Astronomers peered deep into the universe and found that it is flying apart ever faster, suggesting that Einstein was right when he posited a mysterious energy that fills "empty" space

Cosmic Motion Revealed

The nature and ultimate fate of the universe have preoccupied philosophers and scientists for centuries. Scientists discovered decades ago that the universe is now expanding, with its galaxies rushing apart in all directions. But the pull of gravity could slow that expansion, and so researchers have tried to work out the final destiny of the cosmos: whether there is enough matter to cause it to one day collapse on itself, or whether it will expand forever. In 1998 two teams of astronomers peered across an enormous gulf of time and space to answer that fundamental question—and amazed even themselves with what they found.

Not only is there too little matter in the universe to ever halt the expansion on its own, but the outward motion appears to be speeding up, not slowing down. At the same time, the finding raises such profound questions about the nature of space that cosmologists are wondering whether the ultimate fate of the universe can ever be known for certain.

In a triumph for astronomers' ability to look deep into the past, the independent teams came to their conclusions by observing far-off exploding stars called supernovae that turn out to be surprisingly dim, revealing an acceleration that has swept them to unexpectedly large distances from Earth. With these results, reaching billions of light-years into space, astronomers have gained a secure foothold in the deepest and most mysterious reaches of the cosmic past. We name their findings, which transform our view of the universe and pose fundamental new questions for physics, as Breakthrough of the Year for 1998.

Adding to the drama of the find, the simplest explanation for the accelerating expansion is a bizarre energy that on large scales counteracts gravity, pushing matter apart, an idea that Albert Einstein posited in 1917 and later rejected. This year's discoveries suggest that most of the energy of the universe is in this form, which Einstein called the cosmological constant, or lambda. Because matter and energy are interchangeable, this huge energy reservoir means that the universe of matter, from tables and chairs to stars and clusters of galaxies, may be but the minor portion of creation.

These implications are so profound and unsettling that astronomers around the world are still trying to disprove the finding, to uncover anything that could create a false impression of cosmic acceleration. To date they have been unsuccessful, and so physicists are rushing to explain the origin of the cosmic energy. The lambda symbol, λ, is once again sprinkled throughout equations in the astronomy and physics journals, and the new results have inaugurated a small industry of theoretical searches for even quirkier possibilities for boosting the expansion.

Back in 1917, when Einstein proposed the constant, he and other scientists thought that the universe was static, neither expanding nor collapsing. He put the cosmic repulsion into his equations to prevent the universe from collapsing on itself from the gravitational pull of the matter inside it.

But by 1929, astronomer Edwin Hubble had peered into the heavens and startled the scientific world of his day by discovering that the universe is in fact expanding. Born in a hot, dense state called the big bang, the cosmos has been likened to a display of fireworks whose most brilliant moments are behind it. Like fading cinders in the fireworks, galaxies that were initially close to each other are today drifting apart slowly, while those that began slightly further apart are flying away from each other at higher speeds. From our vantage point in the Milky Way, the speed at which any other galaxy is moving away can be clocked using the "redshift" of its light—a drop in frequency and increase in wavelength akin to the dip in pitch of a receding train's whistle.

Cosmic speed trap. The brightness of a fading supernova (upper left to lower right) showed how fast the universe is expanding.

But gauging a galaxy's actual distance is difficult. Hubble managed it by observing the apparent brightness of stars called Cepheid variables, whose intrinsic brightness is known; these stars can thus be used as "standard candles" to measure distance, as more distant Cepheids appear dimmer. Hubble compared the redshifts with the dis-

CREDITS: A. RIESS, W. LI, A. FILIPPENKO/UC BERKELEY

Comeback of the Year: SOHO's Triumphant Return

Early in 1998, the Solar and Heliospheric Observatory (SOHO) was a hugely successful spacecraft, gathering data on solar outbursts from its secure vantage between Earth and the sun. Astronomers were gearing up to observe a maximum in solar activity around 2001. Then, on 24 June, disaster struck: After a series of ground-control errors, the spacecraft spun wildly out of control. Its batteries drained when its solar panels rotated away from the sun, and it lost all contact with Earth.

But the craft was lost in space for only a few months. In an almost miraculous comeback, as SOHO moved on in orbit its orientation changed, so that the solar panels again faced the sun. The batteries recharged and radio contact was reestablished with a cheering ground control on 3 August. By year's end, the craft was back in position, practically all instruments were online—and SOHO was enjoying its place in the sun once more.

tances and discovered the expansion.

