



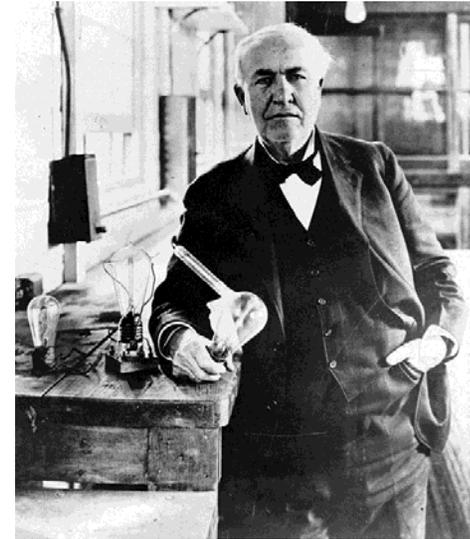
THE ROLE OF METROLOGY IN THE NEW PROJECTS AND PROGRAMS AT NIST

Dr. Richard Cavanagh
Acting Associate Director for Laboratory Programs
NIST

The Importance of Standards

National Bureau of Standards established by Congress in 1901

- Eight different “authoritative” values for the gallon
- Electrical industry needed standards
- American instruments sent abroad for calibration
- Consumer products and construction materials uneven in quality and unreliable



National Archives



National Institute of Standards and Technology (NIST)

Unique Mission within the Federal Government ...

to promote U.S. innovation and industrial competitiveness by advancing
measurement science, standards, and technology
in ways that enhance economic security and improve our quality of life

- **Deep research expertise underpins technological innovation** – e.g., new materials, advanced clinical diagnostics and therapies, advanced communications, forensic science etc.
- **Non-regulatory status** - enables an important role as a convener that facilitates collaboration between agencies of the Federal Government, industry, private organizations, and state and local governments

U.S. Innovation Agenda – NIST has an increasing role

Advanced Manufacturing

- Precision Measurements
- Bio and Nanomanufacturing
- Smart Manufacturing
- Advanced Materials

Cybersecurity and Advanced Communications

Executive Order – Framework for Critical Infrastructure

National Cybersecurity Center of Excellence

Establishing new Center for Advanced Communications with NTIA

Health Care and Bioscience

Measurement tools that will support multiplex analysis of proteins, genetic material, and metabolites.

Forensic Science

Partnering with Department of Justice to enable greater transparency and rigor in forensic evidence use

Climate Change and Clean Energy

Measurement science for buildings



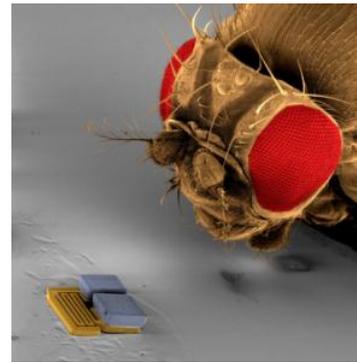
Advanced Manufacturing

Measurements, Standards, and Data for:

- **Biomanufacturing**
- Nanomanufacturing
- Sustainable Manufacturing
- Smart Manufacturing
- Robotics

Manufacturing Extension Partnership

- Technical assistance projects, training programs, networking events, and long-term strategic support



I. Davies/shutterstock.com

ETH Zurich

M. Czamanske/shutterstock.com

Rezacka/shutterstock.com

A Monoclonal Antibody Standard Reference Material (NISTmAb) + Data (SRM/D)

Monoclonal antibodies are the largest class of any chemical or biologic drug. The top 3 selling drugs in the world are mAbs, there are 35 approved mAbs in the US, and worldwide there are over 300 mAbs in late stage clinical trials

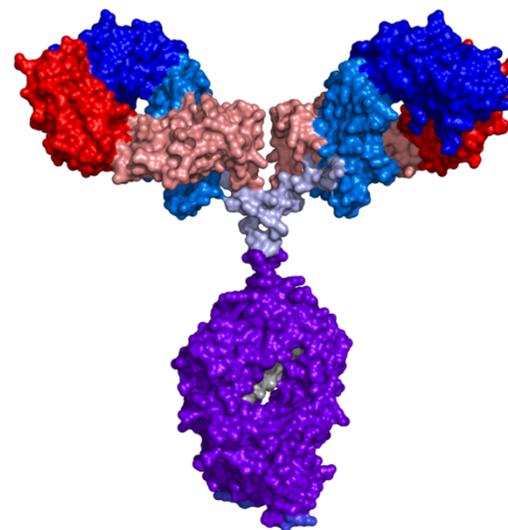
A monoclonal antibody (Immunoglobulin IgG1) reference material could be used for:

