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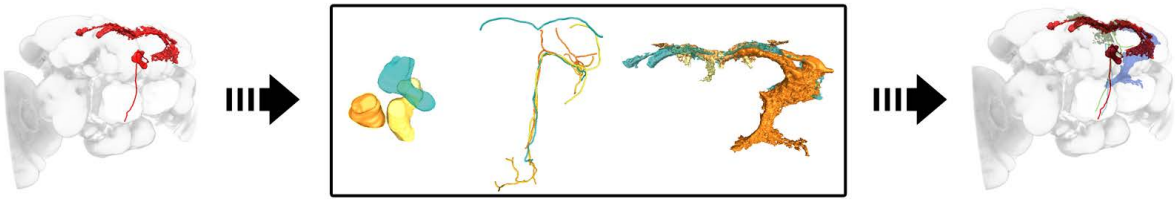
Similarity Based Object Retrieval of Composite Neuronal Structures

F. Schulze[1], M. Trapp[1], K. Bühler[1], T. Liu[2], B. Dickson[2]

[1]VRVis Forschungs GmbH, Austria
[2]Institute of Molecular Pathology, Austria



Abstract

Circuit Neuroscience tries to solve one of the most challenging questions in biology: How does the brain work? An important step towards an answer to this question is to gather detailed knowledge about the neuronal circuits of the model organism Drosophila melanogaster. Geometric representations of neuronal objects of the Drosophila are acquired using molecular genetic methods, confocal microscopy, non-rigid registration and segmentation. These objects are integrated into a constantly growing common atlas. The comparison of new segmented neurons to already known neurons is a frequent task which evolves with a growing amount of data into a bottleneck of the knowledge discovery process. Thus, the exploration of the atlas by means of domain specific similarity measures becomes a pressing need. To enable similarity based retrieval of neuronal objects we defined together with domain experts tailored dissimilarity measures for each of the three typical neuronal sub structures cell body, projection, arborization. The dissimilarity measure for composite neurons has been defined as domain specific combination of the sub structure dissimilarities. According to domain experts the developed system has big advantages for all tasks which involve extensive data exploration.

Categories and Subject Descriptors (according to ACM CCS): I.3.8 [Computer Graphics]: Applications—, I.3.5 [Computer Graphics]: Computational Geometry and Object Modeling —Curve, surface, solid, and object representations, I.3.5 [Computer Graphics]: Computational Geometry and Object Modeling —Object hierarchies

1. Introduction

A mechanistic understanding of brain function must ultimately be built upon a detailed account of how individual neurons are organised into functional circuits, and how information processing within these circuits generates perception and behaviour. Genetic model organisms offer the possibility of applying powerful genetic methods to identify, characterise, and manipulate specific neurons in the brain. In particular, Drosophila melanogaster, the fruit fly, has emerged as one of the leading model systems for exploring how information processing in defined neural circuits generates complex behavioural patterns [OW08]. Central to these approaches are methods to reproducibly label and identify cells of a given type, and to construct digital atlases that ideally would include representations of each neuronal type on a common frame of reference. Molecular genetic methods make it possible to express transgenic markers in various neuronal subsets. In some cases, individual types of neuron can be labelled in this manner, though more often multiple cell types

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are labelled in each brain. Neurons marked in this manner can be visualized using confocal microscopy, resulting in multi-channel volumetric images. To be able to combine images of different fruit flies, i.e. to overcome slight anatomical variations and distortions and to provide a common reference frame, all images are co-registered to a template brain using non-linear registration [RM03]. Interesting neuronal structures are segmented on the registered images and their geometric representations are stored together with their source images and other meta information in a database.

Given the number and diversity of neurons in the fly brain, any systematic mapping of the individual cell types necessarily involves the acquisition, registration, and analysis of many thousands of images. Such constantly growing collections of interrelated spatial data build the basis for further knowledge generation and reasoning, creating the need for effective tools enabling the scientist to explore these large data sets. One urgent need is for a method for efficient similarity searches and 3D object retrieval, as well as robust measures for the classification of neuronal morphologies. Given the representation of a specific type of neuron, or a component thereof, the scientist frequently needs to interrogate the entire database to identify other instances of the same neuron, or distinct neuronal types that share some but not all of its features. Such similarity measures can therefore also form the basis for automatic classification systems that could sort individual representations into distinct morphological classes.

We present a similarity based shape retrieval method tailored to the specific requirements of neuronal structures in the fly brain. The main contribution of this work is the definition of appropriate similarity measures for neuronal (sub-)structures. These methods should be equally applicable to brain atlases for other species.

2. Related Work

Neuroscience is a data intense field requiring specialized and scalable data management, data mining and exploration methods. Data collections and studies in neuroscience are often inter subject, i.e. aim at fusing information from data retrieved from different individuals to a common atlas. A good introduction to this specific kind of image and object data collections and related challenges has been given by Van Essen [Van02] and Hanchuang Peng [Pen08]. Van Essen described the emerging role of databases and atlases for neuroscience research, while Hanchuang Peng listed the main challenges of the new field of bioimage informatics as *clustering*, *classification*, *indexing* and *retrieval* of the data base contents.