Einstein accepted Hubble's find. But he reasoned that if the expansion was a relic of a primeval explosion, the cosmological constant—which he felt made the equations unaesthetic—wasn't needed. He withdrew the idea and called it his "biggest blunder."

As cosmologists continued to work with the notion of an expanding cosmos, they concluded that over the 12- to 15-billion-year life of the universe, the expansion would slow slightly, thanks to the pull of gravity that every galaxy exerts on every other. But spotting such a change requires probing deep into the past by looking at stars glittering billions of light-years away—too far away for Cepheids to be seen.

So for the past 20 years, astronomers have turned to a new kind of standard candle: the brightest kind of supernova, which happens nearly the same way each time. But these bright, massive explosions are rare—only two or three erupt in a typical spiral galaxy per millennium. To find enough of them, astronomers make electronic images of large swaths of sky in a single night, capturing tens of thousands of distant galaxies, and then image the same areas a few weeks later. Once the images are overlaid and subtracted on a computer, any new supernovae leap out and can be observed until they fade away.

The two teams, both of which have members in Europe, Latin America, Australia, and the United States, collected their supernova data with increasing efficiency over the last few years, expecting to find out by how much gravity was slowing cosmic expansion. Early this year, both teams announced that their expectations had been turned upside down: The relative dimness of the supernovae showed that they are 10% to 15% farther out than expected even in a universe with little matter, indicating that the expansion has accelerated over billions of years. At year's end, with dozens of supernovae analyzed, published, or in press, those conclusions stand.

That finding resurrects a mysterious repulsion that counteracts gravity, with lambda as the most likely candidate. There were earlier hints, from theories of cosmic evolution and observations of the large-scale structure of the universe, that the cosmos holds little mass and that there might be a lambda, but the idea was generally considered outlandish. Now lambda is respectable once more, and Einstein is proved right, albeit for reasons he could not have foreseen. In fact lambda appears to be dominant in the universe: In the simplest theoretical picture, the supernova data imply that 70% of the universe's energy is in the form of lambda and only 30% is matter.

Physicists have since interpreted lambda as a quantum-mechanical effect: that the evanescent particles that flicker in and out of existence in "empty" space provide a well of energy that gives space its springiness, shoving it apart. But so far, calculations suggest that such a lambda should be many orders of magnitude larger than the supernova groups have seen. That puzzle has launched a search for new physics principles, such as symmetries in the fabric of space, that might help cancel out huge terms in the equations. Other candidates for this strange energy, which go by names like quintessence and X-matter, have also been put forth, as physicists vie for the prize of explaining what most of the universe is made of. And because some of those forms of energy may change over time, cosmologists have become less confident about declaring the fate of the universe hundreds of billions of years hence.

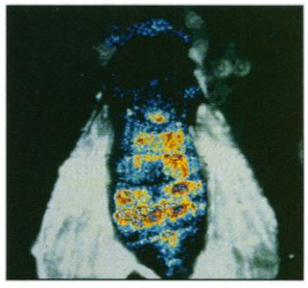
Indeed, at this point the cosmological constant remains in the realm of theory; no one yet knows the precise nature of the energy causing the universe to fly apart ever faster. Astronomers continue to gather data and to search for any effect other than acceleration that could explain their findings. But despite their efforts, they have found no reason to doubt their work. Although the nature of the universe was once chiefly the realm of philosophers, in 1998 it seems that cosmology is grounded in data, as visions of distant supernovae revealed the true nature—and perhaps the future—of the cosmos. Scientists and philosophers both will be grappling with the implications for years to come. **–JAMES GLANZ**

CREDIT: JEFF HALL

THE RUNNERS-UP

Science recognizes nine discoveries that transform our ideas about the natural world and also offer potential benefits to society

First Runner-Up: A remarkable year for clocks. Nineteenth-century philosophers proposed that God was a clockmaker who created the world and then let it run. Modern biologists might in part agree, for it's clear that evolution has carefully crafted clocks that allow almost all organisms to follow the rhythm of the sun. In 1998, a volley of rapid-fire discoveries revealed the stunning universality of the clock workings: Across the tree of life, from bacteria to humans, clocks use oscillating levels of proteins in feedback loops to keep time. Perhaps more amazing, fruit flies and mice—separated by nearly 700 million years of evolution—share the very same timekeeping proteins. Now that they better understand the cellular clock, scientists can begin to manipulate it, with applications from curing jet lag to brightening winter depression.



