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Toolmakers

In this issue:

BRAIN INITIATIVE ALLIANCE

Welcome

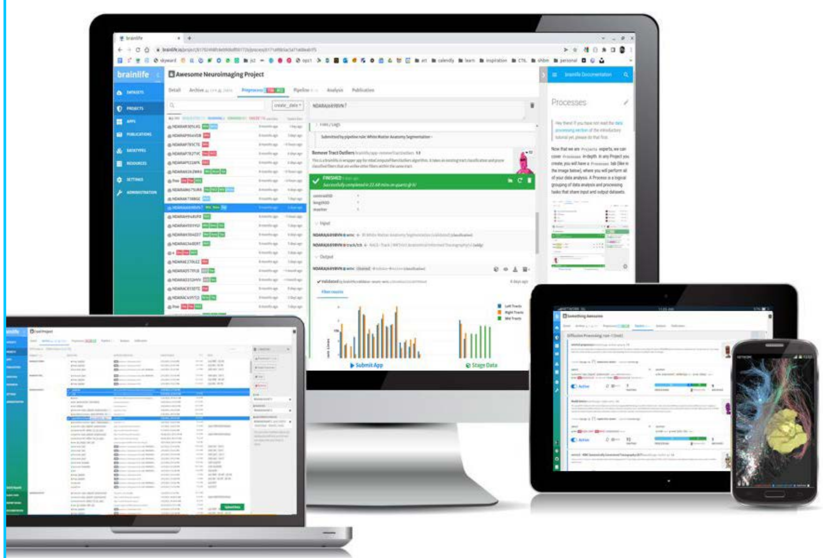

Image: brainlife.io is a free, secure, and reproducible neuroscience analysis platform. Upon signing up, users get immediate access to brainlife.io's apps, data, and computing resources. Source: brainlife.io, 2024.

Welcome to the 2024 premiere of the *Brain Research Through Advancing Innovative Neurotechnologies®* (BRAIN) Initiative Alliance Toolmakers Newsletter. We're kicking off the first issue of the year with a fresh, new look while sharing the same cutting-edge tools with you.

In this issue, we feature three resources that are making it easier to monitor cells and to store and reproduce data: brainlife.io by Dr. Franco Pestilli; CellREADR by Dr. Z. Josh Huang; and the BossDB by Dr. Brock Wester. Let's explore how these tools are progressing neuroscience and learn from the talented investigators behind them.

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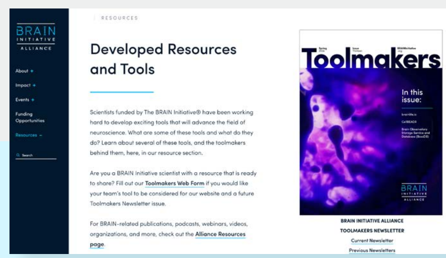


Excited by the potential of the tools in this issue?

Stay tuned for our next issue and explore more products of BRAIN Initiative discoveries in our **Toolmakers' Resources page**.

> BossDB handles astronomical data sets. The ability to work in such large data sets and jump across multiple different neuroscience data repositories is enabling a degree of near real-time brain charting collaboration that has never before been possible. It is vital for tools like BossDB to exist and to be accessible, so these tremendously valuable resources can be made available for the global scientific community without needing special hosting funding.
>
> — **AMY STERLING,** Executive Director, *EyeWire*

