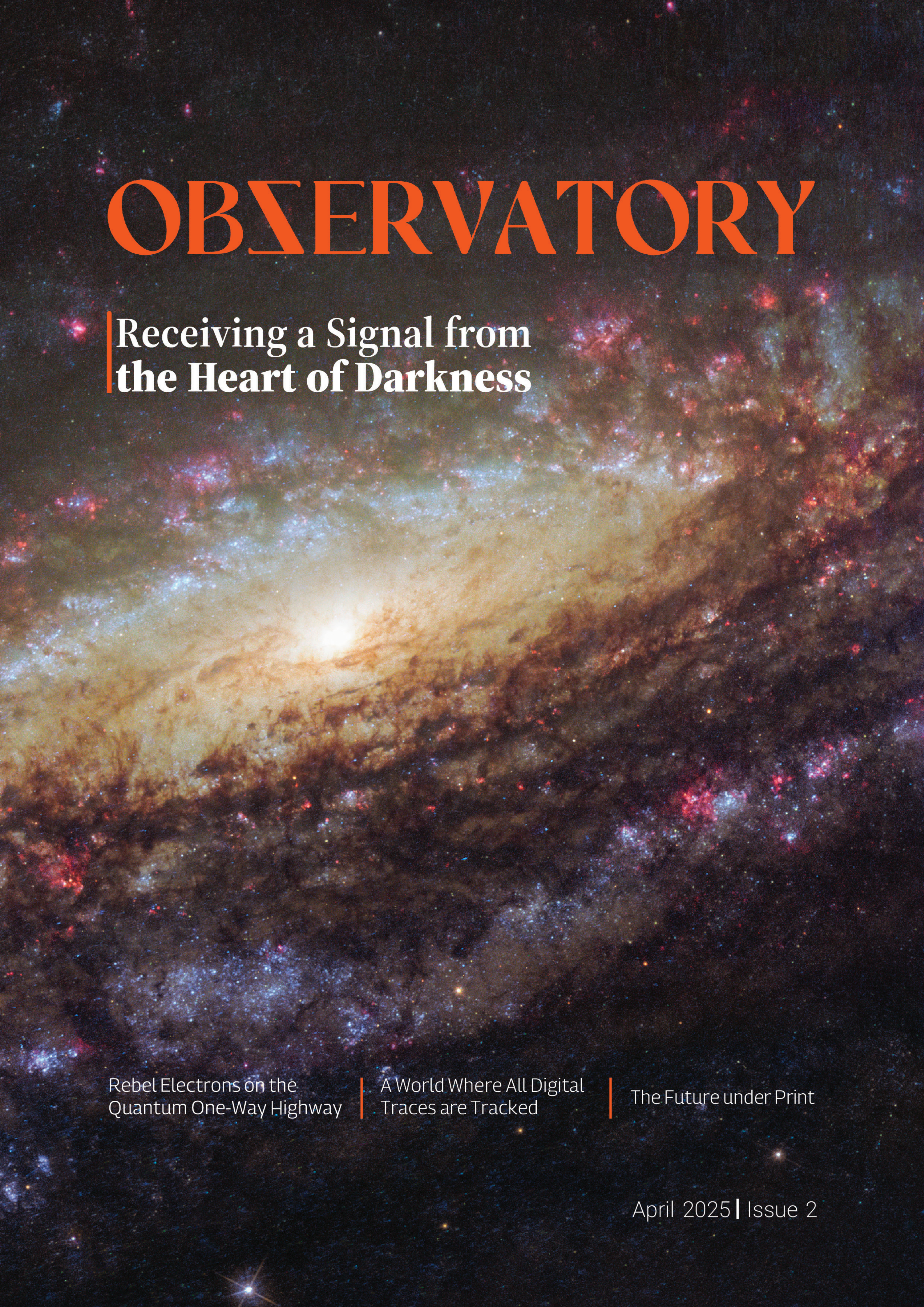

OBSERVATORY

Receiving a Signal from **the Heart of Darkness**

Rebel Electrons on the Quantum One-Way Highway | A World Where All Digital Traces are Tracked | The Future under Print

April 2025 | Issue 2

Cover image:
This image, taken by the NASA/ESA Hubble Space Telescope, features the spiral galaxy NGC 7331, situated approximately 45 million light–years from Earth in the constellation Pegasus.
NGC 7331 closely resembles the Milky Way in terms of its size, morphology, and mass. It exhibits a comparable rate of star formation, contains a similar stellar population, and harbors a central supermassive black hole, along with well–defined spiral arms. The principal distinction between the two galaxies lies in their structure: NGC 7331 is classified as an unbarred spiral galaxy, whereas the Milky Way features a central bar. Like many spiral galaxies, NGC 7331 has a flat rotation curve, which strongly suggests the presence of dark matter.
As residents of the Milky Way, we are unable to capture an external image of our own galaxy. However, by studying galaxies with similar characteristics–such as NGC 7331–we effectively hold up a scientific mirror to the Milky Way. This comparative approach enhances our understanding of our galactic environment, which remains largely unobservable from within, and provides valuable insights into the broader processes of galactic structure, behavior, and evolution.

Credit: ESA/Hubble & NASA/D. Milisavljevic (Purdue University)

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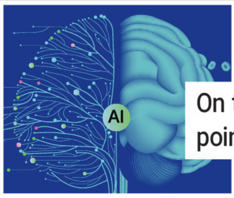

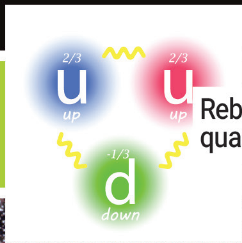

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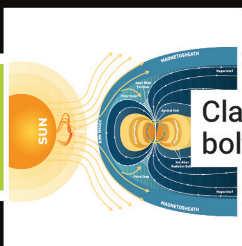

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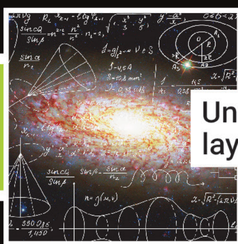


CELEBRATING THE BIRTHDAY OF AN OBSERVATORY

This fall, students and science and technology enthusiasts gathered at the Pardis Technology Park for a one-day scientific adventure. Some were observing sunspots, some were chatting with a scientist at the Science Café, while others were observing microscopic creatures through microscopes and commenting on their subtleties. Yet others were curiously wandering around the laboratories of biotechnology companies, seeking to understand the complexity of the scientific processes at work in these companies.

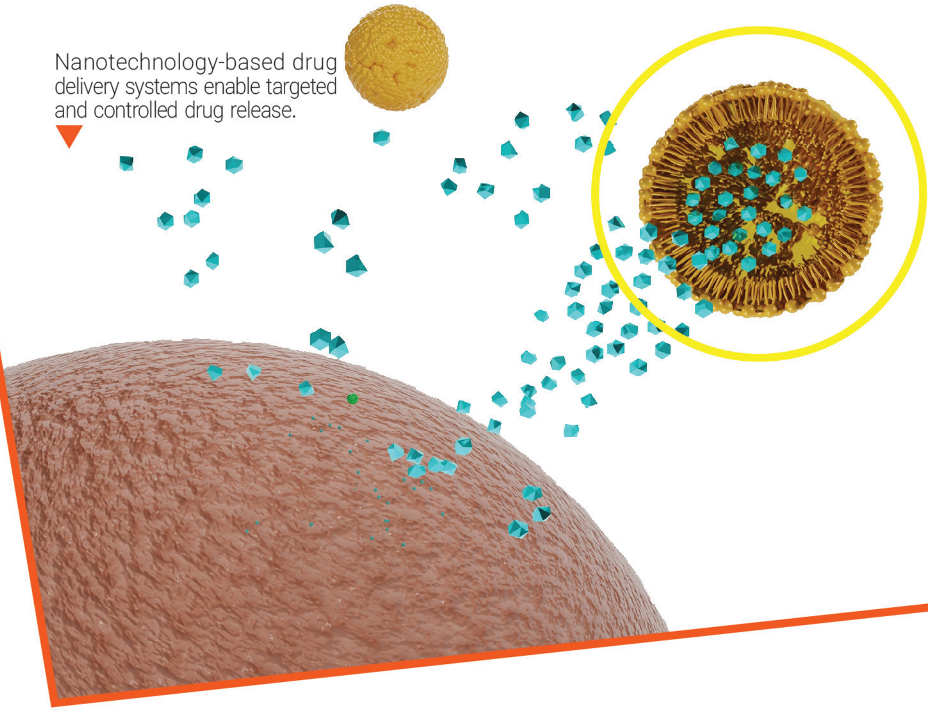
The second 'Sci-Feast,' held on World Science Day, was a grand gathering for science lovers, marking the birthday of the "Observatory." The highlight of the event was the unveiling of the first issue of the Observatory's publication and podcast.

FINDING A NEEDLE IN A HAYSTACK

This was the title of a presentation delivered by one of the sci-questers present at the Sci-Feast. Imagine you have a vast resource full of information about building software. The information includes errors, changes in code, and programmers' and users' experiences, among other information. How can you effectively leverage such rich data to improve software development in a cost-efficient way with the fewest risks possible? Ahmed Hassan, a professor at Queen's University in Canada, dedicated his research to answering this question. He is the inventor of Mining Software Repositories (MSR).

MSR resembles sending a team of scientists to explore a vast land in search of valuable information, which helps programmers solve issues more quickly, build better software, and learn from the mistakes that were previously made. In other words, MSR helps us use these data in the best way possible and build better software. Hassan is the first researcher and pioneer in this field (The research area did not exist beforehand) and the founder of the Mining Software Repositories Conference. He has built an international community of researchers interested in this field.

Nanotechnology-based drug delivery systems enable targeted and controlled drug release.



SMALL PARTICLES, BIG HOPES: DEFEATING CANCER WITH NANOPARTICLES

Amidst the hustle and bustle of the event, the smell of coffee took us to a cozy café in another building, where the 23rd Science Café was going on. The participants in this session were having a discussion about a growing technology, which revolved around the question: "How can we use nano-sized particles to deliver drugs to specific tissues or organs in the body?" This drug delivery method presents a promising prospect for the future of cancer treatment.

Nanoparticles, which typically range in size from 1 to 100 nanometers, can deliver therapeutic agents directly to the tumor site.

This technology increases the efficiency of treatment while minimizing damage to healthy tissues. Omid Farokhzad's achievement in this regard was the focus of this session. He won the 2023 Mustafa(pbuh) Prize for the "Design, Development, and Clinical Translation of Novel Polymeric Nanomedicines." This technology has not only increased the effectiveness of treatment but also reduced its side effects. Farokhzad is now a professor at Harvard Medical School and CEO of Seer Inc. His numerous scientific articles in this field have been cited about 85,000 times so far.

Saturn's rings are almost completely composed of billions (if not trillions) of chunks of water ice, ranging in size from smaller than a grain of sand to the size of a mountain.

RENEWING LIFE: THE FUTURE OF REGENERATIVE MEDICINE AND TISSUE ENGINEERING

Another Science Café, also brimming with science lovers, was going on with a discussion about tissue engineering, hydrogels, and the future of regenerative medicine, the last of which is growing in significance due to factors such as an increase in the global median age and the growing need for new therapeutic methods.

In this session, the condition of companies and products related to tissue engineering in the world was also discussed. Along with that, the achievement of one of the world's leading scientists in biomedical engineering, Ali Khademhosseini, was explained to the participants in simple language. One of Khademhosseini's most important achievements is the development of hydrogels, which are the basis of advanced bioink materials that have wide application in 3D bioprinting. Khademhosseini is now the CEO of the Terasaki Institute in Los Angeles and also the manager of Omeat, a company producing cultivated meat.

UNDER THE STARS WITH THE LORD OF THE RINGS!

Throughout the day, participants observed sunspots through a 14-inch telescope. These spots, which appear temporarily on the sun, are caused by a decrease in the temperature of the surface of the sun. On some days, you can see some gigantic spots even without a telescope; not on the day of our event, though!

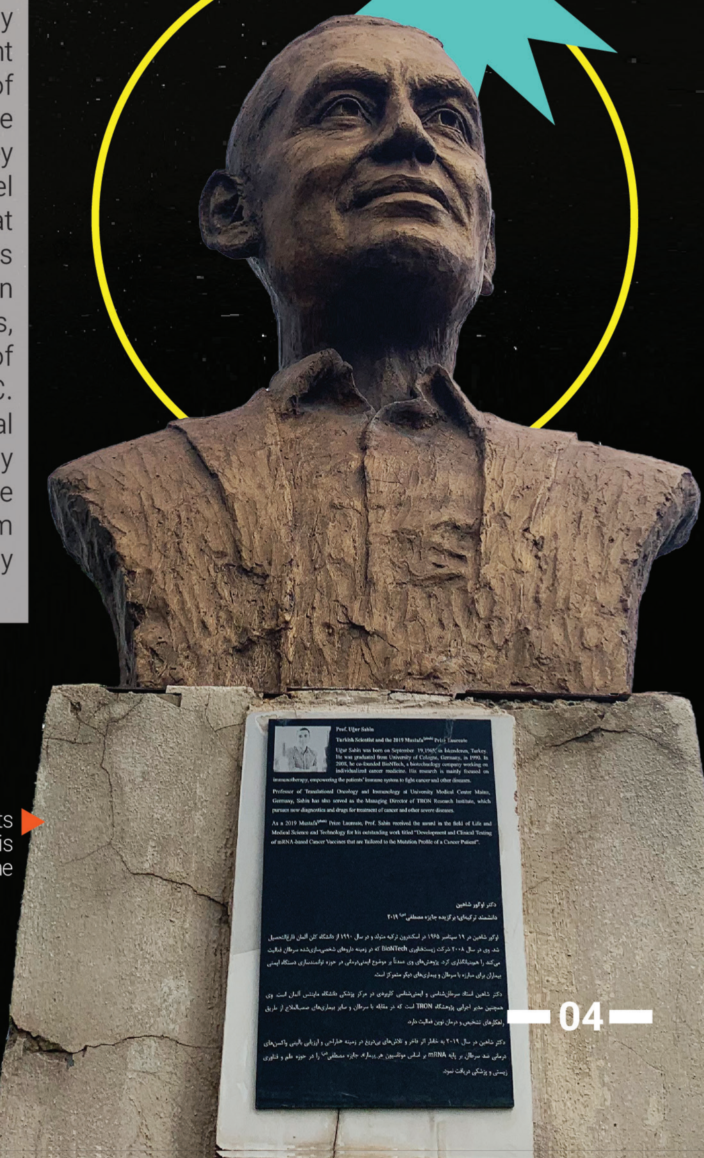
As dusk fell, the moon and some other planets of the solar system gradually replaced the sun in the sky. Watching lunar craters created excitement among the crowd of observers. By watching these craters that were mainly formed as a result of meteorites hitting the moon, the observers were able to imagine the moon's uneven surface.

It was in 1610 that Galileo carried out a detailed study of the moon for the first time (interestingly, he did it in November, the same month that Sci-Feast was held) and later presented a report on his observations. He discovered, for the first time, that the surface of the moon was not as smooth as previously thought and that there were huge mountains and valleys on it.

The night's discoveries didn't stop there. When the telescope was turned towards 'the Lord of the Rings' in the solar system, a vague but magnificent image of a gas giant emerged. Saturn, the second largest planet in the solar system after Jupiter, has 274 known moons, only one of which, Titan, is even larger than the planet Mercury.

TAKING SELFIES WITH SCIENTISTS

The second Sci-Feast came to an end with a warm reception on a cold autumn night in the 'Garden of Scientists,' among the cedars, silver pines, and weeping willows. The final part featured the celebration of the five scientists whose achievements were examined by sci-questers earlier. The busts of these prominent scientists who have pushed the boundaries of science and technology and promoted the application of knowledge were unveiled; they were celebrated thus: Samia J. Khoury for novel approaches to the care of MS patients, Murat Uysal for advancing Optical Wireless Communication Technology, Ahmed E. Hassan for his research on Mining Software Repositories, Ahmad Fauzi Ismail for development of membrane technology applications, and Omid C. Farokhzad for design, development, and clinical translation of novel polymeric nano-medicines. By receiving the Mustafa(pbuh) Prize, these five scientists joined the fourteen laureates from previous years, with their busts now permanently displayed in this garden of scientists.



Uğur Şahin, a prominent immunologist, is one of the scientists whose bust has been installed in the "Scientists' Garden." This bust was unveiled in 2020, one year after he received the Mustafa(pbuh) Prize.

The SEM image of cancer cells dividing on healthy tissue; today, scientists are searching for a way to eliminate these cells effectively while causing minimal damage to the healthy tissue.

PENETRATION OF NANO-AGENT INTO CANCER CELLS

How would you feel if you were told that there are about 8 billion libraries, each with about 46 bookshelves and a total of 20,000 to 25,000 books? Each library is estimated to contain about 3 billion pages of paper.

This incredible example represents us humans. The library indicates the genome that holds all the essential information for human growth. Currently, as we read this, the world's population is about 8 billion people, each possessing 46 chromosomes. A chromosome, like a shelf of books, contains about 20,000 to 25,000 "books," which in biological terms are referred to as genes. A gene is the functional segment of DNA that holds the instructions for producing proteins. But the story does not end there.

Each gene is made up of parts called introns and exons. The exon is the part that remains after splicing and serves as a basis for protein expression. Introns, on the other hand, undergo splicing during transcription and are subsequently deleted. As a result, they don't exist in the RNA. Notably, the human genome is said to contain 3 billion nucleotide pairs!

By performing other calculations with the same numbers, one can reach even more surprising figures and gain insights into the wonders of our world. In this report, we will examine Omid Farokhzad's achievements and talk about his research priorities.

Over the past 20 years, technological advances have enabled deep and broad access to genomic information. The collective efforts of the genomics community have resulted in the sequencing of over 1 million human genomes and over 10 million human exomes (the collection of all the exons within the genome). Across these efforts, scientists have identified over 1.3 billion genetic variants. Genetic variants are different forms of a gene that cause differences among individuals. Nevertheless, we know very little in terms of the functional importance of these genomic variants.

Ultimately, the information contained in DNA is converted into proteins, creating a new term called proteomes. The proteome is a set of all expressed proteins in a cell, tissue, or organism. Understanding the importance and complexity of the proteome paves the way for future advances in biology, while the role of curious scientists seeking a deep understanding of the proteome becomes more prominent.

But why is it important to analyze these small yet impactful details?
By studying the proteome in a deep and detailed manner, it is expected that we'll identify the reason for the difference among the one million proteins that are produced by approximately 20,000 genes. Such variety has different reasons. Differences can be the result of amino acid changes, changes caused by RNA splicing, or even changes following translation. Studies conducted to better understand proteins are essential and ultimately provide a range of applications for biologists. One of the key applications is our enhanced understanding of biology, which will ultimately help us find new biomarkers for diseases. A biomarker is a biological molecule found in blood, other body fluids, or tissues and is a sign of normal bodily function or of an abnormal condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease.
Biomarkers have significantly contributed to the timely diagnosis (detecting cancer in the early stages), monitoring (observing the response to cancer treatments and assessing treatment effectiveness), and prediction (prevention and early diagnosis) of diseases. They assist doctors and researchers in the diagnosis and monitoring of prognostic conditions and stages of diseases.

PROTEOME HELPS NEW DRUGS KICK IN

Examining other applications of biomarkers in the area of disease monitoring will lead to the discovery of new drugs. Studying proteins enables scientists to create new potential drug targets. Molecules or new proteins can be used as a target for developing new drugs. These discoveries open up new markets in the field of biology, which, in addition to having a positive impact on public health, are also economically beneficial. An important achievement that is a result of the convergence of all three applications of proteomic studies is the role of nanoparticles in therapy.

