interband regions. But when they added the antibody to a Z form of a deoxycytosine and deoxyguanine polymer, the antibody would no longer bind to the *Drosophila* chromosomes—presumably it had already combined with the Z-DNA of the synthetic polymer.

What is the biological function of Z-DNA? "We think Z-DNA is one of the elements that regulate gene transcription," says Rich. There are four ways to stabilize the Z-DNA form. It can be methylated, proteins can bind to it (when antibodies bind to Z-DNA, for example, they stabilize it), it can have negatively charged molecules like spermidine bound to it, or it can be supercoiled. All of these ways to stabilize Z-DNA could operate in gene control systems.

"Some people would call this wild-eyed speculation," Rich says as a preface to his theories of how Z-DNA might act as a regulatory structure. But, clearly, Rich himself believes his speculations are not out of line. He proposes two types of control involving Z-DNA, proximal and distal control.

In distal control, the supercoiling of Z-DNA comes into play. "We know that DNA in chromosomes is normally supercoiled and that it is packed with minimal torsional stress," Rich explains. "When a region of Z-DNA is made to convert back to B-DNA, the DNA would have to turn more and so there would be more torsional stress and the DNA would open up, the double helix would unwind." He takes out a rubber band to demonstrate, twisting it tightly. "This is supercoiling," he says. Then he continues to twist and the two strands of the rubber band open up.

Rich proposes that when genes are turned on, regions of Z-DNA which previously were methylated lose their methyl groups. This would destabilize the Z form and the DNA would revert to B-DNA. As a consequence, DNA at some distance from the Z-DNA area would unwind and a so-called hypersensitive region would appear. These hypersensitive regions of DNA are extremely susceptible to degradation by enzymes that break down DNA, including S1 nuclease, which only attacks single-stranded DNA. They are known to appear upstream from genes that are active and to be necessary for gene activity (*Science*, 13 November, p. 775).

Proximal control, Rich speculates, is a bit simpler. He proposes that control regions of DNA adjacent to genes can be in B or Z form. When they are in Z form, certain proteins used in gene transcription cannot bind. When, through demethylation or through one of the other ways of converting Z-DNA to B-DNA, the control regions are converted to the B form, genes adjacent to them can be transcribed.

Now Rich is ready to start looking for evidence that Z-DNA is involved in gene regulation and is ready to look for evidence that gene transcription can be prevented if the Z-to-B switch cannot operate. Why is he so sure this is the way to proceed? "Well," he says, ever the optimist, "we've done some experiments." But, he cautions, he is not ready to discuss his results because "we haven't yet done the controls."—GINA KOLATA

Mauna Kea (II): Coming of Age

The Institute for Astronomy has grown enormously in the last 15 years —but its passage has not been easy

For nearly 18 years it has been John T. Jefferies' ambition to build the University of Hawaii into a world-class center of astronomical research—and, not incidentally, to create on the summit of Mauna Kea one of the great observatories of the world.

In 1965, when the National Aeronautics and Space Administration gave Hawaii the contract to build an 88-inch telescope on Mauna Kea, the university's entire astronomy program consisted of three solar astronomers working under Jefferies within the Institute of Geophysics. But it wasn't long before Jefferies was lobbying for a separate institute. "I felt we were going to grow to such an extent that we would have been disproportionately large within geophysics," he explains now, "and I felt that the specific needs of astronomy should be uppermost in management's mind." He was persuasive, and the Institute for Astronomy was formally established on 1 July 1967.

At first it was hard to hire anyone, Jefferies recalls. For one thing, there were many more jobs than applicants in those days. Worse, too many astronomers seemed to think of Hawaii as some kind of never-never land full of palm trees, pineapples, and tourists. They certainly did not see it as a place to live and to do serious astronomy. "We were engaged in a brand new enterprise in a location not noted for other cultural or academic advantages," Jefferies notes wryly. He was thousands of kilometers from any other graduate university, and in no position to attract academic superstars. So he began to staff his institute with people who were young and adventurous, some just a year or two out of graduate school.

Meanwhile, Jefferies was quietly urging other institutions to consider building telescopes on Mauna Kea. As an observatory site, he pointed out, it is unsurpassed for the clarity, dryness, and stability of its air, the darkness of its night sky, and its relative freedom from clouds.

