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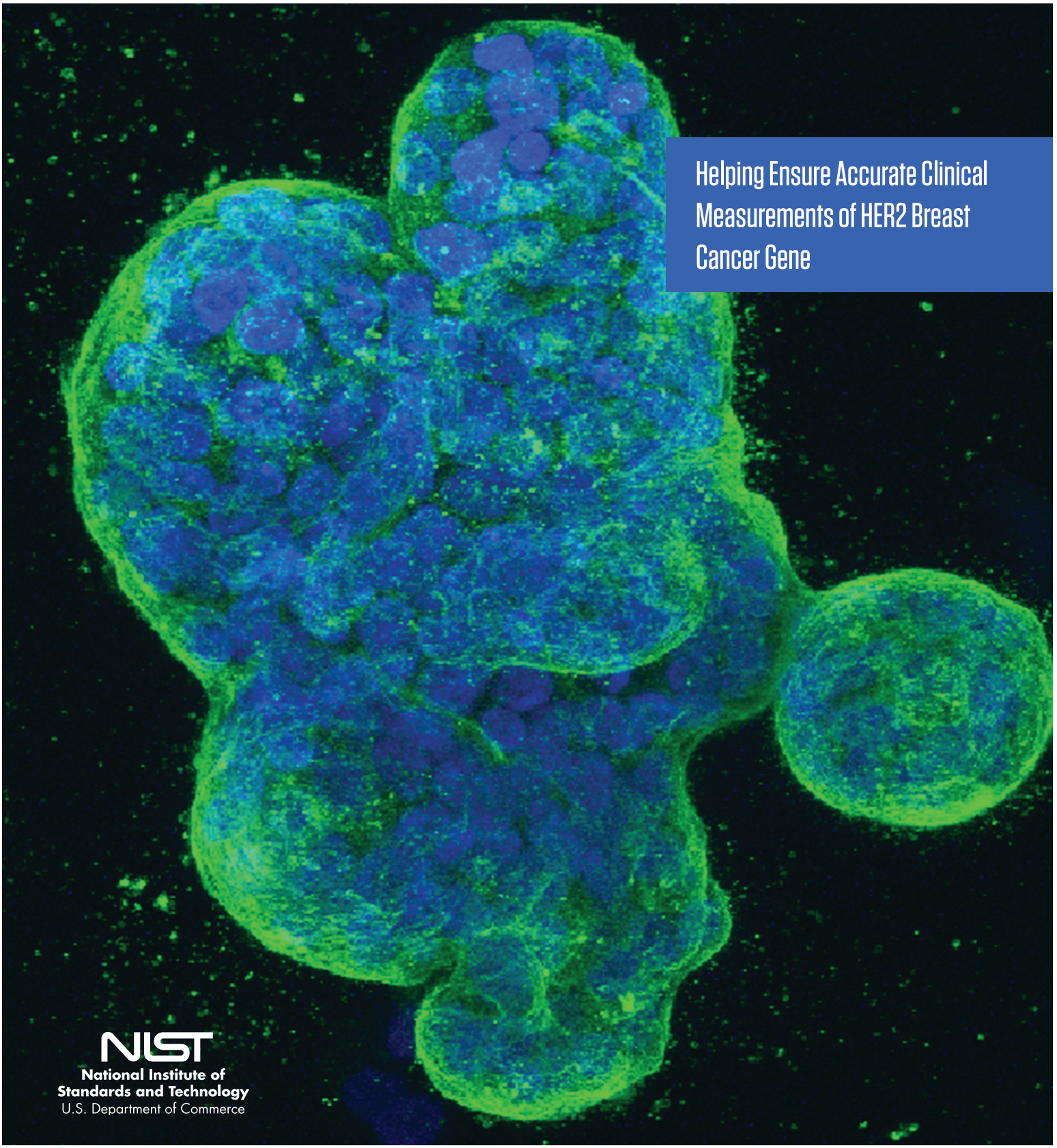
MATERIAL MATTERS

The Quarterly Magazine of NIST's Material Measurement Laboratory



Helping Ensure Accurate Clinical Measurements of HER2 Breast Cancer Gene

NIST
National Institute of Standards and Technology
U.S. Department of Commerce

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A MESSAGE FROM THE MML DIRECTOR

Laurie Locascio, Ph.D.
Director
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About five years ago, scientists from the Material Measurement Laboratory met with representatives from companies that make DNA sequencers and asked, "What can NIST do to help genome sequencing mature into a clinical tool?"

Once limited to research applications, genome sequencing was rapidly becoming fast and inexpensive enough to be used as a diagnostic tool and to guide treatment decisions for patients. It was clear to everyone in the field that sequencing technology had the potential to enable an individual's genetic profile to determine the best therapies for a disease—perhaps before it began to take a toll on a patient's health. To make genome sequencing a valid and powerful clinical tool, however, the field needed to minimize errors in the way a genome is sequenced and analyzed.

To address quality control, industry members said they needed well-characterized genomes. They wanted a widely available sample of DNA that had been extracted, sequenced, and "read" using a combination of different methods to help sequencer developers and clinical and research laboratories check their processes, equipment, and data analysis. This would help ensure that treatment decisions—as well as determinations about where to invest dollars for the development of improved hardware and software, and clinical research—were based on reliable data.

NIST responded with a "genome in a bottle": literally, little bottles of a highly characterized DNA (and the associated data) that are the world's first human genome reference material. Recently, NIST released three additional human genome reference materials, which you can read about on page 5 of this issue of *Material Matters*. A new reference material for bacteria also joins the toolkit.

Development of NIST's human genome reference materials is overseen by scientists at the Joint Initiative for Metrology in Biology, a partnership of the Material Measurement Laboratory and Stanford University, working with representatives from sequencing manufacturers, government agencies, and academia in what is now known as the Genome in a Bottle consortium. The consortium member's input will help NIST continue to enable new sequence techniques and clinical treatments, and is a textbook example of work that meets the NIST mission to assist a whole industry and contribute to the quality of life of all Americans.

NIST AND FREDERICK NATIONAL LABORATORY FOR CANCER RESEARCH HELP ENSURE ACCURATE CLINICAL MEASUREMENTS OF HER2 BREAST CANCER GENE

A new measurement standard developed by NIST has been used successfully by the Frederick National Laboratory for Cancer Research to check the performance of next-generation DNA-sequencing technologies for evaluating gene variations associated with an increased risk of breast cancer.

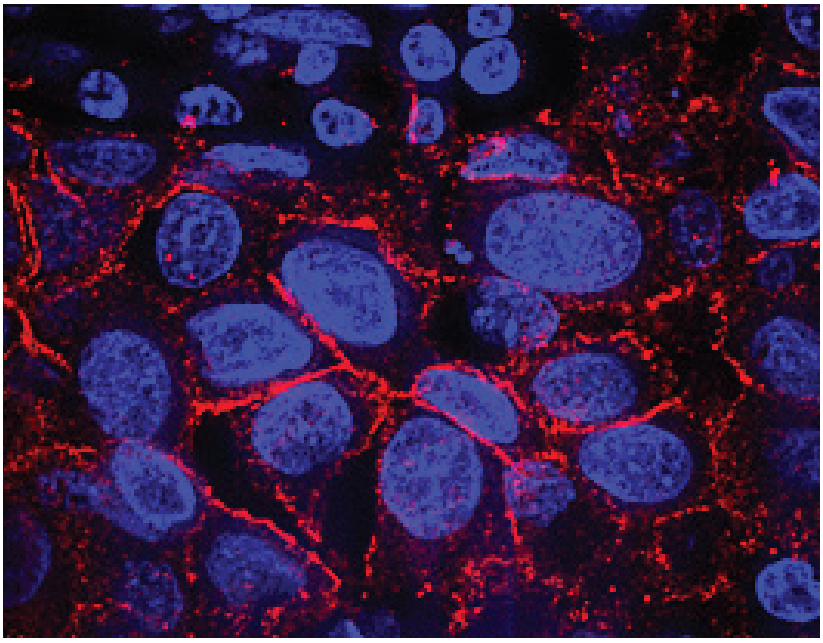
Scientists at the Molecular Characterization Laboratory (MCL) at the Frederick National Lab, which is sponsored by the National Cancer Institute, evaluated the usefulness of the NIST HER2 Standard Reference Material (SRM 2373) for ensuring the accuracy of measurements of HER2 gene copy numbers. Excessive copies of the HER2 gene indicate heightened risk for an aggressive form of breast cancer.

The trial run "clearly demonstrated the value of SRM 2373" for both evaluating assay performance and "increasing confidence in reporting HER2 amplification for clinical applications," Frederick National Lab and NIST researchers report in a recent issue of the *Journal of Molecular Diagnostics*.

"The gene is a biomarker for treatment selection. Diagnostic sequencing tests like HER2 assays make it possible to select the best treatment for individual patients based on the genetic makeup of their tumors," said MCL Director Mickey Williams.

