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THE INTERNATIONAL JOURNAL OF METROLOGY

METROLOGY 101: TESTING LINEARITY ON THE E441XA POWER SENSORS

The Metrology of Counting Protein Particles

Small Current Measurements for a New Standard in Radionuclide Metrology

Gender-Specific Effects on Tympanic Temperature on a Cohort Sample of 15 to 16 Year Old High School Students

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FEATURES

DEPARTMENTS

ON THE COVER: Instructors José Torres and Phil Wright perform measurements during a dry run of the new Fundamentals of Metrology course being offered by the NIST Office of Weights and Measures. Credit: Gentry/NIST, 2013.

CALENDAR

CONFERENCES & MEETINGS 2013

Aug 24-29 Conference on Precision Electromagnetic Measurements (CPEM). Rio de Janeiro, Brazil. CPEM is devoted to topics related to electromagnetic measurements at the highest accuracy levels. These cover the frequency spectrum from dc through the optical region. A major focus of this conference is quantum devices that relate electrical standards to fundamental constants and the international system of units. http://www.icpem.org/

Sep 16-19 AUTOTESTCON. Schaumburg, IL. The world's premier conference that brings together the military/aerospace automatic test industry and government/military acquirers and users to share new technologies, discuss innovative applications, and exhibit products and services. Sponsored annually by the IEEE. The Theme this year is ATS Innovation in the Era of Challenging Budgets. http://autotestcon.com/.

Sep 24-26 15th Annual Sound & Vibration Conference. Detroit, MI. Thousands of sound & vibration professionals have expanded their career horizons by attending Brüel & Kjær courses. Taught by practicing industry experts with many decades of cumulative experience, these courses feature the latest available technology in the latest applications. http://bkhome.com/NewsEvents/News.aspx.

Sep 24-26 The 16th International Flow Measurement Conference (FLOMEKO). Paris, France. Flomeko 2013 will provide the perfect opportunity for practitioners of metrology from a wide variety of industries such as energy, aeronautics, chemicals, healthcare and the environment to exchange ideas with researchers, national laboratories and academics and to explain just how new and improved metrology can play a vital part in all their activities. http://www.flomeko2013.fr/.

Sep 25-27 10th International Congress on Electrical Metrology (X SEMETRO). Buenos Aires, Argentina. This congress is devoted to topics related to electromagnetic measurements and covers high accuracy and industrial measurements in the frequency range from DC to the optical region. It will be organized by the Instituto Nacional de Tecnología Industrial (INTI) of Argentina and the Instituto Nacional de Metrologia, Qualidade e Tecnologia (INMETRO) of Brazil. For further information, please visit http://www.inti.gob.ar/xsemetro/.

Oct 7-10 16th International Congress of Metrology. Paris, France. The 3 day conference in the heart of Paris offers the opportunity to understand the latest technical developments in measurement, explore industrial challenges and develop solutions that will

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EDITOR'S DESK

A Few Good, Young Brains

This past May at the 2013 Water, Energy, Smart Technology (WEST) Summit, California Governor Jerry Brown was presented a document signed by hundreds of scientists around the world declaring a consensus that the earth's environment has reached a tipping point.

Another tipping point to consider is that of the sustainability of qualified personnel in the metrology industry. Much like the tilted environmental dilemma or the hemorrhaging US Social Security fund, the lack of new blood in the metrology industry cannot possibly meet the growing demand in the technology sector. Young adults are running away, rather than running towards a career in metrology. After reading an article in an April 2012 edition of the *Metrologist*, "Status of Metrology Education in North America (a lost science?)," by Michael Taylor, I was a little flustered: If the science of measurement caught the attention of previous generations, then why not now? I don't think it's fair to blame it on the sexy sciences out there (I do all the time… really, who killed the radio star?), but what are the cultural shifts that cause the general public to be complacent about getting something done as well as reasonably possible and striving to control known variables?

So, what are the trends and influences in our culture and educational system that have led us away from metrology? The two big gorillas are the downsizing of the in-house maintenance in the military and the Great Space Race wind-down. But there has to be *something* else besides big government providing momentum—which begs the question: What is the role of government in ensuring the needs of metrology are met per the standards of a well-established, industrialized nation?

What about other nations? From the activity of nations harmonizing standards, forming events & committees, and purchasing calibration equipment for new projects, it would seem like a lot of countries are gearing up, rather than gearing down. So if we include all nations put together, is the US comparatively at a loss for number of people entering the metrology field, or are we descending into Brain Drain on an international scale as well?

Thankfully, there are still a few good, young brains out there. Each year, both NCSLI and MSC foster student involvement with conference presentations and awards. This year, we are including Best Student Papers in Cal Lab Magazine. In this issue, we feature a paper presented by some high-school students at this year's Measurement Science Conference (MSC) in Anaheim, California—"Gender-Specific Effects on Tympanic Temperature of a Cohort Sample of 15 to 16 Year Old High School Students" by Rebecca Choi, Jessica Chung, and Justin Jinwon Lee of Fairmont Preparatory Academy in Anaheim.

Happy Measuring,

Sita Schwartz
Editor

☞ To learn more about introducing metrology to the upcoming generation of young minds, check out: http://www.ncsli.org >> Learning & Development >> Metrology Outreach.

enhance innovation and performance through a varied conference program, an exhibition and technical site visits. http://www.metrologie2013.com.

Oct 14-18 TEMPMEKO 2013 Symposium. Madeira, Portugal. The 12th International Symposium on Temperature and Thermal Measurements in Industry and Science. http://www.tempmeko2013.pt.

Oct 20-25 ASPE 28th Annual Meeting. St. Paul, MN. The 2013 American Society for Precision Engineering Annual Meeting will feature a balanced program combining tutorials, scientific talks, poster presentations and commercial exhibits with networking opportunities, personal exchanges and technical tours. http://aspe.net/.

Nov 13-15 The CEESI International South American Ultrasonic Meter Conference. Lima, Peru. This event, hosted by Colorado Engineering Experiment Station Inc. (CEESI), will provide ultrasonic meter users the opportunity to collectively discuss ultrasonic metering challenges, successes, and lessons learned. http://www.ceesi.com.

SEMINARS: Online & Independent Study

ASQ CCT (Certified Calibration Technician) Exam Preparation Program. Learning Measure. http://www.learningmeasure.com/.

AC-DC Metrology– Self-Paced Online Training. Fluke Training. http://us.flukecal.com/training/courses.

Basic Measurement Concepts Program. Learning Measure. http://www.learningmeasure.com/.

Basic Measuring Tools – Self Directed Learning. The QC Group, http://www.qcgroup.com/sdl/.

Basic RF and Microwave Program. Learning Measure. http://www.learningmeasure.com/.

Certified Calibration Technician – Self-study Course. J&G Technology. http://www.jg-technology.com/selfstudy.html.

Introduction to Measurement and Calibration – Online Training. The QC Group, http://www.qcgroup.com/online/.

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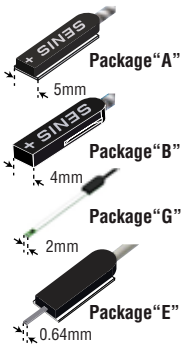

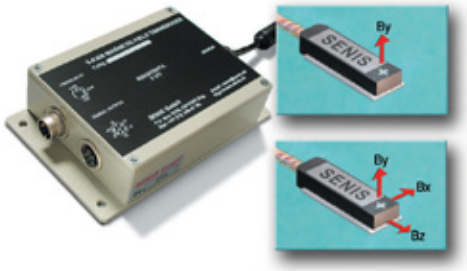

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ISO/IEC 17025 Accreditation Courses. WorkPlace Training, tel (612) 308-2202, info@wptraining.com, http://www.wptraining.com/.

Measurement Uncertainty – Self-Paced Online Training. Fluke Training. http://us.flukecal.com/training/courses.

Measurement Uncertainty Analysis – Online Training. The QC Group, http://www.qcgroup.com/online/.

Metrology for Cal Lab Personnel– Self-Paced Online Training. Fluke Training. http://us.flukecal.com/training/courses.

Metrology Concepts. QUAMETEC Institute of Measurement Technology. http://www.QIMTonline.com.

Precision Dimensional Measurement – Online Training. The QC Group, http://www.qcgroup.com/online/.

Precision Measurement Series Level 1 & 2. WorkPlace Training, http://www.wptraining.com/.

Precision Electrical Measurement – Self-Paced Online Training. Fluke Training. http://us.flukecal.com/training/courses.

Vibration and Shock Testing. Equipment Reliability Institute, http://www.equipment-reliability.com/distance_learning.html.

The Uncertainty Analysis Program. Learning Measure. http://www.learningmeasure.com/.

Do you offer Online Learning you want us to know about? Email office@callabmag.com.

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SEMINARS: Dimensional

Aug 22-23 Hands-On Gage Calibration and Repair Workshop. Colorado Springs, CO. http://www.consultinginstitute.net/.

Sep 5-6 Hands-On Gage Calibration and Repair Workshop. Kansas City, KS. http://www.consultinginstitute.net/.

Sep 12-13 Hands-On Gage Calibration and Repair Workshop. Yorba Linda, CA. http://www.consultinginstitute.net/.

Sep 16-17 Hands-On Gage Calibration and Repair Workshop. San Francisco, CA. http://www.consultinginstitute.net/.

Sep 19-20 Hands-On Gage Calibration and Repair Workshop. Salt Lake City, UT. http://www.consultinginstitute.net/.

Oct 8-9 Hands-On Gage Calibration and Repair Workshop. Indianapolis, IN. http://www.consultinginstitute.net/.

Oct 10-11 Hands-On Gage Calibration and Repair Workshop. Schaumburg, IL. http://www.consultinginstitute.net/.

Oct 24-25 Hands-On Gage Calibration and Repair Workshop. Bloomington, MN. http://www.consultinginstitute.net/.

SEMINARS: Electrical

Sep 16-19 MET-101 Basic Hands-on Metrology. Everett, WA. Fluke Calibration. http://us.flukecal.com/training/courses/MET-101.

Oct 3-4 Essentials of Electrical Metrology. Chicago, IL. WorkPlace Training. http://www.wptraining.com.

Nov 11-14 MET-101 Basic Hands-on Metrology. Everett, WA. Fluke Calibration. http://us.flukecal.com/training/courses/MET-101.

Nov 18-21 MET-301 Advanced Hands-on Metrology. Seattle, WA. Fluke Calibration. http://us.flukecal.com/training/courses/MET-301.

SEMINARS: Flow & Pressure

Sep 10-12 Fundamentals of Flow Measurement Training Course. Loveland, CO. http://www.ceesi.com.

Sep 16-19 Comprehensive Flow Measurement Training Course. Loveland, CO. http://www.ceesi.com.

Nov 11-12 Comprehensive Ultrasonic Flowmeters Training Course. Lima, Peru. http://www.ceesi.com.

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Oct 10 Flow Metrology – Gas & Liquid and Viscosity Fundamentals Hands-on. Irvine, CA. Measurement Science Conference Fall Tutorials. http://msc-conf.com/tech-fall-programs/.

Nov 12-14 Custody Measurement for Hydrocarbon Liquids Training Course. San Antonio, TX. http://www.ceesi.com.

Sep 23-27 Principles of Pressure Calibration. Phoenix, AZ. Fluke Calibration. http://us.flukecal.com/Principles-of-Pressure.

Dec 9-13 Principles of Pressure Calibration. Phoenix, AZ. Fluke Calibration. http://us.flukecal.com/Principles-of-Pressure.

SEMINARS: General & Management

Sep 30-Oct 2 Cal Lab Manager Training; Beyond 17025. Chicago, IL. WorkPlace Training. http://www.wptraining.com.

Oct 7-11 Calibration Lab Operations/Understanding ISO 17025. Las Vegas, NV. Technology Training, Inc. http://www.ttiedu.com/schedule.html.

Oct 10 5S, Lean Thinking and Project Management for Metrology Laboratories. Irvine, CA. Measurement Science Conference Fall Tutorials. http://msc-conf.com/tech-fall-programs/.

Oct 10 Elements of Measurement Techniques. Irvine, CA. Measurement Science Conference Fall Tutorials. http://msc-conf.com/tech-fall-programs/.

Oct 10 Laboratory Project Management. Irvine, CA. Measurement Science Conference Fall Tutorials. http://msc-conf.com/tech-fall-programs/.

Nov 12-14 Cal Lab Manager Training; Beyond 17025. Los Angeles, CA. WorkPlace Training. http://www.wptraining.com.

Nov 4-7 CLM-303 Effective Cal Lab Management. Everett, WA. http://us.flukecal.com/lab_management_training.

SEMINARS: Industry Standards

Sep 16-17 ISO Standard 31000 and ISO 9001 Risk Management Training. La Habra, CA. International Accreditation Service. http://www.iasonline.org.

Oct 10 Traceability To The SI – Educating BioPharma, Medical Device & Healthcare Metrology Professionals On Teaching Their Auditors & Inspectors About Calibration, Traceability and Uncertainty! Irvine, CA. Measurement Science Conference Fall Tutorials. http://msc-conf.com/tech-fall-programs/.

SEMINARS: Mass

Oct 10 Mass Metrology. Irvine, CA. Measurement Science Conference Fall Tutorials. http://msc-conf.com/tech-fall-programs/.

CALENDAR

Oct 21 Mass Metrology Seminar. Gaithersburg, MD. NIST / Office of Weights and Measures. http://www.nist.gov/pml/wmd/labmetrology/training.cfm.

SEMINARS: Measurement Uncertainty

Oct 10 Measurement Uncertainty – Fundamental Applications. Irvine, CA. Measurement Science Conference Fall Tutorials. http://msc-conf.com/tech-fall-programs/.

Oct 17-18 Measurement Uncertainty. Boca Raton, FL. WorkPlace Training http://www.wptraining.com.

Oct 22-24 MET-302 Introduction to Measurement Uncertainty. Everett, WA. Fluke Calibration. http://us.flukecal.com/training/courses/MET-302.

Nov 12-13 Measurement Uncertainty. Los Angeles, CA. WorkPlace Training http://www.wptraining.com.

SEMINARS: Temperature

Sep 17-19 Advanced Topics in Temperature Metrology. American Fork, UT. Fluke Calibration. http://us.flukecal.com/training/courses/Principles-Temperature-Metrology.

Oct 8-10 Principles of Temperature Metrology. American Fork, UT. Fluke Calibration. http://us.flukecal.com/training/courses/Principles-Temperature-Metrology.

SEMINARS: Vibration

Sep 17-19 Fundamentals of Random Vibration and Shock Testing, HALT, ESS, HASS (...). Boxborough, MA. http://www.equipment-reliability.com.

Nov 4-8 Fixture Design for Vibration and Shock Testing. Las Vegas, NV. Technology Training, Inc. http://www.ttiedu.com.

Nov 18-22 Volume Metrology Seminar. Gaithersburg, MD. NIST / Office of Weights and Measures. http://www.nist.gov/pml/wmd/labmetrology/training.cfm.

Nov 13-15 Fundamentals of Random Vibration and Shock Testing, HALT, ESS, HASS (...). Lynchburg, VA. http://www.equipment-reliability.com.

Visit www.callabmag.com for upcoming and future events!

NIST Office of Weights and Measures Receives Important 'Continuing Education' Accreditation

The International Association for Continuing Education and Training (IACET) has awarded the National Institute of Standards and Technology (NIST) Office of Weights and Measures (OWM) an "Authorized Provider" accreditation. IACET Authorized Providers are the only organizations approved to offer IACET Continuing Education Units (CEUs), which certify that IACET has evaluated the NIST OWM training program and found it to be compliant with internationally accepted standards.

