TAUTRENDS

in research 2008

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Tel Aviv University (TAU) prides itself on being the largest and most diverse university in Israel. One of the greatest challenges in the near future is the operation and management of multidisciplinary research. TAU has a big advantage in having its nine faculties on one campus, where different worlds can meet and new research partnerships can be created. These partnerships can be ad-hoc or more formal and long-term joint activities. The latter includes such multidisciplinary research centers as the Adams Center for Brain Studies, the Porter School for Environmental Studies, the TAU Nanotechnology Center and others. In these centers, researchers from different faculties can collaborate using joint research facilities. In scientific fields that require major investments in infrastructure, these centers help raise the funds for the equipment later utilized by all.

TAU provides its researchers state-of-the-art research infrastructure. This year TAU inaugurated a webpage "www1.tau.ac.il/research/equipment" in which all available equipment is presented in a clear and transparent way. TAU constantly upgrades its infrastructure. For example, to enhance research on the living cell, it recently purchased five confocal microscopes at a total cost of over $1 million. They have been installed in a new imaging laboratory for medicine and life sciences that serves some fifty research groups.

In the current issue of TAU TRENDS you can find a description of research topics representing all nine faculties, a sample of the quality and diversity of TAU research.

Hagit Messer-Yaron

Prof. Hagit Messer-Yaron
Vice-President for Research and Development

Faculty of Management – Leon Recanati Graduate School of Business Administration

Why "A Spoonful of Sugar Helps the Medicine Go Down"

Some products, like fitness centers, vitamins, dental floss and condoms promise important future benefits; but, since their consumption experience is unpleasant, consumers use them less frequently then they should. Both policymakers and marketers must find innovative ways to encourage more habitual consumption of such "virtue products," but in dealing with human emotions and motivations, logic is an imperfect guide.

Consider the case of fitness centers. For years, marketers have "educated" the public about the importance of frequent exercise by presenting thin and healthy-looking role models, to highlight the future benefits of exercising. This seemed reasonable, since a major aim of working out is getting into shape; but the impact was minor. Instead, a massive increase in frequent exercise at fitness centers occurred only once cable TVs were installed (see Figure 1). So instead of ads emphasizing the importance of looking fit, seemingly less important inducements, such as having LCD TV screens and cable channels, are now emphasized. Why did cable TV make such a big difference, even to those who had previously been gym-resistant?

Dr. Danit Ein-Gar of the TAU Recanati School of Business – in conjunction with Prof. Jacob Goldenberg and Dr. Lilach Sagiv of the Hebrew University of Jerusalem – has studied this phenomenon in some depth. Although adding any benefit will somewhat increase product demand, The investigators' research shows that the magnitude of its impact depends on the consumer's personality, particularly attitudes towards delayed versus instant gratification. A small, even negligible, benefit that provides present gratification (such as cable TV) can appeal greatly to low self-control consumers – those who do not exercise frequently and who have a short-term time orientation. They focus on the "here and now" and thus want immediate (even if unrelated) benefits while consuming the product. Conversely, future benefits, such as getting into shape are more appealing to consumers with high self-control and a long-term time orientation; and they are more likely to be affected by the classical pitch directed towards such ends. Thus, this research suggests that creating a better "fit" between consumers' self-control and the timing of virtue-product benefits can optimize perceived value, interest and consumption among different marketing segments.

The researchers tested this hypothesis in several experiments. In one experiment participants read a description of vitamins. Then they were asked how far they would be willing to drive to buy them. Some participants read a description in which the new vitamins had an extra sugar supplement (a present benefit); others read a description in which they had an extra fiber supplement (a future benefit). Those participants focused on the future, were willing to drive a greater distance to purchase the fiber-enriched vitamins. In contrast, those focused on the present were willing to drive a greater distance only when offered the sugar-enriched vitamins.

Next, the researchers tested whether high self-control people respond like long-term oriented ones; and low self-control people, like short-term oriented ones (Figure 2). Participants were given dental floss packages for their personal use; and they recorded how many flossing units they used over a period of 2-3 weeks. Some participants got floss with a present benefit (mint flavoring), others got floss with a future benefit (an improved, patented string called "Tuffloss," which better prevents both teeth and gum problems). Participants were categorized as high or low in self-control, based on self-reports. High self-control participants indeed used more units when the floss had the extra (long-term) future benefit. In contrast, low self-control participants used more units when the floss had the extra (short-term) present benefit.

Such findings demonstrate that, although "virtue products" are rarely consumed enthusiastically, it is possible to encourage consumers to use them more frequently by shifting the focus from the product's main goal to seemingly less meaningful – but apparently more persuasive – attributes which tap into a consumer's deep-seated time-orientation.

[Acknowledgement: Dentalon and Placontrol, Inc., and Anna Lotan kindly donated dental and facial products, respectively, for use in this research.]

Figure 1. TV spells the difference between boom and bust for fitness centers – but why?

