Science & Technology Series

Biophysics Research

Life by the Numbers

Tradition of Excellence

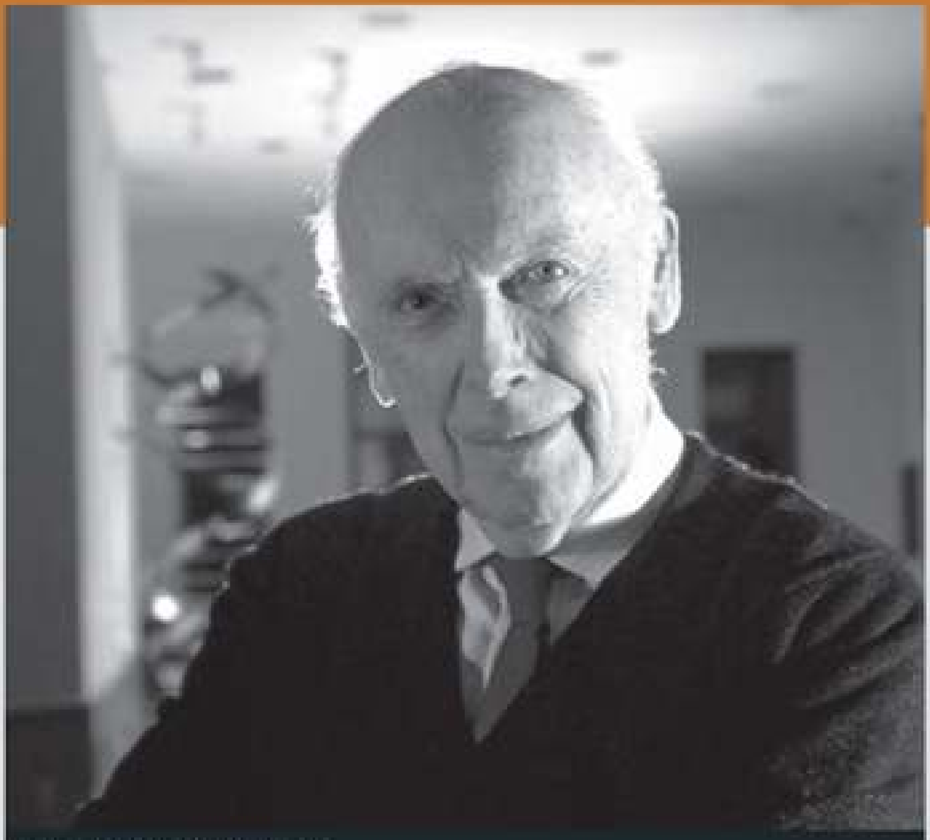
Bar-Ilan University

Bar-Ilan biophysicists are revealing the patterns and principles behind the dynamic process we call life. Their discoveries are creating hope that – in the not-too-distant future – life will be healthier than ever before.

Pictured from left to right:
Dr. Doron Gerber
Prof. Aryeh Frimer
Dr. Yarden Opatowsky
Prof. Benjamin Ehrenberg
Dr. Jordan Chill

Life by the

Numbers



Dr. James D. Watson

Biophysics is the bridge between biology – which studies life in all its variety and complexity – and physics – which seeks out the mathematical laws and patterns that make nature's physical existence both understandable and predictable. From Watson and Crick's 1953 discovery of the structure of DNA to today's ultra-fast "gene-chip" technologies, biophysicists study life at every level, from atoms and molecules to cells, organisms, and environments.

At Bar-Ilan University, a significant number of scientists devote themselves to the study of the membrane – the living "fence" that encircles cells and sub-cellular organelles, stabilizing them energetically and mediating interactions with the outside environment. Other laboratories focus on characterizing fundamental signaling mechanisms in cells, or on quantifying the forces that affect individual proteins. Finally, Bar-Ilan biophysicists are creating important new tools for the observation, measurement and manipulation of biological processes. This "critical mass" of biophysics-oriented researchers is why Bar-Ilan is home to the only undergraduate and graduate study programs in biophysics that are approved by Israel's Council of Higher Education.

From drug discovery to disease prevention, from medical imaging to forensics, and from energy research to environmental protection, Bar-Ilan biophysicists are revealing the patterns and principles behind the dynamic process we call life. Their discoveries are creating hope that – in the not-too-distant future – life will be healthier than ever before.

Membrane Mysteries

Constructed from lipid (fat) molecules together with proteins, sugars and a few other minor components, biological membranes are fairly simple. But by serving as the "gatekeeper" in charge of contact with the extra-cellular environment, membranes play a central role in many complex biological processes. Prof. Benjamin Ehrenberg is examining the forces – related to electric potential – that pump molecules into and out of cells. Using a specially designed membrane model in which the presence of special dyes reveal the fluctuating intensity of an electric field, Ehrenberg quantifies the evolution and collapse of electric forces within membranes.

➔ A "critical mass" of biophysics-oriented researchers is why BIU is home to Israel's only accredited undergraduate and graduate study programs in biophysics.