Lighting up. Clock genes glow in the cells of a fruit fly.

Clocks made the Runner-Up list in 1997 too, after researchers identified the first two mammalian clock genes, *Clock* and *per*. This year a prodigious amount of work from the clock research community filled out the story dramatically. For example, work in fruit flies showed that during the morning hours, CLOCK binds to a protein partner and together they turn on genes for proteins called PER and TIM (Timeless). These two proteins eventually shut down their own genes.

But to keep the proteins on a 24-hour cycle, PER and TIM's turnoff must be delayed. This year researchers found the cause of that delay in flies: a protein called DOUBLE-TIME (DBT) that destabilizes PER, keeping its levels low until enough TIM accumulates to pair with PER and shield it from DBT. Only then do PER and TIM enter the nucleus to turn off their genes, causing levels of the two proteins to wane until morning, when CLOCK and its partner turn on the genes once again.

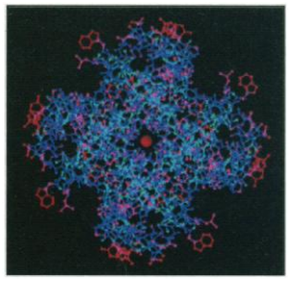
Discovering all this in one organism would be breakthrough enough, but researchers found the same proteins or close variants playing the same roles in mice, too. As reported in June, a negative feedback mechanism appears to power plant clocks as well, albeit with different genes. And in September, a Japanese team showed that the single-celled cyanobacteria's clock is based on the same theme.

Despite this elegant molecular machinery, circadian clocks are imperfect timekeepers: Left on their own, their daily cycles run longer or shorter than 24 hours. Light keeps them in line, like a daily adjustment of a watch. In July researchers showed how: Light causes the rapid destruction of TIM, at least in flies.

Researchers thought that, in mammals, eyes are required for the light signal to reach the clock. But in January a U.S. team made the shocking discovery that light shone on, of all places, the back of the knees seems to reset the clock in humans; several groups have now repeated that finding.

Capping a year of dramatic discoveries, in November researchers fingered three plant pigments that capture light and pass its signal to the clock; one seems to play the same role in animals. For clock researchers already pleased with the pace of findings in 1997, this year's double-quick barrage of discoveries has exceeded all expectations.

An electrifying structure. As you read this page, electric signals flash from your eye to deep in your brain, traveling through millions of neurons. Each signal is successfully passed along courtesy of molecules in the cell membrane, "gates" that allow certain ions—but no others—to pour in and out of the cell, spreading the change in electrical potential throughout the cell.



Passing through. Potassium ion (red) in its channel.

This year, in a landmark discovery that reveals one of the biochemical roots of the nervous system, a New York City team published the three-dimensional structure of one such ion channel—selective for the potassium ion—in a bacterium. This long-awaited finding is a technical marvel that provides new insight into how the nervous system works its magic.

After decades of wondering, electrophysiologists can now understand such riddles as how the potassium channel manages to keep out wrong ions, such as sodium, while shuttling an amazing 100 million potassium ions per second across the membrane. The structure reveals that the ions must pass through a narrow filter, where potassium ions fit snugly and briefly bind to the protein. The slightly smaller sodium ions cannot form this bond, making the filter an energetically unattractive place for them. And there are always at least two potassium ions in the filter, repelling each other just enough to ensure that once in, they quickly make their way out the other end. Membrane proteins are notoriously difficult to crystallize, but this year's triumph may prompt work on the thousands of other such proteins still waiting.

Neutrinos weigh in. The elusive particle called the neutrino has led physicists on a merry chase ever since it was posited in 1930. Researchers have assumed that the ghostly neutrinos lack both charge and mass. But in a stunning announcement in June, an international collaboration running the Super-Kamiokande neutrino detector in Japan showed that these subatomic particles do indeed have a wisp of mass, and physicists are now scrambling to revise their view of how the universe is put together.

Physicists first began to suspect that neutrinos had mass when they aimed neutrino detectors at the sun and found fewer than expected. One possibility was that as neutrinos flew from their origin in the sun to the detector, they changed from one of three types to another type that eludes detection. By the laws of quantum mechanics, this can happen only if neutrinos have mass.

