MoMo - Combining Neuron Morphology and Connectivity for Interactive Motif Analysis in Connectomes

M. Shewarega[*1,2], J. Troidl[*1], O. Alvarado Rodriguez[3], M. Dindoost[3], P. Harth[4], H. Haberkern[5], J. Stegmaier[2], D. Bader[3], H. Pfister[1]

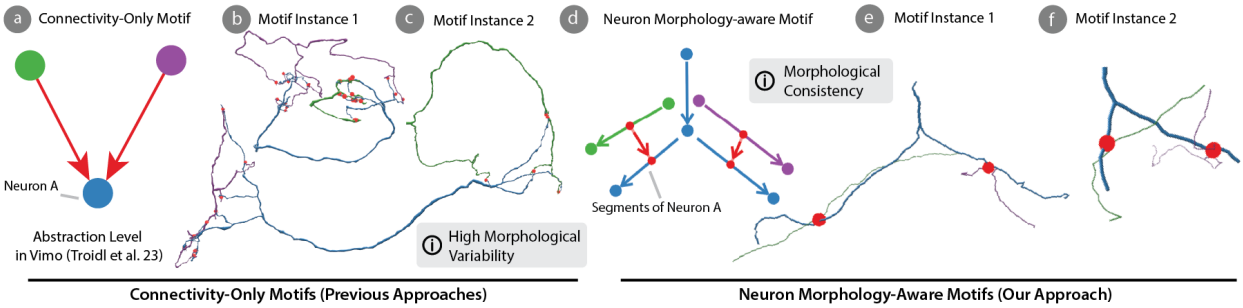


Fig. 1: **Connectivity-only vs. Neuron Morphology-Aware Motif Analysis.** (a) Previous work [39, 67] has focused on interactive motif analysis, where neurons are represented as simple nodes connected through synapses. (b, c) This representation lacks scientifically relevant neuron morphology, leading to ambiguity in motif queries. (d) Our approach integrates neuron morphology into motif queries and enables searching motifs interactively by explicitly sketching neuron segments and their respective synapses. (e, f) Hence, users can perform targeted queries for both morphological and connectivity patterns. Data: FlyEM Hemibrain (a-c) [56], MICrONS (d-f) [64].

Abstract—Connectomics, a subfield of neuroscience, reconstructs structural and functional brain maps at synapse-level resolution. These complex spatial maps consist of tree-like neurons interconnected by synapses. Motif analysis is a widely used method for identifying recurring subgraph patterns in connectomes. These motifs, thus, potentially represent fundamental units of information processing. However, existing computational tools often oversimplify neurons as mere nodes in a graph, disregarding their intricate morphologies. In this paper, we introduce *MoMo*, a novel interactive visualization framework for analyzing *neuron morphology-aware motifs* in large connectome graphs. First, we propose an advanced graph data structure that integrates both neuronal morphology and synaptic connectivity. This enables highly efficient, parallel subgraph isomorphism searches, allowing for interactive morphological motif queries. Second, we develop a sketch-based interface that facilitates the intuitive exploration of morphology-based motifs within our new data structure. Users can conduct interactive motif searches on state-of-the-art connectomes and visualize results as interactive 3D renderings. We present a detailed goal and task analysis for motif exploration in connectomes, incorporating neuron morphology. Finally, we evaluate *MoMo* through case studies with four domain experts, who asses the tool's usefulness and effectiveness in motif exploration, and relevance to real-world neuroscience research. The source code for *MoMo* is available here.

Index Terms—Visual motif analysis, Scientific visualization, Neuroscience, Connectomics.

1 Introduction

Connectomics is a rapidly advancing subfield of neuroscience focused on mapping the intricate network of connections between neurons down to the level of individual synapses. The overarching goal is constructing a comprehensive wiring diagram of an organism's nervous system. Recent breakthroughs [16, 29, 55, 63] in imaging and automated neuron reconstruction have made this vision increasingly tangible. This resulted in the publication of a complete connectome of the fruit fly brain [15] as well as cubic-millimeter-scale connectomes of both mouse [64] and human [59] brain tissue. These datasets now enable scientists to trace complete neural circuits that underlie all aspects of information processing in the brain. Analyzing such circuits has already yielded transformative insights into the neural basis of behavior. For instance, studies of the fly connectome have advanced our understanding of navigation [28], vision [46], and motor control [35], among many others. However, extracting meaningful information from large-scale connectomes remains an enormous challenge due to several key factors. First, modern connectomes are extraordinarily large, exceeding a petabyte size, making them computationally intensive to process. Second, neurons are complex, tree-like structures that extend across significant spatial distances. This morphology complicates the interpretation and querying of connectivity. Third, the connectivity graphs are extremely dense: a single neuron can form synapses with over 1,000 partners, rendering traditional node-link diagrams ineffective for visual analysis. To address this complexity, neuroscientists often employ motif analysis [61] as a divide-and-conquer strategy, breaking down large connectomes into smaller, more interpretable subgraphs. For example, motifs in the H01 dataset [59] have been identified based on strong pairwise connections via multiple nearby synapses. Similarly, motifs involving compass neurons in the fruit fly's central brain have elucidated mechanisms for encoding directional information [28]. Crucially, these analyses consider both synaptic connectivity and neuron morphology. Nonetheless, current interactive tools for connectomic analysis [38, 39, 51, 67] lack support for querying networks based on both synaptic connectivity and morphological structure.

In this paper, we present *MoMo*, a novel interactive visualization and analysis tool designed to enable neuron morphology-aware mo-

- [1] *School of Engineering & Applied Sciences, Harvard University*
- [2] *Institute of Imaging and Computer Vision, RWTH Aachen University*
- [3] *New Jersey Institute of Technology (NJIT)*
- [4] *Zuse Institute Berlin*
- [5] *University of Würzburg*
- * *co-first author*

Manuscript received xx xxx. 201x; accepted xx xxx. 201x. Date of Publication xx xxx. 201x; date of current version xx xxx. 201x. For information on obtaining reprints of this article, please send e-mail to: reprints@ieee.org. Digital Object Identifier: xx.xxxx/TVCG.201x.xxxxxxx

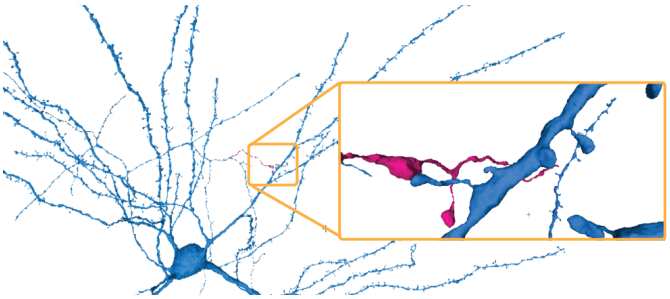


Fig. 2: **Data Overview.** Modern connectomics reconstructs tens of thousands of neurons connected through millions of synapses. Here, we show a single neuron (blue) and a single synaptic connection to a pink neuron (orange box). Data: Human cerebral cortex / H01 [59].

tif analysis in large-scale connectome graphs. Our contributions are four-fold: **(1)** First, we conduct a detailed study of domain-specific goals for interactive motif analysis incorporating neuron morphology. Based on these insights, we derive a set of analytical tasks that *MoMo* must support to meet neuroscientists' needs. **(2)** Second, we introduce a novel graph-based data representation for connectomes that jointly encodes synapse-level connectivity and neuronal morphology (Sec. 6). In this model, each neuron is composed of interconnected segments reflecting its branching structure, and synaptic connections link these segments across neurons. This structure dramatically reduces data size compared to voxel-based representations and enables the use of established graph analysis techniques for efficient data processing. **(3)** Third, we implement a Jupyter-based prototype of *MoMo* that supports the full set of analysis tasks. The tool features an intuitive sketching interface that allows users to draw motifs—including both morphological components and synaptic connections—as query patterns. These sketches are used to search the underlying graph representation, and matching instances are visualized in interactive 3D renderings, allowing detailed inspection of how motifs are embedded within neural tissue. **(4)** Fourth, we evaluate *MoMo* through pilot and case studies on two state-of-the-art connectome datasets, conducted in collaboration with expert neuroscientists. Each neuroscientist selected a phenomenon of interest, such as *shunting/lateral inhibition* or *center-surround receptive fields*, and successfully sketched and queried for corresponding motifs. *MoMo* enabled experts to analyze potential instances of these phenomena by sketching individual neuron segments and synapses—granularity not supported by existing cell-level abstractions (see Section 10 for examples).

2 Related Work

Visualizing Connectomes. Beyer et al. [7] present a comprehensive survey on interactive visualization techniques for connectome analysis. Prior work in this space can be broadly categorized into four areas: (a) data structures and algorithms for interactive connectome analysis [5, 6, 22, 24, 60], (b) interactive spatial exploration [4, 25, 44, 54, 65], (c) connectivity analysis [1, 20, 21, 54, 67–69], and (d) visualization for scientific communication [10, 11]. Ganglberger et al. [22] present a spatially-driven visual analytics framework for iterative exploration of large, heterogeneous brain datasets. While their approach enables flexible navigation and multimodal data encoding, it lacks fine-grained motif search at the level of individual neuron segments and synapses. *MoMo* advances the state of the art at the intersection of interactive spatial analysis, connectivity analysis, and data representations for connectomics. In contrast to previous systems, which typically support separate exploration of neuronal morphology and connectivity [67], *MoMo* enables integrated, interactive queries that jointly consider both aspects. This is achieved through a novel graph-based representation derived directly from neuronal skeletons, allowing morphology-aware motif searches. Existing approaches often abstract the connectome as simple node-link diagrams, with nodes representing entire neurons and edges denoting synaptic connections. While other representations, such as dendrograms [62], embed aspects of neuronal structure, they do not support flexible, targeted motif queries. By bridging structural morphology and connectivity, *MoMo* supports new modes of interactive analysis in large-scale connectomic datasets.

Visual Motif Analysis. Visualizing network motifs is a well-established task in network visualization [9, 18, 33], with conventional techniques primarily applied to domains such as social networks, citation graphs, and web connectivity. However, these approaches do not directly extend to connectomic data due to the inherently three-dimensional spatial structure of neurons—the nodes of connectome graphs—which introduces domain-specific challenges for motif visualization. To address this, Vimo [67] introduced an interactive system for constructing and querying motifs within connectomes. *MoMo* builds on this foundation by enabling the specification and analysis of morphological motifs—substructures that incorporate both neuronal branching geometry and precise synaptic connectivity. This extension allows users to define queries that account for spatially and structurally localized connectivity patterns, a critical feature for understanding neural circuits. In parallel, computational methods have been proposed for motif detection in connectomics. Matejek et al. [37] presented a parallelized algorithm for efficient motif enumeration in large-scale brain datasets. At the same time, DotMotif [39] introduced a domain-specific language designed to express motif queries in a concise, readable form, with backend integration into Python and Cypher [19]. While these systems focus on computational efficiency and query abstraction, *MoMo* complements them by providing an interactive, visual environment tailored to spatially embedded morphological motifs in connectome data.

Visual Graph Query Interfaces. Interactive visual graph query interfaces have been explored in various domains, such as bibliographic data [72], and genomics data [42], among many others. Visage [49, 50] shows how visual graph query interfaces can simplify pattern analysis in simple conventional graphs, such as movie and actor networks derived from Rotten Tomatoes. Follow-up work [48] has investigated new visualization approaches to inspect and analyze motif query results in conventional graphs. However, those previous approaches do not translate directly to morphological brain motif analysis since these approaches are designed for data without three-dimensional spatial context. VisualNeo [27] aims to bridge the design for graph query engines and visual graph query interfaces through a custom-designed software system. VIIQ [30] simplifies interactive query construction using an edge suggestion algorithm. Diehl et al. [13] propose a sketch-based query system for spatio-temporal patterns, allowing users to visually search time-series motifs. While conceptually related to our sketching interface, their approach focuses on temporal data and lacks support for spatially embedded morphology. In contrast, *MoMo* operates on 3D neuron structures, accounting for both spatial positioning and branching geometry during queries.