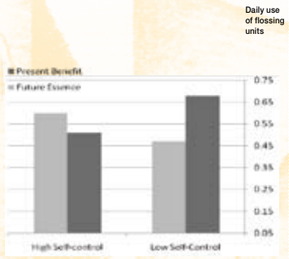


Figure 2. High self-control participants used more dental floss units when a future benefit (grey bar) was highlighted, while low self-control participants used more when a present benefit (black bar) was highlighted.

Iby and Aladar Fleischman Faculty of Engineering

TAU Pioneering Nanoelectronic Circuits

The use of integrated circuit (IC) technology to fabricate electronic devices has led to the rapid development of a major, worldwide microelectronics industry. Typically, high purity crystals of semiconducting materials are doped, chiseled and capped, in a sequential order, with various materials to create extremely complex electronic circuits embedded on a single substrate. For nearly fifty years now, IC technology has continued to develop ever faster and more complex chips, with ever smaller circuit components (which permits compressing more elements into smaller areas). Researchers are constantly searching for new materials and approaches to continue this exceptional progress. One novel idea in the realm of nanotechnology is bottom-up assembly. Unlike the monolithic IC process, in which entire circuit designs are transferred as a unit by photolithography, in bottom-up assembly, tiny building blocks are first produced and then transferred to desired locations.

Carbon nanotubes have spearheaded much current research on nanocircuits, due to their superb electrical properties, ease of fabrication and durability. Devices with unprecedented performance, such as extremely high carrier-mobility, have been shown to be achievable. However, despite their great promise, carbon nanotubes are scarcely used in commercial electronic devices because, despite extensive effort, there has been no practical method for integrating these tiny strands into circuits. A new method, recently developed by Dr. Yael Hanein and her colleagues in the TAU School of Electrical Engineering (TAU/EE), makes it possible to do just that.

Since carbon nanotubes are only several nanometers (millionths of a millimeter) in diameter, they can't be handled by conventional means. Instead, TAU researchers grow the tubes from the top of microscopic silicon pillars and vibrate the tubes by heating, which causes the tubes to stick to each other via short-range interactions (Van der Waals forces). This can be used to connect neighboring pillars with nanotubes. The network of tubes is then mapped with Raman spectroscopy to identify their exact properties and are then transferred using a stamping-like procedure onto a carrier substrate (this step is mediated by the interaction between the tubes and the surface in a similar fashion to the tube-tube interaction). The final step includes metallization of a thin gold layer to form electrical contacts to the tube segments. This process results in the formation of an ordered network of taut, carbon nanotubes

This novel TAU process provides both an innovative way to fabricate carbon nanotube field-effect transistors and a systematic approach for fabricating large quantities of nanotube-based devices on various substrate materials. The many advantages of this approach include the use of long, defect-free tubes grown in the suspended state; the precise structural information revealed by the Raman mapping; the simple, one-shot procedure for creating an entire prearranged network of individual, straight tubes. In short, TAU's pioneering scheme should provide – after optimization – a comprehensive and scalable technique for creating new large-scale devices. The major limitations lie in the yield of transferred nanotubes and in the initial growth of the network of nanotubes between the silicon pillars.

The integration of this technique is already underway in Dr. Hanein's laboratory, for use in various device architectures. Several other TAU research groups have also become involved in specific aspects of this effort. Prof. Ori Cheshnovsky's group (The Raymond and Beverly Sackler School of Chemistry) is helping explore the use of Raman spectroscopy for optimal circuit identification. Prof. Amir Boag and Dr. Koby Schuer (TAU/EE) are helping integrate the nanotube devices with nano-antenna structures. Dr. Slava Krylov and PhD student Asaf Yaakobovitz (TAU School of Mechanical Engineering) are helping explore the integration of the nanotubes with MEMS devices. The original project was initiated by former TAU/EE MSc student Ze'ev Abrams and is now implemented by current TAU/EE MSc student Gabriel Karp, working in Dr. Hanein's laboratory.

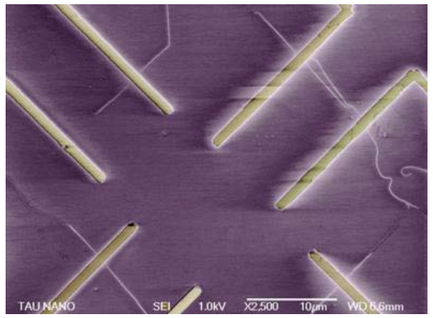


Figure 2. A circuit of carbon nanotubes (thin wires) on a silicon substrate with gold wires (thicker lines) as electrical contacts. These devices operate as extremely high quality field-effect transistors.

