9.01 Introduction to Neuroscience
Fall 2007

Declarative memory

conscious, declared, explicit

Where is declarative memory?

epilepsy

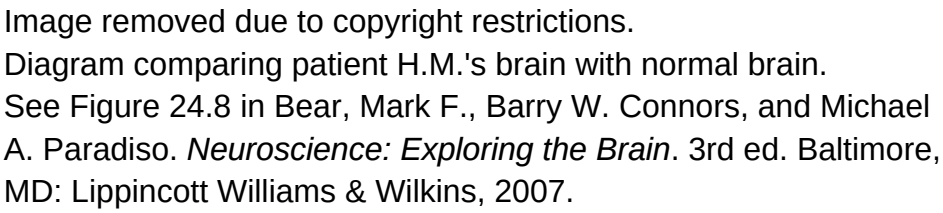
electrical stimulation

lesion

Temporal lobe epilepsy

- sensations
- feelings of familiarity or unfamiliarity
- recollections/flashbacks
- temporal cortex electrical stimulation
  - causes the same effects
  - Wilder Penfield
- medial part of temporal lobe

Bilateral medial temporal lobectomy



H.M.

- long-term memory
  - anterograde amnesia
  - partial retrograde amnesia
- short-term memory intact
- procedural memory intact

Short-term vs. long-term memory

- Short-term memory
  - seconds to minutes
- Long-term memory
  - up to a lifetime
- Consolidation
  - conversion of STM to LTM

Medial temporal lobe lesion in monkeys

- Errors in delayed non-match to sample increase with time delay

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See Figure 24.11 in Bear, Mark F., Barry W. Connors, and Michael A. Paradiso. *Neuroscience: Exploring the Brain*. 3rd ed. Baltimore, MD: Lippincott Williams & Wilkins, 2007.

Strongest effect from lesion of perirhinal cortex

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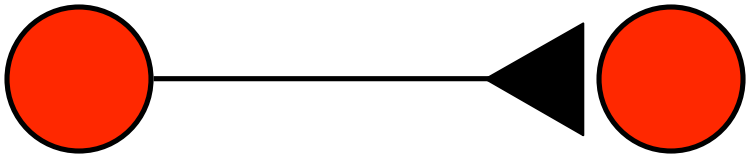
See Figure 24.9b in Bear, Mark F., Barry W. Connors, and Michael A. Paradiso. *Neuroscience: Exploring the Brain*. 3rd ed. Baltimore, MD: Lippincott Williams & Wilkins, 2007.

- weak effect from removal of hippocampus alone

Hypothesis: long-term memories are stored by synaptic modifications

Hebbian synaptic plasticity



- Neurons that fire together, wire together.

Brain slice preparation

- intracellular recording is easier than *in vivo*
- thickness: fraction of a millimeter
- used for studying intrinsic and synaptic conductances

Synaptic plasticity experiment

- Measure EPSP amplitude
- Induce synaptic modification
- Measure new EPSP amplitude

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See Figure 23.27a and b in Bear, Mark F., Barry W. Connors, and Michael A. Paradiso. *Neuroscience: Exploring the Brain*. 3rd ed. Baltimore, MD: Lippincott Williams & Wilkins, 2007.

