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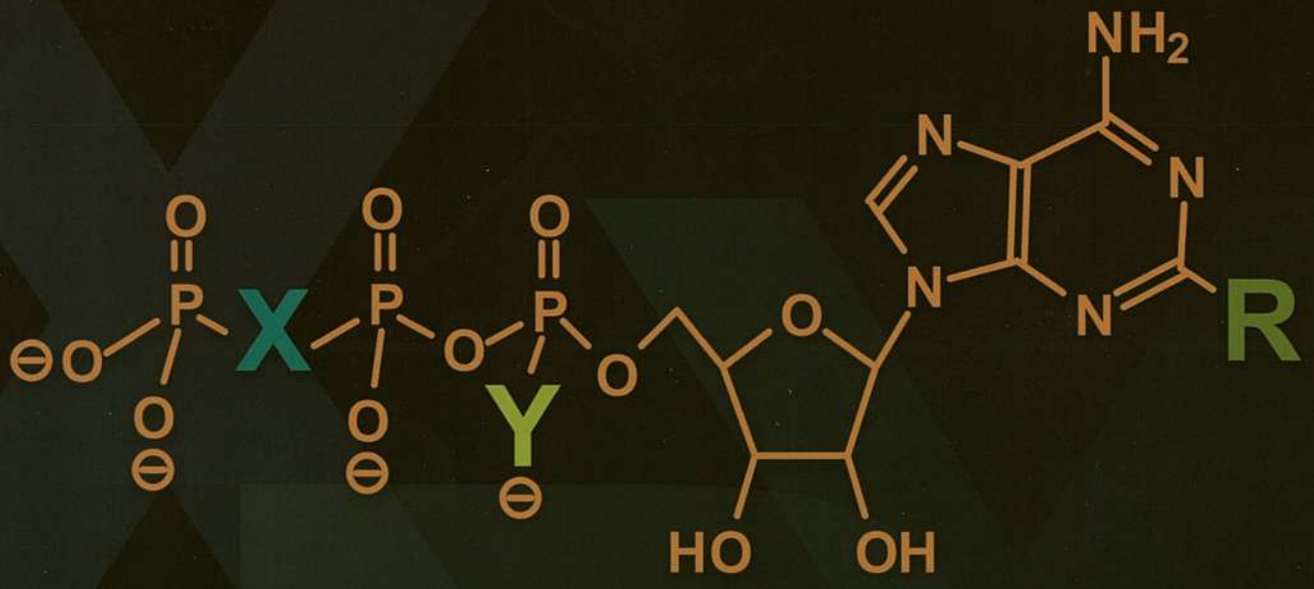

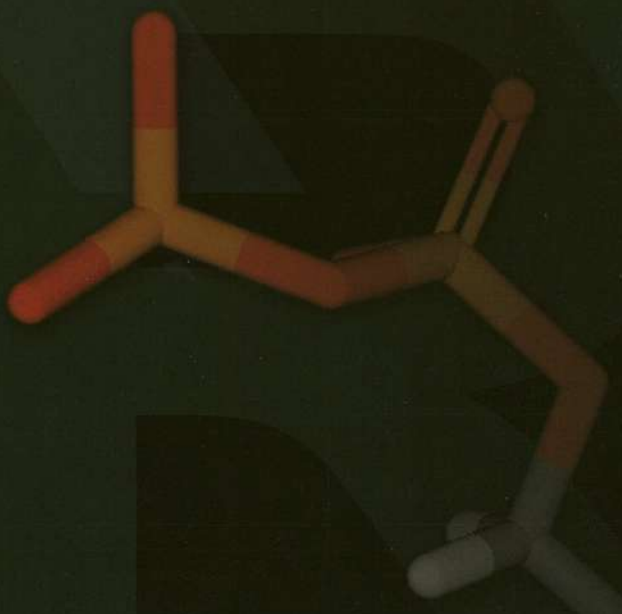

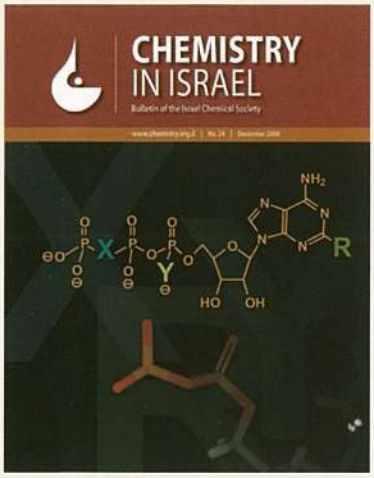

"Nucleotide Based Drugs"
Prof. Bilha Fischer

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בזכות היכולת שלך לחשוב מחוץ לקופסה
מיליוני אנשים יהנו משיפור באיכות החיים

חברת טבע מרחיבה את פעילותה בתחומי הפיתוח והייצור בכל הארץ ומגייסת

כימאים/ות

מהנדסים/ות
תעשיה וניהול, כימיה וביוטכנולוגיה

חוקרים/ות

לכל המשרות נדרשות עברית ואנגלית ברמה גבוהה, יתרון לנסיון מהתעשיה

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המודעה מיועדת לנשים וגברים כאחד

Letter from the president

Prof. Ehud Keinan
President of the Israel Chemical Society

Dear Colleague,

We all share the excitement and pride of being Israeli chemists, with Prof. Ada Yonath becoming the third Israeli Nobel Prize Laureate in Chemistry. About six weeks after the Nobel Prize ceremony in Stockholm we will be celebrating the 75th anniversary of the ICS Meetings in Tel Aviv on January 25-26, 2010. This meeting, which is organized by the School of Chemistry of Tel Aviv University, will be honored by a highly respected delegation of top Japanese chemists. Prof. Shmuel Carmeli, Chairman of the organizing committee, will provide you with more details.

Another rapidly approaching event is the International Year of Chemistry (IYC-2011). The Israel Chemical Society is planning to take advantage of this opportunity to convey three main messages to the general public in Israel, and particularly to the young generation.

Message A: Chemistry plays a central role in any scientific endeavor, because scientific problems have no boundaries and because all major scientific research projects worldwide are now interdisciplinary. All "hot" areas of science, including biochemistry, catalysis, environmental science, materials science, biomedicine, nanotechnology, surface science and opto-electronics are all heavily based on chemistry. Chemistry is the crossroads and main interchange on the information highway that connects mathematics and physics with biology and medicine. Chemistry also connects the basic sciences with the technological and engineering disciplines. While remembering that, we must ensure that the strength of core chemistry is retained and reinforced.

Message B: The explosive growth of the world population challenges humankind with severe problems, such as sustainable energy, food, human health, global warming, lack of water, air and water pollution, disappearing raw materials, future cities, quality of life, etc. If science will ever be able to come up with solutions to these problems, it will be mainly through the chemical sciences. Thus, contrary to the public image of our science, chemistry is not a source of problems in our world; chemistry might be the only way to solve our problems.

Message C: The future of chemistry in Israel is at risk. Since the 1970's there has been a persistent deterioration of science education, and of Chemistry in particular, at our intermediate and high schools. When more than 80% of the high school graduates become ignorant citizens, deprived of the very basic of scientific concepts, our society becomes inferior not only to advanced societies, but also in comparison with nearby societies of the Middle East. Scientific and technological ignorance of the general public, including politicians and other decision makers, poses a severe threat to the long-range existence of the State of Israel. The current situation of chemical education in Israel is unacceptable and unforgivable, and should undergo a major reform.

It is our responsibility to bring these messages to the Israeli public, and the International Year of Chemistry is a good opportunity to do so.

Finally, I wish to thank Prof. Mati Fridkin and Ms. Anitta Harrison for a fine job in continuously upgrading the international stature of Chemistry in Israel. I thank the authors who have contributed articles to this issue and I encourage all of you to contribute future articles to this journal.

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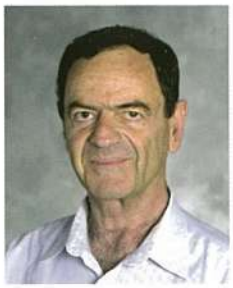


Letter from the editor

Prof. Matityahu Fridkin
Editor-in-chief

In the course of final editing of the present winter issue of Chemistry in Israel **Prof. Ephraim Katzir**, the fourth president of the state of Israel, an internationally highly esteemed scientist and one of the founders of the Weizmann Institute of Science passed away. In his memoriam a press release of the Weizamnn Institute of Science is given herein.

The shortage of fresh water for domestic and for industrial and agricultural use in semi-arid regions, notable in Israel, is the subject of enhanced scientific and technological challenges aiming low-cost water production and purification. Recent achievements and new challenges for "water-oriented" chemists are presented by **Dr. Roni Kasher.**

Prof. Alfred Hassner, the winner of the ICS award for the year 2007 summarizes the highlights of his achievements in the article: Adventures in stereochemistry and cycloadditions.

Ion mobility spectrometry (IMS) is sensitive analytical mean that is used for detection, identification and monitoring of chemicals, mainly explosives, highly toxic gases and drug interdiction. A brief overview of the principle of operation of IMS and applications in the war against terror is presorted by **Dr. Zeev Karpas**.

Prof. Zeev Luz, the winner of the ICS Medal for the year 2008 summarizes some highlights of his work in the article: Pathways of chemical processes in solid by dynamic NMR. The case of the Cope rearrangement in bullvalene.

The 73rd annual meeting of the ICS took place on February 4-5, 2008, at the Jerusalem International Convention Center. The highlights of this multidisciplinary event are given by **Prof. Yoel Sasson** who chaired the organizing committee.

Prof. Noam Adir, chairman of the organizing committee of the 74th ICS meeting, held on February 8-9, 2009, at the David Intercontinental Hotel in Tel Aviv, outlines the highlights of the event.

The highlights of the 7th conference of the Israel Association for Medicinal Chemistry, which took place on the 24th of March 2008 at the Weizamnn Institute of Science, are summarized by **Drs. Michal Sharon, Eylon Yavin and Nurit Livnah**, the organizers of the meeting.

Dr. Bob Weitraub, director of the Libraries, at the Sami Shamoon College of Engineering brings, from the Archives, the stories of five leading chemists whose lives were saved by Raoul Wallenbereg, righteous gentile
On behalf of the editors I urge the members of the community of Chemistry in Israel to suggest and write articles for the journal, moreover, please response positively to our requests for contributions.

The dedicated, professional and creative contributions of the **Graphic Design Section** and the **Photography Section** of the **Weizmann Institute of Science** is highly appreciated.

The invaluable contribution of **Ms. Anitta Harrison**, the spirit, the driving force and the operator of every single aspect of the production of this winter issue of *Chemistry in Israel* is highly appreciated.

Prof. Ephraim Katzir
1916 – 2009

Institute Professor Ephraim Katzir, the Fourth President of the State of Israel, an internationally esteemed Israeli scientist and one of the founders of the Weizmann Institute of Science, passed away on Saturday, May 30, 2009, at his home in the Weizmann Institute. He was 93.

Ephraim Katzir was born in Kiev, Ukraine, in 1916. His parents, Yehuda and Tzila Katchalski, brought him to the Land of Israel in 1922. After finishing high school in Jerusalem, he chose to study botany, zoology and bacteriology at the Hebrew University of Jerusalem, though he eventually focused on biochemistry and organic chemistry. In 1941, he completed his doctoral degree with research in simple synthetic polymers of amino acids, and he continued his studies at the Polytechnic Institute of Brooklyn, Columbia University and Harvard University.

While studying in Jerusalem, Katzir was active in the Hagana and advanced to the rank of field corps company commander. In 1948, after returning from the US, he became involved in military research and development in the Israel Army's Science Corps, Hemed, founded at the start of the 1948 War of Independence, and for a time commanded it as a lieutenant colonel.

At the close of the War of Independence, together with his scientist brother, Aharon, Ephrain Katzir joined the faculty of the Weizmann Institute of Science, where he established and headed the Biophysics Department. Aharon served as Head of the Polymer Department until his murder in a terrorist attack at the Lod airport in 1972.

Over the course of his career, Ephraim Katzir researched synthetic models in order to investigate the principles of polymer structure and function. His pioneering studies

contributed to the deciphering of the genetic code, to the development of synthetic antigens and to the clarification of the various steps in immune reactions. An understanding of the properties of his models ("poly-amino acids") aided, among other things, in the development of the multiple sclerosis drug Copaxone® at the Weizmann Institute.

Another of Katzir's important successes was the development, in the 1960s, of a method for binding enzymes to various substrates. The method is used today as an important tool in the drug and food industries.

Parallel to his scientific research, Katzir was also active over the years in the social and educational sides of science. He headed a governmental committee that set national science policy, raised generations of new scientists, translated important scientific material into Hebrew and helped to establish a Hebrew-language popular science magazine. He served as the head scientist of the Ministry of Defense and chaired the Society for the Advancement of Science in Israel, the Israeli Biochemical Society, the National Council for Research and Development, and the Council for the Advancement of Science Education. In addition, he headed the National Biotechnology Council.

In 1973, Katzir was chosen to be President of the State of Israel (its fourth president), a position he held until 1978. (With his appointment to the presidency, he changed his name from Katchalski to Katzir.) In his term as president, he put special emphasis on societal problems and education, and he regularly went out of his way to become acquainted with all the different groups making up the Israeli population.

Returning to his scientific career, Katzir's research took off in new directions. He headed a team that won an international competition for computerized modeling of proteins and took part in a multidisciplinary scientific team that discovered important features of the effect of snake venom on the human body. He authored hundreds of scientific articles and served on the editorial and advisory boards of many scientific journals. In honor of his 60th, 70th and 80th birthdays, international scientific symposia were held in Rehovot and Jerusalem. On his 90th birthday, an international scientific conference was held at the Weizmann Institute.

Prof. Katzir was a member of the Israeli Academy of Sciences and Humanities and of numerous other learned bodies in Israel and abroad, including the Royal Institution of Great Britain, the Royal Society of London, the National Academy of Sciences of the United States, the Academie des Sciences in France, the Scientific Academy of Argentina and the World Academy of Art and Science. He was a visiting professor at Harvard University, Rockefeller University, the University of California at Los Angeles and Battelle Seattle Research Center.

In addition, Katzir was awarded the Rothschild and Israel Prizes in Natural Sciences, the Weizmann Prize, the Linderstrom Land Gold Medal, the Hans Krebs Medal, the Tchernikovsky Prize for scientific translation, the Alpha Omega Achievement Medal and the Engineering Foundation's International Award in Enzyme Engineering. He was the first recipient of the Japan Prize and was appointed to France's Order of the Legion of Honor. He received honorary doctorates from more than a dozen institutions of higher learning in Israel and around the world, including Harvard University, Northwestern University, McGill University, the University of Oxford and the Technion-Israel Institute of Technology.

The official memorial ceremony, held in the Weizmann Institute's Memorial Plaza, was attended by the President of the State Shimon Peres, Prime Minister Benjamin Netanyahu and Minister of Defense Ehud Barak, as well as many government ministers, Knesset members, educators, scientists and members of the public.

Membrane-based water treatment technologies: Recent achievements, and new challenges for a chemist

Roni Kasher

Roni Kasher was born in 1964. He received his BSc in Chemistry and Geology, MSc in organic chemistry (with Itamar Willner) from the Hebrew University of Jerusalem. His PhD (with Chaim Gilon, H.U.) was on backbone-cyclic peptides synthesis and activity (2000). Roni did a post-doc in Weizmann Institute with Mati Fridkin and the late Prof. Ephraim Katzir on rational design of biologically active peptides, then spent two years as a research associate (H.U., Dep. of Water and Soil Sciences) studying groundwater pollution. Since 2005 Roni is a faculty member at Zuckerberg Inst. for water research, Ben-Gurion University of the Negev. His research interests are design of surfaces resistant to biofilm growth in water treatment systems, novel reverse osmosis (RO) and nanofiltration polymeric membranes for desalination, mineralization and fouling phenomena, surface chemical modification, antimicrobial peptides, and design of peptides with biological activities.

ABSTRACT

The shortage of fresh water for domestic and for agricultural use in semi-arid regions of the world, including Israel, focuses an attention on a growing scientific and technological challenge of low-cost water purification and water production. Membrane processes play a key role in water-treatment technologies, due to their low energy consumption and to advancement in membrane fabrication techniques. This paper describes the chemistry of most important water treatment and desalination technologies with focus on membrane processes and current research of developing water treatment membranes.

Background

Today, access to clean water is becoming a difficult task in many regions of the world. According to the World Health Organization, 1.2 billion people lack access to sufficient amounts of clean fresh water, and 2.6 billions lack adequate sanitation. Poor sanitation combined with unhealthy water quality accounts for the largest single cause for disease and death in the world (1). Fresh water is 2.8% of the total water in the world, whereas among fresh water, only 0.6% is available for use, and the rest is inaccessible, located in the poles (2).

The need for fresh clean water is growing rapidly due to the world population growth that imposes larger demands of water supply for domestic use, agriculture and industry. Another reason is deterioration of fresh water supplies: aquifers, the largest fresh water resource, are being contaminated constantly by industrial and agricultural activities, as well as by intrusions of seawater or saline water due to overuse. Rivers and lakes (surface water

Zuckerberg Institute for Water Research, Jacob Blaustein Institutes for Desert Research, Ben-Gurion University of the Negev, Midreshet Ben-Gurion 84990, Israel

resources) are also in threat. Hence, there is a strong need to increase fresh-water availability either by recycle waste water or by production of fresh-water from seawater (3). In Israel, being located in a semi-arid zone, water scarcity is much more dramatic, and the need to coup with the water problem is crucial and urgent.

The need to increase fresh water supply and more extensive water treatment drove the advancement of new water technologies and the maturity of existing ones, in all fields of water: Desalination and ion removal by reverse osmosis, disinfection techniques by catalysts and by biological treatment, decontamination, new filtration techniques, and monitoring of water quality. Membranes play a key role in many of the modern water technologies, due to recent advances in material chemistry and polymer chemistry, coupled with the need for processes with low energy consumption. Examples for shift to membrane technologies are the use of reverse osmosis instead of thermal desalination, a wide application of polymeric and ceramic filters on account of gravity sand, change of waste-water treatment and decontamination - from pond bio-degradation techniques to membrane-based bioreactors.

The most important membrane-based water technologies include reverse osmosis (RO), electrodialysis (ED), nanofiltration (NF), ultrafiltration (UF) and microfiltration (MF). Ultrafiltration membranes have pore diameters in the range of 10-100 nm, and microfiltration membranes have pores of 0.1-1 μm. Ultrafiltration is a modern solution for removing bacteria and viruses from water, and microfiltration is used for removal of suspended particles, and in some cases filter bacteria and most viruses. Ultrafiltration and microfiltration are used very frequently in combination, in many water treatment processes such as waste-water reclamation, membrane bioreactors, or treatment of surface water. With no doubts, an exciting breakthrough in water treatment technology is the invention of the first RO membranes and development of modern RO membranes, followed by development of NF membranes (see a wonderful review by Linder and Kedem (4)). Both NF and RO membranes are non-porous. Today RO is the most common process for production of potable water from seawater or brackish water. A semi-permeable membrane is used to separate salts from water. A high pressure is induced to overcome an osmotic pressure, and water permeation is induced from saline water to freshwater through the membrane, while salts are rejected. NF membranes are used mainly for removing heavy dissolved salts and large organic molecules from water.

This paper describes chemistry-related aspects of modern water technologies, focusing on membrane processes and current research of water treatment membranes.

Early nanofiltration and reverse osmosis membranes

The first production of potable water from saline solutions was accomplished by Reid and Breton at the University of Florida (5). The separation process employed a cellulose acetate (CA) membrane and had a low flux. Loeb and Sourirajam studied porous CA membranes and in 1959 found that heating CA in water produces a desalination membrane. They pursued the study by development casting techniques that yielded anisotropic CA membranes, called the Loeb-Sourirajam (L-S) membranes, with high flux and equal desalination (6). The mechanism of membrane formation was phase-inversion (7), and the resulting membranes had thin layer (less than 1 mm) on top of a thicker porous layer (8).

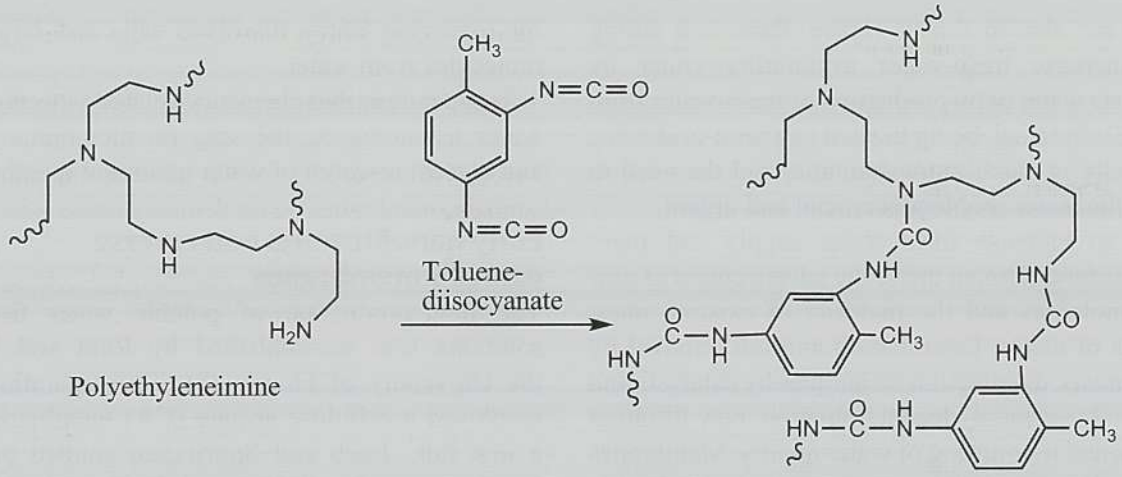
[In 1966 Sidney Loeb came to Beersheva for three years to teach RO technology at the Negev Institute for Arid Zone Research, today part of Ben-Gurion University of the Negev. Loeb met his wife, left Israel, and then came back on aliya. Sidney Loeb set up the first RO pilot project in Israel, located in the Arava at Kibutz Yotvata.]*

The concept of a dense submicron layer on top of porous asymmetric support was named thin-film composite membrane (TFC; see Fig. 1), and laid the basis for modern RO and NF membranes. Variations in the casting solution composition of CA, as well as annealing temperature of the thin top layer, yielded different molecular weight cutoffs (MWCO) for the resulting membranes that extended from tight RO to UF, including the intermediate NF range (9).

