

Medicina sec XXI: **DIGITALĂ – COMPUTAȚIONALĂ - ALGORITMICĂ**

Cris Doloc, PhD.
ALGOMEX & RoGeniX

Timișoara - 26 Iulie 2016

Intro

Cris Doloc

❖ **Education** – Computational Scientist

- Physics PhD from French AEC/EP

❖ **Experience** – Technologist & Entrepreneur

- 25+ yrs. as Computational Expert & Enterprise Software Architect (CTO) – FinTech
- Started 5 tech-ventures (US, RO)

❖ **Expertise** – Applied ML & HPC

- Thermonuclear Fusion Research (90' – 99')
- Computational Finance (1999 - 2015)
- Precision Medicine (2015 - present)

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ALGOMEX(US) - bii(RO)

- ❖ Seed-stage ventures bringing novel technologies from **AI & Cognitive Computing** into the field of **Precision Medicine**

- ❖ **VISION** - leverage an impressive arsenal of technological discoveries in **Next Generation Sequencing, Bioinformatics, ML and HPC** to advance the current state of Medicine and to allow both clinicians and patients to take full advantage of the latest technological advances in **Molecular Biology and Informatics**

Outline

WHY

Needs & Challenges

- The impending **BIG RESET** - need Transformative Innovation
- Health vs. Medicine
- Brief history of Medicine
- Factors governing the dynamics
- Transition from Information acquisition > Knowledge extraction

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WHAT

Digital Medicine

- **Context** – Creativity crisis
- **Solution** – Great Convergence
- **Drivers**
 - Tech advancements
 - Bio-Med advancements
 - Cultural changes
- The **directions** of DigiMed
- **VC funding**

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HOW

Solutions

- **Information vs. Knowledge**
- Data is not enough
- Need for Intelligence- algos
- Tech(tools) vs. Solutions
- Education
- Examples & success stories

DIGITAL MEDICINE

*the most recent and palpable aspect of
the Convergence between Medical, Bio
sciences and IT&C*

- ❖ term was coined by Shaffer in 2002
 - ❖ defined as the “*technology and those products that are undergoing rigorous **clinical validation** and/or that ultimately will have a direct impact on **diagnosing, preventing, monitoring or treating** a disease, condition or syndrome*”
 - ❖ the first attempt to create Convergence between scientific disciplines.
 - ❖ great opportunities & challenges
-

WHY

Needs & Challenges Nevoi & Provocari

- ❖ Is Medicine ready for a BIG RESET?
 - ❖ Transition from Information age to the Cognitive Intelligence era:
INFO(DATA) → KNOWLEDGE
 - ❖ Knowledge accumulation:
 - Past - via exceptionalism & randomness
 - Future - systematic Knowledge Extraction
-

Health - is the level of functional or metabolic or efficiency of a living organism → a **State variable**, a measure of functionality

Influencing factors:

(1) Socio-economic environment:

- **Income & social status**
- **Education**

(2) Physical environment:

- **Habitat** – water, air, workplaces, housing, communities and transportation
- **Social support** networks – families, friends and communities

(3) Individual characteristics & behaviors:

- **Genetics** - inheritance plays a role in lifespan, healthiness
- **Life style**
- **Gender**

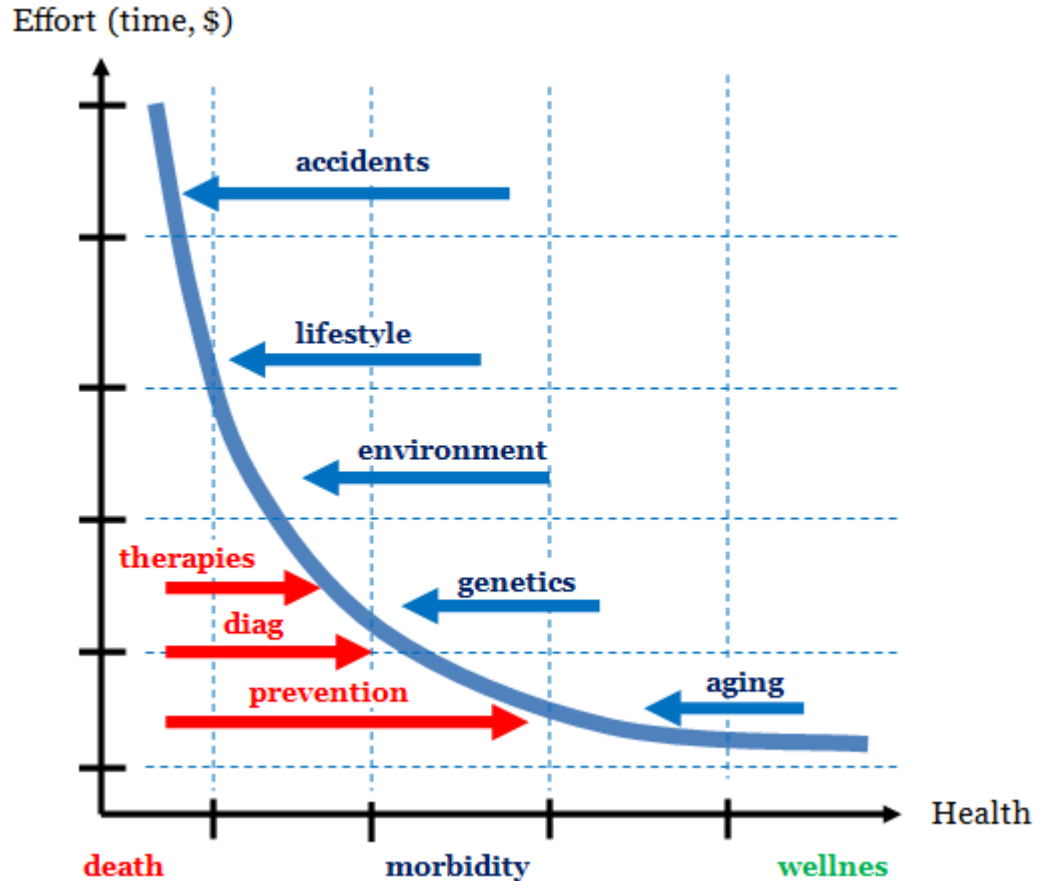
Medicine - is the science or practice of the diagnosis, treatment, and prevention of disease, typically via pharmaceuticals, surgery, therapies and medical devices.

