Reproducibility and ML: We are probably thinking about this wrong….

Carl Kesselman

University of Southern California

How do we create a scientific result

Any time scientists disagree, it's because we have insufficient data. Then we can agree on what kind of data to get; we get the data; and the data solves the problem. Either I'm right, or you're right, or we're both wrong. And we move on. That kind of conflict resolution does not exist in politics or religion.

Neil deGrasse Tyson

- Science is about communities arguing over data
  - How do those communities form
  - How do communities argue: knowledge capture and communication

There be dragons…..

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WILL KNIGHT BUSINESS AUG 10, 2022 7:00 AM

Data leakage causes reproducibility failures in ML-based science

The running list below consists of papers that highlight reproducibility failures or pitfalls in ML-based science. We find 20 papers from 17 fields where errors have been found, collectively affecting 329 papers and in some cases leading to wildly overoptimistic conclusions. In each case, data leakage causes errors in the modeling process.

ım. pers viewed	Num. papers w/pitfalls	Pitfalls
	27	No train-test split
	14	No train-test split; Feature selection on train and test set
	3	Duplicates across train-test split; Sampling bias
	6	Pre-processing on train and test sets together
	4	No train-test split

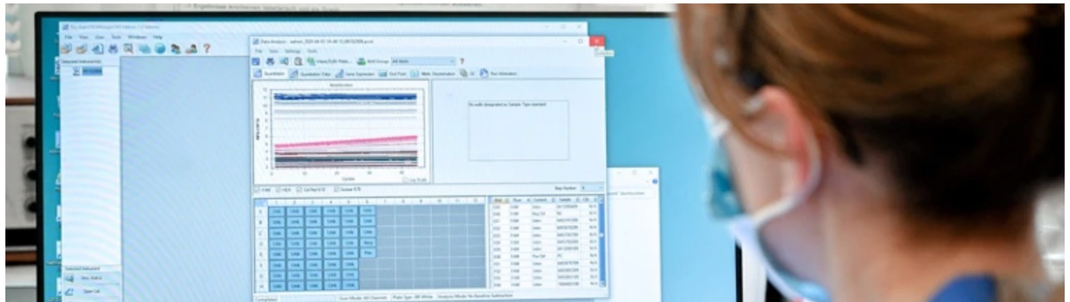
nature > news > article

NEWS | 13 August 2021 | Correction 25 August 2021

Autocorrect errors in Excel still creating genomics headache

Despite geneticists being warned about spreadsheet problems, 30% of published papers contain mangled gene names in supplementary data.

Dyani Lewis



USC Viterbi School of Engineering

Feynman says…..