Microporous support layer

In early composite membranes the micro-porous supports were made by using asymmetric Loeb-Sourirajan cellulose-acetate membranes that were cast in a way to produce high flux. The flux of composite membranes was higher than asymmetric membranes: A typical Loeb-Sourirajan asymmetric CA membrane tested under simulated seawater desalination conditions – 3.5%

* Sidney Loeb had passed away on December 2008.



Scheme 1

aqueous sodium chloride at 102 atmospheres showed only 4.08 lit/m²hr (litters per square meter per hour) with 88% salt rejection, while a comparable composite membrane consisting of 200 nm CA laminated on a loose asymmetric support exhibited 8.5 lit/m²hr with 91% salt rejection (10).

In search for supports that could give better results, in particular higher flux, composite membranes were prepared by using commercial MF membranes as porous sublayers (11). Evaluation of a variety of CA commercial membranes led to the finding that the pore size of the porous support layer should be less than 100 nm. The search for better composites was pursued by preparation and testing noncellulosic microporous support films. Polymers examined included polycarbonate, poly(phenylene oxide), and polysulfone (1). Polysulfone showed the best results (12), and has remained a mainstay in composite membranes to this day. Polysulfone (1) also finds widespread use itself as an UF membrane.

Table 1: Transport properties of selected membranes.

Membrane name and type	Feed solution[a]	Salt rejection	Permeate flux (lit/m²*hr)	Pressure (atm)
NS-100 Polyethyleneimine/ TDI	3.5% Synthetic SW	99%	30	102
PA-300 Polyepiamine	3.5% NaCl	99.4%	39	68
Polypiperazine-amide	Synthetic SW	98%	44.2	102
NS-300 Piperazine-trimesamide	Synthetic SW	99.2%	23.8	102
FT-30 Aromatic polyamide	0.5% NaCl	99.5%	71.4	34
SW-30 Aromatic polyamide	SW	99.1%	43	54

[a] SW=Seawater;

Non-cellulosic composites

The development of microporous polysulfone (1) as a support layer for composite membranes enabled one to use variable types of polymerization methods on top of polysulfone template, since it is stable to either acidic or alkaline solutions. Hence, the active barrier membranes were prepared with materials other than CA or other esters of cellulose, such as polyamides, polyethersulfone (PES), polysulfones, chlorinated polyvinyl chloride (PVC) and polyvinylidene fluoride (PVDF), resulting in non-cellulosic composites.

The field of composite reverse osmosis membranes has overwhelmingly moved to interfacially synthesized membranes (13), dominated by polyamide compositions. It is prepared by amine in the aqueous phase and acyl halide in the organic phase (10, 14). High flux and high rejection polyamide membranes are routinely prepared, with simultaneous crosslinking of the nascent polymer film at an interface. It was demonstrated that interfacial polymerization occurs in the organic phase (13), hence, for film thickness to build up, amine must continuously cross the water-organic interface, diffuse through the polyamide layer already formed, and come into contact with the acyl-halide in the organic solvent side.

The first generation non-polysaccharide membranes

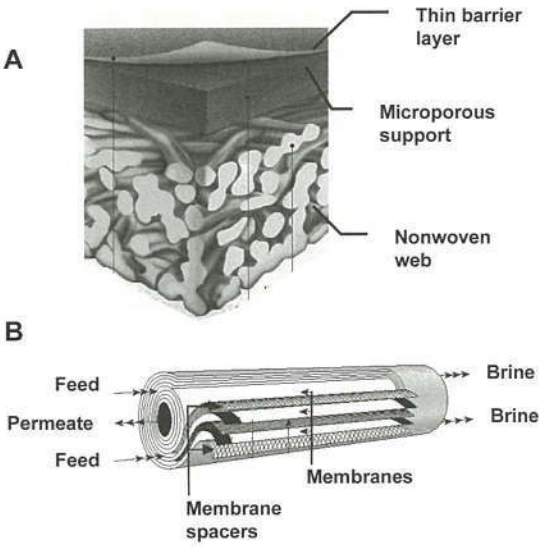


Figure 1: (A) The structure of thin-film composite membrane for water desalination. The top dense barrier layer is obtained on top of porous support layer, with mechanical reinforcement of non-woven web. (B) Schematic view of a spiral-wound membrane module that is widely used in reverse osmosis seawater desalination with composite membranes.

were prepared by interfacial condensation of polymeric polyamines with a crosslinker molecule. The product of polyethyleneimine reacted with toluene-diisocyanate (see Scheme 1) or with isophthaloyl-chloride produced a new membrane named NS-100 (15). NS-100, which was prepared on a microporous polysulfone sheet gave 99% salt rejection and flux of 30 lit/m^2*hr at 102 atmospheres with 3.5% synthetic seawater solution (Table 1). This membrane was a breakthrough in a sense that it was the first successful non-cellulosic composite reverse osmosis membrane, and it had high rejection of small salts. Another polymeric polyamine that was used to prepare RO membrane was polyepiamine (known also as polyether amine). The reaction product of polyepiamine with isophthaloyl chloride as a crosslinker gave a reverse osmosis membrane designated PA-300 (16) with superior fluxes (see Table 1) compared to polyethyleneimine membranes. The first major installation of a composite RO membrane in the world, i.e. the seawater desalination plant in Jeddah, Saudi Arabia, utilized the PA-300 membrane.

Interfacial polymerization using acyl halide functionality > 2.0

Interfacial polymerization with monomeric amines was more difficult, as these resulted in porous films with poor salt rejections. However, through optimization of conditions, composite membranes could be made by interfacial reaction of piperazine with isophthaloyl chloride on polysulfone support with reasonable salt rejections (see Table 1). When isophthaloyl chloride was replaced in part by a triacyl halide, the 1,3,5-benzene-

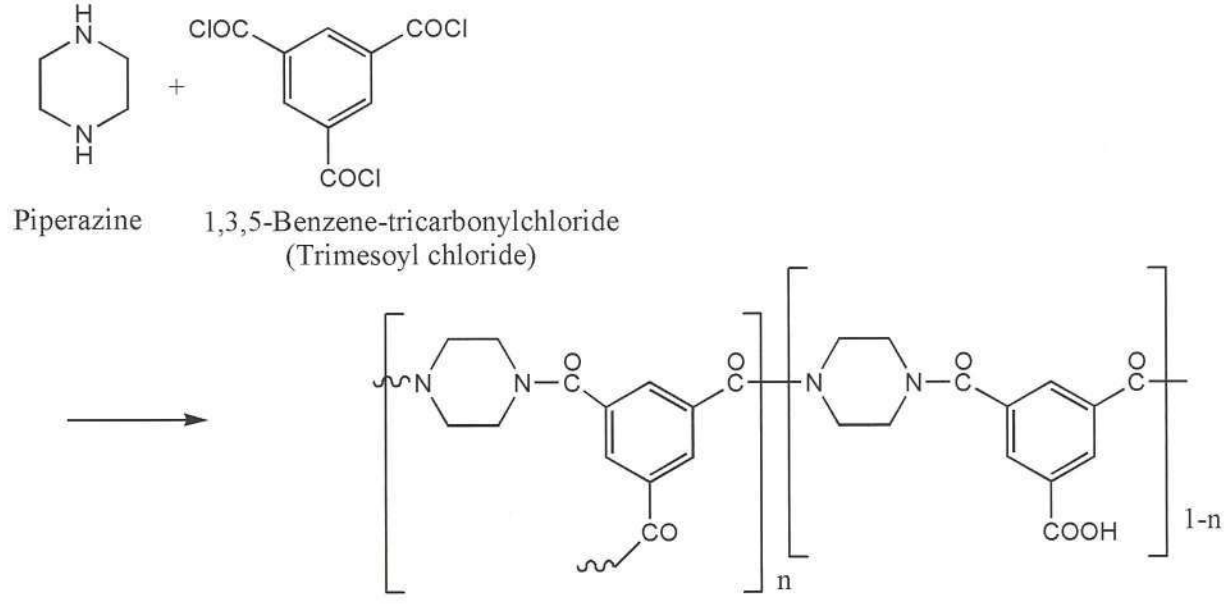


Figure 2: The chemistry of the barrier layer of piperazine-trimesamide membrane (such as NS-300).

tricarbonyl chloride (trimesoyl chloride; see Fig. 2), a dramatic and unexpected changes in flux and salt rejections were obtained. Water flux had a maximum at 1:1 isophthaloyl chloride: trimesoyl-chloride and rejection of magnesium sulfate was higher than 99%. NS-300 is piperazine-trimesoyl-chloride membrane and is used mainly in applications of high flux and high $MgSO_4$ rejection (see Table 1).

The chemistry of NS-300 is described in Fig. 2, assuming partial hydrolysis of the acyl halide groups, to generate carboxylic acid groups. NS-300 has low rejection to monovalent ions, and high rejection for salts with divalent ions such as sulfate, that is in agreement with anionically charged barrier layer, probably due to the presence of carboxylate anions.

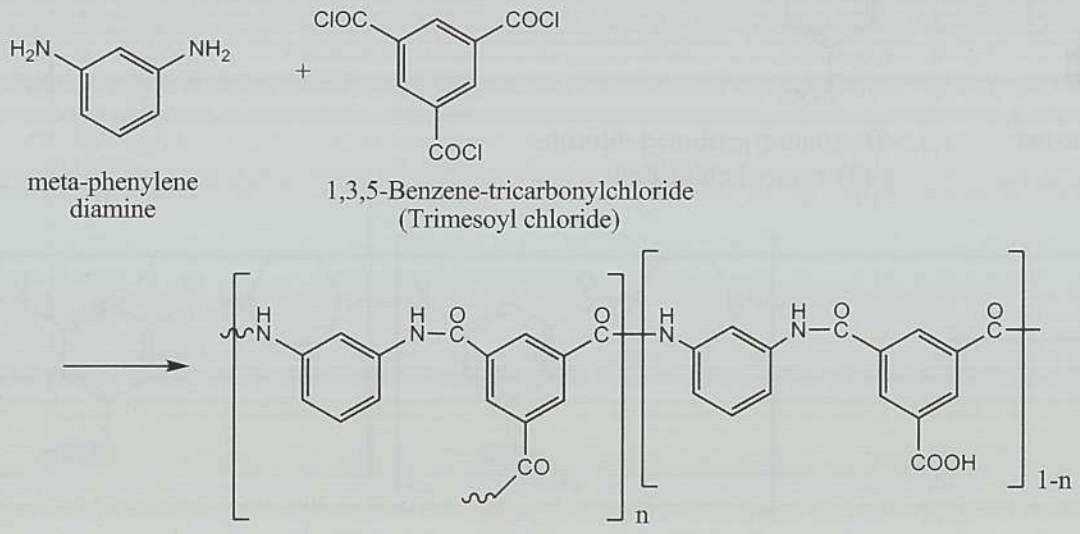
Piperazine-based polyamide membranes (Fig. 2) are most commonly used in nanofiltration applications, due to their wide range of working conditions and poor salt rejection (see Table 1). For example, the NF-40 membrane which has a barrier layer of piperazine-trimesamide, show temperature operating capability from 0 to 45 °C, and pH resistance from 2 to 11 (17). The low monovalent anion rejection and high divalent anion rejection of piperazine-based membranes has led to applications such as salt whey treatment (concentration of sugars and proteins with simultaneous reduction of NaCl), sulfate removal from seawater, recycle of waste dye streams, and color removal from bleach effluents in wood pulping process.

Other aliphatic amines were used and evaluated in composite membranes: Petersen and coworkers compared 1,2-ethanediamine, 1,4-cyclohexanediamine, and 1,3-bis-(aminomethyl)cyclohexane with piperazine when reacted with trimesoyl chloride and converted into trimesamides (18). All three amine-mesamides showed higher NaCl rejection then the poly (piperazineamide), and lower water permeability. This can be explained by the presence of amidic hydrogen that may provide strong inter-chain hydrogen bonds.

Aromatic monomeric amine in composite membranes

Membranes that are made by interfacial polymerization of aromatic monomeric amines with aromatic acyl halides having functionality > 2.0 were found to be the most suitable ones for the conversion of seawater to potable-drinking water. This is due to the requirement of high salt-rejection and high flux under seawater feed conditions. The best results are obtained by using 1,3-benzenediamine (*m*-phenylene-diamine) and trimesoyl chloride as the acyl halide, to give the metaphenylene trimesamide layer, that is described in Scheme 2. The 1,3,5-benzene-triamine monomer, if reacted solely with trimesoyl chloride, would give too rigid crosslinked structure with resulting layer being too brittle.

An example of metaphenylene trimesamide composite membrane is FT-30 (Scheme 2). Salt rejection of FT-30



Aromatic polyamide membrane (FT-30)

Scheme 2

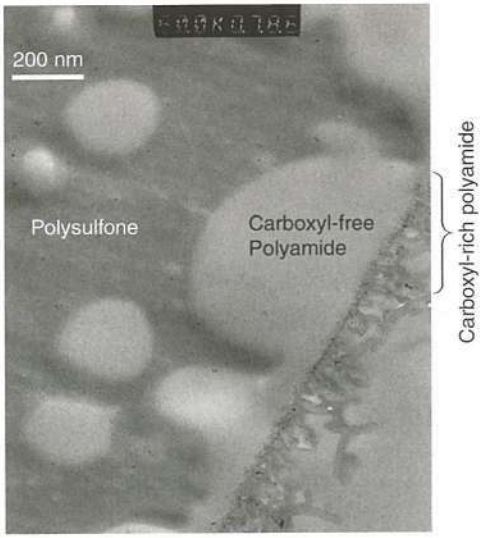


Figure 3: Cross section TEM of the ESPA1 membrane (aromatic polyamide membrane, with similar chemistry as FT-30) stained with uranyl nitrate. The polyamide layer shows two separate domains, with different carboxyl content, that are separated by thin intermediate layer. The figure was taken with permission from V. Freger, Langmuir 19, 4791-4797 (2003).

membrane was found to reach a maximum at pH 8.5 (see Table 1), that is suitable for seawater desalination (19). FT-30 has general applicability of pH range from 5 to 11, wide enough for seawater desalination processes. FT-30 membrane is approved by FDA for food contact use.

Commercial variations of metaphenylene trimesamide composite membranes (Scheme 2) apart from FT-30 are in use for brackish water (BW-30) or seawater conversion to potable water (SW-30), and for municipal tap-water purification (TW-30; see Table 1 for performance properties). The SW-30 membrane has 99.1% salt rejection in seawater operation at 54 atm. Another commercial variation, SW-30HR, has 99.4% salt rejection with lower flux (Table 1), and is increasingly used in seawater desalination plants requiring single-step operation at recoveries of up to 45% (produced potable water per incoming feedwater).

Characterization of aromatic polyamide TFC membranes

The surface of composite interfacial aromatic polyamide membranes has ridge-and-valley structure; the average thickness of the barrier layer in the metaphenylene trimesamide FT-30 membrane has been estimated to be 200 nm, with 40 nm at valley and 260 nm on ridge.

The composition of the barrier layer of FT-30 membrane in terms of carboxyl content in the formula of Scheme 2 has been estimated by ESCA studies to be $n = 0.72$. Freger (20) used transmission electron microscopy (TEM) combined with carboxyl- and amine-selective staining to confirm the presence of nanoscale structural features known by a theory of interfacial polymerization (see Fig. 3). The outer layer contained an excess of negatively charged carboxylic groups binding a cationic uranyl stain while an inner layer was free of carboxyls and showed binding of heavy anions, suggesting an excess of unreacted amine groups.

Fouling phenomena in membrane-based water processes

A major problem in membrane-based water technologies, particularly in non-porous thin-film composite membranes, is membrane fouling, that is the accumulation and formation of solids and gel-layers on the membrane surface, which causes flux decline and increase of operating pressure. Membrane fouling is dominated by a high concentration of a solute on the membrane surface, due to an effect named *concentration polarization* ((21); see Fig. 4), which is typical to many membrane-separation processes.

Different causes of fouling, which influence one another, include (a) precipitation of salts, mainly calcium salts (crystalline or inorganic fouling), (b) suspended solids

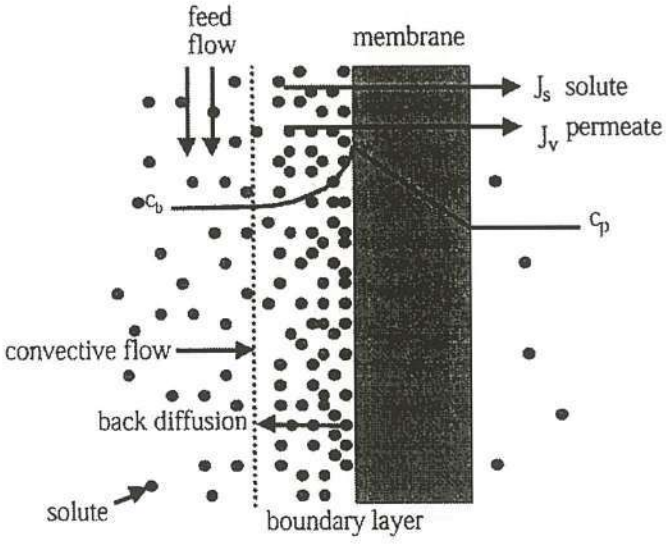
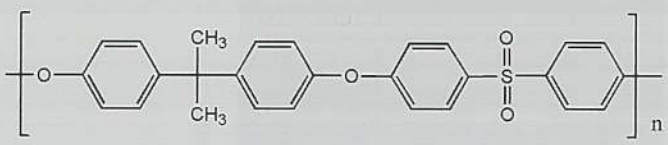


Figure 4: A schematic illustration of concentration polarization on the surface of a membrane and cross-flow operation. The figure was taken with permission from M. Wilf et al., Desalination 141, 269-289 (2001).

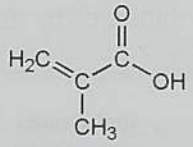
(particulate and colloidal fouling; 22), (c) dissolved organic matter (organic fouling; 23, 24) and (d) biofilm formation by microorganisms (microbial fouling, biofouling; 25-27). Organic fouling and microbial fouling are considered among the more difficult problems in the field because acid wash is not effective. Biofilm formation due to the accumulation and adhesion of microorganisms has additional difficulties: Pretreatment of the feed to limit biofouling is employed today in RO applications, but it is costly (requires additional equipment) and is not very efficient, since microorganisms multiply inside the module due to the continuous supply of nutrients in the feed water (26). Effective prevention of microbial growth on membranes is achieved only when a continuous, high chlorine concentration is maintained. However, chlorine generates harmful byproducts upon reaction with organic matter. In addition, most modern TFC membranes (aromatic polyamide) are sensitive to oxidizing agents, such as chlorine and ozone, and chlorination is therefore not a practical solution.



