SCIENCE NEWS

Higher Dementia Risk Linked to More use of Common Drugs

A large study links a significantly increased risk for developing dementia, including Alzheimer's disease, to taking commonly used medications with anticholinergic effects at higher doses or for a longer time. Many older people take these medications, which include nonprescription diphenhydramine (Benadryl). JAMA Internal Medicine published the report, called "Cumulative Use of Strong Anticholinergic Medications and Incident Dementia."

The study used more rigorous methods, longer follow-up (more than seven years), and better assessment of medication use via pharmacy records (including substantial nonprescription use) to confirm this previously reported link. It is the first study to show a dose response: linking more risk for developing dementia to higher use of anticholinergic medications. And it is also the first to suggest that dementia risk linked to anticholinergic medications may persist and may not be reversible even years after people stop taking these drugs.

"Older adults should be aware that many medications including some available without a prescription, such as over-the-counter sleep aids have strong anticholinergic effects," said Shelly Gray, PharmD, MS, the first author of the report, which tracks nearly 3,500 Group Health seniors participating in the long-running Adult Changes in Thought (ACT), a joint Group Health-University of Washington (UW) study funded by the National Institute on Aging. "And they should tell their health care providers about all their over-the-counter use," she added.

For instance, the most commonly used medications in the study were tricyclic antidepressants like doxepin (Sinequan), first-generation antihistamines like chlorpheniramine (Chlor-Trimeton), and antimuscarinics for bladder control like oxybutynin (Ditropan). The study estimated that people taking at least 10 mg/day of doxepin, 4 mg/day of chlorpheniramine, or 5 mg/day of oxybutynin for more than three years would be at greater risk for developing dementia. Dr. Gray said

substitutes are available for the first two: a selective serotonin re-uptake inhibitor (SSRI) like citalopram (Celexa) or fluoxitene (Prozac) for depression and a second-generation antihistamine like loratadine (Claritin) for allergies. It's harder to find alternative medications for urinary incontinence, but some behavioral changes can reduce this problem.

"If providers need to prescribe a medication with anticholinergic effects because it is the best therapy for their patient," Dr. Gray said, "they should use the lowest effective dose, monitor the therapy regularly to ensure it's working, and stop the therapy if it's ineffective." Anticholinergic effects happen because some medications block the neurotransmitter called acetylcholine in the brain and body, she explained. That can cause many side effects, including drowsiness, constipation, retaining urine, and dry mouth and eyes.

"With detailed information on thousands of patients for many years, the ACT study is a living laboratory for exploring risk factors for conditions like dementia," said Dr. Gray's coauthor Eric B. Larson, MD, MPH. "This latest study is a prime example of that work and has important implications for people taking medications and for those prescribing medications for older patients." Dr. Larson is the ACT principal investigator, vice president for research at Group Health, and executive director of Group Health Research Institute (GHRI). He is also a clinical professor of medicine at the UW School of Medicine and of health services at the UW School of Public Health.

Some ACT participants agree to have their brains autopsied after they die. That will make it possible to follow up this research by examining whether participants who took anticholinergic medications have more Alzheimer's-related pathology in their brains compared to nonusers.

One Nanoparticle, Six Types of Medical Imaging

Using two biocompatible parts, University at Buffalo researchers and their colleagues have designed a nanoparticle that can be detected by six medical imaging techniques:

- computed tomography (CT) scanning;
- positron emission tomography (PET) scanning;
- photoacoustic imaging;
- fluorescence imaging;
- upconversion imaging; and
- Cerenkov luminescence imaging.

In the future, patients could receive a single injection of the nanoparticles to have all six types of imaging done.

This kind of "hypermodal" imaging, if it came to fruition, would give doctors a much clearer picture of patients' organs and tissues than a single method alone could provide. It could help medical professionals diagnose disease and identify the boundaries of tumors.

"This nanoparticle may open the door for new 'hypermodal' imaging systems that allow a lot of new information to be obtained using just one contrast agent," says researcher Jonathan Lovell, PhD, UB assistant professor of biomedical engineering. "Once such systems are developed, a patient could theoretically go in for one scan with one machine instead of multiple scans with multiple machines."

When Lovell and colleagues used the nanoparticles to examine the lymph nodes of mice, they found that CT and PET scans

provided the deepest tissue penetration, while the photoacoustic imaging showed blood vessel details that the first two techniques missed. Differences like these mean doctors can get a much clearer picture of what's happening inside the body by merging the results of multiple modalities.

A machine capable of performing all six imaging techniques at once has not yet been invented, to Lovell's knowledge, but he and his coauthors hope that discoveries like theirs will spur development of such technology.

The research, Hexamodal Imaging with Porphyrin-Phospholipid-Coated Upconversion Nanoparticles, was published online Jan. 14 in the journal *Advanced Materials*.

The researchers designed the nanoparticles from two components: An "upconversion" core that glows blue when struck by near-infrared light, and an outer fabric of porphyrin-phospholipids (PoP) that wraps around the core.

Each part has unique characteristics that make it ideal for certain types of imaging. The core, initially designed for upconversion imaging, is made from sodium, ytterbium, fluorine, yttrium and thulium. The ytterbium is dense in electrons, a property that facilitates detection by CT scans.

