

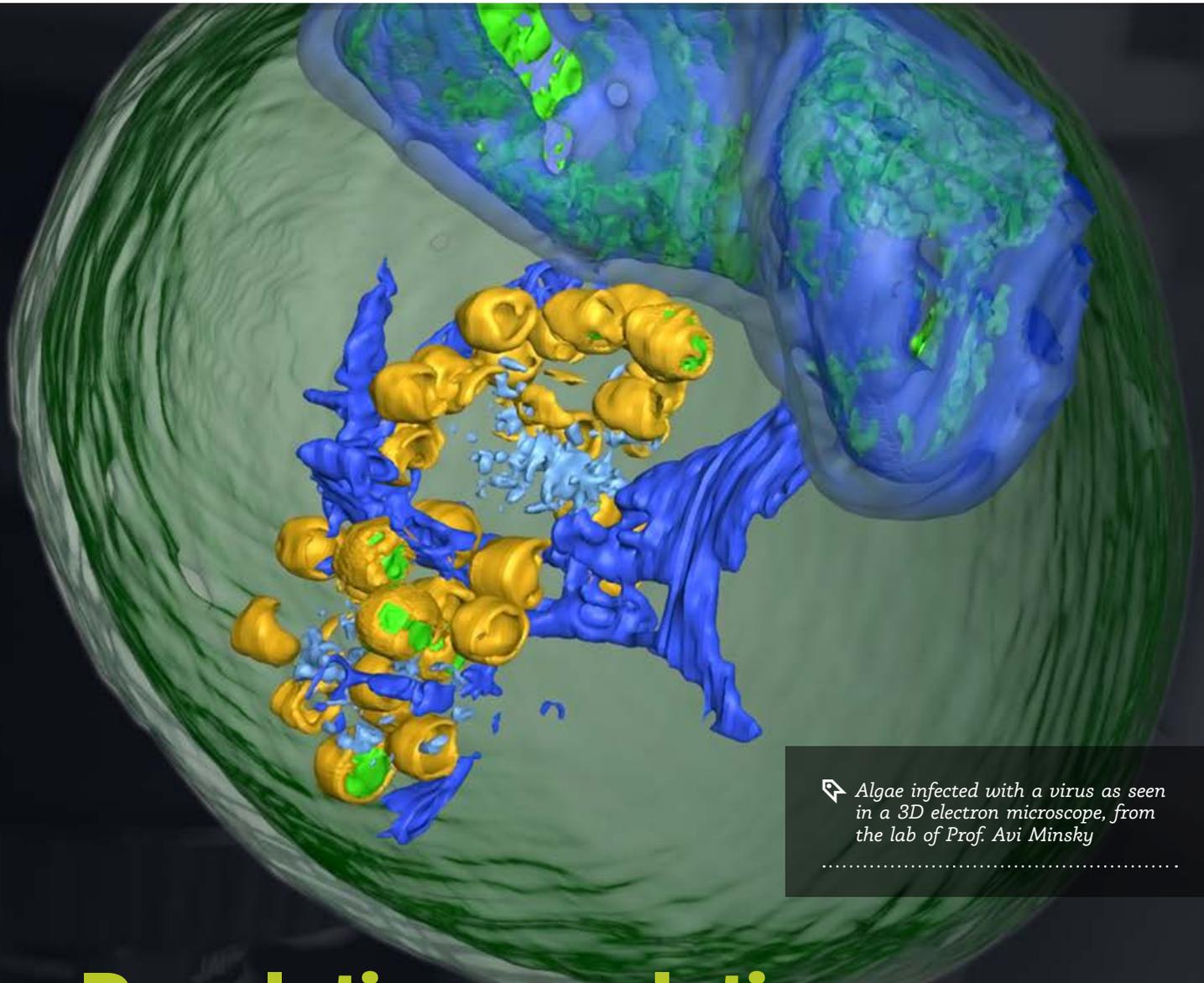
SPRING 2017

מכון ויצמן למדע
WEIZMANN INSTITUTE OF SCIENCE



THE WEIZMANN

INTERNATIONAL MAGAZINE OF SCIENCE & PEOPLE No. 11



🔗 *Algae infected with a virus as seen in a 3D electron microscope, from the lab of Prof. Avi Minsky*

Resolution revolution

Modern microscopy's impact on science

Editing the genome: the story of CRISPR

André Deloro: a builder of Israel's future



From the President

Dear Friends,

I always say that basic science takes years of investment and large sums of money to generate insights that lead to advances in human health and enlightenment about our universe. But some things have just sped up—and dramatically so. Our cover story highlights the revolution in microscopy: Because microscope technology has advanced by leaps and bounds, particularly in the last decade, the pace of research has quickened, allowing our scientists to see the elements of life—from cells to interactions between proteins to the movement of atoms—in vivid detail. That enables them to focus on ever-more-nuanced questions and reach levels of understanding that simply weren't possible even a decade or two ago. The implications for the life sciences, and thereby human health, are substantial.

We are thrilled to congratulate Prof. Yossi Yarden on his winning of the Israel Prize, the country's highest honor. Prof. Yarden has made crucial discoveries in the biochemistry of cancer over the course of his career, which have paved the way for treatment protocols that have entered into clinical practice. Prof. Yarden, who runs the Dwek Institute for Cancer Therapy Research in the Moross Integrated Cancer Center, is a pillar of our cancer research whose lab has generated several generations of scientists. This is a very well-deserved honor.

We have lots to report on about the successful International Board in November, and, as always, stimulating and moving stories about our supporters and their relationships to the Weizmann Institute. Such stories are always a heartwarming indication to me of how expansive and incredibly special our global community is, and how they provide an important engine in the research conducted here at the Weizmann Institute.

With all best wishes for a healthy and pleasant spring,

Sincerely,

Prof. Daniel Zajfman

President, Weizmann Institute of Science

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 *Pictured on cover: Eukaryotic cell chlorella alga infected by Paramecium Bursaria Chlorella Virus -1. The 3D image was acquired by Focused Ion Beam/Scanning Electron Microscope (FIB/SEM). Authors: Elad Milrot, Katya Rechav (Chemical Research Support), and Avi Minsky; the research was performed under the supervision of Prof. Avi Minsky, Department of Structural Biology. It was published in Cellular Microbiology in 2016.*

How did the Moon form?

Weizmann Institute planetary scientists offer a new, plausible answer to the biggest lunar mystery

Although it is a cross-cultural symbol of serenity, when the Moon first made its appearance a few billion years ago, calamity, not calm, was the order of the day.

Now, computational modeling by planetary scientists at the Weizmann Institute has painted a new picture of the violent circumstances accompanying the Moon's birth, one that involves collisions between a number of objects and the Earth's surface. In so doing, they have presented an elegant theory that represents a formidable challenge to the long-favored "giant impact" scenario of the Moon's formation.

In their study, published in *Nature Geoscience*, doctoral student Raluca Rafu and Prof. Oded Aharonson of the Department of Earth and Planetary Sciences set out to seek alternatives to the Moon-formation hypothesis in vogue since the 1970s—in which a single collision of a Mars-sized object produced a hot, massive, and rapidly rotating disk around the Earth from which the Moon then condensed and cooled to its present form.

An alternative theory was necessary because of a vexing problem with the "giant impact" scenario. According to this scenario, 80 percent of the material ejected into space came from the impacting object, with 20 percent emanating from the Earth's surface.

However, modern studies have shown that the chemical composition of the Earth and the Moon are a near-perfect match, indicating that most, if not all, of the Moon's formative material originally came from Mother Earth. The liberation of such a huge amount of material in a single blow—leading to the formation of the Moon we know—would require that the cosmic collision match highly specific criteria, in fact, so specific as to be improbable.

The study presented a compelling model that may solve that mystery. Using Chemfarm, a computational infrastructure consisting of more than 5,000 processor cores, the researchers ran 800 simulations about how, in the early days of our solar system, bombardment of Earth by extra-terrestrial objects may have caused the Moon to emerge. Their investigation suggests that it was a series of run-ins with smaller objects, rather than a single giant punch, that formed the Moon. These smaller collisions could have resulted in the creation of orbiting "moonlets"—which later merged into a single Moon.

Working together with Dr. Hagai Perets of the Technion, Prof. Aharonson's team suggested that a number of smaller collisions might better explain what happened several billion years ago, when the solar system was taking shape. Such smaller bodies would have been more prevalent in the system, and thus collisions with the smaller objects would have been more likely.

According to Prof. Aharonson, the scenario also offers an explanation for the isotope identity crisis: the fact that the chemical signature of the Earth and Moon are so remarkably similar.

"If a number of different bodies collided with Earth over a period of millions of years, their different chemical signatures—for example, ratios of oxygen-16 to its heavier cousins, oxygen-17 and -18—might even out, masking the traces of the various collisions," he says.

According to Raluca Rafu, the new model provides a strong basis for determining the long-term dynamics that may have formed the most familiar face in the night sky. "The new scenario does not require finely tuned initial conditions," she says. "And if the smaller moonlets, as we think, were drawn into the same orbit, they could have merged over millions of years."



Science Briefs

2-3

Israel Prize in Life Sciences

To Prof. Yosef Yarden



Prof. Yosef Yarden, a member of the Weizmann Institute's Department of Biological Regulation, has been awarded the 2017 Israel Prize in Life Sciences. The Prize, which is the country's highest honor, will be presented to Prof. Yarden in celebration of his crucial discoveries about the biochemistry of cancer, in a festive ceremony on Israel Independence Day.

Over the course of his career, Prof. Yarden has made a significant and original contribution to the understanding of cancer, and has paved the way for new treatment protocols that have entered into clinical practice and saved lives. Focusing on the activity of hormone-like molecules called growth factors, Prof. Yarden's discoveries have led to the development of several successful anti-cancer drugs.

Much of Prof. Yarden's research is centered on EGFR and HER2, which belong to a family of growth factor receptors that play a critical role in tumor progression. As a result of his work, several strategies for blocking these receptors were devised and approved for use with cancer patients.

Most recently, the Yarden lab has been investigating strategies for circumventing the resistance that some lung cancer patients develop to anti-cancer immunotherapy. Combining an antibody that blocks EFGR activity with two additional monoclonal antibodies, Prof. Yarden successfully inhibited cancer cell proliferation in a mouse model of lung cancer, and slowed overall tumor growth. This "triple antibody" methodology may someday form the basis of tailor-made, personalized strategies for combating cancer in humans.

An alumnus of the Institute who completed his PhD in 1985, Prof. Yarden has been a faculty member since 1988. He has served as Dean of the Faculty of Biology (1997-1999), Vice President for Academic Affairs (1999-2001), the first Director of the MD Moross Institute for Cancer Research (1999-2001), and Dean of the Feinberg Graduate School (2001-2007). He is the director of the Dwek Institute for Cancer Therapy Research of the Moross Integrated Cancer Center and is the Harold and Zelda Goldenberg Professor of Molecular Cell Biology.

Prof. Yarden is the recipient of a large number of prestigious awards, including the MERIT Award of the U.S. National Cancer Institute, and the 2007 EMET Prize in Biochemistry.

The secret messages of viruses

What convinces an invading virus to hold back and to lie dormant inside a host cell rather than going for the kill? According to new research by Prof. Rotem Sorek, infectious agents “conspire” with each other, coordinating the timing of their attack based on molecular messages left behind by viral “relatives” from generations past.

“When a virus invades, its ultimate goal is to replicate—a process which destroys the host by rupturing the cell wall or membrane,” says Prof. Sorek, a member of the Department of Molecular Genetics. “But if fast-replicating viruses are too gung-ho, there won’t be any hosts left for future generations.” He found that phages—infectious viruses that attack bacteria—secrete small molecules that other phages can later pick up and “read”. These molecular messages help the viruses determine whether to replicate quickly, or to become dormant and lie in wait. This process is the basis of a sophisticated strategy that promotes virus survival.

The study, published in *Nature* in January, represents the first time that viruses have been “caught” communicating with each other. Prof. Sorek’s group, led by research student Zohar Erez, also included Weizmann Institute staff scientist Dr. Gil Amitai, and Dr. Ida Levy of the Israel Institute for Biological Research.

The research group discovered the small communication molecules almost by accident, while searching for evidence of communication between bacteria infected by phages. The team grew bacteria in culture and infected them with phages; they then filtered the bacteria and phages out of the culture,

leaving only the smallest molecules that had been released to the medium. When they grew more bacteria on the filtered medium and infected them with the same phages, they were surprised to find that the new phages became dormant rather than killing the bacteria.

The scientists determined that high concentrations of the communication molecule—a short chain of amino acids called a peptide—caused the phages to “choose” dormancy over the replication that would immediately kill the host cell. Having discovered that such a choice exists, the team named the peptide arbitrium, the Latin word for ‘decision’.

“The molecule we discovered enables each generation of viruses to communicate with successive generations, by adding to concentrations of the arbitrium molecule,” Prof. Sorek says. “Each virus can then ‘count’ how many previous viruses have succeeded in infecting host cells and decide which strategy is best—virulence or dormancy—at any point in time.”

They went on to find similar molecules in dozens of related phages, and ultimately deciphered a phage-specific communication code. “It is as if each phage species broadcasts on a specific molecular ‘frequency’ that can be ‘read’ by phages of its own kind, but not by other phages,” says Prof. Sorek. Like an army bugle, this message “rallies the troops” to attack host cells at the optimum time.

The dormancy strategy may have broader implications: If the viruses that infect humans are found to communicate with one another in a similar manner, scientists might learn to intercept these messages and use them to our advantage.





The brain's GPS

Whoever coined the phrase “blind as a bat” probably didn’t know that bats see almost as well as humans. Bats also hear well, orienting themselves via “echolocation”—a system based on sound. But it turns out that even without such sensory input, bats can navigate successfully, thanks to a special class of neurons in the bat brain recently identified by scientists at the Weizmann Institute.

Located in a part of the brain associated with memory, “navigation” neurons reveal a brain-based link between where we’re going and what we remember. Interestingly, the bat-based study may help explain how memory loss and “getting lost” tend to go together in human Alzheimer’s patients.

The study was performed by Prof. Nachum Ulanovsky and research student Ayelet Sarel, both of the Department of Neurobiology, together with their departmental colleagues Drs. Arseny Finkelstein and Liora Las. Their results were published in *Science* in January.

A calculated flight path

To clarify how bats navigate, Prof. Ulanovsky and his team trained Egyptian fruit bats to fly highly complex trajectories within a specially designed flight room equipped with a landing site where the bat could eat and rest. During flight, a wireless device recorded the activity of 309 single neurons in the bats’ hippocampus.

The scientists discovered that about a fifth of these hippocampal neurons were goal-direction cells, maximally active when the bat was heading toward the goal at a particular angle. In flying sessions in which the goal was obscured by an opaque curtain that blocked sensory input based on vision, echolocation, and olfaction, a substantial fraction of these neurons still exhibited directional firing triggered by

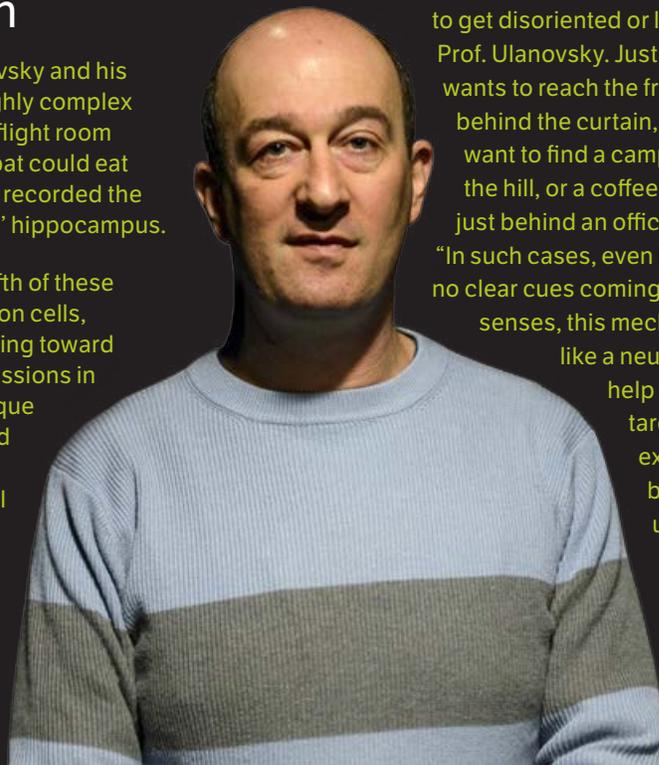
information about the target stored in memory.

The scientists also discovered neurons that fired maximally when the bat was close to the target. Rather than being entirely separate from the directional neurons, a statistically significant number of these “goal-distance” neurons expressed “goal-direction” as well.

The Alzheimer’s connection

The *Science* study helps clarify the connection between navigation and memory—and not just in bats.

“Damage to the hippocampus has been shown to impact navigational functioning, something that may explain the tendency of people with Alzheimer’s disease to get disoriented or lost,” says Prof. Ulanovsky. Just like the bat wants to reach the fruit hidden behind the curtain, humans may want to find a campsite over the hill, or a coffee shop tucked just behind an office building. “In such cases, even if there are no clear cues coming in via our senses, this mechanism works like a neural GPS to help us locate the target. In this experiment, the bats showed us how it’s done.”



Can nature heal nature?

Dr. Ulyana Shimanovich is using silk worms and spiders to fix brain cells ravaged by disease

Anyone who thinks that worms and spiders are simply nuisances can think again. And not just because they keep insects at bay. Now, they may help fix cells ravaged by Parkinson's and Alzheimer's diseases.