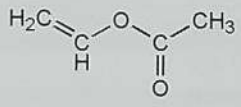
Polysulfone (1)

New approaches to biofouling control

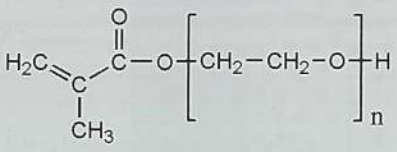
Extensive research efforts are devoted to the prevention of membrane biofouling. For example, in UF membranes, cellulose-based membranes, such as stabilized regenerated cellulose, are the state-of-the-art for low-fouling UF membranes. However, their low chemical stability and relatively low surface porosity are significant limitations. Blending of the membrane polymer (e.g., polyethersulfone) with a hydrophilic polymeric modifier might in some cases improve the fouling resistance (28). However, membrane manufacturing from a polymer blend will yield a different pore structure and hence different flux and selectivity. Surface modification of established commercial membranes, while preserving their chemical resistance and mechanical strength, is therefore of great interest for producing low fouling UF membranes. Two general strategies to reduce the fouling tendency by surface modification have been proposed: The first, introduction of charged groups to promote electrostatic repulsion. The second strategy is based on previous studies that correlated high surface wettability with low sorption of proteins and organic molecules (29). Thus,



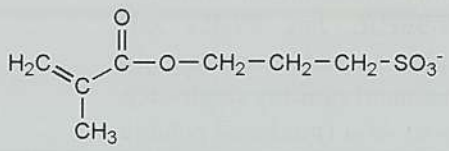
Methacrylic acid (MA)



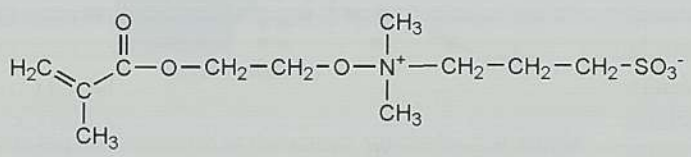
Vinyl acetate (VA)



PEG-MA



Sulfopropyl-methacrylate (SPM)



Sulfo-propyl ammonium-MA betaine (SPE)

Figure 5: Vinyl monomers that are being used in modification of membrane surfaces: Methacrylic acid (MA), polyethylene-glycol ester of methacrylic acid (PEGMA), sulfopropyl methacrylate (SPM), and SPE. Note that the resulting surface charge can be easily controlled by choosing an appropriate monomer.

attempts are made to increase the hydrophilic character of the membrane surface to make it less susceptible to organic fouling and biofouling (30). Numerous methods of initiation of graft polymerization have been used, such as ionizing radiation (31), oxidation by ozone (32) and low-temperature plasma (33). UV radiation is an attractive method (34-36) since it may be performed at mild reaction conditions, and high selectivity may be obtained by choosing well suited photo reactive groups with respective excitation wavelengths (36).

Fouling in composite membranes

In TFC membranes, the most commonly used membranes in desalination, backwash is not applicable therefore the cleaning is very difficult. The most commonly used membranes for seawater desalination, methaphenylene trimesamide TFC membrane (such as FT-30; see Scheme 2) are susceptible to binding and fouling by cationic surfactants because the membrane surface charge is mildly anionic due to partial hydrolysis of acyl halide groups to carboxylic acid groups during membrane preparation (see above).

A modification of the membrane surface to render it less susceptible for biofouling or organic fouling was applied also to TFC membranes. In some membranes, TiO_2 has been incorporated as a bactericidal agent into the aromatic polyamide film of RO membranes, either as a suspended powder (37) or as self-assembled nano-particles (38, 39). Many studies are focused on graft polymerization of ionic and nonionic vinyl monomers (as was described above for the UF membranes; for example methacrylic acid derivatives, Fig. 5) by a variety of methods: S. Belfer and her coworkers (Ben-Gurion University of the Negev, Israel) developed redox-initiated graft polymerization of hydrophilic monomers onto RO (40, 41) and NF membranes (42, 43) which has resulted in improved resistance to fouling without reducing membrane retentive properties (41, 44). In subsequent studies the researchers succeeded to perform graft polymerization of hydrophilic vinyl monomers onto NF membranes inside the membrane-pressure cell (45). NF membranes used for treating industrial and municipal wastewater were modified by numerous hydrophilic monomers such as MA, PEGMA, DMAEMA, SPM and HEMA (Fig. 5). Graft polymerization with PEGMA showed greatly reduced adsorption of certain organic compounds typical of paper mill streams. In tests on tertiary effluent from wastewater treatment plant (Shafdan plant, Rishon-Letzion, Israel) modification with hydroxy-ethyl ester of methacrylic acid lead to significantly reduced salt passage, especially of monovalent anions such as chloride.

New types of vinyl monomers are used for graft polymerization. Their chemical nature has a crucial effect on fouling resistance; Polyethylene glycol (PEG)-derivatives (PEGMA, Fig. 5) are well-known as nonfouling materials (46). However, PEG may be susceptible to oxidative degradation and chain cleavage in aqueous systems, and it looses its resistance to fouling above 35°C (47). Zwitterionic substances such as the ammonium-sulfo betaine SPE (Fig. 5) have been reported as a new family of nonfouling material and were used in UF membranes (48) as well as for modification of nonporous surfaces (47, 49).

Summary

The development of membranes capable of separating dissolved salts from water with high efficiency had two major breakthroughs: The first was development of Loeb-Sourirajan (L-S) anisotropic or asymmetric cellulose acetate membranes for seawater desalination. These membranes constituted the basis for modern membrane development in RO and UF. Within a few years, RO composites comprising a submicron coating of a selective film on an asymmetric UF support were developed. Progress in RO and UF technology gave birth to yet another discipline - NF.

In the search for improved water treatment economics and for other commercial applications, the limitations of CA as a membrane material were, however, quickly revealed. These limitations restricted the range of applications and impeded efforts to expand NF into new areas. One approach to overcoming this problem was the development of integrally skinned asymmetric membranes from materials other than CA, such as polyamides, polyethersulfone (PES), polysulfones, chlorinated polyvinyl chloride (PVC), and polvinylidene fluoride (PVDF). However, the selectivity/flux combination needed for seawater desalination, as well as other applications, could not be achieved. The breakthrough in RO and NF took place with the invention of non-cellulosic composites based on coating UF supports with a submicron selective barrier, mainly by interfacial polymerization.

Polyamide compositions dominate the field as barrier layers of RO and NF membranes. Initially, membranes

were prepared by reacting polymeric polyamine with a crosslinker molecule such as toluene diisocyanate or with isophthaloyl chloride, to yield the polyamide. Membranes prepared by reaction of piperazine with trimesoyl chloride created superior barrier layer in terms of flux and divalent-ion rejection, and were used for composite NF membranes. The most popular RO membrane for seawater desalination is meta-phenylene-tri-mesamide that affords high flux under seawater conditions and high salt rejection.

Membrane fouling is a major problem in RO and in NF applications, and numerous approached are taken to control it. Chemical modification of the membrane to render it less susceptible to fouling, especially to organic- and bio-fouling, is being investigated extensively. Many studies rely on the correlation between increased hydrophilic character of the membrane surface with less fouling. Hence, efforts are made to modify the membrane surface into more hydrophilic one, with minimal change of the transport properties of the membrane.

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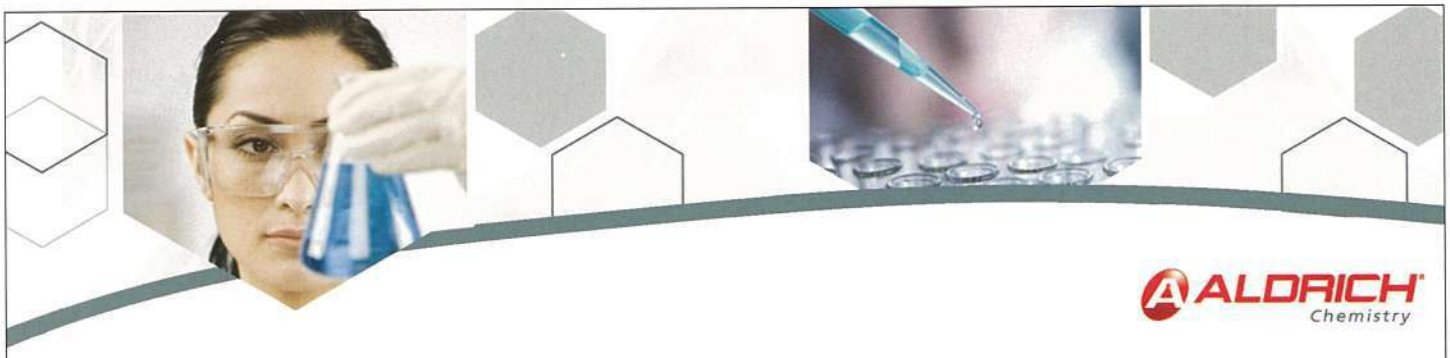

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Adventures in Stereochemistry and Cycloadditions

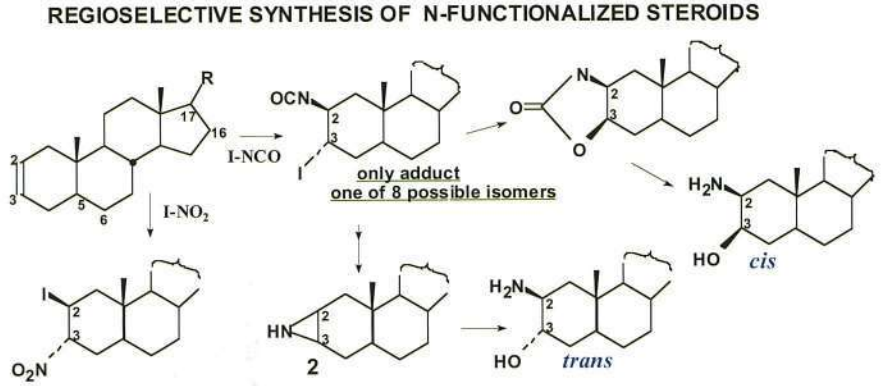
Alfred Hassner

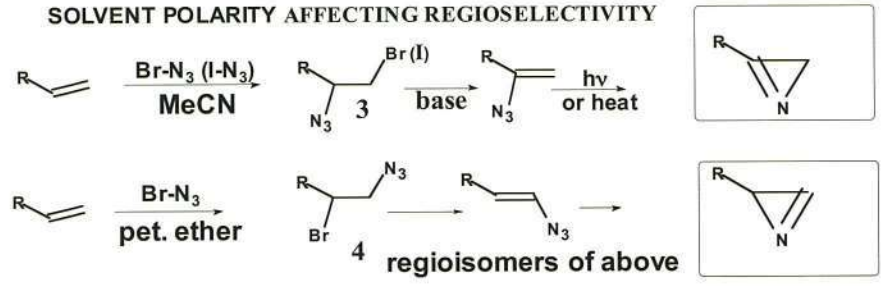
Prof. Alfred Hassner was born in 1930 in Czernowitz, Romania. After surviving the Shoah, he studied in Vienna and then at the Univ. of Nebraska where he received his Ph.D. under N.H.Cromwell in 1956. Following postdoctoral studies at Harvard with Louis Fieser, he joined the faculty at the University of Colorado, Boulder where he advanced to full professor in 1966. In 1975 he became Leading Professor at SUNY Binghamton and since 1983 has been on the faculty at Bar-Ilan University. Hassner was visiting professor at several universities including Univ. Wurzburg, Kyushu Inst. Technology, Univ. Claude Bernard Lyon, Weizmann Inst., Stanford Univ., Univ. California Berkeley. He is the recipient of many honors among them Senior Fulbright, von Humboldt, Lady Davis, Meyerhoff, National Cancer Institute Special Fellowships, A.W. Killam and 2007 Israel Chemical Society Prize. Prof. Hassner's research in organic synthesis, heterocyclic chemistry and stereoselectivity has been an inspiration to many, as has been his monograph on "Organic Syntheses Based on Name Reactions". He has been on the editorial board of several journals among them the Journal of Organic Chemistry, has chaired several symposia including Gordon Research Conferences and was an invited plenary lecturer at many international symposia.

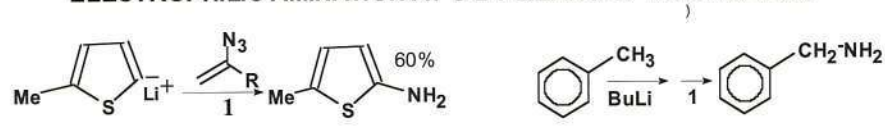
An early interest in steroids led us to investigate the synthesis of steroidal heterocycles, for instance steroidal aziridines, oxazolines, quinolines, indoles which may possess interesting pharmacological properties. To this end we examined the introduction of N-functional groups into steroids. This led to the synthesis of D-norprogesterone[1] and to studies of oxime rearrangements reactions,[2] as well as later to unraveling the mechanism of sugar osazone formation[3], interestingly by using steroids as substrates, where intermediates could be isolated.

In connection with our N-functional group studies, we had become interested in the synthetically versatile, yet potentially explosive, azide functionality. Azides, which due to their dipolar character (see **1**) can act either as nucleophiles or as electrophiles, remained a love affair in our research[4] that later led to stereochemical investigations of dipolar cycloaddition reactions of unsaturated substrates, not only with azides (see IAOC below)[5] but also with nitrile oxides, nitronates, oximes.

Since azide ions react sluggishly in substitution reactions, we prepared from Amberlyte a polymeric azide,[5a] stable to the hammer test and useful for azide substitution reactions at room temperature (r.t.). In fact, as an indication that we lived dangerously, this stable ionic azide allowed us to prepare the highly explosive







triazidomethane $CH(N_3)_3$ from $CHBr_3$. By studying the addition to steroidal olefins of IN_3, as well as of INCO, prepared in situ, we discovered a general stereospecific formation of aziridines (**2**) and of cis as well as trans amino alcohols.[6] Steroidal 2,3-, 5,6- and 16,17-olefins turned out to be useful substrates in the study of stereochemistry of pseudohalogen additions like IN_3, BrN_3, ClN3, INCO, INCS, $ClSO_2NCO$, $PhSeN_3$, NOCl, INO_2, INO_3. Notice below the different regiochemistry for INCO and INO_2 additions.

Unable to describe effectively the preferential formation of what we finally called regioisomers, and after many evening sessions with my research group, we conceived of the now universally accepted concept of regioselectivity.[7] This concept, independent of mechanism and derived from the latin REGIO = direction, now celebrates its 40th anniversary and is a good example of the proverb "necessity is the mother of invention".

Furthermore, structural determinations of our functionalized steroids led us to propose NMR as a stereochemical tool[8] for axial vs equatorial group assignments, before high resolution NMR became available.

Perfect examples of application of regioselectivity are our findings that BrN3 adds to olefins, e.g. 1-hexene, in MeCN to afford exclusively one regioisomer (**3**) while the same reaction in hexane produced a different regioisomer (**4**).[9] These textbook examples (Morrison and Boyd), which highlight the effect of solvent polarity, we explained in one case by a bromonium (or iodonium) ion intermediate, while the second regioisomer **4** was the result of a free radical reaction (by N_3 radical), favored in the nonpolar solvent. Each of these regiosiomers in turn on HBr elimination

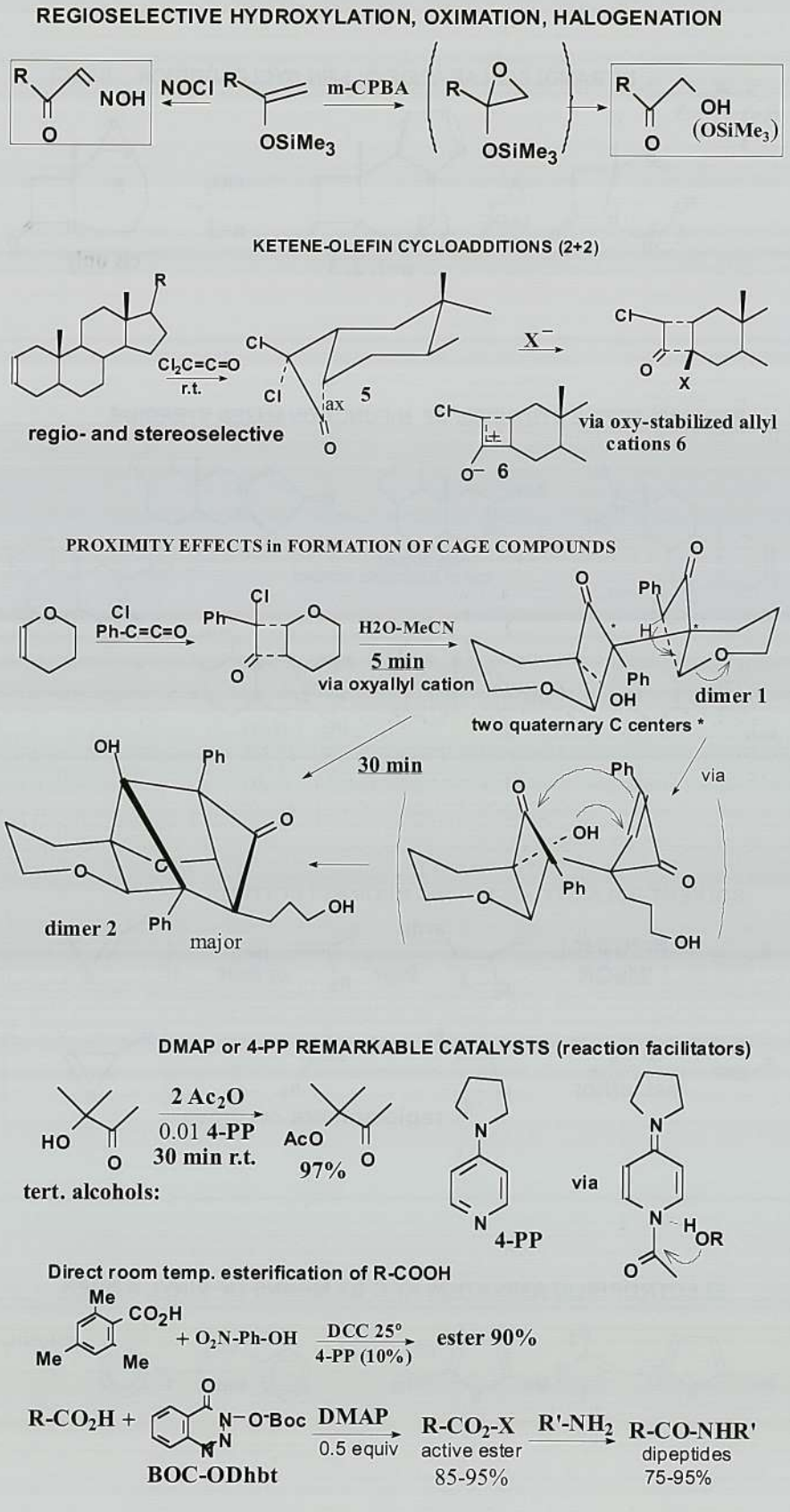
lead to different regioisomeric vinyl azides and from there to different regiosiomeric azirines.[10]

These studies provided us with a general method[11] of synthesis of aziridines and azirines (often referred to as the Hassner reaction), as well as of azetidines (the latter derived from cyclopropyl azides)[12], and from there to a great variety of interesting heterocycles,[13] like 7-ring azepines, diazepines, N-bicyclics etc. Furthermore, vinyl azides proved to be not only useful intermediates in synthesis of new heterocycles but they also were novel electrophilic aminating species (see above) of aromatic and heteroaromatic carbanions (via vinyltriazines).[14] This new electrophilic C-N bond formation, was later supplemented by our discovery of the first electrophilic O-amination of alcohols.[15]

We also succeeded in preparing the first steroidal quinolines, indoles and indoxyls, the latter of which allowed us to decipher an unusual rearrangement involving a novel intramolecular attack of enolates on a nitro group.[16]

Inspired by Herb Brown's hydroboration discovery, we examined but were scooped on the synthesis of amines by hydroboration but did obtain useful results on hydroboration of steroidal olefins, of enol acetates,[17] of acetylenes, of silylacetylenes[17] leading to silaketones and of oxime derivatives.

Our realization of the synthetic and mechanistic importance of 3-membered ring iodonium and bromonium ion intermediates led us to interesting stereochemical and regiochemical studies including rearrangements, the utility of nitrilium ions and a new approach to isoquinolines.[18] Stereoselective opening of 3-membered rings was also examined for aziridines and epoxides, including α-acetoxy- and α-haloepoxides. We were able to



achieve regioselective α-hydroxylation of ketones (Rubottom-Hassner reaction) via epoxidation of silyl enol ethers;[19] furthermore silyl enol ethers also led to a useful synthesis of α-oximino or of α-halo ketones.[19]

Our interest in synthesis of N - phosphorylated aziridines,[20] and oxazaphospholines later led us to formation of phosphorylated cyclopentanes[20] via allyl sulfones (see below).

