repair mechanisms. In addition, carbon beams scatter less—just 3 mm at 27 cm depth in the body, the maximum required to reach most tumors—compared with 13 mm for protons, says Lidestri. That makes for a sharper scalpel and a smaller "lateral penumbra" of damage to surrounding tissue. It also permits more precise beam scanning—so-called painting—to cover the entirety of the tumor mass.

Both protons and carbon ions can treat complexly shaped tumors such as those growing around the spinal cord, where a dose distribution that has a hole in the center can be created, says Jäkel. Carbon-ion beams can be more precisely shaped. Other cancers where carbon treatment is indicated in Germany include skull and brain tumors and a type of salivary-gland tumor.

In Japan, carbon-ion treatment is indicated for a long list of tumors. As of March, of the 14 000 patients that were treated with carbon ions at the Chiba center, prostate cancer was by far the most common, followed by bone and soft tissue, lung, head, neck, lacrimal, pancreatic, and liver cancers and postoperative recurrences of rectal cancers. Prostate cancer, for one, generally responds very well to conventional radiation therapy.

Lidestri notes that 50% of all current cancer patients will receive some form of radiation therapy, and about 15–20% of them are candidates for proton therapy, he says. About 12–13% of proton candidates might better benefit from carbon ions, he estimates. "I'm very careful to say that carbon-ion therapy isn't a silver bullet. It's just a different tool."

One tantalizing implication from Japan's positive results with pancreatic-cancer patients is an observed long-term reduction in metastasis. "The relatively long time from first diagnosis implies that carbon ions are doing something that's improving the metastatic disease problem," says Brenner. "In general, radiotherapy is aimed at the primary tumor, and the goal is to eradicate the tumor cells. If carbon ions are doing something good in two or three years, that tells us that something different is going on."

Cancer grows because it can remain undetected by the immune system. In theory, the prevention of metastasis comes from the carbon-ion-induced double-strand breaks, which somehow create a new signaling path for the immune system to recognize cancer cells throughout the body, says Beltran.

But advanced cancer-treatment modalities other than carbon-ion therapy, including nonradiological ones, are also progressing. NCI has devoted "many millions" to support clinical trials comparing protons to photons, notes Buchsbaum, and it is currently funding four grants totaling between $20 million and $25 million over five years for studying helium- and carbon-ion beams in cells and animal models. NCI paid to have heavy-ion beams at Brookhaven and the Italian center qualified for those experiments. "NCI is supportive of carbon therapy; we've put a lot of money into the research," Buchsbaum says.

Nonetheless, he says, carbon ions need to be evaluated in the context of all other treatment types. "The rest of the world hasn't stood still. There's [chimeric-antigen-receptor] T-cell therapy, immunotherapy, drug therapy, and better surgery. Carbon therapy isn't competing in the same world as when Berkeley was doing experiments."

David Kramer

New telescopes seek the cosmic dark ages

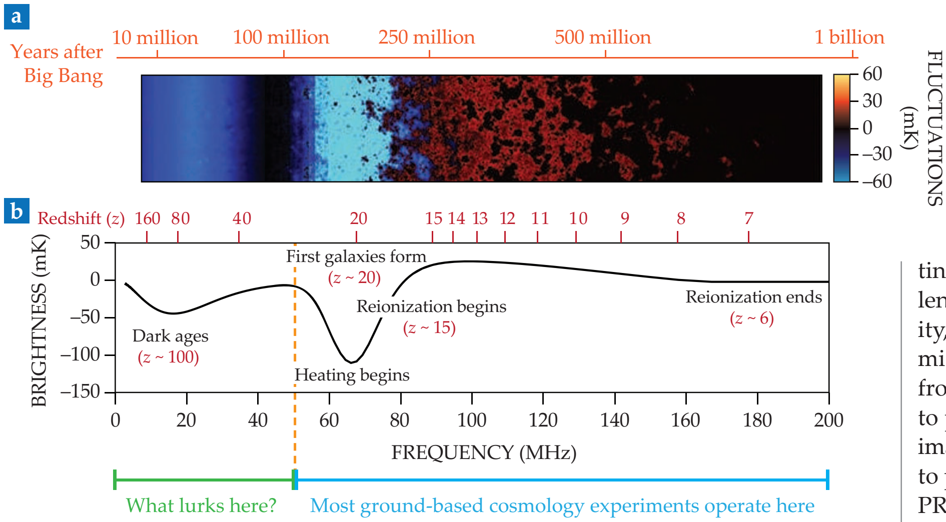
Radio astronomers look to far-flung locations to detect low-frequency signals that emanate from the ancient universe.

