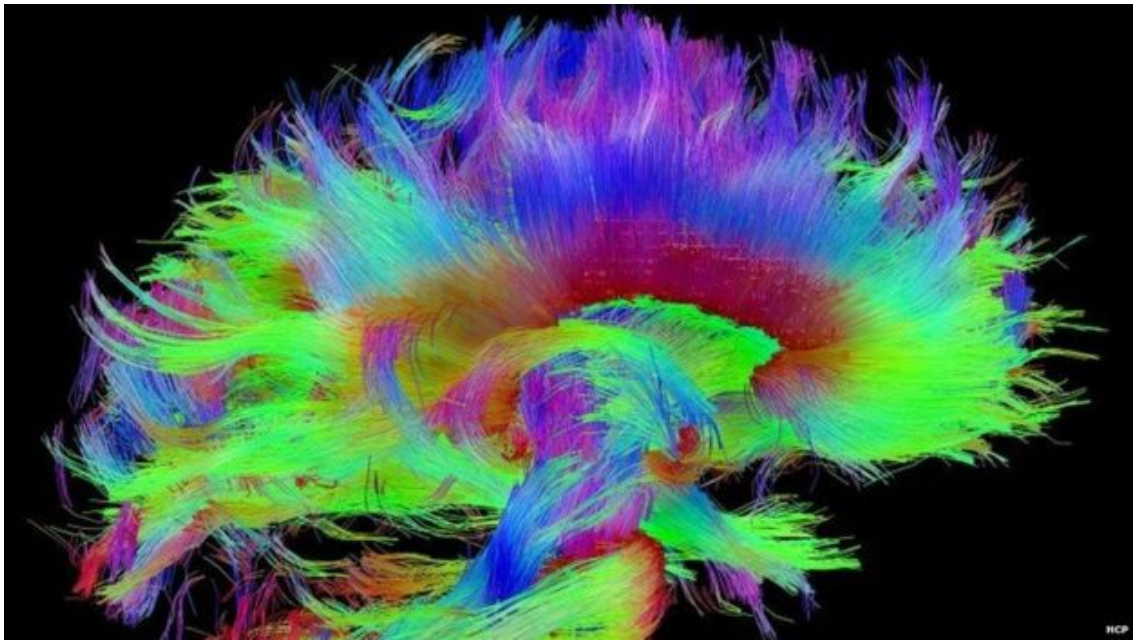
CS 4984: Computing the Brain

T. M. Murali

January 16 and 23, 2018



This course is NOT about

neural networks or deep learning.

Course Information

- Meet on Tuesdays and Thursdays, 12:30pm–1:45pm, MCB 134.
- Office hours: To be decided
- Course website: http://courses.cs.vt.edu/~cs4984/2018-spring-computing-the-brain. Consult this website regularly. Course schedule is subject to change.
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No class on Thursday, January 18, 2018

Textbook

Fundamentals of Brain Network Analysis
ISBN: 9780124079083

Fundamentals of
Brain Network Analysis

Alex Fornito, Andrew Zalesky, and Edward Bullmore

Fundamentals of Brain Network Analysis is a comprehensive and accessible introduction to methods for unraveling the extraordinary complexity of neuronal connectivity. From the perspective of graph theory and network science, this book introduces, motivates, and explains techniques for modeling brain networks as graphs of nodes connected by edges, and covers a diverse array of measures for quantifying their topological and spatial organization. It builds intuition for key concepts and methods by demonstrating how they can be practically applied across many different areas of neuroscience, ranging from the analysis of synaptic networks in the nematode worm to the characterization of large-scale human brain networks constructed with magnetic resonance imaging. This text is ideally suited to neuroscientists wanting to develop expertise in the rapidly developing field of neural connectomics, and to physical and computational scientists wanting to understand how these quantitative methods can be used to understand brain organization.

From the Foreword:

"This much needed primer on brain networks will become an indispensable addition to the bookshelves of all neuroscientists interested in the organization and function of nervous systems, from cellular to systems scales"

— Olaf Sporns, PhD, Distinguished Professor, Robert H Shaffer Chair, Indiana University

Key Features:

- Extensively illustrated throughout by graphical representations of key mathematical concepts and their practical applications to analyses of nervous systems
- Comprehensively covers graph theoretical analyses of structural and functional brain networks, from microscopic to macroscopic scales, using examples based on a wide variety of experimental methods in neuroscience
- Designed to inform and empower scientists at all levels of experience, and from any specialist background, wanting to use modern methods of network science to understand the organization of the brain

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Fornito
Zalesky
Bullmore

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Brain Network Analysis

ACADEMIC
PRESS

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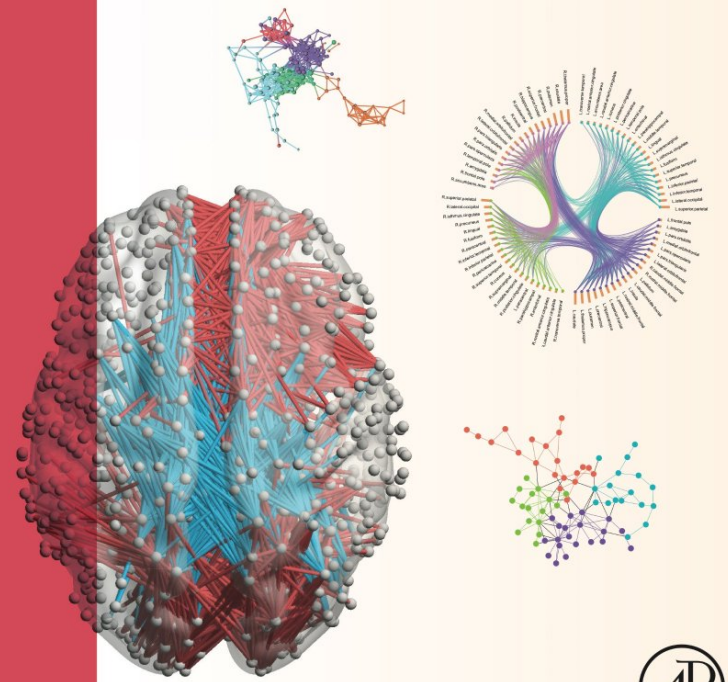
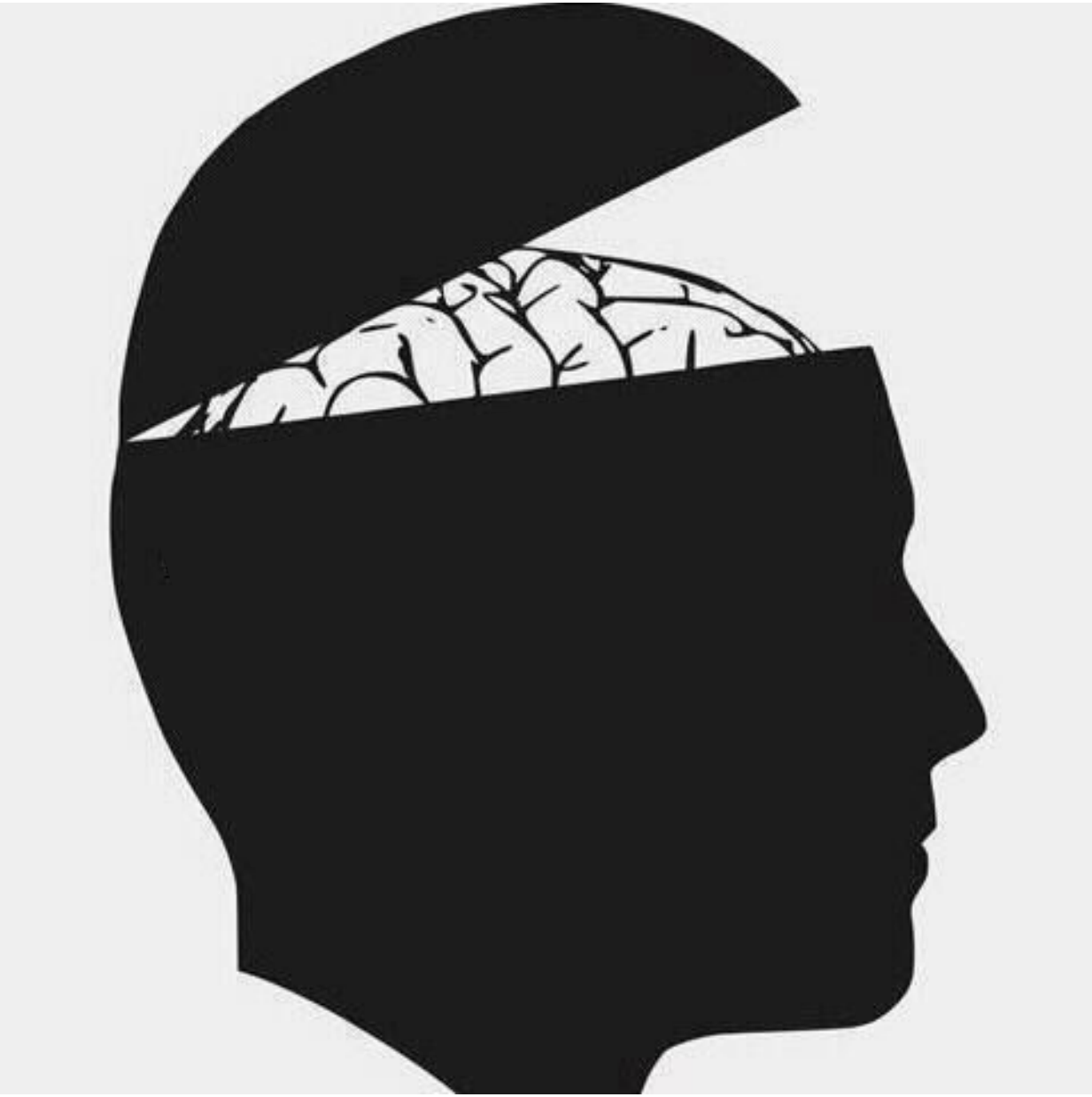


Course Pre-requisite



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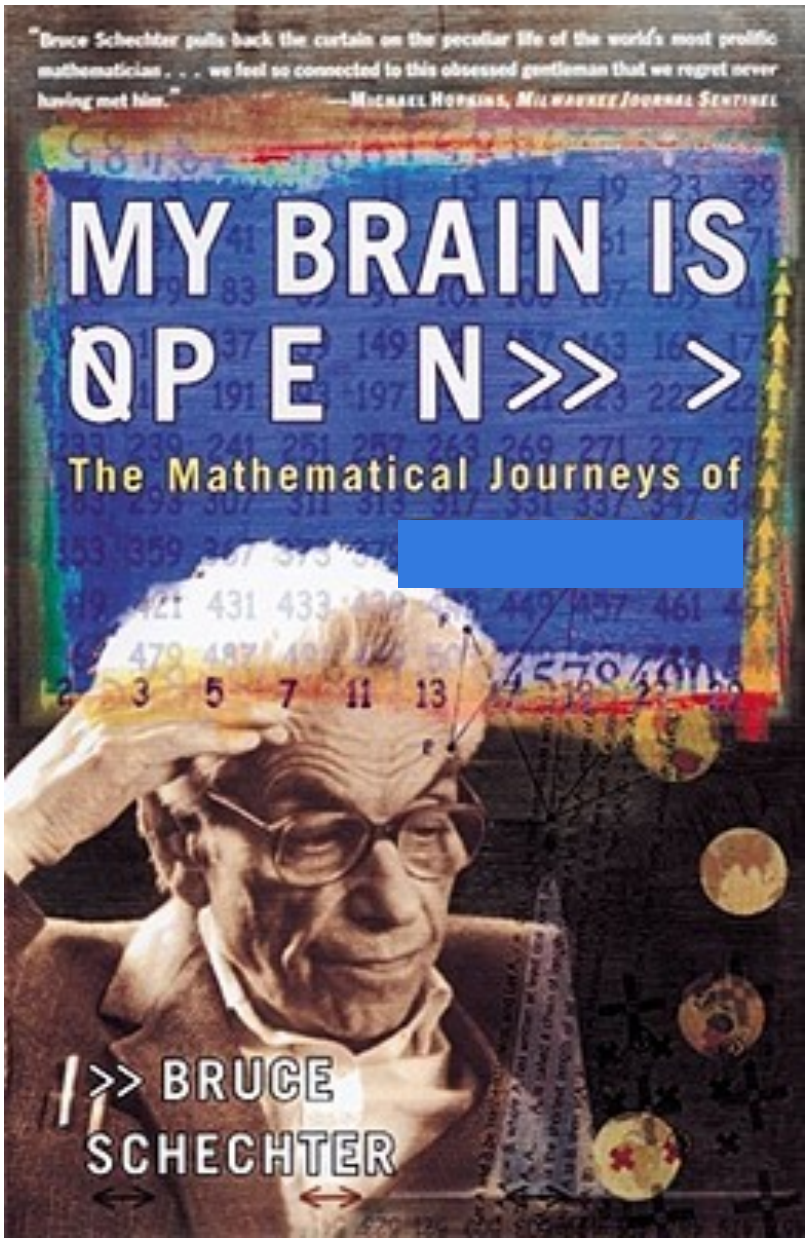

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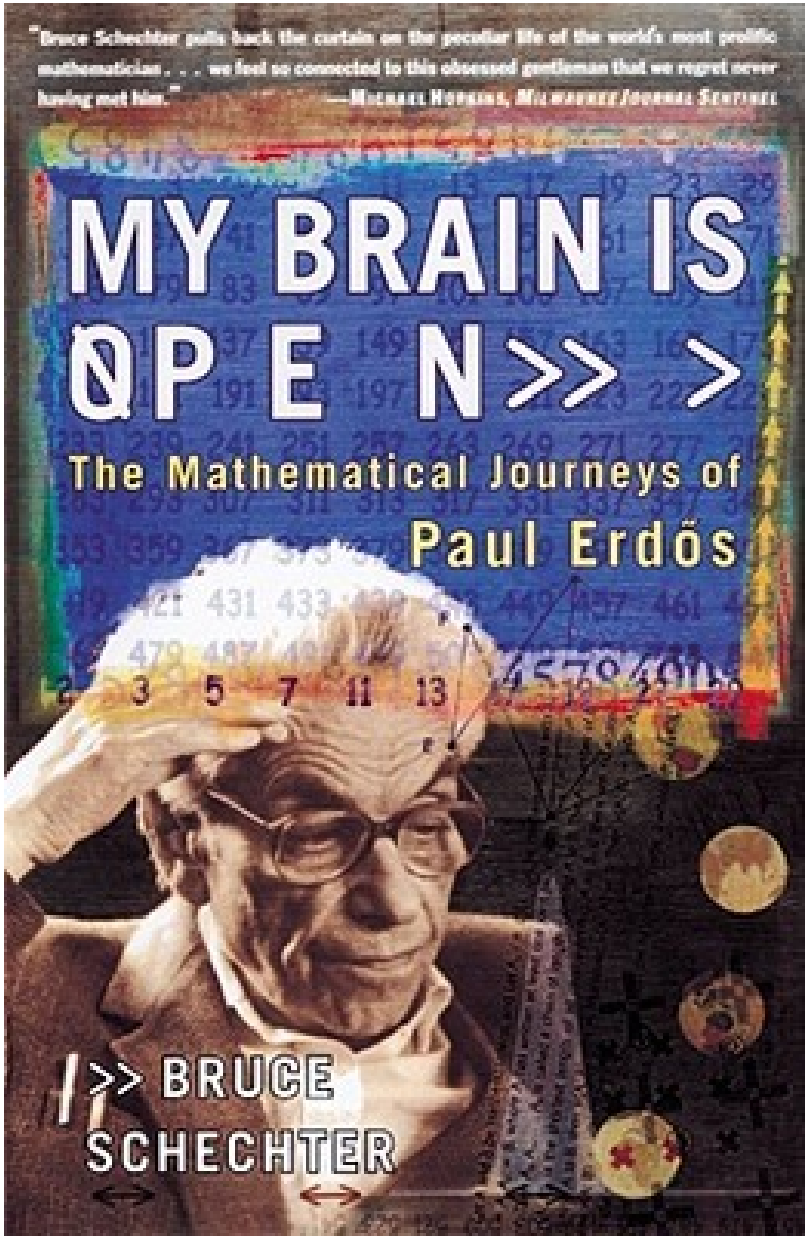

Course Structure

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- Lectures based on the textbook

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- Assignments (3–4)

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- Assignments (3–4)
- Student presentations

Course Structure

- Lectures based on the textbook
- Assignments (3–4)
- Student presentations
- Final project

Grading

- Assignments: 30%
- Presentation: 30%
- Final project: 40%

Assignments

- Typically, I will ask you to write code to replicate analysis in one or two figures in the paper.
- These assignments may organically come about from class discussions.
- You will have about two weeks to complete assignments.
- What do you turn in?
  - Fully working code, e.g., on GitHub.
  - A short report on the results of your analysis, including the figures, discussion of difficulties you faced, how you solved them, and observations on your results.

Goals of the Course

Learn computational methods that use network/graph theory to understand the brain at three levels:

Anatomical

Cellular

Molecular

to gain insights into brain functions in health and disease.

History of the Brain: Pre-History

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- Egypt (c. 3000 BC): Aware of symptoms of brain damage, but considered the heart to the repository of memories.
- India (c. 400 BC): Charaka described symptoms and treatments of epilepsy.

Ancient Greece

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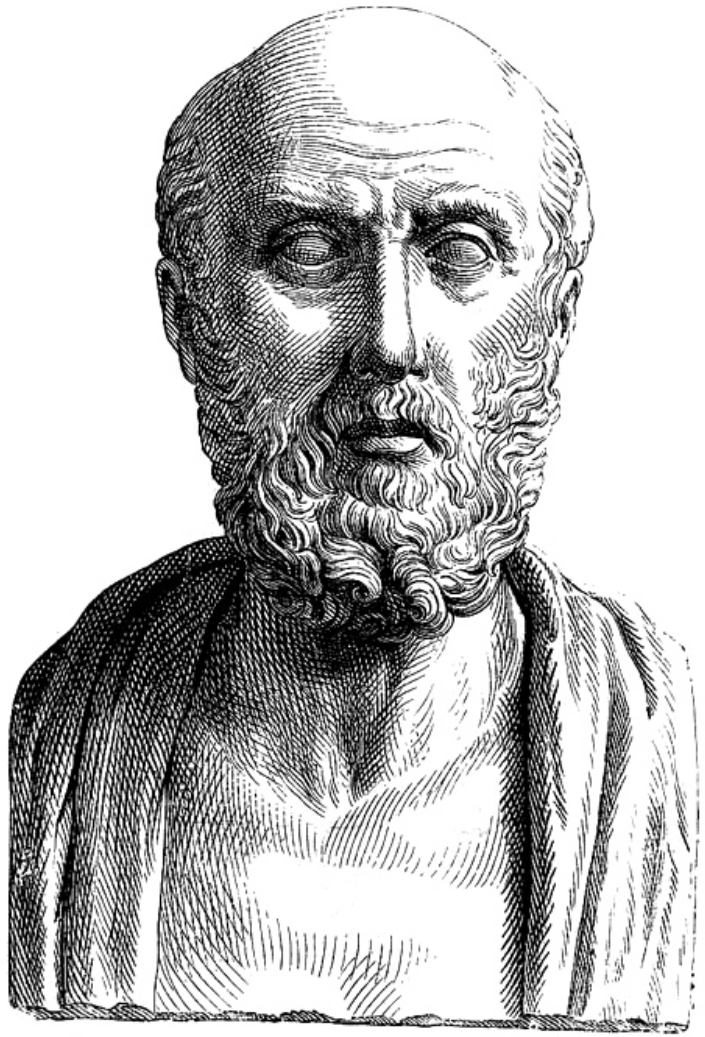
- Hippocrates (460–379 BC): Brain is the organ of sensation and intelligence.



The birth and evolution of neuroscience through cadaveric dissection, Moon K1, Filis AK, Cohen AR. Neurosurgery. 2010 Sep;67(3):799–809

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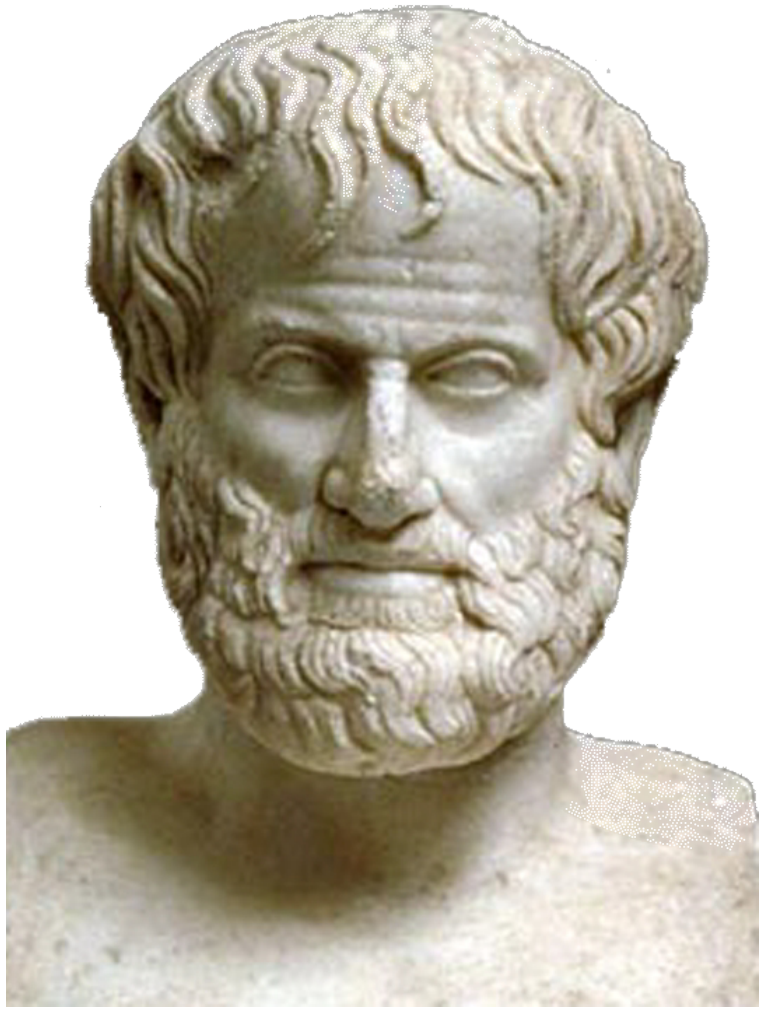

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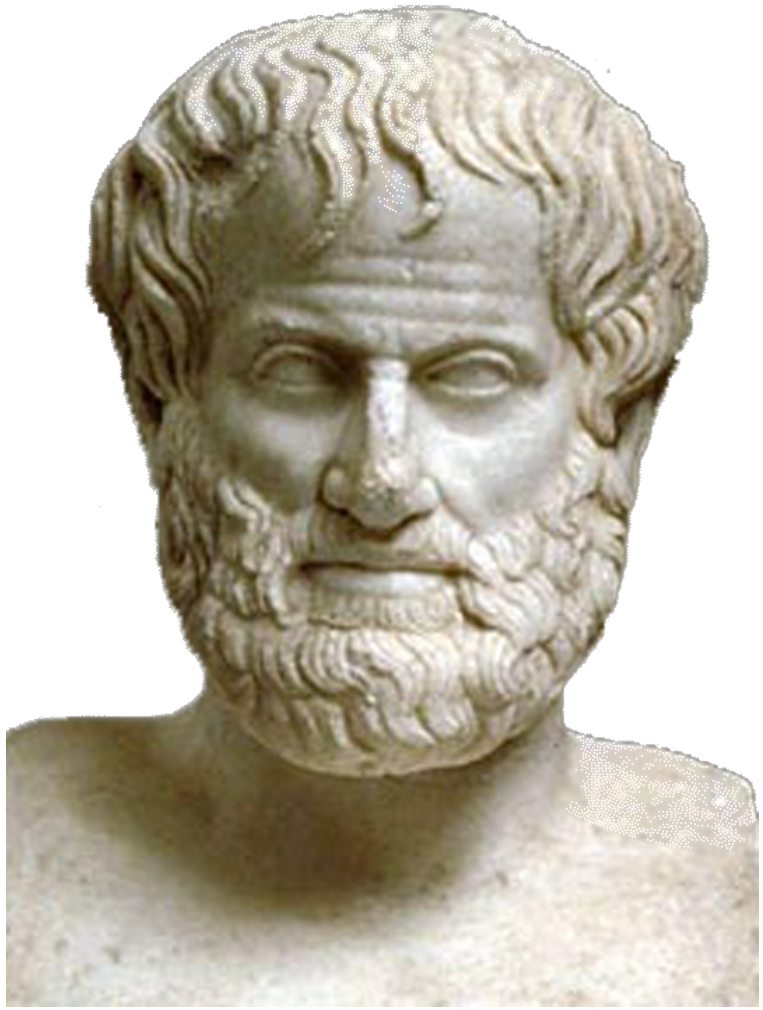

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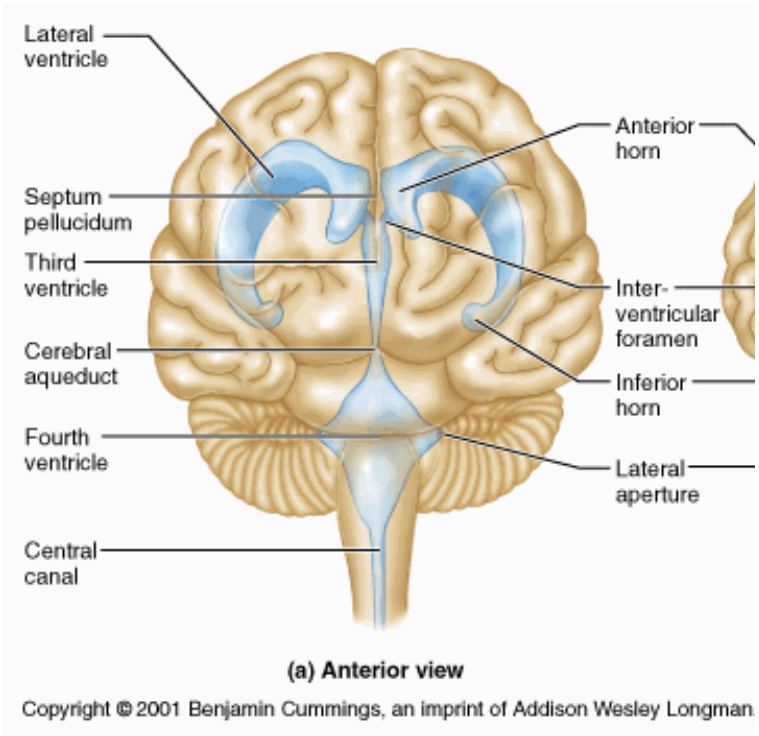
- Herophilus (c. 325–255 BC):
  - Father of neuroanatomy, first dissector in the Western tradition.
  - Discovered ventricles, distinguished between cerebrum and cerebellum.