Dr. Ulyana Shimanovich, a new scientist at the Weizmann Institute in the Department of Materials and Interfaces, is fascinated by the ultra-fine fibers formed by proteins, ranging from the tough, elastic fibrils spun by silkworms to the sticky plaques made up by amyloid protein fibers that affect the brains of those with advanced Alzheimer's and Parkinson's diseases. In fact, her research may lead to a way to use the former to fix the latter.

Traditionally, amyloids have been thought of as purely "bad" because they form toxic plaques or bundles in the brain. However, Dr. Shimanovich's research on the biophysical and biochemical properties of amyloids has shown that they might have positive properties. She wants to figure out the mechanisms for creating useful protein fibrils and for breaking down harmful ones, and how to correlate the structure and functionality of various nano-scale protein fibrils like amyloids, and control their formation.

Doing so, she believes, will be a major step towards designing new nano-scale therapeutic agents such as micro-reactors to encapsulate time-release medications, or nanofibrils with antibacterial properties to resist infection.

Using nature to heal nature

Her approach is all about learning the natural, "positive" properties of proteins in nature to fix nature's deficiencies. Her source is the protein-silk pulled directly out of the silk glands of live silkworms and spiders. She uses these fibers to control the self-assembly processes of the pathological

(diseased) amyloid proteins by converting them into functional biomaterials. In this way, the silk is used to heal the cell instead of using chemical compounds that may cause deleterious effects on surrounding cells—thereby addressing one of the key challenges in drug therapy.

"The silk is a natural resource that, essentially, gives new life to a damaged cell," she says. Her research has implications for diagnostics, the design of new compounds for targeted therapeutic approaches, and materials science more broadly.



Dr. Shimanovich is part of the Weizmann Institute's efforts to expand its research in nanobiology and materials science. This includes the new André Deloro Building, which will house research enterprises in advanced and intelligent materials under the umbrella of a new interdisciplinary center, which will leverage the Institute's strength in this burgeoning and important area. And the implications are vast—including fluorescent biological labels, drug and gene delivery, detection of proteins and pathogens, probing DNA structure, tumor destruction, and tissue engineering.

Uber-scientist from Uzbekistan

Born in Tashkent, Uzbekistan, Dr. Shimanovich moved to Israel at the age of 20. She completed a BSc in pharmaceutical chemistry at Bar-Ilan University, and her MSc and PhD in Chemistry there as well. She performed postdoctoral research at the University of Cambridge and joined the Institute earlier this year. Among her many awards and honors is a Fulbright Ilan-Ramon Post-Doctoral Fellowship from the United States-Israel Educational Foundation and a Fulbright Fellowship, which she declined in order to accept her Cambridge fellowship.

New Scientists

6-7



מכון ויצמן למדע

A man with a goatee, wearing a blue short-sleeved button-down shirt and a straw hat with a black band, stands in a vineyard. He is holding a black cable in his left hand and a small black device in his right hand. The background is filled with green grapevines and leaves.

Dr. Tamir Klein

Trees and the future of climate change

Dr. Tamir Klein lives and breathes trees, studying them and the forests in which they reside using a wealth of measurements and details that try to capture a vivid picture of how trees process water, air, and carbon. And in doing so, he's helping to ensure that as the earth continues to heat up, we are just that much more prepared.

A new member of the Department of Plant and Environmental Sciences, he has discovered new insights into how trees cycle water and nutrients between leaves, stems, and roots—and has even shown evidence for a certain amount of so-called “carbon trade” between roots of nearby trees. Scientists have suspected for years that trees share certain nutrients through intertwining root systems, and have measured the transport of some elements on a small scale in lab experiments. During his postdoctoral fellowship at the University of Basel, Dr. Klein quantified, for the first time, the large transfer of carbon and other nutrients between mature trees of different species—showing in an unprecedented way how trees share resources with one another underground and keep each other healthy.

In his postdoc, Dr. Klein and his colleagues infused industrially produced CO₂ at the leaf canopy level in 40-meter-tall Norway Spruce trees. This CO₂ has an inherently unique signature of carbon isotopes that thus serves as a marker when measuring for its presence in other trees. “We were surprised to find the same isotopes present in the roots of neighboring trees of three different species that were not exposed to the CO₂,” says Dr. Tamir. Delving deeper, they identified symbiotic fungi (called mycorrhiza) associated with the root systems that form “underground highways” for carbon and nutrient exchange between the trees. In an article published in *Science* in 2016, they further showed that 40 percent of the fine root carbon can be traced to these tree-to-tree transfer networks—a thriving interconnected economy.

Preparing for drought, global warming

Dr. Klein was born in Eilat and earned a BSc in biochemistry and food sciences at the Hebrew University of Jerusalem's Faculty of Agriculture, Food, and Environment in Rehovot. He crossed the street for his master's and doctoral degrees in plant sciences at the Weizmann Institute, where he simultaneously lectured and developed courses in the Department of Science Teaching, and taught English and math at the Davidson Institute of Science Education. After he completed his postdoc in Switzerland, he worked as a researcher at Israel's Agricultural Research Organization Volcani Center in Beit Dagan before joining the Institute last year.

“Studying trees matters since they are an essential part of the puzzle of global climate change,” says Dr. Klein. He is especially interested in the role of trees in the global water and carbon budgets, explaining: “Trees form the largest biological carbon pool on Earth, and forests control the water cycle around them through the uptake of water through roots and water loss through leaves.”

And he's thinking forward. In order to mimic what greenhouse gases might have in store for life on Earth 50 years from now, he plans to adapt greenhouses at the Weizmann Institute to create growing areas having atmospheric conditions matching those that existed before the Industrial Revolution, present-day conditions, and double the concentration of greenhouse gases we have today. He is also investigating the drought-resistance mechanisms of lemon trees, work that he started at the Volcani Center. “Even irrigation does not cancel out the exposure of fruit trees to drought, so the development of drought-resistant varieties of lemons, almonds, olives, and other tree crops common to Israel would allow them to grow in even drier areas,” he says. This could be a boon to countries that would like to produce such crops but can't today, given the local climate. And it would help prepare for hotter, drier times.



Often, Thanksgiving dinner wasn't just a family feast in Blythe Brenden's family. "We kind of had to earn it," recalls the Minneapolis native of the traditional November meal around her grandparents' table. Her grandfather, Ted Mann, often required his four grandchildren to come prepared to discuss the charitable organizations where they were investing their time or money.

"I lived and breathed philanthropy from a young age, and my grandfather was the source of that. He believed in giving back and being connected to the community, and he transmitted that to all of us," says Ms. Brenden, who today runs the Blythe Brenden-Mann Foundation, bearing her grandfather's name, in homage to him.

"When you get a table filled with that many generations talking about philanthropy, it gets very interesting. We all had different interests and passions, and we tried to convince each other why our choices were good choices. And those choices evolved from year to year. I told my friends about these dinners, and many of them wanted to join. But I said, 'Are you sure? You'll have to come armed with ideas and have to defend them.'"

Through her foundation, she has given generously to the Weizmann Institute of

Spotlight On

10-11



Blythe Brenden

*Philanthropy and engagement
take center stage*

Ms. Brenden has well exceeded her grandfather's percentage stipulation for giving to a Jewish or Israeli cause. "And it will stay that way. I am a 'lifer' with Weizmann," she says.

Science—to personalized medicine, a new scientist's lab, science education, and women in science. And she has taken a major leadership role, both as a member of the International Board and as a member of the Executive Committee and Board of Directors of the American Committee. She was inducted into the President's Circle in 2016 at the Global Gathering in London. And she is working hard to nurture a community of supporters in the Twin Cities, a new growth area. Most of all, she invests of herself. For the American Committee, she shuns conference calls and prefers a quick jaunt to New York for Board meetings, and meeting other donors.

"I'll take a plane over a phone any day," she says.

"I want to connect with people and potential donors face-to-face, and I feel so strongly about the Weizmann mission that I will fly anywhere to engage wherever I'm needed."

Meanwhile, every description of her foundation work—whether it is related to the Weizmann Institute or to other causes she supports—always winds its way back to a statement of gratitude toward her grandfather. Every gift, she says, is given with him in mind. "The reason that I get to do what I do every day—run the foundation—is because of him," says Ms. Brenden, in an interview in her home in Minneapolis.



 Ted Mann

chain with his brother Marvin. It included some of the Twin Cities' most venerated sites, including the Orpheum and Pantages theaters in the Hennepin Theatre District. In 1970, Ted sold his theaters and moved to Hollywood; later, in a second marriage, he wedded a Hollywood actress. He produced several movies and purchased the National General Theater chain, and thereby temporarily acquired the landmark Grauman's Chinese Theater on Hollywood Boulevard (renaming it the Mann Theater), which attracts millions of tourists every year who come to view the handprints, embedded in the concrete sidewalk, of famous movie stars.

Blythe and her brother Johnny lost their father at a young age, and Mr. Mann wanted to ensure they had a father figure in their lives. So he frequently traveled to Minneapolis at key moments—piano recitals, class plays, graduations. "He would come, watch, clap, give me a hug and a kiss, and turn around and fly home in the same day," recalls Ms. Brenden.

Blythe moved to southern California to attend Pepperdine University, in part to be close to her grandfather. She later moved back to Minnesota, but settled again in California when his health began to suffer; she lived near him in California for a total of 15 years. When she was younger and flew to LA, Mr. Mann made his granddaughter work one week, selling popcorn and soda in his theaters, before taking a vacation.

"His work ethic was unique, and he made sure I absorbed it too. And his integrity was paramount. When he sold his business, he got a better offer—twice as much—a few days later, but he didn't take it because, even though he didn't have anything in writing, he had shaken hands on it," she says. "So people trusted him, and people loved to get his advice... I spent as much time as I could with him. Whether I was there or in Minnesota, I talked to him almost every day. I don't know many people who have had that kind of relationship with a grandparent."

A promise kept, and more

Ted Mann was born in North Dakota and moved to Minneapolis/St. Paul, where he started a theater

in establishing the original family foundation, the Ted Mann Foundation, before his death at age 84 in

 Blythe Brenden


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2001, Mr. Mann stipulated that a percentage of the funds be allocated to Jewish causes; that was his only restriction. (He was Jewish, but Ms. Brenden's side of the family was not.) The foundation evolved through several iterations as it was handed down through two generations, and in 2010 Ms. Brenden began to oversee the new Blythe Brenden-Mann Foundation on a full-time basis.

One of the first items on her agenda was to find a Jewish cause, or one related to Israel.

"I started to do my homework," she recalls. She had lunch with a friend who supported the Weizmann Institute, and who introduced her to a director from the American Committee. At the end of the second meeting, she said, "Sign me up.' I was attracted to Weizmann's global reach, the impact of the science, the diversity of the science, eventually the scientists themselves—whom I started to meet—and the way the best and brightest are changing the world in ways that I can't even imagine. And I didn't just want to write checks. I wanted to be authentically engaged; to participate. Weizmann lets me do all that. Every time I turn around, there is something happening—an opportunity for involvement that I hadn't expected. And it's fantastic."

Given the generous size of her gifts to the Weizmann Institute, Ms. Brenden has well exceeded her grandfather's percentage stipulation for giving to a Jewish or Israeli cause. "And it will stay that way. I am a 'lifer' with Weizmann," she says.

Perfect fits

Her first gift to the Institute was for the establishment of the Blythe Brenden-Mann Genomic Sequencing



A philosophy for philanthropy

Over the years, Blythe Brenden's philanthropy evolved from "giving small amounts to many organizations to giving larger amounts to fewer, favorite organizations," she says. "And my interests will continue to evolve—though with Weizmann, I'm here for the long haul."

She gives generously to medicine and health, the arts, and various local community programs. One of the causes closest to her heart is the Cowles Center for Dance and the Performing Arts, a theater in downtown Minneapolis that her grandfather once owned. She co-chaired a capital campaign for its refurbishment; it is the largest theater in history to be moved in its entirety—a full city block—to ensure its historical preservation.

For her upcoming 50th birthday party in September, she will ask invited guests to give to one of two causes—the Weizmann Institute and Minnesota Masonic Children's Hospital—in lieu of gifts.

Advancing the research of Dr. Rina Rosenzweig

In neurodegenerative diseases, one of the hallmark biomarkers of dysfunction is the mis-folding of proteins in the brain, and the aggregation of toxic, malfunctioning proteins. Understanding the molecular mechanism involved in combating protein aggregation *in vivo*—in the body as it is occurring—is the essence of Dr. Rina Rosenzweig's research in the Department of Structural Biology. Elucidating what is actually happening when the function and structure of proteins go awry is essential in the quest to prevent, slow down, or ultimately reverse the progression of neurodegenerative diseases.

To this end, Dr. Rosenzweig, who joined the Weizmann Institute in 2016, is using nuclear magnetic resonance to see proteins at the highest possible resolution.

In her postdoctoral work, she revealed the inner workings of the so-called chaperone system of proteins. Chaperone proteins are involved in the cellular quality control systems that try to correct protein folding errors and undo the formation of damaging protein plaques, such as the amyloid beta plaques associated with Alzheimer's disease.

"The first time I met Blythe, I was amazed by how passionate and engaged she was in everything she did, from her philanthropy to her many, many interests," says Dr. Rosenzweig. "I feel so lucky to have Blythe's support in starting my lab, and hope to make her proud by bringing her tireless and ever-enthusiastic approach to my own career."

Laboratory in the Nancy and Stephen Grand Israel National Center for Personalized Medicine. She says the lab "fit perfectly" with her interest in integrative medicine, a holistic approach that she has championed through other organizations. The lab is developing new genomic techniques to understand tumor cell behavior, and is serving as an educational center to provide students the opportunity for hands-on experience with genomic sequencing.

She also funded the start-up package of Dr. Rina Rosenzweig of the Department of Structural Biology, who is investigating the mechanisms of neurodegenerative diseases associated with the mis-folding of proteins and toxic protein aggregation (see box).

In deciding to support Dr. Rosenzweig, Ms. Brenden flew to Toronto to meet her at the end of the scientist's postdoctoral fellowship at the University of Toronto, where she was a Revson Fellow of the Institute's Israel National Postdoctoral Program for Advancing Women in Science. "I was especially attracted to Weizmann's approach to hiring new scientists: to hire the best, give them the money they need to pursue their research, and put faith in them, without binding them with restrictions," says Ms. Brenden. "Rina is a young rising rock star, brilliant, has no ego, and is passionate about what she does. The impact that her research is going to have on different diseases is something I hope to live to witness. I love the idea that I'm involved in her career 'at the ground floor,' and I feel it is my obligation to help advance the careers of women scientists. I look forward to watching her career develop."

Of the Science Mobile: "It matters to me that it's going out to kids who would otherwise never have had the opportunity for high-quality education".

14-15

Last year, Ms. Brenden provided funding for the Science Mobile operated by the Davidson Institute of Science Education, a van equipped with science education aids that reaches students in underprivileged areas. Her gift will support new vans which will reach the most at-risk populations, including Bedouin communities and the geographically remote areas.

"It matters to me that it's going out to reach kids who would otherwise never have had the opportunity for high-quality education. In the same way that I support children in the arts, I support the Science Mobile so that we make sure that those minds are ours in the future. How do we know that a child doesn't have an interest in something, unless he or she is exposed to it? I hope it becomes a model worldwide for other countries, even the U.S., where educators could take a page out of the Weizmann playbook and say, 'That works. I want that.'"

Her gift to the Science Mobile program fulfills her commitment to the Women Moving Millions project, a group of women philanthropists who are engaged in their communities and have committed at least \$1 million to causes that benefit women and girls. "Women and children are central in my giving, because they have different challenges than men and I want to see them succeed, so that one day they can be role models for other girls."

One of her favorite milestones in her relationship with the Weizmann



Blythe Brenden and Prof. Daniel Zajfman at the dedication of the Blythe Brenden-Mann Foundation Genomic Sequencing Laboratory

Institute was the 2012 "Women to Women" Mission of the American Committee to Israel, which, she says, afforded her opportunities "to have access to things that are just not in the tour books." The group met with scientists over lunch, visited labs, and toured the country. "I saw the Weizmann approach, which was, 'If you want to talk to a scientist you can. If you want to talk to a student, you can. There is no 'no.'"

She is highly involved in the American Committee's Women for Science (W4S) initiative, spearheaded by ACWIS National Chair Ellen Merlo. W4S engages women philanthropists in supporting Weizmann Institute science, including the advancement of women scientists through initiatives like the Israel National Postdoctoral Program for Advancing Women in Science, which supports female scientists during their postdoc fellowships abroad.

Her time is primarily spent on her foundation work. But she dotes on her two dogs, Lulu and Violet, loves to travel, and is a self-described food and wine connoisseur who likes to spend time in Napa Valley. "If I had it my way, I'd be on a plane and doing my philanthropy work every day. And I'm lucky that I actually do get my way."



Resolution revolution

Modern microscopy's impact on science

Cover Story

16–17

“Like you can’t have a car that can take the kids to schools on Friday and win the Grand Prix on Saturday, you can’t make a microscope that can do it all.”

– Dr. Eric Betzig, 2014 Nobel Laureate in Chemistry

Since their invention in the 1600s, microscopes have opened the window on human and plant biology, allowing scientists to marvel at things unavailable to the naked eye—and explore them in earnest. Developments have occurred over the last 400 years, but scientists agree that the last 15 years has seen nothing short of a “resolution revolution” with dramatic advancements that have ignited a new era in scientific research, allowing scientists to peer into the particulars of life sciences in unprecedented ways.

The secret lives of cells, in health and disease, are increasingly open to view.

