Models of networks - continued

Readings: D&A, chapter 7.

Network models - summary

• Network models: to understand the implications of connectivity in terms of computation and dynamics.

• 2 Main strategies: Spiking vs Firing rate models.

• The issue of the emergence of orientation selectivity as a model problem, extensively studied theoretically and experimentally.
- Two main models: feed-forward and recurrent.
- Detailed spiking models have been constructed which can be directly compared to electrophysiology
- The same problem is also investigated with a firing rate model, a.k.a. the 'ring model'.

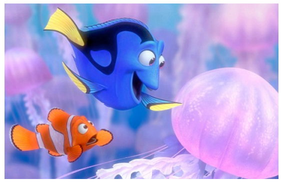
Sustained activity, Working Memory, Associative memory

Readings:

C.Constandinis and XJ Wang, , "a neural circuit basis for spatial working memory", Neuroscientist, 2004

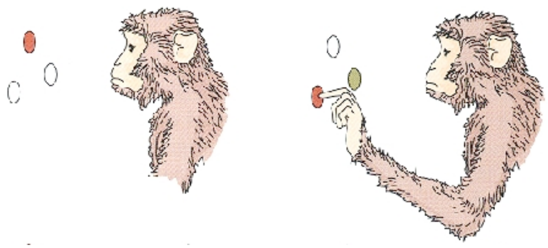
http://www.youtube.com/watch?v=M1Tui0Gbvq4&feature=related

http://news.bbc.co.uk/1/hi/health/4101431.stm



What is working memory ? (a.k.a. short-term memory)

- The ability to hold information over a time scale of seconds to minutes
- a critical component of cognitive functions (language, thoughts, planning etc..)



Delayed match-to sample task:
remember 'red'

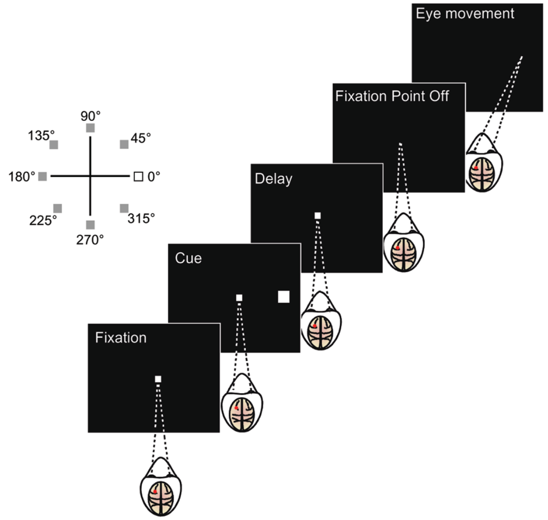
Test your working memory

http://www.ted.com/talks/peter_doolittle_how_your_working_memory_makes_sense_of_the_world.html

TED Ideas worth spreading

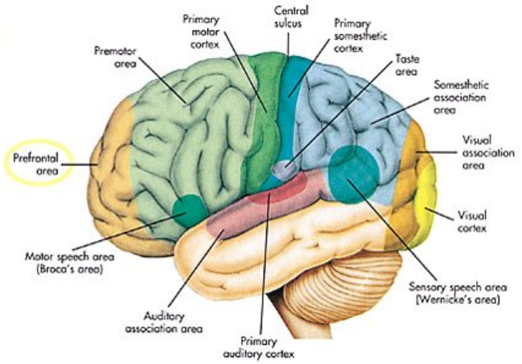
Oculo-motor delayed response task:

remember location of cue.

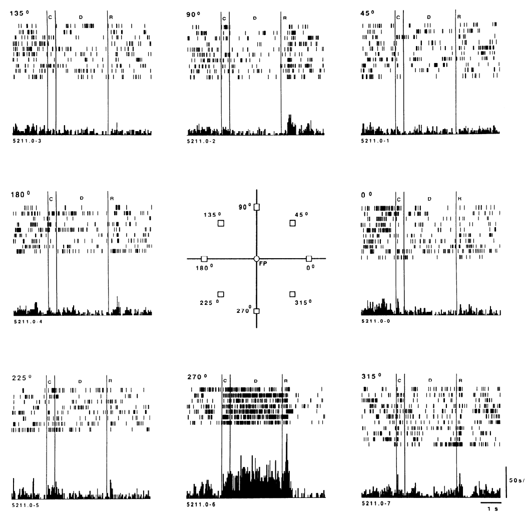


Sustained activity in PFC (1)

- Lesion and inactivation studies demonstrate crucial role of Prefrontal Cortex (PFC) in working memory, in particular dorsolateral PFC (PFdl).