Many states require that their weights and measures officials receive training throughout their careers. Using an accredited training organization gives those officials confidence that the training they will receive is of high quality.

"Our new partnership with IACET is a demonstration of our commitment to lifelong learning and high standards for all of our programs" says Carol Hockert, chief of the Office of Weights and Measures at NIST.

The accreditation period extends for five years and includes courses offered or created that follow OWM procedures during that time. With this accreditation, the NIST OWM joins nearly 650 organizations around the globe that have had their programs vetted by third-party experts in continuing education to ensure the highest possible standards are met.

The NIST OWM analyzes weights and measures training needs, obtains input from the weights and measures community, designs and delivers training for laboratory metrologists and weights and measures officials, measures the impact and effectiveness of training to ensure ongoing continual improvement, and consults with the weights and measures community to ensure ongoing professional development.

In order to achieve Authorized Provider accreditation, NIST OWM completed a rigorous application process, including a review by an IACET site visitor, and successfully demonstrated adherence to the ANSI/IACET 1-2007 Standard addressing the design, development, administration and evaluation of its training program.

Source: NIST Tech Beat for June 25, 2013, http://www.nist.gov/public_affairs/tech-beat/tb20130625.cfm.

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E.U. and U.S. to Extend Scientific Cooperation on Measurements and Standards

The European Commission's Joint Research Centre (JRC) and the U.S. Department of Commerce's National Institute of Standards and Technology (NIST) agreed to expand their current scientific cooperation to include new areas of research, such as energy, healthcare and clinical measurements, and food safety and nutrition.

Under Secretary of Commerce for Standards and Technology and NIST Director Patrick Gallagher and JRC Director General Dominique Ristori held a signing ceremony July 17th, 2013 during Transatlantic Week, an annual event intended to raise the profile of the transatlantic relationship as well as to foster a dialogue on shared purpose and joint action among U.S. and E.U. policymakers.

NIST and the commission have collaborated on many projects since the signing of the U.S.-EU Agreement on Scientific and Technological Cooperation in 1997. The new Implementing Arrangement expands on previous collaboration and provides joint access to scientific infrastructure, the exchange of scientific and technological information and experts, and support for training scientists, engineers and technical experts. The arrangement is initially for five years and can be extended.

While NIST and the JRC, the commission's in-house science service, have a history of working together, this overarching agreement replaces individual agreements on each project. It also provides additional focus on shared research priorities, including potential new areas such as security technology and systems, and environment and climate.

NIST's Gallagher highlighted current collaborative projects, including foundational research that supports the measurements underpinning manufacturing and standards, and also work developing measurement protocols and standards in fields such as homeland security technology.

Both organizations have the strategic goal to support competitiveness and economic growth, and have cooperated on standardization since 2007. The Implementing Arrangement encompasses 10 areas related to standards and measurements. Environment and climate, energy, transportation and security are high on the collaborative research agenda. In addition to reference materials in a range of areas, the cooperation will include research on civil engineering structures (such as bridges, roads and dams) and emerging information and communication technologies, as well as marine optical radiometry.

Source: NIST's Tech Beat July 23, 2013, http://www.nist.gov/public_affairs/tech-beat/.

NEW PRODUCTS AND SERVICES

Crystal Engineering GaugeCalHP

Responding to the need for high-pressure products, Crystal Engineering, a leader in high-end portable pressure calibrators and digital test gauges, has introduced the new GaugeCalHP pressure comparator for test and calibration applications up to 15,000 psi. The highly versatile device is suitable for use with water or oil, either in the field or the laboratory, and is compatible with most-large size pressure gauges.

The GaugeCalHP is designed with Crystal pressure fittings (CPF), a reservoir relief valve, and other safety features that make it the safest comparator available. The patent-pending CPF system adds a unique O-ring sealing system that permits leak-free connections without tools and a self-venting weep hole that alerts users before they disconnect from a pressurized system. CPF fittings and hoses come with an industry first 4:1 safety factor.

Key features of the GaugeCalHP include a fine adjust that is easy to use at 15,000 psi, a connection fitting with quick alignment swivel capability, and a pivoting manifold that rotates to fit large-size gauges. To increase stability, the device's reservoir can be used to quickly add a small amount of pressure to bleed air out of the CPF weep hole. A no mess, drip tray captures excess fluid.

Based in San Luis Obispo, CA, Crystal Engineering produces highly accurate, field-grade testing and calibration equipment for measurement applications in oil and natural gas, offshore drilling, oil refineries, gas distribution, power generation, nuclear power, waste water, water supply, manufacturing, aerospace, and aircraft maintenance.

Crystal Engineering is a unit of AMETEK Test & Calibration Instruments, a division of AMETEK, Inc., a leading global manufacturer of electronic instruments and electromechanical devices with annual sales of more than $3.3 billion.

For more information, contact Crystal Engineering, 708 Fiero Lane, Suite 9, San Luis Obispo, CA 93401, USA. Telephone: 1-(800)-444-1850. Fax: 1-(805) 595-5466. Or visit crystalengineering.net/gaugecalhp.

Mountz TorqueMate® FTA-100

The Torquemate® FTA-100 is a new torque tester by Mountz, Inc. designed for torque testing and calibrating torque tools. The digital torque tester provides exceptional accuracy for measuring torque on various torque tools including pulse tools, hand screwdrivers, torque wrenches and power assembly tools. The small size and portability of the torque analyzer makes it ideal for checking torque tools on production floor daily or weekly to ensure the tools aren't falling out of calibration.

The versatile and cost effective torque calibration instrument features the ability to count pulses, which is a key element for the setting the torque on a pulse tool as well as evaluating the maintenance schedule for a pulse tool. The FTA-100 unit displays both the peak torque reading and the number of pulses performed during a preset time frame to reach the final torque value.

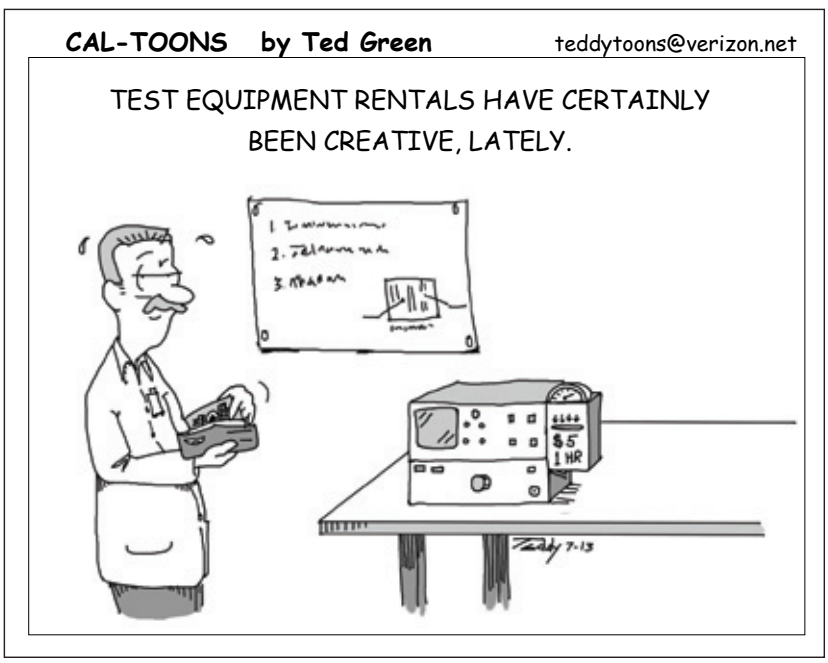
Featuring an intuitive operating system the FTA-100 provides an auto filter frequency selection system based upon type of tool being used in peak mode. The easy-to-use menu structure allows engineers and calibration technicians to quickly perform torque tests and adjust settings as needed on the torque tester. The torque analyzer features an Over Current Protection (OCP) system that protects the unit from damage or malfunction.

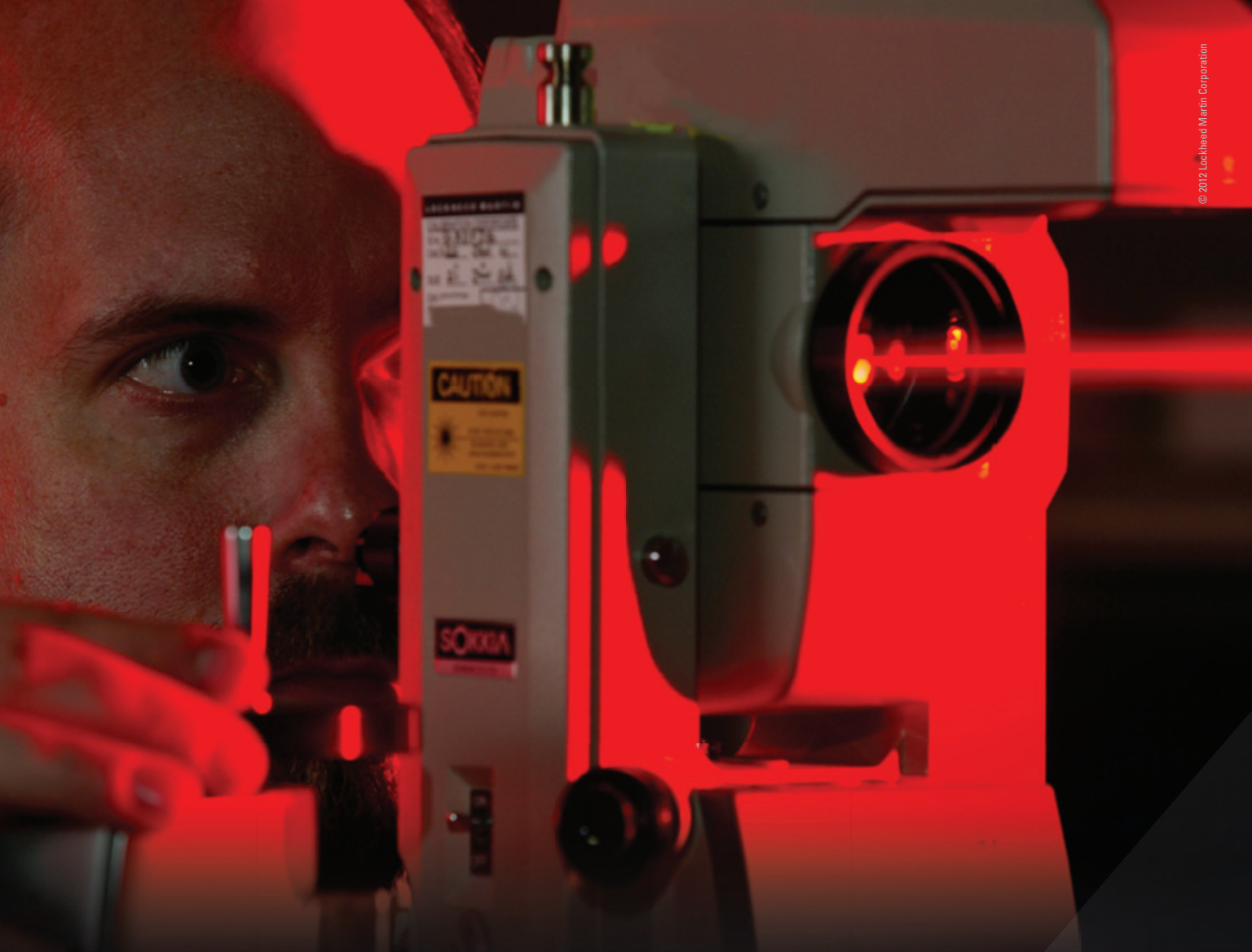
The FTA-100 includes the Mountz Data Manager software that easily allows an engineer to collect and analyze the torque data. Mountz includes a free ISO17025 Calibration Certificate with the purchase of the new torque tester, which is instant cost savings.

Other key attributes the torque meter offers are a USB interface to download torque readings in "real time" and provides "EZ-Plug & Play" with Mountz torque sensors that feature "ARCII" technology, an instant auto-recognition system. Each Mountz torque sensor connected to FTA-100 is recognized automatically by the unit at the time of power-up.

Using a quality torque tester makes a safer world through accuracy and precision. Controlling torque is essential for companies to ensure their product's quality, safety and reliability isn't compromised. The failure of a three-cent fastener that isn't properly tightened can lead to catastrophic or latent failures. Fasteners that are insufficiently fastened can vibrate loose and excessive torque can strip threaded fasteners. Torque measurement should occur in all three facets of the assembly process.

For more information visit: http://www.mountztorque.com/products/torque-analyzers-sensors/torquemate-fta-100.





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NEW PRODUCTS AND SERVICES

ScalesNet-M Software for Mass Metrology

With the release of the ScalesNet-M Software, Maro Elektronik offers innovative solutions to satisfy the more simple requirements of small laboratories all the way up to the complex requirements of mass manufacturers and national institutes. This is made possible through ScalesNet-M's modular design, managed via a hardlock licensed access to enabled modules. More than 16 years of experiences, derived from input of leading mass manufacturers and mass laboratories, have contributed to develop ScalesNet-M, making it the leading professional and commercially available software for efficient mass calibration.

One of the stringent requirements in quality management is providing certification of traceability to a national standard for all calibrated weights. This can be achieved using ScalesNet-M.

ScalesNet-M supports all quality requirements in mass laboratories, from controlling the calibration schedules for the used reference weights and the used comparators, to the connected data logger and their respective sensors.

The calibration of a customer weight is always embedded into a work order process. This work order process includes all customer and weight parameters, including the shape, marking, material, density etc. These unique weight specific parameters are stored in the ScalesNet-M database, ensuring the traceability of the weight.

Each measurement cycle automatically reads real time climate data and reports all calculated results, including all relevant criteria of the weight at the end of the calibration cycle. The calculations include all uncertainties (conventional mass and true mass), air density, standard deviations of the measurement and more.

All applicable formulas for calculating the weight and the calculation of deviations are described in the online help system of ScalesNet-M.

After generating a printout of the customer certificate, ScalesNet-M archives all calibrated weights. The customer certificates are generated via MS-Word© where all text variables and measurement results are displayed via bookmarks in the desired document positions.

ScalesNet-M Features

- Calibration of customer weights, any class and values;
- Suitable for all weight cycles in accordance with international guidelines (OIML R111, ASTM E617);
- Dissemination of mass scale for higher class weights (e.g. E1, ASTM class 0 etc.);
- Calculation and evaluation of calibration results in accordance with international guidelines such as OIML, ASTM;
- Base for an accredited measurement laboratory in accordance with DIN EN ISO/IEC 17025;
- Connecting of comparators, load alternators, robots and climate measurement stations from most manufacturers;
- Plausibility test when standard weights and comparators are selected;
- Quick comparison of weights without logging;
- Monitoring, recording and visual presentation of climate data;
- Display of customer and reference weight calibration histories;
- Cycles with and without additional weights and sensitivity weights;
- All weight classes are already integrated - in accordance with OIML R111 and ASTM E617;
- Creation of own weight classes with user defined permissible errors of nominal values;
- Automatic uncertainty calculation for conventional mass and true mass;
- Automatic creation of multilingual, linguistically accurate calibration certificates;
- SQL database structure for customer, weights, balances and calibration data, etc.;
- Administration of user rights with user defined roles(read, edit and administration);
- Automatic generation of inventory lists (balances, climate stations, reference weights);
- Manual input of weighing data for comparators without RS232 connection;
- Statistic functions (number of weights per defined period, useful life of the balance per defined period etc.).