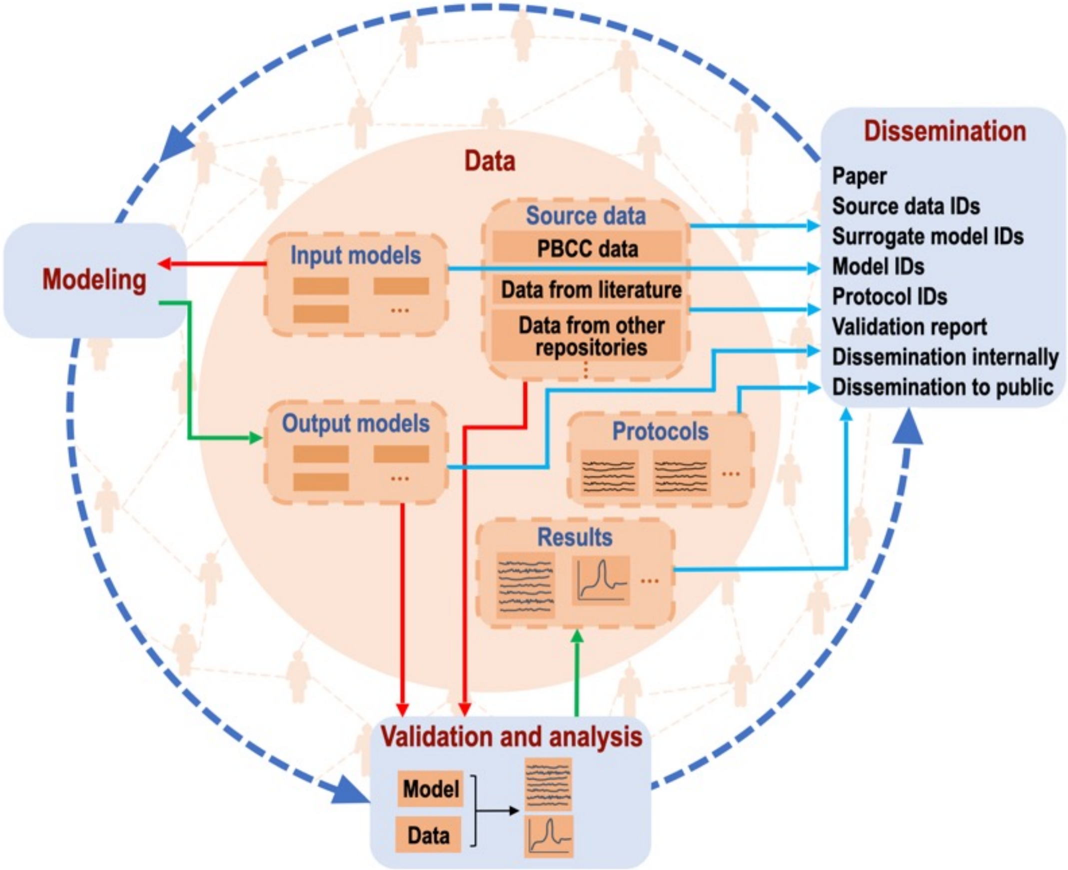
- a kind of scientific integrity, a principle of scientific thought that corresponds to a kind of utter honesty — a kind of leaning over backwards. For example, if you're doing an experiment, you should report everything that you think might make it invalid, not only what you think is right about it: other causes that could possibly explain your results; and things you thought of that you've eliminated by some other experiment, and how they worked — to make sure the other fellow can tell they have been eliminated

Flip the Paradigm....

- **Data Centric vs Compute Centric**
  - Data-Centric Biology A Philosophical Study Sabina Leonell
- Data Centric Architectures
  - Data Centric Discovery with a Data-Oriented Architecture (Kesselman 2015)
- Data Centric Workflows
  - A Data-Centric Design Methodology for Business Processes (Bhattacharya, 2009)
  - A framework for collecting provenance in data-centric scientific workflows (Simmhan, Plale, Gannon, 2006)

FAIR Data is *essential* to good scholarship

- Findable, Accessible, Interoperable, Reusable
- Requires culture and technology
  - Socio-technical approach
  - See: Sharing Begins at Home (doi: [10.1162/99608f92.44d21b86](https://doi.org/10.1162/99608f92.44d21b86))
- Broad issues with policy, privacy, security, IP.
  - There are significant non-protected data sets.