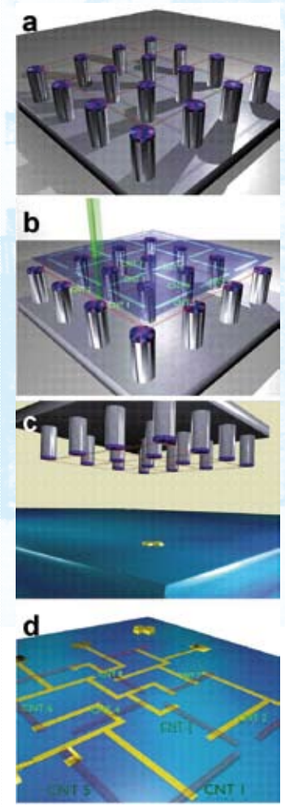


Figure 1. Sequence of steps performed to create carbon nanotube circuits. The nanotubes are grown between specified silicon pillars (a, b) before being transferred to an interconnect-bearing substrate (c, d).

Lester and Sally Entin Faculty of Humanities

Playing with Meaning

Figure 1. When students recently protested the falling apart of higher education, their slogans, although demanding, benefited from their optimal innovativeness. (The large sign reads "The semester is running out," but the two highlighted letters, an abbreviation for "Of Blessed Memory," implies it's as good as dead!).

Speakers love to play with language. Recent research by Miral Ariel and Rachel Giora at the TAU Linguistics Department shows that the way people play with language can be quite revealing about the nature of language and communication – and about playfulness' costs and effects.

Consider this humorous exchange:
A: When you come home, I'll have the food ready on the table.
B: I'd rather have plates.
A: What?
B: I'd rather have plates (not spaghetti, sitting directly on the table. Laughter).

Wasn't A planning on serving the food on plates? Of course, she was. Why didn't she say so? Because she didn't have to. When communicating, speakers rely on a rich body of contextual assumptions that they needn't specify. Note that had B said:
B: I'd rather have food.
the discourse would not be acceptable. Why can B get away with his first "wise-guy" interpretation, but not the second? It all depends on the purely linguistic meaning of "have the food on the table." These two examples teach us that, while contextual assumptions ('food is served on plates') are an integral part of the speaker's message, they are not part of its linguistic meaning, and so, can be ignored. Linguistic meaning itself cannot.

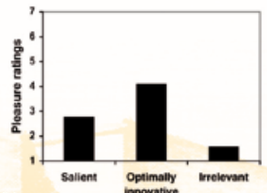
If so, argues Mira Ariel (www.tau.ac.il/~mariel), wise-guy interpretations can provide a useful tool for teasing linguistic meanings from contextual inferences in difficult cases. For example, linguists assume that the number 50 linguistically means 'at least 50.' But consider the following story from Hair (3.9.1990):
[A] couple went into the Allegro record store … to sell two CDs. The store manager offered … 40 shekels. The guy … said that … he could get 50 shekels. The manager … said that not on his life would he get such a sum. They took a bet … The guy … got 55 shekels … "Sorry", said the manager, "you lost. I said you wouldn't get 50 shekels, and indeed, you did not get such a sum".
Just like B, the wise-guy manager sticks to the linguistic meaning. We then see that 50 linguistically means 'exactly 50,' although in context, it could certainly convey 'at least 50'.

Why do speakers play with language? After all, such plays can be costly for the addressees, as can be seen above. Speakers take the risk of introducing novel interpretations to a discourse, because such novelty results in pleasing and witty effects. These plays rely on the listener's automatic activation of salient (coded) meanings, even when not invited to do so by contextual information. Indeed, words and phrases usually have more than one meaning, some of which – whether linguistic or inferred, literal or figurative – are more accessible than others, on account of their frequency, experiential familiarity, conventionality, prototypicality, and the like. These more salient meanings get activated even when unintended; and they affect both processing and its effects.

In a recent study, Rachel Giora (www.tau.ac.il/~giorar), Ofer Fein (The Academic College of Tel Aviv Yaffo), Ann Kronrod, Idit Elnatan, Noa Shuval, and Adi Zur of the Lester and Sally Entin Faculty of Humanities quantitatively investigated the costs and aesthetic effects produced by such innovations. They found that, to be highly aesthetic, a stimulus should be "optimally innovative," in that it should incur a novel (less salient or nonsalient) response (a peace of paper) while allowing for the automatic recoverability of a salient one (a piece of paper), so that both responses make sense despite being different from each other. Such innovations, although less familiar, are more pleasing than pure innovations (a piece of pepper), highly familiar versions (a piece of paper), and slightly less familiar versions (a single piece of paper). This leads to a highly interesting result. It is the ***familiarity*** in the unfamiliar that is responsible for the aesthetic effect (Figure 1). This is clearly seen in their data from a typical study of this effect (Figure 2a).

This pleasure, however, has to be earned. While optimally innovative stimuli were rated most aesthetic, they took longer to comprehend than more familiar stimuli (Figure 2b). Such intriguing studies probe the frontier between linguistics and the social, emotional and aesthetic contexts of communications.

(a)



(b)

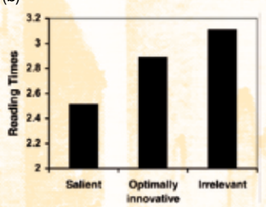


Figure 2. (a) Optimally innovative stimuli, which carefully balance novelty and familiarity, provide the most pleasure, but (b) they also demand more effort from the reader.

