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Medical Histology

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Computer Support (LRC staff):
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Fall 2008

University of Michigan
Medical School

Objectives

To understand:

- How cells and tissues are arranged in the normal organ system of the body, and
- How these cells and tissues are specialized to perform the function(s) most effectively.

The knowledge gained will hopefully provide a cellular and ultrastructural "framework" for all of the other topics (anatomy, physiology, biochemistry, etc.) that you'll learn this year.

Histology is also, of course, a FUNDAMENTAL part of PATHOLOGY.

Correlate

Structure

and

Function

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HISTOLOGY

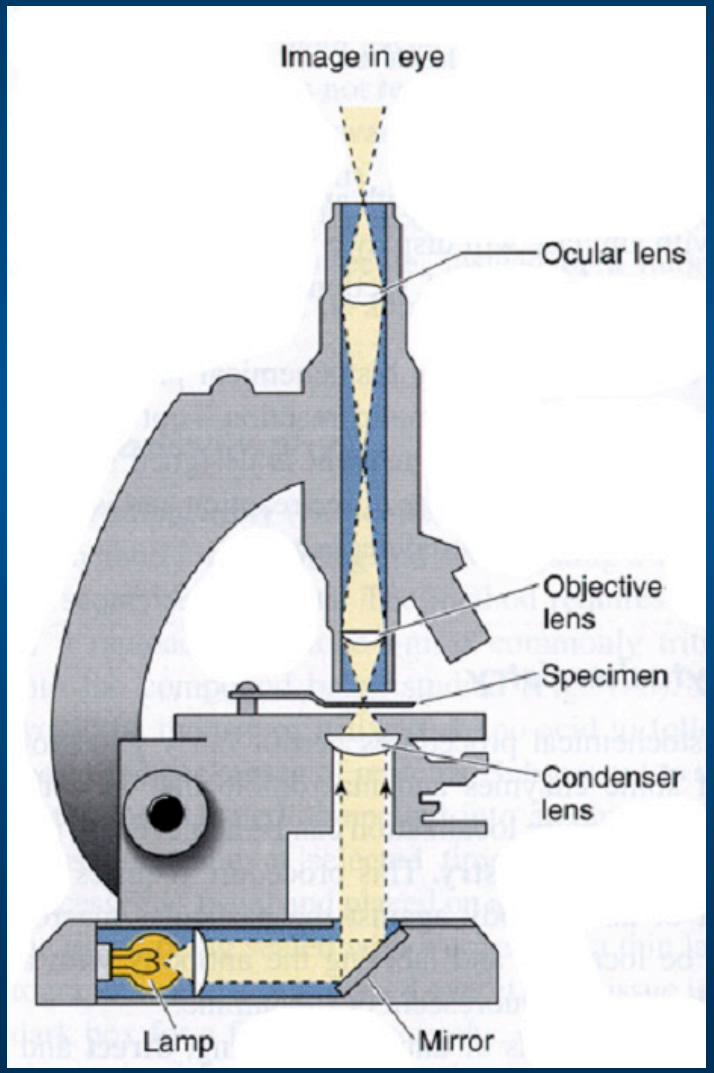
a.k.a. Micro-anatomy

Tissue Preparation for Light Microscopy

1. Stabilize cellular structures by chemical fixation.
3. Dehydrate and infiltrate tissues with paraffin or plastic.
5. Embed fixed tissues in paraffin or plastic blocks.
7. Cut into thin slices of 3-10 micrometer thick; collect sections on slides.
9. Re-hydrate and stain with Hematoxylin (a basic dye): Stains basophilic structures (e.g. nucleic acids) blue/ purple.
11. Counter-stain with Eosin (an acidic dye): Stains acidophilic or “eosinophilic” structures (e.g. proteins, membranes) red/pink.

“H & E” staining is routine, but other dyes and staining techniques may be used to visualize other structures.

Light Microscopy



 Gartner and Hiatt. *Color Textbook of Histology*. 1997. Figure 1.1.

