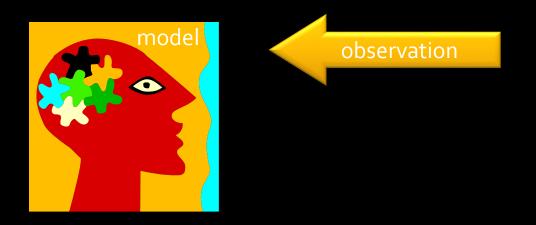
István Csabai Eötvös University, Budapest Department of Physics of Complex Systems

BIG DATA IN BIOLOGY

Evolution of (data) sciences: stone age





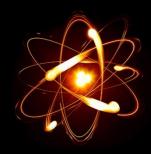
Evolution of (data) sciences: stone age



observation









Evolution of (data) sciences: stone age



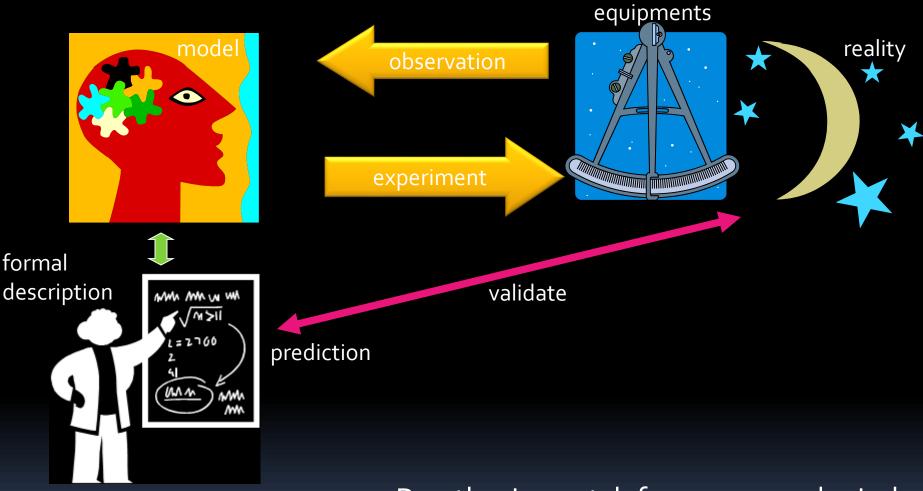
observation







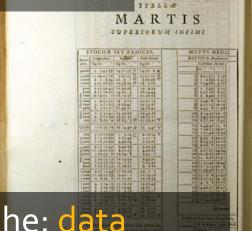
Evolution of (data) sciences: pre-industrial age



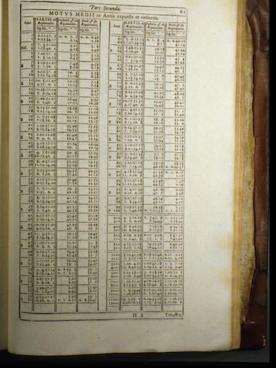
Prosthesis, crutch for senses and mind

First "Data Science"

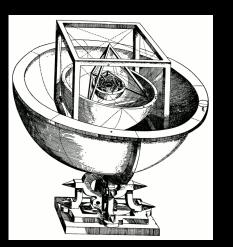


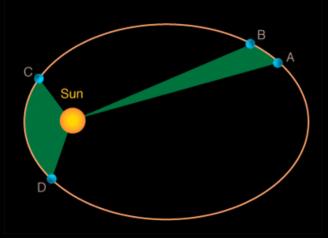


Tycho Brahe: data
Johannes Kepler: model
Isaac Newton: theory



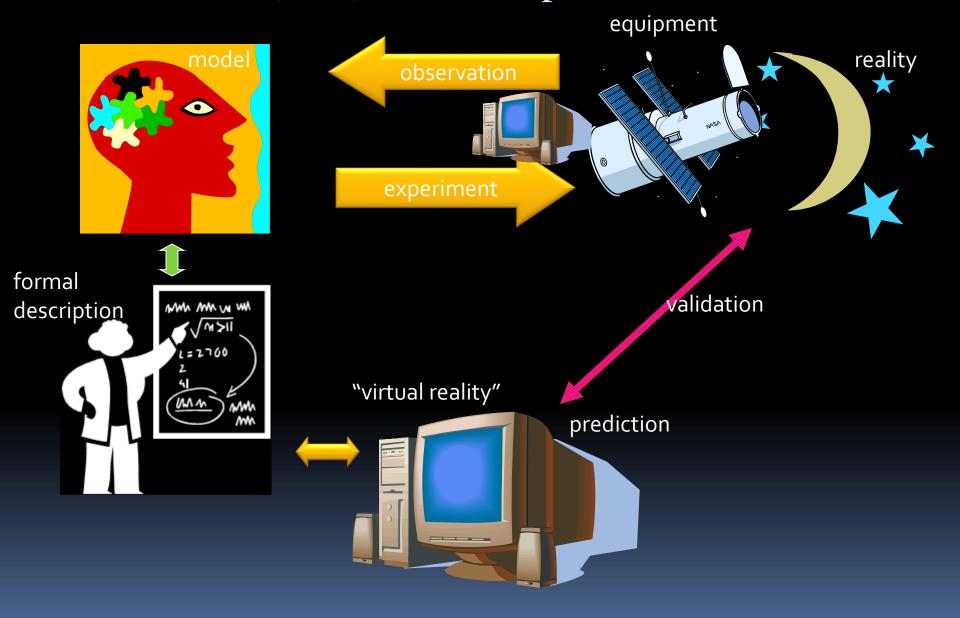
Johann Kepler , *Tabulae Rudolphinae* (1627)



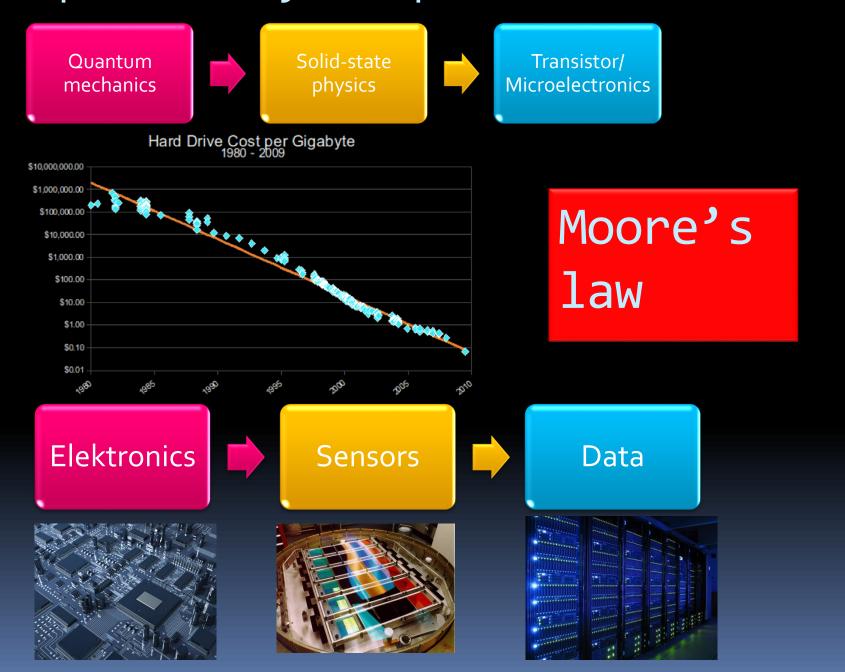


$$F=Grac{m_1m_2}{r^2}$$

Evolution of (data) sciences: present



Exponentially cheaper devices - more data





Prototype of data-intensive science project:

SLOAN DIGITAL SKY SURVEY (SDSS): THE 3D MAP OF THE UNIVERSE 1995-2005...

2.5m

120Mp - 2.5Tp

5 years:10TB

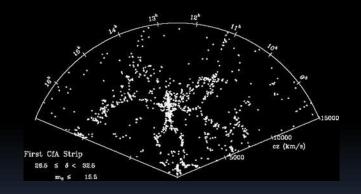




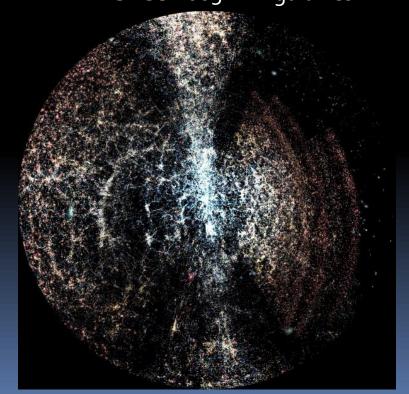


CfA 1989: 1100 galaxies

SDSS 2005: 1M galaxies





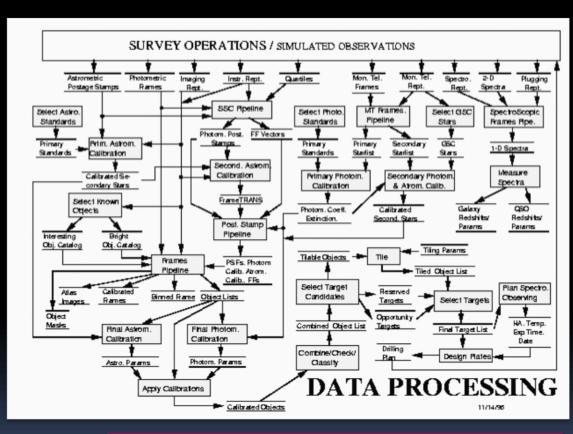


Data processing challenge

- Automatic pipeline
 - More than 150 man year development
 - First astro project where most of the money is spent on software rather on the telescope
- "Big Data"
 - More than 300 million objects, 300+ parameters each
 - 100 TB raw data, 10 TB catalogues, 2.5 terapixels
 - PUBLIC (SQL) DATABASE ("Virtual Observatory")



Tables (SQL) + Raw data (files)



The sloan digital sky survey: Technical summary DG York + SDSS collab.The Astron. J.l 120 (3), 1579 (2000)

PZ Kunszt, AS Szalay, I Csabai, AR Thakar; ADASS IX 216, 141(2007)

