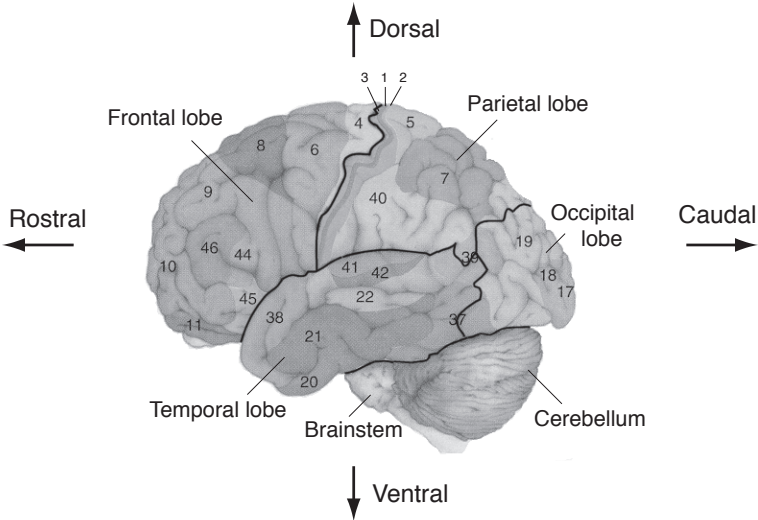


# Neuroinformatics

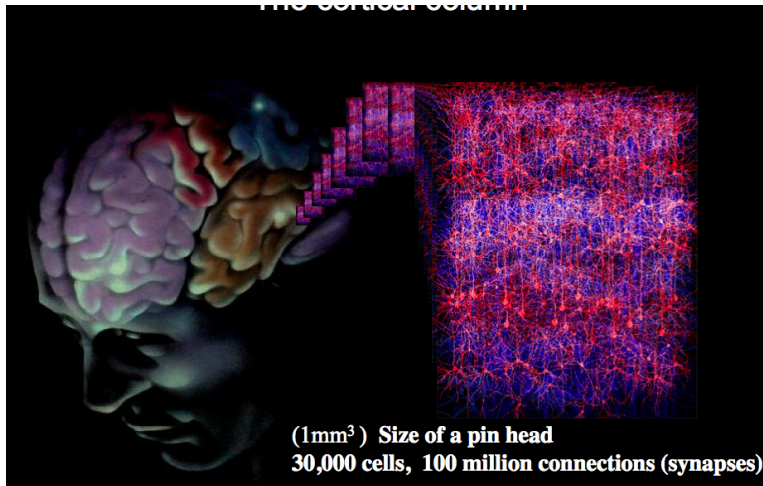
April 10, 2024

Lecture 8: Cortical organization & Random networks

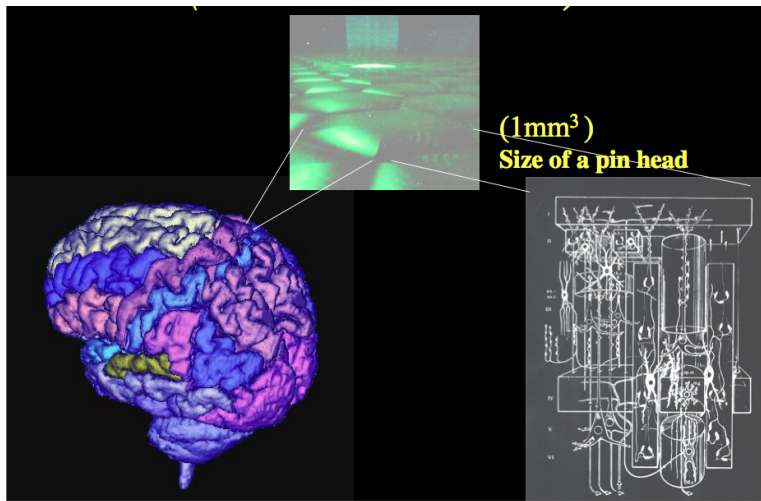
# Brain areas - Brodmann classification



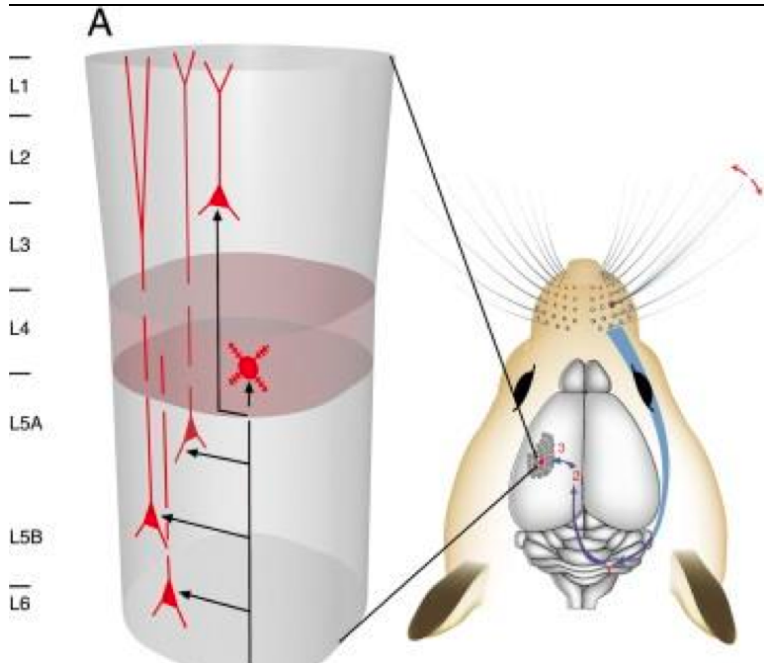
## Cortical column - size



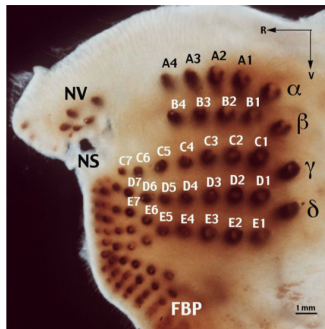
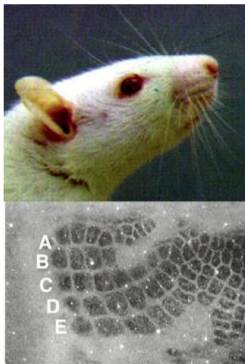
# Cortical column - microcircuit



# Mouse whisker and barrel cortex

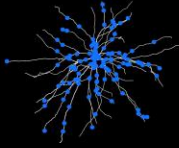


# The excitatory cell types in the cortical column

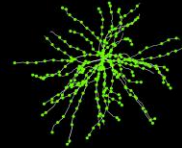


Carol A. Himself's, Peter Land , Sebastian Haidarliu & Ehud Ahissar.

