Synapses, Neurons and Brain Lecture 7-10

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WEEK 7: Cortical Networks - Out of the Blue Project

Mega Projects for the Brain

billions of dollars of new projects for the brain

1. allen institute

   Mouse/Human brain atlas – recently new focus on the mouse visual system

2. Jenelia fram

   Howard Hughes Medical Institute for connecting network level anatomy and physiology to s specific behavior

3. EU human brain project

   ICT-based brain research platform, integrating data and knowledge from different disciplines, and catalyzing world-wide effort to achieve understanding of the brain, propose new treatments for brain diseases and new brain-like computing technologies

4. president obama's brain activity map institute

Creating revolutionary tools to measure/stimulate millions or even billions or neurons simultaneously

> mapping spike in single cell levels
>
> Understanding coding and incoding informations

The Blue Project - The Start

> **The aim of Blue Brain is to establish simulation neuroscience as a complementary approach alongside experimental, theoretical and clinical neuroscience to understanding the brain**, by building the world's first biologically detailed digital reconstructions and simulations of the mouse brain.

from recording only one cell to simulating multiple cells and generating spikes

like "reverse engineering"

The Blue-Gene IBM Computer (10000 processors, 0.05 Peta Flops/sec)

> use it to simulate the brain

Data-basing the brain Major New anatomical methods "Brainbow"

> visualizing in the synaptic level "anatomy jungle"
>
> and the cells will intrinsically have colors

Connectomics

> giving the full detailed network at the level of synapse and connection (with colors but using EM and artificial dyes or colors in order to stain each cell instead of "brainbow")
>
> reconstruct very small piece of cortext (eg. 20 micrometers) using em slices

with all this data, you can now connect structure to functions

> how does this function implemented in

Blue Brain's Scientific Milestone

> ~2007
>
> > **The automatic computer reconstruction of the electrical behavior of any neuron recorded in the brain.**
>
> ~2015
>
> > **An algorithm that can recreate the connectome of a microcircuit of neurons.** This algorithm allowed Blue Brain to capture the way that neurons are connected to each other in the brain and the 3D location of millions of synapses in the modelled microcircuit.
>
> ~2015
>
> > **Reconstruction and Simulation of Neocortical Microcircuitry**

> To bring the different types of neurons and synapses together as a microcircuit, which was demonstrated in the form of the most biologically realistic copy to date of a neocortical column – the “CPU” of the neocortex.

~2015

> **The validation and exploration of the emergent dynamics of the microcircuit in milestone three.** The model gave rise to a whole range of states, solely by integrating measurements. It also provides new insights into the connectivity structure of cortical circuits and provided the key topological features of the neocortical microcircuit.

~2019

> **Blue Brain solved a decade old problem of mathematically growing the shape of neurons (their morphology).**
>
> > this can never yield enough neurons to build whole brain model. This milestone is also important because it provides us with a new way, in the future, to build neurons by reading their genetic information. For example, in the future, we may be able to study the effect of genetic changes in the brain in terms of how they affect the shapes of neurons.

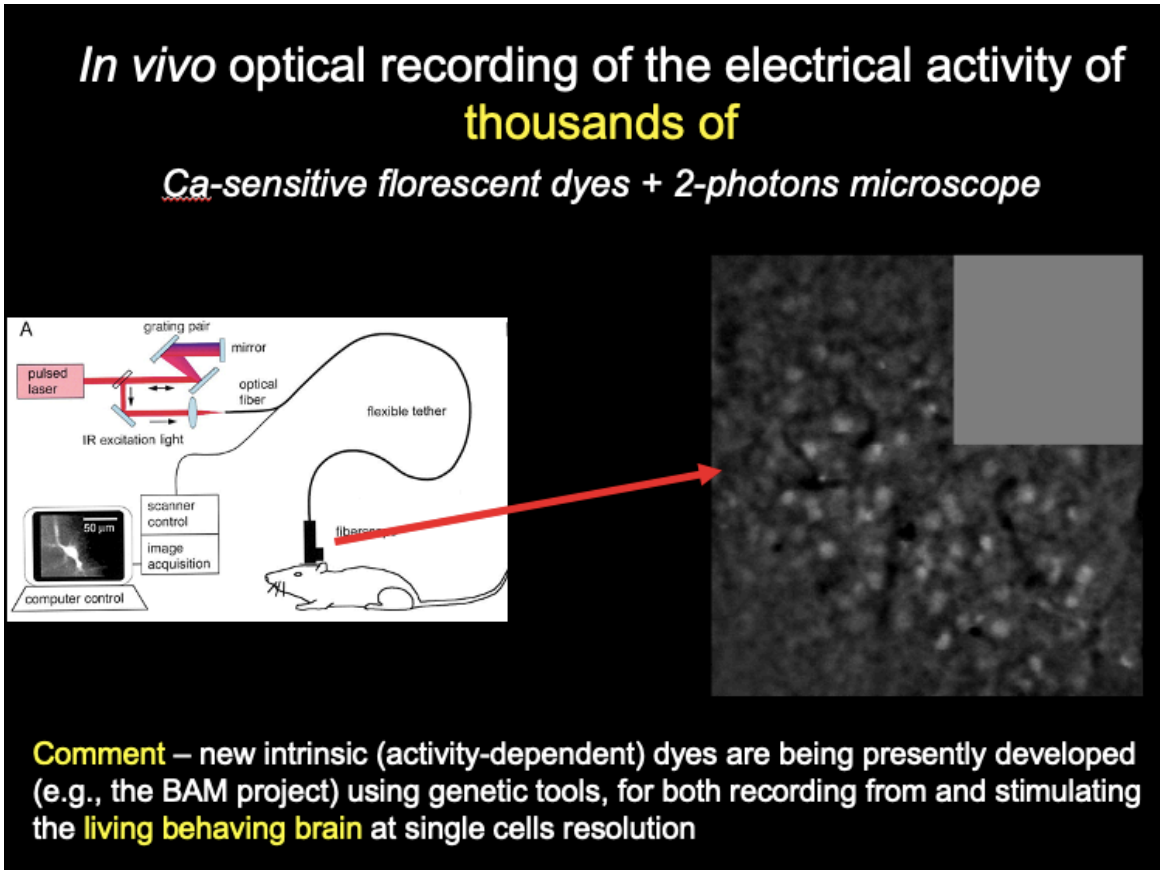
~2020

> **Blue Brain validated that the methods developed to build microcircuits can be generalized to building a whole brain region with curved shape and differences in cellular composition and synaptic properties.** Here we targeted the somatosensory cortex for which a paper is in preparation.

Ann etc. https://www.epfl.ch/research/domains/bluebrain/blue-brains-scientific-milestones/

BAM: Brain Activity Map Project of President Obama

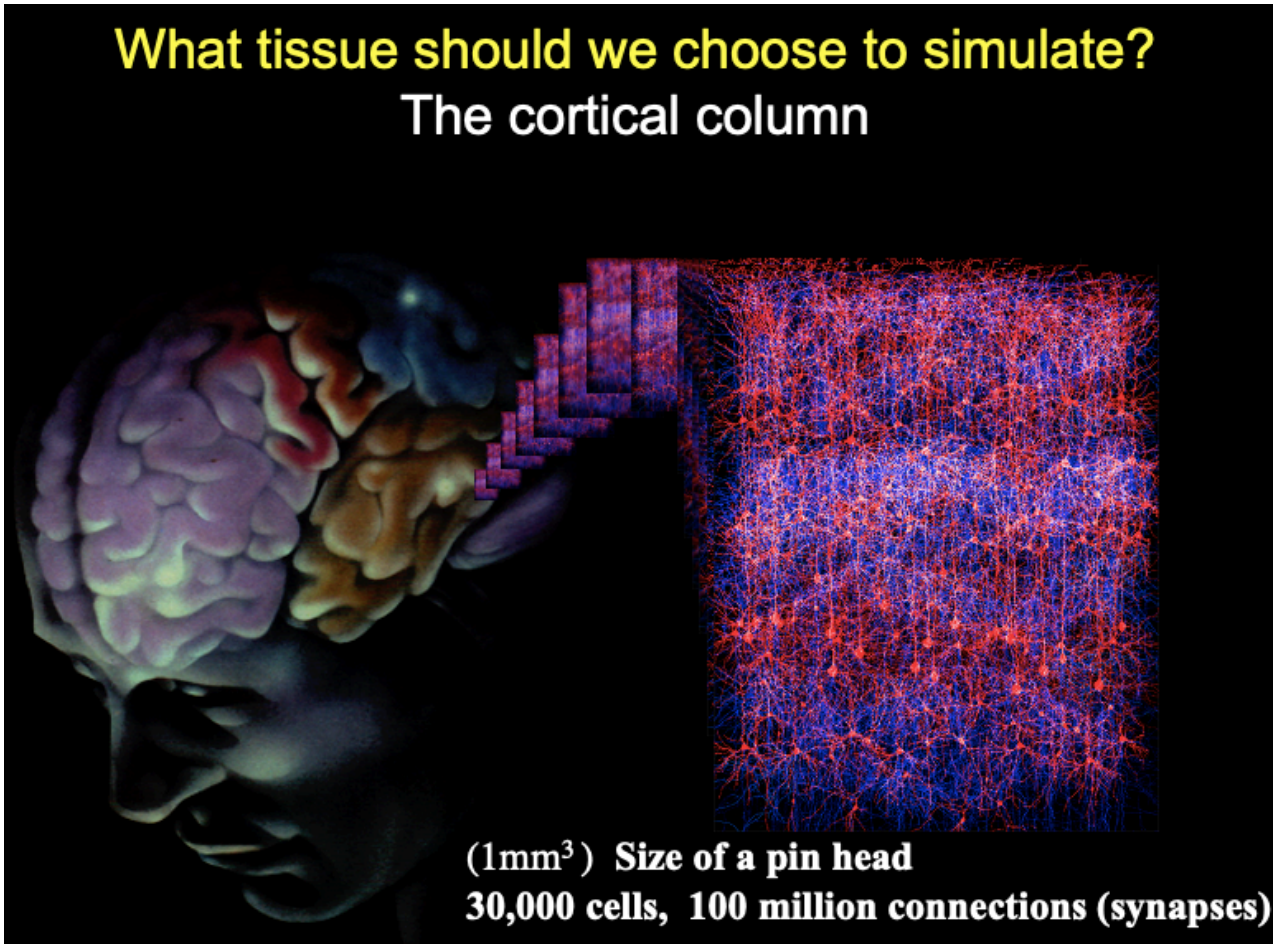
> using relative optics and also the capability to record from many simultaneously thousands cells from a particular brain region
>
> (many other sensitive dyes but not only calcium-sensitive dyes)
>
> but eventually you can see individual cells firing spikes via this calcium image when the system so to speak receives a relevant input, a bars of orientation in different direction, likes to respond to this particular input and so on



and obama's proj improve these optical tools and bring to 2 millions cells not only 2000

The Cortical Column

we want to simulate a particular region of brain in the level of nerve/synapse, so what network should we choose?



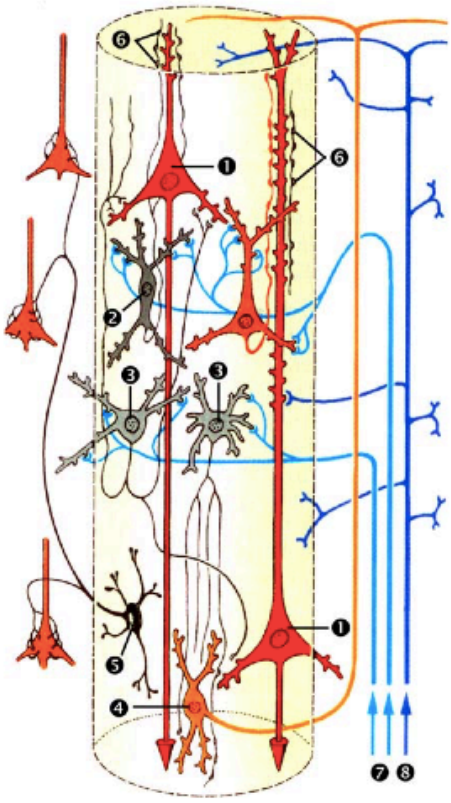
> In the neocortex of mammalian, we may find some similar structure

What is the cortical column

> **Definition**: The cortical column has physiologically many important functions: it is the ubiquitous and universal building block of cortical information processing (a “canonical circuit” found in all areas of the neocortex, Douglas and Martin, 2004).
>
> > Wiki definition: A cortical column, also called hypercolumn, macrocolumn, functional column or sometimes cortical module, is a group of neurons in the cortex of the brain that can be successively penetrated by a probe inserted perpendicularly to the cortical surface, and which have nearly identical receptive fields.
> >
> > cortical columnar is the most widely accepted hypothesis. Cortical column is composed of miniccolumns
> >
> > numbers of cortical columns
> >
> > > There are about 200 million (2×10^8) cortical minicolumns in the human neocortex with up to about 110 neurons each, and with estimates of 21–26 billion ($2.1 \times 10^{10} – 2.6 \times 10^{10}$) neurons in the neocortex.
> > >
> > > With 50 to 100 cortical minicolumns per cortical column a human would have 2–4 million ($2 \times 10^6 – 4 \times 10^6$) cortical columns.

> It allows to combine thalamic inputs with ongoing corticocortical processing, **integrate bottom-up flow of information with top-down processing**, and provides many other modulatory inputs important for incorporating the behavioral context into [sensory processing](#) (Friston, 2010; Harris and Shepherd, 2015).
>
> > for example, in cat's auditory cortex:
> >
> > > notice that connections weakened in deafness

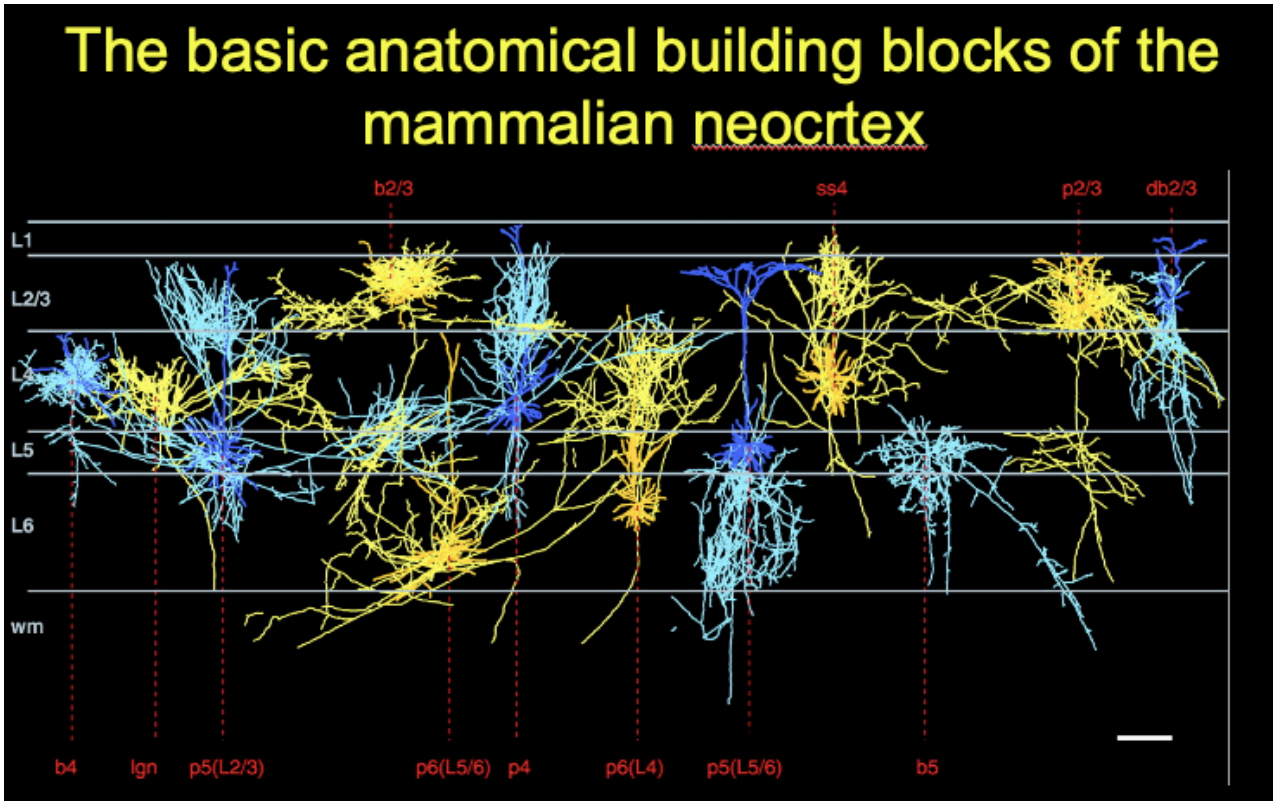
The cortical column, a sophisticated input-output (computational) unit