Among the first to be convinced, in the early 1970's, were the Canadians and the French, who were planning a joint national observatory with a 4-meter class optical telescope. In 1973 representatives of the partnership came out to Hawaii to strike a deal with Jefferies: Canada and France agreed to split the cost of building the telescope; the University of Hawaii, which held the lease on the summit area, donated the land and agreed to build a permanent midlevel facility to house visiting astronomers and staff. Canadian and French astronomers would split 85 percent of the observing time while University of Hawaii faculty got the other 15 percent. Operating costs would be allocated in a like ratio. The Canada-France-Hawaii Telescope (CF-HT) Corporation was born. Completed in 1979, the $30-million, 3.6-meter CFHT is the most lavishly appointed telescope on Mauna Kea. The most obvious detail is an aerodynamically designed dome that looks disconcertingly like a stocky white mushroom—but which allows the CFHT to operate in 100-kilometer-per-hour winds. (The others have to shut down at 60 kilometers per hour.)

About the same time that Jefferies was negotiating with CFHT, he was also concluding a similar arrangement with the

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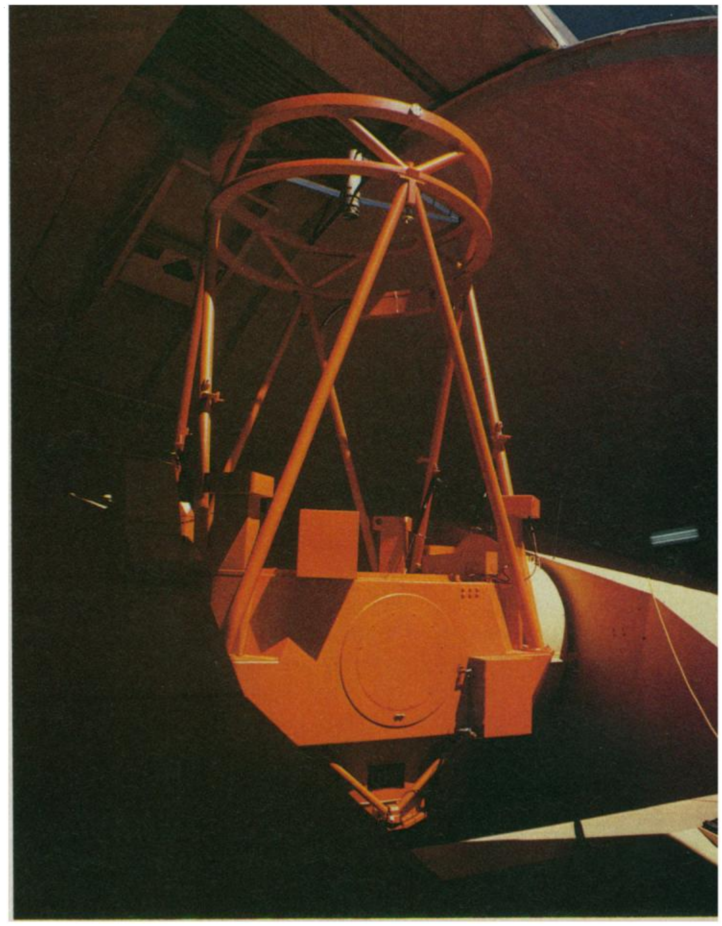
British for the United Kingdom Infrared Telescope, which was also completed in 1979. UKIRT features an advanced-technology, 3.8-meter mirror, made very thin to save weight (and money), but supported by a forest of computer-driven pistons that hold the light-gathering surface steady as the telescope moves.

The third new instrument on Mauna Kea is NASA's Infrared Telescope Facility (IRTF), whose history is a case study in the passions that the building of a new telescope can arouse.

In 1972 a National Academy of Sciences committee on the future needs of astronomy, chaired by Jesse L. Greenstein of the California Institute of Technology, gave high priority to the construction of a 3-meter class infrared telescope. The subject matter of such an instrument would be virtually limitless: planetary surfaces, protostars, gas and dust clouds in interstellar space, galactic nuclei—practically anything above a temperature of absolute zero radiates in the infrared. That same span of wavelengths, from red light at 6000 angstroms to the shortest radio waves at about a millimeter, also contains emission lines of such interstellar molecules as carbon monoxide, ammonia, and water. Moreover, infrared radiation penetrates interstellar gas and dust far better than visible light does.



