Hasselmo's Model of Effects of Cholinergic Modulation of the Hippocampus

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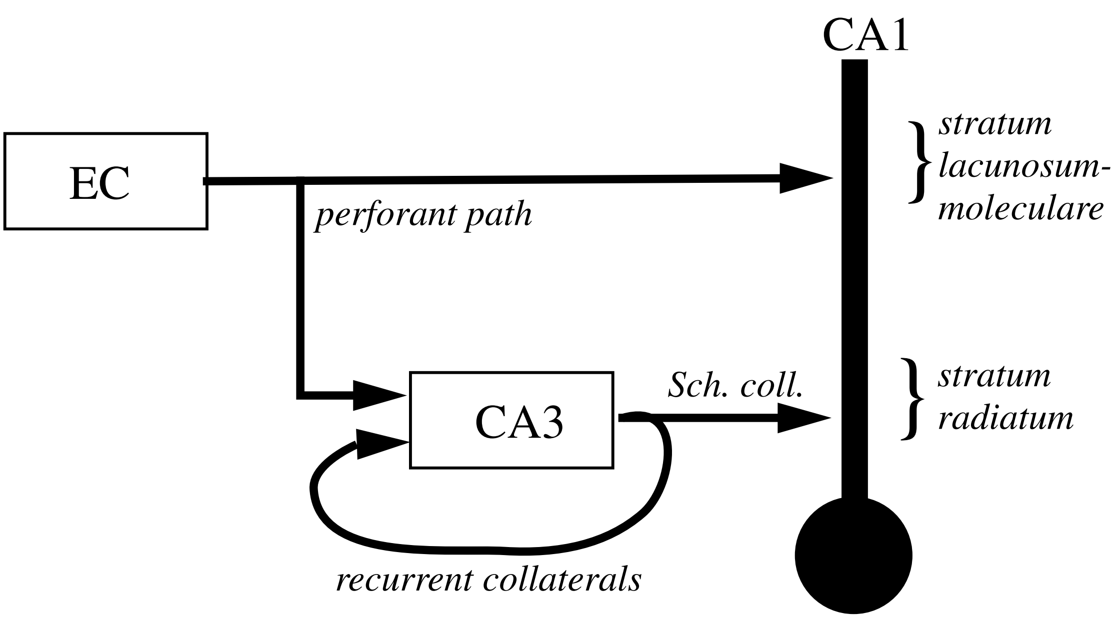
A Theory of Hippocampus

- Suppose CA1 is a hetero-associator that learns to mimic EC patterns and map CA3 patterns to corresponding EC patterns.
- Imagine a partial/noisy pattern in EC triggering a partial/noisy response in CA3, cleaned up by auto-association.
- CA1 could use the CA3 response to call up the complete, correct EC pattern.
- What happens if recall isn't turned off during learning?



Cholinergic Modulation

Acetylcholine (ACh) has a variety of effects on hippocampus:

- Suppresses synaptic transmission in CA1:
  - Mostly at Schaffer collaterals in *stratum radiatum*.
  - Less so for perforant path inputs in *stratum lacunosum-moleculare.*
- Reduces neuronal adaptation in CA1 by suppressing voltage and Ca^{2+} dependent potassium currents: makes the cells more excitable.
- Enhances synaptic modification in CA1, possibly by affecting NMDA currents.
- Activates inhibitory interneurons, but decreases inhibitory synaptic transmission.

CA1 Activation Function

$$a_i(t) = \sum_{j=1}^{n} (L_{ij} - {}_{EC}H_{ij}) \cdot g({}_{EC}a_j(t))$$
$$+ \sum_{k=1}^{n} (R_{ik} - {}_{CA3}H_{ik}) \cdot g({}_{CA3}a_k(t))$$
$$- \sum_{l=1}^{n} {}_{CA1}H_{il} \cdot g({}_{CA1}a_l(t))$$

$a_i(t)$ is activation of unit *i* at time *t*.

g(x) is a threshold function: IF x > θ THEN (x–θ) ELSE 0.
used θ = 0.4.

L_{ij} is feedforward synaptic strength for s. lacunosum (EC input.)
R_{ik} is feedforward synaptic strength for s. radiatum (CA3 input.)

H_{ij} is feedforward inhibition from EC.
H_{ik} is feedforward inhibition from CA3.
H_{il} is feedback inhibition within CA1.

S. Rad. Learning Rule

Note: only learning in this model is in CA3 to CA1 connections.

The learning rule has two factors:

- linear potentiation of synapses when pre - and post-synaptic cells are both firing
- exponential decay of synapses whenever postsynaptic cell fires

$$\begin{aligned} R_{ik}(t+1) = \eta \cdot [\, ({}_{CA1}a_i(t) - \theta) \cdot g({}_{CA3}a_k(t)) \\ - \mu\, ({}_{CA1}a_i(t) - \theta) \cdot R_{ik}(t)\,] \\ + \; R_{ik}(t) \end{aligned}$$

θ is the synaptic modification threshold for LTP to occur.

η is the learning rate (rate of potentiation.)

μ is the synaptic decay rate.

Control of Cholinergic Modulation

Cholinergic modulation was controlled by the amount of activity in CA1.

$$\psi = \left[1 + \exp\left(\xi\left(\sum_{i=1}^{n} g({}_{CA1}a_i) - \nu\right)\right)\right]^{-1}$$

ψ is the level of cholinergic modulation:

- With no CA1 activity, ψ is close to 1.
- With maximal CA1 activity, ψ is close to 0.

ξ is a gain parameter.

ν is a threshold value.

Effects of ACh Modulation

$$a_i(t) = \sum_{j=1}^{n} \left((1 - \psi C_L) L_{ij} - (1 - \psi C_H) H_{ij} \right) \cdot g({}_{EC}a_j(t))$$
$$+ \sum_{k=1}^{n} \left((1 - \psi C_R) R_{ik} - (1 - \psi C_H) H_{ik} \right) \cdot g({}_{CA3}a_k(t))$$
$$- \sum_{l=1}^{n} (1 - \psi C_H) H_{il} \cdot g({}_{CA1}a_l(t))$$

C_L, C_R, C_η and C_ν are coefficients of ACh modulation.

$$R_{il}(t+1) = \eta \bullet [1 - (1 - \psi) C_\eta] \bullet$$
$$[({}_{CA1}a_i(t) - \theta) \cdot g({}_{CA3}a_i(t))$$
$$- \mu ({}_{CA1}a_i(t) - \theta) \cdot R_{ik}(t)]$$
$$+ R_{ik}(t)$$

Note: output threshold θ in g(•) was also reduced, by $(1-\psi)C_\theta$.