CS 4884: Computing the Brain Computional Biology and Bioinformatics Capstone Course

T. M. Murali

January 18 and 20, 2022



This course is NOT about neural networks or deep learning.

Course Information

- Meet on Tuesdays and Thursdays, 2pm-3:15pm, MCB 110A.
- Office hours: by appointment and during class times in second half of semester.
- Course website: http://bioinformatics.cs.vt.edu/~murali/ teaching/2022-spring-cs4884/. Consult this website regularly. Course schedule is subject to change.

Textbook

Fundamentals of Brain Network Analysis

Alex Fornito, Andrew Zalesky, and Edward Bullmore

Finalization of Plant Notes, Analysis is a comprisentine and accussible introductions intercharks for automatic herationhary comparison of measured constructive from emphasis and the strengther and the strengther and the strengtheration of the experiment bulkground in the strengtheration of the strengtheration of the end of the strengtheration of the end of the strengtheration of statistical strengtheration of the strengtheration of the strengtheration of the statistical strengtheration of the strengtheration of the strengtheration of the statistical strengtheration of the strengtheration of the strengtheration of the statistical strengtheration of the strengtheration of the strengtheration of the statistical strengtheration of the strengtheration of the strengtheration of the statistical strengtheration of the strengtheration of the strengtheration of the statistical strengtheration of the strengtheration of the strengtheration of the statistical strengtheration of the str

From the Fore

"This much needed primer on brain networks will become an indispensable as to the bookshelves of all neuroscientists interested in the organization and fur of neuron meters.

- 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





Fornito Zalesky Bullmore

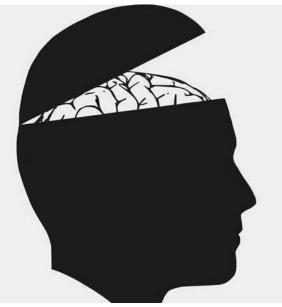
Fundamentals of Brain Network Analysis

Fundamentals of Brain Network Analysis

Alex Fornito, Andrew Zalesky, and Edward Bullmore

Course website contains an online link to the textbook.

January 18 and 20, 2022

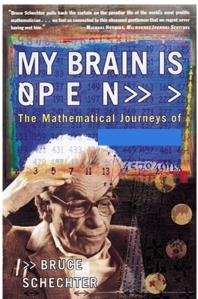


January 18 and 20, 2022



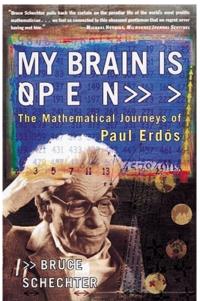
T. M. Murali

January 18 and 20, 2022



T. M. Murali

January 18 and 20, 2022



T. M. Murali

January 18 and 20, 2022

• Lectures based on the textbook

- Lectures based on the textbook
- Assignments (2–3)

- Lectures based on the textbook
- Assignments (2–3)
- Final project

- Lectures based on the textbook
- Assignments (2–3)
- Final project
- Participation in VTURCS Research Symposium in late April.

	C II	
Course Structure		

Grading

- Assignments: 40%
- Final project: 60%

Assignments

- Typically, I will ask you to write code to replicate analysis in one or two figures in a research 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

• Trepanation (6500 BC, Incas, Peru): drilling holes in the skull to expose *dura mater* (outermost layer of the meninges) to treat health problems.



History of the Brain: Pre-History

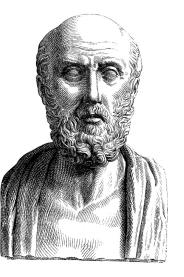
- Trepanation (6500 BC, Incas, Peru): drilling holes in the skull to expose *dura mater* (outermost layer of the meninges) to treat health problems.
- Egypt (c. 3000 BC): Aware of symptoms of brain damage, but considered the heart to the repository of memories.



History of the Brain: Pre-History

- Trepanation (6500 BC, Incas, Peru): drilling holes in the skull to expose *dura mater* (outermost layer of the meninges) to treat health problems.
- 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.

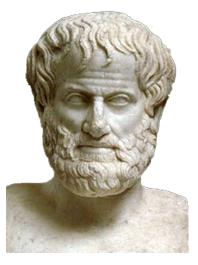
- Study of the brain was not based on dissection.
- Hippocrates (460–379 BC): Brain is the organ of sensation and intelligence.



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

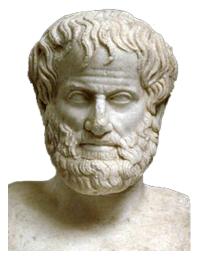
January 18 and 20, 2022

- Study of the brain was not based on dissection.
- Hippocrates (460–379 BC): Brain is the organ of sensation and intelligence.
- Aristotle (384–322 BC): Heart is the center of intellect.



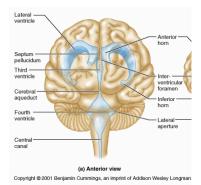
The birth and evolution of neuroscience through cadaveric dissection, Moon K1, Filis AK, Cohen AR. Neurosurgery. 2010 Sep;67(3):799–809

- Study of the brain was not based on dissection.
- Hippocrates (460–379 BC): Brain is the organ of sensation and intelligence.
- Aristotle (384–322 BC): Heart is the center of intellect. Brain is a radiator for cooling blood. Larger brains ⇒ humans are more rational.



