MAXIMUM INNER PRODUCT SEARCH FOR MORPHOLOGICAL RETRIEVAL OF LARGE-SCALE NEURON DATA

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ABSTRACT

Morphological retrieval is an effective approach to explore neurons' databases, as the morphology is correlated with neuronal types, regions, functions, etc. In this paper, we focus on the neuron identification and analysis via morphological retrieval. In our proposed framework, both global and local features are extracted to represent 3D neuron data. Then, compacted binary codes are generated from original features for efficient similarity search. As neuron cells usually have tree-topology structure, it is hard to distinguish different types of neuron simply via traditional binary coding or hashing methods based on Euclidean distance metric and/or linear hyperplanes. Thus, we propose a novel binary coding method based on the maximum inner product search (MIPS), which is not only more easier to learn the binary coding function, but also preserves the non-linear characteristics of neuron morphology data. We evaluate the proposed method on more than 17,000 neurons, by validating the retrieved neurons with associated cell types and brain regions. Experimental results show the superiority of our approach in neuron morphological retrieval compared with other state-of-the-art methods. Moreover, we demonstrate its potential use case in the identification and analysis of neuron characteristics.

Index Terms— neuron morphology, large-scale retrieval, binary coding, inner product

1. INTRODUCTION

How the brain works is one of the most challenging issues in neuroscience. As neurons are the basic elements of brain, understanding their properties and network connectivity is the key step to tackling this challenge. Generally, neurons tend to express distinct morphologies according to their cell types, brain regions, functions, etc. Therefore, it is reasonable and simple to explore the neuronal properties through their morphologies. Current visualization and image processing techniques [1, 2, 3] make it possible to reconstruct 3D neuronal models from microscopic images, and the increasingly 3D neuron image databases such as NeuroMorpho [4, 5] provide a platform to associate their properties and morphologies. Accordingly, neuron retrieval with similar morphology is an effective way to help neuroscientists identify unknown neurons and discover the relationship between their morphology and characteristic.

Recently, the well-studied neuron tracing techniques facilitate the research on neuron morphological retrieval [6, 7, 8, 9]. Costa et al. [10] proposed the concept of neuromorphological space, which analyzed the tree-like shape and identified the most important geometrical features in neuron cell. Then, Wan et al. [11] designed *BlastNeuron* for automated comparison, retrieval and clustering of 3D neuron morphologies. In the retrieval stage, *BlastNeuron* searches for similar neurons via the normalization of rank scores in terms of the closeness of feature vectors. Despite its high accuracy, this method could be inefficient when handling a large-scale neuron database. Therefore, Mesbah et al. [12] proposed a data-driven hashing scheme, i.e., hashing forest, to search among large neuron databases. By establishing multiple unsupervised random forests, 128 or more binary bits are generated to represent morphological features. Hash forest algorithm has achieved efficient and accurate results in neuron retrieval. Nonetheless, it usually needs a large number of bits (e.g., larger than 128), while its efficiency can be further improved with shorter binary codes. More importantly, the encoding process relies on the embedding of the Euclidean distance, which may not be a suitable similarity measure for neuron retrieval issue, as features of neuron data usually lie in complex feature spaces that may not be linearly separable. Therefore, it is desired to explore advanced hashing algorithms to solve these challenges.

As described in [12], binary coding or hashing techniques have achieved great success in efficient retrieval among large-scale databases, with many data-dependent methods proposed in recent years, including, but not limited to, Spectral Hashing (SH) [13], Anchor Graph Hashing (AGH) [14], Iterative