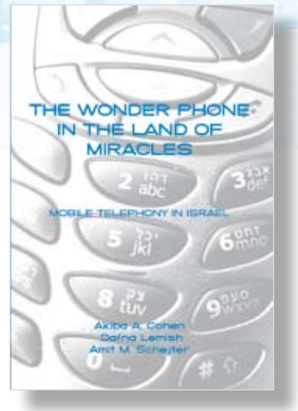
Gershon H. Gordon Faculty of Social Sciences

The "Wonder-Phone" in the Land of Miracles

Pelephone, the name of Israel's first mobile-phone provider, literally means Wonder-Phone; and it has become a fitting generic label for all mobile-phones in the country. The ubiquity and prominent place of these devices in Israeli culture – usage rates are among the world's highest – calls out for explanation. Several characteristics of Israeli society may contribute. First, Israeli society maintains close familial ties and cohesive social networks conducive to interpersonal contact and communication. Second, Israel's complex and trying relationships with its neighbors, and its fragile internal security situation, have created special needs, including those involving terror and military activity (e.g., compulsory active and reserve duty). Third, Israelis have a history of infatuation with and intensive diffusion of technological innovations, particularly those involving communication.

The rapid adoption and use of the mobile phone in Israel raises questions regarding a long list of behavioral and perceptual dichotomies: public and private, work and leisure, freedom and control, male and female, young and old, technology and nature. In addition, questions involving etiquette and values bring to the forefront changes in accepted normative behaviors, as well as the reconstruction of substantive issues such as the nature of "truth" and the social expectation to reveal it (e.g., the whereabouts of the caller and person being called). Finally, it tackles self-perceptions, as people discuss the mobile-phone behavior of "other" Israelis as rude, inconsiderate, pushy and ***chutzpahdik*** (cheeky).

Using a variety of quantitative and qualitative methods, Prof. Akiba A. Cohen and Dafna Lemish of the TAU Department of Communication - in conjunction with Prof. Amit Schejter of Pensylvania State University – have examined the place that the "Wonder Phone" occupies in many facets of Israeli life. Their framework includes historical research on policy and regulation; telephone surveys and face-to-face interviews; real-time measurements of mobile phone use (using sophisticated interactive voice-response technology), semiotic analysis of advertising for mobile phones; and secondary analyses of archival data provided by Cellcom, Israel's largest mobile-phone provider (that graciously funded these studies).



It was concluded that the mobile-phone is "not only talk," as an advertising slogan of one Israeli mobile-phone provider suggests. Rather it is a medium through which Israelis define their gender and national identitites. It offers an experience of "being there," and a security net to hold family members and loved ones together, especially in times of war and terror. It also provides a lifeline during existential crises, such as those involving rituals of mourning.

In analyzing the mobile-phone as it is contextualized in Israeli society, the researchers found clear evidence of two opposing social forces: on one hand, the mobile phone is an expression of modernity and globalization; but, on the other hand, it has been recruited as both a tool and a symbol for the expression of locality and patriotism.

Yolanda and David Katz Faculty of Arts

Old and New: Architecture and Interactive Video Thrive at TAU

Figures 1, 2. Beit Ha'am architecture reflected the interest of Zionist pioneers and architects in traditional local culture (Beit Ha'am Baerwald), international modern forms (Maabaroth Communal Hall), and a creative blending of the two.

TAU's Yolanda and David Katz Faculty of Arts explores artistic expression over a wide range of medias and eras, united by an emphasis on how human creativity impacts our emotions, experience and daily life.

Folk Houses originated in Europe, as one of the most important offshoots of the international workers' movement. The Folk House ***(Beit Ha'am)*** and Culture House ***(Beit Tarbut)*** concept was readily translated to Eretz Israel, where new settlers, mostly from Europe, endowed them with the unique content of the new Zionist culture. Their significance in the new settlements, and the cultural, economic and esthetic values invested in their establishment, were comparable to those of the traditional synagogue for which they often provided a secular substitute. These decidedly modern edifices were planned and executed by renowned Israeli architects who provided their most innovative designs. As such, they represent major architectural developments in the early years of the renewed Jewish settlement, from the end of the nineteenth century until the middle of the twentieth.

Drs. Esther Grabiner and Edina Meyer-Maril, of TAU's Department of Art History and the David Azrieli School of Architecture, are documenting and analyzing the crucial role of these entities in the development of both Israeli architecture and Israel's sociocultural history. Their work is partly supported by a grant from the Israel Science Foundation (ISF). Promoting awareness of this important building type will also help ensure that these buildings are properly documented and preserved. Their project also addresses current Israeli cultural debates and the role of architecture within them. Study of the ***Beit Ha'am*** and ***Beit Tarbut*** will enable a reassessment of the building environment as both an initiator and recipient of culture, and underscores the centrality of architecture as an agent of social change.

