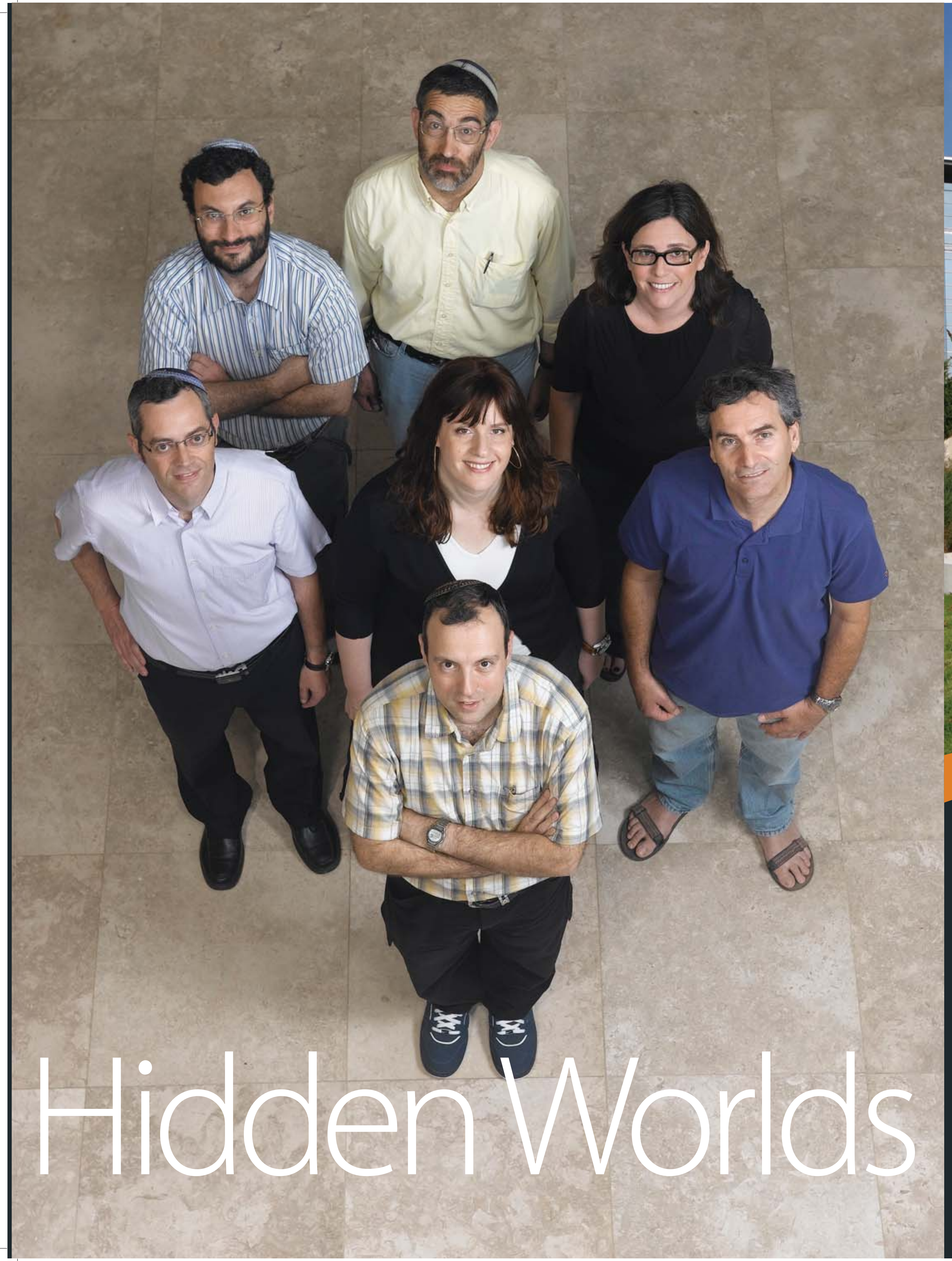


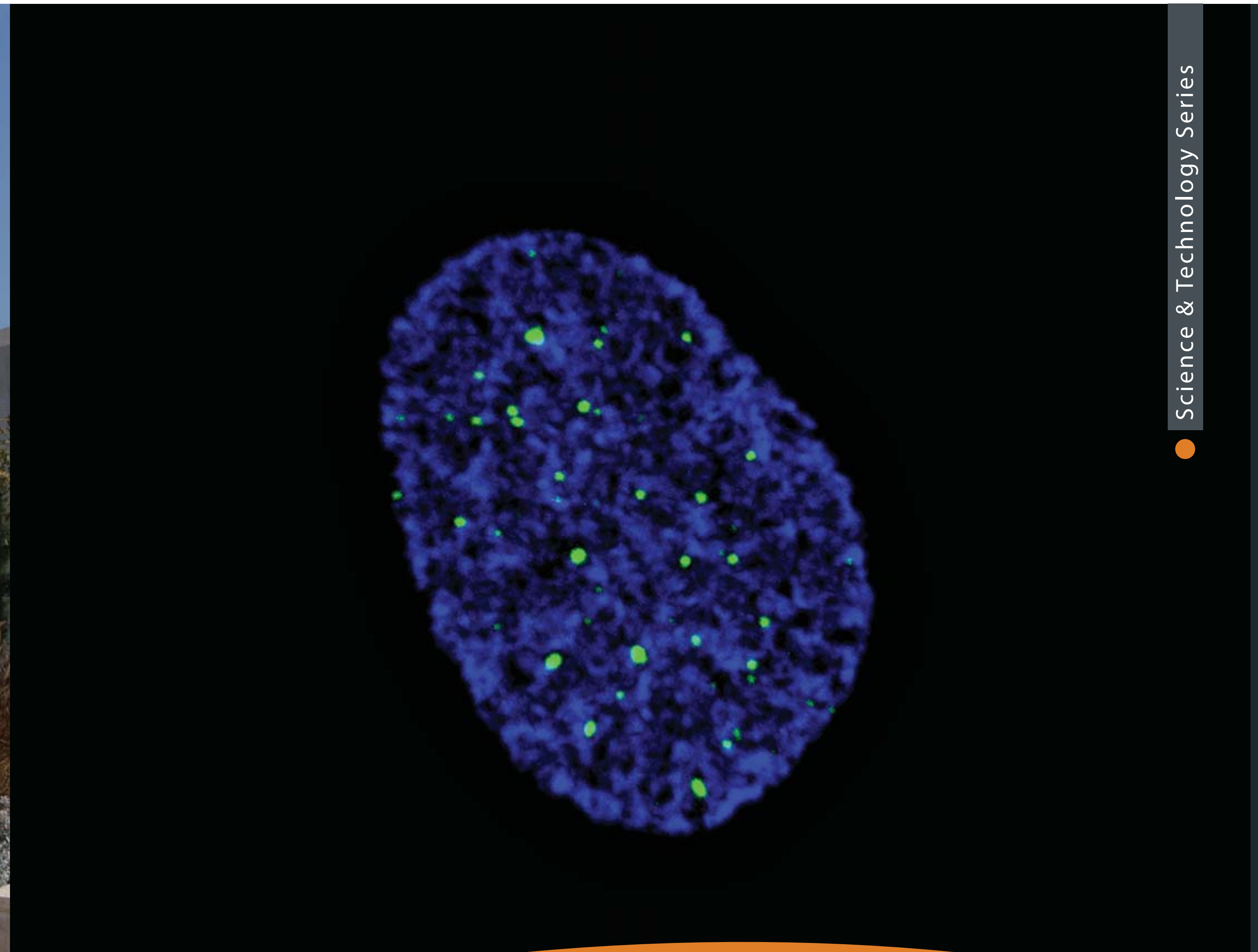
Produced by the Office of the Vice President for Research and Development and the Division of External Relations

↑ BIU's School of Engineering

Bar-Ilan University
Science and Technology

Bar-Ilan University stands at the forefront of cutting-edge research. Bar-Ilan researchers are making breakthroughs that improve life around the globe in areas such as drug-development, nanotechnology, medical research, bio-engineering, microscopy, optics, communications, energy, security, and more. As part of a national program to combat Israel's brain drain, BIU has taken the lead by committing to absorb fifty returning scientists within its world-class research infrastructure. The *Science and Technology Series* highlights some of the University's most exciting research endeavors.

Tradition of Excellence
Bar-Ilan University
Ramat Gan 52900, Israel
www.biu.ac.il



Science & Technology Series

Imaging and Microscopy Research
Exploring Hidden Worlds

Tradition of Excellence
Bar-Ilan University

At Bar-Ilan, imaging and microscopy research is fueling advances related to medicine, communications, advanced materials and nanoelectronics.

