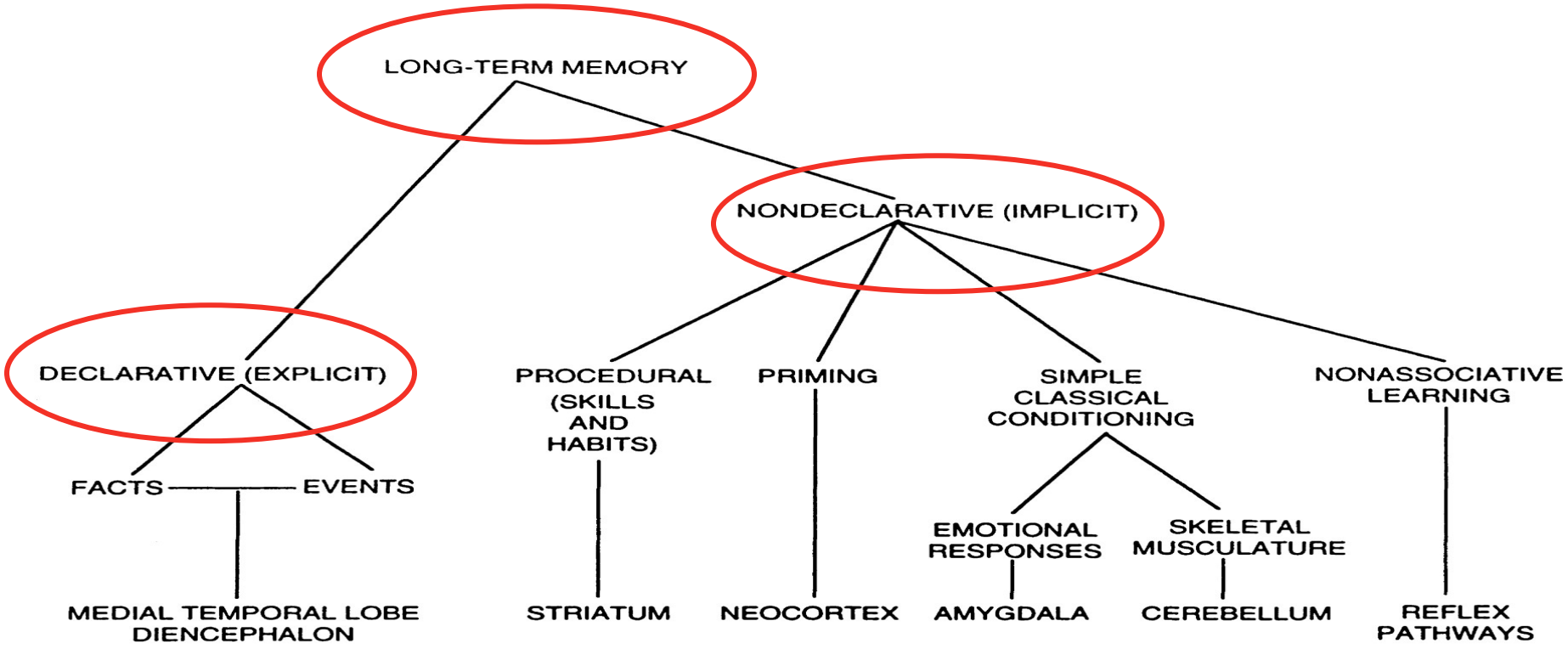
Mmeory Systems
and
Their Neuronal Underpinnings

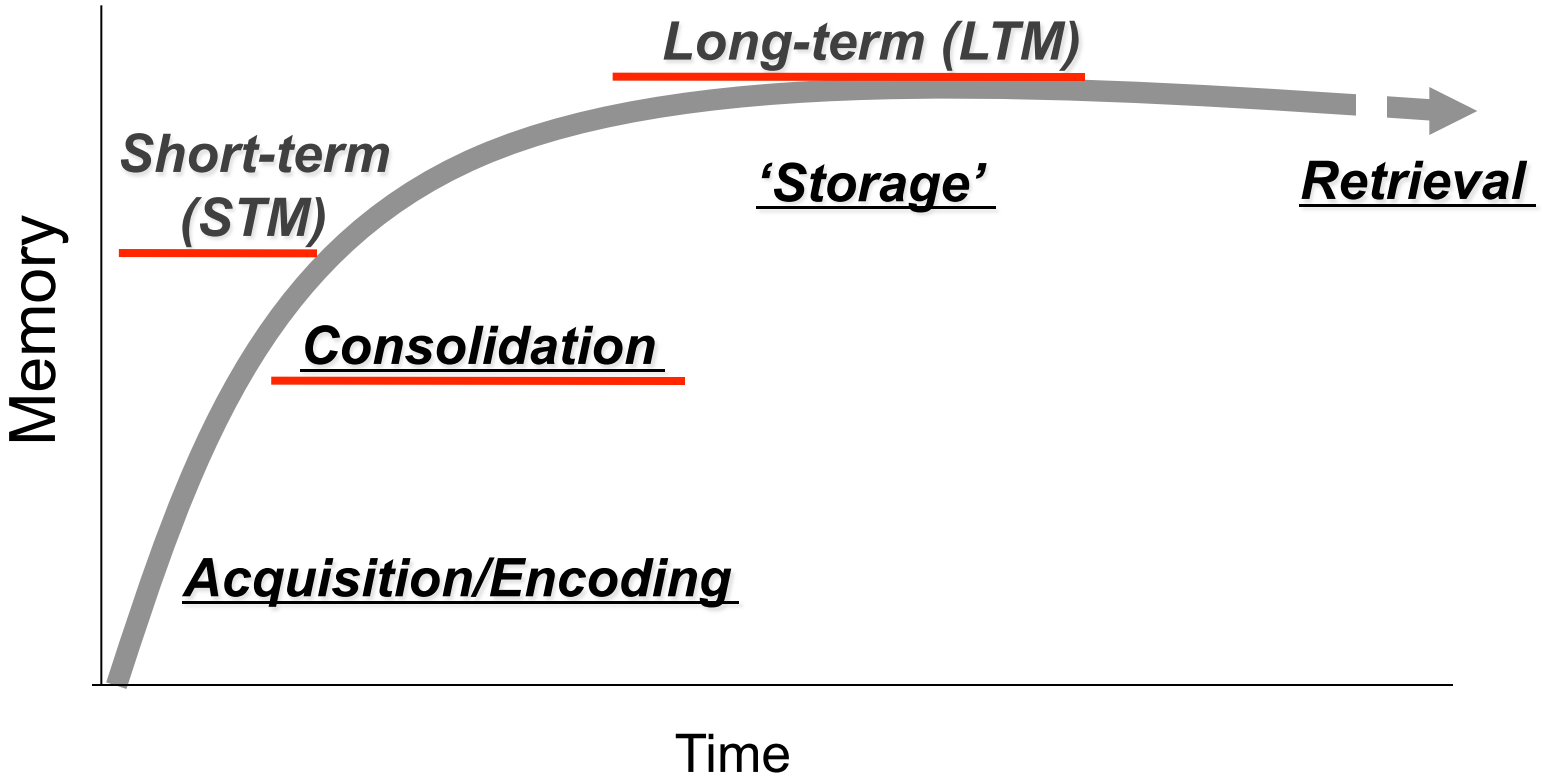
FGS course, January 16, 2013

Taxonomy of Long-Term Memory by Type/Content



(After Squire 2004)

