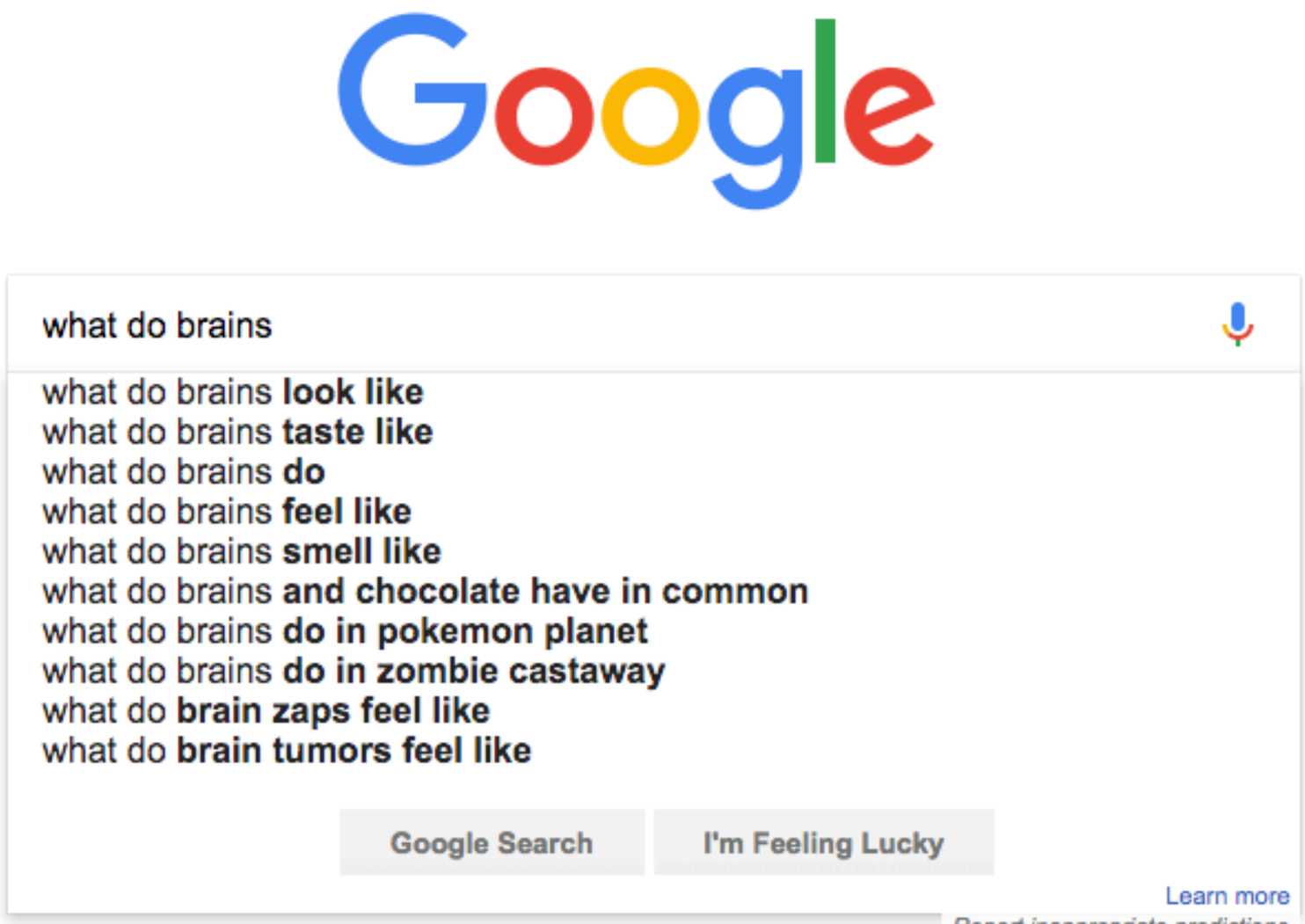
Cognitive Neuroscience

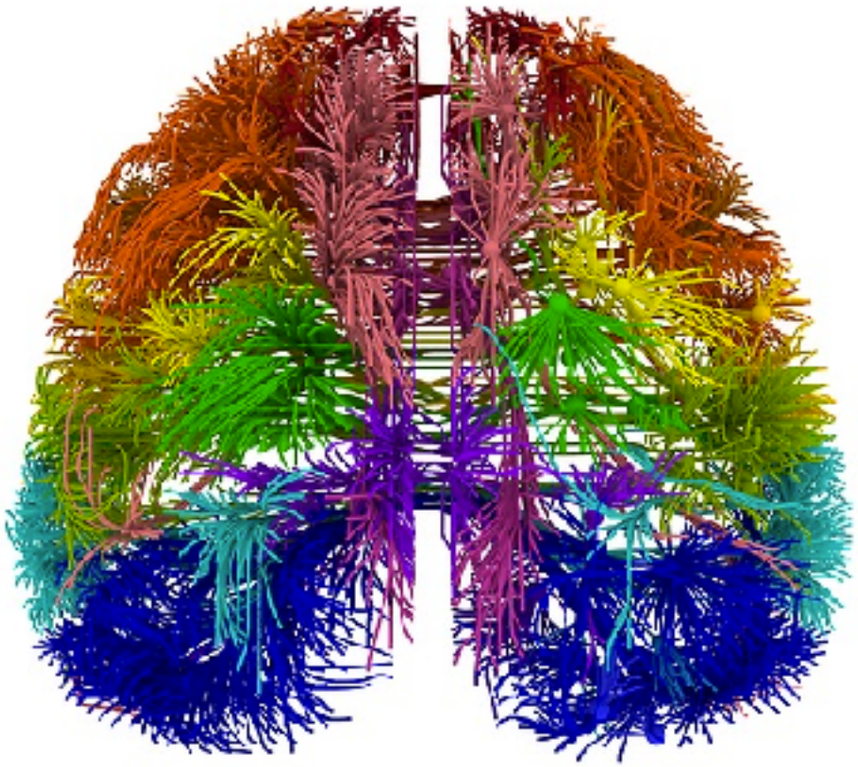
Merely scratching the surface . . .

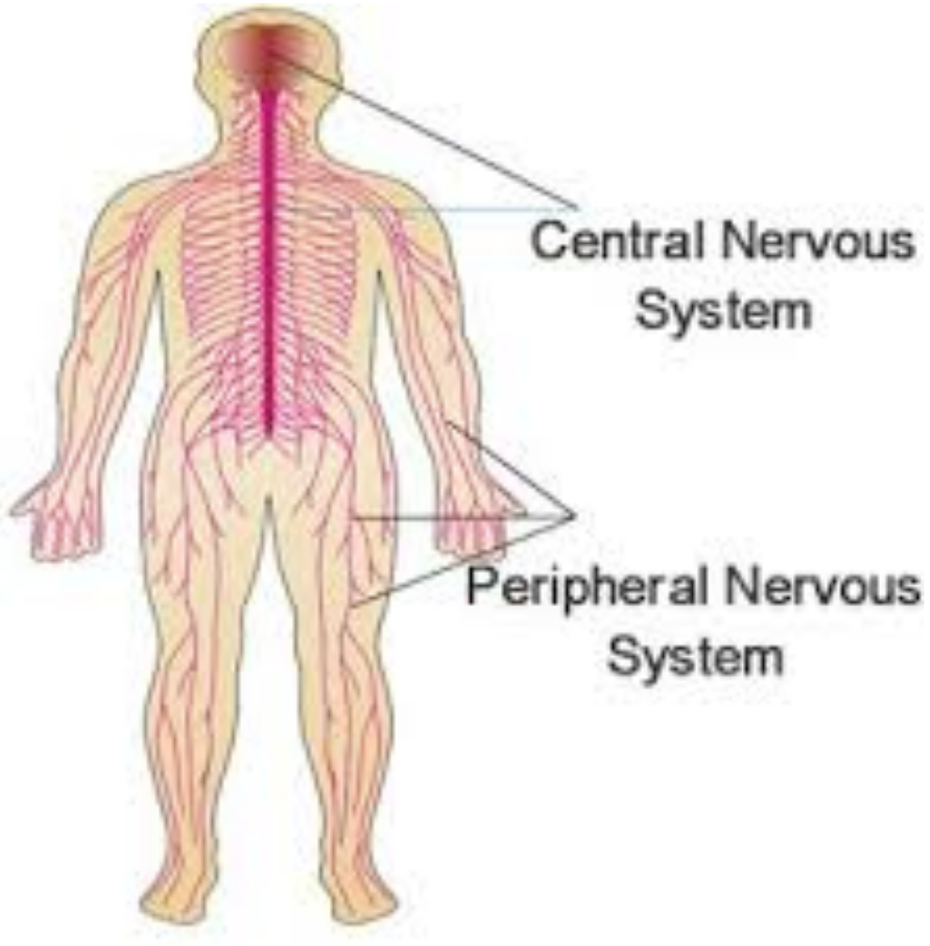


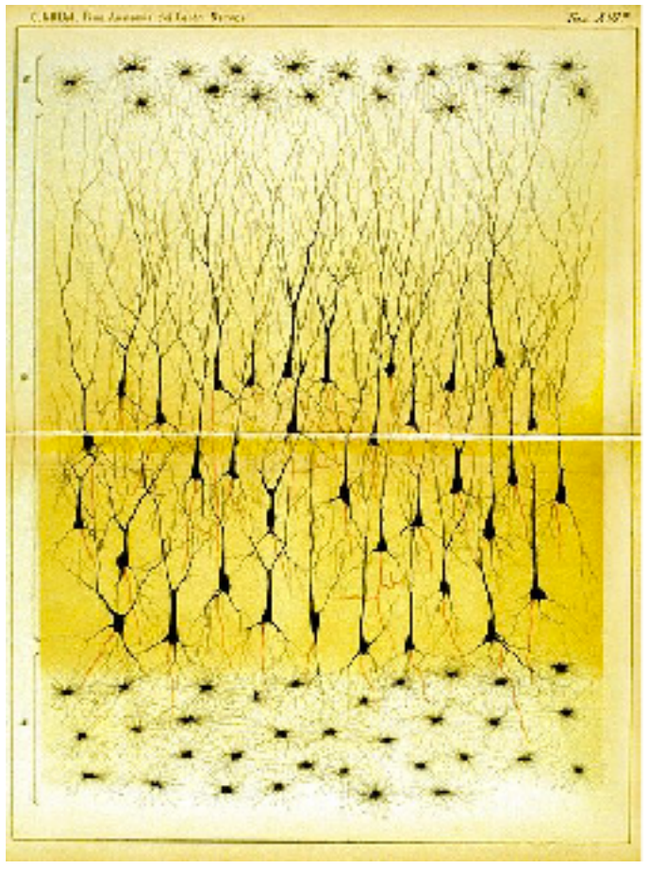
They’re made out of meat

Dir: Stephen O’Regan
Story: Terry Bisson

There's Neuroscience . . .







. . . and there's Cognitive Neuroscience

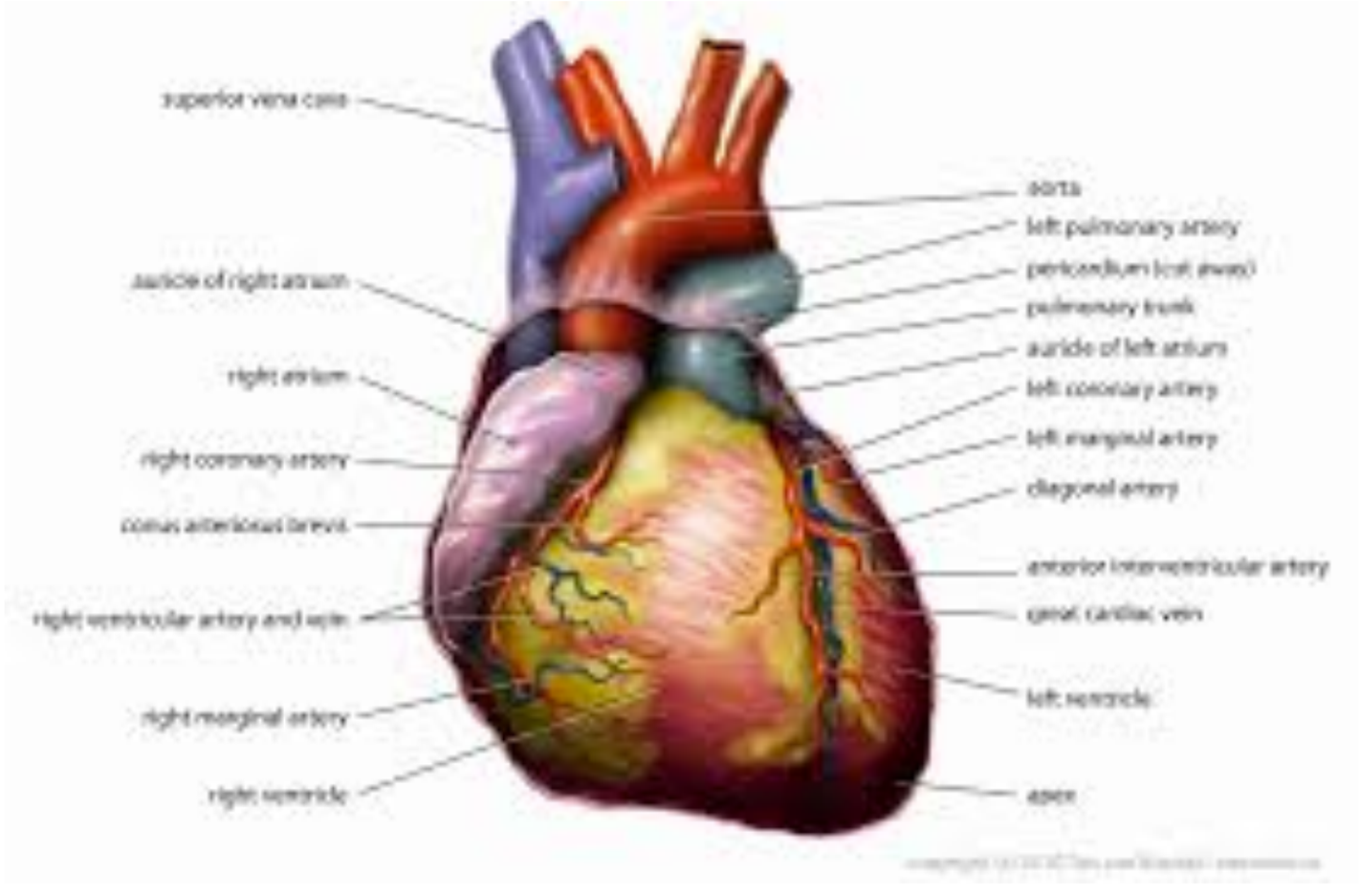
In which we try to understand the structures and processes in the nervous system in terms of . . .

- Psychological predicates (attention, emotion)
- Psychological theory (representations)
- Cognition (what is that?)
- Function

What is all that stuff doing?
What is it for?

Let’s look at that word:

function



What is the function of the heart?

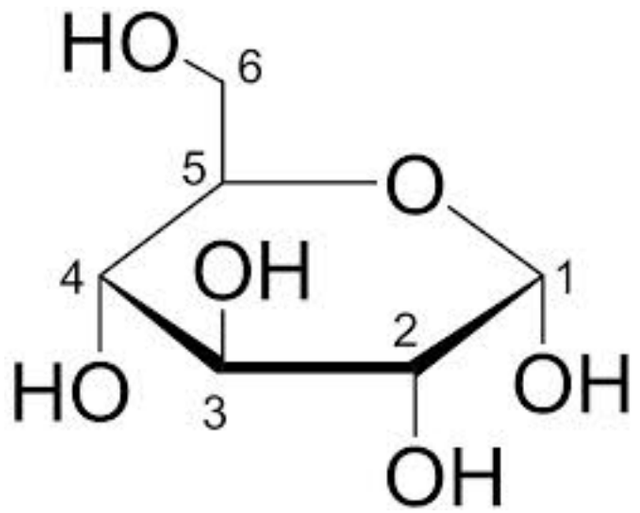
What is it for?

What is the function of litter?

What is it for?

What is the function of glucose?

What is it for?

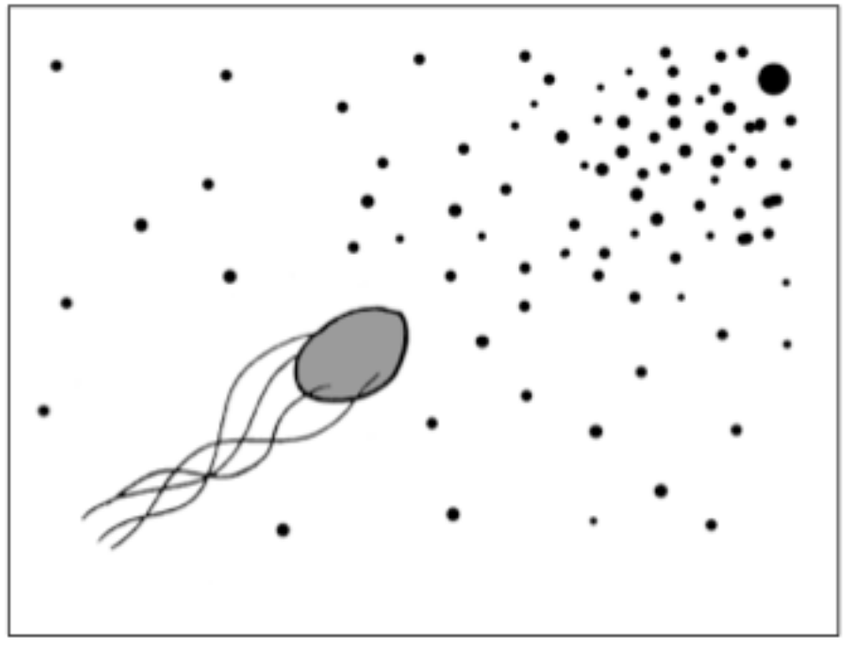


When we say the heart is *for* pumping blood, that statement is licensed by a background assumption that we are talking about a particular systemic perspective: the healthy human body.

“Function” requires framing.

Functions are not simply there.

From a suitably disinterested perspective, glucose is not *for* anything. No more than copper, lead, xenon, hydrogen, or Jupiter



For a bacterium swimming in a glucose-rich medium, glucose is *for* metabolism.

The function is not simply given.

It demands that we frame our statements appropriately.

(A similar point can be made with respect to that vexed term *information*)

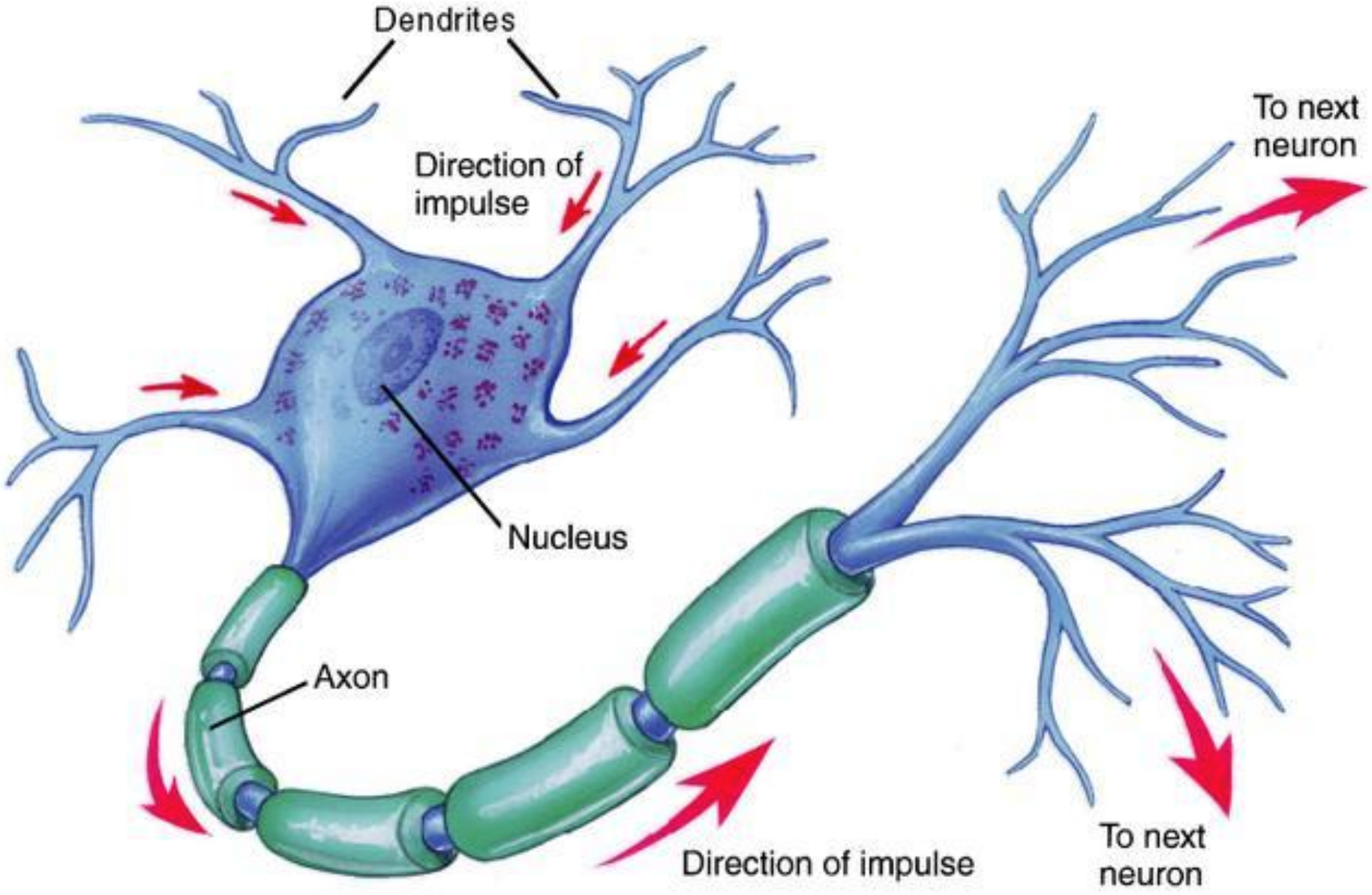
And so the cognitive neuroscience we can do will depend upon our background framing and assumptions.