Sustained activity in PFC (2)



Funahashi et al, 1989

Working memory vs Long-term memory

• Long-term memory : molecular or structural changes

• Short-term/ working memory: dynamic process that has not yielded to molecular characterization. Sustained Activity.

Sustained activity is very widespread

• Sustained activity is a widespread phenomenon

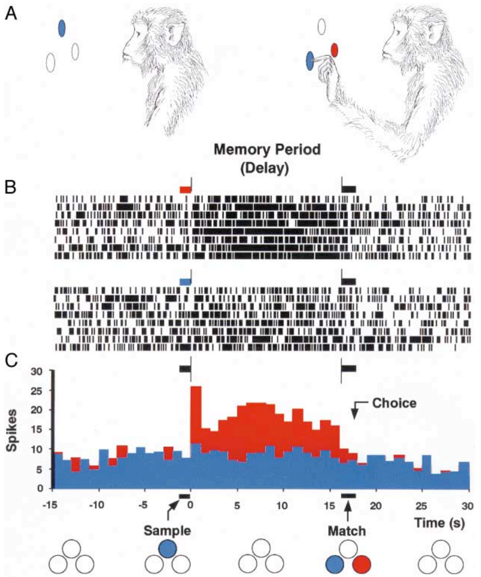
• LIP and PP also have neurons which direction-specific memory fields, similar to PFC.

• Also found in inferotemporal cortex (IT), see e.g. Fuster and Jervey 1982.
Example of a discrete working memory.

• Memory related activity is also described in V3A, MT, V1, entorhinal cortex, Pre motor cortex, SMA, SC, basal ganglia...

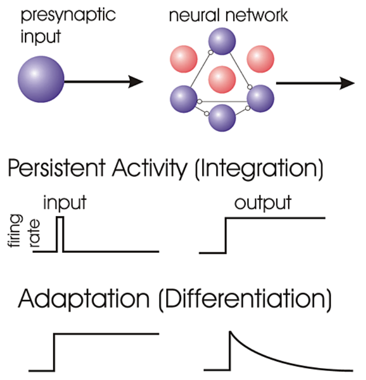
• The distinct and cooperative roles of these areas remain unresolved.

Sustained activity in IT



Fuster and Jervey 1982

Brain calculus : integration and differentiation



• integration (persistent activity) seems to be mainly due to network interactions, while differentiation (adaptation) seems mainly cellular and synaptic depression

Working Memory and Sustained Activity

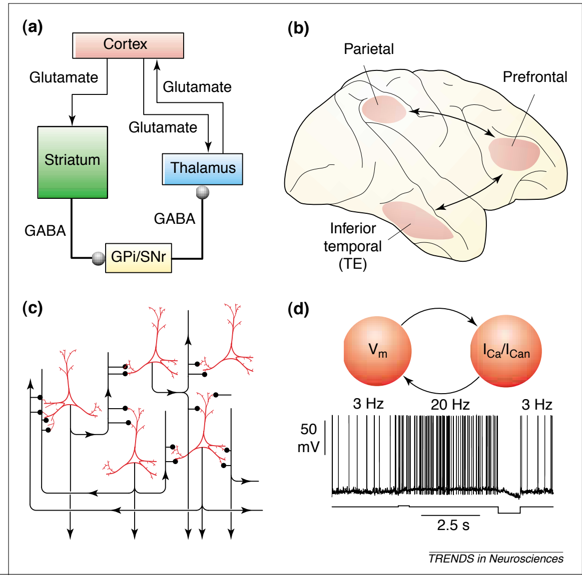
- A theory of working memory should answer:

- how it is initiated?
- why does it persist ?
- what makes it specific?
- how does it end?

