Sncg, Mybpc1, and Parm1 Classify subpopulations of VIP-expressing interneurons in layers 2/3 of the somatosensory cortex

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Introduction

Neocortical vasoactive intestinal polypeptide-expressing (VIP+) interneurons display highly diverse morpho-electrophysiological and molecular properties. To begin to understand the function of VIP+ interneurons in cortical circuits, they must be clearly and comprehensively classified into distinct subpopulations based on specific molecular markers. Here, we utilized patch-clamp RT-PCR (Patch-PCR) to simultaneously obtain the morpho-electric properties and mRNA profiles of 155 VIP+ interneurons in layers 2 and 3 (L2/3) of the mouse somatosensory cortex.

Electrophysiological classification of L2/3 VIP+ interneurons

Electrophysiological properties were analyzed by extracting 25 features for each cell. Cluster stability was assessed using subsampling and clustering analysis. Clear boundaries were observed between three distinct types of cells (E-types) using UMAP. E-type 1 cells showed burst spikes followed by regular spiking, while E-type 2 cells displayed irregular spike frequency after initial bursts. E-type 3 cells exhibited continuous adapting firing. Vector factor map analysis revealed distinct regions for each E-type in a PCA plot of electrophysiological features. These results indicate significant differences among the three E-types, suggesting distinct subtypes of VIP+ interneurons.

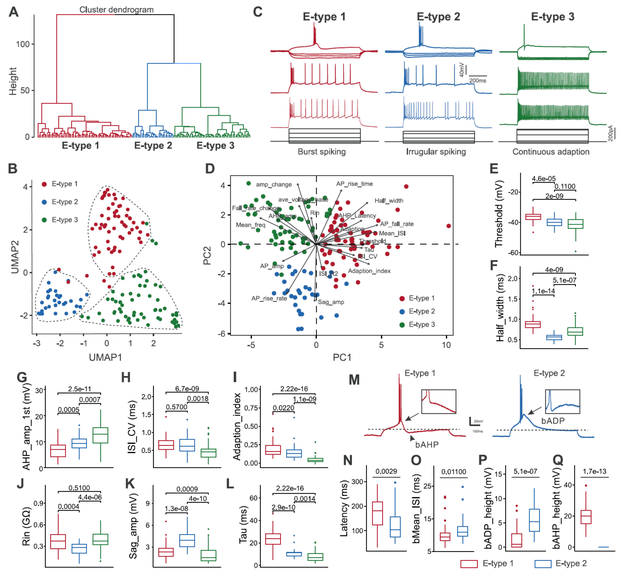

Figure 1. Electrophysiological classification of L2/3 VIP+ interneurons.

My Contributions and Benefits in electrophysiological data analysis

I contribute to build quantitative analysis methods to patch-clamp data using R and Python, original code on my Github. I've honed skills in profiling objects quantitatively, extracting features, and applying classification and clustering methods like random forest and hierarchical clustering.

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Morphological classification of L2/3 VIP+ interneurons

After visualizing neurons, we identified two distinct morphological clusters (M-type 1 and M-type 2) based on 42 extracted features. M-type 1 cells displayed multipolar morphology with descending main and wide horizontal axons, while M-type 2 cells exhibited dendritic features. Axonal distributions primarily characterized M-type 1, while dendritic features dominated M-type 2. Furthermore, M-type 1 cells were concentrated in upper L2/3, whereas M-type 2 cells were distributed throughout L2/3.

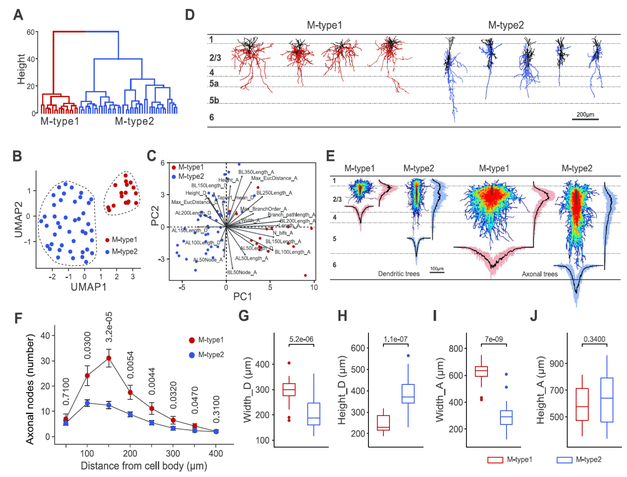

Figure 2. Enter Caption

Morpho-electrophysiological classification of L2/3 VIP+ interneurons

We analyzed both electrophysiological and morphological characteristics together, finding 3 distinct groups (ME-types) using a clustering method. Each ME-type showed consistency in their electrical (E-types) and structural (M-types) characteristics. These 3 ME-types covered about 85% of our sample.