While reading an in-flight magazine article in 2016 about biodiversity on South Africa's Marion Island in the subantarctic Indian Ocean, the cosmologist Cynthia Chiang became intrigued by its remoteness and relative ease of access. Then a lecturer at the University of KwaZulu-Natal in Durban, Chiang submitted a proposal to the South African National Antarctic Programme to conduct the first astronomy experiment on the isolated island. The program, which typically supports climate, weather, and biodiversity studies at the island's research base, agreed to fund it. Now that ongoing experiment is part of a bigger effort to detect the faint, low-frequency radio signals that theorists predict would come from the earliest periods of the universe.

Shortly after the Big Bang, the universe cooled enough for the first neutral atoms to condense and release photons, creating the cosmic microwave background (CMB). Cosmologists refer to the interval between the formation of the CMB and the appearance of the first stars as the "cosmic dark ages." During that period, the universe consisted mostly of neutral hydrogen gas. As a hydrogen atom relaxes from one energy level to another through the flip of an electron spin, it releases a low-energy photon at a wavelength of 21 cm, corresponding to microwave radiation at 1420 MHz. As the universe expanded, that early radiation was redshifted to extremely low radio frequencies. Tuning radio antennas to detect the redshifted hydrogen line at frequency bands below 50 MHz is the only known way to map the distribution of matter in the dark ages (see figure on page 26).

Observing below 50 MHz presents a major challenge because the extremely faint signals are obscured by human-generated radio-frequency interference (RFI) and by radio noise from radiation in the Milky Way and the solar wind interacting with Earth's atmosphere. But it offers a big payoff: Radiation from the cosmic dark ages is unaffected by other astrophysical sources and could provide an untainted map of the early universe's structure. In contrast to the CMB photons, which all originated simultaneously, traveled to Earth uniformly from every direction, and provide a two-dimensional snapshot of the universe's surface at that moment, the dark ages signal contains 3D information. Because the hydrogen emitted radiation over a long period, measuring fluctuations in the signal can establish the distance to each point of emission.

Obtaining upper limits on 21 cm fluctuations during the dark ages could provide powerful constraints on theories about fundamental aspects of our universe, including inflation and exotic dark matter. The 2021 report *Pathways to Discovery in Astronomy and Astrophysics for the 2020s*, by the National Academies



COSMIC DARK AGES. Probing the cosmic dark ages and the first several hundred million years of the universe's history involves detecting the redshifted 21 cm emission from the hydrogen that permeated the ancient universe. **(a)** This timeline shows the evolution of fluctuations in the 21 cm brightness. **(b)** This graph presents the frequency and average brightness of the redshifted 21 cm line in the universe's early epochs. (Adapted from J. Pritchard, A. Loeb, *Nature* **468**, 772, 2010.)

of Sciences, Engineering, and Medicine, stresses the importance of overcoming technology challenges that stand between us and several hundred thousand years of cosmic history. To detect those faint signals, experimental cosmologists are now taking steps to establish radio antennas in locations free of RFI, including in the Arctic, on the Moon, and in space.

Radio challenges

"When scientists first started doing 21 cm low-frequency astronomy, they described it as doing astronomy from the bottom of a swimming pool," says Jonathan Pritchard, a theoretical cosmologist at Imperial College London. That's because Earth's ionosphere reflects and refracts radiation at those frequencies. The result is a distorted, wobbly sky that makes picking out faint low-frequency signals nearly impossible.

One way to detect the redshifted 21 cm line is with a single dipolar radio antenna that measures the average signal over a large swath of sky. Complicating that technique are radio emissions from galaxies between the source and the receiver. It's hard to know if the signal is real, says Philippe Zarka, an astrophysicist at the Paris Observatory. "With just one antenna, galactic foregrounds are all mixed together."

The other established method to detect the 21 cm line uses an antenna array that measures the correlations of signals recorded by different antennas. "You can make resolved images of the sky, where you see the point sources," says Zarka. Analyzing power spectra of the sky background at different frequencies, after detecting and removing the foreground, he explains, could make it possible to detect fluctuations in the remaining cosmological signal.

