Third Faculty of Medicine @ Charles University

CVOL-0161
COURSE SUMMARY

Microscopy (& Histology) Techniques in Health and Disease

Radek Pelc
Czech Academy of Sciences
Prague

radek.pelc@seh.oxon.org

LECTURE LIST in BRIEF

CLINICAL EXAMPLES

Lecture #1 ….. Course summary
Lecture #2 ….. Stereomicroscopy: Operation/surgical microscopes
Lecture #3 ….. Modulation contrast: *In vitro* fertilization
Lecture #4 ….. Phase contrast and darkfield: Abnormal erythrocytes …
Lecture #5 ….. Digital micrographs: Telemedicine & teaching websites
Lecture #6 ….. Histology illustrations: 'Forgotten' teaching aids
Lecture #7 ….. Optical (light-guiding) properties of retinal glia cells
Nobelists in Oxford: The discovery of synapse

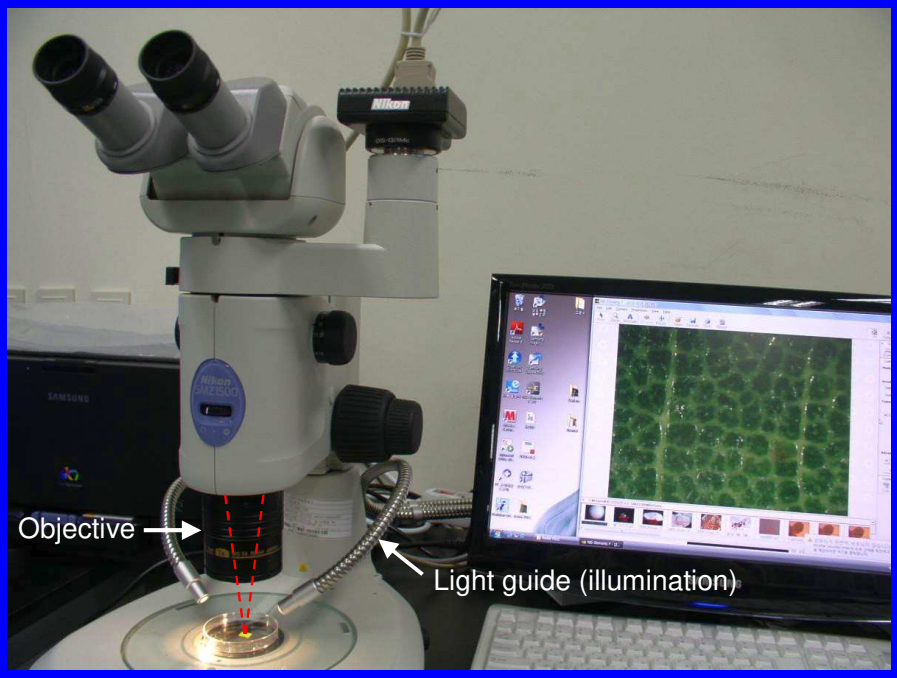
Excursion to the labs (optional)
Purkyně's exposion (optional)

HISTOLOGY TEACHING AIDS for 2nd year students & prospective histology teachers

Lecture #2

STEREOMICROSCOPY:

DISSECTING / OPERATION / SURGICAL MICROSCOPES



Common Main Objective (CMO) design

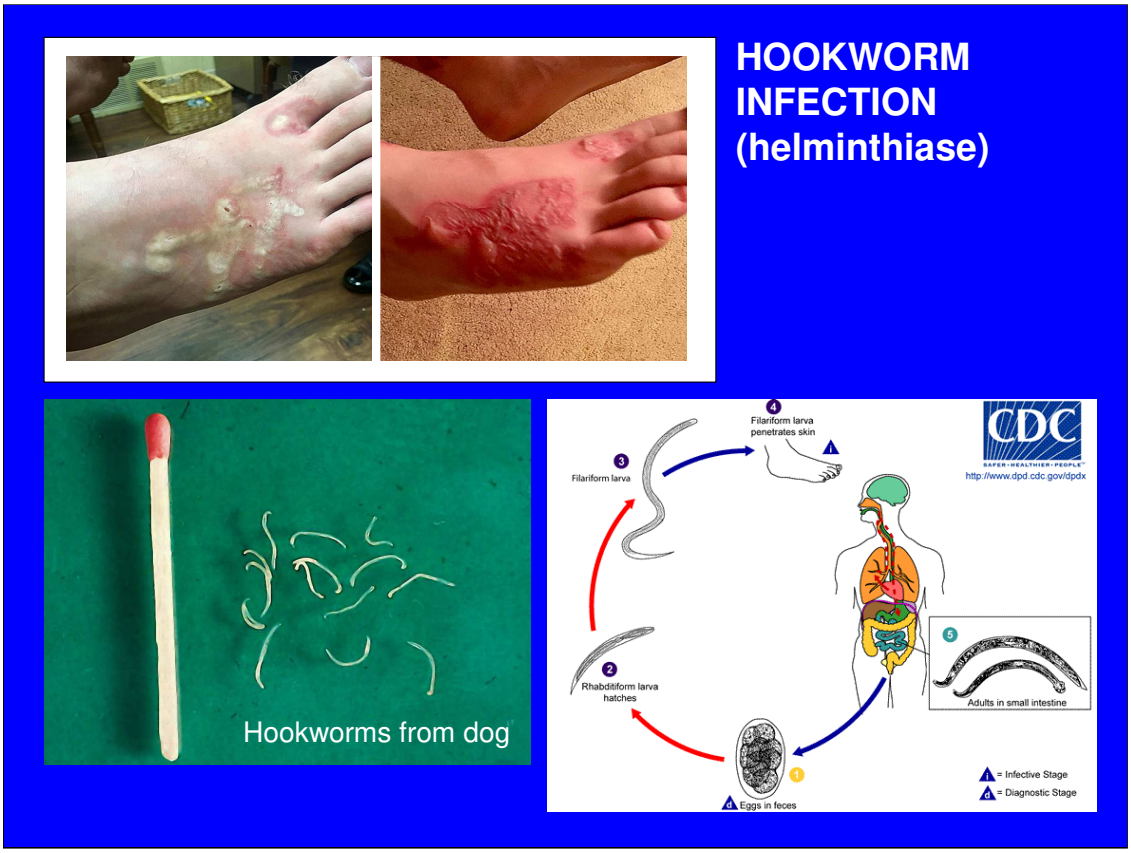
More modern stereomicroscopes (of CMO rather than Greenough design) use a single objective.

It accommodates two separate light paths (dashed red lines) so that the stereoscopic effect is still present.

Flexible light guides (“goose necks” in Czech) are frequently used to illuminate the specimen.

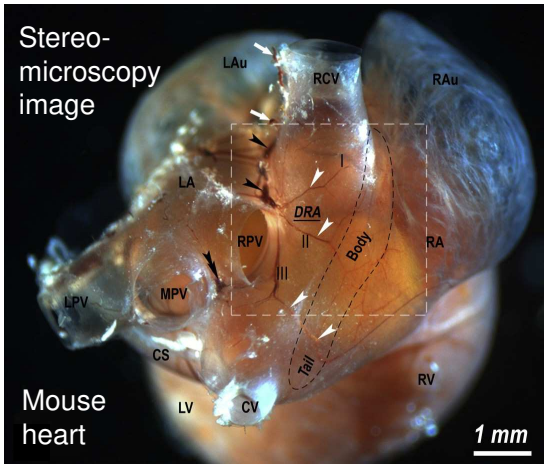
Micrographs may be taken with a digital camera.

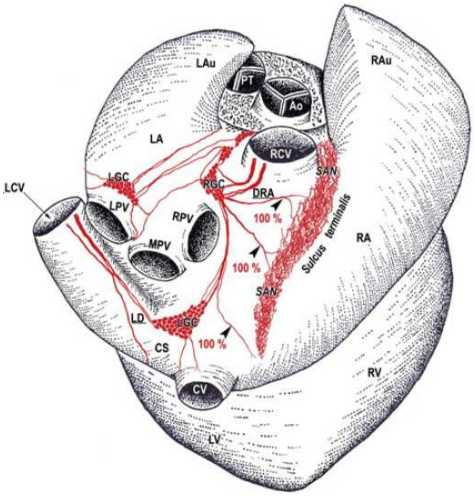
However, the digital image is NOT stereoscopic as only one of the two light paths (dashed red lines) in the objective is used to capture it.

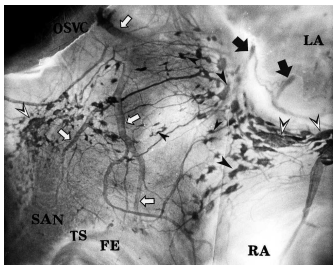


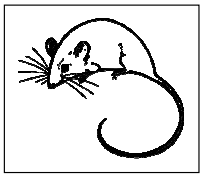
Hookworm infection (one of helminthiases) is encountered in both man, and cats or dogs.

Entering via skin, the milimeter-sized hookworms end up in faeces (stools).









LGC = Left ganglionic cluster
RGC = Right ganglionic cluster
SAN = Sino-atrial node

Contact-microscopy image for enhanced visualization of nerves stained for acetylcholine esterase

Drawing the nerves, ganglions and plexuses observed under the microscope is often helpful.

Their architecture and relationships can be more easily understood than in a micrograph (“raw image”).

To this end, contact microscopy is conveniently employed.

Contact microscope is equipped with a special objective whose protruding front lens

flattens a small part of the heart surface and keeps it in perfect focus.