The Biography of an Item in Memory



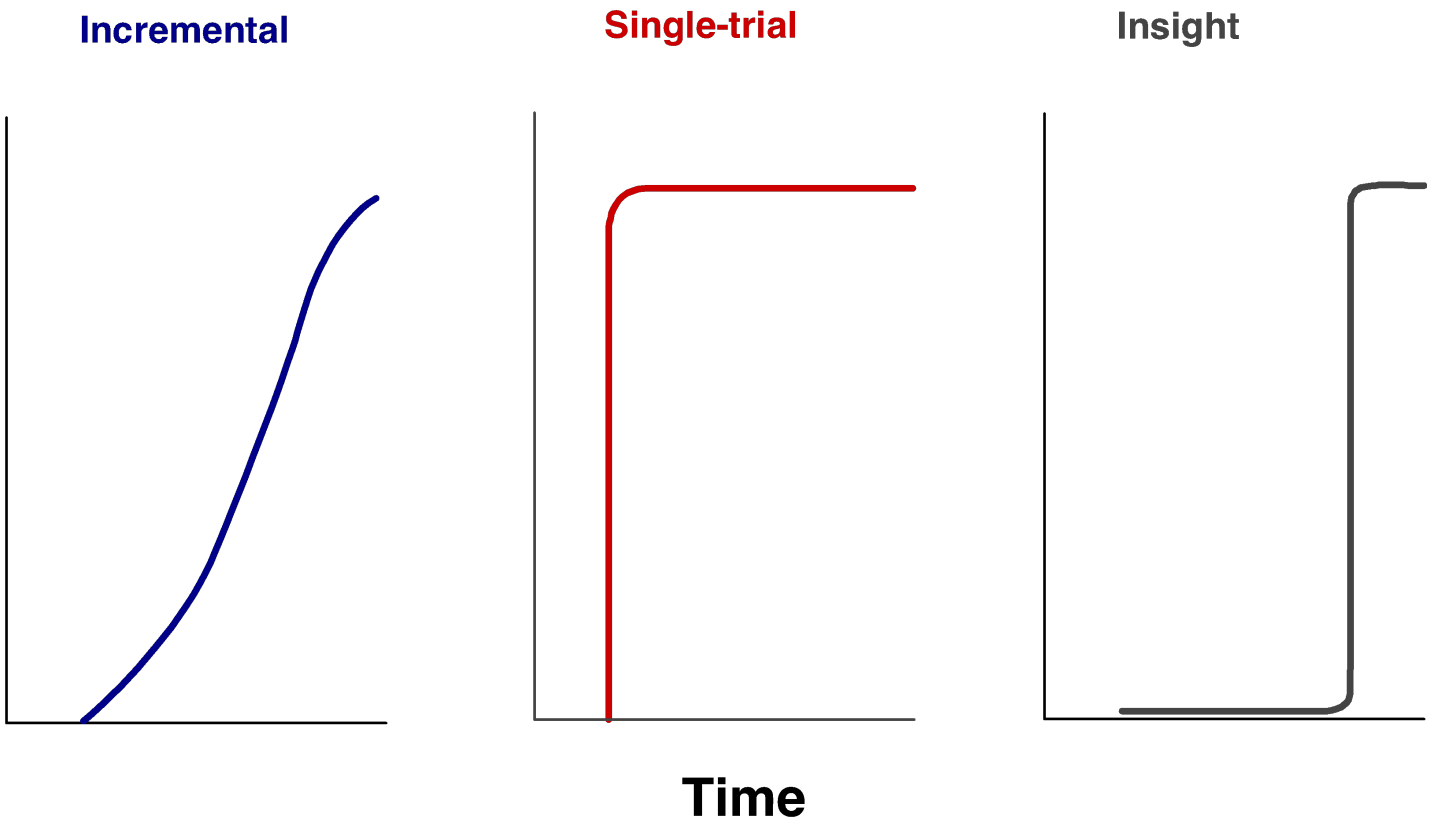
- *The dual-trace hypothesis*
- *The consolidation hypothesis*

} *LTM = f(Growth)*

Acquisition (Encoding):

- The initial phase in the formation of a memory trace
- The process by which new information is converted into a memory trace
- The change in performance during training which is taken to represent the progression of learning

Three types of acquisition modes



Levels of Analysis of a Problem-Solving System

- Computational Theory: *The goal of the system, e.g. register, associate*
- Algorithms: *How is the goal obtained step-by-step, e.g. if X do Y then W etc.*
- Hardware implementation: *How is the algorithm implemented in the hardware of the system, e.g. use receptor to detect X, enzyme to do Y, another enzyme to do W*

(Marr 1982)

Acquisition: The goal(s) of the system

- *Register input*
- *Register associations*

- *Register input:* detect change in intensity or probability
- *Register associations:* detect coincidence detection or contingency

Candidate algorithms:

- **Prime** with a salient *Xi* so that subsequent *Xj* is read out differently (non-associative/ associative)
- **Summate/anticipate** read *Xi, Xj, … Xn,* to detect mismatch of the input, in time or magnitude, with criterion (non-associative /associative)
- Detect **coincidence** (associative)

Summation/Anticipation: The Rescorla-Wagner Model

$$\Delta V_X^{n+1} = \alpha_X \beta (\lambda - V_{tot})$$

and

$$V_X^{n+1} = V_X^n + \Delta V_X^{n+1}$$

where

- ΔV_X is the change in the strength of association of X
- α is the salience of the CS (bounded by 0 and 1)
- β is the rate parameter for the US (bounded by 0 and 1), sometimes called its association value
- λ is the maximum conditioning possible for the US
- V_X is the current associative strength
- V_{tot} is the total associative strength of all CS

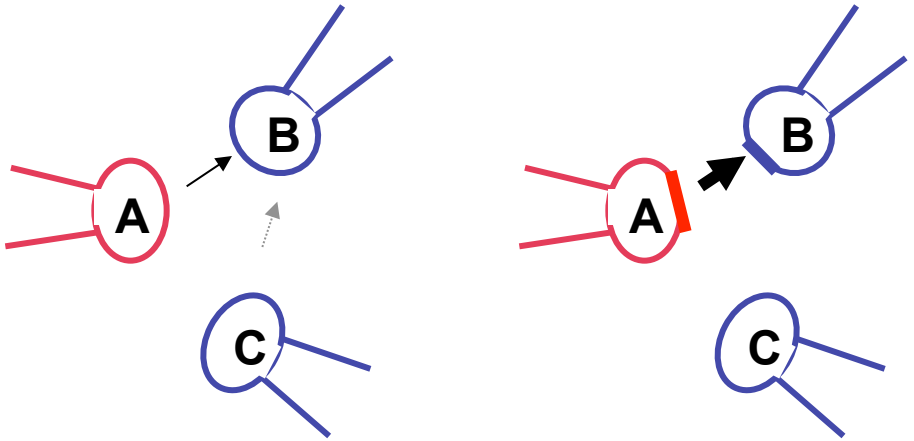
Qualitatively: The more the event is far from the expected, the stronger it is encoded

Coincidence detector:

- A device that responds only on receiving two stimuli simultaneously
- A device that responds only on receiving a complete set of two or more stimuli