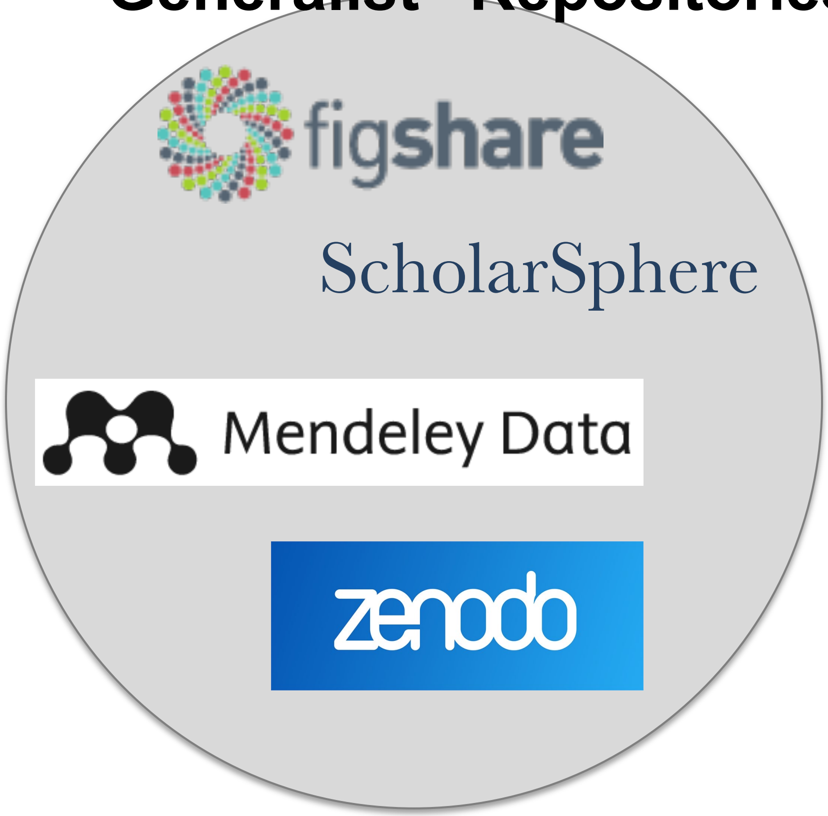


Addressing Gaps in the Data Sharing Ecosystem…

"Domain or Specialized" Repositories

PRO: Highly detailed descriptive information; High quality data
CON: Narrow focus; High cost of biocuration

"Generalist" Repositories



PRO: All types of data and science; Highly scalable
CON: Minimal structure for detail on data; Quality concerns

Addressing Gaps in the Data Sharing Ecosystem…

"Domain or Specialized" Repositories

PRO: Highly detailed descriptive information; High quality data
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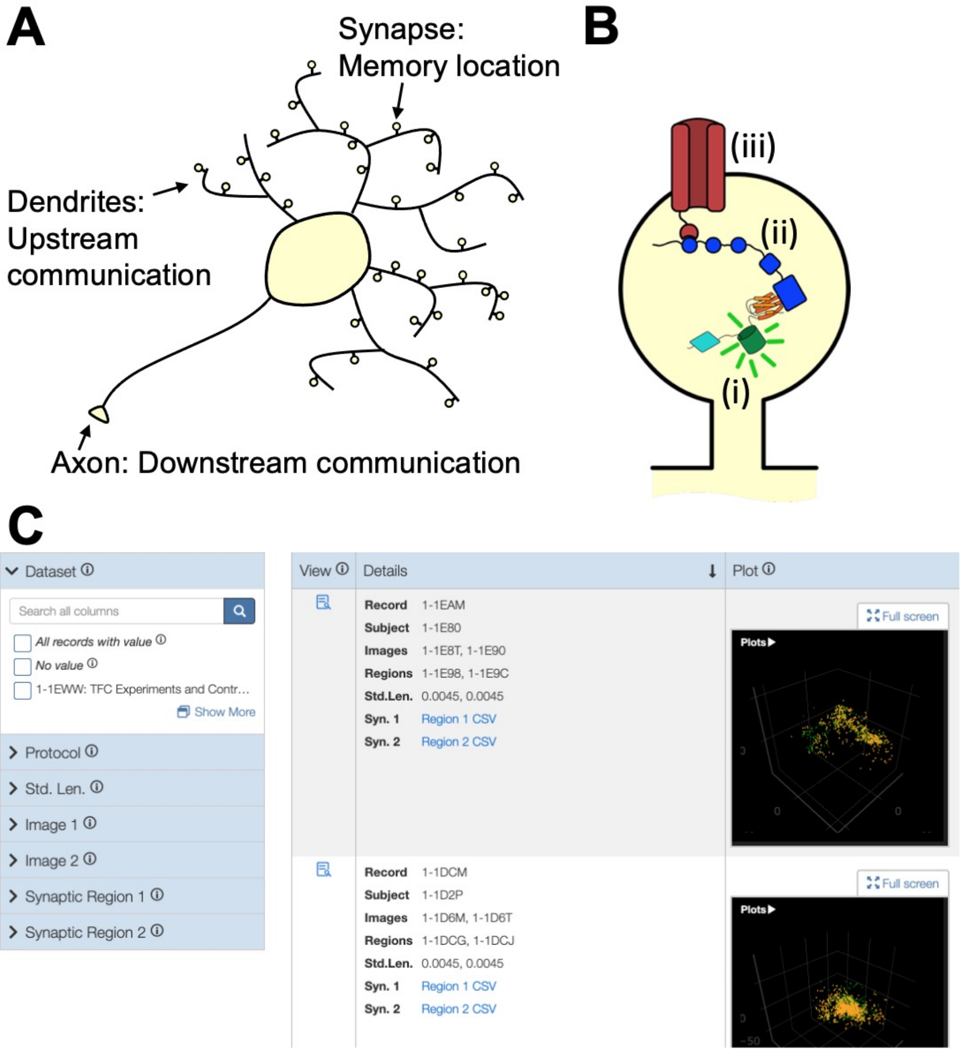
"Hybrid" Repositories

