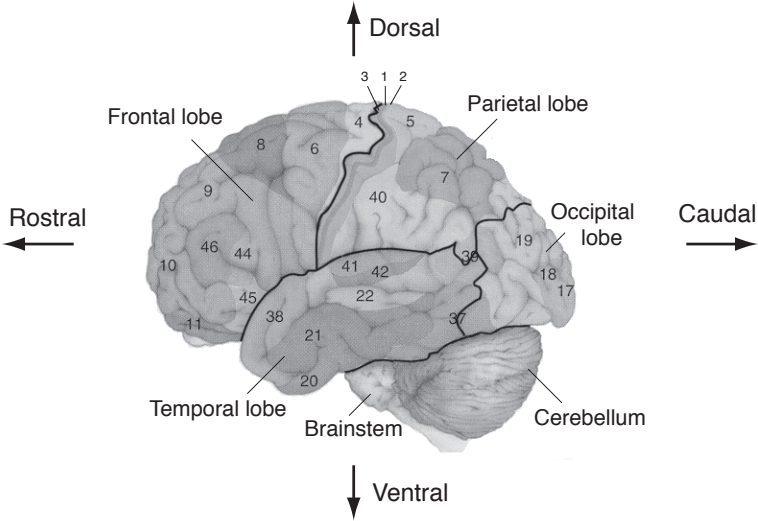


# Neuroinformatics

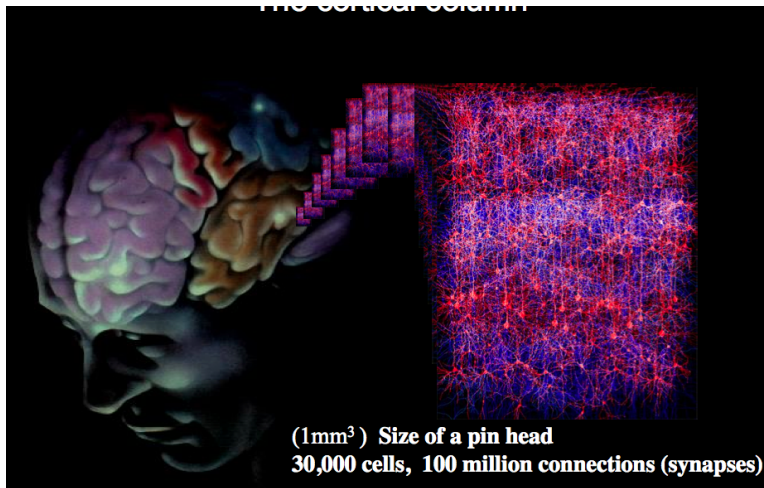
April 2, 2014

Lecture 7: Cortical organization & Random networks

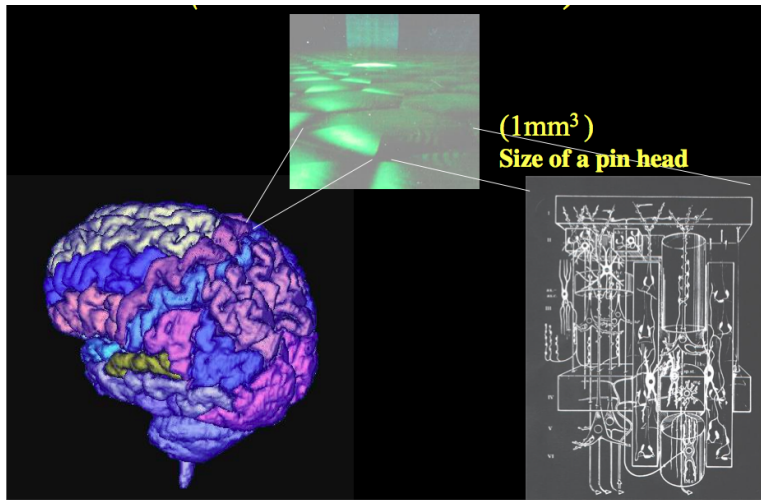
# Brain areas - Brodmann classification



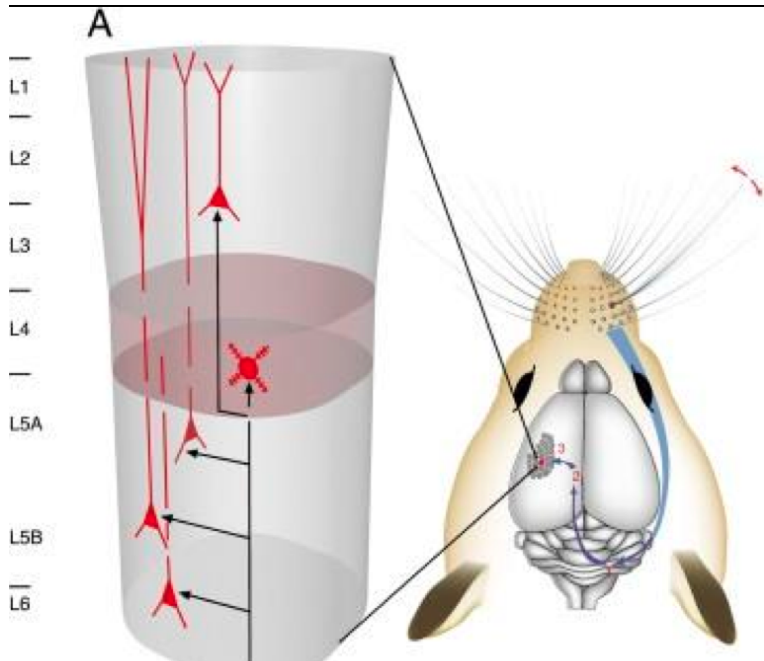
## Cortical column - size



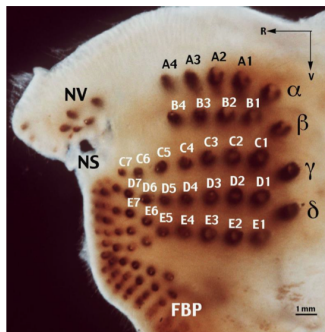
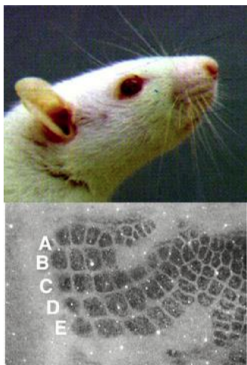
# Cortical column - microcircuit



# Mouse whisker and barrel cortex

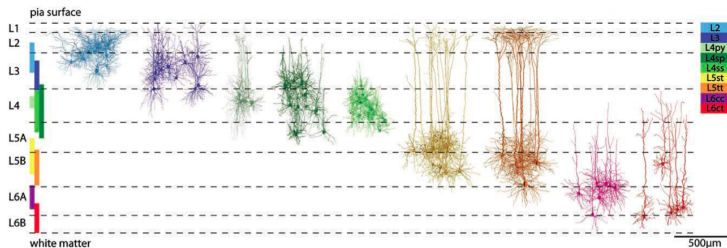


# The excitatory cell types in the cortical column



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