1. ILLUMINATION SOURCE
2. CONDENSER LENS
3. SPECIMEN STAGE
4. OBJECTIVE LENS
5. PROJECTION (OCULAR) LENS
6. OBSERVER

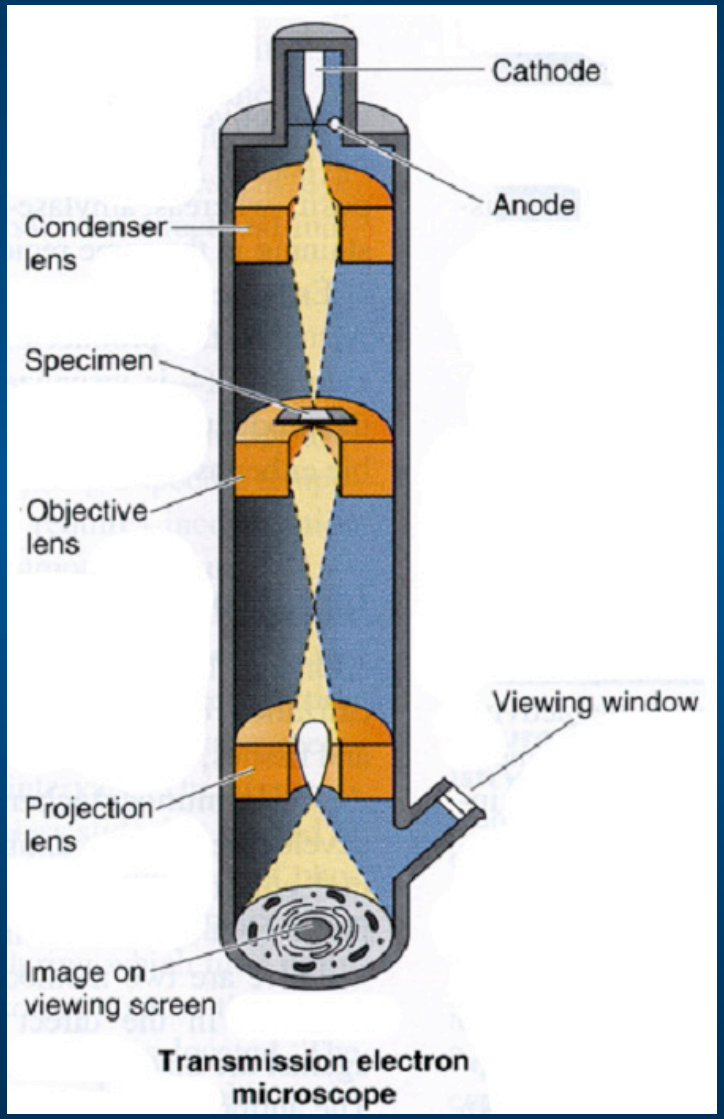
- YIELDS A 2-DIMENSIONAL IMAGE CAPABLE OF 0.2 μm RESOLUTION.
- CELLULAR FEATURES ARE STAINED DIFFERENTIALLY BASED PRIMARILY UPON CHEMICAL PROPERTIES.

Light Microscopy

Tissue Preparation for Electron Microscopy

1. Tissues are fixed with glutaraldehyde (cross-links proteins) and osmium tetraoxide (cross-links lipids); OsO_4 is also an electron-dense "stain"
2. Dehydrate and infiltrate tissues w/ plastic.
3. Embed and block fixed tissues in plastic.
4. Cut into ultra-thin slices (50 nanometers thick); collect sections on slides.
5. Stain sections with heavy metal salts (lead citrate and uranyl acetate) that bind nucleic acids & proteins.
6. Visualize in TEM; heavy metal "stains" block electrons to create contrast