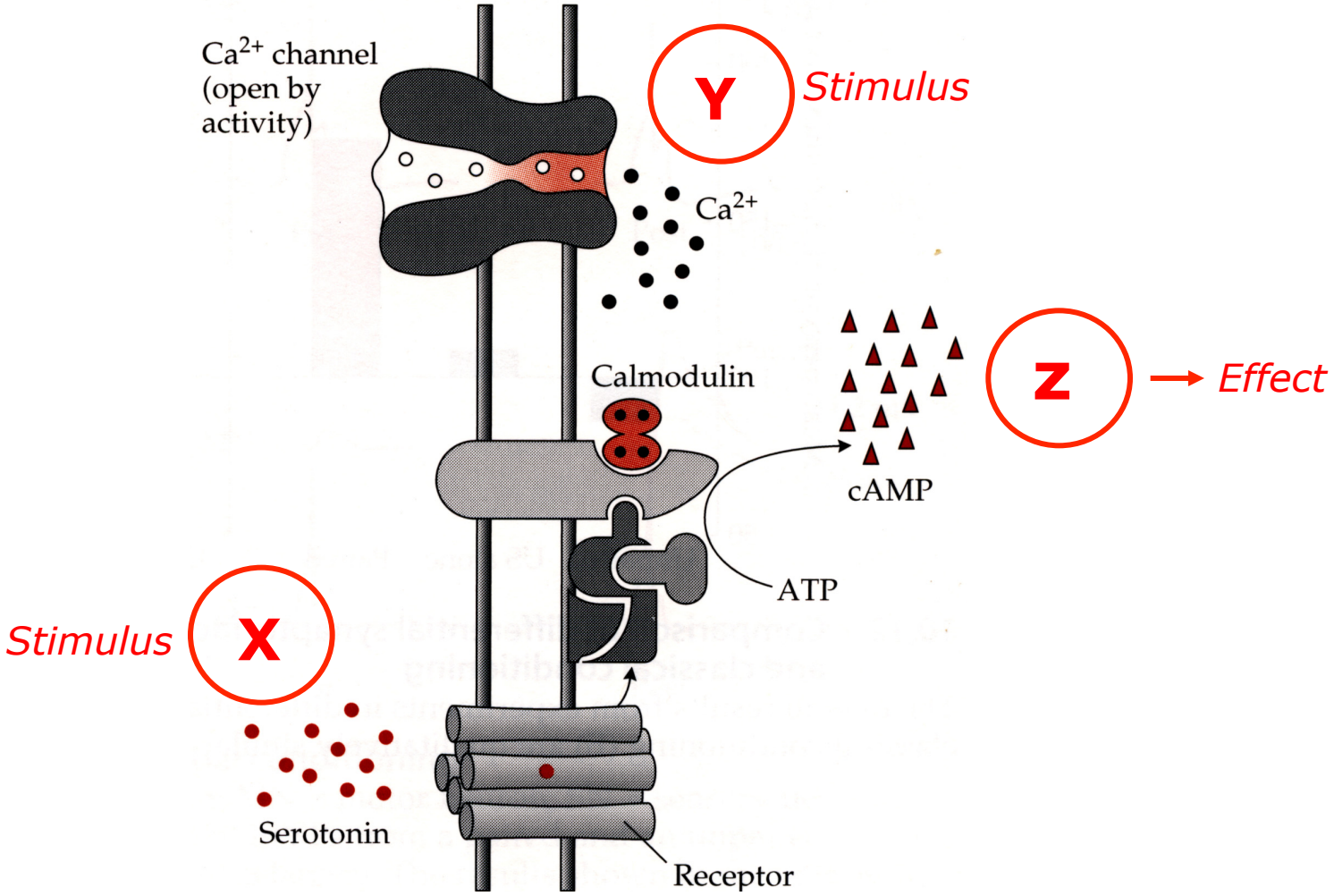
- What is *simultaneously*?

Hebb's postulate:
A cellular/circuit algorithm

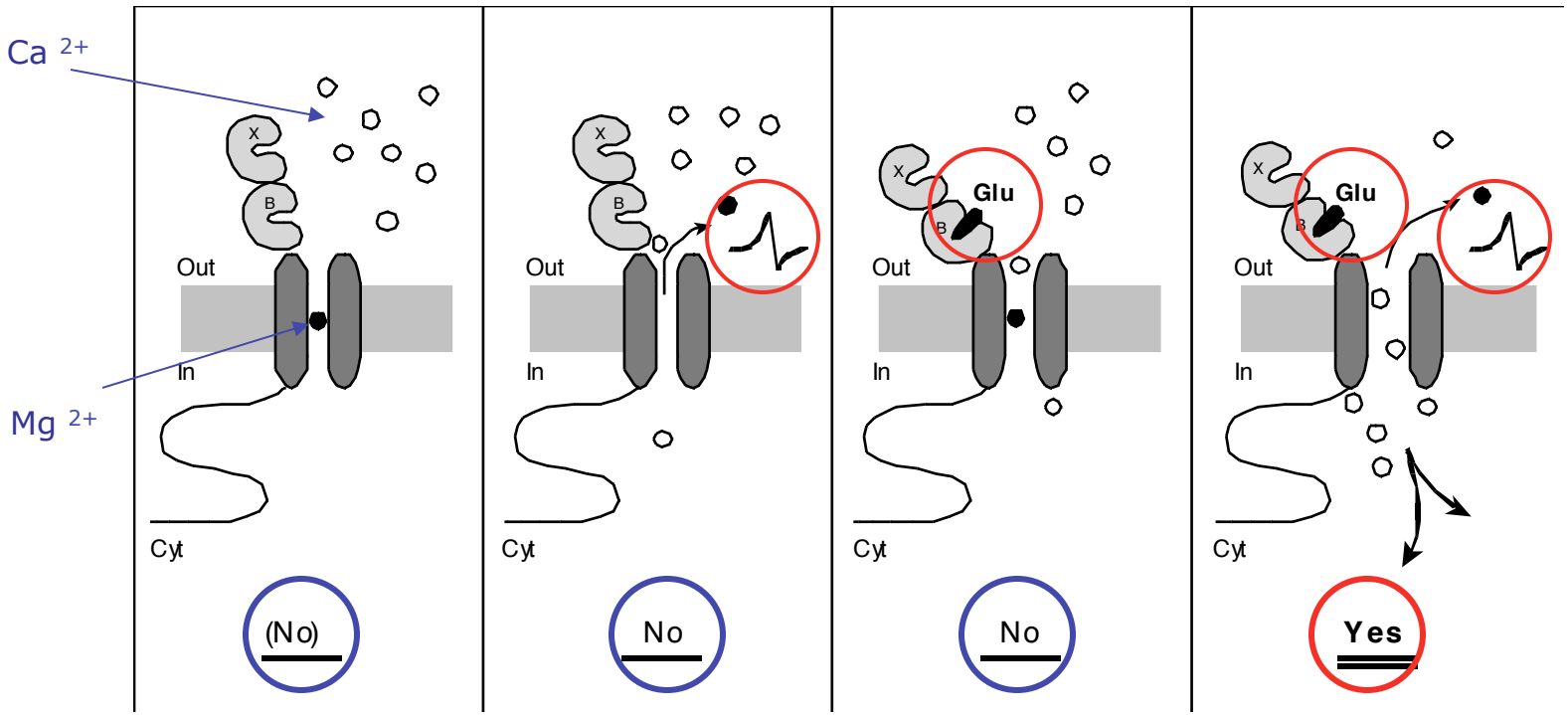


When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth processes or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased ("Darwinian")

A candidate for hardware implementation of coincidence detection: Calcium/calmodulain-dependent adenylyl cyclase



