PSYCH 260

History & Methods

Rick O. Gilmore

2021-09-02 09:13:31

Classic "Powers of Ten" movie by Charles and Ray Eames (10 min).

Today's topics

- History of neuroscience

- Levels of analysis

- Methods to the madness

Warm-up

Neuroscience is harder than physics because…

- A. The brain has more parts than any other physical entity we know about.

- B. Physicists have largely ignored biology.

- C. Nervous systems are influenced by multiple factors we can't (yet) measure effectively.

- D. Physicists only study "toy" problems.

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- C. Interactions among components

- D. Inputs and outputs

- E. Readily predictable behavior

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History of neuroscience

Why study history?

- What can *observation* tell us about brain and behavior?

- Vital role of *tools/methods/techniques* in discovery

- *"If I have seen further, it is by standing on the shoulders of giants."* – Isaac Newton, 1676

The Ascent: A Brief History of the Brain

# What did early humans know about the mind and brain?

- Mental functions controlled by organs in the head, i.e., the brain

- Mental functions can be influenced by substances we consume

- Head injury can impair behavior and thinking

- Something flows from brain to body via nerves

Why didn't they know more?

Why didn't they know more?

- A. Limited technology.

- B. Limited cultural support for systematic observation & description. = SCIENCE

- C. Lack of ability to use knowledge even if it were acquired.

The body as machine (René Descartes – mid 1600's)
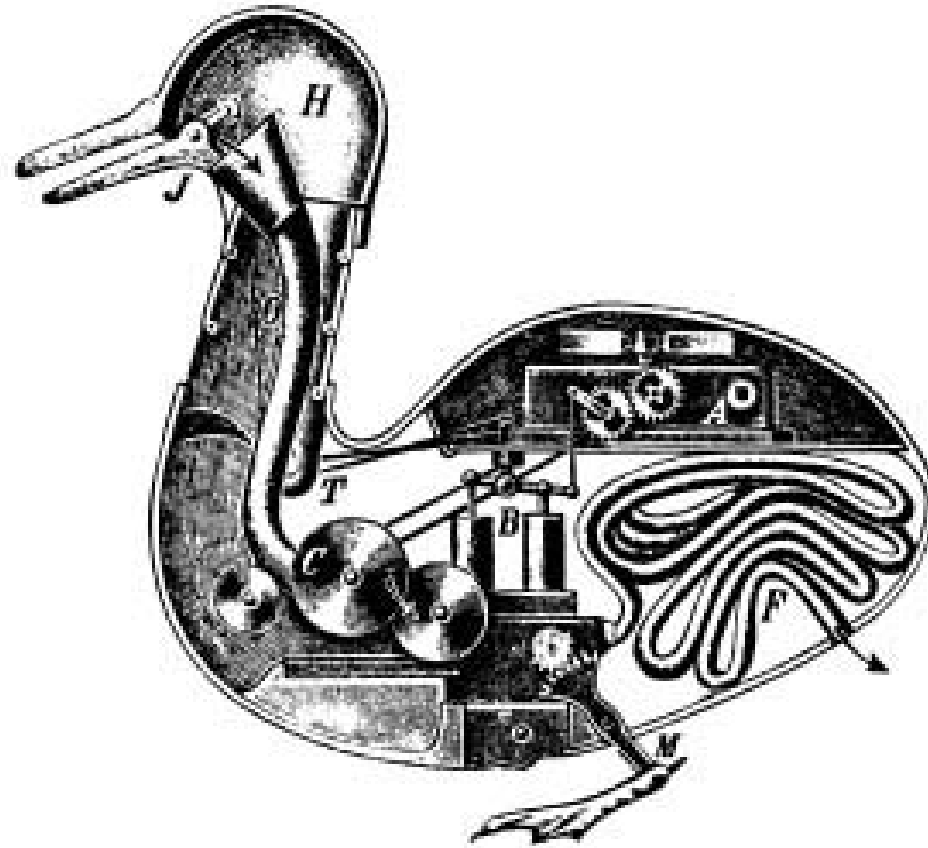
Descartes' 'reflexes'

- Reflexes "reflect" events in the world
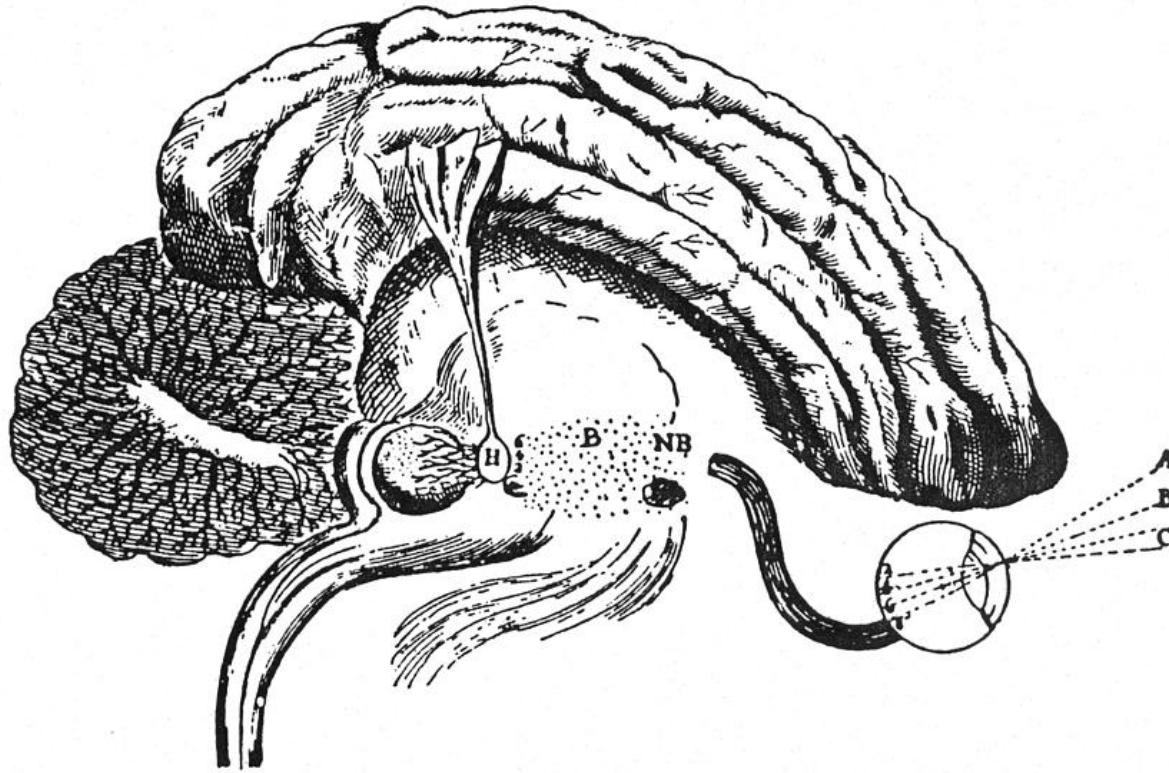
- Not the same as voluntary functions

