Testable predictions made by the semblance hypothesis and how to test them?

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Testable predictions are expected from any causal mechanism for a phenomenon (Douglas, 2009). There is an expectation that testable predictions should come with some surprise and need prospective studies to fulfill the criteria. But this need not always have to be true. The semblance hypothesis has already provided several retrodictive evidence using works that were published after the hypothesis was put forward (see New Findings page in this website). The following are some of the verifications that can be made in the prospective studies.

1. Associative learning will generate new inter-postsynaptic functional LINKs (IPLs)

This is a direct study of the key structural changes proposed by the semblance hypothesis. Total surface area of dendritic spines ranges from 0.61 to 3.14 μm^2 (Wilson et al., 1983). IPLs are expected to be formed at the lateral locations of the spine. At the locations of convergence of sensory stimuli (for e.g. amygdala and hippocampus), experiments can be carried out to stimulate converging paths to generate new IPLs. Then, stimulation of one of the paths can be used to verify the formation of IPLs both functionally (will be able to demonstrate formation of new IPL channel that lead to increase in current flow) and structurally (e.g. injecting different neurons, whose spines can undergo IPLs, with different lipophilic fluorophores to stain their membranes (Floyd et al., 2008) followed by associative learning or by comparable stimulation is expected to demonstrate IPL formation) (Vadakkan, 2013).

2. Firing of laterally located neurons of the same neuronal order need formation of new IPLs.

In a study, artificially triggering several spikes (action potentials) in single neurons in layer 2/3 of mouse visual cortex V1area resulted in spiking activity in a group of sparsely distributed neighboring neurons in the same neuronal order and were correlated in time (Chettih & Harvey, 2019; see also Smith, 2019). The small population of neurons that were excited were located at short distance (25–70μm) from the stimulated neuron. The stimulation had no influence beyond 300μm. The prediction is formation of IPLs between spines of the artificially fired neurons and that of the sparsely located neurons that were fired in a time-correlated manner.

3. Strength of LTP at a particular location depends on the fiber density of the converging input terminals.

For a specific distance between the stimulating and recording electrodes, strength of LTP induced at different locations will depend on the number of inter-spine LINKs formed during the delay time after stimulation (Vadakkan, 2019). This can be demonstrated by correlations between spine density at locations between the stimulating and recording electrodes and the strength of LTP at different locations.

4. Dependence of generation of internal sensations on a narrow range of frequency of oscillating extracellular potentials.

Both associative learning and retrieval of memories take place only during a narrow range of oscillating extracellular potentials. Methods to change the frequency of oscillating extracellular potentials in the olfactory glomerulus in the fly *Drosophila* can alter smell perception (Vadakkan, 2015).

5. Certain dendritic spikes are not followed by somatic action potentials (Golding & Spruston, 1998).

When current is injected into the dendrites of human layer 2/3 neurons they generated repetitive trains of fast dendritic calcium spikes, which can be independent of somatic action potentials (Gidon et al., 2020). So, a route for leakage of potentials from the dendritic area other than its propagation towards the soma needs to be explained. The islet of inter-LINKed spines (IILSs) provides routes for a dendritic spike to propagate. A dendritic spike can propagate to inter-LINKed spines within an IILSs (that offer fewer resistant routes) towards the dendritic trees of those IILSs' neurons. Recordings carried out from neighboring postsynaptic neurons will provide proof for the presence of IILSs.

References

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