found in Agarwood oils were smelled, from those simple like benzyl acetone, furfural, frambinone methyl ether, p-cresol, furfuryl alcohol, creosol, styrene, p-vinyl anisole, etc., molecules which are not important at all. some olfactory important acid molecules as butyric, 3-methylvalerianic, caproic, caprilic, cyclohexanoic etc., and those believed to be really "keys" in the fabulous smell sought for a millennium and being the favorite smell of Asian aristocrats in Vietnam, China, Japan, Thailand or the Indian Maharajas.

It seems that the top note differences in the oils are created by unimportant ingredients while the "treasure" is in the ingredients almost nobody knows. Why do so many different oils have such a different top note, very often unpleasant, and suddenly its odor changes to impart the extraordinary woody note that is so resinous, fragrant, radiant and delicate.

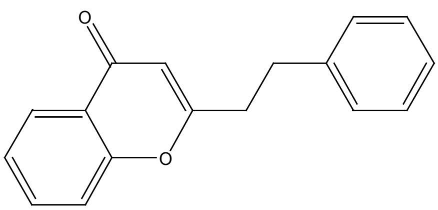
The oils which are fecal, cheesy are less preferred by some of the perfumers. These are mostly the cheesy ones (Boyas from India, Bangla Desh, Laos) or the oils *ex A. Agallocha* or *A. Khasiana*. The more accepted oils are from Malaysia, Indonesia, Papua New Guinea, and those from Thailand (Prachinbury *ex A. Subintegra, Tratex A. Crassna* and those from Cambodia *ex A. Baillonii* and *A. Crassna* too (called in the market KohKhong). These seem to be the best Agarwood oils.

Why do all these oils become so woody and treasure the best smell in the world on its dry down? It is very risky to reply but there are some "key" ingredients than make the miracle as shown below:

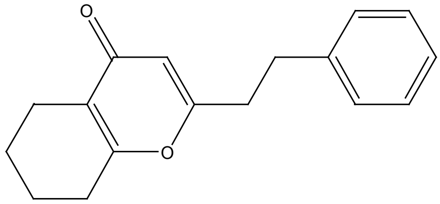
 (+)-(4αS,5R)-Dihydrokaranone	One of the best aroma molecules, being powerfully woody, resinous, timbered extraordinarily diffusive and not easy to forget once known and smelled. This seems one of the best woody chemicals existing. The synthesis of (+)-(4αS,5R)-Dihydrokaranone is described below.
 (-)-Guaia-1(10),11-dien-15,2-olide	Its smell is very strong, as the previous one extremely long lasting, with orris sub notes, clean, radiant, diffusive, bright, woody ambery, smelling a bit of Ambrocenide, Ambrostar, dextro Nor Limbanol, Ambermax, Cachalox, Z-11 and Limbanol whose greatness is to make feel harmony.
 Jinkohol (2-epiprezizaan-7β-ol)	A storm of the noblest woods, a moving smell, sensitive, receptive, insightful that cannot be described, but providing an extremely rich creativity to every good and skilled perfumer.

 (8,12)-Epoxyeremophila-9,11(13)-diene	Softer than Jinkohol or Dihydrokaranone but imparting a special sweetness which combines extremely well with those described before and especially mixed with (-)-Guaia-1(10),11-dien-15-al. The accord of these aroma molecules brings the smell of the mysterious woodiness of Agarwood oils, which bring the same results regardless of the different top note.
 (+)-(4αR,5S)-Karanone.	It is extremely woody but with very important amber gris notes as important as the woody ones. Karanone would mix extraordinarily well with pure amber chemicals such as Ambroxclassique (the original one containing ambrols) and by far the best, α-Ambrinol, Limbanol, Ambrostar, LaevoCetalox, Super Ambrox, Amber Xtreme, Ambrocenide, Cachalox, Ambrinoloxide, Dehydroambrox, Dihydro-γ-ionone, Timbersilk, Dextro Nor Limbanol, Trisamber, etc.
 Jinkohol II	Very woody and smelling of Agarwood smoke

Jinkohol II character is somehow quite strange because when the oils are distilled, no more than 35 chromones present in the woods are detected. The presence of chromones is what makes the smell of the smoke richer, exalted, splendid, high, lofty and even glorious. The chromones do not come on the distilled products and only on the extracted ones by acetone, benzene, supercritical CO_2, etc., being the most important ingredients for the smoke of Agarwood. Among them 2-(2-phenylethyl)-chromones and 2-(2-phenylethyl)-tetrahydrochromenones are more mysterious that the other ones mentioned before.

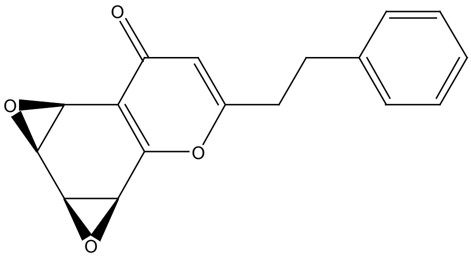


2-(2-Phenylethyl)chromone



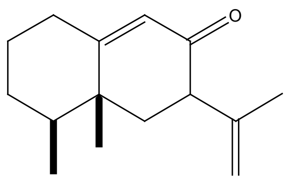
2-(2-Phenylethyl)chromenone

The best smoke comes from woods also rich on diepoxy-tetrahydro-2-2-phenyethyl-chromones.[b] These chromones stabilize and harmonize the smell provided by the volatile ingredients present in the wood and in the oils.

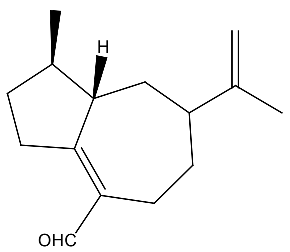


DIepoxy-tetrahydro-2-(2-phenyethyl-chromones

It seems the amount of chromones is what will make the fragrance successful, mostly by Royals, since a wood with 65% of chromones does not burn the same as a wood with only 10%. The chromones have nothing to do with the oils but the burning of these high noble ingredients with the chromones, produces spiritual peace and being in a "Platonic Pink Cloud" as described elsewhere by the author.[2]

 Eremophila-9,11-dien-8-one	Having a lovely smell as other Agarwood ketones

Eremophila-9,11-dien-8-one is a very unstable chemical and very difficult to detect through GC/MS since most of isomerizes to form more Dihydrokaranone during the conditions of the GC injector, being the noblest ingredients as happen in Vetiver too where the best smell is given by α-Vetivone, Dihydro-β-vetivone, Didehydro-β-vetivone, Didehydro-α-vetivone, Dihydro-α-vetivone, Khusimone, β-Vetivone, etc. Both oils are defined as noble "ketone" oils.[3]

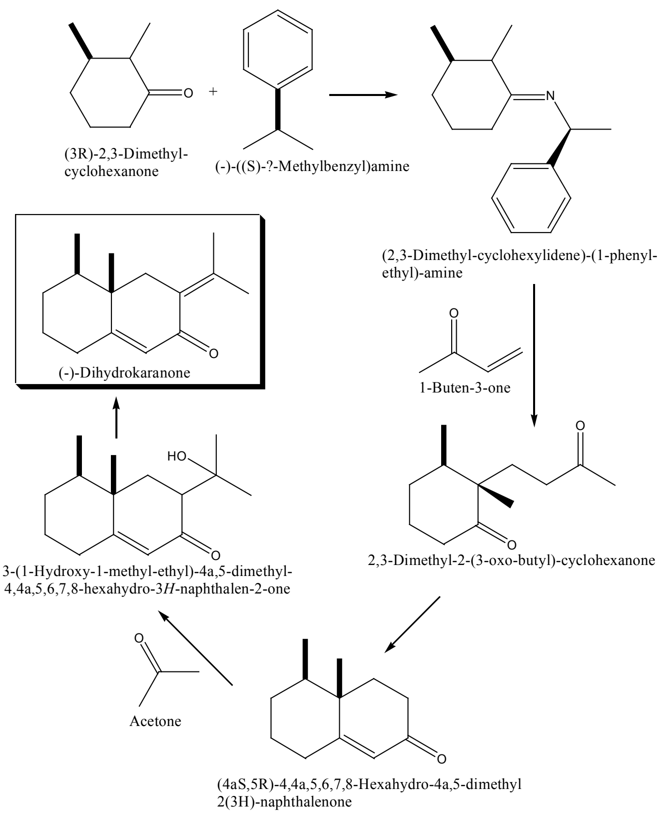


(-)-Guaia-1(10),11-dien-15-al

This molecule mixes very well with epoxieremohilladiene and has a beautiful note of β-Damascenone

The beautiful note of (-)-Guaia-1(10),11-dien-15-al which is very rare on these chemical structures but also an orrisy-diffusive and radiant smell with reminiscences of Irones and Dihydroirone. Its woodiness it is extremely soft, almost having soul and spirit. The studies made on the above sesquiterpenoids showed quite certainly that they are the most important when trying to rationalize this turning of the oils from their original and so diverse top note to the common precious woody note.

A novel diastereoselective route to (4aS,5R)-4,4a,5,6,7,8-hexahydro-4a,5-dimethyl-2(3H)-naphthalenone has been developed. The key step involves an asymmetric Michael addition of the corresponding chiral secondary enamines derived from (S)-(-)-1-phenylethylamine and (3R)-2,3-dimethylcyclohexanone to 1-buten-3-one. This enone was successfully transformed into the eremophilane-type sesquiterpenoid (-)-Dihydro-karanone.[c]



References

a. Sesquiterpenoides – The Holy Fragrance Ingredients – Part 1 M. Zviely and L. Ming, Perfumer & Flavorist (2013) 38(6), 52.
b. The volatile and semi-volatile constituents of agarwood, the infected heartwood of Aquilaria species: a review. Naef, Regula; Flavour and Fragrance Journal (2011), 26(2), 73-89.
c. A practical and efficient preparation of (-)-(4aS,5R)-4,4a,5,6,7,8-hexahydro-4a,5-dimethyl-2(3H)-naphthalenone: a key intermediate in the synthesis of (-)-dehydrofukinone; Schenato, R. A.; dos Santos, E. M.; Tenius, B. S. M.; Costa, P. R. R.; Caracelli, I.; Zukerman-Schpector, J. From Tetrahedron: Asymmetry (2001), 12(4), 579-584.
1. Jeremiah, 6:20
2. Song of Songs, 4:14
3. Myrrh – Commiphora Chemistry, Lumír O. Hanuša, Tomáš Řezankab, Valery M. Dembitsky, Arieh Moussaieff; Biomed. Papers 149(1), 3–28 (2005)
4. Kings I, 10:11
5. Müller PM, Lamparsky D. Perfumes: Art, Science & Technology. Amsterdam, New York: Elsevier; 1991.
6. Bauer K, Garbe D, Surburg H. Common fragrance and flavor materials: preparation, properties and uses. 2nd ed. Weinheim: VCH; 1990. OBS:
7. The volatile and semi-volatile constituents of agarwood, the infected heartwood of Aquilaria species: A review; Regula Naef, Flavour Fragr. J. 2011, 26, 73–89.
8. (a) T. Nagashima, I. Kawasaki, T. Yoshida, T. Nakanishi, K. Yoneda, I. Miura.;IXth Int. Ess. Oil Congress, Singapore, 1983, p.12.; (b) M. Ishihara, T.Kitaura. JP 2004189643, 2004; (c) M. Ishihara, T. Kitaura. JP 2004231519, 2004
9. M. Ishihara, T. Tsuneya, K. Uneyama. Phytochem. 1993, 33, 1147
10. Eudesmane-Type Sesquiterpenoids in the Volatile Oilfrom Burseragraveolens; Chiyoki Yukawa, Hisakatsu Iwabuchi, Sadao Komemushi and Akiyoshi Sawabe; J. Oleo Sci., Vol. 53, No. 7, 343-348 (2004)
11. M. Zviely and C. Hong; Perfumer&Flavorist (2009), 34(1), 26.
12. M. Zviely; Perfumer &Flavorist (2009), 34(12), 20.
13. M. Zviely; Perfumer &Flavorist (2012), 37(2), 46.

Education in Chemical Engineering

Alec Groysman
Israeli Society of Chemical Engineers & Chemists, Tel Aviv, Israel, Technion, Haifa, Israel
E-mail: alecgroysman@gmail.com

Abstract: Humanity faces severe global problems of health and environment. The latter comprises energy (including crude oil, natural gas, coal, and other sources of energy), raw materials (ores, minerals and building materials, excluding crude oil), food, water, air, and soil. Chemistry and chemical engineering deal with all these constituents. New problems of a shortage of skilled knowledgeable specialists in each sphere have appeared. In order to work out this problem, we should improve knowledge management. This includes education and knowledge transfer from older specialists to the younger generation.
The aim of this paper is to show how efficiently and effectively to educate students and to transfer knowledge to young generation of scientists, engineers, educators, and managers.
This approach in some fields of chemistry and chemical engineering has been used in both academy and industry. The philosophy of my work is effective knowledge transfer. For this task, establishing interrelationships between humanitarian aspects, chemistry and chemical engineering is used. Our method attracts students and the younger generation and shows that learning the subject of chemistry and chemical engineering can be more fascinating, creative, and productive. Humanitarian aspects include history, art, philosophy, and humor. Some results are summarized in my books "Corrosion for Everybody" and "Corrosion in Systems for Transportation and Storage of Petroleum Products and Biofuels" published by Springer.

Introduction

"Give a man a fish and you feed him for a day; teach a man to fish and you feed him for a lifetime."
Maimonides (Rambam) (1135-1204), a Jewish philosopher.

Chemical engineers are a unique breed. They are an elite group of engineers who should receive rigorous education, a thorough knowledge of chemistry, physics, physical chemistry, analytical, project-management and problem-solving skills[1]. Many of them work in chemical and other industries and deal with the manufacture of numerous chemicals and fuels, pharmaceuticals, advanced materials, nanotechnology, biotechnology, genetics, microbiology, semiconductors, food processing, agriculture, environment and its protection from pollution, energy producing, and water treatment.

Chemical engineers solve the problems of health and environment, and are responsible for delivering every product we use: from the silicon chips in our computers to the water we drink, food we eat and medicines. Chemical engineers contribute to the prosperity, comfort, health and well-being we enjoy every day and night.

All inventions have two sides of the coin and the achievements of chemical technology are no exception. 'Orange fox tails' of nitric oxides (NO_x), negative consequences of the use of the pesticide DDT (dichlorodiphenyltrichloroethane), use of explosives (ammonium nitrate can served both as fertilizer and as the component of explosives), deleterious effect of chlorofluorocarbons on ozone layer, to name a few. Chemical technology can overcome the problems of harmful effects (fully or partly), for instance, the problem of pollution of atmosphere by NO_x. Nowadays emissions of NO_x in power plants, oil refineries, petrochemical and other chemical plants are reduced by injecting urea which is decomposed by water vapor to ammonia which in turn reacts with NO forming neutral N_2 gas.

Dr. Alec Groysman graduated in 1973 from the Chemico-Technological University named after Mendeleev in Moscow. He received his Ph.D. in physical chemistry and corrosion in 1983 in Moscow.
Alec Groysman has experience in corrosion and corrosion control in the oil refining and petrochemical industry. He is a lecturer of the courses "Materials and Standards in Oil and Gas Engineering" and "Corrosion and Corrosion Control" at the Technion (Haifa, Israel).
His first book "Corrosion for Everybody" published by Springer in 2010 received the innovation award winner of Materials Performance Readers` choice in 2012 year in the USA. His new book "Corrosion in Systems for Transportation and Storage of Petroleum Products and Biofuels" is published in 2014 by Springer.
He has special interests in materials and corrosion education and in searching for relationships between materials, corrosion, art, history and philosophy.
Dr. Alec Groysman is the chairman of the Israeli Association of Chemical Engineers and Chemists.

Risk hazard and safety have become important issues in chemical engineering education. Recycling, environmental protection, and cost efficiency became part of chemical engineering education from its beginning at the end of the 19th century.

The philosophy of chemical technologies is the use of wastes of production of any compound for the manufacture of other needed substances. Thus one of the objectives of chemical engineering is to minimize wastes in chemical processes.

Environmental protection is an important issue for chemical engineers, who continue their work of developing products and processes that could cause less harm to the environment. Biodegradable detergents and polymers are an example. For instance, using platinum catalysts for producing detergent linear molecules allows the detergent to be digested by natural microbes in lakes[1]. However, environmental advances of chemical technologies, notwithstanding, there were more public-relations nightmares for the chemical industry. In 1965, the famous chemical Dow Company made the ill-fated decision to manufacture napalm (a flammable liquid used in warfare). Dow, which was producing about 800 different useful chemical products by the late 1960s, "became famous" for only one, napalm[1].

Many problems of health and environment can be solved by chemical engineers. There are brilliant chemical engineers. However, we are facing a lack of highly qualified specialists, able to solve the above mentioned problems. To improve this situation, we should improve knowledge management, comprising education and knowledge transfer.

The present paper describes the history of education in chemical engineering, some aspects of effective knowledge transfer for students, experienced engineers, educators, and managers, and the use of humanitarian aspects in engineering education with the aim of educating creative, knowledgeable, skillful, qualified and fully developed specialists.

Personal Prelude

My task is to show the 'beauty' and attractiveness of chemical engineering disciplines for students, young and experienced engineers, and other lecturers and managers in order that they understand that these disciplines are not only obligatory but also attractive, interesting and stimulating.

Experience of education both in academy and in chemical industry will be analyzed in this paper. I feel that this experience can be used in the teaching of any scientific or engineering discipline.

1. History of education and knowledge transfer

"Reading makes a person knowledgeable, conversation - resourceful, and the habit of recording - accurate."
Francis Bacon (1561-1626), an English philosopher.

Modern systems of education in Europe derive their origins from the schools of the High Middle Ages around the 11th-13th centuries. Population in Europe was rapidly increasing during this period which brought about great political, social, and economic changes. These changes, in their turn, led to philosophical, technological, art and scientific revival and as a result to the stimulation and emergence of an educational system. The emergence of real science and figurative art, the Renaissance, began later in the 14th century[2, 3]. Despite the emergence of technology already in the Paleolithic era about 2.5 million-10,000 BC (the making of stone tools, the discovery and utilization of fire, clothing, and shelter), engineering as a discipline appeared in the 13th - 14th centuries[4]. Is this simply coincidence or does it have its roots in the interaction between engineering, science, art, and education? Their teaching arose approximately at the same time and education emerged as the need to transfer knowledge in order to prepare new specialists. The first universities were established in Bologna (1088), Paris (1150), Oxford (1167), Modena (1175), and Cambridge (1209). Then in the 13th - 15th centuries, universities were established in Europe like 'mushrooms after the rain'.

In less than a century, there were more inventions developed and applied usefully than in the previous thousand years of human history all over the globe. There were windmills, watermills, printing, gunpowder, a better clock, scissors, spectacles, paper, magnetic compass, to name a few. Philosophical, medical and technological achievements, the appearance of new arts, literature, music, theater, and architecture required the creation of an educational system which was to meet the growing needs of the people.

The educational curriculum in the first universities in Europe included the 'trivium' (grammar, logic, and rhetoric) and 'quadrivium' (arithmetic, geometry, music, and astronomy)[5]. These seven '*Artes Liberalis*' (Liberal arts) were the basics of education throughout the Middle Ages and Renaissance[6]. 'Trivium' and 'quadrivium' mean the '*place where three and four roads meet*' from the Latin (via = road) respectively. In fact, they were used in ancient Greece and Rome. Thus people understood in ancient times that exact and humanitarian disciplines should be taught together (as a crossroad) in order to create well-educated and diversified polymaths.

2. History of chemical engineering

"A pessimist sees difficulties in every opportunity; an optimist sees opportunities in every difficulty."
Winston Churchill (1874-1965), a British politician.

Engineering is the discipline, art (meaning skill) and profession of acquiring and applying scientific, mathematical, economic, social, and practical knowledge to design and build structures, machines, devices, systems, materials and processes that safely realize solutions to the needs of society[4, 5]. Chemical engineering is a branch of engineering that applies physical sciences (chemistry and physics) and life sciences (biochemistry, biology, and microbiology) together with mathematics and economics to produce new compounds and energy. Chemical engineers (industrial chemists, applied chemists) deal with processes that convert raw materials into new useful materials.

In spite of early chemical technologies (producing metals and alloys from ores) that were used by the Egyptians (3,500 BC) and Romans (1-4 AD), the end of the Industrial Revolution in the late 19th century signified the beginning of chemical engineering ('industrial chemistry') as a recognizable discipline. The advent of the steam engine gave rise to the development of the textile industry, in turn launching demand for dyestuffs and other chemicals, such as sulphuric acid, soda ash (sodium carbonate), sodium hydroxide, and bleaching powder (calcium hypochlorite).

Important technological novelties of the First Industrial Revolution (1760-1840) were steam engines, metallurgy (steel making), textile manufacture, machine tools, and manufacture of chemicals (acids, alkalis, salts, dyestuffs) and materials (cement, glass, paper). The production of chemicals and materials was the basis of chemical industry and chemical engineering. The First Industrial Revolution evolved into the Second Industrial Revolution (known as the Technological Revolution) which continued until the World War I (1914)[7]. This period was marked by the development of metallurgy, chemical industry including oil refining and petroleum engineering, electricity and communication technologies (telegraph, telephone, and radio).

Before the 19th century, most products (i.e., soap, dyes, and glass) were produced in batch processing. The Industrial Revolution led to unprecedented escalation in the demand for different chemicals. Chemical engineering technique allowed larger amounts of substances to be produced through continuous chemical processes. Chemical engineering and chemical industry were established and began to be intensively developed when the shift from batch to continuous processes began in the 19th century. Nowadays, commodity chemicals (produced on a very large scale) and petrochemicals (produced from crude oil) are manufactured using continuous processes whereas specialty chemicals (i.e., cosmetics, adhesives, fragrances, surfactants, etc.), fine chemicals (produced in limited amounts) and pharmaceutical drugs (medicines) are produced using batch processes.

The emergence of the chemical industry gave impetus to the appearance of chemical engineering education. The first institutions for technical training and education were established in France in the 18th century. Gustave Eiffel graduated as 'ingénieur chimiste'[8]. The British chemist George Edward Davis gave twelve lectures in 1887-1888 at Manchester Technical School and defined a new discipline 'chemical operations' or '*chemical engineering*'[9]. Really this term was used in England after 1850 to describe the application of mechanical equipment in the chemical industry. Later the lectures of Davis were collected into one of the textbooks on chemical engineering, "*A Handbook of Chemical Engineering*"[8]. The Society of Chemical Industry was founded in London in 1881[1]. An American academic Lewis M. Norton initiated a course 'applied chemistry' at MIT (Massachusetts Institute of Technology, USA) in 1888[1, 8]. Following on from the success of the MIT program, others universities in the USA established chemical engineering programs in 1892-1898[8]. All these programs grew out of chemistry departments. The Chemical Engineer Journal began publication in 1904. The American Institute of Chemical Engineers was founded in 1908[1].

The profession '*chemical engineer*' (industrial chemist, applied chemist) was commonly used in England and USA by 1910. Historically, chemical engineers appeared later than mechanical, civil and electrical engineers. In the 1920s, chemical engineering education focused on the study of unit operations such as reactors, separators and mixers[8]. The importance of safety was emphasized in 1970s; sustainability and "green" engineering became more important in chemical engineering programs in 1990s.

Chemical engineering includes a wide spectrum of topics: thermodynamics; chemical, physical, physico-chemical, biological and biochemical processes (reactions); control of processes; plant and equipment processing design; transport phenomena (fluid flow, mass transfer, heat transfer, materials balances, momentum transport, process dynamics); separation processes; solids handling; safety, and sustainability. Modern chemical engineering includes biotechnology (comprising also genetics and microbiology), nanotechnology, pharmaceutical, fuel cells, hydrogen power, and water technology, to name a few.

The Chemical Engineering Education Committee in the USA was amazed in 1922 by the wide range of subjects and topics offered by 78 institutions and declared: "*Chemical engineering … is not a composite of chemistry and mechanical and civil engineering, but a science of itself, the basis of which is those unit operations which in their proper sequence and coordination constitute a chemical process as conducted on the industrial scale*"[8]. The diversity and richness of the 'chemical engineering' discipline turned it into '*chemical engineering science*' in the 1950s. Over the last 20-30 years, great attention in chemical engineering education has been paid to bioprocesses, energy, environmental and safety issues.

There are more than 100 chemical plants in Israel, manufacturing fuels, fertilizers, polymers, paints, drugs, cosmetics, various chemicals, such as solvents, acids, sulphur, alkalies, bromine and its derivatives, minerals, magnesium, materials for computers, food, textile, paper and others where more than 4,000 chemical engineers work. Such diverse substances and processes for their production make the profession of chemical engineer particularly attractive and interesting. Although we will talk about education in chemical engineering, our approach can be applied to the education and teaching of any engineering discipline.

3. Andragogy and Pedagogy

"The great aim of education is not knowledge but action."
Herbert Spencer (1561-1626), an English philosopher.

Each historical era creates a system of education that addresses its needs. Prehistoric people documented by means of symbols and signs. Probably the main function of prehistoric painting was documentation and communication, and not creativity, which is a modern ritual[10, 11]. Education in the form of teaching and learning perhaps appeared in that ancient period[12].
The First Industrial Revolution in 1760-1840 in Europe contributed to education and knowledge transfer of innovations in several ways. Specialists moved to another employer, but a common method was a study tour (traineeship, probation) and collection of information. Another method of knowledge dissemination resulted from the creation of networks of philosophical societies where members discussed 'natural philosophy' (science), its application in industry, publications of transactions, periodicals and encyclopedias.
New direction arose in education towards the end of this period (1830s) - andragogy (*teaching of adults* or *adult education*). We will describe the difference between andragogy and pedagogy.
Pedagogy deals with theory and practice of education. It is the instrument of education, namely, how best to teach. *Pedagogy* means *'to lead the child'* in Greek. The *andragogy* is the term firstly used by German educator Alexander Kapp in 1833[13]. Andragogy was developed into a theory of adult education by the German-American philosopher Eugen Rosenstock-Huessy (1921) and later by the American educator Malcolm Knowles in 1970-1980s[14-16]. Andragogy requires special teachers, methods, philosophy, approaches, and should be differentiated from the more commonly used pedagogy. The theory of andragogy has six assumptions related to the motivation of adult learning[17]:

(a) *Need to know:* Adults need to define the objectives for learning.
(b) *Foundation (experience):* Adults have life experience and based on it, acquire new knowledge.
(c) *Self-concept:* Adults themselves decide what to study, plan and estimate. They take part in a discussion of which problems should be studied.
(d) *Readiness to learn:* Adults learn subjects having immediate relevance to their work and personal life.
(e) *Orientation to learn:* Adult learners become more problem-centered than subject-centered[14-16].
(f) *Motivation to learn:* Adults' motivation to learn is much higher than that of children.

People are trained more successfully, if they are given practical training rather than just the bare theory. Strategies such as case studies, role playing, simulations, and self-evaluation are most useful. Instructors adopt a role of facilitator or resource rather than lecturer or grader. Thus, 'education from above' is *pedagogy*, while 'education of equals' is *andragogy*[18]. In *andragogy*, curriculum is considered as the transmission of knowledge, process, product, and praxis. *Andragogy* is related to people who work and have some experience. Teaching students who have never worked is related rather to pedagogy. Teaching of students who work and have experience in a specialty can be related to andragogy. This differentiation into two categories is very important in deciding which method to use when teaching this audience.
In *andragogy*, we should guided by the principle discovered by the Swiss psychiatrist Carl Gustav Jung. The difference in psychology of children and adults is that children are searching for how the world is arranged and dismantle a toy in order to learn what is inside; the adults try to connect different things: how this part is connected and works with other parts. Specialization in the last two centuries has led to the splitting of one general culture into many different disciplines (including exact, natural, technical, and humanitarian sciences), while most problems are complex and require an interdisciplinary approach[19]. In addition, the development of any industry requires creative professionals. As a result, attempts were taken at the beginning of the 21st century to unite and include humanitarian aspects in scientific and engineering education[4, 20, 21].

4. Realization of Chemical Engineering Education

"Scientists study the world as it is. Engineers create the world that has never been."
Theodore von Kármán (1881-1963), the Jewish-Hungarian-American aerospace engineer.

The word 'engineer' emerged apparently in the 13th - 14th centuries. The engineer's work is the link between scientific discoveries and their subsequent applications to human needs and to improvement in the quality of life. The engineer organizes links between science, technology and society. Philosophers in the 19th century believed that "*the function of engineer is creative activities, and the function of technician is performance*"[22]. This is not entirely true. Engineers (like all people) can be separated into two categories: performers (the majority) and creators (innovators). Engineers in addition to knowledge of technology must learn the laws, regulations, standards, codes, specifications and their application in practice. An engineer-creator is a person who creates something new.