Multi-layer & Micro-vascular networks. McGee et al. [41] survey the state of the art in multi-layer network visualization. Most relevant to our work are multiplex network visualizations [8, 45], which are defined by the presence of various edge types. However, most use cases center around applications in sociology. Most similar to our work is the visualization of vascular networks [23]. For example, Mayerich et al. [40] visualize volumetric vascular data using techniques from volume rendering and do not explicitly extract the graph information.

Previous Connectivity Motif Workflow. Vimo [67] offers a user-friendly interface that allows users to draw motifs using a data abstraction where each node represents an entire neuron and each edge represents a synaptic connection between neurons. While this abstraction simplifies the visualization and allows for an overview of which neurons are connected, it has significant limitations. One major limitation of Vimo's approach is its lack of detailed morphology information. In Vimo, each neuron is represented as a single node, which means the internal structure—such as the exact locations of synapses, branching points, and neuron morphology—is completely lost. This makes it impossible to perform fine-grained analyses that require insight into the internal pathways and synaptic organization within a neuron.

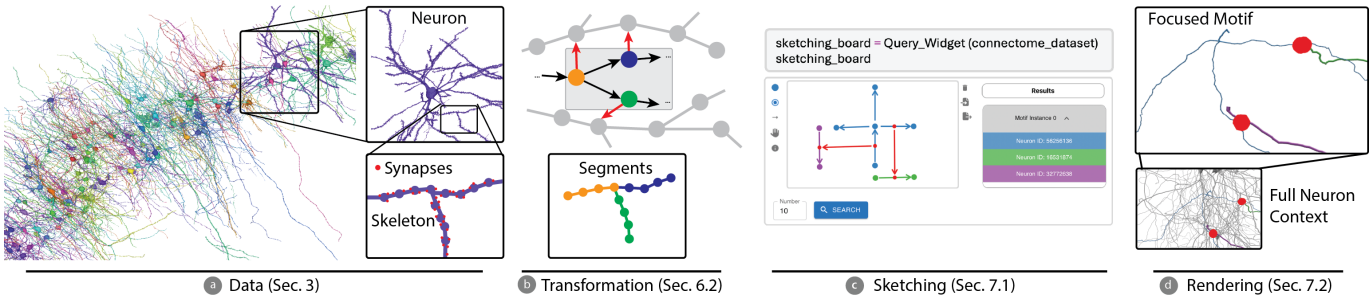


Fig. 3: ***MoMo* Workflow.** (a) Given a connectome dataset, we (b) transform the respective neurons and synapses into our neuron morphology-aware graph representation. Each node in the graph depicts a neuron segment that is connected to other segments through synaptic connections (red arrows) or to neighboring segments (black arrows). (c) The transformed dataset is interactivley queried by sketching motifs. (d) Finally, users can explore identified motif instances in interactive 3D renderings and highlight the motif's morphology through a focus & context approach. Data: Human temporal cortex / H01 [59] (a), MICrONS [3] (d).

3 Biological Background

Neuroscience Fundamentals. Brain tissue consists of neurons, among other cells, that are connected through synapses [26] (see Fig. 2). Neurons are complex, tree-like spatial structures that connect in various spatial configurations. The spatial configuration of neuron connectivity can heavily influence the underlying function of the respective neuronal circuit. The resulting network diagrams are exceptionally dense, with current connectome datasets exceeding tens of thousands of neurons interconnected through millions of synapses.

Connectomics Data. Creating connectomes is an involved process that starts with acquiring 3D image volumes, typically using electron [55] or optical [63] microscopes. The resulting volumes are then segmented using 3D convolutional neural networks [29]. Next, the automatically reconstructed neurons and synapses undergo human or automated proofreading [16, 32, 66, 71], eliminating errors from the previous steps. Here, we demonstrate our approach on two exemplary state-of-the-art connectomes. We use the *FlyWire* connectome [15] for insect neurons and the *MICrONS* dataset [64], which reconstructs approximately one cubic millimeter of mouse visual cortex. For both datasets, *MoMo* uses neuron skeletons and synaptic point annotations.

Motif Analysis in Connectomes. Neuronal connectivity motifs are fundamental building blocks of computation in the brain. Many neuroscientific studies [15, 28, 59] are searching and analyzing structural and connectivity motifs in the brain. For example, Hulse et al. [28] report a group of neurons in the fruit fly's central brain that form motifs, which allow flexible spatial navigation and action selection. Another exemplary motif that combines specific connectivity and neuron morphology patterns is the concept of *shunting inhibition* [31, 43]. Shunting inhibition is a fundamental mechanism in neural computation, where inhibitory synapses modulate the excitability of a neuron by altering its input resistance. This mechanism effectively "shunts" incoming excitatory signals, thereby regulating synaptic integration and influencing the neuron's ability to fire an action potential. Shunting inhibition is crucial in various neural processes such as sensory processing or network synchronization, among others. We report an example of *shunting inhibition* in the case study (see Sec. 10).

4 Goals and Task Analysis

The idea of integrating neuron morphology into tools for motif analysis originated while struggling to represent biologically relevant motifs [59] during the development of Vimo [67]. As a result, we discussed extending Vimo to morphological motifs in informal interviews with four domain experts at an international connectomics conference and research visits at both the Harvard Center for Brain Science and Howard Hughes Medical Institute (HHMI) Janelia. All scientists are leading experts in analyzing neuronal circuits reconstructed from high-resolution electron microscopy data. Two experts focus on analyzing mammalian brain tissue, while the others specialize in the fruit fly (*Drosophila*) brain. Following the design study methodology from Sedlmair et al. [58], we distilled the following goals and tasks.

4.1 Domain Goals

G1 - Quick Identification of Motifs. Hypothesis generation and exploratory analysis are critical while analyzing connectome circuits. Additionally, data exploration may generate new hypotheses, which in turn requires rapidly iterating specific motifs of interests. Thus, domain experts need tools to quickly identify various motifs of interest.

G2 - Precise Connectivity and Morphology Searches. The function of neuronal circuits is governed by both neuron morphology and synaptic connectivity [28, 59]. Queries such as *"Which neurons have multisynaptic connections on the same neuronal branch?"* or *"Which neuron pairs have connectivity clusters on separate branches?"* are common questions in connectome analysis. Thus, neuroscientists need tools to find morphological motifs in conjunction with network motifs.

G3 - Accurate Spatial Analysis of Motif Instances. After identifying motifs involving neuron morphology and synaptic connectivity, domain experts want to inspect spatial models of the respective neurons and their connectivity. When inspecting neurons and their connectivity, neuroscientists need to (a) view accurate 3D models while (b) correlating the motif query to the original neuronal data.

G4 - Flexibility & Data Adaptability. Connectome analysis is a fast-paced scientific discipline with dozens of datasets published annually. Datasets are typically made accessible to the neuroscience community through various platforms [16, 34, 51], which offer simple pythonic interfaces for targeted data retrieval. Thus, scientists need flexible tools that integrate into established, notebook-based analysis workflows without building custom data interfaces.

4.2 Tasks

T1 - Fast Morphological Motif Queries. Scientists need to define motif queries rapidly but also require computationally efficient subgraph isomorphism searches to identify motifs of interest quickly. (**G1**)

T2 - Interactive Sketching-based Queries. Scientists need to precisely define neuron morphology and synaptic connectivity patterns without learning complex graph query languages like Cypher [19] or Gremlin [52]. Interactive sketching-based drawing interfaces are expressive but do not require extensive graph query coding skills to define morphology-aware motifs. (**G1**, **G2**)

T3 - Correlating Motif Structure with 3D Renderings. After a successful query, users must identify the motif structure in a detailed 3D rendering of the respective neurons. (**G3**)

T4 - Analyze Motifs in Hyrid Code-UI Workflow. The computational Jupyter Notebook environment brings ease of Python-based data handling and interactive visualization components closer together. Here, data can be loaded directly from various hosting platforms into respective interactive visualization widgets. (**G4**)

5 *MoMo* Design and Workflow

MoMo provides an intuitive platform for visualizing and analyzing motifs in connectome data that integrates into the computational analysis workflow of connectomics scientists, which often involves data

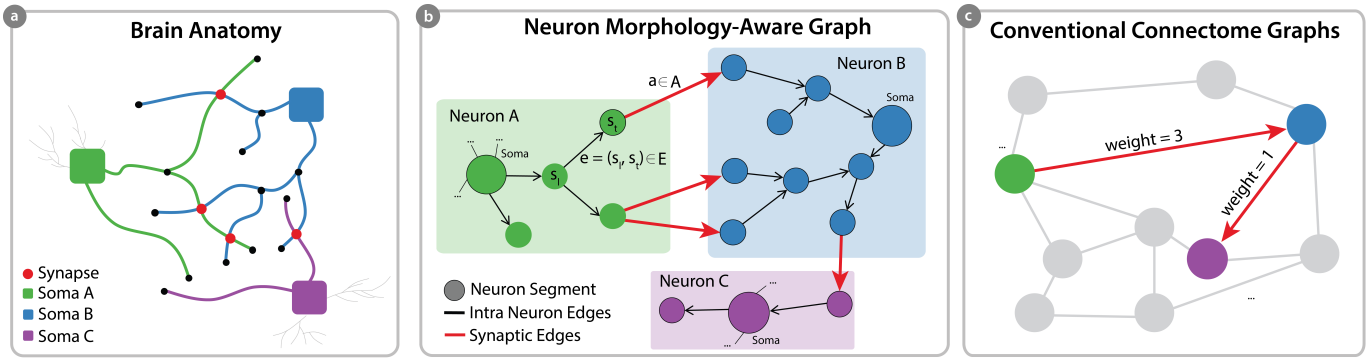


Fig. 4: **Neuron Morphology-Aware Graph**. (a) Neurons build networks through complex tree-like arbors (dendrites/axons) that extend from each neuron's soma. (b) Our graph representation captures the structure of wiring patterns by mapping each branch segment to a single graph node. Synaptic connections between segments are shown as red edges, while neighboring segments are connected through black edges. (c) Conventional connectome graph representations from previous work [38, 67] discard neuron shape information and fully abstract neurons into single graph nodes.

analysis scripts in Python-based Jupyter Notebooks. Jupyter Notebooks provide a robust and interactive environment for quick experimentation and effective visualization. Hence, we designed *MoMo* as a Python package to launch interactive Jupyter widgets for visualization. Users are empowered to programmatically manipulate data before feeding it into *MoMo* but can still use interactive visualization through custom widgets **(G4)**. We designed a simple workflow for *MoMo* (see Fig. 3):
Data Transformation (Sec. 6.2). The first step involves transforming the desired connectome dataset into the *neuron morphology-aware data representation*, which enables efficient motif queries (**G2**).
Sketching (Sec. 7.1). Users interactively draw a motif at the neuron segment level using the *sketching interface* (see Fig. 6) **(G1, G2)**. After the user defines a motif, *MoMo* enables highly performant isomorphic subgraph queries (Sec. 8) to identify sets of neurons that implement the sketched morphology and connectivity pattern (**G1**).
Spatial Motif Rendering (Sec. 7.2). After selecting particular motif instances, *MoMo* allows interactive 3D visualization of the respective neurons and their synapses and highlights the motif's region of interest, such as highlighting the drawn segments in the visualization (**G3**).