Normal cells have two copies of HER2, but about 20 to 25 percent of breast cancers have multiple copies of the gene, resulting in overproduction of the HER2-encoded protein. This gene amplification stimulates tumors to be particularly fast growing in this subset of breast cancer patients—about 40,000 women in the United States annually.

Fortunately, these patients can be treated with a monoclonal antibody called trastuzumab (brand name Herceptin) that targets and inhibits the growth of tumor cells with higher-than-normal levels of the HER2 protein. The combination of more traditional chemotherapy drugs plus trastuzumab has been found to increase long-term survival rates significantly.



Immunohistochemical detection of HER2 cancer biomarker with IgY antibody and quantum dots in breast cancer cells. Cell nuclei are stained blue, quantum dots responding to the HER2 protein light up in bright red at the cell membranes. Credit: NIST

The treatment also can have adverse side effects, so it's important to screen for those patients who would benefit from it by testing them. However, the two primary tests used prior to the ongoing transition to genomic screening—one relying on fluorescent probes and the other on tissue staining—have been prone to error. An estimated 20 percent of tests were estimated to yield inaccurate results, either false positives or false negatives.

In fact, NIST had originally set out to develop measurement tools to improve the accuracy of those diagnostic tests. But with the rapid emergence of next-generation genome sequencing, NIST chose, instead, to focus on developing measurement references that support the more sensitive and more specific detection capabilities of the new technologies.

SRM 2373 consists of DNA extracted from five breast-cancer cell lines, each with a different average number of copies of the HER2 genes, relative to a selected set of unvarying reference genes. Across the five-vial set, NIST-certified ratios of HER2 copies to the reference genes range from just over one to about 18.

"The collaboration with the Frederick National Lab is very valuable for NIST to ensure that the reference materials we develop are relevant and timely to meet the needs of the clinical and research communities in the rapidly changing field of molecular diagnosis of cancer," said NIST biochemist Kenneth Cole.

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NIST RELEASES NEW "FAMILY" OF STANDARDIZED GENOMES

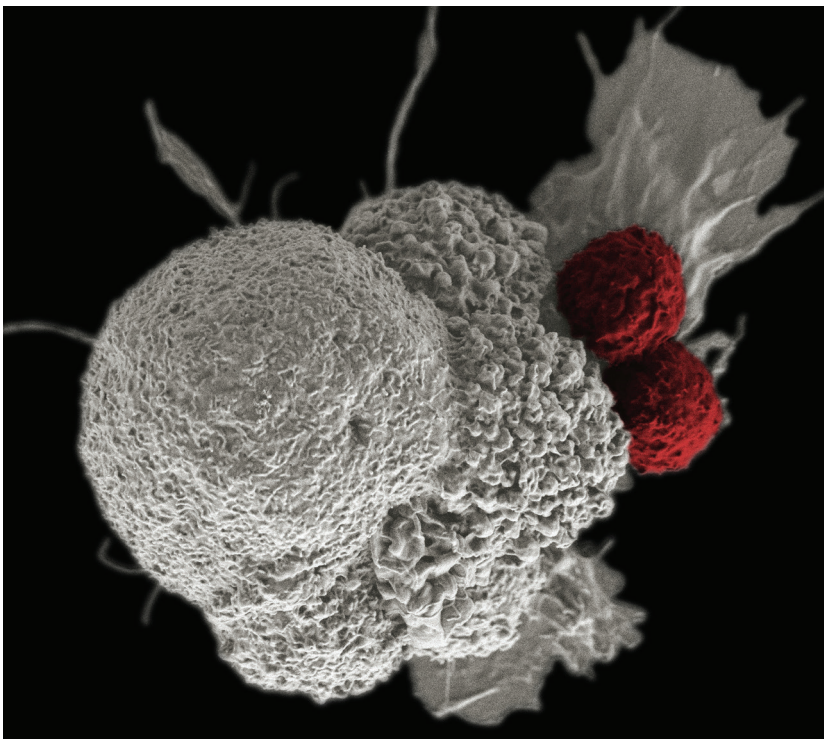
With the addition of four new reference materials (RMs) to a growing collection of "measuring sticks" for gene sequencing, NIST can now provide laboratories with even more capability to accurately "map" DNA for genetic testing, medical diagnoses and future customized drug therapies. The new tools feature sequenced genes from individuals in two genetically diverse groups, Asians and Ashkenazic Jews; a father-mother-child trio set from Ashkenazic Jews; and four microbes commonly used in research.

NIST issued the world's first genome reference material (NIST RM 8398)—detailing the genetic makeup for a woman with European ancestry—in May 2015. Together, all five RMs serve as a collection of well-characterized, whole genome standards that can tell a laboratory how well its DNA sequencing processes are working by measuring the performance of the equipment, chemistry and data analysis involved.

The latest reference materials are:

- NIST RM 8391—male of Eastern European Ashkenazic Jewish ancestry
- NIST RM 8392—male son, father and mother who are a family of Eastern European Ashkenazic Jewish ancestry (with the son's genome being the same released as NIST RM 8391)
- NIST RM 8393—male of East Asian (Chinese) ancestry
- NIST RM 8375—genomes for four bacterial species: Salmonella typhimurium LT2, Staphylococcus aureus, Pseudomonas aeruginosa and Clostridium sporogenes

The individual human RMs provide a baseline for comparing and contrasting genes from distinctly different lineages while the Ashkenazic trio set aids the analysis of genetic links between family members. The bacterial genomes come from species that challenge the technical performance of sequencing methods and have been determined by the Food and Drug Administration (FDA) to have significant relevance to the research of public health issues such as food contamination, antibiotic resistance and hospital-acquired infections.



This electron micrograph shows an oral squamous cancer cell (white) being attacked by two cytotoxic T cells (red). The tumor-specific T cells were developed from the patient's own immune system, a "personalized cancer vaccine" like those that may be developed in the future with the help of NIST's standardized human genomes. Credit: R.E. Serda/National Cancer Institute and Duncan Comprehensive Cancer Center at Baylor College of Medicine

The three individual and one family set of standardized human genomes were created by NIST and its partners in the Genome in a Bottle consortium, a group that includes members from the federal government, academia and industry. The consortium is managed by the Joint Initiative for Metrology in Biology (JIMB), a collaboration between NIST and Stanford University. Through its effort to develop, produce and distribute a suite of genome RMs, the consortium is providing medical and research laboratories worldwide with the tools they need to advance clinical applications of whole genome sequencing, and the FDA with the ability to conduct science-based regulatory oversight of the technology.

Reference materials are critical to properly evaluate the next-generation of gene sequencing and genetic testing methods that will increase the reliability and effectiveness of precision medicine (also known as "personalized medicine"), in which a person's genetic profile is used to create treatments and therapies unique to that individual.

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NIST TEAM SUGGESTS NANOSCALE ELECTRONIC MOTION SENSOR AS DNA SEQUENCER

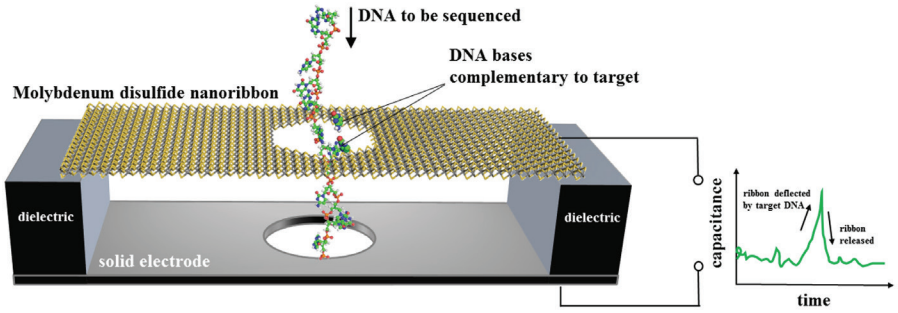
NIST researchers and collaborators have proposed a design for the first DNA sequencer based on an electronic nanosensor that can detect tiny motions as small as a single atom.

The proposed device—a type of capacitor, which stores electric charge—is a tiny ribbon of molybdenum disulfide suspended over a metal electrode and immersed in water. The ribbon is 15.5 nanometers (nm, billionths of a meter) long and 4.5 nm wide. Single-stranded DNA, containing a chain of bases (bits of genetic code), is threaded through a hole 2.5 nm wide in the thin ribbon. The ribbon flexes only when a DNA base pairs up with and then separates from a complementary base affixed to the hole. The membrane motion is detected as an electrical signal.

As described in a new paper, the NIST team made numerical simulations and theoretical estimates to show the membrane would be 79 to 86 percent accurate in identifying DNA bases in a single measurement at speeds up to about 70 million bases per second. Integrated circuits would detect and measure electrical signals and identify bases. The results suggest such a device could be a fast, accurate and cost-effective DNA sequencer, according to the paper.