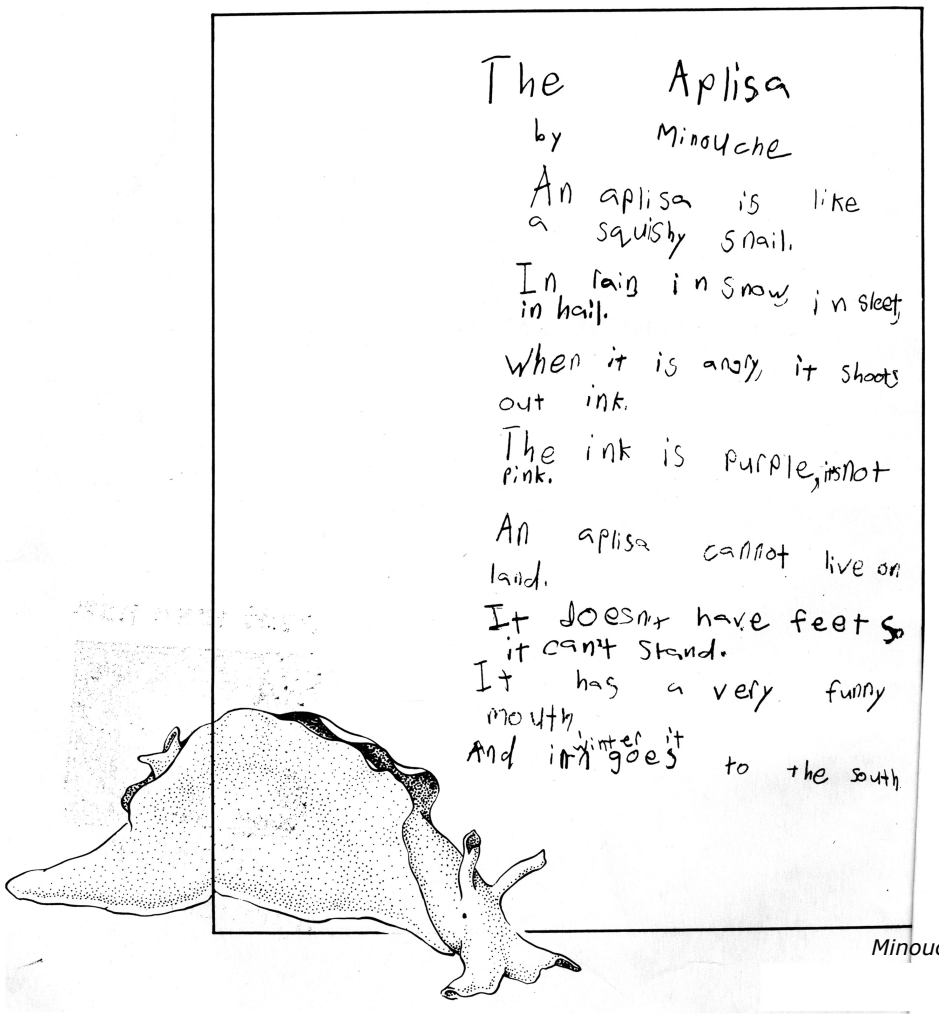
Another candidate for hardware implementation of coincidence detection: The NMDA receptor



How shall we approach the cellular mechanisms

The marine snail *Aplysia* is a convenient 'simple system', which allows investigation of molecular and cellular mechanisms of simple learning

Ode to *Aplysia:*

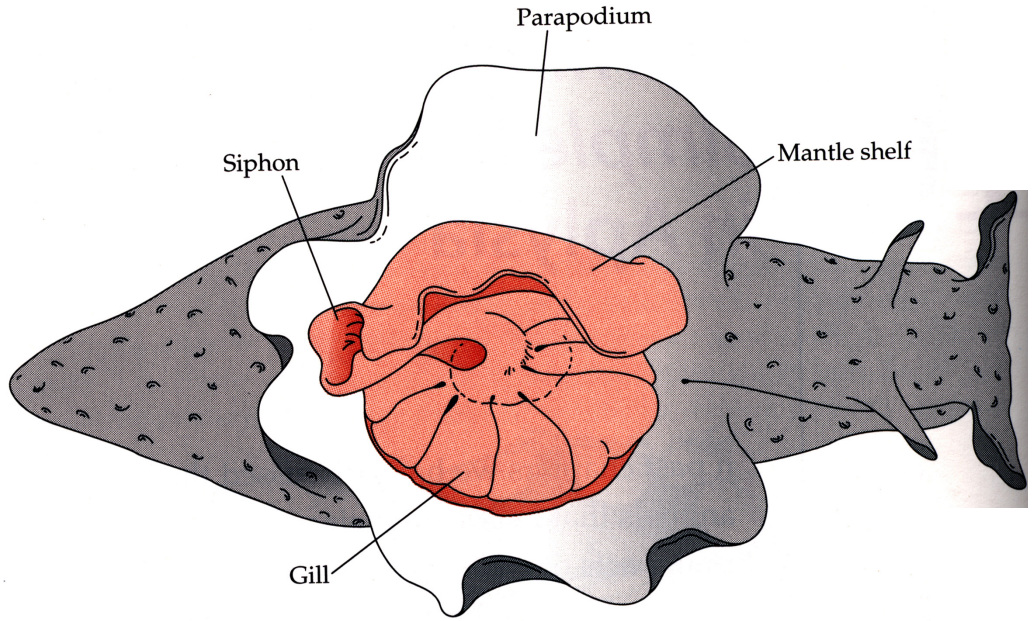


Minouche Kandel, Age 7 (1974)

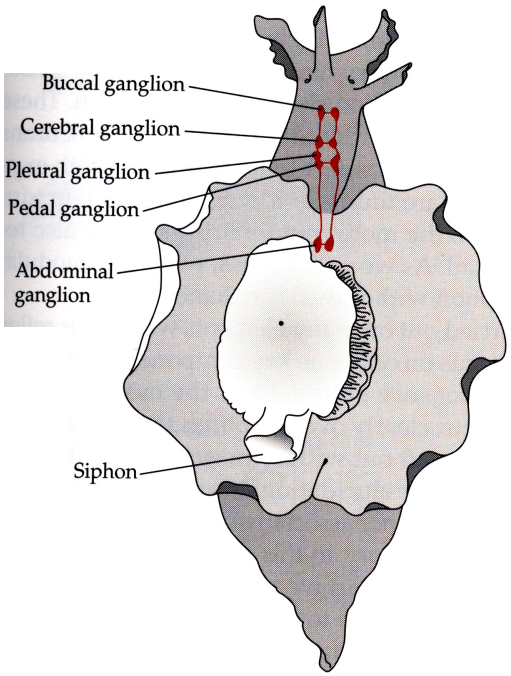
Why Aplysia?

- Reasonable number of neurons (~ 20,000)
- Accessible ganglia
- Large nerve cells
- Identifiable nerve cells
- Simple behvioural repertoire
- Easy to handle

