



RESEARCH
HIGHLIGHTS

EMBRYOLOGY

Deciphering the Complexity of Cellular, Developmental, and Genetic Biology



Cracking the Code in Cell Communication

From the first spark of conception, cells talk to each other to ensure that tissue development stays on course and diseases such as cancer are kept at bay. Scientists in the Chen-Ming Fan lab at the Department of Embryology recently found an entirely new way this communication works. Their discovery could boost the understanding of how stem cells renew themselves and how cancer forms. It has also received enormous attention from the biological community because it calls into question how many cell communication pathways there are and how distinctive they may be.

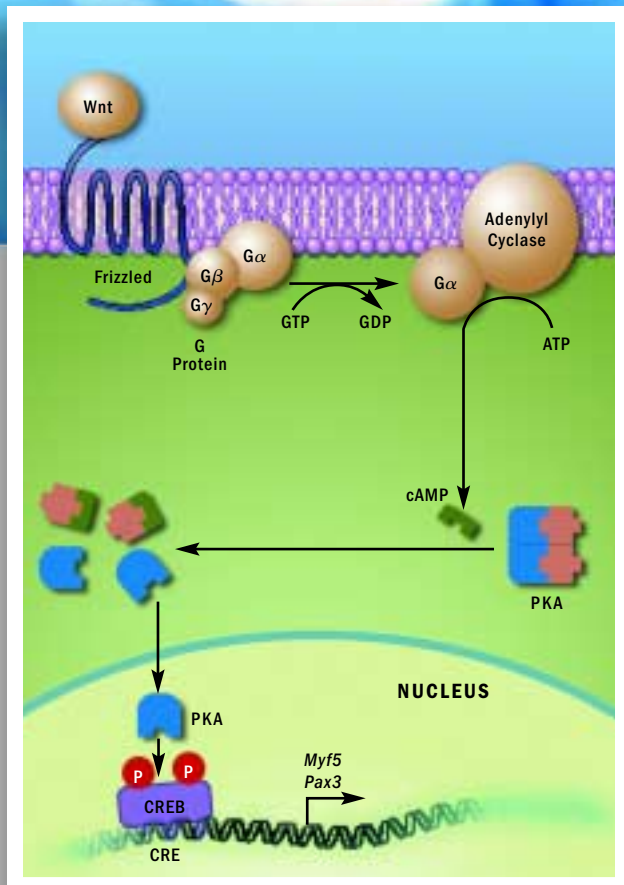
Tissue development involves communication among cells by way of complex molecular relays. A molecule sent from one cell interacts with a surface receptor on a second cell. That receptor relays information to a molecule inside the target cell, which passes the information on to yet another molecule (and so on) until the information gets to the nucleus, where a gene is turned on that will tell the cell what tissue to become—bone, muscle, brain, etc. Remarkably, researchers have identified only seven or eight “signaling pathways” that control tissue development in *all* bilateral animals. And until recently, the pathways were thought to be distinct.

Predoctoral associate Alice Chen, with staff member Chen-Ming Fan and colleagues, discovered an entirely new signaling pathway that appears to be a merger of parts of two other pathways that were believed to be completely independent.

Using skeletal muscles along the backs of embryonic mice, the researchers studied a family of proteins in a pathway called Wnt. The Wnt pathway is important to early embryonic development, stem cell renewal, and tumor growth. The Wnt protein is a ligand—a molecule that binds to a receptor at the surface of a target cell and initiates the relays inside that cell. The team explored the molecules inside the target cell that are involved in turning on the muscle-making genes.

The scientists performed a variety of tests, including a novel technique of infecting mouse embryos with defective forms of two molecules to see how development was affected and to verify which molecules were at work. The researchers found a well-known gene transcription factor—a protein in the nucleus, which begins the process of turning genes on—called CREB near the end of the Wnt pathway. They were surprised because CREB is typically classified in an entirely different signaling chain. They were then able to identify other molecules in the progression, which also turned out to be typically associated with CREB. One of those is a catalyst outside the nucleus called adenylyl cyclase. Another is the molecule PKA, which enters the nucleus and prompts CREB into action.

The discovery that Wnt initiated a cascade that ended with CREB was a surprise to the researchers and the bio-



A chain reaction of molecules turns genes on inside the nucleus of a cell. Members of the Fan lab discovered a previously unknown signaling pathway that begins at the surface of the cell with the Wnt protein. It binds to a receptor and initiates a molecular relay inside the cell. The researchers were surprised to find that CREB, which is a transcription factor that begins to activate a gene, was part of the chain reaction initiated by Wnt.

IMAGE COURTESY NATURE PUBLISHING GROUP.

logical community. The Fan lab will be further examining how this newly discovered pathway affects stem cells in muscle-cell regeneration in the adult.

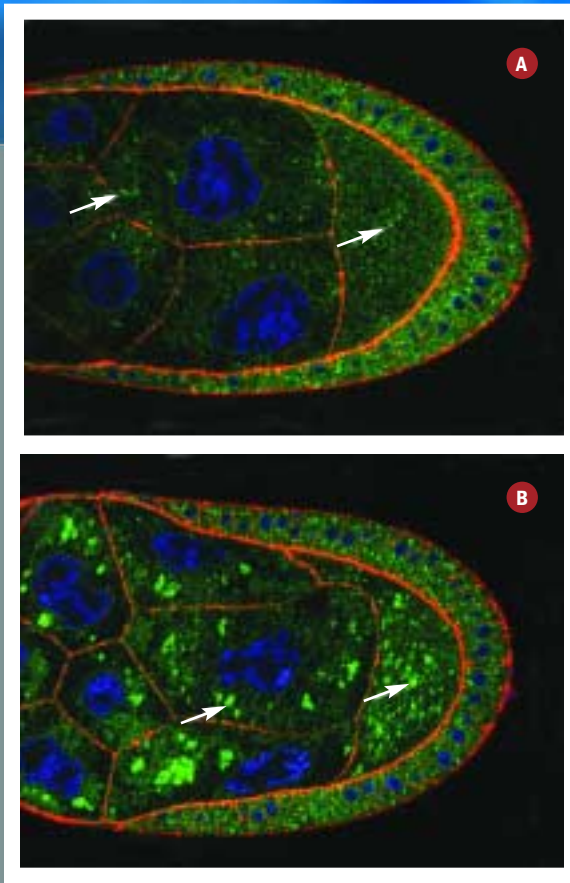
A Genetic Traffic Cop Directs Protein and RNA

Every cell has a traffic system that would astound the most accomplished city planner. RNA and proteins crowd the streets of these microscopic metropolises, rushing to work at particular locations within the cell. Much like human travelers, these biochemical commuters need signals to help them navigate efficiently. James Wilhelm of Carnegie's Department of Embryology has discovered a gene that helps direct traffic in the eggs of the fruit fly, *Drosophila melanogaster*. More importantly, this gene may provide the first known connection between two very different cellular traffic patterns.

Wilhelm and his collaborators found that the gene, which they named *trailer hitch (tral)*, is required to move some key developmental proteins. Their results also suggest that *tral* helps move messenger RNAs—molecules that carry genetic messages from DNA to the cell's protein factories. Until now, scientists believed that these two processes were completely independent.

The movement of proteins to the cell surface depends largely on two protein-processing structures, the endoplasmic reticulum (ER) and the Golgi apparatus, which combine to make a convoluted network of membranes

Embryology, continued



Inside the cell, proteins shuttle through a convoluted network of membranes and channels, including the endoplasmic reticulum (ER) and the Golgi apparatus. But in *tral* mutants, the sites where traffic leaves the ER for the Golgi become muddled by large lumps of mismanaged proteins. These ER exit sites, stained green and marked by arrows, are abnormally large in mutant egg chambers (B) compared with the wild, or normal, chambers (A).

and channels. Proteins shuttle between these two structures and through the entire cell in small membrane sacs. But in fruit fly eggs with a mutant *tral* gene, this process doesn't quite work as it should: the ER exit sites—where traffic leaves for the Golgi—become muddled by large lumps of mismanaged proteins.

One of the proteins trapped in these lumps, called Gurken, normally helps distinguish the top side from the bottom as the egg develops into an embryo. With the Gurken proteins tied up in these lumps a proper top-to-bottom pattern is never established, and the embryo dies early.

Wilhelm's results also suggest *tral* mutants have trouble moving at least one other key developmental protein, a growth factor called "yolkless," from the ER exit sites. Yolkless proteins are normally spread evenly throughout the cell, where they help bring yolk nutrients into the egg. But in *tral* mutants, yolkless proteins collect in lumps much like the Gurken lumps.

Wilhelm's team sequenced *tral* and found that it bears a striking resemblance to genes that code for RNA-processing proteins. The surprised researchers explored the possibility of a functional link between *tral* and RNA, and found that *tral*'s protein forms part of an RNA/protein complex that helps process and shuttle messenger RNAs throughout the cell.

By examining *tral* in fruit fly egg cells, Wilhelm and his collaborators have established the first link between protein shuttling and messenger RNA processing. Once believed to be separate phenomena, it now looks like these two freeways share at least one interchange. ●

GEOPHYSICAL LABORATORY

Probing Planet Interiors, Origins, and Extreme States of Matter

Star Trek Technology Comes Alive

The *Star Trek* crew in the popular TV show of yesteryear used a lightweight device called a tricorder to detect the presence of life on other worlds, as well as pathogens and contaminants that could harm the humans or their craft. Now Jake Maule, Andrew Steele, and the MASSE team at the Geophysical Laboratory (GL) have successfully field-tested a precursor to the tricorder that they, along with Charles River Laboratories and the LOCAD group at Marshall Space Flight Center, have been developing over the past few years. The device, frequently referred to as a lab-on-a-chip, will be permanently installed on the International Space Station beginning in 2006 to identify microbes hazardous to astronaut health. A future adaptation of the instrument is slated to fly the European Space Agency's ExoMars mission to the Red Planet in 2013 to search for evidence of life.

