CN510: Principles and Methods of Cognitive and Neural Modeling

Logistics

Lecture 1 Part 1

Instructor: Anatoli Gorchetchnikov <anatoli@bu.edu>
Readings

Required texts:

Recommended texts:
Other supplemental texts:

Arbib MA (ed.) (1995). The Handbook of Brain Theory and Neural Networks. Referred to as HBT.


Grading

In-class final exam: 30%
Homework (at least 11 assignments) and lab: 70%

All homework assignments are weighted equally. Please see me during office hours if you have questions/problems

Homework has to be computer generated: LaTeX, MS Word, Open Office; there will be a penalty for handwritten pages

All homework should be handed in at the start of class on the due date!

Late homework policy: –10% for each week late, up to –30% (see syllabus for details). No late homework accepted after the final exam

Participation in class discussions will play a role in determining the final grade in borderline cases
Class Readings

All required and some supplemental readings that are not in the D&A book are downloadable from the CN510 web page: http://cns-classes.bu.edu/cn510

Readings should be read before the corresponding lecture
Building Security

A properly coded BU ID is needed to enter the building via the card reader; please provide me your name and BU ID number.

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CN510: Principles and Methods of Cognitive and Neural Modeling

Introduction to Brain Anatomy and Function, Experimental Techniques and Brain Theories

Lecture 1 Part 2

Instructor: Anatoli Gorchetchnikov <anatoli@bu.edu>
Orientation

- Dorsal (superior)
- Caudal (posterior)
- Ventral (inferior)

- Rostral (anterior)
- Caudal (posterior)

- Lateral
- Medial
- Lateral

- Horizontal plane (axial plane)
- Coronal plane
- Sagittal plane
Components of the Central Nervous System

The central nervous system (CNS) can be broken into 7 main parts:
- Spinal cord
- Medulla
- Pons
- Cerebellum
- Midbrain
- Diencephalon (includes thalamus and hypothalamus)
- Cerebrum (includes cerebral cortex, basal ganglia, hippocampus, and amygdala)

The medulla, pons, and midbrain are often considered together as the brain stem. Others distinguish midbrain from brainstem (pons and medulla).

Figure 1-2A The central nervous system can be divided into seven main parts.
Functionality of CNS Components

Roughly speaking:

– The spinal cord transmits sensory inputs from skin, joints, and muscles to higher levels of the CNS

– The spinal cord also conveys motor commands from higher CNS levels to the muscles of the trunk and limbs
Functionality of CNS Components

Roughly speaking:

- The brain stem includes several nuclei (distinct neuron populations) involved with tasks such as:
  - somatic sensation and motor control of the head and face (cranial nerve nuclei),
  - audition (cochlear nuclei, superior olivary complex),
  - regulating arousal (reticular formation),
  - autonomous functions such as digestion, breathing, and heart rate (medulla), and
  - relaying information between the cerebrum and the cerebellum (pons).
Functionality of CNS Components

The midbrain includes areas for identifying target locations and orienting the head and eyes based on visual cues (superior colliculus) and auditory cues (inferior colliculus). The inferior colliculus also passes auditory information to the cortex via the thalamus.

The cerebellum is very important for coordinated movement and aspects of timing.

Most of the sensory and motor information to and from the cerebral cortex passes through the thalamus.

The hypothalamus regulates autonomic, endocrine, and visceral functions.
Functionality of CNS Components

The basal ganglia are involved in action selection and sequencing.

The amygdala is involved in emotional states and reinforcement learning.

The hippocampus is involved in episodic memory formation and the representation of space (e.g., “place” cells) and context.

The cerebral cortex (or neocortex) is involved in the highest levels of cognition, sensation, and behavior.