Transmission Electron Microscopy

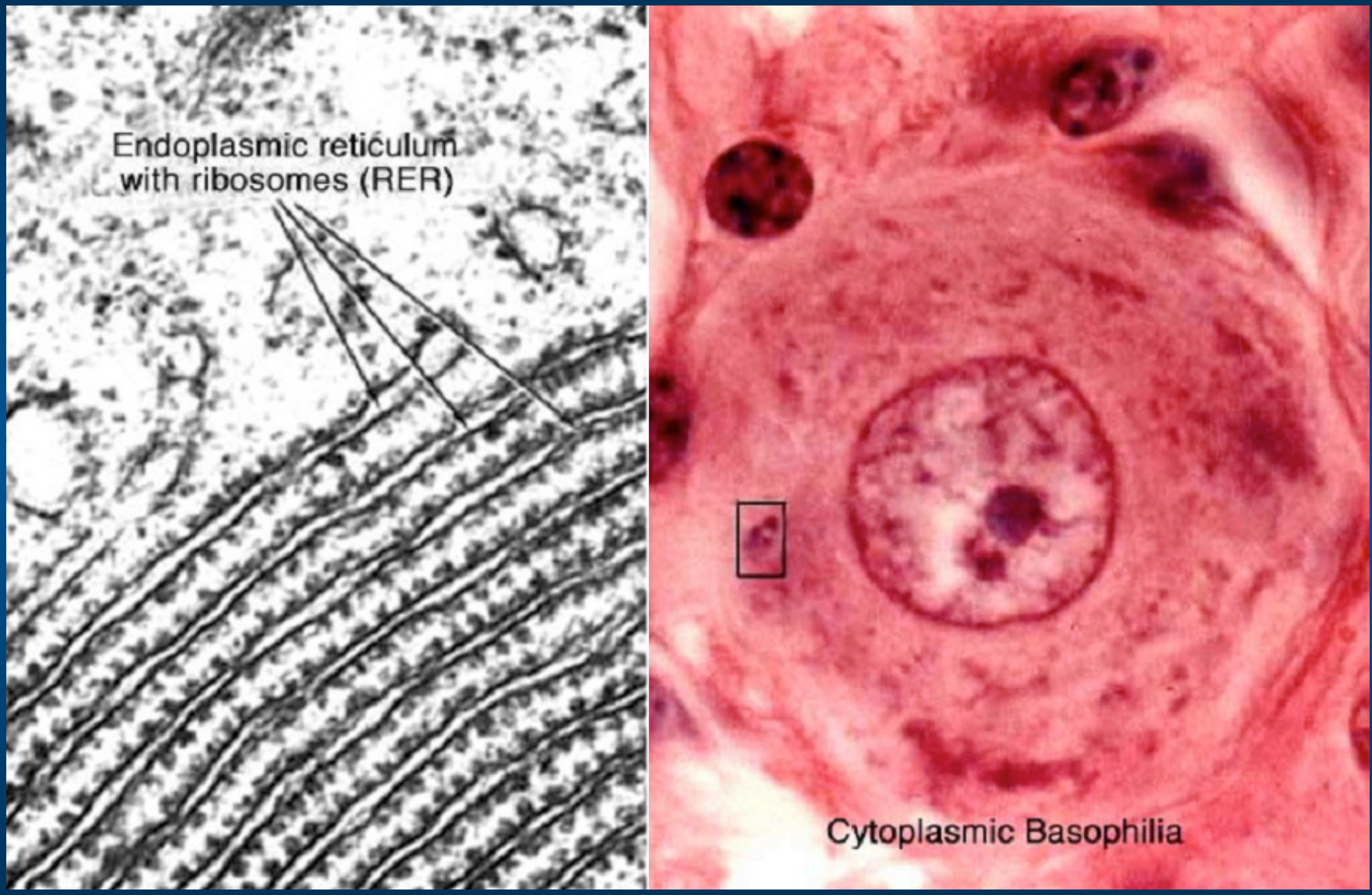


Transmission electron microscope

1. ILLUMINATION SOURCE (generates electron beam)
2. CONDENSER LENS
3. SPECIMEN STAGE
4. OBJECTIVE LENS
5. PROJECTION LENS
6. FLUORESCENT VIEW SCREEN
7. VIEWING WINDOW & OBSERVER

- YIELDS A 2-DIMENSIONAL IMAGE CAPABLE OF 0.2 nm RESOLUTION.
- CELLULAR FEATURES ARE STAINED WITH ELECTRON-DENSE, HEAVY METAL STAINS YIELDING ONLY A BLACK AND WHITE IMAGE

