



# Precision Health and Digital Health: Evolving Inter-Dependencies in the Transformation of Healthcare Delivery

Dr. George Poste, D.V.M., Ph.D, F.R.C. Path., F. Med Sci., CBE, F.R.S.

Chief Scientist, Complex Adaptive Systems Initiative and Regents Professor of Health Innovation
Arizona State University

george.poste@asu.edu www.casi.asu.edu

9<sup>th</sup> Siemens Technology and Innovation Council (STIC) Meeting Farnham Castle, Farnham, UK 7 March 2018

### Aspirations for the U.S. Healthcare System: National Academy of Medicine

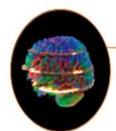
The Triple Aim

- improved outcomes
- reduced cost
- value-based care

- right information
- right decisions
- right culture

The Learning Healthcare System

### Global Healthcare Leader at the Core of Clinical Decision Making



#### Diagnostic Imaging

We help achieve highest diagnostic quality and efficiency

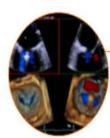
- · Computed Tomography
- Magnetic Resonance
- Molecular Imaging
- · X-Roy Products
- · Imaging IT



#### **Advanced Therapies**

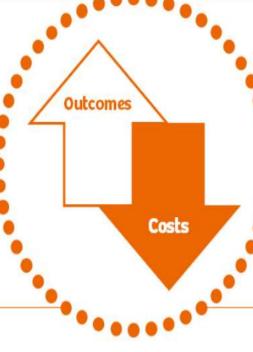
We enable advanced therapeutic procedures

- Cardiologu
- Interventional Radiology
- · Radiation Oncology
- Surgery



#### Ultrasound

We enable real-time access to decision critical information



#### Laboratory Diagnostics

We enable clinical and workflow excellence in the lab

- · Chemistry, Automation & Immunoassay
- Hemostasis, Hematology e Specialty Business
- Business Solutions Group
- · Molecular Diagnostics



We provide fast and accurate results to improve patient outcomes and reduce costs



#### Services

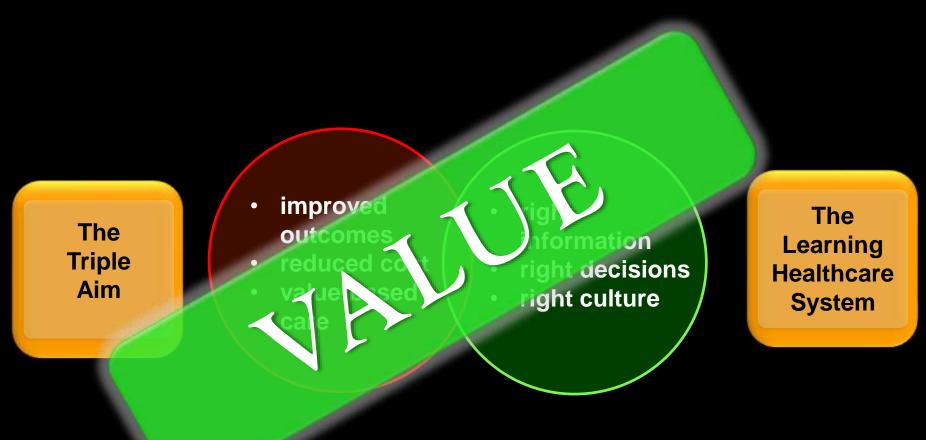
We help achieve best institutional performance

- Customer Services
- · Digital Health Services
- · Enterprise Services & Solutions

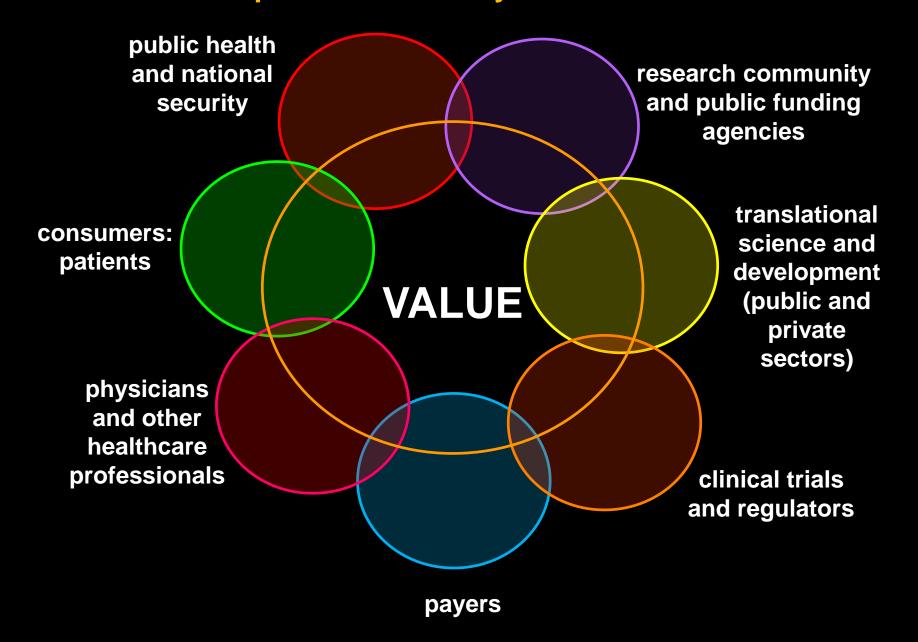




# Aspirations for the U.S. Healthcare System: National Academy of Medicine



## The Complex Ecosystem of Biomedical Research and Clinical Care: Different Perceptions of Value By Different Constituencies



### Biomedical Research and Healthcare Delivery: The Imperative for Major Performance Improvement

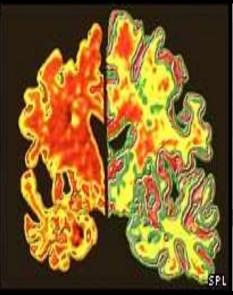
- slow translation of research for patient benefit
- ageing societies, increased chronic disease burden and unsustainable cost of care
- fragmented and uncoordinated expertise and poor continuity in patient care
- wide variation in patterns of clinical care
- error, duplication, waste and administrative bloat
- public dissatisfaction and political turmoil over care access and affordability

### **Biomedical Research and Healthcare Delivery**

- siloed data and poor use of available information
- slow adoption of advanced IT systems relative to other sectors
- implications of advanced computing and decision support systems for medical education and professional competencies