A live demonstration of ScalesNet-M via remote session is available by agreement. For a short period an introductory offer will be available. Please contact our sales department for details: us-sales@maro.de or visit www.scalesnet-m.com.

Pasternack High Frequency Power Dividers

Pasternack Enterprises, Inc., an industry leading manufacturer and global supplier of RF and microwave products, introduces a brand new line of ultra-broadband power dividers capable of 50 GHz. These millimeter wave power dividers (also referred to as RF power splitters) are ideal for use in radar systems, electronic warfare equipment, fiber optic systems, 10G Ethernet and any application that requires high frequency, multi-octave performance.

Pasternack is offering three new configurations of broadband power dividers including two with 2.92 mm connectors, one of which is a low VSWR version. Both 2.92 mm power dividers are capable of frequencies ranging from 10 GHz to 40 GHz and are rated to 10 Watts maximum input power. The third option is a 2.4mm power divider capable of 10 GHz to 50 GHz and also has a power rating of 10 Watts. All three high frequency power dividers are Wilkinson 2-way designs utilizing a compact package that offers low insertion loss and phase stability across their broad operating range.

The new 40 GHz and 50 GHz power dividers from Pasternack have a maximum insertion loss of 1.5 dB and VSWR of 1.6. These ultra-broadband power dividers have a typical phase balance of 6 degrees and carry a maximum isolation rating of 15 dB. Each of Pasternack's newly added 2-way RF power dividers are RoHS compliant.

The new broadband power dividers from Pasternack are in-stock and available now. You can view these new products by visiting http://www.pasternack.com/pages/Featured_Products/ultra-broadband-2-way-power-dividers-up-to-50-ghz.htm directly. Pasternack Enterprises, Inc. can be contacted at +1-949-261-1920.

Bi-Tec Light-Color-Spectral Meter

Gigahertz-Optik's new BTS256-E Light Meter provides all necessary illuminance, color and spectral data to fully qualify solid state lighting and any other type light source. Now lighting designers, engineers, manufacturers and maintenance workers have a cost-effective way to accurately characterize any type light source on site on the fly.

The key component of the BTS256-E is its Bi-Technology sensor that includes both a precision photometric photodiode and diode array spectrometer. Any spectral mismatch error of the photopic sensor is compensated on-line using the diode array's measured spectral data. This reduces measurement uncertainty when evaluating any type of light source. A built-in electro-optical shutter for dark-signal pixel offset compensation increases the highly linear dynamic range of the C-MOS diode array detector.

A large 20mm diameter diffuser provides a precise cosine corrected measurement geometry, a basic requirement for accurate illuminance measurements. This is especially important when measuring oblique angle illuminance as in a parking lot, on the factory floor or in any application involving overlapping light fields. Plus the large input optic averages out any hot-spot effects which can be a problem for smaller diameter optics.

The LED-Luxmeter is built for rugged field portability in a lightweight aluminum housing.

It is powered by a rechargeable lithium battery and features a large size 240x160 pixel resolution transflective display located on the same side of the housing as the input optic. Three front panel control buttons control all meter functions like illuminance area mapping, internal memory and datalogging as well as many advanced settings.

For full PC control, storing data and to recharge its battery a USB2 interface is standard equipment. The supplied S-BTS256-E software controls all functions necessary for measurement, display and data export in the lab, field or in fabrication. The software offers different routines for data acquisition, a selection of numerical and graphical displays for data visualization and different file type export options such as ASCII format and Microsoft Excel.

For system integration SDK software development kits are available for National Instruments LabView, Microsoft .NET, C/C++. The software development kits make it easy for self-progammers to embed the BTS256-E LED-Luxmeter within their own software.

View BTS256-E highlights video at: www.led-measurement.com.

Rohde & Schwarz All-In-One Solution for Testing Broadcast Equipment

The new R&S BTC broadcast test center from Rohde & Schwarz provides a complete testing environment for nearly all audio, video and multimedia applications – in a single device. The RF reference signal generator generates RF signals for all global TV and broadcasting standards and simulates transmissions. The generator can also internally analyze the audio/video functions of DUTs in realtime. The modular design provides a high degree of scalability, allowing the R&S BTC to be configured for any customer requirement.

The R&S BTC reference signal generator enables users to perform complete end-to-end tests in realtime over all open systems interconnection (OSI) levels. DUTs can also be integrated into fully automated test sequences. This all-in-one generator handles today's and tomorrow's transmission standards. Video and audio streams can be generated, played back, fed externally and output in modulated form. The R&S BTC combines signal generation, DUT embedding and video/audio analysis while simultaneously determining the picture failure point (PFP). The result is fast, convenient and reproducible objective picture quality assessment.

Applications include development, certification and quality assurance for chipset and receiver manufacturers as well as test houses. Manufacturers of professional satellite equipment, network operators, rental companies, regulatory authorities and the A&D industry will also benefit from this scalable test solution.

The R&S BTC high-end broadcast signal generator has two separate realtime signal paths, each with a modulation bandwidth of 160 MHz. The R&S BTC comes with a comprehensive range of analysis features and supports all common digital and analog standards for cable, satellite and terrestrial television as well as digital and analog audio broadcasting standards and second-generation DVB standards such as DVB-T2, DVB-C2, DVB-S2 and their interfaces.

Thanks to its modular design, the R&S BTC can be optimized to perform a variety of tasks. This saves money since it eliminates the need for expensive and time-consuming test setups with many separate T&M instruments. Integrated, automated test sequence control and test suites, such as DTG d-book, e-book and NorDig, reduce test times. The repeatable tests allow otherwise time-consuming certification and logo tests to be carried out quickly and reliably.

One of the main tasks when developing broadcast equipment is to test the equipment under realistic and complex interference conditions. The R&S BTC covers this requirement by offering up to eight arbitrary waveform generators (AWG) per RF path in addition to the two independent realtime signal paths. The AWGs generate complex interference scenarios with a maximum dynamic range over the entire frequency bandwidth. Realistic environmental conditions can be simulated using various noise sources (broadband and bandlimited AWGN, impulse or phase noise), predistortion, nonlinearities, filtering, fading and MIMO.

Developers of chips and tuners need I/Q data to be highly flexible in terms of data rates and data formats. The R&S BTC is equipped with digital I/Q

data interfaces and flexible I/Q data input/output for ideal test and design capabilities.

The high resolution, 8.4-inch touchscreen display and the graphical user interface with hierarchical function blocks allow users to quickly and easily operate the R&S BTC. The entire test setup, including signal generation, sequence control, analysis and the DUT, can be graphically displayed for a clear overview of even complex measurement tasks. The remote control commands are compatible with the successful R&S SFx family, also with the R&S SFU, an internationally established multistandard reference signal generator. This simplifies the integration of the R&S BTC in existing test environments.

The R&S BTC reference signal generator is now available from Rohde & Schwarz. For more information, visit: http://www.rohde-schwarz.com/btc.

Yokogawa Announces New Portable Pressure Calibrator

The new Yokogawa CA700 Portable Pressure Calibrator is equipped with a silicon resonant sensor that uses Yokogawa proprietary DPHARP technology. The CA700 can measure pressures with an accuracy that is within ±0.01% of rdg*, making it one of the most accurate portable pressure calibrators on the market. This highly accurate portable pressure calibrator features a variety of functions that includes a wide selection of measuring ranges, as found/as left data storage, and memory capacity to store calibration procedures. The Yokogawa CA700 provides an accurate and efficient calibration and verification tool for pressure/differential pressure transmitters and other types of field devices for commissioning or regular inspection.

Product Features

1. Best-in-class accuracy - The CA700 can measure pressures with an accuracy that is within ±0.01% of rdg* and can also output and measure current and voltage within ±0.015% of rdg. The CA700 is the only pressure calibrator in its price range that can generate and measure both current and voltage.
2. Functions that improve calibration efficiency - For more stable and efficient calibration, the CA700 is able to store the calibration procedures for pressure transmitters and switches in its internal memory. It also records data and error rates before and after calibration.
3. Wide measurement range - The CA700 comes in three models with a wide variety of measurement ranges. Users can thus choose the model with the desired measurement range, eliminating the need for the purchase of multiple calibrators.

For more information, please visit our website tmi.yokogawa.com.

NEW PRODUCTS AND SERVICES

Agilent Technologies New 6½ Digit Digital Multimeters

Agilent Technologies Inc. (NYSE: A) introduced the Truevolt Series digital multimeters, offering several advantages over previous models. They help engineers see their measurement data in new ways, get actionable information faster, and document their results more easily. Exclusive Truevolt technology reduces extraneous factors such as noise, injected current and input bias current for increased measurement confidence.

The Agilent 34461A DMM is a direct replacement for the industry-standard Agilent 34401A DMM, and was designed to make migration easy for current users of the 34401A. The Agilent 34460A offers engineers a basic entry point to the 6½ digit class of DMMs.

Compared with the 34401A DMM, the new 34461A offers expanded current ranges from 100 μA to 10 A. Both the 34460A and 34461A have a temperature measurement function (RTD/PT100, thermistor) and expanded diode measurement capability to allow engineers to measure a larger full-scale voltage (5 V) so they can test more diode types, such as LEDs.

Most DMMs show results on a low-resolution numeric display. With the Agilent Truevolt Series, engineers get a 4.3-inch, high-resolution, color display to view numerical readings, long-term trends (34461A only), measurement histograms and statistical information. They can also set display preferences and pull them up automatically the next time they start up the instrument.

Driverless easy file access USB file transfer provides simple USB connectivity between an Agilent Truevolt DMM and a PC, using the standard USB media transfer protocol. Engineers can drag and drop measurement data, instrument settings and screen images into PC applications without any additional software.

The Digital Multimeter Connectivity Utility software lets engineers control, capture and view the Agilent DMMs on their benches. With a single click they can transfer data to a PC via USB, GPIB, LAN or RS-232 (when used with older-generation Agilent DMMs).

Real-world signals are never flat. They have some level of AC signal riding on top from power line noise, other environmental noise, or injected current from the meter itself. How well a DMM deals with extraneous factors and eliminates them from the true measurement makes a big difference to its accuracy. Using patented analog-to-digital converter technology, Agilent Truevolt Series DMMs account for measurement errors created by these real-world factors, so engineers can be confident in their measurements.

Agilent Truevolt DMMs have less than 30 percent of the amount of injected current attributed to the meter compared with DMMs made by other vendors.

In real measurement situations, input currents create measurement errors, adding voltages to DMM results. Truevolt DMMs take care of input bias current. Other vendors' DMMs offer 20 percent to infinitely poorer performance (some are too noisy to get any measured results).

In the 6½ digit class of meters, only Agilent uses digital direct sampling techniques to make AC rms measurements. This results in a true rms calculation and avoids the slow response of analog rms converters used in all other vendor's 6½ digit DMMs, allowing for crest factors up to 10 without additional error terms.

Additional information about Agilent's Truevolt Series DMMs is available at www.agilent.com/find/Truevolt.

Whitehouse Scientific Sieve Aperture Size Calculator Now on Flash Drive

Whitehouse Scientific's Sieve Aperture Size Calculator, for use with the company's NIST-traceable sieve calibration standards, is now provided in a convenient flash drive format and is free of charge to purchasers of sieve standards. With standards available in a variety of different sizes, Whitehouse Scientific's unique microsphere method of sieve calibration enables sieve users to quickly and easily calibrate on-site rather than having to send sieves away for third party analysis.

A two-minute sieve calibration video on the Whitehouse Scientific website is proving to be a popular learning tool taking viewers through each step of the procedure: http://bit.ly/WHTSC.

Calibration using the Whitehouse Scientific method uses microsphere standards supplied in single shot bottles. Standards are available in sizes from 20 μm to 3.5 mm, enabling users to select the size range appropriate to their sieve. The calibration method involves measuring the weight of standards of a given size passing through the sieve. The percentage passing through is then referenced to the calibration curve supplied or entered into the Sieve Aperture Size Calculator to give the mean aperture size. Results have accuracy and repeatability better than 1 μm and are traceable to both NIST and NPL. Calibration time is typically around one minute and results are independent of the shaking method used.

For further details of available calibration standards go to www.whitehousescientific.com

Oven Industries Inc. Lab Temperature Controllers

Oven Industries Inc. announces new laboratory temperature controllers with ramp/soak capabilities. The 5R6-900 benchtop controller has many outstanding user-friendly benefits. Contained all in one enclosure, the device can be plugged into the wall as a self-contained temperature control system, which has its own power supply. This distinctive detail makes the device unique, as well as highly convenient for users.

The temperature controller can also be used universally, which allows the user to use the device wherever they are located. As a solid state MOSFET bidirectional compact unit featuring an internal power supply, it is also capable of loading currents up to 10A. The compact size, as well as the isolated communication port, makes using the 5R6-900 benchtop temperature controller a breeze.

User-friendly and PC programmable, the electronic controller easily connects to a computer through the electrically isolated RS232 communications port. The computer can be utilized as a connector and the unit can stand alone, once the desired parameter settings are in place.

Great for usage in universities, science laboratories, PCR research and any businesses that specialize in temperature control. The controller features an easy-to-read digital display for controlling functions, including adjusting output voltage and setting the desired temperature. Complete with an auto output shutdown if the sensor is opened or shorted, the unit also includes high, low and no alarm settings.

Oven Industries has many unique options for customized, industrial quality temperature controllers and sensors. All products are designed by experts and have been used in a wide variety of applications, including commercial, industrial, military, medical equipment and food processing. http://www.ovenind.com.

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Testing Linearity on the Agilent E441xA Power Sensors

Michael Schwartz
Cal Lab Solutions, Inc.

Today's new high dynamic range power sensors are not built the same as the older generations of sensors. Older generations of power sensors only had a correction table for their frequency response. This was a simple number that could be easily dialed or entered into the power meter allowing the power meter/sensor to make accurate measurements.

The advent of the EPROM embedded power sensor allowed manufacturers to store more correction tables with greater complexity. It is not uncommon to have power sensors with multiple cal factor tables, linearity corrections, temperature correction, modulation corrections, and more. Periodically, we have to test these operations to ensure the power sensors are making accurate measurements.

In this example, we will be focusing on the linearity accuracy of the Agilent E441xA series power sensors. Keep in mind that all the Agilent E-Series power sensors require this test and, if not working correctly, can dramatically affect the accuracy of your measurements.

First we have to understand the design of the E441xA series power sensors. These sensors are a single diode based power sensor. They have a power operating range of -70 to +20 dBm. However, the square law region of the power sensor only covers a small portion of the lower power range -70 to about -20 dBm. Measurements made in the square-law region have a linear power to voltage conversion, while measurements made above -20 dBm have to be corrected. Figure 1 is a representation of uncorrected power measurements made both inside of outside of the square law region of a diode.

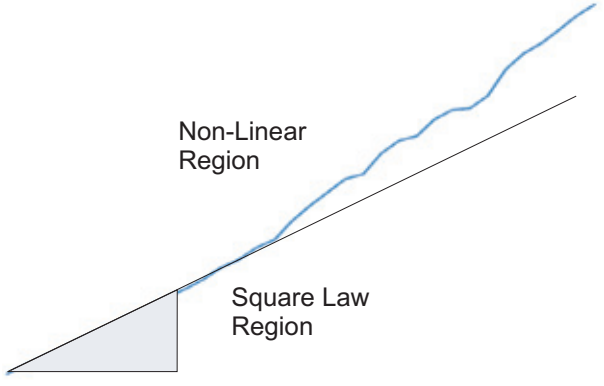

Figure 1.

