scientific reports

OPEN

Visualization and simulation of full-scale point-neuron circuits via the Neural Circuit Visualizer web platform

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Brain modeling has emerged as a fundamental tool for understanding neural mechanisms and information processing across different spatial and temporal scales. However, the simulation and visualization of realistic full-scale neural models remain a challenge. To address this, we developed the Neural Circuit Visualizer (NCV), a web-based platform for the flexible simulation and visualization of full-scale point-neuron circuits. We integrated state-of-the-art scientific advances, such as region-specific connectivity and the anatomical reconstruction of the mouse right hippocampal CA1 region, with resources and services from mature research infrastructures (e.g., Hippocampome.org, ebrains.eu, ebrains-italy.eu) and high-performance computing (HPC) facilities. The resulting online tool provides a public resource for the simulation and visualization of neural dynamics in full-scale point-neuron models and fosters the comprehension of neural mechanisms under physiological and pathological conditions. The tool is released as open source to encourage further collaborative development and integration.

Main

The hippocampus plays a fundamental role in cognitive functions such as learning, memory formation, and spatial navigation in both humans and rodents[1–7]. Research in data-driven rodent models has greatly improved our understanding of hippocampal dynamics, while direct experimental access to the human brain is still limited due to ethical and technological constraints[8,9]. Nonetheless, recent advances have allowed the collection of high-quality cellular human data[10–15]. In this context, computational modeling and interactive visualization have become essential tools in neuroscience that allow researchers to investigate how cellular-level characteristics, such as firing properties and connectivity, give rise to emergent large-scale dynamics within neural circuits[16,17]. Recently, browser-native applications have emerged and proven effective in their role of exploring simulations and large multimodal datasets using the web[18–20]. The number of studies integrating experimental and computational approaches are rapidly increasing and allow researchers to investigate brain dynamics and mechanisms across species. The growing availability of large-scale neural data, point-neuron, biologically and biophysically detailed models of brain cells and circuits requires the development of scalable and intuitive visualization platforms that enable exploratory analysis of neuronal dynamics[20,21]. In particular, tools provided with real-time interactivity to analyze multimodal spatiotemporal data can aid researchers in effectively interpreting how regional anatomy and neuron type-specific cellular properties may together give rise to observed activity patterns in brain tissue[22–25]. An adaptive, web-accessible framework may be especially useful when studying brain regions with large amounts of available data and complex neural anatomy and dynamics, such as the hippocampus, the cerebellum, and the cortex[8,26,27]. Recent improvements in extracellular electrophysiology, calcium imaging, and anatomical reconstruction have enabled the collection of rich high-dimensional datasets of subcortical and cortical regions, including the hippocampus[28–31]. Several neural modeling frameworks are widely used in the computational neuroscience community, such as NEURON[32–34], Brian[35,36], GENESIS[22], and NEST[37,38]. Also, open online resources have been recently developed to facilitate model building and optimization[39], such as

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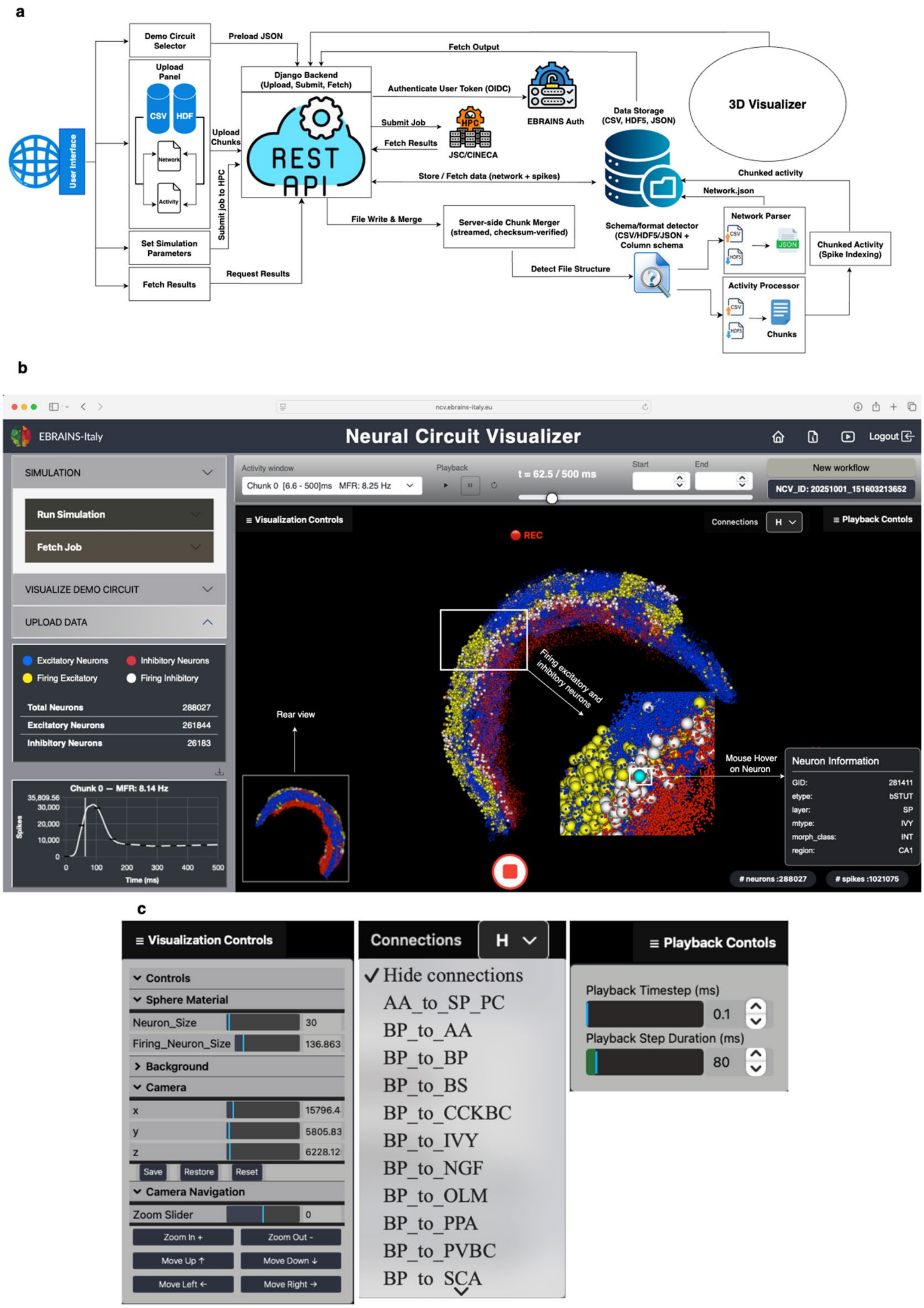

the EBRAINS Hodgkin-Huxley Neuron Builder[40] and the Hippocampus Hub[41]. These tools have facilitated in silico modeling and simulations from individual cells to a large ensembles of neurons with specific connectivity rules[42–44]. However, visualization tools have often provided only static figures and were implemented through desktop-based applications[23,26,45–47], with limited interactivity and scalability[48,49]. Parallel to this, the scientific and educational literature, together with current technological and computing resources, guide and support small and large-scale model building and selection[50–54]. Several public repositories have also emerged that facilitate sharing, collaboration, transparency, data reuse, and model interoperability. The OpenSourceBrain[55] and ModelDB[56] offer a collaborative platform to share and visualize neural models in standardized formats, e.g., NeuroML[57] and PyNN[58], and provide access to thousands of peer-reviewed neuron models implemented across simulators. The NeuroML-DB[59] provides a cross-indexed database of hundreds of standardized neural models, and the Blue Brain Project Cell Atlas[60] integrates neurotransmitter-based neuron types with region-