Conventional sequencing, developed in the 1970s, involves separating, copying, labeling and reassembling pieces of DNA to read the genetic information. Newer methods include automated sequencing of many DNA fragments at once—still costly—and novel "nanopore sequencing" concepts. For example, the same NIST group recently demonstrated the idea of sequencing DNA by passing it through a graphene nanopore, and measuring how graphene's electronic properties respond to strain.

The latest NIST proposal relies on a thin film of molybdenum disulfide—a stable, layered material that conducts electricity and is often used as a lubricant. Among other advantages, this material does not stick to DNA, which can be a problem with graphene. The NIST team suggests the method might even work without a nanopore—a simpler design—by passing DNA across the edge of the membrane.



NIST's proposed design for a DNA sequencer based on an electronic motion sensor. A nanoscale ribbon of molybdenum disulfide is suspended over a metal electrode and immersed in water. Single-stranded DNA, containing a chain of bases (bits of genetic code), is threaded through a hole in the ribbon, which flexes only when a DNA base pairs up with and then separates from a complementary base affixed to the hole. The membrane motion is detected as an electrical signal. Numerical simulations and theoretical estimates show the membrane would be 79 to 86 percent accurate in identifying DNA bases in a single measurement at speeds up to about 70 million bases per second. Credit: NIST

"This approach potentially solves the issue with DNA sticking to graphene if inserted improperly, because this approach does not use graphene, period," NIST theorist and lead author Alex Smolyanitsky said. "Another major difference is that instead of relying on the properties of graphene or any particular material used, we read motions electrically in an easier way by forming a capacitor. This makes any electrically conductive membrane suitable for the application."

Nanomaterials expert Boris Yakobson of Rice University, a co-author on the paper, suggested the capacitor idea. Computational support was provided by the University of Groningen in the Netherlands.

DNA has four bases. For the simulations, cytosine (C), which naturally pairs up with guanine (G), is attached to the inside of the pore. When a piece of DNA passes through the pore, any G in the strand temporarily attaches to the embedded C, pulling on the nanoribbon and signaling the electrode. The DNA sequence is determined by measuring how and when electrical blips vary over time. To detect all four bases, four nanoribbons, each with a different base attached to the pore, could be stacked vertically to create an integrated DNA sensor.

The molybdenum disulfide ribbon is flexible enough to deform measurably in response to the forces required to break up a DNA pair, but rigid enough to have less ongoing, meaningless movement than graphene, potentially reducing unwanted noise in the sequencing signals. The deflection of the ribbon is exceedingly small, on the order of one angstrom, the size of a hydrogen atom. Its pulling force is on the order of 50 piconewtons, or trillionths of a newton, enough to break up the delicate chemical bonds between DNA bases.

Researchers estimated how the device would perform in an integrated circuit and found the peak currents through the capacitor were measurable (50 to 70 picoamperes), even for the small nanoribbons studied. The current peaks are expected to be even larger in physical systems. The device size could be tweaked to make it even easier to measure sequencing signals.

The NIST authors hope to build a physical version of the device in the future. For practical applications, the chip-sized DNA sequencing microfluidic technology might be combined with electronics into a single device small enough to be handheld.

The research was funded in part by the Materials Genome Initiative.

A. Smolyanitsky, B.I. Yakobson, T.A. Wassenaar, E. Paulechka and K. Kroenlein, A MoS2-based capacitive displacement sensor for DNA sequencing, *ACS Nano*, **September 13, 2016**, http://dx.doi.org/10.1021/acsnano.6b05274

LET'S ROLL: MATERIAL FOR POLYMER SOLAR CELLS MAY LEND ITSELF TO LARGE-AREA PROCESSING

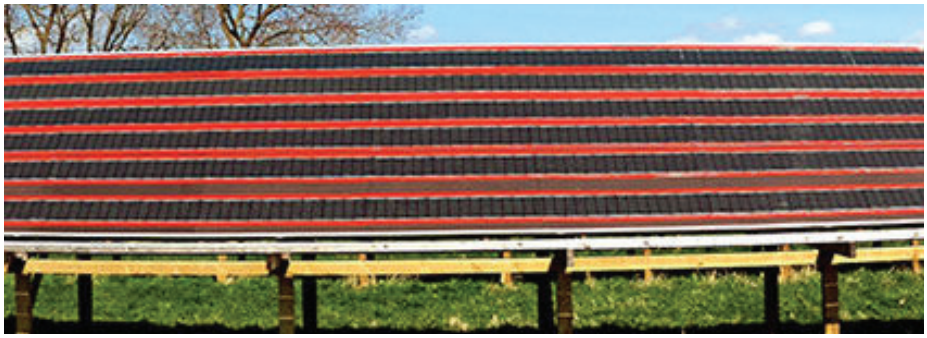
For all the promise they have shown in the lab, polymer solar cells still need to "get on a roll" like the ones employed in printing newspapers so that large sheets of acceptably efficient photovoltaic devices can be manufactured continuously and economically. Polymer solar cells offer advantages over their traditional silicon-based counterparts in numerous ways, including lower cost, potentially smaller carbon footprint and a greater variety of uses.

New research results reported by an international team led by NIST indicate that the "sweet spot" for mass-producing polymer solar cells—a tantalizing prospect for decades—may be far larger than dictated by the conventional wisdom. In experiments using a mock-up of a high-volume, roll-to-roll processing method, the researchers produced polymer-based solar cells with a "power conversion efficiency" of better than 9.5 percent, just shy of the minimum commercial target of 10 percent.

That's almost as good as the small-batch devices made with spin-coating, a method that produces high-quality films in the laboratory but is commercially impractical since it wastes up to 90 percent of the initial ink.

Somewhat surprising to the researchers, their mass-produced versions exhibited molecular packing and texture that only slightly resembled that of lab-made varieties, which at their best convert about 11 percent of incident sunlight into electrical energy.

"The 'rule of thumb' has been that high-volume polymer solar cells should look just like those made in the lab in terms of structure, organization and shape at the nanometer scale," said Lee Richter, a NIST physicist who works on functional polymers. "Our experiments indicate that the requirements are much more flexible than assumed, allowing for greater structural variability without significantly sacrificing conversion efficiency."



A demonstration solar park based on polymer solar cells at the Technical University of Denmark in Roskilde, Denmark. Credit: DTU Energ

"Efficient roll-to-roll fabrication is key to achieving the low-cost, high-volume production that would enable photovoltaics to scale to a significant fraction of global energy production," explained He Yan, a collaborator from Hong Kong University of Science and Technology.

The team experimented with a coating material composed of a fluorinated polymer and a fullerene (also known as a "buckyball"). Going by the technical name PffBT4T-2OD, the polymer is attractive for scaled production—achieving a reported power conversion efficiency of more than 11 percent. Importantly, it can be applied in relatively thick layers—conducive to roll-to-roll processing.

However, the top-performing solar cells were produced with the spin-coating method, a small-batch process. In spincoating, the fluid is dispensed onto the center of a disk or other substrate, which rotates to spread the material until the desired coating thickness is achieved. Besides generating lots of waste, the process is piecemeal—rather than continuous—and substrate size is limited.

So the research team opted to test commercially relevant coating methods, especially since PffBT4T-2OD can be applied in relatively thick layers of 250 nanometers and more, or roughly the size of a large virus. They started with blade-coating—akin to holding a knife edge at a fraction of a hair's breadth above a treated glass substrate as it slides by, painting the PffBT4T-2OD onto the substrate.

A series of X-ray-based measurements revealed that the temperature at which the PffBT4T-2OD was applied and dried significantly influenced the resultant coating's material structure—especially the orientation, spacing and distribution of the crystals that formed.

The substrates blade-coated at 90° Celsius (194°F) were the highest performing, achieving power conversion efficiencies that topped 9.5 percent. Surprisingly, at the nanometer level, the end products differed significantly from the spin-coated "champion" devices made in the lab. Detailed real-time measurements during both blade-coating and spin-coating revealed that different structures arose from the rapid cooling during spin-coating versus the constant temperature during blade-coating.

