Data Management

Niclas Jareborg & Yvonne Kallberg, NBIS
niclas.jareborg@nbis.se

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Bioinformatics for Principal Investigators course

NBIS
NATIONAL BIOINFORMATICS INFRASTRUCTURE SWEDEN

SciLifeLab

Do you think data management is important?

The Research Data Life Cycle

Study & Analysis

Uppsala Multidisciplinary Center for Advanced Computational Science UPPMAX

"rackham"

"bianca"

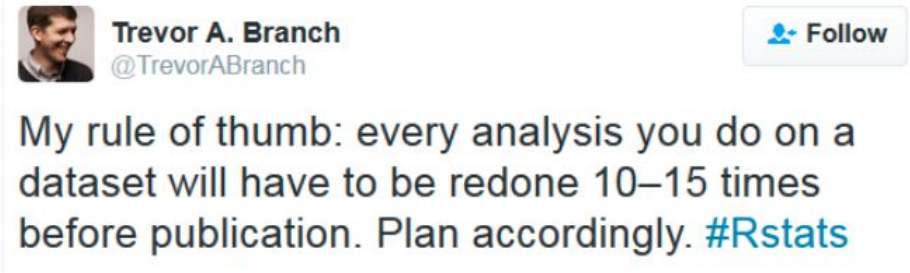
Human derived data

How do you know how an old result was generated?

Structuring data for analysis

- Guiding principle
  - *“Someone unfamiliar with your project should be able to look at your computer files and understand in detail what you did and why.”*

- Research reality
  - *"Everything you do, you will have to do over and over again”* – Murphy’s law

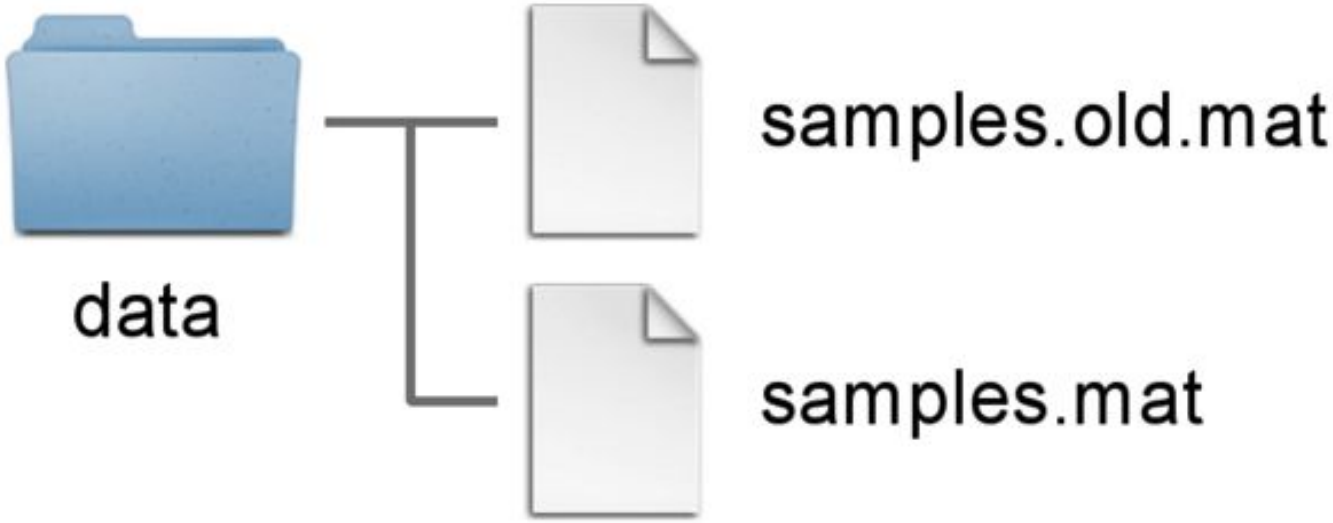


Poor organizational choices lead to significantly slower research progress

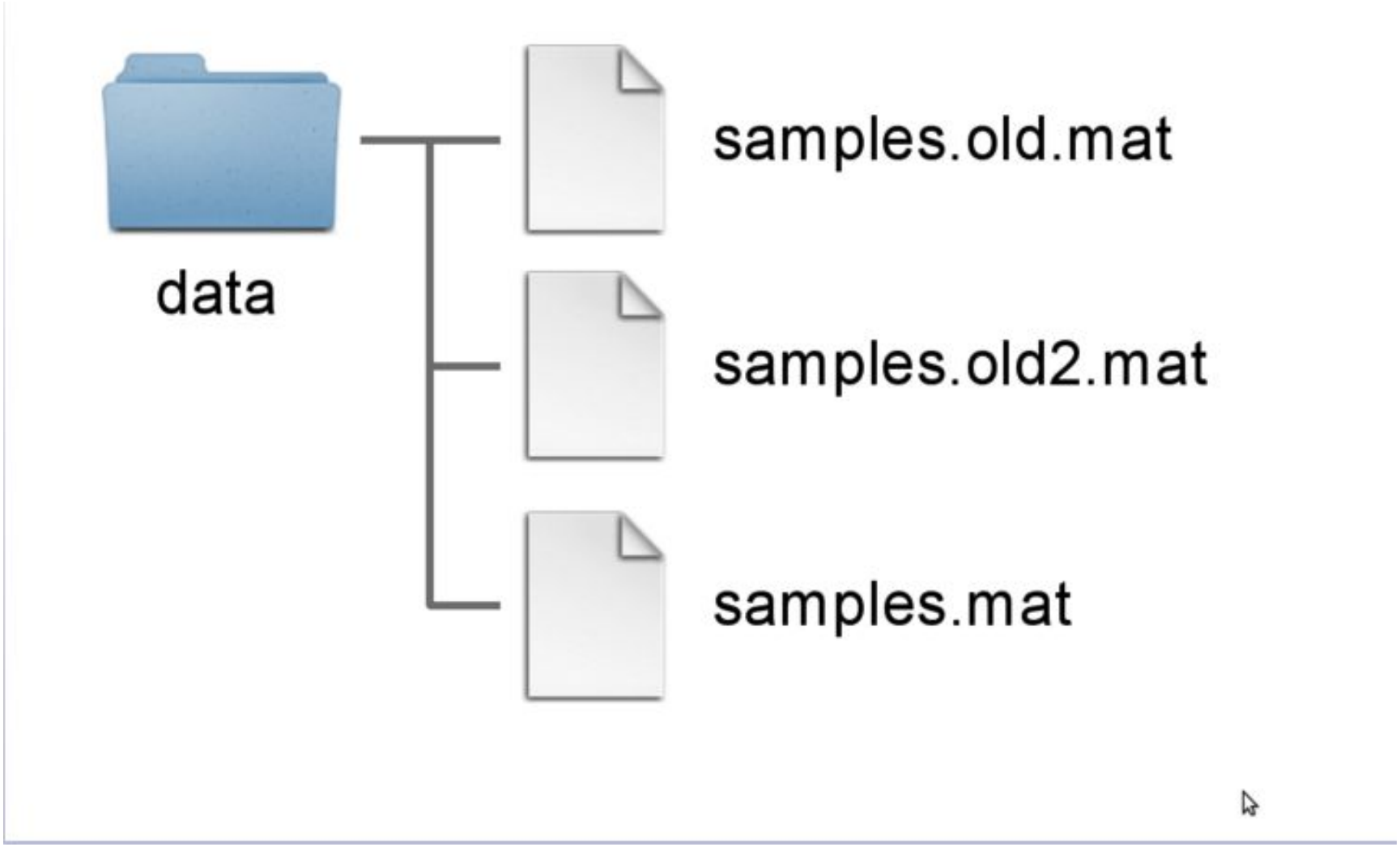
"Your primary collaborator is yourself six months from now, and your past self doesn't answer e-mails."

First step - Organization

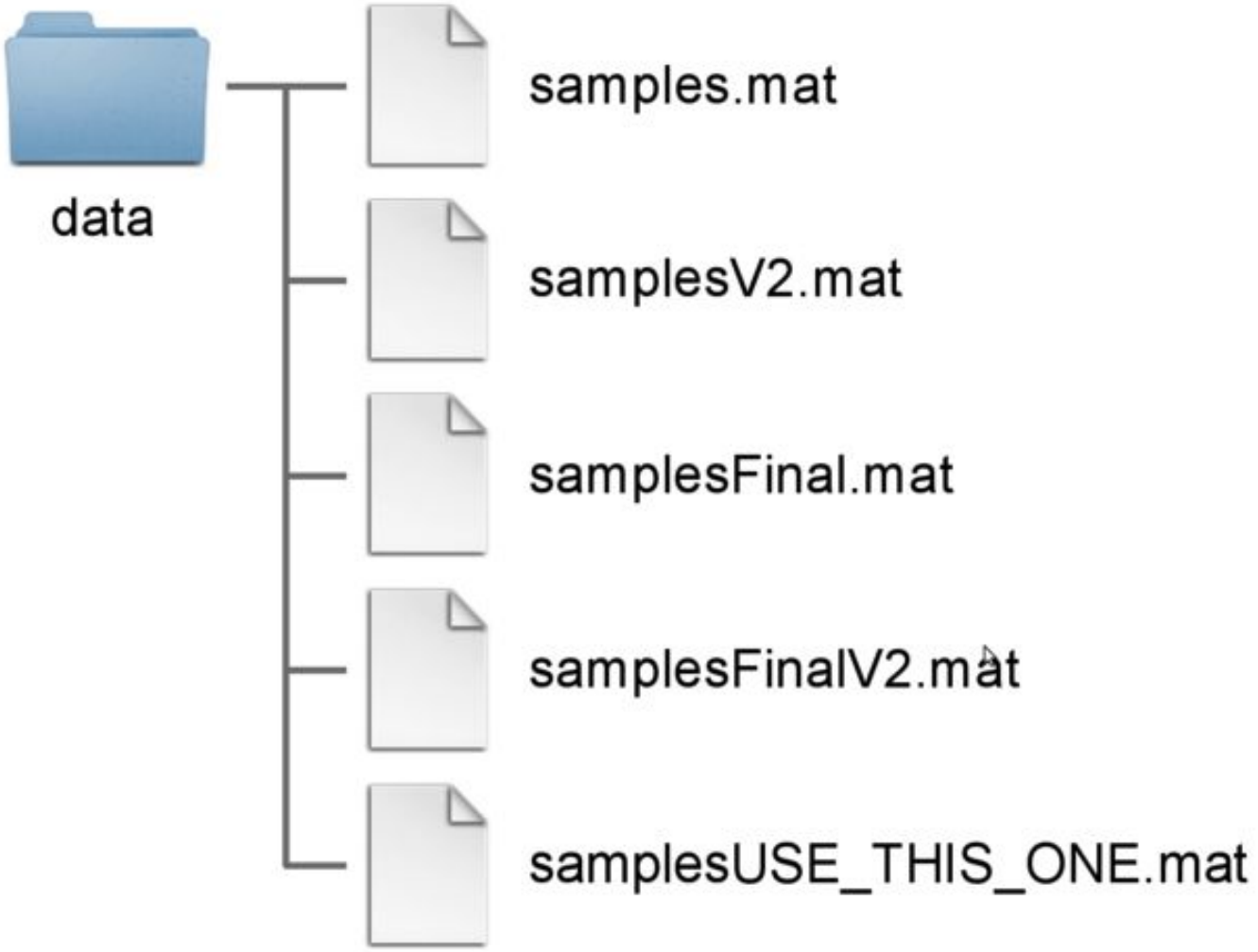
Now what?



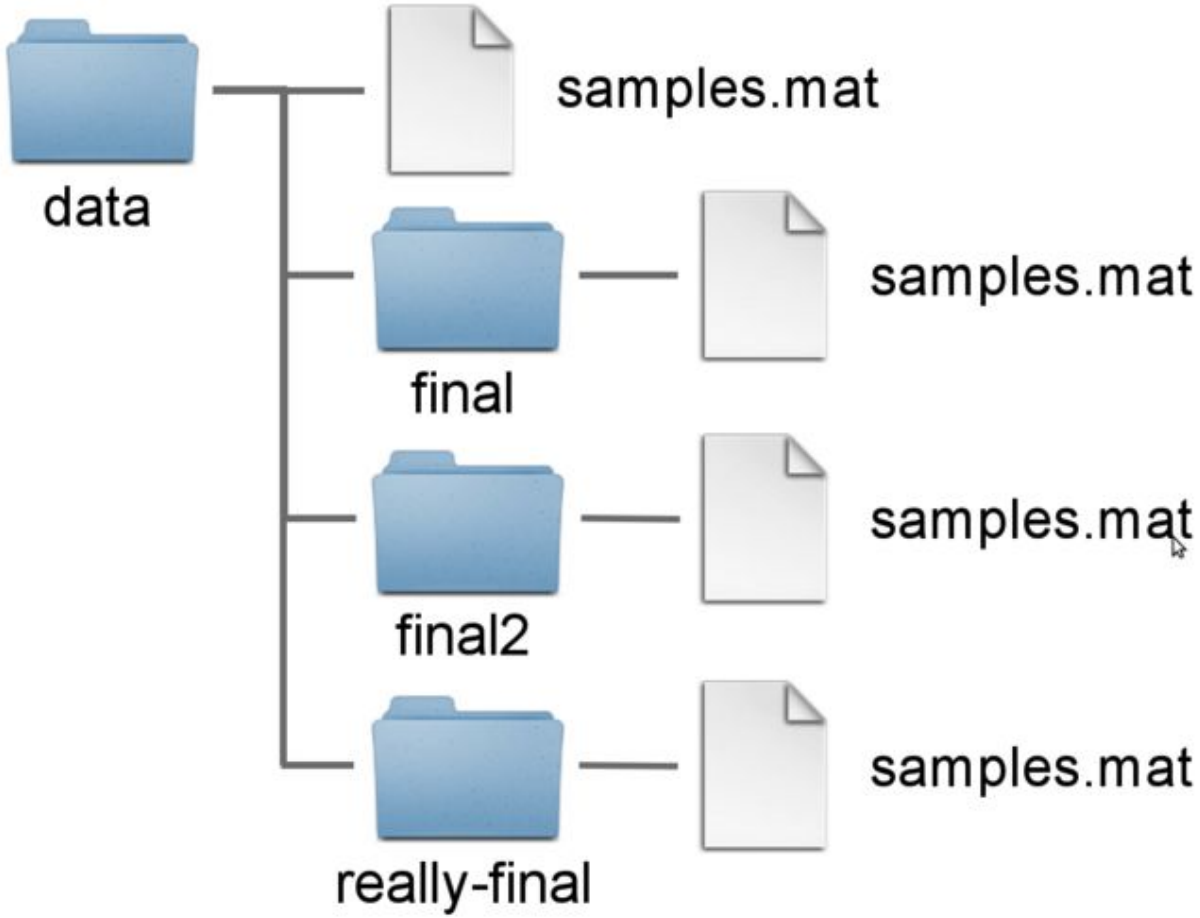
I guess this is alright



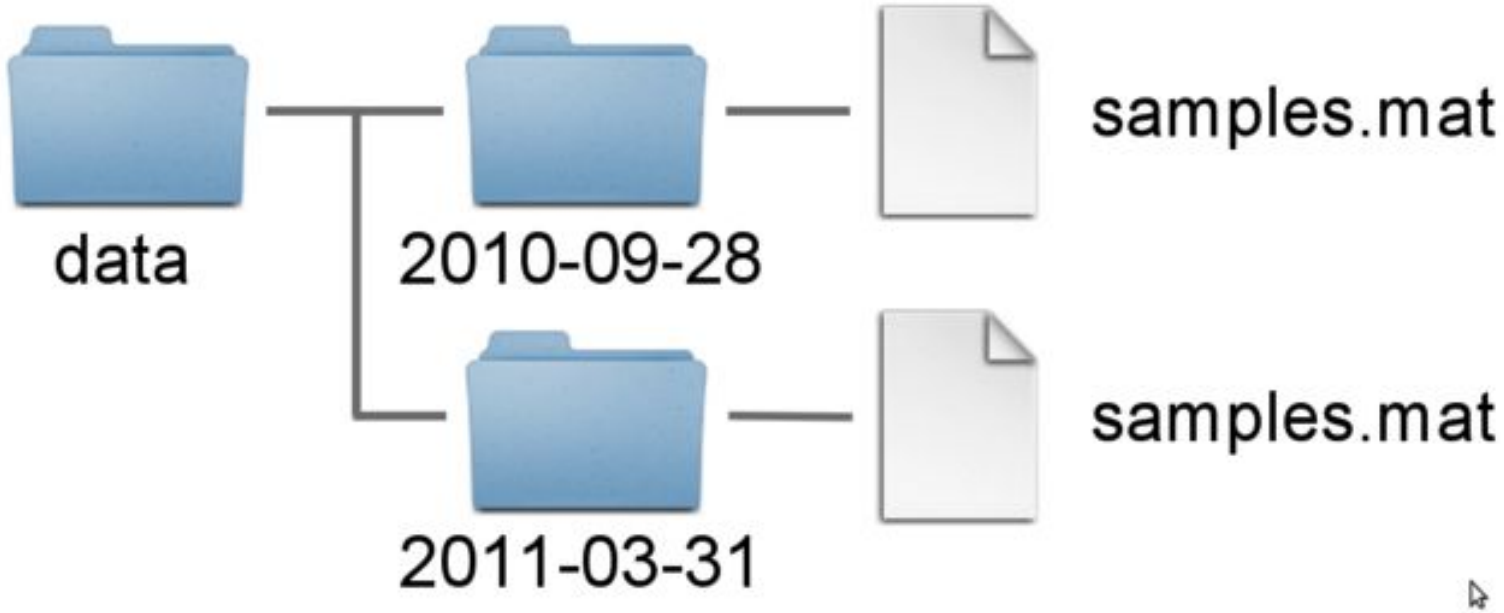
Which one is the most recent?