Aplysia: Outside and inside



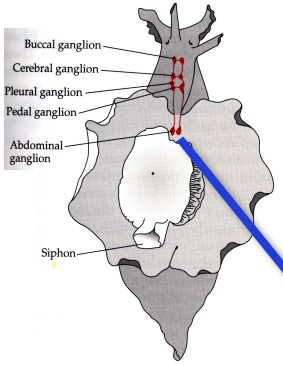
A dorsal view with its gill exposed

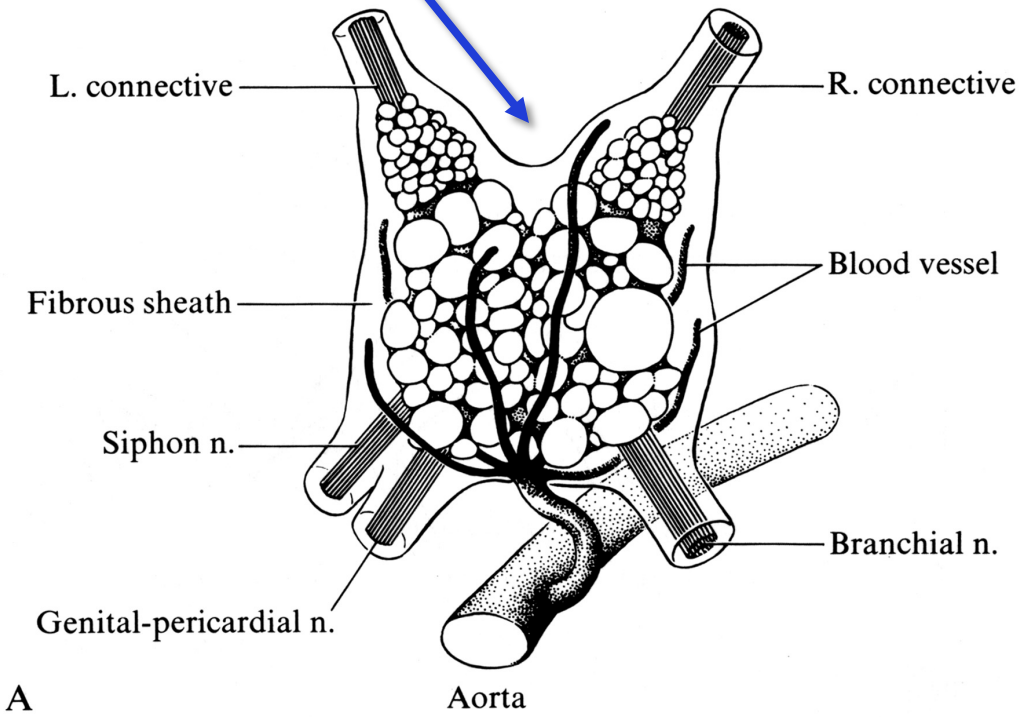


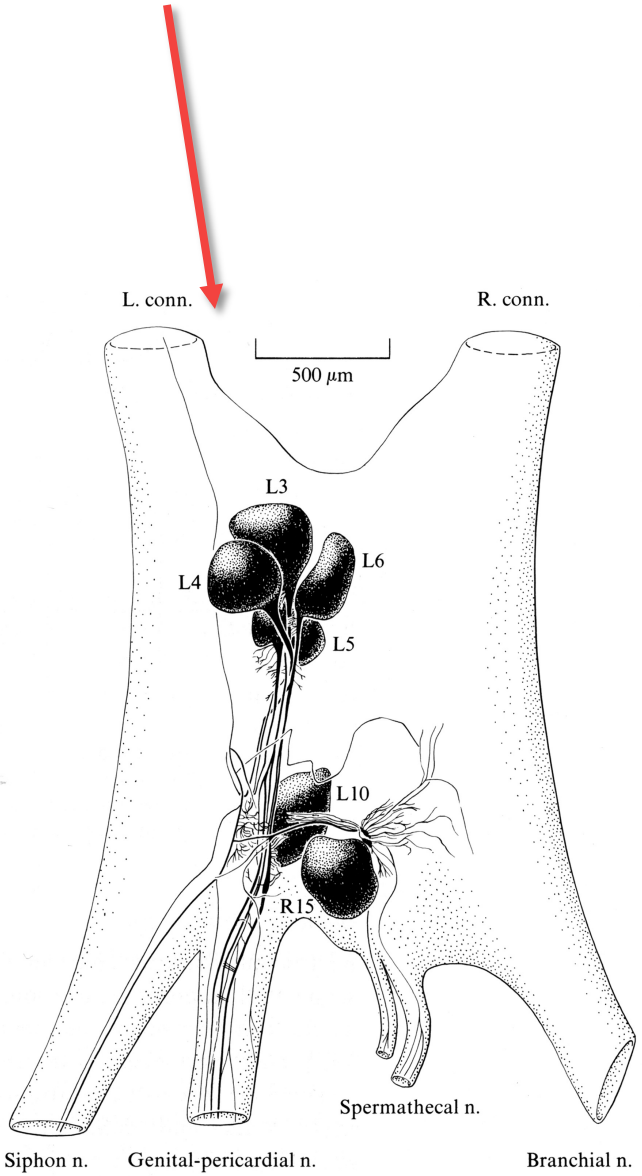
The central nervous system (transparent view)

(Kandel et al. 1984-2010)

The abdominal ganglia and some identified nerve cells



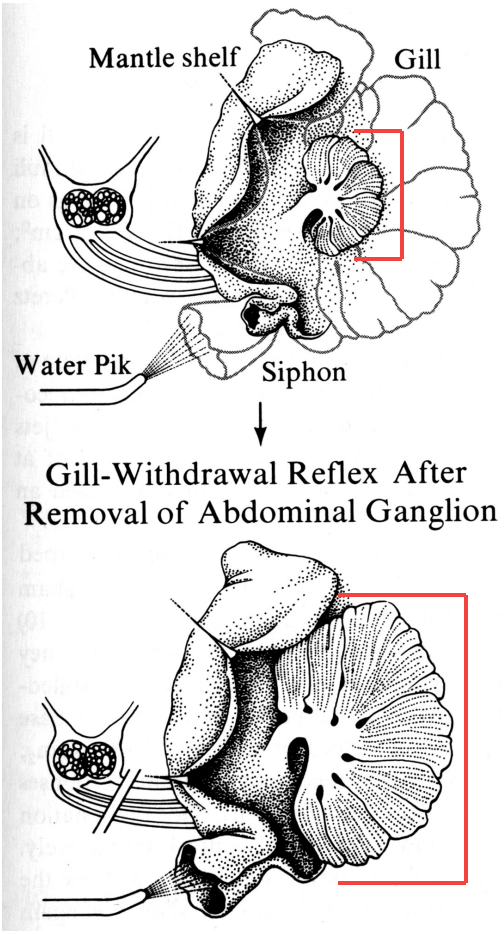




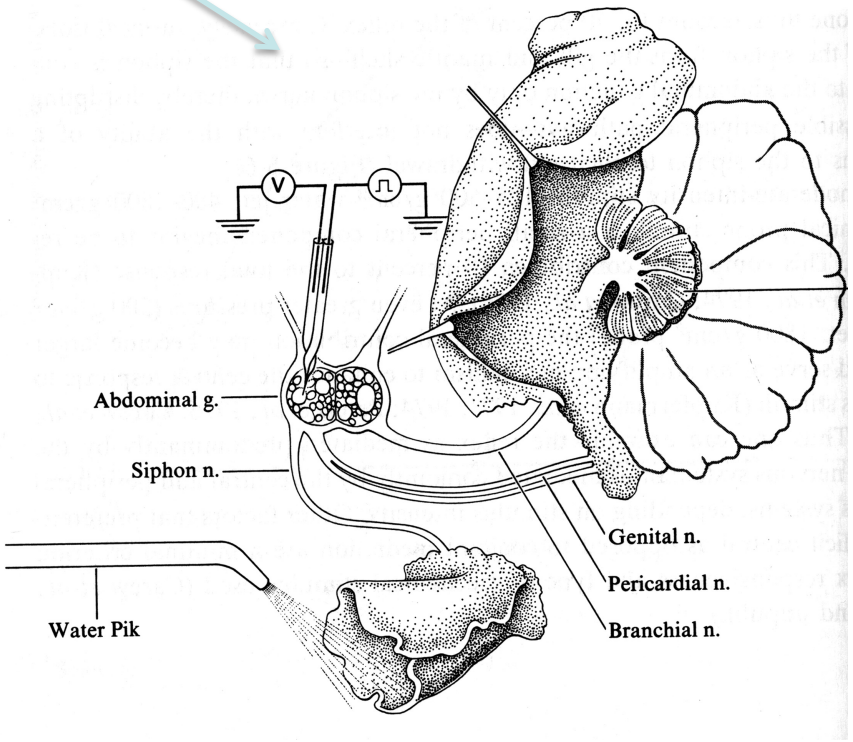
(Kandel et al. 1984-2010)