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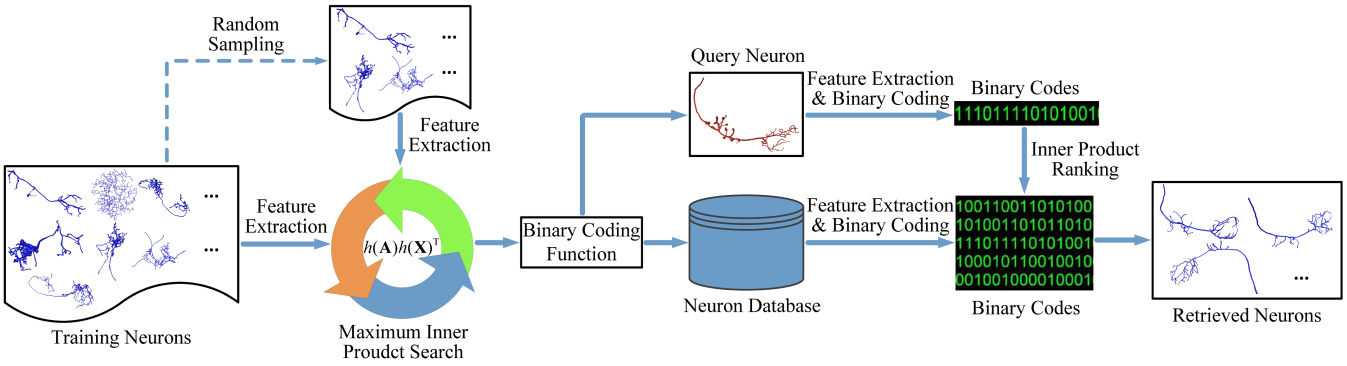

Fig. 1. Overview of the proposed neuron morphological retrieval framework.

Quantization (ITQ) [15], Inductive Manifold Hashing (IMH) [16], etc. However, they may not be directly applicable to the neuron retrieval problem, as the features of 3D neuron morphological data are dramatically different from 2D natural images. For example, the arborization structure can make different types of neurons hard to differentiate. In addition, although supervised binary coding and hashing methods have already been investigated in medical image analysis [17, 18], it is preferred to employ unsupervised methods for neuron retrieval, since there may not be accurate annotations for all neurons.

In this paper, we aim to investigate binary coding algorithms that can accurately perform large-scale neuron morphological retrieval, which is critical for neuron identification and analysis. Specifically, we design a novel binary coding method to retrieve neuron data with high precision and efficiency. Unlike prior methods learning hashing functions to embed Hamming distances and Euclidean distances, our method obtains effective coding functions for maximum inner product search (MIPS), which has the flexibility to differentiate complex features that are linearly inseparable in the original feature space. In fact, this strategy is particularly suitable for the neuron morphology data, which is usually nonconvex and nonsmooth. Moreover, we introduce an auxiliary variable such that the challenging MIPS problem can be efficiently optimized by several iterations. We validate the efficacy of the proposed method in the neuron retrieval problem with a large database, and it outperforms several other binary coding or hashing methods. In addition, according to the neuron information provided by NeuroMorpho [5], our proposed method can retrieve similar neurons not only in morphology, but also in cell type, brain region, etc.

2. METHODOLOGY

2.1. Overview

Fig. 1 shows the overview of our neuron retrieval method. At first, we extract both global and local morphological features to represent 3D neuron data, which is consistent with [10, 11, 12]. Global features such as neuronal width, height and depth are used for revealing the whole morphologies, and local features include the bifurcation and compartment information which represent the particular diversity among neurons. Subsequently, the neuron morphological retrieval problem can be regarded as the similarity search of their features. Although directly measuring the similarity between morphological features offers an accurate solution, the computational efficiency is an issue, especially when searching in a large-scale database. Therefore, we aim to learn a binary coding function which can maximize inner product between the feature of training neurons and a set of randomly sampled neurons. With this coding function, the features of query neuron and every neuron in the database can be compressed into short binary codes. Then, their inner product can be calculated and ranked with descending order. Finally, select neurons in the database with top-K largest inner product, and the characteristics of query neuron can be identified based on these retrieved neurons.

2.2. Binary Coding for Maximum Inner Product Search

In this section, we introduce a novel binary coding method based on maximum inner product search to solve the neuron morphological retrieval problem.