- reason for capacity limit?
- relationship with attention, long term memory?

- Mechanism : reverberations through connections (which?), or cellular?
- Lots of experimental and theoretical work to answer these questions, in PFC, HD, Oculo-motor system

How does a transient stimulus cause a lasting change in neural activity?



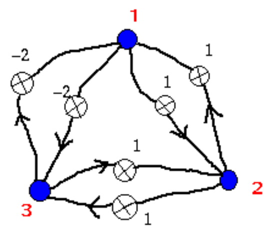
Attractor paradigm for persistent activity

- Since the 1970s it has been proposed that delay activity patterns can be theoretically described by 'dynamical attractors'

Hopfield Networks

- A Hopfield net is a form of recurrent artificial neural network invented by John Hopfield (1982).
- Hopfield nets typically have binary (1/-1 or 1/0) threshold units:

$$s_i = \begin{cases} 1 & \text{if } \sum_j w_{ij} s_j > \theta_i, \\ -1 & \text{otherwise.} \end{cases}$$



weights in black
Nodes numbers in red

where s_j state of unit j, and θ_i is the threshold

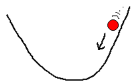
The weights have to follow: $w_{ii}=0$, $w_{ij}=w_{ji}$

- Hopfield nets have a scalar value associated with each state of the network referred to as the "energy", E, of the network, where:

$$E = -\frac{1}{2}\sum_{i<j} w_{ij} s_i s_j + \sum_i \theta_i \ s_i$$

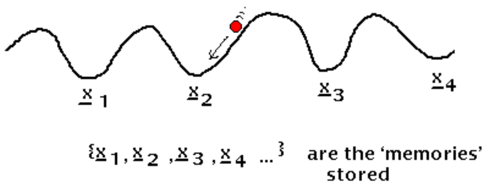
Hopfield Networks

• Running: at each step, pick a node at random and update (asynchronous update)
The energy is guaranteed to go down and the network to settle in local minima of the energy function.



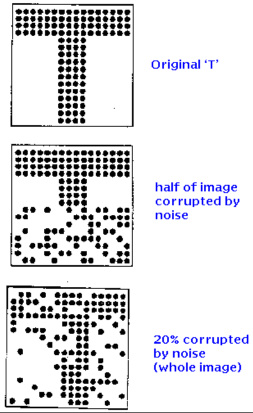
• Learning: the weights are learnt, so as to 'shape' those local minima.
The network will learnt to converge to learnt state even if it is given only part of the state

$$w_{ij} = \frac{1}{N} \sum_{k=1}^{k=N} \xi_i^k \xi_j^k$$



Associative memories

• The Hopfield network is an associative/content addressable memory. It can be used to recover from a distorted input the trained state that is most similar to that input. E.g., if we train a Hopfield net with 5 units so that the state (1, 0, 1, 0, 1) is an energy minimum, and we give the network the state (1, 0, 0, 0, 1) it will converge to (1, 0, 1, 0, 1).

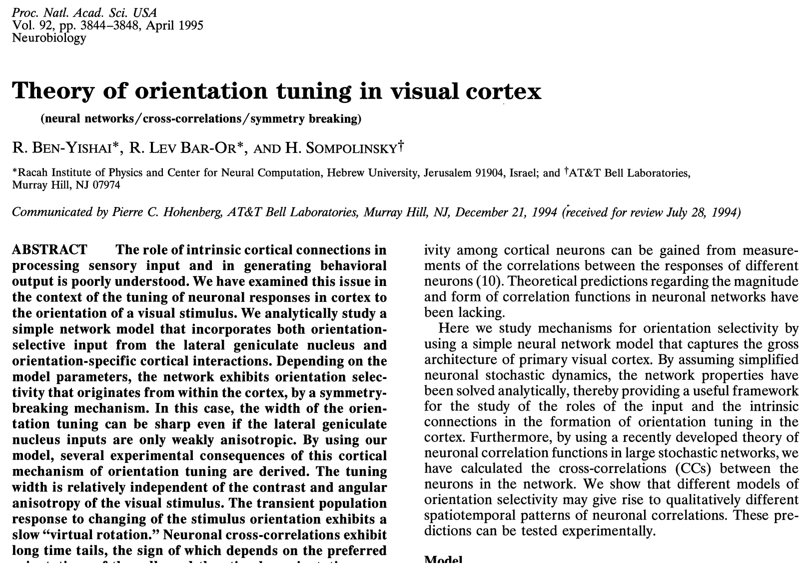


Attractor paradigm for persistent activity

• Since the 1970s it has been proposed that delay activity patterns can be theoretically described by 'dynamical attractors'

• Recently, a great effort to build biophysically plausible model of sustained activity / attractor dynamics for memory.

