



# The Accelerating Trajectory of The Life Sciences: Implications for Health, Industrial Innovation and National Security

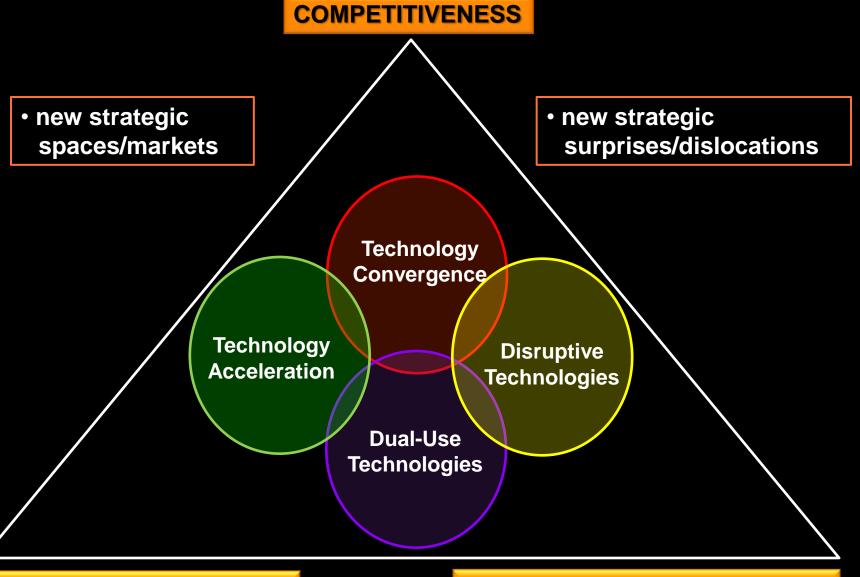
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Keynote Presentation to In-Q-Tel CEO Summit
The Portola Hotel and Monterey Conference Center
4 February 2015

### Slides available @ http://casi.asu.edu/



### The Strategic Environment for Technology



**New Business Models, Networks and Alliances** 

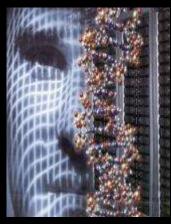
**Technology Diffusion and New Global Competitors** 

### Accelerating Technology and Escalating Complexity: Conceptual, Technological, Informational and Commercial

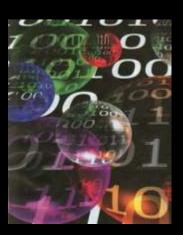
Biomedicine, Biotechnology, Synthetic Biology Ubiquitous
Sensing/
Devices &
Social Networks

Advanced Computing Mega-Metadata

Robotics and Advanced Autonomous Systems Neurosciences and Human-Machine Interactions



"Bio-Space"



"Connected Space"



"Analytics Space" and "Surveillance Space"



"Design Control Space"



"Cognitive Space"

New Patterns of Technology Fusion, Evolution and Adoption

New Knowledge Networks

New Participants New Markets and Business Models

#### Convergence and Acceleration in Advanced Technologies



space"

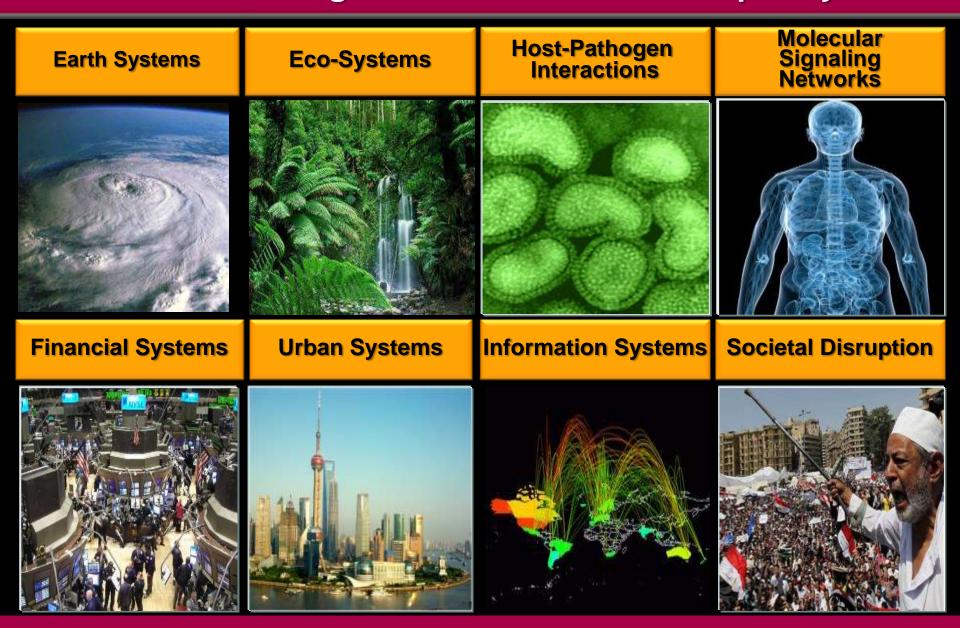




#### **Monitoring and Analysis of Complex Adaptive Systems**

- connectivities of complex networks (systems of systems)
- escalating complexity and decision making in the face of uncertainty

### The Ubiquity of Complex Systems: Understanding the Determinants of Complexity



## Complex Systems and New Challenges in National Security and Military Strategy

#### **Expanding Conflict Zones, Political Instabilities and Terrorism**











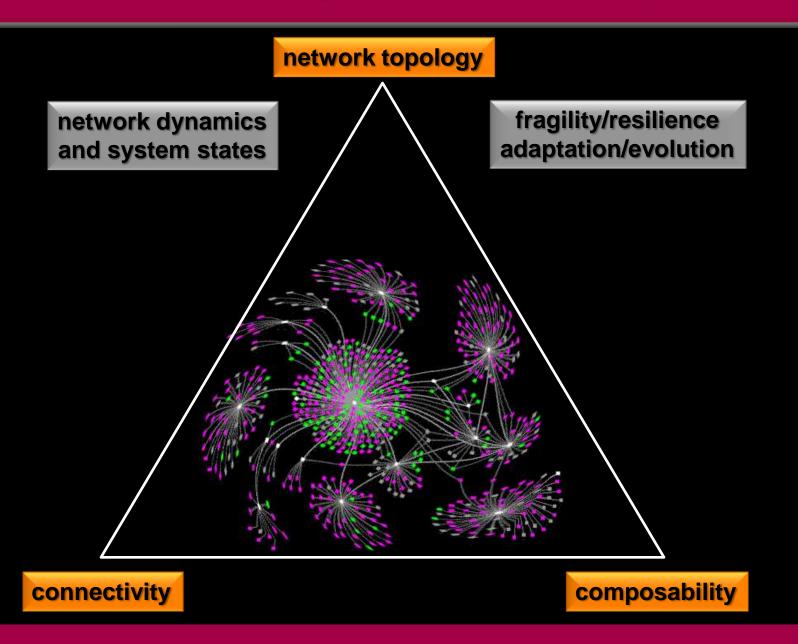


WMD Proliferation

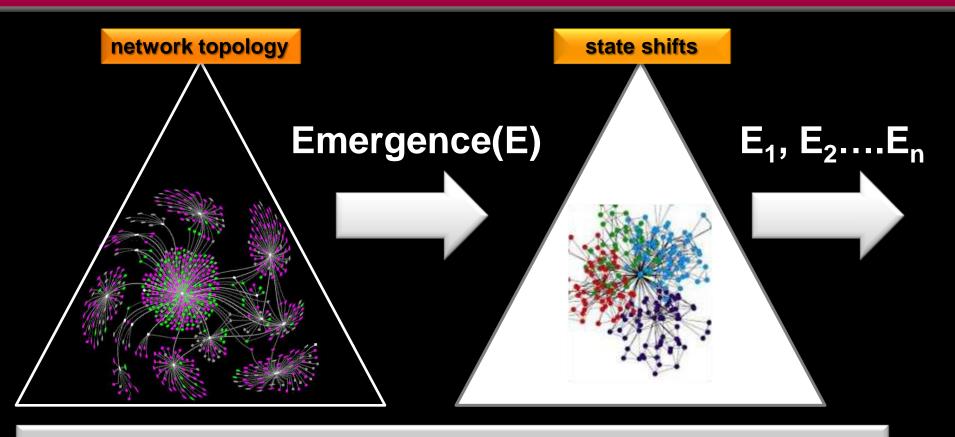
New Power Centers

**US Retrenchment: Geopolitical/Fiscal** 

### **Network Design in Complex Systems**



### Understanding State Shifts in Complex Adaptive Systems and Identification of Triggers of Emergence



- Black Swans
- dislocations
- tipping points
- irreversible cascades

- phase shifts
- perturbations
- inflection points
- critical thresholds
- bifurcations
- trigger points
- unintended consequences

## Convergence of Large Scale Biology with Engineering, Computing and Digital Technologies

**Precision Medicine** 

Outpacing Infectious Disease

Urbanization and Sustainable Ecosystems

Securing a Safer World

Synthetic Biology











#### **Shared Cross-Domain Technology Platforms**

**Unique Signatures of Biological System States** 

Multiplex Signature Detection Systems: Diagnostics, Sensors & Taggants

**Ubiquitous Sensing: Remote Monitoring of Network Architectures and Dynamics** 

Massive Data: Complex Signal Deconvolution, Data Formats & Visualization

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Common Themes: Multiplex Profiling, Integrated Analytics, Informed Decisions