MEDICINE is a toolset for:

- **diagnostic** - measure & detect
 - **treatment** - therapeutics - change/alter diseased state and eventually heal
 - **management** of chronic conditions - maintain, avoid degradation
-

BIG Question:

- ❖ What is the interaction mechanism between the Health degradation factors and the Medical tools available to counter and heal?
- ❖ Understanding this Dynamics is at the core of the Medical model
- ❖ Healthcare includes Medical interventions, but also concepts as PREVENTION and HEALING (coming into wholeness)



Brief history of Medicine



Individual skills - experience

- Artsy & not really Science
- “Flying blind“ era
- Trial & error – no data, K-Bases

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Evidence based

- “Population Medicine” – the Science of the Average/Median
- Statistical modeling
- Data collected @ low frequency (EHR, EMR, medical imaging)
- building & maintaining Knowledge bases & protocols

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P-4 Medicine

- Predictive - **Prognosa**
- Preventive - **Preveni**
- Personalized - **Personaliza**
- Participatory – **Participa direct**
- Massive data collection @ high freq:
 - ✓ Molecular – omics
 - ✓ Physiological – bio-sensors
 - ✓ Imaging
 - ✓ Behavioral
- Algo models – Mol / Phys / Functional
- Calibrate – make predictions

WHY – governing Factors

Commercial (\$\$\$)

- Should HC be a For-Profit activity?
- If not, how is going to be paid for?
- If yes, what are the boundaries of commercial profit?
- the actors:

Providers: Doctors, Hospitals, Labs,
Tech companies

Pharma

Payers: Gov. & private Insurance Co.

Consumers / Patients

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Regulations

Regulators – FDA, EMA, MHRA

- Heavy regulated industry
- Origins – *“turf wars between opposing interests”* Gov. vs. Private
- balance between public health safety and scientific innovation made available to clinicians & patients
- LE: Bureaucracy + Pharma
- SE: MDs, patients & society

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Quality of Life

- Quality-of-Life (**QoL**) is a determining factor - driven by Consumers of healthcare
- Empowering Consumers with:
 - **access** to both Information and Knowledge
 - **control** of the process (choices) and costs (price transparency)

WHAT – Digital Medicine

CONTEXT

Spectacular Tech progress

- labor productivity
- communications
- entertainment & leisure
- more informed consumer
- longer life span

Is Tech keeping up with Society?

- great societal challenges
 - sustainability: energy, food
 - healthcare access, rising costs

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Drivinging needs

Contemporary realities

- B of people are const. connected
- Human Genome was sequenced
- New nano-materials are developed
- ML algos to process Big Data
- IoT and epic data deluge

Is Healthcare taking advantage?

- cures: cancer, ALZ, obesity
- prevention vs. therapies
- empowering the consumer

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SOLUTION

Transformative Innovation

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- Past - Knowledge acquired via exceptionalism & randomness → systematic Knowledge Extraction

Advent of Inter-disciplinary field

- Life sciences: Bio-Medicine
- Informatics: Data & Software
- AI: Machine Learning & Algos

WHAT – Drivers

TECH advances

Constant Connectivity

- Internet & social media: FB 1.3 B
- wireless sensors / IoT
- Billions of devices ~ 7/indiv
- 90% world population will have MP

Compute Power

- > 2B transistors on cell phones
- 40,000 + health apps
- IT&C cloud computing
- 55 Peta FLOP or 10^{15} flpt-op/sec

Table. The Digitally Connecting World 2010-2020

	2010	2015 ^a	2020 ^a
World population, billion	6.8	7.2	7.6
No. connected			
Devices, billion	12.5	25	50
Devices per person	1.8	3.5	6.6
No. of smartphone subscriptions, billion	0.5	3.0	6.1
No. of wireless hotspots, million	3	47	500
No. of transistors, million/chip, nm	16/40	19/16	22/8
No. of sensors	20 Million	10 Billion	1 Trillion
No. of individuals sequenced	<10	400 000	5 Million

WHAT – Drivers

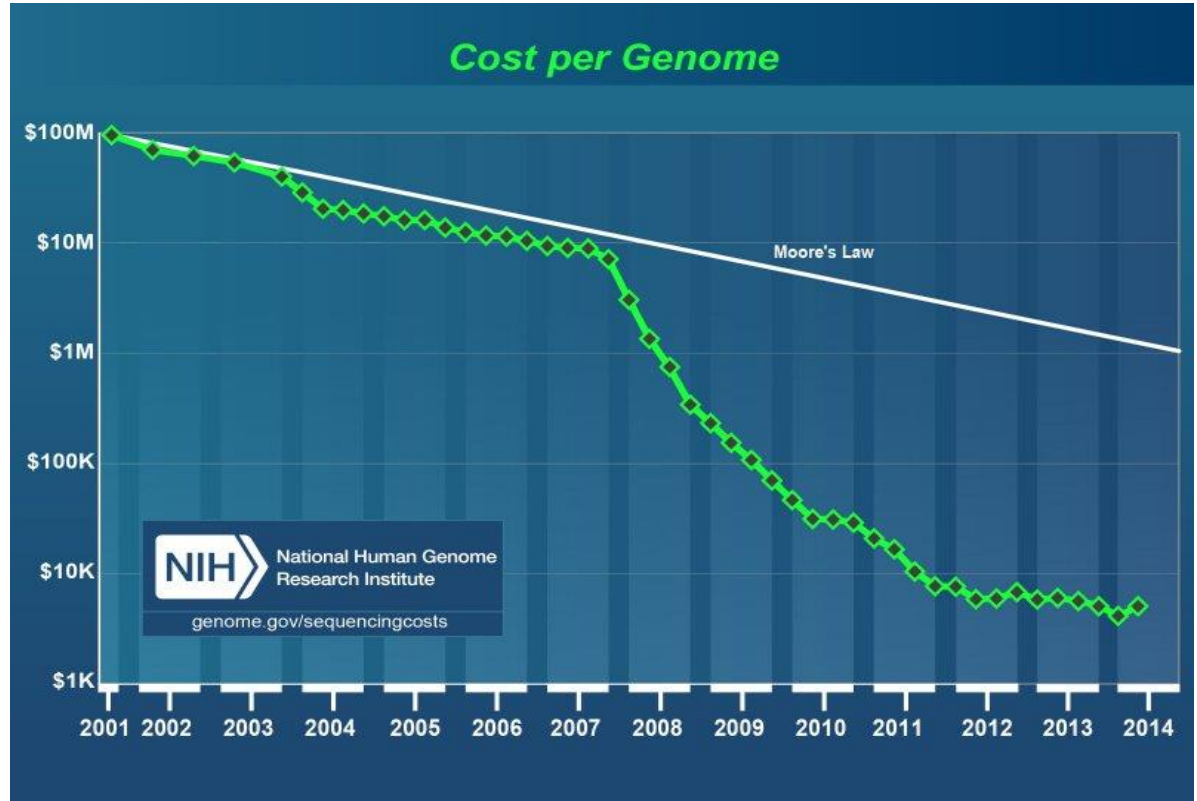
MEDICINE progress

Genomics




- Human Genome proj. – 3B, 10 yrs
- Next Generation sequencing
- Immunotherapy

Biomarkers

- Molecular
- Medical Imaging
- Physiological
- Behavioral



Utility of Biomarkers

PLAYERS	Potential Use case	Diagnosis	Prognosis	Prediction
Bio-Pharma 	<ul style="list-style-type: none"> Optimize patient-targeting for clinical trial recruitment (faster trials powered by smaller sample size) with improved eligibility criteria Continuously track disease progression and outcomes via real world evidence Develop low-cost, enhanced diagnostic solutions to personalize drug recommendations 	•	• •	• •
Providers 	<ul style="list-style-type: none"> Stratify patient populations to identify high, risk-high-cost individuals (predict readmission) Improve objectivity of diagnosis and selection of best treatments Monitor disease progression for appropriate interventions 	•	•	• •
Payers 	<ul style="list-style-type: none"> Individualize medical policy plans, including prior authorization schedules, for patients Track outcomes to design reimbursement policies for Bio-Pharma and providers 	•	• •	• •

WHAT – Drivers

CULTURE changes

Collaboration & Crowd sourcing

- Sharing data & knowledge
- Websites & blogs
- Online patient networks

Customized consumption has the potential to make medical practice:

- more precise,
- more effective,
- more widely distributed, and
- more patient centric

patientslikeme*

Already a member? Sign in.

