

## Module V: Physiology of Specialized Cells GMS FC

Spring 2012

Thursdays, 1:00 pm to 2:20 pm

Fridays, 9:00 am to 10:50 am

### Course description:

This course is one of the elective course modules (Module V) of the Foundations in Biomedical Sciences Curriculum. Knowledge of cellular and molecular physiology is critical to understanding the higher order functioning of tissues, organs and organ systems. *The objective of Physiology of Specialized Cells is to discuss the specialized adaptations of cells that help them to function in their respective tissues and organs. This course will also provide a frame work to bridge the gap between the biochemistry and the molecular and cellular biology that students have acquired in the core modules (I through IV) and organ physiology and pharmacology that will be addressed in the second year.*

Physical and chemical principles will be presented in the context of physiological concepts and further explained with clinical examples. The course will cover basic cellular processes including homeostasis, Ion Channels and Excitable Membranes, and Solute Transport. The course will highlight the specific adaptations of various cell types that allow them to perform their distinct physiological functions. Detailed content is described in the following pages.

Three text books: Cellular Physiology by Blaustein, Kao and Matteson, Random Walks in Biology by Berg, and Vander's Human Physiology by Widmaier, Raff and Strang are recommended. Readings from current and classic literature will reinforce the material covered in lectures. The class will be taught by members of the Division in a variety of Departments utilizing a combination of traditional lectures and discussion sections focusing on clinical examples and primary research to total 3.5 hours of class time per week over a 10 week period. Lecture notes, supplementary materials and figures will be available to students online. Students will be evaluated based on their performance on exams along with problem sets and participation in the discussion sessions.

### Course Learning Objectives

By the end of this course, students should be able to:

1. Explain the molecular mechanisms for maintaining solute and solvent homeostasis.
2. Describe the principles of diffusion and osmosis as they apply to gas transport in the lung and fluid movement across a capillary wall in normal physiological and diseased (pathophysiological) states.
3. Explain the role of electrochemical energy in transport processes and distinguish between passive and active transport mechanisms.
4. Describe the mechanisms responsible for generation and conduction of electrical signals and how pathological disruptions of electrical properties result in cellular dysfunction.
5. Describe ion channel diversity and regulation in a physiological context as well as pathologic changes in response to toxins and pharmacological agents.
6. Describe how the body utilizes transport processes in nutrient and waste absorption.

7. Describe the specialized adaptations of basic cellular processes found in: absorptive cells, secretory cells, olfactory cells, photoreceptor cells, muscle, cardiac muscle.

### Course Managers:

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Dr. Christopher Gabel, Ph.D.  
Assistant Professor  
Department of Physiology and Biophysics  
Room L713, 84267  
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### Additional Participating Faculty:

Dr. Atkinson	Department of Physiology and Biophysics
Dr. Steven Borkan	Department of Medicine
Dr. Carter Cornwall	Department of Physiology and Biophysics
Dr. Fernando Garcia-Diaz	Department of Physiology and Biophysics
Dr. Terrill Gibbs	Department of Pharmacology
Dr. Simon Levy	Department of Physiology and Biophysics

### Grading:

Correlation Sessions/Problem Sets	30%
Midterm Exam	30%
Final Project	40%
Total	100%

Correlation Session: The correlation session grade will consist of two parts: participation in the class discussion and written problem sets. Class participation will be based on attendance, class preparation (did they clearly read the required material before hand) and additional contribution to class discussion. The written homework will consist of a number of problems that are related to the required reading for each discussion session. Students are expected to research and formulate answers before the discussion meets (thus facilitating class participation) and afterward finalize and hand in written answers.

Final Project: The Final Project will consist of an independent, 5-8 pages research paper (fully referenced) describing the physiological characteristics and/or specific mechanisms of a particular specialized cell type. This could be based on and expand the discussion of a cell type discussed during the second half of the course. Alternatively, students could choose a novel cell type. Topics will be submitted and approved before hand.