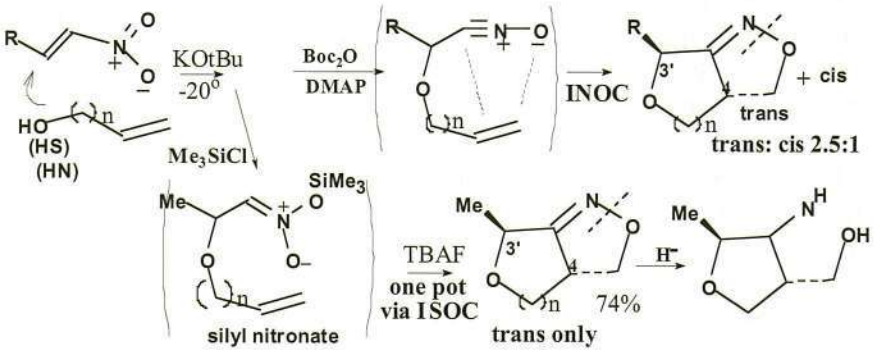
Our study of ketene cycloaddition to azirines, imines, enamines and vinyl azides led us to examine the stereochemistry and regiochemistry of 2+2 cycloadditions of ketenes to olefins including silyl enol ethers[21]. Little was known about stereoelectronic effects influencing these reactions and we were able to formulate a preferential axial approach in a non-parallel transition state by the ketene C=O electrophile to 6-membered ring olefins; furthermore, we described the importance of steric effects operating in these reactions.[22]

Fused α-halo-cyclobutanones (e.g.**5**), resulting from haloketene additions to 2-cholestene and to other cycloalkenes, led to rearrangements that opened up a fruitful inquiry into facile formation of oxyallyl cations **6** and their reaction with nucleophiles.[23] In the case of cycloadditions of chloroketenes to cyclic enol ethers, like dihydropyrans, we discovered novel dimeric products.[24] We were able to unravel the mechanism of formation of such compounds as **dimer 1** and **dimer 2** resulting from unusual proximity effects.[24]

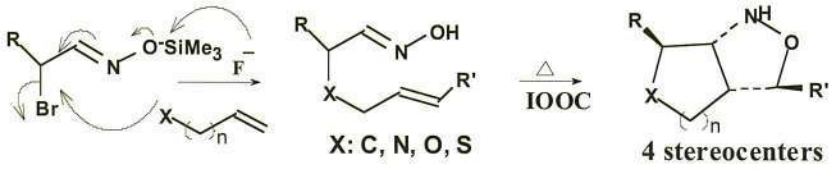
Our interest in silyl derivatives became the object of a study leading to α-silaketones, vinyl silanes as well as metallacycloalkanones.[25]

Among the systems that we investigated were also highly conjugated pyridine derivatives, which in collaboration with Prof. Loew, proved to be very

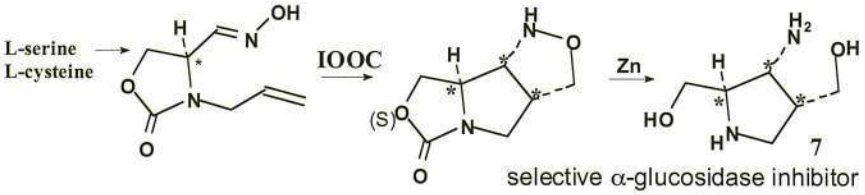
SYNTHESIS of SUBSTITUTED 5- and 6-RINGS via INOC or ISOC



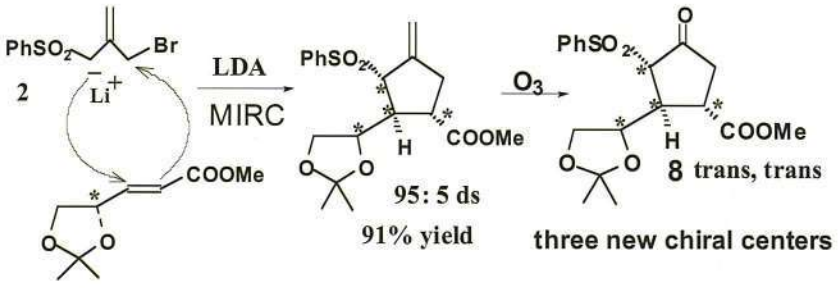
FUNCTIONALIZED CARBOCYCLES and HETEROCYCLES via IOOC



SYNTHESIS of CHIRAL AZASUGARS as GLYCOSIDASE INHIBITORS



MIRC in SYNTHESIS of OPTICALLY ACTIVE CYCLOPENTANONES 8

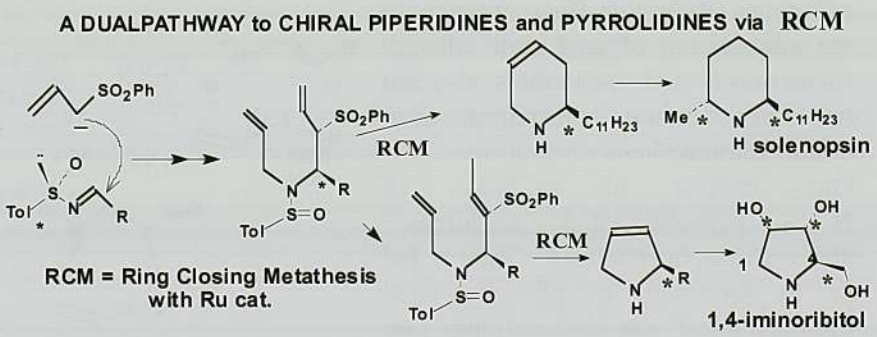


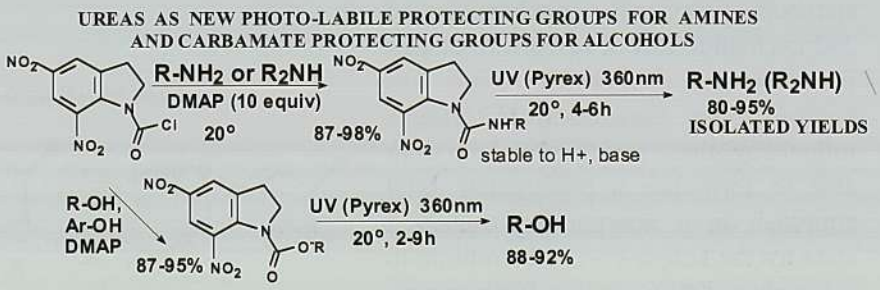
useful electrochromic probes of membrane potential.[26] At that point our interest in 4-dialkylaminopyridines was developed and we showed how DMAP (4-dimethylaminopyridine), 4-pyrrolidino- (4-PP) and 4-guanidinopyridine can accelerate r.t. esterification even of hindered carboxylic acids or of alcohols by as much as 10,000 fold.[27] These studies later branched out into a most effective synthesis of nitrile oxides from nitro compounds utilizing DMAP and Boc_2O, as well as other utilizations of these reagents.[28] In addition the duo, DMAP and Boc_2O together with a benzotriazine, provided us with a new amide coupling as well as peptide coupling system.[29]

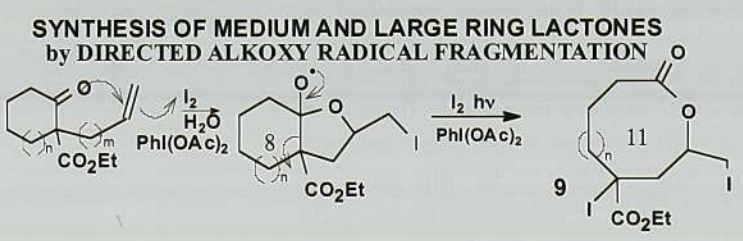
Our infatuation with azides also led us to examine not only their intramolecular cycloadditions with alkenes (see IAOC above) but also intramolecular nitrile oxide-olefin cycloadditions (INOC) or the even more stereoselective intramolecular silyl nitronate-olefin cycloadditions (ISOC).[30]

These studies led to the discovery of highly stereoselective IOOC (intramolecular oxime - olefin cycloadditions) that provided formation of functionalized 5- and 6-membered carbocycles and heterocycles with an introduction in one step of as many as 4 stereo centers.[31] These reactions also have led to active glycosidase inhibitors like 7.[32] Other investigations comprised the chemistry of oxazoles including their intramolecular Diels - Alder cycloadditions, that led to novel heterocyclic systems.[33]

Another fruitful exploration for us has been in the area 3+2 cycloadditions of sulfone carbanions to unsaturated substrates. Employing the lithio derivative of a bromoallyl sulfone as a trimethylene-methane equivalent, we were able to realize the synthesis of stereo- and regioselectively







functionalized methylenecyclopentanes.[34] These MIRC (Michael initiated ring closures) reactions, using a chiral auxiliary, provided us with trisubstituted enantiomerically pure cyclopentanones, e.g. **8**.

Furthermore by applying simple sulfone carbanion chemistry in additions to optically active sulfinimines, we were able to synthesize chiral non-racemic pyrrolidines, or piperidine alkaloids by RCM.[35] Sulfone carbanion additions also provided a synthesis of chiral cyclohexane derivatives.[35]

Recently, we introduced an efficient photo-labile protecting group for amines in the form of urea derivatives. Such a protecting group is also applicable to alcohols and phenols.[36]

Returning recently to free radical vs ionic additions of iodine species, as well as to ring expansions[37], we were successful in obtaining n+3 and n+4 ring enlargements of cyclic ketones to medium size or large ring lactones (e.g. **9**) by directed alkoxy radical fragmentation.[38]

Finally, I wish to thank all my former co-workers, students and postdocs, both in Israel and in the USA who made this report possible. I must apologize that due to space restriction only a fraction of the over 300 publications resulting from their research can be mentioned here.

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Ion Mobility Spectrometry: A tool in the war against terror

Zeev Karpas

Zeev Karpas. Received his Ph. D. in 1976 (Weizmann Institute of Science, Rehovot, Israel) after which he spent two years as a post-doc Research Fellow at CalTech and JPL (Pasadena, California). In 1978 he joined the Nuclear Research Centre, Negev (Beer-Sheva, Israel) and eventually served as Head of the Analytical Chemistry Department (1989-92). In 1984-85 he spent a sabbatical at the National Bureau of Standards in Gaithersburg, Maryland and another sabbatical at New Mexico State University (1992-93). He co-authored with Prof. Gary Eiceman, the monograph entitles Ion Mobility Spectrometry (CRC Press, 1993 and a Second Edition in 2005). Since 1994 he has been involved in trace-analysis by ICPMS and radio-toxicological research. He is co-founder of Q-Scent Ltd. an Israeli company involved in development of diagnostic applications for IMS. Dr. Karpas has interest mainly in the technology and science of IMS and toxicological and environmental applications of laser-ablation and ICPMS.

Abstract

Ion mobility spectrometry (IMS) is a sensitive analytical technique that is used for detection, identification and monitoring of chemicals, mainly explosives, highly toxic gases and drug interdiction. Vapors of these compounds are ionized according to atmospheric pressure chemical ionization processes and then the ions are separated on the basis of their mobility in an electric field. A brief overview of the principle of operation of mobility spectrometers and applications in the war against terror is presented here.

Introduction

How many times was your hand luggage tested for the presence of explosives, while you were watching, after passing through a metal detector and X-ray machine? This would happen especially if you were carrying a laptop computer or other electronics equipment that looks quite opaque in the X-ray image. The luggage you deposited at the check-in counter may have been similarly examined while you were going through passport control, drinking coffee or shopping at the duty-free stores. Most probably, screening for explosives was carried out by a device called an ion mobility spectrometer (IMS) that can pick up minute traces of explosives and identify their specific signature. You may have also seen emergency teams or troops dressed in protective gear and wearing gas masks approaching an area where hazardous chemicals, particularly chemical warfare agents (CWAs), may be present while holding in their gloved hand something that looks like a cell phone or a funny clothes iron. This too could well be a hand-held IMS device set up for detection and identification of toxic gases or vapors. How does this device work and what gives it its high sensitivity and specificity? In the following sections the principle of operation and some applications of mobility spectrometry in the war against terror will be discussed. A comprehensive description of mobility spectrometry, the science, technology and applications was published in a monograph a few years ago[1] and the technology was very recently reviewed[2]. Special emphasis on applications of ion mobility spectrometry for homeland security was also discussed in detail[3].

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Description of the Technique

Principle of operation and design of mobility spectrometers

There are several designs of mobility spectrometers[1], but here we will focus on the two main types: low electric field linear ion mobility spectrometers (IMS) and differential mobility spectrometers (DMS).

A swarm of ions moving through a bath gas (usually air at atmospheric pressure) under the influence of a low strength electric field obtains a certain velocity (mobility). The mobility, K, depends on the strength of the electric field, the bath gas (drift gas) pressure and temperature and on characteristics of the ion (mass, charge and shape) and its interaction with the drift gas molecules, as shown in Equation (1):

$$(1) \quad K = [3 \cdot e \cdot (2 \cdot \pi)^{1/2} (1+\alpha)] / [16 \cdot N \cdot (\mu . k . T_{eff})^{1/2} \cdot \Omega_D \cdot (T_{eff})]$$

Where e is the charge of an electron, α is a correction factor (usually below 0.02 under low electric field conditions), N is the number density of the neutral drift gas molecules, μ is the reduced mass of the ion mass (m) and drift gas (M) molecules [μ=m*M/(m+M)], k is the Boltzmann constant, T_{eff} is the effective temperature of the ion and Ω_D is the effective cross section for collision of the ion with the drift gas molecules. In practice, a simplified formula is used for calculation the mobility at standard temperature (273 K) and pressure (760 torr) conditions, called the reduced mobility, K_0, shown in Equation (2):

$$(2) \quad K_0 = K \cdot (273/T) \cdot (P/760)$$

Where T and P represent the temperature and pressure of the drift gas. The mobility is expressed in units of $cm^2\ V^{-1}\ sec^{-1}$. The time required for an ion to traverse a given distance is inversely proportional to its reduced mobility. Thus, it is common practice to use a reference compound with known reduced mobility, K_{ref}, to calibrate the mobility scale, as the ratio between the measured drift time of the reference ion, t_{ref}, and that of the analyte ion, t_a, is inversely proportional to the reduced mobility ratio:

$$(3) \quad K_a/t_a = K_{ref}/t_{ref} \quad \text{or} \quad K_a = (K_{ref} \cdot t_a)/t_{ref}$$

The design of an ion mobility spectrometer is very simple as shown in the schematic (Figure 1). Vapors of the sample are introduced into a tube that comprises an ionization sector, where some of the vapors are ionized, and a drift sector, where ions are separated according to the time that is required to reach a detector plate that depends on their mobility (drift velocity). A pulsed electronic shutter separates the two sectors and allows a discrete package of ions to enter the drift sector. Ions with high mobility, generally small ions, travel faster than large ions and cover the distance between the shutter and detector in a shorter time. The mobility spectrum (Figure 2) depicts the ion current measured at the detector plate as a function of time.

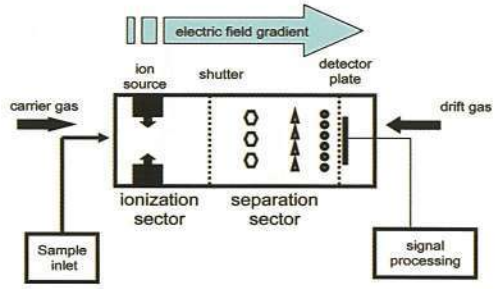

Figure 1: Schematic diagram of a linear ion mobility spectrometer. Molecules are carried from the sample inlet into the ionization sector where ions are produced. The ions drift under the influence of the electric field and a package of ions passes through the shutter into the separation region. Small ions (circles), travel faster than heavier ions (triangles and hexagons) until they reach a detector plate and the signal is processed.

The common ionization sources are radio-active beta emission (^{63}Ni is the most popular such source), corona discharge and photo-ionization. The description presented above pertains to the classic, linear ion mobility spectrometer where a relatively low electric field (~250 V cm^{-1}) is used to transport the ions along a drift tube.

During the last 15 years the concept of differential mobility spectrometry (DMS), also known as field asymmetric ion mobility spectrometry (FAIMS), was developed, and is gaining popularity among practitioners of mobility measurements. Ions that are carried by a stream of air through a strong perpendicular electric field are displaced by the field at a velocity, $v_\perp$, that is proportional to the field strength, E(t) and the field dependent mobility of the ion, K(E):

$$(4) \quad v_\perp = K(E) \cdot E(t)$$

If the strength of the electric field is changed periodically by an asymmetric rectangular shaped waveform, between for example 20,000 V cm^{-1} to 1000 V cm^{-1}, the motion of the ions would follow the waveform, as shown schematically in Figure 3.

The mobility of a given ion under high field conditions would differ from its mobility under low field conditions

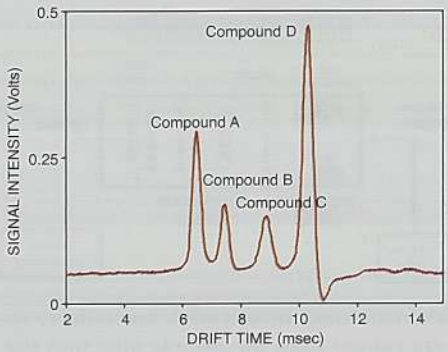

Figure 2. Typical mobility spectrum: Three amines (Compounds A, B and C) in the presence of a reactant ion (Compound D).

and different ions would be affected and displaced to a different extent. Thus, under given conditions only ions with the appropriate mobility would pass through the plates and reach the detector. A mobility spectrum is obtained by sweeping the compensation voltage setting on one of the plates. More details about DMS and its applications may be found in a recent review[5] and the principle of operation of such a device was recently mathematically modeled[6]. The main advantages of DMS compared with IMS are the possibility of miniaturization and of using micro-fabrication techniques for less expensive production of sensors.

Gas-phase ion chemistry underlying ion mobility measurements

The ionization processes that take place under the conditions of atmospheric pressure chemical ionization (APCI) are quite complex and can not be discussed here, but the end result is that a relatively small number of different ions emerge once these processes are completed. If positive ions are considered, these would usually be protonated species of the compounds with the highest proton affinities (PA) that are present in the ionization sector. In clean air these would be mainly clusters of protonated water molecules, $(H_2O)_nH^+$, where n is the number of water molecules in the cluster and depends mainly on the humidity and temperature. If negative ions are considered then the compounds with the highest electro-negativity (EN) would be preferentially ionized. In clean air the dominant ions would be $O_2^-(H_2O)_n$ where n is the same as described above. Under atmospheric pressure conditions, ions may also be formed through more complex reaction mechanisms, like association of an ion onto a molecule (ion attachment), exchange of a one clustered molecule on the ion by another (substitution), formation of clustered ions, etc. The ion formation processes will depend on the chemical environment (mainly humidity), residence time in the ionization sector, concentration of the compounds present, as well as external factors like the temperature and electric field strength.

The identification of the compounds from which ions are formed is based on the measured reduced mobility, calculated from the observed drift time that is compared with a reference compound. This is similar to using the retention time for compound identification in gas-chromatography (GC). However, mobility spectrometry has a lower resolution than GC, but knowledge and control of the gas-phase ion chemistry can greatly reduce the number of possible hits, making mobility spectrometry a viable method for detection and identification of a suite of analytes.

Thus, even in a very complex mixture, like that obtained when ambient air is sampled, the available charge from the ionization source would be concentrated on a few type of ion species. By controlling the ion chemistry, sometimes through addition of reagent compounds in the ionization sector, and by selection of analytes that either have a high PA or EN one can obtain the best performance from the technique. This is the reason underlying the high sensitivity and selectivity of mobility spectrometers.

Counter-Terror Applications

Detection and identification of explosives

Most commercial explosives have several nitro groups and relatively low vapor pressures. There are several

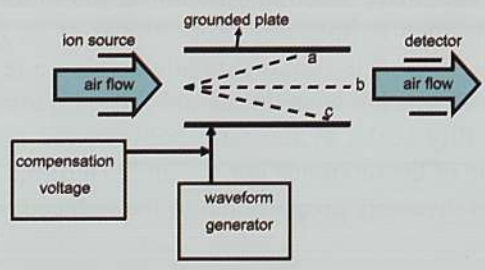

Figure 3: Schematic diagram of a differential mobility spectrometer. Ions are carried by a stream of air from the ion source into the space between two plates. A waveform with alternating high (20 kV/cm) and low (1 kV/cm) electric fields is applied to one plate and the other plate is grounded. Ion a is pushed toward the upper plate, ion c toward the bottom plate, while ion b passes through and reaches the detector. By changing the compensation voltage, different ions (a or c) will reach the detector.

explosives, mainly improvised explosive devices (IED) that do not conform with this, like the organic peroxides that do not have nitro groups but may have high vapor pressures and inorganic compounds like perchlorates that do not contain nitro groups and have a low vapor pressure. Detection of such compounds requires non-standard techniques and operating conditions, so adaptation of the sensor is necessary.

Presence of nitro groups renders the compounds highly electro-negative thus making them suitable for detection by mobility spectrometers operating in the negative ion mode. Negative ions may be formed in the ionization sector directly by electron capture (5a) or by dissociative electron capture (5b).

(5a) $M + X^-(Z) \rightarrow [MX]^- + (Z)$

(5b) $M + e^-(Z) \rightarrow [M\text{-}H]^- + H(Z)$

However, negative ion attachment or association (6) is frequently the dominant mechanism for ionization of explosives under atmospheric ionization conditions, and is often enhanced by intentional addition of a reagent that will produce the appropriate reactant ion (as shown in Figure 2, above).

(6) $M + X^-(Z) \rightarrow [MX]^- + (Z)$

Where Z is a neutral molecule that does not participate directly in the reactions (third body) and X^- is an ion like Cl^-, NO_2^-, Br^-, NO_3^-. Sometimes several negative ions from the explosive compounds and their adduct ions may be observed simultaneously in the mobility spectrum.

Positive ions originating from explosive compounds may also be formed under APCI conditions, but usually with lower efficiencies and with more interference from other chemicals present in the sample. For explosive compounds that do not contain electronegative groups, like the peroxide molecules, detection in the positive ion mode may be preferable, especially if they tend to form adduct ions with suitable reagents. For example, there have been reports[7] that triacetone triperoxide (TATP), a favorite improvised explosive among terrorists due the ease of its production, can be detected by IMS as it may form an adduct ion with ammonium ions[8] (NH_4^+).

Low vapor pressure implies that sampling ambient air ("sniffing") for vapors of the explosive compound would not be effective, and other techniques are needed to transport enough molecules from the suspect object to the sensor. The common practice is to swipe the surface of the suspect object mechanically with a piece of cloth or filter material, insert the sample into a small oven at the front end of the sensor, and after rapid heating the vapors are carried directly into the ionization sector. The sensitivity of mobility sensors is such that the presence of sub-nanogram quantities of explosives on the swipe is sufficient for detection within a few seconds.