How should we develop the natural gifts of a person studying engineering in order to be able to answer questions posed today and be ready to meet the challenges of tomorrow? We need to educate the modern generation of professionals, using the experience in education on the one hand, and on the other hand boldly introducing new methods of teaching.

Working for many years in the chemical industry (including oil refining and petrochemical) and teaching chemical thermodynamics, corrosion and corrosion control, materials and standards in oil and gas engineering, and chemical resistance of materials, in universities and colleges, I would like to share experience of teaching of these disciplines, mostly corrosion of metals.

Fast aging of equipment in chemical industry, aggressive chemicals and harsh conditions result in high corrosion risk. For instance, corrosion failures are responsible for one of five major refinery accidents that have occurred in European countries since 2000[23]. Half of the accidents had very high consequences on the environment, economics of the refinery, and surrounding community. Significant corrosion failures occur either because the hazard was not identified or ignored. Therefore corrosion education for chemical industry is of paramount significance.

Usually students studying chemistry, chemical engineering, oil and gas engineering, refining and petroleum engineering, mechanical engineering, materials science, metallurgy, learn the subject of corrosion briefly or do not study it at all. An engineer becomes the corrosion engineer during his work at a chemical plant. In this regard, we need to teach the subject of corrosion not only to students, working (experienced) engineers, but also to managers and administrative personal; and each group separately.

Nowadays, as at all times, there is a need to transfer knowledge from older specialists to the younger generation. There is printed knowledge presented in encyclopedias, books, and journals. And there is 'tacit knowledge' which is possessed only by specialists. This knowledge is not easy to get, as many experts are reluctant to share it. We also should instruct educators how to efficiently and effectively teach three different groups of listeners.

Four target audiences for corrosion education as a part of chemical engineering teaching are considered in this work: a) students, b) experienced engineers, c) educators, and d) managers in industry. It is necessary to use different curricula for these four groups of people.

4.1. Students.

Curricula study for one semester.

a. Lectures (28 hours). These are for students in their last or penultimate year of study: chemical engineering, mechanical engineering, and materials engineering faculties. Lectures include consideration of the causes of corrosion, corrosion factors, mechanisms of corrosion, forms of corrosion damages, methods of corrosion protection, control and monitoring, chemical resistance and choice of materials, corrosion failure analysis, economic and environmental aspects of corrosion[20]. Some students participating in the course have traineeships in chemical plants. This allows them to solve their problems during the course.
b. The video of the lectures recorded on the camcorder based on previous course (42 hours for self-view) are on the Internet website of the university/college.
c. Seminars (14 hours). Numerous practical problems are solved with concrete examples.
d Laboratory and practical works (14 hours).
e. Excursions to the chemical enterprises (4-8 hours). The tour includes a general introduction to a plant and its function, lecture about materials used at the plant units, corrosive environments, ways of selecting the corrosion resistant materials, corrosion control (coatings, inhibitors, cathodic protection, technological measures), and methods of corrosion monitoring. Students present reports after such tours at the enterprises.
f. Traineeship of students with the definition of the theme performance of the work (600 hours in one semester). A student has two supervisors: from the enterprise and from academia. This is the "immersion method" for students who work together with engineers, where "real" skilled engineers (not the lecturers from academia) tell, show and explain to them (even the course is not a course) and talk about their technological problems and decisions. Examples of those traineeships are:
    - f.1. Identification and analysis of corrosion rates of aboveground storage tanks containing crude oils and fuels. The result is published as the paper and a part of a monograph[24, 25].
    - f.2. Corrosion of carbon steel and anti-corrosion measures in the presence of naphthenic acids. The result is the patent and published articles[26-28].
    - f.3. Examination of a "green" corrosion inhibitor and corrosion resistant alloys for the overhead of the crude oil distillation unit[29].
    - f.4. Analysis of corrosion damages, economic losses and control of corrosion at the oil refinery units.

At the end of such traineeships, students write reports (~70-100 pages) and defend them in academia in the presence of the supervisor from industry. The traineeship is very important step in establishing a direct "educator-educable" bond. This bond in academia, as a rule, is weak: a lecturer in many cases does not know his students. The Middle Age education established a system of direct knowledge transmission ('direct bond') between teachers and students. In modern education in universities there is danger of alienation between professors and students. The introduction of traineeship for students with concrete topics at chemical plants will restore these disrupted bonds.

4.2. Practising engineers and technical personal at chemical plants

Systematic seminars and courses (6-12 hours) are organized in the oil refinery. The program of these courses depends on the specialization of engineers and technicians: chemical engineers, chemists, material engineers, mechanical engineers, quality control and processes, purchase of crude oil and marketing of fuels, supply of materials and equipment. Engineers and technicians can watch three-hour video, created according to our scenario and located on the Internet of the oil refining company. This is a film about technological processes, the materials used in oil refining, corrosion, methods of anti-corrosion protection and monitoring. Engineers and technicians can watch it by means of computer at any time convenient for them, stop, repeat, and continue to browse and study, call the author (corrosion expert) of the film, write him, meet and consult.

Like doctors who have refresher courses every few years, engineers have to raise their qualification every 3-5 years. New technologies and processes, materials, methods of monitoring, detection (with instrumental base) and corrosion protection technology are being developed intensively. How can an engineer acquire new knowledge and be up-to-date? The following ways are recommended.

a. Organization and participation in the annual conferences, seminars, symposia, and courses.
b. Reading of journals, conference proceedings, reports, encyclopedias, and books.
c. Constant pursuit of standards, codes, and specifications.
d. Meetings and consultations with colleagues.
e. Membership in professional organizations and participation in their working committees.

4.3. Teachers, lecturers, educators and instructors of engineering disciplines

The main mission when training teachers, lecturers, educators and instructors is to explain them how they should teach students and practising engineers, as well as pay attention to a particular approach to the administrative personnel in chemical industry. Who should be the ideal teacher of engineering disciplines?

A leading role in the formation of engineering outlook must be given to a lecturer. It is desirable that the educator would be simultaneously a specialist-engineer-practitioner-scientist. A good lecturer is a person who has wide knowledge and wonderful expressive speech, who can establish contact with students, engineers and technicians, managers, other teachers and educators, in short, with all categories of learners. The most important and necessary feature of the teacher is the ability to communicate with the audience (both with performers and creators). Educators as a rule do not learn this skill, and it would be necessary to teach them, as a Russian theatre director Konstantin Stanislavski trained actors to communicate[30]. The personal qualities of a lecturer play a crucial role in the appeal or rejection of the subject of engineering. The main aim and objective of a teacher is the development of independent analytical thinking of a trainee. For this, a teacher must know as much as possible and more of the subject that he teaches. Interdisciplinary communication helps a lecturer in that, for example, humanitarian aspects related to history, art, music, literature, poetry, philosophy, and … humor. Several examples are given below.

4.3.1. Use of Historical Aspects in Education

Any topic is recommended to be represented in a historical context, especially as a struggle between different directions. For example, Luigi Galvani ("animal electricity") and Alessandro Volta ("voltaic pile") about the behavior of two dissimilar metals in contact in an electrolyte solution, invention of stainless steels, metalizing coatings, and volatile corrosion inhibitors.

4.3.2. How to educate creative chemical engineer?

"Every great advance in science has issued from a new audacity of imagination."
John Dewey (1859-1952), an American philosopher.

We must distinguish two levels of learning and knowledge[31]. The first level is *skills*. There are skills in our lives which we do not need to know how to do them, but simply to do them. A typical example - cycling. We can explain to someone many times how to ride a bicycle, but as long as a person does not try to ride, he will not learn to do it. These are *skills*. The second level: "*you must be able to see the problem. Do not need to have the skills already, but the ability of the creative approach, creative thinking.*" It is a totally different level of knowledge. You need a different approach. Exactly this level of knowledge does not tolerate "lack of freedom". If his consciousness is not "free", he will never be able not only to solve the problem, but also to pose a challenge (problem formulation).

Usually an engineer is "burdened, connected" by different algorithms, standards, codes, and specifications. An engineer works in "rigid frames". Our objective as an educator is to "emancipate" him, to give freedom for creative work, creative thinking. Who is not fraught by "rigid frames" of thinking?

Artists: painters, composers, writers, sculptors, and poets. Thus we conclude that we should teach engineers to think freely, without restraints, to be creative like people of art. We speak about interdisciplinary, humanitarian and artistic thinking of engineers and scientists. Let us see how art media can help in engineering-scientific education. We can establish interrelationships between the "three cultures" (science, engineering and art), studying new inspirations and creativity in engineering, and to show the younger generation of students, engineers, scientists and educators how learning, education and our very existence may be interesting, fascinating, creative, productive, efficient, exciting, attractive, rich, and as a result *beautiful*.

4.3.3. Poetry in engineering-scientific education

"Poetry is important. No less than science, it seeks a hold upon reality, and the closeness of its approach is the test of its success."
Babette Deutsch (1895-1982), an American poet.

Poetry is probably one of the most philosophical branches of art. When you teach *entropy* you can talk about the poet Wystan Hugh Auden who has been admired by physical laws and wrote brilliant poem "Entropy" which is well studied by students and perceived with great pleasure.

I'm not being negligent
Nor plain, messy no!
But somebody intelligent
Once made up a law:

This is not a simple verse,
It's a scholar rhyme –
Entropy in the universe
Increases all the time.

From Big Bang to Bigger Boom
One thing just we may assume:
Universe-roulette-wheel spins –
Order loses! Chaos wins!

4.3.4. Music in engineering - scientific education[21]

"Life without music would be a mistake."
Friedrich Nietzsche (1844-1900), a German philosopher.

Music has always been among the leading arts, and therefore has been used for different studies. Plato (428-348 BC), the founder of Western philosophy, declared in the "*Republic*": "*Education through music is extraordinary important because rhythm and harmony penetrate to the depths of the soul, seize and ennoble it*"[32, 33]. Children learn the alphabet "*ABC*" to the tune of "*Twinkle, Twinkle, Little Star*", and the states of the USA in the alphabetical order from a song "*Fifty Nifty United States*"; students learn some chemical reactions to the tune of "*Oh, my darling Clementine*". Thus, music can be useful in learning and remembering the basics of language, social disciplines, and science.

For a better understanding of the role of music in engineering-scientific education, we should mention that music is the most abstract form of art, but word is a real and concrete form of expression of our thoughts. We use mostly visual and hearing perception in education. Thus, we can connect music, word and picture or writing and use them in education. Such education by means of humanitarian topics turns any dull discipline into an aesthetic form of engineering-scientific education.

a. When you explain what happens with crude oil in distillation column during rectification, how different organic substances containing in crude oil move and boil, are separated according to their boiling temperature, and gasoline, kerosene, gas oil, fuel oil are produced, try listen to the music composition "*Rhapsody in Blue*" by George Gershwin.
b. Thermodynamic reversible processes (a 'quasi-static' process that happens infinitely slowly) can be associated with the eternal motion, namely, with the "*Flight of the Bumblebee*" by Nikolai Rimsky-Korsakov, or the "*Perpetual Motion*" by Edward MacDowell. When we are listening to these music compositions we feel that this music is eternal as well as that there is no end both for it and for any thermodynamic reversible process.
c. The 2nd law of thermodynamics (the entropy of the universe tends to a maximum) can be associated with the "*Bolero*" by Moris Ravel or "*In the Hall of the Mountain King*" (suite "Peer Gynt") by Edvard Grieg or "*Polovetzkian dances*" (opera "*Prince Igor*") by Alexander Borodin. The analogy is in the 'expansion' of music during its development. Similar phenomenon occurs with the universe – its expansion.

4.3.5. Humor in engineering education

"There is nothing more frustrating than a world without laughter."
"The human race has one really effective weapon, and that is laughter."
Mark Twain (1835-1910), an American writer and humorist.

The sense of humor is associated with the ability of human to detect contradictions in the world around us. The Russian philosopher Vl. S. Soloviev (1853-1900) noted that comedy arises from contradictions between the reality and the ideal[34]. Two examples are given below[21, 35, 36].

a) The German physico-chemist Walther Hermann Nernst, a founder of the 3rd law of thermodynamics, commented in

1937, that it had taken three scientists (Mayer, Joule, and Helmholtz) to formulate the 1st law of thermodynamics, two scientists (Clausius and Thomson-Kelvin) to formulate the 2nd law, but that he (Nernst) had been obliged to do the 3rd law all by himself. He added that it followed by extrapolation that there could never be the 4th law of thermodynamics[37]. This is a fine joke, as in the 1930s scientists understood the importance of the law of thermal equilibrium, and they called it the "*Zero Law*". Not the fourth one!

b) When we explain what the rate of corrosion is, we can give humorous definition: *corrosion rate is the reciprocal value of the time it takes a corrosion engineer to remain on duty*. Here is the humoristic definition of microbiological induced corrosion: *this is a kind of corrosion, when none of the known mechanisms of pitting formation can be fitted*.

4.3.6. General recommendations

It is necessary to conduct propaganda to attract people to the specialty of 'chemical engineering'. An interesting project is running by NACE (National Association of Corrosion Engineers) International "*Corrosion - it's more than a job. It's a passion. Corrosion career. Professionals of different ages from different countries share their stories how they came into the world of corrosion*"[38].

4.4. Managers and administration of chemical enterprises

"Only fools and charlatans know everything and understand everything".
Anton Chekhov (1860-1904), a Russian writer.

It is important to explain and to show the importance of corrosion problems and their solutions in terms of economy, risk, safety and reliability in operation of equipment, possible damages to the environment, impact on health service staff, and depletion of sources of metals in the earth's crust. For instance, evaluation and analysis of the causes of corrosion damages at the oil refinery (Haifa, Israel) were carried out in 1991-2012. The result was an annual report of economic losses from corrosion (corrosion cost)[39-41]. These figures are so impressive that managers ask "*what to do?*" Our recommendations are:

a) To organize courses for the personnel with acquiring knowledge of corrosion protection required at the design stage of equipment and processes up to control and monitor corrosion.
b) To send engineers to specialization, conferences, seminars, courses.
c) To improve the control of process parameters (as their noncompliance can lead to corrosion and then to explosions, fires, damage to units, the environment, injuries, and even death of people).
d) Necessity of use of anticorrosion actions and corrosion monitoring.
e) To increase the interest of the staff in the implementation of anti-corrosion programs and corrosion monitoring. As a rule, the implementation of these programs is an additional function of engineers, operators, and technicians. Therefore it is proposed to set bonus (for the initiative in their implementation) and penalties (for negligence and disregard of corrosion problems). Only financial incentives can improve the situation and attitude to corrosion problems in the workplace.
f) To include an anti-corrosion program in annual funding plan of enterprises.
g) To enhance the cooperation of all services and departments in realization of anti-corrosion program.

Every opportunity must be used to talk through mass media about the problems associated with corrosion and thus to inform the general public and make them aware of the issues involved.

4.5. The role of an educator (teacher, lecturer)

"I am always ready to learn, but I do not always like being taught."
Winston Churchill (1874-1965), a British politician.

The problem is that usually nobody checks if a person can teach. A person can be a fine scientist or an excellent engineer with deep and diverse knowledge and experience, but this does not mean that this person can be a good educator. When a person wants to learn play piano or to sing it is easy to examine his aptitude: hearing, voice, sense of rhythm. How can one check if a person has the ability to teach? It is not easy but probably possible. It is possible to educate a person some teaching methods and technique but the phrase 'a teacher from God' works in the same way as a talent to play the violin, sing or write poetry.

My daughter is a professional tour guide and is learning in the university. During preparation to the conference "Science, Technology and Art Relations" that I organized a year ago, she said me: "*My lovely dad, people will not come. Today you can read all that you want to know on the Internet.*" She was right. I asked for her: "*Probably, should not you also go to the lectures in the university?*" She replied: "*Yes and No*". The role of an educator is great. Some months after our conversation, she had a group of forty young Jews from Moscow on the program "Taglit (Discovery)" to travel in Israel. After 10 days of training of this group, she received a verse from the young people in Russian (my translation into English):

Ты поделилась с нами сущим,	You shared your passion and knowledge with us,
Что в магазине не купить,	That is not bought in the store,
Не прочитать и не услышать –	Not read and not heard at once.
Такое можно лишь прожить.	This can only be lived anymore.
Ты нас не укольнула в сердце,	You did not prick the heart,
Идеи не вложила в нас ...	You did not invest ideas in us …
Быть может, прозвучит зловеще:	Maybe it sounds ominously but:
Как вирус заразила в раз.	Like the virus you infected us.

This was symbolic. A teacher can do things that no book or encyclopedia can do. Fates of young people depend on a teacher. One can give many examples how young peoples went to learn chemistry and chemical engineering due to the personality of a teacher in chemistry in a secondary school. Nobody can define "this is good or not good", this is a philosophical problem. However we give a significant role to the individuality of a teacher, his knowledge, behavior, uniqueness, ability to "ignite" and inspire young souls.

5. Insight into the Future

"I cannot teach anybody anything. I can only make them think."
Socrates (470-399 BC), a Greek philosopher.

Education (as teaching and learning) probably will change drastically in the near future as a result of technological, information and knowledge 'singularity': when the amount of knowledge will exceed the human intellectual capacity and control (like 'Big Bang' – an explosion from one very dense 'single' point during creation of the universe). Knowledge increases exponentially and grows twofold every 1.5 years. Specialists in each field (and in education too!) cannot follow all the publications in encyclopedias, books, journals, proceedings of conferences, minutes and reports, on Internet. No seminar and conference will help to be familiar with everything that will be researched and published. Only computer treatment will be able to follow and analyze all news. However, the final analysis and decision should be made by qualified specialists.
The question is how to match modern and future education with the achievements of science and engineering? Educators teaching the basics of fundamental knowledge simultaneously will teach how not drown in the "sea" of diverse information, how efficiently, effectively and fast to find needed data for decision of problems.

Conclusions

"Arriving at one goal is the starting point to another."
John Dewey (1859-1952), an American philosopher.

An educator should find the form of communication with listeners.
Theoretical material should be grounded in practice.
Try to defuse 'tension' in the classroom with a joke.
Students are on the top of human intellectual perception of new information and knowledge. Therefore we should use methods of interaction between engineering, science and humanitarian aspects in order to educate creative specialist (chemical engineer) in chemical engineering who can solve current problems, set new targets and solve the tasks of the future, and to "beautify" education.
There are definite limitations in knowledge transfer. First, it is impossible to impart (transfer) all existing knowledge, even if you really want. The aphorisms "*One cannot embrace the unembraceable*" by Kozma Prutkov and "T*he more I learn, the more I realize how much I don't know*" by Albert Einstein are actual for all times. Second, information like memory is associative and we can extract (recover) personal (tacit) knowledge depending on the situation.

This topic is eternal. Therefore it is impossible to put an end to our subject. Like in science, in technology and in art ... Only ... three dots ... And to continue to develop this theme in the next paper ...

References

1. Irene Kim (2002), *Chemical Engineering: A Rich and Diverse History*, CEP, pp. 2S-9S.
2. Butterfield H (1959), *The Origins of Modern Science: 1300-1800*. The Macmillan Company, New York, 242 p.
3. Subrata Dasgupta (1996), *Technology and Creativity*, Oxford University Press, New York, Oxford, USA, 233 p.
4. Groysman A (2012), *Art, Science and Technology: Interaction Between Three Cultures*, In Proceedings of the 1st International Conference "Art, Science and Technology: Interaction Between Three Cultures", 1-2 June 2011, ORT Braude College, Karmiel, Israel, Domus Argenia Publisher, Milano, Italy, pp.1-8.
5. *The Oxford Dictionary of English Etymology* (1991), Editor Onions CT, p. 944.
6. *Medieval France: A Companion to French Studies* (2010), Editor Arthur Augustus Tilley, Cambridge University Press, 326 p.
7. Vaclav Smil (2005), *Creating the Twentieth Century: Technical Innovations of 1867-1914 and Their Lasting Impact*, Oxford University Press, Oxford, New York, 350 p.
8. Shallcross D, *Chemical Engineering Education*, Chemical Engineering and Chemical Process Technology, Vol. 5. http://www.eolss.net/sample-chapters/c06/e6-34-08-00.pdf
9. Clive Cohen (1996), *The Early History of Chemical Engineering: A Reassessment*, The British Journal for the History of Science, 29(2):171-194.
10. Tsion Avital (2003), *Art versus Nonart. Art out of Mind*,

Cambridge University Press, New York, USA, 445 p.
11. Plekhanov GV (1948), *Art and Literature*, Publisher "Гос. изд-во худож. Лит-ры", Moscow, 887 p. (In Russian).
12. Koshkin VM (2010), *Senses and symbols*, Folio, Kharkov, 184 p. (In Russian).
13. http://en.wikipedia.org/wiki/Alexander_Kapp
14. Knowles MS (1975), Self-Directed Learning. Chicago: Follet.
15. Knowles MS (1984), *The Adult Learner: A Neglected Species* (3rd Ed.). Houston: Gulf Publishing.
16. Knowles MS (1984), *Andragogy in Action*. San Francisco: Jossey-Bass.
17. Knowles MS (1988), *The Modern Practice of Adult Education: From Pedagogy to Andragogy*, Cambridge Book Co, 400 p.
18. Jarvis P (1985) *The Sociology of Adult and Continuing Education*, Beckenham: Croom Helm.
19. Dénes Nagy, *Harmonia and Symmetria: Bridges in our "Split Cultures" between Art and Science, In: Symmetry: Art and Science*, 8th Interdisciplinary Festival-Congress of International Society for the Interdisciplinary Study of Symmetry, Gmünd, Austria, August 23-28, 2010,Editors: George Lugosi and Dénes Nagy, Special Issue for Festival-Congress, 2010/1-4, pp. 3-9.
20. Groysman A (2010), *Corrosion for Everybody*, Springer, Dordrecht, 368 p.
21. Groysman A (2011), *Use of Art Media in Scientific and Engineering Education*, In: Proceedings of the 14th Generative Art Conference GA 2011, 5-7 December, Domus Argenia Publisher, Rome, Italy, pp.32-46.
22. Engelmeir PK, *Technical result of the XIXth century*, Typography of K.A. Kaznacheev, Moscow, 1898. (In Russian).
23. Wood MH, Vetere Arellano AL, Van Wijk L, *Corrosion-Related Accidents in Petroleum Refineries* (2013) JRC Scientific and Policy Reports, European Commission EUR 26331 EN, Institute for the Protection and Security of the Citizen, Italy, 94 p.
24. Groysman A and Siso R (2012), *Corrosion of Aboveground Storage Tanks Containing Fuels*, Materials Performance, 51(2):52-56.
25. Groysman A (2014), *Corrosion in Systems for Transportation and Storage of Petroleum Products*, Springer, Dordrecht, 297 p.
26. Groysman A, Penner J, Brodsky N, Skorodinsky S (2008), *Naphthenic Acids Combat Naphthenic Acid Corrosion*, Paper No. 2257, (In) Proc. 17th Intl. Corr. Cong., Las-Vegas, USA, p. 16.
27. Groysman A, Penner J, Brodsky N, Skorodinsky S, *Naphthenic Acid Corrosion Study*, Paper 1081, (In) Proc. European Corrosion Congress EUROCORR 2007, Freiburg im Breisgau, Germany, 2007, p. 23.
28. Groysman A and Penner J (2007), *Process for Inhibiting Naphthenic Acid Corrosion*, WO/2009/053971, USA.
29. Groysman A, Penner J, Mizrahi L, Brodsky N, *Examination of a "Green" Corrosion Inhibitor and Corrosion Resistant Alloys for the Overhead of the Crude Oil Distillation Unit*, Paper No. 2134, NACE International Conference, 2013, Orlando, Florida, USA, p. 13.
30. German Andreev (Fain), *Reminiscences and Reflections of a Russian Emigrant*, OAO "Moscow Textbooks", Moscow, 2008, p. 480 (In Russian).
31. Ivan Illich (1995), *Deschooling Society*, Marion Boyars Publishers Ltd., 116 p.
32. Reichold K and Graf B (2003), *Paintings that Changed the World, From Lascaux to Picasso*, Prestel-Verlag, Munich, 192 p.
33. West ML (1994), *Ancient Greek Music*, Oxford University Press, USA, 440 p.
34. Soloviev VlS (2001), *General meaning of art*, Library "Vehi".
35. Groysman A (2004), *Aesthetic, philosophical and historical aspects in the physical chemistry education*, In: Trends in Electrochemistry and Corrosion at the Beginning of the 21st Century, Dedicated to Professor Dr. Josep M. Costa on the occasion of his 70th birthday, Editors: Enric Brillas and Pere-Lluís Cabot, Universitat de Barcelona, Barcelona, pp. 1203-1225.
36. Groysman A (2014), C*orrosion Education: Present and Future*, In: Proceedings of the 19th International Corrosion Congress, Jeju, Korea, 2–6 November, 2014, 10 p.
37. Laidler KJ (1995), *The World of Physical Chemistry*, Oxford University Press, Oxford,476 p.
38. http://nace.org/Membership/Profiles-Gallery/
39. Groysman A (2004), *Corrosion and Quality*, (In) Proc. 15th Intl Conference of the Israel Society for Quality, Jerusalem, Israel, p. 223.
40. Groysman A (2004), *Corrosion Problems and their Solutions in the Refining Industry*, (In) Proc. European Corrosion Congress EUROCORR 2004, Nice, France, p. 9.
41. Groysman A and Brodsky N (2006), *Corrosion and Quality*, Accreditation and Quality Assurance: Journal for Quality, Comparability and Reliability in Chemical Measurement, Springer (Publisher) Berlin/Heidelberg, 10(10): 537-542.

Insights on learning and grading processes in laboratory courses

Ruthy Sfez
Department of Advanced Materials, Azrieli College of Engineering Jerusalem, Israel
Email: ruti@jce.ac.il

Abstract: Laboratory courses are an important part in any curriculum of students learning for science or engineering degrees. They give the student the opportunity to apply theoretical principles which were learned in frontal courses. Moreover, it enables the student to deal with experimental results which deviate from the expected one, and evaluate the accuracy and precision of his results. Laboratory courses require a major effort on behalf of the students at three levels: preparation, performance and reporting, i.e. writing a scientific report and analyzing the experimental results. Usually, a laboratory session starts with a short pre-lab quiz and colloquium which examines the student' knowledge in usual known parameters of evaluation. The report can be evaluated in that way too. However, the evaluation of the performance in the lab, which can sometimes consist in about 50% and more of the final grades, is given intuitively by the instructors or teaching assistants (TAs). This situation implies a lack of clarity and consistency between the students and teachers, and can cause biased grading depending on a specific instructor with no standardization in the evaluation and grading. Moreover, it is very difficult to estimate the learning process of the student during the lab course.
In our institution (Azrieli College of Engineering, Jerusalem, ACE) we have developed in the past years a rubric score based on specific chosen parameters which was examined on more than 100 students and more than 20 TAs and heads of laboratories in various Chemistry courses. Analysis of the grading process showed that the rubric-based grading enables a systematic and standardized evaluation of experimental performance of the students. A comparison between grades based on intuition and on the developed evaluation method was done showing an expansion in the grading range. Following these results, a second step was taken in which a self-evaluation of the students was conducted and compared to the rubric parameters. This comparison gave an insight on the learning curve of types of students and can be used for real-time intervention during the lab course.

Keywords: laboratory courses, evaluation, assessment, standardization, instructor-student interface

Introduction:

Science and engineering education in the 21st century may be influenced by the development of distance learning[1]. However, laboratory courses are currently less affected by these changes. Laboratory courses have been for many years an essential part of the learning experience for every science or engineering student due to the special environment they provide which enables learning on various levels[2-7]. The main goals of laboratory courses have shifted during the years from learning factual information[8] to developing concepts[9] and scientific processes[10]. In a recent review dedicated to the goals of laboratory courses in the USA, group work and broader communication skills were also mentioned[11]. In any case, it is clear that laboratory courses can develop multiple skills, implying the major role of the laboratory instructor in defining what main skills are desired for a specific course[12]. Laboratory courses in chemistry are varied and serve different purposes and students. The courses range from general basic chemistry courses to specialized and advanced courses. Many laboratory courses are part of general courses, and are usually integrated in the course [9]. It is also important to note that laboratory courses require great effort on behalf of the student and are time consuming. A lab course is composed of several sections which require multiple skills. Usually, it can be

Ruthy Sfez got her Ph.D. in Chemistry at the Hebrew University of Jerusalem, in 2003. She continued as a researcher at the Hebrew University for several years. Since 2011 she is a senior lecturer at the department of advanced materials engineering and head of academic studies in Chemistry at Azrieli, College of Engineering, Jerusalem. Since 2013 she holds the position of students' dean. Her current research interests are self- assembled monolayers for various applications, hybrid nanomaterials and learning and grading process in laboratory courses.

regarded from the student's and instructor's points of view, as composed of three components:

1. Preparation – the student learns the theoretical concepts required for the lab, and the instructor evaluates this knowledge by a pre-lab quiz or/and direct questions.
2. Performance – the student performs the experiment while keeping safety rules and understanding experimental observations, which requires concentration and focus. The instructor usually gives an intuitive estimation of the student's performance.
3. Report – the student writes a scientific report and analysis of the results obtained during the lab, while the instructor has to evaluate it.