Recommended reference materials to supplement reading of the literature include:  
Blaustein, Kao, and Matteson *Cellular Physiology*. Elsevier (Mosby Monograph Series), 2004.  
Berg, H *Random Walks in Biology* Princeton University Press, Chichester. 1993.  
Widmaier, Raff, and Strang *Vander's Human Physiology*

Dates	Class	Instructor
Thursday Feb 16	<b>Introduction to Cellular Homeostasis</b> <b>Random Walks in Biology (Microscopic Theory)</b> <p><u>Objectives:</u></p> <ul style="list-style-type: none"> <li>-Explain that diffusion is the movement of molecules down a concentration gradient</li> <li>-Explain that diffusion results from the random movement of molecules</li> <li>-Describe diffusion in quantitative terms</li> </ul> <p><u>Readings:</u></p> <ul style="list-style-type: none"> <li>-Chapter 1 Blaustein et al., Cellular Physiology 2004</li> <li>-Chapter 2 Blaustein et al., Cellular Physiology 2004</li> <li>-Chapter 1 Berg, Random Walks in Biology 1993</li> <li>-Berg and Purcell (1977) Life at Low Reynolds Number. Journal. Volume: Page-Page.</li> </ul>	Dr. Gabel
Friday Feb 17	<b>Diffusion and Permeability (Bulk Properties)</b> <p><u>Objectives:</u></p> <ul style="list-style-type: none"> <li>-Explain how Fick's law illustrates the intuitive understanding of diffusion</li> <li>-Describe the relationship between the concepts of flux and membrane permeability</li> <li>-Explain how diffusion constrains Cell Biology and Physiology</li> </ul> <p><u>Readings:</u></p> <ul style="list-style-type: none"> <li>-Chapter 2 Blaustein et al., Cellular Physiology 2004</li> <li>-Chapter 2 Berg, Random Walks in Biology 1993.</li> </ul>	Dr. Gabel
Thursday Feb 23	<b>Correlation #1</b> <b>A. Diffusion in cellular processes: DNA repair enzymes</b> <p><u>Objectives:</u></p> <ul style="list-style-type: none"> <li>-Compare and contrast diffusive and directed intracellular transport processes.</li> <li>-Explain how diffusion constrains cellular processes using DNA repair enzymes as an example.</li> </ul> <p><u>Readings:</u></p> <ul style="list-style-type: none"> <li>-Halford (2004) How do DNA enzymes find their targets. <i>Nucleic Acids Research</i>, 2004, Vol. 32: 3040-3052</li> <li>-Von Hippel and Berg (1989) Facilitated Target Location in Biological Systems 264: 675-678.</li> <li>-Gorman Greene (2008) Visualizing one-dimensional diffusion of proteins along DNA Nature Structural and Molecular Biology 15:768-774</li> </ul> <p><b>B. Diffusion in physiological processes: Gas exchange in the lungs</b></p> <p><u>Objectives:</u></p> <ul style="list-style-type: none"> <li>-Explain how Fick's law describes gas exchange in the lungs</li> <li>-Explain how diffusion constrains cellular processes using DNA repair enzymes as an example.</li> </ul> <p><u>Readings:</u></p> <ul style="list-style-type: none"> <li>-Chapter 13 Vander's Human Physiology pp 434-438, 448-454,</li> </ul>	Dr. Gabel and Dr. Moore
Friday Feb 24	<b>Solute Transport, Water Movement and Osmotic Pressure</b> <p><u>Objectives:</u></p> <ul style="list-style-type: none"> <li>-Explain how transport proteins facilitate the movement of solutes across the cell membrane</li> <li>-Describe how the ATP dependent transport of ions maintains membrane gradients</li> <li>-Explain the nature of osmosis.</li> </ul>	Dr. Garcia-Diaz

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- Define the driving forces that control solvent flow across membranes
  - Explain how cell volume changes in response to alterations in permeant and impermeant solutes in the extracellular fluid.

Readings:

-Chapter 3 Blaustein et al., Cellular Physiology 2004

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Thursday  
March 1

**Correlation #2**

*Clinical Correlation Capillary Permeability and Edema  
Bee sting allergy, kwashiorkor, filariasis, Severe dehydration effects on brain*

Dr. Moore and  
Garcia-Diaz

Objectives:

- Explain that fluid movement across the capillary wall is determined by the balance of hydrostatic and osmotic (oncotic) forces.
- Explain how disruption of these balanced forces can result in edema.
- Explain adaptations to maintain cell volume in response to hyperosmotic conditions (severe water deprivation).

Readings:

-Chapter 12 Vander's Human Physiology pp 353-356, 385-392.