Maximum Inner Product Search (MIPS): The problem of MIPS plays a critical role in computer vision and machine learning domains. For the features of neuron database $\mathbf{A} = \{\mathbf{a}_1; \cdots; \mathbf{a}_n\} \subset \mathbb{R}^{n\times d}$ and a query neuron $\mathbf{q} \in \mathbb{R}^{1\times d}$, the MIPS problem can be defined as:

$$\mathbf{p} = \arg\max_{\mathbf{a}\in\mathbf{A}} \mathbf{a}\mathbf{q}^{\mathrm{T}} \tag{1}$$

which means finding the largest inner product between $\mathbf{q}$ and each element in $\mathbf{A}$. As demonstrated in [17], the Hamming distance and code inner product has a one-to-one correspondence. To accelerate computation and save storage, it is practical to employ binary coding method to implement MIPS

problem. A coding function h are learned to map original feature vectors to r bits of binary code. Thus, problem (1) is reformulated as:

$$\mathbf{p} = \arg\max_{\mathbf{a}\in\mathbf{A}} h(\mathbf{a})h(\mathbf{q})^{\mathrm{T}} \tag{2}$$

Compared with common binary coding methods based on Hamming distance minimization, h is likely to be a non-linear function through MIPS [19], which is more suitable for the neuron retrieval dataset that is linearly inseparable. Now the question is how to obtain the binary coding function h via the neuron database.

Coding Function Optimization: As shown in Fig. 1, optimize coding function for MIPS problem is the key step in large-scale neuron morphological retrieval. Assume $\mathbf{A} = \{\mathbf{a}_i\}_{i=1}^{n}$ are the feature vectors of n training neurons with d dimensions, and $\mathbf{X} = \{\mathbf{x}_j\}_{j=1}^{m}$ is random sampling from $\mathbf{A}$ with ratio of k. Denote $\mathbf{S} = \mathbf{A}\mathbf{X}^{\mathrm{T}}$ as the similarity matrix between $\mathbf{A}$ and $\mathbf{X}$. After binarizing $\mathbf{S}$ by its mean value, we aim to learn a coding function h for $\mathbf{A}$ and $\mathbf{X}$, which can well approximate $\mathbf{S}$ in the form of binary codes:

$$\min_{h} \left\| h(\mathbf{A})h(\mathbf{X})^{\mathrm{T}} - \mathbf{S} \right\|^2 \tag{3}$$

As this highly non-convex formula is hard to solve, we discard its quadratic part (i.e., normalization term) after expansion and only focus on the correlation between similarity matrix $\mathbf{S}$ and $(h(\mathbf{A})h(\mathbf{X})^{\mathrm{T}})$. Thereby, the objective can be re-defined as:

$$\max_{h} \mathrm{trace}(h(\mathbf{A})^{\mathrm{T}}\mathbf{S}h(\mathbf{X})) \tag{4}$$

In practice, we find that omitting the quadratic part does not affect the binary coding performance, and makes the highly non-convex problem easy to optimize, which is more efficient for the non-linear differentiation of neuronal morphologies. With the binary coding matrix $\mathbf{W} \in \mathbb{R}^{d\times r}$ and the *sign* function, which $h(\mathbf{A}) = \mathrm{sgn}(\mathbf{A}\mathbf{W})$, we obtain eq. (4) in a new form:

$$\max_{\mathbf{W}} \mathrm{trace}(\mathrm{sgn}(\mathbf{A}\mathbf{W})^{\mathrm{T}}\mathbf{S}\mathrm{sgn}(\mathbf{X}\mathbf{W})) \tag{5}$$

To optimize (5), we first assume that the right part is fixed as a constant matrix $\mathbf{Z}= \mathrm{sgn}(\mathbf{X}\mathbf{W})$. Then, we introduce an auxiliary variable $\mathbf{B}$ as the binary codes of $\mathbf{A}$ to replace the left part $\mathrm{sgn}(\mathbf{A}\mathbf{W})$, and eq. (5) can be separated into two terms:

$$\max_{\mathbf{B},\mathbf{W}} \mathrm{trace}\left[(\mathbf{B}^{\mathrm{T}}\mathbf{S}\mathbf{Z}) - \lambda\|\mathbf{B} - \mathbf{A}\mathbf{W}\|^2\right] \tag{6}$$