Location or euclidean distance based search for neuronal structures have been addressed by Bruckner et al. [BSG*09]. They described a system which allows to retrieve neuronal objects from an atlas by visual queries. The user marks a location or object of interest with a brush gesture in space and the system immediately returns a list of close (minimal distance) or overlapping objects. A similar method for exploration of pathways and connectivity of neurons has been presented by Lin et al. [LTW*11]. The framework offers a variety of tools which allow to combine several location based queries to retrieve connected objects or to identify neurons sharing the same pathways through the brain. Fly Circuit [NB12] is a web based database for Drosophila image and object data. It offers the possibility to search for neurons or cell bodies by similarity. Similarity is defined either by spatial distance in case of cell bodies or by a spatial distribution matrix in case of whole neurons. Non of the three mentioned methods addresses a shape or similarity based search of neurons.

A method for interactive exploration of neuronal pathways in diffusion tensor imaging (DTI) of the human brain has been presented by Sherbody et al. [SAM*05]. A set of regions of interest can be interactively defined and manipulated while the algorithm returns all fiber tracts connecting these regions. Besides such manual exploration of fiber tract data, clustering methods have been used to automatically identify bundles of similar fibers. Similarity between fiber tracts is often defined by their euclidean distance. Demiralp and Laidlaw [Dem09] describe a weighted mean distance metric which favors the middle section of the fiber tract and use it for similarity coloring of fiber tract bundles. Moberts et al. [MVvW05] evaluated different clustering methods and reported that *hierarchical clustering using single-link and mean distance between fibers gives the best results*. These two methods explore the space of fiber tracts either by location, distance or connectivity. Appearance or shape is not directly considered.

A different approach is proposed by Scorcioni et al. [SPA08]. Neurons are characterized by more then 40 different metrics which describe the morphology of the structure. However, it becomes apparent that morphology is a very variable feature on our data. Algorithms which capture similarity on our data must be able to cope with variable morphology and partial matching shape.

Cardona et al. [CSA*10] presented a method which improves reconstruction of brain circuitry of the larval Drosophila by automatically assigning neurons to their respective lineages based on a shape based similarity measure and can be therefore considered as closest to our work. Unknown secondary axon tracts are automatically assigned to a lineage by matching them to previously labeled corresponding axon tracts. The proposed similarity measure for the tube like axon tracts is based on the curve morphing method of Jiang et al. [JBAK02] and relies on a combination of shape similarity, mean euclidean distance and shape homogeneity.

Several general approaches for rigid and non-rigid shape retrieval have been proposed. Their discussion goes beyond the scope of this paper. For a detailed survey on shape re-

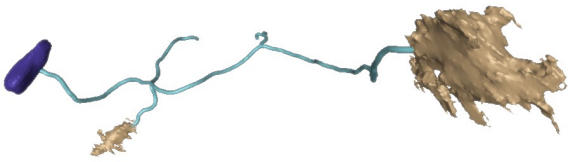

Figure 1: *Rendering of an neuron as it is stored in the fly brain atlas. Blue = cell body, green = projection, brown = arborizations.*

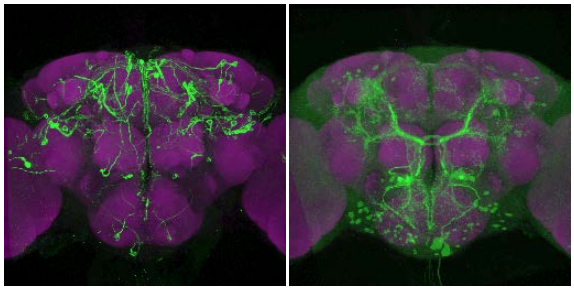

Figure 2: *Maximum intensity projections of volume image data. Green channel: Fluorescence staining of neurons. Magenta channel: Brain template. Left, basic image. Right, averaged image based on five basic images.*

trieval we refer to Tangelder and Veltkamp [TV07]. To the best of our knowledge non of these methods has been applied up to now to realize a shape based retrieval method for similar neurons.

3. Data and Methods

The nervous system of the Drosophila as in any invertebrate organism consists mainly of unipolar neurons (for more informations refer to [BH12]). This means that from a nerve cell body only one process extends from it, which typically later bifurcates into a dendritic branch and an axonal branch. A typical example of a neuron as it is stored in the database is depicted in Fig. 1.

The neuronal objects (cell bodies, projections and arborizations) are segmented on co-registered confocal microscopy images of the brain (see figure 2 left). The volumetric image has a size of $420\mu m \times 420\mu m \times 165\mu m$ and is sampled with a resolution of $768 \times 768 \times 165$ voxels.

