

BIO390: Introduction to Bioinformatics

Lecture I: What is Bioinformatics?

Michael Baudis | 2021-09-21

Course Information BIO390

- Tuesdays at 08:00; 2x45min
- 13 presentations by different lecturers
- (unchecked) homework / preparation exercises w/ focus on test topics
- course language is English
- course slides may/should be made available through the website
- written exam at end of course (== 14th course - December 21st)
- Organizer:

Prof. Dr. Michael Baudis

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web info.baudisgroup.org

**Please use website & OLAT for
additional course information**

<https://comppbiozurich.org/UZH-BIO390/>



UZH BIO390

Introduction to Bioinformatics

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[Examples, Guides & FAQ](#)

Related Sites

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[UZH392 course](#)
[Baudisgroup at UZH](#)

Github Projects

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Tags

[2020](#) [2021](#) [FAQ](#) [Markdown](#) [code](#)
[days](#) [documentation](#) [exam](#)
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UZH BIO390 - Introduction to Bioinformatics Lecture Series

This is a repository for materials related to the BIO390 *Introduction to Bioinformatics* lecture series at the University of Zürich.

Programme

Please see the [listing of lectures here](#).

Time & Place

- 1 x 2h / week
- Tue 08:00-09:45
- UZH Irchel campus, Y03-G-85
- OLAT [lecture recordings](#)

Course Language

- English

2021 COVID19 Regulations

As per current rules for labs/block courses, BIO392 is held with "in person" attendance. Please follow the UZH [Coronavirus Guidelines](#).

We provide [lecture recordings](#) through OLAT. In the case of changing situation with canceled on-site attendance or inability of lecturers to attend in person a ZOOM link will be provided.

Summary

The handling and analysis of biological data using computational methods has become an essential part in most areas of biology. In this lecture, students will be introduced to the use of bioinformatics tools and methods in different topics, such as molecular resources and databases, standards and ontologies, sequence and high performance genome analysis, biological networks, molecular dynamics, proteomics, evolutionary biology and gene regulation. Additionally, the use of low level tools (e.g. Programming and scripting languages) and specialized applications will be demonstrated. Another topic will be the visualization of quantitative and qualitative biological data and analysis results.

Learning Goals

The overall learning goals - especially the (limited) set necessary for passing the test - will be updated throughout the semester.

- Core [Learning Goals](#)

This list is not exhaustive; additional information about "need to know" topics will be provided during the individual lectures.

Literature and Resources

- [Literature links](#) and recommendations
- [Resource links](#) (browsers and online repositories)





UZH BIO390

Introduction to Bioinformatics

News and Updates

BIO390 HS21 Programme
BIO390 HS20 Programme
BIO390 HS19 Final Programme

Lectures

Teachers

Examples, Guides & FAQ

Related Sites

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Tags

2020 2021 FAQ Markdown code
days documentation exam
teachers website

BIO390 HS21 Programme

In the following you will find the program for the 2020 Autumn lectures in the "Introduction to Bioinformatics" series at the University of Zurich.

For on-site access information or live streaming please see the relevant information in UZH's "OLAT" platform (registered participants only):

- OLAT [BIO390 HS21](#)

Individual Lectures

2021-09-21

What is Bioinformatics? Introduction and Resources

Michael Baudis

The first day of the "Introduction to Bioinformatics" lecture series starts with a general introduction into the field and a description of the lecture topics, timeline and procedures.

@mbaudis 2021-09-21: [more ...](#)

2021-09-28

Biological Sequence Informatics

Christian von Mering

@mbaudis 2021-09-28: [more ...](#)

2021-10-05

Statistical Bioinformatics

Mark Robinson

@mbaudis 2021-10-05: [more ...](#)

2021-10-12

Machine Learning for Biological Use Cases

Valentina Boeva (ETHZ)

Brief note: In this lecture V. Boeva will cover the standard machine learning methods used in the analysis of biological data: dimensionality reduction, clustering, classification and regression.

2021-10-12: [more ...](#)

2021-10-19

Regulatory Genomics and Epigenomics

Izaskun Mallona

@mbaudis 2021-10-19: [more ...](#)

2021-10-26





UZH BIO390

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News and Updates

General Info

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Teachers

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FAQ Jekyll Markdown code days
documentation exam teachers
website

UZH BIO390 - Learning Goals

This page indicates some of the learning goals, as emphasised by the different lecturers. Some points will have been discussed in different lectures; accordingly, exam questions may not refer to information of one specific presentation.

Bioinformatics: Definition & Concepts

- definition of "Bioinformatics" (cf. Anna Tramontano)
- categories of informatics tools used in bioinformatics
- hypothesis versus data driven science
- areas of bioinformatics/bioinformaticians, in contrast to ("pure" modelling, statistics etc.)
- 3 main categories of biological data, and example resources
- definition of API
- common sequence related file formats
- hierarchies and relationships as 2 main principles of ontologies
- areas of "not-bioinformatics", and why

Sequence Analysis

- substitution matrices
- BLAST

Statistical Bioinformatics

- statistical evidence for a change in the means
- usage of gene expression profiling
- dimensionality reduction
- central limit theorem
- multiple testing correction
- parameters for hierarchical clustering

Bioinformatics tools: Statistics & Graphics in R & BioConductor

- What is tidy data?
- ideas behind ggplot: components of a ggplot, arrangement of input data ... (no actual code writing needed)
- interpret common types of plots, e.g. barplot, boxplot, histogram
- effect of data transformation (e.g. log) on common types of plots

Regulatory Genomics and Epigenomics

- secondary/tertiary human genome structure
- functional genome content
- transcription factors & genome interaction
- chemical genome modifications, their effectors and results
- Chip-Seq



Some Recommended Books

- Anna Tramontano: Introduction to Bioinformatics
- Susan Holmes and Wolfgang Huber: Statistics for Biology
- Robert Gentleman: R Programming for Bioinformatics
- John Maindonald & W. John Braun: Data Analysis and Graphics Using R
- Andy Hector: The New Statistics with R
- Neil C. Jones & Pavel A. Pevzner: Bioinformatics Algorithms
- Edward Tufte: The Visual Display of Quantitative Information (& other works by Tufte)



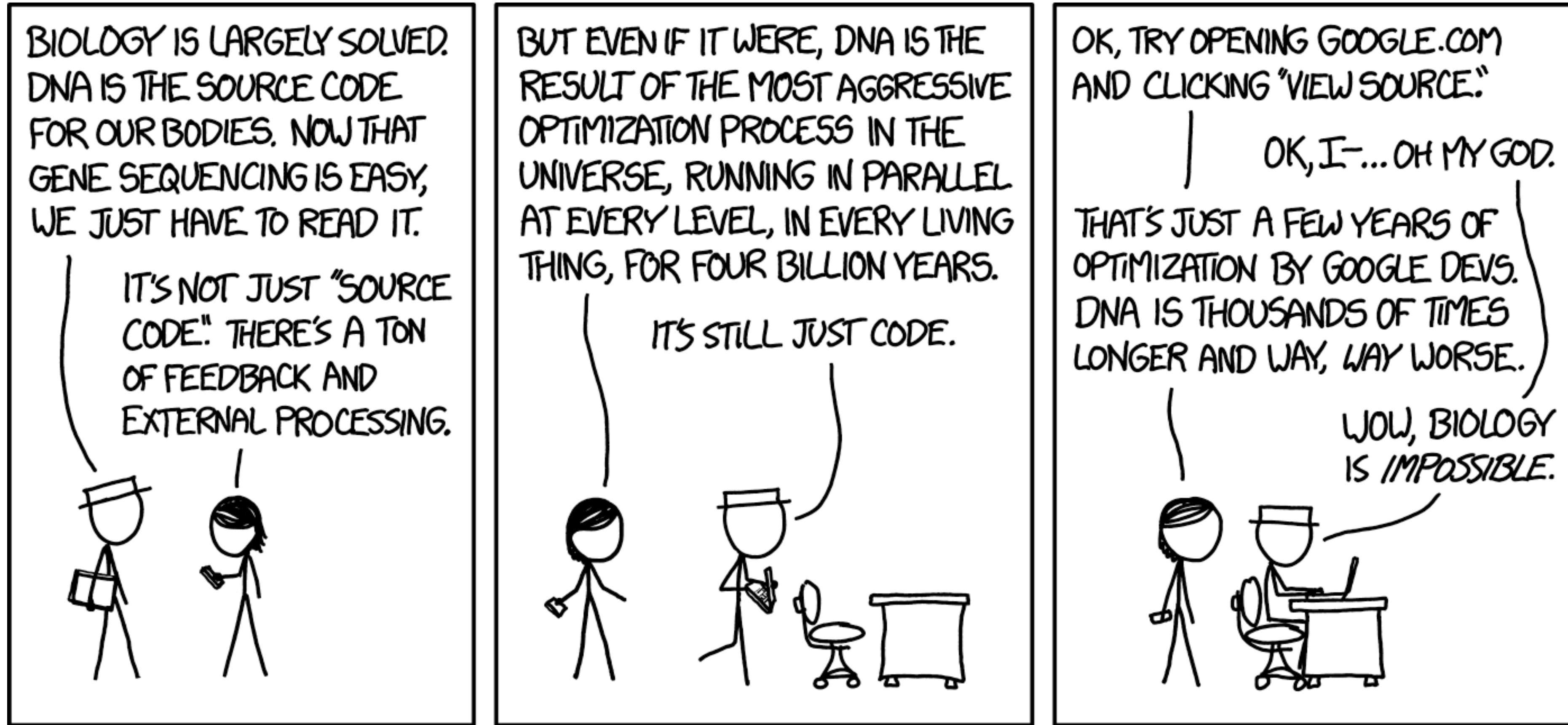
BIO390: Course Schedule

- 2021-09-21: Michael Baudis - What is Bioinformatics? Introduction and Resources
- 2021-09-28: Christian von Mering - Sequence Bioinformatics
- 2021-10-05: Mark Robinson - Statistical Bioinformatics
- 2021-10-12: Valentina Boeva (ETHZ) - Machine Learning for Biological Use Cases
- 2021-10-19: Izaskun Mallona - Regulatory Genomics and Epigenomics
- 2021-10-26: Shinichi Sunagawa (ETHZ) - Metagenomics
- 2021-11-02: Katja Baerenfaller (SIAF) - Proteomics
- 2021-11-09: Puria Dasmeh - Biological Networks
- 2021-11-16: TBD - Text Mining topic
- 2021-11-23: Fabio Rinaldi - Text Mining
- 2021-11-30: Michael Baudis - Building a Genomics Resource
- 2021-12-07: Valérie Barbie (SIB) - Clinical Bioinformatics
- 2021-12-14: Michael Baudis - Genome Data & Privacy
- 2021-12-21: Exam (Multiple Choice)

Why Bioinformatics?

- **hypotheses** are the basis of biological experiments
- biological experiments produce **data**, the quantitative and/or qualitative read-outs of experiments
- both quantitative as well as qualitative data need to be **processed** for
 - **statistical significance**
 - **categorisation**
 - **communication**
- many datatypes are **beyond** the proverbial "**intuitive** understanding"
- analysis of data **confirms** or **refutes** initial **hypotheses** - or requires new hypotheses and new data

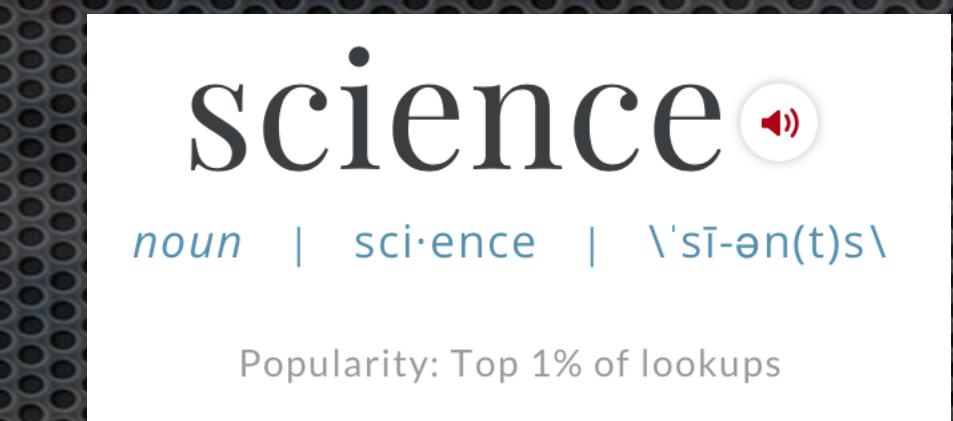
Biology is *impossibly* complex - But bioinformatics might help



So, What is Bioinformatics?

- Bioinformatics is "the science that uses the instruments of informatics to analyze biological data in order to formulate hypotheses about life." (Anna Tramontano)

What is Bioinformatics?



- Bioinformatics is "the **science** that uses the instruments of informatics to analyze biological data in order to formulate hypotheses about life." (Anna Tramontano)

a : knowledge or a system of knowledge covering general truths or the operation of general laws especially as obtained and tested through **scientific method**

b : such knowledge or such a system of knowledge concerned with the physical world and its **phenomena** : NATURAL SCIENCE



What is Bioinformatics?

Bioinformatics **uses** informatics tools for analyses

- Bioinformatics is "the science that **uses** the instruments of informatics to analyze biological data in order to formulate hypotheses about life." (Anna Tramontano)
- **software** (programming languages, statistics & visualisation, program and web APIs, databases, hardware drivers)
- **hardware** (HPC, data storage, signal measurement & processing)
- **algorithms** (modeling, encryption...)

What is Bioinformatics?

Bioinformatics **develops** informatics tools for analyses

- Bioinformatics is "the science that uses the **instruments of informatics** to analyze biological data in order to formulate hypotheses about life." (Anna Tramontano)
- **software** (statistics & visualisation packages, program and web APIs, file formats)
- **hardware** (drivers and procedures...)
- **algorithms** (modeling, encryption...)

What is Bioinformatics?

biological data

- Bioinformatics is "the science that uses the instruments of informatics to analyze **biological data** in order to formulate hypotheses about life." (Anna Tramontano)

sequences, graphs, high-dimensional data, spatial/geometric information, scalar and vector fields, patterns, constraints, images, models, prose, declarative knowledge ... *

What is Bioinformatics?



Bioinformatics **analyzes**

- Bioinformatics is "the science that uses the instruments of informatics to **analyze** biological data in order to formulate hypotheses about life."
(Anna Tramontano)

1 : to study or determine the nature and relationship of the parts of (something) by **analysis**

What is Bioinformatics?



- Bioinformatics is "the science that uses the instruments of informatics to analyze biological data in order to **formulate hypotheses** about life." (Anna Tramontano)

b : an interpretation of a practical situation or condition taken as the ground for action

What is Bioinformatics?