Similar to the cal factor correction table, these sensors also store a linearity correction table in the EPROM. The linearity table corrects for variations in the power level measurement and like the cal factor table, it also needs to be periodically updated.

Recently a customer of ours discovered the results of a poor calibration on an E4412A. The unit was passing on a calibration station that was only testing Cal Factors / Power Flatness, but the sensor was having a problem making accurate measurements:

Applied	Measured
+20 dBm	+20.61
+16 dBm	+16.55
+10 dBm	+10.36
0 dBm	0.00
-10 dBm	-10.25
-20 dBm	-20.30
-30 dBm	-30.32
-40 dBm	-40.32

This is the typical result when this series of power sensor's linearity is not properly calibrated. Because the sensor is zeroed and calibrated using the power meter's Ref Output, the 0 dBm measurements at, and even near, the 0 dBm point are within specifications. But as the power levels applied move away from that 0 dBm calibration point, the delta power error of the applied versus measured power widens.

You can see from the data points above, this improperly calibrated power sensor making a 16 dBm measurement is off by 0.61 dBm (or 15.8%); at the low end, making a measurement at -40 dBm and below, you are off by 0.32 dBm (or 7.1%).

It is apparent that the linearity tables in the power sensors are off and need to be re-characterized or adjusted back into specification. The linearity table is off by a suspected 0.32 dB at the 0.00 dBm calibration point. This offset error will affect every power measurement except ones made at or

near 0 dBm. This is why many systems that only test Cal Factor and rho will unknowingly pass power sensors with huge measurement errors.

Every time these power sensors are calibrated, the linearity must be verified to maintain the accuracy of these power sensors. Skipping linearity verification presents a huge risk to your measurement accuracy. Only a few calibration labs have the technology to adjustment on these power sensors back into specification. But every lab should, at the very least, spot check the linearity of these and other power sensors requiring linearity verification. If problems are spotted, the power sensor can be sent back to Agilent Technologies or any calibration lab running PS-CAL™ from Cal Lab Solutions for alignment.

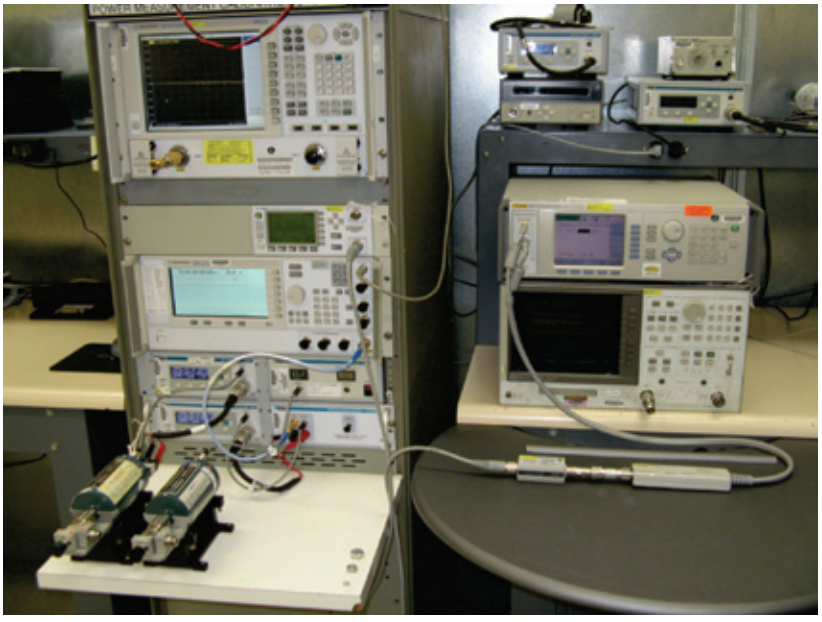

Figure 2.

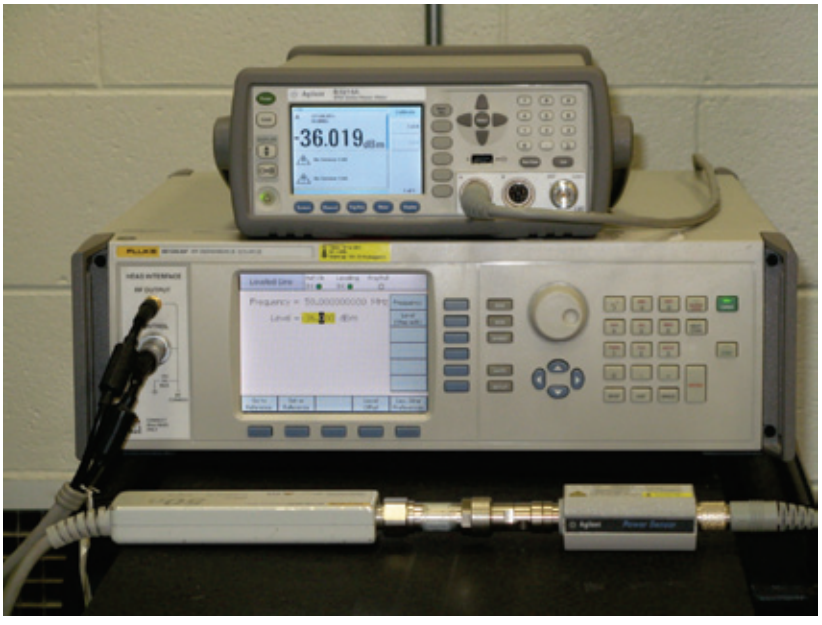

Figure 3.

One of the simplest ways to verify the linearity of the E441xA series power sensors is with the Fluke 9610A or 9640A. Because the Fluke 9640A has absolute accuracy from -130 to +24 dBm, it is a great tool for quickly verifying a power sensor's linearity.

The following procedure steps check the linearity of the power sensor from the top portion of the square-law region all the way through its maximum power measurement point. It is a very fast method of verifying a sensor's linearity and can be completed in under an hour by an experienced technician.

Procedure Steps

1. Set the frequency in the power meter to 50 MHz, then zero and calibrate the E441xA power sensor with a compatible power meter.

   Note: When zeroing the power sensor, keep it disconnected from any RF Source including the Ref Output of the power meter.

2. Connect the DUT power sensor to the Fluke 9640A output (refer to Figures 2 and 3).
3. Apply 0 dBm @ 50 MHz from the Fluke 9640; this will show you the delta between the power meter's Ref Power Output and the Fluke 9640.
4. Re-cal the power sensor to the Fluke 9640A's 0 dBm 50 MHz output, by pressing the cal button on the power meter with the signal applied. The power meter should indicate 0.00 dBm.
5. Change the power level of the Fluke 9640 to -36.00 dBm and compare the readings to the limits in the following table.
6. Repeat for each power level.

Power	Spec	Lower	Reading	Upper	Unc
-36.00	3.0%	-36.132		-35.872	0.05 dBm
-35.00	3.0%	-35.132		-34.872	0.05 dBm
-34.00	3.0%	-34.132		-33.872	0.05 dBm
-33.00	3.0%	-33.132		-32.872	0.05 dBm
-32.00	3.0%	-32.132		-31.872	0.05 dBm
-31.00	3.0%	-31.132		-30.872	0.05 dBm
-30.00	3.0%	-30.132		-29.872	0.05 dBm
-29.00	3.0%	-29.132		-28.872	0.05 dBm
-28.00	3.0%	-28.132		-27.872	0.05 dBm
-27.00	3.0%	-27.132		-26.872	0.05 dBm
-26.00	3.0%	-26.132		-25.872	0.05 dBm
-25.00	3.0%	-25.132		-24.872	0.05 dBm
-24.00	3.0%	-24.132		-23.872	0.05 dBm
-23.00	3.0%	-23.132		-22.872	0.05 dBm
-22.00	3.0%	-22.132		-21.872	0.05 dBm
-21.00	3.0%	-21.132		-20.872	0.05 dBm
-20.00	3.0%	-20.132		-19.872	0.05 dBm
-19.00	3.0%	-19.132		-18.872	0.05 dBm
-18.00	3.0%	-18.132		-17.872	0.05 dBm
-17.00	3.0%	-17.132		-16.872	0.05 dBm
-16.00	3.0%	-16.132		-15.872	0.05 dBm
-15.00	3.0%	-15.132		-14.872	0.05 dBm
-14.00	3.0%	-14.132		-13.872	0.05 dBm
-13.00	3.0%	-13.132		-12.872	0.05 dBm
-12.00	3.0%	-12.132		-11.872	0.05 dBm
-11.00	3.0%	-11.132		-10.872	0.05 dBm
-10.00	3.0%	-10.132		-9.872	0.05 dBm
-9.00	3.0%	-9.132		-8.872	0.05 dBm
-8.00	3.0%	-8.132		-7.872	0.05 dBm
-7.00	3.0%	-7.132		-6.872	0.05 dBm
-6.00	3.0%	-6.132		-5.872	0.05 dBm

Power	Spec	Lower	Reading	Upper	Unc
-5.00	3.0%	-5.132		-4.872	0.05 dBm
-4.00	3.0%	-4.132		-3.872	0.05 dBm
-3.00	3.0%	-3.132		-2.872	0.05 dBm
-2.00	3.0%	-2.132		-1.872	0.05 dBm
-1.00	3.0%	-1.132		-0.872	0.05 dBm
0.00	3.0%	-0.132		0.128	0.05 dBm
1.00	3.0%	0.868		1.128	0.05 dBm
2.00	3.0%	1.868		2.128	0.05 dBm
3.00	3.0%	2.868		3.128	0.05 dBm
4.00	3.0%	3.868		4.128	0.05 dBm
5.00	3.0%	4.868		5.128	0.05 dBm
6.00	3.0%	5.868		6.128	0.05 dBm
7.00	3.0%	6.868		7.128	0.05 dBm
8.00	3.0%	7.868		8.128	0.05 dBm
9.00	3.0%	8.868		9.128	0.05 dBm
10.00	3.0%	9.868		10.128	0.05 dBm
11.00	3.0%	10.868		11.128	0.05 dBm
12.00	3.0%	11.868		12.128	0.05 dBm
13.00	3.0%	12.868		13.128	0.05 dBm
14.00	4.5%	13.868		14.128	0.05 dBm
15.00	4.5%	14.868		15.128	0.05 dBm
16.00	4.5%	15.868		16.128	0.05 dBm
17.00	4.5%	16.868		17.128	0.05 dBm
18.00	4.5%	17.868		18.128	0.05 dBm
19.00	4.5%	18.868		19.128	0.05 dBm
20.00	4.5%	19.868		20.128	0.05 dBm

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The Metrology of Counting Protein Particles

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A common degradation pathway for protein-based drugs is the growth of protein aggregates or particles. Counting and characterization of these particles is needed to assure the quality, efficacy, and safety of this type of drug. The unusual physical attributes of protein particles lead to difficulties in obtaining accurate particle counts with traditional calibration standards and methods. We describe the development of instrument-response models, novel instrumentation, and novel reference materials to address this metrology issue.

Introduction

Protein-based drugs are a rapidly growing class of pharmaceuticals, driven by the ability of these drugs to treat conditions that do not respond to traditional small-molecule drugs and by the increased sophistication of protein design and manufacture. One degradation path for these drugs is the formation of particles, consisting of aggregated protein and possibly a non-protein nucleating core [1, 2]. Stresses that can lead to the formation of protein particles include changes in chemical environment, exposure to interfaces, agitation, elevation of temperature, or the introduction of non-protein particles. There is some evidence that these particles, although constituting a very small volume fraction of the administered drug, may trigger an immune response [3]. In some cases, the immune response has no effect on the patient or on the drug efficacy, but in other cases, the response can lead to altered efficacy, or in very rare cases, development of patient antibodies that cause an auto-immune attack of the patient's own proteins. Figure 1 shows examples of bright-field microscopy images of protein particles.

Regulatory bodies and industry both desire to count and characterize the particles occurring in protein drugs. Particle characterization has important roles throughout the drug development process. Early in the development process, drug candidates are screened to see if they have acceptable resistance to aggregation. Prior to and during clinical trials, the product formulation is adjusted to give maximum stability, including resistance to aggregate formation. Characterization of the nature and count of intrinsic protein aggregates on exposure to various stresses is useful to assess the level of risk posed by particles. Once drug products are in production, simplified methods for particle counting are used as a release test to verify the quality of drug lots.

The size of protein aggregates varies from 10s of nanometers to 100s of micrometers. Protein particles have an irregular morphology and low optical contrast (equivalent to a small refractive index difference from the matrix fluid). Another complication is that protein particles are subject to dynamic changes in size.

The terminology for particle detection in the biopharmaceutical field reflects the evolution of particle counting efforts. Historically, the term 'aggregates' has been used primarily to refer to small protein oligomers with diameters below 100 nm, whereas 'particle' has been used to refer to larger objects that may or may not be composed of protein. In another category, silicone used to coat syringes pre-filled with drug product can leach into the drug product and form droplets. In cases where a particle counting instrument cannot differentiate between a protein aggregate, a silicone oil droplet, and foreign matter, or when only the total count of all objects is desired, the word 'particle' is used for all objects.

Methods used for particle and aggregate detection depend on the particle size. At the lower end of the range, for aggregates consisting of small protein oligomers, industry relies on size exclusion chromatography and analytic ultracentrifugation to monitor the level of aggregated protein. These methods are well established, and interferences to the methods are well understood [4].

Drugs that are administered by other than oral or topical routes are visually inspected, which is effective at detecting particles greater than ≈ 70 μm diameter. Detection of visible particles in biopharmaceuticals presents a number of challenges. First, traceability of any sort for visible detection

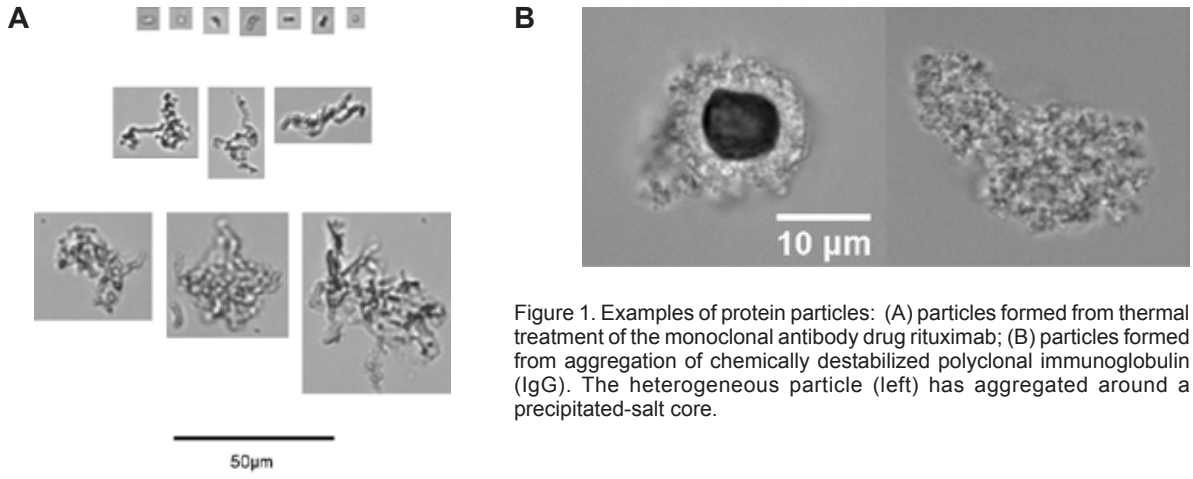

Figure 1. Examples of protein particles: (A) particles formed from thermal treatment of the monoclonal antibody drug rituximab; (B) particles formed from aggregation of chemically destabilized polyclonal immunoglobulin (IgG). The heterogeneous particle (left) has aggregated around a precipitated-salt core.

requires training of inspectors using a challenge set of drug vials intentionally containing particles of known size and composition. At present, there are no existing standards for visible particles that mimic the optical properties of large protein aggregates. Another issue is that biological drugs are often opalescent, due to the very high protein concentrations (> 100 mg/mL), and this opalescence can obscure particles.