◀**Fig. 1**. NCV Software Architecture and homepage. **a**, The system architecture of the NCV comprises a browser-based frontend and a RESTful Python Django backend with three main components: (i) data ingestion, (ii) simulation submission and results fetching via communication with HPC job managers, and (iii) 3D visualization. Users interact with different panels for uploading files in CSV, HDF5 or SONATA H5 format, loading a demo circuit, configuring the simulation job, and fetching the simulation results. The user-uploaded files are submitted in chunks to the backend for faster delivery and browser timeouts prevention. They are merged back into a single file and classified by a schema/format detector for network and activity datasets. The network file is parsed into a JSON structured (i.e., network.json) file containing four columns, while the two-column activity file is divided into spike-timing chunks of 200 MB or less. These are stored in a shared data repository. The system logs users through the EBRAINS authentication system to grant them access to the HPC facilities. Job outputs are fetched from the HPCs, stored on disk and served to the frontend for display. The network structure and the dynamic spiking activity are then visualized using a GPU-accelerated WebGL frontend, offering exploration tools and spatiotemporal playback. **b**, From the top control panel, above the visualization canvas, users can select an activity window and play, pause, or reset the simulation using standard controls. The simulation time (t) is shown, and a slider allows manual browsing of the animation. Users can also set the visualization start and end times. The "New workflow" button generates a unique session identifier, which persists across the session, to track, log, and manage simulation runs. In the visualization canvas, blue and red spheres represent excitatory and inhibitory neurons, respectively, that turn yellow and white when emitting a spike. Detailed metadata about the neuron (e.g., global identifier, type, morphology type, and location) can be viewed in the bottom right panel, by hovering the mouse over the sphere. A rear-view inset provides an alternative perspective of the circuit, aiding orientation and spatial context. The interface also displays overall network information, including the total number of neurons and spikes (bottom right panel and labels). Additionally, a record button in the bottom part, allows to capture the neural activity and the user's action rendered in the main canvas. On the left, the "SIMULATION", "VISUALIZE DEMO CIRCUIT" and "UPLOAD DATA" panels enable users to either run or fetch jobs, view demo circuits, or upload user datasets (CSV, HDF5, SONATA H5). The number of excitatory and inhibitory hippocampal cells, along with an interactive (for activity browsing) firing rate histogram for the selected activity chunk, are also shown. **c**), control panels allowing the visualization to be customized in a fine-grained manner. The "Visualization Controls" panel enable users to set the neuron size and the firing neurons size, change the background color, and control the camera movements (translation, zoom, saving/restoring/resetting the circuit position). The "Connections" panel enables the visualization of a subset of synaptic pathways between specified neuronal classes (e.g., AxoAxonic (AA) to Stratum Pyramidale Pyramidal Cells (SP PC), Backprojection (BP) to AxoAxonic (AA), Bistratified cells (BS) to Parvalbumin positive cells (PVBC)), allowing the isolation of individual network motifs. The "Playback Controls" panel provides a high-level control of the visualization timing, allowing to set the simulation time steps to be displayed and the playback step duration.

specific anatomical details to facilitate data-driven modeling initiatives. Most of the modeling and repository tools require three-dimensional real-time interactivity functionalities to monitor the neural networks activity. Nonetheless, while many of these resources support relatively advanced features, they mainly focus on static models rather than supporting an intuitive interface to interactively visualize circuit dynamics within anatomically realistic 3D models of the brain. Additionally, several resources are not freely accessible online. Existing solutions often require technical setup, local installations, or HPC access[55,61–63], factors that limit their accessibility and usability for widespread scientific exploration. For example, ViSimpl[26] allows researchers to view and interactively playback neural simulation output data at the particle level, leveraging GPU power and providing multiple views across both space and time. This is useful for exploratory analysis of large cellular ensembles but can only be run locally after software installation and does not provide online functionalities. VisNEST[23] focuses on exploring large scale brain simulations at the population and brain area level, linking brain geometry with raster visualizations and spike-derived activity measures, but lacks spike-resolved interactive playback and three-dimensional, online views. Brainrender[62] addresses a different visualization issue and can produce high quality renderings of anatomically registered, atlas-based multimodal data. It supports interactive exploration, scripted workflows, and rendering benchmarks for large datasets. However, it is not intended to serve as an interface for spike-resolved neural simulations. Finally, TVB[63] is a whole-brain simulation platform that uses neural mass and field models and integrates the simulation and visualization of region-level signals into a single desktop and web-based application. Nonetheless, it lacks an online interface for single cells activity playback. A detailed comparative description of the above-mentioned tools with the NCV is provided in Table S1 of the Supplementary Materials.

To address current tools' and frameworks' limitations, we developed the Neural Circuit Visualizer[1] (NCV), a web-based platform for: (1) running the simulation of a full-scale circuit of the mouse right CA1 hippocampal region, fetching and visualizing the results; (2) uploading and visualizing the network topology and the spatial-temporal activity patterns of any brain region in three-dimensional views; (3) control the visualization and playback parameters through an interactive user-friendly interface (Fig. 1). The simulation of the full-scale hippocampal circuit is possible through a seamless integration of NCV with remote HPC systems (JSC-JUSUF[2]

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[1] https://ncv.ebrains-italy.eu.

[2] https://www.fz-juelich.de/en/ias/jsc/systems/supercomputers/jusuf.

and CINECA-G100[3]), where the circuit is hosted. At the same time, users can upload their own network and activity files in standardized formats (i.e., CSV, HDF5, and SONATA H5) for interactive exploration. Thanks to its filtering and simulation playback features, this visualization resource helps researchers to investigate region-specific brain dynamics at different temporal and spatial scales and in multiple conditions and activity regimes (e.g., physiological and pathological). Also, unlike existing visualization tools, NCV allows the playback of activity patterns from millions of neurons to flexibly investigate the dynamics in local microcircuits as well as in full-scale networks. Crucially, NCV allows to record and download a movie of the network and activity rendering, thus enabling users to capture the neural dynamics and their own actions during the interaction with the views. The movie can then be used for further analysis, reproducibility, and dissemination purposes.

