BI 358 Lecture 2

I. **Announcements**  
Douglas Bovee, MD, Addiction & Internal Medicine Specialist next session! **NB**: Sign-in + e-feedback < 24-48 hr. Quiz 1 + Outline due next Tues. Q? Great drug overview for Quiz. U Utah Addiction website!  
http://learn.genetics.utah.edu/content/addiction/mouse/  
Common linking mechanisms: COME Cocaine & Meth HEMA Heroine & Marijuana, LSD & Ecstasy (S? Serotonin!)

II. **Homeostasis Connections**  
Model, BP e.g. Q? Gain? G&H p 8

III. **Addiction Medicine: Homeostasis & Overdose Story!**  
G&H ch 59 pp 751-61…Additional Information as Review? →

IV. **Organization of the Nervous System**  
G&H ch 46 pp 582-7, LS1/2 ch 5  
A. Central vs peripheral, computer analogy fig 46-4  
B. Neurons, neuronal classes, neuroglia, connections

V. **Autonomic Nervous System**  
G&H ch 61 pp 773-85 + LS +…  
A. Sympathetic vs. parasympathetic fig 61-1,61-3  
B. Neurotransmitters, receptors, actions tab 61-2, 61-1  
C. Nicotine & adrenal hormonal disruption

Come see us during office hr! Dr. Bovee next session, Tuesday! No more Pat 'til Thursday! Hooray!
### BI 358 Office Hr Winter 2018

<table>
<thead>
<tr>
<th>Day &amp; Time</th>
<th>Instructor</th>
<th>Place</th>
<th>e-mail</th>
</tr>
</thead>
<tbody>
<tr>
<td>M 11 am-12n</td>
<td>Pat†</td>
<td>65A Klamath</td>
<td>lombardi</td>
</tr>
<tr>
<td>R 10-11 am</td>
<td>Pat†</td>
<td>65A Klamath</td>
<td>lombardi</td>
</tr>
<tr>
<td>R 10-11 am</td>
<td>Courtney</td>
<td>276 ONY</td>
<td>czesbau3</td>
</tr>
<tr>
<td>F 12n-1 pm</td>
<td>Nelson</td>
<td>129 HUE</td>
<td>nugobor</td>
</tr>
</tbody>
</table>

† and by appointment.

For Pat, please call 541-346-6055/4525 or e-mail.
For Courtney, please e-mail.
For Nelson, please e-mail.

Come see us!
Invariably, Negative Feedback
**NB:** Though most often negative feedback, there are exceptions:

**Selected +FB e.g.:**

- LH Surge → Ovulation
- Oxytocin → Uterine Contraction
- Blood Clotting Cascade
- cAMP Cascade
- Na+ influx during AP

Nonpathological! Temporarily amplifies, but ultimately turned off by FB!
Venous Pooling

Baroreceptors/Pressure Receptors e.g., in Carotids & Aorta

NB: Corrective Change Opposes Original Input

Seated to Standing

- FB eg

Electrochemical Signal

CV Control Center Brain Stem

Electrochemical Signal e.g., Symp Accelerator N

Baroreceptors/Pressure Receptors e.g., in Carotids & Aorta

BP

HR

VC

FB eg
How Effective is a System at Maintaining Relative Constancy? Feedback Gain?

\[
\text{Gain} = \frac{\text{Correction}}{\text{Error}}
\]

e.g., Transfuse large volume of blood into person with non-functioning Baroreceptor system

BP: 100 mm Hg $\rightarrow$ 175 mm Hg

...into person with functioning system

BP: 100 mm Hg $\rightarrow$ 125 mm Hg
Gain *for Human Baroreceptor System*?

Gain = \frac{-50 \text{ mm Hg}}{+25 \text{ mm Hg}} = -2

cf: Gain for Human Body Temperature = -33
Neurotransmitter (NT) Balance: Diseases/Addictions/Moods?