Another (bad) common approach



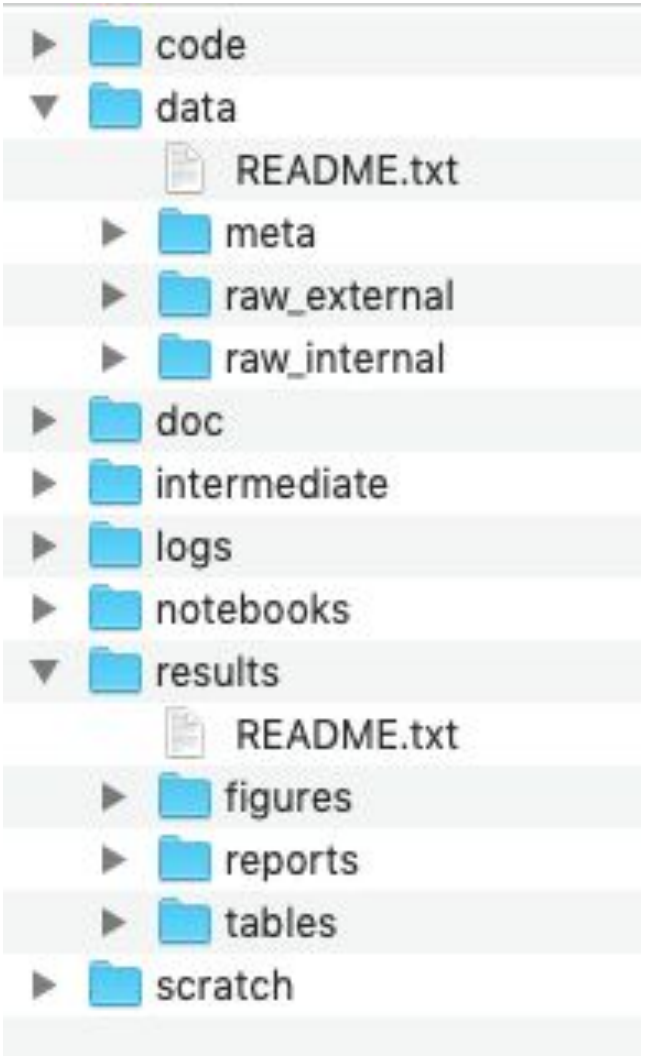
A possible solution



Suggested best practices

- Directory Structure
  - There is a **folder for the raw data**, which do not get altered, or intermixed with data that is the result of manual or programmatic manipulation. I.e., derived data is kept separate from raw data, and **raw data are not duplicated**.
  - **Code is kept separate from data**.
  - There is a **scratch directory for experimentation**. Everything in the scratch directory can be deleted at any time without negative impact.
  - There should be a **README in every directory**, describing the purpose of the directory and its contents.
- Use **file naming schemes** that makes it easy to find files and understand what they are (for humans and machines)
- Use a **version control system** (at least for code) – e.g. **git**
- Use **non-proprietary formats** for files– *.csv* rather than *.xlsx*
- Etc…

Directory structure for a sample project



all code needed to go from input files to final results

raw and primary data, essentially all input files, **never** edit!

documentation for the study

output files from different analysis steps, *can be deleted*

logs from the different analysis steps

output from workflows and analyses

temporary files that can be safely *deleted or lost*

Noble WS (2009) A Quick Guide to Organizing Computational Biology Projects. PLoS Comput Biol 5(7): e1000424.
http://journals.plos.org/ploscompbiol/article?id=info:doi/10.1371/journal.pcbi.1000424

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File naming

- Three principles
  1. Machine readable
  2. Human readable
  3. Plays well with default ordering

NO

myabstract.docx
Joe's Filenames Use Spaces and Punctuation.xlsx
figure 1.png
fig 2.png
JW7d^(2sl@deletethisandyourcareerisoverWx2*.txt

YES

2014-06-08_abstract-for-sla.docx
joes-filenames-are-getting-better.xlsx
fig01_scatterplot-talk-length-vs-interest.png
fig02_histogram-talk-attendance.png
1986-01-28_raw-data-from-challenger-o-rings.txt

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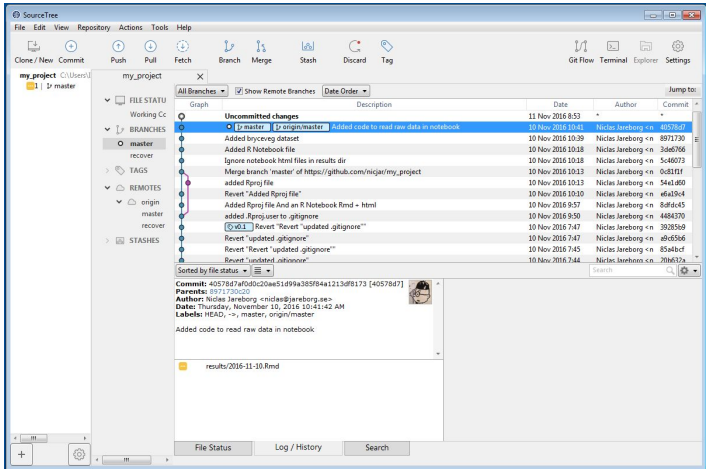
Version control

- What is it?
  - A system that keeps records of your changes
  - Allows for collaborative development
  - Allows you to know who made what changes and when
  - Allows you to revert any changes and go back to a previous state
- Several systems available
  - git, RCS, CVS, SVN, Perforce, Mercurial, Bazaar
  - git
    - Command line & GUIs
    - Remote repository hosting
      - GitHub, Bitbucket, etc



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Non-proprietary formats

- A text-based format is more future-safe, than a proprietary binary format by a commercial vendor
- ***Markdown*** is a nice way of getting nice output from text.
  - Simple & readable formating
  - Can be converted to lots of different outputs
    - HTML, pdf, MS Word, slides etc

- *Never, never, never use **Excel** for scientific **analysis**!*
  - Script your analysis – bash, python, R, …

Tabular data / Spreadsheets

DO

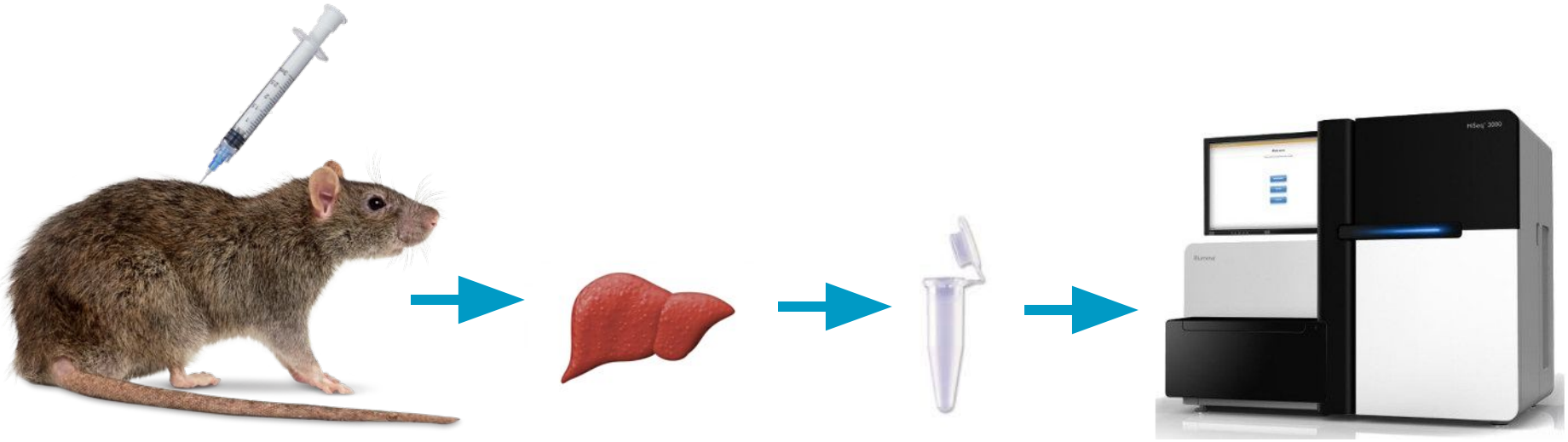
- Keep your raw data raw; calculations and analyses should be done in a copy of the file
- Put variables in columns and observations in rows
- Give each column a descriptive heading that does not include spaces, numbers, or special characters
- Differentiate between zero and null values
- Validate your data
- Keep a separate txt file with a title and a legend describing your dataset, and outlining any steps you take to tidy your data
- Use a version control system and back up your files
- Export each data file in an open non-proprietary format such as CSV or TAB, with a name that appropriately reflects the content of that file
- Check your data thoroughly. Your data should receive the same care as your publications

DO NOT

- Put more than 1 piece of information in a cell
- Use colour coding, embedded charts, comments or tables – your spreadsheet is not a lab book
- Include special (i.e. non alphanumeric) characters within the spreadsheet, including commas
- Use merged or blank cells
- Create multiple worksheets within a spreadsheet

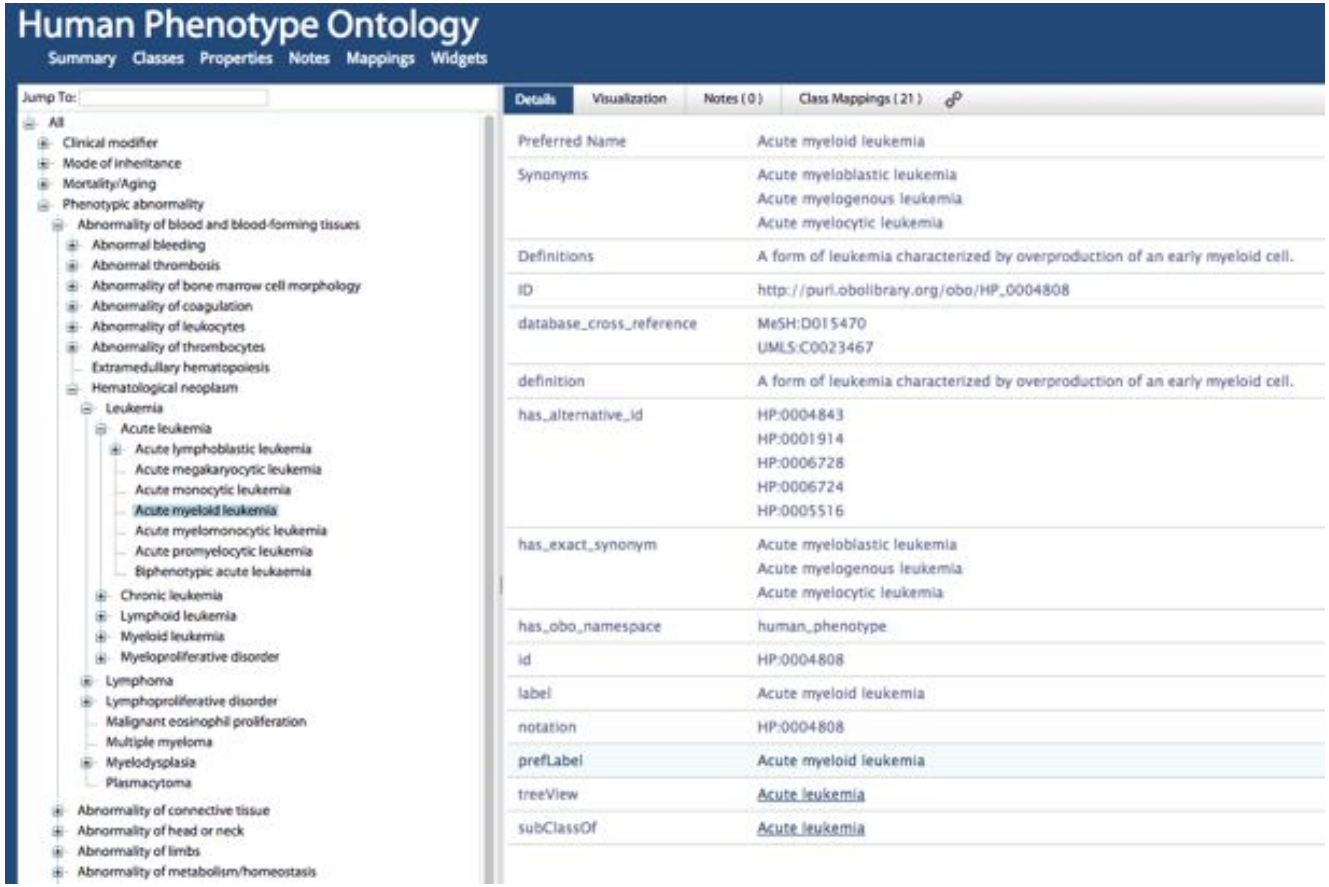
Still missing something

- Need context → document **metadata**
  - From what was the data generated?
  - How do the samples differ?
  - What where the experimental conditions?
  - Etc

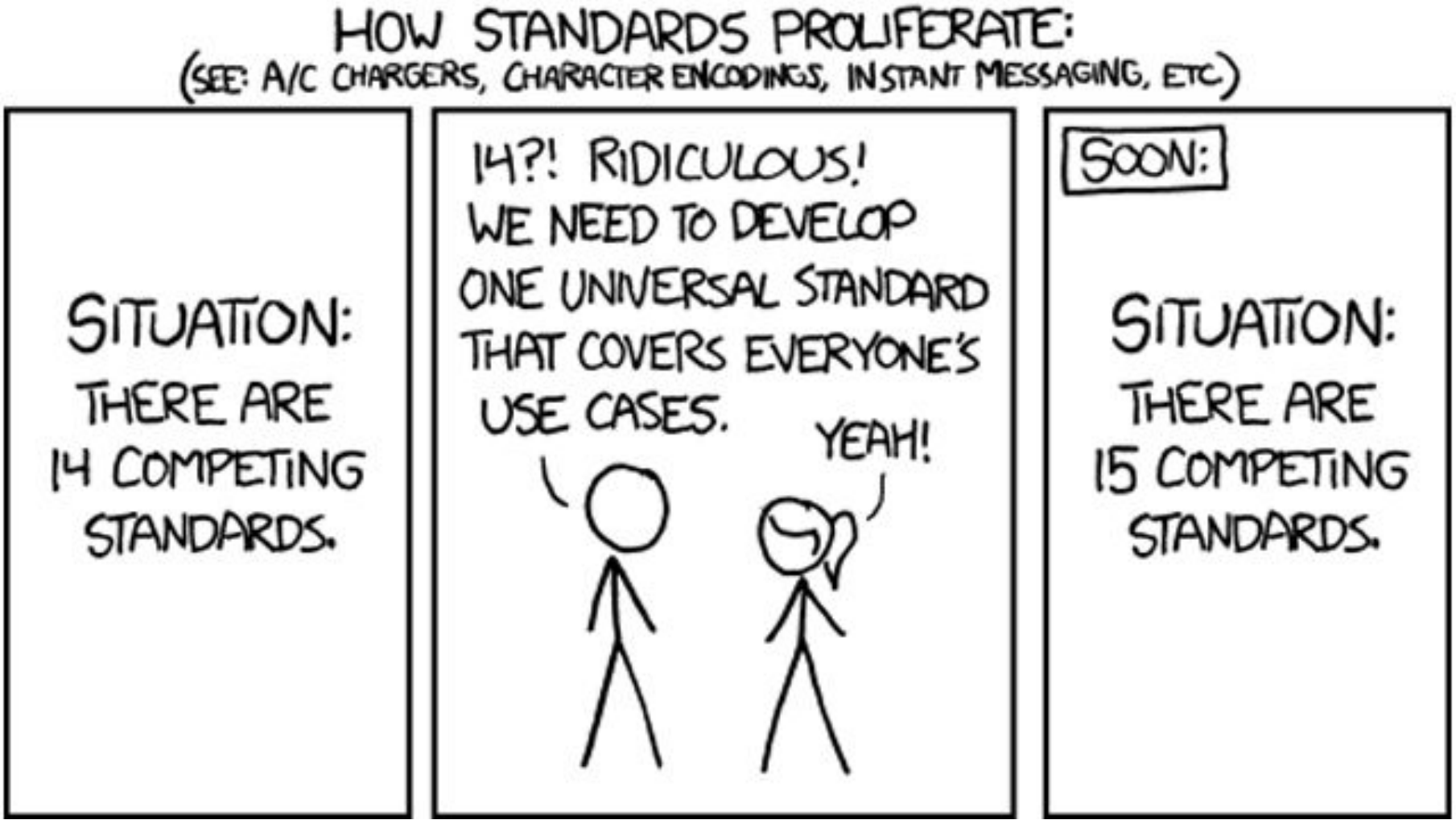


Metadata

- Standards
  - Controlled vocabularies / Ontologies
    - Agreed terms for different phenomena



Metadata


HOW STANDARDS PROLIFERATE:
(SEE: A/C CHARGERS, CHARACTER ENCODINGS, INSTANT MESSAGING, ETC.)
SITUATION: THERE ARE 14 COMPETING STANDARDS.
14?! RIDICULOUS! WE NEED TO DEVELOP ONE UNIVERSAL STANDARD THAT COVERS EVERYONE'S USE CASES.
YEAH!
SOON:
SITUATION: THERE ARE 15 COMPETING STANDARDS.