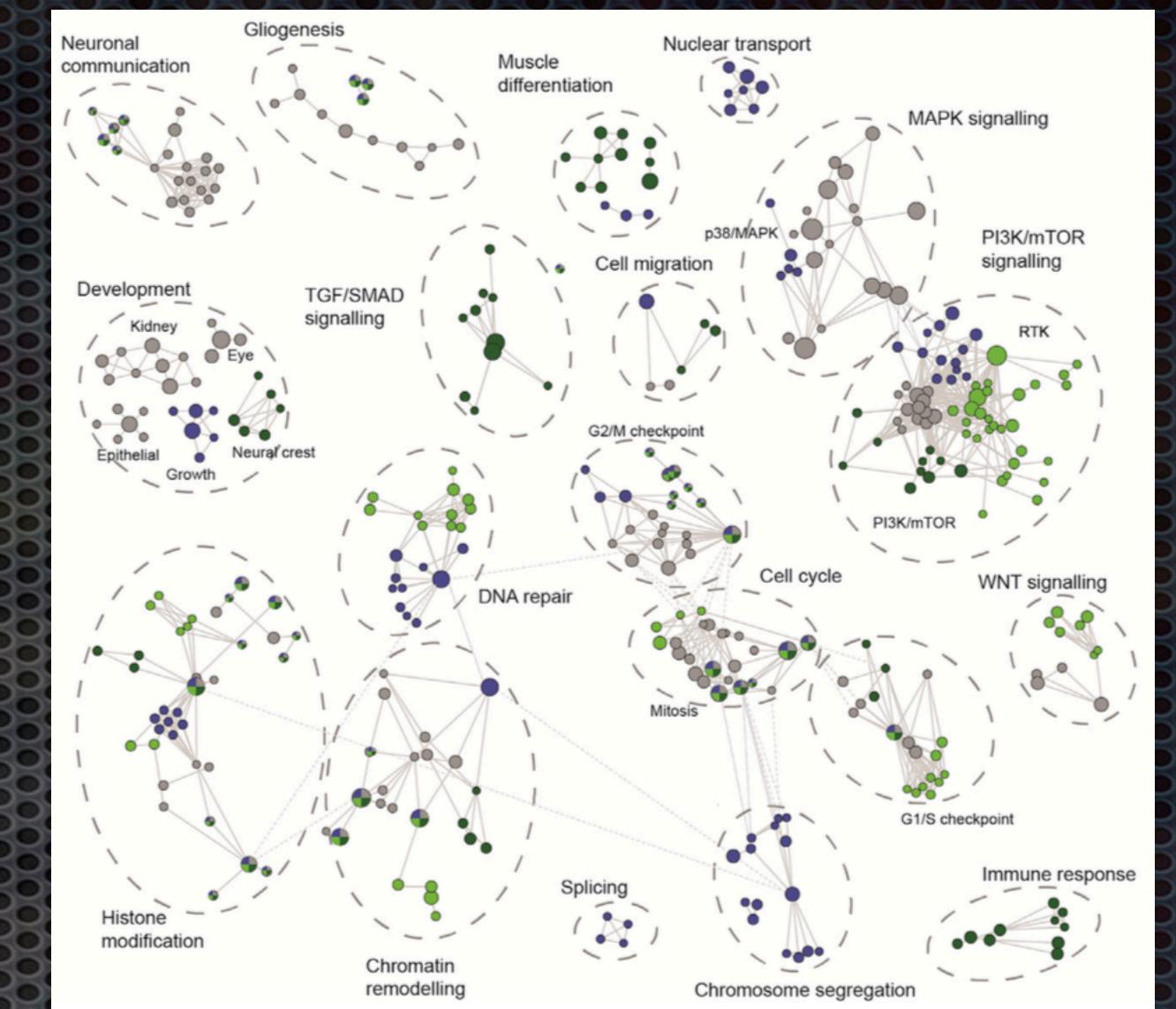
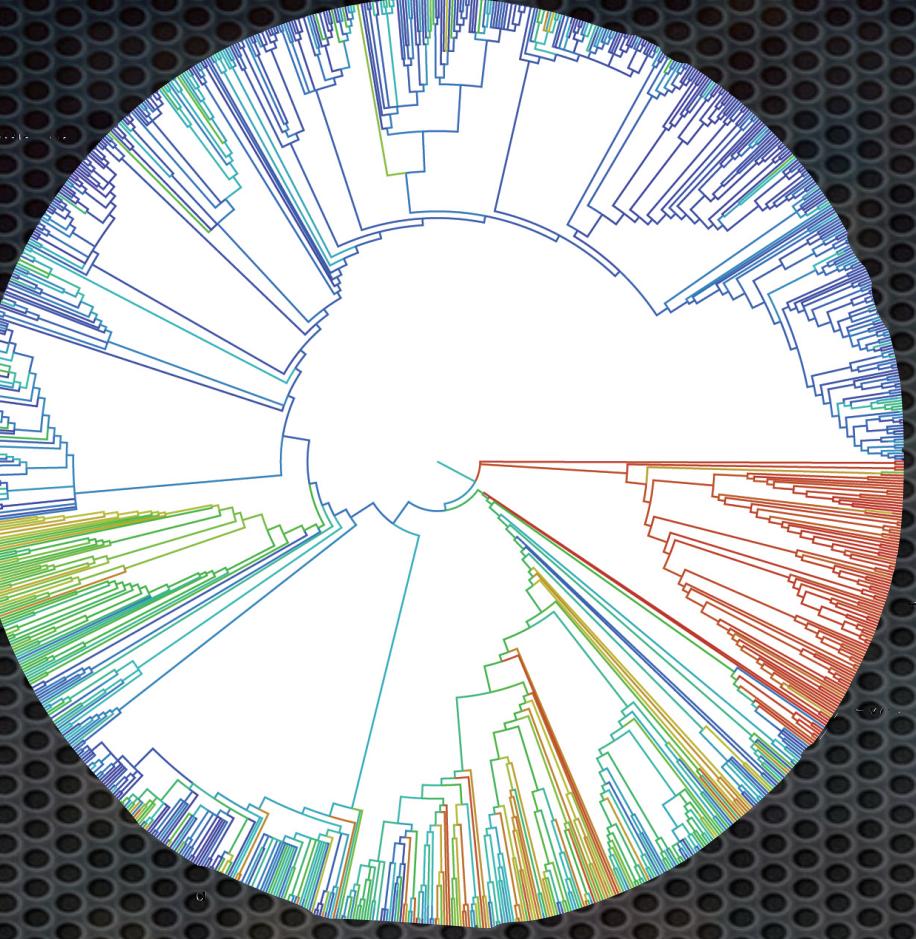


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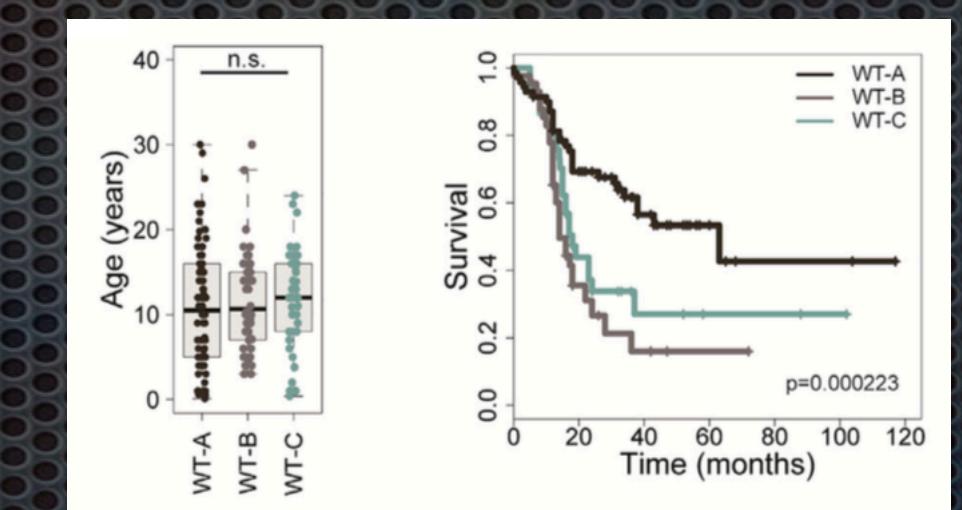
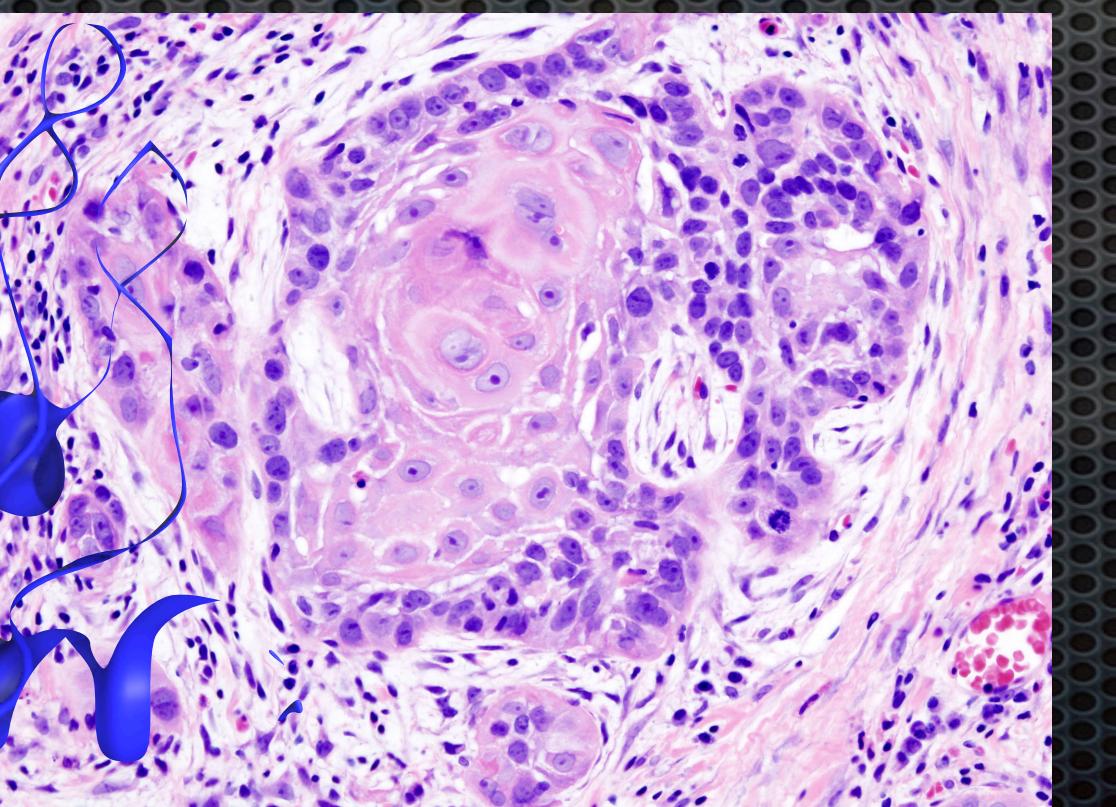
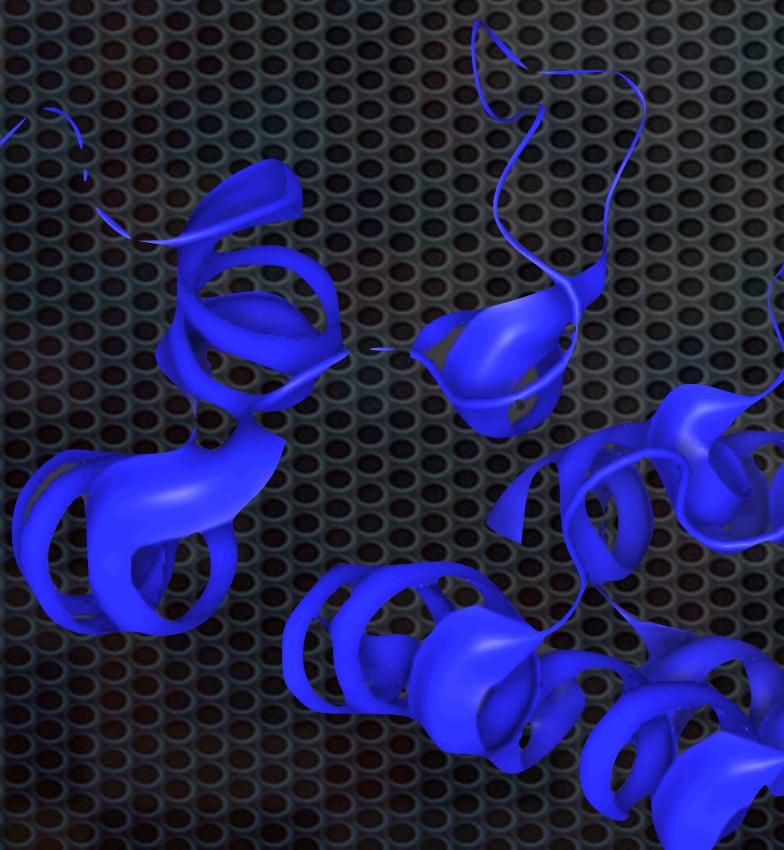
b : an interpretation of a practical situation or condition taken as the ground for action



42



- Bioinformatics is "the science that uses the instruments of informatics to analyze biological data in order to formulate hypotheses about **life.**" (Anna Tramontano)

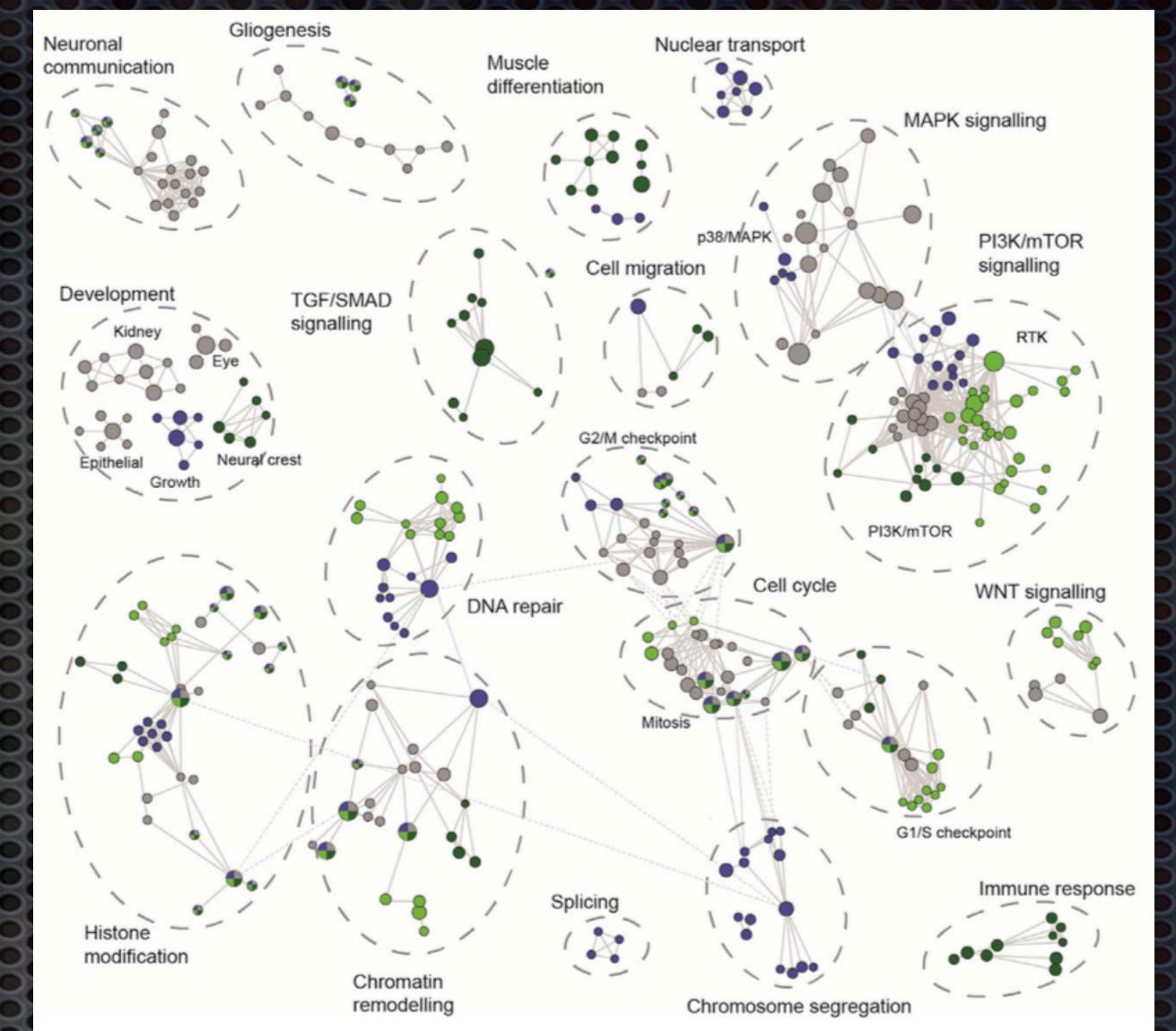


Sources: nextprot | opentreeoflife | wikipedia | MacKay et al., Cancer Cell (2017) | original photos