In contrast to the first and third parts of the evaluation, which can use standard methods of evaluation such as quizzes and usual feedback on written assignments, the evaluation of the performance in the lab (which can sometimes consist of about 50% and more of the final grade), is often given intuitively by the instructors (usually teaching assistants (TAs)). This situation leads to a lack of clarity and consistency between the students and teachers, in the evaluation and grading process.

Often enough there is a lack of understanding by the student as to how the TA is evaluating him. Assessment is almost never used during the labs and the students find themselves very frustrated. Moreover, even the TAs (both inexperienced and experienced) have difficulties in evaluating the practical work conducted by the student, due to lack of defined parameters for evaluation.

In Azrieli College of Engineering, Jerusalem, we wanted to develop a tool in which parameters for evaluation of practical work are defined in order to improve the TA-student interface and improve the learning and teaching process[8]. We started to check the concept of chemistry laboratories, both for first year as well as advanced students.

Our objectives were as follow:

1. Standardization of grading for practical work in laboratory courses – the challenge to quantify a qualitative estimation.
2. Improvement of student-TA interface
3. Improvement in the teaching and learning processes in laboratory courses.
4. Confidence in TA's grading system
5. Real-time analysis and feedback with possible intervention in special cases.

Methodology:

Our methodology consisted of a rubric score based on well-defined parameters which are relatively easy to quantify by the teaching assistants, which was used along with a self-assessment process conducted by the student.

An evaluation system was developed both for TAs and for students in the chemistry lab courses. A rubric score consisting of eight parameters was designed for practical work evaluation, based on discussions with more than 10 laboratory directors in various chemistry lab courses, both basic and advanced. About 20 TAs participated in the research described here, both experienced and inexperienced. More than 100 students were evaluated.

The chosen parameters and their weights are described in Fig. 1:

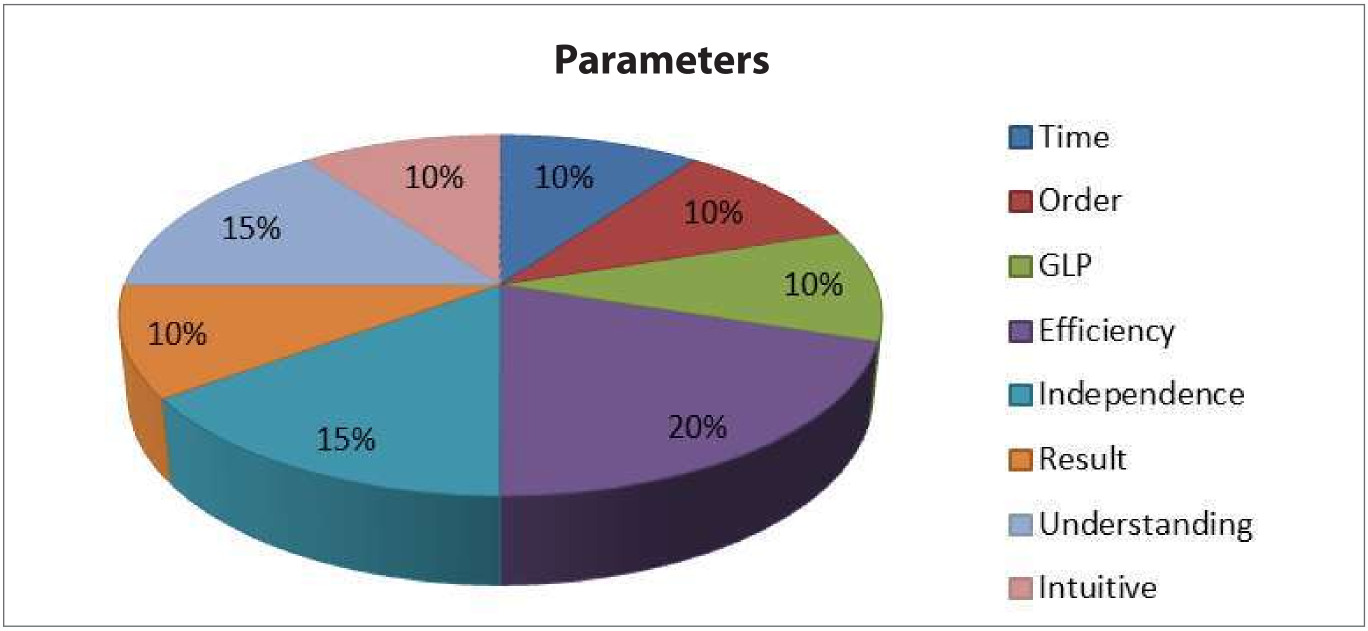


Fig. 1: Coefficients of the eight parameters of the developed rubric score.

- Time required for beginning the work (10%)
- Order and organization (10%)
- Working procedures according to good laboratory practice (GLP) (10%)
- Efficient work in the time frame: division of tasks in a useful way (20%)
- Independence during the work: confidence and understanding of the experimental details (15%)
- Evaluation of the obtained results in terms of accuracy and reproducibility (10%)
- Understanding the results, conclusions based on the experimental work (15%)
- Intuitive qualitative evaluation of the work (10%) – since we try to quantify a qualitative impression, it was important to include an intuition based parameter.

During each lab, the TAs were asked to evaluate the students both intuitively and by using the rubric score. Moreover, in order to estimate the TA-student interface, we asked students to fill out their own evaluation, based on similar parameters, masked in self-evaluation questions without knowing the relevant coefficients. A comparison between the three sets of data, i.e. intuitive estimation, rubric score TA based evaluation, and student self-evaluation was conducted. The two TAs grading systems were compared (Fig. 2) as well as the TAs rubric score and student self-evaluation based grading (Fig. 3-5), From a comparison of students' and TAs' evaluation, an estimation of the TA-student interface was obtained and an insight into the students' learning process was achieved. In some cases an intervention was conducted on the basis of major differences between the TA and student's evaluation.

Results:

A comparison between the two TA evaluation methods is shown in Fig. 2. In general it can be said that the developed methodology gives larger span of grading, as indicated by the minimal and maximal notes as well as larger variance, as can be seen in Fig. 2.

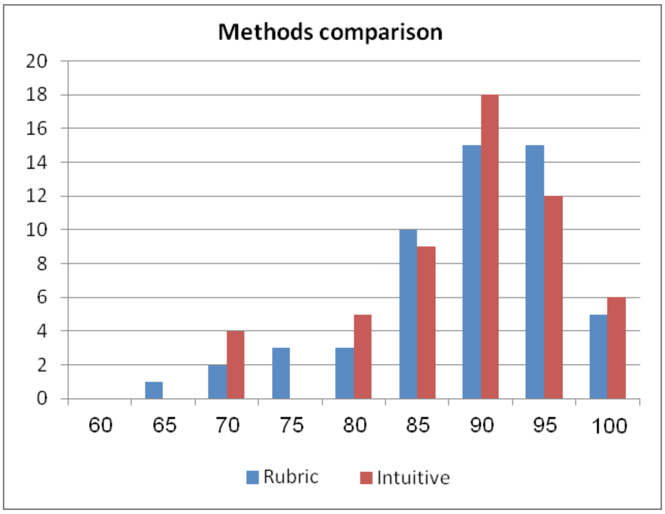


Fig. 2: Intuitive and score based comparison based on 20 TAs and about 100 students.

The average differs by two points, which is negligible. Usually, the intuitive grading was higher than the systematic grading, but in some cases it was not, regardless of the particular TA.

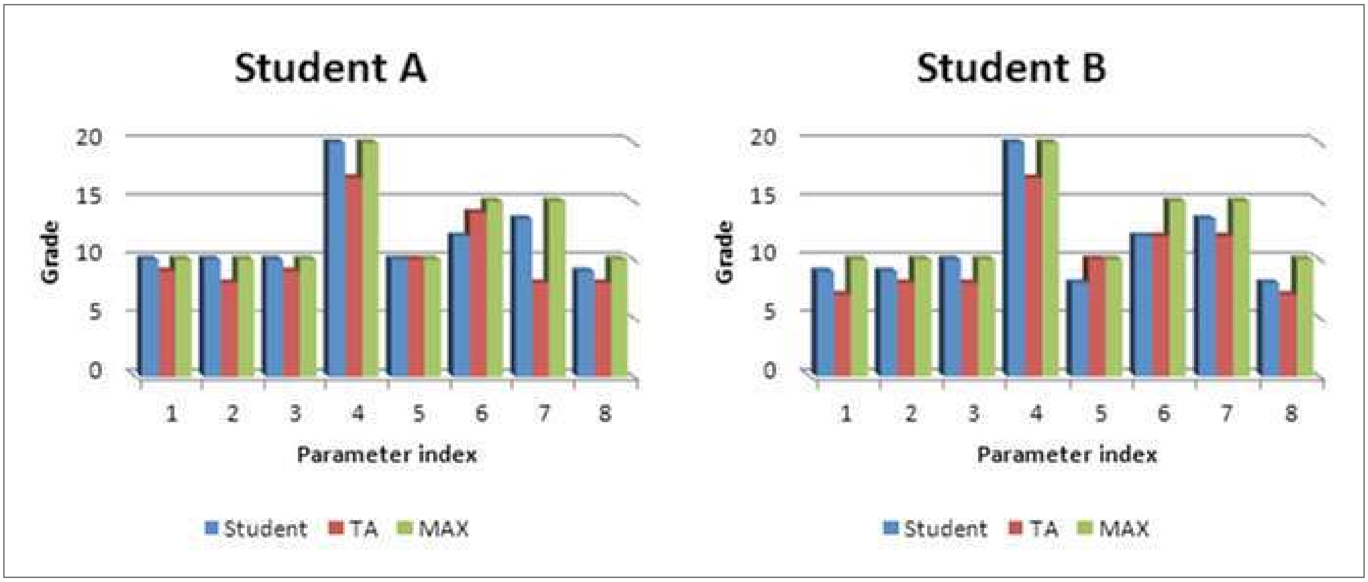


Fig. 3: Comparison of student and TA rubric scores evaluation for each parameter (described earlier) for the first lab session. Maximal value (green), TA evaluation (red) and student estimation at the end of the lab session (blue).

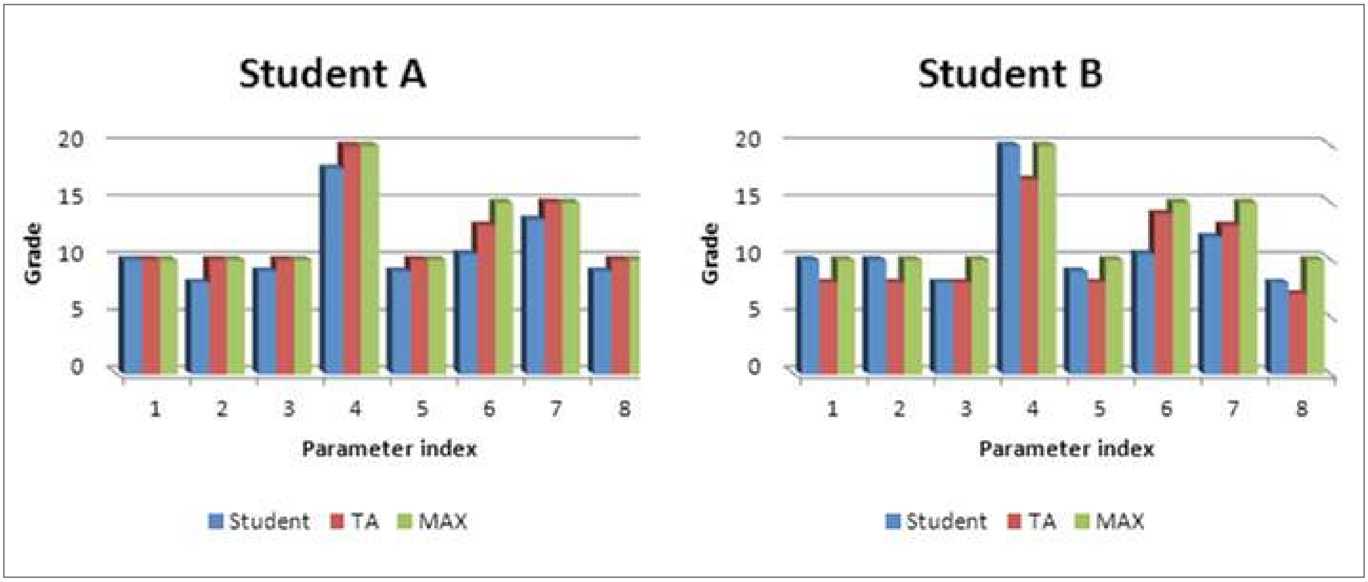


Fig. 4: Comparison of student (A and B) and TA based rubric scores evaluation for each parameter (described earlier) for the second lab session. Maximal (green), TA evaluation (red) and student estimation at the end of the lab session (blue) values.

No major differences were observed between experienced and new TAs.

Besides the differences obtained between the two evaluations, there is the important point of being able to rationalize the grading, a parameter which was evoked by most of the TAs (about 70%) as an important factor that helps the grading process and its validity, and is important of course from the ethical point of view. While asking for feedback from the TAs on the grading process, a difference was observed between new and experienced TAs. Five parameters were checked in the feedback as can be seen in Table 1.

Table 1: TAs' feedback on rubric score based evaluation

Parameter	New TAs	Experienced TAs
Practical	63%-very much, 25% medium, 12%- not at all	67% - very much 33% - not at all
Fair	75% - very much 12% - not at all	67% - very much 33% - not at all
Adequate criteria	yes	70% - yes 16% - no
Reliable	87% - yes	67% - yes
Helps the evaluation process	87% - yes	50% - yes Too many parameters

Analysis of the TAs' answers gave as a whole positive feedback. It is clear that for inexperienced TAs this method of evaluation was found to be most useful. The major problem evoked by the experienced TAs was the number of parameters and the need for a more user-friendly interface. However, in general the rubric score was considered to be a positive tool for evaluation. There is no doubt that a grading process like this requires effort and willingness on part of the TAs. Indeed, an improvement is been made now toward a more user-friendly interface using tablets, and optimized specific parameters for each lab course.

The number of parameters was evoked; however important information was obtained while using this detailed rubric score both for students and TAs. Interesting insights were obtained by comparing the students' self-evaluation and the TA evaluation after each lab session regarding the learning process during laboratory courses.

While comparing the student's self-evaluation of his work at the end of each lab session, with the TA's
evaluation, both based on the rubric score parameters, two different types of students were observed, depending on their learning capabilities and achievements. Figures 3-5 describe the evolution in the self- evaluation of the two types of students. Student A is considered to be a good student, while student B is a "less good" student based on their previous achievements. A major difference was observed in their learning curves through three lab sessions. Following the suggestion that a detailed description of the lab should be included[13], Fig. 3 shows the comparison between the TA and the students in the

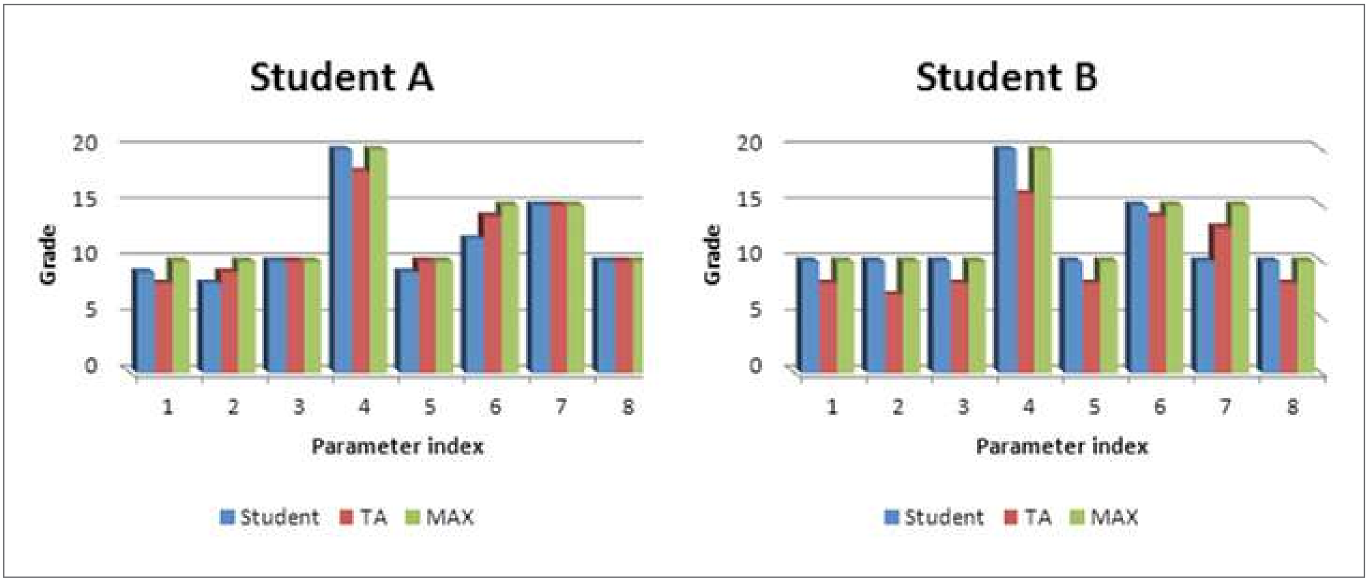


Fig. 5: Comparison of student (A and B) and TA rubric scores evaluation for each parameter (described earlier) for the third lab session. Maximal (green), TA evaluation (red) and student estimation at the end of the lab session (blue) values.

first lab session of mechanical engineering first-year students in a general chemistry course which included a lab session. As can be seen, at the first lab session, both students tend to evaluate themselves higher than the TA evaluation in most of the parameters.

Figures 4 and 5 show the evolution of the self-evaluation process for both students, in the second and third lab sessions. It can be seen that for these sessions, student A's self-evaluation is much closer to the TA's evaluation. A sort of non-verbal comprehension was obtained. On the other hand, student B keeps giving a higher evaluation for most of the parameters, compared to the TA's evaluation. These results suggests that there is a lack of understanding of what is expected from him during the lab, thus, indicating an inefficient student-TA interface.

The same types of students were found also for advanced specialized third-year advanced material students, showing a problem in the interface between the TA and the student even after some years of learning. Based on these results, we have tried to talk to students who self-evaluated themselves (both higher and lower) compared to the TA's evaluation. The students were happy and grateful to participate in the analysis of their results, and understood much better what was expected from them in order to perform efficiently during the laboratory. Moreover, sometimes they pointed that the identified problem, such as organization or work in a specified time frame, is a general problem which must be dealt with.

Conclusion:

We have shown a way to quantify experimental work of students in laboratories with a rubric score developed for chemistry laboratory courses. The main goals were to increase the self-regulated learning process for the student as well as increasing the TA's confidence in the grading process and improve its validity. A more user-friendly tool should be used in order to improve the grading process. In addition, by comparing students' own evaluation with the systematic TA evaluation, it is possible to analyze the actual effectiveness of the learning process by giving specific and real-time feedbacks, as well as reinforcing the student-TA interface.

Acknowledgement:

We thank our dear students of Advanced Materials, Pharmaceutical and Mechanical Engineering in Azrieli College of Engineering, Jerusalem, as well as the instructors who participated in this research. R. S. wishes to thank Hefer E, Lewinstein T. and Dr. Harel A. from the Industrial Engineering department in Azrieli College of Engineering, Jerusalem, for their assistance.

References:

[1] See for example: Academic Instruction 4, 2015, Editor: Hativa, N.

[2] Hofstein, A. , Lunetta, V. N. (1982), The role of the laboratory in science teaching: neglected as [ects of research. *Rev. Educ. Res*. 52, 201-207.

[3] Hofstein, A. (2004) The laboratory in Chemistry education: thirty years of experience with developments, implementation and evaluation, *Chemistry Education research and Practice*, 5, 247-264.

[4] Hofstein, A. , Lunetta, V. N., (2004) The laboratory in science education: foundation for the 21st century, *Science Education*, 88, 28-54.

[5] Hofstein, A. , Navon, O., Kipnis, M., Mamloc-Naaman R., (2005), Developing students' ability to ask more and better questions resulting from inquirytype chemistry laboratories, *Journal of Research and Science Teaching*, 42, 791-806.

[6] Feisel, L. D., & Rosa, A. J., (2005), The role of the laboratory in undergraduate engineering education, *Journal of Engineering Education*, 121-130.

[7] Hofstein, A., Mamloc-Naaman, R. (2007), The laboratory in Science education: The State of the Art, *Chemistry Education research and Practice*, 8, 105-108.

[8] Zuckerman, J. J., (1986), The coming renaissance of descriptive chemistry. *Journal of Chemical Education*, 63, 829-833.

[9] Abrahams, M. R., Cracolia, M. S., Palmer Graves, A., Aldhamash, A. H., Kihega, J. G., Palma Gil, J. G., & Varghese, V. (1997). The nature and state of general chemistry laboratory courses offered by colleges and universities in the united states. *Journal of Chemical Education*, 74, 591-594.

[10] Lloyd, B. W., (1992), The 20th century general chemistry laboratory: its various faces. *Journal of Chemical Education*, 69, 866-869.

[11] Bruck, A. D., Towns, M., (2013) Development, Implementation, and Analysis of a National Survey of Faculty Goals for Undergraduate Chemistry Laboratory, *Journal of Chemical Education*, 90, 685-693.

[12] Reid, N., Shah, I., The Role of Laboratory Work in University Chemistry, (2007), C*hemistry Education research and Practice*, 8, 172-185.

[13] Sadler, D. R., (2010), Beyond feedback: Developing student capability in complex appraisal. *Assessment & Evaluation in Higher Education*, 35, 535-550.

Three Chemists Who Found Refuge in Turkey.

Bob Weintraub* and Geoffrey Boner**

* Director of the Library, Sami Shamoon College of Engineering, Beersheva and Ashdod, Israel. bob@sce.ac.il

** Director, Institute of Hypertension and Kidney Diseases (Nephrology), Rabin Medical Center - Beilinson Campus. Center, Petah Tikva, Israel, (Retired 2002) and Associate Professor, Sackler Faculty of Medicine, Tel Aviv University, Israel (Retired 2003). gboner1@013.net

Fritz Arndt: "The Leader of Modern Chemistry in Turkey"; First proposed the "Resonance Hybrid" idea. Developed the "Arndt-Eistert Reaction."

Felix Haurowitz: Discovered that the human fetus contains a different kind of haemoglobin from that of an adult and made other fundamental discoveries about haemoglobin; First proposed the "Template Theory" of the immune system.

Kurt Steinitz: "Father of Haemodialysis (Artificial Kidney) in Israel"; Pioneer in the development of the clinical laboratory in Israel.

Between the years 1933 and 1945, the Republic of Turkey invited first-rank persecuted scholars to participate in the reform of Turkish higher education. In this way some 190 victims of National Socialism found refuge in Turkey.[1]

Arnold Reisman: "In this case, the Nazis' plans to rid themselves of Jews, beginning with intellectuals with Jewish roots or spouses, became a windfall for Atatürk's determination to modernize Turkey. The select group of Germans and later Austrians with a record of leading-edge contributions to their respective disciplines came to Turkey to transform Turkey's system of higher education and the new Turkish state's entire infrastructure, with the Reichstag's understanding. Occurring before the activation of death camps, this arrangement served the Nazis' aim of making their universities, professions, humanities, and their arts *Judenrein*, cleansed of Jewish influence and free from intelligentsia opposed to fascism. Because the Turks needed the help, Germany could use this situation as an exploitable chit on issues of Turkey's neutrality during wartime. Thus, the national self-serving policies of two disparate governments served humanity's ends during the darkest years of the 20th century."

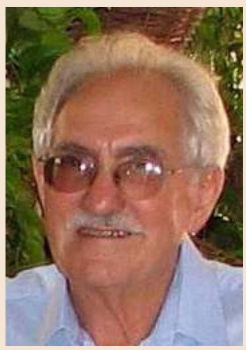
Fritz Arndt (1885-1969):

Fritz Arndt was born in Hamburg. He earned his doctorate in Chemistry at the University of Freiberg in 1908 and then held a series of positions in German universities. In 1915, Arndt accepted a position at the Imperial Ottoman University of Constantinople. In 1918 he returned to Breslau, where he remained until 1933, when dismissed under National Socialism. At the invitation of Sir Robert Robinson, he accepted a position at the Department of Organic Chemistry at Oxford. In 1934, he accepted the chair of General Chemistry at the University of Istanbul. He remained in Turkey until his retirement in 1955 and returned to Hamburg.[2]

Lale Aka Burk:[3] "For the author, a chemist whose native country is Turkey, Fritz Arndt holds a special place. He is remembered with great affection as the "the leader of modern

Bob Weintraub is the Director of the Library, The Sami Shamooon College of Engineering, Ashdod and Beersheva. He holds the Ph.D. in Physical Chemistry from the Massachusetts Institute of Technology and the Diploma in Library Science from the Hebrew University of Jerusalem. He has an interest in the history of chemistry and in scientific and technical librarianship.

Geoffrey Boner completed his medical training in South Africa and after immigrating to Israel, specialized in Nephrology. He is now retired after having been the Director of the Department of Nephrology and Hypertension at the Rabin Medical Center (Beilinson Hospital) and Associate Professor at the Sackler Faculty of Medicine at the Tel Aviv University. His main interest is the prevention and treatment of chronic kidney disease, especially secondary to diabetes mellitus. He has an interest in the History of Nephrology in Israel.



chemistry in Turkey."

"In 1915 the Ottoman government invited, as part of an educational reform initiative, a German mission to help upgrade the Dar-ül Fünun [house of knowledge, in Arabic]. Twenty German academics from a variety of fields were given teaching posts at the institution. One of the most significant achievements of the German professors was the establishment of the first academic department of chemistry, Yerebatan Kimya Enstitusu (The Chemistry Institute at Yerebatan), founded under the leadership of Fritz Arndt from Breslau University. For the first time in Turkey, chemistry became an independent discipline, separate from medicine and biology. The institute was housed in a new building planned by Arndt and equipped with supplies and chemicals from Germany. The curriculum was based on the German model, and the facilities were modern for the times. The institute trained students who eventually received chemistry degrees.

Arndt was also invited back by the Turkish government to come back to Istanbul University to head the department he had founded some two decades earlier. He returned to Turkey in 1934. Fritz Arndt's second sojourn in Turkey was as productive as the first. For the next twenty years, he helped train a new generation of Turkish chemists. His Turkish students were among the first in the world to learn about resonance from the expert himself."

Resonance Theory:

E. Campaigne (1959): "In 1924 Fritz Arndt published the first paper containing the 'resonance hybrid' idea which within the next ten years was firmly established as the proper explanation of aromatic behavior by the molecular orbital calculations of Hückel (1932) and the valence-bond treatment of Pauling and Wheland (1933). Fritz Arndt "was one of the very first to clearly appreciate the difference between tautomerism and resonance, and to conceive of a stable resonance hybrid structure for aromatic compounds."

Arndt (1957): "Kekule's idea of the oscillating double bonds in benzene was the closest approximation to the resonance interpretation of benzene and similar molecules achieved during all the time from Kekule up to 1924. I think this is so because Kekule's idea represented the state of benzene as one in which both Kekule formulas have equal shares, without altering the valencies as such; whereas all the later theories of Thiele, Kauffmann, Werner, Weitz, and others, introduced "partial valencies," "secondary valencies," "free valencies," etc., which turned up and disappeared again arbitrarily. All these attempts within the framework of unitarian theory, though useful in detail, were contradictory to the fundamentals of stoichiometry which are based on the indivisable units of valence. So Kekule's idea, and the theories of Thiele, Weitz, and others cannot be regarded as anticipations of the theory of resonance because they missed the main point, namely, the interrelation between valencies and *ionic changes*. In all resonating systems zwitterionic structures are involved, even in the case of benzene where the reaction formulas for aromatic substitution are zwitterionic."

The Arndt-Eistert Synthesis:

The name of Fritz Arndt is memorialized in the name of a reaction that he worked out with his colleagues, known as the The *Arndt-Eistert Synthesis*.[4] This is a comparatively simple procedure for converting an acid to the next higher homolog or to a derivative of the homologous acid, such as an ester or amide. The synthesis is applicable to aliphatic, aromatic, alicyclic and heterocyclic acids. The overall reaction is the insertion of a methylene group between the alkyl and carboxylic groups.

