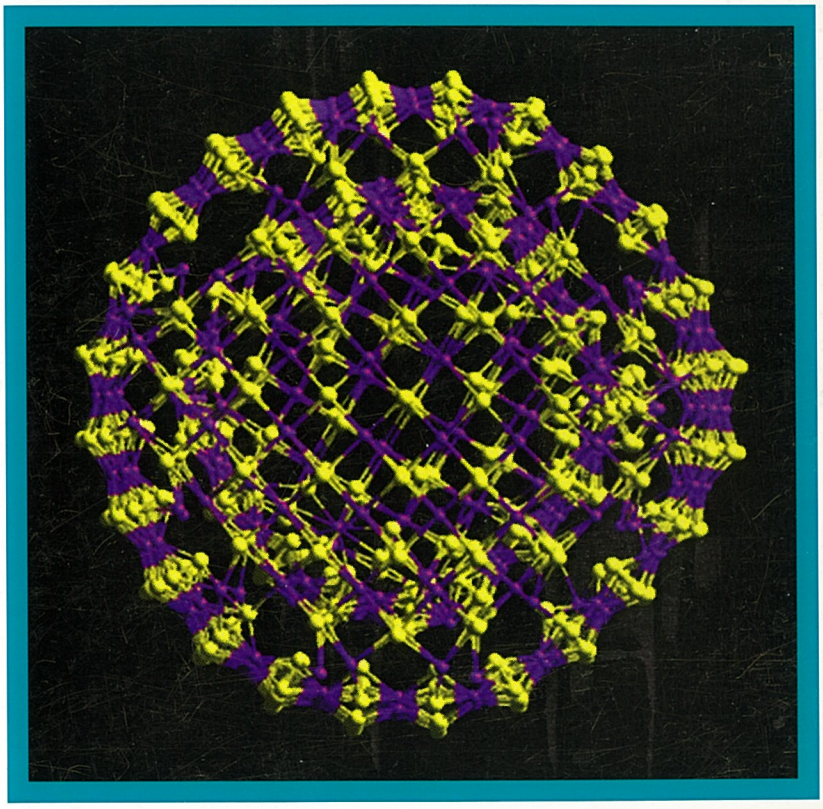
כימיה בישראל
CHEMISTRY IN ISRAEL

Bulletin of the Israel Chemical Society בטאון החברה הישראלית לכימיה

Issue No. 20 December 2005 גליון מספר 20, כסלו תשס"ו



Inorganic Fullerenes - IFs

See article by Reshef Tenne, p. 5

כימיה בישראל - בטאון החברה הישראלית לכימיה

גליון מספר 20, כסלו, התשס"ו, דצמבר 2005 http://www.weizmann.ac.il/ICS

כתובת המערכת: פרופ' משה לוי, מחלקה לחומרים ופני שטח, מכון ויצמן למדע, רחובות 76100 moshe.levy@weizmann.ac.il

תוכן העניינים

דבר המערכת

בבחירות שהתקיימו בחודש נובמבר השנה נבחר פרופ' שלמה מרגל, מאוניברסיטת בר-אילן, לנשיא הבא של החברה. כמו כן נבחרו 9 חברי הועד המנהל. ברכות לנבחרים ואיחולי הצלחה במילוי תפקידם.

במאמרו על "פולרנים אנאורגניים - IFs" מביא פרופ' רשף טנא את ספור פריצת הדרך שנבעה מעבודתו החלוצית ב-1992, שבה הראה שפולרנים וננו-צינוריות אינם בלעדיים לאטום הפחמן, וניתן להכינם גם מיסודות אחרים בטבלה המחזורית. מאז דווח בספרות על מאות מבנים סגורים מן הסוג הזה, ועל תכונותיהם המיוחדות והמעניינות ביותר. בזכות עבודותיו אלה זכה פרופ' טנא בהכרה בינלאומית וקבלת מדליה מטעם ה - Materials Research Society וכן למאמר מערכת מרכזי בבטאון של האגודה האמריקאית לכימיה Chemical & Engineering News, August 29, 2005, p. 30.

פרופ' מאיר וילצ'ק ושותפיו מביאים במאמרם על הכרה ביולוגית ושימושיה, את התפתחות שיטת ה- Affinity Chromatography שנתגלתה על ידי וילצ'ק ושותפיו, ושעיקרה ניצול תכונות ההכרה המיוחדות של מולקולות ביולוגיות, להפרדה בין מולקולות ביולוגיות שונות. מעטים המדענים בעולם היכולים לזקוף לזכותם ש - 95% מכל שיטות ההפרדה הספציפיות של מולקולות ביולוגיות, משתמשות עד היום בשיטה שפותחה על ידם ב- 1968. הערך המסחרי של המוצרים המיוצרים בעזרת השיטה נאמד כיום בסכום של 40 מיליארד דולר בשנה. לפרסים הרבים שבהם זכה פרופ' וילצ'ק עד היום, הצטרף השנה גם פרס א.מ.ת.

חברת Peptor החלה את דרכה בפארק המדע רחובות/נס-ציונה. לימים הפכה לחברת DeveloGen. החברה מתמקדת בפיתוח פפטידים כתרופות, בעזרת מתודולוגיה פפטידומימטית, שפותחה על ידם. סיפורה של החברה ותוכניותיה לעתיד מובאות ע"י ד"ר נורית ליבנה וד"ר תמר יחזקאל.

ויקטור גולדשמידט נחשב לאבי הגיאוכימיה. הוא קבע כללי יסוד לגבי התגבשות המינרלים בטבע, והפך את הגיאוכימיה מאוסף עובדות ניסיוניות,למדע שמסביר את המחזוריות המתבקשת מתכונות היסוד של היסודות. את סיפור חייו המעניין של ויקטור גולדשמידט, מביא כתבנו הנאמן להיסטוריה של הכימיה, ד"ר בוב וינטרוב.

לבסוף נזכיר לקוראינו שהכינוס השנתי ה- 71 של החברה יתקיים במלון אינטרקונטיננטל בתל-אביב, ב- 27-28 בפברואר, 2006 ואנו מצפים להשתתפות ערה.

פרטים על הכינוס ניתן למצוא בתמונת השער האחורי של הבטאון ובאתר www.congress.co.il/chemistry2006

בחירות למוסדות החברה הישראלית לכימיה

בבחירות שהתקיימו בחודש נובמבר 2005 נבחר

לנשיא החברה:

פרופ' שלמה מרגל - אוניברסיטת בר־אילן

לחברי הועד המנהל:

פרופ' טימור באזוב - הטכניון
פרופ' סילביו ביאלי - האוניברסיטה העברית
ד"ר חיים טוביאס - הקריה למחקר גרעיני
פרופ' רז ילינק - אוניברסיטת בן־גוריון
ד"ר מרדכי ליבנה - אוניברסיטת בר־אילן
ד"ר רמי לידור־הדס - טבע תעשיות פרמצבטיות בע"מ
פרופ' רוני נוימן - מכון ויצמן למדע
ד"ר מירה פרייברג - תרכובות ברום בע"מ
פרופ משה קול - אוניברסיטת תל־אביב

לחברי ועדת הביקורת:

פרופ' זאב גולדשמידט - אוניברסיטת בר־אילן
פרופ' מנחם כפתורי - הטכניון
פרופ' משה לוי - מכון ויצמן למדע

ה"כימיאדה" התשיעית

ה"כימיאדה" התשיעית יצאה לדרך

פרופ' גבי קוונצל וגב' מירה כ"ץ מהמחלקה לכימיה בטכניון מוסרים כי התחרות השנתית לתלמידי כימיה בארץ יצאה לדרך. זו התחרות השביעית ברציפות (התשיעית בסדרה) המתקיימת מדי שנה בטכניון. הדווח מפרט כי ההתענינות בקרב תלמידי התיכון עולה גם השנה ומספר הבקשות לבחינה הגיע לכדי חמשת אלפים. לא ברור עדין מספר הנבחנים בפעל, אך מספר זה גבוה באפן משמעותי משנים קודמות. אין ספק שהפעילות הברוכה והרמה הגבוהה ב"כימיאדה" הם גורמים חיוביים ביותר בקדום הנושא. פרטים מלאים יותר ימסרו בגליון הבא של "כימיה בישראל".
יבורכו כל העוסקים במלאכה וברכת הצלחה לכל הנבחנים.

נשמרת היציבות במספר הסטודנטים הלומדים כימיה

ארנון שני, המחלקה לכימיה, אוניברסיטת בן-גוריון בנגב

בשנים האחרונות היינו עדים לעליה מרשימה במספר התלמידים המתחילים למודי כימיה באוניברסיטאות בארץ. אשתקד, לראשונה, נעצרה העליה במספר התלמידים החדשים, דבר שהוא טוב לכשעצמו. אם נוסיף לכך את הידיעה כי במקביל הועלה סף הקבלה והמתקבלים החדשים הם בעלי נתוני פתיחה טובים יותר, הרי מקצוע הכימיה זוכה בשתי הטבות: האיכות והכמות האופטימלית של תלמידי כימיה (ראה: "התיצבות במספר הלומדים כימיה במוסדות להשכלה גבוהה", כימיה בישראל גליון 18, עמוד 3). הנתונים המופיעים בטבלה מס. 1 מראים על מספר תלמידים חדשים הקרוב למספרים של אשתקד.

טבלה מס. 1. מספר הלומדים כימיה במוסדות להשכלה גבוהה בשנת הלמודים תשס"ו (2005/6)

אוניברסיטה/ מכון	תאר ראשון		תאר שני		תאר שלישי	
	שנה א'	סה"כ	חדשים	סה"כ	חדשים	סה"כ
הטכניון	94 (104)	420 (432)	14 (20)	61 (65)	10 (2)	54 (61)
בר־אילן	101 (121)	429 (435)	54 (32)	88 (65)	13 (9)	76 (74)
תל־אביב	98 (93)	280 (284)	26 (21)	60 (56)	18 (15)	84 (65)
ירושלים	75 (103)	243 (299)	39 (61)	123 (121)	12 (7)	125 (101)
בן־גוריון בנגב	77 (81)	248 (248)	18 (9)	32 (28)	4 (7)	43 (42)
מכון ויצמן למדע	------	-------	22 (25)	46 (48)	36 (31)	128 (121)
סה"כ	445 (502)	1620 (1698)	173 (168)	410 (383)	93 (71)	510 (464)

המספרים בסוגריים הם נתוני הלומדים בשנת תשס"ה.

העליה ברמת המתקבלים (לפחות לפי נתוני מבחני הבגרות ו/או המבחן הפסיכומטרי) משיגה שתי מטרות - האחת היא העלאת רמת הלמודים בשנות הלמוד ומתן אפשרות למרצים לדרש יותר מהתלמידים ובכך להעלות את רמת ההבנה והידע הנרכשים במהלך הלמודים; והשניה - עליה ברמת הבוגרים אשר יצאו לשוק העבודה עם תום למודיהם, בכל רמה בה יסיימו. אלה הן חדשות טובות הן למרצים והן למעסיקים של הכימאים במגוון התחומים והמגזרים.

ניתן לצפות כי מספר תלמידי המחקר יעלה בשנים הבאות, עם השלמת הלמודים לתאר ראשון של המחזורים הגדולים. מגמה זו כבר מתחילה להסתמן בשנה הנוכחית.

INORGANIC FULLERENE-LIKE STRUCTURES - IFS

Reshef Tenne, Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot

1. Introduction

It was proposed in 1992 [1] that the propensity of graphite to form fullerenes and nanotubes is not unique and is not limited to only one element in the periodic table. In fact this property is likely to occur in nanoparticles of any compound with layered structure. Fig. 1 shows a nanocluster of MoS_2 emphasizing the difference between fully bonded bulk atoms and rim atoms with dangling bonds.

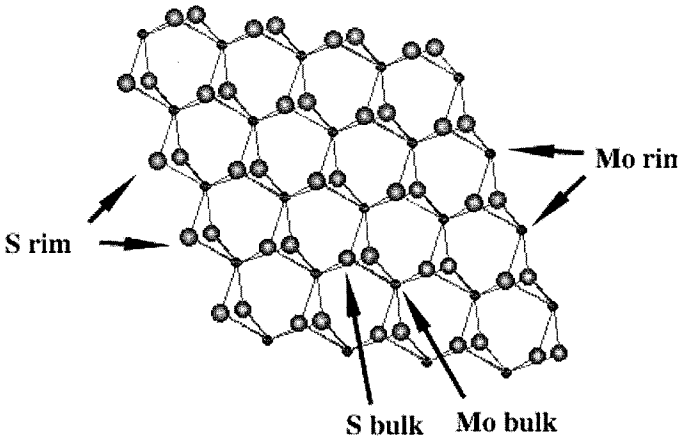


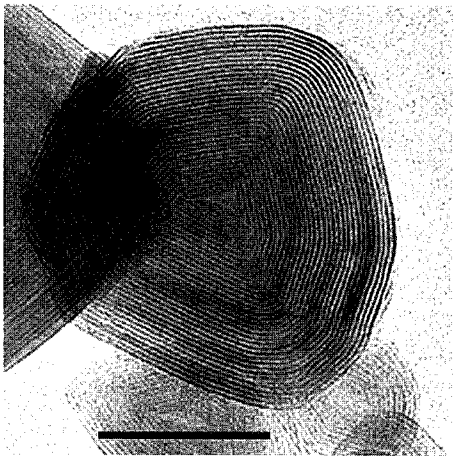
Fig. 1. Schematic drawing of MoS_2 nanocluster from the [001] direction. Note that while the bulk Mo and S atoms are 6-fold and 3-fold bonded, respectively, the rim atoms are only 4-fold and 2-fold bonded only, making the planar nanostructure chemically unstable and forcing it to fold and close onto itself.

It was suggested therefore that the formation of closed polyhedra (fullerene-like structures) and nanotubes is a generic property of (2-D) layered materials and this was indeed demonstrated for W and Mo chalcogenides [1-3]. These structures were termed **Inorganic Fullerene-like materials *(IF)***. Multilayer polyhedra (onions or nested structures) and nanotubes make also part of the *IF* family and in fact might be the most stable of all *IF* structures. **Fig. 2** shows a transmission electron microscope (TEM) image of a multiwall MoS_2 nanoparticle with fullerene-like structure (a) and a multiwall WS_2 nanotube (b). The existence of *IF* structures was confirmed through numerous studies during the last few years.

Nanotubes and fullerene-like nanoparticles of various 2-D compounds have also been studied extensively theoretically in recent years. These observations suggest that indeed the *IF* phase makes part of the phase diagram of elements, which form layered compounds, like Mo and S, or Ni and Cl [4]. If the otherwise planar crystallites are not allowed to grow beyond a certain size (less than say 0.2 microns) the closed cage phase becomes the thermodynamically favorable state. Globally however, the *IF* phase is less stable than the bulk 2-D material, which often comes in the form of platelets.

In practice, the synthesis of *IF* phases proved to be exceedingly difficult in several cases [4,5]. The synthesis and structural elucidation of *IF* materials rely primarily on transmission electron microscopy (TEM) and its associated techniques, like electron diffraction (ED), energy dispersive X-ray spectroscopy (EDS) and more recently, electron energy loss spectroscopy (EELS) [6].

Nanotubular structures from various 3-D compounds, like GaN [7], InN [8] and many others were also recently reported. A clear distinction holds between nanotubular structures obtained from isotropic (3-D) and layered (2-D) compounds. 2-D compounds form energetically stable and perfectly crystalline closed-cage structures by folding the molecular sheets into a nanotube. In the case of polyhedra of 2-D



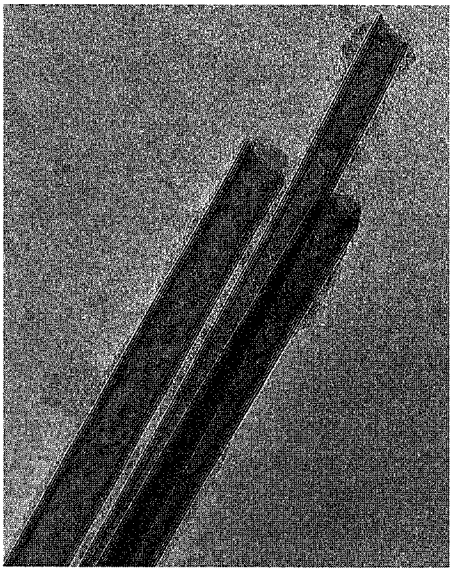


Fig. 2. TEM image of a multi-wall MoS_2 fullerene-like particle with 30 closed layers (a). Scale bar is 20 nm. Three WS_2 nanotubes 15-20 nm in diameter (b). The distance between each two layers is 0.61 nm. The c-axis [001] is always normal to the surface of the nanotube.

compounds, they are obtained by introducing elements of lower symmetry, like pentagons or rhombi (squares) into the otherwise hexagonal (trigonal) lattice. Clearly, a pure 3-D compound cannot form a perfectly ordered, flawless nanotubular or polyhedral structure by folding. The hollow nanotubes are thus obtained either by using a solid [7] or a molten [8] template.