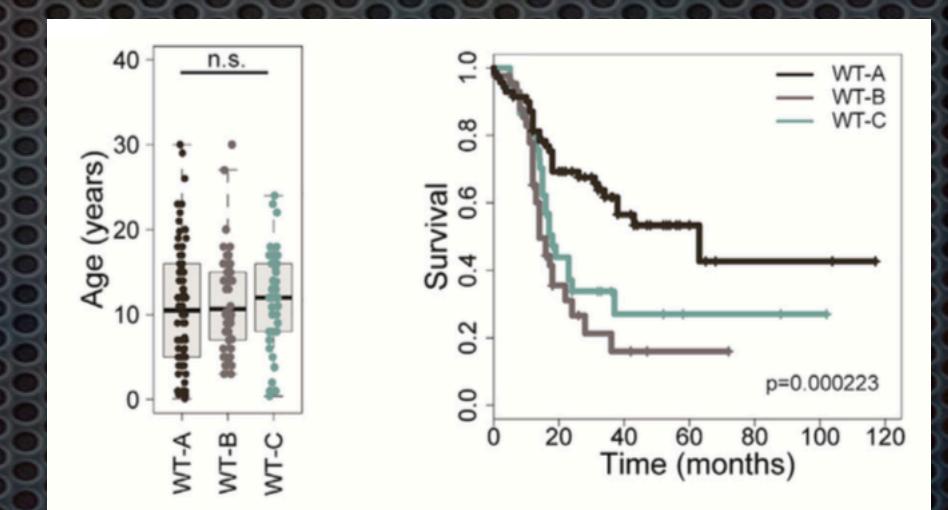
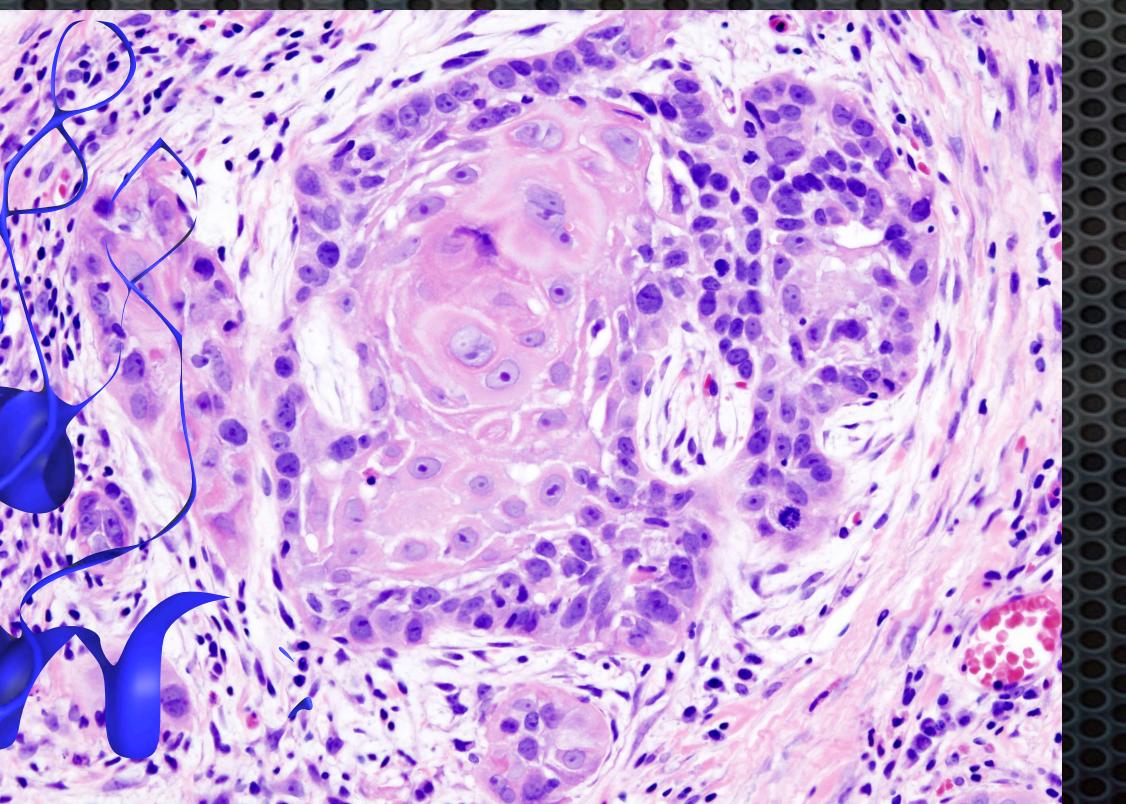
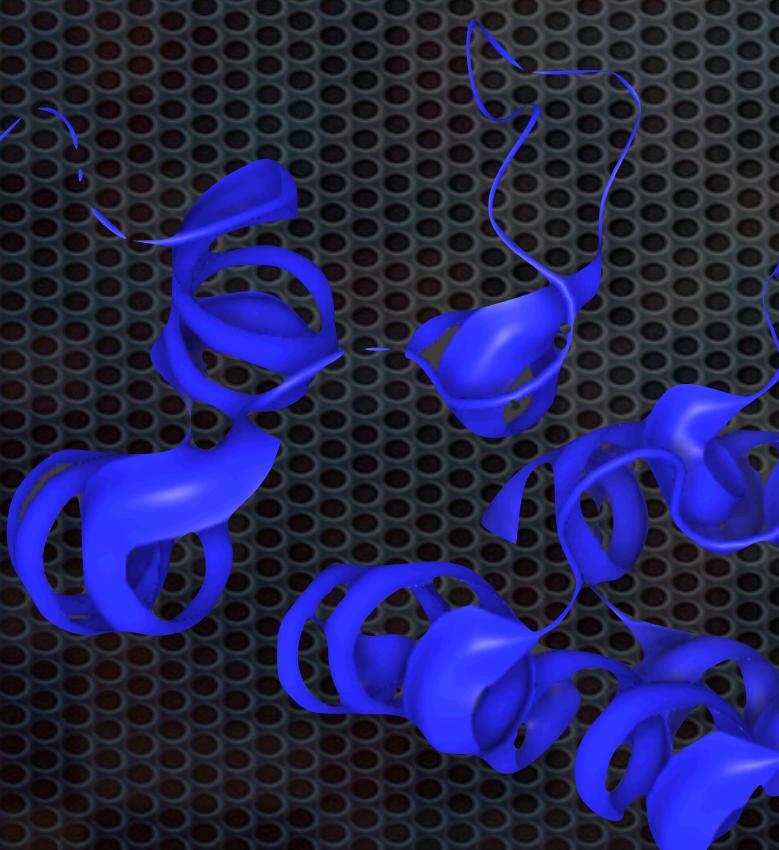


Homework Assignment - How can Bioinformatics help with the **42** of Life Sciences?

42



- Bioinformatics is "the science that uses the instruments of informatics to analyze biological data in order to formulate hypotheses about **life**." (Anna Tramontano)



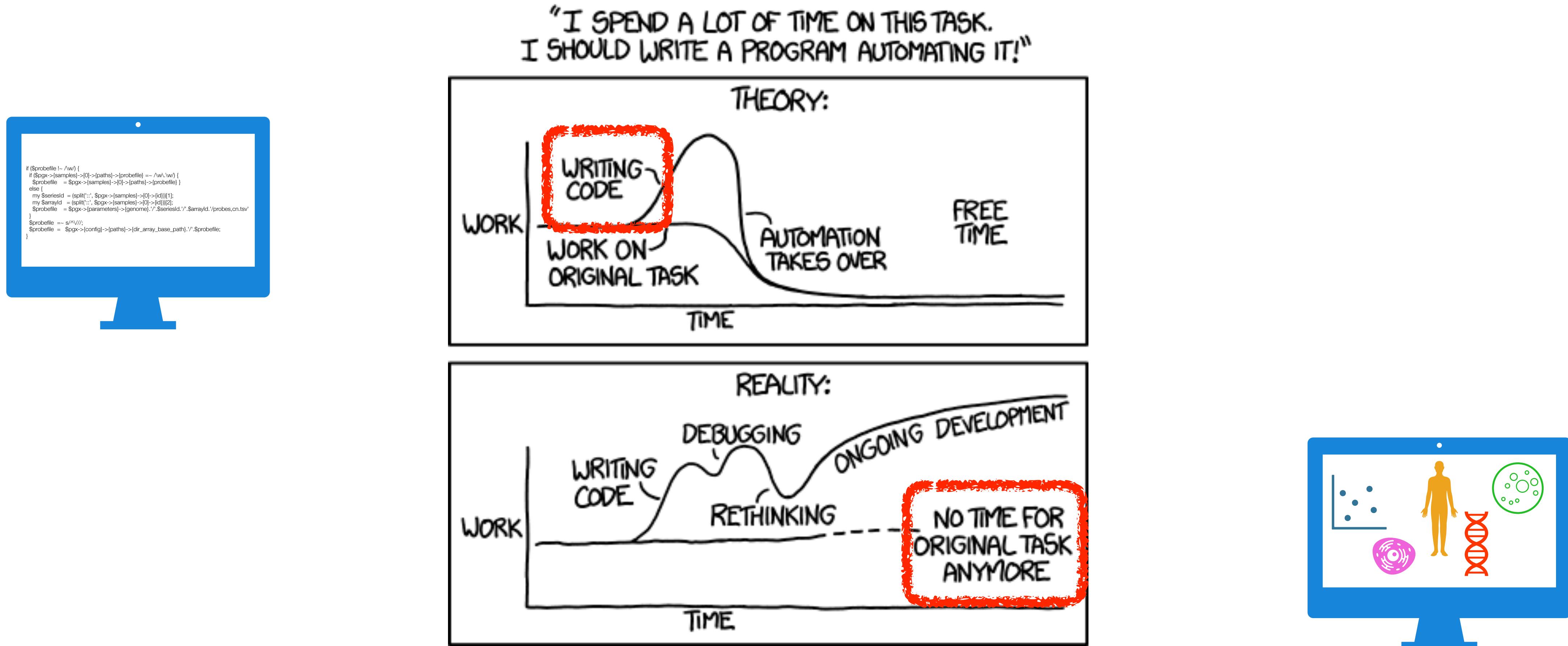
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{bio_informatics_science}



{bio_informatics_science}



Bioinformatician

strong biological knowledge

provides hypothesis and / or dataset

sufficient statistical and
computational expertise to correctly
use bioinformatics tools & develop
workflows (scripting ...)

expert **user** of informatics tools

may get a Nobel

Bio**informatician**

sufficient biological background

provides statistical, analysis methods

sufficient biological or **medical**
background to understand problems
presented and identify pitfalls and hidden
biases arising from data generation

developer of informatics tools

may get rich

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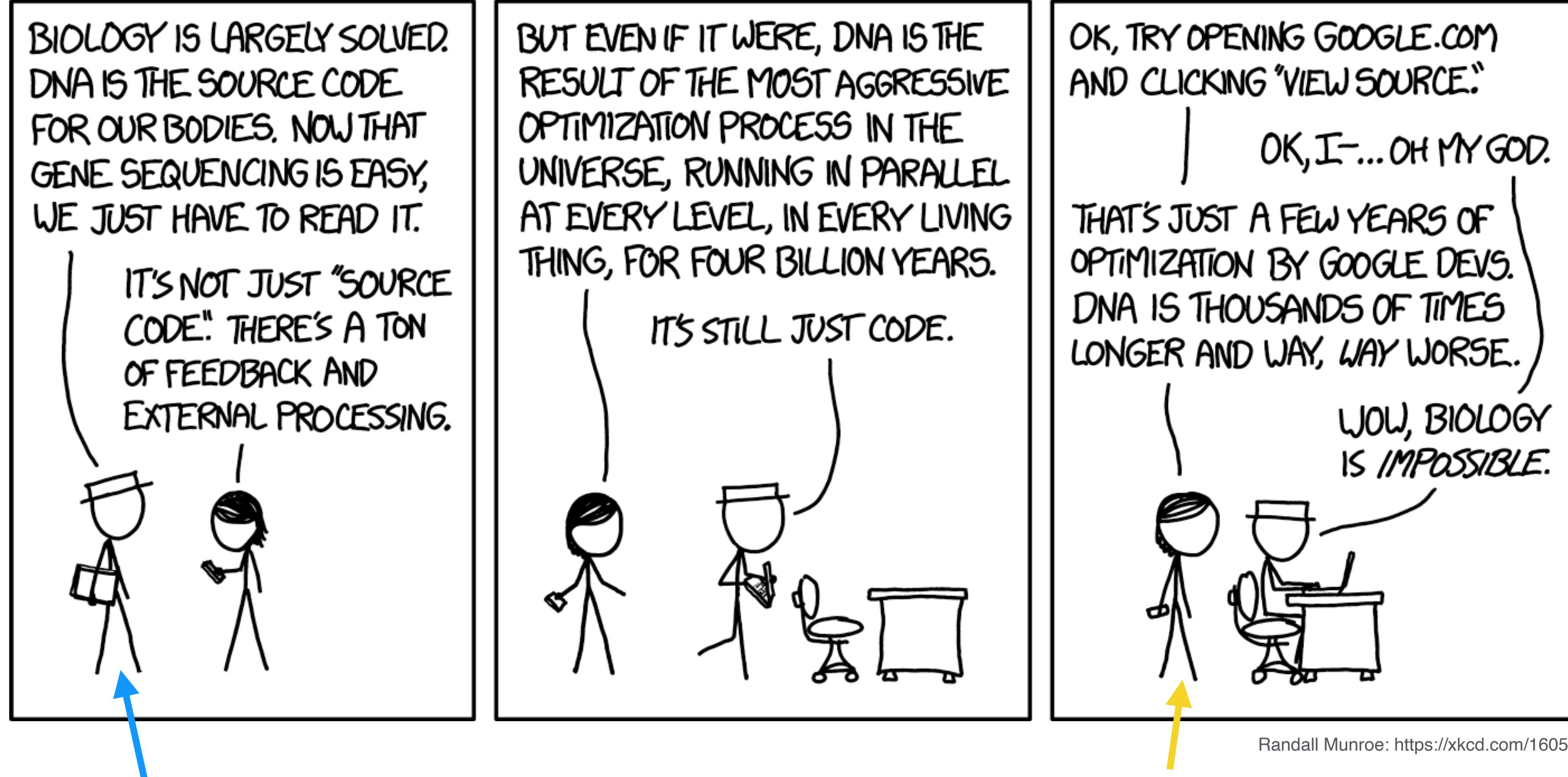
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may get rich

Who is a Bioinformatician?



What do Bioinformaticians work on?

- protein **structure** definition
- DNA/RNA/protein **sequence** analysis
- **quantitative** analysis of "-omics" and cytometry data
- **functional** enrichment of target data (e.g. genes, sequence elements)
- **evolutionary** reconstruction and "tree of life" questions
- **image processing** for feature identification and spatial mapping
- **statistical** analysis of measurements and observations
- **protocols** for efficient storage, annotation and retrieval of biomedical data
- **information extraction** from prose & declarative knowledge resources (think publications & data tables)
- **clinical** bioinformatics - risk assessment and therapeutic target identification
- ...

Bioinformatics: Data **Categories** & **Databases**

- biological data comes in **3 main categories**:
 - **sequence** data (nucleic acids, aminoacids)
 - **structural** data (DNA, RNA, proteins; intracellular organisation, tissues ...)
 - **functional** data (interactions in time and space)
- data storage & retrieval: importance of local and connected **databases**
 - **primary databases** - for deposition of original, raw data (e.g. SRA - sequence read archive; ENA - European Nucleotide Archive; GEO - NCBI Gene Expression Omnibus; EBI arrayExpress...)
 - **derived databases** - information resources providing agglomerated & **curated** data derived from primary sources (e.g. UniprotKB, nextProt, String, KEGG, arrayMap...)