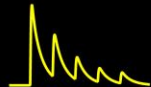
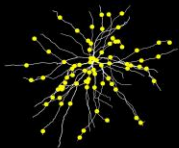
*Synapses formed by  
Smooth Cells*



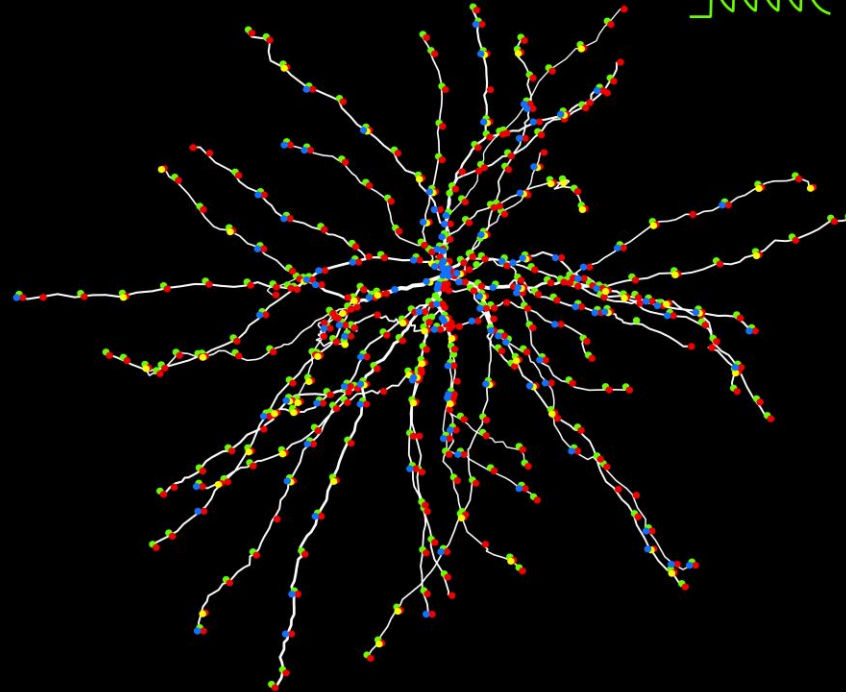
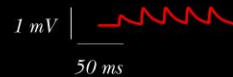
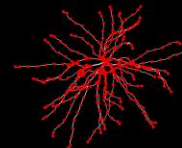
*Synapses formed by  
other Spiny Stellate Cells*



*Synapses formed by  
Thalamic Neurons*



*Synapses formed by  
Layer 6 Pyramidal Neurons*



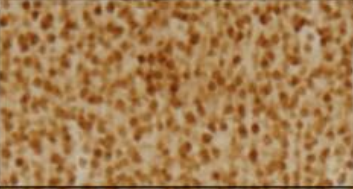

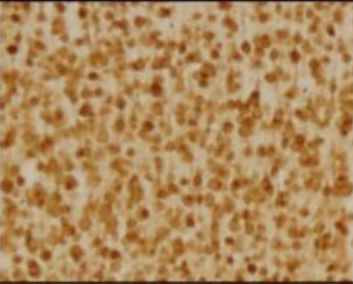
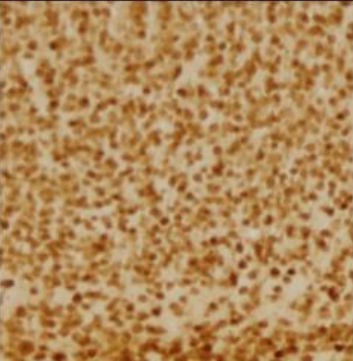


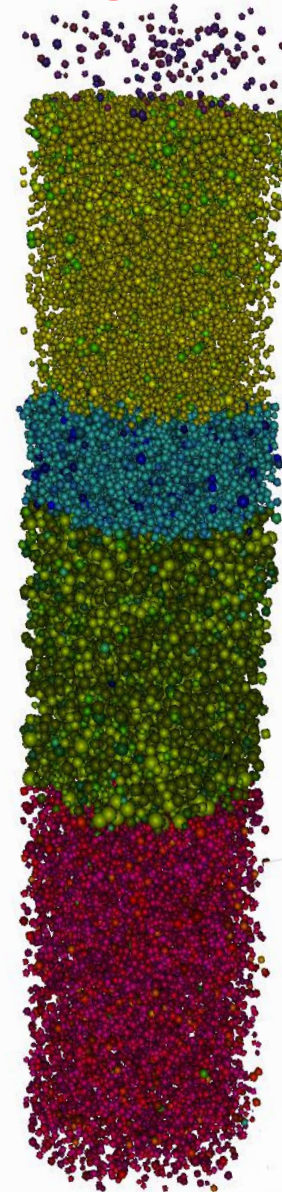
spiny stellate cells  
in cat V1

*Kevan Martin et al*

# The Dimensions of a Cortical Column

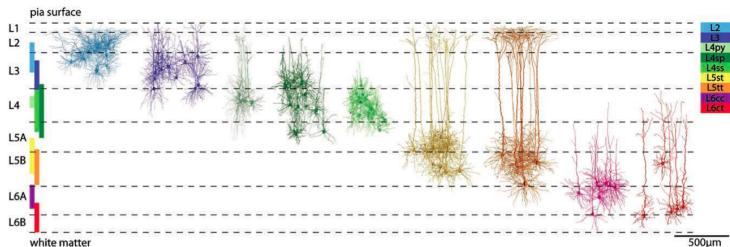
*a local microcircuit, 2000  $\mu\text{m}$  height x 460  $\mu\text{m}$  wide*

Layer I	159 $\mu\text{m}$	
Layer II	143 $\mu\text{m}$	
Layer III	340 $\mu\text{m}$	
Layer IV	182 $\mu\text{m}$	
Layer V	506 $\mu\text{m}$	
Layer VI	675 $\mu\text{m}$	





# Excitatory cell types in the cortical column

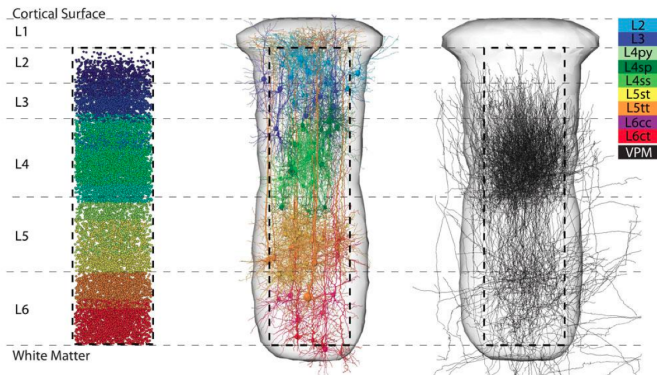


*Sakmann et al.,*

- ▶ Bert Sakmann - Nobel prize in 1991

## Input (axons) from the thalamus

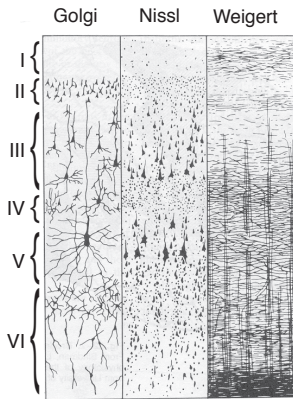
# Input (axons) from thalamus



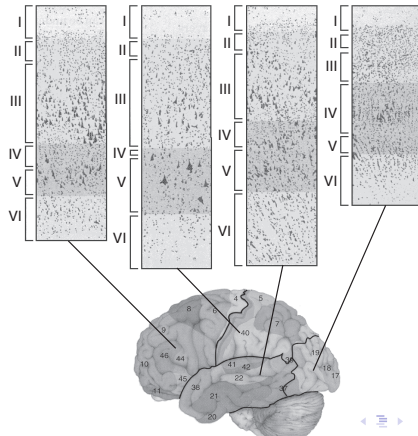
# Cortex column

- ▶ neocortex-no horizontal anatomic segregation, rat column: 6-10.000 neurons, 10 mil synapses
- ▶ 86 % synapses are excitatory, 14 % are inhibitory
- ▶  $\frac{1}{3}$  excitatory synapses: (i) axon from the column, (ii) axons from neighboring columns, (iii) more distant regions, most inhibitory connection from the columns