6 Neuron Morphology-Aware Motifs

Neuron morphology-aware motifs combine patterns related to neuron shape and their synaptic connectivity. In our proposed graph representation, a set of segments represents a single neuron (see Fig. 4b). Each segment is connected to neighboring segments or, through synaptic connections, to segments of another neuron. This contrasts previous connectome graphs where each neuron is represented as a single node connected by weighted edges indicating synapse count (see Fig. 4c).

6.1 Formal Definition

Fundamentally, we construct a two-layer network, where one level describes *neuron connectivity* and the other layer *neuron morphology*. The connectivity layer abstracts the connectome as a directed graph $K = (N, C)$, where a set of neurons $N = \{n_0, ..., n_v\}$ is connected through at set of synapses $C = \{c_0, ..., c_u\}$. In the morphology layer, each tree-like neuron $n \in N$ can be formalized as an acyclic skeleton graph $n = (V, E)$. V is a set of 3D coordinates (vertices) connected through a set of edges E that describe the neuron's centerline. Each synapse $c_{ij} = \{p \in \mathbb{R}^3, (i, j)\} \in C$ stores both a spatial position p and the indices (i, j) of the respective pre- and postsynaptic neurons. Here, we build a graph G that captures *both* neuron morphology *and* neuron connectivity. First, we partition each neuron skeleton $n \in N$ into segments (Fig. 5). A segment s is a set of vertices V_s and edges E_s between two consecutive branching or terminal vertices. Formally, a segment s is defined as

$$s = (V_s, E_s),\ E_s = \{(v_i, v_{i+1}) | 0 \leq i < k\},\ V_s \subset V, E_s \subset E. \quad (1)$$

Additionally, all vertices but the start v_0 and endpoint v_k must have degree 2. Each segment always consists of two or more vertices.

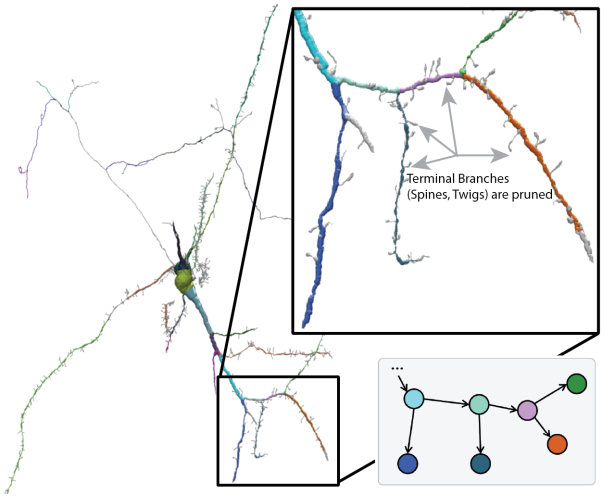


Fig. 5: **Neuron Segments**. We partition each neuron into a set of segments. In our graph structure, each node represents a single segment. Neighboring segments are connected through edges. Terminal branches, such as spines or skeletonization artifacts/twigs, are being pruned during the data transformation. Data: Human temporal cortex / H01 [59].

$$\forall v \in V_s \setminus \{v_0, v_k\}, \deg(v) = 2 \quad \text{and} \quad |V_S| \geq 2 \quad (2)$$

For each segment s, we also store a set of synapses $C(s)$ that connect s to another neuron's segment. Finally, we combine both layers in a neuron-morphology-aware graph $G = (S, E, A)$. The vertices $S = \bigcup_{i=0}^{v} s_i$ are the union of all previously computed segments. There are two types of edges. The first edge type E connects neighboring segments s_l, s_t of the *same* neuron n_m,

$$E = \{(s_l^{n_m}, s_t^{n_m}), ...\}. \quad (3)$$

The second edge type A defines neuron connectivity and thus connects two segments of *different* neurons if they share synapses.

$$A = \{(s_l^{n_i}, s_t^{n_j}) |\ c_{ij} \in C(s^{n_i}) \wedge c_{ij} \in C(s^{n_j})\}. \quad (4)$$

Next, given a motif M, we search for isomorphic subgraphs in G, such that

$$M \cong G' \subseteq G,$$

where G' is an induced subgraph of G. M and G' are isomorphic.

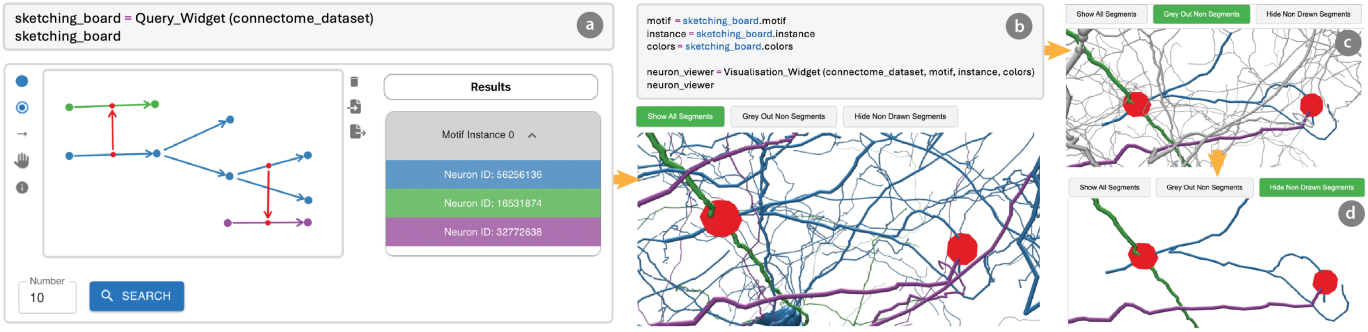


Fig. 6: **Interactive Motif Sketching & Interactive 3D Rendering.** (a) Users start by sketching neuron segments and their synaptic connectivity using an interactive drawing board within a jupyter widget. Next, users can search for matching instances. A list of found motif instances is then displayed in the results panel. (b) Neurons of identified motif instances can be inspected in an interactive 3D rendering shown in a jupyter widget. Synapse locations are shown in red. (c) We allow users to grey out interactively or (d) hide neuron arbors not involved in the sketched motif to simplify creating correspondence with the motif sketch and the 3D spatial neuronal anatomy. Data: MICrONS [3].

6.2 Data Transformation

Connectome data must be transformed into our graph representation. Skeletons are a standard and readily available format for representing 3D neuron data in connectomes. Skeletons store sample x,y,z coordinates and the radius along the centerline of a neuron. Transforming a set of skeletons and their respective synapses into our graph representation involves the following steps:

Pruning Terminal Branches. Neurons frequently contain numerous small terminal branches, such as spines or artifacts from the skeletonization procedure, that can obscure meaningful segment creation (see Fig. 5). Thus, we iteratively prune terminal branches below a specified threshold t. Determining t depends on the properties of the datasets and is a hyperparameter of our graph representation. The goal is to suppress non-meaningful fine-scale morphology (e.g., spines or skeletonization noise) while preserving subcellular structures relevant for motif detection. As a rule of thumb, the pruning threshold should exceed the average spine length to avoid losing meaningful structures. We evaluated thresholds ranging from 1–5 µm on pilot datasets, assessing their impact on noise reduction and motif preservation. Based on empirical results and expert feedback, we selected dataset-specific pruning factors, with exact values reported in Section 9.

Synapse to Skeleton Mapping. Next, we establish a mapping between the location p of synapse and the closest skeleton vertex of its pre- and postsynaptic partner neuron. This mapping is necessary to determine which synapses correspond to which neuron segments.

Skeleton Downsampling. Next, we abstract the pruned neurons by focusing on more significant structural elements—the paths between branching points and endpoints. The exact curvature of these paths is disregarded to reduce computational complexity while maintaining essential connectivity. Thus, we downsample each neuron skeleton, so only branching points and endpoints remain. Branching- and endpoints are shown as black dots in Figure 4a. Those remaining points are a compact representation of the neuron's arborization patterns.

Graph Assembly. The next step is restructuring the downsampled neurons into our neuron morphology-aware data representation. Neuron segments, defined as paths between branching points or endpoints, are represented as individual *nodes*. Neighboring segment nodes are connected through *intra neuron edges* (Fig 4b - black arrows). Synaptic connections between segments of different neurons become *inter neuron edges* types (Fig 4b - red arrows). Note that other properties such as neuronal compartmentalization (axon/dendrite) or synapse polarity (inhibitorty / excitatory) can be easily mapped to nodes and edges as well. The final graph can now be used to query morphological motifs.

Complexity. The transformation of skeleton and synapse data into our graph representation scales linearly with dataset size. Let N be the number of neurons, E the average number of skeletal segments per neuron, and S the average number of synapses per neuron, yielding a total time complexity of $\mathcal{O}(N \cdot (E+S))$.

The pipeline includes loading skeletons, pruning small branches, downsampling, snapping synapses to skeleton nodes, and graph assembly. Each neuron is processed independently, making the pipeline easily parallelizable.

On standard hardware, we construct a morphology-aware graph for 12,000 neurons and 500,000 synapses (FlyWire) in under 10 minutes on a 64-core machine with 256 GB RAM. For smaller datasets like MICrONS (1,700 neurons, 150,000 synapses), processing takes under 90 seconds. Memory usage scales linearly with neuron segments and synapses, driven mainly by connectivity and metadata storage.

For very large datasets (>100k neurons), users can parallelize processing across cores or machines, as neurons and their synapses are handled independently, supporting distributed execution at connectome scale.

7 Motif Visualization

In *MoMo*, visualizing neuron morphology-aware motifs is done through motif sketching and interactive 3D rendering of motif instances. We considered alternatives like visual subgraph selection, where users pick observed multisynaptic patterns directly from the visualization, and rule-based motif definitions using logical or structural constraints. While visual selection is intuitive for highlighting known patterns, it relies on clean subgraph separation and does not scale well. Rule-based queries offer flexibility but are harder to express and computationally intensive. We chose sketch-based input for its speed, intuitiveness, and support for hypothesis-driven exploration.MS: TODO: citations

7.1 Motif Sketching

The sketching board provides an interface for users to create motif sketches by defining neurons with distinct colors and specifying synaptic connections (Fig. 6a). Each node in the sketch represents either a branching point or an endpoint, while neuron segments are drawn in different colors selected from a menu, where each color corresponds to a distinct neuron. Users can add synaptic connections by selecting the appropriate tool and linking previously drawn segments (red edges). Both neuron segments and synaptic connections are directed, reflecting the natural flow of signals within and between neurons.

For example, Figure 6 illustrates a motif composed of three neurons (green, blue, and purple) and two synaptic connections. The *sketching board* accepts connectome datasets formatted in the neuron morphology-aware graph representation, allowing users to query the dataset based on the drawn motif. Matched motifs are dynamically displayed in a results list for exploration.

Querying for Morphological Motifs. Once the sketch is complete, users can initiate a query by pressing a designated button and specifying the desired number of results. The *MoMo* backend processes the request and returns a list of motifs matching the drawn example.