Astronomical data setsastronomical queries

Star/galaxy separation

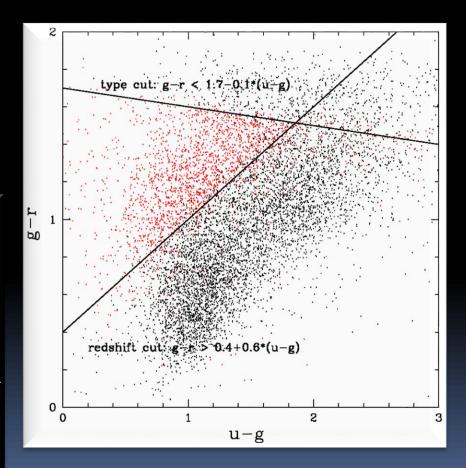
Quasar target selection

"cuts"

Multi-dimensional polyhedra

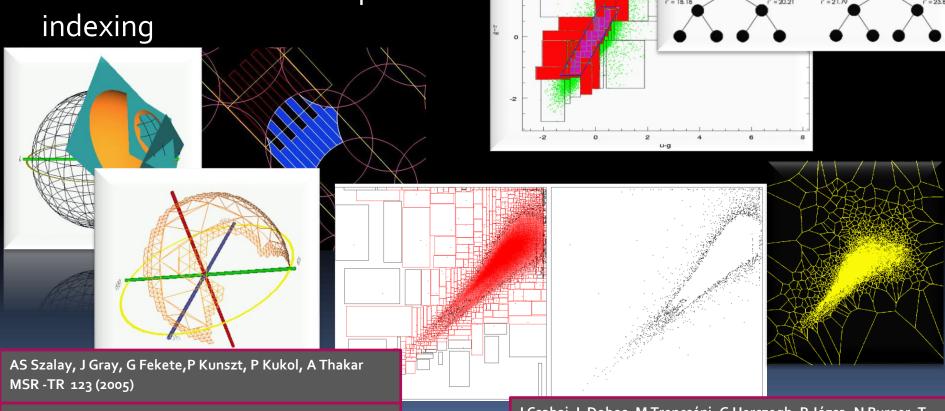
Skyserver: several million queries per year

```
\label{eq:petroMag_i} \begin{subarray}{l} petroMag_i > 17.5 and (petroMag_r > 15.5 or petroR50_r > 2) \\ and (petroMag_r > 0 and g > 0 and r > 0 and i > 0) and (\\ (petroMag_r-extinction_r) < 19.2 and (petroMag_r - extinction_r < (13.1 + (7/3) * (dered_g - dered_r) + 4 * (dered_r - dered_i) - 4 * 0.18) ) and ( (dered_r - dered_i - (dered_g - dered_r)/4 - 0.18) < 0.2) and ( (dered_r - dered_i - (dered_g - dered_r)/4 - 0.18) > -0.2) and ( (petroMag_r - extinction_r + 2.5 * LOG10(2 * 3.1415 * petroR50_r * petroR50_r)) < 24.2) ) \\ or ( (petroMag_r - extinction_r < 19.5) \\ and ( (dered_g - dered_i - (dered_g - dered_r)/4 - 0.18) > (0.45 - 4 * (dered_g - dered_i)) ) and ( (dered_g - dered_r) > (1.35 + 0.25 * (dered_r - dered_i)) ) ) and ( (petroMag_r - extinction_r + 2.5 * LOG10(2 * 3.1415 * petroR50_r * petroR50_r)) < 23.3 ) \\ ) \\ \end{subarray}
```



New skills: Indexing, databases SDSS data "read through"~1 day

- Astronomers should learn: Database programming, computer geometry, search trees, ...
- Multidimensional- and spherical indexing



T Budavari, L Dobos, AS Szalay, G Greene, J Gray, AH Rots ASP Conf . Ser. 376, 559 (2007)

I Csabai, L Dobos, M Trencséni, G Herczegh, P Józsa, N Purger, T Budavári, AS Szalay Astr. N. 328 (8), 852 (2007)

New skills: Database management systems, virtualization

RDBMS

- +Developed for business purposes, optimised IO/memory accsess, declarative language (SQL), parallel queries, standard API (ODBC, JDBC)
- -Relation data model is often not enough (matrices, graphs, [arrayLib]), not distributed [skyQuery, Graywulf]
- New technologies: NoSQL,BigTable, Hadoop/MapReduce, column store, -> distributed servers
- Virtual Observatory (now: "cloud")
 - "If the data mountain does not go to
 - OpenStack, Docker, Jupyter
 - SciServer
- L Dobos, AS Szalay, J Blakeley, B Falck, T Budavári, I Csabai Astronomical Data Analysis Software and Systems XXI 461, 323 (2012)

L Dobos, I Csabai, AS Szalay, T Budavári, N Li Proceedings of the 25th International Conference on Scientific and Statistical Database Management, ACM, (2013)

SkyServer

- Web browser-based synchronous access
- Meant to support several levels of users
 - From casual to moderately advanced gueries
 - From simple form-based to direct SQL queries
 - From cone (radial) search to crossid type searches
- Visual tools to browse image and catalog data
- Stored procedures
- API access, e.g. emacs interface, sqlcl (command-line)
- Strict limits on <u>execution time</u> and <u>output size</u>
 - Fair use for everyone, robots/crawlers discouraged
- Introduction to SQL and Sample Queries

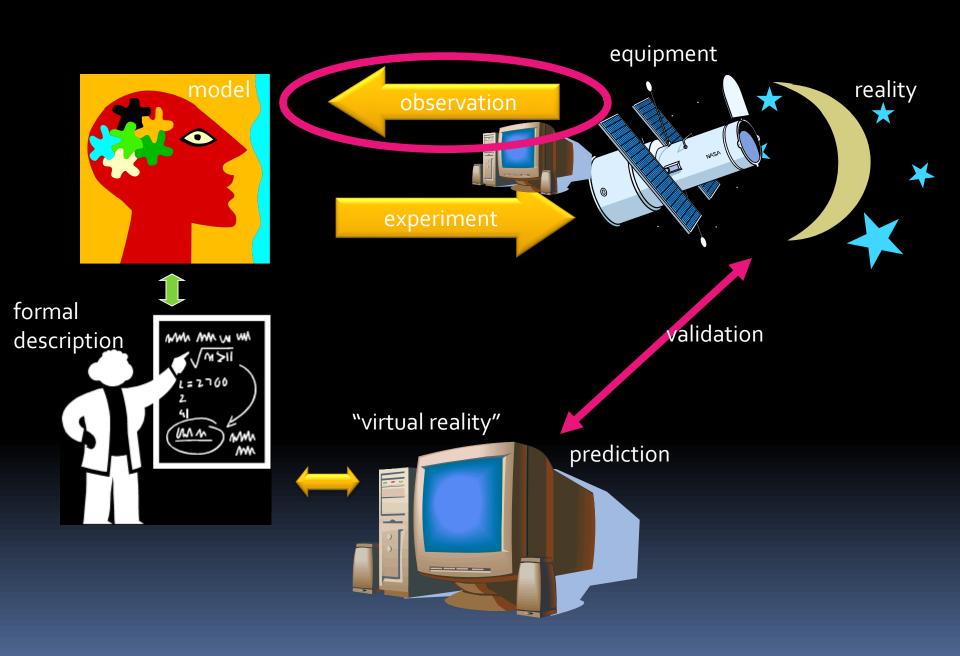
Cas Jobs

- Batch Query Workbench, personal user DB (MyDB)
 - Quick mode: 1 minute cutoff
 - Submit mode: up to 8 hours in "long" queue
 - 24-hr queue for collab members
- MyDB database to save results of your queries
 - Define your own functions, procedures too
 - Share your tables with collaborators (groups)
- Job history, plotting, FITS/CSV/VOTable output
- Restricted (collab-only databases)
- Table Import (upload) for your own data
- Groups to share your results with collaborators
- Command-line access Java tool also downloadable
- SOAP/Web Services access

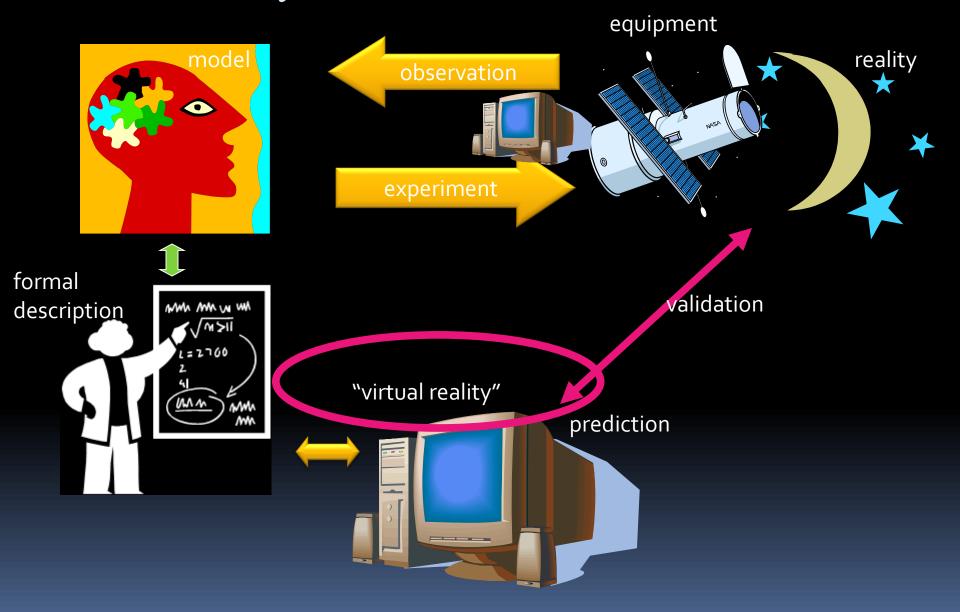
L Dobos, T Budavári, N Li, AS Szalay, I Csabai Scientific and Statistical Database Management, 159-167 (2012)