## A. Different staining techniques



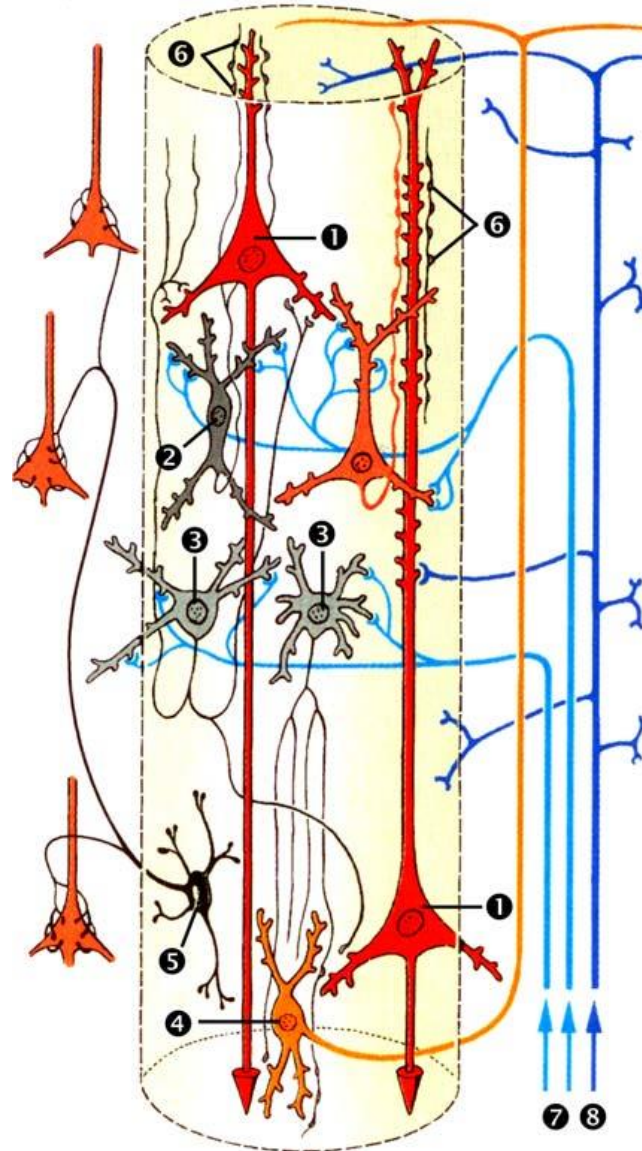
## B. Variation in cortex



## Cortical parameters

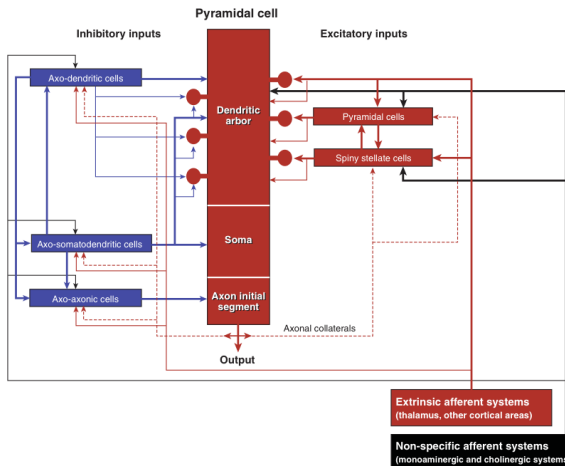
Variable	Value
Neuronal density	40,000/mm <sup>3</sup>
Neuronal composition:	
Pyramidal	75%
Smooth stellate	15%
Spiny stellate	10%
Synaptic density	8 10 <sup>8</sup> /mm <sup>3</sup>
Synapses per neuron	1000–20000
Distribution of synaptic types on pyramidal cell	
Inhibitory synapses	10%
Excitatory synapses from remote sources	45%
Excitatory synapses from local sources	45%
Asynchronous gain (relative synaptic efficiency)	0.003–0.2
Time duration of spike	~ 1 ms
Velocity of spike (myelinated axon of 0.02 mm diameter)	120 m/s
Length of axon	few mm to ~ 1 m
Synaptic cleft	20 nm
Synaptic transmission delay due to diffusion	0.6 ms

# The cortical column, a sophisticated input-output (computational) unit



## Basic cortical microcircuit-general

- ▶ 70-80 % - pyramidal cell,
- ▶ spiny nonpyramidal cells (short-axon cells)
- ▶ 15-30 % Aspiny nonpyramidal cells (short-axon cells without dendritic spines)
- ▶ red: glutamatergic (excitatory) , blue: GABAergic (inhibitory), black: others



## Basic cortical microcircuit-cats and monkeys

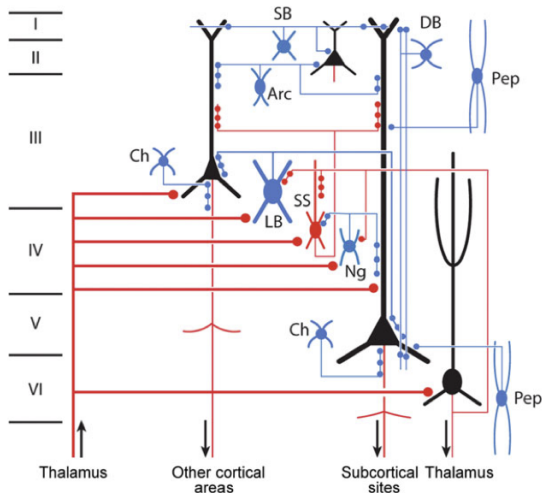
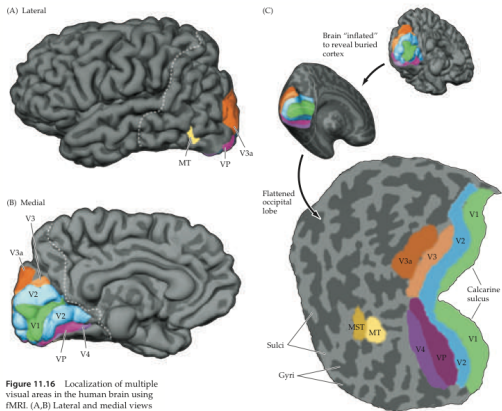