The PoP wrapper has biophotonic qualities that make it a great match for fluorescence and photoacoustic imagining. The PoP layer also is adept at attracting copper, which is used in PET and Cerenkov luminescence imaging.

"Combining these two biocompatible components into a single nanoparticle could give tomorrow's doctors a powerful, new tool for medical imaging," says Prasad, also a SUNY Distinguished Professor of chemistry, physics, medicine and electrical engineering at UB. "More studies would have to be done to determine whether the nanoparticle is safe to use for such purposes, but it does not contain toxic metals such as cadmium that are known to pose potential risks and found in some other nanoparticles."

"Another advantage of this core/shell imaging contrast agent is that it could enable biomedical imaging at multiple scales, from single-molecule to cell imaging, as well as from vascular and organ imaging to whole-body bioimaging," Chen adds. "These broad, potential capabilities are due to a plurality of optical, photoacoustic and radionuclide imaging abilities that the agent possesses."

Lovell says the next step in the research is to explore additional uses for the technology.

For example, it might be possible to attach a targeting molecule to the PoP surface that would enable cancer cells to take up the particles, something that photoacoustic and fluorescence imaging can detect due to the properties of the smart PoP coating. This would enable doctors to better see where tumors begin and end, Lovell says.

Functional Tissue-engineered Intestine Grown from Human Cells

A new study by researchers at Children's Hospital Los Angeles has shown that tissue-engineered small intestine grown from human cells replicates key aspects of a functioning human intestine. The tissue-engineered small intestine they developed contains important elements of the mucosal lining and support structures, including the ability to absorb sugars, and even tiny or ultra-structural components like cellular connections.

Tissue-Engineered Small Intestine (TESI) grows from stem cells contained in the intestine and offers a promising treatment for short bowel syndrome (SBS), a major cause of intestinal failure, particularly in premature babies and newborns with congenital intestinal anomalies. TESI may one day offer a therapeutic alternative to the current standard treatment, which is intestinal transplantation, and could potentially solve its largest challenges donor shortage and the need for lifelong immunosuppression.

NASA finds good news on forests and carbon dioxide

A new NASA-led study shows that tropical forests may be absorbing far more carbon dioxide than many scientists thought, in response to rising atmospheric levels of the greenhouse gas. The study estimates that tropical forests absorb 1.4 billion metric tons of carbon dioxide out of a total global absorption of 2.5 billion.

"This is good news, because uptake in boreal forests is already slowing, while tropical forests may continue to take up carbon for many years," said David Schimel of NASA's Jet Propulsion Laboratory, Pasadena, California. Schimel is lead author of a paper on the new research, appearing online in the Proceedings of National Academy of Sciences.

Forests and other land vegetation currently remove up to 30 percent of human carbon dioxide emissions from the atmosphere during photosynthesis. If the rate of absorption were to slow down, the rate of global warming would speed up in return.

The new study is the first to devise a way to make apples-to-apples comparisons of carbon dioxide estimates from many sources at different scales: computer models of ecosystem processes, atmospheric models run backward in time to deduce the sources of today's concentrations (called inverse models), satellite images, data from experimental forest plots and more. The researchers reconciled all types of analyses and assessed the accuracy of the results based on how well they reproduced independent, ground-based measurements. They obtained their new estimate of the tropical carbon absorption from the models they determined to be the most trusted and verified.

"Until our analysis, no one had successfully completed a global reconciliation of information about carbon dioxide effects from the atmospheric, forestry and modeling communities," said co-author Joshua Fisher of JPL. "It is incredible that all these different types of independent data sources start to converge on an answer."

The question of which type of forest is the bigger carbon absorber "is not just an accounting curiosity," said co-author Britton Stephens of the National Center for Atmospheric Research, Boulder, Colorado. "It has big implications for our understanding of whether global terrestrial ecosystems might continue to offset our carbon dioxide emissions or might begin to exacerbate climate change."

As human-caused emissions add more carbon dioxide to the atmosphere, forests worldwide are using it to grow faster, reducing the amount that stays airborne. This effect is called carbon fertilization. "All else being equal, the effect is stronger at higher temperatures, meaning it will be higher in the tropics than in the boreal forests," Schimel said.

But climate change also decreases water availability in some regions and makes Earth warmer, leading to more frequent and larger wildfires. In the tropics, humans compound the problem by burning wood during deforestation. Fires don't just stop carbon absorption by killing trees, they also spew huge amounts of carbon into the atmosphere as the wood burns.

For about 25 years, most computer climate models have been showing that mid-latitude forests in the Northern Hemisphere absorb more carbon than tropical forests. That result was initially based on the then-current understanding of global air flows and limited data suggesting that deforestation was causing tropical forests to release more carbon dioxide than they were absorbing.

In the mid-2000s, Stephens used measurements of carbon dioxide made from aircraft to show that many climate models were not correctly representing flows of carbon above ground level. Models that matched the aircraft measurements better showed more carbon absorption in the tropical forests. However, there were still not enough global data sets to validate the idea of a large tropical-forest absorption. Schimel said that their new study took advantage of a great deal of work other scientists have done since Stephens' paper to pull together national and regional data of various kinds into robust, global data sets.

Schimel noted that their paper reconciles results at every scale from the pores of a single leaf, where photosynthesis takes place, to the whole Earth, as air moves carbon dioxide around the globe. "What we've had up till this paper was a theory of carbon dioxide fertilization based on phenomena at the microscopic scale and observations at the global scale that appeared to contradict those phenomena. Here, at least, is a hypothesis that provides a consistent explanation that includes both how we know photosynthesis works and what's happening at the planetary scale."