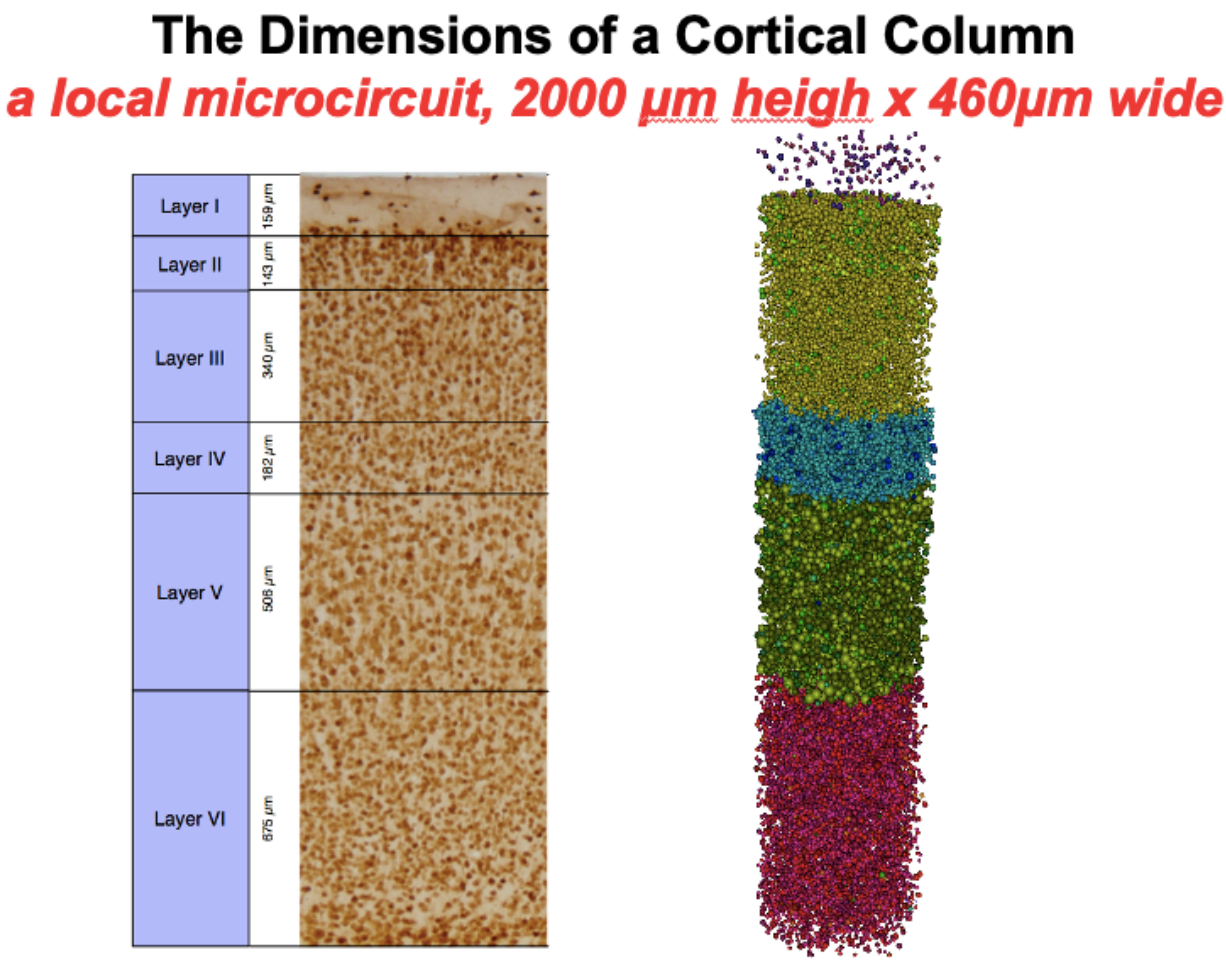
> from the surface of neocortex into the 2-millimeters deep
>
> may contain pyramidal cells, spiny stellar cells, inter-neurons, inhibitory neurons and excititary neurons
>
> the input may come from elsewhere into the network from the thalamus into the network or from other modestal regions and go to different layers

the cortex is relatively new in revolution, enabling mammalians would go generate new behaviors even language

> the neocortex is about 200-million years old



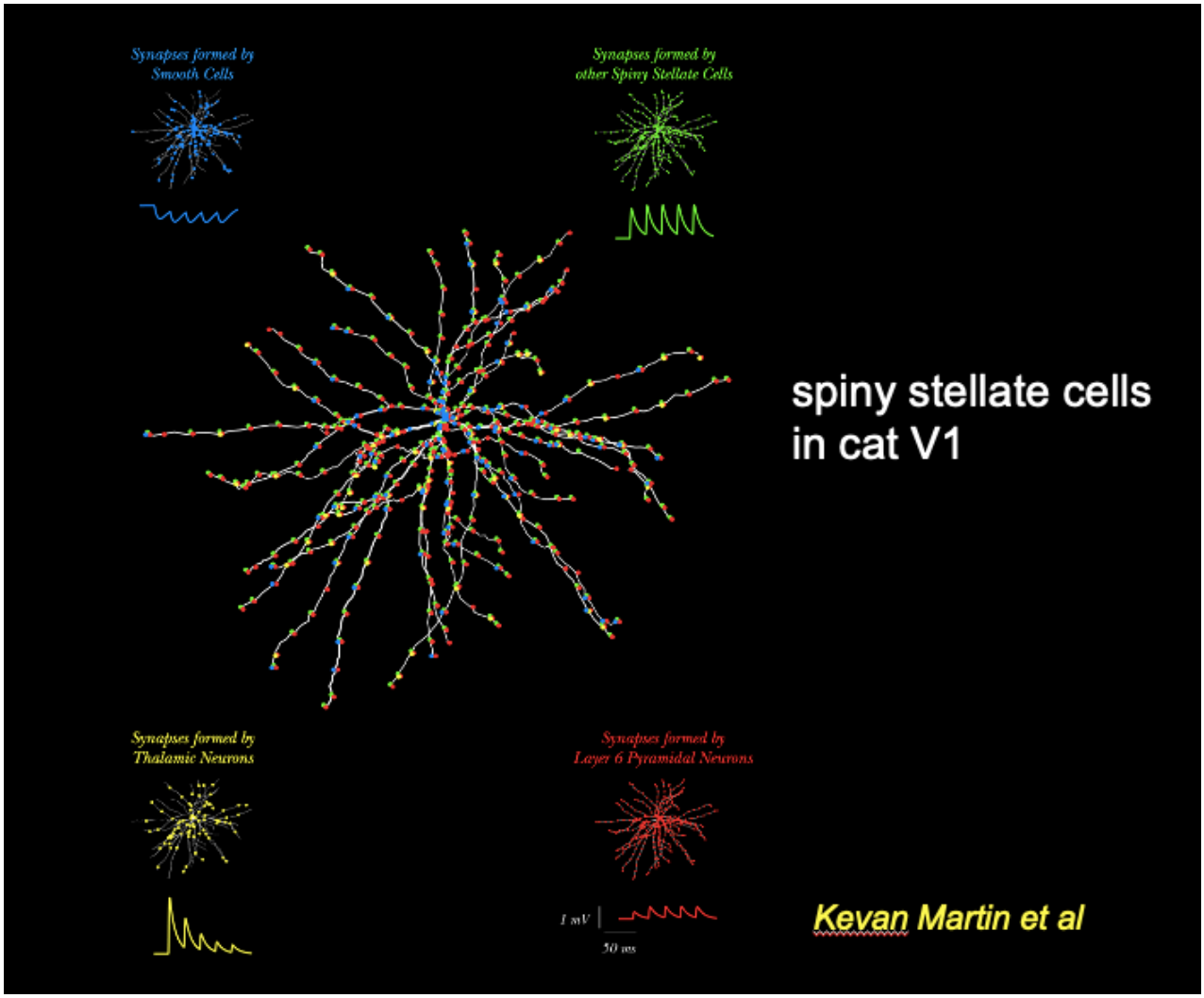
> When we say "layers" we actually think about the high density of cell bodies



> cortical column

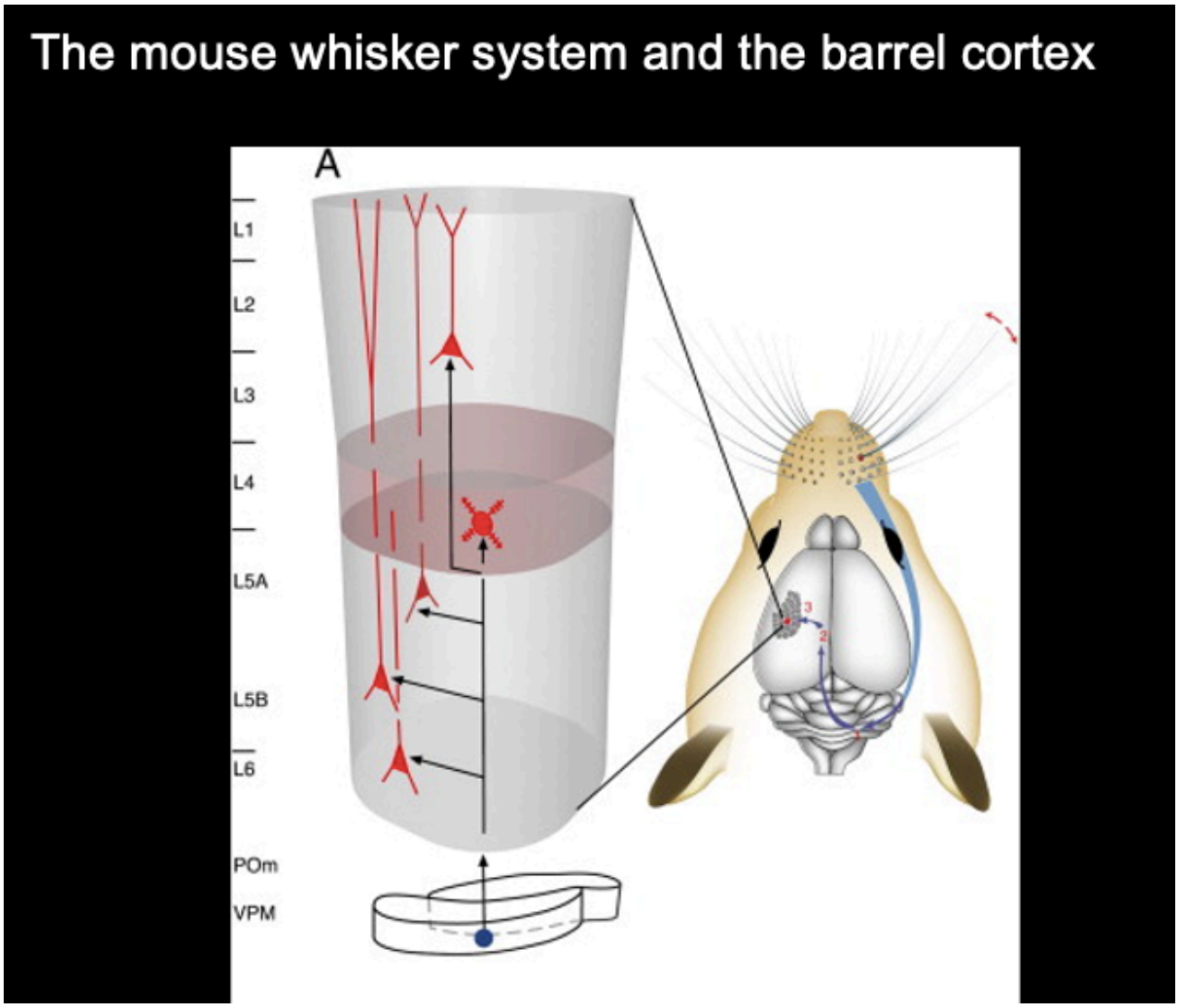
> > the anatomical structure is based on some foundation because the input is not going everywhere (so we are trying to make some order, hopefully, the order will help us to understand some function)
>
> > cell types are different in some sense from on layer to another

Synaptic Mapping

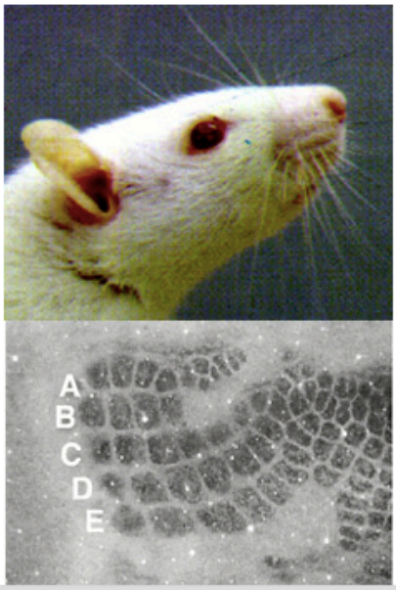


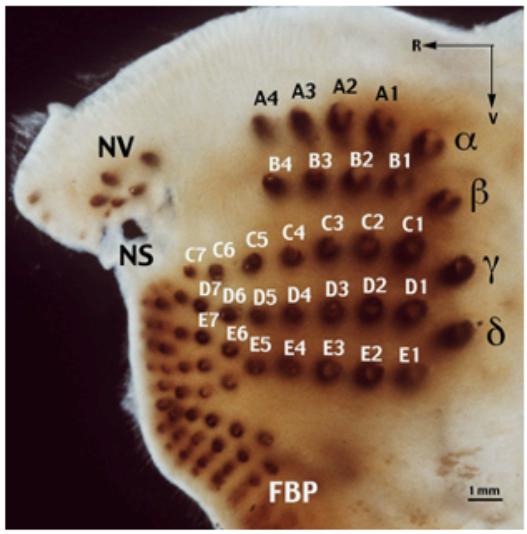
> What is the synaptic environment around you?
>
> What/who is the source of input?
>
> all the inputs may finally generate a "yes" or "no" in the spiny stellate cell
>
> > but this synaptic mapping won't give you the exactly message sent from the pre-synaptic to the post-synaptic
> >
> > > we need these information to decipher the activity of this particular cell resulting from the activity of it's neighbors
> > >
> > > and when the animal is doing some particular motions, we want to know what activity of these synapses will look like
> >
> > it just give you the map of synopsis with out any activity

A Cortical Column Networks



> in this region, there are these columns that each represent the information primarily, information flowing from the particular whisker
>
> the information flowing from a particular whisker may flow and eventually goes into a particular column (a group of 10000-20000 cells)





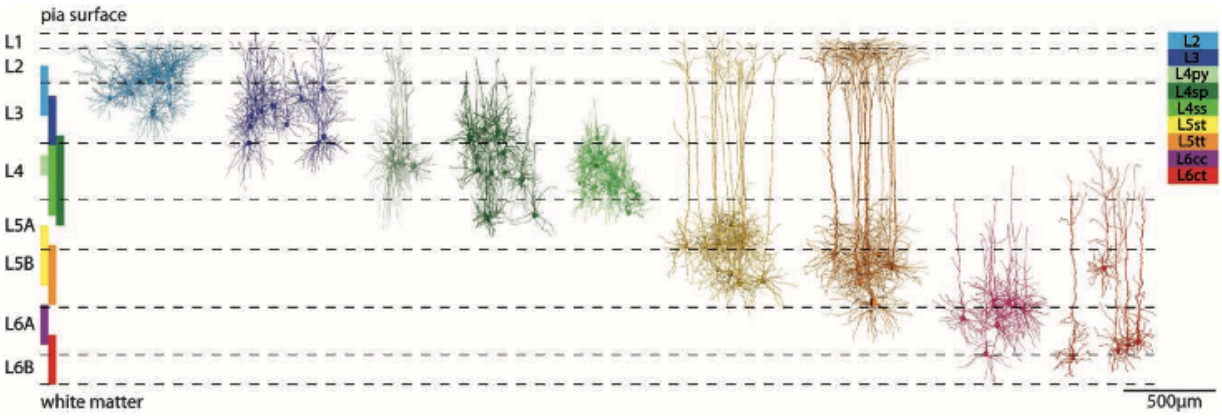
Carol A. Himsel's, Peter Land , Sebastian Haidarliu & Ehud Ahissar.

each whisker has a name (because it is repetitive)

and there is a very clear mapping between the location of a whisker and a particular barrel-a particular column in the cortex of the mouse.

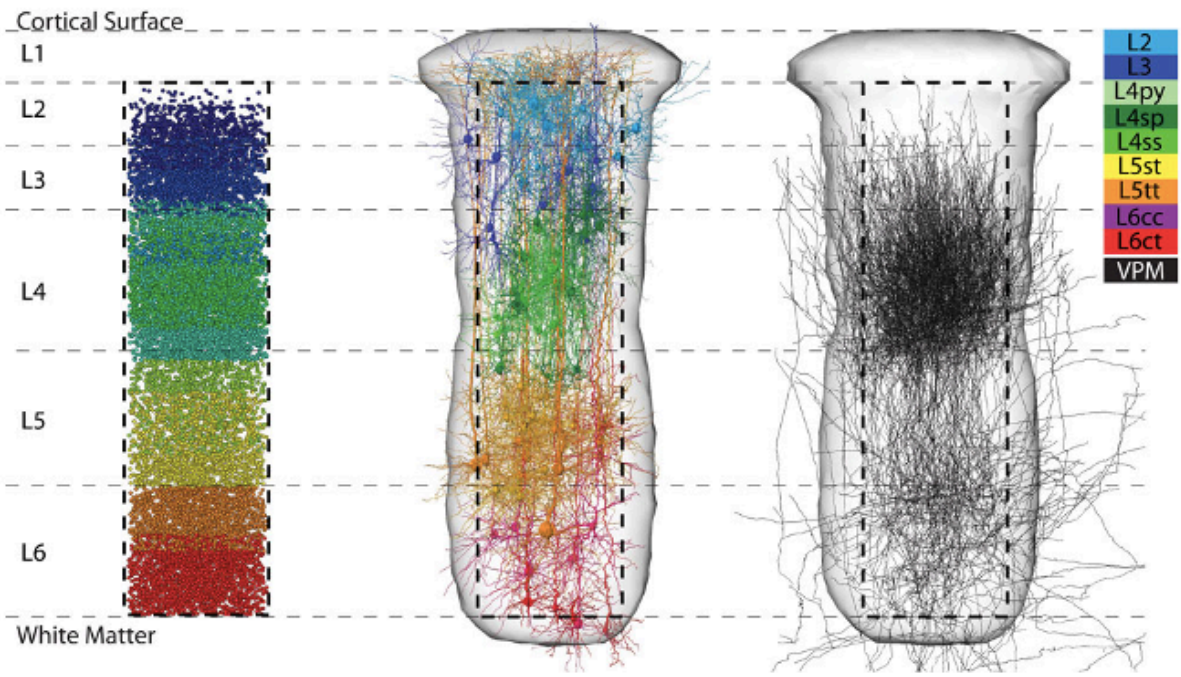
now many people today are trying to understand the columnar organization or the columnar representation of whisker information onto the cortex