FIGURE 1-2. A schematic circuit based upon the known cortical cells upon which thalamic afferent fibers terminate in cats and monkeys. The GABAergic smooth interneurons (blue) are identified by the names that they have received in these species. Arc, neuron with arciform axon; Ch, chandelier cell; DB, double bouquet cell; LB, large basket cell; Ng, neurogliaform cell; Pep, peptidergic neuron. Excitatory neurons (red) include pyramidal cells of layers II-VI and the spiny stellate cells (SS) of layer IV. (Based on Jones, 2007)





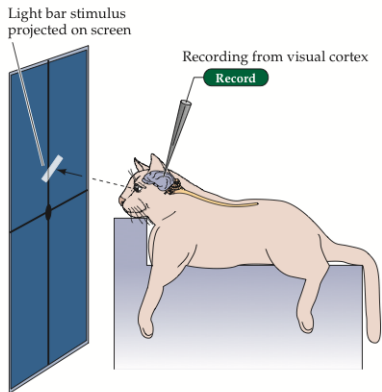
# Example - visual system



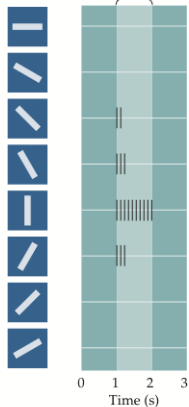
**Figure 11.16** Localization of multiple visual areas in the human brain using fMRI. (A,B) Lateral and medial views (respectively) of the human brain, illus-

# Cat's famous experiment - Hubel, Wiesel

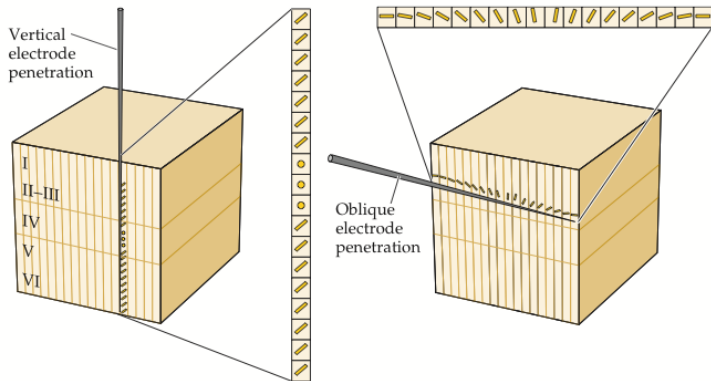
(A) Experimental setup



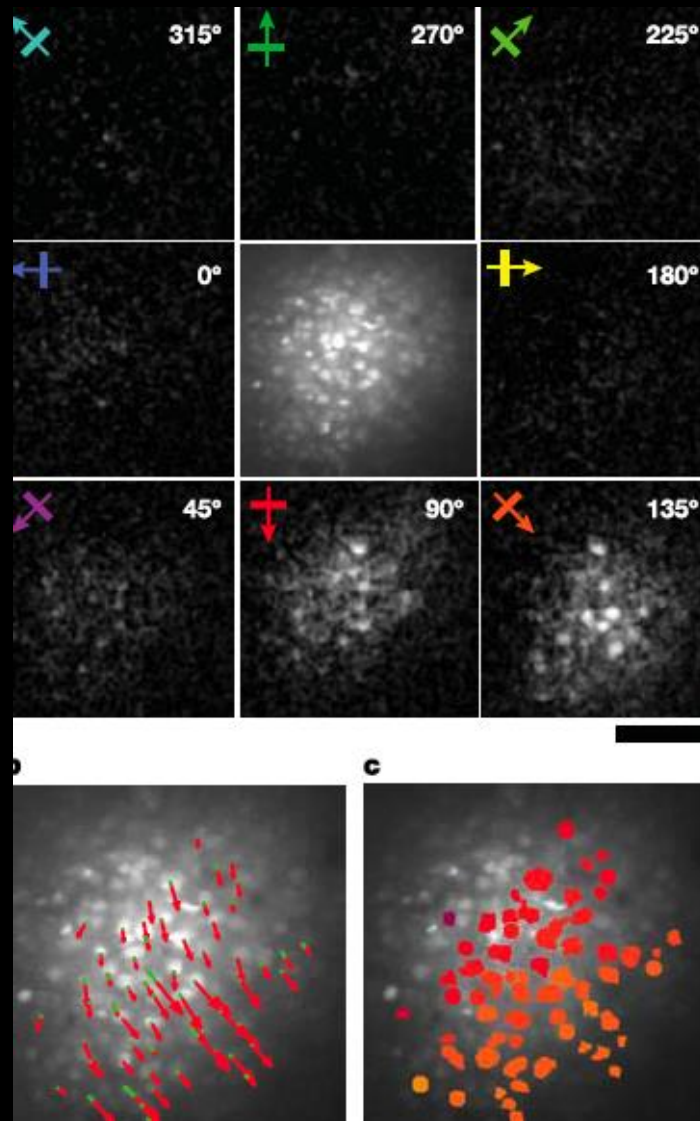
(B) Stimulus orientation



# Columnar organization

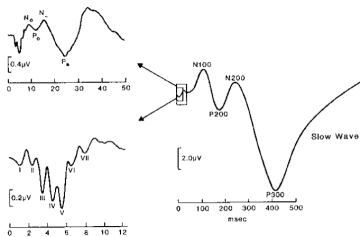
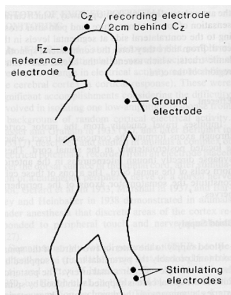


# Functional organization of the cat V1 – columnar organization



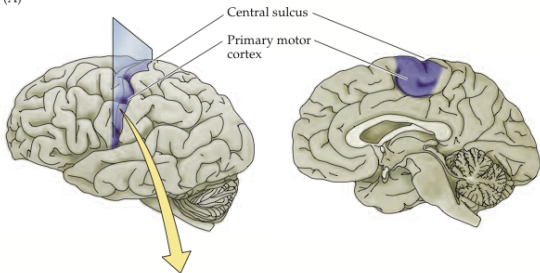
# Evoked potentials - EEG averaging (100-1000)

- ▶ EEG surgery or Macroelectrodes recording (contribution of thousands neuron cells)
- ▶ low amplitudes → low signal-to-noise ration (SNR)
- ▶ averaging is used (noise is random) → signal is time-locked to stimulus → over 100-1000 trials
- ▶ Above example is somatosensory evoked potentials (SSEP), compared to visual EP (VEP)

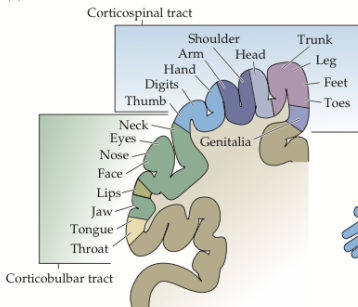


# How do we measure cortical maps - Evoked potentials

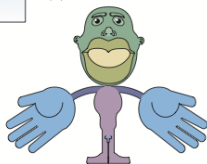
(A)



