

Genomics, Demographics, Epidemics, Economics and Ethics: The Complex Forces Shaping Healthcare

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**First Constantin Spiegelfeld Lecture,
Research Center for Molecular Medicine
Austrian Academy of Sciences, Vienna
8 November 2010**

**Slides available @
www.casi.asu.edu**

Challenges for Healthcare Delivery Systems

Cost



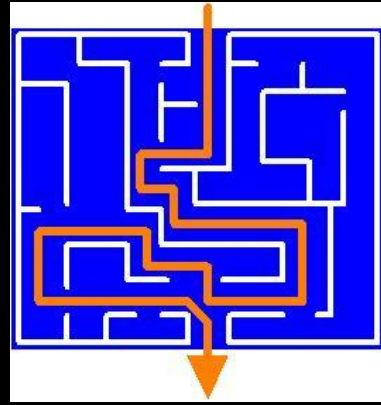
**Inefficient use
of Information**

Demographics



**Fragmented,
Compartmentalized
Services**

Chronic Diseases



**Protracted
Adoption of
Best Practices**

Life Style Disease



**Subsidiarity
and Policy
Complexity**

The Impact of Market Forces on Health Systems

A Review of Evidence in the
15 European Union Member States



European Health Management Association

European
Observatory
on Health Systems and Policies

ENSURING VALUE FOR MONEY IN HEALTH CARE

The role of health technology assessment
in the European Union

Corinna Sorenson, Michael Drummond,
Panos Kanavos

Observatory Studies Series N° 11

eu2006.fi

Health in All Policies

Prospects and potentials

Edited by
Timo Ståhl, Matthias Wismar, Eeva Ollila,
Eero Lahtinen & Kimmo Leppo



MINISTRY OF
SOCIAL AFFAIRS AND HEALTH
Finland



European
Observatory
on Health Systems and Policies

A EUROPEAN CAMPAIGN ON RISK ASSESSMENT



HEALTHY WORKPLACES
GOOD FOR YOU. GOOD FOR BUSINESS

<http://hw.osha.europa.eu>



European Agency
for Safety and Health
at Work



Healthy Workplaces



European
Observatory
on Health Systems and Policies

ASSURING THE QUALITY OF HEALTH CARE IN THE EUROPEAN UNION

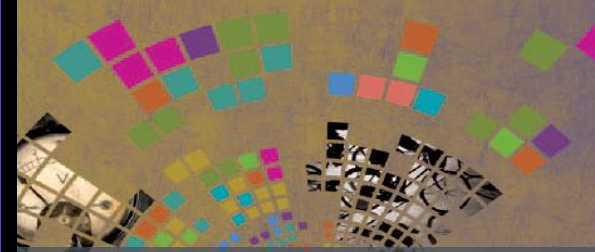
A case for action

Helena Legido-Quigley
Martin McKee
Ellen Nolte
Irene A Glinos

Observatory Studies Series N° 12



EUROPEAN COMMISSION / European
Research Area / Social sciences
& humanities

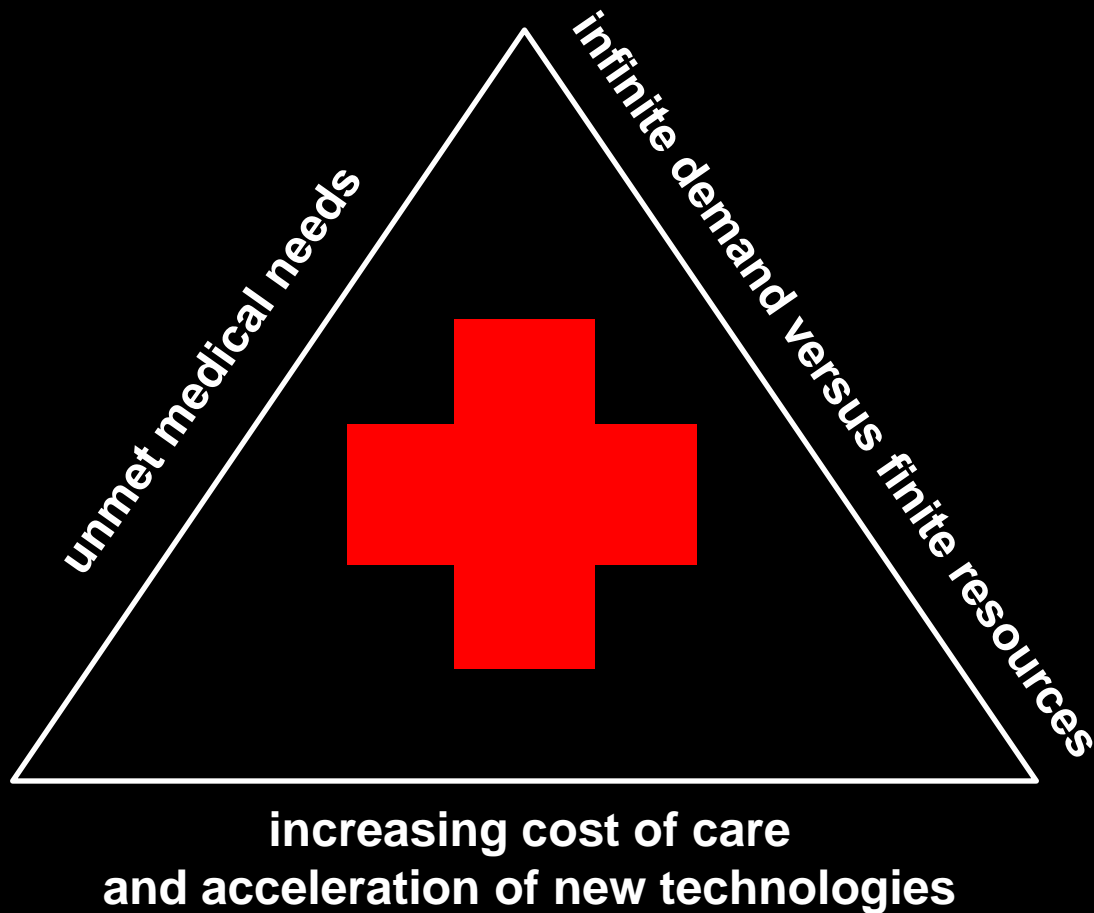


New societal challenges
for the European Union
New challenges for social sciences
and the humanities
Thinking across boundaries
Modernising European research



PRACTICAL INFORMATION

The Healthcare Challenge



The Healthcare Challenge

Outcomes

clinical, economic, quality-of-life

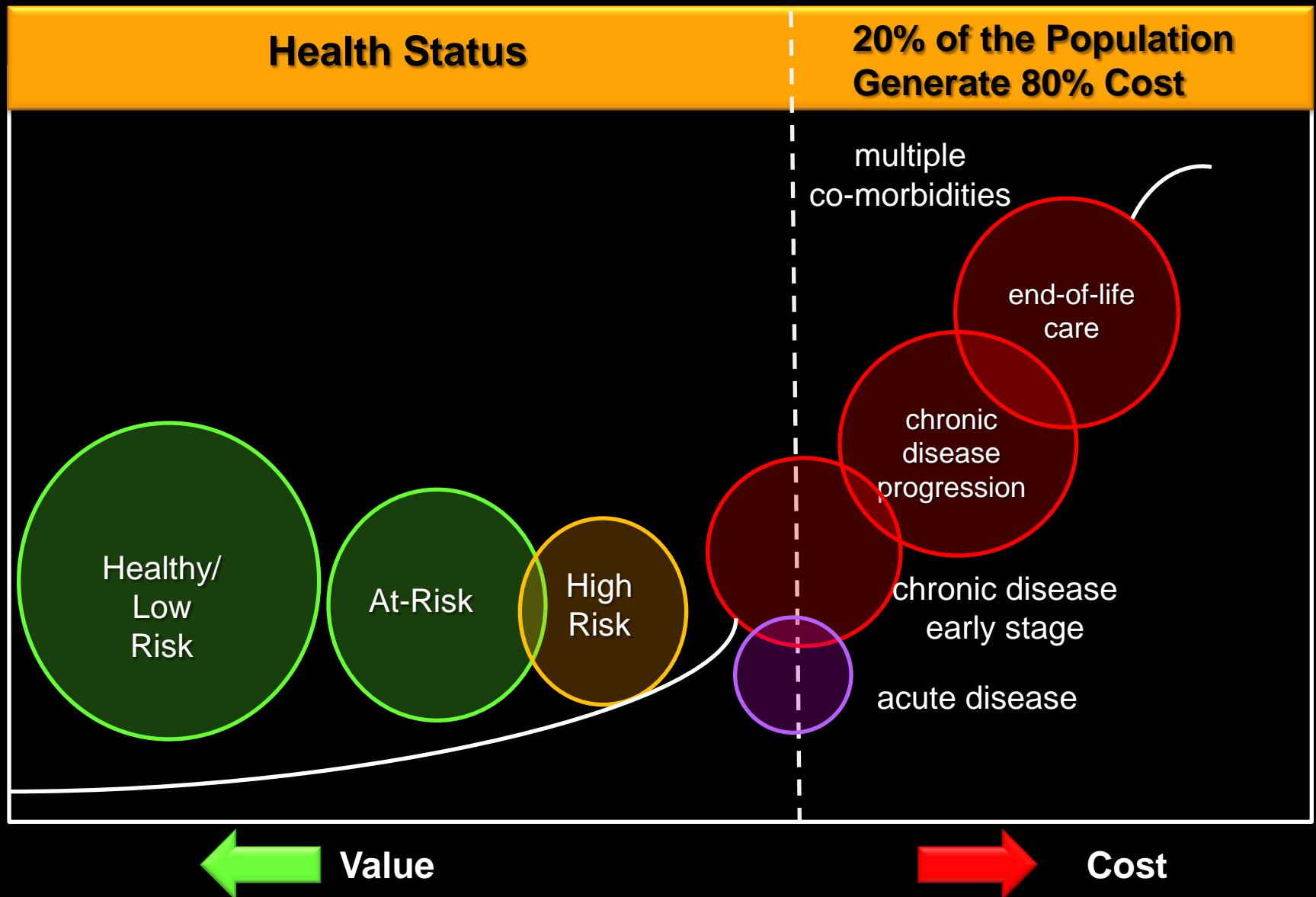


**Innovation
and
Cost of Care**

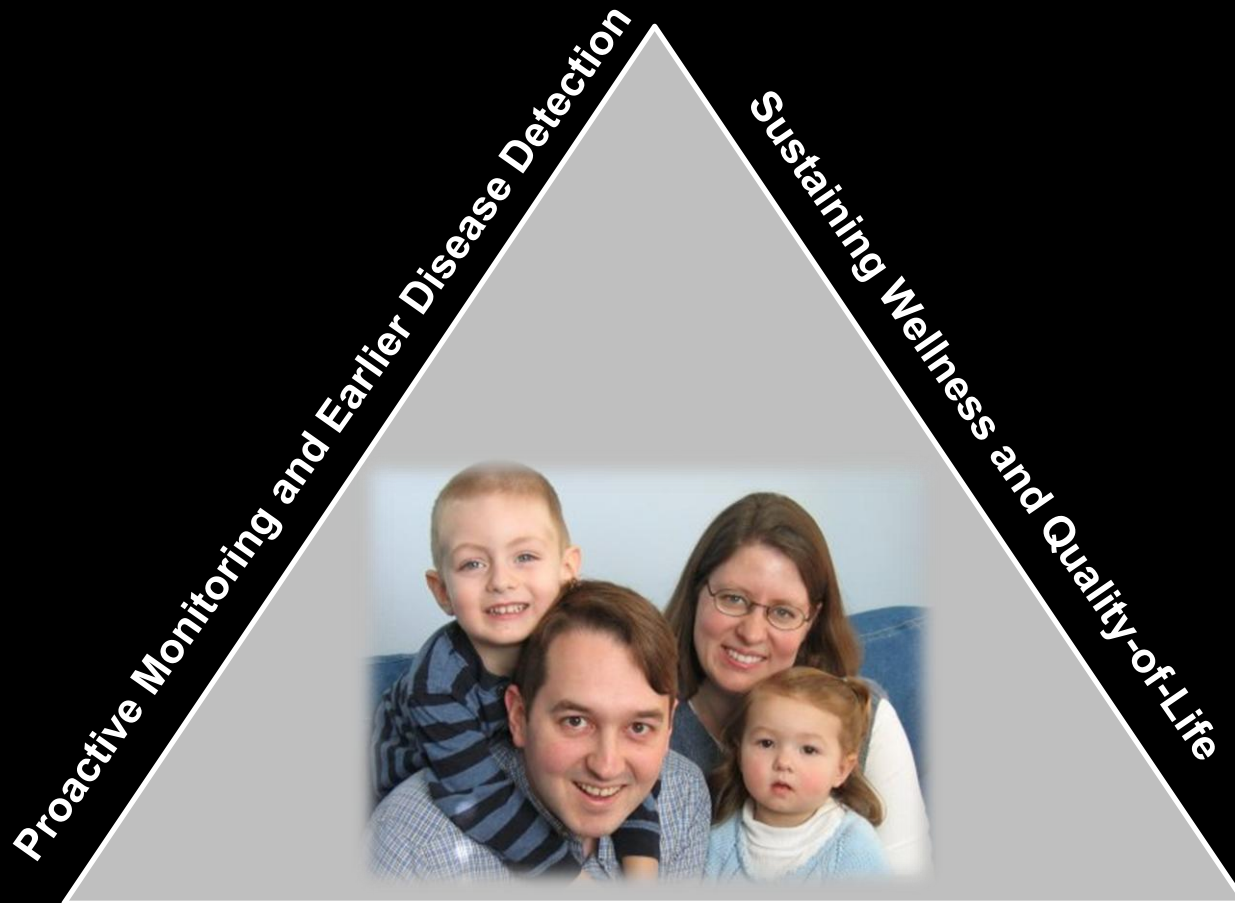
increasing cost of care
and impact of technology acceleration

**Access
to
Care**

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



Designing Delivery Systems to Sustain Health (Wellness) Versus Systems for Treating Illness



Shift from Diagnosis and Treatment of Ongoing Disease
to Disease Prediction and Prevention

The Intellectual Frontiers of Medicine

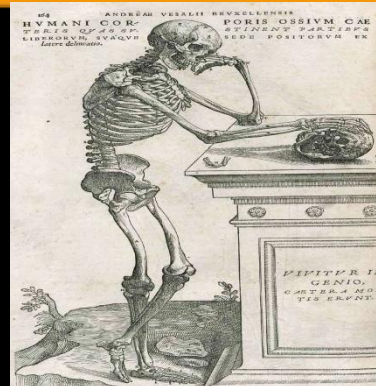
Antiquarian



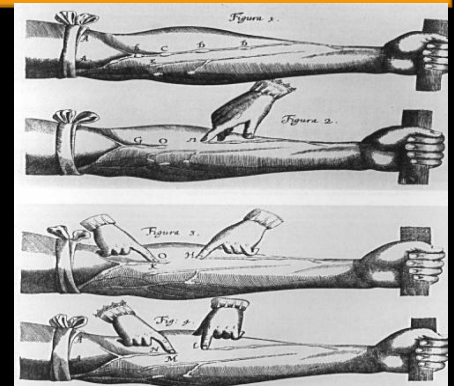
Medieval



Renaissance



Enlightenment



**Microbial
Pathogens**



**Cellular
Pathology**



**Molecular
Mechanisms**



**Mechanism
Based Rx**

The Intellectual Frontiers of Medicine

Anesthesia



Hygiene



Sanitation



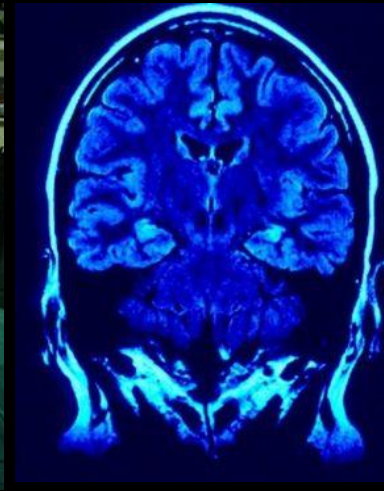
Vaccination



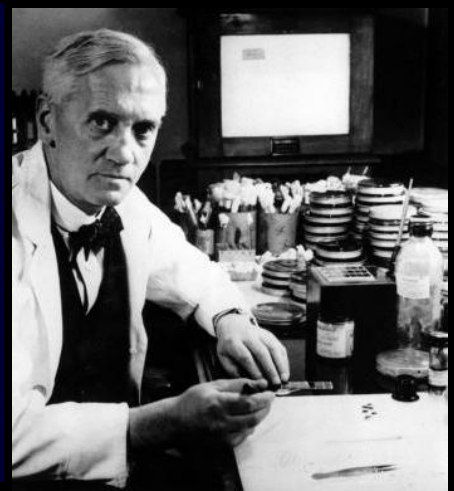
Nutrition



Surgery



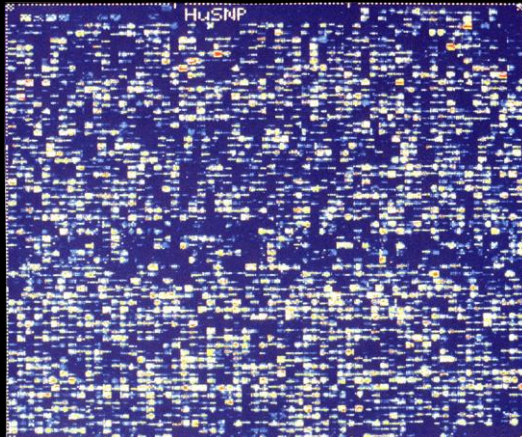
Imaging



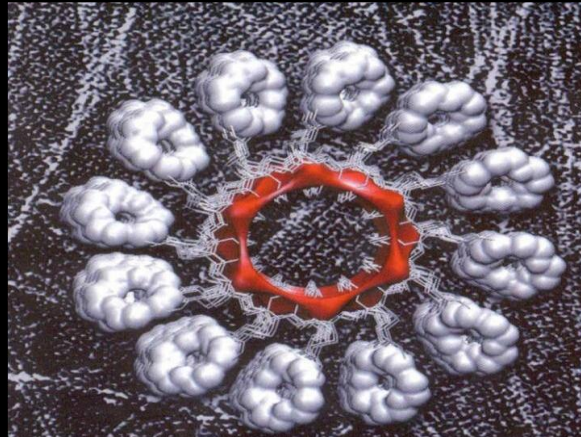
**Revolutionary
Rx**

Systems Biology: Mapping The Design of Complex, Adaptive Networks of Increasingly Higher Structural Order

