Learning and memory

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place avoidance
fear
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Reviews of experimental LTP:
  - Kandel and Schwartz book
  - Hippocampus book

Theory of Hopfield networks and Backpropagation
  - Herz, Krogh and Palmer

Neural computation theory
  - Dayan & Abbott
  - Trappenberg
Priming

Think of a zoo...
Think of a zoo….

Now think of words starting with ‘T’
Priming

Think of a hospital....

Now think of words starting with ‘T’
Measuring memory: perceptual learning

Finger sensitivity

Humans [Dinse ‘03]
Measuring memory:
Classical conditioning
Measuring memory: Classical conditioning

A. Delay-Conditioning

B. Trace-Conditioning

Graph showing the relationship between Performance index and CS-US interval (s).
Measuring memory: Classical conditioning

Functional perspective
Measuring memory: Inhibitory avoidance
Measuring memory: Inhibitory avoidance

A) Training session:
- Mouse is shocked on the lower platform.

24h later:
- Mouse is shocked on the higher platform.

B) Extinction training session:
- Mouse is shocked on the lower platform.

24h later:
- Mouse is shocked on the higher platform.

Test session:
- Mouse is shocked on the higher platform.
Reward dependent on action. Which action?
Human memory systems

Psychologists (e.g. Tulvin 1972) have split up memory in:

**Working memory** (likely activity based)

**Non-declarative memory**
Motor skills, sensory, priming, emotional, procedural...

**Declarative memory**
* Episodic memory
  - recollection memory/familiarity
* Semantic memory: General facts about the world

Are there specific brain regions for each?
Episodic memory

- Episodic memory: what, where, when?
- Can link things that are not naturally linked
- Hippocampus (or Medial Temporal Lobe) based.
- Has been modeled as Hopfield network
- Patient H.M.
Medial temporal lobe
Semantic memory

- Statistical information about the world.
- Stored in neocortex
- Localized cortical lesions can lead to limited dysfunction (e.g. speech, faces, ...)
- H.M. showed
  - normal priming,
  - skill, grammar and motor learning
  - liked doing cross-words(!)
- What is Hippocampus (or MTL) responsible for:
  explicit (vs implicit) memory?
  episodic (vs semantic) memory?
  relational memory?
  relational processing [Eichenbaum]?
Semantic memory

- HM did have remote memories. How can that be?
- During systems consolidation, memory is transferred/copied from hippocampus to cortex. During sleep?
- Is long-term memory only cortical, or is there still a hippocampal component?
- It is possible to store information in cortex without HPC, but typically more slowly.
Episodic memory
Recollection vs. Familiarity

**Recollection**

Example: remember where, when..
Low capacity
Hippocampus dependent
Asymmetric ROC (binary)
Long lasting

**Familiarity memory**

Example: faces, pictures
High capacity
Spared with HC-lesions
Symmetric ROC (confidence)
Short lasting
Episodic memory
Recollection vs. Familiarity

Familiarity memory appears located in Peri-rhinal cortex

[Fortin & Eichenbaum]
Familiarity memory

- High capacity ($\sim N^2$) [Bogazc], cf Hopfield ($\sim N$)
- Use scenario 1: If something is not familiar, don’t even bother remembering.
- Use scenario 2: Search for novelty (exploitation)
- Bloom-filter in software (cache system)

Combined model [Greve & MvR 09]
Memory systems

Declarative memory
* Episodic memory
  - recollection
  - familiarity
  - hippocampus (patient HM)

* Semantic memory: General facts

Non-declarative memory
Motor skills, sensory processing, ...

All done with Synaptic plasticity?
Measuring memory: Mazes

If start point is not varied, can be learned with procedural learning (without HPC)
Measuring memory: Mazes
Measuring memory: Object-place tasks
Models of memory
Modeling classical conditioning

conditioned stimulus

Bell

unconditioned stimulus

Food

‘Saliva’-neuron

NB: just a cartoon!
Modeling classical conditioning

Rescorla-Wagner (delta-rule)

Reward prediction model:

$$\Delta w_i = \epsilon x_i \delta$$

$$\delta = r - y$$

For instance describes blocking:

Lacks temporal effects
[Dayan and Abbott book]
Correlation-based learning

• [James 1898] Objects once experienced together tend to become associated in the imagination, so that when any one of them is thought of, the others are likely to be thought of also, in the same order of sequence or coexistence as before.