Descartes' reflexes

Descartes' 'dualism'

- Reflexes and animal "minds" are physical, machine-like

- Human mind is not

    - "Dual" influences on behavior

    - Physical + spiritual

- Soul controls body via *pineal gland*

    - Causes muscles to "inflate"

Pineal gland

Do you agree with Descartes?

- A. **Yes**, human minds are fundamentally different from animal minds. The human mind is influenced by both physical and extraphysical processes.

- B. **No**, human minds are similar to animal minds. The human mind arises solely from physical processes.
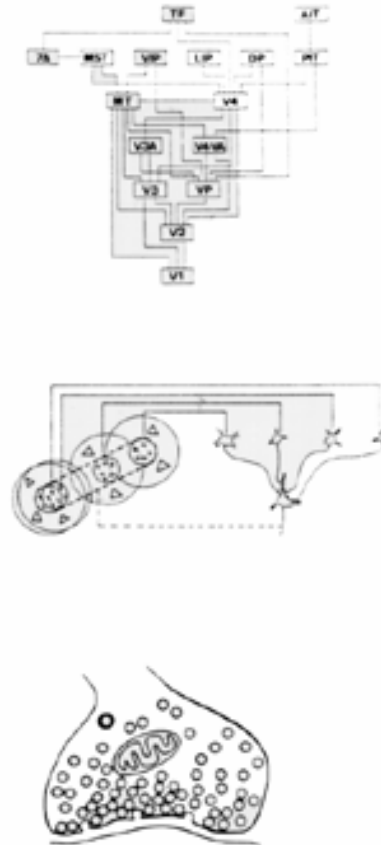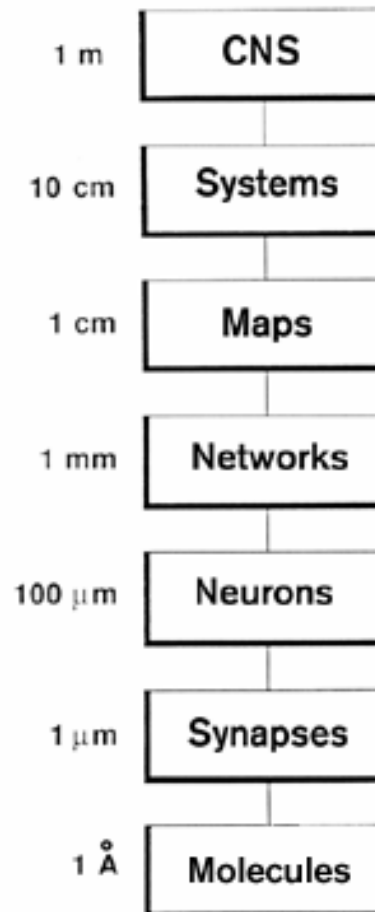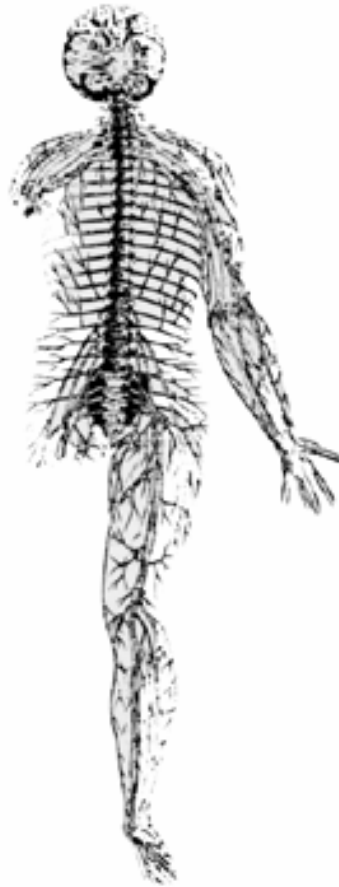
How would you test Descartes idea about the role of the pineal gland?

The lessons from history

- Neuroscience shaped by new methods, tools

- Neuroscience shaped by great debates

    - Mind == brain debate

    - Are functions local or distributed?

    - Do neurons connect like pipes or pass info like relay runners?

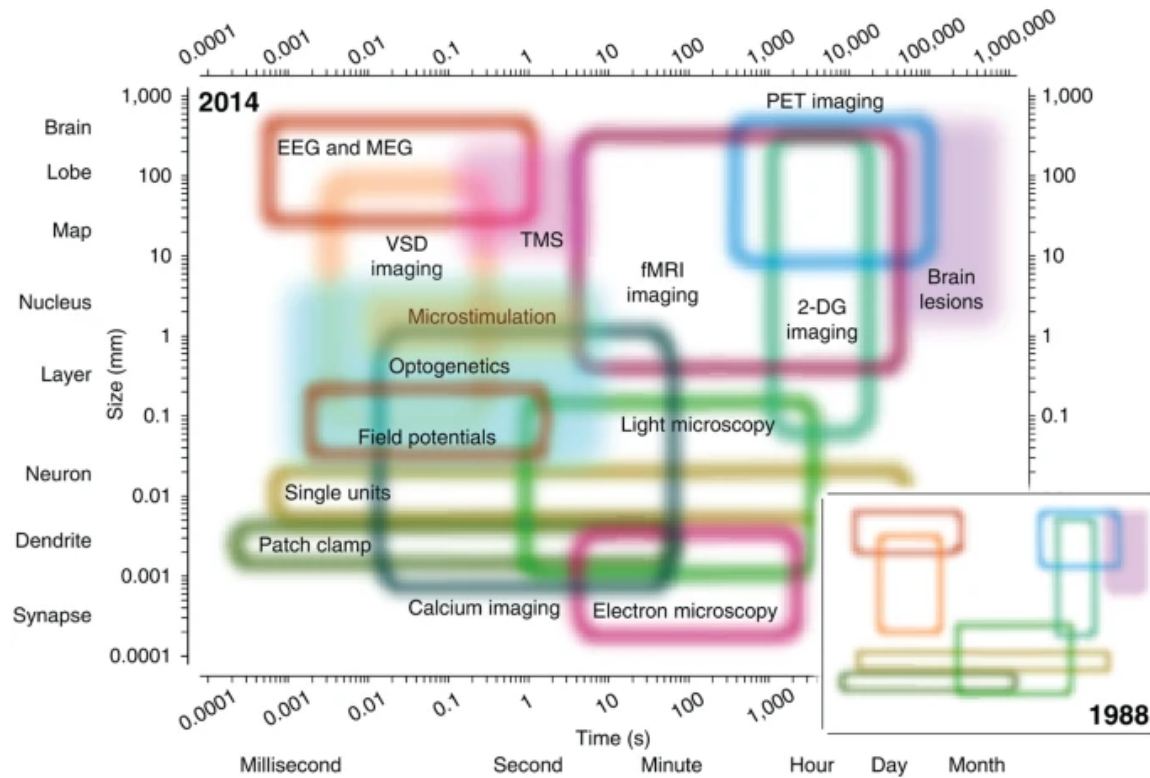- Forms at multiple levels of analysis contribute to function

