

L'activité persistante

Un mécanisme de la mémoire  
de travail

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# Différents types de mémoires

Des aspects variés:

Mémoire procédurale (comment faire)



Mémoire déclarative (informations verbales)

Échelles de temps multiples:

Mémoire sensorielle (~1s)

Mémoire à court terme (~10s)

Mémoire à long terme

A K C D  
G E P M  
T E N D

# Localisation de la mémoire

Le cas du patient HM:

- Amputé de l'hippocampe

Conséquences:

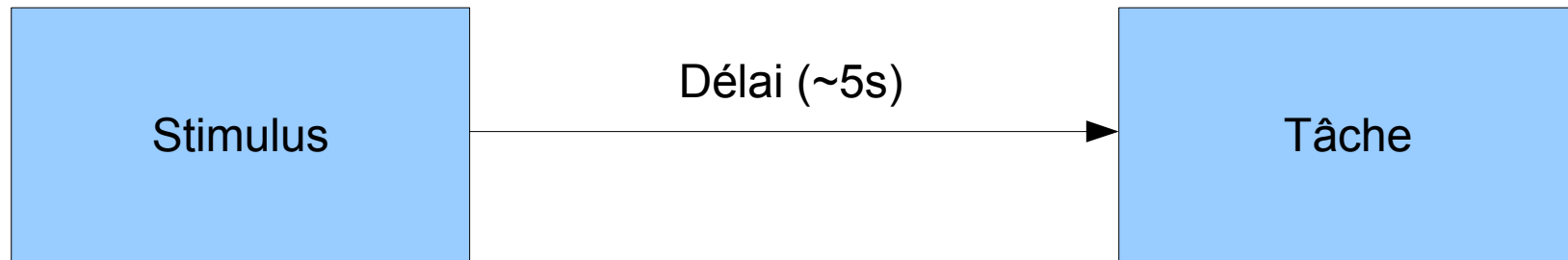
- Impossible de former de nouveaux souvenirs
- Mais capable d'accéder à ses anciens souvenirs

Conclusion:

- La mémoire est un processus partagé dans l'ensemble du cerveau

# Mémoire à court terme

## Expérience type



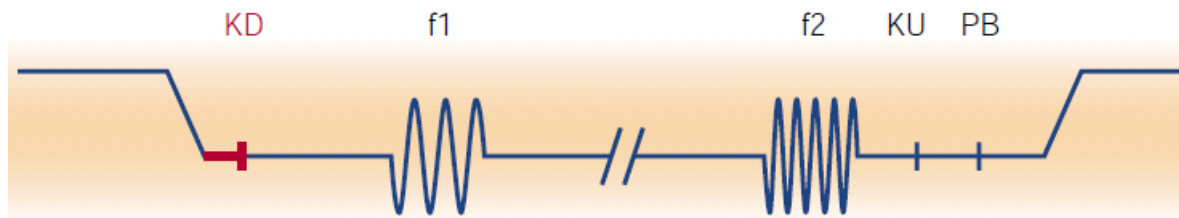
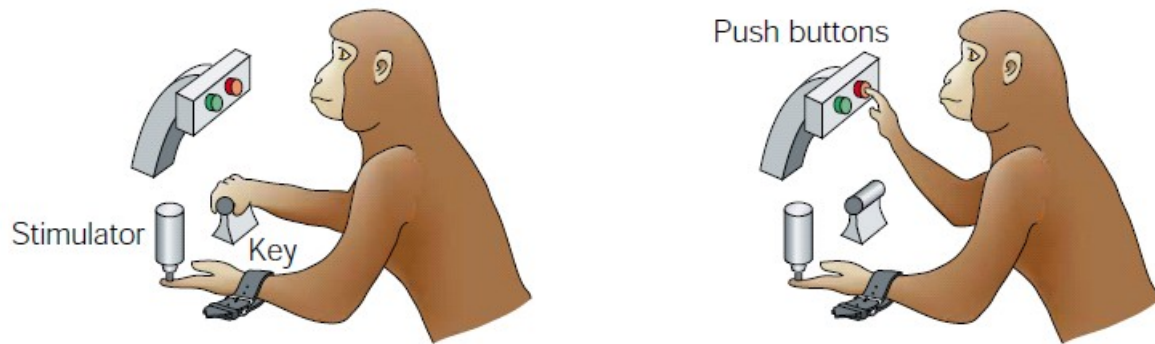
## Nécessite:

- Extraction de l'information utile
- Stockage pendant le délai
- Récupération et travail

# Flutter discrimination: Neural codes, perception, memory and decision making

Romo, R. and Salinas, E. (2003)

# Mountcastle (1960)



Stimulus fréquence  
f1

Stimulus fréquence  
f2

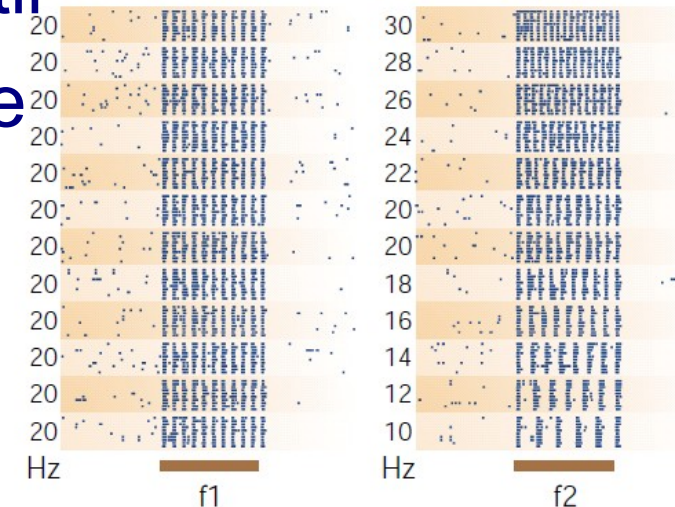
f1 est il plus grand que f2 ?

# Processus cognitifs intervenant

- Stimulus 1
- Mémoire immédiate
- Stimulus 2
- Comparaison
- Décision

# Assimilation et mémorisation du premier stimuli

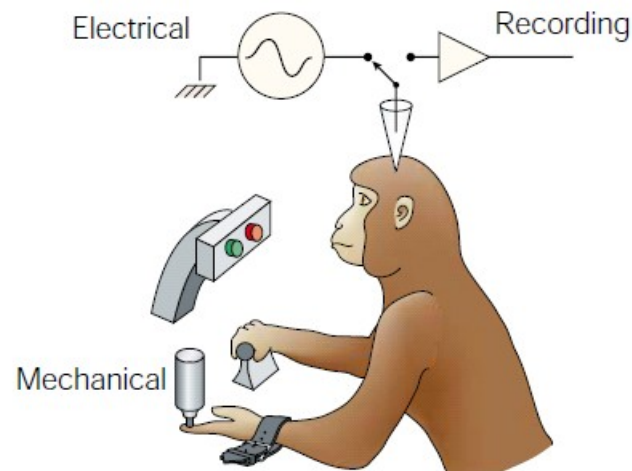
- Signal périodique et tactile
- Neurone du cortex somatosensoriel primaire S1
- Premiers bilans:
  - Importance de la cadence de tir
  - Neurones sensibles à la phase
- Seul le taux de décharge est considéré par le cerveau