### Ageing Societies and the Chronic Disease Burden: Confronting the Largest Clinical and Economic Disruptions and Threats to Sustainable Healthcare









cancer

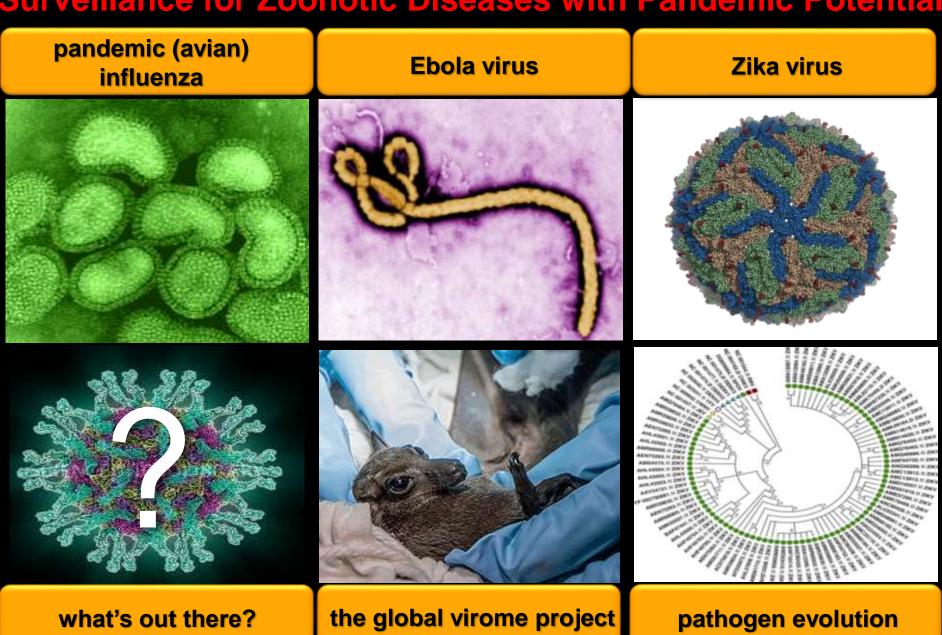
neurodegeneration

cardio-vascular/ metabolic disease

mental illness

### 'One Health':

### **Surveillance for Zoonotic Diseases with Pandemic Potential**



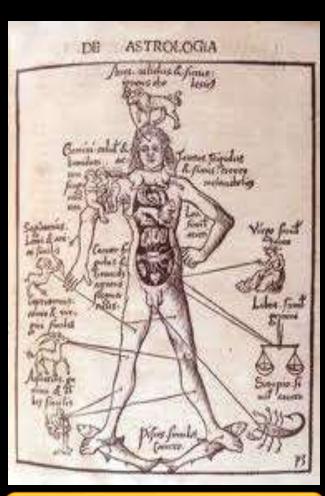
# Technology Acceleration and Cross-Sector Convergence: Blurring the Boundaries of Biomedicine



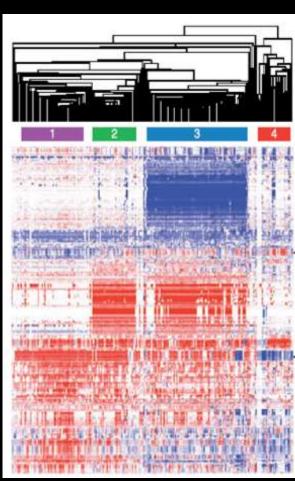
Convergence of Advances in Biomedicine, Materials Science, Engineering, Telecommunications, Robotics, Advanced Computing and Data Science

### **The Path to Precision Medicine:**

### From Superstitions to Symptoms to (Molecular) Signatures







"humors", astrology, shamanism, sin and divine fate

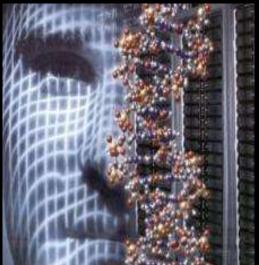
biochemistry and organ-based pathophysiology

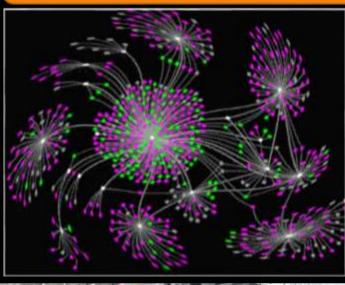
molecular biology and multi-omics profiling

### **Precision Medicine:**

(Epi)Genomics

Causal Relationships Between Disruption of Molecular Signaling Networks and Disease







Patient-Specific Signatures of Disease or Predisposition to Disease

001111110110000000000000000011110000

- terabytes per individual
- zettabyte yottabyte population databases

Big (Messy) Data

# Molecular Diagnostics and Biomarkers as the Intellectual Drivers of Precision Medicine

- disease predisposition risk
- increased accuracy of disease classification (molecular subtypes) and staging
- more rational treatment selection based on presence/absence of specific molecular targets for R<sub>x</sub> action
- pharmacogenetic profiling to avoid R<sub>x</sub> adverse events
- monitoring R<sub>x</sub> efficacy
- detection of emergence of R<sub>x</sub> resistance (microbiology; oncology)
- earlier alert of pending relapse and detertion minimal residual disease

### **Still Two Largely Separate Worlds**

precision medicine

routine healthcare delivery and SOC

research and early clinical adopters

\$100-125\* billion (estimated)

slow and erratic adoption of technological advances

\$3.4 trillion (19% GDP)

## Large Scale Genome Sequencing Projects: The Dangers of Reductionism and Ignoring Biological Complexity

















### **Individual Variation and Genotype-Phenotype Relationships**

**Junk No More: Pervasive Transcription** 

- alternate transcription /translation/ (co)splicing
- · SNPs, CNVs
- pseudogenes
- indels, SVs
- phasing
- epistasis
- imprinting
- cis-and trans regulation
- RNA universe

recognition of (epi)genome organizational and regulatory complexity

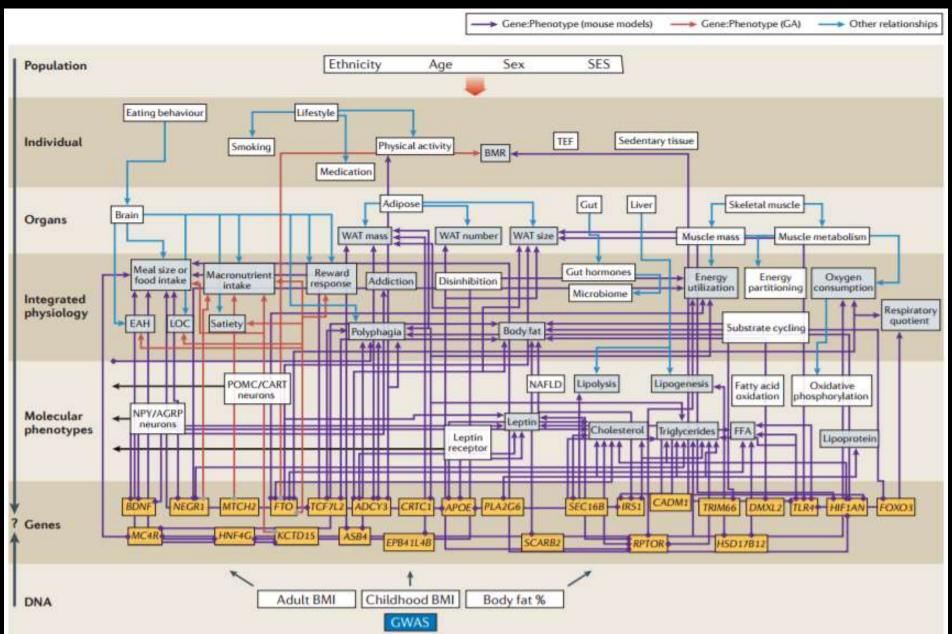
**Cell-specific Molecular Interaction Networks** 



**Perturbed Networks** and Disease



### Interaction Network of Genotypes and Phenotypes in Obesity



From: S. Ghosh and C. Bouchard (2017) Nat. Rev. Genetics 18, 731

# Precision Medicine and Digital Medicine: Obligate Inter-Dependencies

**Individual Data** 

### **Population Databanks**



of
large scale,
diverse
data classes

"matching" individuals to 'best match' cohorts using data on similarities of molecular profiles and treatment outcomes