In addition to its handy size, the lab-on-a-chip cuts sample analysis time from about two to three days in a typical lab to some 10 minutes. Samples are also assessed in the field immediately upon collection. A researcher prepares a sample in an aqueous solution and introduces it into a small plastic cartridge, which slides into a slot of the tiny lab. The lab unit incubates the sample in the cartridge with a chemical preparation that turns yellow in the presence of microorganisms. The intensity of the yellow color is proportional to the number of microbes in the sample.

A fully suited astronaut uses the handheld detection device during a training session at Meteor Crater in Arizona. On the International Space Station the unit will be able to detect microbes that may be hazardous to crew health. In the future, an advanced version of the instrument will be able to screen thousands of molecules to monitor astronaut health and the environment, and to detect evidence of life.

IMAGE COURTESY JAKE MAULE.



Geophysical Laboratory, continued

Jake Maule, project scientist for the handheld lab-on-a-chip, tests the device on a NASA KC-135 aircraft during a parabolic microgravity flight over the Gulf of Mexico. Beginning in 2006, the minilab will remain on the International Space Station permanently to help the crew identify microorganisms that may be hazardous to their health or cause corrosion of panels, wires, and other components.

IMAGE COURTESY JAKE MAULE.



Currently in development is a unit that will determine the chemical signature of a sample and compare it with 100s to 1000s of chemical signatures of known molecules or pathogens that are stored in the unit's memory. A description of the sample then pops up on the LCD display. The team has been developing the library and testing the implement's accuracy over several years. This summer the minilab was subjected to the rigors of extreme environments to mimic future space missions.

Jake Maule joined a NASA Desert Research and Technology Studies (RATS) team at Meteor Crater in Arizona to see how the device performed in heat and dust, and to train fully suited astronauts in the use of the system. He, Charles River's Norm Wainwright, and GL staff member Marilyn Fogel also took the minilab aloft in a NASA KC-135 aircraft to see how it worked under conditions of microgravity (0g), lunar gravity (0.16g), and Martian gravity (0.38g). The minilab passed the

tests with flying colors. Meanwhile Steele, with team members, tested the small lab in the frozen environment of Svalbard, Norway—an area with a geology that is analogous to Martian geology. They successfully detected living organisms—the kind of evidence that will be sought on Mars. They were also able to maintain sterile sampling procedures and avoid contamination—a real challenge in the field.

Meteorites—Historians of the Solar System

Scientists are one step closer to understanding how our solar system formed by studying the most primitive objects around—carbonaceous chondrite meteorites. They are emissaries from a long-gone era in the earliest

solar system and contain clues, in the form of their carbon, which can reveal the temperatures, pressures, and other chemical processing that occurred as the interstellar medium coalesced into the solar system billions of years ago. A challenge to understanding these meteorites, however, has been the establishment of the chemical signatures of specific reactions that altered the parent body, such as an asteroid, and meteorite over time. The Geophysical Laboratory's George Cody and colleague Conel Alexander of the Department of Terrestrial Magnetism are the first to decipher and compare the chemical constituents of four meteorites from distinct groups and relate these chemical differences to their processing histories. The evidence suggests that their organic matter shares a specific reaction pathway—important information for piecing together what happened in the dark reaches of time.

More than 70% of the organic matter in carbonaceous

chondrites is insoluble. Insoluble organic matter (IOM) is difficult to break down and analyze by standard molecular methods. But Cody and Alexander have overcome this hurdle using solid-state nuclear magnetic resonance (NMR) spectroscopy, which reveals molecular information when certain atomic nuclei, aligned by an enormous magnetic field and irradiated with radio-frequency pulses, resonate with characteristic frequencies. The researchers undertook a painstaking analysis of samples from four meteorites—EET92042 (CR group), Orgueil (CI group), Murchison (CM group), and Tagish Lake (a unique group). With a custom-designed procedure developed by Terrestrial Magnetism's Fouad Tera, they extracted the IOM and used a protocol including eight different ^1H and ^{13}C NMR measurements to verify the hydrogen and carbon molecular environments.

The scientists found remarkable variation in the chemical composition of IOM across the meteorite



The carbonaceous chondrite meteorite Allende (near left) exhibits the dark fusion crust formed during atmospheric heating. The mottled white and light gray interior is pristine meteorite, with various mineral phases and very little extraterrestrial organic carbon. The vial contains about 400 milligrams of extracted, pure insoluble organic matter from a carbonaceous chondrite. It records history from before the formation of the solar system.

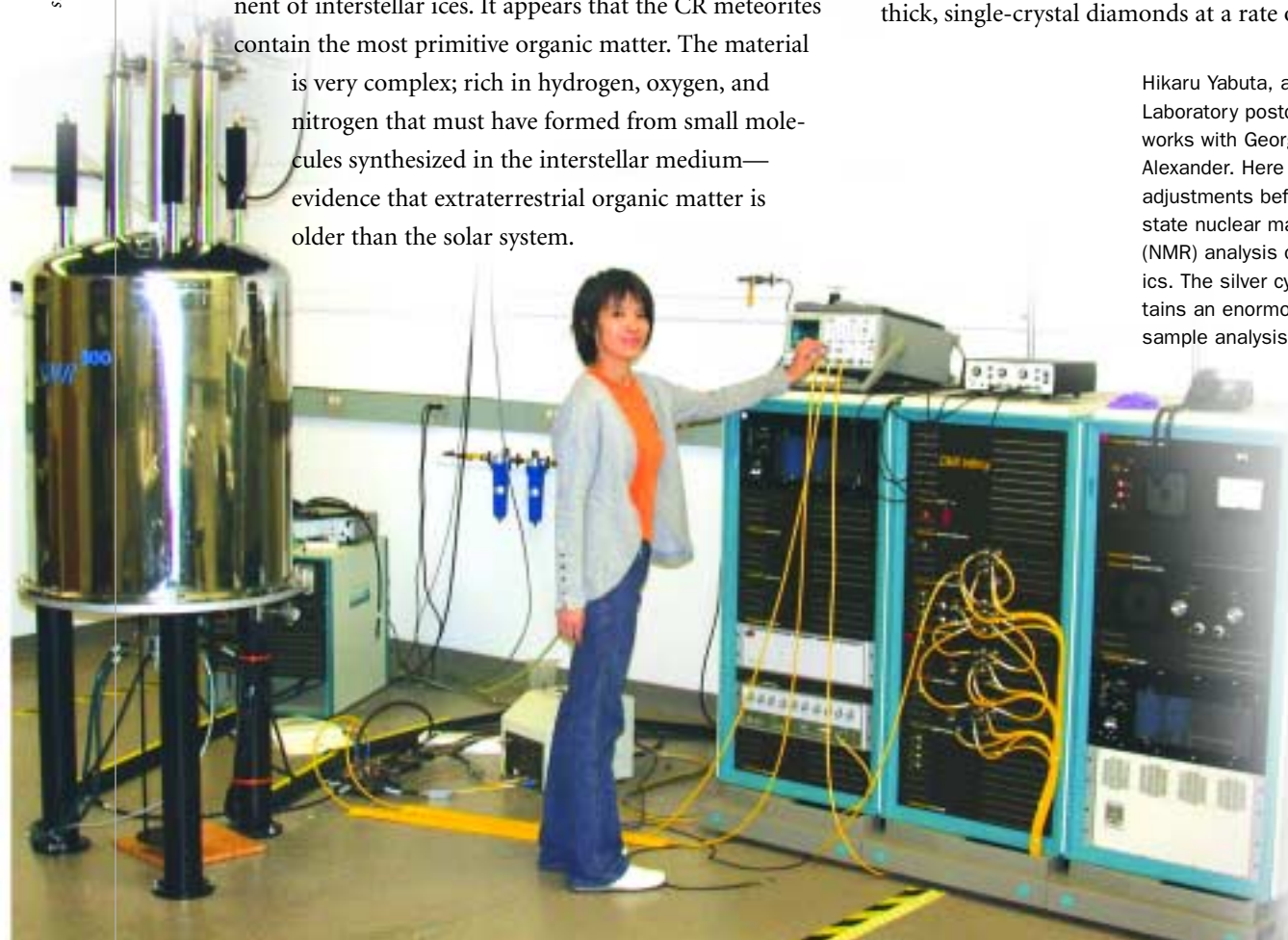
Geophysical Laboratory, continued

groups. The proportion of aromatic carbon increased significantly from the CR to Tagish Lake, and there was a parallel increase in the abundances of tiny nanodiamonds, vestiges of ancient stars. With multiple NMR experiments, the researchers showed that the increase in aromatic carbon was due to a loss of other forms of carbon—crucial evidence for a low-temperature, chemical-oxidation reaction in the meteorite parent body. They suspect the oxidant is hydrogen peroxide, a likely component of interstellar ices. It appears that the CR meteorites contain the most primitive organic matter. The material is very complex; rich in hydrogen, oxygen, and nitrogen that must have formed from small molecules synthesized in the interstellar medium—evidence that extraterrestrial organic matter is older than the solar system.

Nurture Beats Nature in Diamond Making

A team at the Geophysical Laboratory (GL) is surpassing Mother Nature by breaking speed, size, and strength records to lead the world in diamond making. The team, led by research scientist Chih-Shiue Yan and staff member Russell Hemley, has produced 10-carat, half-inch-thick, single-crystal diamonds at a rate of 100 microme-

Hikaru Yabuta, a new Geophysical Laboratory postdoctoral fellow, works with George Cody and Conel Alexander. Here she is making adjustments before starting solid-state nuclear magnetic resonance (NMR) analysis of meteoritic organics. The silver cylinder at left contains an enormous magnet for sample analysis.

