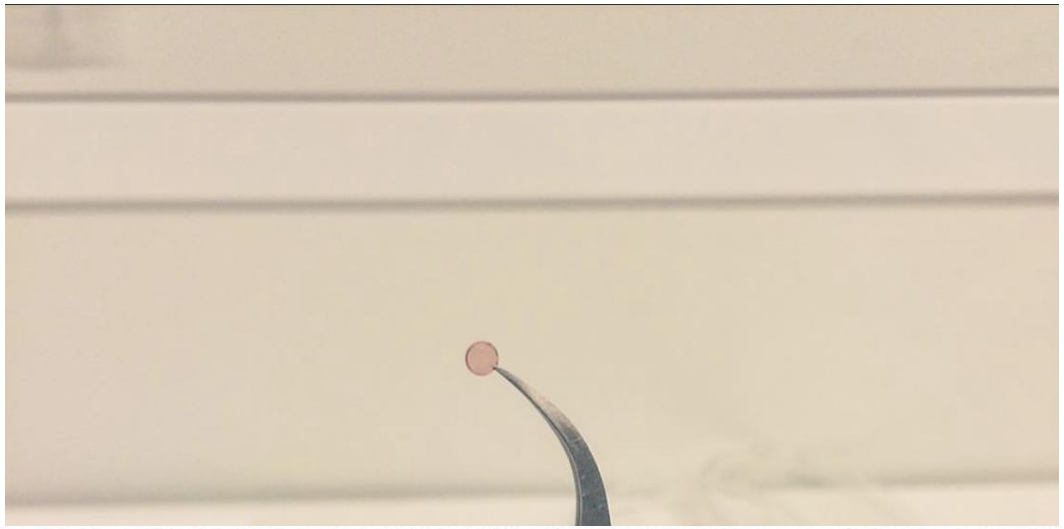
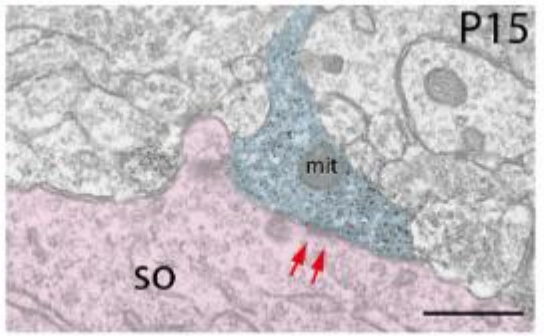
Use (and re-use) of animals in neuroscience

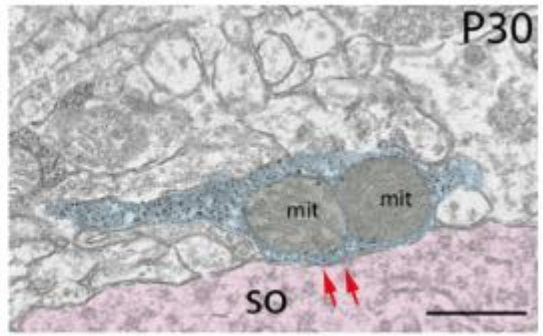
How data sharing and re-use can make our science more ethical