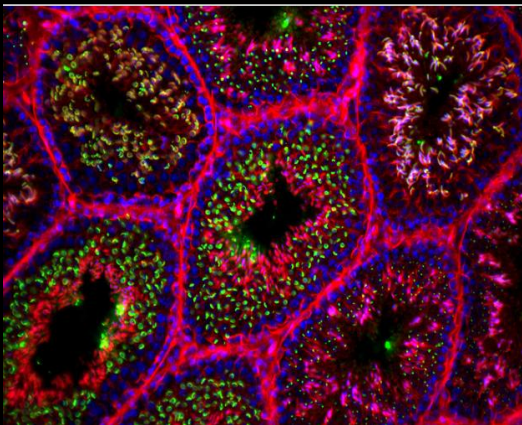
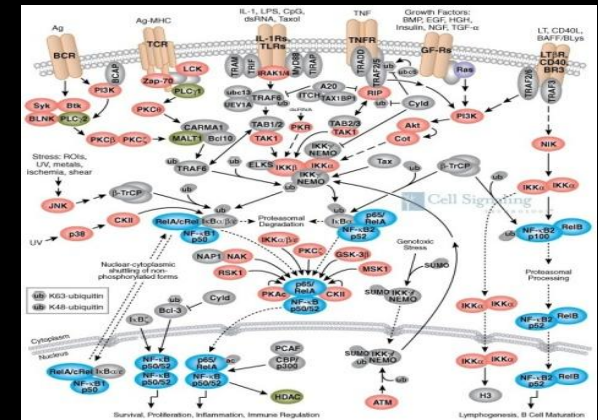
Gene Expression



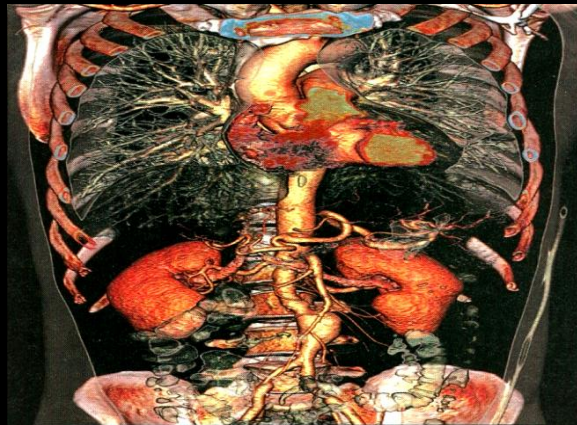
Protein Structure and Function



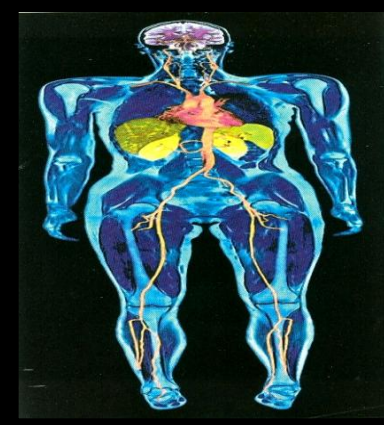
Molecular Pathways



Cells and Tissues



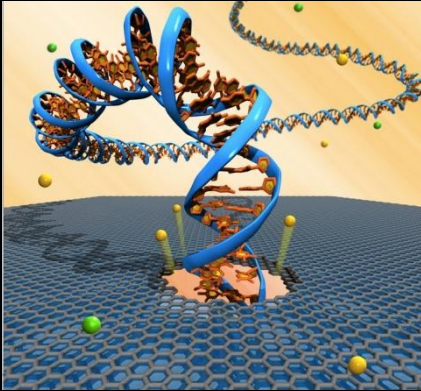
Organs and Homeostasis



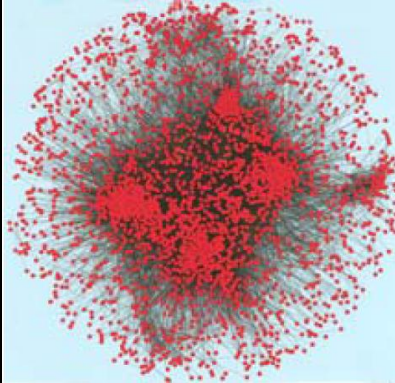
Whole Organism (System)

The Intellectual Frontiers of Medicine

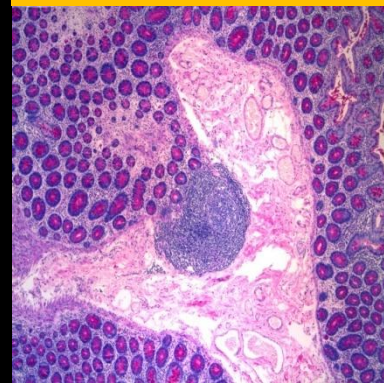
Biology as Information



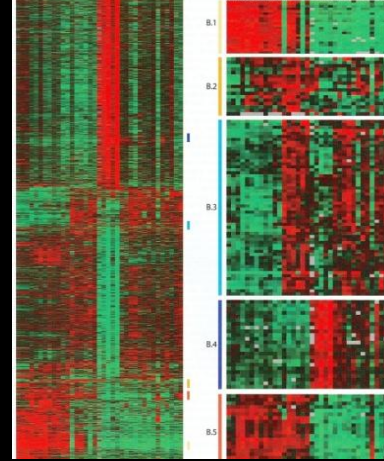
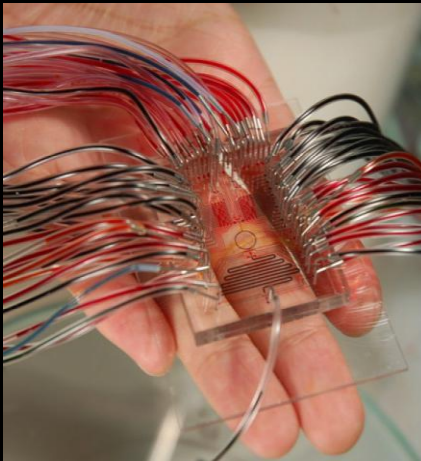
Pathways, Models Networks



Differentiation of Multiple Cell Types



Systems Biology



Analytical Technologies (Platforms)

Integrated Analytical Technologies

Dysregulation (disease)

Massive Data Analysis

GENOMFORSCHUNG IN ÖSTERREICH

Forschen für Gesundheit

Die Genomik untersucht die Erbanlagen des Menschen, von wissenschaftlich und wirtschaftlich bedeutsamen Tieren, Pflanzen und Mikroorganismen.

Wählen Sie ein Thema

FÖRDERN

Das Österreichische
Genomforschungsprogramm

AKTUELL

21.10.2010
PhD Award

Das Programm →

- Programmmanagement
- Förderungen
- Technologietransfer
- International
- Timeline

GEN-AU III



Dritte Phase von GEN-AU gestartet

Den Startschuss gaben Minister Hahn, Henrietta Egerth (FFG) und Giulio Superti-Furga (CeMM) bei einem Pressegespräch.

GENOMFORSCHUNG IN ÖSTERREICH



Was ist GEN-AU?

Genomforschung ist eine Schlüsseltechnologie. GEN-AU fördert und vernetzt Forschung für Gesundheit in Österreich.

FORSCHEN

Geförderte Projekte 2001-2006

AKTUELL

08.10.2010

**Call For Entries -
Science, Art & Film
Festival zur
Synthetischen
Biologie**

Die Projekte →

- Aktuelle Projekte
- Abgeschlossene Projekte
- Institutionen
- Personen
- Publikationen

PORTRÄTSERIE PROJEKTLITER



Wie bitte? Auch Pflanzen haben Stress?

Ein Interview mit GEN-AU Projektleiter und Pflanzenforscher Wolfram Weckwerth

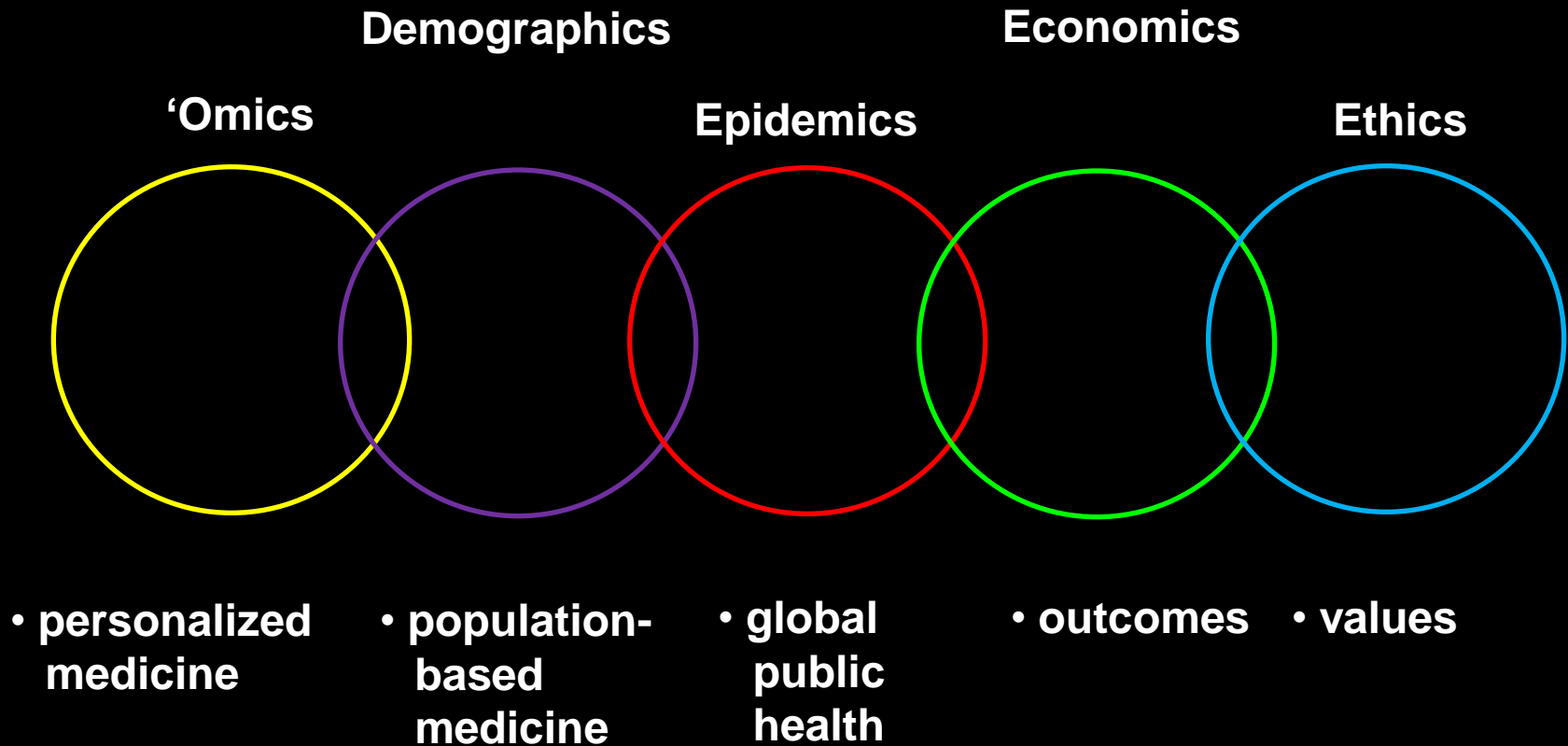
PORTRÄTSERIE PROJEKTLITER



Vakzinologie ist kein Penny-Markt

Die Impfstoffforscherin Eszter Nágy im Gespräch mit Bert Ehgartner

The Complex Inter-Relationships Shaping the Future of Healthcare

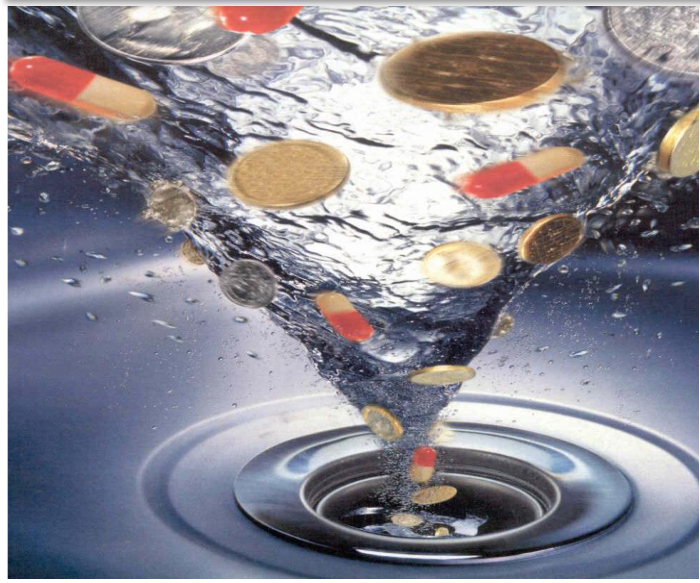


**The Molecular Profiling of Human Diseases:
Biomarkers, Biosignatures as the Foundation for
Accurate Diagnosis and Rational Treatment Decisions**

The Waste and Risk of Empirical Rx: Ignoring The Obvious in Clinical Practice

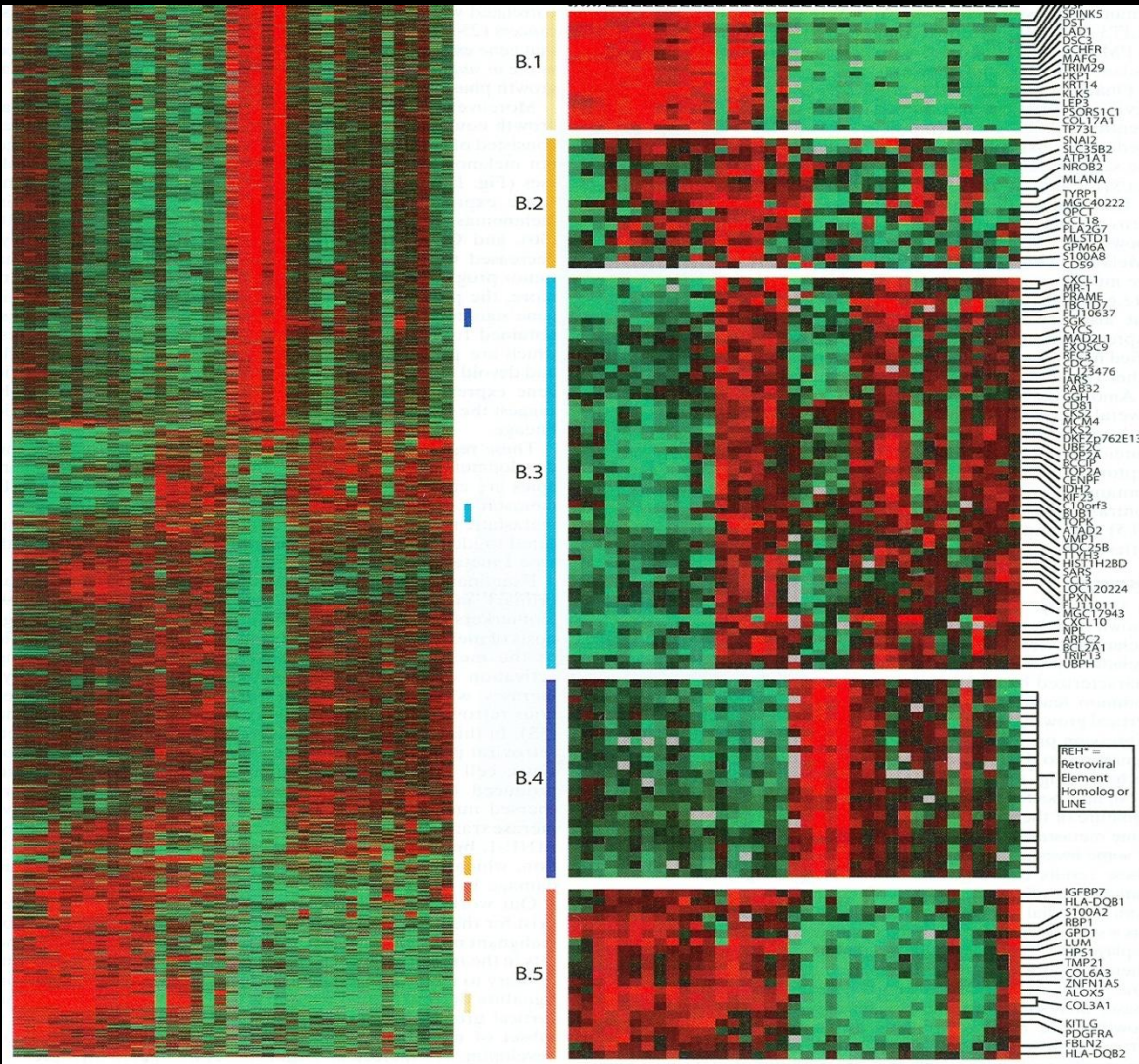


- diseases are not uniform
- patients are not uniform
- a “one-size fits all” Rx approach cannot continue



- inefficiency and waste of empirical Rx
- cost of futile therapy
- medical error and adverse events (AEs)

Disease Subtyping: Next-Generation Molecular Diagnostics (MDx) and A New Molecular Taxonomy of Disease



MDx Platforms

- massive parallelism
- miniaturization
- automation
- rapid
- POC

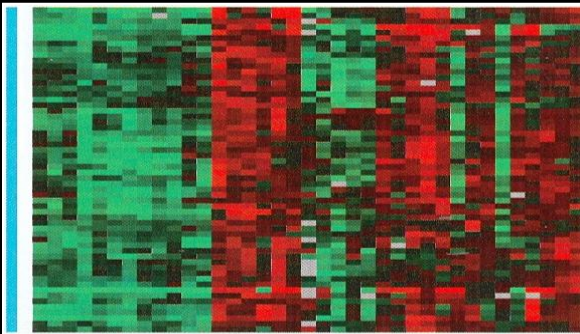
**RIGHT Rx
for
RIGHT DISEASE
SUBTYPE**

Molecular Diagnostics (MDx)