(Teacher-only information)

Barskii I.Y., Polekov N.M., Jakubenas V.A.V. (1976)

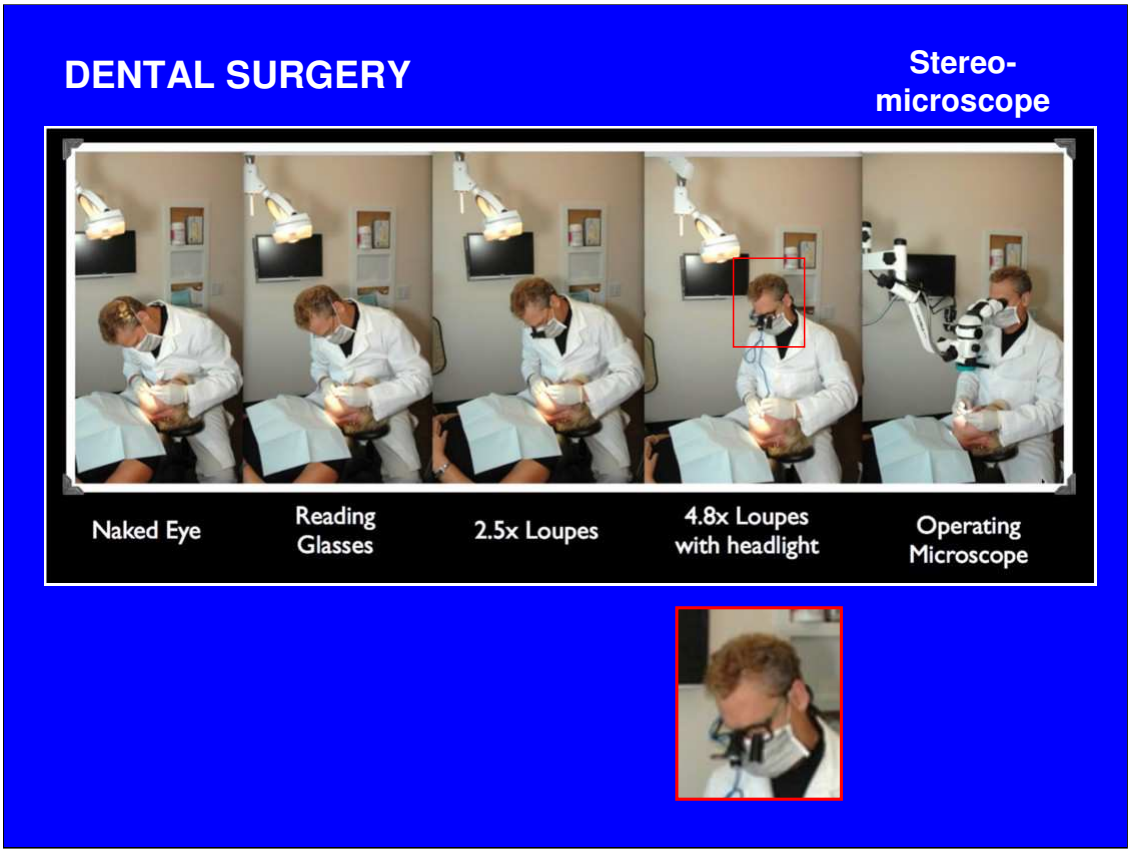
Contact microscopy.

Medicina, Moscow.

Quoted in:

Pauza et al. (1999) *Anatomical Record* **255**: 271-294

https://doi.org/10.1002/(SICI)1097-0185(19990701)255:3<271::AID-AR4>3.0.CO;2-2



Operating microscope represents a special category of a stereomicroscope.

Typically, it is fixed to a stand or mechanical arm.

It provides greater comfort e.g. to a dentist who no longer has to use magnifying glasses or loupes mounted on his head.

As the image quality is better surgery is done with greater confidence.

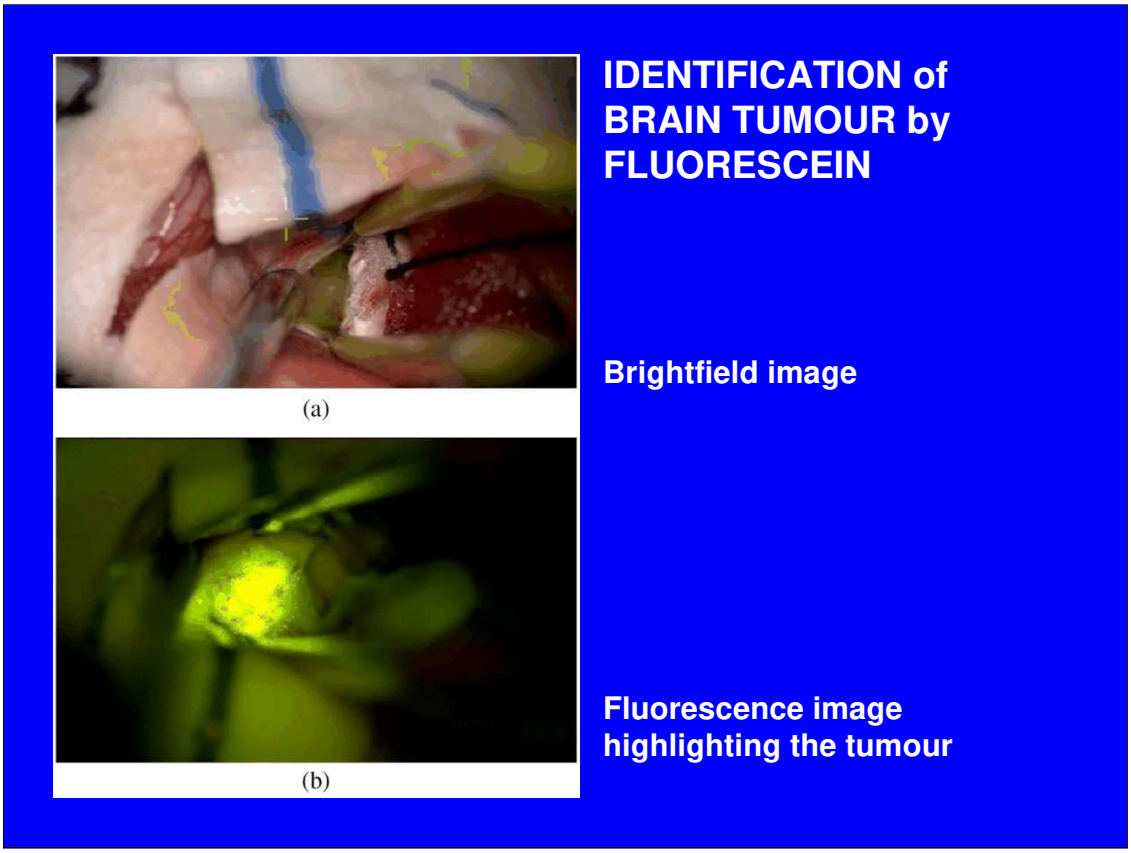
IMAGE from (not original source):

Ma L. & Fei B. (2021)

Comprehensive review of surgical microscopes: technology development and medical applications.

Journal of Biomedical Optics **26**(1): 010901.

https://doi.org/10.1117/1.JBO.26.1.010901



Brain tumour identification is aided by injecting fluorescein into the blood stream. As the blood-brain barrier is compromised in tumours fluorescein enters them. This aids their identification during surgery.

IMAGE from (not original source):

Ma L. & Fei B. (2021)

Comprehensive review of surgical microscopes: technology development and medical applications.

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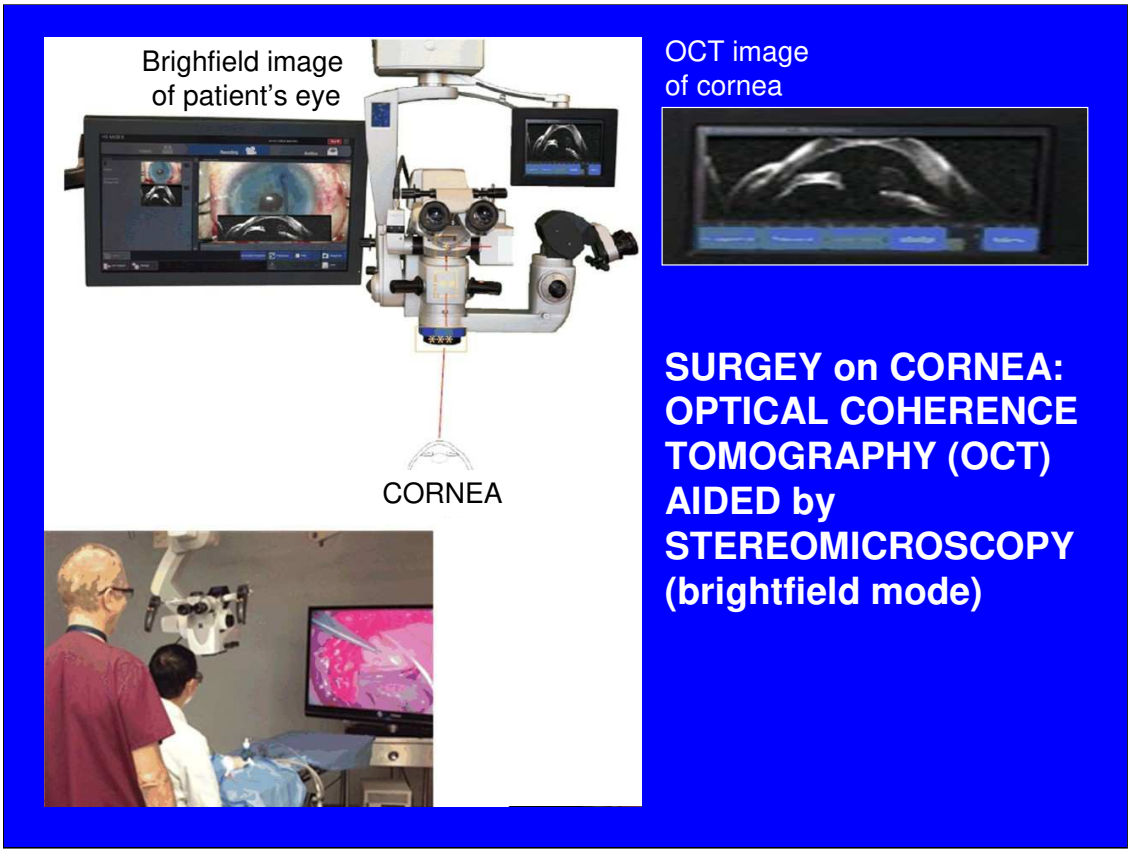
https://doi.org/10.1117/1.JBO.26.1.010901



Surgery on cornea is difficult because it is transparent and hard to see.

A special imaging technique called Optical Coherence Tomography (OCT) is employed to visualize it.

However, the rest of the eye is invisible in the OCT image.

Stereomicroscopy is thus used to obtain morphological context,

i.e., to properly see the rest of the eye and navigate during surgery.

IMAGE from (not original source):

Ma L. & Fei B. (2021)

Comprehensive review of surgical microscopes: technology development and medical applications.