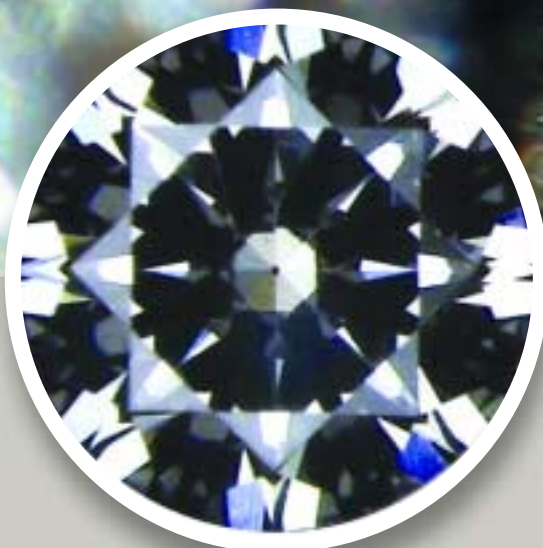


ters per hour using its patented chemical vapor deposition (CVD) process. It has also made colorless, single-crystal diamonds that are transparent from the ultraviolet to infrared wavelengths, and it has fabricated new shapes from blocks of the CVD single crystals.

The 10-carat diamond is about five times the size of commercially available diamonds produced by the conventional methods, typically the high-pressure/high-temperature (HPHT) technique. Although the ultimate goal is to produce extremely large diamonds for instrumentation to maintain GL's leadership in high-pressure research, the new breakthroughs have broad applications that could include a new generation of semiconductors.

The team's CVD process begins with a seed diamond placed in a specially designed chamber. The seed is subjected to a gas mixture consisting mainly of methane and hydrogen and then bombarded with intense microwaves to make charged particles, or plasma. A carbon "rain" falls on the seed, and the carbon atoms arrange themselves in the proper crystalline structure, resulting in the growth of the diamond. The scientists can also subject the diamonds to high temperatures and pressures, hardening the crystals and further improving the clarity.

Large, transparent, and high-purity diamonds are especially valuable. These characteristics are particularly challenging and costly to produce with traditional methods. The Carnegie team has overcome these obstacles with the aim of revolutionizing diamond making. The highest growth rate reached thus far is in excess of 300 micrometers per hour. The goal is to grow diamonds as large as 100 carats.



This colorless diamond (top) was cut from a 1-carat block created by the Geophysical Laboratory's diamond-making team using its unique chemical vapor deposition (CVD) process.

This $\frac{1}{2}$ -inch, 5-carat diamond (bottom) came from a 10-carat block produced by the Carnegie CVD process. It is laser cut, inscribed, and partly polished.

IMAGES COURTESY CHIH-SHIUE YAN AND RUSSELL HEMLEY.

GLOBAL ECOLOGY

Exploring Ecosystems from the Smallest to the Largest Scale



California Climate: Major Impacts on the Horizon

Greenhouse-gas emissions will have major impacts on California's future, states a study in which Christopher Field participated. Field, Department of Global Ecology director, was part of a group of leading scientists from major institutions that investigated greenhouse-gas emissions in California, climate change, and the consequences on the agriculture and economy of the Golden State.

Using results from two of the latest-generation climate models, the team was the first to look at a broad range of impacts for a particular region and assess the sensitivity of the impacts to the future pattern of greenhouse-gas emissions at the global scale. The study showed that more frequent heat waves and dramatically reduced Sierra snowpack are in California's future without aggressive near-term action to minimize greenhouse-gas emissions.

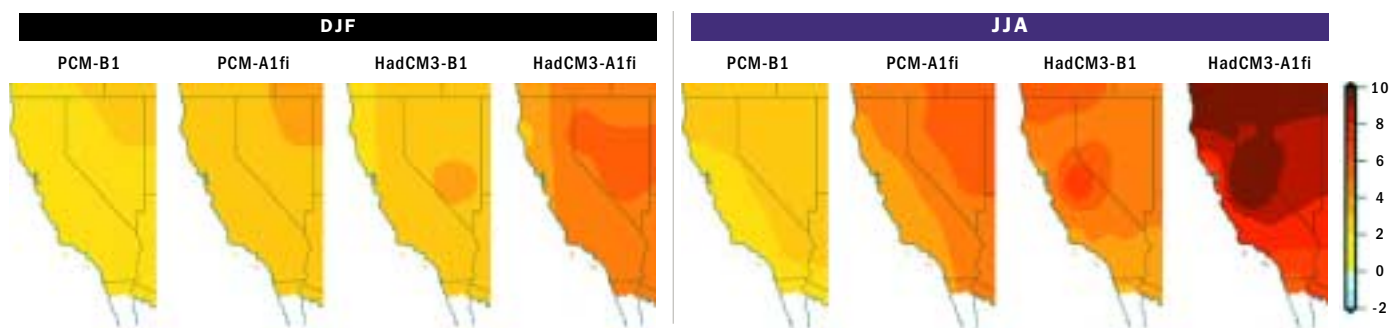
The amount of climate change in the state and the severity of its impacts strongly depend on the level of emissions of heat-trapping gases, such as carbon dioxide. Stanford/Carnegie Ph.D. students Elsa Cleland, Claire Lunch, and Kim Nicholas Cahill participated in the study, which compared an expected future climate with humans heavily using traditional fossil energy (the

source of most of these heat-trapping gases) with a future climate in which people primarily use energy sources that do not emit heat-trapping gases. The results showed that both scenarios result in significant climate changes over the coming decades; but the amount of climate change could be cut by half, or more, if emissions were dramatically reduced.

All of the model simulations showed increased temperatures by midcentury. Even with lower emissions, heat waves, extreme heat, and heat-related human mortality in Los Angeles could double to quadruple by century's end. The warming could be great enough for widespread impacts on agriculture.

Forest Destruction in Brazil Is Twice That of Previous Estimates

Until now it has been almost impossible to detect how much area is logged selectively under the forest canopy in Brazil or elsewhere. Global Ecology staff member Greg Asner led a new large-scale, high-resolution satellite study, which showed that when selective logging is taken into account, forest degradation in the Brazilian Amazon has been underestimated by half. The first-of-its-kind study also showed that there are far-reaching ecological impacts for the region and beyond.



The scientists used two different models—the low-sensitivity Department of Energy Parallel Climate Model (PCM) and the medium-sensitivity U.K. Met Office Hadley Centre Climate Model 3 (HadCM3)—to project future temperatures in California under lower (B1) and higher (A1fi) greenhouse-gas emission scenarios. The left series of images shows what the two models predict for winter temperatures with lower and higher emissions for the years 2070 to 2099. Depending on the model, summer temperatures at the end of the century (right) with higher emissions could rise by 8°F or 15°F, with increased warming in the north and northeastern parts of the state. As predicted by the two models, reducing emissions could result in temperatures increased by 4°F or 7°F.

IMAGE REPRINTED WITH PERMISSION FROM *PNAS* 110 (NO. 34), 12422-12427.

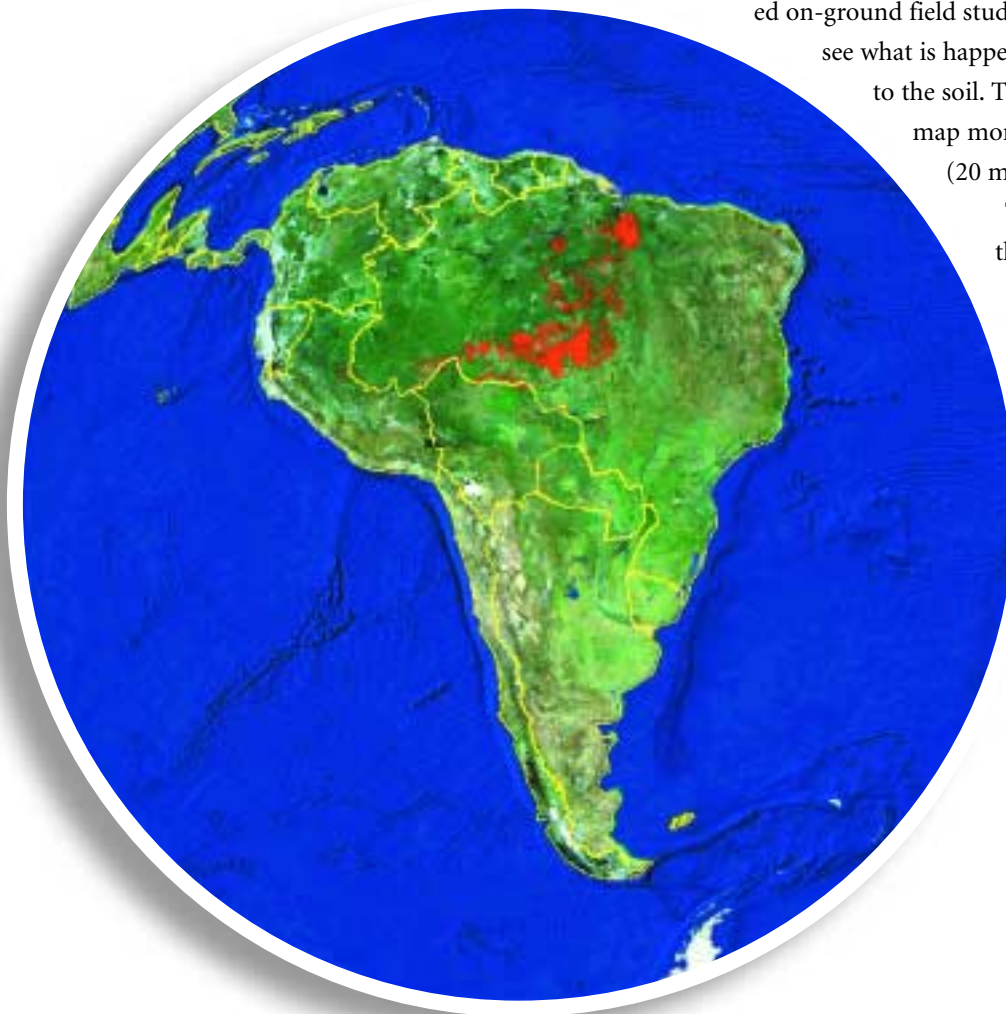
Selective logging is a technique whereby loggers extract specific types of commercially valuable trees one by one from the fragile rain forest, while the forest canopy covers their tracks. Although it is relatively straightforward to use satellite data to estimate large-scale deforestation from clear-cutting, Asner's group is the first to detect both the extent of selective logging in the Amazon and its impacts on the structure of the forest.