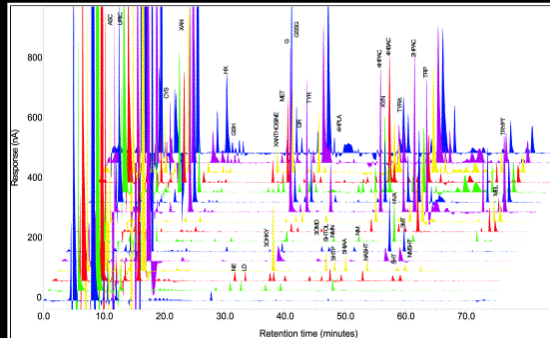
The Convergence of Molecular Biology, Engineering and Computing

Complex Biosignature Profiling

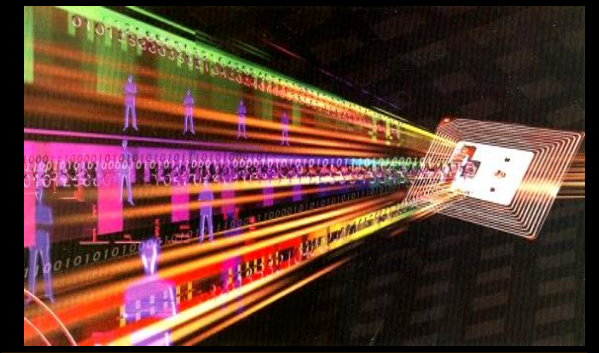
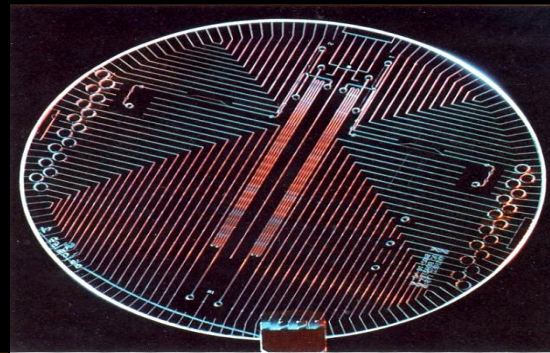
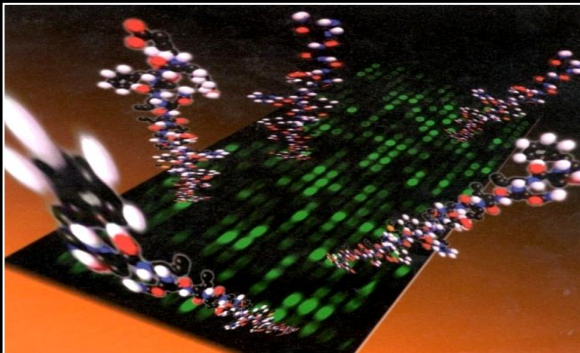
genomics



proteomics



immunosignatures



Signature Detection, Deconvolution and Multivariate Analysis

**automated,
high throughput
multiplex assays**

novel test formats and devices for point-of-care (POC)

**new algorithms
for complex
signal/deconvolution**

Molecular Diagnostics (MDx)

The Convergence of Molecular Biology, Engineering and Computing

Complex Biosignature Profiling

genomics

proteomics

immunosignatures



PROFILE



SENSE



ACT

Signature Detection, Deconvolution and Multivariate Analysis

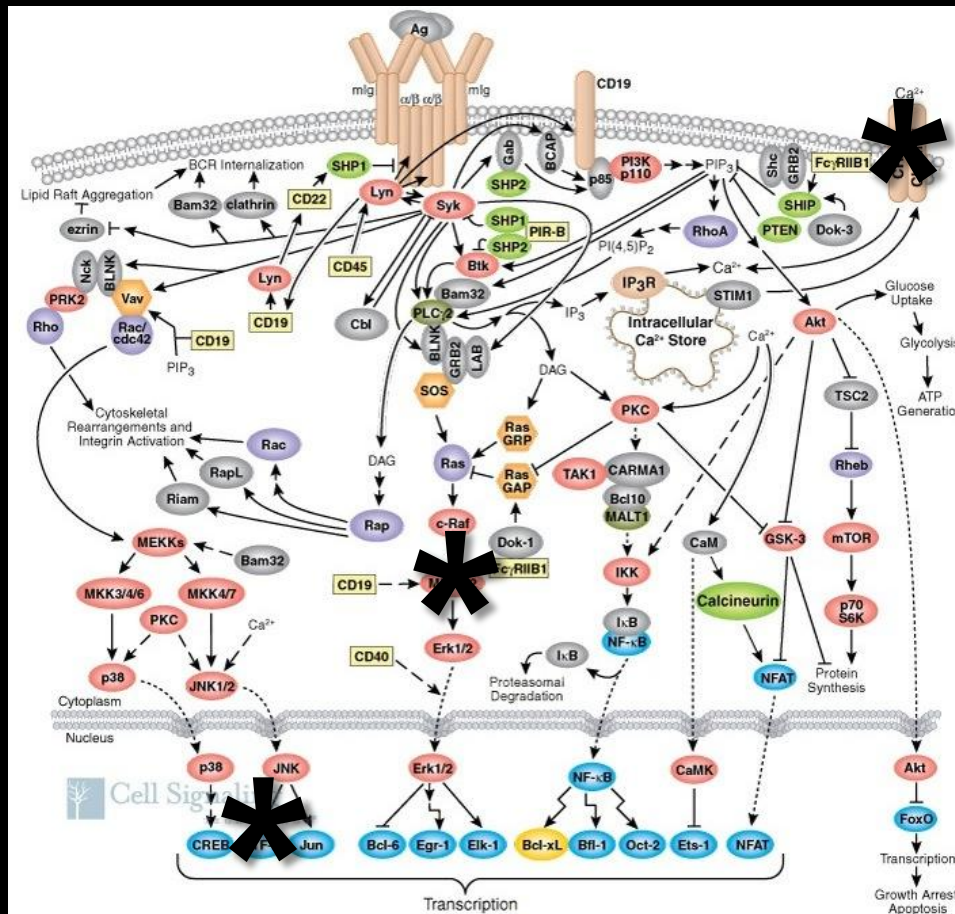
automated,
high throughput
multiplex assays

novel test formats
and devices for
point-of-care (POC)

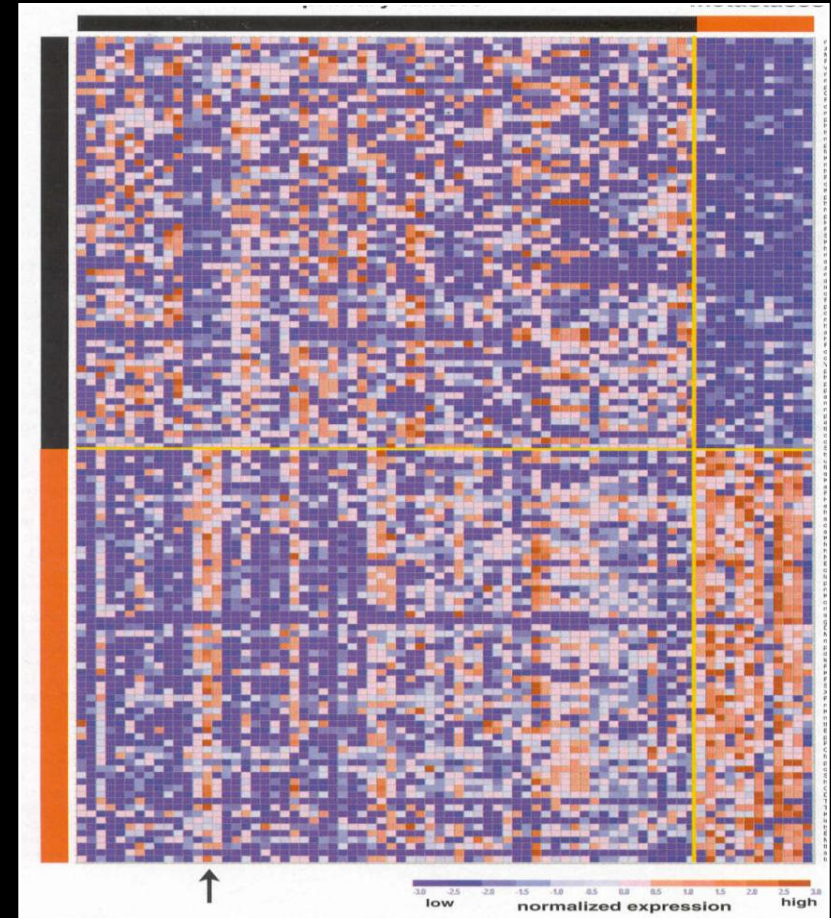
new algorithms
for complex
signal/deconvolution

From Pharmaceuticals to Pharmasuitables: Right Rx for the Right Disease (Subtype)

ID Molecular Targets for Rx Action



Disease Profiling to Identify Subtypes (+ or - Rx Target)



K-RAS Profiling and Anti-EGFR Monoclonal Antibody Therapy



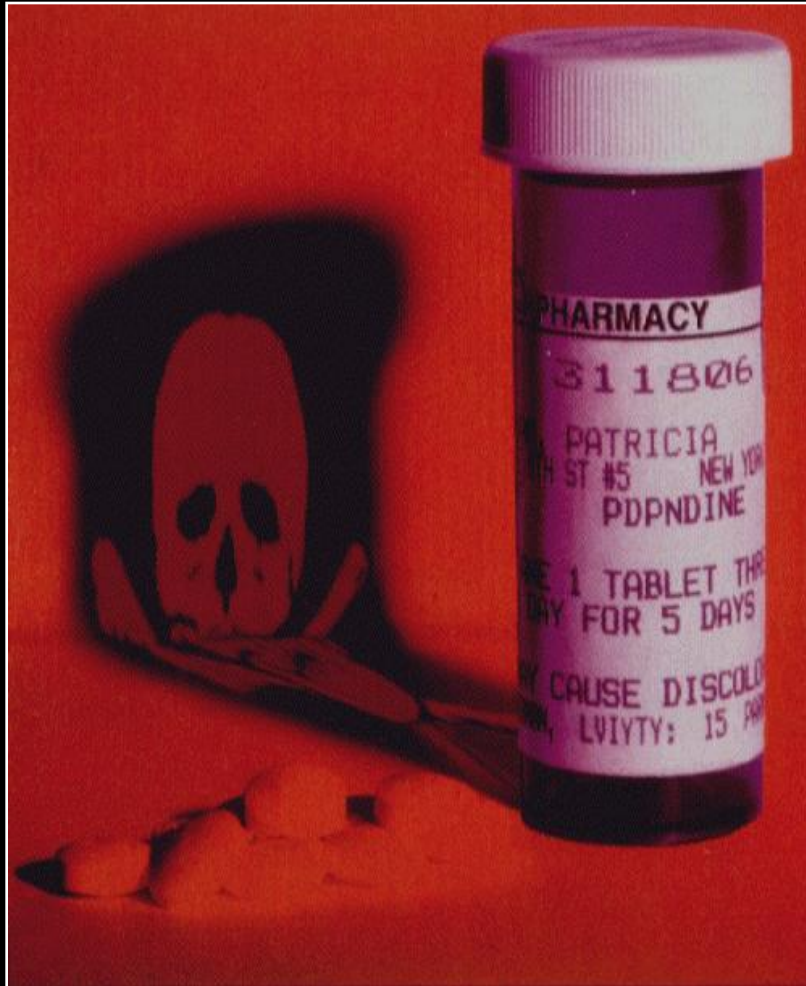
clinical guidelines

- higher response in patients with K-RAS versus mutant-K-RAS
- estimated \$604 million/year savings (ASCO)



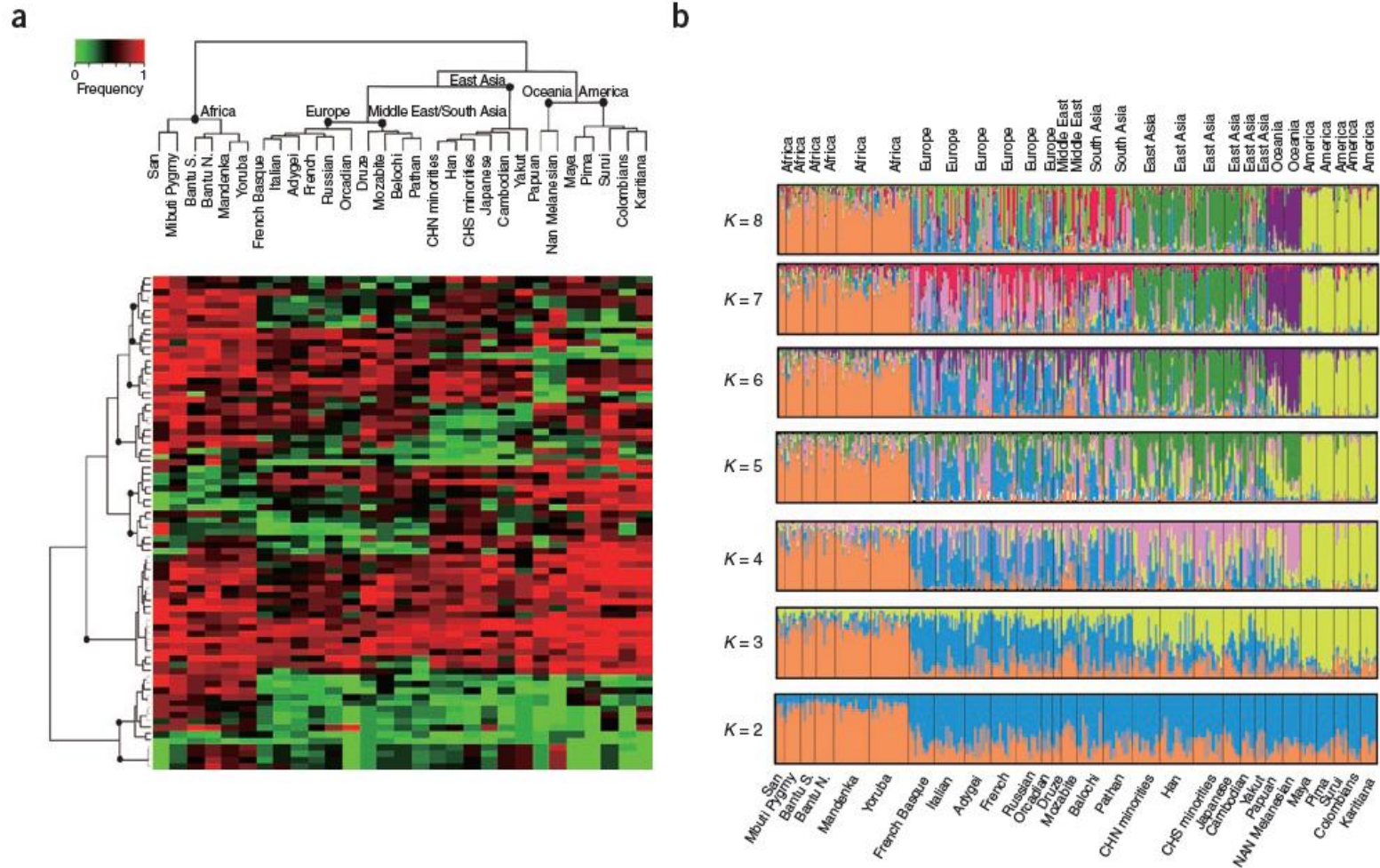
- regulatory endorsement in product labeling

From Pharmaceuticals to Pharmasuitables: The Right Rx for the Right Patient



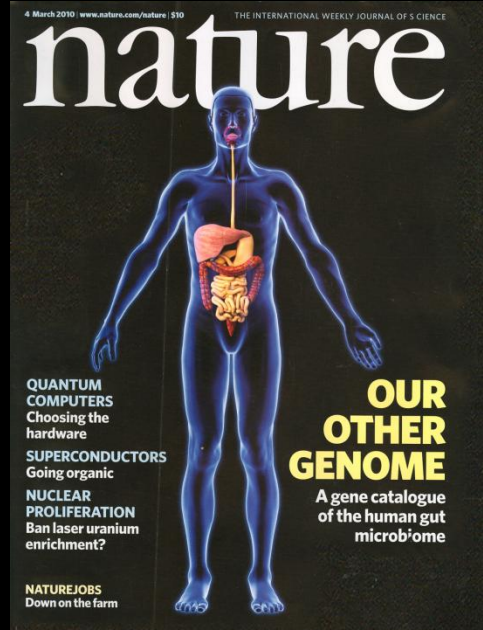
- Rx adverse events (AE) as major source of injury and death
- AEs due to genetic variation in drug transport and metabolism systems
 - fast and slow metabolizers
- AE due to drug interactions
 - action of one Rx in inhibiting metabolic capacity to handle second drug
- AE due to Rx and OTC drugs/supplements
 - latter not tracked

Identification of Ethnic Differences and Implications for Rx Efficacy and Safety



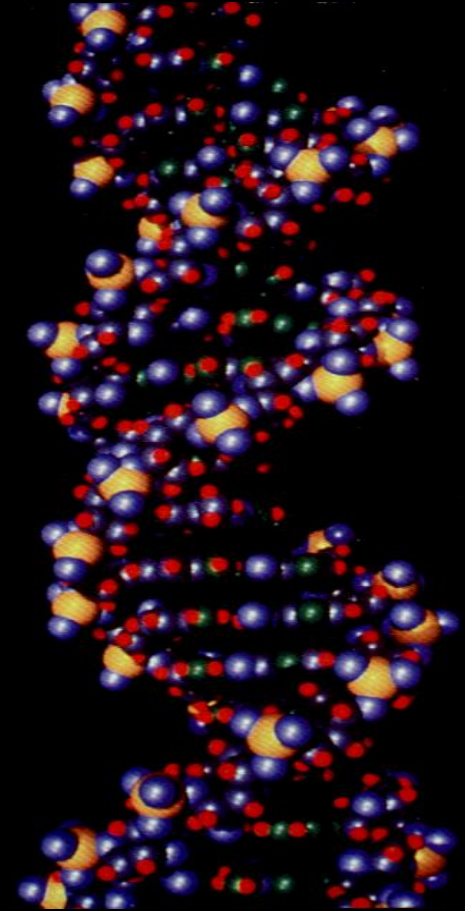
From: Ruiqiang Li et al. (2010) Nature Biotech. 28, 59

We Are Not Alone: The Human Microbiome – A Barely Understood Factor in Human Health and Disease



- human body contains 10x more bacterial cells than human cells
- complex meta-system
 - host, microbes, viruses, other organisms, metabolites, xenobiotics
 - is there a core microbiome?
 - how do perturbations affect disease and vice-versa?
 - does the microbiome influence xenobiotic metabolism and the metabolite spectrum?

