Buckyballs: Wide Open Playing Field for Chemists

The roundest, most symmetrical large molecule found so far, buckminsterfullerene, continues to astonish with one amazing property after another. Named for American architect R. Buckminster Fuller, who designed a geodesic dome with the same fundamental symmetry, C_{60} is the third major form of pure carbon; graphite and diamond are the other two.

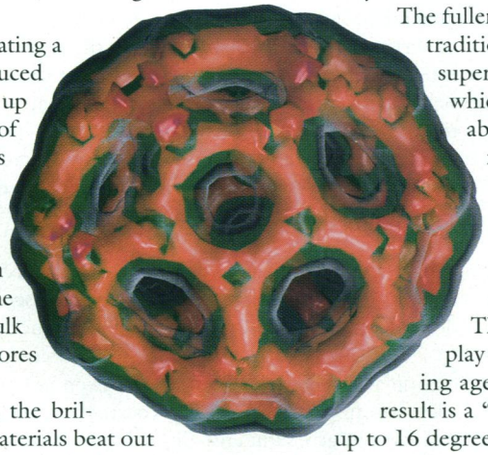
Buckyballs were discovered in 1985—the by-product of an experiment on carbon molecules in space—but it was in 1991 that buckyball science came into its own. This year scientists flocked to the buckyball court, entranced by the molecule's unusual bonding behavior, its hollow symmetry, and its amazing electronic properties. Rarely has one molecule so swiftly opened the door to a new field of science.

Papers hit top journals every week or so; scientists scramble to keep up by fax and E-mail, and month-old information is probably out of date.

In the past year, properly doped C_{60} was found to be both superconducting and magnetic, and the fullerene family expanded to include asymmetrical forms as well as cylindrical fibers nicknamed buckytubes. In a steady stream of firsts, fullerenes were found in flames, decorated with free radicals, hung with fluorine atoms, inflated by carbon rings, and stuffed with metals. With potential applications in such commercial basics as catalysis and polymerization as well as the more distant realms of superconductivity and ferromagnetism, buckyball may soon become one of industry's favorite sports.

All-star teams. From the beginning, buckyballs have been the sport of physicists, materials scientists, and inorganic as well as organic chemists. At first physicists led the way, pointing out the exceptional electronic properties of the fullerenes, but this year, with grams of C_{60} available, chemists also have taken to the field in full force, and interdisciplinary teams of scientists are together exploring the round world of buckyballs.

In the fall of 1990, scientists found that heating a rod of graphite in a helium atmosphere produced C_{60}. Labs around the country began cooking up bins of buckyballs, sparking an explosion of research. And in July, buckyball genesis was made potentially even easier by the discovery that they are found in the sooting flames of burning benzene. Although C_{60} is still relatively expensive—at least $2,000 per gram in purified form—many predict that fullerite (the pure, solid form of C_{60}) ultimately will be a bulk commodity, sold in local chemistry supply stores for dollars per pound.



J. BERNHOLC ET AL., NCSU/T. PALMER NC SUPERCOMPUTING CENTER

Marriage of the molecules. Last year, the brilliance of synthetic diamonds as superhard materials beat out buckyballs for Molecule of the Year. But one shadow dimmed diamond's luster: A polish of diamond itself was often required to grow synthetic diamond film—an expensive and often impractical beginning. This year, buckyballs came to the rescue. Researchers coated silicon with C_{70}, then grew diamond on top. Voilà! The rugby ball-shaped fullerenes increased diamond formation by 10 orders of magnitude over the untreated silicon.

Playing ball in three dimensions. Just how do buckyballs manage their chemical and physical feats? In C_{60}, hexagons and pentagons of carbon link together in a coordinated fashion to form a hollow, geodesic dome with bonding strains equally distributed among 60 carbon atoms. Some of the electrons are delocalized over the entire molecule, a feature even more pronounced in that workhorse of organic chemistry, benzene. But benzene is flat, and many of its derivatives also tend to stack in flat sheets. Spherical buckyballs literally add a new dimension to the chemistry of such aromatic compounds.