brainlife.io

Dr. Franco Pestilli

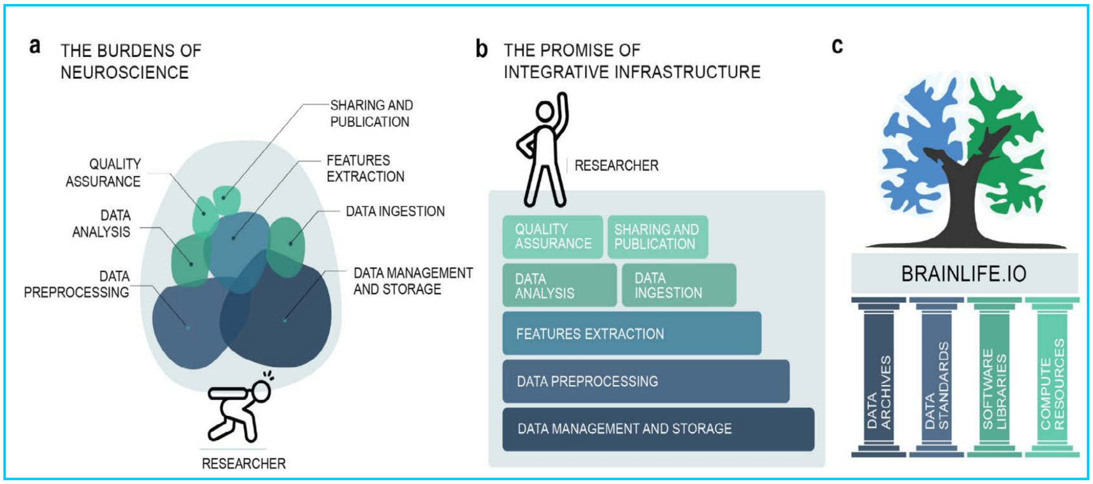


Image: a. The major burdens of performing neuroimaging investigations. **b.** brainlife.io's proposal for integrative infrastructure for findable, accessible, interoperable, and reusable (FAIR), reproducible, rigorous, and transparent neuroimaging research. Adapted from Eke et al. (2021). **c.** The foundational pillars of the open science community that brainlife.io rests upon. Credit: Hayashi et al., 2023, *arXiv*.

As the amount of neuroimaging data grows over time, it is imperative to have platforms that can host and share large data sets with findable, accessible, interoperable, and reusable (FAIR) principles. brainlife.io is a large, free cloud computing platform for neuroimaging data analyses. It features over 400 applications that help build customized workflows to process magnetic resonance imaging (MRI), electroencephalography (EEG), and magnetoencephalography (MEG) data.

With a user base of over 1,500 active users from around the world, brainlife.io is helping students, computer scientists, and data scientists find open resources to analyze their neuroimaging data while encouraging reproducibility and collaboration within the scientific community. Users can develop their own apps to process their data or use apps that have already been created for existing data to reproduce data processing results with their data. For example, FreeSurfer is a popular app that processes anatomical MRI data using algorithms that quantify brain properties. Other popular apps include fMRIPrep, used to clean and standardize functional MRI data, and MRtrix3 for processing diffusion MRI data.

In addition to apps, brainlife.io grants users access to resources and supercomputers to help researchers with high-throughput computing. Supercomputers from advanced computing centers across the nation have lent their storage and computing capabilities to brainlife.io, including The University of Texas at Austin (UT Austin), Indiana University, University of Pittsburgh, and University of Michigan.

> The future of brainlife.io is bright. We are expanding the types of data modalities served and the number of services provided to the community.
>
> **— DR. FRANCO PESTILLI,**
> Founder/Director, *brainlife.io*

Dr. Franco Pestilli, a professor at UT Austin, founded and directs brainlife.io. He created the platform to connect data processing pipelines and end users. Thanks to brainlife.io, over 500 data sets are being used for neuroimaging data analysis projects. Dr. Pestilli hopes that his platform will continue growing. The brainlife.io team is currently working to expand its scope to include positron emission tomography (PET) data, and to extend its reach by conducting workshops in other countries.