# Excitatory cell types in the cortical column

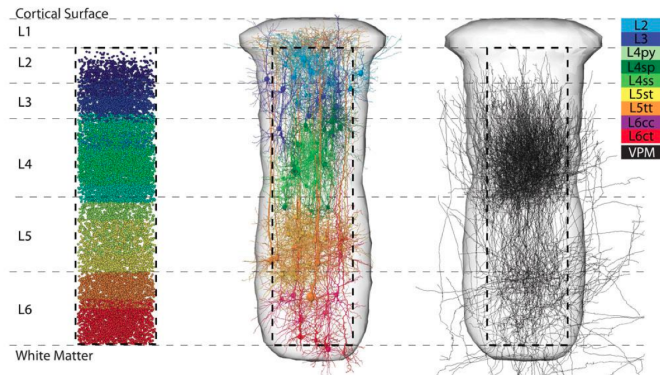


*Sakmann et al.,*

- ▶ Bert Sakmann - Nobel prize in 1991

## Input (axons) from the thalamus

# Input (axons) from thalamus

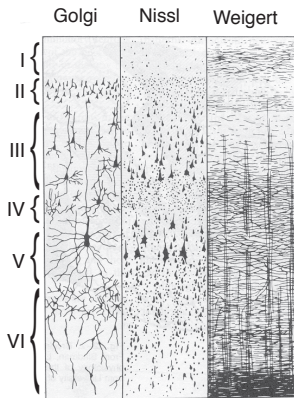




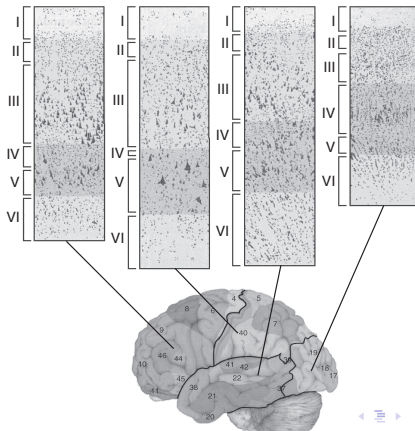
# Cortex column

- ▶ 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

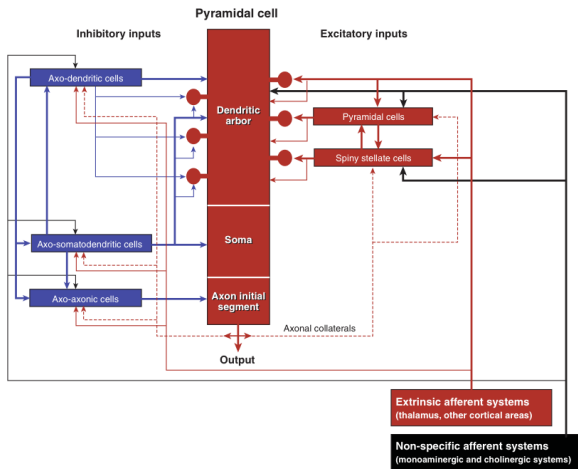


## Cortical parameters

| 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                             |