arrayMap 



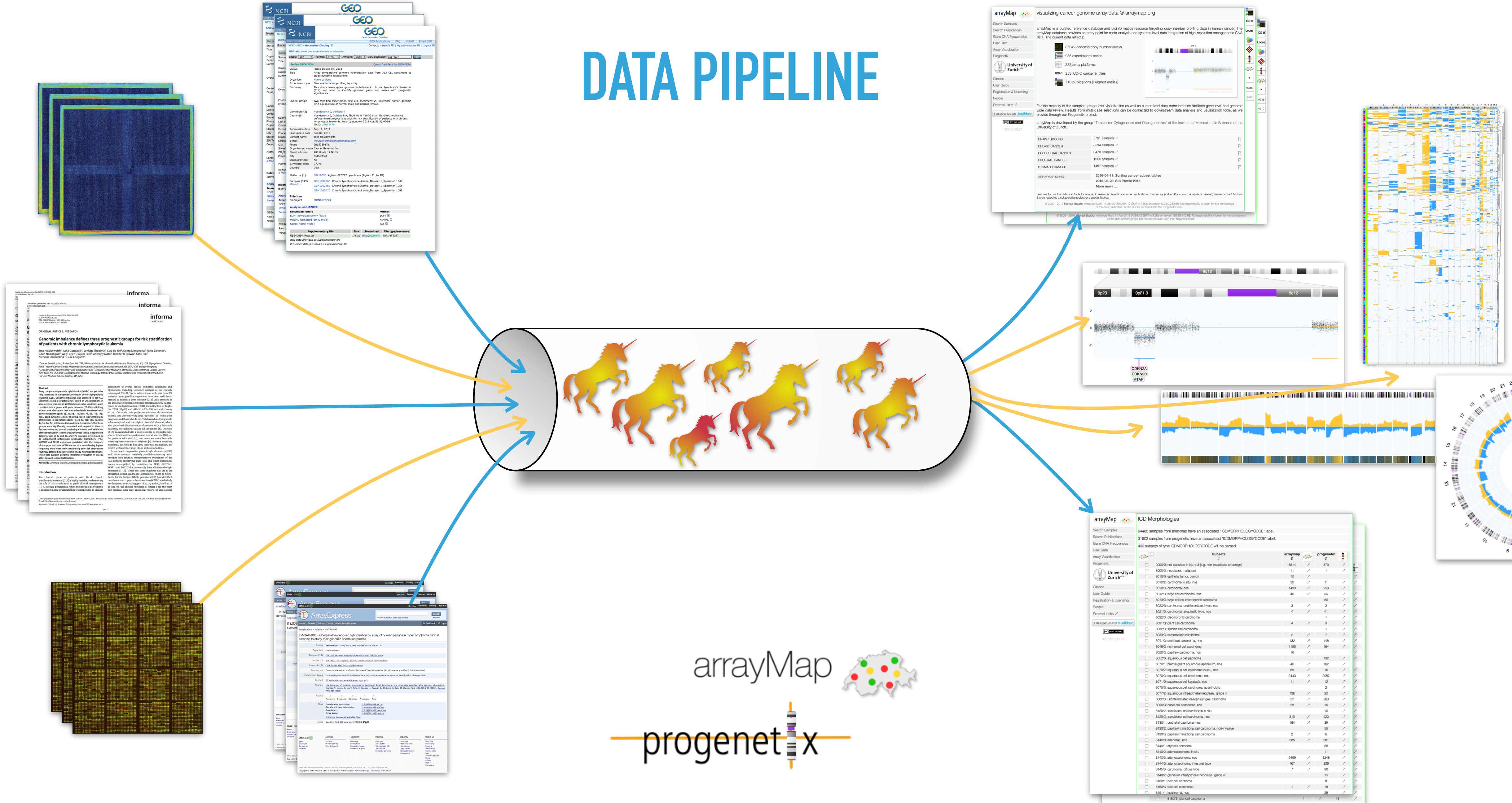
nextprot



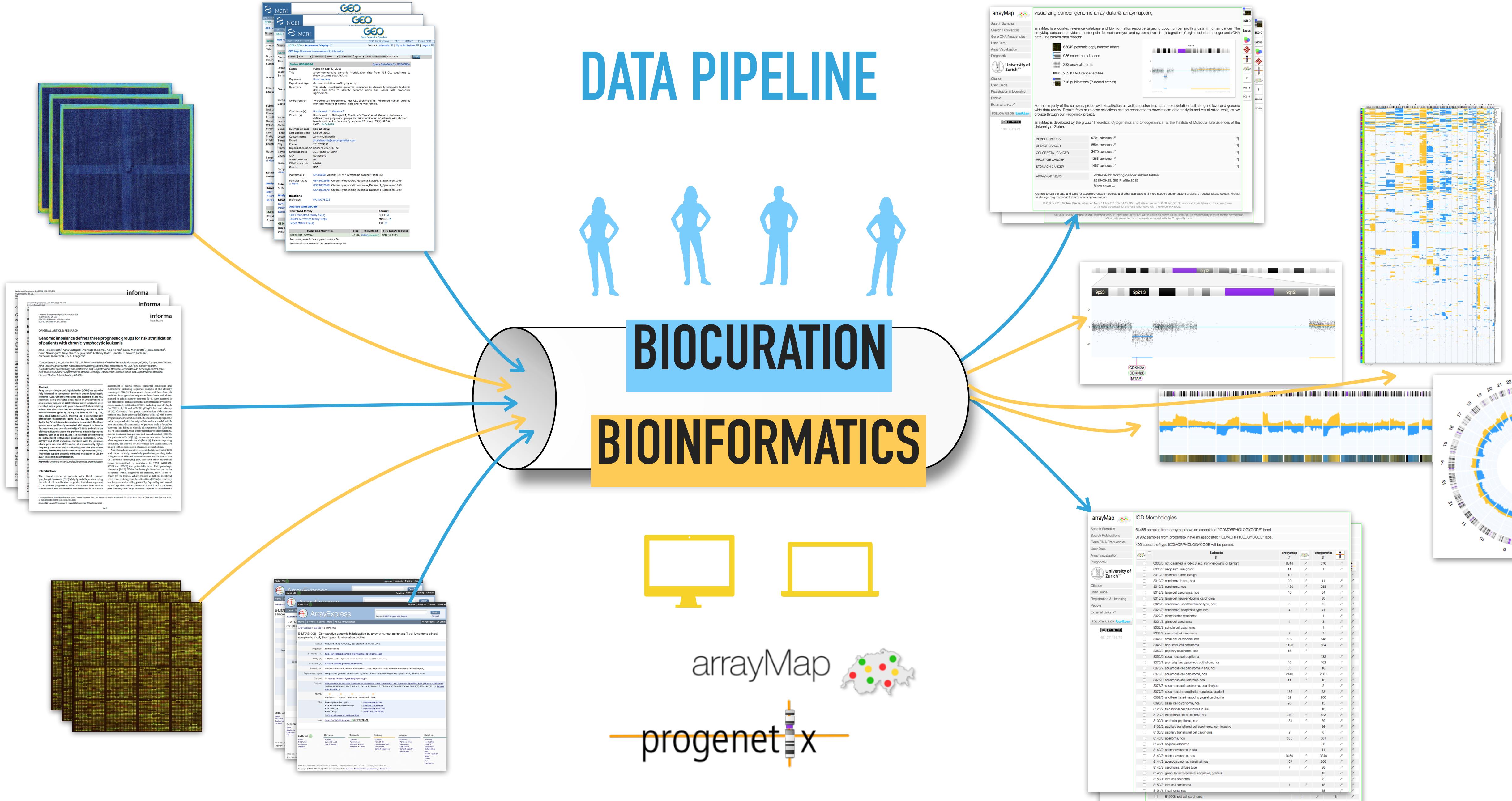
SRA



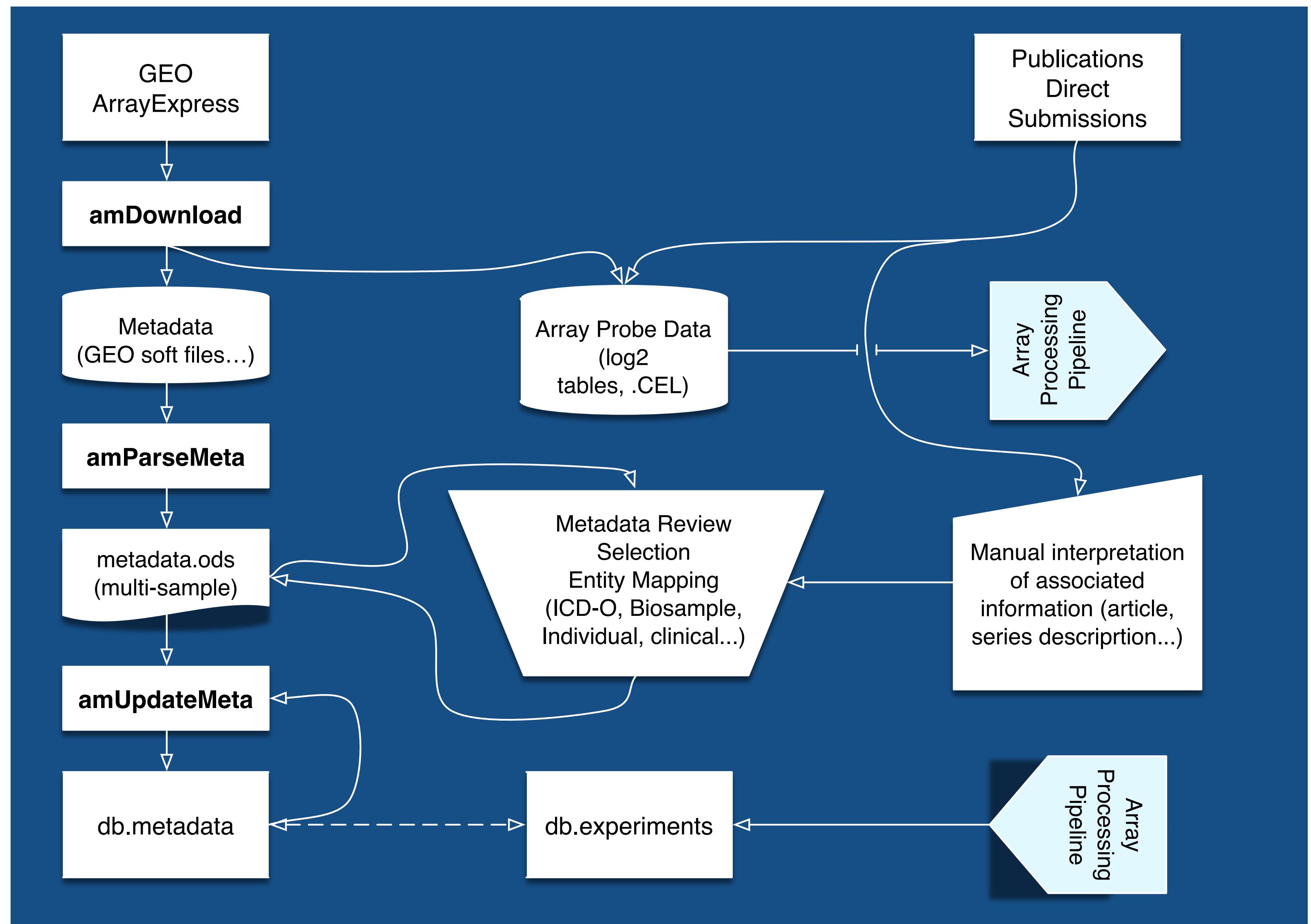
DATA PIPELINE



DATA PIPELINE



Bioinformatics & Data Curation - arrayMap data “Pipeline”



Bioinformatics: File Formats, Ontologies & APIs

- **text** or **binary** file formats, optimised for specific types of biological data
- examples from genomics:
 - **BAM** - compressed binary version of Sequence Alignment/Map (SAM)
 - **BED** (Browser Extensible Data) -flexible way to define the data lines in an genome browser annotation tracks
 - **VCF** (Variant Call Format)

The image consists of three main parts. At the top right is a file information dialog box for a file named "GSM1904006.CEL" which is 69.1 MB in size and was modified on 3 February 2016 at 17:46. The file is identified as an "FLC animation". Below this is a "General" section with details like kind, size, where it was located, and creation/modification times. A note says "Use this application to open all documents like this one." with a dropdown set to "QuickTime Player (default)". A red arrow points from the text "not a movie..." to the file icon in the preview section, which is a movie camera icon with a large red X over it. To the right of the file info is a vertical list of file formats, many of which are preceded by a small blue square icon. At the bottom left is a screenshot of a BED file content, showing genomic coordinates and itemRGB values.

File Formats List:

- Axt format
- BAM format
- BED format
- BED detail format
- bedGraph format
- barChart and bigBarChart format
- bigBed format
- bigGenePred table format
- bigPsl table format
- bigMaf table format
- bigChain table format
- bigWig format
- Chain format
- CRAM format
- GenePred table format
- GFF format
- GTF format
- HAL format
- MAF format
- Microarray format
- Net format
- Personal Genome SNP format
- PSL format
- VCF format
- WIG format

genome.ucsc.edu/FAQ/FAQformat.html

BED file example:

```
browser position chr7:127471196-127495720
browser hide all
track name="ItemRGBDemo" description="Item RGB"
chr7 127471196 127472363 Pos1 0 + 127472363 127473530 255,0,0
chr7 127472363 127473530 Pos2 0 + 127472363 127473530 255,0,0
chr7 127473530 127474697 Pos3 0 + 127473530 127474697 255,0,0
chr7 127474697 127475864 Pos4 0 + 127474697 127475864 255,0,0
chr7 127475864 127477031 Neg1 0 - 127475864 127477031 0,0,255
chr7 127477031 127478198 Neg2 0 - 127477031 127478198 0,0,255
chr7 127478198 127479365 Neg3 0 - 127478198 127479365 0,0,255
chr7 127479365 127480532 Pos5 0 + 127479365 127480532 255,0,0
chr7 127480532 127481699 Neg4 0 - 127480532 127481699 0,0,255
```

not a movie...

File Formats: VCF

Genomic variant storage standard

- The VCF Variant Call Format is an example for a widely used file format with "built-in logic"
- has been essential to master the "genomics data deluge" through providing "logic compression" for genomic annotations which rely on the notion of "assessed variant in a population"
- very expressive, but complex interpretation
- mix of "observed" and "population" variant concepts confusing for some use cases
- no replacement in sight (but new versions)

The Variant Call Format (VCF) Version 4.2 Specification

25 Jun 2020

The master version of this document can be found at <https://github.com/samtools/hts-specs>. This printing is version 09fbcec from that repository, last modified on the date shown above.

1 The VCF specification

VCF is a text file format (most likely stored in a compressed manner). It contains meta-information lines, a header line, and then data lines each containing information about a position in the genome. The format also has the ability to contain genotype information on samples for each position.

1.1 An example

```
##fileformat=VCFv4.2
##fileDate=20090805
##source=myImputationProgramV3.1
##reference=file:///seq/references/1000GenomesPilot-NCBI36.fasta
##contig=<ID=20,length=62435964,assembly=B36,md5=f126cdf8a6e0c7f379d618ff66beb2da,species="Homo sapiens",taxonomy=x>
##phasing=partial
##INFO=<ID=NS,Number=1,Type=Integer,Description="Number of Samples With Data">
##INFO=<ID=DP,Number=1,Type=Integer,Description="Total Depth">
##INFO=<ID=AF,Number=A,Type=Float,Description="Allele Frequency">
##INFO=<ID=AA,Number=1,Type=String,Description="Ancestral Allele">
##INFO=<ID=DB,Number=0,Type=Flag,Description="dbSNP membership, build 129">
##INFO=<ID=H2,Number=0,Type=Flag,Description="HapMap2 membership">
##FILTER=<ID=q10,Description="Quality below 10">
##FILTER=<ID=s50,Description="Less than 50% of samples have data">
##FORMAT=<ID=GT,Number=1,Type=String,Description="Genotype">
##FORMAT=<ID=GQ,Number=1,Type=Integer,Description="Genotype Quality">
##FORMAT=<ID=DP,Number=1,Type=Integer,Description="Read Depth">
##FORMAT=<ID=HQ,Number=2,Type=Integer,Description="Haplotype Quality">
#CHROM POS ID REF ALT QUAL FILTER INFO FORMAT NA00001 NA00002 NA00003
20 14370 rs6054257 G A 29 PASS NS=3;DP=14;AF=0.5;DB;H2 GT:GQ:DP:HQ 0|0:48:1:51,51 1|0:48:8:51,51 1/1:43:5:,,,
20 17330 . T A 3 q10 NS=3;DP=11;AF=0.017 GT:GQ:DP:HQ 0|0:49:3:58,50 0|1:3:5:65,3 0/0:41:3
20 1110696 rs6040355 A G,T 67 PASS NS=2;DP=10;AF=0.333,0.667;AA=T;DB GT:GQ:DP:HQ 1|2:21:6:23,27 2|1:2:0:18,2 2/2:35:4
20 1230237 . T . 47 PASS NS=3;DP=13;AA=T GT:GQ:DP:HQ 0|0:54:7:56,60 0|0:48:4:51,51 0/0:61:2
20 1234567 microsat1 GTC G,GTCT 50 PASS NS=3;DP=9;AA=G GT:GQ:DP 0/1:35:4 0/2:17:2 1/1:40:3
```

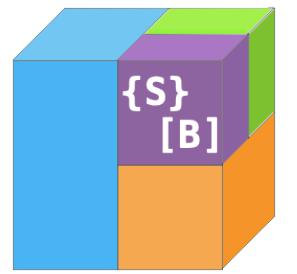
Bioinformatics: File Formats, Ontologies & APIs

- databases can be accessed through Application Programming Interfaces
- *API : set of routines, protocols, and tools that specifies how software components interact, to exchange data and processing capabilities*
- web API example: implementing geographic maps, with parameters provided by the client (e.g. location coordinates, quantitative payload)
- web APIs provide a *machine readable* response to queries over HTTP
- bioinformatic applications frequently make use of web APIs for **data retrieval** or genome browser APIs for **data display**
- bioinformatics software libraries for API functionality are usually implemented in **Perl**, **Python** and/or **R**

Bioinformatics: File Formats, Ontologies & APIs

```
{"api_params": {"genome": "hg18", "db": "progenetix", "datatype": "sampledata", "count": 20, "call": "api_doctype=json&api_out=samples&db=progenetix&icdm_m=817&randno=20", "scope": "samples"}, "data": [{"ICDMORPHOLOGY": "Liver cell adenoma", "NCIT:CODE": "C3758", "ICDTOPOGRAPHYCODE": "C22", "_id": {"$oid": "558e5c2ead9a82d95838f76c"}, "CLINICALGROUP": "Carcinomas: hepatic ca.", "PMID": "15765123", "FOLLOWUP": "", "BIOSAMPLEID": "AM_BS__HKCI-C2-D0R", "ICDMORPHOLOGYCODE": "8170/0", "NCIT:TERM": "Hepatocellular Adenoma", "UID": "HKCI-C2-D0R", "DIAGNOSISTEXT": "Hepatocellular carcinoma [cell line, doxorubicin resistant subclone]", "DEATH": "", "ICDTOPOGRAPHY": "liver", "AGE": ""}, {"FOLLOWUP": "", "PMID": "14578863", "ICDMORPHOLOGYCODE": "8170/3", "BIOSAMPLEID": "AM_BS__PHCC-30", "ICDMORPHOLOGY": "Hepatocellular carcinoma, NOS", "_id": {"$oid": "558e5c36ad9a82d9583901bf"}, "CLINICALGROUP": "Carcinomas: hepatic ca.", "ICDTOPOGRAPHYCODE": "C22", "NCIT:CODE": "C3099", "ICDTOPOGRAPHY": "liver", "DEATH": "", "DIAGNOSISTEXT": "Hepatocellular carcinoma", "AGE": "", "NCIT:TERM": "Hepatocellular Carcinoma", "UID": "PHCC-30"}, {"DEATH": "", "DIAGNOSISTEXT": "Hepatocellular carcinoma [chronic Hepatitis B]", "ICDTOPOGRAPHY": "liver", "AGE": "P54Y2M", "NCIT:TERM": "Hepatocellular Carcinoma", "UID": "HCC-1997-14", "PMID": "8993981", "FOLLOWUP": "", "BIOSAMPLEID": "AM_BS__HCC-1997-14", "ICDMORPHOLOGYCODE": "8170/3", "ICDMORPHOLOGY": "Hepatocellular carcinoma, NOS", "NCIT:CODE": "C3099", "ICDTOPOGRAPHYCODE": "C22", "_id": {"$oid": "558e5bfccad9a82d95838b62a"}, "CLINICALGROUP": "Carcinomas: hepatic ca."}, {"FOLLOWUP": "", "PMID": "11485905", "BIOSAMPLEID": "AM_BS__HCChypo-won-H18", "ICDMORPHOLOGYCODE": "8170/3", "ICDMORPHOLOGY": "Hepatocellular carcinoma, NOS", "CLINICALGROUP": "Carcinomas: hepatic ca.", "_id": {"$oid": "558e5c48ad9a82d95839185a"}, "NCIT:CODE": "C3099", "SEX": "male"}]
```

http://progenetix.org/api/?db=progenetix&api_out=samples&api_doctype=json&icdm_m=817&randno=20



BeaconAlleleRequest beacon ↗

{S}[B] Status [i]	implemented
Provenance	◦ Beacon API
Used by	◦ Beacon ◦ Progenetix database schema (Beacon+ backend)
Contributors	◦ Marc Fiume ◦ Michael Baudis ◦ Sabela de la Torre Pernas ◦ Jordi Rambla ◦ Beacon developers...
Source (v1.1.0)	◦ raw source [JSON] ◦ Github

Attributes

Type: object

Description: Allele request as interpreted by the beacon.