Massive Data and New Analytics for Non-Linear Events: Intelligence at Ingestion

Cognitive Systems, Human-Machine Interactions and Artificial Intelligence

Managing Complexity: Decision-Making, Regulation and Public Policy

Ethical, Legal and Societal Implications of New Technologies

### Challenges and Ugly Realities Facing US Healthcare

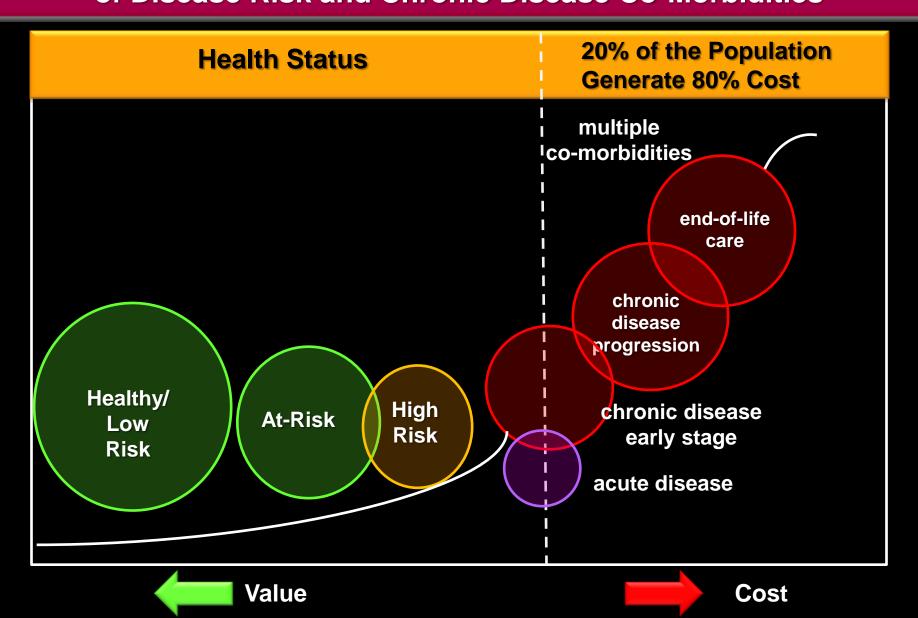
**Balancing Infinite Demand Versus Finite Resources** 

More Effective Management of Chronic Diseases in Aging Populations

Improving Clinical Outcomes at Lower Cost and the Wellness Premium

**Technology, Innovation and New Value Propositions** 

### The Economic, Social and Clinical Benefits of Proactive Mitigation of Disease Risk and Chronic Disease Co-Morbidities

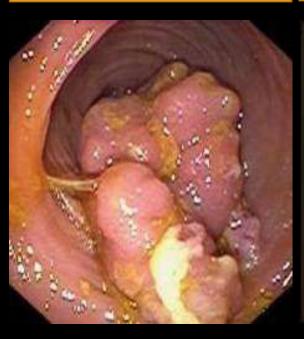


#### **Economic and Clinical Icebergs About to Collide with US Healthcare**

#### Cancer

#### **Neurodegeneration**

### **Chronic Disease, Frailty and QOL**







- 20-30% projected increase by 2025
- inadequate clinical and infrastructure resources
- economically unsustainable

- ageing well
- new products and services

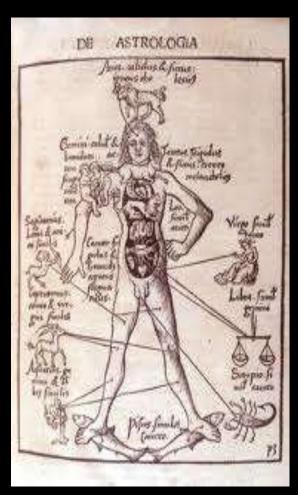
### **Extending Life: Balancing Time, Cost and Quality of Life**



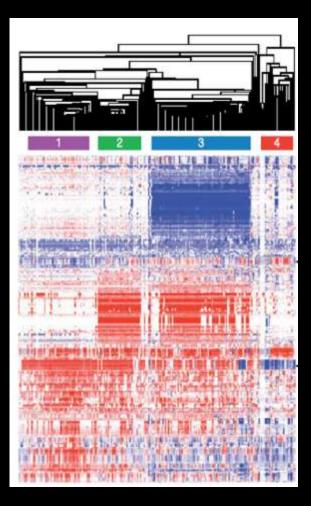




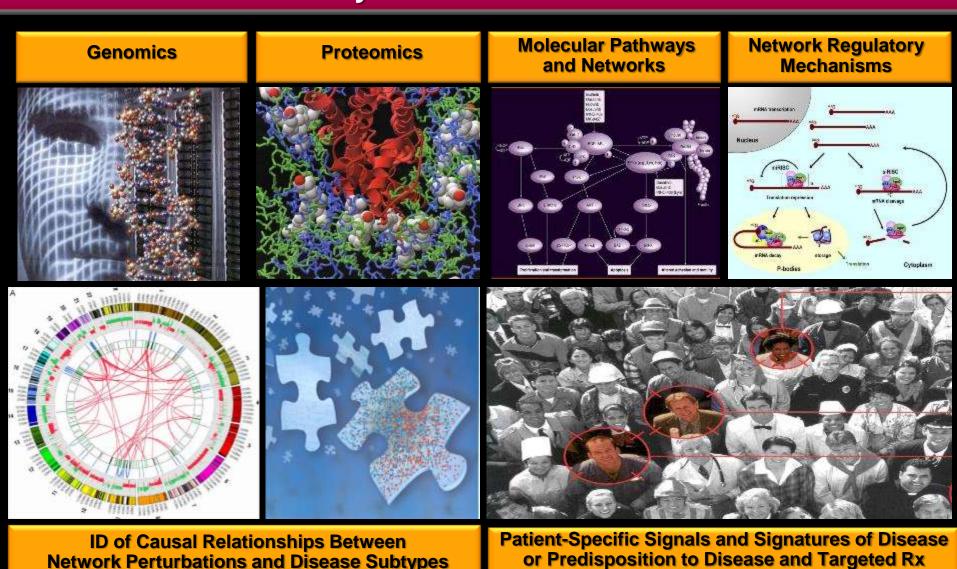
## Medical Progress: From Superstitions to Symptoms to Signatures







## Precision Medicine: Understanding Molecular Signaling (Information) Pathways in Health and Disease



## The Principal Forces Shaping Biomedical R&D and Healthcare Delivery

molecular diagnostics

sensors

device-based medicine

- remote health monitoring
- telemedicine

molecular (precision)
medicine

- panOmics profiling
- integrated analytics of biological networks

information-based healthcare

- m.health/e.health
- data- and evidence- based decisions and Rx selection

outcomes-based healthcare and sustainable health

new value propositions, new business models and services

#### Genome Sequencing and Precision Medicine

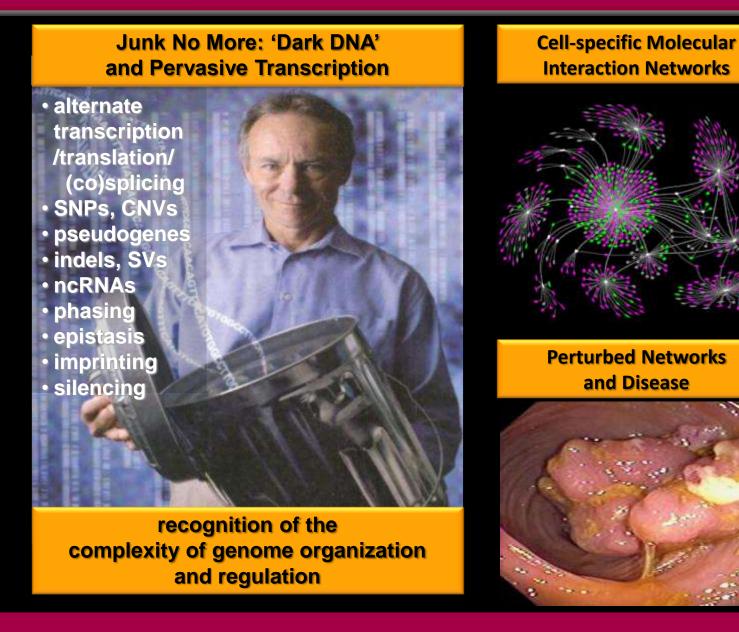




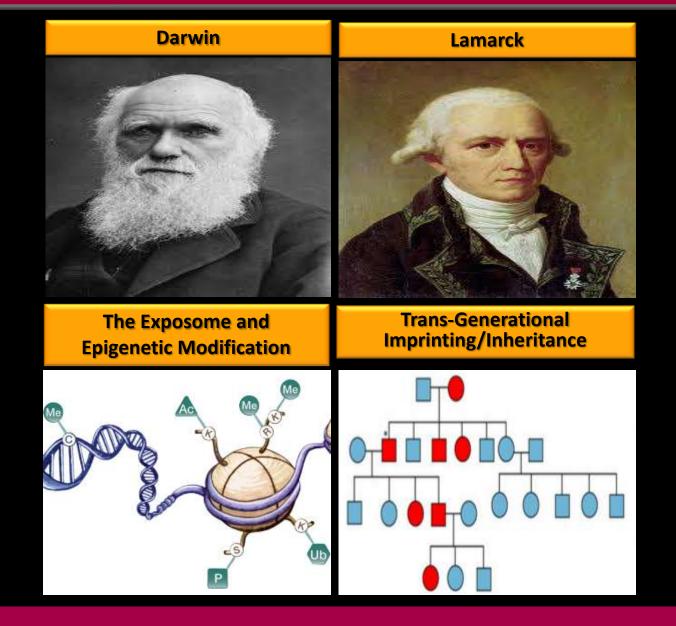


- Clinical Utility: Not If, but When and What
- Hype Is Always Followed by the Hard Work of Demonstrating Value