Cell bodies and arborizations are marked supervised using a region growing tool on averaged image data (see figure 2 right). The resulting binary masks are automatically converted into triangle meshes for rendering and further processing. Projections, semi-automatically traced [LCCC08], are thin elongated tree-like structures which are represented as skeleton graphs with radii.

The composition of one cell body, one projection and any number of arborizations form a neuron. Each neuronal structure belongs to exactly one neuron, but a neuron stored in our database is not necessarily complete, i.e. only a subset of the three components might be available.

Since all structures are segmented based on co-registered image data, the objects share a common reference frame and form an atlas, i.e. they are directly comparable based on their location in space. However the locational invariance undergoes a significant uncertainty. This stems from an average registration error $\approx 5\mu m$ and biological variability between individual flies.

In the following we describe how dissimilarity between neuronal structures is modelled (section 3.1, 3.2 and 3.3) and how dissimilarity between whole neurons is defined (section 3.4).

3.1. Cell bodies

Cell bodies (soma) are blob-like structures located within the cortex of the fly brain (see fig. 1 left). Shape and size varies heavily on segmented data mainly because cell bodies are floating structures on the cortex. Therefore, the shape, gathered from averaged images captured from several genetically identical flies, represents the density of the cell body position.

The only discriminative feature of a cell body C is the location in space. Therefore dissimilarity can simply be computed using the euclidean distance between cell bodies center of mass $\mathbf{m}(C)$ and we define the dissimilarity function for two cell bodies C_a and C_b as follows:

$$D^c(C_a, C_b) = \|\mathbf{m}(C_a) - \mathbf{m}(C_b)\| \quad (1)$$

3.2. Projections

Projections (axons and dendrites) are thin elongated tree-like structures which are represented as skeleton graphs with radii. Discussions with domain experts revealed that the most characteristic features are location and shape, whereas other morphological features (e.g. number/ location of branches or terminals) are very variable and therefore misleading. Furthermore direct pairwise similarity computation is expected to be unrewarding and too expensive because of the expected growth of data. Therefore the presented approach aims to characterize projections by a small set of feature vectors which reflect the invariant properties of the structure and enables fast dissimilarity computation.

The most descriptive feature of a projection in an atlas is the position and shape of its traces. The morphology on the other hand can be different between instances of the same neuron. Therefore we transform a projection into a set of feature vectors which describe the properties of subparts of the skeleton graph, but ignore the morphology. Projection

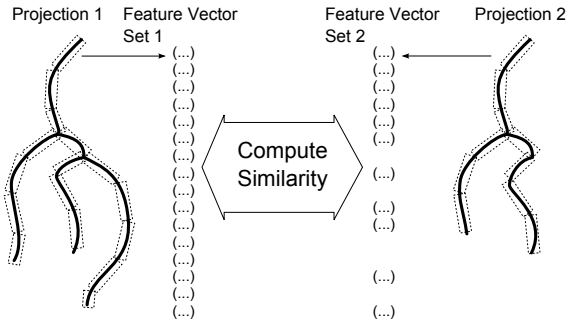

Figure 3: *Transformation of a projection skeleton graph into a set of feature vectors.*

skeleton graph P is split in n non branching sub-traces p_i. The length $|p_i|$ of the traces is a parameter of the algorithm and influences directly the number of feature vectors in the set. For each trace p_i a feature vector is assembled consisting of two three dimensional vectors:

$$\mathbf{f}(p_i) = (\mathbf{m}(p_i); \omega_{\mathbf{d}} \cdot \mathbf{d}(p_i)) \tag{2}$$

where $\mathbf{m}(p_i)$ denotes the center of mass of p_i and vector $\mathbf{d}(p_i) = (d_x^i, d_y^i, d_z^i)$ denotes the main direction of trace p_i. In order to be invariant against point order of the traces we demand that $d_x^i \geq 0$. If this is not the case the alignment is negated. $\mathbf{m}$ is normalized by dividing each component by the corresponding extension of the base volume, the alignment vector is normalized to $\|\mathbf{d}\| = 1$. The scalar $\omega_{\mathbf{d}}$ denotes a weighting parameter which defines the influence of the alignment on the feature vector. The whole projection is therefore described by a set of feature vectors:

$$\mathbf{F}(P) = (\mathbf{f}(p_1); ...; \mathbf{f}(p_n)) \tag{3}$$

Figure 3 shows an example where two different skeleton graphs should be compared. The comparison of both corresponding feature vector sets is not straight forward as the number of feature vectors varies and association between vectors is therefore undefined. Furthermore the distance measure should be able to detect partial matches.