- Qualifying test methods
- Testing new measurement technologies
- Comparing changing analytical test methods
- **Will not** replace in-house reference standard for a product

Possible uses for IgG SRM:

Amino Acid Sequencing
Amino Acid Analysis
N-terminal Sequencing
C-terminal Sequencing
Peptide Mapping by MS
S-S Bridge Analysis
Glycosylation Analysis

Molecular Weight Information
Isoelectric Focusing
SDS-PAGE
Extinction Coefficient
Post-Translational Modifications
Spectroscopic Profiles: CD, NMR
LC: SEC, RP, IEX

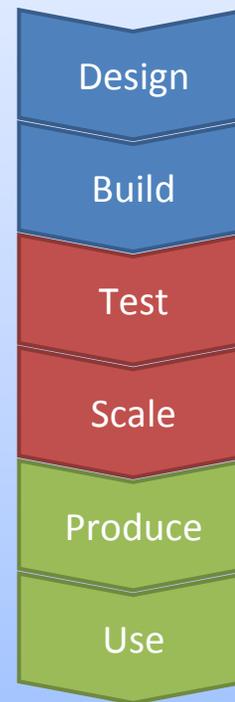


Metrology for Synthetic Biology

Biosciences and Health

- Need
 - Synthetic biology will lead to more effective engineering of biological systems to produce chemical feedstocks, drugs, fuels, and other commodities, and in the process, will lead to a better understanding of biological systems
- Objectives
 - Assure confidence in rapid technologies to “read” and “write” DNA
 - Work with experts to develop metrology roadmap
 - Establish experimental platforms to study the rules of biology and validate models
- Achievements and Impact
 - Developing metrology roadmap with industry
 - Collaborating with DARPA Living Foundries

Engineering Cycle and Planned NIST Work



Data and metadata standards

Sequence quality standards/RMs

Models to predict function from sequence

Phenotypic characterization

Real-time monitoring

RMs to enable confidence

Methods and models to enable scalability

Characterization of products, including tissues, cells, proteins

Ongoing, online QC

Customers and Partners



Improving Critical Infrastructure Cybersecurity Cybersecurity Executive Order

“...America must also face the rapidly growing threat from cyber attacks. I signed a new executive order that will strengthen our cyber defenses by increasing information sharing, and developing standards to protect our national security, our jobs, and our privacy...”

- President Obama in the 2013 State of the Union Address



Credit: K Talbot/NIST & Shutterstock



Author: Pkkao
Creative Commons License

Cybersecurity Framework (CSF)

- **Standards Framework -based on existing standards, guidelines, and practices– to reduce cyber risks to critical infrastructure.**
- **Five workshops between March – November 2013**
- **Draft Cybersecurity Framework was issued October 22, 2013 for public comment.**
- **NIST has released the first Cybersecurity Framework (Version 1.0) along with a companion Roadmap in early February 2014.**

Table 2: Function and Category Unique Identifiers

Function Unique Identifier	Function	Category Unique Identifier	Category
ID	Identify	AM	Asset Management
		BE	Business Environment
		GV	Governance
		RA	Risk Assessment
		RM	Risk Management
PR	Protect	AC	Access Control
		AT	Awareness and Training
		DS	Data Security
		IP	Information Protection Processes and Procedures
		PT	Protective Technology
DE	Detect	AE	Anomalies and Events
		CM	Security Continuous Monitoring
		DP	Detection Processes
		CO	Communications
RS	Respond	AN	Analysis
		MI	Mitigation
		IM	Improvements
		RP	Recovery Planning
RC	Recover	IM	Improvements
		CO	Communications

Credit: Yuval V, Wikimedia Commons



Cryptography

- Cryptography provides the basis for many security and privacy technologies used to support eCommerce.
- NIST works with academia, industry, and SDOs to build strong and interoperable cryptographic standards that can be leveraged throughout the digital infrastructure.
- NIST provides the USG library for cryptographic and key management standards and best practices including a testing program to support conformance.
- The development process for NIST's cryptographic program is transparent, traceable, and inclusive.

NIST is committed to increasing its resources and expertise in creating and maintaining cryptographic standards and guidelines.