The abdominal ganglia control a substantial part of the gill reflex

Lesion experiment

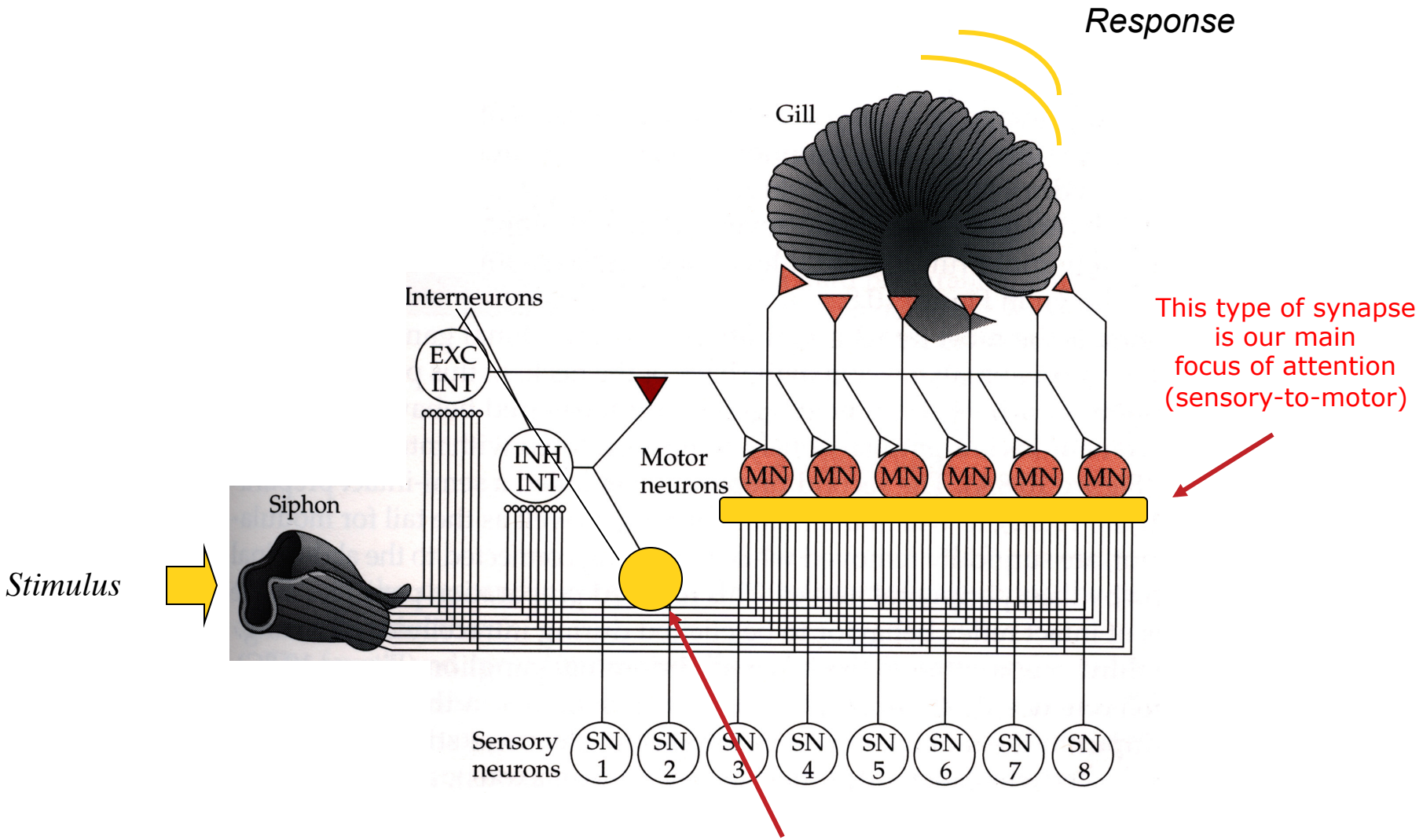


Justification for an easier preparation to work with



(Kandel et al. 1984-2010)

The minimal reflex circuit



(Kandel et al. 1984-2010)

Methods used in the *Aplysia* projects

- Lesions: Inference of function from dysfunction
- Correlations: Concomitant activity in identified neurons and effector organs
- Simulation (mimicry): Activation of effector organ by stimulating neurons

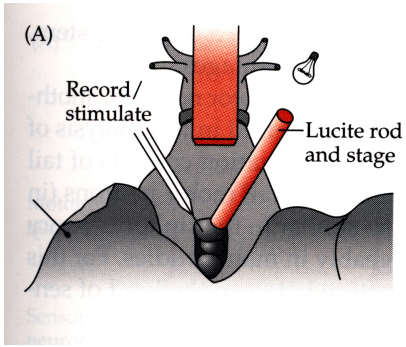
Conceptual and pragmatic steps:

- Reductive step: A shift from one level of analysis to the other (e.g., behavioural to circuit)
- Simplifying step: A down shift in the complexity of the preparation without abandoning levels of analysis

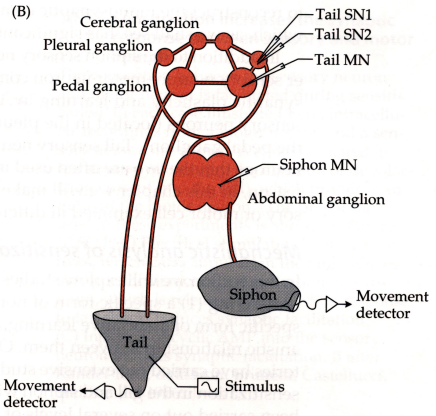
(What is a simple system?)

Reductive and simplifying steps in the analysis of *Aplysia*

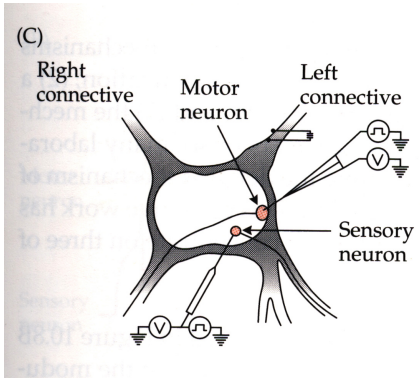
The behaving organism



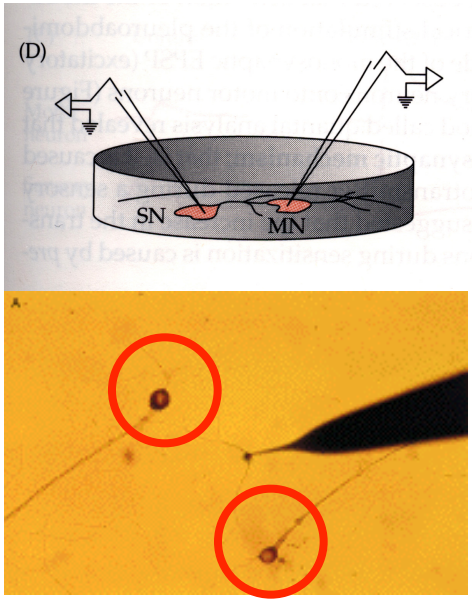
Cellular analysis in the intact organism (reductive step)



Cellular analysis in a Nerve-muscle preparation (simplifying step)