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Galen (130–200 AD)

- Theories dominated Western and Byzantine medicine till the 16th century.
- Used animal dissections.
- Structure-Function: cerebellum (hard) receives sensations and cerebrum (soft) stores memories.
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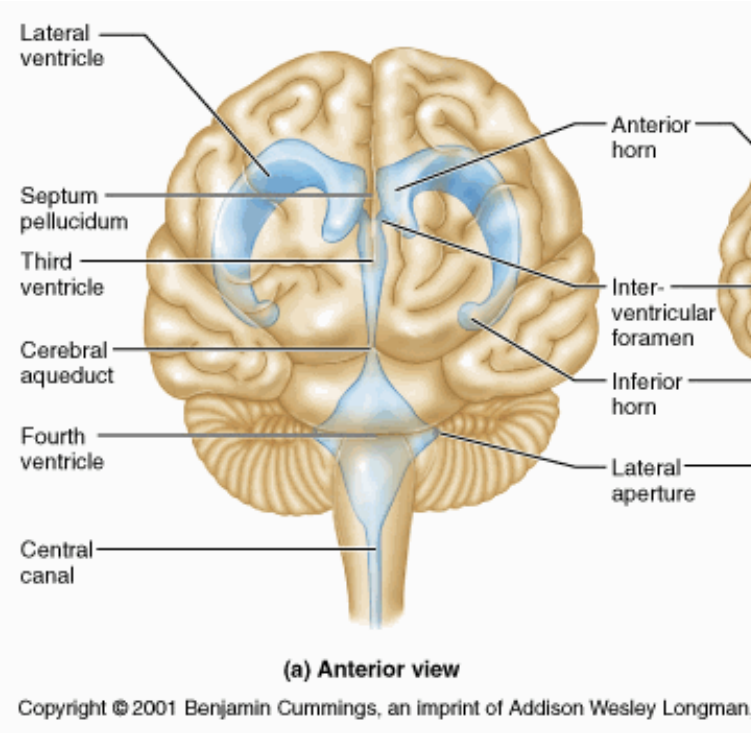
- The brain is the location of the mind.
- Brain controls senses and motor functions by movement of fluids to and from ventricles through nerves (which are hollow, cf. arteries).



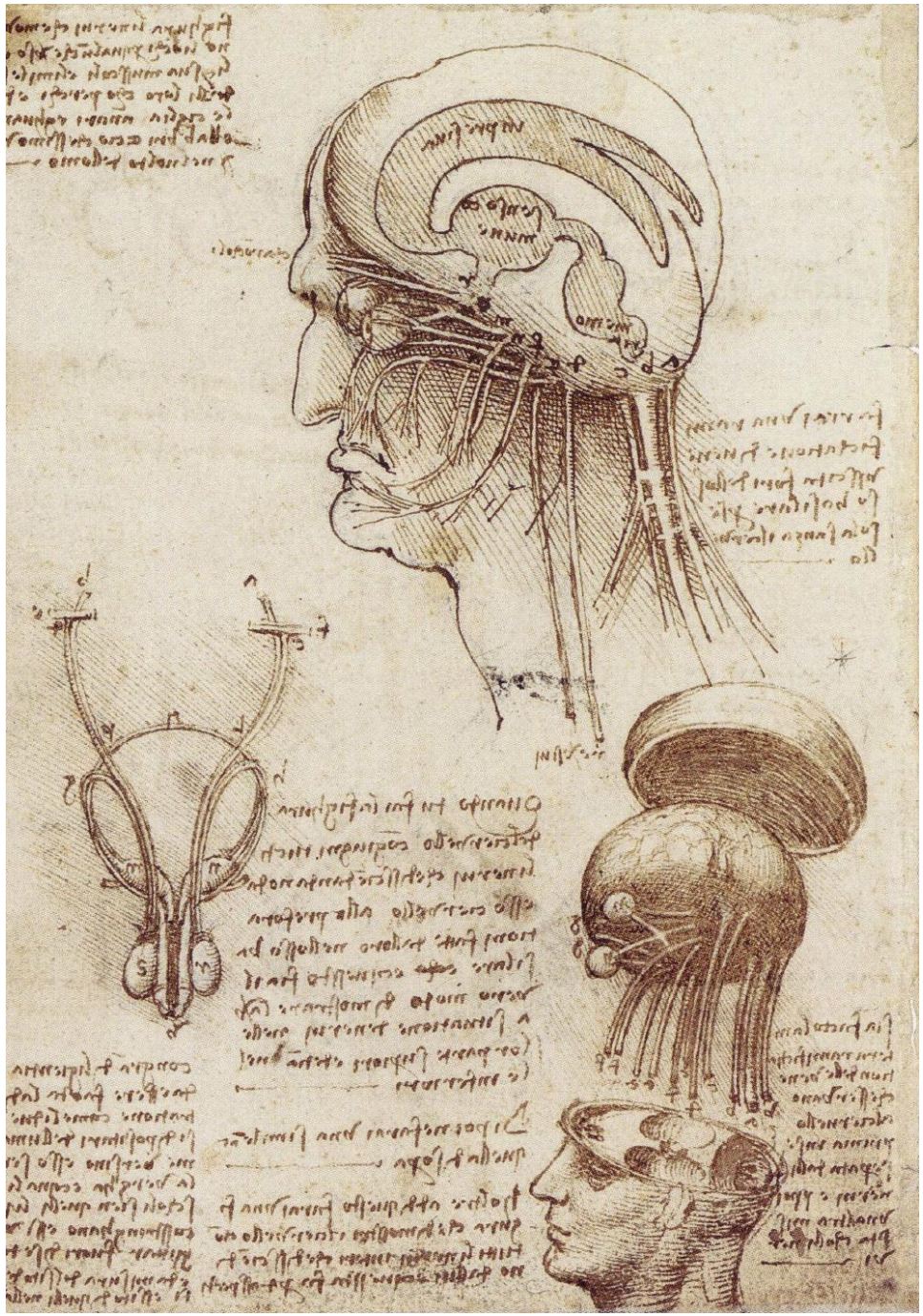
(a) Anterior view

The Next 1300 Years

- Dark Ages in Europe.
- Arabs copied Galen's text among others.
- Islamic surgeon Abu al-Qasim al-Zahrawi (1000 AD) described several treatments for neurological disorders.

Renaissance (14th–16th Centuries)

- Increased recognition of need for dissection to acquire new knowledge about the body's internal organs.
- Printing press (1439 AD) circulated Galen's works.
- Renaissance and Reformation of the Church promoted fresh thinking.
- Dissection resulted in detailed anatomical drawings.

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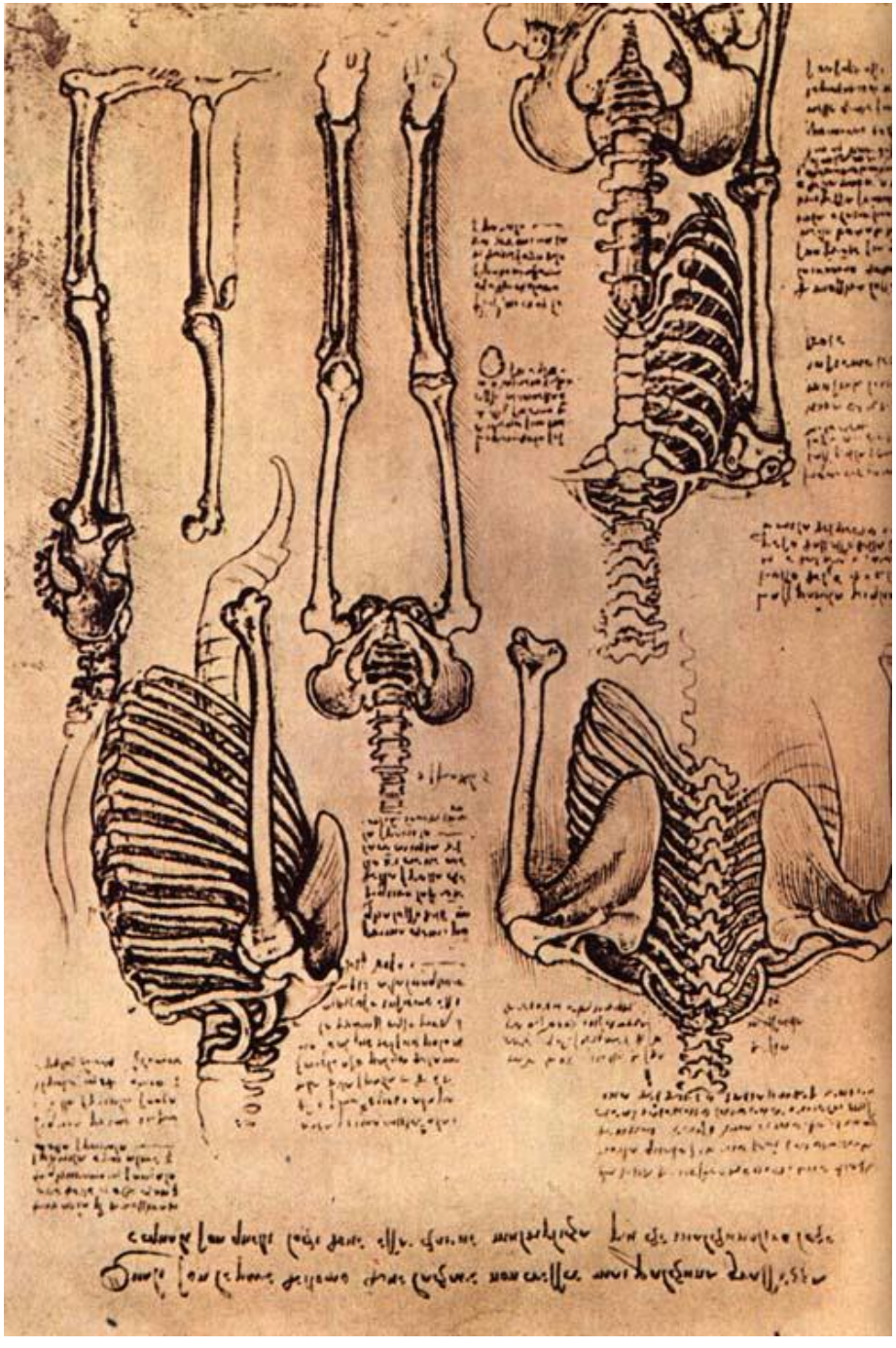
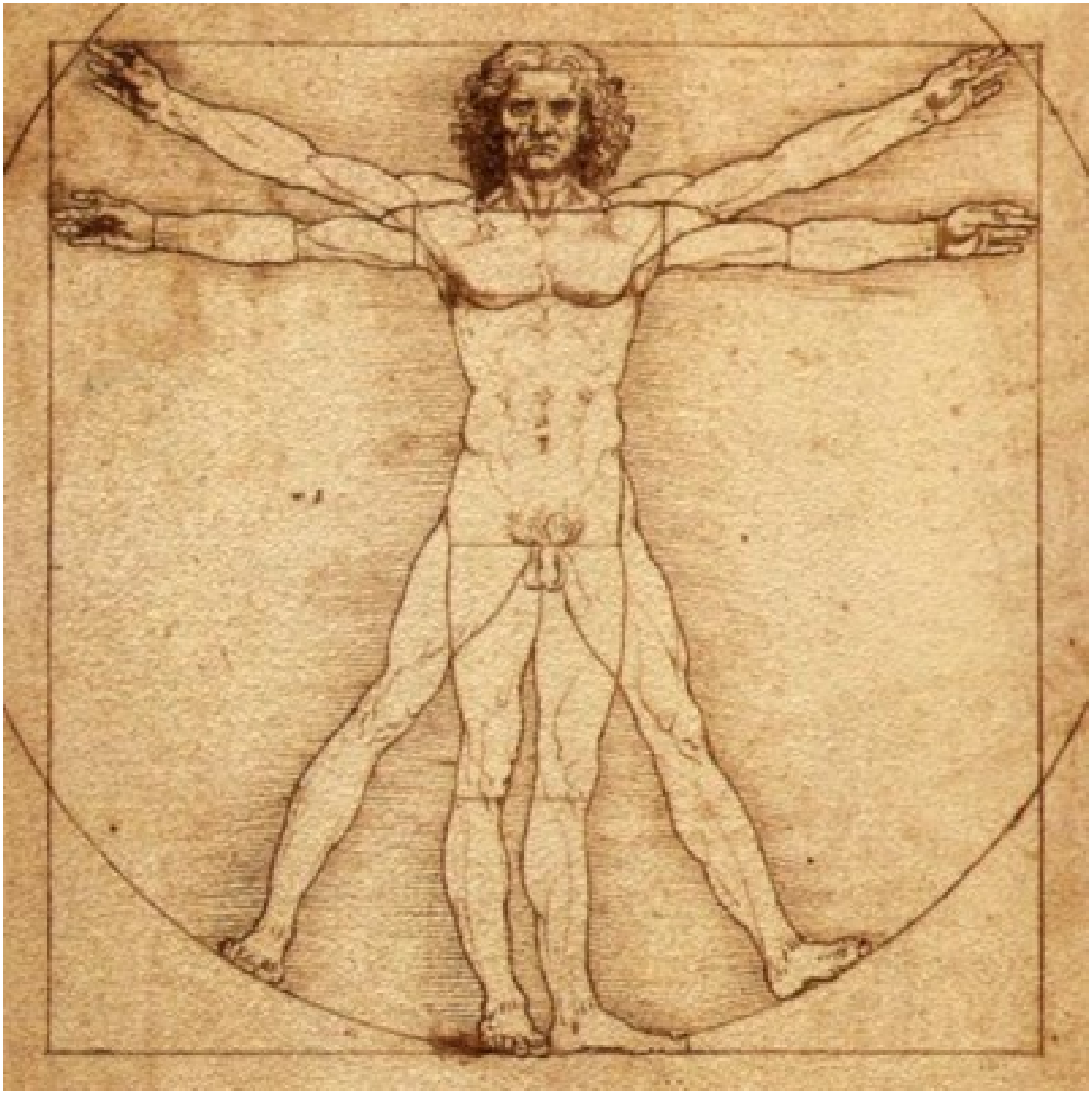
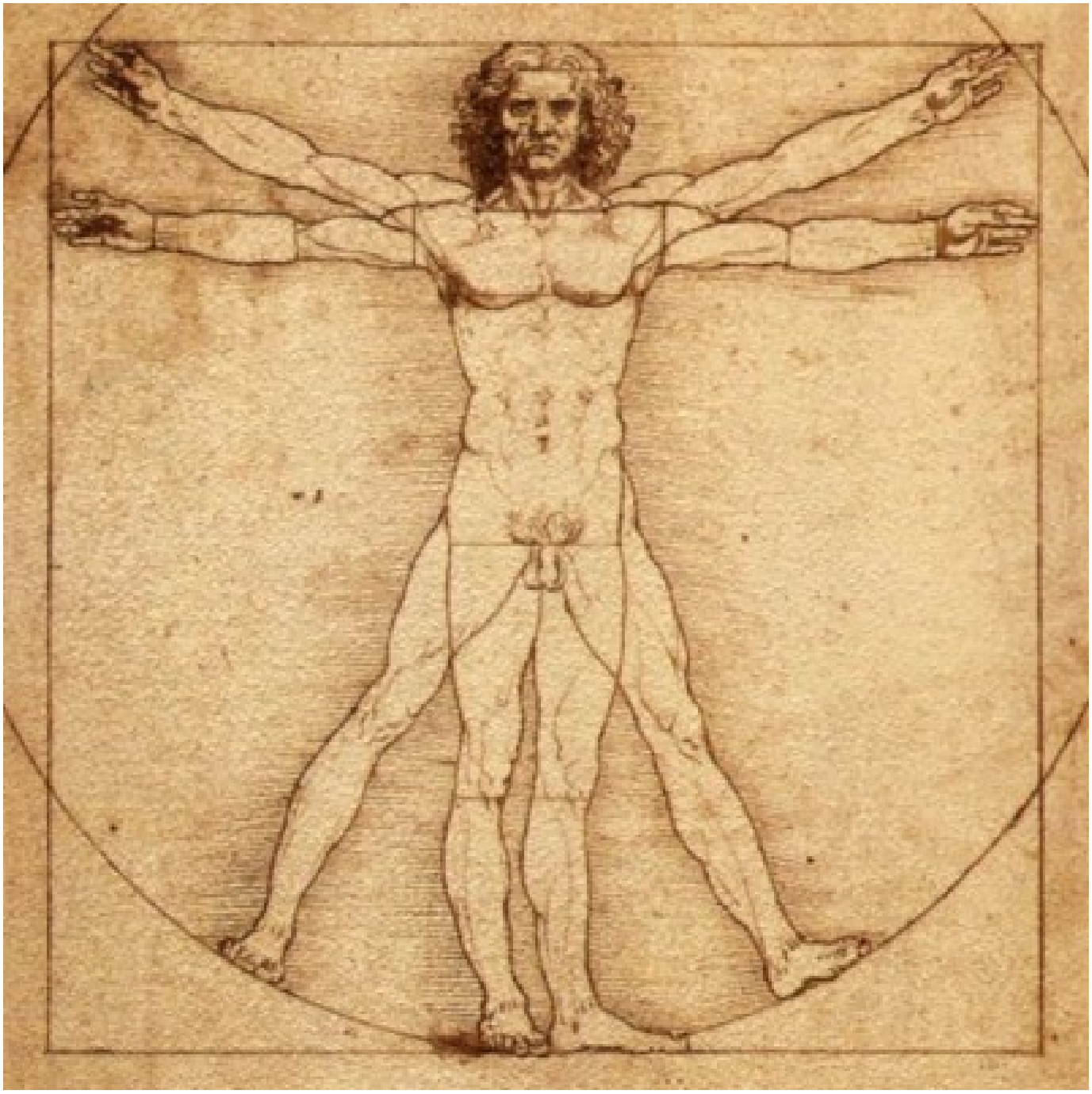


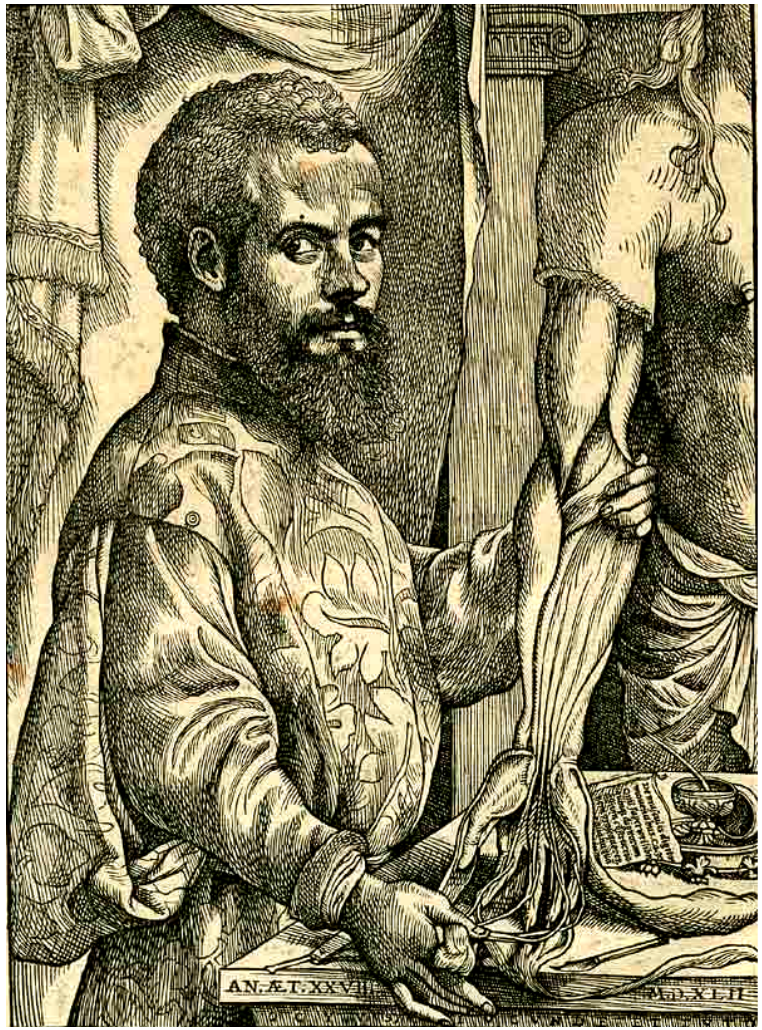




Leonardo da Vinci (1452–1519)

Andreas Vesalius (1514–1564)

- Used skillful dissection of cadavers.