If you frame the issue one way, you may identify this or that function.

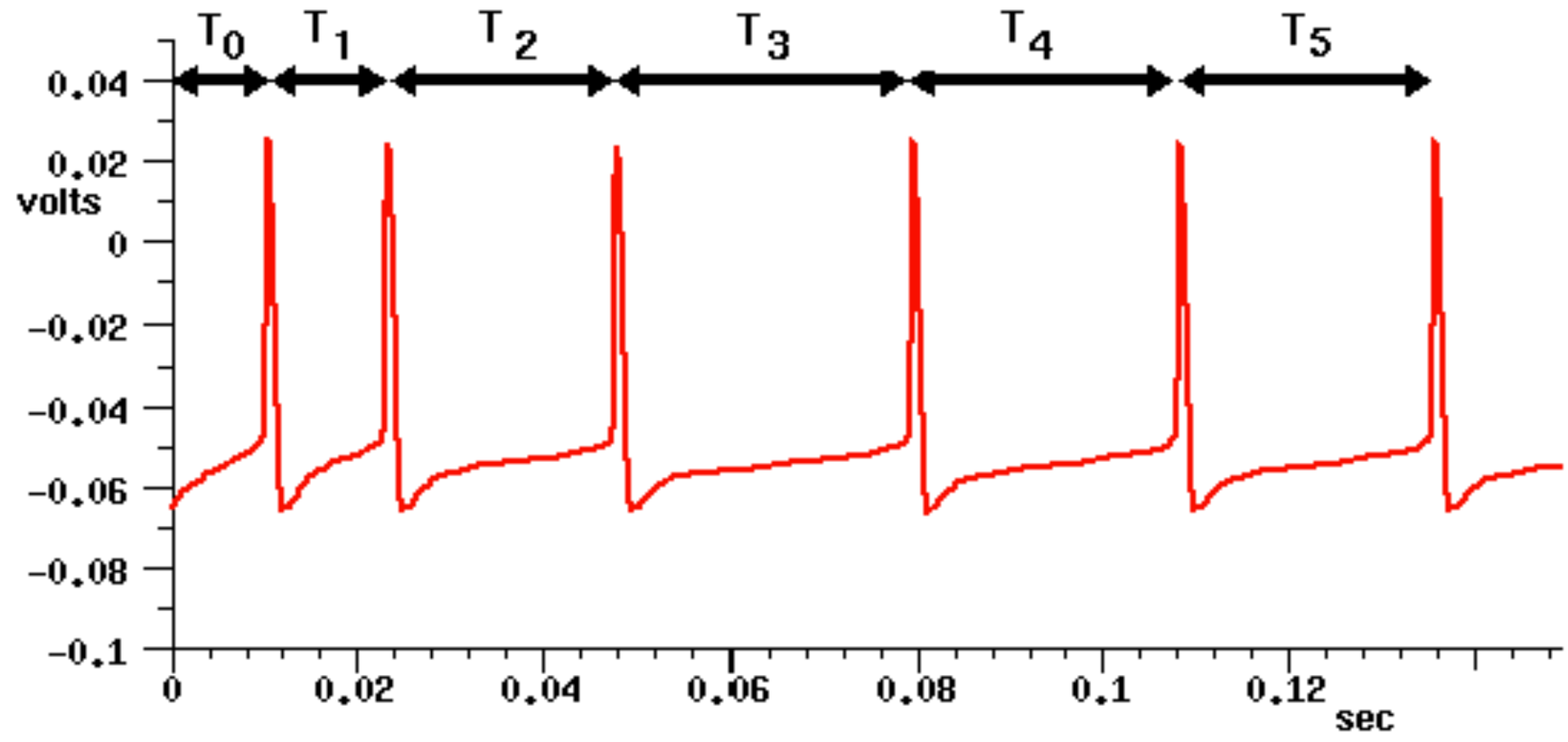
If you frame it differently, you may see something different.

There is little agreement on such matters, and in practice, scientists are terrible at providing the necessary framing considerations before launching into talk of function.

The Neuron Doctrine



The neuron as we now know it (grossly simplified)



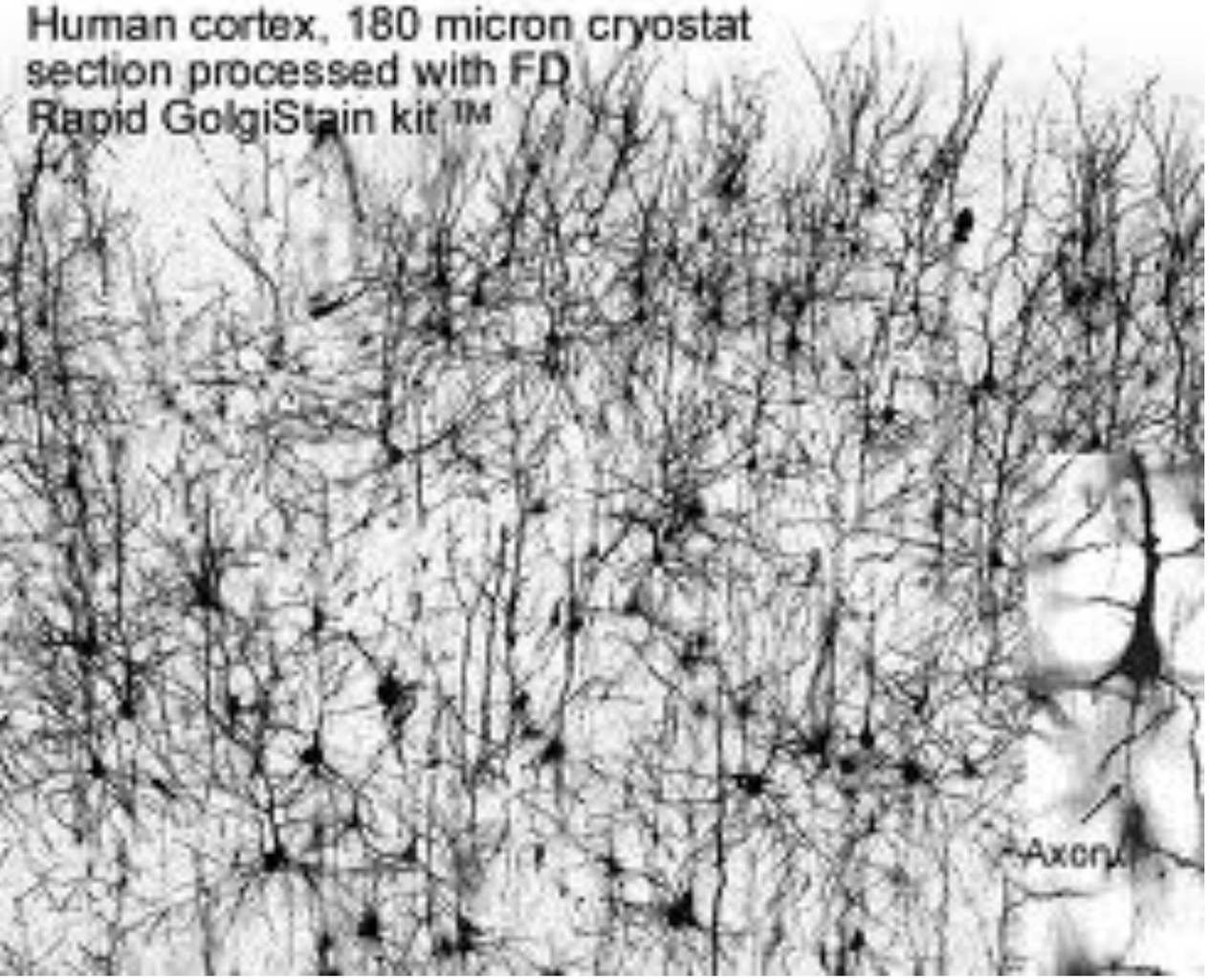
Action potentials (spikes) as discrete events.

A historical debate:

1906, the Nobel Prize for Physiology or Medicine is shared for the first time.

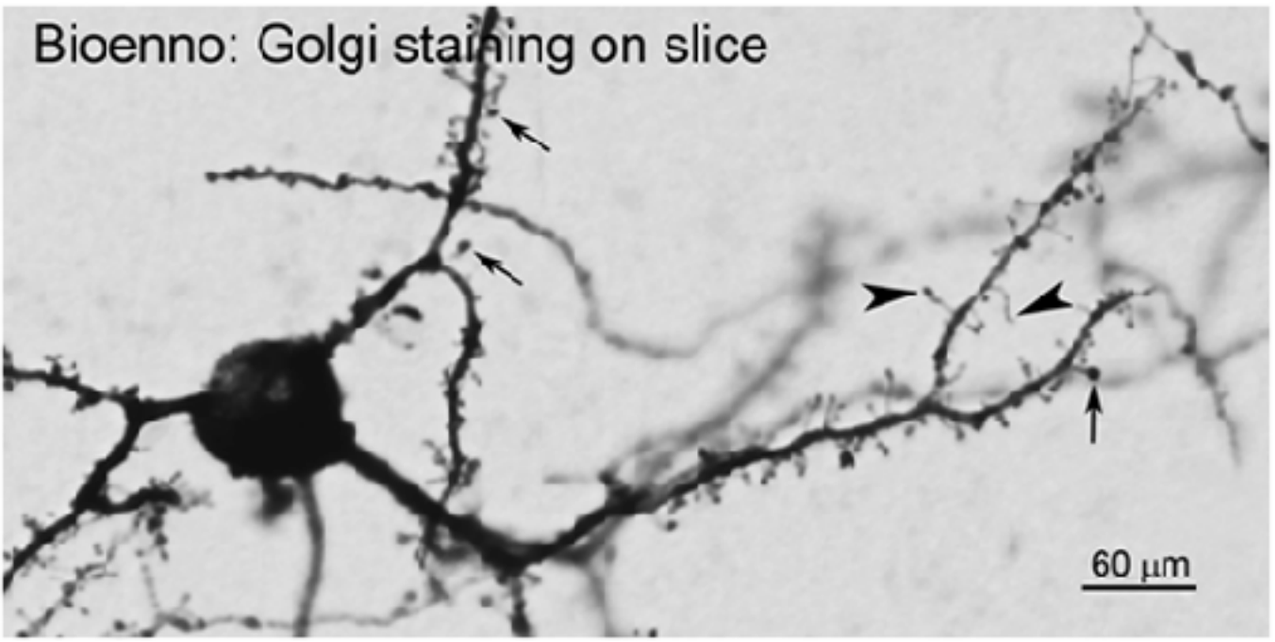
Ramón y Cajal

and Camillo Golgi



Golgi's staining technique with silver nitrate allowed unparalleled imaging of individual neurons and their connections.

Both men worked with these techniques



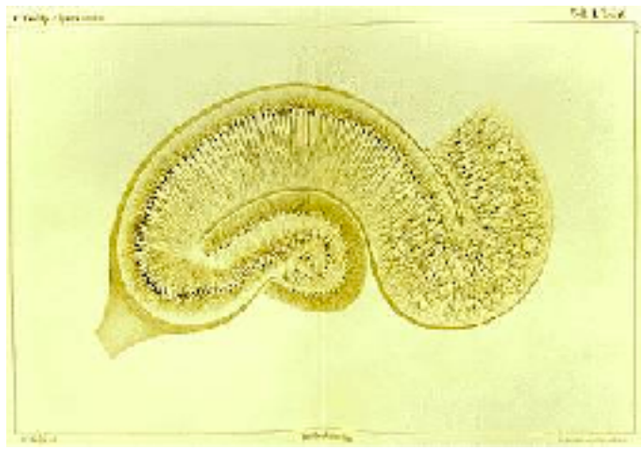
But they differed greatly in what they thought the basic *functional* element of the nervous system was

Golgi: Reticular theory

Neurons were not functionally, developmentally, or structurally independent.

The basic functional element within the nervous system was the distributed nervous network.

There was a unity to the nervous system that defied decomposition into independent units.



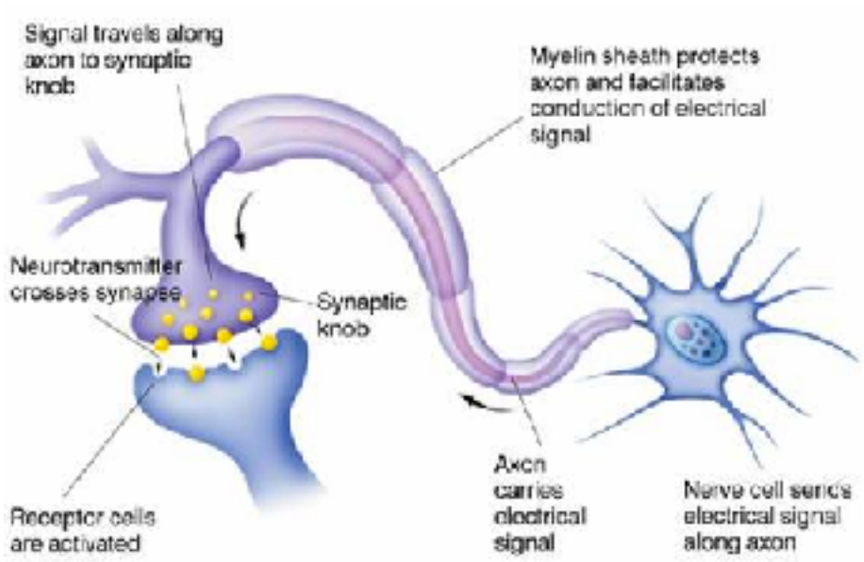
Cajal: The Neuron Doctrine

Each neuron was autonomous, receiving inputs at the dendrites, generating an all-or-nothing action potential that travelled down the axon.

Connections to other neurons were across a gap.

Neurons were thus each individual entities.

Many details we now take for granted (e.g. the role of neurotransmitters) were still unknown



The acceptance speeches must have been something to see.

Golgi spoke first. Everything he said was anathema to Cajal.

Cajal later accused him of having a “strange mental constitution” that was “hermetically sealed” against criticism by its “egocentricity”.

Cajal’s view won the day though, and the neuron doctrine has reigned supreme for 100+ years.

But it is in sore need of qualification. Since then, we have discovered:

* direct electrical connections between neurons
* spikes going the “wrong way”
* apparent computational activity in glial cells (previously thought to be mere insulation)
* dendrites producing spikes
* tri-partite synapses (the synapse as complex feedback modulated system)
* etc etc etc

See the required reading for more

Fast forward to 2014

Human Brain Project

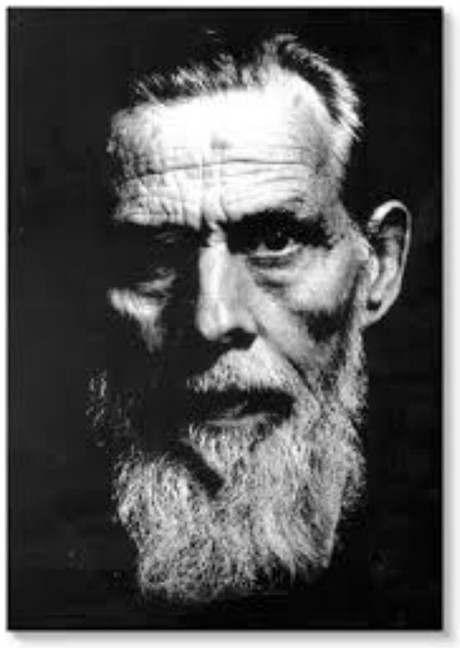
THE BRAIN INITIATIVE℠

the noble goal of making major advances in our understanding of both normal and pathological brain function

600+ European scientists sign an open letter stating that the EU HBP will not meet its goals (and is being mismanaged)

Shades of 1906?

From Neuron Doctrine to A Logical Calculus



Warren McCulloch (1898 - 1969)

Walter Pitts (1923 - 1969)

(1943), "A Logical Calculus of the Ideas Immanent in Nervous Activity". *Bulletin of Mathematical Biophysics* 5, pp 115–133.

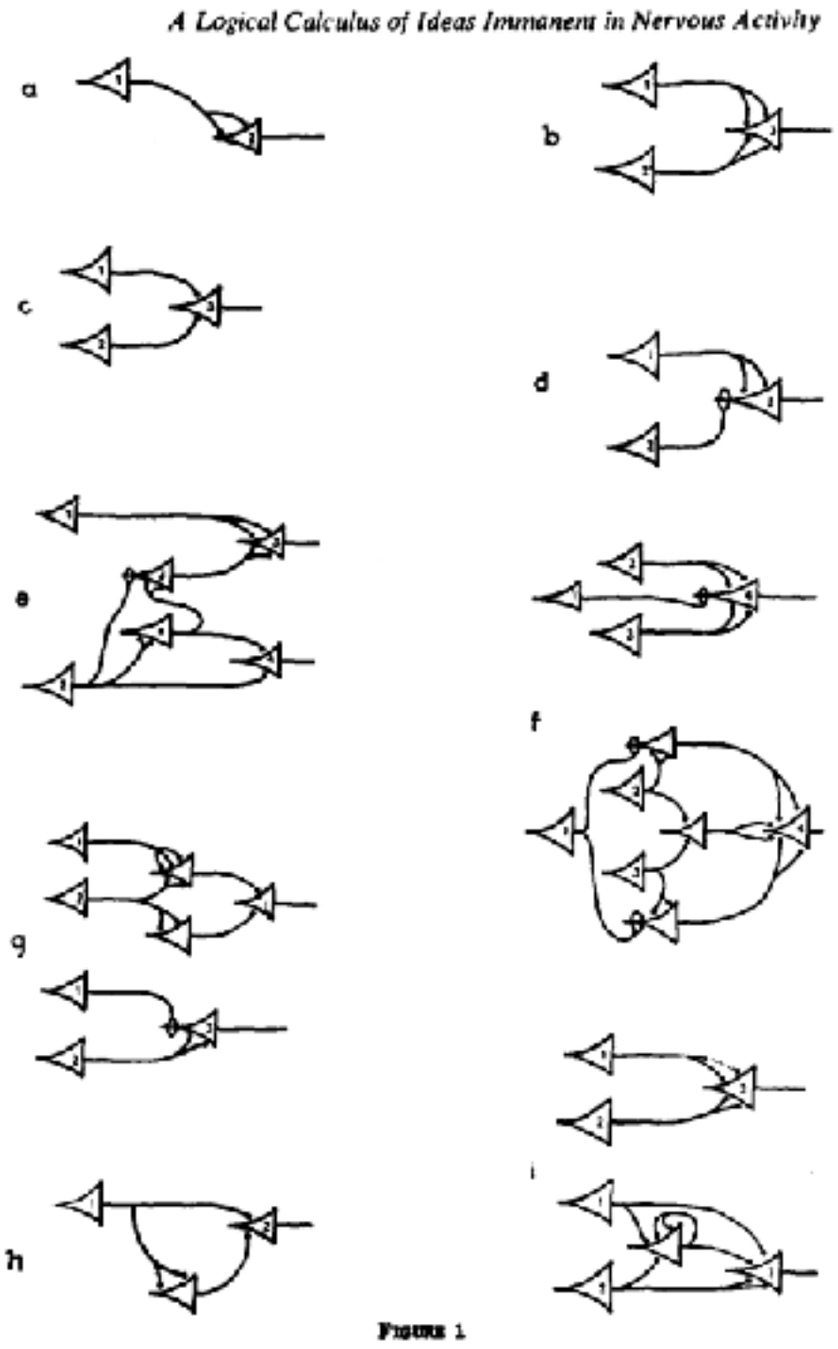
A LOGICAL CALCULUS OF THE IDEAS IMMANENT IN NERVOUS ACTIVITY

WARREN S. MCCULLOCH and WALTER H. PITTS

Because of the "all-or-none" character of nervous activity, neural events and the relations among them can be treated by means of propositional logic. It is found that the behavior of every net can be described in these terms, with the addition of more complicated logical means for nets containing circles; and that for any logical expression satisfying certain conditions, one can find a net behaving in the fashion it describes. It is shown that many particular choices among possible neurophysiological assumptions are equivalent, in the sense that for every net behaving under one assumption, there exists another net which behaves under the other and gives the same results, although perhaps not in the same time. Various applications of the calculus are discussed.