My background

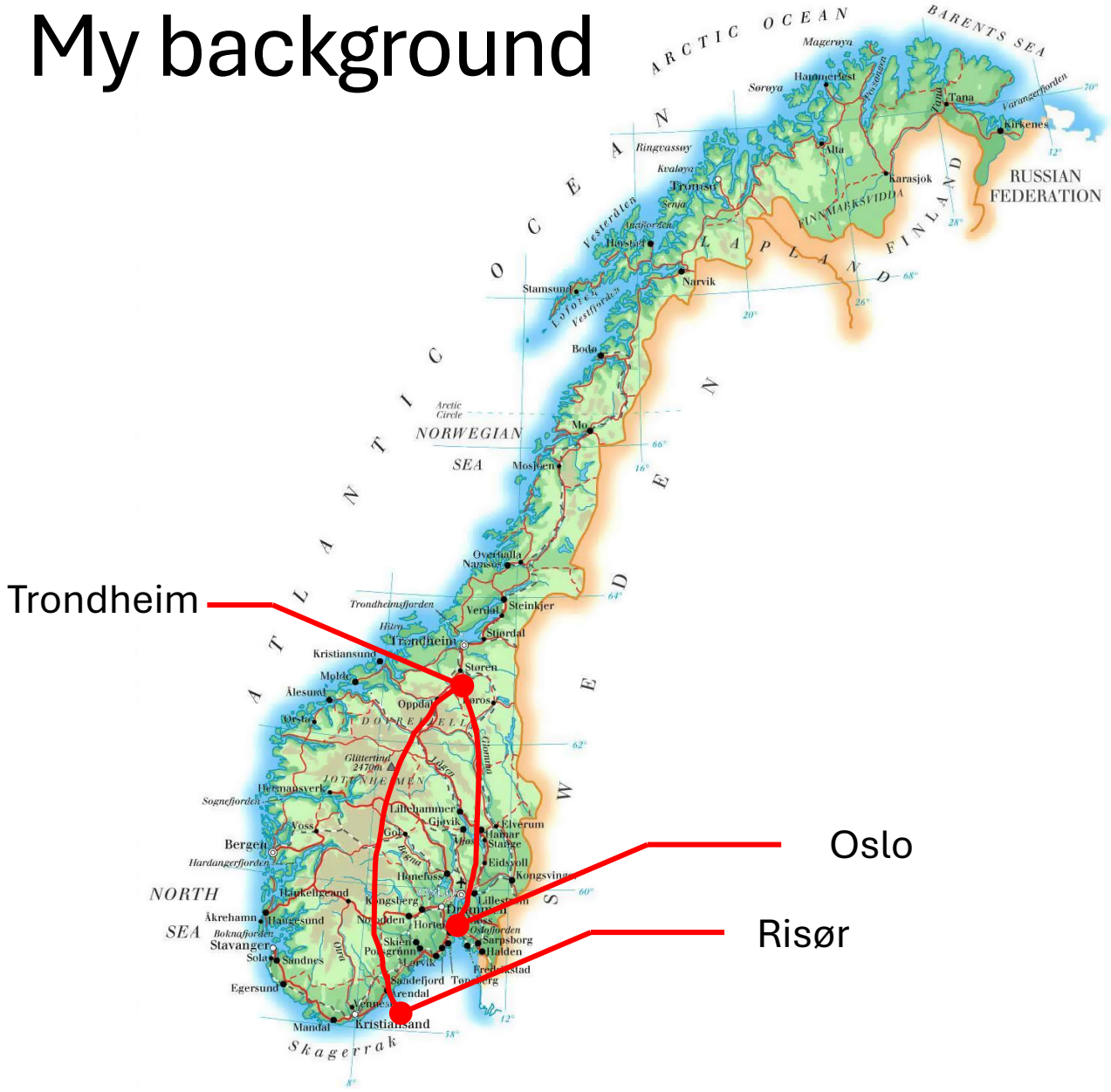
Trondheim







My background



Jan Bjaalie

Trygve Leergaard

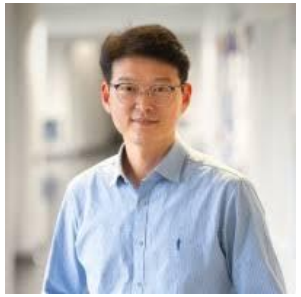
Human Brain Project

UiO : University of Oslo

EBRAINS

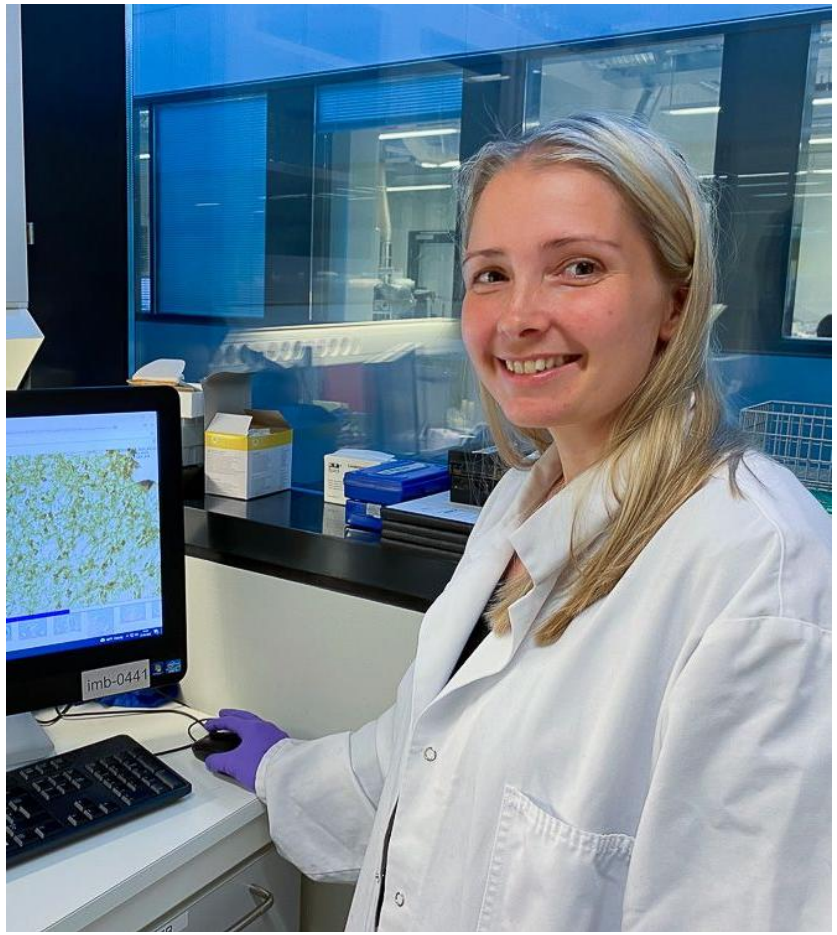
My background

- Currently postdoc at Penn State University with Professor Yongsoo Kim



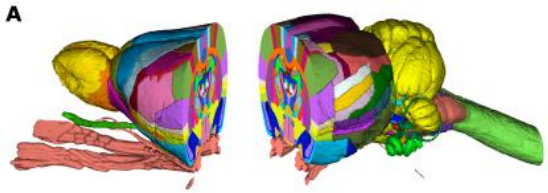
PennState

My research



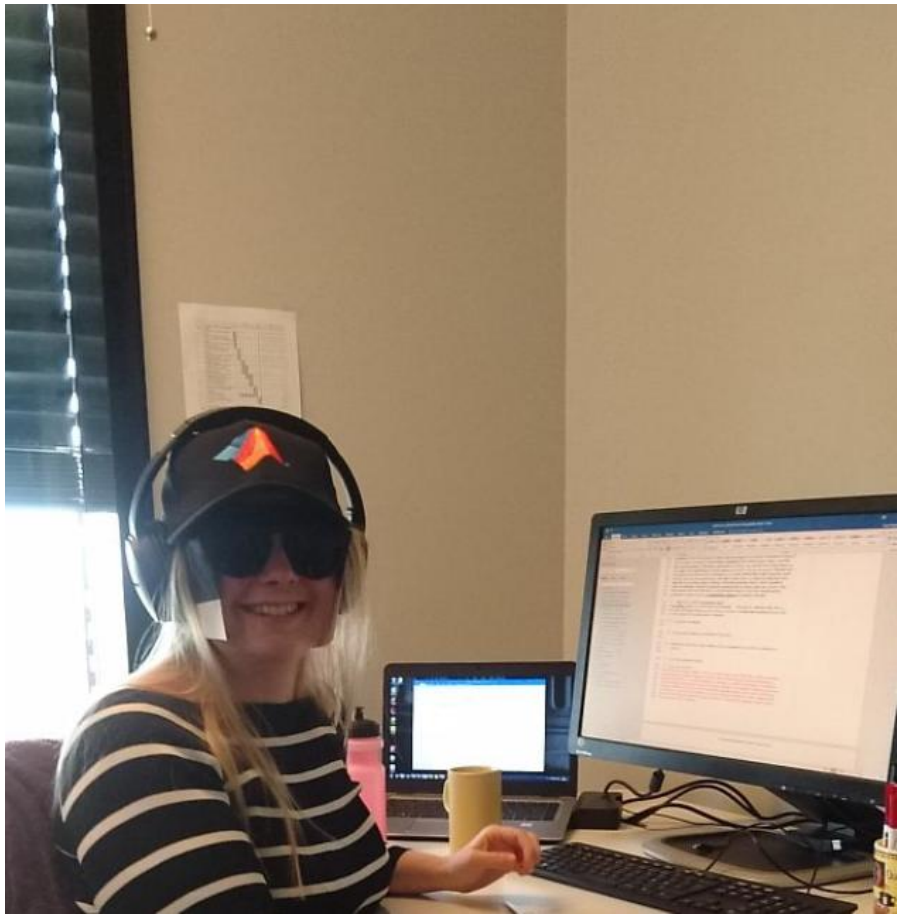
- Rats and mice

- Neuroanatomy and brain development through neuroinformatics



- Data sharing

Domus Medica, Oslo, 2019



- I was a PhD student trying to build a database based on literature

- A rude awakening to some of our scientific practices…
  - Lack of information
  - Partial data reporting
  - Raw data almost always unavailable

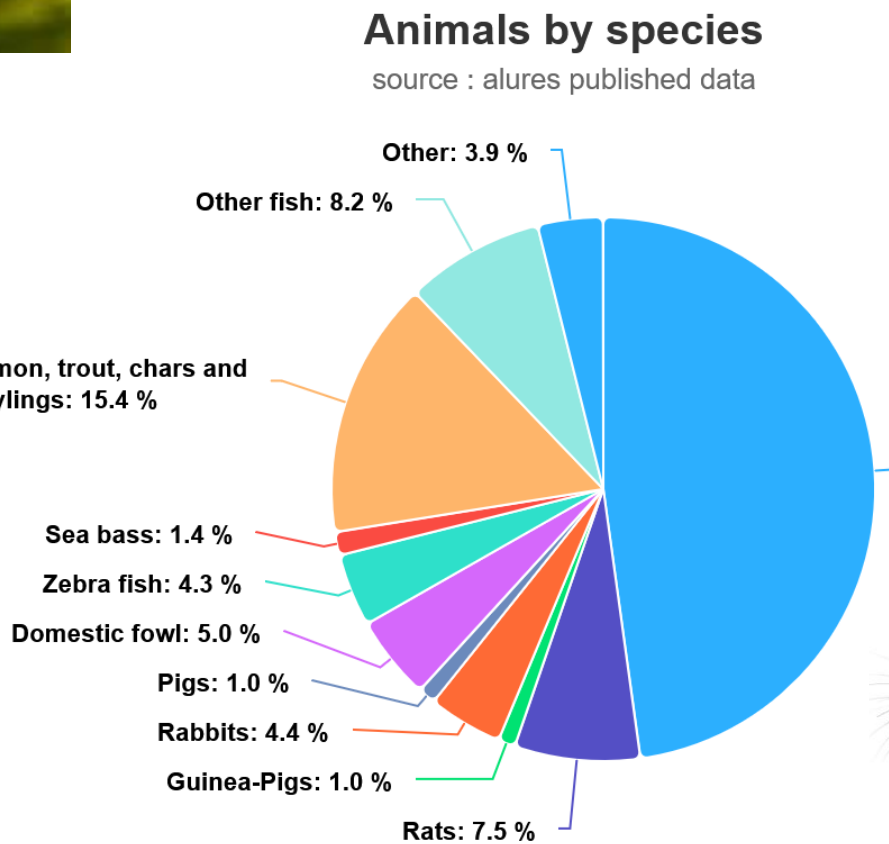
FENS, Paris, 2022

- Seminar about intentions of EU to phase out animal research by 2030

- Researchers concerned about
  - The future of basic medical science
  - How to persuade the public on neccessity of continued use of animals

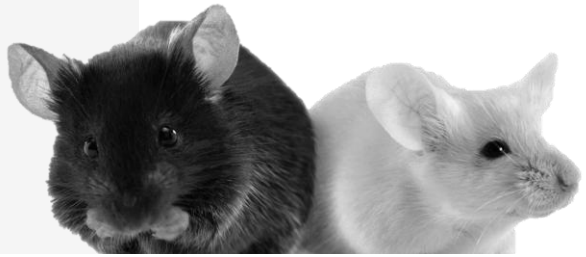
8 385 397

8 385 397

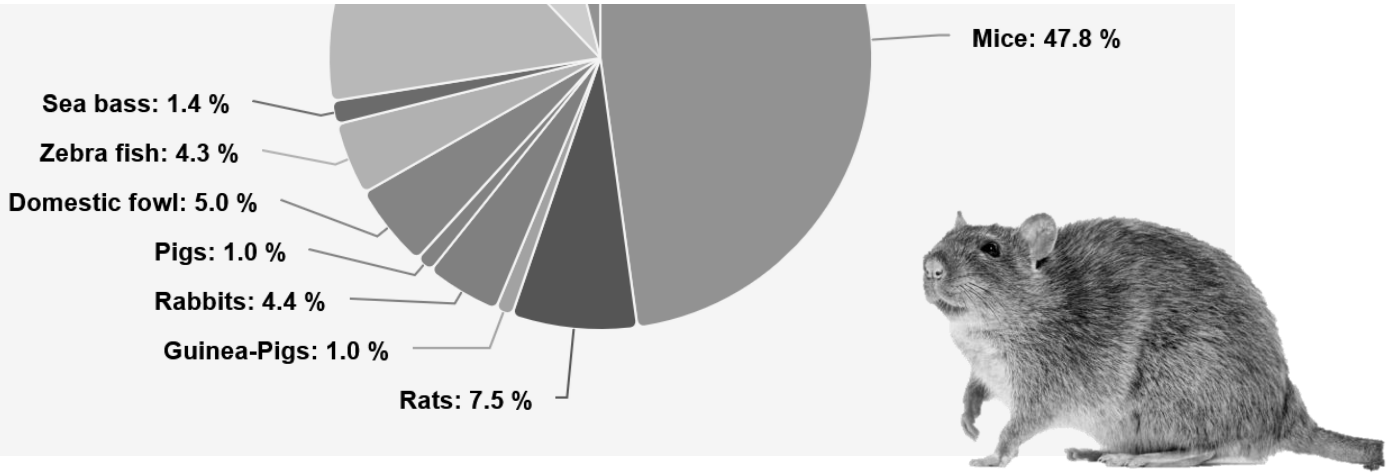


https://webgate.ec.europa.eu/envdataportal/content/alures/section1_number-of-animals.html