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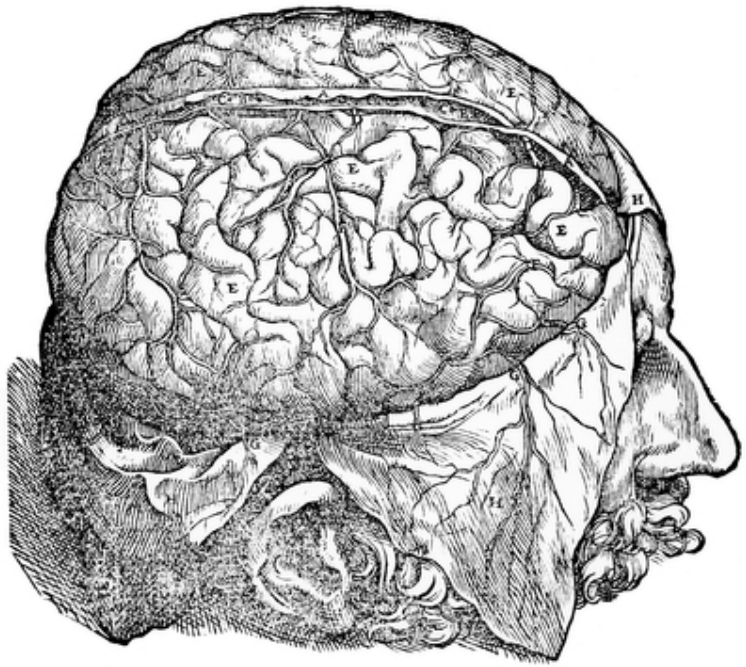

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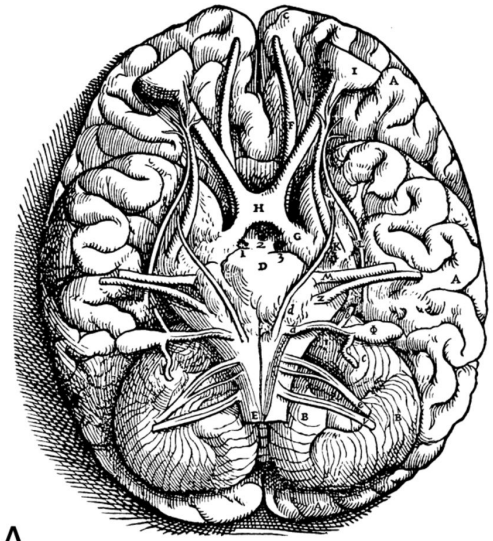

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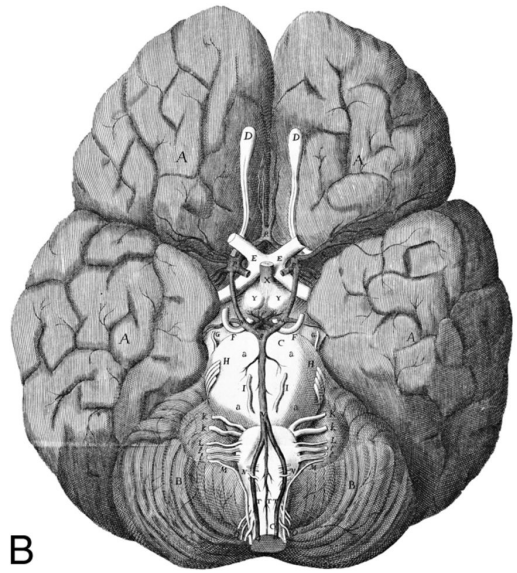
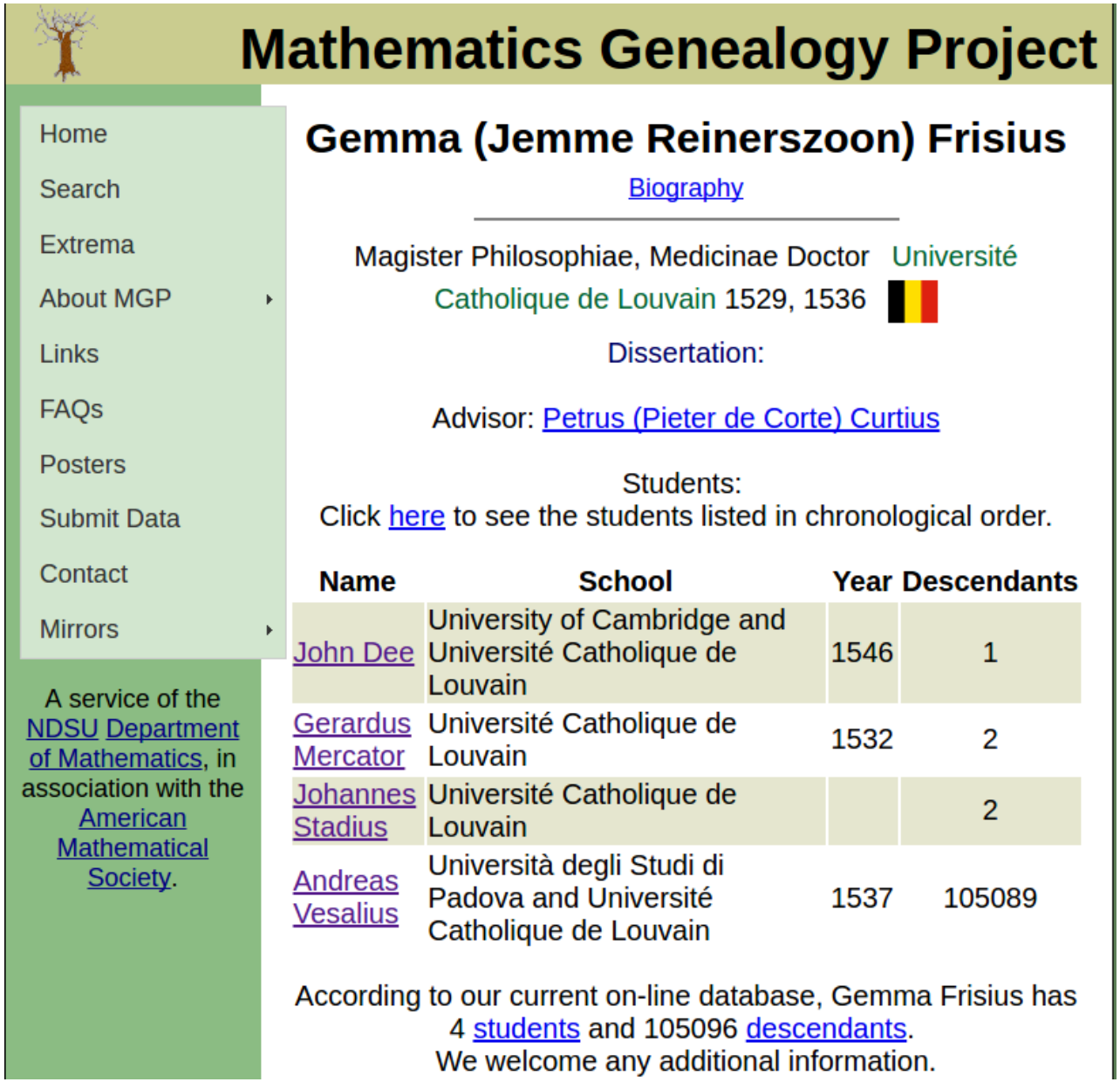


B

Contemporaries and Descendants of Vesalius



Mathematics Genealogy Project

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A service of the NDSU Department of Mathematics, in association with the American Mathematical Society.

Gemma (Jemme Reinerszoon) Frisius

Biography

Magister Philosophiae, Medicinae Doctor Université Catholique de Louvain 1529, 1536

Dissertation:

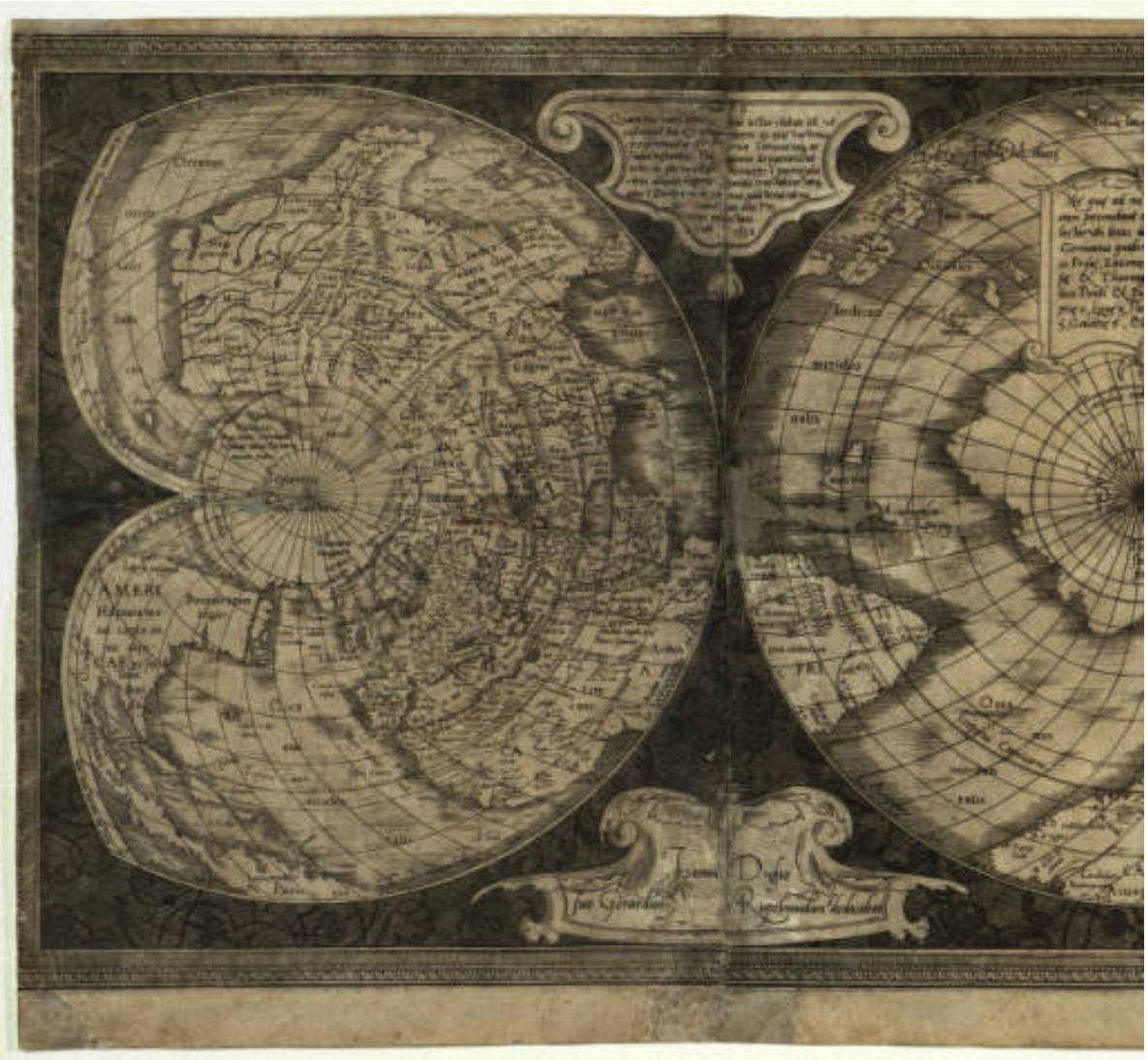
Advisor: Petrus (Pieter de Corte) Curtius

Students:
Click here to see the students listed in chronological order.

Name	School	Year	Descendants
John Dee	University of Cambridge and Université Catholique de Louvain	1546	1
Gerardus Mercator	Université Catholique de Louvain	1532	2
Johannes Stadius	Université Catholique de Louvain		2
Andreas Vesalius	Università degli Studi di Padova and Université Catholique de Louvain	1537	105089

According to our current on-line database, Gemma Frisius has 4 students and 105096 descendants.
We welcome any additional information.

Gerardus Mercator



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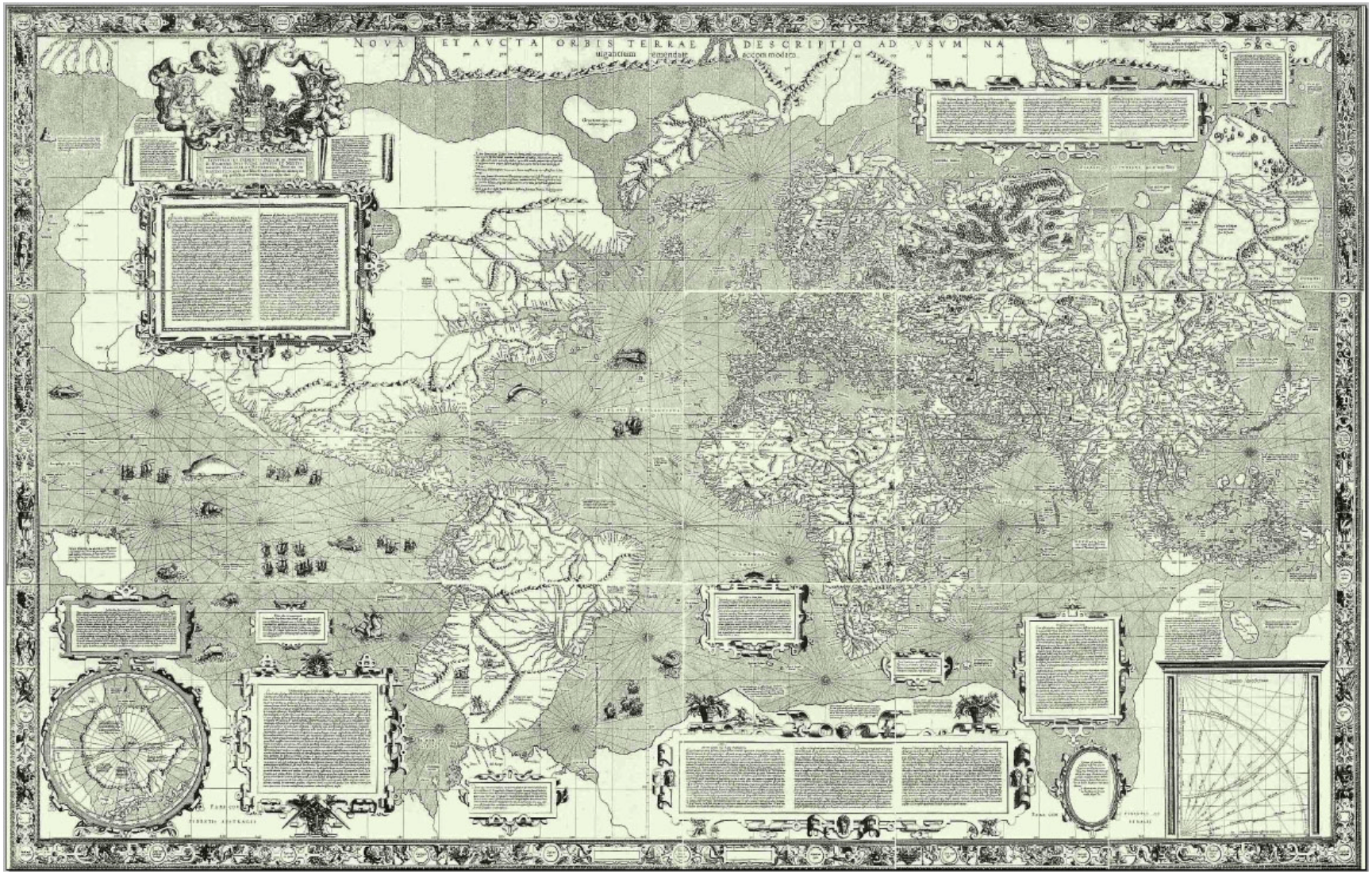

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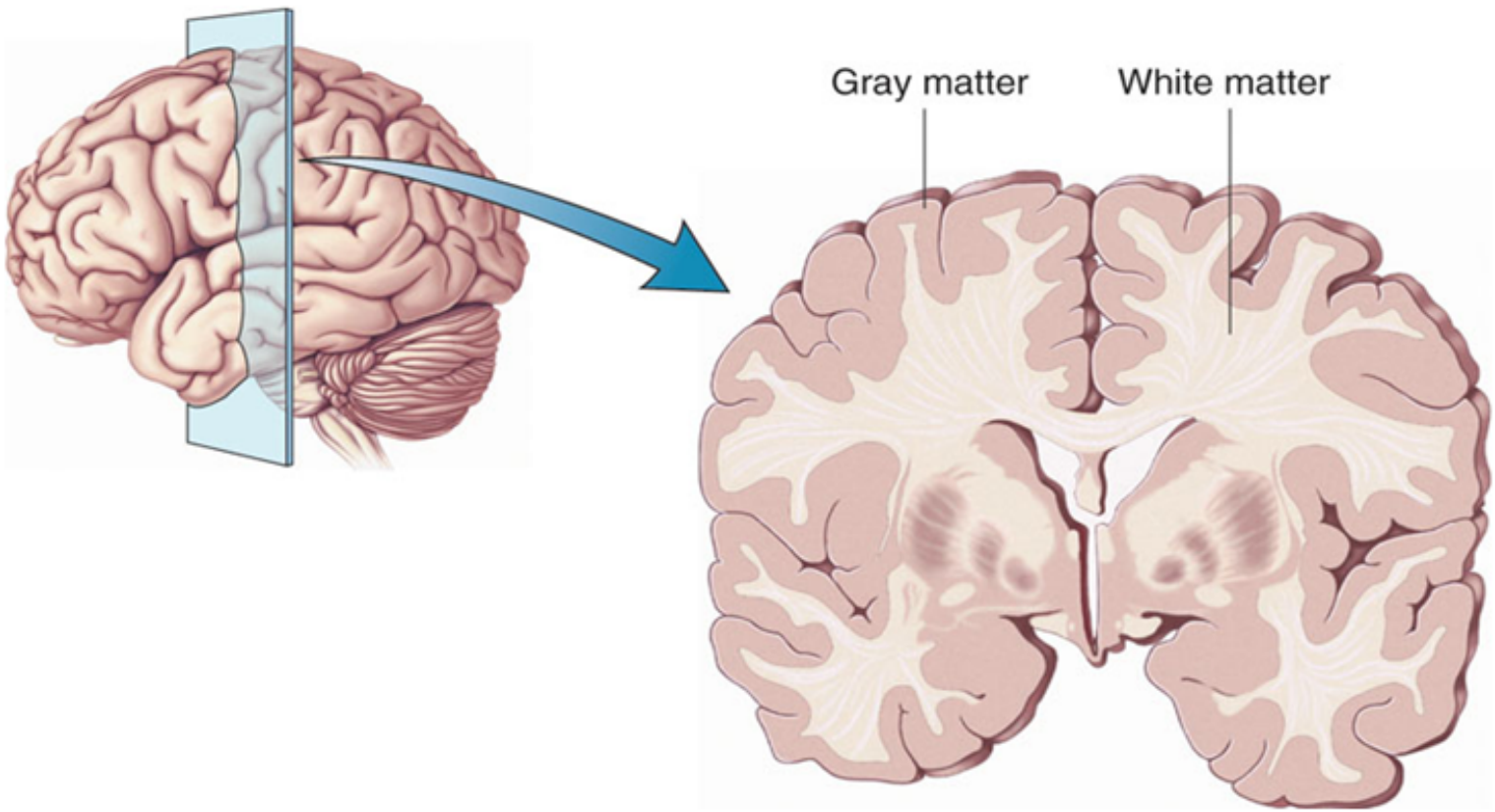
White Matter and Grey Matter (17th–18th centuries)

White matter Generic term for "stuff" that appears white in freshly dissected brain.

Grey matter Generic term for "stuff" that appears grey in a freshly dissected brain.



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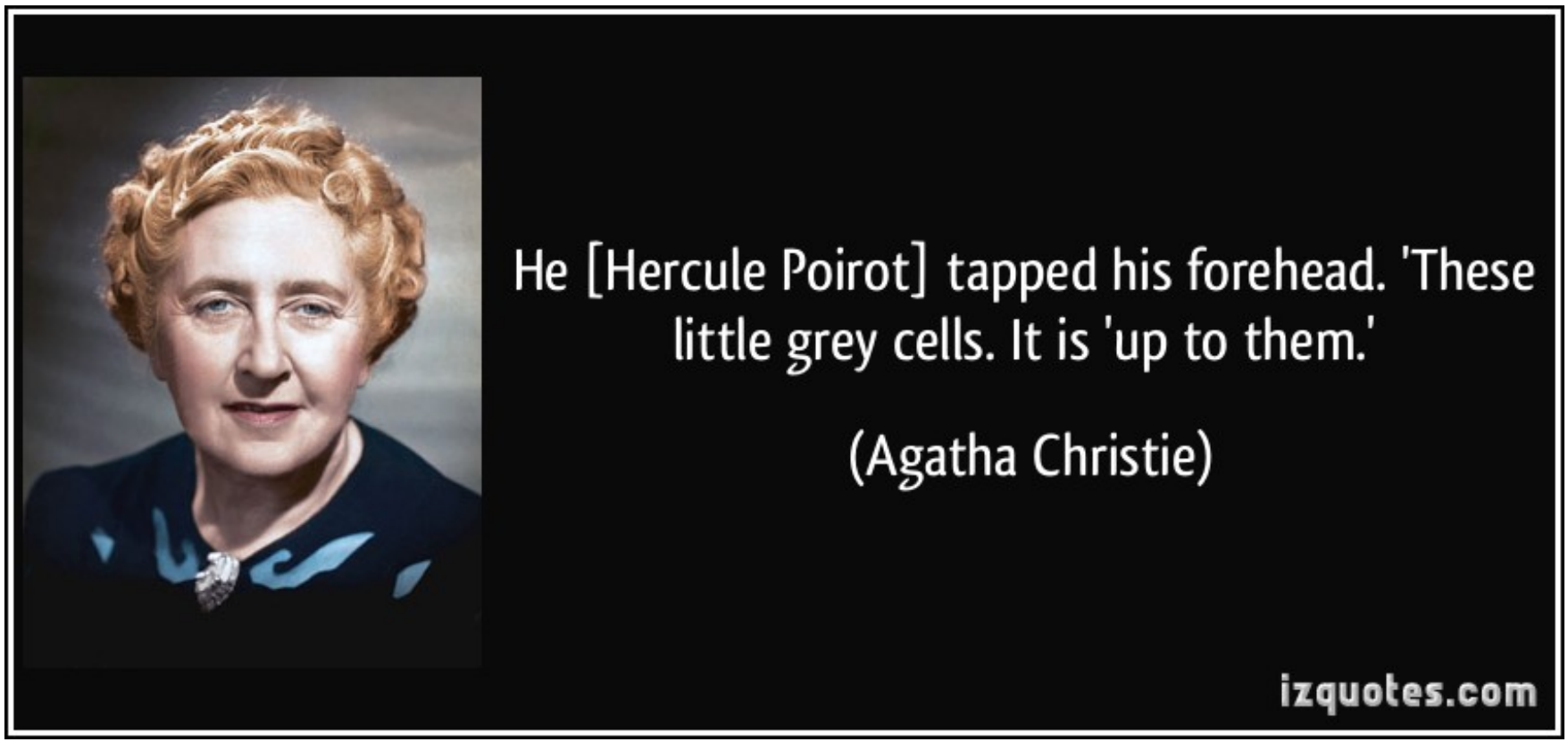