For diameters greater than 10 µm, pharmacopeial methods for particle detection in therapeutic products were designed to identify manufacturing debris, such as glass, rubber or steel, that could cause blockage of patient capillaries [5]. For these types of particles, two effective counting techniques are filter microscopy and light obscuration. In filter microscopy, particles are collected on a membrane filter and the filter is then inspected under a microscope. In light obscuration, a stream of test sample passes through a flow cell traversed by a light beam; when a particle scatters light from the beam, the intensity of the beam drops. The magnitude of the intensity drop may be mapped to particle size. In each case, the particle size distribution of the particles is obtained.

When applied to biopharmaceutical products, traditional pharmacopeial methods give mixed results. Filter microscopy does not work at all for protein particles because the highly hydrated and flexible protein particles distort, flatten, and become invisible on the filter. Light obscuration can give highly repeatable measurements, but the reported particle counts can be in error because the physical properties of protein particles differ substantially from that of the polystyrene latex (PSL) beads commonly used to calibrate instruments.

Recently, a number of new technologies have been adopted by the biopharmaceutical industry to address the difficulty of counting and sizing protein particles [6]. The most common of these new techniques is the flow microscope, which consists of a microscope and camera, a flow cell for passage of the test sample through the focal plane of the microscope, and software that enables automated acquisition of images and identification of particles. Comparisons of the counts obtained from light obscuration particle counters and flow microscopes often give light obscuration counts that are a factor of ten or more lower than the particle counts obtained from flow microscopy.

Below the range of flow microscopy, but above the range of size exclusion chromatography, a number of novel methods are being developed, including field flow fractionation, nanoparticle tracking analysis, and resonance mass measurements [6]. Establishing traceability for each of these requires investigation into the principle of operation of each, and a review of the applicability of existing methods and reference materials.

Calibration Challenges

As defined by the International Vocabulary of Metrology, calibration consists of relating the indication of the instrument to the defined values of a measurement standard [7]. In the case of protein particles, the available standards consist of spherical beads of high optical contrast, and the relation of instrument indication to the values of the standards is not sufficient when the instruments respond to actual particles differently than to the standards. In other terms, the calibration process in no way guarantees that the indication of the instrument will be correct for a particle of properties far different than a PSL bead. In fact, accurate measurements are guaranteed only by:

- developing appropriate models for the instrument response,
- identifying and characterizing the physical properties of protein particles relevant to the counting method considered, and
- developing reference standards that mimic protein particles.

At NIST, we are conducting a program expanding on each of these themes. Our initial work focuses on providing methods and reference materials to enable traceability to the SI for equivalent diameters of 1 μm and greater.

Models of Instrument Response

Two examples of the development of instrument response models are: a) the modeling of the light scattering process in light obscuration counters, and b) the simulation of electrical-sensing-zone (ESZ) counters for the detection of porous and irregularly shaped particles.

To model the light scattering process, we treat the protein particles as randomly oriented spheroids with an effective refractive index, and determine the scattering amplitude from an eikonal approximation [8]. This optical approximation is appropriate for particles with small refractive index difference from the surrounding matrix, which is the case for protein particles. The extinction efficiency factor Q (the ratio of the scattering cross section to the geometric cross section of the particle) is then calculated by integrating the scattering amplitude over the appropriate range of angles for the particle detector considered. These calculations reveal that the finite detection aperture of the light obscuration counter must be accounted for, and that the most important particle attribute is the refractive index difference between the particle and the matrix liquid, as shown in Figure 2. Modeling of the particle scattering process demonstrates why light obscuration tends to undercount the number of particles above a given threshold: the light obscuration counter interprets the reduction in transmitted light as the diameter of a PSL bead that would create the same reduction in transmitted light. Since the Q of protein particles is substantially less than that of PSL beads, across the whole size range of the instrument, the equivalent PSL diameter is less than the actual protein particle size. In contrast, a flow microscope has better abilities at correctly identifying the size of low-contrast particles.

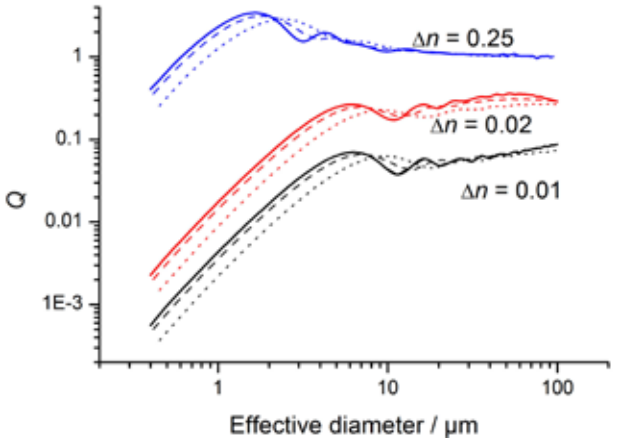

Figure 2. Extinction efficiency factor Q as a function of particle diameter, for prolate spheroids of refractive index difference from the matrix fluid, Δn, and for different aspect ratios (1 for solid lines, 2 for dashed lines, and 4 for dotted lines). For PSL beads in water, $\Delta n \approx 0.25$; for protein particles, Δn may range from ≈ 0.005 to 0.07.

To model the electrical sensing zone counters, we have used finite element modeling to understand the perturbation in ionic conductance as a particle passes through the orifice. The amplitude and shape of the electrical resistance variation depend on the path of the particle through the orifice, the particle geometry, and the particle orientation inside the orifice. Predictions of the model can be confirmed by measuring non-spherical particles of known geometry.

To further investigate the differences between optical imaging and the ESZ technique, we have developed a device that combines optical imaging and a microfluidic electrical sensing zone counter, as shown in the schematic of Figure 3A. The electrical sensing zone technique measures the increase in ionic resistance across an orifice when a particle passes through this orifice. To make an ESZ device that is compatible with optical microscopy, we have fabricated the orifice and flow cell using microfluidic techniques. As the sample flows through the orifice, electrical detection of a particle triggers illumination and capture of the particle image by the camera. For simple solid shapes, such as cells, the resistance increase can be related to the volume of the particle. For more complex shapes, such as irregular aggregates of protein particles, it is not clear if the particle volume can be inferred from the resistance increase. Figure 3B shows the optical image (by bright field microscopy) of a particle passing through the microfluidic orifice along with the corresponding increase in an electrical signal proportional to resistance change. Image analysis of the microscopy results will give a measure of typical morphological parameters, such as the apparent particle area and aspect ratio. Comparison of these parameter values with the electrical-sensing-zone signal for individual particles will give us insight into the differences in response of the two counting methodologies. We are improving the device further by adding a high-speed fluorescence camera to the microscope, which will enable us to take real-time pictures of fluorescently dyed particles passing through the orifice.

In the area of reference materials, we are developing a reference material consisting of a polydisperse distribution of abraded ethylene-tetrafluoroethylene (ETFE) particles [9]. ETFE has several desirable properties: it is chemically inert and very rugged, and has a refractive index (1.40) very close to that of amorphous protein adsorbed on surfaces [10]. When abraded from a solid block, the morphology of the resulting particles

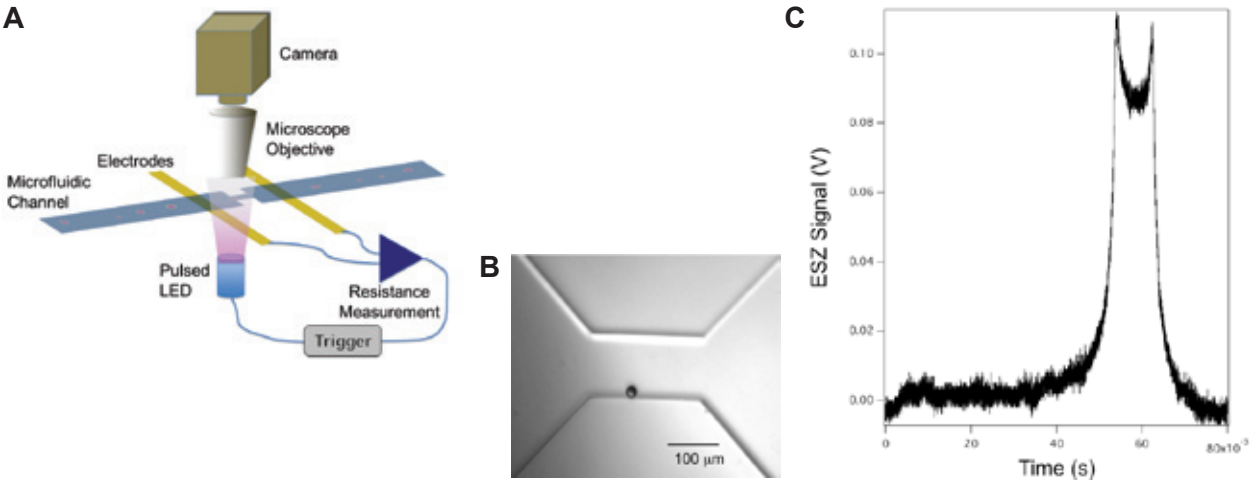

Figure 3. (A) Schematic of a microfluidic, electrical-sensing zone particle counter combined with a flow microscope, (B) a particle traversing the orifice of a microfluidic electrical-sensing-zone counter, and (C) the corresponding electrical signal.

closely mimics that of typical protein particles, as seen in Figure 4, even though the mechanism for protein particle formation is completely different than the abrasion process. Oscillatory motion of a piece of ETFE tubing against a diamond abrasive creates a dilute slurry of highly contorted ETFE particles. The resulting particles are suspended in a pH 7 to pH 8 buffer with an anionic surfactant to promote particle dispersion. The particle size distribution is very broad, depending on the size of the abrasive grains used to produce the particles. We are focusing our present efforts on creating a reference material with effective diameters certified over a range from 0.5 µm to 30 µm.

Once generated, the particle suspension must be characterized in a manner traceable to the SI. We intend to spike into the ETFE suspension a known concentration of PSL spheres, collect samples of the spiked suspension on alumina filters, and then count the collected particles using scanning electron microscopy (SEM). Existing NIST reference materials for PSL beads are certified for diameter, but not concentration. We plan to calibrate the PSL bead concentration by modifying a light obscuration apparatus that will measure in a single pass an initial prime volume of particle-free water, a known volume of PSL bead suspension, and finally a rinse of particle-free water. Bracketing the PSL beads with water volumes will make the measurement independent of start/stop transients and will also reduce the loss of PSL beads by diffusion into

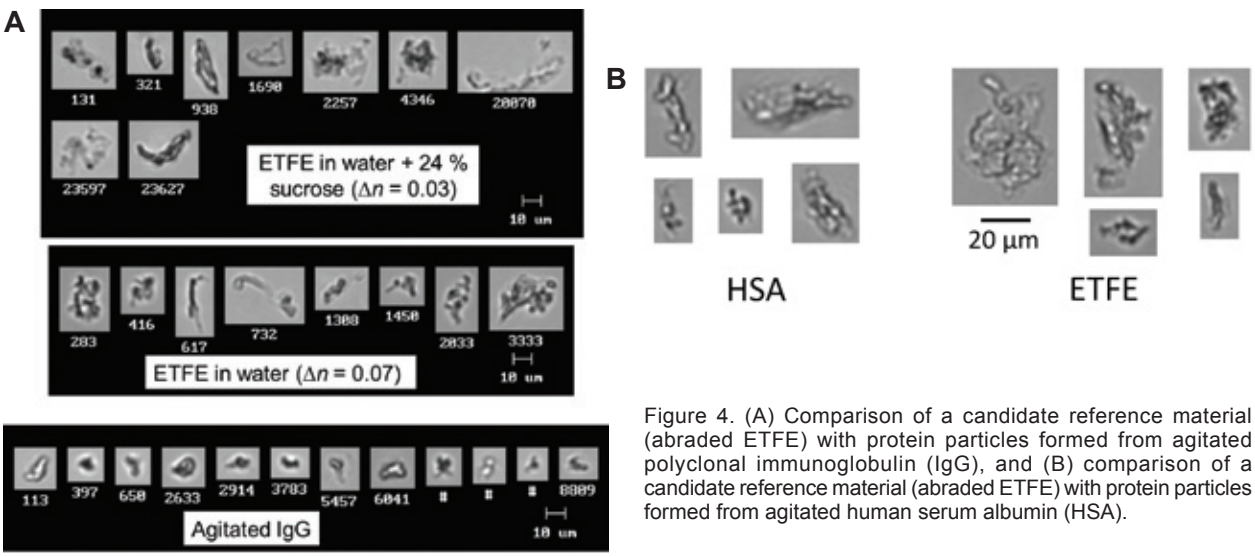

Figure 4. (A) Comparison of a candidate reference material (abraded ETFE) with protein particles formed from agitated polyclonal immunoglobulin (IgG), and (B) comparison of a candidate reference material (abraded ETFE) with protein particles formed from agitated human serum albumin (HSA).

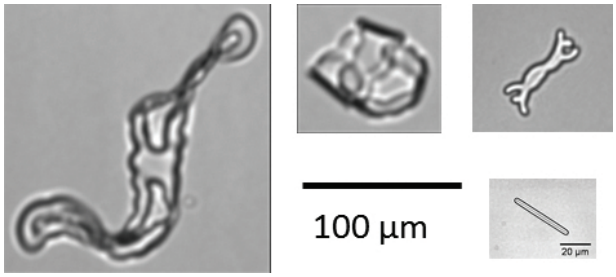

Figure 5. Examples of polymer particles produced by lithographic techniques over a range of sizes.

dead volumes or by adsorption on the walls. By spiking the ETFE suspension, all of the counts obtained by SEM are relative to the number of observed spheres, which is significantly simpler than performing SEM in an absolute counting mode. Success in using PSL beads as a reference for concentration will require understanding the filtration process in detail and ensuring that both PSL beads and ETFE particles are captured equally effectively. Use of the ETFE standard will, we hope, provide a means of quantifying the instrument response for particles of both low optical contrast and irregular morphology.

As an alternative method, we are also developing particles using lithographic techniques. An epoxy-based photoresist (SU-8) was deposited over a release layer on a silicon wafer; the SU-8 was exposed to ultraviolet light through a mask and baked to selectively polymerize the particles, and then the particles were released from the wafer by dissolving the release layer. Examples of these particles are shown in Figure 5. We have produced particles as large as 300 µm and as small as 50 µm long rods with a 2.5 µm x 2.5 µm square cross section. As one example of the utility of this type of particle, the elongated particles in the upper right corner of Figure 5 were measured using a calibrated, standard microscope and by two automated flow microscopes, all using bright field microscopy. The uncertainties of the NIST measurements are dominated by the ambiguity of the physical edge of the particles [11]. Table 1 presents the results, demonstrating that both instruments achieve acceptable performance for the measurement of perimeter and area of an irregular particle. Even larger particles may be useful as a standard for the counting of visible particles. When released from the silicon wafer, large planar SU-8 particles if sufficiently thin are flexible and take on three-dimensional shapes, as seen in Figure 5. PSL beads scatter light evenly regardless of orientation. The lithographic particles, like protein particles, have a 'twinkling' appearance as they rotate relative to the light source and observer. One disadvantage of the lithographic particles is their relatively large density. PSL, with a density of 1050 kg/m^3, is nearly neutrally buoyant in water. SU-8 has a density of 1200 kg/m^3, although the rate of fall of flexible sheets (see Figure 5) is significantly smaller than if the SU-8 were fabricated as spheres.