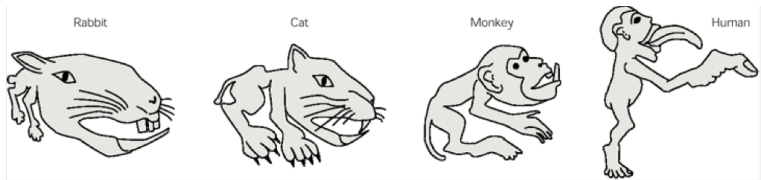
(B)



(C)

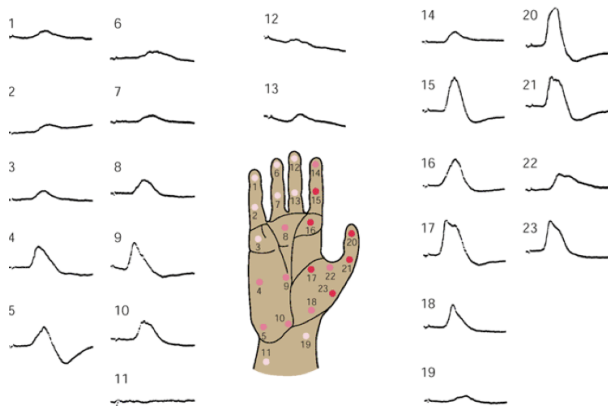


# Adaptive sematosensory information



# Topographical sematosensory maps

Evoked potentials in the somatosensory cortex

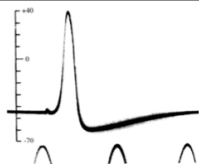
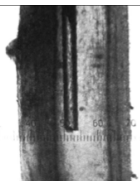




# Simulation - neurons modelling



Sir Alan Lloyd  
Hodgkin



Sir Andrew Fielding  
Huxley

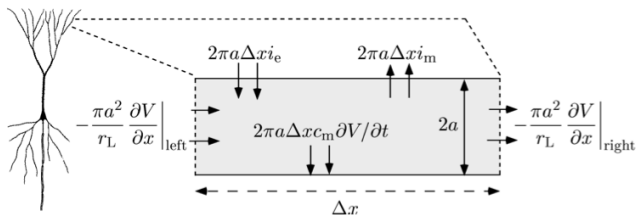
$$I = C_m \dot{V} + g_{Na} h m^3 (V - V_{Na}) + g_K n^4 (V - V_K) + G_L (V - V_L) \quad (1)$$

$$\frac{d}{dt} m = \alpha_m (V) (1 - m) - \beta_m (V) m \quad (2)$$

$$\frac{d}{dt} n = \alpha_n (V) (1 - n) - \beta_n (V) n \quad (3)$$

$$\frac{d}{dt} h = \alpha_h (V) (1 - h) - \beta_h (V) h \quad (4)$$

## Passive cable equation



$$\frac{r_m}{r_i} \frac{\partial^2 V(x,t)}{\partial x^2} - r_m c_m \frac{\partial V(x,t)}{\partial t} - V(x,t) = 0$$

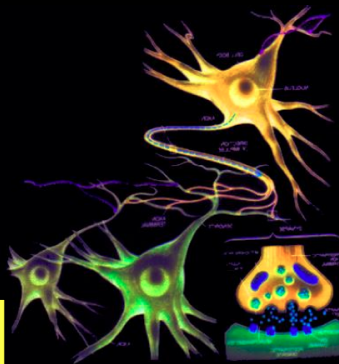
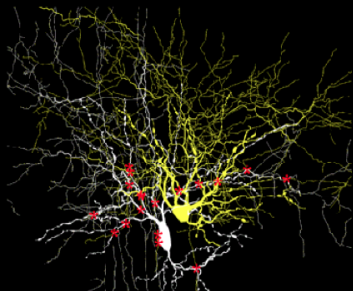
$$\frac{\partial^2 V}{\partial X^2} = \frac{\partial V}{\partial T} + V(X,T)$$

$$X = x/\lambda$$

$$T = t/\tau_m$$

# Learning - plasticity

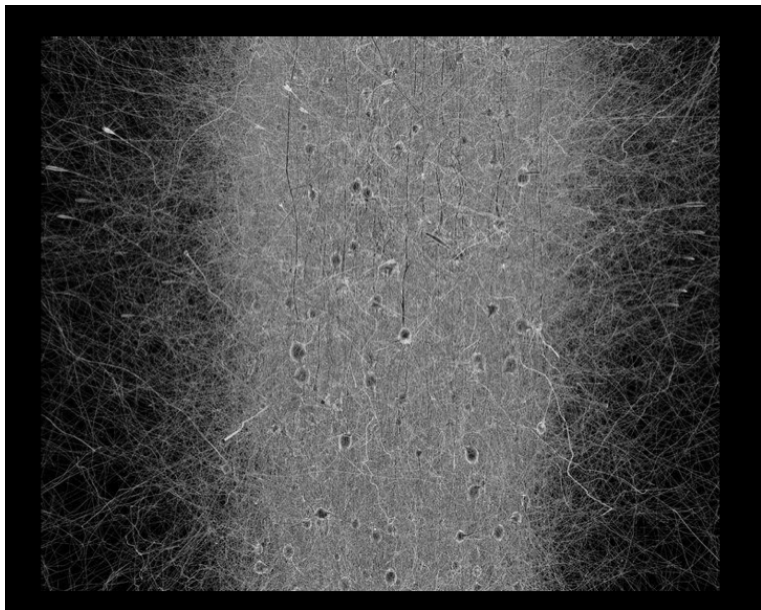
## Modeling synapses (PSP's) as R-C circuits and as **plastic device**



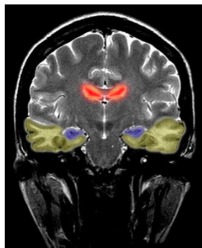
$$\Delta w_+ = A_+ e^{\frac{-(t_{post} - t_{pre})}{\tau_+}} \text{ when } (t_{post} > t_{pre})$$

$$\Delta w_- = A_- e^{\frac{-(t_{post} - t_{pre})}{\tau_-}} \text{ when } (t_{pre} > t_{post})$$

# Blue Brain Project

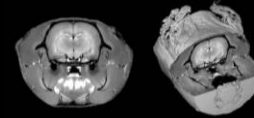
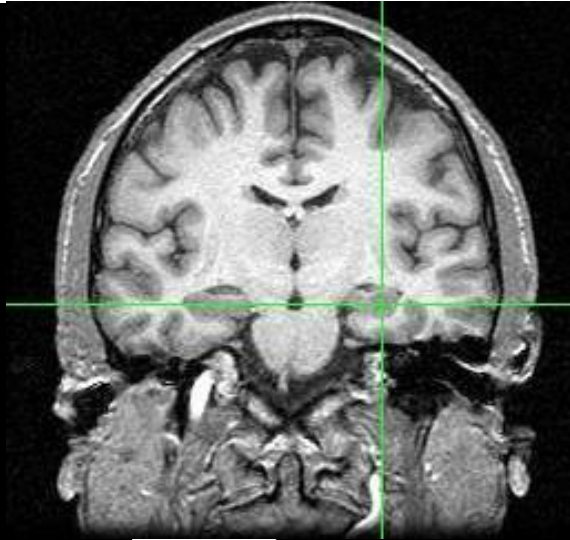