Properties

Property	Type
alternateBases	string
assemblyId	string
datasetIds	array of string
end	integer
endMax	integer
endMin	integer
mateName	https://schemablocks.org/schemas/beacon/v1.1.0/Chromosome [HTML]
referenceBases	string
referenceName	https://schemablocks.org/schemas/beacon/v1.1.0/Chromosome [HTML]
start	integer (int64)
startMax	integer
startMin	integer
variantType	string

alternateBases

- type: string

The bases that appear instead of the reference bases. Accepted values: [ACGTN]*. N is a wildcard, that denotes the position of any base, and can be used as a standalone base of any type or within a partially known sequence. For example a sequence where the first and last bases are known, but the middle portion can exhibit countless variations of [ACGT], or the bases are unknown: ANNT the Ns can take any form of [ACGT], which makes both ACCT and ATGT (or any other combination) viable sequences.

Symbolic ALT alleles (DEL, INS, DUP, INV, CNV, DUP:TANDEM, DEL:ME, INS:ME) will be represented in variantType.

Optional: either alternateBases or variantType is required.

alternateBases Value Example

assemblyId

- type: string

Assembly identifier (GRC notation, e.g. GRCh37).

assemblyId Value Example

Curie sb-vr-spec ↗

{S}[B] Status [i]	implemented
Provenance	◦ vr-spec
Used by	◦ vr-spec
Contributors	◦ Reece Hart ◦ Michael Baudis

Attributes

Type: object

Description: A CURIE is a Uniform Resource Identifier (URI) that identifies a single entity. It consists of a prefix followed by a namespace and a local identifier. The prefix is typically a well-known identifier for a specific domain, such as 'http://www.w3.org/2002/07/owl#' for the Web Ontology Language (OWL). The namespace is a URI that identifies the vocabulary or ontology being used. The local identifier is a unique identifier within that vocabulary.

VR does not impose any constraints on strings used as identifiers, the VR Specification RECOMMENDS that implementers use standard CURIEs.

String CURIEs are represented as [prefix:reference](#) (W3C Recommendation) or [namespace:accession](#) or [namespace:local_id](#) colloquially.

The VR specification also RECOMMENDS that [prefix](#) be

The [reference](#) component is an unconstrained string. A CURIE is a URI. URIs may [locate](#) objects (i.e., specify where they are located) or identify resources (i.e., specify what they are).

A CURIE is a URI. URIs may [locate](#) objects (i.e., specify where they are located) or identify resources (i.e., specify what they are).

VR uses CURIEs primarily as a naming mechanism. Implementations MAY provide CURIE resolution mechanisms.

Using internal IDs in public messages is strongly discouraged.

Curie Value Examples

"ga4gh:GA_01234abcde"

"DUO:0000004"

"orcid:0000-0003-3463-0775"

"PMID:15254584"

Biosample sb-phenopackets ↗

{S}[B] Status [i]	implemented
Provenance	◦ Phenopackets
Used by	◦ Phenopackets
Contributors	◦ GA4GH Data Working Group ◦ Jules Jacobsen ◦ Peter Robinson ◦ Michael Baudis ◦ Melanie Courtot ◦ Isuru Liyanage
Source (v1.0.0)	◦ raw source [JSON] ◦ Github

Attributes

Type: object

Description: A Biosample refers to a unit of biological material from which the substrate molecules (e.g. genomic DNA, RNA, proteins) for molecular analyses (e.g. sequencing, array hybridisation, mass spectrometry) are extracted.

Examples would be a tissue biopsy, a single cell from a culture for single cell genome sequencing, or a fraction from a gradient centrifugation.

Several instances (e.g. technical replicates) or types of experiments (e.g. genomic array as well as experiments) may refer to the same Biosample.

FHIR mapping: Specimen.

Properties

Property	Type
ageOfIndividualAtCollection	https://schemablocks.org/schemas/sb-phenopackets/v1.0.0/Age.json [SRC] [HTML]
ageRangeOfIndividualAtCollection	https://schemablocks.org/schemas/sb-phenopackets/v1.0.0/AgeRange.json [SRC] [HTML]
description	string
diagnosticMarkers	array of https://schemablocks.org/schemas/sb-phenopackets/v1.0.0/OntologyClass.json [SRC] [HTML]
histologicalDiagnosis	https://schemablocks.org/schemas/sb-phenopackets/v1.0.0/OntologyClass.json [SRC] [HTML]
htsFiles	array of https://schemablocks.org/schemas/sb-phenopackets/v1.0.0/HtsFile.json [SRC] [HTML]
id	string
individualId	string
isControlSample	boolean
phenotypicFeature	array of https://schemablocks.org/schemas/sb-phenopackets/v1.0.0/PhenotypicFeature.json [SRC] [HTML]
procedure	https://schemablocks.org/schemas/sb-phenopackets/v1.0.0/Procedure.json [SRC] [HTML]
sampledTissue	https://schemablocks.org/schemas/sb-phenopackets/v1.0.0/Tissue.json [SRC] [HTML]

Checksum sb-checksum ↗

{S}[B] Status [i]	proposed
Provenance	◦ GA4GH DRS (`develop` branch)
Used by	◦ GA4GH DRS ◦ GA4GH TRS
Contributors	◦ Susheel Varma
Source (v0.0.1)	◦ raw source [JSON] ◦ Github

Attributes

Type: object

Description: Checksum

Properties

Property	Type
checksum	<ul style="list-style-type: none"> • type: string <p>The hexadecimal encoded (Base16) checksum for the data.</p>
checksum Value Example	"77af4d6b9913e693e8d0b4b294fa62ade6054e6b2f1ffb617ac955dd63fb0182"

type

- type: string

The digest method used to create the checksum. The value (e.g. [sha-256](#)) SHOULD be listed as [Hash Name String](#) in the [GA4GH Hash Algorithm Registry](#). Other values MAY be used, as long as implementors are aware of the issues discussed in [RFC6920](#).

GA4GH may provide more explicit guidance for use of non-IANA-registered algorithms in the future.

type Value Example

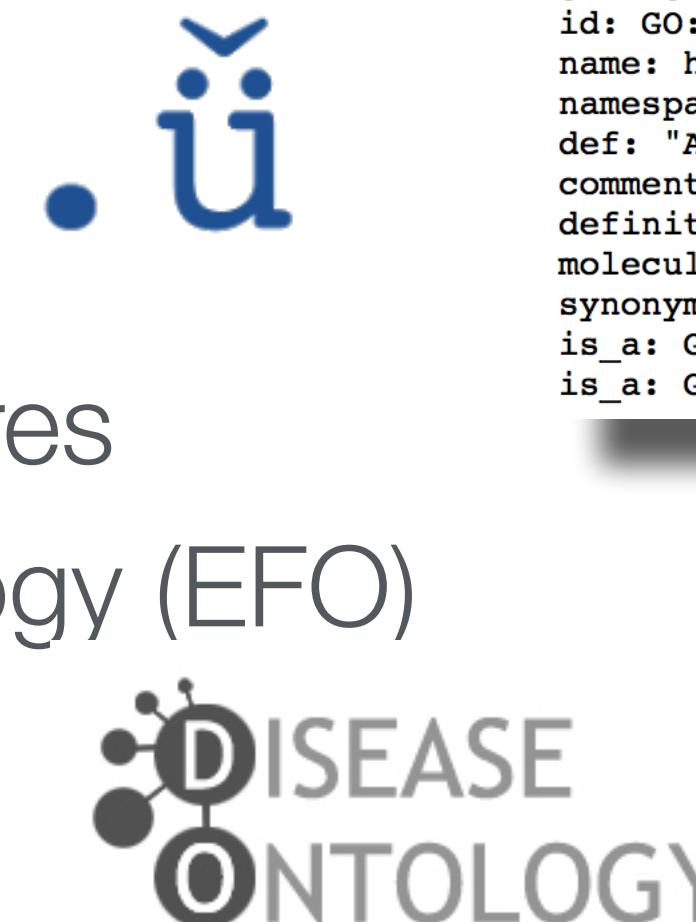
"sha-256"

Bioinformatics: File Formats, Ontologies & APIs

- ontologies in information sciences describe concrete and abstract **objects**, there precisely defined **hierarchies** and **relationships**
- ontologies in bioinformatics support the move from a descriptive towards an **analytical science** in describing biological data and relations among it

"The widest use of ontologies within biology is for conceptual annotation – a representation of stored knowledge more computationally amenable than natural language."^{*}

- Gene ontology (GO)
- NCI Neoplasm Core
- Uberon anatomical structures
- Experimental Factor Ontology (EFO)
- Disease Ontology (DO)



id: GO:0000118
name: histone deacetylase complex
namespace: cellular_component
def: "A protein complex that possesses histone deacetylase activity." [GOC:mah]
comment: Note that this term represents a complex, not a single protein.
definition for the purpose of this ontology:
molecular function term 'histone deacetylase activity'
synonym: "HDAC complex" EXACT [C3709]
is_a: GO:0044451 ! nucleoplasm
is_a: GO:1902494 ! catalytic complex

complex is mentioned in the
lex is represented by the

- ☐ Neoplasm by Morphology
 - ☐ Epithelial Neoplasm [C3709](#)
 - ☐ Germ Cell Tumor [C3708](#)
 - ☐ Giant Cell Neoplasm [C7069](#)
 - ☐ Hematopoietic and Lymphoid Cell Neoplasm [C27134](#)
 - ☐ Melanocytic Neoplasm [C7058](#)
 - ☐ Benign Melanocytic Skin Nevus [C7571](#)
 - ☐ Dysplastic Nevus [C3694](#)
 - ☐ Melanoma [C3224](#)
 - ☐ Amelanotic Melanoma [C3802](#)
 - ☐ Cutaneous Melanoma [C3510](#)
 - ☐ Epithelioid Cell Melanoma [C4236](#)
 - ☐ Mixed Epithelioid and Spindle Cell Melanoma [C66756](#)
 - ☐ Non-Cutaneous Melanoma [C8711](#)
 - ☐ Spindle Cell Melanoma [C4237](#)
 - ☐ Meningothelial Cell Neoplasm [C6971](#)

Standardized Data

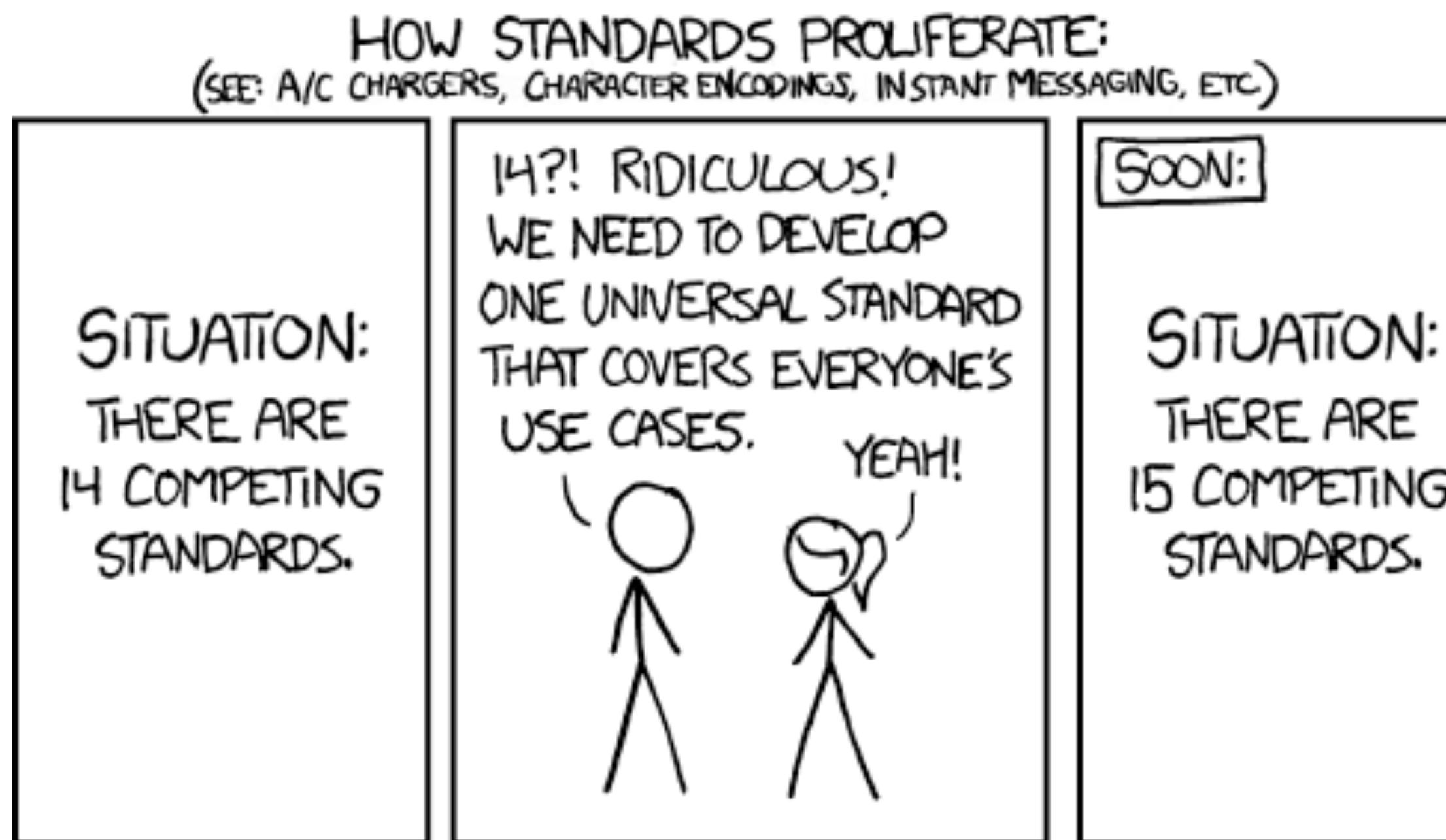
Data re-use depends on standardized, machine-readable metadata

- Multiple international initiatives (ELIXIR, GA4GH, MONARCH...) and resource providers (EBI, NCBI ...) work on the generation and implementation of data annotation standards
- emerging / established principles are the use of **hierarchical** coding systems where individual codes are represented as CURIEs
- other formats for non-categorical annotations based on international standards, e.g.
 - ISO (ISO 8601 time & period, ISO 3166 country codes ...)
 - IETF (GeoJSON ...)
 - W3C (CURIE ...)
- these standards become pervasive throughout GA4GH's ecosystem (e.g. Phenopackets ...)

```
"data_use_conditions" : {  
    "label" : "no restriction",  
    "id" : "DUO:0000004"  
},  
  
"provenance" : {  
    "material" : {  
        "type" : {  
            "id" : "EFO:0009656",  
            "label" : "neoplastic sample"  
        }  
    },  
    "geo" : {  
        "label" : "Zurich, Switzerland",  
        "precision" : "city",  
        "city" : "Zurich",  
        "country" : "Switzerland",  
        "latitude" : 47.37,  
        "longitude" : 8.55,  
        "geojson" : {  
            "type" : "Point",  
            "coordinates" : [  
                8.55,  
                47.37  
            ]  
        },  
        "ISO-3166-alpha3" : "CHE"  
    },  
    {  
        "age": "P25Y3M2D"  
    }  
}
```

