



A High-Performance Computing Portal Applied to 3D Electron Microscopy

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Abstract

The continued expansion in size and resolution of volumetric datasets generated by electron microscopy (3DEM) is making high-performance computing (HPC) an essential component. HPC provides the scalable, parallelized infrastructure required to process and analyze these increasingly large datasets. The Texas Advanced Computing Center's (TACC) Core Experience Portal (CEP) is a science gateway specialized for leveraging HPC. The CEP can be adapted into customized versions based on a research community's needs. Here we have constructed 3dem.org as a gateway for the community exploring volumetric data generated by electron microscopy (3DEM). This gateway provides the 3DEM community with user-friendly browser-based access to raw and processed datasets including both private and shared data, image processing tools for alignment and segmentation, and simulation and analysis environments. All this is linked to the underlying HPC environment at TACC with the ability to connect to other data storage and compute systems. 3dem.org bridges advanced electron microscopy with HPC, providing the research community with scalable, accessible infrastructure for discovery.

Keywords Science gateways · Sustainable cyberinfrastructure · 3DEM · Volumetric image processing · Synapse modeling and simulation

Introduction

3-dimensional electron microscopy (3DEM) is rapidly expanding the size of ultra-high-resolution datasets being acquired to further our understanding of biological systems.

For example, a cubic millimeter of imaged tissue can now exceed one petabyte, necessitating the use of large-scale computational resources for storage and analysis. To support broadening access to the many computationally demanding domains such as 3DEM, the Texas Advanced Computing Center (TACC) Core Experience Portal (CEP) was developed as a template science gateway that can be readily deployed in support of a wide variety of disciplines [1]. The design of the CEP reflects both the technical demands of high-performance computing (HPC) and the collaborative priorities of the broader research ecosystem. A key component of the CEP is the Application Programming Interface (API) that provides the link between the web-browser and HPC. CEP uses the TACC API (Tapis) as the RESTful API layer that serves as the secure connection between the web gateway and the data storage and computing resources, as well as managing user access [2]. This approach forms a foundation of scientific community data sharing that

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supports the Findability, Accessibility, Interoperability, and Reusability (FAIR) principles [3].

The 3dem.org web-based research platform was developed as part of the Next Generation Network for Neuroscience (NeuroNex) program [4]. 3dem.org is focused on supporting and disseminating new technologies for enhanced resolution 3DEM, with a specific emphasis on applications involving the ultrastructure of synapses [5]. By integrating this new data collection technology with publicly funded high-performance computing (HPC), the additional computational power is leveraged to process even larger datasets, and to promote reproducibility and sharing of techniques. 3dem.org is designed to serve not only the project team, but all researchers interested in the tools and capabilities. All visitors to 3dem.org may download the latest public datasets. Users with active TACC accounts and allocations may request access to the interactive 3DEM Workbench. Within the Workbench, users can access community datasets, workflows, and applications. Applications are focused on those that support processing for enhanced resolution 3DEM. Users may also share their data and processes with other users.

3DEM is an appropriate domain for demonstrating the utility of the CEP. Image volumes are increasing in size as instrumentation improves, and the research is focused on seeking to further our functional understanding not only of cells but also the cell neighborhoods. These larger datasets increasingly depend on HPC for processing. Having a common portal allows shared access to the large datasets and processing applications. We describe here the application of the CEP and Tapis to this large-scale collaborative effort toward 3DEM of synapses.

Results

Public Front End

Visitors to 3dem.org can access a customized front end of the CEP that describes the domain and gives public access to project information, recorded workshops, and instructional materials (Fig. 1). Information on how users can access gated resources and tutorials on using 3dem.org are provided publicly. In addition, publicly shared datasets can be downloaded.

Workbench Analytical Environment

After creating a TACC account, users can request and be granted access to the full features of 3dem.org. To facilitate access to data and analysis resources, the CEP provides a customized web-based graphical user interface (GUI)

Workbench. Upon logging in via a laptop or even a smart-phone, users first access their dashboard. The dashboard lists the user's most recently run HPC jobs, provides easy access to the user's support tickets, and lists the operational status of the HPC systems. The Workbench also provides access to data and registered applications on HPC systems. Addressing project security needs, users can keep their data and applications fully private, share with specific users, or share with all members of the program. The infrastructure supports batch applications that submit jobs to HPC systems to run when resources are available, as well as interactive applications that open direct web-access to HPC nodes for more exploratory analysis.

Data Management

Integral to collaboration on 3dem.org is the capability to access and generate data and metadata from interactive environments and HPC resources. Within the GUI Workbench, 3dem.org has a "Data Files" tab that allows users to access various HPC filesystems. This includes TACC's Corral system which is used by 3dem.org as the central repository to facilitate sharing within custom workgroup projects as well as public data sharing, and TACC's Stockyard "\$WORK" filesystem within which each TACC user has 1 TB available for their private data and active analysis. Users also have access to their home directories and unrestricted temporary storage on scratch filesystems on TACC's Lonestar6 (<https://docs.tacc.utexas.edu/hpc/lonestar6/>).

For custom workgroup projects, any user can also create these private directories and manage access with collaborators. This access uses both the fine-grained access control lists as well as TAPIS permissions. Together, this allows users to manage and share the data via the 3dem.org web-browser interface, while also making the data simultaneously available to both API-calls and direct command line access.

Featured Datasets

When research data is ready to be more broadly accessible than custom workgroups, 3dem.org provides two options, Community Data and Public Data.