More often cited than read

The foundation for interpreting brains as computing machines



Logical units that compute simple functions such as

AND
OR
NOT
XOR
etc.

THE THEORY: NETS WITHOUT CIRCLES

We shall make the following physical assumptions for our calculus.

1. The activity of the neuron is an "all-or-none" process.

2. A certain fixed number of synapses must be excited within the period of latent addition in order to excite a neuron at any time, and this number is independent of previous activity and position on the neuron.

3. The only significant delay within the nervous system is synaptic delay.

4. The activity of any inhibitory synapse absolutely prevents excitation of the neuron at that time.

5. The structure of the net does not change with time.

THE THEORY: NETS WITH CIRCLES

The treatment of nets which do not satisfy our previous assumption of freedom from circles is very much more difficult than that case. This is largely a consequence of the possibility that activity may be set up in a circuit and continue reverberating around it for an indefinite period of time, so that the realizable ***Pr*** may involve reference to past events of an indefinite degree of remoteness. Consider such a net $\mathfrak{N}$, say of order p, and let $c_1, c_2, \ldots, c_p$ be

We will encounter this distinction next Semester when we contrast feed-forward neural networks with recurrent neural networks.

Information theory (Shannon)

Brains as computers (McCulloch)

Generative Linguistics (Chomsky)

Von Neumann computer architecture

McCulloch/Pitts interpretation of the neuron

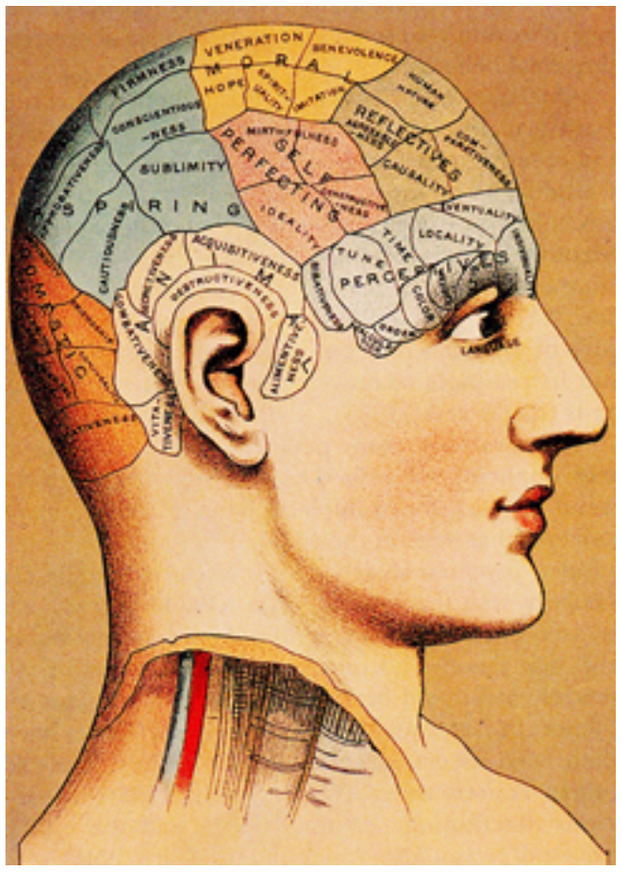
A powerful mixture!

Studying Brains

How do we find out stuff about the brain?

- Pathology (syndromes, lesions)
- Animal experiments
- Imaging (and similar)
- Behavioural studies

Phrenology (not respectable!)



Franz Josef Gall, ca. 1800

Believed the brain consisted of 27 distinct organs. Others went up to 40.

Gall's Assumptions

- The Brain is the organ of the mind
- The brain is not a homogenous unity, but an aggregate of mental organs with specific functions
- The cerebral organs are topographically localized
- Other things being equal, the relative size of any particular mental organ is indicative of the power or strength of that organ
- Since the skull ossifies over the brain during infant development, external craniological means could be used to diagnose the internal states of the mental characters

Phrenology was thoroughly discredited by 1840.

It remains as an important warning about the dangers of premature association of place and function.

Modern cognitive neuroscience is frequently criticised for being *phrenological*.

Table 1. A Mapping of Gall's 27 Faculties to Potentially Related Neuroimaging Research

Faculty	Modern equivalent for neuroimaging	Regions implicated	References
Impulse to propagation	Viewing of romantic lover versus other individuals	Basal ganglia	Aron et al. (2005)
Tenderness for the offspring or parental love	Mothers viewing own versus other child	Amygdala, insula, anterior cingulate, superior temporal gyrus	Leibenluft, Gobbini, Harrison, & Haxby (2004)
Friendly attachment or fidelity	Viewing friend versus a stranger	Right temporoparietal cortex	Sugiura et al. (2005)
Valour, self-defense	Punishment of defectors in economic games	Dorsal striatum	de Quervain et al. (2004)
Murder, carnivorousness	Less active in murderers	Prefrontal cortex	Raine et al. (1994)
Sense of cunning	—	—	—
Larceny, sense of property	Activated in relation to hoarding behavior in OCD	Left precentral gyrus and right orbitofrontal cortex	Mataix-Cols et al. (2004)
Pride, arrogance, love of authority	Related to arrogance scores	Prefrontal cortex	Yang et al. (2005)
Ambition and vanity	Activation for judgment about self versus others	Medial prefrontal cortex	Ochsner et al. (2005)
Circumspection	Activation correlated with harm avoidance	Nucleus accumbens	Matthews, Simmons, Lane, & Paulus (2004)
Aptness to receive an education or the memoria realis	Activation during reasoning tasks correlated with general intelligence	Parietal cortex	Lee et al. (2006)
Sense of locality	Scenes versus nonscenes	Parahippocampal cortex	Epstein & Kanwisher (1998)
Recollection of persons	Activated by judgments about face identity versus occupation	Fusiform gyrus	Turk, Rosenblum, Gazzaniga, & Macrae (2005)
Faculty for words, verbal memory	Use of memory strategies	Prefrontal cortex, extrastriate visual cortex	Kirchhoff & Buckner (2006)
Faculty of language	—	—	—
Disposition for coloring, and the delighting in colors	Greater activity in grapheme–color synesthetes	Area V4	Hubbard, Arman, Ramachandran, & Boynton (2005)

Sense for sounds, musical talent	Activation in MEG and gray matter volume correlated with musical aptitude	Auditory cortex	Schneider et al. (2002)
Arithmetic, counting, time	Activity correlated with arithmetic skill	Angular gyrus	Menon et al. (2000)
Mechanical skill	Greater activity for observing actions in skilled versus unskilled groups	Left premotor, intraparietal, superior temporal cortex	Calvo-Merino, Glaser, Grèzes, Passingham, & Haggard (2005)
Comparative perspicuity, sagacity	—	—	—
Metaphysical perspicuity	—	—	—
Wit, causality, sense of inference	More active for viewing causal events than for noncausal events	Area MT, superior temporal sulcas, inferior parietal sulcus	Blakemore et al. (2001)
Poetic talent	Generation of creative versus uncreative narrative	Right medial frontal cortex	Howard–Jones, Blakemore, Samuel, Summers, & Claxton (2005)
Good nature, compassion, moral sense	Judging personal versus impersonal moral dilemmas	Medial prefrontal cortex, posterior cingulate, angular gyrus	Greene, Sommerville, Nystrom, Darley, & Cohen (2001)

Note. The 27 faculties are from Whye (2004). OCD = obsessive–compulsive disorder.

Pathology

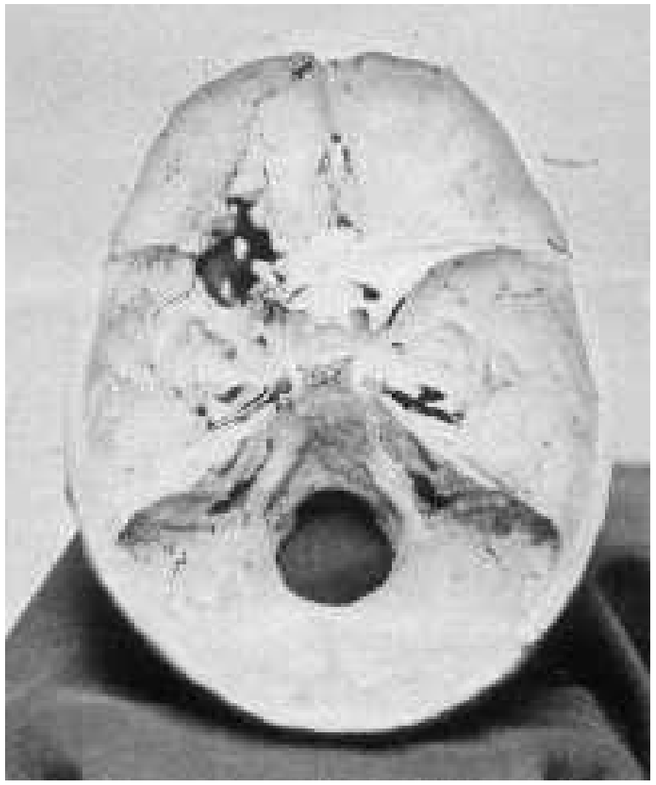
Pathology can provide information that is otherwise utterly unattainable

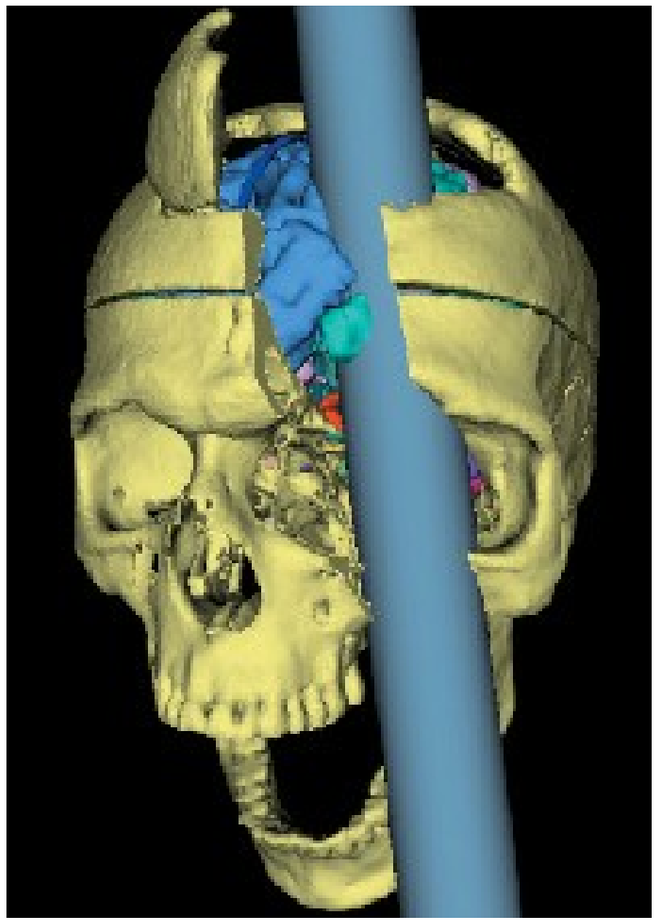
. . . but each case is individual

. . . and pathologies are messy, uncontrolled

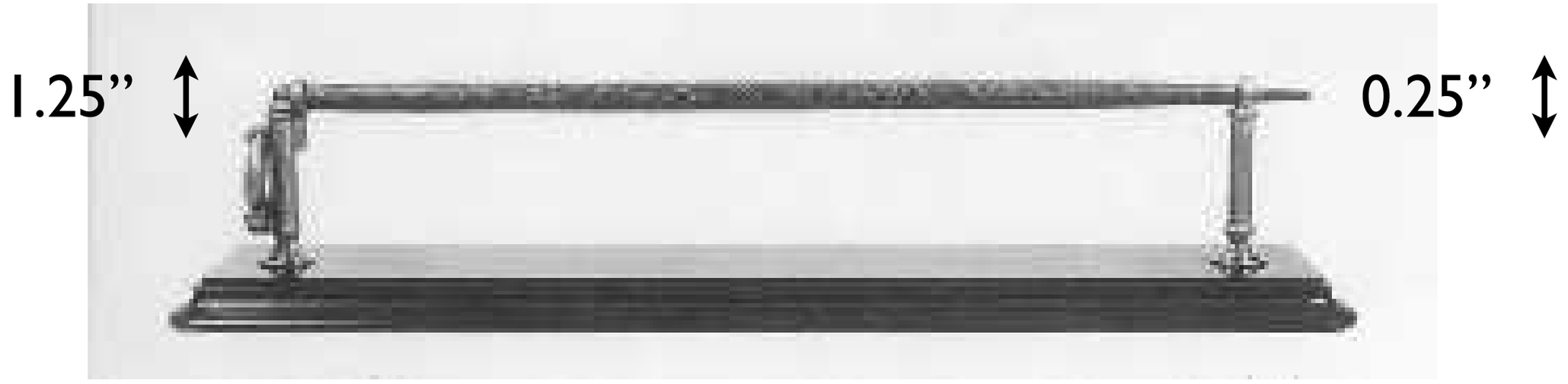
. . . and they only allow inference to be drawn about a damaged system

Phineas Gage was the foreman of a railway construction gang working for the contractors preparing the bed for the Rutland and Burlington Rail Road near Cavendish, Vermont. On 13th. September 1848, an accidental explosion of a charge he had set blew his tamping iron through his head.





The tamping iron went in point first under his left cheek bone and completely out through the top of his head, landing about 25 to 30 yards behind him. Phineas was knocked over but may not have lost consciousness even though most of the front part of the left side of his brain was destroyed. He returned home 10 weeks later.



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."

Animals

Nervous systems must share very many properties and operating principles, from the simplest to the most complicated.

Mammalian brains all have very similar structures.

There are essentially no structural differences between ape brains and human brains — though there are differences in relative size

The single most remarkable feature of the human brain is the relative size of the frontal lobe

Consider the suitability of animal models for studying the following topics:

- smooth eye pursuit
- schizophrenia
- reasoning
- memory

Technologies for studying brains: A Sampling

Anatomy (structure)

Physiology (activity)

Given our previous discussion, be wary of any uncritical discussion of such technologies as studying *function*.

Brain Anatomy

Dissection (see this week's "reading")

X-rays (CT scan)

Magnetic Resonance Imaging

Diffusion Tension Imaging/Diffusion Spectrum Imaging


PHILIPS

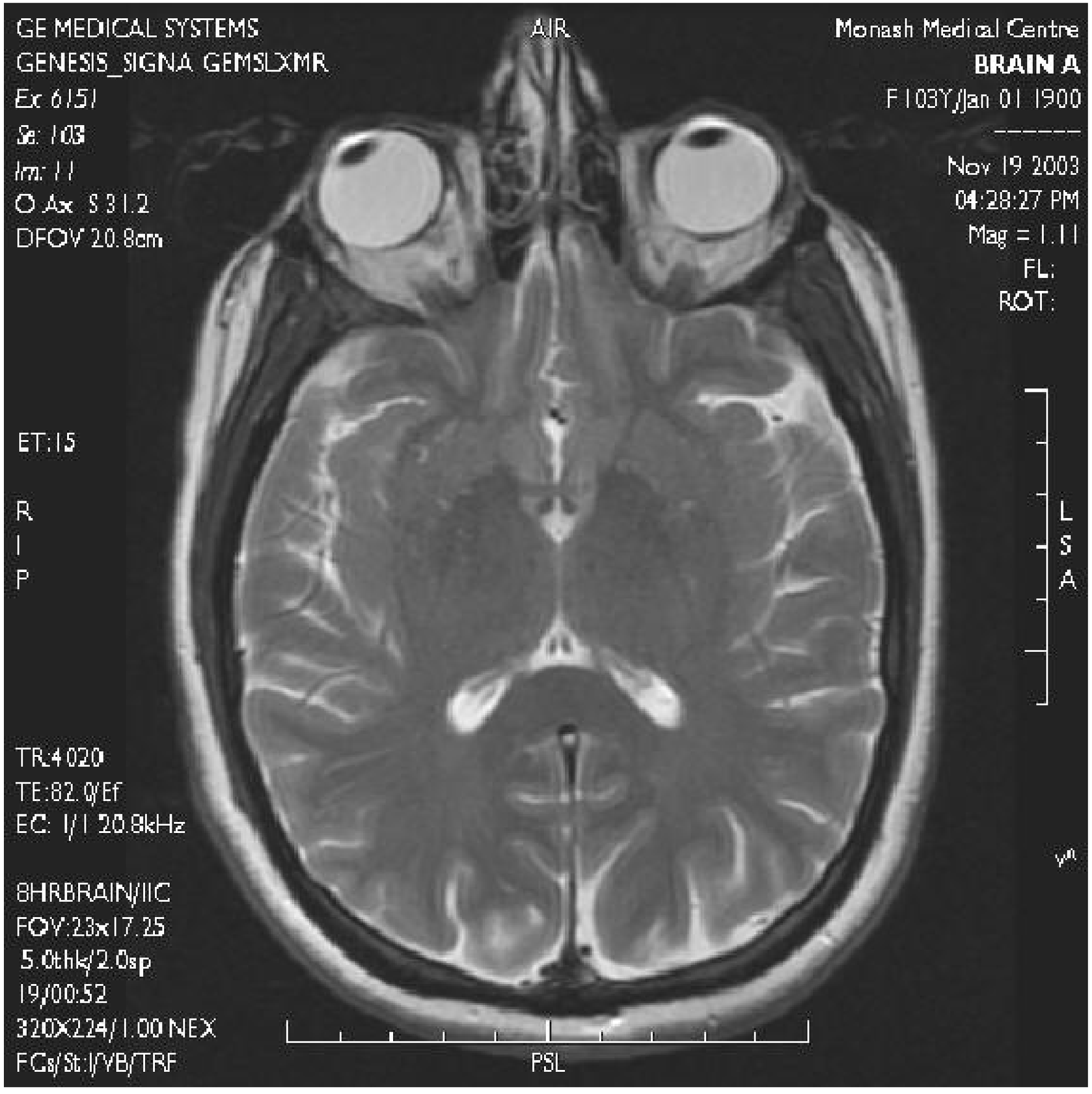
- Not X-rays!!!! Uses very high intensity magnetic field to alter spin of protons

- Typical human strength: 3 tesla. Earth's magnetic field: ca. 50 μT

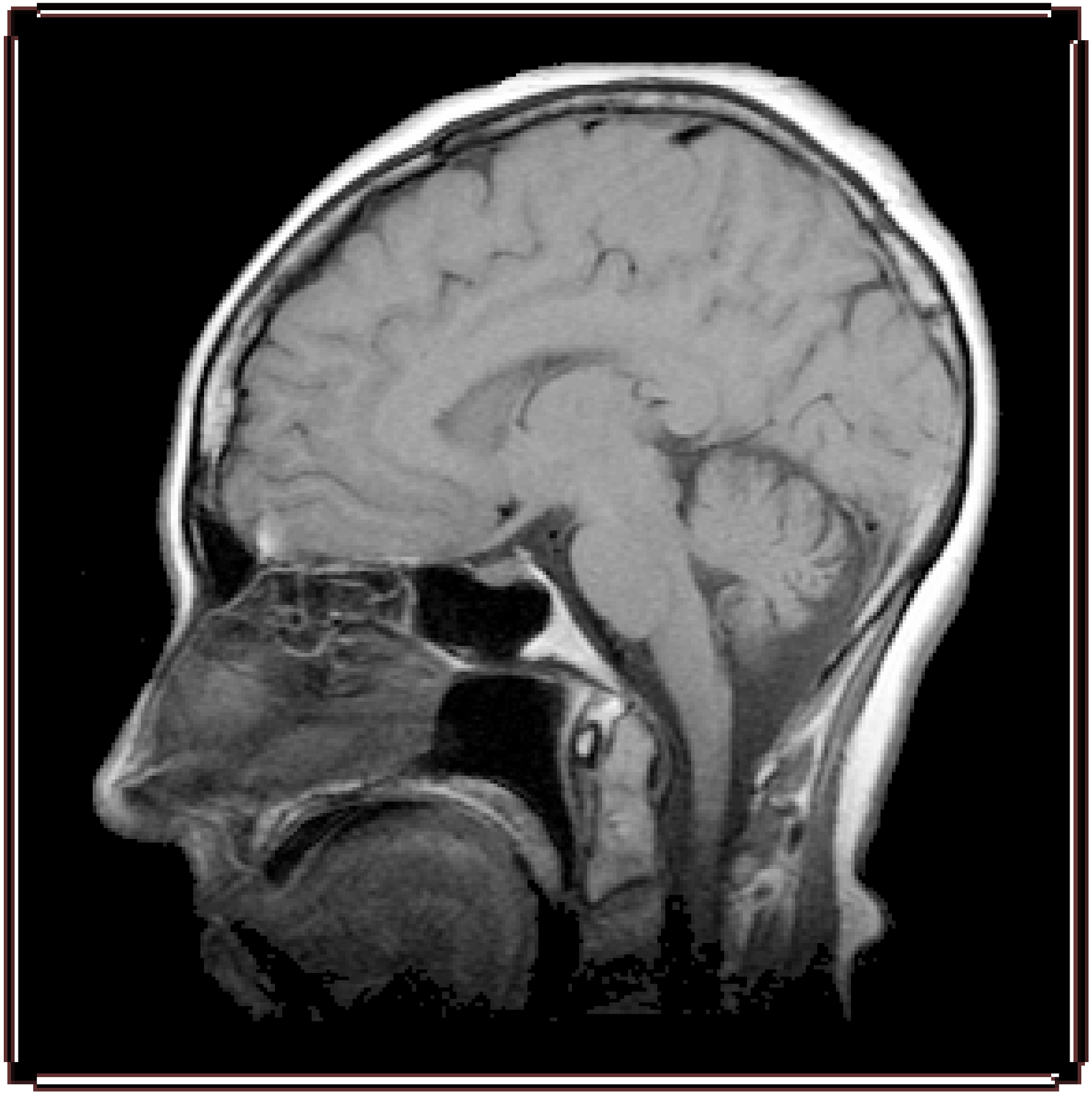
- Images soft tissue with great accuracy. Spatial resolution < 1 mm^3