8 385 397

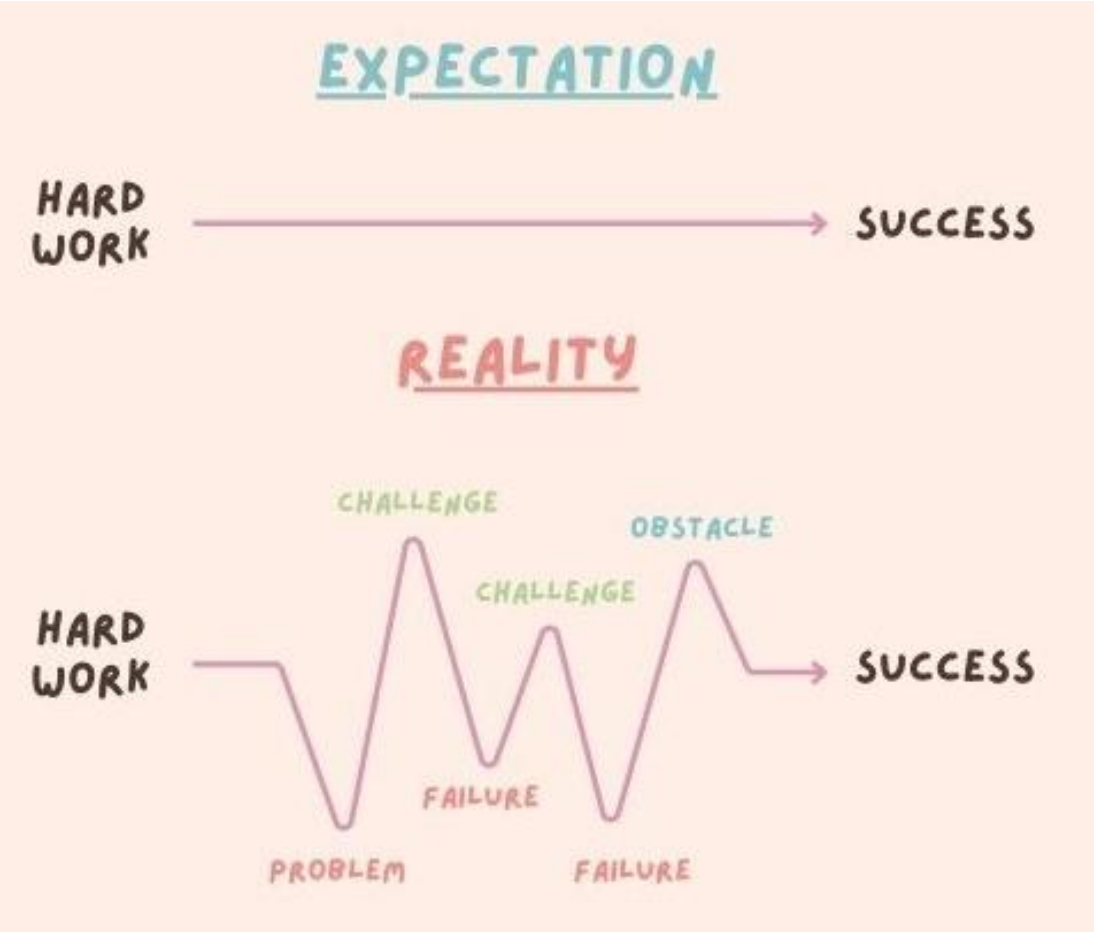


Less than 50% of conducted research is published



https://webgate.ec.europa.eu/envdataportal/content/alures/section1_number-of-animals.html

Less than 50% of conducted research is published*



- Negative findings
- Data that don’t fit the main story of the paper
- Data that’s not considered substantial enough for publication
- Data that no-one found time to publish

* Chan et al., 2014; Song et al., 2010; Van Der Naald et al., 2020

For most publications, the underlying data is not available

- Selected data presented in text and figures
- Underlying data in a drawer or on a hard drive somewhere
- Interpretation, replication and re-use of information can be challenging

Can we do better?

My answer is a clear yes.

«Lack of access to data generated by other researchers or institutions is a major impediment to progress in science»

Tenopir et al., PLOS ONE, 2011

«Lack of access to data generated by other researchers or institutions is a major impediment to progress in science»

67% of scientists agree

Tenopir et al., PLOS ONE, 2011

«Lack of access to data generated by other researchers or institutions has restricted my ability to answer scientific questions»

Tenopir et al., PLOS ONE, 2011

«Lack of access to data generated by other researchers or institutions has restricted my ability to answer scientific questions»

50% of scientists agree

Tenopir et al., PLOS ONE, 2011

Data sharing and the 3R's

- Studies or part of studies replaced by *in silico* studies
- Phasing out animal use sooner

- Maximizing scientific value gained from the animals used

RDN REPAIRER DRIVEN NEWS

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EU mandates fair data

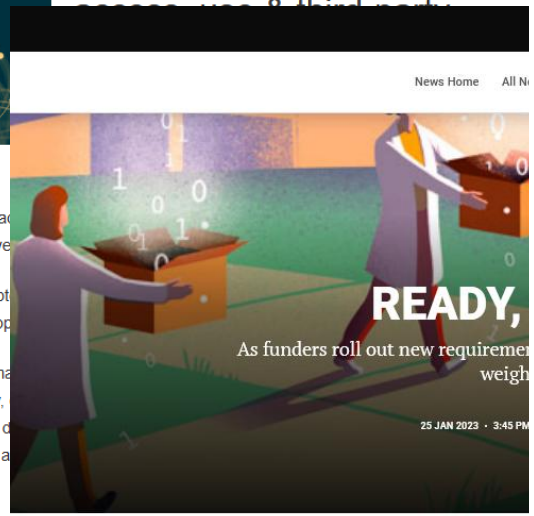
The Council of the European Union has a
data for individuals, businesses, and gove

Following the Data Governance Act adopt
of legislation that is the result of the Europ

The new regulation puts obligations on ma
access and reuse the data generated by,
the Council. It also allows users to share d
future, to share certain vehicle data with a

The purpose of the act is to:

- "Ensure fairness in the allocation of v
- "Stimulate a competitive data market;
- "Open opportunities for data-driven i
- "Make data more accessible to all;



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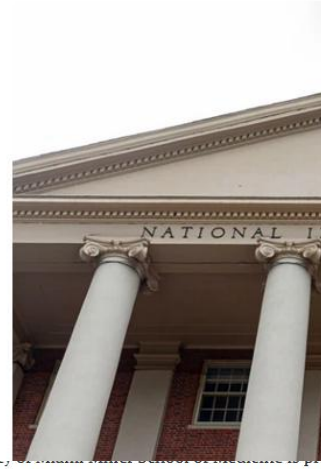
NEWS | 16 February 2022 | Correction 16

NIH issues a se
data publicly

**The data-sharing policy could set a
say, but they have questions about**

By Max Kozlov



A version of this story appeared in Sc

Physiologist Alejandro Caicedo of the Univers
proposal to the U.S. National Institutes of Health (NIH). He is feeling unusually stressed b
new requirement that takes effect today. Along with his research idea, to study why islet c
pancreas stop making insulin in people with diabetes, he will be required to submit a plar
the data the project produces and sharing them in public repositories.

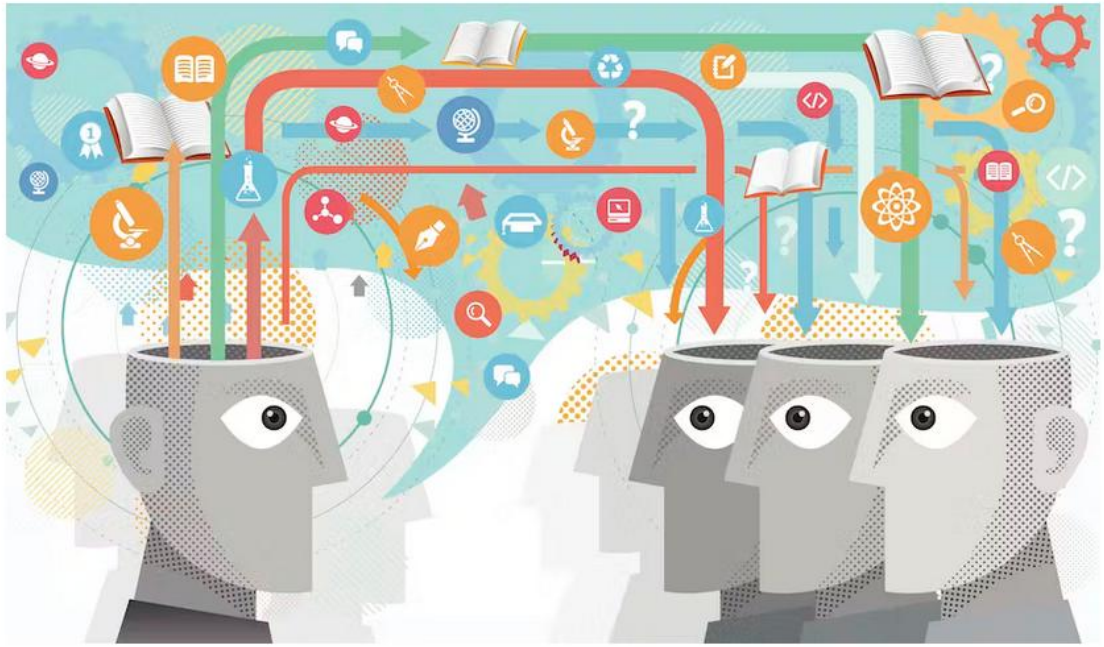
For his lab, that's a daunting task. Unlike neuroscience or genomics, Caicedo's field has n
platforms or standards for storing and sharing the kinds of data his lab generates, such as
pancreatic islet cells responding to a glucose stimulus. The "humongous" raw imaging fil
stored in an on-campus database, notes Julia Panzer, a postdoctoral researcher in the lab.