Excitatory cell types in the cortical column



Sakmann et al.,

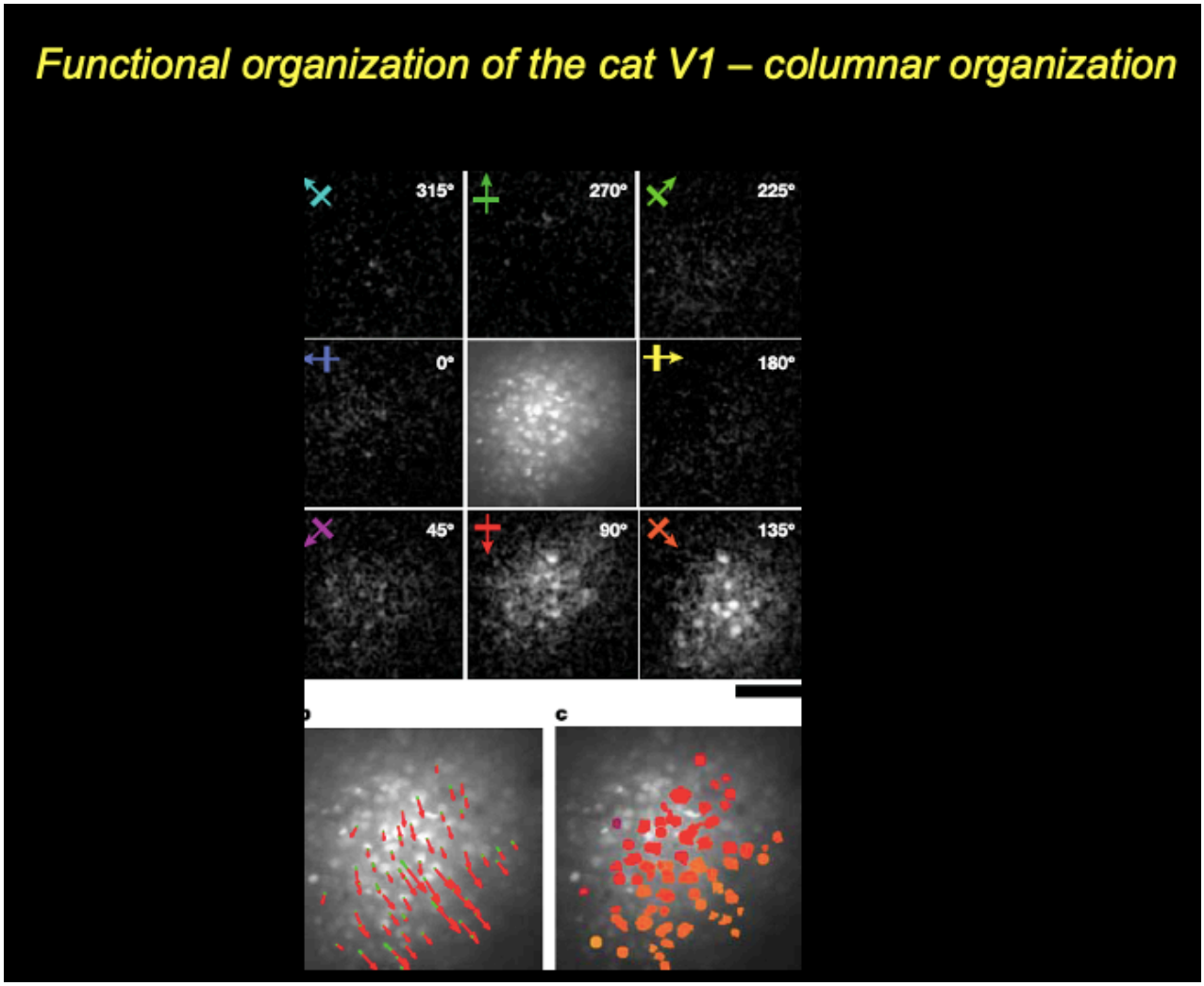
Input (axons) from thalamus



Sakmann et al.,

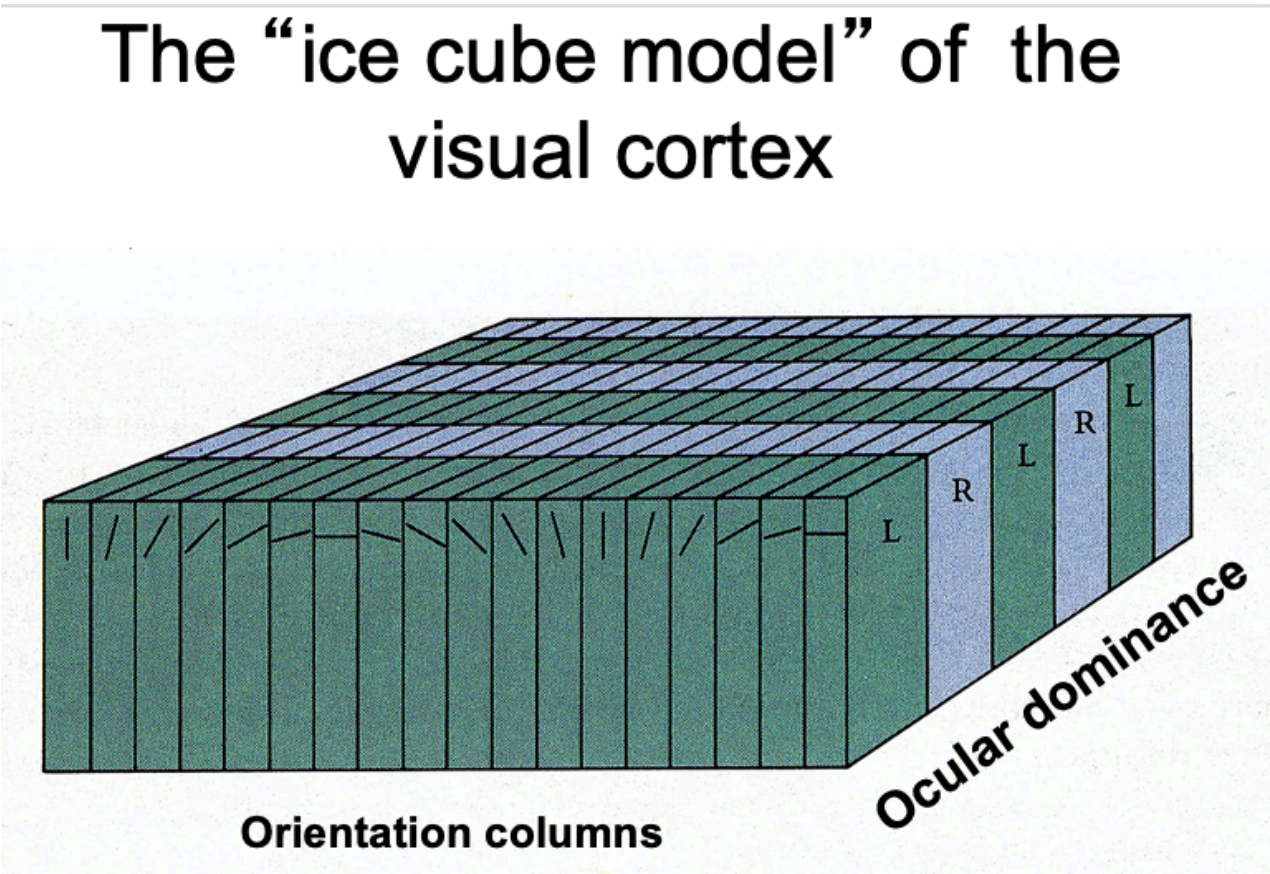
> the fig above shows an axon coming from the thalamus into the cortex. we can see a dense termination in layrer 4
>
> Actually, a particular column is anatomically very clear and functionally. Because each times after you touch the whisker, this particular column will be ignited.

when the line moves in a particular direction, the bunch of the columns will be activated



We can use **the ice cube model of the visual cortex** to summarise what we know about the visual input

> The ice-cube model of the cortex. It illustrates how the cortex is divided, and at the same time, into two kinds of slabs, one set of ocular dominance (left and right) and one set for orientation. *The model should not be taken literally: Neither set is as regular as this, and the orientation slabs especially are far from parallel or straight.*



> in cat's V1 visualization structure, you can see that the orientation gradually changes between one column to another column
>
> so all the cells in the column tend to respond mostly to this orientation. (not all the cells but many of the cells)
>
> also, there is another systematic ordering in V1 because you see that the particular column likes to responds to input from left eye and the next one into the axis (LRLRLRLR... response to input from the right ear and so forth)

The cortical column is the target tissue for the blue brain simulation.

In addition to function, the column unit is also **plastic.**

> Neuron is plastic
>
> synapse is plastic
>
> the column is changing plastically depending on the early experience in life and maybe later on of the animal
>
> > Column is not a static tissue but a dynamical plastic tissue may change depending on experience
> >
> > e.g., if only limited visual angles are experienced in early age (critical period) than only the respective oreintation columns are formed in the cat V1

we need to model the cortical column mathematically

> *We have all this data - cell types, firing properties, connectivity, dendritic anatomy, synaptic dynamics,.... But we don't understand how these ingredients generate a dynamic/functional response*
> *We need to model* it

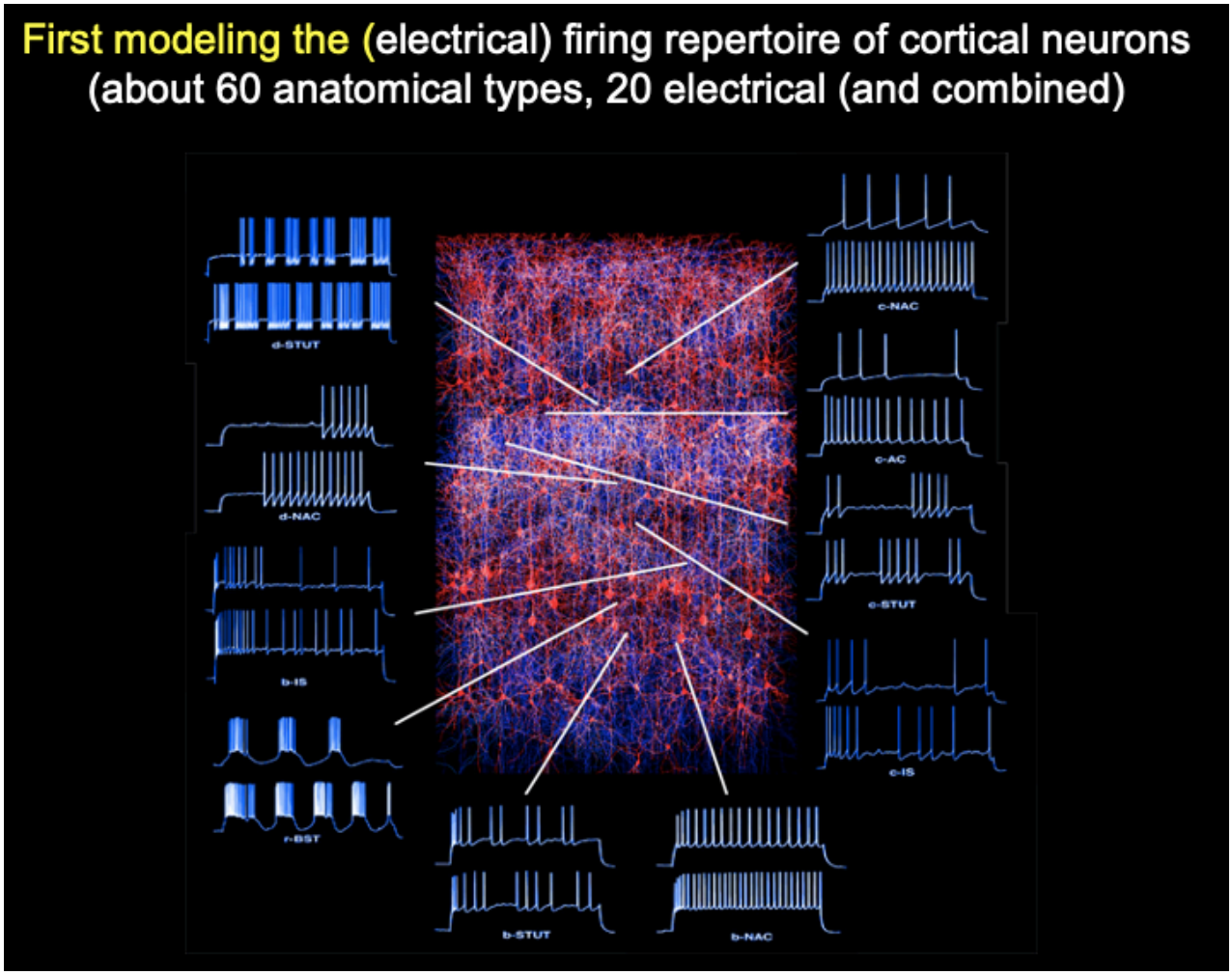
We need to understand how the global dynamical property of a whole network

The network theory about columns and layers

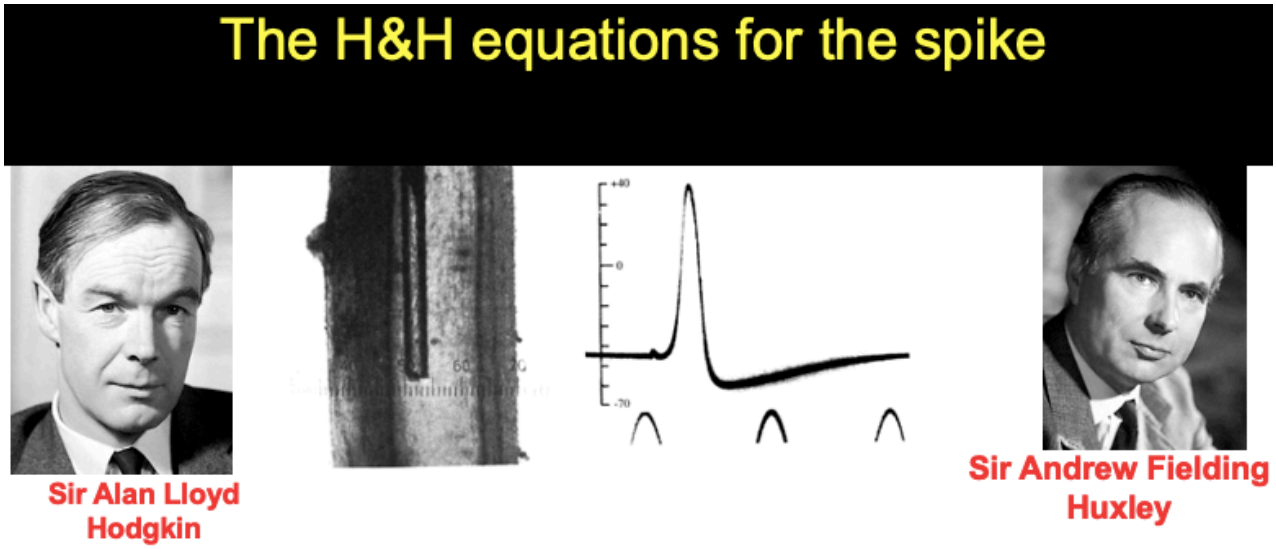
Paer

> This paper propose a network model composed of columns and layers that performs robust object learning and recognition. Each column integrates its changing input over time to learn complete predictive models of observed objects. Excitatory lateral connections across columns allow the network to more rapidly infer objects based on the partial knowledge of adjacent columns. Because columns integrate input over time and space, the network learns models of complex objects that extend well beyond the receptive field of individual cells.
>
> This paper propose that a representation of location relative to the object being sensed is calculated within the sub-granular layers of each column. The location signal is provided as an input to the network, where it is combined with sensory data.
>
> > The present paper about the network model

Blue Brain Simulations



> notice that each cell has its own electrical properties
>
> so we need to find mathematical ways to write the equations to replicate the firing properties not only the individual spike of different cell types



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

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

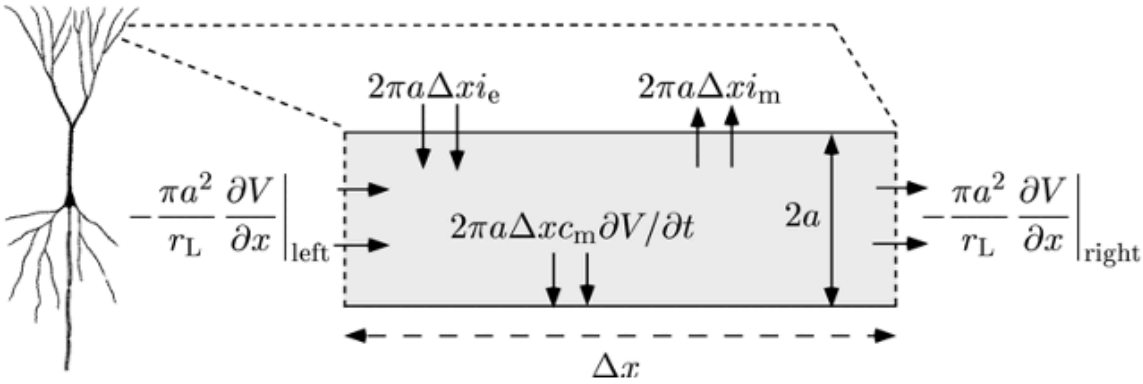
$$\frac{d}{dt} n = \alpha_n (V)\ (1 - n) - \beta_n (V)\ n \qquad (3)$$

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

> Hodgkin-Huxley equations just capture the single spike but not the firing properties

we need to use extended Hodgkin-Huxley equations and passive cable equation now also the active cable equations

Passive cable equation



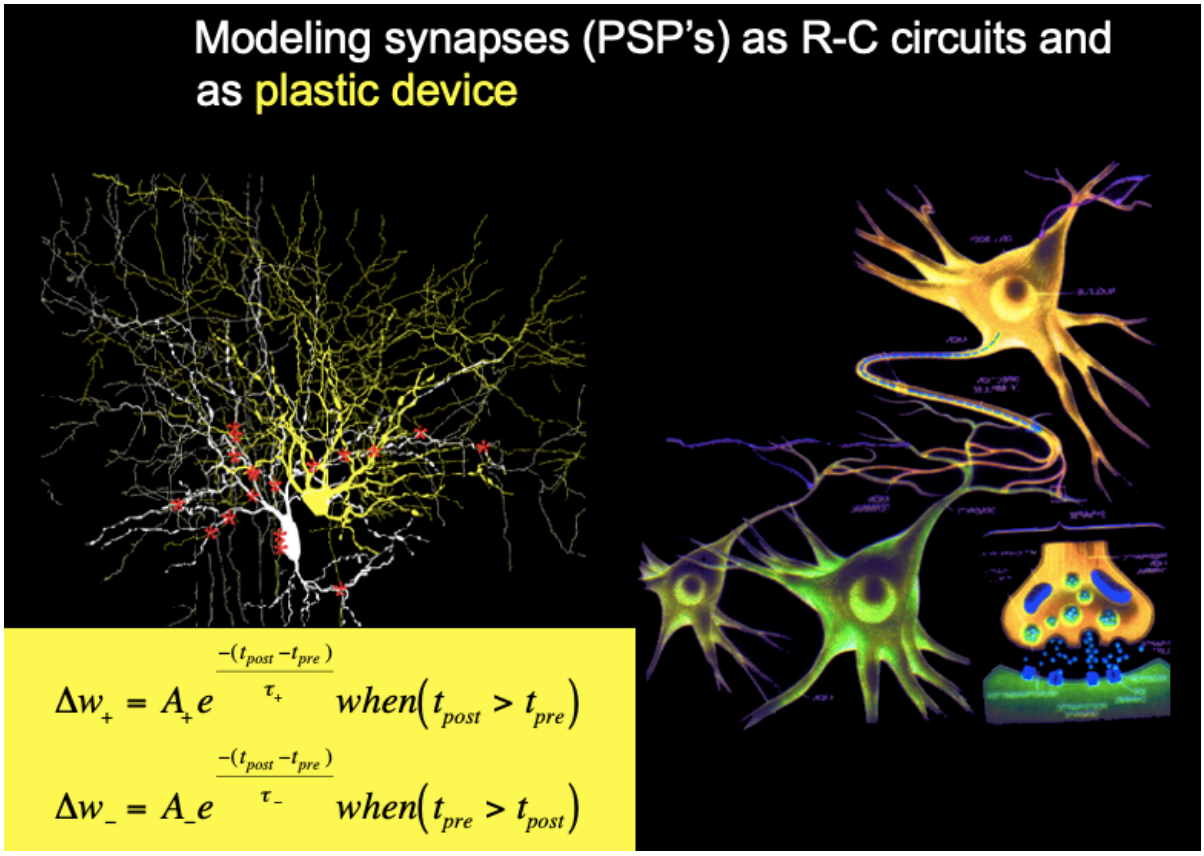
$$\left(\frac{r_m}{r_i}\right)\frac{\partial^2 V(x,t)}{\partial x^2} - r_m c_m \frac{\partial V(x,t)}{\partial t} - V(x,t) = 0$$