Felix Haurowitz (1896-1987):

F. W. Putnam:[5] "He was of a generation that will not be seen again. The product of centuries of European intellectual tradition-learned scholars, dedicated scientists, enlightened human beings-they were driven by barbaric intolerance to a new land to which they contributed so much. Their impact will be enduring, and Felix Haurowitz was one of the great ones among them."

Haurowitz was born in Prague and earned his M.D. in 1922 and his D.Sc in 1923 from the German University of Prague. In 1925, he began to give courses there and stayed on until 1939. During Haurowitz' years in Prague he studied haemoglobin and other proteins and methods of protein chemistry, in which he made a series of fundamental discoveries. In 1929 he started his studies of immunochemical problems which he kept up for the rest of his life.

On October 5, 1938, German troops marched through the Sudetenland. On January 31, 1939, Haurowitz wrote to his German colleague Hans Winterstein, already living in Istanbul, "It is strange, though, that among my German gentile colleagues, the same denunciation and mean-spirited rage has manifested itself as was evident when the Nazis were victorious in Germany's Vienna and the Sudetenland." At this time he was offered the position of the chair of biochemistry at the University of Istanbul. On March 5, 1939, German troops invaded Prague. Haurowitz fled to Turkey two weeks later. In Istanbul he conducted research in immunochemistry.

In 1948, Haurowitz accepted a position in the Department of Chemistry, Indiana University, Bloomington. He remained active in Bloomington until his death.

Haemoglobins:

Haurowitz determined the absorption spectra of methamoglobin and crystallized several haemoglobulin derivatives for the first time. He was the first to isolate fetal haemoglobin from fetal blood. He later pointed out that this was the first step in the search for other haemoglobins and showed that in the newborn the haemoglobin is a mixture of adult and fetal forms. Haurowitz, in an autobiographical note:[6] "Kinetic analysis of the decomposition rate of the haemoglobin of newborn children revealed that the blood of the newborn contains a mixture consisting of 70-85% of fetal and 15-30% of adult haemoglobin. Haurowitz succeeded in isolating and crystallizing the human fetal haemoglobin, whose crystals were quite different from those of adult haemoglobin. The affinity of the fetal haemoglobin to O_2 was found to be higher than that of the adult hemogloblin as long as both were in the red cells; after haemolysis of the red cells, O_2 was bound more firmly by the adult haemoglobin. In both fetal and adult haemoglobin the same heme was found; they differed from each other in their globin moieties."

Max Perutz (1997):[7] "In 1938 Felix Haurowitz, a biochemist in Prague, made a crucial observation. He placed hexagonal plates of horse deoxyhaemoglobin bathed in their mother liquor on a microscope slide and put a cover slip over them. The crystals had the purple colour of venous blood. While he watched, the air penetrated the liquid between slide and cover slip, dissolved the purple plates and replaced them with a growth of monoclinic needles with the scarlet colour of arterial blood. The change of crystal structure signified a change of shape of haemoglobin on reaction with oxygen, implying that it is not a static oxygen tank, but a molecular lung. This was to prove the key to the understanding of haemoglobin's functions, which turned out to be far more subtle and complex than was realized in the thirties." In 1937, Haurowitz showed Max Perutz this reaction and suggested to him that he take on the problem of solving the crystal structure of haemoglobin. Pertuz took up the challenge and in 1962 was awarded the Nobel Prize in Chemistry for his life-time work in this area - which included the first three dimensional model of the haemoglobin molecule.

The Template Theory:

Haurowitz:[6] "In 1929 Haurowitz became interested in immunochemical problems and started a series of investigations with the virologist F. Breinl in Prague. Although it was known then that the antibody properties are linked to the globulin fraction of the immune serum, it was not clear whether the antibodies are indeed globulins, or whether they are substances of an unknown nature, contaminated by globulins. To answer this question, Haurowitz isolated antigen-antibody precipitates and determined their amount gravimetrically; the antigens used were haemoglobin, azoproteins, or iodoproteins, which, owing to their color or their content of a specific constituent, could be determined quantitatively. The antibody content of the precipitates was obtained as the difference between the total weight and the weight of the antigen. The analyses showed that the substance which combined with the antigen had the properties of the serum globulins, and that the amount of globulin bound per milligram of antigen increased when the number of determinant groups per antigen molecule was increased. Haurowitz concluded that the antibodies are indeed serum globulins and that the specific combining site of an antibody molecule is complementarily adjusted to the determinant group of the homologous antigen. The mutual attraction of antigen and antibody was attributed to the mutual close fit which enables the combining sites to approach each other to such an extent that the short range intermolecular forces become efficient. Haurowitz introduced the idea that the antigen may act as a template (or mold) in the formation of the antibody…" Linus Pauling became interested in this model and further developed it. This theory was prominent for over twenty years. The template model replaced the side-chain model first proposed by Paul Ehrlich and itself was replaced by the clonal selection model of Burnett in 1957. The template model was of fundamental importance for biochemistry.[8,9]

Kurt Steinitz (1907-1966) :

Kurt Steinitz was born in Breslau, where he earned his medical degree in 1931. In 1932 he received his medical license and was registered as a specialist in Laboratory Medicine and Clinical Chemistry. Steinitz studied at several universities, including Breslau, Heidelberg and under Karl Thomas in Liepzig from 1928-29. Prof. Thomas instituted a course of study that included inorganic, organic, analytical and physiological chemistry. Steinitz found employment at the Breslau Municipal Hospital. With the rise of National Socialism, he was dismissed.

Steinitz went first to Milan where he worked in a hospital with no remuneration. In 1933 he reached Palestine and received his Medical License in 1934. In Palestine he worked in Ramat Hashavim, near Tel Aviv, raising chickens and bees. He was offered a position in Turkey at the newly established Gurabe, Istanbul University Hospital for Internal Diseases, as head of the clinical laboratory and instructor of students in clinical pathology. His research in these years was on renal function and methods for its determination. During this time, he established in Turkey the infrastructure for transferring conserved blood. In 1943 his contract expired and he returned to Palestine.

In Palestine, Steinitz worked for the Kupat Holim (the major health care organization) and became head of its clinical laboratory both in Haifa and Afula. From 1945 to 1960 he was head of the clinical laboratories of the Rothschild Municipal Hospital. During 1949 he spent a year at the Rambam Government Hospital in Haifa. From 1960 to 1966 he directed the chemistry laboratories of Beilinson Hospital in Petah Tikva. He lectured in biochemistry at the Tel Aviv University School of Natural Sciences, gave courses in biochemistry as part of Postgraduate Medical Studies and also lectured in the School of Medicine. Kurt Steinitz built the first artificial kidney in Israel. He was one of the first to introduce into Israel the use of radioisotopes for the diagnosis of thyroid disease and also organized a thyroid counter.

Renal Function

The amount of fluid filtered in the glomerulus in an accurate determination of the function of the kidney. The most accurate measurement of the glomerular filtration rate (GFR) is achieved by infusing a very special sugar, called inulin, and measuring its clearance. It is difficult to obtain and difficult to measure. Dr. Steinitz reported on a method for measuring inulin in 1938.[10] Another method for assessing GFR is to measure the clearance of creatinine, an endogenous break-down product. Dr. Steinitz reported on this in 1940.[11] He published other articles referring to the function of the kidneys.[12,13,14]

The Artificial Kidney

In the 1940's with the development of cellophane paper and heparin to prevent blood coagulation, attempts were made to develop artificial kidneys using a dialysis apparatus. Kolff was the first to describe the successful use of an artificial kidney in humans.[15] The following year Alwall described a similar but smaller apparatus.[16] Steinitz had read these studies and in 1947 wrote to both Kolff and Alwall requesting details on their experiments. He decided to build an artificial kidney using the Alwall design. He treated three patients with acute renal failure. His first patient developed renal failure following a mismatched blood transfusion, the second following gun-shots to the chest and abdomen and the third following abdominal surgery for an extra-uterine pregnancy. It was only the third patient that he managed to keep alive until her kidneys started to function again. When he moved to the Rambam hospital in 1949, he discontinued his treatment of renal failure. He wanted to continue using this method but for various reasons was unable to do so. It was only in 1957 that dialysis treatment of renal failure was reintroduced into Israel. This time Prof. David Ullman of Hadassah Hospital was instrumental in introducing the treatment.

Dr. Steinitz built his own dialysis equipment based on the design of Alwall and used it for treatment of patients with renal failure long before it was used in most countries of the world. Dr. Steinitz was a true pioneer in introducing hemodialysis to Israel.

The Thyroid Gland

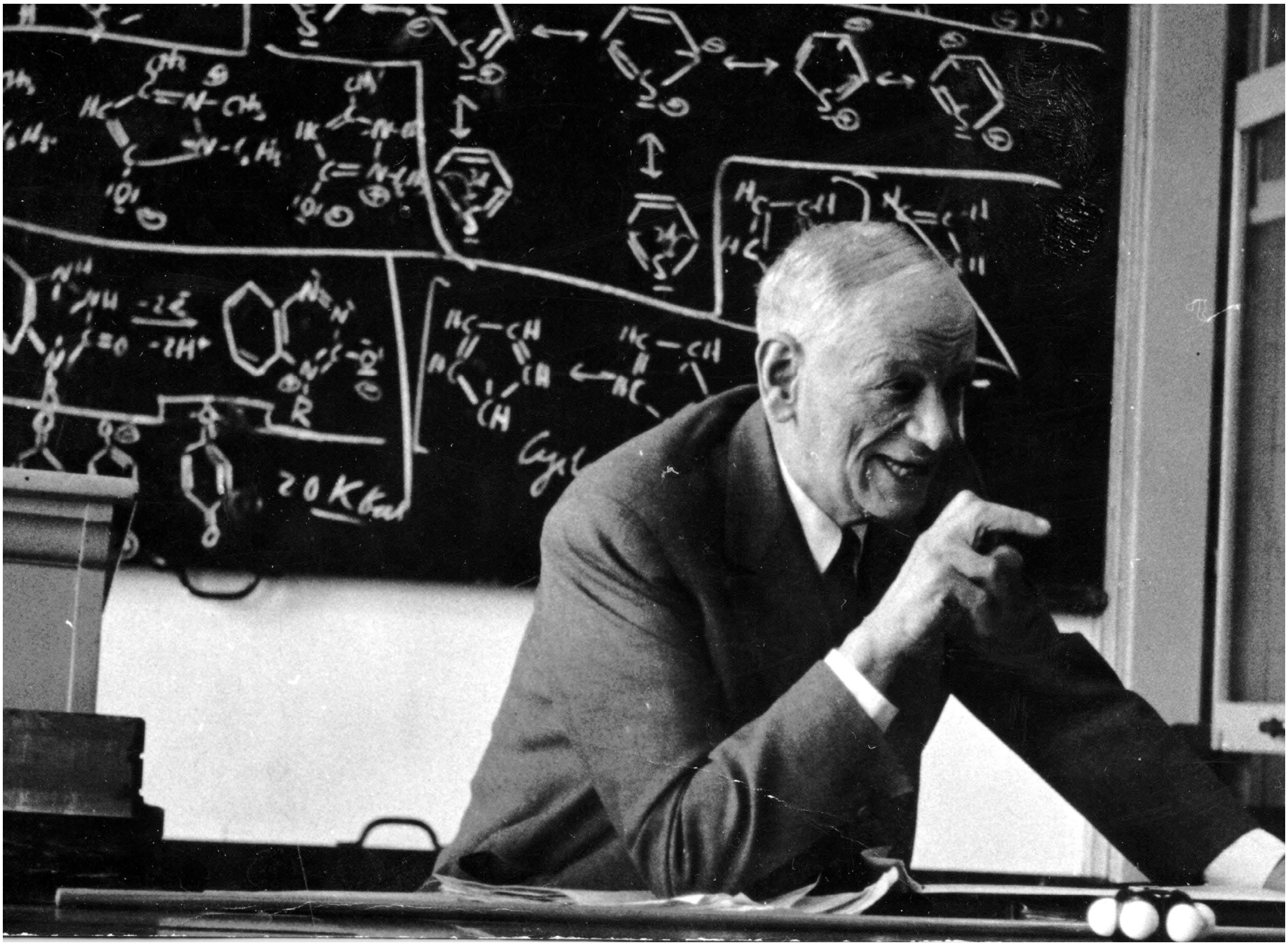
Iodine is avidly taken up by the thyroid gland and used in the production of thyroid hormone. As isotopes of iodine became available it became clear that these isotopes could be used in the study of the thyroid gland. Dr. Steinitz was a pioneer in applying isotopes of iodine. In 1953 he reported on the use of radioactive iodine in the diagnosis of hyperthyroidism.[17] He then went on to describe the use of radioactive iodine in an international journal.[18]

Steinitz' contribution to the development of the clinical laboratory in Israel was tremendous. He developed many new tests for the clinical laboratory. His ability to realize the importance of hemodialysis and to build an artificial kidney in the months before the establishment of the State of Israel was his outstanding achievement. He should be remembered as the father of dialysis in Israel and a pioneer in the laboratory investigation of many diseases.

Reflecting Back:[19,20,21]

After a few years, the majority of the refuge scientists who fled to Turkey were not wanted and their contracts were not renewed. To each had been attached a few young Turkish students who were supposed to learn the necessary skills so as to replace him.

Prof. Philip Schwartz, a Hungarian by birth, held the chair of Pathology at Frankfurt University. In March 1933 he was dimissed. Schwartz left for Zürich where he was one of the founders of the Notgemeinschaft (Emergency Service of German Scholars Abroad) and directed it for 6 months. During that time the Turkish Government asked him to establish the new University of Istanbul. Towards this purpose, within three weeks he drew up a list of thirty candidates. The Turkish Parliament dissolved the old High School and established in its place a modern University with five faculties. On Nov 1,



Fritz Arndt. I am grateful to Ms. Bettina Arndt , Fritz' granddaughter, for this photograph.

the new University opened. Schwartz went there himself and headed the Pathological Institute for twenty years. During that time he was instrumental in founding a medical school in Ankara and became advisor to the government in the recruitment of scientific and government specialists.

"I personally was able to engage, directly or indirectly, about 250 first-rate scientists (émigrés) for the Turkish Government. My friends, active in every governmental and organizational field, changed profoundly the face of Turkey, giving a mighty impulse to similar developments in the surrounding Musseulman countries."

Professor Schwartz, reflecting on the story eighteen years after, wrote: "The hopes that were bound up with the foundation of the new Universities have not been fulfilled in every aspect. Nevertheless, all of us foreign and Turkish professors, who collaborated in so many new cultural Institutes of the Republic, must be content. We have been able to remain loyal to the spirit which is the foundation of modern civilization and humane feeling, and to impart that spirit, even in these dark days of history, to thousands of gifted young persons. Happy are we who could carry on our work uncompromisingly, and happy the people whose leaders opened the doors to productive men compelled to leave their former place of work for grotesque reasons."

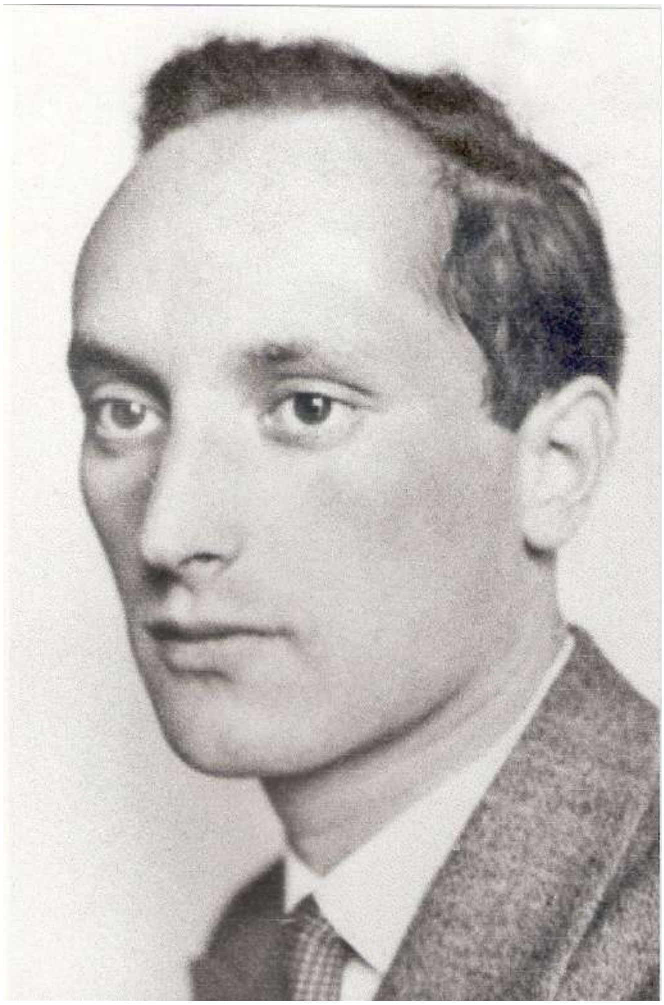
References:

1 Reisman, A. *Turkey's Modernization*. New Academia, 2006. Also Resiman's related papers.

2 Campaigne, E. The contributions of Fritz Arndt to resonance theory. JCE 36: 337, 1959.

3 Burk, LA. in Rose, PI ed. *The Dispossessed -An Anatomy of Exile*. Univ Mass, 2004.

Felix Haurowtiz, 1960. Photograph courtesy of Indiana University Archives.



Kurt Steinitz.

4 Bachmann, WE. and Struve, WS. The Arndt-Eistert synthesis. Organic Reactions 1: 38, 1942.

5 Putnam, FW. Biog Mem Natl Acad Sci. 1994;64:135-63.

6 Haurowitz, F. in *McGraw-Hill Modern Scientists and Engineers*. 1980.

7 Perutz, M. *Science is Not A Quiet Life*. Imperial College /World Scientific, 1997.

8 Morange, M. *A History of Molecular Biology*. Harvard Univ Press, 1998.

9 Golub, ES. and Green, DR. I*mmunology, A Synthesis*, 2nd ed. Sinauer, 1991.

10 Steinitz K. A colorimetric method for the determination of Inulin in blood, plasma and urine. J Biol Chem 126: 589, 1938.

11 Steinitz K. The determination of the glomerular fitration by the endogenous creatinine clearance. J Clin Invest 19: 285, 1940.

12 Steinitz, K. Studies on the conditions of glucose excretion in man. J Clin Invest 19: 299, 1940.

13 Steinitz, K. The determination of urea in blood and urine by Conway units. J Lab Clin Med 25: 288, 1939.

14 Steinitz, K. The renal excretion of sucrose in man. Comparison with inulin. Amer J Physiol 129: 252, 1946.

15 Kolff, WJ and Berk HTJ. Artificial kidney dialyzer with a great area. Acta Med Scand 117: 121, 1944.

16 Alwall, N. On the artificial kidney, 1. Apparatus for dialysis of blood in vivo. Acta Med Scand 128:317, 1947.

17 Steinitz, K. The use of radioactive iodine in the diagnosis of hyperthyroidism. (Hebrew). Harefuah. 14, March 15, 1953.

18 Steinitz, K. The clinical value of radioactive iodine tests for the assessment of thyroid function. Acta Med Scand. 149; 187, 1954.

19 Bentwich, N. *The Rescue and Achievement of Refuge Scholars*. Martinus Nijhoff. 1953.

20 Beveridge, L. *A Defence of Free Learning*. Oxford University Press. 1959.

21 Weizmann, C. *Trial and Error*. East and West Library. London. 1950.

Profile of Arnon Shani: 2014 Honorable Member of the ICS

by Simone Somekh

When Arnon Shani was born back in 1935, his hometown Ness Ziona was just a tiny colony. In a land that one decade later would be called Israel, Shani not only built his career in terms of achievements, but also virtually built the institutions which made him a great scientist.

Shani began his chemistry studies at Hebrew University in Jerusalem in 1957, and moved to the Weizmann Institute for his doctorate, which he completed in only two years thanks to a successful research project in aromatic compounds, synthesizing 1,6-oxido[10]annulene, a missing system in the annulene family, confirming the Huckel rule for aromaticity. He then switched to organic photochemistry during his postdoctoral research in Chicago.

“For a native Palestinian like me, the United States was a new, fascinating world,” he says while sitting in his spacious living room in North Tel Aviv. “My wife and I would take the car, a tent and sleeping bags and would take our three daughters to explore the country. My oldest daughter learned a lot about geography, geology, and zoology during those trips.”

Once he returned to Israel, Shani merged his photochemistry studies with research on natural plants and their active components. Together with Prof. Raphael Mechoulam he proved that THC (Tetrahydrocannabinol) is the only psychoactive component in hashish. Shani's career, however, went much further than lab research. The chemist was one of the pioneers who started working at Beer Sheba's Institute of Higher Education in 1968, before it was declared to be the University of the Negev, later on Ben-Gurion University (BGU).

"We all took a big risk," he recalls. "The students didn't even know if they were going to receive a degree, since we got the academic accreditation only in 1973." Shani believes that a collective inferiority complex helped the institution succeed: "In order to raise the bar, we demanded from our students much more than the regular curriculum required. The studies toward the B.Sc. in chemistry included 50% of new topics and subjects not studied in chemistry degrees 10 years before." Shani later served as chairman, vice-rector, and director of the Institute of Applied Research at BGU. In the eighties, when the university almost collapsed due to the staggering inflation that had hit the country, Shani pushed the institution to make drastic cuts in salaries and accept funds from international donors. The budgets were then redistributed among departments according to new parameters, based entirely on performance and achievement.

When the Institute of Applied Research went through a rough time, Shani once more demonstrated his ability as an entrepreneur. "I looked into the activities of the Institute and found that some of them were old-fashioned and not useful anymore. We fired many people, but we helped them transfer to new positions."

Later in 1997, Shani was elected as president of the Israel Chemistry Society (ICS), right when the institution was facing economic collapse. The membership fee was very low, so he talked to the representatives of about 200 chemical industries about joining and supporting the ICS. "It was a great chance to revive the Society, especially considering that the following year we had the International Year of Chemistry, which gave us another boost."

One of the major achievements in his research was the confirmation that mating disruption of insect pests with sex pheromones leads to a significant increase in the pheromone titer by insect females in laboratory mating disruption studies. As a member and chairman of the chemistry curriculum in high school committee, he insisted on demonstrating how much chemistry is relevant to everyday life and strengthening the connection with chemical industry and related topics.

Besides being a chemist and entrepreneur, Shani is an archeology enthusiast. When he was teaching at BGU, sometimes he would join a friend who was an archeologist for a few expeditions in the Sinai.

Today he recalls all of these experiences – his (not so good) chemistry teacher in high school, the establishment of Ben-Gurion University, the road trips in America, his sabbatical year in New Zealand – with a gentle smile on his face. He points at the window of his living room, facing North Tel Aviv, and says he and his wife are enjoying the vibrant cultural scene of the White City.

"When I meet high school students, I tell them the following," he concludes. "There are two types of occupations: Either you create a product and make money from it (Natural Sciences and Engineering), or you don't produce anything and play with other people's money." No wonder Shani met many students who originally aimed at studying business, economics, and law who ended up going into chemistry thanks to his persuasive arguments.

Simone Somekh was born in Italy in 1994. He studies at Bar-Ilan University and works as a freelance writer. His works have been published in The Jerusalem Post, The Times of Israel, and Wired Italy.

His Twitter account: (@simonsays101) and his website: www.simonesomekh.com

Profile of Eliezer Gileadi: Recipient of 2014 ICS Gold Medal

by Lior Elbaz
Department of Chemistry, Bar-Ilan University, Ramat Gan 5290002, Israel
lior.elbaz@hotmail.com

Eliezer Gileadi was born in 1932 in Hungary and immigrated to Israel together with his family in February 1940, at the age of 8, escaping from the hands of Nazi Germany. As they arrived in Israel, they were imprisoned in Atlit by the British army for 6 months. Eliezer likes to joke about this experience, and calls it his "criminal record". He still recalls the high fences and the barbed wire in the camp. This was a pivotal time in his life, which shaped him as a person and scientist as he grew up.

After his release, Eliezer was sent with his family to Jerusalem and lived there for a couple of years until they moved to Haifa, where he lived until joining the IDF. Eliezer was always interested in mathematics and fascinated by science. In high school he thought that he would like to study economics, but since there did not seem to be any prospects in this profession in Israel at that time, he decided to learn something more "practical". Although he never learned chemistry in school, the few articles he read in the Israeli popular science magazine, "Hatechnai Hatzair", including one on the Bohr's theory of the structure of the atom, made him decide to go and study chemistry. In 1951, he decided to join the second cycle of the Atuda (IDF's academic reserves), and obtained his bachelor's and master's degrees from the Hebrew University, Jerusalem, specializing in physical chemistry. This was the second chemistry class of the Hebrew University's Chemistry Department, after the war of independence. Later he began to work in the early stages of the atomic energy commission and opened a geochemistry lab conducting studies with rare-earth elements. After his military service, he decided to obtain a PhD degree in electrochemistry for two simple reasons: he was interested in the field, and at that time, there were no electrochemists in Israel, which made him think that this could help him get an academic position in Israel after his return. Eliezer applied to several universities and received positive answers from all of them, and decided to go to work with the late Prof. Brian E. Conway at the University of Ottawa in Canada. Electrochemistry received very high attention in those days. The Western world's leading laboratories at the time were those of Prof. J.OM. Bockris in the University of Pennsylvania in Philadelphia and Prof. Conway whereas the East had the famous lab of Prof. A.N. Frumkin in Moscow. Eliezer quickly became a leading student in Conway's group. He relates that one day, after his first year, Conway came to the students' room and wrote an equation on the board describing the effect of the lateral interactions between particles on the reaction kinetics and asked his students to try to solve it. All of the other students went back to their work and Eliezer decided to solve this problem. He worked on it all night and solved it. The next day he showed his solution to Conway, who was amazed by Eliezer's exceptional ability. After that, Eliezer became Conway's protégé, working closely together with him at the lab and often continuing the work in the evening at Conway's home. A year later, in 1963, Eliezer submitted his PhD dissertation. According to Eliezer, this is a classic case where opportunity knocks on the door and one needs to be smart enough to open it. Conway convinced him to stick around for six more months until he received an offer to become a team leader in John Bockris's lab in the University of Pennsylvania, US, with six students working under his supervision, state-of-the-art instrumentation and what seemed to be limitless funds.

While working with Bockris, he studied Fuel Cells technology. Eliezer worked in Bockris's lab for three years and then felt it was time to move on. After working with the two biggest names in electrochemistry in the western world at the time, with very strong recommendations from both of them, Eliezer could get almost any academic or industrial job in his field. Despite the tempting job opportunities in the US, Eliezer decided to come back to Israel and was willing to consider both academic positions and industrial positions. He says his reason for coming back to Israel was pure patriotism – he wanted to live and raise his children in Israel.

Eliezer decided to accept an offer from Tel-Aviv University, where he stayed for all his career. When asked, "What is your most significant scientific achievement?" he answered, "I think my biggest achievement was the simple derivation of a general form of the adsorption isotherm of Temkin, which unlike the Langmuir isotherm, takes into account the lateral interactions of adsorbed species. This lead to a better understanding of the Adsorption Pseudo Capacitance and of the mechanism of electrode reactions". This was later published in volume 3 of the prestigious series of "Modern Aspects in Electrochemistry" edited by Bockris and Conway.

Eliezer says that apart from research, he also enjoys teaching and interacting with fellow scientists. He is the author of three textbooks in Physical Electrochemistry, which are still being taught and used by graduate and undergraduate students. According to him, the most important thing he did in his life was the program he envisioned and lead, together with Prof. D. Huppert and the late Prof. B. Fein, for the absorption of talented Russian immigrants, who came to Israel after the fall of the USSR, in Israeli academia – The Gileadi Program. He fought for several years to incorporate these researchers in all the universities in Israel, give them a chance to continue their work and receive a respectable salary. He worked with government officials and senior faculty members of the Israeli academia to avoid what he called "a catastrophe if these researchers were not absorbed". Again, he looked at this blessed immigration as an opportunity knocking on the door and was smart enough to open it. These actions were driven by the history of his family and his patriotism.

Eliezer has published more than 200 scientific papers, books and book chapters. He has written several patents on a wide spectrum of electrochemical applications, received numerous prizes for excellence and recognition, and is a fellow of the Electrochemical Society, the American Association for the Advancement of Science, the International Society of Electrochemistry and the International Society for Pure and Applied Electrochemistry. He is also the only Israeli scientist ever who is a Fellow of the Royal Society of Canada and a member of its Academy of Sciences.