The Infrared Telescope Facility

Because infrared photons are absorbed by water vapor in the lower atmosphere, however, the instrument would have to be located on some high, dry mountaintop. Because those photons reflect from a silvered telescope mirror just as visible light does, the instrument would look much like an optical telescope, but its framework would have to be carefully designed to keep the thermal glow of the telescope itself from overwhelming the dim glimmer of infrared photons coming down from the sky.

NASA was willing to fund such a telescope, primarily because of its importance for planetary astronomy, and in the early 1970's the agency commissioned Caltech astronomer James Westphal to survey potential sites in the United States, Mexico, and Chile. It quickly became apparent that Mauna Kea was by far the best. Not only was the air above the summit very dry, but its water vapor content showed little of the marked seasonal variations seen elsewhere. Moreover, there were long intervals in which the "sky noise" was essentially zero. (Sky noise is a measure of how the infrared brightness varies from point to point across the sky, as a function of time. Even on the coldest nights, the thermal emissions of the atmosphere are about a million times brighter than the objects astronomers are trying to observe; the greater the sky noise, the harder it is to pick out faint signals from the background.)

When Westphal's results were announced, however, some astronomers who had been advocating their own pet sites started denouncing his tests as "meaningless." Pointed (and cogent) remarks were also made about the difficulty of the logistics at such a remote site as Mauna Kea. And it was suggested that the tiny infrared group at the Institute for Astronomy was not among the best.

NASA's advisory committee on site selection for IRTF took such factors into account for all the sites. Arizona's Mount Lemmon rose to second place in its listing largely because of its proximity to Tucson and a large, vigorous community of infrared astronomers. But the committee's first choice was still Mauna Kea. In February 1974 NASA awarded the IRTF contract to the University of Hawaii.

At the Institute for Astronomy there were many people who did not want to get involved with IRTF, says Eric Becklin, who is now Jefferies' deputy in charge of the facility. "The institute was already involved with the CFHT. It was trying to get it's own 88-inch telescope working more effectively, it was going through all the growing pains of developing a new mountain—they were taking on too much, with too young and inexperienced a staff."

But Jefferies had worked hard to get IRTF. He forged ahead, setting his staff to work on detailed designs for the telescope with Charles W. Jones in Los Angeles, the same consulting engineer who had designed the 88-inch. Eighteen months later the designs had been finalized and the project was moving steadily toward its scheduled completion in 1977—when it was brought up short by a disaster 5000 kilometers away.

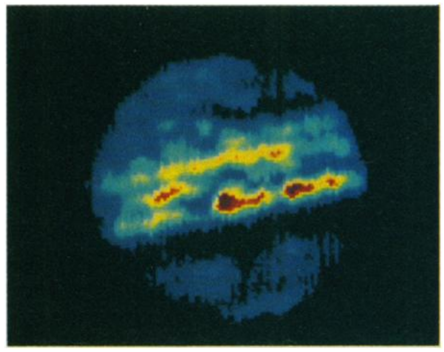
IRTF's mirror blank was one of several that NASA had procured for testing during the development of the Space Telescope, and the IRTF project had gotten it free. By late 1975 it had been transferred to Kitt Peak National Observatory in Arizona for grinding and polishing. The technicians had just bored the hole through the middle (through which light would pass into instruments mounted on the rear of the telescope) and had gone home for the Labor Day weekend. They returned to find a crack in the mirror, running radially outward from the central hole.

It was small comfort to anyone that such events are extremely rare. A new blank would cost hundreds of thousands of dollars; starting over with grinding and polishing would delay the project a year or more. To this day, no one knows what caused the crack, or who, if anyone, was to blame. The agonizing over how to save the old mirror was resolved when the manufacturer, Owens-Illinois, provided a second blank at cost. But meanwhile, the setback catalyzed a rising opposition within the infrared community to the whole project.

"About half the infrared astronomers wanted to cancel it," says Becklin. "It came down into camps: 'Tucson' versus 'Hawaii.' The Tucson side had a gut feeling that Hawaii's IRTF would never work well, that it would never produce major science, that it would siphon money away from other projects, and that it would certainly never be ready in time to support the Voyager Jupiter encounter in 1979, which had been one of its major rationales. They called it NIRD—the National Infrared Disaster." Other infrared telescopes were coming along—UKIRT, among others—and it wasn't even clear that IRTF was needed anymore.