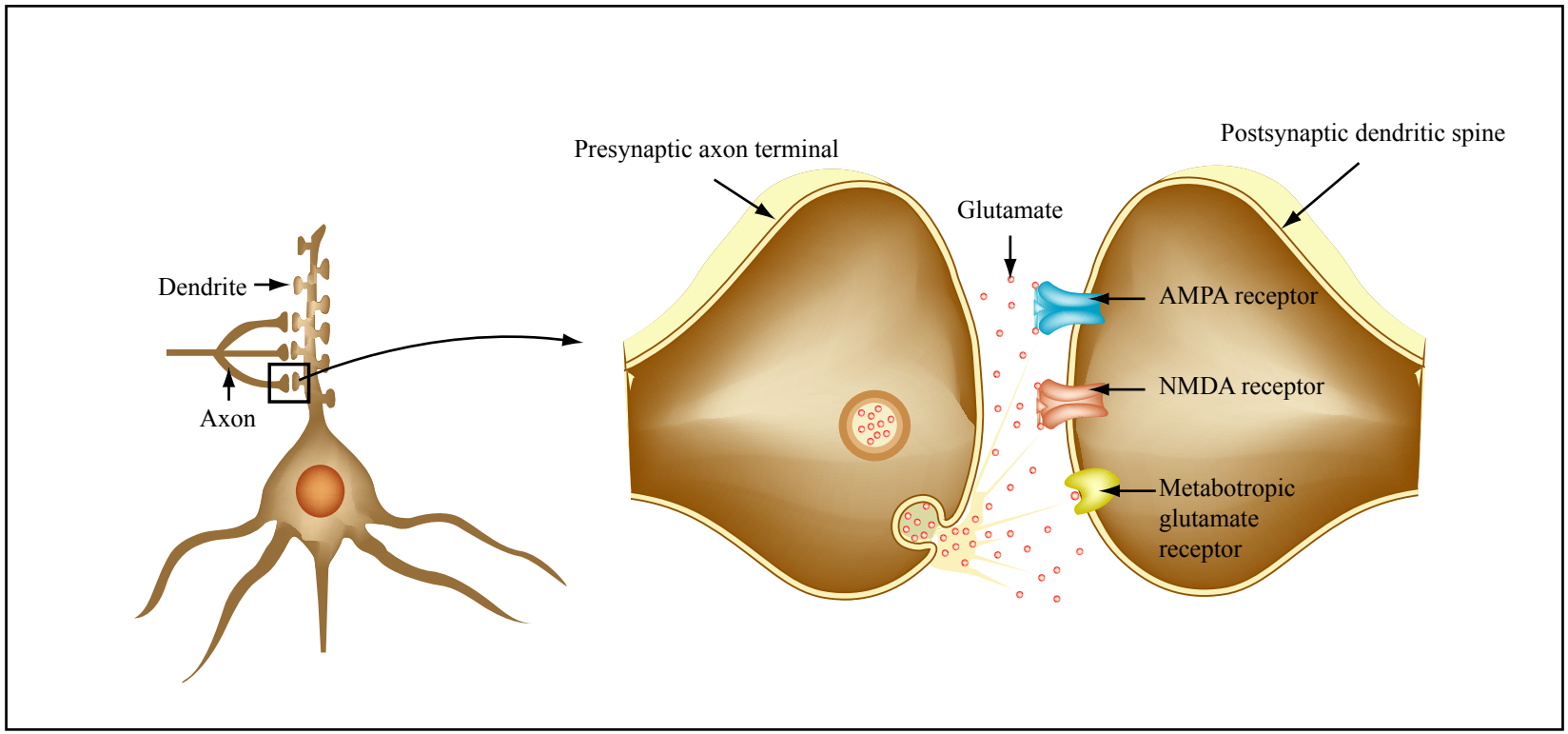
Long-term potentiation (LTP)

- activity-dependent synaptic modification
- lasts for tens of minutes or longer
- induction
  - high-frequency stimulation
  - postsynaptic depolarization
- found in cortex, hippocampus, etc.

Long-term depression (LTD)

- Neurons that fire out of sync lose their link.
- induction: low-frequency stimulation