From the writer: both as a student and as a researcher, I have been learning electrochemistry from Eliezer's books and papers. I consult with him whenever I have a question related to electrochemistry. Eliezer's door seems to be always open to those who seek it. On top of being, as I like to call him, "the father of the Israeli electrochemistry" and one of the world leaders in the field, he is a wonderful person, always willing to listen, and give advice and help. It is a privilege and pleasure to interact with him.

Dr. Lior Elbaz has a B.Sc., M.Sc. and Ph.D. in chemical engineering, all from the Ben-Gurion University, Israel. During his graduate studies, he became an expert in electrochemistry and electrocatalysis. He used his expertise to develop alternative energy technologies. After finishing his Ph.D. he joined the MPA11 group, at the Materials Physics & Applications Division at the Los Alamos National Laboratory, a world leader in the development of fuel cell technology, where he developed new catalysts, and materials for fuel cells, in order to reduce their price and increase their durability. After almost four years at Los Alamos, Lior came back to Israel to take a faculty position at the Department of Chemistry, Bar-Ilan University, where he heads the alternative Energy Lab.

Profile of Arie Zaban: Recipient of 2014 ICS Prize for the Outstanding Scientist

by Simone Somekh

According to Prof. Arie Zaban, if you want to make a difference in the world, excellence is an indispensable prerequisite. Head of a renowned renewable energies lab at Bar-Ilan University and former director of the Bar-Ilan Institute for Nanotechnology and Advanced Materials, Zaban knows what the word "excellence" stands for: "It means having the skills and the notions, but also being focused and determined."

Born in Ramat Gan in 1961 to a family of intellectuals – two of his grandparents earned a Ph.D. in Germany right before moving to Palestine in the early thirties – Zaban developed an interest in chemistry when he was in high school, thanks to a good teacher who made him appreciate the "clean, precise aspect of the subject."

"I liked that there was so much mystery behind it," he says. "The idea of solving issues gave me an exciting feeling – the thought that I could see beyond what regular people see."

After being part of the Nahal program – which combined the military service with the establishment of new kibbutzim – and serving in the air force for 7 years, Zaban started his academic studies at Bar-Ilan, the same university where he eventually earned a Bachelor's, a doctorate, and where he is currently teaching and researching. His lab develops new materials for sustainable energy, mainly for photovoltaics.

"I like the environment at Bar-Ilan very much," he says. "The colleagues here are friends, they are people I can always share and exchange ideas with. The university has experienced a dramatic growth in the past 10 years, and you can see it constantly improving." Zaban stresses how warmly welcomed he felt when he returned to Bar-Ilan after his post-doctorate in Denver, Colorado: "I had become the colleague of my own teachers, and I felt very accepted."

The outstanding successes earned by Zaban did not come without an equal dose of challenges. He recalls a specific night, after one year of research for his Ph.D., when he realized that the work he had done for the past twelve months was worthless. "The setup of the experiment I was doing was not controlling one of the parameters, so I realized that the results were useless," he says.

In that moment, he had to ignore his emotions and display emotional strength to proceed with his research.

"I had to correct the experiment and start again."

Coming from a Zionist family, Zaban feels a strong connection to Israel and doesn't see himself living in any other country. Though he has many international collaborations and often travels abroad, he loves being in Israel with his family.

Israel should always strive for excellence, he claims. "I believe it should improve its education system. When it comes to the socioeconomic gap, education is the best way to help the poor. Through quality schooling, the State can give them the tools to be more significant – both for themselves and for the whole country."

Simone Somekh was born in Italy in 1994. He studies at Bar-Ilan University and works as a freelance writer. His works have been published in The Jerusalem Post, The Times of Israel, and Wired Italy.

His Twitter account: (@simonsays101) and his website: www.simonesomekh.com

Profile of Ronny Neumann: Recipient of 2014 ICS Prize for the Outstanding Scientist

by Simone Somekh

It only takes a few minutes of walking around Prof. Ronny Neumann's chemistry lab at Weizmann Institute to breathe a remarkably international atmosphere. Students come from all parts of the world, and it's common to hear them alternate between English, Italian, Hebrew, and Indian. This is not by chance – Neumann himself comes from a multicultural background and every time he hires new researchers he makes sure to recreate the international environment in which he grew up.

"The teaching methods are different in each country," says Neumann, explaining that this results in different approaches to research. "For instance, I noticed that students from Ukraine are very attentive to the smallest details, while the Israelis tend to concentrate on the larger picture. It's important for me to have both approaches in my lab."

Born in New York City in 1953 to Jewish immigrants from Germany and Switzerland, Neumann grew up in the States, curious about both history and science. After visiting Israel at the age of 16, he decided to move there as soon as he would graduate from high school. "While in the States people tended

to be very materialistic, I was fascinated to see that in Israel people put their individual desires behind the nation's needs." Is it still the case? No, he answers.
"Israel has become Americanized today. I can't see the difference anymore."

Neumann moved to Kibbutz Mishmar Hasharon – not far from Netanya – in 1972 and stayed there for many years, commuting to Jerusalem when he started studying chemistry at the Hebrew University. "In my first year of studies, I was at the Mount Scopus campus, which was still being built," he recalls, stressing how different was the Israel he experienced then to the Israel in which he lives today. After completing his undergraduate degree, Neumann served in the military. During this time, he realized he wanted to continue following his passion for chemistry and discovery. The field of research he chose for his Master's – catalysis – would become the same in his own lab at Weizmann decades later.

It was at Hebrew University, in a class on colloids, where Neumann met his wife, a chemist as well. In 1982, after attempting to build a chemical industry in the kibbutz where he lived, he decided to leave Mishmar Hasharon. "It had been my home since I moved to Israel," says the professor, who defines the decision as "emotionally complicated." However, he planned on building a family and embarking on an academic career, and Jerusalem seemed to be the best place to do it. During his doctorate at Hebrew University, he successfully worked on phase-transfer catalysis (PTC) and had two of his four children.

Neumann started working on catalytic oxidation at Princeton University, in the States, in 1985, and has been researching that field since then. This research has resulted in several achievements in the field of "Green Chemistry," which attempts to reduce any negative impact chemistry may have on the environment. "I believe there are many important issues that chemistry can solve," he says about eco-friendly science. In addition, "the development of alternative energies is the key aspect in the survival of the human species."

For ten years, Neumann has been the head of the Organic Chemistry Department at Weizmann. "It's important to shape the future of the department. Organic chemistry is changing a lot now, and we need to focus on new topics and techniques." The multiple tasks, however, don't take Neumann away from his own students. As he says, he wants his lab to be a "home away from home," and he follows each student's individual project. "I value excellence and creativity," he claims, explaining how carefully he selects his new recruits to form an international and dynamic working environment.

"At night, when I finish working, I get in the car and play some classic rock." It's during those rides home, with the Rolling Stones in the background, that Neumann digests his day and often gets his best ideas. When he is not working, Neumann is a relentless traveler. Together with his family, he has visited tens of countries around the world, from Alaska to China, from Morocco to Nepal. Once a year, he also travels to Austria for a ski trip.

Life in Israel is good, but there are plenty of things that Neumann would change if he could. "I would like the society to be more open, to accept minorities, to separate between religion and state. I'd like it to be less capitalistic. And of course, I'd like the government to invest more money in science." However, he claims to be an optimist: Not by chance, science is based on overcoming obstacles. Therefore, as Neumann concludes, "All scientists should be optimistic."

Simone Somekh was born in Italy in 1994. He studies at Bar-Ilan University and works as a freelance writer. His works have been published in The Jerusalem Post, The Times of Israel, and Wired Italy.

His Twitter account: (@simonsays101) and his website: www.simonesomekh.com

Profile of Ed Narevicius: Recipient of 2014 ICS Prize for the Outstanding Young Scientist

by Simone Somekh

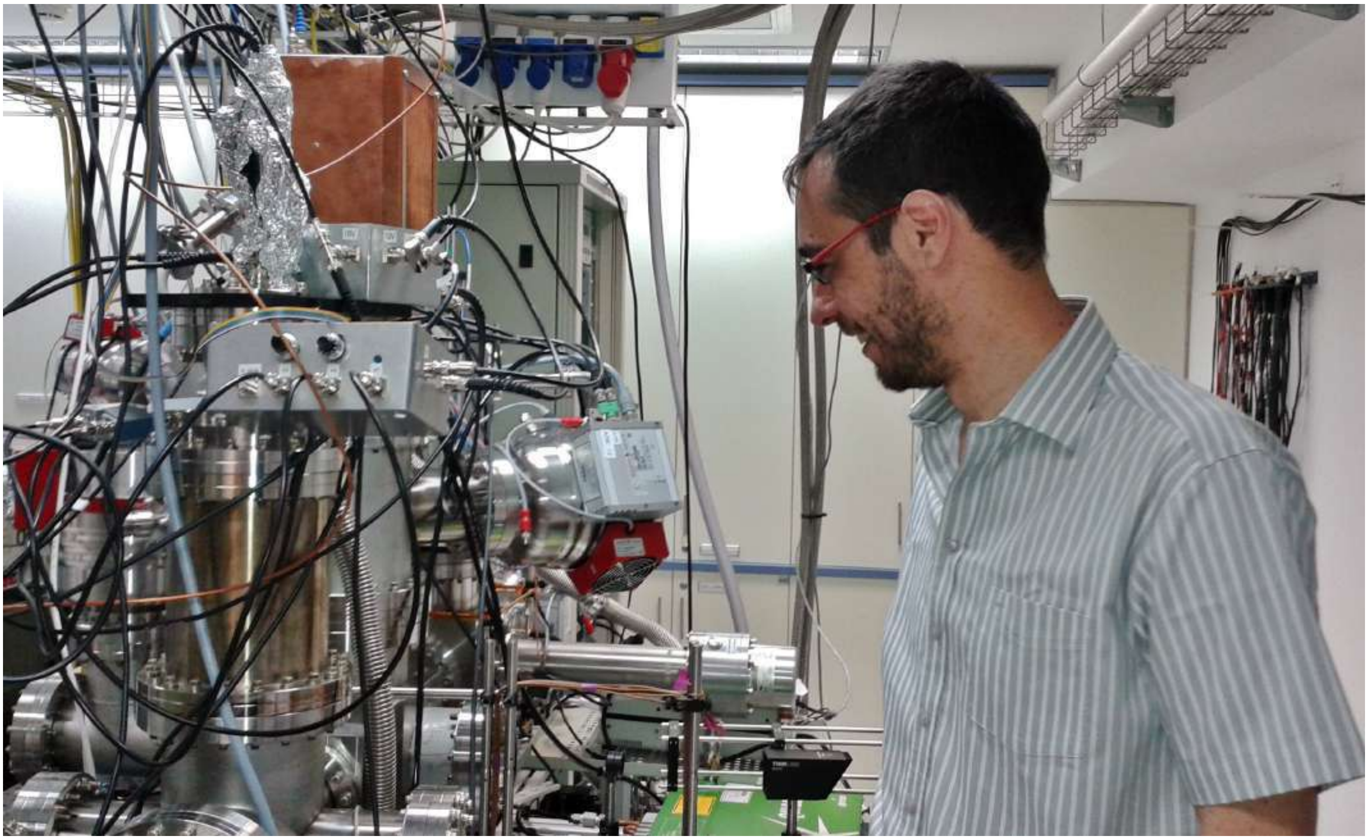


Photo by Simone Somekh

When Ed Narevicius was ten years old, he would head to the kitchen in his house in Vilnius, Lithuania, and attempt to trigger chemical reactions with his mother's baking ingredients. Twice he accidentally started a fire. "My parents supported my interest in chemistry," he laughs as he recalls that time. "Now that I have my own children I admire their patience!

"Decades later, Narevicius, 42, has a Ph.D., leads his own lab at Weizmann Institute in Israel, and is still fascinated by chemistry, although now instead of working with high temperature reactions he has gone to the other extreme of testing reactions taking place near absolute zero.

Coming from a mixed background, he visited Israel on a one-month program during high school and was deeply fascinated by the contrast with his native country. "I was struck by the freedom of action," he says. After spending one year learning Hebrew in a kibbutz, Narevicius began his academic journey at the Technion, where he started researching with Prof. Nimrod Moiseyev while he was still an undergraduate student. "He taught me a course in quantum mechanics, and I got fascinated by the curious world where atoms and molecules behave as waves." He ended up staying in Moiseyev's lab for seven years, as he completed his Ph.D. and worked with a start-up company which developed optical switches.

Being exposed to the entrepreneurial field was an eye-opening experience for Narevicius. There, he even met his wife Julia, an engineer, who is sitting in the same office at Weizmann as the interview takes place and after twelve years of marriage still works alongside him. When the start-up relocated to the States, the two moved to the Silicon Valley and Narevicius experienced for the first time the conflict between management and the development of a project. He left the company and began a post-doctorate with Prof. Mark Raizen at the University of Texas in the field of chemical physics.

"Raizen has the reputation of being most creative experimental physicist," he explains. "He took a risk when he accepted me into his lab, since I had not been working with experiments before." The risk resulted in being a great success: in three years, Narevicius helped building two new experiments from scratch, aiming at taking control over fast and cold atomic and molecular beams that ideally suit the low temperature research.

When Narevicius and his wife decided to return to Israel, it took year and a half for him to establish his own lab at Weizmann, where he intended to take the research he had been doing with Prof. Raizen in the States into the direction of chemical physics. "Weizmann is the ideal place to do research in Israel, it's like a kibbutz of scientists." There, he developed a new experiment with cold atoms, which today is the successful result of Narevicius' creative approach.

"Sometimes, if you work in the same field for many years you become confined by the accumulated knowledge and it gets harder to think out of the box," he explains. "I think that moving among different fields during your career helps to apply ideas across different disciplines. For example when I hire a new student in my lab, I don't care if he has experience related to my research field. It is the creativity and curiosity that I value the most."

As for the atoms, it took that creativity Ed refers to in order to reach the low temperatures he had been seeking. "Supersonic expansion produces extremely cold beams, but the beams are so fast that when they collide you gain nothing from the low beam temperature." Narevicius was on a plane from Berlin to Tel Aviv, returning from a meeting with some German colleagues, when he got the idea of how to solve the issue. In midair, he took pen and paper and did some calculations. The day after, he ran to the lab and explained the idea to his students: instead of making the beams collide, he would deflect one of them so that they would merge and travel together, with collisions now taking place in the cold moving frame of reference. With the help of his wife, Narevicius proved his idea to be successful.

Ed and Julia's kids – respectively eleven and seven years old – are just as curious as their parents and dream of being scientists. "They love to inquire into things and always seek for explanations." With a pianist as a father and a violinist as a mother, both kids are also interested in music and love exploring nature, as the family travels to a different country twice a year.

Exploration is key to Narevicius' scientific approach. "I'm not looking for convenient research. Every wall I hit, it's a new challenge that stimulates me. And the truth is, I love surprises."

Simone Somekh was born in Italy in 1994. He studies at Bar-Ilan University and works as a freelance writer. His works have been published in The Jerusalem Post, The Times of Israel, and Wired Italy.

His Twitter account: (@simonsays101) and his website: www.simonesomekh.com

Profile of Efrat Lifshitz: Recipient of 2015 ICS Prize in Memory of Lea Tenne for Nanoscale Sciences

by Arlene Wilson-Gordon
Department of Chemistry, Bar-Ilan University, Ramat Gan 5290002, Israel
gordon@biu.ac.il

Efrat Lifshitz, Professor of Chemistry at the Technion, is the descendent of three generations of professional musicians. Her grandfather moved from Russia to Vienna before the First World War and from there emigrated to Haifa, then in Palestine, in 1926. He managed to forsee the fate that awaited European Jewry and convinced his family to accompany him. Once in Haifa, he changed the family name to Abileah (Father of Leah) and became well-known as a musician and composer. Indeed, he composed the popular tune for "Ma Nishtana" which is sung at the traditional passover meal (the seder). Efrat's father taught the violin and was an expert in Bach. It was into this intellectual musical home that Efrat was born in 1956 and, under her parent's direction, she trained to become an accomplished pianist as well as an excellent student. From an early age, she absorbed the values of intellectual rigor and insatiable curiosity, creativity, hard work, determination, perseverance and self-discipline that characterize her approach to science and, indeed, to life itself. It is these values that she endeavors to impart to her three children and to the many research students that she has trained. She is a strong believer that a student with original and imaginative thinking, hard work and perseverance, can become an outstanding researcher.

Efrat studied for her BA in Chemistry at the Hebrew University. The excellent education she received there stood her in good stead in her doctoral studies at the University of Michigan at Ann Arbor. There, she chose to study layered semiconductors, laying the foundation for her future work in nanotechnology. After short postdocs at the University of Michigan and the Weizmann Institute, she was appointed as a Senior Lecturer in the Faculty of Chemistry at the Technion in 1990, rapidly rising through the ranks to become a Full Professor in 2005.

At the Technion, she built her research group which specializes in the development of novel nanostructures and the understanding of their fundamental properties, using an impressive suite of magneto-optical characterization tools, such as optically detected magnetic resonance and microwave modulated photoluminescence. By studying the properties of the materials they synthesize in intricate detail, she and her group gain deep understanding of their fundamental characteristics that allows them to engineer specific properties and to overcome many of the physical barriers that have previously impeded progress. Although Efrat collaborates with many industrial companies in implementing these materials in applications such as solar cells, light emitting diodes, lasers, spintronics and biological platforms, it is evident that her main focus and passion lie in exploring the fundamental physics of the nanostructures she creates. She is a champion of long-term incremental progress rather than quick ephemeral achievements. This approach undoubtedly arises from her "yekke" background.

Efrat contributes to the future generation of scientists by supervising graduate and undergraduate students, as well as high-school students in her group. She is undoubtedly a role model for young woman scientists. When reflecting on the reasons why there are so few women faculty members in Israeli chemistry departments, despite the fact that over half of the PhDs are women, she has some interesting insights. In addition to the obvious difficulties experienced by young women in persuading their partners and children to join them in the mandatory postdoctoral study period overseas, she cites the feminist approach of some women students who wish to go into industry in order to compete with their male counterparts in gaining promotion and a high salary. In addition, she notes that some young women are deterred by the lack of well-defined work hours in academic life, often not realizing that the work day in high-tech industry can be very long and inflexible. Efrat thrives on a long work day – indeed she is fortunate that she throughly loves her work any time of the day. And she is doubly lucky that her husband of many years shares her enthusiasm.

When asked whether there is anything she would change in modern academic life, she says that she sometimes feels the need for more time for reflection and deep scientific thinking and mentions her dismay at the loss of balance in university life, characterized by the constant pressure to write grant proposals, review journal articles and grant proposals, and attend university and national committees. She does, however, mention that these activities often lead her to new research directions and collaborations. Despite these reservations, she would not change anything in the path she has chosen – truly blessing the enjoyment she derives from science and the opportunities it continues to give her.

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. 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.

The 80th Annual Meeting of the Israel Chemical Society & Exhibition

February 17-18, 2015, David Intercontinental Hotel, Tel-Aviv, Israel[1]

Ehud Keinan
The Schulich Faculty of Chemistry, Technion - Israel Institute of Technology, Haifa 32000, Israel.
Email: keinan@technion.ac.il

In 1933, a group of chemists in Palestine, most of whom were new immigrants from Europe, particularly from Germany, decided that they should organize in order to solve their unemployment problems. They met at the campus of the Hebrew University of Jerusalem on Mount Scopus, announced the establishment of the "Union of Chemists in Eretz-Israel (Palestine)" and decided on the aims and by-laws of the Union. Prof. Mordechai Bobtelsky of the Hebrew University was elected as the first Chairman of the Union. About 20 years later, after the establishment of the State of Israel, the name of the Union was changed to the "Union of Chemists in Israel." In 1960, under the leadership of Prof. Shalom Sarel of the Hebrew University, the name was again changed to the "Israel Chemical Society" (ICS).

With almost no interruption since 1933 the ICS has kept its tradition of Annual Meetings, each providing an opportunity for students, faculty members, industrial chemists and chemistry teachers to refresh their networking, exchange scientific and social information and establish fruitful collaboration projects. Typically, each of these vibrant meetings featured heterogeneous scientific programs that included reports from academic labs and industrial research centers, as well as lectures by international guests.

The ICS meetings are usually held every year in early February, which is the inter-semester break of all Israeli universities at the end of the short rainy season in Israel. The responsibility for the meetings has been revolving in a 6-year cycle among the chemistry departments of the 6 major research universities. Thus, looking back at the ICS history of the past 2 decades, the Technion has taken responsibility for organizing the 62nd Meeting (1997), the 68th Meeting (2003), the 74th Meeting (2009), and now the 80th Meeting (2015).

Another unique tradition of the ICS, which had already attracted much worldwide attention and interest, has been the hosting of high profile delegations of scientists from top academic institutions worldwide who present plenary and invited lectures. This initiative has created outstanding opportunities for many Israeli scientists, and particularly for graduate students, to interact with top-tier chemists, thus enhancing prospects for networking and scientific collaboration. Each visit of these delegations has left a long trail of mutual visits of students and faculty members, postdoctoral and sabbatical programs, joint research proposals and other fruitful international activities. The ICS has hosted distinguished delegations from The Scripps Research Institute (1997), California Institute of Technology (1998), University of Cambridge, UK (1999), ETH–Zurich (2000), Columbia University (2001), University of California at Santa Barbara (2006), the Max Planck Society (2009), the Chemical Society of Japan and the Japan Society for the Promotion of Science (2010), Academia Sinica (2011), the University of California at Berkeley (2012) and the University of Oxford (2014). This year we had the pleasure of hosting a delegation of 9 outstanding scientists from Stanford University (Figure 1).

Figure 1: A traditional ICS autographed poster, displaying members of the Stanford delegation (top two lines) and laureates of the major ICS prizes.

The Technion Organizing Committee, which was chaired by Prof. Mark Gandelman, comprised professors of the Schulich Faculty of Chemistry, including Sahar Rahav, Gil Alexandrowicz, Noam Adir, Aharon Blank, Zeev Gross and Ilan Marek. Ms. Paula Lam-Haim, CEO of the ICS, provided much additional help. The actual operation, including all technical aspects, administration, organization of the exhibition, promotion, etc. was carried out by an experienced team of Bioforum Ltd., mainly by CEO Mr. Amir Malka and Conference Coordinator Ms. Reut Lazar. Bioforum is an integral part of the diverse Israeli chemical, bio-pharmaceuticals and biotechnology industries. Through its education and training services, which include courses, personal training, consultation and project support, Bioforum promotes employee professionalism, organizational performance, career development, efficacy, safety and quality in these industries and in the entire chemical community. In addition, Bioforum provides clinical data management services and prepares, publishes and compiles submissions to regulatory agencies worldwide.

About 800 participants enjoyed a broad range of over 100 lectures on diverse subjects, including more than 20 plenary and keynote lectures, over 200 posters, special symposia and discussion groups, as well as a large commercial exhibition by over 20 providers of lab equipment, scientific instrumentation, chemicals, materials, services of analytical chemistry and diagnostics, publishing houses and management of intellectual property. The companies represented in the exhibition included Eldan, Arad-Ophir, New Road, Bargal, Dr. Golik, Mercury, Bruker, Tzamal D-Chem Laboratories, Pearl Cohen, ICL Innovation, Bioanalytics, PerkinElmer, Agentek ,Interview Information Resources, Idbs, Holland-Moran, Meir – Science Technologies, Labotal Scientific Equipment, Waters and Meshulam Avni & son.

As in previous years, the conference center of the David Intercontinental Hotel offered convenient space for the parallel sessions, exhibition and poster sessions, along with excellent food services. The Hotel location at the Mediterranean beaches at the southern part of Tel Aviv offered pleasant strolls along the coastal promenade to the scenic harbor of ancient Jaffa, to outdoor cafés and art galleries, the famous flea market and the adjoining historic neighborhoods of early Tel Aviv, such as the trendy Neve Tzedek district. The Tel Aviv weather in this period of early February was typically dry, sunny and pleasant, not too cold for outdoor activities. Indeed, this attractive setup provided good reasons for several participants and guests to extend their stay by few more days to explore the country.

Welcoming reception

The welcoming reception dinner in honor of the two Nobel Prize Laureates, Profs. Michael Levitt and William E. Moerner and the Stanford delegation took place in the evening of February 16th in the Hilton Tel Aviv Hotel. Adi and Ishay Zalmanovitz of the Lakers Holding Group sponsored the event, which was jointly organized by the Wolf Foundation and the ICS. Dr. Liat Ben David, CEO of the Wolf Foundation greeted the audience of 100 guests, including most of the Israeli Wolf Prize Laureates, members of the Wolf Foundation Council and the ICS Executive Board. In their short lectures, Prof. Levitt spoke about "Getting used to being in the limelight and concerns for the future of scientists worldwide." Prof. Moerner, who is a Laureate of the 2008 Wolf Prize in Chemistry, spoke about "How single-molecule detection, imaging, and photo-control act as foundations for super-resolution microscopy."

Opening Ceremony

On Tuesday morning, February 17th, **Prof. Mark Gandelman,** Chairman of the Organizing Committee, opened the 80th ICS Annual Meeting by greeting the large audience and the distinguished guests, particularly Prof. Keith O. Hodgson, Head of the Department of Chemistry at Stanford University, the two Laureates of the Chemistry Nobel Prize, Profs. Michael Levitt and William E. Moerner, the other Stanford delegates, Mr. Daniel Shapiro, USA Ambassador to the State of Israel, and Mr. Yaron Razon, Director of the Israel Philatelic Service. He expressed his immense delight and pride at welcoming all participants to this historical event, organized by the Schulich Faculty of Chemistry of the Technion. He explained that the meeting aimed at bringing together Israeli scientists, practitioners, students, industrial leaders and teachers, as well as representatives from several other countries. Excited by the intensive and broad scientific program that the Organizing Committee had managed to put together, he indicated that the program included many aspects of experimental and theoretical science, industrial chemistry and chemical education. Gandelman invited the audience to enjoy the gathering, learn about new discoveries, present their scientific findings and create new connections for future collaborations. Finally, he acknowledged the significant help of all members of the Organizing Committee, the ICS CEO, Ms. Paula Lam-Haim, ICS President, Prof. Ehud Keinan, and staff of Bioforum.

In his welcoming address, ICS President **Prof. Ehud Keinan** pointed out that it had been an exciting decade for the Israel Chemical Society and for the community of chemists in the State of Israel. In 2004, no one could anticipate that in less than a decade there would be 6 Israeli Nobel Prize Laureates in Science, or expect that all six would win the Nobel Prize in Chemistry. This decade has also witnessed the fruitful collaboration between the ICS and the Israel Philatelic Service, already yielding four Chemistry stamps. In 2015 we celebrate the International Year of Light, amazed by how light-based technologies have been promoting sustainable development and solving worldwide challenges. Light is all about chemistry. We use chemical technologies to convert electricity, heat and chemical reactions to light and use it in communication, electronics, materials, photography, medicine and entertainment. Photodynamic therapy represents a major weapon to fight cancer. Chemistry helps save energy, helps harvest sunlight with solar cells and artificial photosynthesis and helps generate hydrogen, which is the cleanest possible fuel, by catalytic water splitting. All Israeli chemists, chemical engineers and chemistry teachers share the excitement and pride of being members of the Israeli chemistry community.

Keinan then referred to his role as Editor-in-Chief of the Israel Journal of Chemistry (IJC), which is the official journal of the ICS. We are all very pleased with the statistics and the increasing worldwide visibility and popularity of the Journal. Clearly, the IJC has already become a major player among the chemistry journals, and we expect this trend to continue. Keinan took this opportunity to encourage ICS members and guests to consider becoming Guest Editors of future issues on specific topics at the forefront of all chemical sciences.

Keinan also indicated that the numerous activities of the ICS have lead to increased popularity of chemistry and chemists among young people and the public at large. The main event of last year was the 79th ICS Meeting, held at the Dan Panorama Hotel in Tel-Aviv in February 4-5, 2014. The Meeting was organized under the responsibility of the Hebrew University of Jerusalem with Prof. Dima Gelman serving as Chairman of the organizing committee, Prof. Roy Shenhar as Co-Chairman and Bioforum as the organizing company. Last year we hosted a delegation of 8 outstanding scientists from Oxford University, who presented plenary and keynote lectures. We also celebrated then the launching of a new Israeli stamp commemorating the International Year of Crystallography and the 2011 Nobel Prize in Chemistry awarded to Dan Shechtman of the Technion for his discovery of quasi-periodic crystals. A full report on the 79th meeting was published in the IJC.[2]

For the fourth year in a row, two teams of chemists from all universities and the chemical industry participated in the internationally known Mountain-to-Valley (M2V) relay race along more than 220 Km, and both teams completed this route in less than 20 hours. The 2014 race took place in May 15-16 and included several thousand runners who met non-trivial challenges of hot weather and difficult night-navigation. The representation of the ICS in the 2015 M2V race will increase with 3 teams of 8 runners each already registered for the next race, which was scheduled to take place on April 30, 2015 (see report on the 2015 race in this issue of the magazine LINK).