Pictured clockwise from bottom:
Dr. Yaron Shav-Tal
Dr. Dror Fixler
Dr. Eli Sloutskin
Prof. Aryeh Weiss
Dr. Orit Shefi
Dr. Yuval Garini
Dr. Rachela Popovtzer (center)

Imagin
Exploring

Imaging Microscopy Research

Antony van Loeowenhauk

Great science requires vision. That's why advanced microscopy and imaging technologies play such an important role in the scientific achievements emanating from the laboratories of Bar-Ilan University.

Scientific intuition and visual technology have always gone hand in hand. The Romans were the first to note how magnification could be achieved by peering through plates of clear glass. In the 1600s, Dutchman Antony van Loeowenhauk was startled to discover the existence of single-celled organisms using a primitive microscope. In the mid-20th century, electron microscopy revealed an entirely new biological world, teeming with mysterious subcellular structures. As electron microscopy pioneer Albert Claude put it when he received the Nobel Prize for Medicine in 1974: "The facts have been far better than the dreams… We have entered the cell, the mansion of our birth, and started the inventory of our acquired wealth."

At Bar-Ilan, imaging and microscopy research is fueling advances related to medicine, communications, advanced materials and nano-electronics. Multi-disciplinary collaborations between professionals trained in biology, chemistry, physics and engineering are expanding technological horizons, and sharpening the tools that allow us to see – and manipulate – the building blocks of life.

Getting to the Small Picture

Modern microscopy can reveal what happens on the cellular and even the molecular level in biological systems. However, when we rely on light-based "optical" microscopes – descendants of van Loeowenhauk's simple apparatus – the results are limited. This is because such microscopes cannot distinguish between points closer together than approximately half a wavelength of light. Although a short distance in absolute terms, this is still far larger than the infinitesimal "playing field" where biologically significant interactions take place. Most breakthroughs in the field of biotechnology depend on scientists' ability to distinguish between structures measured in nanometers – a distance about half the diameter of a DNA molecule's "double helix."

The work of Dr. Dror Fixler in the School of Engineering is one example of how a multi-disciplinary approach can lead to technological breakthroughs – breakthroughs that overcome the inherent limitations of optical microscopy.

➔ The multidisciplinary approach in the School of Engineering leads to technological breakthroughs that overcome the inherent limitations of optical microscopy.

In order to scan areas smaller than half a wavelength in size, Fixler – working together with his Engineering School colleague, Prof. Zeev Zalevsky – has improved conventional microscopy with a method known as "super-resolution." First, he introduces a filter of randomly moving reflective nanoparticles, which he places between the light source and the target area. While using an optical microscope to record a series of images over time, Fixler shifts the filter slightly, creating a movie-like collection of dynamically changing pictures. He then correlates these pictures mathematically, revealing a composite "portrait" of the previously invisible target situated under the filter.

Fixler's lab is also advancing other super-resolution methodologies that could eventually be used together with nano-medical devices, or provide a boost to industrial microelectronics by providing a low-cost, easy-to-integrate tool for verifying the structure of manufactured chips. Whatever the outcome, however, Fixler's basic research – which has been published in top bio-engineering journals – is attracting attention worldwide.

