UPWARD

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THE ISS & Household Products:

HOW P&G IS USING SPACE TO IMPROVE YOUR CUSTOMER EXPERIENCE

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Below, ISS Chief Scientist Julie Robinson discusses how the 2016 annual ISS R&D Conference served as a representation of the breadth, success, and forward momentum of space-based research. Some of the innovative research from this conference is also highlighted on pages 10-14 in this issue.

THE VIEW FROM THE CUPOLA

BY JULIE A. ROBINSON, NASA'S JOHNSON SPACE CENTER

Julie A. Robinson is the Chief Scientist for the International Space Station

The maturation of the International Space Station as a National Laboratory was on display at the recent ISS Research and Development (R&D) Conference in San Diego, California. This conference represents a broad focus across all disciplines that use the space station laboratory. It complements the different discipline-specific conferences that are attended by researchers that use the ISS by providing results across different disciplines from biology and physics to Earth science and technology development. I would like to take this opportunity to share some perspectives from the conference.

With record attendance, the conference drew a large number of users who have not done space research before. This is a key objective of the declaration of the ISS as a U.S. National Laboratory by Congress and of this unique conference. These potential new researchers came for information on past research results, facilities, and sources of funding. Their goal was not to answer questions of interest to NASA, but to make novel connections that would allow the ISS National Lab to contribute to the economy and quality of life on Earth.

Keynote addresses from innovative researchers and technology leaders were there to inspire creativity, including Dr. Eric Topol from Scripps University talking about translational medicine, Dr. Peter Diamandis of the XPRIZE Foundation talking about the future of technology, and Scott and Mark Kelly talking about the recent One-Year Mission to the ISS and the Twins Study with medical journalist Dr. Sanjay Gupta. A number of key results presented at the conference are summarized in this issue of *Upward*.

One thing that stood out across the conference was the type of partnerships that are growing and developing. The first is the partnership between NASA and the Center for the Advancement of Science in Space (CASIS), which manages the ISS as a National Laboratory. Across many different events and speeches by leaders at NASA, CASIS, and private companies, it was clear that the National Laboratory approach for the space station is facilitating economic development in low Earth orbit.

The international partnerships that are the core of the space station were also dynamic at the conference. One example is a special pre-conference meeting that was held by NASA and the Japanese Aerospace Exploration Agency (JAXA) to share information about unique Japanese facilities available to American researchers. Two teams of Japanese investigators also received awards for their innovative results in the past year. The five international partner agencies—NASA, JAXA, the Canadian Space Agency, the European Space Agency, and Roscosmos coordinate facilities to enhance capabilities for researchers around the world.

A third set of partnerships that showed their strength at the conference were the relationships between researchers, who may not know NASA's processes and approaches, and implementation partners—companies with the expertise to help researchers transfer Earth-based experiments to the ISS. It was clear that the productivity of the National Laboratory is linked to companies such as NanoRacks, Space Tango, Made in Space, Techshot, and Bioserve Space Technologies, and that these companies are helping to make it easier and faster than ever before to access the ISS National Lab. Under an initiative called RISE (Revolutionize ISS for Science and Exploration), NASA has been using feedback from companies such as these and streamlining requirements and processes to make space access simpler and more cost effective than ever.

Perhaps most exciting to me was the new set of funding partnerships that were developing and emerging at the conference. One of the key principles of the ISS as a National Laboratory is that Congress intended for funding from the private sector and other government agencies to provide part of the research support, while NASA would continue to fund exploration-related research and ISS operations. Conference attendees had the opportunity to participate in business-to-business sessions for pitching R&D concepts and business models for providing services in low Earth orbit. Between sessions, the conference space was filled with side meetings, as companies met and forged new business relationships and scientists traded observations and brainstormed new experiments. What an amazing week!

For more information on the annual ISS R&D Conference, visit www.issconference.org. ■

THE ISS & Household Products:

HOW P&G IS USING SPACE TO IMPROVE YOUR CUSTOMER EXPERIENCE

BY EMILY TOMLIN

In an era of increasing commercial innovation in space, many big-name companies are taking to the skies to explore how microgravity research might enhance their products. But for Procter & Gamble (P&G), a giant among household product providers, spaceflight has been a part of their R&D portfolio for almost a decade—and recently, they have shared exciting progress from their ISS experiments investigating the new science of polydisperse systems.

A common problem in the consumer product world is how to develop new and clever ways of suspending materials in fluids. Consumer foams and gels—such as the familiar products from Gain®, Dawn®, Tide®, Olay®, Gillette®, Pantene®, and many other P&G brands—depend on the stability of such mixtures. This is particularly true for polydisperse mixtures; that is, liquids or gels that contain particles of different sizes in suspension. Unfortunately, how these mixtures move and break down is often not fully understood, which poses a challenge to product designers and manufacturers: ***How to create better, longer-lasting products that maintain all their desired features.***

For example, shampoos contain oils that give the product nice characteristics for a consumer; for example, the oils condition hair and make it easier to brush. But oil droplets suspended in a liquid tend to separate over time, because the oil tends to float to the top. So how does a manufacturer keep these droplets suspended in solution without changing the product so much that it loses its functional and preferable characteristics?

BUILDING MICROSCOPIC NETS

One way to keep droplets suspended is to introduce tiny sticky particulates into a mixture. These micro- and nano-sized particles stick together to create strands that form a net structure within a fluid, stabilizing the movement and dispersity of larger droplets in the mixture. The behavior and effectiveness of such "nets" is the focus of P&G research on the ISS, led by P&G Principal Scientist Matthew Lynch.

> *"We need overarching mathematical models to describe interactions within these complex mixtures," said Lynch. "We need to build predictability to model, improve, and design for commercial product development."*

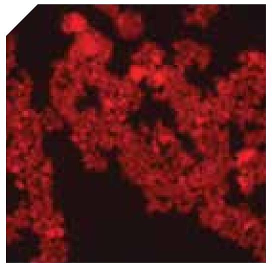


photo credit: Procter & Gamble

For nets to stabilize a complex mixture, they have to possess mechanical strength. The net must "catch" larger droplets responsible for product benefits (such as oils), keeping the droplets from separating out of solution. But the net also has to be flexible—it must stretch and even break so the mixture can flow like the commercial foams and gels a consumer is used to.

For example, the fluid mixture that makes up a shampoo must flow like a liquid when a consumer squeezes it out of the bottle. However, while the shampoo sits in the bottle, both the manufacturer and the consumer ideally want the solution to behave almost like a solid—keeping the droplets of active materials in place, dispersed throughout the bottle. An ideal product thus acts like a solid as it sits on a shelf in the store or in your home—or even as it is transported down a bumpy road—but under the influence of mechanical force (such as squeezing the bottle), the product flows like liquid.