Remember, these are just basic guidelines, the real life is always more complicated.
Roughly speaking:

- **Occipital lobe** is concerned with early vision
- **Temporal lobe** is concerned with hearing, speech perception, and object recognition
- **Parietal lobe** is concerned with representation of the body and external spaces
- **Frontal lobe** is concerned with movement control and high-level cognitive tasks (e.g., grammatical processing, action planning)
Structural and Functional Asymmetries

The brain is largely, though not entirely, symmetric. Structural asymmetries include the larger speech and language areas in the left temporal lobe (Martin, p. 218):

Functional asymmetries are also found, particularly in cortex.
Sulci and Gyri

A sulcus or fissure is a groove in the brain.
A gyrus is a convolution (bump) in the brain.
What is the reason for convoluted structure of the brain?
The most prominent sulci and gyri are found in almost all human brains in approximately same positions and serve as a means for separating the cortex into different regions (cortical parcellation).
The parcellation system used by the Center for Morphometric Analysis at Massachusetts General Hospital is schematized at right.
Staining Techniques: Weigert Method

Introduced by Carl Weigert in 1882
Stain binds to myelin on axons
Connectivity Tracing

A NETWORK CABLE IS UNPLUGGED
Staining Techniques: Nissl Method

Proposed by Franz Nissl in 1894
Uses common agents such as thionin, cresyl violet, or neutral red
Stains “Nissl bodies” (rough endoplasmic reticulum) in cell bodies
Staining Techniques: Golgi Method

Discovered by Italian physician and scientist Camillo Golgi (1843-1926) in 1873

Staining is achieved by impregnating fixed nervous tissue with potassium dichromate and silver nitrate

Cells thus stained are filled by microcrystallization of silver chromate
The Six Layers of Neocortex

Cortical sheet contains six layers of cells
Different staining techniques can be used to highlight different aspects of this organization

**Figure 17-6** The neurons of the cerebral cortex are arranged in distinctive layers. The appearance of the cortex depends on what is used to stain it. The Golgi stain reveals neuronal cell bodies and dendritic trees. The Nissl method shows cell bodies and proximal dendrites. A Weigert stain for myelinated fibers reveals the pattern of axonal distribution. (From Heimer 1994.)
Roughly speaking:

• Layer I (molecular layer) – mostly dendrites and axons of cells in deeper layers
• Layer II (external granule layer) – comprised largely of granule cells
• Layer III (external pyramidal layer) – variety of cell types, including pyramidal neurons that project mainly to targets in other parts of cortex
• Layer IV (internal granule layer) – like layer II, composed primarily of granule cells. Typically receives inputs from layer III in other parts of cortex
• Layer V (internal pyramidal layer) – contains mainly pyramidal cells that are typically larger than those in layer III and often project to subcortical targets or to layers I/II or VI of “lower-level” parts of cortex
• Layer VI (polymorphic or multiform area) – mix of different cell types and white matter
Cytoarchitectonic Differences

Different parts of the cortex have different distributions of the layers.

For example, the primary motor cortex includes lots of very large “output” cells in layers III and V, whereas the primary visual cortex includes lots of “input” cells in layer IV.

This type of difference was used by Brodmann in his parcellation scheme.
Brodmann’s Cytoarchitectonic Parcellation

A brain parcellation proposed by the German anatomist Brodmann in the early 20th century

Brodmann divided the cortex into 52 regions

Divisions were based on differences in cell types and characteristic arrangements of cell layers

Cytoarchitecture – the cellular makeup of a body tissue or structure

*Figure 1-5* In the early part of the twentieth century Korbinian Brodmann divided the human cerebral cortex into 52 discrete areas on the basis of distinctive nerve cell structures and characteristic arrangements of cell layers. Brodmann’s scheme of the cortex is still widely used today and is continually updated. In this drawing each area is represented by its own symbol and is assigned a unique number. Several areas defined by Brodmann have been found to control specific brain functions. For instance, area 4, the motor cortex, is responsible for voluntary movement. Areas 1, 2, and 3 comprise the primary somatosensory cortex, which receives information on bodily sensation. Area 17 is the primary visual cortex, which receives signals from the eyes and relays them to other areas for further deciphering. Areas 41 and 42 comprise the primary auditory cortex. Areas not visible from the outer surface of the cortex are not shown in this drawing.
Brodmann’s areas correlate only crudely with the locations of the sulci and gyri, and this correlation varies from brain to brain:

Duvernoy et al. (1999):
Connectivity Tracing

Techniques for identifying axonal tracts (i.e., connections between brain regions):

Tracer techniques
- Anterograde tracers travel from the cell body down the axon
- Retrograde tracers (e.g. horseradish peroxidase) travel up the axon toward the cell body
- Must be used in living animal or very shortly post-mortem

Diffusion-weighted (DW) or diffusion tensor (DT) MRI
- Can identify axonal fiber tracts by analyzing directions of water diffusion in vivo
- Not as accurate as tracer techniques
Degeneration Patterns

When a nerve fiber is severed, myelin from the “downstream” portion of the axon breaks apart and can be detected with stains.