The allure of C_{60} goes beyond the beauty of its symmetrical shape. First considered a paragon of physical stability, it has turned out to be one of the most chemically versatile molecules known. This year, among other pioneering steps, chemists learned how to make fullerene derivatives, inflating the C_{60} balloon by one or more carbons, in some cases still preserving its aromatic electron structure. In the same week, it was reported that C_{60} acts as a veritable sponge for free radicals, able to absorb dozens of these reactive chemical species. Free radicals with one unpaired electron are crucial to the economical polymerization processes, and fullerene compounds may one day be useful in such industrial processes.

Superballs. A simple C_{60} cage easily accepts electrons, so solid fullerite doped with an alkali metal like potassium forms a stable compound of the family called fullerides with increasing amounts of the alkali metal. Some fullerides become chameleons, changing from insulator to semiconductor to superconductor and back to insulator again. Pure C_{60}, for example, is an insulator. K_3C_{60} is a superconductor; K_6C_{60} is an insulator. The superconductive properties have unfolded at astonishing speed. In April, the critical temperature was 18 K; by November, maybe 45 K, thanks to novel dopings of C_{60} and its rugby ball-shaped cousin, C_{70}, with metals and alloys of rubidium, cesium, and thallium.

The fullerides can't yet run in the same league as the traditionally hot candidates for high-temperature superconductivity, the metallic copper oxides, which have set the superconductive record at about 125 K. But because the fulleride materials are a much simpler system, they may offer a window into the still mysterious mechanisms of superconductivity.

Magnetic buckys. Ferromagnetism, like superconductivity, remains a mysterious electronic property of certain materials. This year, buckyballs proved that they can play magnetic games too. Add an organic reducing agent to fullerides and the totally unexpected result is a "soft" organic ferromagnet at temperatures up to 16 degrees K. The new material won't stay magnetic in the absence of an outside field, and so in itself may not have practical applications. But the ongoing quest for an organic ferromagnet, which would be prized for its light weight and ability to be polymerized, suddenly broadened its scope to include the fullerenes.

Cagey chemistry. For years chemists have been painstakingly building molecules with cavities, and fine-tuning the properties of those cavities in order to hold and transfer different atoms and

ions. Now, with a naturally hollow molecule dropped into their laps, chemists are eagerly discovering the rules for how buckyballs can be filled. Eventually, by combining approaches, chemists may tailor-make stuffed buckyballs to serve as molecular containers, shields for radioactive compounds, or drug-delivery agents. This year, lanthanum atoms were stuffed inside buckyballs using the ship-in-a-bottle trick: form the cage around the stuffing. The next goal is to open a door into the fullerene cage, while still preserving that fragile electron structure, to allow direct movement of atoms or ions inside.

Twist and shout. Not all the fullerenes have the perfect symmetry of C_{60}—but even a lopsided structure can be promising. C_{76} and C_{84} have been found to have a helical form. C_{78} also has a chiral form, explored on page 1768 of this issue. Starting with planar graphite and ending with chiral carbon is surprising enough, but the asymmetrical forms may have fancy applications too, such as the creation of nonlinear optical materials. When exposed to light of one frequency, such a material would emit light of another, acting as an optical switch.

Buckytubes. One of the year's most exciting developments turned up in the dirt piles of old fullerenes. In the soot on a carbon electrode used to make fullerenes were found needles of carbon, composed of very thin nested tubes. Within each individual rolled-up sheet, the carbon molecules were apparently arranged in a helical structure. Fullerene tubes may possess an amazing mix of properties—including great strength, since fibers of conventional forms of carbon are already the strongest known. Evidence is mounting that the higher fullerenes—such giant molecules as C_{240}—may not be symmetrical like the prototypes, C_{60} and C_{70}. Rather, the larger molecules may be asymmetrical and incorporate buckytubes in their structures.

Starting reactions. Carbon cages are likely to make good catalysts, thanks to their bonding behavior and geometrical features, so industrial chemists are watching the buckyball play closely. This year, the outside of carbon cages was decorated with complexes of nickel, palladium, and platinum complexes, a feat that may eventually offer more than just a pretty molecule.

Injuries on the field? Many potentially useful organic compounds have a crippling fault: They tend to be intercalated into DNA and thus promote cancer. But buckyballs suffer no such flaw. They appear to be too big and round to be incorporated into DNA as are some of their planar cousins.