Few telescopes have surveyed the radio sky at tens of megahertz. State-of-the-art ground-based measurements date from the 1950s, when pioneering radio astronomer Grote Reber caught glimpses of the 2.1 MHz sky at 5° resolution from an antenna array that he built in Tasmania. In 1974 the *Radio Astronomy Explorer-2* lunar orbiter made observations at 4.7 MHz with a resolution of 10°. And in 1976 and 1999, the Dominion Radio Astrophysical Observatory in Canada surveyed the northern sky at 10 MHz and 22 MHz, with 2° and 1.5° resolution, respectively. Modern radio antenna arrays can make observations with resolutions of less than 1° but only at much higher frequencies.

"Background noise has been the limiting factor for many surveys to date," says Chiang, who is now at McGill University in Montreal. Her Marion Island astronomy proposal led to a field study to measure emissions in a range of 50–150 MHz, corresponding to the time when hydrogen was beginning to heat up as the first stars formed. The name of the experiment was Probing Radio Intensity at High-Z from Marion, or PRI^{Z}M.

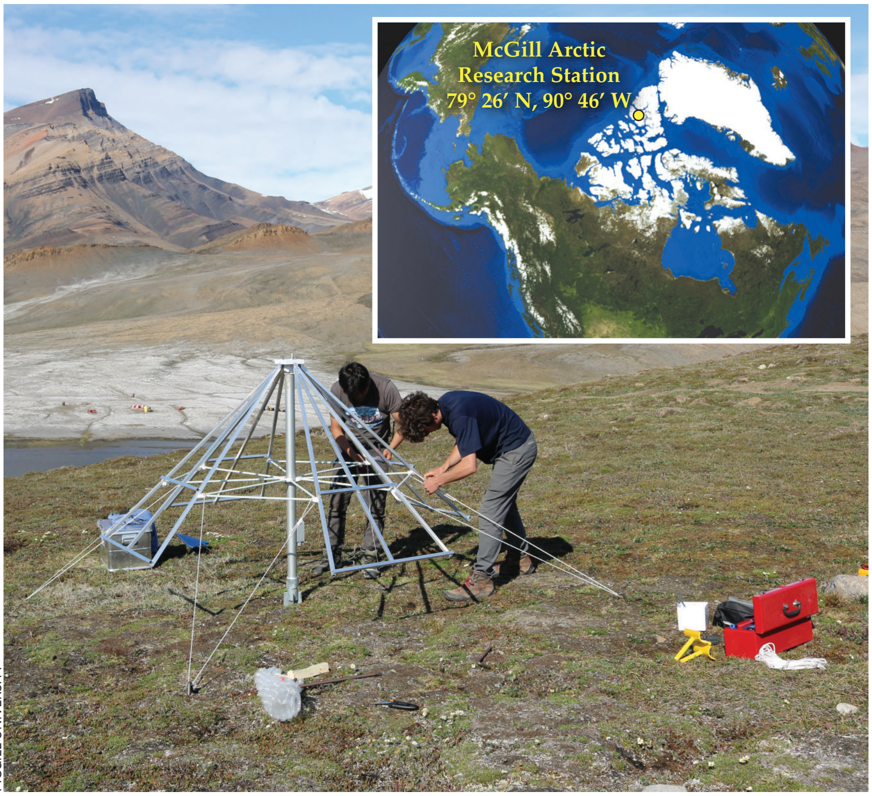
One of PRI^{Z}M's goals was to learn about RFI in the remote setting of Marion Island. Logistical challenges included once-per-year accessibility, harsh weather, and wire-chewing mice. But unparalleled low-RFI spectra from the experiment led Chiang in 2017 to propose an array of radio antennas to image the low-frequency sky. "We wanted to push toward the dark ages," she says. PRI^{Z}M led to the Array of Long Baseline Antennas for Taking Radio Observations from the Subantarctic, or ALBATROS.

Marion's quiet RFI environment and staff-supported research station made it ideal for ALBATROS. Pursuing yet more-remote locations, Chiang looked to expand the experiment from a latitude of 46° S in the subantarctic to the McGill Arctic Research Station, a seasonal field facility located on a Nunavut island at 79° N in northern Canada (see inset next page). Not only is the island far removed from terrestrial RFI sources, but the Arctic winter offers six months of darkness, without solar reflection from Earth's ionosphere.

With support from Natural Resources Canada's Polar Continental Shelf Program, the Canada Foundation for Innovation, and the National Sciences and Engineering Research Council of Canada, Chiang locked in a multiyear commitment in 2018 to set up 10 antennas at the McGill outpost. Making sure the instruments operate reliably is a challenge because "you can't have someone stay over winter in the Arctic to fix things," notes Taj Dyson, then an undergraduate at McGill who helped with the first test in Nunavut. (Dyson is now a graduate student at Stanford University.)

