not respond to agents that normally induce gene expression. Both groups are now searching for ways to get the genes to produce much larger quantities of mRNA. In a very controversial experiment, Martin Cline of the University of California at Los Angeles has attempted much the same feat in humans (*Science*, 19 December 1980, p. 1334).

The final category of potential therapeutic agents includes those that act on the erythrocyte membrane. One of these is Cetiedil, a local anaesthetic that is used clinically in Europe for treating chronic cardiovascular disease. Physicians there observed that it also inhibits sickling. Charles M. Peterson of Rockefeller University has examined Cetiedil and found that it does not interfere with polymerization or oxygen affinity. The lipophilic molecule does insert itself in the erythrocyte membrane and stays there for a long time, but no one knows what it does there. Preliminary uncontrolled studies in the Ivory Coast have shown that the drug alleviates sickle cell crises, and Peterson hopes to begin controlled clinical trials within the year.

Another attack on membranes has been conducted by George J. Brewer and his colleagues at the University of Michigan. They have treated a small number of patients with zinc acetate and thioridazine, a tranquilizer. Both thioridazine and zinc are inhibitors of calmodulin, a naturally occurring substance that, in response to the sickle erythrocytes' increased concentration of calcium, causes the cell membrane to stiffen so that the cell becomes permanently sickled. The combination of reagents increases the half-life of sickle erythrocytes by as much as 75 percent, but there is no evidence yet that they decrease the frequency or severity of crises. Like Cetiedil, though, these agents could prove very useful in conjunction with antipolymerization agents.

Two points should be made about prospective agents. They must almost certainly be prophylactic rather than curative: It is substantially more difficult to depolymerize HbS than it is to prevent it from polymerizing in the first place. In fact, there are very few agents that have been shown to depolymerize gelled HbS. A potential new antisickling agent must thus be very safe since it will be used on a daily basis throughout the patient's life.— THOMAS H. MAUGH II

Massive Neutrinos: Masters of the Universe?

Neutrinos with mass would explain a lot about the distribution and dynamics of galaxies; they might even suffice to close the universe

For cosmologists, the idea of a universe filled with massive neutrinos carries the Copernican principle to its extreme: first the earth was not at the center of the solar system; then the sun was not at the center of the galaxy; and finally the galaxy was not at the center of the universe. Now, says University of Chicago astrophysicist David N. Schramm, it seems that the stuff we are made of may not even be the dominant kind of matter in the universe.

Relic neutrinos—those left over from the Big Bang—are thought to outnumber the protons, neutrons, and electrons of ordinary matter by about 10 billion to 1, he said last month at the Tenth Texas Symposium on Relativistic Astrophysics in Baltimore. On the average, every cubic centimeter in the universe contains some 450 of them. Their ghostly indifference to ordinary matter is famous: supposedly massless, moving at the speed of light, they are capable of passing through the earth as if it weren't there.

But if 40 years of neutrino theory is wrong, if those 450 particles per cubic centimeter have even a tiny mass, then their cumulative gravitational pull would be immensely greater than theorists have imagined. Massive neutrinos, in fact, could explain a number of cosmological puzzles related to the structure and expansion of the universe as a whole and to the formation and mass distribution of the galaxies.

While such speculations are more than a dozen years old, the revived interest in massive neutrinos so apparent at the Texas Symposium was sparked in part by two independent experiments last year, one by Soviet physicists and the other by a group from the University of California, Irvine. These experiments produced the first direct, albeit controversial, evidence that even the lightest neutrinos have masses of a few tens of electron volts (*Science*, 16 May 1980, p. 697). For comparison, 10 electron volts is 0.002 percent of the mass of the electron.

But physicists and astrophysicists would be taking the idea of neutrino mass very seriously in any case, because such masses are also predicted in many of the so-called Grand Unified Theories of elementary particle interaction. Such theories typically give a different mass to each of the three known types of neutrinos; some of the particles may even be unstable. Floyd W. Stecker of NASA's Goddard Spaceflight Center in Greenbelt, Maryland, has suggested, for example, that a feature in the ultraviolet spectrum of the sky near the north galactic pole may arise from the decay of heavy neutrinos in a neutrino halo surrounding the Milky Way galaxy. He estimates a mass of 14 electron volts for the particle, consistent with the laboratory experiments.

There is a vast difference between neutrinos having even the tiniest mass, and neutrinos having zero mass. Zero-mass particles, such as photons, are constrained by relativity to move only at the speed of light. At that speed, they can carry energy even without mass—in fact, according to Einstein, their energy content alone would allow them to exert gravitational forces on other bodies—but they could never slow down.

