Information Technology for the Health Care Enterprise

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Outline

• Healthcare Vision
• Health IT at NIST
• Standards & Testing
• Security
• Biomedical Imaging
• Bioinformatics
• Summary
Healthcare Facts

• $3.5 Trillion dollars spent in 2017 on healthcare in the U.S. (http://www.cms.gov)

• It is estimated that approximately $750 billion is lost due to inefficiencies in the system
  – Effective use of IT may help reduce these costs

• Multiple parties playing different roles
THE NATION’S HEALTH DOLLAR ($3.5 TRILLION), CALENDAR YEAR 2017: WHERE IT CAME FROM

Health Insurance, 75%

Private Health Insurance, 34%
Medicaid (Title XIX) Federal, 10%
Medicaid (Title XIX) State and Local, 6%
Medicare, 20%
VA, DOD, and CHIP (Titles XIX and Title XXI), 4%
Out of Pocket, 10%
Other Third Party Payers and Programs, 8%
Investment, 5%
Government Public Health Activities, 3%

1 Includes worksite health care, other private revenues, Indian Health Service, workers’ compensation, general assistance, maternal and child health, vocational rehabilitation, Substance Abuse and Mental Health Services Administration, school health, and other federal and state local programs.
2 Includes co-payments, deductibles, and any amounts not covered by health insurance.
Note: Sum of pieces may not equal 100% due to rounding.

THE NATION’S HEALTH DOLLAR ($3.5 TRILLION), CALENDAR YEAR 2017, WHERE IT WENT

- Hospital Care, 33%
- Physician and Clinical Services, 20%
- Prescription Drugs, 10%
- Other Professional Services
- Dental Services, 4%
- Other, 14%
- Nursing Care Facilities and Continuing Care Retirement Communities, 5%
- Government Administration and Net cost of Health Insurance, 8%
- Investment, 5%
- Durable Medical Equipment, 2%
- Other Non-Durable Medical Products, 2%
- Other Health Residential and Personal Care, 5%
- Home Health Care, 3%
- Public Health Activities, 3%
- Other Health

*Includes Noncommercial Research and Structures and Equipment.

†Includes expenditures for residential care facilities, ambulance providers, medical care delivered in non-traditional settings (such as community centers, senior citizens centers, schools, and military field stations), and expenditures for Home and Community Waiver programs under Medicaid.

Note: Sum of pieces may not equal 100% due to rounding.

## Levels of Biological Information

### HEALTH CARE
- Ecologies
- Societies/Populations
- Individuals
- Organs

### BIOSCIENCES
- Tissues
  - Cells
    - Protein and gene networks
    - Protein interaction networks
  - Protein
  - mRNA
  - DNA
Advances Making Future Health Vision Attainable

Advances in Computing, Imaging, and Information Technology

Software (Internet, Cloud, Data Analytics, Etc.)

Speed and Storage

Networking Communications and Imaging

mPCD

Advances in Healthcare Practice

Disease Management

Evidence-Based Healthcare

Continuum of Care

Future Health Vision

Advances in Healthcare Technology

Human Genome Project

Pharmaceuticals and Nutraceuticals

Medical Devices

Advances in Healthcare Practice
The P7 Concept

1. Personalized
2. Predictive
3. Participatory
4. Precise (recommendation, decision analytics)
5. Preventive
6. Pervasive (including point of care)
7. Protective (Privacy and security)

Based on discussions with Leroy Hood and Ramesh Jain
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• Healthcare Vision
• **Health IT at NIST**
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Key Activities in Health IT

• NIST enables **interoperability** and **adoption** by:
  – Accelerating **standards** development and harmonization
  – Developing a conformance **testing** infrastructure
  – Expanding R&D and deployment of **security** protocols
  – Leveraging testing infrastructure to assist with **certification** process

• Leading to an emerging health IT network that is correct, complete, secure and testable.

• In addition to exploring standards and measurements for emerging technologies in health care.
NIST Health Care: IT Projects

- Health Information Technology: Standards & Testing
- Medical Devices: Interoperability
- Biomedical Imaging
- Bioinformatics
- Text Retrieval (Past)
- Usability (Past)
- Security
Outline

• Healthcare Vision
• Health IT at NIST
• **Standards & Testing**
• Security
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Standards and Testing

Provide technical expertise to leverage industry-led, consensus-based standards development and harmonization as well as develop a conformance testing infrastructure to enable interoperability and adoption.