At the other extreme of modern Israeli history, the ubiquitous and versatile internet has opened new opportunities for creativity, which both compete with and contribute to preexisting media. The standard movie is a continuous, fixed, non-interactive narrative, which coherently leads to a specific, preplanned emotional impact on the viewer. The standard computer game, by dividing the narrative into a series of alternative segments, is anything but. Now a host of new forms, such as interactive internet video, are springing up in between. How are these alternative forms of presentation influencing each other, and what can each learn to expand the limits of their own form of artistic expression?

Figure 3. As this homepage suggests, interactive video is both new and real and surely will change the way we view things – but what are its implications for conventional media such as movies? TAU researchers see an interactive future.

Drs. Nitzan Ben-Shaul and Duby Rubinstein of the TAU Faculty of Arts' Film and Television Department, recently received a grant from NDS, a leading digital pay-TV technology developer, to research the impact of the internet on video production and its reception by audiences. Their pioneering research seeks to analyze new and emerging internet video formats, highly interactive and selectable contents, and a wide variety of new user interfaces (e.g., interactive movies, iptv, YouTube, blogs). Their work should provide important insights into how these new developments are changing movie and video production and viewer reception.

Analysis of audiovisual media reception suggest a gradual trajectory from film, which provides viewers with a self-contained narrative that tightly directs and facilitates their cognitive and emotional construct of the experience, to television, in which those must be construed out of disjoint audiovisual segments, to interactive and internet video which complicates these tasks by adding interaction and choice. Internet video actively splits the user's attention and enhances choice (via segmentation and interaction), running the risk of evoking viewer distraction or frustration. The latter might be avoided by internet platforms and strategies that facilitate the user's personal research objectives, gaming involvement or narrative motivations, while helping them to cognitively reestablish coherence and deepen their emotional involvement. In particular, the TAU researchers will explore the development of flexible, novel video categorizations, personal customizations and multi-threaded venues for following the same event.

Dr. Ben-Shaul is also in the process of devising an authoring software tool for the production of interactive movies, together with his former students Noam Knoller and Udi Ben Arie. At present, interactive movie experiments have failed, mostly because their interactions are more gaming than narrative directed. Ben Shaul seeks to produce more engaging interactive movies by devising interactions according to dramatic-narrative considerations. TAU's Fund for Applied Research has expressed interest and patenting is underway. Handled properly, interactive movies could provide added-value for narrative-motivated consumption and complement – or even surpass – the popularity of standard film and television. Thanks to such initiatives, the TAU Film and Television Department should step to the forefront of innovative computer-based movie research and production.

George S. Wise Faculty of Life Sciences

Glia Cells: A Key to Neurological Diseases?

In 1856, the famous German pathologist Rudolf Virchow, first used the term glia (glue in Greek) to describe a new type of brain cell he found surrounding and interconnecting neurons. Glia cells maintain brain plasticity, protect the brain during functional recovery from injury and, once properly activated, are the first defense against the pathological abnormalities of neurodegenerative diseases. Activation signals are numerous; and their actions, complex. For example, they can make specific subsets of glia cells either neuroprotective or neurotoxic. (e.g., by producing reactive oxygen species, proteases and pro-inflammatory cytokines). Glial cells can also produce nerve growth factor and mediate neuronal growth in neurodegenerative diseases.

Dysfunctional glial-cell receptors, that alter the cells' sense of their environment, can lead to neurological diseases, as can age-related changes in glial cell division. Since glia cells constitute the largest cell population in the brain, and since they continually renew themselves over a human lifetime, they are a prime target for therapeutic intervention. However, the diversity of glia families (astrocyte, microglia and oligodendrocyte) makes this difficult. Finally, glial-cell plasticity and diversity may allow the maturation of new functional cells, to aid in neuronal repair.

Dr. Dan Frenkel's laboratory, in the TAU Department of Neurobiology, investigates glial-neuronal cell interactions to clarify their role in neurological diseases, both in culture ***(in vitro)*** and in animal models of Alzheimer's disease and stroke ***(in vivo)***. The researchers use advanced gene array techniques as well as immunological approaches using fluorescent activated cell sorting (FACS) to shed light on the genes – and thus proteins – involved in glial cell function. Modifying the activity of glial cells to reduce their neurotoxic effects and to enhance their neuroprotective effects, could lead to new therapeutic interventions in neurological diseases, including new drug-target candidates.

For example, Alzheimer's disease, which affects more than 20 million people worldwide, is associated with the increased production and accumulation of the waxy amyloid-beta protein. Microglial cells provide a natural mechanism by which amyloid protein aggregates and debris could be removed from the brain; and Dr. Dan Frenkel together with master student Dorit Farfara are investigating mechanisms that could activate microglia to promote the clearance of amyloid-beta (Figure 1) and prevent neuronal death in Alzheimer's disease.