Levels of analysis

Spatial resolution

Spatial and Temporal Resolution

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knitr::include_graphics("https://media.springernature.com/lw685/springer-static/image/art%3A10.1038%2Fnn.3839/MediaO
```


[@sejnowski2014putting]

Spatial Resolution in Detail

- Within an individual
  - molecular
    - genetic
    - receptor
  - chemical
    - neurotransmitter/hormonal
  - cellular
    - neuronal firing

Spatial Resolution in Detail

- Internal to individuals
    - network
        - lateral inhibition
    - area
        - V1 varies by ~2x
    - region
        - Wiring/connectivity differences
    - system

Spatial Resolution in Detail

- External to individuals
    - Social
        - Friends, family, teachers, others
    - Non-social
        - Neighborhood, school, state/region, country
        - Physical environment

Temporal Resolution in Detail

- Within one lifetime
    - Microseconds
        - detection position from acoustic stimulation
    - Milliseconds
        - action potential
    - Seconds
        - changes in EEG power
        - short-term memory

Temporal Resolution in Detail

- Within one lifetime

    - Minutes

        - synaptic plasticity

    - Hours

        - memory consolidation

        - Hormone (melatonin, cortisol) levels

    - Days

Temporal Resolution in Detail

- Within one lifetime

    - Weeks

    - Months

    - Years

        - education & training

        - disease processes

        - cultural change

Temporal Resolution in Detail

- Across lifetimes

  - Centuries

    - cultural changes

  - Millenia

    - Natural & sexual selection

Why does this matter?

- Different methods, different levels of analysis
- Challenge of linking phenomena across levels
    - How does the micro affect macro or vice versa?
- Challenge of interpretation

Neuroscience methods

Methods to the madness