On the other hand, relativity dictates that massive particles must never travel at the speed of light. Like protons or electrons, massive neutrinos could indeed slow down and come to rest. And therein lies the difference for cosmology. Not only would a tiny mass increment enhance the gravitational effect of the relic neutrinos enormously, but those moving slowly enough could become gravitationally bound in galaxies or clusters of galaxies, and thereby participate in the evolution of these objects. The only thing that could bind a massless neutrino, by contrast, is a black hole.

Schramm told the symposium that massive relic neutrinos bound in large clusters of galaxies might in fact offer a straightforward resolution of the "miss-

0036-8075/81/0130-0470$00.75/0

ing mass" problem—that there is literally more to the universe than meets the eye.

The problem is that the amount of visible matter in the universe, the stars and luminous gas, falls far short of the total amount of matter estimated from gravitational dynamics, Schramm explains. Moreover, the discrepancy seems to become larger and larger as one ascends the mass scale from individual galaxies to small groups of galaxies to the giant clusters.

In a spiral galaxy, for instance, the orbital velocities of stars about the center are related by simple Newtonian physics to the distribution of mass in the galaxy—*all* the mass, not just the visible component. From spectroscopic data, astronomer Vera Rubin and her colleagues at the Carnegie Institution of Washington have measured orbital velocities in some 50 spiral galaxies. They find that the mass density in the galactic disk typically falls off as the inverse of the radius. Yet the luminosity falls off much faster—exponentially, in fact. Thus most of the material in the outer reaches of such a galaxy is dark; the photogenic spiral itself is just a tiny lens of glowing matter embedded in some immense, invisible halo.

Velocity measurements can also yield mass estimates for giant clusters, where the individual galaxies dart about randomly like swarming bees. Assuming that a cluster is stable, the overall gravitational field must keep the fastest-moving galaxies from flying away. By this measure, says Schramm, the total mass in large clusters is as much as 100 times the visible mass in the galaxies.

Speculations about the identity of the dark material have ranged from the conventional—gas, dust, rock, even very dim stars—to exotica such as small black holes and magnetic monopoles. Schramm and Gary Steigman of the Bartol Research Institute in Newark, Delaware, have reviewed the latest data and conclude that normal matter (often called "baryonic matter," since particle physicists place the proton and neutron in the baryon family) will suffice for the dark component of individual galaxies and small groups of galaxies. But for the large clusters something else is needed.

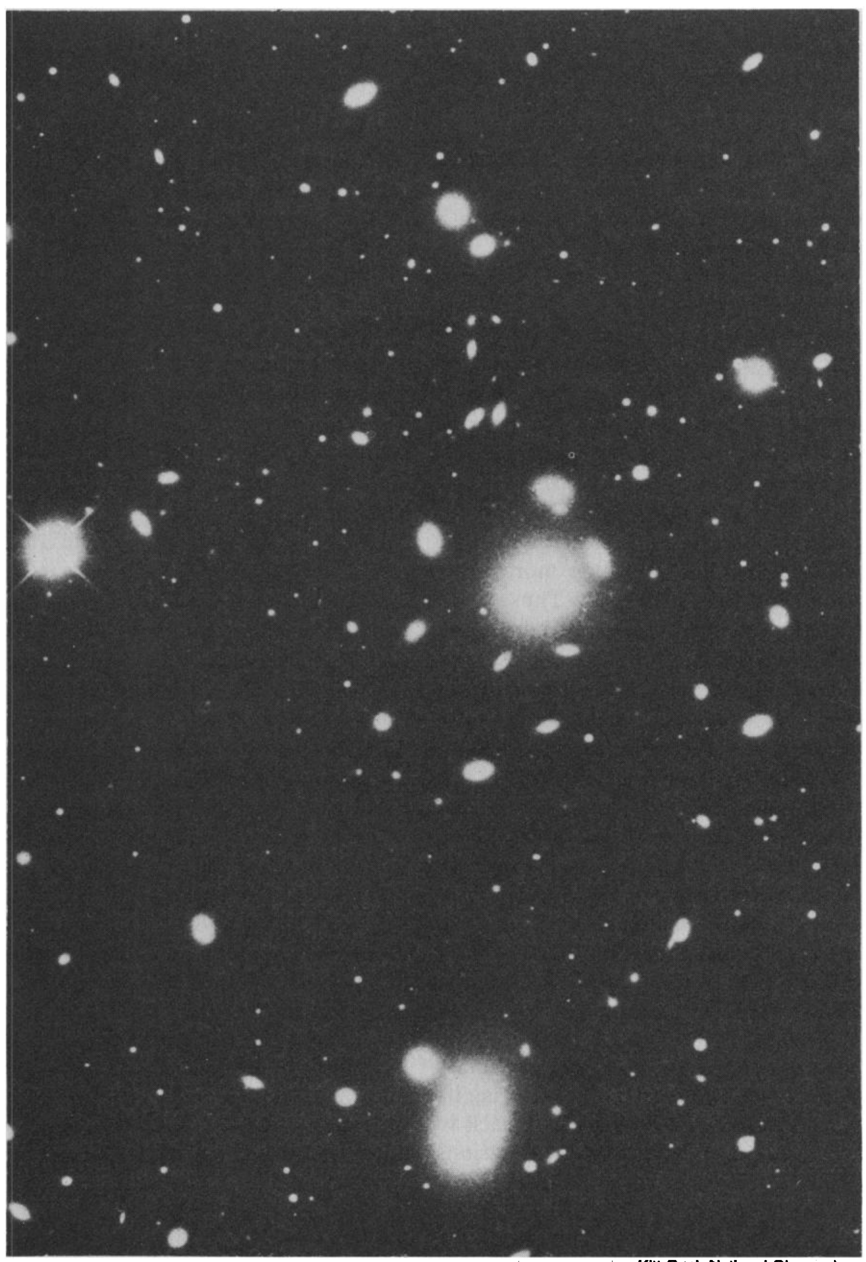
There is simply too much mass in the clusters, Schramm explains. If it all consisted of baryons it would violate other mass constraints, particularly that based on the cosmic abundance of helium.