Glutamate receptor subtypes



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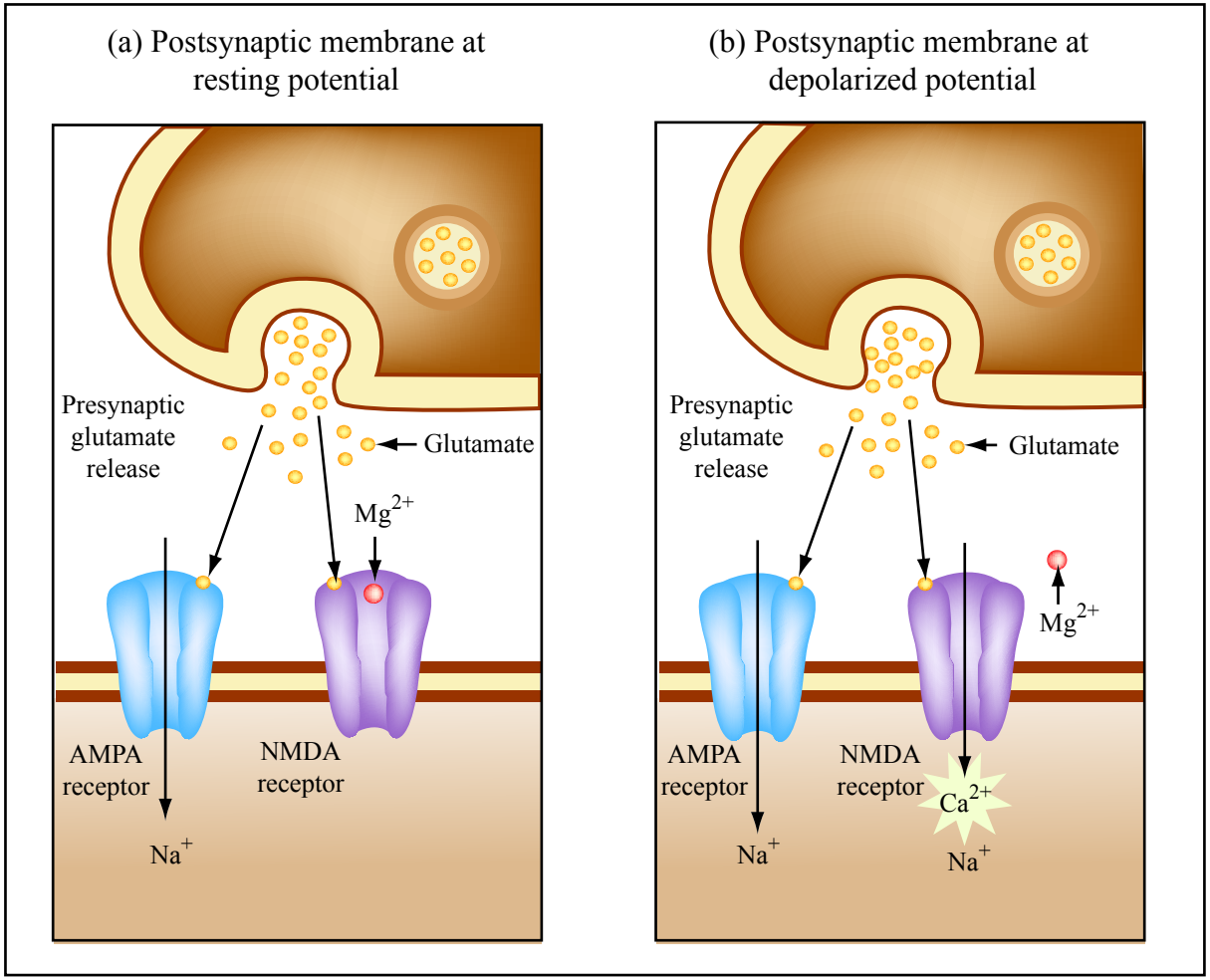
NMDA receptor

- transmitter-gated
- magnesium block: voltage-gated
- permeable to calcium

NMDA receptor as a coincidence detector



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The evidence

- NMDA receptor
  - LTP is blocked by the antagonist AP5
- Calcium
  - chelators (such as EGTA) block LTP
  - release of caged calcium mimics LTP

Morris water maze

- swimming pool with opaque water
- submerged platform
- measure time for rodent to swim to platform
- learning is impaired by AP5