Need for advanced communications

- The global Internet Provider (IP) traffic has increased 5x in the past 5 years and will increase 3x in the next 5 years
- Video use is 79 % of all global IP traffic

You **Tube**

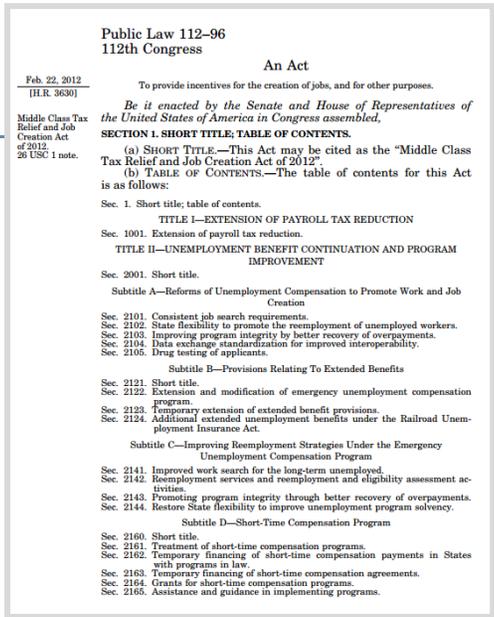
NETFLIX

- Traffic from wireless and mobile will exceed wired use by 2018 (internet of things)



Advanced Communications Research

- The *Middle Class Tax Relief and Job Creation Act of 2012*
 - Created **FirstNet** to provide emergency responders nationwide, high-speed, broadband network dedicated to public safety.
- NIST research plan includes activities involving:
 - Mission Critical Voice over LTE (4G LE)
 - LMR to LTE integration/migration
 - Expanded 700 MHz Demonstration Network
 - Identify/incorporate public-safety requirements into standards
- NIST’s plan engages all stakeholders
 - Stakeholder-driven R&D roadmaps
 - Competitive industry collaboration program
 - Partnerships with Federal agencies



• Proceeds from wireless auctions provide NIST \$300M through 2022 for Public Safety Communications

NIST involvement in Healthcare

Health IT

- Standards for EHRs, conformance testing
- Technical Guidance for Securing EHRs
- Practical Guidance for Securing Health environments

Standard Reference Materials

- Cholesterol, vitamin D, toxins, etc.

Calibration Standards

- Radiation, MRIs

Vaccines

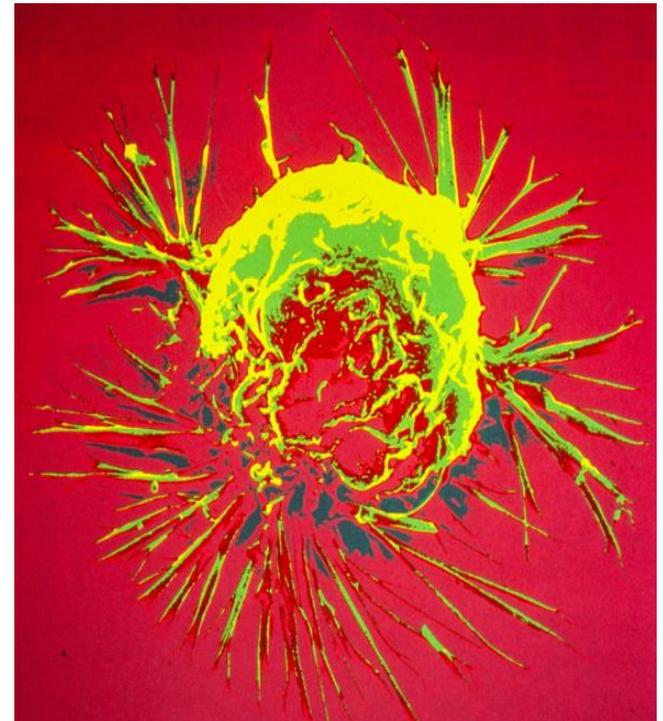
- Storage, preservation, quality

Disease assays

- Imaging, lab-on-a-chip

Medical Technologies

- Bioreactors, tissue scaffolds, therapeutic nanoparticles



Physical Measurements at the Bedside and Beyond

Physical Measurement and Standards Supporting the Clinic

Mass standards and force measurements

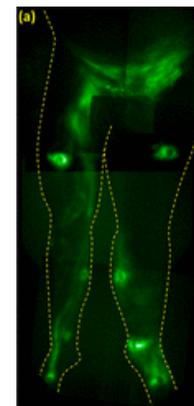
- Hearing aid testing and evaluation

Standards for temperature

- Patient temperature
- Device sterilization

Standards in ionizing and non-ionizing radiations

- National standards for x rays (dental, medical)
- National standards for color (data readout)
- National standards for fluorescence (cell/tissue labeling)



Genomic Quality Assurance



Genome in a Bottle
Consortium



- NIST led consortium with more than 75 public, private, academic partners
- Developing whole genome reference materials and bioinformatics tools for quality assurance of whole genome sequencing technologies (next gen and next/next gen).
- FDA used this to approve the first high-throughput DNA sequencer.