Super-Kamiokande, a 50,000-ton tank of water in which 11,200 light sensors detect the faint glow created when a neutrino

Best Bets for 1999

To find future winners in the research game, *Science*'s editors turned to our crystal ball and saw six fields emerge:

Maturing research. Genes that extend life in the fruit fly and worm have now confirmed the notion that individual genes can regulate aging. Next up: more genetics, plus a flurry of mechanistic work to try to pinpoint how certain enzymes, hormones, and cellular structures mold the aging process. Also expect a continuing flurry of studies of the now-trendy telomeres—DNA sequences on chromosome ends—whose shortening over time may contribute to cellular aging. Top priority: to test these ideas in human cells.

Bioterror troubles. The superpowers halted aggressive biowarfare R&D 30 years ago, but a new threat is emerging, as smaller nations such as Iraq and even cults like the Aum Shinrikyo sect in Japan seek to exploit the deadly power of nature's toxins. In response, a worried U.S. Congress this year approved $150 million for civilian bioterrorism defense, funding medical supplies, disease surveillance, and new vaccine research.

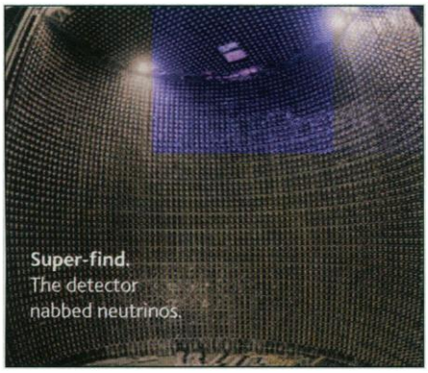
Crystal power. New Agers claiming that crystals channel vibes have it almost right. Specially tailored photonic crystals have latticelike structures that can transmit certain wavelengths of light while excluding others. This year researchers created the first optical fibers based on such crystals, which promise to carry light pulses farther without losing the signal. Look for a new world of crystal applications in areas from advanced sensors to telecommunications equipment.

Sink search. One burning question in climate research concerns the so-called "missing sink": Terrestrial plants seem to be sopping up carbon dioxide—staving off some greenhouse warming—but no one knows just where this sponge is or whether it's forests, croplands, or both. A controversial modeling study this year pointed to North America, but more debate is sure to come in 1999, as other modelers compare their results and new data come in from a worldwide network of towers measuring CO_2 flowing in and out of forests.

Take a deep breath. Allergies and asthma made headlines in 1998, as some U.S. schools and airlines banned peanuts to accommodate allergy sufferers and asthma cases rose to an estimated 155 million worldwide. But peanut butter could make a comeback if advances in understanding the dozens of molecules involved in allergic responses pay off. Trials for DNA vaccines and antibodies that block key steps in runaway immune reactions are set to begin in 1999, and nearly 200 different asthma treatments are in development or clinical trials. Expect some relief for sneezing and wheezing in 1999.

Once and future climate. A growing torrent of data is revealing why climate has varied, often abruptly, over the millennia. As researchers tie together climate records from oceans, lakes, and glacial ice, they are discovering the global nature of climatic jitters that can drive the planet halfway to an ice age in a decade—and that might pop up in a greenhouse world. As records are linked from pole to pole, expect the research flurry to move from the North Atlantic, where swings are strongest, to the tropics, where the trigger for millennial change may lie.

CREDITS: (TOP) R. MACKINNON; (BOTTOM, LEFT TO RIGHT) P. HOLDEN/VISUALS UNLIMITED; TERRY E. SMITH; WILLIAM J. WEBER/VISUALS UNLIMITED



Super-find. The detector nabbed neutrinos.

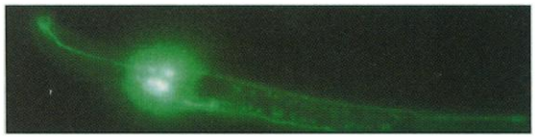
slams into a water molecule, found strong evidence for such shape-shifting by tracking atmospheric neutrinos. These particles are the products of cosmic rays and so should rain down on Earth in equal numbers from all directions. But the detector found fewer neutrinos coming from Earth's far side than streaming down from above, presumably because far-side neutrinos change types during their longer route.