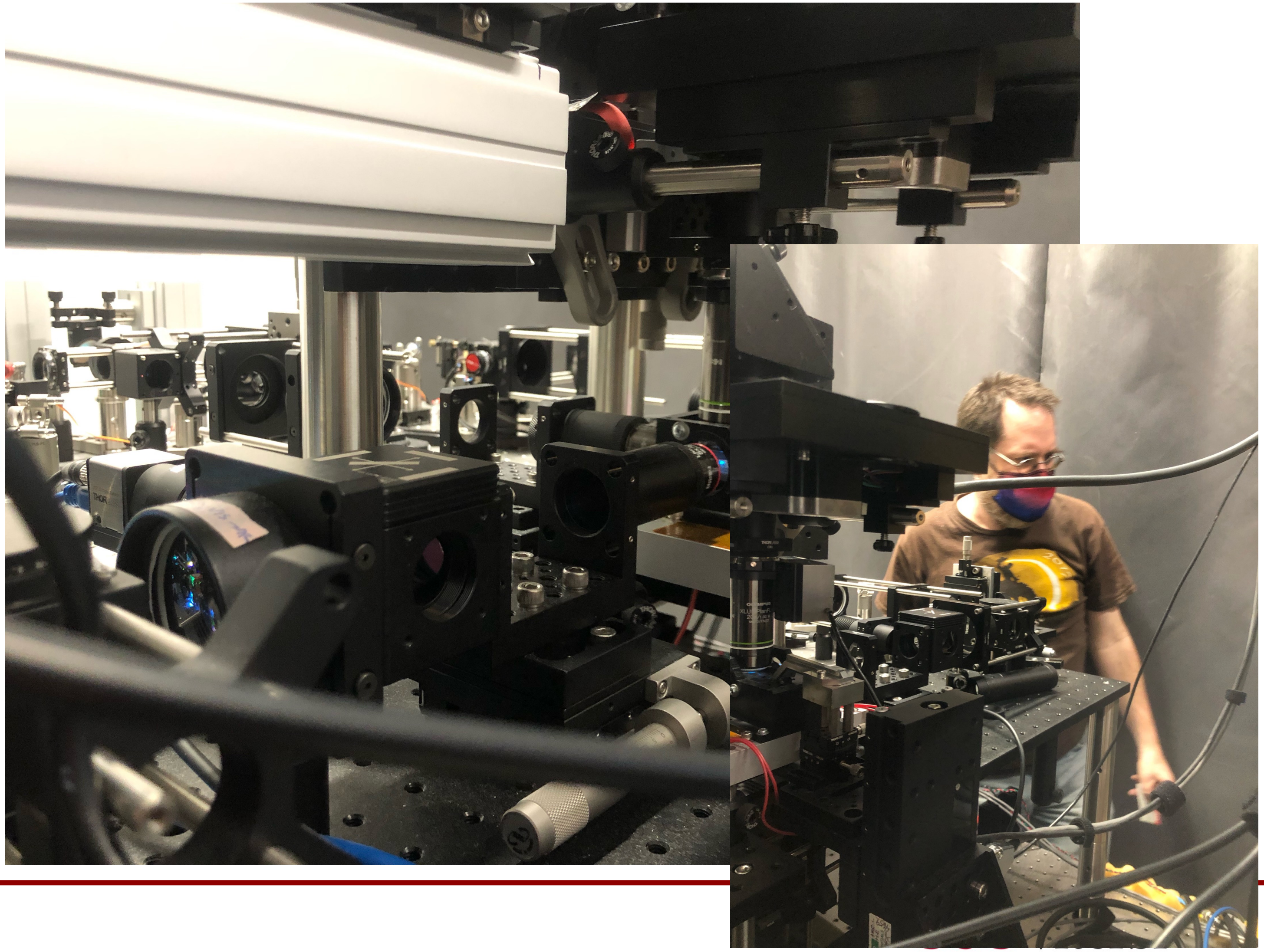
Addresses Gaps: Flexibility to adapt to new species and assays, with minimum viable information for reusability; "Self-serve" style of data curation with structure to guide scientists to produce quality (meta)data.