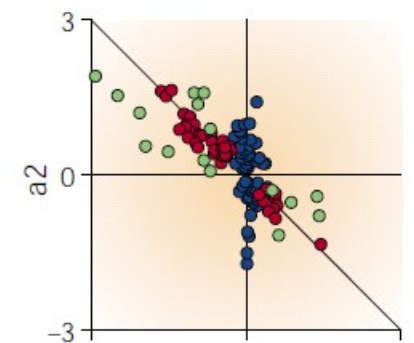
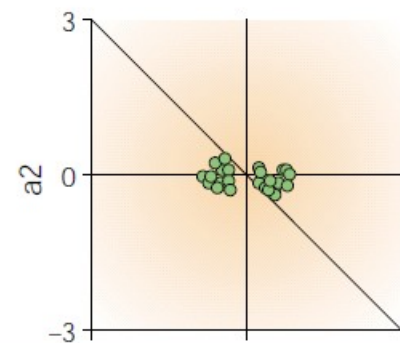
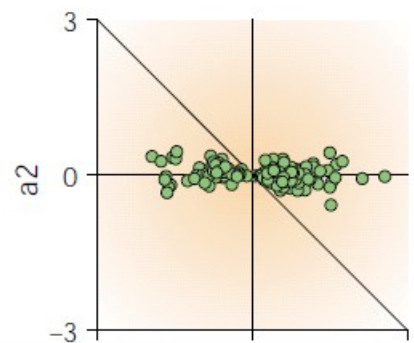
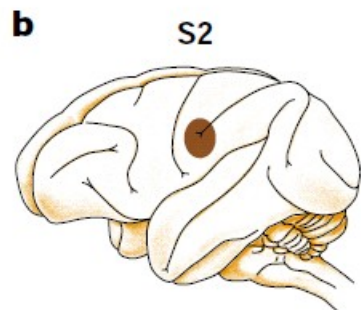
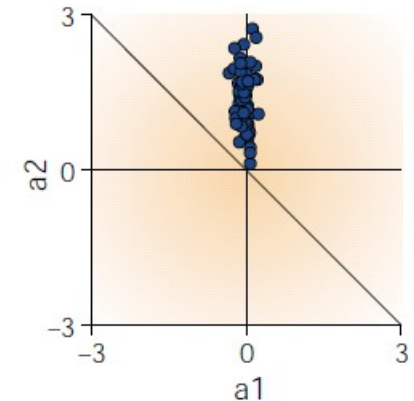
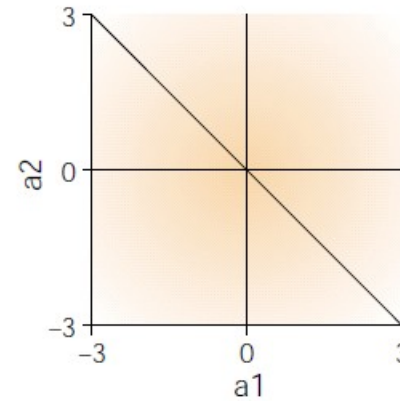
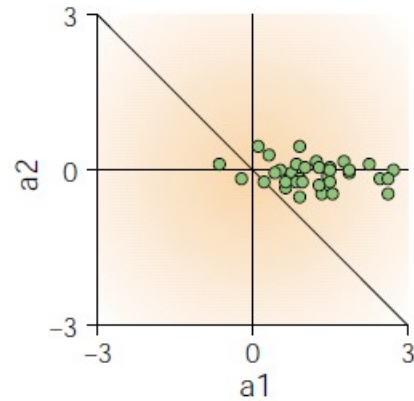
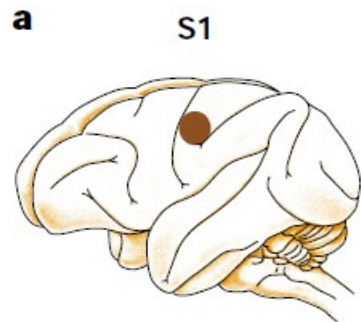


