CubeSats set to tackle living systems, effects of deep space radiation

Stephen Battersby, *Science Writer*

Human beings will soon be heading into deep space again, decades after the Apollo missions. Out there, beyond Earth's magnetic shield, they will be exposed to intense radiation for months or years, a cosmic onslaught that could cause all sorts of damage. But a fleet of tiny bio-laboratories may offer up insights that will help protect future astronauts.

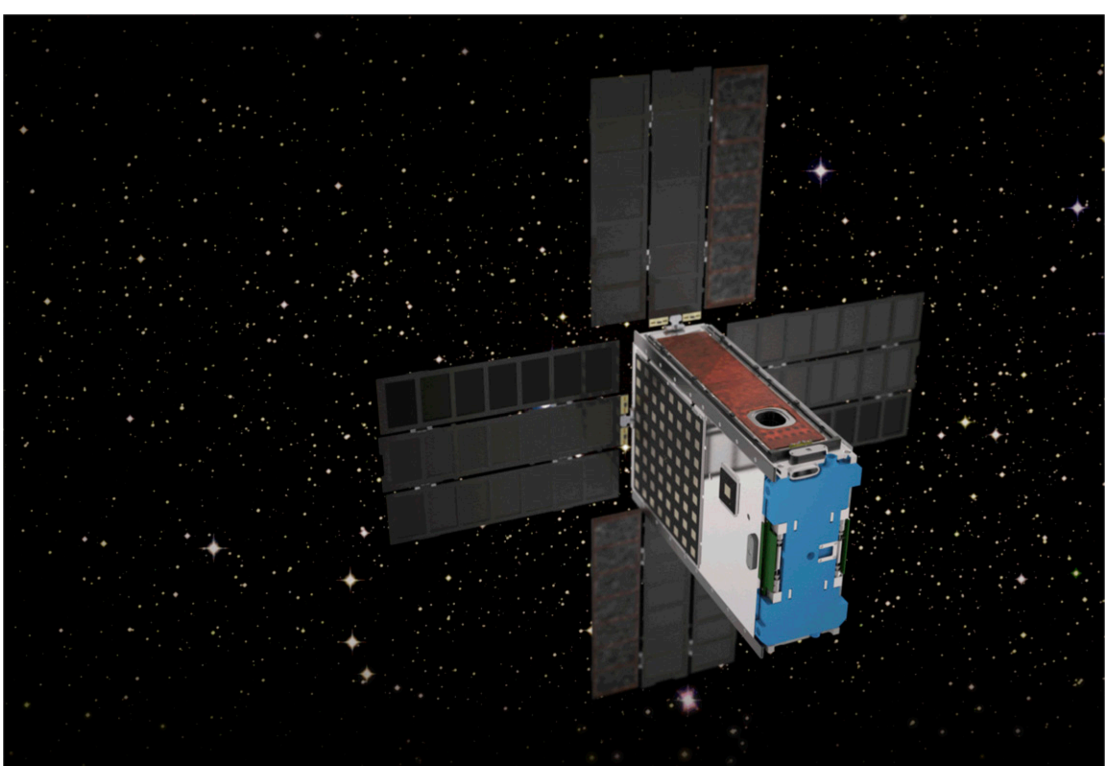
These intrepid explorers are CubeSats, built up from 10 × 10 × 10-centimeter units, in a somewhat standardized format originally laid out in 1999. CubeSats are cheap and quick to build, making them popular with telecommunications companies and scientists alike. In May, for example, a small fleet of CubeSats, called QB50, set off from the International Space Station to explore a little known layer of the Earth's outer atmosphere between 100 and 300 kilometers in altitude.

And now these tiny satellites are being adapted to pave the way for human missions to the moon, Mars, and beyond. These marvels of miniaturization will squeeze in samples, nutrients, plumbing, and even microscopes, to send back images and other data on suffering cells millions of miles away—all to help us understand and maybe reduce the pernicious effects of space radiation.