Biomarkers are essential tools for the early diagnosis of diseases such as cancer. They enable us to predict treatment responses and provide precise information about the development of the disease.

SCAN TO LISTEN

THE LEVERAGE TO BEAT CANCER

Among the most important applications of nanoparticles is the treatment of the emperor of all diseases: cancer. Cancer is one of the greatest medical challenges, and common treatments such as chemotherapy and radiation therapy have numerous side effects. Our trump card against cancer is the magical particles called nanoparticles. The importance of these particles can be examined from several aspects. Crossing biological barriers, precise targeting of cancer cells, drug delivery to specific body parts, and maintaining the health of non-cancerous tissues are among the properties of nanoparticles that bring great hope to scientists and patients.

You may wonder what the connection between the proteome, cancer treatment, and nanoparticles is. The answer to this question lies in Omid Farokhzad's research findings. This question was also answered at the 23rd Science Café, the main focus of which was the use of nanoparticles in cancer treatment. The guest of this session, a bioinformatics professor at Tehran University, introduced the distinctive features of nanoparticles and the challenges of using them.

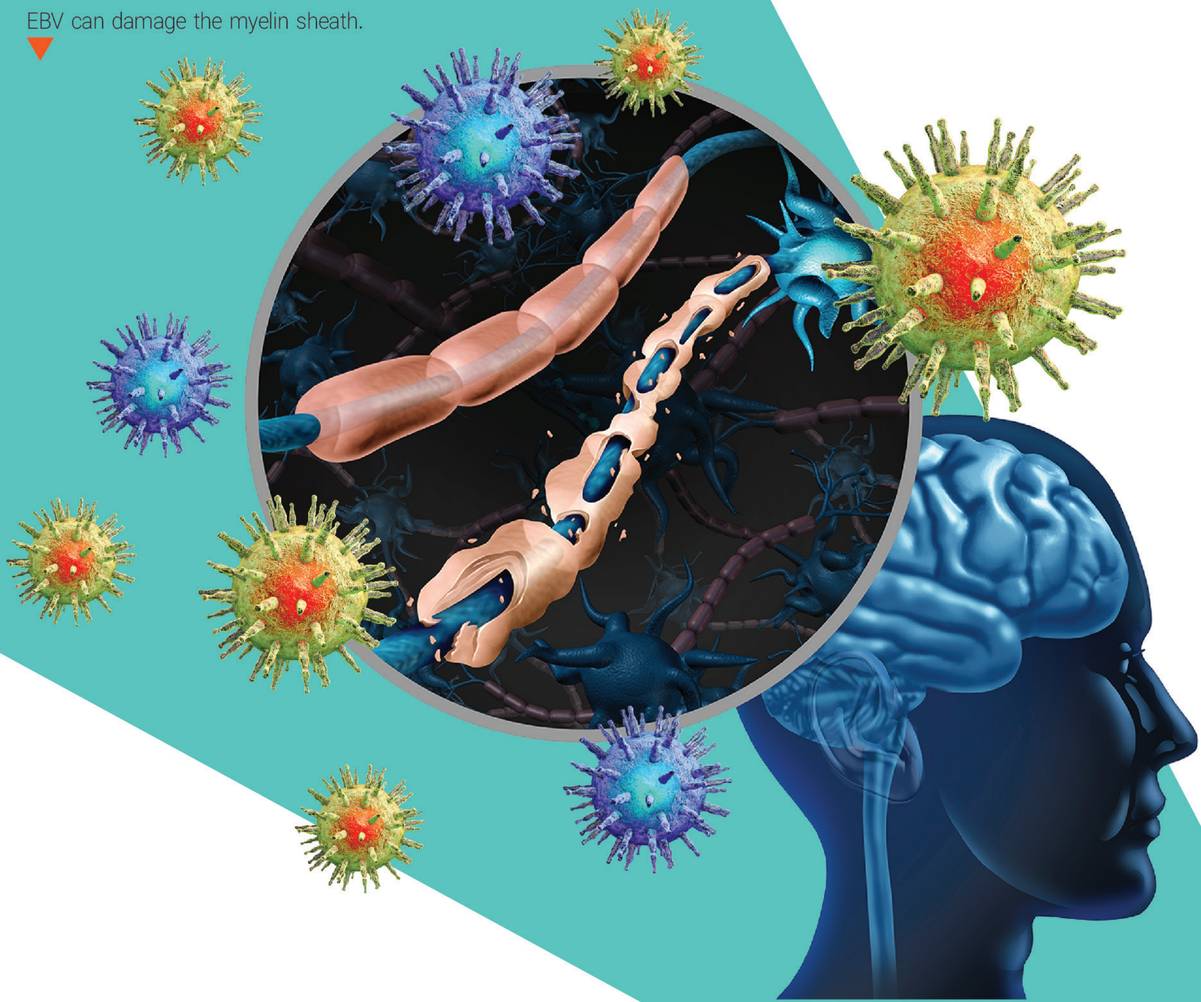
"The body's biological system is very complex, and every molecule or particle injected into the body must be able to pass through the lipophilic coating of cells if necessary. On the other hand, despite their high effectiveness, a number of drugs cannot dissolve well in aqueous environments or flow through the blood due to their high lipophilicity. Therefore, the use of 'smart nanoparticles or carriers' in therapeutic methods becomes important," reviewing Farokhzad's achievements.

"Since nanocarriers are extremely accurate in identifying the target cells and releasing drugs directly in that area, using them for targeted drug delivery to the location of cancer cells can greatly reduce the side effects that come with common methods of treating this disease," he added, pointing out the need to design new treatment methods with fewer side effects. In his research, Farokhzad has shown that specific conditions must be provided when releasing drugs at the target site.

According to these studies, in order for nanoparticles to be able to identify cancer cells, specific functional groups must be placed on them. For example, folic acid—recognized by specific receptors on ovarian cancer cells—can bind specifically to the target cell and release the drug. In some cancers, specific proteins are expressed in target cells; therefore, nanoparticles must be designed to bind to these proteins and release the drug.

Such discoveries result from paying attention to small, yet impactful details in biology such as studying the proteome. Technological advances over the past 5 years have enabled access to deep unbiased proteomics at an unprecedented scale. These advances include the convergence of the Proteograph Product Suite, which enables deep unbiased sampling of the proteome with next-generation mass spectrometers that are faster and more sensitive. It also enables precise detection of proteins and their variants at the peptide level resolution. Our current knowledge has only scratched the surface of the proteome. We may have gained few insights into nanoparticles and cancer, but the iceberg remains to be discovered.

EBV can damage the myelin sheath.



THE FOOTPRINT OF EBV IN MS:

WHEN LIFE ASSERTS ITS POWER ON THE SMALLEST SCALE

With a microscopic view of our surroundings, we step into a realm of the unknown—a world where countless microorganisms thrive, each telling a different story of life's complexity. Among them, viruses, despite their relatively simple structure, remain some of the most enigmatic entities in existence. These beings blur the line between life and non-life. Their survival depends entirely on their unfortunate hosts, and outside their target cells, they are nothing more than dormant genetic packets.

Viruses do not breathe, eat, or even reproduce on their own. Yet, these seemingly harmless entities come to life the moment they find their target cell. By taking full control, they transform it into a factory dedicated to producing more copies of themselves. These cellular factories can be bacterial, plant-based, or from any living organism. But our story begins when human cells fall prey to an opportunistic virus.

INFILTRATING THE HEART OF IMMUNITY

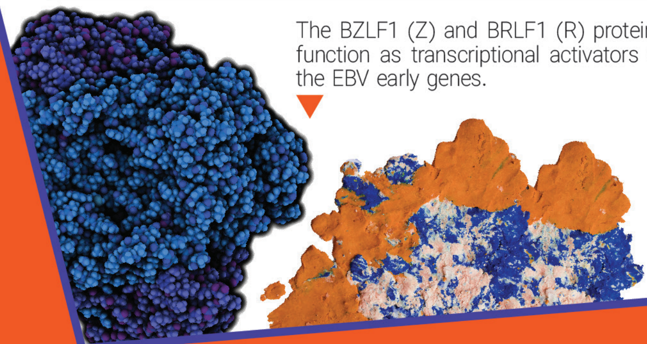
If you were told about a virus that has infected over 90% of people worldwide, what would be your first guess? You might think of viruses like COVID-19 or the varicella-zoster virus (which causes chickenpox). But this time, the discussion is about a different virus—Epstein-Barr virus (EBV). This virus circulates widely among humans, and many of us have encountered it without even realizing it. EBV stealthily enters our bodies through the mouth. Its first stop is the epithelial cells of the throat, where it begins replicating—especially in individuals with a weakened immune system. After this initial phase, the virus moves toward its primary target: B lymphocytes, which are crucial cells of the immune system. However, instead of defending the body, these infected B cells become safe havens for EBV. At this point, the lytic phase begins—a stage in the virus's life cycle characterized by high activity and rapid replication. During this phase, EBV aggressively invades host cells, hijacking them to produce more viral copies. Ultimately, this virus can cause a range of illnesses, from mild infections to severe diseases. Some of the conditions associated with EBV include respiratory infections, infectious mononucleosis, Kawasaki disease, and even certain types of cancer. More broadly, EBV has been linked to oncogenesis (cancer development) and autoimmune diseases, as it can induce genetic changes in cells, leading to uncontrolled proliferation.

One of the biggest challenges with EBV is the complexity of diagnosis and treatment. Since many of its early symptoms resemble those of other viral infections, timely and accurate diagnosis can be difficult. A diagnostic delay increases the risk of long-term complications or progression to more severe conditions.

THE BODY TAKES ACTION

To replicate, Epstein-Barr viruses (EBV) require specific proteins, such as BZLF1 and BRLF1. The production and release of these proteins act as an alarm signal for the immune system, alerting key immune cells—particularly cytotoxic T cells (killer T cells)—to the infection. These veteran soldiers of the immune system recognize and destroy virus-infected cells, preventing further viral spread. This immune battle manifests in some individuals as symptoms like fever, sore throat, and fatigue, creating the classic picture of infectious mononucleosis.

Over time, as the immune system gains partial control, most of the virus is eliminated. However, EBV does not surrender easily. Instead, the remaining viruses enter a latent phase, stealthily hiding within B lymphocytes, where they lay low and strategize their next move.



The BZLF1 (Z) and BRLF1 (R) proteins function as transcriptional activators of the EBV early genes.

FROM A SIMPLE INFECTION TO A COMPLEX DISEASE

EBV is a silent and mysterious guest, often lingering in the body for years without causing noticeable symptoms. However, recent research has uncovered a disturbing possibility—this virus may contribute to the development of severe diseases, including multiple sclerosis (MS).

MS is an autoimmune disease, meaning that the immune system mistakenly identifies the body's own cells as enemies and attacks them. In this case, the central nervous system (CNS) becomes the battleground, and the mistaken targets are oligodendrocytes—cells responsible for supporting and insulating nerve fibers. The resulting inflammation and damage disrupt neural communication, leading to serious neurological impairments.

The exact cause of MS remains unknown, but researchers believe it results from a combination of genetic and environmental factors. Among the potential environmental triggers, EBV has been a major focus of scientific investigation.

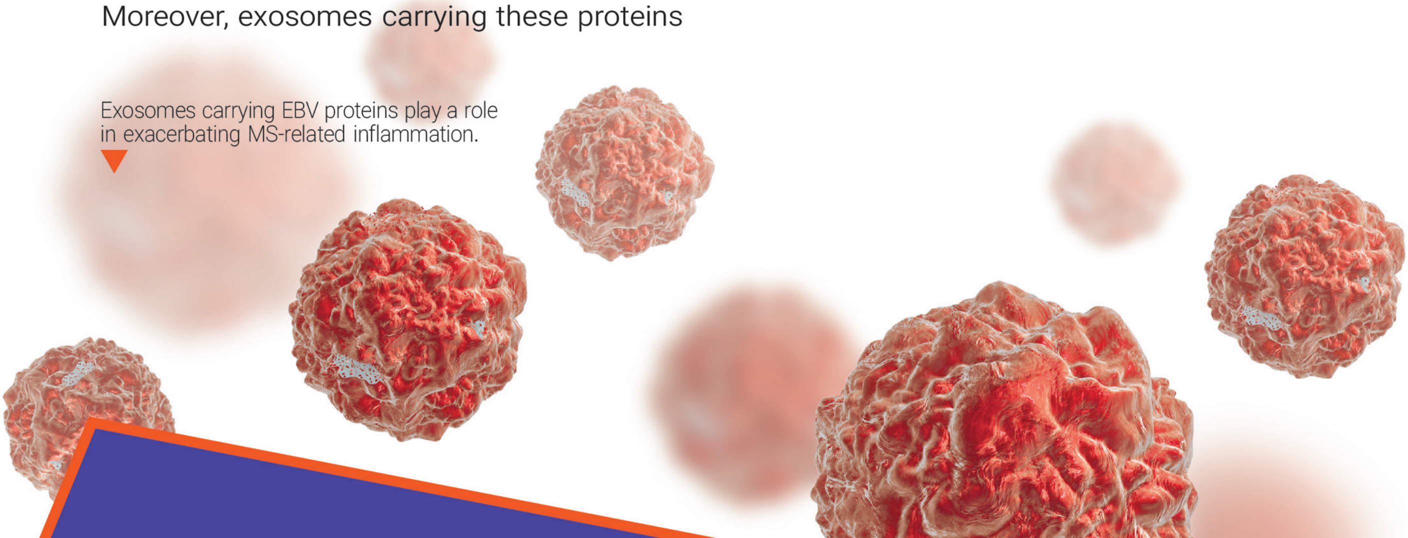
Samia Khoury, a leading MS researcher, has extensively studied the role of EBV in MS pathogenesis. She states: "There is a significant association between Epstein-Barr virus positivity and the risk of developing MS."

A LOOK AT SAMIA KHOURY'S RESEARCH

Khoury's scientific research seeks to unravel complex mysteries by focusing on the study of exosomes in the serum of MS patients. Exosomes are tiny particles (about 30 nanometers in diameter) that act as microscopic messengers, transferring biological molecules—such as proteins and lipids—from one cell to another.

Regarding the exosomes found in MS patients, Khoury states: "We discovered that the serum exosomes of MS patients, especially during active disease phases, express Epstein-Barr virus (EBV) proteins. Moreover, exosomes carrying these proteins were able to activate monocyte-derived macrophages outside the cells."

In other words, the presence of EBV proteins such as EBNA1 and LMP1 in the exosomes of MS patients indicates that the virus is active within their bodies. Furthermore, the findings revealed that these EBV-positive exosomes trigger the release of cytokines—immune signaling molecules—from macrophages, a type of immune cell. This amplifies inflammation, ultimately contributing to the development and progression of MS.



Exosomes carrying EBV proteins play a role in exacerbating MS-related inflammation.

EXPLORING OTHER POSSIBLE MECHANISMS LINKING EBV TO MS

One of the proposed mechanisms by which Epstein-Barr virus (EBV) may contribute to multiple sclerosis (MS) is molecular mimicry. In this process, due to the similarity between EBV proteins and the body's own proteins, the immune system becomes confused. When it produces antibodies against the virus, these antibodies may mistakenly attack the body's own proteins.

For instance, BFRF3, a protein found in the EBV viral envelope, closely resembles Septin-9, a crucial human protein involved in cell structure and function. As a result, when the immune system encounters EBV, it generates antibodies against BFRF3. However, due to their similarity, these antibodies may also target Septin-9, leading to the destruction of supportive cells in the nervous system and increasing the risk of MS.

Another proposed mechanism is abnormal B cell activation. EBV can manipulate B lymphocytes using proteins like LMP1 and LMP2A. These viral proteins mimic normal immune signals, tricking B cells into excessive growth and replication. The consequence is the production of a large number of abnormal or dysfunctional B cells, which may contribute to autoimmune diseases like MS.

Additionally, EBV can cause indirect damage. When immune cells become highly activated to combat the virus, they may unintentionally harm nerve cells. This situation is comparable to a battle where friendly fire damages the body's own structures, further fueling the inflammatory process associated with MS.

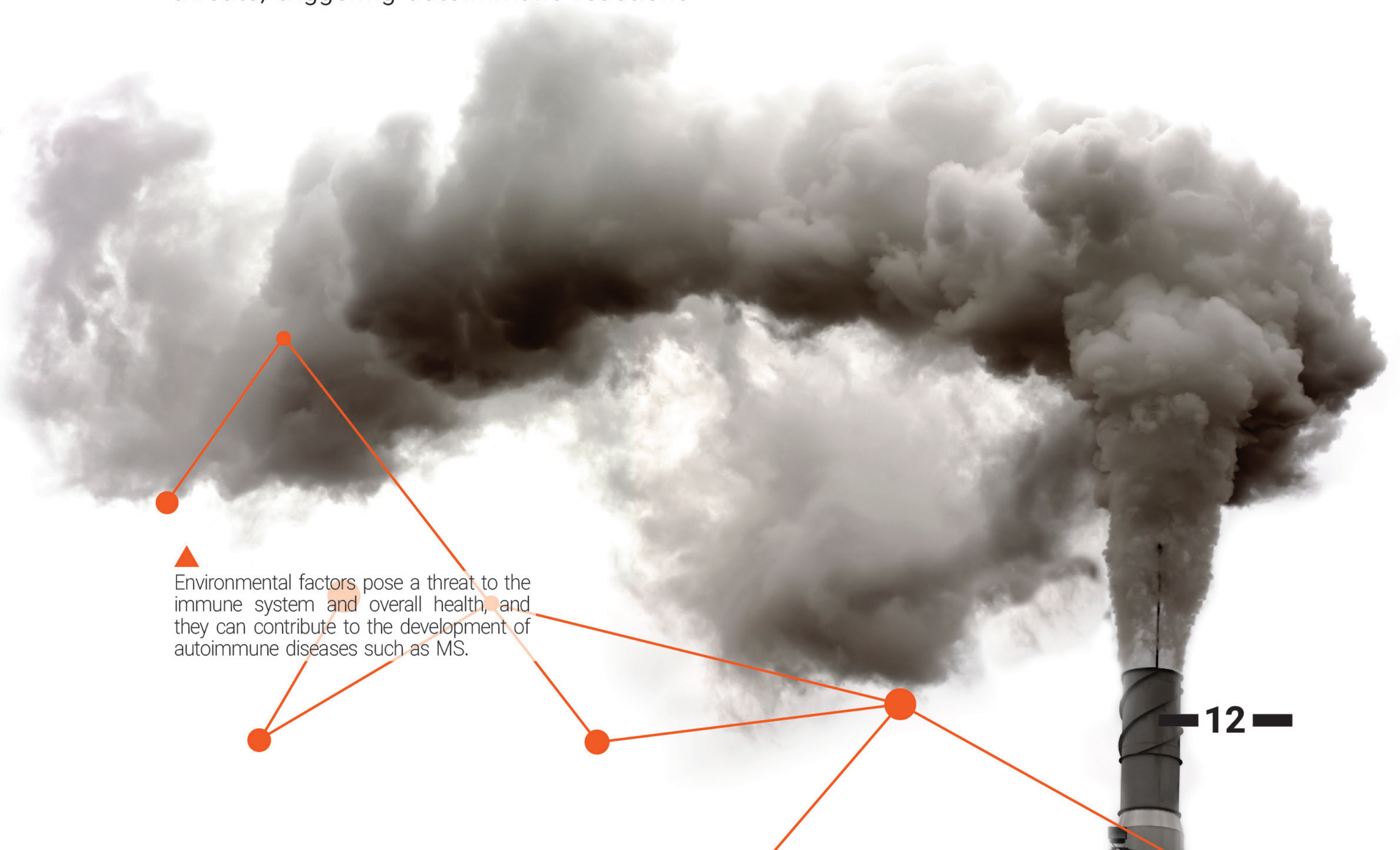
THE MYSTERY OF IMMUNITY

If nearly everyone is infected with EBV, why do only a small percentage develop multiple sclerosis (MS)? As previously mentioned, MS is influenced by a wide range of genetic and environmental factors, meaning EBV alone cannot fully explain its development.