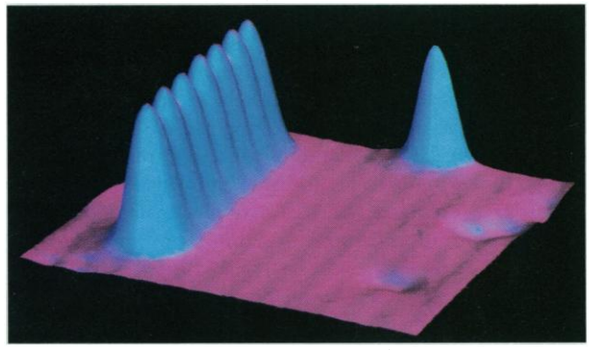
Buckyballs face a potential red flag of their own, however. In the presence of light and oxygen, the C_{60} molecule can pass its superfluous excitation energy onto nearby oxygen molecules, creating a long-lived but very reactive form of oxygen called singlet oxygen. Bucky boosters point out that even such a threat may hold promise. When not in an excited state, C_{60} quenches the reactivity of other singlet oxygen species. Unmodified fullerenes are insoluble in water, suggesting that they may react very little with biological tissue. Carcinogenicity tests are ongoing, but thus far buckyball looks like one of the safer games in town.

As fullerene science takes off in all directions, speculations as to its uses abound. Will it be superconductivity that makes fullerenes commercially important? Super-strong fibers? Catalysts? Too soon to say, but buckyball players aren't exactly worried about a lack of applications. At this point, the heady atmosphere of discovery is too strong. After all, so far fullerene science exhibits the classic profile of a major scientific breakthrough. Buckyballs were found by accident by researchers asking a completely different question. Then they were steadily explored—until they became widely available and the field exploded. Now, buckyball scientists are enjoying the exponential phase, in which almost everything is new and the unexpected is expected. Eventually, the action will focus on a few promising research veins, and then practical applications will bloom. For now, chemists, physicists, and materials scientists are simply having a ball.

And the Runners-Up Are...

Scientists hit homeruns in many fields this year, as they explored new territories ranging from planets to atoms. *Science*'s nine runners-up for Molecule of the Year—exciting discoveries need only be "honorary" molecules—are described below.

Microscopic manipulations. Extending human perceptions into the atomic realm has been a scientists' dream for decades, but in 1991, that dream became a useful part of reality, thanks to the scanning tunneling microscope (STM). An STM initially offered the perception aspects at the atomic level, but recently the microscope has been shown to be able to pick up atoms and move them about. The scope works by inducing a tunneling current of electrons between its tungsten tip and the sample. If the current is kept constant, the probe rises and falls, creating a map of the sample's topography. Sharply increasing the current allows the tip to pick up atoms delicately and transport them. As an imaging tool, the STM is available from about 20 commercial sources and is already a workhorse of materials science. As an atomic forceps, STM applications are just beginning. For their first attempts at moving atoms, scientists pulled stunts like writing "I love STM" in xenon atoms. But in the past year, they systematically explored the tricks of atomic manipulation. Atoms were dragged along a surface, picked up and set down somewhere else. A single atom can be induced to diffuse by applying a voltage between the surface and the STM tip. Practical applications are still years away, but the possibilities for atomic assembly are endless, including creating new molecules or building synthetic versions of precious natural ones. Atomic switches, which flip a current on and off by moving a single atom and which were demonstrated for the first time this year, could theoretically shrink computers by several orders of magnitude—and allow readers to store a year's worth of *Science* on a disc the size of a penny.

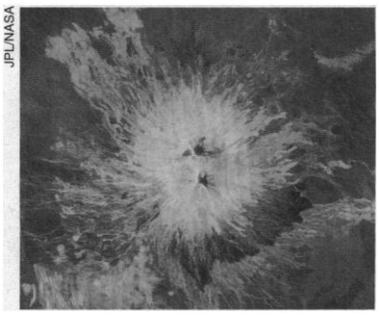


The first hand-built atomic structure. Seven Xe atoms banded together to form a linear chain on the Ni (110) surface. The image is 50Å x 50Å.