Digital Medicine

Live better, together!™

Making healthcare better for everyone through sharing, support, and research

Join now

(it's free!)

Learn from others
Compare treatments, symptoms and experiences with people like you and take control of your health

Connect with people like you
Share your experience, give and get support to improve your life and the lives of others

Track your health
Chart your health over time and contribute to research that can advance medicine for all

Member Stories: How Paul Dalio thrives with bipolar

News
PatientsLikeMe and M2Gen Announce Partnership and Plans for Landmark Cancer Experience Study

We're giving patients and researchers a more complete picture of patients' experiences with cancer treatments and helping to shed new light on the factors that may affect outcomes and quality of life.

RWJF Awards Grant to PatientsLikeMe to Develop New Measures for Healthcare Performance

Jamie & Ben Heywood
Co-founders, PatientsLikeMe

"Our brother Stephen was living with ALS and we thought, 'there has to be a better way.' There is. By sharing our experiences, we can all contribute new data that can accelerate research and help create better treatments. Our experiences can actually change medicine... for good."

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TECH advances

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The great CONVERGENCE

"Medicine is about to go
through its biggest shake-up."

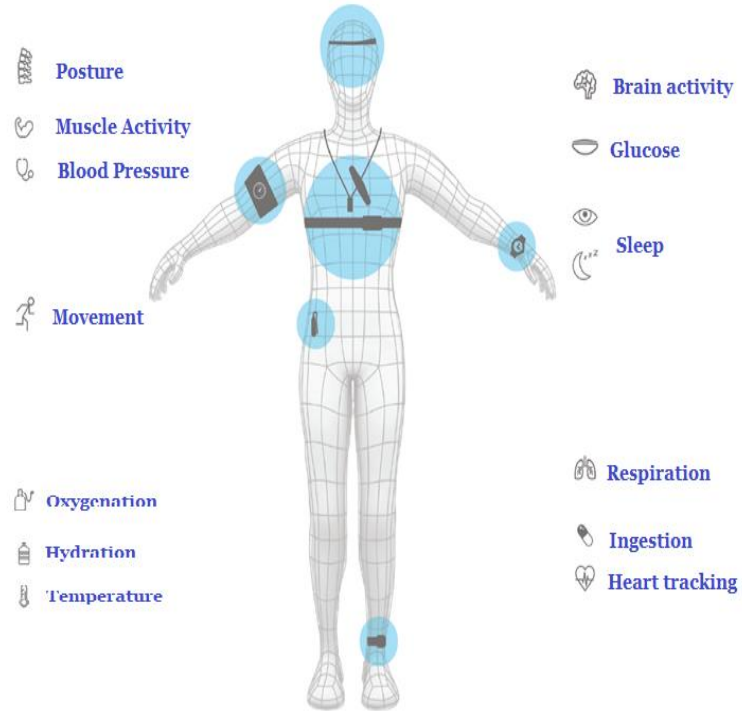
—Eric J. Topol, MD,
Scripps Translational
Science Institute

- ❖ “*The creative Destruction of Medicine*” by Eric TOPOL: “The ability to digitally define the essential characteristics of each individual – high def human – sets up a unique era in medicine”
 - ❖ Currently Medicine relies on the median, but in the near future it will be anchored to the individual.
 - ❖ The Consumer will need to step up, get involved, demand more!
 - ❖ the 4-C’s: **Connectivity**, **Collaboration**, **Customization** & **Computing** will converge into a new kind of Medicine
-

WHAT – Directions

Continuous Monitoring

- human Physiology & Biology via remote sensing technology
- tracking & analyzing data gathered in a longitudinal manner
- reveal new patterns of biomarkers that are informative of disease severity or progression
- open up new lines of investigation for researchers in Bio-Medicine
- *Virtual Physiological Human* – EU project: data collection, Phys models, simulators



WHAT – Directions

Digital Phenotype

- combining physiological data with other types of molecular data:
 - ✓ Genomics
 - ✓ Transcriptomics
 - ✓ Metabolomics
 - ✓ Proteomics
- **Behavior & environment** → Dawkins(1982) - extended Phenotype
- **Integrative approach** could reveal a highly complex & dynamic multi-dimensional picture of transitions between healthy & diseased states

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Systems Biology

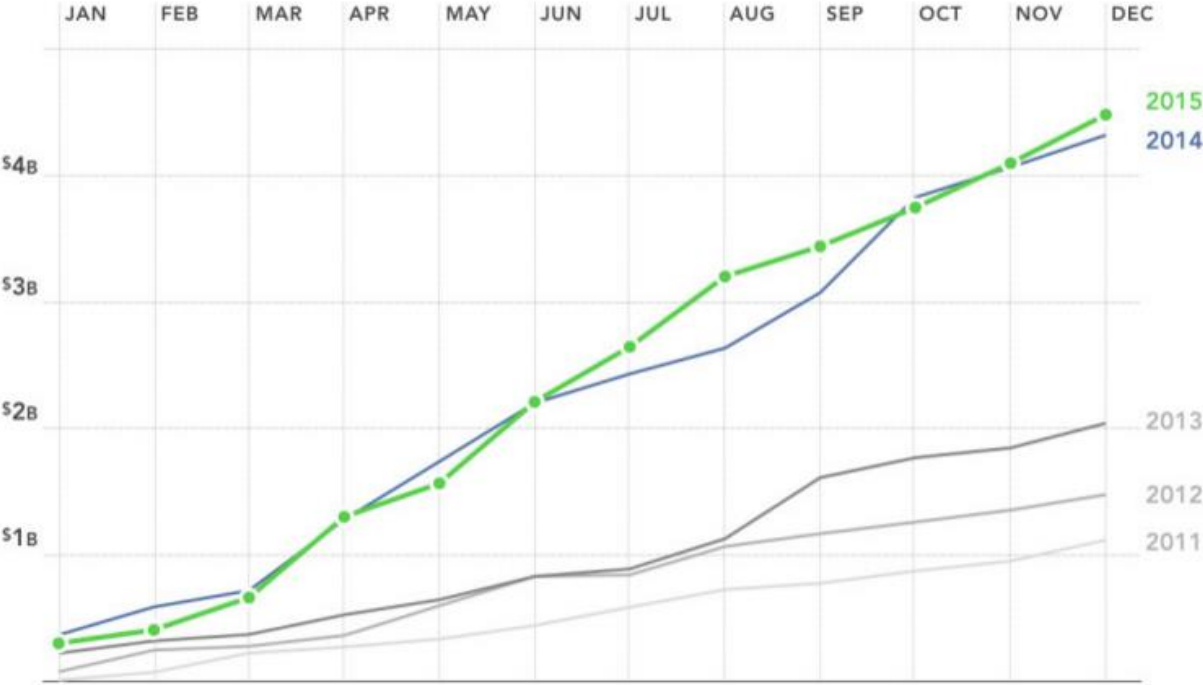
- **Field of study**: interactions between the components of biological systems, and how these interactions give rise to the function and behavior of that system
- **Paradigm**
- Set of **operational protocols**
- application of **Dynamical System** theory to Molecular Biology
- System Biology vs. **Bioinformatics** – tool set combining CS, Stats, Math & Engineering