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NOVEL 3-IN-1 "RHEO-RAMAN" MICROSCOPE ENABLES INTERCONNECTED STUDIES OF SOFT MATERIALS

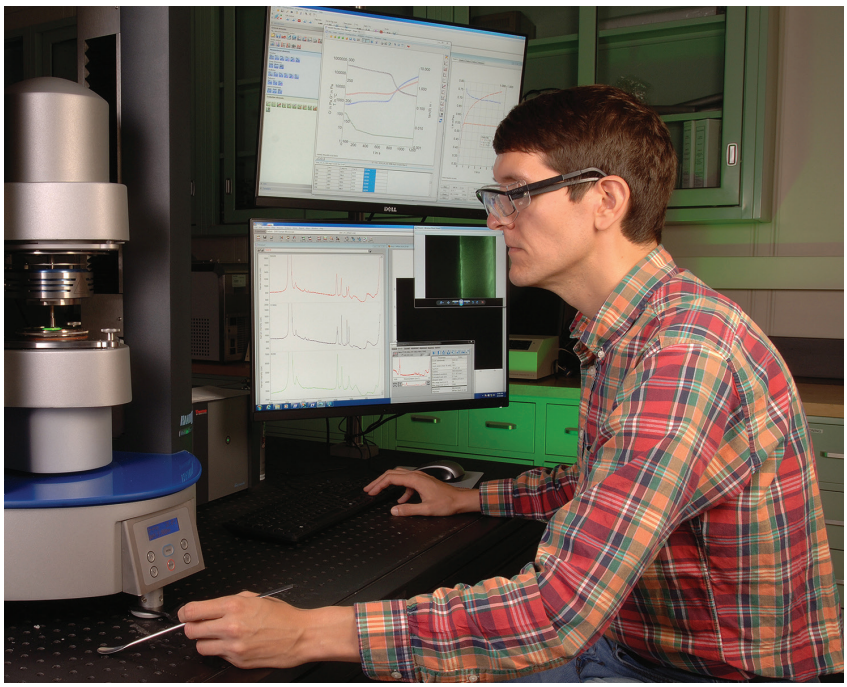
An innovative three-in-one instrument that allows scientists to correlate the flowability of soft "gooey" materials such as gels, molten polymers and biological fluids with their underlying microstructure and composition has been developed by scientists from NIST and Thermo Fisher Scientific.

Simultaneous measurements yield a clearer picture of how structural make-up and flow behavior during processing dictate the macroscopic properties—such as strength, hardness, or electrical conductivity—that make so-called soft materials desirable for certain products or applications.

A novel combination of off-the-shelf instruments, the new research tool—called the rheo-Raman microscope—integrates:

- a Raman spectrometer, which shines a laser on the sample and measures the tiny portion of scattered light that reveals vibrational energy levels of molecules in the sample, providing the equivalent of molecular fingerprints showing how atoms are arranged;
- a rotational rheometer to track and measure how a liquid, suspension or slurry flows in response to stress—or, put another way, the degree to which the sample deforms; and
- an optical microscope that collects polarized light reflected from a sample to increase contrast, enabling measurements of a specimen's structural features at microscopic scales.

The new instrument is designed for "multitasking," said Anthony Kotula, a NIST materials scientist. "It allows you to trace the evolution of microstructure across a range of temperatures and to do it in one controlled experiment rather than in two or three separate ones. It provides insights that would be very difficult to obtain through measurements made one at a time."



NIST's Anthony Kotula using the new rheo-Raman microscope, a three-in-one instrument that enables researchers to measure the flow properties of a material along with its microscopic structure and composition.Credit: Denease Anderson/NIST

Homing in on the flow behavior is especially important, because it is intimately coupled with the microstructure and ultimate properties, Kotula explained.

Soft materials share features of liquids and solids. They range from plastics to liquid crystal displays and from contact lenses to biopharmaceuticals. For these "in-between materials," even slight variations in processing conditions can alter internal structures and drastically change material properties, which can open the way to improved performance or entirely new technological applications.

As they report in the *Review of Scientific Instruments*, the team used their prototype rheo-Raman microscope to follow and measure changes before, during and after melting a cosmetic material composed of coconut and almond oils and about 10 other ingredients. They also present simultaneous "melt" measurements taken on high-density polyethylene, which is used to make plastic bottles, corrosion-resistant pipes and many other items, as liquid molecules arrange and solidify into crystals.

Both demonstrations yielded a detailed, unfolding picture of how flow behavior and other phenomena during melting and crystallization correspond to changes in the shape and arrangement of molecules due to processing conditions.

"Based on the possibilities for direct correlation between chemical, structural and mechanical properties, we expect the rheo-Raman microscope to be critically relevant to both academic and industrial interests," the researchers concluded in their article.

"The rheo-Raman microscope is a general purpose instrument with lots of potential uses," Kotula said. "At NIST, one of our first applications pertains to 3D printing. We'll use it to better understand how polymer crystallization proceeds during the layer-by-layer printing process."

A.P. Kotula, M. Meyer, F. De Vito, J. Plog, A.R. Hight Walker and K.B. Migler, The rheo-Raman microscope: Simultaneous chemical, conformational, mechanical, and microstructural measures of soft materials, *Review of Scientific Instruments*, **October 4, 2016**, http://dx.doi.org/10.1063/1.4963746

NIST UNVEILS FORENSIC TECHNIQUE TO MEASURE MECHANICAL PROPERTIES OF EVIDENCE

You may have seen it on CSI: The star examines hair from a crime scene and concludes its color or texture looks like the defendant's hair, or maybe his dog's. Case closed.

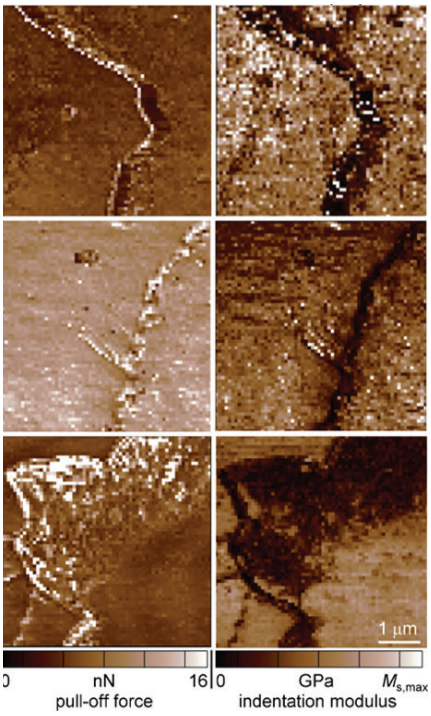
But looks can be deceiving, as well as vague and subjective. In real life, the FBI is now reviewing thousands of cases involving hair comparisons going back to the 1980s because traditional identifications—often based on looks alone—have been called into question.

Instead, what if investigators could precisely measure a hair's mechanical properties—its stiffness and stickiness? In fact, they can, according to recent experiments at NIST, which is developing science-based methods to help ensure rigorous forensic practices.

"Lots of forensics is based on how the evidence looks," NIST engineer Frank DelRio says. "We are trying to add another dimension, how things feel. How an object feels—its mechanical response—depends on the material and the object's history."

DelRio is an expert in atomic force microscopy (AFM), a precision tool with a mechanical probe typically used in basic sciences for imaging but also to measure responses to force, or pulling. He usually measures industrial materials like silicon. But he also watches a lot of CSI and thought his expertise could help answer national calls to enhance the accuracy, reliability and statistical rigor of forensics.

DelRio and NIST physicist Robert Cook recently used AFM to demonstrate quantitative methods for measuring—nondestructively and at the nanometer size scale—the mechanical properties of four types of evidence: hair, documents, fingerprints and explosives.



NIST researchers used atomic force microscopy (AFM) to measure the stickiness (pull-off force) and stiffness (plane strain modulus) of hair that was untreated (top), bleached (middle), and conditioned (bottom). The clear differences in the measured results for various hair treatments suggest that AFM might be used to analyze forensic evidence. The measured forces are very small, in units of nanonewtons or nN (1 nanonewton is about the weight of a pollen grain). Modulus is in units of gigapascals or GPa and ranges from 1-5 for the hair samples (for comparison, the plastic lens material polycarbonate measures about 3).Credit: DelRio/NIST

The researchers measured the stiffness and pull-off force (stickiness) for hair as a function of treatment, specifically conditioning and bleaching. They also measured these properties for test documents made to mimic forgeries marked with both ballpoint ink and printer ink, impression and pattern evidence such as how fingerprints change over time, and interactions of explosive particles and surfaces as a function of fabric type, rayon versus cotton.

The measurement results clearly distinguished various treatments of hair, types of ink, age of fingerprints and composition of fabrics, and related these data to the structure of the sample such as broken bonds in the hair and the smooth ballpoint ink versus the rough printer ink. Importantly, the measurements were rigorous—that is, precise enough to allow for tests and quantitative specifications of the statistical significance of the similarities or differences in properties. DelRio imagines that someday AFM might be used, for example, to measure old hair evidence and determine the probability that a criminal used a certain shampoo.

"This is all theoretical at this point," DelRio notes. "For this to be an effective practical tool, a lot of baseline measurements and in-depth studies would need to be done to develop a good sense of how these properties change over time."

In addition, DelRio notes that AFM calibration methods and standard samples or other methods for specifying accuracy would need to be developed to enable accurate comparison of measurements across laboratories. Also crucial would be the development of an experience base to build trust in AFM techniques, requiring widespread availability of instruments, training, protocols and standards for forensics labs, the paper notes.