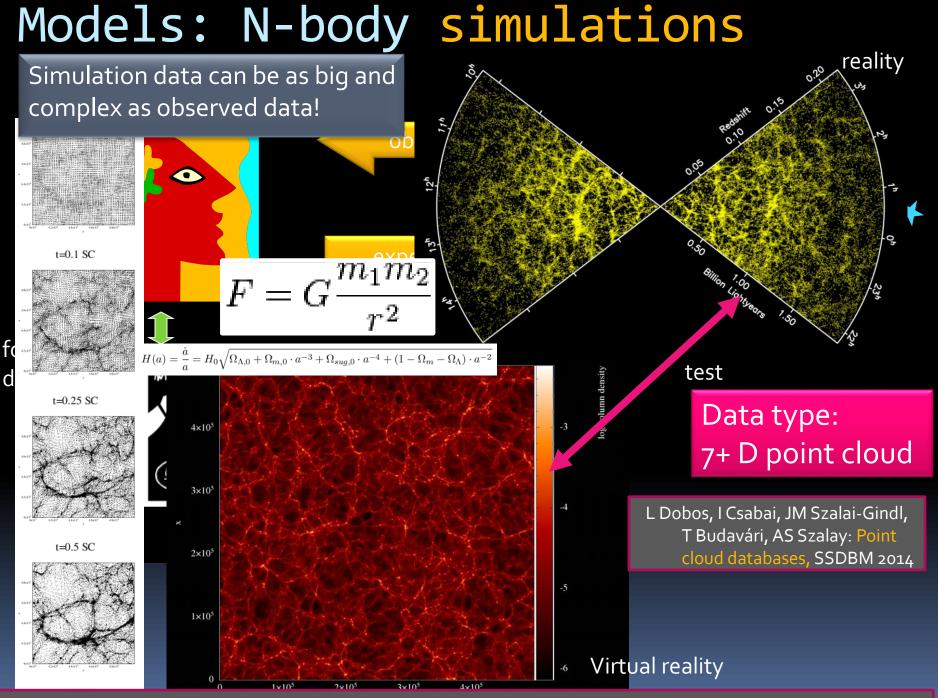
L Dobos, T Budavári, I Csabai, AS Szalay Astronomical Data Analysis Software and Systems (ADASS) XIII 314, 185 (2007)

T Budavári, L Dobos, AS Szalay, G Greene, J Gray, AH Rots Astronomical Society of the Pacific Conference Series 376, 559 (2007)



"Virtual reality"



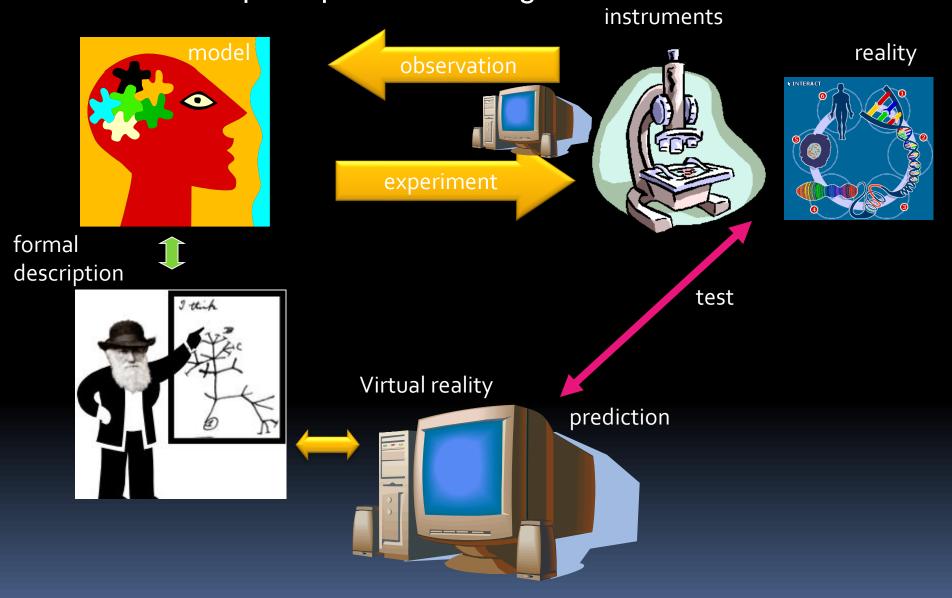


G Rácz et al., Concordance cosmology without dark energy, Mon Not R Astron Soc Lett (2017) 469 (1)

Real Universe - Virtual Universe



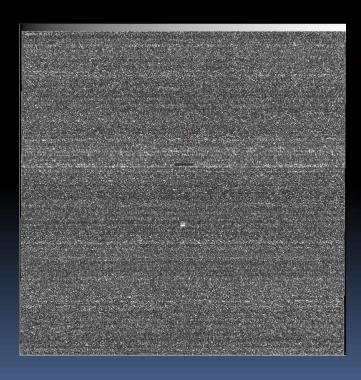
Not only astronomy: genomics, environmental sciences, social sciences... Complex questions – large datasets



DATA-INTENSIVE GENETICS NEXT GENERATION SEQUENCING

Expression microarray study (2010)

- Affymetrix HG U133 Plus2
 - Raw data 67Mpix (photometry!)
 - 604258 probes
 - 54675 probe set (~gene)
 - 207 samples (colorectal cancer)



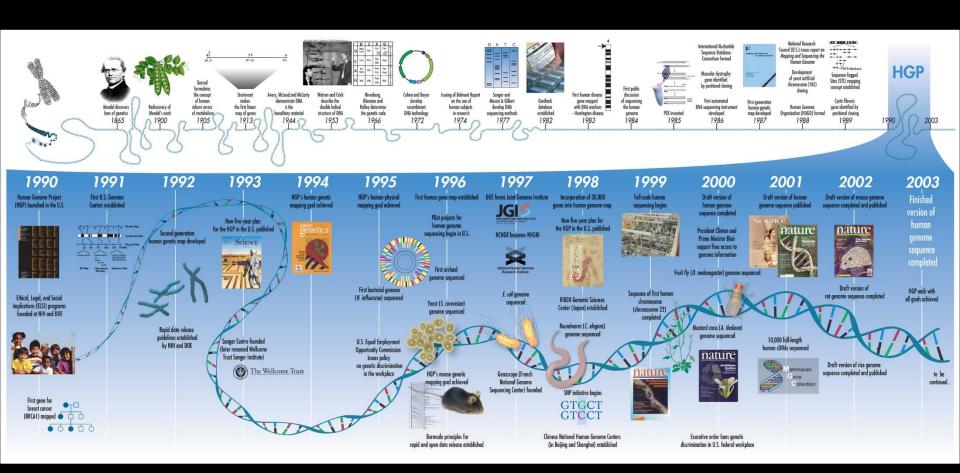
Raw data: Image Processed data: 54675D vectors + metadata



"similar" to astronomy

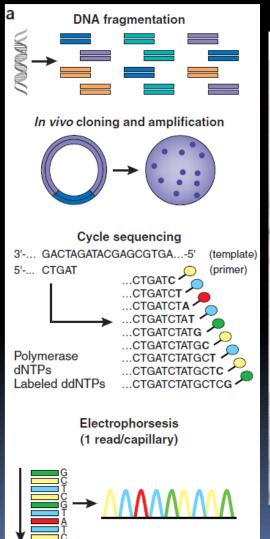
- Large databases (own + public)
- Computer-intensive data analysis

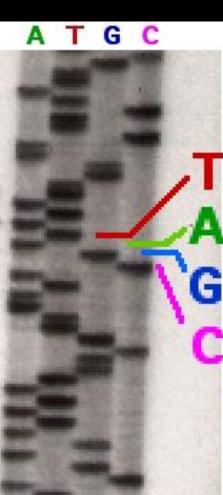
Map of the genome

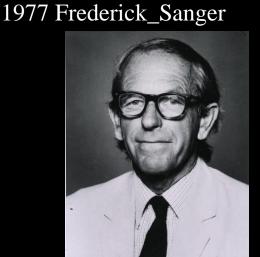


High througput sequencing history:

Sanger

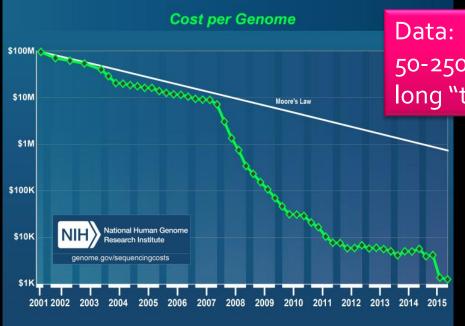






- DNA is fragmented
- Cloned to a plasmid vector
- Cyclic sequencing reaction
- Separation by electrophoresis
- Readout with fluorescent tags

Moore's law in gene sequencing



50-250 or 3Bn letter long "texts"

Human genome sequencing 1990-2003: 13yrs /2.7 Bn USD

2016: ~days/1000 USD

2020: ?????

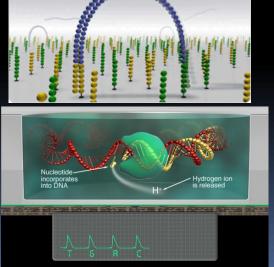
CCD!

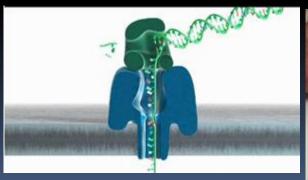
- X Prize, 100 genom, 30 days, \$10k – cancelled (2006)
- Microarray
- Mass spectroscopy
- Digital microscopy

. . . .