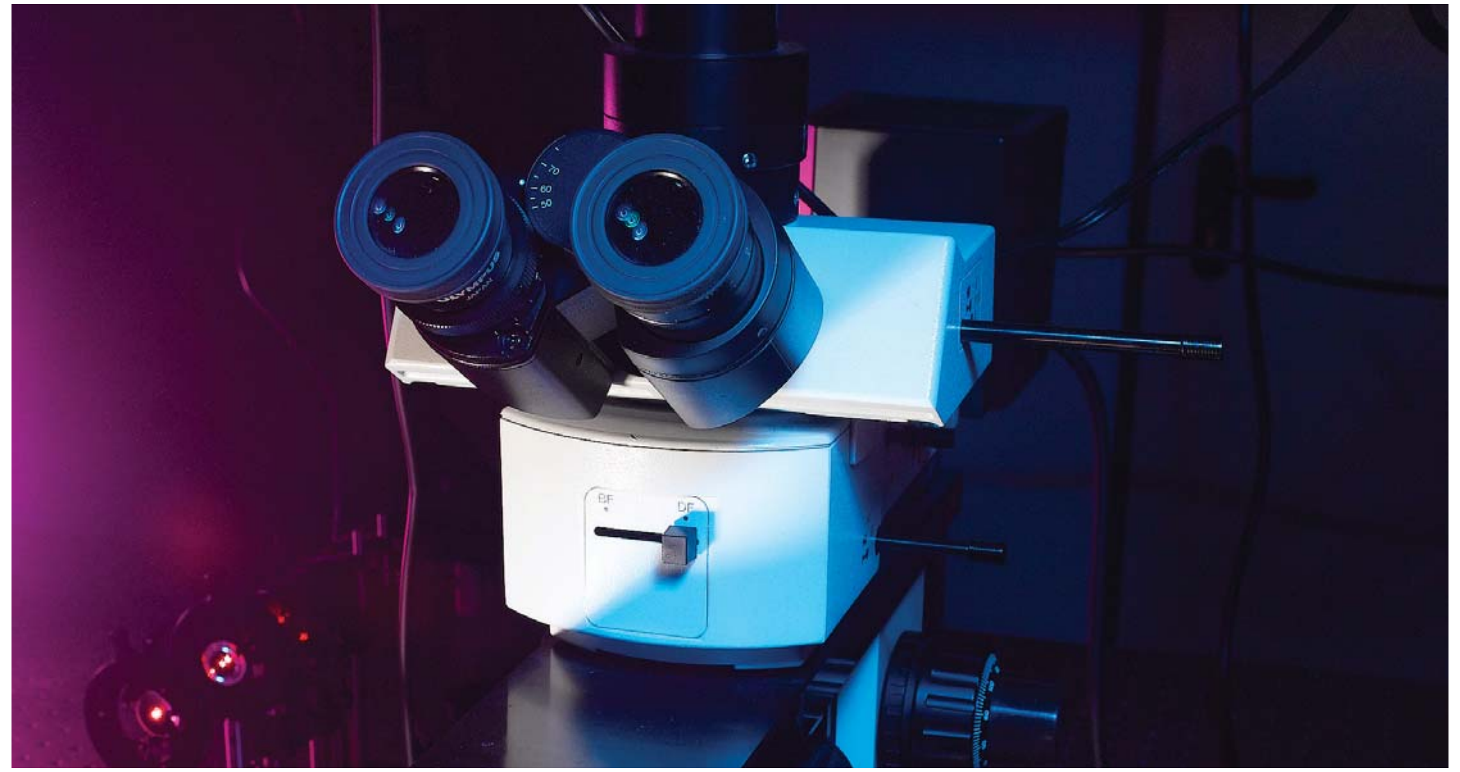
Life, As It Happens

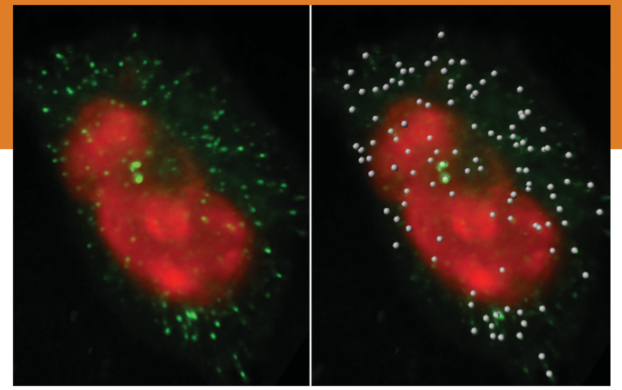
At the Bar-Ilan Institute of Nanotechnology and Advanced Materials (BINA), microscopy experts are revealing the secrets of basic biological mechanisms.

In the laboratory of Dr. Yaron Shav-Tal, techniques taken from the world of molecular cell biology are combined with time-lapse microscopy to quantify the rate at which individual genes are switched "on" and "off" in the cell nucleus. In Shav-Tal's unique set-up, the "on" state is provided by fluorescent markers – molecules engineered to light up when they bind to the RNA produced by activated genes. These markers act like torches, illuminating – for the first time in any lab – the path that genetic signals follow on the road to protein production.

Also at BINA, Dr. Yuval Garini has developed an optics-based method that allows scientists to measure the physical changes that occur in DNA when it comes into contact with individual proteins, something that may be useful for screening molecules for drug design. A multiple patent holder who invented a highly acclaimed imaging method for the study of human chromosomes, Garini's microscopy expertise allows him to characterize a dynamic process that keeps genetic material stable and organized inside the watery world of the cell nucleus.