THE CONVERSATION

Academic rigour, journalistic flair

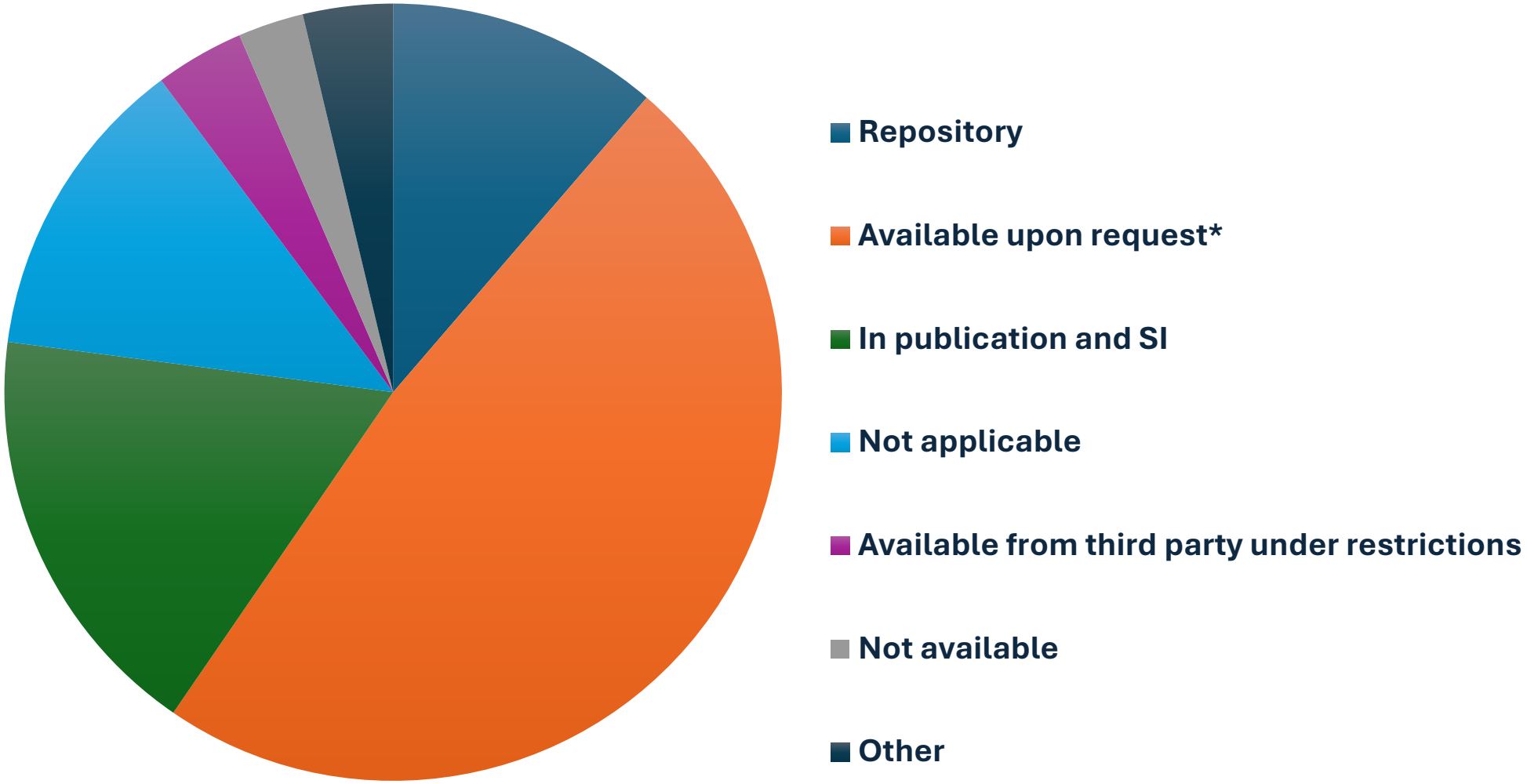
New data-sharing requirements from the National Institutes of Health are a big step toward more open science – and potentially higher-quality research

Published: March 24, 2022 1.16pm CET



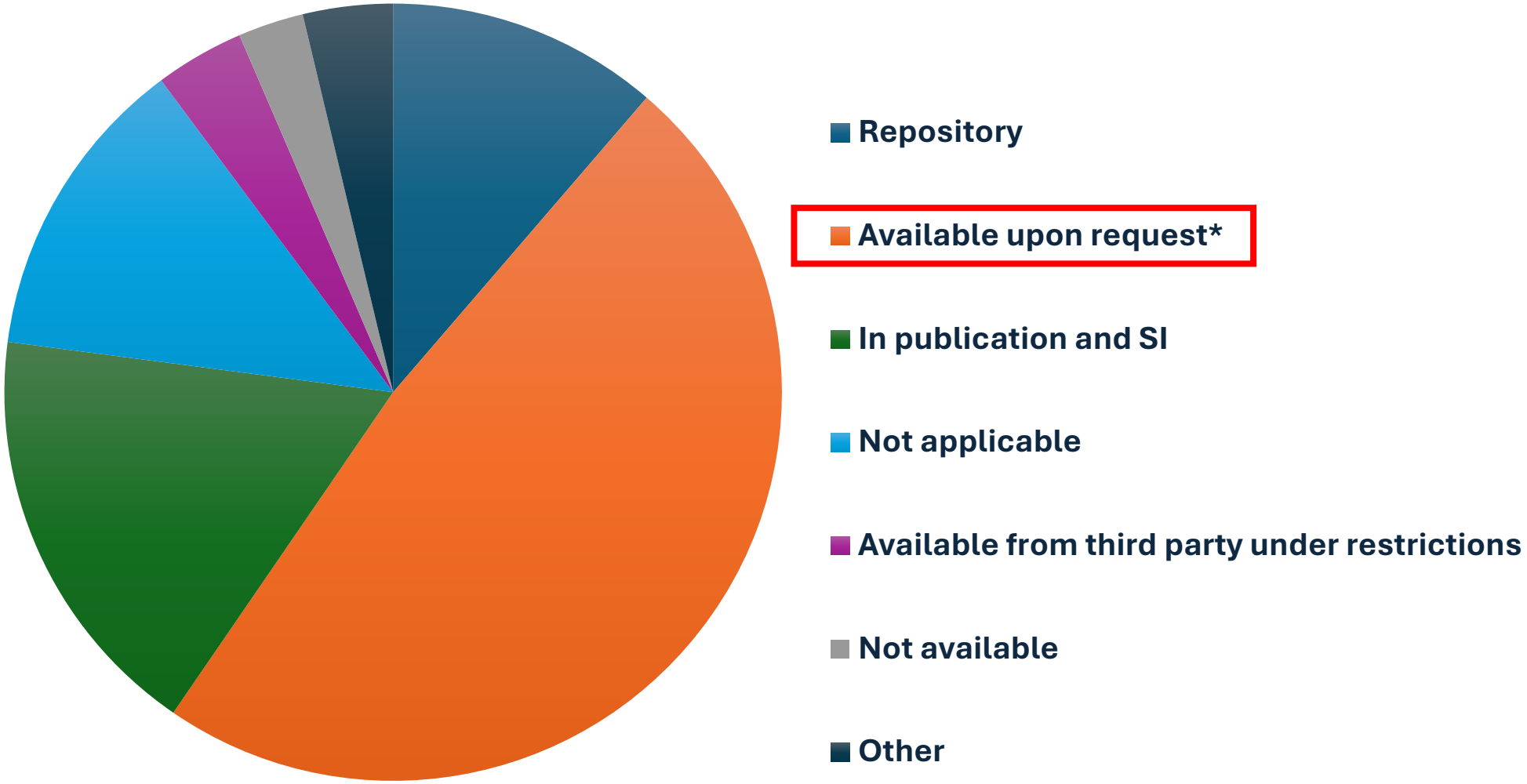
In order to get funding from the National Institutes of Health, researchers now need a plan for sharing and managing their data. Exdez/Digital Vision Vectors via Getty Images

Data availability from biomedical publications



Data from Gabelica et al., 2022, Journal of Clinical Epidemiology (Table 2, charted for this illustration)
** Categories 2 and 4 from the original table combined*

Data availability from biomedical publications



Data from Gabelica et al., 2022, Journal of Clinical Epidemiology (Table 2, charted for this illustration)
** Categories 2 and 4 from the original table combined*


And then, I wrote :
“Data available upon reasonable request”

«Among authors whose DAS indicated data are available on request, we received responses from 14% of the contacted authors, and data were shared by 6.8% of the contacted authors. The percentage of useable data sets was 6.7%»

Gabelica et al., 2022, Journal of Clinical Epidemiology

«Among authors whose DAS indicated data are available on request, we received responses from 14% of the contacted authors, and data were shared by 6.8% of the contacted authors. **The percentage of useable data sets was 6.7%**»

Gabelica et al., 2022, Journal of Clinical Epidemiology

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WORLD VIEW | 05 September 2022

Without app data-sharing pointless

Funders and inves take data from fou

By Mark A. Musen

Last month, the US government generated with federal funds sh implemented by the end of 202 programme for science funding FAIR (that is, findable, accessibl data-sharing policies is to make results and conduct further ana

But just getting those data sets really be FAIR, because most wil to organize metadata.

Humanities & Social Sciences Communicat

Explore co

nature > h

Article | Op

Percei scienti

Joshua Bory

Natalie M. R

Humanities

2319 Acces

Abstrac

Addressing trustworthy research data. Identifying the factors that influence widespread data sharing will help us understand the limitations and potential leverage points. We used two well-known

THE Times Higher Education

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News

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Few researchers get open data training despite mandates to share

Lack of institutional support in meeting the growing demand for data sharing must be addressed, says global study of attitudes towards publishing

October 13, 2022

Jack Grove

Twitter: @jgro_the

«I would use other researchers' datasets if their datasets were easily accessible»