Possible approaches to define a dissimilarity function for projections are for instance the *Bag of Words* [LG09] and the *Bag of Features* (BoF) [FSB09] algorithms. We propose to use the *Pyramid Match Kernel* (PMK) [GD05] because we found that a multi-scale method adapts better to the variability of the domain specific data. The PMK method builds a histogram pyramid over the feature space. The resolution of each histogram starts by 1 for each dimension and is doubled on every higher level. The pyramid match kernel K for the feature vector sets $\mathbf{F}_a := \mathbf{F}(P_a)$ and $\mathbf{F}_b := \mathbf{F}(P_b)$ of projections P_a and P_b is computed as follows:

$$K(\mathbf{F}_a, \mathbf{F}_b) = \sum_{k=0}^{L} \frac{1}{2^k} N_k \tag{4}$$

with

$$N_i = I(H_k(\mathbf{F}_a), H_k(\mathbf{F}_b)) - I(H_{k-1}(\mathbf{F}_a), H_{k-1}(\mathbf{F}_b)) \tag{5}$$

, where H_k denotes the histogram at level k and I is a function computing the overlap between histograms. Finally the kernel function K is turned into the dissimilarity function:

$$D^p(\mathbf{P}_a, \mathbf{P}_b) = 1 - \frac{1}{\sqrt{c}} K(\mathbf{F}_a, \mathbf{F}_b) \tag{6}$$

where $c = K(\mathbf{F}_a, \mathbf{F}_a) \cdot K(\mathbf{F}_b, \mathbf{F}_b)$ normalizes the similarity value.

3.3. Arborizations

Arborizations are dense terminal branching structures which enable neurons to intercommunicate. It is important to determine the similarity of arborizations to figure out if they correspond to the same neurons. Similarity between arborizations can be defined by their shape. Because of the generation process similar arborizations tend to differ by small distortions or sometimes only parts are segmented. We decided to use shape context because it benefits from being insensitive to small distortions and is easy to compute, yet still has a high accuracy. Originally proposed for 2D shape similarity [BM02], the shape context has also been generalized for 3D shapes [MBM05].

For each vertex $\mathbf{v}_i, i = 1..,n$ of the mesh representation of an arborization A a coarse log-polar histograms H_i with $k = 1, ..., l$ bins of the connection vectors of $\mathbf{v}_i$ with all other vertices is computed. Thus, H_i describes implicitly the relative positions of all other vertices of the shape in respect to v_i.

$$H_i(k) = |\{\mathbf{v} \in A | \mathbf{v} \neq \mathbf{v}_i;\ (\mathbf{v} - \mathbf{v}_i) \in bin(k)\}| \tag{7}$$

The bins of the histograms $H_i, i = 1, ..., n$ used for the shape context of the shape are uniform in log-polar space to make the descriptor more sensitive to near by sample points. The shape context descriptor is translation and rotation-invariant, and can be made scale-invariant by an additional normalization step.

As arborizations consist out of up to 800.000 vertices, and the runtime is dominated by the vertices, the general shape context is not appropriate for our application. Moreover, as sometimes only parts of arborizations are segmented, we also have to solve the problem of partial matching. Therefore, we propose to use the bag of features (BoF) based fast pruning algorithm using shape context (shapemes) by Mori et al. [MBM05].

To realize BoF we have to obtain a vocabulary of geometric words $W = \{w_1, \ldots, w_m\}$ that is representative for the full set of shape contexts of the known shapes. We use vector quantization through k-means clustering for our purpose. The corresponding BoF histogram $H_W(A)$ will be obtained

by counting the occurrences of the geometric words for the shape A.

Because the relation between the words is lost using BoF, we use a spatial-sensitive bag of features (SS-BoF) approach by Bronstein et al. [BBG11] to improve the results. In the case of SS-BoF, the frequency of word pairs $f_{ij}(A)$ for spatial close shape context histograms of the shape A will be used as feature descriptor. We use diffusion distance [Lin06] to measure the spatial distance. The resulting feature descriptor for the whole shape A is the $m \times m$ SS-BoF histogram $\mathcal{F}(A) = (f_{ij}(A))$.

In order to additionally strengthen discriminative word pairs, Bronstein et al. use the text retrieval inspired weighting proposed by Sivic and Zisserman [SZ03]. Word pairs with a high frequency are less discriminative then those with low frequency, therefore spatially-close geometric words will be weighted by their *inverse document frequency*

$$\omega_{ij} = log\left(\frac{N}{n_{ij}}\right) \tag{8}$$

where N is the number of objects in the database and n_{ij} is the number of occurences of the word pair (w_i, w_j) over all objects.

In order to compute the dissimilarity function for two arborizations A_a and A_b, we simply compute the L_1 distance between the weighted SS-BoF histograms $\mathcal{F}(A_a)$ and $\mathcal{F}(A_b)$

$$D^A(A_a, A_b) = \sum_{i=1}^{m}\sum_{j=1}^{m} \omega_{ij}\,|f_{ij}(A_a) - f_{ij}(A_b)| \tag{9}$$

3.4. Neurons

As neurons comprise cell body, projection and arborizations, similarity between neurons is defined by the similarity of these components. Therefore, the similarity of each component has to be computed and the result set of each component has to be combined in a rank-aware manner to one single result set.