Mapping Genetic Predisposition to Disease

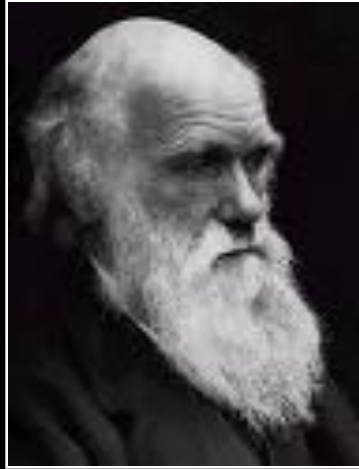


Nature (2010) 467, 832

Hundreds of variants clustered in genomic loci and biological pathways affect human height



Mapping Human Diversity



“Our ignorance of the laws of variation is profound”

Charles Darwin

**CGCCME!CAGGCATGCA
CAGTGCCAGGCATGCAT
CATGCGAGME!GCACT
TGCTAGGCATGCATGA
TCATGCCAGTCATGCA**

Mapping the Complexity of Genome Organization and the Cause of Multigenic Diseases



- recognition of increasing levels of organizational and regulatory complexity
 - haplotypes
 - CNV
 - indels
 - RNA universe
 - ‘dark’ elements
 - epistasis
 - epigenetics
 - nuclear compartmentalization and *trans*-expression
- impact of environmental factors
- gene-RX interactions



US Regulatory Action Against Direct-to-Consumer Genetic Testing



Consumer Genetics
Bringing Science Home

DNAdirect

Your Genes In Context

CyGene
LABORATORIES

GeneLink

GENECARETM
Medical Genetics Center



**GENETIC
TECHNOLOGIES, INC.**
DNA / FORENSIC / PATERNITY TESTING

genele

g-Nostics

**INTERLEUKIN
GENETICS**

Empowering

MediChecks.com



ScientificMatch.com
"The Science of Love"

NEUROMARK

SURACELL
Personal Genetic HealthTM



23andMe



Navigenics

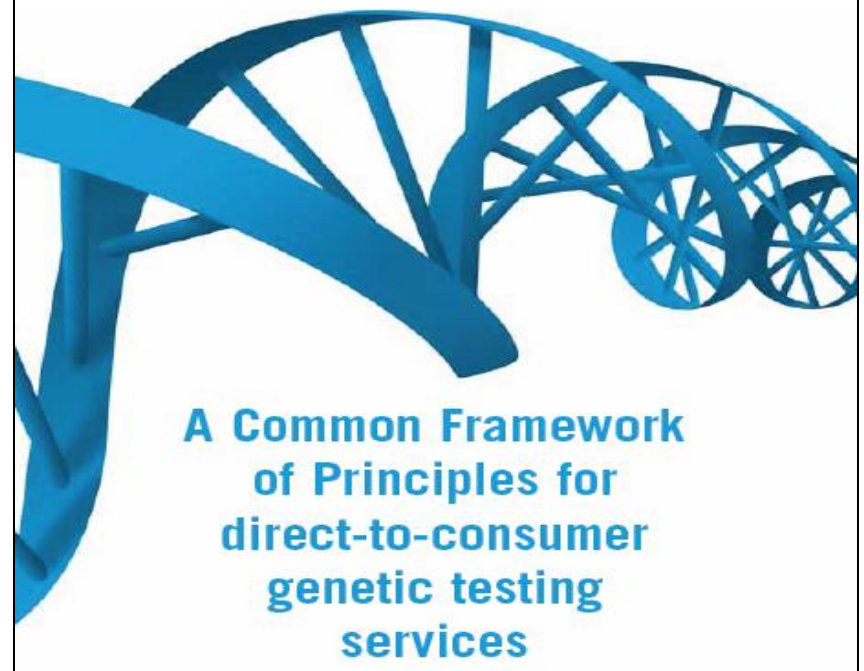


Knome

POLICY

Statement of the ESHG on direct-to-consumer genetic testing for health-related purposes

European Society of Human Genetics*

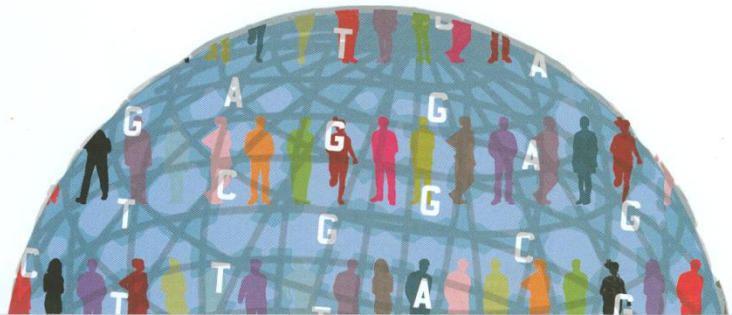


Whole Genome Sequencing

28 October 2010

nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE



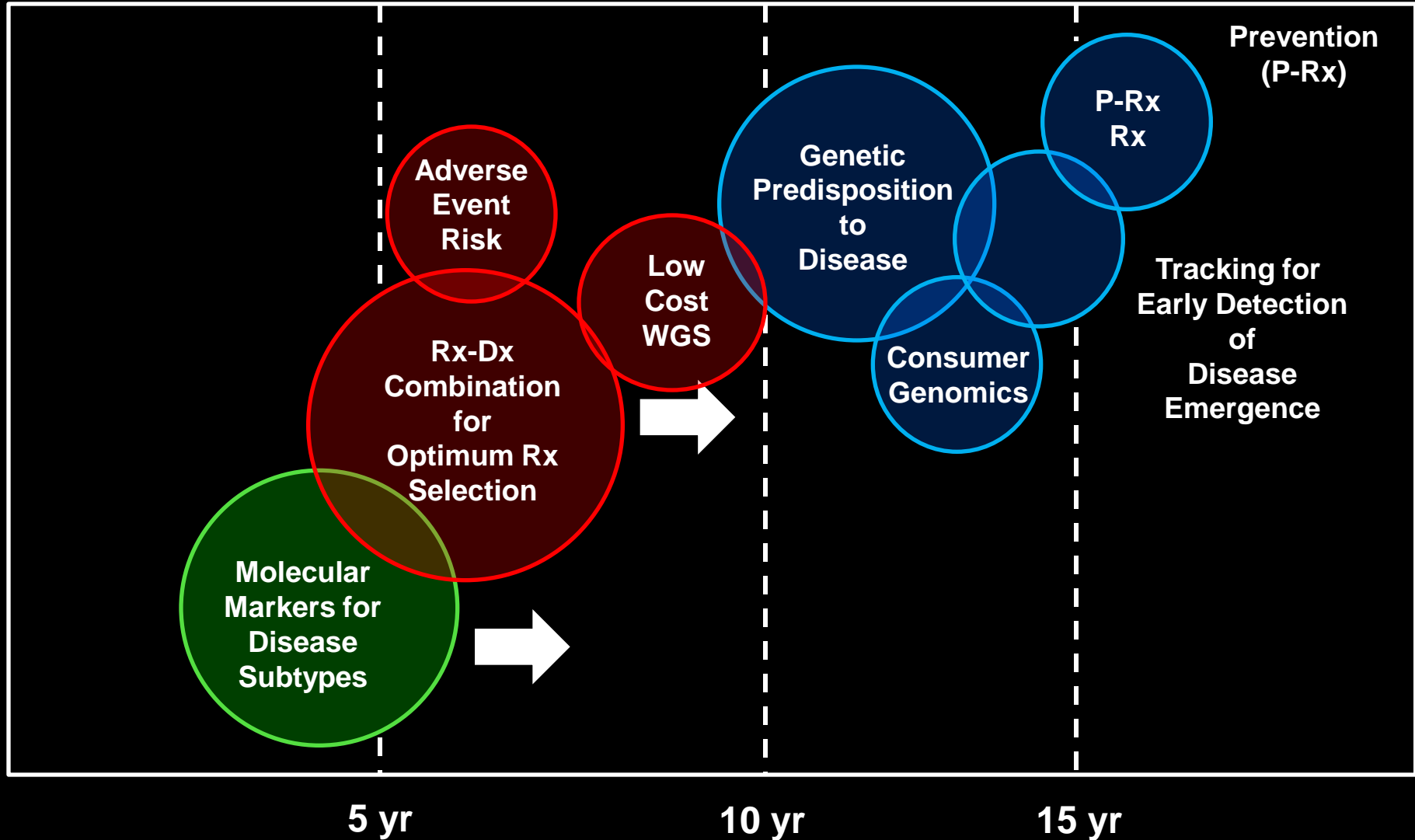
A THOUSAND GENOMES

Pilot studies prepare the way for population-scale gene sequencing PAGES 1050 & 1061



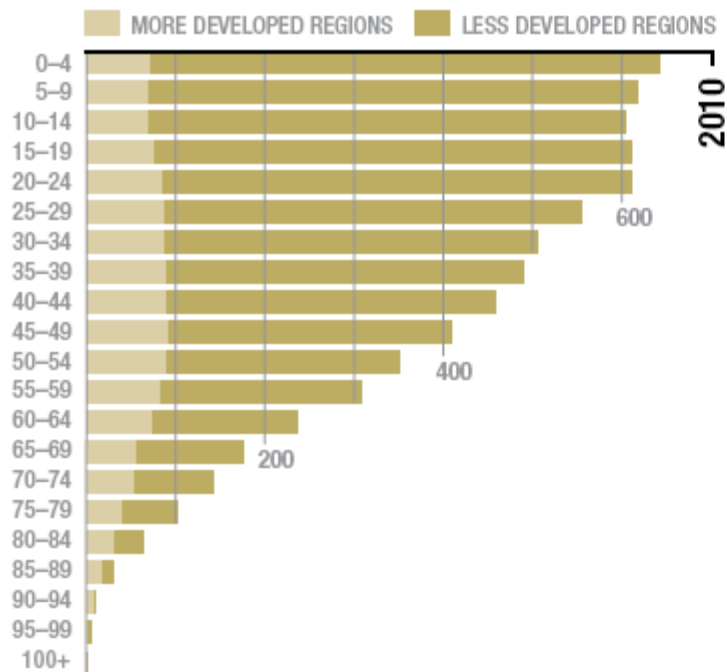
\$1000 Genomes

Evolution of Molecular Profiling and Diagnostics for Improved Disease Detection, Classification and Risk Evaluation



Global Population Demographics

(millions)



SOURCE: Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, World Population Prospects: The 2008 Revision, <http://esa.un.org/unpp>

The Disease Burden in Europe

Disease Category

- cardiovascular
- cancer
- tobacco
- obesity
- diabetes
- depression
- schizophrenia
- Parkinson's disease

Impact

4.3 million deaths/yr
1 in 3 men, 1 in 4 women
650,000 deaths/yr
30-80% adult population
246 million cases/3.8 million deaths/yr
23 million cases
1.5 million cases
800,000 cases, 75,000 new cases/yr

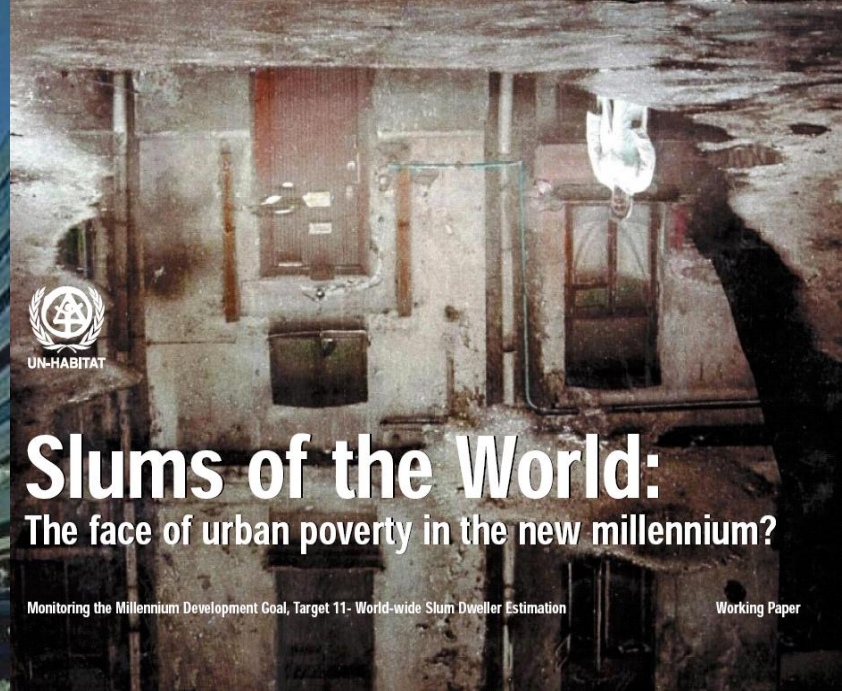
Urbanization

- 2 billion increase in world's urban population by 2030
- 90% of world's urban population will be in DCs by 2030
- 35% of current 3 billion urban residents reside in slums (UN-HABITAT)



- accelerating deterioration of physical and social well-being
- worsening morbidity and mortality for both communicable and non-communicable diseases
- polar demographics
 - aging urban populations in G8/OECD
 - record cohort of population younger than 25 yrs in DCs

Urbanization: A Bipolar World but Shared Risks



Slums of the World:
The face of urban poverty in the new millennium?

Monitoring the Millennium Development Goal, Target 11- World-wide Slum Dweller Estimation

Working Paper

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

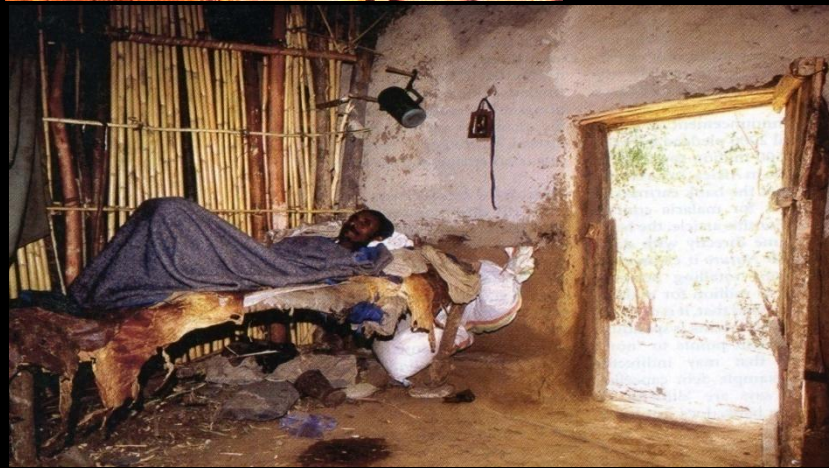
High Disease Transmission



Lack of Safe Water



Toxic Waste

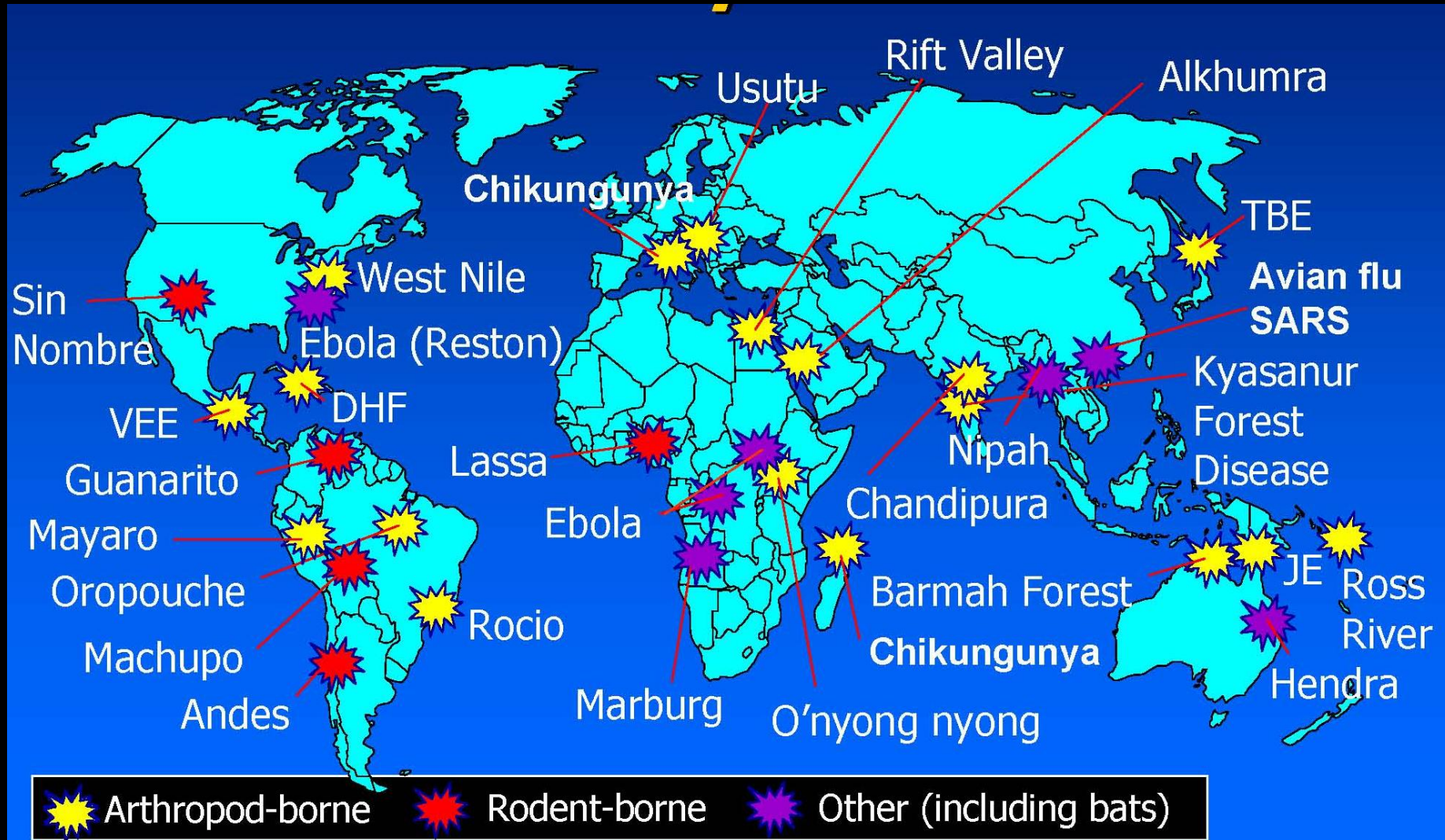


Major Deficits in Health Infrastructure



Expanded Eco-niches and Increased Zoonotic Risks

Emerging Infections:



The Super Vector



A stylized map of Africa is shown against a dark background. The map is composed of a dense network of red lines connecting various points across the continent, symbolizing a complex network or infrastructure. The lines are thin and numerous, creating a web-like pattern. The map itself is a light green color, and the background is dark, making the red lines stand out.

