Aperio

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LOOKING BEYOND

SEARCHING FOR DISTANT LIFE IN SPACE AND SCIENTIFIC BREAKTHROUGHS ON EARTH

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Understanding how animals make crystals and see the world

Building Blocks
Exploring the processes and unlimited potential of chemical evolution

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Navigating a new paradigm in natural language processing and AI

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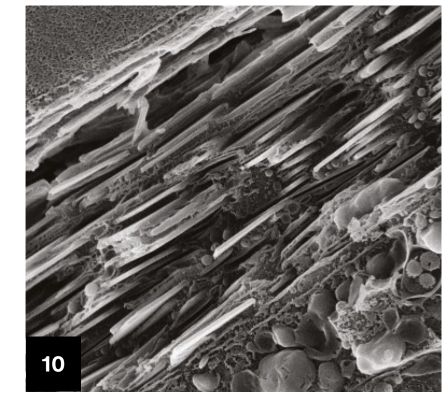
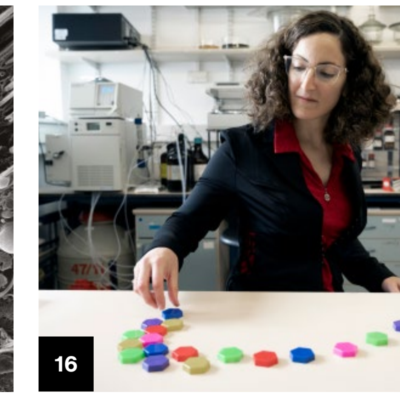
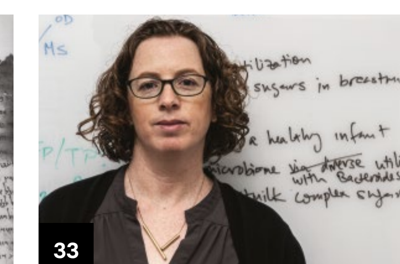
On the cover: A rendering of the Giant Magellan Telescope, currently under construction at the mountaintop Las Campanas Observatory in Chile's Atacama Desert, for which Azrieli Early Career Faculty Fellow Sagi Ben-Ami is building a spectrograph. Image courtesy GMTO Corporation.







By Lisa Gregoire

Breaking The Mould

Fusing architecture with physics and drawing inspiration from the natural world, Arielle Blonder reimagines how we build things

Architect Arielle Blonder has a radical vision for the future of architecture — not about how we design buildings but how we fabricate the materials we build them with. And it begins with smashing the mould.

Fibreglass, a lightweight, resilient and durable composite that resists fire, water, corrosion and insects, is popular in the aerospace, automotive and construction industries. But before components can be made, money and energy must first be sunk into building a mould and shaping the product, which amounts to an estimated forty per cent of the total cost. But what if we could eliminate the one-time need for a mould and all that throwaway material and labour?

Blonder, who holds postdoctoral research positions at the Racah Institute of Physics in Jerusalem and École nationale supérieure d'architecture Paris-Malaquais, believes we can and is working across disciplinary boundaries to prove it. "Composite materials represent the present and future of architecture, or at least they offer a lot of opportunities," she says. "But they have

PHOTOGRAPH BY DACIAN GROZA

limitations which, for a large part, lie in the moulding process that turns the raw materials into shape and into service."

When people talk about composites, they typically mean fibre-reinforced polymer, or FRP, a highly versatile material that's made of a polymer matrix, usually epoxy, vinyl or polyester, and reinforced with fibres such as glass, carbon or basalt. (Fibreglass is the most common form of FRP.) Yet, despite its proven attributes, the use of FRP in architecture has been limited, mainly due to stubborn building codes, opposition to plastic production and a profession that's generally slow to adapt.

PHOTOGRAPH BY HENRIK KAN, COURTESY SFMOMA

Inspired by the water and fog of San Francisco Bay, the expanded SFMOMA's façade showcases the architectural possibilities of FRP.

But change is afoot. The new 12-storey San Francisco Museum of Modern Art, adorned with an undulating white skin, has the tallest façade ever to be clad entirely in FRP. And although the building is groundbreaking, its FRP panels still had to undergo an expensive, multi-layered moulding process.

Blonder, the first architectural PhD student at the Technion – Israel Institute of Technology to focus on material research in a thesis, which she completed in 2019 as an Azrieli Graduate Studies Fellow, is exploring new ways of forming FRP without moulds. She is hoping to transform how we imagine small-to-medium structures and exterior façades by studying the fibre part of FRP, which is usually a woven textile.

As the former CEO of American Supply Paris, which creates and customizes materials for everything from haute couture to furniture, Blonder knows fabric can morph into any shape. She calls this "fabric materiality" or FM: "the essential material qualities, attributes and design paradigms of textiles with their associated techniques and technologies of fabrication and transformation." Based on its intrinsic materiality — and with help from computer simulators, mechanical manipulation, or both — fabric impregnated with resin polymers can assume any shape, if we let it.

"When we put FRP into a mould, we don't let any textile aspect of the material be expressed because we make it into a piece of plastic," says Blonder. "When you take a piece of fabric," she continues, pinching her shirt sleeve, "you can get an incredible shape. You see folds and curvature, things that we try to do in some of our building façades and envelopes."

As an Azrieli Graduate Studies Fellow, Blonder examined how fibreglass that is pre-impregnated with resin and then gathered through pleating can form a porous laminate. After being cured in an oven, the resulting stiff, rippled panels — a variety of which were produced through multiple gathering methods — underwent tensile, compression and bending tests, both singularly and stacked together. Further testing and scaling up are required but Blonder believes these are crucial first steps toward confirming the suitability of such FRP materials in architectural façades and cladding.

Blonder's FM research helped inspire Israel's 2016 contribution to the prestigious Venice Biennale of Architecture exhibition. This project manifested two other influential forces in her work: nature and interdisciplinarity. As one of the Israeli pavilion's curators, Blonder and her colleagues designed a structure inspired by a three-dimensional scan of a bird's nest. The unique, bio-architecture installation, "LifeObject," consisted of more than 1,500 free-formed, fibreglass tubes — or "twigs" — that were combined into a porous, resilient structure. Eventually, that is. In the weeks leading up to the Biennale, the structure kept failing, despite the team's valiant efforts. Panicked, Blonder consulted Oded Rabinovitch, a structural engineering professor who is now the Senior Executive Vice President at the Technion.

"He told me — and this was surprising, coming from an engineer — listen, it won't work," recalls Blonder. "You have to stop thinking like an engineer and start thinking like a bird." In other words: control what you can, accept limitations and embrace partial randomness, like a bird building a nest, piece by piece, from found objects. So,

'He told me — and this was surprising, coming from an engineer — listen, it won't work,' recalls Blonder. 'You have to stop thinking like an engineer and start thinking like a bird.'

Arielle Blonder (top) transcends boundaries between architecture, physics and art in projects such as "LifeObject" (previous pages and bottom), Israel's contribution to the 2016 Venice Biennale of Architecture.

PHOTOGRAPHS BY BOAZ PERLSTEIN (TOP) AND EYAL TAGAR

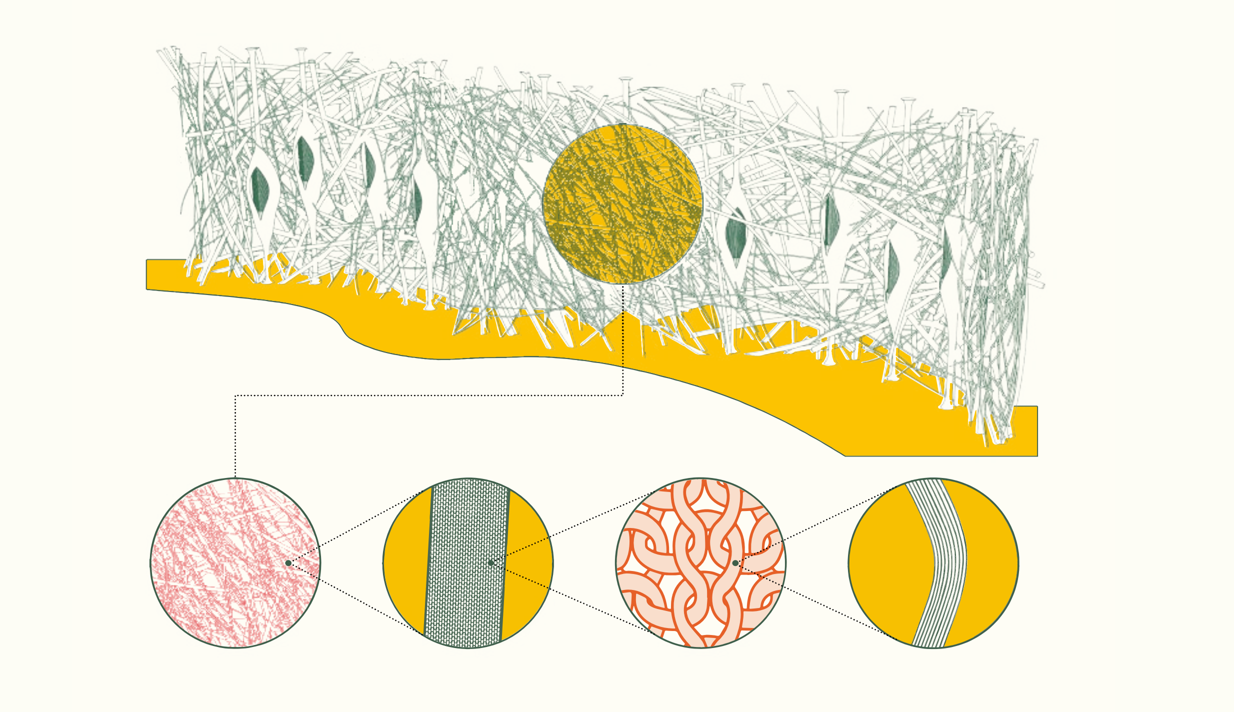


DIAGRAM BY DALBERT B. VILARINO; SOURCE: ARIELLE BLONDER

Zooming in on one of the 1,500 fibreglass tubes used to build LifeObject, a simultaneously flexible yet solid structure.

after scanning the nest, analyzing it by algorithm and determining how many rods were needed per section to make the structure sound, Blonder's team of biologists and architects placed approximately ten per cent of the rods in fixed places and then randomly installed the rest to satisfy the density requirements. It worked.

"My biggest revelation, apart from the material, the structure and the proof of mechanics, was the understanding of the potential of partial control," she says. The bent twigs, with their inherent tension, need friction and contact points, she explains, but they are free to move, which makes the nest simultaneously flexible and solid. You couldn't live in the LifeObject, but the piece proved you could build an adaptive, resilient structure with a bunch of cheap, lightweight and randomly placed elements. LifeObject also proved that collaboration between architects and biologists was not just possible, but worthwhile. Continuing her commitment to teamwork, she's now moved on to physics.

Some people go into architecture for artistic, social or urban planning reasons. Blonder was drawn to numbers and angles, which is why, as a postdoctoral fellow, she feels comfortable in physicist Eran Sharon's lab at the Racah Institute.

Blonder first met Sharon at a design conference on the outskirts of Tel Aviv. His talk about how complex shapes form in natural elements, such as flowers, and the parallels with contemporary design prompted her to update some scientific elements of the Biennale installation when it came to Israel. Later, she met physicist Ido Levin, another Azrieli Graduate Studies Fellow, at an Azrieli Fellows Program event that brought together researchers from a range of disciplines; upon discovering that Levin had also been supervised and mentored by Sharon, she decided fate or coincidence was pushing her toward a formal partnership. Blonder brings architectural knowledge to their collaboration, building on the science of complex, self-shaping materials and applying them to her field, even if it is, at present, purely experimental and futuristic work with FRP, textiles and ceramics in her lab.

Together, they are diving deeper into FM and mould-free fabrication by exploring "frustrated materials," a term used to describe a material in which an incompatibility has been introduced. For example, if you stretch a latex membrane in opposite directions, it becomes "frustrated." Cut a V shape into it and the latex will release energy and the edges of the V will curl up to a relaxed state and create a complex shape. Blonder is examining how these principles, applied to specially designed and layered textiles and ceramics, can create unique and even predictable self-shaping morphologies. Being able to ship flat textiles or morph composites into shape on location has the potential to maximize and streamline the transportation of materials.

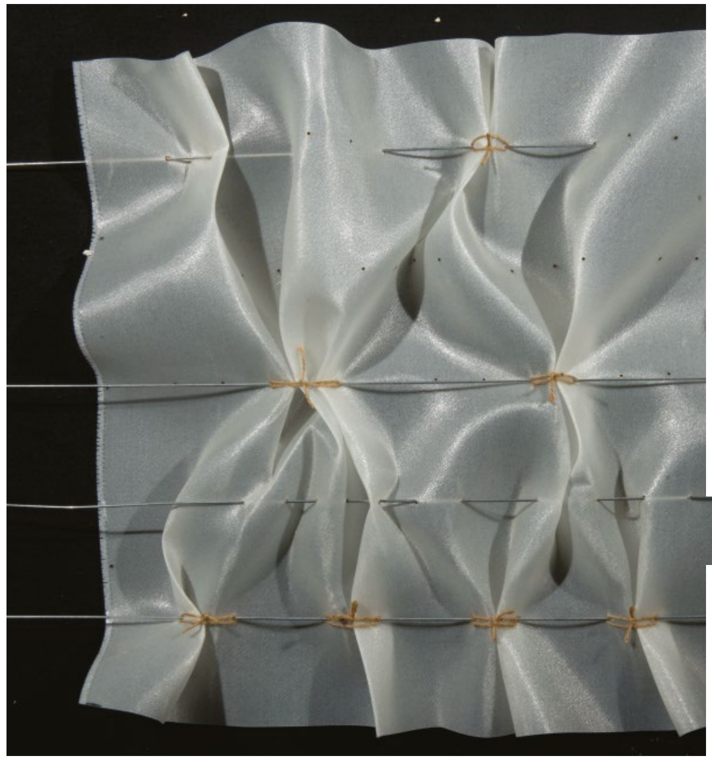
In a research article discussing their initial findings, Blonder and Sharon explained how traditional clay and FRP fabrication are strictly controlled to minimize shrinkage and avoid incompatibilities that could deform the product. "Here, we harness the shrinking phenomenon and its subsequent internal stresses for the generation of complex morphologies," they stated. A single layer of fibre composite, for instance, contracts in the direction perpendicular to fibre orientation. If you layer a composite with opposite fibre orientations, it will form a saddle-like shape when cured. Another experiment involved sandwiching a low-shrinkage ceramic between layers of higher shrinkage ceramic and cutting opposing grooves in the clay on the outer layers, which resulted in twisted ribbons after firing in an oven.

As part of their work, Blonder and Sharon are attempting to design exterior building panels using 3D software and its parametric design platform, incorporating "a simulation engine that allows the determination of the properties of a sheet in order to emulate its mechanical properties." Digital panels are divided into smaller squares and, using surface pixelation, each square is given a particular fibre orientation. If you layer two sheets together with different fibre "maps," the simulator predicts how the squares will contract and thus how the panel will shrink and warp once they do. This simulation can also be done in the inverse — conceiving a particular surface and then determining which fibre orientation map renders it.