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

$X = x/\lambda$
$T = t/\tau_m$

we also need to model synases (PSP's) as R-C circuits and as plastic device

mathematically write down the plasticity rules



> this equation describing spike timing dependent plasticity

Challenge 2: Modeling mathematically the connections between neurons (Synapses) - Done

Challenge 3: Modeling plastic (learning) processes in networks (synaptic plasticity) – Ongoing

> plasticity is more difficult because there are many plastic rules not easy to implement in a network
>
> now scientists are trying to embed plasticity into the the cortical network

Challenge 4: Connecting the cortical networks (a-la-experiments) – Ongoing

> we don't fully have all the anatomy as yet
>
> but we have a lot of the anatomy and we may now predict what would be the connection between pairs of cells that we did not record from

then put all the information into the simulation computer

> now the blue brain proj can simulate a single cell, a whole network about 100000 real cells (10 columns)
>
> and visualize a single cell, a whole network (axon jungle) and hundred million of synapses (labeled excitatory and inhibitory)
>
> and now it allows us to look at the activity

the question is how to relate this activity to a particular behavior

Supplemental materials

> now there are many cortical column simulation papers and network models

From Mouse to Human

we can simulate a column or several columns of humans and this will be hopefully enough to already understand some diseases emerging within sub-networks

The Human Brain Project

the notion: to develop a platform for understanding the brain but also using this platform but also develop new technologies like new super computing capabilities, new visualization of activity anatomy of large networks, new microchips

the project is not about finding details but about developing approaches both in neuroscience and in medicine and in future computing

> Basic notion: brain is a computing device

QUIZ

1. What is common to Parkinson, Alzheimer and Autism?

   > The electrical activity of the brain is different comparing with a non sick brain.

2. Mammals are different from other animals by having the neocortex.

   > The neocortex typically consists of 6 layers
   >
   > In different brain regions, the neocortex is specialized in different computational tasks
   >
   > ❌Only in the neocortex one finds pyramidal cells
   >
   > ❌The neocortex in all regions shows clear structural partition into columns

3. In a cubic mm of a mammalian cortex

   > There are ~ 30,000 neurons and ~10^8 synapses

4. Layer 5 pyramidal cell in a mammalian neocortex:

   > Receives input from different types of cells
   >
   > May receive input also from neurons outside the cortex, sending their axon to the cortex
   >
   > Receives input from different layers in the cortex
   >
   > ❌Its dendritic tree resides only at layer 5 of the neocortex

5. In the mouse barrel cortex:

   > There is a clear anatomical separation among the columns
   >
   > Each column receives primary input from a particular whisker
   >
   > ❌The sensory information that reaches each column remains sensory throughout the whole brain of the mouse
   >
   > ❌The computations performed within each column are isolated from those of other columns

6. Input (axon) from the thalamus to the mouse barrel cortex:

   > Impinges mainly onto layer 4 of the cortex

7. Mark the correct sentences:

   > Cells in cat V1 are plastic – experience can change the orientation selectivity of the column
   >
   > In cat V1 there are functional columns – most of the cells in the column respond to the same orientation of the visual input
   >
   > ❌As in the mouse whisker system, cat V1 also consists of anatomically-identified columns

> ❌The orientation of the column is defined by its physical orientation with respect to the skull

8. Different types of cells in the cortical column are different from each other in:

> By their target output and by their synaptic effect (e.g., inhibitory/excitatory)
>
> Their anatomy
>
> Their electrical characteristics
>
> ❌Different cells have significantly different spike shape.

9. Models of a cells in the blue brain project (BBP) include:

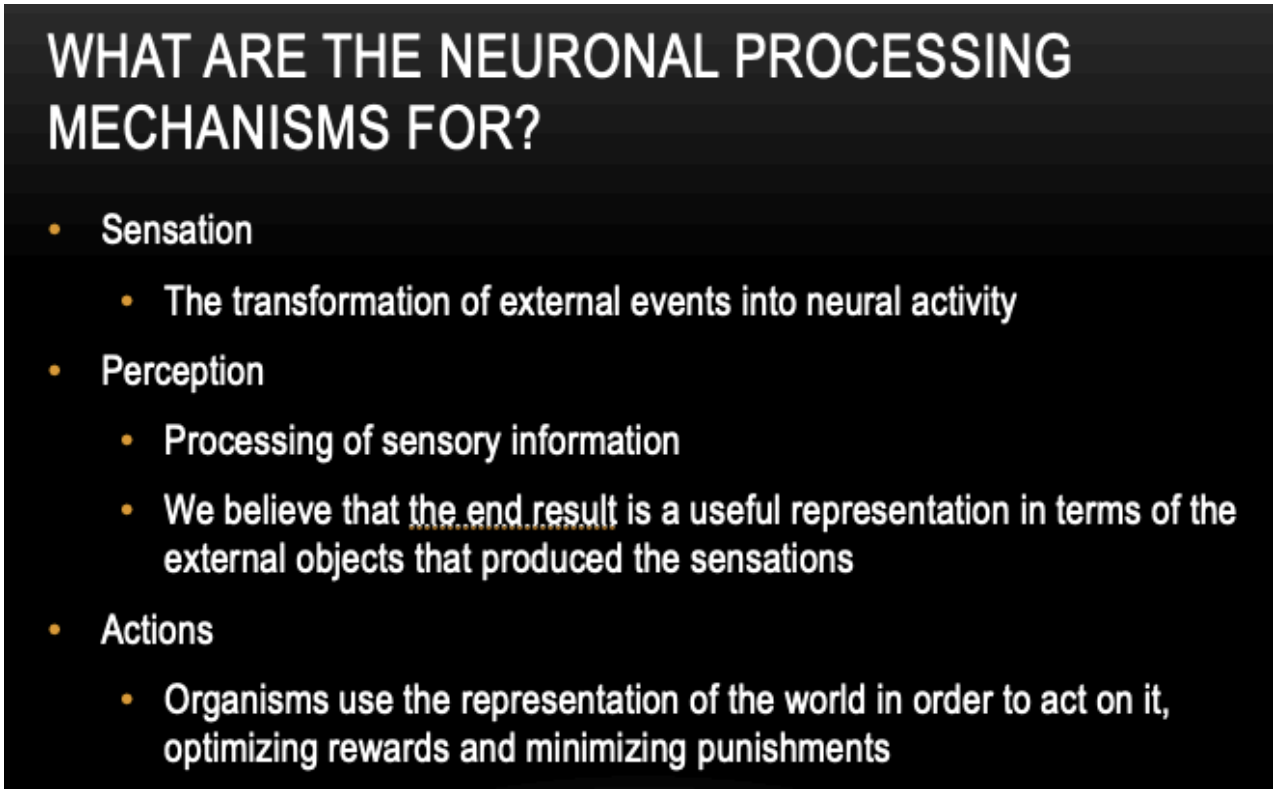
> The cell morphology – the size and the location of its dendrites and axon
>
> The cell electrical properties – a set of equations that replicates the firing properties of a similar cell in the cortex
>
> The synaptic properties impinging on other neurons in the network
>
> ❌Each cell is represented as a single compartment cell (“point neuron”)
>
> ❌Simulations also include the activity of various genes and proteins

10. Simulation of a particular disease in the BBP means

> That the dynamic properties of the simulated network replicate closely to that of the corresponding disease
>
> That the spiking activity of different electrical-neuron types is replicated closely in the simulations
>
> That the simulation enables the identification of possible (synaptic, excitable or anatomical) changes underlying the disease
>
> ❌That the genes expressed in that disease are simulated in details
>
> ❌That we can repair the disease via interaction between the computer simulation and the sick brain

WEEK 8: Perception, Action, Cognition and Emotions

Sensory Transduction



sensation

> The transformation of external events into neural activity

perception

> processing of sensory information

The view of a linear order of sensation, perception and actions is actually a little bit naive and probably wrong.

Now people mainly talk about **perception-action loop**

> action and perception are not separated things
>
> they act in a loop and modify each

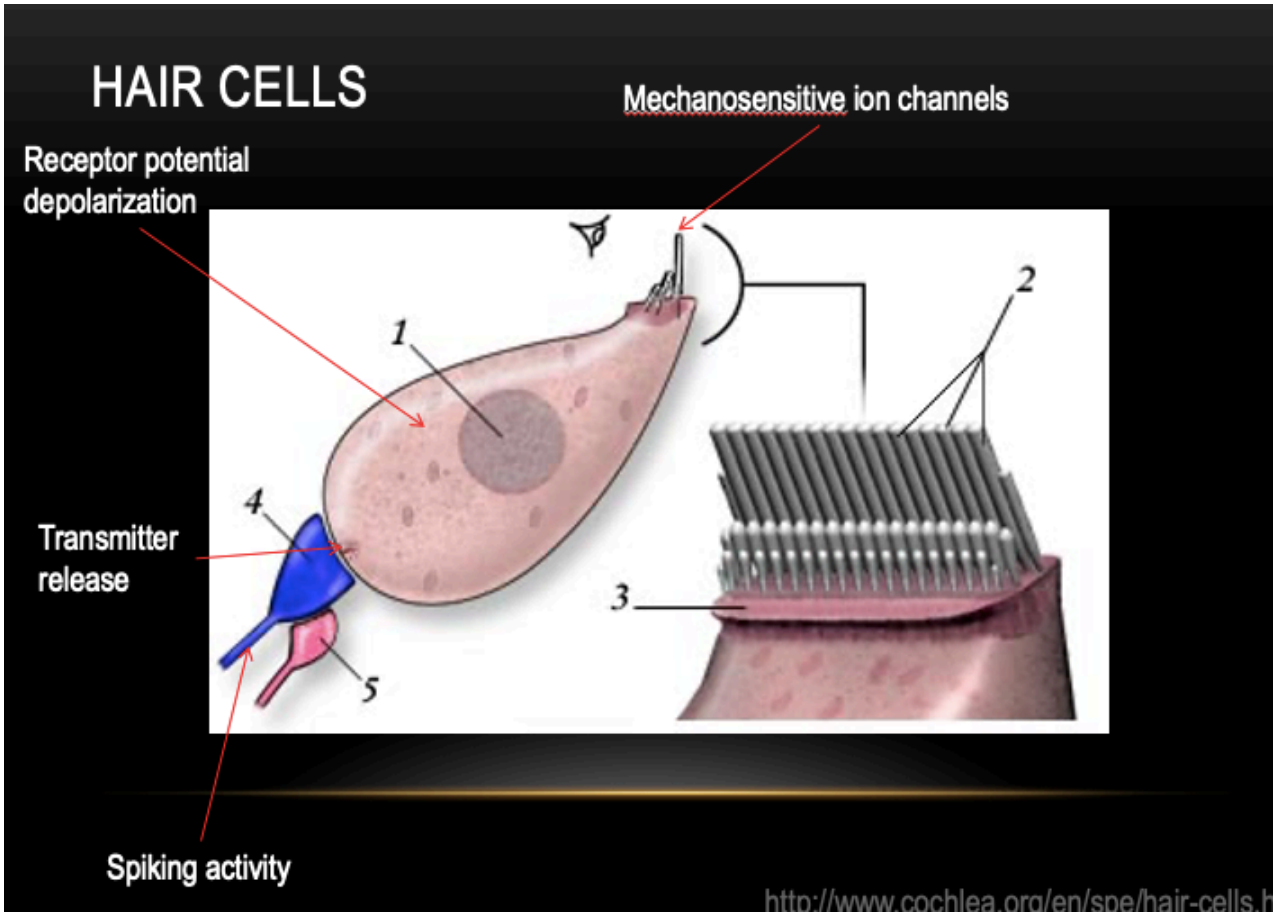
The problem from Marr's book

> You have 2-D image on retina - and your brain will reconstruct 3-D visual scene

But the problem that we facing today is

> **2-D image on retina → recover the latent variables.**
>
> > latent variables as the cause is for the things fall on the retina

Sensory Transduction: how do sound become electricity?



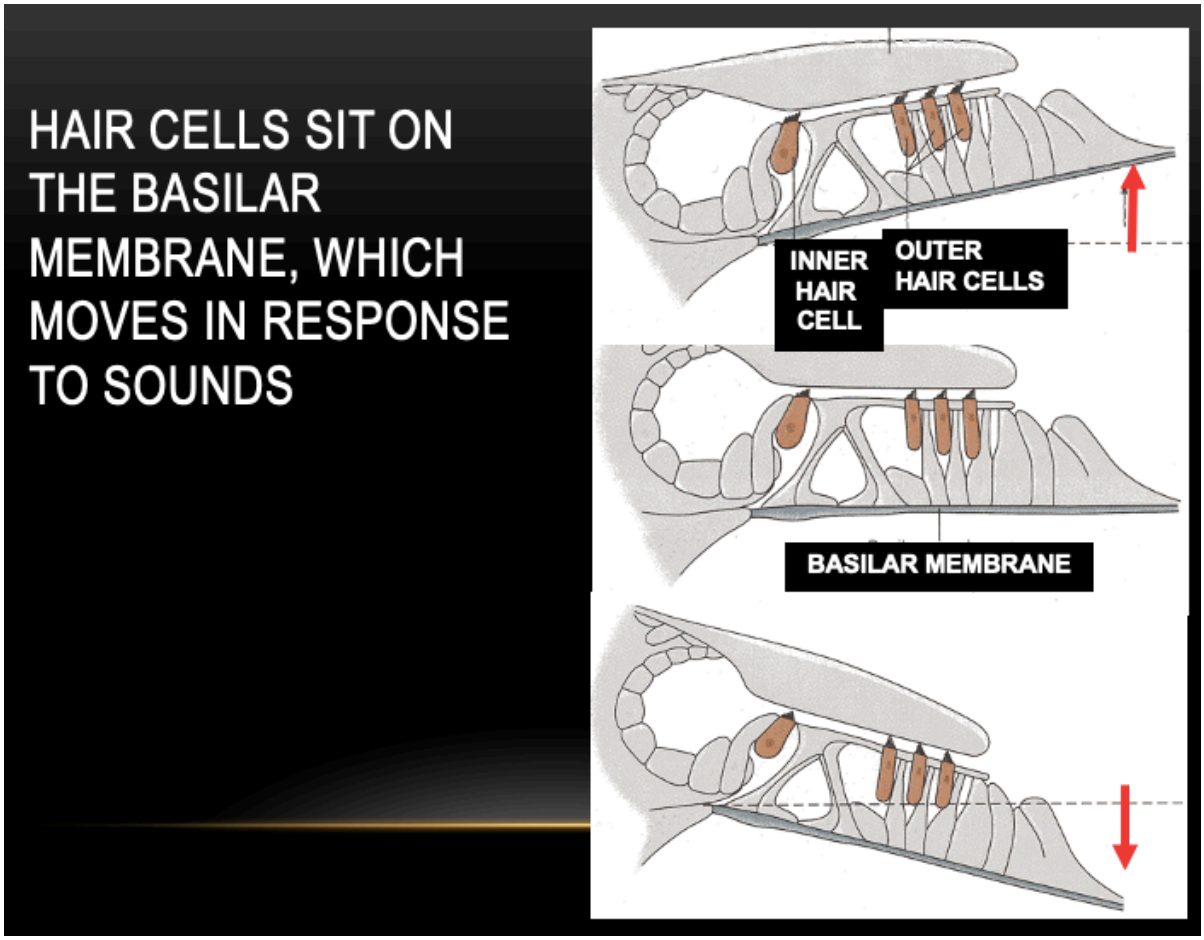
The notion is that when sounds come, they cause movements of the hairs. The mechanic sensitive ocean signals the hills and the motion of the hill open and close.

These mechanosensitive ion channels will cause currents into the neuron and the currents into the hair cell cause depolarization in the hair cell.

This depolarization like in all neurons acts on a synapse. It modulates the amount of transmitter that is released in synapses between the activity of the auditory nerve fiber.

Now this auditory nerve fiber has one end, contacting the hair cell in the ear, and its other end is inside the brain. And so the brain gets to know the motion of the hairs.

But how dose sound cause vibration of the hairs?