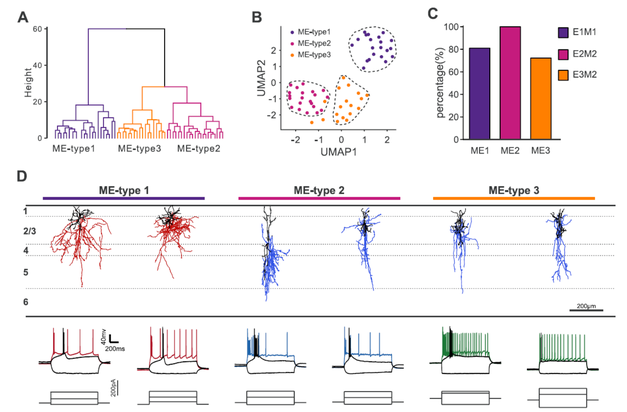

Figure 3. Morpho-electrophysiological classification of L2/3 VIP+ interneurons.

My contribution and benefits in morphological data analysis

In this journal paper, I didn't contribute much on morphological analysis, but I extensively studied neural morphological and electrophysiology quantification and discussed its advantages in my master's thesis. I have a strong understanding of morphological quantitative profiling systems. Specifically, I excel in reconstructing neuron shapes into standardized data formats, assessing the quality of this data, extracting features, and creating clustering or classification models. I think these skills will be helpful in my future research because analyzing research subjects quantitatively is crucial but difficult in science. In neuroscience, studying both electrical signals and neuron morphology is essential.

My exploration of quantitative neuron electric and morphological features (part from my this stage thesis)

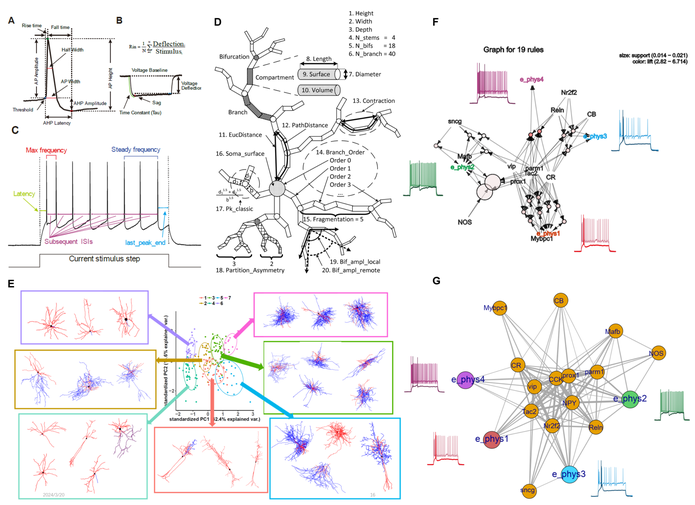

Figure 4. My exploration of quantitative neuron electric and morphological features. A-C. Quantitative Electric Parameters. D. Quantitative morphological Characteristics [1]. E. PCA clustering of morphological features. F-G. Apriori correlation (F) and Complex networking (G) analysis of neuron multi-layer features.

Conclusion

Together, our results suggest that Sncg, Mybpc1,andParm1 define 3 major VIP+ interneuron populations within L2/3 of the somatosensory cortex. We expect that these 3 signature genes can serve as a valuable genetic entry point for experimentally investigating VIP+ interneuron subpopulations.

Personally, I delved into quantitative methods in electrophysiology and neuron morphology, grasped the purpose and significance of classification, and enhanced my understanding of complexities within neuroscience. Additionally, this project effectively nurturing my data mining skills.

[1] Luciano Da Fontoura Costa, Krissia Zawadzki, Mauro Miazaki, Matheus P. Viana, and Sergei N. Taraskin. Unveiling the Neuromorphological Space. *Frontiers in Computational Neuroscience*, 4, 2010.