Results

The NCV is a public online resource for the simulation and interactive visualization of full-scale neural circuits, with a focus on the hippocampal formation. The primary goals of this platform are: (1) to provide the neuroscience community with a user-friendly tool for configuring, simulating, loading, and visualizing a full-scale model of the mouse hippocampal CA1 region and (2) to allow the uploading and visualization of any neural circuit and its spiking activity-provided by the user- in an agnostic manner. For a better understanding of the anatomy and activity of the mouse hippocampal circuits, the resource includes a pre-integrated demonstration model comprising different regions, layers, and neuron types that the user can selectively filter in/out for visualization (preloaded explanatory spiking activity is also provided). As an example of a larger model, and to show the visualization capabilities of the tool when adopted for circuits with millions of neurons, a demo human CA1 model is also available. A user-friendly graphical interface allows to easily navigate the 3D circuit and its activity dynamics. The backend performs file handling, data validation, session management, and communication with HPCs systems (see Fig. 1a). Users can initiate new processes or retrieve previously launched simulation results by using a unique session ID. Neuron positions and spike data are processed by the system, after the files are loaded and displayed, via colored and size-changing particles that show excitatory and inhibitory neurons firing in an animated 3D space (see Fig. 1b). This architecture allows interactive spike dynamics exploration and submission and monitoring of computationally intensive simulations by keeping data preparation and visualization independent of each other (see Fig. 1c). Thanks to its features, the NCV offers an accessible and scalable solution for interactive neuroscience research at the circuit level.

Model parameter setting and job submission

To run mouse CA1 model simulations (see *Methods*), users are required to configure a basic set of execution parameters via the NCV interface before submitting full-scale simulations to the HPC facility of choice (see *The HPCs* and Fig. 2a). For configuring the mouse model, six parameters must be set: *INH2INH*, *INH2PYR*, *PYR2PYR*, and *PYR2INH* are dimensionless multiplicative factors of the synaptic weights that control the inhibitory-to-inhibitory, inhibitory-to-excitatory, excitatory-to-excitatory, and excitatory-to-inhibitory synaptic strength, respectively. Altogether, they influence the excitation–inhibition balance and their default values are tuned to match available experimental results[64].

Background weight represents the strength of the stimulating synaptic signals (i.e., spikes) individually delivered to all neurons in the network.

Background frequency represents the mean number of external stimuli delivered per second to each neuron, according to a Poisson distribution.

The job name corresponds to the unique ID of the session to facilitate tracking and reproducibility. Upon submission, the system validates the input data and transfers the job to a remote scheduler using a secure backend service. Through this interface, it is possible to access the HPC resources with no need for SLURM scripting or command-line operations, making the use of HPC resources accessible to non-experts. This design promotes reproducibility, scalability, and accessibility of data-driven modeling workflows (Supplementary Video 1 shows the full workflow, namely parameter configuration, job submission, and results fetching and visualization).

Model activity fetching and visualization

After the simulation job has been successfully executed on the HPC systems, NCV allows users to fetch, download and visualize the resulting data using an integrated "Fetch Results" panel (see Fig. 2b). Once the "Fetch jobs" button is clicked, a list of submitted jobs is displayed, and the users can choose the simulation to be fetched from the remote system. To perform the "Submit" and "Fetch" operations, users must have logged in (with their EBRAINS credentials[4]) through the "Login" button in the top panel of the GUI. This step ensures secure session-specific access to completed and active jobs. The retrieved results include a downloadable structured dataset (in. hdf5 format) containing a Global neuron Identifiers (GID) for each neuron, the corresponding spatial coordinates (x, y, z) and spike time vectors (see *File Formats and graphical representation*). The data are automatically parsed and loaded into the NCV front-end, the circuit is spatially rendered, and the spike activity is animated over the simulation period so that the user can observe the temporal evolution of neuronal dynamics in 3D. The NCV playback speed control, zooming, and camera navigation allows optimal exploration of neural dynamics such as pattern propagation, background activity and stimulus-response dynamics, in different regions, from diverse viewpoints, at different velocities and sampling values (see Fig. 1b).

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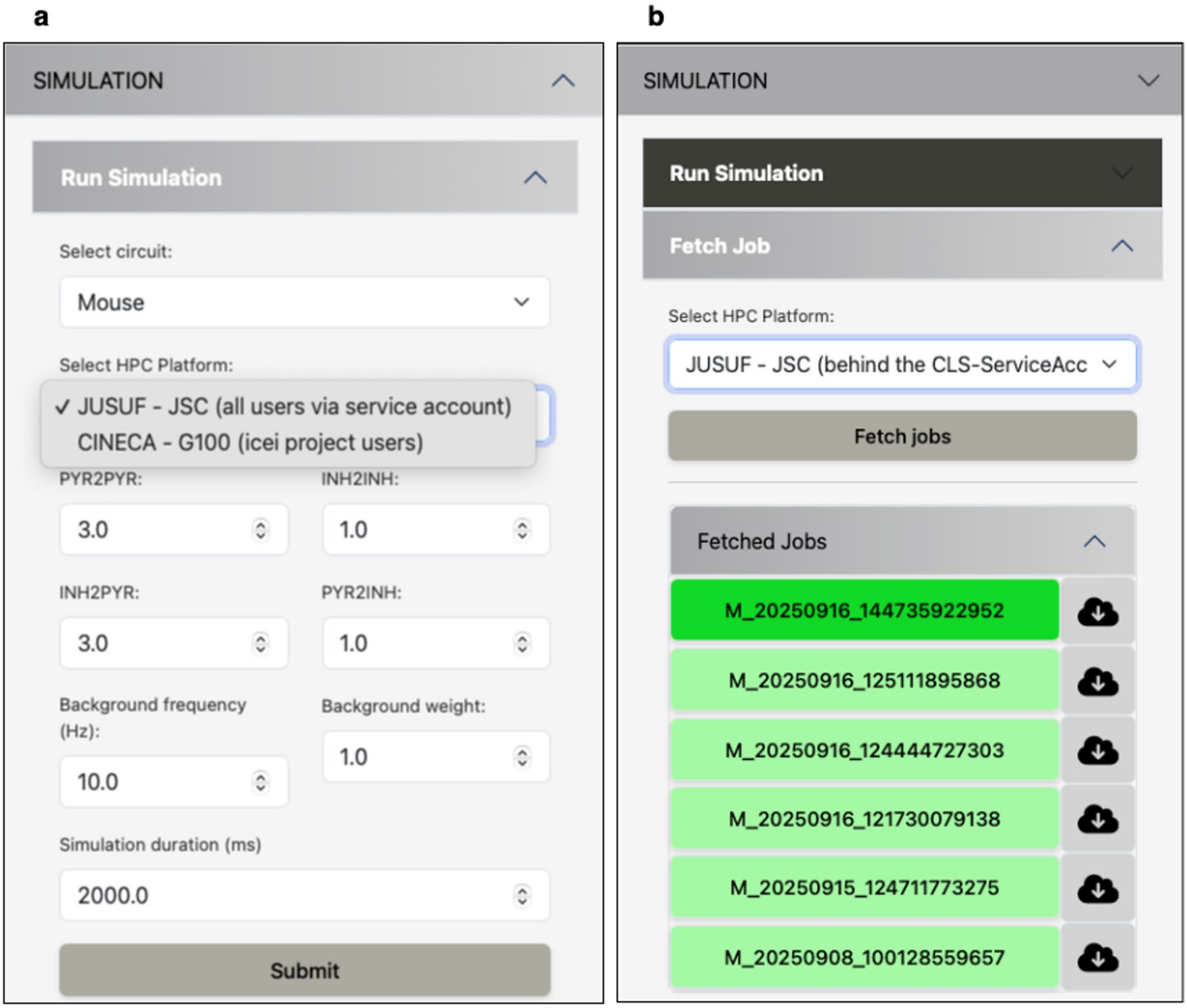
[3] https://www.hpc.cineca.it/systems/hardware/galileo100/.