Many other events and symposia took place in the past year, including the annual meetings of the chemistry teachers (the Weizmann Institute, March 17 and December 23, 2014), the National Chemistry Olympiad, Chemiada, and the associated Assi Prize for excellent pupils from the Arab sector (Baqa al-Gharbiyye, February 26, 2015), the continuation of Nobel Negev project that enhances chemistry teaching in Southern Israel and many more. The Nano-Israel conference (Tel Aviv, March 24-25, 2014) provided an opportunity to award the ICS-Tenne Prize for Nanoscale Sciences to a young scientist, and this time the award was presented to Prof. Hossam Haick of the Technion.

Following the long collaboration between the ICS and the Wolf Foundation, the ICS held a special symposium in honor of 2014 Wolf Prize Laureate in Chemistry, Prof. Chi-Huey Wong (Technion, June 2, 2014) under the heading "Chemical Biology and Biomedical Science." The Symposium, which was organized by Ehud Keinan, also a member of the Scientific Council of the Wolf Foundation, included lectures by international guests, Prof. Wong of the Academia Sinica, Prof. Richard Lerner of the Scripps Research Institute, California, Dr. Michael Chang, from OBI Parma, Taiwan, Dr. Jim Lund of Codexis, California, and Dr. Jane Hsiao of Opko, Florida, as well as distinguished Israeli lecturers.

The annual conference of the Medicinal Chemistry Section (MCS) of the ICS (Weizmann Institute, June 23-24, 2014) provided an opportunity to present the prestigious the 2014 MCS-ICS Award in Memory of Barry Cohen to Prof. Richard B. Silverman for his outstanding contributions to the field of enzyme inhibition and the development of new compounds for treatment of neurological disorders.

The 6th symposium of graduate students in organic chemistry (Bar-Ilan University, October 21, 2014), which was well attended, offered an exceptional opportunity for our graduate students not only to present their work, but also to establish the Graduate Students Division (GSD) of the ICS and elect their Executive Board members (see GSD report in the current issue of the magazine LINK). The GDS is already affiliated with the European Young Chemists' Network (EYCN), which is the younger members division of the European Association for Chemical and Molecular Sciences (EuCheMS).

The ICS has also organized a special symposium titled "Chemistry and Biotechnology at the Service of Mankind" (Technion, November 18, 2014) to mark 100 years of the acetone technology of Dr. Chaim Weizmann. The symposium, which was attended by several hundred high-school pupils who take enhanced chemistry programs, was organized by Ehud Keinan, the CEO, Paula Lam Haim, Chief Inspector of Chemical Education, Dr. Dorit Taitelbaum, and Ms. Rachel Weizman Shneorson. The conference sent a message to students and the general public that Weizmann was a pioneer in the field of biotechnology even before the term was invented, and his legacy as a scientist as important as his heritage as a Zionist leader. Technion President Prof. Peretz Lavie noted that the Technion owes its existence largely to Dr. Weizmann, who back in 1901 was appointed by the World Jewish Congress in Basel, together with Berthold Fable and

Martin Buber, supported the idea of a Jewish university and recommended the establishment of a technical college. This initiative has eventually led to the establishment of the Technion. Professor Aaron Ciechanover, Nobel Prize winner for chemistry in 2004, delivered the keynote lecture on the revolution of personally adapted medicine.

The year of 2014 was particularly fruitful for the ICS in terms of international cooperation. The ICS has initiated a framework agreement for collaboration between the chemical societies of Spain and Israel, and it was endorsed by the Israeli Ambassador in Madrid and the Spanish Ambassador in Tel Aviv. The agreement, which was signed in Barcelona (October 2, 2014) during the huge chemical fair of Expoquimia, Eurosurfas and Equiplast, included the Real Sociedad EspaÇola de Quimica (RSEQ), the Asociacion Espanola de Quimicos (ANQUE), the ICS, the Israel Society of Chemical Engineers and Chemists (ISCEC) at the Association of Engineers and Architects, and the Israel Institute of Chemical Engineers (IIChE). All five societies are public, non-profit entities that have similar missions of promoting scientific research, technological development, and training. Consequently, the five societies agreed to join forces in order to enhance the scientific and technological relationships between the two countries, as well as specific relationships between universities, research centers, industries, and other institutions of scientific, educational, and cultural nature. The first binational conference within this agreement was scheduled to take place in Tarragona, Spain at the end of February 2015, seeking modes of cooperation between the Schulich Faculty of Chemistry at the Technion and the Institute of Chemical Research of Catalonia (ICIQ).[3]

A similar cooperation agreement was also signed with the chemical societies of the Czech Republic (for a full report, see LINK). The ceremony took part in the King David Hotel in Jerusalem (November 25, 2014) as part of a visit by the Czech government to Israel, in the presence of the Czech Ambassador to Israel, the Czech Prime Minister and 5 Ministers of his government. The agreement was signed in Jerusalem by the Israeli presidents, Prof. Keinan on behalf of the ICS, Dr. Alec Groysman on behalf of ISCEC and Ami Alexandron on behalf of IIChE, and in Prague by Prof. Jiří Drahoš, President of the Czech Society of Chemical Engineering, Prof. Jan John, President of the Czech Chemical Society and Doc. Ing. Jaromír Lederer, President of the Czech Society of Industrial Chemistry.

Finally, Keinan announced that the 81st Annual Meeting will take place in February 2016 under the aegis of Tel Aviv University with Micha Fridman and Amir Goldbourt serving as Chairman and Co-Chairman of the organizing committee. The expected delegation will comprise scientists from several Texan Universities, including UT Austin, Texas A&M and Rice University. Thus, we hope to see again the USA Ambassador, **Mr. Daniel B. Shapiro**, in the opening ceremony of the 81st Annual ICS Meeting.

Mr. Daniel B. Shapiro, the 19th and current USA Ambassador to the State of Israel, greeted the audience and expressed his great pleasure in joining this very special occasion. Knowing that science is at the center of the Israeli success story, he recognized the instrumental role of the ICS in building this tradition, which is much longer than the history of the State of Israel. The centrality of science to this country is reflected by the facts that two of the State Presidents, Chaim Weizmann and Ephraim Katzir, were chemists and all six Israeli Nobel Prize laureates in science, won the prize in chemistry.

Mr. Shapiro expressed his pride that the United States had also played an important role in furthering the advancement of chemistry in Israel. The delegation from Stanford includes two laureates of the Nobel Prize in chemistry, along with seven other highly distinguished chemists. Stanford University, which produces some of the best minds in the USA, demonstrates the on-going cutting edge collaboration in chemistry between the two countries.

As the USA Ambassador to Israel he expressed his strong commitment to fostering the growth of scientific collaboration between the two nations. Although much of this happens without any government involvement, as it should, the US Embassy tries to support these relationships while fostering new ones. The three binational science foundations, BIRD, BARD, and BSF, are instrumental in these efforts, nurturing the many excellent scientific connections. He announced that this year an umbrella science and technology agreement between the USA and Israel will be negotiated, to make the government-to-government science relationships even more efficient and effective.

The Ambassador stressed that while the US Embassy may help grease some wheels, much of the strength of the science connections is inherent in the nature of the two societies. Both countries share the tradition of emphasizing excellence in higher education, creating a climate ripe for innovation, and demonstrating a willingness to take risks and reach for new ideas. He expressed his confidence that these traditions will continue to cement the enormously important science relationship, encouraging all Israeli chemists to do what they already do so well. He concluded by stating that he is truly honored to take part in this event surrounded by hundreds of brilliant minds and wished all fruitful discussions and exchange of new ideas over the coming days.

Dr. Diane G. Schmidt, 2015 ACS President, could not attend the meeting but sent her videotaped greetings. She congratulated all members of the ICS, the Stanford delegation and guests and expressed her pleasure of joining the audience by this video and welcome all to the 80th ICS Meeting. She said that the central theme of the 2015 ACS presidency is "inspiring and innovating for tomorrow", and that it is through meetings like the ICS annual gathering that we can inspire and innovate by creating conditions for researchers and educators from different nations to exchange ideas, collaborate and evolve in mutually beneficial directions. She noted with admiration and respect that among the aims of the ICS is an enduring dedication to nurture and advance the science of chemistry and its applications, and to foster chemistry teaching and the image of chemistry among the public. She expressed her pleasure that also in the objects of the ICS one can explicitly recognize that the chemical industry plays a major role in Israel's economy and call out the contribution of Israeli chemists to national prosperity. It is not surprising that the ACS shares similar aims, because there is a border character to the endeavors of both societies. Chemists, chemical engineers and allied practitioners work across national boundaries, both physical and virtual. They teach and conduct theoretical, experimental, and applied research in industrial, utility, health, educational, and government laboratories. Over the next two days, the ICS scientific program carries a promise for researchers, engineers, and entrepreneurs to exchange ideas, share new results, create new collaborative projects, and discover new networks and employment opportunities – on both a national and a global scale. It is in this spirit of formulating new and strengthening existing collaborative relationships that ideas and possibilities for solutions can and do emerge. She concluded by looking forward to hearing of many mutually beneficial programs in the future and wished us all a successful meeting.

Prof. Keith O. Hodgson, Chairperson of the Department of Chemistry at Stanford, who led the Stanford Faculty Delegation assembled by the previous Chairperson, Prof. W. E. Moerner, thanked the organizers of the meeting, particularly Prof. Ehud Keinan, for their invitation to come to Tel Aviv as a delegation to participate with colleagues, students and postdocs in what was sure to be a vibrant and exciting exchange of scientific ideas. The Stanford delegation of 9 included 8 faculty members from Chemistry and one from Structural Biology. Among the delegation were two recent Nobel Prize winners in Chemistry (Professors Michael Levitt, 2013, and W. E. Moerner, 2014), who described their work leading to the Nobel Prize in detail in subsequent plenary lectures.

Hodgson briefly described Stanford University and within that context, the Department of Chemistry. Stanford currently has about 7,000 undergraduates, 11,400 graduate students and 2,000 postdocs. Beyond the organization into Schools (most relevant to the sciences being the four Schools of Humanities and Sciences, Medicine, Engineering and Earth Sciences), there are 18 independent institutes and centers, which facilitate innovative multidisciplinary research among the faculty and their students. Among these are the new ChEM-H Institute, which brings together chemists, engineers, biologists, and clinicians to understand life at a chemical level and apply that knowledge to improving human health. There is also SLAC, which provides innovative world-class x-ray light sources and instrumentation for the study of matter in space and time and enriches the research and education mission of Stanford.

The Chemistry Department at Stanford has a rich history, admitting its first students in 1891. Today there are 25 faculty members representing all disciplines of chemistry and 4 lecturers. The Department strives for world-class excellence in research and teaching. There are 225 graduate students and 81 postdocs forming a vibrant, creative research and teaching environment. The core curriculum includes large undergraduate service courses as well as providing for about 45 chemistry majors.

Prof. Hodgson noted that while there are already many well-established links between faculty colleagues in Israel and at Stanford, the interactions and exchange of ideas that would happen over the two days of the ICS meeting would foster even stronger ties and opportunities, both benefitting collaborative research programs and contributing to the training and education of young scientists. On behalf of the Stanford Delegation, he also thanked the Office of the Dean of Humanities and Sciences at Stanford for their generous financial support that allowed the group to travel to Israel.

Later, at the end of the meeting, all members of the Stanford delegation agreed that this was a truly wonderful trip to Israel to help celebrate the 80th annual meeting of the Israel Chemical Society. Not only did the delegates enjoy presenting their latest work, but also the discussions throughout and after the meeting will certainly lead to a variety of interactions and potential future collaborations between Israeli and Stanford scientists.

Mr. Yaron Razon, Director of the Israel Philatelic Service at the Israel Postal Company highlighted the intense collaboration between the Philatelic Service and the ICS. The fruitful relationshipss started with the planning and issuing of two Israeli stamps on January 4, 2011, commemorating the International Year of Chemistry, the 2004 Nobel Prize in Chemistry awarded to Aaron Ciechanover and Avram Hershko of the Technion and the 2009 Nobel Prize in Chemistry awarded to Ada Yonath of the Weizmann Institute. The third stamp, which was issued on December 3, 2013, commemorates the International Year of Crystallography and the 2011 Nobel Prize in Chemistry awarded to Dan Shechtman of the Technion for his discovery of quasi-periodic crystals. This stamp was chosen by the Israel Philatelic Federation (IPF) to represent them in the Philately Day, which was held in Tel Aviv in December 4th, 2013. Now, the fourth stamp in this series is being issued to commemorate the International Year of Light 2015 and the 2013 Nobel Prize in Chemistry awarded to the Israeli citizens, Arieh Warshel and Michael Levitt, jointly with Martin Karplus of Harvard University, for their development of multiscale models for complex chemical systems.

Mr. Razon repeated his promise made last year that the relationships between the Israel Philatelic Service and the ICS will continue and intensify and hoped that future Nobel Prizes in Chemistry to Israeli citizens will provide the Philatelic Service with additional opportunities to design and produce new Israeli stamps.

Figure 2: Top right: Stamp exposure ceremony, from right: Mr. Amir Malka, Mr. Daniel Shapiro, Prof. Michael Levitt, Mr. Yaron Razon and Prof. Ehud Keinan. **Bottom right:** Mr. Razon awards the framed stamp set to Profs. Michael Levitt and Ehud Keinan. **Left:** The Souvenir Leaf.

First-day-issue ceremony of a new Israeli stamp

A stamp release ceremony concluded the opening ceremony immediately after the greetings of Mr. Razon. The new stamp was revealed by Prof. Michael Levitt, Mr. Daniel Shapiro, Mr. Amir Malka, Mr. Yaron Razon and Prof. Ehud Keinan. Keinan explained that in addition to celebrating the light sciences, light-based technologies and their importance to humankind, all world cultures refer to light in positive philosophical terms of knowledge, education, enlightenment and human values. The story of the creation of light is of unique significance in Jewish culture and scriptures, and the Souvenir Leaf presents this theme via a wood engraving by the French artist Gustave Doré (Figure 2).

The new stamp recognized the 2013 Nobel Laureates' revolutionary contributions during the years 1968–1976, which created the new field of computational molecular biophysics and provided new approaches and techniques for understanding complex biological molecules. Their approach changed the way we think about proteins and defined a new area of science, which has influenced and inspired many other fields. A substantial portion of the honored work was undertaken at the Weizmann Institute of Science when Warshel and Levitt were working as students under the supervision of Shneior Lifson (1914-2001). Martin Karplus also conducted some of his research during a sabbatical year he spent working with the Lifson research group. It was a happy coincidence that the Nobel Prize committee recognized this group effort very close to what would have been Shneior Lifson's 100th birthday.

One of the most impressive achievements of these Nobel laureates' work is the molecular dynamics simulations of biological processes, which provide a computerized description of the events that actually occur in nature. One of the earliest and most significant examples of this strategy is the deciphering of the precise molecular events that occur during the process of vision. Arieh Warshel was the key researcher who deciphered the role played by the protein rhodopsin, which is the biological pigment in retina cells. The right side of the stamp features the protein rhodopsin, which is a bundle of seven helices connected to each other by peptide loops. This protein, which is embedded within the cell membrane, binds retinal, a small light-sensitive molecule shown as a group of grey spheres that represent atoms. The left side of the stamp exhibits the Schrödinger equation, which is the most fundamental tool of quantum mechanics.

The stamp tab features the logo of the International Year of Light as well as a schematic representation of the two major types of light-sensitive cells in the human retina: the rods (shown in yellow) and the cones (shown in blue, green and red). The rods are responsible for black-and-white vision and the cones are responsible for color vision. The human eye contains three types of cone cells, which discern red, green or blue light. All of the retinal cells translate the light stimulus to chemical changes and electrical impulses, which are transmitted to the vision centers in the brain via the optic nerves.

Keinan and Razon awarded Professor Michael Levitt with a framed set of the recently issued stamp along with the newly issued Souvenir Leaf of this stamp. A second set was awarded 4 months later to Prof. Arieh Warshel on the occasion of receiving a Honorary Doctorate degree from the Technion. Mr. Razon awarded a third framed set to Prof. Keinan for his help in the proposal, design and production of the new stamp. Enlarged images of all four stamps decorated the main lecture hall of David Intercontinental Hotel during the entire meeting.

The ICS Awards Ceremony

Following the ICS tradition, all prizes were awarded either at the Awards Ceremony (Figure 3), which took place in the afternoon of February 17th, or during the Gala Dinner the same evening.

Prof. Arnon Shani of Ben-Gurion University of the Negev became a **Honorable Member of the ICS** (see his profile in the current issue of the magazine LINK) for his major contributions to the community and to chemistry education in the State of Israel. Prof. Shani was born in Ness Ziona in 1935, received his BSc and MSc with Distinction from the Hebrew University of Jerusalem, (1961, with E. D. Bergmann) and PhD from the Weizmann Institute of Science (1965, with F. Sondheimer). Following two postdoctoral research periods with Prof. N. C. Yang (University of Chicago) and R. Mechoulam (Hebrew University of Jerusalem) he joined Ben-Gurion University (1968) and was one of the three founders of the Department of Chemistry at BGU. His scientific achievements span from insect pheromones, including isolation, identification, synthesis and application in integrated pest management to the chemistry and applications of the Jojoba wax, natural products from desert plants and organic photochemistry. At Ben-Gurion University he served twice as Chairman of the Chemistry Department, Deputy Rector, Director of the Institute for Applied Research in addition to numerous executive committees and boards. He also served on many committees on the national and international levels, focusing on higher education and chemical ecology and working with the Ministry of Agriculture, Ministry of Education and IUPAC Committees.

Prof. Shani served as President of the ICS for two terms (1997-2003). Using his rich managerial experience he rebuilt the ICS on strong financial foundations by partnering with major chemical industries and by expanding the membership. He initiated many significant projects, including restructuring and promotion of the ICS Bulletin, he established the Chemiada (national chemistry Olympiad), created major ICS prizes, initiated various projects related to the first International Year of Chemistry, etc. Under his leadership the ICS flourished and gained national and international reputation. Responding to the award Prof. Shani thanked the anonymous people who nominated him for the award and the anonymous jury who selected him. Most importantly, he thanked his wife Mira and the family who supported him all along his long career and many activities, both at Ben-Gurion University and in the ICS.

The 2014 Tenne Family Prize in memory of Lea Tenne for Nanoscale Sciences was awarded to **Prof. Efrat Lifshitz** (see her profile in the current issue of the magazine LINK) of the Schulich Faculty of Chemistry, Technion – Israel Institute of Technology, for her pioneering work in the synthesis and characterization of nanoscale semiconductors and magnetic materials, and for the development and application of advanced magneto-optical methodologies for the study of the properties of tailor-made nano-scale materials.

Prof. Lifshitz has developed novel nanostructures and enhanced our understanding of their most fundamental physical properties using advanced magneto-optical characterization tools, such as optically detected magnetic resonance and microwave-modulated photoluminescence. She pioneered the development of colloidal core/shell hetero-structures, developed and implemented advanced characterization techniques to detect ensembles as well as individual nanostructures. These methods enabled identification of carrier trapping sites, exchange interactions, angular momentum, and spin properties. In her response Prof. Lifshitz thanked the Tenne Family and to the ICS prize jury, mentioning that she personally knew Leah Tenne, and thus felt honored receiving the prize in her name. She pointed out that her career started with exploring two-dimensional transition metal layers, continued with the exploration of multiple quantum wells and organic thin films, and finally merged into the rich field of colloidal nanocrystals, such as dots, rots, polypods or platlets/ribbons, exploring these new materials at the nanoscale using dedicatedly developed magneto-optical methodologies. She said that she had always found great satisfaction and enthusiasm in research, citing Albert Einstein: "Learn from yesterday, live for today, hope for tomorrow. The important thing is not to stop questioning."

The ICS-ICL Prize for Technological Innovation was awarded to **Prof. Shlomo Magdassi** of the Casali Center for Applied Chemistry, the Institute of Chemistry, the Hebrew University of Jerusalem, for developing the technology of conductive inks composed of silver nanoparticles for printed electronics.

Printed electronics refer to the application of printing

Figure 3: The ICS Prizes Award Ceremony. **Top row from left:** the Honorable Member Award to Arnon Shani of Ben-Gurion University of the Negev, the Tenne Family Prize in memory of Lea Tenne for Nanoscale Sciences to Efrat Lifshitz of the Technion (with Reshef Tenne) and the ICS-ICL Prize for Technological Innovation to Shlomo Magdassi of the Hebrew University of Jerusalem (with Dani Chen of ICL). **Second row from left:** the ICS Prize for Excellence in Chemistry Teaching to Yonat Shamai of the Aviv high school in Ra'anana (from left: Shifra Strusky, Aviv School Principal, Dorit Taitelbaum, Yonat Shamai, Ayala Miller, VP Global Corporate Social Responsibility in Teva Pharmaceuticals, and Ehud Keinan) and the ICS Prize for Excellence in Chemistry Teaching to Dafna Shellem of the Reali School in Haifa (from left: Dorit Taitelbaum, the Reali Principal Yossi Ben Dov, Dafna Shellem, Ayala Miller and Ehud Keinan) and the ICS Prize for the Chemical Green Industry to Dor Chemicals Ltd. (from left, Yossi Antverg, Ehud Keinan, Gil Dankner, Carmel Feldman of the Manufacturers Association of Israel, Dani Chen of ICL and Shaya Baitel). **Third row:** the Yanai Prize for Excellence in Academic Education to Mark Gandelman of the Technion (with Yitzhak Apeloig and Zeev Gross), First and third poster Awards to Regev Parnes and Yakov Ginzburg, both of Ben Gurion University (with Dani Shahar of Bioanalytics Ltd.) and second poster Awards to Yael Ben-Nun of the School of Pharmacy, the Hebrew University of Jerusalem.

technologies for the fabrication of electronic circuits and devices, particularly on flexible substrates to form flexible electronics. Magdassi has demonstrated the persistence needed to take the very long route from basic science all the way to successful commercialization. By patterning of nanometric silver particles he successfully replaced the widely used indium tin oxide (ITO) as a transparent conductive electrode, with a product that is devoid of the many problems of ITO, including the unstable market and unstable costs of indium, its brittleness and inflexibility. His technology enables the direct patterning of electrodes on glass and on plastic substrates by inkjet printing. His most recent invention of a new process for the synthesis of silver nanoparticles and conductive inks, and their utilization for printing of transparent conductors for touch screens was promptly licensed by the Hebrew University to two companies, Hyrax and Xjet, and a startup company, ClearJet, for the manufacturing of touch screens for smartphones and automotive panels.

The ICS Prize for Excellence in Chemistry Teaching was awarded jointly to Ms. Yonat Shamai of the Aviv high school in

Ra'anana and **Ms. Dafna Shellem** of the Reali School in Haifa for their outstanding achievements in chemistry education at high schools. **Yonat Shamai** received her BSc in Medicinal Chemistry from Bar Ilan University and MSc in pharmacology from the Faculty of Medicine at Tel Aviv University. She began her professional career in Eilon High School in Holon. In 2001 she established the chemistry division in Aviv high school and since then serves as the division's head and teaches chemistry. Dafna Shellem received her BSc in biotechnology and food engineering from the Technion, and MSc in education, with honors, from the Open University. She began her career in the food industry and later switched to a teaching career in 1995. Since 2000 she has been a teacher and coordinator chemistry division of the Reali High School in Haifa.

The ICS Excellent Graduate Student Prize is awarded every year to a group of seven graduate students, one from each of the research universities. The winners are selected by the teaching committees of each university and the prizes are contributed by the Chairpersons/Deans of the universities during the annual ICS meeting. The 2014 prizes were awarded to: Tamara Brider of Ariel University (with advisors Gary Gellerman and Dan Meyerstein), Michael Layani of the Hebrew University (with advisor Shlomo Magdassi), Rita Schmidt of the Weizmann Institute of Science (with advisor Lucio Frydman), Meital Shviro of Bar Ilan University (with advisor David Zitoun), Adar Sonn-Segev of Tel Aviv University (with advisors Yael Roichman and Haim Diamant), Tommy Tomov of Ben-Gurion University (with advisor Eyal Nir) and Roman Vaxenburg of the Technion (with advisor Efrat Lifshitz) (Figure 4).

The Lise Meitner Prize for an outstanding work in the field of theoretical and computational quantum chemistry is awarded annually by the Lise Meitner-Minerva Center for

Figure 4: ICS Prizes for excellent graduate students. **Top row from left:** Tamara Brider (with Gary Gellerman) of Ariel University, Michael Layani (with Roy Shenhar) of the Hebrew University, Lucio Friedman representing Rita Schmidt of the Weizmann Institute. **Second row from left:** Meital Shviro (with Yitzhak Mastai) of Bar Ilan University, Adar Sonn-Segev (with Gil Markovich) of Tel Aviv University and Tommy Tomov (with Gabriel Lemcoff and Eyal Nir) of Ben Gurion University. **Third row from left:** Roman Vaxenburg (with Alon Hoffman) of the Technion, Barak Hirshberg of the Hebrew University (with Miri Karni) and Binju Wang of the Hebrew University (with Miri Karni).

Computational Quantum Chemistry, administered jointly by HUJ and Technion. The prize encourages young scientists to engage and excel in computational quantum chemistry and quantum theory. The 2014 Prize was awarded jointly to two winners. The first winner was graduate student Barak Hirshberg of the Hebrew University (with advisor Benny Gerber) for his contribution to the prediction of the existence of a new molecular crystal made of nitrogen only, and to the calculation of its structure and thermodynamic properties. The second winner was Dr. Binju Wang, a postdoctoral fellow of the Hebrew University (with advisor Sason Shaik) for uncovering the correct mechanism of repair of DNA lesions using quantum mechanics/molecular mechanics calculations (Figure 3).

The 2014 ICS Prize for the Chemical Green Industry was awarded to Dor Chemicals Ltd. for their contributions to the protection of the environment by advancing methanol-based technologies and demonstrating that methanol, which is significantly less polluting than oil-based fuels, can be used for transportation and for production of electricity. Methanol is a clean and cheap alternative fuel, easily produced from natural gas and significantly less polluting than oil-based products. Burning methanol produces lower carbon monoxide, far less carbon particles and no oxides of sulfur and nitrogen. These advantages, as well as the fact that methanol is easy to store and transport, make methanol a very environmentally-friendly liquid fuel. Indeed, the first Sheila and Eric Samson Prime Minister's Prize for Alternative Fuels for Transportation was awarded in 2013 to G. K. Surya Prakash and George A. Olah for advancing the concept of methanol economy worldwide. Dor Chemicals is leading the national effort to implement methanol as a clean fuel for transportation and electricity. In 2012 they began testing methanol as transportation fuel in various vehicles. In October 2014, Dor Chemicals and the Israel Electric Corporation successfully converted the turbo-generator in Eilat to produce electricity. This was the first gas turbine worldwide to be fueled by methanol instead of diesel oil. Switching to methanol was found to involve only minor modifications and was proven to be cost-effective. The award was received by three representatives of Dor Chemicals: Gil Dankner, Chairman of the Board; Shaya Baitel, Vice CEO Business Development; and Yossi Antverg, Methanol Development Director (Figure 10).

The Yanai Prize for Excellence in Academic Education has been awarded this year to ten outstanding Technion faculty members. This was the fourth year in a row that this prestigious prize was given for significant contribution to the advancement of higher learning "In appreciation of faculty members, who set an example through their endless contributions to teaching and learning and for their efforts to improve student involvement and sense of belonging to the Technion." Moshe Yanai, a global pioneer in the field of information storage, in making his contribution, sought to give back to the Technion in gratitude for the life skills that he gained during his studies at the institute 40 years ago. As his memories of life as a Technion student includes periods of difficulty, he decided to contribute 12 million dollars to award lecturers who have demonstrated teaching excellence, a gift that also greatly benefits Technion students.

One of the winners of the 2015 Yanai Prize was **Prof. Mark Gandelman** of the Schulich Faculty of Chemistry, Chairman of the 80th ICS Meeting. Unfortunately, the Award Ceremony was scheduled to take place at the Technion on February 17 at 18:00, clashing with the ICS events. Nevertheless, the ICS has found an original solution to this spatio-temporal problem. In collaboration with the Technion President Prof. Peretz Lavie and VP Prof. Boaz Golany, the signed prize certificate and check of 100,000 ILS were transferred to Ehud Keinan before the ICS Meeting and the entire "campaign" was kept confidential.

At the end of the ICS Prize Ceremony, Prof. Keinan surprised the audience, as well as Prof. Gandelman himself and awarded him the 2015 Yanai Prize, being helped by two Technion representatives: former Technion President Prof. Yitzhak Apeloig and Prof. Zeev Gross of the Schulich Faculty of Chemistry. The photos of this surprise ceremony were immediately sent to the Technion and were projected on the screen of the actual Yannai Prize ceremony that took place two hours later on the Technion campus, attended by the Yanai family, the other award recipients and their families, and Technion lecturers and students.