For example, some individuals carry defective versions of certain genes, such as those involved in producing HLA (human leukocyte antigen) proteins. HLA proteins display cellular proteins on the cell surface, acting as an immune surveillance system. If a cell contains abnormal proteins—due to infection or mutations—HLA presents them as a warning signal to the immune system. However, mutations in HLA genes can cause the immune system to mistakenly recognize the body's own proteins as threats, triggering autoimmune reactions.

Beyond genetics, environmental factors like vitamin D levels, smoking, and geographical location also play significant roles. EBV infection is only one piece of this complex puzzle. For MS to develop, a unique combination of genetic predisposition and environmental triggers must align. These intricate interactions explain why some individuals with EBV remain completely healthy while others develop one of the most serious autoimmune diseases.

While the link between EBV and MS still requires further research, each new discovery brings us closer to understanding and combating the disease. Samia Khoury's research not only sheds light on this complex relationship but also paves the way for more targeted treatments and potential vaccines. Perhaps one day, not just MS but many other diseases will be fully controlled, freeing future generations from the shadow of these health threats.



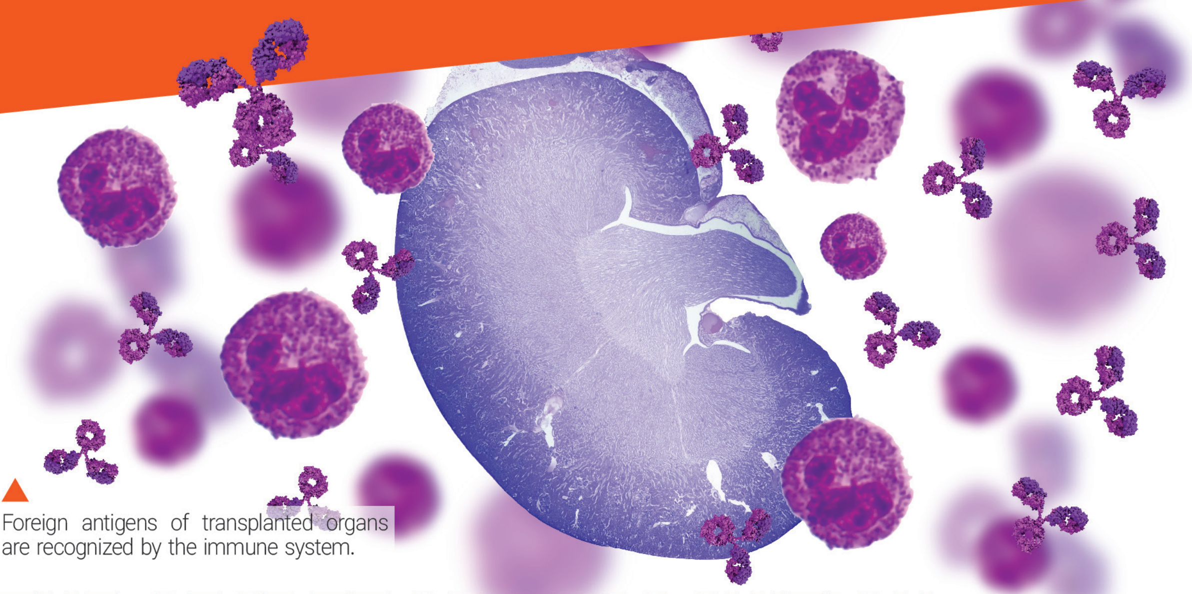
Environmental factors pose a threat to the immune system and overall health, and they can contribute to the development of autoimmune diseases such as MS.

A HIDDEN BATTLE WITHIN THE BODY

Organ transplantation, one of the most advanced medical treatments, offers patients with organ failure a second chance at life, restoring the function of vital organs like the heart, kidneys, liver, and lungs. Among these, kidney transplantation is the most common. In recent years, the number of transplants has increased, with significant advancements having been achieved in the field. Most transplants are allogeneic. This type uses transplants from someone other than the patient with similar genetic characteristics (except an identical twin). A major challenge in allogeneic transplantation is the immune system's reaction to the new organ, which can lead to its rejection. To prevent this, patients have to continuously take immunosuppressive drugs, which help the body accept the new organ but weaken the immune system and increase the risk of infections and complications such as high blood pressure and kidney damage.

THE IMMUNE SYSTEM: PROTECTOR OR ATTACKER?

The body's immune system acts as an army, defending it against external entities such as viruses, bacteria, and even transplanted organs. When an organ from a donor is transferred to the recipient's body, the immune system has to decide whether to accept it as a new part of the body or identify it as a threat. In most cases, the immune system naturally identifies the transplant as a danger, causing a reaction called transplant rejection. The rejection signifies that the body has identified the transplanted organ as foreign and has started attacking it. Such an attack can seriously damage the organ, disrupt its function, and damage the recipient's body.



Foreign antigens of transplanted organs are recognized by the immune system.

THE SECRET OF RECOGNITION

The immune system employs several mechanisms to identify threats, one of the most important of which is using antigens. Antigens are special molecules that enable the immune system to identify threats. They are typically found on the surface of the major histocompatibility complex (MHC) molecules, which help the immune system distinguish between "self" and "non-self." For example, if the host's MHC molecules do not match those of the transplanted organ, the immune system gets alarmed and initiates a defensive response against it. The immune system's reactions are highly complex, mostly caused by the recognition of molecular differences among various tissues. To put it succinctly, the greater the match between MHC molecules, the lower the chances of rejection and the higher the chances of organ survival. During the process of assessing compatibility, dendritic cells, known as the "messengers of the immune system," collect antigens from the transplanted organ and send them to T-cells. This information transfer activates immune responses, ultimately leading to organ rejection. One of the leading scientists working to overcome challenges in organ transplantation is Mohamed Sayegh. Research in this area, particularly by Sayegh, who is a prominent scientist developing therapeutic strategies in the field, promises remarkable progress in medicine. To better understand his contributions, we must first take a step backwards to see how the immune response to the transplant is formed.

UNLOCKING PROTECTION

One of the methods researchers use to prevent transplant rejection is to block the pathways that allow the immune system to initiate an attack on the transplanted organ. One such pathway, highlighted in the research of Mohamed Sayegh, is the CD28-B7 pathway (the interaction of B7 proteins on antigen-presenting cells with the CD28 molecule on immune cells), which plays a role in T-cell activation. When this pathway is blocked, T-cells can no longer become activated and attack the transplanted organ. Sayegh's 1995 research findings showed that using the CTLA4Ig molecule can block this pathway, effectively reducing immune responses and preventing the immune system from attacking transplanted tissues.

DECODING THE MISSING PIECE

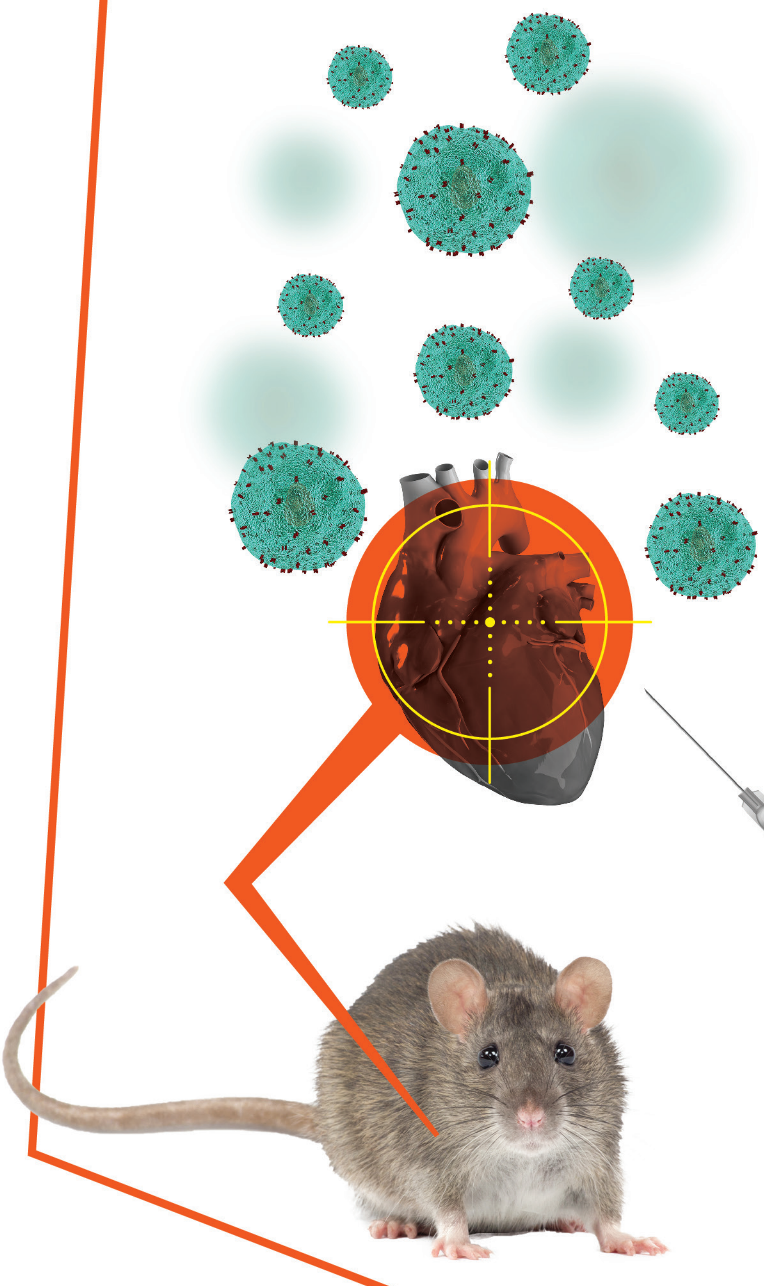
Sayegh's research contributed to the study of other T-cell stimulatory molecules, including members of the CD28 and B7 families. In 2003, he published a paper reporting the complex functions of a new T-cell stimulatory molecule, ICOS (Inducible Costimulator). The CD28 family includes multiple molecules, one of which is CD28 itself. Interestingly, ICOS is also a part of this family, but unlike CD28, which is permanently present on the surface of T-cells, ICOS appears only after T-cell activation and in response to specific stimuli. This makes ICOS a key molecule in the processes that help regulate immune responses.

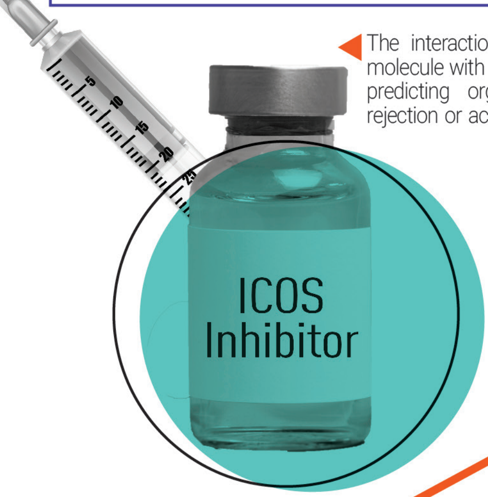
Sayegh has shown that ICOS plays a crucial role in predicting transplant acceptance or rejection and influences how T-cells recognize transplant antigens. This recognition can occur directly, by detecting foreign antigens, or indirectly, after antigens are processed by the recipient's "self" cells and presented to T-cells. Moreover, the interaction between ICOS and similar molecules on the surface of dendritic cells and other immune cells plays a vital role in regulating and boosting immune responses. Research has also shown that inhibiting ICOS during the early or late stages of transplantation can affect organ survival and acceptance.

SHUTTING DOWN THE ATTACK

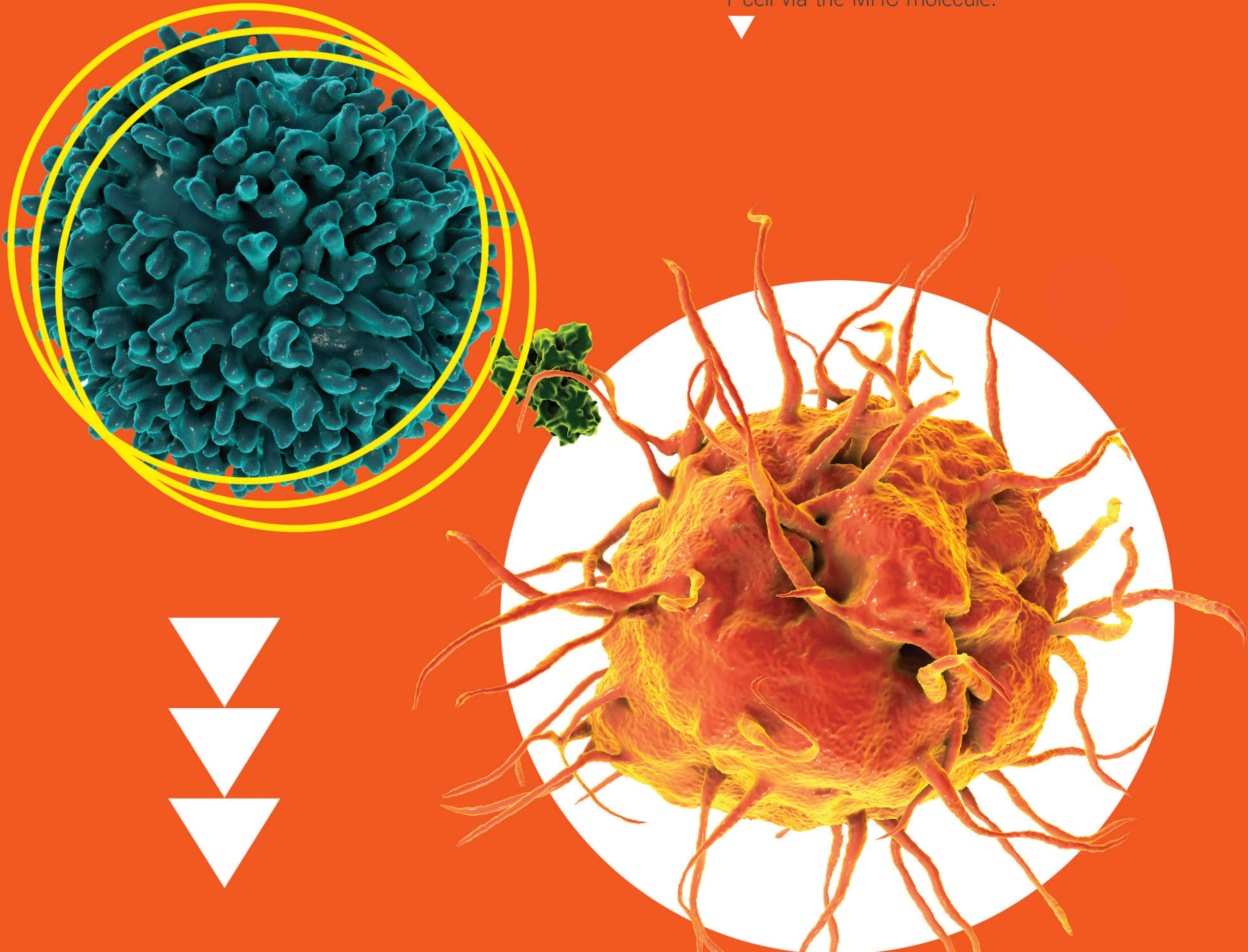
As mentioned earlier, after an organ transplant, T-cells can attack and reject the transplanted organ. Also, ICOS is a key molecule that strengthens immune responses. To study this pathway in detail, Sayegh's research team conducted experiments using animal models, in which new hearts were transplanted into mice. They inhibited the ICOS pathway at two different time points. Early inhibition led to severe immune reactions and quick rejection, while late inhibition reduced inflammation and increased the chance of transplant acceptance.

When the ICOS pathway is blocked, T-cells can no longer interact effectively with dendritic cells. This has led recent findings to establish ICOS as a promising therapeutic target, thus enabling the development of new drugs that reduce immune responses through inhibiting this pathway. During clinical trials, these drugs have prevented inflammation in transplanted tissues and reduced the risk of rejection.





The interaction of the ICOS molecule with T cells is key to predicting organ transplant rejection or acceptance.



The dendritic cell is presenting the antigen to the T cell via the MHC molecule.

FROM TISSUE COMPATIBILITY TO TRANSPLANT SUCCESS

The major histocompatibility complex (MHC) in humans is known as the human leukocyte antigen (HLA). HLA testing is one of the most important tools that enables doctors to increase the chances of transplant success. By analyzing tissue compatibility between donor and recipient through MHC molecule identification, these tests help predict whether the recipient's immune system will reject the transplanted organ or accept it. The more precise the match, the lower the risk of rejection and the greater the chances of transplant survival.

One of the major challenges in organ transplantation is that each person's immune system reacts differently to transplanted organs due to genetic differences. Some individuals' immune systems may easily accept the transplanted organ, recognizing it as part of the body, while others may quickly reject it as a threat and start an immune attack. Therefore, advanced and precise testing is essential before transplantation to assess tissue compatibility. Despite significant advancements, organ transplantation remains one of the most complex and challenging medical treatments, requiring deep knowledge of how the immune system interacts with transplanted organs. In general, by inhibiting T-cell activation pathways and reducing the production of harmful antibodies, transplant rejection can be prevented, and immunological tolerance can be strengthened. This approach is particularly important in critical stages of the immune response, including T-cell differentiation, function, and interactions with other immune cells.

According to Mohamed Sayegh, the most fundamental question in this field is: "What are the mechanisms of immunological tolerance, and how can we trick the immune system into accepting a foreign organ without rejection and without immunosuppression?"

UNLOCKING NATURE'S SECRETS

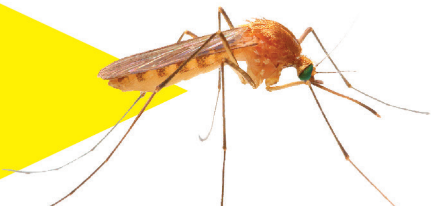
There have been times in our lives when we felt relaxed after drinking a mug of chamomile tea or when that one nasty cold was soothed with a lemon tea. These moments of calm and contentment may have made us appreciate these natural products and think about other benefits we can receive from flowers, fruits, herbs, and spices. We may have asked ourselves: Can natural remedies replace the conventional synthetic methods that we receive when we have an illness? Does the latter need to be altogether discarded, or can both methods coexist and provide us with more effective medicine? We asked for an expert opinion in the field, Muhammad Iqbal Choudhary, to explain these issues. Choudhary enlightened us on nature's healing legacy, his ongoing research on curing "neglected diseases," and the importance of creating a "seamless healthcare system."

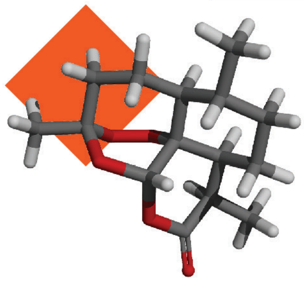
PLANTS:
A TREASURE HOUSE OF FASCINATING MOLECULES

According to Choudhary, since ancient times, humanity has depended on plants for various needs, including food, shelter, and medicine. Many of them have helped humanity to survive against pandemics, epidemics, and various diseases. Over time, human experiences and accumulated wisdom have contributed to the development of traditional medicine. "This collective knowledge of humanity was built over generations, and it is a treasure that we should never lose," he said. He believes that nature is "the best synthetic chemist" and plants are "the treasure house of fascinating molecules," molecules that have an effective role to play in human well-being and health. Choudhary thinks we have a responsibility toward nature to conduct research on traditional plants.