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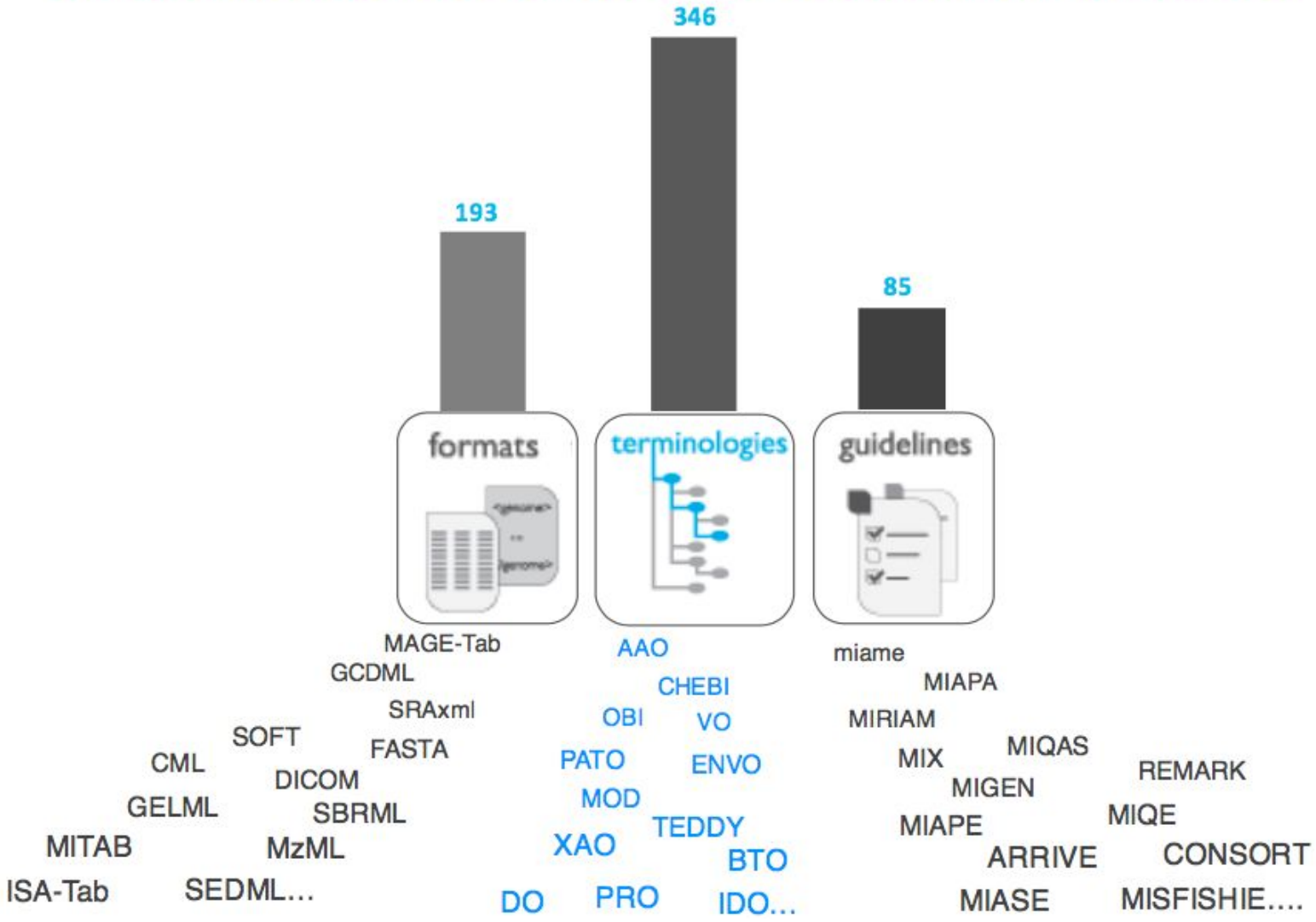
FAIRsharing.org

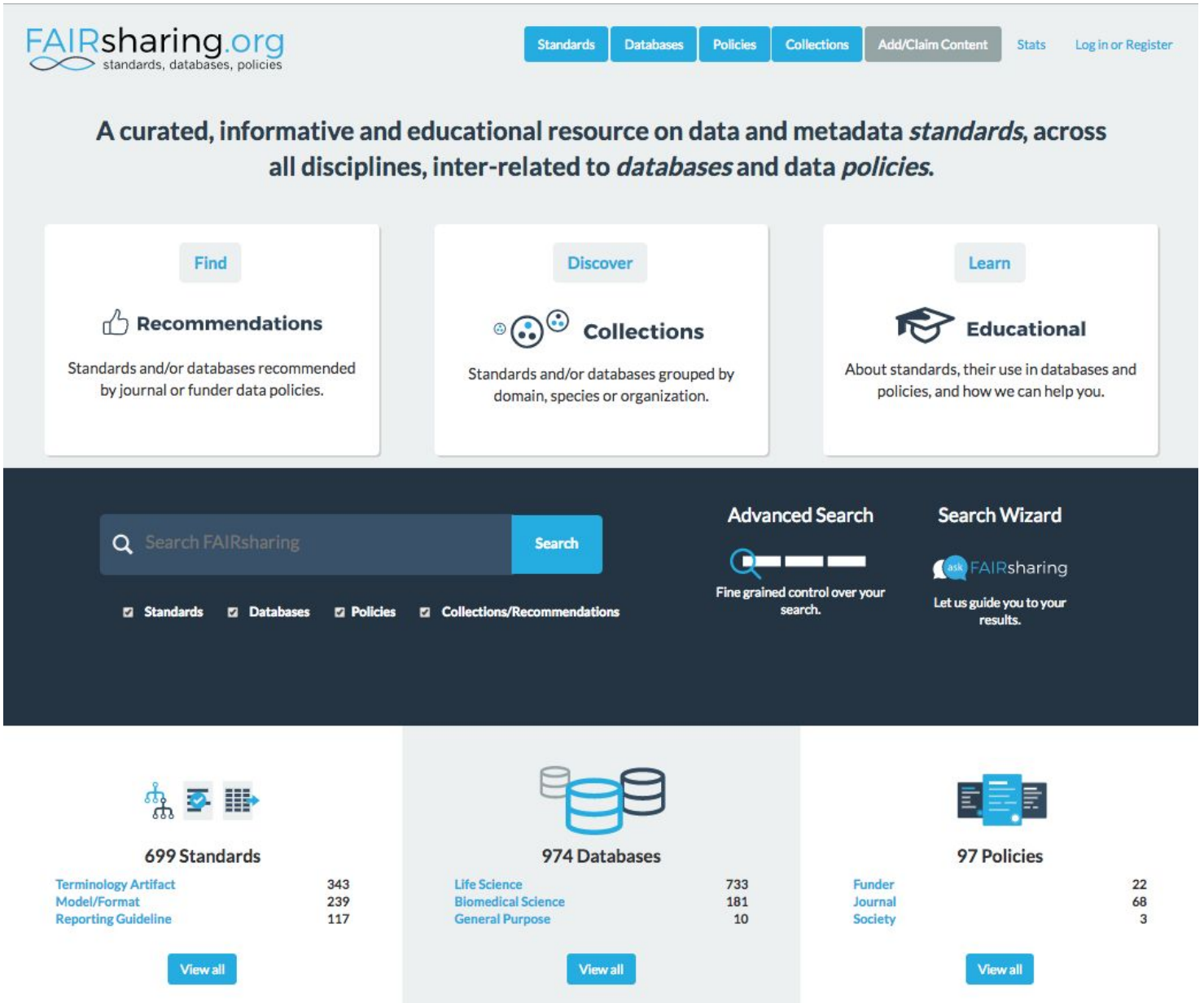
SciLifeLab

In the life sciences there are >600 *content standards*



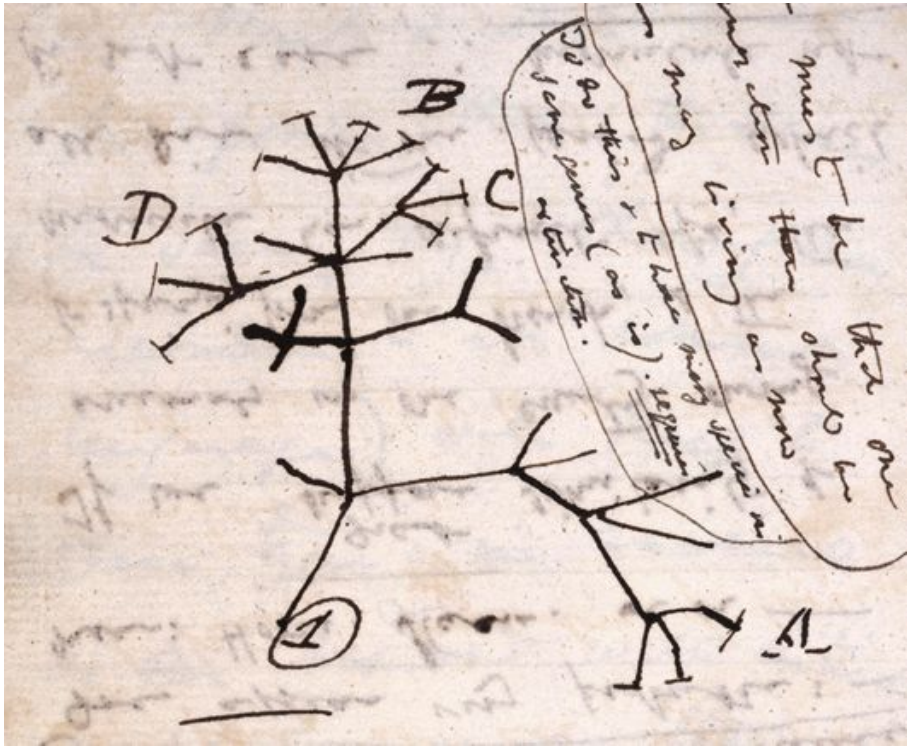
FAIRsharing.org

(was biosharing.org)



Lab notebooks

- Why?
  - You have to understand what you have done
  - **Others should be able to reproduce what you have done**

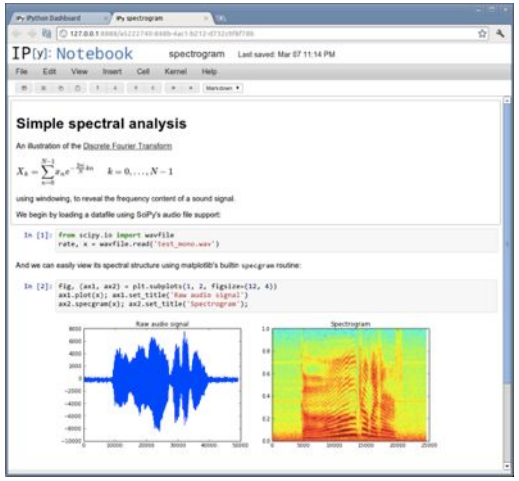


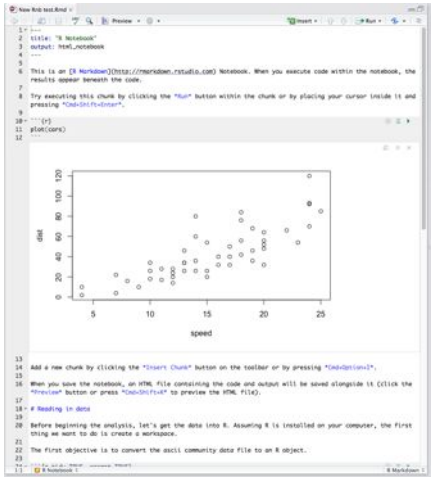
Lab notes – useful practices

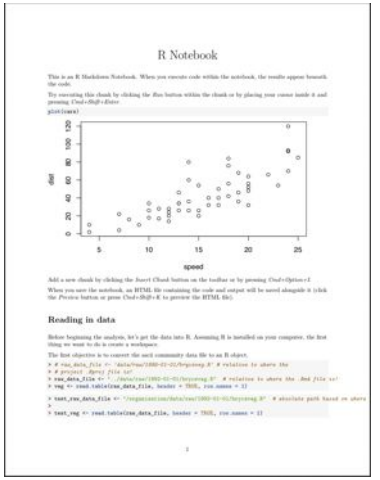
- Put in *separate* directory (e.g. *results*, *documentation*)
- *Dated* entries
- Entries relatively verbose
- Link to *data* and *code* (including versions)
    - Point to commands run and results generated
- Embedded images or tables showing results of analysis done
- Observations, Conclusions, and *ideas* for future work
- Also document analysis that *doesn't* work, so that it can be understood why you choose a particular way of doing the analysis in the end

Where to take down notes

- Paper Notebook
- Word processor program / Text files
- Electronic Lab Notebooks Systems
- 'Interactive' Electronic Notebooks
  - e.g. jupyther, R Notebooks in RStudio
  - Plain text - work well with version control (Markdown)
  - Embed and execute code
  - Convert to other output formats
    - html, pdf, word

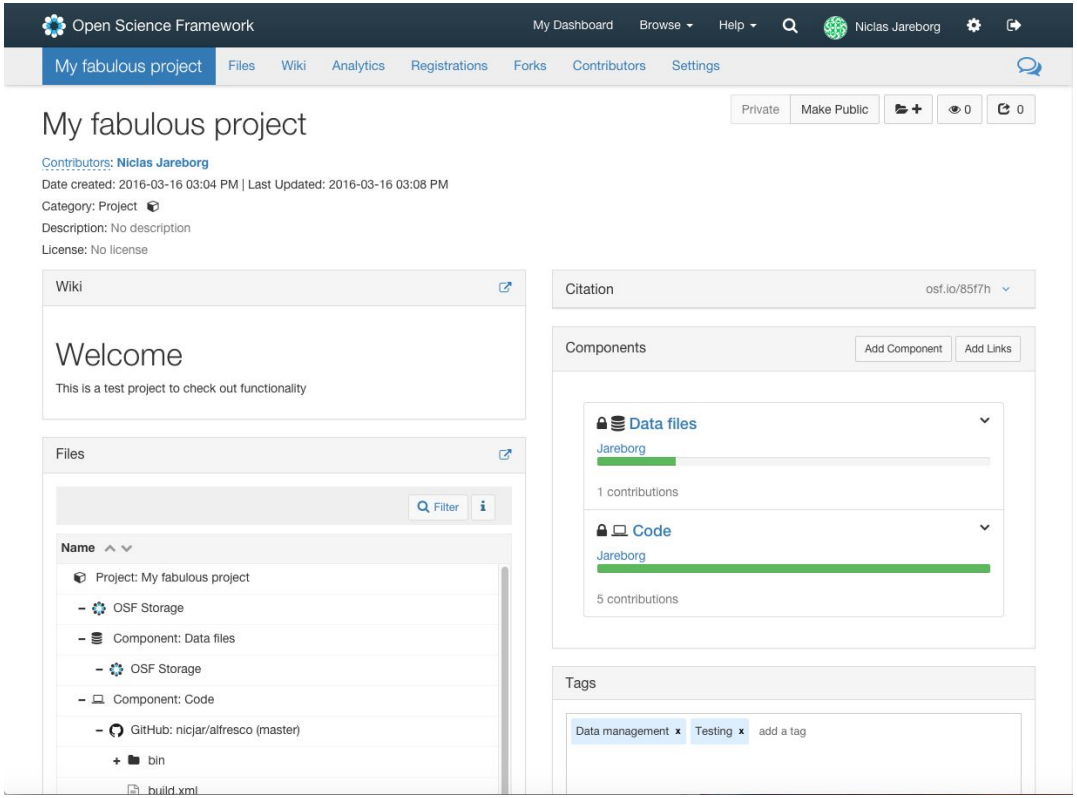




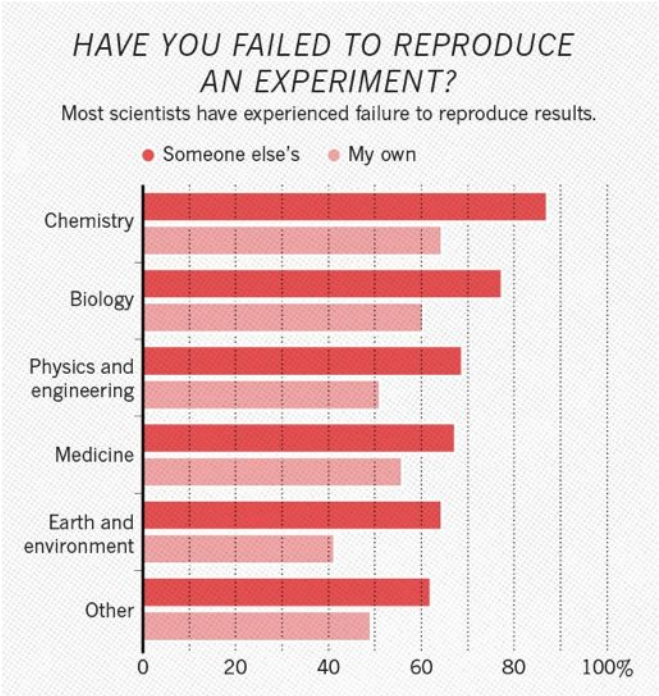


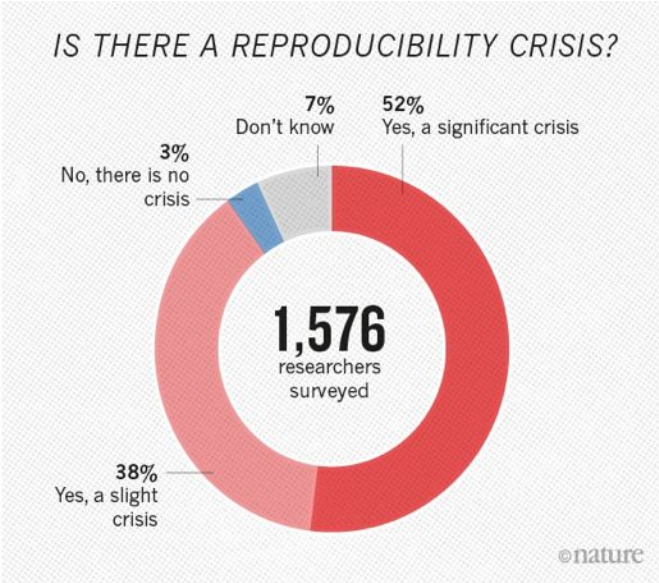
Project collaboration tools

- Open Science Framework – http://osf.io
  - Organize research project documentation and outputs
  - Control access for collaboration
  - 3rd party integrations
    - Google Drive
    - Dropbox
    - GitHub
    - External links
    - Etc
  - Persistent identifiers
  - Publish article preprints



A reproducibility crisis

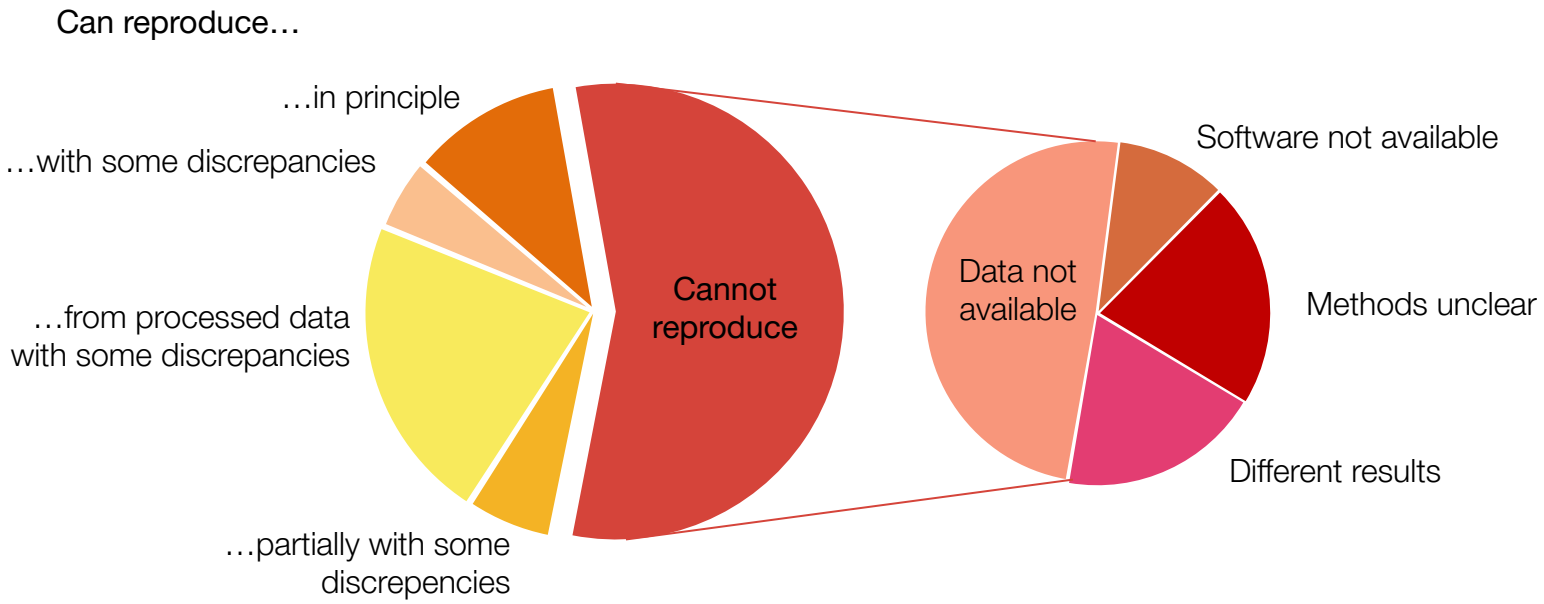




[1] "1,500 scientists lift the lid on reproducibility". Nature. 533: 452–454
[2] Begley, C. G.; Ellis, L. M. (2012). "Drug development: Raise standards for preclinical cancer research". Nature. 483 (7391): 531–533.