[4] Registration, with an institutional email address, is available at https://www.ebrains.eu/page/sign-up.



Select circuit: Mouse

Select HPC Platform:
✓ JUSUF - JSC (all users via service account)
CINECA - G100 (icei project users)

PYR2PYR: 3.0

INH2INH: 1.0

INH2PYR: 3.0

PYR2INH: 1.0

Background frequency (Hz): 10.0

Background weight: 1.0

Simulation duration (ms): 2000.0

Select HPC Platform: JUSUF - JSC (behind the CLS-ServiceAcc

M_20250916_144735922952
M_20250916_125111895868
M_20250916_124444727303
M_20250916_121730079138
M_20250915_124711773275
M_20250908_100128559657

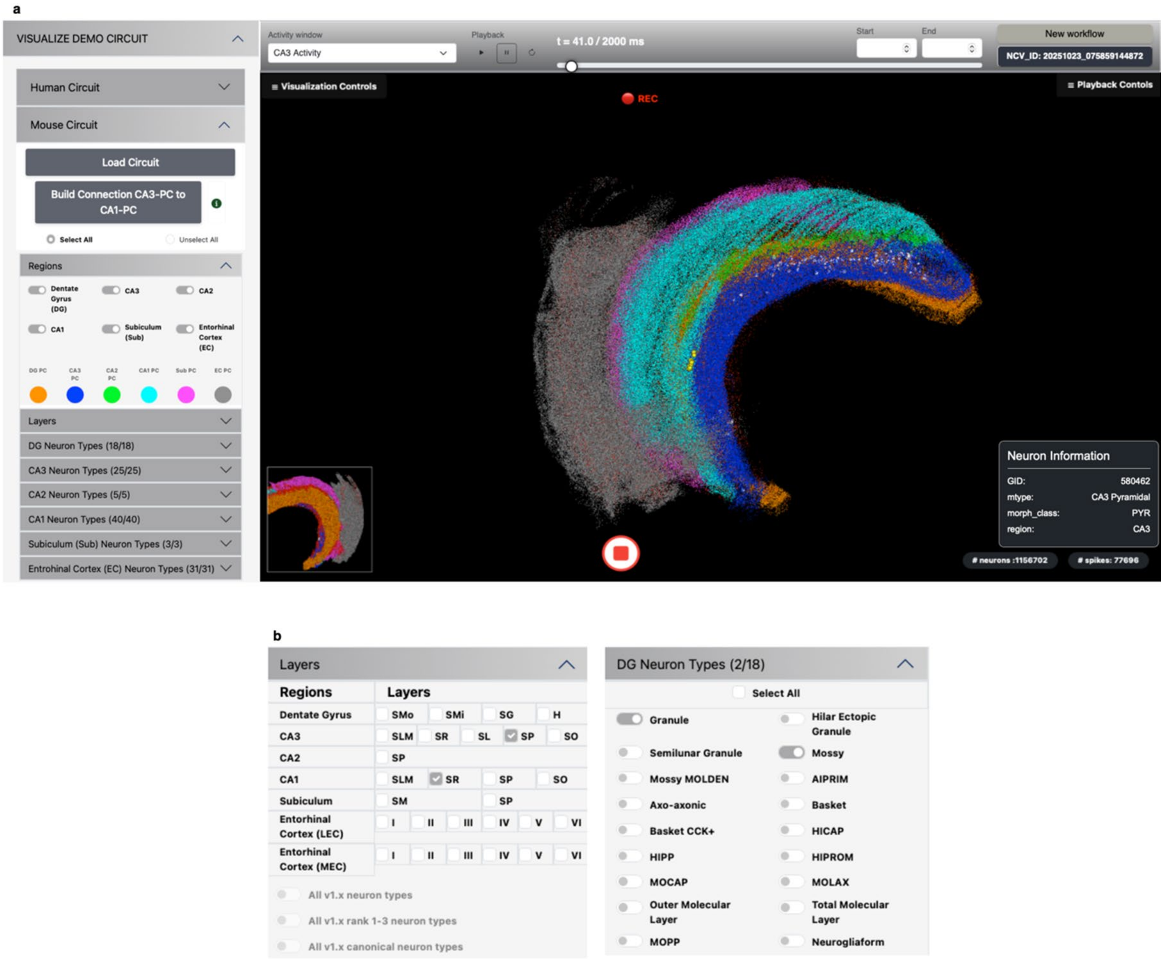
Fig. 2. Job submission and fetching. **a**, Users configure the model parameters in the "Run Simulation" panel. The circuit configuration file is filled in the backend and transparently sent to the HPC for job submission. **b**, users retrieve and load jobs output data into the visualization interface by accessing the Fetch Results panel. Spiking activity and neuron spatial coordinates are included in the returned files, which are automatically parsed and 3D-rendered. Both job submission and result fetching require the users to be authenticated through their EBRAINS credentials.

Case studies: mouse and human hippocampus

Two built-in demonstration circuits are included in the NCV to help the users familiarize themselves with the web-app features while providing activity visualization of two hippocampal networks. Both circuits are accessible from the "VISUALIZE DEMO CIRCUIT" dropdown panel.

Mouse hippocampus

The mouse hippocampal formation is a highly ordered structure comprising different subregions called CA3, CA2, CA1, subiculum, entorhinal cortex (EC), and dentate gyrus (DG). Each subregion has distinct cell types and layers. For every subregion, the NCV sources the list of all known neuron types from Hippocampome.org. Specifically, the Neuron Type Census section of Hippocampome.org provides the counts (population size) for 122 neuron types for both rats and mice across all six subregions, also specifying the neurotransmitter (glutamate or GABA). Moreover, the Morphology section indicates the laminar soma location for each type (e.g., DG mossy cells have soma located in the hilus). For every neuron type, the NCV samples from the mouse brain cell atlas[60] a number of locations in the appropriate subregion and layer corresponding to the Hippocampome.org count. When a neuron type has somata across multiple layers (e.g., CA3 bistratified interneurons having soma in both stratum oriens and stratum pyramidale), the NCV splits the count equally between them (see *Methods*). The interface supports fine-grained loading of partial or full circuits for interactive, detailed visualization and allows customizable color coding for improved anatomical contrast. Specifically, selections can be filtered by anatomical subregion (e.g., only neurons in DG) and/or neuron types (e.g., only granule cells and DG axo-axonic cells) by toggling intuitive check-boxes in real time on the graphical interface. Users can also load pre-integrated activity datasets from recently released, large-scale, data-driven spiking neural network simulations of specific hippocampal subregion dynamics, namely resting-state oscillations in CA3[65] and grid cell firing during exploratory navigation in medial EC[66] (Fig. 3 and Supplementary Video 2). Moreover, users can invoke a projection module to generate connections from CA3 pyramidal cells (CA3PCs) to CA1 pyramidal cells (CA1PCs) based on canonical topological rules. Specifically, the neuron type counts provided by Hippocampome.org are used to calculate divergence ratios (see *CA3 to CA1 Pyramidal Neurons Projections*). Spike propagation across the laminar structure of mouse CA1 is displayed and can be interactively controlled by playback speed, zoom, and recording of the movie as shown in (Fig. 4).