The Ring Model (1)



Proc. Natl. Acad. Sci. USA
Vol. 92, pp. 3844–3848, April 1995
Neurobiology

Theory of orientation tuning in visual cortex

(neural networks/cross-correlations/symmetry breaking)

R. Ben-Yishai*, R. Lev Bar-Or*, and H. Sompolinsky†

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Communicated by Pierre C. Hohenberg, AT&T Bell Laboratories, Murray Hill, NJ, December 21, 1994 (received for review July 28, 1994)

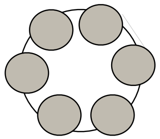
ABSTRACT The role of intrinsic cortical connections in processing sensory input and in generating behavioral output is poorly understood. We have examined this issue in the context of the tuning of neuronal responses in cortex to the orientation of a visual stimulus. We analytically study a simple network model that incorporates both orientation-selective input from the lateral geniculate nucleus and orientation-specific cortical interactions. Depending on the model parameters, the network exhibits orientation selectivity that originates from within the cortex, by a symmetry-breaking mechanism. In this case, the width of the orientation tuning can be sharp even if the lateral geniculate nucleus inputs are only weakly anisotropic. By using our model, several experimental consequences of this cortical mechanism of orientation tuning are derived. The tuning width is relatively independent of the contrast and angular anisotropy of the visual stimulus. The transient population response to changing of the stimulus orientation exhibits a slow "virtual rotation." Neuronal cross-correlations exhibit long time tails, the sign of which depends on the preferred

ivity among cortical neurons can be gained from measurements of the correlations between the responses of different neurons (10). Theoretical predictions regarding the magnitude and form of correlation functions in neuronal networks have been lacking.

Here we study mechanisms for orientation selectivity by using a simple neural network model that captures the gross architecture of primary visual cortex. By assuming simplified neuronal stochastic dynamics, the network properties have been solved analytically, thereby providing a useful framework for the study of the roles of the input and the intrinsic connections in the formation of orientation tuning in the cortex. Furthermore, by using a recently developed theory of neuronal correlation functions in large stochastic networks, we have calculated the cross-correlations (CCs) between the neurons in the network. We show that different models of orientation selectivity may give rise to qualitatively different spatiotemporal patterns of neuronal correlations. These predictions can be tested experimentally.

Model

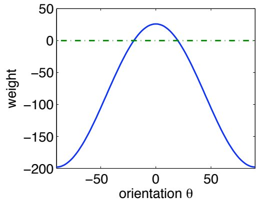
The Ring Model (2)



- N neurons, with preferred angle, θ_i ,evenly distributed between $-\pi/2$ and $\pi/2$
- Neurons receive thalamic inputs *h.*

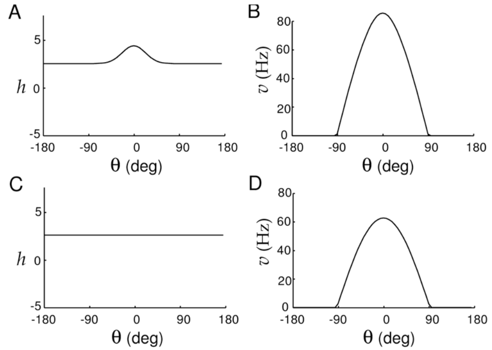
\+ recurrent connections, with excitatory weights between nearby cells and inhibitory weights between cells that are further apart (mexican-hat profile)

$$\tau_r \frac{dv(\theta)}{dt} = -v(\theta) + \left[h(\theta) + \int_{-\pi/2}^{\pi/2} \frac{d\theta'}{\pi} \left(-\lambda_0 + \lambda_1 \cos(2(\theta-\theta'))\right) v(\theta') \right]_+$$



The Ring Model (5): Sustained Activity

- If recurrent connections are strong enough, the pattern of population activity once established can become independent of the structure of the input. It can persists when input is removed.
- A model of working memory ?



