

Debating the Big Questions

Cosmologists squared off recently over the most contentious questions about the history and nature of the universe. Points of consensus emerged—but so did new disputes

PRINCETON, NEW JERSEY—Vera Rubin, an astronomer at the Carnegie Institution of Washington, summed up the most important gathering of cosmologists in years with a story about the wise rabbi who was called on to mediate a marital dispute. In a field that has a history of highly polarized scientific disagreements, the story couldn't fail to resonate. Rubin told the audience that each time the husband visited to complain about his wife, the rabbi said, "You're right." Each time the wife visited to complain about her husband, the rabbi said, "You're right." Finally, the rabbi's own wife emerged from behind a curtain, where she had been hiding, and asked with some dismay, "How can you tell them both they're right?" The wise rabbi replied: "You're right, too."

The parallel with cosmology is no joke, said Rubin: The data have been so thin and theorists so resourceful that warring theories about the history and nature of the universe can all seem to be "right." But now, as observations pour in from new telescopes and satellites, cosmologists have more data to reckon with, and the room for competing theories may have narrowed. The purpose of "Critical Dialogues in Cosmology," which took place here on 24 to 27 June, was to throw together the world's most influential cosmologists in hopes that some of those disputes could actually be settled. As Robert Kirshner of the Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts, put it, the question was whether the various disagreements "could come down to hand-shaking distance rather than fist-shaking distance."

To find out, participants first took off their gloves. The conference, organized by Princeton University researchers David Spergel, James Peebles, and David Wilkinson, and Neil Turok of the University of Cambridge, adopted what one participant called a "confrontational astronomy format." Free-style presentations were followed by often raucous exchanges among the 200 or so astronomers and cosmologists in attendance. The aim was to break down scholarly reserve and highlight the points of dispute and con-

sensus. "The things we really believe," explained Malcolm Longair of the University of Cambridge, "we tend to tell to our bartenders and not our colleagues." When the laughter subsided, Longair insisted that "I've often been asked by bartenders about inflation," a theory holding that the universe experienced a sudden growth spurt when it was a fraction of a second old.

The debates covered virtually all of cosmology's outstanding issues, and the convergence in some areas, said Longair, was "historic": For the first time, proponents of two different values for the Hubble constant—the universe's current rate of expansion—presented measurements in which the error bars, or uncertainties, overlapped, raising hopes of a consensus. On other questions, though, agreement still seemed out of

reach. Is there evidence for inflation? Will the universe expand forever or ultimately slow to a stop? Is there a real conflict between the age of the universe as a whole and that of its oldest stars? At the Princeton conference, all sides staked their claim to cosmic truth.

Adaptable inflation

Alan Guth of the Massachusetts Institute of Technology, for example, gave a spirited defense of inflation, a theory he originated. Simply put, inflation theory explains how the big bang got started. "Inflation actually sets off the Hubble expansion," said Guth, giving the universe a kick-start that otherwise has to be assumed. The key event, Guth explained, came when the universe's forces split away from an initially symmetric condition. According to inflation, the energy from this symmetry-breaking drove a tremendous growth spurt and later spent itself in creating all the matter in the cosmos.

The universe we observe today, Guth argued, "has the fingerprints of inflation all over it." Because the growth spurt would smooth out any primordial lumpiness in the fabric of the early universe and leave only subtle ripples, for example, the theory can help explain the near-smoothness of the cosmic microwave background (CMB)—the

fossil remnant of the radiation that streamed through the infant universe. Future measurements of the CMB's ripples will firm up the case for inflation, he predicts, by eliminating rival theories of the early universe.

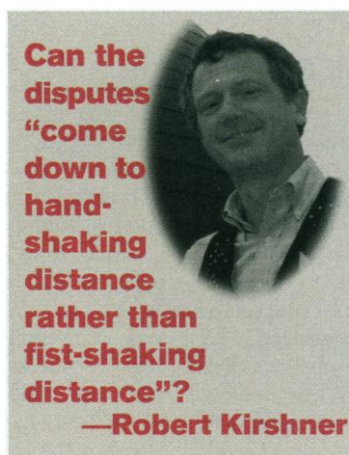
But William Unruh of the University of British Columbia in Vancouver—while calling inflation "beguiling and attractive"—argued that the theory isn't likely to get a definitive test, because theorists have come up with so many variants of it, tailored to explain almost any observational data. That's a weakness in the theory, not a strength, he said: "If you can find an inflationary theory which gives anything you want, it's useless as a predictive theory."