# Deuxième expérience

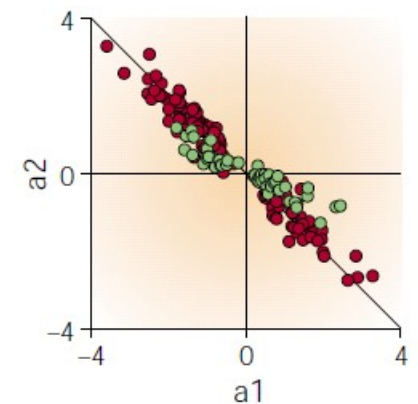
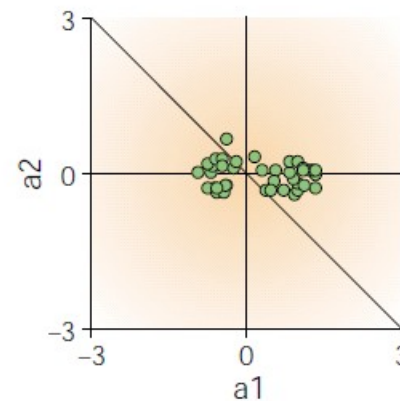
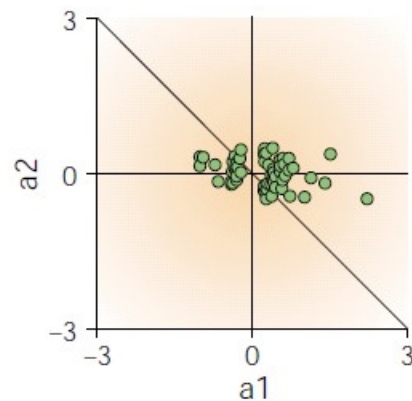
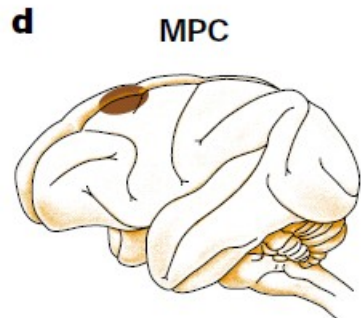
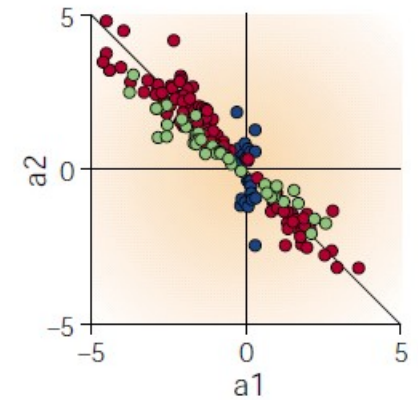
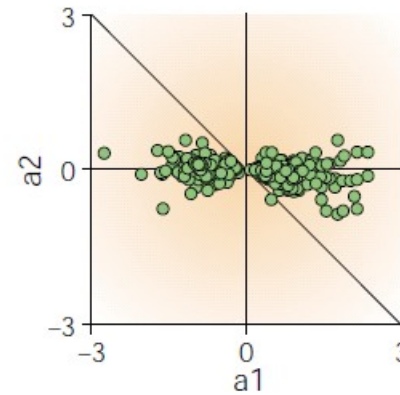
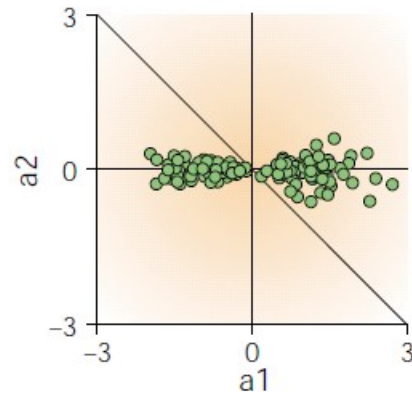
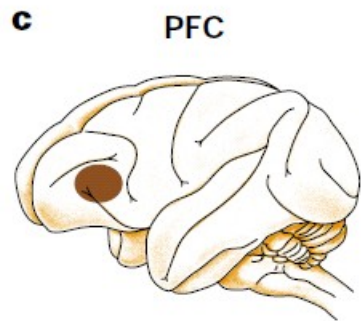
Comparaison stimulus mécanique / stimulus électrique appliqué directement au cerveau



# Activité observée dans différentes parties du cerveau



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# Mémorisation du signal

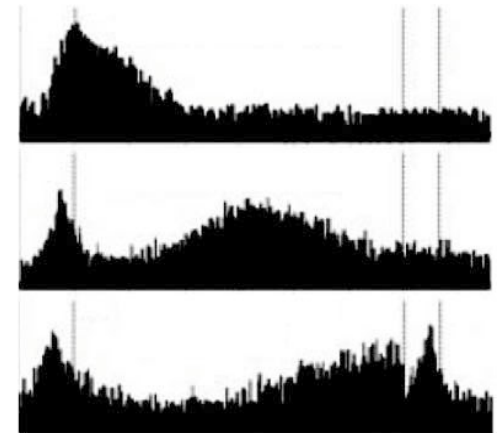
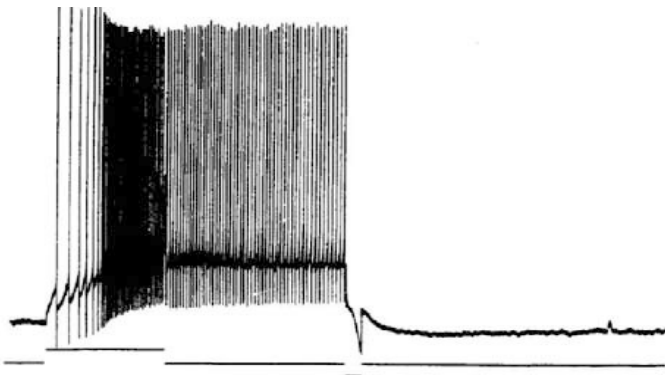
- Activité des zones S2, PFC (mémoire à court terme) et MPC (motricité) pendant le délai.
- Forte adaptabilité des circuits neuronaux de la mémoire à court terme

# PERSISTANT NEURAL ACTIVITY

Persistent neural activity: prevalence and mechanisms

Major, G. and Tank, D.