In another area of his work, Ehrenberg studies photodynamic therapy (PDT) – a clinical treatment in which light-activated compounds that target the cellular membrane generate a toxic molecule that kills malignant cells. Ehrenberg's improvements to PDT – some of which were achieved in collaboration with Prof. Zvi Malik – include quantum-dot enhanced nanoparticles with improved light-absorbing ability, "delivery vehicles" that help cancer-killing compounds reach malignant tissues, and a cream-based photosensitizer that can be illuminated for the treatment of skin cancer and other surface tumors.

Prof. Aryeh Frimer is another scientist looking at how toxic compounds interact with biological membranes. His particular focus is on oxygen radicals – highly reactive, damage-causing compounds. Oxygen radicals are linked to the natural aging process, but also contribute to the genetic damage associated

with more than a hundred human diseases, including cancer, multiple sclerosis, Parkinson's and senile dementia. In order to achieve a clearer understanding of oxygen radical activity and its relation to disease onset, Frimer has created a quantitative tool for pinpointing the exact location of these compounds within the cellular membrane. Frimer's "molecular ruler" – interpreted with the help of a technology called Nuclear Magnetic Resonance, or NMR – allows him to measure the depth to which oxygen radicals penetrate, and identify the exact spot where damage occurs.

Some 70% of drugs target proteins associated with the cellular membrane. However, the physical shape of membrane proteins is almost completely unknown. Dr. Jordan Chill seeks to close this gap, by acquiring reliable structural data about membrane-embedded proteins. In one of his projects, he uses NMR techniques to map the binding interface between two proteins associated with multiple sclerosis – something that will aid in the design of optimal inhibitors for MS that produce limited side-effects. In another area of his research, Chill is looking at the molecular mechanisms involved in the cross-membrane infection of Hepatitis C. Using a membrane-mimicking model, Chill examines the activity of two proteins – each containing a trans-membrane domain – that must assemble into a single structure for infection to occur. By determining the molecular interactions that mediate this process, Chill hopes to suggest possible inhibitors that will halt progression of the disease.

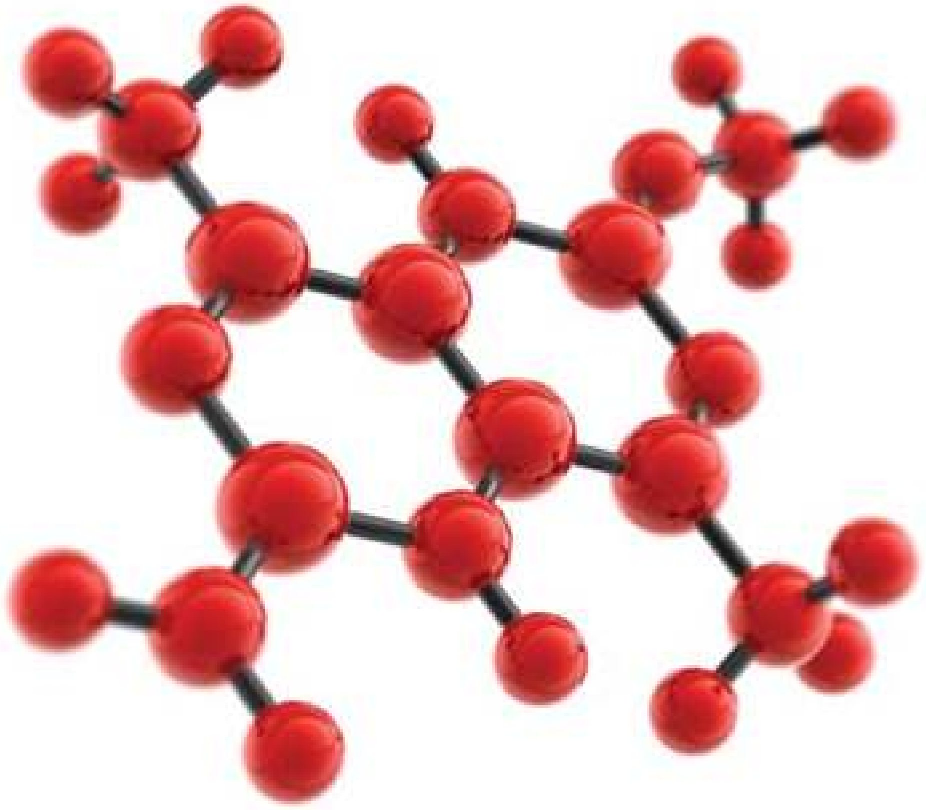
Dr. Yarden Opatowsky – another BIU structural biologist – uses X-ray crystallography to characterize the protein- and membrane-based processes that can lead to disease. Taking advantage of X-ray crystallography's ability to capture pictures of biologically significant processes at the atomic level, Opatowsky is revealing how exposure to infectious agents can cause a normal cell surface receptor to generate protein-based signals involved in cancer onset, neurodegeneration and a number of other pathological conditions. In other projects, Opatowsky is examining the structural basis of axon formation in the developing nervous system, as well as the worrisome emergence of multi-drug resistance in a bacterium associated with conditions including pneumonia, gastrointestinal infection and septic shock.