So, what he and his team have been doing is analyzing plants used in traditional medicine and trying to understand their chemistry and how they function with biological systems. They study the interaction of plant products with the biological system and manifest their therapeutic activity.

In simple words, plants produce many molecules to defend themselves against extreme weather, insects, infections, and other things. These are organic compounds that are made of carbon, hydrogen, sometimes nitrogen, and other elements like oxygen. These molecules have different structures, shapes, and sizes. He described these compounds as "keys" that unlock disease mechanisms. They help us control several disease processes and treat various diseases.





The chemical structure of Artemisinin, a drug isolated from the plant Artemisia, used to treat malaria—a disease spread by the bite of female Anopheles mosquitoes.

WHERE MODERN MEDICINE FAILS, TRADITIONAL MEDICINE ENTERS

Choudhary's specific interest has been identifying those compounds that can help in the treatment of prevalent and neglected diseases. This scientist explains that "there are so many diseases which cannot be treated by modern medicine, but it's possible to use plant constituents on natural products for the treatment of those diseases, as we [our predecessors] have done that in the past."

For example, there was a time when malaria was at its peak, infecting and killing large numbers of people. Effective treatments for this disease, however, were provided thanks to artemisinin, a key drug used in every cure of the disease. Choudhary mentioned that artemisinin was isolated from a plant called Artemisia by the Nobel Prize winner Tu Youyou. Other examples include Taxol, an anti-cancer drug, and morphine, a drug used to reduce chronic pain.

"So, there are many molecules that are present in nature and can help us improve the quality of life," he maintained. So far, his team has isolated natural products that show promise in treating prevalent and neglected diseases like leishmaniasis and neurological disorders such as Parkinson's and Alzheimer's. Choudhary contended that these diseases cannot be treated by conventional medicine; they can just be controlled and managed. This is a serious issue with today's conventional medicine, also called biomedicine, allopathy, or Western medicine. For example, patients afflicted with high blood pressure, diabetes, dementia, or chronic pain are provided with medicines that only manage their disease. For many of such prevalent diseases, there are no treatments, and people have to live with them for the rest of their lives. So, he believes, "There is no single system or a medicine which can treat all diseases."

WHAT DOES A "SEAMLESS HEALTHCARE SYSTEM" LOOK LIKE?

Now, the question comes to mind: Is traditional medicine effective or reliable? The answer is yes. Through years of research, Muhammad Iqbal Choudhary has proven that human wisdom and human experiences, which are called traditional systems of medicine, complementary systems of medicine, or alternative systems of medicine, provide very good and important treatment. These include biomedicine, complementary medicine, the Persian system of medicine, traditional Chinese medicine, traditional Ayurvedic medicine, and traditional Unani medicine, all of which are well-developed systems of medicine. He strongly believes that after being meticulously tested and fulfilling the scientific criteria of efficacy and safety, traditional medicine needs to be integrated into the healthcare system, creating a "seamless healthcare system." As a result of such assimilation patients have the opportunity to be treated with the best medicine available, regardless of what system they belong to.

Choudhary points out that at the end of the day, what is truly important is that patients get treated and be relieved of pain, benefiting from the best approach possible. He believes that the world is going towards an integrated healthcare system and integrated medicine, combining all of these human healing practices and knowledge.

TACKLING DISEASES THE WORLD IGNORES

Currently, Choudhary is focusing on inventing treatments for neglected tropical and neurological diseases. "We are using nature's molecular diversity and the traditional knowledge with science to develop medicine which is effective and safe and that can be used by a large number of people for diseases with unavailable treatments," Choudhary observed.

Neglected diseases, also called "poor man's diseases," are prevalent in poor regions of the world. They include schistosomiasis, leprosy, leishmaniasis, Chagas disease, etc. According to Choudhary, they receive no attention or very little attention from pharmaceutical industries since it is not financially viable for pharmaceutical companies to invest in creating drugs for them. Choudhary and his team have been conducting research on a neglected disease called leishmaniasis, a parasitic and potentially deadly disease that is spread through the bite of a sand fly. They are also working on identifying herbal products or natural compounds that can prevent the onset of neurological diseases such as Alzheimer's disease, Parkinson's disease, and epilepsy and lower their symptomatic burden.

Their formulation against Parkinson's is currently under clinical trials. They have also isolated compounds that can improve the symptoms of Alzheimer's and have registered multiple patents.

A groundbreaking discovery by his team is ISOX, a new plant-derived molecule that has potent anti-epileptic properties. This isomeric mixture is one of the most effective anti-epileptic compounds and offers a potential treatment for epilepsy, particularly in cases resistant to Western medicine.

WHAT'S PLAN B IF THE MEDICAL INDUSTRY SHUNS YOUR PRODUCT?

Carrying out research and putting it into practice comes with challenges. A challenge that their team has faced is the lack of funding due to the pharmaceutical industry's focus on managing diseases rather than treating them. A second and closely related issue is that even after they are produced, the industry shows a complete disregard for traditional medications as they do not seem viable enough or commercially feasible.

He believes that the challenges of funding and pharmaceutical disinterest can be easily overcome if "the developing world, particularly the Muslim world, unite their resources and knowledge and try to move into the pharmaceutical sector, developing their own pharmaceuticals, biopharmaceutical, and vaccines." Choudhary finds research exciting, especially when working with nature, as it often leads to unexpected discoveries. He stated that these discoveries drive research forward and motivate scientists with the ultimate goal of benefiting humanity.

He ended his remarks by offering a piece of advice to young scientists and science communicators: "Always remember that science should benefit humanity. Your discoveries should improve lives and make the world more sustainable and broadly beneficial."

Regenerative medicine can replace human tissues and organs to restore normal function.

THE FUTURE UNDER PRINT

Nowadays, the shortage of transplantable organs has become a critical challenge in the medical field. Despite advancements in medical science and numerous preventive measures, thousands of patients worldwide still require transplants of vital organs such as the heart, kidneys, or liver due to various reasons, ranging from severe injuries to chronic diseases and congenital disorders. In the 24th Science Café, titled "The Future of Regenerative Medicine and Tissue Engineering," recent developments in these emerging fields and the limitations of pre-existing technologies before their emergence were discussed.

In organ transplantation, finding a suitable donor is one of the most challenging and time-consuming stages of treatment. It is important to note that even in successful transplant cases, numerous challenges persist. Transplant recipients typically need to take immunosuppressive drugs for the rest of their lives. These medications increase the risk of severe infections and impose significant financial burdens on both patients and healthcare systems. Additionally, the body's immune system may recognize the transplanted organ as something foreign and reject it.

As a result, the complexity and high costs of transplantation procedures have made this treatment inaccessible to many patients. Tissue engineering has emerged as one of the most promising solutions to address these challenges. By utilizing techniques such as tissue culture, stem cells, and 3D bioprinting, this technology aims to create organs and tissues that can function similarly to natural human tissues. By reducing transplantation-related complications, it seeks to improve patients' quality of life.

THE ART OF CREATION FROM SCRATCH

In modern laboratories, scientists like Ali Khademhosseini are turning a visionary dream into reality—one that could revolutionize the treatment of diseases forever: creating living tissue from scratch. Khademhosseini has developed nanohydrogels and bioinks, which serve as fundamental building blocks for fabricating and cultivating tissues in processes such as bioprinting. These efforts fall within the domain of tissue engineering, a field dedicated to naturally replacing damaged organs and tissues. Tissue engineering lies at the intersection of advanced biology, cutting-edge materials science, and advanced engineering technologies. Scientists in this field meticulously cultivate cells in precisely controlled laboratory environments, guiding them toward the formation of structures that are virtually indistinguishable from natural tissues in both architecture and function.

With this technology, traditional methods such as organ transplantation or simple prosthetics are being replaced by more sustainable and biocompatible solutions. The use of biocompatible materials, bioprinting, and advanced cell culture techniques enables patients to receive healthy, living, and fully natural tissues.

Ears and noses produced using bioprinting technology are examples of engineered tissues.

THE SCAFFOLD OF LIFE

To create fully functional living tissues, scientists utilize three-dimensional biological scaffolds—structures made from biocompatible materials that act as a robust framework, providing an environment similar to the natural body for cell growth, proliferation, and organization. These scaffolds not only support tissue development but also grant it its initial shape and structural integrity. Beyond scaffolds, the use of specialized natural and synthetic materials that are chemically and mechanically optimized to match human tissues is crucial. These materials—including compounds like collagen, hyaluronic acid, or biopolymers—create the ideal microenvironment for sustaining and nurturing living cells.

Another crucial element in this process is cell culture. Researchers utilize stem cells, adult cells, or engineered cells to generate the necessary cellular population for tissue production. These cells are cultivated in advanced laboratories under precisely controlled conditions of temperature, humidity, and nutrient composition to develop healthy, living, and fully functional tissues.

The engineered miniature liver is an example of progress in creating transplantable organs using bioprinting.

Bioprinting is used to produce functional organs and tissues for medical purposes.

THE PRINTER OF THE LIVING WORLD

Bioprinting technology is an innovation in tissue engineering. By employing specialized bioinks and high-precision printing techniques, this technology has enabled the fabrication of structures that not only visually resemble natural body tissues but also replicate their biological functions. Bioinks, composed of living cells and biocompatible materials, serve a dual role: They create robust physical structures while also providing an optimal environment for natural cell growth. These bioinks enable organized and cohesive cell development, allowing cells to mature and integrate into a functional, tissue-like architecture.

One of the key applications of this technology is the production of artificial cartilage and bone, which play a crucial role in treating joint diseases. These engineered tissues provide a biocompatible alternative to traditional metal and synthetic prosthetics. Additionally, tissue engineering has made significant strides in developing complex organs, such as artificial kidneys and livers.

While these bioengineered organs are still in the early stages of development, advancements in this field hold promise for future treatments of chronic conditions such as kidney failure and liver disease. Another successful and practical application of tissue engineering is the production of artificial skin for burn victims. These bioengineered skin grafts enhance wound healing and significantly reduce the risk of infection.

Another groundbreaking innovation in regenerative medicine is organ-on-a-chip (OOC) technology, a field of research that has also captured the attention of Ali Khademhosseini. This technology, by producing miniature models of human organs and tissues in controlled laboratory conditions, allows scientists to examine cellular and biological responses with unprecedented precision. organ-on-a-chip models provide a platform for the in-depth study of cellular responses, paving the way for the production of larger and more complex tissues.

THE WINDING ROAD TO ARTIFICIAL ORGANS

Despite the remarkable advancements and numerous benefits of tissue engineering, some of which were mentioned in the 24th Science Café, this field still faces significant challenges that hinder its rapid development and widespread adoption. One of the most critical obstacles is the intrinsic complexity of recreating complex organs such as the heart and kidneys. These organs not only require precise physical reconstruction but also demand accurate replication of complex mechanical and electrical functions to ensure seamless integration with the body's other systems.

Beyond technical hurdles, regulatory approvals and medical licensing also pose significant barriers to the progress of tissue engineering. While technologies like artificial skin and cartilage have successfully received regulatory approval, more complex bioengineered organs remain stalled due to lengthy and costly clinical trials. These extended approval processes often dissuade companies from continuing research and development in this field.

Another major challenge is the high cost of large-scale production. Many of the materials, equipment, and procedures currently used in tissue engineering are designed for laboratory-scale research rather than mass production. Transforming these innovations into an economically viable and widely accessible industry will require substantial investment and the development of infrastructure. Nevertheless, tissue engineering is recognized as a high-potential sector within biotechnology, with significant economic growth potential. The growing demand for advanced, personalized medical treatments is a key driver of this market. In countries with aging populations, the need for organ repair and replacement is increasing rapidly. This demand incentivizes companies in the field to develop innovative solutions that improve treatment efficacy while reducing long-term healthcare costs. However, regulatory compliance complexities remain a major challenge. Organizations like the FDA and international regulatory bodies are still in the process of establishing clear guidelines for tissue-engineered products. The lack of well-defined regulatory pathways creates uncertainty, leading to delays in product development and market introduction.

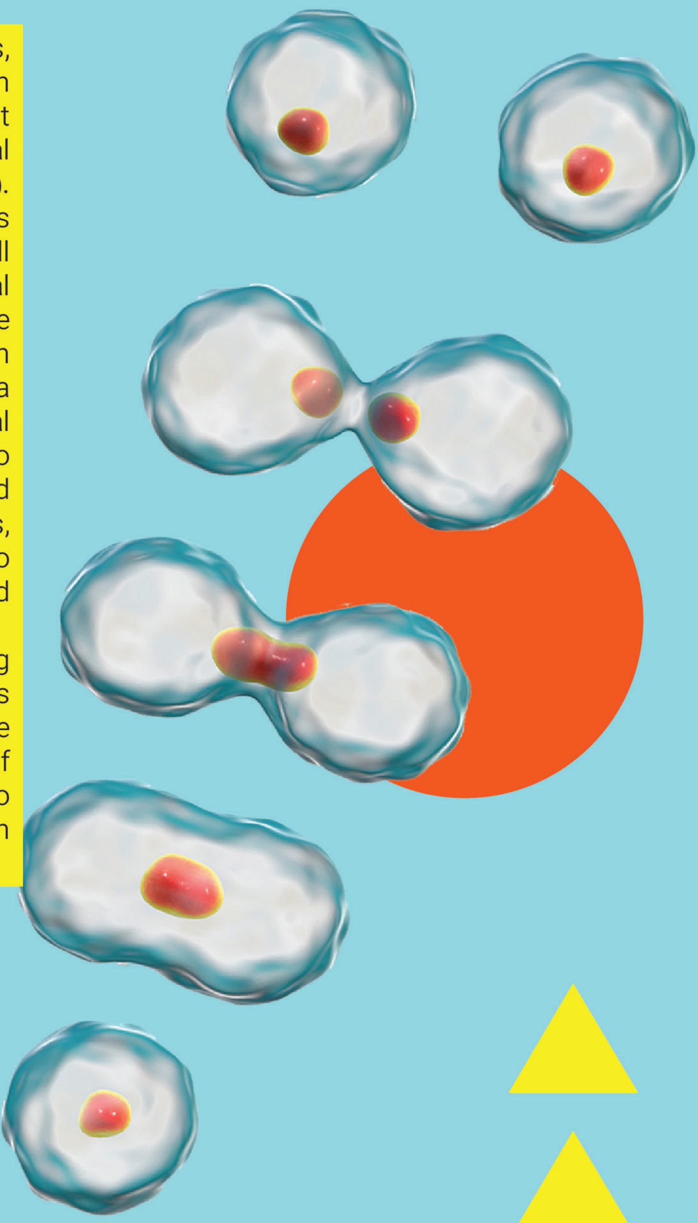
Finally, long-term studies are essential for thoroughly evaluating the functionality and durability of engineered tissues. Even after obtaining initial regulatory approvals, these studies must continue for years. Again, this issue requires long-term investment and meticulous planning.

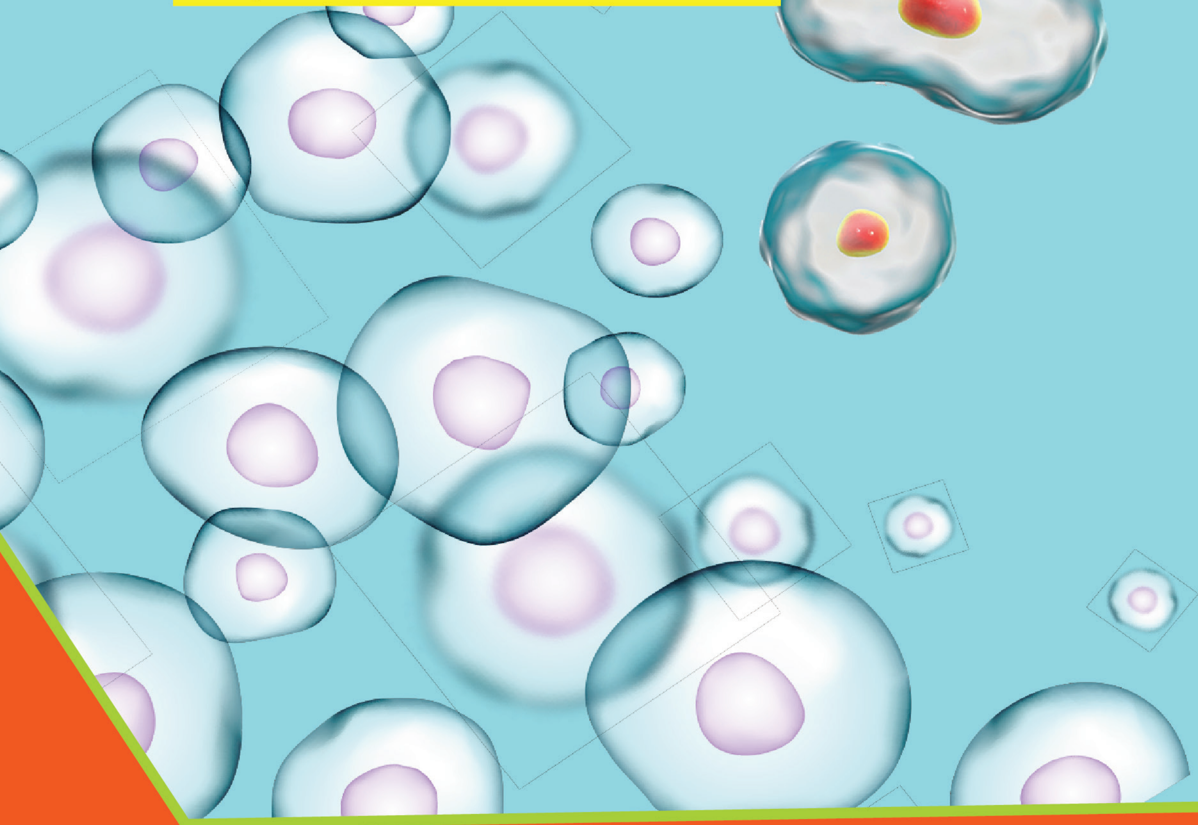
Cell culture and the use of biomaterials are among the most important components in the process of producing engineered organs.

CELLS IN THE EMBRACE OF ALGORITHMS

To achieve breakthrough advancements, tissue engineering must integrate with complementary technologies, the most transformative of which is artificial intelligence (AI) and machine learning (ML). Advanced algorithms can help researchers analyze biological data, precisely predict cell growth patterns, and optimize biomaterial selection for scaffolds, ultimately enabling the design of more efficient artificial organ models. In this pursuit, bioinformatics plays a crucial role. By analyzing complex biological data, this field provides valuable insights into cellular interactions, genetic sequences, and molecular changes. With bioinformatics tools, scientists can predict cellular responses to different conditions and refine tissue and organ design with greater accuracy.

Additionally, genetic engineering is emerging as a crucial complementary technology in this field. Techniques such as CRISPR gene editing enable the precise modification of cellular characteristics, allowing scientists to create engineered cells that flourish in biological environments.





Lab-grown meat is an alternative to traditional livestock farming.