"We need to get the interactions just right to meet both sets of conditions," said Lynch. "By performing experiments on the ISS, we can ask basic science questions about how these mixtures behave and eventually have a tangible impact on product definition."

Basic (rather than applied) science works to answer these fundamental questions and build a foundation for new technologies and new ideas. Lynch's team works on "upstream R&D" at P&G, performing investigations in such basic sciences—and eventually improving mathematical models to describe the underlying phenomena responsible for the behavior of fluid mixtures.

ESTIMATING SHELF LIFE

Technically termed complex fluid physics, the basic science P&G is performing onboard the ISS is the study of colloids, or mixtures of particles dispersed in fluids. On the ISS, the complexity of the mixtures in the P&G experiments is somewhat balanced by the simplified elegance of fluid physics in microgravity. Changes in product behavior happen more slowly in microgravity because of reduced buoyancy-driven fluid movement. Moreover, there are fewer confounding factors to studying these systems on the ISS (for example, sedimentation, which is gravity driven).

The ISS has thus allowed P&G to isolate and study the interactions within complex systems under time scales not possible on Earth. Specifically, Lynch's team has been investigating how the nets within fluids keep droplets dispersed and maintain a product's functional characteristics. The ultimate commercial application of this science is something every consumer can appreciate—shelf life, which is dependent on how long these nets stay intact.

photo credit: Procter & Gamble

"Imagine you have a strand of sticky particles that hold all this stress," said Lynch, "but there's a characteristic time scale for how this strand will change and break down over time." As the many strands within a product break down, the product's structure will eventually collapse, and the various components of the mixture will separate. The product then becomes unusable.

Companies currently have some understanding of the probability of strand breakdown within nets over time, and they use this to predict shelf life. But current models for how this occurs are one-size-fits-all, best describing only simple systems with sticky particles of uniform dimensions. True product chemistry involves polydispersity—interacting particles of many sizes. Breakdown within polydisperse mixtures is complex and difficult to model or predict, let alone to exploit for design of better product formulations.

In other words, current models can give companies indications of how product breakdown will occur, but in the real world, mixtures are not simple, static systems—they are dynamic and complex. Therefore, pragmatic approaches to not only predict shelf life but also improve product design must be driven by a better understanding of the underlying fundamental physics—and the ISS is ideal for this kind of investigation.

STUDYING PRODUCT BEHAVIOR

For P&G, the robust history of colloid physics investigations onboard the ISS also paved the way for a streamlined, effective R&D experience in space. In collaboration with NASA, CASIS, Harvard, Case Western Research, and service provider ZIN Technologies, Inc., two series of P&G experiments were conducted over the past decade, with complementary goals and results building a new knowledge base for understanding polydispersity.

"Typically, the more complex experiments can have timelines of three years or more," said Christopher Sheehan, area manager at ZIN Technologies, "but in this case we were able to leverage lessons learned from previous NASA experiments to enable flight of multiple payloads within a comparatively short time frame."

The experiments—one series through NASA sponsorship and the other through CASIS and the ISS National Lab—involved the study of complex fluids at both ends of the spectrum: microscopic and macroscopic.

photo credit: NASA

In the NASA-sponsored experiments (part of the Advanced Colloids Experiment, or ACE, series on the ISS), P&G studied colloid dispersions—the fundamental physics of how suspended particles move and evolve over time within a fluid. The systems studied not only varied particle size but also differing levels of particle stickiness—which can also be controlled as part of product design.

Basic science knowledge about how these varied mixtures and particles behave will allow manufacturers to predict characteristics, including shelf life, of commercial products that depend on this physics and chemistry.

In contrast, the CASIS-sponsored experiments (part of the Binary Colloidal Alloy Test, or BCAT, series) looked not at microstructure but rather at the ensemble, over longer time scales. Functionally, this allowed P&G to assess the "aging" of a mixture at a very detailed level, because the separation of mixtures occurs more slowly and evenly within spaceflight samples than on Earth.

BRINGING HOME THE BENEFITS

The parallel approach of P&G's multiple investigations, correlating the microscopic data from ACE with the macroscopic phenomena from BCAT, has allowed the company to see evolving "textures" at the product level that correlate with microscopic events. In this way, the ISS is providing a robust, repeatable platform for P&G to diagnose observable behavior of consumer products on Earth.

"The CASIS model for commercial research lends itself to fast, recurring access to ISS assets," said Sheehan. "This experiment also moved quickly through development and build cycles thanks, in no small part, to previous research and technology investments made by NASA in the colloids field. In both cases, helping get P&G's science to station quickly was very rewarding."

Ultimately, the P&G experiments seek to improve product chemistry—tying the spaceflight investigations back into tangible benefit to consumers on the ground. And the story continues, as future P&G experiments are already scheduled to launch later this year and take advantage of upgraded ISS hardware.

With colloids that improve daily life, from showering to cleaning to caring for a baby, it is estimated that P&G products are used by 4.8 billion people every day—more than half of Earth's population. "The success of the P&G spaceflight experiments is more than just a compelling business impact," Lynch said. "More importantly, what we learn here is going to help a lot of people." ■

THE PROBLEM OF POLYDISPERSITY

If a company creates sticky particles of the same size and introduces them into a mixture, the particles organize themselves into strands. These individual strands interact to form the net structure product chemistry seeks to exploit.

But the behavior of sticky particles of varying sizes—the attractive interactions of polydisperse systems—is not well understood. It is these more complex systems that may hold the key to better products with enhanced features and longer shelf life. Polydisperse mixtures behave very differently than the more well-defined systems with uniform particle size.

RESULTS: A SNEAK PEAK

P&G ***The success of P&G products depends on novel and powerful ideas, so the results from their spaceflight experiments are still somewhat confidential—but Lynch and his team intend to publish some of their results to share the details with the scientific community at large.***

Some of the early indications that will be expanded upon in future publications include the fact that smaller particles tend to segregate themselves to the outsides of very sticky strands. Moreover, if the stickiness is decreased, the smaller particles do not join in the net formation at all—only the larger particles form strands. Interestingly, these observed changes appear to be associated not with absolute particle size but rather with the proportionalities of the various sizes.