Rank-aware queries, also known as top-k queries [IBS08], only retrieve the k objects that are highest ranked in the subqueries. For example, consider a top 5 similarity query on flags to a query flag in terms of color and texture. The top-k algorithm has to return those 5 flags that match best the criteria of the user in short computation time and determine a score value for each flag. An approach for fast processing of complex queries consisting of several subqueries has been presented by Güntzer et al. [GBK00] based on the approach of Fagin [Fag96].

To answer similarity queries on neurons our application has to return the top-k ranked neurons based on their subqueries. We use QuickCombine [GBK00] for fast subquery combination based on an aggregating dissimilarity function.

The selection of a dissimilarity function $D(X,Y)$ that maps the distances of each of the subqueries to a single score value is crucial for good results. As mentioned by Grosser et al. [GDC00] using domain knowledge for selecting a proper dissimilarity function improves the results of exploration algorithms.

Determining similarity between two neurons N_a and N_b based on their anatomy is a multi-step procedure. Neurobiologists first evaluate the similarity of the projections of the two neurons. If the projections are very similar it is very likely that the neurons also share an anatomical structure. In the next step, the similarity between the cell bodies and the arborizations will be determined. If those structures are also very similar it is very likely that both neurons are similar. Moreover if one of the two stages respond with a low similarity but the other with high similarity the neuron can still be of interest for the researchers.

Therefore we propose a structure-sensitive dissimilarity function between neuron $N_a = (C_a, P_a, A_a^1, ...A_a^m)$ and $N_b = (C_b, P_b, A_b^1, ...A_b^n)$.

$$D^{CA}(N_a, N_b) = \omega^C D^C(C_a, C_b) + \frac{\omega^A}{n+m}\sum_{i,j}^{m,n} D^A(A_a^i, A_b^j) \tag{10}$$

$$D(N_a, N_b) = \sqrt{\omega^P\, D^P(P_a, P_b)\, D^{CA}(N_a, N_b)} \tag{11}$$

4. Evaluation

For evaluation we used the following parameters: Projection feature vectors are computed from $40\mu m$ long traces. The weight of the alignment fraction is set to $\omega_{\mathbf{d}} = 0.2$. The shape context of arborizations is described by $4 \times 4 \times 8$ (α, β, radius) log-polar histograms. The vocabulary size is set to $m = 20$ geometric words and therefore each arborization is described by a 20×20 SS-BoF. For neuron similarity we used the following weighting parameters $\omega^C = 0.5$, $\omega^P = 1.0$ and $\omega^A = 1.0$. Cell body similarity is weighted by 0.5 because it is less discriminative than the other parts of a neuron.

Quantitative Evaluation: We asked the domain experts to select retrieval classes for 50 randomly chosen query objects from each of the projection, arborization and neuron collections. Cell bodies where not evaluated because dissimilarity is in this case defined only by euclidean distance. Hence assembling ground truth retrieval class would involve the definition of a distance threshold which recreates the ranking method and is therefore trivial.

The retrieval classes contain between one and 25 similar instances. The retrieval result was scored based on the manual composed ground truth data. Figure 4 shows the three resulting recall vs. precision plots.

We received unexpected good results for neuron retrieval which is due to the fact the experts selected just very few

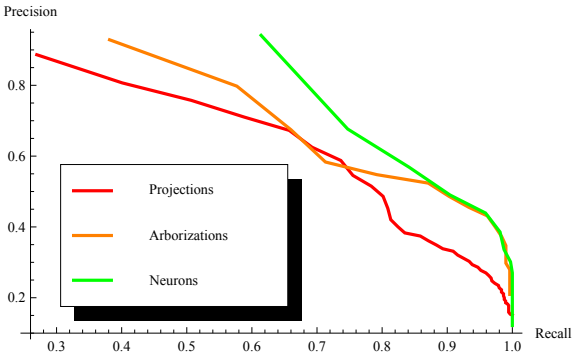

Figure 4: *Recall vs. Precision plots for projection, arborization and neuron retrieval.*

neurons into the retrieval classes because of the high variability and the low number of currently available complete neurons. Fortunately these neurons could be retrieved with very high ranks. This demonstrates the performance of the sub-structure dissimilarity models as well as composition method. On the other hand the recall vs. precision curve of projection retrieval has relatively low precision values together with high recall rates. Despite that the retrieval performance is still sufficient, this shows that the emphasis for similarity rating from the experts side goes beyond a pure geometrical definition, also knowledge about important pathways and anatomy plays a role.

Qualitative Evaluation. Domain experts evaluate the retrieval system and its performance in respect to the following use case: the assignment of new and unknown sub-structures (cell bodies, projections and arborizations) to already known neurons. The task usually either requires a very good knowledge of the data or involves lengthy manual search in the database. Therefore the problem gets more and more complex as the database grows.

For this task the domain experts reported a substantial gain of efficiency compared to manual assignments. The similarity search narrows down the amount of data which has to be compared visually dramatically. Tests showed for all sub-structure types that appropriate results are almost always retrieved within the top 20 ranks.