New remote sensing techniques, developed in Asner's lab, are used for projects ranging from quantifying forest disturbance to identifying the chemical composition of forest canopies and undergrowth. Over five years of field-based studies, the scientists discovered that, annually, selective logging disturbs an area about the size of Connecticut (between 4,685 and 7,973 square miles) over the five states that account for 90% of all deforestation in the Brazilian Amazon. The destruction adversely impacts many plants and animals and increases erosion and fires. Additionally, up to 25% more carbon dioxide is released to the atmosphere each year, above that which would be

Global Ecology, continued

The red areas (hot spots) show where the Asner-led team found selective logging in Brazil.

IMAGE COURTESY THE CARNEGIE INSTITUTION AND GOOGLE EARTH.



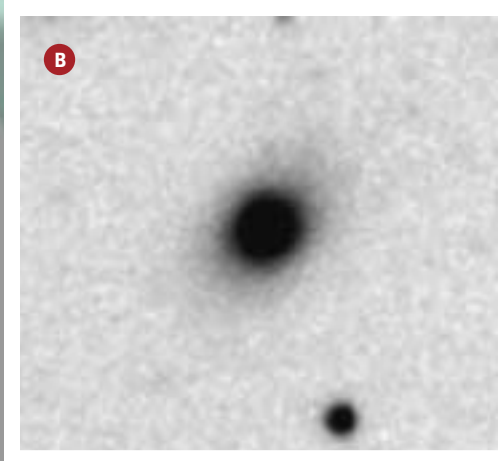
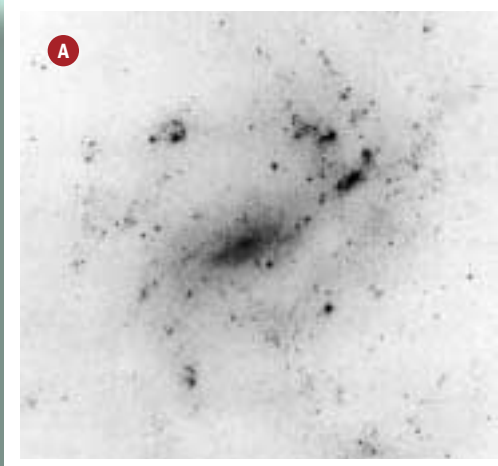
released by clear-cutting alone.

Along with technicians David Knapp, Paulo Oliveira, and Eben Broadbent, Asner developed the Carnegie Landsat Analysis System (CLAS) to penetrate the canopy by analyzing satellite imagery with advanced computational methods and corroborating the results with selected on-ground field studies. The researchers can now see what is happening from the top of the forest to the soil. The group is now using CLAS to map more than 7.7 million square miles (20 million km²) of forest.

The researchers are hopeful that their new techniques can be expanded to monitor logging in other tropical forest countries. One goal is to provide the satellite results to government officials in Brazil to help in enforcement of the laws that prohibit illegal logging. ●

OBSERVATORIES

Investigating the Birth, Structure, and Fate of the Universe



The Ho-led team found “miniquasars” in unlikely places: NGC 4395, a very late-type spiral galaxy with no bulge (A), and POX 52, a dwarf elliptical galaxy (B). Both of these objects, along with many others like them, were found to contain black holes in the previously unknown mass range of 10^4 to 10^6 Suns.

“Tiny” Black Holes Discovered in “Tiny” Galaxies

Once thought a rarity, black holes—those extremely dense objects with a gravitational force so strong that not even light can escape—turn out to be quite common. In fact, supermassive black holes exist at the center of most large galaxies. Observatories astronomer Luis Ho, with Harvard graduate student Jenny Greene and University of California, Irvine, associate Aaron Barth, has discovered an entirely new population of these powerhouses—“tiny” black holes that reside in “tiny” galaxies. This discovery may help decipher the origin of their heavier counterparts. Ho thinks that small black holes were more common in the past and could be the “seeds” of their supermassive cousins.

Supermassive black holes have masses that range from millions to billions of Suns. Astronomers believe that somehow their formation and growth are integral to galaxy life cycles, particularly the central concentration of stars known as the bulge. Our Milky Way, a common spiral with a modest bulge, harbors a 3-million-solar-mass black hole. Hefty ellipticals and early-type spiral galaxies also have bulges, but late-type spirals and tiny dwarf galaxies do not. Every bulge has a black hole, and the mass of the black hole is proportional to the size of the bulge.

Observatories, continued

Ho asked: Do black holes *require* a bulge? Do galaxies without bulges—the smaller systems that make up the bulk of the galactic population—truly lack black holes? If black holes do reside in small, bulgeless galaxies, the galaxies would probably have masses from a thousand to a million Suns. These black holes are likely to be quite rare today, and current technology cannot detect their dynamical signature except among a handful of our nearest neighbors. People have looked, but to no avail.

The Ho-led team overcame this obstacle. They reasoned that small galaxies, with small black holes, should glow as miniquasars, signposts of the tremendous energy released as material falls into these gravitational pits. They combed through mountains of data from nearby galaxies and were the first to find the elusive signal indicating that small black holes reside in this bulgeless galaxy population.

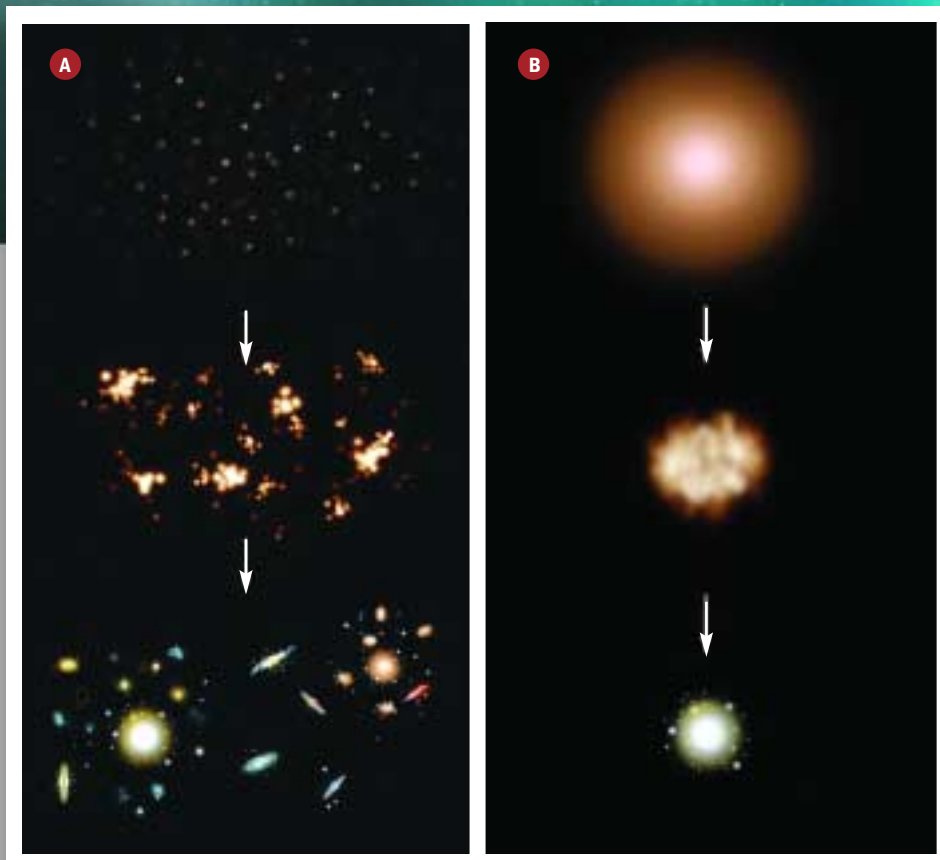
Ho believes that small black holes could be seeds of supermassive black holes that could have coalesced through the hierarchical merging of galaxies over time. In the process, they would release tiny ripples of space-time—gravity waves—that physicists hope to detect in the coming decades.

Galaxy Formation: Top Down or Bottom Up?

Get out of town on a clear night and you can see into the heart of the Milky Way; millions of distant stars blend into a luminous band, while the closer stars form familiar constellations that march across the sky. The origin of large galaxies like the Milky Way is one of the great unsolved mysteries of astrophysics. One outstanding question is whether galaxies form “bottom up” from the gradual assembly of smaller building blocks, or “top down” from the collapse of large gas clouds that fragment into smaller star-forming clusters. Carnegie Observatories staff member Patrick McCarthy and his colleagues are bringing this conundrum into clearer focus.

The bottom-up model has prevailed over the past decade because it offers a good explanation for the distribution of galaxies. This scheme suggests that the most massive objects should be the youngest, because their assembly would have taken the most time. But astronomers have found that the most massive galaxies consist almost exclusively of old stars. It could be that the individual building blocks are old, while the galaxies themselves are young. To sort out the issue, scientists need to peer back in time to when massive galaxies were first formed.

While simple in concept, this effort has proven challenging in practice—the galaxies in question are faint, and most of their radiation has shifted to lower-energy, non-



In the “bottom-up” scenario (A), galaxies form via the clustering of smaller building blocks. The smallest galaxies form first, and large galaxies build up slowly as smaller galaxies merge together.

In the “top-down” model (B), galaxies form from the rapid collapse of a single cloud of gas. As the cloud collapses it breaks into fragments, forming star clusters and smaller groups of a few stars.

visible infrared light. McCarthy’s team surmounted this challenge with an ambitious infrared study using the du Pont telescope at Carnegie’s Las Campanas Observatory. Their results were surprising—the young universe contained 50 to 100 times as many massive galaxies as the bottom-up model would predict. If these massive galaxies existed when the universe was relatively young, then they probably did not form from the gradual assembly of smaller building blocks.