Global Food Networks

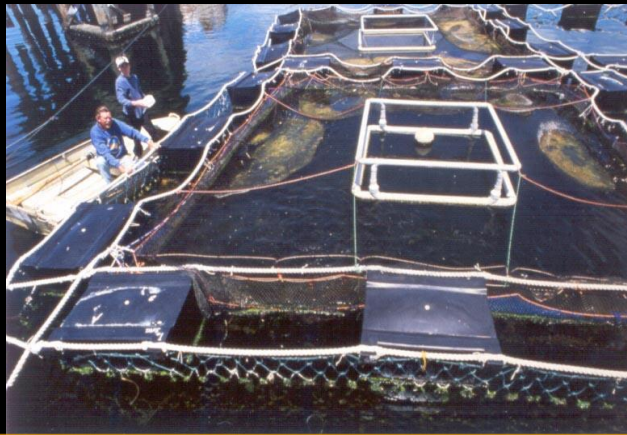


Factors Driving the Evolution of Microbial Drug Resistance

Intensive Agriculture



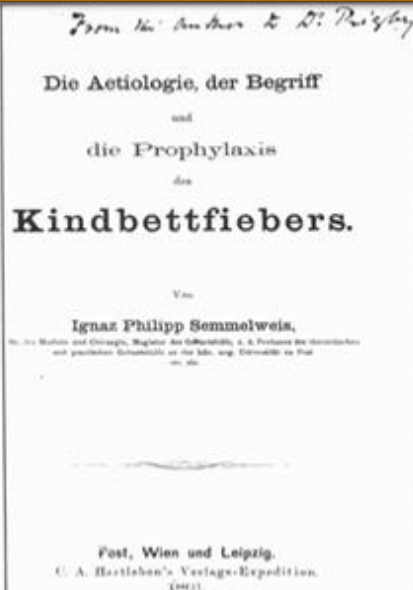
Aquaculture



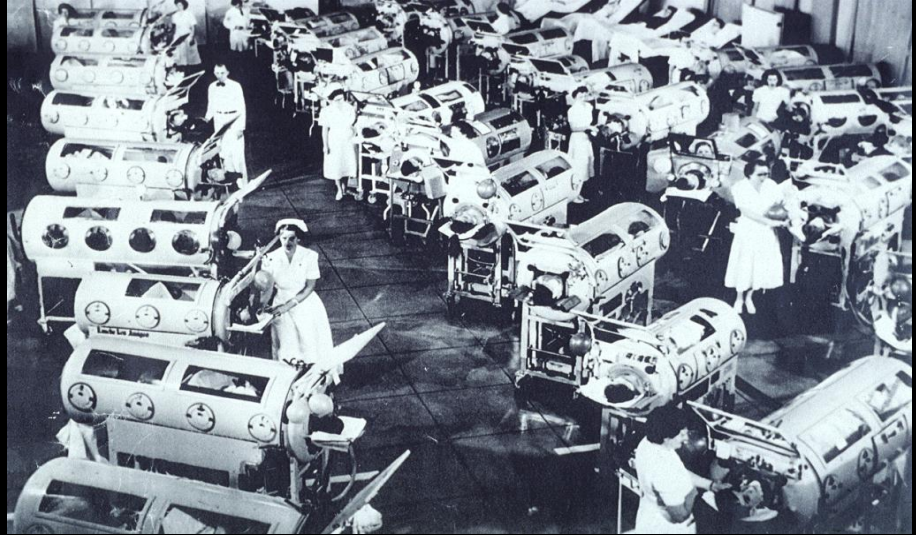
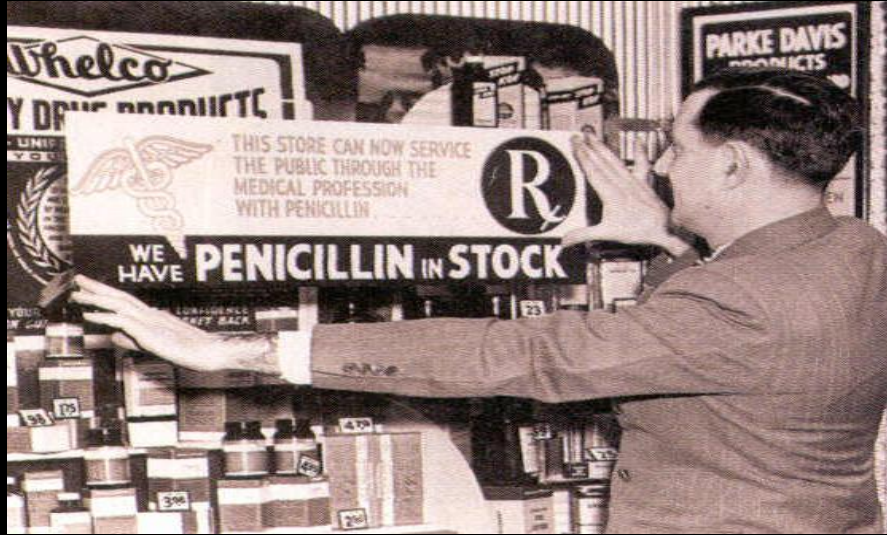
Empirical Rx



Poor Infection Control in Healthcare Facilities



Comfort and Complacency: The Enemies of Vigilance and Preparedness



The Growing Challenge Posed by Antimicrobial Drug Resistance (AMR)



NO ESCAPE

Enterococcus faecium

Staphylococcus aureus

Klebsiella Pneumoniae

Acinetobacter baumannii

Pseudomonas aeruginosa

Enterobacter species





New US-EU Task Force (2 Nov. 2009)

- encourage R&D on new antimicrobial drugs
- yet to be defined strategy/funding



The 10 X '20 Initiative (20 Nov. 2009)

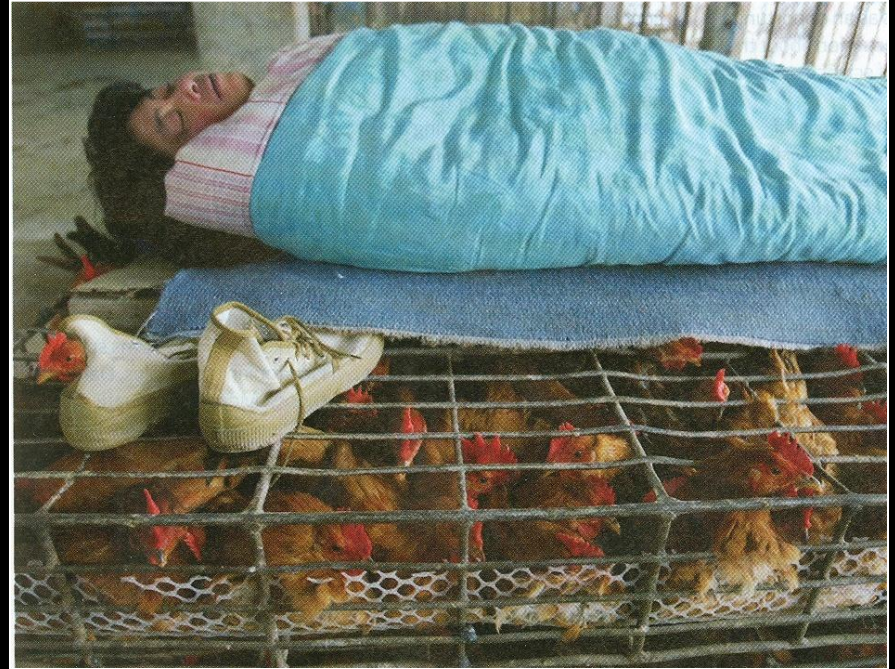
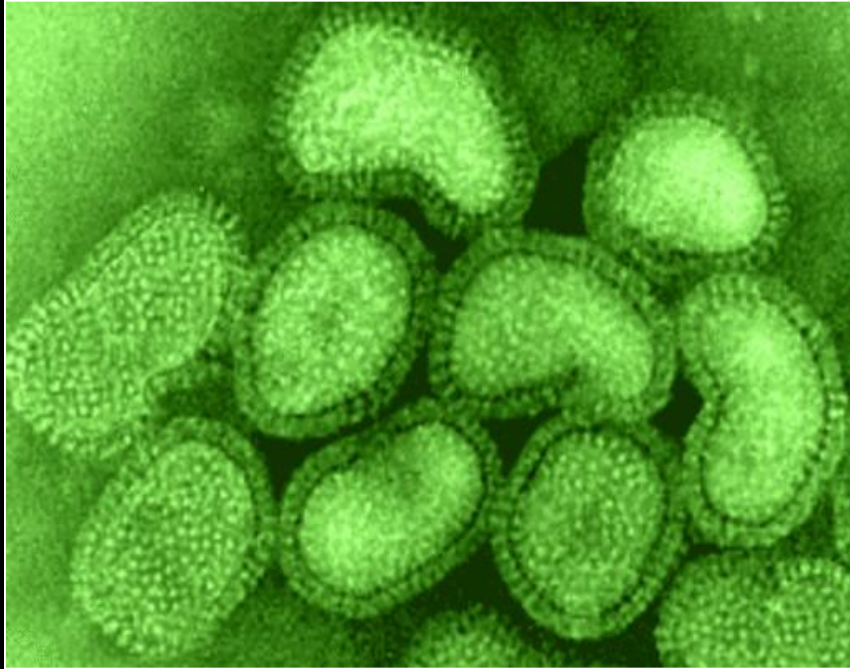
- grand challenge to develop 10 new antibiotics by 2020



Multi-Country Program on AMR (12 Jan. 2010)

- € 12.4 million

Maintaining Global Preparedness for a High Virulence Pandemic



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

Epidemics

**New
Zoonotic
Threats**

**Drug-
Resistance**

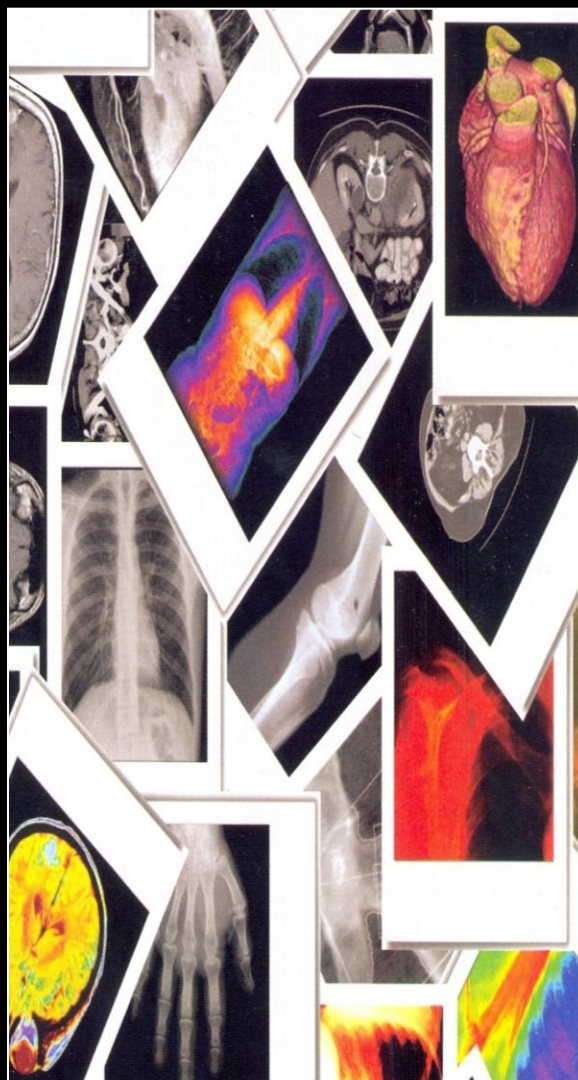
Sustainable Resources

- food production
- food safety
- water resources

Instability and Conflicts



How Much New Technology Can We Afford?



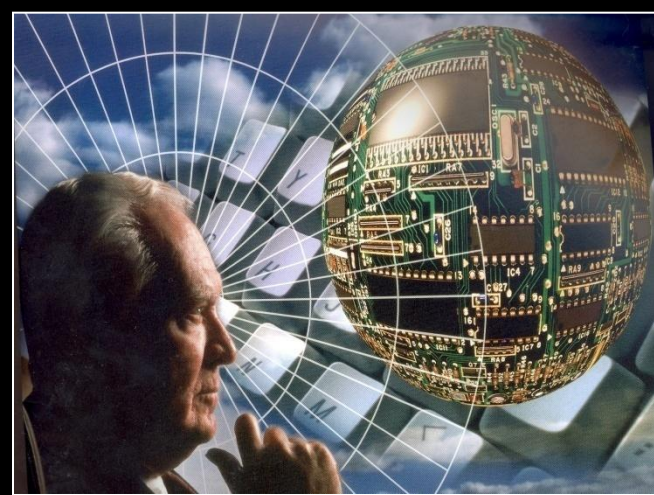
UK National Institute for Health and Clinical Excellence (NICE)



NICE Gets Nasty (or Rational?)

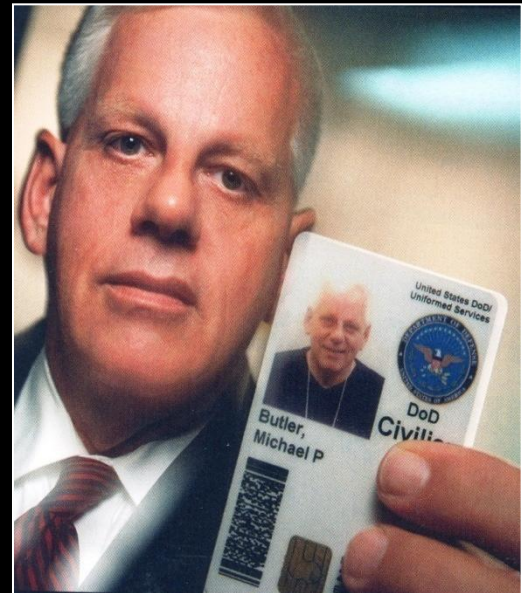


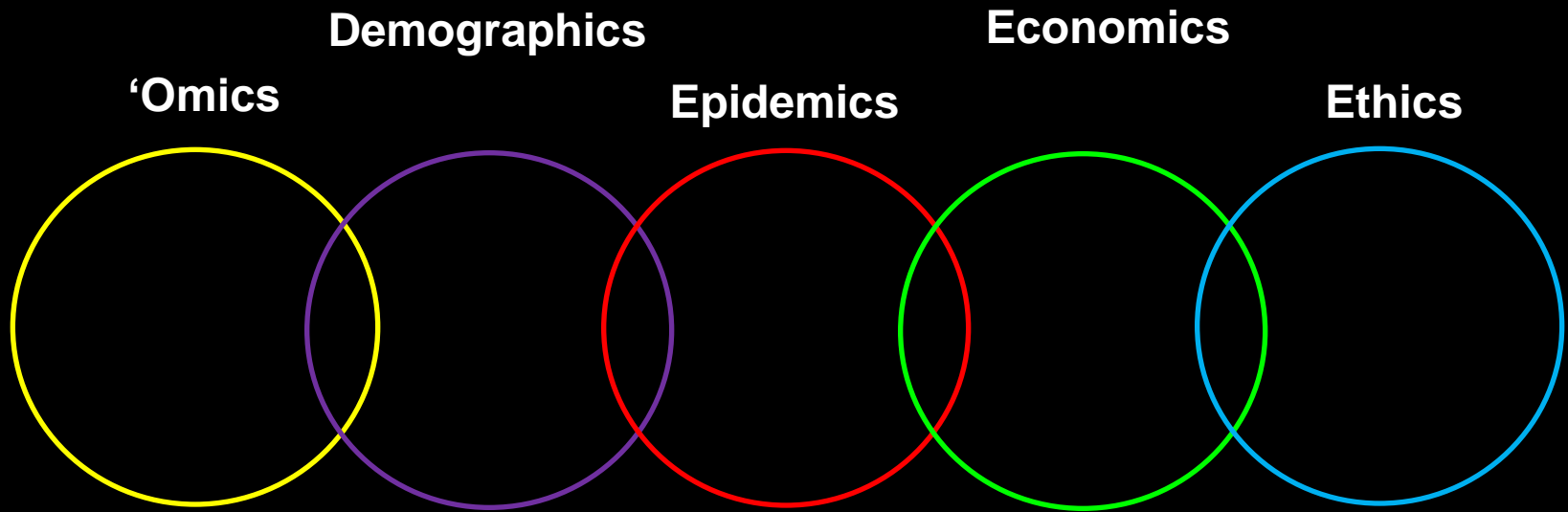
The Infocosm: Emerging Networks of Global Connectivity



Life's a game

Manipulating society has traditionally been the preserve of politicians and the gods. Does the current boom in virtual worlds give social scientists and economists an opportunity to join them? **Jim Giles** investigates.