(2004)

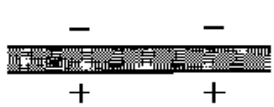




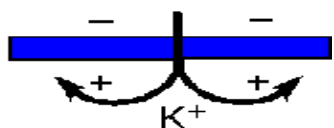
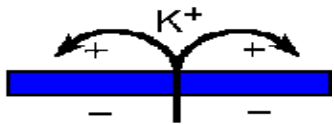
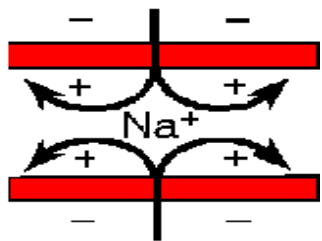
# Introduction: simple explication

- Persistent firing:

- Can be easily generated within an isolated neuron by depolarizing membrane



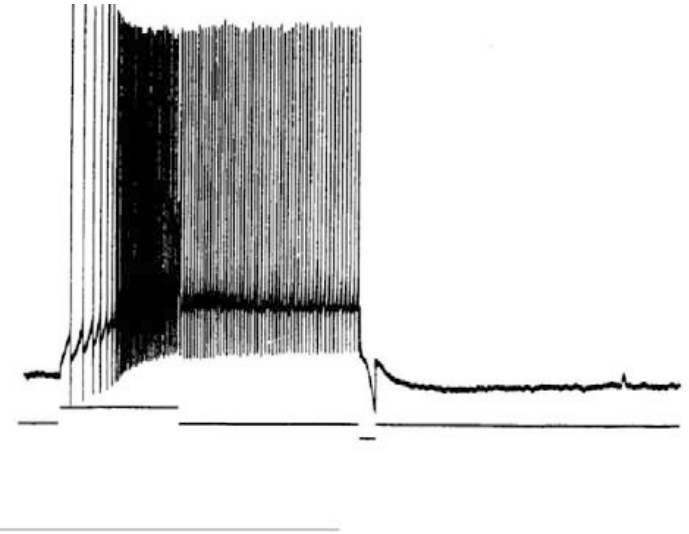
- Firing cycle:



- Membrane polarized: sodium channels closed
- Membrane perturbed: depolarized: sodium channels open and lead to further depolarization
- Saturation reached: sodium channels close, potassium escapes, repolarizing membrane
- Rest cycle: mandatory / optional rest

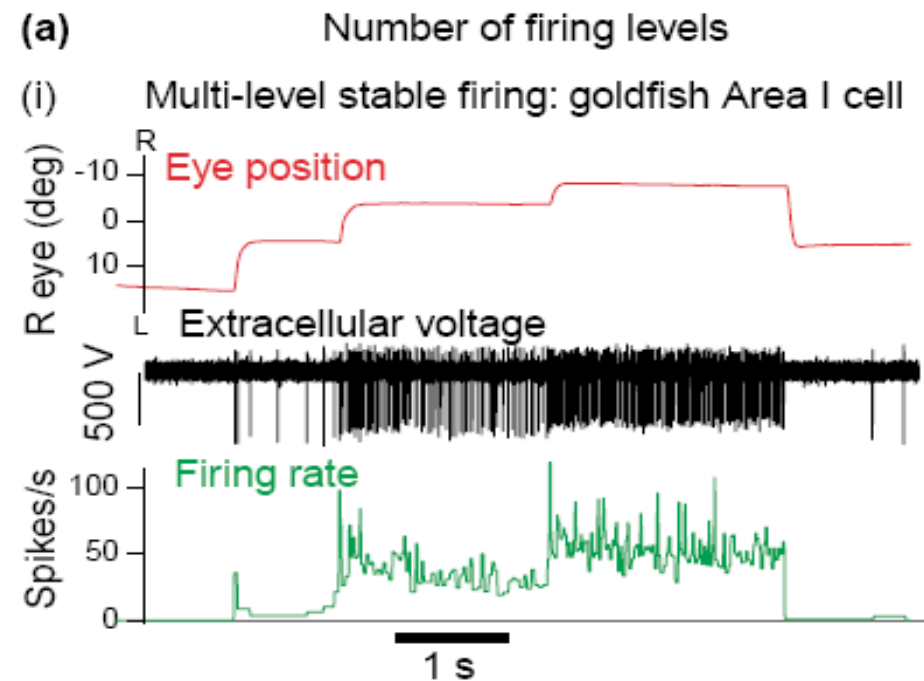
# Persistent activity characterization

- Length : 100ms-10s
- Starting/ termination
  - Started externally, 100 ms
  - Treshold
  - Generally self-terminating, can be inhibited
- During firing:
  - Multiple levels: bi-stability
  - Level transitions: (fish nerve experiments)