Figure 4: Ionscan Sentinel II, Commercialized Version of Explosives Detection Personnel Portal with IMS Detection, developed by Smiths Detection and Sandia National Laboratories. (Photo by Sandia National Laboratories – used with permission).

A different approach is needed for non-intrusive and non-invasive screening of people entering a controlled area. The idea of using portals for explosive detection, similar to magnetometer portals for metal detection, is being actively pursued by the major manufacturers of mobility sensors (Figure 4).

When a person enters the portal pulsed streams of air are used to detach minute particles from the person's body (mainly hands and head) and clothing. These are carried to a fine metal filter that serves as a preconcentrator for collection of the particles. Rapidly heating the filter releases vapors that are carried to the sensor and the presence of explosives would be detected by the mobility spectrometer. The whole process lasts just a few seconds for sampling, preconcentration, desorption and detection.

Detection and identification of chemical and biological warfare agents

Although chemical warfare agents (CWAs) have not yet been used by terrorists (with the exception of the 1995 sarin gas attack in Japan), an increase in the state of preparedness and awareness is called for. Future trends would probably see widespread application of sensors for CWA detection in places where large crowds are present and a central air supply and air conditioning is used like train stations, airports, shopping malls, stadiums and possibly even office buildings and such places.

CWAs are generally divided into two groups: nerve

agents that are usually derivatives of organo-phosphorus compounds, and blister agents that usually contain chlorinated sulfur or arsenic derivatives. Under APCI conditions the former tend to form stable positive ions while the latter group may form negative ions. The sensor should therefore be able to rapidly respond to both types of threats and be able to switch between positive and negative ion modes or measure both simultaneously.

There are two main types of IMS based sensors for CWAs: the handheld detectors that are used mainly for inspection of objects for traces of CWAs, either as a precaution or after decontamination has been carried out, and fixed point monitors that serve as alarms in case of a CWA attack. IMS based technology combined with gas-chromatography, has also been used for on-site screening of CWA degradation products[9]. IMS sensors can also be mounted on an unmanned aerial vehicle (UAV) or drone to monitor the air above strategic positions or troops and give an early warning[10].

Application of mobility spectrometry for detection of biological warfare agents (BWAs) has also been studied, mainly by the US Army[11] and other research groups[12]. The combination of an ion mobility spectrometer with a pyrolysis fast gas chromatograph has been described as a potential detection system.

Summary

Going through Newark airport, on the way to the annual meeting of the International Society for Ion Mobility Spectrometry (ISIMS), I saw a red screen flashing and heard an audible alarm coming from one of the IMS instruments that had supposedly detected traces of explosives on the laptop of a passenger. The passenger was then asked to open his hand luggage and take out all items. Every single item he handled that was swiped and tested also gave an explosives alarm. After calling the supervisor, several repeated tests and a brief interrogation; the passenger was allowed to continue his travel. I approached him and asked if he used any medication (like nitroglycerine for a heart condition) that could be responsible for the false alarm. He mentioned that he traveled several times a month and never had any problems, but then recalled that he had just changed the hand lotion he used for a persistent skin condition. I asked him to show me the new lotion and saw that one of the ingredients was a chloro-anisole compound that could well be responsible for the false alarm. Though inconvenient and even embarrassing, it is better to delay several innocent passengers for a short while than to miss one bomb. We expect to see more counter-terrorism applications for ion mobility spectrometry in the future for explosive detection, through extensive use of portals, improved luggage screening techniques and use of spot checks to monitor people and controlled areas. We should also expect to see pocket size miniature detectors of chemicals warfare agents widely distributed to soldiers or first responder personnel to give a timely and sensitive alert as well as sensors mounted on drones flying ahead and above armed forces. Another future trend will be monitoring of central air supplies in buildings and crowded areas for chemical and biological warfare agents.

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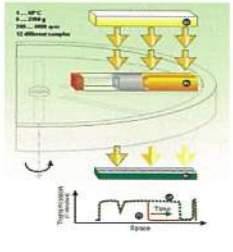

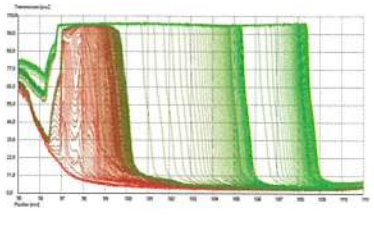

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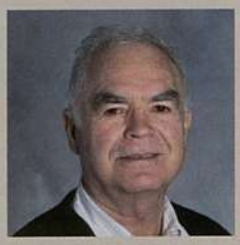
Pathways of Chemical Processes in Solids by Dynamic NMR. The case of the Cope rearrangement in bullvalene

Zeev Luz



Professor Zeev Luz was born in Munich, Germany in 1932, emigrated to Israel (then Palestine) in 1934, grew up in Binyamina, (1935/50), graduated from the Agricultural High School in Pardess-Hanna (1950). After military service (1950/52) he studied Chemistry (M.Sc.) in the Hebrew University, Jerusalem (1952/57) and did his Ph.D. in the Weizmann Instititue (1957/61). At the same time (57/61) he also served as as Chemistry and Physics teacher in his Alma Mater. After a postdoctoral period at the Bell Telephone Laboratories, Murray-Hill, N. J. (1961/64) he joined the Scientific stuff of the Weizmann Institute (1964 –) and became Professor Emeritus after retirement (1997). During this period he served as Chairman of the Chemistry Teaching Committee of the Feinberg Graduate School (1973/76), Dean of the Chemistry Faculty (1978/85), Vice president for Academic Affairs (1985/88) and Chirman of the Scientific Council (1992/94). He spent long-term periods at Oxford University (1966/67), Bell Laboratories, Murray-Hill (1971/72), University of California, Berkeley (1976/77), Experimental Station, E. I. Du-Pont, Wilmington De (1984/85), the MPI for Polymer Research, Mainz, (1990/91) and the MPI for medical research, Heidelberg, (1996). He received the Somech-Sachs award (WIS, 1961, with B. L. Silver), Koltoff award (Technion 1979), Friedenberg award (Bank Leumi 1986), Lisa Meitner – Alexander von Humboldt award (1994), Weizmann Prize (Tel-Aviv Municipality 1999), Rothschild Prize (2000), Doctor of Philosophy honoris causa (Faculty of Chemistry, Stockholm University 2004), elected Fellow of ISMAR (2008) and awarded the 2008 ICS Medal. He is married to Abigail. They have four children.

During the opening ceremony of the 74th Israel Chemical Society (ICS) meeting I was awarded the 2008 ICS Medal for "... using magnetic resonance to unravel molecular dynamics and chemical exchange in liquids, liquid crystals and solids". I am proud to have been chosen although I am well aware that many of my colleagues are much more worthy of the recognition than I.

The first paper which I co-authored as a graduate student was published 52 years ago.[1] I was assigned to help David Gil to prepare aqueous samples at different pH's. It turned out that the proton transverse relaxation rate in aqueous solutions was pH dependent, being slightly faster in neutral water than in higher or lower pH's. The phenomenon was interpreted in terms of exchange between hydrogen bonded and non-H-bonded water molecules. The paper became a citation classic because it contained a very useful equation for the NMR linewidth in the fast exchange regime. Needless to say, I had nothing to do with the derivation of the equation neither with the interpretation of the effect.

When I was a post-doc with Saul Meiboom at Bell Laboratories I extended the earlier work of Aaron Loewenstein on the protolysis reaction in aqueous solutions of methylamines. Before leaving for a conference Meiboom mentioned to me a dispersion effect which he had discovered, namely that in the CPMG experiment, in the fast exchange regime, the effective T_2 should depend on the pulse repetition rate in the range where the latter is of the order of the exchange rate. When he returned

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from the conference I presented him with nice results of dispersion experiments performed on my aqueous trimethyl ammonium solutions. We described the result in a paper submitted to the Journal of Chemical Physics, with Meiboom's derivation of the dispersion equation in an Appendix.[2] This paper too became a citation classic, not because of my protolysis measurements, but because of Meiboom's dispersion method, which had become increasingly popular throughout the years.

Receiving undeserved credit would repeat itself throughout my career. I worked with many senior associates and never managed to fit in their shoes, and my junior associates and students in the academia surpassed me many folds. At the Weizmann Institute I had the fortune of bridging between the early and present-days generations of superb scientists in the field of magnetic resonance. My own research during this period mostly involved topics related to what is commonly referred to as dynamic NMR.

The effect of dynamic processes on magnetic resonance spectra not only serves as a unique tool for studying their rates and mechanisms, but it also provides a means for developing methodologies and for demonstrating general principles related to magnetic resonance spectroscopy. As recipient of the ICS Medal I was invited by the Editor of *this Journal* to contribute a short article related to my own work. I choose to briefly describe our work on the Cope rearrangement in solid bullvalene. I do so in tribute to the late Professor Gerhard Schmidt, who for many years advocated the importance of dynamic processes in the solid phase. Such processes involve, besides the electronic and nuclear redistribution, also space requirements to allow this to occur under the stringent environment of the packed crystalline state. The bullvalene case provides an excellent example for demonstrating the complexity of such problems and of the power of NMR to decipher them. I think that Gerhard Schmidt would have enjoyed the work. I limit the list of references to papers actually mentioned in the text. For details and a more general background the papers cited in these references should be consulted.

The Cope rearrangement in solid bullvalene

The Cope rearrangement in bullvalene is one of the more interesting examples of valence bond tautomerism (Fig. 1a). It will be noticed that a single rearrangement results in an effective near-inversion of the molecule, an effect which does not perturb the statistical distribution of the molecular orientation in solutions. The spatial symmetry of the molecule renders the process highly degenerate leading to 10!/3=1209600 tautomers, which in principle could be distinguished by NMR, where there sufficient stable carbon and hydrogen magnetic isotopes.

In the solid state, bullvalene forms well ordered crystals

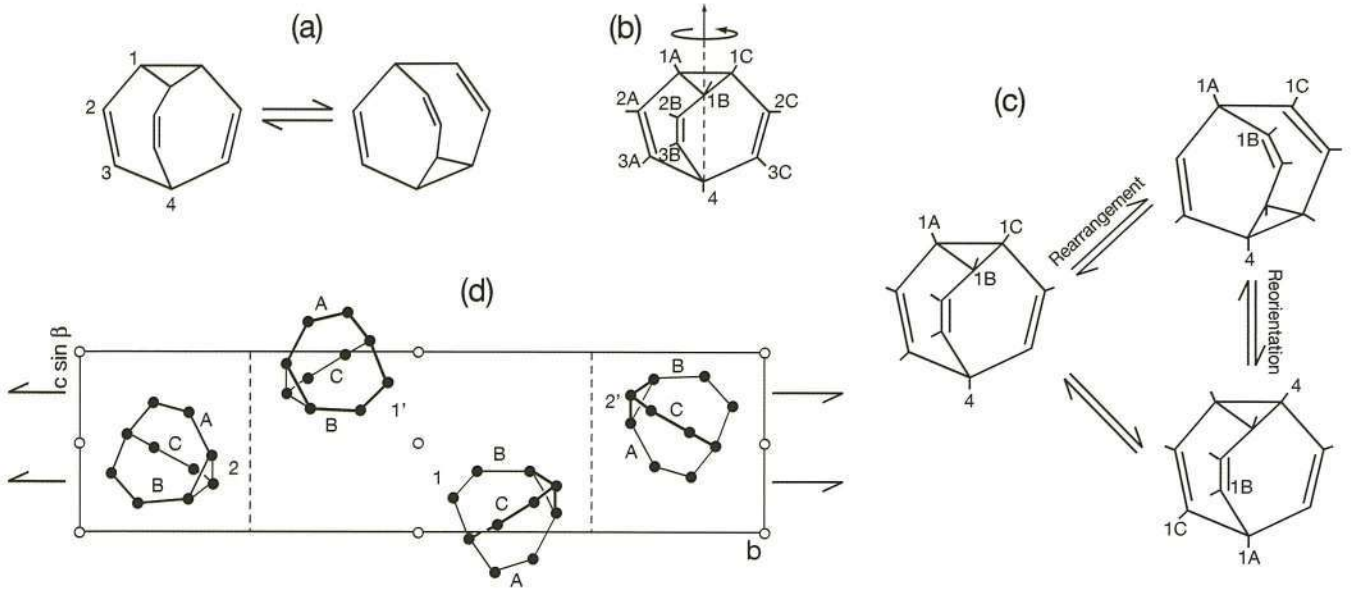

Figure 1. (a) The Cope rearrangement of bullvalene. (b) The 3-fold jump process in crystalline bullvalene. (c) The Cope rearrangement/reorientation process in crystalline bullvaleene. (d) The crystal structure of bullvalene. The numbers 1, 2, 3, 4, label chemical types of C-H (C-D) groups, while the letters A, B, C, label the three wings of the bullvalene molecule.

(monoclinic group $P2_1/c$) with four molecules per unit cell (Fig. 1d). The possibility of the Cope rearrangement taking place in solid bullvalene was therefore largely dismissed because such a process was thought to lead to disorder in the crystal. It thus came as a surprise when in 1985 Meier and Earl[3] observed in the ^{13}C magic angle spinning (MAS) NMR spectrum of solid bullvalene dynamic effects that could only be interpreted in terms of the Cope rearrangement. They proposed that the reaction involves a combined rearrangement/reorientation process that preserves the crystal order (Fig. 1c), however, they did not analyze their results quantitatively. During the 1990's my colleagues and I performed extensive quantitative dynamic NMR studies on solid bullvalene (and many of its derivatives). The first such work[4] used deuterium NMR on a perduterated single crystal of bullvalene. The results confirmed the earlier hypothesis that the rearrangement proceeds in concert with molecular reorientation, however, they also showed the presence of an independent process, namely three fold jumps about the unique axis of the bullvalene molecule (Fig. 1b). Samples of (experimental and calculated) dynamic deuterium NMR spectra on which this analysis is based are shown on the left hand side of Fig. 2. The Arrhenius plots for the two processes are depicted on the right hand side of the figure.

These results were subsequently confirmed using several advanced solid state NMR methodologies, involving natural abundance carbon-13 under magic angle spinning (MAS) conditions. They include "Rotor-Synchronized" experiments[5] and the quantitative analysis of the dynamic broadening of spinning side band.[6] In Figure 3 are shown typical results, but I shall not elaborate on them in the present article.

From Fig. 1c it follows that the valence bond isomerization in solid bullvalene can actually proceed along nine distinct pathways (see Fig. 4); three bond-shift rearrangement channels, depending on which of the three cyclopropane bonds breaks, and for each of these there are three different final orientations in the crystal.[7] As in the crystalline state the bullvalene molecules occupy a general sites in the cell (Fig. 1d) their symmetry is no longer strictly C_{3v}, as it is in the gas or liquid states. This breaking of symmetry could, in principle, lead to different rearrangement probabilities for the different pathways. In the earlier works[4-6] the dynamic measurements were performed at temperatures above about 0°C where the three-fold jumps are faster than the

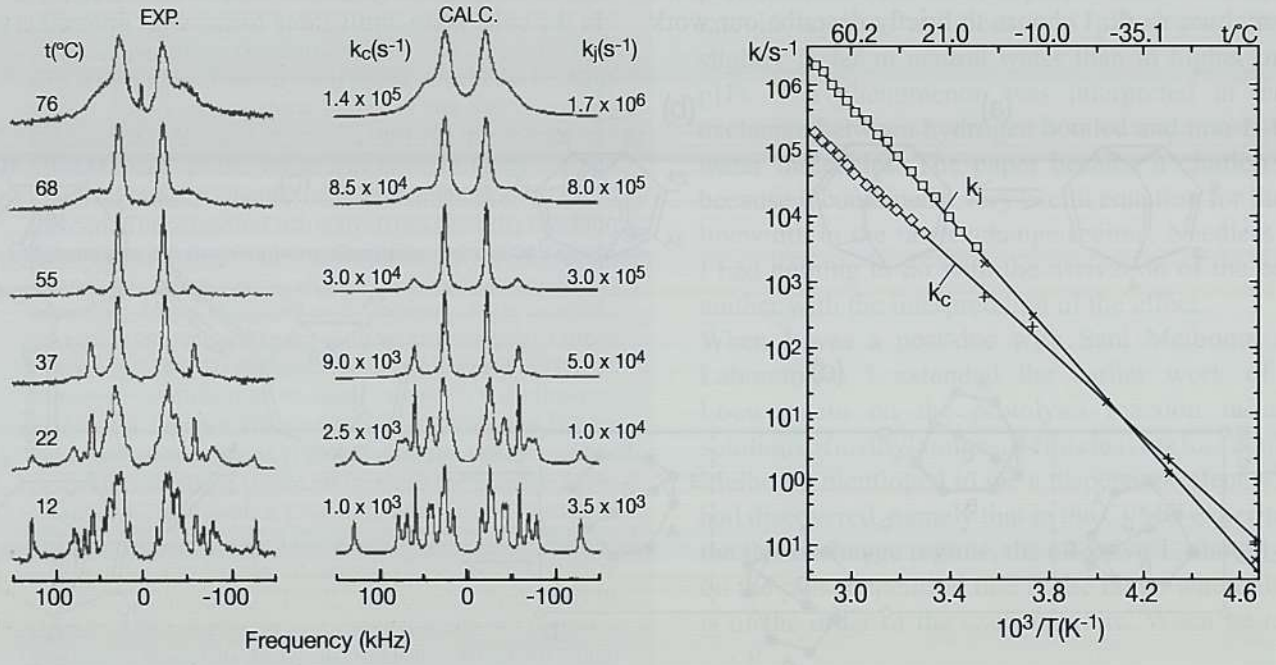

Figure 2. Left: Experimental and calculated deuterium NMR spectra of a single crystal of deuterated (50%) bullvalene. In the calculated spectra, kJ and kC correspond to the 3-fold jump and Cope rearrangement/reorientation rate constants.[4]
Right: Arrhenius plots for k_J and k_C.

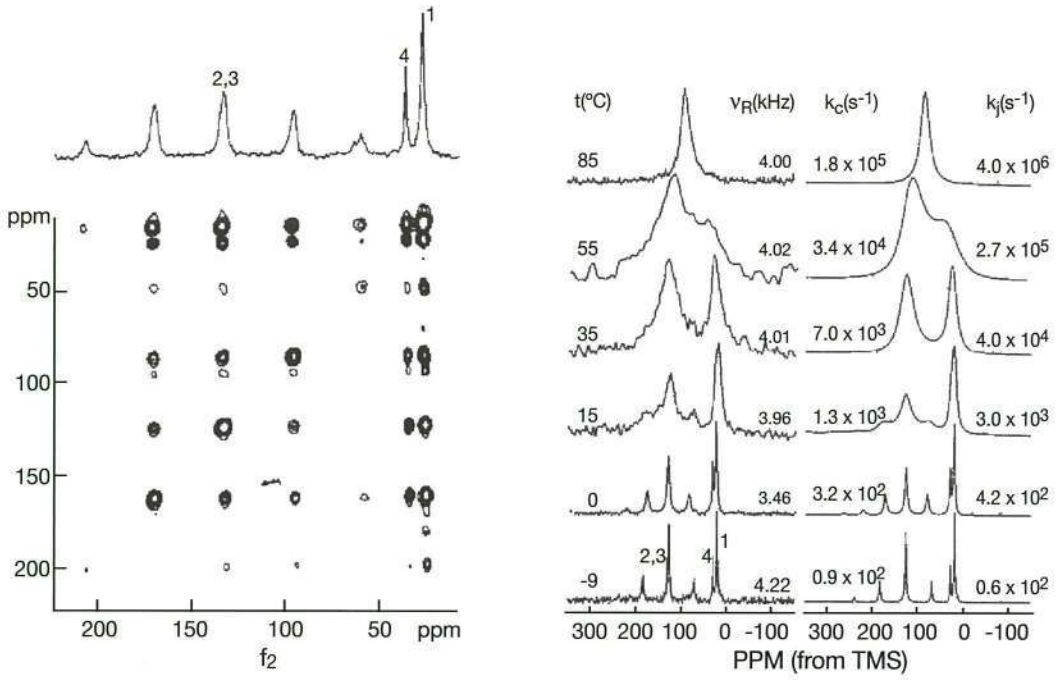

Figure 3. Carbon-13 dynamic spectra of solid bullvalene under MAS conditions. Left: Rotor Synchronise 2D exchange.[5] Right: Experimental and calculated MAS spectra.[6]

rearrangement (Fig. 2). This washes out any selectivity effect that might occur in the Cope rearrangement/ reorientation pathways. To detect such selectivity it is necessary to perform experiments at low temperatures where the three-fold jumps are slower than the rearrangement, and on single crystals where the different sites can be distinguished. The most suitable experiment for this purpose is the deuterium 2D exchange method performed on single crystals of deuterated bullvalene. In Fig. 5 is shown a spectrum of such a sample at a magnetic field orientation at which all four molecules are equivalent. Also indicated is the labeling of the various sites as derived from rotation experiments.[8] In the spectra of 2D exchange experiments off diagonal peaks (cross peaks) are obtained which link between signals from different sites, say X and Y. The intensities of these cross-peaks are proportional to the probability that an atom initially at site X ends up at site Y after an experimentally preset mixing time, τ_m. Such spectra may therefore provide detailed information about possible discrimination between the various pathways of Fig. 4. In particular if certain cross-peaks expected from a particular pathway are missing in the experimental spectrum, it may be concluded that this pathway is not active.