Several theorists replied that it would be "miraculous" if a spurious theory matched the wealth of data expected from future CMB instruments—to which Unruh shot back: "I'll fit any dog's leg that you hand me [using] inflation." As if to illustrate Unruh's point, Princeton University's Richard Gott reprised his own brand of inflation, which readily copes with recent evidence challenging a simpler version of the theory. That version predicts that our universe should have almost exactly the "critical" matter density needed for gravity to slow cosmic expansion to a halt, given infinite time.

There is, however, a mounting observational case for a low-density universe. Neta Bahcall of Princeton University presented results from several techniques for weighing large, rich clusters of galaxies (*Science*, 7 June, p. 1426). Extrapolated to the rest of the universe, they imply that it probably has no more than 20% of the critical density. "Where is the matter?" asked Bahcall. Marc Davis of the University of California, Berkeley, who has deduced higher matter densities in the past by tracking how galaxies flow through space under the pull of gravity, now admits, "You should mark that as unresolved." And Gott's variant of inflation works fine either way. It envisions multiple inflationary universes burgeoning in the first instant of creation, like bubbles in a hot pan of broth. Some of the bubbles—including the one in which we find ourselves—could have less than the critical matter density.

Cease-fire in the Hubble wars?

That kind of theoretical flexibility suggests that the debate over inflation isn't likely to be settled anytime soon. Hints of a possible



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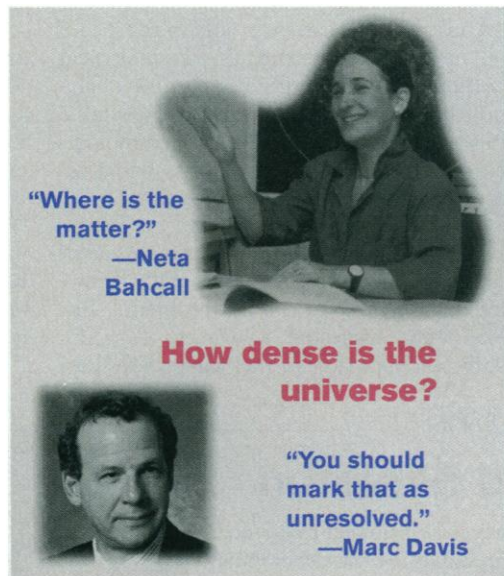
resolution did appear, though, in the long-running debate over the Hubble constant. A group led by Wendy Freedman of the Carnegie Observatories in Pasadena, California, had staked out one pole in the debate by observing fluctuating stars called Cepheids in nearby galaxy clusters, using the orbiting Hubble Space Telescope. The rate at which Cepheids flicker indicates their intrinsic brightness, making it possible to infer their distance from their apparent brightness as seen from Earth. By relating a Cepheid's distance to its redshift, which indicates how fast it is hurtling away from Earth, Freedman and her colleagues calculate a velocity-distance ratio—the Hubble constant. So far, they have consistently come up with high values, indicating a rapidly expanding, presumably young universe.

By contrast, a team led by Gustav Tammann of the University of Basel in Switzerland, Allan Sandage of the Carnegie Observatories, and others has used Cepheids to calibrate a different distance gauge: type Ia supernovas, exploding stars that are believed to reach roughly the same maximum brightness, so that their apparent brightness is a direct indicator of distance. These researchers have consistently reported drastically lower Hubble constant values, implying an older universe that has had more time to slow down. While each team has been accumulating data for years, the conflict has shown no sign of abating—until now. Freedman began her presentation by declaring, "In the last 6 months there has been enormous progress in measuring distances to Cepheids"—including a larger sample and data from a new cluster. Then she revised her team's value to 70 ± 10 kilometers per second per megaparsec, in the units traditionally used for the Hubble constant—down more than 10% from earlier figures.

That range overlaps for the first time with Tammann and Sandage's value, 55 ± 10 , which has itself crept upward over the past several years. Although Tammann seemed encouraged by the drop in Freedman's value, both he and Freedman jabbed away at what they saw as residual errors by the opposing corner. Tammann, for example, accused Freedman of taking some of her data from "the worst place to determine the Hubble constant"—regions of the local universe contaminated by other motions. "Tammann gave a take-no-prisoners talk," said Michael Turner of the University of Chicago. "He smells blood." But onlookers expressed relief that the end may be in sight for one of their field's most visible disputes. "I

would recommend a total moratorium on further talks about the confrontation between the two values," said Longair, adding, "let's get on with the job" of refining a single value for the constant.