# Persistent activity characteristics

- Information encoding?
  - Linear link to eye position (golden fish)
  - Linear link to vibrotactile excitation (monkey experience)
  - That's about all





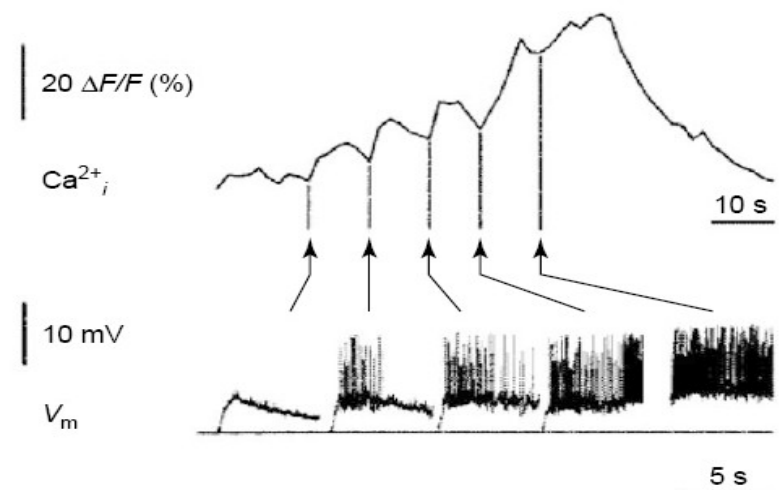
# Framing theories

- Single neuron biological properties:
  - The persistent activity is due solely to the properties of the neuron: one single neuron can be isolated and still be persistently firing
- Networking:
  - The persistent activity is due to the properties of the network formed by a subset of neurons: the persistent activity is nothing but a stable attractor.

# Lamprey spinal cord neurons basic functioning

- NMDA – dependant calcium entry is activated
- Intracellular calcium increases
  - Increase the potential of the neuron membrane
  - Creates CAN current that maintains this potential
- Stable plateau potential
- Persistent firing

Multi-level single cell persistent firing  
lamprey reticulospinal neuron



# Regulation of persistent activity: isolated spinal and cerebral neurons

- Bi-stable activity with transitions, studied *in vivo*
  - Persistent firing
  - Plateau potential, supported by L-Type Ca-channels and resulting CAN currents
- Firing rate and plateau potential increased:
  - mGluReceptors
  - Brief stimuli opening L-Type Ca channels
  - Muscarinic cholinergic agents
- Decreased: GABA<sub>A</sub> Receptors

# *In vitro* - *in vivo* transition: cortical pyramidal cells

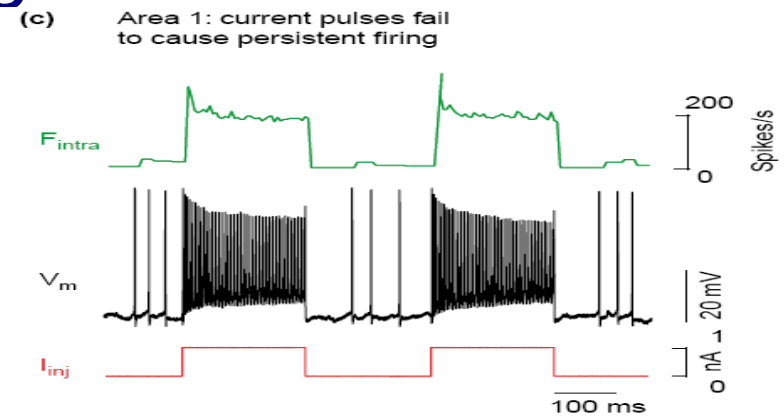
- In vitro, under muscarine modulation:
  - Plateau potentials with stable firing levels
  - Transitions: synaptic and current stimulation
    - Short depolarisation: stimulation
    - Long hyperpolarisation: inhibition
  - CAN current: slow transition
- In vivo:
  - Input signal noise add jitter: too quick switching for CAN?
  - No plateau potentials, yet persistent firing

# And how about switching off?

- NMDA-Receptors generate Ca plateau potential
  - Generates persistent activity
- CAN maintain it
- At the same time Ca-activated K channels compensate CAN and cause extinction of persistent activity