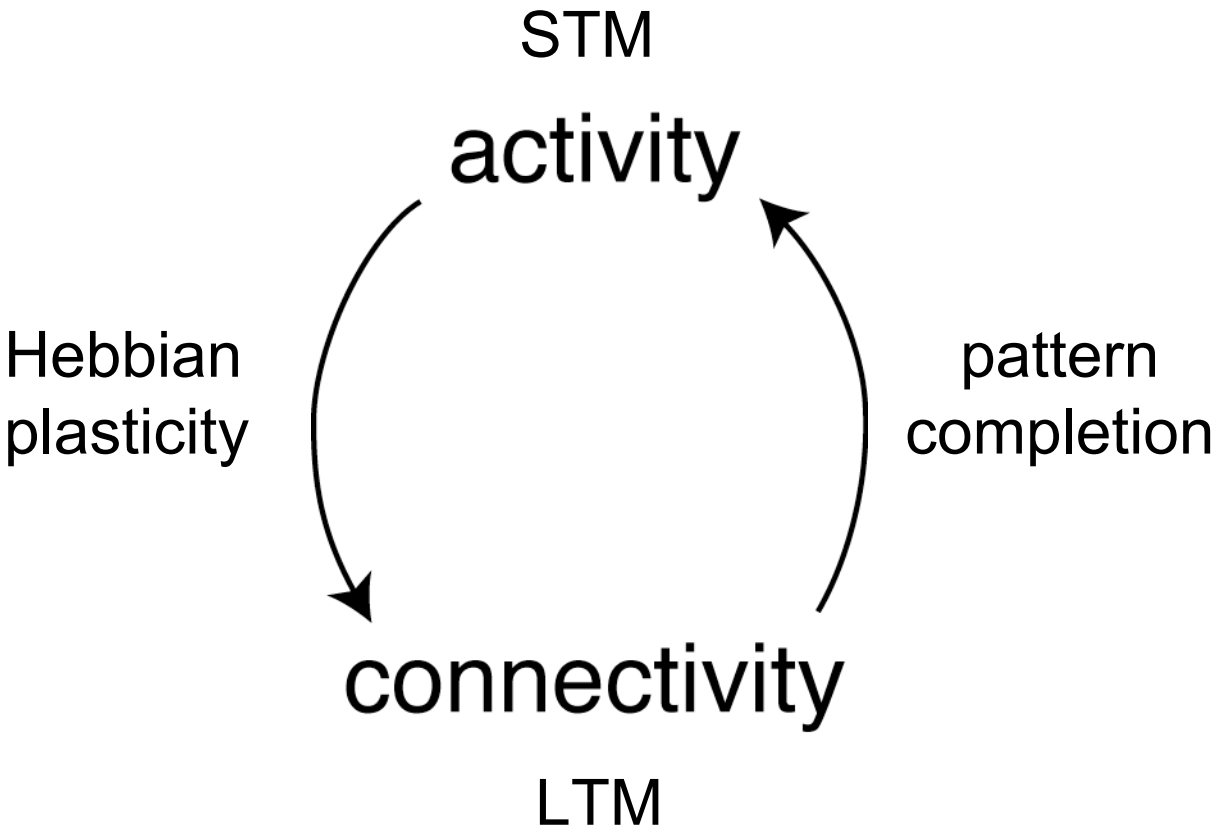
NR1 knockout mouse

- NMDA-R has seven subunits
- NR1 knockout is lethal.
- Site-specific knockouts can be viable.