Except for the few traces that later formed in stars, helium was entirely created from hydrogen in a burst of nucleosynthesis during the first few minutes of the Big Bang. Moreover, the rate of nucleosynthesis was critically dependent on the (baryonic) matter density in those minutes. Thus, it is possible to go from the observed cosmic abundance of helium, roughly 25 percent, to an upper limit on the current density of baryons in the universe.

That limit, says Schramm, is about 5×10^{-31} gram per cubic centimeter, which easily accommodates the dark matter found in the smaller galactic systems. But the dark matter found in the large clusters implies an average cosmic mass density of at least 2×10^{-30} gram per cubic centimeter. This fits the helium limit only if the observational uncertainties are stretched to their utmost.

The limit applies only to baryons, however (even if the baryons have later fallen into black holes). Schramm emphasizes that it does not apply to neutrinos. Neutrinos never participated in nucleosynthesis. They formed earlier in the Big Bang and have little to do with heavy-element abundances.

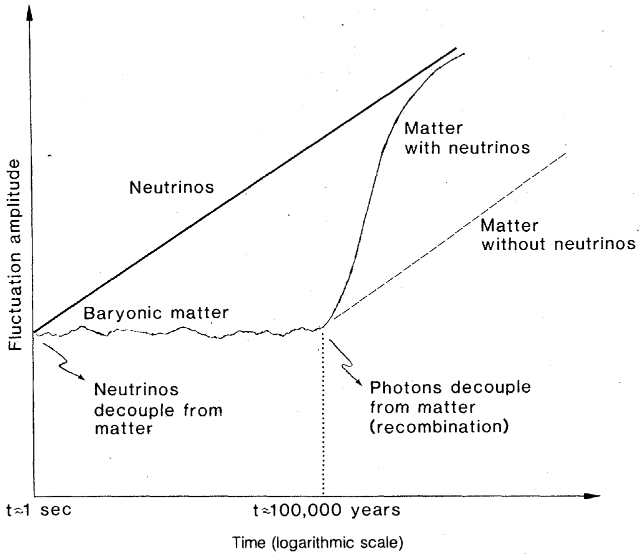
So if relic neutrinos really are massive, they are natural candidates for the missing mass, says Schramm. By now they would have been slowed by universal expansion to speeds of only a few kilometers per second—slow enough, in fact, that a galactic cluster could capture and bind them in its deep gravitational field. And as each neutrino pursued its own slow orbit among the visible galaxies, it



Kitt Peak National Observatory

Cluster of galaxies in Coma Berenices

Bound by massive neutrinos?



As shown here schematically, neutrinos decoupled from baryonic matter about 1 second after the Big Bang. As the universe expanded they continued to cool, much like gas in an expanding cylinder; when they had lost sufficient kinetic energy, density fluctuations began to grow by self-gravitation. But high energy photons continued to disrupt the baryonic fluctuations for another 100,000 years. Only after recombination, when the baryonic matter had cooled enough for neutral atoms to form, did the photons decouple. According to Zeldovich and his collaborators, the baryons were then free to fall into the gravitational field of the preexisting neutrino clumps, developing density fluctuations much more rapidly than they would have otherwise.

would make the overall field infinitesimally stronger; together the neutrinos would form the massive, invisible halo that keeps the cluster bound.