## 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

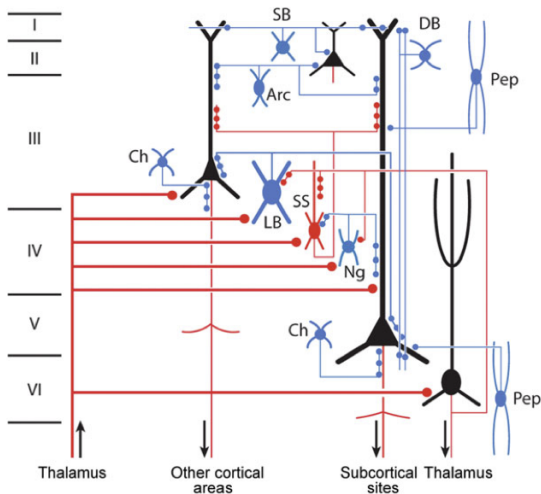
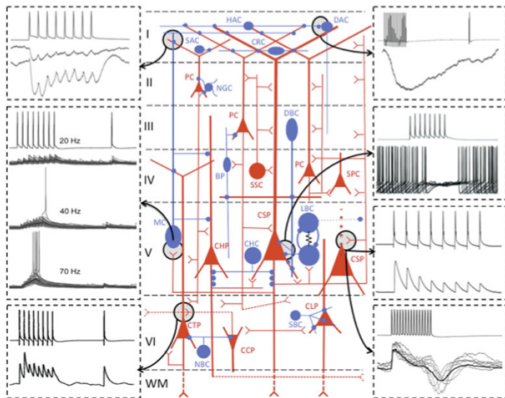


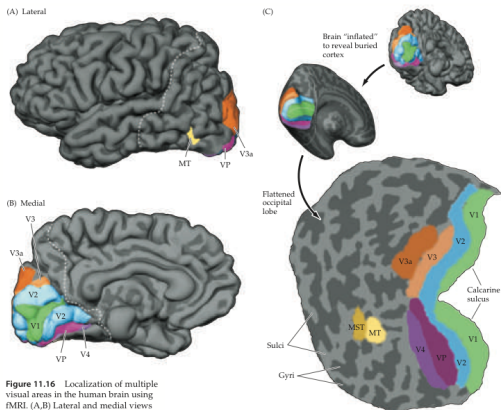
FIGURE 1-2. A schematic circuit based upon the known cortical cells upon which thalamic afferent fibers terminate in cats and monkeys. The GABAergic smooth interneurons (blue) are identified by the names that they have received in these species. Arc, neuron with arciform axon; Ch, chandelier cell; DB, 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)

# Presynaptic and postsynaptic AP



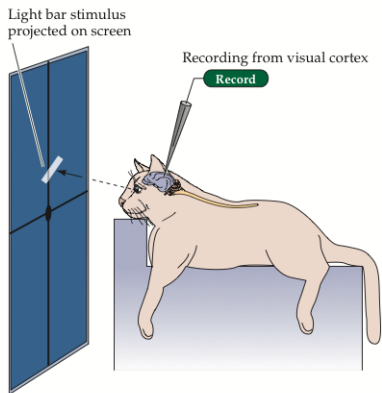
**FIGURE 3-1.** Simplified schematic representation of the neocortical microcircuitry. Red indicates excitatory neurons, dendrites, and axons; blue indicates inhibitory neurons, dendrites, and axons. Inhibitory synapses are marked in blue dots, and excitatory synapses are marked in red forks. From the top left and down, the insert illustrates a synaptic response from an MC onto a PC, a PC onto an MC, and a CCP onto a CTP. From top right and down, the inserts illustrate synaptic responses from an HAC on a VAC, an LBC on a PC, a PC response on a PC, and a disynaptic PC response on a PC via an MC. In all cases the presynaptic action potentials are above and the postsynaptic responses are below. Layers are indicated in roman numerals. Axons projecting beyond the neocortical dimensions are indicated by dotted lines. For the PCs, axons are thin lines relative to the dendrites; for the inhibitory neurons, only axons are schematized. Black arrows from grayed background circles indicate the synaptic locations for the inserted illustrated responses. BP, bipolar cell; CCP, cortico-cortical pyramid; CHC, chandelier cell; CHP, cortico-hemispheric pyramid; CLP, cortico-claustral pyramid; CRC, Cajal-Retzius cell; CSP, cortico-spinal pyramidal; CTP, cortico-thalamic pyramid; DBC, double bouquet cell; HAC, horizontal axon cell; LBC, large basket cell; MC, Martinotti cell; NBC, nest basket cell; NGC, neurogliaform cell; PC, pyramidal cell; SBC, small basket cell; SPC, star pyramidal cell; SSC, spiny stellate cell; DAC, descending axon cell; SAC, short axon cell; WM, white matter.