NASA monitors Earth's vital signs from land, air and space with a fleet of satellites and ambitious airborne and ground-based observation campaigns. NASA develops new ways to observe and study Earth's interconnected natural systems with long-term data records and computer analysis tools to better see how our planet is changing. The agency shares this unique knowledge with the global community and works with institutions in the United States and around the world that contribute to understanding and protecting our home planet.

Record-breaking Black Hole Outburst Detected

Last September, after years of watching, a team of scientists led by Amherst College astronomy professor Daryl Haggard observed and recorded the largest-ever flare in X-rays from a supermassive black hole at the center of the Milky Way. The astronomical event, which was detected by NASA's Chandra X-ray Observatory, puts the scientific community one step closer to understanding the nature and behavior of super massive black holes.

Haggard and her colleagues discussed the flare today during this year's meeting of the American Astronomical Society in Seattle.

Super massive black holes are the largest of black holes, and all large galaxies have one. The one at the center of our galaxy, the Milky Way, is called Sagittarius A* (or, Sgr A*, as it is called), and scientists estimate that it contains about four and a half million times the mass of our Sun.

Scientists working with Chandra have observed Sgr A* repeatedly since the telescope was launched into space in 1999. Haggard and fellow astronomers were originally using Chandra to see if Sgr A* would consume parts of a cloud of gas, known as G2.

"Unfortunately, the G2 gas cloud didn't produce the fireworks we were hoping for when it got close to Sgr A*," she said. "However, nature often surprises us and we saw something else that was really exciting."

Haggard and her team detected an X-ray outburst last September that was 400 times brighter than the usual X-ray output from Sgr A*. This "megaflare" was nearly three times brighter than the previous record holder that was seen in early 2012. A second enormous X-ray flare, 200 times brighter than Sgr A* in its quiet state, was observed with Chandra on October 20, 2014.

Haggard and her team have two main ideas about what could be causing Sgr A* to erupt in this extreme way. One hypothesis is that the gravity of the super massive black hole has torn apart a couple of asteroids that wandered too close. The debris from such a "tidal disruption" would become very hot and produce X-rays before disappearing forever across the black hole's point of no return (called the "event horizon").

"If an asteroid was torn apart, it would go around the black hole for a couple of hours, like water circling an open drain before falling in," said colleague and co-principal investigator Fred Baganoff of the Massachusetts Institute of Technology in Cambridge, MA. "That's just how long we saw the brightest X-ray flare last, so that is an intriguing clue for us to consider."

If that theory holds up, it means astronomers have found evidence for the largest asteroid ever to be torn apart by the Milky Way's black hole.

Another, different idea is that the magnetic field lines within the material flowing towards Sgr A* are packed incredibly tightly. If this were the case, these field lines would occasionally interconnect and reconfigure themselves. When this happens, their magnetic energy is converted into the energy of motion, heat and the acceleration of particles which could produce a bright X-ray flare. Such magnetic flares are seen on the Sun, and the Sgr A* flares have a similar pattern of brightness levels to the solar events.

"At the moment, we can't distinguish between these two very different ideas," said Haggard. "It's exciting to identify tensions between models and to have a chance to resolve them with present and future observations."

In addition to the giant flares, Haggard and her team also collected more data on a magnetar, a neutron star with a strong magnetic field located close to Sgr A*. This magnetar is undergoing a long X-ray outburst, and the Chandra data are allowing astronomers to better understand this unusual object.

As for the G2: Astronomers estimate that the gas cloud made its closest approach, still about 15 billion miles away from the edge of the black hole in the spring of 2014. The researchers estimate the record breaking X-ray flares were produced about a hundred times closer to the black hole, making it very unlikely that the Chandra flares were associated with G2.

Toxic Ebola Protein Fragment Identified

William Gallaher, PhD, Emeritus Professor of Microbiology, Immunology & Parasitology at

LSU Health New Orleans School of Medicine, has discovered a fragment of an Ebola virus protein that is toxic to cells and may contribute to infection and illness. The findings were published online January 20, 2015, in the open access journal, Viruses.

The fragment was found within a grouping of amino acids that is made in parallel with the protein involved in attachment of the virus to cells. Called the "Delta peptide," it has been shown recently to block the Ebola virus from attaching to already-infected cells. The new findings suggest that Delta peptide possibly functions by changing membrane permeability.

Following his discovery, Dr. Gallaher contacted Robert Garry, PhD, Professor of Microbiology and Immunology at Tulane University School of Medicine, a longtime collaborator, to produce a structural model and potential mechanism of action. The results of that modeling work were fashioned into a manuscript that was subjected to rigorous peer view by experts in the field and are being made public only after acceptance into a special issue on "Advances in Ebolavirus, Marburgvirus, and Cuevavirus Research 2014-2015" in Viruses.

Although preliminary studies using synthetic peptides have confirmed the potential of the fragment, its specific role and potency in its natural environment within Ebola virus-infected cells are yet to be determined. However, Dr. Gallaher and his colleagues have determined how to deactivate the toxic properties of the Ebola protein fragment in the laboratory environment. He and his colleagues are also developing inhibitors of the toxic mechanism, which may ultimately be useful as drugs, should a role for Delta peptide in Ebola virus disease become established by future studies.