Key activities include:

- Developed the conformance test method (test procedures, test data, and test tools) to ensure compliance with the Stage 1 and Stage 2 Meaningful Use technical requirements and standards.
- Under HITECH, developing a health IT standards testing infrastructure to provide a scalable, multi-partner, automated capability for current and future testing needs within the healthcare domain.
- Developing conformance test tools for fully integrated health IT systems to assure that the standards are implemented consistently.

Collaborating with industry including Health Level Seven (HL7), IEEE, and Integrating the Healthcare Enterprise (IHE).
Health IT Interoperability

- Hospital
- Radiology
- Administration
- EHR
- Personal Health Record
- Pharmacy
- Laboratory
- Health Info Exchanges
- Homecare devices
EHRs: Key Issues

- Input (user interfaces)
- Store (representation and persistency)
- Manipulate (search, mining, knowledge creation)
- Exchange (syntactic and semantic interoperability)
Interoperability

Electronic Health Record (EHR) System

Laboratory Information systems (LIS)

Public Health

Information Technology Laboratory, National Institute of Standards and Technology
Interoperability

- Electronic Health Record (EHR) System
- Pharmacy
- Medical Device
- Medical Device
Semantic Mapping Techniques
The Medical “Tower of Babel”

Some terms for “Hypersomatotropic Gigantism”:

<table>
<thead>
<tr>
<th>Vocabulary</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>UMLS Metathesaurus</td>
<td>Hypersomatotropic Gigantism</td>
</tr>
<tr>
<td>ICD-9-CM</td>
<td>No direct translation</td>
</tr>
<tr>
<td>MeSH</td>
<td>No direct translation</td>
</tr>
<tr>
<td>DXplain</td>
<td>Pituitary Gigantism</td>
</tr>
<tr>
<td>Read Codes</td>
<td>No direct translation</td>
</tr>
<tr>
<td>SNOMED</td>
<td>Hypersomatotropic Gigantism</td>
</tr>
</tbody>
</table>
True EHR Interoperability

Syntax
Context
Semantics

Conformance to raw message specifications in the Standard
Conformance to Specific Clinically Relevant Test data to exercise all options
Conformance to Specified Vocabularies in clinically relevant test data
• **Standards** are essential to achieving conformance and interoperability

• **Rigorous** testing is critical to achieving **conformance** and enabling **interoperability**

• Conformance CAN NOT be definitively determined* - but gives a level of confidence based on quality and quantity of test(s) performed
  (*unless specification is very basic)

• Conformance  
  ![Not equal sign](https://via.placeholder.com/150)  
  Interoperability

— A is Conformant, B is Conformant
  • The above does not say anything about interoperability between A and B
Standards That Link to an EHR
Standards in HealthCare

• Terminology
  – SNOMED, LOINC
• Classification Systems
  – ICD9 & 10, CPT
• Devices
  – IEEE 11073
• EHR-Related
  – DICOM, HL7 (CDA)
• Interoperability
  – DICOM, HL7 Messaging, HIPAA Transactions, NCPDP
• Language Formats
  – XML, X12
• Internet Protocols
  – HTTP/HTTPS → TCP/IP
### Four Levels of HIT Interoperability

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organizational Interoperability</strong></td>
<td>Standardized process (workflow) elements using business process modeling tools</td>
</tr>
<tr>
<td><strong>Semantic Interoperability</strong></td>
<td>Standardized meaning (model element) and terms / vocabulary for data interpretation, e.g., LOINC, ICD-10CM</td>
</tr>
<tr>
<td><strong>Syntactic Interoperability</strong></td>
<td>Standardized data exchange formats, e.g., HL7, XML</td>
</tr>
<tr>
<td><strong>Technical Interoperability</strong></td>
<td>Signals using standard protocols for technically secure data transfer, e.g., TCP/IP</td>
</tr>
</tbody>
</table>

#### Standards

Based on Oemig F, Snelick R, Healthcare Interoperability Standards Compliance Handbook. Springer International Publishing Switzerland. 2016. Page 13, Figure 1.3.
PROCURING INTEROPERABILITY