The method is well demonstrated in the 2D spectra shown in Fig. 6, which were performed on the same crystal used for Fig. 5. The spectrum on the left was recorded at 10°C, where the three-fold jumps process is faster than the rearrangement (Fig. 2). The mixing time used (τ_m=0.5ms) was long enough for one or several jumps to occur but too short for the rearrangement process to leave its marks on the spectrum. Hence only cross peaks linking between chemically equivalent deuterons are observed which are interchanged by the jump process (for example, 3A, 3B, 3C, see dashed lines in the figure). In contrast, the spectrum shown on the right of Fig. 6 was recorded at -40°C with τ_m=300ms. Under these conditions the probability of jumps is too small to produce observable cross peaks, but on the average a single Cope rearrangement step is expected. This is well demonstrated in the ample cross-peaks linking between chemically non-equivalent atoms (for example 4↔1A, 4↔1B, 4↔1C). However, a close examination of the 2D pattern shows that not all cross-peaks expected by the nine pathways in Fig. 4 are actually observed in this 2D spectrum. For example the cross peaks 1A↔3A and 1C↔3A, are completely missing in the spectrum, thus excluding pathways AC, CA, BB, BC and CB (see Fig. 4). Extensive measurements and a detailed analysis

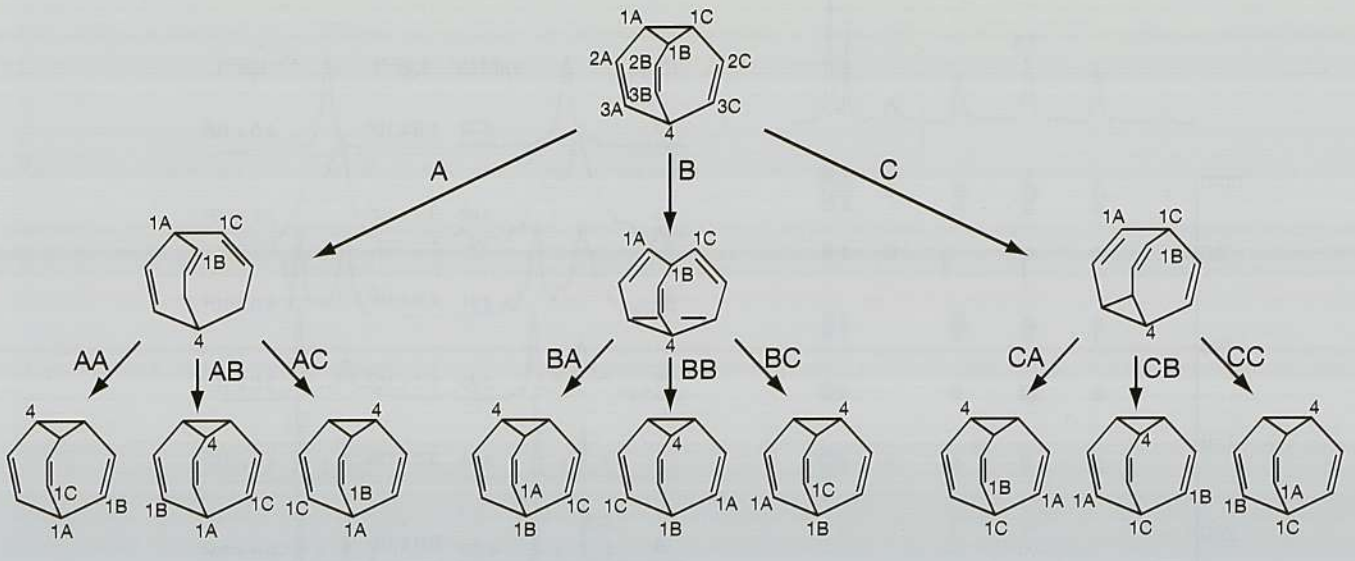

Figure 4. The nine different Cope rearrangement/reorientation pathways in solid bullvalene. They are labeled (IJ) according to the wing opposite which bond cleavage takes place (I) and according to the wing which carbon 4 occupies in the final orientation (J). The only active pathways, detected experimentally are, AA, AB, BA and CC.

indicate that, in fact, only four out of the possible nine pathways are active: They are those labeled as AA, AB, BA and CC.[7]

The Cope rearrangement/reorientation process in solid bullvalene is thus highly selective. As the activation energy of the process in solid bullvalene is similar to that in solution, the rate determining step for the reaction in the solid most likely involves the bond shift tautomerism.

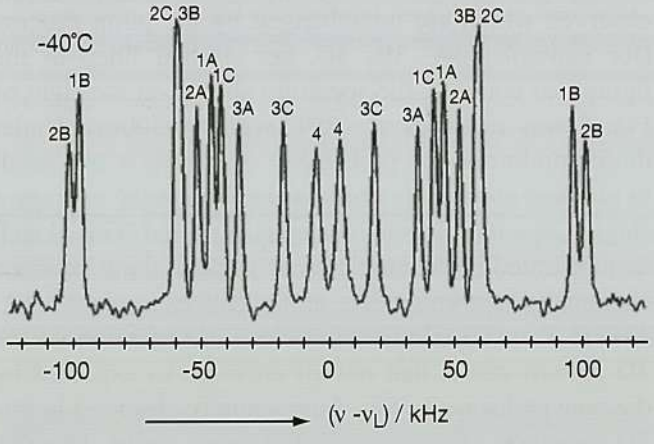

Figure 5. Deuterium NMR spectrum of a single crystal of deuterated (50%) bullvalene at -40°C and at a magnetic field orientation for which all four molecules are equivalent. The labels indicate the sites according to Fig. 1.

This step, however, cannot be the source for the pathway selectivity as the lengths of the three cyclopropane bonds in the crystalline state are essentially identical as in solution. A more likely source for the selectivity of the Cope rearrangement/reorientation in the solid state is therefore the accessibility of a suitable reorientation channel for the process to be completed.

A related point concerns the accessibility of the tautomers in the solid state. In the solid the bullvalene molecules can form 10!=3628800 different tautomers (all possible permutations of the C-H groups on ten sites). This number is a factor three bigger than in solution since the three wings (A, B, C) are distinguishable in the solid. The question then arises whether all these tautomers can be obtained from any given initial one by just the four active channels. Clearly none of the channels alone can produce all tautomers, but as can be proved by permutation theory[7] any pairs of symmetric and corresponding antisymmetric, such as AA and AB, can do the job. Thus at sufficiently long times all tautomers will be produced from any single one.

I doubt that there is any other physical method, besides NMR, that can match this level of analyzing reaction pathways in solids. The situation becomes even more interesting when the bullvalene is substituted with bulky substituents. Such substituents tend to stick in the crystal

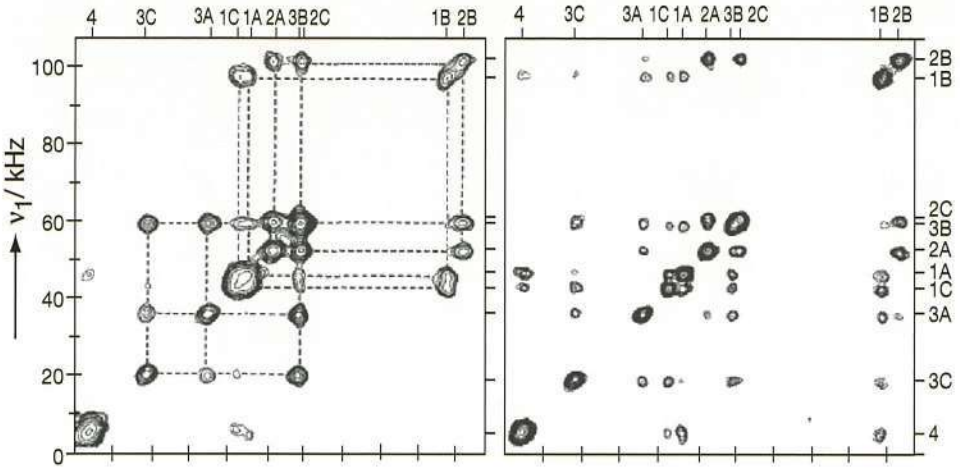

Figure 6. Deuterium 2D exchange spectra measured on the same single crystal as in Fig. 5. Only one quadrant (corresponding to half of the 1D spectrum) is shown. Left: T=10°C, τ_m=0.5ms. The dashed lines connect peaks of chemically equivalent sites, as expected from 3-fold jumps. Right: T=-40°C, τ_m=300ms. Ample cross-peaks between chemically non-equivalent sites are observed, indicating the occurrence of active Cope rearrangement/reorientation pathways.

and force the bullvalene cage to undergo special acrobatic motions to complete a rearrangement process, without disturbing the crystal order. A short time before my retirement I wrote a research proposal aimed at studying such processes. The project was turned down, apparently because of a comment by a referee that "it is time that the PI will do other things than coping with the Cope rearrangement". I never wrote a research project again, but I continued to work on the dynamics of substituted bullvalene in the solid state, leading to new surprises.[9-14] Admittedly, the research and the results described above are more of an intellectual academic interest and less of an applied nature. But, as often happened in the past, somewhere, sometime it may turn out to be useful for some unforeseen purpose.

Acknowledgement

My research on dynamic processes in solids, an example of which I described above is a result of an intimate team work with many colleagues and associates. I am grateful to each one of them for their collaboration, but I refrain from listing names, lest I miss a few and because the list is excessively long. Most are co-authors of the cited references or have been otherwise mentioned. But there is also a long list of advisors and colleagues who remain anonymous.

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The 73rd Annual Meeting of the Israel Chemical Society

Danny Porath (HUJI) and Ernesto Joselevich (WIS)

Abraham Nudelman (BIU)

Summary by Yoel Sasson

Yoel Sasson is a Professor of Applied Chemistry at the Hebrew University of Jerusalem (since 1983) and the incumbent of the Lester Aronberg Chair of Applied Chemistry. He served as a visiting scientist and visiting Professor at the University of Waterloo (Ontario), at Virginia Polytechnic Institute, at the University of Paris Sud and at the Experimental Station in Du-Pont (Delaware). For 12 years (1994-2005) He held the post of VP of R&D at Makhteshim-Agan Industries in Beer Sheva, Israel.

He is active in the area of environmental and process catalysis, mainly phase transfer catalysis, and has published more than 200 articles and reviews and 30 patents in these fields. He has coached 130 graduate students in their Ph.D. and M.Sc. theses.

The 73rd Annual Meeting of the Israel Chemical Society took place on February 4-5, 2008 at the Jerusalem International Convention Center (Binyanei Hauma) and was organized by the Institute of Chemistry, The Hebrew University of Jerusalem. Your loyal servant chaired the organizing committee with Avi Bino, Dima Gelman, Eli Grushka and Ronnie Kosloff as members. The logistics was brilliantly handled by Dan Knassim and by the dynamic secretary of the ICS, Ms. Anitta Harrison.

The conference organization started on the left foot due to the general strike of the faculty in the Israeli Universities which lasted for 90 days. Consequently the academic year started only on January 20 and the conference fell right at the beginning of the first Semester. We were also worried with the weather forecast which projected a snow storm in Jerusalem in the beginning of February. Fortunately the snowfall ended couple of days before the meeting and the attendance to the conference was not notably affected by the parallel teaching duties of the participants.

The 73rd meeting set some new records by all viable standards. Number of participants was the highest ever (887) more than half were graduate students (472). The number of exhibitors and sponsors and the amount of donations were unprecedented. Same for the number of posters presented (278), number of parallel sessions (21) and number of plenary lectures (8).

Our original idea was to invite each of the Israeli chemistry department heads to propose a plenary lecture of his faculty. This worked out only partially and the final list of plenary speakers included three guests from abroad (Alan Heeger, Nobel laureate from Santa Barbara; Peter J. Sadler from Warwick and Robert M. Waymouth from Stanford) and five Israeli speakers (Aharon Gedanken and Alfred Hassner from Bar Ilan, Itamar Willner and Ronnie Kosloff from the Hebrew University, Eli Kolodney from the Technion and Jacob Klein from the Weizmann Institute). Hassner and Kosloff were the recipients of the ICS Prize for 2007.

On the left: Ronnie Kosloff (HUJI)

Dan Meyerstein (AUCS), Shlomo Margel (BIU) and Yoel Sasson (HUJI)

Alfred Hassner (BIU) and Bilha Fischer (BIU)

The oral presentations were all invited and the 20 parallel sessions were organized with the help of an advisory committee. These were as follows: Biomaterials (D. Cohn), Advanced Inorganic Materials (R. Tenne), Theoretical Chemistry (R. Baer), Renewable Energy Sources (M. Asscher), Electrochemistry in Material Science (D. Mandler), Polymer Chemistry (M. Kol), Drug Design (A. Goldblum, A. Shurki), Advanced Functional Materials (S. Magdassi), Advances in Food and Technology (N. Garti), Novel Synthetic Methods (S. Rozen), Analytical and Forensic Chemistry (E. Grushka), Nanocomposite Materials (G. Marom), Chemistry of Fuels (Z. Aizenshtat), Green and Sustainable Chemistry, Cleantech (H. Wiener), Materials for Catalysis (D. Gelman, M. Srebnik), Intellectual Property in Chemistry (E. Bressler), Molecular Electronics (D. Porath), Chemical Education (R. Blonder), Combinatorial Chemistry (G. Gellerman), Physical Organic Chemistry (S. Biali, M. Rabinovitz) and Industrial Chemistry (Y. Sasson, A. Zoran). Typically, in each session we had one keynote speaker and four invited speakers. All the sessions were very well attended but there was sufficient room for all.

Two individuals were awarded with the prize for the Outstanding Young Scientist 2007 – Danny Porath from the Hebrew University and Ernesto Joselevich from the Weizmann Institute. The two laureates submitted keynote lectures at the session for molecular electronics.

Ms Otilia Rosenberg from Rishonim High School in Herzelia was awarded with the ICS 2007 Prize for Excellence in Teaching of Chemistry. The prize was granted in the session of Chemical Education.

Keynote speakers from abroad included A.S. Hoffman from Seattle in Biomaterials, Y.D. Tretyakov from Moscow in Advanced Inorganic Materials, J. Mayer from Stuttgart in Electrochemistry in Material Science, R. Mezzenga from Fribourg in Advanced Food and Technology, G. Rothenberg from Amsterdam in Materials for Catalysis, C. Schonenberger from Basel in Molecular Electronics, I. Parchmann from Oldenburg in Chemical Education and A. Albericio from Barcelona in Combinatorial Chemistry.

The traditional conference dinner (with more than a hundred attendants) honoring the ICS Prize winners, took place at the Indian Restaurant Kohinor at the Crowne Plaze Hotel. The two laureates, Professor Ronnie Kosloff and Professor Alfred Hassner were introduced in several presentations by friends and colleagues.

The atmosphere and the spirit at the conference throughout the lecture halls, the poster sessions, the exhibitions and the coffee and lunch breaks were lively and vibrant and very well reflected the current dynamic and growing status of the chemical sciences in Israel. We are confident that this spirit will be maintained and intensified in the forthcoming 74th meeting to be organized by the Technion.

I wish to take this opportunity to thank all the organizers, contributors and participants who made this conference a success and a memorable event.

The ICS Prizes for 2007

Prize for Excellence

Prof. Alfred Hassner

Prof. ALFRED HASSNER
Bar Ilan University
For his life-long achievements in chemical research and his groundbreaking contributions to synthetic and heterocyclic organic chemistry in Israel and abroad.

Prof. Ronnie Kosloff

Prof. RONNIE KOSLOFF
Hebrew University of Jerusalem
For his pioneering contributions to the development of time dependent quantum mechanical studies of chemical systems and their application to reality.

Excellent Young Scientist Prize

Dr. Ernesto Joselevich

Dr. ERNESTO JOSELEVICH
Weizmann Institute of Science
For his ground-breaking studies involving the synthesis and electromechanical characterization of carbon nanotubes and their noteworthy contribution to nano-science and –technology.

Dr. Danny Porath

Dr. DANNY PORATH
Hebrew University of Jerusalem
For his ground-breaking studies involving the measurement of charge transport properties of DNA and its derivatives using scanning probe microscopy, and its contribution to the possible development of DNA-based nanoelectronics.

Excellent Teacher

Mrs. OTILIA ROSENBERG
The 2007 Israel Chemical Society Prize for excellent teacher is awarded to Mrs. Otilia Rosenberg , from Rishonim High School, Herzliya for devoting her professional life to raising the reputation of chemistry in Israel and training the next generation of teachers and by so doing has made a major contribution to the development of Israeli high school chemistry teaching.

The ICS Prizes for 2007

Ph.D. Excellent Student

Lise Meitner Prize

Dr. HUI CHEN
Hebrew University of Jerusalem

SHACHAR KLAIMAN
Technion Israel Institute of Technology
Supervisor: **Prof. Nimrod Moiseyev**

ARIEL ISMACH
Weizmann Institute of Science
Supervisor: **Dr. Ernesto Joselevich**

ZVIKA POMERANTZ
Bar Ilan University
Supervisor: **Prof. Arie Zaban**

SARA WISHKERMAN
Ben Gurion University of the Negev
Supervisor: **Prof. Joel Bernstein**

ZVI HAYOUKA
Hebrew University of Jerusalem
Supervisors: **Dr Assaf Friedler,**
Prof. Abraham Loyter

AHMAD BASHEER
Hebrew University of Jerusalem
Supervisor: **Prof. Zvi Rappoport**

ANETTE YAHAV-LEVI
Tel Aviv University
Supervisor: **Dr. Arkadi Vigalok**

EMIR HALEVA
Tel Aviv University
Supervisor: **Prof. Haim Diamant**

The 74th Annual Meeting of the Israel Chemical Society

The Opening Ceremony: in the front row: past ICS presidents and guests from the Max Plank Society.

February 8-9 2009 David Intercontinental Hotel, Tel Aviv

by Prof. Noam Adir

The Israel Chemical Society held its 74th annual meeting at the David Intercontinental Hotel in Tel Aviv on the 8-9th of February 2009. Over 700 researchers, lecturers and students took part in ICS09, which strived to offer a challenging program that would successfully blend both classic and cutting-edge themes in our field.

I would like to thank the members of the organizing committee - comprised of Profs. Timor Baasov, Alon Hoffman, Ehud Keinan, Uri Peskin and Asher Schmidt, of the Technion's Schulich Faculty of Chemistry - for their dedication in the planning and preparation of this event.

This year's opening session honored the recipients of the ICS prizes for 2008. The ICS Medal was awarded to Prof. Zeev Luz of the Weizmann Institute of Science (WIS) for his role in the development of Magnetic Resonance in Israel. The ICS Prizes for Excellence were awarded to Prof. Reshef Tenne from the WIS and to Prof. Raphael Mechoulam of the Hebrew University of Jerusalem (HUJ). The ICS Young Scientist Prizes were awarded to Prof. Deborah Fass of the WIS and Dr. Assaf Friedler of HUJ.

In keeping with recent ICS tradition, ICS09 celebrated the staunch ties between the Israeli chemistry community and the international one with the attendance of a truly exceptional delegation from the Max Planck Society of Germany. Our guests included Profs. Klaus Kern (Stuttgart), Werner Kuhlbrandt (Frankfurt), Benjamin List (Muelheim), Klaus Muellen (Mainz), Peter Seeberger (Berlin), Joachim Spatz (Heidelberg) and Walter Thiel (Mulheim). The delegation gave a series of brilliant plenary and keynote lectures on a broad variety of topics, which spanned nanotechnology, material chemistry, catalysis, structural biology, computational methods and organic chemistry. Their contribution provided a unique insight into the future of modern chemistry. Further plenary and keynote lectures were given by both local and additional foreign participants.

Prof. Noam Adir. B. Sc.: Chemistry. Hebrew University of Jerusalem, 1984. Ph.D: Biochemistry. Hebrew University of Jerusalem, 1990. Post Doctoral Research: Biophysics/ Protein Crystallography, University of California, San Diego, 1990-1995. Faculty Member, Schulich Faculty of Chemistry, Technion since 1995.

Yehiam Prior (WIS)

L to R: Shlomo Margel (BIU), Ehud Keinan (Technion), Zeev Luz (WIS), ICS Medal 2008

Reshef Tenne (WIS) and Gitti Frey (HUJI)

L to R: Raphael Meschoulam (HUJI) and Shlomo Rozen (TAU)

Eighteen parallel sessions took place over the course of the two-day conference, with subjects ranging from 'Molecular Electronics' to 'Industrial Chemistry' and everything in between. Each session began with a keynote lecture by prominent researchers in each of the given fields, followed by 3-5 additional contributions. Many of the lectures were given by participants selected by the session chairs after reviewing the numerous submitted abstracts. In this way session participants had the opportunity to hear not only renowned researchers, but also some of the brightest minds of the burgeoning new generation of Israeli chemists.