Venusian visions. Planetary scientists have always had a basic problem: Studies of active geologic and atmospheric processes on Earth-like planets were chiefly based on one planet—Earth. In 1991, detailed information was obtained for another planet, thanks to an interplanetary voyager called Magellan, which began to orbit Venus in August 1990. Despite some early problems, Magellan's big radar antennae sent back eerily beautiful radar photos of the surface of Venus. The new photos (which Magellan gathered by beaming microwaves to the surface through the clouds that shroud the planet, picking up the echoes and sending records back to Earth for processing) are a technological triumph, 10 times as sharp as any

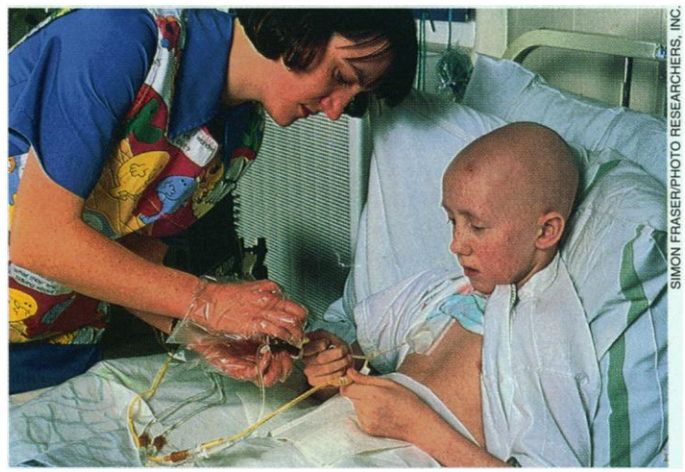
previous Venusian views. They show huge impact craters flooded with radar-dark material, giant volcanic calderas, dramatic mountain ranges, and evidence of Silica-rich volcanism, such as thick lava puddles 25 km in diameter. Already it's clear that Venus is no twin to Earth, bearing little evidence of Earth-like plate tectonics. One other 1991 Venusian news flash: more proof that the planet's heavy sulfuric clouds are sometimes pierced by lightning. The lightning's telltale radio signals were picked up by a plasma wave instrument aboard the Galileo spacecraft, which enjoyed a brief rendezvous with Venus in 1990. Meanwhile, Magellan's work was so successful that its mission has been extended; a third mapping rotation begins in January. For those who have seen Venus with new eyes, the twinkling star of evening and morning will never look quite the same.

That sinking feeling. Stratospheric ozone, or rather the lack of it, has been a scientific concern for several years, but in 1991 public awareness reached a new high, as the ozone hole over Antarctica expanded. This year, ozone losses hit home for denizens of the Northern Hemisphere too. The protective layer has thinned by about 3% over northern latitudes in the past decade. Even during northern summers—typically a seasonal high for ozone as well as prime time for sunbathing—ozone has declined. As a consequence, human exposure to ultraviolet light is expected to increase. If ozone drops by an average of 10%, the United Nations Environmental Program predicts that there will be 1.6 million new cataracts and 300,000 skin cancers worldwide annually. On the positive side, the Montreal Protocol, which calls for phase-out of ozone-eating halons and chlorofluorocarbons by 2000, was implemented this year. Environmentalists say faster phase-out is needed, but even critics agree the protocol deserves respect as the first international treaty to tackle a global environmental problem. Meanwhile, using satellites and aircraft, scientists continue to explore the dynamics of ozone destruction. But even if ozone loss can be slowed, how can the existing hole be filled? Some atmospheric scientists suggested one possibility this year: break the ozone-destroying chain reaction by dumping 50,000 tons of ethane or propane into the Antarctic stratosphere to scavenge reactive chlorine free radicals.


JPL/NASA

The volcano Sapas Mores on Venus erupts with molten lava 250 miles across with some similarity to eruptions in Hawaii.

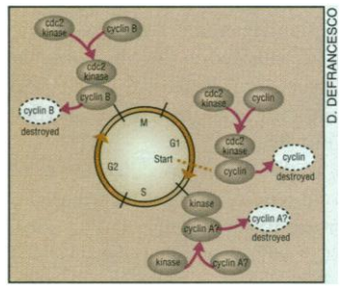
Growth factor. True to their name, colony stimulating factors (CSFs) spur colonies of immune cells to grow in Petri dishes. But in 1991, CSFs swept into clinical medicine, with two factors approved by the Food and Drug Administration. Naturally produced in the human body, recombinant CSFs can be used to stimulate production of key white blood cells, which destroy bacteria and viruses. Chemotherapy kills such cells, leaving patients vulnerable to infection and dependent upon antibiotics. To regain their health, tens of thousands of patients getting chemotherapy also receive granulocyte colony stimulating factor, (GCSF), which allows more intense and frequent doses of chemotherapy. Patients who receive GCSF need fewer antibiotics, recover earlier, and go home sooner, making the medicine a cost-effective strategy. It's not only cancer patients who benefit. GMCSF (for granulocyte-macrophage colony stimulating factor) was approved for bone marrow transplantation this year. Meanwhile, basic research on the factors continues; the molecular structure of GMCSF is presented by