Journal of Biomedical Optics **26**(1): 010901.

https://doi.org/10.1117/1.JBO.26.1.010901

Lecture #3

MODULATION and INTERFERENCE MICROSCOPY

MODULATION RELIEF-CONTRAST SETUP (schlieren imaging)

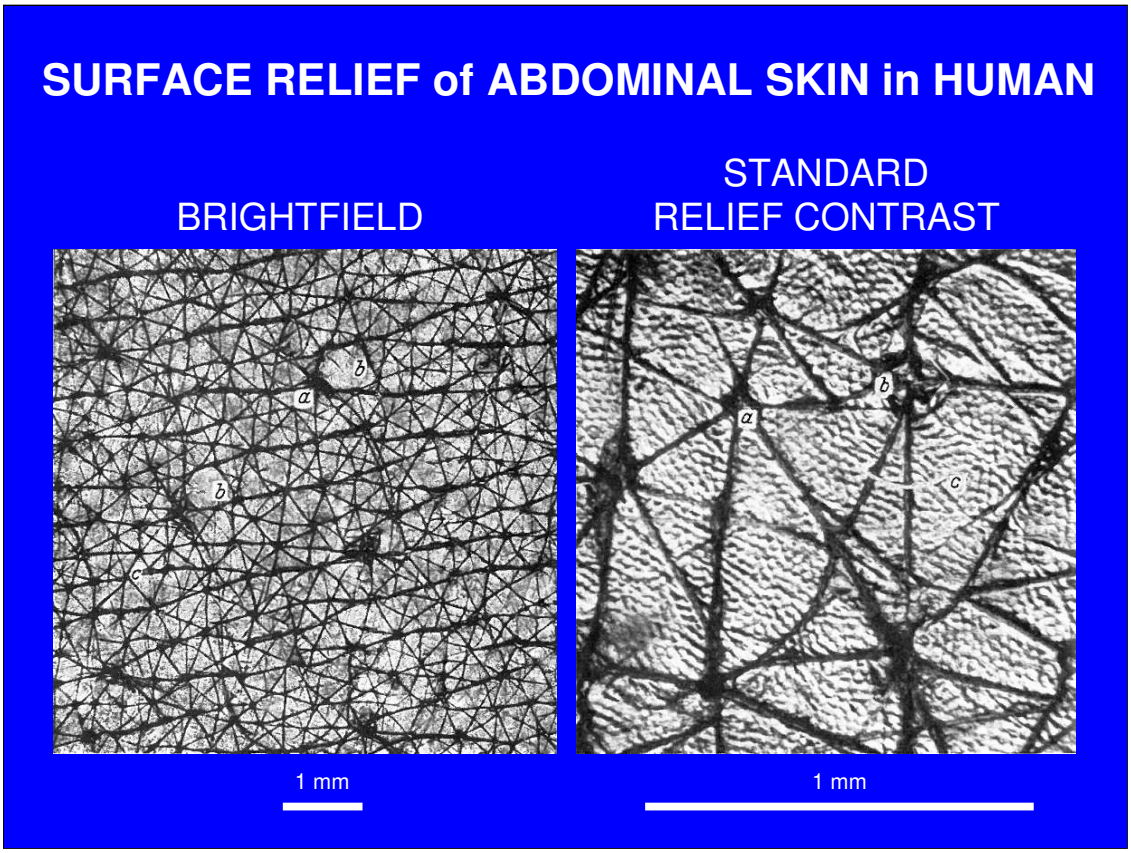
A simple adaptation of a substage condenser (B) for standard and modulation relief-contrast microscopy

Standard Relief Contrast = Relief diaphragm (RD) only
Modulation Relief Contrast = Relief diaphragm (RD) + Modulator (M)
“Schlieren” (from German) = streaks (refractive index variations)

The “relief diaphragm” (RD) is inserted into the condenser to produce STANDARD relief contrast.

A similar asymetric diaphragm (so-called modulator, M) may additionally be used just above the objective lens to produce MODULATION relief contrast.

The latter modality is often referred to as SCHLIEREN contrast (“schieren” in German = “streaks” = dark/bright regions in the image, i.e., the shading patterns serving as visual cues to depht structure).



This is how a replica from human skin looks like.

Epidermal cells (ca 20 to 30 µm in diametre) are highlighted by the relief-contrast illumination.

Reprinted from:

Horstmann E. (1957)

Haut und Sinnesorgane.

In: Handbuch der mikroskopischen Anatomie des Menschen (von Mollendort W. & Bartmann W., eds.), vol. III, Pt. 3 (Horstmann E. & Dabelow A., eds.), pp. 1-276.

Springer, Berlin.

Original source listed as (**to be verified**):

Wolf J. (1940)

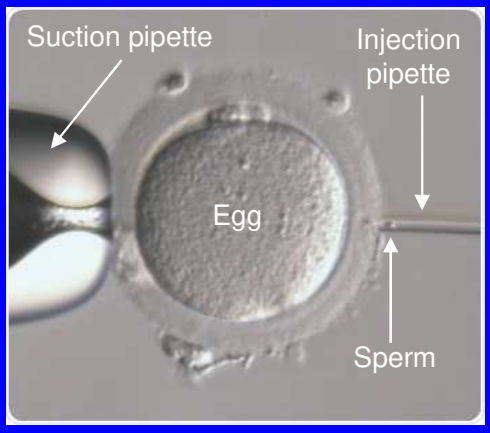
Das Oberflächenrelief der menschlichen Haut.

Zeitschrift fur mikroskopisch-Anatomische Forschung **47**: 351-400

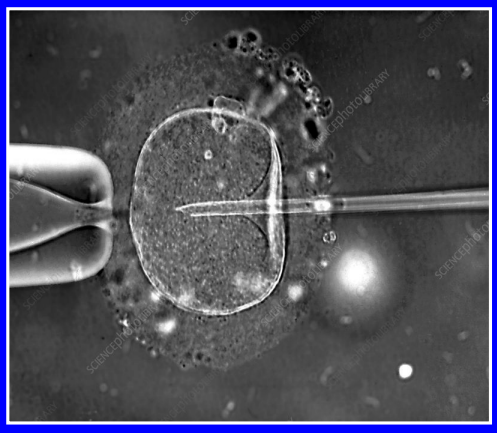
(= Jahrbuch für Morphologie und Mikroskopische Anatomie, Pt. 2)

ISSN: 0044-3107

IN VITRO FERTILIZATION



HOFFMAN MODULATION CONTRAST



BRIGHTFIELD

VIDEO
https://www.youtube.com/watch?v=D4VHJC2uS_A

Hoffman Modulation Contrast (HMC) microscopy is often found at in vitro fertilizatin (IVF) clinics as it is very convenient in visualizing human oocytes (ca 100 µm in diametre).

The oocyte (egg) is held in place by a suction pipette.

The injection pipette introduces the sperm into the oocyte.

The quasi-3D image HMC microscopy generates makes it easier for the technician to properly position the injection pipette relative to the oocyte (otherwise, the pipette may be above or below the oocyte).

This is owing to shading (the bright and dark areas) in the image, serving as a visual cue to depth structure, i.e., aiding the perception of depth.

A brighfield image lacking the visual cue to depth structure is shown for comparison.

Ooocyte in 3D:

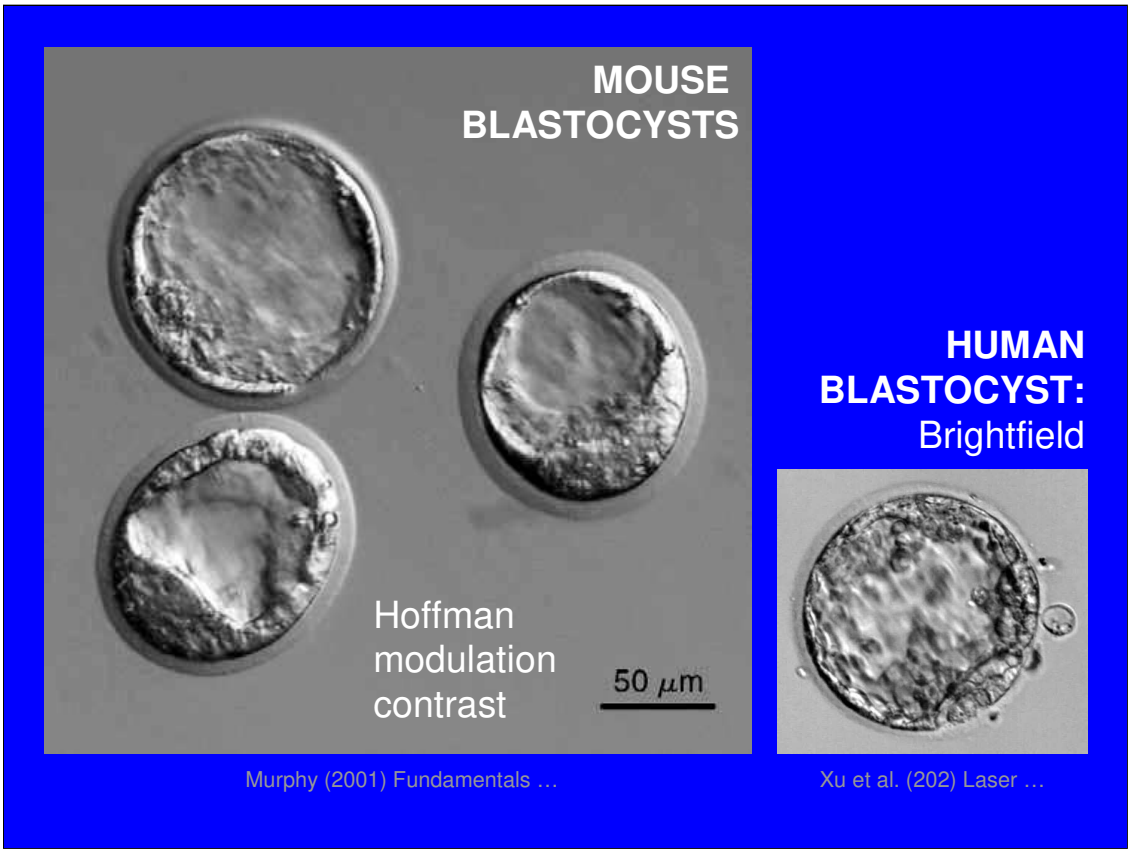
https://www.news-medical.net/whitepaper/20160321/Intracytoplasmic-Sperm-Injection-Using-Eppendorf-Transferman-4m-Micromanipulator.aspx