Community Data

Community Data is a form of broad data access that allows anyone with a TACC account and 3dem.org access to also access Community Data. Currently, Community Data includes example datasets for trying out 3dem.org applications and testing application development. Also included in Community Data are datasets used in NeuroNex workshops,

3-D ELECTRON MICROSCOPY

A web-based research platform focused on developing and disseminating new technologies for enhanced resolution 3-dimensional electron microscopy.

SHARED DATA

Interactively access the latest datasets and workflows available in the 3DEM Data Depot and Discovery Environment.

WORKSHOPS

Mitochondria Workshop Series
The University of Texas at Austin | Online
Workshop exploring current knowledge of the morphology and function of Mitochondria.

First NSF NeuroNex Workshop on Super 3DEM
Texas Advanced Computing Center | Austin, TX
3DEM users and developers shared experiences and tools for the management and reconstruction of objects from serial section transmission electron microscopy.

Blender Scripting Tutorial Series
Salk Institute for Biological Studies | Online
Hands on how-to series of tutorials on using Blender for cell simulations.

Public Data

As with Community Data, 3dem.org users can readily access Public Data for use with 3DEM applications. However, Public Data is an even broader form of data access that allows anyone with a web-browser to download the data, even without a TACC account. For 3dem.org, the Public Data includes video recordings and transcripts from past NeuroNex workshop series presentations, as well as data made public as part of publications, which can serve as a complement to repositories that may have data size limitations (e.g., the Texas Data Repository at <https://datavers.e.tdl.org/>). Publication data includes: deep learning-based

access to the same set of queues. Users can also control their data sharing, from private, to selected collaborators via Shared Workspaces, to making their data Public

pretrained models as well as all training and testing data for point-scanning super-resolution imaging that includes both volumetric EM and non-EM data [6]; serial EM images from hippocampal area CA1 from acute slices prepared from P15 rats along with trace, and series files analyzed for synaptogenesis [7] and for dendritic spine density and microtubules [8]; serial EM images acquired from hippocampal area CA1 from acute slices prepared from adult rats (P60-61), two hours following either control or theta burst stimulation [9]; serial-section EM images along with a corresponding.

PyReconstruct trace files collected from the middle and outer molecular layers of the hippocampal dentate gyrus of adult male rats (P121-185) [10]; and EM tomography images for analysis of presynaptic vesicles in long term potentiation [11].

Fig. 1 The 3DEM Science Gateway provides a browser-based access point to advanced computing resources. Users can launch both interactive and batch applications on HPC systems, with both styles having

including 3DEM datasets from [5]. Community Datasets can be easily accessed by 3DEM applications as well as by command line. In addition, users can download the data if so desired.

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Applications

To support best practices in software development the use of software containers and public code repositories is encouraged for applications integrated into 3dem.org and other CEP gateways. Reproducibility is further supported by allowing users to individually or collaboratively develop and share their data processing workflows and analysis pipelines. Provenance of software versions is tracked by Tapis as well as inputs, outputs, and parameters for every job launched, allowing specific reproducibility and interactive development applicability. 3dem.org has a collection of cutting-edge applications, both pre-release and full-featured, designed to support the volumetric data community that span the processing workflow, including generating a coherent 3D voxelated volume from acquired images, segmenting morphological features, simulation, and analysis.

AlignEM-SWIFT

AlignEM-swift is an open-source software application under development for high-throughput alignment of serial EM images (<https://github.com/mcellteam/swift-ir>). As such, this tool is fundamental to the creation and curation of 3DEM datasets. AlignEM-swift, written in Python, is based

upon the powerful SWiFT-IR (Signal Whitening, Fourier Transform Image Registration) toolkit [12], encapsulating the individual tools in the toolkit, which are written in C. The graphical user interface of AlignEM-swift streamlines the workflow of 3DEM dataset curation from intake of a raw image dataset, alignment of the dataset, analysis and evaluation of the quality of the alignment, and remedies for problematic alignments. AlignEM-swift also encapsulates high-performance viewing of the dataset, in zarr format (<https://zarr.dev/>), via Neuroglancer (<https://github.com/google/neuroglancer>).

Figure 2 shows a screen capture of a typical use case: a stack of images from a 3DEM dataset is loaded into the tool (297 images in this example). The images are then aligned to their previous neighbor in the stack in a pairwise manner. Because the alignment process involves evaluation of pairwise images, it is highly parallelizable on HPC platforms such as LoneStar6 at TACC. Alignment requires finding the affine matrix that maximizes the goodness of fit between a given pair. This is accomplished by employing the signal whitening image matching (swim) function of the SWiFT-IR toolkit. Swim measures the displacement of the signal whitening FFT match signals (dark spot images displayed on the right panel in Fig. 2) for several corresponding image patches in neighboring images in the stack. Here 4 patches