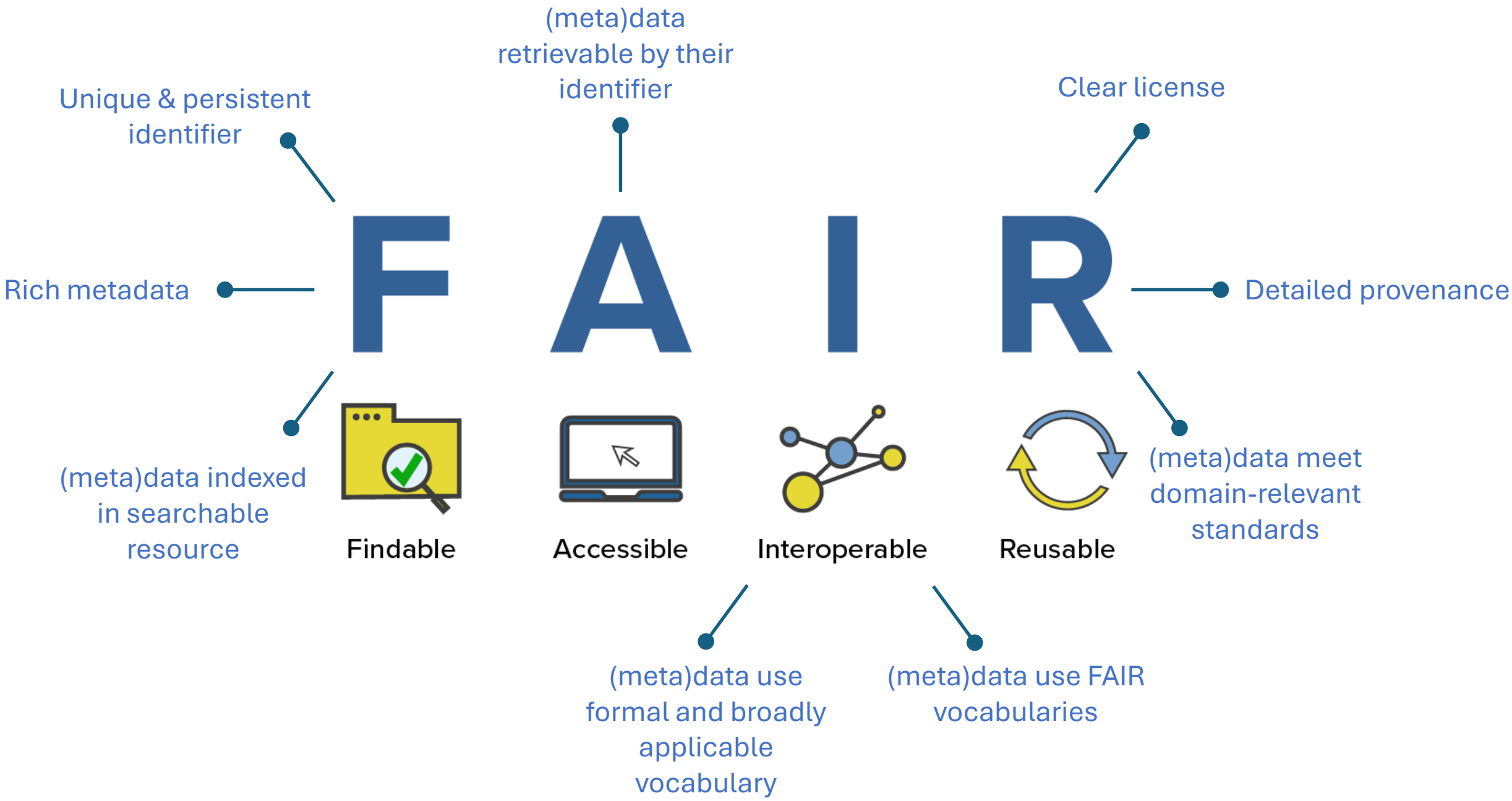
Tenopir et al., PLOS ONE, 2011

«I would use other researchers' datasets if their datasets were easily accessible»

83% of scientists agree

Tenopir et al., PLOS ONE, 2011

How do we get there?


(meta)data retrievable by their identifier
Unique & persistent identifier
Clear license
F A I R
Rich metadata
Detailed provenance
(meta)data indexed in searchable resource
(meta)data meet domain-relevant standards
Findable
Accessible
Interoperable
Reusable
(meta)data use formal and broadly applicable vocabulary
(meta)data use FAIR vocabularies

EBRAINS

Share data About

Search (e.g. mouse hippocampus or calbindin)

SEARCH

CATEGORIES

Project	125
Dataset	**1032**
Model	253
(Meta)Data Model	4
Software	224
Web service	18
Contributor	2152

FILTERS

Reset

ACCESSIBILITY

- [ ] free access 898
- [ ] under embargo 93
- [ ] controlled access 38
- [ ] restricted access 3

SPECIES

add species filters

EXPERIMENTAL APPROACH

add experimental approach filters

STUDIED BRAIN REGION

add studied brain region filters

TECHNIQUES

add techniques filters

KEYWORDS

add keywords filters

Viewing **1-20** of **1032** results.

Top trending

The Swedish National Facility for Magnetoencephalography Parkinson's Disease Dataset

Released: 2023-11-17

Accessibility: controlled access

Custodians: Lundqvist, D.

Parkinson's disease (PD) is characterised by a loss of dopamine and dopaminergic cells. The consequences hereof are widespread network disturbances in brain function. It is still an ongoing topic of investigation how ...

brain | electrocardiography | electromyography | electrooculography | magnetic resonance imaging | magnetoencephalography | motor behavior | Movements | Parkinson's disease

Top trending

Julich-Brain Atlas, cytoarchitectonic maps

Released: 2023-07-13

Accessibility: free access

Custodians: Amunts, K.

This dataset contains the Julich-Brain Atlas, Cytoarchitectonic maps in different coordinate spaces. The parcellation provided by the Atlas is derived from the individually released probability maps (PMs) of cytoarchi...

anatomical parcellation technique | brain | brain mapping | cytoarchitectonic mapping | magnetic resonance imaging | maximum probability projection | silver staining

Top trending

The Digital Brain Tumour Atlas - an open histopathology resource (v1.0)

Released: 2022-01-20

Accessibility: controlled access

Custodians: Roetzer-Pejrimovsky, T.

Currently, approximately 150 different brain tumour types are defined by the WHO. Recent endeavors to exploit machine learning and deep learning methods for supporting more precise diagnostics based on the histologica...

brain | cancer | clinical annotated tissue | H&E staining | high-resolution scanning | histopathology | qualitative analysis | quantitative analysis | tumour

Search (e.g. mouse hippocampus or calbindin)

SEARCH

CATEGORIES

Dataset 79

FILTERS Reset

ACCESSIBILITY

- [ ] free access 71
- [ ] under embargo 8

SPECIES

add species filters

- [x] Mus musculus 79

EXPERIMENTAL APPROACH

add experimental approach filters

- [x] histology 79

STUDIED BRAIN REGION

add studied brain region filters

TECHNIQUES

add techniques filters

KEYWORDS

add keywords filters

CONTENT TYPES

add content types filters

Viewing **1-20** of **79** results.

Investigating cellular diversity in a novel Alzheimer's disease mouse model using the optimized QUINT workflow (v1)

Released: 2023-04-06

Accessibility: free access

Custodians: Kaczorowski, C.

This study includes 40 mice (20 at 6 months(m), 20 at 14 months(m); 2 males and 38 females). Of the mice, 29 are from 14 AD-BXD strains, 2 are the C57B1/6J founder strain, 6 are the F1 B6/DBA/2J (D2) 5XFAD founder str...

Alzheimer's disease | amyloid pathology | anatomical segmentation technique | cell composition | genetic diversity | mouse model | Nissl staining | primary antibody staining | quantitative analysis | secondary antibody staining ...

X-ray virtual histology for the investigation of temporal lobe epilepsy in a mouse model (v1)

Released: 2023-02-01

Accessibility: free access

Custodians: Tanner, C.

This study evaluates virtual histology with synchrotron radiation-based X-ray microtomography to track the histopathological progression of mesial temporal lobe epilepsy (mTLE) in a mouse model. The kainate (KA) model...

anatomical segmentation technique | brain | convolution | deep learning | epilepsy | epilepsy model | epileptogenesis | injection | kainate | synchrotron radiation | transcardial perfusion fixation technique | virtual histology | X-ray microtomography ...

Distribution of dopamine 1 receptor positive neurons in the adult male mouse brain

Released: 2022-12-22

Accessibility: free access

Custodians: Kim, J. H.

High-resolution bright-field microscopy images of coronal brain sections showing dopamine 1 receptor positive neurons across the adult (70 days old) male mouse brain. The dataset consists of image series covering the ...

anatomical delineation technique | basic cell groups and regions | brain mapping | Chemoarchitecture | cryosectioning | D1 receptor | DAB staining | image registration | immunohistochemistry | Transgenic animal ...