SIMON FRASER/PHOTO RESEARCHERS, INC.

Pediatric nurse adjusting an intravenous line being used to deliver chemotherapy drugs to a young boy with leukemia.

Diederichs *et al.* on page 1779 of this issue. Theoretically, anyone who suffers from impaired immunity may profit from CSFs; trials with AIDS patients are under way. Trials are also under way on people who have normal immune cell counts but are fighting serious infections, like pneumonia, and could use an immune cell boost. The CSFs are also pretty good at stimulating stock portfolios. Amgen stock rose by 180% this year. The two approved CSFs are expected to garner $450 million in sales in 1992, and that's only the tip of the iceberg, with more than a dozen CSFs and their cousins, the interleukins, waiting in the wings.

Cycling into cancer research. Like miners following their separate veins of gold, basic scientists for years have explored the subtleties of the cell cycle while cancer researchers explored the genetics and pathology of the disease. This year, both groups have found themselves digging away at one promising vein, which could lead to the motherlode: proteins called cyclins and their working partners, the cdc kinases. Originally, researchers thought that one or two cyclins paired up with a kinase (enzymes that modify proteins by phosphorylation) to trigger cell division. This year the cyclins and kinases have multiplied into a complex cast of characters, including five distinct families of cyclins and perhaps 10 cdc kinases. Together, these proteins may regulate the cell cycle at a series of key points. For example, this year researchers looking for a gene involved in a benign parathyroid tumor stumbled into cyclin research, finding that the protein encoded by their tumor gene is a cyclin. Other groups (who were actually looking for cyclins) found the same cyclin, now called cyclin D. Meanwhile, cyclins are suspected of binding with the protein encoded by a well-known tumor suppressor gene, the retinoblastoma gene. There are even tantalizing hints that cyclins are involved with the protein product of the *p53* gene, a tumor suppressor that is the most frequently mutated gene in some human cancers. This year, the cell cycle picture became much more complex and a little less mysterious. Eventually, resetting the cellular clock could stop the wild reproduction of cancer cells or nurture the regrowth of cells in damaged organs.



D. DEFRANCESCO

Cyclins and the kinases related to them have key roles in controlling the cell cycle.

Immunologists look inward. In the past few months, a series

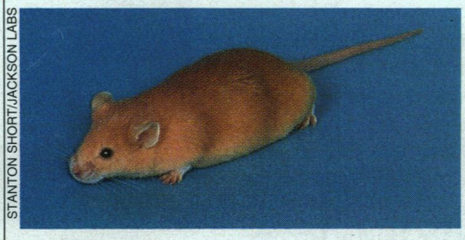
of fast-paced developments in immunology has begun to unravel the story of the way antigens are processed into strips of peptide and displayed for recognition by lymphocytes. For this internal processing duty, the immune system has coopted existing cellular machinery. In one antigen-processing pathway (class I) there are two steps—first, digesting the proteins and second, transporting the peptides to the binding site. The new genes were found in a small area of the genome that contains other genes of the major histocompatibility complex (MHC). Also in late 1990 and in 1991, several of the peptides bound to the MHC molecules (both class I and class II) were sequenced for the first time. Since vaccines mimic these peptides in order to arouse an immune response, knowing the detailed sequence is likely to lead to more potent vaccines. For example, MHC class I molecules incorporate surprisingly short peptides, typically only nine amino acids long. Most current vaccines are generated by a much longer and therefore less effective chain. Since the immune system sometimes attacks its own proteins (the autoimmune diseases), knowledge of these peptides may also be the first step to creating drugs to block the unwanted response.