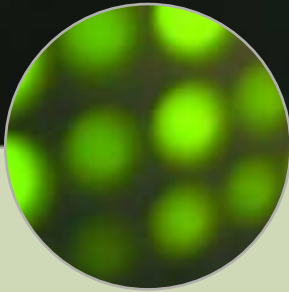
Directly measuring the age of galaxies can help settle the matter. But determining a galaxy’s age, specifically that of its stars, is not easy. Conventional wisdom says that a galaxy’s hottest, most massive stars will die first, leaving cooler, less massive stars as the galaxy matures. It should therefore be possible to estimate a galaxy’s age by measur-

ing the temperatures of its hottest stars. McCarthy and his team found many distant, massive galaxies composed of stars hotter than the Sun. These galaxies are also old, having formed only 1.5 to 3.5 billion years after the birth of the universe.

The formation of smaller galaxies is still best explained by the bottom-up model, but McCarthy’s work provides strong evidence that the most massive stellar systems formed early, and from the top down. ●

PLANT BIOLOGY

Characterizing the Genes of Plant Growth and Development



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Research Highlights

A Glimpse at Cellular Construction Crews

Much like buildings, plant cells have rigid walls to define their shape. These walls take many forms, from spiky, thornlike trichomes that fend off hungry bugs, to sausage-shaped guard cells that regulate the plant's breathing pores. David Ehrhardt and colleagues at Carnegie's Department of Plant Biology and Stanford University use groundbreaking imaging techniques to

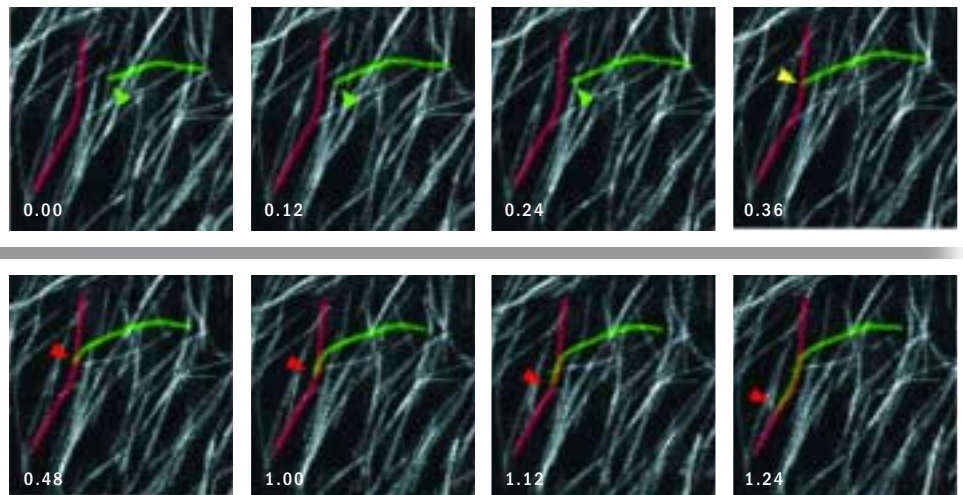
observe the proteins that create this array of shapes. They are the first to watch these molecular construction crews at work during cell growth. This important basic research has already revealed plants to be as dynamic and complex as their animal counterparts.

These proteins help plant cells work around a unique problem: unlike animal cells, plant cells have rigid walls and cannot easily change shape. Once they are in place, plant cells can only grow outward. To get it right the first time, plant cells rely on scaffolding made of microtubules—stiff rods made from a protein called tubulin. Microtubules constantly move and change shape as the cell wall pushes outward, but until now scientists knew very little about how the cell controls this process.

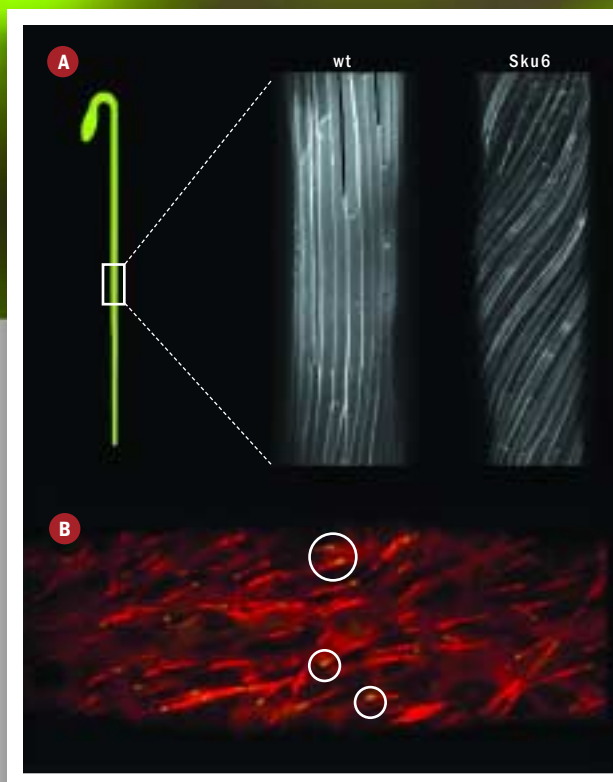
To get a closer look, Ehrhardt and collaborators fused

A growing microtubule (green) “bundles” (A) with a second microtubule (red) as it advances. A drawing of microtubules “treadmilling” and “bundling” is shown in B (opposite). As new tubulin molecules (green) attach to the growing end (top), they are also lost from the trailing end (bottom). The loss of tubulin from the trailing end is especially important because it erases old, less organized microtubule structures, allowing more ordered structures to replace them. Researchers believe a specialized protein (orange dots) helps the microtubules bundle together.

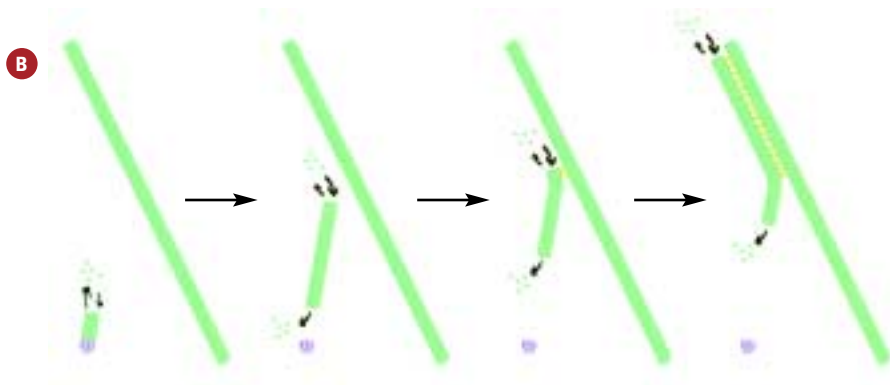
A



Normal *Arabidopsis thaliana* stems (wt) grow vertically (A), but plants with a defective form of the SPR1 protein (Sku6) grow in a spiral pattern. SPR1 proteins marked with a fluorescent dye (circled yellow dots in B) can be seen at the growing ends of microtubules. The red streaks, created by superimposing a time series of false-colored images, trace the paths that the SPR1 molecules followed.



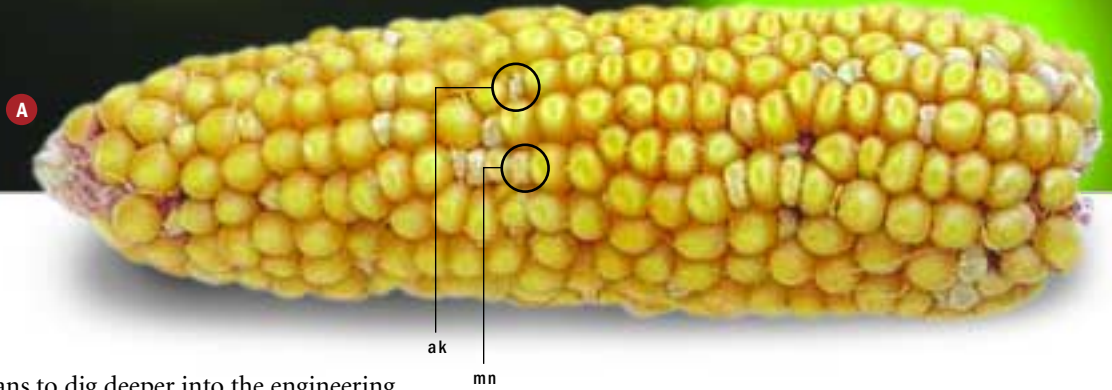
a tubulin gene from the model plant *Arabidopsis thaliana* with a fluorescent protein gene to express fluorescent tubulin protein. Using a specialized confocal microscope, they watched these proteins reorganize themselves in living cells. Ehrhardt found that microtubules move just under the surface of the cell, shortening at one end while lengthening at the other end. They do this one tubulin molecule at a time, in a process the researchers call treadmilling.



Treadmilling microtubules inevitably bump into stationary microtubules as they explore new territory in the cell. Instead of shoving past these obstacles, the growing fibers will often link up with the older ones and follow the same path. Ehrhardt believes this process, called bundling, helps the cell forge a strong, highly organized lattice from a random patchwork of microtubules.

Ehrhardt's lab is searching for the molecules that guide treadmilling and bundling, and they have found a possible candidate: a protein called SPR1 that attaches to the growing end of treadmilling microtubules. Cells with nonfunctional SPR1 proteins grow in an abnormal spiral pattern, as does the entire plant. Although the exact function of the protein remains unknown, the spiraling defect suggests that SPR1 is a major player in either configuring microtubules or control-

Plant Biology, continued



ling their function.

Ehrhardt's lab plans to dig deeper into the engineering of plant cells. For example, they want to find other proteins that help guide treadmilling and bundling, and determine whether and how microtubules guide other construction processes in the cell. Recent work suggests that microtubules might directly guide construction of the cell wall. By snapping real-time imagery of tubulin molecules at work, Ehrhardt and his colleagues are helping to illuminate the structure and organization of plant cells.

In ears of maize with a mutant *ig1* gene (A), many kernels do not grow to full size (mn), or completely abort early in development (ak). The embryo sac in *ig1* mutant maize (C) contains extra cells and malformed structures as compared with the wild-type embryo sac (B).