Informatics

Assembly, Integration and Analysis of Massive Data

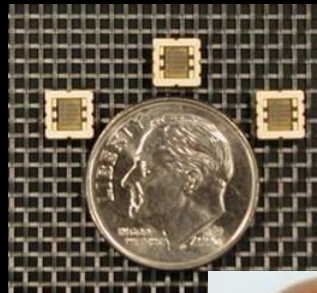
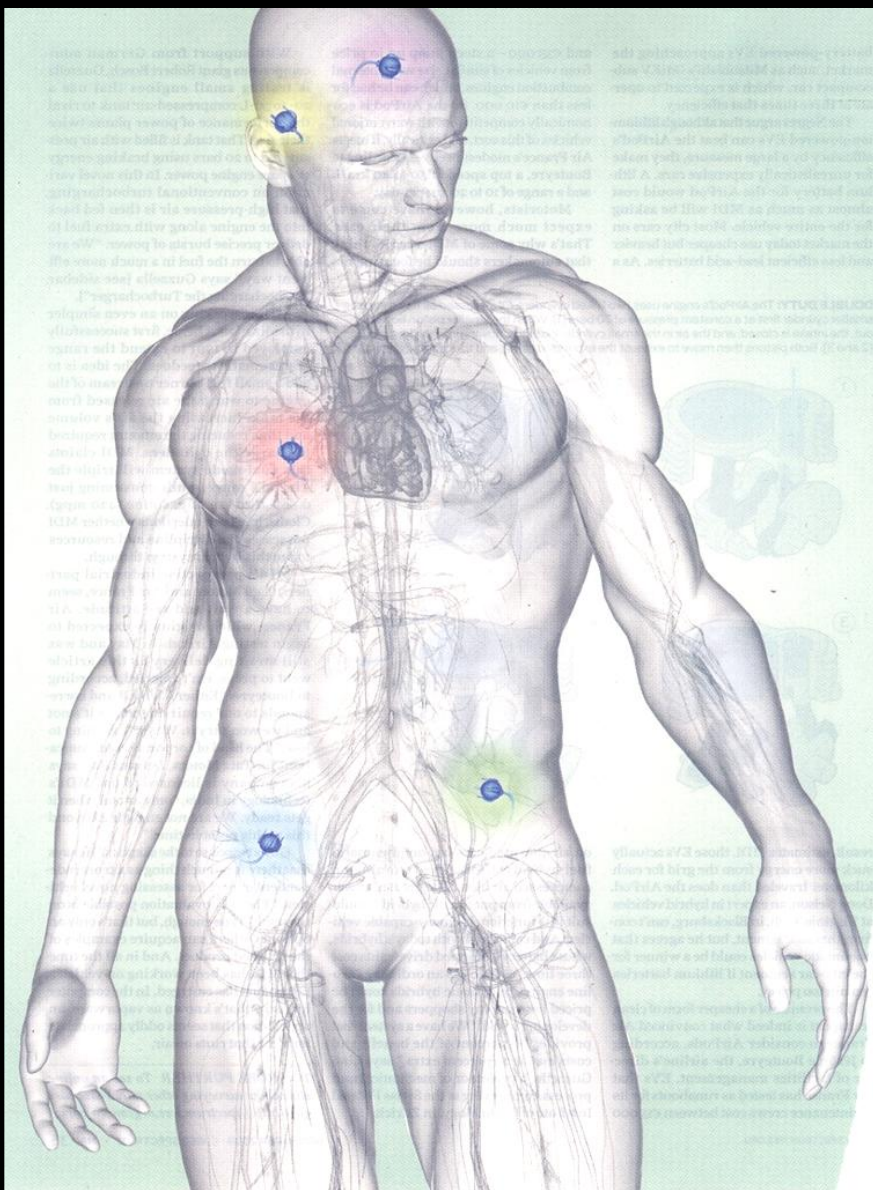
- **better diagnosis and treatment decisions (individuals)**
- **population data and evidence-based guidelines for best practices (health professionals)**
- **improved allocation of scarce/expensive resources (society)**
- **global health surveillance and risk reduction (global)**
- **acceleration of research discoveries and translation for improved care (academia, industry)**

Sensor Networks for Remote Health Status Monitoring via Wireless Integrated Data Systems

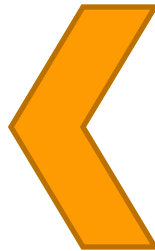
- geolocation data (where)
- temporal information (when)
- contextual information (what)



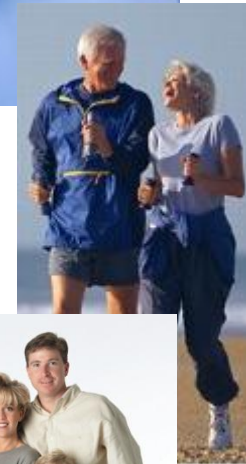
On Body: In Body Sensors/Devices For Real Time and Remote Monitoring of Individual Health Status



m.Health



**Remote
Health
Monitoring
and
Chronic
Disease
Management**



**Lifestyle
and
Fitness**

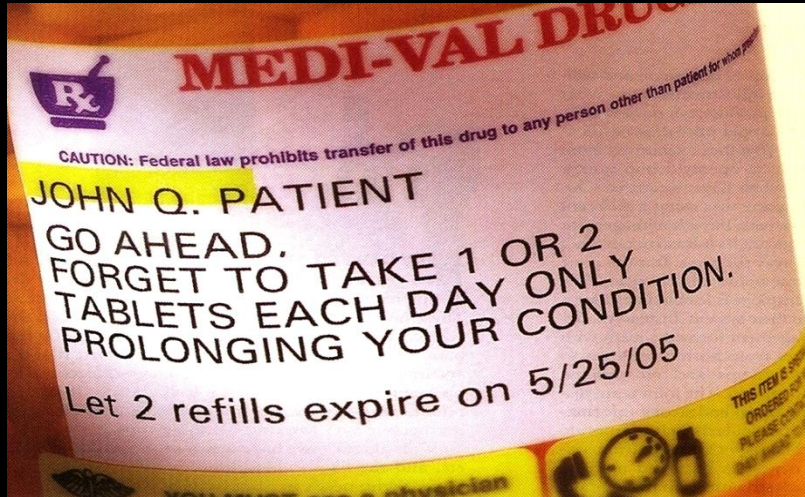


**Information
for
Proactive
Health
Awareness
(Wellness)**

Wireless Devices for Health Status Monitoring



The Costs of Non-Compliance with Rx Regimens



- \$177 billion projected cost
- 20 million workdays/year lost (IHPM)
- 40% of nursing home admissions
- projected 45-75% non-compliance (WHO)
- 50-60% depressed patients (IHPM)
- 50% chronic care Rx (WHO)

Intelligent Medicine Dispensers for Enhanced Rx Compliance

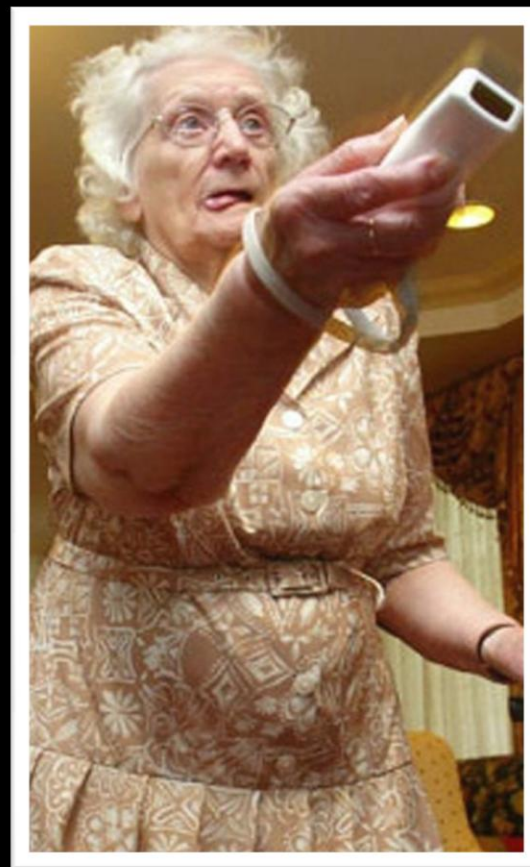


Gaming for Health:





Wii *Fit*.Plus



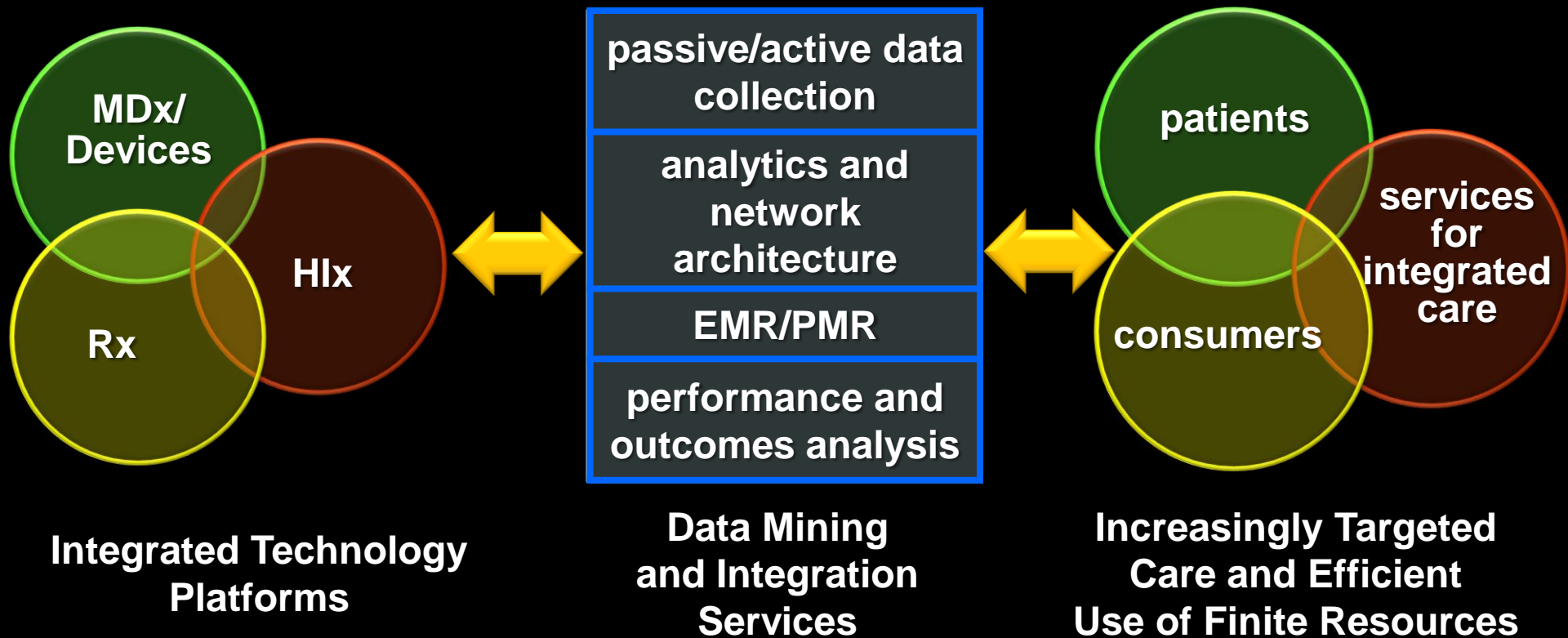
Social Networks and Consumer: Patient Empowerment



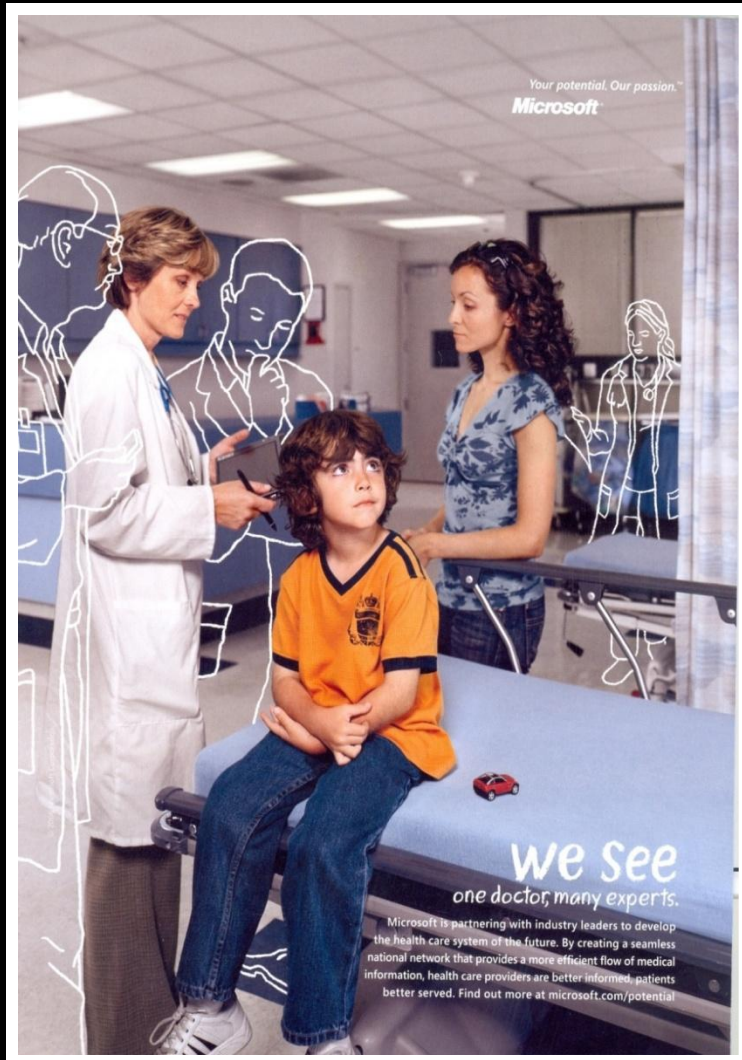
In-Home Health Connection: Engaging the Elderly



A New Healthcare Ecosystem Arising From Technology and Market Convergence



Virtual Medicine Networks: Increasingly Integrated Care and Continuity of Care



Rx

- rapid, real time access to expertise
- broader range of clinical specialties
- integrated health records
- availability of lab and Rx lab data
- drug interactions risk
- electronic Rx prescribing

OTC

Consumer Health

- optimum use of 'wellness' products and
- databases on OTC product performance to accelerate Rx to OTC conversion for products that regulators would otherwise be reluctant to grant full OTC approval

e.Health, m.Health and Patient Empowerment

- **greater access to information on treatment options**
- **generation-dependent ease and expectations for shared role in decisions**
- **new doctor-patient relationships**
- **new ‘cultural’ skills for healthcare professionals**
 - **less paternalism**
 - **patient education**
- **major gaps in professional familiarity and competencies in molecular medicine**

European Journal of Human Genetics

Article

European Journal of Human Genetics **18**, 972-977 (September 2010) | doi:10.1038/ejhg.2010.64

Genetic education and the challenge of genomic medicine: development of core competences to support preparation of health professionals in Europe

Heather Skirton, Celine Lewis, Alastair Kent and Domenico A Coviello





Global Disease Surveillance

Eurosurveillance

EMERGENCY ID NET



Public Health Department's Surveillance



U.S. Influenza Sentinel Provider Surveillance Network



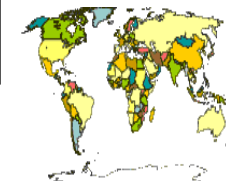
biocaster



GIDEON

Quarantine Activity Reporting System (QARS).

google.org

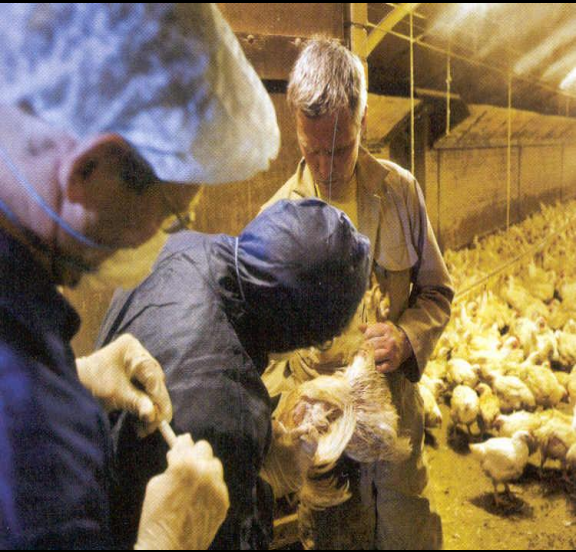


GeoSentinel

The Global Surveillance Network of the ISTM and CDC
a worldwide communications & data collection network of travel/tropical medicine clinics

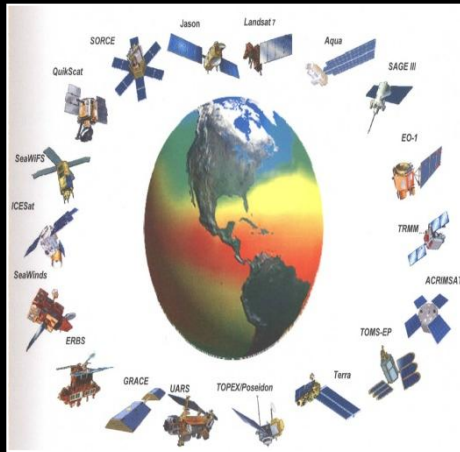
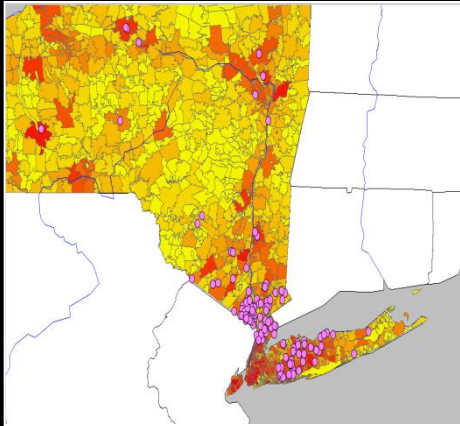


Geodemographic Information Systems (GIS): Real-Time, Front Line, Ground Zero Data from Field Sampling and Sentinels