# Example - visual system

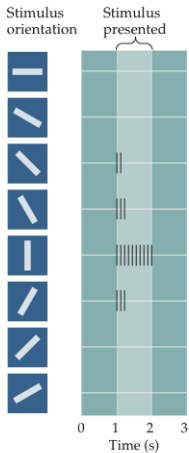


# Cat's famous experiment - Hubel, Wiesel

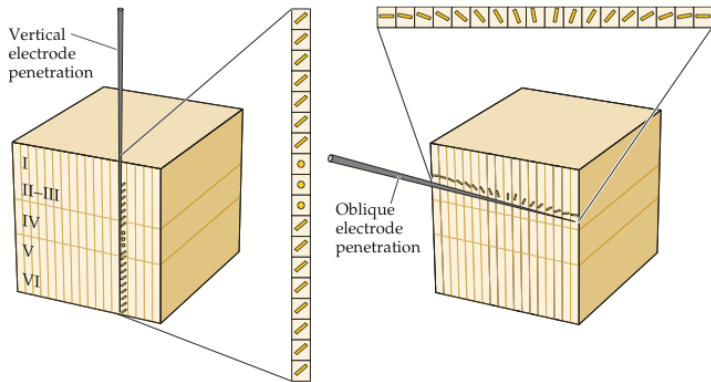
(A) Experimental setup



(B) Stimulus orientation



# Columnar organization

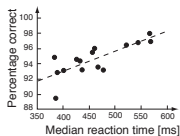




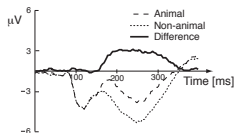
## Rapid transmission in brain

- ▶ Object recognition is fast - 20 ms: experiments of Simon Thorpe
- ▶ Presence of animals in visual scenes presented by short time - 20ms → subject released button when animal was present
- ▶ Evoked potentials by surface EEG → frontal cortex indicates correct answer after 150 ms!
- ▶ Each neuron in hierarchical level process and pass on information of the order of 10-20ms!

A. Recognition performance

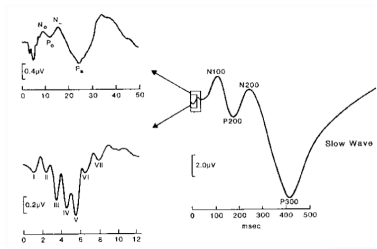
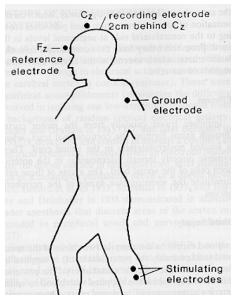


B. Event-related potential



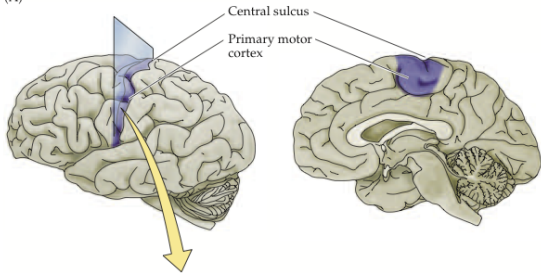
## Evoked potentials - EEG averaging (100-1000)

- ▶ 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)

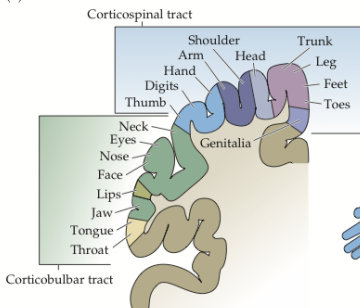


# How do we measure cortical maps - Evoked potentials

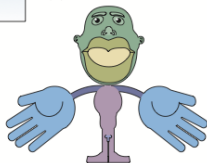
(A)



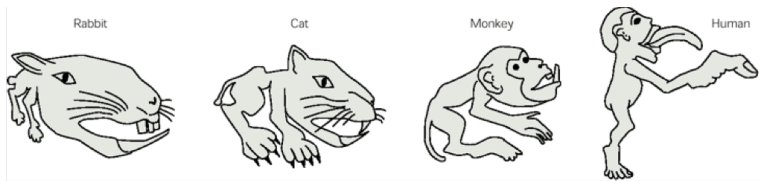
(B)



(C)