We now have the ability to zoom in on the minutest workings of the molecules of life in a more naturalistic setting—and to do so at speeds that would have astonished researchers a mere 20 years ago. Weizmann Institute Prof. Ada Yonath’s painstaking work to understand protein structure, beginning in the 1980s—a herculean, Nobel Prize-winning effort of perseverance that lasted almost two decades—may now be accomplished in a comparative blink of an eye.

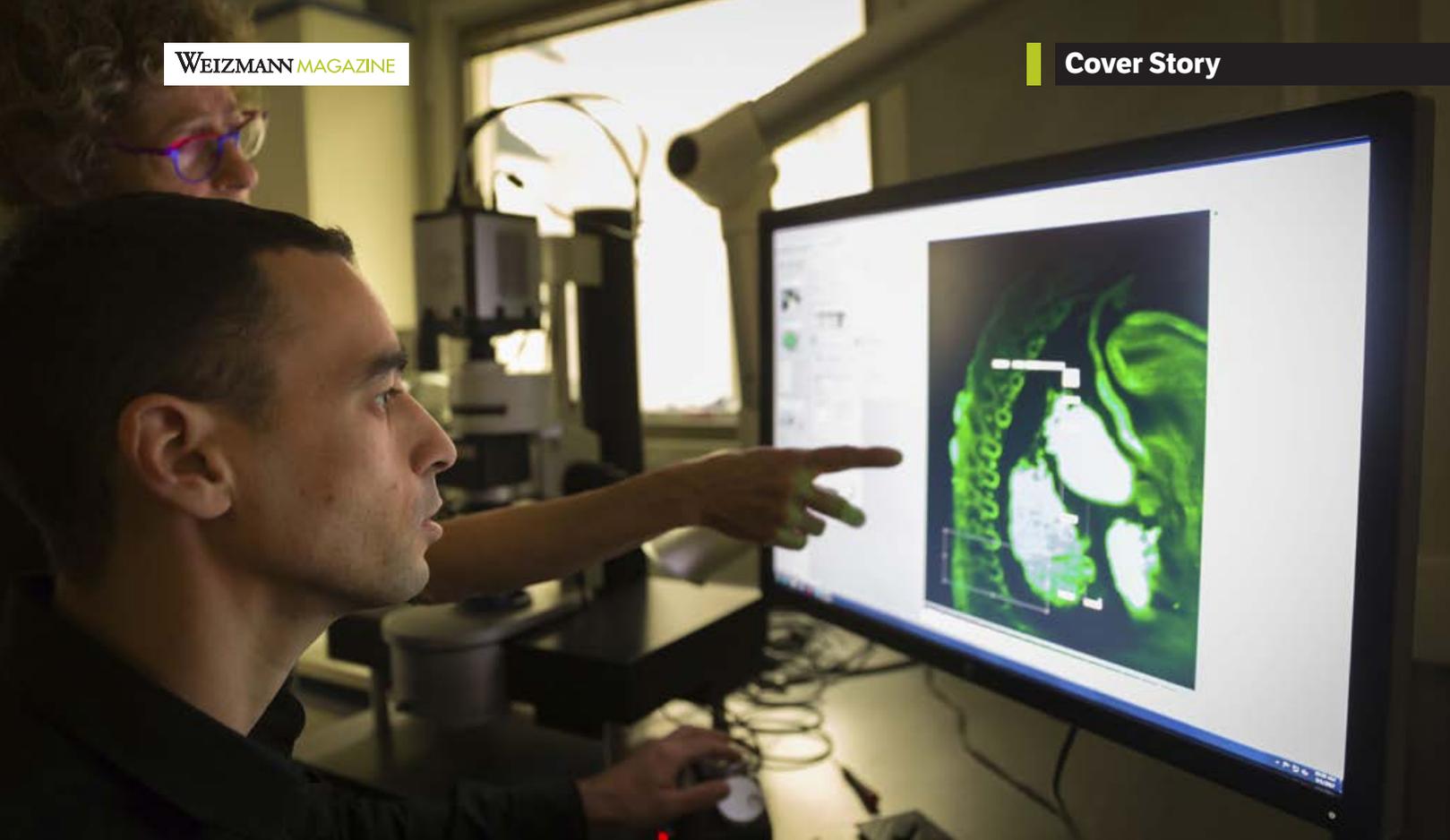
“We are in a new era of microscopy, which is throwing open the doors to countless new avenues of scientific exploration,” says Prof. Neeman of the Department of Biological Regulation and Institute Vice President, who also heads the Henry Chanoch Kreter Institute for Biomedical Imaging and Genomics. “Every new advance is contributing a puzzle piece of information to help illuminate biology, insights that will

translate into meaningful results in human health.”

The earliest microscopes utilized light to image the sample, and thus were called optical microscopes. In the early 20th century, electron microscopy entered the scene, utilizing electrons to generate the images. Even today, the world of microscopy can be divided into two hemispheres: light (optical) microscopy (LM) and electron microscopy (EM). Although electron microscopes have long outpaced the resolution of their optical cousins, light microscopes have experienced a resolution revolution over the past decade and a half, thanks to advances in applying fluorescence to microscopy. At the same time, EM has experienced its own resolution revolution thanks to advances in single-particle imaging, allowing for near-atomic-level resolution of biological samples.

The Weizmann Institute of Science has capitalized on these parallel bouts of imaging innovation through active recruitment of talented microscopy experts, acquisition of state-of-the-art microscopy equipment, and the infrastructure needed to support mighty explorations on the smallest of scales—improving the power and quality of Weizmann research on cancer, stem cells, bones, muscles, tissues, and more.

Both LM and EM use illumination to form larger and more detailed images of objects than the human eye can produce unaided. LM illuminates an object with photons of various sources of visible or



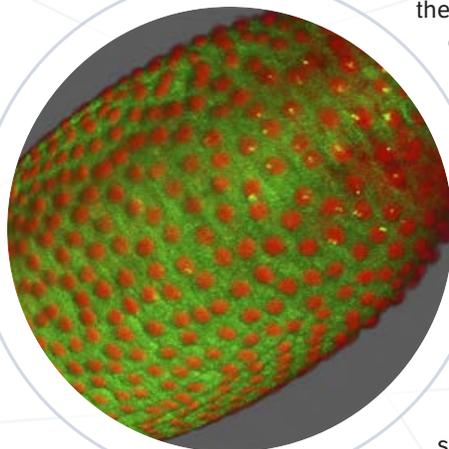
 *Dr. Yoseph Addadi, scientific head of the de Picciotto-Lesser Cancer Cell Observatory in Memory of Wolfgang and Ruth Lesser in the MICC.*

infrared light in a natural setting, forming an image via the absorption and/or emission of light by the object. Meanwhile, EM illuminates the object with a beam of electrons emitted in a vacuum, forming the image via the scattering of electrons by the object. Electron microscopes are thus significantly more powerful than optical ones, but also more expensive, requiring painstaking sample preparation and, because of the need for a vacuum, applicable to non-living specimens only.

A glowing solution

Scientists determined to image living biospecimens on the smallest of scales have long been stymied by the limits of LM. That is, there's only so much you can magnify a sample and still be able to preserve resolution—a law of nature referred to as Abbe's Diffraction Limit, which sets the limit at 200nm when using

natural light. This phenomenon has withstood human ingenuity until 20 years ago, when scientists Eric Betzig, William Moerner, and Stefan Hell (separately, in parallel) developed super-resolved fluorescence microscopy, for which they jointly received the 2014 Nobel Prize in Chemistry. In awarding the honor, the Royal Swedish Academy of Sciences said the trio “brought optical microscopy into the nanodimension.”



 *A live fly embryo, with red marking the nuclei and green marking the intensity of gene expression. Courtesy of Neta Strasser-Rahimi from the lab of Prof. Benny Shilo.*

The three co-Laureates showed, in different ways, that it is possible to use so-called fluorophores—fluorescent chemicals that can absorb and then re-emit light when excited—to enhance resolution. For example, Stefan Hell and his colleagues developed stimulated emission depletion (STED) microscopy, which uses laser pulses to excite and then de-excite the fluorophores, producing a focal spot of light surrounded by a donut of darkness. The precision and power of

the laser beams combine to break Abbe's Diffraction Limit.

"It is an exciting time to be involved in the field of microscopy," says Dr. Tali Dadosh, a staff scientist in the Weizmann Institute's Electron Microscopy Unit. She specializes in super-resolution fluorescence LM, and in particular, **stochastic optical reconstruction microscopy (STORM)**. The STORM method is based on randomly glowing fluorescent molecules which are used to label the sample (picture different colors for components of a cell). Unlike the precise glow of STED, in the STORM process the fluorescent dyes blink on and off at a rate that can be controlled by the chemical environment of the sample, so that the glow can be tuned.

Through a careful process of "glow-tuning", Dr. Dadosh is able to explore the fine details of cells with nano-level precision. Dr. Dadosh helps Institute scientists design, conduct, and optimize a variety of exquisitely sensitive fluorescence microscopy experiments. She also makes use of a new technique that combines all these improvements in LM with the power of EM which offers a unique, high-resolution method for visualizing structural information about aspects of a cell.

Resolution evolution

Other forms of LM have been experiencing a steady and remarkable evolution. One of them is **lightsheet microscopy**, which allows for imaging intact organs, organisms, and embryos in 3D. It is also faster and more efficient than many other imaging techniques and gentler on biospecimens, causing far less photo (light) damage. The Institute plans to expand its capacity in LM in order to enable its scientists to conduct their research at the highest levels possible.



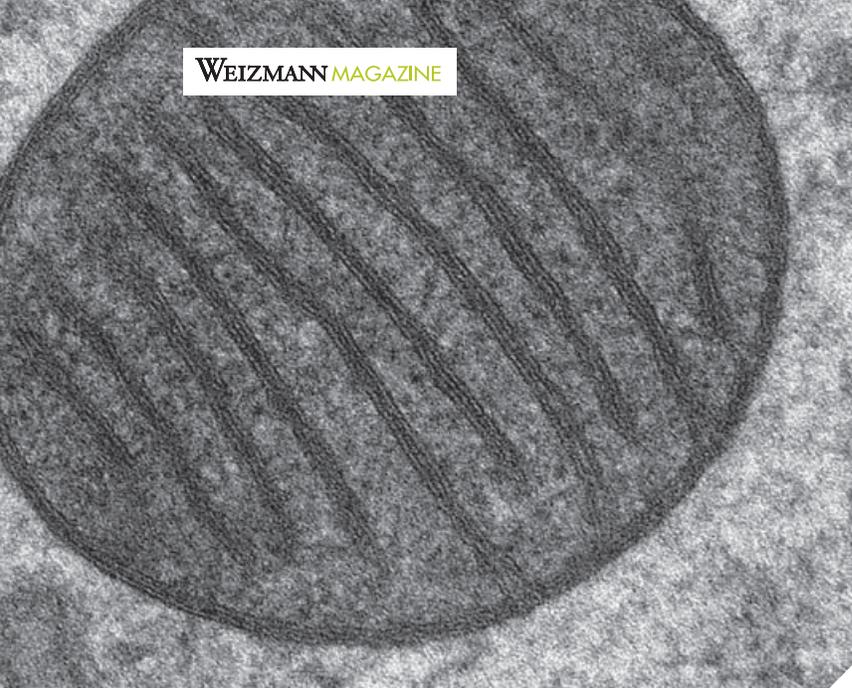
 Prof. Nir Davidson

Pushing technology forward

As microscopy is already helping elucidate a panoply of important investigations, other scientists at the Weizmann Institute are forging ahead in the physics of it all, which undoubtedly will lead to further improvement in resolution.

For one, pushing past Abbe's Diffraction Limit is an ongoing goal. Prof. Dan Oron, who heads the Department of Physics of Complex Systems, is exploring new approaches to simplify current microscopy techniques that can transcend the limit, and is applying these techniques to study biological systems. Prof. Nir Davidson, Dean of the Faculty of Physics, is an expert on laser physics and ultra-cold atomic physics who is hard at work focusing and shaping diffuse light beams, to this end.

Other scientists are trying to better understand how light behaves at very high intensities. Prof. Yaron Silberberg is a leader in laser technology, also referred to as nonlinear optics. His team has developed an approach that utilizes nonlinear optics in microscopy to uncover details about the behavior and dynamics of molecules. His approach may be particularly useful for learning about the dynamics of large molecules found within biological systems, revealing subtle, dynamic changes in a molecule's structure, which affects how a molecule will interact with other molecules in its environment—e.g., the particular way in which a protein is folded determines its function in the human body.



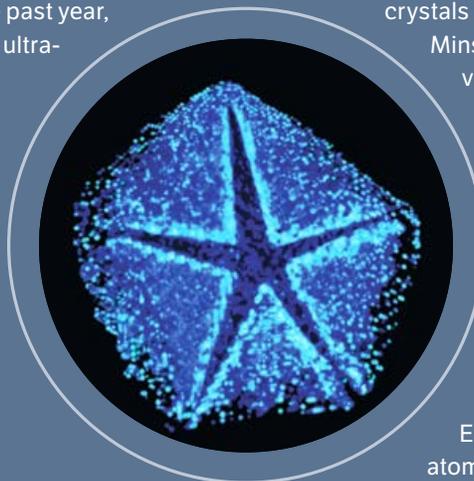
➤ *Mitochondria, the energy-production factory of a cell, within a HeLa cell line (an immortal cell commonly used in scientific research). Image taken with high-pressure freezing TEM, by Dr. Helena Sabanay for the research of Dr. Miriam Regev in the lab of Prof. Benny Shilo.*

Moskowitz Center makes (light) waves in imaging

Meanwhile, as LM is going nano, EM is going sub-nano. The revolution in EM involves single particles, stemming from transmission electron microscopy (TEM). The Irving and Cherna Moskowitz Center for Nano and Bio-Imaging, established in 2006 by Prof. Avi Minsky and now headed by Prof. Michael Elbaum, supports research in the Electron Microscopy Unit. Over the past year, the Unit has seen the integration of ultra-high resolution light microscopy and electron microscopy. The Center helped purchase major equipment for one of the scanning EM microscopes, and will support the installation of a new camera for the TEM that allows determination of the structures of biomolecules at superb resolution.

In recent years, more than 30 publications by a wide range of Institute research groups used microscopy supported by the Moskowitz Center (and thus

cite the center). Such investigations include those done by Prof. Reshef Tenne on new materials; Prof. Ernesto Joselevich on growing nanowires for electronics; Prof. Boris Rybtchinski on developing nanowires; Prof. Assaf Vardi on marine photosynthetic microorganisms; Prof. Lia Addadi on the formation of cholesterol crystals in atherosclerosis; and Prof. Avi Minsky on the replication cycles of giant viruses.



In TEM, the microscope emits an electron beam that interacts with the sample as it passes through the entire (very thin) sample. It can “see” objects with varying internal structures and the resulting image is a 2D projection of the sample. But while TEM, like other forms of EM, is a great method for obtaining atomic-resolution of inorganic materials, it is a killer on biospecimens. How then can

➤ *Derived from electron tomography, this image shows a modified vertex of the Mimivirus, one of the largest viruses ever discovered. The opening of this vertex, coined the “stargate”, generates a large portal through which the huge DNA genome of the virus is released into the host cytoplasm. Image taken with high-pressure freezing TEM, by Dr. Nathan Zauberman for his research on giant viruses in the lab of Prof. Avi Minsky of the Department of Structural Biology.*

*“Because of advances in light microscopy, scientists started to re-visit **lightsheet microscopy**, and now it is considered a relevant and highly valuable technology for biological sciences,” says Dr. Yoseph Addadi.*

20–21

“Because of advances in light microscopy, scientists started to re-visit lightsheet microscopy, and now it is considered a relevant and highly valuable technology for biological sciences,” says Dr. Yoseph Addadi, who heads the de Picciotto-Lesser Cancer Cell Observatory in Memory of Wolfgang and Ruth Lesser (in the Moross Integrated Cancer Center, or MICC). He assists a range of Weizmann Institute life scientists

with this technique, one of the newest technologies available in the MICC’s dedicated microscopy unit, thanks to the generosity of the Henry Kreter Foundation. In the past, this technology was used to image non-biological samples. But now, scientists can use it to follow the behavior of cancerous cells in live tissues for prolonged periods. Because it can penetrate deeper into tissues without damping

scientists resolve protein structure, and thereby gain an understanding of protein function?

The most popular solution to this problem has been to use X-ray crystallography, in which the sample is crystallized and the protein structure is determined from a diffraction pattern. This technique is largely successful for analyses of biospecimens, but not for all proteins. That is, many proteins are very difficult to crystallize and researchers may spend years to find adequate crystallization conditions, so the process becomes a significant bottleneck. Consider that Prof. Yonath made a staggering 25,000 attempts before she succeeded in creating the first ribosome crystals.

So how can scientists obtain the extraordinary resolution of EM with recalcitrant proteins, without frying their samples to a crisp in the process? The answer today is a revolutionary technique of single-particle analysis conducted at cryogenic temperatures called **single-particle cryo-EM**.

In single-particle cryo-EM, a sample (e.g., a purified protein) is spread out sparsely and evenly on a grid, which is then plunged into a cryogenic liquid and flash-frozen—a process that preserves the sample’s natural structure. Next, the scientist uses an electron microscope to obtain multiple 2D images of each of the sparsely spread protein particles (hence the name ‘single-particle’), after which these images are used to construct a 3D model of the protein. Refinement of the 3D model to high

resolution involves elaborate and intense computing. In this way, single-particle cryo-EM provides atomic and near-atomic imaging of viruses, ribosomes, ion channels, and various enzyme complexes.

The freezing process helps scientists contend with the unavoidable damage that all EM techniques cause to samples because the low temperatures protect sample integrity for the duration of the experiment. Nevertheless, no sample can withstand an electron beam’s intensity forever, and therefore the beam must be of low strength, administered bit by bit, so that the final 3D image is normally an average of tens of thousands of individual particles collected at low dose conditions.