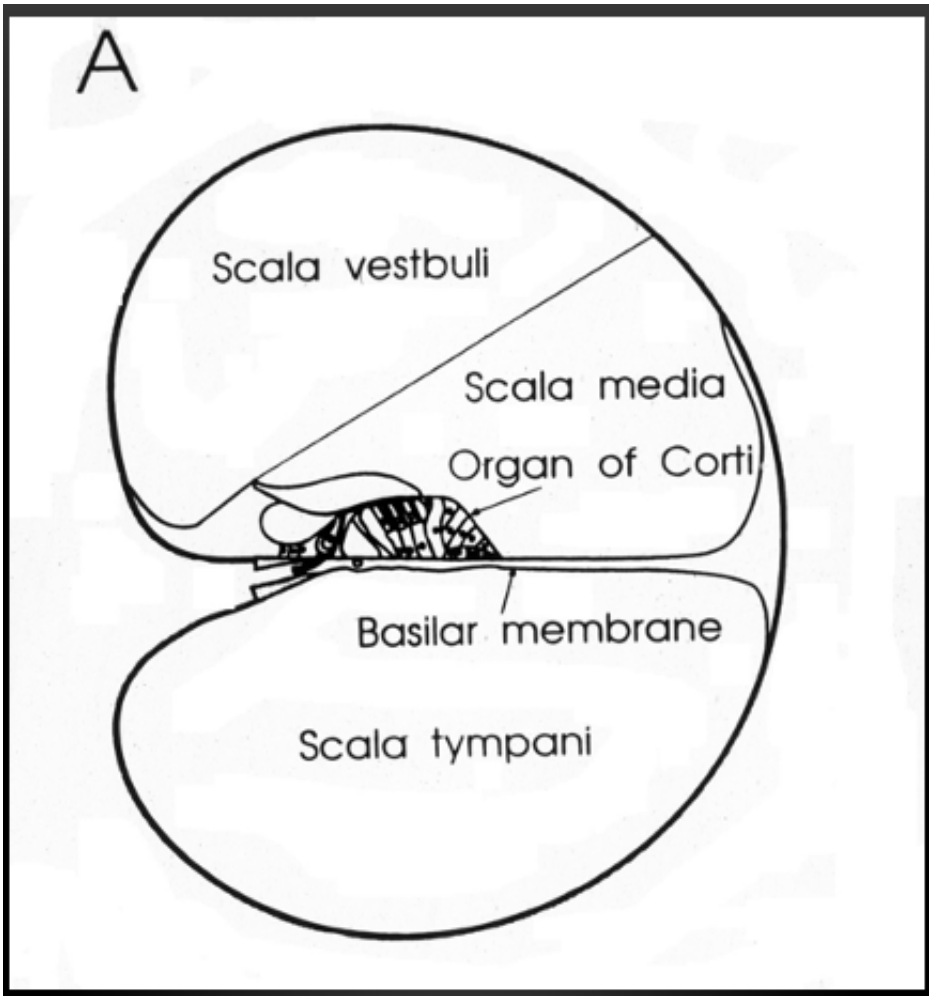


It's because the hair cells sit on the top of a membrane, called "basilar membrane", again in the ear. The hair cells are embedded in a structure which is very stiff. It's called the organ of corti, and caused by vibration of the basilar membranes. So the basilar membranes sometimes goes up and sometimes goes down.

So when the basilar membranes goes up or down, where this causes a relative motion of the hair we suspect to this huge copula this kind of a roof that lies above them.

The motion of the basilar membrane is translated into motion of the hair bundle and this causes the opening and closing of ion channels and the polarization, the transmitter release and spikes.

And why basilar membrane vibrate in response to sound?



> So it turns out that the basilar membrane itself sits inside a long tube. This long tube is a divided in the middle by the basilar membrane.

Emotions

Involved by physiological activation (eg. you can measure emotions by changes in skin conductance which is used in lie detectors)

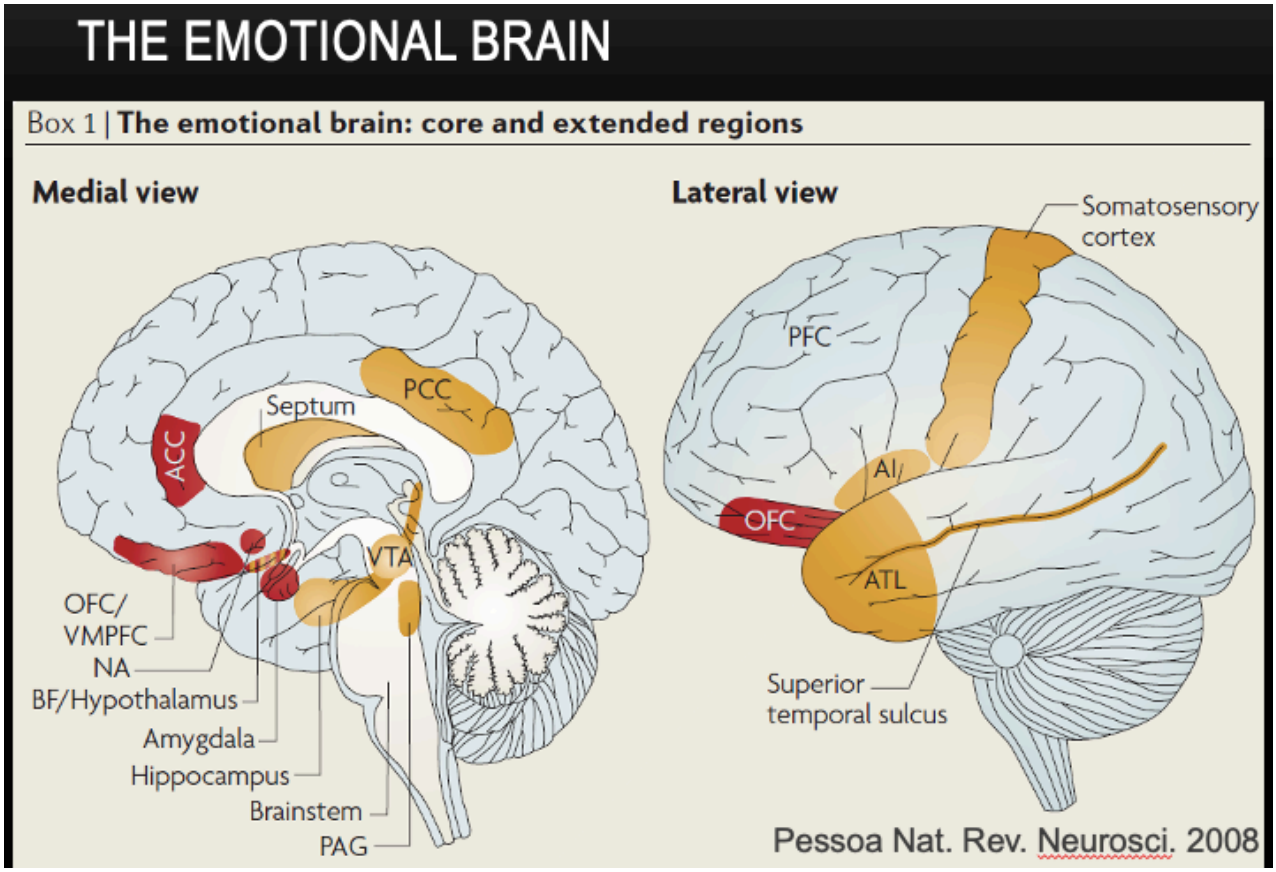
emotions are different from cognitive processes

> these are not emotions:
>
> memory
>
> attention
>
> language
>
> problem solving
>
> Planning

Edmund wrote that emotions are states elicited by rewards and punishers:

> •Emotions are states elicited by rewards and punishers (E.T. Rolls)
>
> •Emotions are involved in the conscious (or unconscious) evaluation of events (M.B. Arnolds)
>
> •Emotions are pre-programmed set of coordinated bodily reactions with adaptive values; affect is secondary (A. Damasio)

the emotional brain



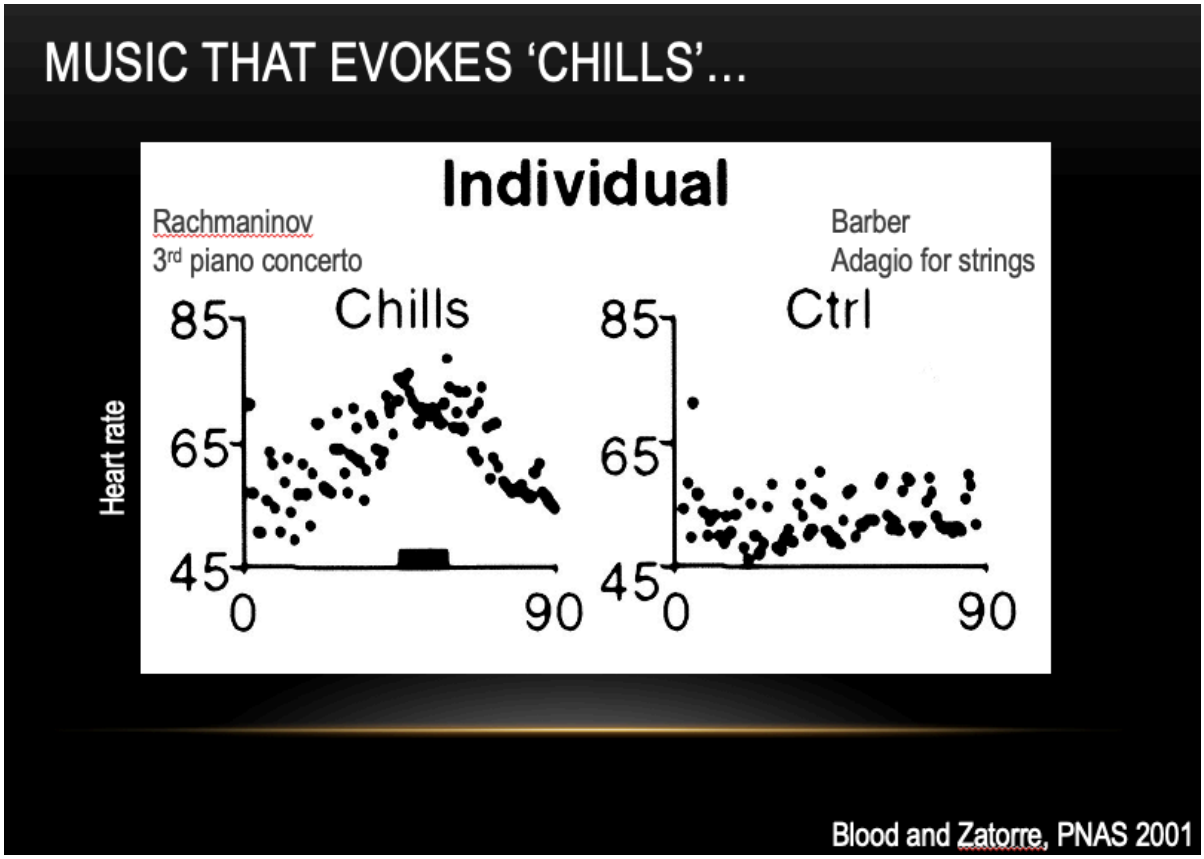
> Amygdala has been associated with fell reactions

the most extreme view of dopamine

> the goal of the mammalian vein in the world is to maximize the dopamine released over its lifetime

Notion: *emotion complex*

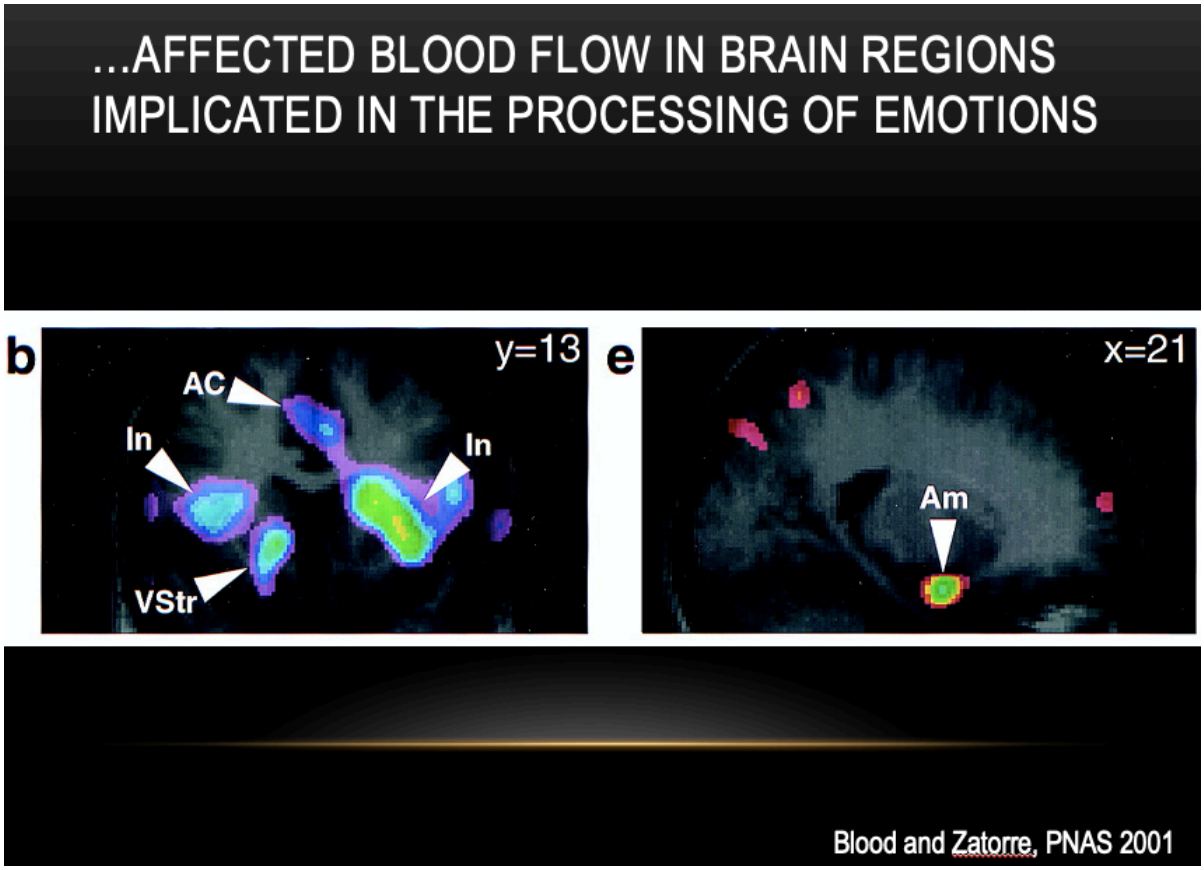
Music that evokes "chills"



many people have this piece of music that when they hear it, it creates in them such strong emotions that they have chills, shivers like very strong bodily actions

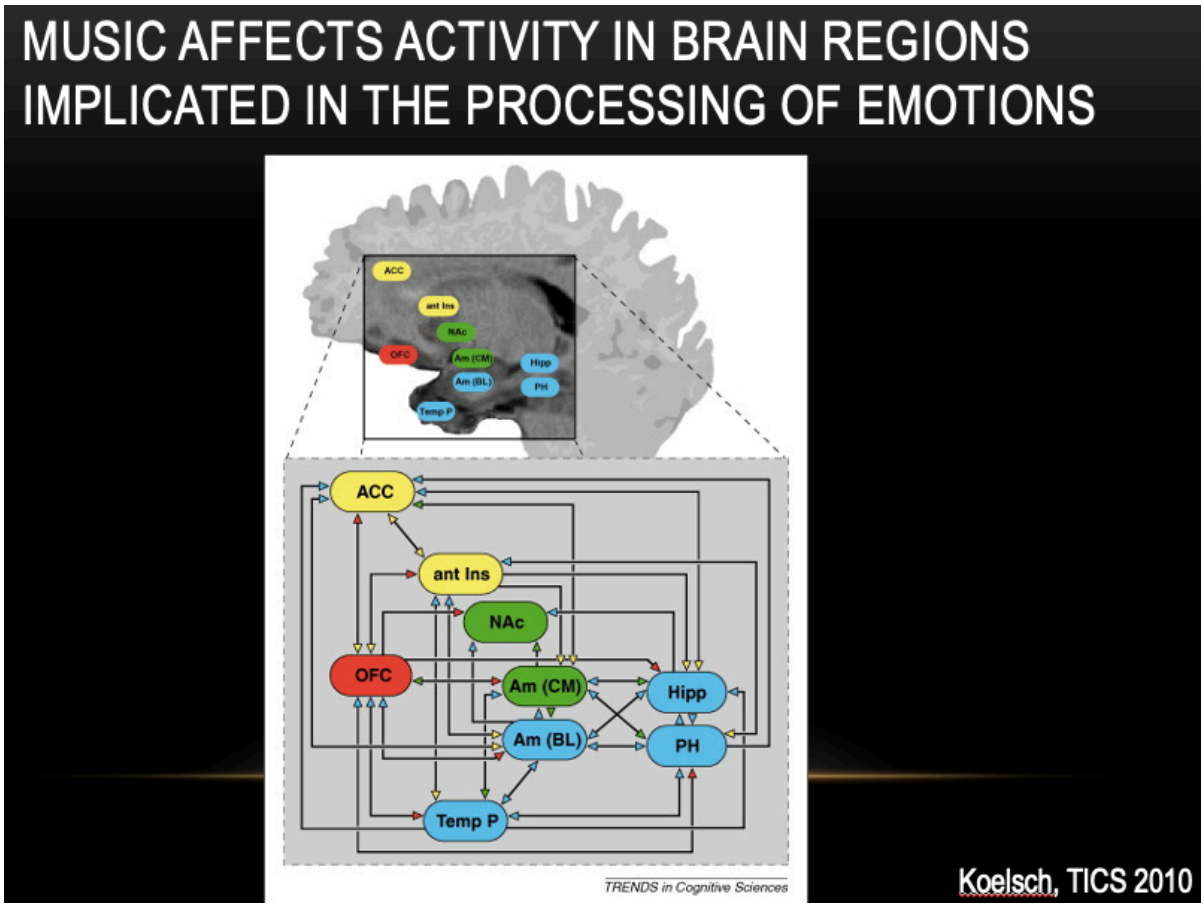
(in this study, "chills" are measured by heart rate)

Blood flow in brain regions when "chills"