The 210 posters displayed in two separate sessions were of truly superb quality, and generated a great deal of on-the-spot discussion between senior and junior researchers. Good poster sessions are in many cases the true measure of a scientific meeting, and judging by the crowds surrounded this year's presentations ICS09 was indeed a great success. I am sure that many of the young presenters will take the new ideas that resulted from these discussions back with them.

A gala dinner honoring the recipients of the ICS prizes was held at the beautiful *'Le Relais Jaffa'* restaurant in Jaffa. The audience was entertained by Schulich Faculty graduate students Rennana Poranne (née Gershoni) and Yuri Tulchinsky, and each of the ICS Prize recipients was introduced by a former student or colleague.

The organizing committee would like to thank all of those that helped in making ICS09 a success. The professional organization of the conference was managed and supervised by the excellent team from Deisenhaus – Anat Reshef, Magali Mizrachi and Tsipi Lasker. From overall planning to micro logistics, the conference ran without a glitch. Thanks to Anitta Harrison, the secretary of the ICS who tirelessly helped in facets of the organization. The meeting could not have come together without the monetary assistance provided by many commercial and academic institutions, their support helped keep the fees manageable while allowing the community to enjoy the facilities of the Dan Intercontinental Hotel.

In summary, I hope that this vitalizing conference will be remembered by all as an exciting meeting of minds and we can now all look forward and prepare ourselves for the next year's ICS2010 and the celebration of the ICS's 75th anniversary!

On behalf of the organizing committee,
Noam Adir, ICS09 Chair

The gala dinner honoring the recipients of ICS Prizes for 2009 at the 'Le Relais Jaffa'.

The ICS Prizes for 2008

Prize for Excellence

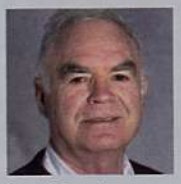
Prof. Rafi Mechoulam

Prof. RAFI MECHOULAM
Hebrew University of Jerusalem
For his unparallel contributions to the isolation and synthesis of the active compounds of the Hashish and mapping the receptors in the brain for these compounds. Professor Mechoulam also discovered the family of Anandemides found in the above receptors which are responsible for many desirable effects in the brain such as easing pains, control coordination and much more.

Prof. Reshef Tenne

Prof. RESHEF TENNE
Weizmann Institute of Science
For his pioneering studies which extended the fullerene and nanotubes realm to the inorganic chemistry. This work opened new research fields in nanotechnology and solid state science, subjects which already are starting to affect and benefit our lives.

ICS Medal



Prof. Zeev Luz

Prof. ZEEV LUZ
Weizmann Institute of Science
For using magnetic resonance to unravel molecular dynamics and chemical exchange in liquids, liquid crystals and solids; For his enormous contribution in establishing Israel as an internationally renowned center for magnetic resonance research.

Excellent Young Scientist Prize

Dr. Assaf Friedler

Dr. Deborah Fass

Dr. ASSAF FRIEDLER
Hebrew University of Jerusalem
For his ground-breaking studies on protein-protein interactions and for the development of molecules with therapeutic potential based on improved understanding of such interactions.

Dr. DEBORAH FASS
Weizmann Institute of Science
For her ground-breaking studies on the mechanism of disulfide bond formation in proteins and its central role in protein folding and assembly.

Excellent Teachers

Mrs. Afrah Assi

Mrs. Suzanna David

Mrs. AFRAH ASSI
The 2008 Israel Chemical Society Prize for Excellent Young Teacher
The Israel Chemical Society Prize for the Outstanding Young Teacher for 2008 is hereby rewarded to mrs. Afrah Assi Jaljulia High School - Jaljulia for extraordinary devotion to chemistry teaching that produced outstanding students , for making chemistry a prestigious , highly demanded subject at her school.

Mrs. SUZANNA DAVID
The 2008 Israel Chemical Society Prize for excellent teacher is awarded to Mrs. Suzanna David, from Wizo – Hadassim High School, Hadassim for devoting her professional life to raising the reputation of chemistry in Israel and training the next generation of teachers and by so doing has made a major contribution to the development of Israeli high school chemistry.

Ph.D. Excellent Student

Lise Meitner Prize

NATALIA ZAMOSCHCHIK
Weizmann Institute of Science
Supervisor: **Dr. Michael Bendikov**

GREGORY MOLEV
Technion Israel Institute of Technology
Supervisor: **Prof. Yitzhak Apeloig**

GOREN GORDON
Weizmann Institute of Science
Supervisor: **Prof. Gershon Kurizki**

DANA. D. MEDINA
Bar Ilan University
Supervisor: **Dr. Yitzhak Mastai**

INNA BARSKY
Ben Gurion University of the Negev
Supervisor: **Prof. Joel Bernstein**

ITZIK YOSEF
Hebrew University of Jerusalem
Supervisor: **Prof. David Avnir**

AMNON BAR-SHIR
University of Tel-Aviv
Supervisor: **Prof. Yoram Cohen**

The 75th Annual Meeting of the Israel Chemical Society

January 25-26, 2010

David Intercontinental Hotel, Tel Aviv


Prof. Tohru Fukuyama


Prof. Shunichi Fukuzumi


Prof. Eiichi Nakamura


Prof. Yoshio Okahata


Prof. Hiroaki Suga


Prof. Daisuke Uemura


Prof. Erick M. Carreira


Prof. Scott E. Denmark


Prof. Ada Yonath


Prof. Lia Addadi


Prof. Steve Weiner


Dr. Michael Bendikov

Dear Colleagues,

The Israel Chemical Society will hold its 75th annual meeting at the David Intercontinental Hotel in Tel Aviv on January 25-26, 2010. The ICS annual meetings are major scientific events of the Israeli Science, bringing together researchers from academia, chemical education, R&D and industry interested in the structure and dynamics of molecules and materials.

The meeting will encompass all facets of modern interdisciplinary chemical research in 9 plenary lectures, 18 symposia and two poster sessions. The symposia will include invited Keynote and regular talks, as well as 1-2 talks that will be selected from abstracts submitted in response to the present call for papers. The two poster sessions will allow young scientists to present their most recent achievements.

This year the Sackler School of Chemistry of Tel Aviv University is organizing the meeting. We are delighted to announce that The 2009 Nobel Laureate in Chemistry, Prof. Ada Yonath, will be our special guest and will deliver the opening ceremony lecture. ICS Prize Laureates will also deliver plenary lectures. This year we are particularly proud to host a delegation of leading scientists from Japan in addition to guests from the USA and Europe.

We look forward to seeing all of you in Tel Aviv in January!

Prof. Shmuel Carmeli,
Chairman of the Organizing Committee

The 7th Congress of the Israel Association for Medicinal Chemistry

Meeting Report

Monday, March 24, 2008
Ebner Auditorium, Weizmann Institute of Science

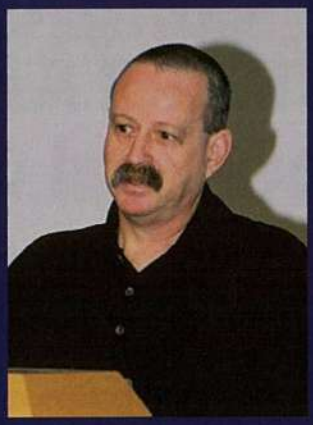
Organizing Committee:
Michal Sharon, Weizmann Institute of Science
Eylon Yavin, The Hebrew University of Jerusalem
Michael Meijler, Ben-Gurion University
Nurit Livnah, Pharma Two B Ltd.

Advisory board:
Matityahu Fridkin, Weizmann Institute of Science
Avi Domb, The Hebrew University of Jerusalem

Secretary:
Malka Nehemia, The Hebrew University of Jerusalem

On the 24th of March 2008 the 7th Congress of the Israel Association for Medicinal Chemistry was held at the Weizmann Institute of Science. The aim of the meeting was to enable a broad view of the field. Medicinal chemistry is a multidisciplinary field that brings together synthetic chemistry, molecular modeling, computational biology, structural genomics, and pharmacology' in order to discover and design new drugs, and investigate their interaction at the molecular, cellular, and whole-animal level. The scientific program comprised 12 invited lectures divided into four sessions. The first session was "structural aspects in drug design" followed by "anti-cancer and anti-inflammatory agents" and "small molecules in biomedicine" and ending with "genes and their products". The meeting attracted around 220 participants from different research areas, biology, chemistry and pharmacology as well as industrial entities.

Prof. Bilha Fischer from Bar-Ilan University presented the first talk in the symposium. In her presentation, Bilha elaborated on her groups efforts in the past decade to develop a nucleotide based drug as an antagonist to P2Y receptor/s; a target that is involved in the modulation of many physiological conditions. Several nucleotide-based analogs were synthesized where one of the crucial criteria in the design of such analogs was to develop antagonists that are metabolically stable. In this regard, several analogs were quite resistant to alkaline phosphatase (no degradation after 30 minutes incubation at 37°C) and very stable when exposed to conditions that mimic the gastric fluid acidity. She concluded her talk by describing potent and selective nucleotide analogs that were specific to the P2Y1 receptor with EC50 values in the sub-microM region.
Lara Golender from accelerys presented a talk describing several computational chemistry metodologies used to aid medicinal chemists in the drug discovery process, by an example of a successful study case. She presented a pharmacophore-based drug discovery strategy which was behind a successful early discovery process of several novel active inhibitors of a target enzyme in TEVA. The inhibitors discovered showed activity *in-vitro* as well as efficacy *in-vivo*. She discussed ligand-based pharmacophore identification procedure in a condition of scarce and poorly comparable experimental data. Using model examples the researchers were able to demonstrate the techniques of activity prediction, the creation of the pharmacophore-based queries, searching of commercial compound databases, rational hit optimization and building of expansion libraries as they were employed in the project. This talk was an interesting demonstartion of the potential of computational approaches to facilitate drug discovery.



Prof. Oded Livnah, Hebrew University. Chair of the Structural Aspects in Drug Design session.

In the third talk, Prof. Yitzhak Tor from the University of California, San Diego, presented his breakthrough studies on the interactions between RNA and small molecules. The specific binding of aminoglycoside antibiotics to the bacterial ribosomal decoding site (A-site), their cognate "receptor", has inspired the study of RNA–small molecules interactions and the search for novel RNA binders. Of interest is the potential use of such small molecules to interfere with the action of RNA binding proteins, and particularly with the replication of retroviruses that rely on the formation of key RNA–protein complexes. Yitzhak's group synthesized aminoglycosides with guanidinium groups displacing the amine moieties, that displayed enhanced affinity and selectivity to specific RNA targets. Moreover, his group showed that viral RNA sites were successfully targeted, resulting in inhibition of HIV replication 100-fold more effectively than their amino precursors. Yitzhak concluded his presentation by showing that the synthetic guanidinoglycosides are very effective cellular transporters, capable of carrying large (>300 kDa) bioactive molecules across cell membranes, without observable toxicity.

After the coffee break, Prof. Ehud Keinan of the Technion continued the morning session with a fascinating presentation on newly discovered functions of ozone. The assumption that ozone is not only a strong oxidant, but also an important inflammatory mediator, is heavily supported by the ample literature on the pulmonary toxicity and biological effects of environmental ozone and by the recent discovery that antibodies, human neutrophils, and inflammatory lesions catalyze the formation of ozone *in-vivo*. Ehud's group proposed that the pulmonary inflammation in asthma involves a vicious circle of ozone production and recruitment of white blood cells, which produce more ozone. If this hypothesis is correct, electron-rich olefins, which are known ozone scavengers, could be used for prophylactic treatment of asthma. His group tested whether volatile, unsaturated monoterpenes, such as limonene, could saturate the pulmonary membranes and thereby equip the airways with local chemical protection against ozone. Examination of the pulmonary function of sensitized rats that inhaled either limonene or eucalyptol (a saturated control terpene, inert to ozone) showed that limonene inhalation significantly prevents bronchial obstruction while eucalyptol inhalation does not cause any effect. Ehud concluded his talk by showing that the anti-inflammatory effects of limonene could also be observed by a marked decrease in peribronchiolar and perivascular inflammation.

The next speaker was Dr. Ronit Satchi-Fainaro, from the Sackler School of Medicine, Tel Aviv University. She gave an exciting presentation on the use of polymer-based anti-cancer therapeutics. Her focus is on the treatment of cancer by inhibition of angiogenesis in combination with tumor inhibition. It is conceptually accepted that angiogenesis inhibitors alone may not be sufficient to eradicate prostate cancer. Therefore, the generation of a combination of drug delivery systems with bi-specific antiangiogenic and antitumor properties is a novel approach. Ronit showed that her group employed an orthotopic prostate cancer mouse model which could be detected by non-invasive intravital microscopy and MRI. They synthesized and characterized a novel polymer conjugate bearing an antiangiogenic and an anticancer drug. Polymer

conjugation improved the therapeutic index of the two drugs, targeting the conjugate selectively to the prostate cancer-derived bone metastases, which also reduced toxicity. The development of a multistage prostate cancer progression model followed by non-invasive intravital imaging will allow the evaluation of targeted therapy at different stages of disease. Ronit concluded her talk by explaining that the development of these novel non-toxic therapies and understanding the cellular and molecular mechanism of action may lead to a paradigm shift into an era of personalized treatment and into a transformation of cancer to a chronic manageable disease.

Joel Van Gelder from Insight Pharmaceuticals Ltd. spoke about Heparanase inhibition as basis for anti-cancer drug development. Heparanase plays an important role in pathologic processes such as inflammation, autoimmune diseases and cancer. It mediates the release of growth factors from the ECM storage and thus induces angiogenesis. Moreover, its activity is essential in the disassembly of the basement membrane by invading metastatic tumor cells. Therefore, heparanase is an attractive target for the discovery of novel anti-cancer agents. A drug discovery program on-going at Insight yielded a potent lead compound, by screening of a chemical library for heparanase inhibitors using a cell-based assay. The lead inhibits pro-heparanase activation through a novel mode of action, by inhibiting the binding of heparin to latent heparanase and inducing changes its conformational state, thereby exposing the proteolytic cleavage sites to processing and allowing pro-heparanase activation. It has also been shown to inhibit binding to heparin of other heparin-binding proteins involved in cancer. Moreover, this compound inhibits angiogenesis, migration and invasion in vitro and significantly reduces tumor growth *in vivo*. On the basis of three-dimensional analysis and structure-activity relationships, NCE pro-heparanase activation inhibitors have been designed and synthesized. The lead candidate INS10197 has shown efficacy and improved oral bioavailability and pharmacokinetic properties.

Following the lunch break Prof. Eli Breuer announced the 2008 Annual Chorev Awards for Excellence in Medicinal Chemistry and invited Prof. Michael Chorev to hand the prize. Jeffrey Sterling from Teva received the award for life achievment in the medicnal chemistry industry. In addition, prizes were given to Esther Eljarrat-Binstock and Zvi Hayouka from the Hebrew University for excellent PhD studies. During her research Esther Eljarrat-Binstock from the group of Abraham J. Domb has developed hydrogel iontophoresis for ocular drug delivery. Her work reveals an effective and comfortable method for delivering charged drugs or particles into the anterior and posterior segments of the eye. Her recent breakthrough is the use of charged nanoparticles as drug carriers for the iontophoretic delivery. This method provides a uniform drug penetration regardless of the drug's ionic strength and diffusion properties. Esther's research has yielded 14 publications. Zvi Hayouka from the lab of Assaf Friedler has developed a new approach for drug design. His "shiftide" strategy is based on inhibition of proteins by peptides that shift their oligomerization equilibrium towards an inactive state. This is a general approach that could be applied for any disease-related protein that is in equilibrium between various oligomeric states. He succesfuly applied this for the development of a novel anti-HIV lead compound. Zvi published six papers and is involved in three patent applications.

The second speaker in the afternoon session on "Small Molecules in Biomedicine" was Dr. Roni Kasher from the Ben-Gurion University of the Negev (Sede-Boqer). Roni described his work as a postdoctoral fellow at the Weizmann Institute prior his recent appointment at Ben-Gurion. In his presentation, Roni elaborated on the elegant combinatorial approach that was initiated, leading to the discovery of a family of peptides with estrogen-like activity. After a few minutes into his presentation, we were pleased and excited to see the renowned Prof. Ephraim Katzir (Roni's postdoctoral

mentor) enter the auditorium. Roni discussed two promising peptides that exerted estrogenic activity *in-vivo*. One active peptide (a hexa-peptide-VSWFFE) acted like a mixed agonist/antagonist, whereas another active peptide (a hepta-peptide –VSWFFED) behaved like an agonist. The biological activity of the agonist was determined on a mouse model (in collaboration with Prof. Itai Bab) in which the active hepta-peptide was shown to restrain bone growth *in-vivo*. Furthermore, it was shown that the active peptide had a profound effect on the longitudinal growth of the femora in ovariectomized (OVX) mice; as corroborated by micro-computed tomography (μCT).

Continuing this session was Prof. Ron Kohen from the school of Pharmacy in Jerusalem. Ron presented a really intriguing talk regarding the so-called anti-oxidant paradox. On one hand, there is accumulating evidence that point to the beneficial effect of consuming fruits and vegetables on reducing the risk for various diseases that are associated with oxidative stress (e.g. cancer and Alzheimer's).Yet recent studies have shown that the consumption of low-molecular weight anti-oxidant (LMWA) supplements (e.g. Vitamin E and β-carotene) have no beneficial effect and at higher doses might even be harmful (e.g. Mayo Clin. Proc.2008, Jan; 83(1):23-34: "Beta carotene supplementation appeared to increase cancer incidence and cancer mortality among smokers, whereas vitamin E supplementation had no effect.").

The first part of his talk presented data that could explain the way antioxidants act in vivo and why swallowing anti-oxidant pills are not so beneficial. Experiments in cell culture to which various anti-oxidants were added showed that the overall antioxidant capacity of cells remains constant and since the cells tightly regulate this antioxidant network, supplementation with exogenous antioxidants cannot enhance the total antioxidant capacity of the cells.

In the second part of Ron's talk, an elegant study conducted in his laboratory shed some light on the anti-oxidant paradox by looking at the effect of consuming anti-oxidants (in the form of poly-phenols from red wine) while eating a fat-rich meal (red meat). In this study it was clearly seen that the levels of MDA (malonedialdehyde – the product of cytotoxic lipid peroxidation) was maintained at a minimal level in the blood serum for those individuals that ate their red meat which was cooked in red wine along with a glass of red wine. Whereas those that had no red wine had high levels of MDA. Hence, it seems reasonable to suggest that unhealthy oxidation processes (leading to the production of reactive oxygen species (ROS)) that take place in the stomach may be minimized by the consumption of anti-oxidants in the form of fruit, vegetables and red wine in the diet.

The last speaker of the session was Shmuel Carmeli from the School of Chemistry, Tel-Aviv University. His talk focused on the biological activity of microcystins which are active cyanobacteria metabolites. These cyclic peptides are stable in the mammalian gastrointestinal system and are transported and accumulated in the liver. Within the liver cells, the microcystins, inhibit protein serine/threonine phosphatases 1 and 2 (PP1 and PP2), which are key components for the control of the cell structure and function. Recently it was found that the inhibitory activity against protein phosphatases is not always related to the apparent LD50 level but depends on the balance between their accumulation and metabolism in the liver. In addition, comparisons of the toxicity of pure microcystins with the toxicity of intact cells from toxic cyanobacteria-blooms, or their crude extracts, suggest that other compounds that accompany the microcystins enhance their activity. Shmuel demonstrated that microcystins, are usually accompanied by a considerable amount of protease inhibitors from five different groups, namely – micropeptins, aerugenosins, microginins, anabaenopeptins and microveridins.

Fuad Fares from the department of Molecular Genetics, Carmel Medical Center and Faculty of Science and Science Education, Haifa University opened the last session. Fuad reported his findings regarding the development of new agonists and antagonists of glycoprotein hormones. Using molecular biology techniques the Thyrotropin hormone (TSH), Human Stimulating Hormone (hFSH) and Human Chorionic Gonadotropin (hCG) heterodimers were converted to a biologically active single-peptide chain. This was done by fusing the common α subunit to the carboxyl-terminal end of hTSHβ subunit in the absence (hTSHβα) or presence of a ~30 amino acid peptide from hCGβ (CTP) as a linker (hTSHβCTPα). Fuad demonstrated that the ligation of the CTP containing 4 O-linked oligosaccharide chains to the carboxyl-end of hFSH, hCGα subunit and to hTSH resulted in increasing the biological activity and longivity in vivo. He suggested

that in general ligation of the CTP cassete gene to different proteins could be an interesting strategy for increasing the in vivo half-life and bioactivity. In the next step of the study two deglycosylated variants were prepared using site-directed mutagenesis and gene transfer; one lacks both N-linked oligosaccharide chains on α subunit (hTSHβCTPα1+2), and the other lacks also the N-linked oligosaccharide chain on β subunit of the single chain (hTSHβCTPα(deg). Interestingly, it was found that the N-linked oligosaccharide units are not important for hTSH receptor binding, however, they play a dominant role in signal transduction of hTSH. In addition, deletion of the N-linked oligosaccharides from TSH resulted in partial antagonists of TSH and TSI at the level of the receptor binding site. Fuad concluded that such a deglycosylated variant may offer a novel therapeutic strategy in the treatment of Grave's disease, the most common form of hyperthyroidism.