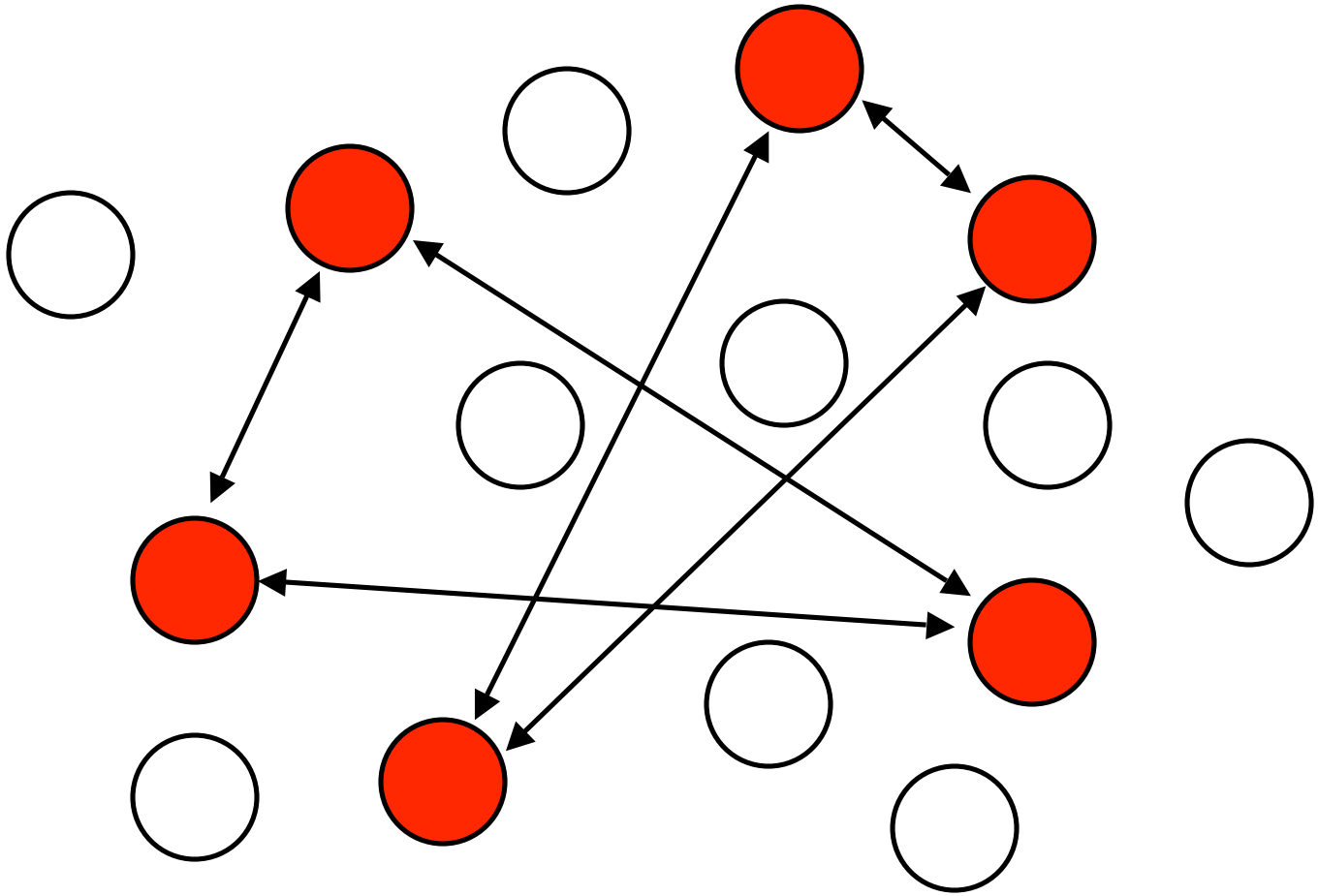
CA3 specific NR1 knockout

- no effect on Morris water maze performance
- if visual cues are reduced, then performance suffers