F.W. DelRio and R.F. Cook, Quantitative Scanning Probe Microscopy for Nanomechanical Forensics, *Experimental Mechanics*, Posted online **October 31, 2016**, http://dx.doi.org/10.1007/s11340-016-0238-y

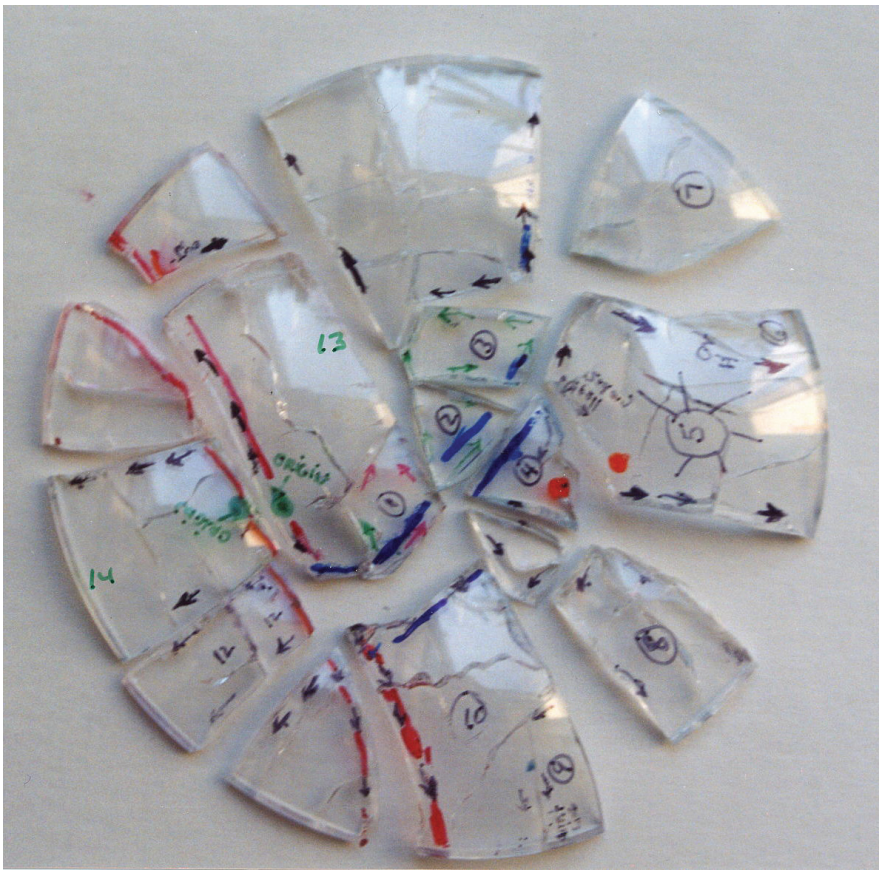
NIST RELEASES EXPANDED "FRACTOGRAPHY" GUIDE FOR ANALYZING, UNDERSTANDING MATERIAL FAILURES

Studying the fractures of industrially important materials such as ceramics and glasses provides important clues on why these materials can fail and how to make them more durable. The practice of "fractography," however, has been an underutilized science. NIST is working to change that.

NIST has released a new, expanded edition of the NIST Recommended Practice Guide, "Fractography of Ceramics and Glasses" (NIST Special Publication 960-16e2). First issued in 2007, the guide was developed to help engineers and scientists analyze the patterns in fractures of ceramics and glasses used for household items and other consumer goods, building materials, and medical devices and implants.

Since it was first published, "Fractography of Ceramics and Glasses" has been used in training courses and by members of industry for failure analysis, helping to improve production methods and product quality.

The new edition of the guide, which is 15 percent larger than its predecessor, includes 300 new illustrations and covers the state of the art in fractography, including descriptions of new documentary standards. The guide, with nearly 1,000 images, covers various topics including equipment (with updates on new microscopy techniques), patterns in glass and ceramic fractures (the "fingerprints" that make failure analysis possible), an expanded chapter on quantitative analysis of fractures, and composites—including new materials used in dentistry. Actual case studies help readers see how the guide is used in practice.



Fracture of a sapphire missile nose cone. Credit: NIST

Mechanical engineer George Quinn, the author of both the original and expanded editions, joined NIST in 1990 to perform strength testing on ceramic materials. In collaboration with ASTM, an international standards organization, Quinn helped to develop two world-first ceramic strength tests. Since formally retiring from NIST in 2009, Quinn has continued to serve the organization as a research associate.

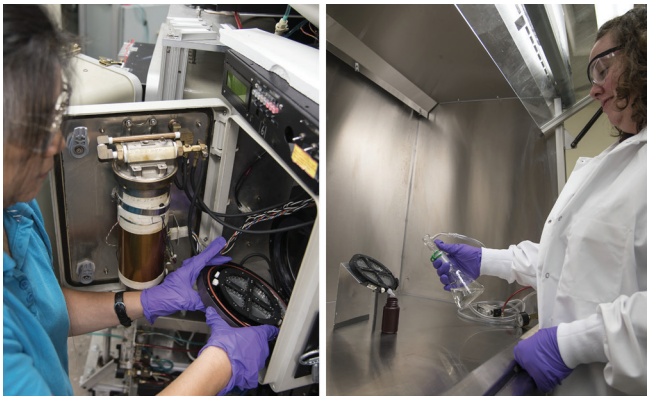
The guide may be accessed online (http://nvlpubs.nist.gov/nistpubs/specialpublications/NIST.SP.960-16e2.pdf). Hard copies are available upon request (george.quinn@nist.gov).

NIST-MADE "SUN AND RAIN" DETAIL HOW NANOPARTICLES CAN ESCAPE FROM PLASTIC COATINGS INTO THE ENVIRONMENT

If the 1967 film "The Graduate" were remade today, Mr. McGuire's famous advice to young Benjamin Braddock would probably be updated to "Plastics … with nanoparticles." These days, the mechanical, electrical and durability properties of polymers—the class of materials that includes plastics—are often enhanced by adding miniature particles (smaller than 100 nanometers or billionths of a meter) made of elements such as silicon or silver. But could those nanoparticles be released into the environment after the polymers are exposed to years of sun and water—and if so, what might be the health and ecological consequences?

In a recently published paper, researchers from NIST describe how they subjected a commercial nanoparticle-infused coating to NIST-developed methods for accelerating the effects of weathering from ultraviolet (UV) radiation and simulated washings of rainwater. Their results indicate that humidity and exposure time are contributing factors for nanoparticle release, findings that may be useful in designing future studies to determine potential impacts.

In their recent experiment, the researchers exposed multiple samples of a commercially available polyurethane coating containing silicon dioxide nanoparticles to intense UV radiation for 100 days inside the NIST SPHERE (Simulated Photodegradation via High-Energy Radiant Exposure), a hollow, 2-meter (7-foot) diameter black aluminum chamber lined with highly UV reflective material that bears a casual resemblance to the Death Star in the film "Star Wars." For this study, one day in the SPHERE was equivalent to 10 to 15 days outdoors. All samples were weathered at a constant temperature of 50 degrees Celsius (122 degrees Fahrenheit) with one group done in extremely dry conditions (approximately 0 percent humidity) and the other in humid conditions (75 percent humidity).



NIST researchers simulate "sun and rain" to determine if weathering causes polymer coatings to release the nanoparticles they contain into the environment. On the left, Li-Piin Sung places a commercially available polymer with silicon dioxide nanoparticles into a chamber of the NIST SPHERE, a device for accelerated weathering that in one day subjects samples to the equivalent of 10-15 days of outdoor exposure. On the right, Deborah Jacobs applies "NIST simulated rain" to the weathered sample to collect any shed nanoparticles in the runoff. Credit: F. Webber/NIST

To determine if any nanoparticles were released from the polymer coating during UV exposure, the researchers used a technique they created and dubbed "NIST simulated rain." Filtered water was converted into tiny droplets, sprayed under pressure onto the individual samples, and then the runoff—with any loose nanoparticles—was collected in a bottle. This procedure was conducted at the beginning of the UV exposure, every two weeks during the weathering run and at the end. All of the runoff fluids were then analyzed by NIST chemists for the presence of silicon and in what amounts. Additionally, the weathered coatings were examined with atomic force microscopy and scanning electron microscopy to reveal surface changes resulting from UV exposure.

Both sets of coating samples—those weathered in very low humidity and the others in very humid conditions—degraded but released only small amounts of nanoparticles. The researchers found that more silicon was recovered from the samples weathered in humid conditions and that nanoparticle release increased as the UV exposure time increased. Microscopic examination showed that deformations in the coating surface became more numerous with longer exposure time, and that nanoparticles left behind after the coating degraded often bound together in clusters.

"These data, and the data from future experiments of this type, are valuable for developing computer models to predict the long-term release of nanoparticles from commercial coatings used outdoors, and in turn, help manufacturers, regulatory officials and others assess any health and environmental impacts from them," said NIST research chemist Deborah Jacobs, lead author on the study published in the *Journal of Coatings Technology and Research*.