Thus at least one kind of neutrino must have mass. The results have spawned a furious debate over whether a new theory of particles is needed, and heated up a long-running argument over whether neutrinos are part of the unseen "dark matter" thought to make up much of the mass in the universe. 1998 marked a new understanding of the neutrino, but this wily particle is still a few steps ahead of the scientists pursuing it.

Genomics takes off. This year it seemed that every month brought another milestone in sequencing work, fueling an explosion in the new field of genomics—analyzing and comparing whole genomes. Researchers bagged the first complete sequence of a multicellular organism, as well as those of several feared microbes, bringing the total of fully sequenced genomes to nearly two dozen. These achievements were also accompanied by new experimental and computer programs to explore the wealth of data.

In December a British–U.S. sequencing alliance reported virtually all 97 million bases that make up the genome of the multicellular nematode *Caenorhabditis elegans*. By comparing the worm genome with yeast's 12.5 million bases, researchers are beginning to glean what genetic changes were necessary for life to move beyond single cells. But about a third of the worm's 19,000 putative genes are novel, suggesting that much experimental work lies ahead to determine their functions.

This year's newly completed microbial genomes include those of some of humankind's worst enemies: the bugs for syphilis, tuberculosis, and typhus, as well as a *Chlamydia*, which causes venereal disease and blindness. The genomes reveal proteins unique to these pathogens, molecules that may be targets for drug or vaccine development. Genomics spread its wings in 1998, and it's likely to soar for years to come.



Gene at work. An active developmental control gene lights up nematode nerve cells.

CREDITS: (TOP TO BOTTOM) ICRR/THE UNIVERSITY OF TOKYO; TERRY E. SMITH; O. HOBERT AND G. RUVKUN/MGH

Quantum leaps. Beaming the Captain and his stalwart crew up to the bridge of the *Starship Enterprise* remains the stuff of science fiction, but this year physicists boldly went where no one has gone before, turning teleportation at the quantum level into lab reality.

In science fiction, teleportation moves people and things around, but in physics it means reconstructing a quantum state at a new location, so that information, rather than matter or energy, is moved about. Such information transfer lies at the heart of quantum computing, which offers the prospect of lightning-fast, superparallel calculations. This year physicists made great strides toward building such devices, "soldering" quantum links between ions, devising schemes to find and fix quantum data errors, and performing simple calculations.

The key to teleportation is the odd phenomenon known as quantum entanglement, in which the fates of two or more particles are entwined without physical contact. For example, when a single photon is split by a crystal, the two daughter photons retain a connection as they travel their separate ways: An action performed on one daughter will dictate the state of the other.

A year ago, teams using a roomful of lasers and mirrors in Innsbruck and in Rome teleported information on the quantum states of single photons. Then in October, a U.K.–Danish–U.S. group teleported information on the amplitude and phase of an entire light beam to another beam. In November, U.S. physicists teleported quantum information from the nucleus of a carbon atom to that of a neighboring hydrogen atom. This last feat hints at the real utility of teleportation—the reliable transmission of information between ions that serve as the elements of a quantum computer. That technology may be worthy of inclusion in a *Star Trek* episode: It's teleportation, Jim, but not as we know it.

Scorecard '97

Last December, we picked six fields to watch in 1998. Here's what happened to our favorites, showing whether our crystal ball was cloudy or clear.

Personalized prescriptions. Ever faster, cheaper DNA screening techniques have made so-called pharmacogenetics—tailoring drug treatment to patients' genetic makeup—all the rage. But although one breast cancer treatment now targets women with a particular genetic makeup, there's no real proof that such genotyping is yielding better therapies.

Forecasting future shocks. Score two for climate forecasters, who in 1998 pitched timely forecasts of both the weather effects of the 1997–98 El Niño and last spring's switch to the opposite condition, La Niña. In the new frontier of decadal predictions, researchers pinned down oscillations in the ocean-atmosphere system from the Arctic to the Pacific and the tropics.

The expanding universe. Last year when a few distant stellar explosions showed that cosmic expansion wasn't slowing as expected, *Science* predicted that more data would yield big news. In this case our crystal ball saw as clearly as the finest telescope: Results from dozens of explosions are the basis of 1998's Breakthrough of the Year (p. 2156). But we also got a surprise: The new data show that the cosmos isn't slowing at all but speeding up, with profound implications for physics and cosmology.