The domain experts also assessed the performance of the neuron retrieval method. The biologists reported that the method retrieves and ranks neurons in a comprehensible way. Furthermore they expect that, with regards to the advancing growth of the database, neuron object retrieval will become an important tool which will help to keep the neuron database explorable.

5. Results

Results of different neuronal object similarity queries are depicted in table 1. Query objects are at the first column followed by the top four result objects.

The first row shows an example query on cell bodies. As the only discriminative feature for cell bodies is the Euclidian distance between their center of mass, the query results are as expected.

Results for two projection retrieval cases are depicted in row two and three. The first case is relatively typical because the search results contain the three other instances of the same projection ranked as the top three results. In the second case the query is performed with an object that does not have any other instances but runs through a very common pathway. Rank one to three are set with completely unrelated projections and the rank four result is an instance of the same projection placed on rank one.

Results for two arborization retrieval cases are depicted in row four and five. The first case is based on unrelated geometric very similar shapes, whilst the second case also contains partial matches in the top ranks.

Results for neuron retrieval depicted in table 1 row six and seven. The first case demonstrates that our approach retrieves neurons that are of anatomically similar even if they are completely unrelated to each other. Moreover, in the second case the most similar neuron in the database are retrieved on the first place.

6. Conclusion

We have presented an effective object retrieval method for neuronal sub-structures as well as composite neurons. Our main contribution is the definition of dissimilarity functions for various neuronal structures which reflect the special needs in the domain of circuit neuroscience. Furthermore we defined a domain specific composition of sub-structure results which enables similarity based retrieval of complete neurons.

As domain experts have reported, the retrieval results for neuronal structures are absolutely appropriate. Apart from the currently low number of admissible composite neurons this even applies to neuron retrieval.

Despite the already good performance, future work must be the further enhancements of retrieval performance. This involves further exploitation of domain knowledge into the discrimination process. Furthermore, the next logical step would be a semi- or fully-automatic labeling of neuronal structures based on the proposed retrieval system.