# Precision Medicine and Digital Medicine: Obligate Inter-Dependencies

### **Individual Data**

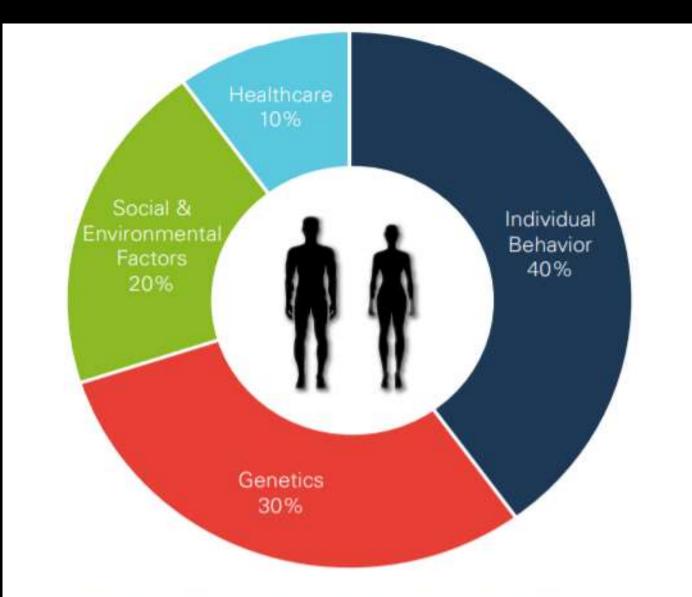
### **Population Databanks**



of
large scale,
diverse
data classes

"digital phenotypes" and "digital siblings"

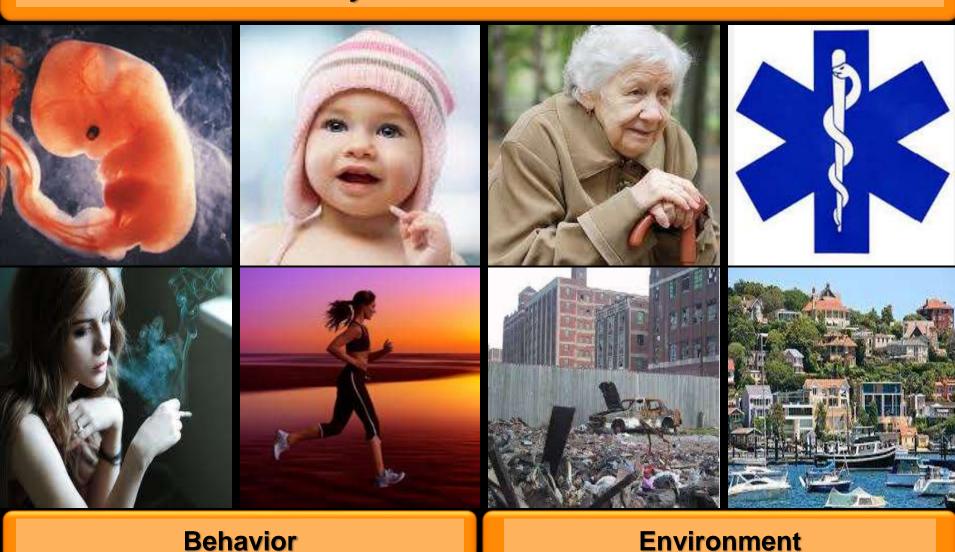
### **Impact of Different Factors On The Risk of Premature Death**



Source: Beyond Health Care: The Role of Social Determinants in Promoting Health and Health Equity. Kaiser Family Foundation, 2015.

## Most Events That Affect Our Health Occur Outside of the Healthcare System And Are Not Monitored

**Need for Continuity of Care Record: From Womb to Tomb** 



### Consortium for Exome Sequencing of 500,000 **UK Biobank Samples by 2020**



### REGENERON













- announced January 2018
- integration with medical records, lab test data and psychological assessments

### Healthcare Beyond the Clinic: Remote Health Status Monitoring

- smartphones, wearables, sensors and self-reported data
- telemedicine and virtual consultations
- environmental sensor networks
  - biosurveillance and EID/pandemic monitoring
  - smart homes
- POC/PON distributed diagnostic test capabilities
- loT and loHT
- AORTA: Always On, Real Time, Access

### **Wellness Apps for Fitness, Diet and Exercise**



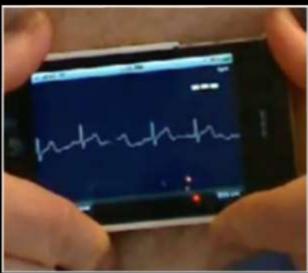


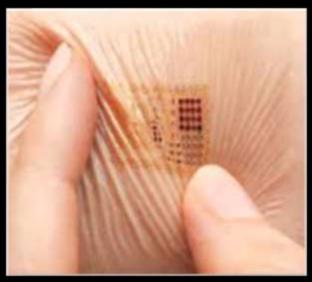




## Remote Monitoring of Health Status













# Limitations of Consumer-Based Wearables for Health Status Monitoring

- restricted analyte menu
- clinical value still viewed as marginal by physicians/payers
- novelty item, rapid abandonment and lack of user 'stickiness'
- regulation as medical devices
- erratic integration into electronic PHR/HER and anomaly alerts requiring intervention
- limited adoption incentives
  - users, payers and physicians

## Gray Technologies and Ageing in Place: The Rapid Expansion of Telemedicine for Remote Health Monitoring





### Rx adherence

cognitive stimulation







reduced office visits



### syngo.via

Reading as it should be: simple and cinematic.



# The Growth of Telehealth and Telemedicine: Expanding the Care Space

- estimated use by 60% HCl's and 50% hospitals (NEJM 2017, 377, 1585)
- virtual consults in Kaiser Permanente exceeded in-person visits in 2016
- healthcare consumerism and Ux expectancy
- 21<sup>st</sup> Century Cures Act and efficacy evaluation projects for Medicare

### **Chatbots and Support Robots in Healthcare**























### **VR/AR and Training for Complex Tasks**



### **VR/AR** and **Neuromodulation**



- promote behavior change via altered sensory inputs and feedback reinforcement learning
- mental illness, PTSD, physical rehabilitation, substance abuse and pain control

# **Computer-Based Facial and Voice Recognition and Idiosyncratic Patterns of Body Language, Gait and Behavior**



# "People Analytics" Social Activities and Behavior Become Quantifiable

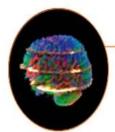
- who knows why people do what they do?
  - the fact is that they do!
- these actions can now be traced and measured with unprecedented precision
- with sufficient data, the numbers reveal increasingly predictable behavior and individual risk patterns
- the confessional of social media
- the blurring of private and public spaces
- complex ethical and legal issues
  - consent, privacy, security, surveillance

## Digital Psychometrics in Psychiatry and Evaluation of Mental Illness

- high variation in clinical assessment of same patients by different psychiatrists
- major need for objective measurements of nuanced behavior
  - (micro) saccades, facial dynamics
  - motor functions, gait
  - speech prosody (rhythm, tone, volume, construct)
  - stimulus response reactions and interaction speed
- analysis of conversations with chatbots
- machine learning and Al analytics of large video banks
  - bipolar disorder, schizophrenia, depression, PTSD and suicidal ideation
- alerts to care teams when intervention is indicated