Although Blonder's research unfolds in the lab, her motivations are firmly rooted in the real world. By exploring the principles and physics of textiles and materials, she is part of a growing architectural movement pushing to transform how we design and build things. To those opposed to increasing plastic production, Blonder paints a bigger picture. FRP is efficient, resilient, durable and requires less framing and infrastructure because of its light weight — all of which could exponentially reduce costs, energy consumption and maintenance. Research into composites made from hemp and flax embedded in organic resins is also advancing and will likely proliferate as demand for FRP increases. All these things, Blonder says, will help integrate FRP into architecture in the future, both as exterior building covers and perhaps even small, lightweight, free-standing shelters.

Many of Blonder's academic revelations have come through collaborations with colleagues in other fields — cross-pollination that picked up steam during her Azrieli fellowship, which is one of the goals of the program. She hasn't been teaching much lately because of all her research, but if she could pass on one bit of advice to incoming architecture students, it would be to remain open and receptive to other fields of inquiry. "This is the future," she says. "Points of convergence are where science becomes exciting and architecture becomes sensible. You have to use multiple languages and multiple approaches to be able to really suggest something valid. Not for today, for tomorrow." ▲●■

PHOTOGRAPHS BY AMIT OFEK (TOP), COURTESY ARIELLE BLONDER (LEFT) AND SHAY BEN EPHRAIM (RIGHT)



Although Blonder's research unfolds in the lab, her motivations are firmly rooted in the real world. She is part of a growing architectural movement pushing to transform how we design and build things.

A close-up look at some of the tubes from LifeObject (top), a curled multi-layered panel from Blonder's research into fabric materiality (left) and mandala-like patterned tiles of frustrated membranes (right) made by Blonder and physicist Eran Sharon.

By Zac Unger
Photographs by Ariel van Straten

CRYSTAL CLEAR

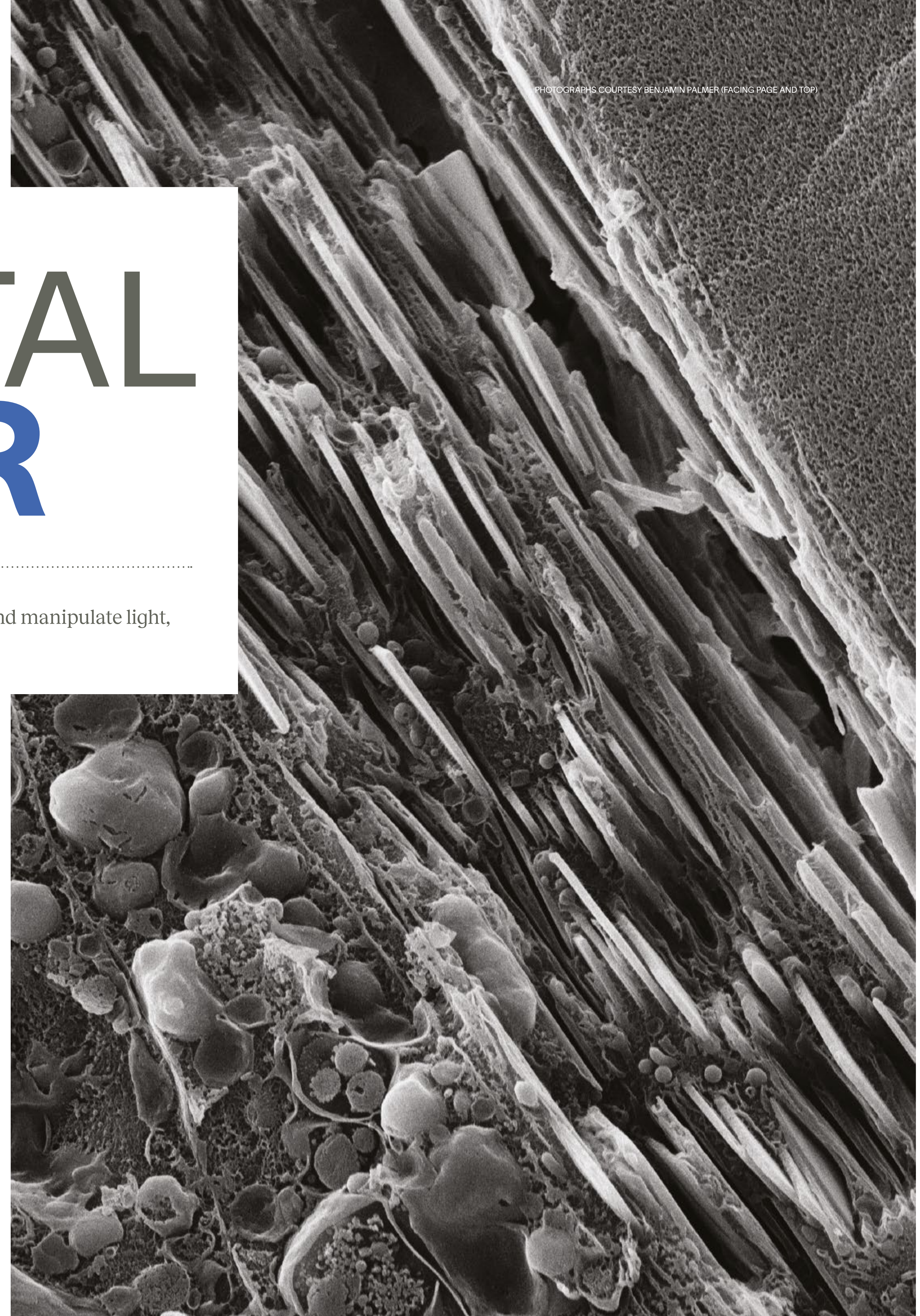
Benjamin Palmer explores how animals make crystals and manipulate light, with an eye toward creating novel organic materials

If you've never thought about how a scallop sees the world, you're probably not alone. Conjure a mental image of a scallop. Does it even have eyes? And even if you can picture where its eyes are, can you imagine a scallop seeing anything other than butter, garlic and the bottom of a sauté pan?

As it turns out, a scallop does have eyes. Up to 200, in fact, along the edge of the soft tissue that lines its shells. This allows the saltwater mollusc to see approximately 250 degrees around itself. Scallops use their eyes to help them escape from starfish and other predators — scallops aren't always permanently attached to rocks like their cousins the clam — and to determine which bits of floating material are food-worthy enough to risk opening their shells for.

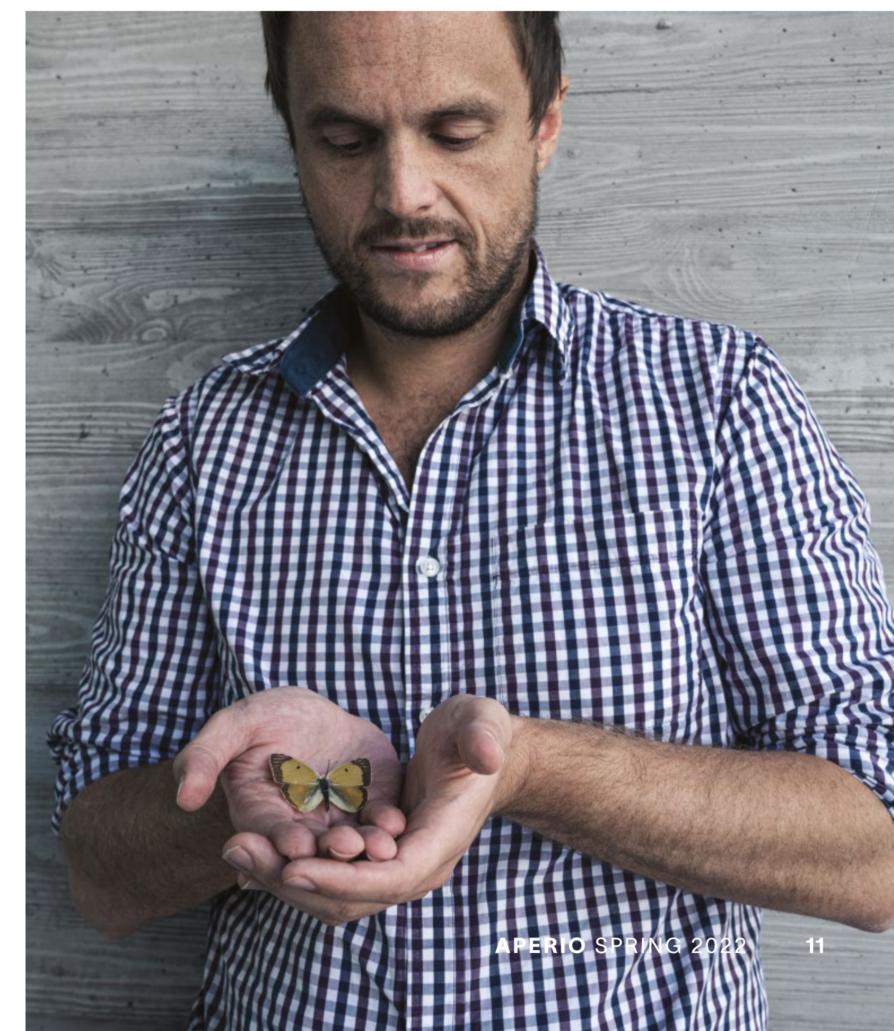
But all that is just a prelude to what's truly impressive about scallop eyes. They're nothing like human eyes. Scallop eyes are actually more akin to complicated telescopes, containing thousands of tiny, crystalline mirrors that allow scallops to see their environment.

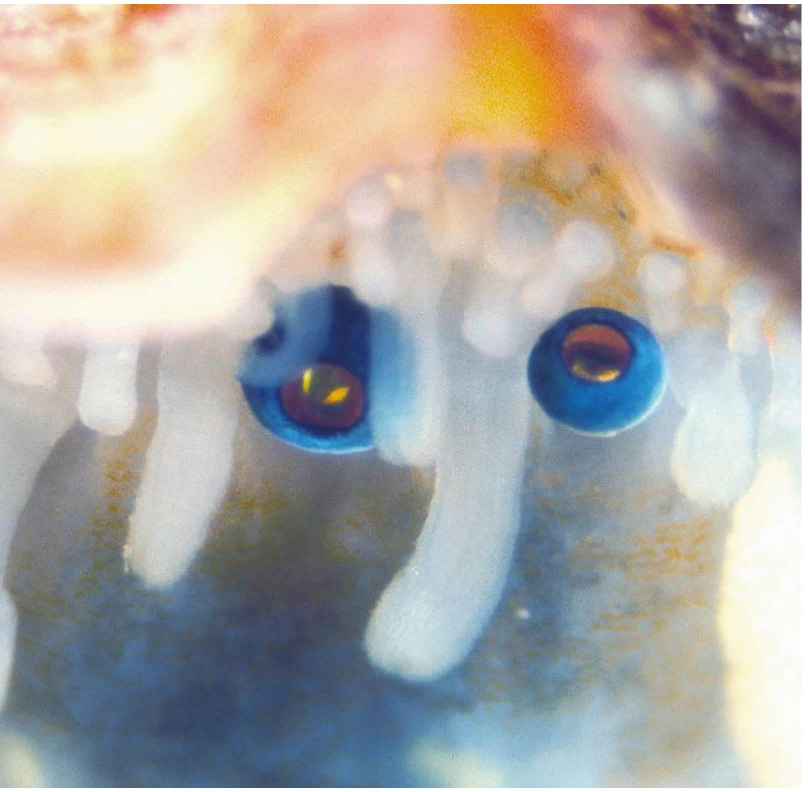
Benjamin Palmer, a chemistry professor at Ben-Gurion University of the Negev and Azrieli Early Career Faculty Fellow, originally thought his academic career would focus on the pure, technical science of



PHOTOGRAPHS COURTESY BENJAMIN PALMER (FACING PAGE AND TOP)

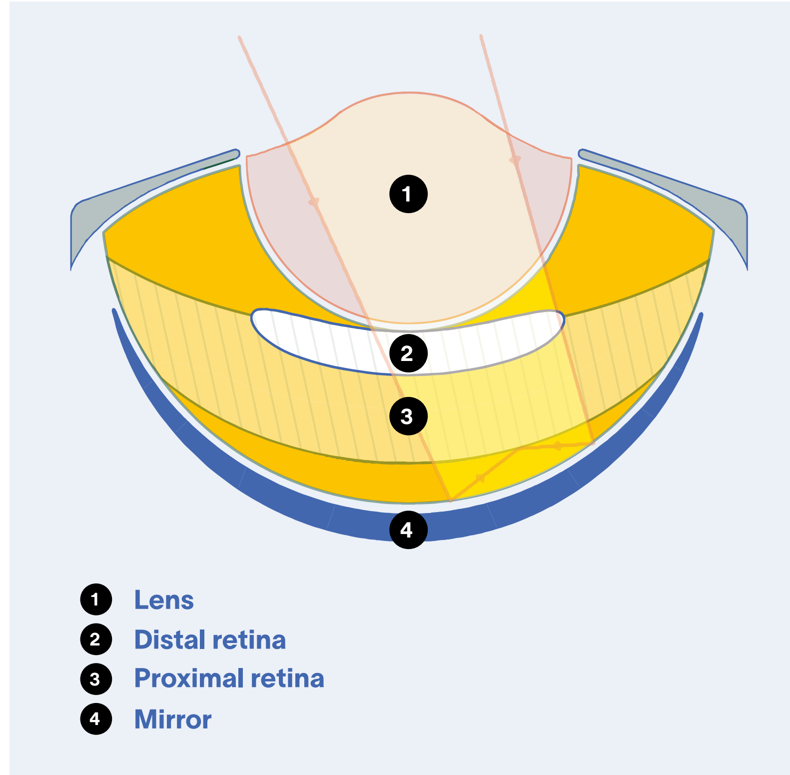
The tiny, crystalline mirrors inside a scallop's eye (facing page), as well as the eyes of shrimps (this image) and butterflies (below), illustrate the diverse range of Benjamin Palmer's research.





The eye of a scallop is an ancient evolutionary masterpiece that prefigured human engineering of telescopes by a few hundred million years.

PHOTOGRAPH COURTESY DAN-E NILSSON, LUND UNIVERSITY



Scallop eyes contain both a distal and proximal retina. The former is focused on detecting moving predators, while the latter receives light reflected from the mirrors at the rear of the eye for enhanced peripheral vision.

DIAGRAM BY DALBERT B. VILARINO; SOURCE: JOURNAL OF EXPERIMENTAL BIOLOGY

Scallop eyes are nothing like human eyes. They're actually more akin to complicated telescopes, containing thousands of tiny, crystalline mirrors that allow scallops to see their environment.

After being drawn to crystallography by its symmetry and aesthetic, Palmer was struck by the ability of animals to manipulate light more intricately than people. "I should go and learn what animals are doing," he thought, "because they clearly do it much better."

crystallography, or the arrangement of atoms in crystalline solids, a field that can help us understand the atomic structure of almost anything. That goal lasted until he encountered scallop eyes, an ancient evolutionary masterpiece that prefigured human engineering of telescopes by a few hundred million years.

