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Detecting Memory-Related Gene Modules in sc/snRNA-seq Data by Deep-Learning

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Abstract : To understand the detailed molecular mechanisms of memory formation in engram cells is one of the most fundamental questions in neuroscience. Recent single-cell RNA-seq (scRNA-seq) and single-nucleus RNA-seq (snRNA-seq) techniques have allowed us to explore the sparsely activated engram ensembles, enabling access to the molecular mechanisms that underlie experience-dependent memory formation and consolidation. However, the absence of specific and powerful computational methods to detect memory-related genes (modules) and their regulatory relationships in the sc/snRNA-seq datasets has strictly limited the analysis of underlying mechanisms and memory coding principles in mammalian brains. Here, we present a deep-learning method named SCENTBOX, to detect memory-related gene modules and causal regulatory relationships among themfromsc/snRNA-seq datasets. SCENTBOX first constructs codifferential expression gene network (CEGN) from case versus control sc/snRNA-seq datasets. It then detects the highly correlated modules of differential expression genes (DEGs) in CEGN. The deep network embedding and attention-based convolutional neural network strategies are employed to precisely detect regulatory relationships among DEG genes in a module. We applied them on scRNA-seq datasets of TRAP; Ai14 mouse neurons with fear memory and detected not only known memory-related genes, but also the modules and potential causal regulations. Our results provided novel regulations within an interesting module, including Arc, Bdnf, Creb, Dusp1, Rgs4, and Btg2. Overall, our methods provide a general computational tool for processing sc/snRNA-seq data from case versus control studie and a systematic investigation of fear-memory-related gene modules.

Keywords : sc/snRNA-seq, memory formation, deep learning, gene module, causal inference
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