Digital Health VC FUNDING

- ❖ We are in a **Creative Destruction** moment in healthcare, but it's still very early
 - ❖ Very experienced serial Hi-tech entrepreneurs & VC money are starting to pour in
 - ❖ a budding Digital Health ecosystem is emerging – tremendous opportunity
-

Digital Health FUNDING

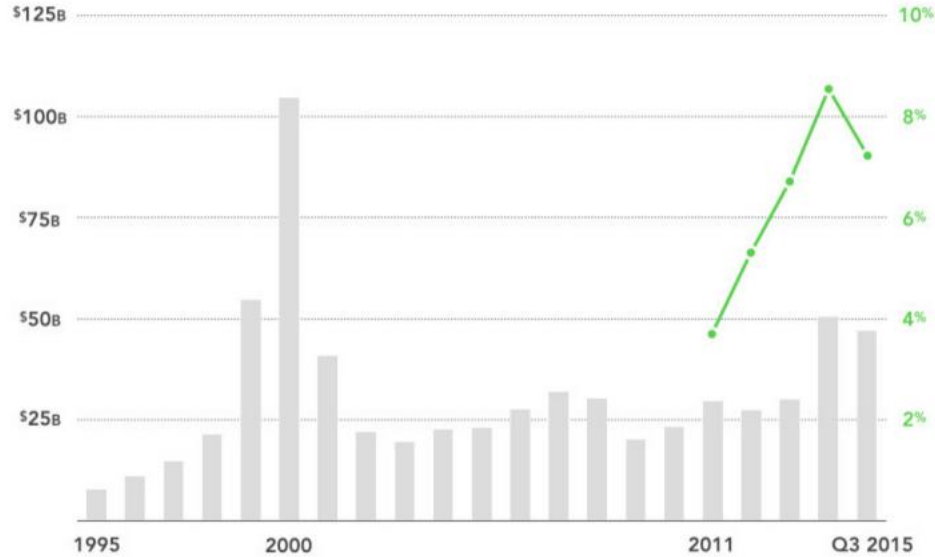
2011-2015



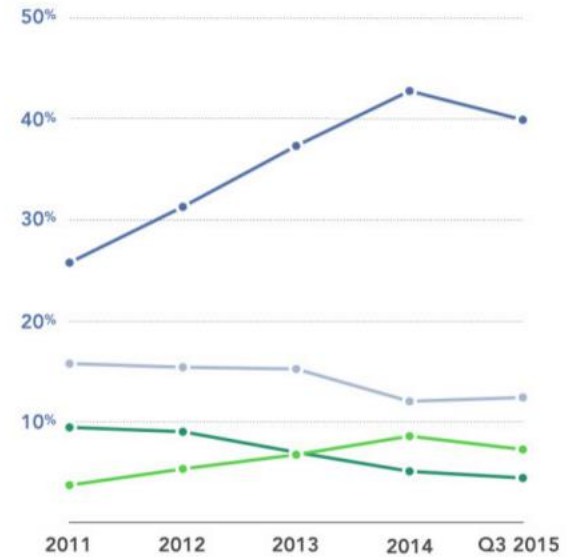
VENTURE FUNDING

2011-Q3 2015

VENTURE FUNDING



PROPORTION OF FUNDING BY SECTOR



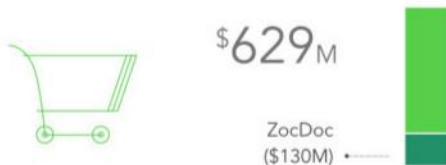
AVERAGE Deal Size & Count

2011-2015



DIGITAL HEALTH FUNDING by sectors

2011-2015



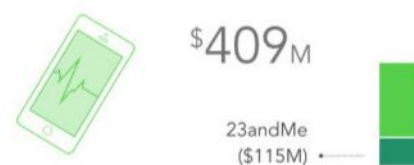
HEALTHCARE CONSUMER ENGAGEMENT

Consumer tools for the purchasing of healthcare products and services or health insurance (B2B and B2C)



WEARABLES AND BIOSENSING

Wearable or accessory devices that detect specific biometrics and are designed for consumers



PERSONAL HEALTH TOOLS AND TRACKING

Software platforms to support the delivery of medicine customized to an individual's genetics (or other 'omics profile or phenotype)



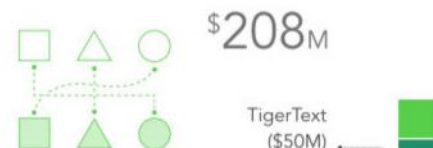
PAYER ADMINISTRATION

Management and administration tools for payers (e.g. fraud detection, third-party payment, portal management)



TELEMEDICINE

Delivery of healthcare services (synchronous or asynchronous) through non-physical means (e.g. telephone, digital imaging, video)



CARE COORDINATION

Coordination and management of care for a patient, across providers or other caregivers

WHAT Conclusions

- ❖ DIGITAL MEDICINE is both a tremendous **opportunity** & a great **challenge** to the medical profession!
 - ❖ There will likely be a **significant change** in the **patient-physician relationship**: much of the diagnostic and monitoring functions performed by physicians today can be offset to computers and algorithms for patients
 - ❖ Hospital rooms could be replaced by remote monitoring via the patient's bedroom; many office visits will change from **physical** to **virtual**
-

HOW

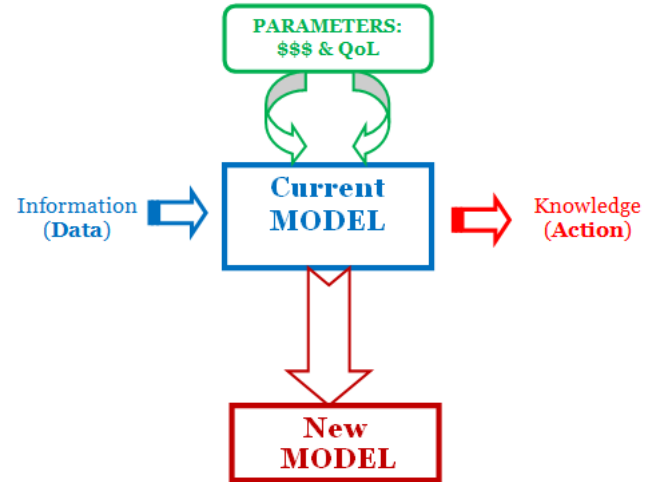
Knowledge & Solutions

- ❖ Information vs. KNOWLEDGE
 - ❖ Tools vs. SOLUTIONS
 - ❖ EDUCATION
 - ❖ Examples of success stories
-