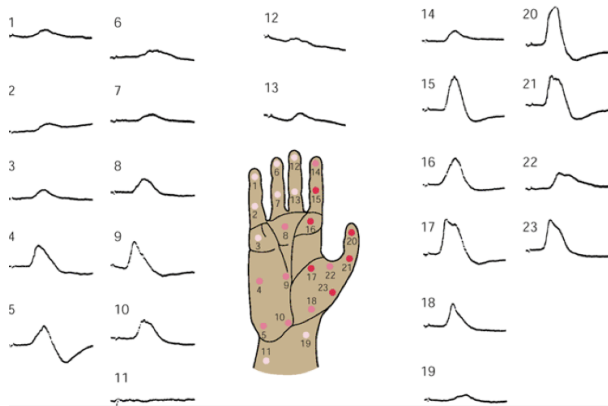


# Adaptive sematosensory information



# Topographical somatosensory maps

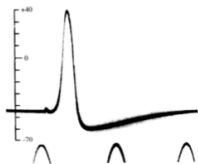
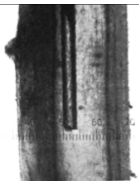
Evoked potentials in the somatosensory cortex



# Simulation - neurons modelling



Sir Alan Lloyd  
Hodgkin



Sir Andrew Fielding  
Huxley

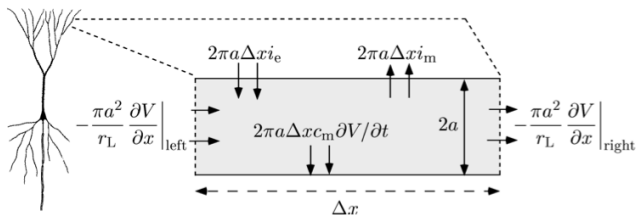
$$I = C_m \dot{V} + g_{Na} h m^3 (V - V_{Na}) + g_K n^4 (V - V_K) + G_L (V - V_L) \quad (1)$$

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

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

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

## Passive cable equation



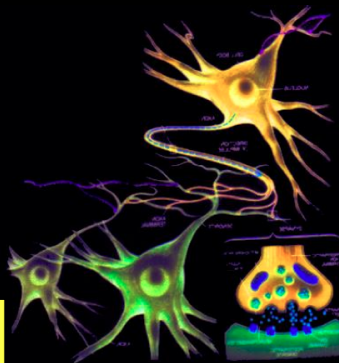
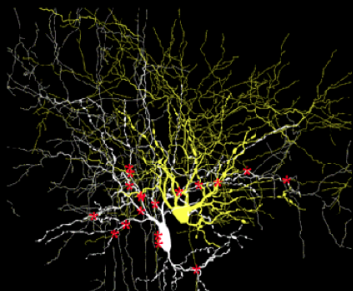
$$\frac{r_m}{r_i} \frac{\partial^2 V(x,t)}{\partial x^2} - r_m c_m \frac{\partial V(x,t)}{\partial t} - V(x,t) = 0$$

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

$$X = x/\lambda$$

$$T = t/\tau_m$$

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

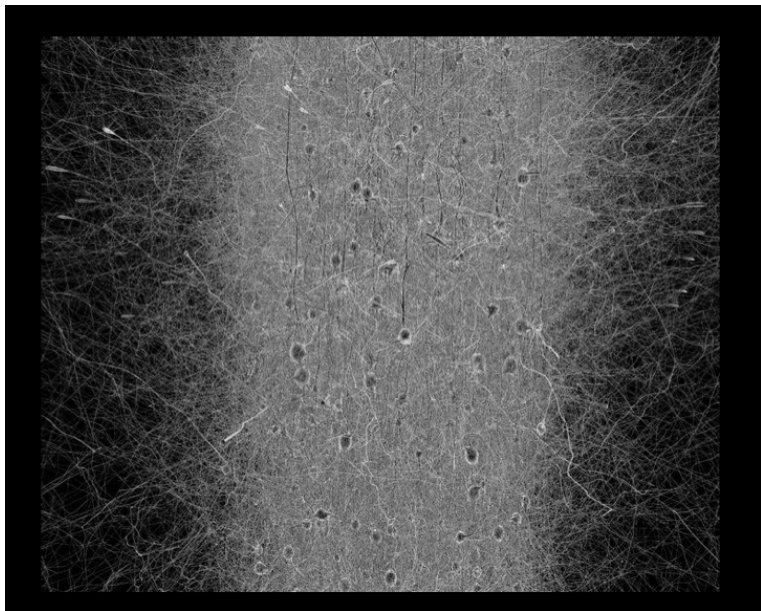


$$\Delta w_+ = A_+ e^{\frac{-(t_{post} - t_{pre})}{\tau_+}} \text{ when } (t_{post} > t_{pre})$$