Part of the skepticism may have stemmed from Hawaii's continuing problems with the 88-inch. Nearly 6 years after the telescope's completion, the Mauna Kea repair crews were still spending a good fraction of their daylight hours getting the telescope's cranky mechanical and electrical systems working well enough for the next night's observing. (The 88-inch had been a pioneering effort in computerized telescope guidance. Many of its problems were finally solved in 1976 by the simple, if expensive, expedient of ripping out the old electronics and starting over.)

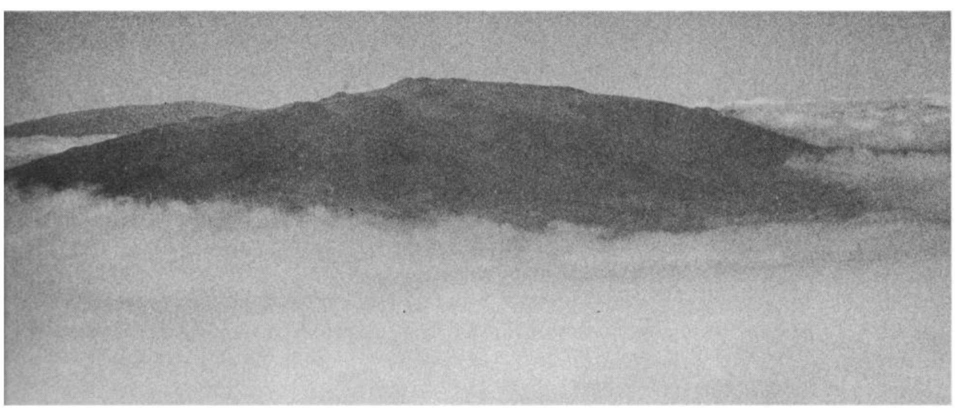
But more specific criticisms were aimed at plans for IRTF's mount. The members of NASA's design advisory committee, chaired by Fredric C. Gillett of Kitt Peak, were very unhappy, and their concerns were arousing the whole community.



Jupiter in the Infrared

Colors range from the cool blues to the warm reds of the "hot spots"

Ideally, an infrared telescope like IRTF or UKIRT should be able to make observations 24 hours per day. The atmosphere is already so bright in the infrared that moonlight or even sunlight does not make all that much difference. But observing in daylight means that the operator is forever pointing the telescope at things he cannot see. A few of the brightest stars are detectable as points of reference, but the operator might have to move the telescope as much as 15° from such a star to find the object of interest. Thus NASA had imposed the unheard of requirement that IRTF be able to move 15° from its guide star with a final pointing error of only 2 seconds of arc.



M. Mitchell Waldrop

Mauna Kea

The tropical inversion layer holds the clouds a kilometer or more below the summit. In the background is Mauna Loa.

Jones had convinced the Hawaiian group, and NASA, that he could meet this specification with a simple fork mount. In such a setup the telescope pivots between the tines of a giant, two-pronged fork whose "handle" is aligned with the earth's rotational axis. Once the telescope has been pointed, a simple rotation of the handle allows it to track its quarry across the sky.

But Gillett and his colleagues argued that such a mount would flex unpredictably. They wanted a much stiffer yoke mount, in which the telescope pivots within a closed frame supported at both ends. The upper support would block the telescope from pointing at the far northern sky, they agreed, but the arrangement would meet the specifications easily.

By the spring of 1975 the committee had made NASA headquarters acutely aware of its concern. But rather than delay the project the agency officials decided to go ahead with Jones' design—until Labor Day, and the cracked mirror.

No one will ever know if Jones' mount would have met specifications because it was never built. During the delay caused by the cracked mirror, NASA's Office of Space Science embarked on a complete reevaluation of the project and soon decided that this time it would listen to Gillett and his colleagues, not to Jones. Agency officials also decided to press for an upgraded facility, with more instrumentation than originally planned. If there were going to be expenses and delays anyhow, why not turn them into an opportunity?