Structure to Function

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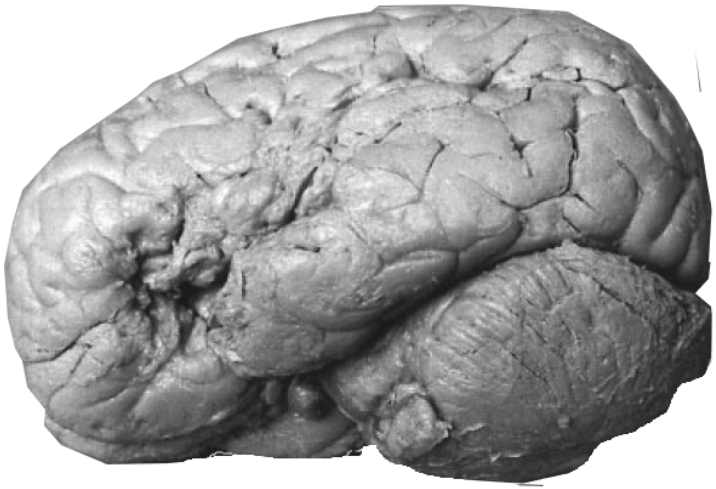
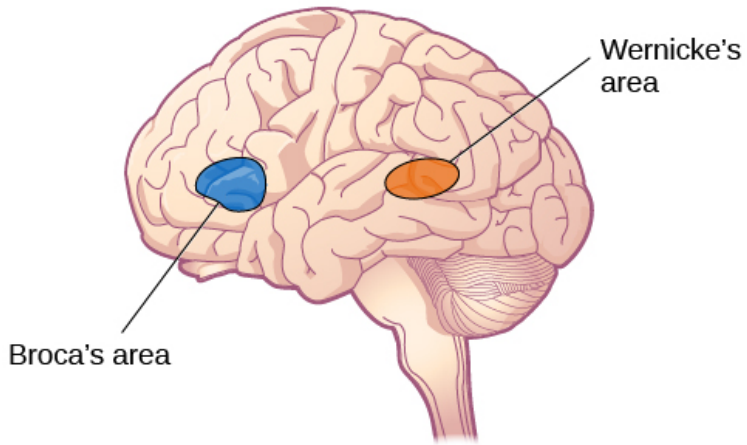


Structure to Function

- Broca's area (1861): production of speech and language
- Wernicke's area (1874): comprehension of spoken and written word



Brodmann Areas (1909)

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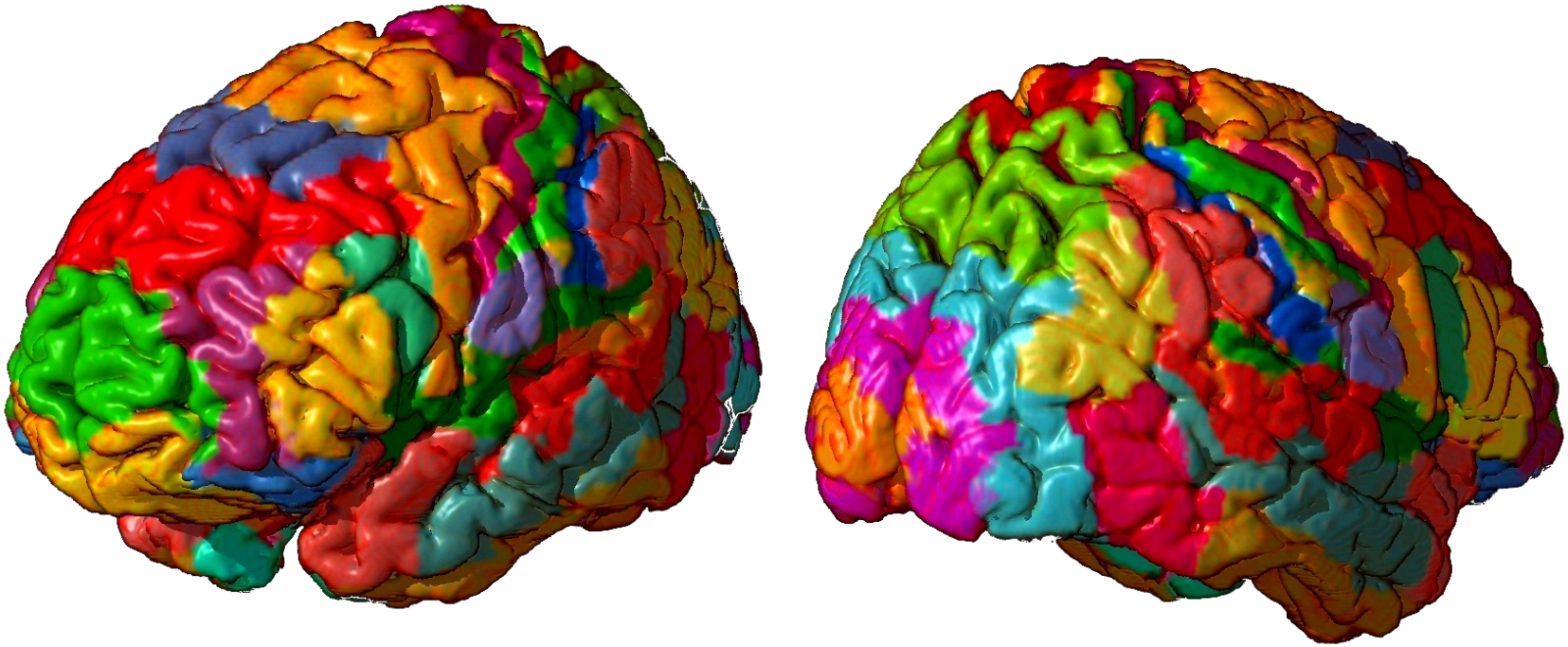

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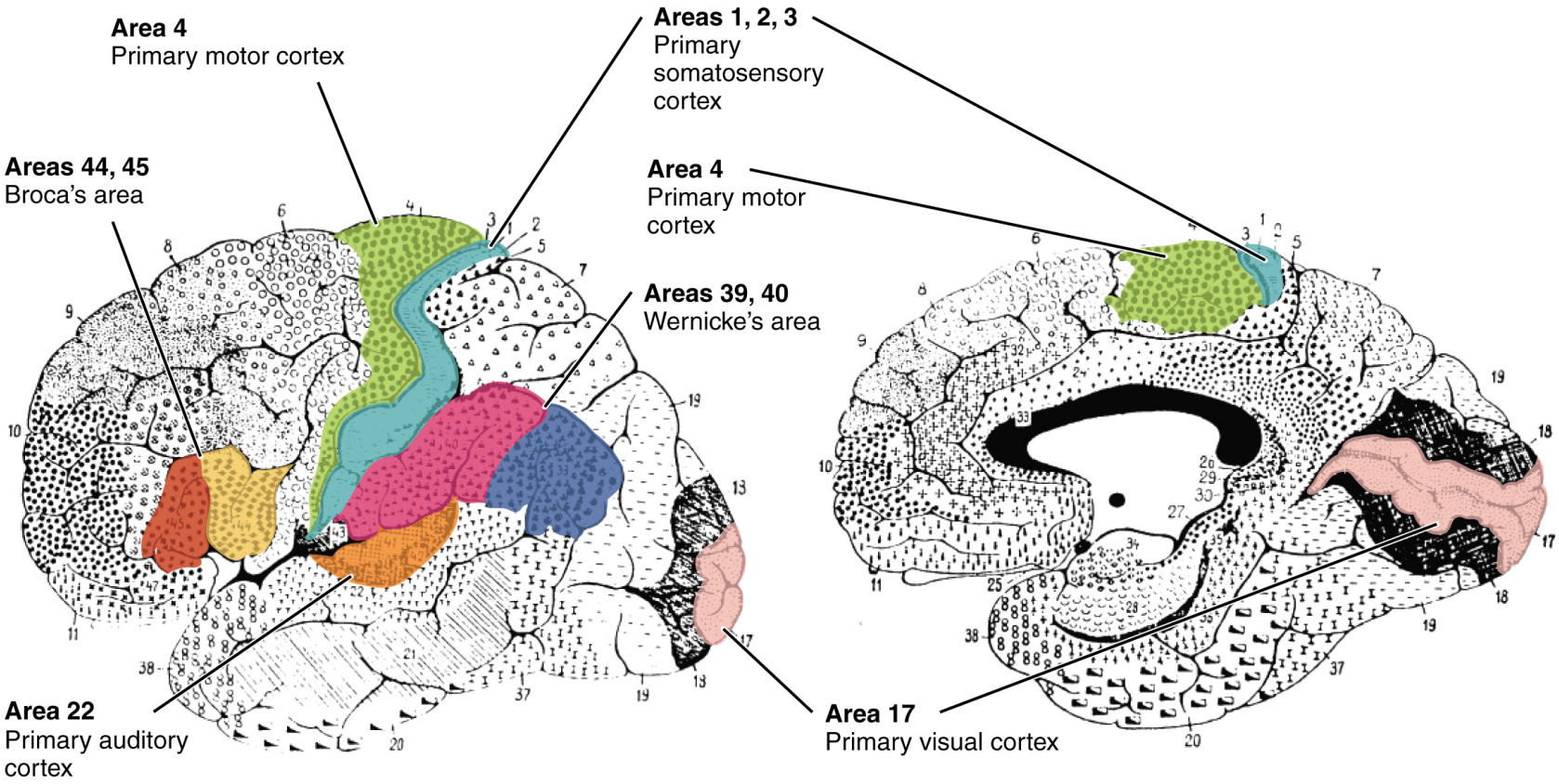
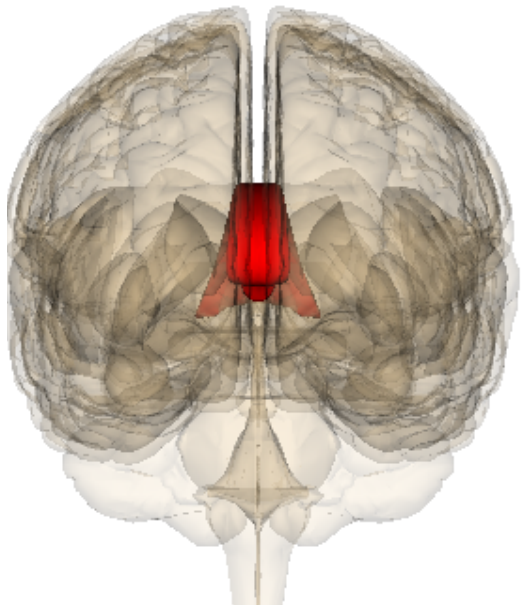


Brodmann's cytotechtonic map (1909):
Lateral surface

Brodmann's cytotechtonic map (1909):
Medial surface

Left and Right Brains (1960s)

- If the two hemispheres of the brain are separated by severing the corpus callosum,
  - information transfer between the hemispheres ceases,
  - an individual has two functionally different brains.



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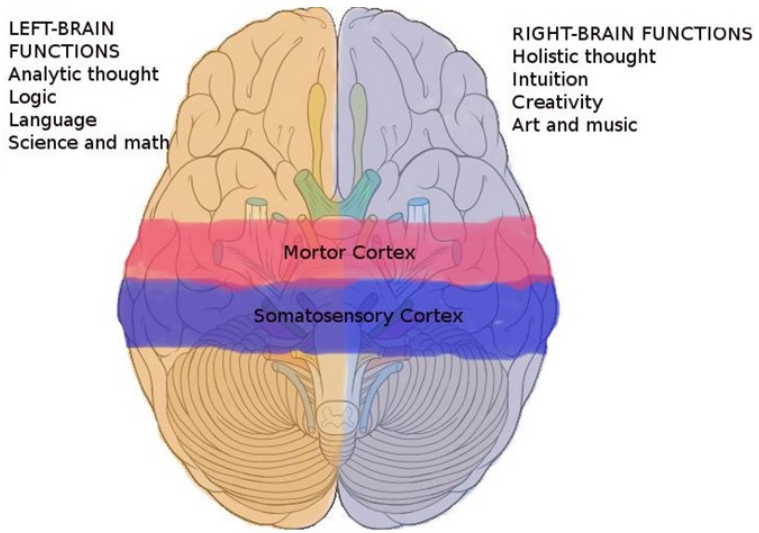

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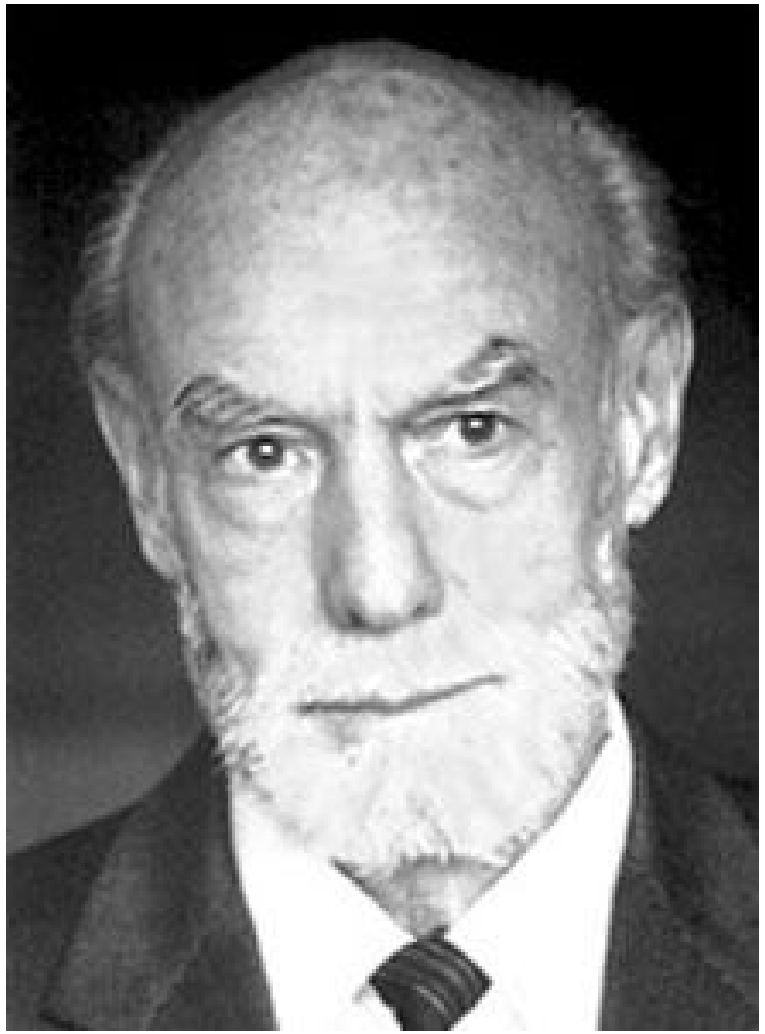
- Roger Sperry received the Nobel Prize in 1981.



"The great pleasure and feeling in my right brain is more than my left brain can find the words to tell you."

Left and Right Brains in Culture

The New York Times Magazine/September 9,1973

Two astonishingly different persons inhabit our heads

We are left-brained or right-brained

By Maya Pines

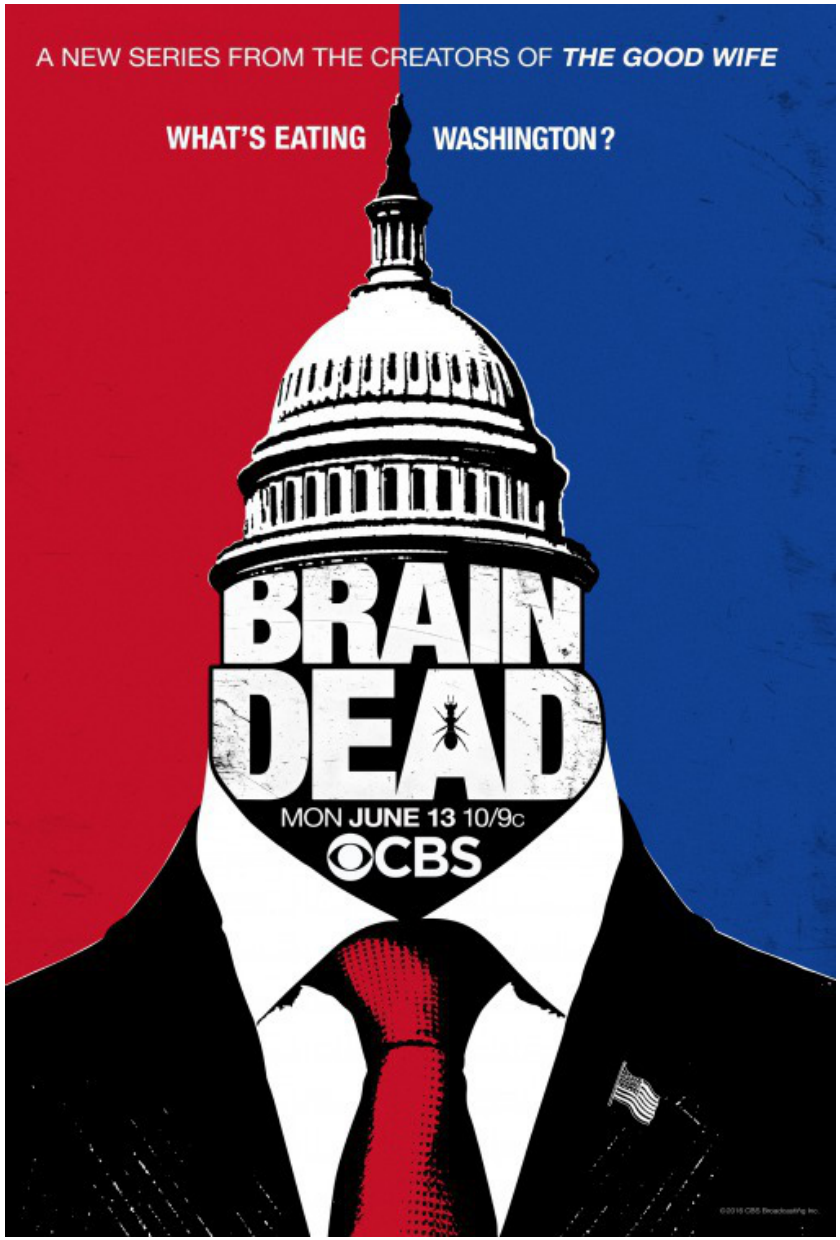
Two very different persons inhabit our heads, residing in the left and right hemispheres of our brains, the twin shells that cover the central brain stem. One of them is verbal, analytic, dominant. The other is artistic but mute, and still almost totally mysterious.

This nonspeaking side of the human brain—the right hemisphere—is now the focus of intensive research by brain scientists. This sudden surge of interest is probably no accident at a time when Yoga, Arica, Tibetan exercises and other nonverbal disciplines are enjoying such a vogue. Some research, for example, those concerned with vision—to find their way through a tangle of other nerve fibers, even when obstacles are placed in their path, and somehow connect with the appropriate cells so as to reach specific terminals in the visual cortex. Next, he began to study visual perception and memory. He wanted to find out what happened when an animal learned certain discriminations that involved the visual cortex—when it learned, for instance, to push a panel marked with a circle rather than a square. Where in its brain was that knowledge stored?

He put the question to a young graduate student, suggesting that he investigate how cats that learned to distinguish between a circle and a square, knowing that the information they acquired would go to only one hemisphere. When he switched their eye patches to cover their trained eyes, however, the cats performed just as well as before. Their memory of this skill was intact. This meant either that the knowledge was stored in the central brain stem, well below the twin hemispheres, or that the knowledge acquired by one hemisphere had somehow been transmitted to the other.

"Obviously the *corpus callosum* was the next thing to test," recalls Dr. Myers. "But from the available evidence, cutting it would have no effect. If the surgery is properly done, the animals are

Left and Right Brains in Culture



Left and Right Brains in Culture

QUIZ

Are You More Right-Brained Or Left-Brained?

Research says it doesn't exist, but let's see where your personality falls.

Erin La Rosa
BuzzFeed Staff

justtransparentthings.tumblr.com

Check off all that apply:

☐ 1. You're better with faces than names.

Left and Right Brains in Culture

LIVESCIENCE NEWS TECH HEALTH PLANET EARTH SPACE STRANGE NEWS ANI

Left Brain vs. Right: It's a Myth, Research Finds

By Christopher Wanjek | September 3, 2013 12:21pm ET

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BAD MEDICINE CHRISTOPHER WANJEK COLUMNIST

The idea that one side of the brain is dominant is a myth, researchers say.

Credit: Human brain image via Shutterstock

Parts of the Brain (Now)

The Brain: Structure and Function (Video, 13:55)

Automated Parcellation of the Human Brain

NATURE | ARTICLE

日本語要約

A multi-modal parcellation of human cerebral cortex

Matthew F. Glasser, Timothy S. Coalson, Emma C. Robinson, Carl D. Hacker, John Harwell, Essa Yacoub, Kamil Ugurbil, Jesper Andersson, Christian F. Beckmann, Mark Jenkinson, Stephen M. Smith & David C. Van Essen

Affiliations | Contributions | Corresponding authors

Nature **536**, 171–178 (11 August 2016) | doi:**10.1038/nature18933**
Received 12 November 2015 | Accepted 15 June 2016 | Published online 20 July 2016

NATURE | NEWS

Human brain mapped in unprecedented detail

Nearly 100 previously unidentified brain areas revealed by examination of the cerebral cortex.

Linda Geddes

20 July 2016

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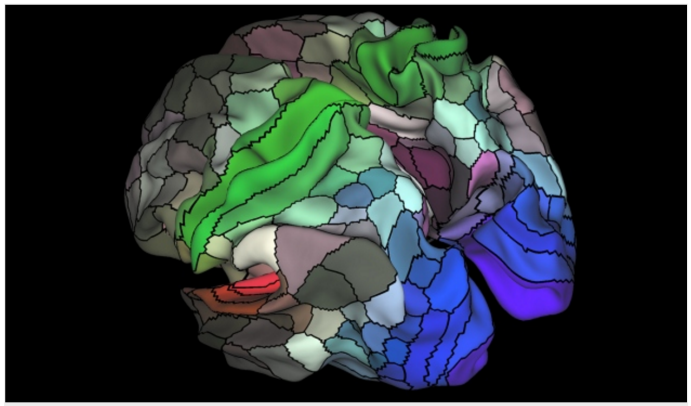


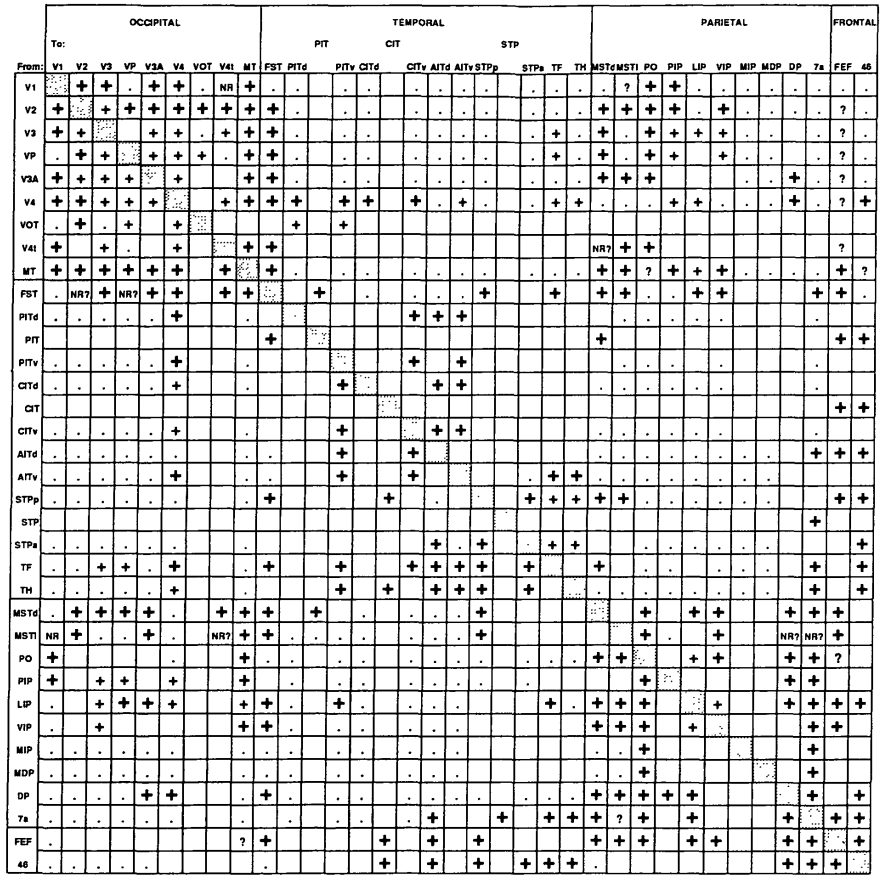
Matthew F. Glasser, David C. Van Essen

Researchers have divided the brain into discrete areas based on structure and function.