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

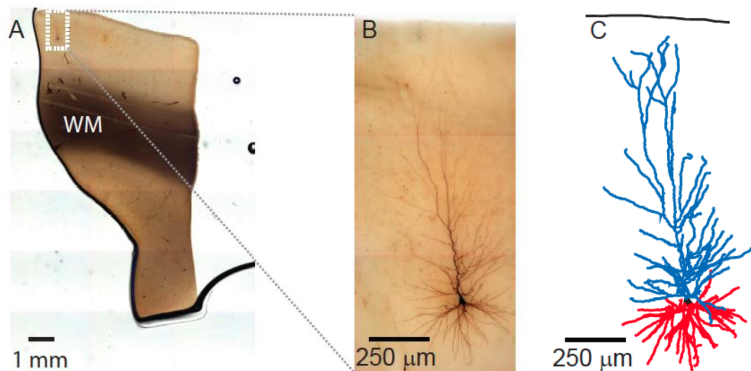


# Blue Brain Project



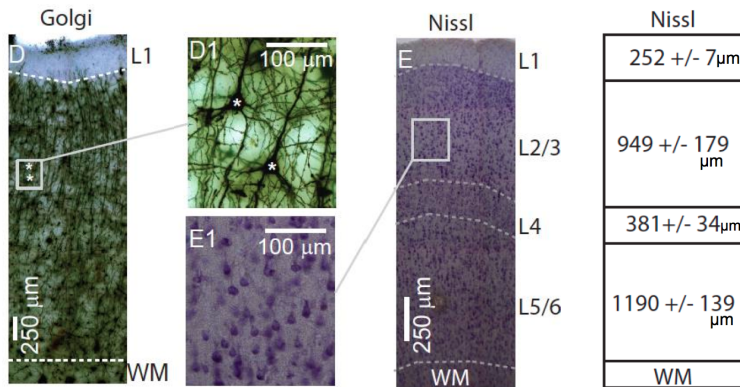


# Recording and reconstructing Human Neurons

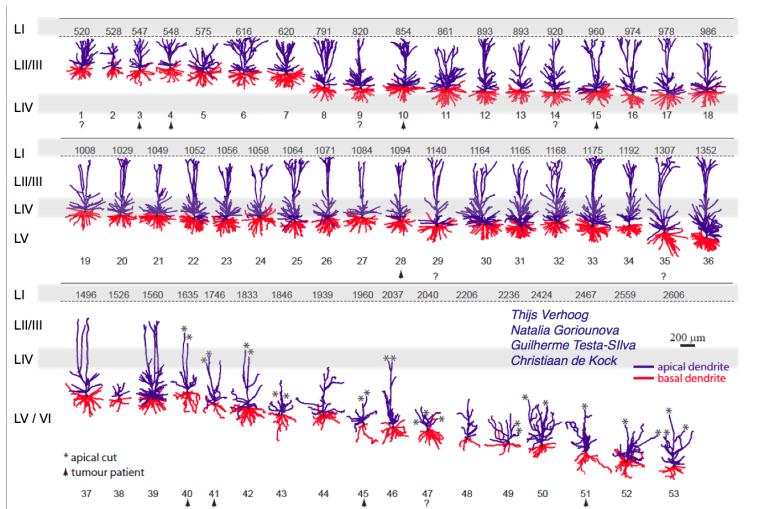


*Thijs Verhoog  
Natalia Goriounova  
Guilherme Testa-Silva  
Christiaan de Kock*

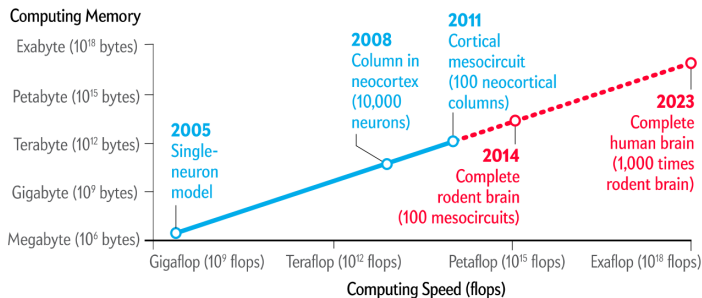
# Histological characterization



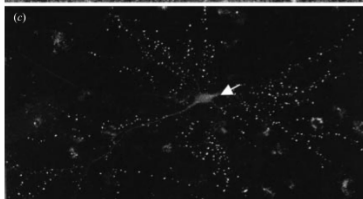
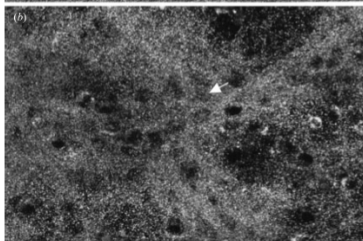
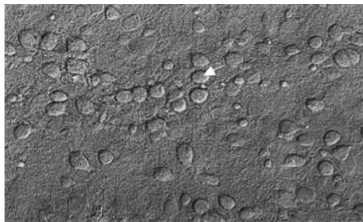
# Human pyramidal neurons across cortical layers



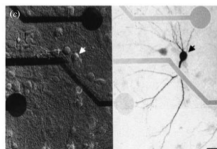
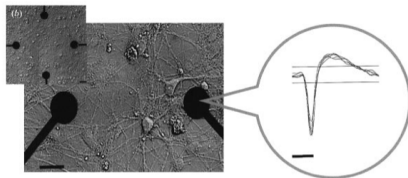
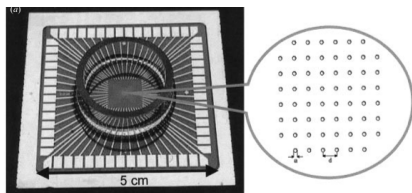
# Expected growth in computational power