"Generalist" Repositories

PRO: All types of data and science; Highly scalable
CON: Minimal structure for detail on data; Quality concerns

Example: Mapping the Synatome





RESEARCH ARTICLE | NEUROSCIENCE

Regional synapse gain and loss accompany memory formation in larval zebrafish

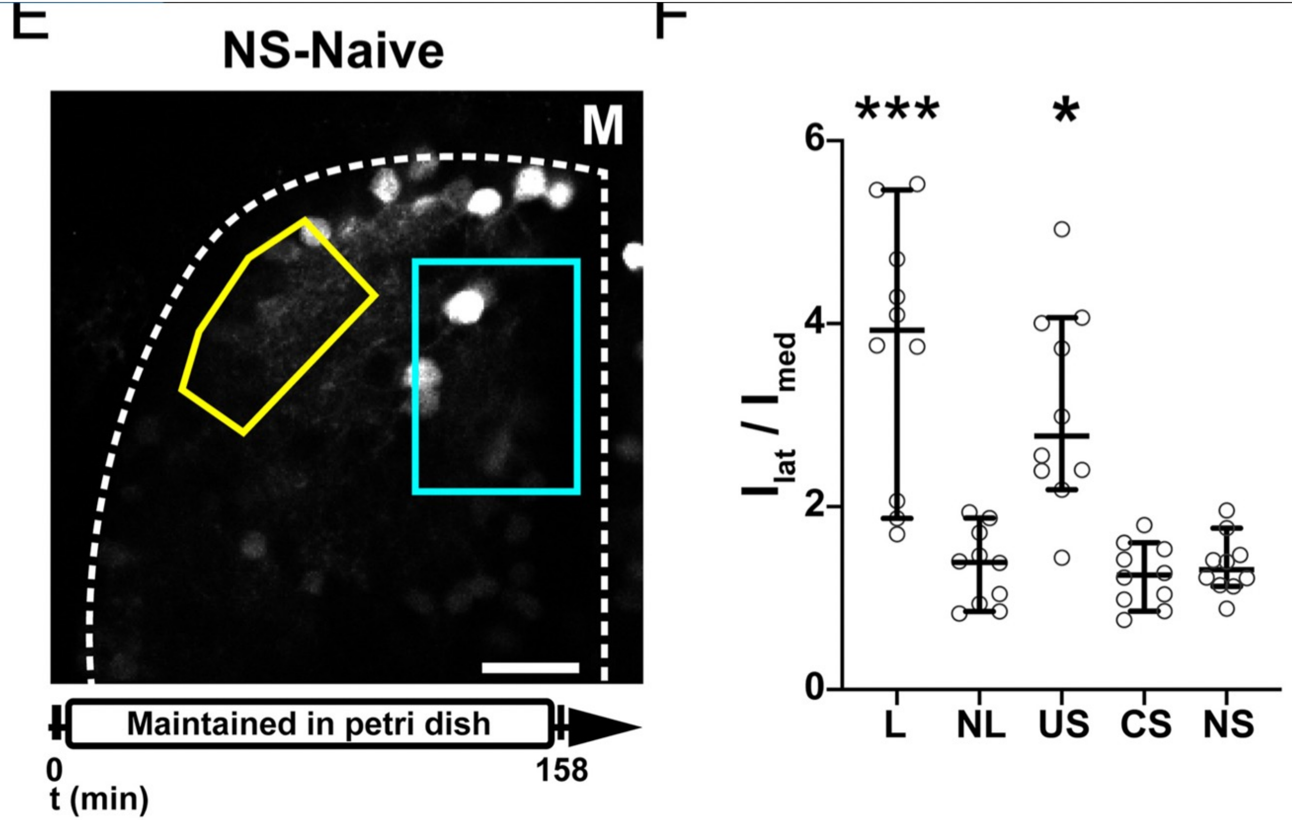
William P. Dempsey, Zhuowei Du, Anna Nadtochiy, +9, and Don B. Arnold Authors Info & Affiliations