Jefferies, however, would have to pay NASA's price if IRTF was to continue at Mauna Kea: Jones was out. The telescope would be mounted on a yoke. Engineers from Kitt Peak would do a new conceptual design for the upgraded facility, and an experienced manager, Gerald M. Smith of the Jet Propulsion Laboratory, would come to Hawaii to oversee the project during the construction phase.

"I was irritated by the high-handed way in which it was done," says Jefferies, "but I was very anxious that IRTF not disappear. It was in critical danger of doing just that." Ignoring the advice of disgruntled colleagues who were ready to abandon the project, Jefferies accepted NASA's terms as gracefully as possible.

Smith arrived in January 1976 and, looking back on it, Jefferies says he was delighted to have him. Smith displayed a tremendous diplomatic ability, says Becklin. "He overcame the initial negative feelings for him here, he straightened the project out, and he made John happy. From that point on there was a real reversal."

With the mount redesigned and a new manager in place, infrared astronomers started to pull behind the project. At a meeting in Tucson that spring they reassured NASA that IRTF was indeed worthwhile. The mood improved even more about a year later, when Becklin himself, already a well-known infrared astronomer, arrived to become IRTF's chief scientist. He and another new colleague, Richard W. Capps, formerly of Kitt Peak, have added considerable luster to the institute's infrared group.

"I feel badly that things got to the stage that it did," says Jefferies. "I feel the whole thing was handled ineptly on all sides. But I'm glad that we—most of us—put the project ahead of our feelings. The differences and controversies have long since healed over. Those of us who stuck with it have produced a fine facility, far better than it started out to be."

Dire prophecies to the contrary, IRTF was ready in time for the Voyager mission. It was dedicated in July 1979. Among the imaging targets during the Voyager 2 encounter with Jupiter that month were atmospheric "hot spots" that had been pinpointed by IRTF images at the 5-micrometer wavelength.

Shortly after the encounter, IRTF followed the volcanically active moon Io as it passed into Jupiter's shadow, and found that it stays warmer in eclipse than the other satellites. This could prove a good way of monitoring the frequency of eruptions. (Actually, this observation is not new to IRTF. Infrared astronomers could have predicted Io's vulcanism long before Voyager, had anyone realized what they were looking at.)

IRTF spends 50 percent of its time on solar system studies. The rest of the time it ranges farther. Becklin, Gareth Wynn-Williams, Reinhart Genzel, and Dennis Downes, for example, have been using IRTF to study the vast gas and dust clouds of Orion, of which the famous Orion nebula is a very small part. Only 1600 light-years away, the Orion complex has long been known as a kind of stellar nursery, in which cold clouds of hydrogen are slowly collapsing under the influence of their own gravity to give birth to new stars. The latest IRTF work—which includes a very high resolution map of the region at 20-micrometers wavelength—shows strong infrared emission from a cluster of perhaps a half-dozen discrete objects buried deep within the densest part of the cloud, just

FDA Approves Hepatitis B Vaccine

The U.S. Food and Drug Administration (FDA) last month approved a new vaccine for hepatitis B, a particularly debilitating form of liver disease. The vaccine, developed by Maurice R. Hilleman and his colleagues at the Merck Institute for Therapeutic Research in West Point, Pennsylvania (*Science*, 14 November 1980, p. 760), is produced from viral particles isolated from the blood of human carriers of the disease. These particles—called hepatitis B surface antigen (HB_sAg)—contain proteins that are recognized by the immune system. FDA Commissioner Arthur Hull Hayes, Jr., noted that the new vaccine is "the first completely new viral vaccine in 10 years and the first ever licensed in the United States that is made directly from human blood."

An estimated 80,000 to 100,000 new cases of hepatitis B occur in the United States each year, with a fatality rate somewhere between 1 and 2 percent. The incidence is much higher elsewhere in the world, particularly in Africa and Asia. As many as 10 percent of those infected become chronic carriers of the disease, displaying relatively high concentrations of HB_sAg in their blood serum. There are an estimated 800,000 carriers in the United States and more than 200 million throughout the world. The first step in production of the vaccine is collection of blood from such carriers at special donor centers throughout the country (the hepatitis B virus cannot readily be grown in culture). The HB_sAg is isolated via a 65-week cycle of purification and safety testing before it is available for use—by far the longest production and testing cycle of any vaccine now being marketed. The first batches of the new vaccine will not be available until mid-1982.