(Video, 2")

Brain Structure to Graphs

Table 3
Matrix of connections in visual cortex



This table is a connectivity matrix for interconnections between visual cortical areas in the macaque. Each row shows whether the area listed on the left sends outputs to the areas listed along the top. Conversely, each column shows whether the area listed on the top receives inputs from the areas listed along the left. Large plus symbols (+) indicate a pathway that has been reported in 1 or more full-length manuscripts; small plus symbols indicate pathways identified only in abstracts or unpublished studies. Specific citations are listed in Table 5. Dots (·) indicate pathways explicitly tested and found to be absent. Blanks indicate pathways not carefully tested for. Question marks (?) denote pathways whose existence is uncertain owing to conflicting reports in the literature. "NR" and "NR?" indicate nonreciprocal pathways, i.e., connections absent in the indicated direction even though the reciprocal connection has been reported. Shaded boxes along the diagonal represent intrinsic circuitry that exists within each area; these are not included among the pathways tabulated in the following table.

Distributed Hierarchical in the Primate Cerebral Cortex, *Daniel J. Felleman and David C. Van Essen, Cereb. Cortex, 1: 1–47, 1991.*

Brain Structure to Graphs

Neuroinformatics
June 2004, Volume 2, Issue 2, pp 145–162

The small world of the cerebral cortex

Olaf Sporns ✉, Jonathan D. Zwi

Review Article
DOI: 10.1385/NI:2:2:145

Cite this article as:
Sporns, O. & Zwi, J.D. Neuroinform (2004) 2: 145. doi:10.1385/NI:2:2:145

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Cells in the Brain (Late 19th and early 20th Century)

Cell theory: Cell is the fundamental unit of all living organisms (Video, 1:40")

Wikimedia Commons

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- Brain is an exception: complex cell shapes, extensive branching, and dense packing.

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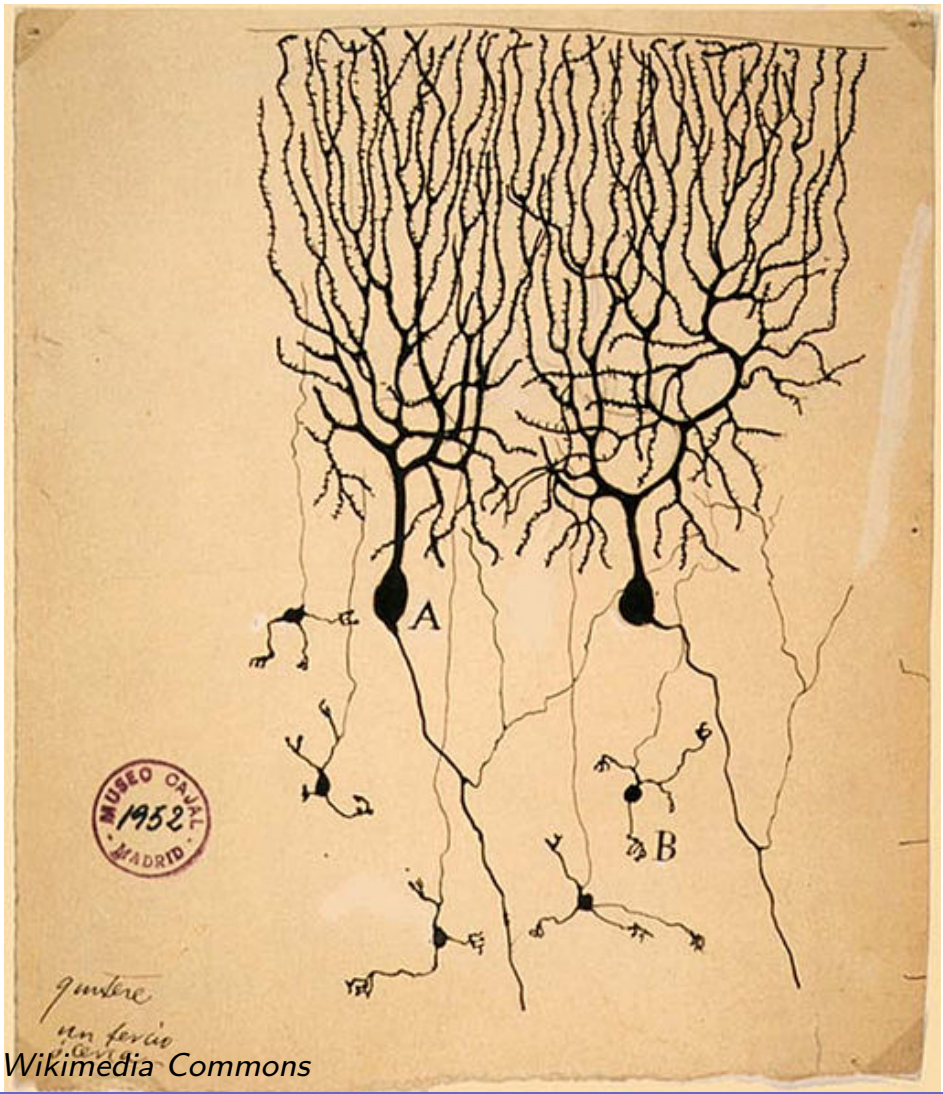
- Brain is an exception: complex cell shapes, extensive branching, and dense packing.
- How many neurons in the brain? 100 billion and many more glial cells.
- Golgi and Nissl stains: allowed cells to be visualised and traced under the microscope.
- Cajal: catalogued many different types of nerve cells.



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Reticular Theory vs. Neuron Doctrine

- "Neuron" coined by Waldeyer in 1891.
- In 1896, Rudolph Albert von Kolliker coined the term "axon" to describe the long slender cables that transmit signals away from cell bodies.
- In 1889, William His used "dendrites" to name the thin branching fibers that ferry signals toward the cell body.

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Reticular theory Nerve cells are fused to each other to form a continuous network, much like blood vessels (Golgi)

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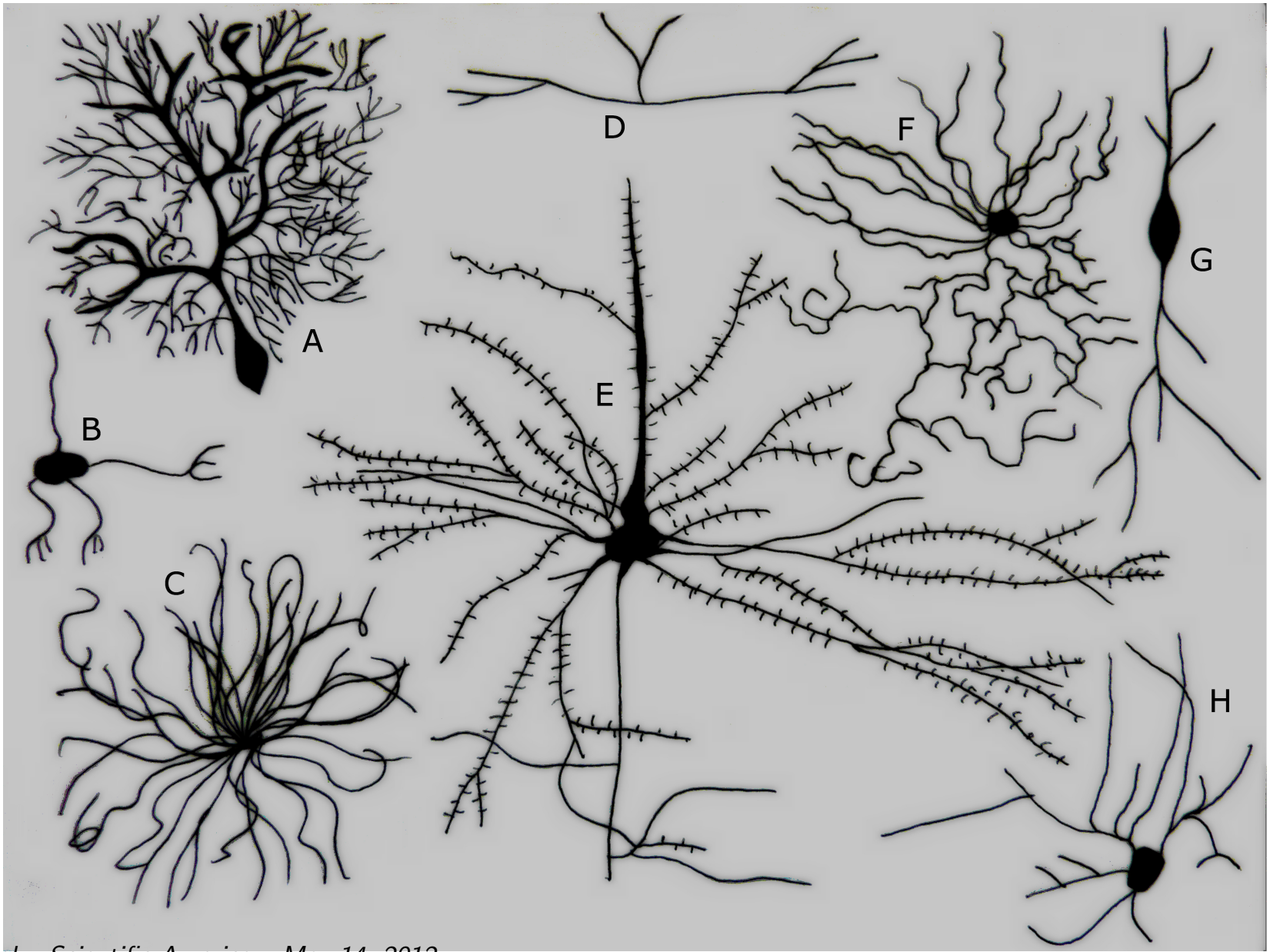
- Both Golgi and Cajal received the Nobel prize in Physiology or Medicine in 1906.

Cells in the Brain



Ferris Jabr, Scientific American, May 14, 2012

Cells in the Brain

Types of Brain Cells (Video, 18:54")

Types of Neurons

- 100s of types of neurons, differentiated by structure, function, genetics ...
- neuromorpho.org: archive of digitally reconstructed neurons.
- neurolex.org

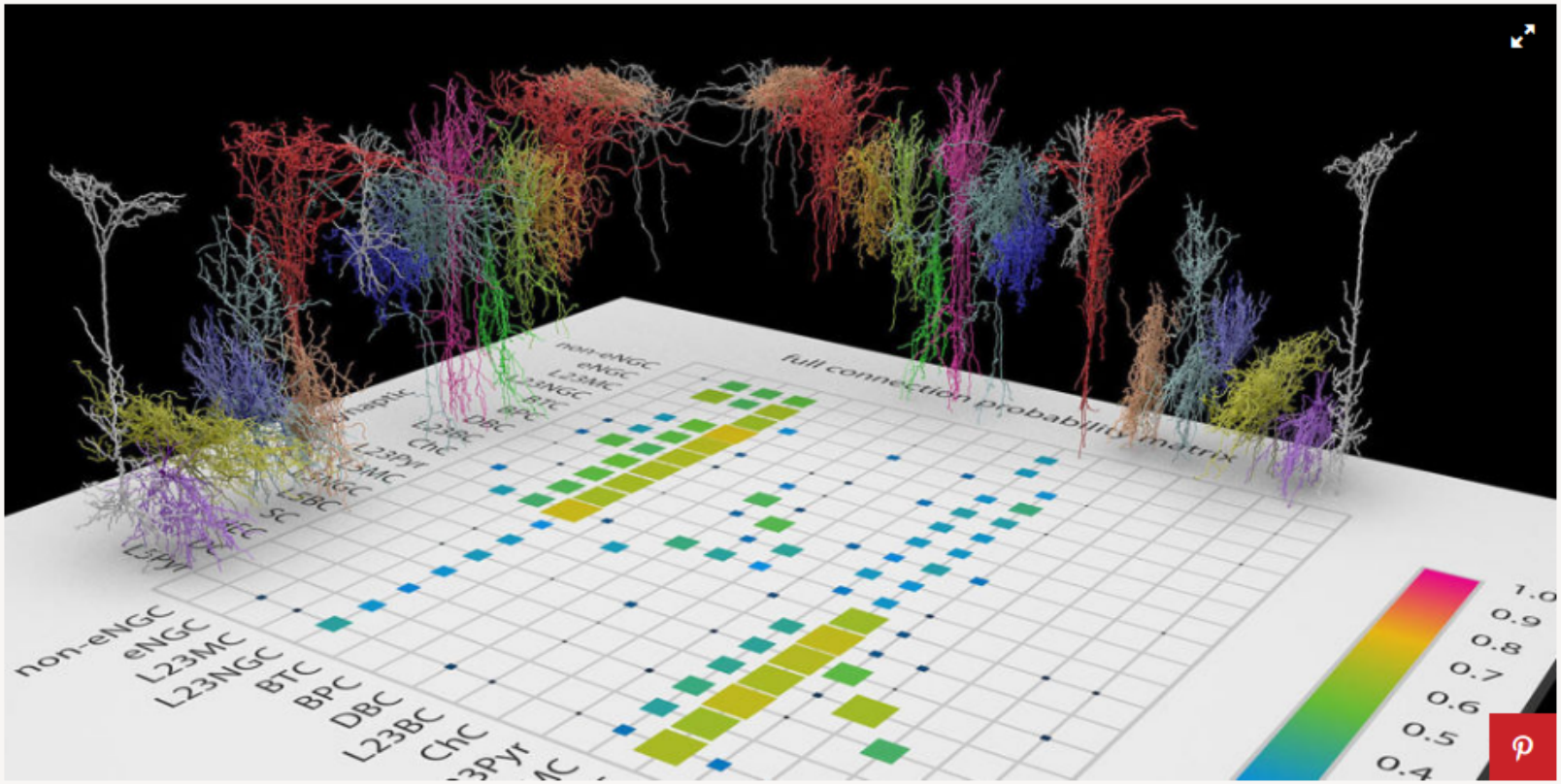
Welcome to NeuroLex, the Neuroscience Lexicon.

A dynamic lexicon of **34,533** neuroscience terms , including 754 neurons and 1303 parts of the nervous system supported by The Neuroscience Information Framework and the International Neuroinformatics Coordinating Facility

Types of Neurons

We Just Discovered 6 New Kinds of Brain Cells

The map of the human brain gets a little more complete.



Daniel Berger, Xiaolong Jiang, Fabian Sinz, Xaq Pitkow, Andreas Tolias

By William Herkewitz NOV 26, 2015

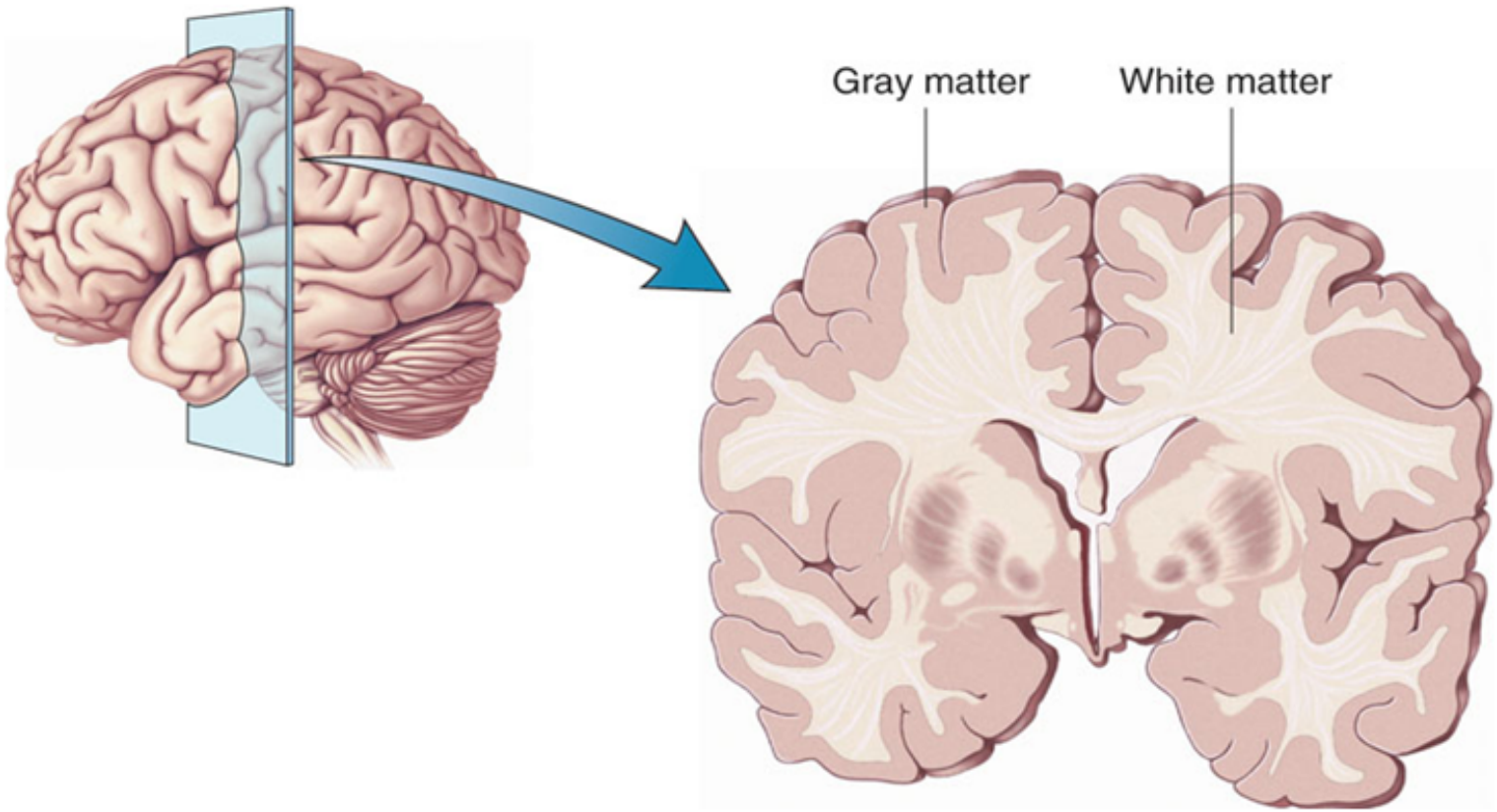
13.2k

Thanks to a handful of newly discovered neurons, the brain just became a little bit less mysterious

White Matter and Grey Matter (17th–18th centuries)

White matter Generic term for "stuff" that appears white in freshly dissected brain.

Grey matter Generic term for "stuff" that appears grey in a freshly dissected brain.



White Matter and Grey Matter (17th–18th centuries)