- Noisy, slow, but non-invasive

- Produces *structural* images



Transverse cross-section



Saggital cross-section

Coronal cross-section

Mapping Brain Connectivity

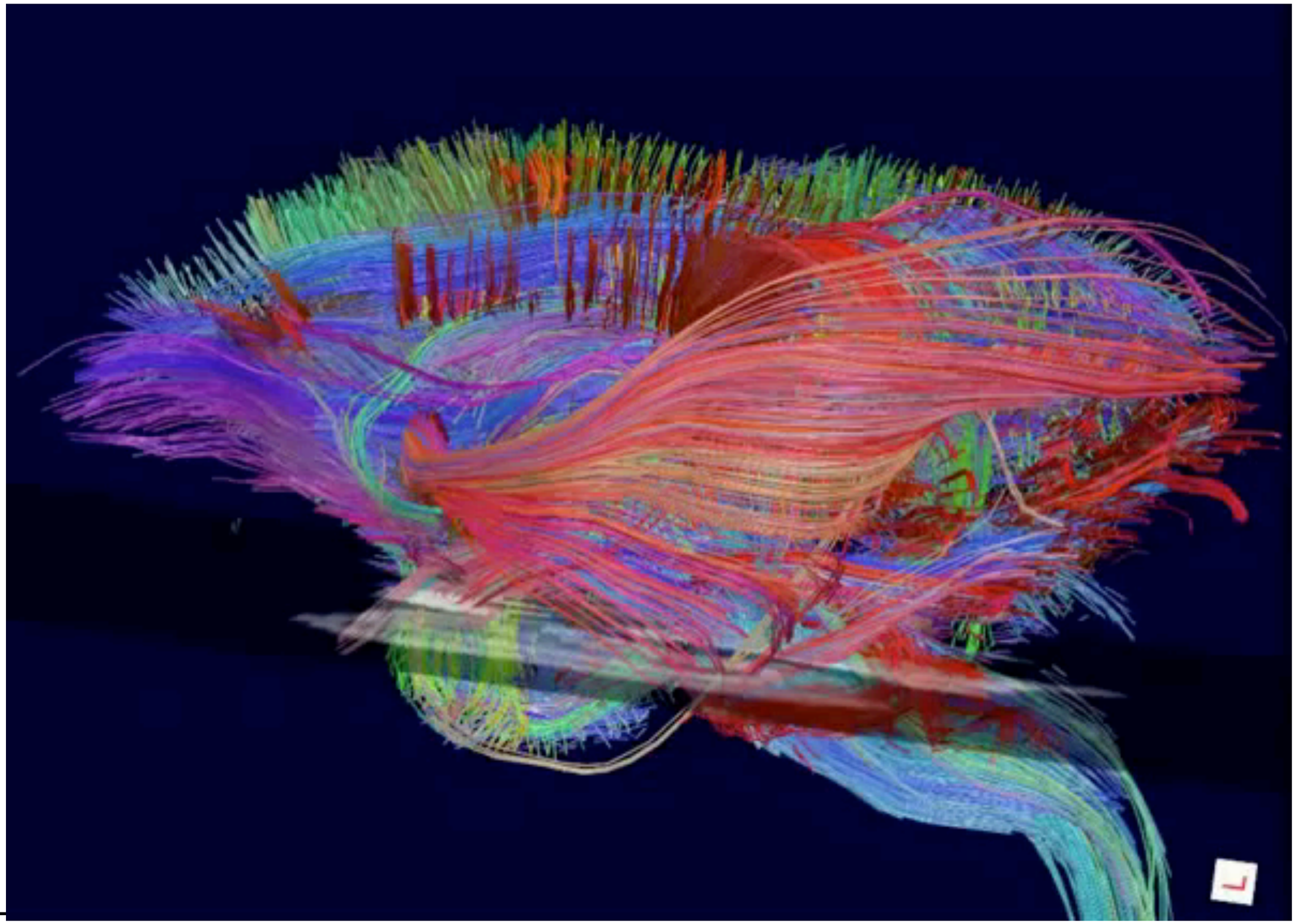
The brain contains massive interconnectivity.

In general, if Area A connects to Area B, then Area B will connect back to Area A

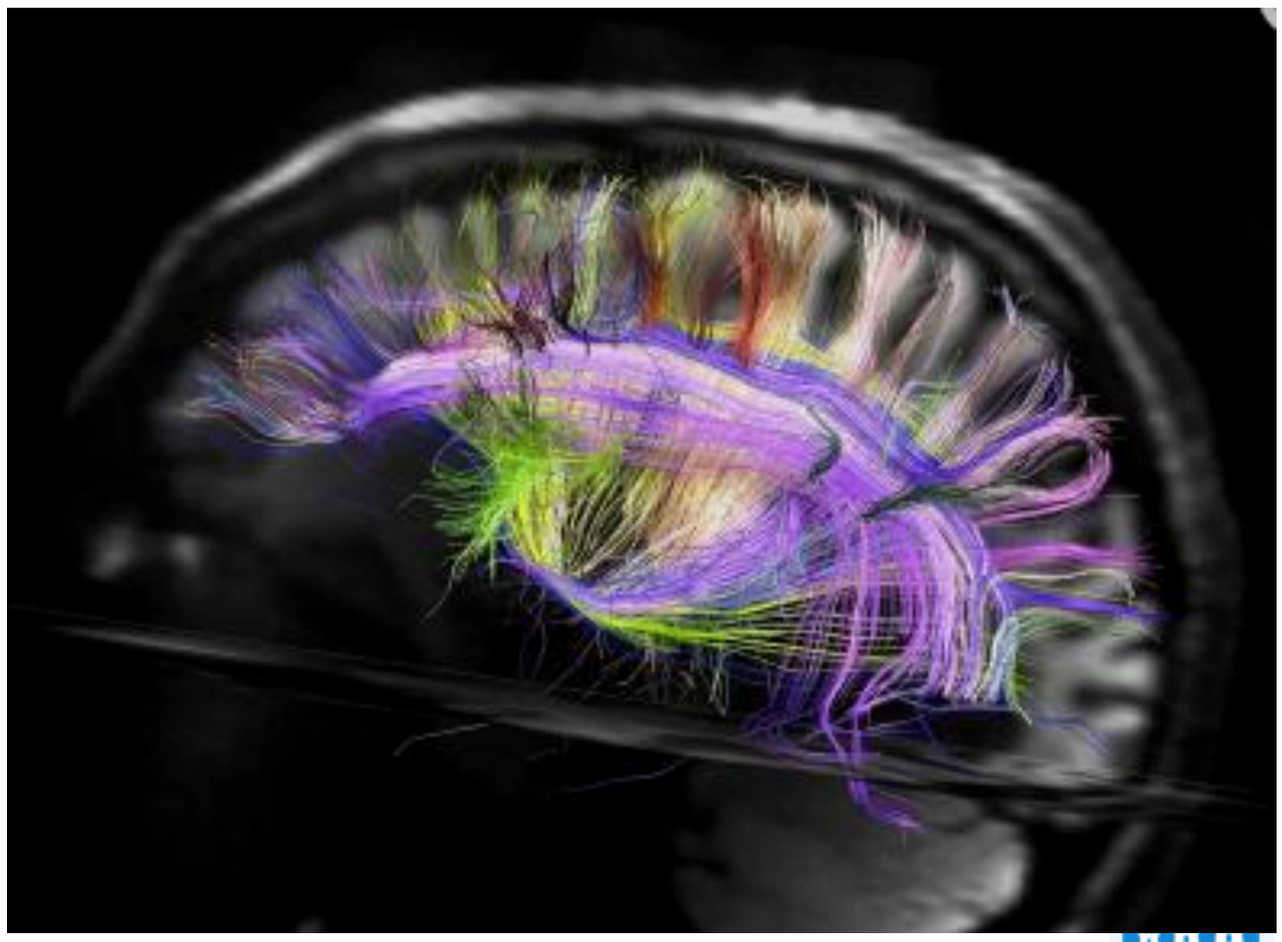
Modern techniques are just uncovering the richness of connectivity

Techniques: Diffusion Tensor Imaging (DTI) and Diffusion Spectrum Imaging (DSI)

Diffusion Tensor Imaging (marmoset brain)



March 2012: Diffusion Spectrum Imaging shows the existence of a fabric or grid like structure in long range connections in the human brain



Physiology: the Brain in Action

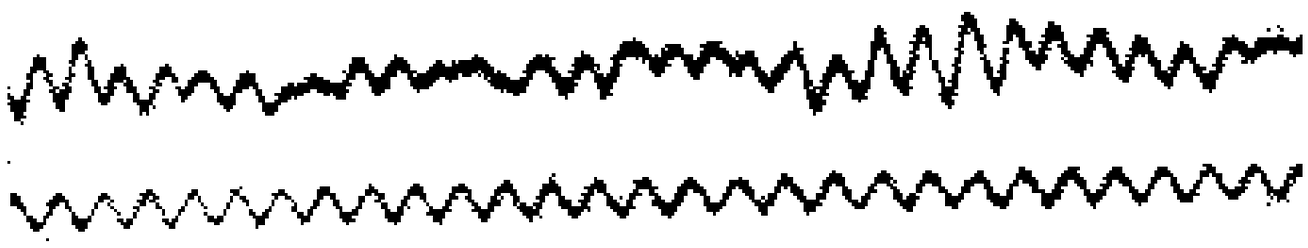
Brief overview of timeline of direct neural recordings:

- 1790's: Galvani demonstrates electrical activity in nervous systems by applying a spark and making a dead frog's leg twitch
- 1928: First recording from a single nerve fibre
- 1952: development of action potential in giant squid neuron documented using glass micro electrodes

Brief overview of timeline of direct neural recordings 2:

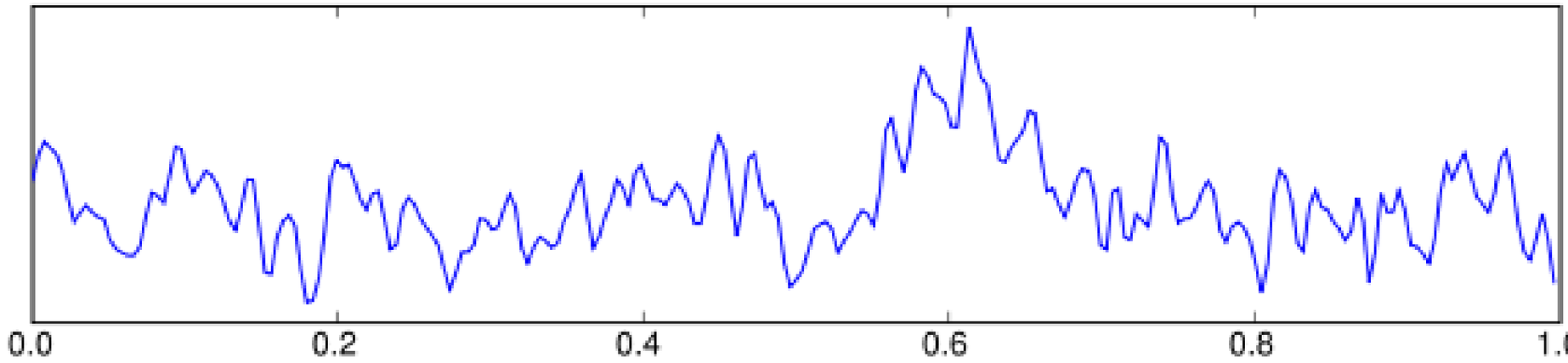
- 1957: first intra-cellular single-unit recording (John Eccles)
- Hubel & Wiesel single unit studies on anaesthetised cats
- 1967: first use of multi-electrode single unit recording in human patients

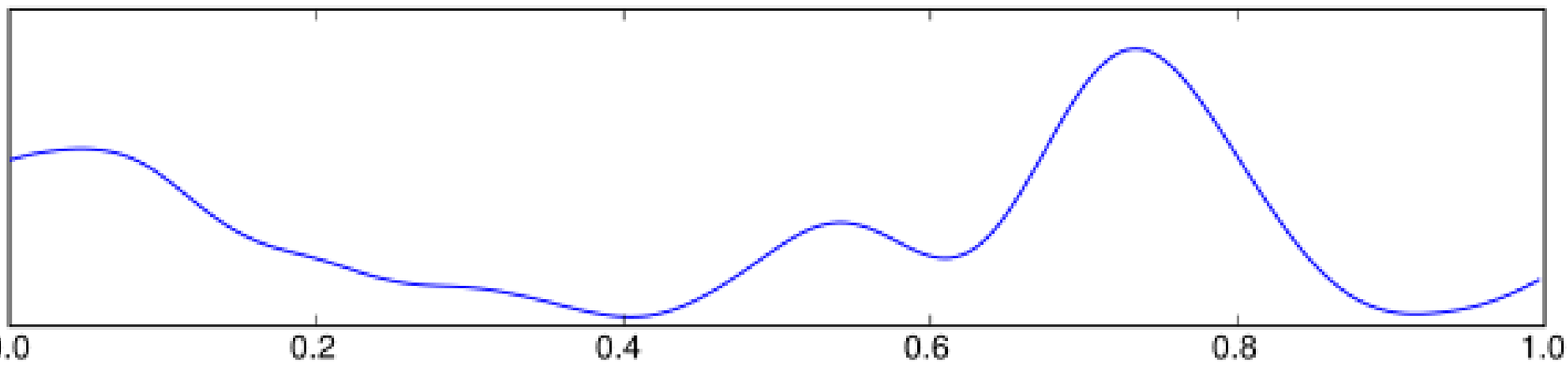
- EEG: Electroencephalography
- Non-invasive technique: uses scalp electrodes
- Excellent temporal resolution/lousy spatial resolution
- Oldest imaging method (Berger, 1924)



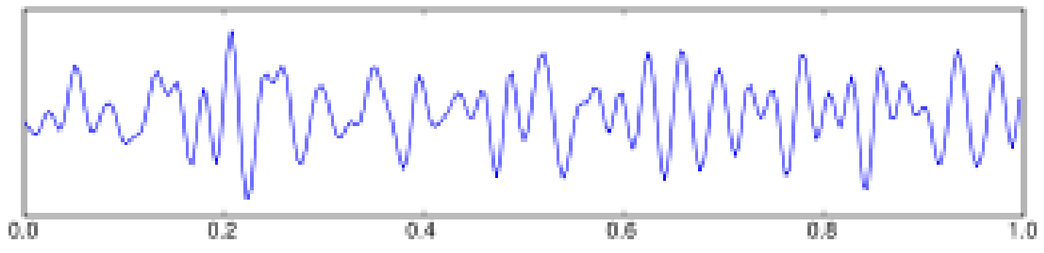
One of Hans Berger's original recordings from 1924.

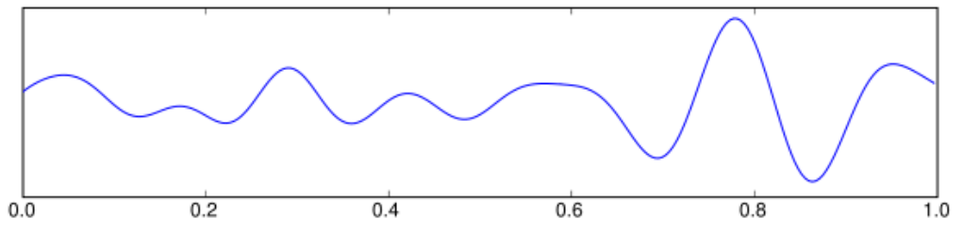
What do you make of it?

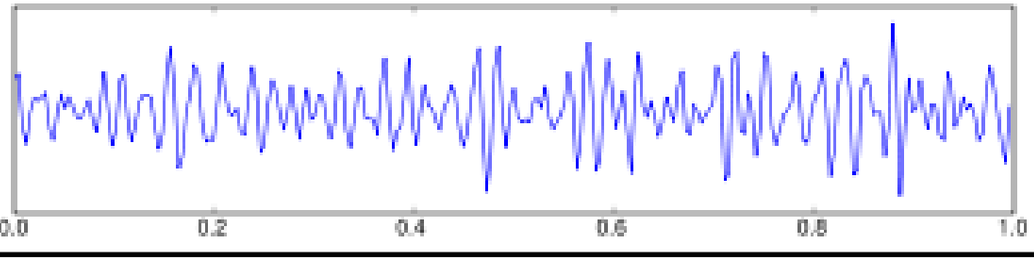


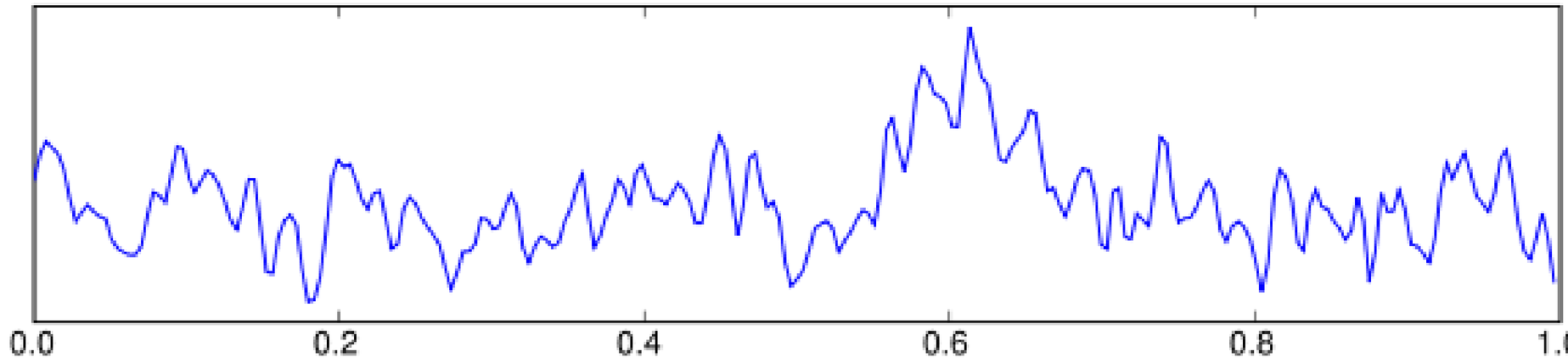


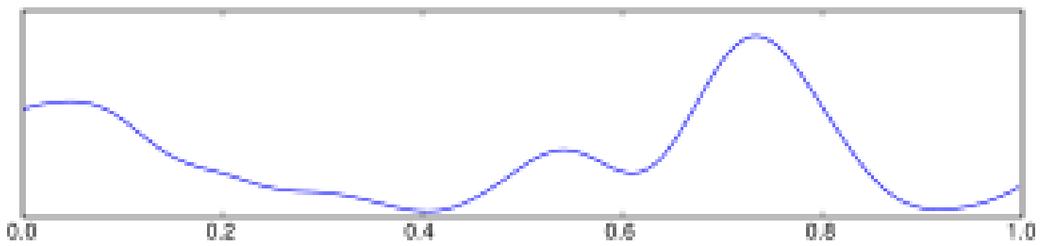
Delta component: some sleep stages; some pathologies; very young subjects