A reproducibility crisis

Reproduction of data analyses in 18 articles on microarray-based gene expression profiling published in Nature Genetics in 2005–2006:

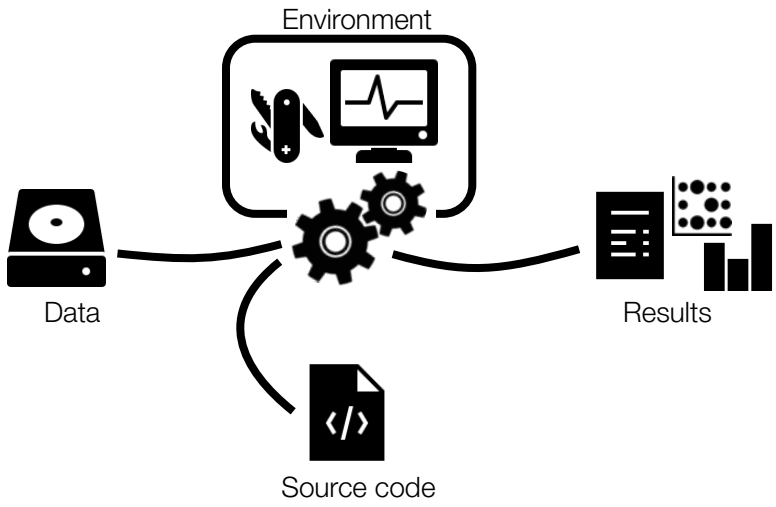


Summary of the efforts to replicate the published analyses.
Adopted from: Ioannidis et al. Repeatability of published microarray gene expression analyses. *Nature Genetics* 41 (2009) doi:10.1038/ng.295

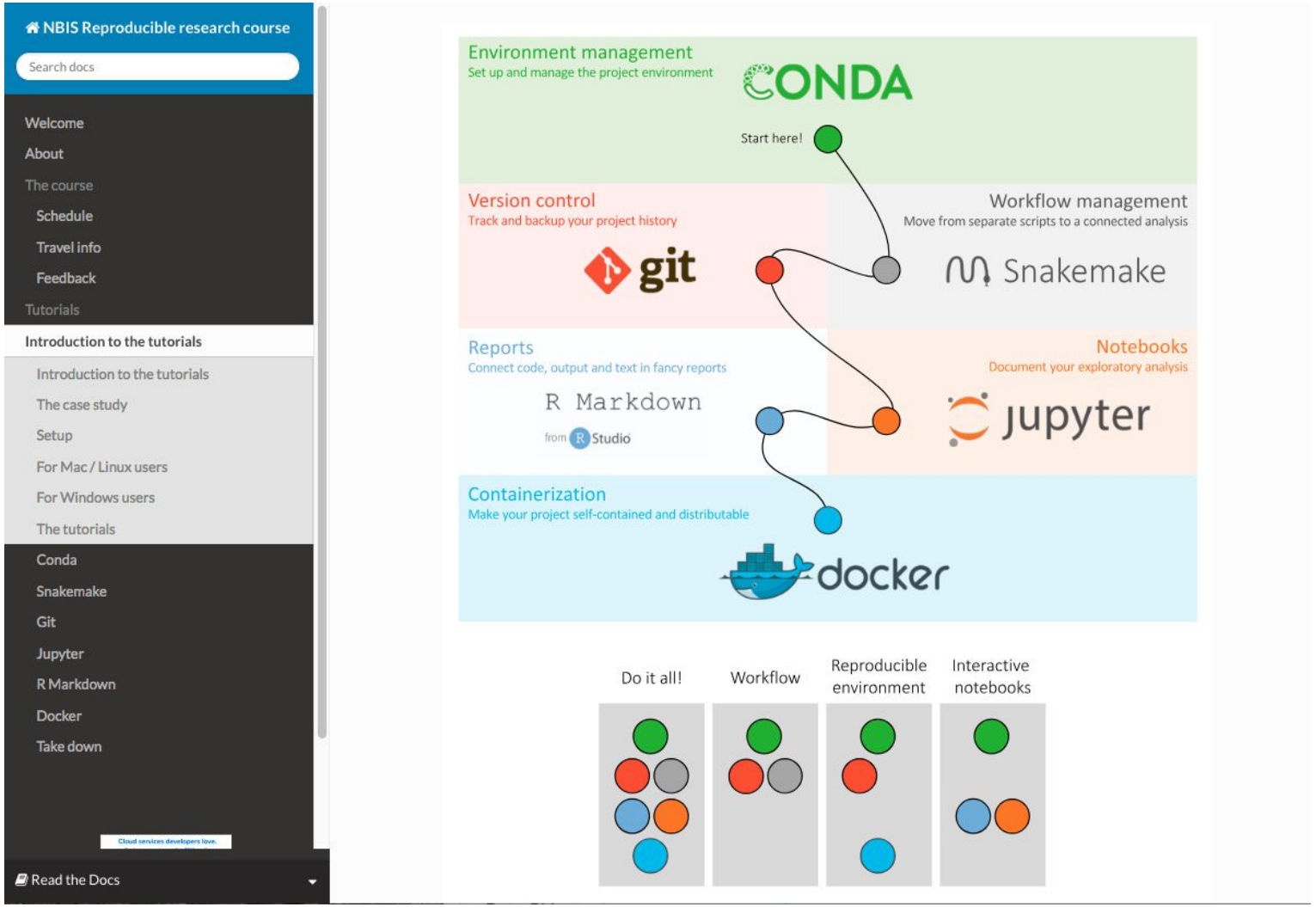
What do we mean by reproducible research?

		Data: Same	Data: Different
Code	Same	Reproducible	Replicable
Code	Different	Robust	Generalizable

All parts of a bioinformatics analysis have to be reproducible:



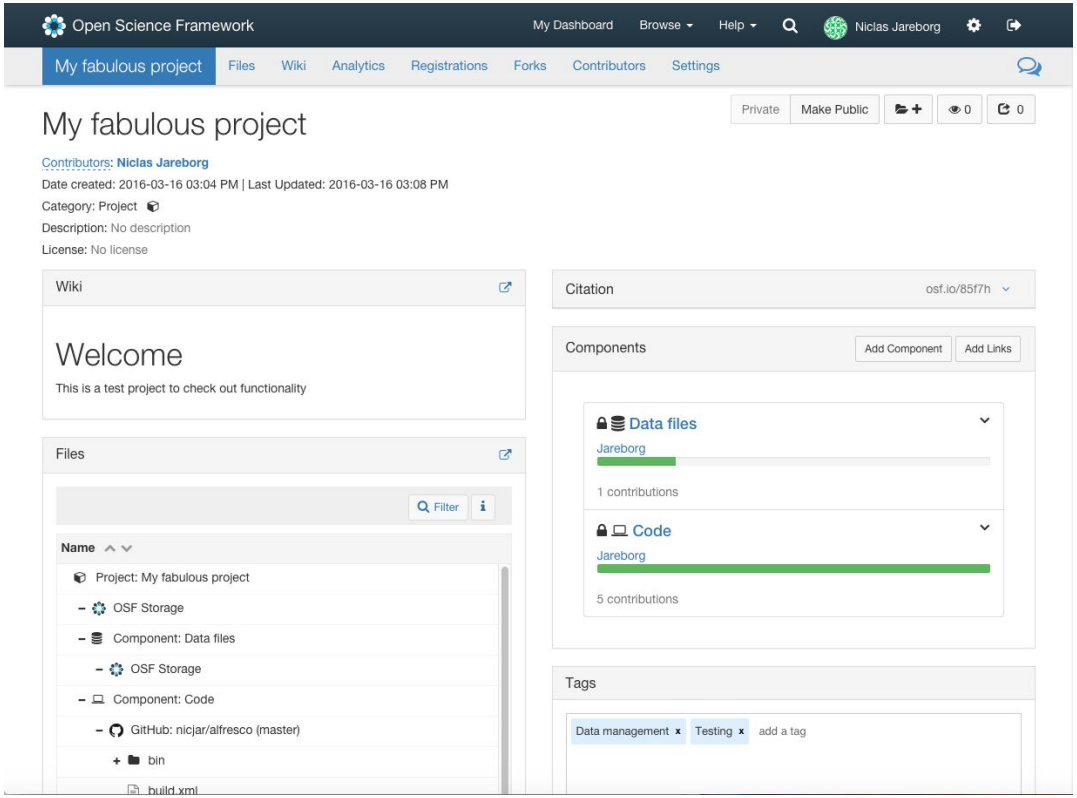
Reproducible Research tutorials



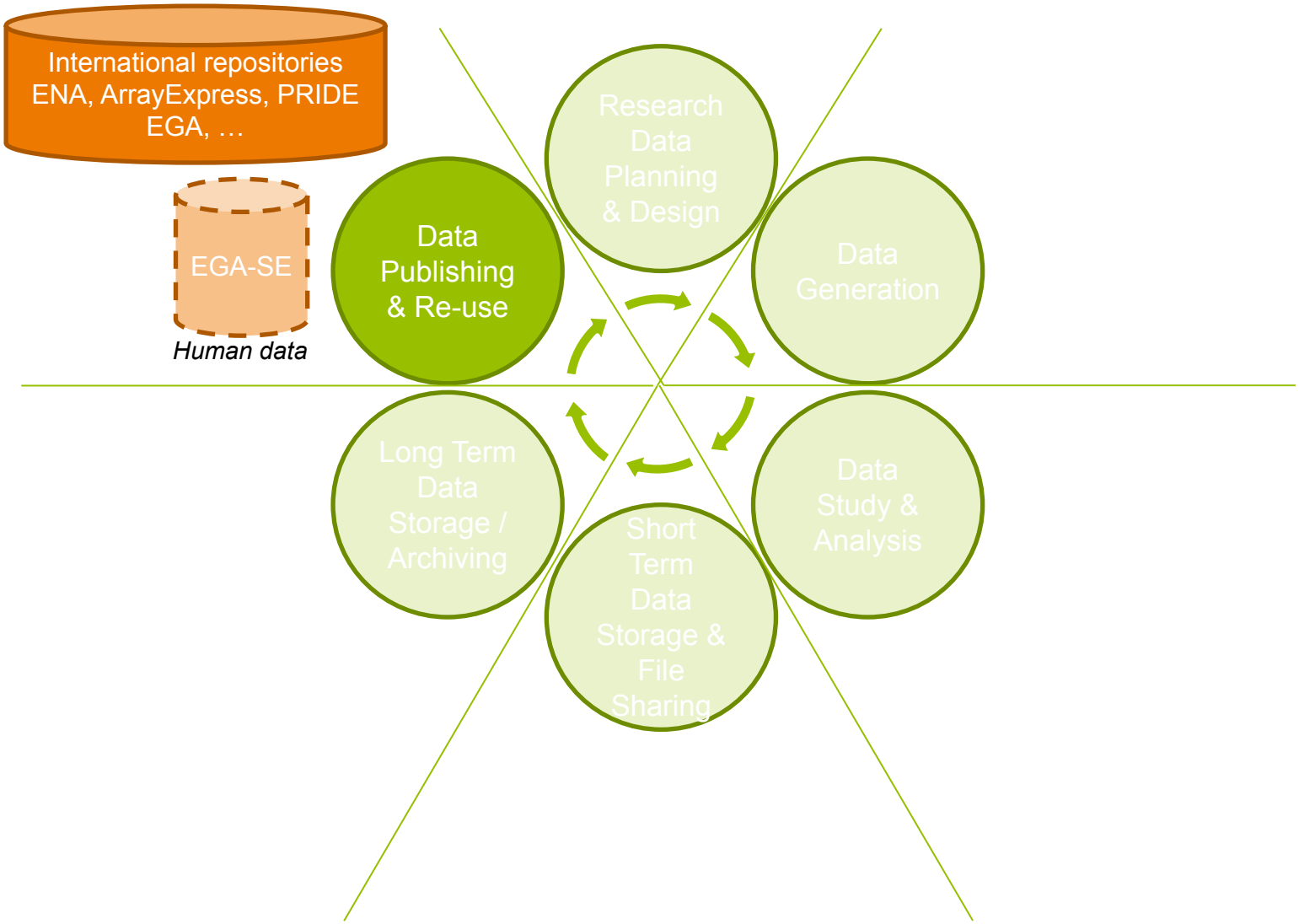
https://nbis-reproducible-research.readthedocs.io/en/latest/

Project collaboration tools

- Open Science Framework – http://osf.io
  - Organize research project documentation and outputs
  - Control access for collaboration
  - 3rd party integrations
    - Google Drive
    - Dropbox
    - GitHub
    - External links
    - Etc
  - Persistent identifiers
  - Publish article preprints



Data Publishing & Re-use



Data Management Snafu

https://www.youtube.com/watch?v=N2zK3sAtr-4

Reflections?

Open Access

- Democracy and transparency
  - Publicly funded research data should be accessible to all
  - Published results and conclusions should be possible to check by others
- Research
  - Enables others to combine data, address new questions, and develop new analytical methods
  - Reduce duplication and waste
- Innovation and utilization outside research
  - Public authorities, companies, and private persons outside research can make use of the data
- Citation
  - Citation of data will be a merit for the researcher that produced it

Open Access to research data

- Strong international movement towards Open Access (OA)
- European Commission recommended the member states to establish national guidelines for OA
  - Swedish Research Council (VR) submitted proposal to the government Jan 2015
- Research bill 2017–2020 – *28 Nov 2016*
  - "*The aim of the government is that all scientific publications that are the result of publicly funded research should be openly accessible as soon as they are published. Likewise,* ***research data*** *underlying scientific publications should be* ***openly accessible*** *at the time of publication.*" [my translation]
- 2018 – VR assigned by the government to coordinate national efforts to implement open access to research data

FAIR

- To be useful for others data should be
  - ***FAIR*** - Findable, Accessible, Interoperable, and Reusable
    … for both Machines and Humans

Wilkinson, Mark et al. *"The FAIR Guiding Principles for scientific data management and stewardship"*. Scientific Data 3, Article number: 160018 (2016)
http://dx.doi.org/10.1038/sdata.2016.18

www.nature.com/scientificdata

SCIENTIFIC DATA

OPEN

SUBJECT CATEGORIES
» Research data
» Publication characteristics

Received: 10 December 2015
Accepted: 12 February 2016
Published: 15 March 2016

Comment: The FAIR Guiding Principles for scientific data management and stewardship

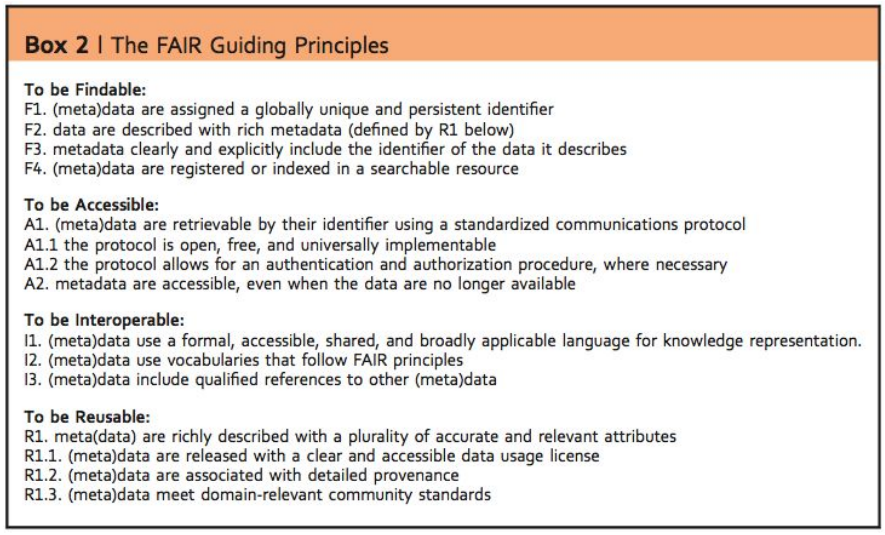
Mark D. Wilkinson *et al.*#

There is an urgent need to improve the infrastructure supporting the reuse of scholarly data. A diverse set of stakeholders—representing academia, industry, funding agencies, and scholarly publishers—have come together to design and jointly endorse a concise and measureable set of principles that we refer to as the FAIR Data Principles. The intent is that these may act as a guideline for those wishing to enhance the reusability of their data holdings. Distinct from peer initiatives that focus on the human scholar, the FAIR Principles put specific emphasis on enhancing the ability of machines to automatically find and use the data, in addition to supporting its reuse by individuals. This Comment is the first formal publication of the FAIR Principles, and includes the rationale behind them, and some exemplar implementations in the community.