INFO vs. KNOWLEDGE

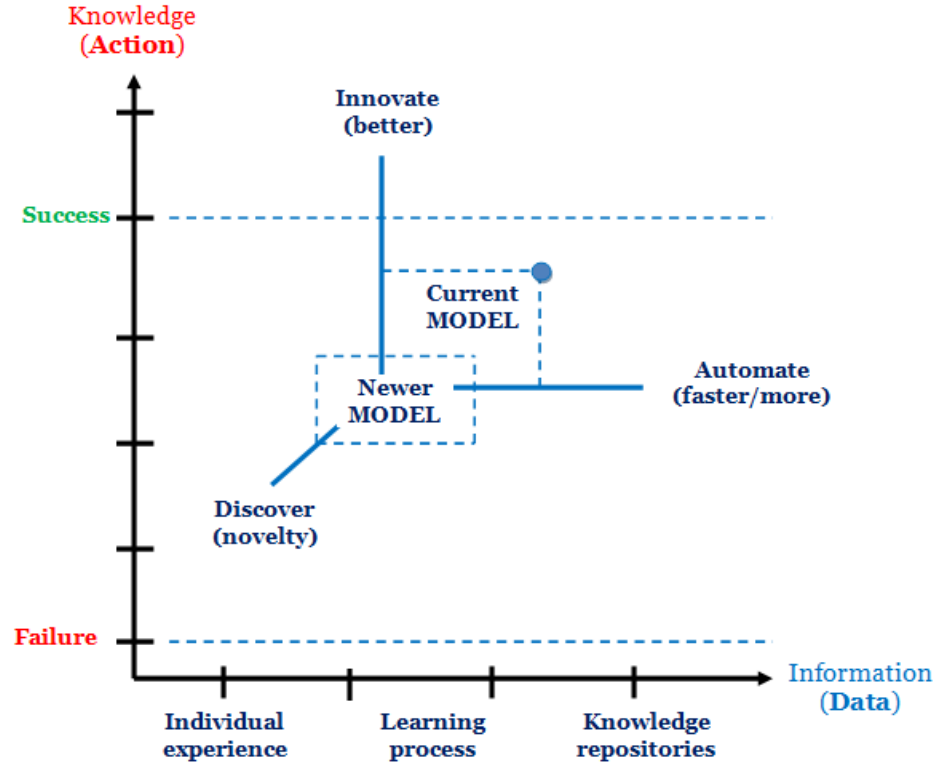
- **Scientific & tech discoveries** → a plethora of gizmos and gadgets, together with an epic flood of data
- The world has generated 5 Exabytes (10^{18}) of data by 2003, and it generates that much every other day!
- 2010 the **Digital universe** - the zettabyte threshold (10^{21})
- **Supercomputers** operate at 2,500 trillion ops/sec
- Much of the data in the future is going to come from Omics and Physiological sensors
- For each fully sequenced human genome (depth 40) we ~250 GB, x 1M humans to be seq. in the next 5 years

This blitzkrieg of information has had little effect on providing solutions to solving major scientific puzzles that threaten our very existence!!!



Priviledged info domains

- Aviation
- Capital Markets
- Media
- Meteo
- Sports



TECHNOLOGY – Tools

The world is not just flooded with DATA it is also brimming with TOOLS:

- devices,
- software,
- methods,
- models,
- languages,
- protocols,
- theories, etc...

SOLUTIONS

❖ We are living a very rapid transition from the **Information Age** → the **Cognitive Intelligence era**

❖ **Information** → **Knowledge** ~ **Wisdom**

❖ Knowledge needs to be **acquired by design** through systematic knowledge extraction

❖ The paradox of great technological accumulation not having the desired impact on solving the most important societal problems could be addressed by **Transformative Innovation** - and this will require Inter-disciplinarity, Convergence & Disruptive spirit

❖ **The world needs Technological solutions (platforms) to REAL world problems!!!**

EDUCATION

- ❖ This brave new world needs **experts** that simply do not exist now!
- ❖ **Develop educational curricula** & graduate programs to educate the new workforce → **partnerships Gov – Academia - Industry**
- ❖ Example: Quant in Finance!
- ❖ **Educate the Consumer** – empower the general population with Information & Knowledge
- ❖ Healthcare needs to be really democratized – **share knowledge & responsibility!**

SUCCESS Stories

Examples from the recent past: Manhattan project & the Space program

What money, good planning & VISION could buy (or not?):

- 100 B\$ - 1956 - built the largest hwy system in the world (160,000 miles)
- 100 B\$ - 1974 - DARPA created the Internet (Defense Advanced Res. Project Agency)
- *200 B\$ - 1990' - promoted the use of EHR - "the place where data goes to die..." Dr. Dona Edelson - Univ. Of Chicago School of Medicine*

OPPORTUNITIES

New era MEDICINE

- Emerging diagnostic & therapeutic **digital health interventions** have the potential to alter the way medicine is practiced & experienced

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Modeling the Human

- The patients are representing an **enormous repository of information** that needs to be harvested as a partnership not only in clinical care but in research and discovery

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New Businesses

- The winners in this emerging space will be the companies that can successfully **blend both technology & medical expertise**

CHALLENGES

SKEPTICISM

- The existence of large numbers of digital health companies with unsubstantiated claims whose medical value is untested has muddied the waters
- Key opinion leaders in certain areas have publicly expressed their skepticism *vis-à-vis* this space

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REIMBURSEMENT

- Reimbursement has historically been both a driver & a limitation to market uptake of new medical products, and digital medicine will likely be no exception.
- Patients may be willing to pay out of pocket for certain types of digital medicine products, i.e. therapeutics that represent a safe, non-pharma alternative.