## Random networks - ex vivo

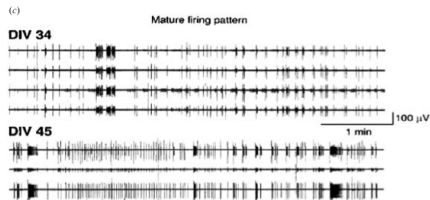
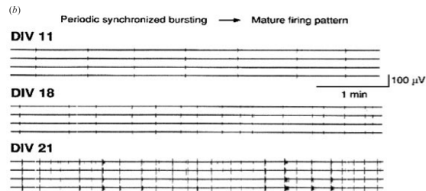
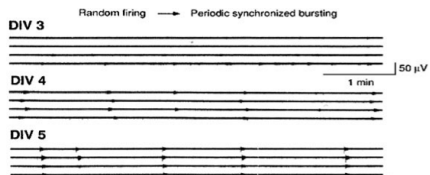


# Random networks - microelectrode array



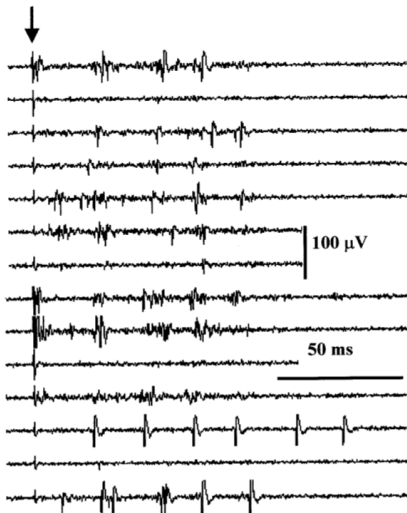


# Random networks - Development changes in neocortical activity

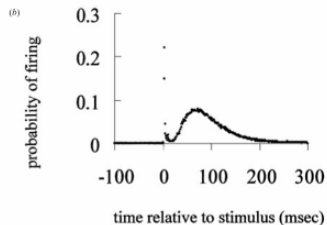
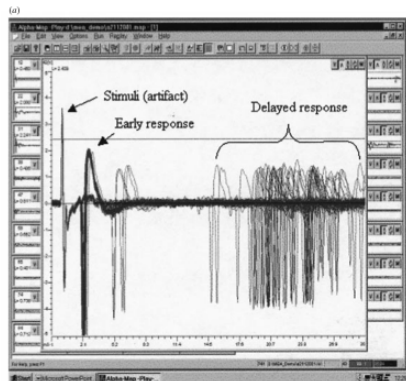


## Random networks - stimulation

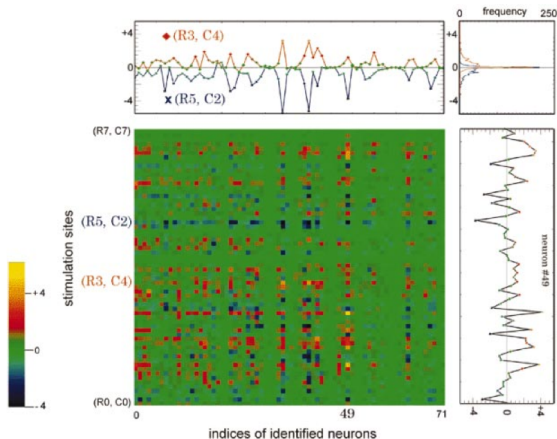
- ▶  $50\mu A$  stimult lasting  $420\mu s$
- ▶ three responses: (i) early componet, (ii) refractory period (iii) late component



# Random networks - response to stimulation: 3 components

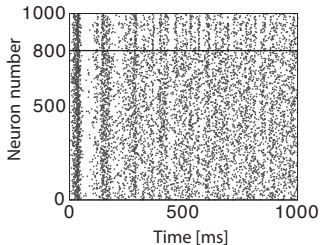


# Random networks - response to stimulation: Hebb's rule

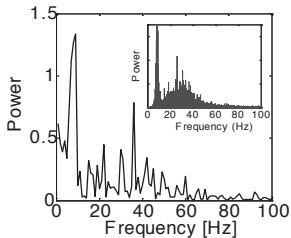


# Random networks with axonal delay

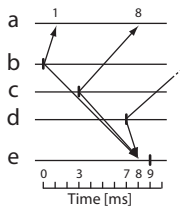
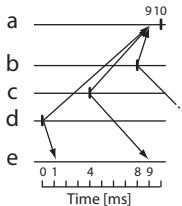
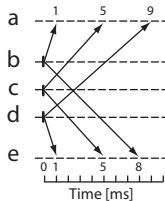
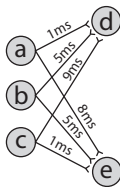
A. Spike trains in random network