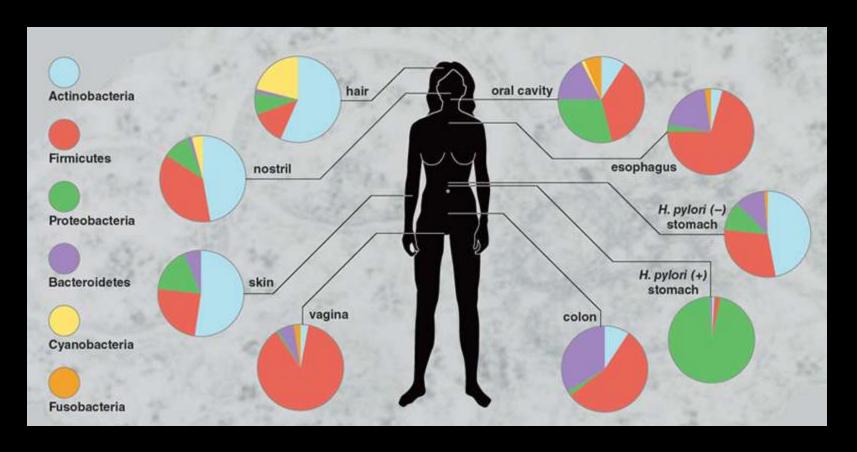
### Precision Medicine: Individual Variation, Genome Complexity and the Need for Systems-Based Approaches to Analyze Disease



## The Inheritance of Acquired Characteristics Epigenetics, Imprinting and Inter-generational Inheritance of Environmentally-Induced Genome Changes



### We Are Not Alone: Microbiome Metagenomics Mapping the Human Microbiome and Its Role in Health and Disease



From: R. Dorit (2014) Am. Sci. 102, 330

Variation of Microbial Species Across Anatomical Sites Within the Same Individual

The Changing 'Touch Points' in Healthcare Delivery

Sensors, Smart Devices, Social Media and New Distributed Channels for Remote Health Monitoring

**M4: Making Medicine More Mobile** 

### m.Health



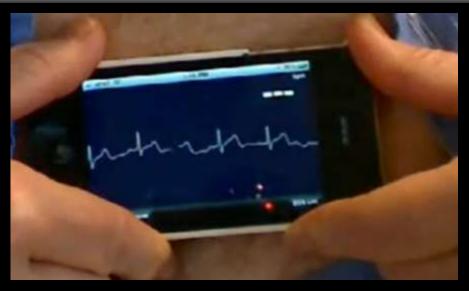


Real Time
Remote
Health
Monitoring
and
Chronic
Disease
Management

Lifestyle and Fitness

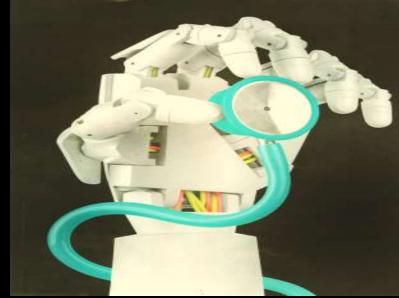


### **Telemedicine: Diagnosis, Monitoring and Education**

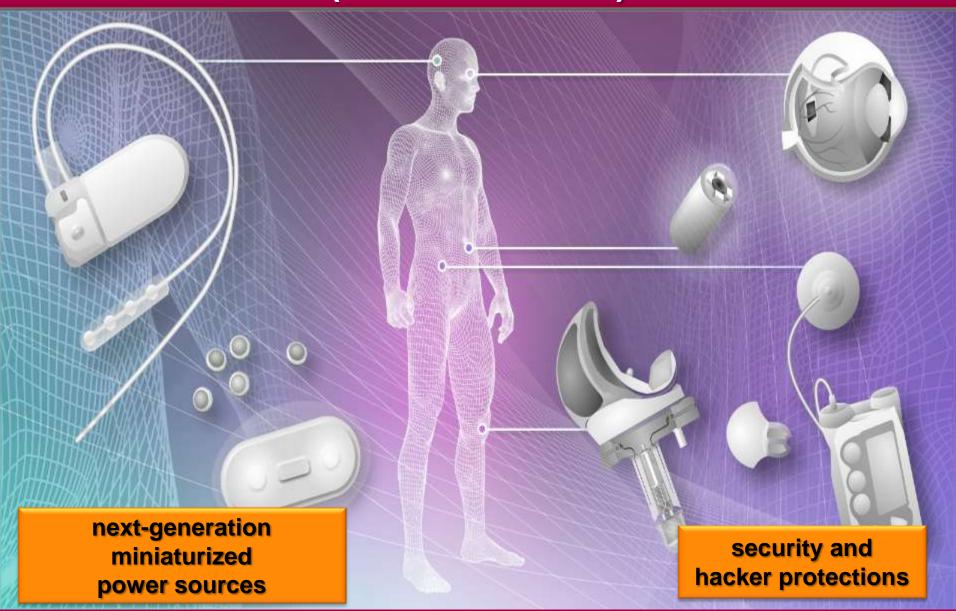




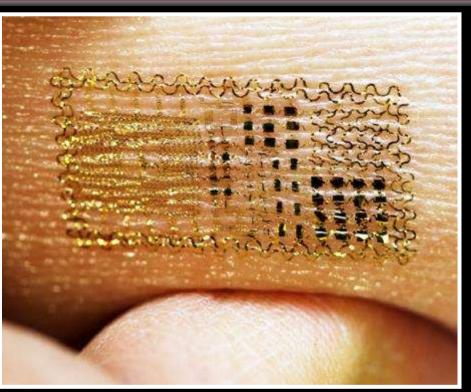


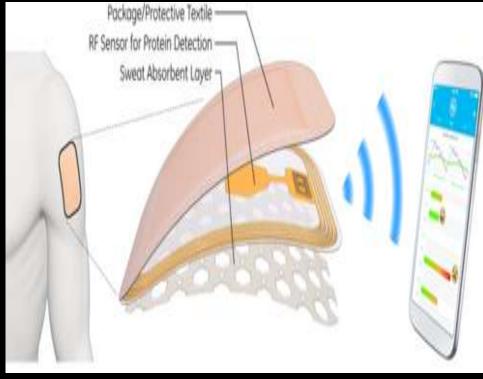


## Implantable Devices and Wireless Monitoring (and Modulation)



## "Lab-On-Me" and "Lab-Always-On" Dissolvable Electronics and Biodegradable Sensors





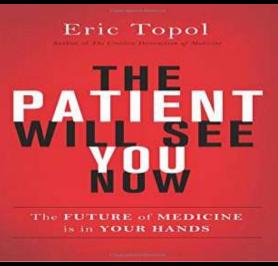
- dissolution of electronic circuits in physiological conditions
- construction from water-soluble, non-standard electronic materials with specific dissolution rates

### Retail Healthcare: New Services and Value-Based Shopping for Healthcare





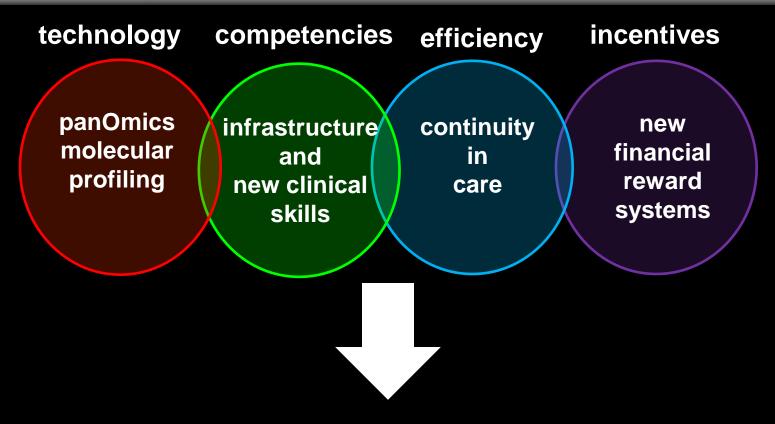




#### **Consumers and Digital Health**

- generational differences in receptivity
- increased personal responsibility for wellness and treatment compliance
  - economic carrots and sticks
  - pricing transparency and shopping for services
- e.health and m.health
  - real-time monitoring:
  - individuals become their own controls (delta)
  - passive versus active monitoring
- behavioral economics and new models for health engagement

## Leveraging the Potential of Precision Medicine Will Require Changes in the Organization and Proficiency of Healthcare Services



- earlier intervention to reduce/prevent disease impact
- seamless integration of healthcare data for real-time access and improved care decisions

# Biosecurity and Global Health: Understanding the Implications of Major Economic Disparities and Environmental Dislocations



### The Biosecurity Triad

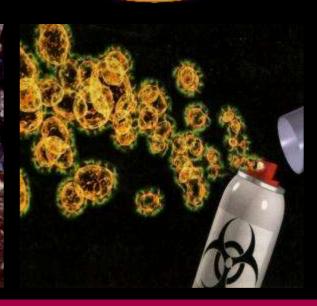
Infectious
Diseases
of
Natural
Origin

Urbanization,
Environmental
and
Ecological Impacts
on
Disease
Emergence

Bioterrorism,
New Dual-Use
Technologies
and
Expanded Threat
Spectrum







### Asleep at the Switch!

The Resurgence of Infectious Diseases

Major Gaps in US and Global Preparedness for a Major Pandemic (or Bioattack)

