A community-developed open-source computational ecosystem for big neuro data

To the Editor — Recent technological developments, such as high-throughput imaging and sequencing, enable experimentalists to collect increasingly large, complex, and heterogeneous 'big' data. These studies result in terabytes of data per day, yielding petabytes across experiments and laboratories. These experimental capabilities exceed the scale or feature set of existing software. For example, such data cannot be stored, processed, and visualized on a laptop or workstation. Instead, big data must be stored on data centers and processed on high-performance compute clusters.

In 2011, we launched Open Connectome Project1, an open-access data repository powered by open-source web-services software applications that store, analyze, and visualize large imaging datasets. However, as technology changed, features were added, and scale increased, our academic development team and resources became overwhelmed. We overhauled our custom stack into a community-built and -maintained software ecosystem deployed in the commercial cloud, integrating multiple open-source projects and extending them for our needs (https://neurodata.io). The ecosystem makes it possible to analyze disparate datasets by reusing components originally designed for other applications.

All datasets use NeuroGlancer for visualization in a browser, bossDB—a cloud spatial database—for data management, NDWeb to store visualization links, NDeX to exchange data into and out of the system, and Jupyter notebooks for data analyses. Spatial data derivatives are uploaded and coregistered for quality control. The other software tools are for subsets of the data types, and make the ecosystem flexible and extensible. Figure 1 shows our reusable tools and web visualizations of two exemplary datasets described below.

Conjugate array tomography images ≥20 channels of microscale protein expression in three dimensions, and can be followed by nanoscale serial electron microscopy2. Our workflow for these data aligns and stitches a collection of 2D images with custom scripts based on TrakEM2’s nonlinear registration. After data have been ingested and visualized, probabilistic synapse detection3 is run on the entire dataset. We study the statistics of the synapses using multiscale graph correlation4.

CLARITY—a brain-clearing method5—collects data from multiple channels, including background for registration, and a ‘signal’ channel that exhibits protein expression localized to a particular subpopulation of cells. Our workflow uses TeraStitcher to align and stitch the collection of raw 2D image tiles, and registration to the Allen Brain Atlas with NDReg6, a multiscale, multichannel implementation of large deformation diffeomorphic metric mapping.

To date, NeuroData holds ≥100 public and private datasets, with ≥200 teravoxels from 30 collaborators, making it the world’s largest and most diverse public neuroscience data repository (the up-to-date listing can be found at https://neurodata.io/). We add new data based on our collaborations and community input (data incur ongoing costs for cloud storage and computation). Without running any code or downloading any data, anyone with internet access can visualize image data from different data types.
technologies to generate hypotheses or plan new experiments. If investigators choose to download data and/or code, they can access and analyze disparate data with the same functionality and syntax, which allows for faster comparisons and scientific discoveries. Because all of the code is open source, anybody can download, set up, and modify this ecosystem.

Data availability
All code is available from https://neurodata.io/tools/ under an Apache 2.0 license unless otherwise specified. All publicly available data are accessible at https://neurodata.io/data/ under an ODC-By v1.0 license, unless otherwise specified.

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Competing interests
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Striped UniFrac: enabling microbiome analysis at unprecedented scale

To the Editor — The UniFrac metric is used frequently in microbiome research, but it does not scale to today’s large datasets. We propose a new algorithm, Striped UniFrac, which produces results identical to those of previous algorithms but requires dramatically less memory and computing power. A BSD-licensed implementation is available that produces a C shared library enabling scientists to derive new biological insights. As a consequence of rotation, diagrams are shown in Supplementary Fig. 1e). The key advances with Striped UniFrac are improved space complexity, obtained through aggregation of metric constituents in post-order traversal, and rotation of proportion vectors for pairwise comparisons (methods, pseudocode, and complexity analysis are provided in the Supplementary Note). The post-order aggregation removes the dominant scaling factor for space complexity in Fast UniFrac (Supplementary Fig. 1c,d). Vector rotation (expressed by embedding; Fig. 1a) allows compilers to use single instruction multiple data (SIMD) operations. As a consequence of rotation, pairwise distances are computed along diagonals of the distance matrix (Fig. 1b), which results in more cache utilization, task-level parallelism, and hardware-level prefetch. We also introduce an optional heuristic that reduces compute by 50% by ignoring tips of the phylogeny (correlations with exact calculations are shown in Supplementary Fig. 1e). Empirical scaling results show that Striped UniFrac outperforms current popular implementations of UniFrac (time in Fig. 1c; space in Fig. 1d; benchmark and algorithm in the Supplementary Note).

Reporting Summary
Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Code availability
An optimized implementation of Striped UniFrac is available on GitHub (https://github.com/biocore/unifrac) under a BSD license (implementation details are provided in the Supplementary Note),