Plenary lectures

Michael Levitt (Stanford University), 2013 Nobel Laureate in Chemistry, presented the first plenary lecture on "The Birth and Future of Multiscale Modeling of Macromolecules." He explained that the development of multiscale models for complex chemical systems began in 1967 with publications by Warshel and Levitt recently recognized by the 2013 Nobel Committee for Chemistry. The simplifications used then at the dawn of the age of computational structural biology were mandated by computers that were almost a billion times less cost-effective than those we use today. These same multiscale models have become increasingly popular in applications that range from simulation of atomic protein motion, to protein folding and explanation of enzyme catalysis. In his talk he described the origins of computational structural biology and then went on to show some of the most exciting current and future applications.

Ronny Neumann (Weizmann Institute), winner of the 2014 ICS Prize of Excellence (see his profile in the current issue of the magazine LINK), delivered the second plenary lecture on "Catalysis, Mechanisms and New Reactions for Sustainable Chemistry." Pulled by a societal need for new sustainable oxidative transformations and the use of renewable resources especially in the transportation sector, this presentation described how the development of new mechanistic paradigms involving the reactivity of polyoxometalates (anionic metal oxide clusters) has led to new reactions with low environmental signatures and new vistas towards the utilization of renewable resources. Among the reactions now possible, he emphasized how new carbon-carbon and carbon-oxygen bond cleavage reactions and insertion of oxygen into carbon-hydrogen and carbon-metal bonds might continue to bring about new solutions to these serious problems.

W. E. Moerner (Stanford University), 2014 Nobel Laureate in Chemistry, started the morning program of February 18th with a plenary lecture on “Single Molecules as Light Sources for Super-Resolution Imaging and Sensors of Nanoscale Transport Properties.” He explained that since the first optical detection and spectroscopy of a single molecule in a condensed phase host in 1989, a wealth of new information has been obtained from time-dependent measurements and single-molecule probability distributions. When single-molecule imaging is combined with active control of the emitter concentration, enhanced spatial resolution well beyond the optical diffraction limit can be obtained for a wide array of biophysical structures in cells. Single-molecule emitters also provide precise and accurate 3D position as well as orientation when combined with a double-helix point spread function polarization microscope or with a number of additional new point spread functions. He stressed that if high-resolution spatial information is not needed, a machine called the Anti-Brownian ELectrokinetic trap provides real-time suppression of Brownian motion for single molecules in solution. By extracting multiple parameters from each molecule, this device has been used to explore the detailed dynamics of photosynthetic antenna proteins, multisubunit enzymes, redox enzymes, and even single fluorophores. With advanced analysis of the motion of the molecule in the trap, the diffusion coefficient and electrokinetic mobility can be estimated in real time, providing new variables for single-molecule studies. This lecture was sponsored by **Ehrlich & Fenster Patent & Trademark Attorneys**.

Arie Zaban (Bar-Ilan University), winner of the 2014 ICS Prize of Excellence (see his profile in the current issue of the magazine LINK), delivered the fourth plenary lecture on “There is Something New under the Sun: Materials for New Solar Cells.” He explained that photovoltaics (PVs) installation around the globe approached 180GW by the end of 2014, with annual growth of 45GW. Maintaining the current growth rate will enable more than 400GW installed by 2018 with an annual growth rate of about 55GW. These numbers represent a dramatic decrease in module and installation cost, which lead to grid parity, the holy grail of renewable energy. Though dominated by silicon based systems, PV research seeks new systems that beyond low cost will involve low energy of production, earth abundant materials and longer service life. Since 2011 the organic-inorganic halide perovskites have emerged as one of the most promising competitors of the silicon-based PVs. The unique properties of this earth-abundant family of materials, which are processed at very low temperatures, allow for high power conversion efficiency (>20%) though still challenged by stability issues. Following the same design rules, another PV family, which is solely based on metal oxides, also shows promising results. The raw materials are also earth abundant, the fabrication process is inexpensive and involves higher conversion efficiencies with perovskite crystals as solar absorbers. Encouraged by the intrinsic stability of metal oxide based systems these cells have reached 8.1% conversion efficiency. He also indicated that possible connections between the two advanced systems are being examined.

Keynote lectures

Edward I. Solomon (Stanford University) opened the session on Inorganic Chemistry & Catalysis by a lecture on “Geometric and Electronic Structure Contributions to Cu/O2 Reactivity.”

Shlomo Magdassi (The Hebrew University), winner of the ICS-ICL Prize for Technological Innovation, opened the session on Industrial Chemistry by a lecture on “Nanomaterials for Functional and 3D Printing.”

Barry M. Trost (Stanford University) opened the session on Organic & Organometallic Chemistry by a lecture on “Self-Assembly of Main Group Complexes for Asymmetric Catalysis.”

Dmitri Gelman (Hebrew University), winner of the ICS Excellent Young Scientist Prize, lectured on “It's all about FA (Formic Acid).”

Ron Naaman (Weizmann Institute) opened the session on Nanochemistry & Materials by a lecture on “Chirality and Spin - a Match for Spintronics and for Electron Transfer in Biology.”

Steven G. Boxer (Stanford University) opened the session on Biophysics by a lecture on “Vibrational Stark Spectroscopy Connects Electrostatics to Catalytic Rates at Enzyme Active Sites.”

Robert M. Waymouth (Stanford University) opened the session on Organic & Organometallic Chemistry II by a lecture on “Catalysis: Opportunities for Sustainable Polymer Chemistry.”

Efrat Lifshitz (Technion) opened the session on Nanochemistry & Materials II by a lecture on “The impact of alloying or/and core/shell hetero-structuring on the physical properties of colloidal quantum dots, examined by specialized magneto-optical methodologies.”

Figure 5: Guest speakers. First row from left: Michael Levitt, Keith O. Hodgson, W. E. Moerner and Edward Solomon. Second row from left: Robert M. Waymouth, Chaitan Khosla, Barry M. Trost and Hema Karunadasa. Third row from left: USA Ambassador Daniel Shapiro, Steven Boxer and the entire Stanford delegation.

Hemamala Karunadasa (Stanford University) opened the session on Analytical and Environmental Chemistry by a lecture on “Hybrid Perovskites as White-Light Phosphors and Solar-Cell Absorbers.”

Milko van der Boom (Weizmann Institute) opened the session on Supramolecular Chemistry by a lecture on “Pyridine Coordination Chemistry for Molecular Assemblies.”

Keith Hodgson (Stanford University) opened the session on Bio-Organic & Bio-Inorganic Chemistry by a lecture on “X-ray Free Electron Lasers in Structural Biology – From Slow to Ultrafast.”

Uri Banin, (Hebrew University) opened the special session on Physical Chemistry in Honor of W.E. Moerner by a lecture on “Dimensionality matters: dimensionality effects on the opto-electronic properties of semiconductor nanorods.”

David Cahen (Weizmann Institute) opened the session on Sustainable Chemistry by a lecture on “How Materials Affect Energy Sustainability.”

Roi Baer (Hebrew University) opened the session on Transport: Theory and Experiment by a lecture on “Stochastic density functional and GW theories scaling linearly with system size.”

Chaitan Khosla (Stanford University) opened the session on Bio-Organic and Medicinal Chemistry by a lecture on “Assembly Line Biosynthesis of Polyketide Antibiotics.”

Micha Asscher (Hebrew University) opened the session on Physical Chemistry II by a lecture on “Plasmonic Nanostructures Induced Photochemistry on Surfaces.”

Edvardas (Ed) Narevicius (Weizmann Institute), winner of the ICS Excellent Young Scientist Prize, spoke in the same session about “Chemistry with Cold Molecules: from Universality to Quantum Resonances”.

Gala Dinner

The Gala Dinner, which represented the main social event of the congress, took place in the evening of February 17th in David Intercontinental Hotel. About 80 participants attended this festive dinner, including the Stanford delegation members, ICS prizewinners, their families, many of their past and current students, friends and colleagues (Figure 7). The gala dinner has always provided the best opportunity to award the most prestigious ICS prizes.

Representing Teva Pharmaceuticals, which sponsored the evening, Inon Schenkar mentioned that as global powerhouse in generic pharmaceuticals, Teva touches the lives of millions of patients every day. With one of the broadest product portfolios in the industry, Teva has an unmatched impact on healthcare worldwide. As the leading generic company Teva produces every year 10 tablets for every person on the planet. Teva is also a leader in innovative pharmaceuticals, including Copaxone for Multiple Sclerosis and Azilect for Parkinson’s Disease. It is no coincidence that both innovative drugs were developed in Israel by, respectively, the Weizmann Institute and the Technion. Teva's faith in the Israeli scientific community leads it to collaborate with and closely support a multitude of research institutes and scientists. He mentioned the Israeli National Network of Excellence (NNE) in Neuroscience, which was created by Teva. Teva is proud of being part of Israel’s scientific community and proud to play its role in leading the advancement of science and scientific excellence in Israel. Teva's commitment to the NNE is to the tune of 15 million dollars over 5 years, and joins other long-term commitments, such as the 4 million dollar grant to establish two new research centers in the new Galilee Medical School, and in annual funds dedicated to awarding breakthrough scientific work through the Eli Hurvitz and Teva's Founders prizes. Teva also do this in the formative years of our young scientists, as early as in elementary school. Teva is proud to be part of such projects and is dedicated to continue to encourage and lead scientific excellence in Israel. In the name of Teva he saluted the ICS prizewinners for their admirable achievements.

Prof. Keinan thanked again all nine members of the Stanford delegation and awarded each one of them with a lifetime honorary membership of the ICS. He described the way by which the relationships between the ICS and Stanford have developed, all the way from the initial request by the Organizing Committee to this moment. He thanked Prof. Barry Trost, his postdoctoral mentor, long ago at the University of Wisconsin at Madison, for jumpstarting the whole process. Much of the work was done in close and informal relations with Prof. W.E. Moerner, before we all received the news from Stockholm. Finally, after the change of guards at the Stanford Department of Chemistry, the final phase of these successful relations were carefully followed by the current Chairman, Prof. Keith O. Hodgson. Keinan expressed his thanks to the many people who were involved in organizing this successful meeting and expressed his confidence that the visit will create many future collaborative projects between Stanford and Israeli chemists and will continue through many mutual visits in the future.

The ICS Gold Medal is the highest recognition awarded by the ICS to Israeli citizens who have demonstrated outstanding contribution to chemistry worldwide. Since 2002 the ICS medal was awarded to 14 scientists, 6 of them are Nobel Prize laureates. The list includes Ada Yonath (2002), Joshua Jortner (2003), Ruben Pauncz (2004), Avram Hershko and Aaron Ciechanover (2005), Zeev Luz (2008), Meir Lahav and Leslie Leiserowitz (2009), Meir Wilchek and Eli Hurvitz (2010), Dan Shechtman (2011), Raphael D. Levine (2012), Michael Levitt and Arieh Warshel (2013). The 2014 ICS Medal was awarded to **Prof. Eliezer Gileadi** (see his profile in the current issue of the magazine LINK) and **Prof. Abraham Nitzan**, both of the School of Chemistry, Tel Aviv University, for their exceptional contributions to science, education and society.

Figure 7: Memorable moments from the Gala Dinner and major ICS Prizes. **Top row from left:** the ICS Gold Medal is awarded to Abraham Nitzan, Eliezer Gileadi and his wife celebrating the ICS gold Medal, general view of the dinner hall. **Second row from left:** the ICS Prize of Excellence is awarded to Ronny Neumann and to Arie Zaban, and Zaban celebrating with family members. **Third row:** Dmitri (Dima) Gelman and to Dr. Edvardas (Ed) Narevicius celebrate their shared ICS Excellent Young Scientist Prize with friends.

Prof. Gileadi was born in Budapest (1932) and immigrated to Israel in 1940. He received his BSc from the Hebrew University of Jerusalem and PhD (with B. E. Conway, 1963) from the University of Ottawa. Since joining Tel Aviv University in 1966 he became a recognized leader of the domestic and international electrochemistry communities, educating generations of world-renown electrochemists and influencing the community by his widely used books. Gileadi developed the combined electrosorption isotherm, which provided the first understanding of the effect of molecular size on electrode kinetics. Measuring Tafel slopes with unprecedented accuracy, Gileadi could establish the temperature dependence of the transfer coefficient, a central question in electrode kinetics. He has also demonstrated that Grothuss-type hopping conductivity, believed to apply solely to protons in protic solvents, can also occur with halide ions in liquid and solid bromine and iodine, showing for the first time that unusual conductivity mechanisms can involve ions other than protons. His long list of achievements includes also the theory of microelectrode assemblies, electro-deposition of active metals in non-aqueous solutions, corrosion in non-aqueous media, and the development of new methods for studying adsorption isotherms using electrochemical quartz crystal microbalance (EQCM) in both gas and liquid phases. Prof. Gileadi's contribution to society is exceptional. In 1994 he established the Gileadi Program, which provided over 500 university research positions to first-class immigrant scientists who came from the former Soviet Union. That program was later extended to the Kamea Program. The highly successful Gileadi and Kamea Programs, which affected science in Israel, were highlighted in a study conducted by Science magazine.

Prof. Nitzan was born in Tel Aviv (1944), received his BSc and

MSc from the Hebrew University of Jerusalem with G. Czapski (summa cum laude, 1965) and PhD from Tel Aviv University with J. Jortner (summa cum laude, 1972). In 1975 he joined Tel Aviv University and since 2003 he serves as Director of the Sackler Institute of Advanced Studies. Nitzan has made pioneering contributions to the theory of chemical reactions, of energy transfer and of charge transfer in condensed phases and at interfaces. He also contributed profoundly to the understanding of molecular interaction with light. Together with Jortner, he developed a general theory of electronic radiationless transitions in large molecules, and an equivalent theory for molecular vibrational relaxation in condensed environments. Later, he has generalized the Kramers theory of activated rate process to the non-Markovian solvent regime and to the multidimensional case, making it valid for realistic chemical reactions.

Nitzan introduced the electromagnetic theory of surface enhanced Raman scattering, then extended it to other processes involving light interacting with adsorbed molecule, including surface enhanced energy transfer and surface enhanced photocemistry. Together with Ratner and Druger he has introduced and developed the dynamic percolation theory for transport in systems characterized by time dependent disorder, with important applications to transport properties of polymeric ionic conductors. Together with Landman he has developed numerical and theoretical methods to describe electron solvation and transport in polar environment. Furthermore, he has used similar methodologies to study electron transmission through water layers. He has made pivotal contributions to the understanding of electronic and heat conduction, inelastic and dephasing processes and optical processes in molecular conduction junctions, and elucidated the connection between molecular conduction and molecular electron transfer.

Abraham Nitzan responded by thanking the ICS for this wonderful show of recognition to his research accomplishments: "I am very happy to see many friends here in the audience, some of whom also recipients of ICS awards. And I am very happy to have several of my family members here with me - I would not be able to do my research without their presence in my life and their support. But I want to say special thanks to my colleagues and friends in the Chemistry community in Israel. Much is said about the difficulties in carrying world-class research in Israel. At the same time, I strongly feel that it has been a great advantage for me to do the bulk of my scientific work within our scientific community. Honestly, I cannot think of another place in the world where I could have had such a stimulating and exciting environment. I take this opportunity to thank my colleagues in the chemical physics community in Israel for making my scientific life so rewarding, and again, I thank all of you for being here tonight and the ICS for this recognition."

The 2014 ICS Prize of Excellence was awarded to **Prof. Arie Zaban** of Bar Ilan University (see his profile in the current issue of the magazine LINK) and **Prof. Ronny Neumann** of the Weizmann Institute of Science (see his profile in the current issue of the magazine LINK) for their outstanding contributions to renewable energy sources and chemical catalysis, respectively.

Prof. Arie Zaban is awarded the prize for his outstanding, innovative, and prolific contributions to renewable energies, and particularly to photovoltaics, batteries, and materials science for energy applications. His pioneering research has resolved an array of challenges in this field, and his innovative thinking has taken these ideas from the intellectual sphere to the practical realm. Zaban's combination of scientific innovation, academic excellence, entrepreneurship and community service are unique and are highly appreciated worldwide.

Prof. Ronny Neumann is awarded the prize for his seminal work in the field of catalytic oxidation, which has resulted in major achievements in ‘Green Chemistry’, particularly in the usage of benign oxidants and water as a solvent, for selective oxidation of a great array of organic compounds, and in reductive chemistry of carbon dioxide as well as in the quantitative conversion of cellulose and hemicellulose to synthesis gas. He is highly recognized for his pioneering research in the usage of polyoxometalates for catalytic oxidations.

The 2014 ICS Excellent Young Scientist Prize was awarded to **Prof. Dmitri (Dima) Gelman** of the Hebrew University of Jerusalem for the development of novel pincer complexes for catalytic transformations, and to **Dr. Edvardas (Ed) Narevicius** of the Weizmann Institute of Science (see his profile in the current issue of the magazine LINK) for his pioneering contributions to the field of Cold Chemistry and molecular beam experiments.

Dima Gelman (b. 1974) received his BSc (1996) and PhD (2002 with Prof. Jochanan Blum, Summa Cum Laude) from the Hebrew University. In 2004, after two years of a post-doctoral research with Prof. Stephen L. Buchwald at MIT, he joined the Institute of Chemistry at the Hebrew University. Focusing his research on organometallic catalysis, his highly prolific research group has designed and prepared novel catalytic systems for organic synthesis. In particular, they developed practical catalysts capable of activating and functionalizing inert carbon-hydrogen and carbon-carbon bonds via hydrogen transfer reactions. They developed a new class of electron-rich 3-D bifunctional PC(sp3)P pincer complexes with pendant functional groups that allowed for unique chemical transformations, such as mild and selective acceptor-less dehydrogenation reactions and controlled hydrogen formation from formic acid. They utilized this process as a key step in highly selective hydrogen transfer reactions and also discovered new modes of CO_2 fixation, which could lead to the utilization CO_2 as a raw material for organic synthesis.

Ed Narevicius (b. 1973) received his BSc in Chemistry

(1995, summa cum laude) and PhD (2002 with Prof. Nimrod Moiseyev) from the Technion. In 2008, after a post-doctoral research with Prof. Mark G. Raizen at the University of Texas at Austin he joined the Chemical Physics Department at the Weizmann Institute of Science. He has succeeded with brilliant originality and hard work to make a major breakthrough in experimental low temperature physics and chemistry and this work has been published in Science and Nature Chemistry, attracting worldwide attention. Reaching the quantum regime in chemistry has been a long-standing goal. Following the first experiments of Lee and Herschbach that earned them the 1986 Nobel Prize in chemistry, many groups tried to push the collision energy down using cold molecular beams formed by supersonic expansion. These experiments met a "magical" limit of about 5 Kelvin, which was just not enough to reach the energies where quantum phenomena start dominating the reaction dynamics. The main obstacle was the high mean velocity ranging from several hundred to a few thousand m/s. Many groups raced to stop the cold beams over the past 40 years, but with limited progress. In 2012 Ed proposed and demonstrated a new way to break the 5 K limit with a new type of experiment. Instead of trying to stop the molecular beam, Ed used two beams and deflected one of them in such a way that it overlapped with the other. Although both beams were travelling fast, the relative velocity in the moving frame of reference vanished, reducing the relative collision energy to 0.01 K. This breakthrough enabled Ed to observe a long sought quantum behavior in chemical reactions at ultra-cold energies, as well as an unusual isotope effect, taking place in the cold energy domain.

Closing Ceremony

The Closing Ceremony of the conference, which took place on the evening of February 18th, included awards for excellent posters, sponsored by Bioanalytics Ltd. (Figure 3). The first poster award was presented to Regev Parnes of Ben Gurion University for his poster "Thiol-Promoted Selective Addition of Ketones to Aldehydes." The second poster award was presented to Yael Ben-Nun of the School of Pharmacy, the Hebrew University of Jerusalem, together with Emmanuelle Meriquiol, Alexander Brandis, Boris Turk, Avigdor Scherz and Galia Blum, for their poster "Photodynamic Quenched Cathepsin Activity Based Probes for Cancer Detection and Macrophage Targeted Therapy." The third poster award was presented to Yakov Ginzburg of Ben Gurion University, together with Eyal Tzur and N. Gabriel Lemcoff for their poster "S-Chelated Ruthenium Alkylidenes: Expanding the Latency Gamut."

In his closing remarks, Keinan acknowledged again those who contributed to the great success of the 80th ICS Meeting, particularly Prof. Mark Gandelman as Chairman and the entire organizing committee, Ms. Paula Lam-Haim, CEO of the ICS, the stuff of Bioforum Ltd., particularly Mr. Amir Malka and Ms. Reut Lazar, and the entire delegation of Stanford University, particularly Profs. W. E. Moerner and Keith O. Hodgson. Finally, he reminded the audience that the 81th Annual Meeting will take place in February 9-10, 2016 under the aegis of Tel Aviv University with Micha Fridman and Amir Goldbourt serving as Chairman and Co-Chairman of the organizing committee, and with a respectable delegation from several Texan Universities, including UT Austin, Texas A&M and Rice University.

References:

1 For the full version of this report, see Keinan, E. *Isr. J. Chem*. **2015**, *55*, in press.

2 Keinan, E. *Isr. J. Chem*. **2014**, *54*, 395–412.

3 Keinan, E. *Isr. J. Chem*. **2015**, *55,* 114–123.

Framework Agreement for Collaboration between the Chemical Societies of the Czech Republic and Israel

November 25, 2014, Jerusalem

Ehud Keinan[1] and Alec Groysman[2]
[1] The Schulich Faculty of Chemistry, Technion - Israel Institute of Technology,
[2] Israeli Association of Chemical Engineers and Chemists

The State of Israel and the Czech Republic maintain a long history of friendly relations. Already in the 1920s, under the leadership of Tomáš Garrigue Masaryk as the first President, Czechoslovakia was the first country to recognize the Jewish people as a legitimate nation. In 1948, immediately after Israel's Declaration of Independence, Czechoslovakia was one of the first countries to recognize the new State. Furthermore, refusing to cooperate with the worldwide embargo on arms supply to the State of Israel, Czechoslovakia provided the young country with much weapons, ammunition and airplanes. In fact, Czech pilots trained the first pilots of the Israeli Air Force. Prime Minister David Ben Gurion had stated that without the essential help from Czechoslovakia it would be impossible for Israel to win its War of Independence, and the people of Israel will never forget it.

Although the relations between the two countries worsened under the Soviet occupation, the diplomatic relations were reinstated in 1990 immediately after the Velvet Revolution and the Czech Republic became Israel's most friendly European country. Over the years the two countries have signed many agreements of collaboration in multiple fields, including the economy, culture, science, education and security. The special cultural and economic relations between the two countries enjoy the support of an influential community of more than 25,000 Israeli citizens of Czech origin. Many Israeli artists, authors, musicians, filmmakers and scientists are very welcome guests in the Czech cities, and this friendly attitude is reciprocal. In 2010, the Czech Ministry of Foreign Affairs established the Czech Centre in Tel Aviv, focusing on many areas of the rich Czech cultural tradition, including film, theatre, music, fine arts, literature and others.

When we envision the Czech Republic we recall beautiful Prague, the UNESCO World Heritage Site, which attracts annually more than 4.1 million tourists, we recall composers Bedřich Smetana and Antonín Dvořák, writers Franz Kafka, Jaroslav Hašek, brothers Josef and Karel Čapek (they introduced the word robot), painter Alphonse Mucha with his Art Nouveau, Pilsner beer, and the car Škoda. The list of famous Czech scientists includes the geneticist Gregor Mendel, chemists Jaroslav Heyrovský (the inventor of polarography and electroanalytical chemistry), Otto Wichterle and Drahoslav Lím (the inventors of soft contact lenses) and many others.

The year of 2006 was declared by the Czech government as the Czech Jewish Heritage, commemorating the 100 anniversary of the Jewish Museum in Prague. The Museum displays an impressive 1000-year Jewish presence in Czechoslovakia. Of the 325,000 Jews who lived in the country before World War II, over 270,000 died in the Holocaust and most of the survivors left to Israel and other countries. The current Jewish population in the country is less than 5000.

The Czech Republic has always been the most industrially developed country in central and Eastern Europe and it is still one of the most stable and prosperous of the post-Communist states of Central and Eastern Europe. Prague is not only the capital and largest city of the Czech Republic and the historical capital of Bohemia, but also a political, cultural, and economic center of central Europe with a rich history of over 1,100 years. Prague was the capital of the Holy Roman Empire and was later an important city of the Austro-Hungarian Empire. Bohemia and Moravia were the economic heartland, producing over 70% of all industrial goods in the Austro-Hungarian Empire.

Although the population of the Czech Republic is only 10.5 million, it is highly educated and technologically-oriented, and enjoys a well-developed infrastructure. Consequently, the country has undergone very fast recovery from decades of occupation and exploitation by the Nazi and Communist regimes. The GDP is now 85% of the EU average and the principal industries include heavy and general machine-building, metallurgical products, electronics, transportation equipment, and a very strong chemical industry, with special emphasis on pharmaceuticals.

About 100-150 chemical enterprises function in both Israel and the Czech Republic. Both the their chemical sectors include basic chemistry, crude oil processing, petrochemistry, pharmaceutical industry, polymeric materials, paper industry, as well as many startup companies that develop advanced technologies. The Czech chemical industry is concentrated in large production complexes. Bohemia is home to the Elbe chemical region and Moravia houses the Moravian chemical region. The crude oil processing and petrochemical industries

Figure 1: The Prague Nobel Get-Together events. **First row from left**: the Israeli delegation at the Ambassador's home; Festive Gathering at the Garden of the Senate of the Parliament of the Czech Republic. **Second row:** Ciechanover, Shechtman and Hershko receive medals of honor at the Czech Parliament; The Major of Prague Bohuslav Svoboda (center) receives the Israeli Nobel stamps from Ehud Keinan. **Third row:** Formal lunch hosted by the Czech Minister of Foreign Affairs, Mr. Karel Schwarzenberg (standing in front of Prof. Ada Yonath); the entire group at the Ministry of Foreign Affairs with the Minister.

are located near the oil pipeline (Litvínov, Kralupy nad Vltavou).

Chemistry has always been a prominent area of scientific and technological excellence in the State of Israel. The chemical industry has contributed significantly to the national economy, with chemical products forming over 40% of the industrial production and 25% of the country's exports. Most of the Israeli chemical plants are located in the Haifa Bay area, Ne'ot Hovav, Ashdod and the Dead Sea. Of the approximately 2000 Israeli industrial companies in all fields, only ten companies make 50% of all Israel's exports, and five of those ten companies are chemical companies. Remarkably, two State Presidents, Chaim Weizmann (first President), and Ephraim Katzir (fourth President), were professors of chemistry. Furthermore, all six Nobel Prizes awarded to Israeli scientists were in Chemistry. These achievements are remarkable, considering the fact the Israeli chemistry community is quite small with only 6000 chemists, 5000 chemical engineers and 800 teachers.

Since its establishment in 1933, the Israel Chemical Society (ICS) has been striving to promote chemical research and development, the chemical industry, and chemistry education, as reflected in its diverse membership, including academic faculty members and students, industrial chemists, chemical engineers, and chemistry teachers. The Czech Chemical Society (CCS) is much older, representing the Czech chemists since 1866. The CCS publishes (since 1876) one of the oldest chemistry journals, the Chemicke Listy, which is published in the Czech language. Through the ChemPubSoc Europe, CCS has the privilege of partially owning and influencing the leading European chemistry journals. Besides that, The CCS, which has about 2500 members, collaborates with the Academy of Sciences, schools, and chemical industry, as well as the Slovak Chemical Society. The Association of Czech Chemical Societies (AČCHS) includes the CCS, the Czech Society of Industrial Chemistry, Czech Society of Chemical Engineering, Czech National Committee for Chemistry and the Czech National Committee for the Chemistry Olympiad.

Since the population of Israel is of comparable size to the Czech Republic and shares a strong presence in both academic and industrial chemistry, it became obvious that the two countries should enhance their cooperation in all fields of chemistry.

The idea of signing a collaborative agreement between the chemical societies of the Czech Republic and Israel was born during multiple discussions between Prof. Ehud Keinan and Prof. Pavel Drašar, past president of the CCS when they both served as members of the Executive Board of EuCheMS. They anticipated that a binational agreement would be fruitful for all parties because the chemical research in both countries has intensified over the past few decades and collaboration between Israeli and Czech entities could be highly complementary. They could foresee much synergism based on the innovative power of Israel and the large production capacity of the Czech Republic, highly trained work forces, and the ability to put together long range programs.