Domus Medica, Oslo, 2019

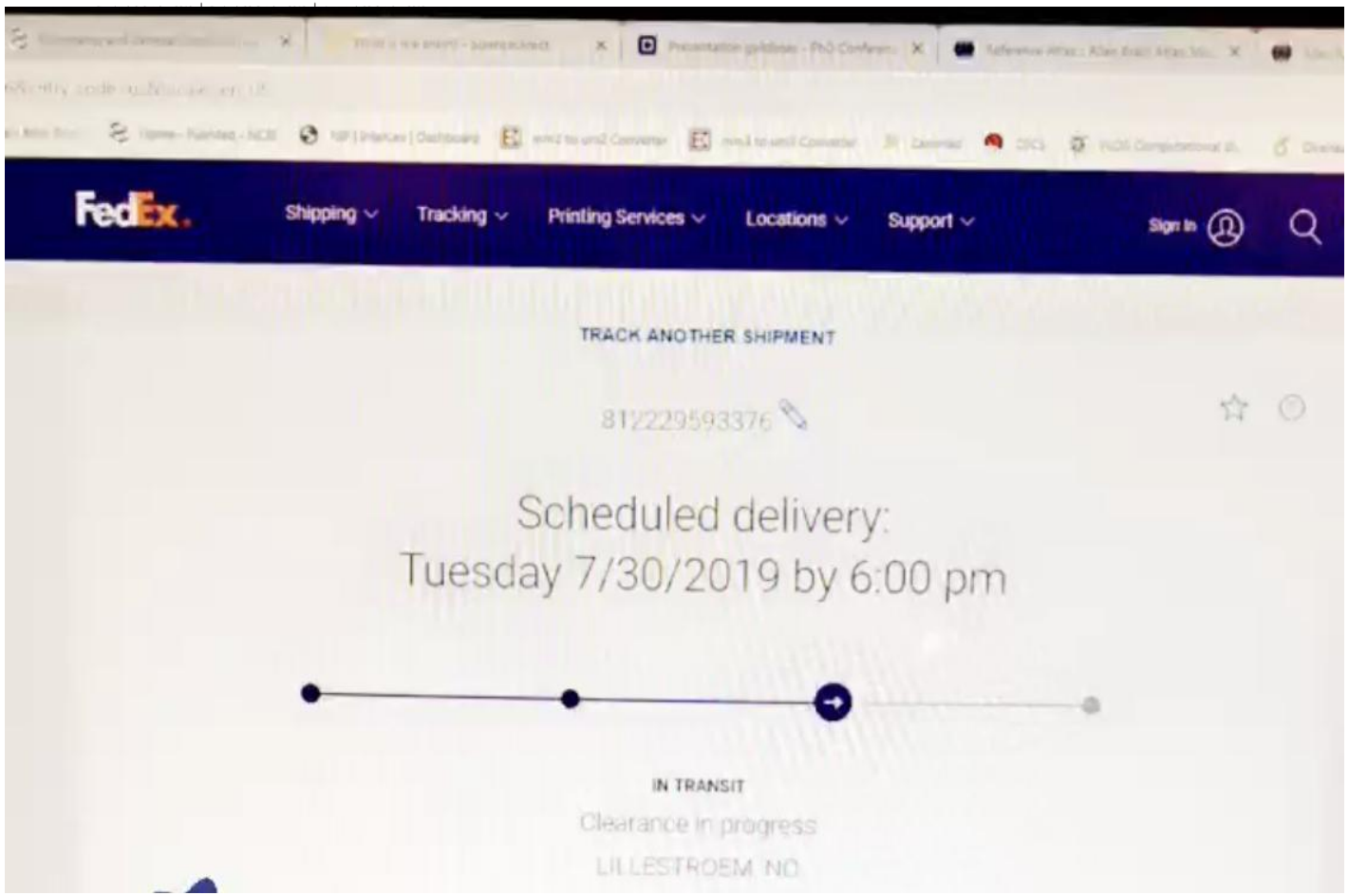
2 | METHODS

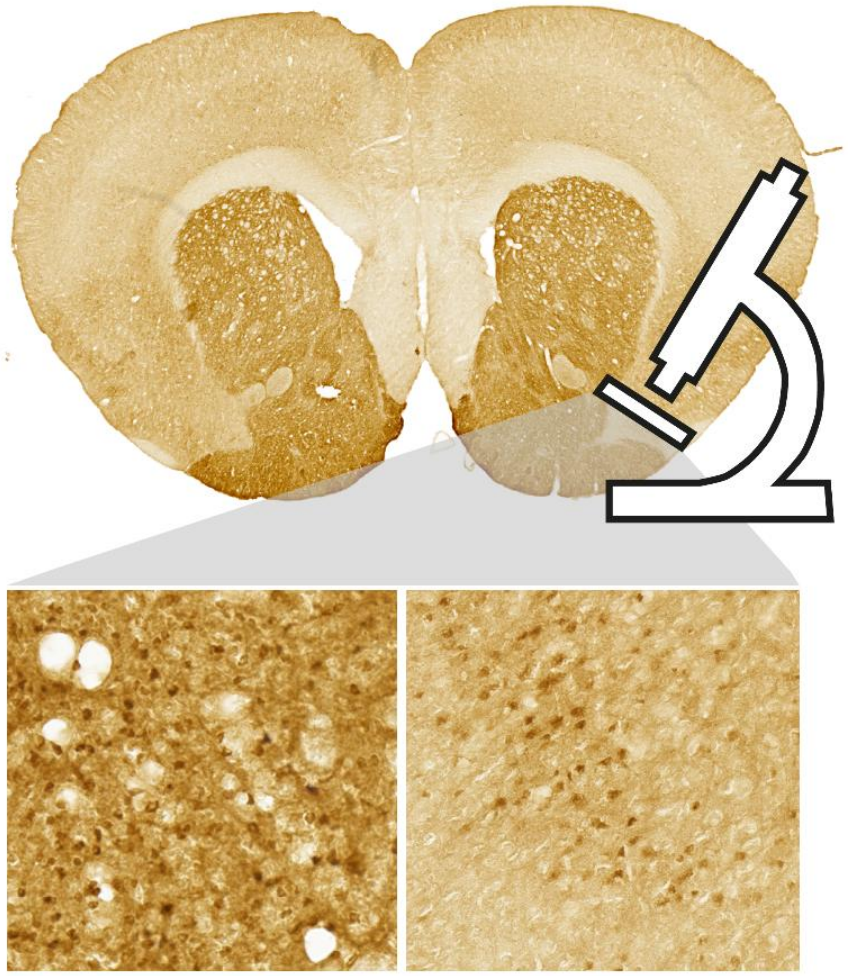
2.1 | Animals

A total of 81 male and 76 female mice were used in this study (see Table 1 for *n* per group). The mice came from separate breeding colonies of Drd1a-EGFP and Drd2-EGFP mice bred on a Swiss background, established at the Florey Institute of Neuroscience and Mental Health, Melbourne, Australia. Mice were originally generated by the Gene Expression Nervous System Atlas (GENSAT) program at the Rockefeller University, New York, USA (Gong et al., 2003). Mice were perfused on postnatal day (P) 17 ± 1 (juvenile), P25 ± 1 (preadolescent), P35 ± 1 (early adolescent), P49 ± 1 (late adolescent), or P70 (adult), and only mice hemizygous for the EGFP reporter gene were used in the study. P17 mice were weaned 30 min before being perfused. All other groups were weaned at P18-P21, and then were housed in same-sex groups of 3–5 littermates in open-top cages (34 cm x 16 cm x 16 cm) and maintained on a 12 hr light/dark cycle

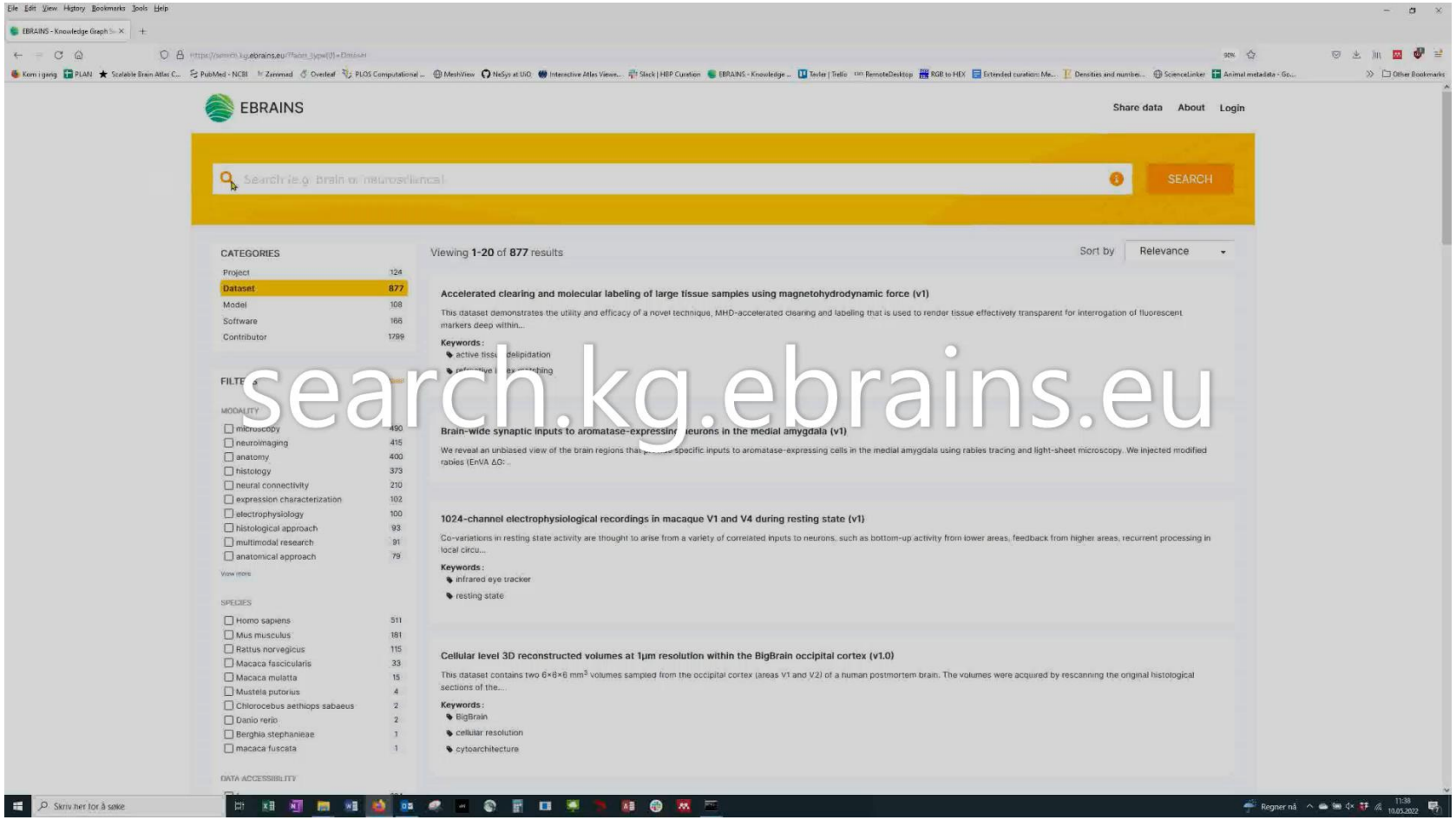
- Collaboration with Prof. Jee Hyun Kim (Deakin University)

Domus Medica, Oslo, 2019





Immortalizing the data online



https://search.kg.ebrains.eu/

Sharing data is about...