Neurons deprived of input from a severed nerve may degenerate (anterograde degeneration).

Neurons with major projections to a dead area may also degenerate (retrograde degeneration).
Anatomical Magnetic Resonance Imaging (MRI)

Sometimes called structural MRI to distinguish from functional MRI
Resolution of approximately 1mm
Uses a powerful magnetic field to align the nuclear magnetization of (usually) hydrogen atoms in water in the body
Radio frequency (RF) fields are used to systematically alter the alignment of this magnetization, causing the hydrogen nuclei to produce a rotating magnetic field detectable by the scanner

A sample structural MRI image:
Neurophysiological Techniques

Techniques for studying human brain activations:
Direct measurement of electrical activity, or direct stimulation of neurons
  – In animals: plenty of studies (e.g. Mike Hasselmo, Howard Eichenbaum here at BU)
  – In humans: usually prior to open brain surgery in severe epileptics (e.g., Penfield in 1950’s, Ojemann more recently, Mike Kahana)

Very high spatial and temporal resolution

Techniques that measure cerebral blood flow non-invasively
  – Functional Magnetic Resonance Imaging (fMRI)
  – Positron Emission Tomography (PET)

Spatial resolution is OK (fMRI: ~5mm “cubes”, or voxels) but low temporal resolution
Sample fMRI image of brain activations in auditory cortical areas while listening to vowel sounds:

From Guenther, Nieto-Castanon, Tourville, and Ghosh (2002)
Evoked potential, or event-related potential (ERP), techniques
  – Electroencephalography (EEG)
  – Magnetoencephalography (MEG)

High temporal resolution, low spatial resolution, measure combined effects of large numbers of neurons

Transcranial Magnetic Stimulation (TMS)
  – In single pulse TMS, a very brief and focused magnetic field transiently interrupts the functioning of a small patch of cortex (about 1-10 cubic cm)

Very high temporal resolution for single-pulse TMS but not repetitive TMS
  – High-frequency repetitive TMS can sometimes induce seizures but is used experimentally, e.g. for treating severe cases of depression
Optical imaging
- A near-infrared laser is positioned on the scalp
- Detectors composed of optical fiber bundles are located a few centimeters away from the light source
- These detectors sense how the path of light is altered, either through absorption or scattering, as it traverses brain tissue
- Much higher resolution is possible when brain is exposed (in animals)
Psychophysical Techniques

In addition to measuring brain activations directly, we can measure the function of the brain by measuring perceptual or motor abilities.

A large number of computer-based apparati have been developed for measuring movements or perceptual abilities.

Examples include:

- Eye and head trackers
- Transducer-based movement trackers
- Computer-based audio and visual stimulus presentation
Sample video from a “McGurk Effect” psychophysical experiment

Visually presented “gi”
Auditorily presented “bi”
Subject reports what consonant he/she heard
Subjects usually report hearing neither “bi” nor “gi”; instead, they perceptually fuse the two into “di”

For more info on the McGurk effect:
Another example of psychophysics: study of visual illusions

What does this example tell us about the visual system?
What experiments should be run using these tools?

Two primary sources of new experiments:

Variations or extensions of previous experiments
  – There are always unanswered questions at the end of each study
  – Can forget the forest behind the trees

Tests of (some aspect of) a theory or model
  – A good theory should provide testable predictions
  – Hard to verify testability without familiarity with experimental techniques
Theories of Brain Function

Concerned here with (often vague) theories of overall function, as compared to the more detailed models encountered elsewhere in the course.