Supporting discovery through good data management

Good data management is not a goal in itself, but rather is the key conduit leading to knowledge discovery and innovation, and to subsequent data and knowledge integration and reuse by the community after the data publication process. Unfortunately, the existing digital ecosystem surrounding scholarly data publication prevents us from extracting maximum benefit from our research investments (e.g., ref. 1). Partially in response to this, science funders, publishers and

DOI: 10.1038/sdata.2016.18



Box 2 | The FAIR Guiding Principles

To be Findable:
F1. (meta)data are assigned a globally unique and persistent identifier
F2. data are described with rich metadata (defined by R1 below)
F3. metadata clearly and explicitly include the identifier of the data it describes
F4. (meta)data are registered or indexed in a searchable resource

To be Accessible:
A1. (meta)data are retrievable by their identifier using a standardized communications protocol
A1.1 the protocol is open, free, and universally implementable
A1.2 the protocol allows for an authentication and authorization procedure, where necessary
A2. metadata are accessible, even when the data are no longer available

To be Interoperable:
I1. (meta)data use a formal, accessible, shared, and broadly applicable language for knowledge representation.
I2. (meta)data use vocabularies that follow FAIR principles
I3. (meta)data include qualified references to other (meta)data

To be Reusable:
R1. meta(data) are richly described with a plurality of accurate and relevant attributes
R1.1. (meta)data are released with a clear and accessible data usage license
R1.2. (meta)data are associated with detailed provenance
R1.3. (meta)data meet domain-relevant community standards

'We support appropriate efforts to promote open science and facilitate appropriate access to publicly funded research results on findable, accessible, interoperable and reusable (FAIR)'

FAIR principles

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F2. data are described with rich metadata;

F3. metadata clearly and explicitly include the **identifier** of the data it describes;

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Interoperable:

I1. (meta)data use a formal, accessible, shared, and broadly applicable **language for knowledge representation**;

I2. (meta)data use **vocabularies** that follow FAIR principles;

I3. (meta)data include qualified references to other (meta)data;

Reusable:

R1. (meta)data are richly described with a plurality of accurate and relevant attributes;

R1.1. (meta)data are released with a clear and accessible **data usage license**;

R1.2. (meta)data are associated with detailed provenance;

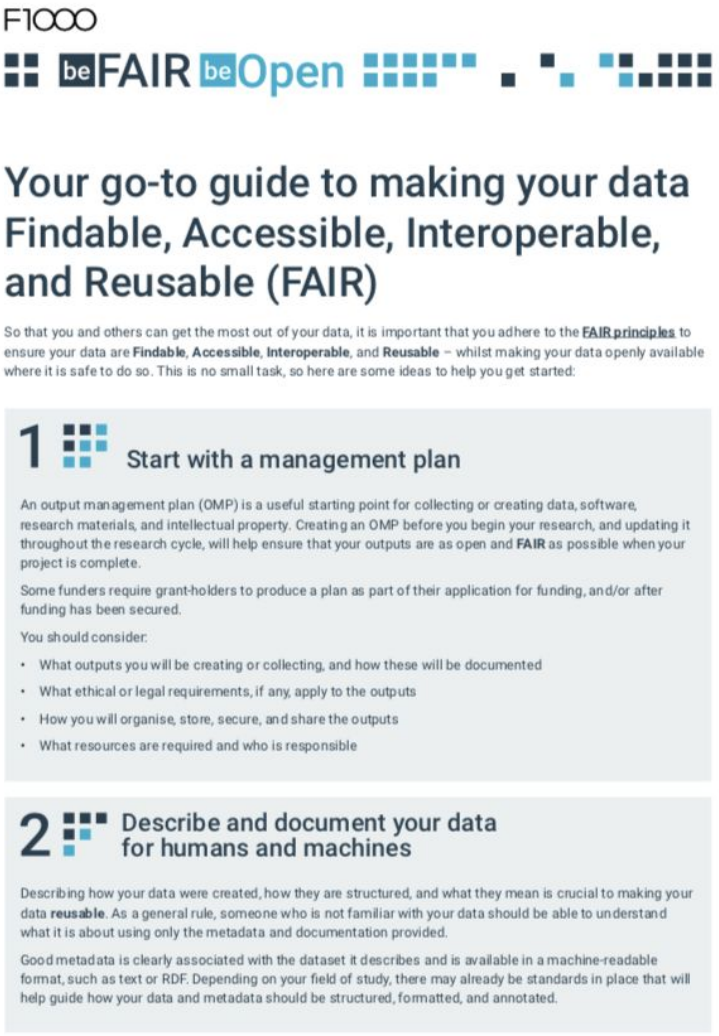
R1.3. (meta)data meet domain-relevant community **standards**;

https://www.nature.com/articles/sdata201618

Derived from slide by Luiz Bonino

FAIR Guide

1. Start with a management plan
2. Describe and document your data for humans and machines
3. Preserve your data



F1000

beFAIR beOpen

Your go-to guide to making your data Findable, Accessible, Interoperable, and Reusable (FAIR)

So that you and others can get the most out of your data, it is important that you adhere to the **FAIR principles** to ensure your data are **Findable**, **Accessible**, **Interoperable**, and **Reusable** – whilst making your data openly available where it is safe to do so. This is no small task, so here are some ideas to help you get started:

1 Start with a management plan

An output management plan (OMP) is a useful starting point for collecting or creating data, software, research materials, and intellectual property. Creating an OMP before you begin your research, and updating it throughout the research cycle, will help ensure that your outputs are as open and **FAIR** as possible when your project is complete.

Some funders require grant-holders to produce a plan as part of their application for funding, and/or after funding has been secured.

You should consider:

- What outputs you will be creating or collecting, and how these will be documented
- What ethical or legal requirements, if any, apply to the outputs
- How you will organise, store, secure, and share the outputs
- What resources are required and who is responsible

2 Describe and document your data for humans and machines

Describing how your data were created, how they are structured, and what they mean is crucial to making your data **reusable**. As a general rule, someone who is not familiar with your data should be able to understand what it is about using only the metadata and documentation provided.

Good metadata is clearly associated with the dataset it describes and is available in a machine-readable format, such as text or RDF. Depending on your field of study, there may already be standards in place that will help guide how your data and metadata should be structured, formatted, and annotated.

F1000

beFAIR beOpen

https://f1000.com/resources/FAIR_Open_Guide.pdf

1. Data Management Plan

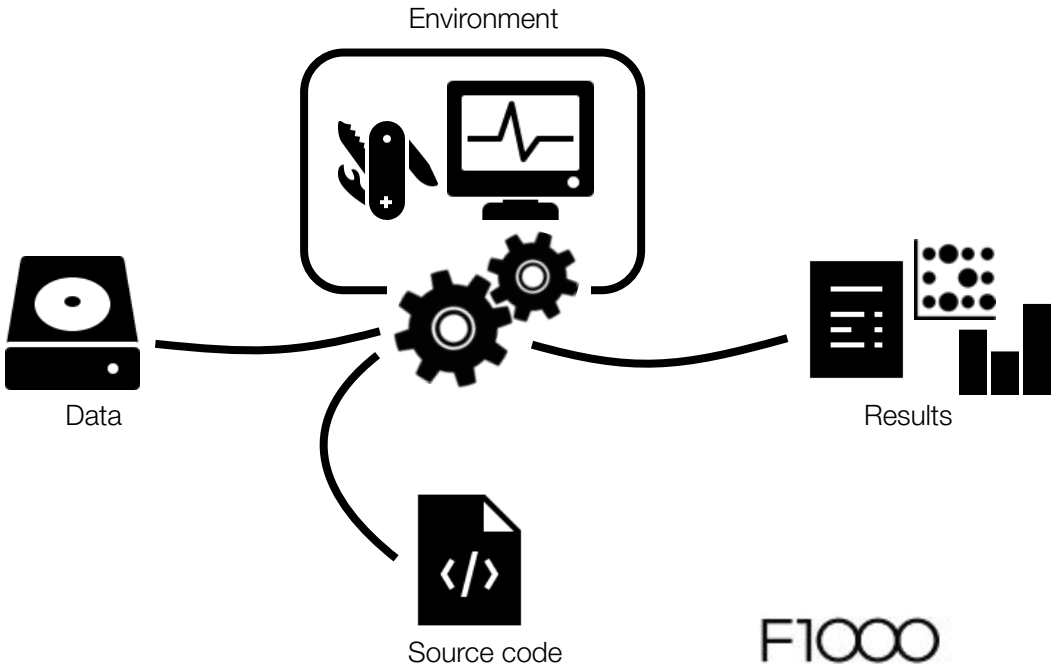
- **Data collection** - data types and volumes, analysis code
- **Data organization** - folder and file structure, and naming
- **Data documentation** - data and analysis, metadata standards
- **Data storage** - storage/backup/protection & time lines
- **Data policies** - conditions/licences for using data & legal/ethical issues
- **Data sharing** - *When* and *How* will *What* data (and code) be shared
- **Roles and responsibilities** - who's responsible for what & is competence available
- **Budget** - People & Hardware/Software

More later...

2. Describe and document

Reusability

As a general rule, someone who is not familiar with your data should be able to understand what it is about using only the metadata and documentation provided.



3. Preserve your data

*Data preservation helps ensure that your data will be **accessible** and **reusable** in the future.*

Best practices include:

- **Backing up** data files regularly
- Storing master copies of data files in **open formats**
- **Validating** preserved data files regularly
- Using **more than one form of storage** for data files
- Appropriately **securing data physically**, and/or on any network or computer on which they are held

Licenses

Data

CC0

Creative Commons Zero is ideal for openly sharing data – it has no restrictions on Reuse whatsoever. CC0 datasets are widely accepted and expected in science.

Other CC licenses

CC-BY – Prevents others from applying legal restrictions beyond the terms of the license to the licensed dataset.

CC BY-SA – Requires outputs derived from licensed dataset to also be licensed as CC BY-SA.

CC BY-NC – *Prevents the licensed data from being used for commercial purpose.*

CC BY-ND – *Prevents the licensed data from being modified.*

CC BY-NC-ND – *Prevents the licensed data from being used for commercial purposes or modified.*

CC BY-NC-SA – *Prevents the licensed data from being used for commercial purposes, and requires outputs derived from licensed dataset to also be licensed as CC BY-SA.*

Code

To allow your code to be freely used, modified, and shared by others it's recommended to use a licence approved by the **Open Source Initiative**, such as

- MIT
- GNU General Public License
- Apache License 2.0

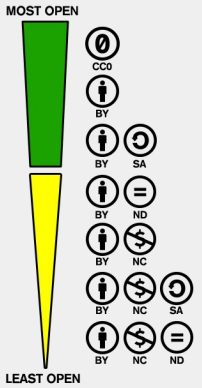
➜ Choose an Open Source License

➜ CC License Chooser

➜ How to License Research Data

Note!

- *NC*, *ND* and *SA* licenses have implications for *reuse* and *inter-operability*
- Be aware of any *licensing restrictions* where your dataset contains *data derived from a 3rd party*.



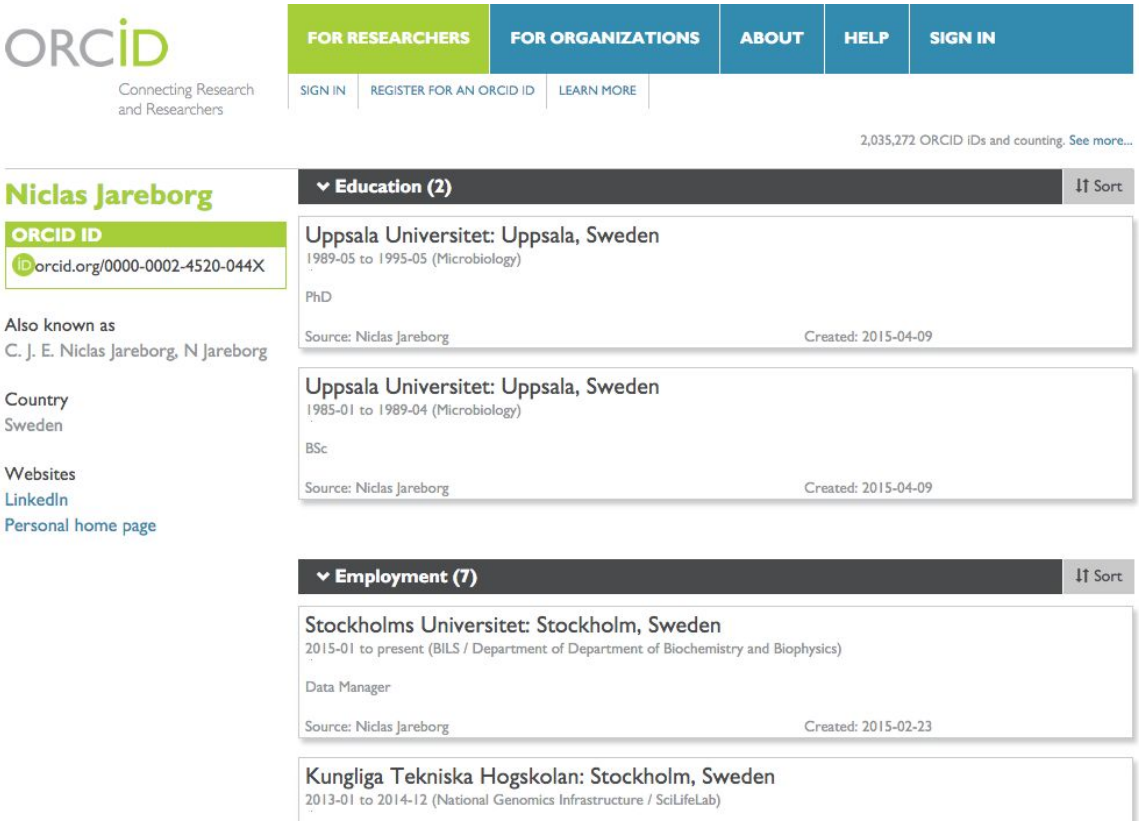
Findable, Accessible

- *Research Data Publishing is a cornerstone of Open Access*

- Long-term storage
  - Data should not disappear
- Persistent identifiers
  - Possibility to refer to a dataset over long periods of time
  - Unique
  - e.g. DOIs (Digital Object Identifiers)
- Discoverability
  - Expose dataset metadata through search functionalities

Persistent identifier for yourself

- ORCID is an open, non-profit, community-driven effort to create and maintain a registry of unique researcher identifiers and a transparent method of linking research activities and outputs to these identifiers.
- http://orcid.org
- Persistent identifier for you as a researcher



Repositories

Does the data contain **personal** or **sensitive** information?

YES → 1. Controlled access repositories

NO → Is there a **discipline-specific** repository for your data?

YES → 2. Discipline-specific repositories

NO → Is there a **institutional** repository for your data?

YES → 3. Institutional repositories

NO → 4. General data repositories

ENA European Nucleotide Archive

BioSamples

EUROPEAN GENOME-PHENOME ARCHIVE

NCBI

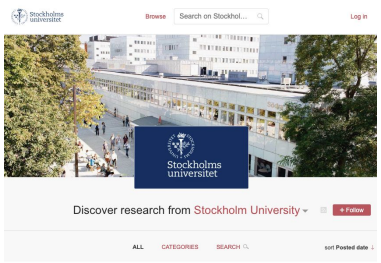
dbSNP Short Genetic Variations

PRIDE

Protein Data Bank in Europe
Bringing Structure to Biology

SND Svensk nationell datatjänst

figshare



zenodo

EUDAT

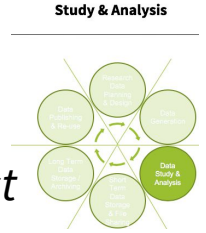
Etc...

Findable, Accessible, Interoperable, Resuable

International public repositories

- Best way to make data **FAIR**
- Domain-specific **metadata** standards

Strive towards uploading data to its final destination already at the beginning of a project



Recommended repositories

ELIXIR Deposition Database list

Deposition Database	Data type	International collaboration framework [1]
ArrayExpress	Functional genomics data. Stores data from high-throughput functional genomics experiments.	
BioModels	Computational models of biological processes.	
BioSamples	BioSamples stores and supplies descriptions and metadata about biological samples used in research and development by academia and industry.	NCBI BioSamples database
BioStudies	Descriptions of biological studies, links to data from these studies in other databases, as well as data that do not fit in the structured archives.	
EGA	Personally identifiable genetic and phenotypic data resulting from biomedical research projects.	European Bioinformatics Institute and the Centre for Genomic Regulation
EMDB	The Electron Microscopy Data Bank is a public repository for electron microscopy density maps of macromolecular complexes and subcellular structures.	
ENA	Nucleotide sequence information, covering raw sequencing data, contextual data, sequence assembly information and functional and taxonomic annotation.	International Nucleotide Sequence Database Collaboration
EVA	The European Variation Archive covers genetic variation data from all species.	dbSNP and dbVAR
IntAct	IntAct provides a freely available, open source database system and analysis tools for molecular interaction data.	The International Molecular Exchange Consortium
MetaboLights	Metabolite structures and their reference spectra as well as their biological roles, locations and concentrations, and experimental data from metabolic experiments.	
PDBe	Biological macromolecular structures.	wwPDB
PRIDE	Mass spectrometry-based proteomics data, including peptide and protein expression information (identifications and quantification values) and the supporting mass spectra evidence.	The ProteomeXchange Consortium

https://www.elixir-europe.org/platforms/data/elixir-deposition-databases

Scientific Data Recommended Data Repositories

SCIENTIFIC DATA

Biological sciences

Nucleic acid sequence

Sequence information should be deposited following the MIxS guidelines.

Simple genetic polymorphisms or structural variations should be submitted to dbSNP or dbVar (please note that these repositories cannot accept sensitive data derived from human subjects); the NCBI Trace Archive may be used for capillary electrophoresis data, while SRA accepts NGS data only.

DNA DataBank of Japan (DDBJ)	view FAIRsharing entry
European Nucleotide Archive (ENA)	view FAIRsharing entry
GenBank	view FAIRsharing entry
dbSNP	view FAIRsharing entry
European Variation Archive (EVA)	view FAIRsharing entry
dbVar	view FAIRsharing entry
Database of Genomic Variants Archive (DGVa)	view FAIRsharing entry
EBI Metagenomics	view FAIRsharing entry
NCBI Trace Archive	view FAIRsharing entry
NCBI Sequence Read Archive (SRA)	view FAIRsharing entry
NCBI Assembly	

Protein sequence

UniProtKB	view FAIRsharing entry

Molecular & supramolecular structure

These repositories accept structural data for small molecules (COD); peptides and proteins (all); and larger assemblies (EMDB).

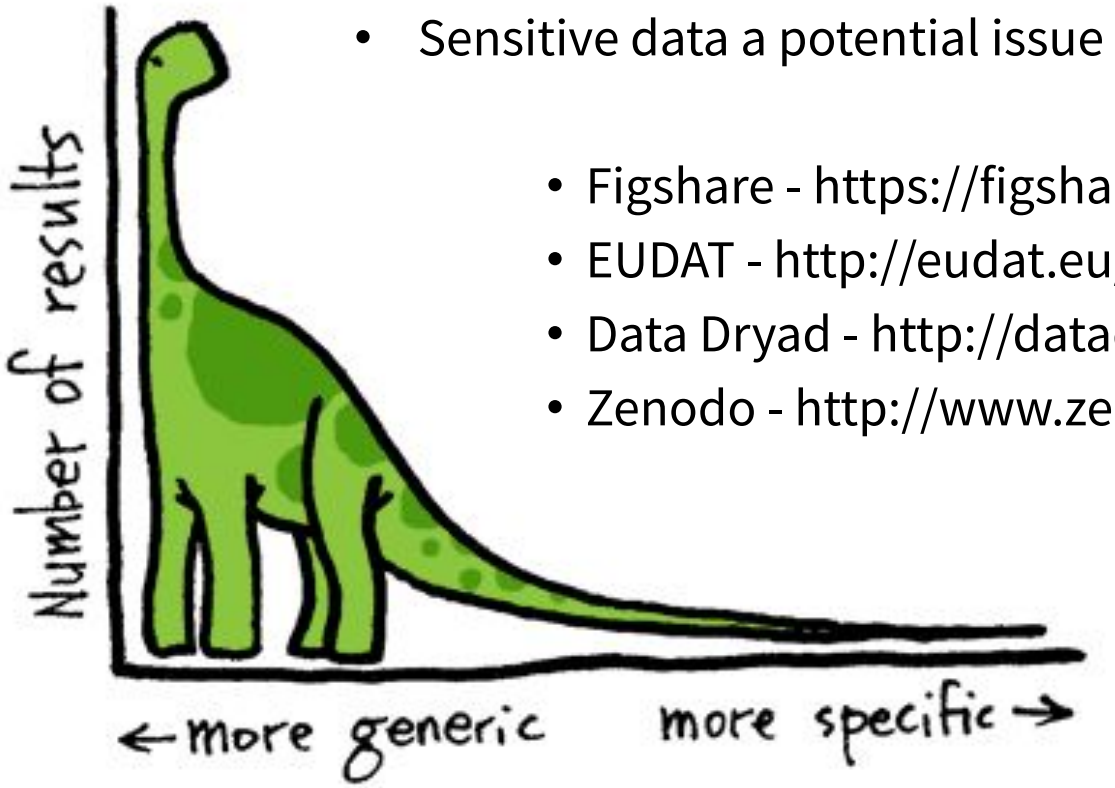
Small molecule crystallographic data should be uploaded to Dryad or figshare before manuscript submission, and should include a .cif file, a structural figure with probability ellipsoids, and structure factors for each structure. Both the structure factors and the structural output must have been checked using the IUCR's CheckCIF routine, and a copy of the output must be included at submission, together with a justification for any alerts reported.