Already the converging values have in-



intensified another problem. Both Freedman's and Tammann's measurements of cosmic expansion imply a universe younger than the oldest stars in globular clusters, ancient hives of stars found in a halo surrounding the Milky Way and other galaxies. Freedman's current estimate implies a cosmic age of 9 billion years, while Tammann's gives 12 billion years. Both ages assume the universe has the critical matter density that theorists cherish; a lower density universe would be somewhat older, because it would be decelerating more slowly—but perhaps not old enough. As Michael Bolte, a stellar modeler

at the University of Chicago argued that the models of stellar evolution are not good enough to rule out maximum ages of 10 billion years. Uncertainties about the internal structure of stars and other potential errors leave enough wiggle room, said Schramm, that "there is no serious age problem at the present time." The soft-spoken Bolte was not swayed. He pointed out that the sunlike stars used for the estimates should have relatively simple structures and held out for an absolute lower bound of 12 billion years.

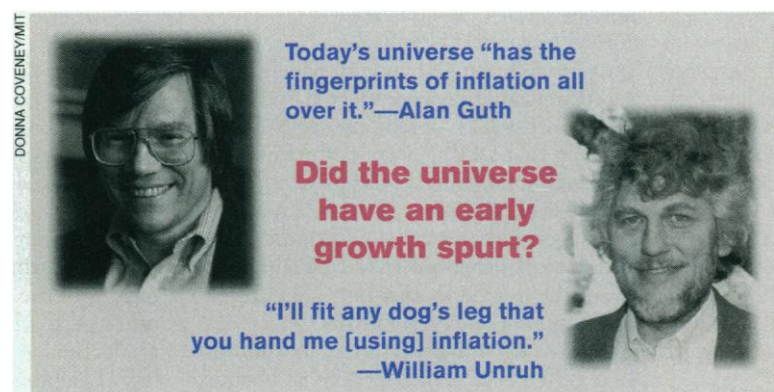
Cosmologists swallow hard

If the age problem proves to be genuine, some cosmologists are prepared to turn to a solution that sparked its own debates at the conference: the cosmological constant. Postulated and then abandoned by Einstein but recently enjoying a renaissance, the cosmological constant implies that empty space is seething with energy, which generates a large-scale, cosmic repulsion. The repulsion would keep cosmic expansion from slowing under gravity, so that the current rate of expansion would translate into an older universe. Some cosmologists regard the cosmological constant as an awkward solution to the age dilemma, but many have "tempered their distaste," says Craig Hogan of the University of Washington, because the alternative—an unresolved paradox—could be worse.

Observers are now studying distant landmarks in the universe for signs that a cosmological constant is affecting the expansion rate (*Science*, 11 August 1995, p. 756). But if a cosmological constant with the right value to solve the age problem is found, an even deeper puzzle will arise, said Steven Weinberg of the University of Texas, Austin: "To particle physicists, all of these values seem absurdly low. We don't understand why [the constant] isn't zillions of times larger."

Weinberg explained that the phenomenon supposedly responsible for the cosmological constant—the swarms of virtual particles and fields that pop in and out of existence throughout space according to quantum mechanics—has a natural energy scale that could produce cosmological constants 50 orders of magnitude larger than cosmologists are now discussing. In the past, physicists

assumed that the relevant terms in the equations governing the quantum vacuum simply cancel out, reducing the energy to zero and eliminating the cosmological constant. But if they failed to cancel, Weinberg said, space would be expected to generate so much repulsion that galaxies could never have coalesced and life couldn't have evolved.



at the Lick Observatory of the University of California, Santa Cruz, explained, increasingly sophisticated computations of how stars age, along with improved observations, strongly imply that the oldest stars top out at some 15 billion years.

Not everyone is convinced that this "age problem" is real. David Schramm of the Uni-

He went on to outline several conceivable resolutions to the problem. One possibility is that the terms for the energies somehow come within a hair's breadth of canceling but don't quite do so, leaving just enough residual energy to explain the constant. But Weinberg, and some other physicists, have a hard time swallowing the idea that the entire universe could be founded on such an unlikely balancing act. Weinberg's response: the so-called anthropic principle, which holds—in logic that many physicists find circular—that fundamental constants have the values they do because only those values allow human beings to exist and measure them.

The principle, which many cosmologists trace back to work by Princeton University's Robert Dicke in the 1960s, assumes multiple universes à la Gott—or multiple regions within a single universe—in which param-

eters like the cosmological constant have different values, making the laws of physics different in different spots. In most of these universes the cosmological constant would take on higher, more plausible values. Our own universe would be peculiar not because of a single mind-bending coincidence but because humans can exist only in those rare universes or regions with tiny cosmological constants. Weinberg's conclusion: "The only kind of theory that is today respectable in which you can understand the cosmological constant problem is theories based on some kind of anthropic reasoning."

Although no one ventured to debate Weinberg formally, Turner declared himself "amazed" by the approach. "It's really throwing your hands up on the problem." But Weinberg suggested a way to test the anthropic approach. Higher values of the cos-

mological constant would be more common in the plethora of universes, so if the cosmological constant in our own universe turns out to be close to the largest values compatible with galaxy formation, "it will be, for me, incomprehensible on any other grounds but the anthropic principle," he said.