According to the Centers for Disease Control and Prevention (CDC), the 2014 Ebola epidemic is the largest in history, affecting multiple countries in West Africa. Two imported cases, including one death, and two locally acquired cases in healthcare workers have been reported in the United States. As of January 16, 2015, the CDC and World Health Organization report 13,510 laboratory-confirmed cases and 8,483 deaths worldwide.

Scientists announce Anti-HIV Agent so Powerful it can Work in a Vaccine

In a remarkable new advance against the virus that causes AIDS, scientists from the Jupiter, Florida campus of The Scripps Research Institute (TSRI) have announced the creation of a novel drug candidate that is so potent and universally effective, it might work as part of an unconventional vaccine.

The study shows that the new drug candidate blocks every strain of HIV-1, HIV-2 and SIV (simian immunodeficiency virus) that has been isolated from humans or rhesus macaques, including the hardest-to-stop variants. It also protects against much-higher doses of virus than occur in most human transmission and does so for at least eight months after injection.

"Our compound is the broadest and most potent entry inhibitor described so far," said Michael Farzan, a TSRI professor who led the effort. "Unlike antibodies, which fail to neutralize a large fraction of HIV-1 strains, our protein has been effective against all strains tested, raising the possibility it could offer an effective HIV vaccine alternative."

When HIV infects a cell, it targets the CD4 lymphocyte, an integral part of the body's

immune system. HIV fuses with the cell and inserts its own genetic material, in this case, single-stranded RNA and transforms the host cell into a HIV manufacturing site.

The new study builds on previous discoveries by the Farzan laboratory, which show that a co-receptor called CCR5 contains unusual modifications in its critical HIV-binding region, and that proteins based on this region can be used to prevent infection.

With this knowledge, Farzan and his team developed the new drug candidate so that it binds to two sites on the surface of the virus simultaneously, preventing entry of HIV into the host cell.

"When antibodies try to mimic the receptor, they touch a lot of other parts of the viral envelope that HIV can change with ease," said TSRI Research Associate Matthew Gardner, the first author of the study with Lisa M. Kattenhorn of Harvard Medical School. "We've developed a direct mimic of the receptors without providing many avenues that the virus can use to escape, so we catch every virus thus far."

The team also leveraged preexisting technology in designing a delivery vehicle an engineered adeno-associated virus, a small, relatively innocuous virus that causes no disease. Once injected into muscle tissue, like HIV itself, the vehicle turns those cells into "factories" that could produce enough of the new protective protein to last for years, perhaps decades, Farzan said.

Data from the new study showed the drug candidate binds to the envelope of HIV-1 more potently than the best broadly neutralizing antibodies against the virus. Also, when macaque models were inoculated with the drug candidate, they were protected from multiple challenges by SIV.

Novel Crumpling Method Takes Flat Graphene from 2-D to 3-D

Researchers at the University of Illinois at Urbana-Champaign have developed a unique single-step process to achieve three-dimensional (3D) texturing of graphene and graphite. Using a commercially available thermally activated shape-memory polymer substrate, this 3D texturing, or "crumpling," allows for increased surface area and opens the doors to expanded capabilities for electronics and biomaterials.

"Fundamentally, intrinsic strains on crumpled graphene could allow modulation of electrical and optical properties of graphene," explained SungWoo Nam, an Assistant Professor of mechanical science and engineering at Illinois. "We believe that the crumpled graphene surfaces can be used as higher surface area electrodes for battery and supercapacitor applications. As a coating layer, 3D textured/crumpled nano-topographies could allow omniphobic/anti-bacterial surfaces for advanced coating applications."

Graphene, single atomic layer of SP2-bonded carbon atoms has been a material of intensive research and interest over recent years. A combination of exceptional mechanical properties, high carrier mobility, thermal conductivity, and chemical inertness, make graphene a prime candidate material for next generation optoelectronic, electromechanical, and biomedical applications.

"In this study, we developed a novel method for

controlled crumpling of graphene and graphite via heat-induced contractile deformation of the underlying substrate," explained Michael Cai Wang, a graduate student and first author of the paper, "Heterogeneous, Three-Dimensional Texturing of Graphene," which appeared in the journal Nano Letters. "While graphene intrinsically exhibits tiny ripples in ambient conditions, we created large and tunable crumpled textures in a tailored and scalable fashion."

"As a simpler, more scalable, and spatially selective method, this texturing of graphene and graphite exploits the thermally induced transformation of shape-memory thermoplastics, which has been previously applied to microfluidic device fabrication, metallic film patterning, nanowire assembly, and robotic self-assembly applications," added Nam, whose group has filed a patent for their novel strategy. "The thermoplastic nature of the polymeric substrate also allows for the crumpled graphene morphology to be arbitrarily re-flattened at the same elevated temperature for the crumpling process."

"Due to the extremely low cost and ease of processing of our approach, we believe that this will be a new way to manufacture nanoscale topographies for graphene and many other 2D and thin-film materials."

The researchers are also investigating the textured graphene surfaces for 3D sensor applications.

"Enhanced surface area will allow even more sensitive and intimate interactions with biological systems, leading to high sensitivity devices," said Nam.

Mixing Plant Waste and Plastic to Obtain Building Materials

A new company PLASTINOVA has intertwined the science of chemical engineering and technology to recycle all kinds of useless plastics and tequila agave bagasse similar to wood, but with greater resistance used as formwork in the construction industry or in the manufacture of benches, tables and chairs.

Generally the falsework used to build roofs, arches or any structure is made of wood or aluminum. However, the offer of the young entrepreneurs in Jalisco, westcoast state of Mexico, aims to achieve a medium point between both materials in terms of physical properties while reducing the cost, as well as recycling organic and inorganic waste.

The composition of the tabloid goes from 10 to 35 percent of agave fiber, completed with recycled plastic, as the latter is the matrix of this building material, said Alberto Medina-Mora Urquiza one of four partners of PLASTINOVA, together with Eloy Aquino Herrán, Milton Vázquez Lepe and Ignacio Reyes González.

PLASTINOVA lasted a year as a project, and in recent months managed to establish itself as a functioning company producing composite materials from recycled plastic and agave bagasse, which after a series of treatments obtains the necessary fiber to make the formwork tabloids.

Although PLASTINOVA was established in an area where tequila is produced, is very difficult to obtain agave bagasse because companies use it as fuel for boilers. The entrepreneurs, however, reached an agreement with two tequila companies to harness the waste plant.

To process one hundred kilograms of agave the machinery requires about 36 hours. And one more day to transform the fiber in a ton of pellets or beads of recycled plastic, with which the tabloids are manufactured, which measure 1.20 meters by one meter and are 10 centimeters thick.

The manufacture of the tabloids requires a three-part process. First, with the help of a physical process the alcohol, sugar, bone and shell is removed from the agave bagasse, leaving only the fiber for cleaning. After that it is dried, ground and pulverized, to obtain a flour-like powder.

During this process a compatibilizing agent is added to the fiber, which is a special substance that serves to alter the chemical composition of the waste, which makes it more resistant and compatible with various types of plastics, such propylene used in spoons or the high density polyethylene used in milk gallons, Medina-Mora explained.

Among the future plans of the company is to replace agave fibers with ones from coconut, since according to their laboratory tests are sturdier and have more suitable physical properties for use in building. Although for this they require further participation in entrepreneurial competitions as they did last year in the Cleantech Challenge or become widely known to attract investors to support them in order to increase the capacity of the machinery.

Sunlight Continues to Damage Skin in the Dark

Much of the damage that ultraviolet radiation (UV) does to skin occurs hours after sun exposure, a team of Yale-led researchers concluded in a study that was published online by the journal Science.

Exposure to UV light from the sun or from tanning beds can damage the DNA in melanocytes, the cells that make the melanin that gives skin its color. This damage is a major cause of skin cancer, the most common form of cancer in the United States. In the past, experts believed that melanin protected the skin by blocking harmful UV light. But there was also evidence from studies suggesting that melanin was associated with skin cell damage.

In the current study, Douglas E. Brash, clinical professor of therapeutic radiology and dermatology at Yale School of Medical, and his co-authors first exposed mouse and human melanocyte cells to radiation from a UV lamp. The radiation caused a type of DNA damage known as a cyclobutane dimer (CPD), in which two DNA "letters" attach and bend the DNA, preventing the information it contains from being read correctly. To the researchers' surprise, the melanocytes not only generated CPDs immediately but continued to do so hours after UV exposure ended. Cells without melanin generated CPDs only during the UV exposure.

This finding showed that melanin had both carcinogenic and protective effects. "If you look inside adult skin, melanin does protect against CPDs. It does act as a shield," said Brash, also a member of Yale Cancer Center. "But it is doing both good and bad things."

The researchers next tested the extent of damage that occurred after sun exposure by preventing normal DNA repair in mouse samples. They found that half of the CPDs in melanocytes were "dark CPDs", CPDs created in the dark.

In searching for an explanation of these results, Sanjay Premi, associate research scientist in the Brash laboratory, discovered that the UV light activated two enzymes that combined to "excite" an electron in melanin. The energy generated from this process, known as chemiexcitation, was transferred to DNA in the dark, creating the same DNA damage that sunlight caused in daytime. Chemiexcitation has previously been seen only in lower plants and animals.

While noting that news of the carcinogenic effect of melanin is disconcerting, the researchers also pointed to a ray of hope: The slowness of chemiexcitation may allow time for new preventive tools, such as an "evening-after" sunscreen designed to block the energy transfer.

Nanotubes Self-organize and Wiggle: Evolution of a Nonequilibrium System Demonstrates MEPP

The second law of thermodynamics tells us that all systems evolve toward a state of maximum entropy, wherein all energy is dissipated as heat, and no available energy remains to do work. Since the mid-20th century, research has pointed to an extension of the second law for nonequilibrium systems: the Maximum Entropy Production Principle (MEPP) states that a system away from equilibrium evolves in such a way as to maximize entropy production, given present constraints.

Now, physicists Alexey Bezryadin, Alfred Hubler, and Andrey Belkin from the University of Illinois at Urbana-Champaign, have demonstrated the emergence of self-organized structures that drive the evolution of a non-equilibrium system to a state of maximum entropy production. The authors suggest MEPP underlies the evolution of the artificial system's self-organization, in the same way that it underlies the evolution of ordered systems (biological life) on Earth. The team's results are published in Nature Publishing Group's online journal Scientific Reports.