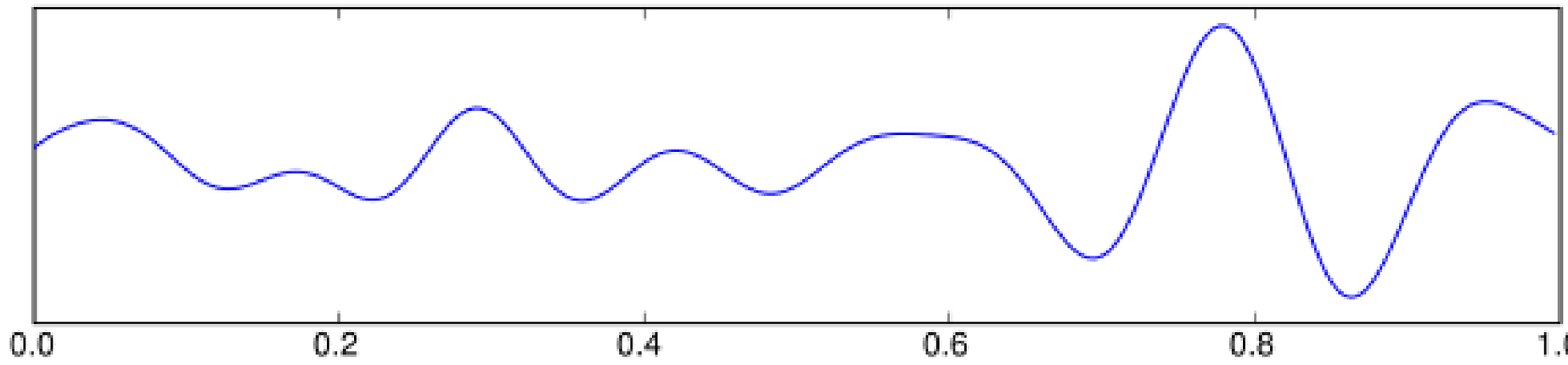




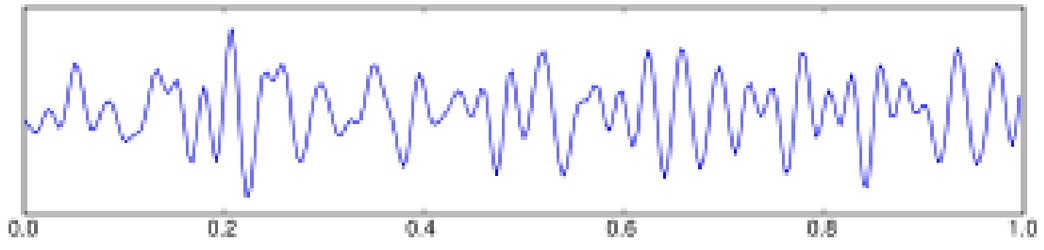


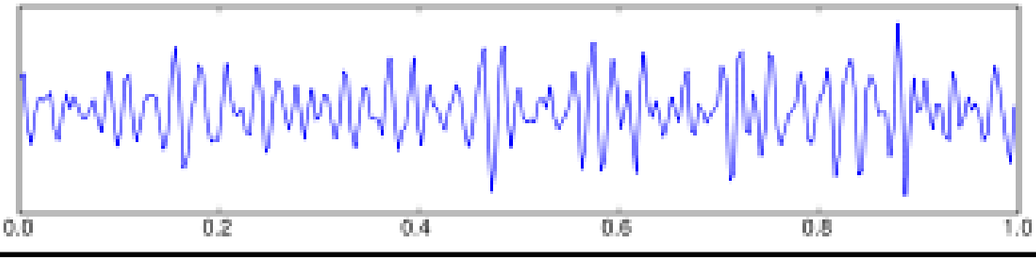


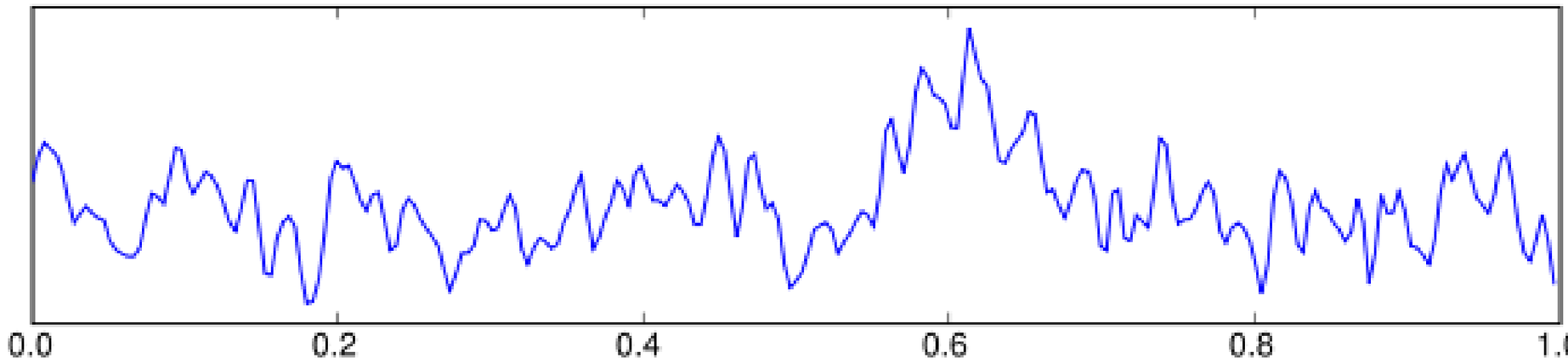


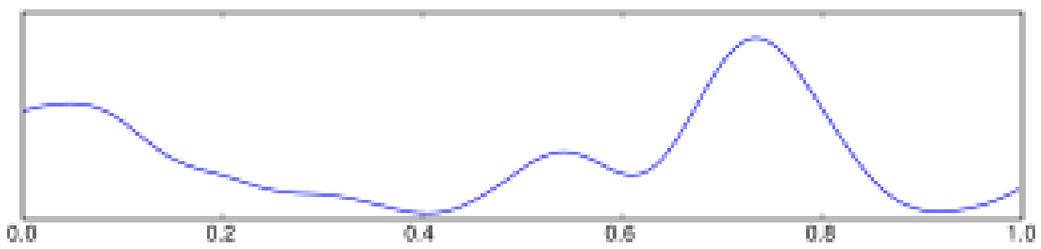


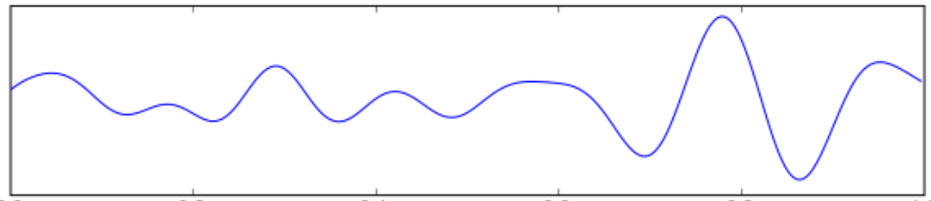
Theta: drowsiness, hypnosis, light sleep



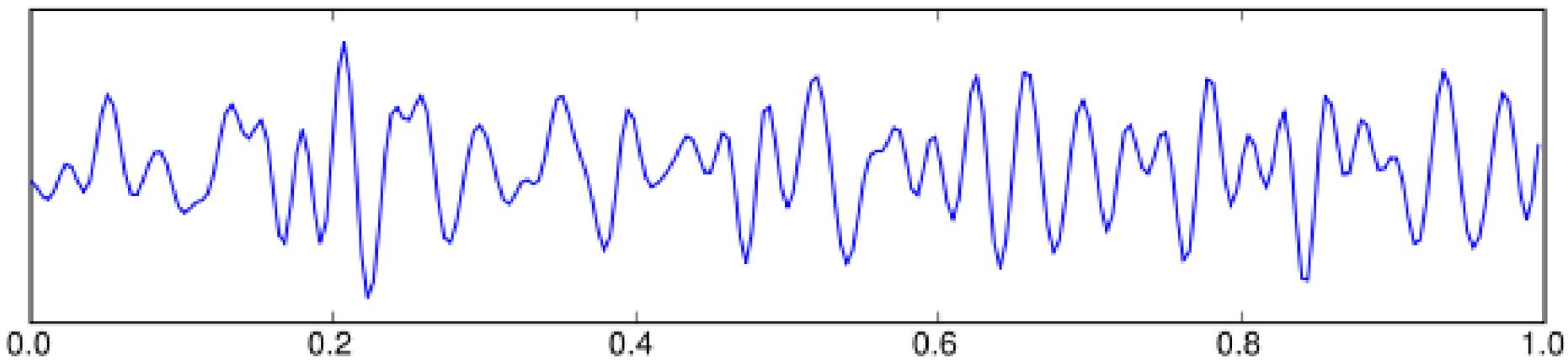


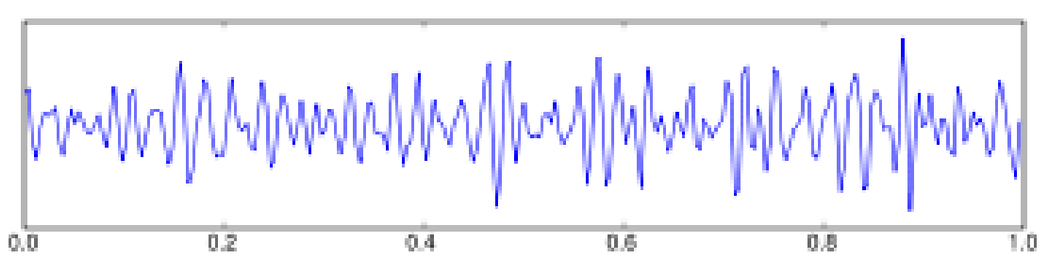


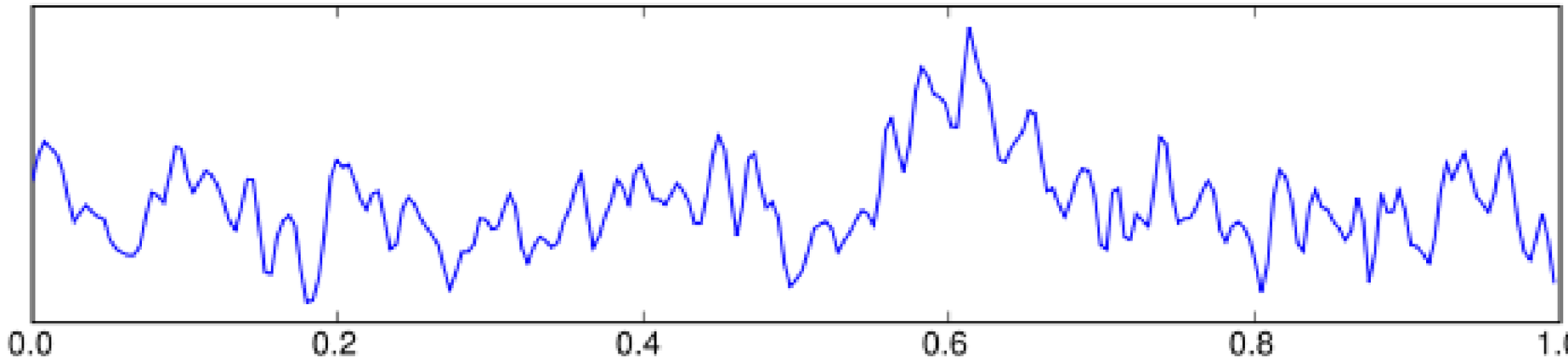


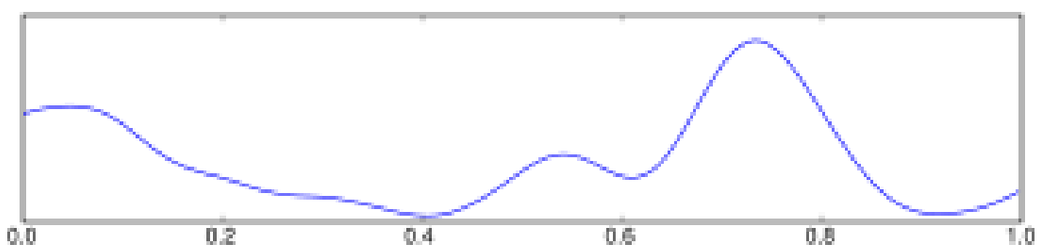


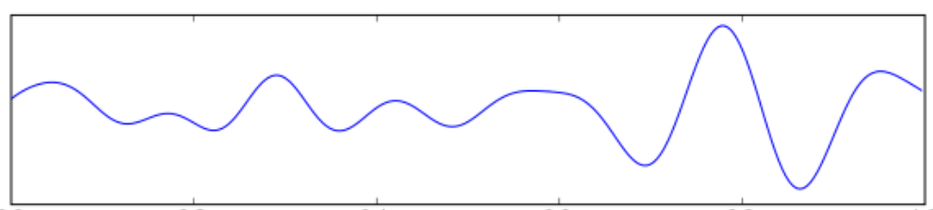
Beta: active concentration, thinking

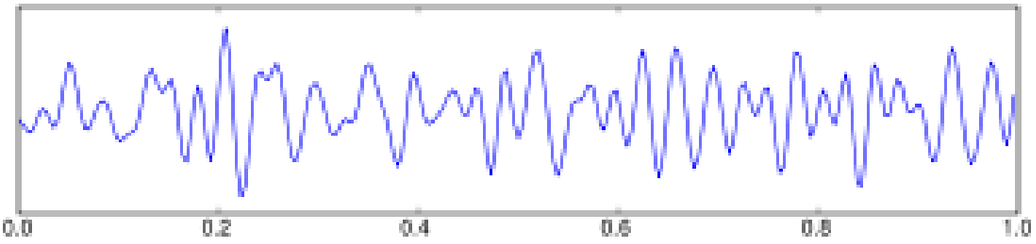




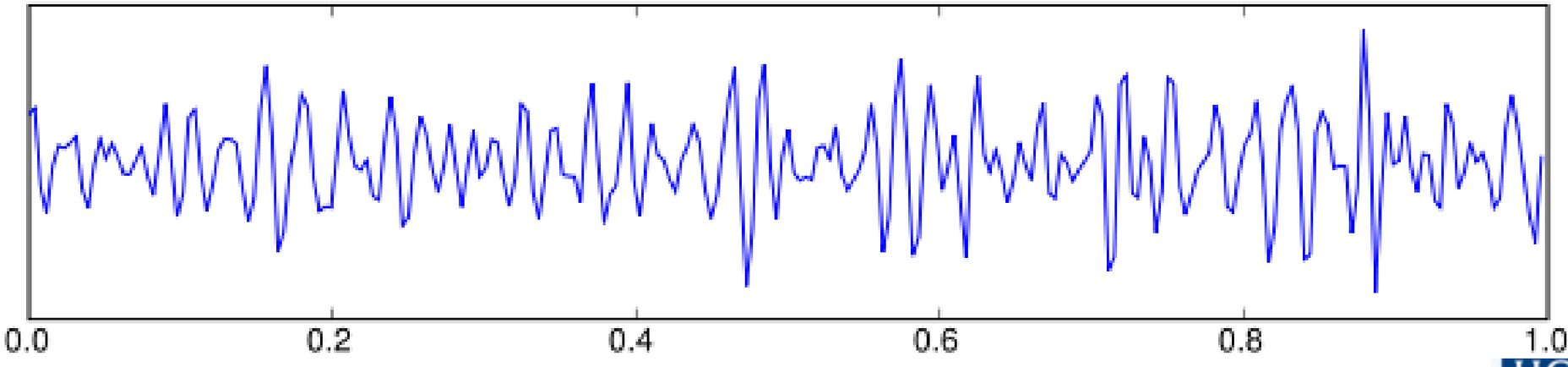








Gamma: intellectual activity? problem solving?



Even if it is difficult or impossible to assign determinate meanings to such frequency bands, they serve an important role in diagnostics:

If you know how things usually are, then you can look out for deviations from the normal patterns.

Many brain imaging successes work in this manner: not by revealing the meaning of any specific pattern of activity, but by allowing comparison across conditions (e.g. healthy/diseased, or awake/asleep/coma).

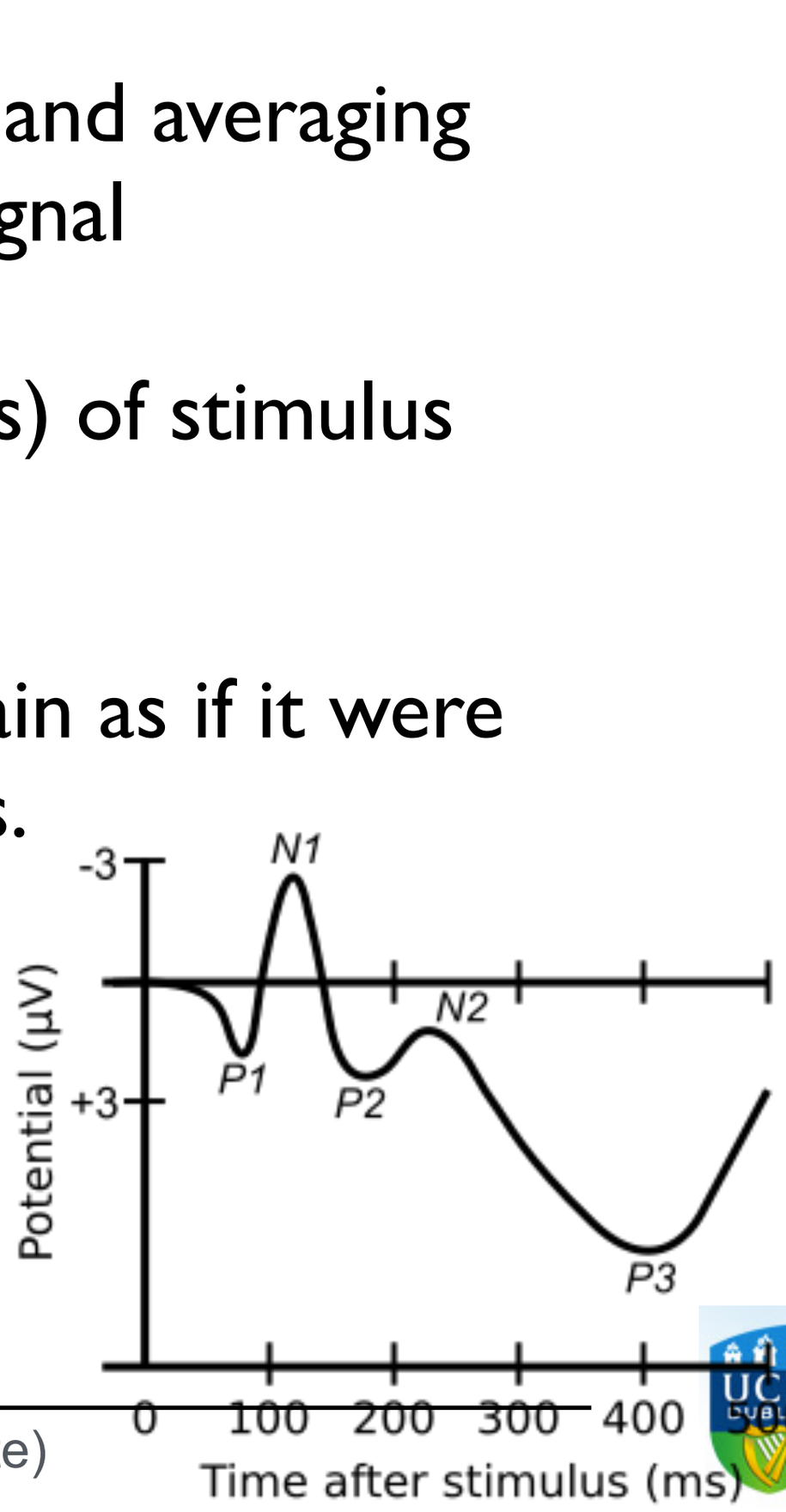
One common technique: Event-Related Potentials:

repeated presentation of a stimulus, and averaging of the immediately following EEG signal

Requires very many (often hundreds) of stimulus presentations.

Treats the (endogenously active) brain as if it were merely "responding" to the stimulus.

Weird convention: negative is up, positive is down.



EEG Limitations

The signal is typically obtained at the scalp, through the skull & several layers of connective tissue

It samples mainly from those bits of cortex that happen, by chance, to lie close to the outer containing surface

Good time resolution (< 1 ms) but terrible spatial resolution

Signal to noise ratio is very very poor

Near Infra-Red Spectroscopy: NIRS

Uses light!