- NT Lack
  - Depression
  - Parkinson's

Balance

Balance

+ NT Excess
  - Serotonin/Norepinephrine
  - Euphoria?
  - Suicidal Ideation?
  - Schizophrenia
  - Cocaine Addiction

Continuum
Chemical vs. Electrical Synapse

1-way

- Action potential
- Ca++
- Mitochondria
- Synaptic vesicle
- Neurotransmitter
- Ionotropic receptor
- Ions
- Second messenger
- Metabotropic receptor
- Cellular response:
  - Membrane potential
  - Biochemical cascades
  - Regulation of gene expression

Ion flow

200-300 A

20-40 A

2-way

G&H 2016 fig 46-5
Chemical Synapse Animations

http://highered.mheducation.com/sites/0072495855/student_view0/chapter14/animation_transmission_across_a_synapse.html

http://thebrain.mcgill.ca/flash/i/i_01/i_01/m/i_01_m_fon/i_01_m_fon.html

Balance!
Table 45-1  Small-Molecule, Rapidly Acting Transmitters

<table>
<thead>
<tr>
<th>Class I</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class II: The Amines</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td></td>
</tr>
<tr>
<td>Serotonin</td>
<td></td>
</tr>
<tr>
<td>Histamine</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class III: Amino Acids</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma-aminobutyric acid (GABA)</td>
<td></td>
</tr>
<tr>
<td>Glycine</td>
<td></td>
</tr>
<tr>
<td>Glutamate</td>
<td></td>
</tr>
<tr>
<td>Aspartate</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class IV</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitric oxide (NO)</td>
<td></td>
</tr>
</tbody>
</table>

Prominent in reward pathways & chemistry of addiction.

G&H 2011 p 550; G&H 2016 p 585
Locus ceruleus = "Blue/azur spot"

Substantia nigra = "Black substance"

Raphe nuclei = "Nut seam/line"

Norepinephrine = NE

Dopamine = D?

Serotonin = SI

G&H 2011 p 713; G&H 2016 p 753
Cocaine prevents re-uptake of Dopamine (1\textsuperscript{st} discovery), Norepinephrine (2\textsuperscript{nd}...) & Serotonin (3\textsuperscript{rd}...) & alters the plasticity of all 3 pathways!!!


Nerve cells eg: Ventral Tegmentum (Substantia Nigra) to Nucleus Accumbens (Limbic System)

http://learn.genetics.utah.edu/content/addiction/
4th Pathway Releases Acetylcholine!

Cortical Alertness!

- Substantia nigra (dopamine)
- Gigantocellular neurons of reticular formation (acetylcholine)
- Locus ceruleus (norepinephrine)
- Nuclei of the raphe (serotonin)

To diencephalon and cerebrum
To cerebellum
To cord
Mesencephalon
Pons
Medulla
Reticular Activating System (RAS)
Overall Cortical Alertness!

Radiations to cerebral cortex

Wake up!
Back row!

Visual impulses

Reticular formation

Pons

Auditory impulses
Spinal cord
Descending motor tracts

Ascending sensory tracts
Cerebellum
Master Controller
Endocrine System+
Good Things Come in Small Packages!

Hypothalamus 
< 1% of Brain Mass
Hormone Master Controller
100s of Functions!

Commissure
Lateral Hypothalamic Area
Lateral Preoptic Nucleus
Medial Preoptic Nucleus
Anterior Hypothalamic Area
Supraoptic Nucleus
Optic Chiasm
Dorsomedial Nucleus
Ventromedial Nucleus
Medial Mamillary Nucleus
Lateral Mamillary Nucleus

Plane of Frontal Section (page 6)
**POSTERIOR**

- Dorsomedial nucleus (GI stimulation)
- Posterior hypothalamus (Increased blood pressure) (Pupillary dilation) (Shivering)
- Perifornical nucleus (Hunger) (Increased blood pressure) (Rage)
- Ventromedial nucleus (Satiety) (Neuroendocrine control)
- Mamillary body (Feeding reflexes)
- Arcuate nucleus and periventricular zone (Neuroendocrine control)
- Lateral hypothalamic area (not shown) (Thirst and hunger)

**ANTERIOR**

- Paraventricular nucleus (Oxytocin release) (Water conservation)
- Medial preoptic area (Bladder contraction) (Decreased heart rate) (Decreased blood pressure)
- Posterior preoptic and anterior hypothalamic areas (Body temperature regulation) (Panting) (Sweating) (Thyrotropin inhibition)
- Optic chiasm (Optic nerve)
- Supraoptic nucleus (Vasopressin release)
- Infundibulum

- = Reward
- = Punishment

**midbrain**
**FIGURE 5-18**

**Limbic system**

This partially transparent view of the brain reveals the structures composing the limbic system.
Memory
Emotion
Motivation
Sociosexual Behavior
Enraged BI 358 student post Quiz 1?