• [Hebb 1949] Let us assume that the persistence or repetition of a reverberatory activity (or ‘trace’) tends to induce lasting cellular changes that add to its stability ... When an axon of cell A is near enough to excite A cell B and repeatedly or persistently takes part in firing it, some growth Process or metabolic change takes place in one or both cells such that A’s efficacy, as one of the cells firing B is increased.

• [Schatz] What fires together, wires together.
Hippocampus

- Essential for declarative memory
- Cylindrical structure
- Longitudinal axis surrounds thalamus
Schaffer collateral LTP (in vitro)

weak
S1

S2
strong

alternate at 15 sec intervals
tetanic stimulation
S1: cooperative
S2: input-specific
S1+S2: associative
Long term synaptic plasticity

What is (activity dependent, long term) synaptic plasticity?

Long term, semi-permanent changes in the synaptic efficacy, induced by neural activity.

In contrast to:
- development
- short term changes
- excitability changes
Synaptic plasticity = memory?

[Martin, Greenwood, Morris]
Synaptic plasticity = memory?

• Detectability
  changes in behaviour and synaptic efficacy should be correlated
  Yes

• Mimicry
  change synaptic efficacies → new ‘apparent’ memory
  Not quite yet...

• Anterograde alteration
  prevent synaptic plasticity → anterograde amnesia
  Yes (e.g. NMDA block)

• Retrograde alteration
  alter synaptic efficacies → retrograde amnesia
  Yes, but...

[Martin, Greenwood, Morris]
Synaptic plasticity = memory?

[Whitlock,.. and Bear '06]
Biophysics of LTP
LTP stages

Induction:
- Requires pre- and post synaptic activity.
- Mechanism: NMDA and Ca influx

Expression / maintenance phases:
- Early LTP
- Late LTP
Model for LTP induction
Magnesium block

cultured hippocampal cells, outside-out patch (Jen and Stevens)
AP5 is a selective blocker
AP5 blocks learning
Ca hypothesis

Pairing high pre- and post synaptic activity => LTP
Pairing with low activity => Long term depression

[Bliss & Lomo '73]

[O'Connor & Wang '05]
LTP stages

Induction:
- Requires pre- and postsynaptic activity.
- Mechanism: NMDA and Ca influx

Expression / maintenance phases:
- Early LTP (1 hr):
  - partly pre-synaptic changes
  - AMPAR phosphorylation
  - AMPAR insertion
- Late LTP
  - ? (requires protein synthesis)
“Post-” model for expression
Changes in AMPA receptor phosphorylation

[Whitlock, .. and Bear '06]
Early phase LTP

Stim.: 1 s @ 100Hz

Rapid and local change

CaMKII
- Can be explained with voltage dependence of NMDA
- Associative learning such as Classical conditioning (Pavlov)
Basis of classical conditioning?

condioned stimulus
Bell

unconditioned stimulus
Food

Saliva
Before
After

For Aplysia see Kandel book

NB: just a cartoon!
Early phase LTP

Stim.: 1 s @ 100Hz

Rapid and local change

But gone after few hours
Late LTP requires protein synthesis

[Fonseca et al 06]
Late phase LTP

Stim: 3x 1s @100Hz

Dopamine

Start protein synthesis

Ship PRPs to tagged synapses

LTP lasts
LTP stages

Induction:
- Requires pre- and post synaptic activity.
- Mechanism: NMDA and Ca influx

Expression and Maintenance phases:
- Early LTP (1 hr):
  - partly pre-synaptic changes
  - AMPAR phosphorylation
  - AMPAR insertion

-Late phase LTP
- requires protein synthesis
Longevity: In vivo physiology

- Strong extracellular stimulation, leads to long lasting strengthening of synapse [Bliss and Lomo '73]

[Abraham '00]
What determines if LTP lasts?

Stimulus protocol

[Abraham '00]

Environnement

[Abraham '02, Li & Rowan '00]
(Dopamine mediated)
Does a novel environment 'reset' hippocampal learning?
What determines if LTP lasts?