ACHIEVING HIGH-QUALITY, CONNECTED, AND PERSON-CENTERED CARE

Peter Pronovost, Michael M. E. Johns, Sezin Palmer, Raquel C. Bono, Douglas B. Fridsma, Andrew Gettinger, Julian Goldman, William Johnson, Meredith Karney, Craig Sarnit, Ram D. Sripam, Ashwini Zenooz, and Y. Claire Wang, Editors
Challenges with HIT Interoperability Standards

- Standards can be non-existent for certain domains
- Existing standards can be poorly defined
- Poorly-defined standards can be poorly implemented
- Well-defined standards can be poorly implemented
- Well-defined standards can be ignored (i.e., not adopted)
- Standards can compete with each other (too many standards)
- Standards can be complex

Use of Standards doesn’t guarantee Interoperability
Common Issues with HIT Standards

- Under specified
- Multiple solutions (occurs at all levels)
- Conflation of requirements (requirement scoping)
- Document current state—not desired state
- Not specific enough—e.g., code system binding
- Too specific
- Poor documentation and typos
- Lack of a consistency
- Conditions w/o Condition Predicates
- Absence of harmonized requirement specification methodology
- Insufficient requirement specification mechanisms
- Lack of reference and pilot implementations
- Lack of testing
- Improper scoping
NIST Standard Activities/Working Group Participation

Office of the National Coordinator (ONC)
- Health IT Standards Committee – Ram D. Sriram

OTHERS
- Cross Federal Workgroup on Telehealth (FedTel) – Ram D. Sriram and John Garguilo
- HITRD/NITRD – Ram D. Sriram

Integrating the Healthcare Enterprise (IHE)
- Patient Care Devices (PCD) Technical Committee – Co-Chair John Garguilo
- Patient Care Devices (PCD) Planning Committee – John Garguilo
- IT Infrastructure (ITI) Planning Committee – Bill Majurski
- IT Infrastructure (ITI) Technical Committee – Bill Majurski
- Testing and Tools Committee – Bill Majurski, Robert Snelick, John Garguilo

Health Level 7 (HL7)
- Conformance & Guidance WG – Co-Chair Robert Snelick
- Healthcare Devices WG – Co-Chair John Garguilo
- FHIR WG – Bill Majurski
- Immunization WG – Sandra Martinez

IEEE
- IEEE 11073 Medical Device Communications – John Garguilo

NCPDP
- Meaningful Use WG11 – Kevin Brady
The American Recovery and Reinvestment Act (ARRA) identifies NIST to lead the development of a health IT testing infrastructure

- ARRA (2009) emphasizes the need to move toward electronic health records
- The legislation calls for National Institute of Standards and Technology (NIST) to contribute:
  - Ensure health IT standards are complete and robust
  - Establish a health IT standards testing infrastructure that supports industry consensus standards development and provides robust conformance and interoperability testing capabilities
  - Deploy those technologies to promote interoperable health IT adoption
Proposed Stages of Meaningful Use

Stage 1
- Electronically capturing health information in a coded format
- Using that information to track key clinical conditions
- Communicating that information for care coordination purposes
- Initiating the reporting of clinical quality measures and public health information

Stage 2
- Stage 1 objectives
- Disease management
- Clinical decision support
- Medication management
- Support for patient access to their health information
- Quality measurement and research
- Bi-directional communication with public health agencies

Stage 3
- Stage 1 and 2 objectives
- Improvement in quality, safety and efficiency
- Decision support for national high priority conditions
- Access to self management tools
- Access to comprehensive patient data and improving population health outcomes
NIST And MU

• NIST developed the tests for compliance with the MU criteria.
NIST Role in ARRA MU EHR Certification Stage 1

MU Recommendations from ARRA
HIT Policy and Standards Committees

CMS Final Rule – Meaningful Use
Objectives and Measures

ONC Final Rule – Certification
Criteria and Standards

ONC-Approved Test Method

Accredited Testing and Certification Bodies**

- Drummond Group, Inc. Complete EHR and EHR Modules.
- InfoGard Laboratories, Inc. Complete EHR and EHR Modules.
- ICSA Labs - Complete EHR and EHR Modules.
- SLI Global Solutions Complete EHR and EHR Modules.
- Surescripts LLC - EHR Modules: E-Prescribing, Security

** Set up by NVLAP

Based on the requirements in the ONC Final Rule, NIST published 45 test procedures which are in use by the accredited testing laboratories to test and certify EHR products for the Meaningful Use Program.