# Towards Human Brain project

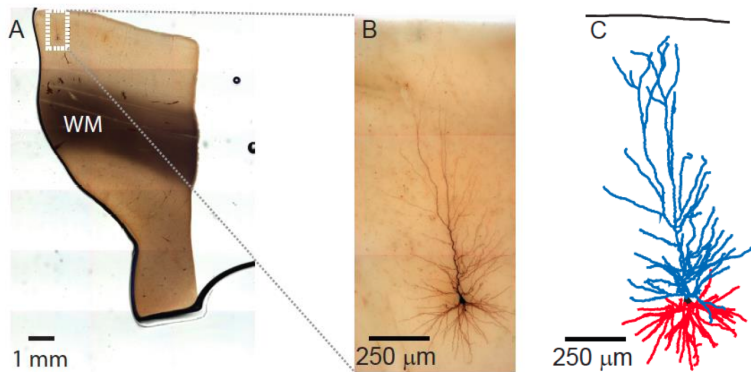


*Hans Baayen, MD  
Neurosurgeon  
VUmc Amsterdam*

# Recording and reconstructing human neurons

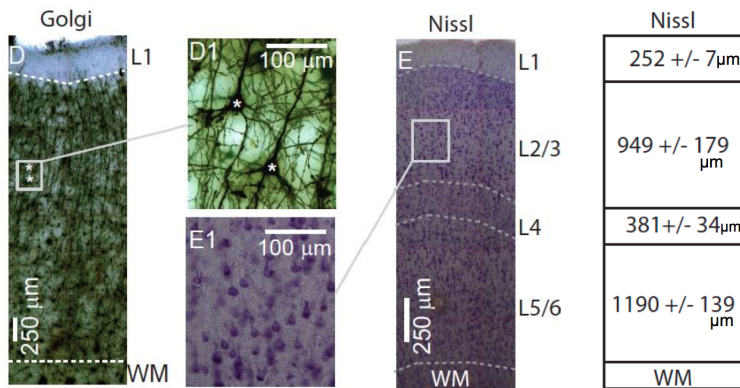


# Recording and reconstructing Human Neurons



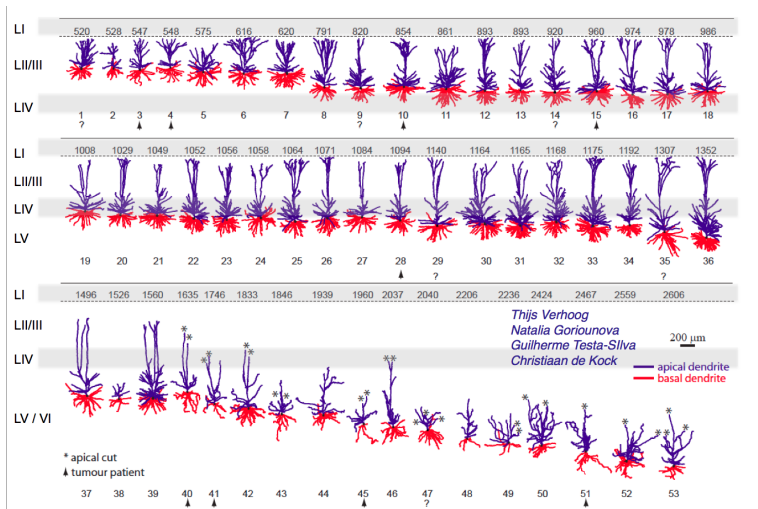
*Thijs Verhoog  
Natalia Goriounova  
Guilherme Testa-Silva  
Christiaan de Kock*

# Histological characterization

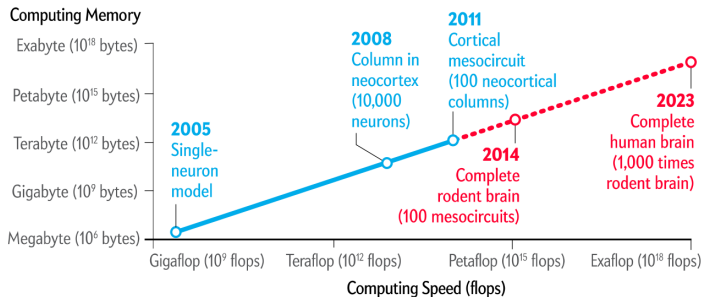




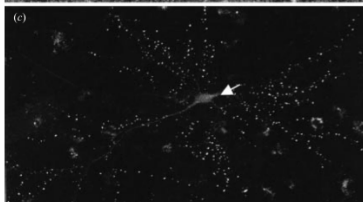
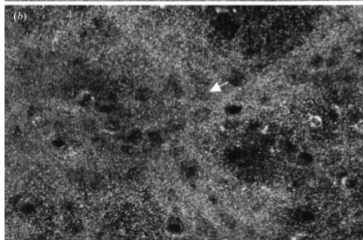
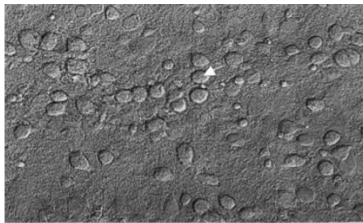
# Human pyramidal neurons across cortical layers



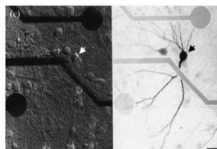
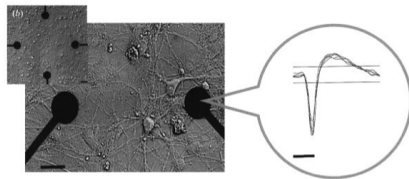
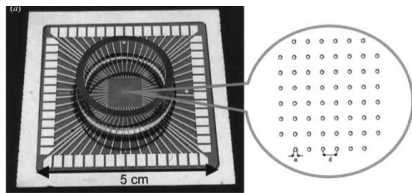
# Expected growth in computational power



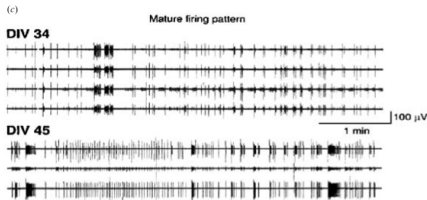
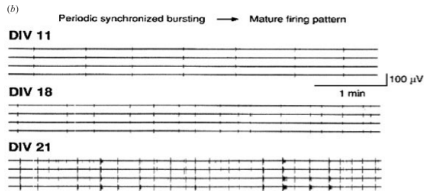
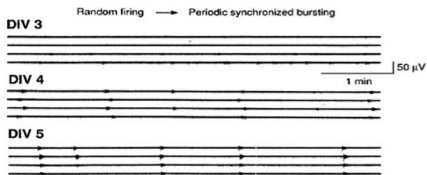
## Random networks - ex vivo