## New Horizons in Diagnostic Medicine

## Diagnostic Laboratory Tests and Imaging: <5% of Healthcare Expenditures But Used in c.70- 80% Clinical Decisions



#### Diagnostic Imaging

We help achieve highest diagnostic quality and efficiency

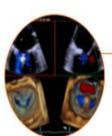
- · Computed Tomography
- Magnetic Resonance
- · Molecular Imaging
- · X-Roy Products
- · Imaging IT



- Cardiologu
- Interventional Radiology

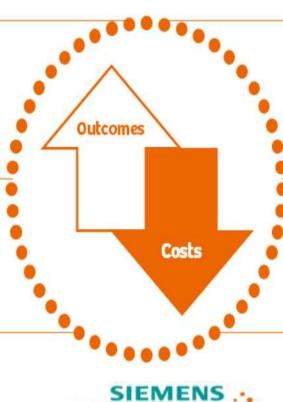
therapeutic procedures

- · Radiation Oncology
- Surgery



#### Ultrasound

We enable real-time access to decision critical information



Healthineers

#### **Laboratory Diagnostics**

We enable clinical and workflow excellence in the lab

- · Chemistry, Automation & Immunoassay
- Hemostosis, Hemotology
   Specialty Business
- · Business Solutions Group
- Molecular Diagnostics



We provide fast and accurate results to improve patient outcomes and reduce costs



#### Services

We help achieve best institutional performance

- · Customer Services
- · Digital Health Services
- Enterprise Services & Solutions



### Faster Diagnosis Saves Lives: POC & PON Multi-Agent 'Stat' Diagnostic Assays for Infectious Diseases



FTD Infectious Disease Detection Kit
- Multiplex Real-time PCR testing -

#### **Faster Diagnosis Saves Lives:**

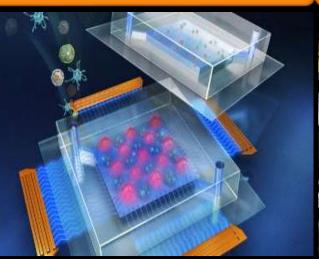
#### The Primacy of Diagnostics in Biosurveillance and Preparedness Mobilization

Profile: signatures of infectious agents

Detect: rapid automated PON/POC diagnostics

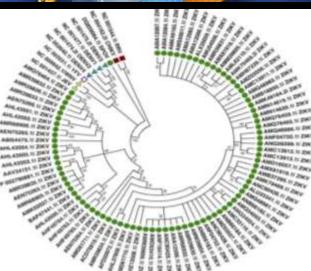
Act: real-time situation awareness, decisions













surveillance sans frontières

pathogen evolution

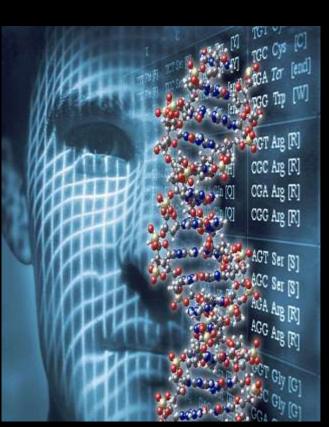
dual-use research and engineered biothreats

## Biomarkers, Molecular 'Multi-Omics' Diagnostics and Mapping the Organization of Biological Signaling (Information) Networks

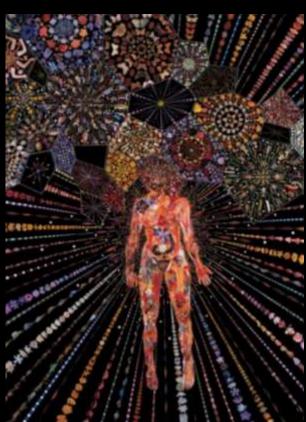
Fundamental Source Data for Making Precision Medicine A Reality

From Reductionist Analysis of Components to Understanding the Assembly, Dynamics and Information Architecture of Complex Biological Systems In Health and Disease

# Defining Individual Uniqueness: Mapping the Organization, Dynamics and Information Architecture of Complex Systems in Health and Disease





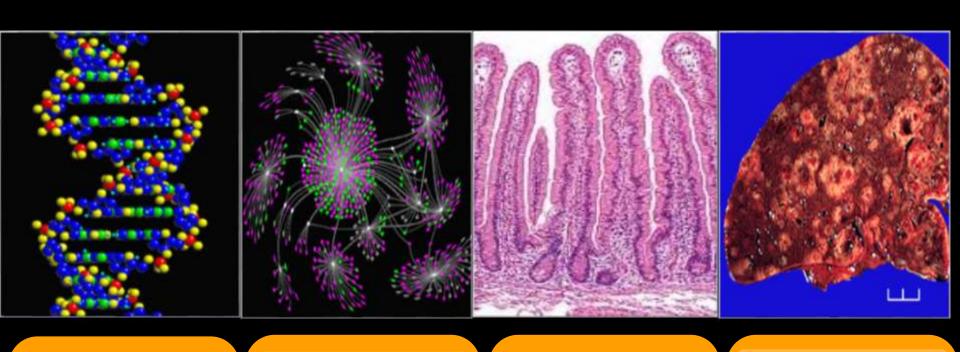


(epi)genome

transcriptome, proteome, immunome exposome

regulation and dynamics of molecular interaction networks

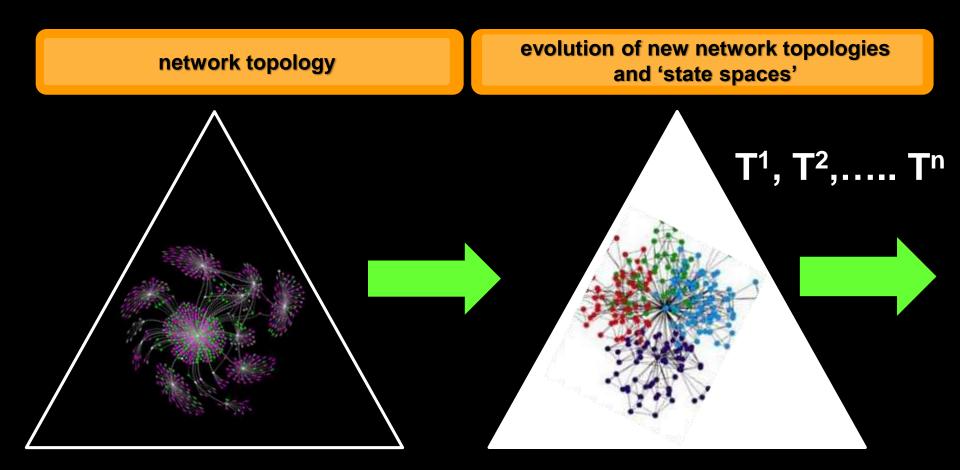
## Precision Medicine: Understanding the Disruption of Molecular Information Networks in Disease



encoded information and expression as cell-specific signaling networks patterns of information flow in signaling networks (network topology)