Off the grid

Chiang and her team began to build antennas based on a design originally developed for the Owens Valley Long Wavelength Array in California, and they added electronics to boost the response at low frequencies. The researchers installed the first two antennas this summer and intend to complete the array, consisting of the 10 antennas separated by up to 20 km, by 2025. A 2019 summer



MCGILL UNIVERSITY

STUDENTS INSTALL a dipole radio antenna at the McGill Arctic Research Station in the summer of 2019. The site is located 8 km inland at Expedition Fjord on the unpopulated Central Axel Heiberg Island of Nunavut (inset). The station consists of a small research hut, a cook house, and two temporary housing structures.

test run at the McGill Arctic Research Station established minimal human RFI from nearby sources. The only RFI detected was from the ionosphere.

During 2020 and 2021, the team developed an off-grid version of their antenna suitable for Arctic winter. On the Marion Island research base, solar panels and batteries could provide year-round electricity, but the dark Arctic winter precluded relying on solar power. So the researchers commissioned a specially designed hybrid system that combined solar panels and fuel cells and could power the antenna through an Arctic winter. Chiang and her team built a custom support structure (see photo at left) for the fuel cell case and solar panels that she "hopes will be able to survive being used as a scratching post by the occasional musk ox."

Because the Arctic wilderness cannot support power-hungry data servers, data storage poses another challenge for the team. Anticipating 100 terabytes of data each year for each antenna station, the researchers took a do-it-yourself approach and constructed shelves of hard drives plugged into a multiplexer. Each antenna will write to a drive until full, then switch that drive off and write to the next one. "Then we'll collect the hard drives and send home hundreds of terabytes in duffel bags," says Chiang.

Pritchard, the Imperial College cosmologist, expects valuable information about dark ages cosmology even if just one antenna survives the Arctic winter. "They'll learn a lot about what's going on in the ionosphere at these low frequencies and map galactic foregrounds in a way that will help with RFI removal more generally," he says.

To the Moon

While the Arctic may be one of the best places on Earth for radio observations, other researchers plan to take dark ages cosmology to the Moon. "Both terrestrial RFI and the ionosphere become negligible on the lunar farside surface," says Jack Burns, a cosmologist at the University of Colorado Boulder who works on the science and data analysis efforts on two

INTUITIVE MACHINES

THE *NOVA-C* lunar lander is scheduled to deliver a radio antenna to the Moon in early 2023 as part of a NASA project to peer into the universe's ancient past.

upcoming missions. Anticipating an RFI spectrum orders of magnitude cleaner than what's available on Earth, Burns and his colleagues in 2018 and 2019 successfully applied through a NASA program that has scheduled putting an antenna on the Moon by early 2023.

From a wide field of proposals, NASA's Commercial Lunar Payload Services project selected two proof-of-concept radio science experiments, led by Robert MacDowall at NASA's Goddard Space Flight Center and by Stuart Bale at the University of California, Berkeley. The first one will launch on a SpaceX Falcon 9 rocket to deliver instruments to the nearside of the Moon to investigate the solar-wind-induced plasma on the surface (see photo at left). The other experiment involves ferrying instruments for cosmological observations to the farside of the Moon, where batteries will power the antenna during the lunar night. Simulations have already identified potential radio-quiet landing sites with low RFI.

Yet another plan to measure the 21 cm line to study the dark ages involves launching satellites into lunar orbit. Xuelei Chen, a cosmologist at the National Astronomical Observatories of the Chinese Academy of Sciences, hopes to find even more ideal observing conditions in space. In addition to avoiding surface reflections, Chen points out one big advantage: "A satellite is simpler than a lander because you don't have to land!"

But space-based observations have their own challenges, including how to calibrate the proposed array of nine dipole antennas in orbit. And the orbiting antennas will require control over RFI generated by both the satellites and by the instruments themselves. Engineers also need to ensure efficient data communications between the satellites. And each satellite will require precise orbital-motion and flight information for interferometry calculations.

The sounds from the early universe will likely be very soft and easily lost in other noise. But according to Chiang, placing antennas in remote areas on Earth and in space will increase the odds of detecting an unambiguous signal that contains information about the origin of the universe.

Rachel Berkowitz PT