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

- Study of the brain was not based on dissection.
- Hippocrates (460–379 BC): Brain is the organ of sensation and intelligence.
- Aristotle (384–322 BC): Heart is the center of intellect. Brain is a radiator for cooling blood. Larger brains ⇒ humans are more rational.
- Herophilus (c. 325-255 BC):
 - Father of neuroanatomy, first dissector in the Western tradition.
 - Discovered ventricles, distinguished between cerebrum and cerebellum.



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

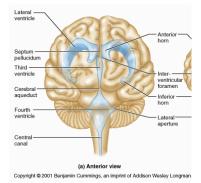
January 18 and 20, 2022

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.
- The brain is the location of the mind.

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.
- 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).

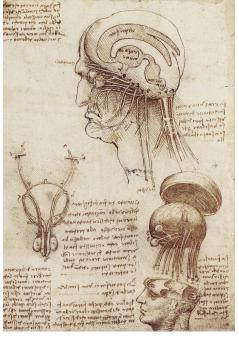


The Next 1300 Years

- 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)

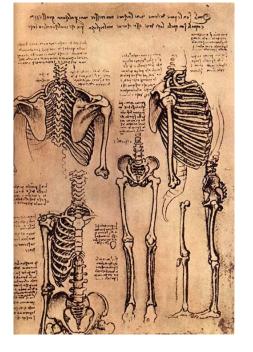
- Increased recognition of need for dissection to acquire new knowledge about the body's internal organs.
- Printing press (1439 AD) circulated Galen's works.
- Renaissance and Reformation of the Church promoted fresh thinking.
- Dissection resulted in detailed anatomatical drawings.

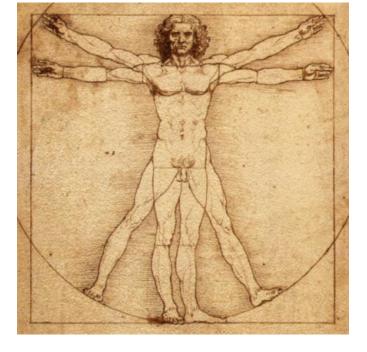


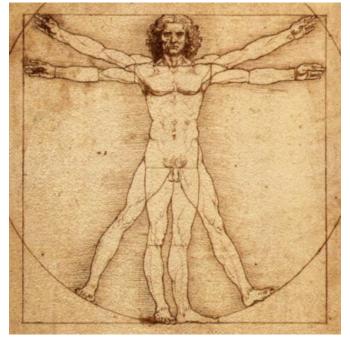
condry & videntur the first friday las protrane come [ight " throfimmer & Lunn me perfine ello for (a principle council

to the oundancelling

quere Constantificate certi qualifone limaficoli Dinif anne nelliomini hans נטווהי ליוויבה demon no fall co fund hum to visituned qualif on familifier ----- 141 (cheffit with minune aboutature y no nimito fel (on old stallow) Buntum Jog winn alon Tomper ono for with hand iten America Strang Matte mafeon Q's comments of TH OTHERNEOLIS when almah prise HUNG & Smil ((a (partala to ifon in workenis הקיויה מיוה A mother [petito ner by the function po por come inter december mo offer to first about win will a first for every belynest Sel - Conull - Countrolo in cline alle to signo get progranto sela of Contransforde . o. . vor mante cupa short for the in antimate by tolgamite on to il's all in the first The weather promo al first a ----- Multipalitation (A MARY D' A MORE TO MARKE)



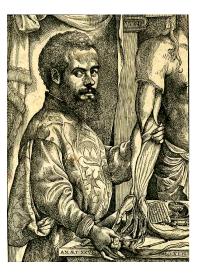




Leonardo da Vinci (1452–1519)

Andreas Vesalius (1514–1564)

• Used skillful dissection of cadavers.



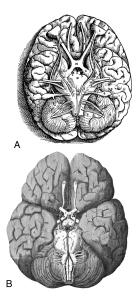
Andreas Vesalius (1514–1564)

- Used skillful dissection of cadavers.
- *De humani corporis fabrica*: Documented and corrected 200 errors by Galen.



Andreas Vesalius (1514–1564)

- Used skillful dissection of cadavers.
- *De humani corporis fabrica*: Documented and corrected 200 errors by Galen.



Contemporaries and Descendants of Vesalius

Mathematics Genealogy Project							
Home	Gemma (Jemme Reinerszoon) Frisius						
Search	Biography						
Extrema	Magister Philosophiae, Medicinae Doctor Université						
About MGP +	Catholique de Louvain 1529, 1536						
Links	Dissertation:						
FAQs	Advisor: Petrus (Pieter de Corte) Curtius						
Posters	Students:						
Submit Data	Click <u>here</u> to see the students listed in chronological order.						
Contact	Name	School	Year	Descendants			
Mirrors >	John Dee	University of Cambridge and Université Catholique de Louvain	1546	1			
A service of the <u>NDSU Department</u> of Mathematics, in	<u>Gerardus</u> <u>Mercator</u>	Université Catholique de	1532	2			
association with the <u>American</u> Mathematical	<u>Johannes</u> <u>Stadius</u>	Université Catholique de Louvain		2			
<u>Society</u> .	<u>Andreas</u> Vesalius	Università degli Studi di Padova and Université Catholique de Louvain	1537	105089			
According to our current on-line database, Gemma Frisius has 4 <u>students</u> and 105096 <u>descendants</u> . We welcome any additional information.							