Ooocyte in non-3D:

https://www.sciencephoto.com/media/288776/view

Another sperm-injection video

https://www.youtube.com/watch?v=IQujLI-ArMY



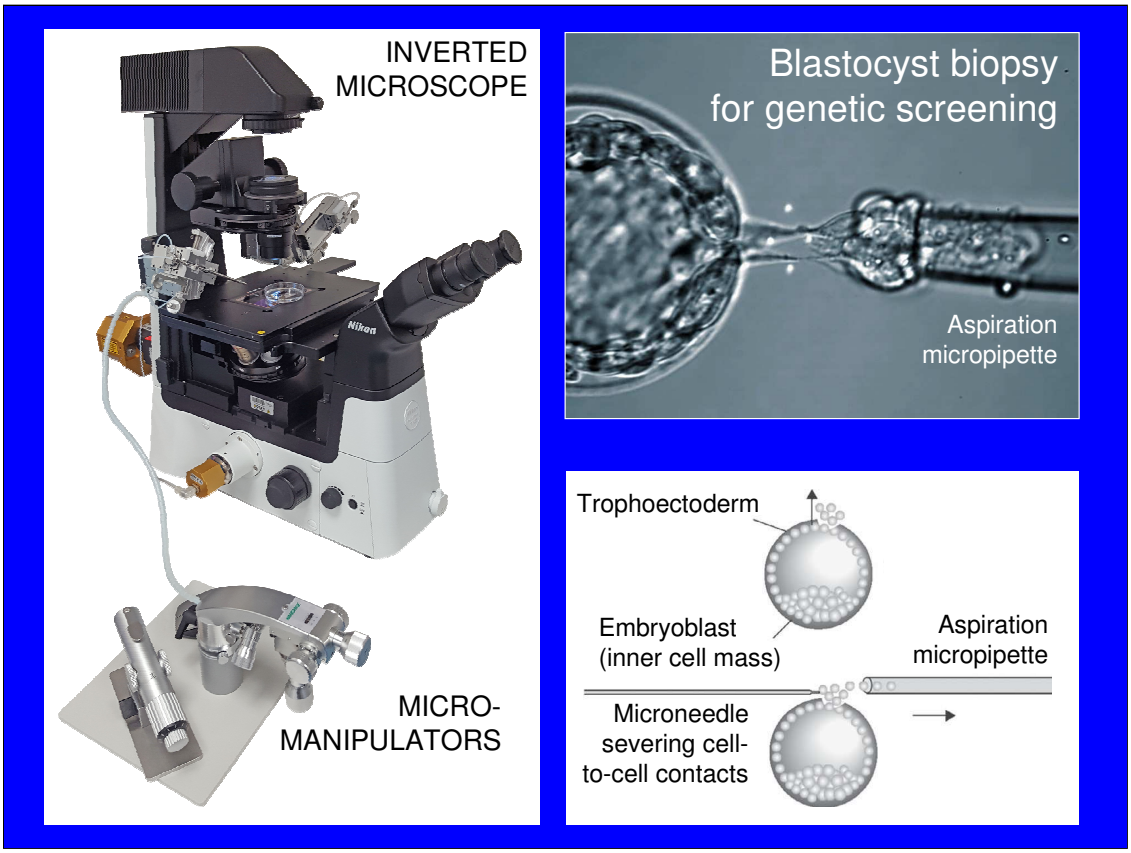
Hoffman Modulation Contrast (HMC) image of mouse blastocysts.
The blastocyst structure is much more obvious in the HMC image than in the brightfield image.
Note the strong contrast (in the form of 3D rendering) even in the absence of any staining.

IMAGE SOURCE(s):

Mouse blastocysts = Fig. 10-10 in:
Murphy D.B. (2001)
Fundamentals of light microscopy and electronic imaging.
Wiley, New York.
ISBN: 047125391X
www.biology.uoc.gr/courses/BIOL493/documents/book.pdf
Credit: image courtesy of Mahmud Saddiqi, Johns Hopkins University

More recent edition of Chapter 10:
https://doi.org/10.1002/9781118382905.ch10

Human blastocyst = Fig. 1 in:
Xu W. et al. (2021)
Laser-assisted hatching in lower grade cleavage stage embryos improves blastocyst formation: Results from a retrospective study.
Journal of Ovarian Research 14: Art. 94
https://doi.org/10.1186/s13048-021-00844-7



Genetic screening of the blastocyst requires that a few cells are taken out from it by biopsy.

These should come only from the **trophoectoderm** so that the **embryoblast (inner cell mass)** critical for proper embryonic development is left intact.

The microscope employed in the *in vitro* fertilization (IVF) and other manipulations with the oocyte or embryo is the so-called “inverted microscope”, i.e., objectives are placed below the specimen stage.

This makes enough room on the specimen stage for a Petri dish with oocytes/embryos, and suction (holding) / injection pipettes.

Microscope and micrographs:

https://www.microscope.healthcare.nikon.com/resources/focus-on/ivf

Drawing:

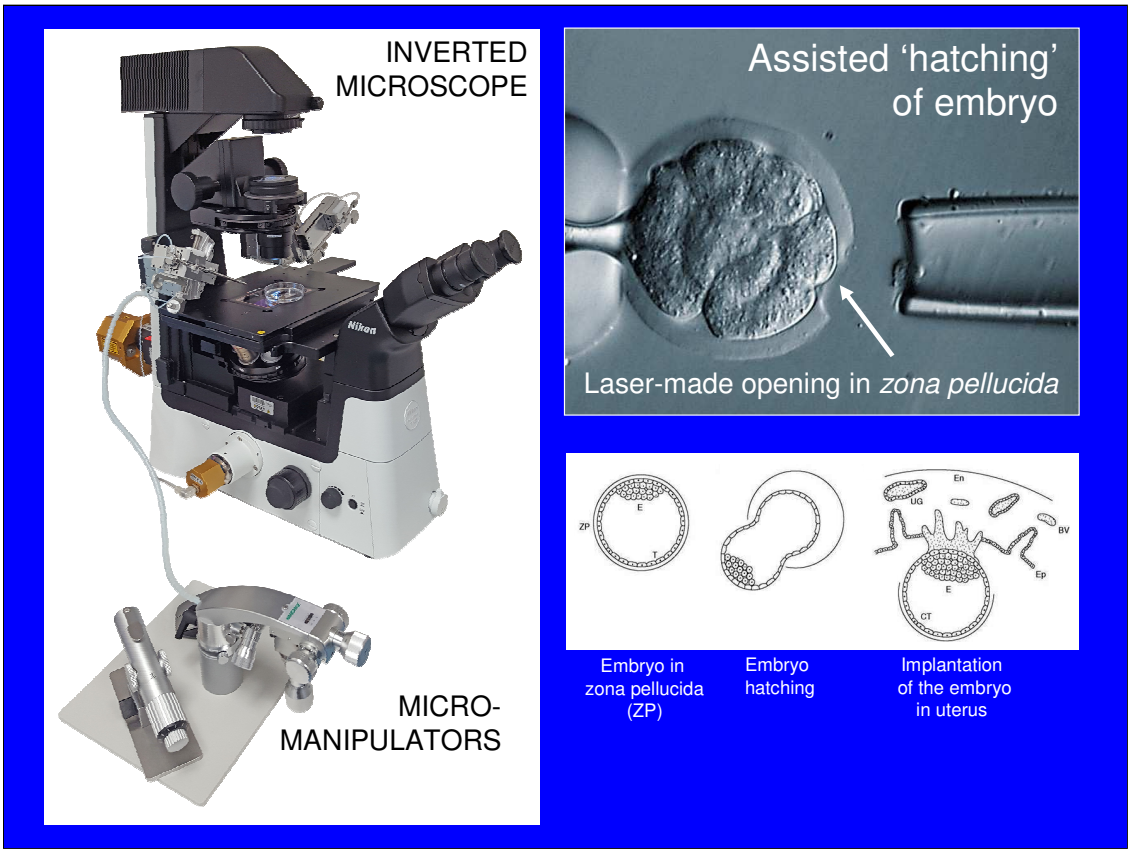
Chapter 13: Micromanipulation techniques (pp. 284-310).

In: Elder K. & Dale B. (2019)

In-vitro fertilization (4th ed.).

Cambridge University Press, UK.

https://doi.org/10.1017/9781108611633.014



In artificially fertilized oocytes, the *zona pellucida* layer is frequently too hard to enable easy release ('hatching') of the embryo required for its successful implantation in the endometrium of uterus.

'Hatching' can be facilitated by making a small opening in the *zona pellucida*. This can be achieved by laser.

BV, blood vessel;

CT, cytotrophoblast;

E, embryoblast ("inner cell mass")

Ep, epithelium;

En, endometrium;

T, trophoblast;

UG, uterine gland

ZP, zona pellucida

DETAILS:

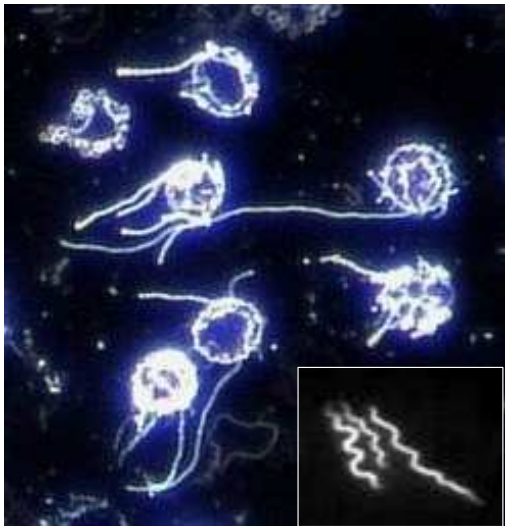
Chapter 13: Micromanipulation techniques (pp. 284-310). In: Elder K. & Dale B. (2019) In-vitro fertilization (4th ed.). Cambridge University Press, UK. https://doi.org/10.1017/9781108611633.014

Microscope and micrograph:

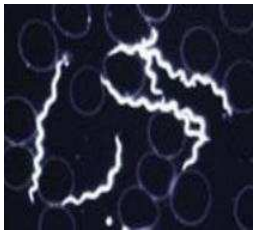
https://www.microscope.healthcare.nikon.com/resources/focus-on/ivf

Lecture #4
PHASE-CONTRAST and DARKFIELD MICROSCOPY

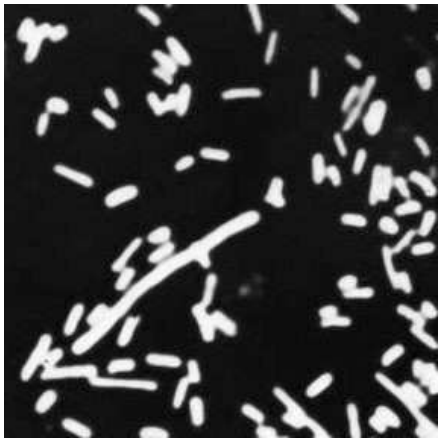
PATHOGENIC BACTERIA in DARKFIELD MICROSCOPY



BORRELIA-infected erythrocytes
(Lyme disease)



Treponema pallidum
(syphilis)



SHIGELLA
(dysenteria)

Darkfield microscopy is very sensitive to detect cell membranes, granules or bacteria

(i.e., objects that are very small or thin).