The Imperative to (Re)Build Robust Global Public Health Capabilities

The Critical Role of the Private Sector: New Incentives for Engagement

## Comfort and Complacency: The Enemies of Vigilance and Preparedness

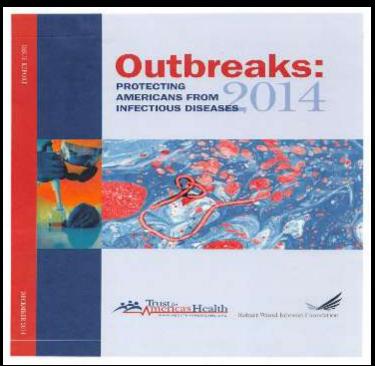


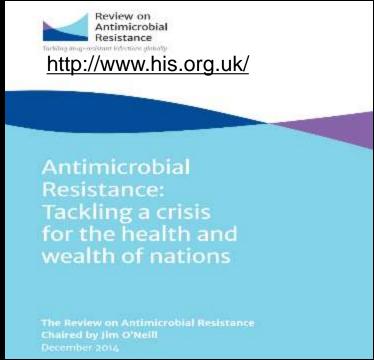






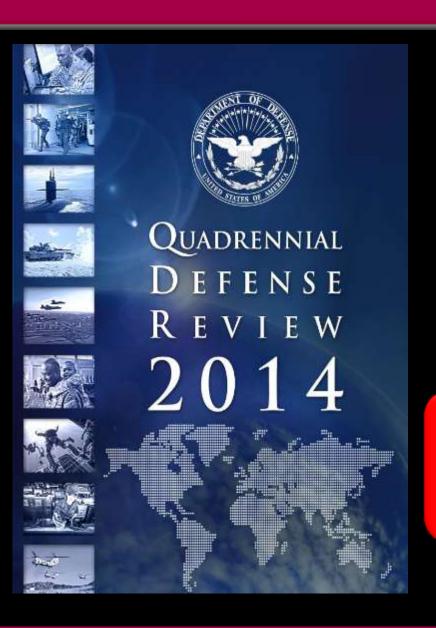
## The Microbial Antibiotic Resistance Problem How Quickly We Forget!





- Darwinian evolution at work
- an entirely predictable (and avoidable!) problem
- industry R&D retreat in late 80's due to lack of financial returns
- new incentives introduced but major gap/risk until 2020/2025
- in 2020/2025 restart new R&D cycle to combat next wave of resistant organisms emerging 2035/2045

#### The VUCA World



- Volatility
- Uncertainty
- Complexity
- Ambiguity

WHAT TO EXPECT,
WHEN NO ONE'S EXPECTING

## DOD Mobilization in Ebola Virus Epidemic: West Africa 2014

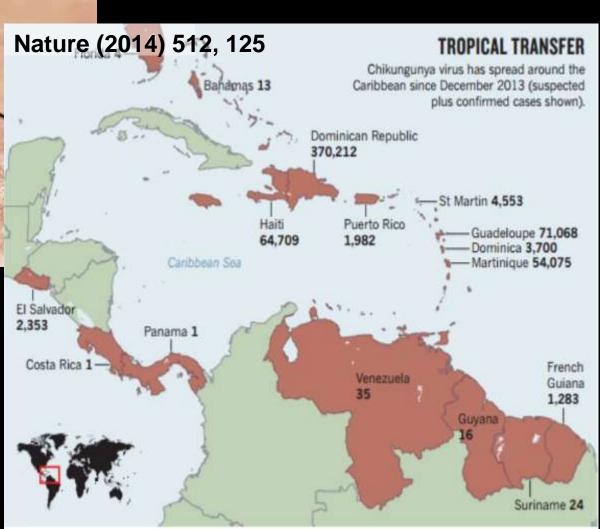








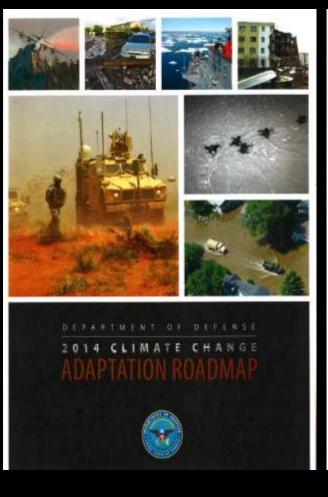


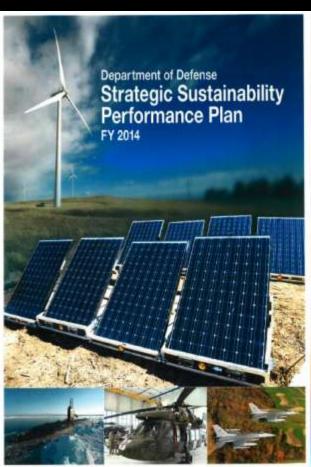


#### **DOD** and **Epidemic/Pandemic Disease**

Pandemic Risk in the Homeland

Posse Comitatus Applies But DOD as the Only USG Agency With the Logistical Resources to Integrate the Complexity of Responding to Major Bioincidents









#### Chief of Staff of the Army, Strategic Studies Group

Megacities Concept Team:

Colonel Marc Harris, Lieutenant Colonel Robert Dixon, Major Nicholas Melin, Command Sergeant Major Daniel Hendrex, Sergeant Major Richard Russo and Mr. Michael Balley

June 2014

#### Megacities and New Biosecurity Challenges





- urban population projected to triple by 2030 with 70% occurring in developing countries (DCs)
- most growth will occur in resource-poor, highly fragile and often politically unstable regions
- many situated in low-lying coastal areas and vulnerable to flooding and sea level changes

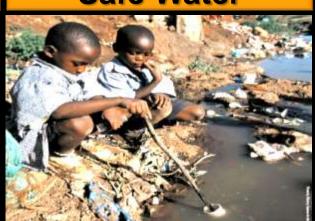
### The Global Public Health Challenge Posed by Rapid Urbanization in Developing Countries

High Disease Transmission

Lack of Safe Water

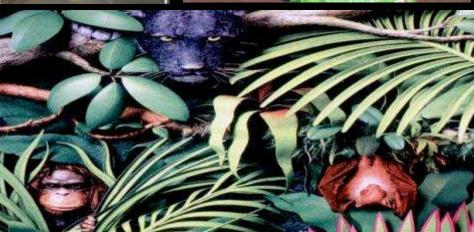
**Bush Meat Food Chain** 







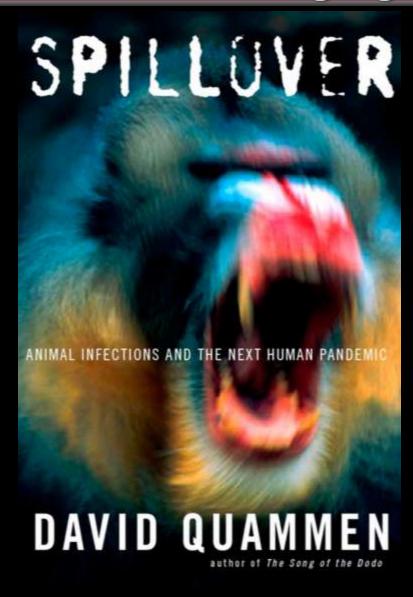




Major Deficits in Health Infrastructure

**Expanded Eco-niches and Increased Zoonotic Risks** 

# The Dominant Role of Zoonoses in Emerging Infectious Diseases





#### Pandemic Influenza: Still the Largest EID Threat?





- H1N1: high transmissibility low virulence/mortality
- H5N1: low transmissibility high virulence/mortality
- H5N1 x (H1N1) or (X): potential for devastating pandemic

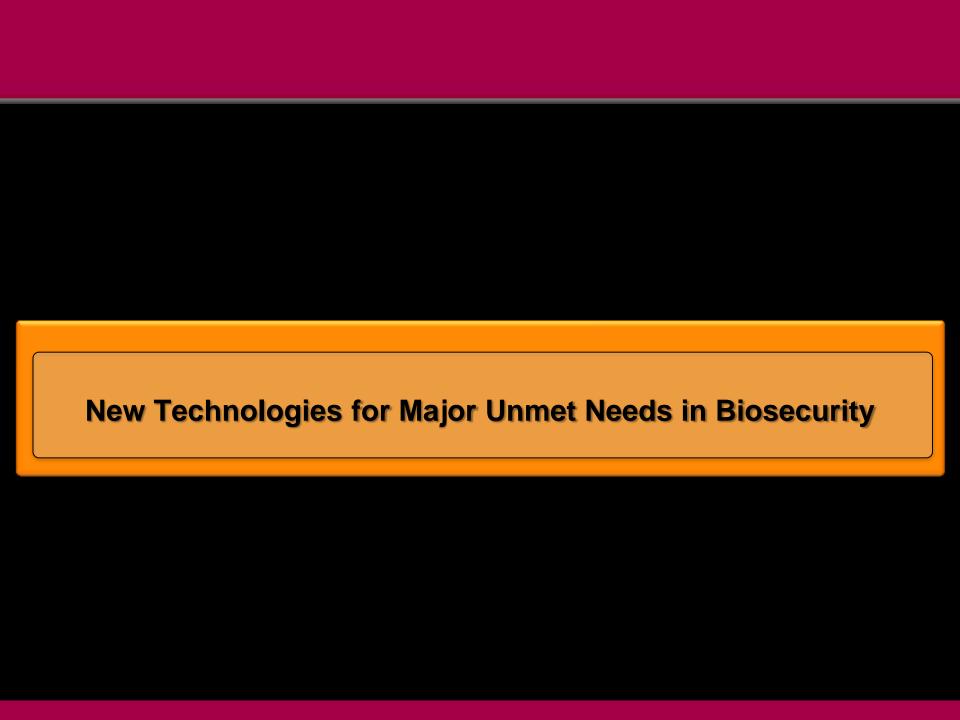
## Biosecurity Implications of the Rise of Intensive Agriculture in BRIC Countries