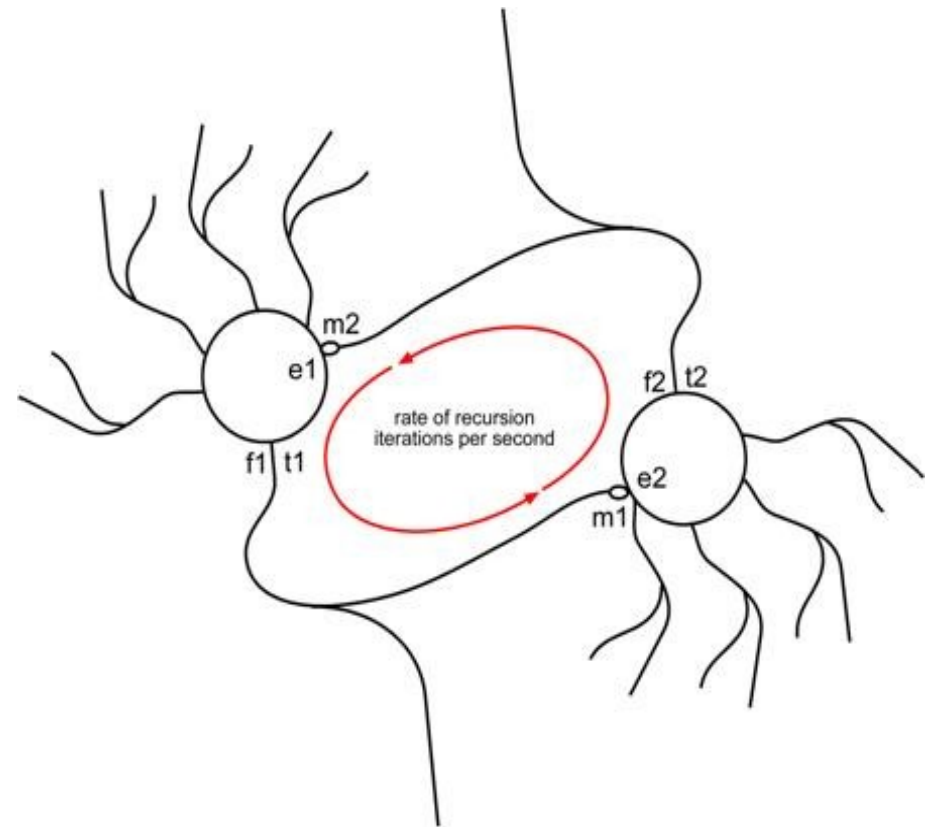
# More problems with one single neuron persistent firing

- Too much persistence of firing activity when firing a potential in one single nerve
  - Oculomotor nerve
  - Higher areas
- Plasticity and adaptability
- Difference of time profile between neurons
- Too much coordination between far-away areas : oculomotor areas on the opposite sides of the brain, goldne fish



# Simple network models explain most of the data

- Background noise
  - In vivo systems
  - Related to feedback signals (PSP)
  - Varies with plateau-potential





# Simple network models explain most of the data

- UP and DOWN states in cortical slices
  - UP = persistent activity varying in time
- Provide evidence for network models:
  - States are synchronized in the nearby cells
  - Depolarization => increases firing rate
    - Increases noise
    - => Increase Post Synaptic Potentials
    - => evidence for some feed-back
  - Blockers of AMPA and NMDA neurotransmitters abolish the UP states



# Return to experiment with cortical pyramidal cells

- *In vitro*, under muscarine modulation:
  - Plateau potentials with stable firing levels
  - Transitions: synaptic and current stimulation
    - Short depolarisation: stimulation
    - Long hyperpolarisation: inhibition
- Yet no effect of hyper/depolarisation on time profile in *in vivo* systems => networks

# Still simple feed-back model is limited

- NMDA repression:
  - firing rate changes,
  - Not the time course
- Isolating neurons (dopamine/serotonergic agents) inside neuronal circuits
  - same effect
- Predicts linear link in firing rates
  - False

# Conclusion: Hybrid Mechanism

- Network mechanisms
  - Time-profile of firing
  - Synchronization of firing
- Single-neuron properties
  - Stability of firing
  - Leveling of firing
- No direct evidence for hybrid mechanism
  - Yet mechanisms are there for both
  - Each model alone do not account for all data

# Résumé

L'activité persistante est associée au maintien d'une information nécessaire au niveau comportemental

Écueil dangereux: l'activité persistante n'est pas caractéristique de la mémoire à court terme