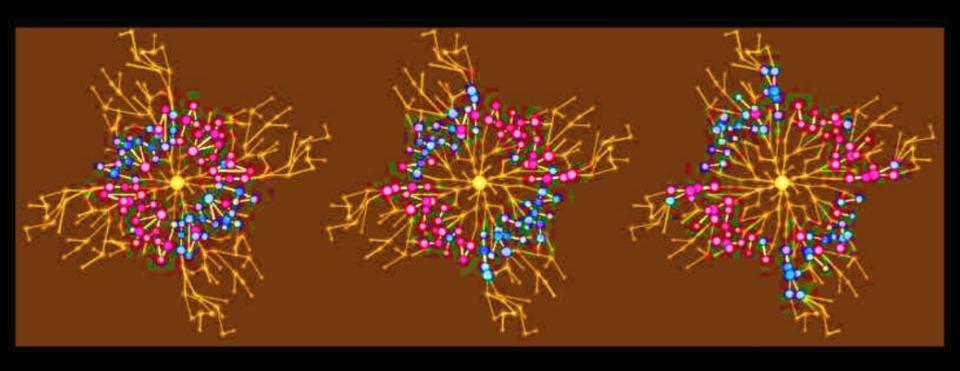
stable networks and information fidelity (health) dysregulated networks and altered information patterns (disease)

## **Understanding System State Shifts and Emergent Perturbations in Molecular Signaling Networks in the Health to Disease Continuum**

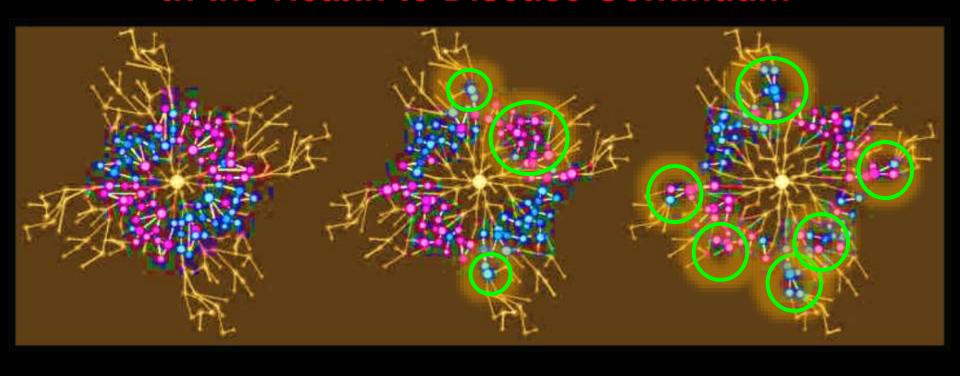


- (epi) genomic, transcriptomic and protein expression networks
- gene-gene interactions (epistasis)
- multi-omic network- environmental interactions
- context: multicellular signaling interactions across multiple levels of biological scale

# Understanding System State Shifts and Emergent Perturbations in Molecular Signaling Networks In the Health to Disease Continuum



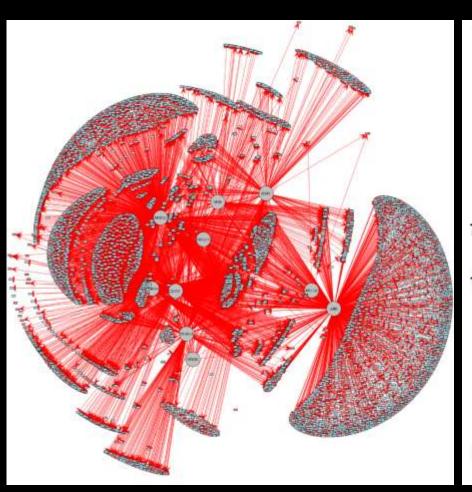
# Understanding System State Shifts and Emergent Perturbations in Molecular Signaling Networks In the Health to Disease Continuum

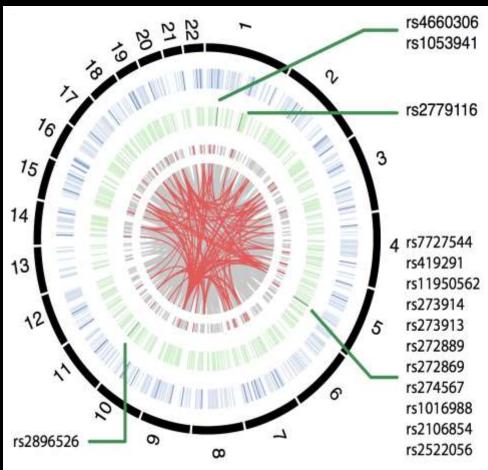


health

subclinical disease overt disease

# Integrative Gene Expression Network Models and Classification of Functional Modules (Communities) That Span Multiple Chromosomes

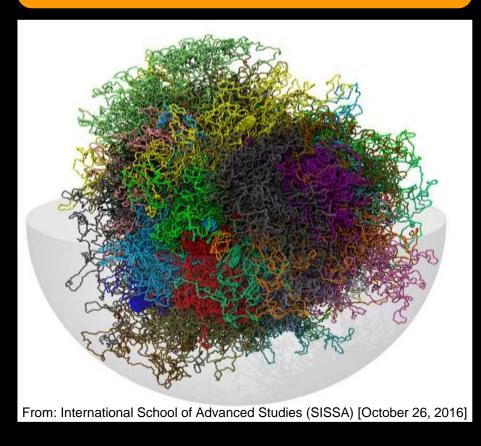


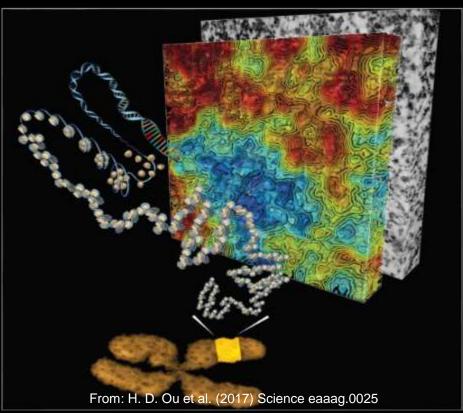


## Defining Short- and Long-Range Cis- and Trans- Regulation of Gene Networks

**Chromosomal Neighborhoods: Understanding the 3-D and 4-D Genome** 

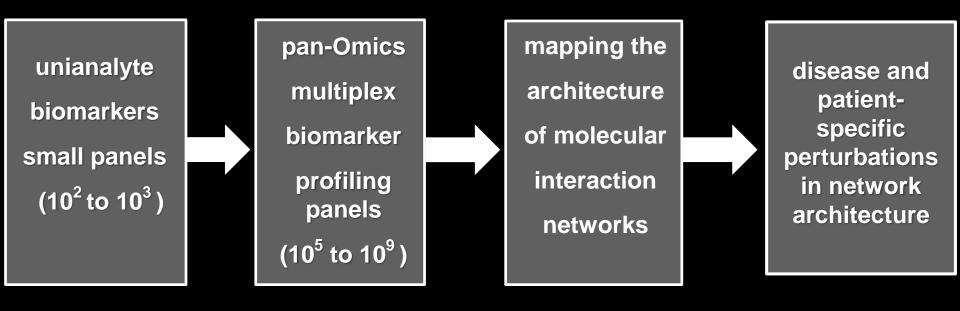
**ChromEMT Mapping of Chromatin Ultrastructure and DNA Packing** 





- spatial and temporal regulation
- inter-chromosomal juxtaposition of TFs, promoters and enhancers