Protein Circular Dichroism Data Bank (PCDDB)	view FAIRsharing entry

https://www.nature.com/sdata/policies/repositories#life

“Long-tail data” repositories

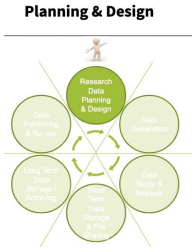
- Research data that doesn’t fit in structured data repositories
- Data publication – persistent identifiers
- Metadata submission – not tailored to Life Science
  - *Affects discoverability*
  - *(Less) FAIR*
- Sensitive data a potential issue



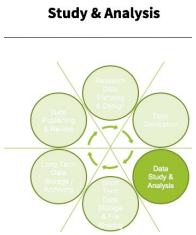
- Figshare - https://figshare.com/
- EUDAT - http://eudat.eu/
- Data Dryad - http://datadryad.org/
- Zenodo - http://www.zenodo.org/

Planning ahead

Consider structuring metadata in the format needed by the repository already at ***planning*** *stage*



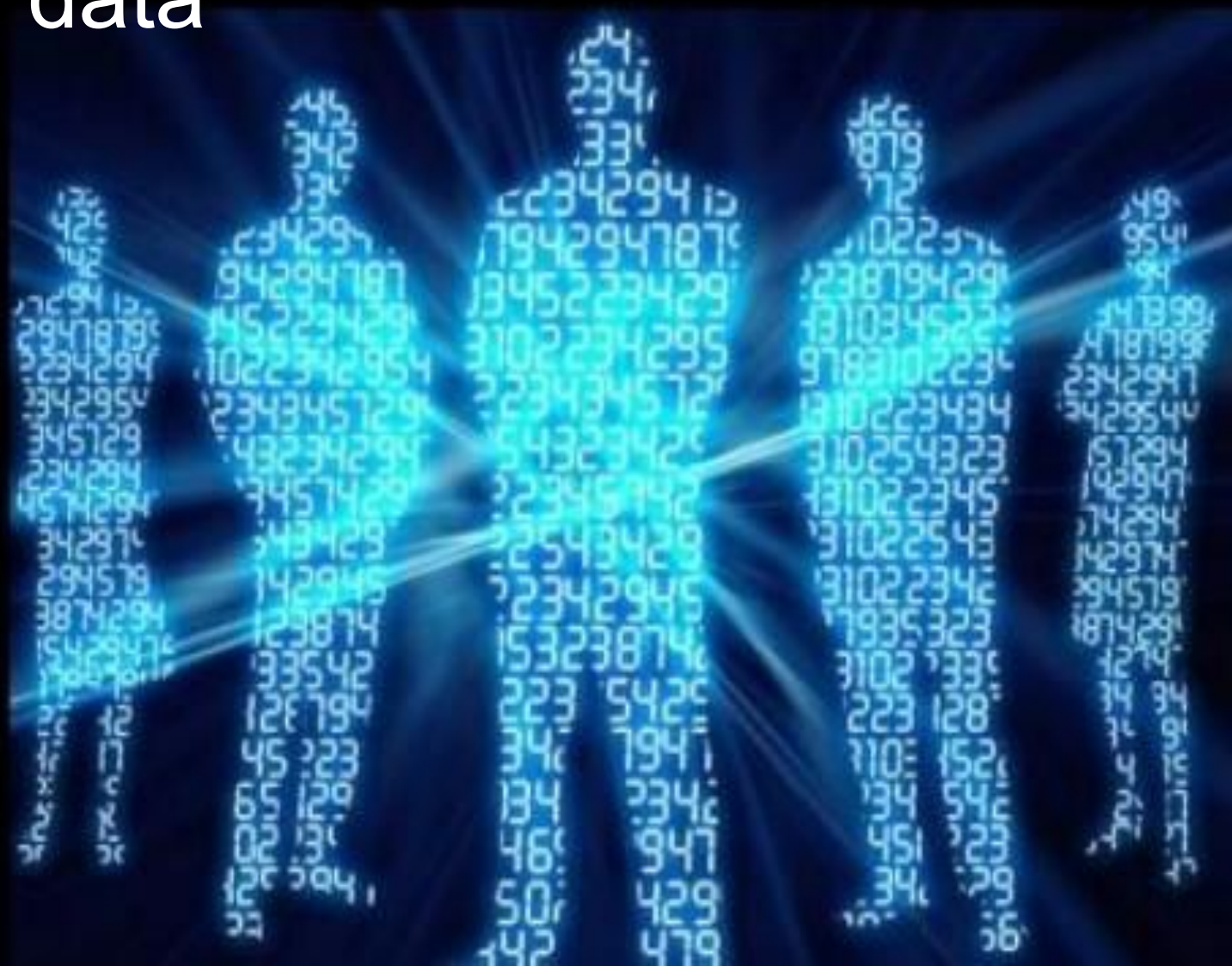
Strive towards uploading data to its final destination already at when it has been ***generated***



NBIS
NATIONAL BIOINFORMATICS INFRASTRUCTURE SWEDEN

SciLifeLab

Personal data



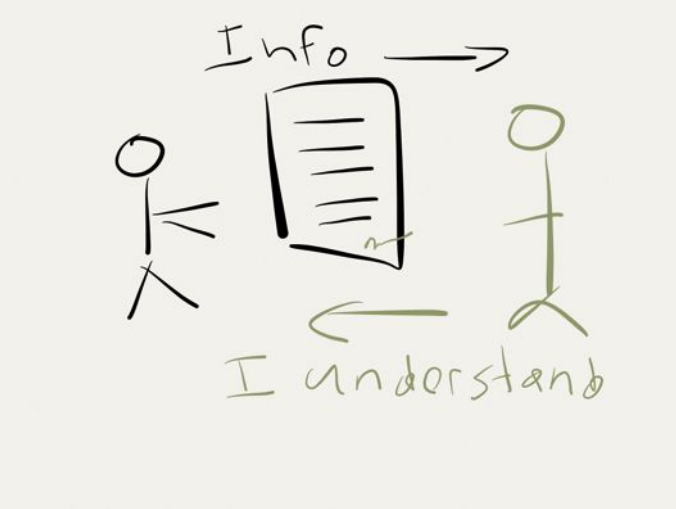
Personal data - Legislation

- GDPR – General Data Protection Regulation (*Dataskyddsförordningen*) + others
- Act concerning the Ethical Review of Research Involving Humans (*Lag om etikprövning av forskning som avser människor*)

Act concerning the Ethical Review

- Research that concerns studies of biological material that has been taken from a living person and that can be traced back to that person may only be conducted if it has been approved subsequent to an ethical vetting

- Informed consent
  - The subject must be informed about the purpose or the research and the consequences and risks that the research might entail
  - The subject must consent



GDPR

- All kinds of information that is directly or indirectly referable to a natural person who is alive constitute personal data
- To process personal data:
  - *All processing of personal data must fulfil the **fundamental principles** defined in the Regulation.*
    - Decide a **purpose** and stick to it
    - Only collect data that is needed
    - Don't collect more data than necessary
    - Don't use data for another incompatible purpose
    - Erase data when no longer needed
    - Ensure that data is correct and updated
    - Protect collected data – confidential and intact
    - Identify the **legal basis** for data processing before it starts
    - Inform in a transparent and honest way

Exemptions for some of these possible for research

- The Data Inspection Board (*Datainspektionen*) is the Swedish Data Protection Authority

GDPR – Legal basis

- **Consent**
- To be able to fulfil contract with data subject
- Legal obligation
- Necessary in order to protect the vital interests of the data subject
- **Public interest**
- Necessary for the purposes of the legitimate interests pursued by the controller

GDPR – Sensitive data

- Special categories (*Sensitive data*)
  - … **racial or ethnic origin**, […] **genetic data**, […], data concerning **health** … Art. 9 (1)
  - Processing is **prohibited** unless…
    - **explicit consent** is given Art. 9 (2)a
    - processing is necessary for **scientific research** in accordance with Article 89(1) based on Union or *Member State law* which shall be proportionate to the aim pursued, respect the essence of the right to data protection and provide for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject. Art. 9 (2)j
    - Member State specific conditions and *limitations possible* for processing of health & genetic data Art. 9 (4)
    - **Sweden**
      - *Consent?*
      - Public interest → Ethical review necessary (often includes consent)

GDPR – Roles

- The (legal) person that decides why and how personal data should be processed is called the **Controller** (*personuppgiftsansvarig*)
  - e.g. the employing university
  - Controller responsible for
    - Has to ensure the **rights of the individuals**
    - **Take measures** to ensure that the Regulation is followed, and be able to **show** that it is
    - **Privacy by Design** as standard
    - Keep a **register of processing**
    - Apply **security measures** when processing data
    - **Report** personal data **breaches** to the Data Protection Authority
    - Perform *Impact Assessments* and consult Data Protection Authority (when necessary)
    - Appoint **Data Protection Officer**

GDPR – Roles

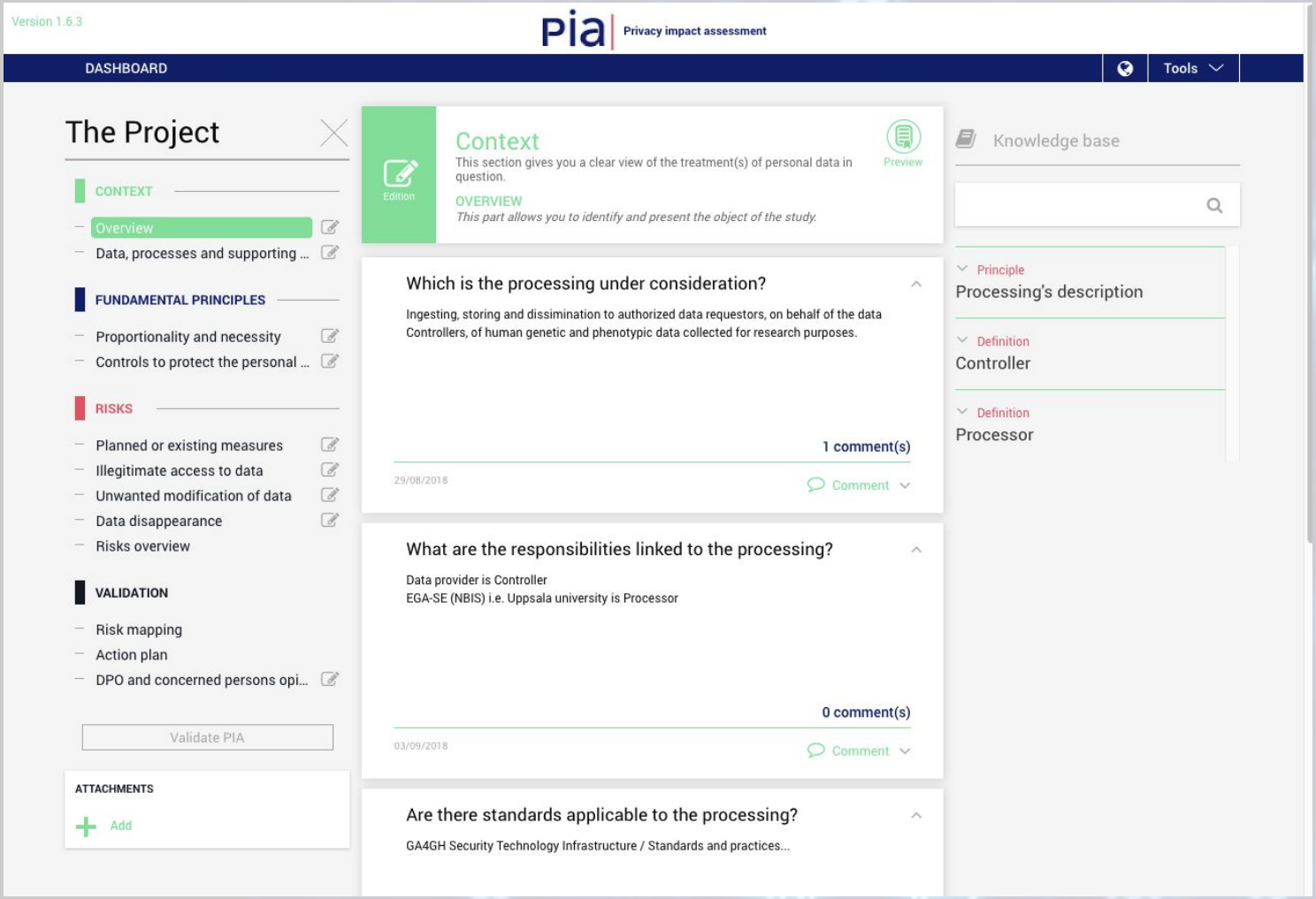
- The controller of personal data can delegate processing of personal data to a **Processor** (*personuppgiftsbiträde*)
  - e.g. UPPMAX/Uppsala university
  - Joint responsibility with Controller
  - A legal agreement **must** be established (Art. 28.3)
    - Instruction from Controller to Processor on how data shall be processed

Data Protection Impact Assessment (Art. 35.1)

- A personal data *controller* must carry out an impact assessment if a type of processing is **likely to result in a high risk to the rights and freedoms** of natural persons. The impact assessment must be carried out **prior** to the processing.
- The Swedish Data Protection Authority has adopted a list of where an impact assessment is required (Swedish, English)
  - 9 criteria
- Example processings requiring a DPIA
  - Processing, including storage for archiving purposes, of pseudonymised sensitive personal data that refers to data subjects from research projects or clinical trials. (Criteria 4 and 7)
  - Organisations that collect and store sensitive data in order to serve as a basis for future research purposes. (Criteria 4 and 7)

GDPR – PIA

- Open source tool for DPIAs from CNIL (French DPA)



https://www.cnil.fr/en/open-source-pia-software-helps-carry-out-data-protection-impact-assesment

GDPR – DPO

- A **Data Protection Officer** (*dataskyddssombud*)
  - The natural person that is responsible for ensuring that the organization/company adheres to the GDPR
  - Educate
  - Audit
  - Contact point between organization and Data Protection Authority

GU

https://medarbetarportalen.gu.se/diarieforing-arkivering-och-personuppgiftsbehandling/rutiner-for-behandling-av-personuppgifter/personuppgifter-i-forskning/?languageId=100001

KI

https://staff.ki.se/gdpr-at-ki

KTH

https://intra.kth.se/en/anstallning/anstallningsvillkor/att-vara-statligt-an/behandling-av-person/dataskyddsforordningen-gdpr-1.800623

LiU

https://insidan.liu.se/dataskyddsforordningen?l=en

LU

https://staff.lu.se/dataprotection

SU

http://su.se/english/gdpr

UmU

https://www.aurora.umu.se/regler-och-riktlinjer/juridik/personuppgifter/

UU

https://mp.uu.se/en/web/info/stod/dataskyddsforordningen

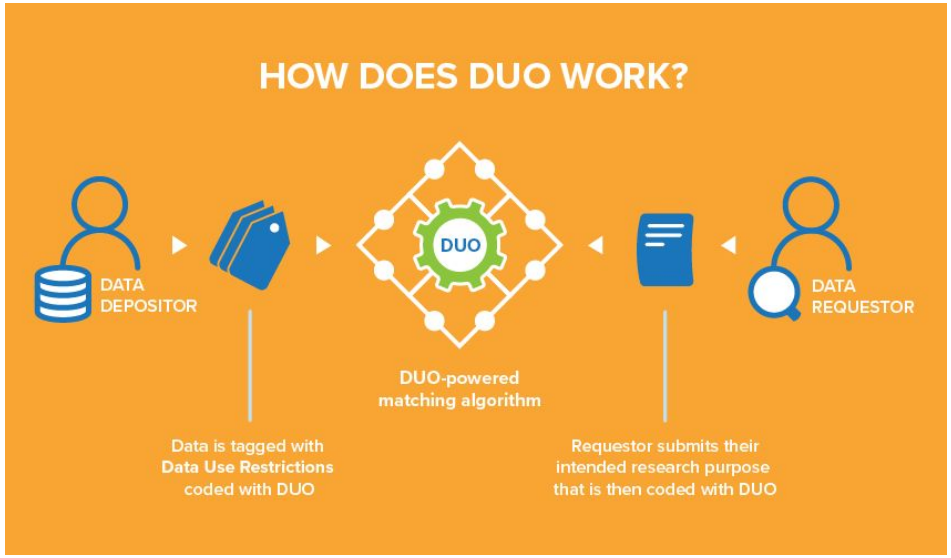
Genetic information

- The genetic information of an individual is personal data
  - **Sensitive** personal data (as it relates to health)
    - Explicitly defining in GDPR
  - Even if *anonymized* / *pseudonymized*
  - In principle, **no** difference between WGS, Exome, Transcriptome or GWAS data

- *Theoretically* possible to identify the individual person from which the sequence was derived from the sequence itself
  - The more associated metadata there is, the easier this gets
  - Gymrek et al. “Identifying Personal Genomes by Surname Inference”. Science 339, 321 (2013); DOI:10.1126/science.1229566

- *Apply technical and organizational measures to protect the sensitive data, e.g.*
  - *Strong IT security and procedures to limit access to data*
  - *Separate from other personal data*
  - *Pseudonymization*
  - *Encryption*.