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Friday  
March 2

**Electrical Consequences of Ionic Gradients**

Dr. Gibbs

Objectives:

- Describe how the movement of ions across a membrane can generate an electrical potential difference.
- Explain the concept of electrochemical potential.
- Explain the concept of chemical potential and how concentration gradients across a membrane store chemical potential.
- Explain how the Nernst equation can be used to calculate equilibrium potential.
- Explain how resting membrane potential is generated.
- Explain how the Goldman-Hodgkin-Katz equation can be used to calculate membrane potential.
- Explain the relationship between the Nernst and GHK equations.
- Explain how alterations in membrane permeability to ions can change the membrane potential.

Readings:

-Chapter 4 Blaustein et al., Cellular Physiology 2004  
-Appendix C Berg, Random Walks in Biology 1993.  
-Goldman 1943, J General Physiology  
-Potential impedance and rectification in membranes  
-Hodgkin and Katz 1949 J Physiology  
The effect of sodium ions on the electrical activity of the giant axon of the squid.

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Thursday  
March 8

**Correlation #3**

*Clinical Correlation: Toxins (e.g., Tetrodotoxin, Saxitoxin), NIDDM can be treated with sulfonurea drugs.*

Dr. Gibbs

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Friday  
March 9

**Generation and Propagation of Action Potentials**

Dr. Gibbs

Objectives:

- Review general electrical properties of the membrane, i.e. the equivalent electrical circuit ( $V=IR$ )
- Describe the equilibrium concentration of ions in a nerve cell (Na, K, Ca, Cl), how it is maintained and how it relates to the resting potential (Nernst equation)
- Describe the role and sequence of channel activity that generate an action potential
- Explain the propagation of an action potential and the effects/benefits of myelination

Readings:

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March 12-  
16

## Spring Break

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Thursday  
March 22

### Correlation #4

*Clinical Correlation: Action potential disease (Multiple Sclerosis),*

Dr. Gibbs

Objectives:

- Describe the effect of demyelination in multiple sclerosis on action propagation,
- Explain the redistribution of Na channels as a result of demyelination in MS and the neurodegenerative effects.

Readings:

Craner et al. (2004) Molecular changes in neurons in multiple sclerosis: Altered axonal expression of Nav1.2 and Nav1.6 sodium channels and Na<sup>+</sup>/Ca<sup>2+</sup> exchanger. PNAS 101: 8168–8173.

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Friday  
March 23

### Ion Channels and Ion Channel Diversity

Objectives:

- Describe the mechanism of ion channel selectivity.
- Describe the structural features of ion channels.
- Compare and contrast cardiac vs nerve action potentials with emphasis on the differences in ion channels.
- Compare and contrast the types of voltage gated ion channels
- Explain the mechanism of action of Ca<sup>++</sup> antagonist drugs.
- Explain the role of K-channels in glucose induced release of insulin from pancreatic beta-cells.

Readings:

-Chapter 8 Blaustein et al., Cellular Physiology 2004  
-Gouaux E, Mackinnon R. (2005) Principles of selective ion transport in channels and pumps Science, 310(5753):1461-5

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Thursday  
March 29

### Correlation #5

*Clinical Correlation: hypokalemic periodic paralysis, cardiovascular disease?*

Dr. Atkinson and  
Dr. Moore

Objectives:

- Explain the role of Na channel mutation in causing hypokalemic periodic paralysis
- Explain the role of Na channel mutation in cardiovascular disease

Readings:

-Catterall WA (2010) Ion channel voltage sensors: structure, function, and pathophysiology. Neuron. 2010 Sep 23;67(6):915-28.

-Ruan et al., (2009) Sodium channel mutations and arrhythmias. Nat Rev Cardiol. 6:337-348.

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March 30-  
April 6

### Midterm exam

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Friday  
March 30

### Specialized Cell: Renal proximal tubule cell

*Transport Processes in the Kidney*

Dr. Borkan

Objectives:

- Explain passive and active transport in the kidney proximal tubule.
- Explain how different transport systems in the apical and basolateral membranes of epithelial cells transfer solute and water between body compartments.