Ribosomal inspection. Parts of the massive protein-RNA complex called the ribosome, where proteins are made, were seen in higher resolution this year. Cell biologists can at last combine data from a variety of imaging techniques to determine how ribosomal proteins interact with nearby RNA. But a full reconstruction of the ribosome has yet to emerge.

Diversity debate. Biologists still suspect that the vast biodiversity in some habitats helps stabilize ecosystems, but evidence has been hard to come by. Ongoing studies suggest that a single key species can dominate the behavior of some ecosystems, while others seem to require more diversity.

Designer crops. In Europe, *Science* predicted a battle over transgenic crops, and indeed the fight has raged all year. At year's end, score 1 for the resistance, which includes environmentalists, consumer groups, and even Britain's Prince Charles. Britain has stalled the commercial release of such crops, and a recent report for the biotech giant Monsanto says that the company's recent ad campaign failed to persuade suspicious European consumers.

New Partnerships for Biology and Business

Futurists predict that in the 21st century, biotechnology will outgrow its academic roots and become a key commercial technology, much as electronics did during this century. In 1998 researchers began to realize just how fast the marriage between biology and industry is taking place—and how turbulent the transition is likely to be. This year company researchers pushed the pace in everything from genomics to cell biology, and in case after case, the advances left publicly funded scientists wondering whether they can compete in areas that were once their exclusive province.

The clash between public funders and industry was painfully obvious last month, when company-sponsored researchers announced the cultivation of "human embryonic stem cells," which can develop into many different tissues in the body (see p. 2161). The U.S. Congress has banned the use of federal funds for such work, which uses cells derived from human embryos, so scientists can't use public grants to explore this research arena.

A public/private schism also split the human genome community this year. In May, gene sequencing pioneer J. Craig Venter announced that he was teaming up with a company that sells gene-sequencing machines to sequence the entire human genome by 2001—4 years ahead of the government's timetable. And he promised to do it for just $300 million, a fraction of the cost of the government's $3 billion Human Genome Project. Three months later another firm upped the pace, promising to finish the sequence in a mere 2 years. Faced with showing up to the party after all the guests had left, Human Genome Project leaders agreed in September to turbocharge their efforts and polish off a "working draft" of the genome by 2001.

Publicly funded plant genome researchers face even stiffer competition from corporate research. In September, the U.S. National Science Foundation awarded the first grants in its new $40 million plant genome initiative; the U.S. government now spends roughly $70 million a year on plant genomics. But giant multinational companies have already set up even larger crop gene sequencing efforts. In just one deal announced late last year, Monsanto and Millennium Pharmaceuticals agreed to spend up to $218 million over 5 years to form a new agricultural genomics company.

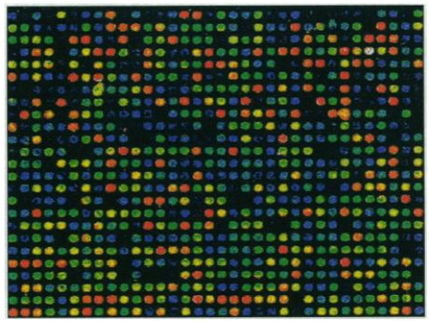
Finally, pharmaceutical firms worldwide continue to industrialize biotech. For example, over the last decade academic labs have pioneered fast new methods for generating and screening novel drugs (see runner-up, this page). Companies have spent billions improving the methods, buying start-up firms, and building high-speed drug labs, again leaving academic researchers with no way to keep pace in a field they founded.

Although ethicists argue that the tremendous power of the new biology cries out for extra care in commercialization, industrialization of novel technologies is nothing new. During this century, the chemical and electronics industries grew from scattered research programs to become global giants, and companies have gradually become the main employer of Ph.D.s in those fields. Yet publicly funded research has remained vigorous, as academic scientists find new problems and often invent the next wave of technology along the way. With the coming of the biotech century, it will be biologists' turn to reinvent themselves.

Boom in biochips. Microchips are already the foundation of the electronics industry, but in 1998 chip technologies left their electronic roots behind and moved decisively into biology and other fields. This year the same miniaturization tools used to make computer chips were used to shrink and speed up everything from DNA sequencing equipment to diagnostics.

