## Seeing All There Is to See in the Universe

Deep in the night sky is a veil of objects that are very faint and very blue; they may be galaxies just coming into existence

BY LOOKING DEEPER INTO THE UNIVERSE than optical astronomers have ever looked before, a team of American and Canadian researchers\* has shown that the night sky is littered with faint blue objects that appear to be galaxies in the act of formation.

"We can now see literally all there is to be seen [at optical wavelengths]," says team leader J. Anthony Tyson of Bell Laboratories. "Light from any earlier luminous phase would have been red-

shifted to infrared wavelengths."

Other astronomers familiar with the work are quick to warn against overinterpreting the data-as does Tyson himself. But they are equally quick to agree that this kind of deep imaging research has the potential for bringing some much-needed clarity to our understanding of the formation and evolution of galaxies, not to mention our understanding of cosmology in general. "I'm pretty conservative, but I think it's really suggestive," says John Huchra of the Harvard-Smithsonian Center for Astrophysics. "This is high-class stuff."

This particular line of deep imaging research had its beginning in 1983, when Tyson and Patrick Seitzer of the Space Telescope Science Institute set out to push the available imaging technology to its theoretical limit. Their targets included 12 different areas of the sky, each covering about 2% of the area of the full moon, and each showing blank on the most sensitive photographic plates. To collect the light they used the 4meter telescope at the Cerro Tololo Interamerican Observatory in Chile, making 6hour exposures of the fields in each of three wavelength bands. To record the resulting images they used a solid-state charge-coupled device (CCD) detector, which comes close to being able to detect individual photons. And to analyze the output they used new image processing software being developed at Bell Laboratories and the National Optical Astronomy Observatories.

The upshot was that by 1986, Tyson and Seitzer had obtained strong evidence for what earlier observations had only hinted at: these "blank" areas are thickly sprinkled with very faint, very blue objects so numerous that they often overlap.



**The universe in depth.** In this negative print, which covers an 11-square arc-minute area in the constellation Sextans, essentially every black spot is a distant galaxy. The faintest images visible are about 28th magnitude.

The obvious and tantalizing interpretation was that these "blue fuzzies" are very young galaxies being lit up by their first frantic episodes of star formation; their blue color would then be the ultraviolet radiation of newborn stars, red-shifted into the visible spectrum by cosmic expansion. Obvious or not, however, this interpretation was far from ironclad. So Tyson, Seitzer, and their colleagues have accordingly spent the past few years on data analysis and followup studies. Their findings are now being published in a series of papers that begins with an article by Tyson in the 1 July issue of *Astronomical Journal*.

To begin with, asks Tyson, are these objects real? He thinks so: when the Cerro Tololo fields were reexamined from the Canada-France-Hawaii telescope on Mauna Kea, every object brighter than 27th magnitude was seen in both. All in all, says Tyson, he and his colleagues have counted more

than 25,000 blue fuzzies in their images. Assuming that there is nothing unusual about these particular 12 fields—which were essentially chosen at random—this corresponds to roughly 20 billion such objects in the entire sky.

Next, are these blue fuzzies really newborn galaxies, or have the images actually turned up a previously unknown class of dim dwarf galaxies lurking relatively nearby?

This is the first and most important objection that skeptics raise. "The problem is that we have absolutely no accurate census of the volume density of little things," says Huchra. "Tony has produced images of these objects that are *probably* galaxies. But we have no idea of what they really are." The crucial missing step is to obtain spectra for the blue fuzzies, which would allow the researchers to measure the objects' red shift and thus to pin down their distances. As Richard Kron of Yerkes Observatory points

> out, "You can't make any definitive progress until you have spectra [down to the faintest limit]. I wouldn't believe any claims at all until then."

> As it happens, Tyson and his colleagues have attempted to do just that. Given that it is much harder to obtain the spectrum of a faint object than to image it, unfortunately, they have only gotten down to objects of magnitude 23. Nonetheless, they still find red shifts in the range of 0.8 to 3, which means that even the brighter blue fuzzies are as far away as most quasars.<sup>†</sup> Add in circumstantial evidence, says Tyson, such as the fact that the blue fuzzies are much bluer

than known dwarf galaxies, and he, for one, is convinced that the dwarf-galaxy alternative is dead. "We've ruled out the hypothesis," he says.

Be that as it may, the evidence is certainly suggestive enough to go on to the final question: assuming that the blue fuzzies are indeed newborn galaxies, what can they tell us about the early universe?

First, says Tyson, we are definitely seeing evolution: the data suggest a sharp falloff in the number density of these galaxies beyond red shifts of 3. (The survey could have detected them out to a red shift of about 7.) The implication is that at larger red shifts that is, at earlier times—the primordial gas that was collapsing to form galaxies had not yet grown dense enough to form stars.

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<sup>†</sup>An object at a red shift of 3 is receding at approximately 88% of the speed of light. We are seeing it at a time roughly 2 billion years after the Big Bang, when the universe was one-eighth its present age.