CONCLUSIONS

❖ This new field of endeavor is still in the **conception phase!**
There is not much to brag about - Big Data, Telemedicine, Health IT, Digital this, that... the truth is that we have created lots of tools & collected Big Data

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- ❖ Need to start learning from it, by extracting **ACTIONABLE Knowledge** that will heal the sick and prevent the healthy one to becoming sick
- ❖ There is a tremendous **OPPORTUNITY** in front of us today
- ❖ And a **BIG CHALLENGE!** It is the challenge of the current and future generation

***“You never change things by fighting the existing reality.
To change something, build a new model that makes the existing
model obsolete”***

Buckminster Fuller

RoGeniX

Platformă Integrată de Valorificare a Inovației Românești



Problema

Problemă **sistemică** foarte serioasă - utilizarea resurselor de inteligență și creativitate Românească

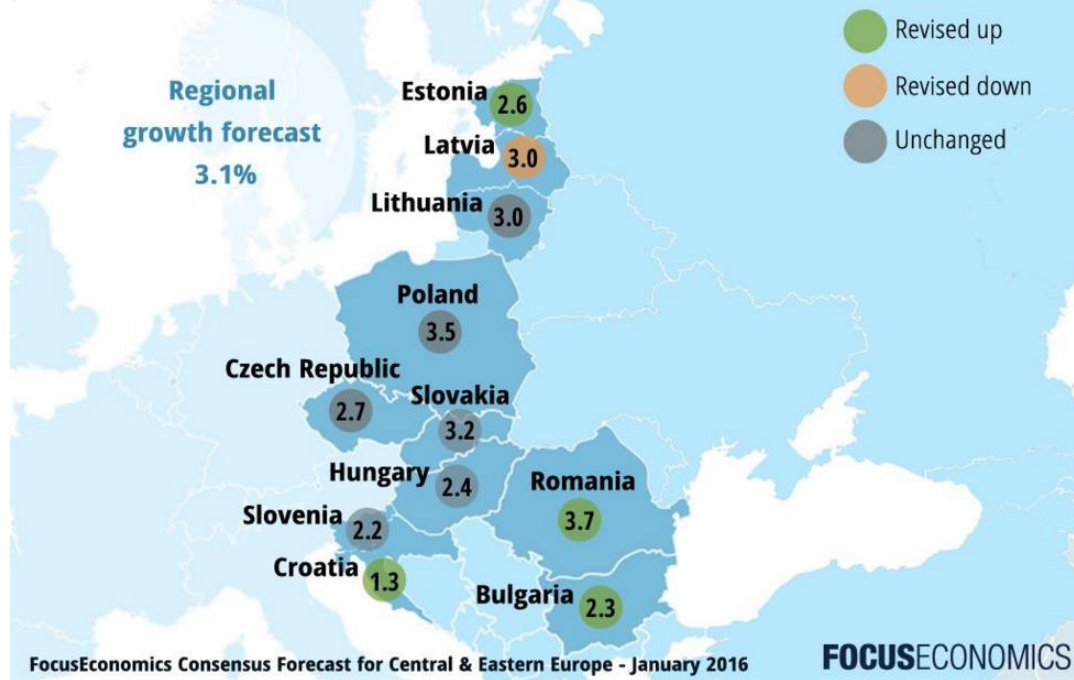
- Implicații profunde la nivelul societății Românești
- Fenomenul de "brain-drain" - scară F.F. mare
- România pierde anual K' de specialiști cu mare potențial de impact în economia locală

Estimări: 10K' de academici și cercetători și 100K' de specialiști au părăsit România în ultimii 25 de ani

Oportunitatea

- România continuă să aibă la dispoziție un rezervor important de capital uman cu **potențial inovativ și creativ**
- Ultimele 2 decenii - fenomen accentuat de "**brain-drain**" → a afectat "productia" științifică și dezvoltarea inovativă din România
- Potențial important de a accesa "know-how" **științific-tehnologic–afaceri-antreprenorial** venind din partea Diasporei, și de a îl utiliza în scopul promovării spiritului inovativ și antreprenorial din România în rândul absolvenților de universități și al tinerilor cercetători

CENTRAL & EASTERN EUROPE 2016 GDP GROWTH FORECASTS (%)



Scopul RoGeniX

- Incuraja academicii și cercetătorii din România să-și dezvolte propriile firme în domeniul științei și tehnologiei, cu suport logistic și financiar venit din partea Diasporei și al partenerilor din SUA.
- România are un potențial real de a deveni "the next Start-up Nation" în deceniul următor
- Dacă **potențialul uman & inovativ** va putea fi aliniat cu o **viziune pe termen lung** și cu **suport material & logistic** adecvat, acest deziderat va putea deveni realitate!

Modalități de implementare

[1] Etapa **SEED**:

S-elecție - prin crearea de **parteneriate** cu centre Universitare și de Cercetare din România, cu Incubatoare și Acceleratoare de afaceri deja existente

E-valuare - prin constituirea unui **Comitet de Selecție** alcătuit din personalități ale lumii științifice și academice românești, experți, oameni de afaceri și investitori din SUA - **alinieră inovației** sub forma unor prototipuri de produse și servicii cu cerințele piețelor este elementul cheie

ED-ucare - prin constituirea de Școli Antreprenoriale de tip **Accelerator**, la care să fie admise Idei și Echipe selectate de către Comitetul de Selecție

[2] Etapa **DCOM**:

D-ezvoltare - prin constituirea unui program de tip **Incubator** care poate dura între 6-12 luni, la care să fie admise Idei și Echipe care au absolvit școala antreprenorială de tip Accelerator

COM-ercializare - prin crearea unui sistem de **comercializare** a inovației produse ca și rezultat al etapei **SEED**

US – Board of Advisors

Edith Nutescu - Prof. of Pharmacy - UIC

Dan Nicolae - Prof. of Statistics - Univ. of Chicago

Dana Tudorascu - Prof. of Biostatistics @ U. of Pittsburgh

Dorin Boldor - Prof. of Biology @ LSU

Sergiu Pasca - Prof. of Neuropsychiatry @ Stanford

Mark Duncan - Prof. of Medicine @ University of Colorado

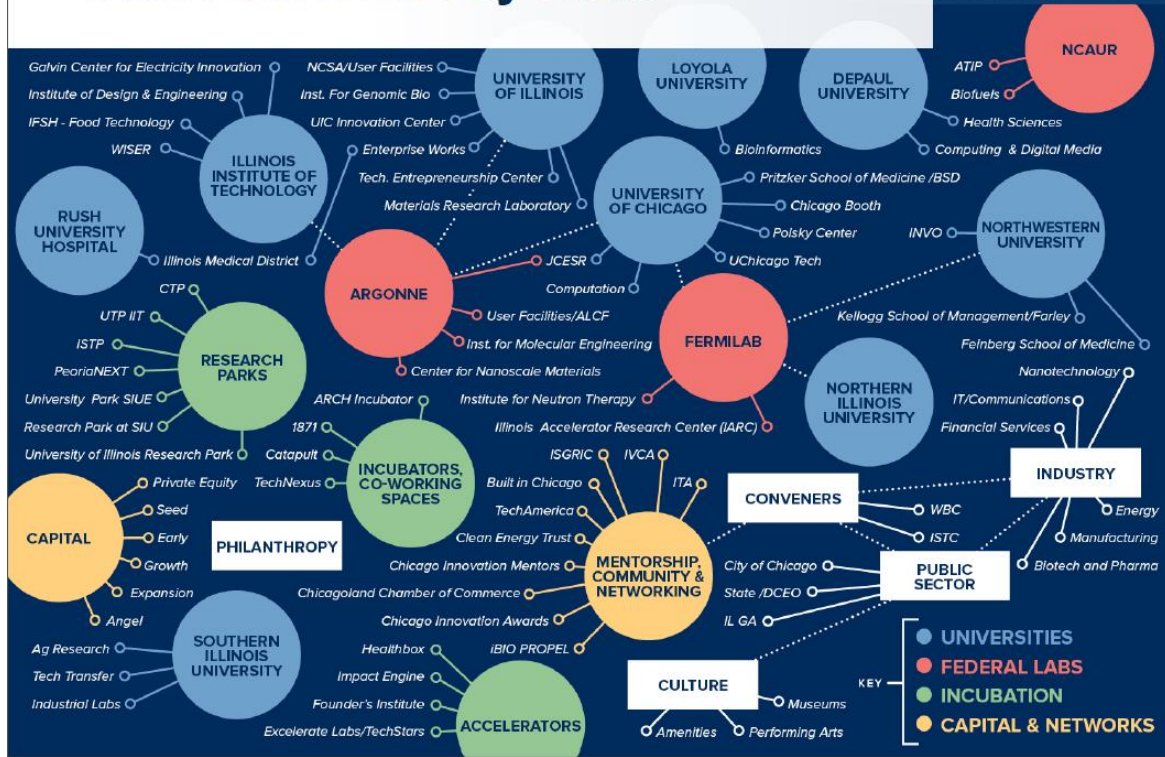
Octavian Bucur - MD, PhD - Harvard Medical School