Sharing data is about…

… increasing the data life-span

… allowing others to build on your data

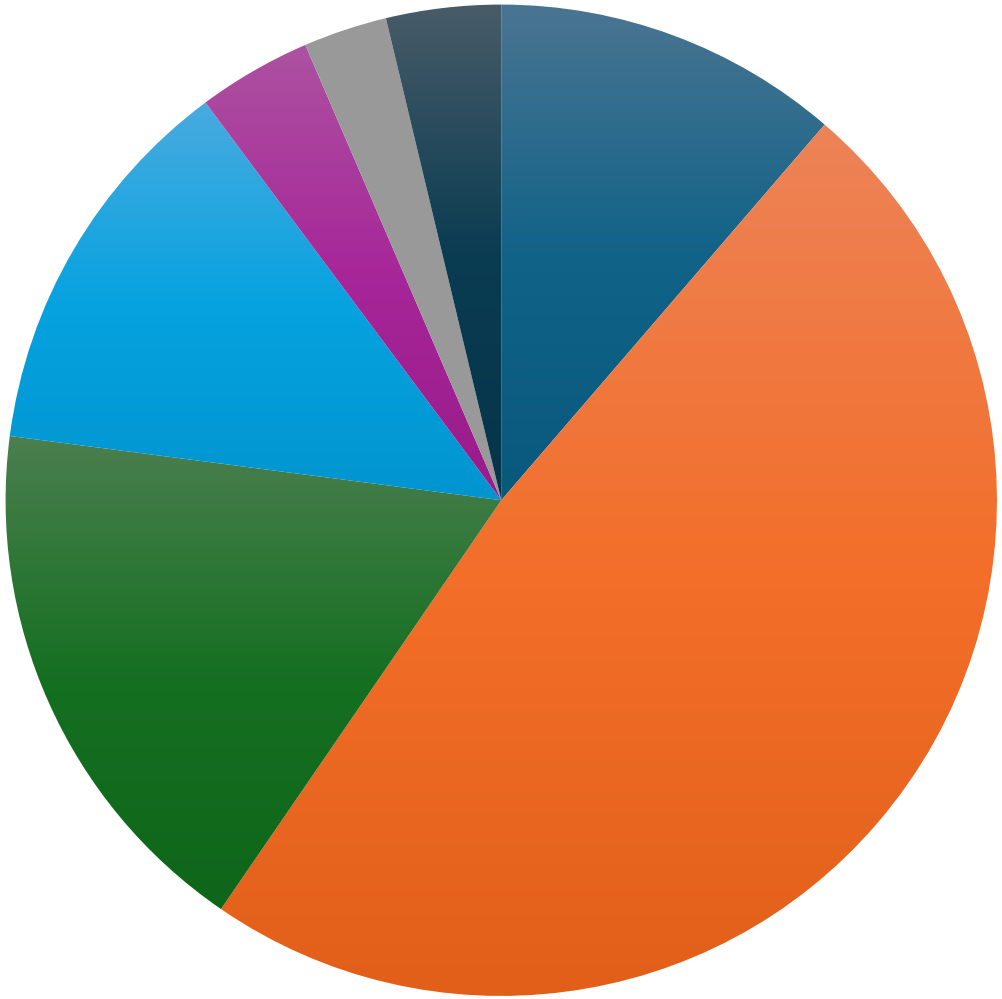
… reducing waste

… maximizing value for the lives sacrificed

If we can do better,

and we know how to get there...

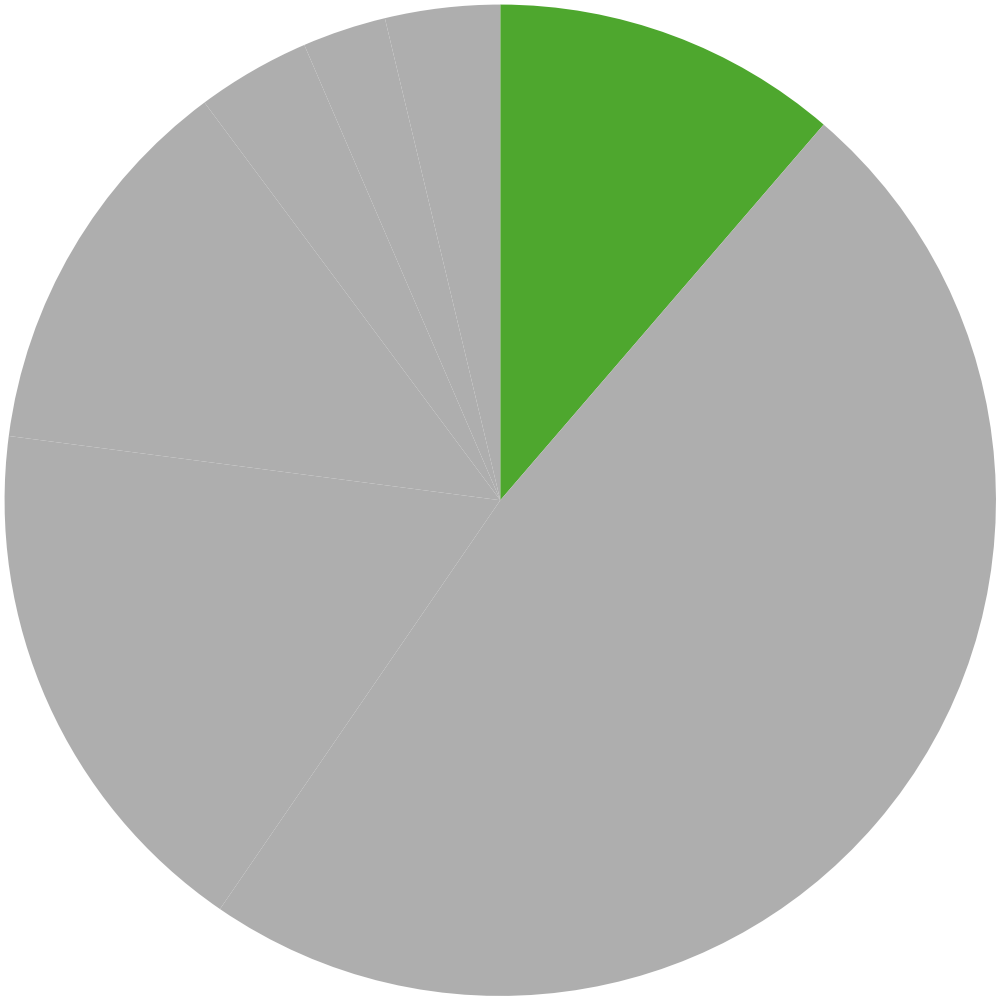
Then why are we still here?



- Repository
- Available upon request*
- In publication and SI
- Not applicable
- Available from third party under restrictions
- Not available
- Other

Data from Gabelica et al., 2022, Journal of Clinical Epidemiology (Table 2, charted for this illustration)
** Categories 2 and 4 from the original table combined*

Then why are we still here?



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- Available from third party under restrictions
- Not available
- Other

Data from Gabelica et al., 2022, Journal of Clinical Epidemiology (Table 2, charted for this illustration)
** Categories 2 and 4 from the original table combined*

Why do researchers choose not to share?

	Responses	Percent
Insufficient Time	603	53.6%
Lack of Funding	445	39.6%
Do not Have Rights to Make Data Public	271	24.1%
No Place to Put Data	264	23.5%
Lack of Standards	222	19.8%
Sponsor does not Require	196	17.4%
Do not Need Data	169	15.0%
Other Reasons For Data Not Available	164	14.6%
Should not be Available	162	14.4%

doi:10.1371/journal.pone.0021101.t012

How do we overcome these challenges?

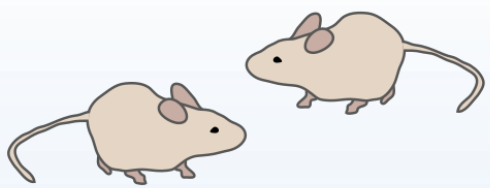
Solutions are emerging

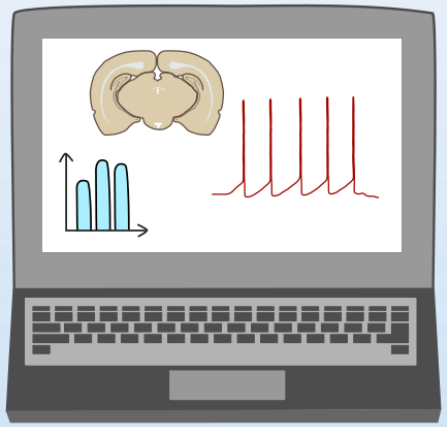
Less relevant in 2025

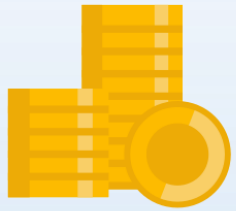
Tenopir et al., PLOS ONE, 2011

Lack of time = lack of incentive?

Lack of time = lack of incentive?







How can we incentivize better practices?

- Enforce data sharing mandates
- Consider data sharing a requirement under the 3 Rs
- Grants for projects to
  - Publish existing data
  - Re-use public data
- Consider datasets to be first-class research objects

What does the future academic CV look like?

DOI:10.1038/s41467-023-41645-4

- A Lorents, M-E Colin, **IE Bjerke**, S Nougaret, L Montelisciani, M Diaz, P Verschure, J Vezoli (2023) ***Human Brain Project Partnering Projects Meeting: Status Quo and Outlook.*** eNeuro. 10(9). DOI:10.1523/ENEURO.0091-23.2023
- **IE Bjerke**, ER Cullity, K Kjelsberg, KC Charan, TB Leergaard, & JH Kim (2022) ***DOPAMAP, high-resolution images of dopamine 1 and 2 receptor expression in developing and adult mouse brains.*** Scientific Data. 9(175). DOI:10.1038/s41597-022-01268-8
- **IE Bjerke**, SC Yates, A Laja, MP Witter, MA Puchades, JG Bjaalie & TB Leergaard (2021) ***Densities and numbers of calbindin and parvalbumin positive neurons across the rat and mouse brain.*** iScience. 24(1), 101906. DOI:10.1016/j.isci.2020.101906
- **IE Bjerke**, M Puchades, JG Bjaalie & TB Leergaard (2020) ***Database of literature derived cellular measurements from the murine basal ganglia.*** Scientific Data. 7(211). DOI:10.1038/s41597-020-0550-3
- **IE Bjerke**, M Øvsthus, KA Andersson, CH Blixhavn, SC Yates, H Kleven, MA Puchades, JG Bjaalie & TB Leergaard (2018) ***Navigating the Murine Brain: Toward Best Practices for Determining and Documenting Neuroanatomical Locations in Experimental Studies.*** Frontiers in Neuroanatomy. 12(82), 1-15. DOI:10.3389/fnana.2018.00082
- N Berggaard, **IE Bjerke**, AEB Paulsen, L Hoang, NET Skogaker, MP Witter & JJL van der Want (2018) ***Development of Parvalbumin-Expressing Basket Terminals in Layer II of the Rat Medial Entorhinal Cortex.*** eNeuro. 5(3). DOI:10.1523/ENEURO.0438-17.2018
- **IE Bjerke**, M Øvsthus, EA Papp, SC Yates, L Silvestri, J Fiorilli, CMA Pennartz, FS Pavone, MA Puchades, JG Bjaalie & TB Leergaard. (2018) ***Data integration through brain atlasing: Human Brain Project tools and strategies.*** European Psychiatry. 50, 70-76. DOI:10.1016/j.eurpsy.2018.02.004