- disruption of global food chain via diversion of grain to animal feed
- new famine risks in DCs



- intensive agriculture and proximity of large avian and mammalian populations
- increased influenza zoonotic risk via bird-pighuman transmission chain

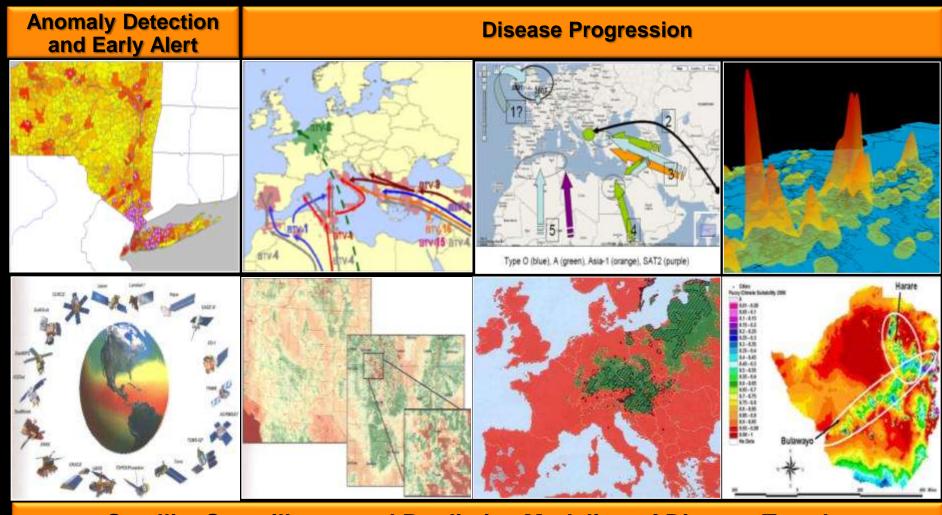


## Biosurveillance and Accurate Diagnosis: Early Detection Saves Lives!



- Ebola: West Africa
  - December 2013 to March 21 2014
  - IHE not declared until August 2014

## Geodemographic Information Systems: Mapping Disease Patterns and Modeling Trends



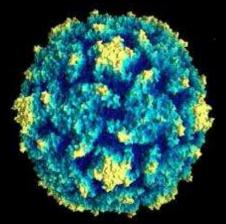
**Satellite Surveillance and Predictive Modeling of Disease Trends** 

### The Imperative for New Platforms for Global Biosurveillance and Rapid Point-of-Need Diagnostics

#### Molecular Signatures of New Classes of Threats......







..... to Detect and Defeat Novel Agents







in their earliest stages of emergence...

... in both rural and urban environments

# Notice the Resemblance? Hygiene and Quarantine as the Only Controls Absent Drugs or Vaccines

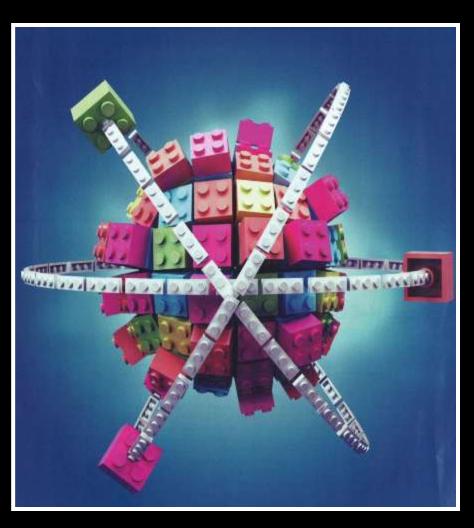
### **Bubonic Plague Physician 15th Century**

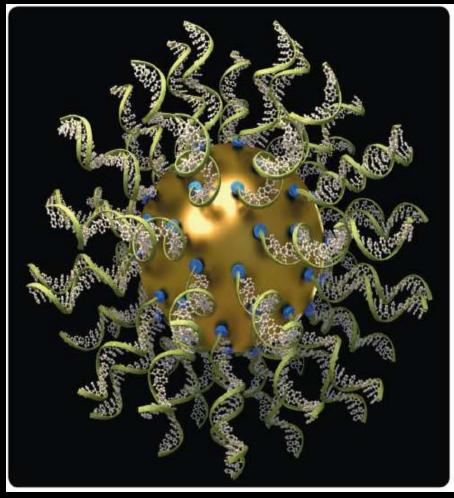
Ebola, Liberia 21<sup>st</sup> Century



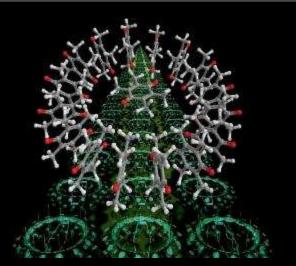


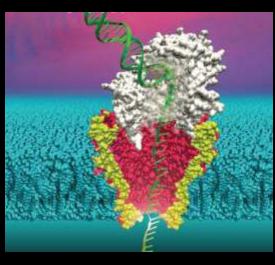
#### Molecular Lego: Ångstrom Level Design Controlled Assembly of Biomolecules and Design of Novel Sensors and Nanoscale Delivery Systems

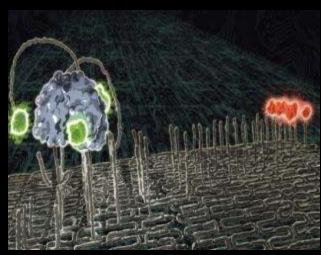




#### **Bio-Inspired Sensor Nets and Robotic Systems**







- miniaturized, automated and PON deployment
- self-assembly (sensors plus robot carriers)
- self-repair and extended duty cycle
- dynamic reconfiguration and swarms

#### **Responding to Agent-X**

Faster Mobilization for Development of Diagnostics and Counter-Measures for Pandemic/Panzootic Risks

#### **Acceleration of Counter-Measure Responses to "Agent-X"**

#### **Pandemics and Epizootics of Natural Origin**





**Bioweapons and Bioterrorism** 

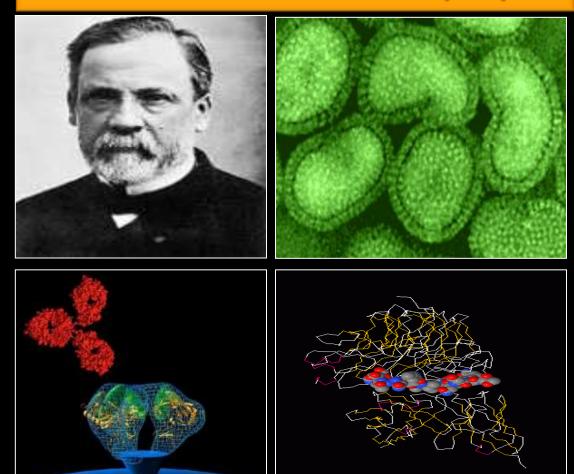
THE SOVIET
BIOLOGICAL
WEAPONS
PROGRAM

A HISTORY

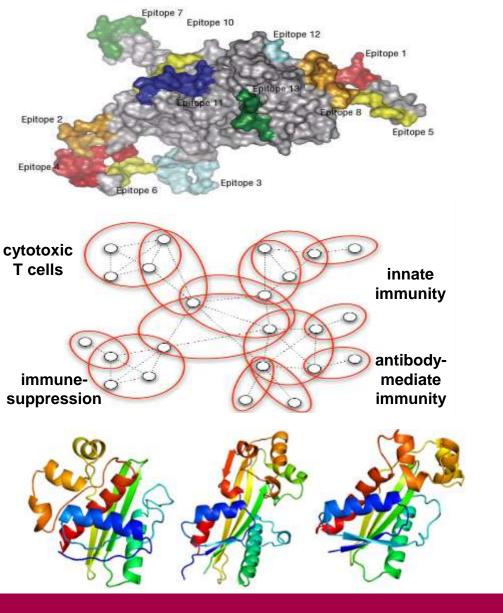


### Transforming Vaccine Technology for Rapid, Agile and Distributed Manufacturing

#### From Pasteur to Predicted Epitopes



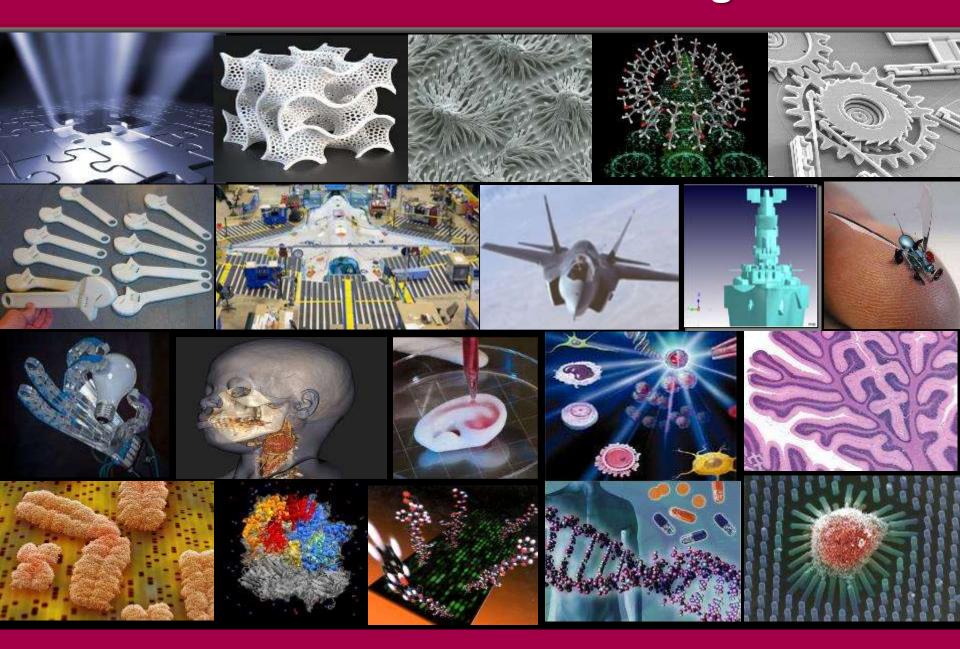
### Conversion of Vaccine Production from Protracted "Biological" Manufacturing to a Rapid "Synthetic" Chemical Process and New PON Capabilities



computational epitope mapping

- analytics to identify commonalities (rule sets) in the composition and structure of proteins that trigger different types of immune responses
- rapid profiling of 'Agent X' for 'epitope rule matching' and chemical synthesis of epitopes at point-of-need facilities