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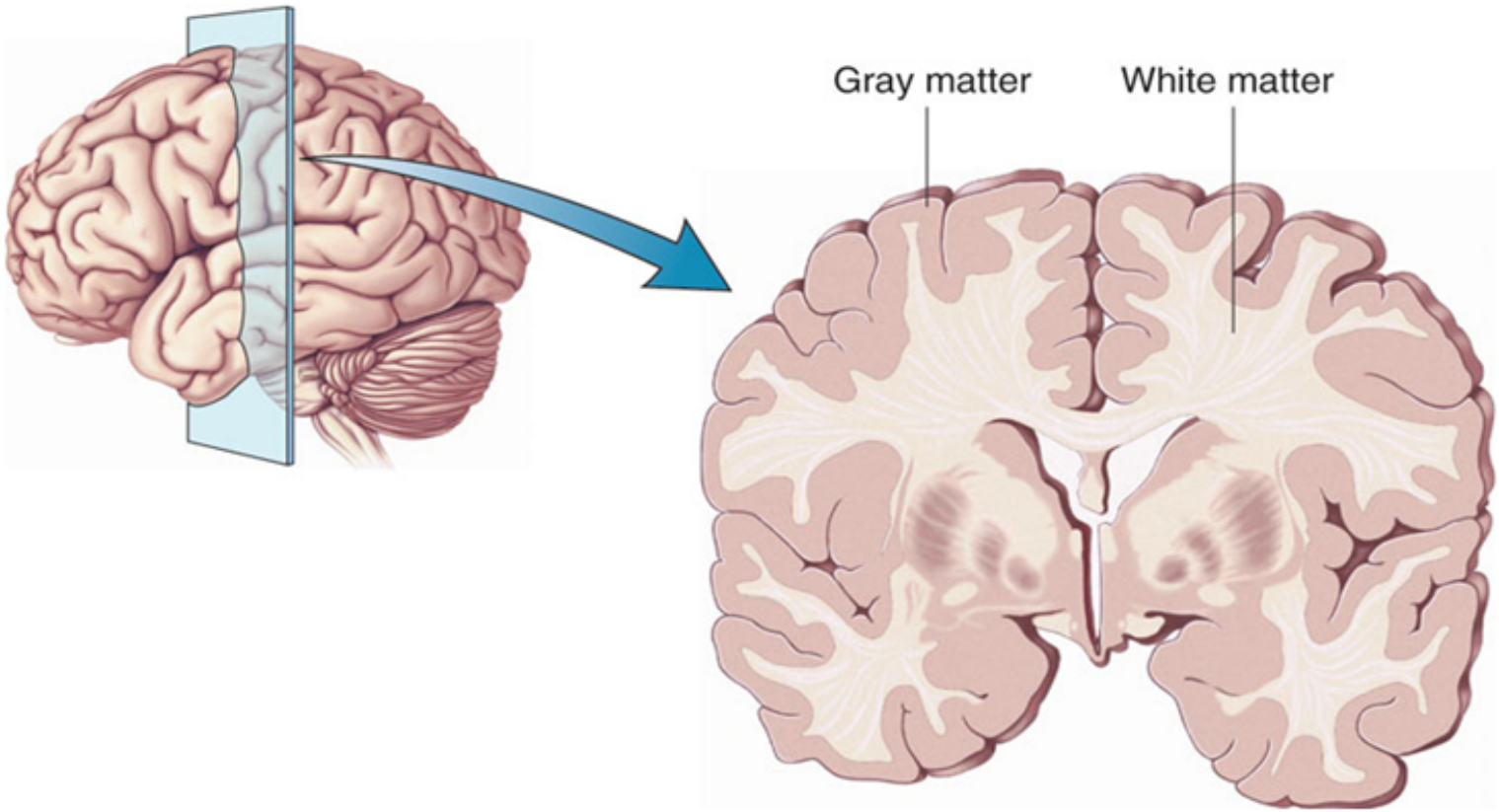
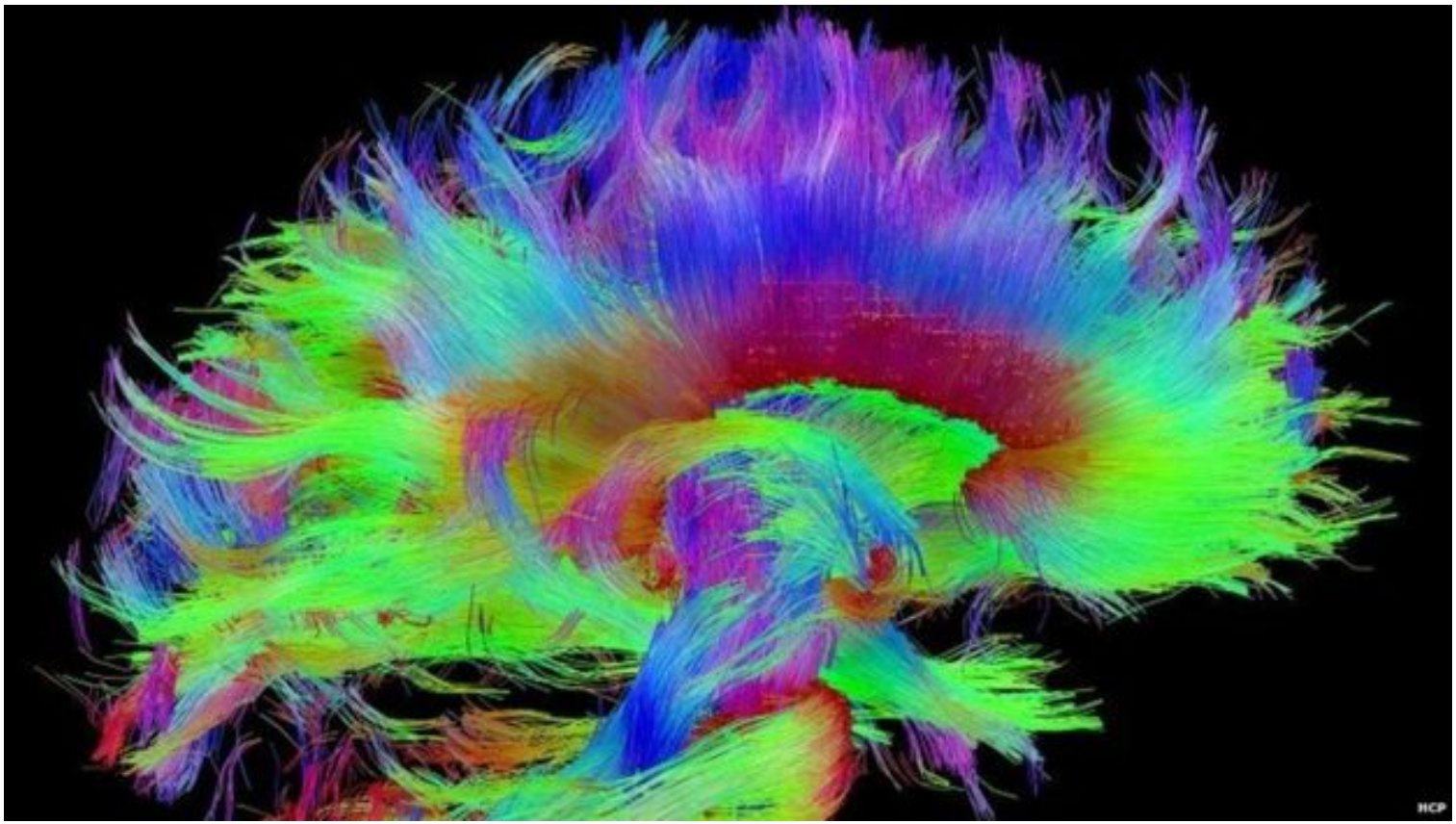
Grey matter Generic term for ~~"stuff"~~ a collection of neuronal cell bodies, which appear grey in a freshly dissected brain.



Brain Structure to Graphs

- Diffusion tensor imaging.
- Tracking white matter (axon) bundles to connect voxels.
- Massive graphs: 15M nodes, 50M edges.

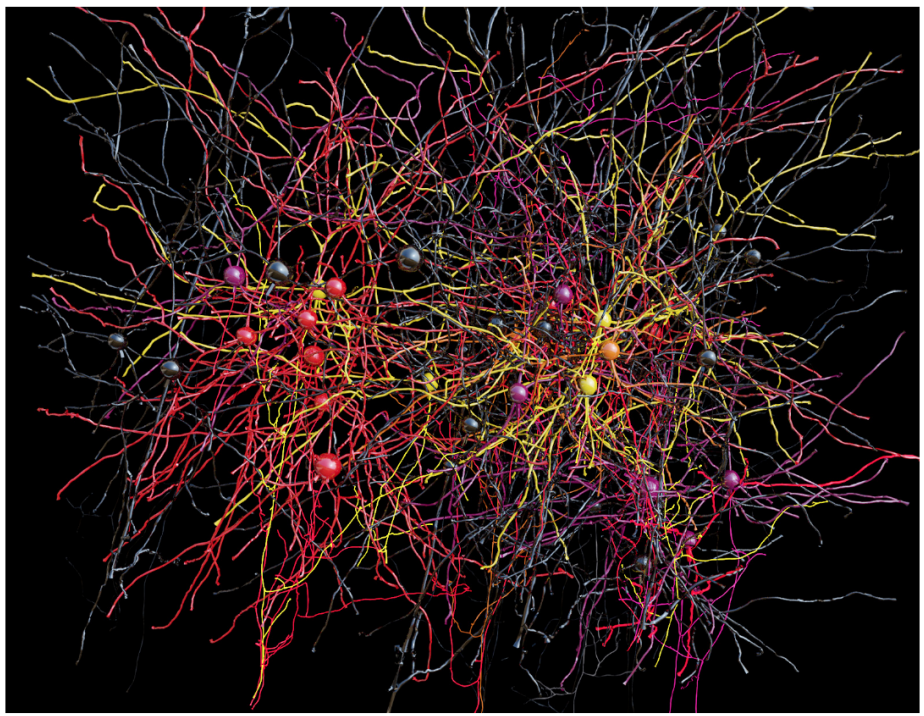


Research on largest network of cortical neurons to date published in Nature

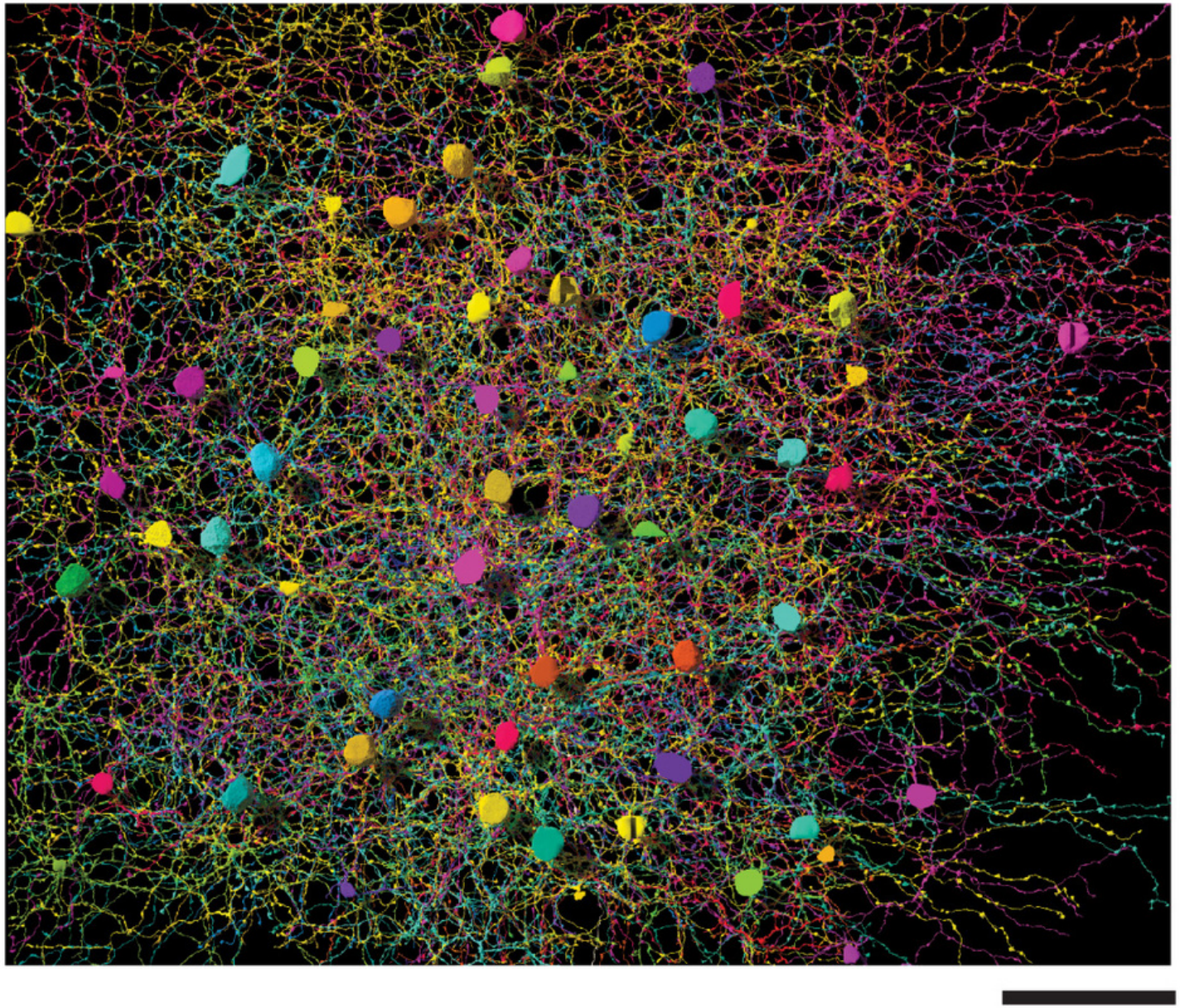
Robust network of connections between neurons performing similar tasks shows fundamentals of how brain circuits are wired

March 28, 2016 | Download PDF

Even the simplest networks of neurons in the brain are composed of millions of connections, and examining these vast networks is critical to understanding how the brain works. An international team of researchers, led by R. Clay Reid, Wei Chung Allen Lee and Vincent Bonin from the Allen Institute for Brain Science, Harvard Medical School and Neuro-Electronics Research Flanders (NERF), respectively, has published the largest network to date of connections between neurons in the cortex, where high-level processing occurs, and have revealed several crucial elements of how networks in the brain are organized. The results are published this week in the journal *Nature*.



Anatomy and function of an excitatory network in the visual cortex, Lee et al., Nature, 532:370–374, 2016.



Spacetime wiring specificity supports direction selectivity in the retina, Kim et al., Nature, 509:331–336, 2014.

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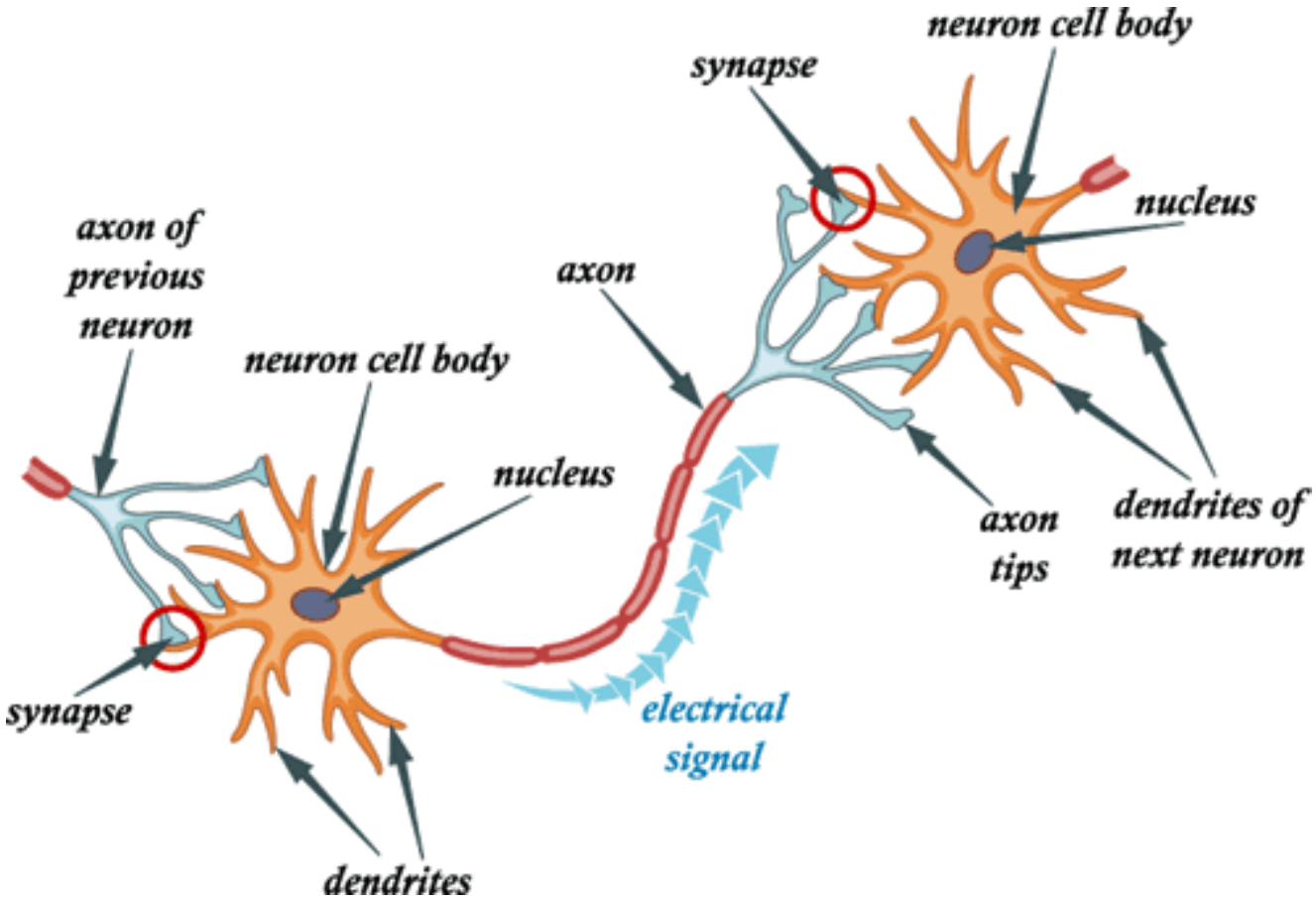
Cellular Communication: Neuron Firing



Neuron, YouTube, 11:20"

www.jasonshen.com

Otto Loewi (1873–1961)

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- How do nerves communicate with muscles: electricity or chemicals?

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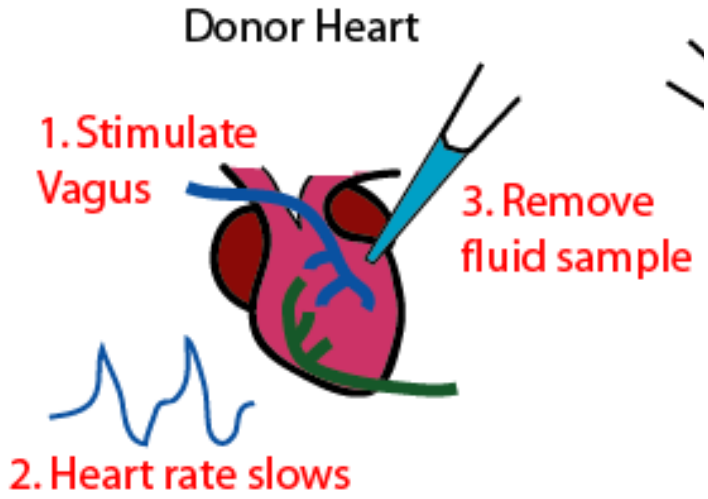

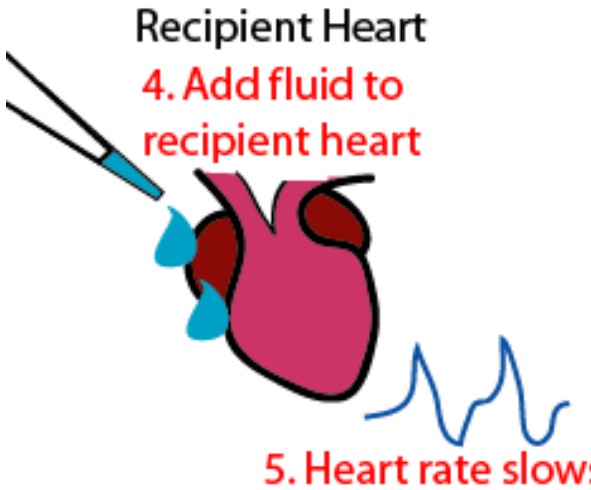

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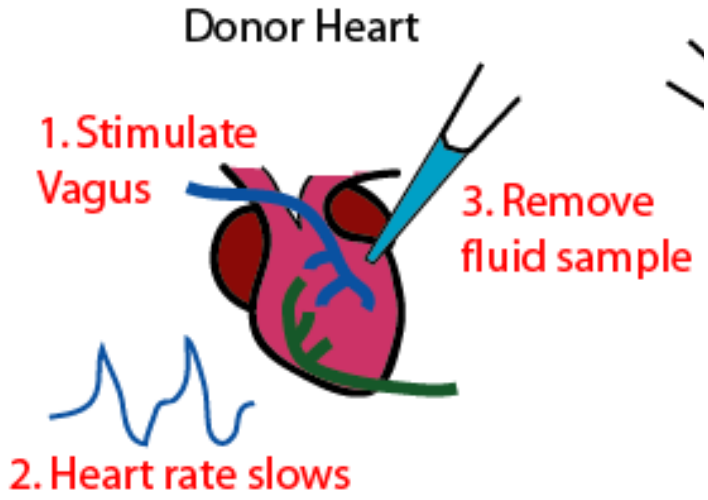
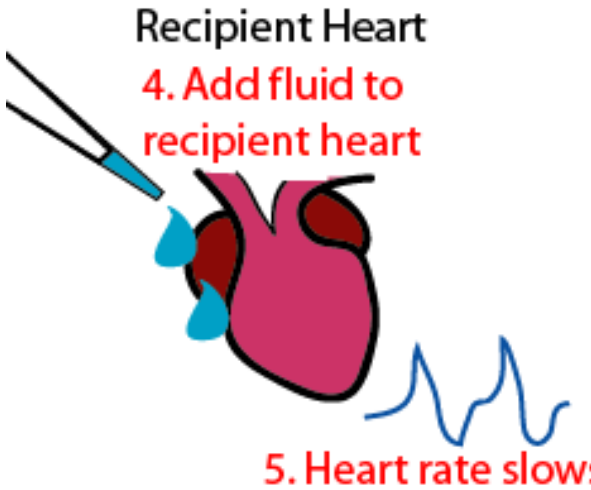
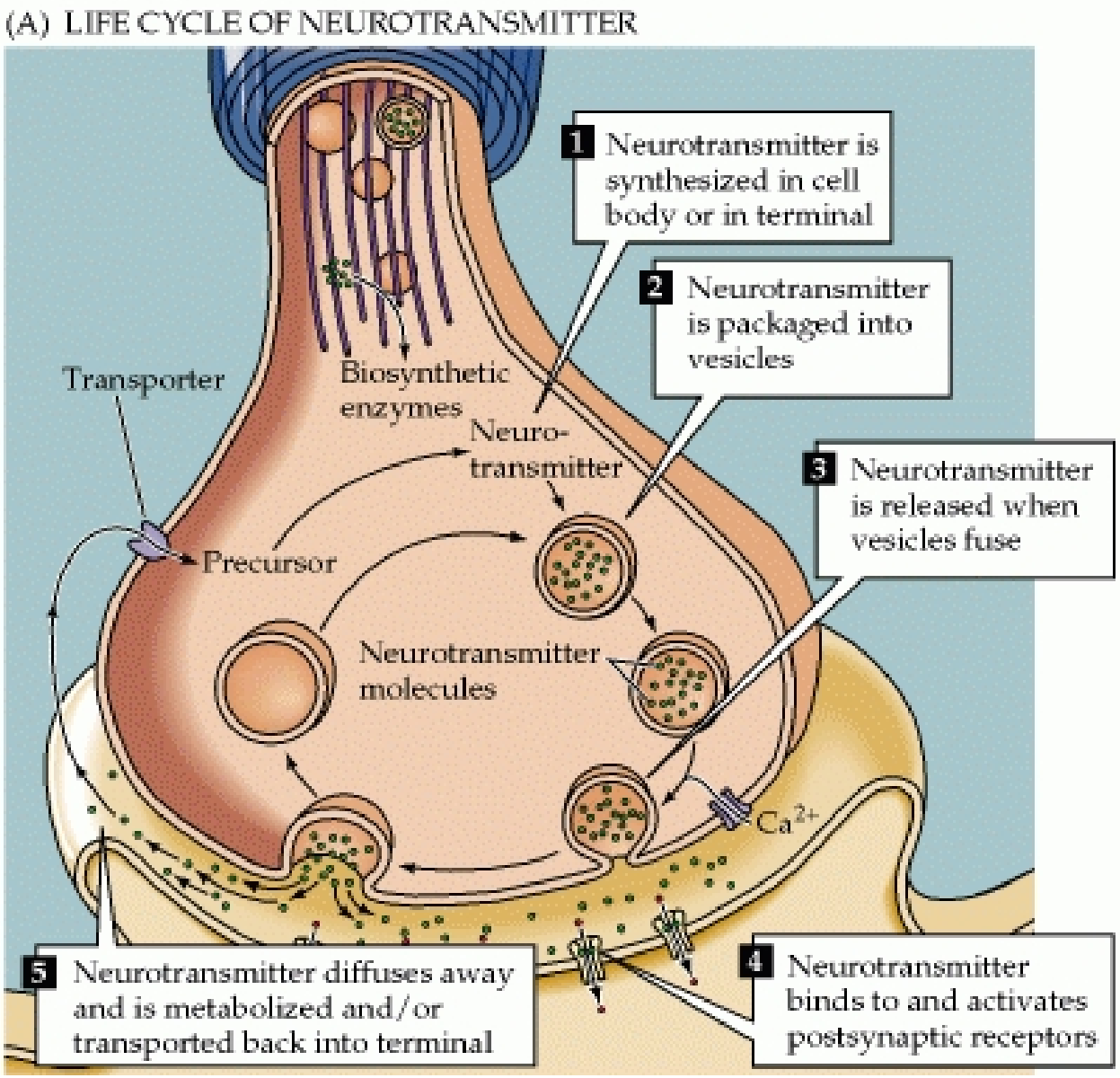
- Later identified as acetylcholine, which had been discovered in 1914 by Sir Henry Dale. *The first neurotransmitter.*
- Loewi and Dale received the Nobel Prize in 1936.