With issues like the cosmological constant and the anthropic principle catching fire even as old conflicts die out, there will be no shortage of topics for future versions of the Princeton conference. In his introductory talk, Martin Rees of the University of Cambridge asked his audience to keep in mind that "as the consensus advances, new questions which couldn't even have been posed in earlier decades are now being debated." At that rate the rabbi's wise words will echo in cosmology for some time to come.

—James Glanz

GENETIC DISEASE

Protein Builds Second Skeleton

In Greek myth, one glance at Medusa's snake-coiled head could turn a man to stone. But the villain in a rare inherited disease that relentlessly converts the body's soft connective tissues into bone—transforming its sufferers into living statues—has proved to be much more elusive. Indeed, it lurks within the victims' own immune systems, scientists in Philadelphia have discovered.

In children with the disease, called fibrodysplasia ossificans progressiva (FOP), the slightest injury to ligaments, tendons, or muscles can cause severe inflammation, followed by the appearance of cartilage, and then ordinary bone, at the site of the injury. As the disease progresses, sufferers' spines, limbs, rib cages, and jawbones fuse in place, leading to complete immobilization.

In the 22 August *New England Journal of Medicine*, a team led by orthopedic surgeon Frederick Kaplan of the University of Pennsylvania School of Medicine now reports that this abnormal bone buildup occurs because the lymphocytes, or white blood cells, of people with FOP erroneously manufacture bone morphogenetic protein-4 (BMP-4), a powerful signaling protein known to help build the skeleton of the developing embryo. "You should be able to repair and remodel bone later in life, but you shouldn't be able to make a new bone," Kaplan says. "That's what's happening here."

While developmental biologists have been studying BMPs and related proteins in organisms from fruit flies to humans since the 1960s, this is the first time a member of the BMP family has been implicated in a human genetic disease. "It's an amazing story," says developmental geneticist William Gelbart of Harvard University, who discovered the first BMP family member, the protein Decapentaplegic (DPP),

which helps establish body and limb axes in the developing fruit fly, among other functions. "It's incredibly gratifying to see how central these molecules are in a whole host of developmental processes—and now in a human disease with heartbreaking effects." The discovery could eventually lead to a therapy to block either the production of BMP-4 or its effects.

The idea that a gene defect might underlie FOP originated about 7 years ago, Kaplan says, after he and geneticist Michael Zasloff, also at the University of Pennsylvania, found a small family in which both a parent and children were affected, indicating that the disorder is hereditary. In 1990, after learning that DPP's relatives, the newly discovered human proteins BMP-2 and BMP-4, help build limbs in the mammalian embryo by triggering bone-cell formation, Kaplan and Zasloff proposed that FOP might be caused by a genetic mutation affecting the production of one of the BMPs.

A test of the hypothesis had to wait until 1993, when Kaplan and Zasloff first obtained blood and tissue samples from patients with FOP. Penn medical student Adam Shafritz, now a resident physician at Manhattan's Hospital for Special Surgery, examined the samples, looking for messenger RNAs that would indicate that the BMP genes were active. He found one—corresponding to the BMP-4 gene—in the lymphocytes of 26 of 32 FOP patients studied, but in only one of 12



Bony prison. FOP fused the spine, shoulders, ribs, and elbows of this man, who died of pneumonia at age 39.

normal subjects.

That finding posed a puzzle, however, because if the lymphocytes were releasing BMP-4 into the bloodstream, it would be so diluted and short-lived that it couldn't account for new bone growth in discrete locations around the body. Then, Kaplan recalls, the team found "the Rosetta stone for this whole condition": a biopsy sample taken 25 years earlier from a 4-year-old boy with FOP.

Under the microscope, the researchers saw masses of lymphocytes surrounding and choking off muscle cells. While a normal response to injury, in FOP patients, the researchers realized, this clumping must create high local concentrations of BMP-4, triggering bone growth. The lymphocytes of people with FOP, Kaplan and Zasloff conclude, probably carry a genetic error that improperly switches on production of BMP-4.

The researchers have now set out to locate this error, which may be in the regulatory regions of the BMP-4 gene itself or in some other gene whose product controls BMP-4 production. Already, however, the findings have heightened hopes for an eventual cure for FOP. "With so much being discovered about how the BMPs act," says Brigid Hogan, a developmental geneticist at Vanderbilt University in Nashville, Tennessee, "it might be possible to develop drugs that would block some part of the BMP-4 pathway—and therefore prevent the progression of what is a horrible, nightmare disease."

—Wade Roush