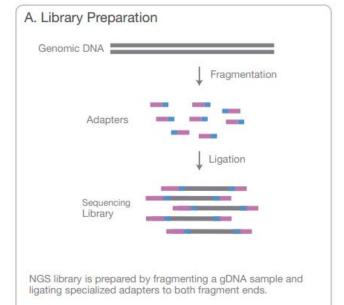
Oxford Nanopore 100Mb,\$900

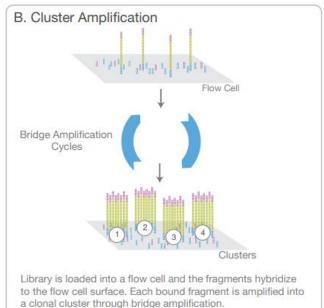


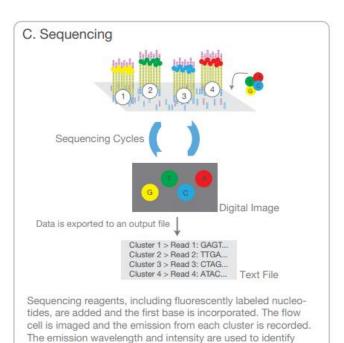






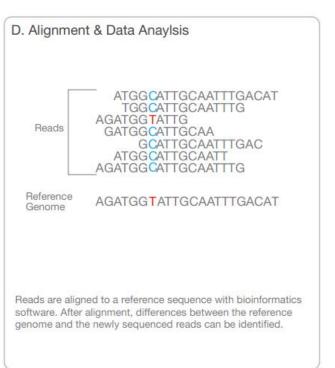


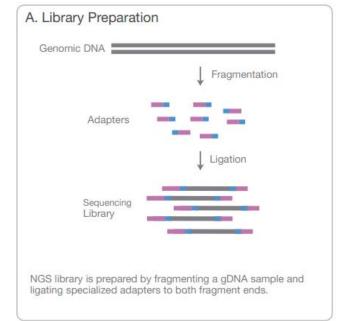


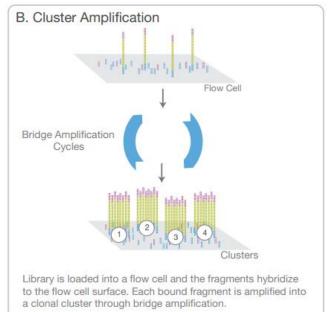


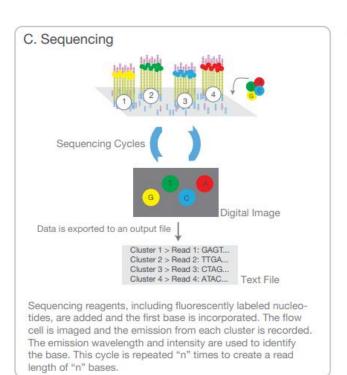
the base. This cycle is repeated "n" times to create a read

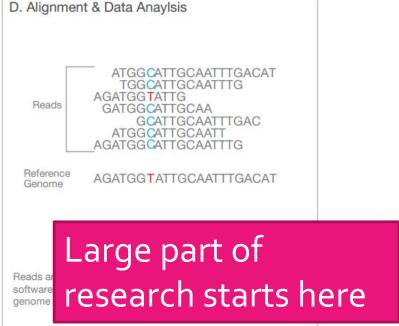
length of "n" bases.



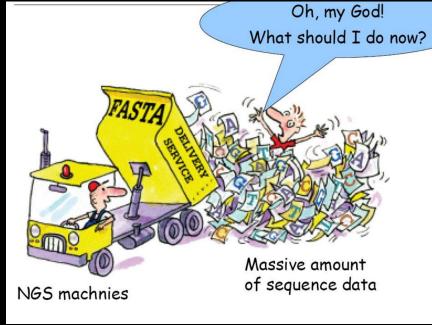








NGS alignment/assembly Big numbers



- Computer speed: ~109 instr./sec
- Genome: ~ 10⁹ nt
- NGS: ~109 short reads
- Brute force: ~10¹⁸ comparisions
- -> Need for clever indexing/search algorithms!



The Cancer Genome Atlas

http://cancergenome.nih.gov/

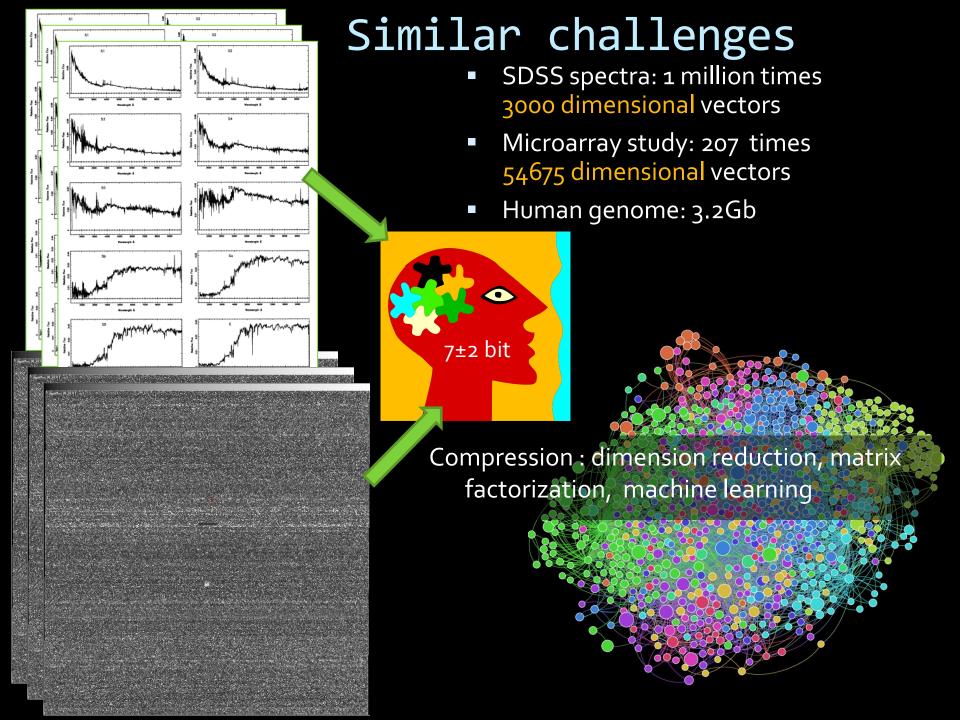
3.2Bn nucleotides / human genome

The Cancer Genome Atlas (TCGA) is a large-scale, collaborative effort led by the National Institutes of Health to map the genomic changes that occur in over 30 types of human cancer, including nine rare tumors. Its goal is to support new discoveries and accelerate the pace of research aimed at improving the diagnosis, treatment, and prevention of cancer.

TCGA is a community resource project. The information generated by TCGA is centrally managed and entered into databases as it becomes available, making the data rapidly accessible to the entire research community. By January 2014, TCGA had generated one petabyte of data for about 10,000 cases of tumor and matching normal tissue samples.

TCGA data are available in two data repositories: the TCGA Data Portal and the Cancer Genomics Hub. All data can be accessed directly from the TCGA Data Portal regardless of which repository houses the data file.

Baroque combination of complex metadata and various raw data file formats



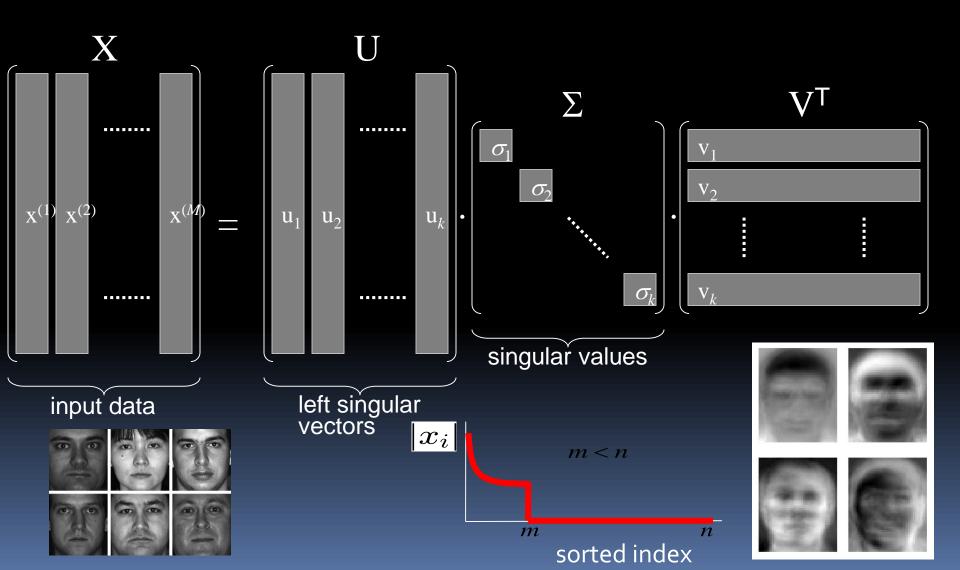
Due to the underlying physical laws, data vectors does not fill the whole space, rather lie on lower dimensional surface/subspace (this is why we can understand the word!)