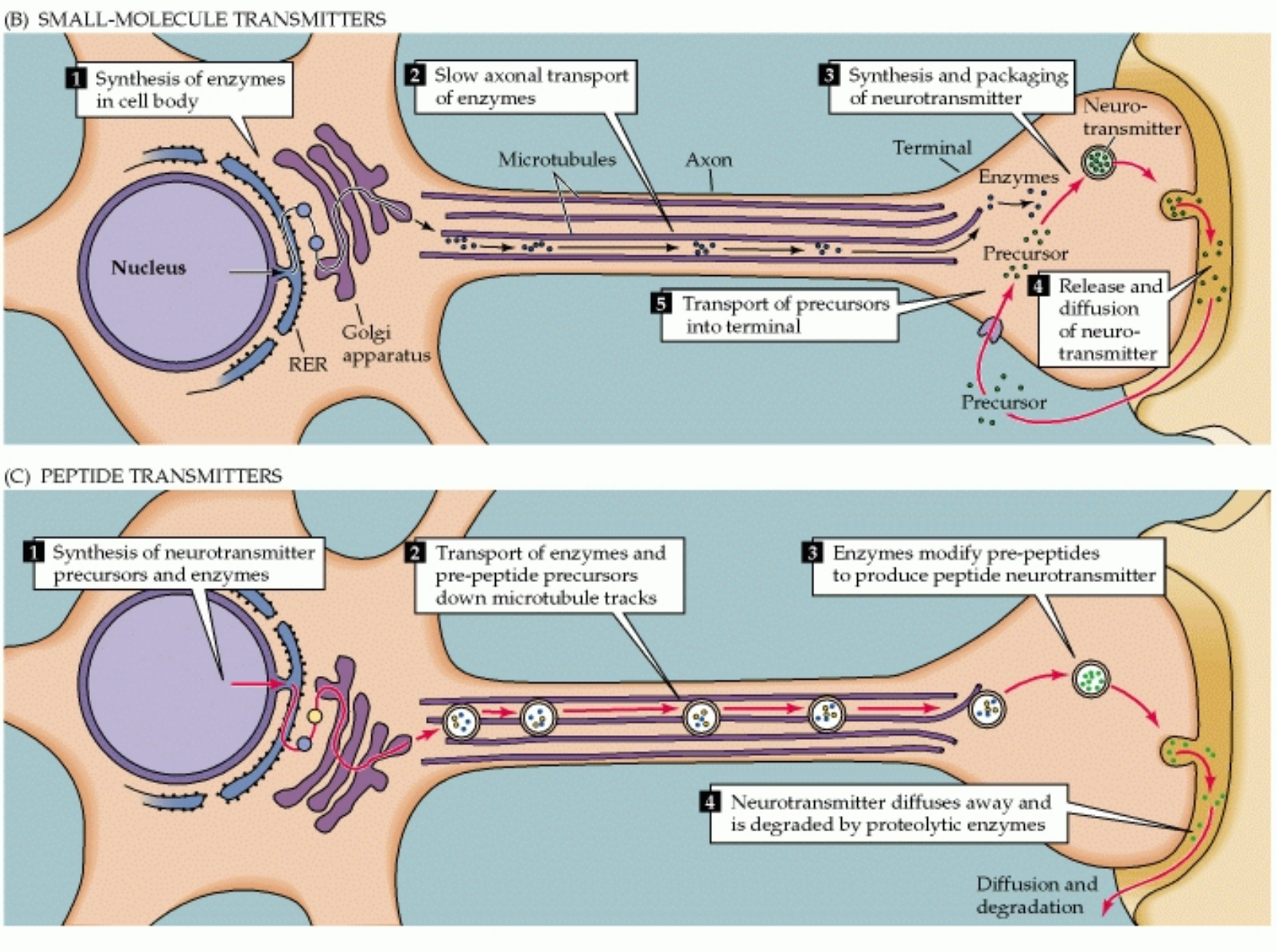




Neurotransmitters



Neurotransmitters



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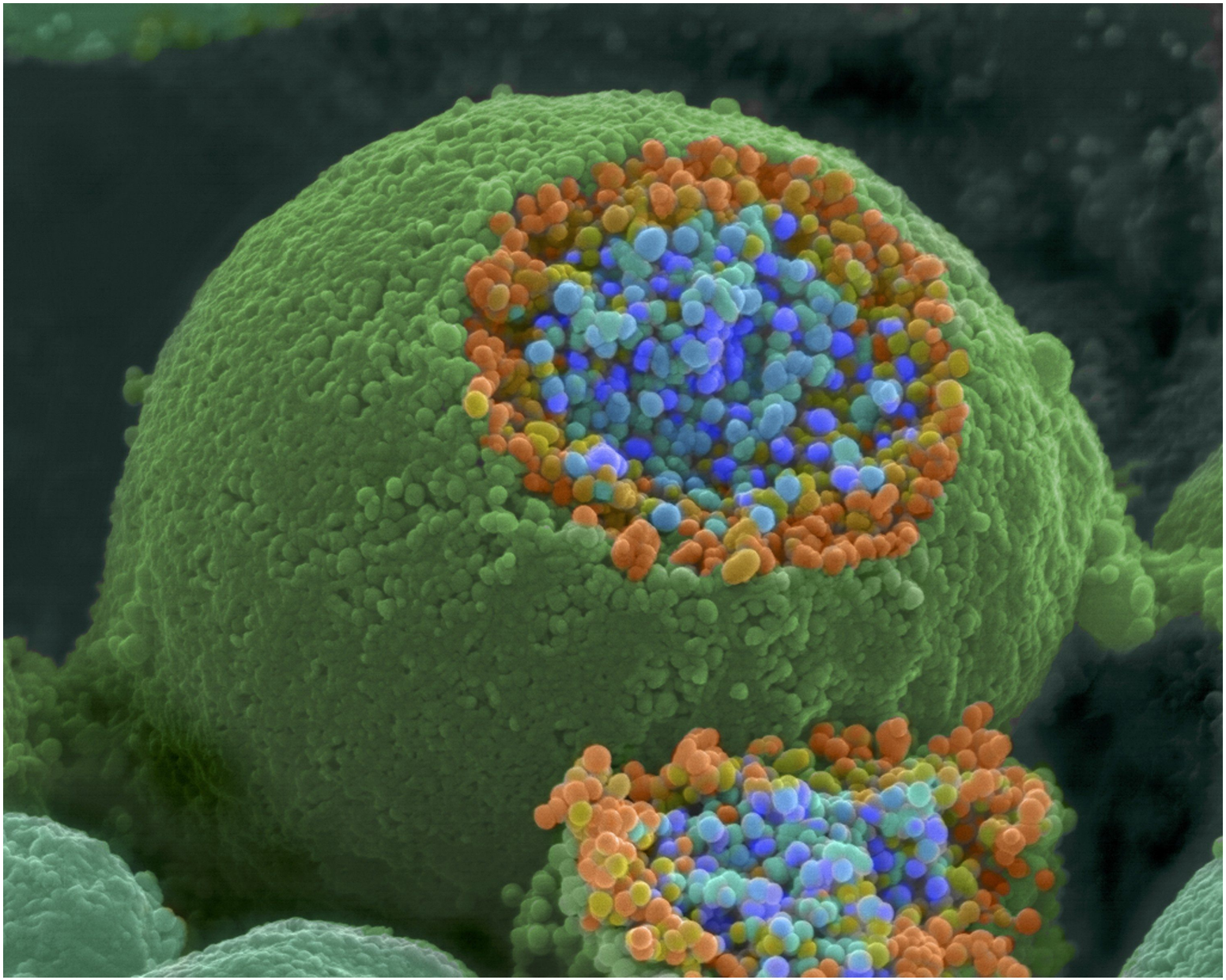

Neurotransmitters

TABLE 47-1

Neurotransmitters and Their Relationship to Mental Disorders

NEUROTRANSMITTER	PHYSIOLOGIC EFFECTS	RELATIONSHIP TO MENTAL DISORDERS
Acetylcholine	Sleep/wake cycle. Signals muscles to become active.	Decreased in Alzheimer's and Parkinson's diseases.
Dopamine	Controls complex movements, cognition, motivation, and pleasure. Regulates emotional responses.	Increased in schizophrenia and mania. Decreased in depression and Parkinson's.
Norepinephrine	Affects attention, learning, memory, and regulation of mood, sleep, and wakefulness.	Decreased in depression. Increased in schizophrenia, mania, and anxiety.
Serotonin	Affects sleep and wakefulness, especially falling asleep. Affects mood and thought processes.	Probably plays a role in thought disorders of schizophrenia. Decreased in depression. Possibly decreased in anxiety and obsessive-compulsive disorder.
Gamma-aminobutyric acid (GABA)	Amino acid that modulates other neurotransmitters.	Decreased in anxiety and schizophrenia.

Alzheimer's Disease

Mechanisms and secrets of Alzheimer's disease: exploring the brain, Video, 6:26"

Rita Levi-Montalcini (1909–2012)

- M.D. at University of Turin (1936).
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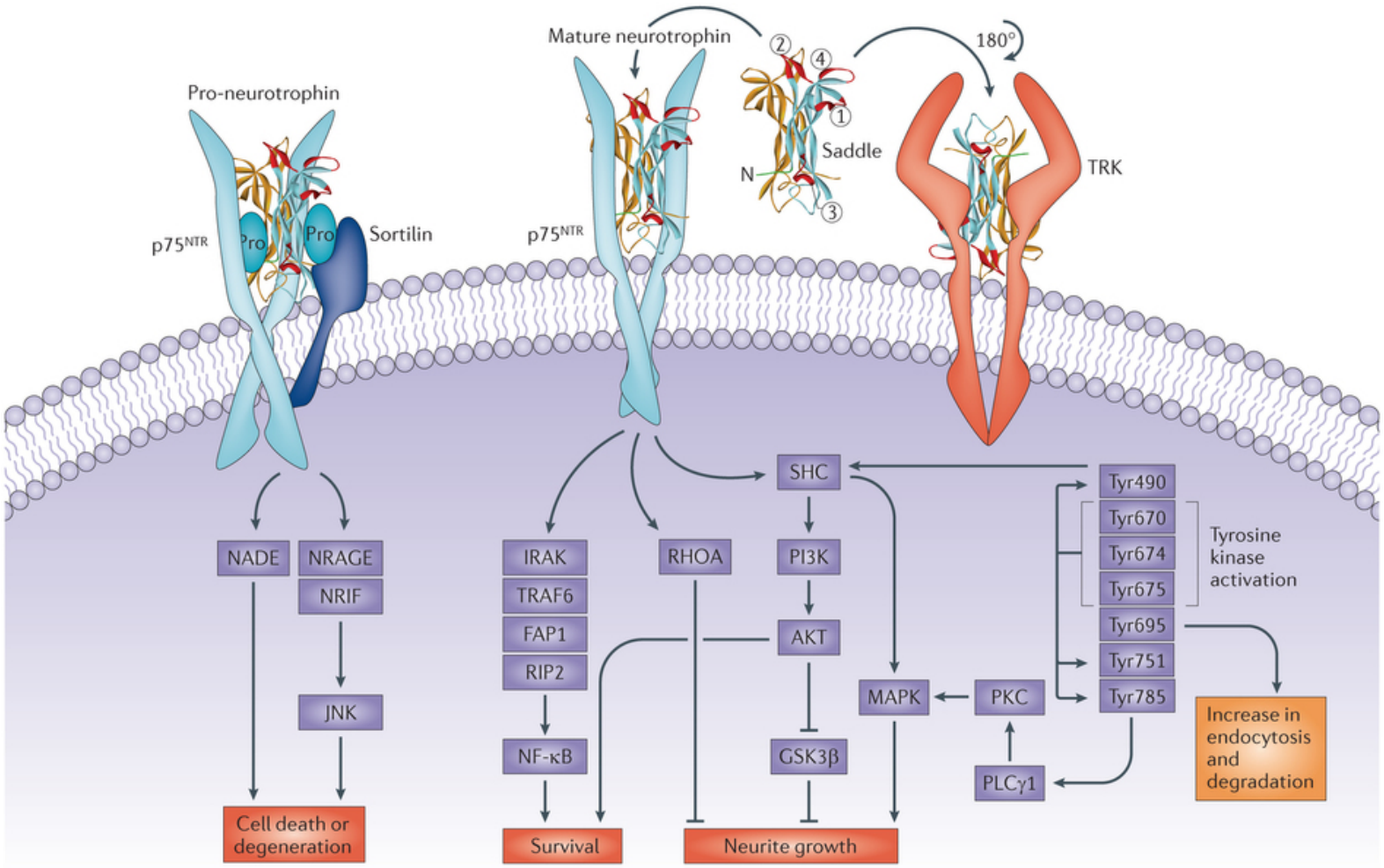
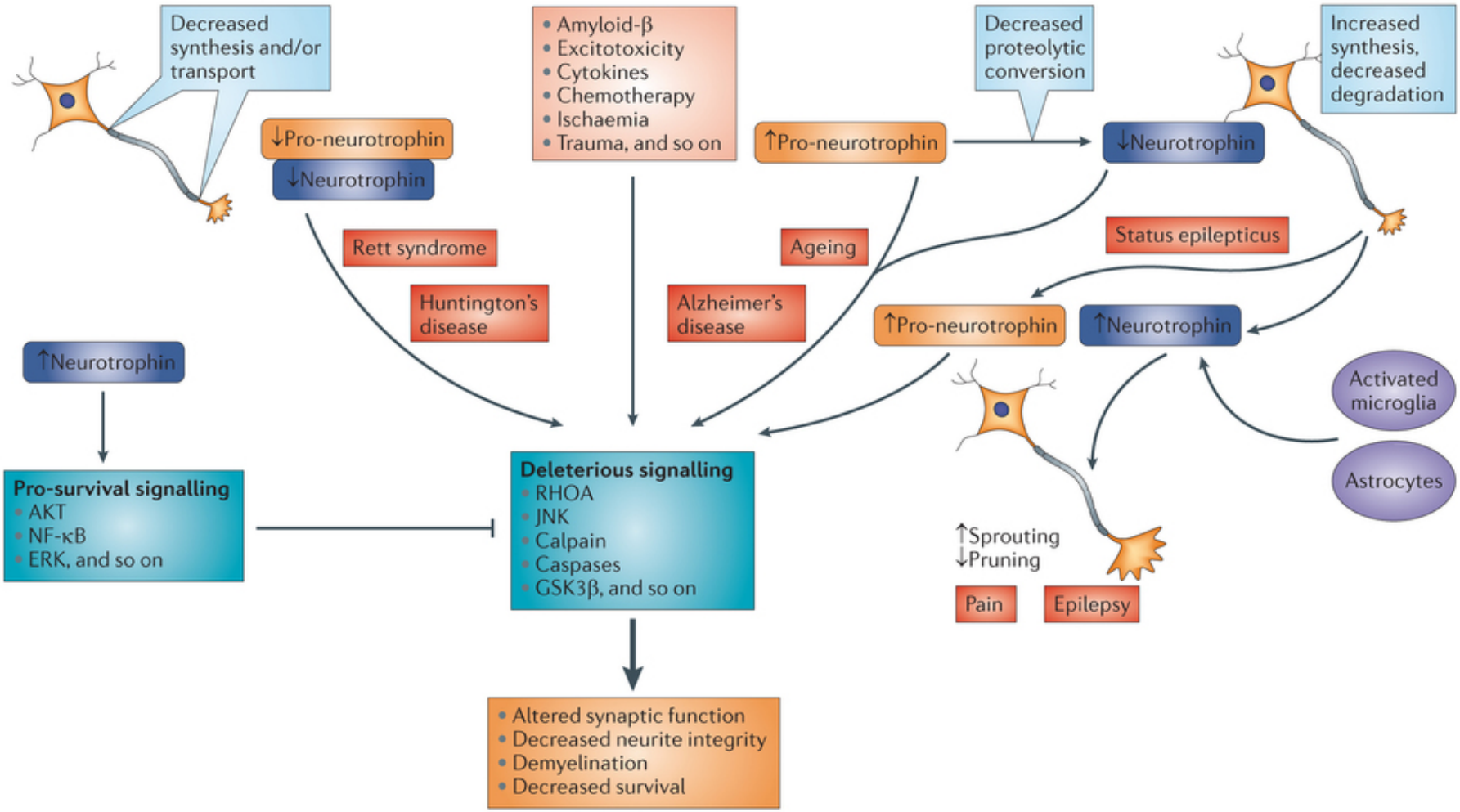
Neurotrophins

Family of proteins that induce the survival, development, and function of neurons.



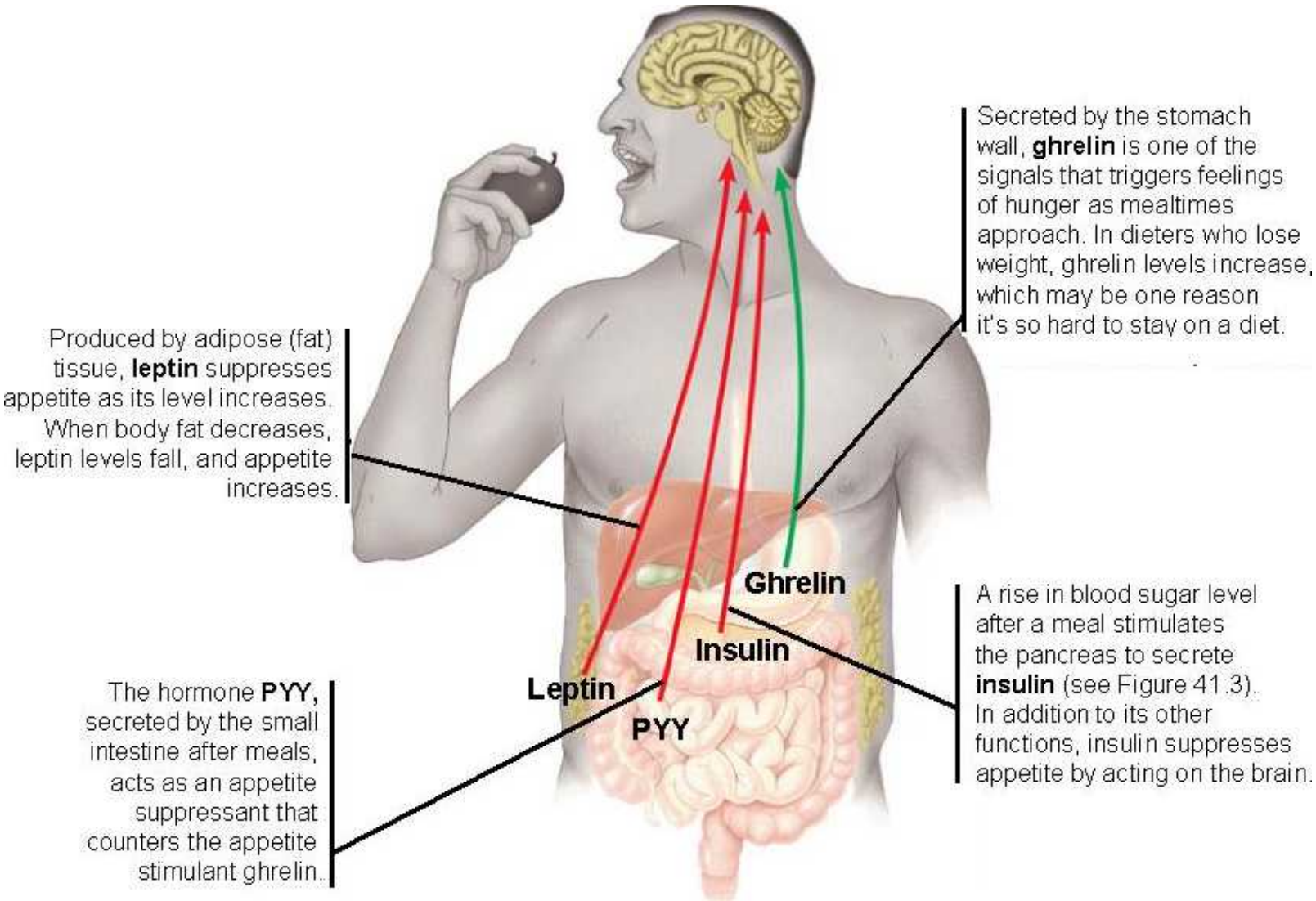
Neurotrophins

Changes in neurotrophin levels or in the ratio of pro-neurotrophin to mature neurotrophin can cause and/or contribute to numerous diseases.