Scott Tremaine and James E. Gunn of the California Institute of Technology have calculated that relic neutrinos will only collapse into clusters of galaxies if their masses are greater than about 3 electron volts, says Schramm. Depending on the details of galaxy formation, neutrinos heavier than 20 electron volts could also contribute to the mass in small clusters and binary galaxies. But in that case they would contribute more mass than is actually observed. Thus, from cosmological constraints, the best guess is that neutrino masses lie between 3 and 20 electron volts, Schramm concludes. This is at least roughly consistent with the current, highly uncertain experimental situation.

It's intriguing, adds Schramm, that with a mass of only 1.4 electron volts, the relic neutrinos would have a density that equals or exceeds the average density of baryons in the universe. Thus, neutrinos could easily be the dominant form of matter in the universe today. And depending on how many kinds there are—and how heavy each kind is—neutrinos could even provide the mass needed to close the universe, to bring its expansion to an end and pull it back in upon itself. If so, then massive neutrinos would solve the biggest missing mass problem of all.

It may be that neutrinos not only explain the missing mass in clusters of galaxies, but are responsible for the very formation of these structures. Alexander S. Szalay of the Roljnd Eötvös University, Budapest, told the symposium about ideas developed during the last decade by a group of Soviet and Hungarian astrophysicists led by Ya. B. Zeldovich of the Institute of Applied Mathematics, Moscow.

The smoothness of the 3 K background radiation has always been difficult to reconcile with the manifest clumpiness of matter in the universe, Szalay explains. The radiation is actually the afterglow of matter recombination, an event which occurred some 100,000 years after the Big Bang. The electrons and nuclei of the original hot plasma, cooling as the cosmos expanded, were suddenly able to form neutral atoms. The universe became transparent to photons (or conversely, the sky for the first time turned dark) and matter was effectively decoupled from light.

The photons released in that event, now cooled by expansion to 3 K, should still reflect any inhomogeneities in the matter, says Szalay. Current measurements, which compare regions as close together as 10 arc seconds, show temperature fluctuations of no more than 1 part in 10,000.

But theorists have a hard time understanding how matter fluctuations starting out that small could have grown enough by self-gravitation to form the galaxies and clusters of galaxies we see in the present epoch.

Yet massive neutrinos resolve the problem very naturally, says Szalay.

Neutrinos interact only very weakly with baryonic matter, he explains. Only at extraordinarily high densities and temperatures can the two kinds of particles remain in thermodynamic equilibrium. Thus, in the cooling, expanding universe, neutrinos decoupled from other particles within 1 second of the Big Bang; these are the relic neutrinos.

Assuming that these neutrinos had masses in the 10 electron-volt range, Szalay and co-workers calculate that within a few hundred or perhaps a few thousand years, they would have begun coalescing under their own mutual gravitation. The baryons were helpless to follow, however. Bathed in high-energy photons, they persisted as a smooth, equilibrated plasma for the next 100,000 years. But after recombination, says Szalay, with the photons decoupled and the now-neutral atoms free to go their own way, they would have fallen into the ready-made potential wells of the neutrino clumps. Baryonic matter would then have proceeded to form galaxies and groups of galaxies much more rapidly than it could have on its own.

It's even possible to estimate the scale on which this clustering took place, says Szalay. For a density fluctuation to grow, its self-gravitation had to overcome the thermal motion of the neutrinos, which tends to smear things out. By calculating the interplay of these two effects within an expanding universe, Szalay and his co-workers find that neutrino clumps first began growing at scales roughly 60 million light years—a size typical of superclusters of galaxies, the largest associations of matter now known. Moreover, Zeldovich has shown that large-scale random motions would make globular clumping of the neutrinos highly unlikely. Far more typical would be thin, sheetlike structures, which Zeldovich calls "pancakes."

Evidence has been accumulating in recent years that matter in the universe is indeed arrayed in a kind of cellular pattern, Szalay points out. The superclusters do tend to be flat, rather than globular; they form membranous "cell walls" around immense voids.

So what does the neutrino mass give to astrophysics? Szalay asked in closing. It provides a high-density universe, perhaps with enough neutrino mass to close the universe. It provides the missing mass, at least for the galactic clusters. It allows deviations in the 3 K background radiation to be small, while matter fluctuations in the universe are large. It provides a characteristic mass and distance scale for superclusters, and it predicts a cellular structure for the large-scale distribution of the galaxies. "This one small fact changes a lot of astrophysics," he says.—M. MITCHELL WALDROP