Smaller size particles are useful to study the response of instruments to non-spherical particles. We have fabricated rod-like particles to study the orientation of particles in flow cells and to understand the response of electrical-sensing zone counters to non-spherical particles. The lithographic particles are highly reproducible; however, the refractive index of SU-8 (1.59) is too high to truly mimic the low optical contrast of typical protein particles. We are engaged in identifying other polymer types that will enable the development of rugged particles with reduced optical contrast.

Future Challenges

Measurement of well-defined reference materials and studies of the operational principles of each type of instrument enable identification of measurement biases and uncertainties. We anticipate this effort to continue

	NIST			% dev. from NIST	
	Mean	S_r	$U_r(k = 2)$	Instr. A	Instr. B
Max. feret, µm	56.0	1 %	3 %	−9 %	2 %
Equiv. diameter, µm	29.1	2 %	6 %	1 %	15 %
Aspect ratio	0.39	3 %	5 %	−11 %	7 %
Area, µm²	666	4 %	12 %	2 %	33 %
Perimeter, µm	189	3 %	3 %	−24 %	−7 %

Table 1. Measurement of a monodisperse, lithographically fabricated particle by three microscope instruments. The maximum feret is the maximum dimension of the particle; S_r denotes the relative standard deviation; U_r denotes the relative expanded uncertainty at a coverage factor of two. Data for instrument A from Clark Merchant, ProteinSimple; data for instrument B from Dave Palmlund, Fluid Imaging Technologies [12].

as new types of instruments come into use. However, any corrections that require extensive knowledge of the properties of the measured particles may prove to be impractical. One of the key challenges is to discern a path to traceable, reproducible measurements, while not burdening biopharmaceutical laboratories with overly complex procedures.

Acknowledgments

We thank M. Halter of the NIST Biosystems and Biomaterials Division for the images in Figure 1B.

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[12] Certain commercial equipment, instruments, or materials are identified in this document. Such identification is not intended to imply recommendation or endorsement by the National Institute of Standards and Technology, nor is it intended to imply that the products identified are necessarily the best available for the purpose.

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Small Current Measurements for a New Standard in Radionuclide Metrology

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The accurate measurement of small electrical currents is essential for the measurement of ionizing radiation as generated by radionuclides. VSL has been involved in the work conducted by IRMM in support of the CCRI(II) Working Group on Realization of the Becquerel, whose objective is the development of a reproducible re-entrant ionization chamber that could ultimately replace the 'Système International de Référence' (SIR), the BIPM facility used for international comparisons of radioactivity measurements, by a worldwide distributed radioactivity standard.

Background: The Becquerel

Radioactive decay is the stochastic process by which the nucleus of an unstable atom loses energy by emitting radiation, such as alpha particles (helium-4 nuclei), beta particles (electrons) and gamma rays (photons). The radiation, which can be either a particle or a photon, is called ionizing when it has sufficient kinetic energy to liberate an electron from an atom. The activity referred to a radionuclide is expressed in the derived SI unit becquerel (Bq) [1]. One becquerel is defined as the activity of a quantity of a radionuclide in which, on average, one nucleus decays per second. There are many ways to measure ionizing radiation, depending on the specific decay type and the quantity. For example, one can use gas-filled detectors such as ionization chambers, proportional counters or Geiger counters. Other ways are by using scintillators, semiconductors, or calorimeters.

Figure 1. The SIR ionization chambers operated by the BIPM.

By means of the SIR (Système International de Référence), the Bureau International des Poids et Mesures (BIPM) provides the method by which National Metrology Institutes from countries which have signed the Meter Convention may compare their results for activity measurements of gamma-ray emitting radionuclides. The SIR consists of two commercial ionization chambers and a current measurement device based on the principle of the Townsend balance. It was not designed for absolute activity measurements, but as a relative transfer standard relating the current generated in the SIR ionization chamber by gamma-ray emitting radionuclides of known activity to that generated by one source of ^{226}Ra chosen among a set of five, as ^{226}Ra provides a sufficiently stable reference given its long half-life of 1600 (7) years. As such, the activity of a radionuclide measured with the SIR is expressed as a so-called equivalent activity of a suitable ^{226}Ra source corresponding to the same ionization current. Consequently, the measurements reduce to precise comparisons of electrical currents. To assure its continuity, the SIR is also capable of measuring the ionization current in an absolute way, providing a way to transfer earlier measurements to a new chamber should this be due necessary [2]. For a picture of the SIR we refer to Figure 1.

Towards a Reproducible Standard for Radioactivity

The European Commission's Institute for Reference Materials and Measurements (IRMM) is an active member of the Consultative Committee for Ionizing Radiation, section II (CCRI(II)), coordinating the Working Group on Realization of the Becquerel. The Working Group was established by the CIPM to study the development of a reproducible radioactivity standard, in the form of a re-entrant ionization chamber that could ultimately replace the SIR. If constructed according to specifications, all chambers built by any laboratory at any time, measuring the

same activity of a given radionuclide, should give the same response (within 0.2 %) for photons with energies ranging from 30 keV to 2600 keV. This very ambitious goal requires that all the physical characteristics affecting the response must be fully defined and traceable to the SI. The description of such a chamber does not only contain the technical blueprints with dimensions and tolerances, but shall also include compositions of materials, composition and pressure of the counting gas and the device measuring the ionization current. When realized and calibrated using primary standardized radionuclides, the traceability to the becquerel will no longer depend on the use of a set of stable ^{226}Ra sources or on the uniqueness of the SIR. The calibration of the first chamber (expressed in current per unit of activity of a nuclide, e.g., pA/MBq) can be transferred to the other chambers reproduced.

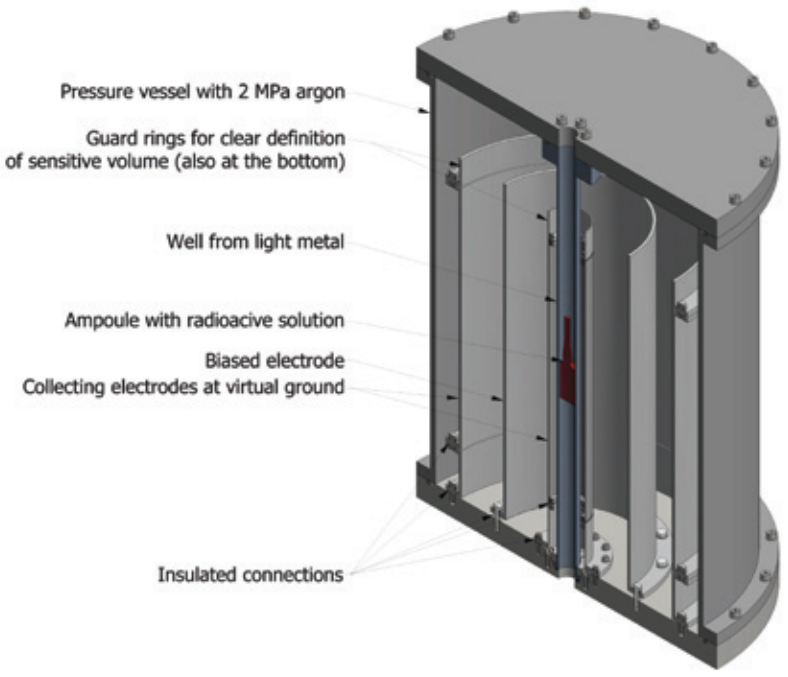

Figure 2. Schematic view of the new ionization chamber developed by IRMM.

Principle of Operation

The ionization chamber envisaged in this project is a cylindrical pressure vessel, filled with 2 MPa of pure argon gas (Figure 2). An ampoule containing the radioactive solution is placed in the middle of the "well," a tube in the center of the chamber. Radiation escapes from the solution and follows a path through different materials until it is absorbed somewhere in the chamber itself or in the surrounding materials. Along their path, the photons also ionize gas molecules. Part of these ionizations takes place in a volume of gas clearly defined by a set of biased electrodes, creating an electrical field in which the electrons and ions will start to drift. The movement of these charges is measurable as an electrical current, proportional to the activity of the radionuclide in the solution. Two essential aspects are involved: the physical interaction of radiation in matter, and the measurement of the electrical current. Of the first aspect, the tolerance on the thickness of the well is the most significant.

Tolerance on the Thickness of the Well

To assure the reproducibility of the amount of ionizations in the sensitive volume, it is essential to control the transmission of radiation through all the materials it will travel, from the solution until the sensitive volume. Both the material composition and the thickness are important. The transmission of photon radiation through a slab of material with thickness t is described by

$$I = I_0 \, e^{-\mu t}, \qquad (1)$$

in which I and I_0 are the intensity of the radiation after and before the slab, respectively, and μ the linear attenuation coefficient, a material property which depends on the photon energy. The effect of a change in the thickness on the transmission can easily be calculated from Equation 1. When the thickness increases from t to $t + dt$, the intensity of the radiation after the slab will reduce from I to $I - dI = I_0 \, e^{-\mu(t + dt)}$. Defining the relative change in transmission as $R = (I - dI)/I = e^{-\mu \, dt}$, the change in thickness dt is given by $dt = -\ln(R)/\mu$. This equation is used to evaluate the tolerance on the thickness of all the materials along the photon's path. Requiring for example $R = 0.999$, corresponding to a 0.1 % change in transmission, yields the following graph of dt as a function of photon energy (Figure 3).

The formula and the graph clearly demonstrate that as the material is less dense, the tolerance is less strict.

The first material the photons encounter is the borosilicate glass of the ampoule itself (ignoring self-absorption in the solution). Recent thickness measurements on a batch of about 200 glass ampoules have shown that it is possible to achieve 0.2 % reproducibility for photons with energies down to 35 keV, approaching the design requirements. To achieve better results, plastic vials could be used for radionuclides that emit low-energy photons.

The selection of the right material is most critical for the well. Not only should the tolerance on the

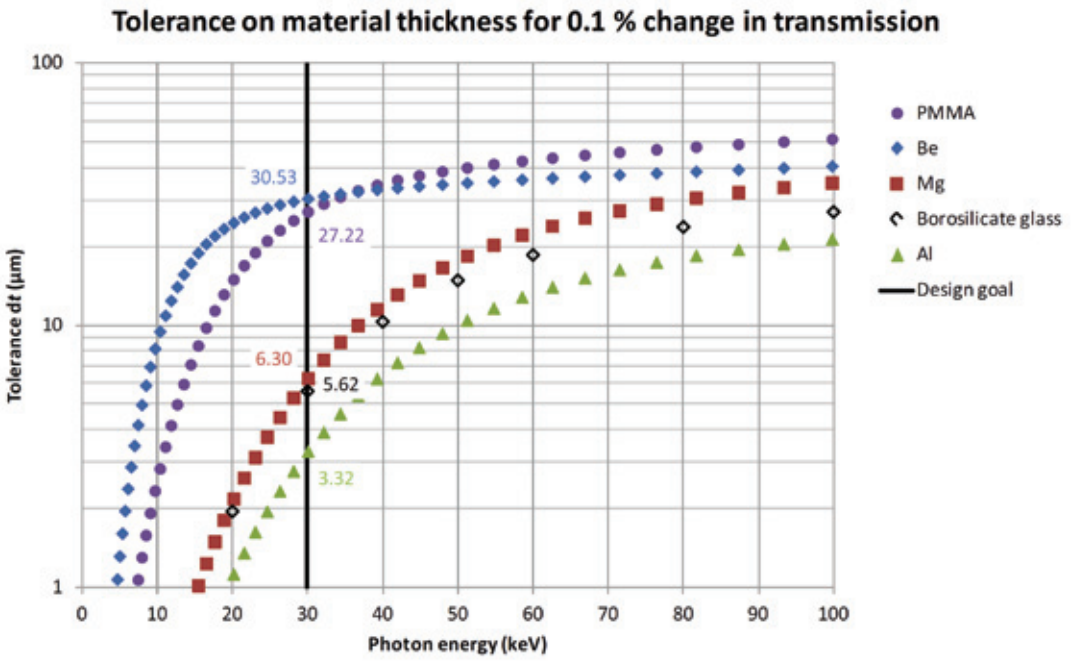

Figure 3. Tolerance on the thickness of the well for a selection of materials, as a function of photon energy, to achieve a reproducibility of 0.1 % on the transmission through the material.

thickness be reasonable, it should also withstand a pressure difference of 2 MPa. For aluminum, the tolerance on the thickness of the tube would be only about 3.3 µm to achieve a reproducible transmission of 0.1 % for 30 keV photons. This is beyond the ability of any highly skilled workshop. The use of the lighter magnesium loosens the requirement on the tolerance by a factor of only two. For plastics, the tolerance is acceptable, but the limited radiation hardness and difficulties to control the precise composition and density make the use of plastics quite risky on the long term. Beryllium is a viable option, but its cost and import/export restrictions might be an issue for some countries. At this moment, the final decision on the material selection has not been made yet.

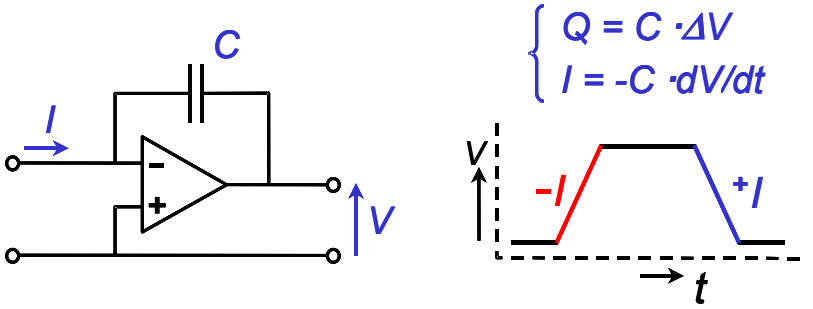

Figure 4. Principle of current measurement by charging a capacitor: the current causes charge to accumulate on the capacitor, which results in a voltage drop $V=Q/C$ over the capacitor. For a DC current, the voltage will increase linearly with time: $I = -C \cdot dV/dt$.

Measurements of Small Currents

The second essential aspect in this project is the measurement of the ionization current, which shall be precise and SI traceable. For the prototype ionization chamber, background radiation typically produces a current of about 45 fA, whereas a relatively strong source results in a current in the nA range. Such low currents can be measured most accurately using an integrator, i.e., an electrometer based on a capacitor charging technique, as illustrated in Figure 4. Using a capacitor C as depicted, and measuring the electrometer output voltage V, the input current I can be determined as

$$I = - C \cdot dV/dt. \qquad (2)$$

VSL has been a major player in the field of small current measurements for more than a decade. During these years, several experimental

realizations have been investigated and published, ranging from measuring the voltage over a high-ohmic resistor to counting individual electrons using single electron tunneling devices, a cryogenic current comparator to scale currents up by several orders of magnitudes, a current source based on a differentiating capacitor with software-controlled non-linearity compensation [3], and a vibrating reed electrometer based on a lock-in technique measuring the charge on a vibrating reed capacitor [4].