NY Times (5/14/15): “The federal government opened a new era of genetic medicine on Thursday by introducing a standard way to ensure the accuracy of DNA tests used to tailor treatments for individual patients.”

NIST RNA Controls played a role in Key Ebola Genetics Study

The New York Times | <http://nyti.ms/1u0Nbms>

HEALTH | NYT NOW

Outbreak in Sierra Leone Is Tied to Single Funeral Where 14 Women Were Infected

By DONALD G. McNEIL Jr. AUG. 28, 2014

Sierra Leone's explosion of Ebola cases in early summer appears to stem from one traditional healer's funeral at which 14 women were infected, according to scientists studying the blood of victims.

The New York Times | <http://nyti.ms/1pUqjH5>

SUNDAYREVIEW | OPINION

Studying Ebola, Then Dying From It

By PARDIS SABETI SEPT. 5, 2014

IN late May, a woman was admitted to the Kenema Government Hospital's maternity ward in Sierra Leone after a bloody miscarriage. Augustine Goba, director of the hospital's diagnostic laboratory and my longtime collaborator

NIST RNA Controls played a role in Key Ebola Genetics Study

Once standards are out in the wild, they have impact in unexpected ways!



VIRAL EVOLUTION

Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak

Stephen K. Gire,^{1,2*} Augustine Goba,^{3,†} Kristian G. Andersen,^{1,2,*} Rachel S. G. Sealon,^{2,4*} Daniel J. Park,^{2,*} Lansana Kaneh,³ Simbirie Jalloh,³ Mambu Momoh,^{3,5}

- This isn't the first time RNA Controls have been used to have accurate results.

Paper helps understand transmission and enable diagnosis

- Stephen K. Gire et al. *Science* 345, 13

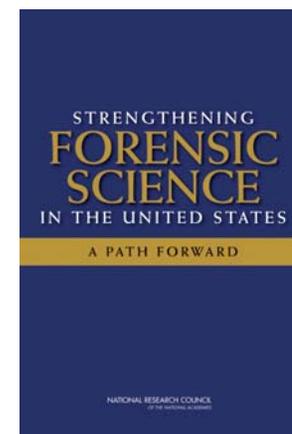
"...controls were used to monitor our library construction process... 500 fg of one, unique synthetic RNA (ERCC, gift from M. Salit, National Institute of Standards and Technology) was spiked in using a different RNA for each individual EBOV sample to aid in tracking our viral sequencing process and potential index cross-contamination."

-- Supplemental Materials and Methods

Helping Ensure the “Science” in Forensic Science

A landmark forensics report by U.S. National Research Council of the National Academies was issued in Feb. 2009.

“With the exception of nuclear DNA analysis, no forensic method has been rigorously shown to have the capacity to consistently, and with a high degree of certainty, demonstrate a connection between evidence and a specific individual or source.”



New Role for NIST:

- **With US Department of Justice, establish a National Commission on Forensic Science**
 - to help improve the reliability of forensic science data/information and to develop policy recommendations for the U.S. Attorney General.
 - to be comprised of forensic science practitioners, academic researchers, prosecutors, defense attorneys, judges, and other relevant stakeholders
- **Administer Guidance Groups of subject-matter experts for specific forensic disciplines**
- **Validate select existing forensic science methods and guidance**
- **Develop and critically evaluate new methods**

NIST Forensic Science Research Themes

DNA

- Reference Materials
- DNA mixture inter-laboratory studies

Ballistics

- Congruent Matching Cells
- Standard Bullets

IT

- Software Libraries
- Databases
- Fingerprint matching

Statistical Methods

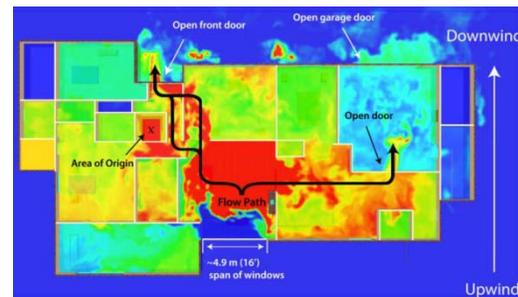
- Probabilistics
- Uncertainty assessment