Standardized Data

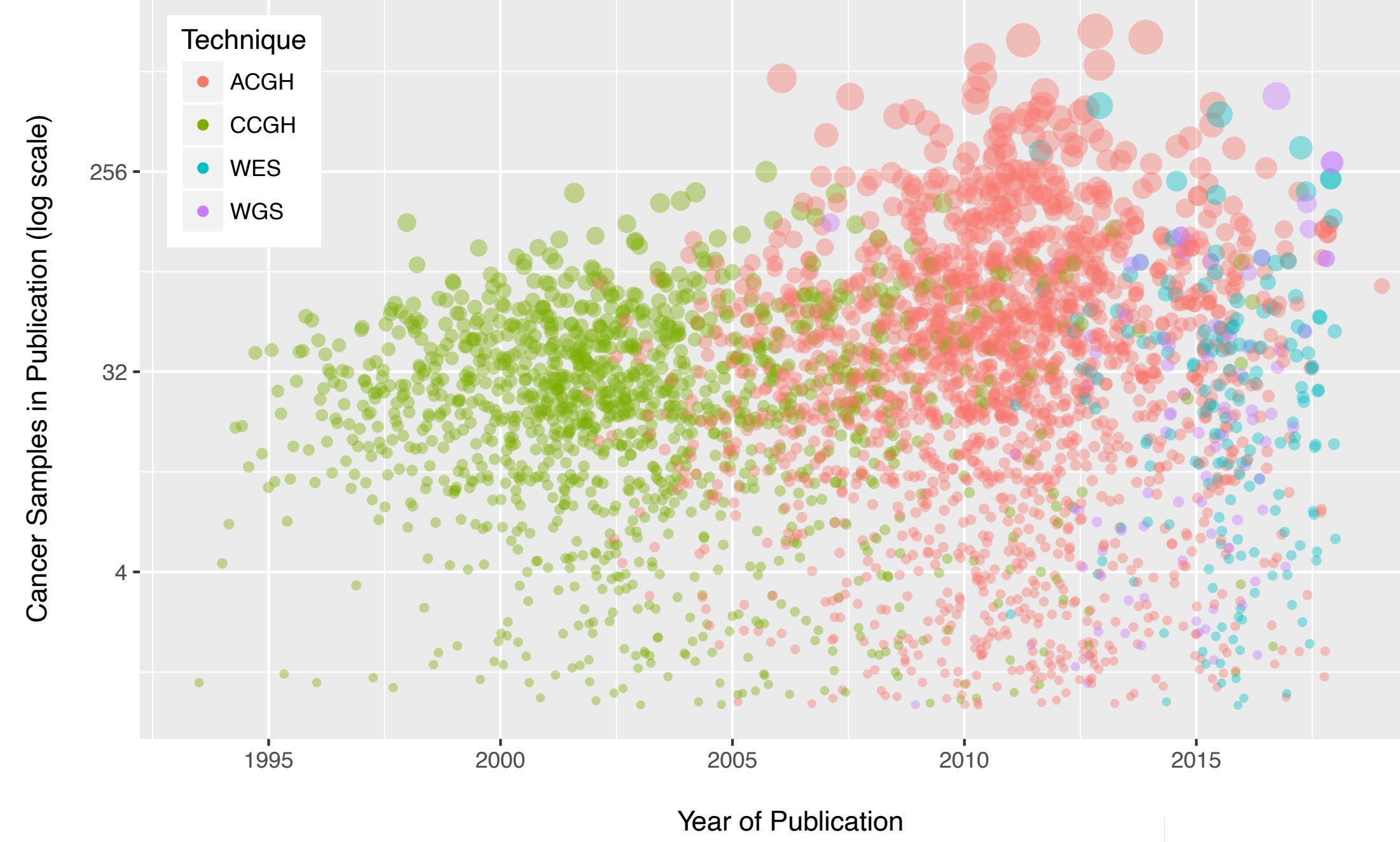
Data re-use depends on standardized, machine-readable metadata



xkcd

```
"data_use_conditions" : {  
    "label" : "no restriction",  
    "id" : "DUO:0000004"  
},  
  
"provenance" : {  
    "material" : {  
        "type" : {  
            "id" : "EFO:0009656",  
            "label" : "neoplastic sample"  
        }  
    },  
    "geo" : {  
        "label" : "Zurich, Switzerland",  
        "precision" : "city",  
        "city" : "Zurich",  
        "country" : "Switzerland",  
        "latitude" : 47.37,  
        "longitude" : 8.55,  
        "geojson" : {  
            "type" : "Point",  
            "coordinates" : [  
                8.55,  
                47.37  
            ]  
        },  
        "ISO-3166-alpha3" : "CHE"  
    },  
    {  
        "age": "P25Y3M2D"  
    }  
}
```

Data Science: Meta-Studies of Metadata



Map of the geographic distribution (by first author affiliation) of the 104'543 genomic array, 36'766 chromosomal CGH and 15'409 whole genome/exome based cancer genome datasets.

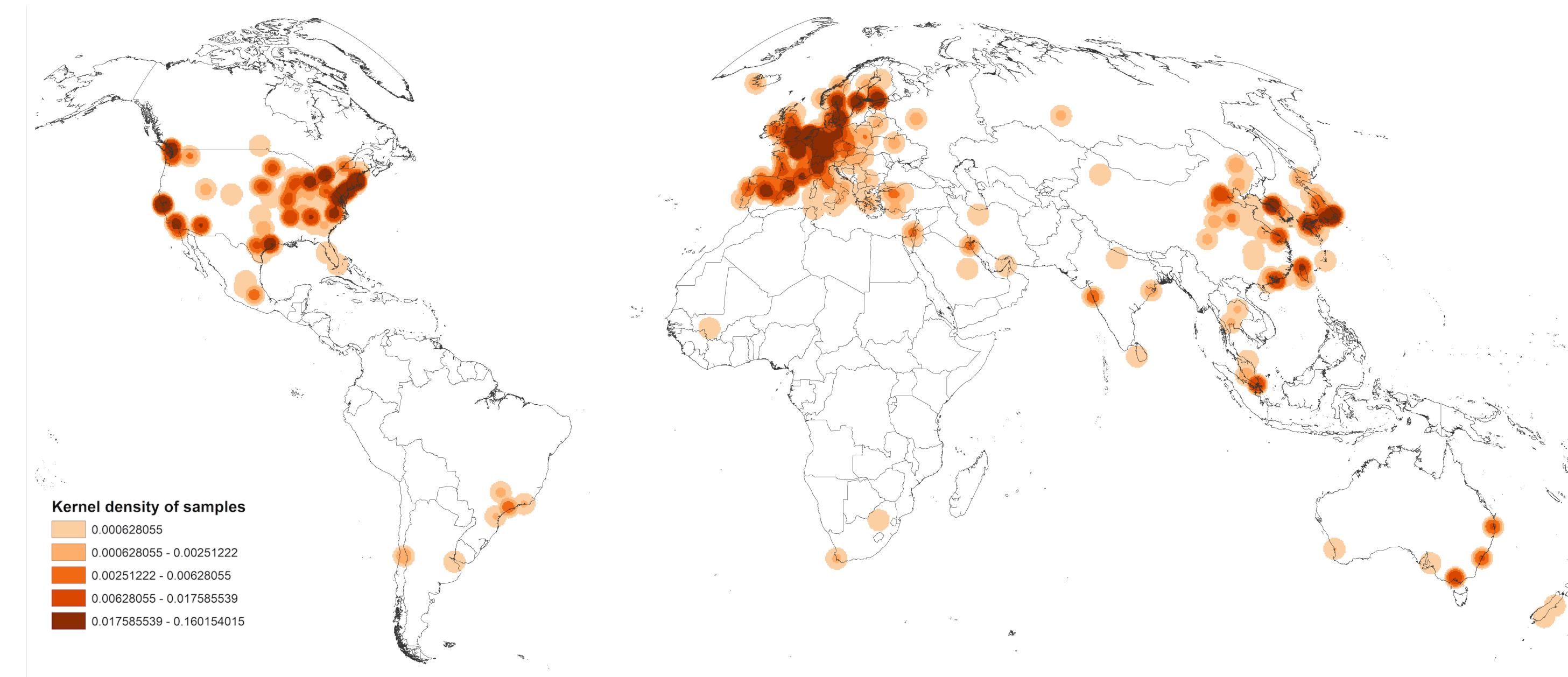
The numbers are derived from the 3'240 publications registered in the Progenetix database.



Publication Landscape of Cancer CNV Profiling

Publication statistics for cancer genome screening studies. The graphic shows our assessment of publications reporting whole-genome screening of cancer samples, using molecular detection methods (chromosomal CGH, genomic array technologies, whole exome and genome sequencing).

For the years 1993-2018, we found 3'229 publications reporting 174'530 individual samples in single series from 1 to more than 1000 samples. Y-axis and size of the dots correspond to the sample number; the color codes indicate the technology used.



But: What is not bioinformatics, though being "bio" and using computers?

- "*I do not think all biological computing is bioinformatics, e.g. mathematical modelling is not bioinformatics, even when connected with biology-related problems. In my opinion, bioinformatics has to do with management and the subsequent use of biological information, particular genetic information.*" (Richard Durbin)
- **biologically-inspired computation** (neural networks etc.) - though their application may be part of bioinformatics
- **computational & systems biology**, where the emphasis is on **modelling** rather than on **data interpretation**

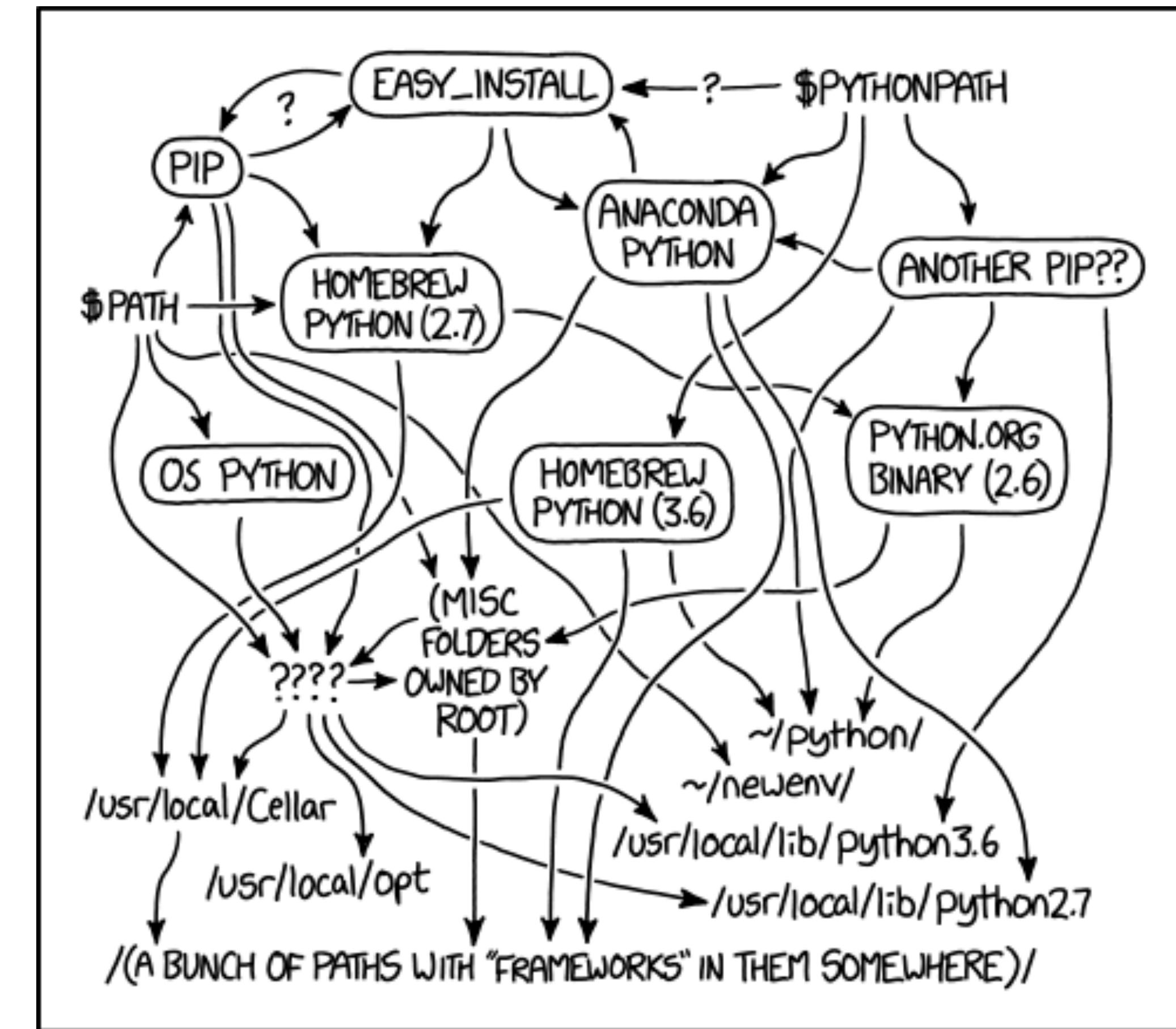
Bioinformatics OR Computational / Systems Biology?

- **Bioinformatics**

Research, development, or **application** of computational **tools** and approaches to make the vast, diverse and complex **life sciences data** more understandable and useful

- **Computational biology**

The development and application of **mathematical** and computational **approaches** to address **theoretical** and experimental questions in biology



MY PYTHON ENVIRONMENT HAS BECOME SO DEGRADED
THAT MY LAPTOP HAS BEEN DECLARED A SUPERFUND SITE.

BIO390: Introduction to Bioinformatics

Lecture I: What are Bioinformaticians doing? Example of Developing "Federated Human Data" concepts

The trouble with human genome variation



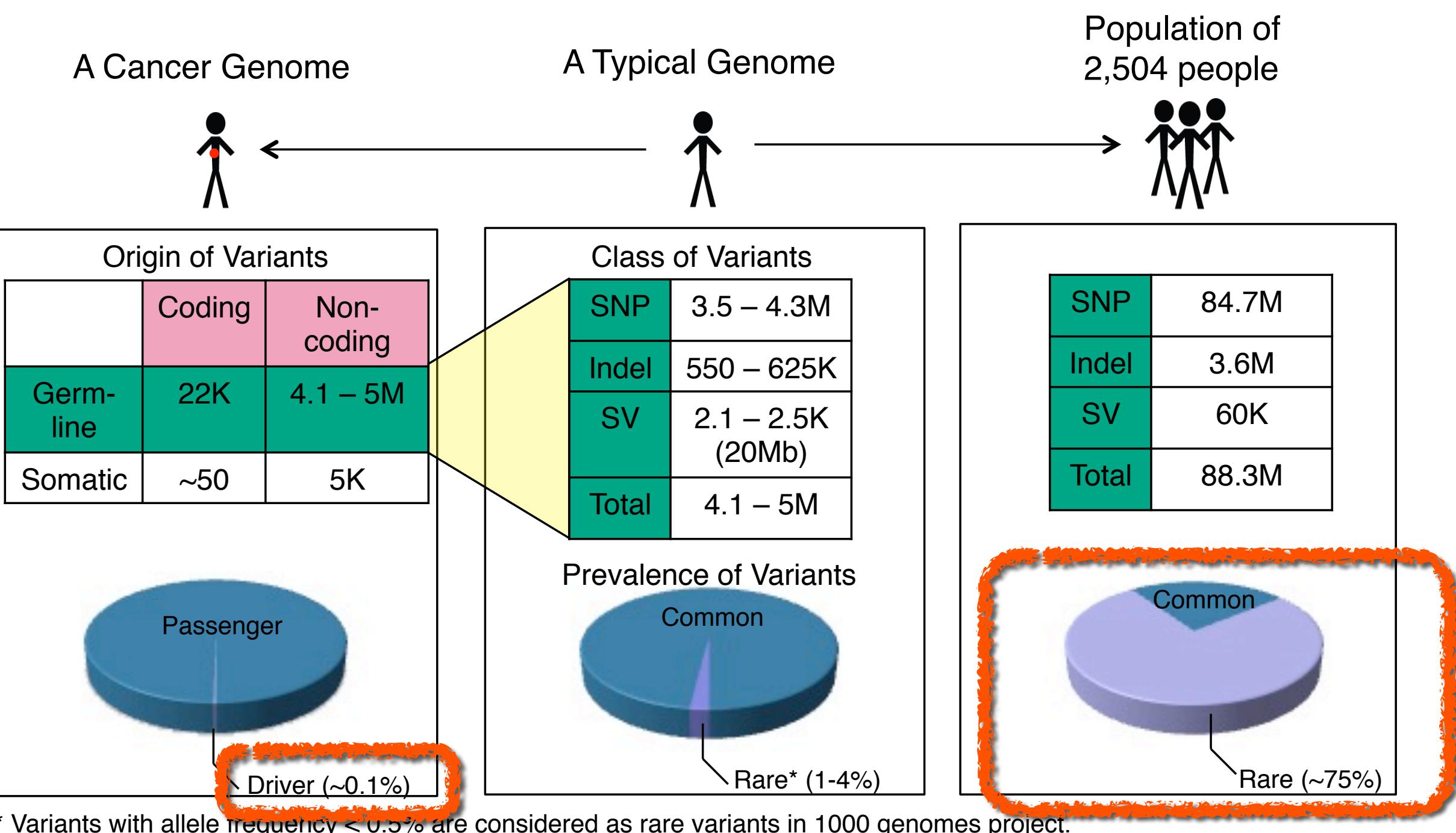
Conclusions from the analysis of variation in the human genome

- 1. Humans are all very similar to each other
 - Two humans will show about 99.9% sequence identity with each other. In other words, only about 1 in 1'000 bp is different between two individuals.
 - Humans show about 98% sequence identity to chimps. So two humans are still much more similar to each other than either is to the monkey.
- 2. Humans are very different from each other
 - Two typical humans will likely have over 1'000'000 independent sequence differences in their genomes.