This project resulted from a collaboration between NIST's Engineering Laboratory and Material Measurement Laboratory. It is part of NIST's work to help characterize the potential environmental, health and safety risks of nanomaterials, and develop methods for identifying and measuring them.

D.S. Jacobs, S-R Huang, Y-L Cheng, S.A. Rabb, J.M. Gorham, P.J. Krommenhoek, L.L. Yu, T. Nguyen and L. Sung, Surface degradation and nanoparticle release of a commercial nanosilica/polyurethane coating under UV exposure, **September 2016**, *Journal of Coatings Technology and Research*, http://dx.doi.org/10.1007/s11998-016-9796-2

PERFLUORINATED COMPOUNDS FOUND IN AFRICAN CROCODILES, AMERICAN ALLIGATORS

American alligators and South African crocodiles populate waterways a third of the globe apart, yet both have detectable levels of long-lived industrial and household compounds for nonstick coatings in their blood, according to two studies from researchers at the Hollings Marine Laboratory (HML) in Charleston, South Carolina, and its affiliated institutions, which include NIST.

Production of some compounds in this family of environmentally persistent chemicals—associated with liver toxicity, reduced fertility and a variety of other health problems in studies of people and animals—has been phased out in the United States and many other nations. Yet all blood plasma samples drawn from 125 American alligators across 12 sites in Florida and South Carolina contained at least six of the 15 perfluorinated alkyl acids (PFAAs) that were tracked in the alligator study.

The two studies are first-of-their-kind examinations of PFAA levels in "sentinel" reptile species, especially useful for investigating the impacts of long-lived chemicals in the environment. PFAAs have been used in products that include water-repellent clothes, stain repellents, waxes, nonstick pans and fire-suppressing foams.

In alligators, plasma levels of perfluorooctane sulfonate (PFOS) ranged from 1,360 to 452,000 parts per trillion. In May 2016, the Environmental Protection Agency issued a drinking-water health advisory for PFOS and another PFAA, recommending a maximum exposure level of 70 parts per trillion for one of the PFAAs or the sum of the two. High PFOS levels reported for alligators at several sites may suggest the need to test drinking water for contamination at those locations, according to the researchers.

This crocodile inhabits waters around Flag Boshielo Dam, a reservoir on the Oliphants River, just upstream from South Africa's Kruger National Park. Researchers from the Hollings Marine Laboratory reported at least four types of perfluorinated alkyl acids in plasma samples drawn from 45 crocodiles at five sites in and around the park. The highest levels were found in animals living in the reservoir. Credit: John Bowden/HML

In a separate study, researchers report that all samples drawn from 45 crocodiles at five sites in and around South Africa's Kruger National Park contained detectable levels of four PFAAs, often in different combinations with others of the 15 fluorinated organic compounds tracked. Present in all plasma samples, PFOS levels ranged from 776 to 118,000 parts per trillion.

"Alligators and crocodiles play a dominant role in their ecosystems," said Jacqueline Bangma, of the Medical University of South Carolina in Charleston. "Similar to humans, they are long-lived top predators. They stay in a select territory—waterways where runoff from human activities accumulates— and their PFAA burden increases through the consumption of fish."

To date, field studies of PFAA levels and health effects in reptiles have been few, focusing mostly on sea turtles. Across studies of animals—from rats to frogs to marine mammals—plasma levels, time required to eliminate PFAAs from the body, and health effects vary greatly, making it difficult to extrapolate from one species to another.

The landmark studies were initiated by the Hollings Marine Laboratory, a partnership including NIST, NOAA's National Ocean Service, the South Carolina Department of Natural Resources, the College of Charleston, and the Medical University of South Carolina. Plans are to continue PFAA monitoring on both continents, according to NIST research chemist Jessica Reiner.

Both studies identified "hot spots," where PFAA levels were significantly higher than in animals tested at other sites, an indication that the contaminants were emitted by a nearby source. In the U.S. study, median plasma levels of certain PFAAs were highest in alligators on Kiawah Island, an Atlantic Ocean barrier island southwest of Charleston, South Carolina, and on Merritt Island in Florida.

Past use of PFAA-containing foams such as those employed in firefighting training may account for the higher levels, the researchers suggest. High environmental concentrations have been reported at fire-training sites and at manufacturing plants.

In contrast, alligators at two sites in the Florida Everglades exhibited some of the lowest levels of the two "highest burden" PFAAs reported across all adult alligators sampled in the U.S. study. The result was somewhat unexpected, Reiner said, because Everglade's alligators have been reported to have some of the highest levels of mercury, a toxic heavy metal, among Florida alligators.

Among the South African crocodiles tested, PFAA levels were highest for animals tested from Flag Boshielo Dam, a reservoir on the Oliphants River, just upstream from Kruger National Park.

Continued on page 15

NEW NIST REFERENCE MATERIAL HELPS ENSURE ACCURATE MEASUREMENT OF CONSTITUENTS IN TOBACCO PRODUCTS

NIST has issued a reference material with certified amounts of nicotine and two carcinogens to help ensure accurate testing of commercial tobacco filler—the blended tobacco found in cigarettes.

Prepared in collaboration with the Food and Drug Administration's (FDA) Center for Tobacco Products (CTP), NIST's new Standard Reference Material "SRM 3222 Cigarette Tobacco Filler" helps companies meet the federal requirement for reporting "harmful or potentially harmful constituents" in tobacco products and tobacco smoke.

The requirement is in the 2009 Family Smoking Prevention and Tobacco Control Act, which assigned FDA the authority to regulate the manufacture, distribution and marketing of tobacco products to protect public health. In 2012, the agency published a list of 93 substances that cause—or could cause—harm from tobacco use or exposure to tobacco smoke.

"It's important to make regulatory decisions with the best information available," said David L. Ashley, director of CTP's Office of Science. "This tobacco standard reference material and others help inform the evaluation of data on harmful and potentially harmful constituents submitted by manufacturers and importers."

NIST SRM 3222 is certified for amounts of nicotine, the primary cause of tobacco addiction, and two tobacco-specific nitrosamines: N-nitrosonornicotine (NNN), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). These nitrogen-containing compounds are among the most carcinogenic chemicals in cigarette smoke.

Levels of each of the three compounds in the reference material are certified by NIST using a combination of mass spectrometry and chromatographic methods—techniques for separating and analyzing complex mixtures. Measurements were made at NIST and the Centers for Disease Control and Prevention and confirmed subsequently at several commercial laboratories.

"The composition of tobacco products can vary greatly," said Lane Sander, the NIST researcher who led development of the SRM. "It's influenced by the tobacco varieties used in production, growing conditions, curing methods and additives. This reference material can serve as a check on composition measurements made during manufacturing and for regulatory purposes."

About 2,500 kilograms (5,500 pounds) of American blended tobacco filler were procured from a commercial source, with established target values for nicotine and nitrosamines. The tobacco was processed and blended by the manufacturer as a cigarette tobacco filler. Dried leaves were chopped to lengths roughly equal to the diameter of a dime and a width equal to the coin's thickness. Each unit of SRM 3222 consists of 20 jars, each containing about 10 grams of filler tobacco.

NIST research chemist Jeanita Pritchett extracts nicotine and tobacco-specific compounds from a candidate Standard Reference Material (SRM) created in collaboration with the Center for Tobacco Products at the Food and Drug Administration. Consisting of a low-level nicotine tobacco filler material, the NIST SRM is intended for use in evaluating the accuracy of measurements of specific compounds and moisture in tobacco. Credit: Earl Zubkoff

NIST AND FREDERICK NATIONAL LABORATORY FOR CANCER RESEARCH HELP ENSURE ACCURATE CLINICAL MEASUREMENTS OF HER2 BREAST CANCER GENE (CONT'D)

The HER2 reference material is the latest addition to a growing list of measurement tools that NIST has developed to help advance genomics-inspired precision medicine. NIST also is working with Frederick National Lab researchers and industry to improve detection and reliable measurement of cell-free circulating tumor DNA, sometimes called liquid biopsies. Circulating tumor DNA has been detected in many cancers and might be used to monitor patients' therapeutic progress and whether tumors mutate to become resistant to treatments.

NIST recently signed a three-year Cooperative Research and Development Agreement with SeraCare Life Sciences to collaborate on an interlaboratory study comparing measurements of the company's circulating tumor DNA reference material.

In 2015, NIST and its partners in the Genome in a Bottle Consortium issued NIST Reference Material (RM) 8398 Human DNA for Whole-Genome Variant Assessment, for which about 77 percent of the genome is characterized with high levels of confidence. The Food and Drug Administration used the genome reference material as its "truth set" for its just-completed PrecisionFDA Consistency Challenge, intended to advance quality standards for whole human genome sequencing.