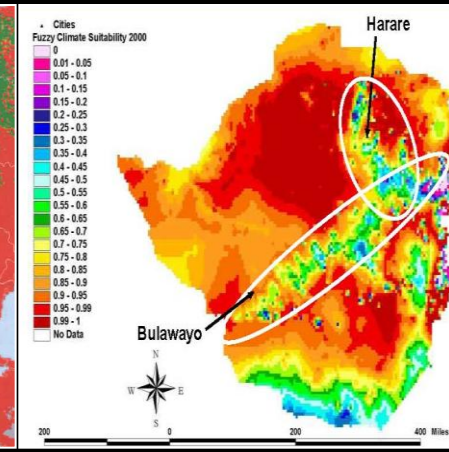
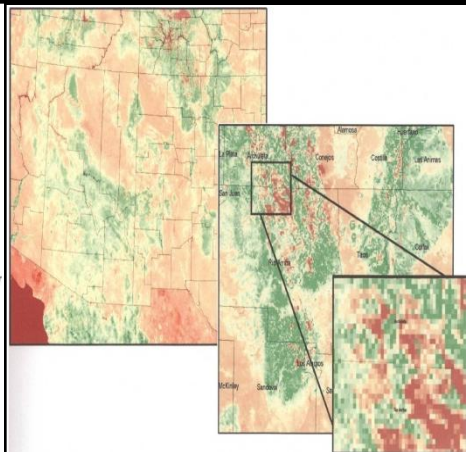
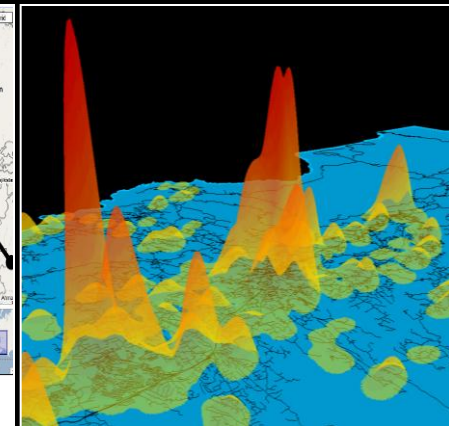
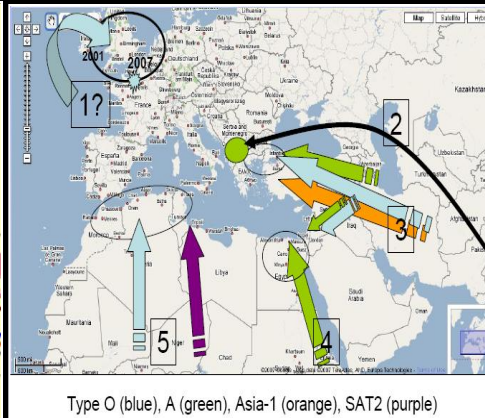
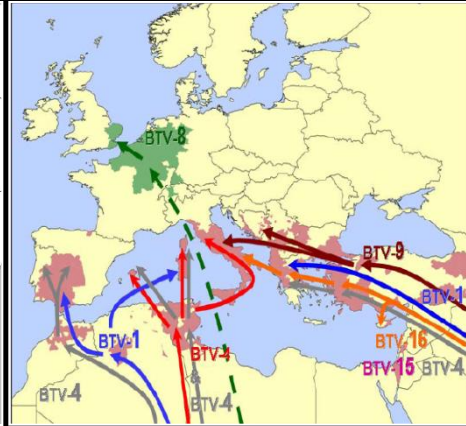


Geo-demographic Information Systems: Mapping Disease Patterns and Modeling Trends

Anomaly Detection and Early Alert

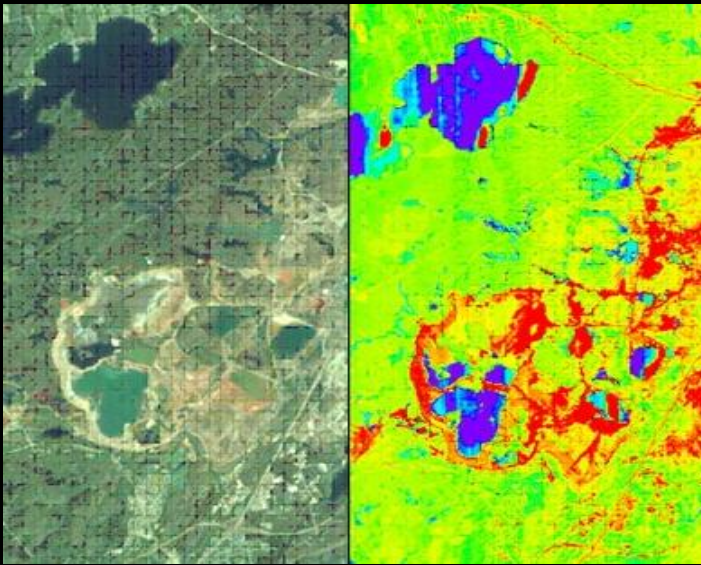


Disease Progression

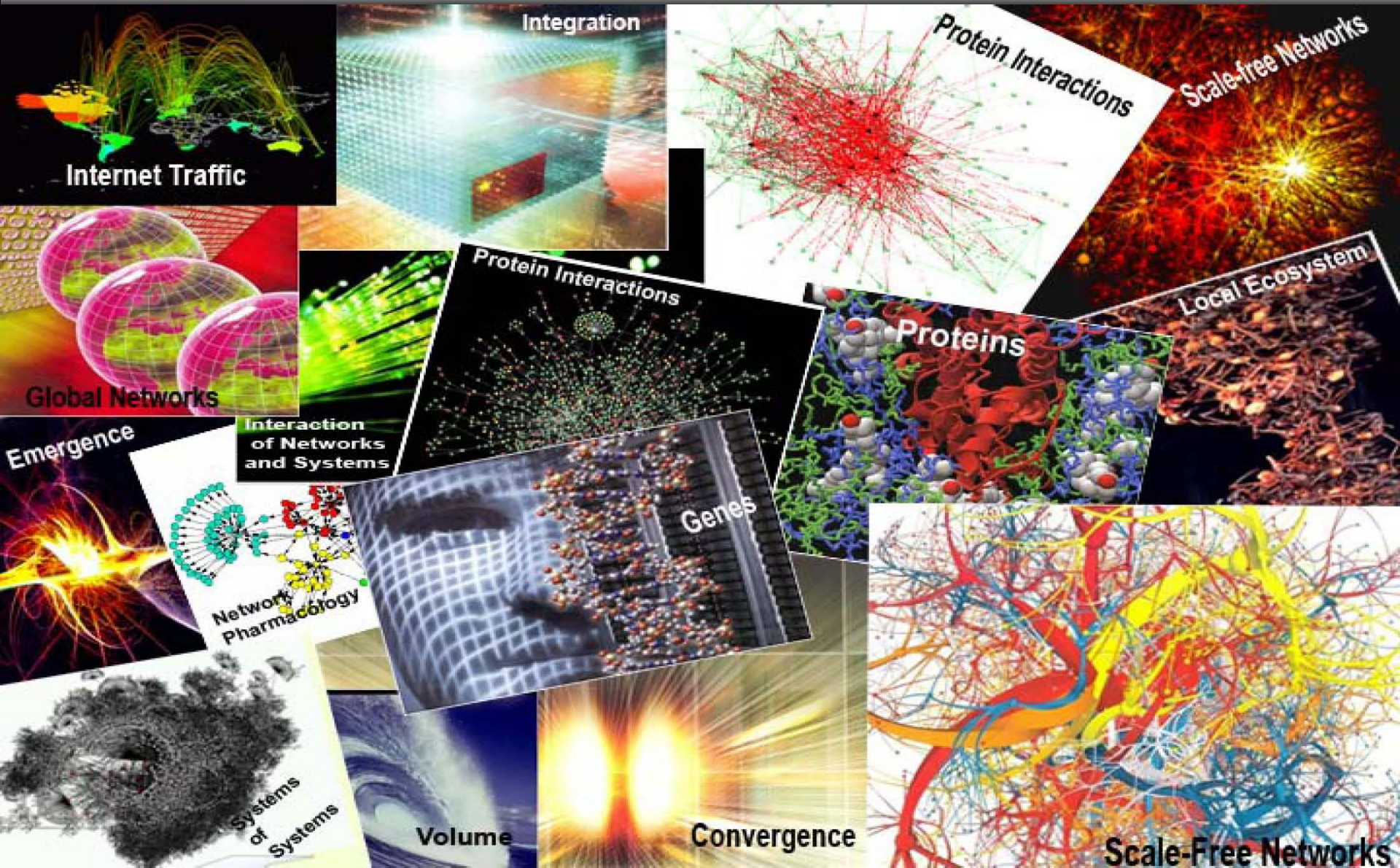


Satellite Surveillance and Predictive Modeling of Disease Trends

Wireless Sensors and Systems for Improved Agricultural Productivity



Data: The Fastest Growing Resource on Earth



“Managing Mega-Data”: (Who Knows Wins)

volume



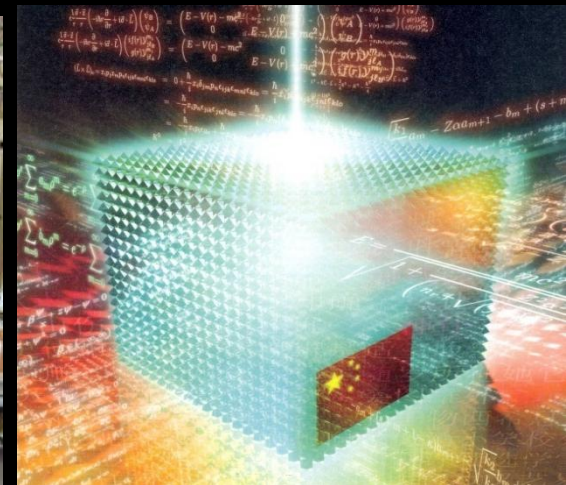
scale



global networks



heterogeneity



integration

Standards for 'Omics' Data Cross-Domain Integration, Open-Source Data Sharing and Computational Analysis



OBO Foundry Ontologies

Nature Biotechnology 25, 1251 - 1255 (2009)



The Open Biomedical Ontologies

Cell Ontology (CL)



Gene Ontology (GO)

Foundational Model of Anatomy

ZFIN

Zebrafish Anatomical Ontology



Chemical Entities
of Biological Interest (ChEBI)

Disease Ontology (DO)



Plant Ontology (PO)

SO
The Sequence Ontology Project

Sequence Ontology (SO)

**Ontology for Clinical
Investigations (OCI)**



The Open Biomedical Ontologies

Common Anatomy
Reference Ontology



The Open Biomedical Ontologies

Environment Ontology



Ontology for Biomedical Investigations

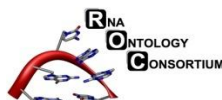
**Phenotypic Quality
Ontology (PATO)**

PIR
A UniProt Consortium Member
Protein Information Resource

Protein Ontology (PRO)



**OBO Relation
Ontology**



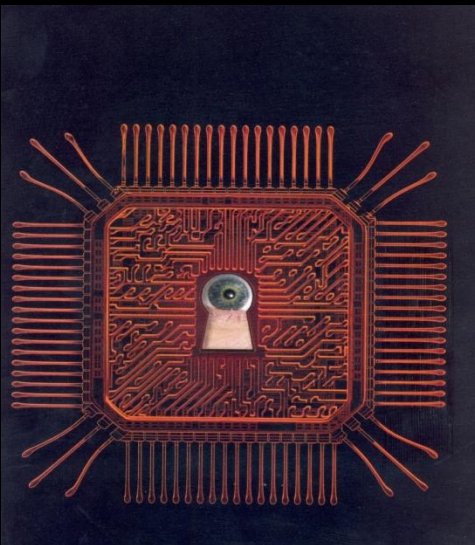
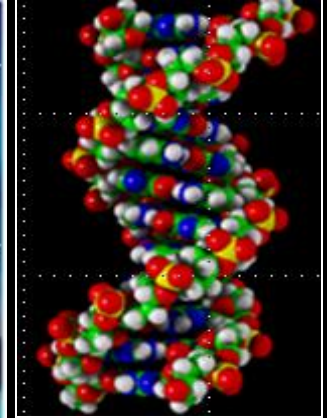
**RNA Ontology
(RnaO)**

Privacy and Health Information

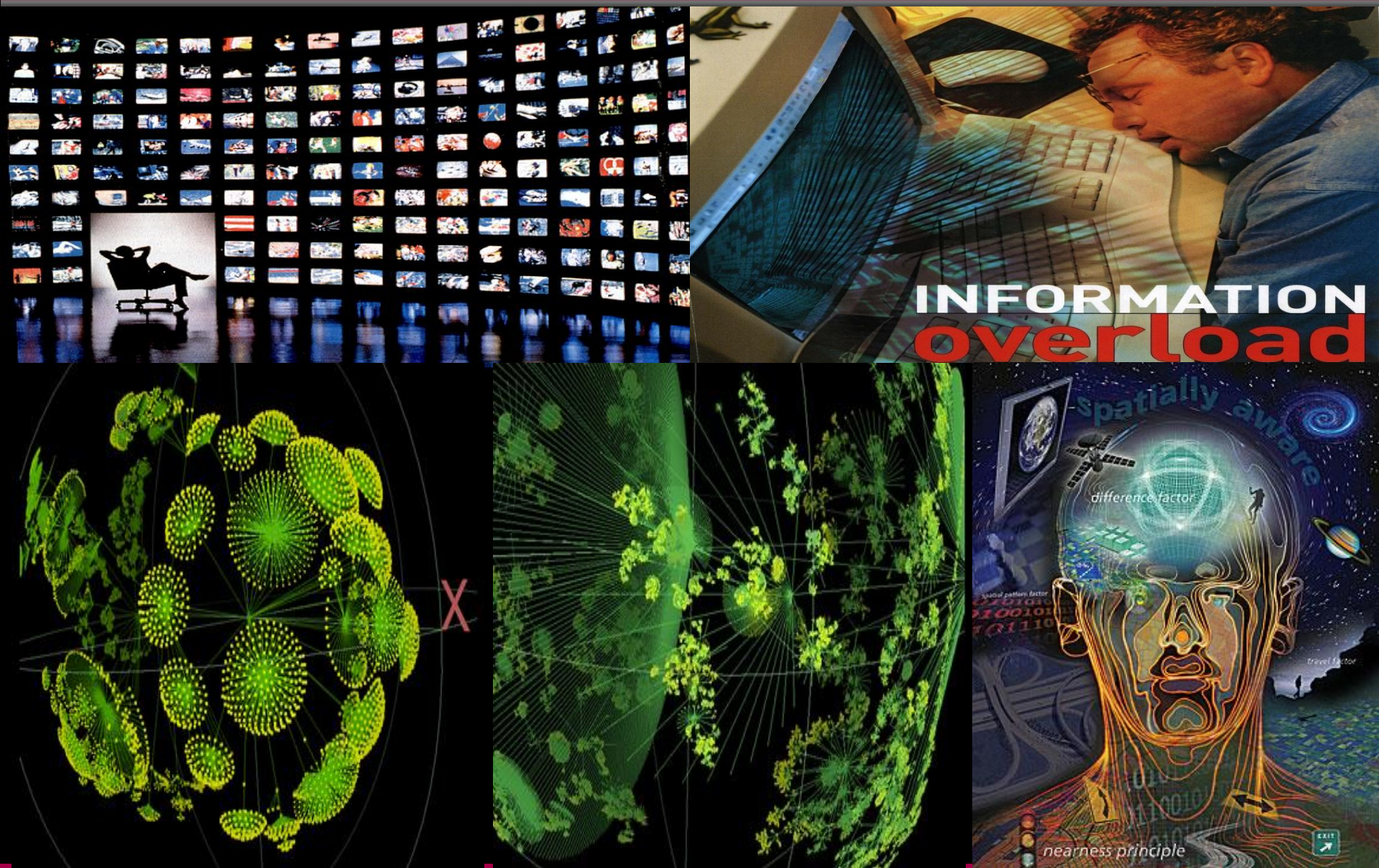
- 2010: 15 Petabits (10^{16}) / \$250,000
- Human Genome: 10 Gigabits (10^{11})

For a few million dollars, one could store the complete genome of every American and European

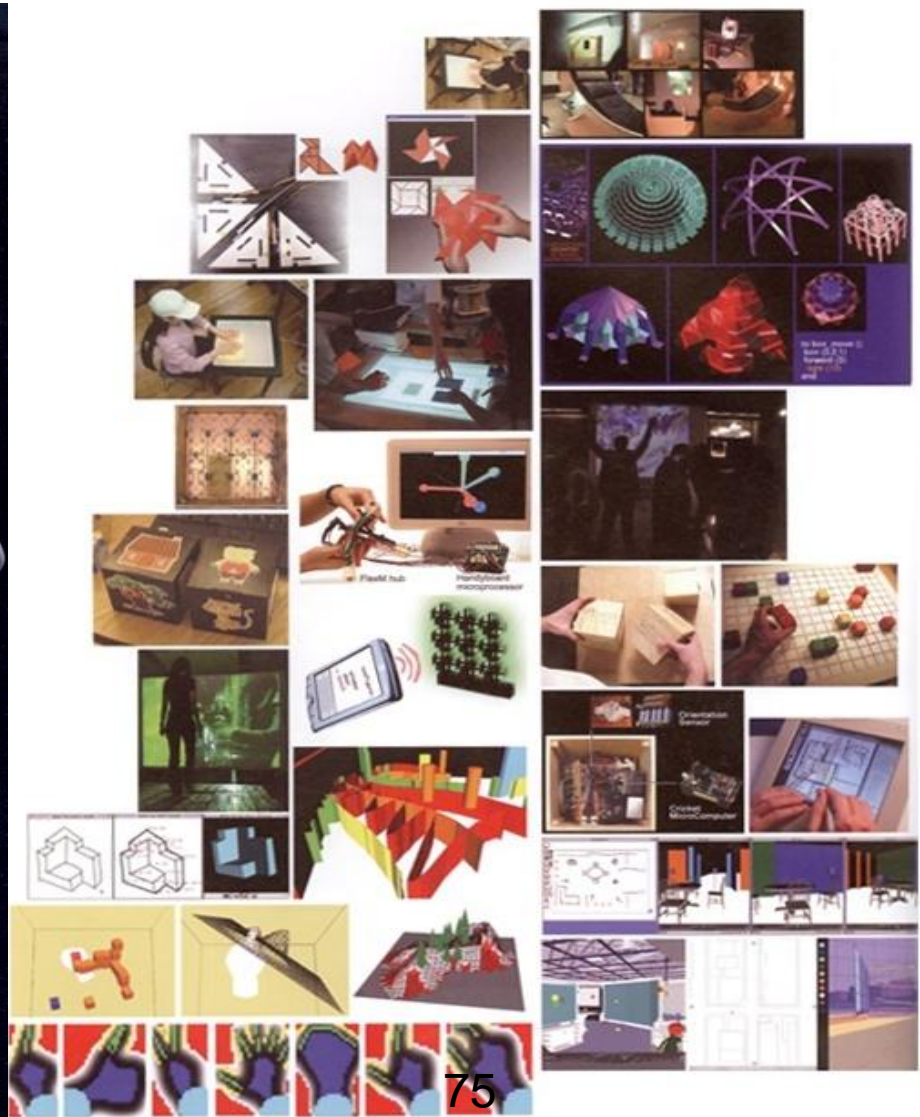
...for several more, could add credit card records, telephone logs, travel history,...