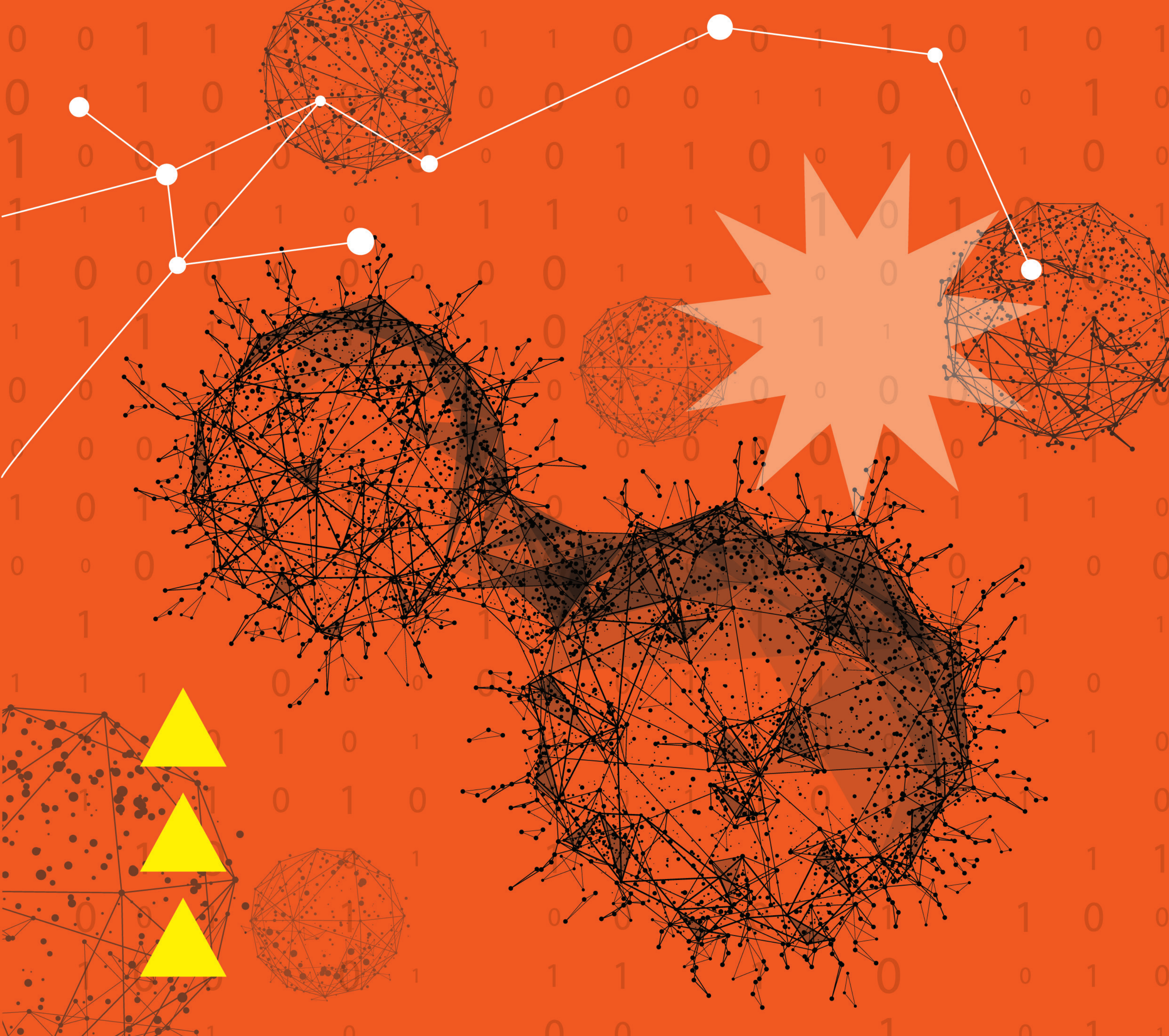
A FARM WITHOUT ANIMALS

The applications of tissue engineering extend far beyond medicine and healthcare, reaching into industries such as food production. One of the most fascinating and controversial examples of this technology is lab-grown meat—real, consumable meat produced through cell culture, bypassing the need for traditional livestock farming and slaughter. By cultivating muscle cells in a controlled laboratory environment, this method offers a sustainable alternative to conventional meat production, significantly reducing environmental impact and resource consumption, while offering a viable solution to the growing global food crisis.

Beyond food production, tissue engineering is revolutionizing agriculture and ornamental plant industries. Advanced plant tissue engineering techniques allow for the mass production of plants with enhanced traits, such as greater resistance to pests, improved crop quality, and even more aesthetically appealing characteristics. This technology not only boosts agricultural efficiency but also enables the cultivation of specialized plants for scientific research, biotechnology, and environmental restoration.

Tissue engineering is no longer just a futuristic concept—it has reached a stage where it is actively revolutionizing treatments for numerous diseases. Recent advancements in bioengineered tissues, biocompatible materials, and cutting-edge medical technologies are shaping a future where precise and reliable organ regeneration becomes a reality. Despite the challenges and obstacles that regenerative medicine still faces, global efforts suggest that tissue engineering will soon become an integral part of everyday life.

Plant tissue culture is a tool for increasing agricultural productivity and producing specialized plants.



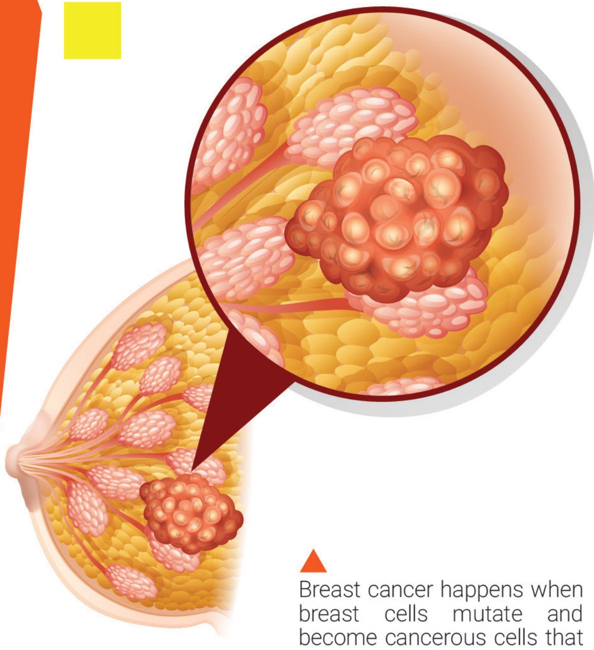
TRANSLATING CANCER CELL BEHAVIOR INTO ELECTRONIC LANGUAGE

A cell is the smallest structural and functional unit of living organisms. It consists of a membrane, genetic material, cytoplasm, and organelles. Cells can grow and divide through a process known as the cell cycle. This division varies depending on its purpose and the type of organism.

The cell cycle is divided into several distinct stages, with specific proteins ensuring the accuracy of the division at the end of some phases. If cells continue to divide indiscriminately beyond the natural cycle, they turn into cancerous cells, which may cluster together to form tumors.

MODERN TECHNOLOGIES IN CANCER DIAGNOSIS AND TREATMENT

According to reports from the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC), over 2.3 million people worldwide were diagnosed with breast cancer in 2020. Among various types of cancer, breast cancer is the most common in women, though men are also at risk. This report covers just one type of cancer. In modern medicine, effective diagnosis and treatment of cancer remain among the greatest challenges. This complex disease demands innovative solutions based on cutting-edge scientific advancements.

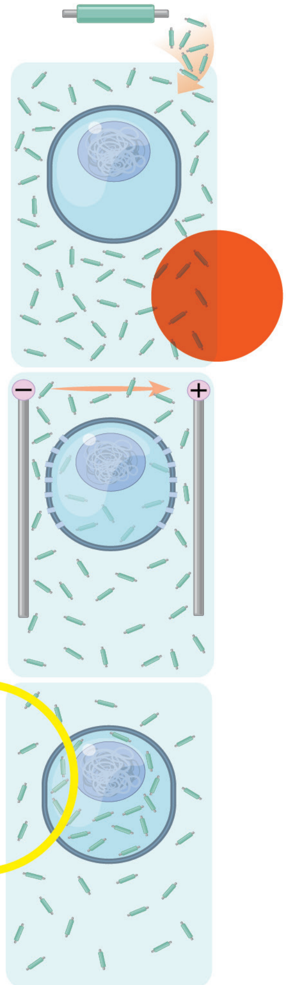


Breast cancer happens when breast cells mutate and become cancerous cells that multiply and form tumors.

THE INTERSECTION OF ELECTRONICS AND MEDICINE

There are two approaches to diagnosing and treating diseases in medicine. The first one is the biochemical approach, which serves as the foundation of medical science. The second one, emerging from successive technological revolutions, is the integration of medicine and electronics, known as bioelectronics.

Mohammad Abdolahad is a pioneer in bioelectronics in Iran. He is a graduate of electrical engineering; however, he entered this interdisciplinary field through collaboration with medical science experts, achieving significant breakthroughs in cancer diagnosis and treatment. In an interview with Observatory, Mohammad Abdolahad describes his work as follows: "My colleagues and I tried to translate the series of events that occur in healthy and cancerous cells into electronic language because everything has signals, even cancer cells." What matters in this approach is understanding the protocol that generated the signal. Only then will the translation demonstrate its effectiveness, and we can perform an accurate analysis of the signal and conclude the effectiveness of our hypothesis.



Electroporation uses electric pulses to create temporary pores in the cell membrane, delivering the molecules to the cells.

HUNTER OF HIDDEN CANCER CELLS

The migration of cancer cells, or metastasis, is one of the greatest challenges in cancer treatment. This cellular migration is the primary cause of recurrence in many cancers. Doctors and researchers strive to detect metastasis with high speed and precision to improve patient survival rates. For example, tumor metastasis is the main cause of 90% of deaths from breast cancer; therefore, determining its extent during treatment is of great importance.

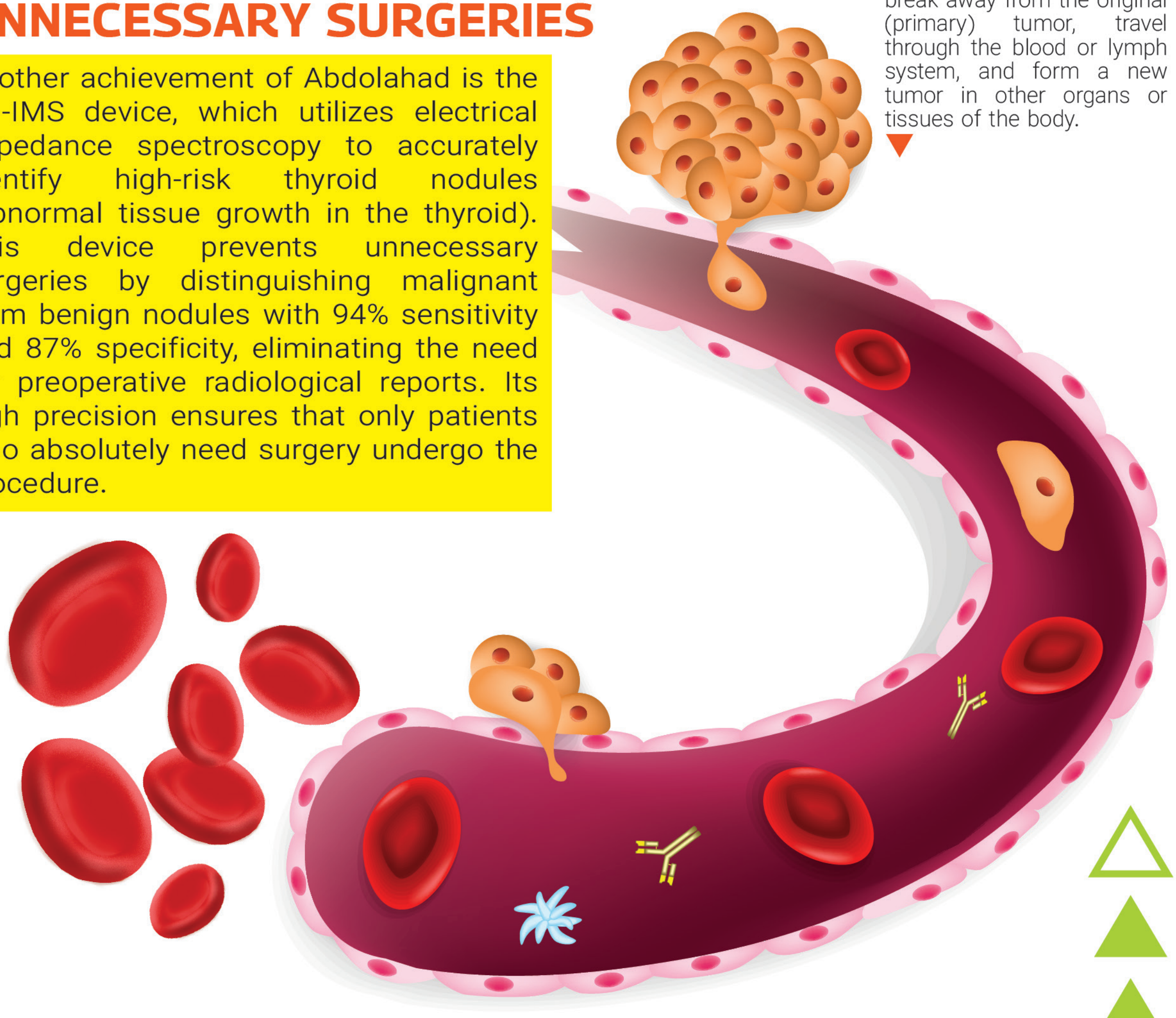
One of Abdolahad and his colleagues' innovations is the CDP probe, a device that identifies residual cancer cells during surgery and assesses tumor metastasis, thus playing a key role in selecting treatment strategies. Another method used in surgery is frozen section analysis, which allows for tissue sampling to determine lymph node involvement—an essential factor in diagnosing cancer metastasis. However, frozen section analysis has only 75% accuracy and is costly and time-consuming.

In contrast, the CDP probe offers real-time detection, enabling surgeons to determine whether removed lymph nodes are cancerous. This feature aids the surgeon to make better decisions throughout the operation. Moreover, it can prevent recurrence by identifying contaminated tumor margins or those suspected of being contaminated. The device is particularly useful for hospitals lacking frozen section facilities.

SAY GOODBYE TO UNNECESSARY SURGERIES

Another achievement of Abdolahad is the TN-IMS device, which utilizes electrical impedance spectroscopy to accurately identify high-risk thyroid nodules (abnormal tissue growth in the thyroid). This device prevents unnecessary surgeries by distinguishing malignant from benign nodules with 94% sensitivity and 87% specificity, eliminating the need for preoperative radiological reports. Its high precision ensures that only patients who absolutely need surgery undergo the procedure.

In metastasis, cancer cells break away from the original (primary) tumor, travel through the blood or lymph system, and form a new tumor in other organs or tissues of the body.



The Cancer Diagnostic Probe (CDP) is a real-time diagnostic system that serves as a complementary surgeon-assisted tool.

INHIBITION OF CANCER CELL PROLIFERATION

The early detection of cancer metastasis or micrometastasis represents a significant therapeutic challenge in oncology. Timely identification is critical for improving patient survival rates. The Metas-Chip device, a groundbreaking innovation by Abdolahad, is a microelectronic biochip engineered to detect micrometastases in biopsy specimens obtained from patients. This device is capable of identifying circulating tumor cells (CTCs) that have disseminated from the primary tumor site.

The device employs specialized traps (sensors) derived from human umbilical vein endothelial cells (HUVECs) to capture cancer cells. In this process, metastatic cells within the biopsy sample are selectively attracted to the HUVECs. After attaching to these cells and inducing measurable changes in the electrical response, they are detected by the device. This enables clinicians to accurately determine the presence or absence of high-risk metastatic cells and implement appropriate treatment methods.

ELECTROPORATION AND TREATMENT-REFRACTORY CANCERS

For patients with cancers resistant to conventional therapies, innovative approaches are essential. One of these methods is irreversible electroporation (IRE), which was introduced by Mohammad Abdolahad. This technique is particularly effective in treating liver metastases, skin, and pancreatic cancers. The procedure involves applying an electric field to create nanoscale pores in the membranes of cancer cells. These pores significantly enhance the intracellular uptake of chemotherapeutic agents, such as bleomycin, by up to 700-fold, leading to targeted cancer cell apoptosis. This method is highly effective, spares healthy tissues, and improves therapeutic precision. As an advanced technology, electroporation holds great promise for improving the life quality of patients with treatment-refractory cancers.

Mohammad Abdolahad began his academic journey in electrical engineering, but his interdisciplinary vision propelled him to the forefront of modern biomedical technologies. Abdolahad and his colleagues have been able to prevent limb amputations in many patients with advanced cancers. Additionally, his innovations have been effective for patients deemed ineligible for surgical intervention. Abdolahad emphasizes the importance of fostering multidisciplinary education and investing in translational research to advance cancer biology understanding and enhance clinical care.

UNDER THE LENS

AHMED E. HASSAN

AND THE ART OF MINING SOFTWARE REPOSITORIES

IF YOU WANT TO GO FAST,
GO ALONE ;

IF YOU WANT TO GO FAR, GO TOGETHER.

ON THE VERGE OF A HISTORICAL TURNING POINT IN SOFTWARE EVOLUTION

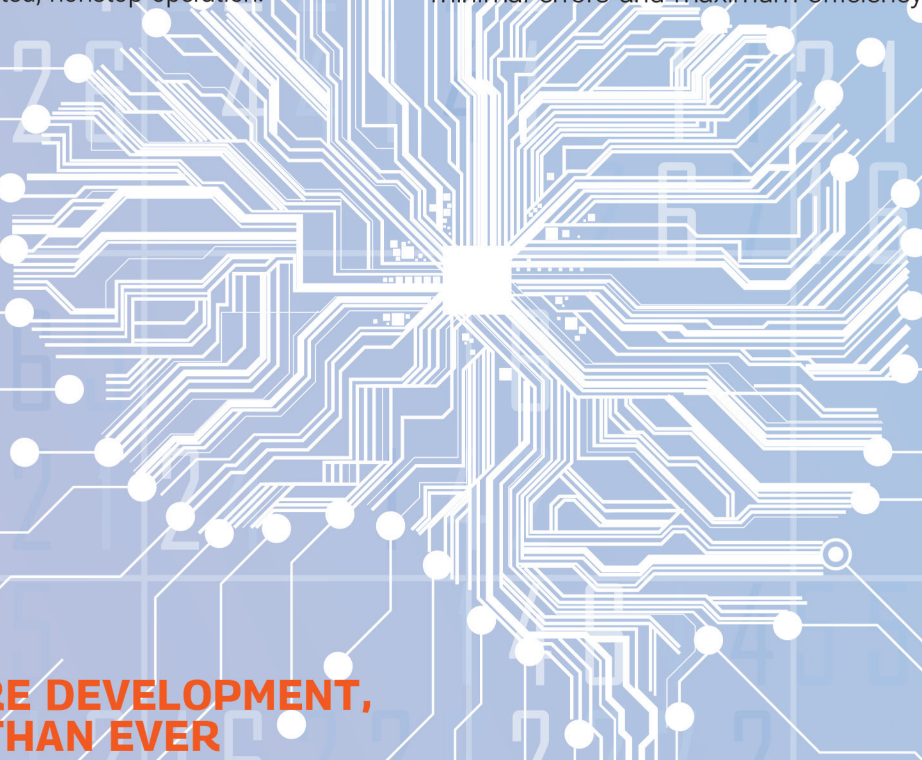
In a world where technology advances at a breakneck pace, software has become the beating heart of digital transformation. Ahmed Hassan, one of the most influential researchers in software engineering and artificial intelligence, has revolutionized the way software is built, maintained, and optimized. Using artificial intelligence (AI), Hassan has provided solutions that can make programming faster, smarter, and less error-prone. In the near future, artificial intelligence will not only help programmers, but it also will turn itself into a skilled programmer, available to the general public. It can even connect natural language and program codes, making codes easier to write and understand.