Second, says Tyson, there is probably not much more to be seen at optical wavelengths, even at very high red shifts. To begin with, the total light from these objects already accounts for virtually all of the background light measured by astronomers in the "empty" sky. Furthermore, the total amount of stellar activity represented by the blue fuzzies is roughly what is required to produce the abundance of heavy elements seen in the universe today. (The key fact here is that all the elements in the universe heavier than hydrogen and helium are primarily made by nucleosynthesis in hot, young stars-the same kind of stars that make the blue fuzzies blue.) And finally, the 10% fraction of the sky covered by the blue fuzzies is strikingly close to the 15% fraction of quasars that show broad absorption lines in their spectra-absorption lines that are thought to result from galaxies lying along the line of sight.

Third, says Tyson, the statistics of the images begin to put some much-needed constraints on models of galactic evolution. For example, one can quickly rule out "star burst" models, in which most of the galaxies form their stars within a relatively short period of time. Such a flurry of activity would have shown up as a distinct peak in the distribution of galaxies plotted as a function of red shift, with the peak corresponding to the epoch of the star burst. And yet the peak simply is not there in the data.

"It's just inconsistent with starting off all the stars at the same time," says Tyson. "Galaxy formation doesn't take place like a horse race." Much more likely is some form of gradualism, he says, with galaxies achieving recognizable structure around a red shift of 4 and then continuing to form stars down to a red shift of 1. (That is, from roughly 1 billion years after the Big Bang to roughly 6 billion years after the Big Bang.)

And finally, says Tyson, once the process of galactic evolution is sorted out-no mean feat in itself-one can begin to address the broader cosmological questions. To take the most obvious and important question: currently fashionable models of cosmology call for a universe containing mass at a certain "critical" density that keeps it precisely balanced at the boundary between infinite expansion and an ultimate recontraction into a Big Crunch. Moreover, about 99% of that mass is supposed to consist of invisible ectoplasm known as Cold Dark Matter, which permeates the galaxies but interacts with them only by gravitation. The question is whether such a model can bring forth galaxies at the right time, around a red shift of 4. Computer simulations suggest that it can. Maybe. But things could be tight.

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In what would be the first experiment of its kind, two National Institutes of Health (NIH) researchers are proposing to insert a genetically altered cell into human beings. On 13 May the protocol, by W. French Anderson of the Heart Institute and Steven A. Rosenberg of the Cancer Institute, was approved by the NIH Institutional Biosafety Committee, the first hurdle for a recombinant DNA experiment. The protocol now moves onto the Recombinant DNA Advisory Committee, or RAC, for consideration.

Although it technically falls under the rubric of gene therapy, the proposed procedure is not, in fact, therapeutic. Rather, the genetically modified cells will be used to monitor the progress of an experimental cancer therapy that Rosenberg has been using since 1986. However, the same procedure could later be used as a means to introduce a therapeutic gene, say, a gene to repair muscular dystrophy, into the body; thus how it fares in the regulatory process, which could take a year or more, is certain to be closely watched.

The goal of the experimental cancer therapy, which this new procedure is intended to augment, is to beef up the patient's own cancer-fighting cells. To do so, a piece of a tumor is surgically removed, and the immune cells that are already invading it, the tumor-infiltrating lymphocytes, or TIL cells, are isolated.

Those cells are then multiplied by culturing them with interleukin-2, which is a growth hormone for white blood cells and is also toxic to tumor cells. After 30 to 50 days, the TIL cells, which now number in the trillions, are infused back into the patient, along with the interleukin-2, where the cells recognize the tumor and attack it.

To date, TIL therapy has been used on 25 patients, all of whom have very advanced cancers, either melanoma or kidney cancer, that have failed to respond to any other treatment. The patients treated are expected to live for only 2 months. In about half the patients the tumor regresses significantly, by 50% or more, following TIL therapy.

No one knows why it fails to work in the other patients, however, and that is what this new experiment is designed to find out. To date, the TIL cells have been labeled with a short-lived radioisotope, which allows their fate to be followed, but only for a few days.

What Rosenberg and Anderson are proposing is to label the cancer-fighting TIL cells instead by inserting a marker gene, in this case, a gene for neomycin resistance, that will be long-lasting. Indeed, it will be a stable part of the cell. Using a mouse retrovirus as a vector, the marker would be inserted into a few percent of the TIL cells. The altered cells would be combined with the larger batch of unaltered TIL cells just before they are given to the patient.

By monitoring the distribution of the TIL cells it should be possible to determine why the therapy works in some cases but not others. In the cases that do not work, is it because the TIL cells are no longer present at the tumor site, for instance, or because they have lost their effectiveness? It should also reveal whether there is a subset of TIL cells that are effective in attacking tumors. If so, then perhaps the therapy could be made more effective.

The experiment will not directly benefit the patients, but the risk to them should also be slight, according to the proposal. The retroviral vector, the N2 vector, has been modified so it no longer contains viral genes; thus, it is no longer infectious. However, the parent virus, the Moloney murine leukemia virus, does cause leukemia in mice, though there is no evidence, after over 2 years of study, that it induces cancer in primates. The researchers note that there is a "remote but finite possibility" that the viral vector could induce cancer through insertional mutagenesis.

If these first experiments work, the same approach, known as retroviral-mediated gene transfer, could later be used to enhance the effectiveness of the cancer therapy, by inserting the gene for interleukin-2 into the TIL cells. And, perhaps more important, it would open the door to other types of gene therapy long envisioned by Anderson and his colleagues around the world.

The protocol next goes to the RAC's human gene therapy subcommittee, which meets on 29 July, then to the full committee in October before going to NIH director James B. Wyngaarden for approval.