While major microelectronics firms entered the biochip business, teaming up with start-up companies to push commercialization, basic researchers forged new chip technologies. For example, this year researchers created a DNA-processing micromachine that may one day be able to sequence DNA. Already this chip, just a few centimeters on a side, can measure out precise amounts of DNA-containing solution, amplify DNA, chop it into small pieces, separate the fragments, and detect their size—all necessary steps in sequencing. Also this year, researchers at a California biotech firm developed a biochip that can screen a blood sample for cancer cells, bacteria, or other cell types and remove their DNA for analysis. Such tools could bring tests now done in the lab into the clinic.

Then there are the DNA chips themselves, in which researchers use arrays of immobilized DNA snippets to search out small genetic variations in genes or to detect RNA messages from the genes turned on in cells. Such chips could one day screen for genetic disease. Their foundations may be in electronics, but microchips have a bright biomedical future.



Chips ahoy. Gene expression levels color a computer simulation of a DNA chip.

New combinations pay off. Researchers pushing the pace of discovery of new compounds put the pedal to the metal again this year. Powering the surge were advances in the high-speed discovery engine known as combinatorial chemistry, which allows researchers to assemble a handful of chemical building blocks into all possible combinations thousands of times faster than before.

Virtually all pharmaceutical companies now rely on combi chemistry to churn out a steady stream of hot prospects. In the field's meteoric climb, 1998 stood out as marked by especially rapid growth and explorations into new arenas. Two new journals were born, and a number of drug candidates, including one to treat inflammation, are now in clinical trials.

And this year, the research took off in new and unexpected directions. For example, one team used the technique to rapidly synthesize a collection, or library, of over 2.1 million complex organic compounds that resemble natural products such as antibiotics. Rather than laboriously test these molecules as drugs, researchers are scanning the library to develop a retinue of small compounds that can activate and deactivate target proteins at will. Such compounds may be new drugs and also may help biologists sort out the roles of the 100,000 or so cellular proteins.

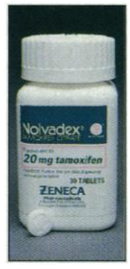
Combinatorial chemists scored victories with other types of compounds, too. For example, U.S. researchers used a variation of the technology to find novel catalysts for fuel cells that convert methanol to electricity. Meanwhile, a Norwegian team created a

CREDITS: (TOP TO BOTTOM) TERRY E. SMITH; INCYTE PHARMACEUTICALS

library of hundreds of zeolites, solid materials shot through with tiny pores that are widely used in the chemical industry as molecular sieves. When the goal is to create new compounds, chemists seem to have hit on a winning combination.

Putting cancer on the defensive. The war on cancer is not a single fight but many far-flung skirmishes, and no superweapon has yet emerged to rout the enemy from all its hideouts. Nevertheless, 1998 saw a host of exciting developments in cancer prevention and treatment, suggesting that this feared enemy is at last losing ground.

The best way to beat cancer is to keep it from taking hold in the first place, and several types of prevention made a splash this year. Researchers can proudly point to a new use for the drug tamoxifen: This estrogen-like molecule was already in use as a breast cancer treatment and this year won rapid approval for prevention in high-risk women. Lower tech lifestyle advice seems to be having an effect too: The American Cancer Society announced in March that U.S. cancer incidence and death rates have been dropping since the early 1990s, due in large part to a drop in smoking.



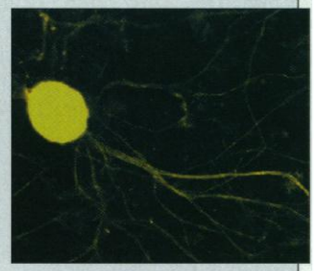
Meanwhile, several promising therapies have emerged. In May, U.S. researchers announced that the antibody Herceptin significantly slows the growth of metastatic breast cancer. And a German team found that the antibody Panorex reduces colon cancer death rates.

False rumors of victory arise in any war, and 1998's award for most overhyped cancer cure goes to angiostatin and endostatin, proteins whose seemingly magical ability to shrink tumors—in mice—was lauded in *The New York Times* before the treatments were even tested in people. Still, therapies that adopt a similar approach—stopping the growth of a tumor's network of blood vessels—are showing some success in clinical trials, as are treatments such as cancer-killing viruses. The war against cancer goes on, but physicians now have a few new weapons to fight with.