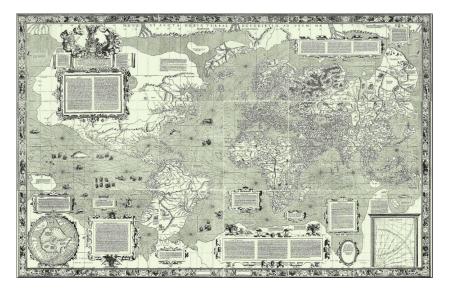
T. M. Murali

January 18 and 20, 2022

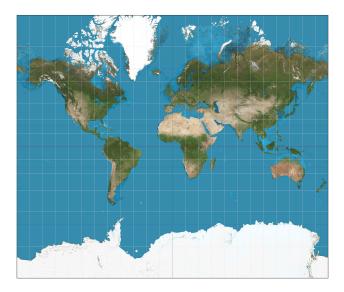
Gerardus Mercator



Gerardus Mercator



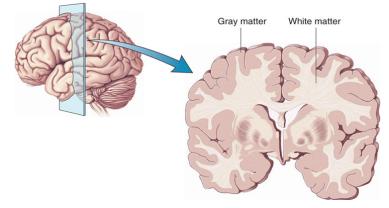
Gerardus Mercator



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

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

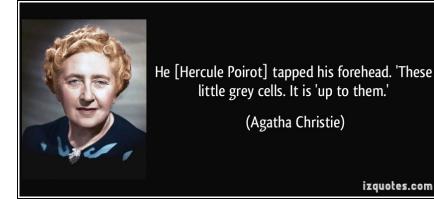
Grey matter Generic term for "stuff" that appears grey in a freshly dissected brain.



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

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.



Structure to Function

• Broca's area (1861): production of speech and language



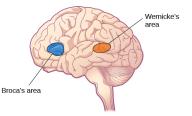
Structure to Function

• Broca's area (1861): production of speech and language



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)

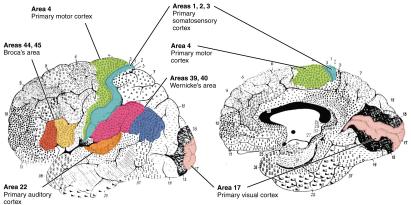
Based on the cytoarchitectural organization of neurons Brodmann observed in the cerebral cortex using Nissl staining.





Brodmann Areas (1909)

Based on the cytoarchitectural organization of neurons Brodmann observed in the cerebral cortex using Nissl staining.



Brodmann's cytotechtonic map (1909): Lateral surface Brodmann's cytotechtonic map (1909): Medial surface

Left and Right Brains (1960s)

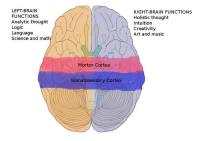
- If the two hemispheres of the brain are separated by severing the corpus callosum,
 - information transfer between the hemispheres ceases,
 - an individual has two functionally different brains.





Left and Right Brains (1960s)

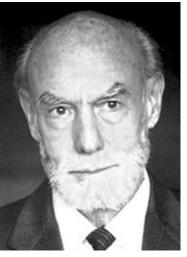
- If the two hemispheres of the brain are separated by severing the corpus callosum,
 - information transfer between the hemispheres ceases,
 - an individual has two functionally different brains.
- Left hemisphere: speech, language, arithmetic, analysis.
- Right hemisphere: spatial comprehension, facial recognition, emotion.



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.
- Left hemisphere: speech, language, arithmetic, analysis.
- Right hemisphere: spatial comprehension, facial recognition, emotion.
- 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."



The New York Times Magazine/September 9,1973

Two astonishingly different persons inhabit our heads

We are left-brained or right-brained

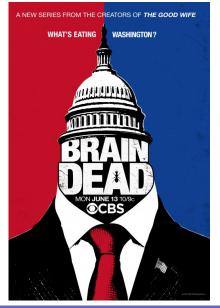
By Maya Pines

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 disciblines are enioving such a vozue. Some reample, those concerned with vision—to find their way through a tangle of other nerver 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 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



T. M. Murali

January 18 and 20, 2022

Computing the Brain



Are You More Right-Brained Or Left-Brained?

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





justtransparentthings.tumblr.com

Check off all that apply:

1. You're better with faces than names.



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

< 0

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 Harvell, 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

Rights & Permissions



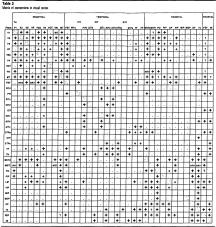
Researchers have divided the brain into discrete areas based on structure and function.