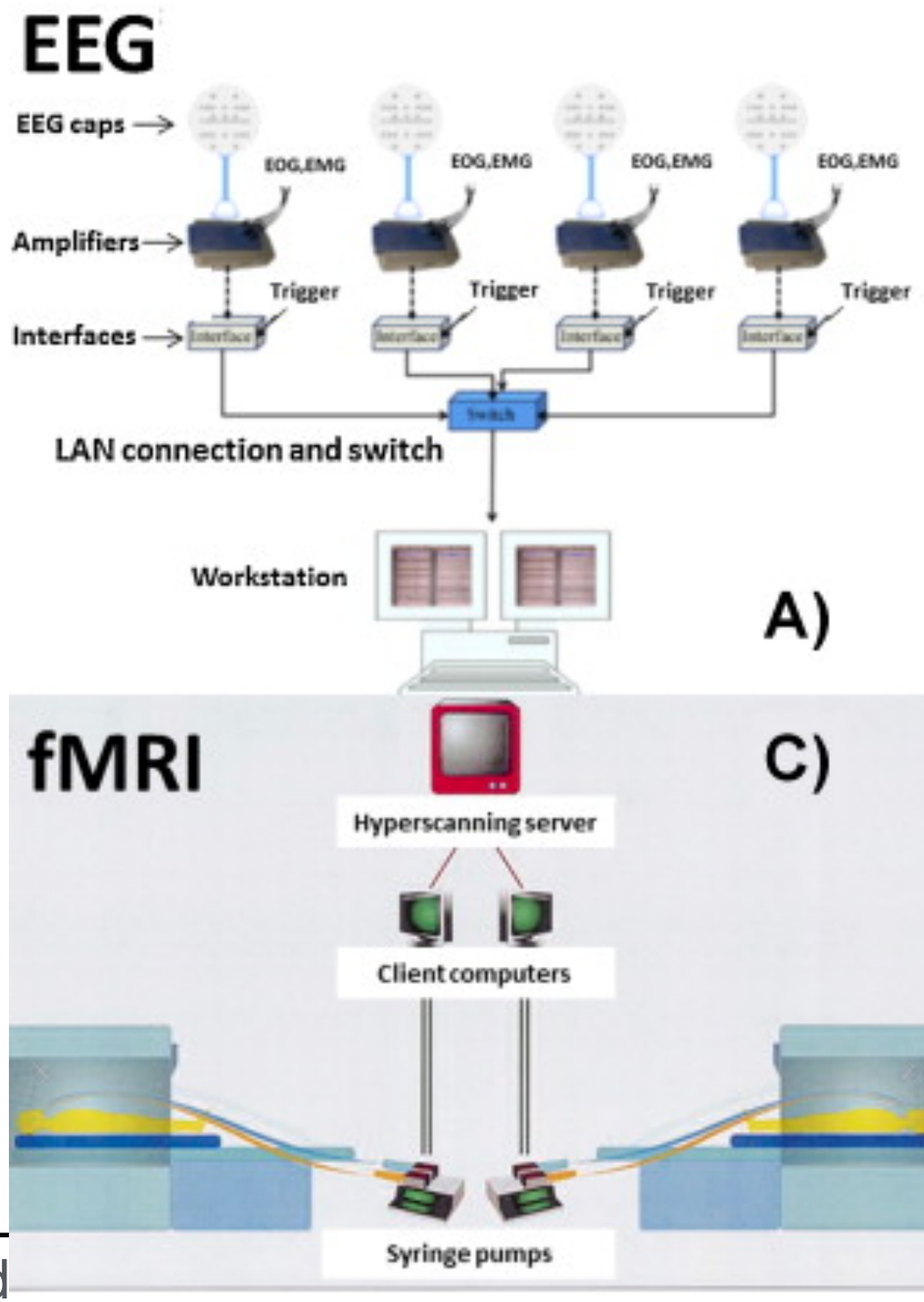
Monitors regional bloodflow (much like fMRI) at the cortical surface.

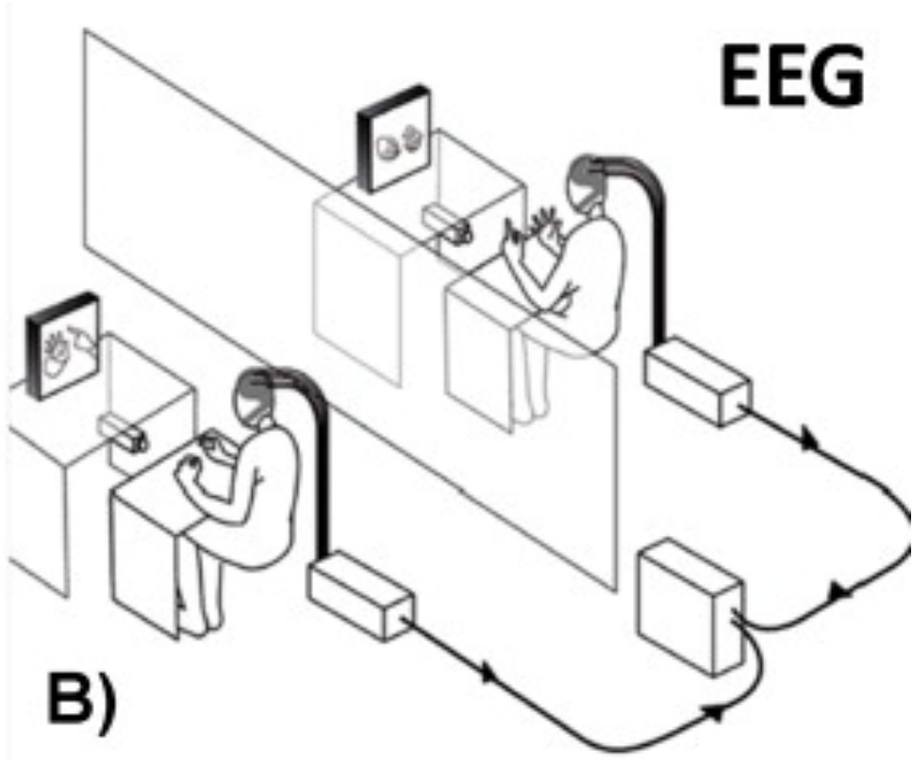
Non-invasive

Relative newcomer, but developing rapidly!

Can be combined with EEG (complex!!)

Imaging more than one brain at a time: HYPERSCANNING!





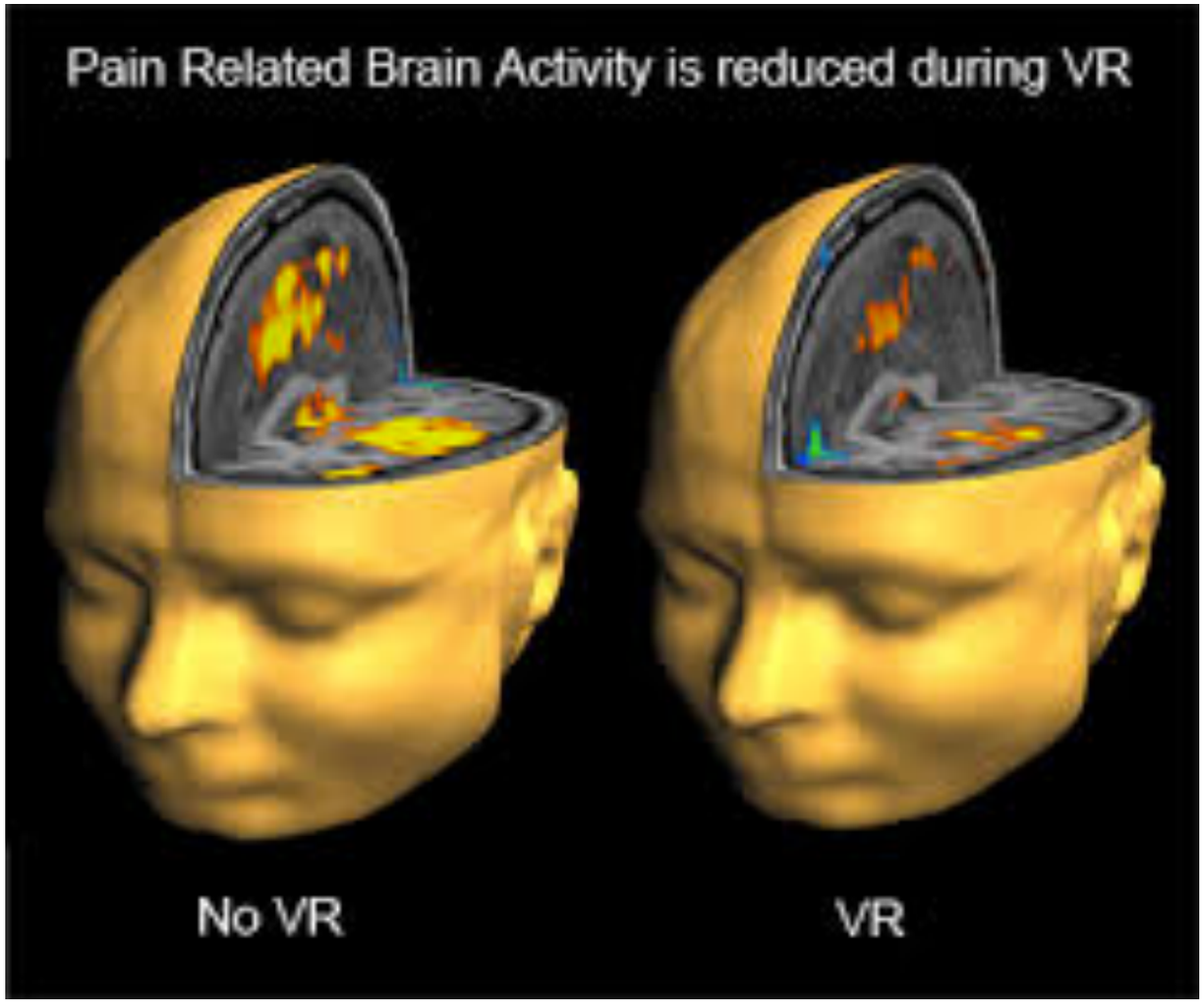
Neuroscience has recently noticed that brain activity is massively different when subjects engage in social interaction.

This has recently been dubbed the “dark matter” of neuroscience

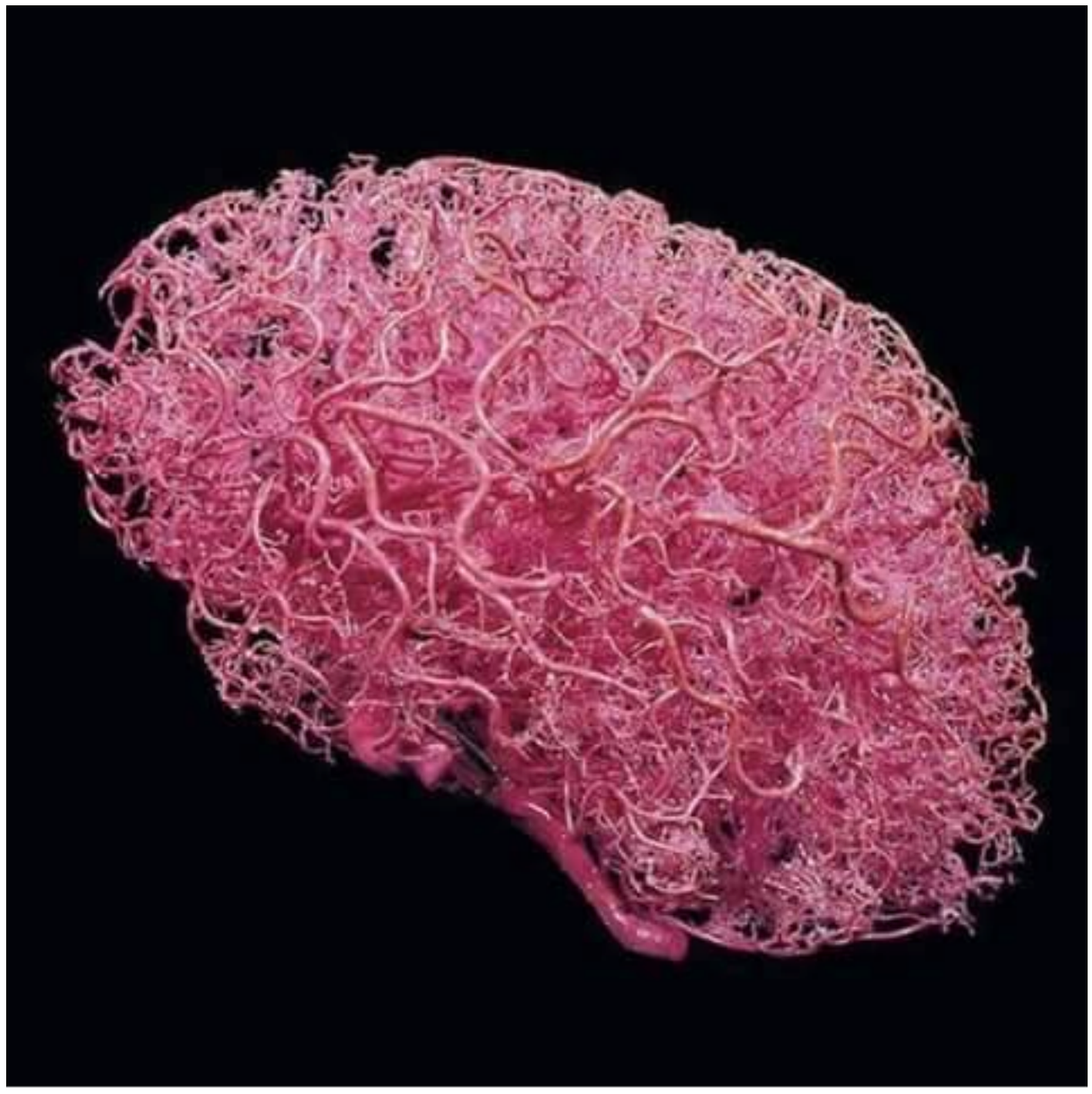
In social interaction, two brains may become coupled!

More on this later . . .

functional Magnetic Resonance Imaging: fMRI



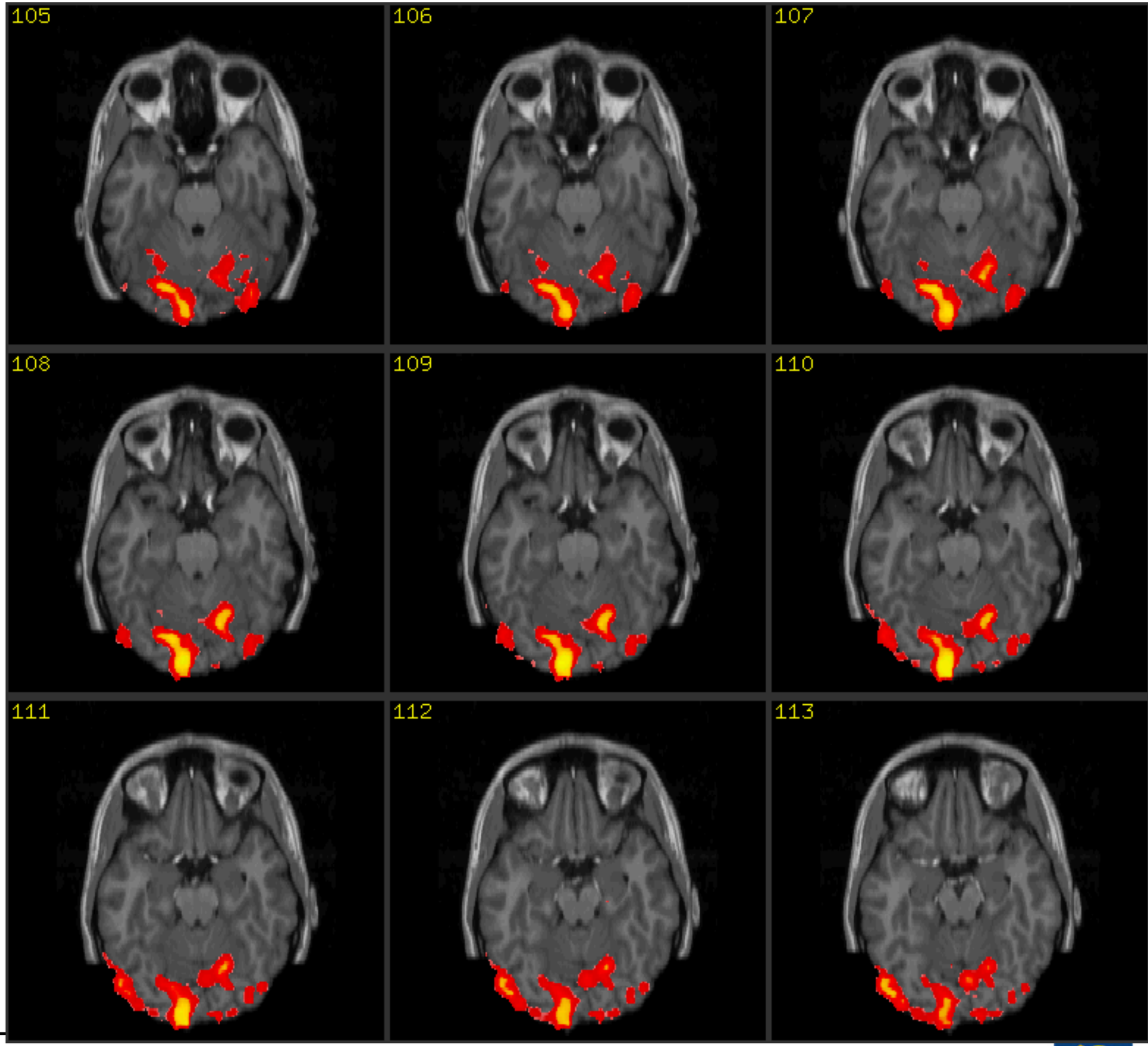
- Same basic principles as MRI
- Sensitive to local blood flow (not to nerve firings directly)
- Blood Oxygen-Level Dependent signal (BOLD)
- Overlaid on structural MRI
- Limited temporal resolution, good spatial resolution



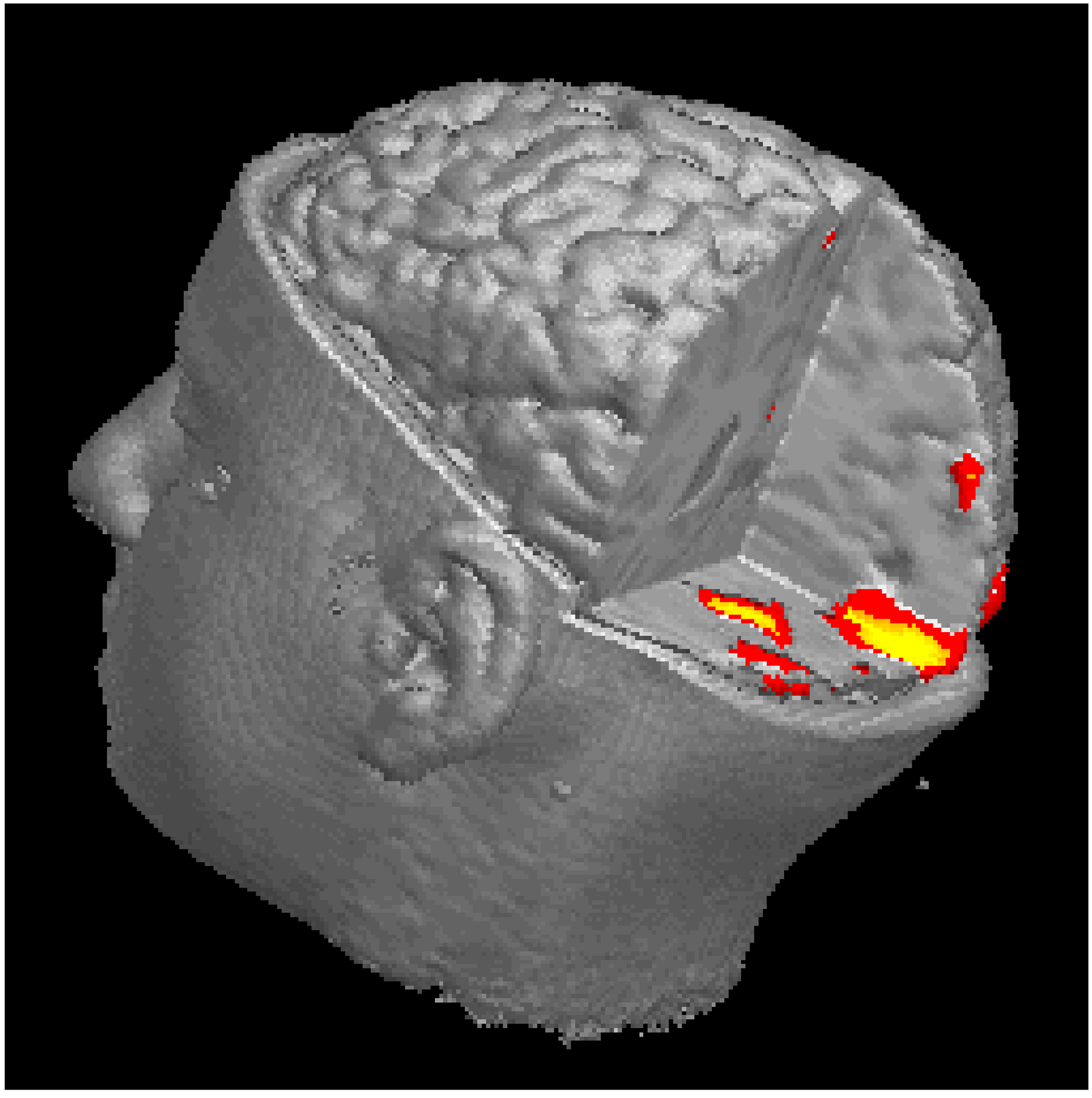
The blood vessels in the human brain.