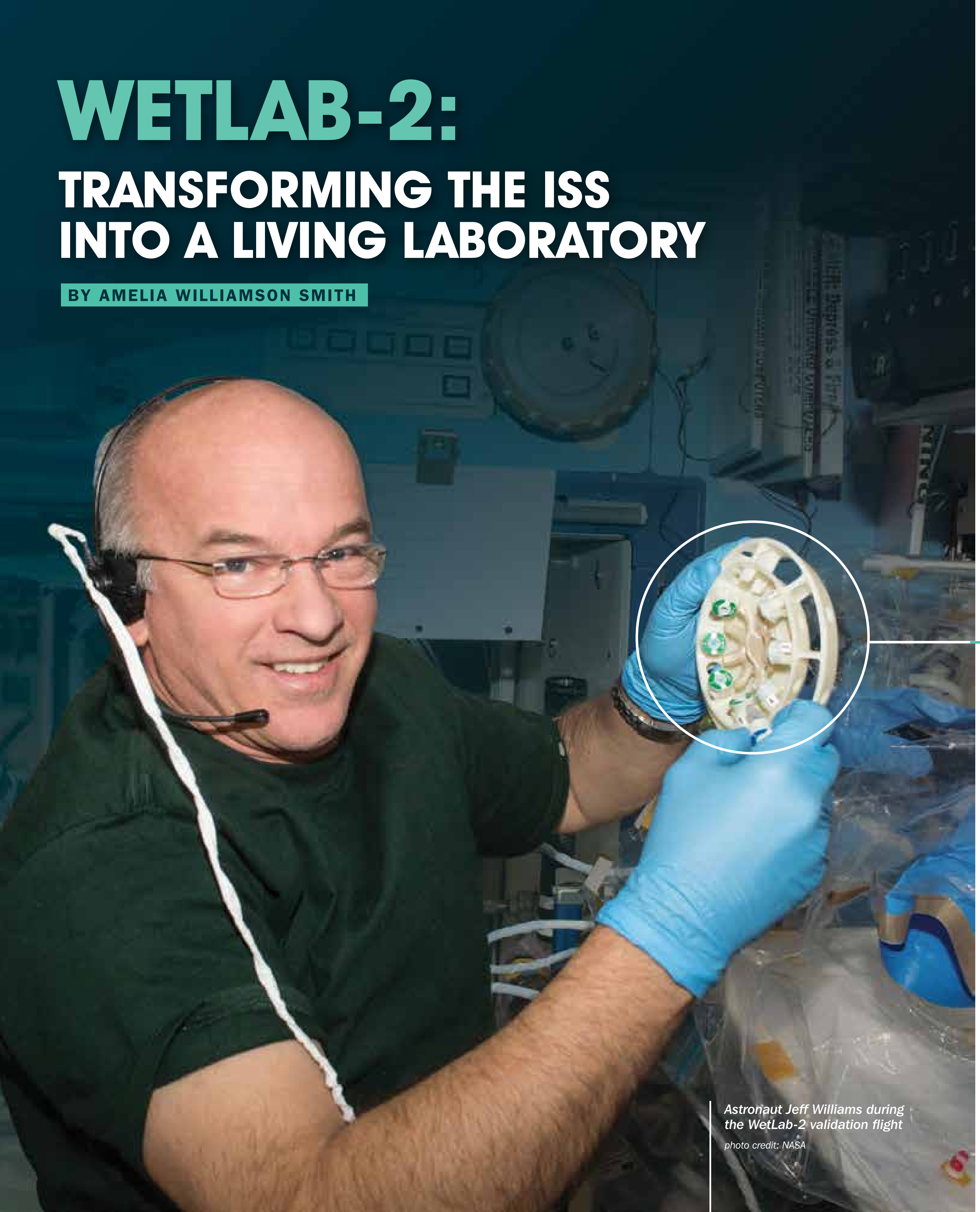
Understanding these nuances of particle behavior and "ordering" will help scientists create mathematical models to describe the behavior of complex mixtures—which is paramount to improving product design.

Lynch cannot share much more detail at this time, but he did indicate that the ultimate goal of better understanding polydispersity and ordering over long time scales had been greatly aided by the ISS experiments. "We've seen unexpected things and learned a lot of interesting science," he said.

WETLAB-2:

TRANSFORMING THE ISS INTO A LIVING LABORATORY

BY AMELIA WILLIAMSON SMITH



Astronaut Jeff Williams during the WetLab-2 validation flight

photo credit: NASA

To study gene expression in a ground-based molecular biology lab, researchers utilize a whole lab bench of tools and equipment. The process of conducting an experiment is interactive and dynamic—researchers can make adjustments as they go or choose to run follow-up tests based on initial results.

On the ISS National Lab, however, conducting an experiment has traditionally been much more constricted and static. Researchers packaged their experiment for loading on a rocket and launch to the ISS, where their samples were exposed to microgravity. While in orbit, the experiment was largely inaccessible to modifications; researchers had to wait for samples to return to Earth before they could perform analyses to determine whether everything worked as expected. After obtaining these results, researchers then had to secure another flight opportunity if they wanted to do something differently or run a follow-up test.

But what if some of the key tools from the molecular biology lab bench were available on the ISS National Lab, allowing researchers to analyze their samples in orbit, obtain the results in near real time, and make adjustments to their experiment while it is still onboard the ISS? For the first time, this is now possible for nucleic acid-based analyses with WetLab-2—a new suite of instruments on the ISS enabling in-orbit gene expression analysis.

“We call the ISS a national laboratory, but it has really felt more like an exposure facility,” said WetLab-2 project scientist Macarena Parra. “Everything for an experiment goes up, is exposed to microgravity, down it comes, and now you get to find out what effect microgravity had on it. Instead, with WetLab-2, researchers can now have more interaction and feel more like they’re really in a lab.”

WetLab-2, developed by NASA’s Ames Research Center in the Silicon Valley, was launched to the ISS National Lab on SpaceX CRS-8. At the ISS Research and Development Conference in San Diego in July, Parra discussed the functionality of WetLab-2 and the successful results of the system’s recent validation experiments.

FROM EXPOSURE FACILITY TO LIVING LABORATORY

WetLab-2 has a wide range of applications and can be used in any experiment that aims to measure gene expression in order to quantify how strongly or weakly a gene is turned on. For example, investigators doing rodent research on the ISS could use WetLab-2 for in-orbit analysis of dissection samples such as blood or tissue to see whether the expression of any genes of interest have been altered. Or, researchers studying the growth or virulence of bacteria in space could use WetLab-2 to analyze samples over time.