(Video, 2")

T. M. Murali

Computing the Brain

Brain Structure to Graphs



This diff is a concretify resist for intramentorie kenners induce strained areas in the respect, factor and new strained areas in the respect, factor and new strained areas in the respect, factor and new strained areas in the respective strained areas in the respective strained areas are the respective strained areas are the respective strained areas are respectively in the respective strained areas areas

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

T. M. Murali

January 18 and 20, 2022

Brain Structure to Graphs

Neuroinformatics

June 2004, Volume 2, <u>Issue 2</u>, 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:<u>10.1385/NI:2:2:145</u>

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

The small world of the cerebral cortex, Olaf Sporns, Jonathan D. Zwi, Neuroinformatics, 2: 145-162, 2004.

T. M. Murali

January 18 and 20, 2022

Computing the Brain

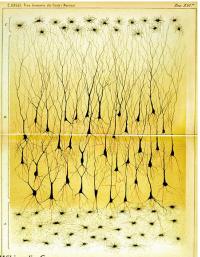
Cell theory: Cell is the fundamental unit of all living organisms (Video, 1:40")

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

- Brain is an exception: complex cell shapes, extensive branching, and dense packing.
- How many neurons in the brain?

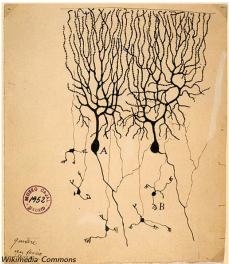
- Brain is an exception: complex cell shapes, extensive branching, and dense packing.
- How many neurons in the brain? 100 billion and many more glial cells.

- 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.



Wikimedia Commons

- 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.



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.

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.

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

Neuron doctrine Nerve cells are discrete entities that communicate by specialised contacts (Cajal and Sherrington)

Reticular Theory vs. Neuron Doctrine

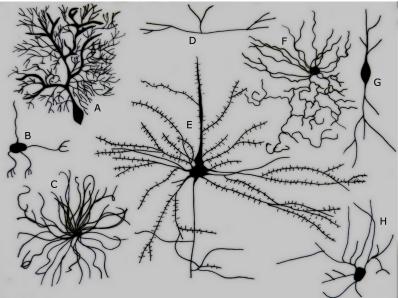
- "Neuron" coined by Waldeyer in 1891.
- In 1896, Rudolph Albert von Kolliker coined the term "axon" to describe the long slender cables that transmit signals away from cell bodies.
- In 1889, William His used "dendrites" to name the thin branching fibers that ferry signals toward the cell body.

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

Neuron doctrine Nerve cells are discrete entities that communicate by specialised contacts (Cajal and Sherrington)

• 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")

T. M. Murali

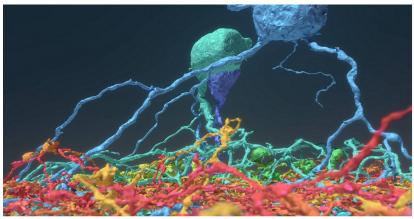
Types of Neurons

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

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



Princeton researchers crowdsource brain mapping with gamers, discover six new neuron types By turning a time-intensive research problem into an intenactive game. Princeton neuroscientist Sebastian Soung has built an unprecedented data set of neurons, which he is now turning over to the public via the Eyewire Naseum. These J' retain a leuros, mapped by Eyewire gamers, include ganglion, edit types in blue and green and amacrine cells in yellow and red.

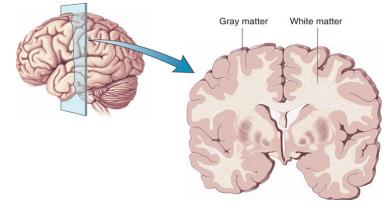
Liz Fuller-Wright, Office of Communications

May 17, 2018 11 a.m.

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

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

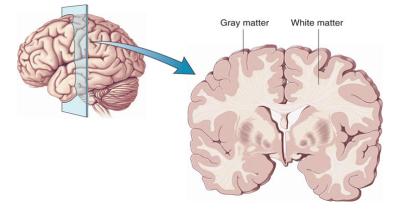
Grey matter Generic term for "stuff" that appears grey in a freshly dissected brain.



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

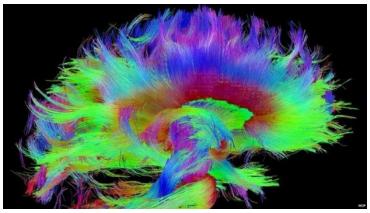
White matter Generic term for <u>"stuff"</u> a collection of axons, which appear white in freshly dissected brain.

Grey matter Generic term for <u>"stuff"</u> 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.

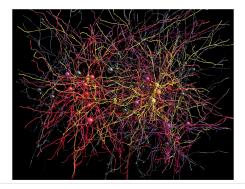


Research on largest network of cortical neurons to date published in Nature

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

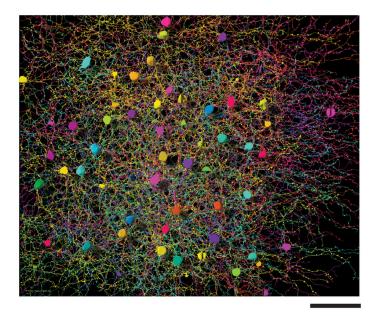
March 28, 2016 | Download PDF

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-Electronic 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 rucial elements of how networks in the brain are organized. The results are published this week in the journal *Netwe*.