It does not visualize well the cell interior, even in eukaryotic (bigger) cells.

Generally, only cell membranes (outline of the cells) are well visible.

This doesn't make any difference in very small cells such as bacteria.

Borrelia are bacteria causing the Lyme disease (borreliosis).

They belong to the *Spirochaeta* group.

Spirochaeta are bacteria of spiral shape, and also include *Treponema pallidum* causing syphylis, and *Leptospira* causing leptospirosis.

Shigella sp. belong to another group of bacteria, and causes dysenteria.

IMAGE SOURCES:

Borrelia: http://microbeon.com/

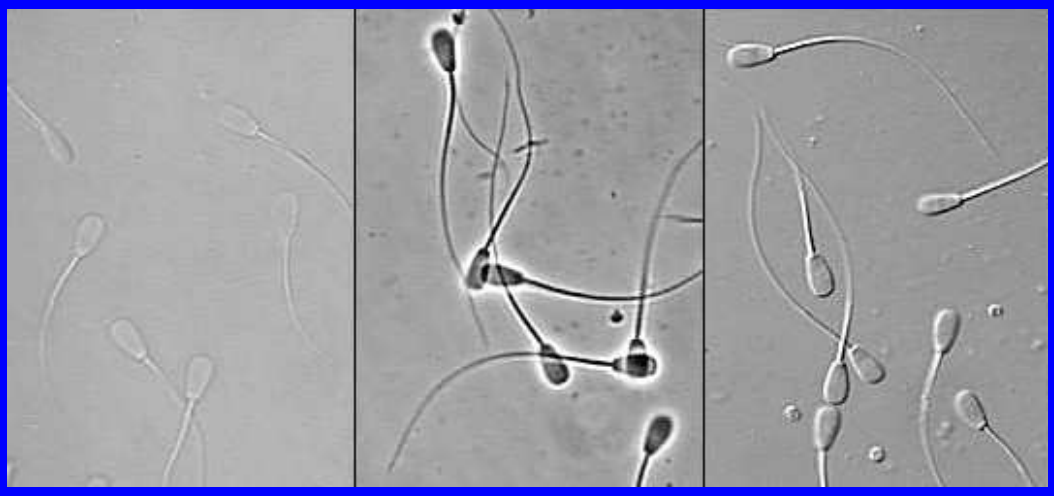
Detail of Borrelia:

https://microbeonline.com/dark-field-microscopy-principles-use-advantages-and-limitations/

Treponema pallidum: https://www.slideshare.net/doctorrao/syphilis-basics

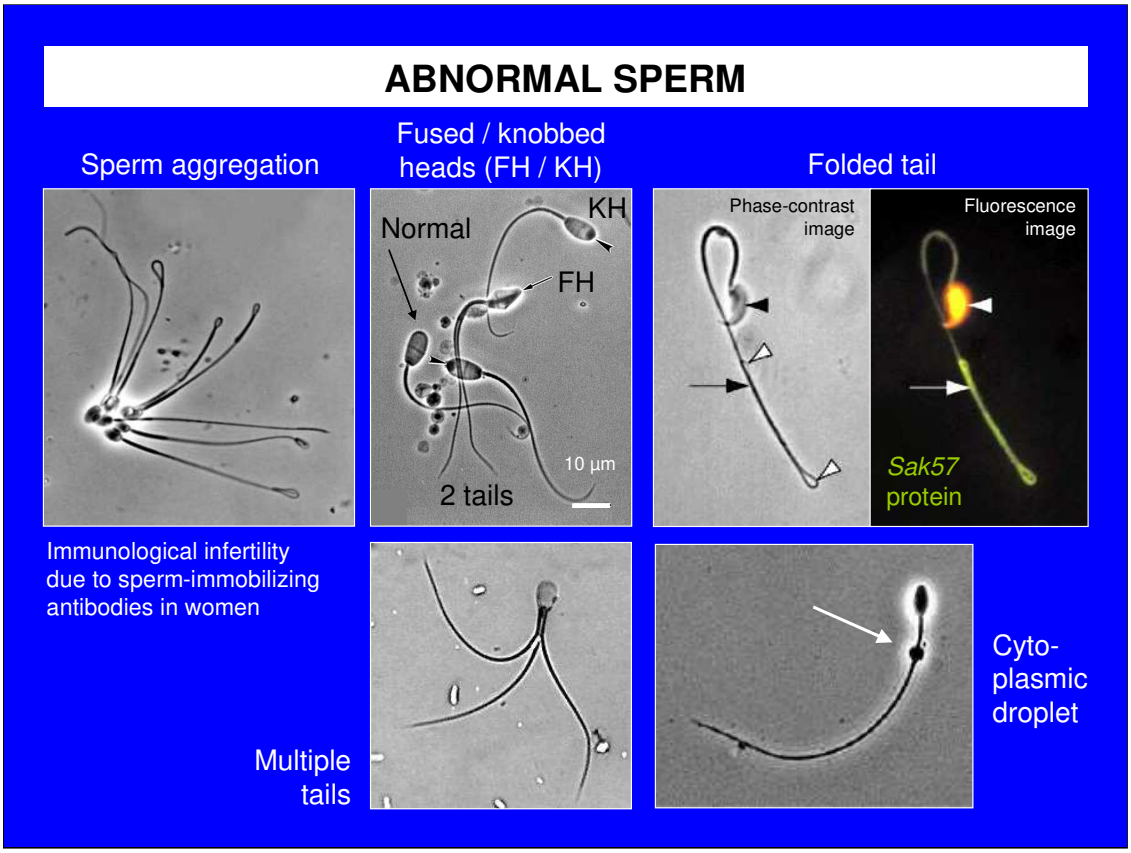
Shigella: https://phil.cdc.gov/Details.aspx?pid=22229

ASSESMENT OF SPERM CELL QUALITY



BRIGHTFIELD PHASE CONTRAST DIC NOMARSKI

Much like the buccal epithelial cells, sperm cells are typical optically thin cells, and as such are best visualized by phase-contrast microscopy.



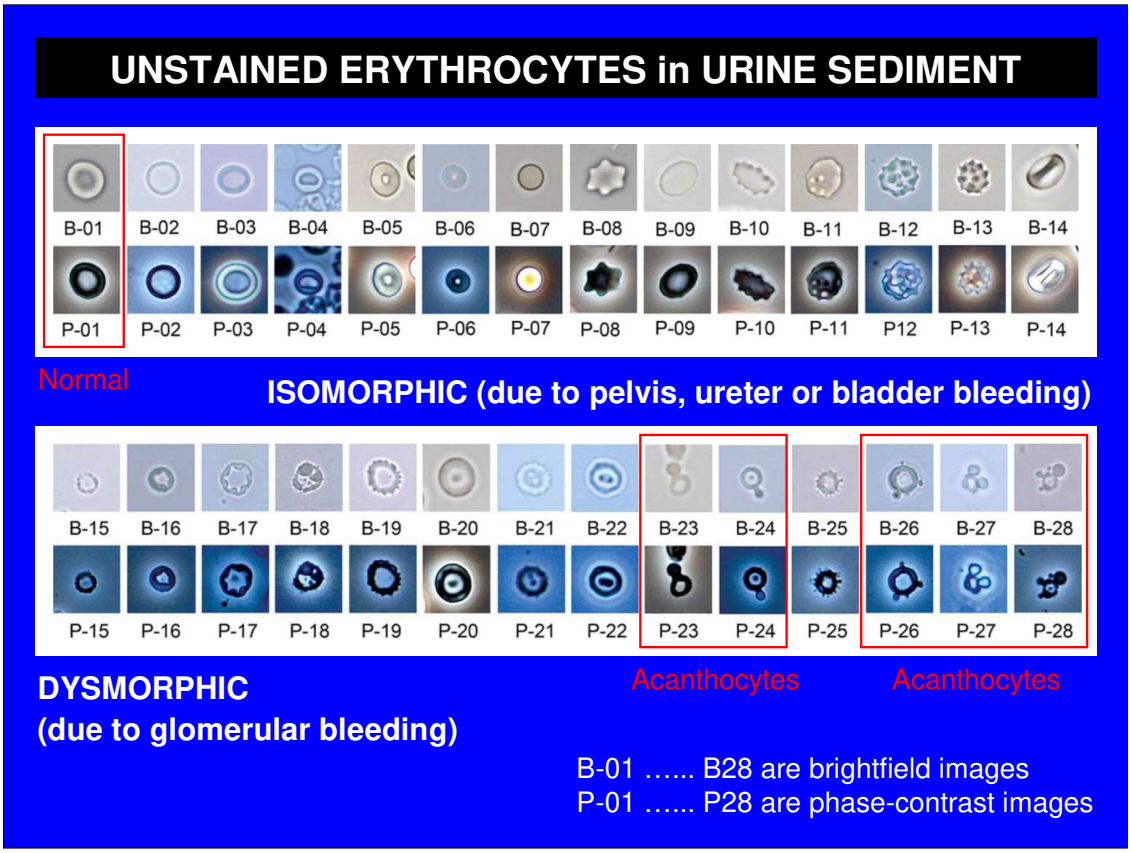
Abnormal sperm include:
-Aggregation due to immunological infertility,
-Fused or knobbed heads (two fused heads imply two tails)
-Folded tail (due to *Sak57* protein identified by fluorescence microscopy)
-Multiple tails
-Cytoplasmic droplets on the tail
In all cases, sperm motility is impaired.

Sperm aggregation:
https://doctorlib.info/anatomy/atlas-clinical-andrology/6.html

Fused heads:
VEERAMACHANENI et al (2001) Long-Term
https://doi.org/10.1093/humrep/16.5.979

Folded tail:
AKUTSU et al (2001) Offspring
https://doi.org/10.1095/biolreprod64.1.249

Cytoplasmic droplet:
PUKAZHENTHI et al (2010) Ejaculate
https://doi.org/10.2164/jandrol.110.011833



Occurence of acanthocytes (cells with prominent blebs) in the urine sediment represents the most conclusive proof of glomerular bleeding.