Acknowledgments

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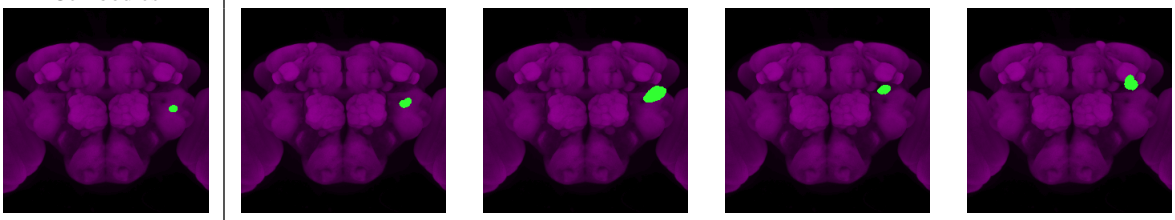
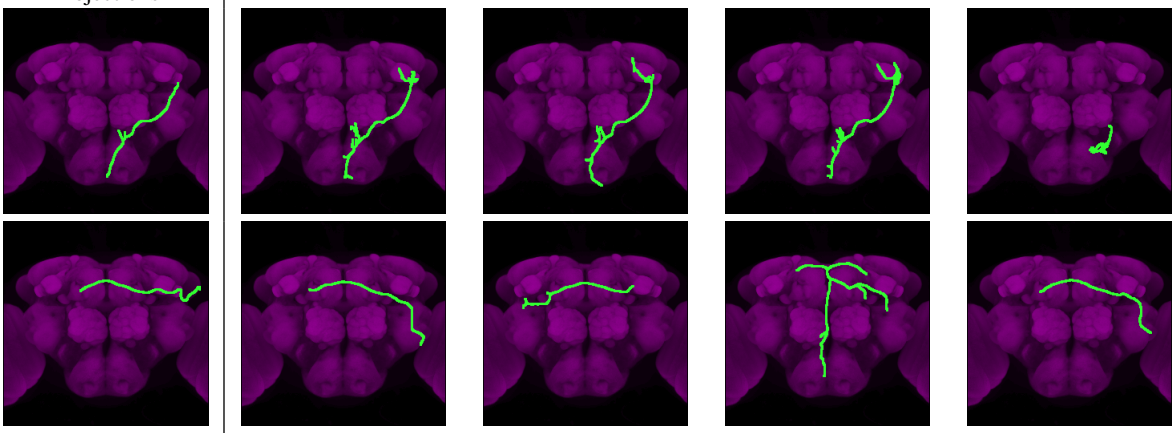
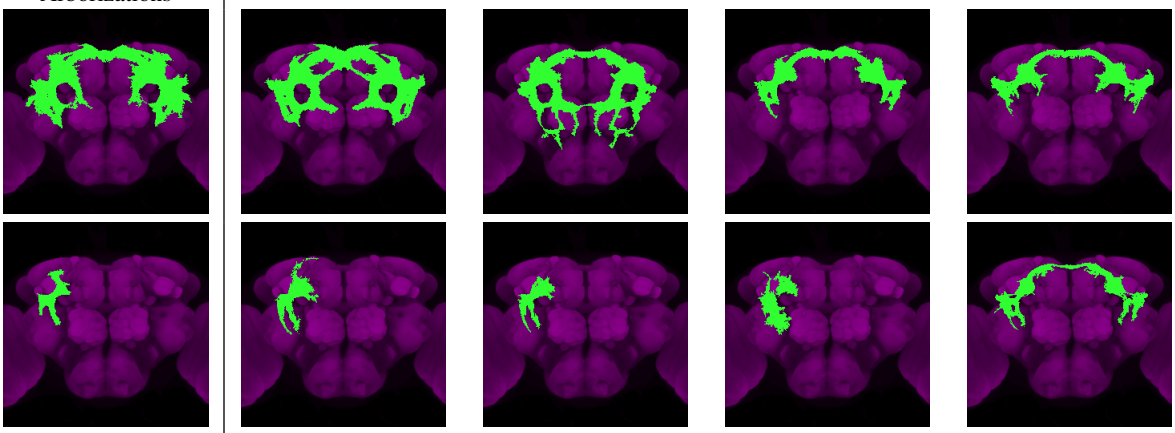
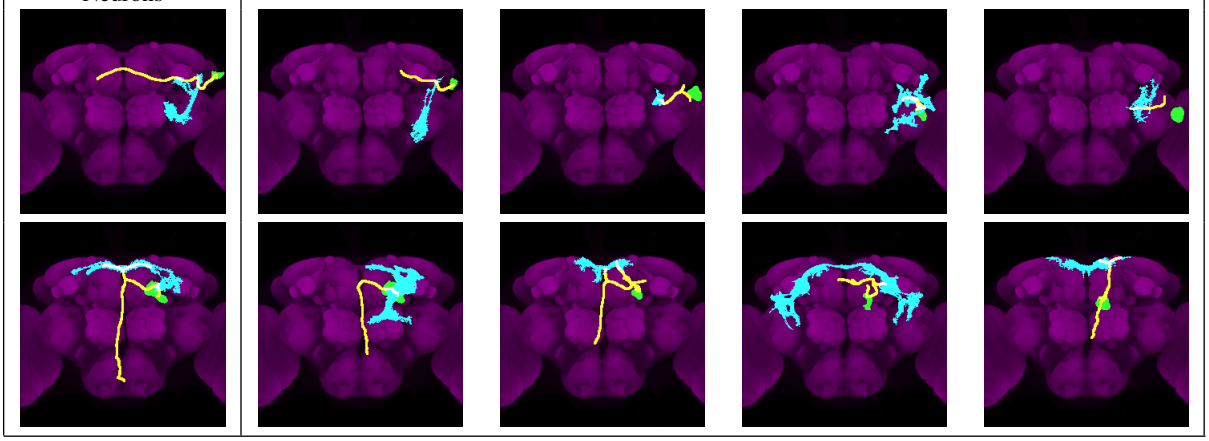
Query Object	1st rank	2nd rank	3rd rank	4th rank
Cell bodies				
Projections				
Arborizations				
Neurons				

Table 1: *Result Images*

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References

[BBG11] BRONSTEIN A., BRONSTEIN M., GUIBAS L.: Shape google: Geometric words and expressions for invariant shape retrieval. *ACM Transactions on* (2011). 5

[BH12] BLANKENSHIP J. E., HOUCK B.: Nervous system (invertebrate), 2012. URL: http://accessscience.com/content/Nervous-system-(invertebrate)/449210. 3

[BM02] BELONGIE S., MALIK J.: Shape matching and object recognition using shape contexts. *IEEE Transactions on Pattern 24*, 4 (Apr. 2002), 509–522. 4

[BSG*09] BRUCKNER S., SOLTÉSZOVÁ V., GRÖLLER M. E., HLADŮVKA J., BÜHLER K., YU J. Y., DICKSON B. J.: BrainGazer–visual queries for neurobiology research. *IEEE transactions on visualization and computer graphics 15*, 6 (2009), 1497–504. doi:10.1109/TVCG.2009.121. 2

[CSA*10] CARDONA A., SAALFELD S., ARGANDA I., PEREANU W., SCHINDELIN J., HARTENSTEIN V.: Identifying neuronal lineages of Drosophila by sequence analysis of axon tracts. *The Journal of neuroscience : the official journal of the Society for Neuroscience 30*, 22 (June 2010), 7538–53. 2

[Dem09] DEMIRALP C.: Similarity coloring of DTI fiber tracts. In *Proceedings of DMFC Workshop at* (2009). 2

[Fag96] FAGIN R.: Combining fuzzy information from multiple systems (extended abstract). *Proceedings of the fifteenth ACM SIGACTSIGMODSIGART symposium on Principles of database systems PODS 96* (1996), 216–226. 5