Navigating a Genetic "Maize"

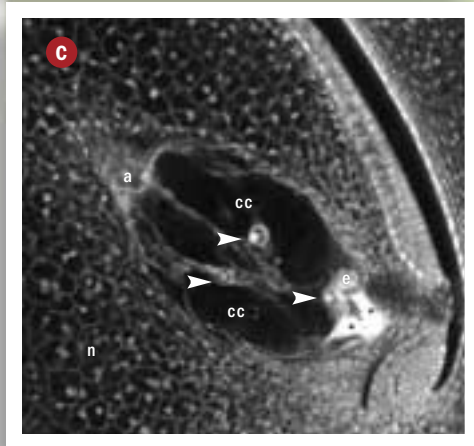
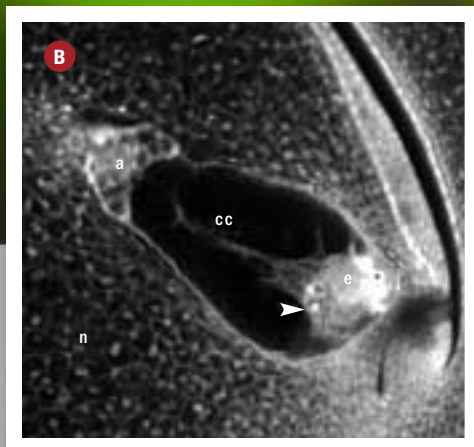
Plants, like animals, depend on specific genes to choreograph the dance of early development. But unlike animals, plants have two distinct generations, one with a single and one with a doubled set of chromosomes. Researchers in Matt Evans's lab at Carnegie's Department of Plant Biology are the first to locate and clone a gene in maize that plays a big role in both generations. The work may allow breeders to produce agriculturally useful varieties of maize, an economically significant crop, more quickly.

The gene is known to affect the embryo sac, the female version of the single-chromosome generation. When the sac combines with a pollen grain—the male version—the two form a seed with a double set of chromosomes. This fertilized seed produces the double-chromosome plant

from which the next generation will arise.

Though Evans's group is not yet sure exactly what purpose the gene, called *ig1*, serves in the developing embryo sac, they do know what happens when the gene malfunctions. Embryo sacs with a mutated form of *ig1* often produce defective seeds riddled with abnormalities, such as a shrunken endosperm (the starchy capsule that feeds the growing embryo) and multiple embryos. The embryo sacs can produce too many cells, some with too many nuclei crammed inside.

Other researchers have documented the effects of *ig1* mutations, but Evans and his colleagues are the first to determine exactly where in the maize genome the *ig1* gene actually resides. To find the locus among tens of thousands of possibilities, the researchers relied on a close cousin of maize: rice. Since maize and rice share much of their genetic order, and the entire genome sequence of rice is known, Evans's group used rice as a genetic roadmap to find *ig1* in maize.



Evans and his colleagues are also the first to determine that *ig1* affects the double-chromosome generation as well as the single-chromosome generation. As it turns out, the gene's sequence is similar to a gene called *AS2* from *Arabidopsis thaliana*, a plant commonly used in genetic studies. *AS2* controls aspects of double-chromosome generation development in *Arabidopsis*, and it appears *ig1* serves a similar purpose in maize.

Evans found evidence to support this idea in one of two distinct *ig1* mutations, called *ig1-mum*. Plants with this mutant have misshapen leaves, much like *Arabidopsis* plants with mutated *AS2* genes. The *ig1-mum* variant also disrupts other vital developmental genes, just as mutant *as2* protein does in *Arabidopsis*. The mutation also causes

an overproliferation of leaf cells, much like the effect it has on the embryo sac.

Because mutations in *ig1* seem to affect both generations, Evans believes there is more regulatory overlap between the phases than was once thought. And by locating the *ig1* gene and identifying its mutations, he and his collaborators have opened up a promising new avenue for maize research.

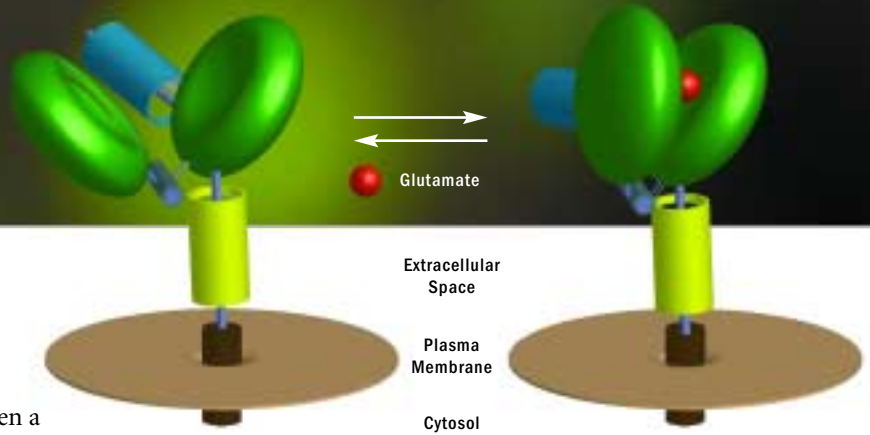
A Tale of Brains over Bran

To the casual observer, brain cells and plant cells might seem a world apart, but they actually have a lot in common. Wolf Frommer and Sakiko Okumoto, of Carnegie's Department of Plant Biology and Stanford University, have designed a way to track a substance called glutamate required by both cell types. In fact, they are the first to measure real-time glutamate changes in single living cells. Their technique holds promise for disease research, since it is suspected that too much glutamate may aggravate conditions like Alzheimer's and Parkinson's diseases.

Glutamate is a mammalian neurotransmitter required for a score of mental processes, from learning and memory to mood and perception. It is also vital for proper growth and chlorophyll production in plants. To study glutamate in both systems, Frommer and Okumoto use a technique called fluorescence resonance energy transfer, or FRET.

FRET detects metabolites such as sugars and amino acids using a "biosensor." Tags made from differently

Plant Biology, continued



colored variants of green fluorescent protein (GFP), one cyan and one yellow, are genetically fused to opposite ends of a protein. When a metabolite such as glutamate binds to this biosensor, it changes the shape of the sensor's backbone, altering the position of the fluorescent tags. When light of a specific wavelength activates the cyan tag, it begins to fluoresce. If the tags are close together, the cyan tag can then trigger the yellow tag to fluoresce.

The tags act like two musical tuning forks with a similar tone. Strike one and it begins to resonate; it can then cause the second to resonate, even if they do not touch.

FRET sensors detect the presence of glutamate by physically changing shape. When glutamate (red sphere) binds to the sensor, it changes from the open, unbound form (left) to the closed, bound form (right). This brings the fluorescent tags (blue and yellow cylinders) at each end of the glutamate-binding protein (green disks) closer together.

Instead of sound, FRET tags produce and transfer fluorescent light when they vibrate. Frommer's sensors have a genetic targeting sequence that places them on the cell's outer surface, where the light they produce provides a sensitive, visible readout of glutamate release.

Frommer's lab has also developed FRET sensors to monitor sugars like glucose, the source of metabolic energy for all cells. With these, they study glucose release from liver cells, a process that assures a constant energy supply to the brain and other organs.

The ability to track when, where, and how such chemicals behave can help answer many complicated questions in both animal and plant cell biology, and might one day help find a cure for debilitating diseases. With the methods developed in Frommer's lab, researchers should be able to engineer FRET-tagged markers to monitor other metabolites, expanding the reach of this useful technique. ●

Fluorescent green FRET nanosensors mark the surface of rat nerve cells grown in culture.

TERRESTRIAL MAGNETISM

Understanding the Earth, Other Planets, and Their Place in the Cosmos



Closing In on Other Earths

The ultimate dream of planet hunters is to identify other worlds around nearby stars that potentially harbor life. This race to find life elsewhere in the galaxy has been heating up in recent years, and researchers at the Department of Terrestrial Magnetism (DTM) are leaders in the quest.

First Light Detected from an Extrasolar Planet

Most of the 150 or so known extrasolar planets have been discovered and studied through techniques such as finding the telltale wobble of a star induced by an orbiting planet, or the “blink” of a star as a planet passes in front of it. Using NASA’s Spitzer Space Telescope a team of astronomers, including DTM’s Sara Seager, have for the first time observed an extrasolar planet through the light it emits in the infrared. This success opens the way to study extrasolar planets’ temperatures and compositions.

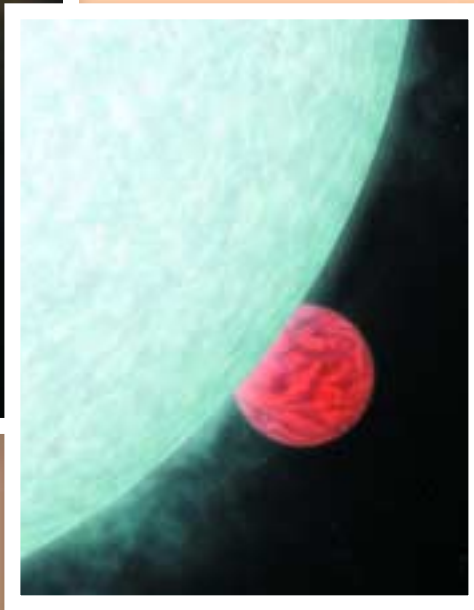
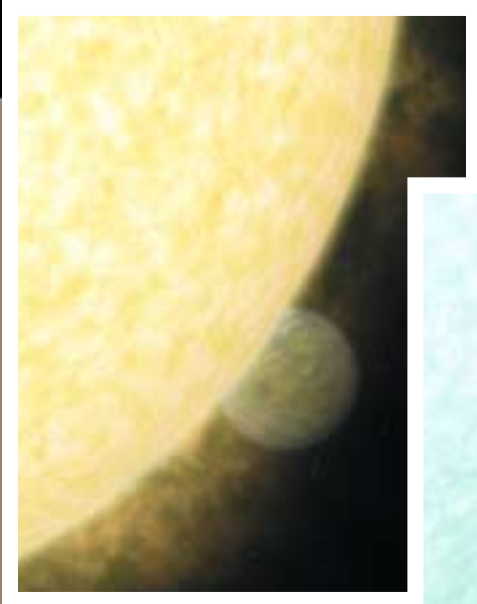
The planet, HD 209458b, is a massive gaseous world that orbits very close to its parent star and is thus known as a hot Jupiter. Astronomers cannot yet see these planets in the visible part of the spectrum because the light from the star vastly outshines that from the planet. In the infrared, however, the planets show up more brightly and can more easily be detected. HD 209458b was discovered indirectly in 1999 and was later found to transit its star—

as the planet passes in front of the star during orbit, the star dims. A planet that passes in front of its parent star also passes behind it. Using Spitzer, Seager and colleagues measured the combined infrared light of the planet and the star before the planet went out of sight behind the star. When the planet was out of view, they measured how much energy the star emitted on its own. The difference between those readings told them how much energy the planet gives off (at the measured wavelength). It is equivalent to a scorching 1570°F (1130 K). That temperature is key to refining atmosphere models created to infer the composition and infrared emissions of hot Jupiters.