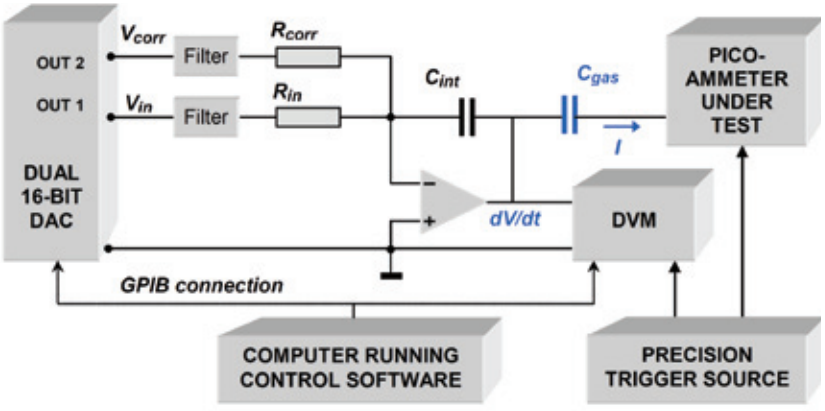

Figure 5. Differentiating capacitor current source with software-controlled non-linearity compensation. The crucial elements are the gas-type capacitor C_{gas} and the generated voltage ramp dV/dt, measured with a high-precision digital voltmeter (DVM) triggered by a high-precision trigger source.

Differentiating Capacitor Current Source

Using the differentiating capacitor current source (DCCS) for calibrations of electrometers under ISO 17025 accreditation, VSL can reach uncertainties as low as 50 ppm for currents between 20 pA and 200 pA, 200 ppm for currents down to 1 pA and 0.2 % for currents down to 100 fA. These low uncertainties make VSL one of the leading institutes in the world for small current generation. The heart of the DCCS setup is in fact a very stable voltage ramp generator. It applies a voltage ramp dV/dt to a gas-type capacitor C_{gas} with a very low AC to DC difference that converts the voltage ramp to a DC current $I = C_{gas} \cdot$ dV/dt. The voltage V can be measured using a high-accuracy and traceable digital voltmeter, whereas the time t between two voltage measurements can be derived from atomic clocks either directly or, for example, by means of a DCF77 receiver.

A schematic of the actual DCCS setup is given in Figure 5 [3]. The voltage ramp is generated by an integrating capacitor C_{int} that integrates a DC current V_{in}/R_{int}, where the voltage V_{in} is delivered to the resistor R_{in} by means of a programmable voltage source such as a digital-to-analog-converter (DAC). The non-linear behavior of the voltage ramp as a function of voltage, caused by stray capacitance and dielectric absorption by the capacitor C_{int}, can be corrected for by injection of a correction current V_{corr}/R_{corr}. This correction current is adjusted almost real time until the difference between two successive voltage measurements dV=V(t+dt)-V(t) is equal to the expected nominal value $(\mathrm{d}V/\mathrm{d}t)_{nom} \cdot \mathrm{d}t$ using a PID control loop. A repetitive symmetrical ramping sequence (hold, ramp up, hold, ramp down, each stage typically during 100 seconds) is generated ramping up and down between $+V_{max}$ and $-V_{max}$. By determining dV/dt during all four stages of the sequence one can correct for offset currents that are present in the setup. The symmetry between $+V_{max}$ and $-V_{max}$ takes care that leakage currents caused by the leakage resistance of the capacitor are averaged out.

The second crucial ingredient of the DCCS is the sealed gas-type capacitor of typically 10 pF, 100 pF, 1 nF or 10 nF. This capacitor is calibrated at 1 kHz by means of a capacitance bridge, whereas in the DCCS setup it is used at quasi-DC. The difference of the capacitance value at 1 kHz and its value at DC is estimated to be less than 10 µF/F. This assumption needs to be verified by experiments. For this reason, the differences of the gas-type capacitors used were determined by comparing the generated current of 1 pA using the 10 pF, 10 pA using the 10 pF and 100 pA using the 1 nF to a current generated by a calibrator applying a DC voltage of 0.1 V, 1 V or 10 V, respectively, to a temperature controlled 100 GΩ resistor. The standard uncertainty of this resistor was 2.3 ppm at 22.945 K, whereas its temperature coefficient was (0.000 ± 0.005) %/K and the temperature during the verification measurements was within 0.2 K of its calibration value. The DCCS current and the V/R current were put in series opposition and fed to an integrating null detector. Table 1 shows the results for the difference between the DCCS current and the V/R current measured this way, including the total standard uncertainty of the measurement. From these results we see that the measured differences fall within the

Capacitor	Nominal Current	Measured Difference	Standard Uncertainty
10 pF	1 pA	7 µA/A	21 µA/A
100 pF	10 pA	8 µA/A	9 µA/A
1000 pF	100 pA	-2 µA/A	8 µA/A

Table 1.

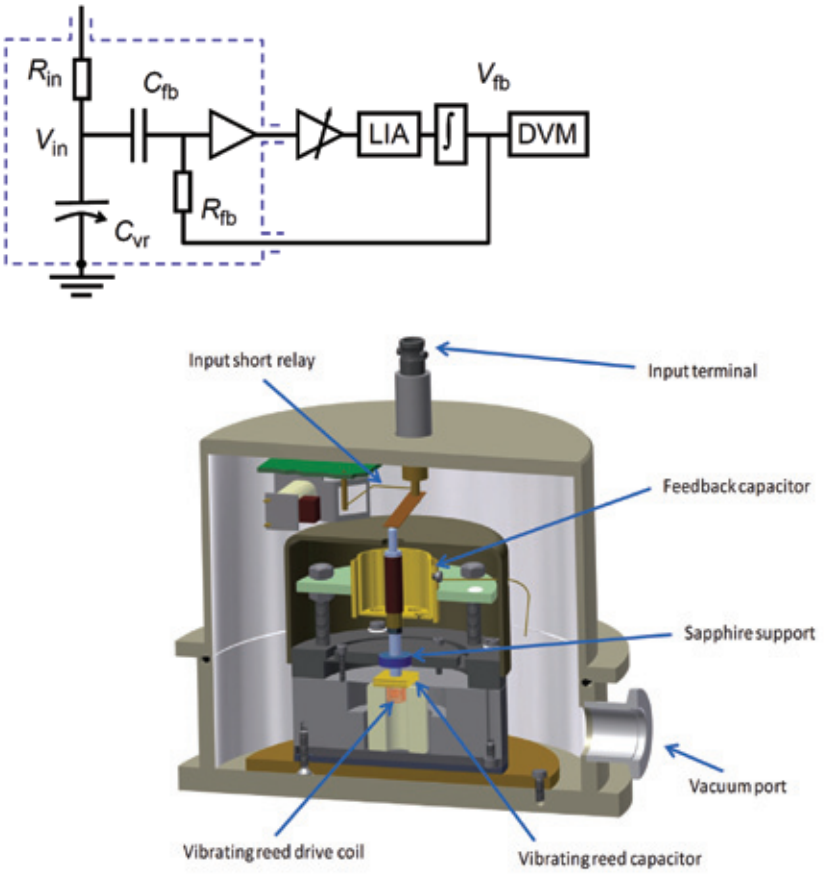

Figure 6. Schematic of the VR electrometer setup (top) and cross-section view of the actual implementation of the sensitive and critical VR input stage (bottom). This input stage is placed in a vacuum chamber (indicated by a dashed line in the top) in order to eliminate humidity effects on C_{fb}.

uncertainty of the measurements. In conclusion, our assumption that the AC to DC difference of the capacitors is smaller than 10 μF/F is justified. We want to emphasize here that this is not automatically true for every gas-type capacitor; some capacitors of the same type were found to have much larger AC to DC difference, probably due to leakage of the seal causing water from the air to stick to the capacitor plate which changes the frequency dependent behavior due to the dielectric absorption of the adsorbed water surface layers [6].

Vibrating Reed Electrometer

Even lower currents and better uncertainties can be obtained using a vibrating reed electrometer. This electrometer can be considered as a special version of the principle depicted in Figure 4, with the operational amplifier replaced by a vibrating reed element. Figure 6 gives an overview of the actual implementation of the VSL vibrating reed (VR) electrometer [4]. Its operation can be explained as follows: any DC charge Q applied to the input generates a DC voltage V_{in} over the vibrating reed capacitor C_{vr}. This induces an AC current, which after passing through C_{fb} is buffered, amplified, and rectified by the lock-in amplifier (LIA). Finally, the output of the LIA is integrated to get an output voltage V_{fb}, which is fed back to C_{fb} via a high-ohmic resistor R_{fb}. The feedback loop changes V_{fb} until the AC signal, and thus, the effect of the DC input charge on V_{in} is nulled. A high-accuracy DVM reads the resulting change in output voltage ΔV_{fb}, after which the applied input charge Q can be determined with

$$Q = C_{fb} \cdot \Delta V_{fb}. \qquad (3)$$

When a DC current I is applied, the VR electrometer output voltage will be a linearly ramping voltage and Equation 2 is used to calculate the value of I.

The most important advantage of the VR electrometer with respect to conventional electrometers is its very small offset current of the input stage. For conventional electrometers using specially compensated field-effect transistors (FETs) as input stage, the best input offset currents that can be achieved that are well below 1 fA. However, the all-vacuum-capacitor input stage of the VR electrometer results in offset currents that are one to two orders of magnitude better, and reach the level of a few aA (1 aA = 10^{-18} A, which corresponds to 6 electrons per second!).

Several important and sensitive small current measurements were performed using the vibrating reed setup, among which the leakage currents of low noise cables [4] and the AC to DC difference of capacitors [5]. An example of such a measurement is given in Figure 7. Here, the electrometer input offset current is shown when different connectors and cables are connected to its input. For the G874 connector, also frequently used in capacitance measurements, both the value of the current and the current noise is close to that of the 'bare' VR electrometer. For the BNC cable and connector, a large decay is seen in the first 12 hours after connection to the VR electrometer. This is due to dielectric desorption effects from the insulating material of the BNC cable [7]. Much to our surprise, the results given in the inset of Figure 7 show that a triax cable, frequently used in low-current

measurements, does not have a very good behavior. The triax design of the cable allows for good shielding and guarding, but apparently the materials and possibly the connectors used in this cable result in an 100 aA current noise which is significantly more than is achieved with the low-current BNC cable.

Summary and Conclusion

In this paper, we present recent developments towards a new approach in realizing the becquerel. At IRMM, a re-entrant ionization chamber is under development that could ultimately replace the SIR facility at BIPM by a worldwide distributed radioactivity standard. The major advantage of the new approach is that any laboratory should be able to reproducibly measure the activity of a given radionuclide within 0.2 % for photons with energies between 30 keV and 2600 keV, as long as the ionization chamber used to measure the activity is constructed according to specifications,

There are two essential aspects in the realization of the new re-entrant ionization chamber: the physical interaction of radiation with matter, and the measurement of the electrical current. Of the first aspect, the tolerance on the thickness of the well is the most significant mechanical factor contribution to the chamber accuracy. Construction tolerances should be within 3 μm to 30 μm depending on the construction material. A final decision of the material selection has not been made yet. For the measurement of the electrical current, commercial electrometers can be used in combination with carefully selected cables and connectors. The electrometers will be calibrated using a differentiating capacitor current source, whereas the cable and connectors as well as the differentiating capacitor itself can be investigated using a vibrating reed electrometer.

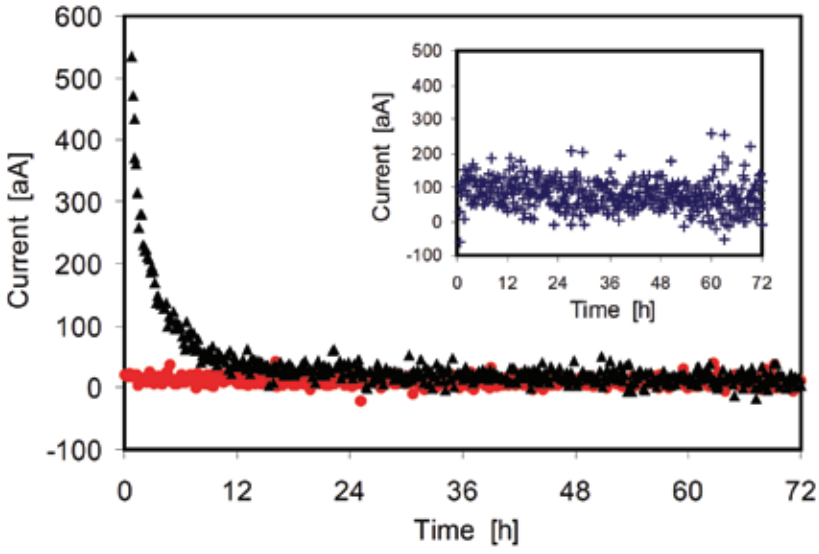

Figure 7. VR electrometer current with different cables and connectors connected to its input. Results are given for a G874 connector (red circles), a BNC connector together with a low noise BNC cable (black triangles), and for a triax input connector with triax cable (inset).

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Gender-Specific Effects on Tympanic Temperature of a Cohort Sample of 15 to 16 Year Old High School Students

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Our experiment consisted of two studies. First we compared two different (based on prices) tympanic thermometers found at local pharmacies, to find the most precise one. The second part applied that finding to question if there is a difference in tympanic temperatures between fifteen-or-sixteen year old boys and girls. The first study aims to educate the public about which ear thermometer is most precise. The second part of the experiment is designed to recognize a difference in body temperature between 15 to16 year old boys and girls, if there is a distinction. We hypothesize that the Braun Thermoscan IR Ear Thermometer IRT4520 ($48) will be the more precise than the Red Cross Rapid Read Thermometer and that boys will have a slightly higher average temperature than girls.

Introduction

In order to most accurately determine the core body temperature, which is the temperature of the vital organs, ear temperatures are taken rather than oral temperature, rectal temperature, or underarm temperature. The reasons for determining body temperature by measuring the ear temperature are the following: tympanic thermometers measure the infrared heat generated by the eardrum and its surrounding tissues, which share the same blood supply with the hypothalamus (Netter), the part of the brain that controls body temperature; and body temperature is more accurately reflected sooner in the ear than at any other place in the body (Guyton). Thus, for children 6 months and older, clinical research has proven that the ear is the ideal site for indicating internal body temperature (American Red Cross).

The topic of the investigation was determining body temperature utilizing tympanic thermometers. The objective of this two-part investigation was to study the effect of gender on body temperature in fifteen to sixteen year old high school male and female students. The first part of the experiment determined the precision of two best-selling tympanic thermometers found at local pharmacies.

The two thermometers chosen were Braun Thermoscan IR Ear Thermometer IRT4520 and Red Cross Rapid Read Ear Thermometer. The second and central part of the experiment applied the most precise thermometer found in Part 1 and tested forty-four students, twenty-two boys and twenty-two girls, to prove or disprove the theory that gender would have an effect on body temperature.

Materials and Methods

Two tympanic thermometers that can be found at local pharmacies (Target, Walgreens, CVS, etc.) were used: the Braun Thermoscan IR Ear Thermometer IRT4520 and the Red Cross Rapid Read Ear Thermometer. First, the three experimenters had their left ear temperatures taken five times sitting down with the Braun Ear Thermometer. These results were recorded into a table (Table 1). The same process was done but with the Red Cross ear thermometer (Table 2). In total, after both ear thermometers were tested on each of the three experimenters, there were 15 temperature readings for each thermometer. Then the average and standard deviation were determined for each set of the 5 ear temperature readings. Whichever thermometer had a lower standard deviation among the sets of data was concluded as the more precise.