Nanotubes of various kinds were synthesized in macroscopic amounts, which permitted systematic studies of their properties and proposing novel applications for such nanostructures. Among them one can find WS2 [9,10], MoS_2 [11], BN [12], V_2O_5 [13], $H_2Ti_3O_7$ [14] and many more. However, by far the successful synthesis of multiwall nanoparticles of WS_2 [15] and MoS_2 [16] with closed-cage (fullerene-like) structure was the most rewarding accomplishment, in this respect. This phase is produced from the respective oxides in a pure form in quantities approaching a kg/day. In view of the large commercial potential, the production of this phase is expected to reach a few tons/day and above in the next few years.

The mathematical theory of polyhedra made of a single layer is well established [17]. The geometrical analysis of polyhedra and nanotubular structures made of two and more interconnected layers has appeared only very recently, as a result of the discovery of the *IF* phases [18-20]. This development reflects the need to address the structure of nanotubes and polyhedral structures of inorganic layered materials. Such compounds consist of a stacking of molecular layers with more than one kind of atom, with strong and oriented chemical bonds interconnecting the different atoms within the molecular sheet.

Among the list of important issues in this area, the making of size and shape selective clusters analogous to C_{60} is perhaps the most important and demanding one. It was found that different growth strategies lead to inorganic fullerene-like nanoparticles and nanotubes with quite different structures. Each method produced nanotubes of different number of walls and chirality with size selectivity remaining illusive target thus far. Some progress was reported in 2001 with the synthesis of bundles of single wall MoS_2 nanotubes [21] using C_{60} as a growth promoter. However, so far this observation did not transpire into a global strategy to synthesize single wall MoS_2 nanotubes

of any desirable diameter and chirality. Notwithstanding this preliminary report, single-wall nanotubes having accurately controlled diameter and chirality of no other metal dichalcogenide compound could be synthesized so far.

The mechanical properties of inorganic nanotubes are being investigated in some detail in recent years. BN nanotubes were shown to exhibit Young's modulus almost as high as that of carbon nanotubes [22]. The mechanical properties of individual WS_2 nanotubes have been investigated in quite a detail using both experiment and theory [23,24]. These studies and others show that despite their smaller Young's modulus and their larger specific weight compared to carbon nanotubes, inorganic nanotubes may find numerous applications in ultra-high strength nanocomposites, mostly due to their high compression strength.

The numerous potential applications of inorganic nanotubes and fullerene-like nanoparticles are highlighted in a number of recent studies [25] and will be discussed in some detail below. Most importantly, *IF*-WS_2 and *IF*-MoS_2 were shown to exhibit superior tribological behavior to all known solid lubricants, particularly under high loads. This behavior offers a plethora of potential applications, which are being contemplated in joint development programs with major industrial manufacturers.

II. Synthetic strategies

The synthesis of nanotubes from inorganic compounds has witnessed a kind of an explosive growth in recent years. Nanotubes of various inorganic compounds have been synthesized by a variety of methods. The availability of some of these nanotubes in large amounts permitted a systematic study into their physical and chemical properties. Thus macroscopic quantities of WS_2 and MoS_2 multiwall inorganic nanoparticles with fullerene-like structure [4,15,16] and various inorganic nanotubes were realized by different strategies [7-13,26-28]. Each of these techniques is very different from the others and produces nanotube and fullerene-like material of somewhat different characteristics. This fact by itself indicates that *IF* materials (including nanotubes) of 2-D metal-dichalcogenides are a genuine part of the phase-diagram of the respective constituents. Of noticeable importance, are the synthesis of bundles of iodine doped single wall MoS_2 nanotubes [21] and MoS_2 nanooctahedra [29].

IIa. *IF*-MX_2 (M=transition metal; X=S,Se,Te)

One of the most successful synthetic methods that leads to a highly crystalline MS_2 (M=Mo,W) nanotubes [21,27,28] is making use of chemical vapor transport, which was used extensively for the growth of high quality single crystals of layered metal-dichalcogenides (MX_2) compounds. Here, MX_2 powder (or M and X elements in the 1:2 ratio) is placed on the hot side of an evacuated quartz ampoule, together with a halogen transport agent. A temperature gradient of 20-100 °C is maintained along the ampoule. After a few days, a single crystal, nanotubes or mixtures thereof are obtained on the colder side of the ampoule.

Synthesis of MoS_2 nanotubes using a solid template was also reported [26]. This synthesis is based on a generic deposition strategy, which was proposed by Martin and further perfected by Masuda and co-workers [30]. Nonuniform electrochemical corrosion of an aluminum foil in an acidic solution produces a dense pattern of cylindrical pores, i.e. anodic alumina oxide (AAO) membrane. This membrane serves as a solid template for the deposition of nanofilaments from a variety of materials. $(NH_4)_2MoS_4$ precursor was deposited from solution and annealed at 450 °C. The AAO membrane was dissolved in KOH releasing a large amount of MoS_2 nanotubes. The limited thermal stability of the

alumina membrane did not allow using annealing temperatures higher than 500 °C, and consequently the crystallinity of the nanotubes was found to be quite poor. In fact, the MoS_2 nanotubes resembled more bamboo-like shaped hollow fibers [26]. More recently numerous 1-D nanostructures, like nanowires and nanotubes were prepared using the AAO membrane.

The growth mechanism of *IF*-MS_2 (M=Mo,W) materials by the sulfidization of the respective oxide nanoparticles, has been elucidated in quite a detail [3,16] and was also described in a number of papers and review articles. In brief, the initial step in this reaction is the sulfidization of the surface of the oxide nanoparticles at temperatures between 750-900°C in an almost instantaneous reaction. This first sulfide layer passivates the nanoparticle surface and prevents coarsening of the nanoparticles into larger platelets. In the next slow step, the partially reduced oxide core is converted into metal-sulfide in a quasi-epitaxial layer by layer process, leading to a nested multilayer core. The growth mechanism of *IF*-MoS_2 nanoparticles was elucidated using a three-region reactor, which permitted a good control over the growth parameters [16].

Pure WS_2 nanotubes, 2-10 mμ long and with diameters in the range of 20-30 nm, were reported by a number of research groups [9-11,31]. An important intermediate in the conversion of oxide nanowhiskers into such nanotubes is the monoclinic $W_{18}O_{49}$ phase with pentagonal columns and hexagonal channels [32]. This phase provides a sufficiently stable but open structure for the sulfidization to proceed until the entire oxide core is consumed and converted into the respective sulfide.

Using a fluidized bed reactor (FBR), synthesis of multi grams quantities of very long WS_2 nanotube phases, was accomplished [33]. The nanotubes obtained in this reaction are open ended, 15-20 nm in diameter and 4-8 layers thick. Some are as long as a few hundred microns, very uniform in shape, many of them have quite perfect crystallinity.

Fullerene-like MoS_2 nanoparticles were also synthesized by using electron beam of MoS_2 crystallites [34], and by microwave irradiation of a gas mixture containing the metal carbonyls [35]. Here, $Mo(CO)_6$ and $W(CO)_6$ powders were vaporized and then mixed with a heated H_2S(1%)/argon atmosphere, under microwave irradiation. *IF* nanoparticles were formed when the reactor temperature was raised to 580°C.

More recently a new strategy has been adopted for the synthesis of *IF*-MS_2 and *IF*-MSe_2 nanoparticles using metal halides and carbonyls as precursors. These compounds have high vapor pressure already at temperatures not higher than 300°C. Furthermore they are very reactive with respect to H_2X vapor, forming MX_2 nuclei which are bound to grow very fast in the reaction atmosphere. The first successful synthesis using this approach was demonstrated for NbS_2 [36]. Subsequently, open-ended TiS_2 nanotubes were synthesized by the reaction of $TiCl_4$ with H_2S [37]. In this kind of reaction, numerous nuclei are formed instantaneously due to the high exothermicity of the reaction and subsequently grow to nanotubes and nested nanoparticles through nucleation and growth mechanism. In another report, fullerene-like TiS_2 nanoparticles with very high degree of crystallinity were obtained using $TiCl_4$ and H_2S as precursors [38]. The perfectness of the nanoparticles topology was attributed to the use of a vertical reactor. Typical nanoparticles contain 80-120 layers; they are almost free of a hollow core and seem to be quite spherical in shape (see **Fig. 3**).

An interesting technique for the synthesis of MoS_2 nanoparticles with fullerene-like structure by the arc-discharge technique was reported as well [39]. Later-on, an alternative version of this technique with the electrodes fully immersed in aqueous solution, which tame the reaction and leads to a better control of the reaction products, was also reported [40].

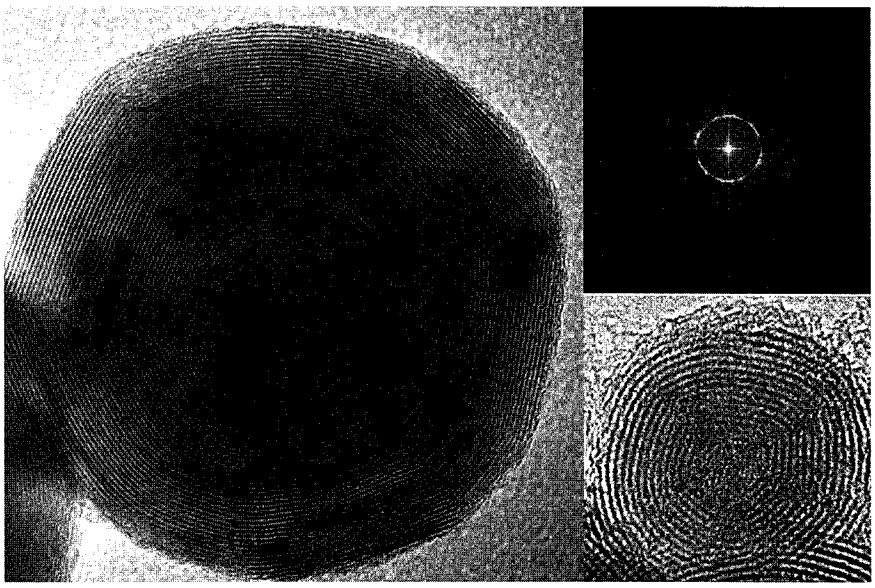


Fig. 3. TEM image of a typical *IF*-TiS_2 nanoparticle (left), produced in the vertical set-up. The interlayer distance is 5.8 Å and the diameter of the nanoparticle is larger than 70 nm. Insert shows the fast Fourier transform (FFT) of the shown nanoparticle. On the right a small nanoparticle of the same kind is shown. Adopted from Ref. [38].

IIb. Metal oxides nanotubes via soft chemistry and other methods

Soft chemistry processes, like hydrothermal, sol-gel, intercalation reactions, sonochemical reactions, etc. play an ever larger role in the chemistry of inorganic compounds and nanomaterials in particular.

Vanadium oxide nanotubes were obtained by first forming V_2O_5 sol which was prepared by mixing vanadium (V) oxide triisopropoxide with hexadecylamine in ethanol. Aging the solution while stirring resulted in the hydrolysis of the vanadium oxide which transformed into a gel [13]. Subsequently, a hydrothermal treatment at 180° C lead to the synthesis of nanotubes with the formal composition $VO_{2.45}(C_{16}H_{33}NH_2)_{0.34}$ (VO_x-alkylamine).

Carbon nanotubes were used as templates for the deposition of V_2O_5 nanotubes; the solid template was subsequently removed by burning the sample in air at 650°C [41]. This strategy can be easily adopted for the synthesis of different oxide nanotubes, as shown below.

One of the most remarkable accomplishments of the soft chemistry processes in this field is the synthesis of what was initially believed to be TiO_2 nanotubes [42]. The structure of these nanotubes was later shown to be related to the series of layered titanates, like $H_2Ti_3O_7$ [14]. Careful inspection reveals that these nanostructures are in fact nanoscrolls, which is not surprising given the low temperatures used for the synthesis. Given the simple synthesis and the importance of titanium oxides for numerous applications, it is not surprising that recently a wave of studies has appeared on the titanate nanotubes (*vide infra*).

A remarkable manifestation of the kinetic stabilization of closed fullerene-like nanostructures was demonstrated recently in the synthesis of tiny amounts of *IF*-Cs_2O nanoparticles [5]. Films of cesium oxides with approximately 2:1 Cs to O ratio and at ~ a monolayer level dimensions are widely applied onto the surface of e.g. S-1 photocathodes, negative electron affinity (NEA) devices, and also discharge

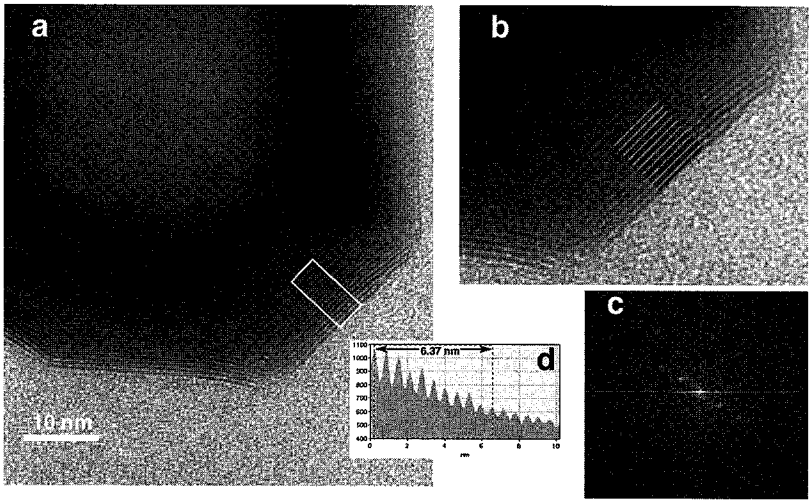


Fig. 4. TEM micrograph showing: (a) A blown-up view of a part of the IF-Cs2O nanoparticle; (b) higher magnification of the IF-Cs2O nanoparticle displayed in (a) with a computer simulation of the image overlaid on the lattice image. Note the good agreement between the simulated and experimentally observed image; (c) Fourier transform (FFT) of the framed area in (a); (d) line profile of the framed area in (a) showing an interlayer spacing of 6.37 Å. Adopted from Ref. [5].

lamps, television cameras, lasers, etc. These films reduce the work-function of the electrode increasing thereby the electron emission currents and the long wavelength response of these devices. Unfortunately, these films are highly reactive and they are damaged or destroyed by short exposure to low vacuum conditions. Crystallites of the layered compound 3R-Cs_2O closed in sealed ampoules were laser ablated and subsequently inserted into the TEM through an air-tight environmental chamber. A few nested closed nanoparticles of Cs_2O were observed (**Fig. 4**). When taken out of the microscope they showed a gradual exfoliation, but even after one hour air-exposure the inner layers of the fullerene-like nanoparticles remained intact though a small lattice expansion, probably due to partial water intercalation, took place.

IIc. Metal halide *IF*'s

Numerous metal halides, hydrates of metal-halides, and metal oxyhalides are known to possess a layered structure and are therefore potential candidates for the synthesis of fullerene-like structures and nanotubes. In contrast to the metal dichalcogenides which are very covalent in nature, the chemical bond in the metal halides, and most particularly in the metal chlorides, is very polarized with large density of electron cloud on the halide atom. Therefore these compounds are in general very hygroscopic and in certain cases ($MgCl_2$) even deliquescent, i.e. dissolve in their own water of hydration. The first demonstration for the kinetic stabilization of the *IF* structures was obtained with the layered compound $NiCl_2$. *IF* nanoparticles thereof were reported using first sublimation-condensation technique and more recently laser ablation [4b]. $CdCl_2$ and its first hydrate $CdCl_2.H_2O$ are compounds with layered structure. $CdCl_2$ has a hexagonal structure with two $CdCl_2$ layers in the unit cell (2H). On the other hand $CdCl_2.H_2O$ has a rhombohedral unit cell with three $CdCl_2.H_2O$ layers (3R). Irradiation of the 3R powder by the electron beam of a transmission electron microscope (TEM) leads to the loss of the water molecules and recrystallization of the powder into $CdCl_2$ nanoparticles with closed cage polyhedral structures [43]. Since bulk $CdCl_2$ is

extremely hygroscopic, it is impossible to handle the bulk material in the ambient atmosphere. In contrast, the fullerene-like structures are perfectly stable in the ambient, which again is a manifestation of the kinetic stabilization of the closed cage structures. *IF* nanoparticles of CdI_2 and $NiBr_2$ were also recently reported.