ATCB Test Scripts
ATCB Testing of EHRs
ONC Certified Products List

Test Procedures
Test Data
Conformance Tools
How we accomplished MU 2

- HL7 CDA Cancer Registry Reporting Validation Tool
- HL7v2 Immunization Information System (IIS) Reporting Validation Tool
- HL7v2 Syndromic Surveillance Reporting Validation Tool
- HL7v2 Electronic Laboratory Reporting (ELR) Validation Tool
- Transport Test Tool (TTT) (includes C-CDA, Direct, and SOAP)
- Electronic Prescribing (eRx)
- HL7v2 Laboratory Results Interface (LRI) Validation Tool

Partner with CDC
Four separate divisions

Partner with DIRECT
Project/NwHIN

Partner with NCPDP
Established MU WG

Partner with S&I
Framework
NIST’s Tools are foundations for MU implementations

**Improved Quality, Access, and Cost of Healthcare**

- Meaningful Use (MU) Attestation by Eligible Entities
- Meaningful use of CEHRT by Eligible Entities
- CEHRT Configuration and Implementation at Eligible Entities’ Sites
- EHR Certification Testing using Test Tools
- Development of Conformance Test Tools by **NIST**
- Development of IG Standards & Other Specifications by Work Groups (with **NIST** participation)

**CMS MU Incentive Payments to Eligible Entities**

- **$10’s of Billions**

- Quality of the CEHRT implementations and the installed sites is directly related to the quality of the Conformance Test Tools and the underlying standards

- Resolving interoperability problems is much less expensive during standards development and testing; after CEHRT deployment these problems would need to be resolved at numerous locations

- **28 Billion Dollars**

- **A few $M**

CEHRT = Certified EHR Technology
The National Coordinator shall, in collaboration with the National Institute of Standards and Technology and other relevant agencies within the Department of Health and Human Services, for the purpose of ensuring full network-to-network exchange of health information, convene public-private and public-public partnerships to build consensus and develop or support a trusted exchange framework, including a common agreement among health information networks nationally. Such convention may occur at a frequency determined appropriate by the Secretary.
The NIST Testing Infrastructure ... will provide a scalable, automated environment for current and future testing needs

- NIST will collaborate with health IT stakeholders to harmonize healthcare standards test development and delivery to ensure conformance and interoperability within the healthcare domain

- NIST will leverage existing tools and work with health IT stakeholders including:
  - Certification Bodies
  - Testing Organizations
  - NwHIN
  - Vendors
  - Implementers
  - SDOs
  - Other Industry Consortia
Conceptual View of HIT Testing Infrastructure

Information Technology Laboratory, National Institute of Standards and Technology
The Big Picture: HL7 V2 End-to-end Testing Support

HL7 v2 Impl. Guide Template

Use Cases

HL7 v2 Standard Message Definition

General Transaction Constraints (e.g., IG, TF, or user input)¹

HL7 v2 Standard Value Sets

Import Value Sets

Domain Experts

IG Template Wizard

Use Case Development

Message Profiling

Vocabulary Profiling

Disposition Traceability

Utilities

Document Generator

Implementation Guide Authoring & Management Tool

Test Plan Development

Test Case Development

Constraint Generator

Test Script Generator

Document Generator

Data Management

Message Generation

Test Case Management and Authoring Tool

User Input Tool Generated

Conformance Profiles (XML)

Vocabulary Libraries (XML)

Test Case Specific Context Files (XML)

Data Sheets

Juror Documents

Test Plan Execution Script (XML)

Test Plan English Document

Domain Experts and Test Case Developers

Software Engineers

Tool Developers

Conformance Profile (XML)

Vocabulary Library (XML)

Specification Validation Context File (XML)

Test Case Requirements

Impl. Guide English Document

Data Sheet and Juror Document Generator

Validation Engine

Message Generation Engine

Report Generation

Artifact Repository

Testing Infrastructure

Web Applications

Domain Specific Tools

Testing Infrastructure Components

Resource Bundle

Resource Bundle Management

Test Plan Integration

Validation

Utilities

Communication

Documentation

Testing Tools

¹ Support existing specifications

R. Snelick May 8th, 2012

Information Technology Laboratory, National Institute of Standards and Technology
Medical Devices

- Interoperability
- Body Area Network Standards
- Security
NIST
Medical Device Communication Testing

Semantic interoperability of Medical Devices
Introduction - Need

As hospitals deploy EMRs into their most critical care areas, the need to acquire data directly from medical devices becomes increasingly evident.