Critically, with WetLab-2, instead of having to stop the experiment and wait for samples to return to the ground for analysis, researchers can now obtain data while the experiment is still in orbit. “This really starts to open up the possibility of using the ISS as a living biology laboratory,” said WetLab-2 NASA project scientist Eduardo Almeida. “WetLab-2 is one of the first sets of instruments and procedures that really lets you do an end-to-end experiment in orbit to live up to the spirit of the ISS as a national laboratory.”

OVERCOMING THE HURDLES OF MOLECULAR BIOLOGY IN MICROGRAVITY

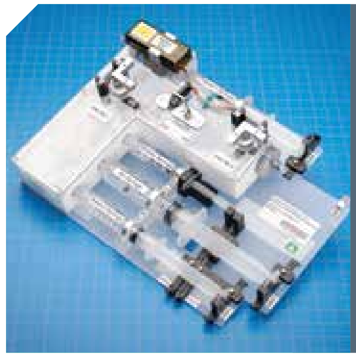
To allow investigators to extract and purify RNA from biological samples in orbit and enable in-orbit gene expression analysis, WetLab-2 uses a method called reverse transcriptase quantitative polymerase chain reaction (RT-qPCR). This common lab technique uses a thermal cycler to amplify DNA using fluorescent probes and primers to quantitatively measure the expression of target genes of interest.

However, although the laboratory procedures from WetLab-2 are done routinely on the ground, they had never been done in space—in part because of the complexity of moving and mixing fluids and operating a thermal cycler in a microgravity environment. To function properly on the ISS National Lab, the WetLab-2 hardware was specially designed to overcome these issues—which influence almost every step of the process.

Extract and Purify

The first step in the WetLab-2 system is to run the biological sample—anything from cells to microbes to tissues—through the sample preparation module. In this module, a nucleic acid, RNA, is extracted and purified, and a crew member uses a syringe to remove the purified RNA liquid. However, when the liquid is removed, some air is removed with it, creating bubbles that can be difficult to separate from the liquid without gravity to keep them at the top.

photo credit: NASA, Dominic Hart



WetLab-2 sample preparation module

"On Earth, it’s very easy to get the bubbles out—you just hold the syringe upright and tap it,” Parra said. “But in microgravity, it’s not so easy.” To address this problem, the WetLab-2 team designed a special device that removes the bubbles as the liquid is injected through. The de-bubbled RNA liquid is then ready to load into commercial reaction tubes (retrofitted with special 3-D-printed caps for use in microgravity) to perform RT-qPCR.

photo credit: NASA, Dominic Hart

Amplify and Analyze

For RT-qPCR, the RNA must be combined with several components. In a ground-based lab, an investigator walks around the lab to collect all of the components needed. Because this is not plausible on the ISS, the WetLab-2 team designed a novel freeze-dried bead to put in the bottom of each reaction tube containing everything needed for RT-qPCR.

> ***"This is really a marvel of biochemistry because we're able to put in a mixture of around a dozen components—the salts, enzymes, primers, and probes—that are usually assembled at the last minute and freeze-dry it," Almeida said. "So everything you need to run RT-qPCR is there, and it can be refrigerated and stored for months until needed."***

photo credit: NASA, Bill Stafford

photo credit: NASA, Bill Stafford

To rehydrate the freeze-dried bead, the RNA liquid must get to the bottom of the reaction tubes; however, the liquid does not immediately fall to the bottom of the tubes. Thus, the WetLab-2 team designed a 3-D-printed rotor to hold the tubes that attaches to the tip of a hand-held drill, allowing a crew member to use the drill to spin the tubes and bring the liquid down.

Next, the activated reaction tubes are loaded into a commercial off-the-shelf thermal cycler—the Cepheid SmartCycler®. The WetLab-2 team chose this specific thermal cycler, in part, because of its durability.

"Most thermal cyclers are designed for a laboratory environment and are delicate instruments," Almeida said. "If you turn them upside down, something will fall off and they won't work." But in the functional absence of gravity onboard the ISS, a more durable instrument was needed. "The SmartCycler® has been used in military field hospitals—it's pretty tough and rugged, making it ideal to use on the ISS National Lab."

Finally, in the thermal cycler, reverse transcription converts the RNA (which is very sensitive to degradation) into complementary DNA (which is much more stable), and PCR is done to amplify the DNA so gene expression can be detected. As the DNA is amplified, fluorescent probes bind to the genes of interest and emit fluorescence. This fluorescence is measured in real time, providing a quantitative measurement of the gene expression. Once the data is collected, the reaction tubes are discarded and the results are sent to the investigators on the ground.

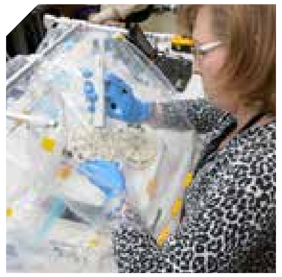


photo credit: NASA

NOW OPEN FOR SCIENCE

Because the WetLab-2 system is the first of its kind, the first test of its functions was a critical demonstration to confirm that the instruments and procedures overcame the numerous hurdles imposed by microgravity. Thus, a series of tests were run both using WetLab-2 on the ISS and using ground controls following the same procedures.

WHAT IS QUANTITATIVE PCR?

PCR is a process that uses cycles of heating and cooling to make copies of specific sections of DNA. These sections are targeted by small pieces of complementary DNA called primers. This cycle is repeated up to 35 times to exponentially amplify the piece of DNA, producing billions of copies.

Quantitative PCR uses fluorescent probes that target genes of interest. When the probe matches up to the targeted gene and binds to it, fluorescence is emitted.

As the DNA is amplified during PCR and more copies of the gene are made, the fluorescence increases. The more of the gene there is in the original DNA sample, the more rapidly the fluorescence increases.

Real-time detection of the fluorescence produces an S-shaped curve that provides a quantitative measurement of the expression of the gene in the sample.

A single-color fluorescent probe only allows for analysis of one gene; however, using multiple colors of fluorescent probes allows analysis of multiple genes at once. WetLab-2 can analyze up to three genes at a time per reaction tube.

BUBBLES IN MICROGRAVITY

The WetLab-2 team did find an unexpected effect from microgravity during the validation experiment—the RT-qPCR data obtained on the ISS had a little more "noise" than you get on the ground. The S-curve plotting from the measured fluorescence was not as smooth and was a little choppier than the curve from the ground data. The team found that the reason for the noise is that some bubbles formed in the reaction tubes.

"On Earth, the air bubbles float to the top, but in microgravity, they stay put," Parra said. "So when an air bubble gets near the fluorescence detector, it suddenly acts like a lens, giving higher readings followed by lower readings as the air bubble moves away."