Reviewing Found Instances. Query results are displayed in a list view, where each detected motif instance is enumerated. Neuron IDs

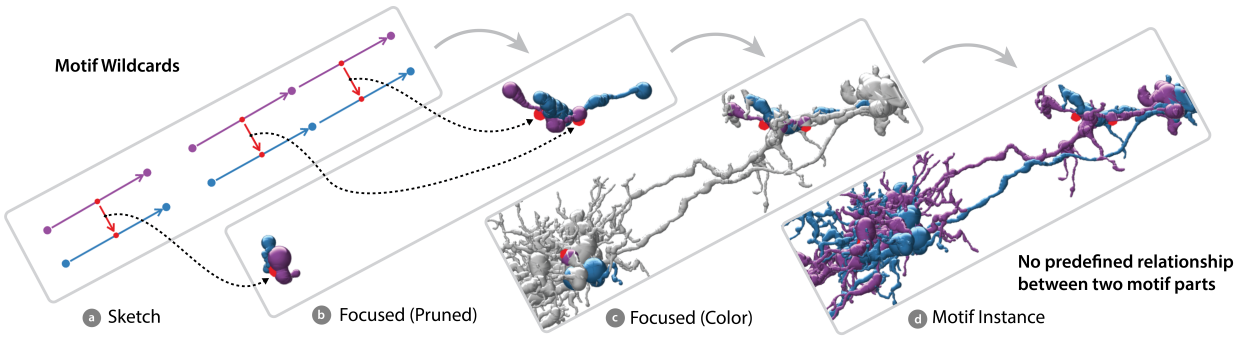


Fig. 7: **Wildcard Feature.** (a) *MoMo* enables users to leave specific parts of the motif query undefined. (b) This enables flexible motif discovery, such as identifying multiple distinct synaptic clusters. (c, d) A focus and context strategy is used to better correlate the motif sketch to the true neuroanatomy rendering. We allow users to gray out or hide neuronal branches unrelated to the sketched motif. Data: FlyWire [15]. MS: TODO Change caption and references to the fig in the text

corresponding to the drawn segments are grouped and highlighted using the same colors as in the sketch for easy interpretation.

Sketch Reproduction and Sharing. Users can import and export motif sketches as JSON files, preserving segment information for future queries or sharing with collaborators, facilitating reproducibility and collaborative research.

7.2 Spatial Motif Rendering

MoMo provides an interactive 3D exploration of motif instances (see Fig. 6). After selecting a queried motif instance from the result list (Fig. 6a), users can visualize the corresponding neurons in 3D. The 3D viewer widget is launched via a Python function call (see Fig. 6b), enabling detailed inspection of the identified structures. *MoMo* provides three visualization modes, following a *focus & context* approach, to enable the user to correlate the sketched motif with the detailed 3D renderings of neurons from a specific motif instance (see Fig. 6b-d).

Full Instance Rendering. The first mode shows the full morphology of neurons involved in a motif instance (see Fig. 6b). This mode provides important spatial context. However, it can be hard to mentally map the sketched motif pattern to the 3D neuron rendering due to the cluttered neuron morphologies.

Focused Instance Rendering (Color). In the second mode, we defocus neuronal branches that are unrelated to the sketched motif by rendering them in gray (see Fig. 6c). This helps to identify the neural processes involved in the motif easily visually but can still be perceived as cluttered due to occlusion effects.

Focused Instance Rendering (Pruning). The third mode prunes unrelated neuron branches that are unrelated to the motif. This enables clear inspection of the neuronal segments that implement a motif pattern (see Fig. 6d). However, this view lacks important spatial context and is thus complemented by the previous two visualization modes.

In all modes, synapses are represented as red spheres within the visualization. The user can switch between those three modes interactively in the user interface (see Fig. 6b-d).

8 Interactive Motif Queries

Our neuron morphology-aware graph representation extends conventional connectome graphs by adding significant complexity through introducing additional nodes and edges. In our exemplary dataset from MICrONS, 1,712 proofread neurons are connected through around 150,945 synaptic edges. Once transformed into our morphology-aware representation, the respective graph contains more than 390,000 nodes and 400,000 edges.

Computational Challenges. Generally, isomorphic subgraph search in a host graph is known to be an *NP-complete* problem [12]. Consequently, in the worst-case scenario, the computational complexity increases exponentially with graph size. While this is manageable for small-scale graphs, larger graphs, such as our representation, cause expensive and long computation times to identify even small motifs. Such long computation times are impractical for interactive applications such as *MoMo*, because users want to sketch motifs and inspect related instances quickly.

Parallel Motif Discovery. To reduce long waiting times and enable rapid data exploration, we integrated the parallel state of the start VF2-PS [14] motif discovery algorithm into *MoMo*. VF2-PS addresses the above challenges by representing subgraph isomorphism queries as a state-space search problem [47]. In this state-space representation, each state encapsulates a partial or complete mapping of vertices from the motif graph M to vertices of the host graph G, which enables highly efficient work distribution over many parallel cores. For example, VF2-PS [14] can reduce query times for simple motifs up to 48× compared to conventional NetworkX-based motif queries (see Supplement).

Custom Motif Discovery Features. We extended the VF2-PS algorithm with three custom features that facilitate interactive motif analysis. First, *wildcards* in queries (see Fig. 7) enable flexible motif queries by allowing users to leave certain attributes of the neuron morphology undefined. Thus, it allows users to explore structural hypotheses without requiring precise knowledge of a neuron's complete morphology. For example, to investigate whether multiple synaptic connections between two neurons exist within distinct spatial regions or clusters, users can draw multiple disconnected neuron segments in different colors and specify synaptic connections as needed. Second, *color matching* ensures that the nodes correspond to distinct neurons and their connections. Hence, we developed a post-processing stage, introducing arrays to track the color assigned to each node and edge. Next, each identified motif instance is checked to ensure its color structure matches the input subgraph, meaning that the colors correspond to distinct neuron IDs. Third, users can define *query limits*. For interactive exploration of motif in *MoMo* it is not necessary to enumerate all instances of a particular motif sketch in the whole connectome dataset. Thus, we allow the user to set an upper bound on the number of motif instances (see Fig. 6a), after which the isomorphic subgraph query algorithm should terminate.

9 Data and Implementation

MoMo requires a connectivity network and proofread reconstructions of neurons represented as 3D skeletons and synapses, along with their spatial locations. *MoMo* then processes the input data and transforms it into the neuron morphology-aware graph representation. Once the data is transformed, all subsequent computations can be executed during runtime. We tested *MoMo* on two different connectome datasets.

FlyWire Data. We tested *MoMo* on a subset of the FlyWire connectome [15] that includes neurons from the *medulla intrinsic* (Mi) and T4 families, *Lamina Intrinsic*, *Lobula Intrinsic*, *Centrifugal*, and *Distal Medulla* neurons. All these neurons are located in the right optical lobe, bringing the total to 12,803 neurons with 532,530 synaptic connections. The final neuron morphology-aware graph has 956,729 nodes and 654,778 intra-neuron edges. Based on experimental evaluations and expert feedback, we set the pruning factor to 3 µm for this dataset.

MICrONS Data. As a second dataset, we tested *MoMo* on a set of 1,712 proofread neurons from the MICrONS dataset [3]. This data describes the detailed synaptic wiring of a mouse's primary visual cortex. The respective neuron morphology-aware graph contains 392,438 nodes, 250,923 intra-neuron edges, and 156,945 synaptic edges. For this dataset, we applied a pruning factor of 1 µm, following the same evaluation process as for the Flywire dataset.

Implementation. *MoMo* is implemented as a modular Python library designed for Jupyter environments. The motif sketching interface (see Fig. 6a) and 3D visualization widget (see Fig. 6b-d) are implemented as separate components, each embedded within a Jupyter cell. *MoMo* uses the *AnyWidget* framework [36] to simplify the integration of custom JavaScript components within a Jupyter widget. Both widgets use JavaScript/React, while the data processing backend is implemented in Python. *MoMo* builds on libraries such as *Navis* [57] for neuron data processing and *Paper.js* as a vector graphics scripting framework to facilitate intuitive motif drawing. The 3D interactive skeleton rendering is based on *Three.js* with SharkViewer [70]. The *VF2-PS* algorithm is implemented in Arachne [2, 17], which provides access to parallel property graph data structures [53]. We have made the *MoMo* code, along with example code for transforming skeletons into our graph representation, publicly available on GitHub (see abstract). The datasets used will be released upon acceptance of this paper.

10 Evaluation

We evaluate *MoMo* through a series of case studies, assessing the usefulness for real-world neuroscience research questions.

Participants. We evaluated *MoMo* with four experts (**P1–P4**): three male and one female, from Harvard University, Janelia Research Campus, the University of Würzburg, and Freie Universität Berlin. The group comprised one professor, one research scientist, and two postdoctoral researchers, all specializing in the analysis of neuronal circuits reconstructed from EM image data. Additionally, two participants had prior experience using graph abstraction tools for connectome analysis. Their diverse expertise provided valuable neuroscientific perspectives, reinforcing the tool's broad applicability.

Session Structure. Each session lasted around one hour and was conducted either in person or via an interactive Zoom call. All but the first participant (pilot study) engaged directly with the tool, either hands-on or through remote screen control. The first participant took part in a pilot study during the tool's development, providing early feedback and use cases that helped shape its design. First, we introduced *MoMo*, outlining its capabilities and the novel integration of neuronal morphology in motif analysis. Next, participants explored example motifs by sketching their own and analyzing the retrieved instances. Finally, the experts discussed their findings, offering insights into their biological relevance, potential applications of the tool, and areas for improvement.

Each case study, details the expert's analysis objective, an overview of the relevant biological context, and how *MoMo* facilitated their investigation. Three out of four case studies explore the interplay between neuron morphology and synapse polarity (inhibition/excitation). While *MoMo* does not explicitly store polarity, experts agreed that analyzing the underlying connectivity is the essential first step in investigating these phenomena. Our approach enables an exploratory analysis of motif instances that *could* support the respective neural computations. Lastly, we synthesize key takeaways across all case studies, identifying strengths, challenges, and opportunities for future enhancements.

10.1 Pilot Study: Investigating Shunting Inhibition

As an initial pilot study, we collaborated with **P1** to explore potential applications of *MoMo* during its development. They suggested investigating the biologically relevant use case of *shunting inhibition*. This phenomenon exemplifies a case where both neuronal morphology and connectivity must be considered, making it challenging to study with existing graph-based tools.

Understanding Shunting Inhibition. *Shunting inhibition* is a neural mechanism in which inhibitory inputs suppress excitatory signals, preventing their propagation. This occurs when an inhibitory neuron synapses onto a neuron receiving an excitatory input, but the inhibitory input is positioned upstream relative to the excitatory one. As a result, the inhibitory signal can cancel or *shunt* the excitatory effect before it travels further through the neuron [31, 43].

Applying *MoMo* to Shunting Inhibition. During the remote session conducted via Zoom, the expert instructed us to sketch multiple motifs representing possible instances of shunting inhibition. One of the sketched motifs can be seen in Fig. 8a. The sketched motif comprises a network of three interconnected neurons: a blue neuron with four horizontally connected segments, a green neuron segment linked to its leftmost part, and a purple neuron segment synapsing onto its rightmost part. Given the left-to-right signal flow, the expert hypothesized that an inhibitory signal from the purple neuron could shunt an excitatory input from the green neuron, preventing its transmission along the blue neuron. The expert also instructed us to iteratively create additional motifs with varying numbers of blue segments to explore how the tool would handle different configurations.

Following the motif query, they explored multiple matching instances within the Flywire dataset [15]. The expert examined the visualized results, assessing whether the retrieved structures aligned with the desired morphological and connectivity patterns. Figure 8 illustrates one of the identified instances across different view modes in *MoMo*. In Figure 8c, only the sketched segments are highlighted in their respective colors, with the rest of the neuron structures grayed out for clarity. Figure 8e shows the four segments of the blue neuron are colored differently to emphasize different segments of the blue neuron in the motif sketch.