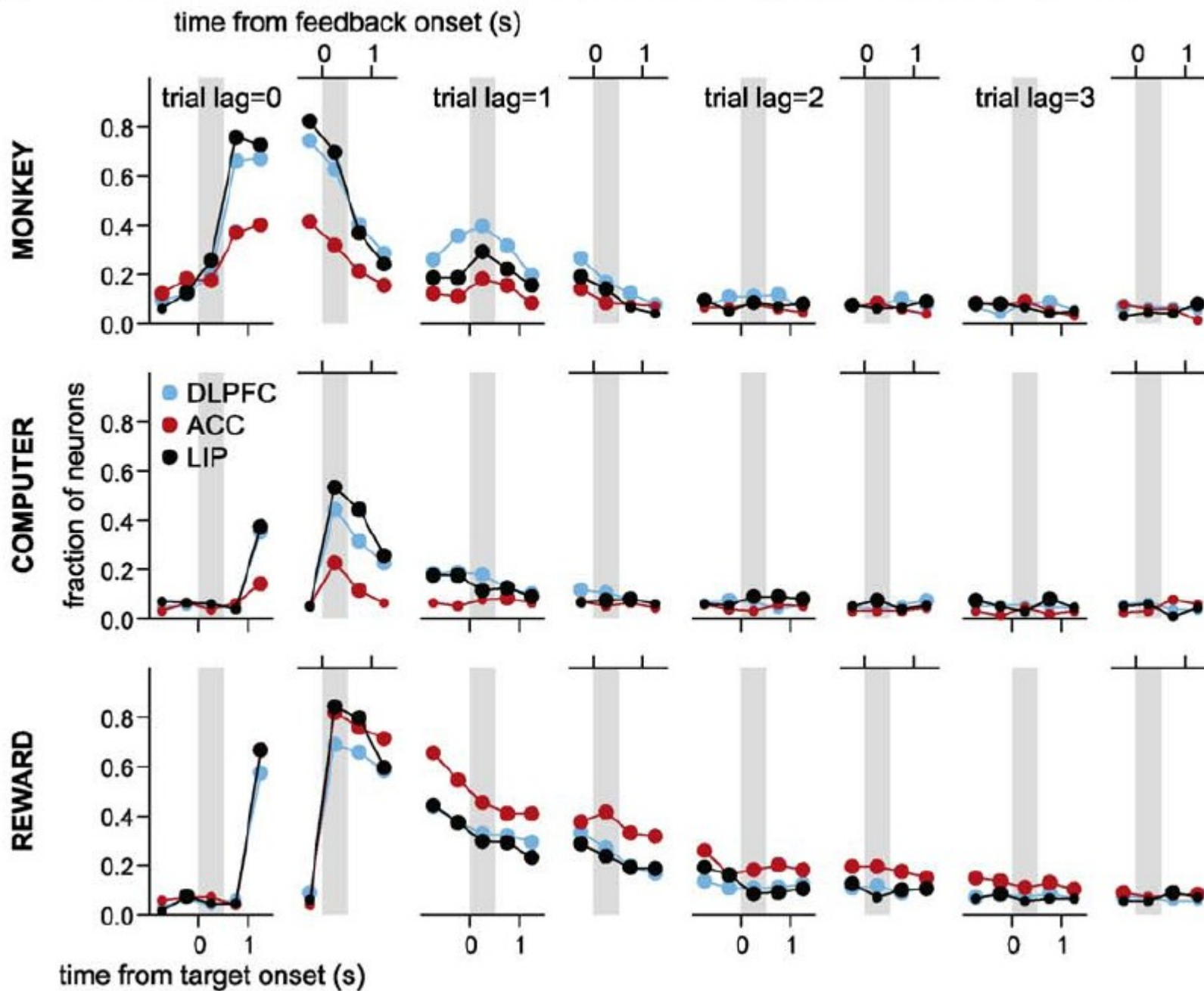
# Activité persistante et reinforcement learning

## « Reinforcement learning »

- Algorithme d'exploration d'un environnement inconnu
- Associe à chaque action des valeurs abstraites qui représentent l'espérance de gain de chaque choix

Est implémenté au niveau neuronal

(c) Persistent activity in DLPFC, ACC and LIP during a decision-making task



# Conclusion

## Activité persistante:

- Sous-tend de nombreux mécanismes
- Pas encore de modèle parfait

## Mémoire de travail:

- Les étapes de sélection de l'information utile et de restitution sont encore mal comprises