Readings:

-Chapter 9 and 10 Blaustein et al., Cellular Physiology 2004

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Thursday April 5	<b>Clinical Correlation #6</b> <i>Clinical Correlation: Renal Ischemia and Fanconi syndrome</i>  <u>Objectives:</u> -Explain the kidney tubule transport and how transport can be disrupted in disease states.	Dr. Borkan
Friday April 6	<b>Specialized Cell: Muscles, Muscle activation, Neuromuscular Junction</b>  <u>Objectives:</u> -Determine the transmission characteristic of the NMJ through analysis of its physical properties (i.e. vesicle trafficking, diffusion times, reuptake etc.) -Explain pre and post-synaptic ionic response to action potential and synaptic transmission in the NMJ. -Identify the major types of synapses and their basic mode of operation: gap junction, inhibitory and excitatory synapses, neuromuscular junction.  <u>Readings:</u> -Chap 11 Principles of neuroscience Kandel, Schwartz, Jessell -Harlow et al., (2001) The architecture of active zone material at the frog's neuromuscular junction, Nature, 409 (2001), pp. 479–484	Dr. Levy
Thursday April 12	<b>Clinical Correlation #7</b> <u>Objectives:</u> -Myasthenia gravis – Explain how blockage of acetylcholine receptors by antibodies leads to NMJ dysfunction -Lambert-Eaton – Explain how antibodies against voltage gated Ca channels reduce acetylcholine release in the NMJ -Discuss additional diseases of the NMJ?  <u>Readings:</u> -Losen et al., (2008) Treatment of myasthenia gravis by preventing acetylcholine receptor modulation. PNAS 113:174-9. -Satoh et al., (1998) Lambert—Eaton syndrome antibodies inhibit acetylcholine release and P/Q-type Ca <sup>2+</sup> channels in electric ray nerve endings. Journal of Physiology (1998), 508: 427-438. -Diseases of the neuromuscular junction. McConville and Vincent (2002) Curr Opin Pharmacol. 2: 296-301.	Dr. Levy
Friday April 13	<b>Specialized Cell: Hepatocyte cellular transport</b>  <u>Objectives:</u> -Explain the physiological mechanisms and role of hepatocyte cells in the liver. -Describe the synthesis of apolipoproteins and the assembly and secretion of lipoproteins by the liver. - Describe lipoprotein uptake, Synthesis and Secretion - Describe the role of ABC transporters in the formation of bile.	Dr. Atkinson
Thursday April 19	<b>Correlation # 8</b>  <u>Objectives:</u> - Explain the cellular basis for various liver diseases. - Describe the consequences of having a defect in an ABC transporters.	Dr. Atkinson
Friday April 20	<b>Specialized Cell: Auditory system (Hair cells):</b> <u>Objectives:</u> - Describe the basic structure and operation of hair cells for auditory sensation within cochlea - Explain the physical gating mechanism of channel activation within a hair cell, their compliance and resonance.	Dr. Gabel

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Readings:

-Chap 6 Sensory Transduction. Gordon Fain  
-Howard and Hudspeth, (1988) Compliance of the Hair Bundle Associated with Gating of Mechano-electrical Transduction Channels in the Bullfrog's Saccular Hair Cell Neuron. 3:189-99.

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Thursday  
April 26

**Correlation # 9**

Dr. Gabel

Objectives:

- Determine the mechanism of tuning/adaptation in hair cells (ie the role of molecular motors and Ca mediation),
- Explain the role of active hair cell movement (ringing) in the sensitivity of its response
- Explain how hair cell malfunction results in various forms of deafness.

Readings:

-Assad and Corey (1992) An Active Motor Model for Adaptation by Vertebrate Hair Cells. J. Neuroscience 12:3291-3309  
-Martin and Hudspeth Active hair-bundle movements can amplify a hair cell's response to oscillatory mechanical stimuli (1999) PNAS. 96:14306-11  
-Hudspeth\* et. al (2000) PNAS  
*Putting ion channels to work: Mechano-electrical transduction, adaptation, and amplification by hair cells*

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Friday  
April 27

**Specialized Cell: Visual System**

Dr. Cornwall

Objectives:

- Describe the basic structure and operation of rod and cone cells in the retina.
- Explain the signal transduction pathway that triggers rod/cone cell activation in response to light.

Readings:

-Chap 9 Sensory Transduction. Gordon Fain

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Thursday  
May 3

**Correlation #10**

Dr. Cornwall

Objectives:

- Explain the basic mechanisms of light adaptation in rod cells.
- Explain how defects in the phototransduction pathway lead to blindness.

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May 7-11

**MODULE V FINAL PROJECT**

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