Earth’s Bigger Cousin

DTM’s Paul Butler and team announced this summer the discovery of the smallest and most Earth-like extrasolar planet yet detected. The new ability to detect the tiny wobbles in the star from a small planet gives astronomers confidence that they will be able to find even smaller rocky planets at orbital distances more conducive to supporting life. The research was conducted at the Keck Observatory in Hawaii as part of the California and Carnegie Planet Search. The program is surveying the nearest 2,000 Sun-like stars and has found more than two-thirds of the 150 known planets, including the transit planet HD 209458b.

Terrestrial Magnetism, continued



The newly discovered Earth-cousin orbits the star Gliese 876, located 15 light-years away in the direction of the constellation Aquarius. The scientists believe that the planet may be the first rocky planet ever found orbiting a star similar to the Sun. It is about seven and a half times as massive as Earth, with about twice the radius. At 0.021 astronomical units (AU), or 2 million miles from its parent star, it is much closer to its star than Mercury is to our Sun, and it makes an orbit in just under 2 days.

All of the other extrasolar planets discovered to date around Sun-like stars have been more massive than Uranus, an icy giant with about 15 times the mass of Earth. Although there is no direct proof that the new planet is rocky, its low mass would prevent it from retaining a huge gas envelope as Jupiter does. The researchers

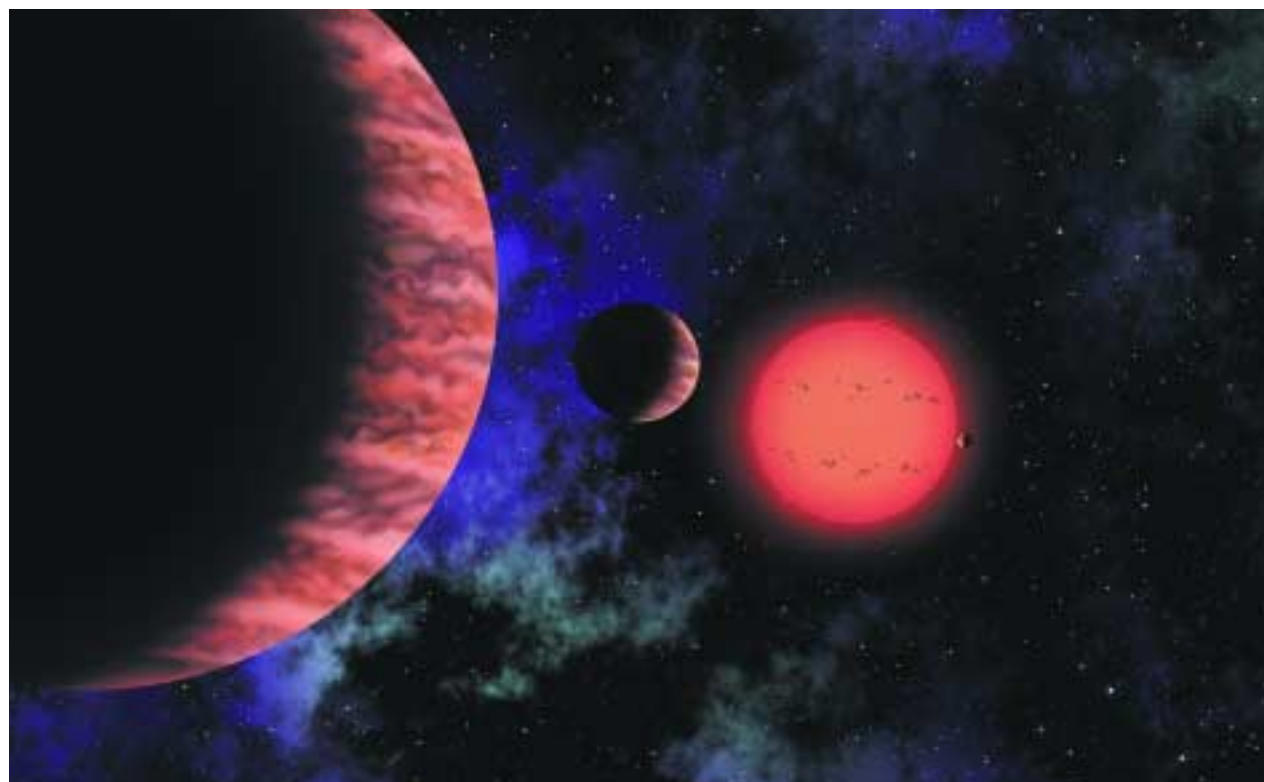
These artist's renderings show what a "hot Jupiter," orbiting close to its parent star, might look like in both the optical and infrared parts of the electromagnetic spectrum. The scene at left represents visible light, where the light of the smaller planet is overpowered by light from the star. In the infrared (right), the hotter star gives off more blue light than red, allowing the planet to be observed with greater clarity.

IMAGE COURTESY NASA/JPL-CALTECH/
R. HURT, SPITZER SCIENCE CENTER.

believe that its composition is probably like the inner planets of this solar system.

The planet's proximity to the star results in a surface temperature between 400° and 750°F—too hot for liquid water and therefore incompatible for life to develop.

Gliese 876 is an M dwarf. M dwarfs are small red stars with less than half the mass of the Sun. They are the most common type of star in the galaxy. Very few Jupiter-mass planets have been found orbiting M dwarfs, but as measurement precision improves smaller planets have begun to emerge, suggesting a large population of Earth-mass planets. Because these stars are cooler and smaller than the Sun, the orbits on which a planet could sustain liquid water on its surface have periods from days to weeks. Precision Doppler monitoring is already capable of detecting such planets.



This artist's rendering depicts three planets orbiting Gliese 876. The outer planets have masses of 2.5 and 0.8 Jupiter-masses. Jupiter is 318 times more massive than the Earth. The new inner planet (far right, nearest the star) has a mass of 7.5 Earth-masses.

IMAGE COURTESY LYNETTE COOK.

Revamping Earth's Early History

Research by Department of Terrestrial Magnetism's Carnegie Fellow Maud Boyet and staff member Rick Carlson challenges the standard model of the geochemical evolution of the Earth. The work was cited by *Science* magazine as a runner-up breakthrough of the year for

2005. According to the standard model, the Earth's mantle, the layer between the core and the crust, has been evolving gradually over Earth's 4.5-billion-year history. These DTM geochemists have found, instead, that the mantle separated into chemically distinct layers within 30 million years of the solar system's formation. Their work substantiates DTM director emeritus George Wetherill's theoretical models of early terrestrial planet formation, where collisions between small, rocky planetesimals, bombardment of the growing planets by large bodies, and the energy released from short-lived radioactive elements created deep, churning magma oceans that cooled and crystallized early in the solar system's history.

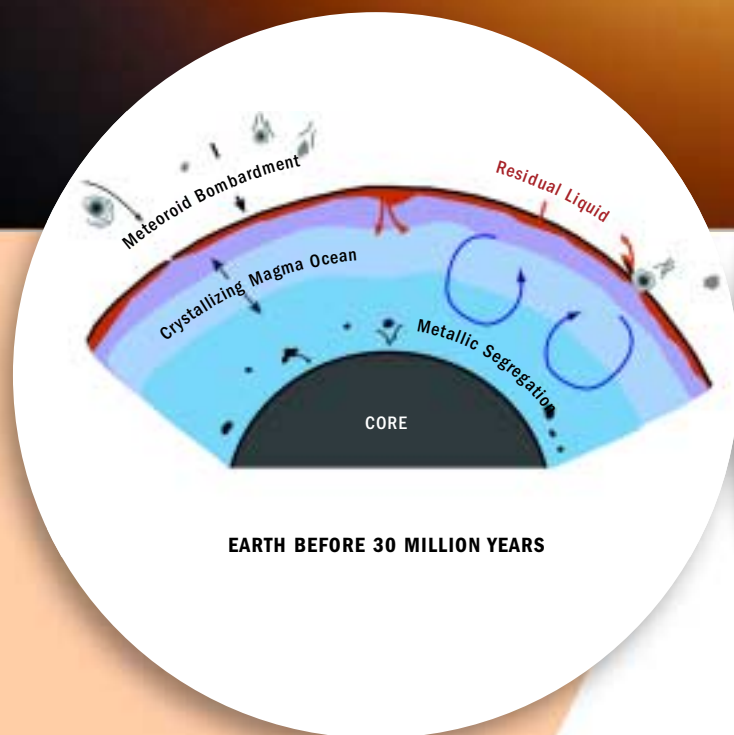
Boyet and Carlson analyzed isotopes contained in rock samples to understand the geochemical history and evolution of the Earth and other bodies in the solar system. Isotopes—atoms of an element with the same num-

Terrestrial Magnetism, continued

ber of protons, but a different number of neutrons— exist naturally in different proportions and can be useful for determining conditions under which rock forms. Radioactive isotopes decay at a predictable rate and can reveal a sample's age and when its chemical composition was established.