Dan Ciresan - Senior Researcher at ISDIA Switzerland - World pioneer in DNN

Serhat Cicecoglu – ANKA Capital, Chicago

Serban Georgescu - MD & serial entrepreneur - Boston

Innovation Ecosystem





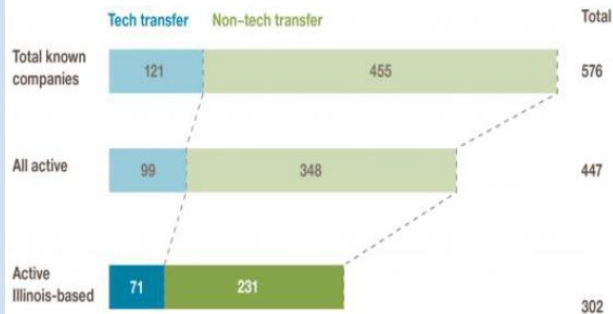
University-Driven Startups



~450 active startups created over last 5 years

Licensing grown double the national rate over last 5 years

All university startups, Illinois, founded 2009-14



Source: ISTC Tech Transfer and University Entrepreneurship surveys, December 2014



University Research and Innovation



University Innovation

Startup and Entrepreneurial Support

Industry Collaboration



- Engineering & Nanotech
- Life Sciences
- Supercomputing

- EnterpriseWorks, ResearchPark, HTI
- Technology Entrepreneur Center
- IllinoisVENTURES and RPOC Fund
- I-Start/I-Corps

- Private Sector Program at NCSA
- Center for Nutrition, Learning & Memory
- UIC Innovation Center
- Technology Innovation Center



- Design & Engineering
- WISER/Electricity Innovation
- Food Technology

- University Technology Park
- Knapp Center for Entrepreneurship

- Idea Shop and Interprofessional Projects
- Illinois Smart Grid Innovation Cluster
- Institute for Food Safety and Health



- Life Sciences
- Engineering
- Nanotechnology

- NUvention and Farley Center for Entrepreneurship and Innovation
- Levy Inst. Entrepreneurial Practice Innovation & New Ventures Office

- NUCATS institute for clinical
- Baxter- Northwestern Alliance
- Center for Hierarchical Materials Design



- Life Sciences
- Physical Sciences

- Polsky Center for Entrepreneurship
- New Venture Challenge
- UChicago Tech and CIE

- Chicago Innovation Fund
- Chicago Innovation Exchange (CIE)
- Center for Computation Biotechnology & Genomic Medicine (CCBGM)



- Agricultural sciences
- Life Sciences
- Advanced energy technology

- Southern Illinois Research Park
- Saluki Innovation Lab and Fund
- Technology and Innovation Expo

- Cooperative Research Center for Embedded Systems
- Center for Advanced Friction Studies



- Physical Sciences
- Mathematical Sciences

- Office of Technology Management

- Engineers in Residence
- EIGERlab
- Microelectronics R&D Lab

Bio-Informatics Intelligence – new start-up based in Romania

Application of AI to Medical Diagnosis & Therapies

1. Development of an Algorithmic Processing Data (APD) platform for **Clinical Oncology**. The platform will allow the extraction of clinically actionable knowledge from Genomic, Clinical & Medical Imaging data
2. Development of Machine Learning Algorithms to speedup Virtual screening of Chemical compounds used in **Drug Discovery** by the Pharmaceutical companies

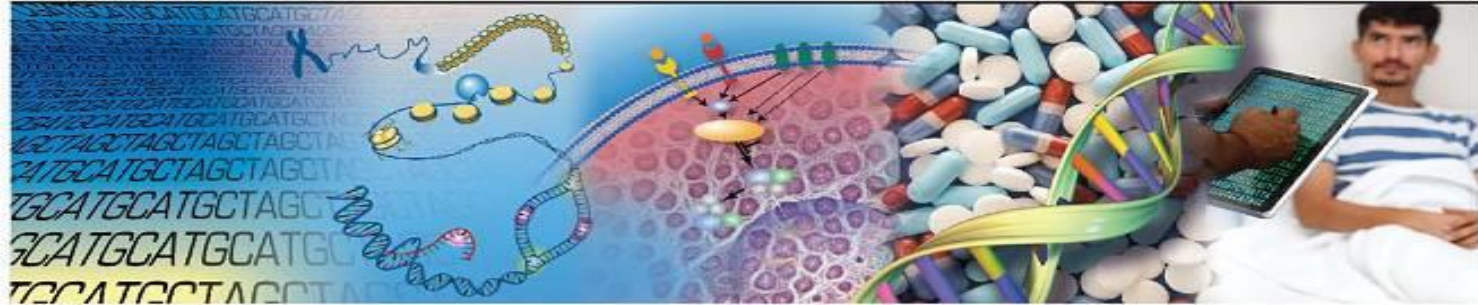
Understanding
the Structure of
Genomes

Understanding
the Biology of
Genomes

Understanding
the Biology of
Disease

Advancing
the Science of
Medicine

Improving the
Effectiveness of
Healthcare



Next Generation Sequencing

focus is on very large data generation, mainly from WE/G seq. and data processing