The interactions of glial cells (particularly astrocytes) with endothelial cells, support and maintain the blood-brain barrier, which is critical for homeostasis. It also regulates amyloid-beta transport to and from the brain. In cerebrovascular amyloidosis (CA), amyloid-beta is deposited on the walls of small blood vessels in the brain, which can lead to stroke, hemorrhage or dementia (Figure 2). Incidence of this disease is about 10% to 40% in the general elderly population, but 80% in Alzheimer's disease. Dr. Frenkel and PhD student Veronica Lifshitz have been studying mechanisms of CA deposition in both animal and cell models in order to identify candidate targets that mediate amyloid deposition for a future novel therapeutic application in CA. The success of this research will constitute a basis for understanding and treating CA as well as other vascular amyloidogenic diseases.

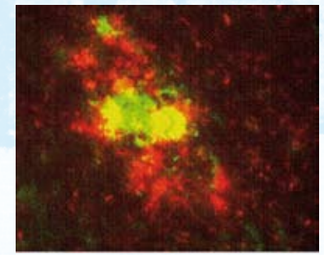


Figure 1. Activated microglial cells (stained red) clear amyloid plaque (green) in an Alzheimer's disease animal model.

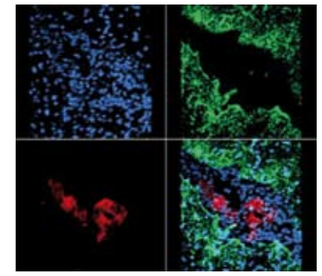


Figure 2. Activated astrocytes (green) surround vascular amyloid (red) in an animal model of Cerebrovascular Amyloidosis. (The cell nucleus is stained blue.)

Sackler Faculty of Medicine

Master Gene Regulates Eye Development

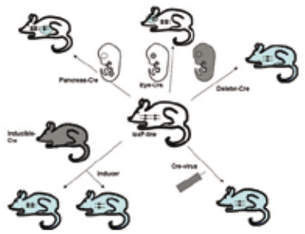


Figure 1. In the Cre/loxP approach for somatic mutagenesis, a mouse line in which the gene of interest is flanked with loxP sequences (arrow heads) is mated with a Cre-expressing mouse line (or injected with a Cre-expressing virus) in order to create somatic mutants. Cre expression is denoted by dark-gray; regions of somatic deletion, by light-blue.

Darwin once described eyes as "organs of extreme perfection and complication," referring to the exceptional number of different tissue types that must function together in vision. Located at the back of the eye, the neuroretina is a complex neural network composed of six different types of nerve cells (neurons). The cones and rods are photoreceptor cells which respond to light and transmit signals to retinal interneurons that further process the information and communicate it to ganglion cells. The ganglion cells extend axons to the brain, where this visual information is processed still further.

Visual acuity also requires focusing external images on the retina. This is accomplished by refraction within the transparent lens and cornea, located at the front of the eye. The contractible iris, located between the lens and cornea, controls the amount of light entering the eye, which also improves acuity. Other ocular tissues, such as drainage structures and the retinal pigmented epithelium, are essential for the survival and function of the retina. Thus, normal vision requires the proper morphology, function and positioning of many diverse types of tissues, and even slight deviations can be associated with blinding diseases, such as retinal degeneration and cataracts.

Intriguingly, a single gene, Pax6, can initiate eye formation in both invertebrate and vertebrate species. The PAX gene family includes several transcription factors that play important developmental roles, so it is perhaps not surprising that Pax6 is also required for normal development of the brain, pancreas and olfactory system. However, it is particularly essential for eye formation. Eyes do not form in its absence and ectopic eyes are induced upon its mis-expression (in flies and frogs). Moreover, its "dosage" directly affects normal eye development in mammals, as loss of one functional allele and increased Pax6 expression both result in severe ocular phenotypes.

Despite its importance, early attempts to study Pax6's tissue-specific roles were limited, due to the early arrest in eye development that occurs in Pax6-mutant embryos. Dr. Ruth Ashery-Padan and her colleagues at the TAU Sackler Faculty of Medicine have now overcome this problem. To study Pax6's spatial and temporal roles in vivo, her group employs a somatic knockout approach for the temporal and tissue-specific inactivation of Pax6 in the developing embryo eye. The somatic mutation is created using Cre, a viral protein which acts like targeted, molecular-level "DNA scissors." When Cre identifies two copies of a specific sequence (loxP), it fuses the two loxP sites together, deleting the intervening DNA sequence. The Cre enzyme and its loxP recognition sites are not normally present in mice. However, using advanced genetic tools, the TAU team (in collaboration with the laboratory of Prof. Peter Gruss, Max-Plank Institute, Goettingen, Germany) introduced a pair of loxP sites around the Pax6 gene of one transgenic mouse line. They then created a second transgenic mouse line containing the Cre gene attached to regulatory elements that permit its expression only in specified tissues (for example in the retina or lens). When mated, the offspring of these two transgenic mouse lines carry both a pair of loxP's around the Pax6 gene and a Cre gene which is expressed only in specific tissue types. The Pax6 (or any other gene so treated) will now be deleted only in the cells that express Cre, but not in adjacent cells (see Figure 1).