Earth formed from the collision and accretion of rocky bodies shortly after solid material began forming in the early solar system 4.567 billion years ago. The chemical composition of these building blocks is preserved today in primitive meteorites called chondrites. In the 1980s, scientists analyzed the ratio of isotopes of the rare Earth element neodymium in chondrites and various terrestrial rocks collected at or near the Earth's surface and found that the samples shared a common composition. Researchers believed that this ratio remained constant from the time the Earth formed. Now, using a new-generation mass spectrometer, Boyet and Carlson found, surprisingly, that the terrestrial samples had an excess of the mass 142 isotope of neodymium (^{142}Nd). ^{142}Nd is the decay product of a now-extinct radioactive isotope of samarium (^{146}Sm). The composition of the part of the Earth that has contributed melts to the surface over time diverged from that of the meteorites' parent bodies within the first 30 million years after solar system formation (less than 1% of the age of the Earth), which was when ^{146}Sm was decaying into ^{142}Nd .

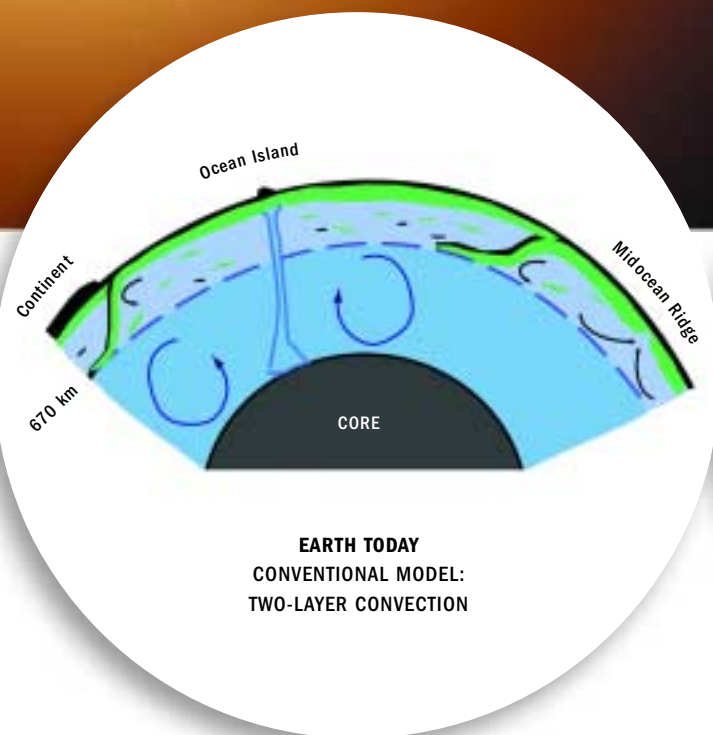
To explain the excess of ^{142}Nd found in the terrestrial samples, the scientists conclude that rapid crystallization of Earth's early magma ocean caused the mantle to sepa-



EARTH BEFORE 30 MILLION YEARS

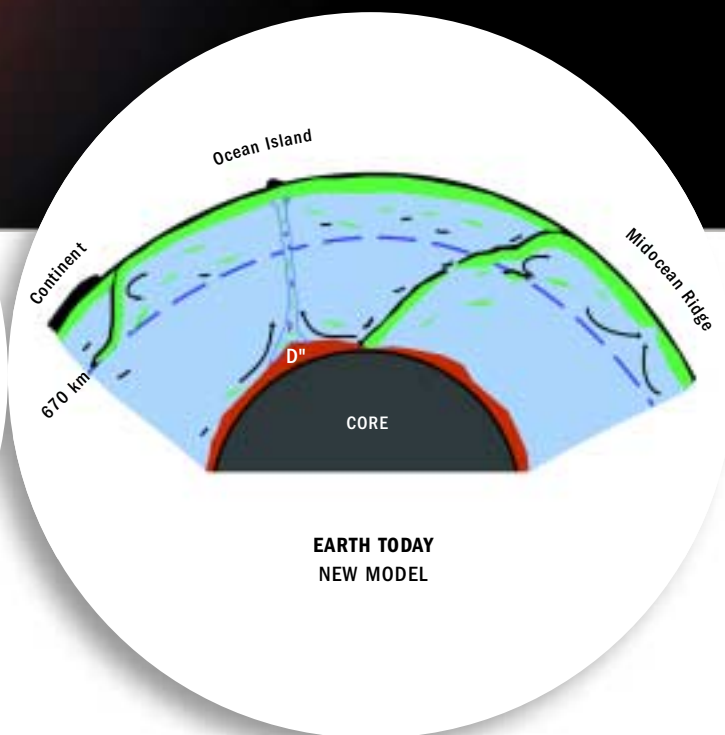
During Earth formation, decay of short-lived radioactive isotopes and surface bombardments from large bodies heated Earth's mantle and created a deep magma ocean. Crystallization of the magma ocean created compositionally distinct layers (blues), while leftover liquid (red) remained just under the primordial crust.

rate into chemically distinct layers, one containing a high ratio of Sm to Nd, similar to that observed today in the mantle source of the volcanism along ocean ridges. The complementary reservoir, with low ^{142}Nd abundance, has never been sampled at the surface and hence could now be deeply buried in the so-called D" layer at the very base of the mantle, above the core. This "missing" layer should be rich in the elements uranium, thorium, and potassium, whose long-lived radioactive decay would heat Earth's interior. This hot layer above the core could



EARTH TODAY
CONVENTIONAL MODEL:
TWO-LAYER CONVECTION

In the conventional model of Earth history, the mixing caused by mantle convection erased this early chemical differentiation. The only chemical variation in the mantle is that caused by the formation of the continental crust, leaving the upper mantle (light blue) deficient in those elements concentrated in the crust (black), while most of the mantle is still similar in composition to the chondritic meteorites from which Earth accumulated.



EARTH TODAY
NEW MODEL

The Boyet and Carlson result requires the Earth to have differentiated early, within 30 million years, leaving most of Earth's mantle (light blue) depleted in those elements that prefer melts over crystallizing solids. The chemical complement to the depleted mantle could be small and quite enriched in radioactive elements, such as uranium and thorium; this complementary material may coincide with the seismically observed D'' layer, located between the core and the mantle some 2700 km deep.

IMAGES COURTESY MAUD BOYET.

help keep the outer core molten so that circulation of liquid iron can produce Earth's magnetic field and instigate the hot plumes of upwelling mantle material that give rise to volcanically active islands, such as Hawaii.

Because lunar rocks have the same abundance of ^{142}Nd as the terrestrial samples, the finding also adds to the evidence that the Moon formed from the Earth. Since

Mars also experienced early melting, as indicated by the chemical and isotopic composition of Martian meteorites, the Boyet and Carlson work now links the Earth, Moon, and Mars and highlights the importance of early events in determining the chemical characteristics of the terrestrial planets. ●

FIRST LIGHT AND THE CARNEGIE

Teaching the Art of Teaching Science



CASE and First Light Graduate!

This was a milestone year for the Carnegie Academy for Science Education (CASE), a program formed 11 years ago to instruct elementary school teachers from the District of Columbia Public Schools (DCPS) in the art of teaching science and mathematics. The long-term goal at CASE has been to turn much of the effort over to the CASE Mentor Teachers, who have been trained by the Carnegie staff over the years, so as to create a self-sustaining program and build capacity within DCPS. This goal was reached this year when 12 Mentor Teachers from the D.C. schools ran the four-week summer institute under the supervision of the CASE staff. For the first time, the Mentor Teachers organized and taught the highly successful and enjoyable approach to teaching science pioneered by CASE, an approach based on conducting scientific experiments while integrating mathematics and technology in the process.

Because of the school system's increasing emphasis on science in secondary school, the CASE staff is moving on to this level. For 15 years the First Light Saturday science school has offered 15 to 20 third to sixth graders exposure to science through innovative hands-on experiments and field trips. Over the years, the students' regular schools

found that the First Light students were performing better than their peers. This success led principals to seek out CASE for teacher training in higher grades. This year CASE received funding from the D.C. State Education Office to improve teacher quality in middle school mathematics and science by helping teachers from public, charter, and parochial schools learn the unique CASE methods.

As part of this new initiative, CASE ran a two-week summer institute that focused on the field of astrobiology—a multidisciplinary approach to understanding the origins of life in the universe. The group, which included teachers of life sciences, Earth and planetary science, and mathematics, looked at questions that integrate these topics. In addition to learning through participating in experiments, the teachers visited the laboratories of Carnegie's Geophysical Laboratory and Department of Terrestrial Magnetism, whose scientists are affiliated with the NASA Astrobiology Institute. The instructors ended their course by developing lesson plans to implement in their own classrooms.

Drawing on its extensive expertise in molecular biology, the CASE staff also ran a new summer program in biotechnology for high school teachers and students. This course, in cooperation with the new D.C. McKinley Technology High School and the DCPS Office of Career and Technology Education, prepares students to work in biotech fields and teaches instructors how to present the curriculum. The staff is also working with the DCPS Central Office, area postsecondary schools, such as nearby Montgomery College and Catholic University, and

ACADEMY FOR SCIENCE EDUCATION



Washington, D.C., middle school teachers receive training in the art of teaching hands-on science, mathematics, and technology at the Carnegie Academy for Science Education (CASE) 2005 summer session. Former Carnegie president Maxine Singer (left), founder of the program and senior scientific advisor for CASE, attends this session.



2005 marked the first year that the First Light Saturday science school opened its doors to middle school students.

local "biotech industries," including the National Institutes of Health and Walter Reed Army Medical Center, to develop an advanced technological education program to help teachers prepare students for careers in the burgeoning field of biotechnology.

First Light middle school students participate in field trips and collect samples as part of the curriculum.

IMAGES COURTESY TOBY HORN.

First Light also graduated to middle school this year. Now every Saturday about 20 sixth through eighth graders from D.C. public and charter schools are immersed in entertaining and instructive laboratory science activities and take field trips throughout the Washington metropolitan area. As CASE and First Light mature, more and more individuals and institutions are becoming exposed to their unique educational techniques. From the very beginning, these programs have sparked curiosity and shown the uninitiated how science touches our lives every day, and how teachers can become classroom scientists along with their students. ●