The session continued with a fascinating talk by Danny Tawfik from the department of Biological Chemistry, Weizmann Institute. His talk covered the application of directed or *in-vitro* evolution. This is a powerful tool that enables the engineering of tailor-made proteins. Danny described the use of these tool towards the engineering of the mammalian dubbed serum paraoxonase enzymes, or PONs. PONs are generally associated with serum HDL (the good cholesterol) and are involved in the prevention of arteriosclerosis and organophosphate detoxification. By applying directed evolution, a series of stable wild-type-like PON variants that are highly stable were engineered, and functionally expressed in *E. coli*. These variants opened the door for the first structural and systematic biochemical studies of PONs, and provided novel insights regarding their biochemical function, mode of binding and activation to HDL, and physiological roles. A range of PON variants were engineered with novel substrate specificities that differ from wild-type PONs, including the ability to catalyze the hydrolysis of ceratin organophosphates and nerve agents. Danny also demonstrated the construction of artificial HDL-particles carrying engineered PON variants that show much improved stability and potency relative to the human HDL-PON complexes.

The meeting was closed by the talk of Noga Yerushalmi from Rosseta genomics, who presented the use of antisense oligonucleotides against miRNA as potential therapeutics against hepatocellular carcinoma.

The organizing committee of the The 7th congress of the Israel Association of Medicinal Chemistry. From left to right: Matityahu Fridkin, Michal Sharon, Eylon Yavin, Nurit Livnah and Michael Meijler

MicroRNAs (miRs) are short non-coding RNA molecules that regulate gene expression through post-transcriptional suppression of miRNA. The regulatory role of miRs makes them attractive potential targets for therapeutics, through either their activation or suppression. In her talk, Dr. Yerushalmi described a study aimed to identify miRs that are deregulated in hepatocellular carcinoma, and inhibit their activity through the use of antisense oligos (ASOs) that target the miRs involved in the carcinogenic process. Expression profiling of miRs was performed on RNA extracted from liver tissue samples of Hepatocarcinoma patients and compared to matched adjacent normal liver samples. The process was done using miRs microarrays containing probes for about 700 human miRs, including Rosetta Genomics proprietary predicted miRs, as well as control sequences. Differentially and highly expressed miRs were chosen as candidate targets for studying their *in-vitro* function. Antisense Oligos that are complementary to the interesting miR candidates were synthesized using Isis' proprietary chemistry. These antisense oligos were transfected into two HCC cell lines chosen after demonstrating the highest correlation of miRs expression to human HCC tissues. Several antisense Oligos were discovered that could slow or diminish hepatocarcinoma cell line proliferation. This talk demonstrated the potential of miRNA therapeutics approach and the promise in its future development.

Five Chemists Whose Lives Were Saved by Raoul Wallenberg:

Raoul Wallenberg
(Photo: Hagstromer & Qviberg Fondkommission AB, courtesy of USHMM Photo Archives)

Raoul Wallenberg saved the lives of Miklós Bodánszky, Margaret Demény, Lars Ernster, Francis Körösy, Gabor Somorjai and of thousands of others.

Miklós Bodánszky and Peptide Synthesis;
Margaret Demény and Spinal Cord Injuries;
Lars Ernster and Bioenergetics;
Francis Dov Körösy and Applied Physical Chemistry;
Gabor Somorjai and Modern Surface Chemistry.

Bob Weintraub

Miklós Bodánszky and Peptide Synthesis:

Miklós Bodánszky developed methods for the synthesis of peptides. He devised a widely accepted method for the construction of peptide chains by stepwise addition of protected activated amino acids from their components and applied it in the synthesis of the peptide hormone oxytocin and in the first synthesis of the gastrointestinal hormone secretin.

His paper together with Vincent du Vigneaud, *A method of synthesis of long peptide chains using a synthesis of oxytocin as an example*, in *JACS* (1959) was cited as a Citation Classic by *Current Contents*. Of this paper, he wrote, "Early in 1957 my wife, our five-year old daughter, and I arrived as refugees in New York City. I came to join du Vigneaud in his studies (recognized a year earlier by the Nobel Prize) on the chemistry of the peptide hormones oxytocin and vasopressin. Our newly acquired freedom, together with the absence of material possessions such as home, car, or television set, allowed me to concentrate on the task at hand: a new synthesis of oxytocin. At the same time, I was still somewhat obsessed by thoughts about my new procedure for the coupling of amino

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

Left: Miklós Bodánszky, in the early 1960's. Bodánszky developed methods for the synthesis of peptides. His life was saved by Raoul Wallenberg. I am grateful to Miklós' daughter, Dr. Eva Bodanszky, for the photograph.
Right: Margit Kelemen (now Demény), 1938. Photograph was taken after she had completed 4 years at the University of Budapest and 1 year of teacher training and was waiting for acceptance as a Ph.D. candidate.

acids to each other, developed before I left Hungary: the nitrophenyl ester method. Thus, the idea to incorporate only protected-activated amino acids in the synthesis of oxytocin, rather than to follow the classical approach of combining segments of the peptide chain, presented itself quite naturally. The stepwise addition of single residues allowed systematic lengthening of the chain, without endangering the optical purity of the amino acid constituents. Du Vigneaud enthusiastically approved the project and supported it with his tremendous knowledge of the problems surrounding oxytocin, his baby protein. The progress of the synthesis appeared breathtakingly fast. Within a short time we had a fairly large sample of oxytocin in our hand in a yield far exceeding the yields of previous syntheses." (CC, July 14, 1980)

Bodánszky (1915-2007) was born in Budapest. He earned his diploma in 1939 and his doctorate in 1949 from the Budapest Technical University, where he later held the position of lecturer in medicinal chemistry. The ten year period between earning his diploma and his doctorate was a struggle for survival, including forced labor camp and hiding from the Nazis. He was saved by Raoul Wallenberg. (I. Hargittai, Candid Science)

Bodánszky left Hungary in 1956. He held positions in the United States at the Cornell University Medical College, the Squibb Institute for Medical Research and from 1966 until his retirement in 1983 at the Case Western Reserve University in Cleveland.

Margaret Demény and Spinal Cord Injuries:

A major part of Margaret Demény's professional life was devoted to biochemical research on spinal cord injuries. Her main work was the study of the blood supply of the brain during physical rehabilitation. She worked at the Mt. Sinai Hospital in New York City and at New York University. Dr. Kristjan T. Ragnarsson of Mount Sinai Medical Center recalled (2007) her work: "She was working under the direction of Dr. Eric Naftchi on various kinds of biochemical research relating to people that have supported spinal cord injury…Her work with her colleagues at NYU resulted in greatly increased understanding of the function of the sympathetic nervous system following spinal cord injury, as well as of the alterations in numerous endocrinologic and metabolic factors."

In 1942 Demény earned her Ph.D. in chemistry in Budapest before the war, under the direction of Gyula Gróh, with a thesis on *Rotary Dispersion of Aqueous and Carbamide Solutions of Proteins*. Gróh was the only Professor of Chemistry that was willing to take on a Jew for graduate work. Demény was 30 years old and a newlywed of a week when the Germans entered Hungary. Her husband was taken away and she never saw him again. Demény recalls that they did not know what Wallenberg was doing or why. "All we knew was that Wallenberg was saving Jews." Her aunt asked her to move to their apartment because it was in a Swedish-protected house. Demeny says that when she tells her

story that at this point she always has to laugh as she recalls keeping a big suitcase full of food and clothing ready just in case they came for her. "I was no naive." She now knows that the people being taken away were usually taken to the bank of the Danube and shot into the river. Recalling the day after the Russians marched into Budapest, "...we heard that Wallenberg had disappeared, taken by the Russians. Nobody was thinking he would never come back." In 1947 Demeny married again and moved to New York. Her second husband was previously married to a cousin of hers who died in Theresienstadt.

Gabor Somorjai: The Father of Modern Surface Chemistry.

"Somorjai is the world leader in developing modern surface science. He established the molecular foundation of many surface-based technologies. His fundamental surface studies over the past 35 years contributed the main lion's share of molecular level understanding of surface structure, the bonding of adsorbates and the concepts and ingredients responsible for the reactivity of surfaces that helped the development of surface technologies.

Somorjai began the process of discovering the fundamental bases of heterogeneous catalysis, without which the chemical industry as we know it today would not exist. His techniques and the results he obtained bear on many surface features of broad technical importance such as adhesion, lubrication, absorption catalysis and other phenomena that depend on surface interactions."

"One of his major discoveries was that defects on surfaces, like steps and kinks, are where catalytic activity takes place. These defects break and make bonds between atoms, allowing, for example, complex organic chemicals like naphtha to be rearranged into chemicals, such as gasoline.

His approach was to work with simple surfaces-single metal crystals-and discover how chemical reactions occur on them, then extrapolate his findings to more complex surfaces like those used in industrial reactions." (National Science Foundation and UC Berkeley Press Release)

John Meurig Thomas: "It is not, however the volume of Gabor's work, impressive as that is, which is the most conspicuous feature of his accomplishments, it is its quality. Many of his admirers will have their own favorite feature of his work which they would select as being the most noteworthy.

For me, if I had to choose just one example, it would be his classic experiments on the notable differences in behaviour between the five principal high-symmetry surfaces-crystal iron (in the synthesis of ammonia) that stands out as the most elegant. But then there is his recent sum-frequency generation work, or his identification of ethylidyne species at a metal surface, and many, many more highlights." (Top Catalysis, (2001) 14,1).

Gabor Somorjai was born in Budapest in 1935. During the war he was saved by Raoul Wallenberg. Somorjai left Hungary for the United States in 1956. He earned his Ph.D. from the University of California at Berkeley in 1960 and then joined the research staff at IBM at Yorktown Heights, New York. He returned to UC Berkeley in 1964, where he has spent his professional career. He is the recipient of the Wolf Prize in Chemistry for 1998.

Lars Ernster: Bioenergetics.

E. Schon and S. DiMauro : "The history of mitochondrial disease goes back to the early 1960's, however, when Lars Ernster and Rolf Luft in Stockholm described a patient who ate voraciously yet stayed thin, sweating profusely even in winter. Ernster and Luft implicated a defect in mitochondrial energy metabolism and showed that this patient's muscle mitochondria could make only a fraction of the energy they should normally produce; the unconverted fuel was diverted into heat production. The exact cause of Luft disease (perhaps the rarest

Left: Dr. Margaret Demény in a family picture at her granddaughter's graduation from NYU Medical School in 2007. Mr. Mark Leeds (back right), Margaret's son-in-law, wrote to me, "...the photo shows Dr. Margit Demény (a professor emeritus of NYU School of Medicine) together with the two generations she inspired to become physicians. None of this would have been possible without the help of Raoul Wallenberg." (Photo by Rabbi Joshua Lobel, husband of Margaret's granddaughter. Also in photograph partially hidden is Aunt of Mr. Leeds. I am grateful to Mark Leeds, for making available the photographs and for his help during the preparation of this article.)
Middle: Gabor Somorjai. Somojai is known as the *Father of Surface Chemistry*. His life was saved by Raoul Wallenberg. (Photograph courtesy of Lawrence Berkeley National Laboratory.)
Right: Lars Ernster. Ernster's life's work was in the field of Bioenergetics. Ernster and Rolf Luft were the first to describe a mitochondrial disease. His life was saved by Raoul Wallenberg. (Photograph courtesy Department of Biochemistry and Biophysics, Stockholm University.)

condition known: only one other patient has been found) remains unknown, but these investigators broke new ground by linking mitochondrial function defects to human disease." (21st C, 2002)

Ernster: "I became interested in ATP function and in ATP synthesis. Mitochondrion was discovered in 1946 to be the site of ATP synthesis in the cell. Mitochondria are small bodies in the plant and animal cells. This is part of a very big topic called bioenergetics. This is my main field and people associate my name with this field. Cell respiration, photosynthesis, metabolic diseases, and energy metabolism all belong to bioenergetics..... However, on my way I happened to discover, by serendipity a number of reactions and enzymes." [ie, DT Diaphorase, diphospho-triphospo-pyridine-nucleotide-dihydrogen, an important enzyme for detoxification of quinines in the body and an anticancer compound]...

I happened to be studying DT Diaphorase, an antioxidant enzyme, and co-enzyme Q, which is a quinone and which acts as antioxidant in its reduced form. Mitochondria are the main producers of oxygen radicals. We happened to be the first group to describe a mitochondrial disease, and we did this together with people at the Karolinksa Institute in 1959." (I. Hargittai, Candid Science)

Lars (Laslo) Ernster (1920-1998) was born in Budapest. He wanted to study medicine but in 1938 Hungary he could not be admitted to medical school because he was a Jew. He went to Paris to study at the Sorbonne. With the outbeak of the war the French ordered him out of the country. He fled though Italy and returned to Budapest. In Budapest Ernster tutored and worked as a volunteer laboratory technician in a Jewish Hospital until 1943. During this period he was called for forced labor for three months. He was married after the German occupation of Hungary. "We were married on the 5th of May [1944] during a bomb raid, and a non-Jewish friend of ours came with us to hide our yellow David stars." Raoul Wallenberg arrived in Budapest in July, 1944 and operated there until January, 1945. Ernster's father-in-law was one of Wallenberg's closest associates during those six months. The whole family was issued with Swedish passports. "In November, 1944, the arrow-cross people killed every single person in that hospital but by then I was already at the Swedish Embassy."

Ernster went to Sweden in 1946. He earned his Ph.D. at Stockholm University in 1956. Ernster was research scientist and later became head of the Department of Physiological Chemistry at the Wenner-Gren Institute for Experimental Biology. From 1967 until 1986 he was Chairman of the Department and Professor of Biochemistry at the University of Stockholm. He was a member of the Nobel Committee for Chemistry (1977-1988) and a member of the board of the Nobel Foundation.

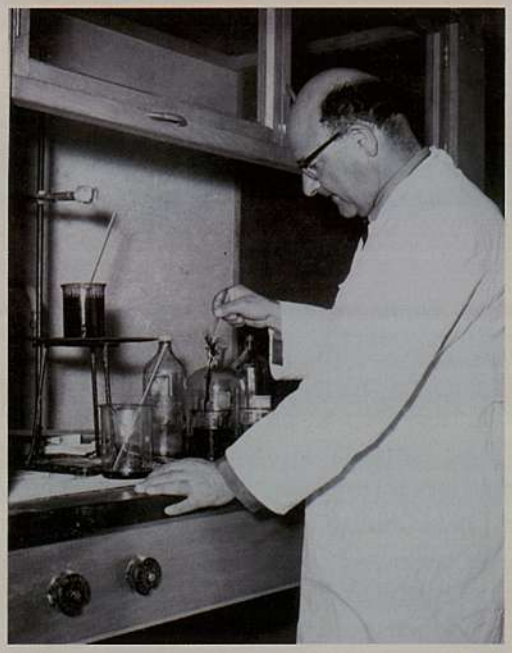
Ernster (1996): "Before the end of the war, we had to move into the cellar of a bank, which was under Swedish protection. Wallenberg, his secretary, his driver, and my whole family lived in that cellar. On the 17th of January,

the Russians were already only a few streets away from us so Wallenberg decided to go over and get in touch with them to inform the Russian commander about what was going on here. He said good bye, and we never saw him again.

I remember an incident in 1944 when I foolishly left the Swedish Embassy without telling anybody about it. I just wanted to meet Edit [his newlywed] who went to a doctor. Across the street there was an arrow-cross guy standing in front of a house, he captured me and took me into the house. I asked him, 'How old are you?' He said, 'I am 16 and I am a student. But now during the day I am involved with capturing people and in the evening we shoot them into the Danube.' I asked him, 'What will happen to me?' He laughed, 'You can guess!' he said. I told him about my papers, but he did not let me show them.

It turned out that they noticed my absence at the Embassy and started to search for me and they found that I was in this house. Around 5 in the afternoon they called me into the commander's office and he told the young boy to take me back to the Embassy building. But this whole incident showed me what people could really turn into. There was this young boy and I asked him, if you had gone to school today, what would have been the subjects today? He said, Well, first we would have had mathematics, then history, and so on. And you don't like to go to school, I asked. No, because I am doing my real duty here and this is more important. This was the general attitude.

When I got back to the Embassy, Wallenberg yelled at me, 'How could you do this? You have your job here, do you have any idea what hell it was for us to find you?' So Wallenberg personally saved my life."



Top: Francis Dov Körösy at the Negev Institutes for Applied Research, 1963. His work was in the field of applied physical chemistry. His life was saved by Raoul Wallenberg.
(Photograph courtesy of Tuviyahu Archives of the Negev, Ben-Gurion University of the Negev.)
Bottom: Edward Teller and Francis Körösy. Tel Aviv, c. 1983. Prof. Teller around this time made frequent visits to Israel and the two old friends tried to meet with each other on each visit. I am grateful to Dr. Yossi Korazim-Korosy for the photograph.

Francis Dov Körösy: Applied Physical Chemistry.

Francis Dov Körösy was born in Budapest in 1906. He earned his Ph.D. from the University of Budpest in 1928. He made aliyah in 1957 and from 1968 was Chemical Laboratory Director at the Negev Institutes for Desert Research, later part of Ben-Gurion University of the Negev. His main areas of work were on barrier layer cells, gas filled lamps, iodides of Ta group metals, solubility of gases, buffers against gastric acidity, electrochemistry of carotinoids and ion-permselective membranes in water desalination.

Körösy: "Everything went well for a while, and there was an agreement between the Swedes and the Szálasi government. However, during the last weeks of the battle for Budapest one such house after another was evacuated by the nyilas (the arrowcross Hungarian Nazis), the inhabitants being led to the nearby banks of the Danube near the Margithid [Margit Bridge] where they were slaughtered and tossed into the icy waters. Only very few managed to escape the shootings by swimming away with their wounds and getting back to dry land further

The Counted Remant:

The following is the preface of the "Counted Remnant: Register of the Jewish Survivors in Budapest." (Hungarian Section of the World Jewish Congress and Jewish Agency for Palestine, 1946):

And the Lord shall scatter you among the nations, and ye shall be left few in number. (Deut. IV, 27.)

This book is one of gladness and of pain. Its editors are glad to publish the names of those who survived all the horrors, all abominations of hatred and war. Each single person mentioned in the columns of this book struggled amidst nerve-killing dread, awful tortures, superhuman sufferings during the last years; each single name was figuring in that collective sentence of death passed by the most barbarous judges of History with a view to exterminate Jews altogether.

The mercy of God, the triumph of eternal justice, the victory of the armies fighting for democracy prevented the Nazi and Nyilas executioners from carrying out their infernal scheme on all who had been sentenced to death.

Everybody turning over the leaves of this book should realize the significance of the fact that also above the will of the power which thought itself to be the strongest there is a higher jurisdiction, preventing the innocent from being entirely exterminated. But he should also realize the heavy burden pressing down upon each single person who is figuring in this book: the dreadful memories of the past, the frightful dreariness of the present, and the unsolved problems of the future.

For we all who remained are now standing here in the world, plundered, humiliated in our human dignity, with souls harassed to death, and alone. Destruction and ruins surround us, the graves of hundreds of thousands of our brethren, and we all are living in the oppressive atmosphere of sorrow... There is not a house where there is not one dead...there is no one among us who would not have lost his dearest ones,-- --those whose names this book can publish no more.

And therefore this book is one of pain at the same time, that of pain and of tears for those who will never return to us. Instead of their names there is only their memory living among us, the memory which the whole of the Jews will never forget.

We have been scattered among the nations and we are left few in number. May the roll of Mtei Mispar, the counted remnant, be received by our brethren in Eretz Ysrael and in the countries of the diaspora as a message, as a hand outstretched towards them, which sends love and which is also awaiting and soliciting for the love missed ever so long.

downriver, to tell their stories. The fortunate inhabitants of some Swedish houses escaped this fate, as the Russians came to occupy Pest in time before their turn was going to come." Körösy was issued a Swedish identity card and was staying in the protected house of the Swedish Red Cross at Károlyi Palota [Károlyi Palace, originally the residence of the Counts Karolyi, an ancient Hungarian artistocratic family]. "After midnight a group of nyilas people came, accompanied with police and Interior Ministry personnel. A woman swallowed poison and collapsed but did not die, and in the ensuing confusion someone managed to contact Wallenberg..." Körösy was saved by Wallenberg's intervention. (Recollections of Francis Körösy, unpublished.)

Acknowledgements:

I am grateful to Prof. István Hargittai for the unpublished transcript of his conversation with Prof. Margaret Demény (2007) and for the use of published conversations in *Candid Science* with Prof. Miklós Bodánszky and Prof. Lars Ernster. I thank Mrs. Rose Post for copies of her relevant newspaper articles (also *Salisbury Post Online*, 2001); Dr. Ragnarsson for his recollections of Prof. Demény; Dr. Jean Kloos-Fishman for making available the relevant sections of the unpublished memoirs of Prof. Körösy. Dr. Kloos-Fishman has been a leader for many years in efforts on behalf of Raoul Wallenberg and now, as hope has faded for Raoul Wallenberg's return, she is active in keeping alive his memory.

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I encourage every one of you to contribute articles to the future issues of *Chemistry in Israel.* These articles could cover your own science or other areas that could be of great interest to our readers. A typical article would span approximately 6 journal pages. Please contact the Editor, Prof. Mati Fridkin in order to discuss with him the topic and size of your proposed contribution.
I appreciate very much your help,

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