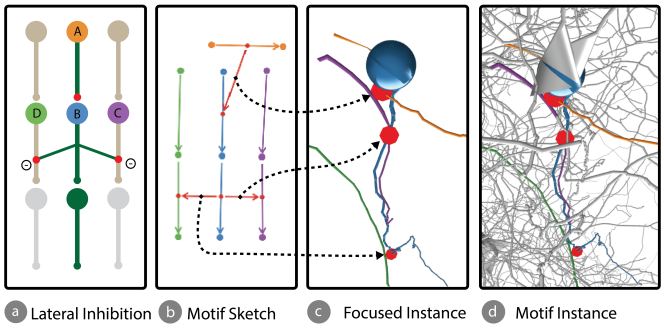


Fig. 9: **Case Study 1. Query for Lateral Inhibition.** (a) A schematic representation of *lateral inhibition*, featuring a four-neuron example (A, B, C, D). Assuming Neuron A sends an excitatory signal to Neuron B, which, in turn, reduces the activity of its neighboring neurons (C and D) through inhibitory connections, preventing the lateral spread of action potentials and enhancing signal contrast. (b) The sketch illustrates the four-neuron example, with connectivity and morphological structure that align with the schematic. (c, d) The renderings show an example motif instance with different levels of focus. Data: MICrONS [3].MS: include the new arrows in the caption

10.2 Case Study 1: Lateral Inhibition

To further assess *MoMo*'s applicability, we conducted a case study with **P2**. They highlighted *MoMo* 's potential as a complementary approach to tools like Vimo that abstract entire neurons as nodes. In their view, Vimo is well-suited for initially defining broader connectivity constraints, while *MoMo* becomes particularly valuable when morphology needs to be considered alongside connectivity for more detailed investigations. They suggested using the tool to investigate *lateral inhibition*. Unlike the pilot study, this expert directly interacted with *MoMo* in person, allowing for more hands-on evaluation of the tool's query and visualization capabilities.

Understanding Lateral Inhibition. *Lateral inhibition* is a key neural process where inhibitory neurons reduce the activity of their neighboring excitatory neurons, thereby enhancing contrast in sensory processing and aiding in pattern recognition. This mechanism typically involves inhibitory connections that synapse onto adjacent excitatory neurons, suppressing their responses and refining signal transmission. A classic example of *lateral inhibition* is depicted in Figure 9a, where

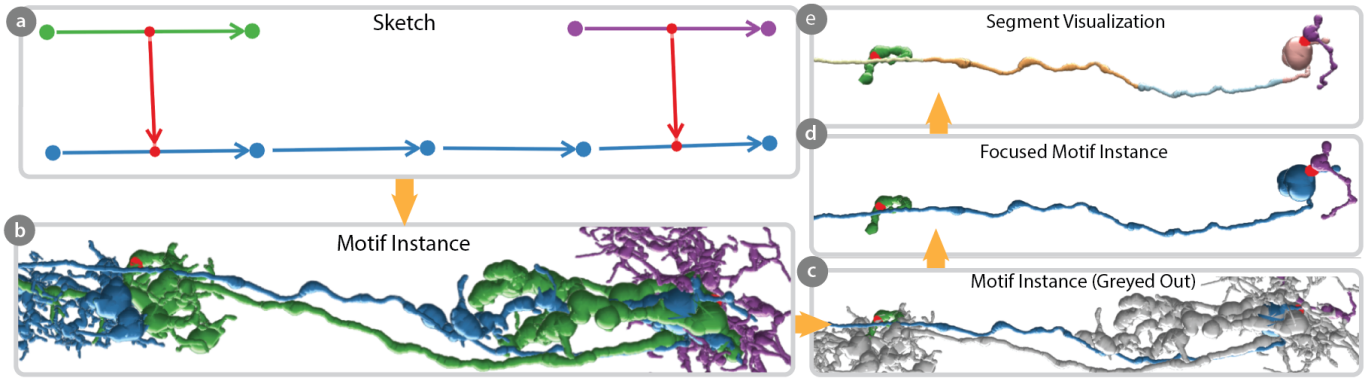


Fig. 8: **Pilot Study: Query for Potential Shunting Inhibition.** (a) The sketch illustrates a three-neuron motif (green, blue, and purple). The green neuron connects to the leftmost segment of the blue neuron, while the purple neuron connects to the rightmost segment. Thus, assuming the purple neuron provides inhibitory input, it could suppress the excitatory input from the green neuron due to the left-to-right signal propagation within the blue neuron. (b-d) The renderings show an exemplary motif instance queried with *MoMo* at different levels of focus. (e) We show the four corresponding segments of the blue neuron by assigning each segment a distinct color. Data: FlyWire [15].

Neuron A could send an excitatory signal to Neuron B. Neuron B, in turn, could inhibit the activity of its neighboring neurons (C and D), preventing the lateral spread of action potentials and enhancing the contrast of the signal. This process is crucial for sensory perception as it helps distinguish between different stimuli by sharpening the response of the excited neuron and reducing the activity of its neighbors. Identifying such motifs within large-scale connectomic data requires tools capable of analyzing both synaptic connectivity and the spatial relationships between neurons.

Applying *MoMo* to Lateral Inhibition. In this case study, the expert used *MoMo*'s sketching interface to draw multiple motifs corresponding to potential instances of *lateral inhibition*. These motifs typically involved central neurons receiving excitatory inputs from neighboring neurons and subsequently potentially inhibiting the activity of these neighboring neurons. Some drawn motifs matched existing structures in the dataset, while others did not. After each motif sketch, the expert utilized *MoMo*'s visualization interface to inspect the identified instances and assess whether they corresponded to the expected anatomical and connectivity patterns of *lateral inhibition*. This process was iterative—after reviewing the results, the expert modified the sketch and conducted another motif search to refine the analysis. The expert highlighted that *MoMo*'s ability to incorporate detailed morphological structure greatly facilitated the investigation of complex phenomena like *lateral inhibition*, enabling a more nuanced exploration than possible with purely connectivity-based tools.

Figure 9b presents an example of a potential *lateral inhibition* motif, derived from the expert's sketched motifs and follow-up discussions. In this case, the orange neuron is depicted as potentially making an excitatory synaptic connection onto the blue neuron, which then forms potential inhibitory synapses onto the neighboring purple and green neurons, dampening their responses and creating a feedback inhibition loop. Figure 9c provides a simplified view of an identified instance from the MICrONS dataset [3], emphasizing only the relevant neuron segments and synaptic connections from the original sketch. In contrast, Figure 9d presents the same instance with the full neurons in grayscale, preserving the sketch's color to provide broader structural context.

10.3 Case Study 2: Feed Forward Excitation

To assess *MoMo* 's usability for researchers who are not familiar with graph-based representations of neuronal data, we conducted a case study with **P3**, an expert specializing in the detailed analysis of physical neuronal structures, such as images and 3D reconstructions, rather than relying on graph abstractions. This expert's perspective was invaluable in understanding how *MoMo* could enhance the study of neuronal morphology using graph-based tools. For this case study, **P3** chose to investigate *feed-forward excitation* and the presence of dense synaptic connections within neurons.

Biological Significance of Feed-Forward Excitation *Feed-forward excitation* involves the transmission of excitatory signals from one neuron to another, often amplifying signals in circuits involved in sensory processing and motor coordination. It plays a vital role in the integration and rapid transmission of information across the brain. Dense synaptic connections occur in regions with a high concentration of synapses, facilitating complex neural processing. These connections are crucial for brain areas involved in learning, memory, and sensory processing, supporting the integration of large amounts of information for tasks like pattern recognition and cognition.

Applying *MoMo* to Feed-Forward Excitation During the Zoom session, the expert engaged with *MoMo*'s sketching interface, using remote control to explore motifs related to *feed-forward excitation* and dense synaptic connections. This was the expert's first time considering a graph-based abstraction of the connectome data, which required a shift in perspective from their typical approach of analyzing physical neuronal structures. They actively explored the found instances of the drawn motifs by leveraging *MoMo* 's various view modes, rotating and zooming in and out of the visualized motifs. The real-time querying feature was particularly advantageous, allowing the expert to refine and visualize their hypotheses iteratively. This dynamic exploration facilitated a deeper understanding of how complex neural circuits are connected and how spatial arrangements of neuronal structures influence connectivity patterns. The ability to interactively adjust the visual representation helped bridge the gap between abstract graph-based data and the expert's more familiar, physical visualization of neuronal morphology.

10.4 Case Study 3: Center-Surround Receptive Fields

This case study was conducted in collaboration with **P4**, who was already familiar with previous tools that utilized a sketch-based graph abstraction for connectomics data. After discussing several initial ideas, the expert chose to investigate the phenomenon of *center-surround receptive fields* for this session.

Understanding Center-Surround Receptive Fields. In sensory neuroscience, neurons process information from their surroundings in structured patterns. A common motif in visual processing is the *center-surround receptive field*, where a neuron's response depends on the contrast between the center and the surrounding region of its input. This structure enhances edge detection and contrast sensitivity, which are critical for vision. Neurons tuned to this pattern fire most strongly when a bright stimulus is in the center and a darker region surrounds it (or vice versa). This mechanism is fundamental in biological vision systems, including those in flies and mammals, and is analogous to computational filters like *Gabor filters* used in artificial vision models.

Applying *MoMo* to Center-Surround Receptive Fields. During the Zoom session, the expert used *MoMo*'s sketching and visualization

interface via remote control to analyze and refine neuron motifs relevant to the study of *center-surround receptive fields*. After several iterations, they finalized the sketch shown in Figure 10a. According to their explanation, the green neuron represents the potential central excitatory unit, which is hypothesized to respond to a bright stimulus in the center of its receptive field. The blue neuron, acting as a localized feature detector, was designed to respond selectively to smaller bright regions, thus enhancing the detection of fine details. Surrounding the central excitatory unit are the purple and orange neurons, which represent the potential surround inhibitory neurons. These neurons are activated by darker areas surrounding the center, contributing to contrast detection. Using *MoMo* 's real-time query feature, the expert successfully identified potential instances of the *center-surround receptive field* phenomenon within the MICrOns dataset [3] (see different views of one identified instance in Figures 10b and c). The expert explored these motifs through *MoMo* 's visualization interface, utilizing its different views to examine the morphological and connectivity patterns that aligned with the expected characteristics of the phenomenon.

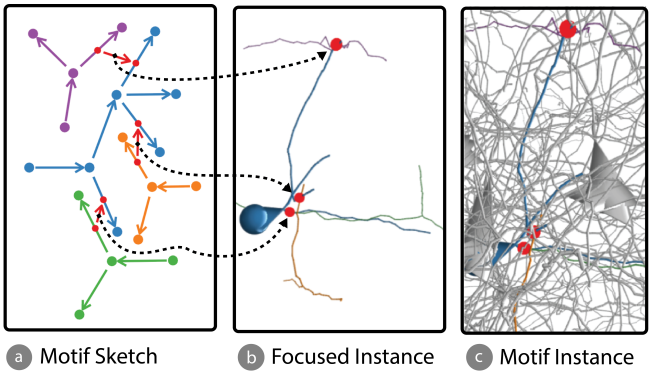


Fig. 10: **Case Study 3: Center-Surround Receptive Fields.** (a) Motif sketch, which could correspond to a potential *center-surround receptive field*. The key components of the sketch include a green neuron (potentially the central excitatory unit), a blue neuron (potentially the localized feature detector), and purple and orange neurons (potentially the surround inhibitory neurons). (b, c) Renderings of the identified instances of the potential *center-surround receptive field* phenomenon, queried using *MoMo*, shown at different levels of focus. Data: MICrONS [3].MS: include the new arrows in the caption

10.5 Key Evaluation Findings

MoMo effectively fulfills its core goals and tasks outlined in Section 4 by offering an interactive, morphology-aware motif analysis tool for connectomics research. Across all case studies, experts highlighted its intuitive interface, real-time querying, and seamless integration of sketching and visualization. However, while the tool offers several advantages, certain limitations and areas for improvement were identified, which are discussed below.

Efficient and Intuitive Motif Identification. One of *MoMo* 's most valued strengths is its ability to facilitate rapid motif identification (**G1, T1**) through an interactive sketching interface (**G2, T2**). Experts particularly appreciated the tool's capacity to refine and adjust queries in real time, especially when no exact matches were initially found, like in the first case study. This flexibility lowers the barrier to entry for researchers unfamiliar with complex query languages (**G4, T4**). However, relying on user-generated sketches introduces subjectivity, as motif definitions may vary across users. Future enhancements could include predefined motif templates or automated suggestions.