Although the flight data is a little noisier, the bubbles do not affect the measurements for the most part, Parra said, and could only potentially interfere if an investigator is looking at incredibly small changes in gene expression.

The first test sought to determine whether quantitative PCR works in space using a standard DNA sample. "PCR involves the rapid heating and cooling of samples, and there was a question as to whether that would work when you don't have thermally driven convection in space," Parra said. "But we ran that test and proved for the first time that quantitative PCR does work in space."

Next, the team tested whether WetLab-2 was able to extract and purify RNA and successfully perform RT-qPCR. This was done using two different biological samples—a nonpathogenic (not disease-causing) strain of *Escherichia coli* bacteria and a mouse liver tissue sample from the ground.

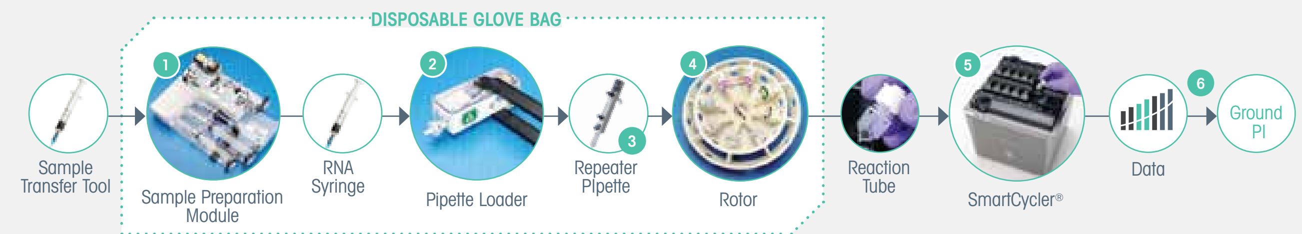
Excitingly, all initial tests were successful in validating the system, which can now be used with confidence for a multitude of scientific investigations. Moreover, the WetLab-2 team was able to obtain the data from each validation experiment within about two hours after the end of each test. This allowed the team to look at the results before the next test was run and request changes.

> ***"The whole idea of WetLab-2 is to give researchers more control over their experiments and enable interactive, in-orbit analysis so they can look at their data and make changes rather than having to wait for everything to come back down," Parra said. "It was an amazing experience to feel like you were really almost having a conversation with the crew member, saying 'hey, could you try this next?'—that's the way a lab is supposed to work."*** ■

• • •

The WetLab-2 team would like to acknowledge ClaremontBio, which helped with the design of the chemistry for the sample preparation, and BioGX, which performed the freeze-drying services. These partnerships were critical to the project and its success.

THE WETLAB-2 PROCESS



1 **SAMPLE PREPARATION MODULE:** A syringe is used to load the biological sample into this module, and RNA is extracted and purified. A disposable glove bag is used to avoid contamination of the RNA by crew members.

2 **PIPETTE LOADER:** A syringe is used to run the purified RNA through this device to remove bubbles from the liquid.

3 **REACTION TUBES:** A pipette is used to remove the liquid from the pipette loader and load it into the reaction tubes that contain the freeze-dried materials for RT-qPCR.

4 **ROTOR:** The tubes are put into a rotor that attaches to a drill, and the rotor is spun to bring the liquid to the bottom of the tubes to rehydrate the freeze-dried materials.

5 **SMARTCYCLER®:** The activated reaction tubes are loaded into the thermal cycler, and RT-qPCR is done. Once complete, the tubes are discarded.

- *Reverse transcription converts RNA to DNA.*
- *DNA is amplified to detect gene expression.*
- *Gene expression is quantitatively measured using fluorescent probes.*

6 **DATA DOWNLINK:** The results are sent through Operations staff to investigators on the ground.

photo credits: NASA, Dominic Hart

PUSHING RESEARCH TO NEW HEIGHTS:

Innovative Research at the ISS R&D Conference

BY AMELIA WILLIAMSON SMITH

What do investigators studying ecosystem productivity, the growth of fungi from the Chernobyl nuclear accident site, the robustness of a new type of osteoporosis drug, and an implantable nanochannel drug delivery system all have in common? These investigators are each using the unique microgravity environment onboard the ISS National Lab to conduct research off of Earth for the benefit of life on Earth.

The annual ISS Research and Development (R&D) Conference brings together a diverse group of investigators from academic, commercial, and governmental communities covering a variety of disciplines—including remote sensing, physical sciences, life sciences, materials science, and technology development—all focused on one thing: leveraging the ISS National Lab to do groundbreaking research not possible on Earth.

The sections below highlight some of the innovative research discussed at the 2016 ISS R&D Conference held in San Diego, California in July.

STUDYING ECOSYSTEM PRODUCTIVITY

Gross ecosystem production (GEP) is a measurement of energy flow in an ecosystem, a biological community of organisms in a geographical location. Ecologists use the movement of carbon dioxide from the atmosphere into an ecosystem to estimate production because plants breathe in carbon dioxide for photosynthesis. Understanding productivity at the scale of ecosystems is important because it provides a glimpse into the ability of agricultural crops, rangelands, and forests to convert rising levels of carbon dioxide into biomass. GEP data enables scientists to model how changes in carbon dioxide levels in the atmosphere will impact future agricultural production and to predict ecosystem stability.

Ecologist Karl Fred Huemmrich, of the University of Maryland, Baltimore County, described the results of his team's research using hyperspectral remote sensing data from the ISS to evaluate ecosystem productivity on the ground. The team used archived imagery from the Hyperspectral Imager for the Coastal Ocean (HICO), which operated on the ISS from 2009 until 2014.

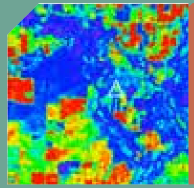
The orbit of the ISS goes through a repeated pattern of visible daytime observations about every 60 days. The advantage of this orbit is that it allows observations of specific locations on Earth's surface at different times of the day and year. Conversely, of course, there are times that a location of interest is passed over by the ISS during darkness and thus cannot be observed with visible light sensors.

Huemmrich and his team developed algorithms to correlate archived hyperspectral reflectance data from HICO with ecosystem productivity as determined on the ground. Ground-based sensors on eddy covariance towers placed at hundreds of sites around the world measure carbon dioxide flux between the surrounding ecosystem and the atmosphere. Huemmrich and his team chose four eddy covariance tower sites with varying types of vegetation in the western U.S. and Canada to compare with archived HICO imagery.