The first term maximizes inner product via the binary coding matrix $\mathbf{W}$, and the second term ensures that $\mathbf{A}\mathbf{W}$ can approximate with the target binary codes $\mathbf{B}$. Denote λ as a trade-off parameter between these two items. Subsequently, $\mathbf{W}$ can be optimized by several alternative iterations with $\mathbf{B}$:

$$\begin{cases} \mathbf{B} = \mathrm{sgn}(\mathbf{S}\mathbf{Z} + 2\lambda\mathbf{A}\mathbf{W}) \\ \mathbf{W} = \mathbf{A}^{\dagger}\mathbf{B} \end{cases} \tag{7}$$

where $\mathbf{A}^{\dagger}$ is the pseudo-inverse of $\mathbf{A}$. We denote such alternative iterations as inner loop and local optimal $\mathbf{W}$ of eq. (6) will be acquired until converge or reach maximum t iterations. Then update eq. (5) and $\mathbf{Z}$ with current $\mathbf{W}$. To obtain more accurate coding matrix for eq. (5), several outer iterations between (5) and (6) are still needed until coverage or reach maximum T iterations.

With acquired coding matrix $\mathbf{W}$, every neuron morphological features $\mathbf{x}_i \in \mathbb{R}^{1\times d}$ can be mapped to binary codes via the coding function $h(\mathbf{x}_i) = \mathrm{sgn}(\mathbf{x}_i\mathbf{W})$. Accordingly, the similarity search problem between query neuron and the neuron database is transformed as the inner product ranking of their binary codes. For a query neuron, the similar neurons are defined as the corresponding top-K largest inner product, and these similar neurons can further be used to interpret biomedical meanings of the query neuron.

	SH [13]	AGH [14]	ITQ [15]	Ours
top5	0.8690	0.8738	0.8627	**0.9048**
top10	0.8087	0.8198	0.8131	**0.8556**
top15	0.7587	0.7860	0.7881	**0.8214**
top20	0.7125	0.7488	0.7673	**0.7863**

Table 1. Average precision of four methods under different number of retrievals for 252 query neurons.

3. EXPERIMENTS

We first compare the proposed neuron retrieval method with other relevant methods in this section. Then we will discuss its use case in neuron identification and analysis.

During the experiment, we use 17,107 public 3D neuron data in NeuroMorpho [5], which are reconstructed from microscopy images of Drosophila Melanogaster. L-measure toolbox [20] is employed to extract morphological features. In total, there are 38 dimensional global and local features extracted from each neuron. In the binary coding stage, we extract every neuron's feature in the database as training data $\mathbf{A}$, and $\mathbf{X}$ is random sampled from $\mathbf{A}$ with 2:1 ratio. Maximum iterations of the inner loop and outer loop during optimization are 100 and 20 respectively. The trade-off parameter λ is set as 34. All experiments are conducted on a desktop with 3.6GHz processor of eight cores and 32G RAM.

To evaluate the efficacy of our method for neuron morphological retrieval problem, we compare the retrieval precision with other three state-of-the-art binary coding and hashing methods, i.e., Spectral Hashing (SH) [13], Anchor Graph Hashing (AGH) [14], and Iterative Quantization (ITQ)

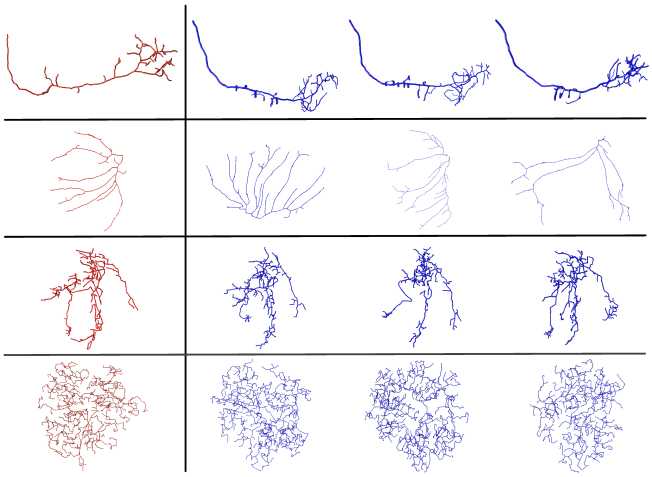

Fig. 2. For each neuron on the left (red), top-3 retrieved neurons on the right (blue) through our method, which illustrate the morphological similarity between query neurons and retrieved neurons.