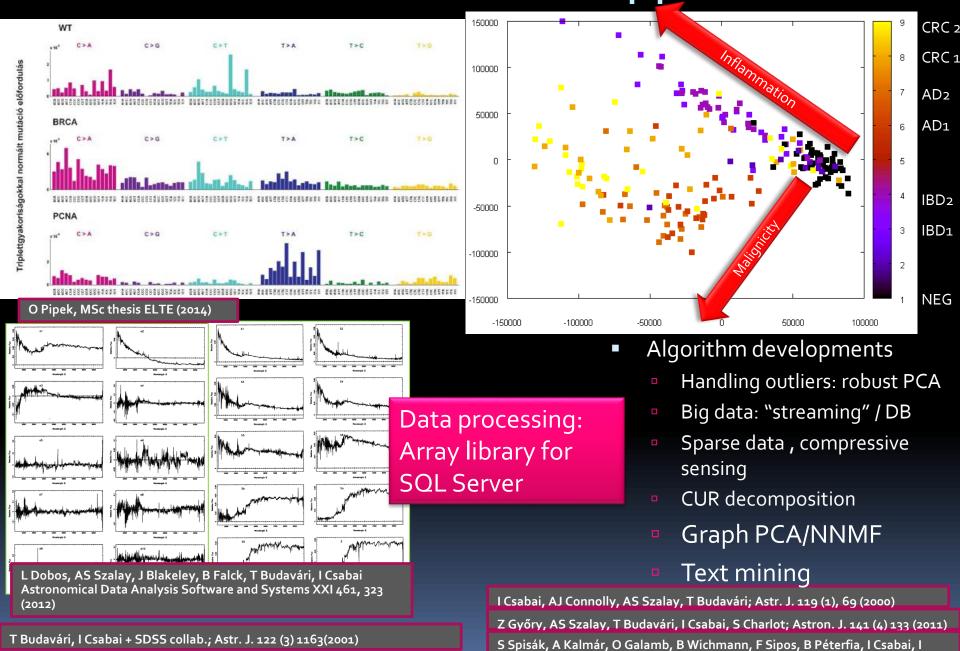
Projection ~ compression ~ model

Linear projection: PCA - SVD

$$X = U\Sigma V^{\mathsf{T}}$$



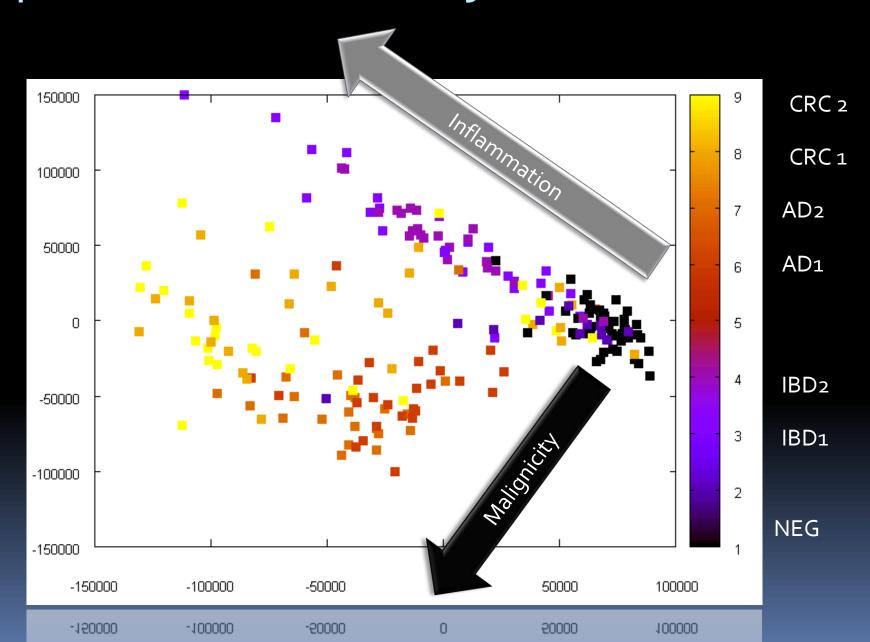
Dimension reduction: applications



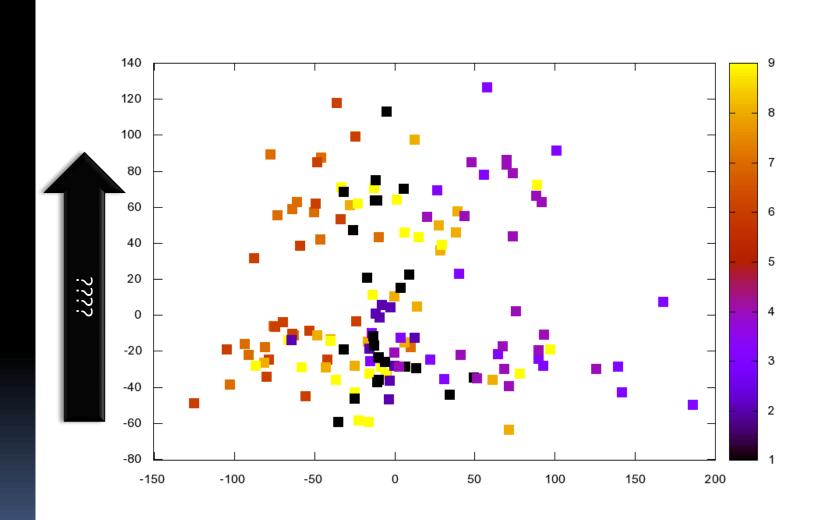
R. Beck, L. Dobos, C. Yip, A. Szalay, I. Csabai; MNRAS 457 (1), 362-374 (2016)

Kovalszky, S Semsey, Z Tulassay, B Molnár; PloS one 7 (10), e46215(2012)

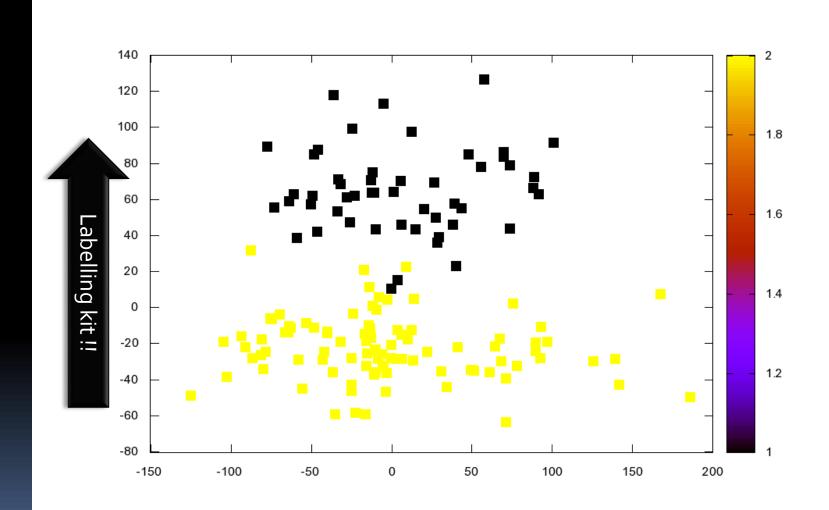
Expression microarray: 54675D -> 2D



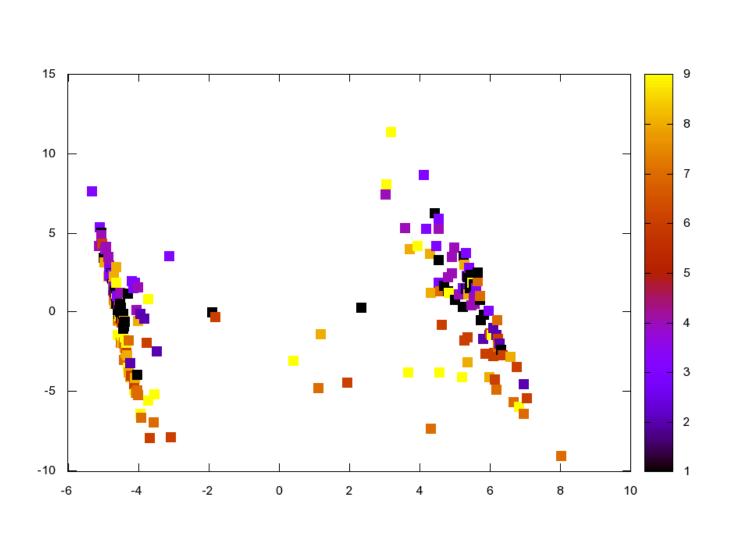
PCA2, PCA3 clusters?



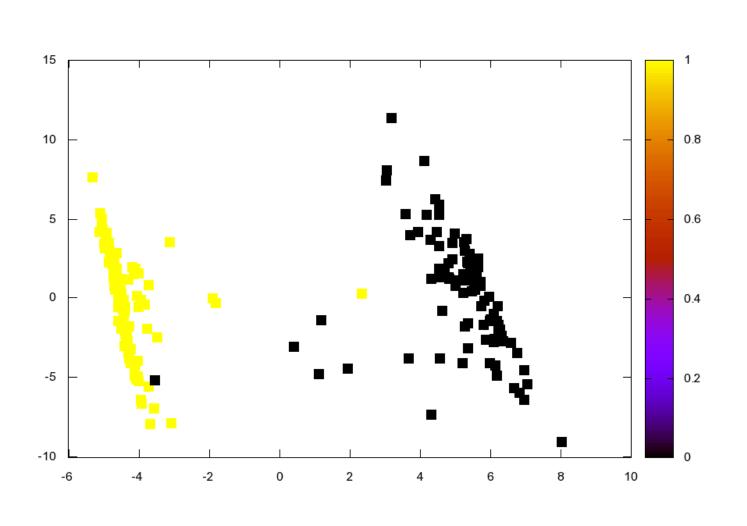
PCA2, PCA3 clusters



PCA - KEGG pathways (ribosome)

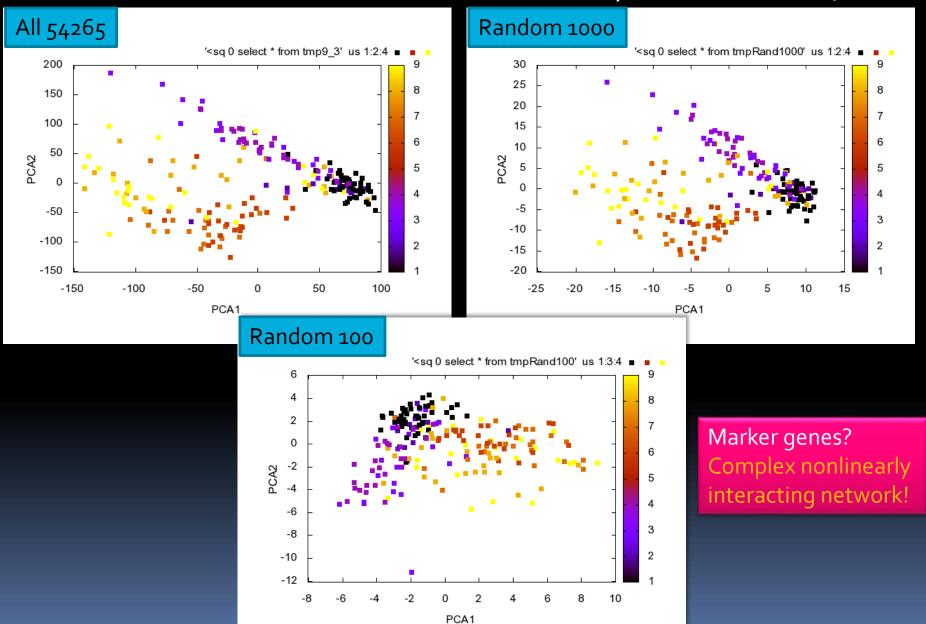


PCA - KEGG pathways (ribosome)