Network Mechanisms & Biophysical Models

- Anatomical organisation of PFC resembles a recurrent network
- Biophysical realistic computational modelling has shown that such recurrent networks can give rise to location-specific, persistent discharges (Compte et al 2000, Gutkin et al 2000, Tegner et al 2002, Renart et al 2003a, Wang et al 2004)

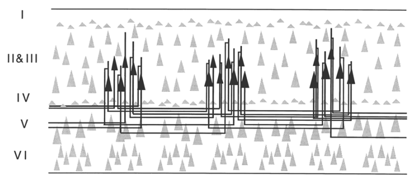


Fig. 4. Schematic diagram illustrating the pattern of connections between prefrontal neurons in the superficial layers. The figure summarizes results of anatomical tracer injection experiments and retrograde labeling. From Kritzer and Goldman-Rakic (1995), with permission.

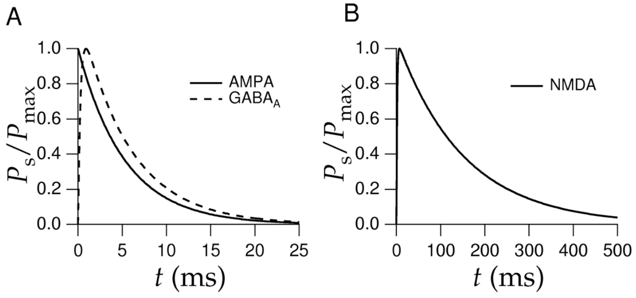
Network Mechanisms & Biophysical Models

- Modelling studies show that stability is an issue in such network.
- Strong recurrent inhibition is needed to prevent runaway excitation and maintain specificity
- Models are also challenged by accounting for spontaneous activity in addition to memory state
- Oscillations can destabilise the memory activity.

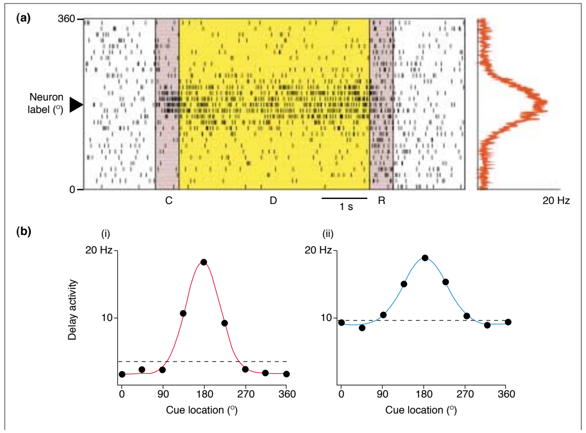
- Working memory is found to be particularly stable when excitatory reverberations are characterised by a fairly slow time course, e.g. when synaptic transmission is mediated by NMDA receptors (prediction)

Synaptic input

- Different synapses have different dynamics.
- Excitatory synapses: AMPA is fast, NMDA slow.
- Inhibitory synapses: GABAa are fast, GABAb slower.