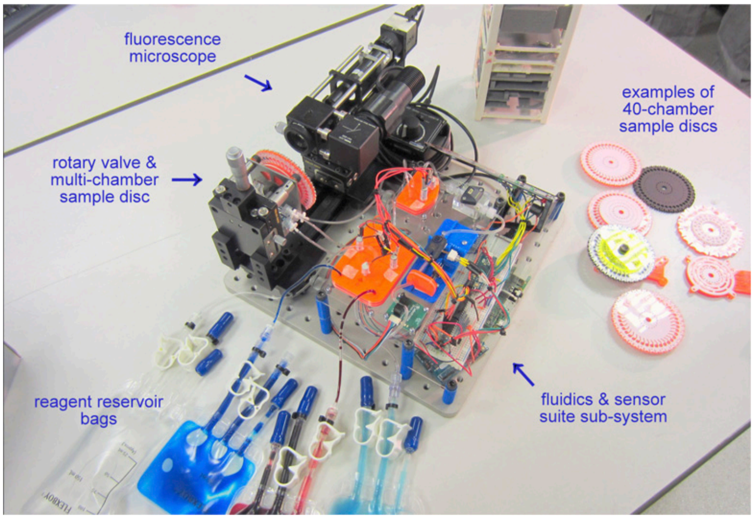
Small Sentinels

The first of these CubeSats should go up a year or two from now. BioSentinel is a six-liter spacecraft built at NASA's Ames research center in Moffett Field, California (1). "We at Ames have been the only ones clever or foolish enough to do live biology experiments on CubeSats," says payload technologist Tony Ricco.

So far the team has flown four biological CubeSat missions. One, O/OREOS, looked at radiation damage in a spore-forming bacterium, comparing their growth with identical samples held on Earth. Unfortunately, the spacecraft overheated toward the end of its mission, so there was no clear conclusion (2). "Radiation effects



BioSentinel, seen here in a conceptual drawing, is the first CubeSat aiming to investigate the pernicious effects of deep-space radiation. Image courtesy of NASA.



Despite their diminutive size, CubeSats that study the effects of radiation can include an array of instruments, as illustrated in this image of a bioscience platform called BAMMsat. Image courtesy of David Cullen.

were probably subtle, and we couldn't tease them apart from thermal impacts," says team scientist Sharmila Bhattacharya. "But the mission gave us an inkling we could do this kind of thing, and paved the way for BioSentinel."

BioSentinel is a much more ambitious project, flying far beyond the confines of low earth orbit. It should take off in late 2018 or early 2019 as part of Exploration Mission 1, the first outing for NASA's new Space Launch System. Exploration Mission 1 will carry an unmanned Orion capsule to the Moon and back, while a cluster of CubeSats rides piggyback, including BioSentinel, which will be sent into its own independent orbit around the Sun, a little closer than Earth.

High Radiation

Missions like this one will help scientists understand the damaging effects of deep space radiation. NASA has plans to send astronauts out to an asteroid by the late 2020s, and on to Mars in the 2030s. China and Europe have held talks about collaborating on a lunar base. Whereas the Apollo missions of the 1960s and 1970s only lasted days, the new plans involve spending months or years exposed to the harsh radiation of deep space. And we don't fully understand what that might do the frail human frame.

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>
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Most of our knowledge of radiation effects comes from nuclear industry workers on Earth, and records from Hiroshima and Nagasaki. All of these sources involve exposure to electrons, γ-rays, and α-particles at relatively low energies, up to a few million electron volts.

Space radiation is very different. Here, the main enemy is high-energy protons. Solar flares can accelerate some protons up to energies of hundreds of millions of electron volts, which can arrive in sudden blasts so intense that they could cause acute radiation sickness in unprotected humans. Then there are galactic cosmic rays: a steady flux of protons from beyond our solar system with energies that may be many trillions of electron volts, which are difficult to shield against. Both solar protons and cosmic rays present a cancer risk.

Experiments on Earth can only go so far. "Radiation in space covers an enormous range of energy, and you can't simulate that on Earth," says David Cullen at Cranfield University in the United Kingdom, who is developing a space-going bio laboratory platform called BAMMsat (Bioscience, Astrobiology, Medical, and Materials) (3). Particle accelerators can only generate protons over a fairly narrow energy range. "There might be issues from simultaneous exposure to different parts of the spectrum," says Cullen. It's vital to get better data in to set new astronaut exposure limits for voyages to Mars and elsewhere. "If we can raise these limits, we could have a massive impact on reducing mission costs," he says.

Experiments on the International Space Station and other orbiting spacecraft can add to our knowledge, but these are also limited. Earth's magnetic field shields astronauts in low orbit from most solar protons and many cosmic rays. Extrapolating to the deep-space environment can only be done by making assumptions. "We want validation in deep space, to highlight where these assumptions are false," says Cullen. CubeSats are the only affordable way to provide this validation.