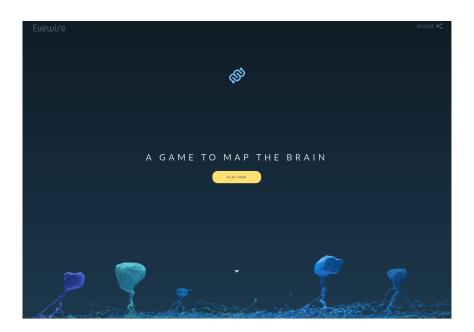


Anatomy and function of an excitatory network in the visual cortex, Lee et al., Nature, 532:370–374, 2016.

◆□▶ ◆□▶ ◆三▶ ◆三▶ 三 のへで



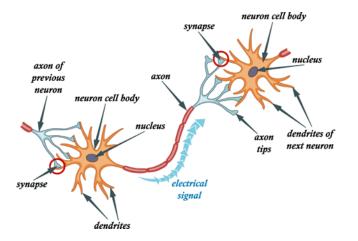
Space-time wiring specificity supports direction selectivity in the retina, Kim et al., Nature, 509:331-336, 2014.



Space-time wiring specificity supports direction selectivity in the retina, Kim et al., Nature, 509:331-336, 2014.

◆□▶ ◆□▶ ◆三▶ ◆三▶ ○□ ● ● ●

Cellular Communication: Neuron Firing



Neuron, YouTube, 11:20"

www.jasonshen.com

Course Structure

Otto Loewi (1873–1961)

- Galvani showed that electric stimulation of sciatic nerve causes muscles in frog legs to twitch (1780).
- How do nerves communicate with muscles: electricity or chemicals?



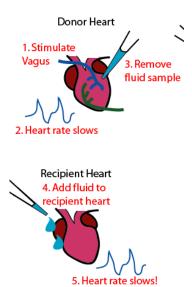
Otto Loewi (1873–1961)

- Galvani showed that electric stimulation of sciatic nerve causes muscles in frog legs to twitch (1780).
- How do nerves communicate with muscles: electricity or chemicals?
- Loewi settled this question through his discovery of *vagusstoff* (1921).



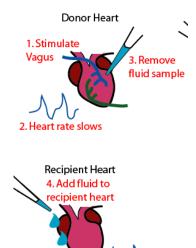
Otto Loewi (1873-1961)

- Galvani showed that electric stimulation of sciatic nerve causes muscles in frog legs to twitch (1780).
- How do nerves communicate with muscles: electricity or chemicals?
- Loewi settled this question through his discovery of *vagusstoff* (1921).

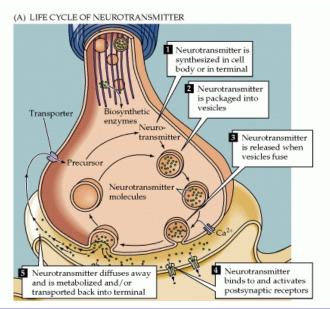


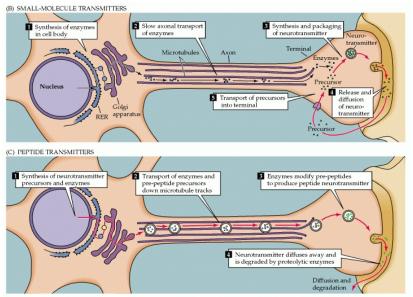
Otto Loewi (1873-1961)

- Galvani showed that electric stimulation of sciatic nerve causes muscles in frog legs to twitch (1780).
- How do nerves communicate with muscles: electricity or chemicals?
- Loewi settled this question through his discovery of *vagusstoff* (1921).
- 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.



Heart rate slows!





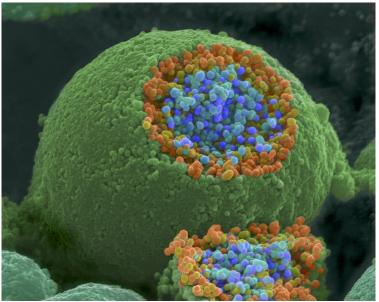


TABLE 47-1

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).
- Lost her job due to laws barring Jews (1938).
- Secret lab in bedroom to study nerve growth in chicken embryos (WWII).



Rita Levi-Montalcini (1909–2012)

- M.D. at University of Turin (1936).
- Lost her job due to laws barring Jews (1938).
- Secret lab in bedroom to study nerve growth in chicken embryos (WWII).
- Received one-semester research fellowship at WUSTL (1946).
- Isolated nerve growth factor (NGF) by observing that cancerous tissues caused extremely rapid growth of nerve cells in chicken embryos (1952). *First growth factor discovered.*



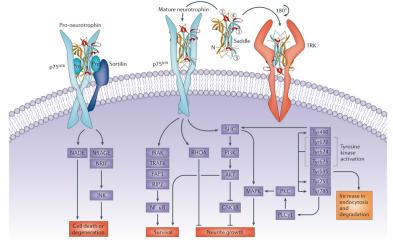
Rita Levi-Montalcini (1909–2012)

- M.D. at University of Turin (1936).
- Lost her job due to laws barring Jews (1938).
- Secret lab in bedroom to study nerve growth in chicken embryos (WWII).
- Received one-semester research fellowship at WUSTL (1946).
- Isolated nerve growth factor (NGF) by observing that cancerous tissues caused extremely rapid growth of nerve cells in chicken embryos (1952). *First growth factor discovered.*
- Received Nobel prize (with Stanley Cohen, 1986).