Enhancing Connectivity and Morphology Analysis. The tool effectively supports combined connectivity and morphology queries, enabling detailed circuit-level analyses (**G2**). This was demonstrated in studies on *shunting inhibition* and *lateral inhibition*, where experts could specify spatial arrangements of potential excitatory and inhibitory synapses and retrieve biologically relevant instances. However, the accuracy of search results remains dependent on the data preprocessing

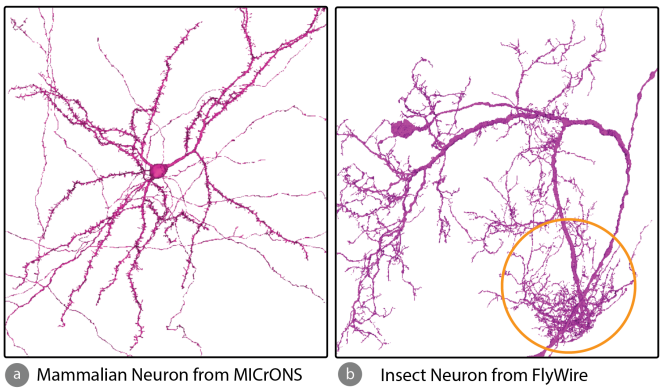


Fig. 11: **Mammalian Neurons vs. Insect Neurons.** Comparison of neuronal structures between the *MICrONS* and *Flywire* datasets. (a) A mammalian neuron from *MICrONS*, characterized by small, uniform terminal branches. (b) An insect neuron from *Flywire*, displaying more intricate and variable terminal branches, particularly in the yellow-circled region. Thus, mammalian neurons are overall better suited for *MoMo*.

of connectome data. While pruning fine structures improves efficiency, it may also lead to omitting crucial neuronal details. Deriving the right pruning factor is key to balancing efficiency and preserving essential structural information. Experts noted that incorporating additional semantic information, such as branch lengths or the ability to query specific regions of the connectome, would enhance *MoMo* 's applicability.

Insect vs. Mammalian Brains. We tested *MoMo* both on the *Flywire* and *MICrONS* datasets, allowing case study participants to switch between them based on their preferences. Thus, participants raised the question of whether our neuronal abstraction approach is better suited for certain connectomes. Our method captures neuronal structure at the segment level, which is much more well defined in mammalian neurons compared to insection neuron, such as flies. In the mammalian brain (*MICrONS*), terminal branches (twigs) are relatively uniform in size and structure, making them easier to manage and more consistently pruned. In contrast, insect neurons (*Flywire*) exhibit greater variability, requiring dataset-specific pruning adjustments. Fig. 11a shows a mammalian neuron with small, uniform twigs, whereas Fig. 11b highlights an insect neuron with more intricate and variable branches, particularly in the yellow-circled region. This variability makes abstraction more challenging in insect neurons. Consequently, our approach is particularly well-suited for mammalian neurons, where uniform twig structures simplify preprocessing, but *MoMo* remains adaptable for more complex insect neurons through parameter tuning.

Improving Spatial Analysis and Visualization. *MoMo* 's ability to correlate motif queries with 3D neuron reconstructions (**G3, T3**) is a significant advantage. Experts appreciated the tool's multiple visualization modes, which aid spatial reasoning about synaptic interactions. However, some participants found interpreting dense 3D structures challenging. Future improvements could include occlusion-aware highlighting or interactive slicing to enhance clarity in highly interconnected regions. Another key challenge lies in the wildcard feature, which allows flexible matching of neuronal segments. While this feature provides adaptability, it currently lacks the ability to constrain wildcard segments to specific neuronal regions. For example, in the *feed-forward excitation* case study, a constraint ensuring that synaptic connections occurred on a particular neuron arbor would have improved specificity. Introducing constraint options for wildcards could enhance motif refinement while preserving flexibility.

Limitations of Motif Querying. While *MoMo* enables segment-level motif sketching and structural queries, some limitations remain. Users cannot specify exact segment lengths or precise synapse positions along a segment, as sub-segment resolution is not supported. Quantitative constraints (e.g., "at least three inputs") are also unavailable, limiting expressiveness for some patterns. While effective for small to mod-

erately sized motifs (typically 3–4 neurons with 3–6 segments and synapses), querying larger or more complex motifs is challenging due to combinatorial search space and sketching usability. As noted by **P2**, *MoMo* works best alongside higher-level tools better suited for motifs with 5+ neurons.

11 Conclusion and Future Work

In this paper, we introduced a novel approach for interactively searching and analyzing neuron morphology-aware motifs in large connectome graphs. This method enables the exploration of complex neural structures and their functional relationships across datasets such as *FlyWire* and *MICrONS*. By focusing on connectivity patterns at the segment level, our approach facilitates the identification of motifs, like lateral inhibition, that were previously difficult to query. Through case studies, we demonstrated the tool's effectiveness in supporting exploratory analysis and providing insights into neuronal function. We also presented a fully functioning prototype that allows users to perform these analyses interactively and efficiently.

We see several exciting directions for future work. First, comparative visualization methods are needed to correlate morphology-aware connectivity patterns across specimens of different sexes or developmental stages, posing challenges such as establishing visual correspondences between comparison targets. Second, *MoMo* currently focuses on morphological motifs and does not support the query or analysis of spatial motifs, such as helix patterns. Spatial motifs incorporate spatial coordinates alongside neuronal morphology, enabling the identification of geometric patterns beyond what morphology alone can reveal. Integrating spatial motif queries would require additional data, significantly increasing computational demands. Third, alternative interactions for motif definition should be explored, such as selecting patterns directly in the 3D rendering or using scribbling-based drawings. Finally, while our current approach investigates the connectome based on detailed hypotheses of motif morphology and connectivity, there is an opportunity to explore unknown motifs by integrating graph-based machine learning with interactive visualization. A major challenge here is effectively visualizing automatically identified morphological motifs.

Acknowledgements

We thank the Chapel and Arkouda communities for their guidance. This research is supported in part by the NSF grants CCF-2109988 and OAC-2402560. JTR: TODO.

References

[1] A. K. Al-Awami, J. Beyer, H. Strobelt, N. Kasthuri, J. W. Lichtman, H. Pfister, and M. Hadwiger. NeuroLines: A Subway Map Metaphor for Visualizing Nanoscale Neuronal Connectivity. *IEEE Transactions on Visualization and Computer Graphics*, 20(12):2369–2378, Dec. 2014. doi: 10.1109/TVCG.2014.2346312 2

[2] O. Alvarado Rodriguez, Z. Du, J. Patchett, F. Li, and D. A. Bader. Arachne: An Arkouda Package for Large-Scale Graph Analytics. In *2022 IEEE High Performance Extreme Computing Conference (HPEC)*, pp. 1–7, Sept. 2022. ISSN: 2643-1971. doi: 10.1109/HPEC55821.2022.9991947 7

[3] J. A. Bae, M. Baptiste, A. L. Bodor, D. Brittain, J. Buchanan, D. J. Bumbarger, M. A. Castro, B. Celii, E. Cobos, F. Collman, N. M. d. Costa, S. Dorkenwald, L. Elabbady, P. G. Fahey, T. Fliss, E. Froudarakis, J. Gager, C. Gamlin, A. Halageri, J. Hebditch, Z. Jia, C. Jordan, D. Kapner, N. Kemnitz, S. Kinn, S. Koolman, K. Kuehner, K. Lee, K. Li, R. Lu, T. Macrina, G. Mahalingam, S. McReynolds, E. Miranda, E. Mitchell, S. S. Mondal, M. Moore, S. Mu, T. Muhammad, B. Nehoran, O. Ogedengbe, C. Papadopoulos, S. Papadopoulos, S. Patel, X. Pitkow, S. Popovych, A. Ramos, R. C. Reid, J. Reimer, C. M. Schneider-Mizell, H. S. Seung, B. Silverman, W. Silversmith, A. Sterling, F. H. Sinz, C. L. Smith, S. Suckow, M. Takeno, Z. H. Tan, A. S. Tolias, R. Torres, N. L. Turner, E. Y. Walker, T. Wang, G. Williams, S. Williams, K. Willie, R. Willie, W. Wong, J. Wu, C. Xu, R. Yang, D. Yatsenko, F. Ye, W. Yin, and S.-c. Yu. Functional connectomics spanning multiple areas of mouse visual cortex, 2021. doi: 10.1101/2021.07.28.454025 3, 5, 7, 8, 9

[4] J. Beyer, A. Al-Awami, N. Kasthuri, J. W. Lichtman, H. Pfister, and M. Hadwiger. ConnectomeExplorer: Query-Guided Visual Analysis of Large Volumetric Neuroscience Data. *IEEE Transactions on Visualization and Computer Graphics*, 19(12):2868–2877, Dec. 2013. doi: 10.1109/TVCG.2013.142 2

[5] J. Beyer, M. Hadwiger, A. Al-Awami, Won-Ki Jeong, N. Kasthuri, J. W. Lichtman, and H. Pfister. Exploring the Connectome: Petascale Volume Visualization of Microscopy Data Streams. *IEEE Computer Graphics and Applications*, 33(4):50–61, July 2013. doi: 10.1109/MCG.2013.55 2

[6] J. Beyer, H. Mohammed, M. Agus, A. K. Al-Awami, H. Pfister, and M. Hadwiger. Culling for Extreme-Scale Segmentation Volumes: A Hybrid Deterministic and Probabilistic Approach. *IEEE Transactions on Visualization and Computer Graphics*, 25(1):1132–1141, Jan. 2019. doi: 10.1109/TVCG.2018.2864847 2

[7] J. Beyer, J. Troidl, S. Boorboor, M. Hadwiger, A. Kaufman, and H. Pfister. A Survey of Visualization and Analysis in High-Resolution Connectomics. *Computer Graphics Forum*, 41(3):573–607, June 2022. doi: 10.1111/cgf.14574 2

[8] R. S. Burt and T. Schøtt. Relation contents in multiple networks. *Social Science Research*, 14(4):287–308, 1985. Publisher: Elsevier. 2

[9] E. Cakmak, J. Fuchs, D. Jackle, T. Schreck, U. Brandes, and D. Keim. Motif-Based Visual Analysis of Dynamic Networks. In *2022 IEEE Visualization in Data Science (VDS)*, pp. 17–26. IEEE, Oklahoma City, OK, USA, Oct. 2022. doi: 10.1109/VDS57266.2022.00007 2

[10] F. Claudi, L. Petrucco, A. Tyson, T. Branco, T. Margrie, and R. Portugues. BrainGlobe Atlas API: a common interface for neuroanatomical atlases. *Journal of Open Source Software*, 5(54):2668, Oct. 2020. doi: 10.21105/joss.02668 2

[11] F. Claudi, A. L. Tyson, L. Petrucco, T. W. Margrie, R. Portugues, and T. Branco. Visualizing anatomically registered data with brainrender. *eLife*, 10:e65751, Mar. 2021. doi: 10.7554/eLife.65751 2

[12] S. A. Cook. The complexity of theorem-proving procedures. In *Logic, automata, and computational complexity: The works of Stephen A. Cook*, pp. 143–152. 2023. 6

[13] A. Diehl, L. Pelorosso, C. Delrieux, C. Saulo, J. Ruiz, M. E. Gröller, and S. Bruckner. Visual Analysis of Spatio-Temporal Data: Applications in Weather Forecasting. *Computer Graphics Forum*, 34(3):381–390, June 2015. doi: 10.1111/cgf.12650 2

[14] M. Dindoost, O. Alvarado Rodriguez, S. Bagchi, P. Pauliuchenka, Z. Du, and D. A. Bader. VF2-PS: Parallel and Scalable Subgraph Monomorphism in Arachne. In *2024 IEEE High Performance Extreme Computing Conference (HPEC)*, Sept. 2024. 6