### **Advanced Manufacturing**

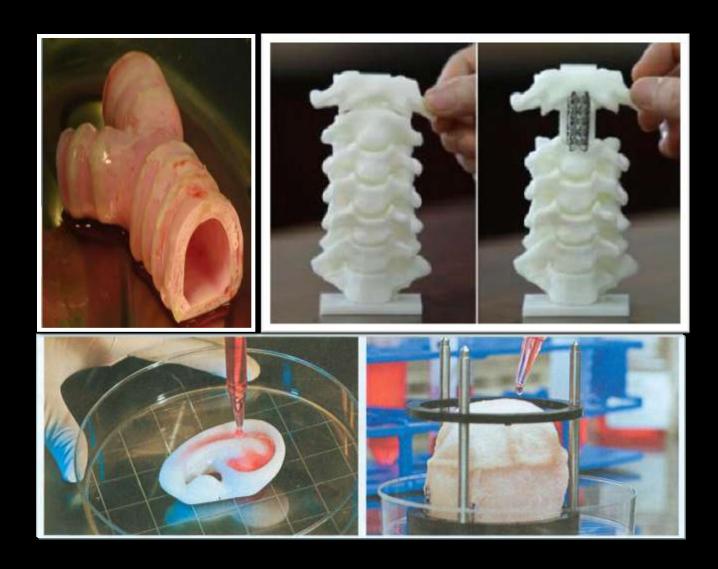


#### **Next Generation Bio-inspired Manufacturing Platforms**

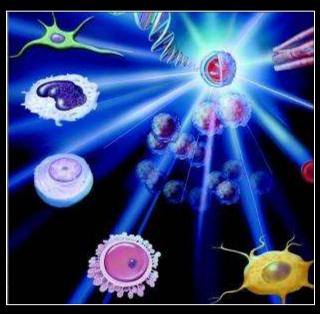
**Regenerative Medicine** 

**Synthetic Biology** 

### 3D Assembly of Biological Cells Seeded Onto/Into Synthetic Biomaterial "Scaffolds"



# Stem Cell Biology and Cell Therapies: Understanding the Genetic Programs Encoding the Development of Specialized Cell Types



 stem cell signatures and molecular pathways for directed differentiated cell fates



embryonic stem cells



reprogramming somatic cells

#### **Synthetic Biology**

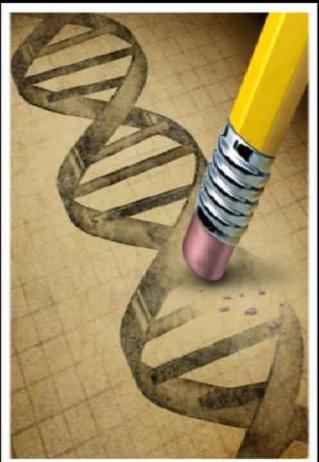
Understanding the Instruction Codes for the Assembly and Control of Complex Biological Systems

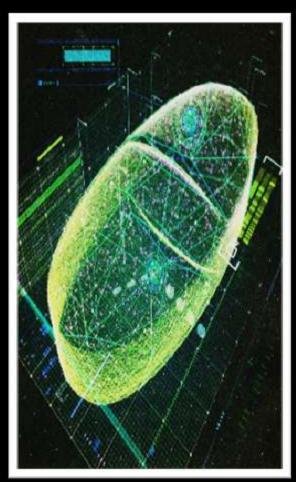
**Reading, Writing and Editing Genomes** 

'Exploring Biospace': Design and Assembly of Genomes and Biological Systems With No Known Evolutionary Predicate

### Emerging Technologies for Precision Modification of Genomes and Their Coding Instructions (Biological Software)







Cost-Effective Synthetic Production of DNA

**Genome Editing** 

Construction of 'Cellular Chassis' For Designed Genes

## Biological Diversity and Variation: "Endless Forms Most Beautiful"



### Biological Diversity and Variation: "Endless Forms Most Beautiful"

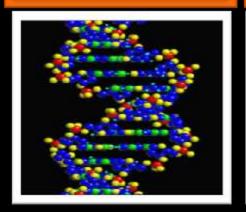


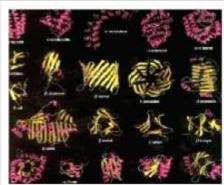
# Understanding Biological Organization: The Construction of Increasing Hierarchical Complexity and Mapping the Underlying Instructional Information

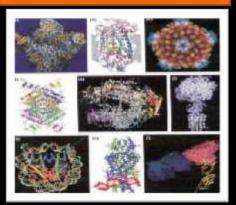
common genetic (digital) code in all life forms tool box of protein motifs for combinatorial assembly ("molecular lego")

assembly of structurally and functionally diverse proteins

protein interactions and nanoscale intracellular structures

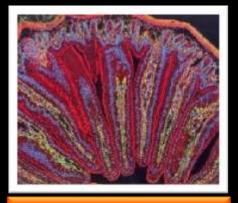
















molecular signaling networks

cells and tissues

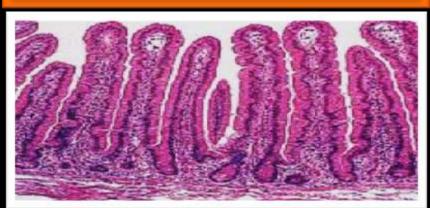
organs

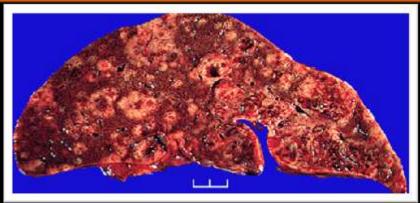
organism

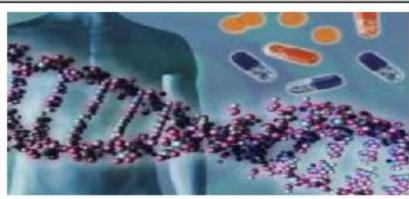
## Digital Biology and Molecular Medicine Mapping Instructional Coding Landscapes and Information Networks

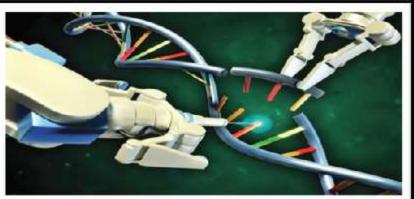
stable information signaling networks (health)











therapeutic modulation of perturbed networks

engineering novel gene constructs (code) to program biological information networks

#### Convergence

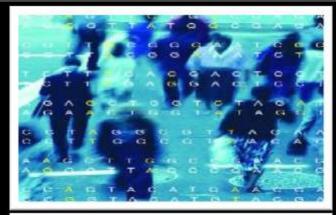
Natural
Digital
Software:
DNA

Artificial
Digital
Software:
Programming
Languages

3 – 4 x 10<sup>9</sup> years old

60 - 70 years old

### Digital Biology and Synthetic Biology "It from Bits"



'It' (hardware, wetware)



• 'Bits' (software)



- Reading and Writing Genomes
- Construction of Desired Network Topology and Control of Information Flow in Biological Signaling Networks

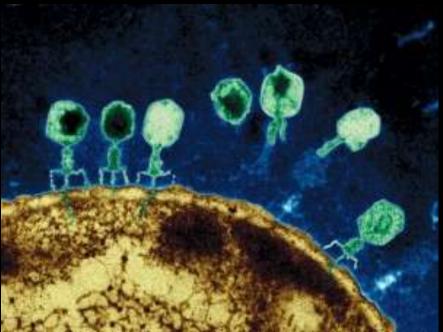
## Exploring Biospace The Power of Combinatorial Interactions and Molecular Assembly

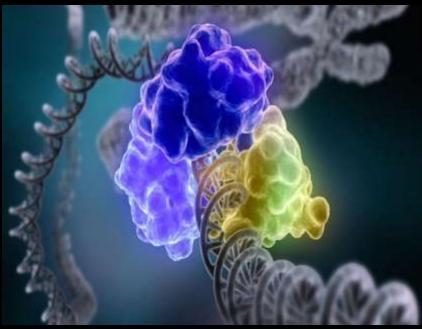
- estimated 22,000 human genes
- two genes cooperate to create a function =(22,000 x 21,999)/2 = 241,989,000 potential combinations
- 100 genes generate a complex function =10<sup>65794</sup> potential combinations
- number of theoretical possibilities for synthetic assembly (biospace) far exceed narrow molecular space sampled in evolutionary time to date