# Random networks - microelectrode array

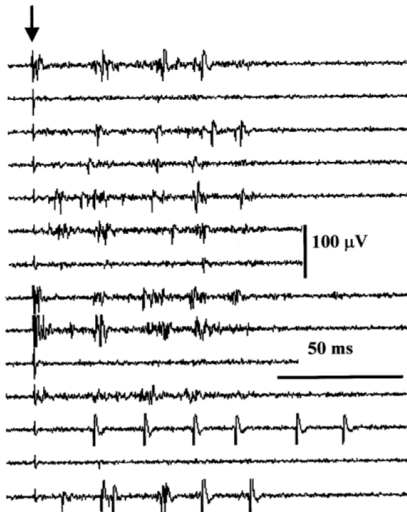


# Random networks - Development changes in neocortical activity

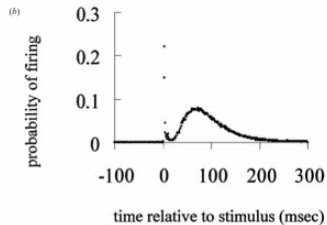
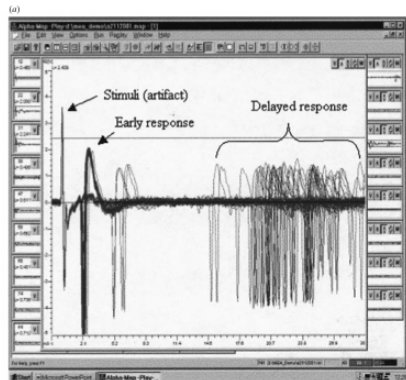


## Random networks - stimulation

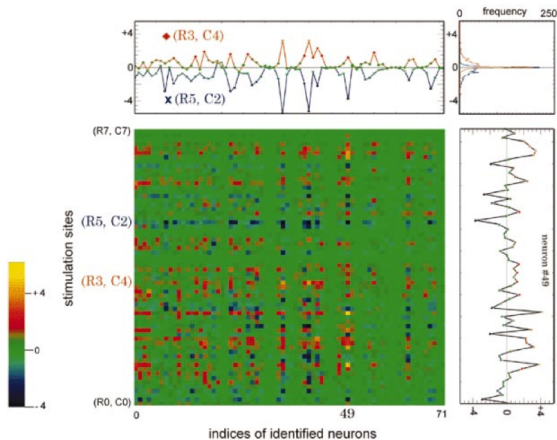
- ▶  $50\mu A$  stimult lasting  $420\mu s$
- ▶ three responses: (i) early componet, (ii) refractory period (iii) late component



# Random networks - response to stimulation: 3 components



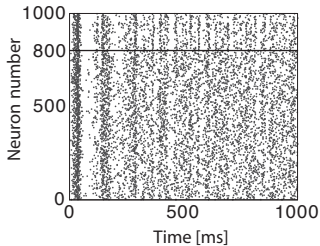
# Random networks - response to stimulation: Hebb's rule



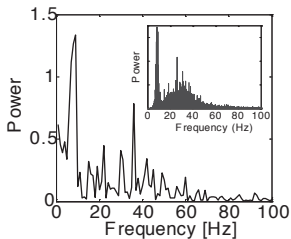


# Random networks with axonal delay

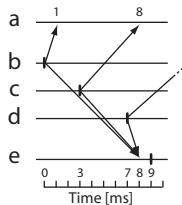
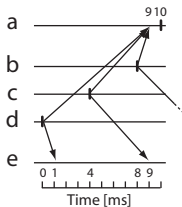
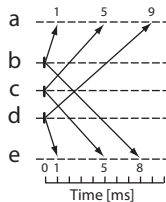
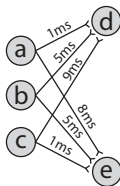
A. Spike trains in random network



B. Power spectrum in random network



C. Spike activation with axonal delay



## Polychronization

- ▶ two groups: i) (d,c,b,a) firing spike time pattern (0,4,8,10) ms / ii) (b,c,d,e) firing spike time pattern (0,3,7,9) ms
- ▶ firing is not synchronous but time-locked, poly → many, chronous → time/clock
- ▶ reproducible time locking pattern
- ▶ spike-timing-dependent plasticity (STDP) can spontaneously organize neurons into such groups
- ▶ main result: the number of coexisting polychronous groups could be far greater than the number of neurons in the network, sometimes even greater than the number of synapses
- ▶ Each neuron is part of many groups, firing with one group at one time and with another group at another time.
- ▶ Simulation on 1000 neurons with STDP and conduction delays
- ▶ mammalian cortex → neuron distribution: excitatory (80%) and inhibitory (20%), 0.1 probability of connection between any two neurons

## STDP rule

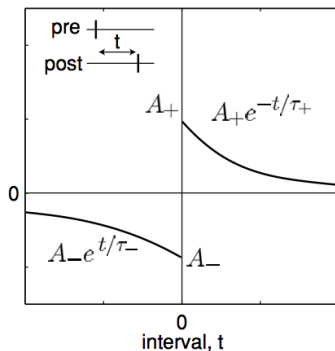
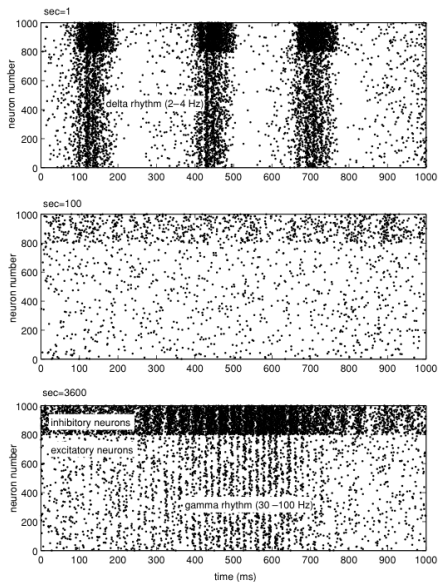
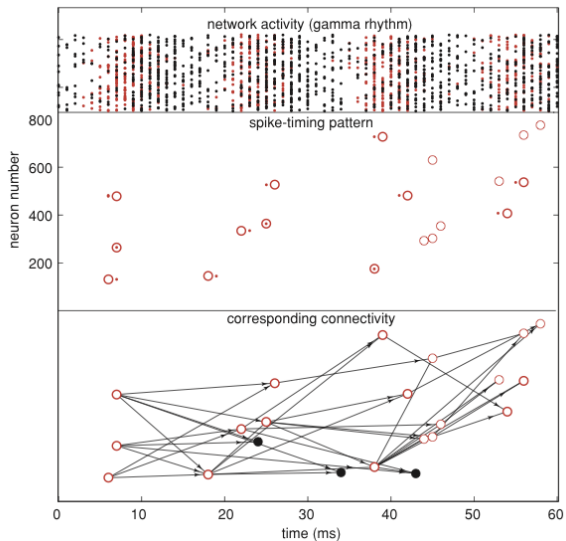


Figure 4: STDP rule (spike-timing-dependent plasticity, or Hebbian temporally asymmetric synaptic plasticity): The weight of synaptic connection from pre- to postsynaptic neuron is increased if the postsynaptic neuron fired after the presynaptic spike, that is, the interspike interval  $t > 0$ . The magnitude of change decreases as  $A_+e^{-t/\tau_+}$ . Reverse order results in a decrease of the synaptic weight with magnitude  $A_-e^{t/\tau_-}$ . Parameters used:  $\tau_+ = \tau_- = 20$  ms,  $A_+ = 0.1$ , and  $A_- = 0.12$ .