"For whatever reason, I was always interested in crystals," says Palmer, who joined Ben-Gurion in 2019 after a postdoctoral fellowship at the Weizmann Institute of Science. "I guess the symmetry appealed to me. There was something very aesthetic about it. Then I read a couple of articles from two professors at Weizmann on animal crystallization and compared what I was doing in the lab with what these animals were doing." He remembers thinking, "Well, there's no point in me carrying on doing my chemistry stuff. I should go and learn what animals are doing because they clearly do it much better." After "blowing through" the articles and sending his CV to the authors, Lia Addadi and Steve Weiner, Palmer flew to Israel from his native Wales and decided immediately that he wanted to stay.

Most animal eyes work by allowing light to pass through a lens at the front of the eye. That light is then projected and focused onto the retina, which lies at the rear of the eye, creating an image that is collected by tiny nerves and then sent to the brain for interpretation. But scallop eyes work quite differently. First of all, the light passes through not one but two retinas, distal and proximal. And, crucially, the retinas are not located at the back of the eye as with humans and other animals, but float in the middle. Light passes all the way through the retinas until it encounters mirrors at the rear of the eye. It's the job of the mirrors, working in a perfectly coordinated array, to bounce the light up to the retinas, where it is finally focused for use. The unusual shape of the mirrors reflects incoming light to different points on the retinas, allowing them to perform two separate functions. The upper retina is specialized for imaging well-focused on-axis light for detecting moving predators, while the lower retina is specialized for imaging off-axis light and providing relatively high-quality peripheral vision.

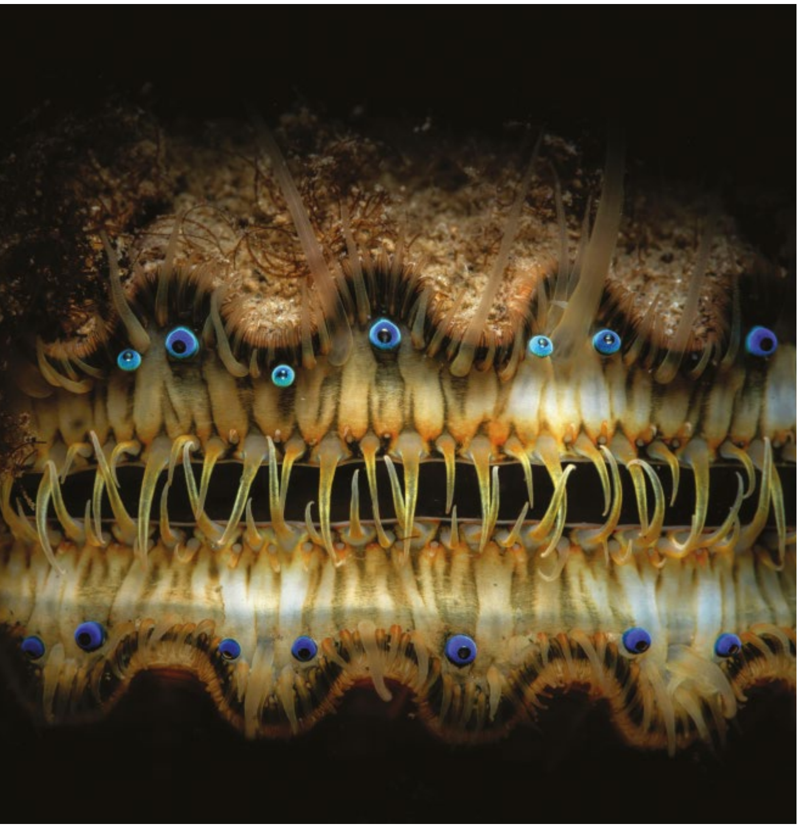
And if all that isn't remarkable enough — remember, we're talking about scallops here, nobody's idea of the most sophisticated animal on Earth — the structure of the mirrors, made of layered crystals, is another marvel of evolution. "The general theme of our lab is to figure out how animals use crystalline materials to manipulate light," says Palmer. Broadly speaking, this area of study is a subset of the field of biomineralization, or the processes animals use to make hard structures like bones, shells and teeth. The big question in that field is how do organisms take ions that they find naturally — in sea water, mother's milk and so forth — and concentrate them into a functional material like bone? "But there is another class of materials that form in animals," Palmer explains, "and these crystalline materials are made by the cells themselves." Instead of being formed using ions found in the surrounding environment, these organic crystals are synthesized internally by specialized cells. A particularly useful building block employed by scallops is guanine, one of the four essential bases that make up the structure of DNA.

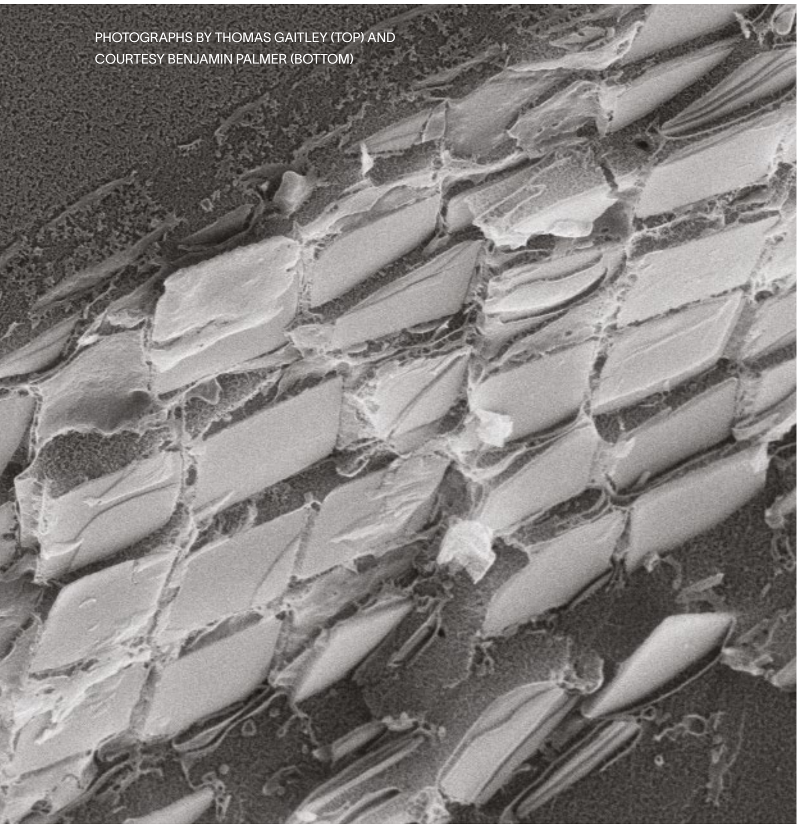
"These guanine crystals are very beautiful, and they also happen to be extremely good at reflecting light," says Palmer. One of the key factors and limitations in optics is the refractive index, a measurement of how quickly light travels through a substance. To see clearly, an animal needs to make a material with a higher refractive index than the medium that surrounds it. "The refractive index of water is 1.3," Palmer says, "and the refractive index of air is one. But these molecular crystals have some of the highest refractive indices of any biological materials." This makes the mirror crystals perfect for the low-light conditions that scallops live in. This critical property, combined with guanine's easy cellular availability, has allowed the scallop to evolve the concave mirrored eye structure that is best suited not only for the murkiness of seawater, but also for the specific spectra of light that penetrate below the surface.

When viewed under a scanning electron microscope, these crystals appear as perfect rows of squares, a tiled mosaic structure that wouldn't look out of place on the floor of the grand entranceway to a luxurious mansion. But what the scallop has created is even more complicated than that — the concave mirror has a structure that isn't flat but is actually three-dimensional. The full structure consists of several dozen layers of crystals, separated by cytoplasm. These layers are perfectly aligned so that each individual tile of crystal directly underlies the one above it, creating a vertical stack. This closely coordinated tiling minimizes defects, which could scatter the light and result in less effective vision.

Palmer gets visibly excited when talking about the wonder of a system this beautiful and well-organized. "If chemists knew how to precisely control crystal form and morphology, it would be a dream for material science," he says, noting that the shape and properties of crystals affect what a structure made with these materials could accomplish. "Animals somehow do this in these specialized cells, and we don't even know the underlying rules behind the formation yet. So that's half of our research, trying to uncover the rules and the crystallization tricks that the animals employ to control crystal morphology."

The lab work itself is no easy task; scallop eyes are incredibly tiny, about one millimetre each, after all. "We have a three-pronged approach to the imaging, basically chemical, physical and biological methods," Palmer says. "But in truth, we're throwing the kitchen sink at it." One critical technique is cryogenic scanning electron microscopy, which utilizes a freezing mechanism to trap the cells





PHOTOGRAPHS BY THOMAS GAITLEY (TOP) AND COURTESY BENJAMIN PALMER (BOTTOM)

The eyes of a scallop (top) are nothing like human eyes. They're more akin to complicated telescopes, with perfectly coordinated arrays of mirrors (bottom).

of the eye in a close-to-life state so that they can be studied and manipulated before they disintegrate as they normally do at room temperature. Palmer and his colleagues also use synchrotron particle accelerators and then "interrogate the structural properties with X-rays." An exciting new avenue of study involves watching how animals create these crystals during different stages of embryonic development, capturing different morphological moments as they occur.

Although guanine crystals are found in seven different animal phyla, Palmer is quick to note that guanine isn't the only biomineral capable of forming complex crystalline structures. "This is a very new field," he says, "and it's just bubbling right now. Guanine has been known and studied for years, but I've been asking 'What else is there?' Because nobody thought to look! In the last couple of years we've found a new class of crystals which have similar structures, but which are based on a different family of crystals."

Additionally, it isn't just scallops that have evolved this remarkable strategy for seeing the world around them. "We have many animal models that we work on," says Palmer. "A lot of them are aquatic, like scallops, shrimp and fish. But we also work on lizards, snakes, butterflies. Maybe ten or so animals right now. So many that I've almost lost track."

Palmer's passions primarily lean toward understanding the basic science of how such a system functions. "If my students go to an electron microscope I always say, 'Call me if you find anything exciting.' And then I run down to the microscope because you never tire of seeing a crystal in an animal cell. Because often it just doesn't make sense, this perfectly geometrical thing that you think of as synthetic and manufactured, yet it finds itself inside a biological cell."

Although the pure science of discovery provides Palmer all the thrills he needs, there is great potential for practical applications to emerge from his research. "This is almost like sci-fi," he says. Knowing which genes are responsible for the size and shape of the crystals allows us to potentially manipulate the process and build new crystals. "If we understand the rules these organisms use to make these materials," Palmer says, "we can apply the principles that animals have taught us to make new optical or electrical materials in a more sophisticated, controlled way."

Palmer's long-term vision is to understand how organisms control crystallization processes and uncover new bio-inspired crystallization techniques for the synthesis of novel organic material, and his enthusiasm for this field is infectious. "The next frontiers are finding out what crystals are out there and then understanding the underlying mechanisms," he says. "But it doesn't just take me; it will take biologists and chemists and physicists to collaborate on everything." The humble scallop has perfected this system over hundreds of millions of years of evolution, but our understanding of how it all works is in its infancy. "Honestly," Palmer says, "I don't understand why everyone in the world isn't working in this area. Even if I didn't get paid, I'd still turn up at the lab every morning." ▲●■

In Israel, Palmer has easy access to places such as the Negev Desert, a prime location for collecting samples to bring back to the lab.

The Specimens In Your Own Backyard

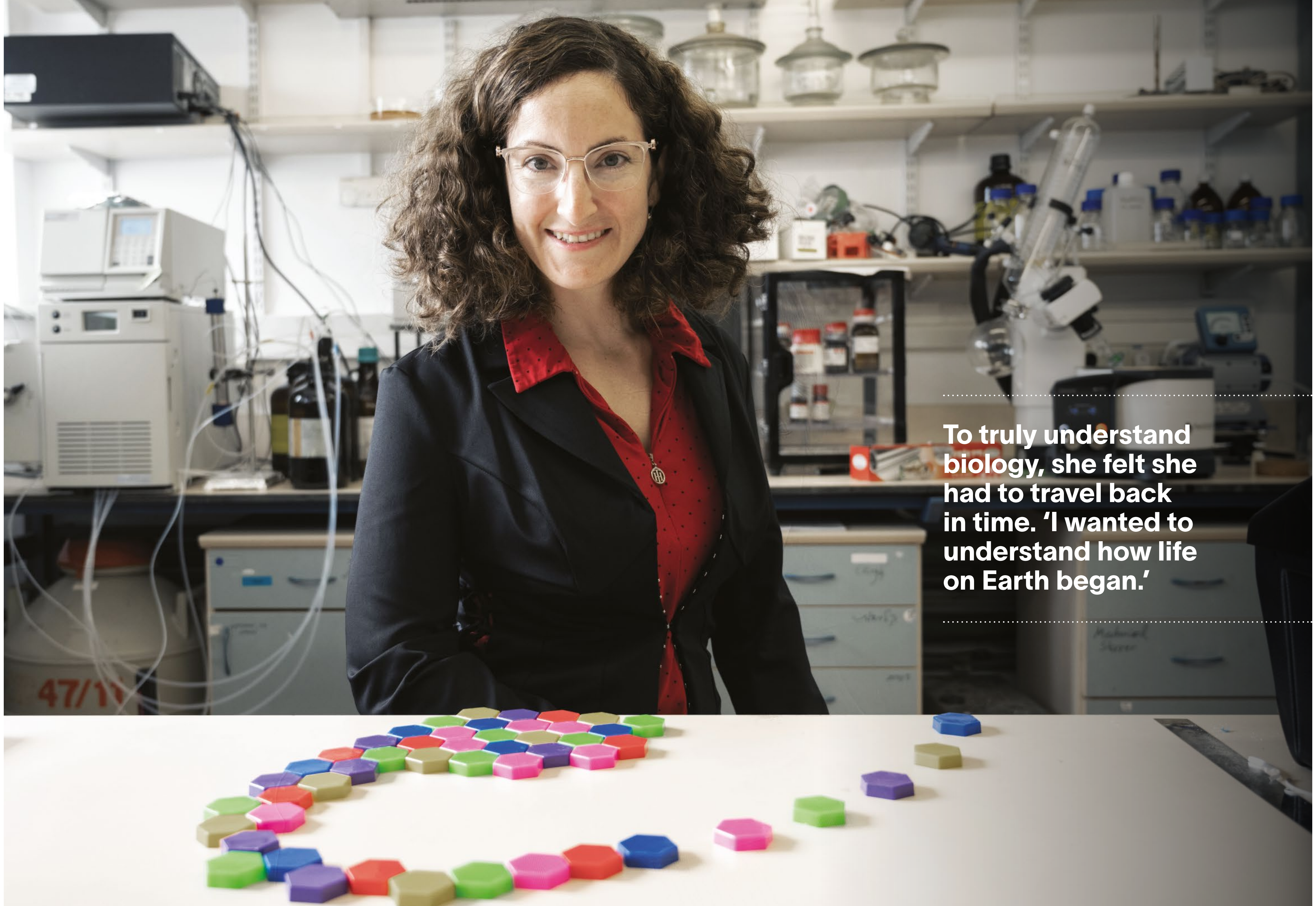
One of the advantages of Benjamin Palmer's work with scallops — and shrimp, lizards, butterflies and more — is that his job requires him to be out in the field finding the animals he needs.