The idea was further discussed on several other occasions, particularly in three major events that took place in 2012. In 2012 Prof. Jitka Ulrichová, President of the CCS, invited Keinan to present a plenary lecture in the 64th Annual Meeting of the CCS (Olomouc, June 25-27, 2012) and that event provided an important opportunity to develop the idea of collaboration between the chemical communities. The details of such an agreement were further discussed during the 4th EuCheMS Chemistry Congress (Prague, August 26-30, 2012) under the leadership of Prof. Pavel Drašar, Chair of the Local Organizing Committee.

Another important joint event that took place earlier in the same year was the visit of the Nobel Laureates to Prague (May 28-31, 2012), which included a delegation six Israeli lecturers: Nobelists Aaron Ciechanover, Avram Hershko, Dan Shechtman and Ada E. Yonath, in addition to Joel Sussman and Ehud Keinan. The program included a festive lunch hosted by Mr. Yaakov Levy, Ambassador of Israel at his Residence with a dozen of other Ambassadors, interviews with prominent Czech media, a Festive Gathering at the Garden of the Senate of the Parliament of the Czech Republic, a formal lunch hosted by the Czech Minister of Foreign Affairs, Mr. Karel Schwarzenberg, and visits to the Jewish Quarter and Jewish Museum (Figure 1).

The key event was the Prague Nobel Get-Together symposium (National Technical Library, Prague, May 30-31, 2012), which was organized by the Czech Academy of Science, the Institute of Organic Chemistry and Biochemistry in Prague, the Israeli Embassy and the Czech-Israeli Chamber of Commerce. The program included, in addition to the Israeli and Czech speakers, distinguished guest, such as Josef Michl and M.G. Finn of the USA.

The framework agreement for collaboration between the chemical societies of the Czech Republic and Israel was signed by six societies. On the Israeli side, it was signed by Prof. Ehud Keinan, President of the ICS, Dr. Alec Groysman, Chairman of the Israel Society of Chemical Engineers and Chemists (ISCEC) at the Association of Engineers, Architects and Graduates in Technological Sciences in Israel, and Eng. Amiad Alexandron, President of the Israel Institute of Chemical Engineers (IIChE) (Figure 2).

The Czech signatories were Prof. Jan John, President of the Czech Chemical Society (Česká společnost chemická. CCS), Prof. Jiří Drahoš, President of the Czech Society of Chemical Engineering (Česká společnost chemického inženýrství, CSCHE), and Prof. Jaromír Lederer, President of the Czech Society of Industrial Chemistry (Česká společnost průmyslové chemie,CSPCH).

All six societies are public, non-profit entities that have similar missions of promoting scientific research, technological development, and training. They all collaborate with the social and economic sectors in order to promote innovation and productivity through science and technology. Consequently, the six societies agreed to join forces in order to enhance the scientific and technological relationships between the two countries, as well as specific relationships between universities, research centers, industries, and other institutions of scientific, educational, and cultural nature on both sides.

The content of this agreement resembles the cooperation agreement between the chemical societies of Spain and Israel, which was signed in Barcelona less than two months earlier (October 2, 2014). In addition to joint projects of research and

FRAMEWORK AGREEMENT FOR COLLABORATION BETWEEN THE CHEMICAL SOCIETIES OF THE CZECH REPUBLIC AND ISRAEL

CONTRACT AGREED BY

Prof. Jan John
President of the Czech Chemical Society (Česká společnost chemická, hereinafter CCS), acting on behalf and in representation of the CCS, bearing Fiscal ID No. CZ00444715, located at Staré Město, Novotného lávka 200/5, Praha 1 (Czech Republic).

Prof. Jiří Drahoš
President of the Czech Society of Chemical Engineering (Česká společnost chemického inženýrství, hereinafter CSCHE), acting on behalf and in representation of the CSCHE, bearing Fiscal ID No. CZ00499692, located at Staré Město, Novotného lávka 200/5, Praha 1 (Czech Republic).

Prof. Jaromír Lederer
President of the Czech Society of Industrial Chemistry (Česká společnost průmyslové chemie, hereinafter CSPCH), acting on behalf and in representation of the CSPCH, bearing Fiscal ID No. 00539171, located at Staré Město, Novotného lávka 200/5, Praha 1 (Czech Republic).

And

Prof. Ehud Keinan
President of the Israel Chemical Society (hereinafter ICS), acting on behalf and in representation of the ICS, bearing Fiscal ID No. 580089936, Located at the Schulich Faculty of Chemistry, Technion-Israel Institute of Technology, Technion City, Haifa 3200003 (Israel).

Dr. Alec Groysman
Chairman of the Israel Society of Chemical Engineers and Chemists (ISCEC) at the Association of Engineers, Architects and Graduates in Technological Sciences in Israel (hereinafter ISCEC), acting on behalf and in representation of ISCEC, Located at 200 Dizengoff St., Tel Aviv, P.O. Box 6429, 61063 (Israel).

Eng. Amiad Alexandron
President of the Israel Institute of Chemical Engineers (hereinafter IIChE), acting on behalf and in representation of the IIChE, bearing Fiscal ID No. 580066660, located at the Faculty of Chemical Engineering, Technion, Haifa 3200003 (Israel).

Figure 2: The first page of the Framework Agreement.

development, the modes of collaboration will include programs that promote dissemination of scientific and technological knowledge via training courses, workshops, conferences, seminars, mutual visits, students exchange programs, and prizes of excellence, as well as joint industrial initiatives in all fields of chemistry and chemical engineering.

A joint committee, consisting of five members, one from each entity, will convert the agreement to practice. A committee chairperson will be appointed for two years, and this appointment will rotate among the five partners. The committee will propose possibilities for collaboration in topics of common interest, prepare agreements for specific matters, and search for funding opportunities for joint projects.

The signing ceremony of the framework agreement took place in the King David Hotel in Jerusalem (November 25, 2014) as part of a formal, widely covered visit of the Czech government to Israel. Thus, the event was attended not only by the Israeli signatories and the Czech Ambassador to Israel, Mr. Ivo. Schwartz, but also by Prime Minister J. E. Bohuslav Sobotka and many of his Ministers, including Deputy Prime Minister Pavel Bělobrádek, Minister of Defence Martin Stropnický, Minister of Trade and Industry Jan Mládek, Minister of Health Svatopluk Němeček and Minister of Agriculture Marian Jurečka. The long list of other distinguished guests included past Minister of Trade and Industry Vladimír Dlouhý, President of the Czech-Israeli Mutual Chamber of Commerce Pavel Smutny, former Ambassador of Israel in Prague, Mr. Jacob Levi and Major General (Ret.) Danny Yatom (Figure 3).

Figure 3: Moments of the agreement signing ceremony. **Top left:** Mr. Pavel Bělobrádek, Deputy Prime Minister receives the signed agreement from Ami Alexandron, Alec Groysman and Ehud Keinan. **Top right:** The Czech government delegation in the signing ceremony. From left: Marian Jurečka, Minister of Agriculture, Svatopluk Němeček, Minister of Health, Jan Mládek, Minister of Trade and Industry, Pavel Bělobrádek, Deputy Prime Minister, J. E. Bohuslav Sobotka, Prime Minister, Martin Stropnický, Minister of Defence, Mr. Ivo. Schwartz, Ambassador of Czech Republic in Tel Aviv, Vladimír Dlouhý, past Minister of Trade and Industry, Pavel Smutny, President of the Czech-Israeli Mutual Chamber of Commerce (ICCCI). **Bottom left:** former Minister of Trade and Industry Vladimír Dlouhý, former Ambassador of Israel in Prague Jacob Levi, Major General (Ret.) Danny Yatom, Alec Groysman, Ami Alexandron, Ehud Keinan and President of the Czech-Israeli Mutual Chamber of Commerce Pavel Smutny. **Bottom right:** Ami Alexandron, Alec Groysman, Ehud Keinan showing the agreement to the former Ambassador Jacob Levi.

The six partially signed agreements started a long journey after that evening. Deputy Prime Minister Pavel Bělobrádek took them with him to Prague and invited the three presidents of the Czech Societies to sign them in his office. Three copies were sent back using diplomatic mail to the Ministry of Foreign Affairs in Jerusalem and then by special delivery to the Technion.

In March 2015, Dr. Alec Groysman visited Prague and met with the CCS president, Prof. Jan John, the President of the Czech Society of Chemical Engineering, Prof. Jiří Drahoš, President of the Czech Society of Industrial Chemistry, Doc. Ing. Jaromír Lederer, and Former President of the Czech Society of Industrial Chemistry, Prof. Ing. Jiří Hanika to discuss the development of mutual contacts based on the Framework Agreement. They agreed to exchange information about chemical research in the universities and in the chemical industry in order to find mutual interests and cooperation; encourage organizing workshops and symposia on topics of mutual interest; develop programs to support exchange by chemists and students; organize specific websites and establish links to websites of chemical societies in both countries.

For example, mutual conferences of the Czech and Slovak Chemical Societies take place in August-September of each year; a conference on "Natural Gas and Future of Chemical Industry" will take place in Tel Aviv in 2016; mutual conference of three Israeli Chemical and Chemical Engineering Societies are planned for February 2016, Tel Aviv; the 12th Conference of Israeli Corrosion Forum, NACE International Central Israel, is planned for May-June 2016 in Tel Aviv; the Czech Republic will host the 20th International Corrosion Congress in 2017 in Prague. Such congresses, which are held once in three years in different continents, will be carried out with the active participation of the Israeli Corrosion Forum.

Mountain-to-Valley Relay

The Mountain-to-Valley race is a 215 km relay, beginning in the northern village of Tel Hai, and finishing in Timrat, in the Jezreel Valley. It has been held annually for the past 7 years and this is the 5th time that Israel Chemical Society (ICS) teams have participated in the race. Over a 1000 teams, totaling approximately 8,500 runners, from Israeli industrial, governmental and private companies, participated. This year, three teams from the ICS, consisting of eight runners each, joined the race. The ICS teams consisted of undergraduates, graduate students, senior researchers and faculty members from all the Israeli academic institutions. They divided the 215 km race into 24 segments, running through ~22 hrs to complete the challenging route.

The experience was summarized by Yaniv Bouhadana and Evan Erickson of Bar-Ilan University as follows. "We set out at Thursday, April 30th, at 8 AM, from the beautiful, mountaintop village of Tel Hai, and ran along the Jordan River, and past the Kinneret. Some runners enjoyed a respite in the cool waters of the Kinneret during their break. Then we climbed diligently westwards past Tzalmon prison, where we were served soup by inmates, one runner taking a selfie with Ehud Olmert. Then we continued running downwards into the picturesque Beit Netofa valley where we ran speedily to the dark and mysterious Solelim forests, finally making our way to Timrat, where we had Café Hafuch at ~ 7 AM. It was a legendary experience, and we thank Rotal for their generous support. They provided accommodation during the race, beautiful athletic shirts, and pita-based bio-fuels to power the runners."

The Rotal Group who sponsored the ICS teams is a family business that was established in 1963 by Bernhard Rosenthal, a descendent of a long line of German industrialists. Since 2003, the business has been managed by Meir Tal (Rosenthal). The Rotal Group consists of three companies: Rotal Industries and Trading Ltd. – representatives of Henkel Loctite since 1963, Rotal Adhesives and Chemicals Ltd. – represents companies in the field of chemical finished products and equipment, and Lachman Ltd. which represents about 40 companies in the field of control and measurement equipment. Their client base consists of the majority of sophisticated industrial companies in Israel to whom they supply industrial adhesives, electronic adhesives, special lubricants, metal work liquids, soot reduction additives, environmentally friendly cleaning products, dispensing equipment, and control and measurement equipment.

Announcing the formation of the Graduate Student Division (GSD) of the Israel Chemical Society!

The GSD is a new organisation under the umbrella of the ICS, devoted to serving the graduate (Masters and PhD students) of Israel in Chemistry, Biochemistry and closely affiliated branches of science.
This unified organization will be a network which allows outside interests — academia, industry, schools and others, to access the diverse pool of talent of our members. At the same time, we are actively building the relationships to allow graduate students access to personal and professional opportunities through organisations with which we have affiliations and relationships, both at home and overseas. We hope that this nexus of contacts and opportunities will serve the interests of Israel's graduate students, and additionally draw in further support from outside organizations and companies.

The concerns of graduate students are not always heard in the academic world. We want to be a voice for the shared experience of our members. An example of a widespread issue for graduate students — particularly when new to the world of research — is the concentration of expertise within particular groups and institutions. Often we face challenges for which solutions are available, but which lie outside the expertise of our immediate research environment. Thus, the GSD sees itself as an organization which is capable of bringing instrumental, practical and theoretical techniques to those who need them, and we have already begun to organize workshops in the use of, for example, analytical instrumentation and subsequent data interpretation when our members demand it. The idea is always to have the maximum benefit from our collective knowledge by sharing it!

Another, more formal aspect of knowledge-sharing among our members will take place this December. We will be integrating the organic and physical chemistry student symposia and holding the inaugural GSD Symposium at Ariel University. This will be the first of an ongoing series of annual conferences which will allow the graduate student population of Israel to share their work. As the GSD grows, we expect to expand this conference toward the invitation of internationally renowned scientists and speakers with support from our affiliates, and we hope this support will allow us to sponsor the travel of Israeli students to conferences abroad.

Figure caption: From left to right: Haim Katz (Ariel), Carl Recsei (Technion), Maya Miller (Hebrew University of Jerusalem), Rami Batrice (Chairman), Oren Meiron (Ben Gurion), Sivan Okashy (Bar Ilan University), Olga Chovnik (Weizmann Institute of Science). Not in picture: Ori Green (Tel Aviv University).

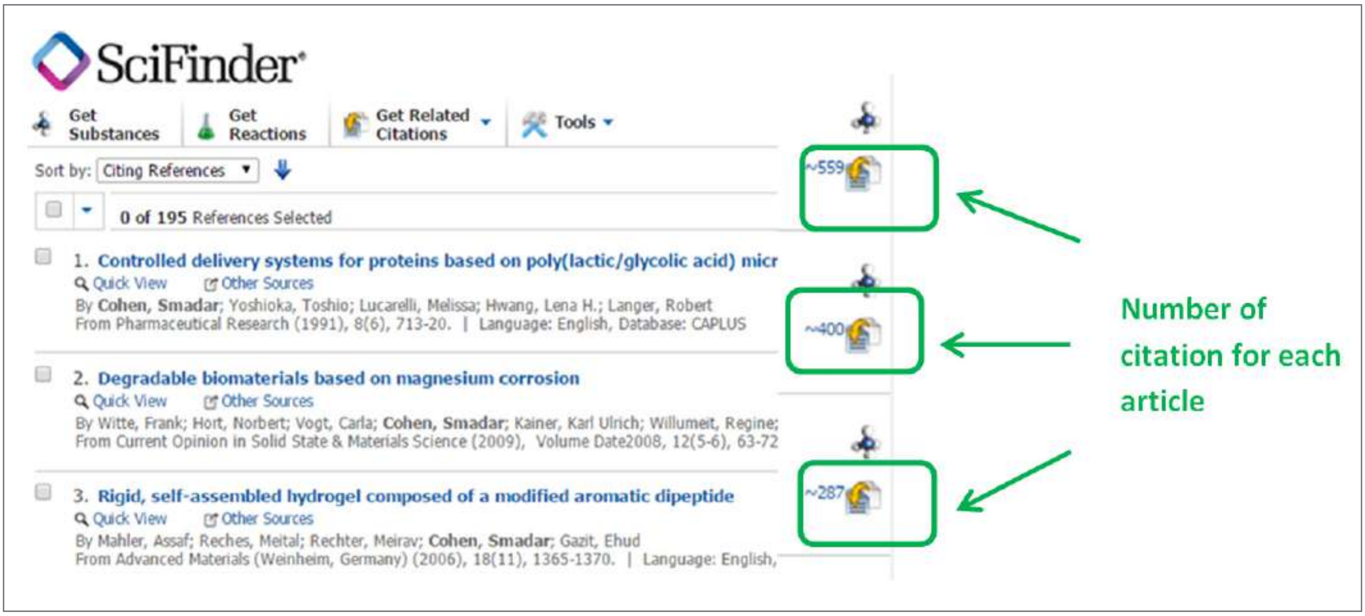
Complementary to our student conference, we are looking to hold career days featuring industry representation, including large companies and startups seeking talented graduates. This is an example of using the GSD as a portal for organizations to access our graduate students' knowledge, but we also want to share this knowledge with the next generation of chemists. It is no secret that attracting students to science is a challenge, but the GSD sees this as an opportunity to recruit other talented students who may otherwise feel that chemistry is inaccessible to them. We want to send our best communicators to share our enthusiasm for science with the broader public. Whether it be in the schools or pubs of Israel, we want everyone to feel connected to science, which is at the very heart of our country's growth and prosperity. Serving the student population of Israel, we hope to spark a new-found curiosity and fascination with science, and we hope to inspire minds everywhere to engage with chemistry and help our members have the best possible start to their careers!

How to analyze an important scientific contribution with SciFinder – Case Study

Rina Labiner
Arad-Ophir Ltd. www.arad-ophir.co.il 03-5409111
Email: info@arad-ophir.co.il

Prof. Cohen is a leading researcher in the Biotechnology Engineering Department of Ben-Gurion University who has won many prestigious awards like the Rappaport Prize and was selected by the magazine "Lady Globes" as one of the 50 most influential women for 2013 thanks to her contribution to biomedical research that allowed treating cartilage degeneration without surgery. Her algea extract "alginate" injected into patients suffering from Acute Myocardial Infraction, is also considered a clinical/biomedical breakthrough. For more information press here.
Prof. Cohen has 35 patents and many articles.

Who cited Professor Cohen's articles?



All together more than 5000 citations sorted on SciFinder in descending order.

Take a look at one of the patents, using a new tool **PatentPac™**, developed by CAS and aimed at the patent analysis process.

1. Injectable cross-linked polymeric preparations and uses thereof
By: Cohen, Smadar; Leor, Jonathan
Assignee: Ben Gurion University of the Negev Research and Development Authority, Israel

A therapeutic compn. for treatment of a body tissue which includes an aq. soln. of a crosslinked polymer being capable of: (i) maintaining a liq. state in storage at room temp. for at least 24 h; and (ii) assuming a gel state following deposition within the body tissue. The therapeutic compn. can be effectively administered into a damaged boby tissue via injection or catheterization, thereby treatingthe damaged body tissue. Thus, cross-linked alginate soln. was made 1% w/v sodium alginate (Avg. Mw = 30 kDa; G/M ratio 2.1) and 0.3% w/v calcium gluconate

Patent Information

Patent No.		Kind	Language	Date	Application No.	Date
US 20060083721	PatentPak	A1	English	Apr 20, 2006	US 2005-229119	Sep 19, 2005
US 8168612	PatentPak	B2	English	May 1, 2012		
JP 2011218186	PatentPak	A	Japanese	Nov 4, 2011	JP 2011-132761	Jun 15, 2011
JP 5492147	PatentPak	B2	Japanese	May 14, 2014		
US 20130272969	PatentPak	A1	English	Oct 17, 2013	US 2013-13893567	May 14, 2013
US 9006213	PatentPak	B2	English	Apr 14, 2015		

One may choose to read the patent PDF in English or Japanese or other languages. PatentPak will help choosing it by easy access to searchable PDF patent documents from the main 11 main authorities in multiple languages.

This tool can bring you directly to the exact location of the relevant molecule within the patent document.

9005-32-7 Alginic acid	Page 3 in PatentPak
7440-70-2 Calcium, uses	Page 9 in PatentPak
56687-62-8 β-D-Mannuronic acid	Page 11 in PatentPak

$(C_6H_9O_6)$ —OH

Rina Labiner received her BSc in chemistry in 2006 from Bar-Ilan University and an MBA in business management in 2009 from Ono Academic College. From 2006 until 2011, she worked as a project manager in the field of hazardous materials. Since 2012, she is an information specialist at Arad-Ophir Ltd.– the Israeli agent for Chemical Abstracts Service and STN International from 1995, and LexisNexis from 2006.

How patent data can be leveraged for business decisions

Dorit Plat
Information Specialist
Email: plat.dorit@gmail.com

Patent information has becoming increasingly relevant, not only for the established IP community, but also for businesses and governments to inform their economic and political decision-making.

Patent information may help innovation-based businesses to

- Gain intelligence about a product or an industry and align their research accordingly
- Identify most active competitors and understand their strategies
- Identify key inventors within a particular organization or technology space
- Identify potential partners for in-house IP
- Identify new licensing, research, and growth opportunities
- Strengthen their patent portfolio by filling up unidentified gaps
- Keep a close watch on the industry trend and make reliable predictions

These capabilities, and others, are among the reasons for the increasing interest in patent analysis capabilities and visualization.
The following graphs show how we can use patent information in order to evaluate the innovation patterns of the Israeli private companies in the field of chemistry.

Figure 1 shows a statistical analysis that has been performed on PCT applications (international applications published in

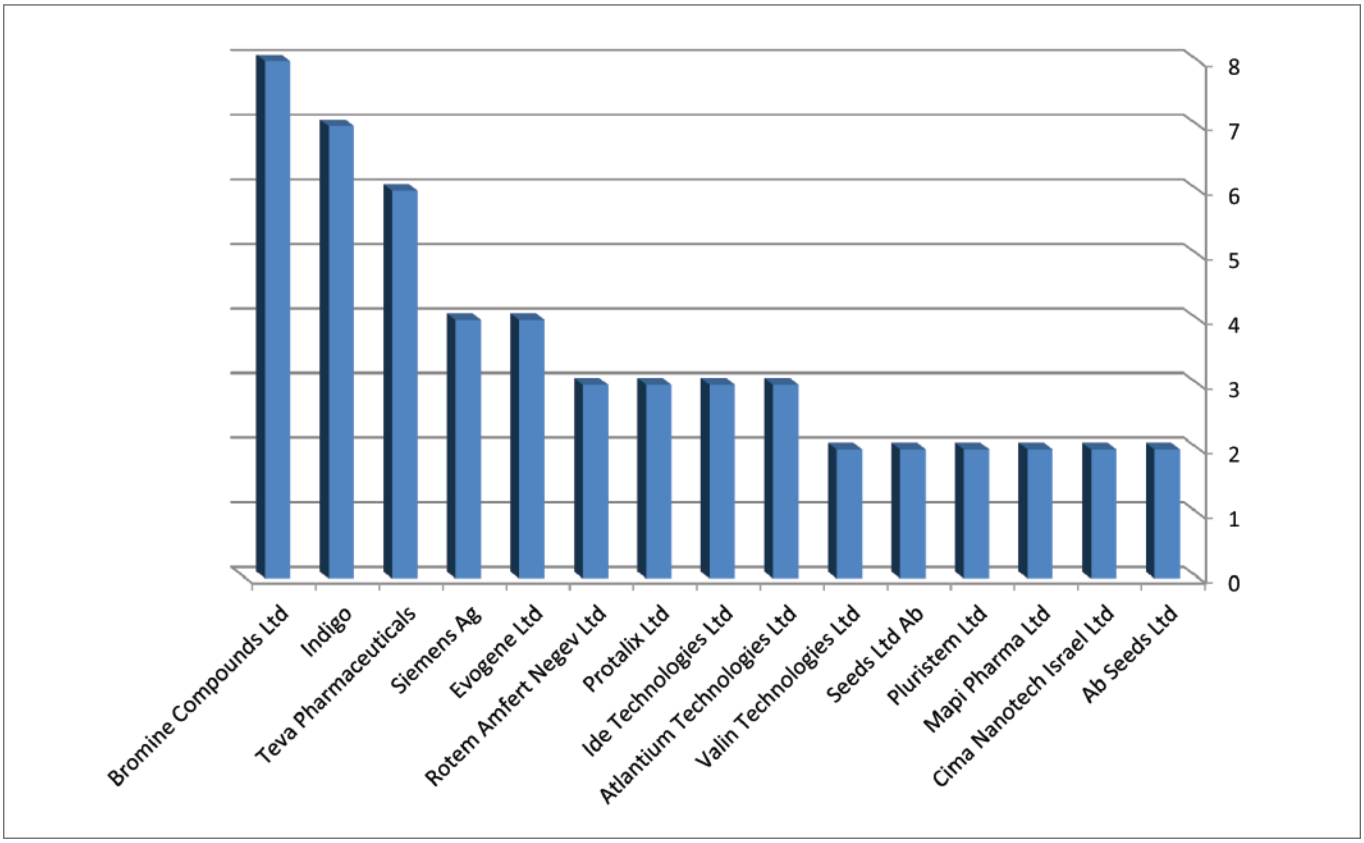


Figure 1: Number of PCT applications of Israeli companies published in 2014

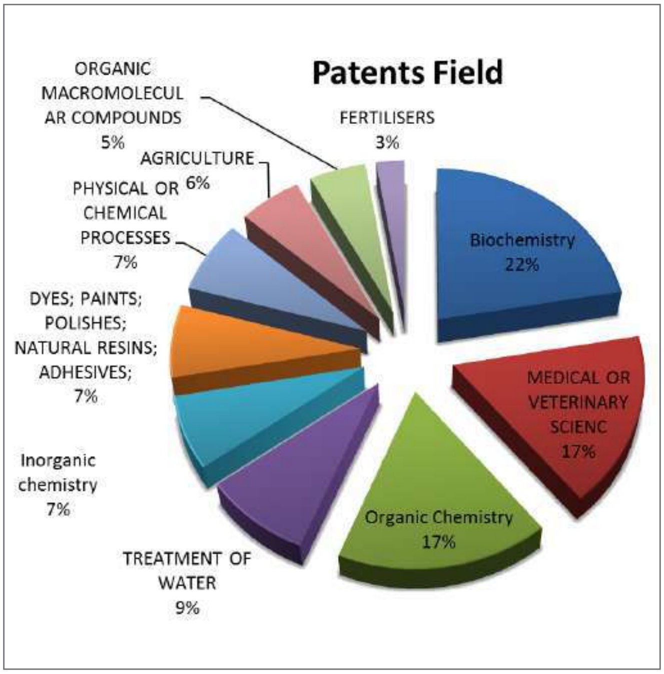


Figure 3: PCT application fields of Israel based companies, published in 2014

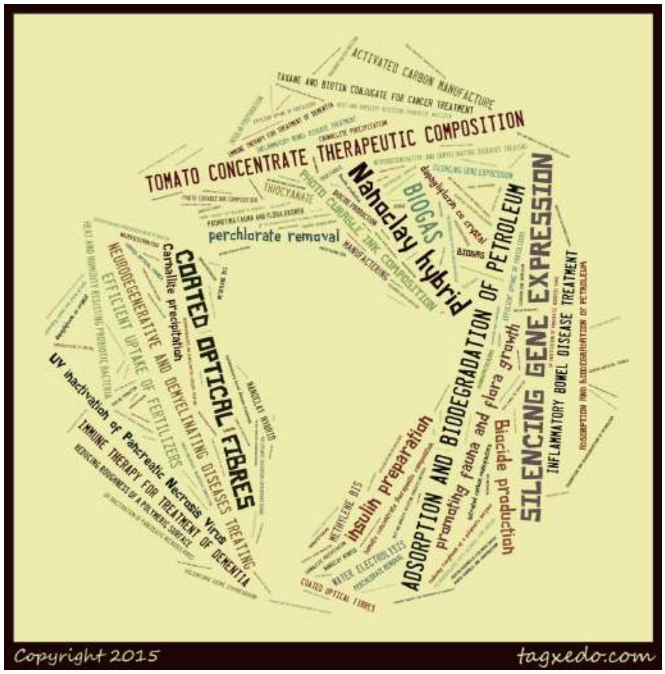


Figure 2: PCT application topics of Israel based companies published in 2014

the Patent Cooperation Treaty, the international patent law treaty) of Israeli based companies that were published during 2014 in the field of chemistry and chemistry- related areas. Patents of academic organizations have been excluded. The analysis has been performed using the **PATENTSCOPE®** and **PatBase** databases with a threshold of 2 (companies with only one patent are not shown).

Some of the main topics of those patents appear in Figure 2 and in Figure 3 there is a summary of the main areas of those patents.
If Patents are Weapons, the bigger companies are well armed and take a leading position in patent submissions (see Fig. 1).

As can be seen from Fig. 3, the main areas of activity are biochemistry, organic chemistry, and medical or veterinary science (in which chemists have a significant role), followed by water treatment.

Using similar statistical analysis we can rate the innovation activity in different industries and graph it over a period.
As can be understand from the above, the patent analysis resource is a meaningful tool for any business related research.

Dorit Plat is an information retrieval specialist. After completing her PhD in chemistry, she worked as an R&D manager. During the last four years, her main focus is on patent searches and analysis as well as on providing information services in the field of Chemistry, Life Sciences and Biomed.