Codifying consents



Consent Codes

Name	Abbreviation	Description
Primary Categories (I^{Y})		
No restrictions	NRES	No restrictions on data use.
General research use and clinical care	GRU(CC)	For health/medical/biomedical purposes, including the study of population origins or ancestry.
Health/medical/biomedical research and clinical care	HMB(CC)	Use of the data is limited to health/medical/biomedical purposes; does not include the study of population origins or ancestry.
Disease-specific research and clinical care	DS-[XX](CC)	Use of the data must be related to [disease].
Population origins/ancestry research	POA	Use of the data is limited to the study of population origins or ancestry.
Secondary Categories (II^{Y}) (can be one or more extra conditions, in addition to I^{Y} category)		
Oher research-specific restrictions	RS-[XX]	Use of the data is limited to studies of [research type] (e.g., pediatric research).
Research use only	RUO	Use of data is limited to research purposes (e.g., does not include its use in clinical care).
No “general methods” research	NMDS	Use of the data includes methods development research (e.g., development of software or algorithms) ONLY within the bounds of other data use limitations.
Genetic studies only	GSO	Use of the data is limited to genetic studies only (i.e., no “phenotype-only” research).
Requirements		
Not-for-profit use only	NPU	Use of the data is limited to not-for-profit organizations.
Publication required	PUB	Requestor agrees to make results of studies using the data available to the larger scientific community.
Collaboration required	COL-[XX]	Requestor must agree to collaboration with the primary study investigator(s).
Ethics approval required	IRB	Requestor must provide documentation of local IRB/REC approval.
Geographical restrictions	GS-[XX]	Use of the data is limited to within [geographic region].
Publication moratorium/embargo	MOR-[XX]	Requestor agrees not to publish results of studies until [date].
Time limits on use	TS-[XX]	Use of data is approved for [x months].
User-specific restrictions	US	Use of data is limited to use by approved users.
Project-specific restrictions	PS	Use of data is limited to use within an approved project.
Institution-specific restrictions	IS	Use of data is limited to use within an approved institution.

doi:10.1371/journal.pgen.1005772.t001

Global Alliance for Genomics & Health
Collaborate. Innovate. Accelerate.

Nordic Collaboration for Sensitive Data

NordForsk neic NORDIC E-INFRASTRUCTURE COLLABORATION elixir DENMARK elixir FINLAND elixir NORWAY elixir SWEDEN

https://neic.no/tryggve/

Tryggve vision

Tryggve2 develops and facilitates access to secure e-infrastructure for sensitive data, suitable for hosting large-scale cross-border biomedical research studies

https://neic.no/tryggve/

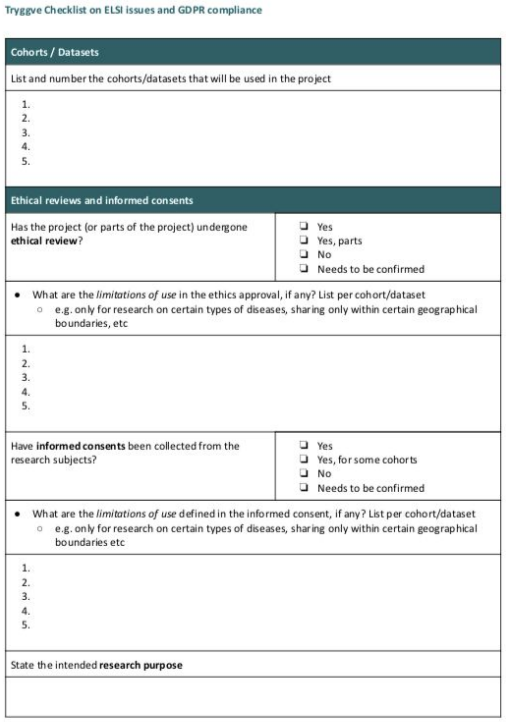
Tryggve2 major deliverables **2017 – 2020**

1. **Sensitive data archiving**
2. Production quality processing services
3. Homogenized user experience
   - User mobility
   - Workflow mobility
   - Data mobility
4. **Nordic use cases**
   - **Research**
   - **Infrastructure development**
5. ELIXIR AAI
6. IT Security
7. **ELSI Topics**

https://neic.no/tryggve/usecase/

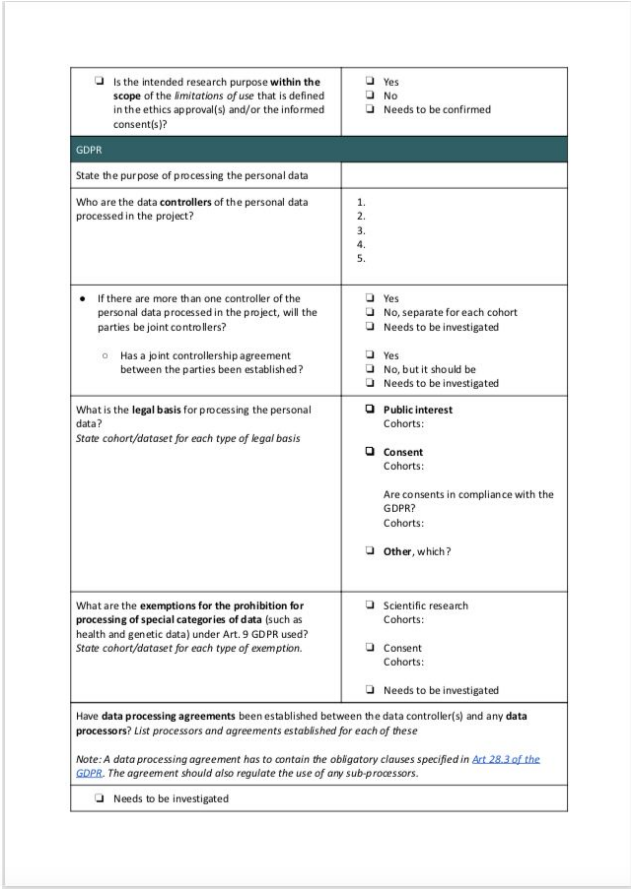
https://neic.no/tryggve/

Tryggve ELSI checklist

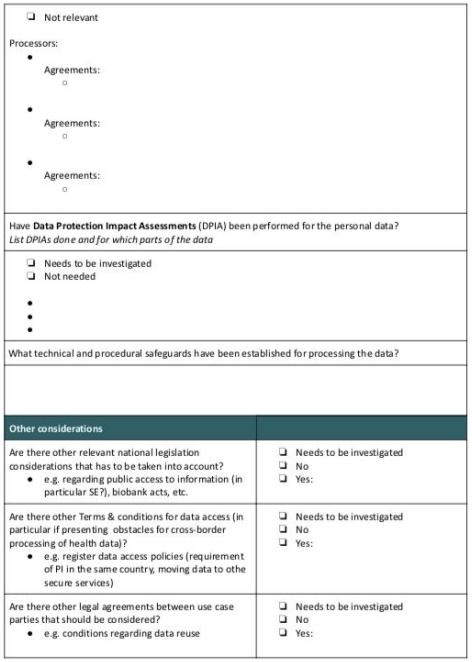


Tryggve Checklist on ELSI issues and GDPR compliance

Cohorts / Datasets	
List and number the cohorts/datasets that will be used in the project	
1. 2. 3. 4. 5.	
Ethical reviews and informed consents	
Has the project (or parts of the project) undergone **ethical review**?	❑ Yes ❑ Yes, parts ❑ No ❑ Needs to be confirmed
• What are the *limitations of use* in the ethics approval, if any? List per cohort/dataset ○ e.g. only for research on certain types of diseases, sharing only within certain geographical boundaries, etc	
1. 2. 3. 4. 5.	
Have **informed consents** been collected from the research subjects?	❑ Yes ❑ Yes, for some cohorts ❑ No ❑ Needs to be confirmed
• What are the *limitations of use* defined in the informed consent, if any? List per cohort/dataset ○ e.g. only for research on certain types of diseases, sharing only within certain geographical boundaries etc	
1. 2. 3. 4. 5.	
State the intended **research purpose**	



❑ Is the intended research purpose **within the scope** of the *limitations of use* that is defined in the ethics approval(s) and/or the informed consent(s)?	❑ Yes ❑ No ❑ Needs to be confirmed
GDPR	
State the purpose of processing the personal data	
Who are the data **controllers** of the personal data processed in the project?	1. 2. 3. 4. 5.
• If there are more than one controller of the personal data processed in the project, will the parties be joint controllers? ○ Has a joint controllership agreement between the parties been established?	❑ Yes ❑ No, separate for each cohort ❑ Needs to be investigated ❑ Yes ❑ No, but it should be ❑ Needs to be investigated
What is the **legal basis** for processing the personal data? *State cohort/dataset for each type of legal basis*	❑ **Public interest** Cohorts: ❑ **Consent** Cohorts: Are consents in compliance with the GDPR? Cohorts: ❑ **Other**, which?
What are the **exemptions for the prohibition for processing of special categories of data** (such as health and genetic data) under Art. 9 GDPR used? *State cohort/dataset for each type of exemption.*	❑ Scientific research Cohorts: ❑ Consent Cohorts: ❑ Needs to be investigated
Have **data processing agreements** been established between the data controller(s) and any **data processors**? *List processors and agreements established for each of these* *Note: A data processing agreement has to contain the obligatory clauses specified in Art. 28.3 of the GDPR. The agreement should also regulate the use of any sub-processors.*	
❑ Needs to be investigated	



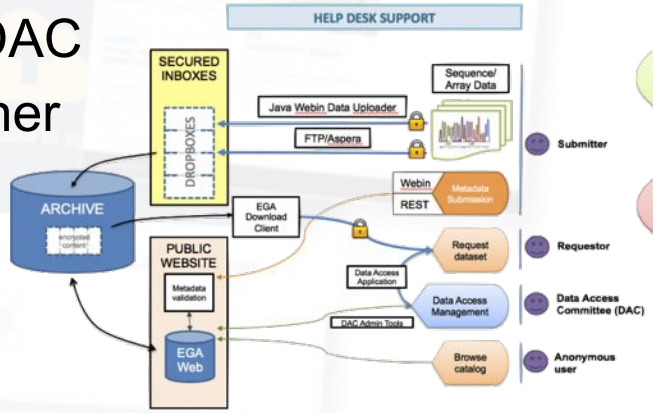
❑ Not relevant Processors: • Agreements: ○ • Agreements: ○ • Agreements: ○	
Have **Data Protection Impact Assessments** (DPIA) been performed for the personal data? *List DPIAs done and for which parts of the data*	
❑ Needs to be investigated ❑ Not needed • • •	
What technical and procedural safeguards have been established for processing the data?	
Other considerations	
Are there other relevant national legislation considerations that has to be taken into account? • e.g. regarding public access to information (in particular SE?), biobank acts, etc.	❑ Needs to be investigated ❑ No ❑ Yes:
Are there other Terms & conditions for data access (in particular if presenting obstacles for cross-border processing of health data)? • e.g. register data access policies (requirement of PI in the same country, moving data to othe secure services)	❑ Needs to be investigated ❑ No ❑ Yes:
Are there other legal agreements between use case parties that should be considered? • e.g. conditions regarding data reuse	❑ Needs to be investigated ❑ No ❑ Yes:

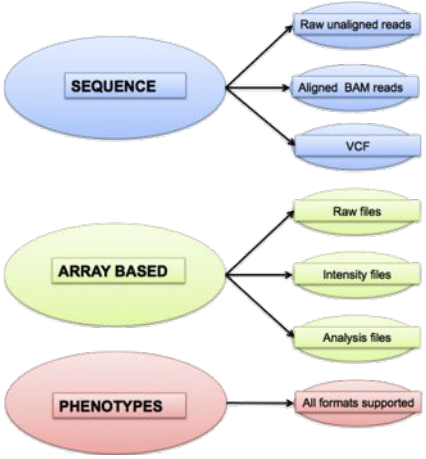
What about publishing sensitive data?

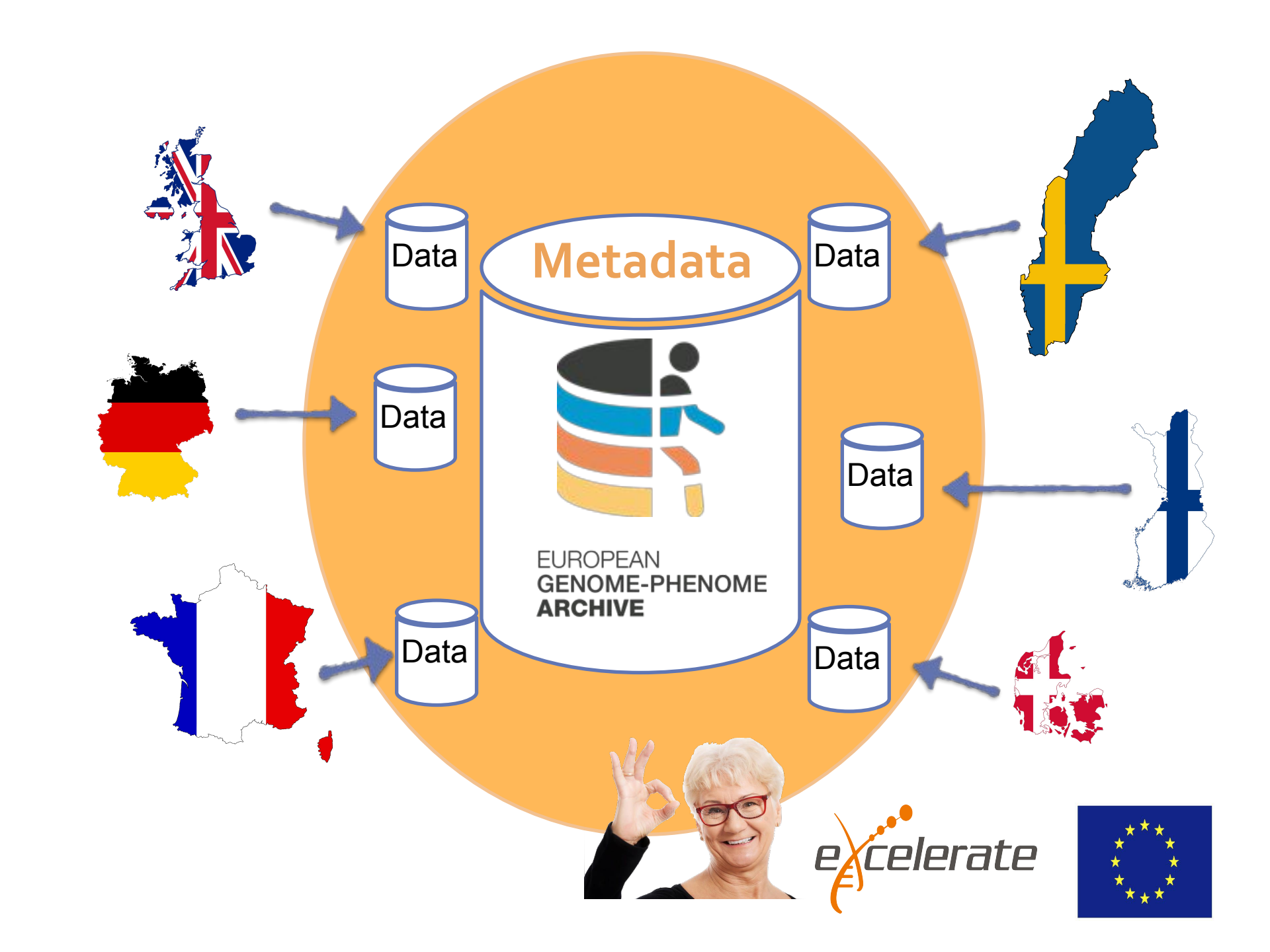
"As open as possible, as closed as necessary"

- **EGA** – European Genome-phenome Archive
  - Repository that promotes the distribution and sharing of **genetic and phenotypic data** consented for specific approved uses but **not fully open, public distribution**.
  - All types of sequence and genotype experiments, including case-control, population, and family studies.

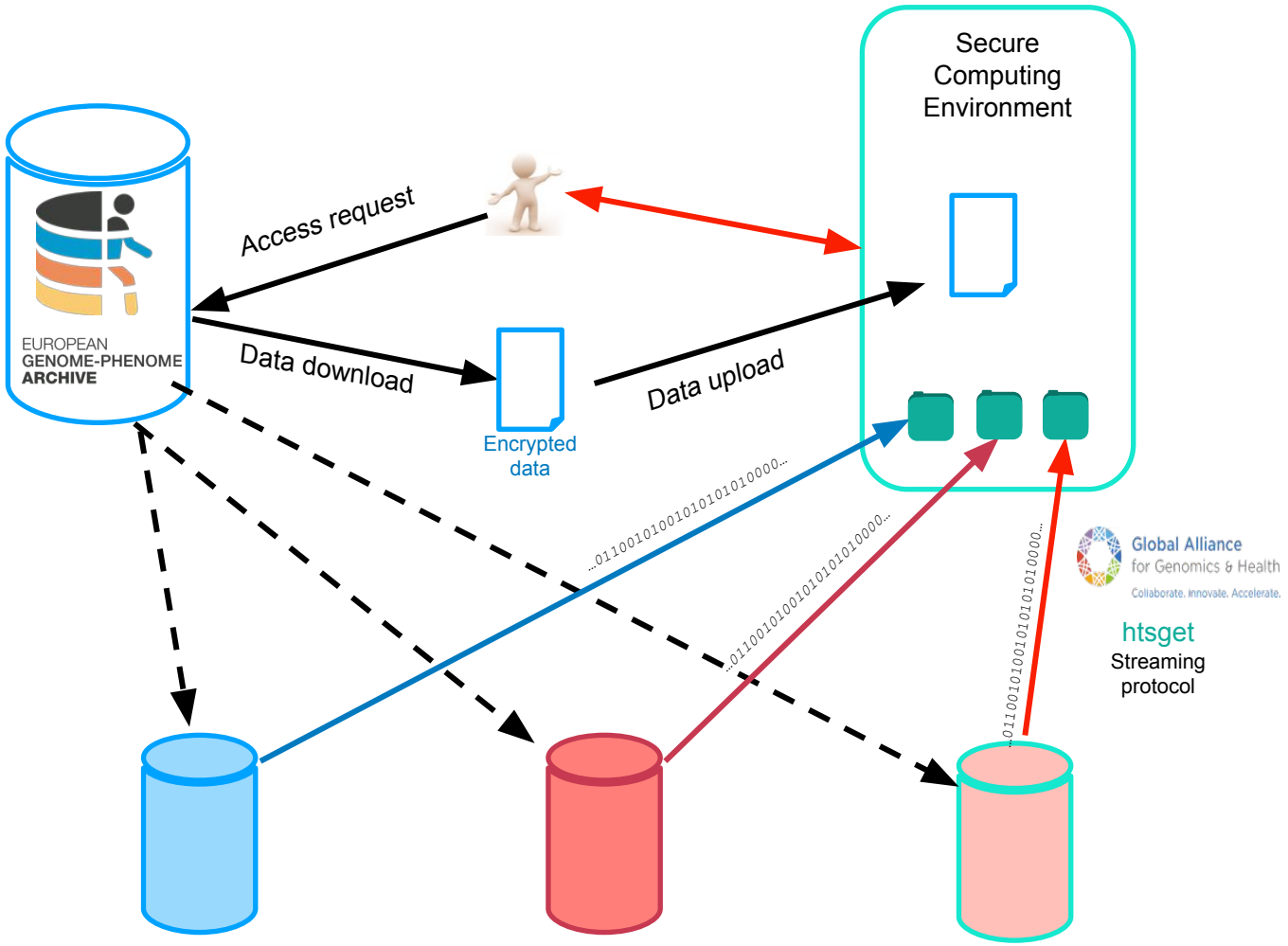
- Data Access Agreement
  - Defined by the data owner
- Data Access Committee – DAC
  - Decided by the data owner