# Rhythmic activity of the spiking model



# Polychronous group activation



## Example of polychronous group

- ▶ Although spiking of excitatory neurons looks random and uncorrelated, there are certain persistent spike-timing patterns that emerge and reoccur with millisecond precision
- ▶ Pattern denoted by circles in the middle of the figure repeats itself a few times per hour with  $\pm 1$  ms spike jitter.
- ▶ activation of the group is locked to the gamma oscillation; that is, the first three neurons fire at the first gamma cycle, their spikes travel 10 to 20 ms and arrive at the next four neurons in the next gamma cycle, and so on, resulting in precise stereotypical activity.

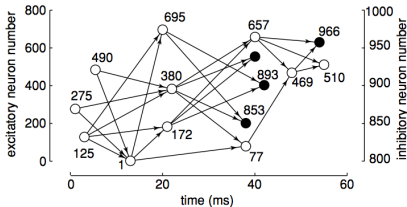
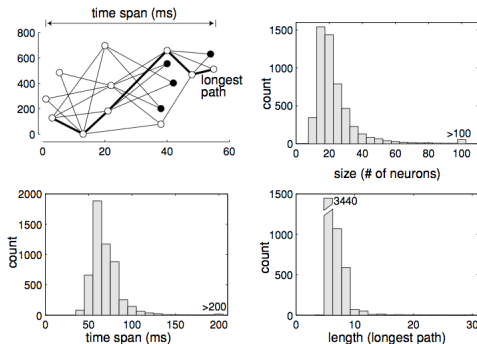


Figure 7: Example of a polychronous group: Firing of neurons (125, 275, 490) with the timing pattern (0, 3, 7) ms results in spikes arriving simultaneously at neuron 1, then at neurons 172, 695, and 380. This multitiming (polychronous) activity propagates farther along the network and terminates at neuron 510.

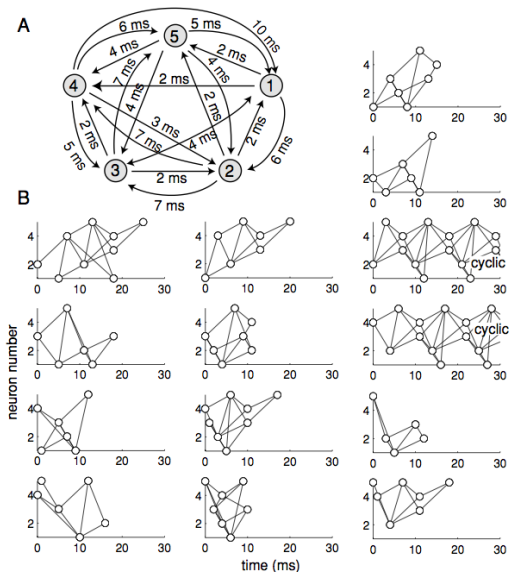
## Group emergence

- ▶ 1000 neurons: 5000 groups, The groups did not exist at the beginning of simulation but appear as a result of STDP acting on random spiking
- ▶ groups constantly appear and disappear; their total number fluctuates between 5000 and 6000
- ▶ a core of 471 groups that appeared and survived the entire duration of 24 hour simulation



# More groups than synapses

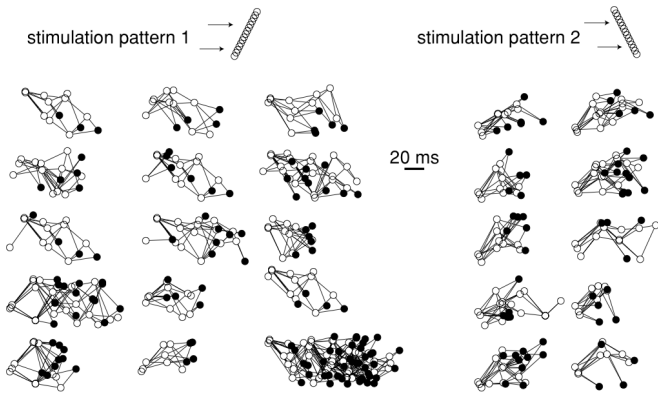
- ▶ 5 neurons: 14 groups, 6 neurons, 42 groups > synapses !





## Representation: Significance of polychronous group?

- ▶ Representation of memories and experience
- ▶ no coherent external input to the system was present, random groups emerge; that is, the network generates random memories not related to any previous experience
- ▶ Stimulation Every second during a 20-minute period, we stimulate 40 neurons, 1, 21, 41, 61, . . . , 781, either with the pattern (1,2,...,40) ms or with the inverse pattern (40,...,2,1) ms
- ▶ after 20 minutes of simulation 25 new groups emerged



## Conclusion

- ▶ minimal model: spiking neurons, axonal conduction delays, and STDP: well-established properties of the real brain
- ▶ Polychronous groups are representations of possible inputs to the network, so that each input selects groups from the repertoire.
- ▶ Learning of a new input consists of selecting and reinforcing an appropriate group (or groups) that resonates with the input, persistent stimuli may create new groups
- ▶ FeedForward: The anatomy of the spiking networks that we consider is not feedforward but reentrant. Thus, the network does not “wait” for stimulus to come but exhibits an autonomous activity.
- ▶ Spiking networks with delays have more groups than neurons. The system has potentially enormous memory capacity and will never run out of groups, which could explain how networks of mere  $10^{11}$  *neurons* (the size of the human neocortex) could have such a diversity of behavior.

```

1  % Created by Eugene M. Izhikevich, February 25, 2003
2  % Excitatory neurons      Inhibitory neurons
3  Ne=800;                   Ni=200;
4  re=rand(Ne,1);           ri=rand(Ni,1);
5  a=[0.02*ones(Ne,1);     0.02+0.08*ri];
6  b=[0.2*ones(Ne,1);      0.25-0.05*ri];
7  c=[-65+15*re.^2;        -65*ones(Ni,1)];
8  d=[8-6*re.^2;           2*ones(Ni,1)];
9  S=[0.5*rand(Ne+Ni,Ne), -rand(Ne+Ni,Ni)];
10
11 v=-65*ones(Ne+Ni,1);    % Initial values of v
12 u=b.*v;                 % Initial values of u
13 firings=[];             % spike timings
14
15 for t=1:1000             % simulation of 1000 ms
16     I=[5*randn(Ne,1);2*randn(Ni,1)]; % thalamic input
17     fired=find(v>=30); % indices of spikes
18     if ~isempty(fired)
19         firings=[firings; t+0*fired, fired];
20         v(fired)=c(fired);
21         u(fired)=u(fired)+d(fired);
22         I=I+sum(S(:,fired),2);
23     end;
24     v=v+0.5*(0.04*v.^2+5*v+140-u+I);
25     v=v+0.5*(0.04*v.^2+5*v+140-u+I);
26     u=u+a.*(b.*v-u);
27 end;
28 plot(firings(:,1),firings(:,2),'.');

```

## Further Readings

Edward L. White (1989) **Cortical circuits**, Birkhäuser

Moshe Abeles (1991) **Corticonics: Neural circuits of the cerebral cortex**, Cambridge University Press