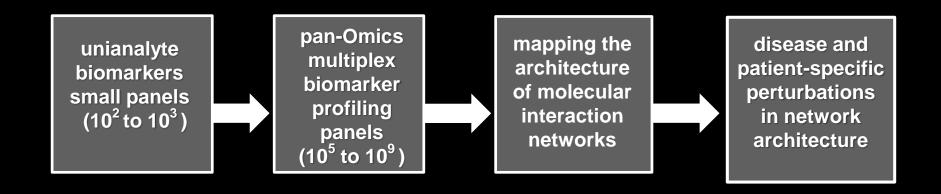
#### Molecular Diagnostics, Biomarkers and Understanding the Dysregulation of Molecular Information Flows in Disease



traditional diagnostics

emerging next-generation molecular diagnostics

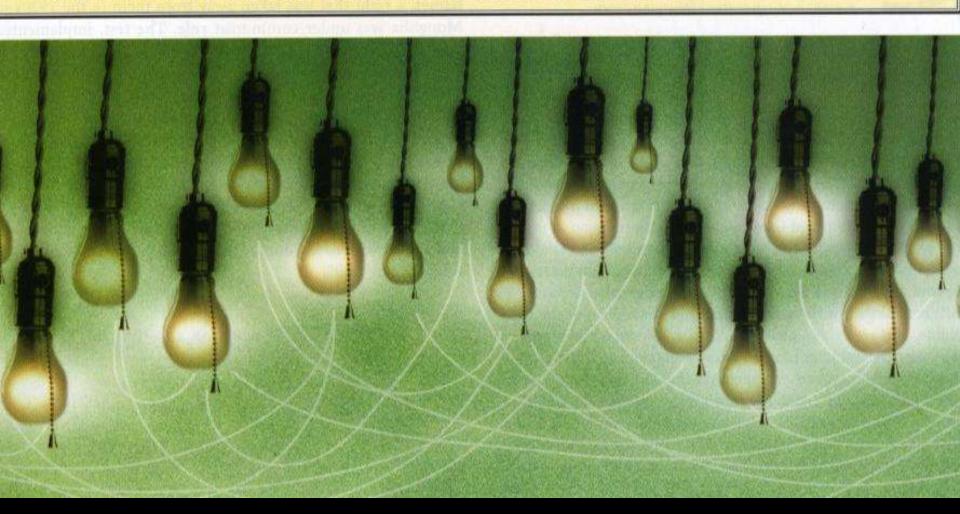
the grand challenge for systems biology



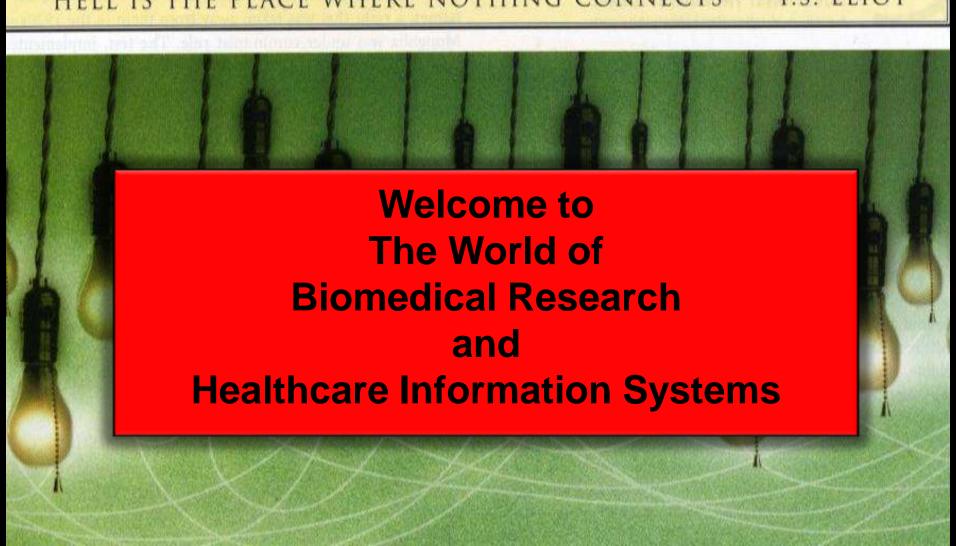
The V6 Data Deluge volume, variety, velocity, veracity, visualization, VALUE

- data production, analysis and storage
  - standards, inter- operability and provenance
    - scalability, infrastructure and cost
      - new conceptual models and analytical platforms for mapping network architectures
        - deep learning and artificial intelligence

#### HELL IS THE PLACE WHERE NOTHING CONNECTS - T.S. ELIOT







# Data Tombs: The Current Status of Too Much Biomedical Research and Clinical Data

- unstructured (semantic chaos)
- hoarded (limited sharing)
- siloed (poor integration)
- incompatible data formats, db interoperabilities
- variable quality, lack of standardization and the reproducibility problem
- immobile (inadequate infrastructure for large scale data transfer)
- static (episodic snap shots of dynamic biological systems and disease processes)

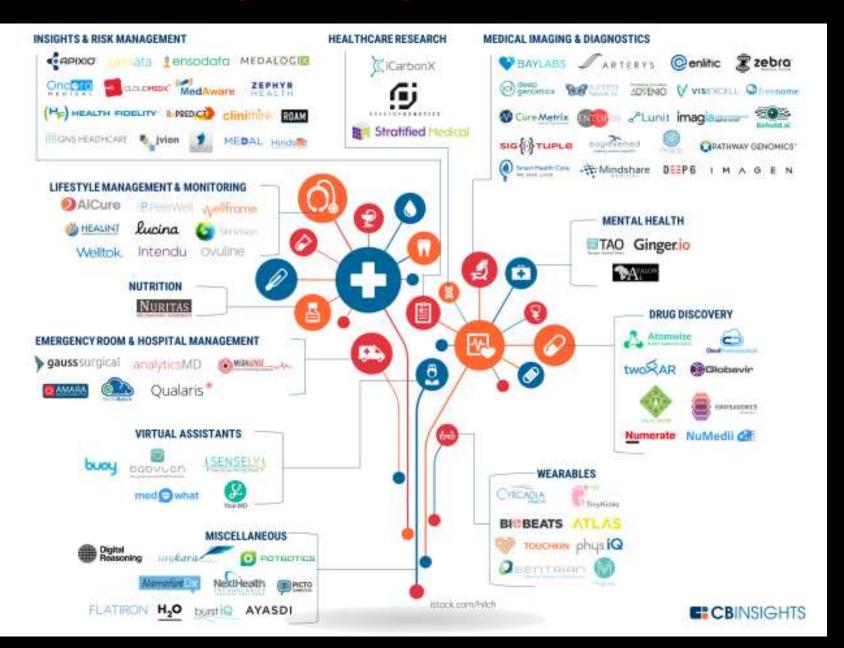
#### Artificial Intelligence, Pattern Analysis and Medical Practice



"I don't think any physician today should be practicing without artificial intelligence assisting in their practice. It's just impossible otherwise to pick up on patterns, to pick up on trends to really monitor care."