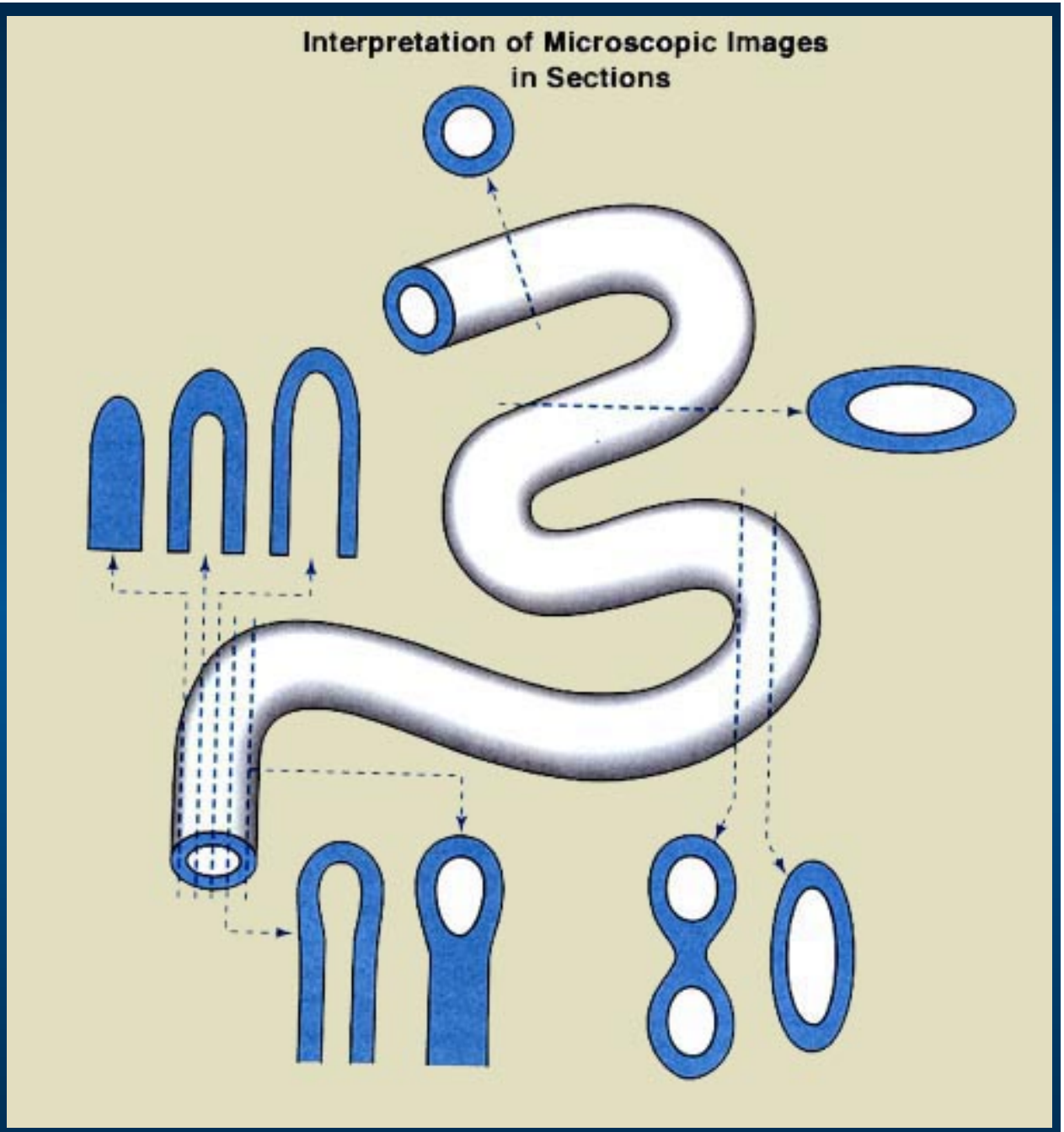
 Gartner and Hiatt. *Color Textbook of Histology*. 1997. Figure 1.1.



The challenge:

3D structures, but viewed only in 2D…

PD-INEL University of Michigan, Histology Slide Collection



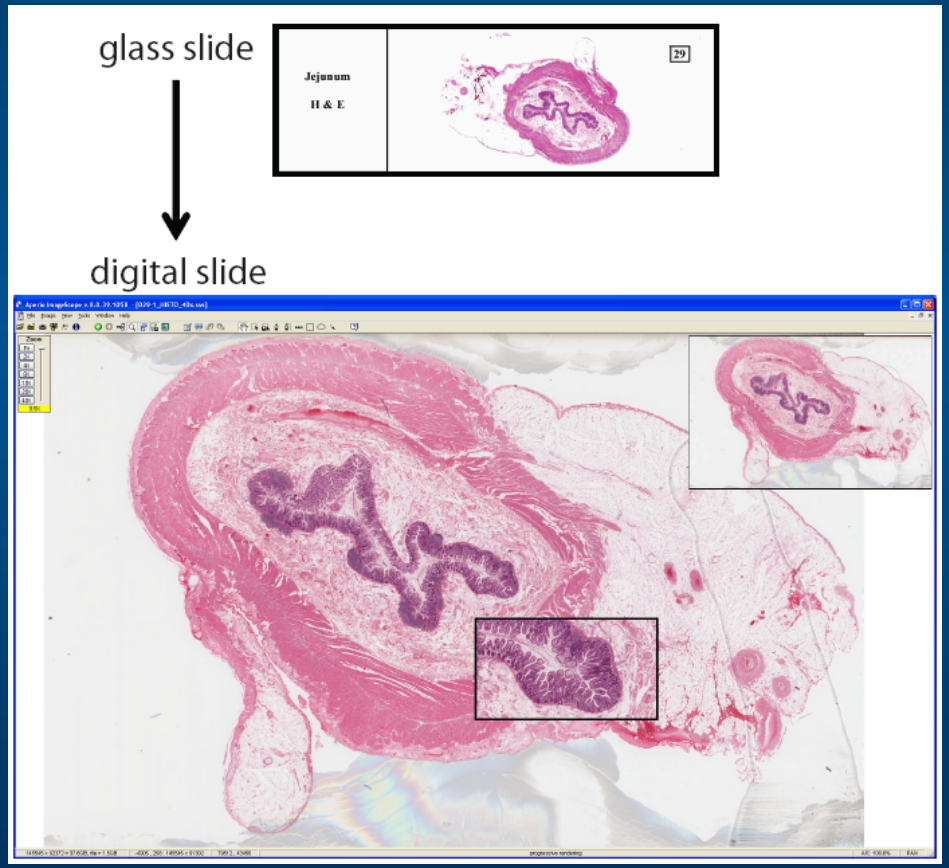
PD-INEL Source Undetermined

Microscopy
→ Virtual Microscopy

Microscope Slides
→ Digital Images

Virtual Microscopy

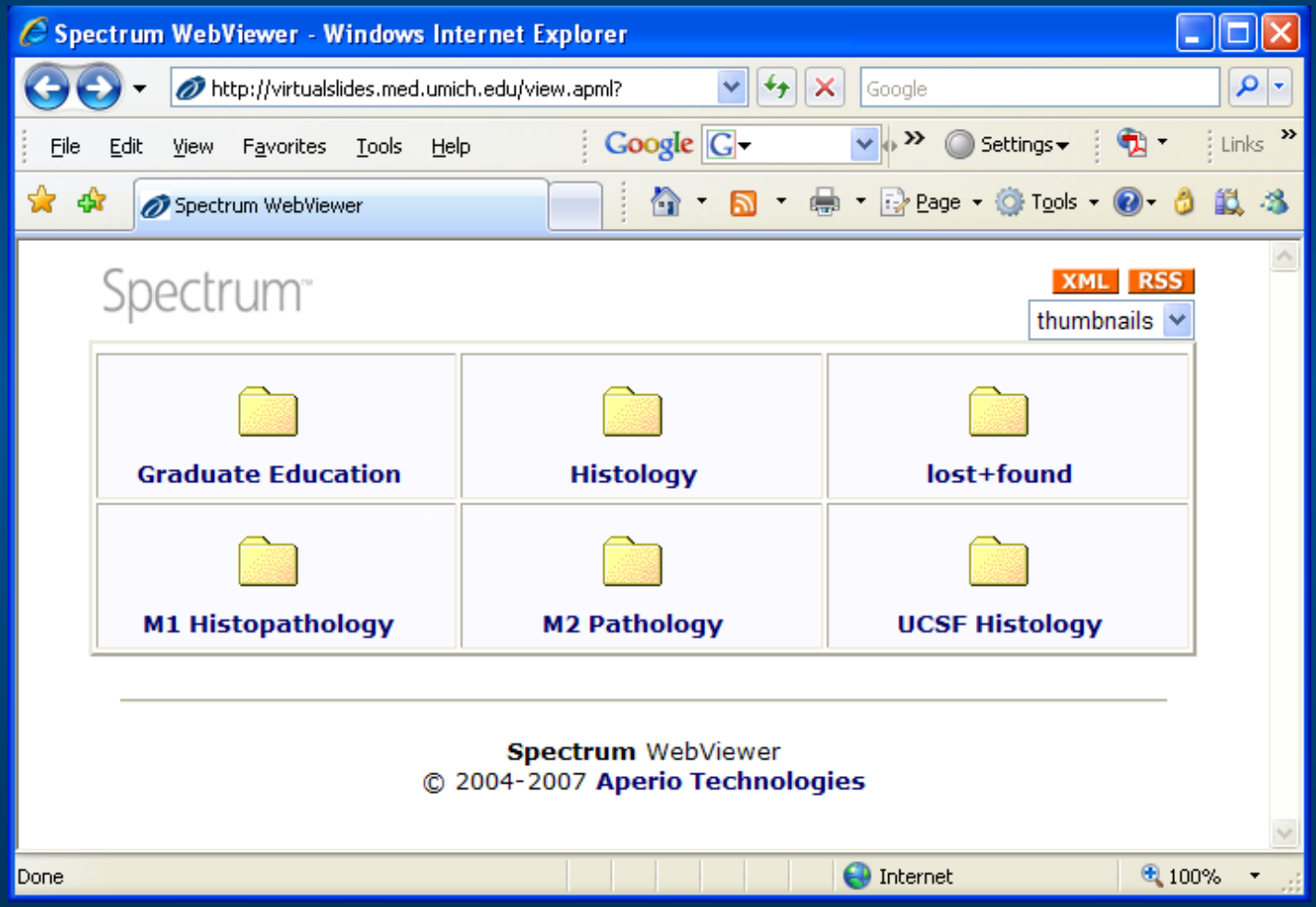
- Glass microscope slides line-scanned using a computer-controlled microscope
- Line scans compiled into single “digital slide” that may be 200k x 200k pixels (that’s 40 GIGApixels!)
- Digital slides stored as compressed files (~1.5 GB) and delivered via Web or file-server
- Digital slides viewable as flash objects within web browser or in proprietary format (e.g. Aperio ImageScope)
- Any region of interest on digital slide may be viewed at a range of magnifications with resolution up to 0.25µm/pixel