[15]. All the neurons are compressed into 32 bits of binary code through these methods during the comparison. As neuron morphology is correlated with their cell types and brain regions, for the Drosophila Melanogaster neuron database which has various cell types (around 100) and brain regions (around 50), we select 233 projection neurons (PN) in olfactory bulb and 19 lateral horn neurons (LH) in protocerebrum as queries, which is consist with [11]. In the testing phase, the correct retrieved neurons are defined as if they present the same cell types and brain regions with the query neuron.

For all the PN and LH queries (252 in total), Table. 1 reports their average retrieval precision of four competitive methods under different number of candidates. Denote retrieval precision as the percentage of correct neurons in the candidates. According to Table. 1, our method can obtain the most precise retrieval results among these competitive methods. It is mostly benefited from the nonconvex optimization strategy of MIPS, which is particularly suitable for the linear inseparable neuron morphological retrieval problem. Fig. 2 present four random selected query neurons and their corresponding top-3 retrieved neurons through our method. We employ *Vaa3D* [1] to display these neurons. Generally, the retrieved neurons present similar morphologies with their query neurons, which verify the effectiveness of feature extraction procedure and the proposed binary coding method.

Beside the retrieval precision, the proposed method also demonstrates the computational efficiency in the testing phrase. Compared with traditional similarity search methods such as k-Nearest Neighbors, our binary coding method is 30 times faster (252 queries' retrieval in 0.17 seconds). This merit will be particularly beneficial in the future when more dimensional features are extracted and larger scale databases

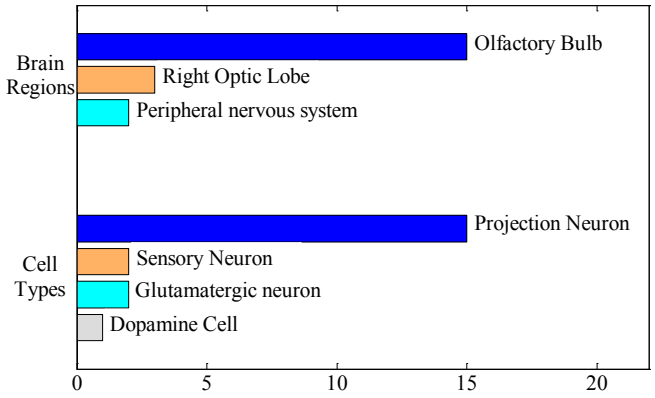

Fig. 3. The distribution of cells types and brain regions for top-20 retrieved neurons.

are used.

With the development of neuron tracing, an increasing number of newly reconstructed neuron morphologies are released in recent years. However, most of them lack basic annotations such as cell types, brain regions, transmitters. Therefore, identifying their characteristics is an urgent need for further exploration [21]. Based on the fine retrieval results, it is reasonable to apply our method for neuron identification and analysis. We select a query neuron and assume that its characteristics are unknown. After running the morphological retrieval procedure by our method, Fig. 3 shows the distribution with respect to top-20 retrieved neurons' cell type and brain region. According to the statistical information presented in Fig. 3, the query neuron most likely locates in olfactory bulb, and it belongs to the class of projection neuron. From these characteristics, we can reasonably infer that the query neuron is relevant to drosophila's olfactory system, and it serves as a connector with other function parts. Meanwhile, the information provided in NeuroMorpho [5] also verified our inference about the query neuron.

4. CONCLUSIONS

In this paper, we introduced a large-scale morphological retrieval framework for neuron identification and analysis. Specifically, we proposed a novel binary coding method based on MIPS, which not only achieved fast retrieval, but also differentiated the linearly inseparable morphological space with high precision. Experimental results verified the efficacy of our binary coding method and also illustrated its application in neuron identification. Based on the present work, we will study how to extract more typical features from 3D neuron image in the future, which can indicate different levels of morphological similarity. We will also apply the morphological retrieval method to explore the relationship between neuronal structure and function.

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