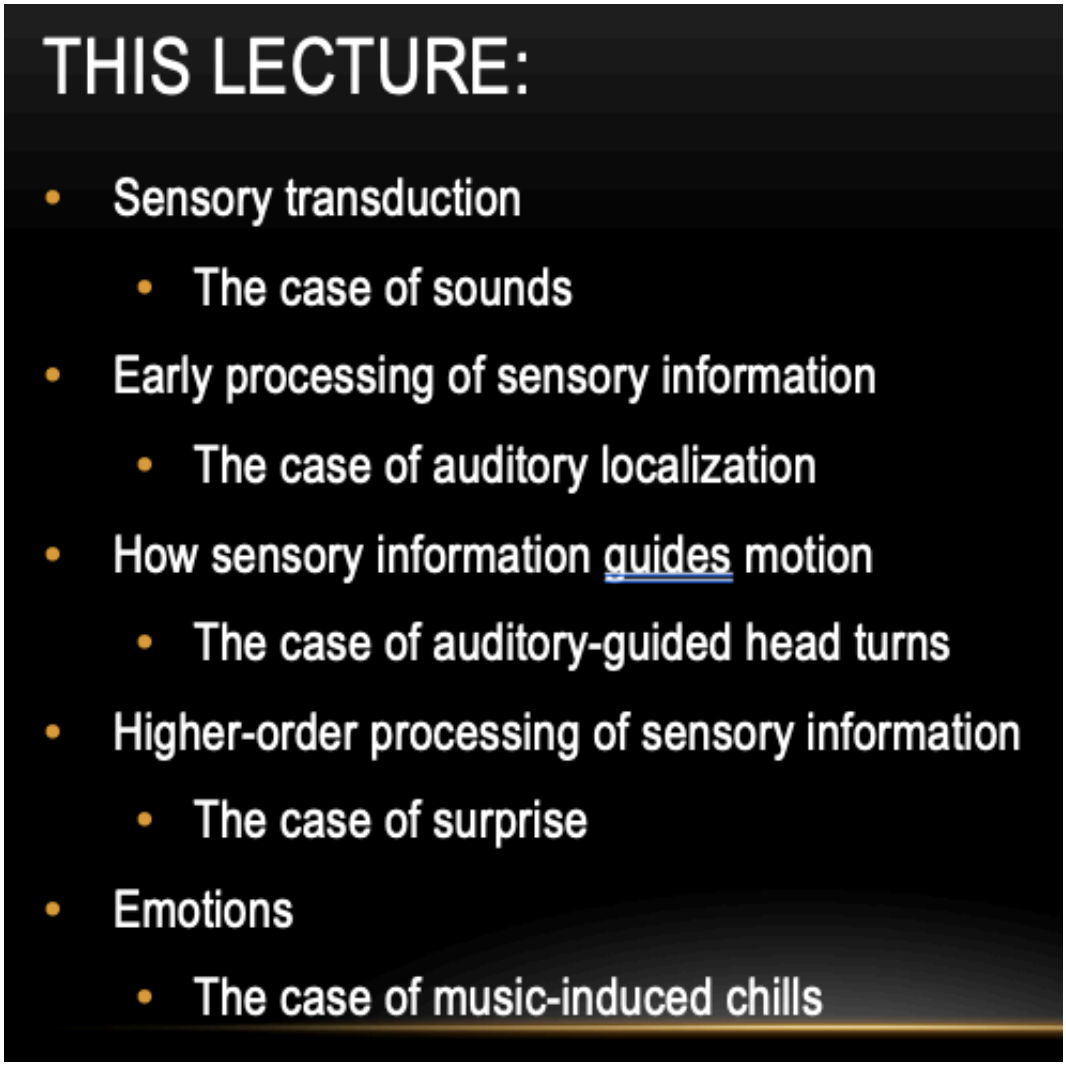
> blood flow increases to a brain structure when this brain structure is active
>
> (in this study, blood flow is measured by functional MRI and o positron emission tomography)
>
> In the fig above, we can see the dopaminergic system and the amygdala which is associated with bad emotions are activated

Music affects activity in brain regions implicated in the processing of emotions

> 
>
>
> the review shows that each of these areas which are associated with emotional processing in general studies of emotions is also associated with an emotional processing in the context of music listening
>
> > auditory structure and auditory thalamus are not shown in the fig

Questions

Summary



WEEK 9: From Synapses to Free Will

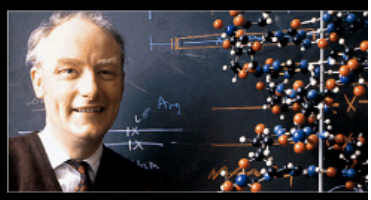
Kick Ending

- What did we learn?
- Neuroethics ("brain reading", brain intervention/augmenting cognition – ethical issues emerging from brain research)
- The question of "free will"?
- Disseminating knowledge at the digital age (*MOOC*, *Frontiers* and *Open Access idea*)
- A personal note, and farewell

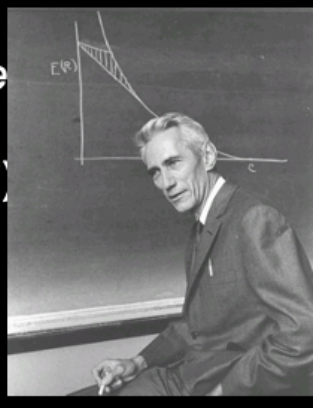
What did we learn?

"You, your joys and sorrows, your memories and your ambitions, your sense of personal identity and your free will are in fact no more than the behavior of a vast assembly of nerve cells and their associated molecules"

(Francis Crick, Nobel Laureate 1962 – "the father of DNA").



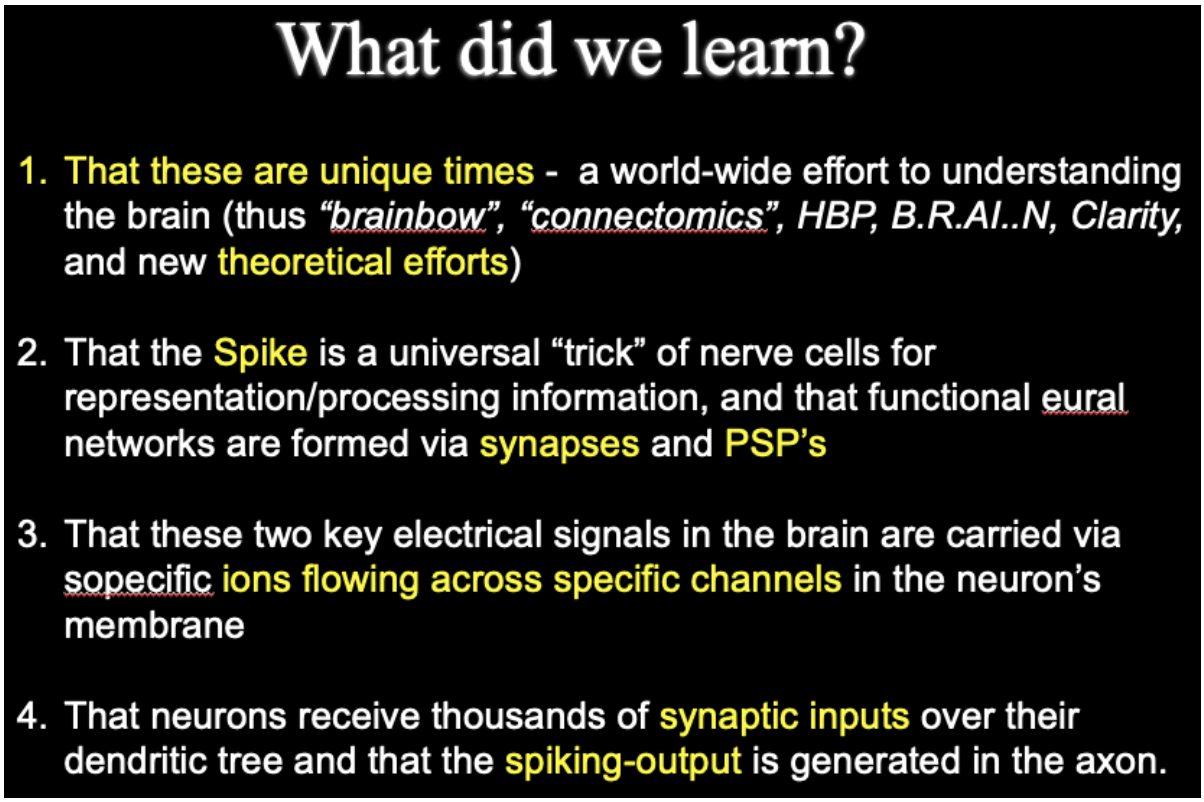
"Machine think? You bet! We're machines and we think, don't we?"
(Claude Shannon – "the father of information age")



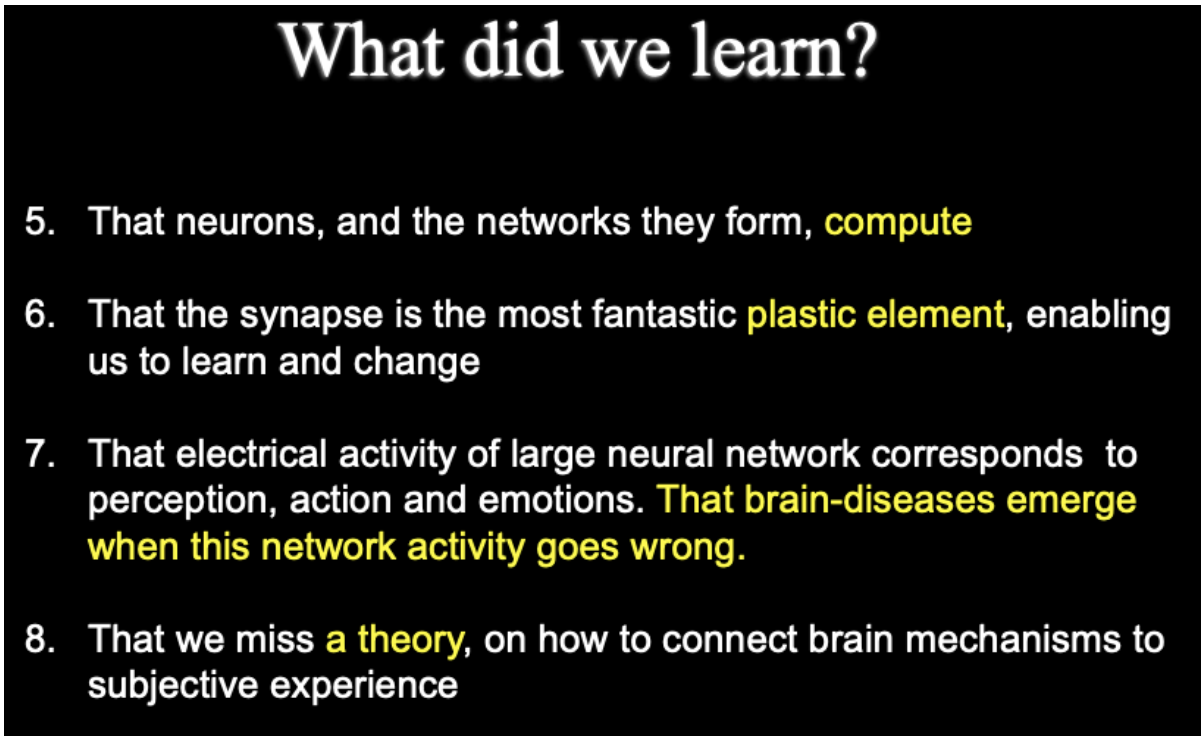
> in some way we are a mechanistic machine, a physical machine
>
> when you look into the brain, you will find the things that make us miracles:
>
> > genes, ions, membrane, channels, neurons, axons, networks
> >
> > and eventually something comes out of it

So what is the route to comprehend the brain?

Essence from the course

> 
>
>
> Techniques: brainbow, connectomics
>
> > Generating amount of anatomical and physiological data like optogenetics
>
> Projects: Human Brain Project, Obama Project
>
> theoretical framework: theoretically mathematical concepts, tools
>
> 2 key signals in the brain:
>
> > spikes mostly in the axon
> >
> > Post-synaptic potential in the dendrites
> >
> > > EPSP or IPSP
>
> the 2 key electrical signals are carried via specific ions flowing across specific channels in the neuron's membrane

Neuron is an input-ouput microprocessor taking many synaptic input converging on its dendritic tree and sum, integrate and eventually come get to the soma near the axon soma region where they spike output is generated (consider neuron cells as very sophisticated microchip with 2 separate regions-the input region, there are many synapses impinging and converging decorating the dendrite and the axon there are the spikes output)



the neurons compute from the information they collect from the environment plus memory processes. during learning, tell them what to do with this information so that the computation will become more and more efficient, more and more relevant, more and more adaptive. So animals could survive.

> we borrowed the notion "compute" from computer science but the it is different from the notion in cs
>
> brain computing is not only used for animals behaving in the environment but also change the environment
>
> > Perception-action loop

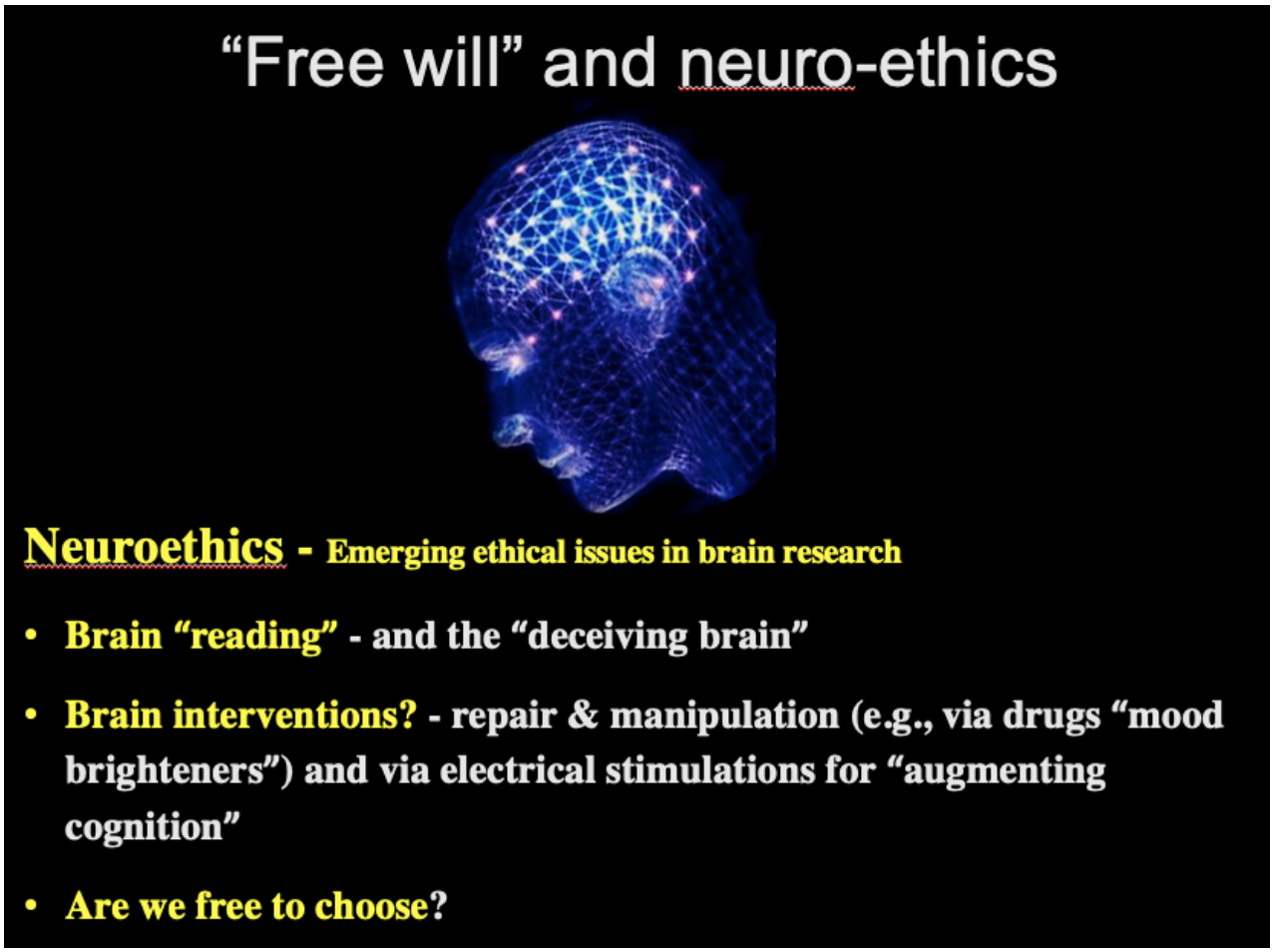
Neuron and synapses (especially synapses) have plasticity

> very minute and plastic
>
> > functional: more or less efficient
> >
> > Structural: more or less synapses
>
> **plasticity underlying the uniqueness of the brain and its capability to interact to the ever changing enviroment**
>
> **Synapses are the miraculous aspects of the brain for its capability to connect and change adaptively**

millions of neural networks exist in our brain

> > diseases will show up when something go out of balance due to connectivity within the network or due to excitability that goes wrong within the network or combination of many parameters go wrong
>
> > so suddenly the whole network starts to generate a new electrical phenomena/activity like Parkinson
>
> > > nowadays the neuroscience needs to go beyond the single cell and gene to the whole network and understand how a connected network of elements interacting in the brain generate a disease/feeling
> > >
> > > Which means we need to go beyond the unit
> > >
> > > so we need a theory for large elements interacting and generating dynamically and adaptively phenomena to behave
>
> Theory: from gene neuron to network neurons

Reading Thoughts



> Neuroethic

Reading Thoughts

“Reading thoughts”?

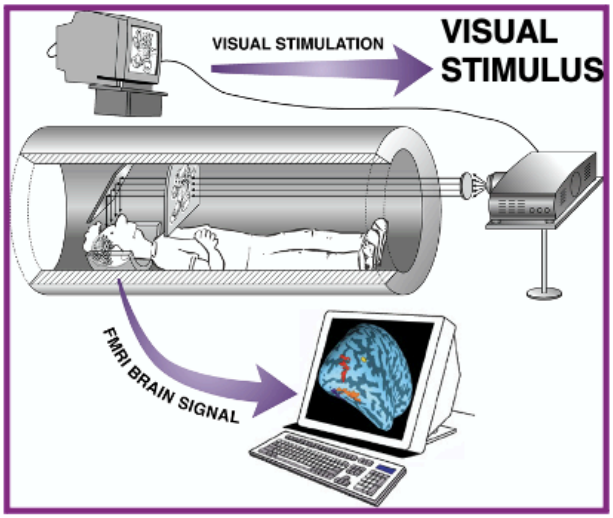
- Privacy
- Reproducibility (accuracy)
- Individuality (how similar/different are our “personal” brains?)