Dr. Nadav Elad, an EM expert and colleague of Dr. Dadosh in the Electron Microscopy Unit, observes that it is the convergence of this technique with advances in technology that is the real revolution.

“People have been solving protein structure for decades,” he says. “But now, with improvements in electron microscopes, detectors, computer hardware and software, we are finally able to achieve atomic resolution of protein structure, making single-particle cryo-EM a valid alternative to X-ray crystallography.” True, there may be no avoiding the damaging effect of the electron beam completely. But scientists are hard at work to push the resolution boundaries even further, and there is much more work to be done in EM to advance capabilities.

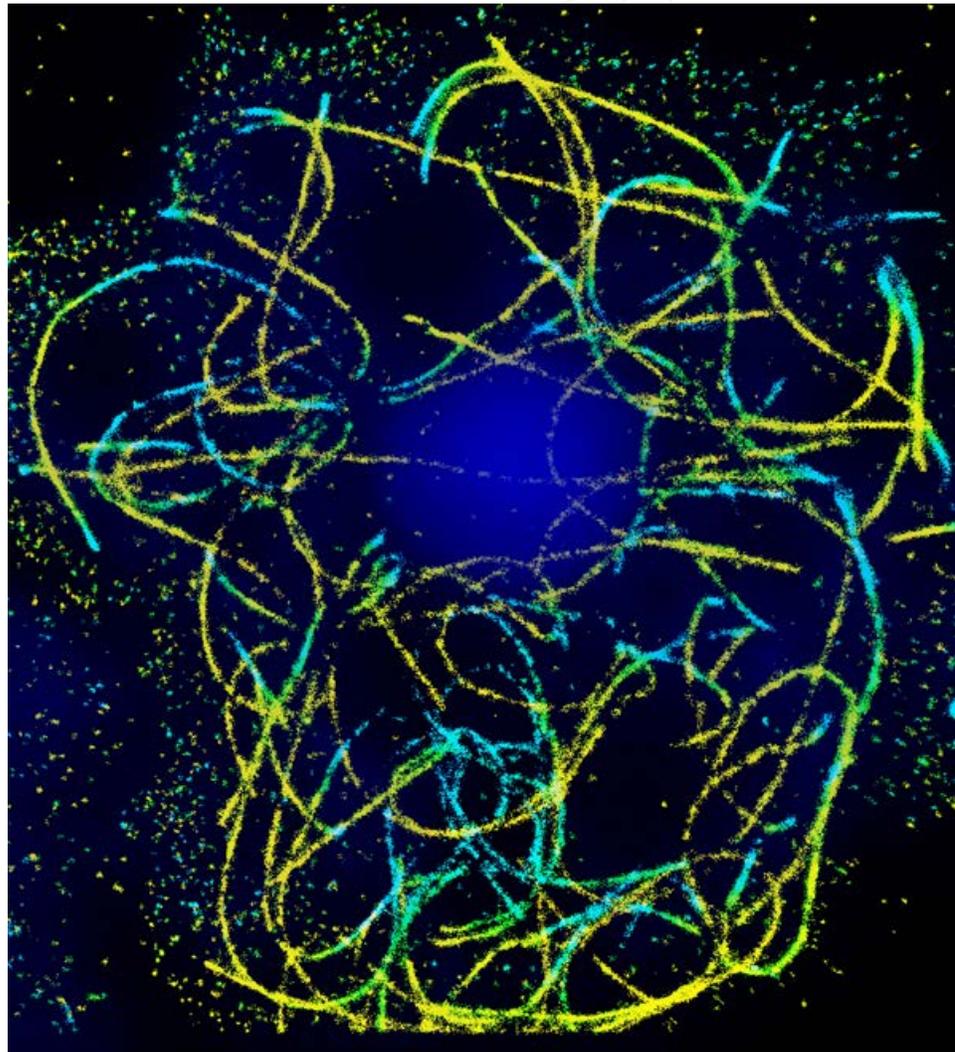
fluorescent signals, scientists can literally watch the interactions between different cell populations in tumors.

Meanwhile, **two-photon excitation microscopy**, allows deep, live imaging of up to a 1mm thickness, and is based in infrared excitation of fluorescent dyes. This method results in a miniscule amount of excitation, in contrast to confocal or wide-field microscopes, and therefore prevents bleaching or other photo-damage to the tissue.

A number of Weizmann Institute scientists are using the extraordinary scanning sensitivity of two-photon microscopy, including scientists associated with the Krenter Institute, the MICC and beyond. For example, Dr. Ruth Scherz-Shouval of the Department of Biomolecular Sciences studies cancer cells and

the way in which they recruit and subvert normal cells to create an environment that promotes tumor progression and metastasis. She uses two-photon microscopy to detect and visualize fine differences in the extracellular environment as a result of cancer progression.

Prof. Neeman developed a method for fluorescently labeling a type of cell normally involved in forming connective tissue—and which is frequently hijacked by ovarian cancer tumors to become part of the malignancy. These fibroblasts are thereby used as a beacon in two-photon microscopy, pointing to the otherwise invisible metastases, like an informant wearing a wire to a meeting with the mafia. This method not only finds hidden cancer cells, but it also enables the researchers to target delivery of anti-tumor therapies with specificity and sensitivity.



 STORM imaging of microtubules in amoebae, courtesy of Dr. Tali Dadosh, pictured left, as part of the studies conducted by Liran Ben Yaacov in the lab of Prof. Avi Minsky

Michael de Picciotto: Celebrating a life to advance life-saving research

Created as a key component of the Moross Integrated Cancer Center (MICC), the de Picciotto-Lesser Cancer Cell Observatory in Memory of Wolfgang and Ruth Lesser, established by Michael de Picciotto, offers scientists in-depth analysis of cancer cells using advanced imaging technologies, which enables viewing live cells in action and at high optical resolutions. Access to these state-of-the-art light microscopy techniques and instruments will allow Weizmann Institute scientists to investigate and analyze cancerous and normal cells in varying experimental modalities and at different scales from single molecules to the whole, functional organism.

“The in-depth analysis offered by the de Picciotto-Lesser Observatory will revolutionize our capacity to image life processes in unprecedented depth, enabling us to monitor specific molecular and cellular changes occurring in the cancer cells, which enable them to invade tissues and organs and grow in a deregulated fashion. Understanding the cellular and molecular hallmarks of cancer cells and gaining insight into the complexity and heterogeneity of cancer can open novel diagnostic and therapeutic avenues,” says Prof. Benjamin Geiger, head of the Observatory and a member of the Department of Molecular Cell Biology.

Michael de Picciotto grew up in Brussels and splits his time between London and Switzerland, where he lives with his wife and two daughters. He made his gift for the establishment of the Observatory

in memory of his maternal grandparents, who were born and raised in Germany. In 1933, barely 20 years old, they fled Nazi Germany to Amsterdam; their own parents followed after the Kristallnacht in November 1938, when Michael's mother was born. They survived deportation to Bergen Belsen and lived in Amsterdam until moving to Jerusalem in the 1980s. “My grandfather, a successful

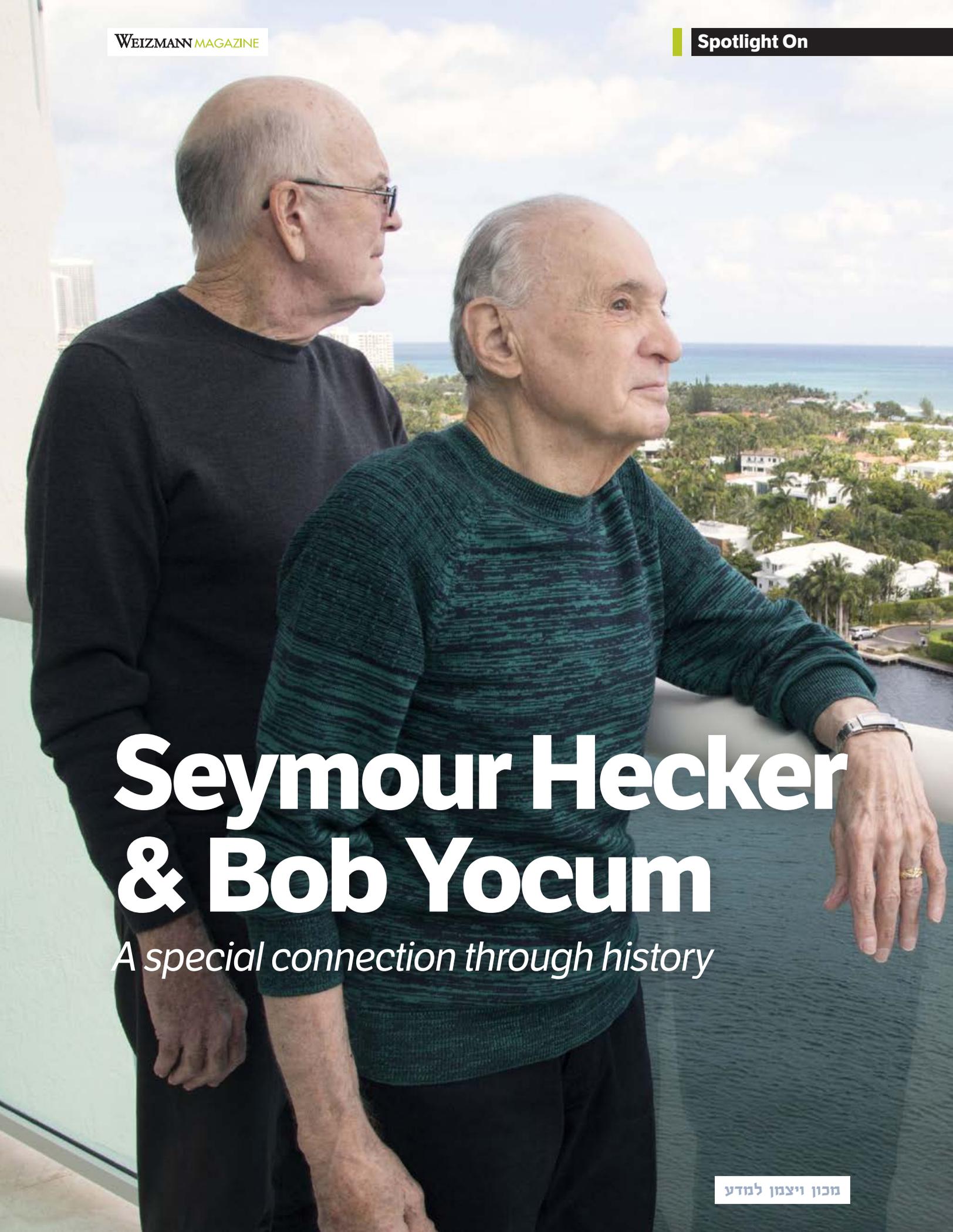
businessman, was a very generous and charitable person with whom I had an extremely close bond. He was also a great supporter of Israel.” Wolfgang Lesser passed away in Jerusalem, in 1995, from pancreatic cancer.

“My contribution to the Cancer Cell Observatory allows me to honor my beloved grandparents, and express my attachment to my roots and my fascination with science,” says Michael de Picciotto, whose father is an engineer—as were his two uncles—and who also has a PhD in organic chemistry from Geneva University.



 Michael de Picciotto

“Science is the dominant field of excellence in Israel, and the Weizmann Institute is one of its most successful ‘engines’. Globally, and in particular over the past 100 years, science has greatly benefited from many important Jewish scientists and represents an impressive contribution by our ‘nation’ to mankind,” he continues. “I am eager to follow and observe the future results of the research done within the Observatory and am grateful to be able to associate my grandparents’ memory and that of my family with this exciting new area at the Weizmann Institute.”



Seymour Hecker & Bob Yocum

A special connection through history

Spotlight On

24–25

Sy Hecker's presence in Tel Aviv upon the establishment of the State of Israel in May 1948, at age 18, and his first visit to the Weizmann Institute of Science shortly thereafter are intricately entwined moments that are imprinted on his memory. They also set in motion a lifetime of commitment, and recently, generous philanthropy to the Weizmann Institute, together with Bob Yocum, his partner, with whom he lives in Miami.

In reality, the story starts even before that—in 1935. That was the year that Sy's grandparents, who lived in Buffalo, New York, traveled to Europe and Egypt. In Egypt, they met a Jewish man from Palestine who told them about a small Bauhaus-style apartment building in Tel Aviv that might be worth purchasing. His grandfather was in the real estate business and was always looking for a good deal. The couple traveled to Tel Aviv and made an offer—\$25,000—on the 16-apartment building on Allenby Street, not far from the landmark Great Synagogue. They sent a telegram to their son, Sy's father, in Buffalo, asking for a wire transfer.

"At first, my father didn't want to send the money because he thought they were kidnapped and he was being asked for ransom money," laughs Sy. But the purchase happened soon enough, and his grandparents sold off the apartments and kept one for themselves, a second home in which they spent their winters to escape from the cold of Upstate New York.

Sy, who was born in 1929, visited them often. In preparation for a visit in 1947, he obtained a visa from the British consulate in Buffalo; when his flight stopped over in Paris on November 29, the U.N. announced its partition plan: the British would withdraw, and the land between the Jordan River and the Mediterranean would be divided into two states, one Jewish and one Arab. With tickets bearing the destination "Palestine," he landed in the nascent state of Israel, where he witnessed triumph and celebration. "I watched the parade from our balcony on Allenby Street. It was so emotional. We were all in tears, so proud. Today, when I think about it, I feel that I was so lucky to have seen everything in the making," says Mr. Hecker.

He spent 10 months in Israel and traveled all over the newborn country. He returned again in 1949, when he visited the Weizmann Institute, which had just been established and consisted of just a handful of buildings. One of them, the Ziv Building, housed the chemistry lab of Dr. Chaim Weizmann; another, Ziskind, housed WEIZAC, the first computer in the Middle East. WEIZAC—which still sits in Ziskind today and takes up an entire wall—made an impression on him, as did "seeing a research institution springing up from the ground, almost from nothing, while the country was just starting," he said.

"I saw that even from the very first days, Israel made science and medicine a top priority," he continued. "The president of the country was also the founder of a scientific institution, which was an incredible thing to me... And while I wasn't a scientist, what mattered to me was the emphasis on bettering humanity."

A photographer snapped a picture of Sy and his uncle on the steps of the Ziskind Building that year, and when Sy and Bob visited the Institute in 2008—nearly 50 years later—they had a photograph taken in the same spot.

"When I met Sy more than 20 years later [in 1971], his early visits to Israel and the one to the Weizmann Institute were still present in his mind," says Bob. They had made a deep and lasting impression on him. And through his emotional connection, I developed an emotional



📍 *“He’s a guten neshama,” says Sy, using the Yiddish word for ‘good soul’ to describe his partner. Says Bob: “And each day we’ve been together, he has made me a better person.”*

connection. Throughout the years, as illnesses occurred among family and friends, the thought was always in our minds: ‘What if there could have been knowledge that could have helped them, or saved them?’ This is why we support Weizmann.”

In 2008, the duo gave their first major gift to the Institute, for scholarships at the Feinberg Graduate School. Most recently, the couple made a testamentary

gift to the Weizmann Institute involving a pledge of 95 percent of their assets, which they have also earmarked for scholarships. The men have met nearly every Institute scientist who has given talks in South Florida.

“Every time we meet a scientist, it is mind-boggling,” says Bob. “The substance and importance of their work encircle you and become part of your thought process, and you want to be part of it.”

Serendipity and purpose

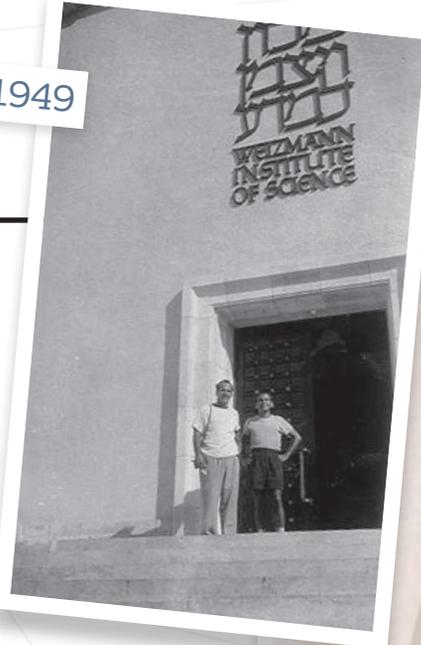
Sy, 87, and Bob, 73, met 46 years ago, at the lunch counter of a Miami restaurant, shortly after Bob moved to the city. Mr. Yocum had relocated from his native Texas as part of a team opening the first Neiman Marcus store in Florida. Sy was in the real estate business; he owned several motels on what was once referred to as Miami Beach’s “strip”, the length of the shore that drew sun-seeking tourists, particularly in the winter months. Today, the area is populated with upscale residential high-rises and luxury hotels. Looking out from their balcony, they can see the breathtaking views of that area and reminisce about what it used to look like.

Bob grew up in a small rural town called Levelland in north Texas—“all cotton and all wheat,” he says. And religion. Without mincing words, the pastor of his church told

The Feinberg Graduate School

Students at the Feinberg School study tuition-free in English and receive a living stipend, freeing them to focus on their studies and research. In a hands-on learning atmosphere that favors interdisciplinary collaboration, FGS students are often first authors on scientific publications that result from research in the labs in which they work. The School, located in the David Lopatie Hall of Graduate Studies, and its five affiliated research schools, awards 140 MSc degrees and 140 PhD degrees annually; about 500 new students and postdocs join the Institute every year, including a large contingent of international students.