"Existing approaches generally use meteorological data and try to predict and model plant responses and therefore productivity," Huemmrich said. "What we're trying to do is observe the biochemical state of the plants to then infer how stressed they are and how productive they are. We want to then be able to apply that over regions so we can map variations in gross ecosystem production."

Huemmrich and his team found multiple promising approaches that allowed them to successfully use HICO imagery to map complex variations in GEP across different types of landscape vegetation (forests, shrubs, and warm and cool season grasslands). The team was able to use the data to map both spatial variations (how GEP varied across a specific geographical area) and temporal variations (how GEP varied depending on the season and time of day).

These results demonstrate that the ISS National Lab can be used as an Earth observation platform to study ecosystem productivity using routinely collected hyperspectral remote sensing data. Data from space can supplement eddy covariance tower data from the ground and help scientists and farmers better manage crops as our climate changes.



Map of gross ecosystem production (GEP) derived from HICO imagery from the ISS for the study area around Lethbridge, Alberta, Canada. Image collected July 2, 2013. The triangle indicates the location of the flux tower. The area is a mixture of grassland and crops, resulting in a complex spatial pattern of productivity.

TESTING A NEW TYPE OF OSTEOPOROSIS THERAPY

Osteoporosis is the most common bone disease, contributing to 1.5 million fractures and more than $25 billion in healthcare spending each year in the U.S. Current osteoporosis treatments work in one of two ways—by slowing bone breakdown (antiresorptive therapies) or increasing the formation of new bone (anabolic therapies). A new drug, PEGylated NELL-1, has been shown in animal models on the ground to do both. If effective in humans, PEGylated NELL-1 could be developed as a therapy to combat extreme cases of osteoporosis on Earth as well as a countermeasure to spaceflight-induced osteoporosis in astronauts on long-duration missions.

Jin Hee Kwak, of the University of California, Los Angeles, discussed her research (as part of a team led by principal investigator Chia Soo) aimed at testing the effectiveness of PEGylated NELL-1 in treating microgravity-induced osteoporosis in mice onboard the ISS National Lab. Kwak discussed the results of her team's ground optimization study and preparations for their upcoming flight project, which is part of the Rodent Research-5 (RR-5) mission scheduled to launch to the ISS in a SpaceX Dragon in 2017.

Microgravity onboard the ISS provides an environment for robust, accelerated testing of potential pharmaceuticals such as PEGylated NELL-1.

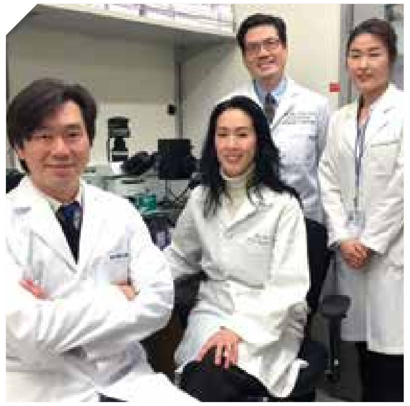


photo credit: Peter Bracke

Drs. Kang Ting, Chia Soo, Ben Wu, and Jin Hee Kwak, the research team behind the Systemic Therapy of NELL-1 for Spaceflight-Induced Osteoporosis.

"Microgravity is known to induce bone loss up to four times faster than models on Earth, and induces an extreme state of osteoporosis that is difficult to mimic by a single osteoporosis model on the ground," Kwak said. "Microgravity-induced bone loss is also an excellent and unique model of disuse atrophy from disability and immobilization on the ground that frequently occurs with osteoporotic fracture patients."

In preparation for their flight experiment, Kwak and her team conducted ground-based optimization studies aimed at addressing two changes in experiment design. One was reducing the frequency of administration of the drug from once every seven days (based on previous research) to once every 14 days, as required on the ISS to reduce crew time and handling of the mice. Additionally, the drug is given intravenously on the ground, but in microgravity, another route of drug administration would be needed.

To address these challenges, the team tested PEGylated NELL-1 administered once every two weeks by one of three ways—injection into the space just under the skin, injection into the abdomen, or a combination of the two. The results showed that PEGylated NELL-1 successfully reversed osteoporotic bone loss in mice on the ground when given once every 14 days and that injection into the abdomen was the most effective route.

The team's flight experiment on the RR-5 mission will be unique because 20 mice will be returned live to Earth from the ISS halfway through the nine-week experiment, while 20 mice will continue treatment in orbit. The mice returned to Earth will recover while continuing treatment in normal gravity until the end of the study period.

GROWING USEFUL FUNGI IN ORBIT

On Earth, certain strains of fungi are known to generate bioactive compounds that have been used to produce important products, such as antibiotics, immunosuppressant drugs, anticancer therapies, and even antifungal agents for crop protection. Research has shown that the production of many bioactive compounds is affected by the fungi's growth environment and response to stress. Thus, growing fungi in the stressful growth environment of microgravity could lead to the production of novel compounds for use in medicine and agriculture on Earth.

Kasthuri Venkateswaran, of NASA's Jet Propulsion Laboratory, discussed his team's research focused on growing certain strains of fungi on the ISS National Lab. The fungal strains chosen for this project were isolated from in and around the Chernobyl nuclear accident site. In the time since the Chernobyl accident in 1986, thousands of fungi from around the accident area have been collected and analyzed. A subset of these fungal strains was found to display a unique phenomenon—instead of growing away from sources of radiation, they actually grow toward the radiation source.

These specific fungal strains have been found in terrestrial studies to produce novel, beneficial compounds useful for humans. Thus, by exposing these unique fungal strains to the added variable of microgravity onboard the ISS, Venkateswaran anticipates that they may produce additional, novel compounds that may be beneficial for use on Earth.

"The strains isolated in and around the Chernobyl accident site produce agricultural- and pharmaceutical-related natural products, so we are trying to see if those strains under the stressful microgravity condition produce different secondary metabolites," Venkateswaran said.

Colony morphologies of the Chernobyl fungal strains that were exposed to microgravity in order to characterize novel bioactive compounds

Based on ground studies to determine which Chernobyl fungi are the most resistant to radiation and the best candidates to send to the ISS, the team selected eight strains to grow for 14 days on the ISS and in ground-based controls. The experiment launched to the ISS on SpaceX CRS-9 in July and returned to the ground on SpaceX CRS-9 in August. The team will analyze the bioactive compounds produced by the fungi in space and on the ground to identify natural compounds to benefit agriculture and medicine.