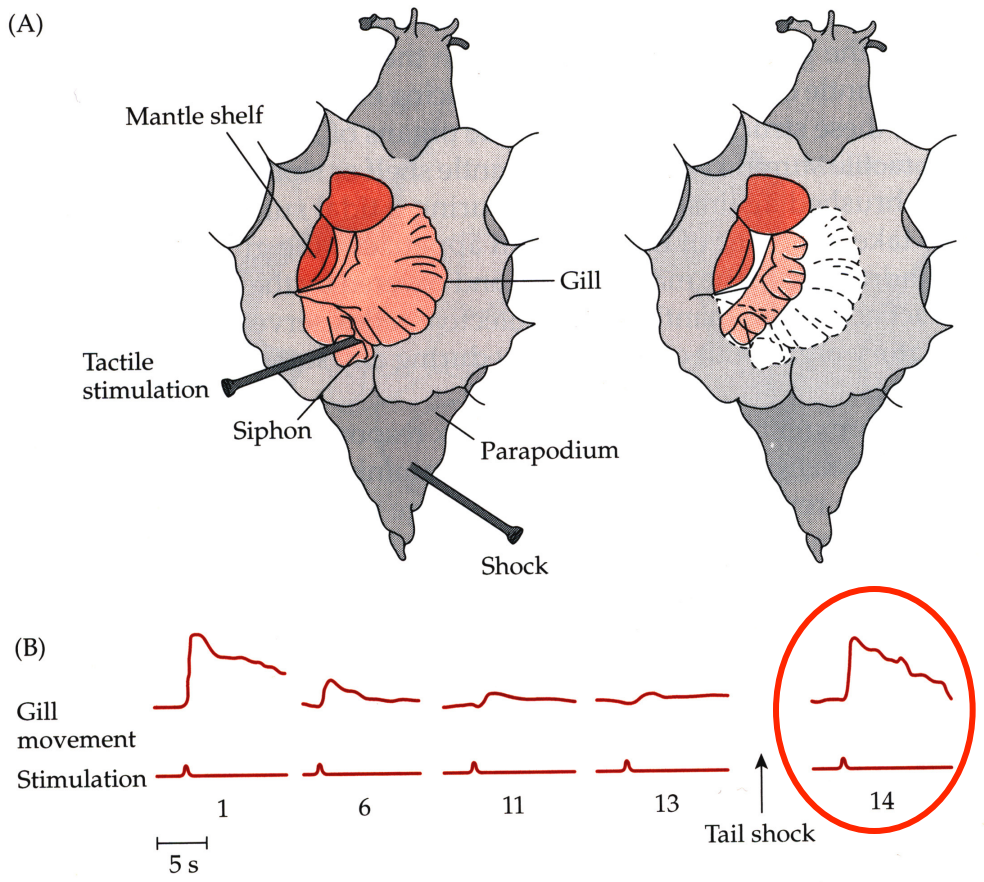
Cellular analysis in the isolated ganglion (simplifying step)



Cellular and molecular analysis of sensory-motor cultures (reductive step)

(Kandel et al. 1984-2010)

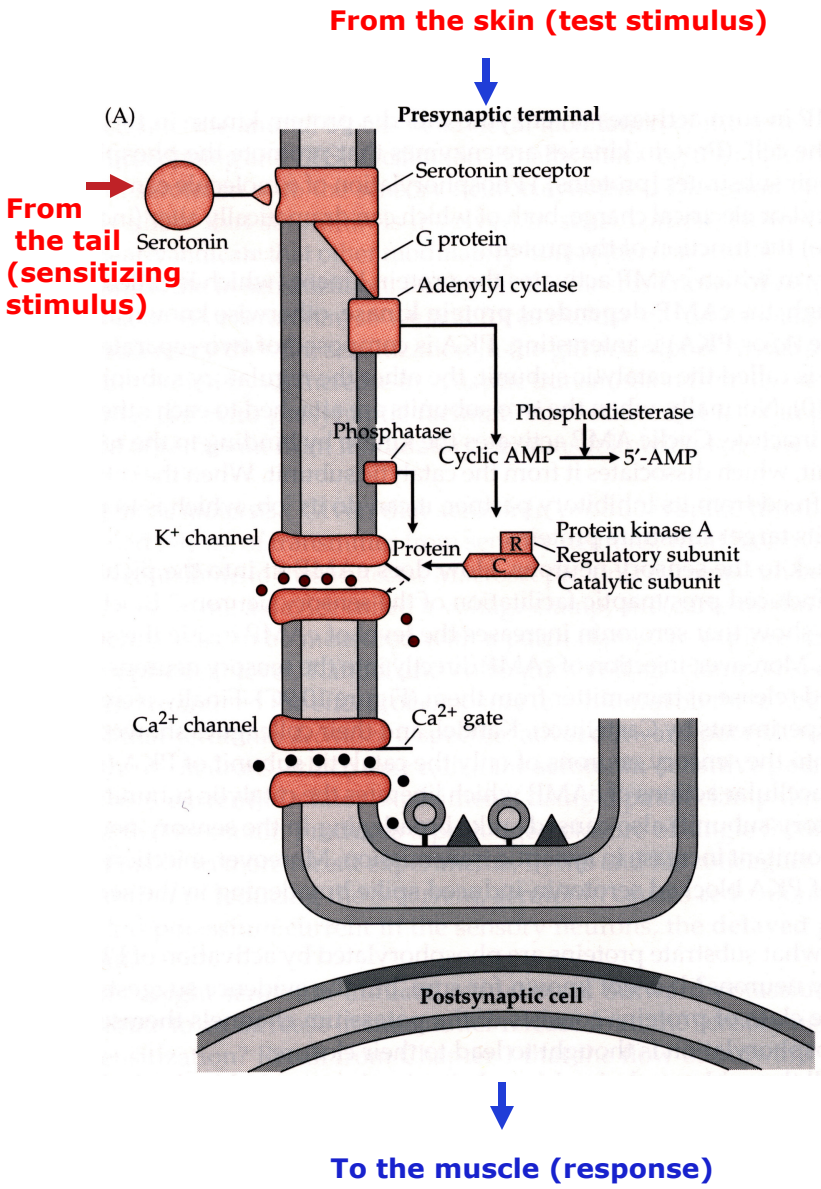
The defensive, gill-and-siphon withdrawal reflex undergoes habituation and sensitization



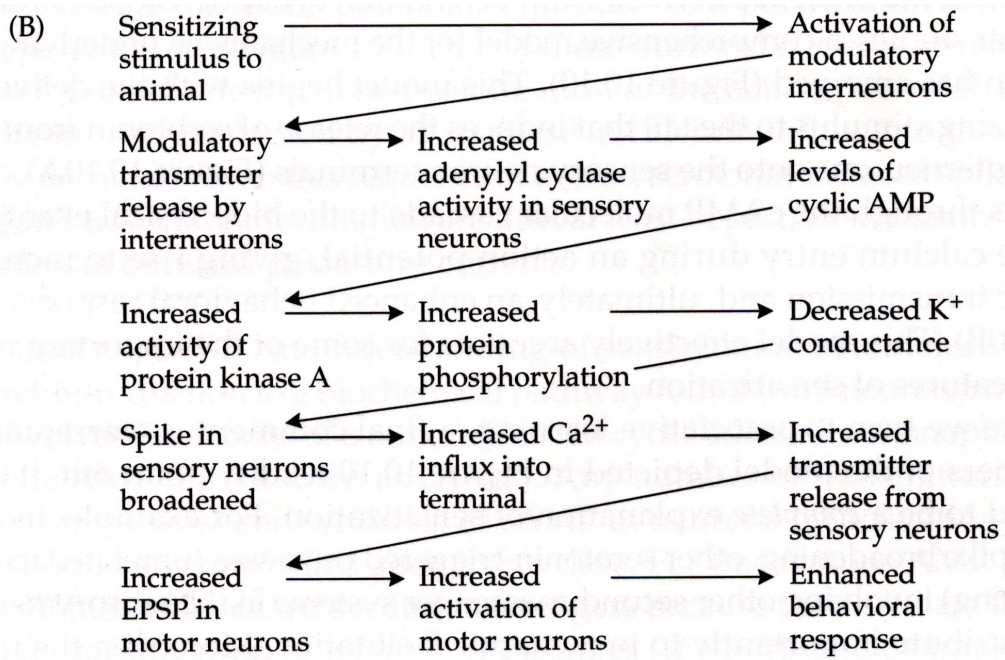
Sensitization

(Kandel et al. 1984-2010)