 University of Michigan, Histology Slide Collection

Virtual slide collection

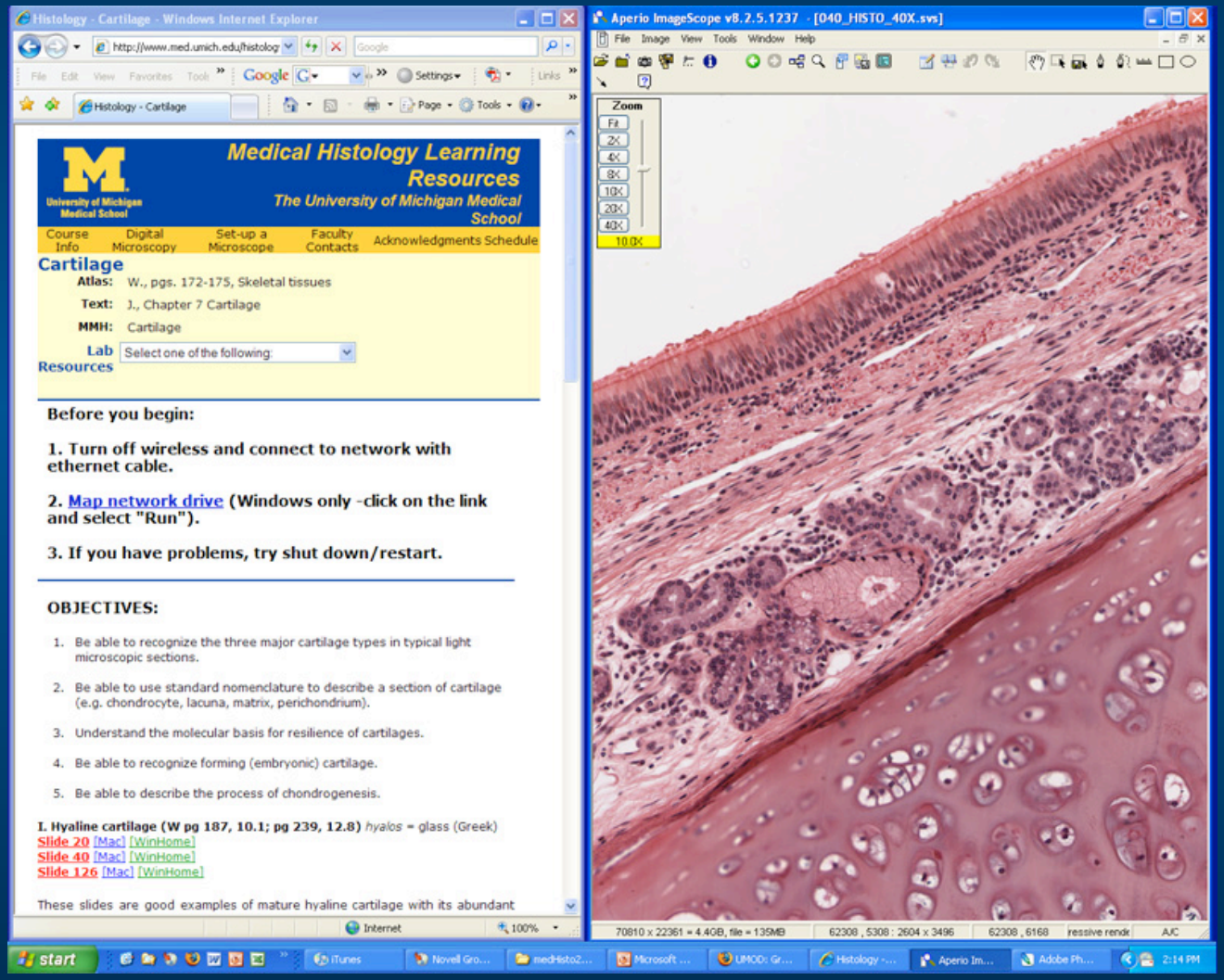
http://virtualslides.med.umich.edu



 Screenshot of Spectrum WebViewer by Dr. Velkey

Medical Histology Website

http://www.med.umich.edu/histology



© FAIR USE **Screenshot of U-M Website by Dr. Velkey**

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Microscopes and glass slides still have their place!

- **The focal plane and depth-of-field (aperture) of the digital slide is fixed**
- **The digital slide is only a representative specimen**
- **Servers crash**
- **Knowing how to use a microscope has its value.**

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 Photo taken by Dr. Sun-Kee Kim

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 Photo taken by Dr. Sun-Kee Kim

BASIC TISSUES

EPITHELIUM

CONNECTIVE TISSUE

MUSCLE

NERVOUS TISSUE

(BLOOD)

Basic tissues combine to form larger functional units, called ORGANS.

CELLS AND TISSUES SEQUENCE

Epithelial Tissue

Connective Tissue

Muscle Tissue

Peripheral Nervous System

Skin / Integumentary System

MEDICAL HISTOLOGY TOPICS per SEQUENCE

Cells and tissues	5
Musculoskeletal	2
Cardiovascular/Respiratory	3
Renal	1
GI / Liver	4
Endocrine/Reproductive	3
Immunology	1
Central Nervous System	3

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MEDICAL HISTOLOGY

Lecture: ~50 minutes

- Lecture Handouts in coursepacks
- Lecture PowerPoints on CTools (also linked from histo web site).

Laboratory: 3 hours

- Laboratory Guide (hard copy or online) - learning objectives
- Microscope and slides ("real" and virtual)

Lab Atlas and Text Book:

- Young, et al.: *Wheater's Functional Histology, 5th ed.* –HIGHLY recommended
- Ross and Pawlina: *Histology: A Text and Atlas, 5th ed.* -recommended

Michigan Medical Histology CD –not issued this year (won't work in Mac OS X)

Review and Lookalike Images (online)

Lab Orientation Presentations (online)

RESOURCES

Histo web site:
http://www.med.umich.edu/histology

CTools (aka "portal"):
https://ctools.umich.edu/portal

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Quizzes and Exams

- **Usually a total of 8 questions per session divided between weekly quizzes and final exam. Questions will weigh equally.**
- **Weekly quizzes and final exams will all be administered online.**
- **Multiple choice questions: some straight text, but MOSTLY image-based (LM, EM, or diagram), or virtual slides**
- **Sample questions may be found in the online syllabus.**

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Issued Histology Materials (in your lockers)

Locker key

Microscope*

Two Boxes of M1 Histology Microscope Slides*

Network Cable

No MMH CD issued this year

* Shared resources (*i.e. MUST stay in locker*)

Sign Loan Agreement Sheet –you acknowledge receipt of EACH item and you agree to return them at the end of the year!