Examples:

Scanning the (“social”) brain:

Functional Magnetic Resonance Imaging (fMRI)

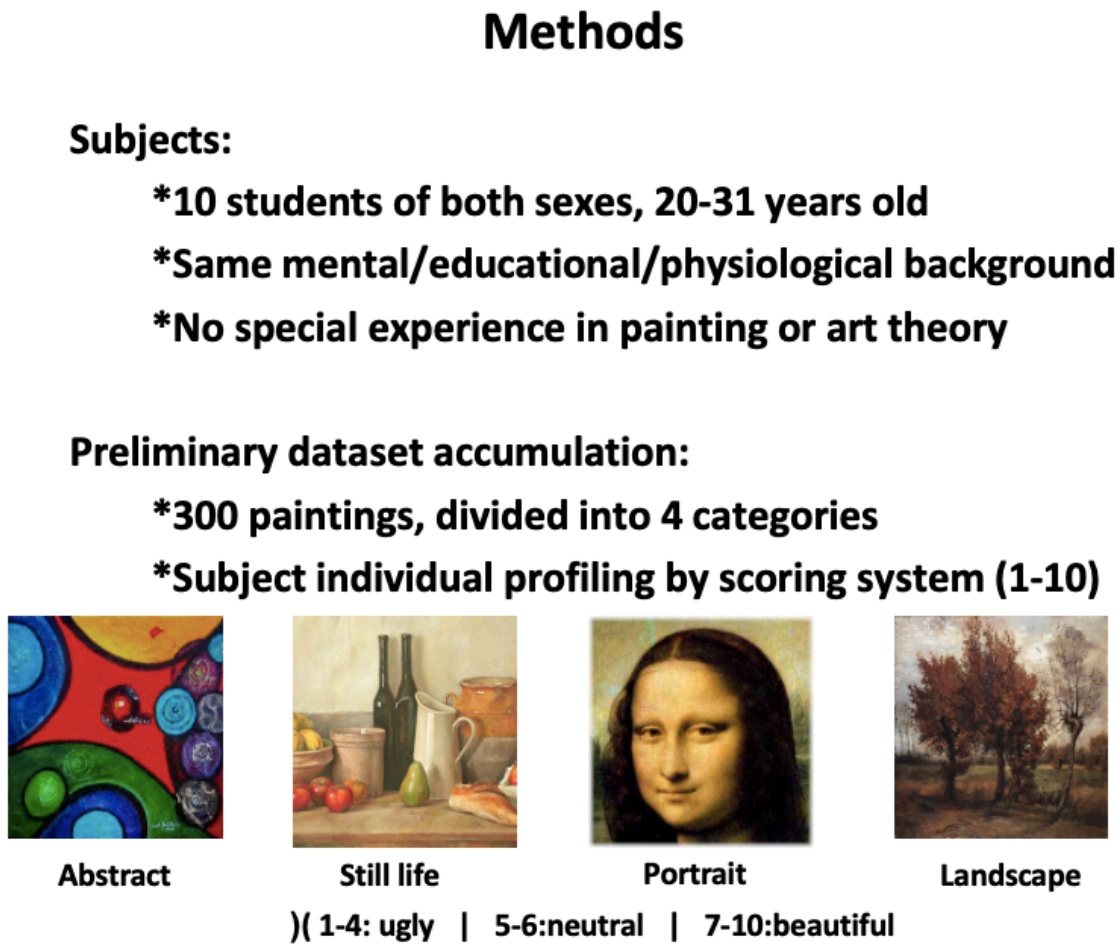
1. Detecting brain functions in health and diseases
2. Communicating with the brain in vegetative states
3. Detecting beliefs? Intentions? (e.g., lie, aggression), tendencies (and more?)



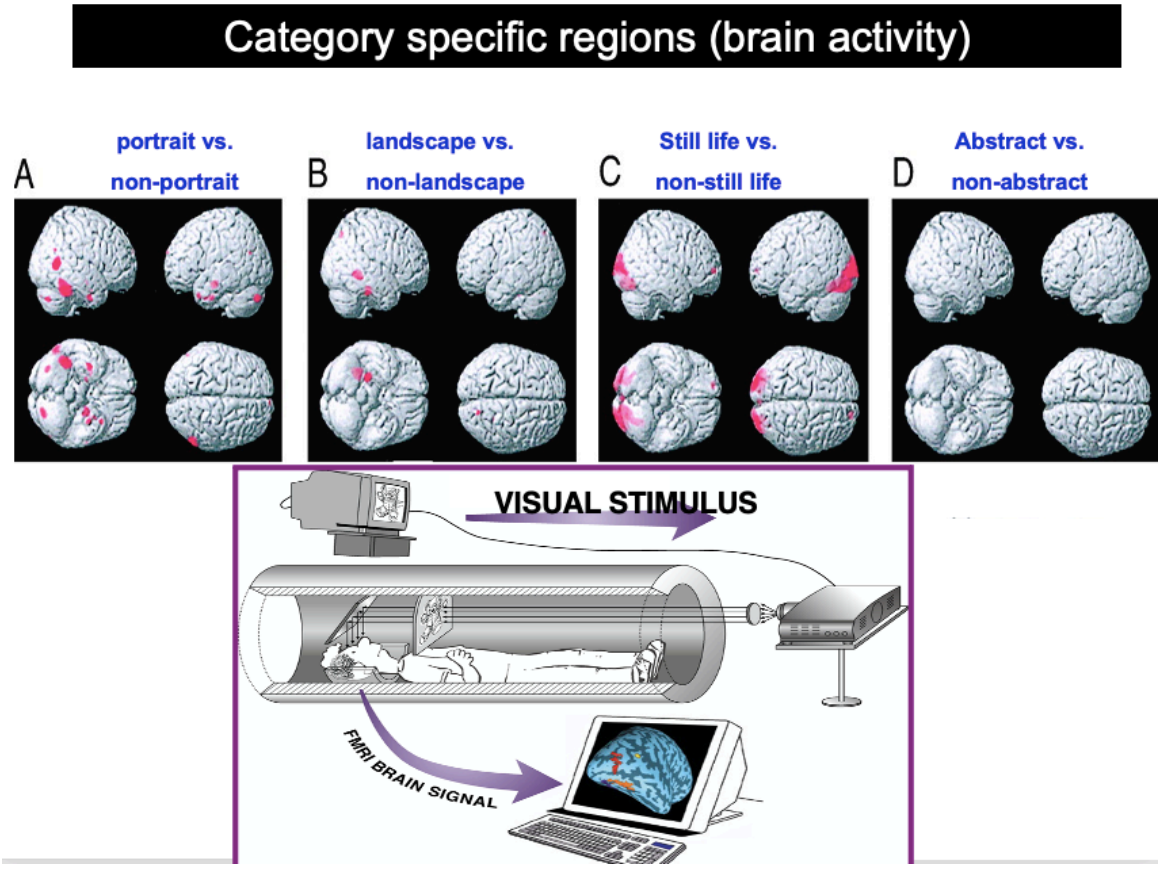
I. Levy, Hebrew University & R. Malach, Weizmann Institute

> functional MRI
>
> > see which region of your brain is now overactive electrically
> >
> > when your brain is active, it will require extra oxygen and energy to build up the electrically active synaptically region. So more oxygenated blood is flowing to this region.
> >
> > So you can see through the MRI to find out the region with more blood flows. MRI records blood flow rather than direct electrical activity.

> we can use the MRI machine to look at normal people and diseased people who cannot interact otherwise, which is called vegetative state.
>
> > now we can know the brain is processing faces by analyzing the MRI pics
> >
> > > which looks almost the same in most people's brain
> > >
> > > *general things*
> >
> > by using machine learning and training people to look at the same face again and again we can know the brain is processing this particular face by calibrating the brain and analyzing the particular detailed activity
> >
> > > personal activities in different brain

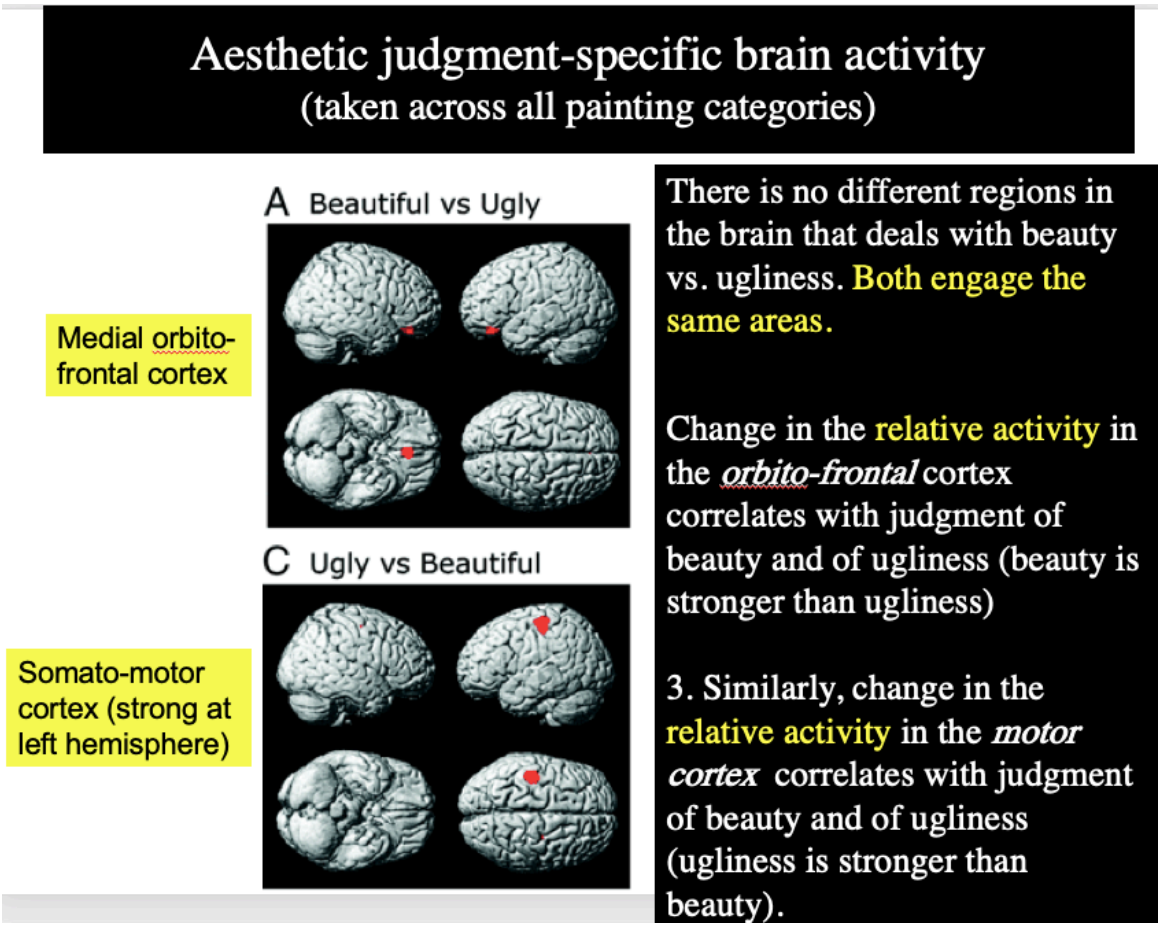


> Imaging the brain during aesthetic experience by Kawabata & Zeki "Neural correlates of beauty"



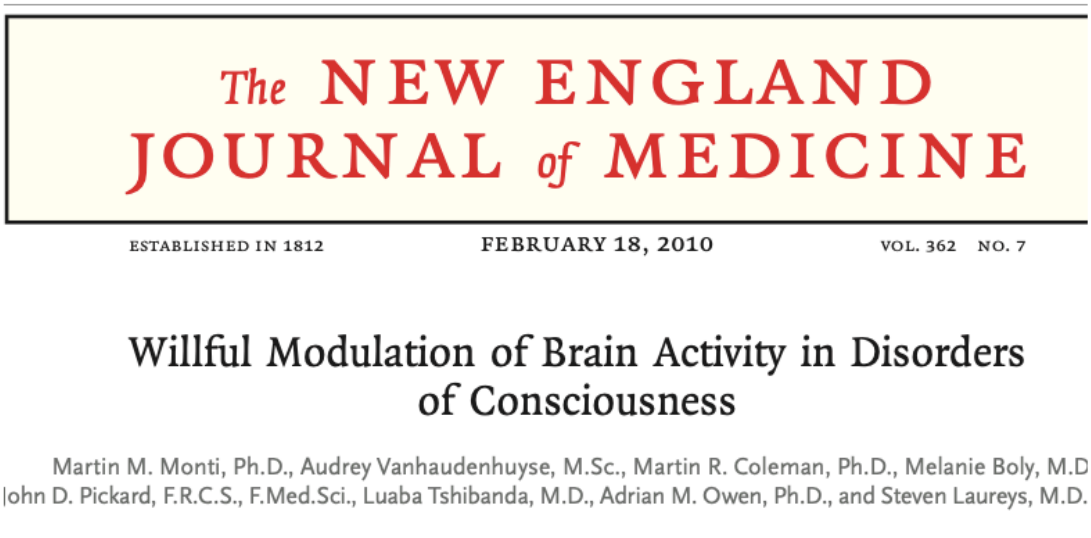
> it shows that there is a particular region in all our brains to process specific class of images

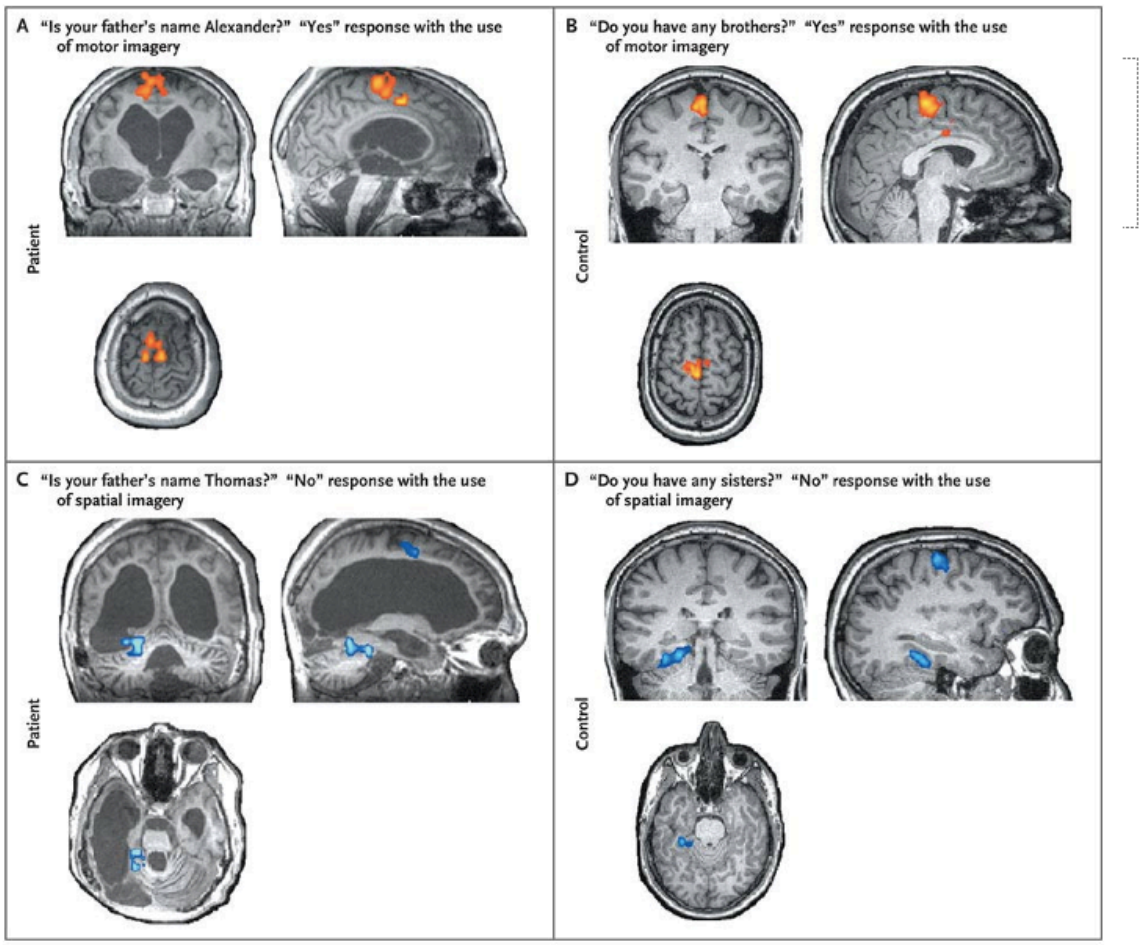
The question are the regions that responds specifically to your liking or disliking? To your personal preference of whether this is ugly or beautiful. Beyond the category, beyond the particular category?



> general region for people like or not
>
> So, so, whenever you see something that is, either you like it or you feel it's ugly Both regions are activated. It's not that this only this region is activated when you like it and only the mortar cortex is activated when you don't like it. **Both regions are activated. But one is activated more than the other**. So both engage the same areas, both ugliness and beautifulness engage the same position but with different proportions.
>
> so these 2 regions response to your private feeling of ugliness or beautifulness.
>
> > the use of MRI to read your preference

So this technique can be used in:





you can ask yes or not questions and instruct the vegetative patients to imagine activity A when the answer is yes and imagine activity B when the answer is yes

then scan their brains with MRI machine

we can interact with unconscious patient

Issues of brain polygraphs

Brain polygraphs?
(EEG and fMRI)

Probing the brain with fMRI for: Lie-detection
"Accessing brain activity goes to the very source of the lie"

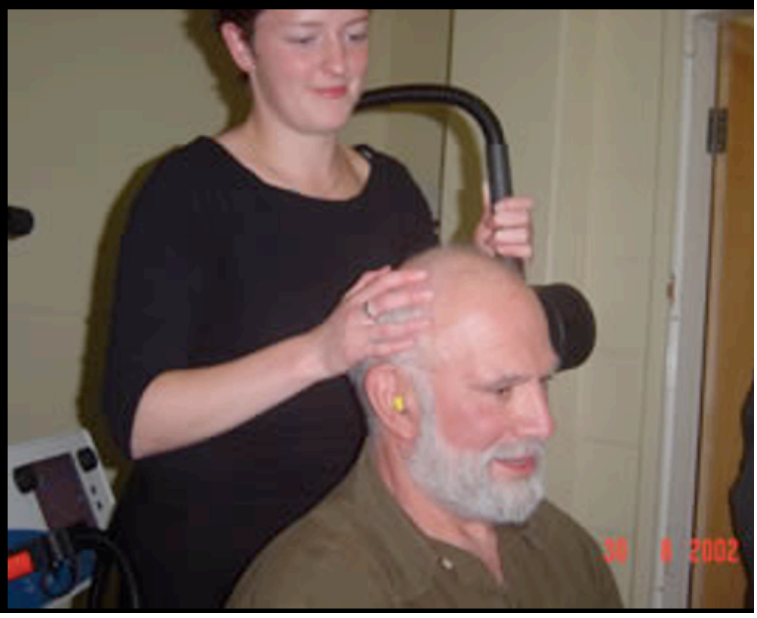
Detecting thoughts and feelings while interacting with someone of a different race.

but no need to be frightened:

> **General Issues for Future Discussions**
>
> - Success rate? (Noise and variability)
> - Calibration (personal)
> - How does it compare with regular polygraphs?
>
> > the MRI/EEG has noise and success rate is low
> >
> > if need to read a particular brain, you need to calibrate this person first (issue of personality)
> >
> > it is not at the level of cell