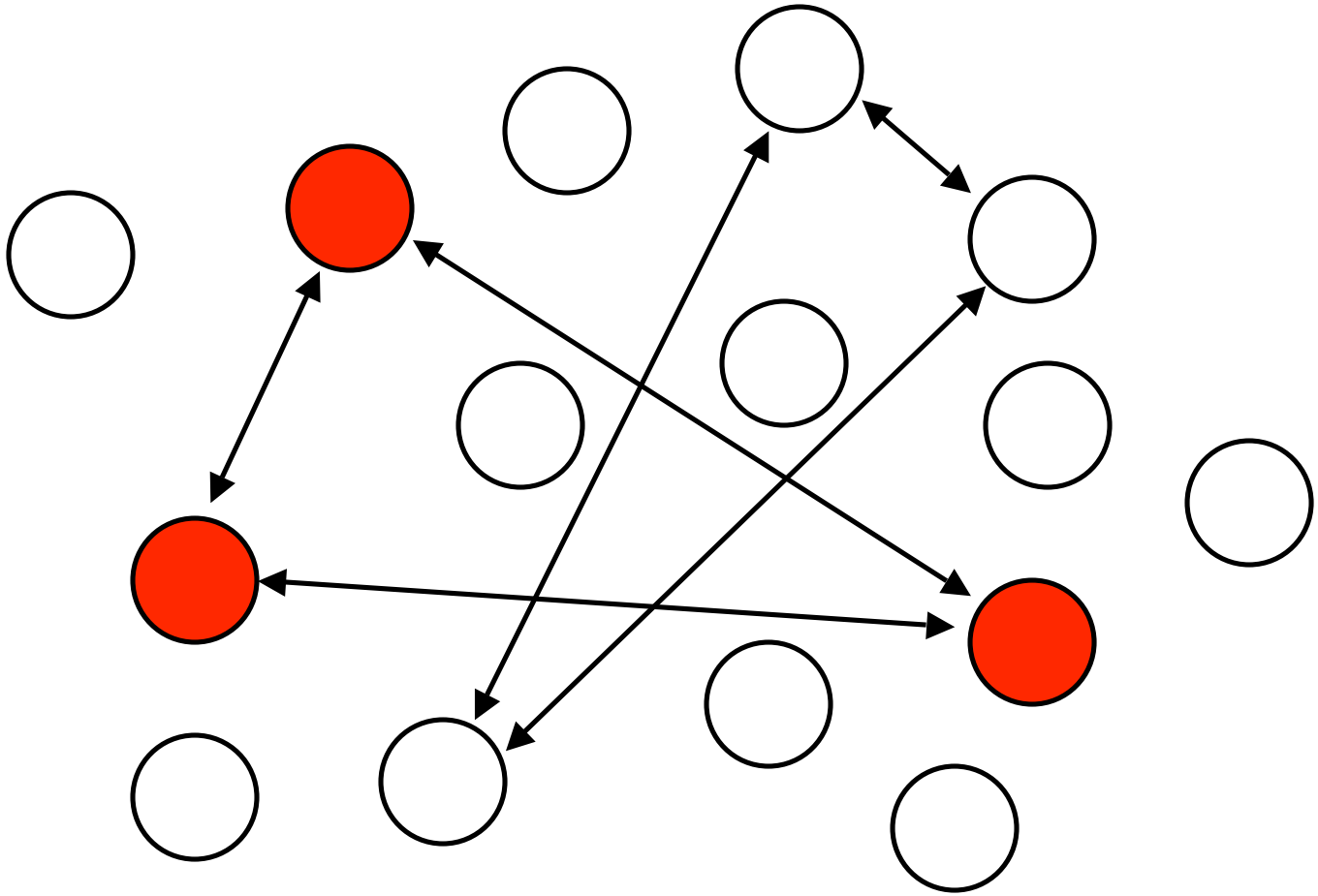
The central dogma



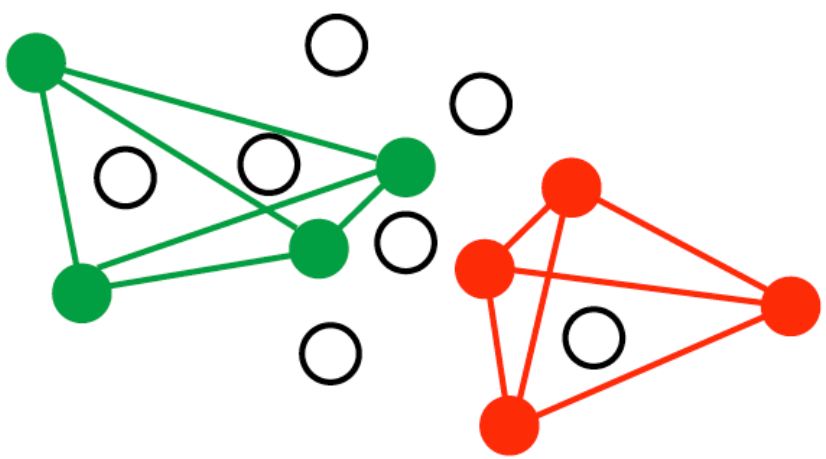
Hebbian plasticity creates cell assemblies

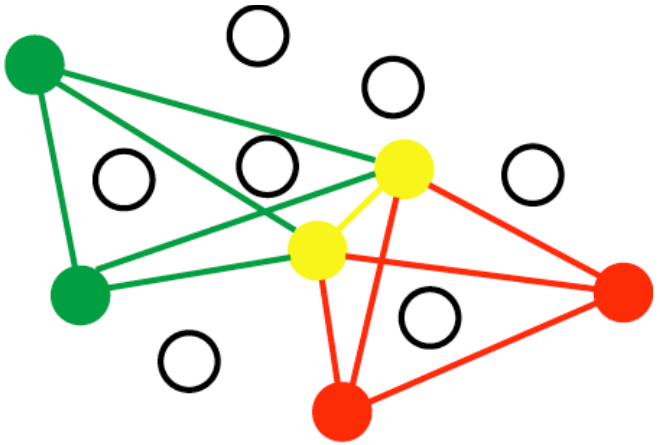


Pattern completion



Interference





- How many memories can be stored?