- Tools in the neuroscientist's toolkit
- What they tell us, and what they don't

Evaluating methods

- What question does method X answer?

- What are we measuring?

  - Structure

  - Activity

- Strengths & Weaknesses

  - Cost (time/$)

  - Invasiveness

  - Spatial/temporal resolution

Spatial and Temporal Resolution
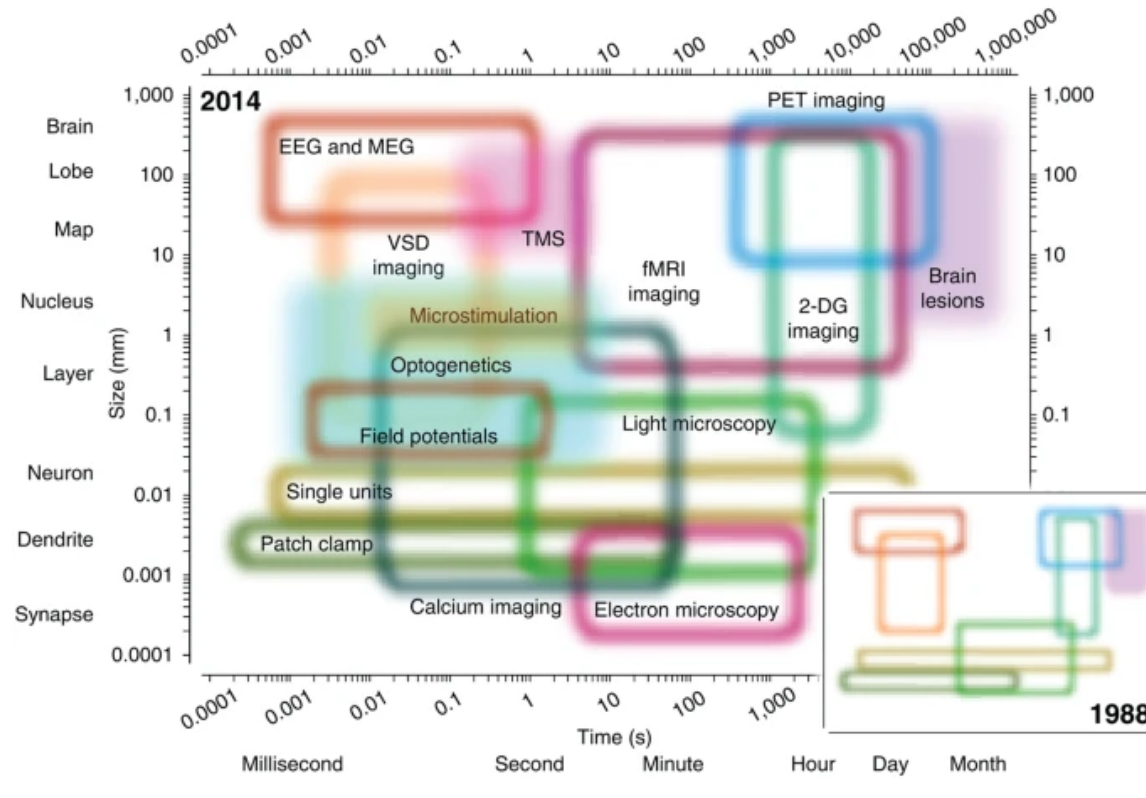
Sejnowski 2014

Types of methods

- Structural
    - Mapping the circuitry
    - Anatomy & connectivity
- Functional (next time)
    - What does it do?
    - Physiology/Activity

Mapping structures

- Cell/axon stains
    - *Golgi stain* – whole cells
        - Camillo Golgi
    - *Nissl stain* – cell bodies only
        - Franz Nissl
    - Cellular distribution, concentration, microanatomy

Golgi stain
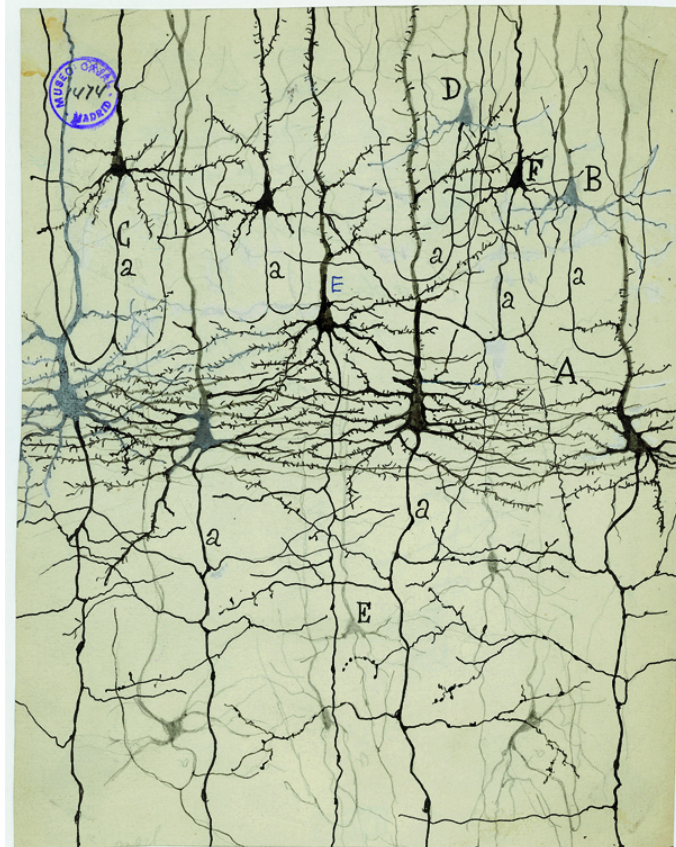
- Complete nerve cells, but only 5-10% of total

Nissl stain
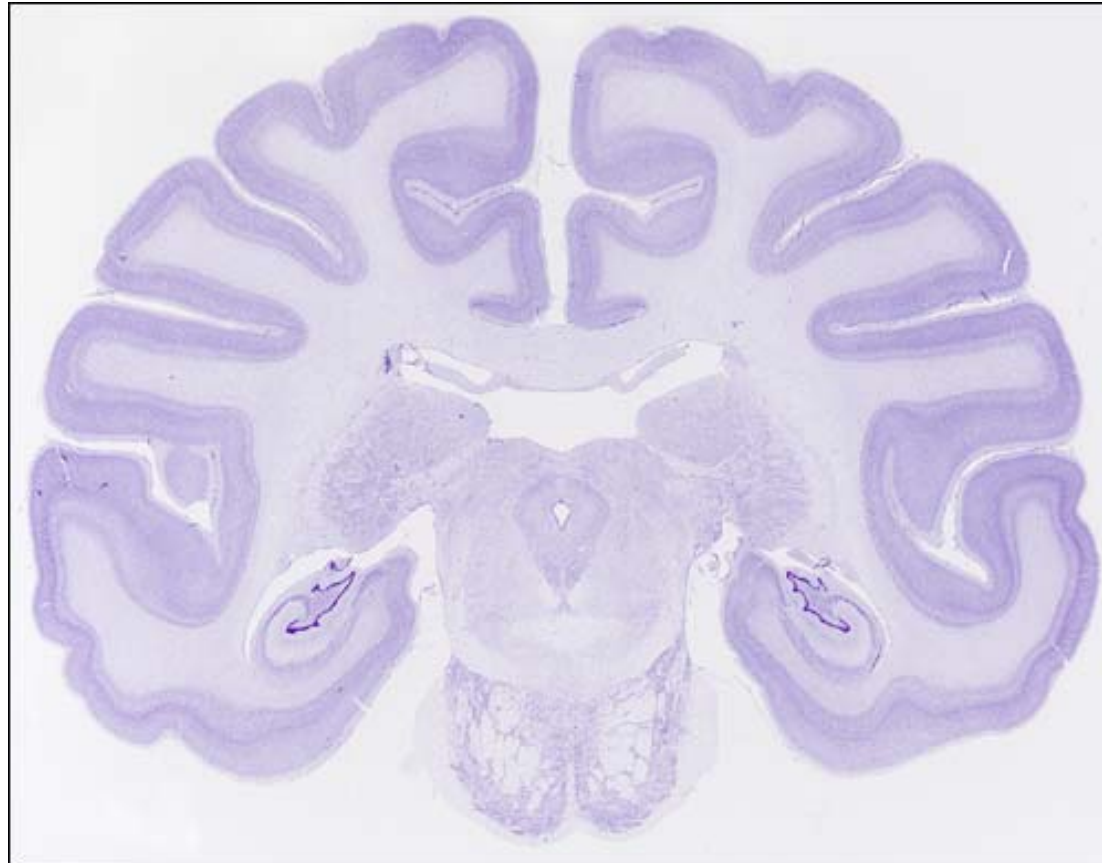
- Only cell bodies