The selective somatic deletion of Pax6 exclusively from the developing lens revealed that this factor is essential for lens formation and that the lens determines retinal polarity (Figure 2). Inactivation of Pax6 exclusively in the developing neuroretina revealed its role in helping retinal progenitors produce a number of different cell types (multipotency). Following Pax6 loss, only a single type of interneuron is formed, and differentiation to the other neuronal fates is lost (Figure 2). The TAU researchers have now successfully used their approach to genetically dissect Pax6 dosage requirements in a number of ocular cell types. For example, they have discovered that Pax6 dosages are required within the iris and lens (cell-autonomously) for the proper growth and differentiation of these tissues.

The TAU research team is now identifying Pax6-dependent pathways involved in the transition of progenitor cell to differentiated ocular cell types. This is accomplished by utilizing their somatic mutants combined with high-throughput genomic approaches. These studies should clarify cellular and molecular events that mediate complexity in organ formation and elucidate the genetic basis of many ocular diseases. Understanding the molecular processes that govern organ formation is also crucial for eventually utilizing stem cells and tissue engineering technologies in regenerative medicine.

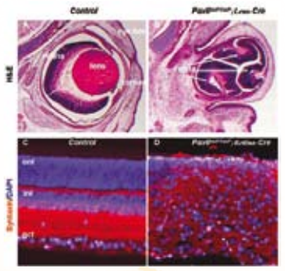


Figure 2. Cre/loxP mediated inactivation of Pax6 in the developing lens and retina reveals the multiple roles of Pax6 in eye development. (A) Stained section of a normal mouse embryo, showing the lens, retina, cornea and eyelids. (B) Inactivation of Pax6 in the lens prevents lens formation, and results in several retinal folds. (C) The normal adult retina is populated by six types of neurons, organized in the three cellular layers shown. In the normal retina the amacrine interneurons (here stained red) populate the inner nuclear layer (inl.). (D) Inactivation of Pax6 in the embryonic retina prevents normal retina development; and only amacrine interneurons differentiate from the Pax6-deficient retina progenitor cells.

Buchmann Faculty of Law

National Courts React to Globalization

The importance of borders between nation states has decreased dramatically due to increasing globalization. Goods, services, money and people are moving across political boundaries at an ever increasing pace; and intergovernmental coordination has become a prerequisite for the regulation of markets, the environment, other human activities, including national security. From a democratic perspective, such transnational coordination lessens opportunities for public participation in decision-making and limits mechanisms that ensure accountability of the coordinating agencies. Intergovernmental coordination offers domestic interest groups and government officials new means to circumvent domestic democratic and supervisory processes that had been developed through years of effort by civil society, legislatures and courts.

In a recent landmark study, Prof. Eyal Benvenisti of the TAU Buchmann Faculty of Law suggests that national courts are now reacting to these trends by coordinating their positions to form coalitions capable of challenging intergovernmental action. Their aim – to reclaim the space for domestic democratic deliberation. Courts have come to realize that interjudicial coordination has become a prerequisite for performing their traditional task of judicial review. To facilitate this, national courts are developing a shared language, based on comparative constitutional law and international law, that enables them to communicate with each other and monitor each other's performance.

It wasn't so long ago that the overwhelming majority of courts in democratic countries shared a reluctance to refer to foreign and international law. They sought to avoid any application of foreign legal sources that could clash with the position of their domestic governments. However, as Prof. Benvenisti demonstrates, this situation has recently changed, as courts in various countries seek to forge a united judicial front by coordinating their policies with similarly positioned courts in other countries.

This coordination strategy seems limited to situations in which national courts perceive that their government, their legislature, or they themselves are threatened by economic or political powers that stifle the democratic process through coordinated supranational standards, be they formal (in treaties) or informal. This suggests that courts might not be equally adamant in purely local disputes, for example, over conditions for detaining local criminals or for displacing indigenous inhabitants to permit dam construction. This also could explain why the U.S. Supreme Court, which, so far, has not had to protect its domestic political process from external pressures, is still not part of this collective effort.

Finally, based on this insight into the driving force behind increased reliance on foreign law, Prof. Benvenisti asserts that this trend is perfectly legitimate, in terms of democratic theory, as it aims to reclaim democracy from the debilitating grip of globalization.

It is, however, too early to assess the success of this trend. Every collective action depends on accumulating a sufficient number of contributors to the joint effort; and changes in domestic rules protecting judicial independence could dampen the willingness of some courts to assume an assertive role. Governments also may be pressured to support intergovernmental efforts that deprive courts of the authority or opportunity

to act. But, following Benvenisti's analysis, it seems unlikely that national courts will sit idly by, while their authority to review the actions of the political branches erodes away. In an era when governments are opting for alternatives to formal internal or international lawmaking, it is the national courts that are turning very seriously to comparative constitutional law and to international law.