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

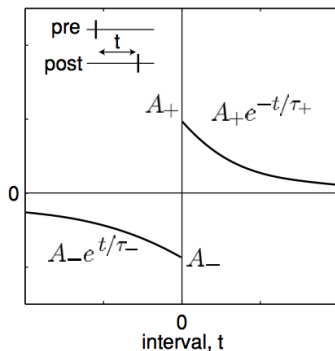
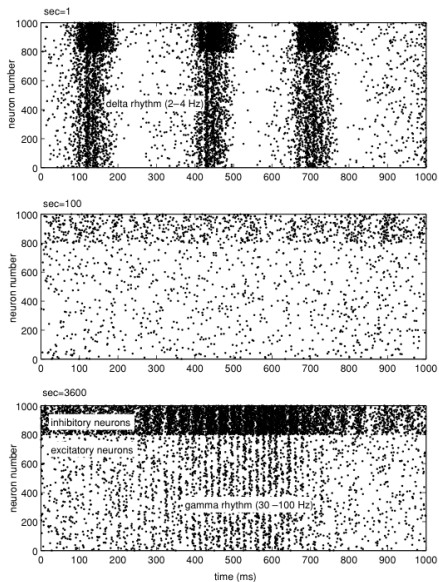


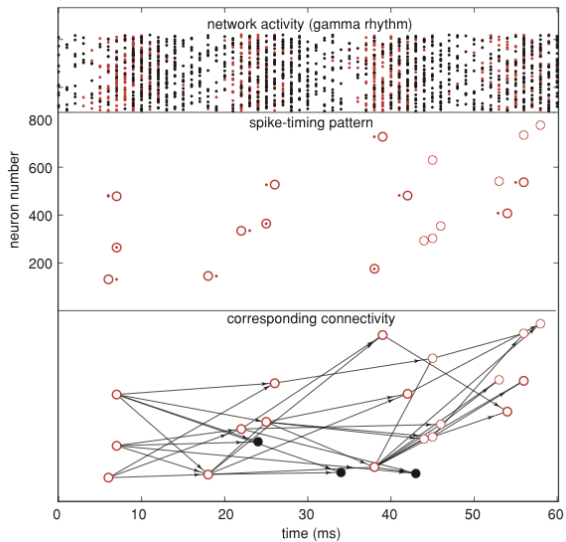
Figure 4: STDP rule (spike-timing-dependent plasticity, or Hebbian temporally asymmetric synaptic plasticity): The weight of synaptic connection from pre- to postsynaptic neuron is increased if the postneuron fired after the presynaptic spike, that is, the interspike interval  $t > 0$ . The magnitude 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 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.

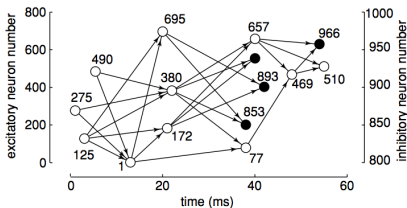
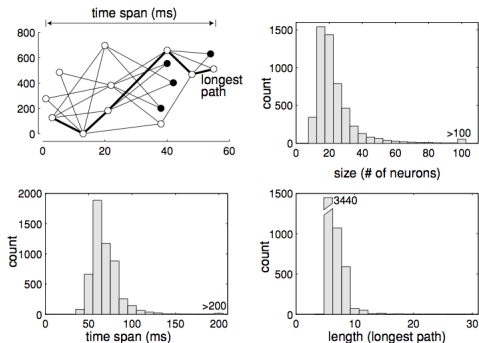


Figure 7: Example of a polychronous group: Firing of neurons (125, 275, 490) with the timing pattern (0, 3, 7) ms results in spikes arriving simultaneously at neuron 1, then at neurons 172, 695, and 380. This multitiming (polychronous) activity propagates farther along the network and terminates at neuron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

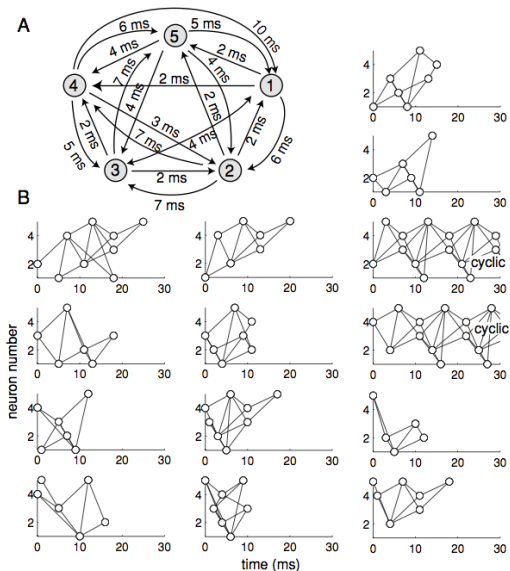
## Group emergence

- ▶ 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 !





## 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