In May 2016, NIST issued a "Peptide Mixture for Proteomics" (RM 8321), which contains 440 synthetic peptides, or segments of proteins. Proteomics is the identification and study of proteins, which are encoded by genes and are, ultimately, the body's "doers," acting alone or in groups to drive processes involved in health and disease.

H-J. He, J. Almeida, S. Lund, C.R. Steffen, S. Choquette and K.D. Cole, Development of NIST Standard Reference Material 2373: Genomic DNA Standards for HER2 Measurements, *Biomolecular Detection and Quantification*, **June 2016**, http://dx.doi.org/10.1016/j.bdq.2016.02.001

C-J. Lih, H. Si, B. Das, R.D. Harrington, K.N. Harper, D.J. Sims, P.M. McGregor, C.E. Camalier, A.Y. Kayserian, P.M. Williams, H-J He, J. Almeida, S.L. Lund, S. Choquette and K.D. Cole, Certified DNA Reference Materials to Compare HER2 Gene Amplification Measurements Using Next-Generation Sequencing Methods, *Journal of Molecular Diagnostics*, Available online **July 25, 2016**, http://dx.doi.org/10.1016/j.jmoldx.2016.05.008

NIST RELEASES NEW "FAMILY" OF STANDARDIZED GENOMES (CONT'D)

Sequencing devices take long strings of a person's DNA and randomly chop them into small pieces that can be individually analyzed to determine their sequence of letters from the genetic code (A, C, G and T representing the four key components of DNA that code for protein production in living organisms: adenine, cytosine, guanine and thymine). The sequenced pieces can then be compared to a well-defined "reference sequence" to identify differences between the two codes. The differences reveal where mutations may have occurred in specific genes.

However, biases and "blind spots" for certain sequences contribute to uncertainties or errors in the sequence analysis. These biases can lead to hundreds of thousands of disagreements between different sequencing results for the same human genome.

To better understand these biases, laboratories can now compare their DNA sequences to those obtained from the DNA in any or all of the human genome RMs. The reference materials have been extensively characterized with multiple techniques, with the results weighted and analyzed to eliminate as much bias and error as possible.

The new NIST human genome RMs increase the ability of DNA sequencing laboratories to be more confident in their reporting of true positives, false positives, true negatives and false negatives, and therefore, significantly improve genetic tests used for disease risk prediction, diagnosis, and progression tracking. They also can be used with tools developed by the Global Alliance for Genomics and Health Benchmarking Team to further raise that confidence level.

Similarly, the standardized microbial genomes in NIST RM 8375 can be used to assess the performance of high-throughput methods for microbial DNA sequencing.

All five of the NIST reference materials are available for purchase from the NIST Standard Reference Material program. Each RM sample is characterized for homogeneity (ensuring that each vial contains similar DNA) and stability (ensuring that the DNA ordered now will be comparable to samples ordered in the future). The original sources for the RMs are from the Personal Genome Project, whose cell lines are hosted at the Coriell Institute for Medical Research.

Future additions to the RM collection may include whole genomes from persons with Hispanic, African and mixed ancestries, as well as a set containing sequenced genes of both malignant tumor and normal cells from the same individual.

LET'S ROLL: MATERIAL FOR POLYMER SOLAR CELLS MAY LEND ITSELF TO LARGE-AREA PROCESSING (CONT'D)

"Real-time measurements were critical to developing a proper understanding of the film formation kinetics and ultimate optimization," said Aram Amassian, a collaborator from Saudi Arabia's King Abdullah University of Science and Technology.

Encouraged by the results, the team performed preliminary measurements of PffBT4T-2OD coating formed on the surface of a flexible plastic sheet. The coating was applied on NIST's slot-die roll-to-roll coating line, directly mimicking large-scale production. Measurements confirmed that the material structures made with blade-coating and those made with slot-die-coating were nearly identical when processed at the same temperatures.

"It's clear that the type of processing method used influences the shape of the domains and their size distribution in the final coating, but these distinctly different morphologies do not necessarily undermine performance," said Harald Ade, a collaborator from North Carolina State University. "We think these findings provide important clues for designing polymer solar cells optimized for roll-to-roll processing."

H.W. Ro, J.M. Downing, S. Engmann, A.A. Herzing, D.M. DeLongchamp, L.J. Richter, S. Mukherjee, H. Ade, M. Abdelsamie, L.K. Jagadamma, A. Amassian, Y. Liu and H. Yan, Morphology changes upon scaling a high-efficiency, solution-processed solar cell, *Energy & Environmental Science*, **August 2, 2016**, http://dx.doi.org/10.1039/c6ee01623e

PERFLUORINATED COMPOUNDS FOUND IN AFRICAN CROCODILES, AMERICAN ALLIGATORS (CONT'D)

Among the American alligators studied, some PFAA levels tended to be higher among males, regardless of locations. Levels also tended to increase with age, as determined by snout length. Age- and sex-related associations with PFAA levels were not found in the crocodiles sampled.

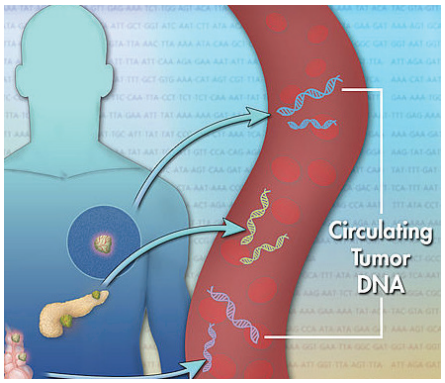
I. Christie, J.L. Reiner, J.A. Bowden, H. Botha, T.M. Cantu, D. Govender, M.P. Guillettee, R.H. Lowers, W.J. Luus-Powell, D. Pienaar, W.J. Smit and L.J. Guillette Jr., Perfluorinated alkyl acids in the plasma of South African crocodiles (Crocodylus niloticus), *Chemosphere*, **July 2016**, http://dx.doi.org/10.1016/j.chemosphere.2016.03.072

J.T. Bangma, J.A. Bowden, A.M. Brunell, I. Christie, B. Finnell, M.P. Guillette, M. Jones, R.H. Lowers, T.R. Rainwater, J.L. Reiner, P.M. Wilkinson and L.J. Guillette, Jr., Perfluorinated alkyl acids in plasma of American alligators (Alligator mississippiensis) from Florida and South Carolina, *Environmental Toxicology and Chemistry*, Accepted manuscript online: **August 20, 2016**, http://dx.doi.org/10.1002/etc.3600

OUTREACH AND PARTNERING

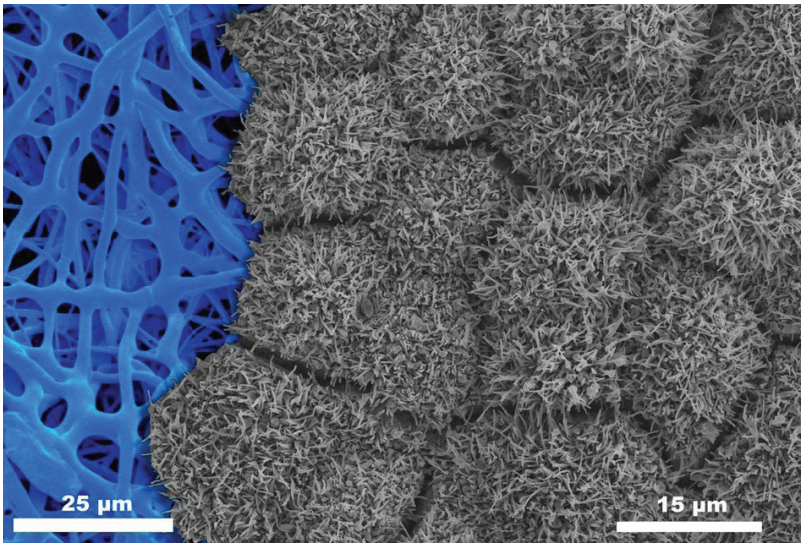
WITH NEW CRADA, NIST UPS ITS MEASUREMENT R&D IN SUPPORT OF PRECISION MEDICINE DIAGNOSTICS

NIST's efforts to support accurate diagnostic testing so that cancer treatments can be tailored to the tumor DNA and other characteristics particular to individual patients continue to gain momentum, as the agency mounts a multi-laboratory study to evaluate candidate reference materials for benchmarking measurements of circulating tumor DNA—so-called liquid biopsies.



Credit: National Human Genome Research Institute

The comparative exercise—sometimes referred to as an interlaboratory "round robin"—benefits from a new three-year Cooperative Research and Development Agreement (CRADA) with SeraCare Life Sciences, of Millford, Massachusetts. Under the agreement, SeraCare will supply its circulating DNA reference material technology to NIST to help further development and refinement of digital measurement methods. NIST will distribute these materials for testing at laboratories in the National Cancer Institute's Early Detection Research Network and to other research and testing organizations.