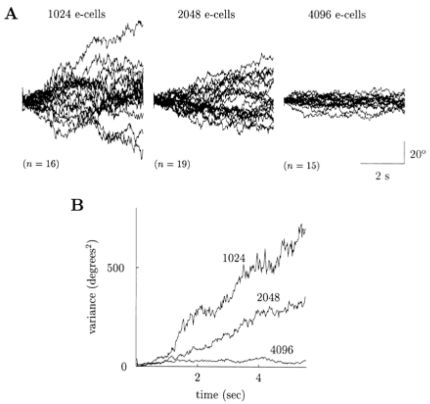
Network Mechanisms & Biophysical Models

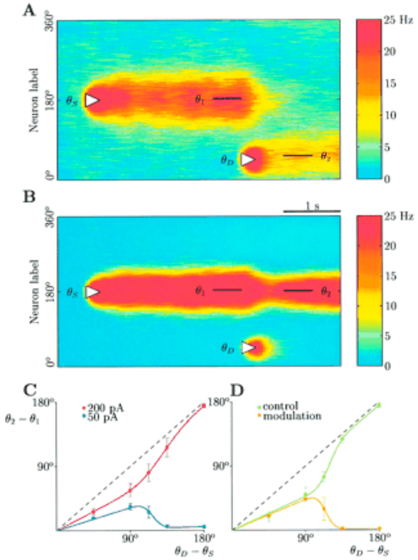


[Compte, Brunel, Goldman-Rakic and Wang, 2000]

- Network of ~2500 integrate and fire neurons, mexican hat connectivity, NMDA excitation.
- Reproduce Funahashi et al 1989.
- Selectivity of memory field, temporal drifts, robustness to distractors.

Biophysical Models -- drift and robustness to distractors.

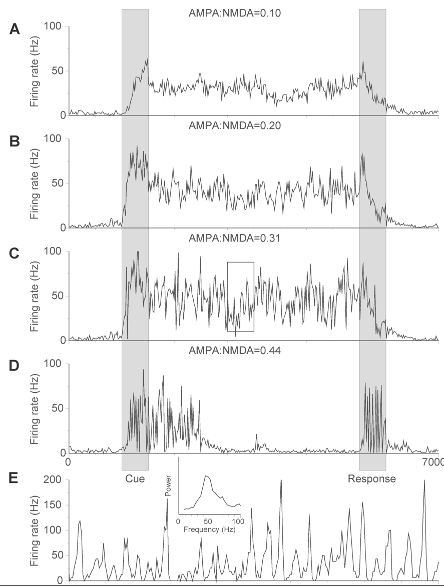




Compte et al 2000

Network Mechanisms & Biophysical Models

Fig. 6. Stability of persistent activity as a function of the AMPA:NMDA ratio at the recurrent excitatory synapses. *A–D*, Temporal course of the average firing rate across a subpopulation of cells selective to the presentated transient input, for different levels of the AMPA:NMDA ratio. As the ratio is increased, oscillations of a progressively larger amplitude develop during the delay period, which eventually destabilize the persistent activity state. *E*, Snapshot of the activity of the network in (*C*) between 3 and 3.5 seconds. *Top*, Average network activity. *Bottom*, Intracellular voltage trace of a single neuron. *Inset*, Power spectrum of the average activity of the network, showing a peak in the γ (40 Hz) frequency range. Persistent activity is stable even in the presence of synchronous oscillations. Adapted with permission from Renart, Brunel, and others (2003).



[Renart, Brunel, Wang , 2003]

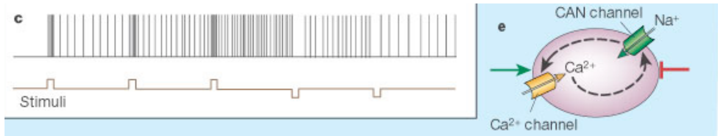
But cellular mechanisms should not be forgotten ...

[Egorov et al, Nature, 2002]

- Layer 5 of rat EC in vitro, intracellular depolarisation + bath application of the ACh-receptor agonist leads to a Ca2+ -dependent plateau potential.
- leads to sustained firing at a constant rate > 13 min
- independent of synaptic transmission.
- activity level can be increased or decreased using repeated inputs.

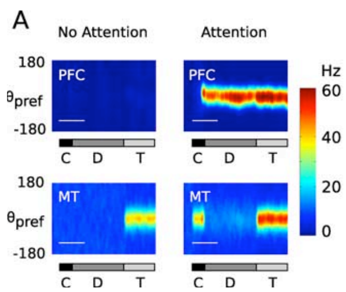
see also [Lowenstein ... and Hausser, *Nat Neuro,* 2005, bistability in Purkinje neurons]

Could attractors be suited for remembering learned stimuli while such a system could help maintaining new stimuli?