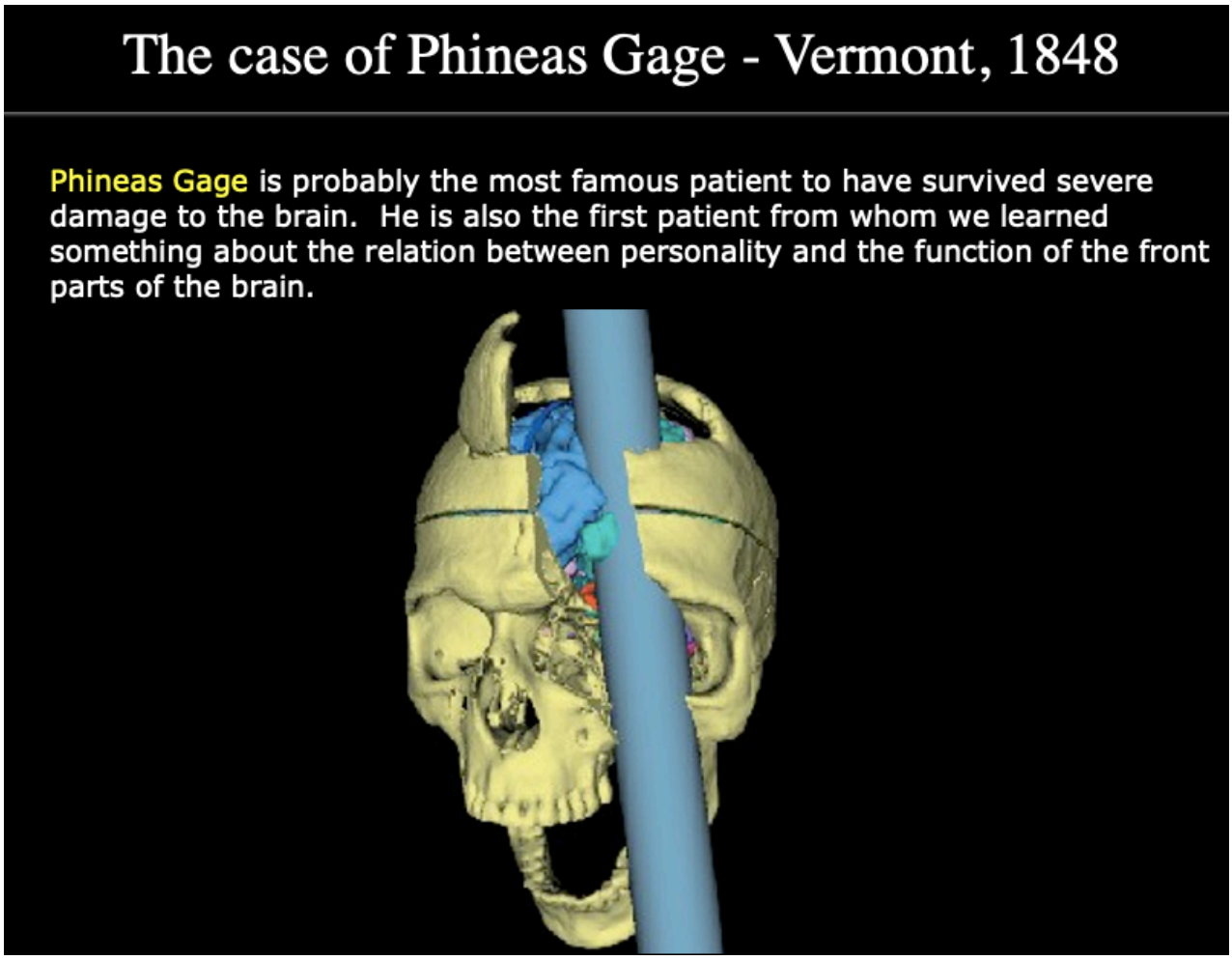
Free Will?

Transcranial Magnetic Stimulation (TMS)

> **Noninvasive Probing of the Living Brain**
>
> e.g., Transcranial Magnetic Stimulation (TMS)
>
> Oliver Sacks
>
> Receiving (TMS) at Snyder's lab. (Australia)
>
> Started to draw better?
>
> 
>
>
> early example:
>
> > used to activate a large region of cells and get to know what this region is responsible for
> >
> > > or sometimes needed to be used for depressive patients (clinical use)
> > >
> > > this machine has already proven itself to be useful for some depressed persons

> But whether the machine will enhance human cognition or not?
>
> > Still question

Free will issue



> Phineas Gage, the very first person (a famous patient) who revealed the relationship between brain region and personality

The case of Phineas Gage - Vermont, 1848

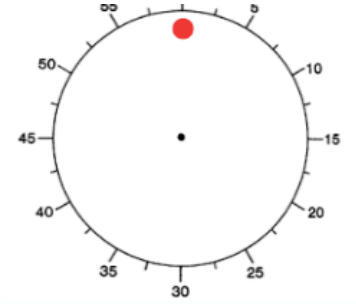
Some months after the accident, probably in about the middle of 1849, Phineas felt strong enough to resume work. But because his personality had changed so much, the contractors who had employed him would not give him his place again. Before the accident he had been their most capable and efficient foreman, one with a well-balanced mind, and who was looked on as a shrewd smart business man. He was now fitful, irreverent, and grossly profane, showing little deference for his fellows. He was also impatient and obstinate, yet capricious and vacillating, unable to settle on any of the plans he devised for future action. His friends said he was "No longer Gage."

Are we completely defined by the deterministic nature of physical laws? Are we essentially sophisticated automatons only, with our conscious feelings and intentions tacked on as epiphenomena with no causal power? (cf. Thomas H.Huxley)

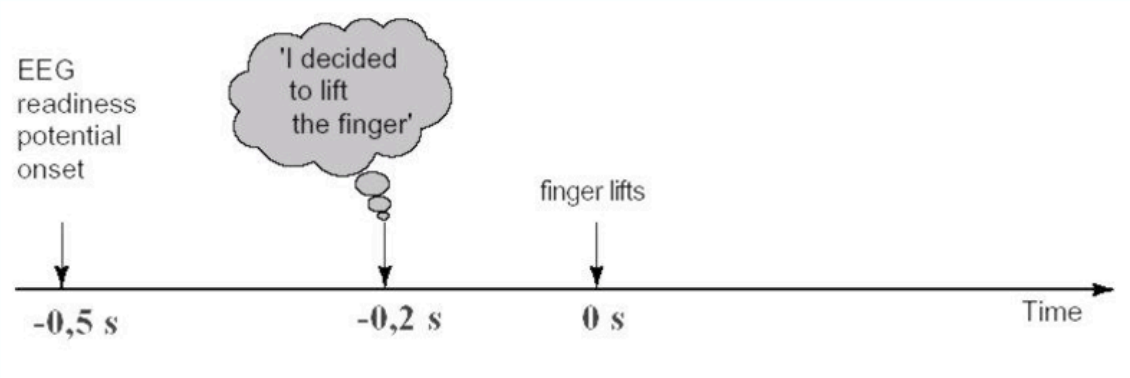
Or do we have some independence in making choices and actions, not completely determined by the known physical laws?

The greatest gift which humanity has received is free choice. It is true that we are limited in our use of free choice but the little free choice we have is such a great gift and is potentially worth so much that for this itself life is worthwhile living. (Isaac Bashevis Singer 1968)

Benjamin's Lab Experiment

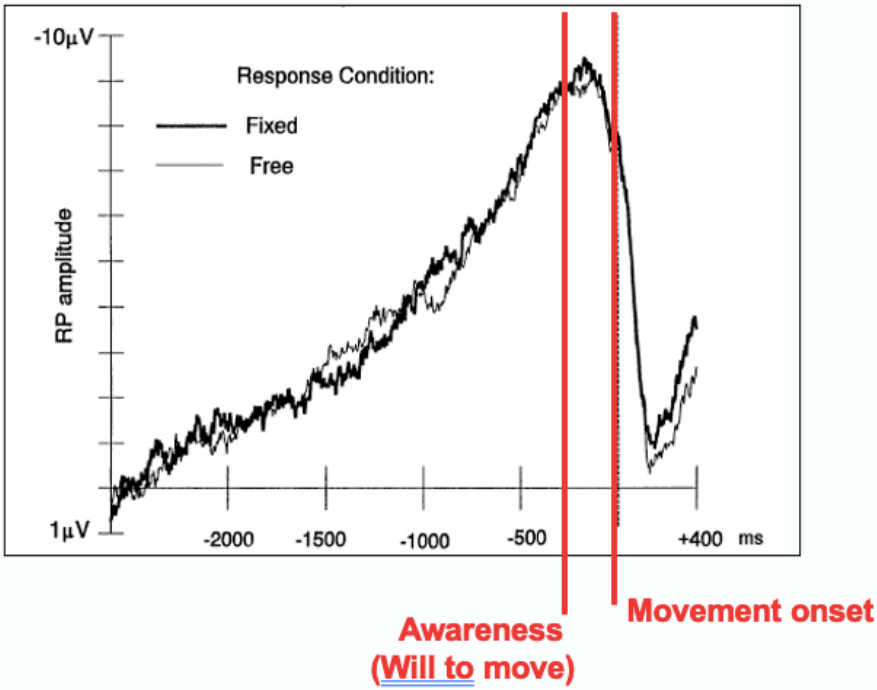


Benjamin Libet's experiment



- Libet et al. (1983). *Time of conscious intention to act in relation to onset of cerebral activity (readiness potential): the unconscious initiation of a freely voluntary act.* **Brain** 106, 623≲642.

The "readiness potential" – Libet experiments



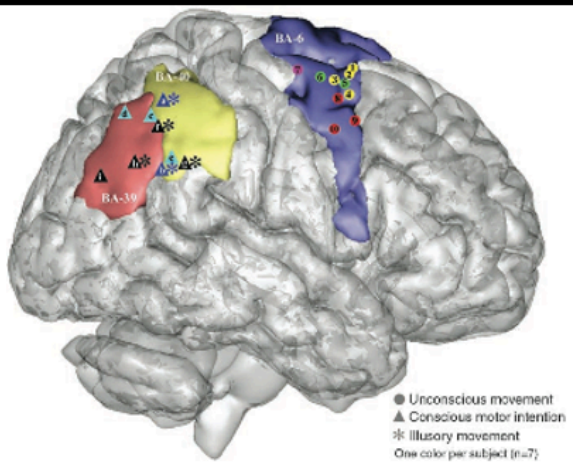
long before your final decision be made, your brain is active for almost 2 seconds and you are not aware of it

so do we have free will? What kind of free will do you have if you are not aware of what you are going to do and you don't know when you are going to do?

Libet's findings have been widely taken to show that since our brain has already started preparing to flex the wrist before we even become aware of our intention to flex it, our supposedly free will is not free at all. Rather, our brain has decided for us and has started a causal chain leading to the finger-bending, before we become aware of our decision.

Thus, our will appears determined and causally irrelevant.

Movement Intention After Parietal Cortex Stimulation in Humans
Michel Desmurget et al., Science 2009



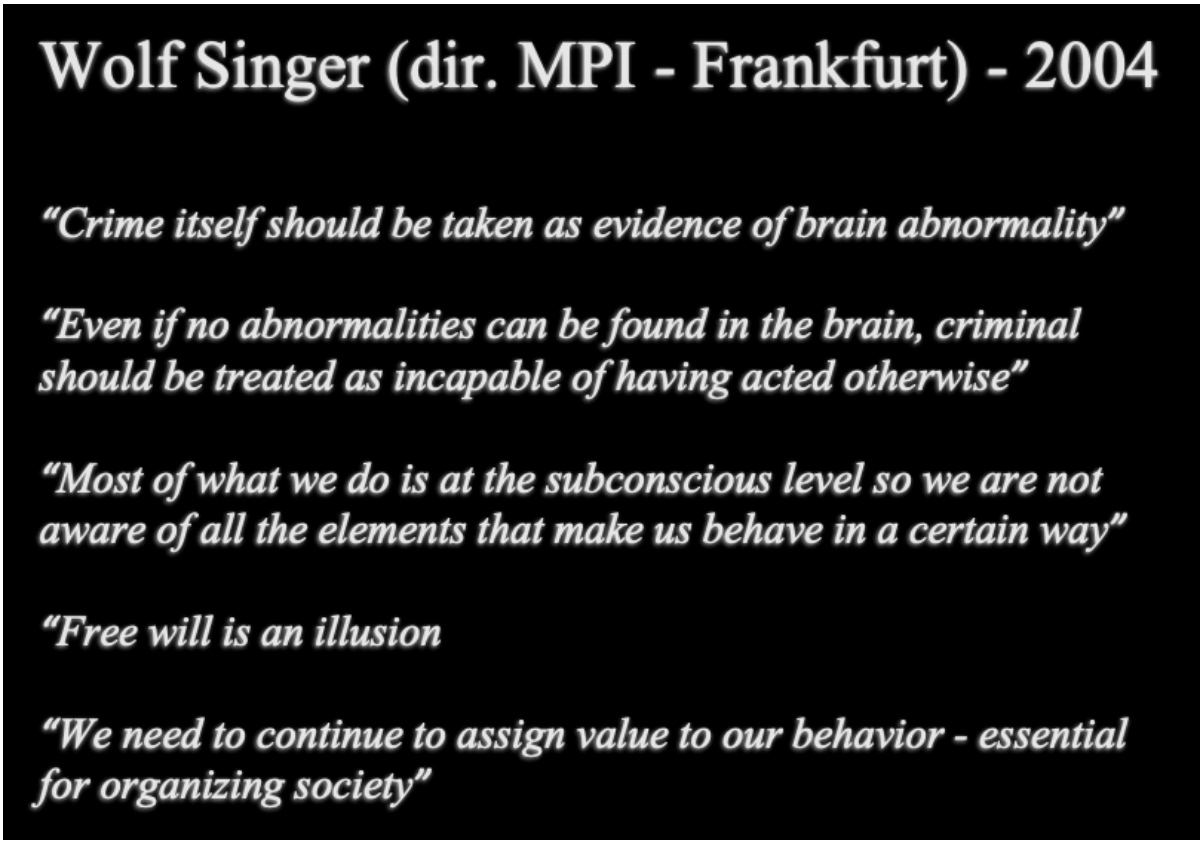
Left/right inferior parietal regions: **No movement, no EMG BUT**

Low-intensity : "I felt a desire to lick my lips" " (▲Conscious motor intention)

Higher intensity: "I moved my mouth, I talked, what did I say?"" (* Illusory movement)

Premotor regions: Low + strong stimulation, **movement without awareness**

> Patients will show particular (simple) behaviors when being stimulated particular brain region and are not aware of it.



> *The other aspect, is that in terms of ethics, because I drive in red light, because I am a criminal, you may continue to put me in jail, not because I decided to be a criminal, but because I am dangerous to you.*

The EEG experiment by Benjamin LIbet is flawed: debate on "readiness potential"

> Libet showed consistently that there was unconscious brain activity associated with the action—a change in EEG signals that Libet called "readiness potential"—for an average of half a second before the participants were aware of the decision to move. This experiment appears to offer evidence of Wegner's view that decisions are first made by the brain, and there is a delay before we become conscious of them—at which point we attribute our own conscious intention to the act.
>
> However, if we look more closely, Libet's experiment is full of problematic issues. For example, it relies on the participants' own recording of when they feel the intention to move. One issue here is that there may be a delay between the impulse to act and their recording of it—after all, this means shifting their attention from their own intention to the clock. In addition, it is debatable whether people are able to accurately record the moment of their decision to move. Our subjective awareness of decisions is very unreliable.
>
> An even more serious issue with the experiment is that it is by no means clear that the electrical activity of the "readiness potential" is related to the decision to move, and to the actual movement. Some researchers have suggested that the readiness potential could just relate to the act of paying attention to the wrist or a button, rather the decision to move.

> > Others have suggested that it only reflects the expectation of some kind of movement, rather being related to a specific moment. In a modified version of Libet's experiment (in which participants were asked to press one of two buttons in response to images on a computer screen), participants showed "readiness potential" even before the images came up on the screen, suggesting that it was not related to deciding which button to press.

QUIZ

1. What are the main factors that limit the capability for "thoughts reading"?

   > The brain is very noisy, its response varies between repetitions of similar "thoughts"
   >
   > Not all brains are alike - Different brains code/represent specific details (e.g., particular face) differently. This implies that one must calibrate the reading machine (e.g., fMRI) to a specific brain
   >
   > ❌It is impossible to read brain activity without intervening and thus changing it

2. Mark the correct sentences about Functional Magnetic Resonance Imaging (fMRI)

   > A fMRI signal detects brain activity at a spatial resolution corresponding to the activity of millions of cells.
   >
   > fMRI measures brain activity of different areas by detecting changes in blood flow.

3. Mark the correct sentences:

   > Different brains detect faces in similar "object related" brain regions
   >
   > We may learn what face is particularly represented in the brain using calibration and repetitive fMRI
   >
   > To date, it is impossible to write down an algorithm that outputs from a single fMRI or EEG trial, what particular face is being processed

4. Mark the correct sentences about the research by Semir Zeki and others regarding the neural correlates of beauty

   > A Particular region in the brain is active when a portrait image is displayed
   >
   > A Particular region in the brain is active for a (subjectively assessed) beautiful painting, independently of the paining category
   >
   > "Beautifulness" is coded in enhanced activity at the orbito-frontal cortex and reduced activity in the motor cortex
   >
   > ❌A Particular region in the brain is active when an abstract painting is displayed

5. Mark the correct sentence:

   > We can use fMRI signals to differentiate between "yes" and "no" by teaching the locked in patient to activate different regions in the brain corresponding to the desired answer.

6. Mark the correct sentences about Transcranial magnetic stimulation (TMS):

> TMS is being used to treat depression
>
> TMS is a noninvasive method that enables the experimenter to induce activity in particular brain region.
>
> ❌TMS is a noninvasive method that generates an electrical field in the brain, enabling the experimenter to induce activity in specific cortical neurons
>
> ❌TMS is being used medically to induce continuous improvement in motor activity

7. From the case of Phineas Gage we may learn that:

> we might have limited freedom to choose also with a non-injured brain
>
> Physical changes (damage) in the brain can induce change in personality

8. According to the (EEG) experiments of Benjamin Libet:

> The movement-related brain activity starts seconds before we become aware that we "decided" to move
>
> There is time gap between the awareness (the will to move) and the onset of the movement
>
> ❌That it is possible to read from brain activity at what time we decided to move (when we became aware of our decision)

9. Using local stimulation in the brain:

> We can trigger the subject's will to perform an action "conscious motor intention" and we can also trigger illusory movement (subject feels he moved, but he did not).
>
> We may trigger an action without the subject's awareness to the action.
>
> ❌We can trigger the will to do an action but not the action itself.

WEEK 10: Final Exam

Basically as sam as quizs