Using the more precise thermometer (Braun IRT4520), twenty-two 15-16 year old girls and twenty-two 15-16 year old boys were asked to volunteer for the experiment and given a consent form (Appendix A) to sign. Additionally, it was very important to ask the volunteers if they were sick as that could result in inaccurate results. A new sanitary cover specifically designed for the Braun IRT4520 was used for each new participant. The participant's temperature was taken 5 times in the left ear, sitting down. The results were recorded in a data table that included the participant's five temperature readings and the participant's gender and age.

After gathering all the data, the average and standard deviation of each participant's temperature readings was calculated followed by the total average and standard deviation of the group of boys and the group of girls. These results were compared and analyzed to finalize a conclusion.

Results

Part 1: Preliminary Test for Precision of the Thermometers

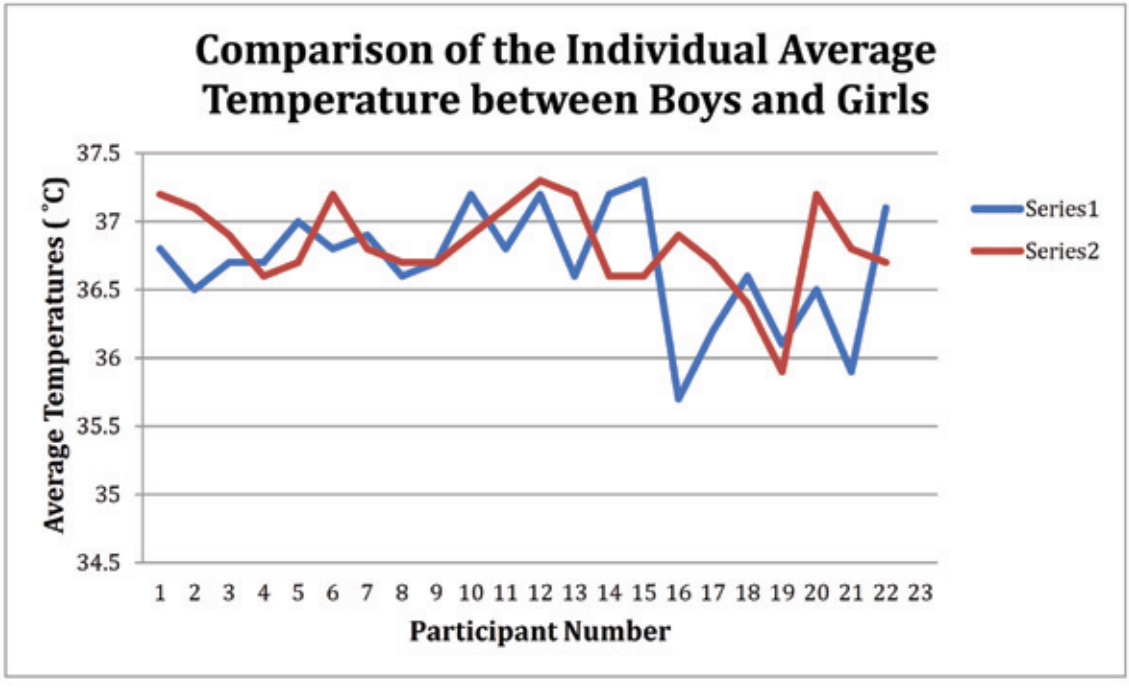
Experimenter	Reading 1 (˚C)	Reading 2 (˚C)	Reading 3 (˚C)	Reading 4 (˚C)	Reading 5 (˚C)	Average (˚C)	Standard Deviation (˚C)
Experimenter1	36.9	36.8	36.8	36.8	36.9	36.8	0.1
Experimenter2	37.0	37.1	37.2	37.2	37.1	37.1	0.1
Experimenter3	37.1	37.1	37.0	37.1	37.0	37.1	0.1

Table 1. Braun Thermoscan Ir Ear Thermometer IRT4520.

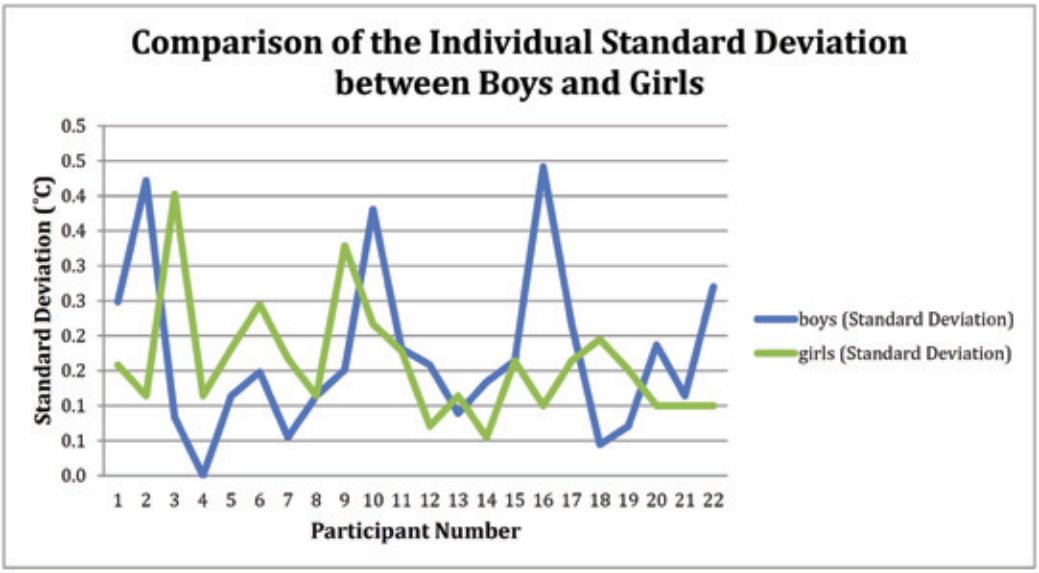
Experimenter	Reading 1 (˚C)	Reading 2 (˚C)	Reading 3 (˚C)	Reading 4 (˚C)	Reading 5 (˚C)	Average (˚C)	Standard Deviation (˚C)
Experimenter1	36.8	36.8	36.7	36.7	36.6	36.7	0.1
Experimenter2	36.5	36.5	36.4	36.3	36.1	36.4	0.3
Experimenter3	36.2	36.2	36.1	35.5	35.6	35.9	0.6

Table 2. Red Cross Rapid Read Ear Thermometer.

Part 2: The Comparison Between Fifteen to Sixteen Year Old Boys and Girls Using the More Precise Thermometer



Graph 1.



Graph 2.

Average Temperature for Boys	36.7 °C
Average Temperature for Girls	36.8 °C

Table 3. Total Average Temperature for Boys and Girls.

SD (Avg) of Boys	0.2
SD (Avg) of Girls	0.2

Table 4. Total Standard Deviation of Boys and Girls.

$$s_x = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}} \qquad (1)$$

The equation above (Equation 1) is used to calculate Standard Deviation, where

n = the number of data points,

$\bar{x}$ = the mean of the x_i, and

x_i = each of the values of the data.

The data charts and graphs above show that individual standard deviation for boys and girls were not statistically significant. However, it must be noted that the highest standard deviation (0.4) came from the boys, as well as the lowest standard deviation (0.0). The girls' average individual standard deviations stayed within a given range.

Secondly, both the highest and lowest average individual temperature, which was 37.3 °C and 35.7 °C, respectively, came from the boys. Similar to the average individual standard deviation, the girls' average individual temperature stayed within a given range.

On the greater scale, the boys' total average temperature was 36.7 °C, while the girls' total average temperature was 36.8 °C. The boys' total average standard deviation was equal to the girls' as approximately 0.2.

Note: All numbers/data collected were rounded to the tenth decimal point because the temperature readings on the thermometers were restricted to the tenth decimal points.

Discussion

The investigation done to study the effect of gender on body temperature in fifteen to sixteen year old high school male and female students did not yield a significant difference between the two groups. Those who participated in this lab experiment were forty-four high school students, twenty-two boys and twenty-two girls. Through the data that we collected from these forty-four participants, we concluded that the boys were generally more sporadic in the consistency of their temperature readings. In addition, the boys had the highest and lowest standard deviation compared to the girls. On the other hand, girls were more consistent in their body temperatures, in both the areas of average individual standard deviation and average individual temperature readings. Despite these differences, the overall results between the girls and boys were similar. Based on these results, we found that there were no differences between genders from ages fifteen to sixteen in high school.

The hypothesis was that the ear temperature of fifteen to sixteen year old girls would be lower than that of boys. However, results we obtained negated this statement. There was an overall 0.3 difference in the total means between the two genders in our representative sample. Therefore, it was concluded that there was not a significant difference

between the temperatures of 15-16 year old boys and girls. However, after analyzing our data tables, an observation was made that although girls were slightly more consistent in their temperature readings than the boys, some male participants had the same exact reading for all or almost all five readings. On the other hand, these consistent individual temperatures were had significant variances between each male individual's temperatures. To further explain this point, all the girls' temperatures were in close proximity of each other, while the temperatures of the boys were set in a larger range of numbers. This observation could lead to a possible question that although males may be consistent in temperature readings, why their temperatures would be set in a wider range than that of the girls.

In this experiment, there were many ambiguities that were discovered after reviewing the experimental design and results. The first uncertainty is the background of the participant and what he or she was doing before the temperature reading. Although our body has the ability to maintain a specific body temperature of 98.5 °F whether we are in cold or warm temperatures, moderate exercise does have a slight effect on our overall body temperature. Therefore, if the participant was involved or partaking in moderate or excessive exercise before coming to be tested, his or her body temperature could have been read as higher than it usually is at standard conditions. In conclusion, the whereabouts and actions of the participants before the temperature readings are unknown. In further experimentation, knowing the connection between previous activity and body temperature would allow experimenters to draw conclusions that exclude any possibility of an unknown variable.

Secondly, whether or not the female participants were on their menstrual cycles was also unknown. This is important because during a menstrual cycle, the hormonal levels of a fifteen to sixteen year old female may affect her body temperature by making it higher or lower than her normal body temperature (Healthwise). The effects of the changes resulting form varying hormonal levels are unclear in our experiment.

In Part 1 of the experiment, we discovered several experimental errors. When we used the American Red Cross Ear Thermometer, it was stated in the instructions about the sanitation of the device to clean the tip of the device with an alcohol wipe or a moistened cloth but to be very careful not to get liquid on or inside the area where the actual infrared readings were taken. However, some of the isopropyl alcohol (70%) used to clean the probe of the thermometer could have entered the interior of the thermometer without our knowledge of this happening. If this did occur, our conclusion on which thermometer may have been the more precise could have been different.

In Part 2 of the experiment, the way that the tympanic thermometer was inserted into the ear may have caused a difference in the temperature readings. This is because we the experimenters were in control of the device and had encountered the possibility of hurting the participants' ear canals; therefore, the thermometer may not have been placed deeply enough into the ear to get an accurate reading of the real body temperature. Secondly, each experimenter may have inserted the thermometer into the participants' ears in different ways, which would have affected the readings and consequently, the results. Although the Braun Thermometer that was used included a flashing light that indicated when the device was in the proper place to take an accurate reading, we did not actually calibrate it and simply assumed it to be correct. Thirdly, although the participants who deemed themselves sick were not tested at all, the participants who stated that they were not sick may have been unaware of their symptoms at that time. This could have been a potential error because the temperature readings of those who were unaware of symptoms of a viral illness, which include fevers, would have been different.

The strengths of our experimental design were that we were able to design our experiment, so it does not depend too strongly on the accuracy of the thermometer. We worked around the likelihood of dealing with the inaccuracy of the thermometer by using precision rather than determining accuracy. If our experiment depended on the accurate values of the temperatures, it would be important to make certain that the thermometers used were calibrated to match the exact temperatures of the participants at all times. A second strength in our experiment was, rather than taking one temperature trial per person, we took five to make sure the conclusion was not based off of too few data.

One limitation of our experimental design was that the number of participants we gathered was too few. A larger pool would have strengthened or perhaps disproved our conclusion. Secondly, the number of thermometers used to test precision in the first part of the experiment was too few. If we managed to find a more precise thermometer out of more thermometers than just two, the data we gathered may have been more concrete.

Unfortunately, access to any clinically significant investigations was unavailable in the literature. Therefore, we could not compare our results to previous experiments regarding the gender-specific effects on body temperature.

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What is the best software to use for automation?

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What is the best software to use for automation? That is the age old question. I remember having this debate more than 20 years ago when I was working at White Sands Missile Range in New Mexico. And today, as I read people's comments online I realize not much has changed. We have made tremendous advancements in technologies, newer protocols, faster computers, and a multitude of automated test software solutions, but the question of what is the best software to use is still unanswered.

Every programming language, when compared to another, has a set of distinct advantages and disadvantages. Some execute faster, some are easier to program in, some have graphical user interfaces, and others are geared to a very specific task.

I have been writing automated software for more than 25 years now. I have written in just about every automation control language out there and I ask this same question regularly: "What is the best language to develop this solution in?" Having done this several times, I have broken the question down into four separate questions to help me pick the right tool for the job.

#1 What is the time to market?

When we answer the 'time to market' question, we are talking about when the software must be complete and operational. For many of us the answer is "Yesterday!" which directs us to the buy versus build decision. In many cases, it is far more costly to build software than to buy it—you should always entertain the idea of buying in your decision tree.

Looking at the time to market question, strictly from the build perspective, we have to approach the problem in terms of man hours multiplied by the cost of an hour, then double the estimate since software is seldom finished on time and on budget.

The knowledge skills and abilities of our developers will be a large factor. Often the best platform is one they already know. The learning curve of a new language is often like retooling a factory; technology changes will cost you down time and productivity in the beginning. Few languages present a large enough advantage in long term savings that justifies the learning curve and productivity loss to switch a whole project. But then again, some do and it is a tough pill to swallow!

What we have to realize here is that "All software is in an investment!" Whether you are buying it, developing it yourself or getting freeware off the web, software is an investment in both time and money. Since we all know time is money, we have to think in both terms of cost and time to market.

#2 What are the future supportability requirements?

The life of any software package is an unknown. During initial development we can speculate as to the expected life but the fact is we really don't know what computing will be like 5 or 10 years down the road. This makes future supportability a difficult question to answer. It is difficult to spot the next great technology or trend in its infancy. We know adaption of a technology is a slow process largely because people in general are resistant to change. Equating this to supportability, one can conclude a more popular, well adopted platform will have a longer life and be easier to support years down the road.

Using the Visual Basic/Delphi example… I am sure most of you have heard of VB, but few have heard of Delphi. Though Borland's Delphi™ was a more robust programming language based on the Pascal, it had limited availability of developers making it much harder to support.

#3 Flexibility and Integration?

This means many things to many people, but to me it means two things: 1) How hard is it to take something and make it do what it was not originally designed to do, and 2) how well does the software play with others? I never ask, "Can a programming platform do something specific?" Instead I ask, "How hard is it to do something it was not designed to do?" If it can be done in a few lines of code, then I see it as having flexibility. Integration in general is a good thing—being able to use other off-the-shelf tools and various languages can help cut time to market. For example, using Microsoft.NET™ you can mix and match programming languages and compile them all into one solution.

#4 What are the requirements of the project?

By far, the biggest factor is always going to be the specifications of a project. The devil is in the details and sometimes the details dictate the technology. Instead, we need to keep the details of the requirements technology neutral, wherever possible. The hardest thing to do in technology selection is to isolate details of real requirements from any technology centric paradigms, leading to a skewed or limited pool of technologies meeting the specific requirements.

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