Some popular views between the late 18th century and early 20th century:

– Phrenology
– Aggregate-Field Theory
– Neuron Doctrine
– Cellular Connectionism
Phrenology

In the late 18th century, the German physician Gall made some radical (at the time) claims:

- The brain is the basis of all behavior
- The cerebral cortex does not act as one organ, but as a collection of specialized regions
- Each region corresponds to a different mental faculty (35 or more in Gall’s scheme)
- Brain regions grow with use, as evidenced by bulges on the skull

Although phrenology has since been discredited, the first two (or even three and a half) of these ideas are accepted by the vast majority of modern neuroscientists
Phrenology

The main problem with phrenology:

- Gall believed that bumps and ridges on the skull reflected growth of the underlying brain structures with use
- To determine the function of a brain region, he correlated the size of the bumps in that region with a person’s personality traits
- Proper experimental approach based on wrong assumption led to Gall’s “map” of the brain being very wrong
Aggregate-Field Theory

French physiologist Flourens removed specific brain areas of experimental animals to try to isolate Gall’s cerebral “organs”

From these experiments, he concluded that, rather than acting as a collection of specialized organs, the entire cortex was involved in every mental action

Flourens (1823): “All perceptions, all volitions occupy the same seat in these (cerebral) organs; the faculty of perceiving, of conceiving, of willing merely constitutes therefore a faculty which is essentially one.”

This is essentially the opposite of phrenology

Experimental technique he used is still widely used and often with different results. Why?
Neuron Doctrine

The neuron doctrine is the principle that individual neurons are the elementary signaling elements of the nervous system.

In late 1800’s, Santiago Ramon y Cajal used the staining technique developed by Camillo Golgi to reveal the structure of individual neurons.

Neuron doctrine was proposed by Heinrich Wilhelm Gottfried von Waldeyer-Hartz in 1891.

Prior to this, the brain was widely believed to be a gland whose secretions were distributed throughout the body via nerves (fitting in well with aggregate-field theory).

Updated through more than a century of research it still is a basis of our view on the brain.
Some Ramon y Cajal diagrams:

**Golgi Stain**

**Silver Nitrate Stain**

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**Fig. 6.** — Cellule de Purkinje; homme adulte.
Méthode de Golgi.

a, cylindre-axe; — b, collatérale récurrente; — c, cavités destinées aux capillaires; — d, vides occupés par les cellules à corbeilles.

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**Fig. 342.** — Cellules nerveuses de la couche des petites pyramidales; cerveau humain.
Méthode du nitrate d’argent réduit (formule 1, sans fixation préalable).

A, cellule pyramidale moyenne; — B, G, petites cellules pyramidales; — C, noyau; — a, nucléoles;
b, région cellulaire où les neurofibrilles s’imprègnent avec difficulté.
Cellular Connectionism

An elaboration of the neuron doctrine
Aggregate field theory was contradicted by studies showing a specialization of the left hemisphere, in particular the left frontal lobe and superior temporal gyrus, in speech and language (Broca, Wernicke)
Scientists such as Wernicke, Sherrington, and Ramon y Cajal suggested that:
  – individual neurons are the signaling units of the brain,
  – neurons are generally arranged in functional groups connected to each other in a precise fashion
This view is known as cellular connectionism
The Current Prevailing View

Most neuroscientists agree on the following:

– The neuron is the basic signaling unit in the brain
– Different parts of the brain have different functional roles (e.g. auditory cortex, visual cortex, motor cortex, etc.)
– The different brain regions project to each other in a fairly precise fashion that is affected by experience
– A given brain region has roughly the same role across individuals
– Damage to one part of the brain may lead to long-term reorganization such that another region takes over the functionality of the damaged region, but there are limits to this type of adaptation
– Most non-trivial tasks involve several different brain regions interacting in a task-specific network
An Editorial Message

Our overall view of brain function has swayed one way, then another way, then back in the original direction, etc., finally settling somewhere in between.

In the early stages of a science, ideas are often stated in absolute or dogmatic forms that do not hold up to scrutiny; e.g., phrenology and aggregate-field theory.

Even though they are eventually replaced with more sophisticated views, these absolute forms are often an important stepping stone toward understanding complicated systems such as the brain.

There still no comprehensive theory of brain function.

In other words we are far from done!
“Would we lie to you?”

Not much in neuroscience (especially cognitive neuroscience) can be considered an irrefutable fact.

Unfortunately, this is not always obvious when reading articles or listening to lectures.

Another major objective of this class: help you develop a healthy cynicism toward cognitive neuroscience research: Read critically, but try to extract “grains of truth” wherever possible.
Next Time

The goals of computational neuroscience, general approaches to modeling of the nervous systems, and various scales the models can concentrate on.

Several example neural models, each defined at a different grain of analysis will be briefly presented.

We will also discuss an idea of multiscale modeling, its advantages, and related issues.

Readings: