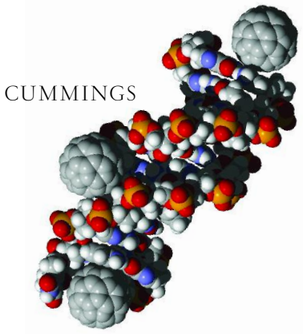
Bright Ideas

"Buckyballs have a potentially adverse effect *on the structure, stability and biological functions of DNA molecules."* – PETER CUMMINGS



Brain Morphing Technology Simplifies Movement Disorder Treatment

Tens of thousands of people who experience movement disorders associated with Parkinson's disease and a variety of other neurological conditions could benefit from a new guidance system that uses computerized brain-mapping to improve an increasingly popular procedure called "deep brain stimulation" (DBS).

DBS has proven highly effective in treating movement disorders when standard drug therapies are not effective. Since the procedure's approval in 1998, the number of DBS operations performed has grown to about 3,000 annually.

But it is arduous, expensive, and therefore not widely available. More than 100,000 people a year could benefit from DBS to treat the tremor, rigidity, stiffness and slowed movement they experience as a result of neurological disorders ranging from dystonia to multiple sclerosis, Parkinson's disease to obsessive-compulsive disorder.

To improve the procedure, a team of electrical engineers and neuroscientists at Vanderbilt has developed a pilot guidance system that automates the most difficult part of the operation: identifying the proper location to insert electrodes. To work, the electrodes must pass through small nuclei deep in the brain that are not visible in brain scans or to the naked eye. The researchers—writing in a special issue of the journal *IEEE Transactions on Medical Imaging,* published last November—report that the new system can do a better job of identifying the location to insert the electrodes than can an experienced neurosurgeon.

"The biggest problem with the procedure is that surgeons cannot see the structure where they have to put the electrode, and as a result, they must spend a considerable amount of time searching for it," says Benoit Dawant, professor of electrical engineering, computer engineering, and radiology and radiological sciences at Vanderbilt, who is developing the guidance system in collaboration with Peter Konrad, assistant professor of neurological surgery and biomedical engineering.

The only way the target region can be identified is by its electrical characteristics. The surgeons must first insert a recording electrode and monitor the electrical activity of the neurons it touches. Sometimes they must remove and reinsert the electrode two or more times; sometimes they must insert three or four electrodes at the same time to find the elusive spot.

Patient Ronald Bradford is awake as electrodes are implanted in his brain.

LARRY MCCORMACK FOR *THE TENNESSEAN*

"I tell patients that it is something like playing a big game of Battleship," says Konrad. "Like the game, you don't know where the target is until you've made a hit."

Each time surgeons reinsert the electrode, it increases the risk of brain damage. When surgeons decide they have hit the right spot, they implant a stimulating electrode and test to determine if it reduces the patient's symptoms.

The operation can take as long as eight to 12 hours to place one electrode. Most patients require two—one in each hemisphere. "This is extremely rough on patients, who have to be awake through the surgery and have to be locked to the bed," says Konrad. "Anybody who performs this surgery appreciates the need to trim the procedure down to a shorter process."

The computer-aided guidance system compensates for variations in the three-dimensional brain structure of each patient, something that is very difficult for surgeons to do on their own. The system consists of a three-dimensional brain atlas that was built up by combining brain scans of 21 post-operative DBS patients into one using sophisticated computer-mapping methods. To predict the location of the target area in a new patient, the researchers map the reference atlas onto the patient's brain scan. When the neurosurgeons have used the system's predictions, they have hit the target area on the first insertion two out of three times, compared to one out of five times when working without it.

"We have reduced a two-day procedure down to five hours," says Konrad.

The researchers have begun to collect data on the effectiveness of the operations and will use that to refine their predictions. They also have set up a system that will collect electrophysiological data from the patients' brains during the procedure so they can add it to the brain atlas. And they intend to begin creating individual atlases for different conditions—Parkinson's, essential tremor, dystonia, etc.—in case the precise location of the neurological damage may differ.

The research was funded by Vanderbilt and FNRS, the Belgian Science Foundation.

Buckyballs: Please Do Not Immerse in Water

Soccer-ball-shaped molecules known as "buckyballs" present prospects of revolutionizing medicine and the computer industry. Since their discovery in 1985, engineers and scientists have been exploring their properties for a wide range of applications and innovations. But could these microscopic spheres also represent a potential environmental hazard?

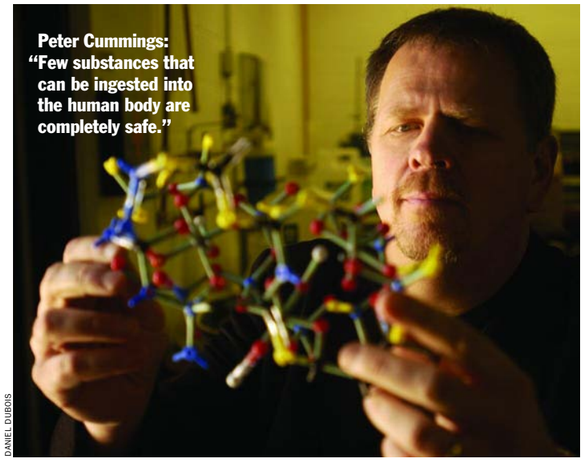
A study published last December in *Biophysical Journal* raises a red flag regarding the safety of buckyballs dissolved in water. It reports results of a computer simulation that find buckyballs bind to the spirals in DNA molecules in an aqueous environment, causing DNA to deform, potentially interfering with biological functions and possibly causing long-term side effects in humans and other organisms.

The research, conducted at Vanderbilt by chemical engineers Peter T. Cummings and Alberto Striolo (now a faculty member at the University of Oklahoma), along with Oak Ridge National Laboratory scientist Xiongce Zhao, used molecular-dynamics simulations to investigate whether buckyballs would bind to DNA and, if so, inflict any lasting damage.

"'Safe' is a difficult word to define, since few substances that can be ingested into the human body are completely safe," says Cummings, the John R. Hall Professor of Chemical Engineering at Vanderbilt and director of the Nanomaterials Theory Institute at Oak Ridge National Laboratory. "What we are doing is looking at the mechanisms of interaction between buckyballs and DNA. We don't know yet what actually happens in the body."

But the research could reveal a serious problem. "Buckyballs have a potentially adverse effect on the structure, stability and biological functions of DNA molecules," Cummings says.

The findings came as something of a surprise, despite earlier studies that have shown buckyballs to be toxic to cells unless coated, and to be able to find their way into the brains of fish. Before these cautionary discoveries, researchers thought that the combination of buckyballs' dislike of water and their affinity for each other would cause them to clump and sink to the bottom of a pool, stream or other aqueous environment. As a result, researchers thought



Peter Cummings: "Few substances that can be ingested into the human body are completely safe."

DANIEL DUBOIS

they should not cause significant environmental problems.

Cummings' team found that, depending on the form the DNA takes, the 60-carbon-atom (C60) buckyball molecule can lodge in the end of a DNA molecule and break apart important hydrogen bonds within the double helix. They can also stick to minor grooves on the outside of DNA, causing the DNA molecule to bend significantly to one side. Damage to the DNA molecule is even more pronounced when the molecule is split into two helices, as it does when cells are dividing or when the genes are being accessed to produce proteins needed by the cell.

"The binding energy between DNA and buckyballs is quite strong," Cummings says. "We found that the energies were comparable to the binding energies of a drug to receptors in cells."

It turns out that buckyballs have a stronger affinity for DNA than they do for themselves. "This research shows that if buckyballs can get into the nucleus, they can bind to DNA," Cummings says. "If the DNA is damaged, it can be inhibited from self-repairing."

Researchers don't know whether these worrisome binding events will take place in the body. "Earlier studies have shown both that buckyballs can migrate into bodily tissues and can penetrate cell membranes," Cummings continues. "We don't know whether they can penetrate a cell nucleus and reach the DNA stored there. What this study shows is that if the buckyballs can get into the nucleus, they could cause real problems. What is needed now are experimental and theoretical studies to demonstrate whether they can actually get there. Because the toxicity of nanomaterials like buckyballs is not well known at this point, they are regarded in the laboratory as potentially very hazardous, and treated accordingly."

Loss of Virginity as a Rite of Passage

3. The loss of virginity is a complex and relatively unstudied rite of passage addressed in a new book by Vanderbilt sociologist Laura M. Carpenter, assistant professor of sociology. *Virginity Lost: An Intimate Portrait of First Sexual Experiences* (NYU Press) is the first scholarly book on virginity loss as a social phenomenon.

During 18 months in 1997 and 1998, Carpenter, then a doctoral candidate at the University of Pennsylvania, interviewed 61 young adults aged 18 to 35 in great detail. Men and women from diverse social backgrounds were asked to share their personal stories in order to understand the variety of meanings and experiences associated with virginity loss.

Carpenter: Men and women view virginity loss similarly.

DANIEL DUBOIS

"We all read and hear the statistics about at what ages men and women begin having sex, but it doesn't tell us what losing their virginity means to them," Carpenter says. "Nor do these figures tell us how teens and young adults made decisions about when, where and with whom to lose their virginity."

Though every story she uncovered was unique in its details, most of the people viewed virginity in one of three ways: as a gift, a stigma, or as a step in the process of growing up.

"Processers" seemed to have the most emotionally satisfying, healthy and safe experiences.

The well-being of "gifters" depended on having partners who reciprocated loving, appreciative feelings. For the women in the study for whom that did not happen, the result was not only disappointment—even devastation—but also a feeling of being deprived of sexual empowerment.

The "stigmatized" group reported mostly positive virginity-loss experiences. Men who saw virginity as a stigma especially felt compelled to conceal their inexperience and felt particularly vulnerable to humiliation and disempowerment at the hands of female partners. Derided as virgins or sexual incompetents, three men in the study avoided sex long after losing their virginity. The intensity with which most in this group wanted to hide their inexperience, along with the circumstances and casual relationships in which many lost their virginity, also resulted in the lowest rates of protected sex in the study.

Carpenter suggests that viewing virginity as a rite of passage or step in the process of growing up is the most conducive to

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physical health, emotional well-being and sexual empowerment. She says parents, policymakers, sex educators and others would do well to encourage young people—one-on-one and through public policies—to approach virginity that way. She believes her findings could be of help in developing sex-education programs.

Regardless of gender, Carpenter found, people who viewed virginity loss through the same metaphor—as a gift, as a stigma, or as a rite of passage—understood and experienced the act in very similar ways.

"Men and women are a whole lot less different than people think they are when it comes to how they view virginity loss," she says.

The 61 young adults who took part in her study included 33 women, of whom 22 self-identified as heterosexual, seven as lesbians and four as bisexual. Of the 28 men interviewed, 17 described themselves as heterosexual, nine as gay and two as bisexual. The group came from diverse racial and ethnic groups, social-class backgrounds and religious traditions. All but five were no longer virgins when Carpenter met them. She also sought to

interview secondary or born-again virgins—people who recommit to abstinence, often after a religious awakening. One man and three women she interviewed described themselves as current or former secondary virgins.

"Growing up in a context of uncertainty, diversity and change, young people benefit from being able to understand virginity loss in ways that help them fashion specific social identities and that bring them one step closer to adulthood," Carpenter says.

"Given these benefits, it makes sense to treat virginity loss as a significant and important life event; however, treating it as one of the most important sexual experiences of a person's life appears to carry real costs as well."

Mapping Orion's Winds

For the past few months, Bob O'Dell has been mapping winds blowing in the Orion Nebula, the closest stellar nursery similar to the one in which the sun was born. New data from the Hubble Orion Heritage Program, a major observational effort by the Hubble Space Telescope in 2004 and 2005, have given the Vanderbilt astronomer information to measure the stellar winds with unprecedented detail. He reported his early results in January at the annual meeting of the American Astronomical Society in Washington, D.C.

"Determining how stellar winds interact with the ambient material in stellar nurseries like Orion is a critical factor in understanding the process of star creation," says O'Dell, distinguished research professor of astrophysics.

All stars, including the sun, give off a stream of particles as they burn. In young, hot stars like those that form the "Trapezium" at the heart of Orion, this stream of particles is millions of times more dense and energetic than the solar wind. Newborn stars, which are still shrouded in thick veils of dust and gas, often eject gas and dust from their polar regions in narrow jets, rather than broadcasting them outward in all directions. When these stellar winds impact floating clouds of dust and gas, they produce shock waves that erode and shape the clouds in a fashion similar to the way in which terrestrial winds sculpt sand dunes. When they are strong enough, such shock waves also can compress the free-floating clouds of dust and gas, triggering the formation of new stars.

O'Dell is using these shock waves as celestial "wind socks" to plot the direction of these winds in different parts of the nebula. By back-tracking older, more distant shock waves to their likely points of origin, the astronomer can also get an idea of how long major currents have been flowing.

"When you look closely enough, you see that the nebula is filled with hundreds of visible shock waves," O'Dell says. In his analysis, he has identified three different types of shock waves.

As a young star ejects material in narrow jets, a cross-current causes the jets to bend.

Bow-shocks are stationary shock waves formed by the collision of two steady winds and are excellent indicators of wind direction. They are present near the hottest stars in the center of the nebula where they show winds flowing outward at velocities of thousands of kilometers per second. They are also present in the outer nebula where they are produced by low-velocity stellar winds of tens of kilometers per second.

Jet-driven shocks are produced when narrow streams of gas and particles traveling at hundreds of kilometers per second pass through gas that is relatively stationary. Many shockwaves of this type in the nebula are produced by jets of material ejected by newly formed stars.

Warped shocks are jet-driven shocks located in areas where the ambient gas is not stationary but is moving in a cross current. This bends the jets and shocks into bow-like shapes.

Using these markers, the astronomer has mapped the outflow from two of the three regions of star formation in the nebula. Both of these regions, labeled "BN-KL" and "Orion-South," are located behind the glowing region of the nebula where the light from the central stars ionizes the outer layers of the parent molecular cloud. The specific objects that are producing these winds in the two regions are not visible to optical telescopes, but they stand out as hot spots in infrared images.

By tracking back the farthest shockwaves produced by these outflows, O'Dell has established that the winds blowing from BN-KL have been doing so for 900 to 1,100 years, while those from Orion-South have been going on for 200 to 1,500 years.

These observations were made during 104 orbits of the Hubble and provide the most comprehensive picture ever obtained of the Orion Nebula. The data will be combined with other Hubble and ground-based telescope observations to create a widely available archive for research scientists interested in this region, in addition to acting as a base for a detailed study that should provide new insights into the conditions required for creating stars like the sun.