Toxicity

Trace Evidence



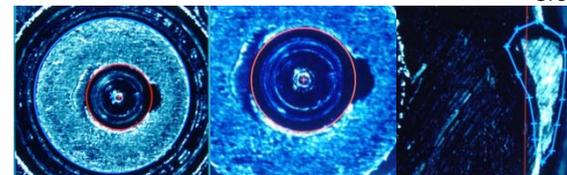
Credit: DHS



Credit: Adam Barowy/NIST



Credit: Michael Indovina/NIST



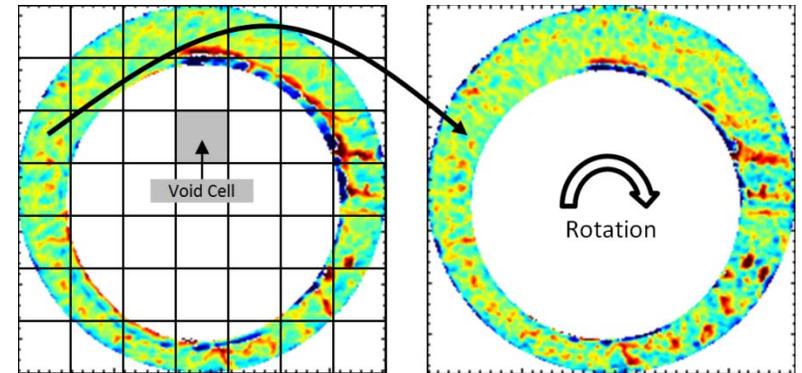
Credit: Theodore Vorbuger/NIST

Congruent Matching Cells

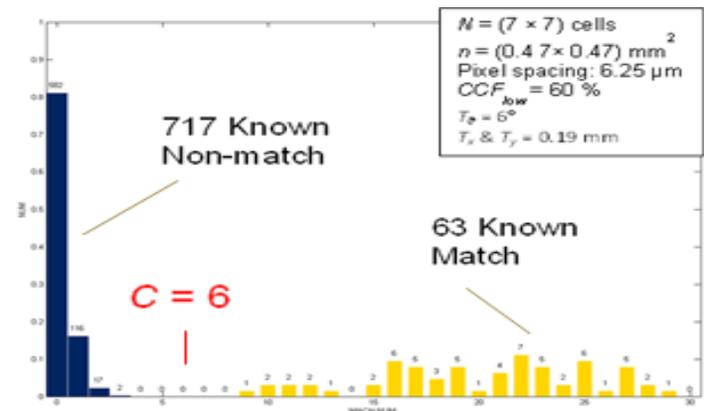
The newly developed Congruent Matching Cell (CMC) method relies on objective measurements and correlations that in turn facilitate error rate analyses for ballistics identifications.

The CMC method separates the ballistic surface into discrete cells that must exceed four similarity thresholds. Each pair of correlated surfaces require at least 6 CMCs to qualify as a match.

The CMC method has now been applied in a realistic blind validation study and was able to correctly identify all cartridge cases.



Example image (left) is divided into correlation cells. Each cell is scanned over the reference image (right) at each rotated position.



Example error rate analysis using the known matching and known non-matching distributions.

NIST Net-Zero Energy Residential Test Facility

- Demonstrate net-zero energy
- Create test bed for in-situ measurements of components and systems for Smart Grid integration
- Quantify impacts of embedded controls intelligence & building-to-grid interactions
- Compare actual installed performance to controlled laboratory measurements



Building to Smart Grid Integration

Home and building energy management in the smart grid

Interoperability standards for buildings communicating with the smart grid

Standard electric price, usage, weather signals

\$, kWh

Smart Meter

Photovoltaic Energy

Air-conditioning, Lights & other building systems

Thermal Storage



Electric Vehicle



Smart Appliances



Conclusion

NIST is working to promote U.S. innovation and industrial competitiveness by **advancing measurement science, standards, and technology** in ways that enhance economic security and improve the quality of life.

- **Advanced Manufacturing**
- **Cybersecurity and Advanced Communications**
- **Health Care and Bioscience**
- **Forensic Science**
- **Measurement science for buildings**

richard.cavanagh@nist.gov