[15] S. Dorkenwald, A. Matsliah, A. R. Sterling, P. Schlegel, S.-C. Yu, C. E. McKellar, A. Lin, M. Costa, K. Eichler, Y. Yin, and others. Neuronal wiring diagram of an adult brain. *Nature*, 634(8032):124–138, 2024. Publisher: Nature Publishing Group UK London. 1, 3, 6, 7, 8

[16] S. Dorkenwald, C. M. Schneider-Mizell, D. Brittain, A. Halageri, C. Jordan, N. Kemnitz, M. A. Castro, W. Silversmith, J. Maitin-Shephard, J. Troidl, and others. CAVE: Connectome annotation versioning engine. *bioRxiv*, 2023. 1, 3

[17] Z. Du, O. Alvarado Rodriguez, J. Patchett, and D. A. Bader. Interactive Graph Stream Analytics in Arkouda. *Algorithms*, 14(8):221, Aug. 2021. Number: 8 Publisher: Multidisciplinary Digital Publishing Institute. doi: 10.3390/a14080221 7

[18] C. Dunne and B. Shneiderman. Motif simplification: improving network visualization readability with fan, connector, and clique glyphs. In *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems*, pp. 3247–3256. ACM, Paris France, Apr. 2013. doi: 10.1145/2470654.2466444 2

[19] N. Francis, A. Green, P. Guagliardo, L. Libkin, T. Lindaaker, V. Marsault, S. Plantikow, M. Rydberg, P. Selmer, and A. Taylor. Cypher: An Evolving Query Language for Property Graphs. In *Proceedings of the 2018 International Conference on Management of Data*, pp. 1433–1445. ACM, May 2018. doi: 10.1145/3183713.3190657 2, 3

[20] F. Ganglberger, N. Swoboda, L. Frauenstein, J. Kaczanowska, W. Haubensak, and K. Bühler. BrainTrawler: A visual analytics framework for iterative exploration of heterogeneous big brain data. *Computers & Graphics*, 82:304–320, Aug. 2019. doi: 10.1016/j.cag.2019.05.032 2

[21] F. Ganglberger, M. Wißmann, H.-Y. Wu, N. Swoboda, A. Thum, W. Haubensak, and K. Bühler. Spatial-data-driven layouting for brain network visualization. *Computers & Graphics*, 105:12–24, June 2022. doi: 10.1016/j.cag.2022.04.014 2

[22] F. J. Ganglberger, J. Kaczanowska, W. Haubensak, and K. Bühler. A Data Structure for Real-Time Aggregation Queries of Big Brain Networks. *Neuroinformatics*, 18(1):131–149, Jan. 2020. doi: 10.1007/s12021-019-09428-9 2

[23] P. Govyadinov, T. Womack, J. Eriksen, D. Mayerich, and G. Chen. Graph-Assisted Visualization of Microvascular Networks. In *2019 IEEE Visualization Conference (VIS)*, pp. 1–5. IEEE, Vancouver, BC, Canada, Oct. 2019. doi: 10.1109/VISUAL.2019.8933682 2

[24] M. Hadwiger, J. Beyer, Won-Ki Jeong, and H. Pfister. Interactive Volume Exploration of Petascale Microscopy Data Streams Using a Visualization-Driven Virtual Memory Approach. *IEEE Transactions on Visualization and Computer Graphics*, 18(12):2285–2294, Dec. 2012. doi: 10.1109/TVCG.2012.240 2

[25] P. Harth, A. Bast, J. Troidl, B. Meulemeester, H. Pfister, J. Beyer, M. Oberlaender, H.-C. Hege, and D. Baum. Rapid Prototyping for Coordinated Views of Multi-scale Spatial and Abstract Data: A Grammar-based Approach. *Eurographics Workshop on Visual Computing for Biology and Medicine*, pp. 99–109, 2023. Artwork Size: 11 pages ISBN: 9783038682165 Publisher: The Eurographics Association. doi: 10.2312/VCBM.20231218 2

[26] C. Henley. *Foundations of Neuroscience*. Michigan State University Libraries, East Lansing, 2021. 3

[27] K. Huang, H. Liang, C. Yao, X. Zhao, Y. Cui, Y. Tian, R. Zhang, and X. Zhou. VisualNeo: Bridging the Gap between Visual Query Interfaces and Graph Query Engines. *Proceedings of the VLDB Endowment*, 16(12):4010–4013, Aug. 2023. doi: 10.14778/3611540.3611608 2

[28] B. K. Hulse, H. Haberkern, R. Franconville, D. Turner-Evans, S.-y. Takemura, T. Wolff, M. Noorman, M. Dreher, C. Dan, R. Parekh, A. M. Hermundstad, G. M. Rubin, and V. Jayaraman. A connectome of the Drosophila central complex reveals network motifs suitable for flexible navigation and context-dependent action selection. *eLife*, 10:e66039, Oct. 2021. doi: 10.7554/eLife.66039 1, 3

[29] M. Januszewski, J. Kornfeld, P. H. Li, A. Pope, T. Blakely, L. Lindsey, J. Maitin-Shepard, M. Tyka, W. Denk, and V. Jain. High-precision automated reconstruction of neurons with flood-filling networks. *Nature methods*, 15(8):605–610, 2018. 1, 3

[30] N. Jayaram, S. Goyal, and C. Li. VIIQ: auto-suggestion enabled visual interface for interactive graph query formulation. *Proceedings of the VLDB Endowment*, 8(12):1940–1943, Aug. 2015. doi: 10.14778/2824032.2824106 2

[31] P. Jonas and G. Buzsaki. Neural inhibition. *Scholarpedia*, 2(9):3286, 2007. doi: 10.4249/scholarpedia.3286 3, 7

[32] J. Joyce, R. Chalavadi, J. Chan, S. Tanna, D. Xenes, N. Kuo, V. Rose, J. Matelsky, L. Kitchell, C. Bishop, and others. A novel semi-automated proofreading and mesh error detection pipeline for neuron extension. *bioRxiv*, 2023. 3

[33] S. Jung, D. Shin, H. Jeon, K. Choe, and J. Seo. MoNetExplorer: A Visual Analytics System for Analyzing Dynamic Networks With Temporal Network Motifs. *IEEE Transactions on Visualization and Computer Graphics*, 30(10):6725–6739, Oct. 2024. doi: 10.1109/TVCG.2023.3337396 2

[34] W. T. Katz and S. M. Plaza. DVID: distributed versioned Image-Oriented dataservice. *Frontiers in neural circuits*, 13:5, 2019. Publisher: Frontiers Media SA. 3

[35] E. Lesser, A. W. Azevedo, J. S. Phelps, L. Elabbady, A. Cook, D. S. Syed, B. Mark, S. Kuroda, A. Sustar, A. Moussa, and others. Synaptic architecture of leg and wing premotor control networks in Drosophila. *Nature*, 631(8020):369–377, 2024. Publisher: Nature Publishing Group UK London. 1

[36] T. Manz, A. Nezar, and N. Gehlenborg. anywidget: reusable widgets for interactive analysis and visualization in computational notebooks. 2024. 7

[37] B. Matejek, D. Wei, T. Chen, and others. Edge-colored directed subgraph enumeration on the connectome. *Scientific Reports*, 12:11349, 2022. doi: 10.1038/s41598-022-15027-7 2

[38] J. K. Matelsky, E. C. Johnson, B. Wester, and W. Gray-Roncal. Scalable graph analysis tools for the connectomics community. *bioRxiv*, pp. 2022–06, 2022. Publisher: Cold Spring Harbor Laboratory. 1, 4

[39] J. K. Matelsky, E. P. Reilly, E. C. Johnson, J. Stiso, D. S. Bassett, B. A. Wester, and W. Gray-Roncal. DotMotif: an open-source tool for connectome subgraph isomorphism search and graph queries. *Scientific Reports*, 11(1):13045, Dec. 2021. doi: 10.1038/s41598-021-91025-5 1, 2

[40] D. Mayerich, L. Abbott, and J. Keyser. Visualization of Cellular and Microvascular Relationships. *IEEE Transactions on Visualization and Computer Graphics*, 14(6):1611–1618, Nov. 2008. doi: 10.1109/TVCG.2008.179 2

[41] F. McGee, M. Ghoniem, G. Melançon, B. Otjacques, and B. Pinaud. The State of the Art in Multilayer Network Visualization. *Computer Graphics Forum*, 38(6):125–149, Sept. 2019. doi: 10.1111/cgf.13610 2

[42] A. Messina, A. Fiannaca, L. La Paglia, M. La Rosa, and A. Urso. BioGraph: a web application and a graph database for querying and analyzing bioinformatics resources. *BMC Systems Biology*, 12(S5):98, Nov. 2018. doi: 10.1186/s12918-018-0616-4 2

[43] S. J. Mitchell and R. Silver. Shunting Inhibition Modulates Neuronal Gain during Synaptic Excitation. *Neuron*, 38(3):433–445, May 2003. doi: 10.1016/S0896-6273(03)00200-9 3, 7

[44] H. Mohammed, A. K. Al-Awami, J. Beyer, C. Cali, P. Magistretti, H. Pfister, and M. Hadwiger. Abstractocyte: A Visual Tool for Exploring Nanoscale Astroglial Cells. *IEEE Transactions on Visualization and Computer Graphics*, 24(1):853–861, Jan. 2018. doi: 10.1109/TVCG.2017.2744278 2

[45] J. L. Moreno. Who shall survive? *Journal of Psychodrama, Sociometry, and Group Psychotherapy*, 6(1-2):118–118, 1953. 2

[46] A. Nern, F. Loesche, S.-y. Takemura, L. E. Burnett, M. Dreher, E. Gruntman, J. Hoeller, G. B. Huang, M. Januszewski, N. C. Klapoetke, S. Koskela, K. D. Longden, Z. Lu, S. Preibisch, W. Qiu, E. M. Rogers, P. Seenivasan, A. Zhao, J. Bogovic, B. S. Canino, J. Clements, M. Cook, S. Finley-May, M. A. Flynn, I. Hameed, A. M. C. Fragniere, K. J. Hayworth, G. P. Hopkins, P. M. Hubbard, W. T. Katz, J. Kovalyak, S. A. Lauchie, M. Leonard, A. Lohff, C. A. Maldonado, C. Mooney, N. Okeoma, D. J. Olbris, C. Ordish, T. Paterson, E. M. Phillips, T. Pietzsch, J. R. Salinas, P. K. Rivlin, P. Schlegel, A. L. Scott, L. A. Scuderi, S. Takemura, I. Talebi, A. Thomson, E. T. Trautman, L. Umayam, C. Walsh, J. J. Walsh, C. S. Xu, E. A. Yakal, T. Yang, T. Zhao, J. Funke, R. George, H. F. Hess, G. S. X. E. Jefferis, C. Knecht, W. Korff, S. M. Plaza, S. Romani, S. Saalfeld, L. K. Scheffer, S. Berg, G. M. Rubin, and M. B. Reiser. Connectome-driven neural inventory of a complete visual system. *Nature*, Mar. 2025. doi: 10.1038/s41586-025-08746-0 1

[47] N. J. Nilsson. *Principles of artificial intelligence*. Springer Science & Business Media, 1982. 6

[48] R. Pienta, F. Hohman, A. Endert, A. Tamersoy, K. Roundy, C. Gates, S. Navathe, and D. H. Chau. VIGOR: interactive visual exploration of graph query results. *IEEE transactions on visualization and computer graphics*, 24(1):215–225, 2017. Publisher: IEEE. 2