Edited by Bernardo Sabatini, Department of Neurobiology, Harvard Medical School, Boston, MA; received April 23, 2021; accepted December 3, 2021

January 14, 2022 | 119 (3) e2107661119 | https://doi.org/10.1073/pnas.2107661119

Significance

Imaging of labeled excitatory synapses in the intact brain before and after classical conditioning permits a longitudinal analysis of changes that accompany associative



Neuronal activation within the anterolateral pallium in response to the CS in learner fish and to the US in naïve fish. (A) Intense immunostaining of pERK in the pallium (magenta highlighted region, Inset) of an L fish exposed to 5 CSs following TFC. The strong signal in an anterolateral region (yellow outline) of this optical section reveals regional neuronal activation. Relatively less immunostaining is present in the medial pallium (cyan outline). (B) An NL fish shows a lack of pERK staining in the anterolateral region (yellow outline) after exposure to 5 CSs in this equivalent optical section. (C) A naïve fish reveals strong pERK staining in the same anterolateral region (yellow outline) after exposure to 10 USs. Equivalent optical section to those in A and B. (D) A naïve fish exposed to 10 CSs does not show concentrated pERK labeling in the anterolateral region (yellow outline). Optical section equivalent to those in A–C. (E) A naïve fish not exposed to a CS or US (NS) does not show concentrated pERK labeling in the anterolateral region (yellow outline). Optical section equivalent to those in A–D. (F) L and US-exposed naïve subjects show a significantly higher lateral:medial pERK intensity ratio compared to NL and naïve untreated subjects (*$P < 0.02$, ***$P < 0.005$, $n = 5$ fish per group, Kruskal–Wallis multiple comparison test). White dashed lines mark the border of the pallium (midline = M) in A–E. (Scale bar for A–E, 20 μm.) Data available at https://doi.org/10.25551/1/1-1JP0 (50).