Really, Jose Delgado, Yale University!
**Reward Centers** = Hypothalamus, lateral & ventromedial n.

**Punishment Centers** = Mesencephalon, central gray area, Hypothalamus & Thalamus, peri-ventricular zones

Animal will self-stimulate \( \geq 5000 \times/hr \) if electrodes planted in reward center!


G&H 11th ed only p 735
Opiates Brain Action + Overdose Story

- **Limbic System**: Change *emotions* & increase feelings of *pleasure*.
- **Brain Stem**: Depress *breathing* by altering neurochemicals.
- **Spinal Cord**: Block *pain* message transmission.

*Source*: National Institute on Drug Abuse
Additional Background Neuronal Physiology
Nervous System

CNS

PNS

input

output

Systems Level
~ 90% of Cells w/in CNS are **Glial Cells/Neuroglia**!

1. Neuron spatial relationships.
2. Scaffolding during **fetal development**.
3. Induce capillary changes to establish **Blood-Brain Barrier**.
4. Transfer **nutrients** from blood to neurons.
5. **Repair** brain injuries & form neural scars.
6. **Uptake & degrade** **neurotransmitters**.
7. Soak up excess K+ to sustain normal neural excitability.
8. Communicate with neurons & each other electrochemically.

100 Billion Neurons → 900 Billion **Glial Cells**!
What the Heck is the Glymphatic System? CNS Functional Waste Clearance Pathway!

Glymphatic Pathway Function

- Para-Arterial Influx
- Convective Flux
- Para-venous Efflux

Astrocyte  Neuron  Interstitial solute  AQP4

http://www.sciencedaily.com/releases/2012/08/120815142042.htm
https://www.ted.com/talks/jeff_iliff_one_more_reason_to_get_a_good_night_s_sleep
~99% of all neurons in humans! CNS ~100 billion interneurons!!
A single nerve cell may have as many as 200,000 inputs!
Neuron 1

Input
Dendrites ≡ Antennae

Controller
Soma ≡ NCB

Output
Axon

Neuron 2

Neuron 3

H. Howard 1980
Figure 45-5 Typical anterior motor neuron, showing presynaptic terminals on the neuronal soma and dendrites. Note also the single axon.
Nerve cell with multiple axons grown by adding a mitogen/neurogen ≡ nerve growth factor!

Courtesy Fengquan Zhou
UNC Chapel Hill
Sensory nerves especially, come in all shapes & sizes!

Figure 46-1
Several types of somatic sensory nerve endings.

G&H 2011 p 547; G&H 2016 p 596
Figure 45-4  Block diagram of a general-purpose computer, showing the basic components and their interrelations.  G&H 2011 p 546; G&H 2016 p 580
CNS Connections: The Central 7!

Fore-

1. Cerebrum

2. Diencephalon – Hypothalamus + Thalamus

Mid-

3. Midbrain

Hind-

4. Cerebellum

5. Pons

6. Medulla – Brain Stem

7. Spinal Cord
Ice Cream Cone Evolution Analogy

Basal Nuclei  Cerebral Cortex

Cerebrum -

Diencephalon -

Hypothalamus  Thalamus

- Cerebellum

- Brain Stem

Medulla  Pons
Homeostasis is a dynamic balance between the autonomic branches.

Rest-and-digest: Parasympathetic activity dominates.

Fight-or-flight: Sympathetic activity dominates.
Autonomic Neurotransmitters & Receptors

**Cholinergic**
- Nicotinic
- Muscarinic

**Adrenergic**
- $\alpha = \text{Alpha}$
- $\beta = \text{Beta}$

G&H 2011 pp 731-3;
G&H 2016 pp 775-8
Ach = Acetylcholine

NE = Norepinephrine

α Receptor (α₁, α₂)

β Receptor (β₁, β₂)
Nicotine activates both Sympathetic & Parasympathetic post-ganglionic neurons!

Problem?

Like hammering the gas pedal & brake at the same time!!
Nicotine also triggers the release of adrenalin & cortical hormones & causes generalized adrenal disruption!

80% Epinephrine/Adrenaline (E)
20% Norepinephrine (NE)

Output to blood

Adrenals = Paired organs above kidneys