[49] R. Pienta, F. Hohman, A. Tamersoy, A. Endert, S. Navathe, H. Tong, and D. H. Chau. Visual Graph Query Construction and Refinement. In *Proceedings of the 2017 ACM International Conference on Management of Data*, pp. 1587–1590. ACM, Chicago Illinois USA, May 2017. doi: 10.1145/3035918.3056418 2

[50] R. Pienta, A. Tamersoy, A. Endert, S. Navathe, H. Tong, and D. H. Chau. VISAGE: Interactive Visual Graph Querying. In *Proceedings of the International Working Conference on Advanced Visual Interfaces*, pp. 272–279. ACM, Bari Italy, June 2016. doi: 10.1145/2909132.2909246 2

[51] S. M. Plaza, J. Clements, T. Dolafi, L. Umayam, N. N. Neubarth, L. K. Scheffer, and S. Berg. neu Print: An open access tool for EM connectomics. *Frontiers in Neuroinformatics*, 16:896292, 2022. Publisher: Frontiers Media SA. 1, 3

[52] M. A. Rodriguez. The gremlin graph traversal machine and language (invited talk). In *Proceedings of the 15th symposium on database programming languages*, pp. 1–10, 2015. 3

[53] O. A. Rodriguez, F. V. Buschmann, Z. Du, and D. A. Bader. Property Graphs in Arachne. In *2023 IEEE High Performance Extreme Computing Conference (HPEC)*, pp. 1–7, Sept. 2023. ISSN: 2643-1971. doi: 10.1109/HPEC58863.2023.10363498 7

[54] S. Saalfeld, A. Cardona, V. Hartenstein, and P. Tomančák. CATMAID: collaborative annotation toolkit for massive amounts of image data. *Bioinformatics*, 25(15):1984–1986, 2009. Publisher: Oxford University Press. 2

[55] R. L. Schalek, X. Lu, M. Petkova, J. Boulanger-Weill, N. Karlupia, Y. Wu, S. Wang, X. Wang, N. Dhanyasi, D. Berger, X. Han, E. Sjostedt, F. Engert, and J. W. Lichtman. Volume Electron Microscopy Workflows for the study of Large-Scale Neural Connectomics. *Microscopy and Microanalysis*, 29(Supplement_1):1209–1211, July 2023. doi: 10.1093/micmic/ozad067.622 1, 3

[56] L. K. Scheffer, C. S. Xu, M. Januszewski, Z. Lu, S. y. Takemura, K. J. Hayworth, G. B. Huang, K. Shinomiya, J. Maitlin-Shepard, S. Berg, J. Clements, P. M. Hubbard, W. T. Katz, L. Umayam, T. Zhao, D. Ackerman, T. Blakely, J. Bogovic, T. Dolafi, D. Kainmueller, T. Kawase, K. A. Khairy, L. Leavitt, P. H. Li, L. Lindsey, N. Neubarth, D. J. Olbris, H. Otsuna, E. T. Trautman, M. Ito, A. S. Bates, J. Goldammer, T. Wolff, R. Svirskas, P. Schlegel, E. Neace, C. J. Knecht, C. X. Alvarado, D. A. Bailey, S. Ballinger, J. A. Borycz, B. S. Canino, N. Cheatham, M. Cook,

M. Dreher, O. Duclos, B. Eubanks, K. Fairbanks, S. Finley, N. Forknall, A. Francis, G. P. Hopkins, E. M. Joyce, S. Kim, N. A. Kirk, J. Kovalyak, S. A. Lauchie, A. Lohff, C. Maldonado, E. A. Manley, S. McLin, C. Mooney, M. Ndama, O. Ogundeyi, N. Okeoma, C. Ordish, N. Padilla, C. M. Patrick, T. Paterson, E. E. Phillips, E. M. Phillips, N. Rampally, C. Ribeiro, M. K. Robertson, J. T. Rymer, S. M. Ryan, M. Sammons, A. K. Scott, A. L. Scott, A. Shinomiya, C. Smith, K. Smith, N. L. Smith, M. A. Sobeski, A. Suleiman, J. Swift, S. Takemura, I. Talebi, D. Tarnogorska, E. Tenshaw, T. Tokhi, J. J. Walsh, T. Yang, J. A. Horne, F. Li, R. Parekh, P. K. Rivlin, V. Jayaraman, M. Costa, G. S. Jefferis, K. Ito, S. Saalfeld, R. George, I. A. Meinertzhagen, G. M. Rubin, H. F. Hess, V. Jain, and S. M. Plaza. A connectome and analysis of the adult drosophila central brain. *Elife*, 9:e57443, 2020. doi: 10.7554/eLife.57443 1

[57] P. Schlegel, C. Barnes, Sridhar Jagannathan, B. Pedigo, and R. Court. navis-org/navis: Version 1.1.0, Nov. 2021. doi: 10.5281/ZENODO.5710143 7

[58] M. Sedlmair, M. Meyer, and T. Munzner. Design study methodology: Reflections from the trenches and the stacks. *IEEE transactions on visualization and computer graphics*, 18(12):2431–2440, 2012. 3

[59] A. Shapson-Coe, M. Januszewski, D. R. Berger, A. Pope, Y. Wu, T. Blakely, R. L. Schalek, P. H. Li, S. Wang, J. Maitin-Shepard, and others. A petavoxel fragment of human cerebral cortex reconstructed at nanoscale resolution. *Science*, 384(6696):eadk4858, 2024. Publisher: American Association for the Advancement of Science. doi: 10.1126/science.eadk4858 1, 2, 3, 4

[60] W. Silversmith, A. Zlateski, J. A. Bae, I. Tartavull, N. Kemnitz, J. Wu, and H. S. Seung. Igneous: Distributed dense 3D segmentation meshing, neuron skeletonization, and hierarchical downsampling. *Frontiers in Neural Circuits*, 16:977700, Nov. 2022. doi: 10.3389/fncir.2022.977700 2

[61] O. Sporns and R. Kötter. Motifs in brain networks. *PLoS biology*, 2(11):e369, 2004. Publisher: Public Library of Science San Francisco, USA. 1

[62] M. Strauch, V. Hartenstein, I. V. Andrade, A. Cardona, and D. Merhof. Annotated dendrograms for neurons from the larval fruit fly brain. In *VCBM@ MICCAI*, pp. 57–66, 2018. 2

[63] M. R. Tavakoli, J. Lyudchik, M. Januszewski, V. Vistunou, N. Agudelo, J. Vorlaufer, C. Sommer, C. Kreuzinger, B. Oliveira, A. Cenameri, and others. Light-microscopy based dense connectomic reconstruction of mammalian brain tissue. *bioRxiv*, pp. 2024–03, 2024. Publisher: Cold Spring Harbor Laboratory. 1, 3

[64] The MICrONS Consortium, J. A. Bae, M. Baptiste, C. A. Bishop, A. L. Bodor, D. Brittain, J. Buchanan, D. J. Bumbarger, M. A. Castro, B. Celii, E. Cobos, F. Collman, N. M. Da Costa, S. Dorkenwald, L. Elabbady, P. G. Fahey, T. Fliss, E. Froudarakis, J. Gager, C. Gamlin, W. Gray-Roncal, A. Halageri, J. Hebditch, Z. Jia, E. Joyce, J. Joyce, C. Jordan, D. Kapner, N. Kemnitz, S. Kinn, L. M. Kitchell, S. Koolman, K. Kuehner, K. Lee, K. Li, R. Lu, T. Macrina, G. Mahalingam, J. Matelsky, S. McReynolds, E. Miranda, E. Mitchell, S. S. Mondal, M. Moore, S. Mu, T. Muhammad, B. Nehoran, O. Ogedengbe, C. Papadopoulos, S. Papadopoulos, S. Patel, X. Pitkow, S. Popovych, A. Ramos, R. Clay Reid, J. Reimer, P. K. Rivlin, V. Rose, C. M. Schneider-Mizell, H. S. Seung, B. Silverman, W. Silversmith, A. Sterling, F. H. Sinz, C. L. Smith, S. Suckow, M. Takeno, Z. H. Tan, A. S. Tolias, R. Torres, N. L. Turner, E. Y. Walker, T. Wang, A. Wanner, B. A. Wester, G. Williams, S. Williams, K. Willie, R. Willie, W. Wong, J. Wu, C. Xu, R. Yang, D. Yatsenko, F. Ye, W. Yin, R. Young, S.-c. Yu, D. Xenes, and C. Zhang. Functional connectomics spanning multiple areas of mouse visual cortex, July 2021. doi: 10.1101/2021.07.28.454025 1, 3

[65] J. Troidl, C. Cali, E. Gröller, H. Pfister, M. Hadwiger, and J. Beyer. Barrio: Customizable Spatial Neighborhood Analysis and Comparison for Nanoscale Brain Structures. *Computer Graphics Forum*, 41(3):183–194, June 2022. doi: 10.1111/cgf.14532 2

[66] J. Troidl, J. Knittel, W. Li, F. Zhan, H. Pfister, and S. Turaga. Global Neuron Shape Reasoning with Point Affinity Transformers. *bioRxiv*, 2024. 3

[67] J. Troidl, S. Warchol, J. Choi, J. Matelsky, N. Dhanysai, X. Wang, B. Wester, D. Wei, J. W. Lichtman, H. Pfister, and J. Beyer. Vimo: Visual Analysis of Neuronal Connectivity Motifs. *IEEE Transactions on Visualization and Computer Graphics (IEEE VIS)*, 2023. Publisher: Cold Spring Harbor Laboratory _eprint: https://www.biorxiv.org/content/early/2022/12/11/2022.12.09.519772.full.pdf. doi: 10.1101/2022.12.09.519772 1, 2, 3, 4

[68] S. K. Vohra, P. Harth, Y. Isoe, A. Bahl, H. Fotowat, F. Engert, H.-C. Hege, and D. Baum. A Visual Interface for Exploring Hypotheses About Neural Circuits. *IEEE Transactions on Visualization and Computer Graphics*, 30(7):3945–3958, July 2024. doi: 10.1109/TVCG.2023.3243668 2

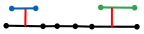
[69] S. K. Vohra, P. Harth, Y. Isoe, A. Bahl, H. Fotowat, F. Engert, H.-C. Hege, and D. Baum. A Visual Interface for Exploring Hypotheses About Neural Circuits. *IEEE Transactions on Visualization and Computer Graphics*, 30(7):3945–3958, July 2024. doi: 10.1109/TVCG.2023.3243668 2

[70] C. Weaver, C. Bruns, and M. Helvensteijn. Sharkviewer 1.1, Aug. 2014. 7

[71] D. Xenes, L. M. Kitchell, P. K. Rivlin, R. Brodsky, H. Gooden, J. Joyce, D. Luna, R. Norman-Tenazas, D. Ramsden, K. Romero, and others. Neuvue: A framework and workflows for high-throughput electron microscopy connectomics proofreading. *bioRxiv*, pp. 2022–07, 2022. Publisher: Cold Spring Harbor Laboratory. 3

[72] Y. Zhu and E. Yan. Searching bibliographic data using graphs: A visual graph query interface. *Journal of Informetrics*, 10(4):1092–1107, 2016. Publisher: Elsevier. 2

Table 1: **Algorithmic Evaluation.** Execution time comparison for motif querying between Arachne and NetworkX. Arachne is utilized in *MoMo*. Performance measured on a system with two AMD EPYC 7713 CPUs (64 cores each) and 1TB RAM. Data: FlyWire.

Subgraph	VF2-PS (sec)	NetworkX (sec)	# Instances
	**2.48**	336.45	696,460
	**3.62**	173.75	191,690
	**2.88**	5,980.54	5,048
	**339.46**	16,436.85	2,308
	**1.56**	435.07	44,657
	**78.77**	810.23	161,842
	**4.10**	1,018.23	179,255
	**38.06**	>12,000	4,992