SOFTWARE WITH MILLIONS OF USERS

Ultra-Large Scale Software Systems (ULSS) are those that make the world go round. They allow us to get millions of results in less than a second when we google or recommend contents we enjoy as we scroll on Instagram or Facebook. These platforms all run on ULSS. Extremely large software systems operate on a global scale, serving millions of users around the clock. They include Google (a search engine that processes billions of requests in real-time), Facebook (a social network in which users from all over the world interact with each other), and Visa (a financial transaction processing system that manages millions of purchases every second). These systems, which serve millions of users daily, require uninterrupted, nonstop operation.

FLAWLESS AND UNSTOPPABLE: ADVANCING LARGE-SCALE SYSTEMS

Big systems also come with big challenges, such as security, regular maintenance and updates, and usability. What is more, the system must always be available and running properly. Since traditional software development approaches are not sufficient to manage these systems, we need new approaches that ensure the high quality and smoothness of the systems. Ahmed Hassan has played a key role in creating and implementing these approaches. Through years of research on these systems and by using AI, he has provided new methods for their development, assessment, and optimization, helping big companies use these systems with minimal errors and maximum efficiency.



SOFTWARE DEVELOPMENT, FASTER THAN EVER

Today, artificial intelligence can play a role in all stages of software development and production and improve this process. Until just a few years ago, the only way to write a program was through programmers. But in 2023, Gartner announced that artificial intelligence in software engineering has attracted a lot of attention, which means that in the near future, all software will be developed with the help of artificial intelligence, and the pace of software development will accelerate. Hassan believes that AI will not replace programmers but rather empower them, much like a friend would. AI can make software development processes faster and more efficient. Other uses of AI in this field include automatically detecting errors at the time of coding, suggesting more optimized codes, and automatically writing parts of the code. The implication of this for technology companies is that they will be able to produce software faster, cheaper, and of higher quality.

WHEN EVERYONE CAN BUILD SOFTWARE

According to Ahmed Hassan, a person with no programming knowledge will soon be able to create an application just by speaking or typing a few sentences. "Alware" means software created and controlled by artificial intelligence. This idea makes software development more accessible. In other words, in the future, anyone, including non-experts, can build software. The software development process will become smart, and systems will be able to automatically write code, optimize it, and even solve its problems.

In the future, the role of software developers will change, and non-specialists will also be able to participate in the software production process. This change allows software to be made with higher quality and easier access. There are five generations of software in the process of software development, which indicates the evolution of software. These include Codeware (software written manually by programmers), Neuralware (software developed using neural networks and early artificial intelligence), Promptware (software produced based on commands and textual inputs), Agentware (software developed in collaboration with humans and intelligent agents), and Mindware (software that works with advanced artificial intelligence models and brain-computer interfaces).

WORDS AS COMPUTER CODES

Natural language processing and programming languages are areas in artificial intelligence that deal with the relationship between natural language (such as English or Persian) and programming languages (such as Java or Python). The main goal of language processing is to enable machines to understand natural human language and use it to generate, search, and understand programming code. In this regard, large and accurate databases such as CoDesc have been created to provide artificial intelligence systems with proper data. This database is a large dataset containing 4.2 million Java code snippets and their equivalent textual descriptions in natural language, designed to train artificial intelligence models to understand and generate code from text and vice versa. The main goal of CoDesc is to strengthen the relationship between natural language and coding, which enables artificial intelligence to understand programming codes, summarize them, and even write new codes based on textual descriptions.

So far, code searching has been dramatically improved with the help of code-NL models. These models are artificial intelligence models that can understand and process programming codes and human language. They are trained to make connections between textual descriptions and programming codes. These models are capable of searching through large amounts of code to find the appropriate piece of code in natural language. One of Hassan's main achievements is pre-training models, which allow AI systems to perform better at complex tasks such as code summarization and code search before being trained to use real data. Pre-training can reduce the volume of data required for training and increase the efficiency of AI models in performing various tasks. When working with programming data and natural language descriptions, noise is one of the big problems that can reduce the accuracy of models. Ahmed Hassan's research team has used advanced methods to clean data and remove common noises, including removing redundant characters, removing HTML and XML tags, and checking for coding errors. Having better communication with software and its code will yield good results; for example, AI-augmented software will revolutionize human lives. In areas where large amounts of data need to be processed, having more optimized software becomes more important.

What was once considered a dream has now become a reality. Through his pioneering research, Ahmed Hassan has shown that future software will not only be faster and smarter but will also be able to sustain itself by developing, optimizing, and even solving its own problems. The entry of AI into software engineering does not mean the end of traditional programming but rather the beginning of an era in which AI works alongside developers as a powerful partner.

A WORLD WHERE ALL DIGITAL TRACES ARE TRACKED

In the early days of software, the typical image that came to mind was of a programmer writing code alone in the confines of their room, isolated from other collaborators, striving to create something valuable. However, today, this image is far from reality, with hundreds of thousands of programmers, each with their own expertise, working collaboratively to develop software systems. This naturally raises a question: Are other skills beyond coding needed to develop software?

About twenty years ago, when the open-source software movement emerged, it allowed anyone to start a project, collaborate with others, innovate, and reach acceptable results on the subject under study. Through these collaborations, many bugs that may go unnoticed by one programmer are quickly identified by thousands of other programmers, thus improving the quality of the project. To understand the importance of software quality, consider those times when you were using your mobile phone, and it suddenly crashed, or maybe the battery drained in an instant, and the phone heated up. These issues indicate the poor quality of your phone's software. Upon facing these issues, you may ignore them and continue using your phone as it is. But the consequences may not always be trivial. In many cases, you are dealing with much more critical software that has access to your bank account, your car, or even an airplane, or a space shuttle. The slightest mistake with these software systems would cost you a ton in terms of money and human lives. This is where software quality becomes vital, and you can't afford to ignore the slightest bug in the software.

Given that widespread interaction is necessary and inevitable in achieving efficient software, another question arises: What is the mechanism by which this cooperation takes place? And how can we access the wealth of information from other programmers, using it to avoid repeating their mistakes? Ahmed Hassan, a professor at Queen's University in Canada, has come up with an ingenious solution to this challenge. He explains, "Today's software systems are highly complex networks of multiple components interacting with one another. With the increasing complexity of software design, the idea of a single person—or even a team of a hundred engineers—working in one place has become obsolete." Instead, Hassan believes, we now have large teams with programmers collaborating across the globe, each bringing their own expertise and integrating it with that of others. This results in the increasing complexity of software systems. As software systems continue to advance and become more complex, user expectations for quality and user-friendliness also rise. According to Hassan, collaboration is at the heart of this process.

Hassan's idea for this all-encompassing collaboration of programmers around the world is reflected in his groundbreaking work, Mining Software Repositories (MSR). He recalls, "About 20 years ago, I had an idea that denoted a new path for software development. It was then that I realized that every step software developers take in their projects leaves a digital footprint." This footprint contains a huge amount of data, ranging from code changes to the data obtained when customers use the software. "In the past, this data was merely stored and never effectively utilized to improve the quality or productivity of software projects. My key idea was to clean and organize this data so that it can be used by developers," Hassan explains. He suggests that developers can use this data to increase productivity or improve the quality of software systems.

Today, we encounter something similar in our daily lives when, for instance, we are shopping online and the website recommends related products based on what other customers have purchased before. Hassan draws a parallel: “When you buy a book from an online bookstore, you are usually presented with suggestions such as ‘customers who bought this book also bought ...’ Now imagine designing a system for programmers that does something similar.” In this system, when programmers change a piece of code, they get the message that ‘99% of developers who have changed this section have changed another related section as well.’ This insight can prevent many problems in the future, minimizing their impact on customers. The well-known tool GitHub Copilot was created based on this idea. This tool can predict and suggest line continuations or even larger sections of code while the developer is writing code. This technology is built on artificial intelligence by analyzing a vast amount of code worldwide and creating statistical patterns. It essentially serves as a predictor that guesses the probability of the next suggested word or phrase. The technology is a deep connection between artificial intelligence, software development, and the challenges that programmers face.

Ahmed Hassan's achievement signifies the unprecedented role of collaboration in software development. His response to the opening question is clear and indeed surprising:

Today, coding takes up 15 or, at most, 20 percent of a programmer’s time. The remaining 80 percent is spent on collaboration, interaction with others, and planning.

SOLO SCIENTIFIC PROJECTS? NO, THANKS.

Having put his idea of Mining Software Repositories into practice, Ahmed Hassan focused on building a scientific community around this area of study. His dedicated efforts in this regard seem to have been as successful as his ideas in the field of MSR.

In October 2023, when Ahmed Hassan came to Isfahan to receive the Mustafa(pbuh) Prize, we had a brief friendly chat with him at the Abbasi Hotel, along with some members of the Observatory. We finally got to ask him a question that had been on our minds for a long time: Why is building a community around Mining Software Repositories crucial, and why has he devoted his focus to it?

His response showed how closely his success is intertwined with this community: "Had I sat alone in my lab, not sharing my ideas with the world, we would not have achieved what we have today. If that had been the case, there would be no prize now, no progress. Many of the technologies developed at MSR have come to fruition and been adopted by companies such as Google, Microsoft, and Facebook. Therefore, the spread of MSR around the world is not solely my work but rather the result of the attention to this field and contributions from many people worldwide. They accepted our idea, which initially sounded ridiculous, and made all these wonderful technologies happen. That's why bringing all these people together to expand this field was a must."

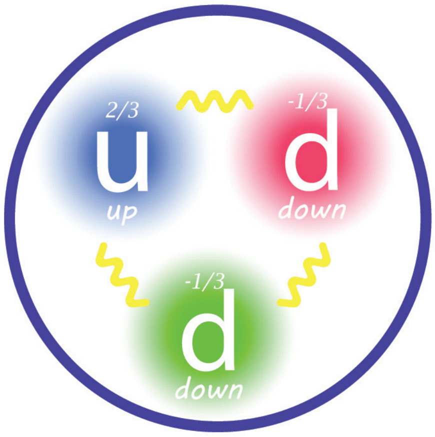
He believes that while it is commendable for an individual scientist to focus on a narrow scientific subject, contributions by other scientists are essential. With their contributions, the heaviest of burdens seem light. He reminds us: "If you want to go fast, go alone; if you want to go far, go together."

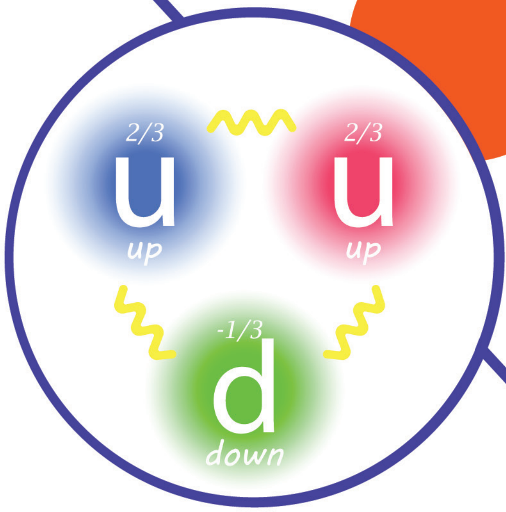
A sculpture depicting the collaboration of James Watson, Francis Crick, and Rosalind Franklin in the discovery of DNA. The double-helix model proposed by Watson and Crick was largely based on laboratory data from Rosalind Franklin and others. This sculpture was created in 2006 by Allan Sly and is located in The Garden of Heroes and Villains in Warwickshire, England.

REBEL ELECTRONS ON THE QUANTUM ONE-WAY HIGHWAY

By taking a look at the world around us, we will notice that, at first glance, the periodic table of elements seems to be the most thorough approach to classifying the matter around us. This table forms the foundation of chemistry and our understanding of matter. Upon closer inspection, however, we will realize that this is only the surface of physical reality. The periodic table is, ultimately, made up of atoms and the bonds between them, but what are the atoms themselves made of?

To answer this question, we need to refer to a more fundamental model of the structure of the universe: the Standard Model of elementary particles. In the Standard Model, matter is not only made up of electrons, protons, and neutrons but also of more fundamental structures called quarks and leptons. These particles—classified into three generations—are the foundation of everything we see in the universe, from massive galaxies to the smallest living organisms.





In the quark model for hadrons, the neutron is composed of one up quark (charge +2/3 e) and two down quarks (charge −1/3 e), and the proton is composed of two up quarks of charge +2/3 e each and one down quark of charge −1/3 e.

If we examine this model through a more fundamental perspective, we find that all the particles we know fall into two main categories: fermions and bosons. Bosons are the carriers of force, like the photon that carries the electromagnetic force and the gluon that holds protons and neutrons together. The category that is important for the structure of matter is fermions. Fermions are particles that make up the fundamental structure of matter. The quarks that make up protons and neutrons and the electrons that form atomic orbitals are all fermions.

The unique property of fermions—which distinguishes them from bosons—is the Pauli exclusion principle. According to this principle, two fermions cannot be in the same quantum state. This simple law is the main reason for the layered structure of electrons in atoms, the formation of solids, and ultimately, the formation of the universe as we know it. If the Pauli exclusion principle did not exist, all electrons within atoms would be arranged in a single energy level, and there would be no structures resembling solids, molecules, or life.

Among the different types of fermions, there is a special type called Weyl fermions that are not only important in the Standard Model but also play a special role in the world of condensed matter physics. Initially proposed as massless particles in fundamental theories, these particles appear as quasiparticles in the world of quantum matter, exhibiting strange properties such as Fermi arcs, chiral currents, and peculiar magnetic effects.

The discovery and study of Weyl fermions have allowed us to explore particle physics on a scale beyond particle accelerators and in solid environments. This discovery builds a bridge between high-energy physics and condensed matter physics and could help develop new technologies such as quantum computation.

Weyl fermions are particles described by the Weyl equation. This equation is the massless version of the Dirac equation. The key feature of this equation is its chiral nature; that is, the Weyl fermions are either left-handed or right-handed, and the two categories remain independent of each other unless a mass is defined for them. Another unique feature of Weyl semimetals is the presence of Weyl nodes in momentum space. These points are locations where energy bands (including the valence and conduction bands) meet and act as topological monopoles in Berry curvature space. As a result, these materials have Fermi curves on their surface, which is one of their experimental signatures.

One of the most important physical effects observed in Weyl fermions is chiral anomaly. First predicted in quantum field theory, this phenomenon signifies that the number of left-handed and right-handed fermions, if in the presence of parallel electric and magnetic fields, is no longer conserved. This leads to an observable phenomenon in Weyl semimetals: their electrical resistance decreases in the presence of a magnetic field, unlike ordinary materials, whose resistance increases under these conditions. This negative magnetoresistance was one of the key experiments to confirm the existence of Weyl fermions in solids. This phenomenon was first observed in the Weyl semimetals tantalum arsenide (TaAs) and niobium arsenide (NbAs) and was used as one of the key experiments to confirm the existence of Weyl fermions.

THE DISCOVERY OF WEYL SEMIMETALS: ROGUE FERMIONS ESCAPE THE PRISON OF PHYSICS

In a world where physics ruled, there was an unwritten law for particles: Either matter or force! All particles in the universe followed this law. Electrons, protons, and neutrons were held together in a regular pattern, and photons, gluons, and other bosons served as force carriers.

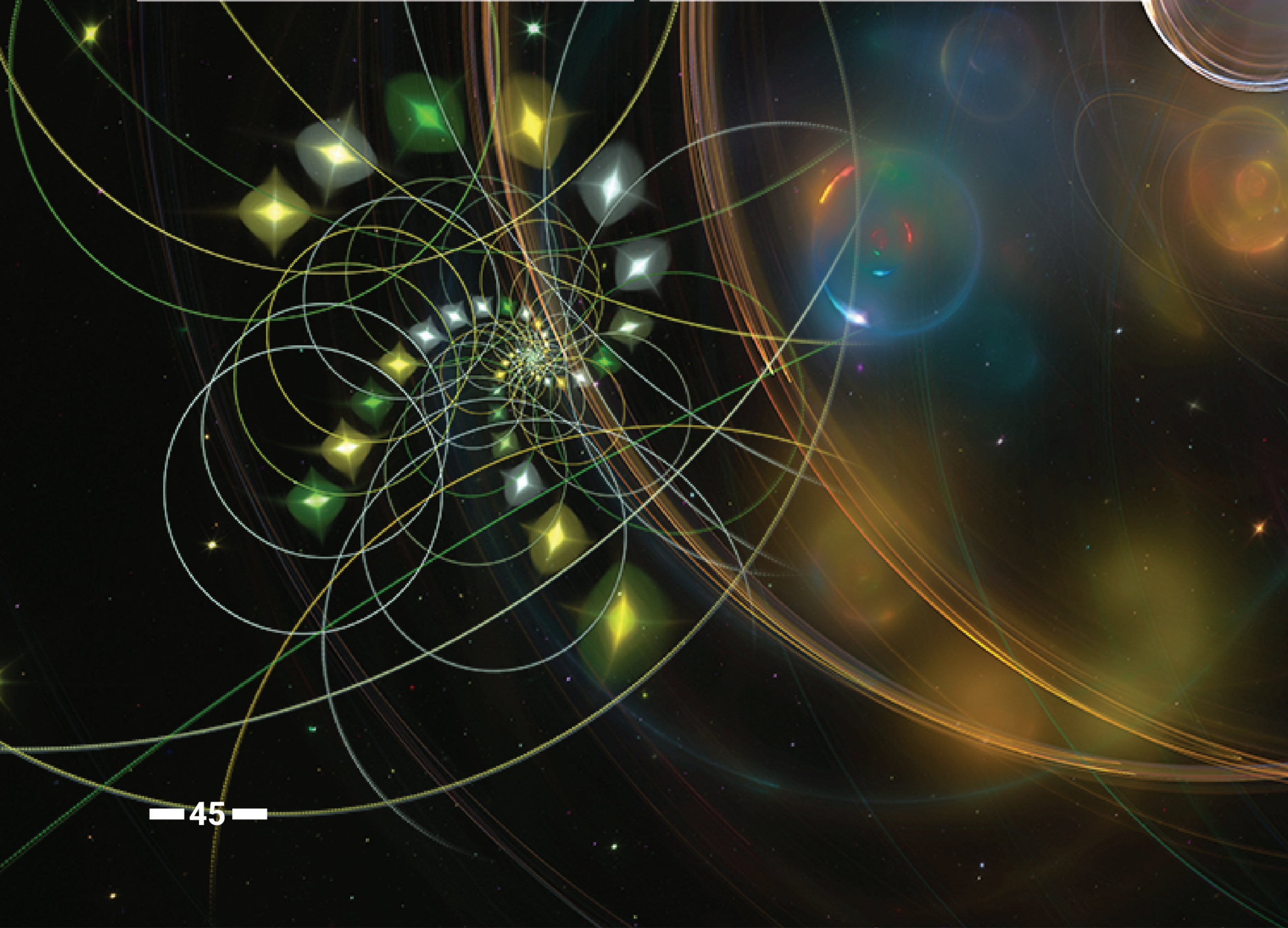
But in a corner of this universe, there were Weyl fermions that were particles that followed no laws. They neither submitted to the constraints of mass nor did they fit into the conventional structures of matter. They were weightless and chiral beings (meaning they only ran in one direction and had no way back!). This was the reason why scientists always thought that these strange fermions only lived in the world of elementary particles and in massive accelerators.

One day, Zahid Hasan and his colleagues decided to put an end to this mystery. Could these rebellious fermions be found in the real world, in the world of matter?

They studied a specific matter called tantalum arsenide using a special technique called Angle-Resolved Photoemission Spectroscopy (ARPES). If Weyl metalloids really existed, there should have been signs of them in this matter. By shining light on the surface of the matter and assessing the behavior of the electrons, something unexpected happened that shook the world of physics: Weyl fermions, free and unbound, were moving in this matter!

They moved through space like one-way passengers on a quantum highway, without any obstacles, creating strange curved paths called Fermi arcs on the surface of the matter, and unlike all known matter, in a magnetic field, their resistance decreased instead of increasing!

It was as if these rebellious fermions had finally escaped the theoretical prison of physics and carved out a new realm for themselves in the world of matter.



Weyl semimetals are natural bridges between entangled particles and quantum material with non-local behavior.

LINKING PARTICLE PHYSICS AND CONDENSED MATTER

The discovery of Weyl Semimetal established a connection between particle physics and quantum materials. As mentioned, in 2015, Zahid Hasan and his colleagues at Princeton University were able to identify Weyl semimetals as a real phenomenon in solids. In fact, before that, physicists only referred to Weyl fermions as theoretical entities that existed in the world of fundamental particles. This success was not only a major scientific breakthrough but also demonstrated that even complex theories of high-energy physics can pave the way for real-world innovations. The discovery of Weyl semimetals is a new chapter in the history of physics, in which particle and condensed matter physics not only came closer together but also became intertwined.

Beyond the event horizon of a black hole, the fabric of spacetime is wrapped so profoundly that nothing -not even light- can escape.

RECEIVING A SIGNAL FROM THE HEART OF DARKNESS

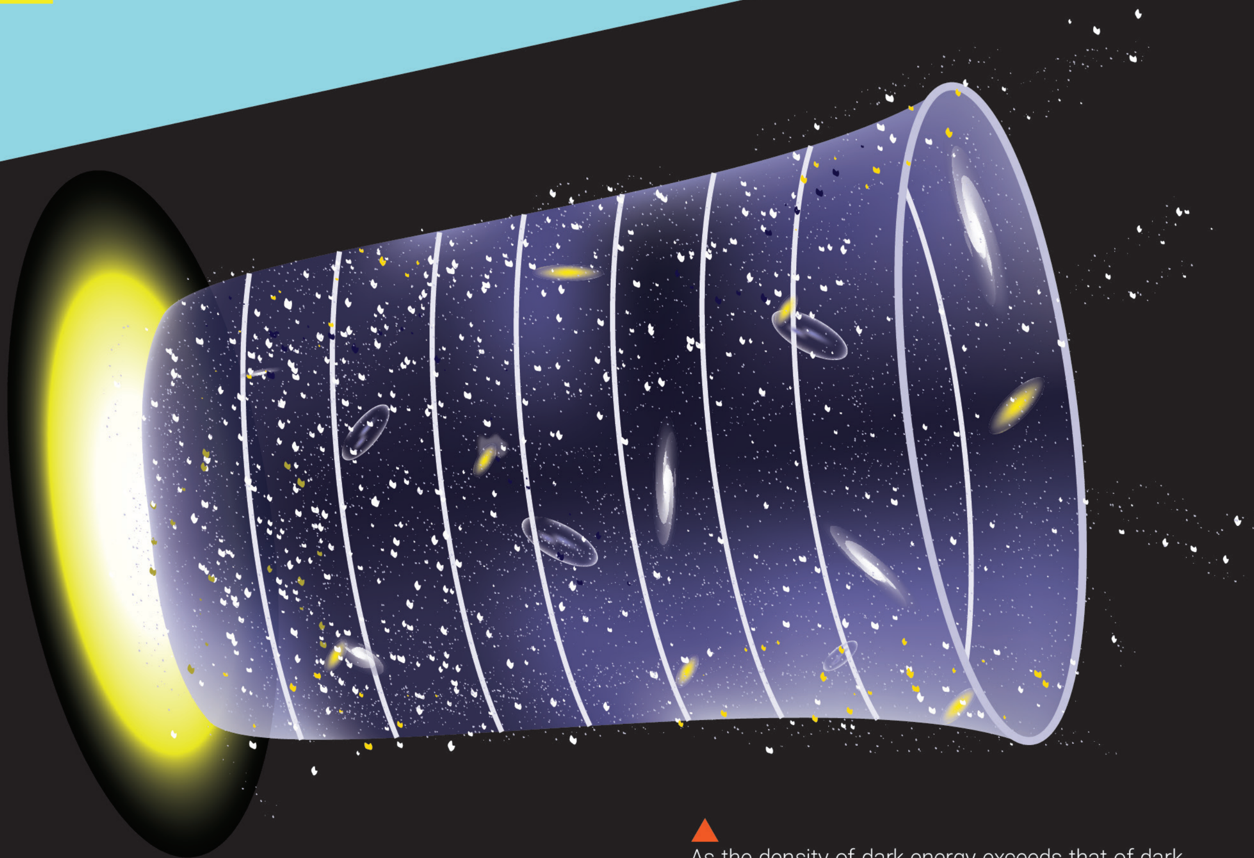
If we take a fleeting glance around us, everything we see consists of matter that makes up the world. But is our universe, like our immediate surroundings, filled with visible matter, and is it taken for granted? Let us step away from this visible matter for a moment and venture into a more enigmatic realm.

Imagine leaving Earth behind and traveling so far that galaxies appear merely as tiny dots among countless others. From that vantage point, we can observe the entire observable universe within a single frame. But is everything before us truly composed of visible matter?

In this frame, by observing the motion of galaxies, we uncover the existence of a substance known as dark matter—a form of matter that neither emits light nor is easily detectable, yet plays a crucial role in the structure of the cosmos. It is an invisible part of space that possesses gravity, and scientists observe its gravitational effects on visible celestial bodies. Dark matter acts as the invisible glue that holds solar systems, galaxies, and galaxy clusters together. It binds stars, dust, and gas within a galaxy, making up the majority of its mass. In essence, it forms the foundation of the cosmic structure that defines our universe.

Accompanying this matter is an even more dominant component—dark energy—whose presence surpasses that of dark matter. Together, these two entities prevent ordinary matter from constituting more than 5% of the entire universe. In reality, about 95% of what exists remains unseen, lying beyond our senses.

For this reason, we refer to it as "dark." This invisible and enigmatic realm serves as a veil behind which hidden secrets await discovery. For years, scientists have meticulously strived to illuminate this cosmic mystery, seeking to unveil the unknown forces shaping our universe. Exploring this darkness is a pursuit that has captivated many scientists, including Yahya Tayalati, whose passion for research has driven significant advancements in the field. Tayalati is one of the pioneers in theoretical physics, contributing to the unraveling of dark matter's mysteries through a unique approach—studying light-by-light scattering. His work has played a crucial role in shedding light on the hidden aspects of the universe. Before delving into the details of light-by-light scattering observations, it is essential to understand a fundamental concept: Objects become visible to us because they scatter light. The rough and uneven surfaces of objects scatter incident light in all directions, allowing the human eye to perceive them.



As the density of dark energy exceeds that of dark matter, the universe's expansion accelerates.

WHICH PARTICLE CONSTITUTES DARK MATTER?

At the beginning of his career, Tayalati worked on the ATLAS experiment at the Large Hadron Collider (LHC) at CERN. His objective in the ATLAS project was to explore light-by-light scattering and search for axion-like particles (ALPs)—hypothetical fundamental particles that are strong candidates for dark matter. Today, scientists believe that axions or axion-like particles, which are lightweight and electrically neutral, could be the very components that make up dark matter due to their unique properties.

To better understand light-by-light scattering and axion-like particles (ALPs), it is useful to first review the Standard Model (SM) of particle physics. To account for all known matter in the universe, scientists predicted that all that there is in the world consists of several fundamental building blocks known as elementary particles, governed by four fundamental forces. Over time, extensive experiments confirmed the existence of these particles, and the Standard Model became an established theoretical framework describing them. In this model, if a particle is a constituent of matter, it is classified as a fundamental fermion, such as electrons, quarks, and neutrinos. If a particle serves as a mediator of interactions or forces between matter particles, it is categorized as a fundamental boson—such as photons, gluons, and others. Despite its success in explaining a vast range of experimental data, the Standard Model has a critical limitation: It does not account for dark matter. Furthermore, it fails to explain the formation of galaxies and the dark energy responsible for the accelerated expansion of the universe. This fundamental gap in the model has driven scientists to search for an additional, undiscovered particle, one that could finally explain the enigmatic nature of dark matter.

Before now, scientists have posited various hypotheses regarding the nature of dark matter, such as Weakly Interacting Massive Particles (WIMPs), Neutralinos, Sterile Neutrinos, and Neutrinos, among others. However, axions and axion-like particles (ALPs) emerged as the most promising candidates for this mysterious form of matter. Axions are theorized to have extremely low mass and no electric charge. Therefore, they cannot be readily observed through electromagnetic radiation, making them suitable candidates for dark matter particles. In other words, they do not interact with light, which makes them invisible despite their existence in the world and galaxies.

SEARCHING FOR AXION-LIKE PARTICLES (ALPS) AT THE LHC

Tayalati took his first steps at CERN using the Liquid Argon Calorimeter Prototype, an advanced detector designed to identify photons and electrons. One of his major achievements, along with the ATLAS collaboration, was the first-ever observation of light-by-light scattering at the LHC in 2019. Light-by-light scattering is an extremely rare phenomenon, making its measurement highly challenging and nearly impossible. For decades, the direct observation of high-energy light-by-light scattering remained unsuccessful. However, at the Large Hadron Collider (LHC)—the world's most powerful particle collider—this elusive process was finally detected using lead ion collisions.

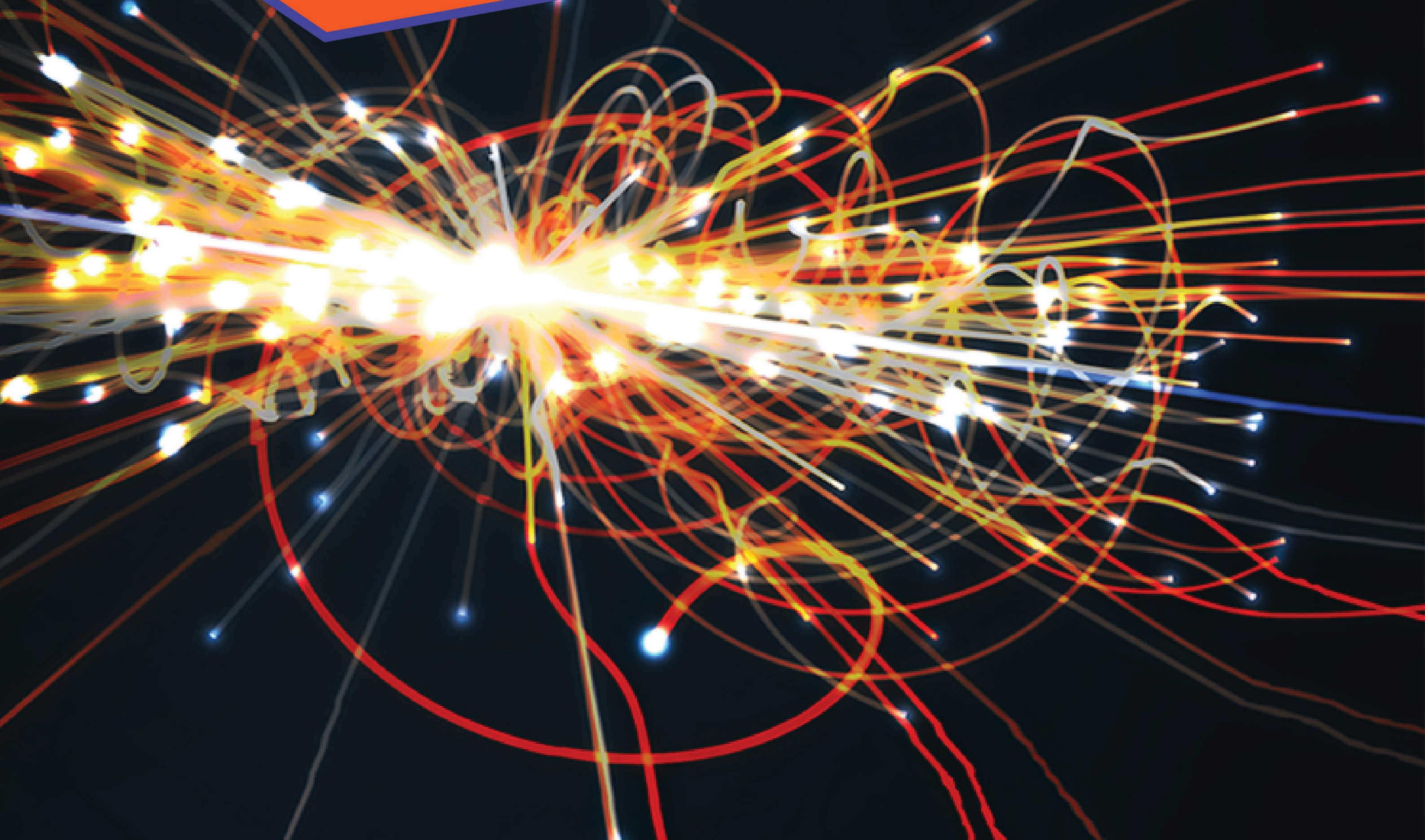
Heavy-ion collisions provide a uniquely clean environment to study light-by-light scattering.

As bunches of lead ions are accelerated, an enormous flux of surrounding photons is generated. When ions meet at the center of the ATLAS detector, very few collide, yet their surrounding photons can interact and scatter off one another. These interactions are known as 'ultra-peripheral collisions.' In this special type of interaction, the distance between the lead ions must be at least twice the radius of a single lead ion. During these photon-photon interactions, various new particles with different energy levels can be produced. Scientists hypothesized that under certain conditions, axion-like particles (ALPs) could emerge from these collisions. Experimental data provided strong statistical evidence supporting the existence of such particles, marking a significant step in the search for dark matter.

WHAT SIGNALS THE PRODUCTION OF AXION-LIKE PARTICLES?

In the ATLAS experiment, strong magnetic fields exist within the LHC. Axion-like particles (ALPs), produced in photon-photon interactions, can themselves decay into photons through interaction with these strong magnetic fields. This photon emission serves as the key signal indicating the presence of axion-like particles.

Through his work, Tayalati was able to extract a distinct and identifiable signal from the vast amount of data collected at the LHC—a signal that could potentially serve as evidence for dark matter. His research, along with the efforts of other scientists in the field, is not only advancing the search for dark matter but also addressing fundamental questions about the universe. The discovery of light-by-light scattering marked a major breakthrough, paving the way for new physics beyond the Standard Model. However, the journey is far from over—it remains long and filled with challenges. Are axion-like particles the long-sought missing pieces that constitute dark matter? Answering this question, along with many others, requires further investigations and experiments. The quest for understanding the dark universe continues.



When particles collide at high energies in the LHC, they can release a tremendous amount of energy. This energy can be converted into mass, creating new particles that did not exist before the collision.

The fleeting and thread-like sparkle of red sprites in the upper atmosphere.

CLASH OF LIGHTNING BOLTS ABOVE THE CLOUDS

Lightning flashes across the sky, briefly illuminating it before darkness reigns again. This dazzling spectacle is the typical image of lightning etched in our minds. This massive electrical discharge, however, gives rise to other amazing phenomena that are very rarely seen.

These lesser-known phenomena differ from the familiar lightning that occurs in the lowest layer of the atmosphere, the troposphere. They typically manifest above the cloud tops and in the upper layers of the atmosphere, i.e., in the mesosphere and lower ionosphere. So, it is only natural that we do not see them! These phenomena are called transient luminous events because they occur within one or a few milliseconds and then disappear. In addition, other phenomena occur during lightning that are not optically visible but have an effect on the atmosphere.

Umran Inan, a Turkish scientist and former professor at Stanford University, is one of the scientists who, along with his team, has researched these phenomena. His area of expertise is very low frequency (VLF) electromagnetic radiation and geosciences. Red sprites, elves, and blue jets are among the mysterious names given to some of these transient luminous events, phenomena that have also been observed from space shuttles.

RED SPRITES, DANCERS OF FIRE

Red sprites are clusters of red light above the cloud tops seen after lightning. They look as if the cloud is shooting one or more red lightning bolts upwards! Of course, it would not be true to say that this phenomenon always occurs above every cloud from which lightning is emitted; rather, its occurrence depends on the conditions. Recorded videos show red sprites at altitudes of 50 to 90 kilometers above the Earth's surface. These light clusters are red from top to bottom, but their lower part has a tinge of blue. Their presence endures for mere milliseconds, vanishing almost instantly after their formation.

In Inan’s theory explaining red sprites, thunderclouds are considered electric dipoles, where the top of the cloud has a positive charge and the bottom a negative one. In this case, there is a system around which an electric field is created, but this field does not have the ability to penetrate the high altitudes of the atmosphere above the cloud. This is because the electrical charges, or electrons, in the atmosphere act like a shield, protecting the upper atmosphere from the cloud's electric field.

After the positive charge of the cloud is discharged to the ground through lightning, the cloud changes from a dipole to a negatively charged electric monopole, and the electric field of a monopole is much stronger than that of a dipole. Then, the cloud's electric field and the electrons in the atmosphere combine to produce a strong field that can penetrate the upper atmosphere. This strong electric field exerts a force on the electrons in the upper atmosphere and gives them energy. The energetic electrons collide with gas molecules in that area. During these collisions, energy is transferred to the gas molecules. Then, gas molecules get excited after receiving this energy and lose the energy they receive through light emission.

The red light is mostly due to the excitation of nitrogen at that height above the ground. The clustered shape of red sprites is also, according to many scientists, due to inhomogeneity in the conductivity of the mesosphere. As mentioned earlier, various light phenomena occur during lightning, one of which is red sprites. Sometimes, before the red sprites appear, a long light is seen in the sky that disappears very quickly, which is known as elves.

ELVES, TWINKLES FROM HEAVEN TO EARTH

Elves are seen at altitudes of 75 to 105 kilometers above the Earth's surface, much higher than cloud level. They are horizontal, 100 to 300 kilometers long, and last less than a millisecond. Named after their shape, these phenomena are called light worms or elves. According to Inan, the most likely source of elves is low-frequency electromagnetic pulses that occur after strong thunderstorms. Pulses that propagate upward give energy to the electrons in the lower layers of the ionosphere, heating them. The energetic electrons also excite the gases in that area and cause them to emit light.

The luminous intensity of this event is very high, which means that the lower layer of the ionosphere receives a lot of heat as a result; therefore, the light creates a noticeable change in the lower region of the ionosphere. We use this region to guide radio waves, and any change in this area itself affects the propagation of radio waves. The electromagnetic pulse generated by lightning is not only a source of elves but also has other effects on the atmosphere that affect our daily lives.

ELECTROMAGNETIC PULSES, BOWS INTO THE SKY

The pulse generated by lightning can interact with the ionosphere, causing ionization and heating of its lower layer. That is, it affects an altitude of approximately 100 kilometers above the Earth and can change the physical properties of the ionosphere, including its refractive index, in a very short time. Inan has calculated that it takes much longer for the conditions to revert back to their original state. Changes in the ionosphere, which are vital for the propagation of radio waves throughout the Earth, cause changes in the characteristics of the emitted waves, such as phase and intensity. This, in turn, causes devices such as radio and television, and even the Global Positioning System (GPS)–which use electromagnetic waves–to stop working during a thunderstorm.

Also, the heating of the ionosphere and the rise in its temperature increase its conductivity, which leads to the creation of an electric current and can produce waves with very low frequencies. According to Inan, the ionization of the ionosphere through a process can generate the X-rays that are observed during lightning.