#### **Genome Editing**

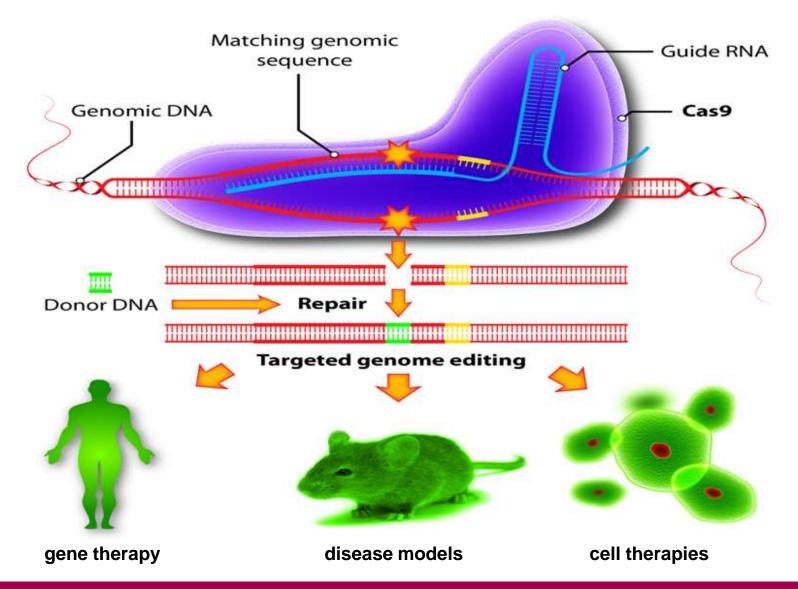
Microbial CRISPR Defense System Against Viruses

**CRISPR-Cas Guided Excision** and Insertion of New Genes





### CRISPR-Cas Guided Gene Excision/Insertion for Genome Modification



#### **Synthetic Biology**

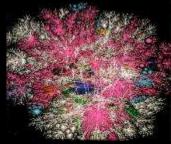
emerging technology with myriad applications across diverse industrial sectors

**Functional** Novel **Public** Healthcare **Agriculture** Foods **Materials** Health **Textiles Ubiquitous** Clean Bioenergy **Industrial** 'Green' Bioand **Sensors** Water **Enzymes** Mfg remediation **Biofuels** 

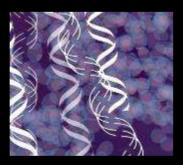
### The Expanded Dimension of the 'Bio' Threat Challenge Dual Use Research of Concern (DURC):



the 'bio' threat becomes more than just infectious agents



- potential targeted disruption of ANY body function
  - novel C and B threats



- synthetic biology
  - exploring biospace: designing new life forms

#### Big Biology and Biomedicine Meets Big Data

The Pending Zettabyte Era 1,000,000,000,000,000,000,000



Volume, Variety, Velocity, Veracity, Value

#### Sensor Webs and the Internet-of-Things (IoT)

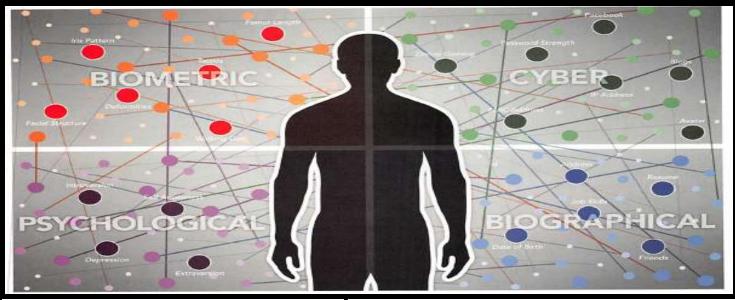


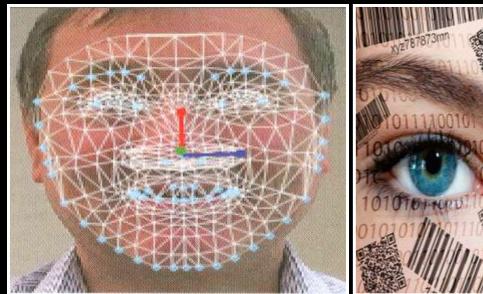
- pervasive/ubiquitous sensing of diverse environments/analytes
- critical features
  - sense-compute-actuate (SCA) loops
- next-generation features/traits
  - reconfiguration, repair and regeneration
  - intelligence and evolvability

#### Social Behavior Becomes 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 patterns reveal increasingly predictable behavior and individual risk patterns
- new opportunities in multiple business sectors
- broad utility in national security, intelligence and military operations
- new ethical and legal issues regarding privacy and data security

### Large Scale Integration of Diverse Data Streams for Situational Awareness of Health Status and Biosecurity Risks

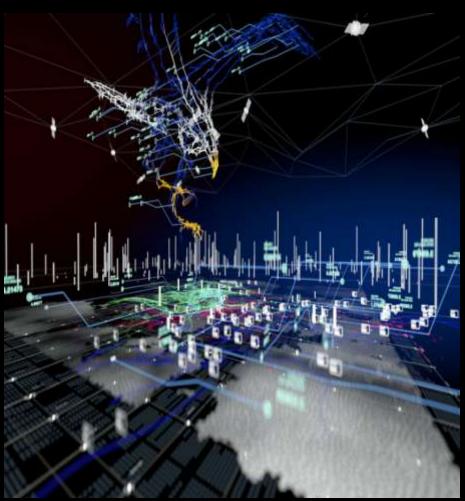






# Integration of Diverse Data Streams for Real-Time Situational Awareness and Preemptive Intervention/Awareness





**Healthcare** 

**Military Operations** 

### Interactive Interfaces and Customized Visualization Formats for Simulation, Education, Training and Decisions



# Brain: Machine Interface Technologies Direct Cognitive Control of External Devices

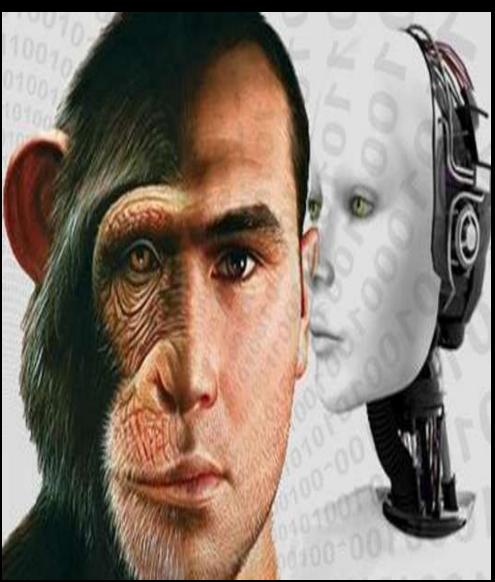






#### **Cognitive Constraints**





### The Pending Era of Cognitive Systems: Overcoming the "Bandwidth" Limits of Human Individuals



- limits to our expertise
- limits to our multi-dimensionality
- limits to our sensory systems
- limits to our experiences and perceptions
- limits to our objective decision-making

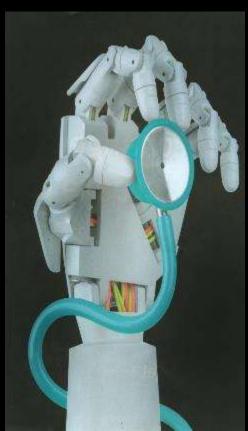
### Advances in Cognitive Neurosciences and New Patterns of Cognitive Processing



- optimize information representation (perception)
- neuroplasticity and selection of new cognitive mechanisms
- modulation of brain function to optimize comprehension

#### Transcending Human Cognitive Bandwidth: The Rise of Robotic Diagnostic Devices and Machine Intelligence for Decisions







Massive Computing Power and Analytic Parsing mega-meta data • open source data • personalized data

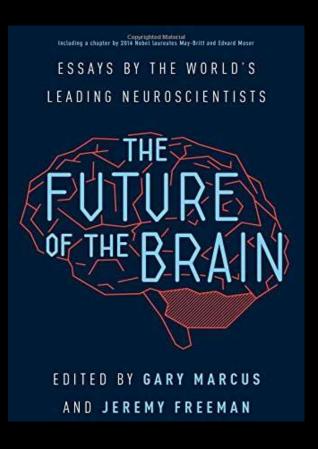
### Original Sin Updated? Artificial Intelligence and the Existential Expulsion of Mankind?