- Density of staining ~ cell density/number

Retrograde vs. anterograde histochemical tracers

- Neuron information flow *polarized*–flows in one direction

  - ≠ electronic wires, but like pipes

- *Retrograde* (from *axon terminal* to *cell body*); *anterograde* (from cell body to axon terminal)

- What connects where

  - inputs to region X

  - outputs from region X
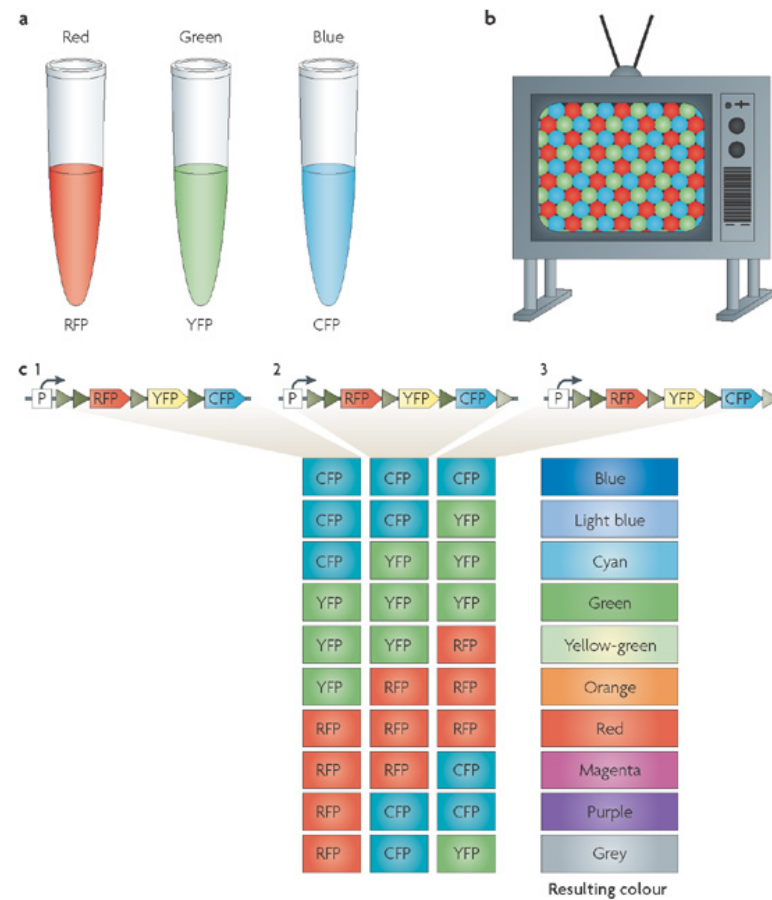
Retrograde vs. anterograde tracers

Brainbow

Nature Reviews | Neuroscience
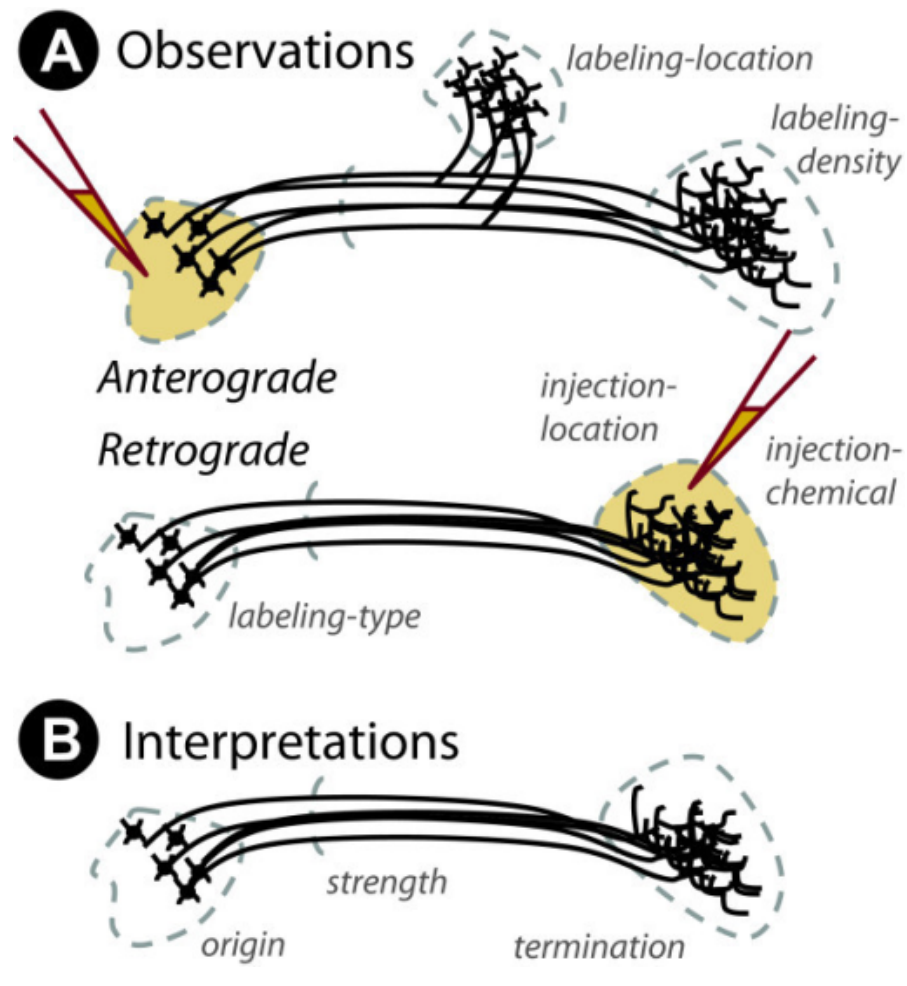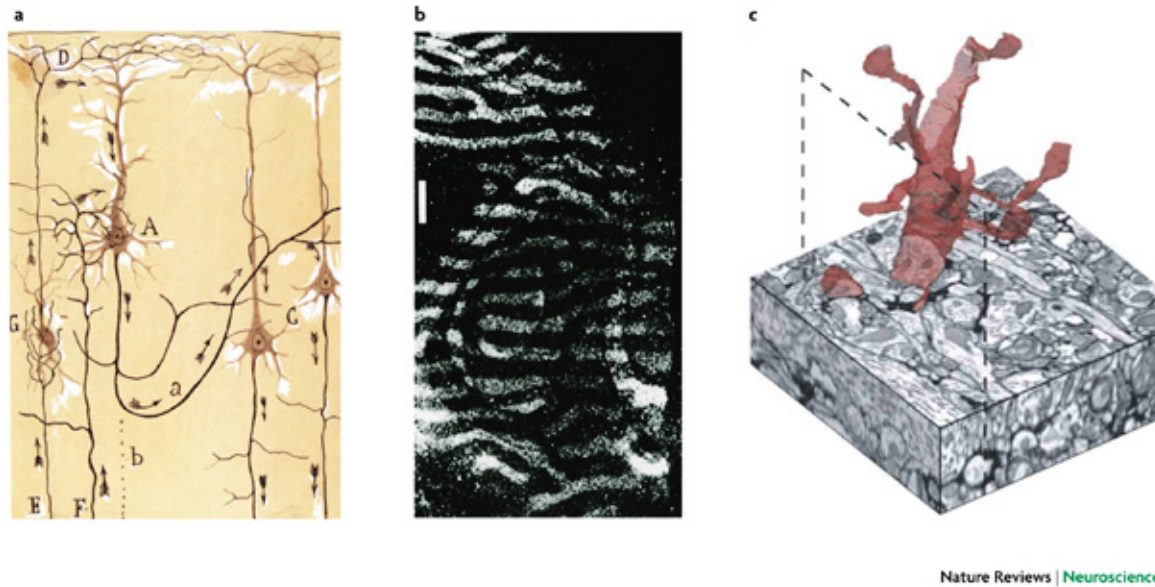
Lichtman, 2008

Brainbow

Lichtman, 2008

Beautiful 3-D Brain Scans Show Every Synapse | National Geographic

"If understanding everything we need to know about the brain is a mile, how far have we walked?" – J. Lichtman
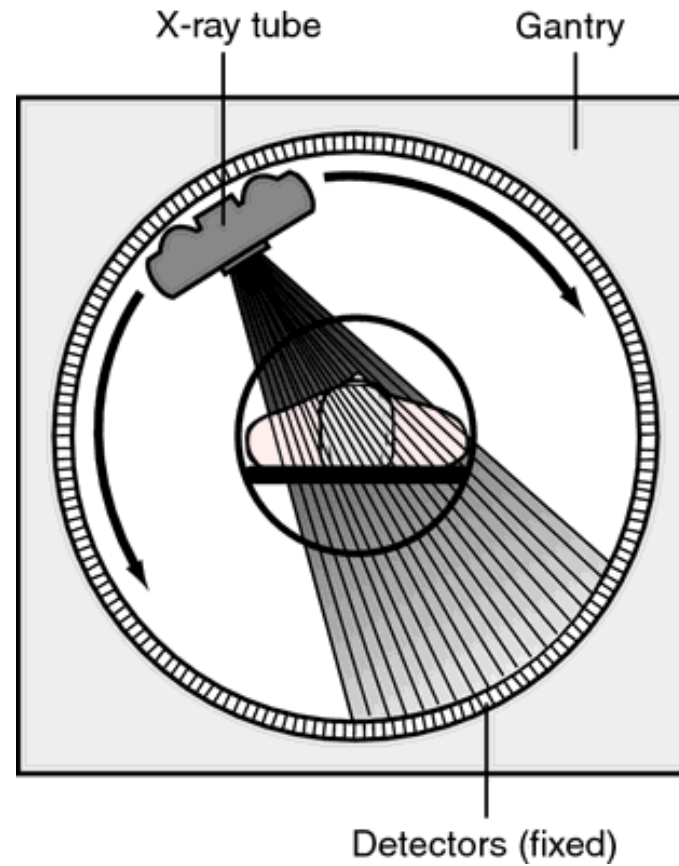
Clarity

See-through brains

Evaluating cellular tracing techniques

- Invasive (in humans post-mortem only)