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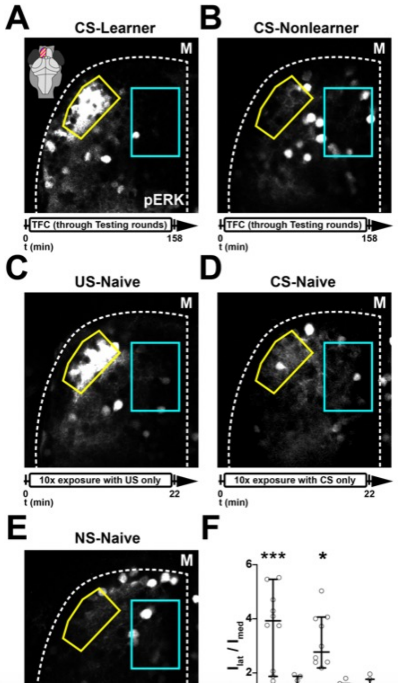
File: 1-1JP0: Fig. 2: Neuronal activation within the anterolateral pallium in response to the CS in learner fish and to the US in naïve fish.

Sections Hide panel

Summary

Belongs to Dataset (1)

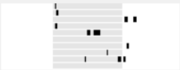
Record ID	1-1JP0
Permanent ID	https://doi.org/10.25551/1/1-1JP0
Title	Fig. 2: Neuronal activation within the anterolateral pallium in response to the CS in learner fish and to the US in naïve fish.
Authors	William Dempsey, Zhuowei Du, Anna Nadtochiy, Karl Czajkowski, Colton Smith, Andrey Andreev, Drew Robson, Jennifer Li, Serina Applebaum, Thai Truong, Carl Kesselman, Scott Fraser, Don Arnold
Year	2020
Description	

Dataset: 1-1F6W: Phosphorylated ERK Immunostaining Experiments (Figure 2, 6, Extended Data Figure 2)

Sections   Hide panel

- Summary
- Behavior in Dataset (10+)
- Image in Dataset (10+)
- File in Dataset (5)
- Part of (1)

Displaying first 10 records

View	Details	Plot
	Record 1-1T8P **Subject** 1-1T7E **Volume** 0.008 L **FScope** 2018-12-12_3Lvl_FScope3 **Grade** bhv_no_aversion	
	Record 1-1T8G **Subject** 1-1T7J **Volume** 0.008 L **FScope** 2017-06-28_3Lvl_FScope2 **Grade** bhv_no_aversion	
	Record 1-1T8E **Subject** 1-1T7C **Volume** 0.008 L **FScope** 2017-06-28_3Lvl_FScope2 **Grade** bhv_no_aversion	
	Record 1-1T88 **Subject** 1-1T7G	

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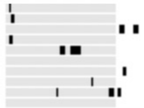
- Summary
- Belongs to Dataset (1)

Behavior: 1-1T8P

Record ID	1-1T8P
Subject	1-1T7E
Image Step	CS Stimulation Behavioral Exposure of SYNAPSE:1-11EC
Volume	0.0080
Trial Counts	List of decimal counts "H,L,T,R" for Habituation, Learning, Testing, Re-Learning rounds, respectively.
Grade	bhv_no_aversion
Raw URL	Behavior_1-1T8P.m4v
Plot	
Download	Behavior_1-1T8P.events.csv
Frames URL	Behavior_1-1T8P.frame_measures.csv
Sums URL	Behavior_1-1T8P.sums.csv

Belongs to Dataset

Explore

Displaying all 1 records

View	Details	Title and Description
	Record 1-1F6W Reference https://doi.org/10.25551/1/1-	*Title:* **Phosphorylated ERK Immunostaining Experiments (Figure 2, 6, Extended Data Figure 2)** *Authors:* William Dempsey, Zhuowei Du, Anna Nadtochiy, Karl Czajkowski, Colton Smith, Andrey Andreev, Drew

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Sections

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- Summary
- Synaptic Pair Study (1)

Image Pair Study: 1-1YRA

Image 1	1-03MJ
Image 2	1-01BA
Nucleic Region 1	1-1YNW
Nucleic Region 2	1-1YNT
Alignment	[[0.9994621779220547,0.004642105303365061,-0.03246237455348768,0.9717546038549336],[-0.006126096091920411,0.9989334398487295,-
Region 1 URL	ImagePair_1-1YRA_n1_registered.csv
Region 2 URL	ImagePair_1-1YRA_n2_registered.csv
Plot	

Full screen