MEPP may have profound implications for our understanding of the evolution of biological life on Earth and of the underlying rules that govern the behavior and evolution of all nonequilibrium systems. Life emerged on Earth from the strongly nonequilibrium energy distribution created by the Sun's hot photons striking a cooler planet. Plants evolved to capture high energy photons and produce heat, generating entropy. Then animals evolved to eat plants increasing the dissipation of heat energy and maximizing entropy production.

In their experiment, the researchers suspended a large number of carbon nanotubes in a non-conducting non-polar fluid and drove the system out of equilibrium by applying a strong electric field. Once electrically charged, the system evolved toward maximum entropy through two distinct intermediate states, with the spontaneous emergence of self-assembled conducting nanotube chains.

In the first state, the "avalanche" regime, the conductive chains aligned themselves according to the polarity of the applied voltage, allowing the system to carry current and thus to dissipate heat and produce entropy. The chains appeared to sprout appendages as nanotubes aligned themselves so as to adjoin adjacent parallel chains, effectively increasing entropy production. But frequently, this self-organization was destroyed through avalanches triggered by the heating and charging that emanates from the emerging electric current streams.

"The avalanches were apparent in the changes of the electric current over time," said Bezryadin.

Following avalanches, the chains with their appendages "wiggled," resembling a living thing, similar to an insect.

"Toward the final stages of this regime, the appendages were not destroyed during the avalanches, but rather retracted until the avalanche ended, then reformed their connection. So it was obvious that the avalanches correspond to the 'feeding cycle' of the 'nanotube inset'," comments Bezryadin.

In the second relatively stable stage of evolution, the entropy production rate reached maximum or near maximum. This state is quasi-stable in that there were no destructive avalanches.

The study points to a possible classification scheme for evolutionary stages and a criterium for the point at which evolution of the system is irreversible--wherein entropy production in the self-organizing subsystem reaches its maximum possible value. Further experimentation on a larger scale is necessary to affirm these underlying principals, but if they hold true, they will prove a great advantage in predicting behavioral and evolutionary trends in nonequilibrium systems.

The authors draw an analogy between the evolution of intelligent life forms on Earth and the emergence of the wiggling bugs in their experiment. The researchers note that further quantitative studies are needed to round out this comparison. In particular, they would need to demonstrate that their "wiggling bugs" can multiply, which would require the experiment be reproduced on a significantly larger scale.

Such a study, if successful, would have implications for the eventual development of technologies that feature self-organized artificial intelligence, an idea explored elsewhere by co-author Alfred Hubler, funded by the Defense Advanced Research Projects Agency.

"The general trend of the evolution of biological systems seems to be this: more advanced life forms tend to dissipate more energy by broadening their access to various forms of stored energy," Bezryadin proposes. Thus a common underlying principle can be suggested between our self-organized clouds of nanotubes, which generate more and more heat by reducing their electrical resistance and thus allow more current to flow, and the biological systems which look for new means to find food, either through biological adaptation or by inventing more technologies.

Vitamin D Deficiency Linked more Closely to Diabetes than Obesity

People who have low levels of vitamin D are more likely to have diabetes, regardless of how much they weigh, according to a study published in the Endocrine Society's Journal of Clinical Endocrinology & Metabolism.

The results help clarify the connection between vitamin D, obesity and diabetes. According to the Society's Scientific Statement on the Non-skeletal Effects of Vitamin D, studies have found that people who have low levels of vitamin D are more likely to be obese. They also are more likely to have Type 2 diabetes, prediabetes and metabolic syndrome than people with normal vitamin D levels.

Vitamin D helps the body absorb calcium and maintain bone and muscle health. The skin

naturally produces this vitamin after exposure to sunlight. People also absorb smaller amounts of the vitamin through foods, such as milk fortified with vitamin D. More than 1 billion people worldwide are estimated to have deficient levels of vitamin D due to limited sunshine exposure.

The cross-sectional study compared vitamin D biomarkers in 118 participants at the university hospital Virgen de la Victoria in Malaga as well as 30 participants from the Hospital Universitari Dr. Josep Trueta in Girona, Spain. All participants were classified by their body-mass index (BMI) as well as whether they had diabetes, prediabetes or no glycemic disorders. Researchers measured levels of vitamin D in the participants' blood streams and vitamin D receptor gene expression in adipose tissue.

The analysis found that obese subjects who did not have glucose metabolism disorders had higher levels of vitamin D than diabetic subjects. Likewise, lean subjects with diabetes or another glucose metabolism disorder were more likely to have low levels of vitamin D. Vitamin D levels were directly correlated with glucose levels, but not with BMI.

"Our findings indicate that vitamin D is associated more closely with glucose metabolism than obesity," said one of the study's authors, Manuel Macías-González, PhD, of Complejo Hospitalario de Málaga (Virgen de la Victoria) and the University of Málaga. "The study suggests that vitamin D deficiency and obesity interact synergistically to heighten the risk of diabetes and other metabolic disorders. The average person may be able to reduce their risk by maintaining a healthy diet and getting enough outdoor activity."

Artificially Intelligent robot scientist 'Eve' could Boost Search for New Drugs

Eve, an artificially-intelligent 'robot scientist' could make drug discovery faster and much cheaper, say researchers writing in the Royal Society journal Interface. The team has demonstrated the success of the approach as Eve discovered that a compound shown to have anti-cancer properties might also be used in the fight against malaria.