– Device data capture is “real-time”
  • Data is up-to-date
  • Decision support algorithms can run on more timely data
– Device data capture is “automatic”
  • Reduce nursing workload
– Device data capture is “accurate”
  • Automated data capture is less error prone than manual charting
Patient Care Health Device Connectivity

Departmental Devices and Mgmt Systems
- Acute care
- Cardiology
- Surgery
- ER, ICU, others …

Hospital Device Gateway(s)
- Internal Hospital Network
- IHE DEC Profiles: PCD+RTM, PIB, SPD, ACM, PIV, WCM, IDCO …

Hospital Health Records

Remote EHRs
- Health Information Exchange
- IHE Content Profiles, XDS, XDR

Note: IHE Profiles shown above were recently (March 2016) demonstrated at HIMSS16; IHE DEC PCD-01 Technical Framework “Final Text” version first became available in Q3 2011.

Slide developed and provided by Paul Schluter, GE Healthcare

Information Technology Laboratory, National Institute of Standards and Technology
Personal Health Device Connectivity

Note: Continua 2014 Version (and subsequent updates) Guidelines available today; The Continua WAN interface uses the IHE DEC PCD-01 transaction over Web Services.
Problem Space Addressed through test methods
How can we Improve Interoperability?

The NIST Approach...

• Use **standards** to provide more economically effective solutions by amortizing the cost of design over many implementations.

• **Profile standards** to reduce optionality and simplify implementation and testing.

• Provide **computable definitions** of message syntax and semantics as well as information models.

• Use **rigorous conformance** (which in turn, used for certification and conformity assessment testing).

• Use other incentives to promote acceptance ...
NIST, SDOs, and (Medical Device) Domain Groups
Test Ecosystem

**ASTM**
- ASTM 2761
  - ICE
  - Patient Safety
  - Standards development framework

**IEEE**
- IEEE 11073
  - Nomenclature
  - Information Models
  - Standards development framework & Conformance

**NIST**
- Conformance, Validation, & Interoperability Testing
  - Test infrastructure
  - RTMMS, Nomenclature
  - Co-constraints
  - Information models
  - Interactions

**HL7**
- HL7 V2
  - Standards Development Framework
  - Transactions
  - Value Sets
  - Conformance

**IHE**
- IHE PCD
  - Pre- & Connectathon Testing
  - HIMSS and other venues
  - Rosetta → RTMMS

**Domain Groups**
- AAMI
- Continua
- MDICC
- WHI
- NCCoE
- C4MI
- FDA
- KP
- MD PnP
- TATRC
- CIMIT
- ICE
- OpenSDC
- KD: Kaiser-Permanente
- WHI: West Health Institute
- C4MI: Center for Medical Interoperability
- FDA: Food & Drug Administration
- MD PnP: Medical Device Plug-n-Play
- TATRC: Telemedicine and Advanced Technology Research Center
- CIMIT: Center for Integration of Medicine and Innovative Technology
- MDICC: Medical Device Interoperability Coordination Council
- OpenSDC: System & Device Connectivity
- NCCoe – NIST National Cybersecurity Center of Excellence

**Key: Relationships**
- Indirect
- Direct
- NIST Tooling

Information Technology Laboratory, National Institute of Standards and Technology
## Work Products:
Standards, Domains & NIST Test Tools

### Medical Device Domain
- IHE-PCD
- HL7 – Health Level 7  
  *Device-to-EHR/EMR*
- ISO/IEEE 11073 Medical Device Communication - Family of Standards  
  *Device-to-Device*

  **Model:** Manager  \(<->\)  Agent  
  *Manager (Receives Data) <-> Agent (Provides data)*

### NIST Tools
- Pre-Connectathon
- Connectathon
- RTMMS - hRTM
- RTMMS - Nomenclature
- ‘DIM Modeling – ‘DIM Editor - DeviceEditor’
- ICSGenerator’ - sunsetted
- ‘ValidatePDU’ – on hold

Information Technology Laboratory, National Institute of Standards and Technology
Medical Devices

- Interoperability
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Healthcare Sector

• Projects
  • Securing Telehealth Remote Patient Monitoring Ecosystem Project Description
  • Securing Picture Archiving and Communication Systems Project Description
  • Securing Wireless Infusion Pumps in Healthcare Delivery Organizations (SP 1800-8)
  • Securing Electronic Health Records on Mobile Devices (SP 1800-1)

• Join our Community of Interest
  • Email us at hit_nccoe@nist.gov
Overview

• PACS is nearly ubiquitous in hospitals, prompting the Healthcare Sector Community of Interest (COI) to identify securing PACS as a critical need.