The vaccine is expected to cost between $75 and $120 for a series of three doses. It is not meant for the population at large, but for the roughly 10 million Americans considered at high risk of developing the disease—health care workers, drug addicts, sexually promiscuous individuals, and male homosexuals. FDA says that this targeted use could cut the incidence of hepatitis B in half.

The exceptionally long period of production and safety testing has been undertaken because of fears that a vaccine from human blood might contain viruses or other unwanted materials. This possibility could be eliminated by alternative ways of obtaining HB_sAg. The most promising route was revealed this summer by William J. Rutter and his colleagues at the University of California at San Francisco. They announced in August that they had induced yeast cells to produce a hepatitis viral coat protein, which then assembled with other molecules inside the yeast cell to produce HB_sAg particles. Rutter says that this is the first time that genetic engineering techniques have been used for production of a complex, biochemical structure that probably combines protein, sugar, and fat-like molecules.

Other investigators, including Walter Gilbert of Harvard University, Pierre Tiollais of the Pasteur Institute in Paris, and Kenneth Murray of Biogene Company in Switzerland have also inserted the gene coding for HB_sAg into bacteria such as *Escherichia coli*. The bacteria do not glycosylate (attach sugar molecules to) the proteins, however, and proteins isolated from such preparations are not as immunogenic as those isolated from yeast.

Some investigators, particularly Arie J. Zuckerman of the London School of Hygiene and Tropical Health, have been critical of the use of vaccines prepared from intact HB_sAg particles. Zuckerman argues that host proteins or other cellular components embedded in the particles may themselves be deleterious to the liver or may provoke other unwanted side effects. Zuckerman and his colleagues have developed a new technique that uses detergents to disrupt the HB_sAg particle and affinity chromatography to isolate two proteins, one of which is glycosylated. They reported earlier this year [*Nature (London)* **290**, 51 (1981)] that when the two proteins are recombined in a micellar preparation they are much more immunogenic in mice than are the HB_sAg particles themselves. Zuckerman speculates that his relatively simple technique could be used with HB_sAg particles obtained from humans or by genetic engineering techniques to produce a second-generation hepatitis B vaccine that could be produced more rapidly and cheaply and that would provoke fewer side effects.

—THOMAS H. MAUGH II

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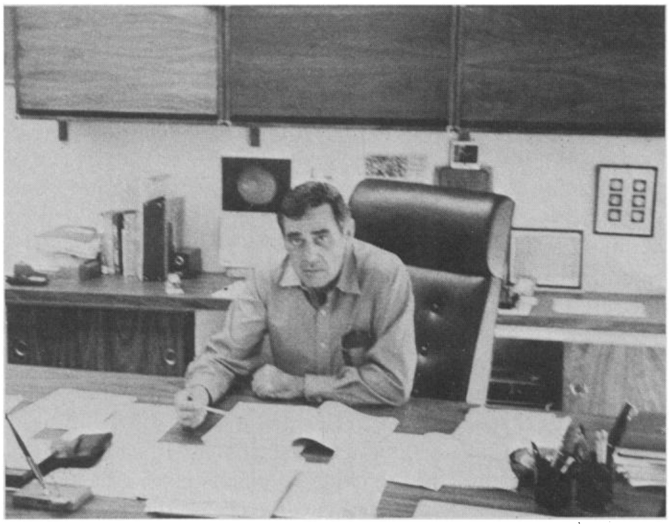

John T. Jefferies

behind the visible nebula. The researchers believe that these objects are very young, dust-shrouded stars expelling fast-moving streams of gas—stars so young that they have barely begun to shine by nuclear fusion.

Looking farther from home, Ian Gatley of UKIRT, Becklin, and Hawaii's Charles M. Telesco have made new high-resolution maps of the central parsec of our own galaxy at 10 to 30 micrometers. They see a peak of temperature centered like a bull's-eye on the galactic core—possible new evidence, says Gatley, that the core is occupied by an immensely massive black hole. In fact, a group at Berkeley has been able to model the observations by assuming a black hole of 3 million solar masses that swallows surrounding material at the rate of 10^{-5} solar mass per year. "The 30 micrometer galactic center work is a good example of why infrared telescopes were built on Mauna Kea," says Gatley. "Before, you had to fly in an airplane to do this kind of thing."