Significant Signals

Brain activity depends on the proper transfer of chemo-electric signals from one neuron to the next. "Catching" these signals is the job of "Cys-loop" receptors – neurological gatekeepers that are the research specialty of Dr. Yoav Paas. When stimulated by the presence of a particular neurotransmitting material, Cys-loop receptors quickly open and close communication channels. The accuracy and efficiency of this process is vitally important; malfunctioning Cys-loop receptors are associated with neurological disorders including epilepsy, irritable bowel syndrome and the addiction to nicotine. Paas is examining molecular aspects of Cys-loop receptors at high resolution, revealing important information about the electro-physical basis of channel gating, and is identifying new targets for rational drug design.

Bar-Ilan scientists are creating the tools and techniques that help us understand and manipulate biological systems.

Another BIU biophysicist studying the brain is Dr. Alon Korngreen. Korngreen – who studied under the Nobel prize-winning inventor of the patch-clamp, a tool that monitors changes in the electric current flowing across a cell's membrane – has shown that single neurons are more than just "components" of a larger machine; in fact, they, can complete complex mathematical functions. Using patch-clamp studies of live cells as well as computer modeling, Korngreen takes simultaneous measurements of electrical activity taking place in neural networks, or in multiple locations on a single nerve cell. In his recent research, Korngreen is examining voltage-gated calcium channels, and is applying genetic algorithms to the creation of more exact models of the electro-physiology of nerve function.



DNA's double helix is the world's most famous biophysical structure. But according to Dr. Yuval Garini, DNA might be better described as a rope ladder – one that twists, bends and coils in the liquid environment of the cellular nucleus. Garini has developed an optics-based method for studying the minute physical changes that occur when DNA comes into contact with an individual protein. In a unique experimental setup, proteins in solution flow past a single DNA molecule that, on one end, is secured to a substrate, and the other end, moves freely in the water. A gold nanoparticle attached to the moving top of the molecule creates a target for optical measurement. Garini's technique has revealed an increase in DNA stiffness during protein binding, creating the most detailed pictures ever achieved of this prelude to gene expression. In another area of his research, Garini – who is the inventor of a fluorescence-based imaging method for examining chromosome organization – is using time-elapsed, three-dimensional imaging of chromosomes to analyze the relationship between genomic structure and gene function.

Bio

Moving from the molecular to the cellular level, Prof. Haim Breitbart, a Bar-Ilan alumnus, is using advanced technologies to characterize signal transduction in the mammalian fertilization process. Not only are Breitbart's studies revealing important information that may lead to the improvement of agricultural livestock, they are contributing to the basic scientific knowledge needed to find improved clinical treatments for human infertility.

BIU researchers are characterizing the physical laws that govern self-assembly of the macro-molecular structures that control biological processes.

Top Tools

One of the most important tools used by biophysicists is NMR – a technology that makes it possible to prove the structure and dynamics of biological molecules and their surrounding liquid environment. Prof. Eva Meirovitch has created a unique NMR-based methodology that provides quantitative information about protein flexibility, revealing a new and detailed picture of protein dynamics and aggregation within [the dynamic environment of] bodily fluids. Another NMR expert is Dr. Gil Goobes, who is characterizing the interactions between biological molecules and surfaces – a line of research with significance for a range of applications in medicine and materials science.

Biological processes are complex, involving the self-assembly of macromolecular structures that perform various functions. To characterize the physical laws governing such processes, Prof. Elisha Haas takes an interdisciplinary approach that combines protein engineering, chemistry, ultra-fast fluorescent spectroscopy and time-resolved measurements using Fluorescence Radiation Energy Transfer, or FRET. His research seeks to identify gene-based signals that underlie the efficient folding of protein molecules, and to characterize the relation of these conformational dynamics to function. Haas is also examining the macromolecular basis of pathological conditions – such as the buildup of protein aggregates in the nervous system that are associated with diseases such as Alzheimer's.

Studying the genetic nature of viral disease has been made easier by a new technology developed by Dr. Doron Gerber. Gerber's invention addresses a vexing biomedical "bottleneck"– the fact that traditional protein replication techniques produce them as inactive viral proteins, or, if active, produce them in insufficient quantities for the many experiments needed to isolate important protein-protein interactions. Searching for a way to do more with less, Gerber designed a tool the size of half a playing card, etched with thousands of "microfluidic" channels. Inside these channels, thousands of experiments – each consisting of a unique interaction – can be performed simultaneously, providing quantitative data about each reaction's intensity.

Dynamics of Discovery

By creating the tools and techniques that help us understand and manipulate biological systems, Bar-Ilan biophysicists are solving important medical and environmental problems, while uncovering new topics for study and exploration. In the spirit of interdisciplinary innovation, Bar-Ilan scientists are leading the way toward a healthier future.

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

physics

The Gonda (Goldschmied) Medical Diagnostics Research Building

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 dozens of returning experimental scientists within its world-class research infrastructure, and has added state-of-the-art physical facilities in engineering, brain sciences and nanotechnology to house these innovative initiatives. The Science and Technology Series highlights some of the University's most exciting research endeavors.

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

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