Data
Metadata
Data
Data
Data
Data
Data
Data
EUROPEAN
GENOME-PHENOME
ARCHIVE
excelerate

Future ways of accessing data

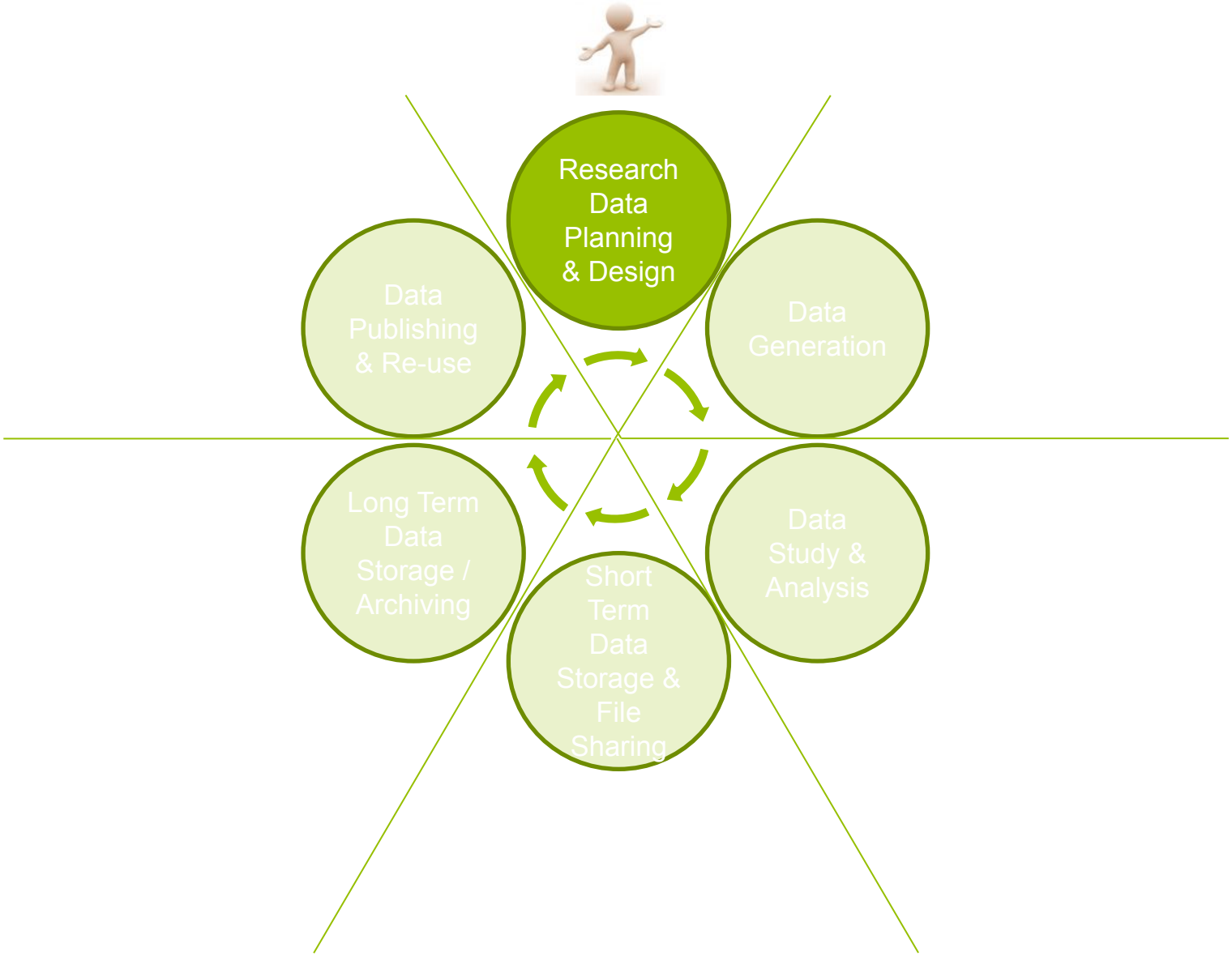


NBIS
NATIONAL BIOINFORMATICS INFRASTRUCTURE SWEDEN

SciLifeLab

When should you start planning for how to manage you data?

Planning & Design



Gaps in the NGS Data Life Cycle

International repositories
ENA, EGA, ArrayExpress, …

Interoperability

Policies

Research Data Planning & Design

Data Generation

Data Study & Analysis

Short Term Data Storage & File Sharing

Long Term Data Storage / Archiving

Data Publishing & Re-use

EGA-SE

Human data

NATIONAL GENOMICS INFRASTRUCTURE

Next-Generation Sequencing and Genotyping for Swedish Research

Uppsala Multidisciplinary Center for Advanced Computational Science UPPMAX

?

Legally, archiving is a responsibility of the universities ***Note****! Higher security for human derived data*

Strategy for this being worked at by SciLifeLab

?

Lower-cost storage from which data can be staged to HPC systems

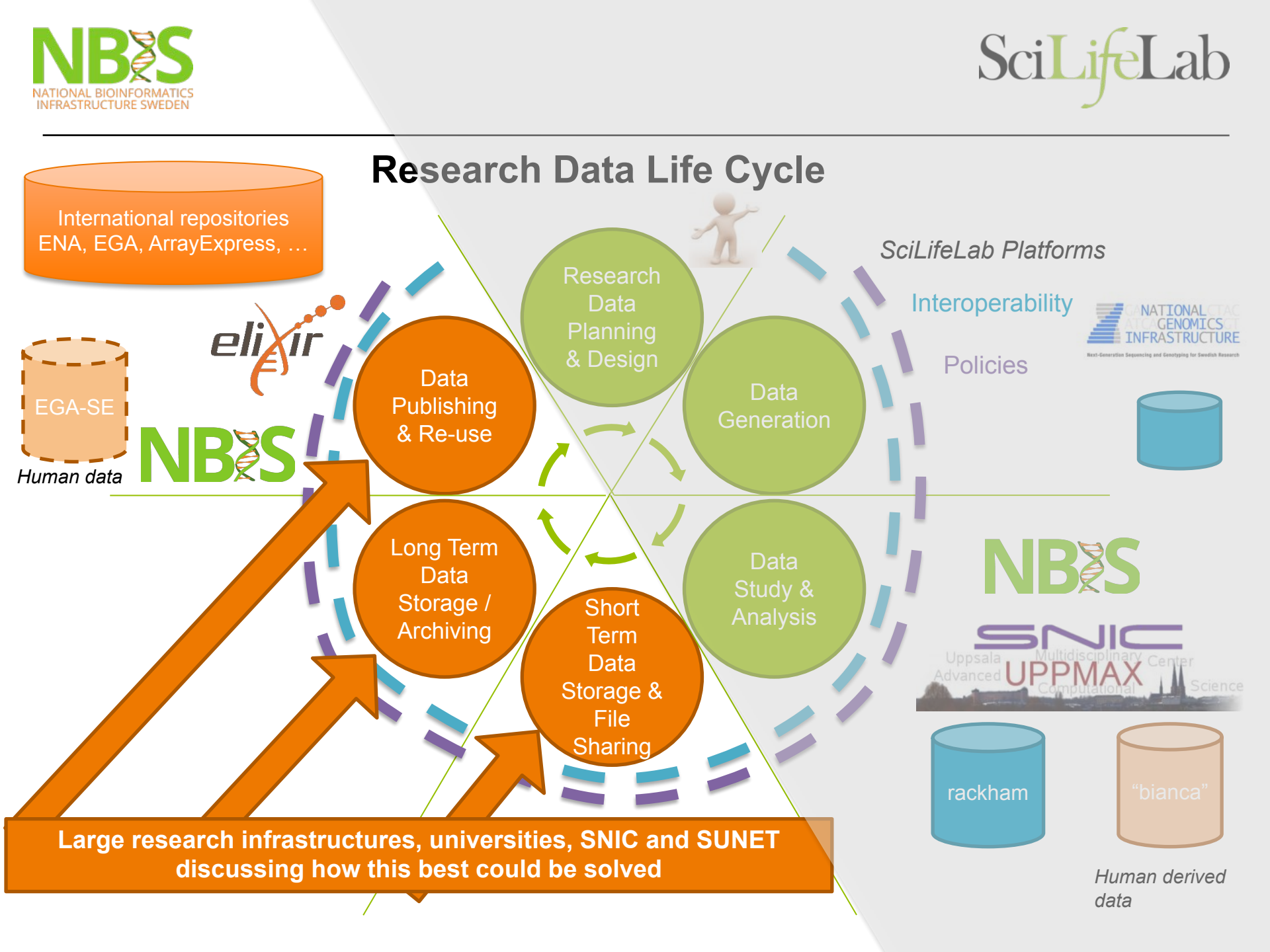
Solutions are planned by SNIC

rackham

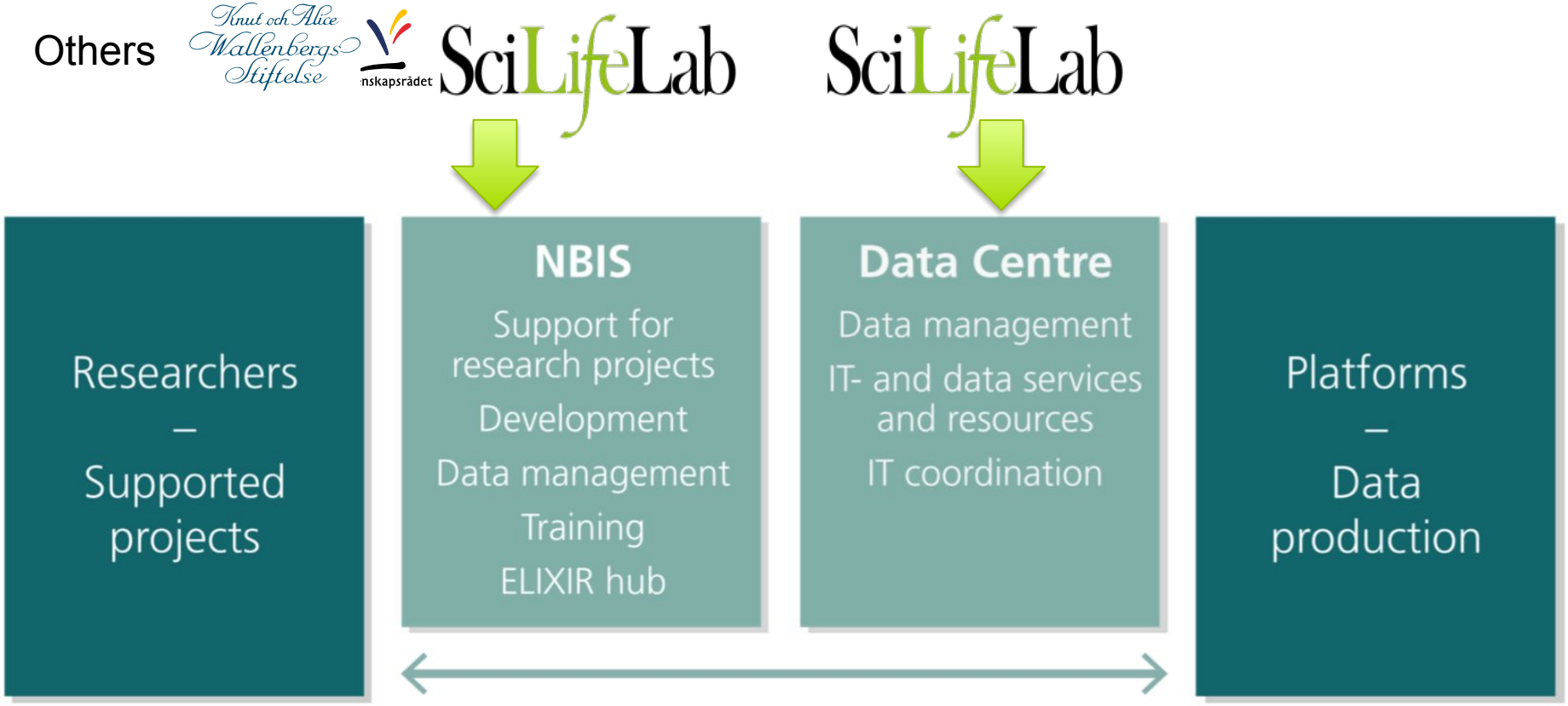
"bianca"

Human derived data

Research Data Life Cycle



Data Centre / NBIS differences



NBIS Data Management support

- Project planning
  - Metadata
  - File formats
  - Licensing
  - *Data Management Plans*

- *(Data analysis)*

- Data publication and submission
  - Support submissions to public repositories
  - Metadata
  - DOIs to dataset (if needed)

Research Ethics

- Is it ethical to do bad/careless science?
  - Wasting resources
    - … or even dangerous medical practices
  - Contribute to the current research credibility crisis
  - harming the profession
  - harming the public trust

- But!
  - Careless science -> longer CV

My take of material by Rochelle Tractenberg "Unexpected Ethical Challenges in Bioinformatics and Genomics."

Take home messages

- You set the culture in your research group
- Promote best-practice data management
  - Pick a thought-through file and folder structure organization for your computational analyses
  - Strive for reproducibility
    - Data & Code
  - Organize project metadata from the start
    - In ways that makes it easy to submit to public repositories
    - Use available standards
  - Plan for submitting ”raw data” to public repositories as early as possible
- Be aware that there are legal aspects to processing human data
- Make Data Management Plans for your projects
  - Ensure that your research output is FAIR
- *Ask for help if you need it!*

Source Acknowledgements

- Research Data Management, EUDAT - http://hdl.handle.net/11304/79db27e2-c12a-11e5-9bb4-2b0aad496318
- Noble WS (2009) A Quick Guide to Organizing Computational Biology Projects. PLoS Comput Biol 5(7): e1000424. doi:10.1371/journal.pcbi.1000424
- FAIR
  - Luiz Bonino - https://indico.neic.no/event/56/sessions/97/attachments/47/77/2.2._Day_2_PM_Late_-_Luiz_-_FAIR_Principles_explained_and_actionized.pdf
- Reproducible research
  - Reproducible Science Curriculum – https://github.com/Reproducible-Science-Curriculum/rr-init
  - Leif Väremo & Rasmus Ågren
    - https://bitbucket.org/scilifelab-lts/reproducible_research_example/src
    - https://nbis-reproducible-research.readthedocs.io/en/course_1803
- GDPR
  - Datainspektionen – https://www.datainspektionen.se/lagar--regler/dataskyddsforordningen/
- Ethics
  - Rochelle Tractenberg "Unexpected Ethical Challenges in Bioinformatics and Genomics."
- … and probably others I have forgotten

Data Management Plans

Will become a standard part of the research funding process

nature
International journal of science

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EDITORIAL · 13 MARCH 2018

Everyone needs a data-management plan

They sound dull, but data-management plans are essential, and funders must explain why.

By 2019, all who receive grants from us must have a data management plan

As from spring 2019, if you are awarded a grant from the Swedish Research Council you must have a plan for how the research data generated within your project shall be managed.

You must not send in your data management plan to us when you apply for a grant, but your administrating organisation will be responsible for ensuring that a data management plan is in place when you start your project or corresponding, and that the plan is maintained.

National guidelines

- VR & SUHF (Association of Swedish Higher Education Institutions)

- **Central parts of a data management plan**
  - Based on Science Europe's "Core Requirements for Data Management Plans"

1. Description of data – reuse of existing data and/or production of new data
2. Documentation and data quality
3. Storage and backup
4. Legal and ethical aspects
5. Accessibility and long-term storage
6. How will the use of unique and persistent identifiers, such as a Digital Object Identifier (DOI), be safeguarded?

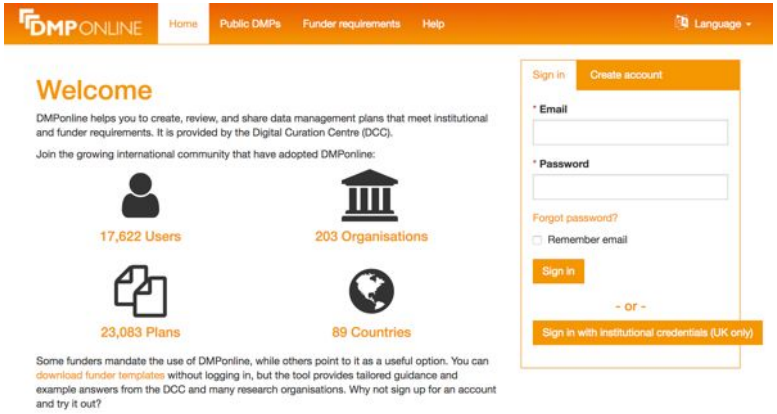
https://www.vr.se/english/calls-and-decisions/grant-terms-and-conditions/data-management-plan.html

VRs recommendations

1. Description of data – reuse of existing data and/or production of new data
   - How will data be collected, created or reused?
   - What types of data will be created and/or collected, in terms of data format and amount/volume of data?
2. Documentation and data quality
   - How will the material be documented and described, with associated metadata relating to structure, standards and format for descriptions of the content, collection method, etc.?
   - How will data quality be safeguarded and documented (for example repeated measurements, validation of data input, etc.)?
3. Storage and backup
   - How is storage and backup of data and metadata safeguarded during the research process?
   - How is data security and controlled access to data safeguarded, in relation to the handling of sensitive data and personal data, for example?
4. Legal and ethical aspects
   - How is data handling according to legal requirements safeguarded, e.g. in terms of handling of personal data, confidentiality and intellectual property rights?
   - How is correct data handling according to ethical aspects safeguarded?
5. Accessibility and long-term storage
   - How, when and where will research data or information about data (metadata) be made accessible? Are there any conditions, embargoes and limitations on the access to and reuse of data to be considered?
   - In what way is long-term storage safeguarded, and by whom? How will the selection of data for long-term storage be made?
   - Will specific systems, software, source code or other types of services be necessary in order to understand, partake of or use/analyse data in the long term?
6. How will the use of unique and persistent identifiers, such as a Digital Object Identifier (DOI), be safeguarded?
   - Responsibility and resources
   - Who is responsible for data management and (possibly) supports the work with this while the research project is in progress? Who is responsible for data management, ongoing management and long-term storage after the research project has ended?
   - What resources (costs, labour input or other) will be required for data management (including storage, back-up, provision of access and processing for long-term storage)? What resources will be needed to ensure that data fulfil the FAIR principles?

DMP tools

DMPonline



https://dmponline.dcc.ac.uk/

ELIXIR Data Stewardship Wizard

https://ds-wizard.org/

https://dsw.scilifelab.se

Hands-on DMP session

- Go to https://dsw.scilifelab.se/
- Create an account, login after confirmation email
- Click on Questionnaires in left-side menu
- Write a name based on your name and project
- Select ‘Common SciLifeLab DMP 1.1.0” as Knowledge Model
- Save and begin answering the questions