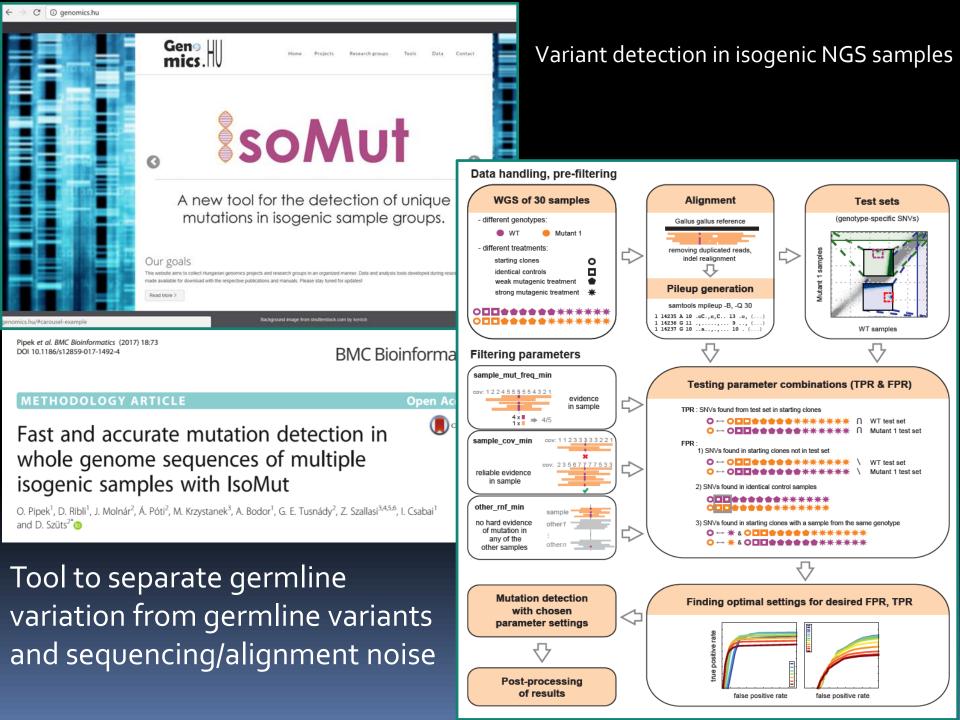


"Realize that everything connects to everything else."

/Leonardo da Vinci/



RECENT PROJECTS



go Advanced search

Journal home > Advance online publication > 25 July 2016 > Full text

Journal home Advance online publication L About AOP **Current** issue **Archive** Press releases ■ Online submission

For authors

For referees

Original Article

Oncogene advance online publication 25 July 2016; doi: 10.1038/onc.2016.243

Loss of BRCA1 or BRCA2 markedly increases the rate of base substitution mutagenesis and has distinct effects on aenomic deletions

OPEN

J Zámborszky¹, B Szikriszt¹, J Z Gervai¹, O Pipek², Á Póti¹, M Krzystanek³, D Ribli², J M Szalai-Gindl², I Csabai², Z Szallasj³,4,5,6, C Swanton⁷,8, A L Richardson⁹ and

D Szüts1

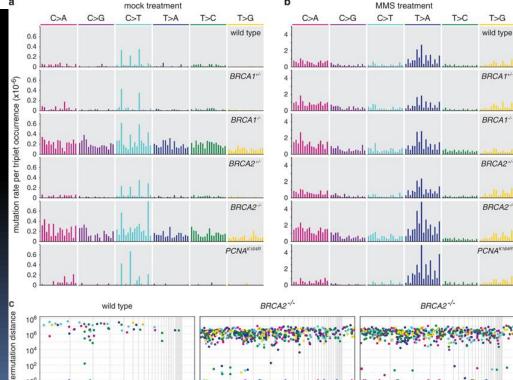
mechanisms

Table of contents Download PDF Share this article View interactive PDF in ReadCube D. Szűts, Rights and permissions Order Commercial Reprints Z. Szállási ▼ Abstract

- ▼ Results mock treatment C>A C>T T>A T>C T>G C>A C>G wild type 0.4
- gene knock-out cell lines, mutagene treatments

understanding DNA-repair

- mutational signatures with non-negative matrix factorization
- mutation spectra compare to TCGA

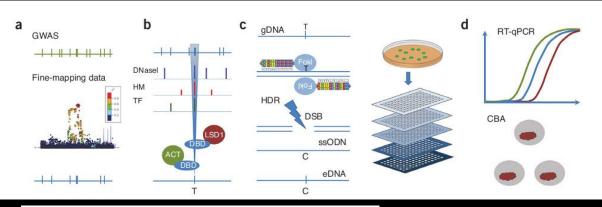


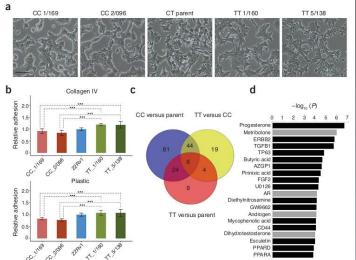
• C>A • T>C • T>A • C>T • C>G • T>G

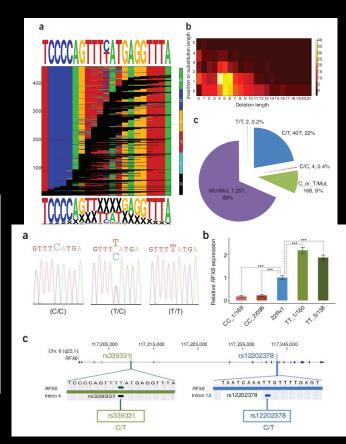


CAUSEL: an epigenome- and genome-editing pipeline for establishing function of noncoding GWAS variants

Sándor Spisák^{1,2,20}, Kate Lawrenson^{3,20,21}, Yanfang Fu^{4-7,20,21}, István Csabai⁸, Rebecca T Cottman^{4-6,9}, Ji-Heui Seo^{1,2}, Christopher Haiman^{3,10}, Ying Han³, Romina Lenci^{1,2}, Qiyuan Li^{1,2,11}, Viktória Tisza^{1,12}, Zoltán Szállási^{12–14}, Zachery T Herbert¹⁵, Matthew Chabot¹, Mark Pomerantz¹, Norbert Solymosi¹⁶, The GAME-ON/ELLIPSE Consortium¹⁷, Simon A Gayther^{3,18}, J Keith Joung^{4-7,9} & Matthew L Freedman^{1,2,19}

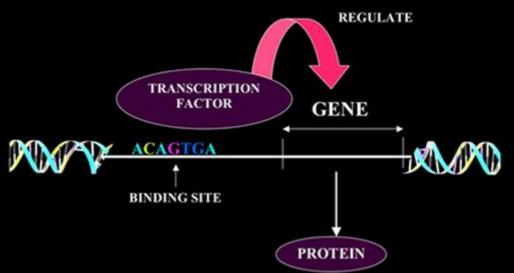




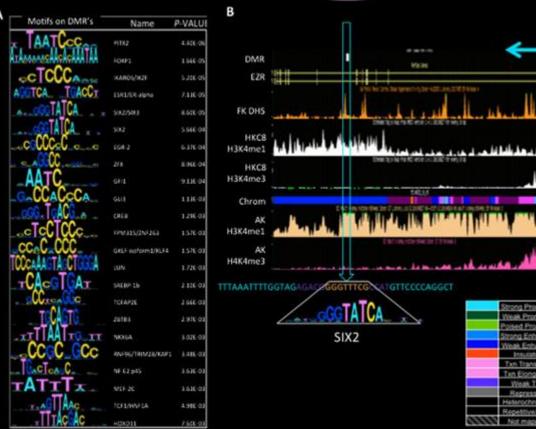


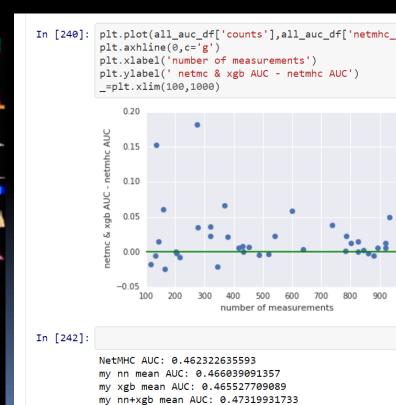
- Genome editing techniques: TALEN, CRISPR-CAS9
- "no averaging" phenomenon:

Strong coupling of micro and macro scales: a single nucleotid in non-coding region can cause phenotypic change

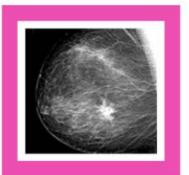


Transcription factor & MHC binding with machine learning





NetMHC + xgb mean AUC: 0.476159451622



The Digital Mammography DREAM Challenge

Build a model to help reduce the recall rate for breast cancer screening

Learn more & register to participate here: www.synapse.org/Digital_Mammography_DREAM_Challenge