• This project will provide a reference architecture and an example solution for demonstrating the capabilities to address the cybersecurity challenges of a PACS ecosystem.

Project Status

Build Phase - Currently building example solution in the NCCoE lab and drafting the NIST Special Publication 1800-series Practice Guide with expected publication date of 09/2019/2019

Collaborate with us

• Read Securing Picture Archiving and Communication (PACS) Project Description

• Email hit_nccoe@nist.gov to join the Community of Interest for healthcare projects
Overview

• Telehealth is one of the fastest growing sectors within healthcare. It leverages network-connected devices to monitor and treat patients outside of a healthcare delivery organization’s (HDOs) closed environment. This project was driven by the NCCoE healthcare Community of Interest (COI) and will demonstrate an example solution with the capabilities to address the cybersecurity challenges of a telehealth RPM ecosystem.

Project Status

• Define Phase – The final project description was published in May 2019. A federal register notice seeking technology collaborators will be published soon.

Learn more:

• Read Securing Telehealth RPM Project Description
• Email HIT_nccoe@nist.gov to join the Community of Interest for healthcare projects
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Medical Imaging

- Change Analysis – Lung Cancer
- NIST/QIBA Activities
- Iterative Reconstruction
- Interpreting Wireless Capsule Endoscopy Images
- From Images to Diagnosis through Ontologies
- Image Quality for Healthcare Applications
- Computational Metrology for Biomedical Imaging
- Performance of Scalable Systems
Confidence in CS Metrology & Big Data Measurements

Biological Metrology
- Experimental design
- Specimen preparation
- Visual inspection
- Definition of biologically meaningful objects & features
- Data-driven hypotheses
- Manual labeling of samples
- Interpretation of measurements
- Decisions

Computational Science
- Image correction
- Stitching
- Image visualization
- Segmentation & tracking & evaluation
- Feature extraction & visualization
- Comparisons & classification & cross-validation
- Confidence in models due to data variations and computational parameters

INTERACTIVITY
SW & HW IMPEDANCE
MACHINE LEARNING

Samples of segments
Quality characteristics

Information Technology Laboratory, National Institute of Standards and Technology
Use Case: Age–Related Macular Degeneration (AMD)

• **11 million** affected people in the US. Leading cause of vision loss in adults.

• Estimates of the global cost is **$343 billion**, including **$255 billion** in direct health care costs.

• Stem cell engineering of retinal pigment epithelium to treat macular degeneration (collaboration with NIH)

Information Technology Laboratory, National Institute of Standards and Technology
Use Case: Age–Related Macular Degeneration (AMD)

20/20 Vision

AMD blurred vision

Scale
- Single Microscope FOV (10X) = 0.034% of 10 cm diameter dish ~1 MB

Complexity
- Phase Contrast
- Fluorescent imaging
- Bright-field imaging

Speed
- Identify & count healthy cells/colonies
- Distribution of cells

Imaging instruments

<1 TB image of total dish over time

Therapy Failed

Therapy Worked
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Bioinformatics: Projects

• Cellular Markers that Report Microenvironment
• Dynamic Measurements in Live Cells
• **Computational Geometry**
• Protein-Protein Interaction Networks
• Precision Medicine
• Performance of Scalable Systems
Motivation

- Cyclin-dependent kinase 5 (*Cdk5*) operates in human brain
  - Involved in cell development, cancer and neurodegeneration
- P25 is a pathological cdk5 activator
  - Cdk5/p25 causes phosphorylation of brain protein tau (Alzheimer’s disease)
- An experimental study of the effects of truncated fragments of p25 on Cdk5 activity is carried out in the Neurochemistry Lab, NINDS
- Inhibitory fragments inhibit cdk5/p25 pathology, but inhibition mechanisms are unknown
- Small fragments are needed for effective clinical trials
  - No side effects, can cross blood brain barrier