DEVELOPING NANOCHANNEL TECHNOLOGY FOR CONTROLLED DRUG DELIVERY

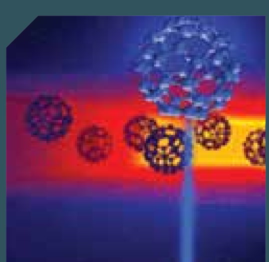
Alessandro Grattoni, of the Methodist Hospital Research Institute in Houston, described his team's research focused on developing nanochannel technology for an implantable controlled drug delivery system. Grattoni discussed his team's recent flight experiment aimed at better understanding how molecules diffuse in confined spaces. He also discussed the team's research on remotely controlled implantable drug delivery systems.

Many chronic conditions require long-term therapeutics that are often administered orally or through injections. When administered in these ways, there is an initial burst of concentrated drug in the patient's blood, followed by a decrease.

> *"For many applications in which you want to maintain a therapeutic range for an extended period of time—for months or even for the lifetime of the patient—this kind of approach is rudimentary," Grattoni said. "We have been looking at ways of targeting the therapeutic range and maintaining it for the entire time that is required."*

To do this, Grattoni and his team are working to develop an implantable device that can deliver a steady and metered dose of the drug through diffusion, without the need for a pump or even power. The nanochannel system consists of membranes with very small channels—roughly two to three times the size of the drug molecule to be delivered. The drug is contained in a reservoir that can be easily refilled by an injection through the patient's skin. The release of the drug can be adjusted by applying an electrical field across the nanochannels in a way that interrupts and then reactivates the release.

In designing these systems, Grattoni and his team needed to understand how molecules of different size, shape, and charge diffuse across the nanochannels. To do this, they needed to explore in microgravity how fluids behave in confined spaces. It is not possible to directly observe individual small molecules diffusing across nanoscale channels; microscopes cannot provide the necessary resolution for that. However, in microgravity, a surrogate model represented by fluorescent microparticles in microchannels can, in specific circumstances, be highly representative of smaller molecules in nanochannels.



3-D rendition of the diffusion of nanoparticles through a confining slit-nanochannel

Thus, Grattoni and his team scaled up their experiment to the microscale, preserving some peculiar features of their nanoscale system, for a study to be carried out using the light microscopy module (which features a modified Leica RXA microscope) onboard the ISS National Lab. The experiment launched on SpaceX CRS-8, and the team is now analyzing the data.

Grattoni and his team are also working to develop technology for remotely controlled implantable drug delivery systems. Such systems would not only benefit patients on Earth but also could be an enabling technology for rodent research on the ISS. The drug delivery implant could be inserted in rodents before flight, and instead of having a crew member perform a complex procedure to administer doses of a drug, an investigator on the ground could remotely control the drug release in the mice.

CASIS President and Executive Director Greg Johnson welcomes investigators from academic, commercial, and governmental communities across a variety of disciplines to the 2016 ISS R&D Conference.

NEW IDEAS AND INNOVATION

Each year, investigators from across disciplines and institutions converge at the ISS R&D Conference to exchange ideas, spark innovation, and push their research to new heights. The ISS National Lab is a research facility unlike any on Earth, opening the door for new discoveries that cannot be made on the ground.

> *"The scale and scope of investigations possible on the ISS National Lab is astounding," said CASIS Deputy Chief Scientist Michael Roberts. "From entire ecosystems to drug molecules in nanochannels, anything is possible."* ■

Tissue Chip and Lab-on-a-chip Technology for Improved Drug Testing

BY AMELIA WILLIAMSON SMITH

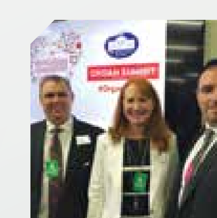
When investigators identify a promising compound for a potential therapeutic drug, there are numerous stages of drug development, preclinical testing, clinical testing in humans, and review before the drug is approved to go to market. This process often takes more than a decade and is astronomically expensive. In 2014, the Tufts Center for the Study of Drug Development estimated the cost of developing a new drug and getting it to market to be more than $2.5 billion. In addition, more than half of all drugs that make it to clinical testing fail—a problem that is in part due to a lack of accurate preclinical testing.

However, "tissue chip" and "lab-on-a-chip" technologies could allow investigators to identify and test potential therapeutics more quickly and with less cost. These microscale systems provide higher-accuracy models for drug testing because they are fabricated using adult human cells. Tissue chip systems (also called microphysiological systems, or MPS) use cells grown on an artificial scaffold to model the detailed physical structure of human tissue, and lab-on-a-chip systems incorporate several laboratory operations on a single chip to better understand the function of cells and their interaction to form tissues.

In response to the 3-D Microphysiological Systems for Organs-on-Chips Grand Challenge, CASIS recently awarded $1 million to two projects. These projects seek to utilize the microgravity environment onboard the ISS to advance tissue chip and lab-on-a-chip technologies for the benefit of patients on Earth with musculoskeletal disorders such as osteoporosis and muscle wasting.

One awarded project, led by Rocky Tuan of the University of Pittsburgh, aims to develop an MPS using human bone cells that can be used to rapidly and reliably test potential therapies to treat and prevent osteoporosis. To validate the MPS, Tuan and his team will confirm that a drug currently used to treat osteoporosis on the ground in normal gravity works to protect against the accelerated bone degeneration caused by long-term exposure to microgravity. Bone pathways in mice differ from those in humans, thus MPS platforms that use human bone cells allow more accurate modeling than animal models, potentially saving millions of dollars in failed clinical testing.

The other awarded project, led by Siobhan Malany of Micro-gRX in Orlando, Florida, aims to validate a fully automated lab-on-a-chip culturing system to monitor the growth of human skeletal muscle cells. The lab-on-a-chip system recapitulates the *in vivo* conditions in which cell growth takes place to provide a more accurate model of cell culture. Malany and her team will use their lab-on-a-chip system to grow human skeletal muscle cells on the ISS and measure changes in cell function resulting from microgravity-induced muscle atrophy. The team's lab-on-a-chip system could be used to more accurately test drugs aimed at treating muscle wasting. The system could also lead to the development of a tissue chip model of muscle wasting with improved accuracy over animal models. ■



The investigators of these two ISS National Lab projects, together with CASIS staff, were invited to attend the White House Organ Summit in Washington, D.C., in June. At the summit, the investigators and CASIS participated in a discussion with 40 leading organ bioengineering experts from a variety of backgrounds who share an interest in advancing biomedical research and technology development to benefit organ donation, transplantation, and regenerative medicine.