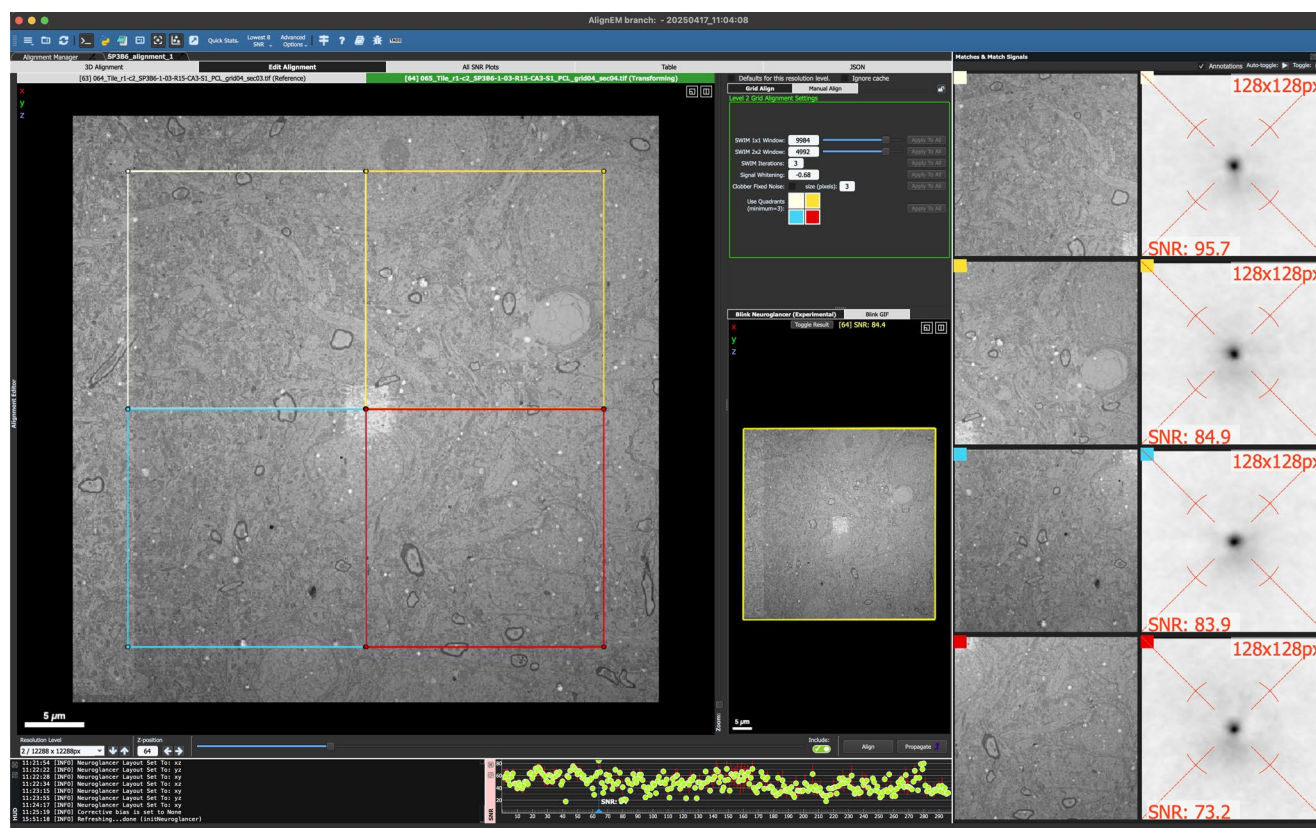


Fig. 2 The GUI of AlignEM-swift under development shown here aligning a 3DEM image stack

are used as indicated by the white, yellow, blue, and red rectangles shown on the left panel. The set of displacements is used to compute the single affine matrix that brings the rectangles into correspondence across the neighboring images. By iterating this process several times, the residual displacements measured by swim decrease to sub-pixel magnitude and convergence to the best affine matrix is achieved. The goodness of fit of the image alignment can be assessed from the signal-to-noise ratio (SNR) of the match signals, which is visually apparent from the shape and compactness of the dark spot and its contrast with the light gray background of the match signal. A graph showing the pairwise average SNR values obtained across the whole stack is shown in the lower middle panel. Generally, SNR values greater than 8 indicate satisfactory alignment. In the example shown, the SNR values across the stack ranged from 17 to 84. The graph can be used to identify quickly any problematic alignments and the match signals for those cases can be assessed to determine appropriate remedies, available via custom settings in the GUI.

The main output of AlignEM-swift is the curated project file which is a database in JSON format containing all settings, steps performed, and results for a given project, including the final affine matrices aligning the stack. PyReconstruct, introduced in the next section, uses the affine matrices in the project file as a fundamental part of its non-destructive display of the 3DEM dataset.

PyReconstruct

PyReconstruct is a powerful, fully open-source application [13] for annotating and analyzing serial electron microscopy data. PyReconstruct was designed as a modern successor to the widely-used legacy software Reconstruct [14]. Created specifically to balance rapid segmentation with detailed structural analysis, PyReconstruct empowers researchers to trace, segment, curate, and visualize 3D cellular structures across serial sections with exceptional precision. The tool features an intuitive GUI with moveable widgets, sophisticated 3D rendering capabilities, and built-in curation systems for team-based quality control. Its rich annotation environment supports the application of tags, flags, and comments to traces and objects, creating a comprehensive documentation system integrated with the image data. PyReconstruct's dynamic alignment strategy enables users to apply multiple alignment profiles on-demand without permanently altering original images, making it ideal for correcting section distortions discovered during annotation. The application excels at nanoscale quantification of structures like synapses while maintaining compatibility with larger-scale connectomics workflows, making it valuable

across neuroscience as well as a variety of diverse fields [15–29].

PyReconstruct addresses key technical limitations through its multi-resolution zarr approach to image handling, breaking through previous RAM restrictions to handle arbitrarily large datasets. PyReconstruct facilitates team-based workflows through its robust import/export capabilities and trace conflict resolution system, which identifies potential conflicts arising during multi-user segmentation efforts. The software accepts standard image formats as input and produces multiple outputs including quantitative measurements, 3D meshes, and labelled zarrs for integration with automated segmentation pipelines. PyReconstruct bridges manual and automated approaches, enabling researchers to generate ground truth for machine learning while maintaining full control over annotation quality. Interactive features like double-clicking on 3D objects to locate corresponding sections facilitate efficient proofreading. Source code is fully open and available under a GNU General Public License (v3), with ongoing development hosted on GitHub (<https://github.com/synapseweb/pyreconstruct>).

Napari

Napari is a Python-based application that supports n-dimensional image visualization, annotation, and analysis [30]. It can input n-dimensional images (2D images, 3D images, multi-channel images, Zarrs, tiffs) and output labels, point annotations, line/curve/polygon annotations. In addition to enabling exploration, overlaying, and editing complex images, Napari has a strong plugin community. Our installation of Napari [31] has several key plugins important to 3DEM workflows. One of these is a Bootstrapper plugin for accessing and editing segmentations using machine learning to generate segmentations from a sparse set of manual segmentation (Fig. 3) [32]. Two other featured Napari plugins are microSAM (Meta's Segment Anything Model finetuned for microscopy) [33] and PSSR2, a deep learning-based point-scanning super-resolution imaging tool for improving image resolution [34]. Though Napari by itself does not have many parallel features, these plugins can have parallelized implementations of functions. For this reason, Napari is best used for viewing, exploring, and annotating smaller cropped volumes.

MCell-CellBlender-NeuropilTools

MCell-CellBlender-NeuropilTools is suite of tools designed for computer simulation and analysis of biochemical reaction-diffusion systems in 3D [35]. MCell is the particle/agent based Monte-Carlo simulation engine in the package. CellBlender is an add-on for Blender, a popular and

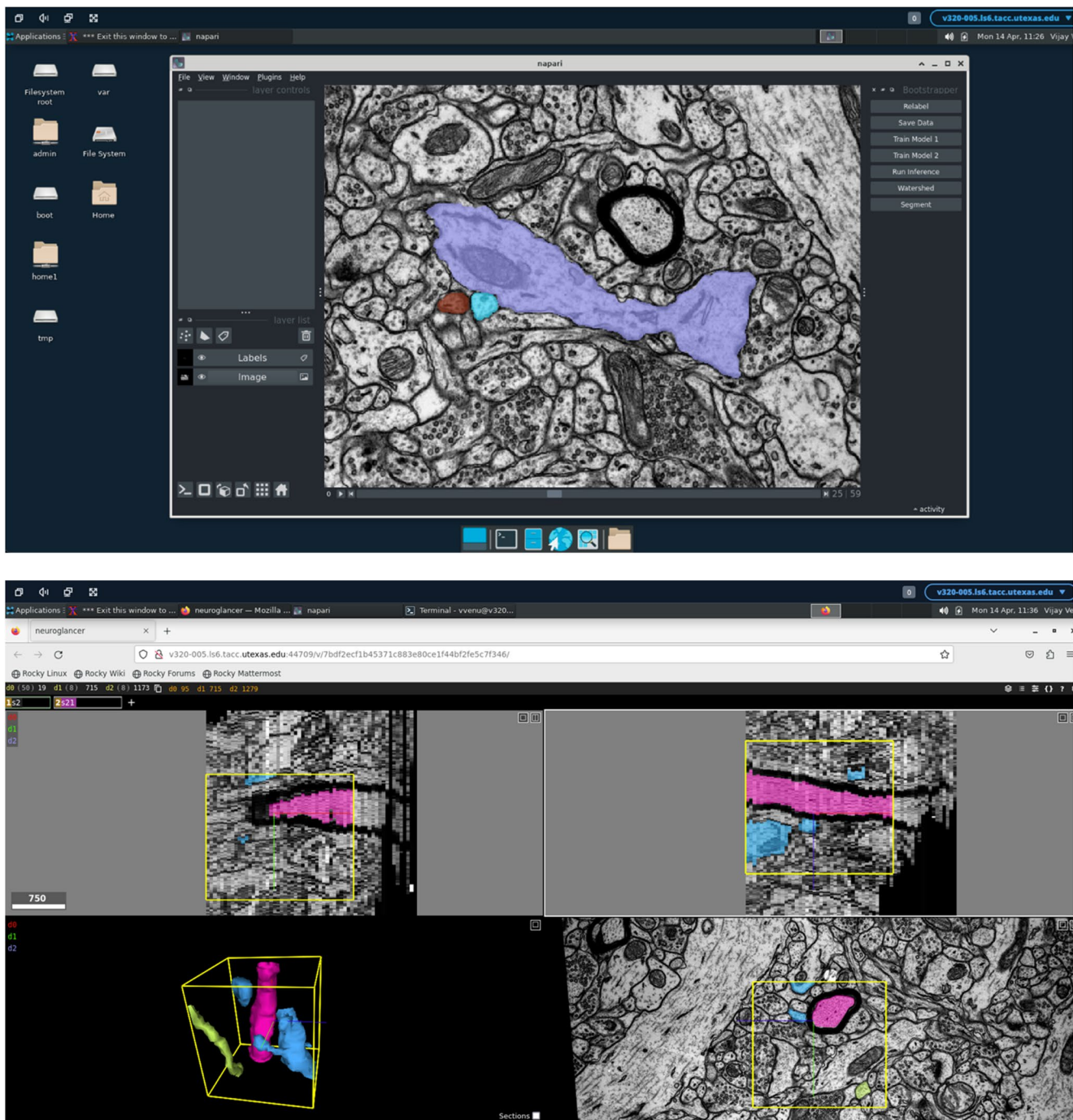


Fig. 3 The Napari application and Bootstrapper plugin. Top: Shown in use on 3dem.org. Sparse label annotations in color. Bottom: Screenshot of Neuroglancer viewer of same dataset illustrates ZY, ZX, and

YX planes as well as 3D rendering of labels. <https://github.com/ucsdmanorlab/napari-bootstrapper/releases/tag/v0.2.0> - <https://github.com/napari/napari>

powerful 3D CAD platform, and serves as the graphical frontend to the MCell physics engine. NeuropilTools works alongside CellBlender to provide computational quality mesh generation, annotation, and analysis of cellular and subcellular membranes (with emphasis on neuronal tissue) from their segmentation contours in PyReconstruct 3DEM datasets. Together this suite of tools allows the researcher

to bridge the gap from structure (given by the cellular ultrastructure in the 3DEM dataset) to dynamic cellular function, in a sense, bringing the tissue back to life in-silico.

Figure 4 illustrates an example of MCell-CellBlender-NeuropilTools used to simulate pre-synaptic release of neurotransmitter and post-synaptic activation at a spine synapse in hippocampal area CA1 [36, 37]. Here the cellular

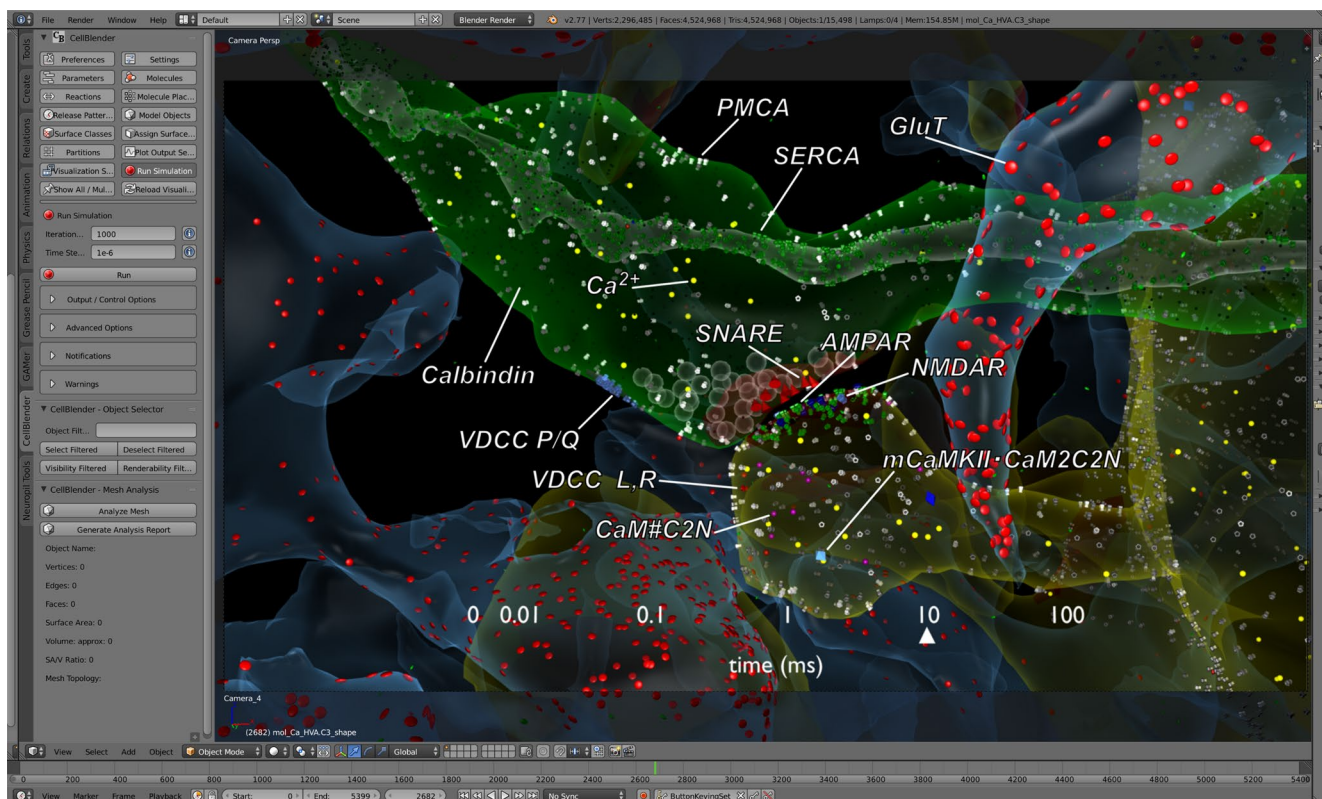


Fig. 4 Computational reconstitution and MCell simulation of glutamatergic synaptic transmission at dendritic spines of hippocampal area CA1 pyramidal neurons. The model encompasses many known components and molecular mechanisms of presynaptic neurotransmitter release (presynaptic axon shown in translucent green, molecular

species as indicated) and postsynaptic activation on the dendritic spine and dendrite (shown in translucent yellow, molecular species as indicated). The width of field of view is ~3 micrometers. This model was constructed and simulated in MCell-CellBlender-NeuroPiTools and is shown in the 3D view panel at $t=10\text{ms}$ into the simulation

structure was hand-segmented in Reconstruct, meshed and annotated with NeuroPiTools, and turned into a functional model of synaptic transmission with anatomically correct distributions of relevant molecular species, biochemical reaction pathways and kinetic rate constants with CellBlender, and then simulated with MCell. CellBlender displays the visualization of the simulation results within the Blender platform.

Additional Applications

In addition to these primary applications utilized by the NeuroNex project, several other software applications relevant to 3DEM are also currently available to all users. These include TrakEM2 [38] as part of Fiji [39] which is used for image registration. Notably, we have customized our Fiji container to allow specifying the number of processes as a parameter when launching the application (<https://github.com/eriks/fiji-openjdk-8-ui>). This is to allow users to ensure that sufficient RAM is allocated to each process, which is important when aligning large images. Other applications include Paraview for 3D visualization [40], Matlab [41],

Jupyter notebooks [42], and Neuroglancer (<https://github.com/google/neuroglancer/releases/tag/v2.40.1>), a fast web browser-based viewer for large zarr arrays which supports customization and workflow automation using Python. Running these applications on one or more HPC nodes provides a powerful approach for working with large 3DEM images and volumes. Beyond these applications, any user can create their own private application for their own use, share the application with collaborators, and if desired, request that the application be made public to all 3dem.org users.

Workflows

Figure 5 illustrates a typical workflow performed using 3dem.org. A raw transmission scanning EM (tSEM) image series collected for each experiment is transferred from the laboratory's local drive to 3dem.org My Data (temporary storage of LS6 Scratch). AlignEM-Swift in Interactive Analysis mode uses SNR to evaluate the quality of the series for issues such as poor focus or astigmatism, displaced region of interest (ROI), section defects, repeated ROIs, missing or out-of-sequence sections that may necessitate re-imaging. After passing the quality check, image series is coded

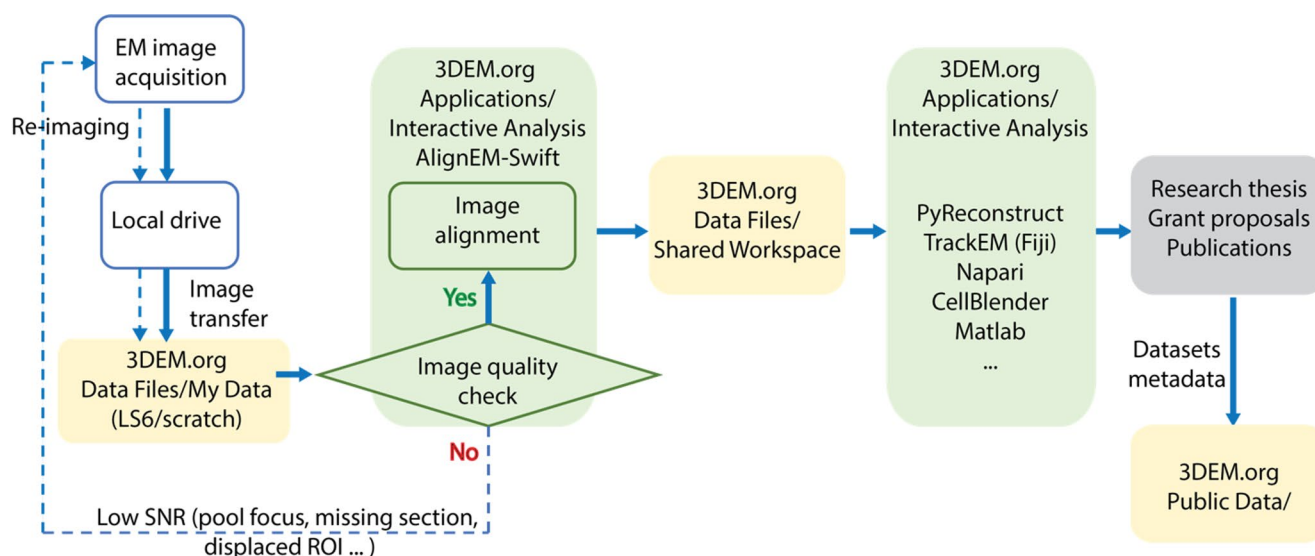


Fig. 5 Workflow of 3DEM image volumes, reconstructions, visualization, analysis and storage on 3dem.org

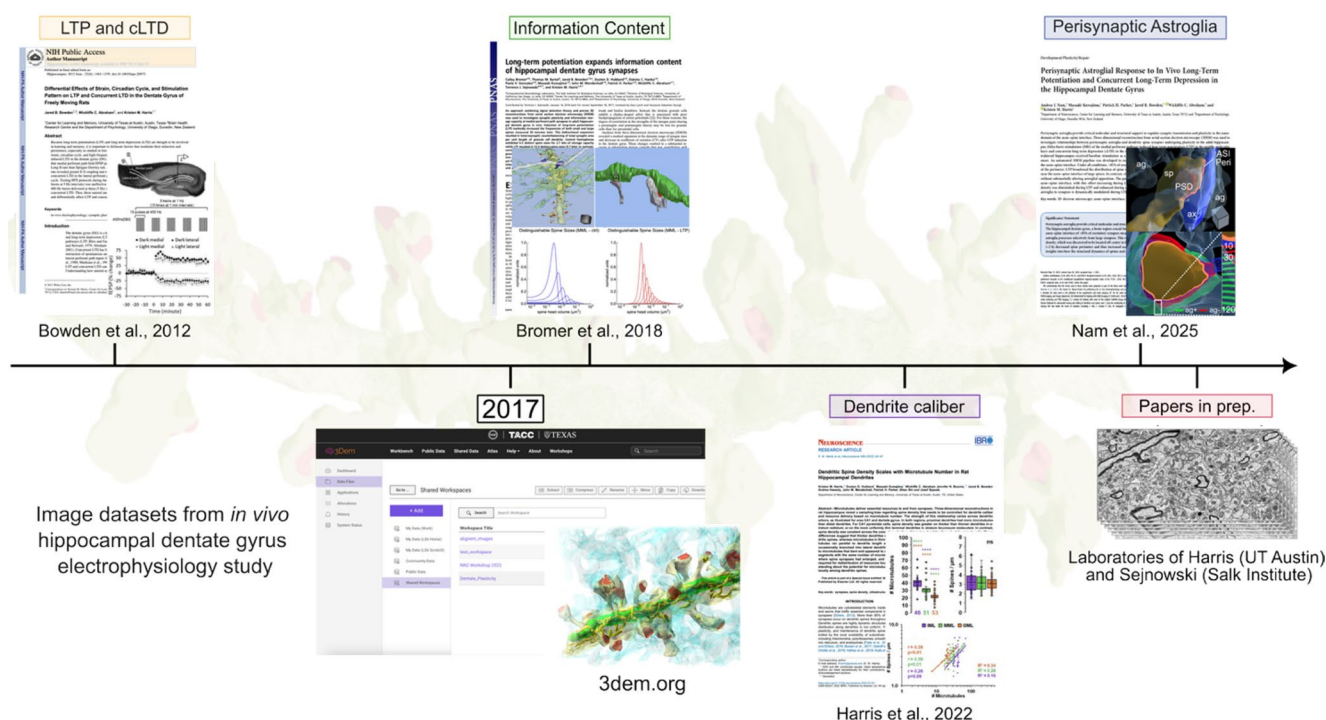


Fig. 6 Integrated data and analysis framework at 3dem.org supports data sharing and streamlined publication workflows

for alignment using AlignEM-Swift in My Data. Aligned image series (.tiff, .swift) are transferred from My Data to project folder in Shared Workspaces for data storage and analysis. PyReconstruct, TrakEM2 (Fiji), Napari, and CellBlender are used for Interactive analysis to prepare data for research thesis, collaborative grant proposals, and publications. Datasets and associated metadata (.tiff, .swift, .json, .zarr, .csv, .blend, .xlsx etc.) generated from experiments are

saved and shared on the 3dem.org portal for easy retrieval and data sharing.

Figure 6 illustrates how 3dem.org has been applied to publication workflows, beginning with ingesting the hippocampal dentate gyrus dataset into 3dem.org. For this dataset, *in vivo* long-term potentiation (LTP) and concurrent long-term depression (cLTD) were induced at granule cell synapses. Interactive applications available through 3dem.

org facilitated sharing and analysis of the large datasets, accelerating research progress.

Methods

Portal Deployment

The 3dem.org instance of the CEP is deployed on a virtual machine on Rodeo, TACC's in-house VMware cluster. The frontend is a web application using the React framework, providing users an interface for managing data and submitting HPC jobs. The backend is built with the Django web framework, providing API endpoints to primarily structure calls to Tapis apps, jobs, and systems and format the results for display on the front end. A PostgreSQL cluster is used for the database layer, which stores user profiles and project metadata. Searches for files, projects, and web content are managed by an Elasticsearch cluster running on a dedicated virtual machine. Search indexing and other long-running tasks are handled by an asynchronous Celery worker with RabbitMQ as the message broker. An Nginx server is placed in front of the rest of the services to route user requests and serve static web content.

The portal itself is completely Dockerized, with each service broken out into containers, with deployments managed by Jenkins, docker-compose, and an in-house customizable deploy-management suite called Camino (<https://github.com/TACC/Core-Portal>). The content management system (CMS) also exists as its own image and container, allowing for seamless upgrades and deployments targeting specific services, maximizing uptime.

API Tools

Agility and portability can be critical to achieving a rapid pace of iteration and discovery. Toward this end, 3dem.org uses Tapis version 3 as a common, unifying platform to harmonize the presentation of data, the publication of software applications (<https://github.com/james-labyer/3dem-apps>), and the provenance of analyses. As discussed, the portals provide a graphical, browser-based interface to the hardware infrastructure. These views were built on Tapis endpoints. Tapis managed the key functionality of the gateways, including managing user and data security.

Tapis is also accessible using powerful python libraries, Tapispy and TapisService (<https://tapis.readthedocs.io/en/latest/technical/pythondev.html>). These libraries enable the creation and maintenance of Tapis entities such as systems, applications, and jobs via a widely used language that is familiar to many scientists.

Application Deployment

Researchers can use the tooling and computing resources provided by TACC to make research software available via the 3dem.org workbench. The process begins with containerization: the desired software must be containerized before deployment via Tapis v3. Once the software has been containerized, it can be tested on TACC systems using an interactive development session or a DCV session that provides a GUI for applications with visualization requirements. Once the container is working, users can systematize the deployment of the container on TACC systems by creating a new Tapis application that stores the information needed to successfully deploy the container. The user can then run the new Tapis application from the 3dem.org workbench. Tapis applications are initially visible only to the user that created the application. Once the application has been tested, the user can request that an administrator make the application public, which makes the application available to all users via the 3dem.org workbench.

User Management

TACC has a robust, facile process for user enrollment into 3dem.org using the TACC User Portal combined with novel automation developed for these projects. Per-user quotas are not enforced, though user usage is tracked to ensure utilization efficiency.

Every user job, whether running on HPC or Cloud infrastructure, can be monitored for resource use efficiency. Metrics tracked include memory footprint, storage I/O, idle CPU, idle GPU, and network traffic. Historical records of each job are available for users to consult. In addition, TACC staff routinely survey the jobs database looking for usage that was less than optimally efficient. Staff members consult as needed with job owners to improve their computations, ensuring efficient use of federally-supported resources.

Hardware

TACC supports hierarchical, high-performance POSIX storage on the Stockyard and Corral filesystems, backed by TACC's Ranch tape archive for disaster recovery support. This storage is accessible to users on all TACC HPC and cloud computing platforms and used for data storage and analysis. TACC provides high-performance networking and data ingress services that demonstrably supports inbound data transfer rates of >1 TB/day. This is accomplished by operating a dedicated MinIO S3 server on an access node with 100GB/sec external networking to the public Internet. In addition, high-speed SSH, SFTP, and HTTPS access are provided.

TACC supports CPU and GPU compute capacity over the course of this program across Vista, Frontera, Stampede2, Stampede3, Lonestar5, Lonestar6, Jetstream, Jetstream2, and Maverick2 HPC systems [43–47]. This complement of systems allows users to run on a wide array of processor architectures including Intel, AMD, and NVIDIA. Cloud computing capacity is delivered via a combination of on-premises OpenStack and VMware clusters. Data storage, compute, network, and data transfer services operate at an availability of over 99%.

Discussion

We have described the capabilities of the NeuroNex 3dem.org portal, one of the many science gateways that have been deployed from the CEP and Tapis in recent years. The success of 3dem.org in serving its research community demonstrates the value of the template gateway approach. Due to the use of the CEP, the initial deployment of gateways can be rapid, with initial customization made available in less than a month. This efficiency highlights the robustness and adaptability of the template gateway model, which can be tailored swiftly to meet specific research needs. Collaboration was significantly enhanced through 3dem.org, with the impact and utility of the gateway in facilitating research and knowledge dissemination. The gateway's design makes it easy for researchers to locate and access relevant data, integrate it with other systems, and reuse it for various purposes.

Importantly, using a common gateway template is a key part of a long-term sustainability plan. This approach ensures that future CEP and Tapis updates can be shared quickly across all gateways, maintaining consistency and up-to-date functionality across the research community. Future functionality enhancements to 3dem.org can leverage these updates, for example, integrating automated workflows into 3dem.org using Tapis v3 workflow capabilities. Tapis v3 also serves as an API interface to external community resources, including software containers, distributed data stores, and external computing environments, enabling scalable and interoperable execution across platforms. While Tapis supports external system integration, 3dem.org currently operates solely on TACC-hosted resources, with the architecture designed to enable future extensions if needed. Users considering external integrations should account for authentication configuration and data transfer times. There are no data transfer fees incurred on the TACC side.

Providing the web-based GUI allows for execution of workflows without requiring command-line interaction or knowledge. Users do not need prior experience with schedulers, batch scripts, or container technologies. More advanced HPC familiarity becomes beneficial when users

wish to optimize application parameters for large-scale runs, develop and deploy new containerized applications, or integrate custom workflows via Tapis. To support onboarding, 3dem.org provides public tutorials, recorded workshops, example datasets, and responsive user support, allowing users to progressively deepen their engagement with HPC concepts as needed.

Leveraging HPC allows for scaling in both speed and size. In practice, application performance is influenced primarily by hardware memory constraints and by data movement. To mitigate this, some workflows on 3dem.org are structured to limit parallelism in order to optimize memory per process and to use in-node temporary storage when practical. As datasets grow, bottlenecks most commonly emerge when per-process memory requirements or shared filesystem I/O exceed the capabilities of a single node, rather than from insufficient aggregate compute capacity. Applications designed to scale across multiple nodes can overcome these limitations.

Adhering to the FAIR principles further supports sustainability by promoting practices that enhance the longevity and usability of the gateway. Long-term stewardship of public datasets on 3dem.org is supported through a combination of curated project spaces, persistent identifiers within the portal, and explicit versioning of both data and associated software artifacts. When public datasets evolve due to, for example, re-alignment or improved segmentation, prior versions are retained, with clear provenance linking derived outputs to their source inputs and software versions. The use of open and widely adopted file formats further reduces the risk of obsolescence as tools and platforms evolve, while containerized applications and shared workflows ensure that historical analyses remain reproducible over time. Community engagement is also central to our roadmap for long-term viability, with ongoing efforts to solicit user feedback and align development priorities with emerging use cases. These strategies aim to reinforce 3dem.org's role as a durable, community-driven gateway for volumetric imaging research.

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Declarations

Conflict of interest The authors have no financial or non-financial competing interests to declare that are relevant to the content of this article.

Research involving Human and/or Animal Participants No human or animal research was performed to produce the work detailed in the Methods of this manuscript. Datasets referenced and figures that include brain images rely on animal procedures approved by the Institutional Animal Care and Use Committees (IACUC) at the respective institutions where live animals were handled.

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