Information Technology Laboratory, National Institute
Problem Formulation

• Fragments are randomly obtained from p25 and tested (years of work)
  – First inhibitor tested, CIP, consisted of 124 amino acids (too big!)
  – Smaller inhibitor tested so far, p5, consists of 24 AAs
    • Can cross the blood brain barrier
    • It is still big, so high probability of side effects

• Computer-based studies should be used to provide insights into Cdk5-inhibitor bindings
  – Binding prediction and simulation

• No more random truncations of p25 fragments, but computer-aided peptide design
Proposed approach

• A method to predict protein-protein association in solution has been defined [1,2]
• Basic idea: in the early stages of complexation, proteins form metastable preferential first-encounter complexes, from which stable binding modes evolve. The main steps are:

1. Protein conformers are obtained using a Monte Carlo (MC) method

2. For each pair of conformers, MC optimizations yield a set of first-encounter modes, defining a probability distribution

3. First-encounter modes are combined into a generalized probability function to simulate protein-protein systems using self-adaptive configurational bias-MC simulations.

4. The binding modes thus obtained are refined using Molecular Dynamics (MD) simulations
Results

- Cdk5-p5 pharmacophore was characterized
  - Strong electrostatic interactions identified
  - Spatial arrangement and critical AAs known
  - Dynamic stability tested
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• Summary: Towards Smart Health Care
Defining Health Persona

Logical Sensor

Fitness Tracking Sensors

Physiological Sensors

Life Event

Food Event

Kinetic Event

Physiological Event

Personicle

Home Drive Walk Meeting Work Walk Exercise

Courtesy: Ramesh Jain, UCI
EventShop: Global Situation Detection

Data Ingestion and aggregation → Predictive Situation Recognition → Evolving Global Situation

- Event: Breathing/cough symptom
  - Posted by: a patient
  - Where: DC
  - When: 2/21/13 2:30 am

Example of Rules
- R1: If (301<AQI<500 at Location DC ) Then (“Health alert”: everyone may experience more serious health effects)
  - http://www.airnow.gov/
- R2: If (Disease = “Asthma” and AQI>200) Then (message...)
- ...

Example of Physical Data
- AQI: 250 (Air Quality Index 0<AQI<500) at Location DC
- GPS: 38, 53, 77, 02, 12:00
- Temperature: 60 F

Personal EventShop

Data Ingestion → Predictive Personal Situation Recognition

- Location identification DC / Map Visualization at time 2:30 pm
- Air quality not suitable for your Asthma – Move Indoors

Need- Resource Matcher

Resources
- Prone to Asthmatic reactions
- Is in outside location DC at time 2:30 pm
- High Probability of attack

Database

Persona

Data Sources

Wearable Sensors
- Air quality not suitable for your Asthma – Move Indoors

Calendar

Location

Environment Sensor Devices

Social Network

Internet of Things

Environmental Sensor Devices

Database Systems

Satellite

Example: Breathing/cough symptom

Poster by: a patient

Where: DC

When: 2/21/13 2:30 am

Example of Rules

- R1: If (301<AQI<500 at Location DC ) Then (“Health alert": everyone may experience more serious health effects)
  - http://www.airnow.gov/
- R2: If (Disease = “Asthma” and AQI>200) Then (message...)
- ...
Overview of Production Support Model for HC Wireless Cart - rev. 1

**Smart Healthcare**
- **Smart** Devices
- **Smart** Networks
- **Smart** Processes
- **Smart** EMRs
- **Smart** Medicine
- **Smart** Organizations
- **Smart** Collaborations
- **Smart** Society
- **Smart** Planet
Smart Doctor
Summary

- We develop measurements, tools, and prototypes, and contribute to voluntary standards to advance the use of information technologies in healthcare systems and achieve an interconnected electronic health information infrastructure.
  - Collaborate with industry to develop clear, testable public specifications
  - Based on industry priority we develop conformance test suites to ensure correct, robust interoperable software
  - Develop prototypes of emerging HC standards to fill in the gaps that are identified by industry
  - Develop the Health IT Testing Infrastructure
  - Research into standards, measurements, and testing methodologies for emerging technologies
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