The observed resourcefulness of national courts suggests that concerns about "the retreat of the state" due to globalization may be overly pessimistic. Although the state has lost much of its ability to affect external and even internal outcomes, its various branches have learned the art of transnational coordination. Such coordination enhances their abilities both to make and enforce policies, and to check other branches of government.

Raymond and Beverly Sackler Faculty of Exact Sciences

Nanowires Detect Biological and Chemical Agents in Real-Time

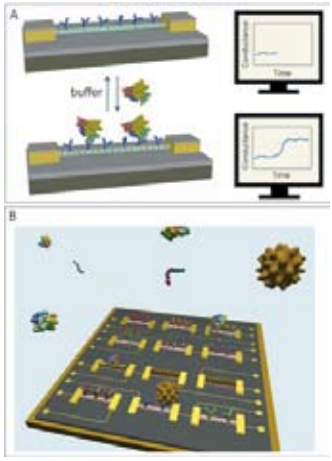


Figure 1A. Binding specific receptor molecules to a nanowire (top) creates a highly sensitive, real-time detector. Nanowire conductance rises when a target molecule binds its receptor (bottom).

Figure 1B. An array of nanowires sporting several different receptors can simultaneously bind and detect several different agents, from small molecules to virus particles.

"Who goes there?" Detecting proteins and other molecular species by high-throughput systems is critical in many areas ranging from medical diagnosis and treatment, drug discovery and biosafety, to elucidating basic protein functions and interactions. Microarray probes, based on target-receptor binding, can now provide selective and rapid screening of proteins, using incredibly small amounts of sample.

Most protein detection methods can be divided into two broad categories: labeled detection (e.g. ELISA, in which the protein is bound to an antibody linked to an enzyme that catalyzes a color change in a reagent) and label-free detection (e.g. surface plasmon resonance, bending microcantilevers, etc.). However, these approaches typically require binding multiple antibodies (which recognize different epitopes of the target protein), fluorescent labeling, and other additional steps which increase the assay's cost, while reducing its quantitative accuracy, reproducibility and sensitivity. They are also too slow for real-time detection, a highly desirable property for high-throughput applications. Thus, no existing sensing platforms have the combination of features required for the rapid, highly sensitive, multiplexed detection of a broad range of biological and chemical agents.

Prof. Fernando Patolsky and his colleagues at the TAU Raymond and Beverly Sackler School of Chemistry and TAU Center for Nanoscience and Nanotechnology, focus on the interface between nanoscale materials and biomaterials, an exciting new multidisciplinary area which combines biology, physics, chemistry, biotechnology, medicine and engineering. More specifically, the TAU group excels in the synthesis, characterization and applications of semiconductor (e.g. silicon) nanowires. A well-developed understanding of nanowire growth mechanisms now allows the reproducible synthesis of inorganic nanowires of homogeneous composition and diameter, with controllable electronic and optical properties suited for a wide variety of important applications.

The TAU researchers are developing nanowire detectors for biomolecules and other chemicals that can provide accurate, label-free electrical readouts in real-time, without the use of bound dyes or fluorescent probes. Their nanowires function as field-effect transistors (FETs), whose conductivity changes in response to variations in the electric field potential at their surface. In a standard FET, the flow of electrons from the source wire to the drain wire is switched off and on by a third electrode ("gate"), capacitively coupled through a thin dielectric layer to the semiconductor. In the case of a p-type semiconductor, applying a negative gate voltage leads to an accumulation of positive charge carriers (holes) and a corresponding increase in conductance. FETs are natural candidates for electrically-based sensing, since the binding of a charged or polar chemical species to the "gate" dielectric is analogous to changing its voltage. For example, binding a protein with a net negative charge to the surface of a p-type FET increases the FET's electrical conductance, a readily measured output.

Nanowire sensors also benefit from their one-dimensional morphology. A chemical binding to their surface leads to the depletion or accumulation of carriers throughout the entire cross-section of the device, versus only a thin region near the surface of typical large-area planar detecting devices. That is, the binding event leads to a much greater change in device conductance (sensitivity). The wires can be turned into sensitive detectors by linking specific receptor groups to their surface. When these surface-modified devices are exposed to a solution containing the macromolecule species of interest, specific binding to the receptor increases or decreases the device's conductance, depending on the net charge of the biomolecule (Figure 1A). The binding process can be viewed in real-time on a computer screen, which monitors the conductance of one or more devices. The small size of nanowire devices also allows packing hundreds of individually addressable nanowire devices within a tiny sensing area. Using distinct receptors on different nanowire elements allows multiplexed, real-time assays of multicomponent solutions, such as the simultaneous detection of proteins, DNA, viruses and small molecules (Figure 1B).

The TAU group is now developing ultrasensitive electronic arrays for sensing disease-related protein biomarkers, and for detecting small molecules of explosives and biological warfare agents. This innovative, general platform should eventually permit screening complex biological fluids and environmental samples for specific agents and have a broad impact on the life sciences, medicine, forensics and security.