Market rules. For more than 70 years, the Soviet Union ran a sweeping economic experiment on a scale so grand no social scientist would ever dare propose it. Spurning free markets, the Soviets did their best to craft a planned economy, setting prices and directing factory output for the entire nation. Meanwhile, from the 1930s to the '50s, Western economic journals hosted a fierce debate. Could a centrally controlled economy run smoothly by mimicking a free market? Socialists argued that inventories could signal supply and demand just as well or better than prices. But other economists insisted that nothing could match the wealth of information about tastes and technologies that is contained in a free market price. Those theoretical debates ended inconclusively, and the journals turned to other issues. But in 1991 the Soviet Union crumbled from within, offering strong support for the market economists. Economists around the world are now concluding that central planning does not motivate citizens and cannot transmit information as efficiently as a free market. The demise of the USSR does not prove, of course, that every aspect of an economy should be left to Adam Smith's famed invisible hand. But in the wake of the Soviet experience, the question is no longer market economy vs. central planning. Rather, it is how best to create a market economy while minimizing hardships.

AP/WIDE WORLD PHOTOS

Lenin's statue comes falling down. A rope removes Lenin from a pedestal in Lithuania as symbol of the collapse of his economic system.

Genes on target. Homologous recombination, the act of slipping a mutated gene into the correct place on a chromosome, was first accomplished about 4 years ago. But in 1991 the technique's chimeric offspring began to appear in large numbers. A zooful of altered mouse lines has now emerged, setting the stage for a new set of powerful mammalian model systems for human diseases. Biologists are working on creating mice to provide models for common human diseases, such as cystic fibrosis and many types of cancer. Before homologous recombination, geneticists working with transgenic mammals could introduce a mutated gene into cells but could not control where the gene went on a chromosome or how many copies were inserted. Only in yeast could altered genes be inserted on target. But now mammalian geneticists can study living mice with carefully targeted mutations, thanks to homologous recombination and another relatively new technique, that of culturing embryonic stem cells and reinserting them into the developing mouse. The scientific rewards are rolling in. For example, in 1991



STANTON SHORT/JACKSON LABS

Yellow obese mouse. The mouse is heterozygous for a gene that alters coat color and tumor susceptibility.

several of the homeobox genes—key genes that regulate development and have been conserved throughout evolution—were disrupted by targeted mutagenesis and put back into mice. Most times homologous genes have homologous effects in different species but sometimes the results are surprising. For example, mutated *Drosophila* show drastic effects if missing a homeobox gene called *engrailed*, but knocking out the homologous gene in mice produced normal mice with only slight changes in brain tissue, suggesting that there is more redundancy than expected in the mammalian genetic plan. Meanwhile, the homologous recombination technique continues to be refined, so that as of this year, the technique can be used extensively.

Rousing receptors. As the most widespread neurotransmitter in the brain, the simple amino acid L-glutamate has powerful and diverse effects, with roles in development, learning and memory, and neurological diseases and stroke. This single molecule triggers a variety of events because different receptors respond to glutamate in very different ways. This year, the genes that code for several receptor types were found, which marks a giant step toward understanding their detailed functions and providing therapy for malfunctioning cells without interfering with normal brain processes. The elusive metabotropic receptor was cloned this year, as was the long-sought NMDA receptor (for N-methyl-D-aspartate, a synthetic compound that activates this receptor). Finding the NMDA receptor was a prize discovery, in part because this receptor, which allows calcium ions into the cell, is involved in the brain damage left by a stroke. The damage is done when cells become overstimulated and calcium floods the cell, in a process called excitotoxicity. Conventional wisdom held that only NMDA receptors were permeable to calcium, but this year scientists revised their views: certain subunits of another class of receptor, the non-NMDA Slutamate receptors called kainate-AMPA receptors, also can trigger the flow of calcium. And this summer two groups independently found that the genes that code for these receptor subunits differ by only one amino acid, which means calcium permeability is genetically controlled by one amino acid in these receptors. These developments suggest that the non-NMDA receptors also may have a role in calcium-dependent processes, which are believed to include learning and memory. And they raise the possibility that some day very specific drugs could turn off calcium permeability in a small subset of brain cells—without turning off the rest of the brain in the process.

—ELIZABETH CULOTTA AND DANIEL E. KOSHLAND, JR.