Scanning electron micrograph of retinal pigment epithelium (RPE) cultured on a nanofiber scaffold. RPE and nanofibers were imaged separately and combined. There are two scale bars since RPE and nanofibers were imaged at different magnifications. Nanofibers were pseudocolored and shadowing was added to the RPE.

Reliably accurate measurements will be critical to the successful introduction and adoption of liquid biopsies for anticipated clinical applications, which include monitoring therapeutic progress and detecting drug resistance mutations.

NEW PUBLIC-PRIVATE PARTNERSHIP TO DEVELOP STANDARDS FOR REGENERATIVE MEDICINE

NIST has partnered with the Standards Coordinating Body for Gene, Cell and Regenerative Medicines and Cell-based Drug Discovery (SCB) to develop industry-wide standard methods and protocols for characterizing and manufacturing these cutting-edge therapies, with an aim of accelerating their use as mainstream treatments for a variety of human diseases and injuries.

The field of regenerative medicine manipulates genes, cells, and tissues to repair or replace diseased, damaged, or missing organs, skin, bone, and other cells and tissues. Regenerative medicine has the potential to alleviate the shortage of donor organs and restore appearance and full function to patients who have experienced severe burns or physical trauma.

Because of the complexity of regenerative medicine treatments, they have been slow to transition from the laboratory to the clinic. The traditional measurements of efficacy, potency, purity, and quality that work with traditional pharmaceuticals aren't always sufficient for regenerative medicine treatments.

To address these issues, NIST and the SCB, a non-profit founded by the Alliance for Regenerative Medicine, announced on September 19, 2016 that they had signed a Memorandum of Understanding, forming a partnership to explore the regenerative medicine industry's needs and develop standards and other products to increase confidence in measurements of gene- and cell-based therapies and manufacturing processes.

AWARDS

HARVEY NAMED IAPWS FELLOW

The International Association for the Properties of Water and Steam (IAPWS) has named Allan Harvey, of MML's Theory and Modeling of Fluids Group, an IAPWS Honorary Fellow. The status of Honorary Fellow is conferred upon select individuals in recognition of outstanding contributions to IAPWS and has been given to only 47 people in the 36 years the award has existed. Harvey's citation reads, "For long-standing efforts in formulating and improving IAPWS releases as member and Chair of the Working Group on Thermophysical Properties of Water and Steam, and Chair of the Editorial Committee. For outstanding scientific work in the field of fluids and aqueous systems, including *ab-initio* calculation of molecular interactions." He is the fifth NIST-affiliated scientist to receive this honor.

KILPATRICK RECOGNIZED BY AACC MASS SPECTROMETRY AND SEPARATION SCIENCES DIVISION

Eric Kilpatrick, of MML's Bioanalytical Science Group, was recently awarded Outstanding Abstract in the 2016 Mass Spectrometry and Separation Sciences Division Abstract Competition. Kilpatrick received the award for his abstract entitled "Amino acid analysis by mass spectrometry for concentration determination of C-reactive protein in candidate reference material SRM 2924" at the Division Annual Meeting.

WARREN, CICERONE ELECTED AMERICAN PHYSICAL SOCIETY FELLOWS

Director of NIST's Materials Genome Program Jim Warren (left) and Marcus Cicerone of MML's Biomaterials Group have been elected Fellows of the American Physical Society (APS).

Warren is recognized for his seminal contributions to the modeling of microstructural development in a broad range of materials. He was elected by the APS Council of Representatives at its September 2016 meeting upon the recommendation of the Division of Materials Physics. Cicerone is recognized for outstanding contributions to the understanding of the dynamics in glassy materials, demonstrating its importance in the stabilization of protein therapeutics, and the development of broadband CARS microscopy for bioimaging. He was nominated by the APS Division of Polymer Physics.

APS Fellowship is a distinct honor for APS members and is a prestigious recognition by their peers. Fellowship is reserved for no more than one half of 1% of APS members in any given year.

SOLES SELECTED AS A FELLOW OF THE AMERICAN CHEMICAL SOCIETY

In July 2016, the American Chemical Society announced the selection of 57 members as ACS Fellows, who are recognized for outstanding achievements in and contributions to science, the profession, and the Society. Christopher Soles leader of MML's Functional Polymers Group Christopher Soles was named as one of the new ACS Fellows. He is recognized for "significant contributions to elucidating the structure and properties of confined polymeric materials, nanoporous films, and nanoscale structures that impact emerging technology areas," and "admirable service to the Polymeric Materials: Science and Engineering Division admirably as Chair-elect, Vice Chair, Treasurer, and Technical Program Chair, including initiating new program development and fiscal reforms."

NIST STANDARD STORY

NIST scientists have thoroughly measured and characterized more than 1,300 physical products, NIST Standard Reference Materials®, to help people in industry, academia, and government agencies calibrate instruments, verify their test methods, and develop new measurement methods. NIST reference materials, for example, help manufacturers make interoperable parts in far-flung facilities, medical labs check the accuracy of cholesterol and other clinical tests, and scientists monitor environmental threats.

FOR LABORATORY USE ONLY

WHAT

Standard Reference Material® 1946 Lake Superior Fish Tissue, and 1947 Lake Michigan Fish Tissue

Mark Cronise isn't lying about the hundreds of pounds of trout that the and two colleagues helped to fillet, ice, and prepare for shipment to NIST after driving the length of Michigan's upper peninsula all night. (The collection of Lake Michigan's trout, scheduled for the same trip, was delayed, so it was shipped to NIST unescorted.) Upon arrival at NIST, each lake's batch of fish was further frozen to -120 degrees Celsius (-184 degrees Fahrenheit) in liquid nitrogen freezers, then ground to a powder, homogenized in a spinning drum, and bottled, all while still frozen. Each SRM is sold as five bottles of about 8 grams (0.28 ounces) of powdered fish tissue stored at -80 degrees Celsius (-112 degrees Fahrenheit). They are each certified—meaning that NIST and collaborators have performed sophisticated chemical analysis and shown that those results can be repeated—for more than a half dozen elements including mercury, plus a selection of industrial chemicals, pesticides, and fatty acids. NIST continues to test for and add values for chemicals, adding to the utility of the SRMs.

WHY

The U.S. Environmental Protection Agency (EPA) has monitored the Great Lakes water quality and ecosystem since the late 1970s. With more than 94,000 square miles of surface area and 30 million people living along their shores, there's not much that doesn't end up in the waters of the Great Lakes, from industrial contaminants like polychlorinated biphenyls (PCBs), to

Mark Cronise (left) of NIST's Office of Reference Materials assists a fisherman in the gutting and filleting of trout from Lake Superior. With further processing back at NIST, the fish tissue is transformed into a reference material that helps environmental monitoring labs with quality control.
Credit: Mark Cronise/NIST.

mercury, to agricultural pesticides, to other chemicals like the flame retardants used in couches and chairs. (Because Lakes Superior and Michigan differ in the types and amounts of chemicals they contain, NIST developed a fish tissue SRM for each.) PCBs and mercury have been shown to harm people and wildlife. The other substances have been shown to harm animals, although their effects on humans are not well understood. While NIST first developed the fish tissue SRMs to assist the EPA, they are used by environmental monitoring labs around the world to check their sample processes and test methods. The EPA, in particular, is interested in an accurate picture of the lakes' recovery from now-banned or regulated PCBs and other chemicals, and helping localities give data-backed advice to their residents about how much Great Lakes fish is safe to eat.

In addition to aiding environmental monitoring efforts, the Great Lakes fish tissue SRMs help food industry labs check their analytical methods for measuring fatty acids.

WHO

Each year, the EPA collects predator fish from the top of the lakes' aquatic food chain from each of the Great Lakes. Top predators—the same types of fish usually eaten by people—accumulate toxins ingested by organisms lower in the food chain, so they are good indicators of the chemicals in their environments. Bernard Crimmins of Clarkson University oversees some of the analyses conducted as part of the EPA's Great Lakes Monitoring Program.

HOW

Crimmins and Clarkson students rely on NIST fish tissue SRMs to diagnose any problems with their laboratory methods. "These SRMs are great because it's the actual fish tissue, the same as what we measure," Crimmins says, adding that just enriching a control with a known amount of chemical doesn't represent the full complexity of the real-world analytical problem. The NIST SRMs also help the Clarkson students determine whether levels of emerging potential contaminants, such as new flame retardants, have increased compared to the historical levels preserved in the nearly-20-year-old NIST SRMs. Despite their age, the fish tissue SRMs have legs: If kept properly frozen, the SRMs will be good on your shelf until December 2026.

Learn more:
https://www-s.nist.gov/srmors/view_detail.cfm?srm=1946

https://www-s.nist.gov/srmors/view_detail.cfm?srm=1947

Technical Contact:
John Kucklick, john.kucklick@nist.gov

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MATERIAL MEASUREMENT LABORATORY

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