[FSB09] FEHR J., STREICHER A., BURKHARDT H.: A bag of features approach for 3D shape retrieval. *ISVC 1*, 4 (2009), 34–43. 4

[GBK00] GÜNTZER U., BALKE W., KIESSING W.: Optimizing multi-feature queries for image databases. In *Proceedings of the 26th International Conference on Very Large Data Bases* (2000), Morgan Kaufmann Publishers Inc., pp. 419–428. 5

[GD05] GRAUMAN K., DARRELL T.: The pyramid match kernel: Discriminative classification with sets of image features. In *Computer Vision, 2005. ICCV 2005. Tenth IEEE International Conference on* (2005), vol. 2, Ieee, pp. 1458–1465. 4

[GDC00] GROSSER D., DIATTA J., CONRUYT N.: Improving Dissimilarity functions with domain knowledge, applications with IKBS System. *Principles of Data Mining and Knowledge Discovery*, 1 (2000), 163–186. 5

[IBS08] ILYAS I. F., BESKALES G., SOLIMAN M. A.: A survey of top- k query processing techniques in relational database systems. *ACM Computing Surveys 40*, 4 (Oct. 2008), 1–58. 5

[JBAK02] JIANG X., BUNKE H., ABEGGLEN K., KANDEL A.: Curve morphing by weighted mean of strings. In *Pattern Recognition, 2002. Proceedings. 16th International Conference on* (2002), vol. 4, IEEE, pp. 192–195. 2

[LCCC08] LEE P.-C., CHING Y.-T., CHANG H. M., CHIANG A.-S.: A semi-automatic method for neuron centerline extraction in confocal microscopic image stack. *Computer* (2008), 959–962. 3

[LG09] LI X., GODIL A.: Exploring the Bag-of-Words method for 3D shape retrieval. In *IEEE Image Processing* (2009), pp. 437–440. 4

[Lin06] LING H.: Diffusion distance for histogram comparison. *Vision and Pattern Recognition, 2006 IEEE* (2006). 5

[LTW*11] LIN C. Y., TSAI K. L., WANG S. C., HSIEH C. H., CHANG H. M., CHIANG A. S.: The Neuron Navigator: Exploring the information pathway through the neural maze. In *Pacific Visualization Symposium (PacificVis), 2011 IEEE* (2011), IEEE, pp. 35–42. 2

[MBM05] MORI G., BELONGIE S., MALIK J.: Efficient shape matching using shape contexts. *IEEE Transactions on Pattern Analysis and Machine Intelligence 27*, 11 (2005), 1832–1837. 4

[MVvW05] MOBERTS B., VILANOVA A., VAN WIJK J. J.: Evaluation of fiber clustering methods for diffusion tensor imaging. In *IEEE Visualization* (2005), pp. 65–72. 2

[NB12] NCHC, BRC/NTHU: Fly Circuit, 2012. URL: http://www.flycircuit.tw/. 2

[OW08] OLSEN S. R., WILSON R. I.: Cracking neural circuits in a tiny brain: new approaches for understanding the neural circuitry of Drosophila. *Trends in neurosciences 31*, 10 (2008), 512–520. 1

[Pen08] PENG H.: Bioimage informatics: a new area of engineering biology. *Bioinformatics (Oxford, England) 24*, 17 (Sept. 2008), 1827–36. doi:10.1093/bioinformatics/btn346. 2

[RM03] ROHLFING T., MAURER C. R.: Nonrigid image registration in shared-memory multiprocessor environments with application to brains, breasts, and bees. *IEEE Transactions on Information Technology in Biomedicine 7*, 1 (2003), 16–25. 2

[SAM*05] SHERBONDY A., AKERS D., MACKENZIE R., DOUGHERTY R., WANDELL B.: Exploring Connectivity of the Brain âĂŹ s White Matter with Dynamic Queries. *Visualization and Computer Graphics 11*, 4 (2005), 419–430. 2

[SPA08] SCORCIONI R., POLAVARAM S., ASCOLI G. A.: L-Measure: a web-accessible tool for the analysis, comparison and search of digital reconstructions of neuronal morphologies. *Nature protocols 3*, 5 (Jan. 2008), 866–76. 2

[SZ03] SIVIC J., ZISSERMAN A.: Video Google: A text retrieval approach to object matching in videos. In *Computer Vision, 2003. Proceedings. Ninth IEEE International Conference on* (2003), no. Iccv, IEEE, pp. 1470–1477. 5

[TV07] TANGELDER J. W. H., VELTKAMP R. C.: A survey of content based 3D shape retrieval methods. *Multimedia Tools and Applications 39*, 3 (Dec. 2007), 441–471. 2

[Van02] VAN ESSEN D. C.: Windows on the brain: the emerging role of atlases and databases in neuroscience. *Current Opinion in Neurobiology 12*, 5 (2002), 574–579. 2