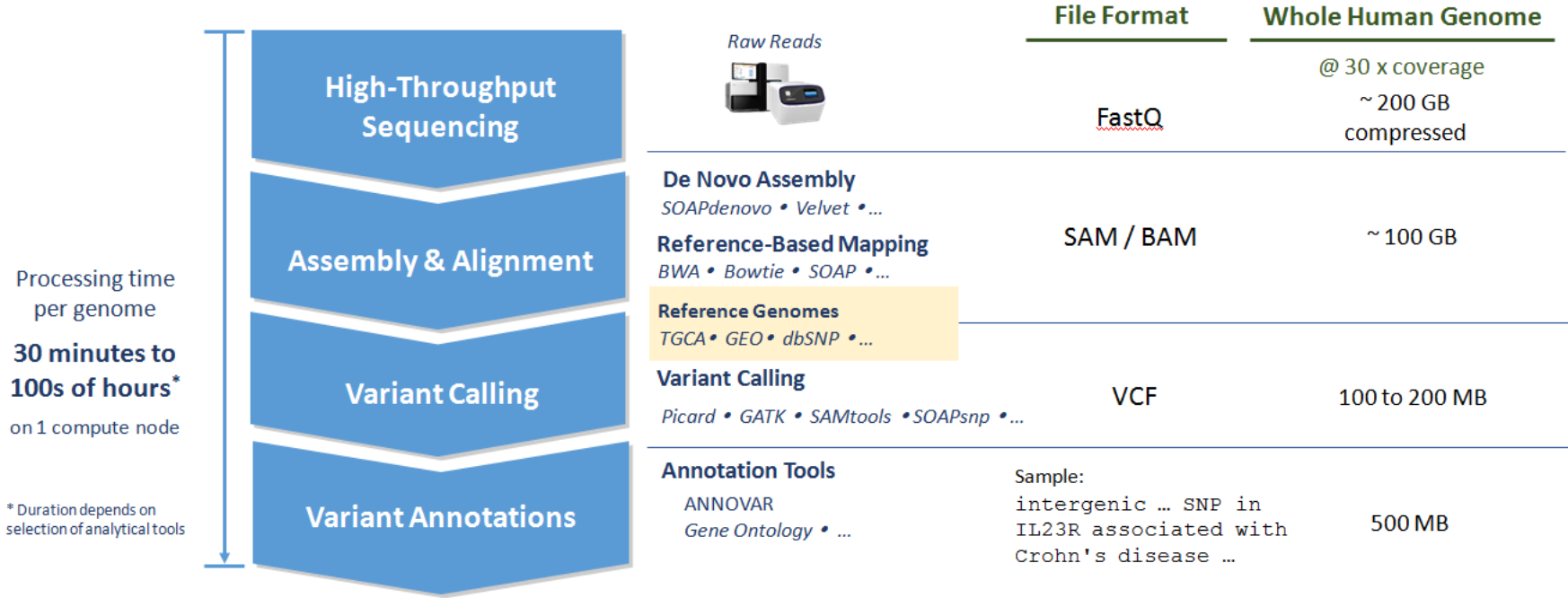
Translational Research/Early Discovery

focus is on data integration and the analytics required to identify biomarkers, understand disease mechanisms

Personalized HC /Clinical Genomics

focus is on delivering genomic medicine to patients to improve outcomes by associating patients with known genomic specific treatments

NGS



Each human genome can have a few million variants




Genome Pipeline

Ultra-Rapid Genome and Exome Data Analysis




22min
FASTQ → VCF

WHG @ 30x
Coverage



99.37%
Precision

SNP + INDEL
Combined



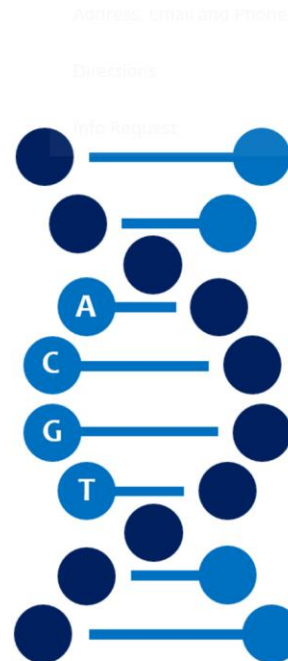
98.31%
Sensitivity

SNP + INDEL
Combined



**Hybrid
Cloud**

Onsite, Cloud, and
Hybrid Solution

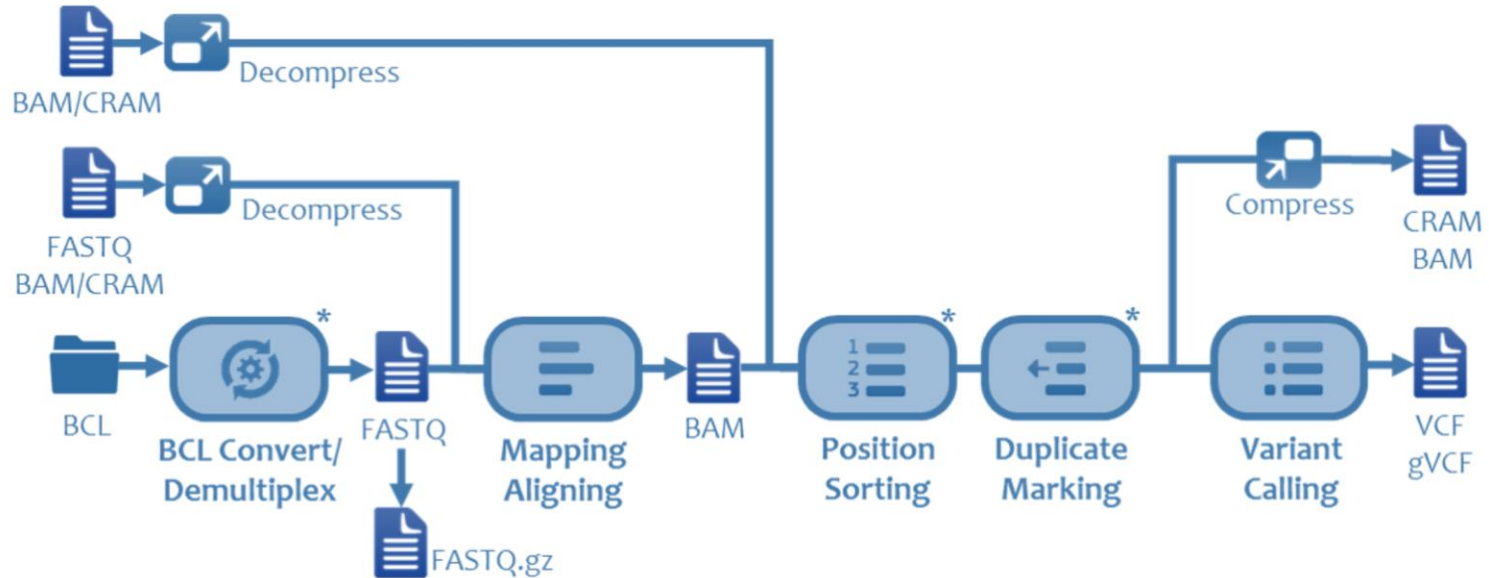


DRAGEN Genome Pipeline

[Directions](#)

[Info Request](#)

The DRAGEN pipeline offers supreme flexibility of data analysis. DRAGEN can handle multiple input formats and produces industry standard output formats compatible for downstream analysis. DRAGEN can stream BCL data directly from sequencer storage, a solution unique to the DRAGEN pipeline, enabling the customer to go directly from raw sequencing data to an output VCF. DRAGEN can also convert BCL to FASTQ or BAM/CRAM, then proceed with the standard DRAGEN pipeline.



Q & A



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