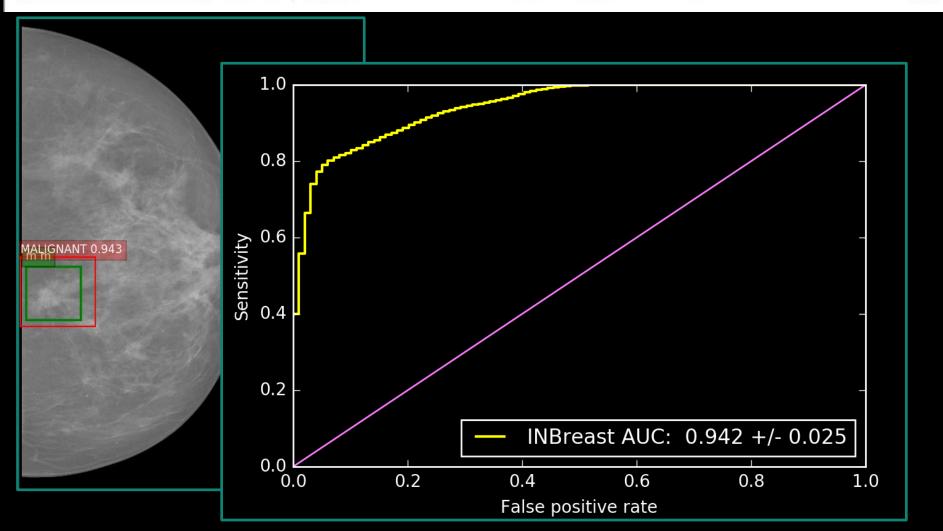


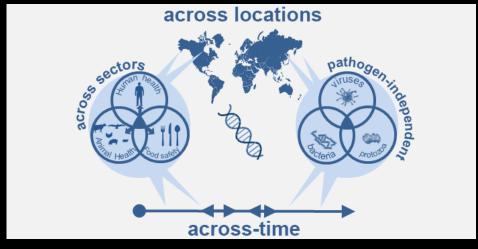


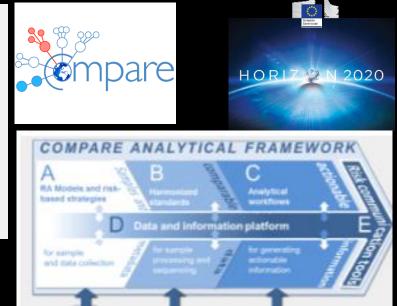












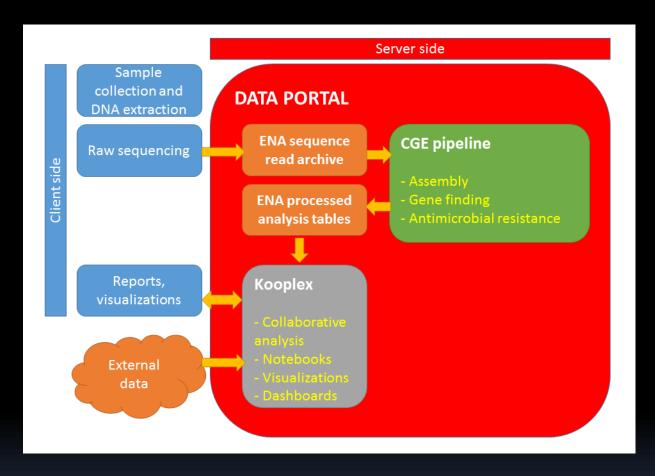
- improve rapid identification, containment and mitigation of infectious diseases and foodborne outbreaks
- cross-sector and cross-pathogen analytical framework and globally linked dataand information-sharing platform
- integrate state-of-the-art strategies, tools, technologies and methods for collecting, processing and analysing sequence-based pathogen data in combination with associated data (clinical, epidemiological, and other), and
- generate actionable information for relevant authorities and other users in human health, animal health and food safety domains.

Examples

Metagenomics - sewage samples from ~100 countries

Antimicrobiotic resistance prediction with machine learning

Cloud based Data Portal



Big Data (EBI ENA 5PB!) — downloading data is not optimal/possible Data sharing is not enough

- share data + complete processing pipeline + result figures, tables, ...
- -> reproducible science

Kooplex

Infrastructure for flexible collaboration





Gitlab

to it, file issues.

Manage your project, add members



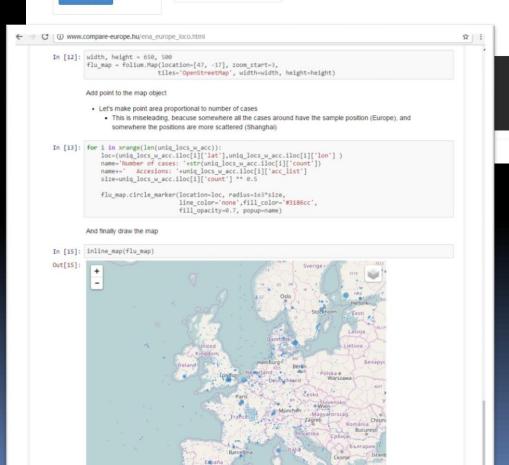
Run existing or create Jupyter notebooks from existing projects to process your data or author your own projects, notebooks and share with others

→ Browse notebooks

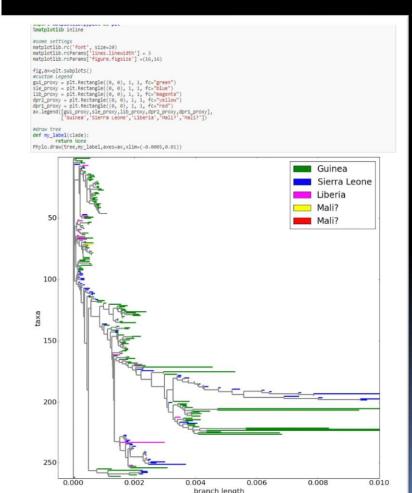
Manage easily your data files through the owncloud... (just as easy as in Dropbox! :))

→ to Owncloud





Collaborative data analytics



New national R&D projects

Biomarker research ELTE, MTATTK, Servier, **CRU**



NEMZETI KUTATÁSI, FEJLESZTÉSI ÉS INNOVÁCIÓS HIVATAL



Cancer genomics, liquid SOTE, ELTE, 3DHISTECH

Magyar Onkogenom és Személyre Szabott Diagnosztika és Terápia program indul Intézetünk irányításával

Közzétéve: 2017. február 19. vasárnap

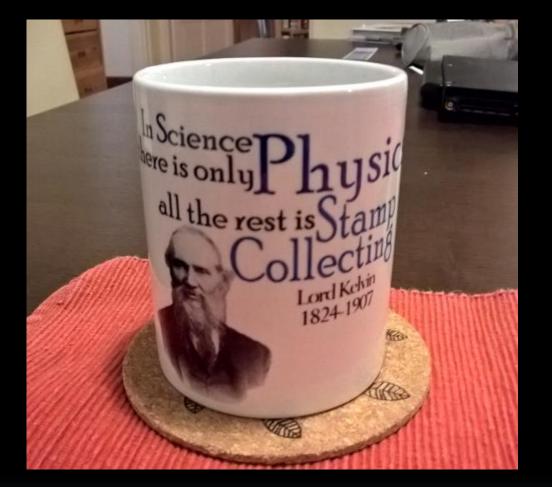
A Nemzeti Kutatási, Fejlesztési és Innovációs Hivatal (NKFIH) 1.5 milliárd forintos támogatásával indul útjára Intézetünk koordinálásával a Magyar Onkogenom és Személyre Szabott Diagnosztika és Terápia Program.

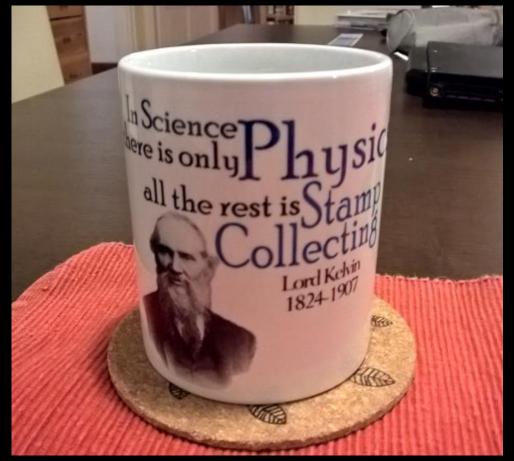
Not only DNA sequencing, but

- Methylation, ncRNA, 3D structure, ...
- Proteomics, lipidomics, ...
- Digital microscopy, medical imaging, ...

Not just sciences, but Everything

- Smart watches, wearable EEG, personal genome sequencers -> better health
- Sensors for cars -> less death on roads
- Sensors for sports -> more enjoyment
- ...
- More "sensors" more data
- better "models" better life





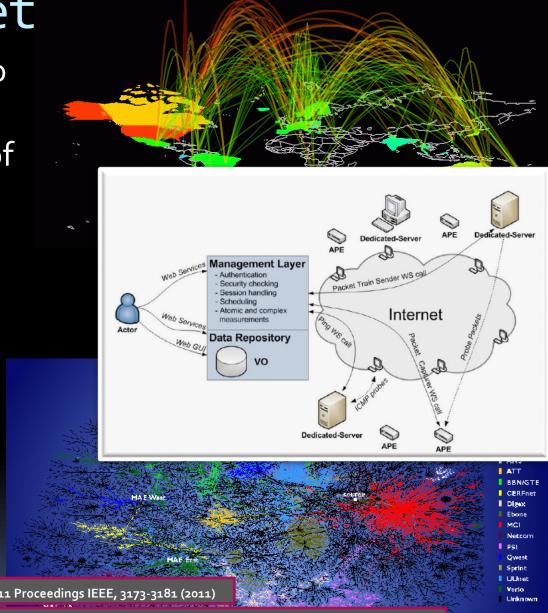
Sorry Dr. Thomson, everything is science, maybe even stamp collecting, too.

Manmade complex systems

COMMUNICATION- SOCIAL- AND FINANCIAL NETWORKS

Map of Internet

- Manmade, but there is no "blueprint"
- "Astronomical" number of non-linearly interacting complex elements
- Scientific approach is required
 - Observation/experiment
 - Modeling
 - -> plan better
- Future internet: selfaware, self-managing, self-healing ...

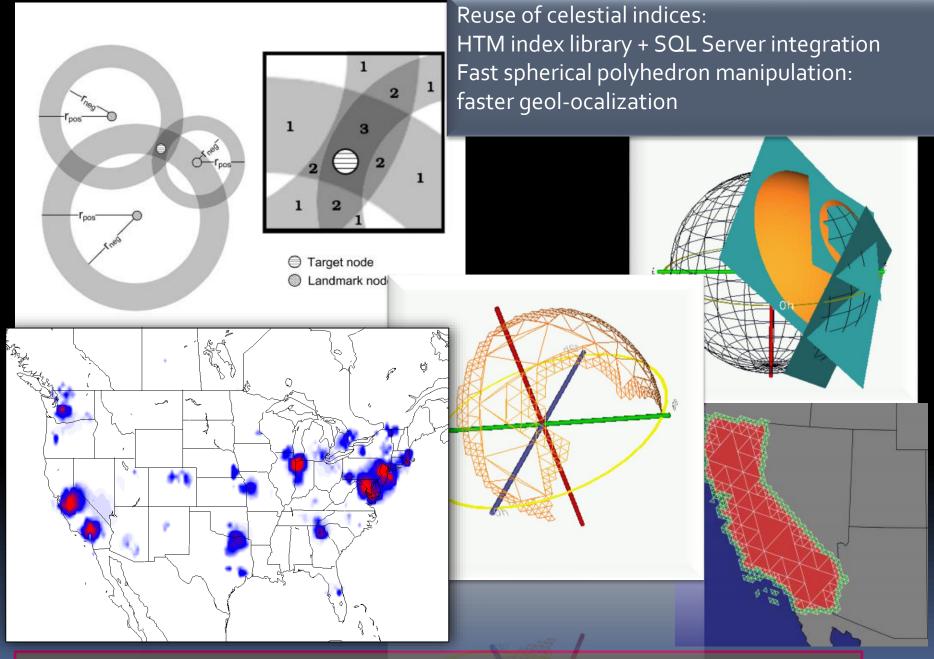


S Laki, P Mátray, P Hága, T Sebők, I Csabai, G Vattay; INFOCOM, 2011 Proceedings IEEE, 3173-3181 (2011)

