

Constraints implicitly used in the book *Semblance of activity at the shared postsynapses and extracellular matrices*

Functional constraints 1. Memory retrieval must occur within physiological timescales. 2. Retrieval must recreate the learned event. 3. **Retrieval must occur without activating the original presynaptic neuron in the path of the item whose memory is being retrieved.** 4. Learning requires **coincidence of at least two inputs (co-activation of at least one pair of synapses).** 5. Memory must remain highly specific.

Cellular constraints. 1. **The elementary mechanism must occur at postsynaptic sites.** 2. Rapid recall cannot require protein synthesis. 3. Repeated learning should stabilize cellular changes. 4. Cellular events should be **reversible and reusable.**

Structural constraints. 1. Existing anatomical structures should support the mechanism. 2. **Closely apposed postsynaptic membranes are required.** 3. Learning should reorganize postsynaptic relationships. 4. **Structural organization must permit enormous combinatorial capacity.**

Physiological constraints. 1. **Single-trial learning should be possible.** 2. Forgetting should occur naturally. 3. Temporary ECM changes and longer-lasting structural changes should be able to explain working memory and long-term memory.

Systems-Level constraints. 1. No separate mechanism should be required for systems memory. 2. **Consolidation** (Cortical mechanism survive hippocampal loss after sufficient learning) **must be explained.** 3. Reconsolidation (temporary lability of memory upon reactivation) must be explained. 4. The mechanism must accommodate ongoing adult neurogenesis.

Plasticity Constraints. 1. The mechanism must **remain compatible with LTP.** 2. Protein synthesis dependence for long-term stabilization must be explained. 3. **Related learning should become easier.**

Network constraints. 1. **Memory codes must be distributed** (Memory should depend on many postsynaptic relationships rather than single neurons). 2. Retrieval should tolerate partial cues. 3. **Degeneracy should exist** (Different but related cues should retrieve the same memory). 4. The mechanism should explain other brain functions such as perception.