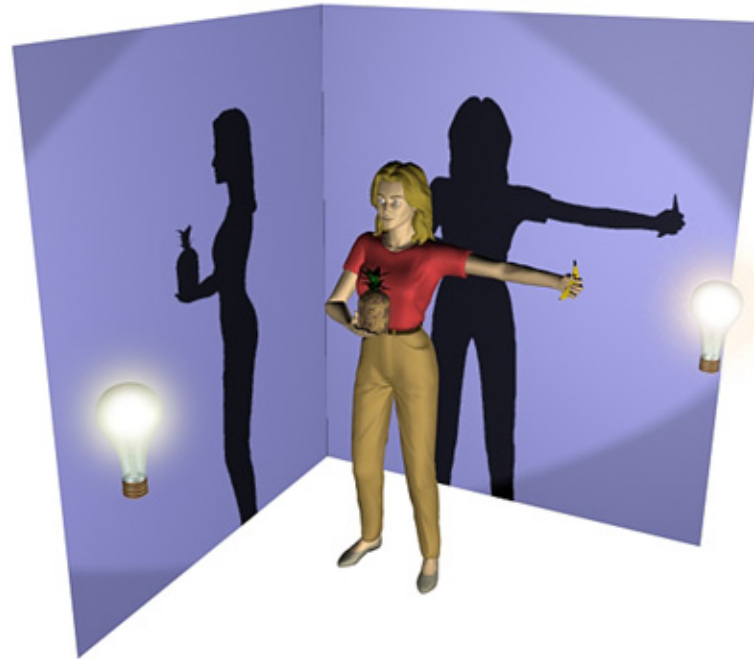- High spatial resolution, but poor temporal resolution

    - Why?

Mapping structures

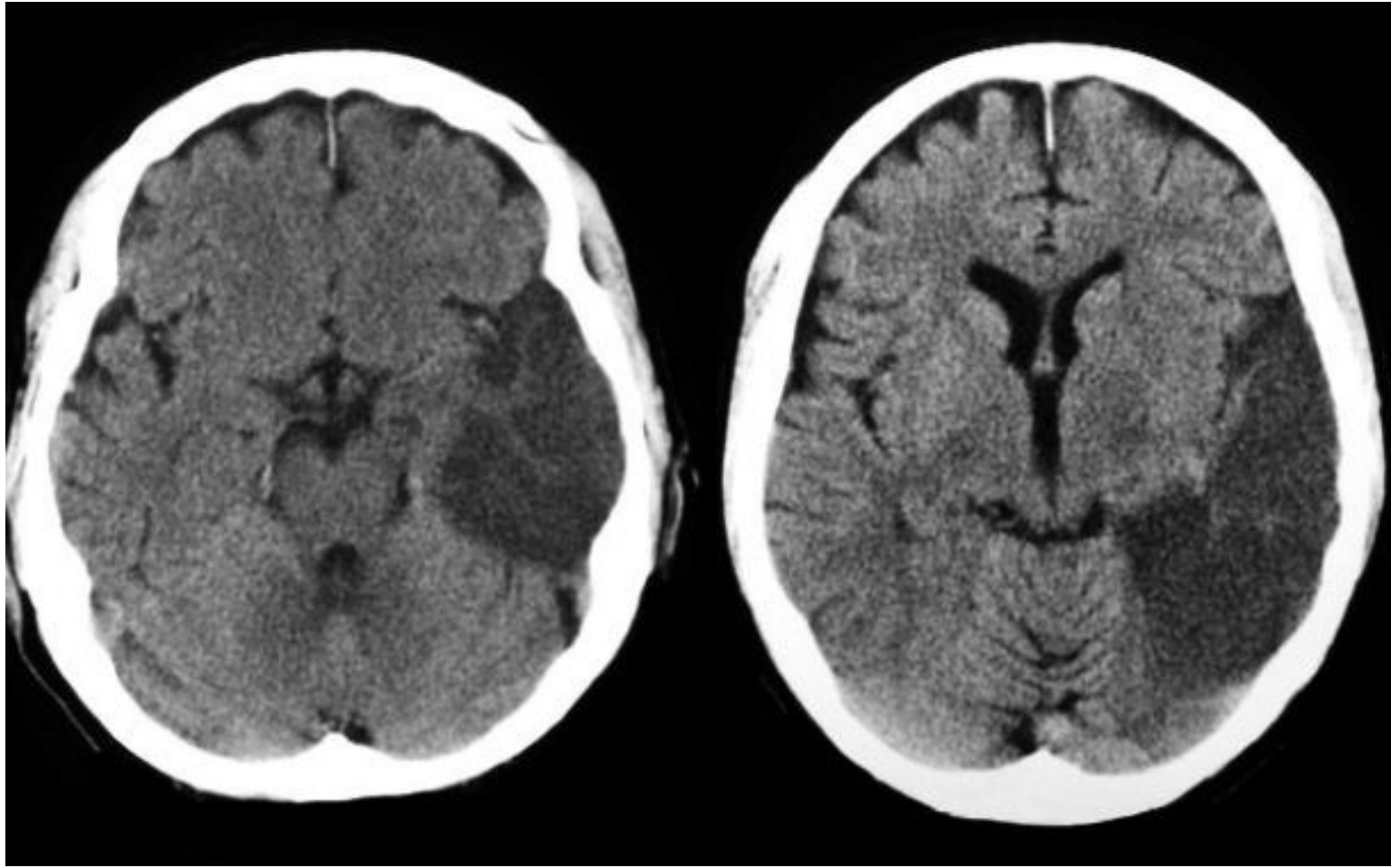- Computed axial tomography (CAT), computed tomography CT

- X-ray based

Tomography

Tomography

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https://cdn.hswstatic.com/gif/cat-scan-pineapple.jpg

CT scan of stroke

Magnetic Resonance Imaging (MRI)

- Magnetic resonance

- Some common isotopes (e.g., H) & complex molecules have a magnetic dipole

- Axes align with strong magnetic field

- When alignment perturbed by radio frequency (RF) pulse, speed of realignment varies by tissue

- Realignment emits RF signals

- How MRI works

MRI

https://cdn.hswstatic.com/gif/mri-steps.jpg
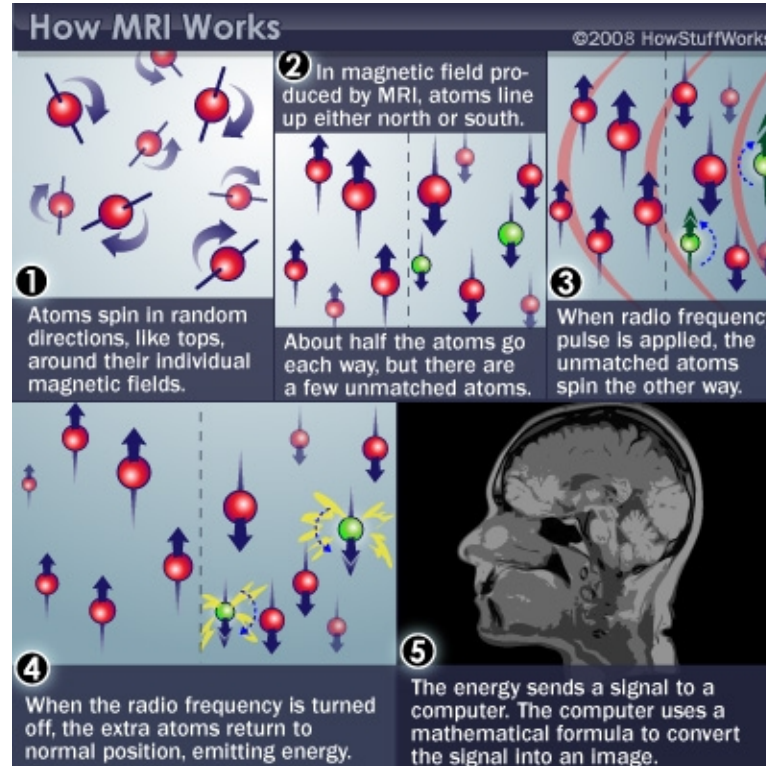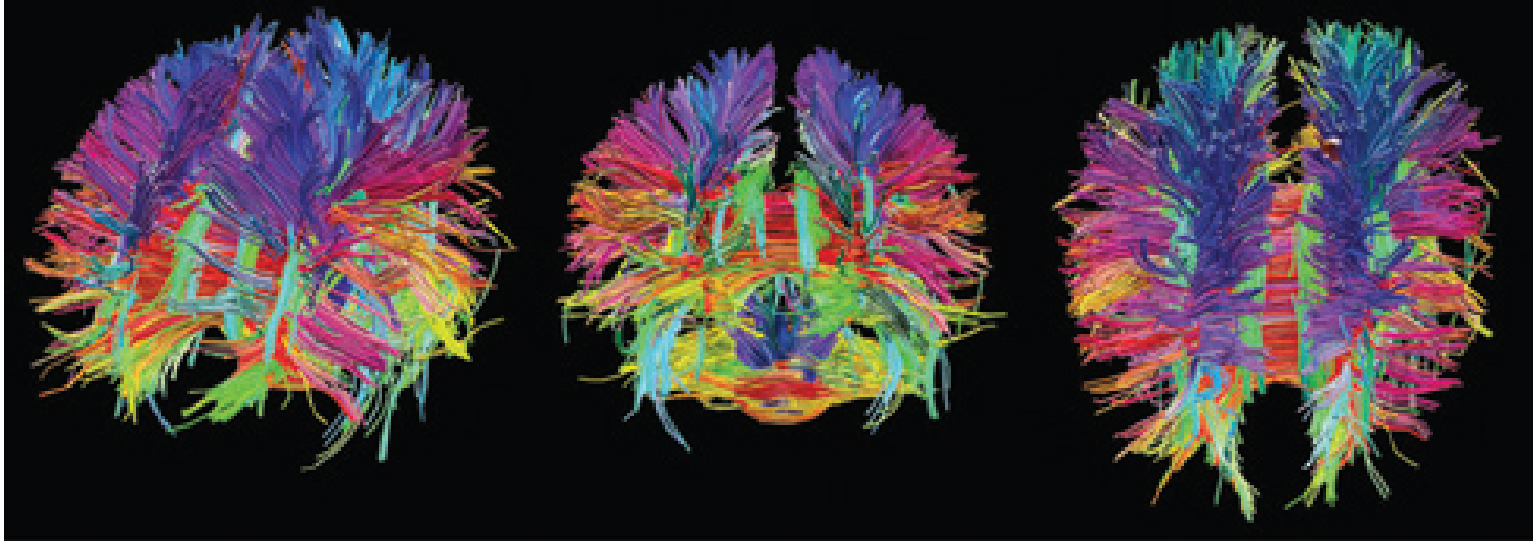
How MRI works

How Does an MRI Scan Work?

Structural MRI

- Reveals tissue density/type differences