Phase-contrast images of unstained erythrocytes are usually of better quality than the brightfield ones.

However, caution is due in case of optically thicker cells exhibiting profound 'halo' artifacts (P-13 and P-14).

There are three possibilities [1-3] to tackle this issue ([2,3] not yet tested on erythrocytes):

[1] Brightfield microscopy (often with partially closed condenser diaphragm to improve contrast and increase the depth of field); see echinocytes (B-13) and knizocytes (B-14).

[2] Conventional (i.e., non-apodized, non-relief) phase contrast combined with refracting index matching (see slide #20).

[3] Apodized phase contrast (slide #21 and #23) or relief phase contrast (slide #15).

Ideally, DIC Nomarski or Hoffman modulation contrast (HMC) microscopy should be carried out as well to better intepret cell shapes.

An expert on dysmorphic erythrocytes (acanthocytes, knizocytes, kodocytes, stomatocytes) at the Vinohrady teaching hospital attached to the Third Faculty of Medicine: Prof. Ivan Rychlík (Head of Internal Medicine).

Useful references from his group:

Rychlík I. (2008) Pacient s hematurií.

Interní medicína pro praxi **10** (10):440-443.

Horáčková M. & Šafářová R. (2006)

Močový sediment: Vyšetřovací technika a interpretace nálezu klinických nefrologem.

Aktuality v nefrologii (volume not numbered, issue 4/2006): 118-127.

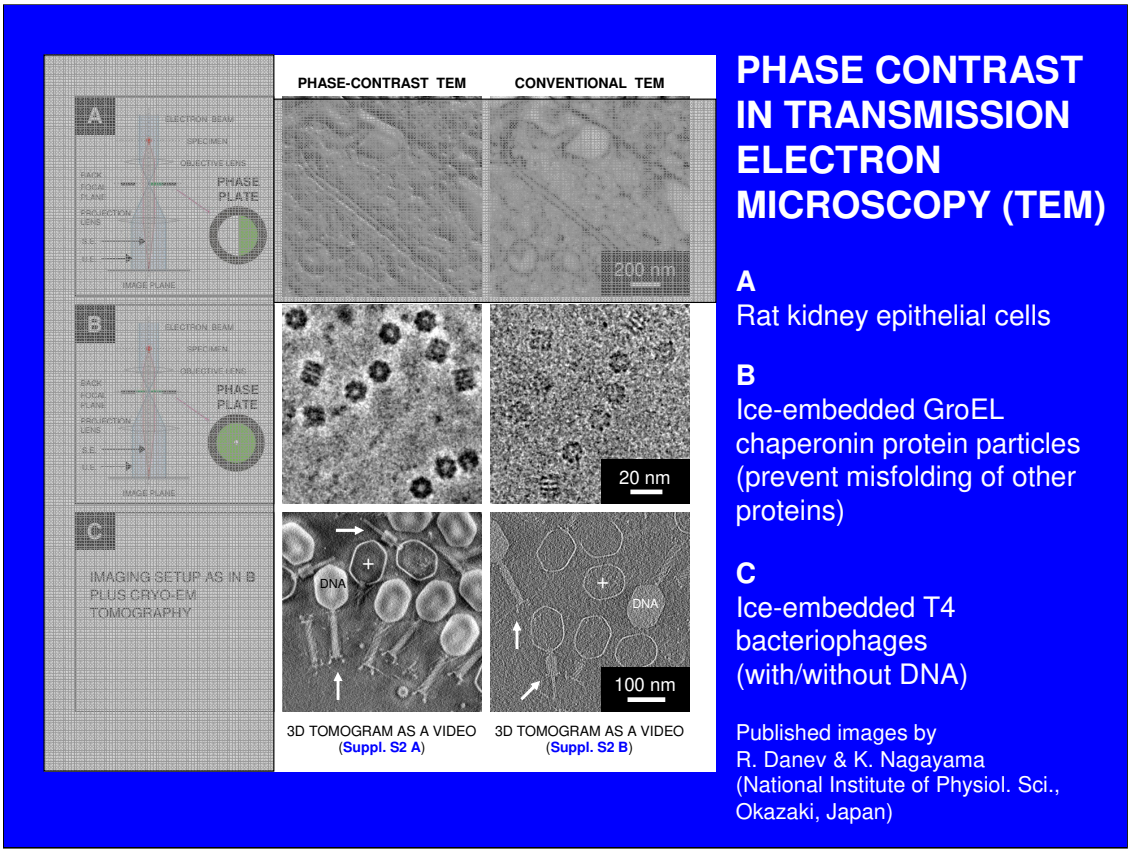
Micrographs from:

Chu-Su Y. et al. (2017)

Enhancing the detection of dysmorphic red blood cells and renal tubular epithelial cells with a modified urinalysis protocol.

Scientific Reports **7**:40521.

https://doi.org/10.1038/srep40521

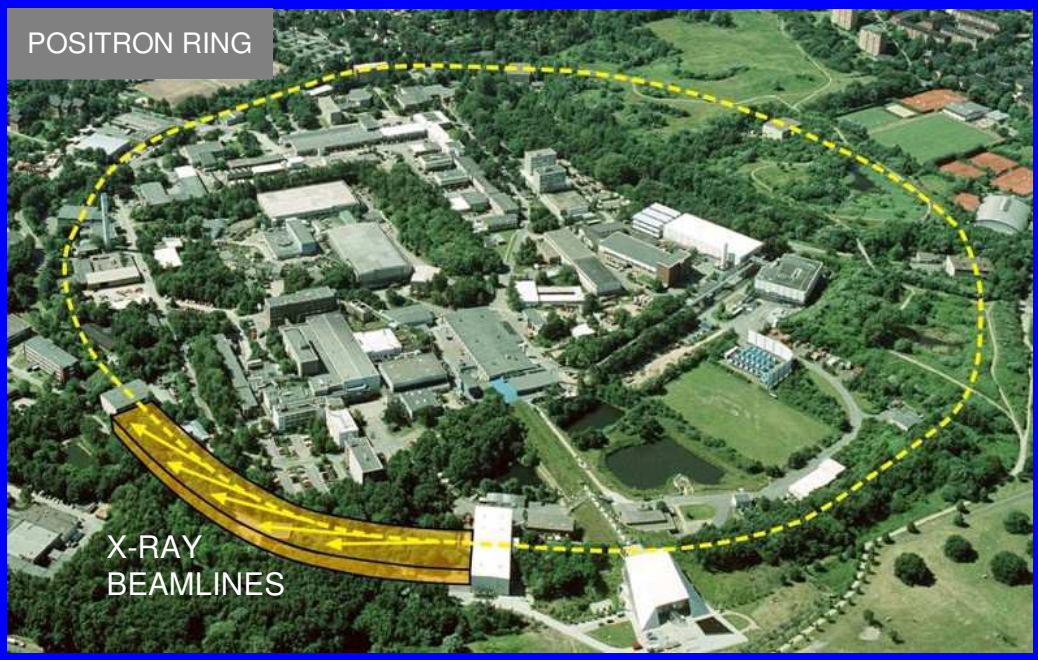


Phase-contrast microscopy is also available in electron microscopy (EM).

While not very useful in studying whole cells it is excellent in visualizing very thin (small) objects such as protein particles if these cannot be stained. This is so when examining them in their close-to-native state, i.e., when they are ice-embedded.

Observation of cells/proteins in solution is not easily possible in EM as the evaporation of the liquid would impair high vacuum necessary for the electrons 'rays' to correctly form the image. Magnetic lenses are used instead of glass ones.

X-RAY ‘MICROSCOPE’ @ HAMBURG SYNCHROTRON



Synchrotron is an elementary-particle (typically positron) accelerator called synchrotron.

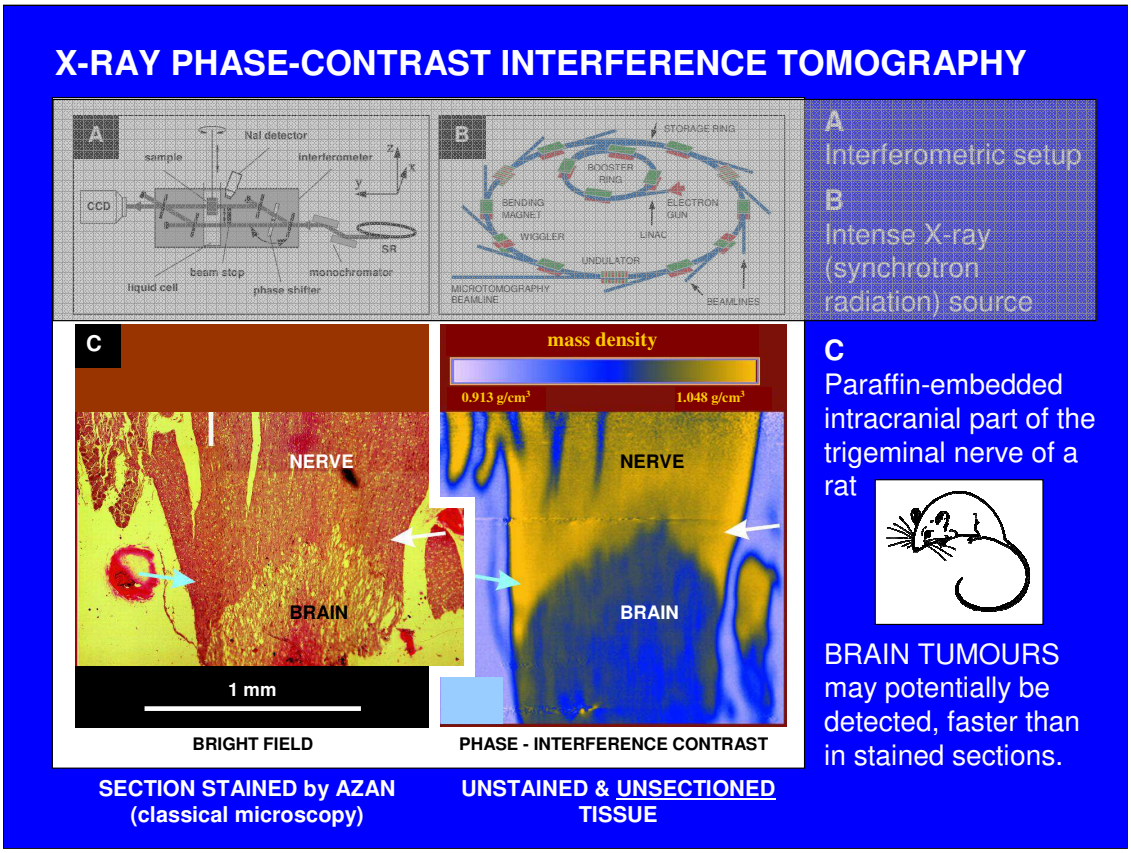
It is a ring several hundred meters in diametre, and the one shown here is in Hamburg.