1949



📍 *Sy and his uncle in 1949 in front of the Ziskind building, and Sy and Bob in the same spot 50 years later.*

Bob that, because of his sexual orientation, he was barred from the church. As a youngster, he felt alienated from his family, and his community. "I had no expectations for myself, because, I think, no one else did... And growing up in the Bible Belt, I didn't want to have anything to do with organized religion," Bob recalls.

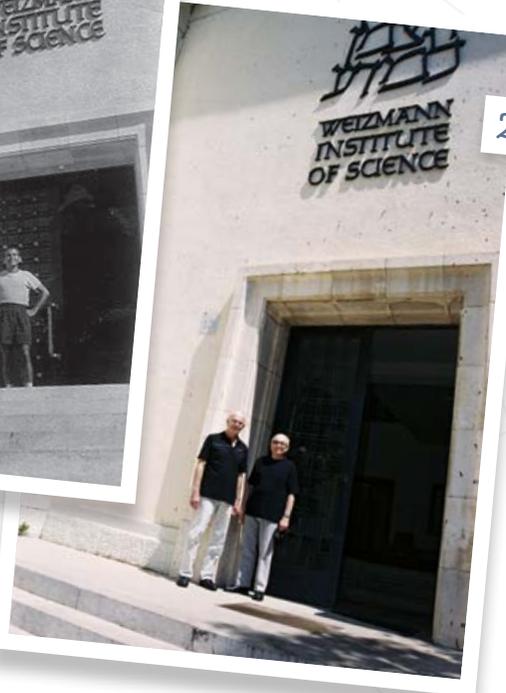
Soon after meeting each other, Sy took him to his synagogue in Miami Beach. The rabbi's speech resonated with Bob and was the trigger that changed his worldview about religion. "The rabbi gave such a meaningful speech. It wasn't hate-filled or judgmental. It was about living your life to be a good person, doing charity, doing good for others, being honest and keeping your integrity," he recalls. "I thought: 'All along, this is what I thought religion should be.' It was a perfect connection for me."

He continued, "We shared a passion for music, art, and opera, but Judaism created a spiritual connection between us. It sealed the deal," Bob says. "It has grounded us and pointed us to who we are today; how we wanted to live." He later converted to Judaism. They are still active in their synagogue today.

Sy's family accepted him, he says, "and his mother even taught me Yiddish. I can speak a little—in a Texas drawl." After gay marriage was approved in Canada, they got married in 2006; and then again, in New York City, in 2013. They traveled the world together; a first order of business in every new city was to find a synagogue, and either attend a service or to wander around inside. "We've been everywhere we've wanted to go, including a survival trip down the Amazon River," says Bob. They were in Israel together a handful of times.

26–27

2008



Eventually, Bob left Neiman Marcus and became a real estate appraiser, and the two formed their own upscale housing construction company, S&B Design. They refurbish properties or build them from

scratch, often living in them for a short time until they are sold. They found their current apartment—with breathtaking views of the Atlantic Ocean and the Intracoastal Waterway—through their work, overhauling it completely. Today it is decorated with art they have collected from their many trips around the world.

"We feel very privileged that we have been successful financially, and that we have been able to act on that in a meaningful way with Weizmann," says Bob. "For us, Weizmann was the right place. It has been so cemented in who we are, and we know we have made the right decision. We feel so blessed to be able to do it. It is validation for our lives."

Taken together, their annuity and their testamentary pledge will fund dozens of scholarships for masters and doctoral students. "We want to allow for knowledge to be incorporated on campus, to develop minds that will become the scientists in the lab," says Sy. "We love the fact that Weizmann doesn't charge its students tuition, and we know this money has to come from somewhere."

Last year, Sy became ill with cancer and their travel ground to a halt. In January, he was pronounced cancer-free and is looking forward to his doctor's approval for him to travel again. His travel bug is back, he admits. "I want to make one more trip to the Weizmann Institute," he says.



Opening of the 68th International Board

Building Excellence

The Opening Gala of the 68th Annual General Meeting of the International Board of the Weizmann Institute of Science started with a bang, as the Revolution Orchestra accompanied the evening's presentations.

The evening, hosted by Weizmann scientist Prof. Roei Ozeri, featured scientific presentations

by Dr. Shikma Bressler of the Department of Particle Physics and Astrophysics, Prof. Alon Chen of the Department of Neurobiology, and Prof. Assaf Vardi of the Department of Plant and Environmental Sciences with his wife, artist Nivi Alroy. The gala was dedicated to the late André Deloro and the ADELIS Foundation (see p. 30).

Special Section

28-29



British tea was the perfect accompaniment to the dedication of the Weizmann UK Building for Biocomplexity Research.



מכון ויצמן למדע

Clore Prize Awarded to Dr. Shikma Bressler

The 2017 Sir Charles Clore Prize for Outstanding Appointment as a Senior Scientist was awarded to Dr. Shikma Bressler of the Department of Particle Physics and Astrophysics. After the traditional address by Dame Vivien Duffield DBE, the board members and guests heard an interesting and topical analysis of the geopolitical situation in the Middle East by the eleventh Mosad Chief, Tamir Pardo.

André Deloro

A builder of Israel's future

Building Excellence' was the theme of the International Board, reflecting a large number of building projects that have come to fruition on campus. And it was no coincidence that the Weizmann Institute chose to shine a spotlight at the Opening Gala on the ADELIS Foundation—whose founder, a French building engineer named André Deloro, devoted himself to building excellence in Israel.

The story of the foundation and its special relationship with the Weizmann Institute, as well as its vast philanthropic initiatives throughout Israel, begins with Mr. Deloro. He passed away in 2012 after an illustrious career in building and public works.

"André did not recognize the word 'impossible,'" said representatives of the foundation.

"André always knew how to recognize excellence. He was a friend of science and was very proud to play a meaningful role in its advancement and development," says Institute President Prof. Daniel Zajfman, who bestowed on him the prestigious Weizmann Award in Science and the Humanities shortly before Mr. Deloro's passing.

Founded in 2006, the ADELIS Foundation has donated generously across Israel, primarily by supporting scientific research, education, and social welfare. This commitment is symbolized in its name, which is an acronym for André Deloro Israel.

"To André, the Institute symbolized scientific excellence in Israel," say the representatives. The foundation's latest gift was for the establishment of the André Deloro Building for Advanced and Intelligent Materials. The facility, currently in its planning stages, will house the future Center for

Advanced and Intelligent Materials, and enable new research in materials science for application in medicine and medical devices, defense and more.

Since its first gift for multiple sclerosis research in 2008, the ADELIS Foundation has given generously to the Institute: for a major collaboration with the Technion in brain research; for the establishment of the André Deloro Institute for Space and Optics Research; and for the André Deloro Research School of Physical Science.

In defense of Israel

André Deloro was born in 1933 in Cairo, where he completed high school before moving to Paris in 1950. In Paris, he studied in two of France's finest universities, École Polytechnique and École Nationale des Ponts et Chaussées (ParisTech).

After a career in construction, he undertook the construction of the last edifice of his life, the ADELIS Foundation. The major proportion of the foundation's giving goes to scientific and medical research.

"André loved Israel," say the foundation representatives. "He was an unusually smart man. He was strict and exact, with an exceptional commitment to hard work and attention to detail, while completely trusting and respecting the people he chose to work with him. André focused all his attention on defending Israel, and that meant ensuring the strength of Israel's economy by building its brain power. His close colleagues told us he was a visionary and was always concerned for Israel's security and future. When asked, 'Who, or what, is going to defend Israel in the long-run, not just in the next four or five years?' he would answer: 'The young minds and ingenuity—so education and science must be a top priority.'"



But he worried about Israeli education. But while he revered its universities and wanted them to work together to expedite discoveries—funding such partnerships with generous sums—he was concerned that the Israeli educational system was not up to the task of adequately training the next generation, mainly in the periphery.

Although he was not a religious man, Jewish values always resonated with him, including *tikkun olam* (literally, “correcting the world”, but essentially

meaning “making the world a better place”). “What interested him was asking questions, never taking accepted views as givens, and furthering education so that life might be better for the next generation than it was for the one before,” say the representatives. “He would say: ‘When a molecule that can cure a disease is discovered and turned into a pill, and a person is sick, he doesn’t ask whether a Jew invented this molecule; he swallows it. Period. In this way we fulfill our role as a people. That is true *tikkun olam*.’”



 Architectural rendering of the Deloro Building

The André Deloro Building

The planned Deloro Building will be a state-of-the-art facility housing the laboratories, instrument systems, and central research service facilities necessary for innovative materials science research. The building will include special features to facilitate research on intelligent materials, including a stable environment to accommodate the strict conditions required for studies on nanomaterials, which are highly sensitive to external contaminants, slight changes in humidity, or fluctuations in temperature and environmental factors. Thus, the building’s lowest floors will be constructed underground, at bedrock, as an

ultra-quiet, i.e., extremely stable and noise-free structure, remote from sources of vibrational or electromagnetic noise. The building will be outfitted with special clean room facilities built to rigorous standards with air locks, ultra-pure air filtration, and a dust-free environment. The air in clean rooms will be repeatedly filtered to remove dust particles and other impurities that can damage the production of highly sensitive technologies. In addition to the communal service laboratories, the facility will also be home to chemistry research groups and intellectual exchange facilities.



PhD *honoris causa* conferred

on 6 visionaries in commerce, science, and the arts

This year honorary doctorates were conferred upon (back row, L to R): businessman and philanthropist Stephen Grand of the U.S.; the Hon. Laura Wolfson Townsley, Chair of the Wolfson Family Charitable Trust of the U.K.; and businessman and philanthropist Sami Sagol of Israel; (front row, L to R): mathematician and Turing Prize winner Prof. Michael Rabin of Israel and the U.S.; Israeli poet Agi Mishol; and neurobiologist Prof. Jean-Pierre Changeux of France.

Dedicating The Schwartz/Reisman Science Education Center

at the Arnon Science Education Campus

Prof. Daniel Zajfman dedicated the new Schwartz/Reisman Science Education Center at the Ruth and Uriel Arnon Science Education Campus. Shabtai Shavit (pictured here), Chair of the HESEG Advisory Board, spoke on behalf of Gerry Schwartz and Heather Reisman. Hundreds of high-school students from Rehovot and Ness Ziona attend classes in physics at the new Center in a new regional model of advanced science education.



Shabtai Shavit, Chair, HESEG Advisory Board, on behalf of Gerry Schwartz and Heather Reisman



Spotlight on Science Education

At a luncheon on science education, Prof. Daniel Zajfman introduced the Institute's new initiative to enrich science education and literacy through modern technology, called *iScience*. The program is run by the Weizmann Institute's Davidson Institute of Science Education. Supporters of the program, the Windsong Trust, Drs. Esther and Michael Pirak, Miriam and Merle Hinrich, Dita and Yehuda Bronicki, and Blythe Brenden were honored at the luncheon.



📍 The Marianne Manoville Beck Research Fellow Chair in brain research was dedicated with its first incumbent, Dr. Yonatan Katz from the Department of Neurobiology, pictured here with Cathy Beck.



📍 Valeria Rosenbloom and her late husband, Mike Rosenbloom, were honored for their support of the research of Prof. Zvi Livneh (pictured here with Valeria) of the Department of Biomolecular Sciences.



📍 Prof. Asaph Aharoni receiving the André Deloro Prize from Albert Deloro, Rebecca Boukris, and Prof. Daniel Zajfman.

Prizes awarded & Scientific Chairs dedicated



📍 Dr. Gil Omenn and Martha Darling, pictured here with the first incumbent of the Dr. Gil Omenn and Martha Darling Professorial Chair in Molecular Genetics, Prof. Maya Schuldiner.



📍 Prof. Ido Amit of the Department of Immunology was the recipient of the Helen and Martin Kimmel Award for Innovative Investigation.



Mandy Moross

Gala dedicated to a friend and supporter exemplar

A special tribute to Mandy Moross, former Chair of the International Board, and founder of the Moross Integrated Cancer Center (MICC), was held at at Beit Hatfuzot (Museum of the Jewish People) with Israeli novelist A.B. Yehoshua as guest speaker. Mr. Yehoshua spoke on the meaning of being a Jew and a Zionist. After the dinner, guests had the opportunity to tour the special exhibits of the museum.

Panel on cancer research

Donors and scientists discuss the future of the MICC

Prof. Israel Bar-Joseph, Vice President of Resource Development and Public Affairs, hosted a special panel on cancer research. Participants of the panel were: Bob Drake, Chair of the European Committee, who, with his wife Renée established the EKARD Institute for Cancer Diagnosis Research; Prof. Yardena Samuels, Director of both the EKARD Institute and the Weizmann-Brazil Tumor Bank; Eric Stupp, President of the Swiss Society of Friends, representing the Swiss Society Institute for Cancer Prevention Research; Prof. Zvi Livneh, Director of the Swiss Society Institute; Mario Fleck, President of the Brazilian Friends, representing the Weizmann-Brazil Tumor Bank; Solo Dwek who, together with his nephew Julian, established the Dwek



Solo Dwek, Mario Fleck, Prof. Zvi Livneh

Institute for Cancer Therapy Research; Prof. Yosef Yarden, Director of the Dwek Institute; and Prof. Moshe Oren, Director of the Moross Integrated Cancer Center (MICC).

After the panel discussion, Prof. Avigdor Scherz discussed his research on prostate cancer.



Panel on prostate cancer research advancements

Prof. Avigdor Scherz, pictured here with Canadian friend Sharon Zuckerman and her daughter Alison Jarvis, gave Board members an in-depth presentation of his collaboration with Memorial Sloan Kettering Cancer Center to advance a prostate cancer therapy called Vascular Targeted Photodynamic Therapy used in concert with **TOOKAD Soluble®** (TS-VTP). Prof. Scherz developed the therapy jointly with Prof. Yoram Salomon of the Department of Biological Regulation.



Celebrating Giving

Board members and guests met at the Donor Wall at the International Plaza, the major site for donor recognition on the Weizmann Institute campus, to honor those supporters who were inscribed on the

wall this year. A mainstay of the International Board meetings, the Celebrating Giving ceremony allows us to publicly thank our many donors and partners in promoting science.



Tribute to Morris Kahn & the Kahn Institute for Human Immunology

Long-time supporter Morris Kahn was honored at a festive gala dinner celebrating the establishment of the Kahn Institute for Human Immunology. Pictured: Mr. Kahn with Dr. Ziv Shulman of the Department of Immunology, and Mr. Kahn with his partner, Ariella Delaney. Iconic Israeli singer Aviv Geffen surprised Mr. Kahn with a few select songs.





Closing Gala



מכון ויצמן למדע



The future of genome-editing

CRISPR cuts through challenges in biological science

Science Feature

38–39

To understand how genes work, scientists need ways to control them. Changing genes in living cells is not easy, but a new method has been developed recently that makes it possible to make specific changes in the DNA of humans, other animals, and plants.

The technology, called CRISPR, is not only faster and easier than any previous technique for modifying DNA—it is radically changing the way basic research is conducted. Advances in CRISPR technology recently achieved by Weizmann Institute scientists give a hint of just how far the CRISPR revolution may yet go.

Early efforts to harness CRISPR—a gene-editing mechanism that occurs naturally in bacteria—focused on using it to improve industrial processes such as the production of yogurt. But according to Prof. Rotem Sorek, who uses CRISPR in his research, CRISPR's potential applications are as vast as the human imagination.

“The discovery of CRISPR is probably one of the next Nobel prizes,” he says.

Illustrating CRISPR's dramatic impact, a group of Chinese researchers recently launched a first-in-human CRISPR trial in late-stage lung cancer patients, using the system to engineer cells of the immune system so that they selectively target and destroy tumor tissue. This experimental addition of CRISPR to the medical toolbox raises fascinating questions: Will CRISPR-ized cells one day be used to cure cancer and other genetic conditions like cystic fibrosis and Tay Sachs? Will it allow us to enhance human intelligence at the embryonic stage? And what about the safety testing needed to prevent the rare yet significant occasions when CRISPR gene editing goes “off-target”—which, in humans, might endanger human health? Only time will tell.

From bacteria to applied biotechnology

CRISPR mimics a system used by bacteria to protect themselves from infection by viruses. It is based on an enzyme called Cas9 whose outstanding feature is that it can cut DNA at specific points. It does this by forming a complex with “guide” RNA produced naturally by bacteria to match the nucleic acid sequence of the invading virus. When this complex finds its target within the viral genome, the enzyme cleaves the target DNA, disabling the virus.

Over the past few years, researchers realized that this gene-editing system could be engineered to cut not only viral DNA, but any DNA sequence, by engineering guide RNA to match a particular target. And this can be done not just in a test tube, but also within the nucleus of a living cell. Scientists around the world are currently using the system to “crop out” specific sections of the code in order to identify gene function. Even more dramatically, they are using CRISPR to replace mutant genes with healthy copies, by “pasting in” another piece of DNA that carries the desired sequence.

In humans, safety testing involves investigating this process, because on rare occasions, Cas will target the wrong DNA, which can lead to potentially lethal autoimmune diseases.

Since the mapping of human DNA with the Human Genome Project, various methods of gene editing have been developed. But unlike previous methods, CRISPR can be used to target many genes at once—a big advantage for studying complex human diseases like Alzheimer's or cancer, which are caused not by a single mutation but by many genes acting together. It is also a powerful, practical tool for plant sciences, making it possible to quickly customize crops according to exacting criteria.

Pursuing very different projects, two senior researchers at the Weizmann Institute have established themselves as world leaders in the CRISPR revolution, by unlocking this technology's potential for improving agricultural crops and for fighting human disease.

