Integrating fMRI and Single-Cell Data of Visual Working Memory

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Extended Abstract

We present a computational neuroscience based approach that integrates, via a detailed large-scale microscopic neurodynamical computational model, single-cell (Rao, Rainer and Miller 1997), and fMRI (Postle and D'Esposito 2000) measurements of the prefrontal cortex associated with working memory processing. We demonstrate that this type of realistic biophysical modeling can be used to investigate the topographical structure of the PFC, providing a specifc way for contrasting different hypothesis concerning the functional organization of the PFC with experimental evidence at both microscopic and macroscopic (single-cell and fMRI, respectively) levels of analysis. For this purpose, we formulated an explicit model of the mechanisms that underly working memory-related activity during the execution of delay tasks with a 'what'-then-'where' design (object and spatial delayed response within the same trial). The model contains different pools of spiking neurons (as found experimentally) in attractor networks that respond during the delay period to the stimulus object, the stimulus position, and to combinations of both object and position information. The pools are arranged in a hierarchical architecture governed by the Biased Competition Hypothesis, which assumes that multiple activated populations of neurons engage in inter-population competitive interactions, implemented through inhibitory interneurons and excitatory top-down interactions. This competition mutually biases the competition in favour of specific neuronal pools. We compared the simulated results for two hypotheses for the organization of the PFC: (1) ventrolateral and dorsolateral prefrontal cortex differ in terms of the type of stimuli they deal with (objects for the former, spatial location for the latter), or (2) dorsolateral and ventrolateral PFC differ in terms of the level of inhibition that they support.

Previous studies using such large-scale models to relate neural activity to functional brain imaging data have employed leaky integrator type neuronal units (e.g., Tagamets and Horwitz (1998), for example, employed Wilson-Cowan units). One novel aspect of our model is that our architecture is implemented with integrate-and-fire neurons (in the theoretical framework of Brunel and Wang (2001)), so that the details of the spiking and synaptic mechanisms involved can be understood, and so that predictions can be made about the effects, for example, of neurotransmitters and pharmacological agents that have particular effects

on synaptic transmission. The processes occurring at the AMPA and NMDA synapses are dynamically modelled in the integrate-and-fire implementation to produce realistic spiking dynamics. Even more, the architecture described is an extension beyond attractor architectures in that different neuronal pools or populations, connected hierarchically, are simulated, and in that an attentional bias is applied that allows the network to select the correct response given the current stimulus and attentional bias. Specifically, we have formulated the biased competition hypothesis for the first time in the framework of a very detailed and biophysically realistic spiking neuronal and synaptic dynamics. This has enabled us to integrate the effects of recurrent maintenance associated with short term memory with the biasing attentional effects associated with a cognitive task. As a result, we have been able to provide not only a quantitative and qualitative description of different experiments, but also to make concrete predictions of experimental effects.

Our modeling specifically compared two different hypotheses concerning the functional organization of the PFC during the delay period of a WM task. One, the organization-by-stimulus-domain hypothesis, posits that ventrolateral cortex contains a large number of neurons that maintain the visual features of objects during working memory delay periods, and dorsolateral cortex contains a large number of neurons that maintain the spatial locations of objects during such delays. The second, the organization-by-process hypothesis, asserts that the main functional difference between ventrolateral and dorsolateral PFC is that the former is concerned with maintenance of the information during the delay period of a working memory task, whereas the latter is involved in manipulation of stored information. Our main finding was that our model could account for both the neurophysiological activity seen in both ventrolateral and dorsolateral PFC during the delay periods of WM tasks, while at the same time providing simulated fMRI patterns that matched experimental findings during a 'what-then-where' short-term memory task for both PFC sectors. However, we could not do this if we assumed that the difference between ventrolateral and dorsolateral PFC followed the organization-by-stimulus-domain hypothesis. Rather, we had to assume that the differences between these two sectors resulted from assigning a greater amount of inhibition to the doroslateral portion of PFC. Our modeling thus suggests that different levels of competition of the networks associated with the ventrolateral and dorsolateral PFC could be the neural basis of the different functions associated with these brain regions. Both brain areas show maintenance capabilities related to their capacities to maintain stable attractors during delay periods, but the increased level of inhibition assumed in the dorsolateral PFC may be associated with the capacity of this brain region to support more complex functions like manipulations.

References

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