Not every country can afford to build it (there is none in the Czech Republic).

Very intense X-rays are generated around its perimeter, and directed into experimental stations called beamlines.

These are multiple laboratories, each using the X-rays for a different purpose.

One of the biggest synchrotrons is in Japan, and has 96 beamlines.



A special type of interference microscopy is available in the X-ray wavelength range.

It is a very unusual X-ray machine capable of visualizing soft tissues in good contrast, but not hard tissues (bones).

For it to be functional, a single-wavelength (monochromatic) X-ray beam must first be generated.

This would be impossible or very difficult using an ordinary X-ray machine.

So-called called synchrotron is used for this purpose.

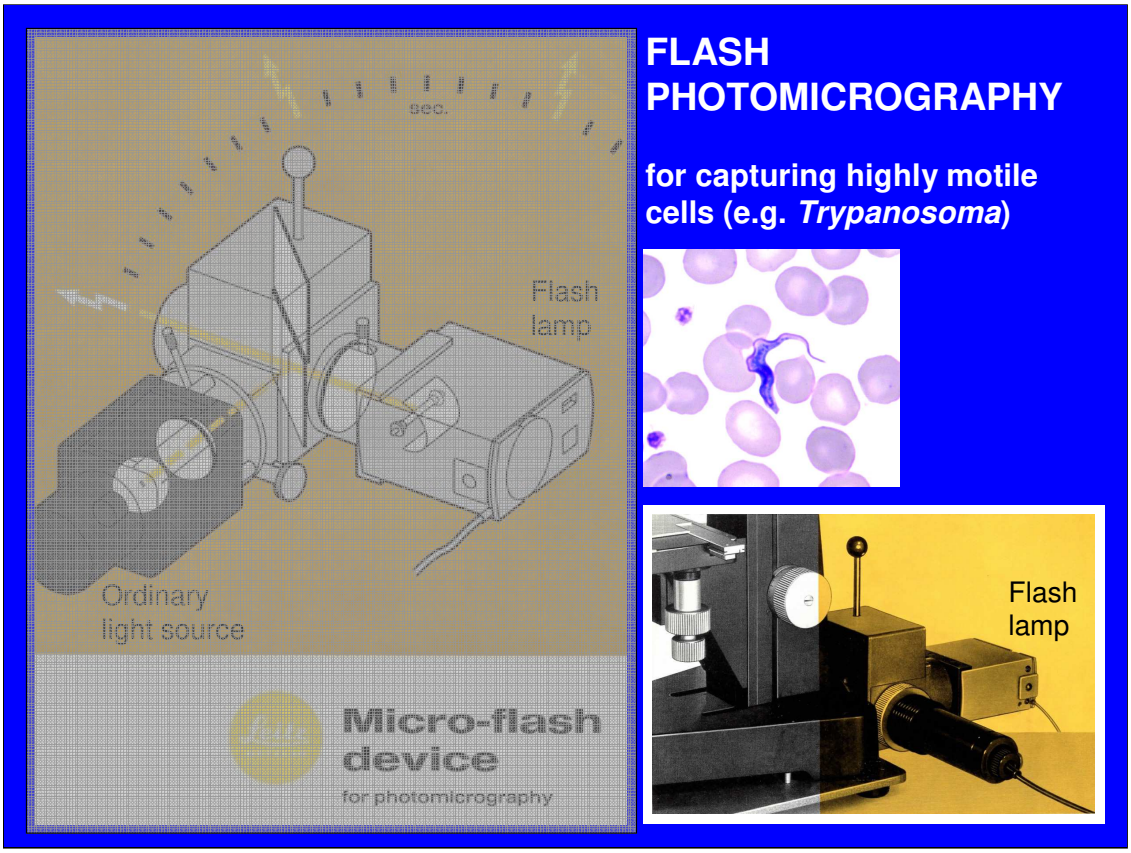
Monochromatic X-rays generated by the synchrotron are directed towards a piece of tissue, in this case rat brain and trigeminal nerve of a rat.

The brain-nerve border is visualized more clearly (C-right) than in sectioned & stained tissue (C-left).

Brain microtumours may potentially be detected without sectioning and staining, thus speeding up diagnosis.

Images:

Lecture #5
PHOTOMICROGRAPHY
& DIGITAL IMAGES



Highly motile cells such as *Trypanosoma*, the cause of the sleeping sickness, are hard to photograph unless fixed.

Micro-flash device is available for such purposes, and accommodates:

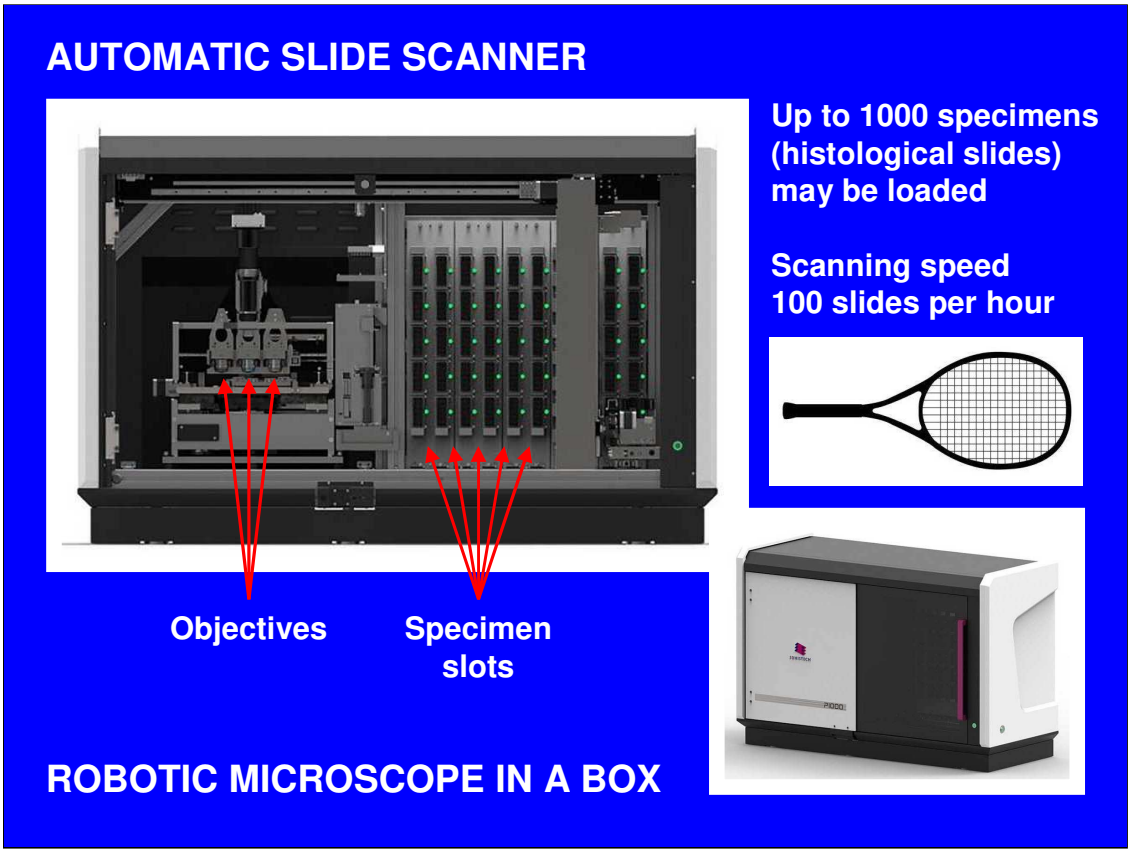
1. Ordinary light bulb for regular observation/photography of fixed specimens

2. Flash lamp to photograph highly motile cells

“Leitz” is the original designation of the “Leica” company making microscopes and their accessories.

It was named after its founder (Ernst Leitz) and was based in Wetzlar (Germany), same as Leica now.

Leitz (Germany), Reichert (Austria), Wild (Switzerland) and American Optical (USA) merged to become Leica.



https://www.3dhistech.com/research/hardware/

This type of scanner (a more simple model) is available at the Pathology Department of the Third School of Medicine.

Once you load the specimens into the scanner you can go playing tennis, or go home.

Upon coming back, hundreds or thousands of images will be waiting for you.

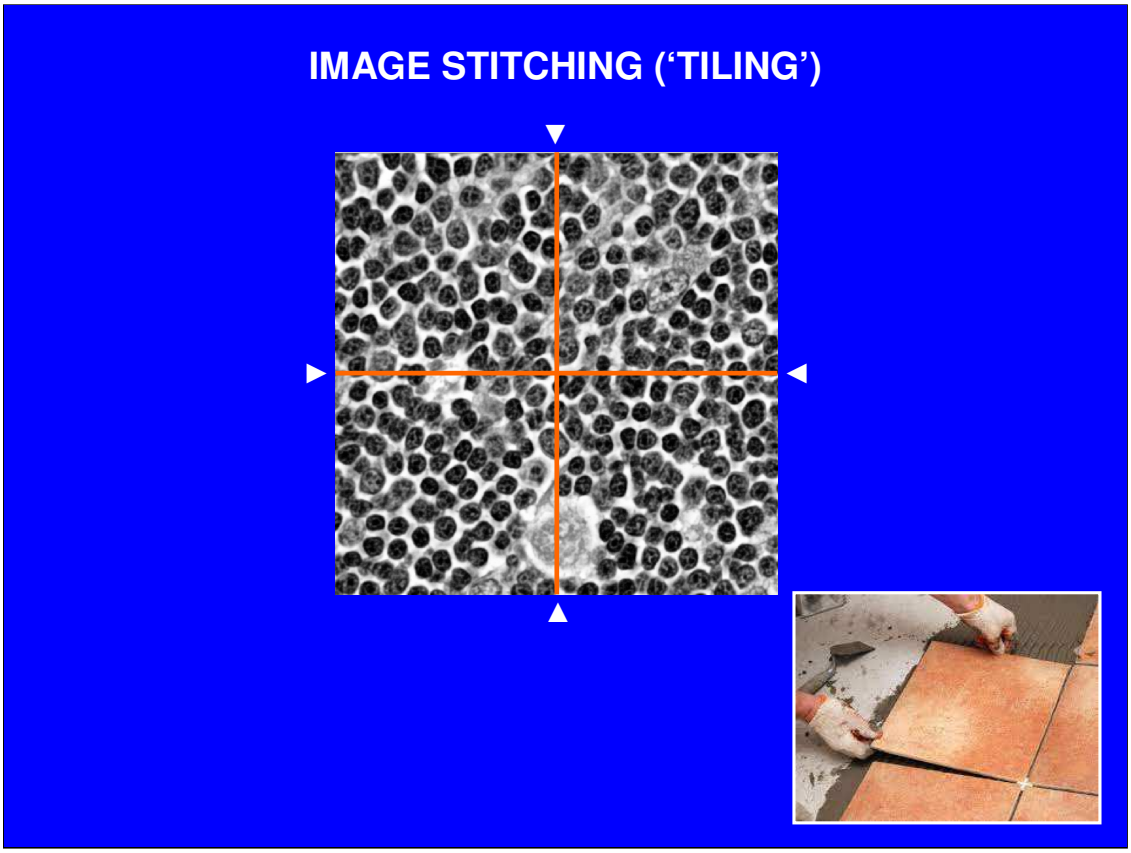
Several other companies offer automated (robotic) slide scanners

(Aperio Technologies, Carl Zeiss MicroImaging, Hamamatsu Photonics, Olympus Optical, Ventana).