IId. Nanotubes from non-layered compounds

Early studies showed that quasi-isotropic 3-D compounds yield mostly amorphous or polycrystalline nanotubes. These nanotubes were obtained, e.g. by depositing a precursor on a nanotube-template followed by calcination. Using solid templates, like carbon nanotubes, nanowire, porous alumina (AAO), or soft templates, like elongated micelles various nanotubes of 3-D compounds were obtained.

Recent studies indicated that almost perfectly crystalline nanotubes of 3-D compounds can be synthesized in a reproducible manner. Thus faceted GaN nanotubes with hexagonal cross-section were obtained by the reaction of trimethylgallium and ammonia on an ordered array of ZnO nanowires, which served as a template [7]. The template was subsequently removed by thermal reduction and evaporation of the zinc metal core. Carbothermal synthesis was used ingeniously to synthesize nanotubes of various 3-D oxides, nitrides and sulfides. For example, in a reaction of this kind [8,44], heated graphite was used to reduce a solid precursor M_2O_3 (M=Al,Ga,In) producing a volatile intermediates: M_2O and CO according to the proposed reaction:

$$M_2O_3(s) + 2C(s) \rightarrow M_2O(g) + 2CO(g) \quad (1)$$

Subsequently, the intermediates reacted with nitrogen gas (ammonia) producing MN nanotubes with faceted cross-section according to the reaction:

$$M_2O(g) + CO(g) + N_2 \rightarrow 2MN(NT) + CO_2(g) \quad (2)$$

M_2O_3 (M=Ga,Al,In) nanotubes stuffed with M in their core [45] and ZnS [46] nanotubes were formed by a similar carbothermal reaction. Here the reduction of the metal oxide by the heated graphite occurs at elevated temperature. The molten metal-M serves as a nuclei and template for furthering the nanotube's growth. **Fig. 5** shows faceted ZnS nanotubes with wurzite lattice prepared in an induction oven at 1700°C under water vapor pressure. The water vapor facilitated the chemical vapor transport by reacting with the graphite crucible forming a reactive reducing mixture of $CO+H_2$ gases.

It must be born in mind however, that unlike nanotubes made of 2-D (layered) compounds, which are

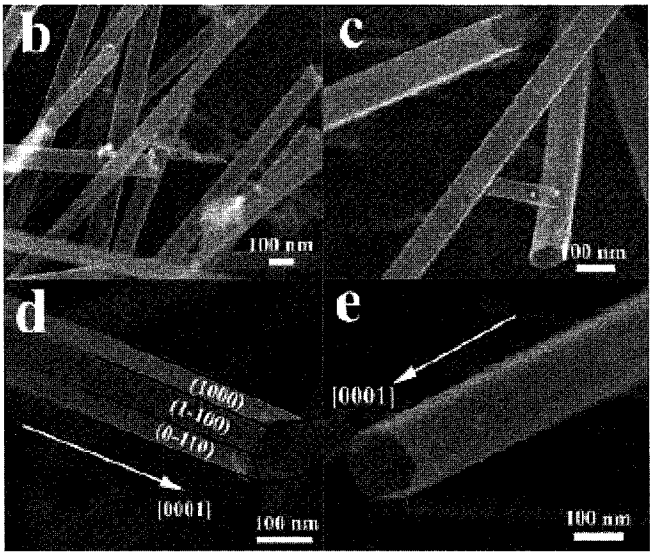
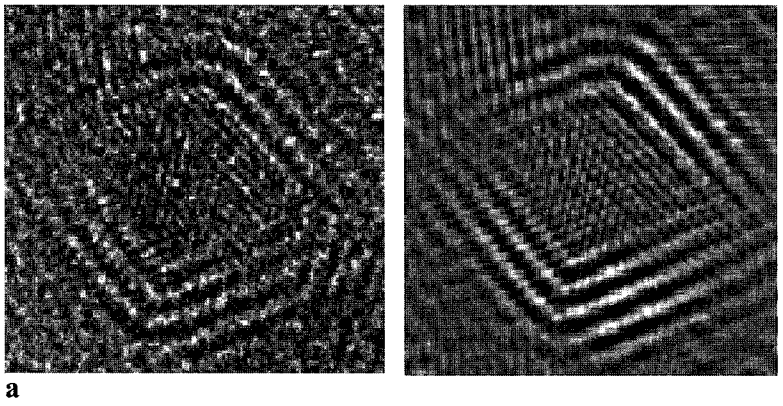


Fig. 5. SEM micrographs of ZnS nanotubes obtained by heating ZnS powder in graphite crucible in the presence of water vapor. The growth axis of the nanotubes is [001]. Adopted from Ref. [46].

inherently stable in the nano-range, those made from 3-D compounds, like ZnS are not. Furthermore, the surfaces of nanotubes made of 3-D compounds are not passivated and often they react with the ambient. Notwithstanding their limited stability, such nanotubes may exhibit rich phenomena and find numerous applications.

The rational synthesis of peptide based nanotubes by self-assembling of polypeptides into supramolecular structures was also demonstrated. This self-organization leads to peptide nanotubes, having hollow channels 0.8 nm in diameter and a few hundred nm long [47]. The connectivity of the proteins in these nanotubes is provided by weak hydrogen bonds. These structures benefit from the relative flexibility of the protein backbone, which does not exist in nanotubes of covalently bonded inorganic compounds. Self-assembly of a very short peptide, the Alzheimer's beta-amyloid diphenylalanine structural motif, led to the formation of discrete and stiff nanotubes [48]. These nanotubes are stabilized by the π–π interaction of the adjacent aromatic groups of the diphenylalanine.

Early on it was recognized that layered compounds made of the X-M-X structure, like MoS_2, can possibly form stable point defects other than pentagons, and most particularly triangles or/and rhombi [2]. Preliminary evidence supporting the idea of nanotetrahedra and nanooctahedra, which have four triangles and six rhombi in their corners, respectively, were found early on. However, the most compelling evidence in support of this idea was obtained in a soot collected from laser ablated MoS_2 [29]. Nanooctahedra consisting of 2-4 layers (see **Fig. 6a**) with the inner one counting about 600 molybdenum and 1200 sulfur atoms, respectively, are routinely found in laser ablated [49a] and arc discharge [40] MoS_2 samples.



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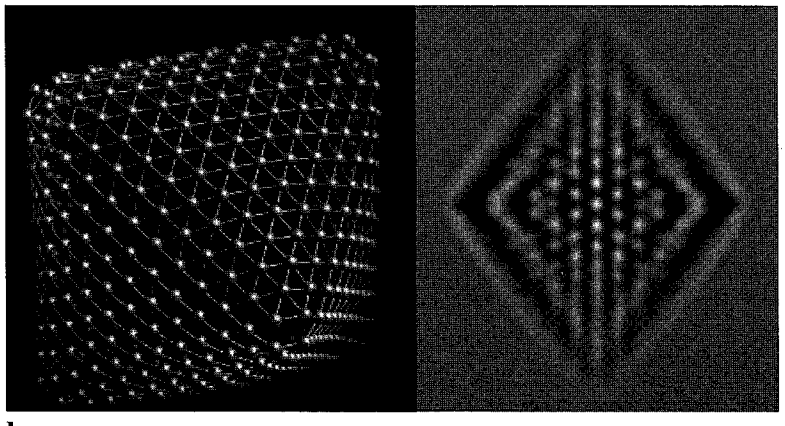

b c

Fig. 6. (a) HRTEM image of a MoS_2 nanooctahedron produced by laser ablation (left) and its filtered image after FFT and back transform (right). (b) Schematic presentation of the molybdenum atoms arrangement in a MoS_2 nanooctahedron consisting of 572 Mo atoms [After 49a]. (c) Simulation of a TEM image of a nanooctahedron [After 49b].

Schematic presentation of the Mo network in such a nanooctahedron is presented in **Fig. 6b**. Fig. 6c shows an image simulation of a TEM micrograph of an individual nanooctahedron [49b]. The rhombi in the corners of such nanooctahedra are clearly delineated. Much effort is currently undertaken to elucidate the structure of such nanooctahedra in various laboratories.

With the advent of computational methods and first principle (density functional theory-DFT) methods in particular, great progress has been accomplished in analyzing the structure and properties of *IF* nanoparticles, and most impressively also the prediction of new such nanostructures which were later on synthesized in the laboratory. The pioneering work of the Cohen/Louie group who studied BN and related nanotubes, and that of other groups who elucidated the structure of the fullerene-like analogues, should be noted [50]. Later on Seifert and co-workers [51] have studied metal dichalcogenide nanotubes in great detail. Numerous kinds of inorganic nanotubes have been studied theoretically ever since and provided a plethora of observations, some are still awaiting experimental confirmation.

Fig. 7 shows a computer simulation of a spherical MoS_2 nanoparticle with fullerene-like structure and its simulated TEM projection [49b]. This analysis helps to elucidate the detailed structure of the synthesized MoS_2 fullerene-like nanoparticles and eventually also their properties.

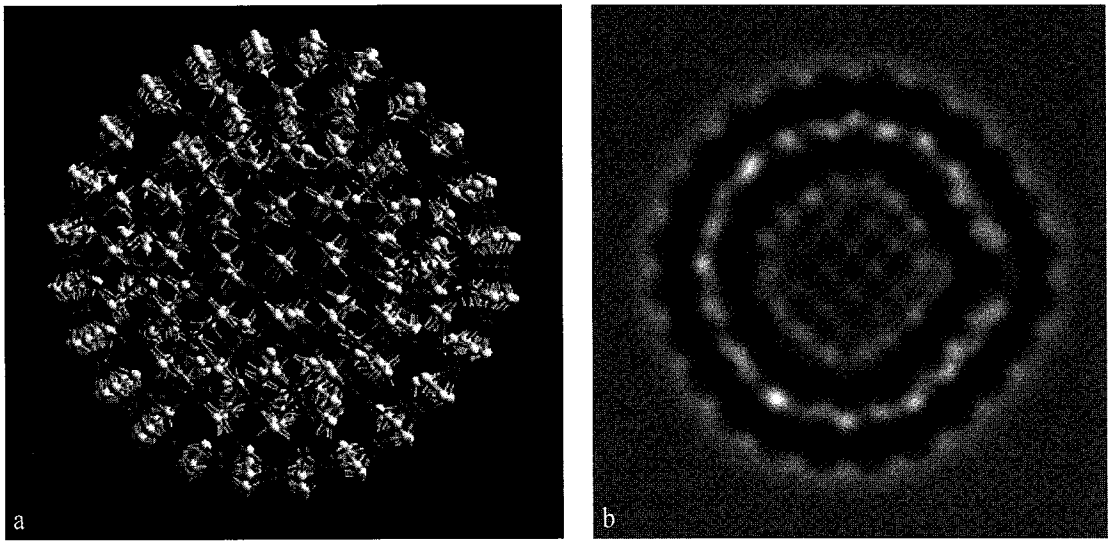

Fig. 7. Computer simulation of a double layer MoS_2 nanoparticle with fullerene-like structure (a) and its simulated TEM image (b) [49b].

III. Physical properties

IIIa. Optical studies in the UV and visible and electronic excitations

In general, measurements of the optical properties in this part of the spectrum, gives information on the fundamental electronic transitions. The optical properties of *IF*-WS_2 nanoparticles, which were prepared by a careful sulfidization of oxide nanoparticles, were studied [52]. The excitonic nature of the optical transition in the nanoparticles was confirmed, which is a manifestation of the semiconducting nature of the material. A red shift of the fundamental transition (bandgap) with shrinking radius of the *IF* nanoparticle was observed. Due to the anisotropic nature of this 2-D compound the exciton is mostly confined in the closed layer and hence the quantum confinement is not expected to be very large. On the other hand, the

elastic strain which is imposed on the folded molecular sheets induces the above red shift in the excitonic transitions.

In another study the radius dependence of the fundamental transition of WS_2 nanotubes was evaluated both experimentally and by theoretical calculations [53]. Here a high resolution scanning tunneling microscopy was used to image the WS_2 nanotubes and to analyze the density of states near the Fermi level. While the quality of the spectroscopic data was far from ideal **(see Fig. 8)**, the overall trend showing a red shift of Eg with shrinking radius of the nanotube was unequivocal and the fit to the theoretical calculations was quite good. These observations suggest that bandgap tuning by varying the nanotube diameter is possible offering various applications for the *IF* phases, in photochromic, electrochromic, photoelectrochemical and photocatalytic devices.

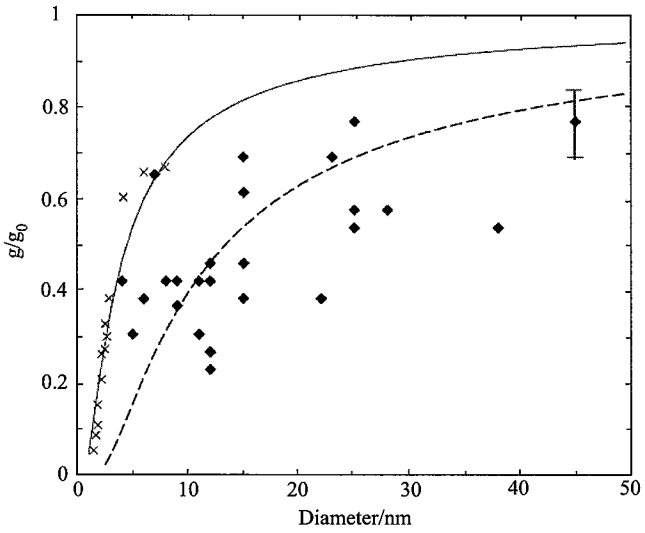

Fig. 8. The dependence of the bandgap of WS_2 nanotubes as a function of their diameter. The diamonds are the experimental data obtained from STM measurements in the ambient. The crosses are values determined from first principle calculations. Note that both sets of data exhibit a decreasing bandgap with shrinking diameter of the nanotubes [53].

IIIb. Raman spectroscopy

Polarized resonance Raman measurements of individual multiwall WS_2 nanotubes were recently described [54]. A strong Raman scattering signal was obtained when the light was polarized along the nanotube axis. Using a fit to a theoretical model, an estimate of the ratio of the perpendicular to parallel polarizabilities $\alpha_{XX}/\alpha_{ZZ} = 0.16$ was obtained, which value is comparable to that obtained for single wall carbon nanotubes (0.09). Symmetry analysis of the Raman and IR active modes of MoS_2 nanotubes was also recently published [55]. The tubular structure was found to be characterized by two Raman active modes. A new high-energy breathing mode transition, which is characterized by the breathing of the sulfur shells in phase and out of phase relative to the molybdenum atoms, was identified.

A Raman study of titania nanotubes [56] produced by the hydrothermal synthesis and VOx-alkylamine nanotubes was undertaken [57]. These studies provided important structural information and are helpful in elucidating the mechanistic details of the *IF* formation.

IIIc. Mechanical properties

There is a surge of interest in measuring the mechanical properties of individual nanoparticles and in particular nanotubes and nanowires. This interest does not stem from pure academic reasons only, but is driven by the search for new high performance nanocomposites. Nonetheless, the mechanical properties of inorganic nanotubes have been investigated to a relatively small extent so far. The Young's modulus of multi wall BN nanotubes was measured individually within the TEM [22], and was estimated at 1.2 TPa, which value is comparable to the one measured for carbon nanotubes. A vertical array of dense and uniform GaN nanotubes was obtained on GaN substrate using metal-organic chemical vapor deposition technique followed by plasma etching with reactive gases [58]. Buckling instability of the nanotubes was observed by nanoindentation. The Young's modulus (250-500 GPa) and the critical strain for buckling (8-22 %) of the nanotubes was found to be both length and model dependent. Since the present nantoubes are made of a cubic GaN (sp^3 bonding), any comparison with theoretical analysis which considers sp^2 bonded GaN nanotubes is questionable. Another difficulty stems from the fact that the present method does not allow for a direct inspection of the nanotube during the buckling test.