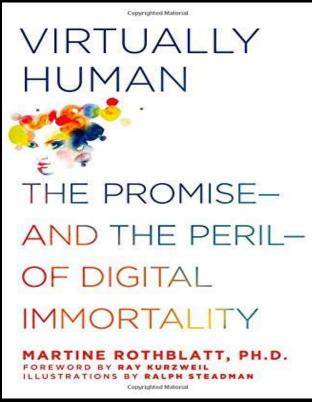


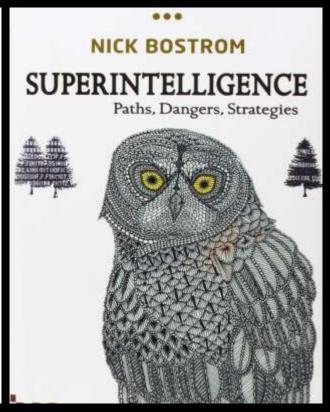
#### Debating the Dangers of Artificial Intelligence (AI)



### Artificial Intelligence and Deep Learning Why Wait for the Slow Brain to Catch Up With the Fast Machine





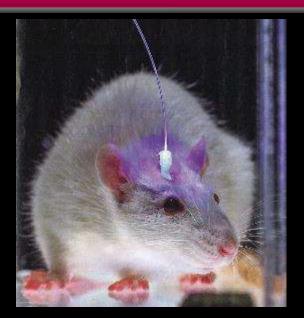


#### 3D Mapping of Brain Structure and CNS Network Functions





#### "Brain Net"



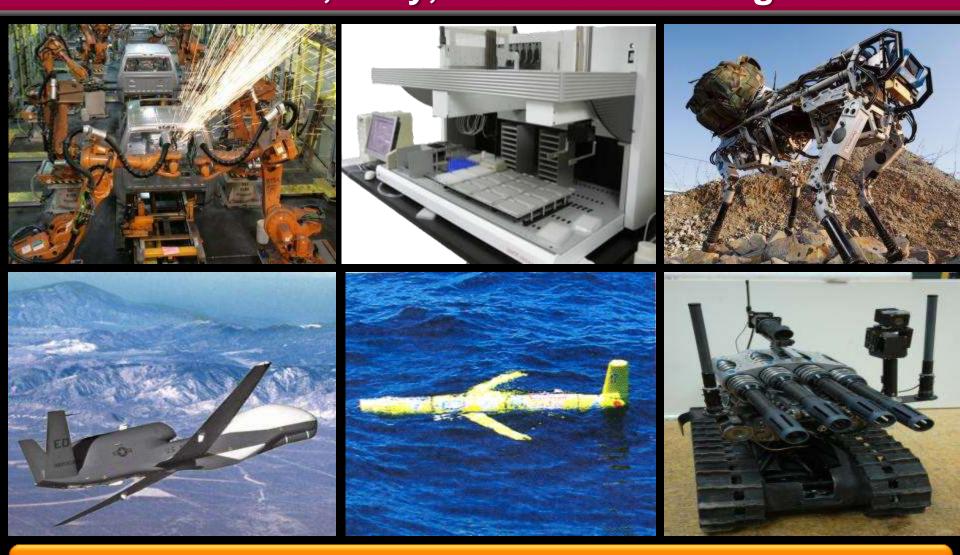


- first brain-to-brain link via remote transfer of encoded brain pattern to decoder animal and triggering of behavioral mimicry
- build inventory of codes to elicit specific behavior in target (decoder)
  - design of new control systems for robots
- legal and ethical implications of extension to elicited behavior (control, modulation) of humans

# Smarter Than The Average Mouse Engraftment and Colonization of Mouse Brain by Human Glial Cells

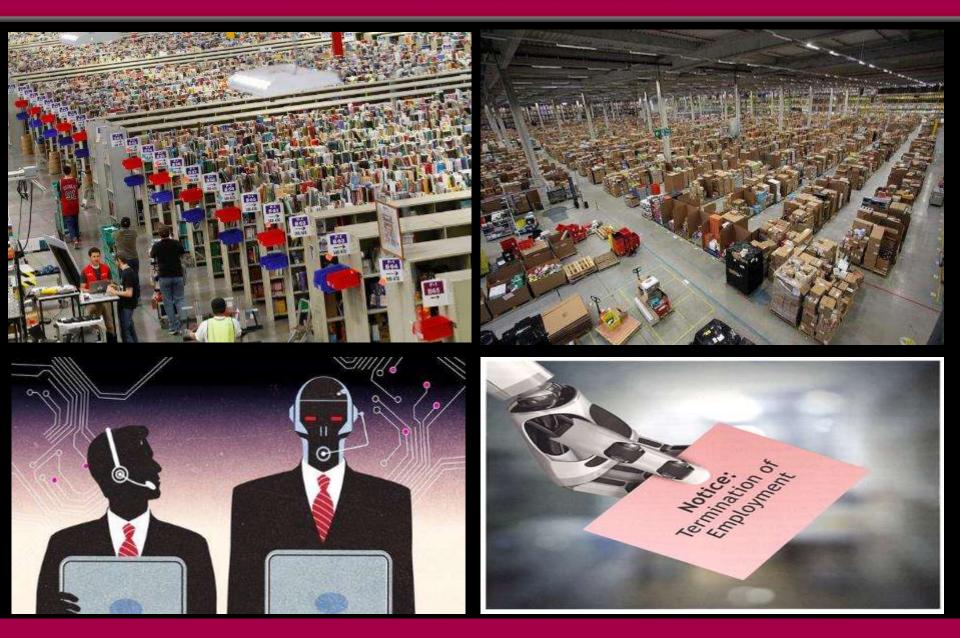
- M.S. Windrem et al. (2014) J. Neurosci. 34, 16153
- immature human glial progenitors engraft and myelinate hypomyelinated shiverer mice
- progressive colonization of host (mouse) glial cells
- human astrocytes x10-20 size of mouse astrocytes and carry x100 times as many tendrils
  - higher level of synaptic plasticity
- glial chimeric mice exhibited improved memory and learning tasks
- ethical barrier to similar transplant into non-human primates?

# Robotics 4D Jobs: Dull, Dirty, Detailed and Dangerous



**The Momentum for Transition to Autonomous Systems** 

### Automation, Robotics, Machine Intelligence and the Future Workforce



#### Living With Systems We Don't Understand

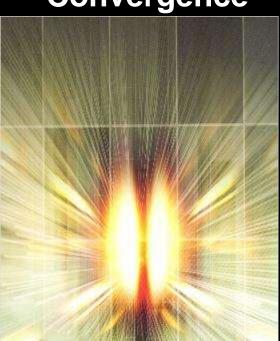
Escalating Complexities Imposed by Technology Convergence and Acceleration and Increased Connectivities of Diverse Global Networks

Reducing Decision Uncertainty and Risk in Increasingly Complex Systems of Systems

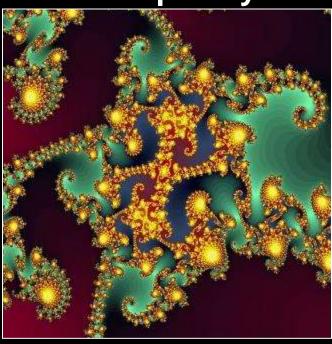
Understanding Complexity: A Dangerous Void in Public Policy and Governance of Advanced and Emerging Technologies

# Features of Complex Adaptive Systems: Highly Optimized Tolerance and Far-From Equilibrium States

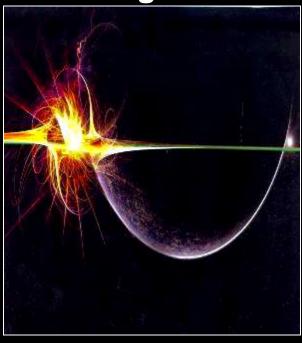
#### Convergence



Complexity



**Emergence** 



- novel interactions between previously distinct agents/ networks/systems
- system behavior cannot be predicated from properties of the component parts
- new patterns of convergence trigger new system with highly different and typically unpredicted and undesired features

### Complex Adaptive Systems: Increasing Design Degrees of Freedom (DDOF)



- increasing number of interacting elements/coding complexity
- graded levels of autonomous behavior (components, system)
- escalating challenge of predicting system behavior and state shifts

### Oversight and Decision Making Regarding Systems | We Don't Fully Understand

Development of Systems Too Complex to be Understood and Too Important to be Turned Off

### Pervasive Problems in Addressing Complexity in Contemporary Government and Industrial Innovation

- silos subvert solutions
  - expertise, turf, budgets, egos
  - protection of the status quo
- comfort and complacency dominates absent a perceived existential threat (national, corporate, academic tenure)
- timid incrementalism versus bold disruptive innovation
- the tyranny of Wall Street
  - quick returns and short-termism
- kicking the can down the road
  - political and media appeal of cosmetic, unidimensional quick fixes for problems that require multi-dimensional solutions and long term commitment

#### The "Too World" and The Retreat from Complexity

- "too hard"
- "too complex"
- "too long"
- "too risky"
- "too uncertain"
- "too unfair"

# Three Epochs in Harnessing Science and Technology for National Security

#### **Big Innovation**



- big bang
- big metal

- cold war existential threat
- unparalleled innovation and leadership by mil. labs/nat. labs/academia with shared goals
- catalyst for myriad new technology industries and US competitiveness

# Three Epochs in Harnessing Science and Technology for National Security

#### **Big Buyer**



- advanced computing
- artificial intelligence

- DOD/IC highly sophisticated users
- primary role as purchaser with majority of innovation in private sector
- strong DOD/IC relationships with private sector for timely, creative acquisition/customization

# Three Epochs in Harnessing Science and Technology for National Security

#### **Big Void**



 life sciences/ biomedicine

- growing USG gap in analysis of technology vectors and implications
- biosecurity largely ignored element in national security calculus
- translation is counter-cultural to biomedical USG agencies and academia
  - ROI/accountability for \$150 billion investment in biodefense since 9/11?



### Innovation Demands Boldness: Reconceptualize, Reset, Redesign and Recommit

- set aggressive metrics to meet grand challenges in education, health and environment sustainability
- more proactive analysis of new national security risks and intelligence requirements arising from technology acceleration and convergence in the life sciences
- accelerate new military capabilities for major shifts in CONOPs
  - urban warfare in unstable/anarchic environments
  - megacities, global health and humanitarian missions
  - robotics, autonomous systems and artificial intelligence

#### 10 C's Shaping the Trajectory of the Life Sciences

- convergence (technology)
- complexity (systems of systems, exponential exponentials, emergence)
- capacity (sustainability)
- cities (megacities and new risks)
- connectivity (massive networks)
- computing (data science, brain:machine interfaces)
- cognition (neuroscience, artificial intelligence)
- competition (new business models, markets, national security)
- consequences (benefit and risk)
- choices (decision making in era of escalating complexity)

#### **CREATIVITY AND COURAGE**

### Slides available @ http://casi.asu.edu/