Dr. Mira Barda-Saad, from the Mina and Everard Goodman Faculty of Life Sciences, is putting high-resolution microscopy to work in the study of the immune system. She has developed a unique, three-color fluorescence methodology that she uses to track





multiple molecular interactions simultaneously in live cells. Barda-Saad is advancing our understanding of immune-cell activation – knowledge that could lay the foundation for the development of therapeutic approaches to cancer and infectious disease.

Advances in imaging technology also play an important role in biological studies being conducted at the School of Engineering. Prof. Aryeh Weiss employs fluorescence to track protein-protein interactions, protein-DNA interactions, and light-induced cell death – dynamic processes that are important to understanding how a drug will work in a living system.

➔ At the Bar-Ilan Institute of Nanotechnology and Advanced Materials (BINA), microscopy experts are revealing the secrets of basic biological mechanisms.

In another lab at the Engineering School, Dr. Orit Shefi uses time-lapse imaging technology to examine genetic factors that affect the growth of nerve cells. Hers is one of the first labs in the world to achieve significant results using a pneumatic capillary gun – a device that allows her to "fire" non-damaging nanoparticles into living tissues. Shefi's use of advanced microscopy to observe growth patterns in these "doctored" tissues has helped her identify genes that influence nerve structure and development – data that may someday be parleyed into new post-trauma therapies for nerve damage.

Moving Microscopy Forward

A number of Bar-Ilan scientists are creating new, cutting-edge imaging technologies that will make microscopy a more powerful tool for basic and applied science.

In the Leslie and Susan Gonda (Goldschmied) Multidisciplinary Brain Research Center, Dr. Hamutal Slovin is characterizing the neural mechanisms behind vision and other higher cognitive functions. Using a special dye that glows in the presence of nerve-to-nerve communication, Slovin is able to isolate brain activity taking place in precincts measured in just hundreds of nerve cells, and to follow this activity at intervals of less than a millisecond – a close approximation of the speed of thought. Using a new "nano-pipette" that transmits light and electrical signals to sensors in the brain – a tool created by the Engineering School's Prof. Zeev Zalevsky – Slovin is increasing the amount of information that can be derived from brain images.

Prof. Shlomo Margel of the Department of Chemistry, an expert in the synthesis and surface modification of nano-sized particles, uses nano-medical techniques to improve the accuracy and usefulness of medical imaging. Margel's ability to link his nano-particles to a variety of contrast agents has rendered them useful tools for medical diagnostics, because they increase the amount of information that can be derived from readings taken by X-ray, CT and MRI.

Another researcher who is improving medical imaging is Dr. Rachela Popovtzer of the Engineering School. Popovtzer has synthesized gold nanoparticles that improve the efficacy of CT scans for cancer diagnosis. Administered to patients through an IV drip, Popovtzer's nanoparticles link up directly with the membranes surrounding cancer cells, creating an unmistakable, "golden" signal on the CT screen that highlights a cancerous tumor.

Microscopy and Materials

Electron microscopy – a powerful technology suited to working with inorganic samples – is the key to actualizing the potential of nanotechnology for the manufacture of super-miniaturized electronic devices.

BINA member Prof. Aviad Frydman has succeeded in fabricating narrow magnetic wires that exhibit unique patterns of magneto-resistance. These unusual patterns – attributed to the quantum phenomena that govern the behavior of materials at a very small scale – make these wires excellent candidates for use in nano-scale magnetic sensors and transistors. Frydman is also using advanced microscopy to see if fabrication methods for semiconductor based quantum dots – tiny crystals that scientists believe may one day be used in "quantum" computers – might be applied to dots made of non-semi-conductor material.

Dr. Eli Sloutskin uses advanced imaging methods to examine the phenomenon of crystallization. His research – based on extensive work conducted during his post-doctoral studies at Harvard – includes an examination of tiny crystal precursors, which appear in a dense system of simple hard spheres prior to crystallization. Using laser-scanning confocal microscopy, Sloutskin has increased our understanding of how liquids freeze – an issue that is fundamentally important for everything from operating engines in cold climates to the formation of kidney stones.

Seeing is Believing

By expanding the technological limits of imaging and microscopy, Bar-Ilan University is shining a light on the complex dynamics of biological systems, and helping to characterize the "brick and mortar" environment in which we live. Bar-Ilan researchers are bringing scientific discovery into focus – for the good of us all.

Exploring

For more about the research of BIU faculty listed in this brochure go to: www.biu.ac.il and click Research.