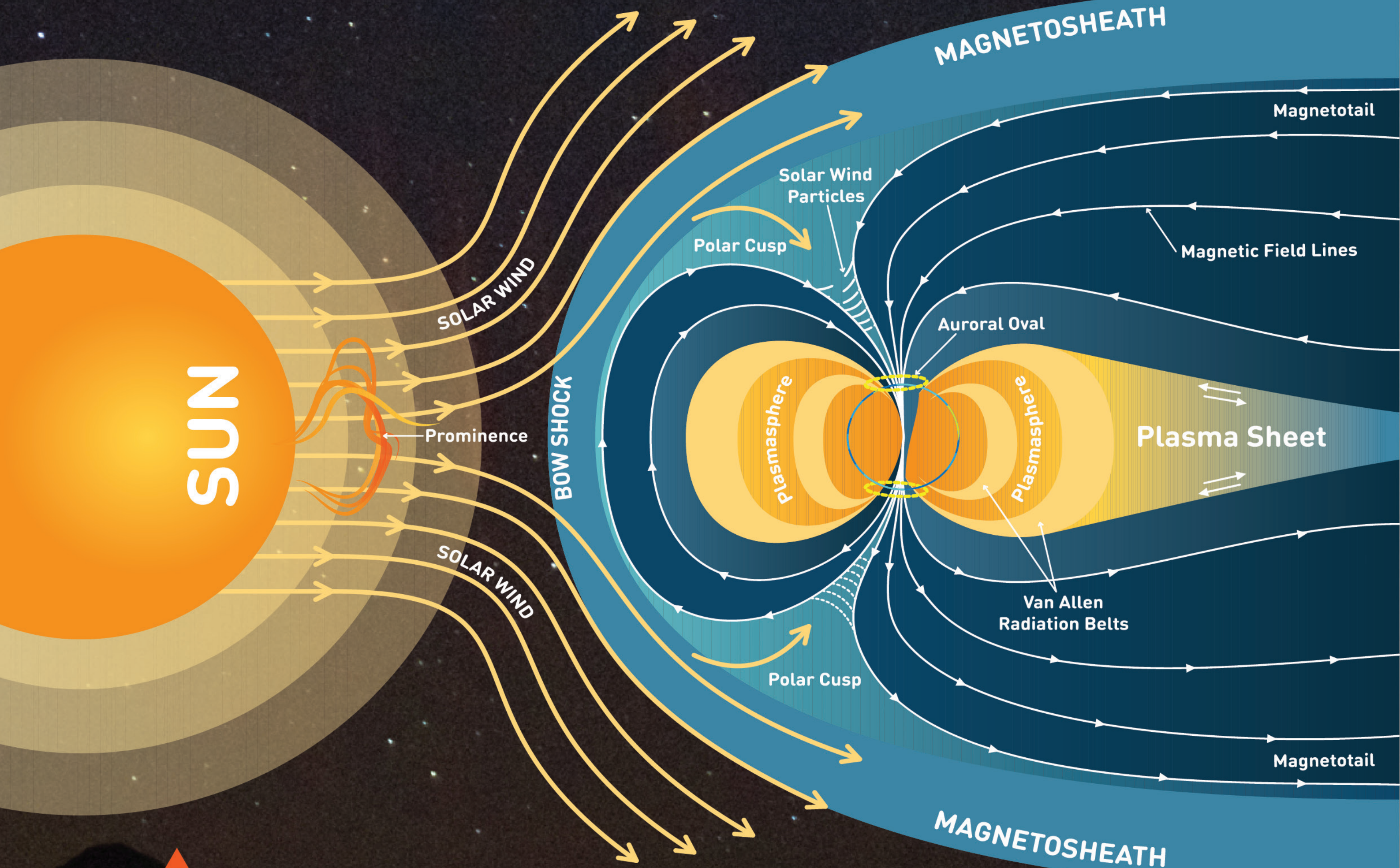
This ionized region behaves like a plasma. Studying very low frequency (VLF) electromagnetic waves and their interaction with charged particles in plasma, such as electrons, is another main focus of Inan's work. To better understand the application of this research, we need to understand some concepts, including the Van Allen radiation belt, which will be discussed.

RADIATION BELT: EARTH'S DEFENDER, SATELLITE ATTACKER

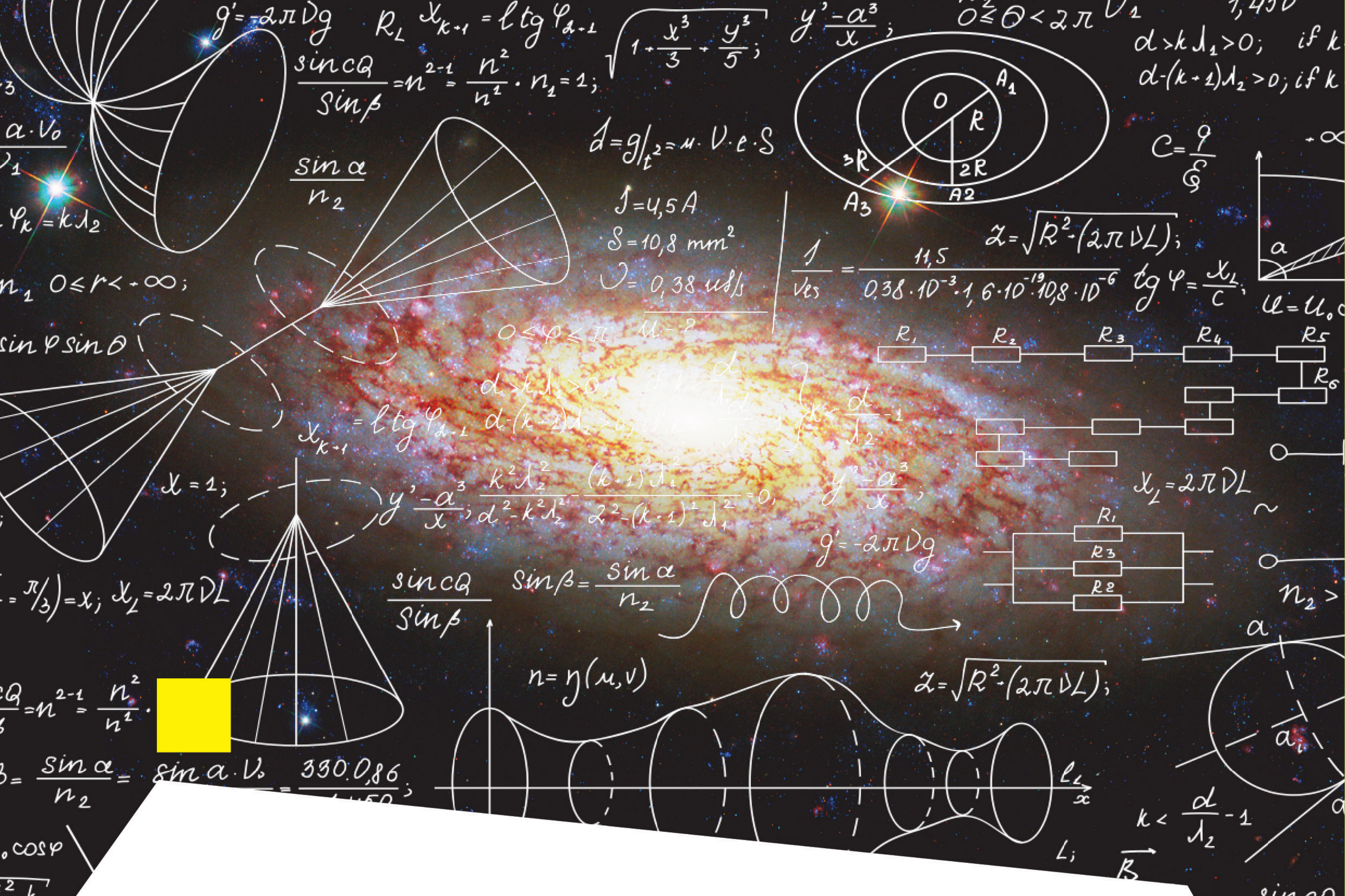
When harmful and charged solar rays reach the Earth, they are trapped by the Earth's magnetic field and cannot hit the Earth's surface. This magnetic field protects us and other living things from these rays. These particles create areas around the Earth known as the Van Allen radiation belt. This belt poses a major challenge for satellites, electromagnetic wave transmission, and GPS because any satellite or electric circuit placed in this area will quickly wear out and fail as a result of the radiation of these particles. Also, the intensity and frequency of electromagnetic waves in this area change, disrupting communications in these areas.

By studying the propagation of low-frequency electromagnetic waves in plasma, Inan has attempted to better understand the interaction of these waves with charged particles. The VLF research team at Stanford University, led by Inan and supported by more than 30 years of research at Palmer Station in Antarctica, has succeeded in making precise VLF measurements. Their studies have made it possible to study wave-particle interactions in near-Earth space. The interaction of these waves with electrons causes the electrons to accelerate and move.

It is possible that in the future, high-power VLF electromagnetic wave transmitters could be made through artificial processes, producing waves that could be used to reduce harmful electrons in the radiation belt. The results of this research and their development will change our understanding of plasma physics, astronomy, and meteorological physics.



A view of Earth surrounded by the Van Allen radiation belts, as streams of solar wind interact with the planet's magnetic field, creating a constantly shifting shield in space.



UNVEILING THE HIDDEN LAYERS OF THE UNIVERSE

Since ancient times, humans have sought to uncover the structures and laws governing the universe. This quest began with observation of the skies and nature and, with the advancement of scientific tools, it led to more complex discoveries. Initially, humans could only observe their surroundings with the naked eye. However, with the invention of the first microscopes and telescopes, they were able to explore both the microscopic and macroscopic worlds. For instance, with the development of advanced telescopes by Galileo and Kepler, humanity was able to observe celestial objects like planets and stars, which were previously beyond reach.

However, these observational discoveries were only the beginning. Today, humanity has proposed theories even for phenomena that we lack the tools to see. At the 25th Science Café, which featured a professor from the Faculty of Physics at Sharif University of Technology, the discussion focused on string theory, the hidden structures of the universe, and recent discoveries in fundamental particles and their interactions at subatomic scales. These discoveries are made possible by tools such as particle accelerators, electron microscopes, and new detection systems, allowing scientists to meticulously examine the universe's hidden properties and behaviors.

At subatomic scales, we encounter particles that exhibit properties such as electric charge, mass, and other characteristics at levels far smaller than what we observe at ordinary scales. For example, at these scales, particles like quarks and gluons, which reside within protons and neutrons, display unpredictable and fascinating behaviors. These hidden subatomic structures have significant effects on the behavior of the universe at larger scales and may even offer explanations for fundamental questions about the nature of space and time. In fact, uncovering these hidden layers in the microscopic world is essential for a better understanding of how the universe operates on macroscopic scales.

PARTICLES THAT WERE NOT SUPPOSED TO BE FOUND

Science continuously seeks to uncover the hidden truths of the universe through advanced tools and precise scientific observations. According to the guest speaker at 25th Science Café, one of the tools used to analyze the behavior of fundamental particles is the Large Hadron Collider (LHC) at CERN. This accelerator propels particles to nearly the speed of light, causing them to collide. These collisions randomly produce new particles, the analysis of which helps scientists understand new features of fundamental structures. These precise observations allow us to study not only particle behavior but also the various forces acting between them, such as electromagnetic forces, strong and weak nuclear forces, and gravity. However, it is essential to acknowledge that these findings are limited to scales we have been able to observe, and smaller scales remain beyond our reach due to multiple reasons, one of which is technological constraints.

THE SHORTCOMINGS OF CLASSICAL PHYSICS

At microscopic scales, particles that are more fundamental than protons and neutrons exhibit behaviors that cannot be measured or explained by classical physics. At these scales, classical physics, formulated by Newton, fails to describe these phenomena accurately. For example, at these scales, fundamental particles exhibit both wave-like and particle-like behavior.

In the following sections of Science Café 25, quantum mechanics was presented as the initial theory for explaining particle behavior at microscopic scales. According to this theory, particles cannot occupy exact positions in space at any given moment.

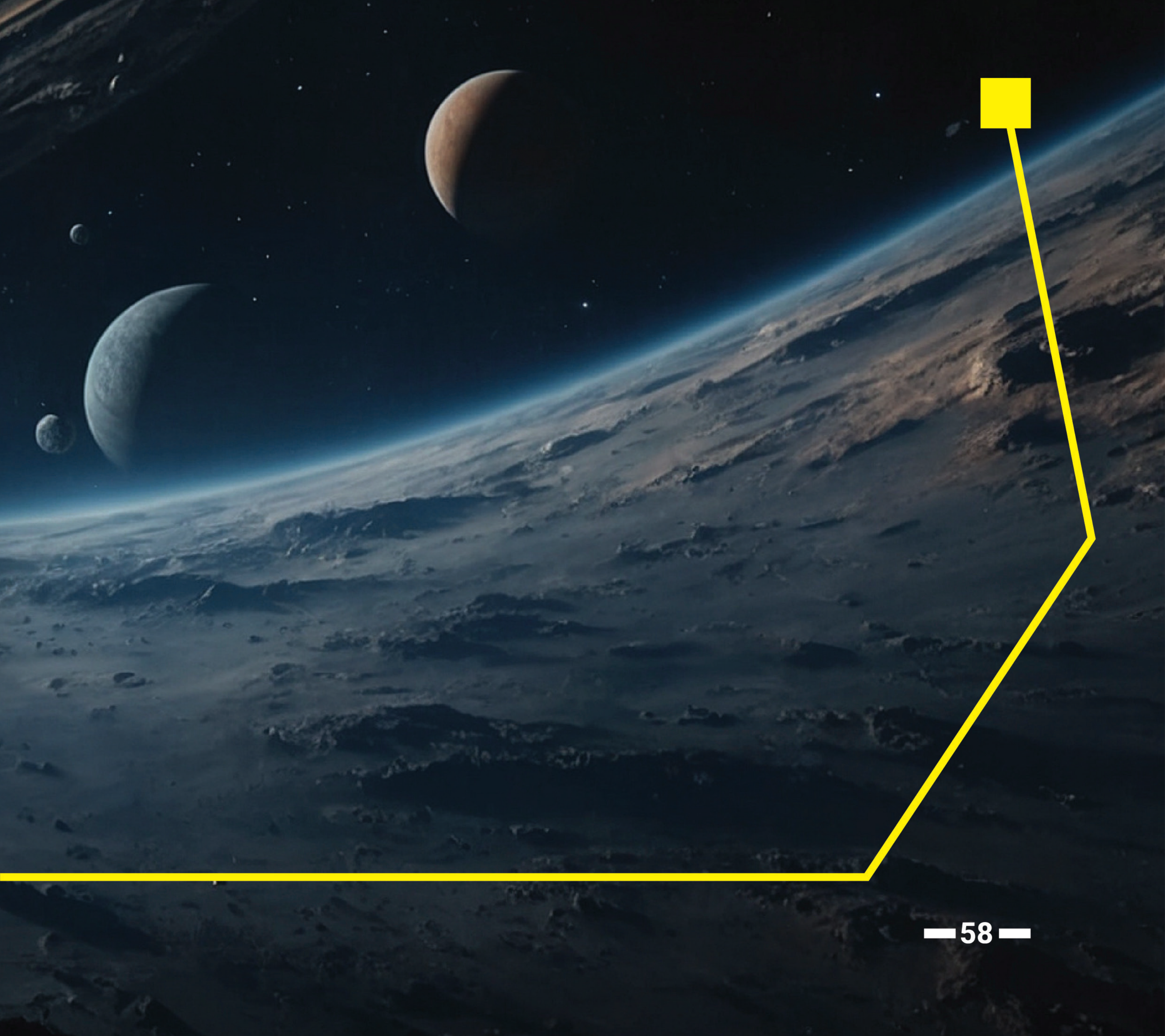
While this concept is incomprehensible in everyday macroscopic reality, it holds true at subatomic scales, such as dimensions on the order of 10^{-18} meters. The limitations of quantum mechanics arise when attempting to bridge these microscopic scales to the cosmic realm. For instance, on cosmological scales, the governing laws are Einstein's theory of gravity and general relativity.

In the macroscopic world, gravity is one of the four fundamental forces of nature, influencing massive celestial bodies like black holes, galaxies, and stars. While gravity operates effectively at large scales, binding cosmic structures together, a significant issue in modern physics is that this force fails to explain phenomena at microscopic and subatomic scales. In fact, at these tiny scales, gravity functions independently of other fundamental forces, lacking any unification with them.

THE PATH TO RECONCILING GRAVITY

To address this and similar problems, string theory has been introduced as a fundamental model explaining the behavior of fundamental forces and particles at scales far smaller than those we have currently explored. This theory is based on the assumption that, at microscopic scales, what we perceive as particles are actually multidimensional vibrations of a fundamental structure called a "string." These vibrations can occur in various dimensions, including extra dimensions that are beyond our observation.
According to string theory, all fundamental particles, such as electrons and quarks, are manifestations of vibrating strings.

In other words, when a string vibrates, it determines different characteristics of particles, including mass, electric charge, and type. These vibrations arise from the interactions of strings and extra dimensions. Thus, in addition to the three spatial dimensions we experience daily (length, width, and height), there exist extra dimensions that are only observable at extremely small scales. These hidden dimensions influence particle interactions and forces, explaining why gravity, at microscopic scales, does not interact uniformly with other forces. Essentially, at these scales, due to the influence of extra dimensions and string structures, gravity operates weaker compared to other fundamental forces.



The Andromeda Galaxy, 2.537 million light-years away, is our nearest spiral neighbor and contains over a trillion stars.

THE COSMIC UNIFICATION

String theory, which seeks to unify all forces at microscopic scales, is intrinsically linked to Grand Unification Theories (GUTs), which aim to merge gravity, electromagnetic forces, and the strong and weak nuclear forces into one single unified framework. The concept of "force unification" in string theory suggests that all particles and forces originate from a single source and do not remain distinct across different scales. For example, the gravitational force that dominates on cosmological scales might simply be a manifestation of specific vibrations within extra dimensions at microscopic scales. This idea is especially significant at the Planck scale (approximately 10^{-35} meters), which may hold the key to many cosmological and theoretical physics mysteries.

THE ARCHITECT OF NEW HORIZONS

One of the main challenges in string theory is the nature of extra dimensions that manifest themselves in complex forms influencing particle behavior in four dimensions. These extra dimensions significantly influence particle behavior, and some of these complex forms lead to inconsistencies and serious issues in the theory.

As the Sharif University professor mentioned: "In 2004 and 2005, it was believed that due to the excessive number of complex structures in string theory, the theory would no longer be useful. However, Cumrun Vafa and his colleagues refuted this view, arguing that not all possible theories had been identified and string theory could still provide a way to recognize viable theories. Ultimately, they concluded that only a limited number of well-founded theories exist within string theory. This discovery led to the development of the 'Swampland Program', which posits that most previously assumed viable theories are, in fact, dead ends—akin to a swamp—whereas only a select few theories prove to be truly useful and effective and should be the center of attention."

Another significant achievement of Vafa relates to black hole entropy. Employing string theory concepts, he successfully addressed the problem of black hole entropy, proposing new models to explain black hole behavior. These advances have not only deepened our understanding of cosmic phenomena but also expanded the practical applications of string theory. Moreover, Vafa has conducted crucial research on mirror symmetry, which aids in understanding interactions between particles and fundamental forces.

The universe has always been filled with profound and endless mysteries for humanity. From the structure of subatomic particles and fundamental forces to the vastness of the cosmos, scientific advancements—particularly in physics—continue to drive us toward new discoveries. String theory, as a fundamental model for explaining particle behavior and forces at microscopic scales, inherently describes all particle properties without the need for additional assumptions. This theory introduces extra dimensions that directly determine particle characteristics such as mass, electric charge, and type from the outset. Despite these strengths, challenges persist, including the limitations of scientific tools in observing extremely small dimensions and the inability to precisely measure subatomic scales. Furthermore, string theory still struggles to fully explain phenomena like dark matter and dark energy. However, with continued advancements in experiments and scientific instrumentation, the theory retains the potential to provide a better understanding of the cosmic structure and the intricate relationship between gravity and quantum mechanics.