Basic transverse MRI

Sequence of BOLD responses from one slice



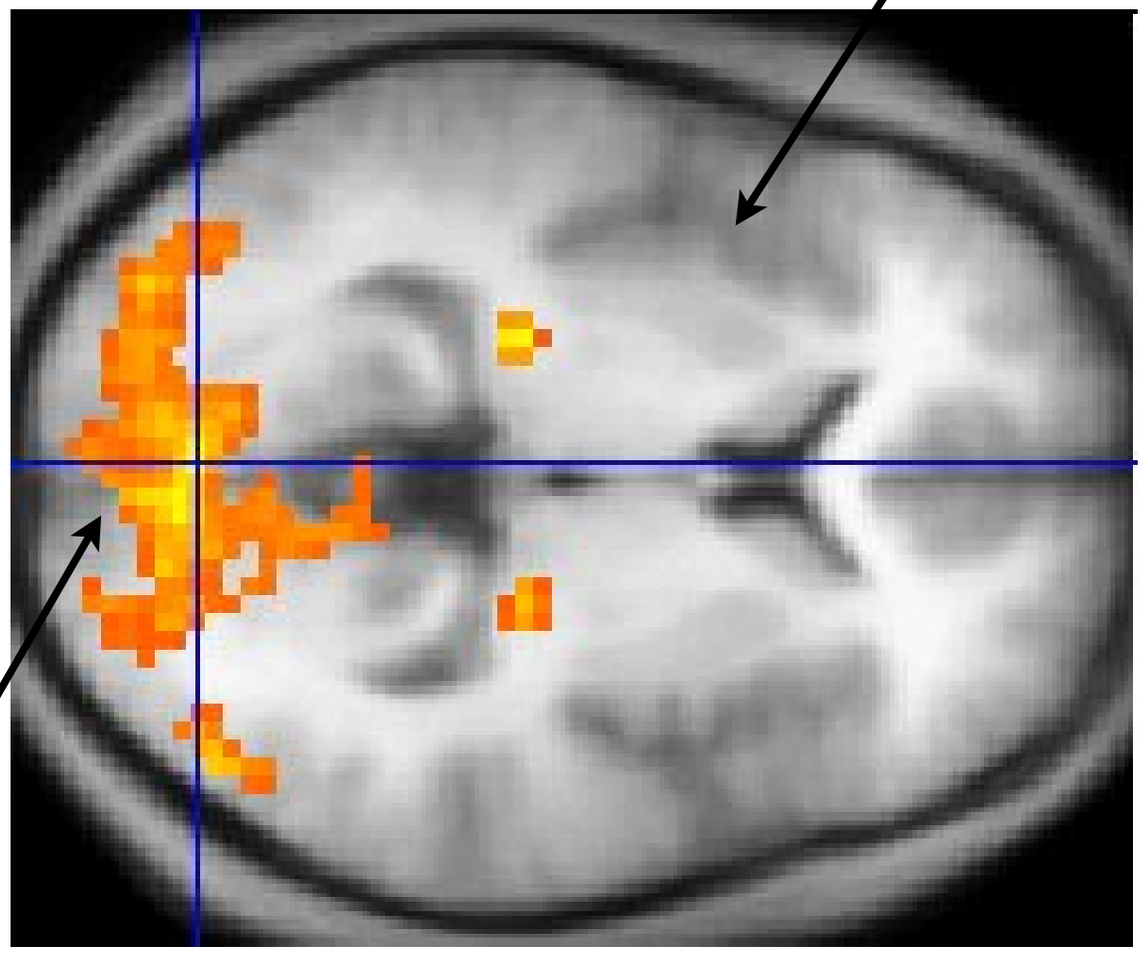
3-D image of brain activity



Typical procedure

- First, do protracted, hi-res, anatomical MRI scan
- Now do ca 150 lo-res scans of about 5 sec each (half with stimulus, half without)
- Compare activation, voxel by voxel, across the two conditions

Structural average MRI



Subjects viewed a complex moving stimulus or a black screen. Areas more active when viewing the moving stimulus are coloured.

Primary visual cortex

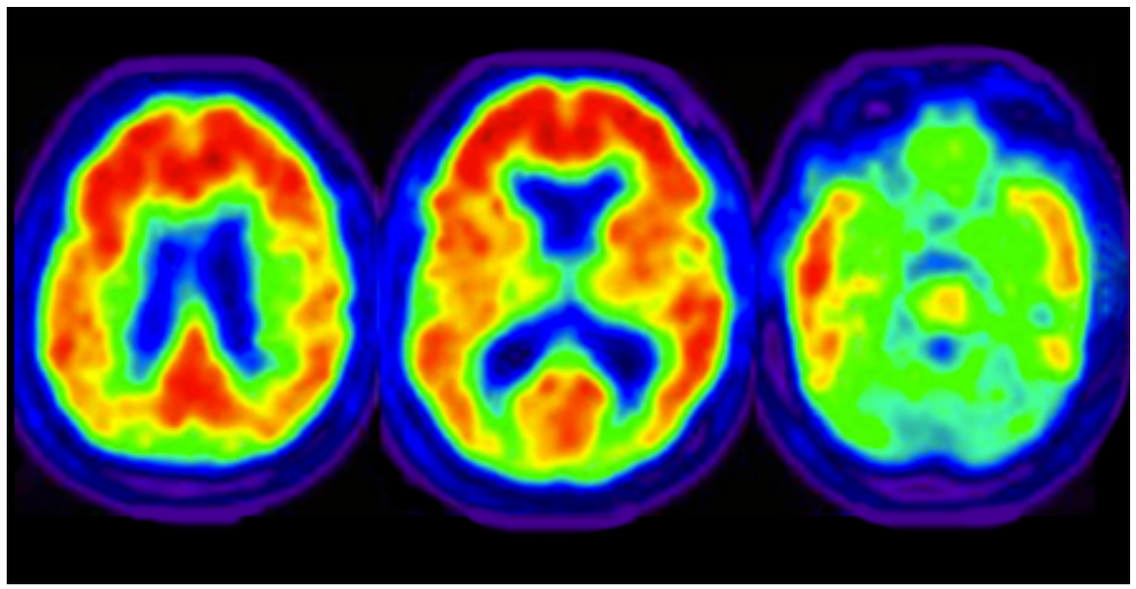
Caveats

- Averaging in time necessary: repeated presentations of stimulus
- Brains differ greatly in their fine structure: averaging among subjects thus inherently fuzzy
- Captures increases in blood flow. Decreases may be very important too
- Danger of premature association of ‘function’ with ‘location’

Other important technologies 1:

Positron Emission Tomatography (PET):

Uses radioisotopes in the bloodstream. Like fMRI, it thus measures blood flow, not neural activity, and has been used for functional imaging.



PET	fMRI
Measures blood flow	Measures blood flow
Allows a limited range of movement	Allows almost no movement
Poorer spatial resolution	
Expensive	

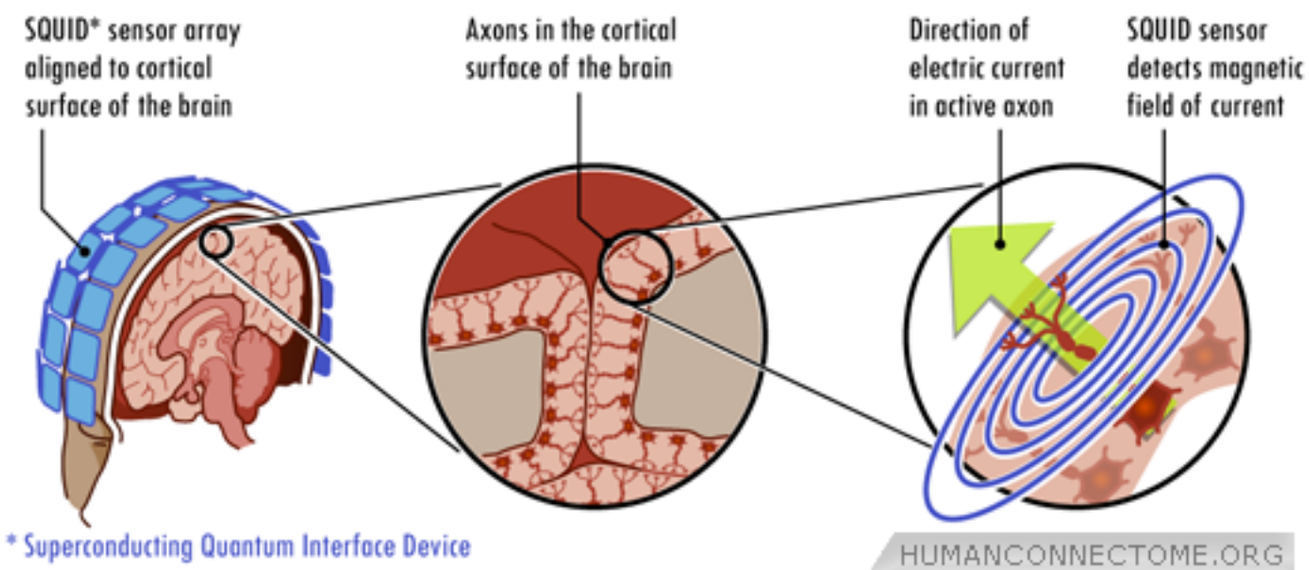
fMRI with two brains at the same time

Other important technologies 2:

Magneto Encephalography (MEG)

Measures changes in magnetic field associated with changing electrical activity.

Excellent temporal resolution.



Hybrid methods are being intensively developed:

fMRI + EEG

EEG + NIRS

EEG + MEG

etc

Two peculiar features of human central neuroanatomy and physiology

(1) Mirror Neurons

(2) Spindle Cell Neurons

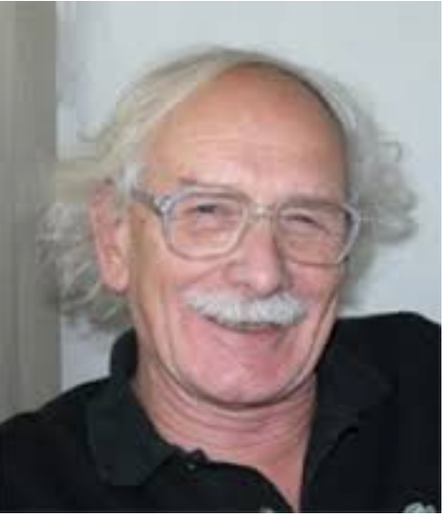
Mirror Neurons

Unknown before 1992, Mirror Neurons jumped onto the stage in the late 1990s.

A quick search of Google Scholar for “mirror neurons” now returns over 27,000 results[1].

A chance finding in a lab in Parma, Italy has led to an enormous amount of kerfuffle. Let’s see why.

1. Last check, Nov 27, 2017



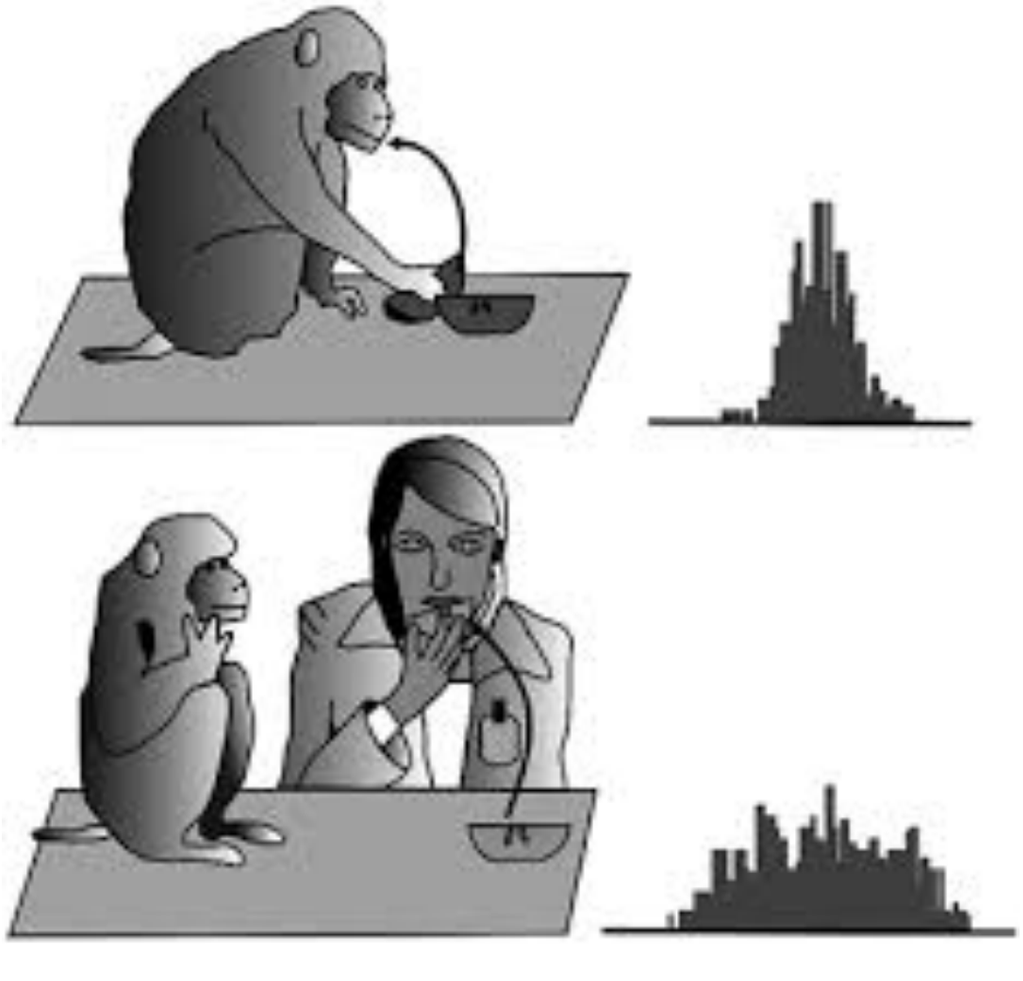
Giacomo Rizzolatti

With Gallese, Fadiga, Di Pellegrino, Fogassi

Studying *ventral premotor cortex* - a *motor* region in rhesus macaque monkeys, using single cell recordings

Repeatedly found neurons that were very active when the monkey was performing a goal directed action (picking up a peanut)

And accidentally found that the same neuron would fire strongly when seeing an assistant do the same action



peanut grabbing

paper ripping

???? more????

2002: similar responses found to sounds of goal directed actions (paper ripping, peanut breaking)

Monkey ventral pre-motor cortex is, in many respects, analogous to Broca's area in human (left) pre-frontal cortex (Brodmann area 44/45)

Broca's area is particularly active when speaking, and for fine, skilled manual movements.

Some estimate that 10% of neurons in monkey ventral pre-motor cortex have mirror properties.

Prevalance in humans is less well documented, though it is suspected that they are widespread.

There has been much (and undisciplined) talk of a mirror neuron *system.* Why have these aroused so much interest?

They suggest (to some) a neural basis for understanding the *intentions* of others.

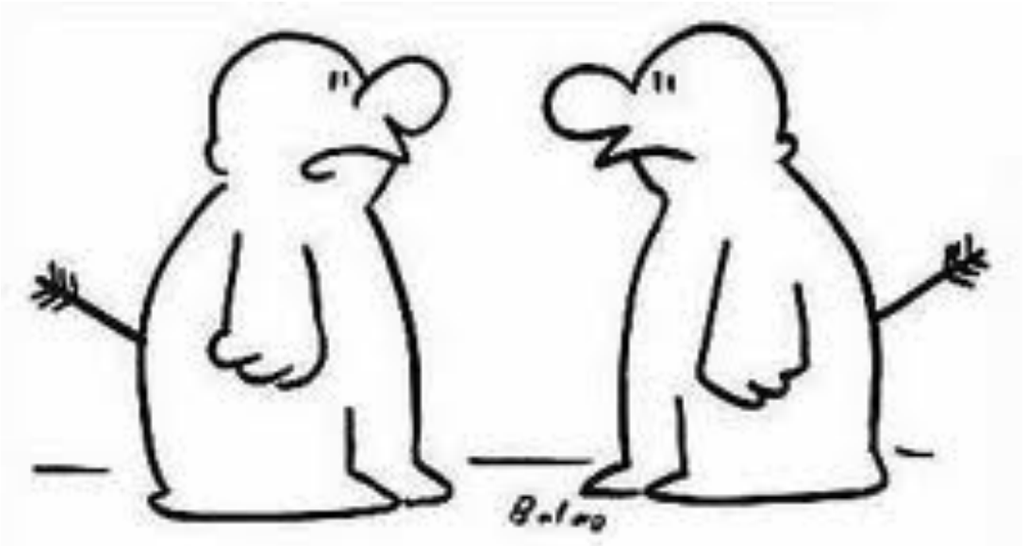
E.g. neurons have been found (in monkey) that fire strongly for “grasp-to-eat”, but not for “grasp-to-place-in-cup”

Does this help bridge the gap from perception to meaning?

Leonardo et al (2005) “Parietal lobe: from action organisation to intention understanding” *Science* 308

Several researchers have argued that a mirror system could provide a neural account of *empathy*.

Frans de Waal, Vittorio Gallese, Christian Keysers etc.



Most of this work is based on fMRI and regional bloodflow, not on direct observation of mirror neurons

Ramachandran has argued that
a mirror system could form the basis
for self-awareness

[T]hese neurons can not only help simulate other people's behavior but can be turned 'inward'—as it were—to create second-order representations or meta-representations of your own earlier brain processes. This could be the neural basis of introspection, and of the reciprocity of self awareness and other awareness

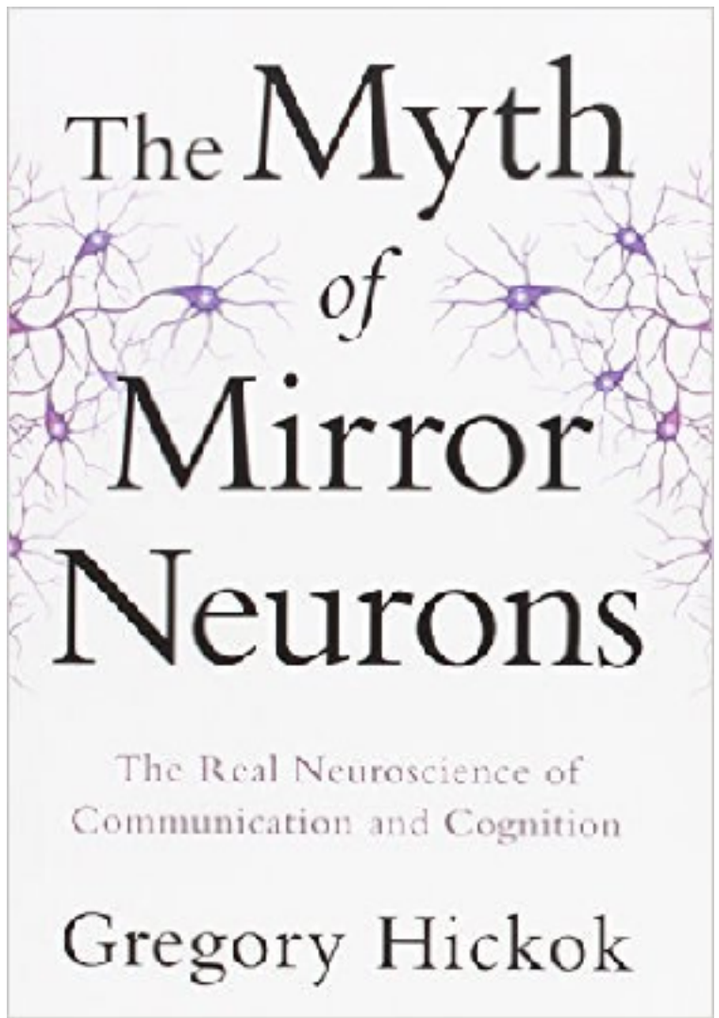
The hand-mouth overlap found in Broca's area has led some (Rizolatti, Arbib) to claim that mirror neurons provide a foundation for the development of *language*.

Rizzolatti, G., & Arbib, M. A. (1998). Language within our grasp. *Trends in Neurosciences*, 21(5), 188-194. (almost 3k citations)

The claimed abilities of neonates (and monkeys) to imitate facial expressions, with no visual knowledge of their own face, has been suggested to be based on the mirror system

Understanding intentions/meaning
Empathy
Self-understanding
Language
Imitation
. . . . .