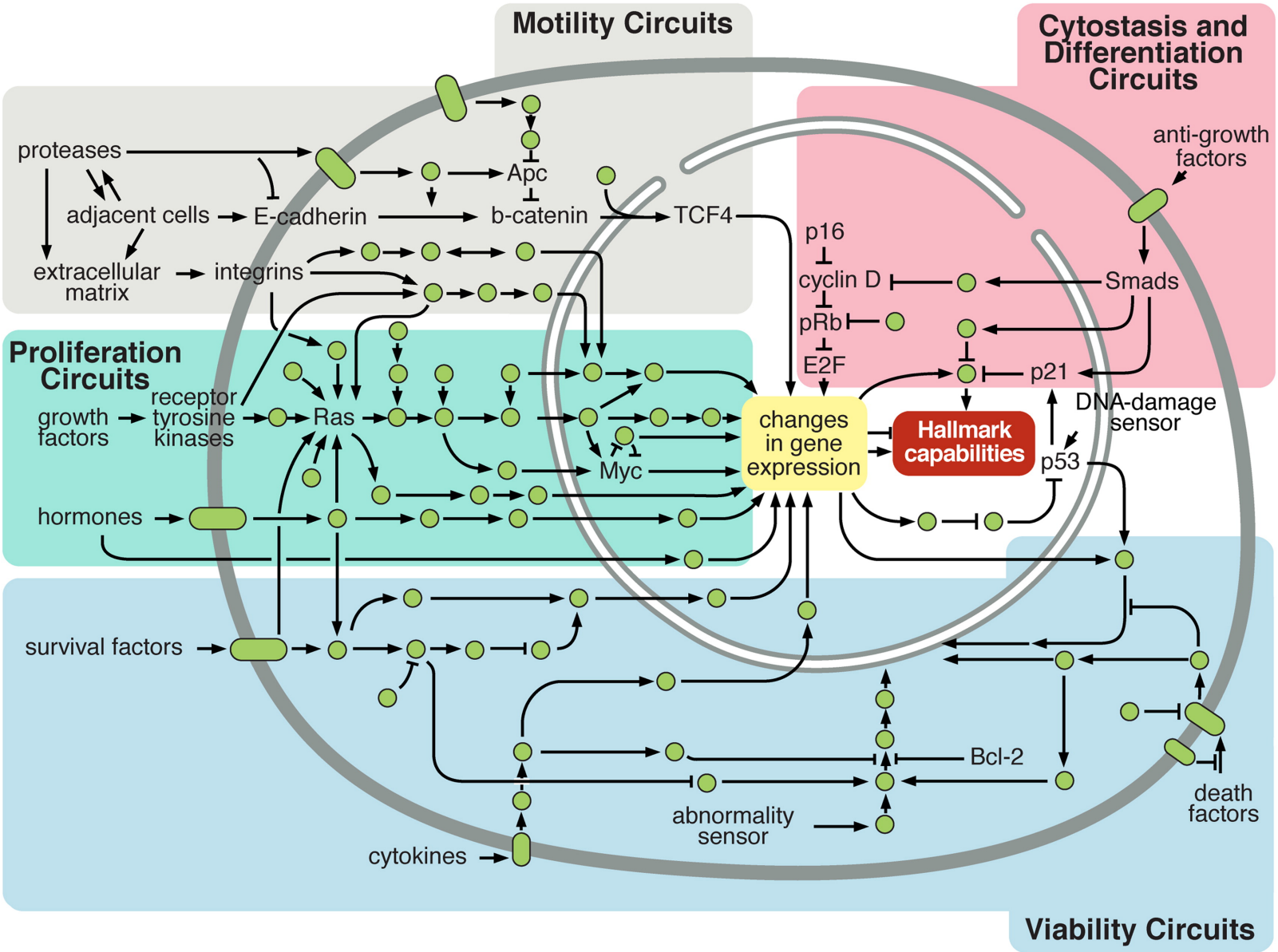
Nature Reviews | Drug Discovery

Cellular Communication: Hunger Response



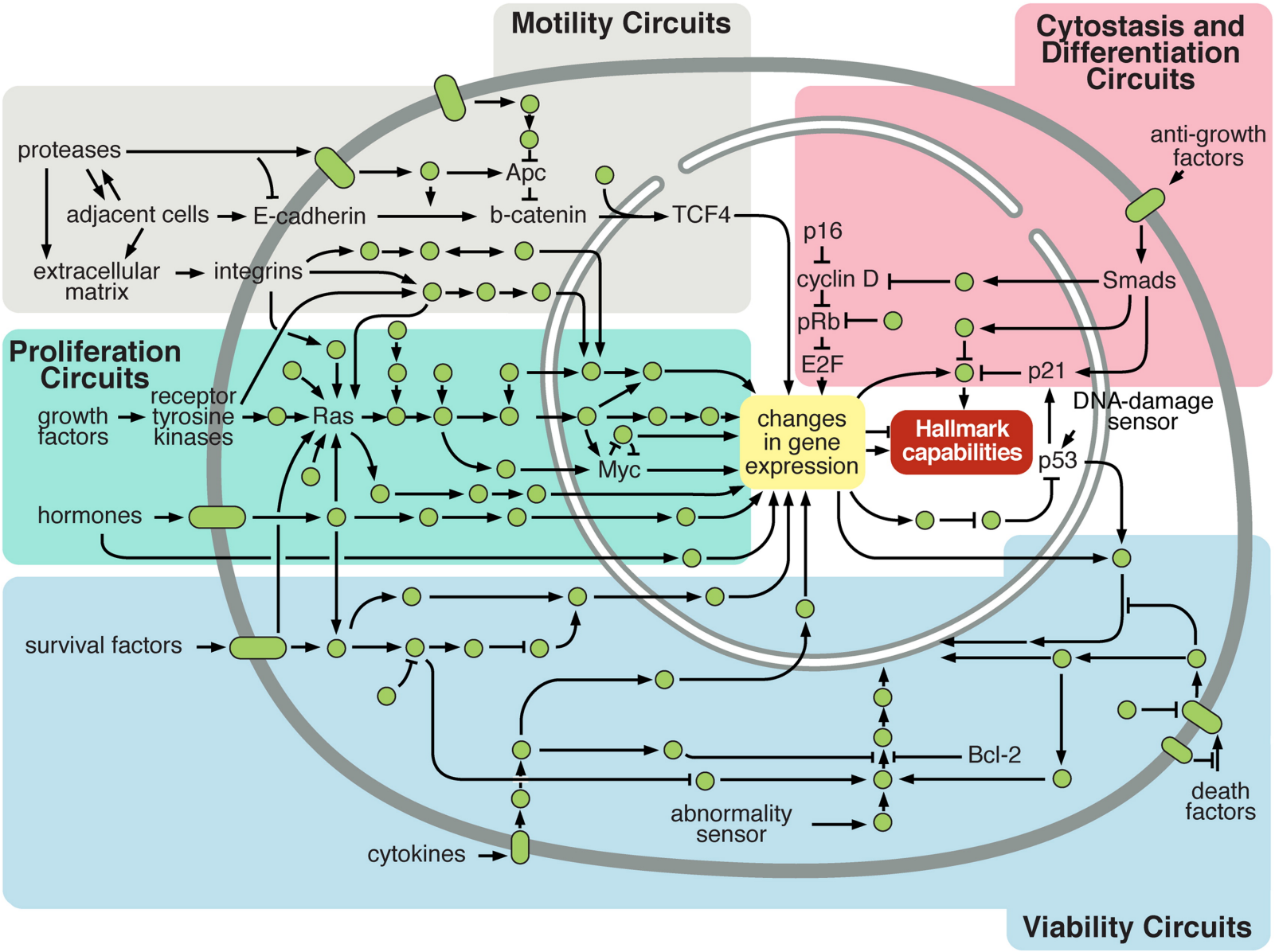
www.barbellmedicine.com

Cellular Response to External Signals



Hanahan and Wienberg. Hallmarks of cancer: the next generation. Cell, 2011.

A Cell is Like



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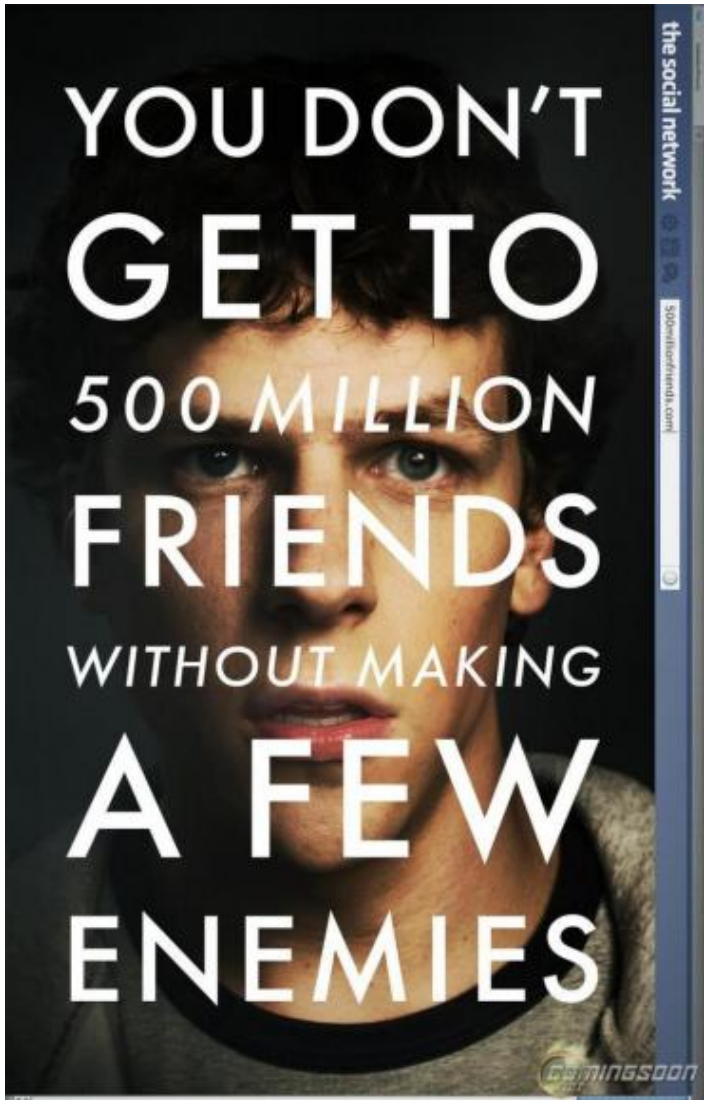
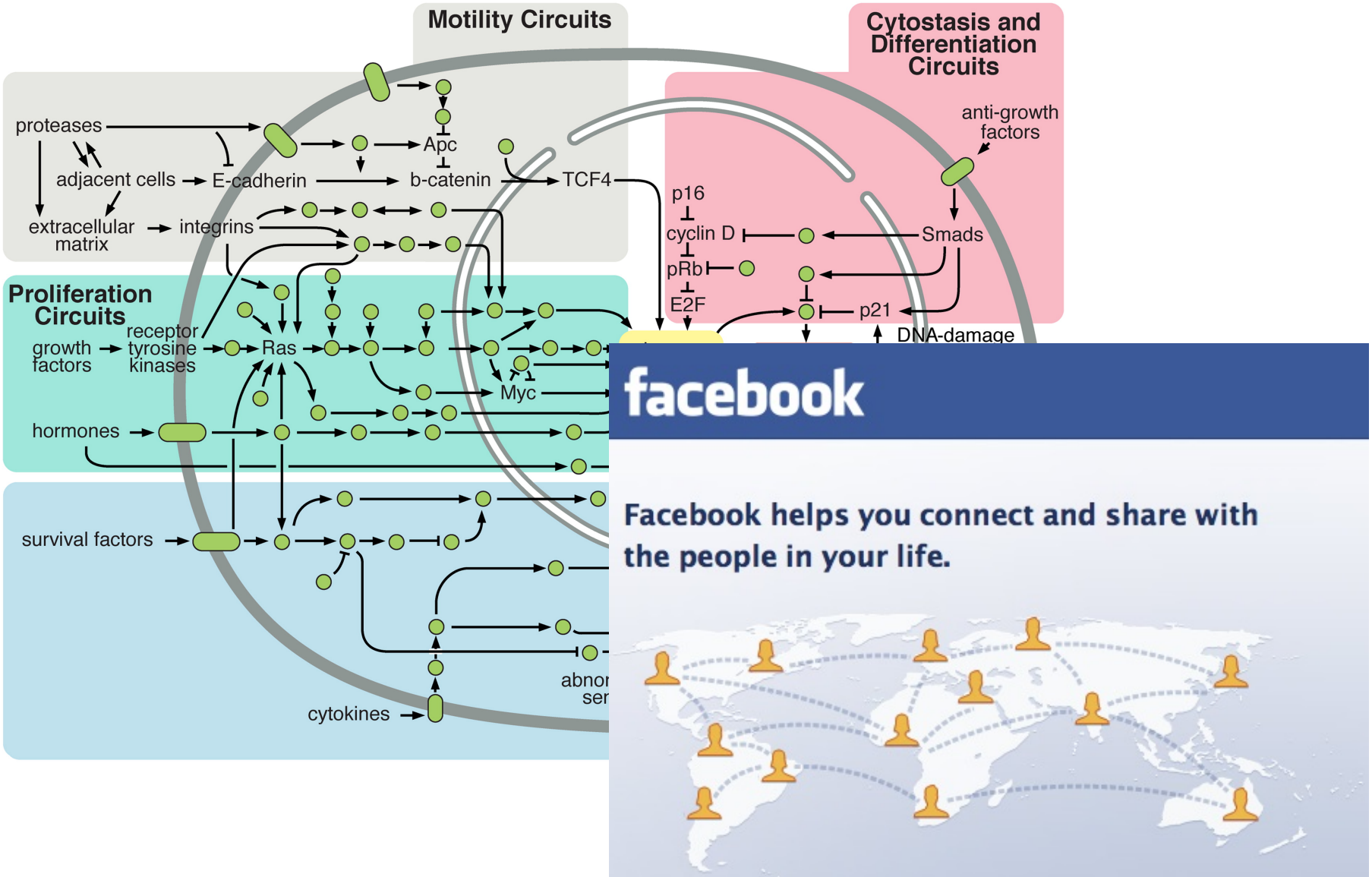
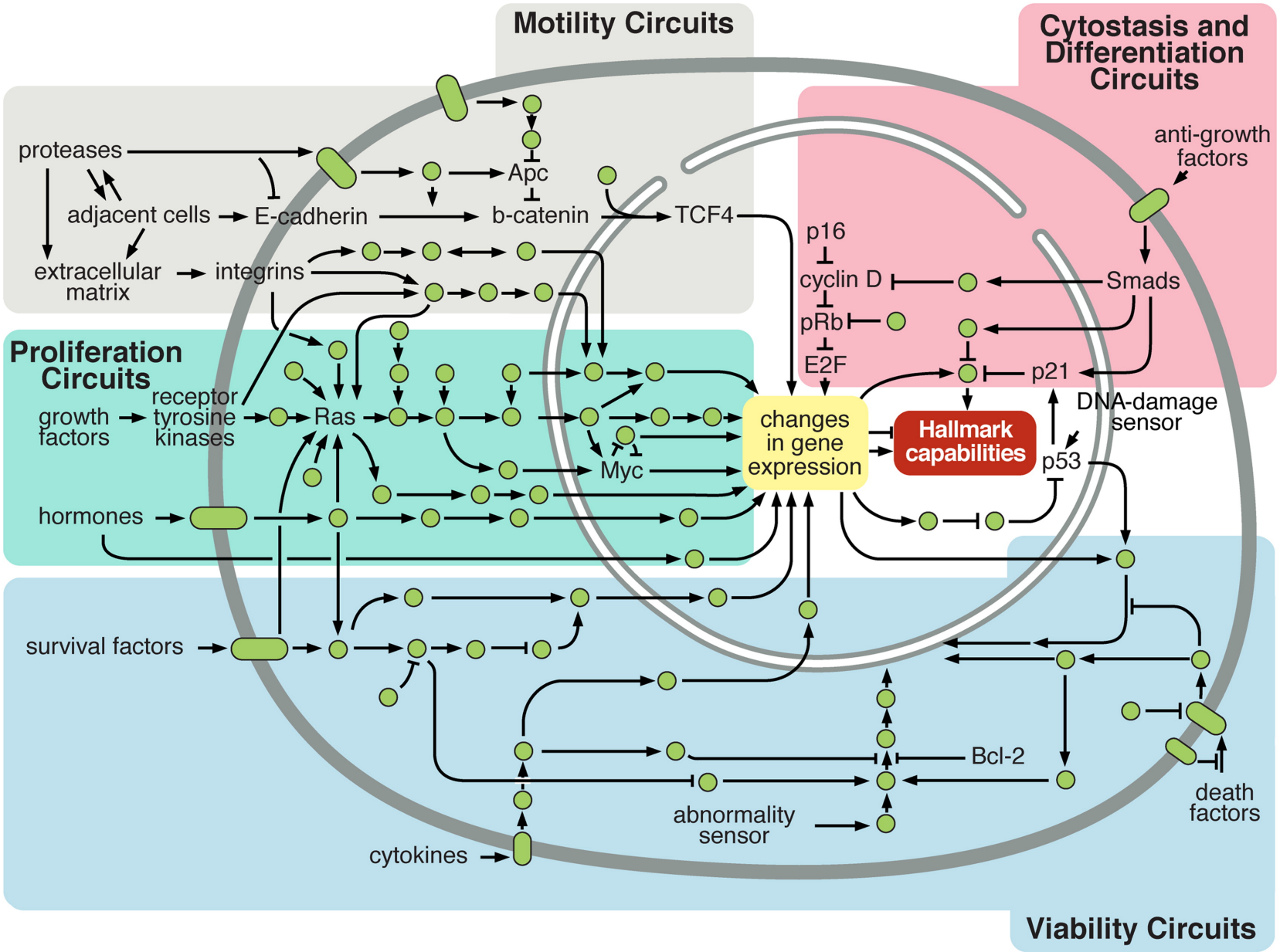


A Cell is Like facebook



Network is Complex



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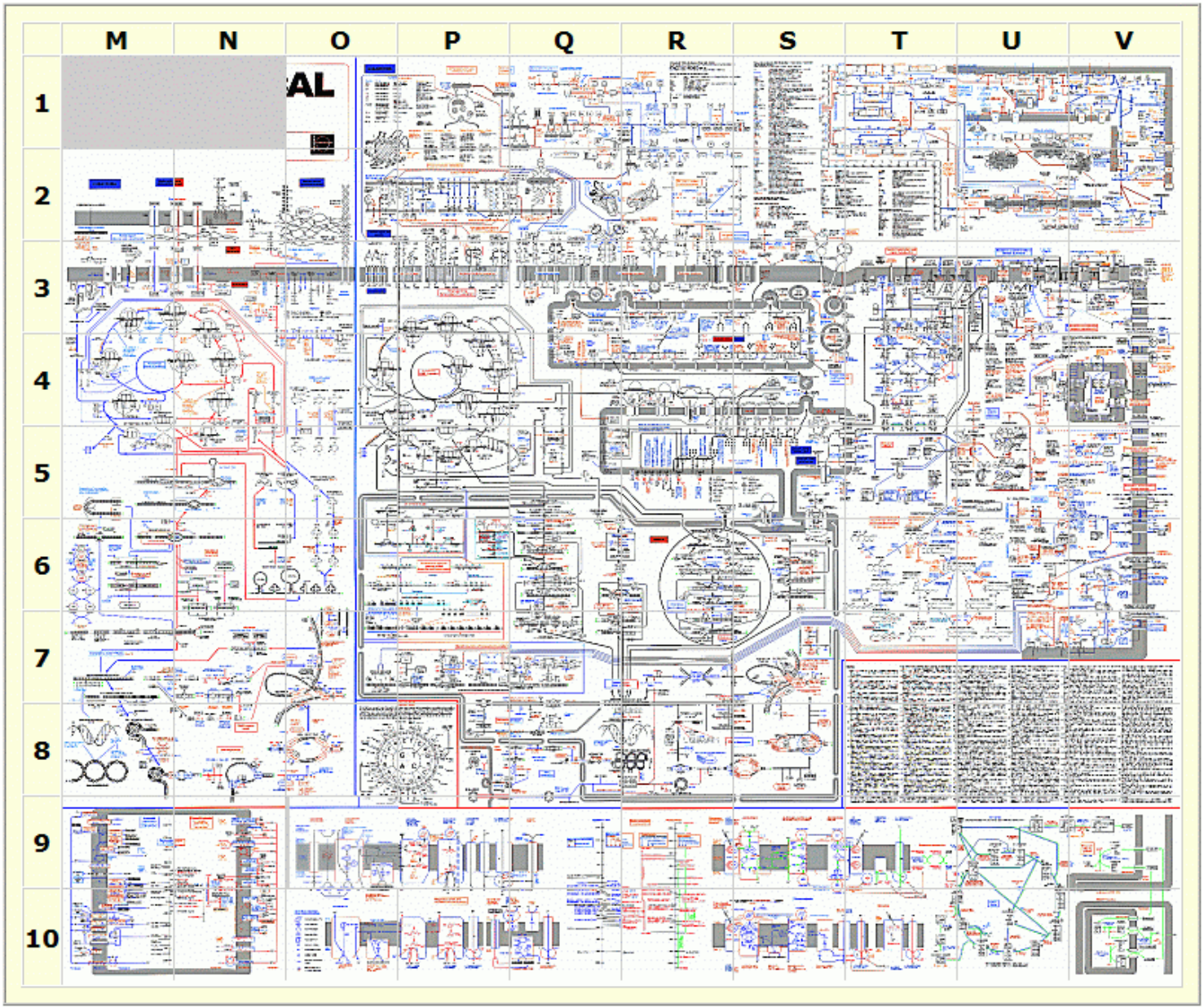
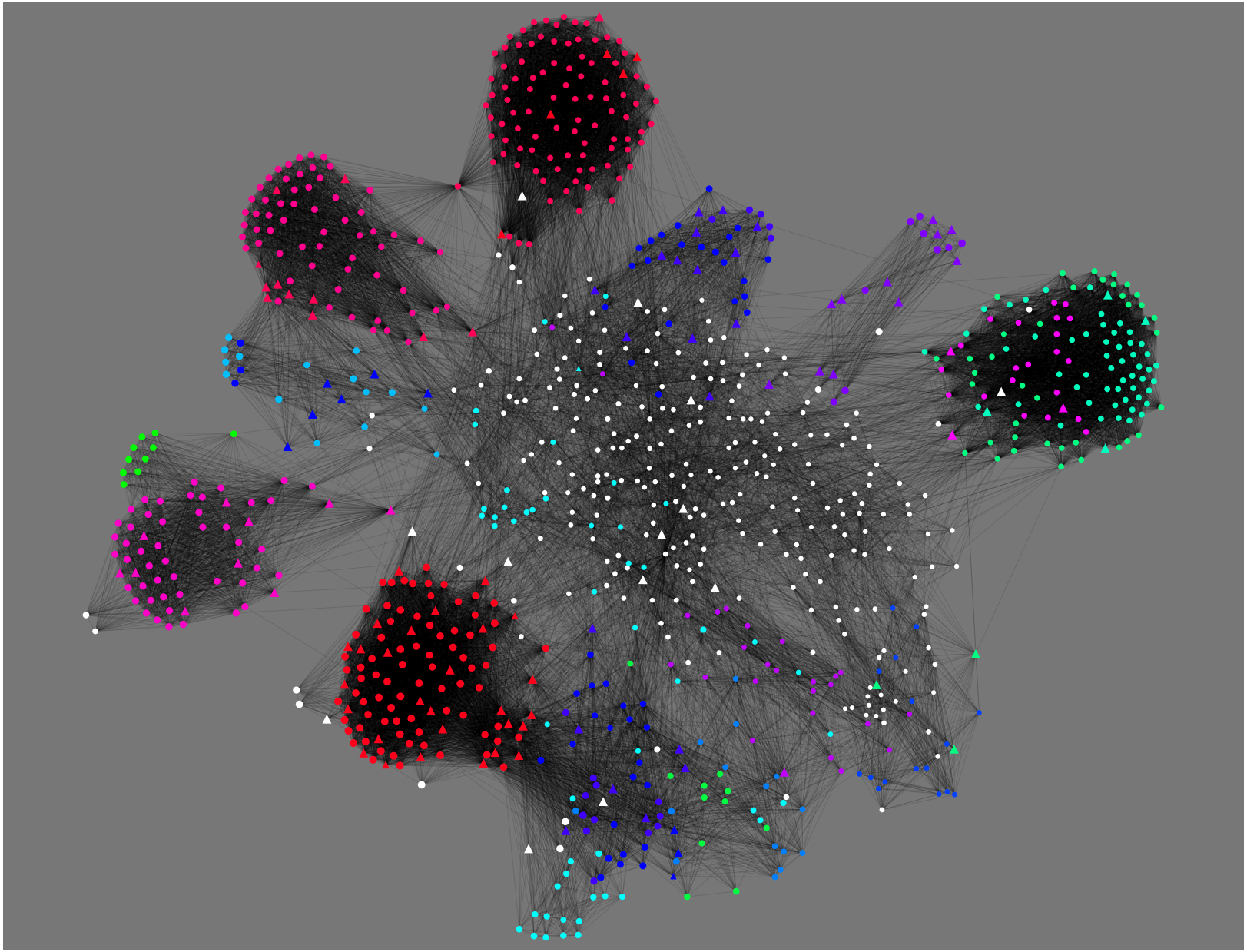


Network is Complex but Very Poorly Understood



Survey Results

What are the most important things you expect from this course? You can select multiple options. If your choice does not appear, please add it in your answer to the third question.

Learn graph theory	8 respondents	50 %	
Learn about the structure of the brain	13 respondents	81 %	
Work on a software project	11 respondents	69 %	
Learn how to work collaboratively in a team	3 respondents	19 %	
Study and present research papers	5 respondents	31 %	
No Answer	1 respondents	6 %	

Survey Comments

- Learn about the brain and graph theory, how CS is used to represent/understand the brain, study brain diseases.
- Learn how to incorporate CS with neuroscience and biology, how CS interacts with other fields, apply CS to solve real-world challenges.

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- Please don't assume yours is the only class we are taking. Don't change project specs. Give us guidance on projects throughout the class.

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- *Definitely the course I'm looking forward to most this semester!*

Modified Course Structure

- Designed with the following goals in mind:
  - Presentation skills are very important in the real world.
  - You will almost always work collaboratively.
  - You will often be called upon to learn independently from multiple sources (life-long learning).

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- Student presentations: after spring break, based on textbook chapters, research papers, and other materials, 30% of grade.

Modified Course Structure

- Designed with the following goals in mind:
  - Presentation skills are very important in the real world.
  - You will almost always work collaboratively.
  - You will often be called upon to learn independently from multiple sources (life-long learning).
- Lectures by me based on the textbook: till spring break
- Assignments (2–3): till spring break, project warm-ups, 30% of grade.
- Group software project: assigned by spring break, 40% of grade.
- Student presentations: after spring break, based on textbook chapters, research papers, and other materials, 30% of grade.
- After spring break, use classroom time as office hours.
- I will give detailed feedback on practice presentations.
- I will give detailed feedback on software projects.
- I will help you with poster presentation for VTURCS Symposium.
- We will have guest lectures from Smith Career Center on collaboration and presentation skills.