P Matray, I Csabai, P Haga, J Steger, L Dobos, G Vattay; Proc. ACM workshop on Mining network data, 23-28 (2007)

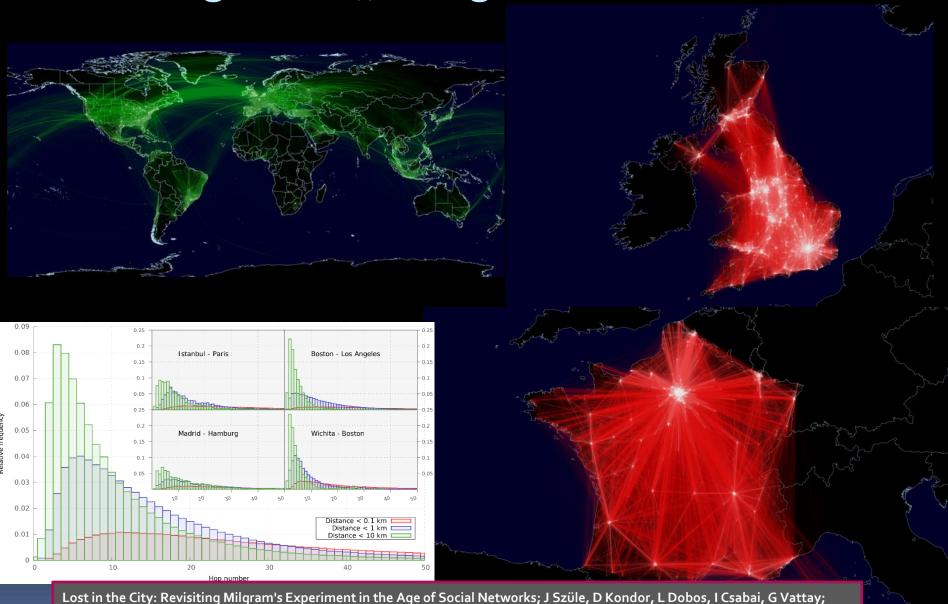
D Morato, E Magana, M Izal, J Aracil, FJ Naranjo, P Astiz, U Alonso, I Csabai, P Hága, G Simon, J Stéger, G Vattay; TRIDENTCOM, 283-289 (2005)

J Szüle, L Dobos, I Csabai, G Vattay; TRIDENTCOM, 137, 65 (2014)



Efficient classification of billions of points into complex geographic regions using hierarchical triangular mesh; D Kondor, L Dobos, I Csabai, A Bodor, G Vattay, T Budavári, AS Szalay; Proc. of the 26th Int. Conf. on Scientific and Statistical Database Management, ACM (2014)

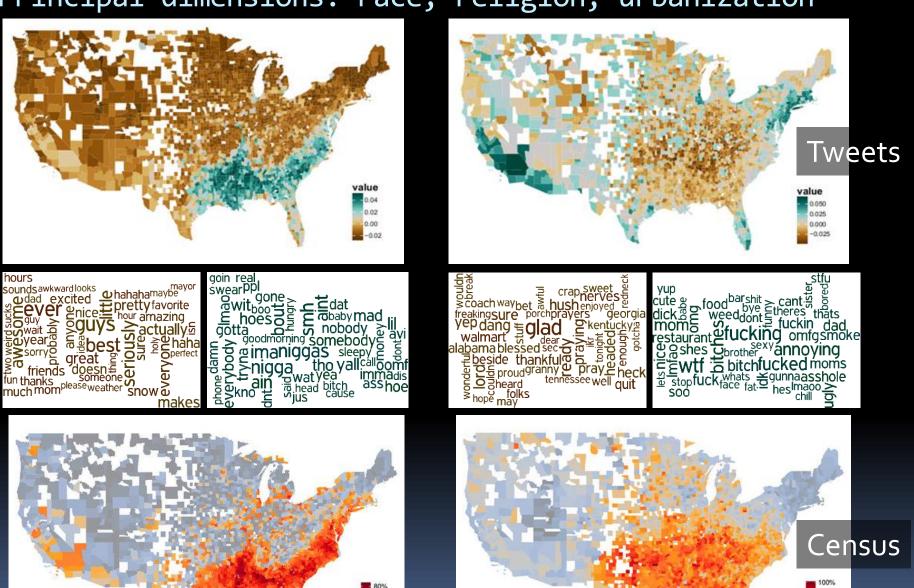
Test Milgram's ,6 degree" on Twitter



Lost in the City: Revisiting Milgram's Experiment in the Age of Social Networks; J Szüle, D Kondor, L Dobos, I Csabai, G Vattay, PloS one 9 (11), e111973 (2014)

Map of society: TwitterDB

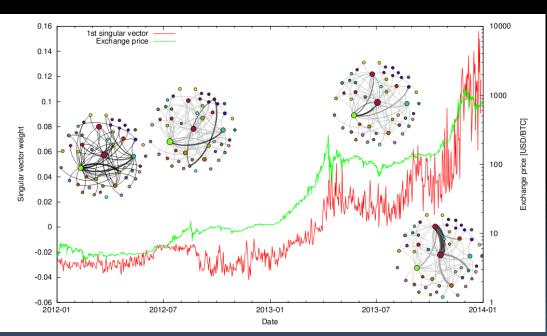
Principal dimensions: race, religion, urbanization



E Bokányi, D Kondor, L Dobos, T Sebők, J Stéger I Csabai, G Vattay Race, religion and the city: twitter word frequency patterns reveal dominant demographic dimensions in the United States, Palgrave Communications 2, 16010 (2016)

Bitcoin financial network. Map of economy

- All (50M) transactions are logged, public
- Dynamic evolving network
- Database
- Dimension reduction (graph non-negative factorization)



Strong random correlations in networks of heterogeneous agents; I Kondor, I Csabai, G Papp, E Mones, G Czimbalmos, MC Sándor Journal of Economic Interaction and Coordination 9 (2), 203-232 (2014)

Do the rich get richer? An empirical analysis of the BitCoin transaction network; D Kondor, M Pósfai, I Csabai, G Vattay; PloS one 9 (2), e86197 (2014)



SCIENCE IS NOT ANY MORE ABOUT 3 LETTER EQUATIONS. THE REAL CHALLENGE IS COMPLEXITY

Take home message

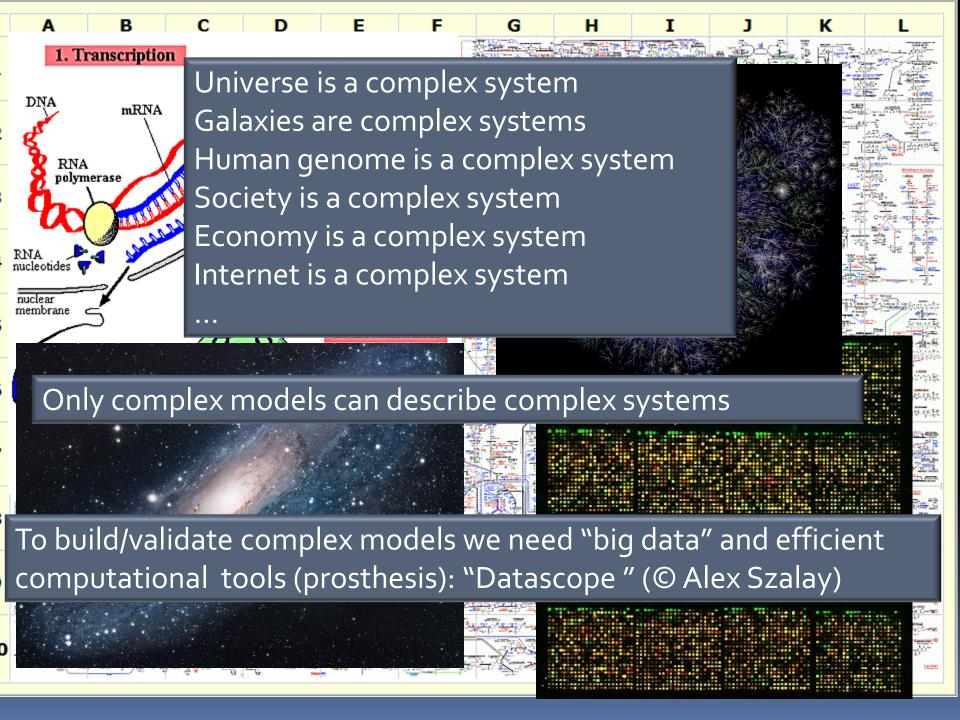
SCIENCE IS COMPLEX MODELING

AND

COMPLEX MODELING IS SCIENCE

 $\nabla \times H = J + \frac{\partial D}{\partial t}$

and then there was light.



Any sufficiently advanced technology is indistinguishable from magic. / Arthur C. Clarke /

"If you think of the phases of the golden age of humanity, once we started to understand the basic laws of physics and made engineering rules to apply them, we saw exponential growth of energy and power use"

Last century we saw a similar breakthrough in our understanding of electricity.

Now, he says, we are ready to tackle another frontier.

"Medicine is the last, because it is the most sophisticated and complex."

/ Dean Kamen, White House Frontiers Conference 2016 October /

Mechanics -> simple machines

Thermodynamics -> steam and internal combustion engines Electrodynamics -> electricity

- + Quantum mechanics -> microelectronics
- ? Biology -> end of diseases, longer healthy life, ...



Who will cure cancer? Who will help to understand **Everything?**

Nobody

Sorcerers

Superintelligent aliens

We! Together.

- ÚJTUDOMÁNYOS MÓDSZERTAN:
 ÚJTUDÓSOK KELLENEK
 - AKIK ÉRTIK A SZAKTUDOMÁNYOKAT
 - PROFESSZIONÁLISAN KEZELIK A
 MATEMATIKAI MELLETT AZ INFORMATIKAI
 ESZKÖZTÁRAT IS



Csabai István

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