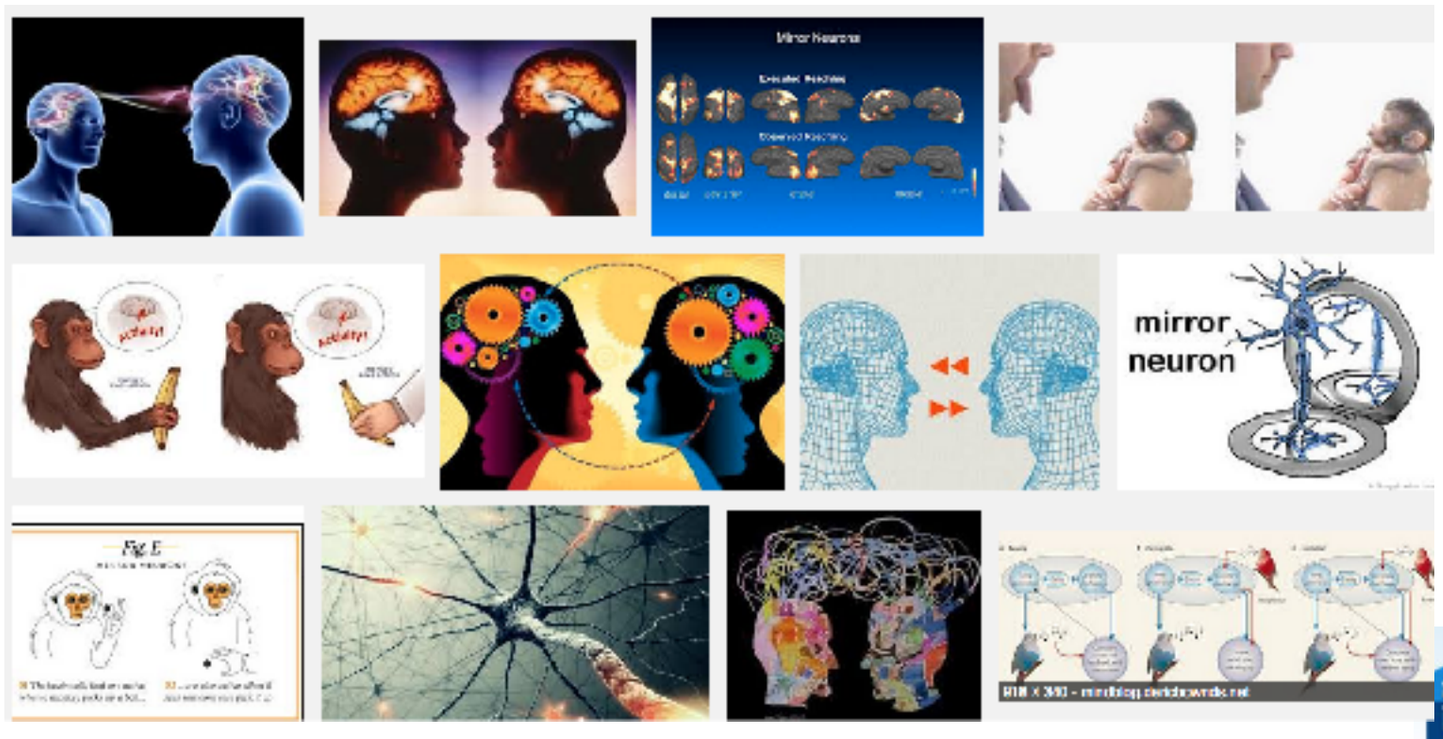
Critics caution:
* no mirror system has been identified
* invoking “mirror-ness” explains nothing at all
* the direct “link” between perception and action could surprise only one committed to a particular, and particularly problematic, view of humans as a linear through put system



Even within representational, information processing accounts, there is no consensus here.

Sound familiar?

Exercise: discuss these images.
What are we projecting onto the brain?

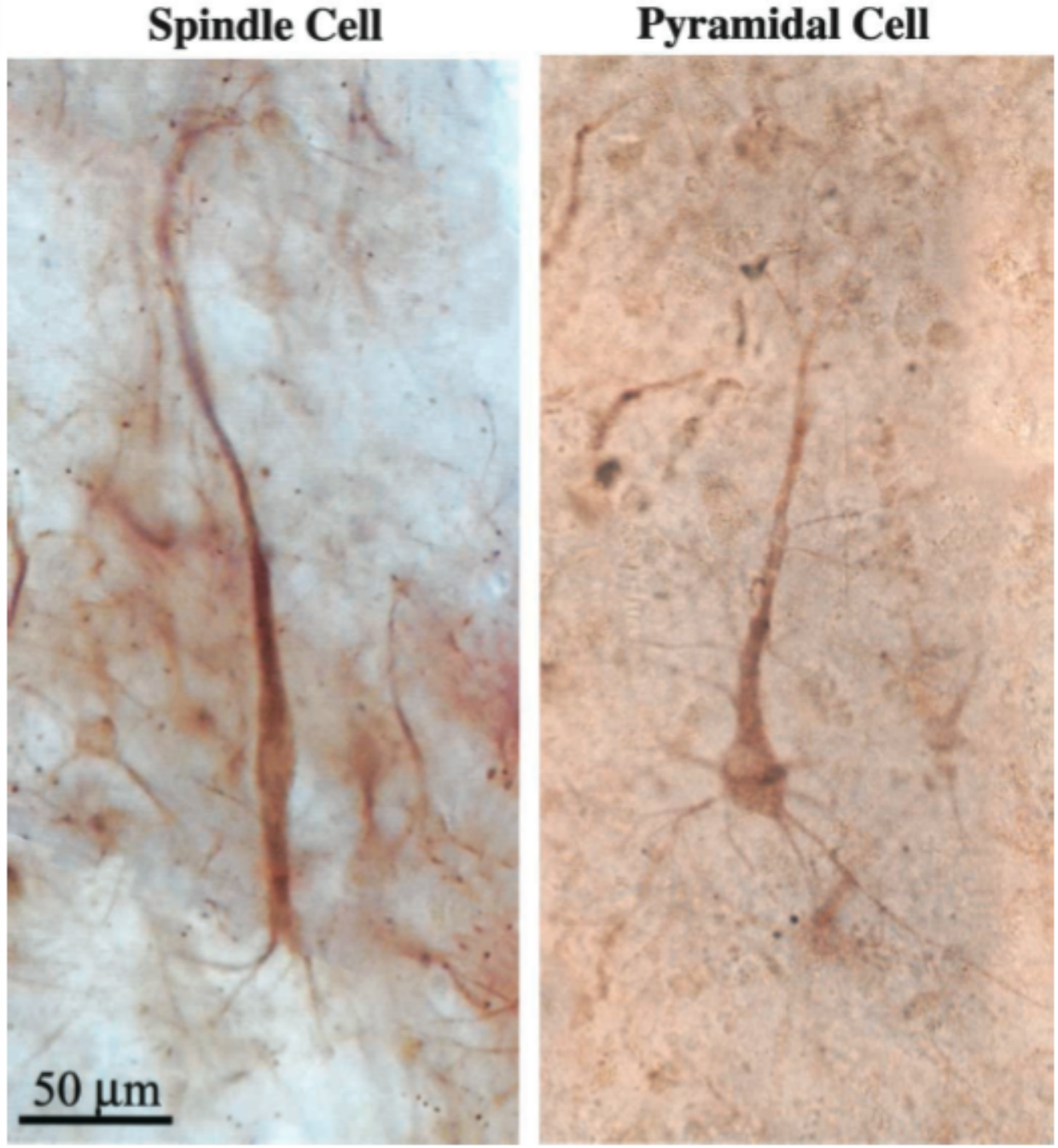


von Economo Neurons (Spindle cell neurons)

Described in 1929 by Constantin von Economo.

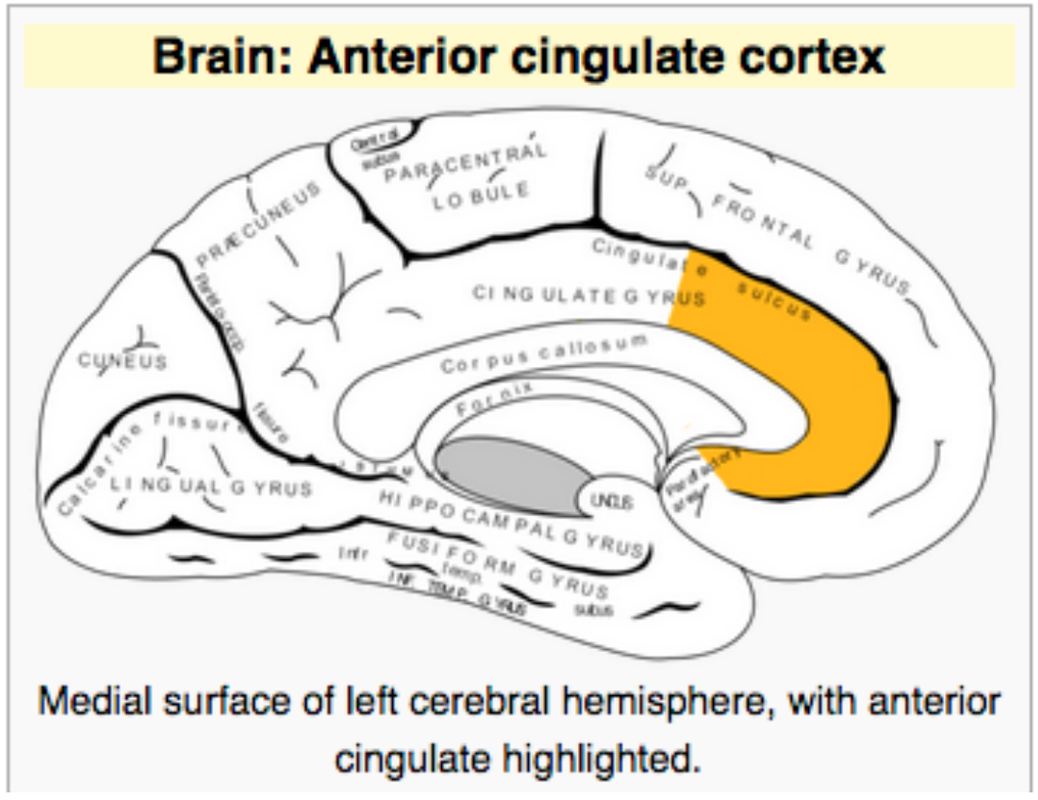
Long thought to be unique to great apes . . .

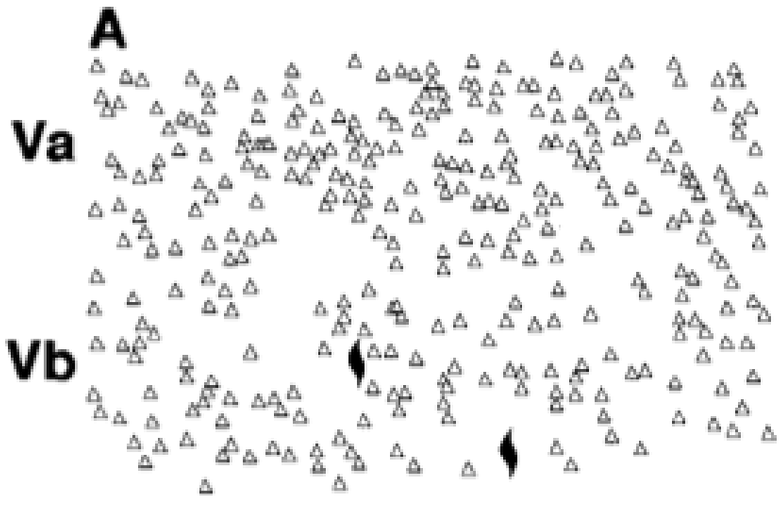
though a very few have recently been found in macaque too.

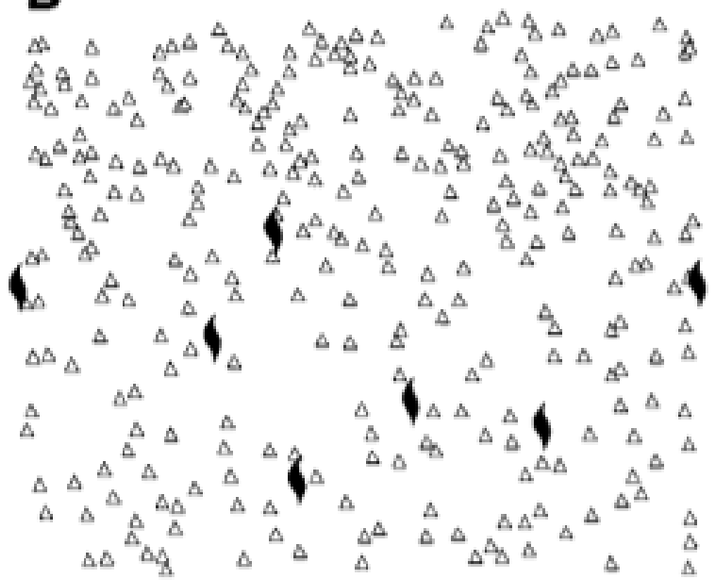


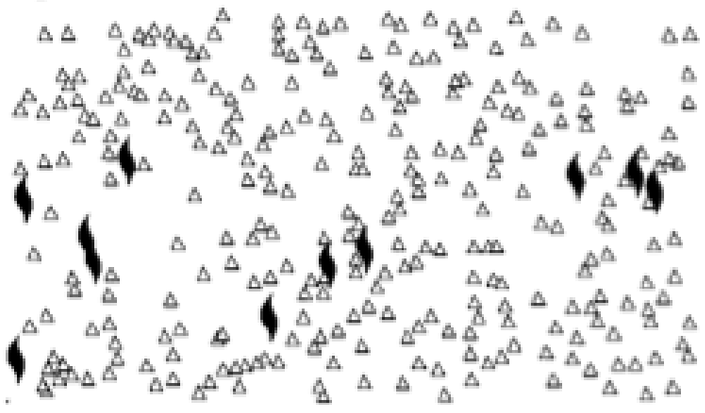
Found in Anterior Cingulate Cortex, and the base of the frontal lobes, above the eye socket.

ACC: the dustbin of cognitive neuroscience, or part of the "social brain"???




A
Va
Vb


B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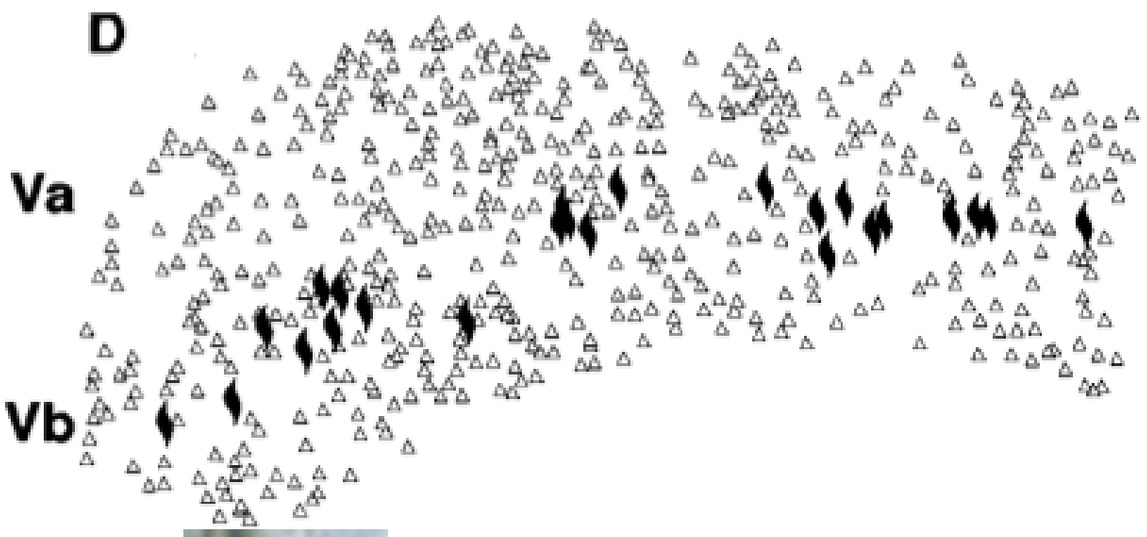
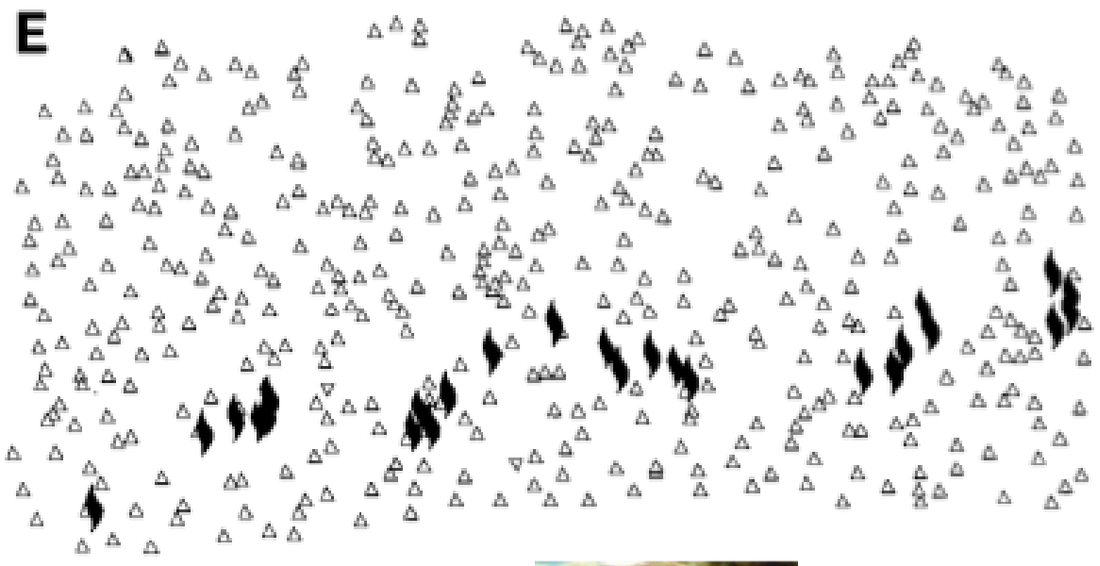
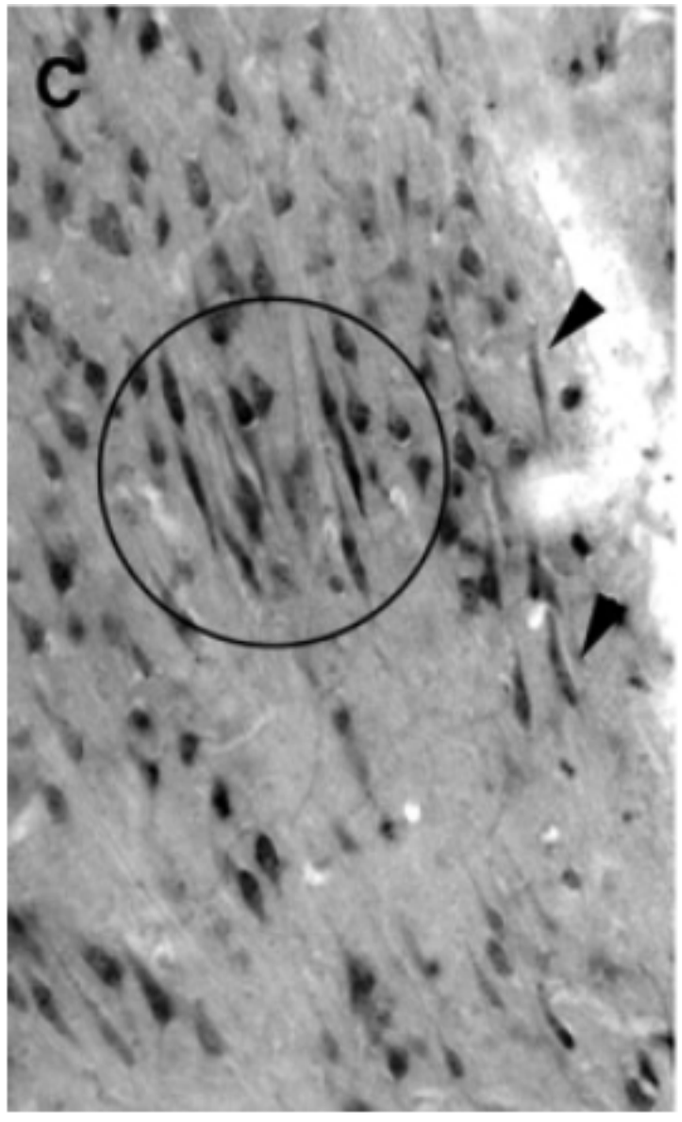

D
Va
Vb


E

Astonishingly, spindle cells have recently been found in the forebrain of a female humpback whale, and in small numbers in a few other cetaceans!



Female humpbacks are richly social, but we know relatively little about their social lives.

Convergent Evolution, but WHY? What is the common (social?) problem that these cells help solve?

Even more recently, spindle cells have also been found in Elephants, another intensely social animal.

Great Apes, Cetaceans, Elephants.

What are we learning here from the brain?