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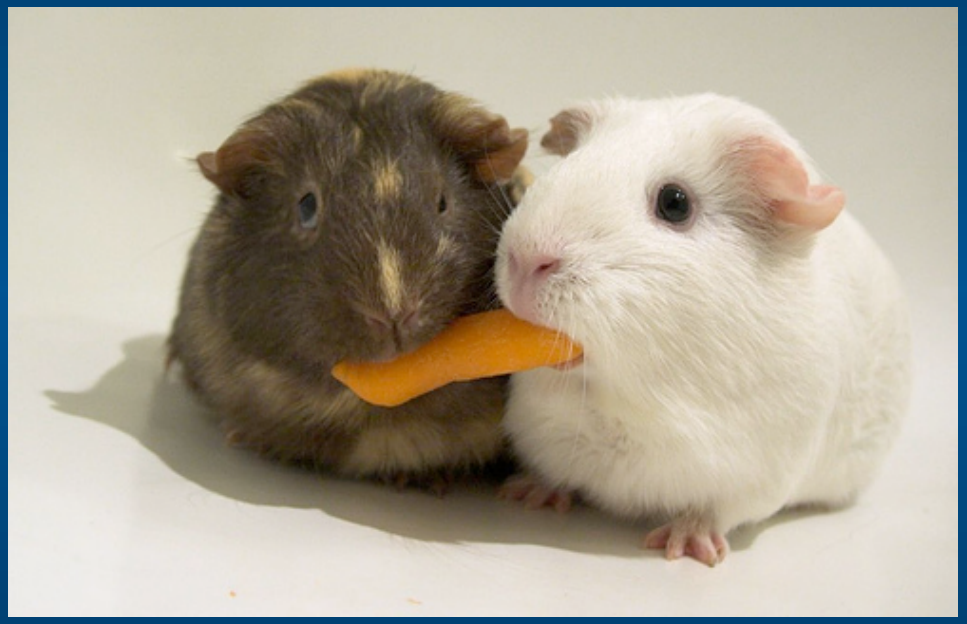
So, what's going to happen in the lab today?

It depends on how you look at it…

 US Army Africa, Flickr

Doctors in training



 Ryancr, Flickr

Test Subjects Pioneers

Tasks in the lab today…

- Making sure your computers are set up to access and view virtual slides
- Explanation of the different links to the virtual slides:
  - "Mac" (for Macs that cannot run Windows)
  - "WinLab" (for Windows machines when **ON CAMPUS**)
  - "WinHome" (for Windows machines **OFF CAMPUS)**
- "Load testing" the servers (requires synchronized activity, so wait for instructions)
- After load testing, work through tutorial to learn basic features of ImageScope (Windows) and WebViewer (non-Windows)
- Sign and turn in Loan Agreement Forms acknowledging receipt of network cable (we'll deal with microscopes and slides NEXT week)

A quick word about ImageScope…

- It is the preferred method of viewing the slides
- Primary advantage is the ability to ANNOTATE slides (for self-study or to mark something about which you have a question)
- Slides are opened into ONE ImageScope window so it's easy to quickly go from one slide to another and/or compare slides side-by-side
- Can adjust image brightness, contrast, and color levels
- 1-click TIFF or JPEG image capture

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The Team

Digital Slide Creation and Management:

Ronald A. Craig, Ph.D., Digital Microscopy Lab Manager, Pathology
Kristopher L. Thompson, Pathology Informatics
Melissa (Colter) Bombrey, Medical School Class 2008
Matthew Velkey, Ph.D., Clinical Lecturer, Cell and Developmental Biology
Sun-Kee Kim, Ph.D., Professor, Cell and Developmental Biology

Server, network and workstation development/support:

Roger Burns, Technical Coordinator, Learning Resource Center
Chris Chapman, Assistant Media Manager, Learning Resource Center
Monica Webster, System Administrator, Medical School Information Systems
Wayne Wilson, Associate Director, Medical School Information Systems
Sue Boucher, Technology Help Desk Manager, Medical School Information Systems
Kristopher L. Thompson, Pathology Informatics (UM Class 2007)
Jason Engling, Learning Resource Center
Matt Undy, Classroom services
Thomas Peterson, Systems Analysis and Programming Manager, Pathology Informatics
Douglas Gibbs, PhD, Network Engineer, Pathology Informatics
Mary Bernier, Programmer Analyst Supervisor, Medical School Information Systems

Additional Source Information

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