Editing the plant genome

Since the earliest days of agriculture, farmers have been selecting plants with desirable characteristics out of natural variants. More recently, crossbreeding helped them make new, even more desirable specimens. But the search for the “perfect plant,” combining the best traits from both parents, requires screening thousands of plants bred over successive generations—a process that can take years.

Now, Weizmann Institute plant scientist Prof. Avraham Levy and his team have achieved proof-of-concept for a CRISPR-based technique that enables precise customization of a plant’s genetic make-up in a single generation. This breakthrough technique makes it possible to redesign plant genomes—from the editing of single genes to the exact engineering of chromosomes—achieving what farmers have always dreamed of: an efficient path to precise crop design.

Genomic editor-in-chief

Prof. Levy is a member of the Department of Plant and Environmental Sciences, and is the incoming Dean of the Faculty of Biochemistry. He is a pioneer in the study of something called DNA double-strand break repair—a natural process in which the plant cell’s genetic machinery fixes damage occurring

in both strands of the DNA double helix. One way that such breaks can be repaired is through genomic “recombination”—a phenomenon in which extended segments from the parental chromosomes are randomly exchanged, generating new genetic combinations as well as new traits.

Prof. Levy and his team recently demonstrated for the first time how recombination can be transformed from a random event into a process that can be scientifically directed, in order to achieve specific agricultural outcomes.

The researchers relied on a revolutionary molecular tool called CRISPR-Cas, which makes it possible to cleave the genome at specific sites (“Cas” is the name of the enzyme responsible for cutting DNA). Using this tool, they directed the recombination of targeted chromosomal segments, allowing the non-random alteration of multiple traits in plant progeny. Significantly, these dramatic changes took place over a single generation, establishing CRISPR-Cas as a highly efficient tool for precise breeding of crop plants.

Prof. Levy’s achievement, for which a patent application has been registered, demonstrates how CRISPR-Cas can drive non-random “chromosome editing” in order to achieve specific results in plants.



 MSc student *Offir Lupu* and Prof. *Avi Levy*

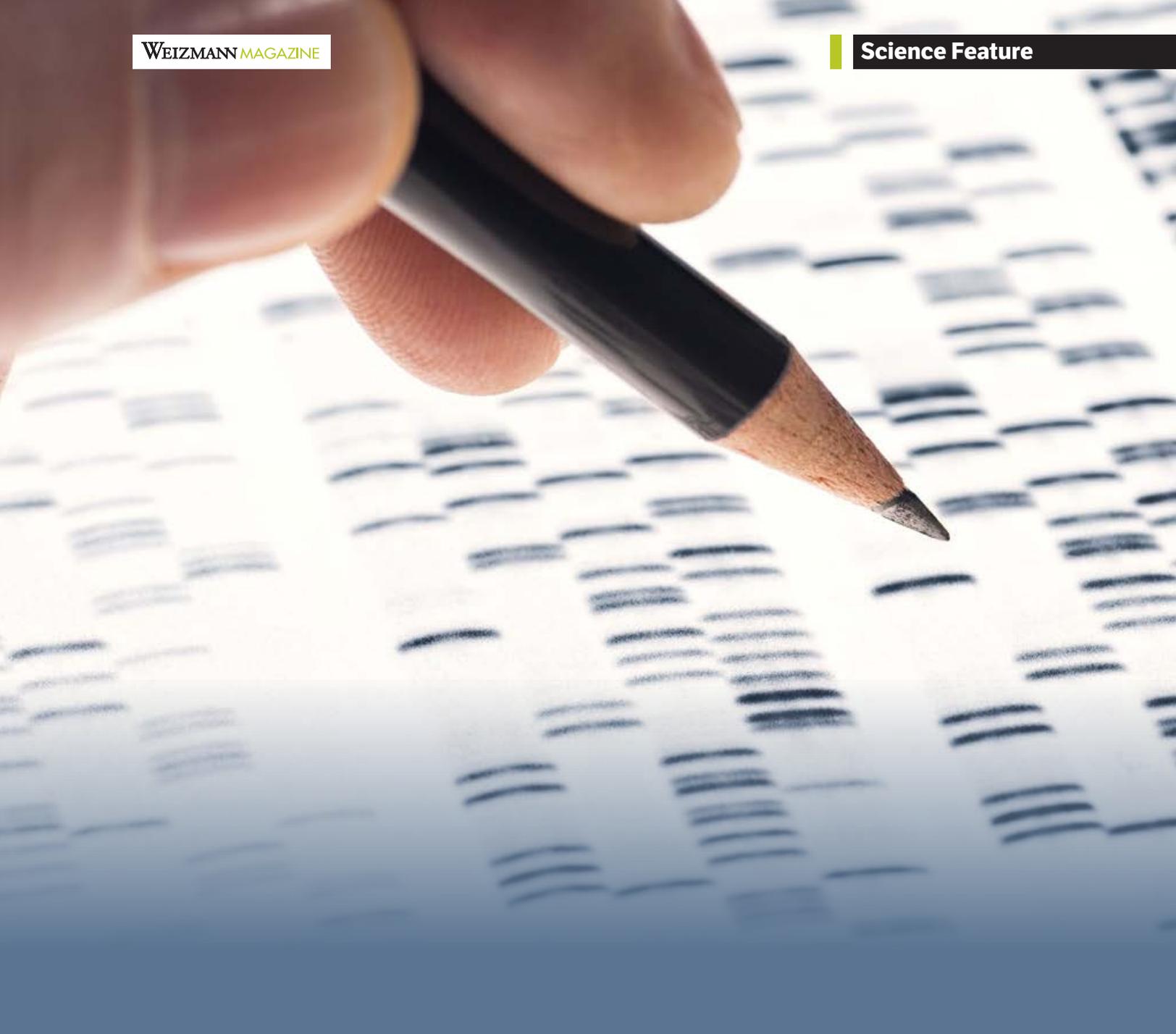
Using this method, he says, “we took advantage of recombination—one of the cell’s natural strategies for repairing double-stranded breaks—and produced a complex desired result. CRISPR-Cas gives us the means to choose the best from both parents, for example, combining the high-yield characteristics of the ‘dad’ plant with the high disease resistance of the ‘mom’, using just a handful of plants.”

Editing individual genes

The recent work also demonstrates how CRISPR-Cas can efficiently target and modify specific gene-linked

traits. As a proof of concept, the Levy team used the method to edit fruit color, producing yellow-colored tomatoes from red tomato parents. This result was achieved using only a few plants—compared to the several thousand required to introduce desired traits into the plant genome by conventional, random methods—and in a single generation.

“With this new technique, we can effect change faster than practitioners of traditional crossbreeding could ever have imagined,” Prof. Levy says. “In terms of both specificity and speed, CRISPR-Cas gives us enormous control over traits in the crops we grow. We’ve just begun to explore it, but it looks like it may be a real revolution in science-driven agriculture.”

A close-up photograph of a hand holding a black pencil, with the tip of the pencil pointing towards a DNA microarray. The microarray consists of a grid of small, dark spots on a light background, representing genetic data. The background is a soft, out-of-focus blue gradient.

A “1-2 punch” against human disease

While Prof. Levy was perfecting genome editing in plants, just across campus Prof. Ido Amit of the Department of Immunology was closing in on another CRISPR-based breakthrough with significant implications for the clinical treatment of a vast array of disease conditions.

By combining CRISPR with massively parallel single-cell RNA sequencing, Prof. Amit has made it possible to manipulate gene functions within hundreds of thousands of single cells—and also to understand the impact of each genetic change, in extremely high resolution. A single experiment conducted

with the new method may be equal to thousands of experiments based on previous approaches, making it a potential springboard for significant progress both in genetic engineering and medical applications.

Prof. Amit chose to demonstrate the new system, which he calls CRISP-seq, by focusing on a particularly busy biological “junction”: the immune system.

Using the new system to probe the “wiring” of innate immune cells that play a critical role in our ability to combat pathogens, Prof. Amit and his team were able to identify genes important for the function of this important network of cells. These experiments also succeeded in illustrating, in high resolution, how these gene circuits direct a complex and concentrated response against invading pathogens.

“There are diverse decision-making circuits in immune cells, but pinning down their activity is difficult, because their function is constantly in flux,” Prof. Amit says, who published this study in *Cell* together with lead authors Drs. Diego Jaitlin, Ido Yofe and Assaf Weiner, and research student David Lara-Astiaso. “Our challenge was to use the CRISPR gene editing technology to target multiple genes simultaneously, including combined targets in the same cell, and then identify resulting changes to the cell and its function.”

The researchers then faced a new type of “big data”—consisting of hundreds of thousands of cells and many thousands of genes expressed in each cell—with quite a few missing values. “By linking

cells with similar behaviors, something like the algorithms Netflix uses to group people who like similar movies, we were able to identify previously unrated function for many genes,” says Dr. Weiner, who developed the algorithms to analyze the data.

‘A new molecular microscope’

Combining CRISPR with massively parallel single cell RNA sequencing can provide insight that neither method alone would be able to yield. Moreover, the versatility of CRISP-seq suggests that it can be used in the future to investigate many open questions, and produce new results that no one can yet predict.

“CRISPR, on its own, is a blunt research tool,” says Prof. Amit. “Most studies so far have looked for black-or-white types of effects, but the majority of processes in the body are complex and even chaotic.”

According to Prof. Amit, the advent of CRISPR revolutionized scientists’ ability to understand and edit immune circuits, and the new combined system may further heighten CRISPR’s impact.

“We hope that our approach will be the next leap forward, providing the ability to engineer immune cells for immunotherapy, while paving the way for many new investigations, in a range of scientific disciplines.”

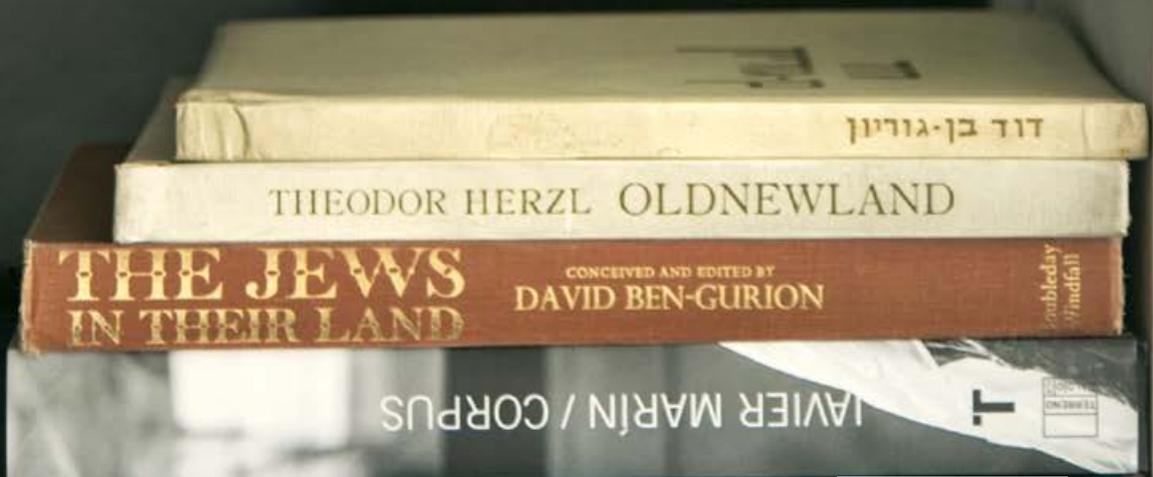
The research results were published together with descriptions of a similar technology developed at the Broad Institute in Boston and the University of California, San Francisco.



Prof. Ido Amit



Miriam & Martin Kushner



מכון ויצמן למדע



Profile of a Pair

44–45

Martin Kushner is a self-described ‘serial science lover’: he and his wife, Miriam, travel to the Weizmann Institute from their home in Mexico City at least once a year, meet with scientists from a variety of fields, and often give philanthropically to many of those they meet. They have supported particle physics, neurobiology, alternative energy, microbial genomics, science education, and have funded a Mexican postdoctoral fellowship at the Institute.

“I just get excited—I get interested in this and that, and fall in love with a new scientific subject after meeting with a scientist and connecting with him or her,” says Mr. Kushner in an interview in the Kushners’ home in Mexico City. “I like to understand a little bit about a lot of things, and there’s no better place for that than Weizmann,” he says.

Martin Kushner is a nuclear physicist by training; he received his degree in physics from the Universidad Nacional Autónoma de México. The “bible” of nuclear physics at the time, from which he studied, was written by two Weizmann Institute physicists, Profs. Igal Talmi and Amos De-Shalit. He taught for a few years at the university level, and went on to work for the Federal Electricity Commission of Mexico, the state-owned national electric power company, as an advisor of the country’s only nuclear-powered electricity facility. There, he tracked radioactive material, ensuring it would not contaminate the local water sources or the nearby coast.

He later moved into the business world, joining the family’s hardware store chain across Mexico. But his interest in science—specifically nuclear physics—remained. That interest led the couple to support

the lab of Dr. Shikma Bressler of the Department of Particle Physics and Astrophysics.

“When I was studying nuclear physics and working in the field, the behavior of the nucleus was reasonably understood,” he says. Particle physics involves the study of the properties, relationships, and interactions of subatomic particles. “Now everything has changed, and scientists are finding more particles, new ways of measuring their properties and understanding their behavior. Shikma is doing incredibly interesting work and I am looking forward to following it.”

The Kushners became involved with the Weizmann Institute about a decade ago, and in 2010 Martin became the president of the Mexican Association of Friends, casually referred to by its members as “the Amigos.” Mexico’s Jewish community is small—about 45,000 people in all—but it has strong ties to Israel. As president, he helped build awareness of the Institute, including through the awarding of the prestigious Weizmann Prize for the best PhD thesis, operated jointly with the Mexican Academy of Sciences. He continued the strong historical legacy of the Mexican committee in nourishing research at the Weizmann Institute, and widened the circle of supporters. He completed his presidency last year.

Miriam and Martin are also members of the Institute’s prestigious President’s Circle, comprising the Institute’s most generous supporters, and they are active members of the Institute’s international community, attending annual International Board events—Martin is a Board member—and the Global Gathering, held every two years in a major city (most recently in London).





Beyond Higgs

When the media headlines revealed triumphantly in July 2012 that the once-elusive Higgs boson particle had been found—and thus a cornerstone of the so-called Standard Model of particle physics clarified—the thousands of physicists who had been working for decades on this puzzle didn't pack their bags, call it a day, and go home. On the contrary—the finding opened the door to reams of new research on the fundamental building blocks of the universe. And Dr. Bressler, too, saw that day not as an end point but a new starting point to explore just what new physics the Higgs might be hiding.

As an active member of the ATLAS collaboration at the Large Hadron Collider at CERN, Dr. Bressler is now spearheading a search for the so-called “lepton flavor violating decays” of the Higgs boson—which might reveal that the Higgs boson

is a lot more exciting than previously assumed. It is true fundamental science: understanding the very building blocks of matter. In preparation for future experiments and future discoveries, she is developing new detection techniques. These studies also have potential for applications in homeland security, medicine, archaeology, and more.

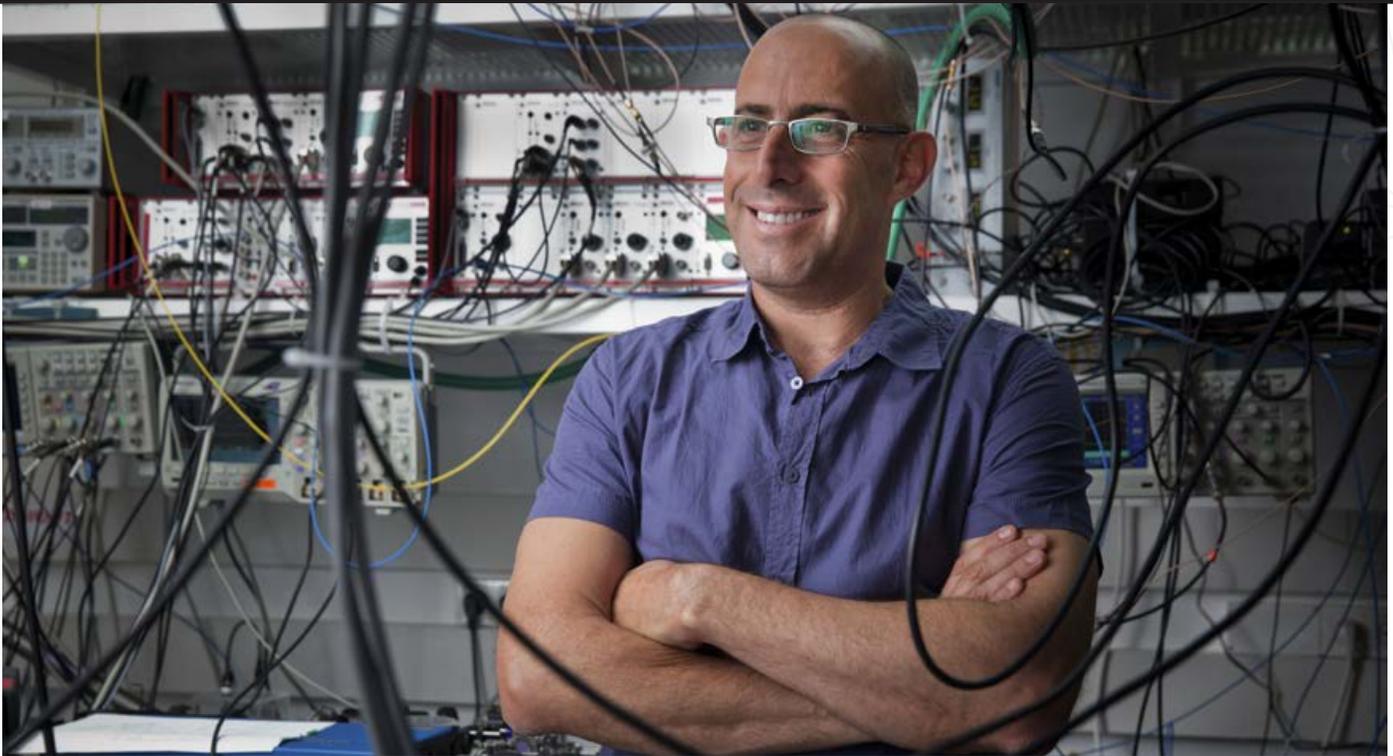
“The Kushners care about this field of work and it is meaningful to have a supporter with whom I can share my ideas and plans. They understand what I'm doing it and, most importantly, why I'm doing it,” says Dr. Bressler. After completing her PhD at the Technion, Dr. Bressler joined the Weizmann Institute as a postdoctoral fellow, moved up to a scientist position, and in 2015 became a principal investigator (PI)—a testament to her talent, because these positions are typically filled by scientists who perform their postdoc studies abroad.