Bernard J. Tyson
CEO, Kaiser Permanente
Cited in Forbes: The Future of Work
1 March 2017

#### 90+ Startup Al Companies in Healthcare



#### **Major Investments in Digital Health by Major Corporations** Within and Outside of Traditional Healthcare



















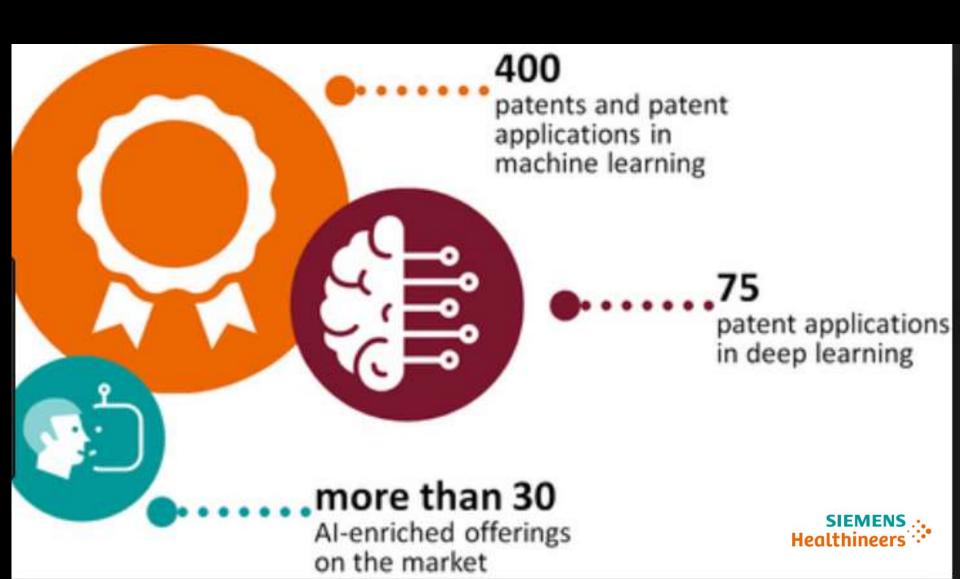




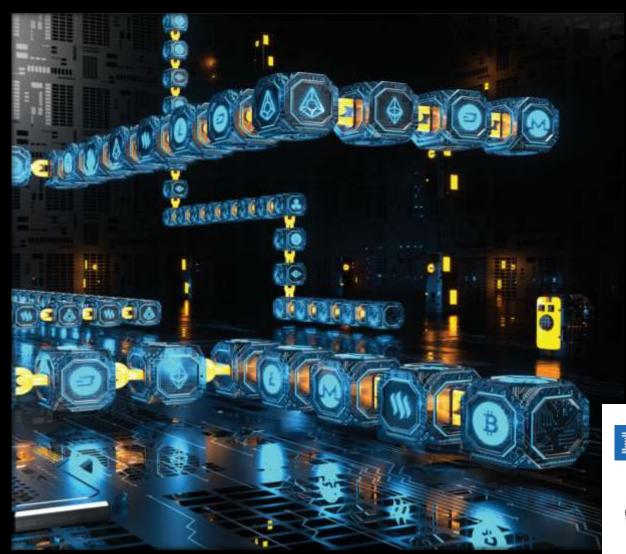








#### Early Entrants Into The Use of Blockchain for Secure Contract Transactions in Healthcare





















#### **Breaching Anonymity in "De-identified" Healthcare Data**

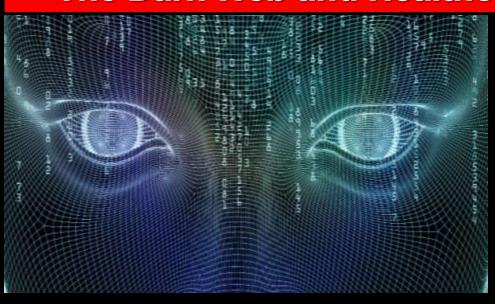


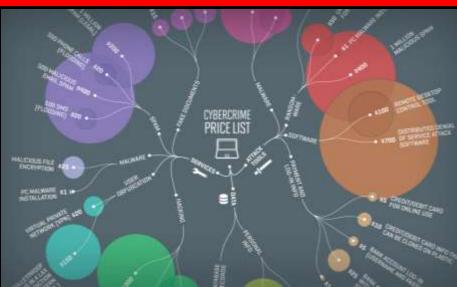
"Mishandling of patient information shows how governments and companies must become more worthy of trust."



Nature(2017) 547, 259

#### The Dark Web and Healthcare Data Theft and Fraud

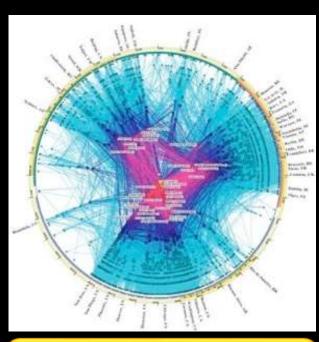




## The Emergence of Big Data Changes the Questions That Can Be Asked





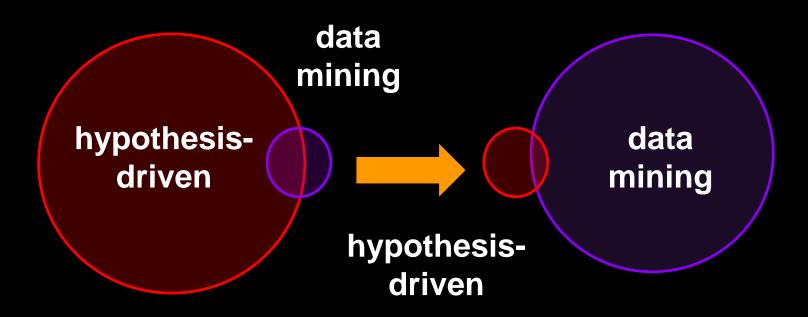


Isolated Data

Complex Networked Data

Complex
Computational Data

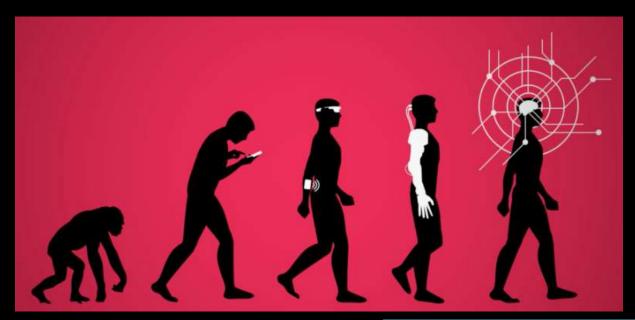
#### A Pending Transition in Scientific Research?