SPOT LIGHT

Commercial Use of the ISS for Maritime Tracking: An Operational Evaluation

BY EMILY TOMLIN

The view of Earth from space is a stunning shift in perspective that is not only beautiful but also valuable—facilitating research in disciplines as diverse as atmospheric and agricultural sciences, maritime operations, and disaster response. Thus, in an era of increasing use of the ISS by commercial companies, one must wonder how the ISS platform might support commercially relevant monitoring of Earth. When SpaceX CRS-9 berthed with the ISS on July 20, it carried a payload poised to ask a question—specifically, can the ISS serve as a commercially viable platform for maritime tracking?

Commercial vessels broadcast important data (such as location, speed, heading, and registration number) through an Automatic Identification System (AIS) transponder, but the signals are limited to line-of-site reception. Improved availability of real-time data from these signals could have substantial value to the safety and security of the crew and vessel, as well as commercial and environmental applications that save money and reduce pollution. In a project to demonstrate the real-world value of the ISS in providing these data, JAMSS America, Inc. is performing an operational demonstration of the Global AIS On Space Station (GLASS) over the next 12 months.

The ISS orbits the Earth every 90 minutes, with an orbital path covering 90% of Earth's population and the vast majority of global ship traffic. GLASS is an applied R&D initiative that will take advantage of this unique observation post to acquire and disseminate data derived from extended-range AIS signals. Through the GLASS operational evaluation, JAMSS America, Inc. hopes to determine the suitability of these data for trade, economic, environment and resource management, safety, and security purposes.

Moreover, in anticipation of expanded opportunities, JAMSS America, Inc. is also preparing a future ISS National Lab payload that will place a new, commercially available wide-band antenna and data processing capability onboard the ISS.

"Many people are interested in using space-based platforms for tracking of assets, recovering remote telemetry, and other purposes," said Rob Carlson, president of JAMSS America, Inc. "The GLASS payload is our entry into this field, and our next payload will open access for many commercial and scientific applications that require access to remote telemetry over a much wider range of the radio spectrum."

This second project, Global Receive Antenna and Signal Processor (GRASP), is a multi-user facility planned for launch to the ISS National Lab in early 2018. "We're really excited to provide an entirely new capability," said Carlson, "one that will strengthen the commercial appeal of the ISS." ■

SPOT LIGHT

Zero Robotics: Helping Students Discover the Digital World Through the ISS

BY AUSTIN JORDAN

Today, the world runs on code. There are a gazillion digital interfaces around us buzzing with information, influencing how we communicate, travel, conduct business, and ultimately how we learn. Within this digital renaissance, the means of human exploration have also evolved: we have the ability to not only visit space but to live there. This is best demonstrated by the International Space Station—entire systems and networked processes working synchronously to support astronauts living in space and conducting scientific research in microgravity.

Within this space where imagination has no boundary, the learning opportunities are endless and students are able to discover and use the building blocks of our digital world in a unique classroom—the space station. Through the Zero Robotics program, middle and high school students in the U.S. and member states of the European Space Agency are immersed into the world of coding and robotics. Between the two grade-level program tracks, students work alongside mentors from the Massachusetts Institute of Technology, the program's organizing sponsor, and aerospace professionals to learn the basics of computer programming and robotics.

Zero Robotics participants' ultimate goal is to master the basics of coding in order to program an experimental satellite (known as SPHERES, Synchronized Position Hold Engage and Reorient Experimental Satellite) onboard the ISS to complete various tasks, with astronauts on-hand to referee. The competition is as diverse as it is intense, with 171 high school teams and 70 middle school teams participating in the 2015-2016 season.

Zero Robotics programming is delivered to students, including under-represented communities, at zero cost. The ISS National Lab supported-program aims to increase access to space science and science, technology, engineering, and mathematics (STEM) enrichment. "Zero Robotics seeks to inspire middle-school children to pursue an education in the STEM subjects," said Katie Magrane, Zero Robotics program manager. "There exist many tools that can create excitement among students in STEM, but too many times these resources are used only as promotional tools rather than to engage and inspire students."

The 2016 Zero Robotics high school program kicked off this month. To learn more about Zero Robotics or to get involved, visit: ***zerorobotics.mit.edu*** ■

SPOT LIGHT

News & Notes

FROM THE ISS NATIONAL LAB

SPACEX CRS-9 MISSION COMPLETION

SpaceX CRS-9 launched to the space station in July, delivering 20 ISS National Lab payloads representing more than 40 investigations. Among the payloads were a wide variety of life sciences experiments as well as investigations aimed at using the ISS as an external platform for materials testing and as an Earth observation platform. Also onboard were several student investigations, helping to inspire the next generation of scientists and engineers. After a little more than a month-long rendezvous with the ISS, the SpaceX CRS-9 Dragon capsule successfully returned to Earth at the end of August.

SAVE THE DATE ISS R&D 2017

The 2016 ISS Research and Development (R&D) Conference continued to provide a forum for information exchange among a growing and vibrant global community of organizations and individuals intent on breaking the bounds of innovation in space. More than 700 scientists, engineers, commercial developers, entrepreneurs, and investors gathered at the San Diego conference to learn about state-of-the-art research in microgravity, opportunities to accelerate the commercialization of low Earth orbit, and the enabling technologies and partners that support opportunities and new discoveries in space. Save the date for the 2017 ISS R&D Conference—July 18-20 in Washington, D.C.

SPACECOM

CASIS is a sponsor of the Space Commerce Conference and Exposition (SpaceCom), a commercial industry event where business leaders, space services providers, and technologists from multiple aerospace sectors learn how to exploit new space technology and enable access to space-based assets to gain a competitive advantage. This year's agenda, themed "Space Applications Fueling Business Innovation," focuses on in-depth education, interactive exchanges, and fostering connections to help attendees explore new markets, improve profits, and close deals. Visit CASIS in the exhibit hall, November 15-17 in Houston, and plan to attend our four expert-panel sessions. View the conference program at spacecomexpo.com for dates and times.

DESTINATION STATION: CHICAGO & PHILADELPHIA

In August, CASIS and NASA's ISS Program Science Office representatives brought the ISS National Lab to Philadelphia and Chicago to showcase the research possible onboard the orbiting laboratory as part of Destination Station outreach. With visits to companies including GlaxoSmithKline, McDonald's Innovation Center, Underwriter Labs, and USG, the ISS team provided an overview of science research on the station and how microgravity enables inquiry not possible on Earth that can accelerate innovation and discovery. The Destination Station outreach model has evolved into a great example of how NASA and CASIS are powered through partnership to fully utilize the ISS and increase its accessibility.