Robot scientists are a natural extension of the trend of increased involvement of automation in science. They can automatically develop and test hypotheses to explain observations, run experiments using laboratory robotics, interpret the results to amend their hypotheses, and then repeat the cycle, automating high, throughout hypothesis, led research. Robot scientists are also well suited to recording scientific knowledge: as the experiments are conceived and executed automatically by computer, it is possible to completely capture and digitally curate all aspects of the scientific process.

In 2009, Adam, a robot scientist developed by researchers at the Universities of Aberystwyth and Cambridge, became the first machine to independently discover new scientific knowledge. The same team has now developed Eve, based at the University of Manchester, whose purpose is to speed up the drug discovery process and make it more economical. In the study published today, they describe how the robot can help identify promising new drug candidates for malaria and neglected tropical diseases such as African sleeping sickness and Chagas' disease.

"Neglected tropical diseases are a scourge of humanity, infecting hundreds of millions of

people, and killing millions of people every year," says Professor Steve Oliver from the Cambridge Systems Biology Centre and the Department of Biochemistry at the University of Cambridge. "We know what causes these diseases and that we can, in theory, attack the parasites that cause them using small molecule drugs. But the cost and speed of drug discovery and the economic return make them unattractive to the pharmaceutical industry.

"Eve exploits its artificial intelligence to learn from early successes in her screens and select compounds that have a high probability of being active against the chosen drug target. A smart screening system, based on genetically engineered yeast, is used. This allows Eve to exclude compounds that are toxic to cells and select those that block the action of the parasite protein while leaving any equivalent human protein unscathed. This reduces the costs, uncertainty, and time involved in drug screening, and has the potential to improve the lives of millions of people worldwide."

Eve is designed to automate early-stage drug design. First, she systematically tests each member from a large set of compounds in the standard brute-force way of conventional mass screening. The compounds are screened against assays (tests) designed to be automatically engineered, and can be generated much faster and more cheaply than the bespoke assays that are currently standard. This enables more types of assay to be applied, more efficient use of screening facilities to be made, and thereby increases the probability of a discovery within a given budget.

Eve's robotic system is capable of screening over 10,000 compounds per day. However, while simple to automate, mass screening is still relatively slow and wasteful of resources as every compound in the library is tested. It is also unintelligent, as it makes no use of what is learnt during screening.

To improve this process, Eve selects at random a subset of the library to find compounds that pass the first assay; any 'hits' are re-tested multiple times to reduce the probability of false positives. Taking this set of confirmed hits, Eve uses statistics and machine learning to predict new structures that might score better against the assays. Although she currently does not have the ability to synthesise such compounds, future versions of the robot could potentially incorporate this feature.

Professor Ross King, from the Manchester Institute of Biotechnology at the University of Manchester, says: "Every industry now benefits from automation and science is no exception. Bringing in machine learning to make this process intelligent.

To test the viability of the approach, the researchers developed assays targeting key molecules from parasites responsible for diseases such as malaria, Chagas' disease and schistosomiasis and tested against these a library of approximately 1,500 clinically approved compounds. Through this, Eve showed that a compound that has previously been investigated as an anti-cancer drug inhibits a key molecule known as DHFR in the malaria parasite. Drugs that inhibit this molecule are currently routinely used to protect against malaria, and are given to over a million children; however, the emergence of strains of parasites resistant to existing drugs means that the search for new drugs is becoming increasingly more urgent.

"Despite extensive efforts, no one has been able to find a new antimalarial that targets

DHFR and is able to pass clinical trials," adds Professor King. "Eve's discovery could be even more significant than just demonstrating a new approach to drug discovery."

The research was supported by the Biotechnology & Biological Sciences Research Council and the European Commission.

SOHO sees Something New Near the Sun: Comet Survives Close Encounter

An unusual comet skimmed past the sun on Feb 18-21, 2015, as captured by the European Space Agency (ESA) and NASA's Solar and Heliospheric Observatory, or SOHO.

This comet was interesting for two reasons. First it's what's called a non-group comet, meaning it's not part of any known family of comets. Most comets seen by SOHO belong to the Kreutz family, all of which broke off from a single giant comet many centuries ago.

The second reason it's interesting is because the vast majority of comets that come close enough to the sun to be seen by SOHO do not survive the trip. Known as sungrazers, these comets usually evaporate in the intense sunlight. This comet made it to within 2.2 million miles of the sun's surface.

"There's a half-decent chance that ground observers might be able to detect it in the coming weeks," said Karl Battams, a solar scientist at the Naval Research Lab in Washington, D.C. "But it's also possible that events during its trip around the sun will cause it to die fairly fast."

Since launching in 1995, SOHO has become the number one comet finder of all time this was comet discovery number 2,875. However, SOHO sees non-group comets like this only a few times a year.

Anti-inflammatory Mechanism of Dieting and Fasting Revealed

Researchers at Yale School of Medicine have found that a compound produced by the body when dieting or fasting can block a part of the immune system involved in several inflammatory disorders such as type 2 diabetes, atherosclerosis, and Alzheimer's disease.

"These findings are important because endogenous metabolites like BHB that block the NLRP3 inflammasome could be relevant against many inflammatory diseases, including those where there are mutations in the NLRP3 genes," said Vishwa Deep Dixit, professor in the Section of Comparative Medicine at Yale School of Medicine.

