



## Highlights of the Biophysical Society 56th Annual Meeting

Protein assassins, hibernating woodchucks, the evolution of neurotoxins, and more

The latest news and discoveries in medicine, physics, environmental science, and interdisciplinary fields will be featured at the 56th Annual Meeting of the Biophysical Society (BPS), held Feb. 25 - Feb. 29, 2012, at the San Diego Convention Center in San Diego, Calif. With more than 4,000 poster presentations, 200 exhibits, 20 symposia, and 6,000 research scientists in attendance each year, the BPS Annual Meeting is the largest gathering of biophysicists in the world.

Journalists are invited to attend the conference free of charge. For more information or to register, please see below.

The following summaries highlight a few of the meeting's many noteworthy talks.

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### HIGHLIGHTS: SUNDAY, FEBRUARY 26

**Microbes May Be Engineered to Help Trap Excess CO<sub>2</sub> Underground:** Among the methods being considered for removing excess carbon dioxide (CO<sub>2</sub>) from the atmosphere is sequestering the gas in porous rock deep underground. But the mineralization process required to permanently trap this greenhouse gas is extremely slow, sometimes taking hundreds to thousands of years. Bacteria might help speed things up, says a team led by researchers at Lawrence Berkley National Laboratory's Center for Nanoscale Control of Geologic CO<sub>2</sub> (NCGC). Using different surface bacteria as proxies for their deeper-dwelling cousins, the researchers first examined the microbes' effect on calcium carbonate formation, and discovered that all of the species accelerated the process. The rate, they report, was highest in microbes whose surfaces had a thin protein shell known as an S-layer. The researchers suspected that the negative charge of the S-layer attracted positive calcium ions and brought them in proximity with carbonate. To test this theory, the researchers engineered artificial S-layers and increased their negative charge by attaching a loop of six amino acids. When carbonate was introduced, nucleation was significantly increased. The next step will be to culture deep subsurface microbes in the lab, make nanoscale changes to increase the negative charge of their surfaces, and see if that "tuning" makes them better able to speed up carbonate nucleation.

Presentation 941-Pos, "Tuning microbial surfaces to control carbonate mineralization," is at 1:45 p.m. on Sunday, Feb. 26.

**Invade and Conquer: A role for nicotine in promoting heart and blood vessel disease:** Irritating smoke from cigarettes has long been considered the main risk factor for heart disease. But new research from Brown University in Providence, R.I., shows that nicotine itself, a component of cigarette smoke, can contribute to the disease process by changing cell structure in a way that promotes the invasion of the smooth muscle cells that line blood vessels. When this invasion occurs, it typically gives rise to the formation of vessel-clogging fatty deposits known as plaque – the hallmark of heart and blood vessel disease. The study illuminates the multistep process of plaque formation, and suggests a new means of intervening on the process: targeting the cell structures that are changed by nicotine and promote invasion of the smooth muscle lining the vessel wall. If a therapy could prevent, slow, or reverse that step, it would likely interrupt the plaque-production cycle. If confirmed in further studies, the finding appears to question the health benefits of helping people quit smoking by prescribing smokeless nicotine delivery agents such as gum or patches.

Presentation 593-Pos, "Cigarette smoke and nicotine-induced remodeling of actin cytoskeleton and extracellular matrix by vascular smooth muscle cells," is at 1:45 p.m. on Sunday, Feb. 26.

**Molding the Business End of Neurotoxins:** For snakes, spiders, and other venomous creatures, the "business end," or active part, of a venomous toxin is the area on the surface of a protein that is most likely to undergo rapid evolution in response to environmental constraints, say researchers from Ben Gurion University in Israel. Understanding these evolutionary forces can help researchers predict which part of unstudied toxins will do damage. Scientists have long suspected that evolutionary forces that encourage diversity could play a role in shaping how a toxin works; if such forces were in play, toxins could rapidly evolve within a single species or change quickly from species to species, supporting predators and prey in the "arms race" that keeps them in competition. Still, it was not clear whether the same rules dictate neurotoxin evolution between animals from different phyla (that is, that have very little genetically in common with each other), or whether there are different rules in play for different organisms. Using the published gene sequences for dozens of different toxins from various species of poisonous scorpions, spiders, and snakes, the Ben Gurion researchers studied toxins that targeted a variety of ion channels and receptors. They found a clear correlation between the active parts of the toxins and the parts that experience these diversifying forces.

Presentation 681-Pos, "Molding the business end of neurotoxins by diversifying evolution," is at 1:45 p.m. on Sunday, Feb. 26.

**Vaccines for HIV: A new design strategy:** Vaccines prime the immune system to target molecular signatures associated with a particular pathogen, but HIV's ability to mutate has made it difficult to identify reliable vaccine targets. Physical scientists and clinical virologists from the Massachusetts Institute of Technology (MIT) and the Ragon Institute in Cambridge, Mass., have identified a promising strategy for HIV vaccine design using a mathematical technique that has also been used in problems related to quantum physics, as well as in analyses of stock price fluctuations and studies of enzymes. The team sought to identify groups of amino acids that are both evolutionarily constrained (meaning that they are not able to change greatly from generation to generation) and that mutate in tandem. By staging a multipronged attack against these groups, the researchers reasoned, they might be able to trap the virus between two bad choices: be destroyed by the immune system, or mutate and destroy itself. With a mathematical tool called random matrix theory, they looked for collectively co-evolving groups of amino acids with a high number of negative correlations (meaning multiple mutations would destroy the virus) and a low number of positive correlations (meaning the virus could survive multiple mutations). They found this combination in a region, which they call Gag sector 3, that maintains the protein shell of the virus. The researchers are currently working to extend their methods to HIV proteins beyond Gag. They are also developing elements of the active components of a vaccine that would prime the immune system to selectively target Gag sector 3 proteins, and they expect to begin testing in animal models soon.

Presentation 114-Plat, "Analysis of collective coevolution in HIV proteins suggests strategies for rational vaccine design," is at 12:30 p.m. on Sunday, Feb. 26.

**Hibernating Woodchucks Offer New Insight into Protection from Cardiac Arrhythmias:** A new study of hibernating woodchucks may provide insight into therapies for cardiac arrhythmias – abnormal heart rhythms such as ventricular tachycardia and ventricular fibrillation that can lead to sudden cardiac death. Bears and bats can be roused from their slumber by external stimuli. But woodchucks (*Marmota monax*), also known as groundhogs, are "true hibernators," which means

they can enter a profoundly altered physiological state: their body temperature drops to near-ambient levels (often as low as freezing) and heart and respiration rates slow dramatically. Despite – or perhaps because of – these changes, hibernating animals have been found to be more resistant to cardiac arrhythmias and sudden cardiac death. Researchers at the University of Medicine and Dentistry of New Jersey (UMDNJ)-New Jersey Medical School in Newark examined muscle cells, or myocytes, isolated in winter and in summer from woodchucks, and monitored the release and uptake of calcium ions when the cells were activated. They found that the myocyte sarcoplasmic reticulum – the membrane system in muscle cells that stores and releases calcium – had less spontaneous leakage of calcium, released more of it during excitation, and took it back up faster than that of summer woodchucks or non-hibernating animals. Understanding cardiac adaptive mechanisms in hibernators may suggest new strategies to protect non-hibernating animals, especially humans, from certain types of fatal cardiac arrhythmias.

Presentation 513-Pos, “Calcium handling properties in a hibernating animal: insights into antiarrhythmic mechanisms,” is at 1:45 p.m. on Sunday, Feb. 26.

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#### HIGHLIGHTS: MONDAY, FEBRUARY 27

Blue Light Culprit in Red Tide Blooms: Though the precise causes of red tides remain a mystery, a team of researchers in the United States and Spain has solved one of the main riddles about these ecological disasters by uncovering the specific mechanism that triggers phytoplankton to release their powerful toxins into the environment. Red tides appear when naturally occurring algae, including *Karenia brevis*, multiply very rapidly, becoming so concentrated that the ocean surface takes on a reddish hue. *Karenia* produces brevetoxin, a powerful neurotoxin that binds to nerve and muscle cells, leading to substantial marine life mortality and human morbidity. The blooms are triggered by some as yet unknown fluctuations in ocean temperature, salinity, and available nutrients. The researchers discovered that *Karenia* and other unicellular microalgae function very much like the secretory cells we have in our bodies. Namely, they store inside membrane-lined microscopic vesicles their active chemicals — such as hormones, antibacterial products, and, in *Karenia*'s case, toxins. When properly stimulated, these cells released their cargo by a process known as exocytosis. The researchers discovered that phytoplankton release their toxin-loaded gels when exposed to sunlight, particularly the blue portion of the spectrum. These observations support the notion that *Karenia brevis* functions as a typical secretory cell, which the researchers believe opens the way for a better understanding of red tide bloom dynamics.

Presentation 1624-Pos, “Exocytic mechanisms of storage and release of brevetoxin in the dinoflagellate *Karenia brevis*,” is at 1:45 p.m. on Monday, Feb. 27.

New Street Drug ‘Bath Salts’ Packs Double Punch: Mimicking effects of two powerful narcotics: The street drug commonly referred to as “bath salts” is one of a growing list of synthetic and unevenly regulated narcotics that are found across the United States and on the Internet. New research on this potent drug paints an alarming picture, revealing that bath salts pack a powerful double punch, producing combined effects similar to both methamphetamine (METH) and cocaine. “This combination of effects is particularly novel and unexpected,” says Louis J. De Felice of Virginia Commonwealth University’s School of Medicine in Richmond. “Methamphetamine and cocaine operate in the brain in completely opposite ways. It would be atypical that both drugs would be taken together, but that’s the effect that occurs with bath salts.” The team’s research reveals that bath salts contain two structurally similar chemicals that produce

quite dissimilar effects on the brain's dopamine transport system. Dopamine is a neurotransmitter that plays an important role in the brain's pleasure and reward centers. Though bath salts' chemicals are structurally similar, both acting as potent psycho-stimulants, they use completely opposite mechanisms in the brain. The surprising finding is that rather than canceling each other out, as would be anticipated, the chemicals combine to enhance the effects of the other. The researchers do not understand the fundamental reason why two structurally similar drugs act oppositely on the dopamine transporter. There also are many questions on the meaning of these findings for the dozens of other illicit synthetic drugs that have found their way to the street," concludes De Felice. "We do suspect, however, that the combination that is found in bath salts could be behind its powerful physiological and neurological effect on users."

Presentation 1086-Plat, "Bath salts': A synthetic cathinone whose two major components act similar to methamphetamine and cocaine on the human dopamine transporter," is at 9:15 a.m. on Monday, Feb. 27.

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#### HIGHLIGHTS: TUESDAY, FEBRUARY 28

**Proteins Behaving Badly:** Researchers develop an algorithm to predict how and when proteins misfold: Several neurodegenerative diseases, including Alzheimer's and ALS (Lou Gehrig's disease), are caused when the body's own proteins fold incorrectly, recruit and convert healthy proteins to the misfolded form, and aggregate in large clumps that gum up the works of the nervous system. "For Star Trek fans, this is like the Borg, a fictional race of cyborgs that abduct and assimilate humans and other species," says Steven Plotkin, a biophysicist at the University of British Columbia who studies the process of protein misfolding. Plotkin's research group has developed an algorithm that can predict which regions of a protein are prone to misfolding, and how mutations in the protein and changes in the cellular environment might affect the stability of these vulnerable regions. The algorithm can also predict which new parts of the protein will be exposed when it misfolds. Researchers can then use the exposed regions as targets for diagnostic and therapeutic treatments. The algorithm can be adapted for different proteins, and the group has used it to study neurodegenerative disease-causing proteins, as well as misfolded proteins that have been implicated in some cancers. More recently, the research group has used the power of computer simulations to manipulate proteins in a virtual environment, testing out how easy it is for misfolding and propagation to occur in mutated proteins. Using this tool has helped the team predict the progression of hereditary ALS disease, and offers the hope that, through better understanding, scientists may one day be able to effectively combat currently incurable neurodegenerative diseases.

Presentation 2414-Pos, "Template-directed protein misfolding in silico and in the cell," is at 1:45 p.m. on Tuesday, Feb. 28.

**A Change of Heart:** Probing how chronic alcoholism alters cellular signaling of heart muscle: Scientists know severe alcoholism stresses the heart and that mitochondria, the cellular energy factory, are especially vulnerable to dysfunction. But they don't know the precise mechanism. Now new experiments led by a team at the Wadsworth Center of the New York State Department of Health in Albany, and Thomas Jefferson University in Philadelphia, may provide insights into possible modes of heart damage from alcohol. Using a technique called electron microscopic tomography, the Albany group produced the first 3-D images of mitochondria and discovered tiny tethers linking mitochondria to another cell compartment, the endoplasmic reticulum (ER), where calcium is stored. A clue about the role of these tethers was provided by collaborative

experiments with the Philadelphia group. Normally mitochondria take up very little calcium but, as mitochondria get closer to the ER, calcium uptake increases. Calcium overload damages mitochondria, shutting down energy production and leading to cell death. The team looked at calcium regulation and cell structure in the pumping chambers of two groups of laboratory rats to find clues to how hearts are damaged by alcohol consumption. One group of rats was healthy and one was fed alcohol for six months. The 3-D images the team produced clearly show that the mitochondria of alcohol-fed rats are disorganized. The primary focus of the team's ongoing analysis is the mitochondrial interface with the ER – in particular, characterization of the length, number, and distribution of tethers, which could explain the observed dysfunction of heart mitochondria.

Presentation 2218-Plat, "SR-Mitochondrial ultrastructure in the heart of normal and ethanol-fed rats," is at 4:45 p.m. on Tuesday, Feb. 28.

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#### HIGHLIGHTS: WEDNESDAY, FEBRUARY 29

**Protein Assassin:** Scientists find that the unfolded end of a protein can kill E. coli-like bacteria selectively: When bacteria wage a turf war, some of the combatants have an extra weapon. Certain strains of E. coli bacteria produce proteins that kill competing E. coli and other like microbes. Researchers from Newcastle University in England have recently discovered something surprising about one of these lethal proteins: even after the toxic folded portion of the protein is removed, the unfolded end is still deadly. The Newcastle research team focused their attention on a specific bacteria-killing protein called Colicin N. Scientists traditionally divide the structure of Colicin N into three separate parts, or domains: a receptor binding domain that helps the colicin latch onto the bacterial membrane; a translocation domain that helps the colicin wiggle into the cells; and a toxic domain that punches holes in the membrane from the inside, so that potassium, an element essential to proper cell function, leaks out of the bacteria. In order to learn more about how the translocation domain, called ColN-T, functions, the Newcastle researchers isolated this part of the protein and added it to a fluid containing Colicin N-susceptible E. coli. Surprisingly, the E. coli started leaking potassium and dying shortly after the ColN-T was introduced into their environment. It turned out the seemingly disarmed protein could still kill. The finding may one day help scientists searching for new, more targeted, ways to kill antibiotic-resistant microbes.

Presentation 3217-Pos, "Targeted killing of Escherichia coli by an unfolded protein," is at 10:30 a.m. on Wednesday, Feb. 29.

**Taking Back the Brain:** New targets of Alzheimer's disease treatment: A promising novel target for potentially treating Alzheimer's disease has been identified in mouse experiments by a team at the University of California-Davis. The team's focus is on controlling cells in the brain known to be major inflammatory agents. These cells, called microglia, are activated by toxic beta amyloid proteins that accumulate as plaques in the brain and disrupt neuronal function, and they are major players in the initiation and progression of Alzheimer's disease. To turn off the microglia, and therefore stop their neurotoxic effects, the UC Davis team blocked the flow of potassium ions through a voltage-gated potassium channel on the microglia membrane. Results showed that the blocker inhibited plaque-induced microglia activation and the toxicity associated with it, but that it did not interfere with the useful "housecleaning" tasks that microglia perform. "Our observations raise the exciting possibility that potassium channel blockers might preferentially inhibit the action of microglia related to killing neurons without affecting the beneficial functions

associated with them, as such as scavenging of debris,” explains UC Davis’ David P. Jenkins, first author of the study.

Presentation 3443-Pos, “Microglial KV1.3 channels as a potential target for Alzheimer’s disease,” is at 10:30 a.m. on Wednesday, Feb. 29.

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This news release was prepared for the Biophysical Society by the American Institute of Physics (AIP).

#### ABOUT THE 2012 ANNUAL MEETING

Each year, the Biophysical Society Annual Meeting brings together over 6,000 research scientists in the multidisciplinary fields representing biophysics. With more than 4,000 poster presentations, over 200 exhibits, and more than 20 symposia, the BPS Annual Meeting is the largest meeting of biophysicists in the world. Despite its size, the meeting retains its small-meeting flavor through its subgroup meetings, platform sessions, social activities, and committee programs.

The 56th Annual Meeting will be held at the San Diego Convention Center (111 W. Harbor Drive, San Diego, CA 92101), located three miles from the San Diego International Airport and less than one mile from the Amtrak station. The San Diego Trolley has two stops directly in front of the Center at Harbor Drive/First Avenue and Harbor Drive/Fifth Avenue.

#### QUICK LINKS

Meeting Home Page:

<http://www.biophysics.org/2012meeting/Main/tabid/2386/Default.aspx>

Housing and Travel Information:

<http://www.biophysics.org/2012meeting/AccommodationsTravel/HotelInformation/tabid/2479/Default.aspx>

Program Abstracts and Itinerary Planner:

<http://www.abstractsonline.com/plan/start.aspx?mkey=%7B5B4BAD87%2D5B6D%2D4994%2D84CE%2DB3B13E2AEAA3%7D>

#### PRESS REGISTRATION

The Biophysical Society invites credentialed journalists, freelance reporters working on assignment, and public information officers to attend its Annual Meeting free of charge. For more information on registering as a member of the press, contact Ellen Weiss, Director of Public Affairs and Communications ([eweiss@biophysics.org](mailto:eweiss@biophysics.org)<<mailto:eweiss@biophysics.org>>, 240-290-5606), or visit

<http://www.biophysics.org/2012meeting/Registration/Press/tabid/2477/Default.aspx>.

#### ABOUT BPS

The Biophysical Society (BPS), founded in 1956, is a professional scientific society established to encourage development and dissemination of knowledge in biophysics. The Society promotes growth in this expanding field through its annual meeting, monthly journal, and committee and outreach activities. Its 9000 members are located throughout the U.S. and the world, where they teach and conduct research in colleges, universities, laboratories, government agencies, and

industry. For more information on the Society or the 2012 Annual Meeting, visit [www.biophysics.org](http://www.biophysics.org) <<http://www.biophysics.org>>.