Acquisition of sensitization in *Aplysia*: The simplest cellular model



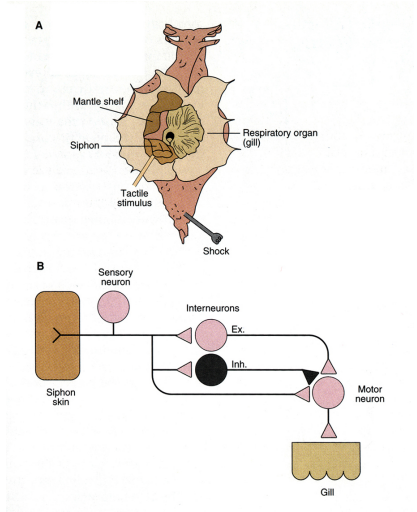
The flowchart

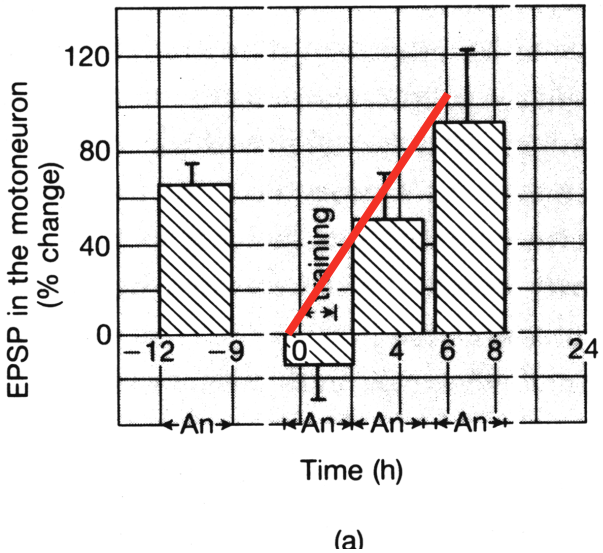


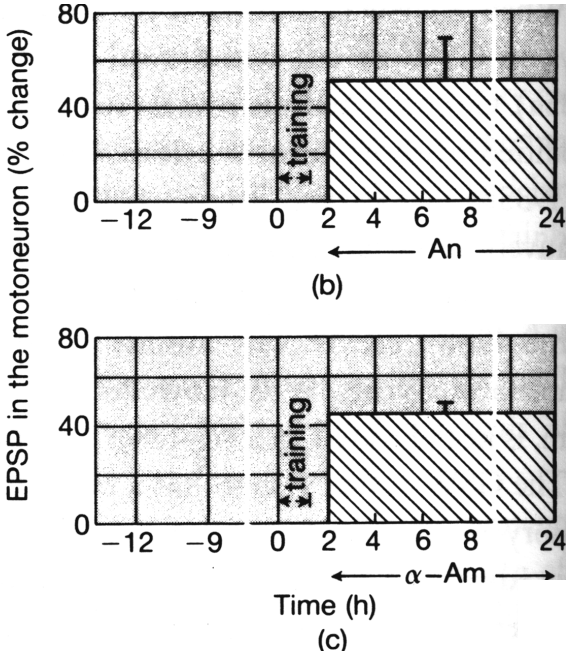
Note: the actual mechanism includes additional components (e.g., PKC) and is context- and history- dependent

(Kandel et al. 1984-2010)

But is the memory stable?



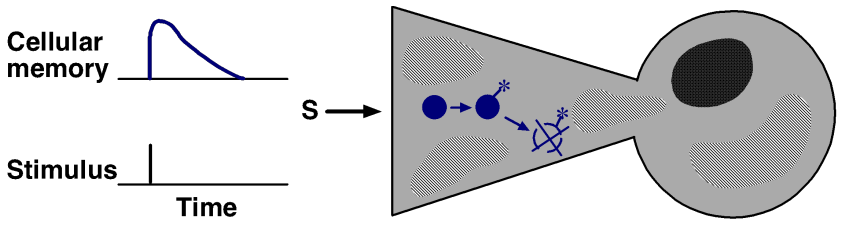




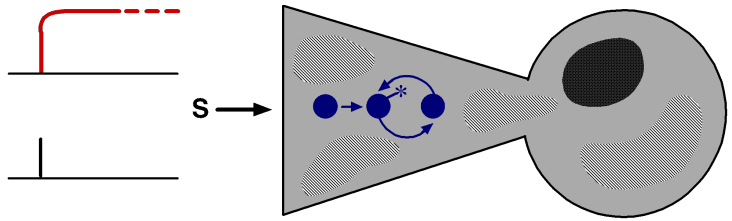
(Montarolo et al. 1986)

Types of cellular models of "storage" (persistence)

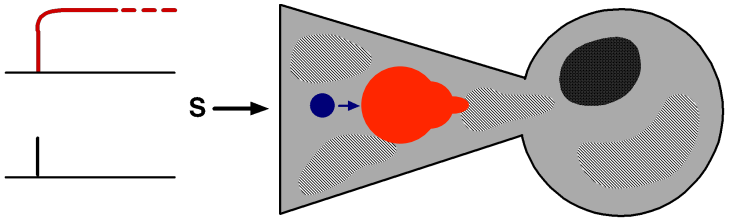
Short-term



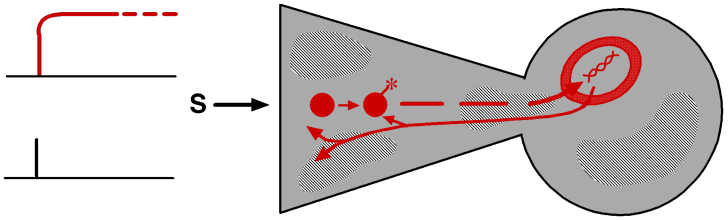
Long-term,
Regenerative switch



Long-term,
Crystalization

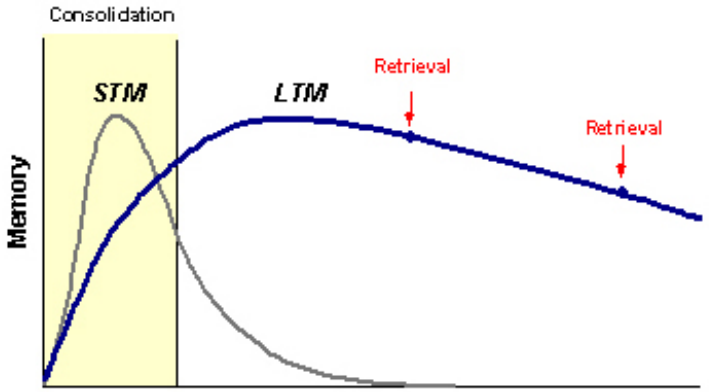


Long-term
Gene expression

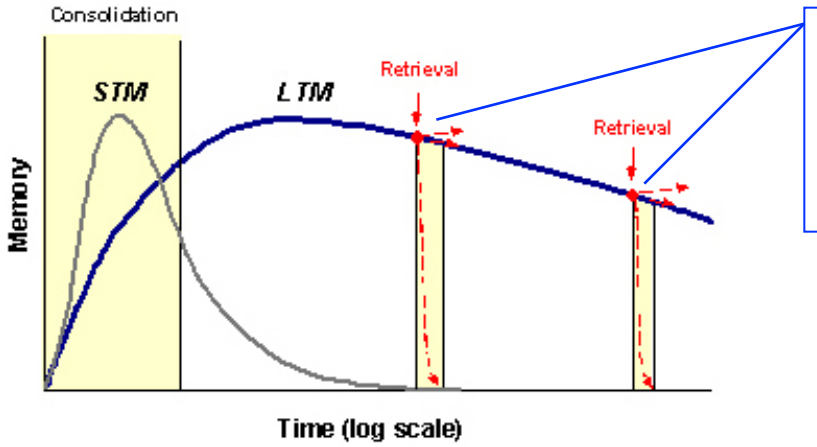


Does consolidation occurs just one per item in LTM?

A *Once-per-item*



B *Reconsolidation, upon reactivation*



Multiple versions: soft, intermediate, ***strong***

(Misanin et al. 1968, Nader et al. 2000, Dudai 2004)