Finding Somatic Mutations In Cancer

Many Needles in a Large Haystack

- a typical human genome (~3 billion base pairs) has ~5 million variants
- most of them are "**rare**"; i.e. can only be identified as recurring when sequencing thousands of people
- cancer cells accumulate additional variants, only **few** of which ("**drivers**") are relevant for the disease

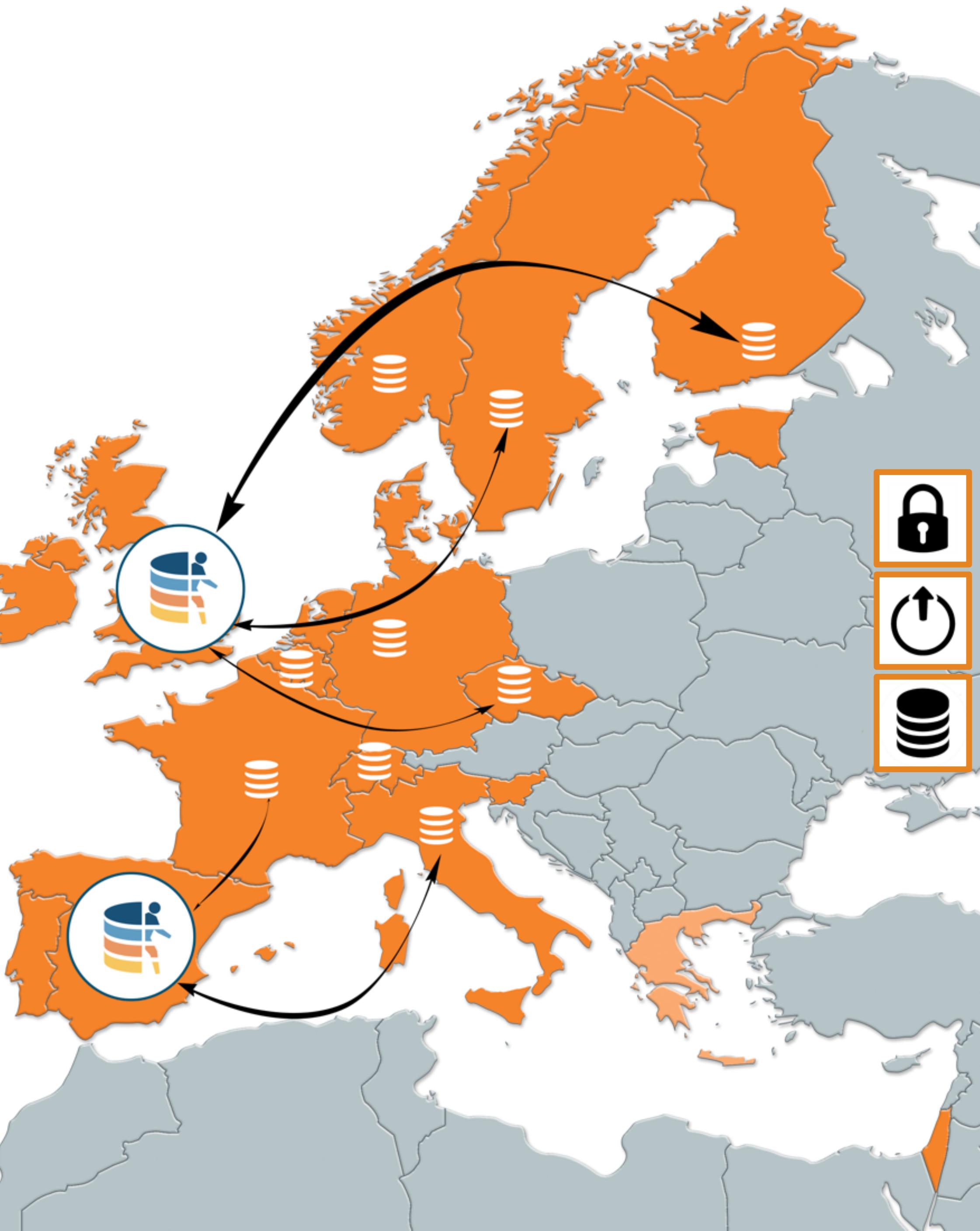


The 1000 Genomes Project Consortium, Nature. 2015. 526:68-74
Khurana E. et al. Nat. Rev. Genet. 2016. 17:93-108

Graphic adapted from Mark Gerstein (GersteinLab.org; @markgerstein)

Federation of human genome data

- Many national datasets from human research participants needs to be stored locally
- ELIXIR developing a federation with shared metadata (FAIR) and local data store (secure)
- Linking local EGA to national clouds – and international access (ELIXIR-AAI)



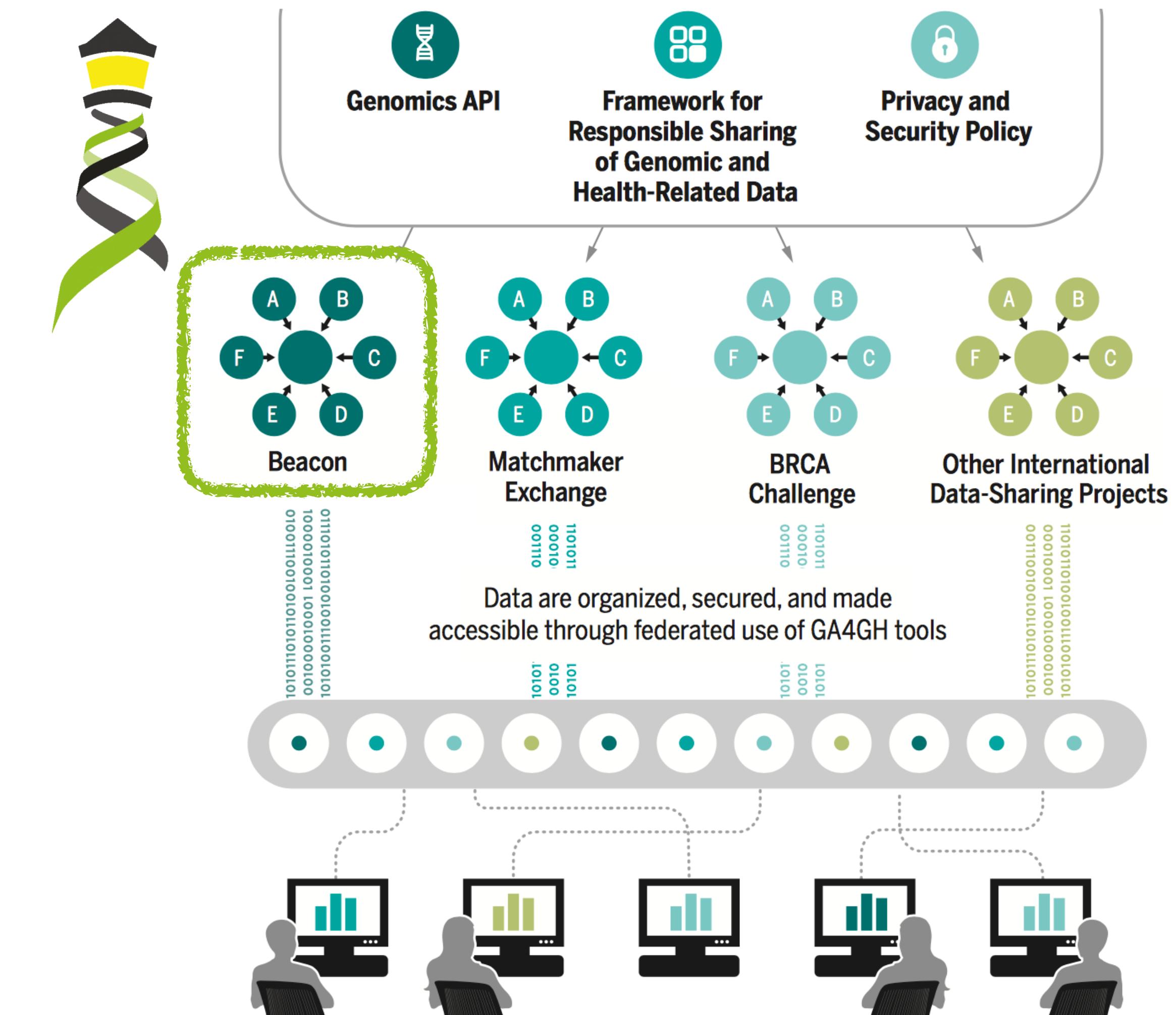


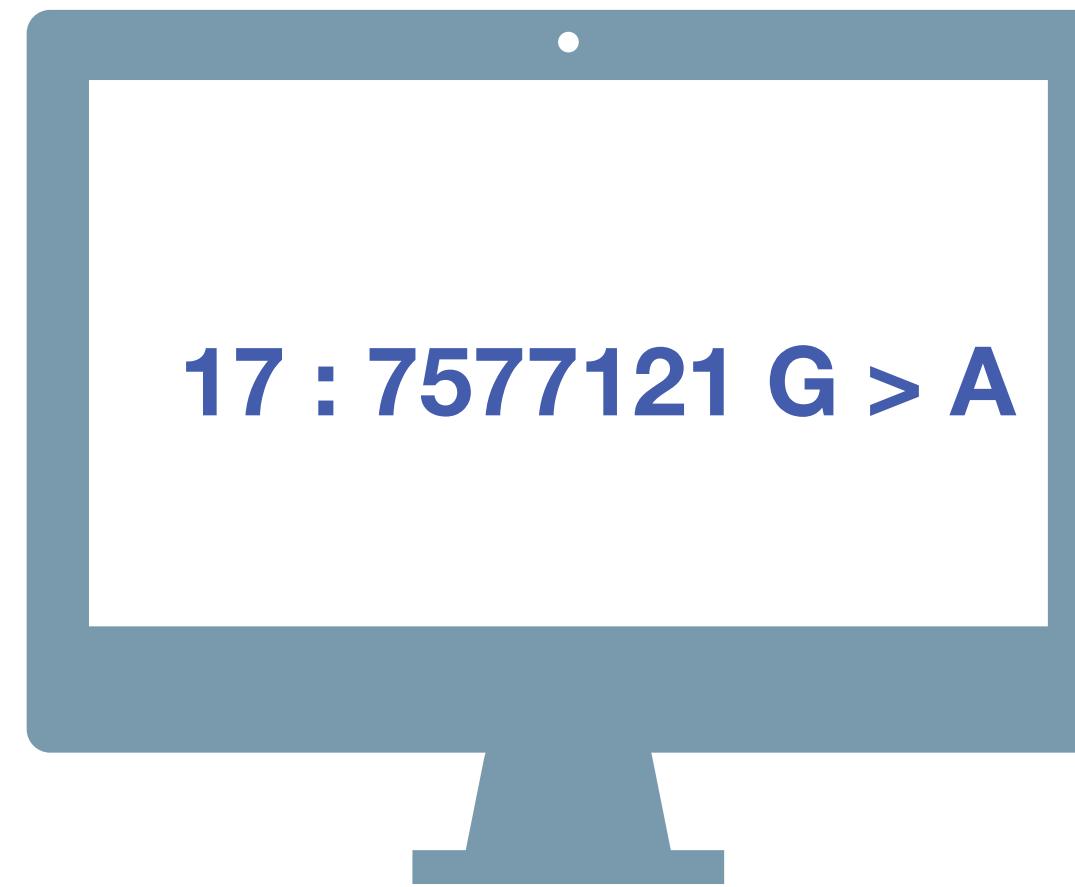
GENOMICS

A federated ecosystem for sharing genomic, clinical data

Silos of genome data collection are being transformed into seamlessly connected, independent systems

A federated data ecosystem. To share genomic data globally, this approach furthers medical research without requiring compatible data sets or compromising patient identity.





Beacon

A **Beacon** answers a query for a specific genome variant against individual or aggregate genome collections

YES | NO | \0

Beacon v2 Requests

POSTing Queries

- Beacon v2 supports a mix of dedicated endpoints with REST paths
- POST requests using JSON query documents
- final syntax for core parameters still in testing stages

```
{  
  "$schema": "beaconRequestBody.json",  
  "meta": {  
    "apiVersion": "2.0",  
    "requestedSchemas": [  
      {  
        "entityType": "individual",  
        "schema": "https://progenetix.org/services/schemas/Phenopacket/"  
      }  
    ],  
    "query": {  
      "requestParameters": {  
        "datasets": {  
          "datasetIds": ["progenetix"]  
        }  
      },  
      "filterLogic": "OR"  
    },  
    "pagination": {  
      "skip": 0,  
      "limit": 10  
    },  
    "filters": [  
      { "id": "NCIT:C4536" },  
      { "id": "NCIT:C95597" },  
      { "id": "NCIT:C7712" }  
    ]  
  }  
}
```



Progenetix & Beacon v1->2

Handover elements in Beacon responses

- Progenetix utilizes handovers to deliver data matched by the Beacon queries
- These handovers are interpreted by the front end to populate different parts of the UI, w/o the need of active selection
- Handovers are either standard Beacon v2 paths or dedicated custom functions

```
"results_handovers": [
  {
    "description": "create a CNV histogram from matched callsets",
    "handoverType": {"id": "pgx:handover:cnvhistogram", "label": "CNV Histogram"},
    "url": "https://progenetix.org/cgi-bin/PGX/cgi/samplePlots.cgi?method=cnvhistogram&accessid=aff0f73f-6dbf-45e5-91ba-04f19e3621bb"
  },
  {
    "description": "retrieve data of the biosamples matched by the query",
    "handoverType": {"id": "pgx:handover:biosamples", "label": "Biosamples"},
    "url": "https://progenetix.org/beacon/biosamples/?accessid=61b68a59-2160-41e4-a17d-0cf128841a57"
  },
  {
    "description": "retrieve variants matched by the query",
    "handoverType": {"id": "pgx:handover:variants", "label": "Found Variants (.json)" },
    "url": "https://progenetix.org/beacon/variants/?method=variants&accessid=5cced529-3acf-4156-b121-6ae7e5e63d0c"
  },
  {
    "description": "Download all variants of matched samples - potentially huge dataset...",
    "handoverType": {"id": "pgx:handover:callsetsvariants", "label": "All Sample Variants (.json)" },
    "url": "https://progenetix.org/beacon/variants/?method=callsetsvariants&accessid=61b68a59-2160-41e4-a17d-0cf128841a57"
  },
  {
    "description": "map variants matched by the query to the UCSC browser",
    "handoverType": {"id": "pgx:handover:bedfile2ucsc", "label": "Show Variants in UCSC" },
    "url": "http://genome.ucsc.edu/cgi-bin/hgTracks?org=human&db=hg38&position=chr9:21531306-22492891&hgt.customText=https://progenetix.org/tmp/5cced529-3acf-4156-b121-6ae7e5e63d0c.bed"
  }
]
```

ELIXIR Beacon Network



- developed under lead from ELIXIR Finland
- **authenticated access** w/ ELIXIR AAI
- **incremental extension**, starting with ELIXIR Beacon resources adhering to the **latest specification** (contrast to legacy networks)
- service details provided by individual Beacons, using **GA4GH service-info**
- **registration service**
 - integrator** throughout ELIXIR Human Data
 - starting point for "beyond ELIXIR"**
feature rich federated Beacon services

GRCh38 ▾ 17 : 7577121 G > A

Example variant query Search

[Advanced Search](#)

baudisgroup at UZH and SIB
Progenetix Cancer Genomics Beacon+

Beacon+ provides a forward looking implementation of the Beacon API, with focus on structural variants and metadata based on the cancer and reference genome profiling data represented in the Progenetix oncogenomic data resource (<https://progenetix.org>).