“Science will be one of the human activities that will remain for generations, like art and music,” says Mr. Kushner. “It is a show of the creativity of humans. I am captivated by science in the way that I am captivated by art and music; it involves a special way of thinking—very methodically.”



“The Kushners care about this field of work and it is meaningful to have a supporter with whom I can share my ideas and plans,” says Dr. Bressler.

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Prof. Roe Ozeri

Among the scientists supported by the Kushners is Prof. Roe Ozeri of the Department of Physics of Complex Systems.

Prof. Ozeri studies the basic building blocks needed for quantum computing—the development of computing systems that make use of the principles of quantum mechanics. Such quantum systems have the potential to perform immense information-processing tasks that are out of reach of regular computers, and they can have a vastly greater capacity for storing information.

If such systems are indeed built, they will revolutionize the world of computing, requiring, for example, an entirely new approach to ensuring the secrecy of information in online banking transactions. Prof. Ozeri focuses on one of the greatest challenges in developing quantum computers: finding appropriate units, or bits, for storing information.

To create the basic building blocks for quantum information systems, Prof. Ozeri and his group use ultra-cold trapped ions. And when he says cold, he

means very cold—as cold as it gets. The Ozeri group laser-cool their ions to a temperature of a few millionths of a degree above absolute zero, where they can only occupy the ground-state of their trapping potential. These trapped ions are well isolated from the noisy lab environment. In fact, the only way the scientists can investigate these super-cold ions is by using laser light. Under these conditions, the laws that govern ion dynamics are those of quantum mechanics.

To this end, Prof. Ozeri and his group succeeded recently in detecting the minuscule magnetic interaction between two individual electrons that were bound to two ions separated by the atomically vast distance of about two micrometers. The background noise was a million times stronger than the weak force he measured. However, his achievement not only taught new information about an essential atomic force, but may also be extremely useful in the emerging fields of quantum sensing and quantum information systems—a whole new era in electronics and computing.



📍 L to R: Prof. Goldfarb; postdoctoral fellows Drs. Shiri Gur-Cohen and Anat Biran; Ellen Merlo; Prof. Neeman; Prof. Dudai; and Prof. Alberini.

Women for Science Symposium & Luncheon

Launched in 2015, the American Committee's Women for Science (W4S) Initiative brings together philanthropists and leaders to advance transformative research and women's-related initiatives at the Weizmann Institute. Recently, 50 supporters attended the W4S Symposium & Luncheon, held at New York University's Helen and Martin Kimmel Center for University Life.

The morning symposium opened with a talk by Prof. Michal Neeman, Vice President of the Institute. Prof. Daniella Goldfarb, the President's Advisor for Advancing Women in Science and a member of the Department of Chemical Physics, described the Institute's efforts to support female scientists at every stage of their careers. She then led a conversation with two young scientists who have received support from the Institute through the Israel National Postdoctoral Award for Advancing Women in Science to pursue their postdoctoral studies in the U.S. Prof. Yadin Dudai of the Department of Neurobiology and NYU's Prof. Cristina Alberini discussed their international neuroscience collaboration.

American Committee National Chair and W4S chair Ellen Merlo moderated a panel discussion, "Women in Philanthropy: A Catalyst for Positive Change," which featured noted philanthropists Patricia Gruber and Marcy Syms, as well as Cheryl Black, Managing Director of J.P. Morgan Private Bank.

Stem cells and beyond, in Toronto

Weizmann Canada hosted an evening of celebration and recognition in honor of its supporters at the Shangri-La Hotel in Toronto on November 3.

The program included Dr. Jacob Hanna of the Department of Molecular Cell Biology (pictured below), who spoke about his research on stem cells. Other highlights included tributes to Sharon Zuckerman and the late Tom Beck for their long-standing support and visionary philanthropy. Board Chair Jeff Cohen spoke about the impact of two transformational gifts: one from the Azrieli Foundation to establish the Azrieli National Institute for Human Brain Imaging



and Research and another from The Gerald Schwartz & Heather Reisman Foundation to establish science education centers in Israel for high school youth.

The annual Outstanding Leadership Award was presented to Michele Atlin, Chair of the Women and Science Committee, in recognition of her dedication and tireless service to Weizmann Canada and the Institute. Several new members were inaugurated into the Honour Society, recognizing those who have chosen to leave a bequest to Weizmann Canada.

Weizmann World

48-49

Garvan-Weizmann partnership building up

Construction of the Garvan-Weizmann Centre of Cellular Genomics in Sydney, Australia, is on track, and the Centre is set to open later this year.

The Garvan-Weizmann partnership will involve a staff and student exchange; the use of sophisticated tools to investigate immunological responses in complex diseases; and cellular genome sequencing for clinical purposes. The center is located at the Kinghorn Cancer Centre at the Garvan Institute. Studies by Institute scientists Prof. Ido Amit (Department of Immunology) and Prof. Yardena Samuels (Department of Molecular Cell Biology) are among the first collaborations with Garvan colleagues.



European Committee hosts annual dinner in Zurich

About 140 philanthropists and friends from Europe gathered on January 11 at the Hotel Baur au Lac in Zurich for the annual gala dinner of the European Committee of the Weizmann Institute of Science (ECWIS). Participants from ECWIS societies celebrated the strong bond between Institute scientists and their supporters in Europe. As a special tribute, the Swiss Society of Friends was honored for its role in the establishment of the Swiss Society Institute for Cancer Prevention Research at the Moross Integrated Cancer Center on campus.

Mr. Bob Drake, Chairman of ECWIS, opened the evening and H.E. Mr. Jacob Keidar, Israel's

ambassador to Switzerland and Liechtenstein, greeted the guests and shared his personal experiences with malaria patients during his service as Israel's ambassador in Kenya and east Africa. Prof. Daniel Zajfman, President of the Weizmann Institute, described new developments on campus, with a specific focus on advancing science literacy. Keynote speaker Dr. Neta Regev-Rudzki from the Department of Biomolecular Science described her research on malaria.

A musical interlude of classical and Jewish Ladino songs was performed by the talented flute player Tama Lalo, accompanied by Mrs. Sara Agueda on the harp.



Tribute to Robert Parienti in Paris



On November 22, the Weizmann Institute celebrated the life and career of Robert Parienti, Delegate General of the French Committee who retired after over four decades. Nearly 600 people attended the event, which took place at the Palais Brongniart in Paris. David Weizmann replaces Robert in that role as Executive Director.

Mr. Parienti was born in Tunisia and moved to Switzerland, and then Paris. He was introduced to the Weizmann Institute by the late Israeli statesman Shimon Peres, who suggested that he become the Institute's representative in France. He took on that role in 1974.

“He had a scientific mission, but he also had another idea, which was to show people a different face of Israel at a time when the atmosphere was particularly unfavorable,” says Prof. Michel Goldberg, a leader of the French Committee. To that end, and with the help of French Health Minister Simone Veil, he initiated a major collaboration between the Pasteur Institute and the Weizmann Institute, which became a gold standard for scientific collaborations by Institute scientists. Mr. Parienti is also responsible for recruiting major philanthropic gifts for the Institute from French donors for buildings, research, scholarships, and more, and he held galas in Paris that drew the elite of French society.

Wild animals and human nutrition: meeting of the Israeli Science Club

The Science Club of the Israeli Friends of the Weizmann Institute of Science gathered on December 14 for an event at the Hilton Hotel in Tel Aviv. More than 250 members, including members of the WeizmannVibe Club, attended a festive dinner featuring a talk by Dr. Eran Elinav of the Department of Immunology.

Dr. Elinav, who specializes in the study of the microbiome—the population of bacteria and other micro-organisms in our gut—told the audience about his studies on personalized nutrition, and how the foods we eat affect everyone differently. Award-winning nature photographer Amos Nachoum (pictured right), who lives in San Francisco and who specializes in photographing large animals,

spoke about his work and the importance of nature preservation.



Friends events in Latin America

A new friends group in Rio de Janeiro, part of the Brazilian Friends of the Weizmann Institute of Science, was launched at a meeting that filled Hillel Rio on February 17, in the presence of Mario Fleck, President of the Brazilian Association of Friends of the Weizmann Institute, and Dany Schmit, the Institute's CEO of External Affairs for Latin America.

The event involved new and existing friends. Mario Fleck spoke about the activities of the Association, including how it has fostered scientific partnerships with entities such as FAPESP (São Paulo Research Foundation), the selection of Brazilian students for the Dr. Bessie F. Lawrence Summer Science Institute on campus, and hosting events like Science on Tap and Weizmann Talks, which creatively engage the public in Weizmann science.

In December, Weizmann Institute President Prof. Daniel Zajfman traveled to São Paulo, Brazil, and Buenos Aires, Argentina, where he met with donors and business leaders. On December 6, Prof. Zajfman met with business and academic professionals at the offices of Grupo Insud in Buenos Aires, hosted by CEO Dr. Hugo Sigman and his wife, biochemist Silvia Gold. Lino Barañao, Argentina's Minister of Science, Technology and Productive Innovation, also participated in the meeting, as well as Israel's Ambassador to Argentina, Ilan Sztulman; resident of the National Scientific and Technical Research Council, Dr. Alejandro Ceccatto; and university rectors, business managers, and researchers.



➤ *New group in Rio, L to R: Ricardo Hechtman, Marcelo Herskovits, Ronaldo Adler (Hillel President), Renato Cohen (Vice President of FIERJ, the Jewish Federation of Rio de Janeiro), Cláudio Goldemberg (also FIERJ Vice President), Mariano Zalis, Marcelo Astrachan (Vice President for Rio of the Brazilian Association of Friends), Eduardo Rabinovitch (Vice President of ARI), and Flávio Stanger (President of the FIERJ council).*



➤ *Visit in Argentina: L to R: Dany Schmit; Prof. Zajfman; Dr. Silvia Gold, President of Mundo Sano; Dr. Sigman; and Israel Ambassador to Argentina, Ilan Sztulman.*

'Girls Choose Science' airs on Israeli TV



A new television series representing a collaboration between the Davidson Institute of Science Education and the Israeli Children's

Channel launched in February, with a goal to ignite curiosity for science among girls and pursue studies in science. The 21-part series of skits appears on the Children's Channel and the Logi Channel. It includes leading Israeli actors Lior Raz and Eliana Magon, whose humorous and entertaining skits of two- to three minutes present accurate simple explanations of key concepts in science and math.

The series—the first of its kind in Israel—aims to help girls overcome obstacles and prejudices that might prevent them from pursuing science and math. It will run every day throughout 2017. In addition to the skits, the popular show "The Real Bell" will feature a recurring "Girls Choose Science" segment.

Weizmann events in South Africa

In February, the Weizmann Institute hosted several events in South Africa to acknowledge the significant contribution of David Lopatie and other leading South African philanthropists to the Institute.

Prof. Israel Bar-Joseph, Vice President for Resource Development and Public Affairs, spoke to the participants about the Institute and about major challenges in science. He was joined by Kelly Avidan, Head of the Department of Resource Development; Sheridan Gould, Executive Director of Weizmann UK; and Yael Goren-Wegman, Executive Director of the Israeli Friends of the Weizmann Institute.

The visit was an opportunity to acknowledge the dedication of those who have supported the Institute for many years, and celebrate the 90th birthday of long-time friend Ann Susman. Several UK philanthropists with connections to South Africa joined in the festivities, including Sir David and Lady Sieff; Sir Sydney and Lady Lipworth, Jeremy Smouha, and Clifford and Soozee Gundle.

"Whenever I visit the Weizmann Institute, I am made so welcome that it feels like I have returned home, but now it is just wonderful to be able to welcome the

Weizmann Institute to South Africa," says Mr. Lopatie. "I hope that fellow South Africans will enjoy as rewarding a relationship with the Institute in Israel as I do."

The wealth management firm Stonehage Fleming graciously hosted two breakfasts, in Johannesburg and Cape Town. Another asset management firm, Investec Wealth and Investment, generously hosted a lunch in Johannesburg and an evening reception in Cape Town. This was a most welcome initiative led by Investec's Jonathan Bloch, brother-in-law of European Committee Chair Bob Drake, who attended the events with his wife Renée.





Alumni conversation in Boston on Weizmann innovation

The New England Weizmann Institute Alumni Initiative of the American Committee hosted a gathering, “From Bench to *Tachlis*,” at the Cambridge Innovation Center (CIC) in Boston. Weizmann Institute alumna Dr. Michal Preminger, who is the executive director of business development for Harvard Medical School, led a dialogue with her Harvard University colleague, Isaac T. Kohlberg (pictured together above). Dr. Preminger is co-chair of the alumni initiative. Mr. Kohlberg, Harvard’s Senior Associate Provost and Chief Technology Development Officer, previously headed the Weizmann Institute’s Yeda Research and Development Company.

Mr. Kohlberg described key Weizmann Institute discoveries that have resulted in lifesaving medications and technologies and the vision of Institute founder Dr. Chaim Weizmann, who believed in combining top-quality basic research and partnership with industry. Mr. Kohlberg and Dr. Preminger engaged in a dynamic conversation with the audience, which included Weizmann alumni and friends from the Boston area.

מכון ויצמן למדע



Heart research from the heart

When International Board member Dan Shapiro (pictured above) passed away last year, his wife Ellen wanted to do something special to memorialize him. Dan had died of heart failure, and had suffered for many years with heart disease and related problems. Ellen, with her three sons, established a fund in Dan’s memory at the Weizmann Institute, the Daniel S. Shapiro Cardiovascular Research Fund.

The fund supports the joint research of Prof. Eldad Tzahor of the Department of Molecular Cell Biology and Dr. Karina Yaniv of the Department of Biological Regulation. The duo is collaborating on research on the vascular system—the vessels and tissues that circulate fluids, including blood, through the body.

In a developing embryo, formation of the vascular system happens early on, guided by a complex set of molecular signals. Prof. Tzahor and Dr. Yaniv’s research grew out of the fact that, in many cases, the same signals involved in embryonic blood vessel formation are re-activated in adulthood during cardiovascular disease. By examining early-stage vascular development, the scientists are identifying key molecular “triggers” that contribute to disease onset. By doing so, they are identifying new targets for drug development, as well as new strategies for clinical treatment.

Dan was a lifelong leader in the Jewish community, and in the last decade, he had come to know and love the Weizmann Institute. He had been an active member of the Board, serving also on its Honors and Executive committees. He was particularly keen on learning as much as he could about neuroscience, and, because of his own health issues, followed developments in cardiovascular research.

Within weeks, the Shapiros’ friends and colleagues in the UK and US—the Shapiros are Americans who resided in London in recent years—had given generously to the fund, more than doubling expectations, and Dan’s law firm offered a major portion of the sum. “We were humbled by the generosity of our friends and grateful to be able to support this area of research, which Dan would have been proud to support,” says Mrs. Shapiro.

In this age of convenience, on-demand car services such as Uber and Lyft have become so popular that city dwellers across America wonder how they survived without them. It's easy to forget that just a few years ago, using a smartphone app to hail a ride was a novel idea. And one of the first to recognize its potential was Weizmann Institute alumnus Dr. Oren Shoval.

Dr. Shoval is a co-founder of Via, a New York City-based startup that is taking the urban transportation space by storm. Since its inception in 2012, the company has provided more than 10 million rides, launched in several markets, and raised \$137 million from investors.

What makes Via stand out from its competition? Rather than providing door-to-door rides, it offers ride shares for passengers traveling in the same direction and drops them off within a couple blocks of their destination. In this way, the company keeps the number of vehicles to a minimum, and guarantees low, flat fares. For New Yorkers, it means

Dr. Oren Shoval

A road paved by science and the founding of Via



being able to travel from lower Manhattan to Harlem for about \$5—“the price of a latte,” as Via’s website points out.

Now running a growing company and raising two young children, Dr. Shoval, 39, admits his life has changed dramatically in the four years since he earned his PhD in systems biology at the Institute. He says Via is the outcome of his thinking in terms of system-level problems—and solutions.

Moreover, he says, “The Weizmann Institute taught me to trust my instincts, to feel comfortable with uncertainty, and to take a complicated problem and try to simplify it,” he says. “It’s a state of mind that is very useful in my day-to-day work.”

This state of mind is vital for game changers in any field, something his mentor at the Institute, Prof. Uri Alon of the Department of Molecular Cell Biology, taught him. “Uri told me that if you ask a question you have no clue how to answer—and it causes anxiety—that’s a good thing,” Dr. Shoval says. “We’re not here to do something that’s already been done.”