Datasets

In addition to my research papers listed above, I have also published more than 60 datasets through the EBRAINS Knowledge Graph. This ensures that all data from my research are available according to the FAIR principles. The most notable dataset collections from my research are the following:

- Map of dopamine receptor positive cell types in the developing and adult mouse brain (DOPAMAP; 21 datasets). This project provides access to a large body of high-resolution image data showing the distribution of dopamine 1- and 2–receptor positive neurons in the mouse brain, with age groups ranging from postnatal day 17 to 70. The age groups included correspond to key developmental milestones, defined as follows: juvenile (17 days), preadolescent (25 days), adolescent (35 days), late adolescent (49 days) and adult (70 days). The data have been analysed to provide quantitative data across age, sex and receptor type.
- Atlas of parvalbumin- and calbindin-positive neurons in the rodent brain (CalciMAP; 8 datasets) This project provides access to series of high-resolution images showing the brain-wide distribution of parvalbumin and calbindin in the rat and mouse brain. The project uses immunohistochemistry, with all images spatially registered to open-access brain atlases. Most recently, this collection has been expanded to include data from developing mouse brains. For the adult data, the project includes data resulting from a semi-automatic analysis of labelled cells.
- Developmental Mouse Brain Atlas (DeMBA; 11 datasets). This project provides access to a continuous 3D reference atlas for the postnatal mouse brain. The atlases are based on spatial transformation of the Allen Mouse Brain Common Coordinate Framework version 3 template (postnatal day 56) to a set of serial two-photon tomography (STPT) templates of developing mouse brains (postnatal day 4, 7, 14, 21 and 28; Newmaster et al. (Nat Comm, 2020), Liwang et al. (biorxiv, 2023)). These are the key ages of the DeMBA atlas. The spatial transformation matrixes were used to create synthetic, interpolated templates for intermediate ages. They provide models of what an STPT-imaged brain would look like at the intermediate ages. The segmentations volumes from the adult Allen Mouse brain Common Coordinate Framework version 3 (2017 and 2022 editions) are transformed and interpolated using the same matrices.

Other scientific communication

- Forskningskampen er mer enn en elitekamp. 2022. Commentary in Norwegian about cuts in research funding, Aftenposten (Norway's largest printed newspaper).
- The critical window for becoming a FAIR researcher 2021. Commentary, INCF Community Blog.
- Improve reporting practices for quantitative neuroscience data. 2020. Behind the paper. Research Data at Springer Nature.
- Hvordan få mer ut av hjerneforskningen? 2020. Bloggpost ved Medisinbloggen, Universitetet i Oslo. Blog post in Norwegian.

GRANTS AND AWARDS

- **UNIFOR Frimed travel grant** 2023. Grant awarded to me for a research visit to collaborator (Professor Jee Hyun Kim).
- **King's gold medal** 2022. Prize awarded to outstanding young researchers for scientific work assessed at the University of Oslo.
- **DLN FAIR data award** 2021. NOK 30000. Prize awarded for my openly shared datasets.
- **UNIFOR Medical Research Grant** 2022-2023. Euros 10000. Grant awarded to TB Leergaard. My role was in planning the project and contributing to write the application.
- **UNIFOR Medical Research Grant** 2021-2022. Euros 17491. Grant awarded to TB Leergaard. My role was in planning the project and contributing to write the application.
- **European Union Human Brain Project Research Infrastructure Voucher.** 2020-2021. Euros 89500 + 3580 travel budget. Grant awarded to JH Kim & TB Leergaard. My role was in planning the project and contributing to write the application.

INVITED TALKS

- ***Experiences with data sharing from the field of neuroscience.*** Online. October 16, 2023. ReproducibiliTea journal club series arranged by the Norwegian Reproducibility Network.
- ***Mapping the developing dopaminergic system.*** Egersund, Norway. September 27, 2023. Symposium talk at the Norwegian Research School of Neuroscience national conference.
- ***En Risørværings guide til nevrovitenskapen.*** Risør, Norway. September 25, 2023. Popular science talk (in Norwegian) at the Risør Rotary Club.
- ***Using EBRAINS tools and atlases: Quantitative analysis of calbindin and parvalbumin positive neurons across the rat and mouse brain.*** Online. November 23, 2022. Webinar series arranged by the Human Brain Project Outreach team. Recording available online.
- ***Mapping cellular parameters in the mouse brain.*** Paris, France. July 8, 2022. Talk at EBRAINS FENS Satellite event.

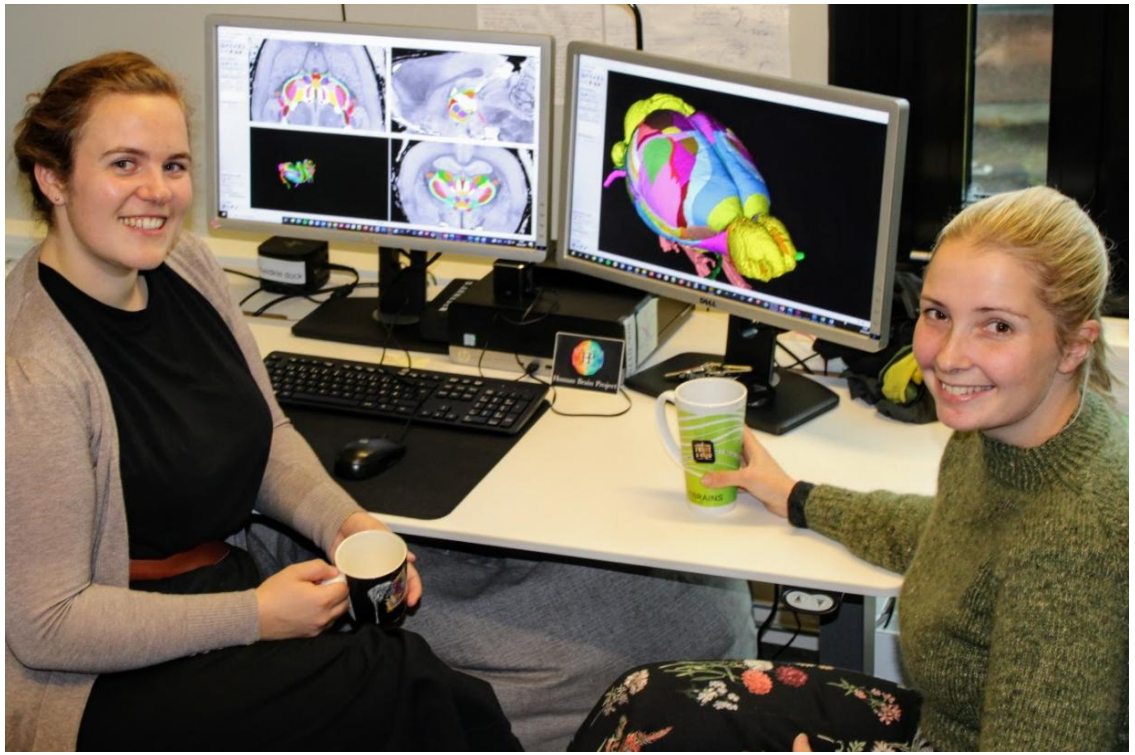
SUPERVISION

- **Medical research student supervision** 2022-current. Elisabeth Mathisen, Cand. med. University of Oslo, Oslo, Norway.
- **PhD student co-supervision** 2021-current. Heidi Kleven, PhD student in neuroscience. University of Oslo, Oslo, Norway.
- **Master student supervision** 2021-current. Olga Rogulina, MSc Neuroscience. Norwegian University of Science and Technology, Trondheim, Norway.
- **Master student supervision** 2021-2022. Monika Overdevest, MSc Neuroscience. Norwegian University of Science and Technology, Trondheim, Norway.
- **Honors student co-supervision** 2020-2021. Kristel Charan, Psychology Honors. Institute for Social Neuroscience (ISN) Psychology, Melbourne, Australia.
- **Master student co-supervision** 2019-2020. Maren Pamas Gulnes, Master of Informatics. University of Oslo, Oslo, Norway.
- **Master student co-supervision** 2018-2019. Arthur Laja, MSc Neuroscience. Norwegian University of Science and Technology, Trondheim, Norway.

TEACHING

- **Mouse and rat brain atlases: Registering and analysing rodent brain data** 2022. Lecture for EBRAINS Training on Brain Atlases and Simulation Services in Vienna, Austria.
- **Assigning location parameters to experimental data: Common practice and best practice.** 2018, 2019, 2021, 2022, 2023. Lecture for the course "Neuroscience data integration through use of digital brain atlases" (IMB9345) at the University of Oslo, Norway.
- **Problem-based learning** Facilitator for first-year medical students working with cases in small groups.
- **Facilitator at conference workshops related to spatial atlas registration, data integration and data curation** 2016, 2017, 2018. Human Brain Project Summit, Firenze, Glasgow, Maastricht.

A critical window for becoming FAIR



- Teach young researchers to:
  - Plan for data sharing
  - Collect metadata systematically
  - Use public data
  - Share their research through repositories

Summary

- There is a large discrepancy between the number of animals used and what gets published
- Improved data sharing practices could help us get more value for the lives sacrificed
- We need incentives for researchers to adopt improved practices

Thank you for your attention!

Data sharing and re-use as a moral imperative in animal research

The critical window for becoming a FAIR researcher