CellREADR

Dr. Z. Josh Huang

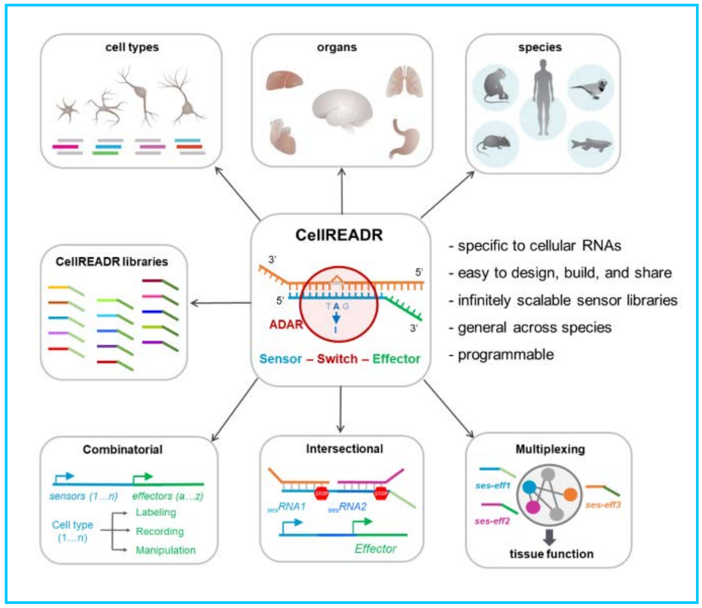
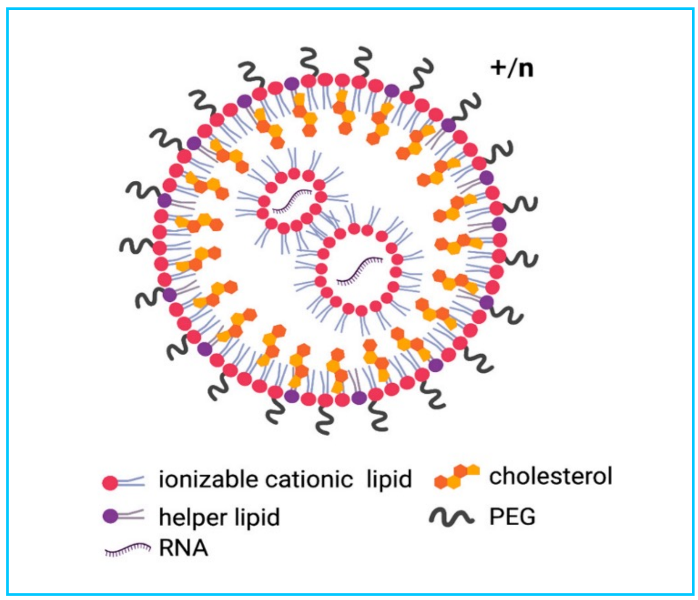


Image (above): CellREADR properties. Credit: Duke University School of Medicine, 2024. **(below):** CellREADR liquid nanoparticle delivery. Credit: Duke University School of Medicine, 2024.



CellREADR stands for Cell access through RNA sensing by Endogenous ADAR (adenosine deaminase acting on RNA). CellREADR is a cell engineering tool that uses a single modular RNA molecule to detect cell-specific RNAs that define distinct cell types or cell states. Once detected, CellREADR translates effector proteins that can monitor cell states, change a cell type's physiology, and even reprogram a cell's identity. The gating of effector translation by RNA sensing is achieved through an RNA editing mechanism mediated by ADAR enzymes.

"Most current approaches to genetic access of cell types are DNA- and transcription-based methods that leverage germline genome engineering or viral vectors harboring enhancer elements to drive the transcription of effector genes," says Dr. Z. Josh Huang, CellREADR's principal investigator at the Duke University School of Medicine. Unlike these approaches, CellREADR uses direct RNA sensing and editing to trigger protein translation. In addition to delivery through DNA expression plasmid using viral vectors, CellREADR can also be delivered *in vitro* through transcribed RNAs directly via lipid nanoparticles. CellREADR creates a user-friendly, easily programmable way to monitor and control animal cells with an approach that is generalizable across animal species.