Yeast in Space

BioSentinel will carry dried yeast cells to give early indications of radiation's cancer-causing effects: *Saccharomyces cerevisiae*, the same species we use to make wine and beer on Earth. These little passengers will cling to the walls of 288 tiny chambers known as microwells. Drying them out helps to keep them viable, but they have to stay cool too. "You might be familiar with keeping dry yeast in your fridge for years," says Ricco. There is not enough room or power for a fridge on board, so the spacecraft will chill one side—where the yeast lives—by keeping it pointed away from the Sun and into the blackness of space.

Once in deep space, fermentation begins. "There are fluid connections to the top and bottom of each cell. When it is time to activate the yeast, valves open and pumps turn on to push water and nutrient in." Micropore filters ensure that yeast cells don't get washed away.

It is a remarkable feat to pack all this equipment—along with computing, power, and communications—into a box measuring about 30 × 20 × 10 centimeters, although sometimes the very smallness brings benefits. "One challenge is displacing air so you don't leave bubbles, which would affect our measurements," says Ricco. "So we use wells of small enough diameter that they fill by capillary action, which happens very smoothly without bubbles."

Light will shine through each little growing culture so that detectors can see what's happening. Yeast cells scatter infrared light, which reveals how many are in each well. Meanwhile, blue and green light reveal a dye that is sensitive to the cell's metabolic activity.

Yeast doesn't get cancer of course. But because it's eukaryotic like human cells, yeast can still tell us about the basic processes of radiation damage—with regard to DNA-repair mechanisms in particular. The NASA Ames team will compare the growth and metabolic rates of yeast on BioSentinel with samples on Earth—including some samples irradiated by particle accelerators—to calibrate the effects of deep-space radiation. They may also send up a strain of yeast that is genetically modified to require the amino acid lycine. Put on a lycine-free diet, this strain's samples will fail to grow until they have undergone and repaired a double-strand break in their DNA, fixing the impairment.

BioSentinel will be a great leap for yeast-kind, but Cullen wants to go further. He and his team at Cranfield are designing a system that will accommodate 40 samples of mammalian cells, with all of the plumbing required, and fit inside a two-unit CubeSat measuring just 20 × 10 × 10 centimeters: "flying humans in a shoebox" as he describes it.

The team has even developed a tiny fluorescence microscope to fly onboard. This could reveal how cells are repairing radiation damage, because researchers can attach the gene for producing green fluorescent protein to a gene for a particular DNA-repair mechanism. Using that information, researchers might identify potential drug treatments to improve the efficiency of DNA repair in space, perhaps protecting future astronauts.

Cubic Conundrums

There are still some unsolved problems, however. It's hard to keep mammalian cells inactive yet robust for the weeks or months of ground handling and prelaunch checks. "In the [laboratory] we'd freeze them at liquid-nitrogen temperatures; then they are stable for years," says Cullen. "That is not an option on CubeSats yet. We have some ideas of how to do it, but I'd prefer not to tell." In the meantime, such missions would have to pounce on any opportunity where they could hand the CubeSat over only hours or days before launch.

Another snag is that many of our tissues are replaced in a matter of days or weeks. These cells would soon fill up a small well and then die out, preventing researchers from seeing the effect of long-term exposure. So Cullen wants to find a way to repeatedly reseed a cell line, moving it to new wells. "That's work in progress," he says.

Bhattacharya notes that we may not need to send mammal cells to learn about genetic pathways important for humans. Instead, researchers could insert human genes into yeast. Even so, as Cullen points out, this will not replicate the complex interplay that occurs in a mammalian cell.

For now, though, yeast is our best emissary. The solar system's smallest microbrewery should soon be operating somewhere between Earth and Venus, helping to make space more hospitable for human explorers.

1 Ricco A, et al. (2016) The BioSentinel bioanalytical microsystem: Characterizing DNA radiation damage in living organisms beyond Earth orbit. *Hilton Head Workshop 2016: A Solid State Sensors, Actuators, and Microsystems Workshop*. June 5–9, 2016, Hilton Head Island, SC.

2 Nicholson WL, et al. (2011) The O/OREOS mission: First science data from the Space Environment Survivability of Living Organisms (SESLO) payload. *Astrobiology* 11:951–958.

3 Cullen D, et al. (2017) BAMMsat—A platform for beyond LEO space environments studies on biological systems in CubeSats and CubeSat-like payloads. *6th Interplanetary Cubesat Workshop*. May 30 and 31, 2017, Cambridge, UK.