## Data-Driven Knowledge Generation and Decision Support Systems

- changing the nature of discovery
  - hypothesis-driven versus unbiased analytics of large datasets (patterns, rules)
- changing the cultural process of knowledge acquisition
  - large scale collaboration networks, open systems versus individual investigators and siloed data
- changing knowledge application
  - increased quantification and decision-support systems
- changing the cognitive and intellectual competencies for knowledge-intensive expertise in multiple domains
- changing education, training and research

## The Co-evolution of Augmented Humans, Robotics and Human-Machine Interactions





#### Robotics, Autonomous Systems, Machine Learning and Artificial Intelligence

4-D Jobs - Dull, Dirty, Dangerous, Digital



**Speed of Progressive Redundancy and Replacement of Human Skills?** 



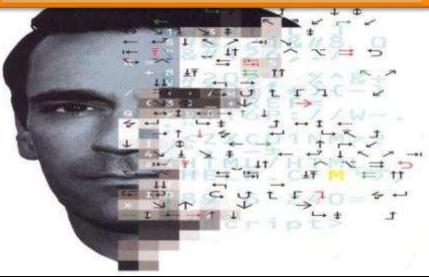
#### "Explainable Al"

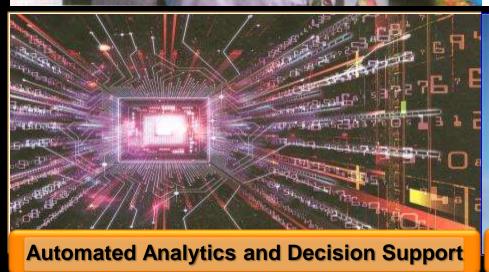
- need to better characterize the evolution of decision algorithms
  - keeping humans in the loop
- deconvolution of how and why machine learning algorithms reach flawed conclusions
- broad national security issues related to data integrity
- concern over Al-directed manipulation of social networks, advertising and personal data
- corruption of critical military and civilian systems and decision tools

## Technology Acceleration and Convergence: The Escalating Challenge for Professional Competency, Decision-Support and Future Medical Education

# Data Deluge

#### **Cognitive Bandwidth Limits**







**Facile Formats for Actionable Decisions** 

#### Machine Learning and Image Analysis in Clinical Medicine



- large scale training sets and classification parameters
- standardized, reproducible and scalable
- 260 million images/day for \$1000 GPU

#### Artificial Intelligence (AI) and Healthcare

- how will Al algorithms/decision analytics be validated/regulated?
- how will Al be integrated into current work flow or will radical reorganization/re-training be required?
- how will Al platforms alter payment schemes?
- which clinical specialties/processes will be at risk of replacement by AI and when?
- how will professional competencies in using Al decision-support tools be evaluated?
  - MD curriculum, CME
- what new malpractice liabilities will emerge by failure to use/interpret Al platforms

## The Future of Healthcare: Precision Medicine and Digital Medicine

new technology platforms

multiplex profiling of molecular network topologies

automation and advanced computing

sensors, robotics

the expanded care space

wearables, sensors, telemedicine

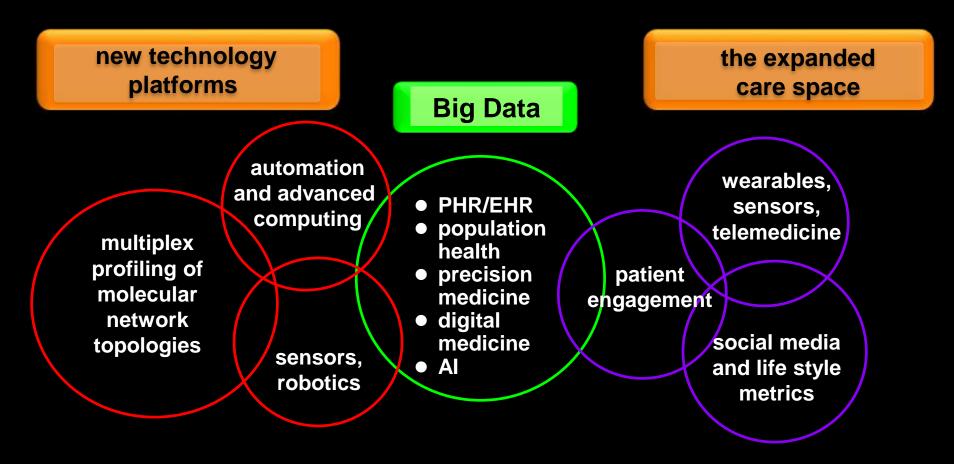
patient engagement

social media and life style metrics

molecular classification of disease

remote monitoring of health status

## The Future of Healthcare: Precision Medicine and Digital Medicine

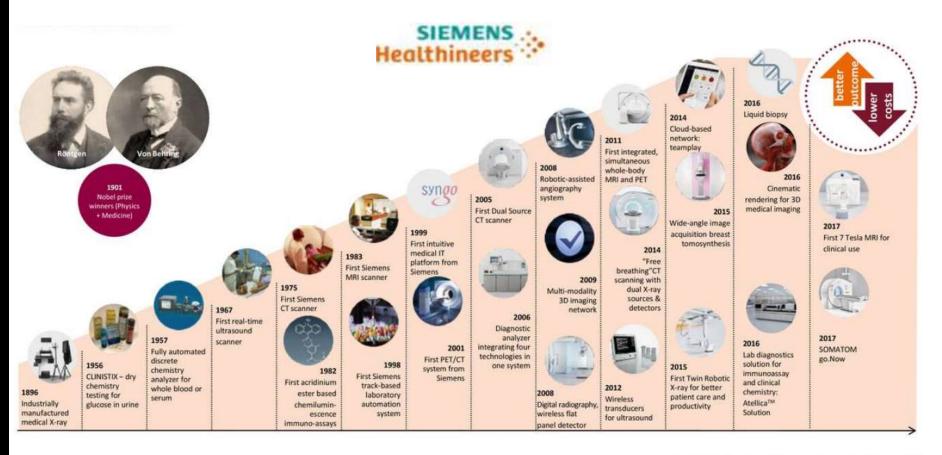


molecular classification of disease

analytics for improved decisions and clinical outcomes at lower cost (value)

remote monitoring of health status

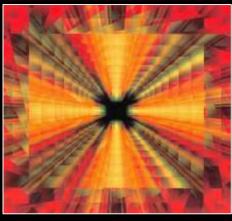
#### **A Long History of Transformational Innovations**



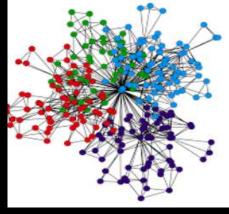
#### The Evolution of Data-Intensive Precision Medicine

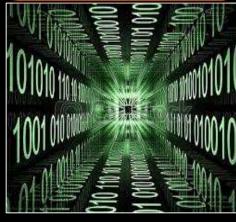
Technology Convergence and Acceleration Mapping Geno-Phenotype Complexity Topology of Biological Information Networks

V6 Big Data



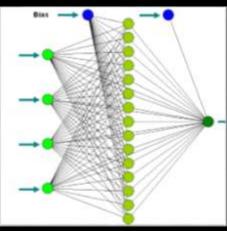












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Data Security and Privacy

**Robotics and Human Machine Interactions** 

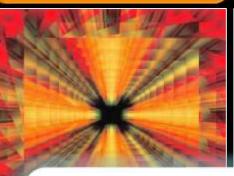
Artificial Intelligence and Decision Support

Identity, Ethics, Risk and Regulation

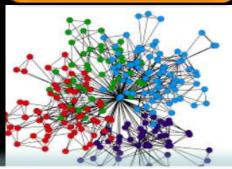
#### The Evolution of Data-Intensive Precision Medicine

Technology Convergence and Acceleration Mapping Geno-Phenotype Complexity Topology of Biological Information Networks

V6 Big Data





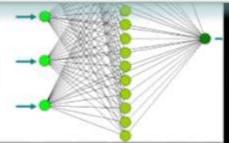




Slides Available @ http://casi.asu.edu/presentations







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Data Security and Privacy

**Robotics and Human Machine Interactions** 

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