[Visit Us](#) · [Beacon API](#) · [Contact Us](#)

NBIS National Bioinformatics Infrastructure Sweden SweFreq Beacon

Beacon API Web Server based on the GA4GH Beacon API

[Visit Us](#) · [Beacon API](#) · [Contact Us](#)

CSC - IT Center for Science
Development Beacon

Beacon API Web Server based on the GA4GH Beacon API

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LCSB at University of Luxembourg
ELIXIR.LU Beacon

ELIXIR.LU Beacon

[Visit Us](#) · [Beacon API](#) · [Contact Us](#)

Research Programme on Biomedical Informatics
DisGeNET Beacon

Variant-Disease associations collected from curated resources and the literature

[Visit Us](#) · [Beacon API](#) · [Contact Us](#)

European Genome-Phenome Archive (EGA)
EGA Beacon

This [Beacon](https://beacon-project.io/) is based on the GA4GH Beacon [v1.1.0](https://github.com/ga4gh/beacon/specification/blob/develop/beacon.yaml)

[Visit Us](#) · [Beacon API](#) · [Contact Us](#)

University of Tartu Institute of Genomics, Estonia
Beacon at the University of Tartu, Estonia

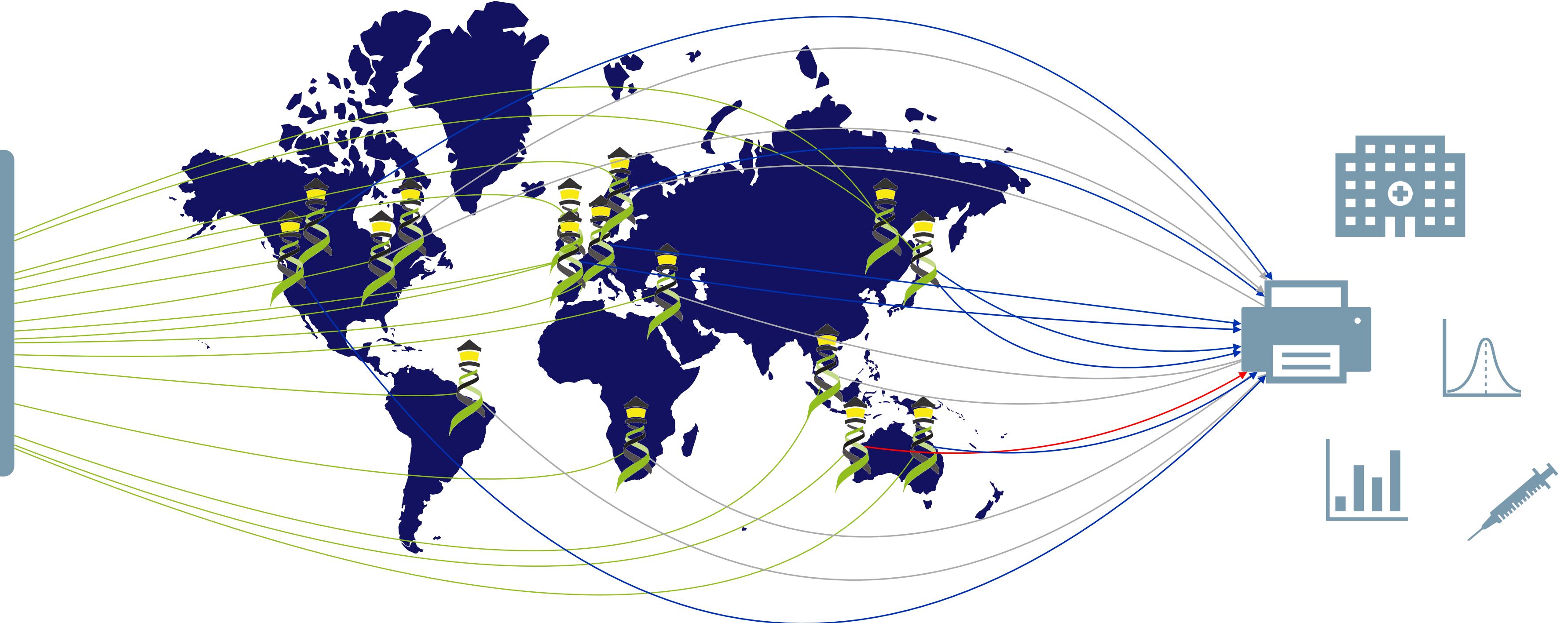
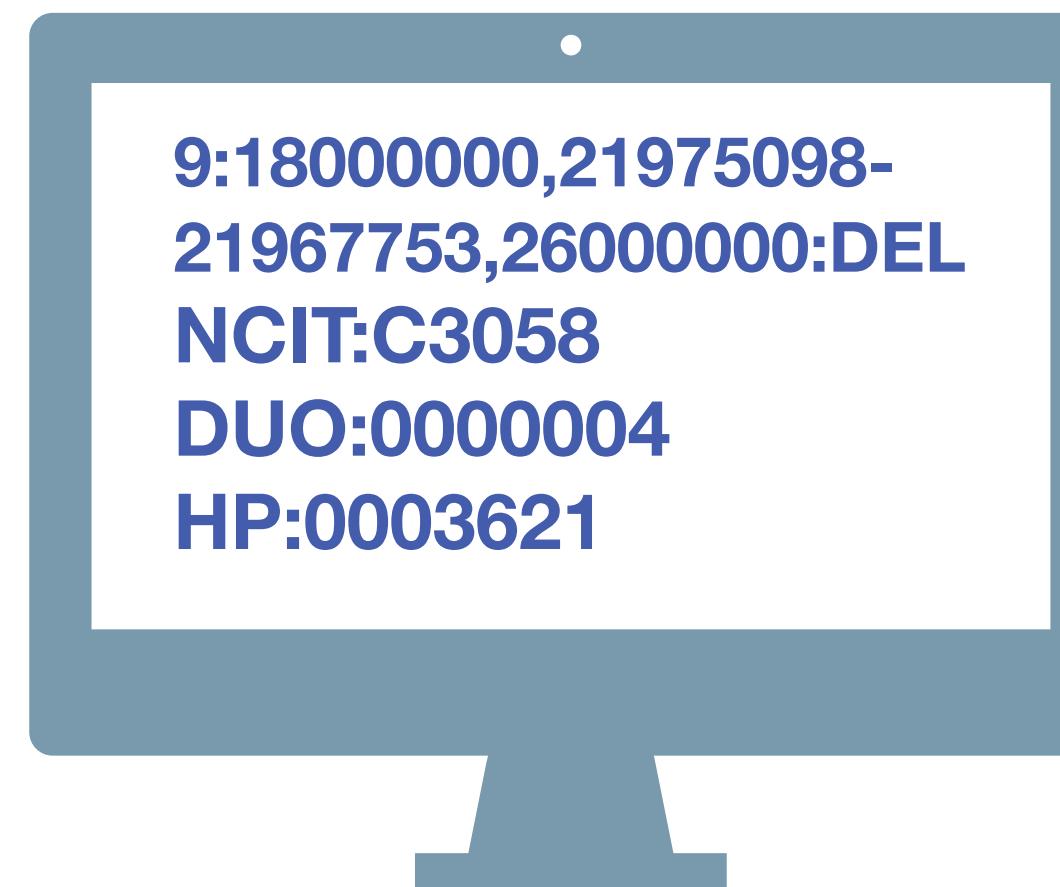
Beacon API Web Server based on the GA4GH Beacon API

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CSC - IT Center for Science
Production Beacon

Beacon API Web Server based on the GA4GH Beacon API

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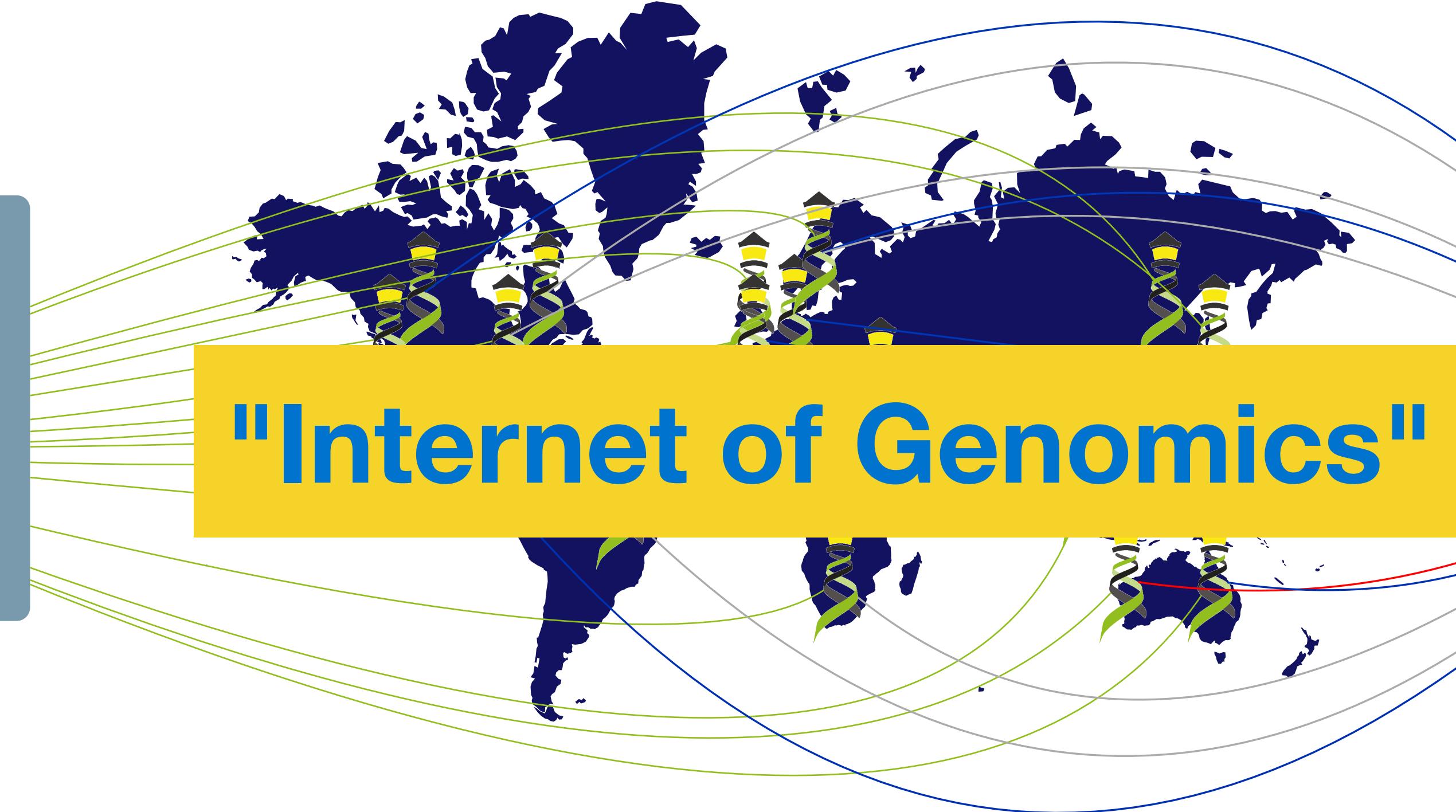
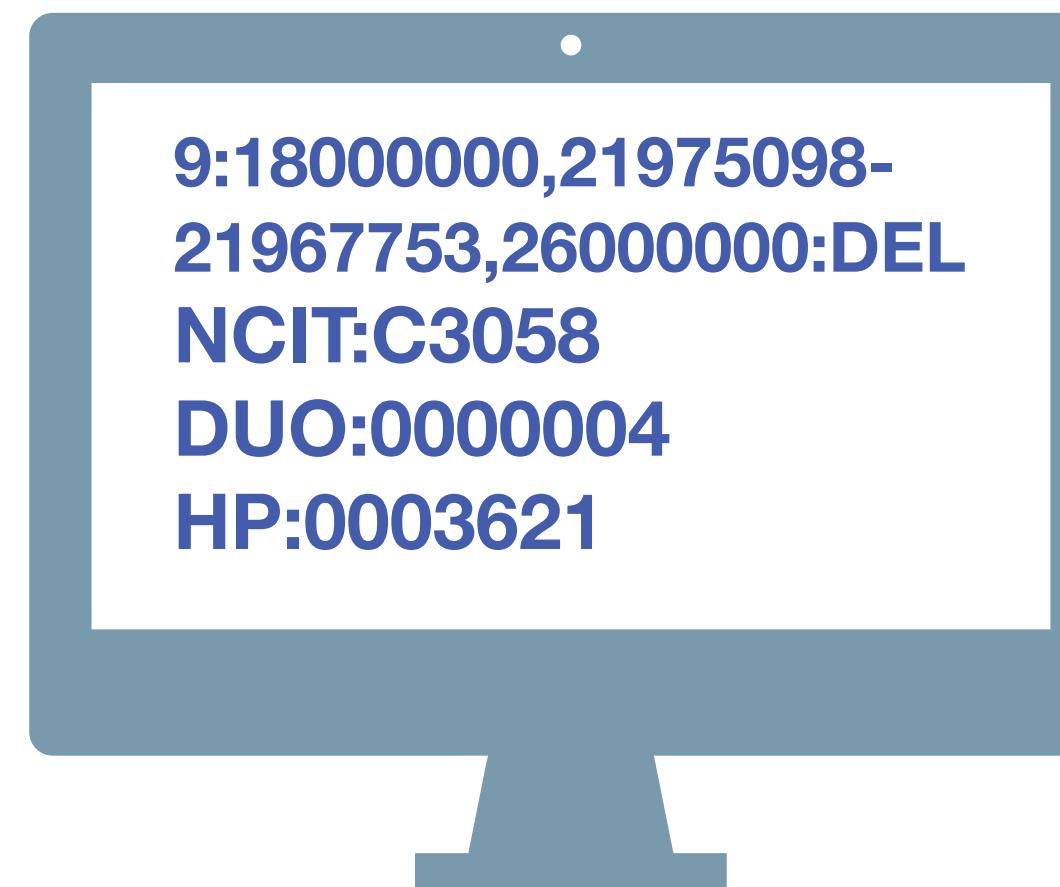


Have you seen deletions in this region on chromosome 9 in Glioblastomas from a juvenile patient, in a dataset with unrestricted access?

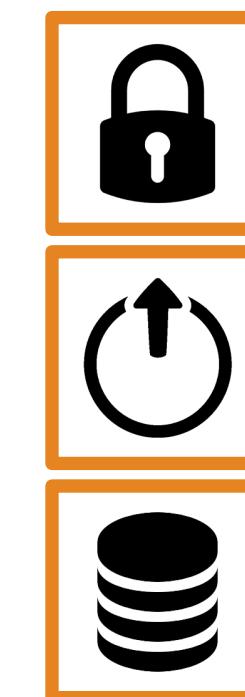


Beacon v2 API

The Beacon API v2 proposal opens the way for the design of a simple but powerful "genomics API".



Have you seen deletions in this region on chromosome 9 in Glioblastomas from a juvenile patient, in a dataset with unrestricted access?



Beacon v2 API

The Beacon API v2 proposal opens the way for the design of a simple but powerful "genomics API".

BIO390: Course Schedule

- 2021-09-21: Michael Baudis - What is Bioinformatics? Introduction and Resources
- **2021-09-28: Christian von Mering - Sequence Bioinformatics**
- 2021-10-05: Mark Robinson - Statistical Bioinformatics
- 2021-10-12: Valentina Boeva (ETHZ) - Machine Learning for Biological Use Cases
- 2021-10-19: Izaskun Mallona - Regulatory Genomics and Epigenomics
- 2021-10-26: Shinichi Sunagawa (ETHZ) - Metagenomics
- 2021-11-02: Katja Baerenfaller (SIAF) - Proteomics
- 2021-11-09: Puria Dasmeh - Biological Networks
- 2021-11-16: TBD - Text Mining topic
- 2021-11-23: Fabio Rinaldi - Text Mining
- 2021-11-30: Michael Baudis - Building a Genomics Resource
- 2021-12-07: Valérie Barbie (SIB) - Clinical Bioinformatics
- 2021-12-14: Michael Baudis - Genome Data & Privacy
- 2021-12-21: Exam (Multiple Choice)



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Zurich^{UZH}



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progenetix.org
info.baudisgroup.org
sib.swiss/baudis-michael
imls.uzh.ch/en/research/baudis
beacon-project.io
schemablocks.org



Global Alliance
for Genomics & Health