Immortal Cells Spawn Ethical Concerns

Developmental biologists grabbed headlines this year by growing a kind of human embryonic cell that can be coaxed to become many different types of human tissue. The work, which starts with cells from human embryos, may lead to safer tissue transplants, but it also fired up a debate about the ethics of using embryos in research. Coming on the heels of Dolly, the cloned sheep and 1997's Breakthrough of the Year, the research offers another dramatic example of how rapid scientific progress is ushering in a new era of control over human reproduction and development—and sparking a host of new ethical questions for a largely unprepared public.

Indeed, although biologists are eager to follow up on the results, legal questions put the work outside the reach of U.S. taxpayer–financed labs. It may take months to resolve the ethical and legal issues, according to members of Congress and National Institutes of Health officials who met at a Senate inquiry in December.



New neurons. These neurons were derived from human embryonic stem cells.

The big news came in November, when two U.S. academic groups reported that they had isolated "embryonic stem cells" from human embryos and fetuses. As these cells divide, they give rise to more specialized cells that can become almost any kind of tissue in the body, including bone, gut, or blood cells.

If the cells live up to their promise, they could lead the way to custom transplant tissues that won't trigger a patient's often-lethal immune response. Already these techniques have produced replacement cells that were successfully grafted onto a damaged mouse heart, and analogous experiments may be tried before long on a human heart. Eventually, lab-grown neurons may be transplanted into the brains of people with Parkinson's disease. For now, the cells will be used mainly to study human development and gene expression and test cellular reactions to candidate drugs.

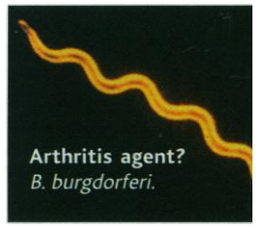
But before any of that happens, more researchers will need to leap into this field—and as of now, taxpayer-financed labs in the United States are hesitant to do so because of hostile federal rules. Cell lines derived from embryos cannot now be used in federally funded research, although the use of tissue from medically aborted fetuses may be permitted. And laws vary widely around the world. In Britain publicly funded researchers can use early embryos, but both private and public labs must obtain a license first; France, Germany, Norway, Denmark, and Austria are even more restrictive.

To avoid tangling with federal regulators, both stem cell developers this year relied entirely on private support from the Geron Corp. of Menlo Park, California. The universities whose faculties did the research hold patents on the technology, which is to be commercially developed by Geron. Thus these cells, which—in theory—have the potential to develop into a human embryo, are treated as commercial products, a notion that sparked concern in a U.S. Senate hearing in December. Committee members said they plan to investigate this aspect further next year, and President Clinton has asked his National Bioethics Advisory Commission to investigate; their complete review is due in mid-1998. Research on these embryonic cells may be dampened by government strictures, but debate is sure to flourish.

Tracking molecular mimics. The acute phase of many infectious diseases is bad enough, but some have long-term effects that are positively chilling. Lyme disease, for example, starts with short-lived flulike symptoms but can end up causing chronic arthritis—even after antibiotics have wiped out the bugs. What causes such delayed damage?

One theory has been that the infection somehow sensitizes the immune system to the body's own molecules. That fits with suspicions that unidentified infections might explain the puzzling onset of some autoimmune diseases, but the idea has been hard to prove. This year two teams convincingly linked infections and autoimmune disorders, paving the way to better understanding and treatment of diseases such as diabetes and multiple sclerosis.

In the first case, researchers created a mouse model of herpes simplex virus 1, which can lead to destruction of corneal tissue and blindness. The team infected the mice's eyes and found that immune cells called T cells reacted against the animals' own tissue and destroyed their corneas. Future work may pinpoint the viral component that triggers the autoimmune response—and lead to treatments to block it.



Arthritis agent? *B. burgdorferi.*

Another team tackled *Borrelia burgdorferi*, the bacterium that causes Lyme disease and, in 10% of cases, chronic arthritis. The researchers found that nine of 11 Lyme arthritis patients have T cells that react to both a bacterial protein and a closely related human one—strong evidence that the T cells trigger the arthritis. Now that this year's discoveries have set the stage, expect a flood of work to track new links between autoimmunity and infection. **–THE NEWS AND EDITORIAL STAFFS**

For an expanded version with references and links, see *Science* Online at www.sciencemag.org/content/vol282/issue5397/#special

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