A systematic experimental and theoretical study of the mechanical properties of individual WS_2 nanotubes is now underway. In the first work, the buckling of WS_2 nanotubes was followed using an atomic force microscope (AFM) [23]. The experimentally determined force-displacement curve clearly showed a singularity point which was ascribed to the buckling of the nanotube. Using the Euler formula, the Young's modulus of the nanotubes was estimated at 170 GPa. First principle theoretical calculations of the Young's modulus were found to be in agreement with the experimental data.

In a follow-up work, the mechanical properties of individual WS_2 nanotubes were measured within the scanning electron microscope (SEM). In-situ tensile and buckling experiments were carried-out [24]. Fig. 9 displays a series of micrographs taken during the tensile test. The strain-stress curve of one such nanotube was thus obtained. The statistically averaged measured Young's modulus, strength and elongation to failure were found to be 150 GPa, 16 GPa and 12%, respectively. First principle calculations were generally in agreement with the experimental findings. The experimentally determined strength of the WS_2 nanotubes is 11% of its Young's modulus, which is an exceedingly high value in comparison to high strength materials. The first principle computations suggest that the onset of failure of the nanotubes comes as a result of excessive distortion of a chemical bond, while the role of macroscopic failure mechanisms, like dislocations' diffusion and propagation of cracks along grain boundaries seem not to be applicable here. Conceptually, nanomaterials of a high crystalline order are expected to show a remarkably different

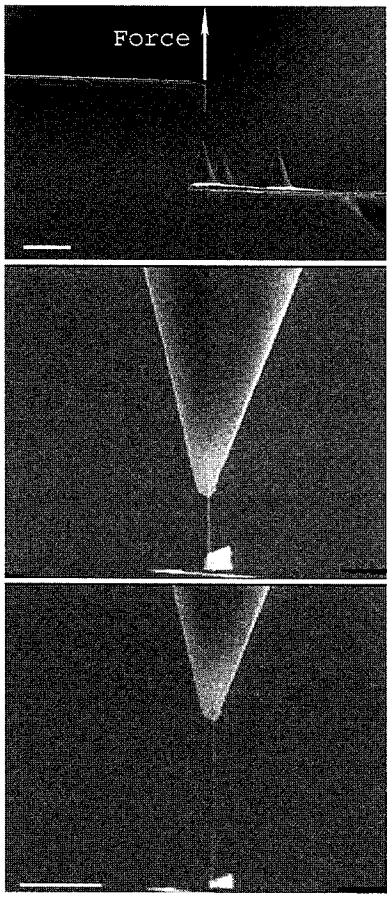

Fig. 9. Tensile test of an individual WS_2 nanotube carried-out within the SEM. The figure shows the nanotube before and after being torn apart. Adopted from Ref. [24].

mechanical behavior as compared to macroscopic solids. The mechanical properties of regular solids are influenced by their intrinsic strength as well as to the distribution of dislocations in the solid. Therefore the strength of macroscopic objects is size dependent and is describable by the Weibull distribution. Contrarily, the mechanical behavior of nanotubes or nanowires with perfectly crystalline structure, reflect the intrinsic strength of the chemical bond of the nanostructure. Consequently a quantitative comparison with first principle calculations becomes possible in the case of nanotubes. Fig. 10 shows an SEM image of a post-buckled WS_2 nanotube. An averaged Young's modulus of 150 GPa was found by applying the Elastica theory to the present results, which value is consistent with all the previous measurements [24]. In a series of works *IF*-WS_2 and *IF*-MoS_2 nanoparticles were shown to exhibit excellent resilience under shockwave pressures of 20-30 GPa with concurrent temperatures of up to 1000°C. No evidence for significant structural degradation or phase change were observed, making these materials probably the strongest cage molecules known today and offering them plethora of applications [59].

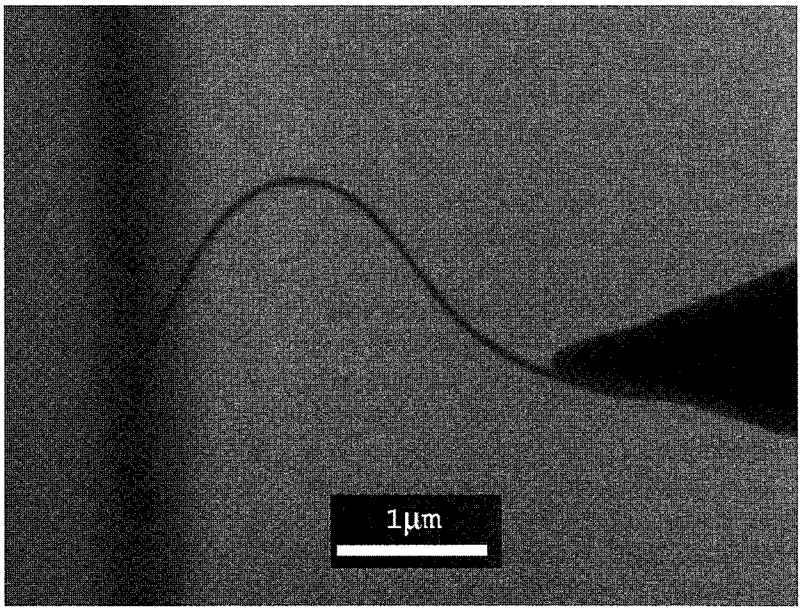

Fig. 10. SEM micrograph showing buckling of a WS_2 nanotube. Adopted from Ref. [24].

IV. Electrochemical measurements

Electrochemical measurements are particularly pertinent to energy conversion and storage and sensorial applications. Inorganic nanotubes could serve as hosts for both alkali metal and for hydrogen atoms. The spacing between the layers, the hollow core in the center of the nanotube, and the voids between the densely packed nanotubes could be used to host guest atoms, with little if any disturbance to the pristine nanotube structure.

IVa. Li and hydrogen intercalation in MS_2 nanotubes

The electrochemical hydrogen-storage properties of the MoS_2 nanotubes were measured in an alkali electrolyte by a three-electrode system at 293°K [60]. The working electrode was prepared by pasting MoS_2 nanotubes onto a nickel-foam matrix. The counter-electrode was made of sintered $Ni(OH)_2$/NiOOH,

and the reference electrode in this experiment was Hg/HgO. The cyclic voltamogram (CV) of the MoS_2 nanotubes electrode showed a cathodic peak at –0.955V, which could be attributed to hydrogen reduction. The anodic peak observed at –0.645 V was assigned to hydrogen oxidation. The nanostructured MoS_2 electrode displayed a discharge capacity of 260 mAh/g (corresponding to the formula $H_{1.57}MoS_2$, i.e. 0.97 wt.% hydrogen) at a current density of 50 mA/g and a temperature of 293°K. The electrode did not lose more than 2% of its original capacity after 30 consecutive charge/discharge cycles (100 % depth of discharge at 150 mA/g to –0.6V versus Hg/HgO).

Adsorption/desorption of hydrogen in MoS_2 nanotubes was also investigated at room temperature [61]. The hydrogen-adsorption kinetics is nearly linear and it exhibits a saturation after about 30 min. Comparison of the gas adsorption (1.2 wt.%) and electrochemical storage (0.97 wt.%) suggests that the gas adsorption process is the result of a physisorption of the hydrogen in the MoS_2 nanotubes. The same group showed also that high-purity TiS_2 nanotubes with open ended tips, which were synthesized by a chemical transport reaction, can efficiently store 2.5 wt.% of hydrogen at 298°K and under hydrogen pressure of 4 MPa [62]. Detailed analysis showed that about 1 wt% of the hydrogen is chemisorbed while the rest of the hydrogen atoms are physisorbed to the nanotubes.

Three moles of lithium could be inserted into $MoS_2I_{0.3}$ nanotube bundles, which were prepared by chemical vapor transport [63]. Comparing their electrochemical properties with those of bulk 2H-MoS_2, one finds a significant increase in the amount of inserted lithium and a decrease by about 0.7 V in the potential at which lithium insertion takes place, for the electrodes made with the nanostructured material. The electron spin resonance (ESR) signal of lithiated $MoS_2I_{0.3}$ nanotube bundles was found to decrease upon exposure to the air but in a much slower rate as compared to 2H-MoS_2 crystals, suggesting that lithiated $MoS_2I_{0.3}$ nanotube bundles are less air-sensitive than the lithiated bulk crystals.

IVb. Li intercalation VOx-alkylamine and titanate nanotubes

The synthesis of VOx-alkylamine nanotubes, by a sol-gel reaction and subsequent hydrothermal treatment was described [13]. Further studies [64] showed that these nanotubes could serve as high capacity Li insertion electrode. Gustafsson and co-workers were able to fabricate VO_x-alkylamine nanotube-based cathode with improved performance [65]. The electrode was tested by galvanostatic cycling in the potential range 1.8–3.5 V versus Li/Li^+. The capacities were found to be closely dependent on the type of lithium salt used in the electrolyte. Three salts were tested: $LiBF_4$, $LiPF_6$ and $LiN(CF_3SO_2)_2$. The imide salt, $LiN(CF_3SO_2)_2$, gave the best result with initial capacities of 200 $mAhg^{-1}$. The electrode cycled reversibly for at least 100 cycles. X-ray diffraction results indicated that the tubular structure is preserved, even after prolonged cycling. In a related study, Whittingham and co-workers studied nanotubes of the partially metal-exchanged manganese compound $Mn_{0.1}V_{0.9}O_x$-alkylamine as electrode material for Li intercalation battery [66]. Li intercalation was studied also in titanate nanotubes [67].

V. Applications

In bulk 2H-MoS_2, which is commonly used as lubricant, the molecular layers are held together by weak van der Waals forces. They can therefore easily shear with respect to each other and with respect to the two mating metal surfaces, which slide past each other. At the same time, the platelets serve as spacers, eliminating the direct contact between the two metal surfaces and minimizing thereby the metal wear. Therefore, MoS_2 powder is used as a ubiquitous solid-lubricant in various systems, especially under heavy loads, where fluid lubricants are squeezed out of the contact area between the two metal surfaces.

Unfortunately, MoS_2 platelets tend to adhere to the metal surfaces through their reactive prismatic (*hk*0) edges and therefore their efficacy as solid lubricants is hampered. In contrast to that, the spherical *IF*-MS_2 nanoparticles are expected to behave like nano-ball bearings and upon mechanical stress they would slowly exfoliate or mechanically deform, but would not lose their tribological benefits, until they are completely gone, or oxidize. The beneficial effect of *IF* powder as a solid lubricant additive and in self-lubricating coatings has been confirmed through a long series of experiments in various research laboratories [25,39,68-72]. These findings lead to a surge of interest in these materials which culminated in the licensing of this technology to "ApNano Materials, Inc" ("NanoMaterials, Ltd"). Currently a prototype of a manufacturing facility for the *IF* nanoparticles is being erected to address the large demand for this material in the car, aerospace, home appliances, medical and numerous other industries.

Another important field where inorganic nanotubes can be useful is as tips in scanning probe microscopy [73]. Here applications in the inspection of microelectronics circuitry have been demonstrated and potential applications in nanolithography are being contemplated. Various inorganic nanotubes exhibit strong absorption of light in the visible part of the spectrum and their electrical conductivity can be varied over many orders of magnitudes by doping and intercalation. This suggests numerous possible applications, in areas such as nanolithography, photocatalysis, sensors and others.

Optical limiting behavior, i.e. opacity of the films under high intensity irradiation was observed in the visible and near IR range in films produced from VO_x-alkylamine nanotubes [74]. Room temperature ferromagnetic material was obtained by lithium and iodine intercalation of VOx-alkylamine nanotubes [75]. The ferromagnetic behavior of the intercalated nanotubes' material was attributed to the lifting of spin frustration in the nanotube lattice, by either pairing (Li) or removal (I) of the highest occupied spin state. Furthermore, the lithium (iodine) doping brought the Fermi level into the conduction (valence) band transforming this Mott-Hubbard insulator into a good conductor. This effect offers intriguing applications for such nanotubes in the field of spintronics.

A number of interesting observations were recently made with titanate nanotubes. Thus, organic light emitting diodes mixed with titanate nanotubes were shown to exhibit stronger luminosity and lower the turn-on voltage [76]. It was suggested that the nanotubes lower the barrier for hole injection and improve the hole transport in the film. In another recent work, films made of titanate nanotubes exhibited enhanced electrochromism compared with films made of TiO_2 nanoparticles [78]. The nanotube films were prepared by alternating layer deposition of the negatively charged nanotubes and the positively charged polyelectrolyte onto a transparent conductive oxide glass. Subsequently, the polyelectrolyte was removed by photocatalytic oxidation using UV light source. The titanate nanotubes films exhibit a faster proton diffusion and higher proton capacity than those made of TiO_2 (anatase) nanoparticles. The significant electrochromism of the titanate nanotube film is attributed to its layered nanostructure. Finally, high efficiency dye-sensitized solar cells were produced using single-crystalline titanate nanotubes as a thin-film semiconductor [76]. Very fast electron transfer rate through the single-crystalline titanate nanotubes films was observed as compared to that through nanoporous TiO_2 films composed of the normal nanoparticles. The dye-sensitized solar cells with single-crystalline titanate nanotubes showed more than doubling of the short-circuit current density compared with those made of titania nanoparticles (Degussa P-25) and overall solar to electrical conversion efficiency of 5 %. Finally, arrays of titania nanotubes were prepared by electrochemical etching of titanium foil [79]. These arrays exhibited very high sensitivity to hydrogen gas, with various possible medical applications.

Conclusions

Inorganic fullerene-like structures and inorganic nanotubes, in particular, are a generic structure of nanoparticles of inorganic layered (2-D) compounds. Various synthetic approaches to produce these nanostructures are presented. In some cases, like WS_2, MoS_2, BN and V_2O_5 both fullerene-like nanoparticles and nanotubes are produced in large amounts. However, size and shape control is still at its infancy. More recently, nanotubes of numerous inorganic compounds with non-layered structure were prepared using various templates. The study of these novel nanostructures has led to the observation of a number of interesting properties and some potential applications in tribology, high energy density batteries, sensors, and nanoelectronics.

Acknowledgement

This work was supported by the Israel Science Foundation. Reshef Tenne is the director of the Helen and Martin Kimmel Center for Nanoscale Science and holds the Drake Family Chair in Nanotechnology.

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BIORECOGNITION AND ITS MANIFOLD APPLICATIONS

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Molecular biorecognition

Molecular recognition or biorecognition is at the heart of all biological processes. How it works is still clouded in mystery. How does a protein recognize another? How does an antibody recognize an antigen? And how does a hormone recognize a receptor? How specific is this recognition and what drives proteins to recognize one another? Does a protein always recognize a single partner or can it recognize a group of related (or even unrelated) proteins? And how does a protein recognize a low-molecular-weight ligand? And how can the immune system generate an antibody that is complementary to virtually any foreign molecule? And how does such a ligand compete with medically relevant protein-protein interactions? One thing is clear, in all of these cases a combination of noncovalent interactions are involved, namely, ionic, hydrogen-bonding and hydrophobic interactions. In addition, shape complementarity appears to play a pivotal role in the process of biorecognition (1).

Scientists pursue different approaches to study biorecognition. Some study protein folding, others focus on protein-protein or protein-ligand interactions (1, 2). In addition, protein-nucleic acid, protein-carbohydrate, protein-lipid and even protein-solvent interactions have been investigated extensively. In order to better understand the principles of biorecognition, we have selected to examine its application in different fields of biology (3). Consequently, the application of biorecognition is now widespread in virtually all areas of biology, medicine, chemistry, molecular biology, biotechnology and nanotechnology. In the following, we will describe some of their applications.

Affinity chromatography

Affinity chromatography is a method in which biospecific and reversible interactions are used for the selective extraction, separation, and/or purification of biologically active material from crude samples (Figure 1). The approach was introduced in 1968 by Cuatrecasas, Wilchek and Anfinsen to purify proteins (4) and is an indispensable tool for studying many biological processes, such as the mechanism of action of enzymes, hormones, protein-protein or cell-cell interactions and others (5). In the initial demonstration of this method, immobilized biotin was used to purify avidin and thymidine 3,5-diphosphate was used to purify nuclease. In both cases, the polymeric carrier was a polysaccharide, Sepharose, and the reaction used to immobilize the ligand was cyanogen bromide (6). In order to increase the efficacy of binding and purification spacers were introduced between the biologically active ligand and the inert polymer. Interestingly, even today affinity chromatography remains the most powerful technique for isolation and purification of biologically active material. About 95% of all affinity purification methods apply

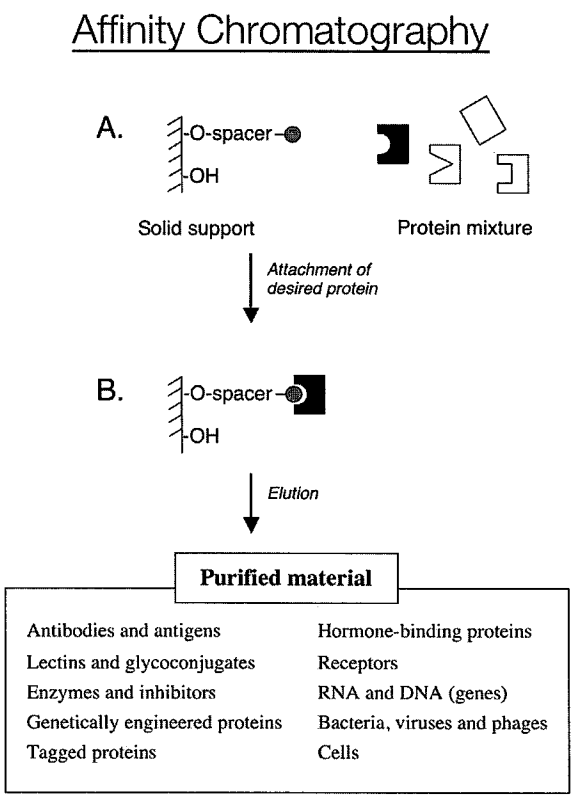

Figure 1. Scheme showing principle of affinity chromatography and short list of target materials that have been purified.

the same general principles outlined in the above publication (see Figure 1 for a short list of types of biomaterials purified by affinity chromatography). The current market value of affinity-purified products is estimated to be about $40 billion per year (7).

Following the initial introduction of affinity chromatography our group continued to develop new carriers and new methods of ligand coupling (8, 9). All of these carriers and coupling methods were immediately adopted by many research facilities as well as biotechnology-based industries worldwide. Quantitative analytical methods were developed for determining the extent of activation, the amount of bound ligand and the chemical mechanism of these reactions (10). These studies were initiated in order to solve many problems that are inherent in the technique of affinity chromatography, such as ligand leakage, hydrophobic interactions and ion-exchange problems. The information gained through these studies has enabled the development of new approaches for coupling proteins and ligands to solid matrices in a leakage-free manner, using carbamate bonds instead of the original isourea bond formed via cyanogen bromide reaction (10).

The chemical nature of this work has not detracted from continued application of these columns for the isolation and study of biologically active molecules. We employed antibody columns for the isolation of antigenic peptides derived from parent proteins (11). The use of antibody columns,, i.e., "immunoaffinity chromatography", continues to be a definitive tool for the isolation of proteins produced by genetic engineering (12). Affinity columns are also used to remove toxic compounds and cholesterol from blood, thus laying the grounds for modern-day hemoperfusion (13). Moreover, we introduced the concept of sandwich-type affinity chromatography, whereby either an antibody to a hapten or avidin was used to isolate a biologically active molecule via the hapten-modified or biotinylated counterpart to a target molecule. This is one of the most important applications in the field of proteomics (14).

The general biorecognition-based approach was subsequently adopted for a variety of other techniques (Table I). Affinity chromatography is thus the grandfather of most modern techniques, including biosensors, DNA and protein microarrays, and their varied application in diagnostics, protein-protein interactions, nanobiotechnology and drug screening.

Table I. Various techniques derived from affinity chromatography

1. Affinity capillary electrophoresis	10. Isotope-coded affinity tag
2. Affinity partitioning	11. Lectin affinity chromatography
3. Affinity precipitation	12. Library-derived affinity ligands
4. Affinity tag chromatography	13. Metal-chelate affinity chromatography
5. Avidin-biotin immobilized system	14. Molecular imprinting
6. Dye-ligand affinity chromatography	15. Receptor affinity chromatography
7. High performance affinity chromatography	16. Tandem affinity purification (TAP)
8. Hydrophobic chromatography	17. Thiophilic chromatography
9. Immunoaffinity chromatography	18. Weak affinity chromatography

Affinity Labeling

Concurrent with affinity chromatography we continued to work in areas in which we could combine chemical reactions with the affinity concept to investigate the phenomenon of biological recognition. A perfect example of such an approach is affinity labeling, by which residues in the binding-active site of proteins can be identified (Fig. 2). Affinity labeling is a method designed to label an active- or binding-site residue of a protein by virtue of a ligand to which a chemically reactive group is bound. Using this technique, we determined which amino acid residues are involved in the active sites of enzymes (such as nuclease, ribonuclease, trypsin and chymotrypsin) (15). In the field of antibodies, we were able to prove that their binding site lies in the Fv portion of the molecule and involves the complementarity-determining regions (CDRs) (16). The latter work was instrumental in the preparation of X-ray models of the antibody molecule and for the preparation of Fv (17), which we synthesized chemically as early as 1977 (18). The use of Fv is very popular today for drug and toxin targeting (19) and for protein purification. We also affinity-labeled and photoaffinity-labeled complex molecules, e.g., ribosomes and receptors in the intact cell (20). These early studies, which were published in the early 1970s, were verified recently by gene sequencing and X-ray structure analysis (21).

With the advancement of X-Ray crystallography, the importance of affinity labeling as a general tool to study binding sites has diminished, but it is still used for crosslinking between biologically active partners (22) and for localization of drug targets and for nanobiotechnology, as shown recently using the avidin-biotin system (23).

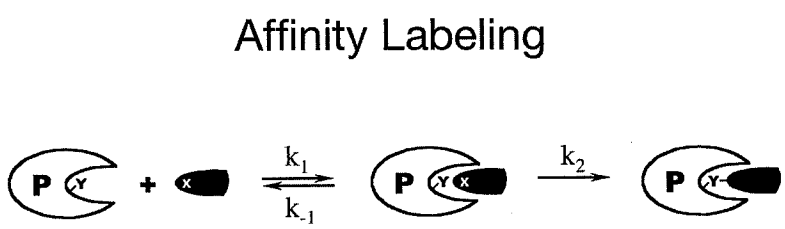

Figure 2. Schematic representation of affinity labeling. A nucleophilic or electrophilic reactive group (X) is introduced into a ligand, which reacts with an amino acid residue (Y) on a protein, thus forming a covalent bond in or near the active site. This enables the determination of the active-site residues of a protein.

Affinity therapy

Affinity therapy is a biorecognition-based approach to selectively deliver a cytotoxic drug or toxin to a given target cell located where the drug is needed (Fig. 3). The cell-associated target molecule can be a defined cell-surface antigen, a surface receptor or other type of biomolecule which bears specificity for a given antibody, hormone, or nutrient. The drug counterpart can comprise the corresponding, antibody, hormone etc. to which a cytotoxic compound (e.g., selected from chemotherapeutic drugs, radionuclide or toxins from different origins) has been chemically attached (24). We called this approach by a general term, affinity therapy, which was later changed by others to the misnomer, immunotoxins (25).

In the field of affinity therapy, which was pioneered together with Michael Sela, Ester Hurwitz and Ruth Arnon as early as 1975 (26), we applied drug- conjugated antibodies for the targeted delivery to

cancer cells of cytotoxic compounds (e.g., doxorubicin, adriamycin, 5-fluorouracyl, cis-platinum and others). We developed methods to conjugate such drugs and toxins to antibodies and demonstrated the advantage of having a polymeric spacer between the antibody and the drug (27). We also showed that the drug, conjugated to simple polymers such as dextran, can be useful for drug delivery and targeting (28), and in a series of surprising control experiments we established that in many cases the best results could be obtained when the free drug was given as a mixture with the free antitumor antibody (27). This approach was recently adopted by others and eventually led to efficient treatment of human breast cancer by recombinant humanized anti-HER2 antibody (Herceptin) in a mixture with paclitaxel and doxorubicin (29).

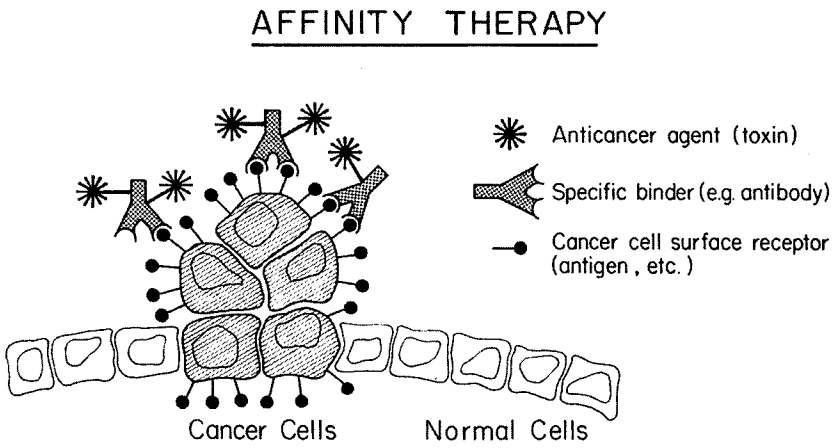

Figure 3. Schematic diagram illustrating affinity therapy. A drug, toxin or radionuclide is attached to a delivery vehicle (e.g., antibody, hormone, etc.), which is recognized by a receptor on an aberrant cell, such as a cancer cell. The resultant drug is thus selectively targeted to the afflicted cell, which is then destroyed by the cytotoxic agent.

We have recently employed antibody-directed enzyme prodrug therapy (ADEPT), using antibody-conjugated alliinase from garlic to produce a cytotoxic agent, allicin (from alliin), in situ at the site of the cancer (30). The affinity therapy is now being pursued in many other laboratories around the world and is already at the stage of clinical trials (19, 31).

The avidin-biotin system

The egg-white glycoprotein, avidin, and its bacterial relative, streptavidin, are known to bind biotin with an affinity constant of 10^{15} M^{-1}. The complex formed represents the strongest biological interaction between a ligand and a protein. Again, the precise reason for such strong binding is still unknown and even less was known about this strong interaction before we began working in this field.

The application of the avidin-biotin interaction, now known as the avidin-biotin system has become a "universal" tool in most of the fields of the biological sciences, thanks to studies we commenced in the early-1970s (32, 33). The avidin-biotin system can contribute to the interaction between any two biomolecules in an indirect manner as follows: biotin can be chemically coupled to a binder molecule (e.g., a protein, DNA, hormone, etc.) without disturbing the interaction with its target molecule; avidin can then be used to "sandwich" between the biotinylated binder and a reporter molecule or probe. This enables a variety of applications with this system, including localization, identification, purification, assay, etc., of the binder or target molecule. Consequently, the avidin-biotin system can emulate in many

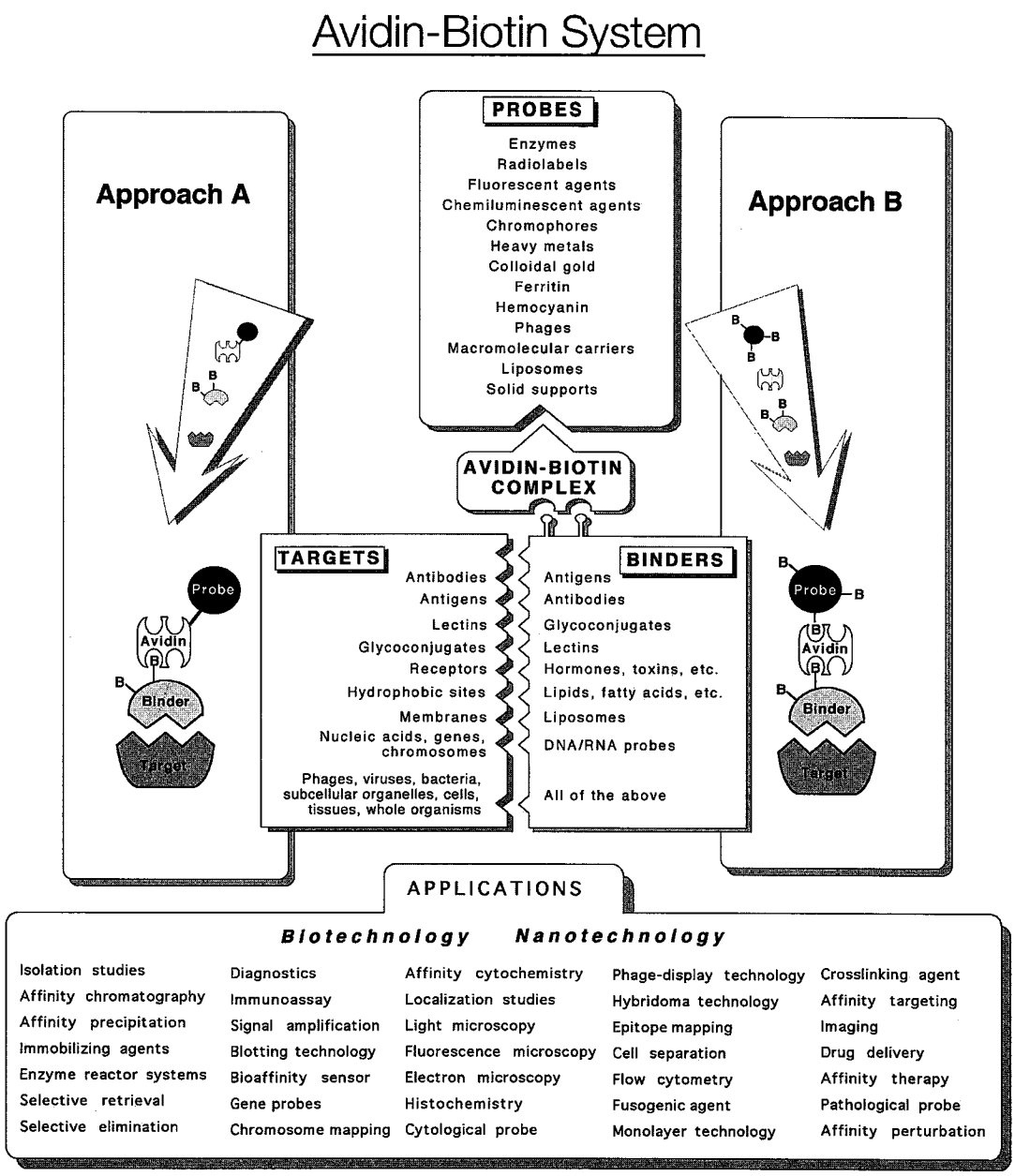

Figure 4. Overall summary of the avidin-biotin system. The principle of the two approaches is shown. In Approach A, the direct approach, a target is labeled with a biotinylated binder, which is labeled subsequently with an avidin-probe conjugate. In Approach B, the sandwich approach, free avidin mediates the binding of a biotinylated probe to the biotinylated binder The various target-binder pairs, the probes and many of the applications are listed.

ways what had previously been accomplished using radioactive probes, which can thus be replaced by a variety of colorful alternatives. The avidin-biotin system thus helped remove radioactivity from many laboratories, clinics and hospitals (34, 35).

The application of this system is really unlimited. The overall approach of the avidin-biotin system and a list of the various targets, binders, probes and many of the applications are shown in Fig. 4. In general, we have no control over the targets and binders if we want to study biological molecules, since the target is an integral part of the experimental system and we are limited to the types of interacting binders. On the other hand, we have complete control over the other parts of the system, including the coupling of biotin and the probe and/or the selection of a capture or detection system.

The covalently coupling of biotin to one or more components of a system is usually done chemically, using a biotin-containing reactive reagent. Many of our originally described biotinylating reagents are now commercially available. Thus, with comparatively little effort, one can insert a biotin molecule into a target, a binder, or a probe, with very little effect on their respective activities.

Avidin and its modified forms (or its bacterial cognate, streptavidin and derivatives thereof) can be introduced into an experimental system for several different purposes: e.g., to capture, to detect, to isolate or to perturb. Historically, we employed these approaches in the initial development of the avidin-biotin system. The biotinylated binder and its target can be any of the molecules listed in Fig. 4, and the system is amenable to an unlimited number of permutations and combinations, dictated only by the purpose and requirements of the experimental system and the imagination and skill of the scientist (36). Throughout the years, the number and nature of the applications has indeed grown, and we certainly have no space to describe them in detail, since we have already described them thoroughly in previous reviews (34).

In recent years, we employed protein engineering studies of the avidin-biotin complex in order to understand how such a strong binding site is being formed. These studies have culminated in the determination of the 3-dimensional structure of the avidin-biotin complex by X-ray crystallography (37). The extension of this investigation enabled the study of protein-ligand, protein-DNA and protein-protein interactions (38). It is hoped that further extension will enable the design and chemical synthesis of improved specific artificial recognition sites, known as molecular imprinting (39), a direction which may eventually prove even more far-reaching in its scope and application than that of the natural system (40).

As we predicted originally (36), the avidin-biotin system continues to display a tremendous level of vitality, proving indispensable for a variety of applications and generally irrepressible in its utility in a growing number of fields. The system continues to develop in many wonderful and surprising directions; many scientists from fields of physics, materials science, nanotechnology and biotechnology and other areas we never could have foreseen, are now devising new and fantastic applications based on the (strept)avidin-biotin complex. Finally, the study of biorecognition and its application is now blooming in many fields, and it seems that any biological research is impossible without taking into consideration its principles. In this regard, we are simply emulating Nature, which has been taking the principles of molecular recognition into account since the beginning of time.

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Prof. Meir Wilchek was born in 1935 in Warsaw, Poland. In 1949 he came to Israel from Germany. He received his B.Sc. degree in chemistry and physics from the University of Bar-Ilan in 1960, and his Ph.D. from the Weizmann Institute of Science in 1965, under Profs. Patchornik and Katzir. He served as Head of the Department and as Dean of the Faculty for Biophysics-Biochemistry. He is best known for the development of affinity chromatography for purification of biologically active molecules and the avidin- biotin system which has a major impact in the fields of chemistry, biology, medicine and nanotechnology.
Prof. Wilchek has published over 400 scientific works. He is a member of many scientific societies, including the Israel Academy of Science and the Institute of Medicine-American Academy of Science. He has received many prizes, among them: the Rothschild Prize in Chemistry; the Wolf Foundation Prize for Medicine, the Pierce Prize for Biorecognition Technology; the Israel Prize for Biotechnology, the Sarstedt Prize, the International Distinguished Clinical Chemistry Award, the Anfinsen award in Protein Science, the Wilhelm–Exner medal, and the EMET Prize, as well as Honorary Doctorates from various Universities in Canada, Finland and Israel.

Dr. Talia Miron was born in Israel in1941. She studied biochemistry at the Hebrew University, in Jerusalem and completed her M.Sc. in 1967. Since 1968 she has been working in the Weizmann Institute. Her doctoral thesis was carried out under the supervision of Profs. Benny Geiger and Meir Wilchek (1991). She has been working with Prof. Meir Wilchek for more than 30 years.

Prof. Edward A. Bayer is an associate professor in the Department of Biological Chemistry at the Weizmann Institute. Since the early 1970s, he has been involved in the development of the avidin-biotin system as a general tool in the biological sciences. This discovery was an outgrowth of his doctoral thesis, under the supervision of Prof. Meir Wilchek. The two received the Sarstedt Award for their contributions to the avidin-biotin system for biomedical analysis. Together with Raphael Lamed, he introduced the cellulosome concept in the early 1980s. During his career, he has collaborated with groups in the United States, Canada, Guatemala, Holland, Belgium, Germany, Great Britain, France, Spain, Finland, Denmark and the Republic of Georgia. He has authored over 200 articles and reviews. In 2002 he was elected as a Fellow of the American Academy of Microbiology.

DEVELOGEN ISRAEL LTD: APPLYING PEPTIDOMIMETIC CHEMISTRY FOR THE DISCOVERY OF NOVEL DRUGS FOR METABOLIC DISORDERS

Nurit Livnah and Tamar Yechezkel

In August 2004, DeveloGen AG aquired DeveloGen Israel Ltd. (previously known as Peptor Ltd.). DeveloGen is a specialty pharmaceutical company, headquartered in Goettingen, Germany, with proprietary innovative technology for discovery and validation of biological targets for metabolic diseases. As a result of the acquisition, DeveloGen's pipeline now includes, among other clinical and pre-clinical stage products, also SomatoprimTM, a peptidomimetic drug candidate in pre-clinical development, indicated for the treatment of diabetes complications. Somatoprim emerged from the peptidomimetic drug discovey platform developed by DeveloGen Israel, that includes parallel synthesis and high-throughput purification of various peptide-based compounds, synthetically modified for optimization of pharmacological propereties. The Israeli research group was successfully integrated into the research and discovery platform of DeveloGen, and is applying the peptidomimetic drug discovery platform to metabolic projects, in full cooperation with the researchers in Goettingen. Work also continues on one cancer project in preclinical stages as a non-core activity.

Peptides as drugs

Peptides and proteins are involved in numerous biological processes and play important roles in the development and progression of various diseases. Protein-protein interactions, such as kinase activation and inhibition, and peptide-protein interactions, like various peptide hormones and their receptors, are just two examples of biological processes with high therapeutic importance that can best be mimicked by peptide-based drugs. However, despite these clear biological advantages, the use of peptides as pharmaceutical agents is limited, due to their poor pharmacological properties, such as high susceptibility to enzymatic degradation, poor bioavailability and limited cellular penetration.

The proprietary technology of DeveloGen Israel Ltd, is focused on optimizing pharmacological properties of peptides, turning them into drug-like molecules, using various peptidomimetic methodologies. This comprehensive synthetic platform is aimed to identify drug-like molecules that combine the highly specific binding ability of the original protein fragment or peptide, with the advantages of improved pharmacological properties, and increased metabolic stability, oral availability and cell-permeability. DeveloGen's discovery process is carried out using an integrated drug discovery platform, including multi parallel synthesis and purification, carried out in Israel, and detailed biological characterization, carried out both in Israel and in Germany.

Peptidomimetic chemistry- turning peptides into drugs

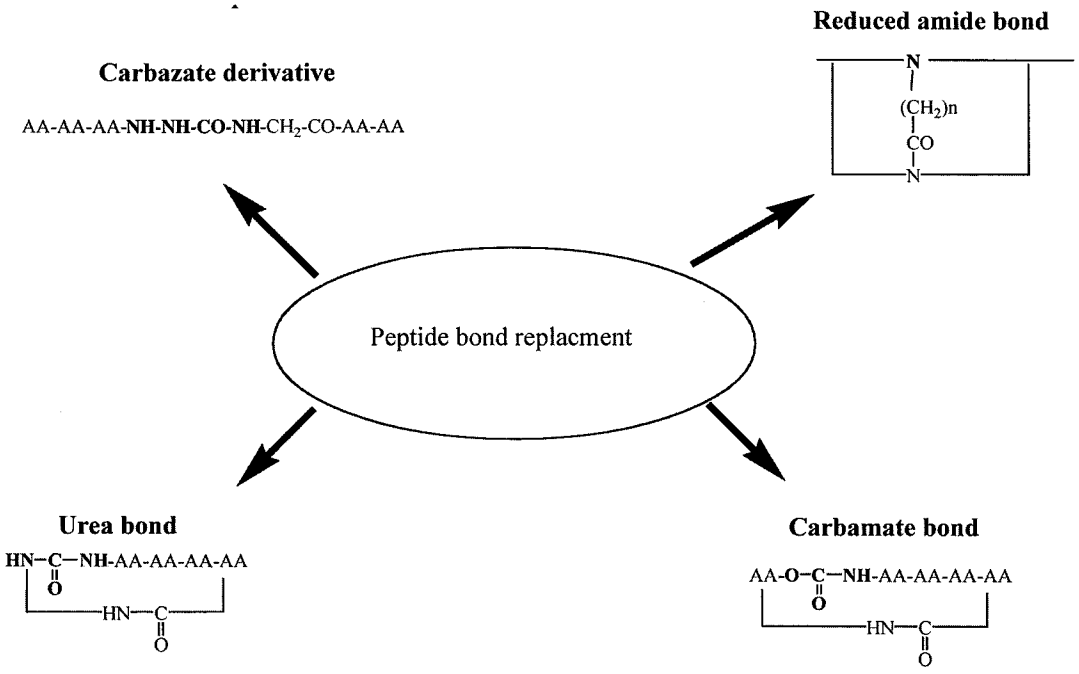
Several methods were developed and used by our chemists in the discovery, development and optimization of peptide-based drugs:

1. Amide bond replacements – replacement of peptide bonds by non-peptide analogs such as carbamate, urea, hydrazines etc.
2. Incorporation of non peptide moieties - insertion of various bi-functional, non-peptidic molecules within the peptide sequence.
3. Peptide small molecule conjugates - small molecules attachment to side chains, and use of N-alkylated and non-natural AA derivatives
4. Backbone cyclization – ring formation using proprietary building units, leads to cyclic peptides in which the amino acid side-chains are unaltered.

Amide bond replacement

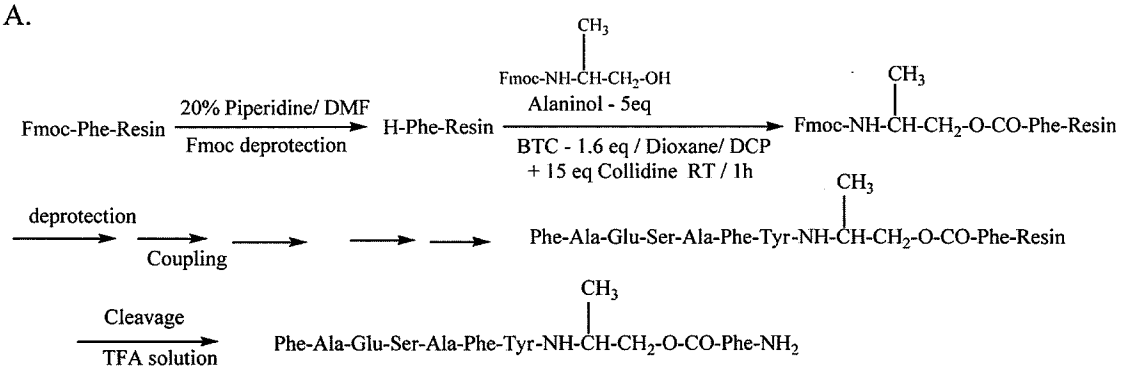
Enzymatic degradation occurs when proteolytic enzymes attack and break the peptide bonds. Thus, replacement of the amide bonds with other covalent bonds, which are less susceptible to enzymatic degradation, significantly improves metabolic stability. Various such replacements are used at DeveloGen, including reduced amides, urea bonds, carbamate bonds, carbazates etc. These modifications are carried out on solid support, using BTC, Bis (Trichloromethyl) Carbonate, as a coupling agent (see scheme 1,2).

Scheme 1. Examples of amide bond replacements

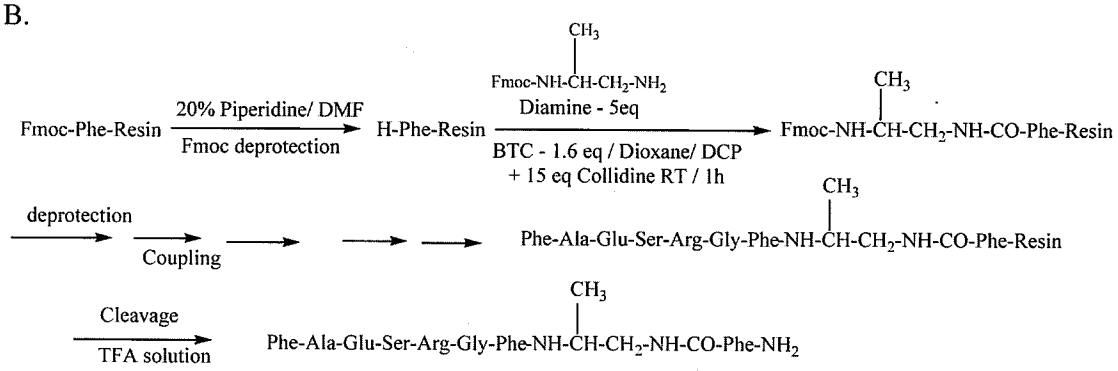


Scheme 2. Formation of carbamate bonds from hydroxyl amino acid derivatives (A) and urea bonds from the corresponding amino derivatives (B) in the peptide sequence, using solid-phase chemistry and BTC.

A.



B.

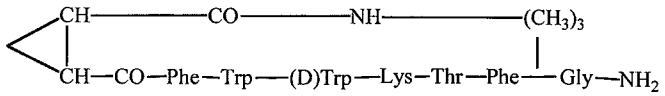


Incorporation of non-peptide moieties

In contrast to the amide bond replacement, where just the peptide bond is altered, we can in some cases insert whole non-peptidic moieties in the sequence. When positions that are not relevant for binding are identified in the sequence (using alanine-scan for example) various units can be inserted, including bi-functional small molecules, non-natural amino acids and N-alkylated amino acids. This modification leads to significant increase in metabolic stability. In several cases, including leads from three different projects that are currently in preclinical stages, we have developed linear peptidomimetics which are stable in serum for 6-24 hours.

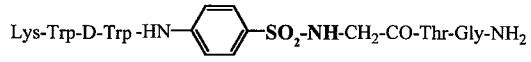
Scheme 3. Incorporation of various bi-functional small molecules and non-peptidic moieties in the sequence. A. Incorporation of diacids, B. Incorporation of diamines, C. Incorporation of amino sulfonyl chloride, D. Linear peptidomimetics stabilized with non-natural amino acids:

A.



B. Tyr-NH-CH_2-NH-CO-Asp-Gly-Thr-Arg-**NH-CH_2-CH_2-NH**-CO-Ala-NH_2

C.



D. Leu-Ile-**HyP*-HyP***-Glu-**HomoPhe**-Glu-Leu-**Cit****-Leu-NH_2

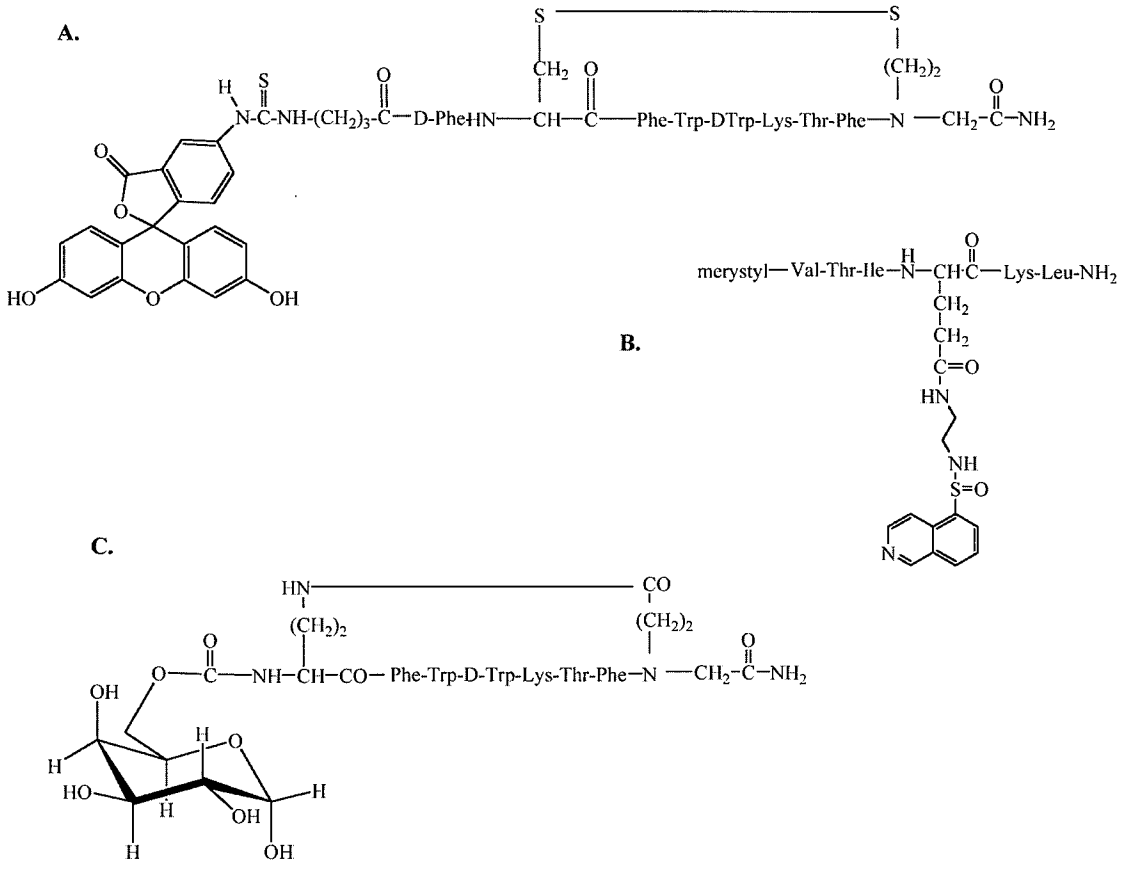
*HyP- Hydroxy Proline
**Cit- Citroline

Peptide-small molecule conjugations

Attachment of various small molecules to peptides through side chains or one of the termini. The conjugation methodologies are utilized to form bi-functional compounds that were used in several of our projects as targeted imaging materials, targeted therapy agents, bi-substrate drugs that bind to two different binding sites of the target, and various carrier-drug systems. In addition, conjugation of hydrophobic moieties

may facilitate cell permeability of peptides, as we have seen in our PKB project aimed to develop kinase inhibitor anti cancer agents.

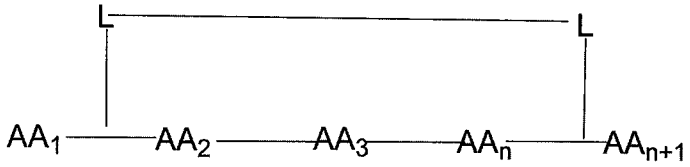
Scheme 4. Selected peptide-small molecule conjugates for various purposes. A. Targeted imaging agent for cancer diagnosis, B. Bi-substrate kinase inhibitor, also modified for cell permeability, C. Currier-drug system.



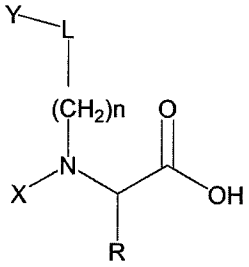
Backbone cyclization

Backbone cyclization allows the formation of cyclic peptides without altering any side chains. The cyclization is done using proprietary building units, which are modified amino acids, bearing functionalized alkyl "arms" attached to the α amine nitrogen, as illustrated in scheme 5. Cyclic peptides will form when two building units with appropriate functional groups are reacted, or one building unit is reacted with the N-terminus or a side chain. The length of the alkyl arm determines the size and flexibility of the resulting ring; the fact that such a unit can be made from any amino acid, allows cyclization at any position along the sequence, without altering the side chains that are usually associated with biological activity. The cyclization leads to fixation around the active conformation, decreased molecular volume, increased metabolic stability and improved bioavailability and cell permeability.

Scheme 5. A backbone cyclic peptide and cyclization building units. The structure of the units is an amino acid, N-protected by X, alkylated by an n-length carbon chain, and substituted by L which is, in turn, protected by Y.



Building units Structure



X = Fmoc			Deprotection
L= NH	**Y**= Alloc	**N**-building unit	Pd(PPh3)4
L= COO^-	**Y**= Allyl	C- building unit	Pd(PPh3)4
L= S	**Y**= Acm, Trt	S- building unit	I_2

Multi parallel synthesis (MPS)

The early stages of discovery are done using parallel synthesis approaches. An initial peptide sequence, derived from the active site of the relevant protein target, is usually used as a starting point for library design. We use solid phase synthesis with Fmoc chemistry, and the libraries are synthesized on an automated 96-well ACT instrument. A typical synthetic scale for such a library is 6μmol, and the yields range from 70% –85% of crude peptide.

The 96-well plates are subjected to high throughput purification, where each well is purified to >90% purity. Characterization is done by mass spectrometry, and occasionally, LCMS. The pure peptides are screened for activity and the most active hits identified from the libraries are re-synthesized as single compounds, in 100-mg quantity scale or larger, with full characterization and complete purification. They are used for enhanced biological and pharmacological evaluation, which feeds back into the optimization process.

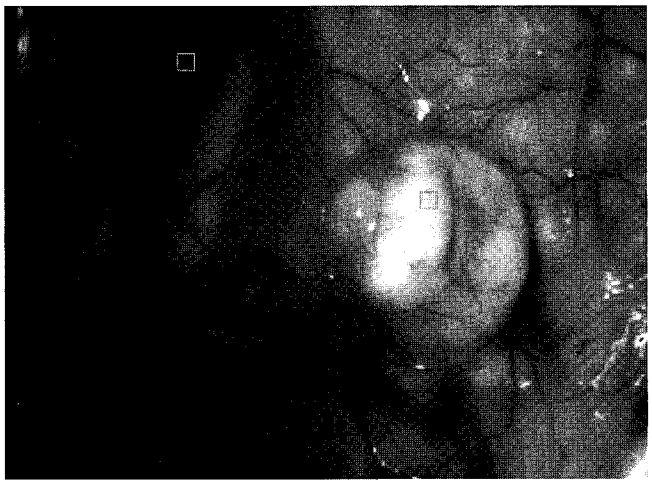
Technology application: Peptide-Small Molecule Conjugation Chemistry for Photodynamic Diagnosis

DeveloGen's peptidomimetic product, Somatoprim™, which is currently in advanced preclinical studies for treatment of diabetes complications, provided our research team with deep knowledge and understanding of this type of peptides, and many potent SST analogs with diverse selectivity profiles. Somatostatin receptors are significantly over expressed in tumors, thus a highly potent ligand is expected to selectively bind these receptors, leading to increased accumulation in the tumor compared to normal tissue. The conjugation chemistry that was developed at DeveloGen allowed us to design compounds in which therapeutically relevant small molecules are attached to SST ligand peptides, where the peptide

portion is aimed to target the drug selectively into a tumor, using its high affinity to the SST receptors that are overexpressed in the tumor. In this example project, we developed, in collaboration with Sheba hospital, a series of conjugates bearing light-active molecules, for the purpose of photodynamic diagnosis-tumor imaging using light-sensitive compounds.

Photodynamic Diagnosis (PDD) is fluorescence-based detection of cancer using selectively accumulated photosensitiser - dye compounds that absorb and emit visible light, which can be detected and used for diagnostic processes. In collaboration with the Center for Advanced Technologies in the Sheba Hospital, we identified, out of a combinatorial library, several highly selective PDD agents, one of which, PTR-1023 (scheme 4A), gave outstanding results in in-vivo (mouse model) distribution studies. After 24 hours from IV injection, the compound accumulated over 20-fold more in the tumor than in any other tissue and allowed clear visualization of the tumor with remarkable tumor-to-healthy tissue ratio (picture 1). This compound is one example of the many advantages of peptidomimetic chemistry: A specific, tageted peptide, was optimized for stability by backbone cyclization, demostrated improved pharmacokinetic properties (several hours in the blood stream, compared to about 30 minutes of the natural SST-14 peptide). This optimized peptide retained its pronounced affinity to the SST2 receptor, thus when conjugated to a light active moiety, it serves as an excellent targeting molecules that leads the compound selectively into tumors over expressing the SST2 receptor.

PTR 1023 is a novel compound with high potential for cancer imaging, especially in early detection of small tumors. Since the cancer orientation of project is not in the current core activity of DeveloGen, the lead compound is now in advanced preclinical studies in collaboration with the Sheba hospital in Israel. This research was published in Lung Cancer, 2005 Sep 10; [Epub ahead of print].

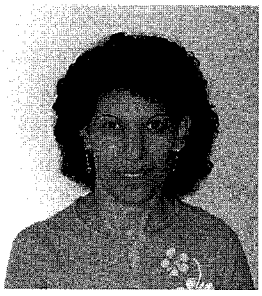


Picture 1. Fluorescence image of H69 tumor nodule near normal body tissue of a mouse, 24 h post administration of conjugate PTR 1023.

Summary

DeveloGen will continue to develop its peptidomimetic drug discovery platform in order to discover novel peptide-based compounds for the treatment of metabolic disorders. The modern drug discovery approaches, targeting specific biologically active proteins invloved in the progression of diseaes, give new horizons to the peptidomimetic field, that may enable research groups and companies all over the world to design and produce novel compounds that mimic those important proteins, and use them to develop potent, selective and safe drugs.

Dr. Nurit Livnah received her B.Sc. in Chemistry, from Ben Gurion University and her M.Sc and Ph.D. from the Weizmann Institute of Science.
Her Post Doctoral work was done at the Department of Medicinal Chemistry, Alanex Corporation , San Diego, CA. She was involved in a project for the development of NPY antagonists as obesity drugs. She was then promoted to Research Scientist and was involved in a project for the development of κ-opioids as novel pain control agents.
Since 1998, she is at Peptor LTD , first as Project leader for development of PKB inhibitors as anti-cancer agents, then as Head of Chemistry, Vice President for R&D, and since 2004 she is the Director of Research, DeveloGen Israel ltd.



Dr. Tamar Yechezkel received her B.Sc., M.Sc. and Ph.D.degrees in chemistry, from Bar Ilan University.
In 1996 she became Research Scientist in Peptor Ltd., developing new peptide chemistries.
She then became Project leader in the development of backbone cyclic Substance P analogs and Bombesin analogs for imaging and isotope therapy, followed by becoming Group leader in the chemistry department, and then Head of Chemistry.
Since 2004 she is Chemistry Manager, DeveloGen Israel Ltd.

AWARDS

Ada Yonath, Weizmann Institute of Science
received the Louisa Gross Horwitz Prize of Columbia University NYC, the Fritz Lipmann Lectureship, of the German Biochemical Society, the Datta Lectureship Award, IUBMB, Budapest, Hungary, the Massry Foundation International Award and Medal for ribosome research, and the Paul Karrer Gold Medal, Zurich, Switzerland.

Joshua Jortner, Tel-Aviv University
was awarded a Doctorate of Philosophy, Honoris Cause
from the Technion and from the Weizmann Institute of Science.

Zeev Tadmor, Technion and **Meir Wilchek**, Weizmann Institute of Science
were awarded the Emet Prize for exact sciences, established by the A.M.N. Foundation.

Reshef Tenne, Weizmann Institute of Science
was awarded the RAFAEL Research Excellence Prize, at the annual meeting of the Israel Vacuum Society, 2005. He was also awarded the Materials Research Society Medal for 2005, at the Boston meeting of the MRS "for realizing that nanoclusters of layered compound materials (e.g. MoS_2, WS_2) can be made to fold into hollow cage structures, in analogy to graphitic carbon. These structures, known as "Inorganic Fullerene-like structures" constitute a materials class with exciting new properties".

Menachem Lewin, Former Founder and Head of the Polymer and Textile Chemistry Division of the Faculty of Science at the Hebrew University
was honored with the Geza Zemplen Award, the highest Hungarian award in chemistry a non-Hungarian can receive. The awarding ceremony took place at a special session of the 8th Symposium of Polymers for Advanced Technologies (PAT2005) held in Budapest, September, 2005.

The Lise Meitner Prize for 2004
was awarded at the 70th Annual Meeting of the ICS on February 2005 to:
Dr. Yair Kurzweil, Hebrew University, Jerusalem
"For a pioneering study in time-dependent density-functional theory. An exchange-correlation potential which incorporates 'memory' effects (non-local time dependence) while retaining Galilean invariance is proposed for the first time, enhancing significantly the applicability of TDDFT to molecular electronic excited state".
And **Dr. A. Daniel Boese**, Weizmann Institute of Science
"For the development and implementation of a novel DFT exchange-correlation functional that accurately reproduces transition states and reaction barrier heights without compromising other properties".

The 34th Annual Meeting of the Israel Polymers and Plastics Society

was held on December 5, 2005, at the Beit Heyl Haavir in Herzelia

Organizing Committee:
Prof. H. Daniel Wagner, Chairman,
Prof. Moshe Levy, and
Prof. Arnon Siegman, President of the Society.

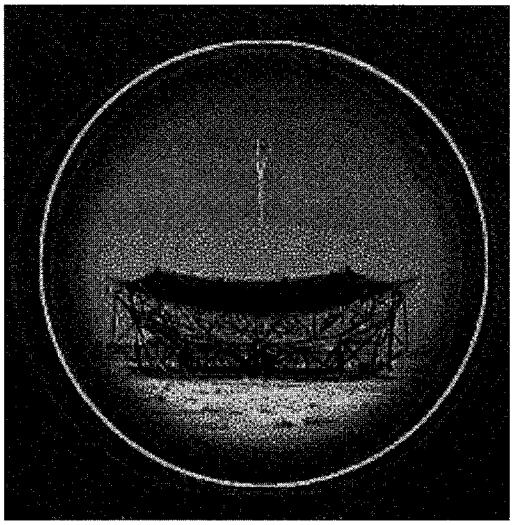
The Plenary Lectures were:

Effect of Processing on Polymer/Polymer Adhesion
Chris Macosko, Department of Chemical Engineering,
University of Minnesota, Minneapolis MN USA

Polymers and carbon nanotubes - dimensionality, interactions and nanotechnology
Rachel Yerushalmi – Rozen, Department of Chemical Engineering,
Ben-Gurion University of the Negev, Beer-Sheva

Composites of polymers with ceramics and metals
David Avnir, Institute of Chemistry, Hebrew University, Jerusalem

Following the plenary lectures a poster session was held with 22 posters presented.
In the afternoon, 18 lectures were delivered, in two parallel sessions, covering various subjects in polymer science and technology.



The Big Solar Dish at the Ben-Gurion National Solar Energy Center in Sede Boqer

The 13th Sede Boqer Symposium on Solar Electricity Production

Was held in October, 2005, in Sede Boqer

The Keynote Lectures were:
Environmental costs of fossil fuels and benefits of solar
Ari Rabl, Armines/Ecole des Mines, Paris, France

Solar power from space: current status and prospects
Leopold Summerer, European Space Agency, Noordwijk, The Netherlands

Sessions were held on the following subjects:
Solar thermal systems
Concentrated photovoltaics
Photovoltaic devices
Photovoltaic cells
Improvement of system efficiency and economics

VICTOR MORITZ GOLDSCHMIDT (1888-1947): FATHER OF MODERN GEOCHEMISTRY AND OF CRYSTAL CHEMISTRY

Bob Weintraub, Director of the Libraries, Sami Shamoon College of Engineering, Beersheva and Ashdod.

"The primary purpose of geochemistry is on the one hand to determine quantitatively the composition of the earth and its parts, and on the other to discover the laws which control the distribution of the individual elements."(Goldschmidt)

"During the preceding hundred years geochemical research was largely synonymous with the analysis of those parts of the earth accessible to visual inspection and chemical assay. From the nature of things it could be little more; interpretative geochemistry, the creation of a philosophy out of the mass of factual information, had to wait upon the development of the fundamental sciences, physics and chemistry. Fundamental advancements in these sciences were made in the early years of this century, such as the discovery and exploration of radioactivity, the Rutherford-Bohr atomic structure, the discovery of x-ray diffraction and its application to chemical analysis and crystal structure. It is the mark of Goldschmidt's genius that he seized upon these discoveries. His insight and intuition, his ability to plan and expedite extensive research programs, and not least, his recruitment and inspiration of devoted research associates, revolutionized geochemistry. Thanks largely to his work and stimulus, geochemistry has developed from a somewhat incoherent collection of factual data to a philosophical science based on the geochemical cycle, in which the individual elements play their part according to established principles." (Brian Mason, 1991).

Victor Goldschmidt

Victor Mortiz Goldschmidt was born in Zürich to Jewish parents. He grew up in a series of European capitals where his father held professorial appointments. He earned his doctorate at the University of Christiania (later Oslo) in 1911, with a thesis entitled, "The Contact Metamorphism in the Kristiania Region," which has become a classic in geological literature. In 1914 he accepted the position as professor and director of the Mineralogical Institute of Oslo, where he remained until 1929, at which time he moved to Göttingen. .

(Victor Moritz Goldschmidt, Father of Modern Geochmistry: B. Mason, 1992; Prin. Goechem: B. Mason and C. B. Moore, 1982; G.B. Kaufman, Chem Educ., 1997; E.D. Goldberg, Dict. Sci. Biog.; The Griffin, A. Kramish; and references therein.)

Metamorphism

Metamorphism is the processes that cause the recrystallization of rock material that take place below the zone of weathering. Metamorphism is induced in solid rocks as a result of pronounced changes in temperature, pressure and chemical environment. The changes affect the physical and chemical stability of the minerals in equilibrium and metamorphism results from the effort to establish a new equilibrium. The rocks remain solid during this process.

Goldschmidt's thesis dealt with thermal metamorphism in the Oslo region, induced at the contacts between the Permian plutonic igneous masses with the varied groups of Palaeozoic sediments. The phenomenon is called contact metamorphism and the resulting rock types are known collectively as hornfels. He applied physical chemistry and the recently "popularized" Gibbs Phase Rule - due to the work of Roozeboom - to geological problems and in particular to rock metamorphism. Goldschmidt used his data on the hornfels to arrive at the general principal which he called the Minerological Phase Rule. This powerful rule states that the maximum number of crystalline phases that can exist in rocks in stable equilibrium is equal to the number of components. This rule limits the number of minerals present in a rock.

Goldschmidt showed the value of the phase rule in setting limits to the p-t curve of rock formation by applying it to the metamorphic reaction of siliceous limestone being converted into wollastonite:

$CaCO_3 + SiO_2 = CaSiO_3 + CO_2$
Calcite + quartz = wollastonite + CO_2.

For the next ten years he continued his work on rock metamorphism and expanded it to include all of the mountains in the south of Norway.

The Differentiation of the Earth

Goldschmidt (1922): It is conceivable that the original state of the Earth was a homogenous or nearly homogeneous mixture of the chemical elements and their compounds. Today, however, the Earth is far removed from a homogeneous state. The material distribution within the Earth has by no means reached a final equilibrium state; we observe instead an active redistribution of matter and energy. The processes which have resulted in the inhomogeneity of our planet and still contribute to the migration of material I would summarize in the expression "The Differentiation of the Earth." Godlschmidt established the basis for the new geochemistry.

Goldschmidt pointed out the importance of the primary geochemical differentiation of the elements during geological evolution. He classified the elements in the earth into four groups: siderophile, chalcophile, lithophile, and atmophile. These are groups such that the elements have an affinity for metallic iron, for sulfide, for silicate, or for the atmosphere, respectively. (Later he added biophile, for those elements commonly concentrated in organisms). The geochemical character of the element is determined to a large extent by its electronic configuration, and thus related to its position in the periodic table. It was during this period of study that Goldschmidt showed the significance to geochemistry of meteorite compositions. Astronomical and chemical evidence, point to the fact that the earth and meteorites have a common origin.

Crystal Chemistry

During World War I, Norway was largely cut off from overseas sources of supply. In 1917 Goldschmidt was appointed the Chairman of the State Raw Materials Committee. In this capacity he found local sources to replace previously imported materials. This period led Goldschmidt to the study of crystal chemistry. Goldschmidt: "The experimental work in the field of crystal chemistry which in recent years the Mineralogical Institute of the University had undertaken had as objective to throw light on the geochemical distribution and technical properties of practically important materials. During the carrying out of these researches, which for the most part, was by means provided by the Raw Materials Committee of the Norwegian State, there appeared a series of generally crystallo-chemical relationships which made possible a notable deepening of the principles and data of crystal chemistry."

Bernal (1948): He wanted to start work straight away, but, realizing his limited knowledge and apparatus he could not compete with the Braggs in the analysis of complex minerals like the silicates, he began on simple structures - the AX and AX2 compounds which were mostly of the rock salt, cesium chloride, rutile, corundum, and calcium fluoride types. Goldschmidt's original approach was to examine systematically binary compounds of most of the elements. What he did was a model of extensive work. In that sense he was a real chemist; a physicist would spend years working out one structure, but he spent a few months working out a very large number. In two years he and his coworkers, several of whom like Barth, Oftedal, and Zachariasen were to become noted geochemists and crystallographers, worked out structures of 200 compounds of 75 elements and in that way established the extensive basis on which to found general laws...Goldschmidt's characteristic contribution was that of using this new view of ionic size to explain

the morphotrophy, or the changes of structure, which occurred in passing along any series of similar compounds on changing the atomic number. He noticed that this transition from one crystal type to another occurred when the radius of one or other of its constituent ions was altered, and, by considering groups of compounds with ions of different charge such as the halides and the oxides, that it was the radius ratio that determined the structure. This led him directly to the most fundamental concept of crystal chemistry, the importance of coordination."

He proposed the first general law of crystal chemistry: The structure of a crystal is determined by the numerical proportions, the ratio of radii, and the polarisability of its ions.

In 1925, based on his extensive studies on ionic compounds, Goldschmidt was able to draw up the first tables of empirical atomic radii for most of the ions in the periodic table. He was thus able to understand clearly for the first time the significance of the replacement laws that had made mineralogical chemistry such a confusing subject. A year later, Linus Pauling at the California Institute of Technology, published a similar table based on wave mechanic calculations. Mason: "The correspondence between the two tables was a brilliant confirmation of the theoretical background."

Goldschmidt stated the rules that relate ionic size to atomic structure: for the elements in the same group (vertical column) of the Periodic Table, the ionic radii increase as the atomic numbers of the elements increase; for the positive ions of the same electronic structure the radii decrease with increasing charge; for an element that can exist in several valance states, that is, form ions of different charge, the higher the positive charge of the ion, the smaller the radius.

Bernal: "Before leaving this field, Goldschmidt entered the last remaining large area of chemical ignorance, that of the metals and alloys. Here he early realized that the effective diameters of atoms were quite different from those in the ionic state and were always larger. The differences varied very much between the alkali metals, where they were more than twice, and the transition metals, where they were hardly anything at all..." Goldschmidt compiled the first table of metallic radii. In recognition of his work in this field, J.D. Bernal refers to Goldschmidt as one of the founders of modern alloy chemistry.

In 1924 Richard Willstätter proposed Goldschmidt to the faculty at the University of Munich as the replacement for the retiring Prof. Paul von Groth. Golschmidt's appointment was rejected by the faculty because they did not want another Jewish faculty member. Willstätter, himself Jewish, in protest announced his own resignation the evening after the faculty vote.

Even before the vote, Goldschmidt had his doubts about the appointment. He wrote to Willstätter with alarming foresight: ...Racial fanaticism is one of the evil phenomena of the present day, and I fear it will spread over the whole world...In the spring of 1914 the choice between Munich and Kristiania would not be in doubt; today I have serious reservations about Munich; no one knows what will be the state of the world in 1934."

In 1929 Goldschmidt accepted a Professorship at Gőttingen. Here he studied the abundance and distribution of the individual elements and its implications for the geochemical cycle. He worked on both terrestrial materials and extraterrestrial meteorites. He studied the geochemistry of germanium, gallium, scandium, beryllium, the noble metals, boron, the alkali metals, selenium, arsenic, chromium, nickel, and zinc. In 1934, in the course of this work, Goldschmidt published the geochemical cycle of carbon. His cycle showed overwhelmingly that the cycle of carbon is determined by biochemical reactions. In 1936 he wrote the following, in which he anticipated the significance of man-made carbon-dioxide emissions: "The carbon cycle is of special interest because it demonstrates the great significance that the industrial combustion of coal and other fuels has already had on the carbon dioxide content of the atmosphere. The amount of carbon dioxide which each year is added to the atmosphere by the combustion of fuels is

two hundred times greater than that contributed by the world's volcanoes. This demonstrates that human activity in our time is a highly important factor."

Goldschmidt:

"Then in spring 1935, on May 1, there was placed in Gőttingen a big sign board, not far from the road to my institute, with the inscription, 'Jews not desired.' I gave notice that I was resigning my professorship if such board was not taken off, as I could not reconcile my presence in Gőttingen with such an open attack against Jews in the same town. Before 24 hours had gone the thing had been taken off. However, several months later (in August) a signboard of the same kind was reerected, that time just opposite my institute. I renewed my action of protest, and that time it was not removed even at my request, as such boards at the same time had been placed in all German towns by direct order of the uppermost party rulers. Consequently, next day, August 11, as an ultimate protest I resigned my position, and designated my intention to leave the country."

Goldschmidt returned to Oslo where a position was made available to him. He worked now on the cosmic and terrestrial distributions of the chemical elements and studied the significance of the isotropic compositions of the elements in minerals. Hans Suess later wrote that the concept of "magic numbers" that define the structure of the nucleus of the atom was first discussed by Victor Goldschmidt in a 1938 paper, and that he and Jensen had appropriated the idea without giving credit. For work in this area, Jensen was awarded the 1963 Nobel Prize in Physics. Between the years 1929 and 1936, Goldschmidt was ten times unsuccessfully nominated for the Nobel Prize, twice by Max Planck and twice by Fritz Haber, among others.

Occupied Norway

In April 1940 the Germans occupied Norway. Until January 1942, Goldschmidt continued to work without interference of the Germans. He was interested in the work of Fritz Houtermans and Robert Atkinson and their theories of the fusion of the elements that created thermonuclear reactions in the sun and stars. That January, Goldschmidt completed his work on the chemistry of what he called "superuranium", or plutonium, and published it in Norwegian. His work paralleled the secret work of Glenn Seaborg in the United States. According to A. Kramish, had Heisenberg and his colleagues come to a proper appreciation about plutonium, "The one person under Hitler's control who might have put the German atomic program on the right track was the Norwegian Jew Victor M. Goldschmidt, still in occupied Norway."

In February 1942, the 2000 Norwegian Jews were required to fill out questionnaires about their "ancestry." Goldschmidt's passport was now stamped with the letter J. In March, Vidkun Quisling decreed all Jews to be illegal aliens. In October 1942, Goldschmidt was arrested and sent to the Berg concentration camp near Tönsberg, 50 miles south of Oslo. He was released in early November. He was rearrested later on in November and was sent to the docks for immediate deportation to Poland. He was again released. Goldschmidt believed that his life was saved due to the importance placed on his current work by the Ministry of Agriculture. The carbonates in the Fen area contain the phosphate mineral apatite. During this period, Goldschmidt was working to extract the phosphate mineral for use as fertilizer.

On December 18, 1942, Goldschmidt was picked up by Norwegian Resistance and transported to Sweden. During the war, the resistance sent 1100 Jews to Sweden. Of the 760 Jews that were sent to Poland, only 24 survived the war to return to Norway.

Goldschmidt was offered the chair of mineralogy at Uppsala University. He felt strongly, however, that

it was his duty to continue on to England, that his knowledge of technical developments in Norway and of the German interest in them would be of great value to the allies. He went to London in March 1943, and attended 150 conferences in which he detailed the German exploitation of Norwegian raw materials, the production of heavy water, among others. He accepted a position in Scotland, and in 1944 moved to the Rothamsted Experimental Station near Harpenden, England. In June, 1946, he returned to his former position in Oslo. He died in March, 1947.

The Wisdom of Moses Katz and Lesser Rosenblum

Paul Rosbaud related the following (Goldschmidt's friend; WWII hero who under the cover of scientific advisor to Springer-Verlag in Germany was a secret agent who provided vital intelligence on weapons systems to the British; Rosbaud made use of Norwegian students studying in Germany to transport intelligence to occupied Norway, and from there it was sent to neutral Sweden.):

"One episode influenced V.M. deeply and occupied his mind until the end of his life: it happened early in November 1942, in the County Hospital in Tönsberg, Norway, which was then the internment camp for Norwegian Jews. After a day of humiliation and torment by his jailers, V. M. talked to two other prisoners, whose names deserve to be recorded: Moses Katz, an orthodox Jew, and a hosiery peddler, and Lesser Rosenblum, socialist, atheist, and manufacturer of umbrella handles. V.M. suggested that they should remember the names of their tormentors, so that any survivors might extract retribution. The reply of the pious Moses Katz was a surprise to V.M.: 'Revenge is not for us; that must be left to the Almighty.' With the arrogance of a scientist confident of his superior knowledge, V.M. asked what prayers would be permissible to God from men in their position. Katz replied without hesitating a moment: 'You may pray that the hearts of your enemies may be enlightened.' Goldschmidt, still not admitting defeat, turned to the atheist Rosenblum and asked for his view. His reproof was equally unexpected: 'We must break the evil circle of retribution, or there can never be an end to evil.'

Goldschmidt became very humble after this experience. He had escaped, but his two friends from Tönsberg were facing death in Poland's gas chambers. He regarded their sayings as lucid and practical improvements on the Old Testament. Through them he learned not to forget, but to forgive...

In one of his last letters to me he wrote:

The wisdom of the Moses Katz principles is undeniable...And I am fully convinced that it is my duty towards science and decency to stand firm in continuing my work as long as health permits, thus giving an example to at least some of my junior colleagues. Often I think that (to maintain principles) to be even more important than my contributions to scientific and industrial research, and my scientific teaching. To set a new standard of morality is a matter of great urgency in these times...

ABSTRACTS

Inorganic Fullerene-like structures - IFs

R. Tenne, Materials and Interfaces, WIS, Rehovot

Following the discovery of carbon Fullerenes and carbon nanotubes, it was hypothesized that nanoparticles of inorganic compounds with layered (2-D) structure, like MoS_2 and WS_2 will not be stable against folding and form closed structures. These were indeed synthesized and were nick-named Inorganic Fullerene-like structures – *IF*s [1]. The synthesis of numerous other nanotubes and fullerene-like nanoparticles has been reported in recent years. Various techniques for the synthesis of *IF*s, including high temperature reactions and strategies based on soft chemistry processes, are described. First principle, density functional theory based calculations is able to provide substantial information on the structure and properties of such nanotubes. Various properties, including mechanical, electronic and optical properties of inorganic nanotubes are described in brief. Applications of *IF*-WS_2 (MoS_2) in the field of tribology, protection against impact, catalysis, photo-catalysis, batteries, etc, are briefly discussed.

Biorecognition and its Manifold Applications

Meir Wilchek, Talia Miron and Edward A. Bayer, Biological Chemistry, WIS, Rehovot

In this article, we describe four different applications of biorecognition, which are leading techniques in molecular biology, medicine, diagnostics and nanotechnology. 1) Affinity chromatography is a method for purification of biologically active molecules, based on biological interaction rather than their chemical or physical properties. It opened the door for modern-day biology and biotechnology by providing readily purified materials for research and use. 2) Affinity labeling is a method for determining the identity of binding-residues of a protein even without knowing its structure. This procedure enables the development of irreversible inhibitors to enzymes and the development of new drugs. 3) Affinity therapy involves the binding of a drug to a carrier molecule, which delivers the conjugate to a target cell using the carrier-receptor interaction. Examples of this approach are currently in the process of preclinical evaluation, particularly using antibodies against specific markers on cancer cells. 4) The avidin-biotin system applies the high-affinity interaction of the glycoprotein avidin (or its bacterial relative streptavidin) with the vitamin biotin, and is used as a mediator in all of the above-mentioned methods. It is an indispensable tool for diagnostics, biotechnology and nanotechnology.

DeveloGen Israel Ltd: Applying Peptidomimetic Chemistry for the Discovery of Novel Drugs for Metabolic Disorders

Nurit Livnah and Tamar Yechezkel

The research at DeveloGen Israel Ltd. (Formerly Peptor) is focused on the development of peptidomimetic drugs for metabolic diseases. Using DeveloGen's peptidomimetic technology, biologically active peptides are structurally modified in order to optimize their activity, selectivity and pharmacological properties, leading to highly potent and specific compounds with favorable pharmacological properties, such as Plasma stability, cell permeability and resistance to enzymatic degradation. The peptidomimetic technologies used, include replacement of peptide bonds by various covalent non-amide bonds, insertion of bi-functional small molecules and non-natural amino acids to the sequence, backbone cyclization, conjugation to hydrophobic moieties and more. The discovery process employs Multi-Parallel-Synthesis methods, that allow the screening of one-compound-per-well libraries, high-throughput purification and full characterization of each compound in each well, and rapid biological screening that feeds back into the design of the optimization process. The technology was applied to various projects throughout the last several years, and one example, of a peptidomimetic imaging agent in preclinical development, is presented.

CHEMISTRY IN ISRAEL - Bulletin of the Israel Chemical Society

Issue No. 20, December 2005 http://www.weizmann.ac.il/ICS

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TABLE OF CONTENTS

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Graphic Department, Weizmann Institute of Science, Rehovot.
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Printing:
Publishing Department, Weizmann Institute of Science, Rehovot

Ben-Gurion University of the Negev

הכינוס ה-71 של החברה הישראלית לכימיה

The Israel Chemical Society החברה הישראלית לכימיה

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