Alumni

54–55

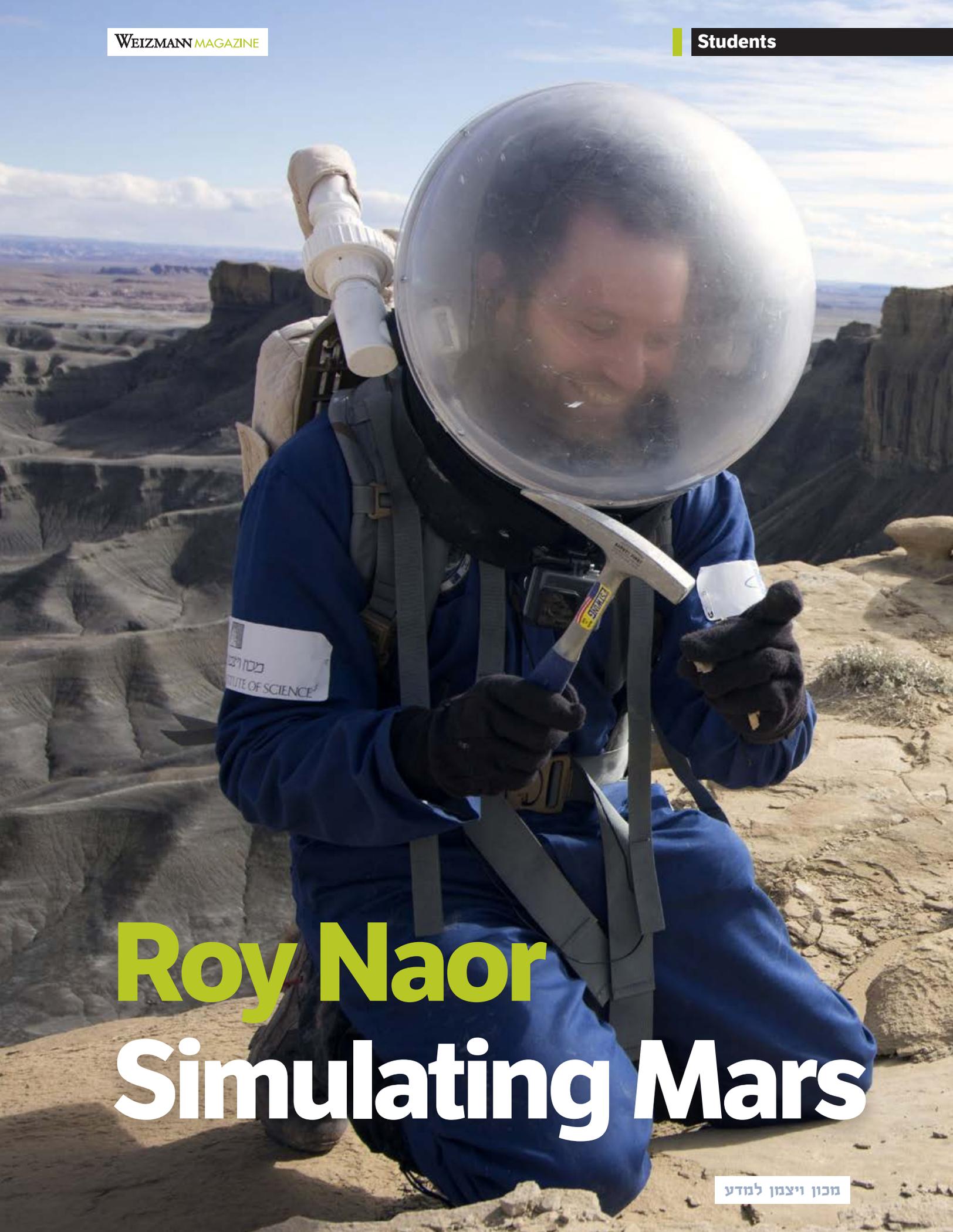
He grew up in Rishon LeZion and was always interested in math and science. He was accepted into a prestigious program in the army where he pursued his studies in tandem. He earned a BSc in physics and mathematics from the Hebrew University of Jerusalem, and an MSc in electrical engineering from Tel Aviv University. He spent almost 10 years in the IDF, during which he led engineering projects for the Air Force.

The modern way to hitch a ride

He had planned to pursue a postdoc, but he and Dr. Daniel Ramot, a friend from the Air Force, came up with the idea for Via. It was based on shared taxis in Israel called *moniot sherut*; anyone who has landed in Ben-Gurion Airport and needs to get to Jerusalem knows this is a popular option. They thought that combining this concept with mobile technology would create a “dynamic bus system,” he says, that is both efficient and eco-friendly. At the time, however, they faced naysayers who were convinced Via would fail. Undaunted, he says, “I recalled my training with Uri, who taught his students about the importance of venturing bravely into the unknown.”

He and Dr. Ramot, who holds a PhD in neuroscience from Stanford, brought their research backgrounds to bear while developing Via. While the platform appears simple and intuitive, behind the scenes Via requires complex algorithms and data to build, mix, and match the routes—all in real time. Today, Via provides more than 200,000 rides weekly in New York City, Chicago, and Washington D.C., with plans to expand to other cities. It is also marketing its technology to public transit agencies, and college and corporate campuses; the technology was deployed in Paris through a partnership with the public transit operator, Keolis. Via’s team has grown to include about 100 employees at three offices.

Like in the lab, he says, “The process of building Via has involved coming up with an idea, developing it, testing it, deploying it, and tweaking it.”



Roy Naor

Simulating Mars

Students

56-57

It looks like Mars and feels like Mars but—it's Utah

For two weeks at the end of January, Roy Naor lived in a simulation of a Mars research station as a representative of the Israel Space Agency. The Weizmann Institute masters student and a team from four other countries were in an isolated capsule in the Utah desert, carrying out studies similar to those that might be carried out in the future on the Red Planet.

Naor, a native of Kibbutz Naan near Rehovot, is studying geology in the Department of Earth and Planetary Sciences, where he plans to pursue his PhD.

The Mars Desert Research Station is run by the Mars Society; in the 172 team simulated missions executed so far, members work in the arid, Mars-like environment to develop new technologies and gain insight into how people could live on Mars. The Utah desert's topography, isolation, and soil quality is as close to what Mars is expected to be like as one could get in North America. This mission also included the head of the Slovakian Space Agency, a French mechanical engineer, an Australian astrobiologist, and an Irish artist.

The Israel Space Agency invited the public to participate in Naor's adventure by voting on the Israeli food that he would bring with him—Israeli salt and the peanuty snack *Bamba* won—and the song he should play for his team—“Halalit” (spacecraft) by Gazoz.

One of the team's goals was to investigate carbonate minerals, which have been found on Mars and could provide evidence for liquid water in the planet's past. Naor had an additional goal: to investigate the possibility of using the soil to create housing structures. One of the biggest technical hurdles to overcome in exploring Mars is its habitability—shelter, food, water. (Not to mention the ability to return home; it takes 7 months to get there and two years to return. But astronauts would die of starvation first, if not exposure to radiation or the loss of fuel.)

One of the Utah mission scientists investigated the crops that might be grown on Mars, for instance.

Naor sampled and analyzed the geology of the environment, investigating the properties of the soil and using a 3-D printing technique, which involves synthesizing a three-dimensional object with a computer using successive layers of material. He then tested it to see whether the material has the required strength and the durability to withstand the radiation on Mars, to use for building structures.

So, how did it go? “I learned a lot,” he says, “but I brought back samples to the Institute for further testing. It's a work in progress. And of course, it's Utah soil—not Mars. I have to compare our results with what we know about the soil on Mars.”

To simulate living in a Mars station, the group lived together in cramped conditions, eating, working, and sleeping in a single structure, with showers limited to once every three days. They could only venture outside the station in groups, in full suits—including helmets and oxygen tanks. They were only allowed to communicate with “Earth”—the outside world—once a day, with a delay of several minutes; cell phones were forbidden. They had to ration their food over two weeks.

“It was intense and it was important,” he says, adding that the experience only heightened his desire to “inspire the next generation.” The mission generated media headlines and Naor described his experience on a series of Israeli news programs upon his return, which he hopes will kindle curiosity among youth. To that end, he teaches a course at the Davidson Institute of Science Education for high schoolers interested in space exploration. His dream: to create a Mars simulation habitat in Mitspeh Ramon in the Negev Desert, where the terrain and climate are similar to Utah—and as similar to Mars as possible here on Earth.

As for traveling to Mars, Naor says he's game, “but I'll wait patiently until they figure out how to get us back.”

New hope for ALS patients

Kadimastem's new approach to a devastating illness

Amyotrophic lateral sclerosis, or Lou Gehrig's disease, will forever be associated with the legendary baseball player whose diagnosis in 1939 brought this neurodegenerative condition to the public consciousness. ALS continues to affect two out of every 100,000 people each year, driving a devastating trajectory that begins with the death of motor neurons in the brain and spinal cord, and ends with losing the ability to walk, talk, swallow, and breathe. During this process, the mind otherwise remains completely intact, silent witness to a progressive decline that typically culminates in fatal respiratory failure within five years.

With only one FDA-approved drug in existence—a compound that extends ALS patients' lifespan by no more than three months—there is a critical need for new medical strategies. One strategy currently in development is based on the work of an emeritus Weizmann Institute faculty member, drug discovery pioneer, and Israel Prize winner, Prof. Michel Revel, of the Department of Molecular Genetics.

Prof. Revel is Chief Scientist of Kadimastem, a company based on stem cell technology he developed while at the Institute. Kadimastem's focus is regenerative medicine—a clinical approach that seeks to harness the potential of stem cells to repair or replace damaged tissues in order to combat disease.

“Traditionally, drugs have been created by chemists, who use the tools of bioengineering to design molecules that can perform specific tasks in the body,” says Prof. Revel who, following his retirement from the Institute, co-founded Kadimastem together with company CEO Yossi Ben-Yossef in 2009. “But today, cells—not molecules—can be the medication. We are using human embryonic stem cells to produce precursor cells that—when transplanted into the spinal cord—differentiate into non-neural brain cells that slow the progression of ALS in a rat model. We believe this can work in human ALS patients as well.”

Kadimastem's human trials on ALS patients are scheduled to begin at Jerusalem's Hadassah Hospital in September 2017.

The path to the new, stem cell-based approach to ALS therapy began when Kadimastem licensed



Beyond the Bench

58–59

Prof. Revel's stem cell patents from Yeda, the Weizmann Institute's commercialization arm. But as Yeda CEO Gil Granot-Mayer explains, the most valuable intellectual property is human expertise. "In his long career at the Weizmann Institute, Prof. Revel was extremely successful in the bioengineering of molecules to create new drugs to fight disease. Our hope is that Prof. Ravel and his team's unique expertise in stem-cell-based drug design will address this unmet need," he says.

A regenerative approach

Prof. Revel is the creator of Rebif[®], a multiple sclerosis drug now marketed by Merck, with sales on the order of \$2.5 billion per year. At a time when most researchers were engineering medically useful protein molecules within yeast and bacteria, Prof. Revel took a more "exotic" route of using cells taken from the Chinese Hamster in order to obtain the protein interferon-beta in a form identical to the natural protein found in the human body. Rebif[®] was recently shown to prevent the more serious symptoms of advanced MS in 80 percent of early-stage patients who had been using the drug for 15 years.

In addition to Copaxone[®], another MS drug developed at the Institute, Rebif[®] contributes to quality of life by slowing down disease progression. However, it was Prof. Revel's desire to achieve a complete cure for MS that led him to the stem cell approach he is now using in the fight against ALS.

In 2000, he began to explore the use of stem cells to regenerate the neuron-insulating material lost as a result of MS. "But since MS is a diffuse process that occurs throughout the brain, it was not a practical target for stem cell therapy," he says. "That's when I turned my attention to generating a class of cells called astrocytes, which can mitigate the loss of motor neurons characteristic of ALS."

Astrocytes are non-neural cells critical for maintaining chemical balance in the environment surrounding motor neurons. "The significance of these cells for promoting motor neuron survival

has been well documented," Prof. Revel says. "Kadimastem's achievement is producing precursor cells that, once transplanted into the spinal cord, differentiate into the mature astrocytes that motor neurons need to survive. This is what we believe may be a real breakthrough for human ALS patients."

Kadimastem is pursuing additional avenues, including a stem-cell derived approach to insulin production for diabetics (see box), and a technology for optimizing insulin generation by selecting the right stem cells, developed by Weizmann Institute professors Yoav Soen and Michal Walker, and recently licensed to the company by Yeda. Carried out by the Kadimastem's 35 employees—including 12 research scientists—these projects are a continuation of the applicative approach that Prof. Revel developed over a 40-year career.

"In industry, the goal is to create a working technology that's safe, and that meets all the regulatory requirements," says Prof. Revel. "It's a challenge, but if we can prolong and improve the lives of people suffering from disease, it's all worth it."

A device for diabetes?

With a global population of 150 million diabetics relying on injected insulin, the creation of a device for generating insulin in the body would be a revolutionary event. Kadimastem is collaborating on a system that uses human embryonic stem cells as a platform for creating the beta cells that produce insulin. The company's goal is to create an encapsulated system that could be implanted in patients, constantly sensing blood glucose levels and secreting insulin accordingly, while avoiding rejection by the body's immune system. Kadimastem is configuring the device and is aspiring for clinical trials in humans.

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Yosef Yarden

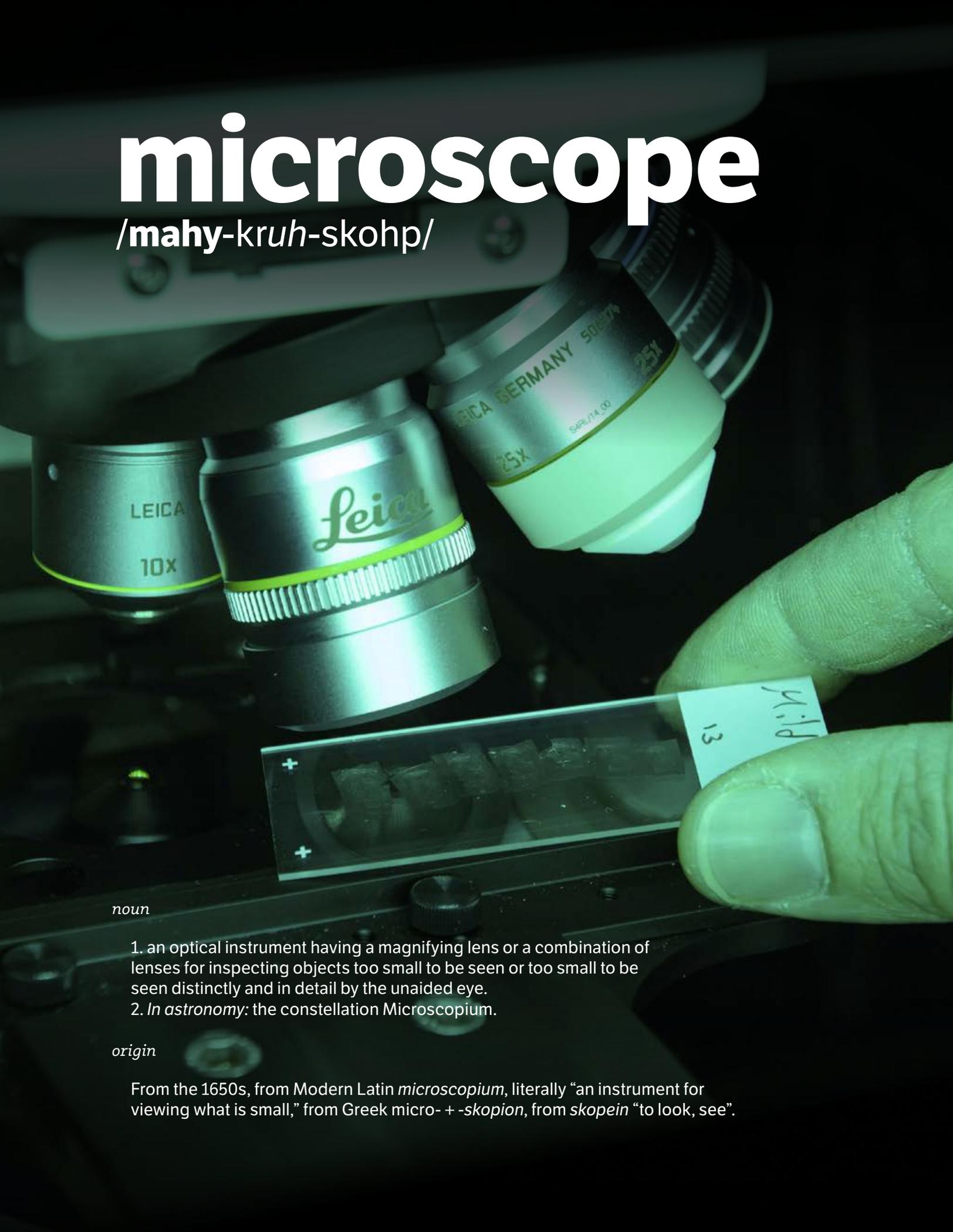
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microscope

/mahy-kruh-skohp/



noun

1. an optical instrument having a magnifying lens or a combination of lenses for inspecting objects too small to be seen or too small to be seen distinctly and in detail by the unaided eye.
2. *In astronomy:* the constellation Microscopium.

origin

From the 1650s, from Modern Latin *microscopium*, literally “an instrument for viewing what is small,” from Greek *micro-* + *-skopion*, from *skopein* “to look, see”.



↗ *Dr. Chaim Weizmann's microscope from his laboratory in the original building of the Daniel Sieff Institute (later renamed the Weizmann Institute of Science).*