CellREADR was first published in *Nature* in 2022, in a paper describing how it targets and controls cell types in different organs and animal species. The paper demonstrated CellREADR's design and how its viral delivery gains access to cell types in rodent brains of behaving animals and in *ex vivo* human brain tissues. Since then, Dr. Huang's lab has been experimenting with sensor design and prediction algorithms to help improve its tool's reliability and specificity. The lab has also been working to improve payloads for cellular gene expression so that CellREADR can manipulate cells and prompt therapeutic effects. Dr. Huang hopes that technology like CellREADR will eventually be able to precisely target and treat brain disorders through cell editing.

> CellREADR can potentially enable highly scalable, generalizable, and programmable analysis of animal cell types and cell states across species.
>
> **— DR. Z. JOSH HUANG,** Principal Investigator, *CellREADR*

Brain Observatory Storage Service and Database (BossDB)

Dr. Brock Wester

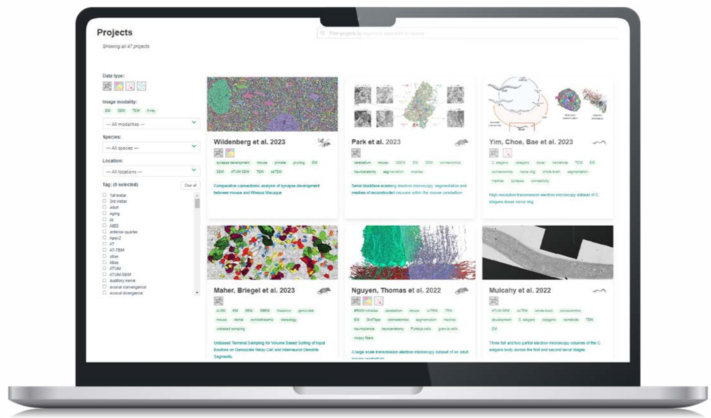


Image (top left). BossDB logo. Credit: BossDB, 2024; **(above)** BossDB's projects' page highlighting various public volumetric neuroimaging data sets. Credit: BossDB, 2024.

At the Johns Hopkins University Applied Physics Laboratory, Principal Investigator Dr. Brock Wester and his team created the BossDB, a large neuroscience data ecosystem. The database provides a storage solution for large-scale volumetric imaging modalities, primarily including electron microscopy and X-ray microtomography data. It also helps connect neuroscience resources in hopes of accelerating research and encouraging scientific collaboration.

No data set is too large for BossDB—it hosts over 1PB (compressed) of high-resolution, publicly available neuroimaging data. In addition, BossDB partners with Amazon Web Services to make sure all data are highly accessible and scalable. Currently, BossDB stores nearly 50 data projects and over 1,000 imagery data channels. "Our data is supporting neuroscience research in connectomics, neural architectures, cell typing, data processing and analysis tool development, and cellular and tissue neuroanatomy," says Dr. Wester.

BossDB began as a data storage solution for the Intelligence Advanced Research Projects Activity's (IARPA) MICrONS program to enable sharing and neural circuit reconstruction assessment. It has since integrated into a larger neuro-data ecosystem, and is supporting a variety of additional neuroscience projects, like Princeton University's Flywire application, which enables community proofreading and analyses of an adult female fruit fly brain. Other data sets in BossDB come from around the world and across multiple species, including nematodes, zebrafish, mice, and more.

> Some of our data sets include high resolution multi-petavoxel contiguous image volumes with dense segmentation and mesh data.
>
> — **DR. BROCK WESTER,** Principal Investigator, *BossDB*

In addition to its storage capabilities, BossDB has tools to help with data access, data processing, visualization, and more. For example, DotMotif is one of its powerful network science tools that was designed for finding graph motifs. DotMotif performs large-scale graph and connectomics analysis and mining by interfacing with graph management systems. Other tools integrated into the BossDB ecosystem help researchers perform tasks like visualizing 3D data, proofreading image data segmentation, generating meshes from segmented data, and analyzing neuronal connectivity.

The team at BossDB welcomes new data contributions and collaborations. Researchers interested in using or storing data in BossDB can find tutorials and video walkthroughs on its website.