"It's very important," adds Becklin, "that when you're developing a department or a program, you exploit the unique quality of the site. Because that's what excites people, what makes for a growing, vibrant situation." Thus, the Institute for Astronomy's infrared program has flourished with the advent of IRTF and UKIRT. Jefferies now counts six infrared specialists on his staff and a number of others who are actively involved with infrared research.

The same thing is happening with extragalactic astronomy because of the dark sky and excellent seeing on Mauna Kea. Alan Stockton, for example, has spent a great deal of time at the 88-inch working on quasar redshifts. The question about quasars has always been whether they are extraordinarily bright and far way, with redshifts due to the expansion of the universe, or dimmer and close by, with redshifts caused by some unknown new physics. Stockton investigated the question by taking very long time exposures of quasars and the much fainter, normal galaxies around them, relying on the dark sky and the seeing to distinguish the galaxies from the background. And when he measured the redshifts he found that galaxies and quasars that were nearby on the sky had identical redshifts. "It is probably the strongest support for the idea that quasar redshifts are cosmological," says Sidney Wolff, associate director of the Institute for Astronomy.

The completion of IRTF, CFHT, and UKIRT has given Mauna Kea a curious ambiguity. It is far from being a single unified institution like Kitt Peak. But it is also far more than a random collection of telescopes.

For historical reasons the offices of UKIRT are in Hilo, near the airport. The offices of CFHT are an hour-and-a-half's drive away in Weimea, in the cool, grassy uplands on the dry side of the island. The Institute for Astronomy is in the Manoa suburb of Honolulu, adjacent to the main campus of the university. Everybody says it would be nice if they could all be next door and have seminars together, but nobody seems to want to move. The dream of a single, integrated astronomical community remains elusive.

Yet, on the mountain itself the various organizations share shop facilities, spare parts, dormitories, a mess hall, and camaraderie. UKIRT staffers often observe at IRTF, and so on through all the permutations. Perhaps it is the chill desolation of the summit area, the sense of remoteness. The people who work there say they feel like part of a team.

The telescopes are also united by the Institute for Astronomy, the one institution that is part of all of them. If Jefferies has not yet achieved his goal of making it a world-class research center, he has brought it a remarkably long way from its beginning. "Bearing in mind that we have no 'superstars,' " says Dale Cruikshank, "we can hold our own with any university-based faculty in the country."

"Look around you," adds Robert Milkey, the institute's assistant director for administration. "There's the new building [a $3-million structure completed in 1975]. We have a scientific staff of 30, and each nighttime observer has as much as 20 nights of telescope time per year. We have the 88-inch all to ourselves. We have pieces of CFHT, UKIRT, and IRTF. That's quite a resource."

Much remains to be done, however. The mountain is still very difficult to reach (the original jeep road to the summit has yet to be paved). The observatories at the summit are still powered by diesel generators, and the plywood eating and sleeping facilities at Hale Pohaku still resemble a not-very-prosperous dude ranch in the Sierra foothills. But the environmental controversies that have slowed further improvements are now close to a resolution. (Not everyone on the island of Hawaii is enchanted with the sight of little white dots on their mountain.) And a comprehensive plan for the future development of the summit is now close to approval.

Jefferies looks forward to seeing five and perhaps eight new instruments on Mauna Kea by the end of the century. The summit has plenty of room, he points out. Already proposed are the University of California's 10-meter telescope, twice the diameter of the Mount Palomar instrument, and a 15-meter behemoth called the New Technology Telescope. Also, the California Institute of Technology, the National Radio Astronomy Observatory, and the United Kingdom are each planning radio telescopes on Mauna Kea for observations at submillimeter wavelengths. Assuming that there will be money for any new construction in the 1980's and 1990's, most of the major new American telescopes planned for those decades will be built here.

"The quality of the site is high," says Cruikshank. "The quality of the instruments is high. The quality of the work is good and getting better rapidly. There is every indication that Mauna Kea will become one of the great observatories of the world. And in retrospect, I think John Jefferies will be remembered, on a level with George Ellery Hale, as one of the great observatory builders."

—M. MITCHELL WALDROP