Lots of interesting questions

- How are these attractors learnt?
- What is the relation with Attention?
- What is the relation with Long-term Memory ? (Is sustained activity helpful for storage of memory?) http://www.youtube.com/watch?v=k8Bgs8EarR0&feature=related



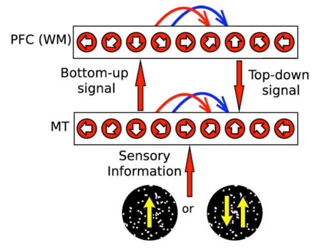


Figure 1. Scheme of the loop architecture (red is excitation, and blue is inhibition). Two kinds of motion stimuli are considered (random-dot patterns; yellow arrows indicate signal

Ardid, Wang and Compte 2007

Link with disease (schizophrenia)

- Working Memory deficits core of cognitive deficits in Scz
- Schizophrenia associated with reduced function of NMDA receptor (and ketamine blocks NMDA).
- Instability of attractor states, shallower basins of attraction
- spontaneous attractors: positive symptoms?

Review

A computational neuroscience approach to schizophrenia and its onset

Edmund T. Rolls[a,*], Gustavo Deco[b,c]

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ABSTRACT

Computational neurosci
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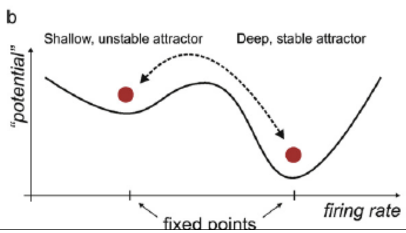


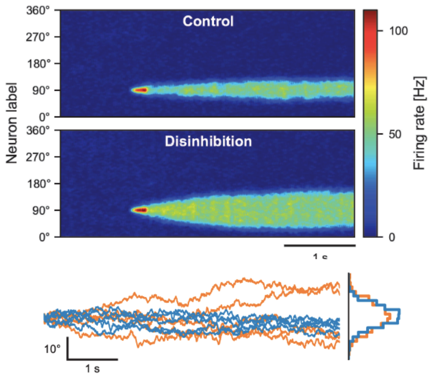
Link with disease (schizophrenia)

Cerebral Cortex Advance Access published November 29, 2012

Cerebral Cortex
doi:10.1093/cercor/bhs370

Linking Microcircuit Dysfunction to Cognitive Impairment: Effects of Disinhibition Associated with Schizophrenia in a Cortical Working Memory Model

John D. Murray[1,2], Alan Anticevic[3,4,5], Mark Gancsos[3], Megan Ichinose[3], Philip R. Corlett[3,5], John H. Krystal[3,4,5,6,7] and Xiao-Jing Wang[2,8]



- Desinhibition via perturbation of NMDA receptors on Inhib cells.
- broadens selectivity, increases drift and vulnerability to distractors

Ageing and working memory

LETTER

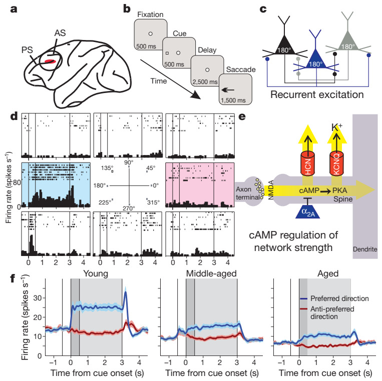
doi:10.1038/nature10243

210 | NATURE | VOL 476 | 11 AUGUST 2011

Neuronal basis of age-related working memory decline

Min Wang[1], Nao J. Gamo[1], Yang Yang[1], Lu E. Jin[1], Xiao-Jing Wang[1], Mark Laubach[1,2], James A. Mazer[1], Daeyeol Lee[1] & Amy F. T. Arnsten[1]