BHB is a metabolite produced by the body in response to fasting, high-intensity exercise, caloric restriction, or consumption of the low-carbohydrate ketogenic diet. Dixit said it is well known that fasting and calorie restriction reduces inflammation in the body, but it was unclear how immune cells adapt to reduced availability of glucose and if they can respond to metabolites produced from fat oxidation.

Working with mice and human immune cells, Dixit and colleagues focused on how macrophages specialized immune cells that produce inflammation respond when exposed to ketone bodies and whether that impacts the inflammasone complex.

The team introduced BHB to mouse models of inflammatory diseases caused by NLP3. They found that this reduced inflammation, and that

inflammation was also reduced when the mice were given a ketogenic diet, which elevates the levels of BHB in the bloodstream.

In the Quantum World, the Future Affects the Past: Hindsight and Foresight Together more Accurately 'Predict' a Quantum System's State

We're so used to murder mysteries that we don't even notice how mystery authors play with time. Typically the murder occurs well before the midpoint of the book, but there is an information blackout at that point and the reader learns what happened then only on the last page.

If the last page were ripped out of the book, physicist Kater Murch, PhD, said, would the reader be better off guessing what happened by reading only up to the fatal incident or by reading the entire book?

The answer, so obvious in the case of the murder mystery, is less so in world of quantum mechanics, where indeterminacy is fundamental rather than contrived for our reading pleasure.

Even if you know everything quantum mechanics can tell you about a quantum particle, said Murch, an assistant professor of physics in Arts & Sciences at Washington University in St. Louis, you cannot predict with certainty the outcome of a simple experiment to measure its state. All quantum mechanics can offer are statistical probabilities for the possible results.

The orthodox view is that this indeterminacy is not a defect of the theory, but rather a fact of nature. The particle's state is not merely unknown, but truly undefined before it is measured. The act of measurement itself that forces the particle to collapse to a definite state.

It's as if what we did today, changed what we did yesterday. And as this analogy suggests, the experimental results have spooky implications for time and causality.

Measuring a phantom

Until recently physicists could explore the quantum mechanical properties of single particles only through thought experiments, because any attempt to observe them directly caused them to shed their mysterious quantum properties.

But in the 1980s and 1990s physicists invented devices that allowed them to measure these fragile quantum systems so gently that they don't immediately collapse to a definite state.

The device Murch uses to explore quantum space is a simple superconducting circuit that enters quantum space when it is cooled to near absolute zero. Murch's team uses the bottom two energy levels of this qubit, the ground state and an excited state, as their model quantum system. Between these two states, there are an infinite number of quantum states that are superpositions, or combinations, of the ground and excited states.

The quantum state of the circuit is detected by putting it inside a microwave box. A few microwave photons are sent into the box, where their quantum fields interact with the superconducting circuit. So when the photons exit the box they bear information about the quantum system.

Crucially, these "weak," off-resonance measurements do not disturb the qubit, unlike "strong" measurements with photons that are

resonant with the energy difference between the two states, which knock the circuit into one or the other state. A quantum guessing game In Physical Review Letters, Murch describes a quantum guessing game played with the qubit.

"We start each run by putting the qubit in a superposition of the two states," he said. "Then we do a strong measurement but hide the result, continuing to follow the system with weak measurements."

They then try to guess the hidden result, which is their version of the missing page of the murder mystery.

"Calculating forward, using the Born equation that expresses the probability of finding the system in a particular state, your odds of guessing right are only 50-50," Murch said. "But you can also calculate backward using something called an effect matrix. Just take all the equations and flip them around. They still work and you can just run the trajectory backward.

"So there's a backward-going trajectory and a forward-going trajectory and if we look at them both together and weight the information in both equally, we get something we call a hindsight prediction, or "retrodiction."

The shattering thing about the retrodiction is that it is 90 percent accurate. When the physicists check it against the stored measurement of the system's earlier state it is right nine times out of 10.

Down the rabbit hole

The quantum guessing game suggests ways to make both quantum computing and the quantum control of open systems, such as chemical reactions, more robust. But it also has implications for much deeper problems in physics.

For one thing, it suggests that in the quantum world time runs both backward and forward whereas in the classical world it only runs forward.

"I always thought the measurement would resolve the time symmetry in quantum mechanics," Murch said. "If we measure a particle in a superposition of states and it collapses into one of two states, well, that sounds like a process that goes forward in time."

But in the quantum guessing experiment, time symmetry has returned. The improved odds imply the measured quantum state somehow incorporates information from the future as well as the past. And that implies that time, notoriously an arrow in the classical world, is a double-headed arrow in the quantum world.

"It's not clear why in the real world, the world made up of many particles, time only goes forward and entropy always increases," Murch said. "But many people are working on that problem and I expect it will be solved in a few years," he said.

In a world where time is symmetric, however, is there such a thing as cause and effect? To find out, Murch proposes to run a qubit experiment that would set up feedback loops (which are chains of cause and effect) and try to run them both forward and backward.

"It takes 20 or 30 minutes to run one of these experiments," Murch said, "several weeks to process it, and a year to scratch our heads to see if we're crazy or not."

"At the end of the day," he said, "I take solace in the fact that we have a real experiment and real data that we plot on real curves."