Normally Palmer would be out with his colleagues and students "disappearing into the desert," he says. "We're off-road trying to get spiders, we're floating in the Jordan with nets, we've got head torches in the middle of the night, searching for shrimp with shiny eyes." Unfortunately, he is currently stuck in his office at Ben-Gurion University putting the finishing touches on multiple papers, and he has to settle for staring at the Negev through the window instead.

Because this is such a new field, opportunity abounds. "Serendipity and opening your mind as much as possible has started half of these projects," Palmer says. His signature project on scallops began with a chance encounter in Wales with a friend of his father's, a scalloper who dives for scallops at night and described scallop eyes as thousands of undersea "diamonds" reflecting back in his torchlight. "I asked him if maybe he could grab one for us," Palmer recalls. "He said, 'Sure, sure.' I took it back to Israel and within a week we had it under the microscope." Another of Palmer's projects started from overhearing a Negev ranger talk about a lizard that can change its pale colour. Sure enough, when Palmer and his students studied it in the lab, they found precisely the kind of crystal morphology they'd been working on. "Things like this happen all the time," Palmer says. "Israel facilitates this stuff because people are so inquisitive and so curious that there's no limit to what you can end up doing."

Palmer adds that, before he moved to Israel, he didn't expect the country's geography to play such a crucial role in his research. "We have a huge advantage in that we can go to Eilat or the Negev any time of year to collect specimens, whereas other people in Britain or America might have to make one special trip to Australia a year. But we have these animals that do funky things with crystals on our doorstep pretty much all the time."

'Israel facilitates serendipitous opportunities because people are so inquisitive and curious that there's no limit to what you can end up doing.'



> To truly understand biology, she felt she had to travel back in time. 'I wanted to understand how life on Earth began.'

BUILDING **BLOCKS**

From the origins of life to a new approach to pharmaceuticals, Moran Frenkel-Pinter explores the processes and potential of chemical evolution

By Brian Owens
Photographs by Ariel van Straten

For as long as she can remember, Moran Frenkel-Pinter has attempted to piece together puzzles both small and large, such as how basic things function and how the world works. In a sixth-grade science project, she was determined to engineer purple strawberries and cows that produce chocolate milk. Three years later, when a friend's mother spoke to her class about genetic engineering, she realized for the first time that nothing is set in stone, that humans can chart their own biological path.

Frenkel-Pinter's restless scientific curiosity continued throughout her studies, leading from a BSc in biotechnology to a PhD exploring some of the chemical mechanisms underlying Alzheimer's disease. Afterward, to truly understand biology, she felt she had to travel back in time. In her postdoctoral research, Frenkel-Pinter probed how life on Earth first arose. Now, as a chemistry professor at the Hebrew University of Jerusalem and Azrieli Early Career Faculty Fellow, she is combining these biological and chemical strands into one by setting up a laboratory to create new chemicals that are economical, sustainable and conducive to drug development.

Frenkel-Pinter's PhD at Tel Aviv University focused on how the proteins related to neurodegeneration fold, and how this affects the progression of Alzheimer's disease. This research could eventually lead to the identification of biomarkers in the blood to help track the development of Alzheimer's in patients and to effective therapeutics. After completing her PhD, however, Frenkel-Pinter turned her attention to a much deeper question. "I wanted to understand how life on Earth began," she says. "Why did twenty particular amino acids become the building blocks of all proteins in biology? Could there have been other forms of life?"

In 2016, after winning a NASA postdoctoral fellowship, Frenkel-Pinter went to the Georgia Institute of Technology's Center for Chemical Evolution in Atlanta. As a team leader, she researched how primordial molecules formed and interacted on pre-biotic Earth, before there were any enzymes to catalyze reactions. "Before biology there were just molecules and chemistry," she says, "and there were forces that led to the selection of some molecules over others from a very messy soup."

Untangling the mysteries of chemical evolution is much more challenging than understanding biological evolution, according to Frenkel-Pinter. "With biological evolution we can look at how species evolved over time by sequencing their DNA and looking at fossils," she says. "But I'm asking what happened *before* life started? How did we get from that messy soup to the structure and function of life as we know it?"

Addressing those questions involved thinking about whether alternative forms of life could have arisen instead. Is there something special about the subclass of amino acids that founded biology? Could other, similar molecules have given rise to a different form of life had things gone their way? Frenkel-Pinter and her colleagues discovered that a subset of the twenty amino acids found in today's proteins are able to form peptides more readily in the absence of enzymes than non-proteinogenic amino acids. "Every molecule has an intrinsic reactivity to form larger molecules, and the amino acids we have in today's proteins do that better," she says. "The best molecules won."

As these molecules grew more complex, other selection forces came into play based on the larger molecules' tendency to form stable three-dimensional structures. This stability helped the molecules last longer and increased their tendency to undergo chemical reactions with other molecules, which could then produce new compounds with new functions. These insights offered a fresh perspective. "For the first time," says Frenkel-Pinter, "we were able to understand the selection forces that shaped protein evolution from a chemical point of view."

Next, she looked at whether interactions between different kinds of molecules were important for chemical evolution. There has been long-standing debate within the origin-of-life field about which molecules came first. Was it only RNA? Only peptides? Or a mixture of both? It's a bit of a chicken-or-egg problem because RNA is needed to make proteins, but proteins are also needed to make RNA. What Frenkel-Pinter found in her experiments was that because primordial RNA and primordial peptides interact to stabilize each other, the chicken and egg could have appeared alongside one another and worked in tandem to improve each other. "It was never a dilemma, because they evolved together," she says. "It was co-evolution, just like in biology."

This does not mean that Frenkel-Pinter and her colleagues have fully solved all of these origins-of-life mysteries. The question of which molecules took the lead — just one kind, such as RNA or peptides, or a more chaotic system — remains open. "But if we understand the process," she says, "we can learn a lot."

Aiming to merge her studies in biotechnology with the chemical evolution research she explored at Georgia Tech, Frenkel-Pinter began her current position as an Azrieli Fellow at the Hebrew University's Institute of Chemistry in July 2021. Once her new lab is ready, her first experiment will be screening lab-generated polymers for potential nucleic acid–binding properties. Those polymers could be useful in applications like RNA vaccines, such as the ones currently used to address COVID-19, by providing chemical scaffolds that help to stabilize the RNA in the body long enough for the vaccine to do its work.

This will be just the first step. Based on the techniques she used in her postdoctoral research, Frenkel-Pinter aims to develop a novel, high-throughput synthesis platform to chemically evolve libraries of small nucleic acid–binding polymers to cultivate the chemicals involved in the origin of life. Once the platform is up and running, it could have many other applications, such as designing molecules to inhibit the aggregation of proteins associated with degenerative diseases like Alzheimer's or to act as scaffolds for regenerative medicine.

Using chemical evolution platforms to design novel molecules has several advantages over traditional combinatorial chemistry and engineering approaches, says Frenkel-Pinter. Typically, if a researcher wants to look for molecules that bind nucleic acids, they will start with a library of possibilities and choose the best option. They will then tweak and play with the molecule, swapping out a methyl group here, or a hydroxyl group there, to try and improve it. But this is inevitably a slow, expensive and wasteful process as engineers methodically work their way through one iteration after another.

Chemical evolution, in contrast, can be cheaper and greener. Because it uses processes that laid the basis for biology, the molecules that are generated will degrade in water without leaving any toxic by-products. The process itself is also much faster and can lead to better results than human designers can produce. By selecting promising starting molecules and controlling the environmental conditions to push them toward the desired end point, researchers can allow the molecules to find their own path to the optimal outcome through open-ended evolution and intrinsic chemical selection.

Frenkel-Pinter sees almost unlimited potential for this system, with the ability to keep evolving new and better chemical products indefinitely. "When we use the power of evolution to create molecules with specific functions," she says, "the sky's the limit." ▲●■

As an Azrieli Early Career Faculty Fellow, she is combining biological and chemical research strands into one by setting up a laboratory to create new chemicals that are economical, sustainable and conducive to drug development.

In her new lab, Moran Frenkel-Pinter will be cultivating polymers that could be useful in applications such as RNA vaccines and designing molecules to address the aggregation of proteins associated with degenerative diseases like Alzheimer's.

One of seven massive mirrors being built for the Giant Magellan Telescope, which is under construction in Chile and will provide an unprecedented resolution ten times greater than that of the Hubble Space Telescope.

PHOTOGRAPH COURTESY GMTO CORPORATION

EYES IN THE SKY

By Dan Rubinstein

ASTROPHYSICIST SAGI BEN-AMI BUILDS INSTRUMENTS TO PROBE THE ORIGINS OF THE UNIVERSE AND SEARCH FOR DISTANT LIFE

Growing up north of Tel Aviv, Sagi Ben-Ami spent as much time as possible in the fields and hills outside town, bringing a pair of binoculars and a notebook and scanning the sky for birds. He meticulously documented all the eagles, storks and vultures he saw — Israel is a stopping point on an important migratory flyway — and read all the birding and popular science books he could get his hands on. Today, Ben-Ami is still looking for life in the skies, only now as an astrophysicist who helps satellites and some of the world's most powerful telescopes search for clues about the origins of the universe and exoplanets with atmospheres that contain oxygen.

Ben-Ami, an Azrieli Early Career Faculty Fellow, is the head of the instrumentation group in the Department of Particle Physics and Astrophysics at the Weizmann Institute of Science. He moved back to Israel in spring 2020 after six years at the Center for Astrophysics | Harvard & Smithsonian, where he did a postdoctoral fellowship and then worked as an instrument scientist for five years. During his time in the United States, Ben-Ami continued to develop the type of technology that he began tinkering with when he was a PhD student at Weizmann.

Despite his omnivorous interest in all facets of science, Ben-Ami has become a specialist in the design and construction of spectrographs and fibre optic systems — instruments and interfaces that allow satellites and telescopes to capture and analyze light from distant stars. He was drawn to this area from high-energy physics because, unlike particle accelerators such as the Large Hadron Collider at CERN in Geneva, Switzerland (which he contributed to while working on his master's degree at the Technion – Israel Institute of Technology), astrophysics experiments tend to involve smaller teams and shorter timeframes. The $10 billion USD James Webb Space Telescope notwithstanding, astrophysics projects usually involve just a few dozen people, instead of several thousand collaborators chipping away for a couple decades, and projects can become operational within a few years, meaning that the impact one can have as an individual is more direct.

"There's something very physical about this work that I love," says Ben-Ami, whose PhD studies helped lead to the completion of a spectrograph called the SED Machine. It began collecting data at California's Palomar Observatory in 2016; since then, it has classified more supernovae — the source of virtually every element in the universe — than any other instrument. This has allowed researchers to sample rare celestial events such as superluminous supernovae (stellar explosions ten times more luminous than standard supernovae) and learn about the origin of heavy elements. Another spectrograph interface that Ben-Ami helped design, TRES, allows astrophysicists to distinguish between stars in binary systems and actual exoplanets. "You build a device for a telescope, it works, you get data," he says, noting that he is an "enabler" who builds instruments that others use to make illuminating discoveries. "There are some grey areas and approximations, of course, but we're studying things that are not based on what we think should happen. We're outside observers, trying to understand processes governed by laws we do not fully understand."

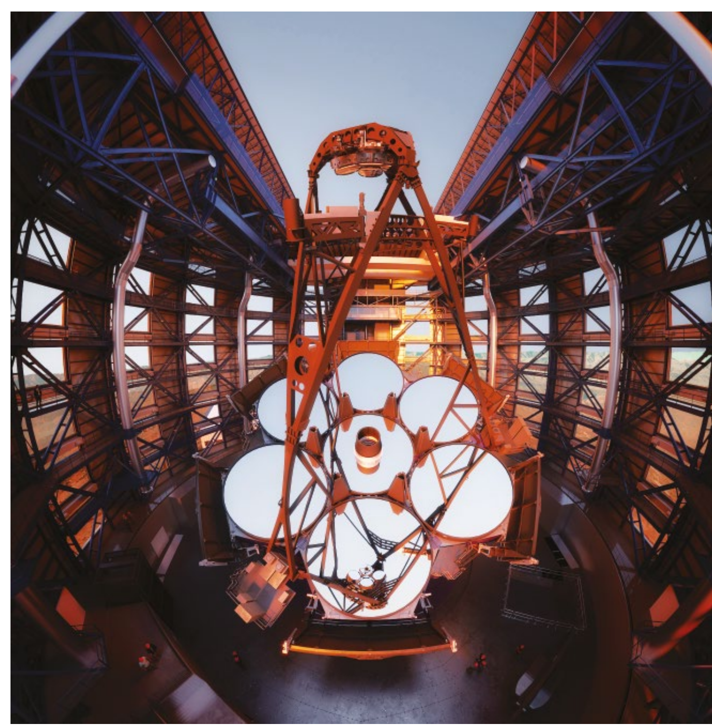
Ben-Ami is busy these days with a trio of major projects: designing a scientific payload for ULTRASAT, an Israeli-led satellite that's expected to launch within the next three years; collaborating with colleague Eran Ofek on the Weizmann Astrophysical Observatory, a network of telescopes that's being built in the Negev Desert; and building a spectrograph for the Giant Magellan Telescope (GMT) in Chile. The GMT, currently under construction at the mountaintop Las Campanas Observatory in the Atacama Desert, should be ready by the end of the decade. Its seven large mirrors are set in a hexagonal pattern and act in concert, forming a 24.5-metre diameter optical surface, and it will be able to collect 368 square metres of light — an unprecedented resolution ten times greater than that of the Hubble Space Telescope and four times greater than that of the recently launched James Webb Space Telescope.

Ben-Ami and principal investigator Andrew Szentgyorgyi at the Center for Astrophysics | Harvard & Smithsonian developed the GMT-Consortium Large Earth Finder (G-CLEF) spectrograph to be able to detect whether a star has an orbiting planet based on tiny movements caused by the gravitational pull of the planet. This will allow astronomers to determine the mass of Earth-sized planets, including some in a habitable zone that is far enough but not too far from their stars, where water could exist in liquid form on the planet's surface. When it is operational, G-CLEF will also be able to detect molecules in the atmospheres of these exoplanets, including oxygen, a biosignature that indicates the possibility of past or present life. There are already several strong candidates. Considering that scientists confirmed the existence of Earth-sized exoplanets for the first time about twenty-five years ago, this represents a tremendous leap forward.

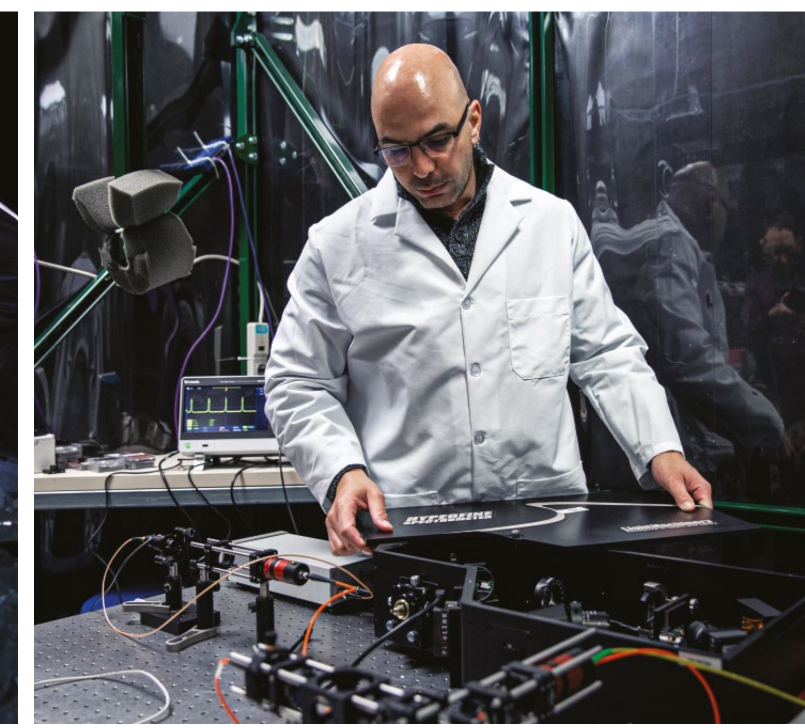
Spectrographs work by breaking light into a spectrum of its constituent colours or wavelengths. The G-CLEF spectrograph, which will be connected to an already active pair of 6.5-metre Magellan telescopes in 2024 until the GMT is finished, will use a mosaic of dispersion grating to separate wavelengths of light based on the angle at which they emerge from the grating and record these wavelengths in a detector for analysis. When elements interact with light, unique information about those elements remains on the light. Every element leaves a specific fingerprint, allowing scientists to infer what the light touched on its journey toward Earth.

With this ability, and because the GMT will be able to observe faint targets, Ben-Ami believes that it could reveal whether any of these exoplanets have atmospheric oxygen. "One of the things we've learned from studying our own planet is that oxygen is the best sign of life," he says. "Given the fact that our planet is the only example of life that we have, it makes a lot of sense to look for oxygen."

Nearly twenty tons of glass (below) are put into a mould for each of the Giant Magellan Telescope's primary mirrors (left). The instrument will give astrophysicists such as Ben-Ami (below right) new insights into the origins of the universe.

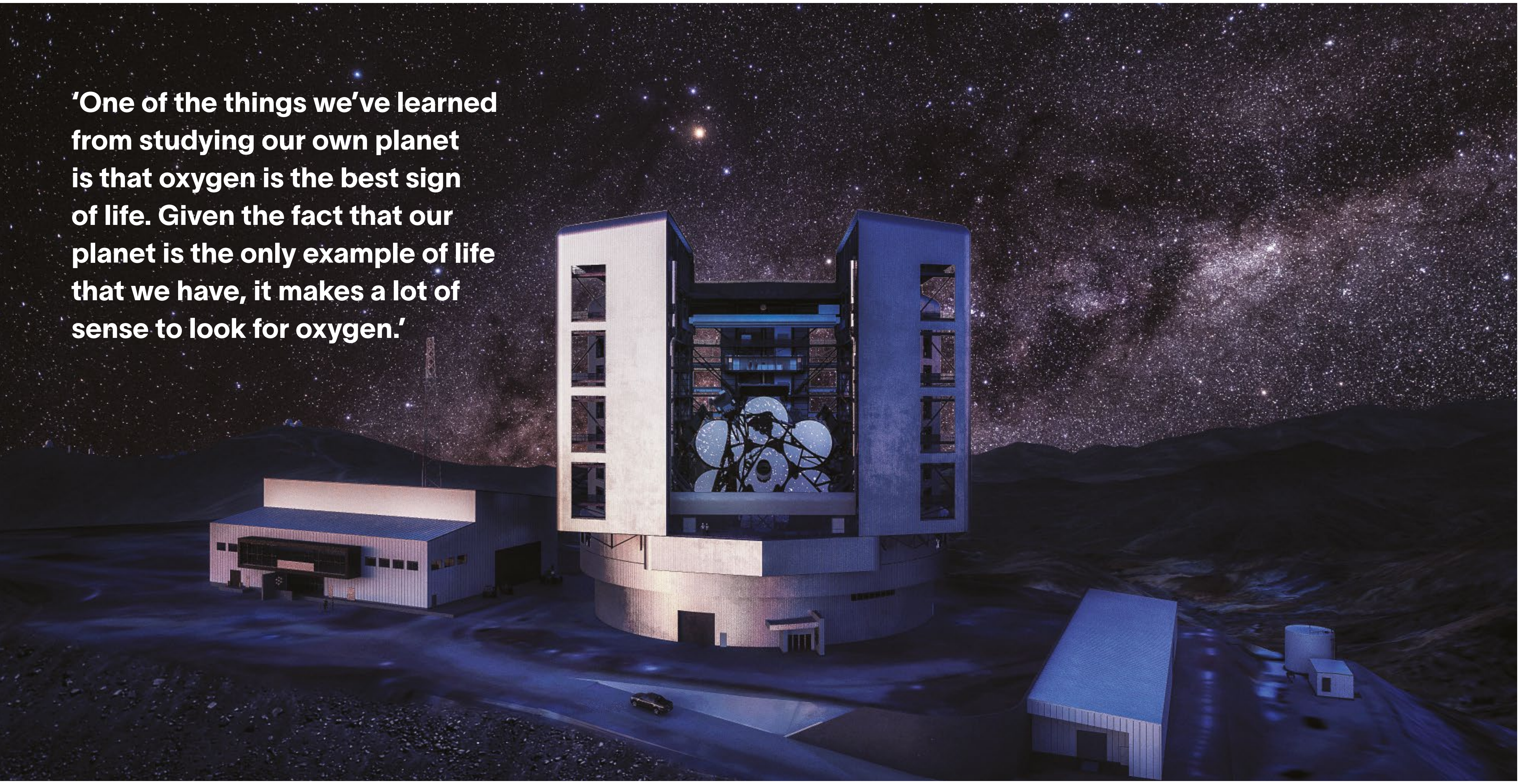


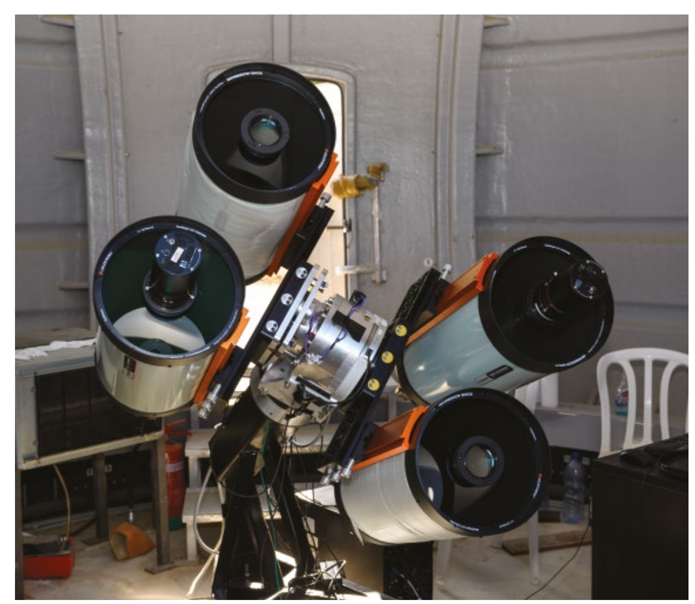
Sagi Ben-Ami is working on a spectrograph for the Giant Magellan Telescope (rendering above) that will help search for oxygen in the atmospheres of distant exoplanets, a biosignature that could indicate the possibility of life.



IMAGES (FACING AND ABOVE) COURTESY GMTO CORPORATION; PHOTOGRAPH (RIGHT): CENTER FOR ASTROPHYSICS | HARVARD & SMITHSONIAN

'We're outside observers, trying to understand processes governed by laws we do not fully understand.'





Ben-Ami and colleagues Juliana Garcia-Mejia and Surangkhana Rukdee (middle, left to right) at work at the Center for Astrophysics | Harvard & Smithsonian before he moved to the Weizmann Institute of Science. In addition to the Giant Magellan Telescope (top and left), Ben-Ami is also contributing to the Weizmann Astrophysical Observatory, which has set up some of its telescopes on the university's campus (right) while the full network is being built in the Negev Desert.

IMAGES (TOP AND ABOVE LEFT) COURTESY GMTO CORPORATION; (MIDDLE) CENTER FOR ASTROPHYSICS | HARVARD & SMITHSONIAN; (RIGHT) WEIZMANN INSTITUTE OF SCIENCE

For the G-CLEF spectrograph to achieve the precision needed to measure the velocity of a distant star within ten centimetres per second, the spectrograph will be housed in a vacuum vessel about twenty metres away from the telescope to avoid any vibrations. Ben-Ami is designing a novel fibre optic system to connect the two, work that's predominantly taking place in his fibre lab at Weizmann, where he can determine the transmission properties of different types of fibre. He is using a unique twenty-five-micron fibre (a micron is one millionth of a metre) that will allow spectra to be captured by the detector in real time at an extremely high resolution.

"At the end of the day, one of the things that I think is really astounding is that it'll be a 24.5-metre telescope feeding a 25-micron fibre," says Ben-Ami. "This is a very difficult task that will require a closed loop of alignment across all the different components in our system. We're now testing different optical fibre geometries to make sure that the mating of the telescope to the instrument actually works.

"One of the biggest advantages of working in the academy is that you never need to do the same thing twice," he continues. "I don't want to build the same instrument I built yesterday. I want to work on something new. In the academy, unlike a company that needs to manufacture a product, we manufacture one-offs. We do one product and when it's finished, we move on to something new."

This fibre optic system can be adapted for use in other projects, such as linking a network of seventeen telescopes at the Weizmann Astrophysical Observatory, which is projected to be running within the coming year. This modular network is a powerful, cost-effective way for researchers to gain a large amount of spectroscopic data from various sources and phenomena, and decide which of these targets should be further observed with larger telescopes such as the GMT.

Meanwhile, for the ULTRASAT project, Ben-Ami is designing an ultraviolet (UV) telescope that will be able to take 200-square-degree images of UV light, which doesn't penetrate Earth's ozone layer. Ultraviolet light is important in astrophysics for several reasons. The first emissions from a supernova emerge in the UV range, Ben-Ami explains, so if you want to learn about the radius and other characteristics of a star that has exploded, you can't wait for the visible light. ULTRASAT will be able to detect and measure the emissions from explosions minutes after they occur, much faster than today's telescopic systems. "It's very difficult to know what a glass looked like after you throw it onto the floor and it breaks into a thousand pieces," says Ben-Ami. "If I can observe it at the moment that it hits, it has more of the shape of a glass. This is why we want UV."

Measuring the UV emissions from various stars is another way to look for environments that could support life. Ultraviolet light was also an important source of energy during Earth's early stages. Too much UV radiation would have broken biomolecules apart, but high enough levels were necessary to generate the chemical reactions that led to prebiotic molecules and the origins of life. "Characterizing UV radiation from stars will tell us which ones are more likely to host planets that can harbour life," says Ben-Ami.

"I don't think we're unique, that Earth is the only place with life," he adds. "I don't think I'll ever see little green men coming to visit us and I don't know if we'll find anything in my lifetime. But I won't be disappointed, because the journey is at least as much fun as the discovery itself. And if this is your approach, then you'll do good science because you're allowing yourself to be open to new things." ▲●■

Nobel
Israel ranks 1st in the world
for Nobel Prizes per capita in chemistry and economics

6 Israelis
have won the Nobel Prize in Chemistry since 2004

Elite Scholars
Azrieli Fellows are recognized internationally for original research

European Research Council Grants

Azrieli Fellows 1 in 3
One-third of Azrieli Early Career Faculty Fellows have won ERC grants

Top 100 Universities in the World
Three of Israel's 10 universities rank in the top 100 in the Academic Ranking of World Universities, or Shanghai Ranking, for 2021.

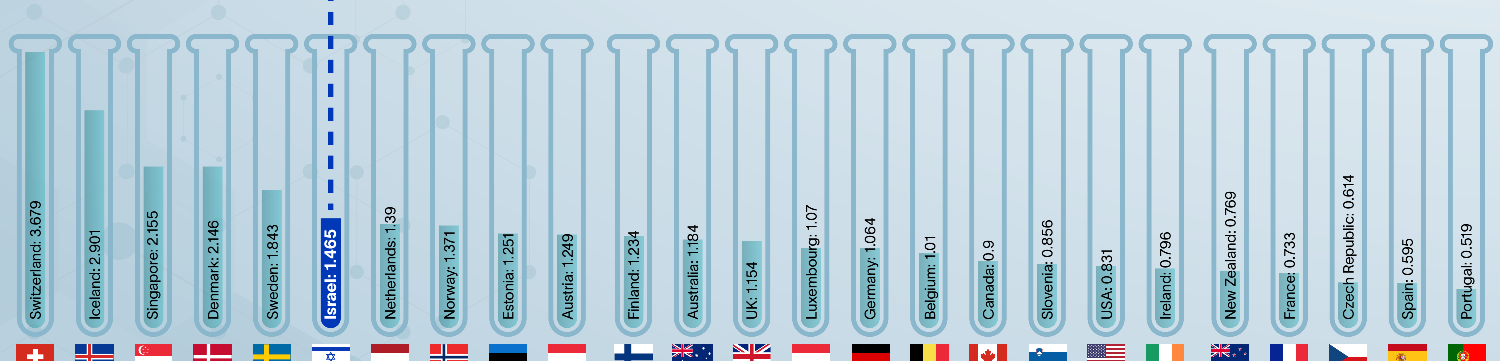
- Weizmann Institute of Science
- Hebrew University of Jerusalem
- Technion – Israel Institute of Technology

Azrieli Fellows Areas of Study
Fellows conduct research in multiple and diverse fields

- Life Sciences
- Computational Biology
- Bioengineering
- Neuroscience
- Chemistry
- Computer Science
- Physics
- Architecture
- Education
- Political Science
- Psychology

Top 6 in the World
According to the Nature Index, **Israel ranked 6th** among all countries in the world for publication of scientific articles in high-impact journals per capita from September 2020 to August 2021.*

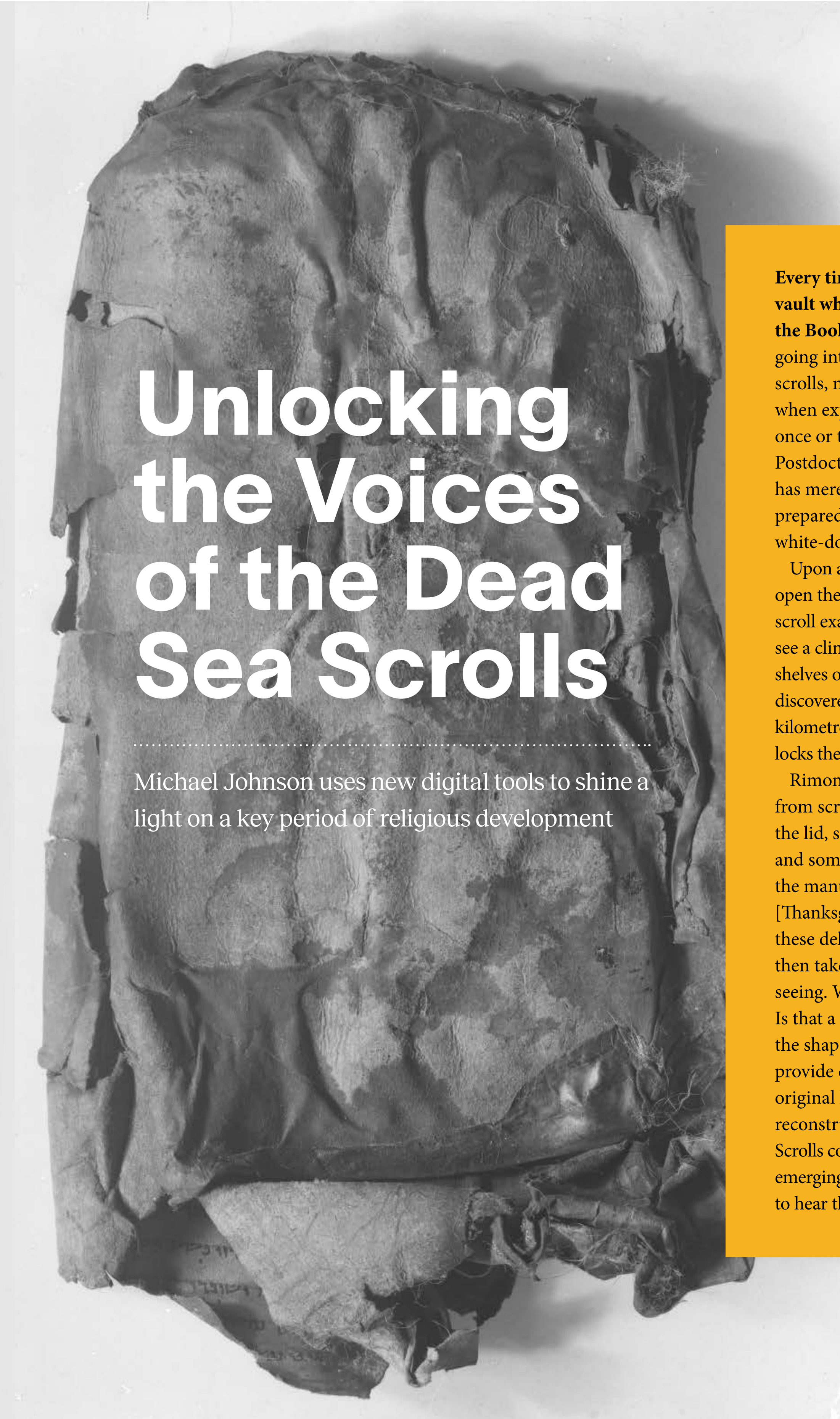
Articles per 10,000 inhabitants



* The Nature Index, compiled by Nature Research, is a database of author affiliation information collated from research articles published in an independently selected group of 82 high-quality science journals.

Israel's Academic Excellence

Nobel Prizes. Global university rankings. Per capita scientific output. By any meaningful measure, Israel displays remarkable academic excellence. The Azrieli Fellows Program contributes to this success by generously funding young scholars at Israel's leading academic institutions, promoting cutting-edge scientific and scholarly innovation for the betterment of society. Azrieli Fellows are an elite group of scholars focused on original, internationally recognized research that strengthens the links between the Israeli and international research communities.



Many more than 2,000 years old, the Dead Sea Scrolls — including 1QH^a — opened a window onto a lost world of Jewish religious practice during a critical juncture in the development of traditions that would eventually shape Western worldviews.

Unlocking the Voices of the Dead Sea Scrolls

Michael Johnson uses new digital tools to shine a light on a key period of religious development

Every time Michael Johnson enters the high-security vault where the Dead Sea Scrolls are held in the Shrine of the Book in Jerusalem, it feels a bit mystical — “like you’re going into the holy of holies,” he says. The parchment scrolls, many more than 2,000 years old, deteriorate rapidly when exposed to air and light, so his access is limited to once or twice a year. Johnson, an Azrieli International Postdoctoral Fellow at the Hebrew University of Jerusalem, has mere hours to work through months’ of painstakingly prepared research questions during each of his visits to this white-domed repository at the Israel Museum.

Upon arrival, conservator Hasia Rimon unlocks and cranks open the vault’s huge steel door and leads Johnson into the scroll examination room. Through a set of glass doors he can see a climate-controlled storage area with floor-to-ceiling shelves of boxes containing the first Dead Sea Scrolls to be discovered in 1947 in Cave 1 at Qumran, located about 50 kilometres east of the vault. After an armed guard shuts and locks the door behind them, they settle in to work.

Rimon brings one of the day’s predetermined boxes from scroll 1QH^a to the examination table and removes the lid, sometimes revealing large sections of a manuscript and sometimes boxes of smaller fragments. (1QH^a is the manuscript number for Cave 1, Qumran, Hodayot [Thanksgiving], scroll A.) Only Rimon is allowed to handle these delicate parchments. Like detectives, she and Johnson then take measurements and talk through what they are seeing. What can this fragment’s damaged edge tell us? Is that a linen fibre attached? Are there changes in the shapes of the fragments? Such minute details can provide compelling new clues, helping us determine the original location of the fragments and test current scroll reconstructions. Far from inert and silent, the Dead Sea Scrolls continue to be deciphered — and Johnson is part of an emerging generation of scholars using powerful digital tools to hear their voices.

By Chris Wiebe
Photographs by Ariel van Straten

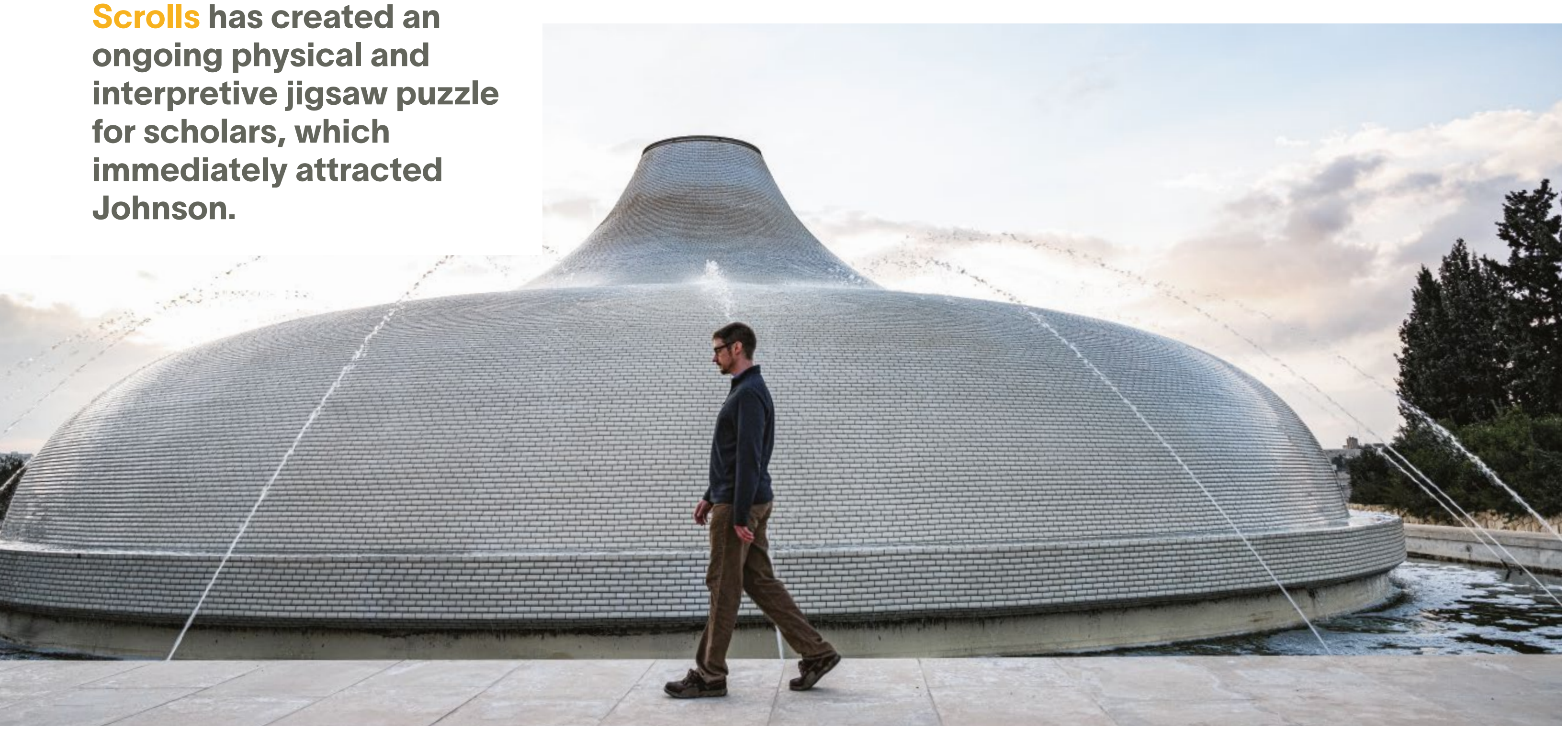
The discovery of the first seven Dead Sea Scrolls by Bedouin shepherds created an international sensation, which was compounded by the discovery over the following decade of nine more caves at Qumran containing the fragments of 950 additional Jewish and Hebrew scrolls from 445 different literary compositions. That only a handful of scrolls in this miraculous cache were intact — many were just heaps of confetti — did nothing to blunt their collective impact. These scrolls threw open a window onto a lost world of Jewish religious practice. Composed between 300 BCE and 70 CE, they fill in our picture of what was happening at a critical juncture in the development of Jewish religious traditions that would eventually feed into and shape Western worldviews, explains Johnson, whose specialty is early Judaism and psalms and prayers from the Second Temple period (515 BCE to 70 CE). "Before the Dead Sea Scrolls," he says, "there was much less indication of how ancient Jews conceived of their scriptures as a corpus, or to what extent they were moving towards the codification of those scriptures into a formal canon resembling the Bibles we have today. It turns out that their conception of authoritative scripture was much more fluid and broader than we realized."

Although revolutionary in content, the fragmented state of the scrolls has created an ongoing physical and interpretive jigsaw puzzle for scholars, which immediately attracted Johnson. "I started out in biblical studies," he recalls, "and one of the first things you learn is that this material has been researched for thousands of years and it is very challenging to say something new." Early in his graduate studies, which began at Emory University in his native United States and culminated in a PhD at McMaster University in Canada, his interest in the Hodayot began with a paper on the scroll 1QH^a, which contains collections of previously unknown ancient psalms or hymns. Johnson soon learned the texts were incomplete, their interpretation uncertain and the position of the scroll fragments unsure. He grew excited by the opportunity to contribute to their refinement. The liturgical dimensions of the texts, such as the communal blessing and praise of the deity alongside the angels at the prescribed times for prayer, also drew him in because they are some of the only surviving texts illuminating these aspects of ancient Jewish religious life in this period.

Johnson is working with renowned scrolls scholar Esther Chazon at the Hebrew University, seeking to resolve critical facets of the Hodayot puzzle. His time in Israel as an Azrieli International Postdoctoral Fellow is simultaneously accelerating his innovative work and knitting him into the scholarly community. "The research I'm doing now," he says, "would have been impossible without access to the Shrine, the photographic archives and the ability to learn at the feet of conservators like Hasia Rimon who are working with these scroll materials on a daily basis." While thematically linked, the two Hodayot scrolls at the centre of Johnson's research agenda have taken him down starkly different research paths — one quite traditional and the other stridently new.

Although revolutionary in content, the fragmented state of the Dead Sea Scrolls has created an ongoing physical and interpretive jigsaw puzzle for scholars, which immediately attracted Johnson.

Michael Johnson outside the Israel Museum's Shrine of the Book, a repository for the first seven Dead Sea Scrolls discovered at Qumran in 1947. The shrine's white dome symbolizes the lids of the jars in which the scrolls were found.



PHOTOGRAPH COPYRIGHT THE ISRAEL MUSEUM, JERUSALEM; DIGITAL RECONSTRUCTION COURTESY MICHAEL JOHNSON

Because some of the scrolls he studies were found wadded (left), Johnson is developing new approaches to 3D modelling (above) to confirm which fragments belong to which scroll.

The scroll 1QH^a is unique because it was found in two bundles — one roughly wadded and the other more carefully folded — and is about 75 per cent complete. German scholar Hartmut Stegemann's first reconstruction of the scroll was developed as an unpublished dissertation in the 1960s, but questions about whether the two bundles are indeed part of the same scroll, or if it is even a liturgical document as some scholars have claimed, have continued unabated. Like a forensic cold case investigator, Johnson went back to the Shrine of the Book to examine the unpublished photos that were taken when the bundles were first opened by James Bieberkraut and photographed by Helene Bieberkraut around 1948. Methods for photographing and conserving scrolls were still being developed at the time, and their process had significant scientific gaps: not enough photos were taken, the sequence of photos is not clear, and the process for separating the parchment layers in the bundles and flattening them likely caused irreversible damage.

Nevertheless, by comparing the bundle opening photos with the scroll fragments in the Shrine's vault and Stegemann's work, Johnson submitted two major scholarly papers for review in the summer of 2021. The first affirms that columns 1 to 8 and 9 to 28 of 1QH^a are indeed from the same scroll, not parts of two separate scrolls that were accidentally combined. The second paper proposes new fragment placements in columns 1 to 8 that deviate from Stegemann's original reconstruction. "This new ordering of the psalms is quite a big change," Johnson says, "as the psalm arrangement puts even greater emphasis on praising God with the angels and drawing in the audience to participate. There is a stronger liturgical orientation reflected in my revised reconstruction than scholars at first realized."

Johnson's 1QH^a work involved conventional research techniques; however, his research on 4QH^a builds on his pathbreaking work using three-dimensional digital modelling to check the accuracy of previous scroll reconstructions. The standard approach to reconstructing a scroll involves not only fitting fragment shapes together, but also examining the repeating sequence of damages (chips, breaks, holes, or the impressions of stitched seams) in the manuscript. The guiding principle is that as you get closer to the core of the scroll, where the diameter of the turns of the scroll becomes narrower, the damage to these edges decreases in distance from each other at a regular mathematical rate. Researchers use this information to determine the positional layers of scroll fragments even if they were not immediately connected. Unfortunately, the measurements used to make reconstructions are not always published and errors have sometimes crept into this theoretical modelling.

Johnson's innovative response — successfully test driven on the relatively intact War Scroll (1QM) — is to stitch together scroll photographs and roll the resulting two-dimensional plane around an Archimedean spiral to check whether the damage patterns line up. "I'm checking the work earlier scholars have done on material reconstructions," says Johnson, "by seeing if the rationale for those reconstructions holds up when you visualize the entire scroll as a 3D model."

The 1QM test helped him weigh in on disagreements in the literature about where some fragments belong in the reconstruction or whether they belong with the same scroll at all. The fragments making up column 19, for instance, are physically detached from the rest of the scroll, but the three-dimensional modelling

Johnson's research would not be possible without access to the scrolls, archives and expertise of conservators at the Shrine of the Book.

'Everyone is scrambling to do the best work while we still can. The parchments are darkening and as that process moves on it will be increasingly difficult to distinguish writing from the parchment. So, the critical issue is to use the best cameras and techniques to capture this material, because we are slowly losing it.'

showed that the patterns of damage cohere well with the damages in several layers of the scroll beneath, strengthening the case for associating column 19 with 1QM. This capability will be especially important for Johnson's ongoing work on 4QH^a because the scroll is exceptionally fragmented and its original length unknown. While Stegemann boldly forged ahead and created a reconstruction of the scroll between 1994 and 1998, he didn't provide technical notes on his measurements and damage pattern analysis; Johnson hopes a three-dimensional model will help him reverse engineer Stegemann's process and explore ways to place new fragments or adjust currently placed fragments.

Once completed, Johnson is hopeful that his work with 4QH^a will demonstrate the exciting potential of three-dimensional modelling to the scrolls research community and prompt broad uptake. The inexorable deterioration of the Dead Sea Scrolls gives the use of new technological tools fresh urgency. "Everyone is scrambling to do the best work while we still can," says Johnson. "The parchments are darkening and as that process moves on it will be increasingly difficult to distinguish writing from the parchment. So, the critical issue is to use the best cameras and techniques to capture this material at its best now, because we are slowly losing it."

Living on the Mount Scopus Campus of Hebrew University has given Johnson the opportunity each day to put his research in fresh new contexts. On his morning runs, half the time he is looking over the Temple Mount, and the other half gazing over the Dead Sea toward Qumran. "It's amazing to live here," he enthuses, "because you are in a place that was such an epicentre for ancient Jewish scribes laying down the traditions that shaped generations." Johnson's meticulous, trailblazing work recovering the Dead Sea Scrolls is bringing us closer to the voices of those scribes and the vibrant lives of their communities. ▲●■

Baby's First Microbiome

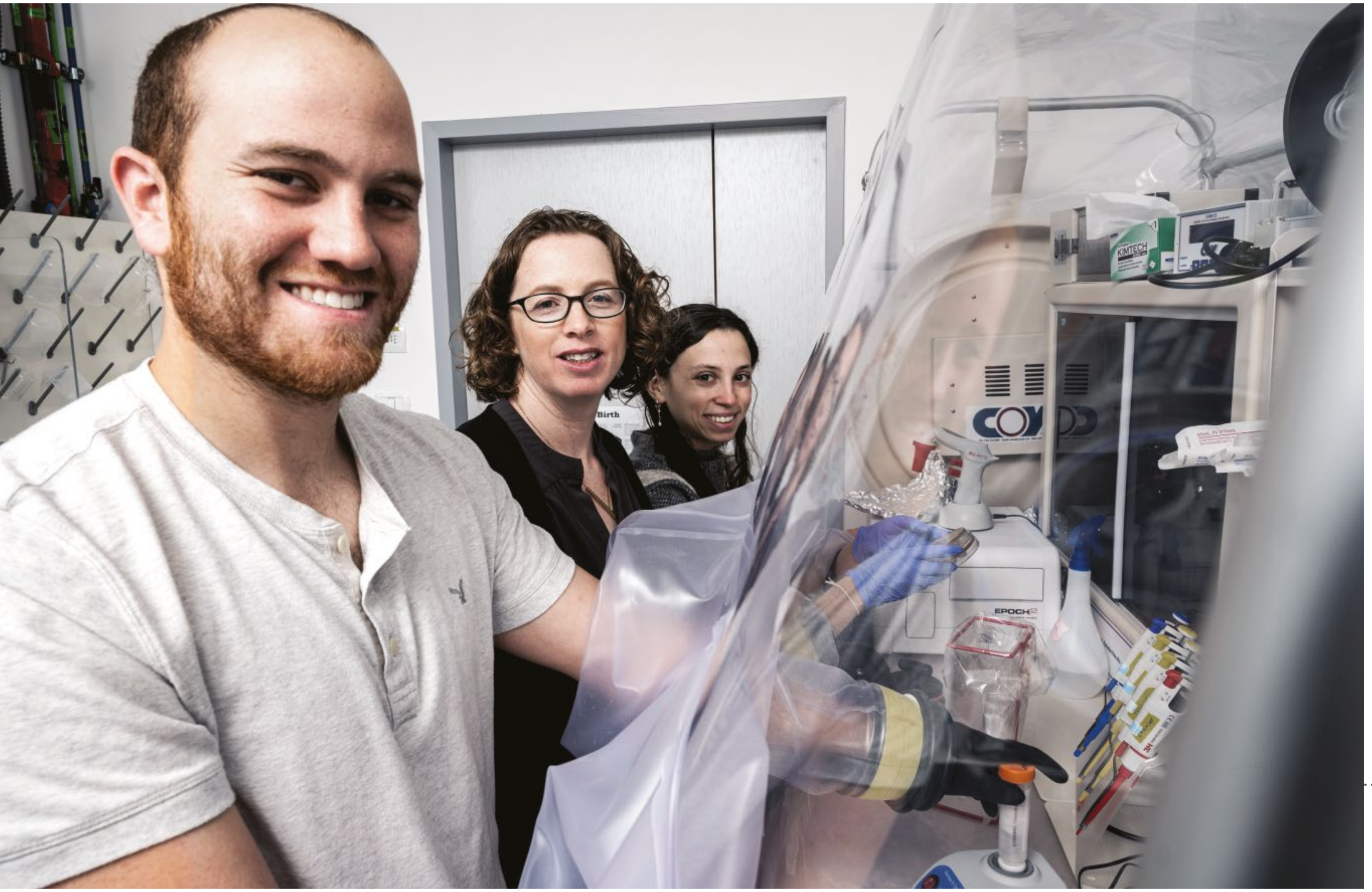
An infant's gut is one of the keys to developmental health, and Moran Yassour wants to decode the role that microbes play

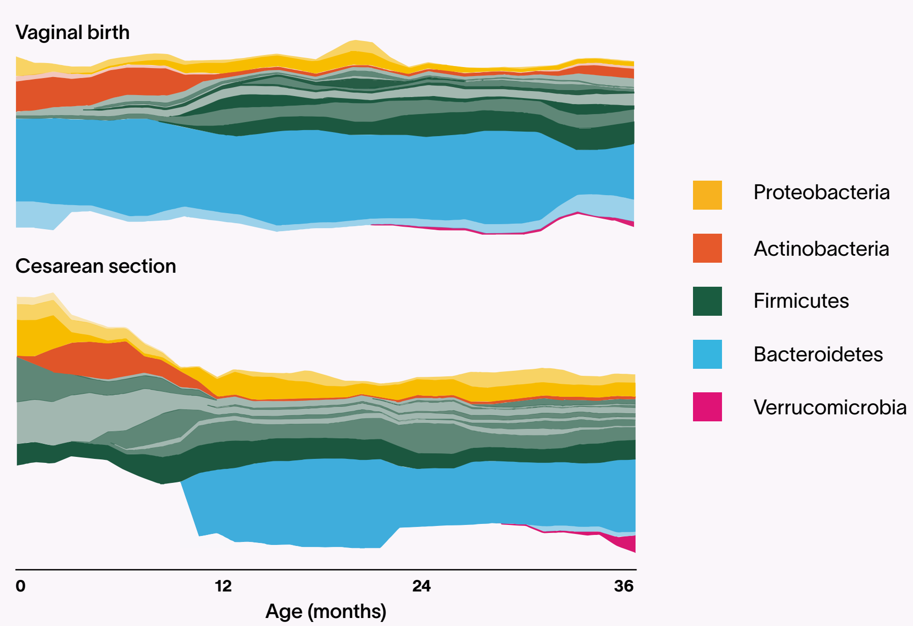
Computational biologist Moran Yassour, an Azrieli Early Career Faculty Fellow at the Hebrew University of Jerusalem, researches a vital but often overlooked aspect of human development: the newborn gut.

More specifically, she is studying how the gut is colonized by microbes, how sugars found only in breastmilk nourish beneficial microbes, and how the establishment of this critical community of microorganisms — known as the human gut microbiome — affects the health of not only babies but children and adults too.

There is a bustling assemblage of bacteria, archaea, fungi and viruses within our gastrointestinal tract, and this microbiome is one of the keys to well-being. The important roles that these microbes play has become increasingly evident in the fifteen or so years

By Anne Shibata Casselman
Photographs by Ariel van Straten





The microbial signatures in the guts of infants borne vaginally and by cesarian section differ and change over time. The differences are so pronounced that by analyzing a stool sample, Moran Yassour can determine how a baby was born. By studying changes in this community of microbes, she aims to address questions such as why infants born by caesarian have a greater chance of developing autoimmune diseases.

DIAGRAM BY DALBERT B. VILARINO; SOURCE: MORAN YASSOUR

Autoimmune disorders arise when the immune system incorrectly identifies elements within our bodies as foe. A healthy gut microbiome appears to be an important training ground for early lessons that lessen the chance of developing an autoimmune disorder.

Moran Yassour (middle) with students Nadav Moriel and Sivan Kijner in her lab, where their research is deepening our understanding of the infant gut microbiome.

ILLUSTRATION COURTESY PEANUTS CREATIVE STUDIO

since genetic sequencing began providing a more detailed picture of what's happening inside our bodies. The microbiome is home to trillions of microbes and it is proving to be as critical to development as any organ. It is implicated in a long list of ailments, from inflammatory bowel disease and type 2 diabetes to colorectal cancer and rheumatoid arthritis, among others. The microbiome helps regulate everything from our metabolism and sleep patterns to our immune system, the majority of which is found in the gut. Autoimmune disorders arise when the immune system incorrectly identifies elements within our bodies as foe; a healthy gut microbiome appears to be an important training ground for early lessons that lessen the chance of developing an autoimmune disorder.

In other words, the formation of this community of microorganisms during infancy has lifelong consequences. Despite this great impact, however, very little is known about how microbes colonize the gut during infancy or how the composition of the microbiome affects pediatric disease. Yassour, who is cross-appointed to the Faculty of Medicine and the School of Computer Science and Engineering, explores this scientifically rich niche at the Hebrew University, where she earned all three of her degrees and to which she returned in 2018 after a postdoctoral fellowship at the Broad Institute of MIT and Harvard. While in Boston, she found herself wondering about the factors contributing to differences in infant gut microbes. "Being a mother myself," she says, "it intrigued me."

Today, Yassour works in her lab with a dozen or so students, from undergraduates to PhDs, with backgrounds ranging from microbiology and medicine to pure computer science. Together, they grow bacterial cell cultures in anaerobic environments that simulate the infant gut, sequence bacterial DNA from stool samples and use machine learning algorithms to map out not only what type of microbes inhabit our guts, but also the specific strains and their functionality, and how they may play a role in pediatric health.

Yassour has made significant progress in the eight years since starting her research in this field. She has debunked the belief that the vaginal microbiome seeds the infant gut microbiome during birth (the source appears to be rectal) and traced mother-to-child transmission of the microbes that colonize the infant gut. She has also continued to lay the groundwork for more ambitious and applied work. Eventually, thanks to her research, infant formula could better mimic breastmilk's ability to nurture healthy children, and lifesaving caesarean deliveries won't deny babies the microbial boost experienced from vaginal births.

"We still need to answer many of the basic science questions," says Yassour, "before we can move on to address the big important ones." Infants born by caesarian, for example, have a greater chance of developing autoimmune diseases than those who are born vaginally. Yassour wants to find out whether differences in their microbiomes are at the root of this disparity. At six months of age, a child born by caesarian has a different microbial signature in their gut than one who is born vaginally. The signs are so strong that if you were to give her a stool sample from an infant's diaper, she could tell you how that baby was born with 80 per cent accuracy. Breastfed infants also have unique signatures in their gut microbes compared with formula-fed infants.

Yassour is interested in teasing apart the precise impact of these variations. One way to do this is by decoding the microbial make-up of stool samples collected from individuals across multiple points in their early lives. "We can collect longitudinal cohorts of infants or older children that have a medical condition that is associated with immunity early on in life, profile their microbiome and search for differential features, such as specific microbial taxa," she says. She is collaborating with researchers at Massachusetts General Hospital in Boston to study an allergy that some infants develop to the proteins in cow's milk. Although the allergy resolves on its own, children who develop it have a higher chance of developing life-threatening food allergies, such as to nuts or shellfish, later in life.

Yassour and her colleagues are analyzing stool samples from ninety babies who developed this allergy during the first year of their lives and ninety who did not to compare their gut microbiomes. "We find some overall differences in microbial diversity between the groups," she says of their findings so far, "and also identify bacterial species that have a higher abundance in one group than the other." Moreover, the researchers found differences during the period that the allergy presents and after it resolves, and they are examining the specific bacteria at play.

Human breastmilk is another key to fostering beneficial gut microbes in infants. To better understand its impact, Yassour must first clarify the effect that the complex sugars found only in breastmilk have on the infant gut microbiome. These sugars, known as human milk oligosaccharides (HMOs), are the third most

common component of breastmilk. A mother's body invests significant energy making these complex sugars, which can only be broken down by the beneficial microbes in her baby's gastrointestinal tract. These HMOs seem to act as a baby's first prebiotic, a food that will encourage the growth of the microbes that use it as an energy source (compared to probiotics, which involve administering live microorganisms).

There are between fifty to two hundred different structures of HMOs. Yassour and her team are currently feeding various HMOs to bacteria collected from the infant gut to determine which bacteria thrive on which HMOs. From there they hope to find the simplest combination of HMOs that best mimics a "universal breastmilk." Yassour is quick to aver that she is not taking sides in the formula versus breastfeeding conversation. "Infant formula is really important," she says. "We all agree that its intention is to mimic breastmilk, so let's think about how we can mimic it in all possible ways." At the same time, Yassour is thinking about myriad ways to gain a better understanding of the infant gut microbiome and its long-term health implications. ▲●■

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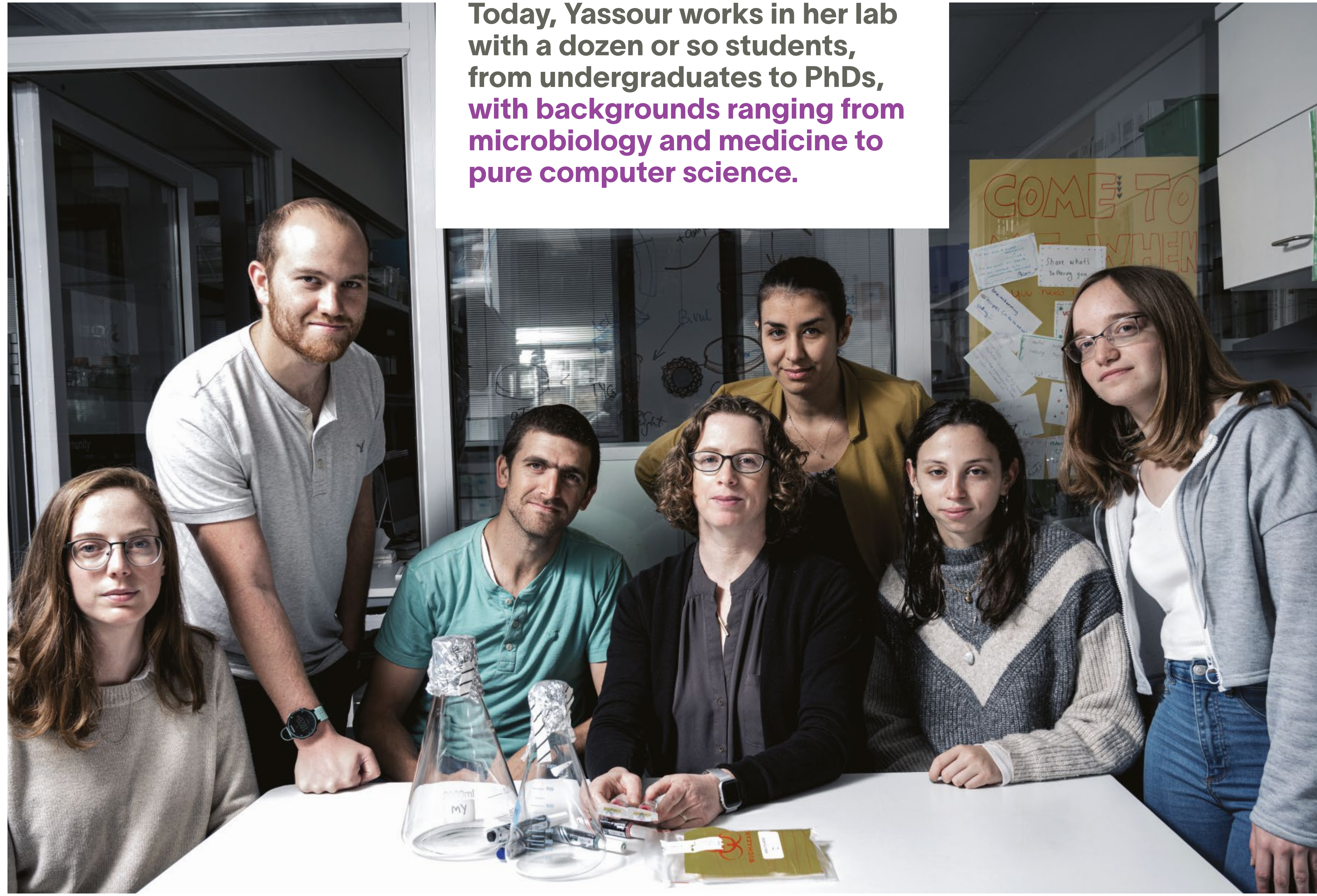


Yassour (facing page), who grows bacterial cell cultures in her lab that simulate the infant gut and performs computational analyses, gathers with students (above, left to right) Netta Barak, Nadav Moriel, Ehud Dahan, Chiara Mazzoni, Sivan Kijner and Lior Merav.