Many of the cognitive deficits of normal ageing (forgetfulness, distractibility, inflexibility and impaired executive functions) involve prefrontal cortex (PFC) dysfunction[1–4]. The PFC guides behaviour and thought using working memory[5], which are essential functions in the information age. Many PFC neurons hold information in working memory through excitatory networks that can maintain persistent neuronal firing in the absence of external stimulation[6]. This fragile process is highly dependent on the neurochemical environment[7]. For example, elevated cyclic-AMP signalling reduces persistent firing by opening HCN and KCNQ potassium channels[8,9]. It is not known if molecular changes associated with normal ageing alter the physiological properties of PFC neurons during working memory, as there have been no *in vivo* recordings, to our knowledge, from PFC neurons of aged monkeys. Here we characterize the first recordings of this kind, revealing a marked loss of PFC persistent firing with advancing age that can be rescued by restoring an optimal neurochemical environment. Recordings showed an age-related decline in the firing rate of DELAY neurons, whereas the firing of CUE neurons remained unchanged with age. The memory-related firing of aged DELAY neurons was partially restored to more youthful levels by inhibiting cAMP signalling, or by blocking HCN or KCNQ channels. These findings reveal the cellular basis of age-related cognitive decline in dorsolateral PFC, and demonstrate that physiological integrity can be rescued by addressing the molecular needs of PFC circuits.



Trends in Cognitive Sciences 14 (2010) 365–375

Opinion

Dynamic Network Connectivity: A new form of neuroplasticity

Amy F.T. Arnsten, Constantinos D. Paspalas, Nao J. Gamo, Yang Yang and Min Wang

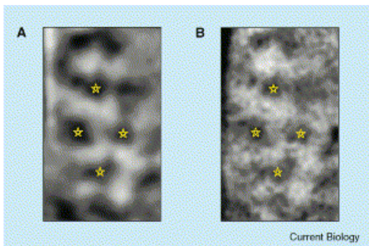
Department Neurobiology, Yale Medical School, 333 Cedar St., New Haven, CT 06510, USA

Prefrontal cortical (PFC) working memory functions depend on pyramidal cell networks that interconnect on dendritic spines. Recent research has revealed that the strength of PFC network connections can be rapidly and reversibly increased or decreased by molecular signaling events within slender, elongated spines: a process we term Dynamic Network Connectivity (DNC). This newly discovered form of neuroplasticity provides great flexibility in mental state, but also confers vulnerability and limits mental capacity. A remarkable number of genetic and/or environmental insults to DNC signaling cascades are associated with cognitive disorders such as schizophrenia and age-related cognitive decline. These insults can dysregulate network connections and erode higher cognitive abilities, leading to symptoms such as forgetfulness, susceptibility to interference, and disorganized thought and behavior.

- Strength of PFC connections are rapidly and reversibly modulated by molecular signaling events (e.g. cAMP gates potassium channels, ACh, NE, DA)
- to accommodate the state of arousal and cognitive or physiological demands
- Link with ageing and disorders

A related problem: spontaneous activity

- Where does it come from?
- How is it maintained? How does it 'move'?
- Are these 'attractor states'?
- Is it structured?
- Why is it there? (any functional advantages?)
- Is it noise?
- Is it the brain trying to 'predict' the input?



evoked (horizontal orientation) spontaneous (one frame)

Arieli et al 1997; Tsodyks et al, 1999; Fiser et al, Nature, 2004

Conclusions

- attractor networks as (main) model of working memory / sustained activity
- effort to provide biologically plausible spiking models, comparable to recordings in PFC
- currently, interesting link with disease and ageing
  -- working memory impairments as instability of attractor states e.g. due to deficits in NMDA, changes in E/I balance.
- spontaneous activity as a similar problem.

Assignment 3 : choice of paper

- computational : has equations in it
- cognitive: talks about some aspect of cognition
- neuroscience: at a level that can be compared with data from the brain

- not a review ! (but read reviews too).

- best if published in a good journal
- recent.
- best if well cited and had important impact on the field.

Assignment 3 : structure of essay

- background: what was known before this paper. (litterature review)
- motivation for this paper / hypothesis
- what the paper shows : describe methods and results in a simple way (description)
- discussion: strengths and weakness of paper, what makes it interesting? important ? how could it be extended? validated? was it followed up by other studies?

Assignment 3 : how I mark

- Background knowledge and scientific maturity
- Description and interpretation
- Discussion, criticism
- Style and writing.

Assignment 3 : common mistakes

- not giving big picture --> focussing immediately on details
- not being critical of the paper's limitations
- not offering more discussion/ extensions/ thinking than presented in the paper