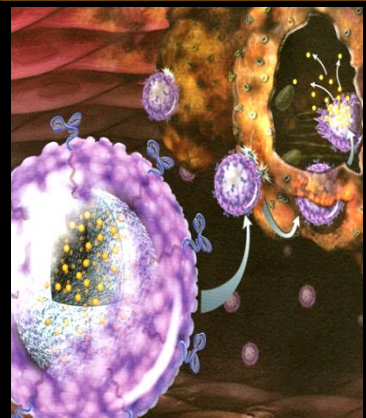
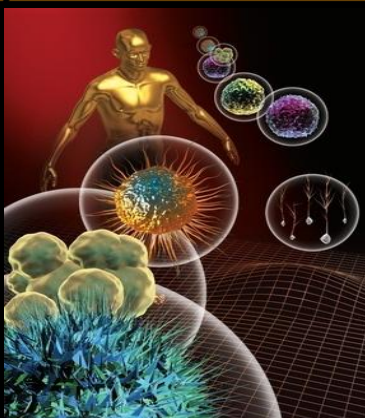




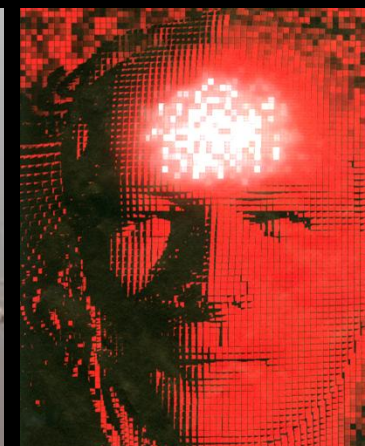
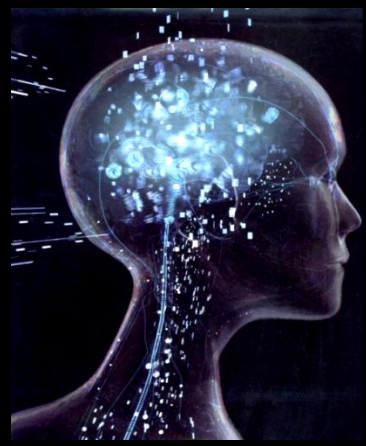
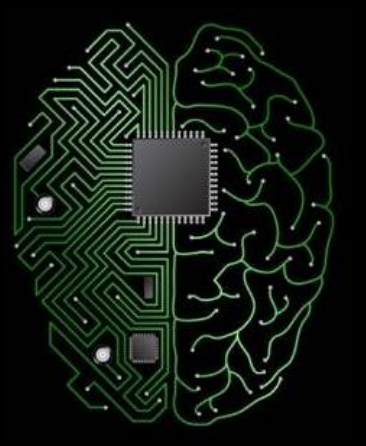
Enhancing Human Capabilities to Use the Increased Volume, Diversity and Complexity of Information Flows



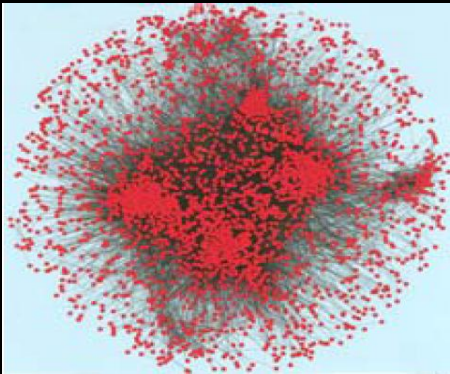
Cognitive Biology, Customized Data Formats and Visualization for Improved Decision-Making



Transcending Boundaries: Emergent Domains Arising from Technology Convergence

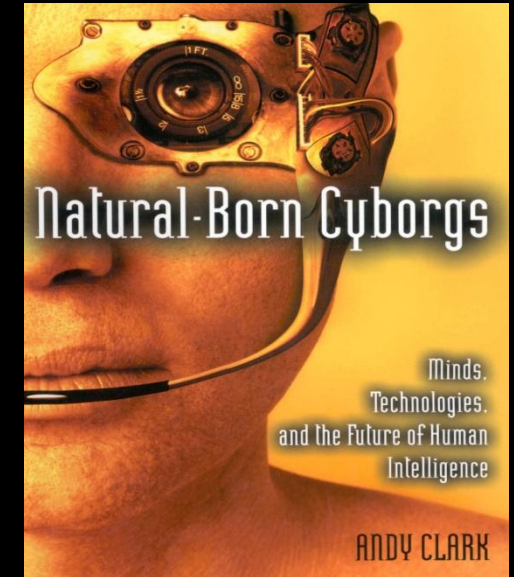
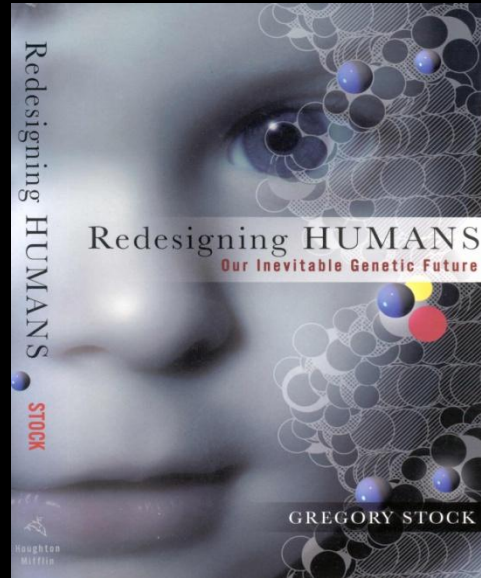
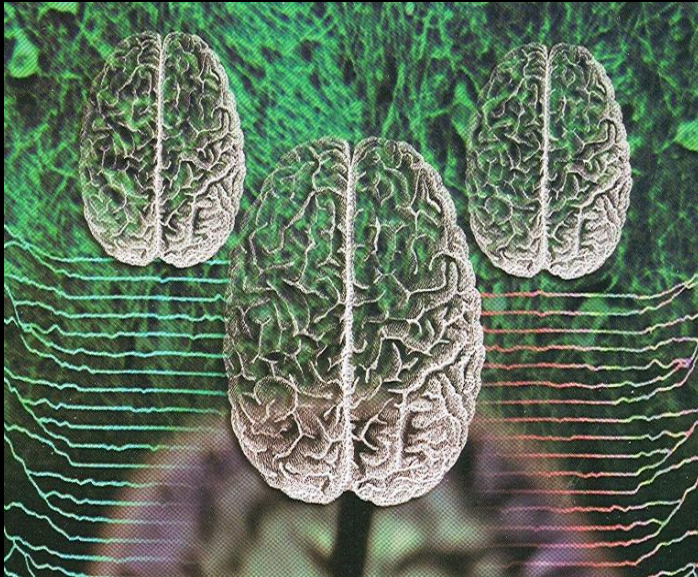
Systems and Synthetic Biology	Targeted Rx	Regenerative Medicine	HPO	Genetic Identity
				
Bio-Enhancement	Bionic-Enhancement	Cognitive Enhancement	Cogint	Brain-Machine Interactions
				

Mapping Biological Control Circuits and the Expanded Dimension of the Chem-Bio (CB) Challenge



- **thinking beyond 'bio' as just infectious agents (bugs)**
- **systems biology**
 - **targeted disruption of ANY body function**
 - **novel CB threats**
- **synthetic biology**
 - **exploring biospace: designing new life forms**
 - **designer organisms to attack materials/infrastructure**

The Accelerating Convergence of Neurobiology with Advances In Engineering and Computing



- **“Brains on Target”: Bio-Info-Cognitive (BIC) technologies**
- **“Borg Drift”: On-Body/In-Body (OBIB) devices and brain: computer interface technologies**

New Strategic Technology 'Spaces' Created by Technology Acceleration and Convergence

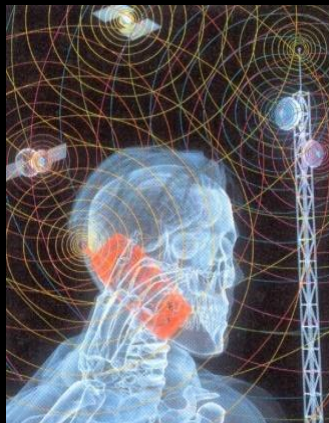
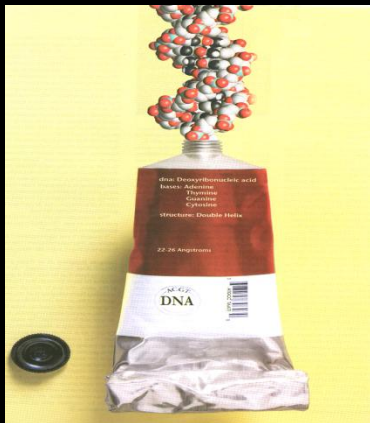
**Systems
and
Synthetic
Biology**

**Ubiquitous
Sensing**

**Infocosm
and the
Metaverse**

**Dual-Use
Technologies**

**Education
and
Research**



“Bio-Space”

**“Monitored
Space”**

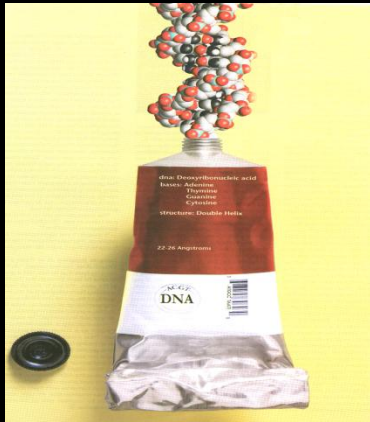
**“Networked
Space”**

**“Controlled
Space”**

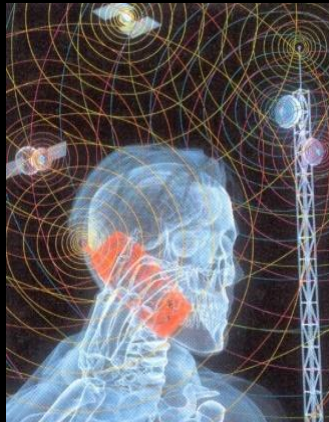
**“Aspirational
Space”**

New Strategic Technology 'Spaces' Created by Technology Acceleration and Convergence

**Systems
and
Synthetic
Biology**



**Ubiquitous
Sensing**



**Infocosm
and the
Metaverse**



**Dual-Use
Technologies**



**Education
and
Research**



“Bio-Space”

**“Monitored
Space”**

**“Networked
Space”**

**“Controlled
Space”**

**“Aspirational
Space”**

**Rapidly Changing and Evolving
Multi-dimensional Matrices of
Knowledge Ecologies**

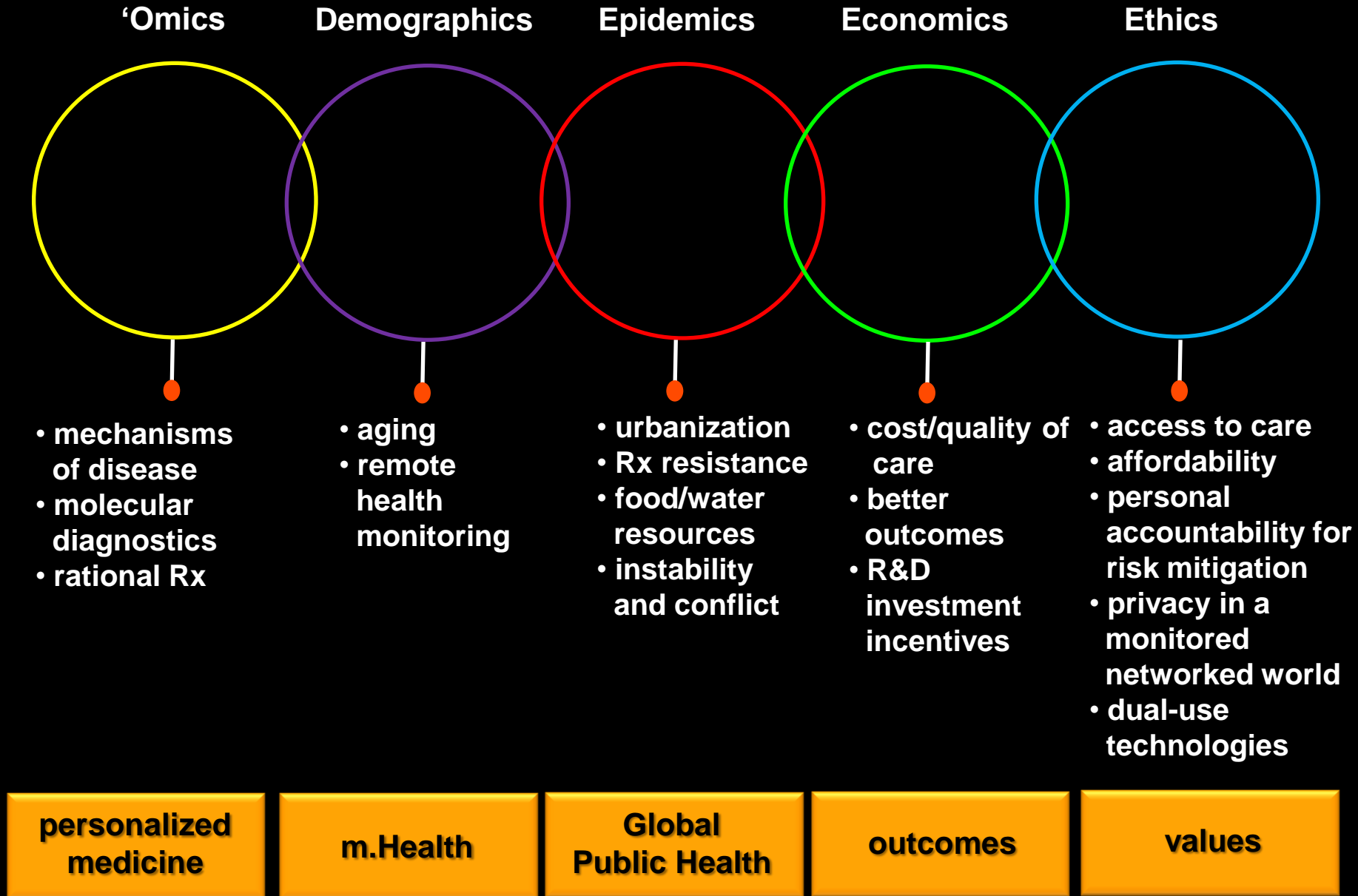
**Innovation
Systems**

**Organization
of Research**

Dangerous Assumptions

- **the future will be similar to the recent past**
- **policy makers understand the forces that are driving ever-faster disruptive changes**
- **national governance institutions, laws and regulations are adapting to the accelerating pace of discovery and globalization of technology**

The Complex Inter-Relationships Shaping the Future of Healthcare



The Complex Inter-Relationships Shaping the Future of Healthcare

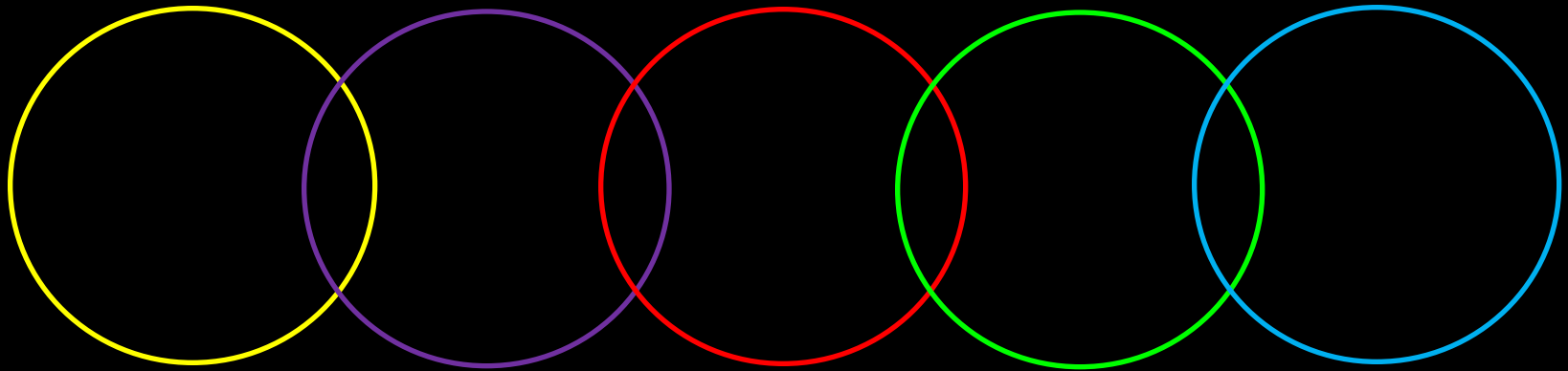
'Omics

Demographics

Epidemics

Economics

Ethics



wellness: predict and prevent disease versus diagnose and treat

sustainable health: wellness + economic thresholds for acceptable 'outcomes'

reducing risk: remote health monitoring + personal accountability

knowledge networks: distributed information systems for smarter decisions and better use of scarce/expensive resources

The Future of Academic Biomedical Research: Adaptive Agility or Denialism and Decline?

- **myriad inefficiencies arising from the organization and performance of academy and its funders**
- **single discipline specialization creates isolated silos**
- **hubris of dangerous belief in perceived competency in an era of dramatic change**
- **reward systems (internal promotion, external funding) weighted to individual versus team performance**
- **scale, cost and logistical complexity of multidimensional**
- **multidisciplinary projects and funding policies**
- **proficient translation of academic discoveries to productive use requires expanded academy-industry interactions**
- **imperative for new cross-disciplinary curricula and training**