Reward and punishment

[Seidenbecher '95]
Hypotheses for long term stability

Slots for AMPA receptors

[Turrigiano '02]

GluR2 trafficking

[Yao & Sacktor '08]
Late LTP maintenance as an active process

ZIP disrupts one month old memory

[Pastalkova et al '06]

(movie demo)
Spike Timing Dependent Plasticity: Experimental data

[Bi & Poo 1998]
Learning models
Why modelling plasticity

1) Artificial neural networks, engineering approach
   - make a network do something
   - now somewhat superseded by more formal machine learning

2) Insight in biology
   - extrapolate single neuron plasticity to network level
   - how can organisms adapt?
Models of plasticity and memory

Supervised learning
- tell network exactly what desired output is
- train network by changing the weights

Reinforcement learning
- Only give reward/punishment

Unsupervised learning
- Let the network discover things (statistics) about the input, e.g. Create representations that are useful for further processing (V1)

Animals can do all three presumably
Supervised: Perceptron

Categorize inputs into two classes

Perceptron learning rule [Rosenblatt 1952]
- If it can be learned, the rule converges
- Not all classification problems can be learned

\[ y = \phi(\sum_{i} w_i x_i) \]
Linear separability

Separable
Perceptron can classify

Non-separable
Perceptron can't classify
Need multiple layers
Multi-layer perceptron

Network to approximate any function with arbitrary number of inputs and outputs
Back propagation

\[ E = \sum_{\text{pattern}} (\text{out}_{\text{actual}} - \text{out}_{\text{desired}})^2 \]

\[ E (\text{in}, \text{out} | w_1, w_2, \ldots) \]

\[ \Delta w_i = -\epsilon \frac{\partial E}{\partial w_i} \]
Back propagation

General approach:
- Come up with cost function, (objective function)
  Examples: #errors, sparseness, invariances
- Take the derivative wrt synaptic weights.
- You have created a learning rule
Hopfield network

- Model for CA3
- Recurrent network
- Auto-associator (i.e. Pattern completion)
Hopfield network

One shot learning: \( w_{ij} = \sum_{\text{patterns}} x_i^\mu x_j^\mu \)
Phenomenological models of plasticity (unsupervised)

Vanilla model: \[ \Delta w_i = \epsilon x_i y \]

Covariance rule: \[ \Delta w_i = \epsilon (x_i - \langle x_i \rangle) \cdot (y - \langle y \rangle) \]

Assumptions made:
- \( w \) can change sign
- \( w \) is unbounded
- \( \Delta w \) independent of \( w \)
- linear
- \( \Delta w \) independent of other synapses
- changes are gradual and small
Unsupervised learning

\[ \Delta w_i = \langle \epsilon x_i, y \rangle \]
\[ \Delta w_i = \epsilon \langle x_i, \sum_j w_j x_j \rangle \quad (\text{slow, linear}) \]
\[ \Delta w_i = \epsilon \sum_j \langle x_i, x_j \rangle w_j \]
\[ \Delta w_i = \epsilon Q_{ij} w_j \]
\[ \frac{\partial \tilde{w}(t)}{\partial t} = Q \cdot \tilde{w}(t) \]

PCA

\[ \tilde{w}(t) = \sum_i c_i \tilde{w}_i e^{\lambda_i t} \]

Diverges

OOPS...
Constraints and competition

**Constraints**
Keep each weight within bounds

**Normalization**
Make sure that $\sum_i w_i$ is constant
This leads to competition
- Divisive normalization (weak competition)
- Subtractive normalization (strong competition)
Constraints and competition

The outcome of the learning is strongly determined by the constraints [Miller & Mackay] (Alternatives: BCM, Oja's rule)

Practical tip:

Use subtractive normalization
Formation of V1 receptive fields

- A wide class of learning rules lead to V1 like receptive fields [Britto & Gerstner '16]
- Lateral inhibition ensures complimentary RFs [Dayan and Abbott book]
- Unless lateral interaction, there will be no map.
Rate-based Hebbian learning, subtractive normalization, can lead to realistic maps.

[Bednar, 2012]
V4 and IT “match” machine learning [Yamins 2014]
Unsupervised learning

Development of realistic receptive fields using generative models.

V1 (1997)

IT [Le ... Ng, 2012]