Activity window: CA3 Activity

t = 41.0 / 2000 ms

NCV_ID: 20251023_075859144872

Neuron Information

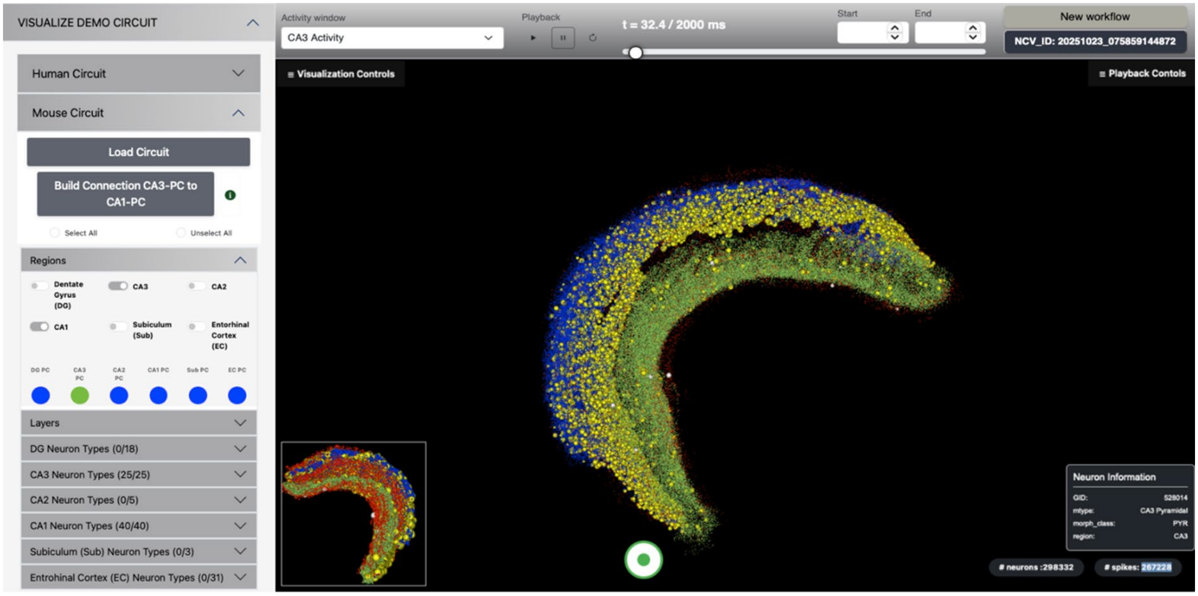
GID: 580462
mtype: CA3 Pyramidal
morph_class: PYR
region: CA3

neurons :1156702

spikes: 77696

Regions	Layers					
Dentate Gyrus	☐ SMo	☐ SMi	☐ SG	☐ H		
CA3	☐ SLM	☐ SR	☐ SL	☑ SP	☐ SO	
CA2	☐ SP					
CA1	☐ SLM	☑ SR	☐ SP	☐ SO		
Subiculum	☐ SM	☐ SP				
Entorhinal Cortex (LEC)	☐ I	☐ II	☐ III	☐ IV	☐ V	☐ VI
Entorhinal Cortex (MEC)	☐ I	☐ II	☐ III	☐ IV	☐ V	☐ VI

Fig. 3. Full mouse hippocampal formation.**a**, The Visualize Demo Circuit panel allows users to load pre-integrated mouse hippocampal circuits and activities. Selecting Mouse Circuit will automatically populate the canvas with the network's 3D rendering. The user is then able to load the network activity, build the CA3-PC to CA1-PC connections (via dedicated buttons) and launch the spiking activity playbacks. Once the circuit is loaded, the anatomical regions, layers and neuron types to be displayed can be selected and the visualization colors customized. Neuron types can be filtered based on versioned types (canonical, ranked types) and grouped by region in collapsible lists **b**, filtering menus offer hierarchical selection of layers and neuron types of the full mouse hippocampus. Different laminae can be selected (e.g. CA1: Stratum Radiatum (SR), Stratum Pyramidale (SP), Stratum Oriens (SO); Dentate Gyrus (DG): Stratum Moleculare outer (SMo), Stratum Moleculare inner (Smi), Stratum Granulosum (SG), Hilus (H)) and individual cell classes toggled (e.g., granule, mossy, basket, axo-axonic). Users can also visualize hippocampal diversity at three levels of granularity according to hippocampome.org, v1.x: (i) all neuron types, the full set of known cell types in terms of both axonal-dendritic distribution and neurotransmitter and molecular and electrophysiological properties; (ii) rank 1–3 neuron types, a more confident category with the most confident experimental evidence; and (iii) canonical neuron types, a smaller set whose prototype morphology is one cell class and provides a simplified but comprehensive view of hippocampal circuit. This hierarchical selection enables precise tailoring of the circuit reconstructions, facilitating analyses of regions, layers, and cell types within hippocampal networks.



Activity window: CA3 Activity

t = 32.4 / 2000 ms

NCV_ID: 20251023_075859144872

Neuron Information

GID: 528014
mtype: CA3 Pyramidal
morph_class: PYR
region: CA3

neurons :298332

spikes: 267228

Fig. 4. CA3 to CA1 Pyramidal cells projections. When loading the mouse model via the "Load Circuit" button, the entire mouse hippocampal neuron census data from Hippocampome.org is fed to the NCV frontend. CA1 (blue) neurons are activated by CA3 (red) cells firing. In both regions, yellow and white neurons represent excitatory and inhibitory firing neurons, respectively.

CA3 to CA1 pyramidal neurons projections

The CA3 pyramidal cells (CA3PCs) create long-distance excitatory projections to CA1 pyramidal cells (CA1PCs) through the Schaffer collaterals. The large number of connections between these two layers has been one of the excitatory pathways most extensively characterized within the mammalian hippocampus. The NCV mouse hippocampus demonstration circuit has a special module that replicates the large-scale organization and sparse connectivity of CA3-to-CA1 connections in an understandable biological way. The census ratio between CA1 and CA3 pyramidal populations is then used to compute the number of postsynaptic targets per CA3PC and, only for demonstration and ease of visualization purposes, connections are produced within each regional pair through a Gaussian-weighted distance sampling (see *Methods*).

The adaptation of this scale parameter will ensure that neurons that are physically close to one another are more likely to connect while ensuring that the connectivity patterns maintain a global sparse structure throughout the entire CA1 region and the anatomical connectivity was also established to provide a network mapping in line with existing anatomical data (see *Methods*).

The propagation of excitatory activity of CA3 to CA1 pyramidal neurons is demonstrated in Fig. 4 and Supplementary Video 2, where simulated spike events represent how localized CA3 activity (from 267,228 neurons) causes spatially structured and temporally consistent patterns of activation in CA1.

The resulting connectivity map is anatomically constrained, quantitatively grounded, and modularly extensible, forming a robust basis for circuit-scale simulation and visualization within the NCV platform.

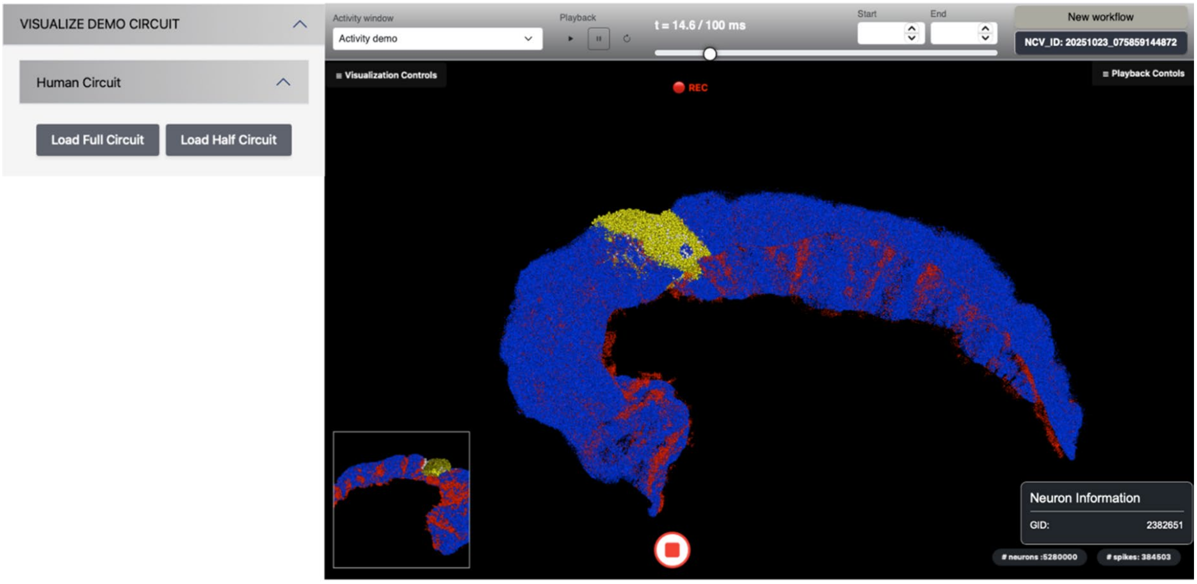
Human hippocampus

An example activity of the human hippocampus model, described in *Case studies* section, is presented. The neural activity available for this demo use case counts 384,503 spike events and lasts 100 ms. The pre-loaded spike dataset shows an example of how neural dynamics can propagate throughout the entire brain structure, and it can be used for teaching and exploratory analysis demonstrations. Exploration through the human CA1 scaffold can be viewed in Fig. 5, which shows the capability of exploring through the curved structure of a human hippocampus in real-time.

Discussion

The Neural Circuit Visualizer (NCV) addresses a significant gap in computational neuroscience: the lack of an online, interactive, anatomically grounded tool for simulating and visualizing neural spiking behavior in large-scale neural networks. Several frameworks exist for model building and optimization, such as NEURON[33], NEST[37], Brian[36], and BluePyOpt[39]. While enabling biologically realistic neural simulations, however, most of them lack intuitive and interactive frontends for anatomically represented data exploration; even when present, they require local installation or are limited to small ensembles of neurons.

NCV fills this gap with a full-stack web application for interactive exploration and simulation of biologically structured neural circuits. This resource provides support for both pre-integrated and user-uploaded hippocampal network data in common standard formats (CSV, HDF5, SONATA H5) and allows online rendering of spike activity in 3D networks. Integration with the EBRAINS[8] and EBRAINS-Italy infrastructures and HPC resources



Activity window: Activity demo

t = 14.6 / 100 ms

NCV_ID: 20251023_075859144872

GID: 2382651

neurons :5280000

spikes: 384503

Fig. 5. View of human CA1 circuit. Users can load either the full-scale or the half-scale version of the reconstructed CA1 region on the Human Circuit, load the network spiking activity and finally play it back with the dedicated controls.

such as JSC JUSUF and CINECA Galileo100 ensures scalability and reproducibility. The tool supports mouse circuit configurations and simulations, allowing the comparative exploration of diverse hippocampal dynamics in silico. Thanks to its fine-tuned visualization functionalities, the NCV helps researchers explore region- and cell type-specific activity to disentangle the role of anatomical domains (e.g., dorsal vs. ventral, proximal vs. distal) in regulating emergent spatiotemporal dynamics. NCV is based on community-curated resources such as Hippocampome.org[67,68] to provide biologically grounded inputs. Also, in the pre-loaded demo mouse circuit, CA3-CA1 pyramidal connections are modeled using a scaled Gaussian-weighted approach and anchored to empirical synaptic density estimates from Hippocampome.org[69].

One of the key features of the NCV is the opportunity for users to upload their own network and activity data. Potentially, any brain region can be explored, provided that the uploaded files fulfill the format requirements. In fact, different simulation frameworks and tools have specific input/output data formats, and it is a common practice for users to perform post-processing operations with ad-hoc code, for visualization purposes. Thanks to the NCV, users are spared this additional work, and the only required operation is the conversion of the neuron positions and spike timings in one of the open formats compatible with the tool (i.e.,.csv,.hdf5 and SONATA.h5, see *File Formats and graphical representation*).

While the current version of the NCV allows interaction with HPCs and exploration of mouse hippocampal circuits, different upgrades and additional functionalities are being designed and implemented for future releases. The CA1 mouse model we make available for simulation through the NCV (i.e., a circuit featuring the complete connectivity map and the neuron copies covering the experimental variability range, as described in[70]) is unprecedented and unpublished. Although in this version, a limited set of parameters can be configured (i.e., the background characteristics and the connection strength between different types of neurons), we believe that users can take advantage of the current ensemble of configurable network properties to investigate the behavior of the full-scale hippocampal model in different conditions, where connection strength and background activity are affected. Nonetheless, we are also currently investigating the model's behavior, in additional different scenarios, following a stimulation protocol (manuscript in preparation, code and algorithm to be released upon publication). Hence, a future release of the NCV will be extended with additional features such as the possibility to deliver specific stimulation to circuit slices or selected neuron ensembles, giving the possibility to investigate more complex dynamics such as oscillations and neural avalanches. Furthermore, while the main objective of the resource presented here is to provide a stable and robust visualization and simulation tool and the analysis provided are minimal, we plan to integrate the NCV with additional quantitative analysis tools, such as studies in the frequency domain at different spatial scales and the investigation of repeated spike patterns. In addition, even though the model is not suited to integrating neuronal morphological details (to the advantage of execution speed and spatial scale) we plan to make available to the users -in a dedicated section of the User Guide- the 3D morphological representation of the neural cell types implemented in the circuit.

The NCV brings together structural, functional, and anatomical dimensions of large-scale neural circuits in a unified framework, thereby expanding the computational neuroscientist's toolkit to validate, analyze, and interpret neural models in a tractable and scalable way. We believe that this novel resource provides new opportunities to leverage in silico models simulation with the aim of analyzing and visually exploring neural circuit activity. This may lead to better decoding the brain mechanisms underlying higher functions, such as memory and navigation, in both physiological and pathological conditions.

Methods

Mouse CA1 model

Users can configure and run a network model of the mouse CA1 circuit constructed according to a previously developed anatomy-driven strategy[29]. The circuit is available on the EBRAINS Knowledge Graph[5] and on the ModelDB portal[6]. In this approach, the placement and connectivity of neurons are determined from volume-based connection rules and biologically motivated spatial distributions. Each neuron's probabilistic axonal and dendritic fields are thus modeled as ellipsoidal volumes that approximate the neuritic arborizations observed in reconstructed morphologies. Synaptic connectivity is established by the spatial overlap between pre- and postsynaptic fields, and the resultant network topology adheres to known anatomical restrictions like cell density, laminar structure, and layer-specific targeting (e.g., CA3 pyramidal axon projecting to CA1 stratum radiatum). The model's distance-dependent connection probability, modulated by the spatial relationship between regions helps to preserve dorsal-ventral and proximal-distal topography in the circuit. Individual neurons are implemented by point-neuron models previously presented and validated[70]. The single cell model captures important electrophysiological characteristics common to rodent species, including firing thresholds, integration dynamics, and synaptic responsiveness -despite initially being created for the rat hippocampal region- and allows to simulate large populations in a scalable manner. For the circuit visualization in the NCV we used a tiling technique[68] to scale the network to biologically realistic dimensions. This method replicates a validated local microcircuit consisting of anatomically limited neuron placements and connection patterns over space to cover the entire hippocampal region. While spatial alignment among adjacent tiles preserves anatomical continuity and avoids edge artifacts, each tile maintains internal consistency regarding cell type distribution, density, and connectivity. This approach effectively builds morphologically faithful circuits on a large scale without sacrificing computational scalability or biological realism.

Human CA1 model

To help users familiarize with the tool and experiment circuit and activity visualization of large networks (i.e., comprising millions of cells), a model of the CA1 region of the human hippocampus is available in the demo section. The model was recently introduced by[72] and its scaffold maintains laminar structure, spatial curvature and somatic density gradients recovered using high resolution BigBrain histological data[73]. A total of 5.28 million neurons were placed within three-dimensional space comprising approximately 4.8 million pyramidal cells and 0.48 million interneurons, which are spatially distributed based on experimentally determined excitatory-inhibitory ratios[72,74]. The morphologies of neurons were parameterized by probability density functions dendrite cones, axon tubes or ellipsoids scaled to human dimensions with scaling based on rodent morphology[72,75]. The connectivity was created by overlaying axonal convex hulls on dendritic point clouds, and then pruned to remove likely connections according to connection probabilities in rodent hippocampal data, by class[69].

To demonstrate this point, NEST simulations of the scaffold were performed with point-neuron models (HT_neurons) and standard Tsodyks-Markram synapses[76]. An example simulation is made available as pre-integrated model in the NCV.

Whole hippocampal formation mouse model

In addition to the mouse and human CA1 models described above, whole mouse hippocampal formation model is available as a pre-loaded demo use case. This model encompasses all subregions of the hippocampus such dentate gyrus, CA3, CA2, CA1 Subiculum and the medial and lateral Entorhinal Cortex (MEC, LEC) I through VI and is detailed at the level of neuron types. Specifically, NCV sources the spatial distribution[77] and population size[78] of over 100 morphologically, molecularly, and biophysically identified neuron types -including both glutamatergic principal cells and GABAergic interneurons- from the open access knowledge base Hippocampome.org[72,73]. To ensure realistic spatial embedding throughout the hippocampus formation, neuron somata were spatially distributed using 3D coordinates derived from the Blue Brain Project (BBP) Cell Atlas[60]. An interactive menu allows users to toggle on or off any desired subsets of neuron types, entire sub-regions, and layers.

CA3-CA1 Pyramidal cell connectome model

On top of this 3D model, NCV includes a biologically realistic model of hippocampal CA3-CA1 pyramidal cell projection, implemented using literature-based connectivity rules[79] and anatomically anchored data sources[80]. A multi-step approach, based on anatomical domains and synaptic stoichiometry, was used to establish connectivity according to the values reported in Table S2 in the Supplementary Materials. To obtain quantitative estimates of the number of synapses, the average dendritic length of CA1 pyramidal cells in the Stratum Radiatum (SR) and Stratum Oriens (SO) was first extracted from the "Synaptic Probability" menu on Hippocampome.org[69]. The volume-based scaling factors translated rat-derived values into mouse-specific estimates[69]. The full SR length was kept since it is the primary input zone for CA3 projections, but the SO length was cut in half to discount CA1-CA1 connectivity. Scaled dendritic length multiplied by average linear spine density (spines/μm) was used to determine total synapse counts. The number of presynaptic CA3PCs innervating each CA1PC was then estimated by dividing these by the average number of synapses formed per axon (~ 7.24, based on CA3→CA3 connectivity data from Hippocampome.org), and divergence was calculated by normalizing the convergence ratio to the known population sizes of CA3PCs and CA1PCs[68]. To produce the connectivity map, a Gaussian

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[5] https://search.kg.ebrains.eu/?category=Model&q=gandolfi#d4cbd970-057a-4b75-8228-dbe603d765ac.

[6] https://modeldb.science/267531.

weighted distance function was applied to each pair of neurons, CA3-CA1 in which the likelihood of connection formation declined exponentially with square of the Euclidean distance between somata.

The following Gaussian kernel was used:

$$P_{ij} = exp\left(-\frac{d_{ij}^2}{2\sigma^2}\right)$$

where $\mathbf{d}_{\mathbf{ij}}$ is the three-dimensional distance between neurons i and j and σ (sigma = 0.3) is the scale parameter that is adapted based on the average geometric dimensions of the CA1 pyramidal layer.

To ensure physiological sparsity and avoid network over-connectivity, a maximum in-degree of 510 CA3 Cellular inputs per CA1 Cell and a mean out-degree of about 54 CA3 cell targets per CA3 cell were imposed (5% of the maximized anatomical fan-out). For an exhaustive view of the model parameter, see Table 2 in the Supplementary Materials.

Network topology and activity visualization

The spatiotemporal data considered for 3D neuron visualization represent the dynamics of neuronal activity within a defined network. The 3D spatial coordinates position cell bodies to visualize a full-scale neural circuit of excitatory and inhibitory neurons, while the temporal dynamics of their activity are captured by their spike times (see *File Formats and graphical representation*). Specifically, the position of each neuron j (x_j, y_j, z_j) is associated with a discrete sequence of spike times S_j = {ts_j}. Spikes are displayed as animations appearing at the location of the 3D neurons during specified time points ts_j. Neuronal firing is indicated by single neurons turning yellow for excitatory (blue) cells and white for inhibitory (red) cells. For better visualization, firing neurons (i.e., yellow or white) are displayed with a larger diameter and stay active for 2ms simulation time. Zooming, rotating, and panning features enable an interactive exploration of the neuronal population. By integrating structural and functional aspects, this framework provides an effective way to visualize the dynamic activity of neuronal networks in 3D space. Additionally, any neuron can be hovered over to provide detailed metadata in real-time (including global identifier (GID), electrophysiological type (etype), laminar position, morphological class, and regional attribution), allowing interactive exploration of individual cell contributions to circuit activity (see Fig. 1b). Importantly, users can also record movies of these visualizations to capture the neural activity and the users' actions for further investigations, qualitative and quantitative analysis.

The NCV software architecture

The NCV interactive web-based platform consists of a client-side frontend and a server-side backend component (see Fig. 1a). The source code is publicly available online (see *Code availability*). The user-friendly frontend is implemented using HTML, JavaScript, and CSS, enabling easy point-and-click interactions. The 3D rendering for neurons relies on a three.js[7] wrapper and WebGL content, which is natively supported by the engine of modern browsers. The backend, implemented through the Python Django web framework[8] based on Python[9], is deployed on a dedicated virtual machine (VM), in the EBRAINS-Italy research infrastructure, hosted on the CINECA supercomputing center[10]. The VM configuration has 32 VirtualCPUs (VCPUs) and 24GB RAM. The frontend and backend reside on the same VM; however, they are logically separated, and their communication takes place via dedicated Representational State Transfer (REST) application programming interface (API) calls. The backend is responsible for data fetching, management, file generation, and replies to requests by the frontend. It manages the VM file system and is run by a dedicated system user with limited rights, in order to increase security and diminish vulnerability. The web server uses NGINX and the uWSGI web interfaces, which serve client requests and guarantees scalability. The Hypertext Transfer Protocol Secure (HTTPS) ensures client-server communication security. To test the robustness of the NCV software architecture and implementation, we performed scalability and reproducibility tests by benchmarking the system on networks of increasing size of 10k, 100k, 1 M and 5 M neurons (see section tests are reported in Table S3 of the Supplementary Materials).

File formats and graphical representation

NCV allows users to upload network and activity file(s) with spatial coordinates and spike data to be visualized for arbitrary neuronal populations. The platform accepts data representing the temporal dynamics of neuronal activity and topology of neural circuits in three structured formats:.csv (Comma-Separated Values),.hdf5 (Hierarchical Data Format version 5) and SONATA.h5 files. If.csv or SONATA.h5 files are adopted, users must upload two files: one for the network topology (e.g., network.csv) and one for the network activity (e.g., activity.csv). The network file includes spatial information in four columns; the first column contains the GIDs for each cell j, while columns 2–4 specify the corresponding spatial coordinates x_j, y_j, and z_j in micrometers (μm). In addition, for the.csv network file, users can add a fifth column indicating the cell type (i.e., inhibitory or excitatory), thus affecting the color-based visualization interface. The same holds for the SONATA.h5, for which cell type can be uploaded in.csv format (when this file is not uploaded, all cells will be considered excitatory – see the NCV online User Guide). The activity file contains two columns. The first column includes the neurons' GIDs, while the second contains the floating-point data type corresponding to spike times ts_j in milliseconds (ms). In case the.hdf5 is adopted, the network topology and the neurons' activity are contained in the same file under

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[7] https://threejs.org.
[8] www.djangoproject.com.
[9] http://www.python.org.
[10] https://www.cineca.it/en.

different data structures (i.e., network and activity) implemented using the same formatting as the.csv file (i.e., the same number of columns and data content). This format is particularly suitable for large simulations because it allows faster data access[81] and is the default spike data output format for the NEST simulator. When files are uploaded, the backend automatically verifies and parses them for rendering. If the uploaded files are larger than 200 MB, they are split into 200 MB chunks (this value can slightly change, depending on the splitting process performed on the backend), representing specific activity time windows (see Fig. 1a) that can be individually selected for visualization. The formats accepted by NCV ensure compatibility with standard simulation tools, aiming at providing greater flexibility in using the NCV with neural circuits of varying scales and complexity.

The HPCs

The full-scale model of the CA1 mouse hippocampus, comprises hundreds of thousands of neurons and requires HPC resources for a simulation run able to provide scientifically meaningful results. To allow any user -including those with no credentials on any supercomputer, such as students or independent researchers- to submit a simulation job, we installed the circuit on the JSC-JUSUF system and appropriately configured a dedicated service account utility, thoroughly described in[40]. Briefly, this backend service first verifies that the users have correctly logged in, via their EBRAINS credentials, in the NCV (see *Model activity fetching and visualization*). After the credentials verification is performed successfully, the user is allowed to submit a simulation job in a transparent way (no system configuration, such as setting the number of nodes or the job duration, is required. Users are granted a predefined quota (initially, 5000 node/hours) that is decremented after every job execution. In case an individual user's quota has been entirely consumed, the user can request additional resources by writing to the corresponding author of this article.

In addition to the JUSUF supercomputer, we also installed the model on the CINECA Galileo 100 system, leveraging HPC resources made available through the EBRAINS-Italy computational resources. Currently, the latter can be exclusively used by CINECA users, as the service account is not yet available on the Galileo 100 system. NCV users with or without account and resources on CINECA that are interested in using this HPC facility can contact the corresponding author of this manuscript. Through the Run Simulation panel (see Fig. 2a) users can monitor the status of the submitted jobs (e.g., QUEUED, PENDING, SUCCESSFUL) and fetch the completed job results for visualization and data analysis.

To evaluate the performance metrics on the resource requirements, we simulated 35 s activity of the mouse CA1 hippocampus on CINECA Galileo100[11], by adopting four different configurations: connectivity and background weights set to 1 in all cases and background frequency set to 1 Hz, 5 Hz, 10 Hz, 20 Hz, respectively. Each simulation ran on 2 nodes (equipped with 384GiB/node) and used 24 CPUs per node. The four simulations generated an increasing number of spikes (i.e., ~ 4.4 M, ~ 6.4 M, ~7 M and ~ 7.7 M) and output files size (i.e., ~ 64 MB, ~ 85 MB, ~ 91 MB, ~ 100 MB) as the background frequency increased but used approximately the same amount of memory (~ 18.7 Gb) each. As per the wall-clock time, little variations were observed (i.e., ~1h10min, 1h11min, 1h12min and 1h13min, in the four configurations) thanks to the optimized implementation of the point-neuron hippocampal models[71].

Data availability

The simulation data are generated (via HPC systems) by individual users and are only accessible to them for download and visualization through the NCV tool (https://ncv.ebrains-italy.eu/).

Code availability

NCV code is publicly available at the following link:
https://github.com/cnr-ibf-pa/NeuralCircuitVisualizer.

Received: 23 December 2025; Accepted: 12 March 2026

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[11] https://docs.hpc.cineca.it/hpc/galileo.html.

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Author contributions

M.M., G.A.A., L.L.B. designed the research; M.A., L.L.B., R.S., E.S., S.A.M. and S.M.G.S. conceived the software architecture; M.A. implemented the code with help from R.S., E.S. and L.L.B.; M.A. and L.L.B. designed the supplementary materials and made the videos; M.A. wrote the manuscript with help from L.L.B. and G.A.A.; All authors reviewed the manuscript.

Funding

This work was supported by the European Union, NextGenerationEU (Project IR0000011, CUP B51E22000150006, “EBRAINS-Italy”), the EU project 101147319 (EBRAINS2.0) and by NIH grant R0139600 to G.A.A. This work was also supported by the Italian Ministry of University and Research through the “FeNeL” project, PNRR M4.C2.1.1 – PRIN 2022 – No. 2022JE5SK2 – CUP G53D23000380006 and PRIN 2022 (20228RMXBE, project HIPPOCOMP).

Declarations

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-026-44588-0.

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