Neurotrophins

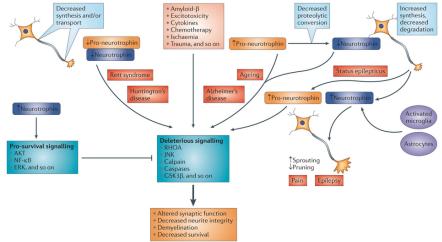
Family of proteins that induce the survival, development, and function of neurons.



Nature Reviews | Drug Discovery

Neurotrophins

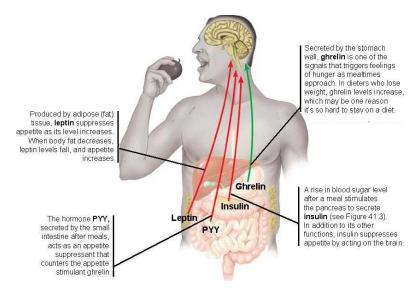
Changes in neurotrophin levels or in the ratio of pro-neurotrophin to mature neurotrophin can cause and/or contribute to numerous diseases.



Nature Reviews | Drug Discovery

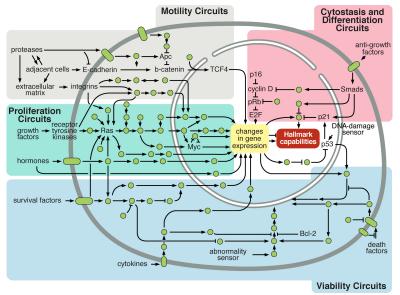
Computing the Brain

Cellular Communication: Hunger Response



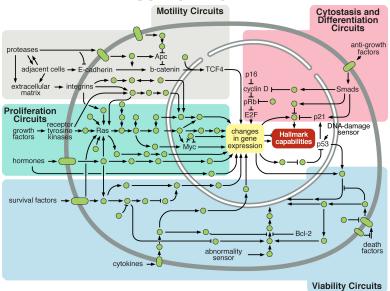
www.barbellmedicine.com

Cellular Response to External Signals

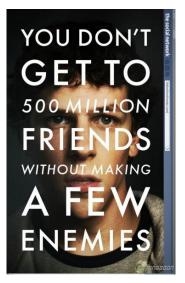


Hanahan and Wienberg. Hallmarks of cancer: the next generation. Cell, 2011.

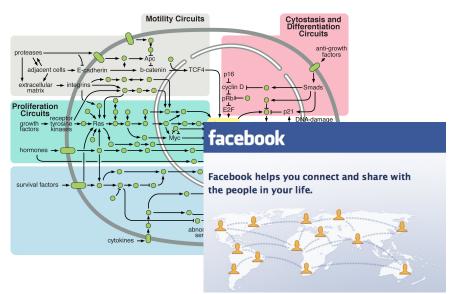
A Cell is Like



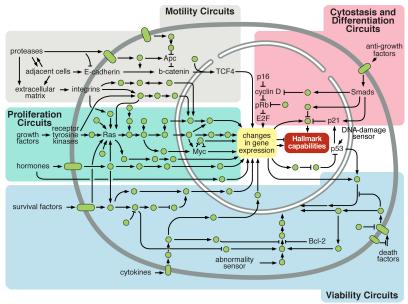
A Cell is Like



A Cell is Like facebook



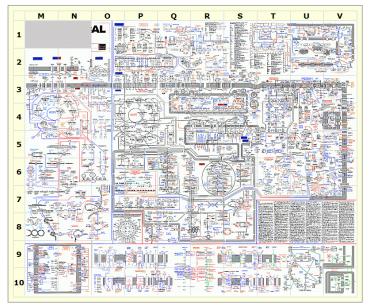
Network is Complex



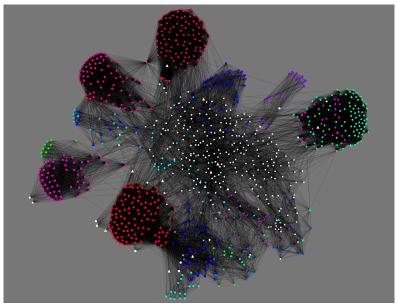
T. M. Murali

Computing the Brain

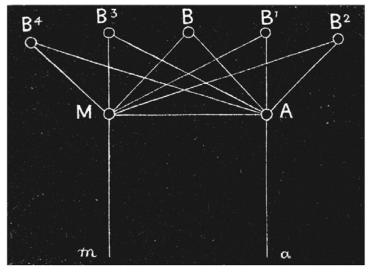
Network is Complex



Network is Complex but Very Poorly Understood



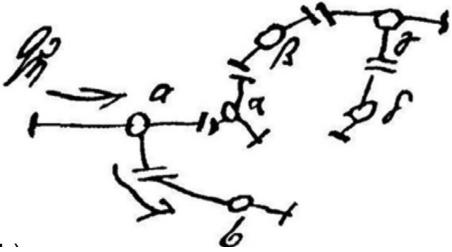
Early Brain Graphs



Large-scale human network for language (Lichtheim, 1885)