- Gray matter (neurons & dendrites & axons & glia) vs. white matter (mostly axons)

- MR Spectroscopy

    - Concentration of specific chemical substances (only some have MR signature)

- Region sizes/volumes

Structural MRI of the brain

Diffusion tensor imaging (DTI)

Diffusion tensor imaging (DTI)

- Type of structural MRI

- Measures patterns of movement/diffusion of H_2O

- Reveals integrity/density of axon fibers

- Measure of connectivity

Voxel-based morphometry (VBM)

- Voxels (volume-based elements)

- Morphometry, measure ("metry") form/morphology

- How does brain size or thickness vary by age, disease status, etc.?
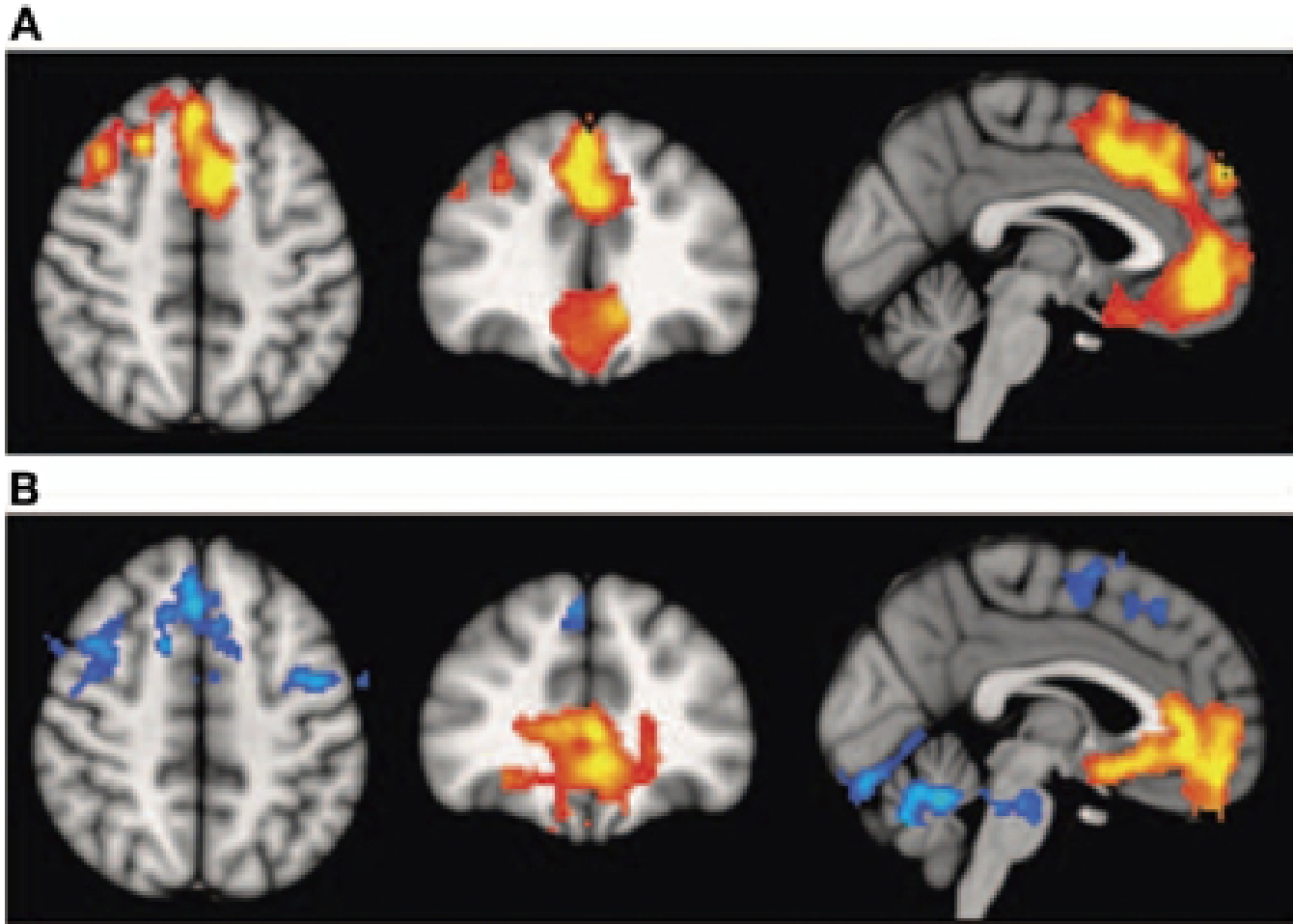
http://www.frontiersin.org/files/Articles/18691/fnhum-06-00184-HTML/image_m/fnhum-06-00184-g003.jpg

Main points

- Spatial vs. temporal resolution

- Structural methods (parts, sizes, connectivity)

Next time…

- *Functional* neuroscience methods

- Neuroanatomy