

FIGHTING ANTIBIOTIC RESISTANCE



Today, antibiotics are under siege.

Bacteria and other organisms, many displaying multi-drug resistance, are rapidly gaining ground. This poses one of the most serious challenges for medical science. As IIT Coleman Faculty Scholar and Assistant Professor of Physics David Gidalevitz points out, “Bacteria only need to undergo a slight mutation to make traditional antibiotics ineffective.”

David Gidalevitz

Photo: Bonnie Robinson

research

Many antibiotic drugs act by attaching to specific cell-surface receptors. When a bacterium mutates, it changes these binding sites so that the antibiotic either cannot attach, or binds to the membrane but loses its bactericidal effect. Gidalevitz believes a unique class of compounds known as antimicrobial peptides (also known as host defense peptides) may help humanity out of its antibacterial rut.

Antimicrobial peptides, or AMPs, occur naturally in organisms ranging from microbes to mammals. In humans, AMPs are part of our innate immune response—the first line of defense against infection. As Gidalevitz explains, these peptide defenders have some remarkable qualities. They can target an extremely wide range of pathogens, including two broad categories of bacteria (known as either Gram positive or Gram negative, based on their staining properties), as well as some viruses, protozoa, tumors, and even fungi. More importantly, AMPs are able to hunt and kill prokaryotic cells like bacteria while leaving eukaryotic cells—the healthy cells in our bodies—undisturbed.

Gidalevitz's work involves the construction of membrane mimics, manmade nanostructures imitative of natural cell walls. He uses these mimics to better understand the precise mechanisms that allow AMPs to recognize and disrupt bacterial cell membranes, despite their structural variation.

Although some experimental drugs composed of naturally occurring AMPs have been attempted, such compounds are quickly recognized by proteases in the body and destroyed before they are able to act. On the other hand, ampetoids—mimics of natural

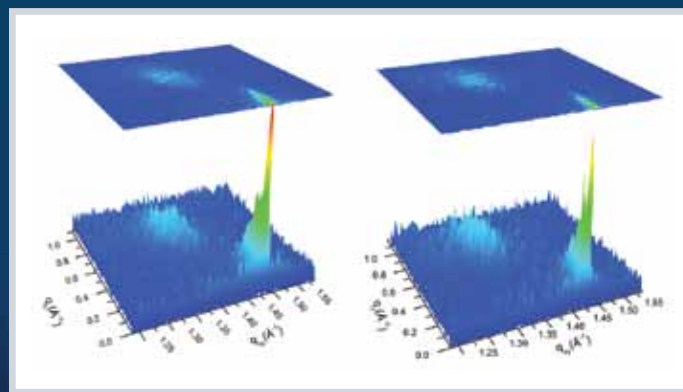
AMPs—are different.

“Antimicrobial peptide mimics won't interfere with general biological systems,” Gidalevitz says. “They're not recognized as such.”

How do AMPs target bacterial cells for destruction? Part of the trick occurs through recognition of the lipid matrix of the bacterial cell wall, which carries an electrically negative charge (unlike eukaryotic cell membranes, which are electrically neutral). Generally, the kinds of mutations bacteria undergo in order to outwit traditional antibiotics can't save them from a frontal assault on their membrane chemistry by an antimicrobial peptide. Because of this, AMPs offer an attractive weapon in the pitched battle against resistant pathogens.

To study the structure of membrane mimics and their interactions with AMPs, Gidalevitz takes a new approach, using sensitive technologies, including synchrotron-grazing incidence X-ray diffraction and X-ray reflexivity, in collaboration with Argonne National Laboratory. “To investigate the action of the peptides and membrane mimics with these techniques is fairly novel,” Gidalevitz notes. “These are definitely not tools used by a majority of biologists.”

Unlike natural cell walls, which are composed of a lipid bilayer, Gidalevitz's membrane mimics are monolayer structures



Grazing incidence X-ray diffraction pattern of phospholipid monolayer mimicking the surface of the red blood cell; [left] before injection of human antimicrobial peptide LL-37; [right] after peptide injection

applied to an aqueous surface in which natural AMPs are dissolved. The AMPs themselves are supplied by Gidalevitz's collaborators, including Annelise Barron of Stanford University.

A \$1.3 million National Institutes of Health grant will help Gidalevitz pursue this research for the next three years, though there is so much to learn about the subtleties of these powerful compounds, and their potential benefits so great, that he expects his work will likely continue long thereafter.

Research into membrane dynamics and AMP mechanisms of action bring promise for the development of an entirely new class of peptide antibiotics, which will target pathogenic invaders and circumvent antibacterial resistance.

—Richard Harth

MORE ONLINE

Roles of antimicrobial peptides in immune defense: <http://download.cell.com/trends/immunology/pdf/PIIS1471490609000052.pdf?intermediate=true>

Antimicrobial peptides and lethal infections in mice: www.sciencedaily.com/releases/2009/06/090619124928.html

Antimicrobial peptides and applied biotechnology: www.ejbiotechnology.info/content/vol6/issue3/full/1/index.html

Rising energy costs, dwindling fossil fuel reserves, and threats of climate change are central challenges for this century. As IIT Professor of Architecture Peter Land points out, we need only look around us to see the biggest consumer of this energy: the built environment.

At IIT, a research initiative takes aim at tall buildings, focusing on refining their design and equipping them to extract the maximum benefit from two primary forms of energy: sunlight and wind. Although his interdisciplinary team came together under the umbrella of the Wanger Institute for Sustainable Energy Research (WISER) just a year ago, Land has wrestled with architectural challenges of sustainable tall buildings for two decades.

Now WISER is harnessing university-wide resources, uniting the College of Architecture with Armour College of Engineering faculty and researchers from other domains, to provide a comprehensive platform to address issues of tall structure sustainability.

New building designs, some appearing to materialize from the realm of science fiction, are being developed by Land and his colleagues, and tested at IIT under rigorous conditions. One day, such ultra-efficient tall buildings may gather all the energy powering them from renewable sources—a synthesis of design and construction Land refers to as the stand-alone concept. Emancipated from the grid, these carbon-free structures could provide living and working space for a burgeoning population, generating their own energy onsite through sustainable technology. “We really are the first school to come together to try to make this a reality,” Land says.

Within WISER, Land has formed a consortium consisting of himself and 15 engineers, to investigate the sustainable built environment. “The design concepts are worked out under my direction with advanced-level students,” he says. Currently, some 12–15 building forms are in testing phases. These unorthodox structures are variously shaped to optimize their ability to extract energy from clean sources.

A key focus of this research is wind turbines. Tall buildings can take advantage of greater wind velocities at higher altitudes, providing significantly more energy than other types of buildings. To be used effectively, incoming wind flow must be accelerated, and then focused onto the turbine’s rotors, which may be located on the structure’s roof or on the building façade. Single-, bi-, and omni-directional turbines may be used, depending on the particulars of building design and the prevailing wind conditions.

In order to further optimize a tall building for wind energy, Land called on the fluid mechanics expertise of Henry R. Linden Professor of Energy and WISER Director Hamid Arastoopour, and Associate Professor of Mechanical and Aerospace Engineering Dietmar Rempfer.

Rempfer stresses the importance of maximizing wind velocity, as the energy content of the wind varies with the cube (or third power) of the average wind speed. “If the average wind velocity doubles,” he says, “I can extract eight times the power from the wind compared to lower wind velocity.”

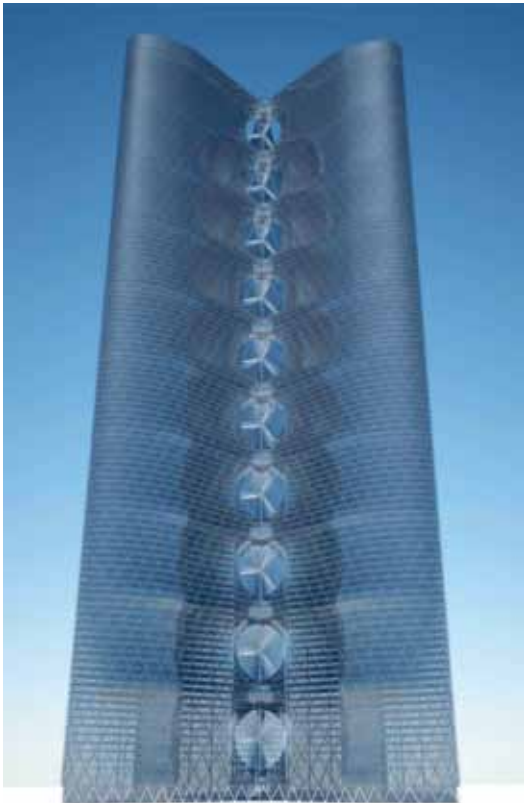
Once Land has completed the building’s conceptual design, an accurate physical model of the structure is produced and subjected to wind tunnel testing. Rempfer gathers the resulting data and uses computational fluid mechanics to accurately model the wind flow. To optimize the building’s shape, he digitally tinkers with the geometry of his computational model, performing simulations to see how the power output changes through repeated iterations.

As Rempfer explains, one such tall building design [see inset] features paired towers, between which a series of wind turbines are suspended. The two towers are shaped in such a way that they form a flow duct or nozzle to increase the wind flow velocity, focusing the accelerated stream onto the turbines.

Other sustainable designs use photovoltaic (PV) elements as integral design features, inseparable from building structure. These may take the form of transparent PV cells embedded in a building’s window glass, or solar concentrators capable of focusing solar radiation on parabolic reflectors. Incident sunlight is used to heat surfaces of the solar-thermal collectors to more than 1,000 degrees, in order to drive conventional steam turbines or for solar thermal heating of the building’s air or water.

Eventually, the use of wind and solar, as well as other renewable resources including geothermal, will guide not only tall building design, but also city planning in general. Land says that changing the political will of developers and governments of the world will be as important as design evolution in the promotion of pollution-free environments for future generations.

—Richard Harth



SKY-HIGH SUSTAINABILITY

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Council on Tall Buildings and Urban Habitat: www.ctbuh.org

Wind turbines in the Bahrain World Trade Center: www.inhabitat.com/2007/03/28/bahrain-world-trade-center-has-wind-turbines