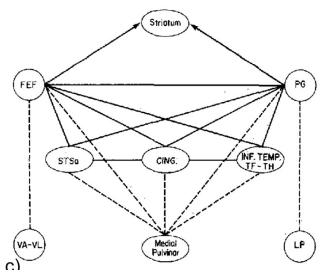
۱

Early Brain Graphs

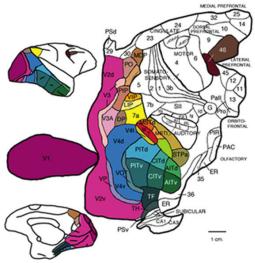


Neuronal network for psychoanalysis (Freud, 1891, 1895)

Early Brain Graphs



Hub-and-spoke model of spatial attention (Mesulam, 1990)

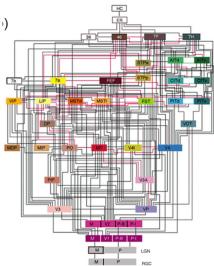


Macaque visual cortex (Felleman and van Essen, 1991)

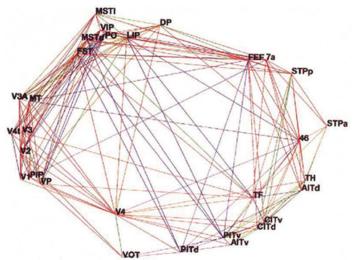
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Table Matria		orre	ancit	in v	istal	œn	n																												
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $										Γ														Γ	m	rnow: a										
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Fran					120		vol	ve		FRE	en la			• a1												1 PO	89			-	825		74		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	1	20	1+	+	T.	1+	+			+			Г		Τ.	Τ	T.	Τ.	Τ.	Τ.	Τ	Ť.	Ť.	Τ.	1.	1,	+	+	١.	١.	Γ.	Γ.				Τ.
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	112	-	12	+	+	+	+	+	+	+	+		Г		1.	Γ	١.	1.	1.	1.	Г	t	1.	1.	+	+	+	+	1	+	1.	Γ.		1.	2	1.
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	1 11	Ð	•	100		+	+		+	+	+						Γ.	Γ.	Ŀ	1.	Γ	Τ.	+	1	+		+	+	+	+					?	Γ.
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	199	Ŀ	+	+	Ð	+	+	+		+	+						1.		1.			Ŀ	+		+		+	+		+					?	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	124	Ŀ			+	Ľ.	+			+	+	1.							ŀ		Г	Γ.	1.		+	÷	÷								?	1
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	74	Ŀ	+	+	+	+	1		+	+	+	+		+	+		+	1.	+		1		+	+				+	+	.			+		7	+
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	101	Ŀ	+	1.	+		+	12		1		+		+																					1	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Ve	+			Ŀ	1		1	£												L	L					+		_				L		1	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	MT	+			+			1_					1	<u>.</u>	1.			·				<u>.</u>					2	+					Ŀ		+	2
m m	FUT	Ŀ	101	+	AL.	+		⊢	+	+	4	1	+			1		ŀ		+		L	+		+	+			+	+				+	+	ŀ
Matrix And	PITE	Ŀ	1.	ŀ	Ŀ	Ŀ	+	L	_	Ŀ	_				⊢	⊢	+	+	+		1	⊢	⊢	L										· .	⊢	1
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	1	L	+	-	_	1	-	-	-	1	+		1.7		1	_	⊢		1	-	-		-	_	+	_			_			-	-	ļ	+	+
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	1	Ŀ	÷		ŀ	Ŀ		L_	-	ŀ	_	L	-		1	-	Į+			-	-	1	1	_					-			-	-		ļ	1
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Ŀ	÷		ŀ	Ŀ	+		-	ŀ		_		+	1	L	1	+	+	-		1	_	-								L			_	-
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		1	+	-	1	L_	-	_	_	L_	_	L	_	-	1		1.	-	⊢		⊢	-	_	_						_		L	-	_	+	+
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Ŀ	·	· ·	ŀ	Ŀ	+	-					_		1	_	÷	+	+	ļ	1			_									-		_	ļ
$ \mathbf{m}_{1} \mathbf{m}_{2} \mathbf{m}_{$		ŀ		÷	÷	ŀ	÷	-	_			-	_		_	_			1	-	⊢	+	L	_	-							-	-	+	+	+
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		ŀ	ŀ	÷.	÷	ŀ	+	-	_	· ·			-	+	-	L.	+	-		-	+	+÷							-		· ·	-	-	_	-	-
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	1	ŀ	ŀ	÷	÷	ŀ.	Ŀ	L		· ·	+			_	-	+	-	ŀ	-	Ľ.,	<u> </u>	+	+	+	+	+			4			1	L		÷	+
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		-	+	-	_	-	-	-	_	-	_		-		-	-	-		-		-	+-		-	-		_	-	-	-			-	+	-	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		ŀ-	÷	÷	÷	÷			-	÷		-	-		+				÷		-	<u> </u>	+	+		-	-	-			÷				-	++
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		÷	÷	+	+	÷	÷.	-	-	-	+	-	-		-	+	۰				-		-		+	-		-	-	•	1	-	-			+
Import Import<		ŀ	÷	÷	÷	÷	+		-	÷			-	+	-	+	-	+	+		-	+			÷	÷		-	÷	÷	r i l	1	-		+	+
N N				7	Ŧ		·						Ξ		÷	-	÷	+·	ŀ		-	+	-	-	- 1	-		-	-			-			+	
M M B			T	÷		-		-	ART		-	-	-	÷	÷	-		÷	÷	7	-	-		-		4	T				-	-			7	H
Image: Constraint of the state of			-	-					-		÷	÷	-	-	÷	-	÷	-		÷	-	+÷	÷.	-	-+	-1		20	-	-	-	-			Ċ.	c l
W S		÷	-			4		-			+	-	-	÷				÷		-	-	1 ·		-	+	4		-	10		-	-			+	+
10		÷	-			-	*	-	-			÷	-	-	÷	-	÷	÷	÷	-	-		-	-				+	÷	÷	-	-			+	÷
Image: Section 1 Image: Section 2 Image: Section 2<		ŕ	-	Ľ			-	-	-		÷	-		-	÷	-	÷	Ľ.	÷		-	-		-	-	-		-	÷	-	-	-			÷	
0 . <td></td> <td>÷</td> <td>+÷</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> <td>÷</td> <td></td> <td>-</td> <td>-</td> <td>-</td> <td>÷</td> <td>L.</td> <td>÷</td> <td></td> <td>-</td> <td></td> <td></td> <td>-</td> <td>÷</td> <td>-</td> <td></td> <td>-+</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> <td></td> <td>-</td> <td></td>		÷	+÷	-	-	-	-	-	-	-	-	÷		-	-	-	÷	L.	÷		-			-	÷	-		-+	-	-	-	-	-		-	
n . <td></td> <td>÷</td> <td>Ľ.</td> <td>÷.</td> <td>÷</td> <td>+</td> <td>+</td> <td>-1</td> <td></td> <td></td> <td>÷</td> <td>÷</td> <td></td> <td>÷.</td> <td>í.</td> <td>- 1</td> <td>ń</td> <td>÷.</td> <td>÷.</td> <td></td> <td>-</td> <td></td> <td></td> <td></td> <td>+</td> <td>÷</td> <td></td> <td>÷İ</td> <td>+İ</td> <td></td> <td>-†</td> <td>-</td> <td></td> <td></td> <td>-</td> <td>÷</td>		÷	Ľ.	÷.	÷	+	+	-1			÷	÷		÷.	í.	- 1	ń	÷.	÷.		-				+	÷		÷İ	+İ		-†	-			-	÷
re		÷		÷.	÷.	÷	-	-		÷	÷	-		- 1			÷		ŕ	Ť.	+	t i	÷	+							-f	-	+	74		÷
		ŕ.	÷.	-	-	-	÷	-		1	÷İ	÷	-	÷	Ť	+	ń			+	ŕ	-	Ť	÷						ŧ.	+			+	Ċ,	÷
		÷				-1	-	-	-	-	÷	-	-		-	÷	-	÷	-	÷		+	+	+	÷	÷	1	+	÷	÷	-+	+		+	ᆉ	÷