Giant Shift Forward

Jonathan Berant navigates a new paradigm in natural language processing and artificial intelligence

By Alex Hutchinson
Photographs by Boaz Perlstein

In the fall of 2019, Google tweaked its search algorithm. The company knew that people tended to type their queries in "keyword-ese," rather than phrasing them the way they would speak to another human, so its researchers developed a new technique that sought to glean meaning from whole phrases or sentences rather than individual keywords. With this change, when presented with a search like "brazil traveller to canada need visa," Google can now spot the crucial word "to," assess its context, and return only results about travelling from Brazil to Canada and not vice versa.

Such advances often feel small or incremental. Who has not become a bit blasé about the steadily growing competence of Siri and her virtual peers? But Google's development, which it dubbed Bidirectional Encoder Representations from Transformers, or BERT, marked a bigger step. "Everything changed afterwards," says Jonathan Berant, a former postdoctoral researcher at Google who is now a professor at Tel-Aviv University's Blavatnik School of Computer Science. "And BERT is the model that started this revolution."

Berant, who started his PhD at Tel Aviv University as an Azrieli Graduate Studies Fellow in 2007, the first cohort of the program, studies natural language processing, a field that has always loomed large in our conception of what it means for a machine to be "artificially intelligent." Most famously, the British mathematician Alan Turing proposed in 1950 that a computer's ability to carry on a human-like conversation would be a reasonable proxy for whether the computer could "think."

The field has undergone several dramatic shifts since Berant finished his doctorate: chatty digital assistants have become ubiquitous, the Turing Test was beaten (albeit controversially) in 2014, and the success of new approaches like BERT has forced everyone in natural language processing to rethink their research agendas. "When a field is exploding, you need to think more about what it is that you do exactly," Berant says. "What is your advantage?"

Berant's interest in natural language processing began with a linguistics course he took at the Open University during his military service. "My head exploded," he recalls. "I thought this was amazing." He wanted to pursue the topic, but he also recognized that he had some "exact science tendencies," so after his service was finished, he enrolled at Tel Aviv University in a joint computer science and linguistics program. Four years later, Berant started his PhD as an Azrieli Fellow, eventually zeroing in on a problem in natural language processing called textual entailment.

Given two statements, can you infer one from the other? To humans, it's clear that if Amazon *acquires* MGM Studios, that means that Amazon *owns* MGM Studios. But these leaps are trickier for a computer to make. After all, if you acquire a second language, that doesn't mean that you own it. Berant's thesis focused on using the underlying structures of language — properties like transitivity, which means that if A implies B and B implies C, A must imply C — to help computers make better inferences. Despite all the progress over the past decade, textual entailment is a problem that researchers are still grappling with, Berant says: "It kind of encapsulates a lot of the things that you need to do in order to understand language."

After completing his PhD, Berant headed to Stanford University in California for a postdoctoral fellowship. He began working with computer scientists Percy Liang and Christopher Manning and shifted his focus to semantic parsing, which is the task of taking a single sentence of natural language and translating it into a logical form that a computer can understand and act upon. If you tell the virtual assistant on your phone, "Book me a ticket on the next flight to New York, but only a morning flight, with no connections," that's a very specific set of instructions that the software has to understand, no matter how you phrase it.

The first attempts to build computer systems that could understand natural language, starting in the 1960s, relied on rules. In a sufficiently narrow domain, you could tell the computer everything it needed to know in order to answer questions. But that approach has limits. “There’s a lot of world out there,” as Liang once put it, “and it’s messy too.”

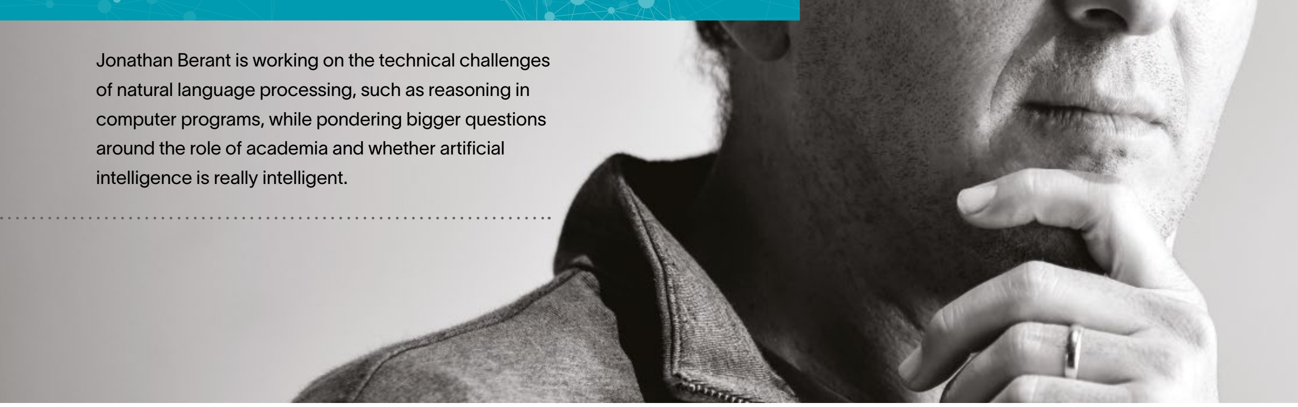
In the 1990s, these rules-based systems were supplanted by statistical approaches, in which computers were programmed to “learn” by adjusting their own parameters after, say, answering a question correctly or incorrectly. To outperform rules, the statistical approach requires huge numbers of human-generated examples. While at Stanford, Berant and his colleagues used Google Suggest to generate a million sample questions, then enlisted human workers on Amazon Mechanical Turk to answer 100,000 of them at three cents per question. This approach can be enormously powerful: it’s how IBM’s computer system Watson beat record-holding game show champion Ken Jennings on *Jeopardy* in 2011. But the statistical approach, too, is limited by the sheer scale of human-provided data required.

What makes BERT and its successors (known collectively by the proposed name “foundation models”) so special is that they’re easy to train. A 2012 breakthrough led by Google’s Quoc Le showed that if you use a big enough neural network — a type of algorithm in which the flow of information is modelled after the nerves and synapses of the human brain — then you don’t need to feed it specially prepared data with pre-labelled answers. Instead, you can simply feed it a massive pile of previously existing data, like ten million still frames lifted from YouTube videos, and the algorithm learns to recognize recurring features, such as cats, without ever being told what a cat is. This approach is known as unsupervised learning, and it was quickly adopted in natural language processing with great success by using existing troves of fact-rich natural language like Wikipedia. “Everything became neural networks in natural language processing,” Berant says, “and it works very well for most things — much better than everything we had before.”

In a word, BERT’s impact was “huge,” says Liang, who launched the Center for Research on Foundation Models at Stanford in August 2021. “Shortly after it came out, essentially all state-of-the-art natural language processing models became based on BERT or some other foundation model.” There’s now a Hebrew version of BERT, AlephBERT, and a French version, CamemBERT. The success of these models sparked a flurry of interest that crossed discipline boundaries. BERT’s successors are being used in neighbouring fields such as computer vision and robotics, and for more exotic applications such as predicting the three-dimensional structure of proteins, where their performance is revolutionizing the field.

But the scale of computing resources required has created a dilemma for academics like Berant. The Google algorithm introduced in 2012 used a neural network with more than a billion synapses that ran on a cluster of 1,000 powerful computers yoked together into a single system. The price of entry also continues to climb: the current state-of-the-art neural network, known as GPT-3, boasts a staggering 175 billion synapses. “The places where you can actually build models that are the best in the world are now more or less restricted to Google, Facebook and Microsoft,” Berant says. “So, academia needs to reposition itself and figure out: What is our role?”

Who has not become a bit blasé about the steadily growing competence of Siri and her virtual peers?



Jonathan Berant is working on the technical challenges of natural language processing, such as reasoning in computer programs, while pondering bigger questions around the role of academia and whether artificial intelligence is really intelligent.

One possibility is to ask uncomfortable questions that Google and its peers may neglect in their rush to develop ever more powerful algorithms. For example, Berant and his colleagues published an article in 2019 on the biases that creep into natural language systems thanks to the quirks of the individual humans who provide the computer with its initial data. The same is true even with supposedly neutral datasets like Wikipedia. “On the web, if there’s a correlation between being a woman and being a nurse,” Berant explains, “then of course the models will absorb these biases.”

As foundation models are deployed in more and more disciplines — health care, biomedicine, law, education — Berant sees a crucial role for university researchers in tackling issues such as bias, privacy, security and inequity. “There’s a lot of interest in academia in these things, which are not about making money for large companies,” he says, “but about making sure that these models are deployed in a safe way and that we’re aware of both the advantages and the limitations.”

That’s not to say that the technical challenges of natural language processing have been fully solved, as anyone who has asked Siri, Alexa or Google Translate to tackle anything more than a simple sentence knows. One focus of Berant’s current research is the role of reasoning for a question-answering computer program. As presented in a 2021 article by Berant and several colleagues, if you ask a Wikipedia-trained computer whether Aristotle died before the invention of the laptop computer, it won’t have any trouble getting the answer, but if you ask it whether Aristotle ever owned a laptop, getting the right answer requires a logical leap. It involves reframing the implicit question as a series of explicit logical steps: When did Aristotle live? When was the laptop invented? Was the former before or after the latter? Training a computer to reliably reason like this remains an ongoing challenge.

A related goal, which Berant tackled in another 2021 paper, is called compositional generalization. Humans are good at putting together pieces of previously learned information to answer questions they’ve never explicitly seen before. If they know the capitals of every state in the United States, and they know what states border New York, then they can generalize that knowledge to answer the question “What are the capitals of the states that border New York?” Computers, on the other hand, struggle with this. Berant’s approach to the problem builds on earlier approaches used by pre-foundation models to break down complex questions into simple components and integrate them into the latest neural network systems.

Where is this all headed? That’s a tricky question, Berant acknowledges. The Turing Test was cracked in 2014 when a computer program that pretended to be a thirteen-year-old Ukrainian boy fooled some judges into thinking that it was human. However, no one in the field really believes that makes computers as intelligent, or even as conversationally adept, as humans. “Trying to solve the Turing Test doesn’t lead to intelligence, but leads to deceit,” Berant says. The same thing happens whenever researchers come up with new benchmarks: computers adopt specific strategies to ace the test, which is done without any need for the general intelligence that the test was designed to elicit.

This problem — what scientists in the field refer to as the “evaluation crisis” — is one of Berant’s next targets. “This is something that people in academia, including myself, have been working on a lot.” After all, he says, the incredible progress of the last few years toward the ultimate goal of a computer that’s fully conversant in natural language raises a crucial question: “How will we know that we got there?” ▲●■

‘There’s a lot of interest in academia in these things, which are not about making money for large companies, but about making sure that these models are deployed in a safe way and that we’re aware of both the advantages and the limitations.’

PHOTOGRAPH BY YURI DOJC

While it may be a cliché, it's true: Life isn't about the destination — it's the journey that matters.

At the Azrieli Foundation, we connect and nurture potential with the resources and wisdom it needs to open doors to a better world. For nearly 400 Azrieli Fellows, these doors have opened onto a new journey.

Azrieli Fellows are brilliant, out-of-the-box thinkers with the drive to make an impact. The Azrieli Fellowship encourages and supports them as they travel on their academic expeditions of research, innovation, creativity and personal growth.

Aperio magazine was created to share these journeys toward discovery. Since the program began in 2007, I have found it fascinating to learn about the array of subjects that captivate each of our Fellows — in this edition alone, they range from supernovas to architecture! While the subject matter itself is thought-provoking, it is also apparent that Fellows are open to new ideas coming from multiple and varied sources and disciplines, which allows them to view their world through different lenses.

Arielle Blonder is an architect who is now working with a physicist. The silo-breaking part of her journey incorporates natural systems into her architecture, which enables her to see problems from different perspectives.

Michael Johnson's work also aims to see things from a range of angles — in this case, by using cutting-edge 3D modelling technology to interpret an ancient religious manuscript.

Benjamin Palmer shifted his research from studying crystals to studying what animals do with crystals. He embarked in this new direction when he read academic papers by two Weizmann professors, flew to Israel and started a postdoc.

Aperio means uncover, reveal or make clear. Azrieli Fellows remind us that amazing things can happen en route to somewhere else, if we are open to it. It is our honour to be part of their journey.

Naomi Azrieli, DPhil
Chair and CEO, The Azrieli Foundation

Aperio

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Aperio: Latin for *uncover*, *reveal* or *make clear*; the source of the English word "appear."

Aperio is a magazine of the Azrieli Fellows Program, which empowers promising academics worldwide through opportunities to conduct cutting-edge research at elite institutions of higher education in Israel, a country long recognized for outstanding achievements in research. The program is operated by the Azrieli Foundation, which aims to improve the lives of present and future generations through philanthropic initiatives in education, research, health care and the arts in Canada and Israel.

PHOTOGRAPH COURTESY ARIELLE BLONDER

Using both computer simulation and mechanical manipulation, architect Arielle Blonder is exploring the design possibilities of textiles.