This stift is a concepting result for increasing the energy of the start of the company of the start of the s

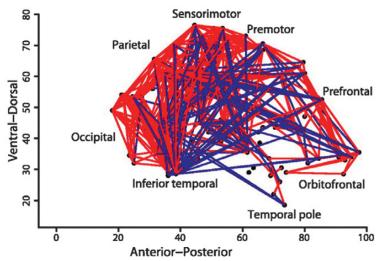
Tract-tracing in the macaque visual cortex (Felleman and van Essen, 1991)



Wiring diagram of macaque connectome (Felleman and van Essen, 1991)

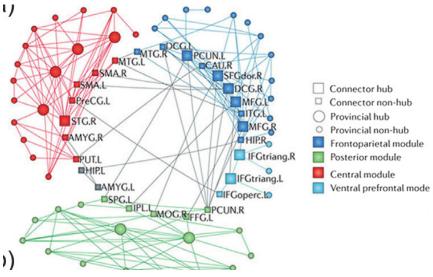


Topological representation of macaque connectome (Young, 1992)

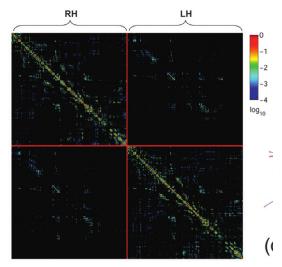


Functional connectivity network from functional MRI data

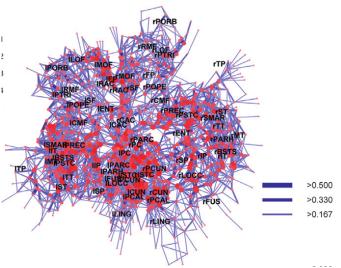




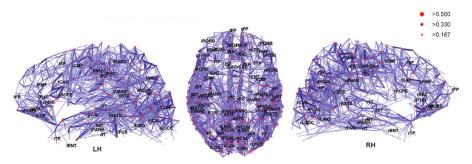
Modular organisation of network



Connectivity network from diffusion MRI data



Toplogical layout of network



Anatomical layout of network