Their characteristics are listed in Supplement S2 to Chapter 14 by Riley et al. (2020):

https://experiments.springernature.com/articles/10.1007/978-1-0716-0428-1_14

(see “Supplementary Information” ….. Table S2)

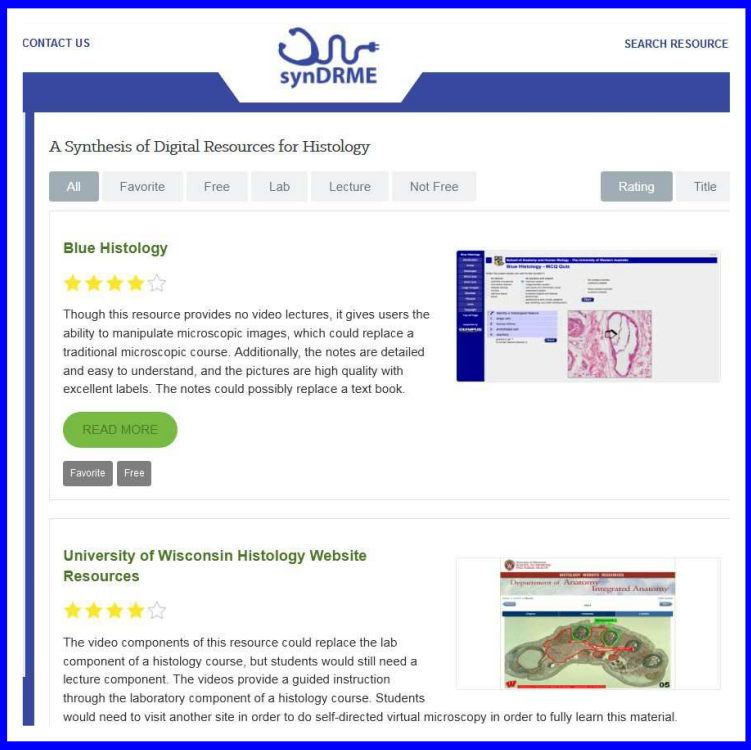


Individual images from the automatic slide scanner are automatically stitched together by a special software.

Often, the individual images are taken to overlap a bit as it facilitates the stitching process.

‘Tiling’ is an alternative term borrowed from the building industry, as it reminds of laying floor tiles.

http://www.syndrme.org/index.php/histology



DIGITAL IMAGES in HISTOLOGY EDUCATION

22+ teaching websites

Electronic highlighting

Dry-run (mock) tests in some of them

Ranked 1 to 5 (by yellow stars)

http://www.syndrme.org/index.php/histology

A portal of 22+ histology-teaching websites around the world (mostly USA).

- Electronic highlighting of the structures of interest.
- Some of them enable dry-run (mock) specimen tests.
- Ranked by quality/popularity (1 to 5 yellow stars).

Lecture #6
HISTOLOGICAL ILLUSTRATIONS

Frank H. Netter (1906-1991) was a medically-educated academic illustrator in USA.

His illustrator career started with the CIBA Pharmaceutical Company.

They commissied from him a small illustration of heart to promote the sale of digitalis.

Physicians liked it enormously, and soon Netter was asked to draw other organs for CIBA.

He is best known for “Netter's Atlas of Human Anatomy” on which he worked for most of his life:

Netter drew ca 100 illustrations per year, in total ca 4,000.

https://en.wikipedia.org/wiki/Frank_H._Netter

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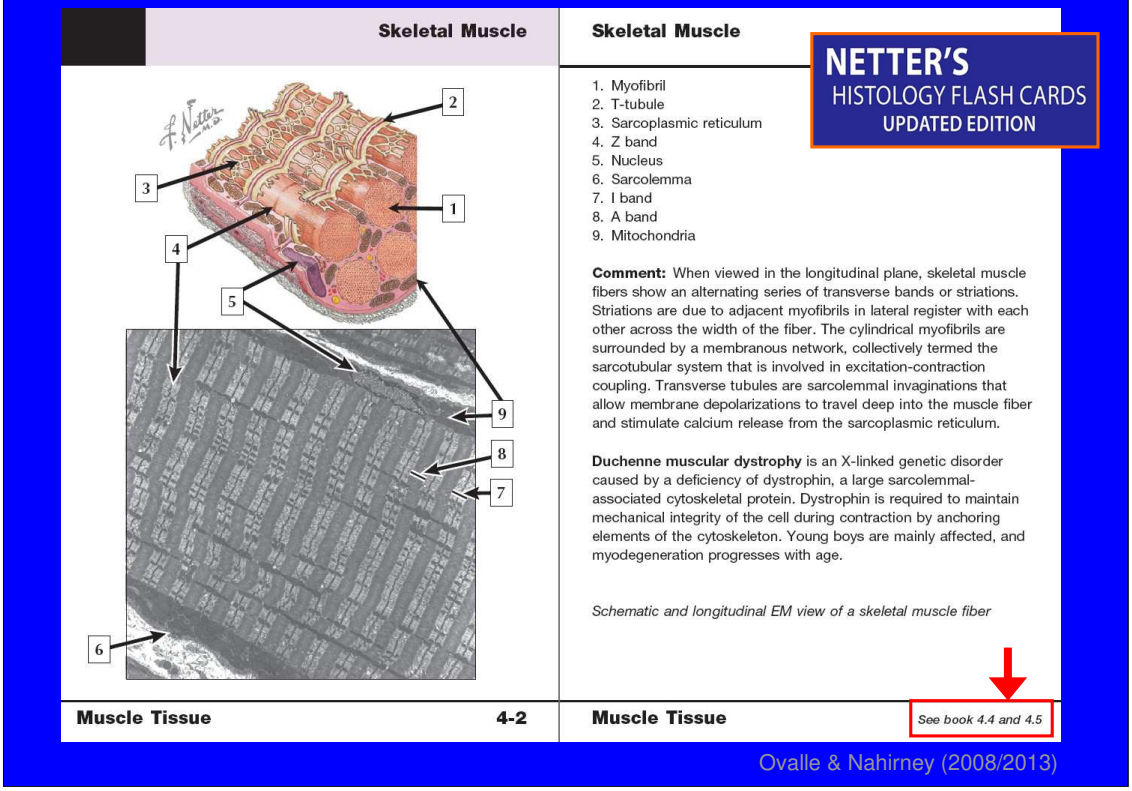
https://dangerousminds.net/comments/the_morbidly_beautiful_medical_illustrations_of_dr._frank_netter

HISTOLOGY PRIMER + REVIEWING before EXAMS



Ovalle & Nahirney (2008/2013)

This book is best as a quick introduction to histology, and then for reviewing before exams.

Each topic is neatly summarized on two pages (a single “flash card“).

1 “flash card“ = 1 illustration page + 1 text page.

At the bottom of the text page, reference is given to a textbook (Netter’s Essential Histology).

The Flash Cards represent a condensed version of the textbook.

Ovalle W.K. & Nahirney P.C. (2008)

Netter’s histology flash cards.

Saunders (Elsevier), Philadelphia.

ISBN: 978-1455776566

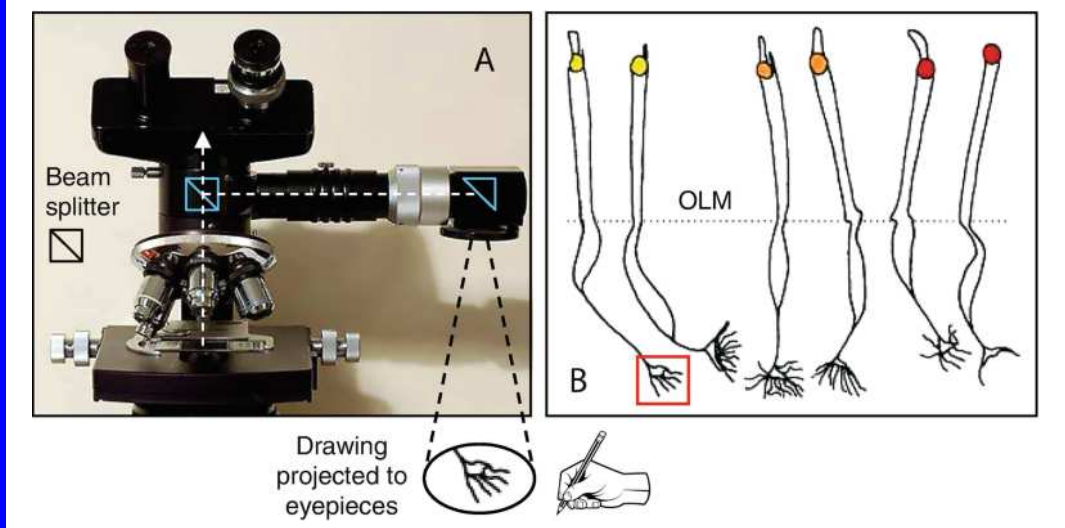
Ovalle W.K. & Nahirney P.C. (2008)

Netter’s essential histology.

Saunders (Elsevier), Philadelphia.

ISBN: 978-1-929007868

CAMERA LUCIDA (a DRAWING ACCESSORY)

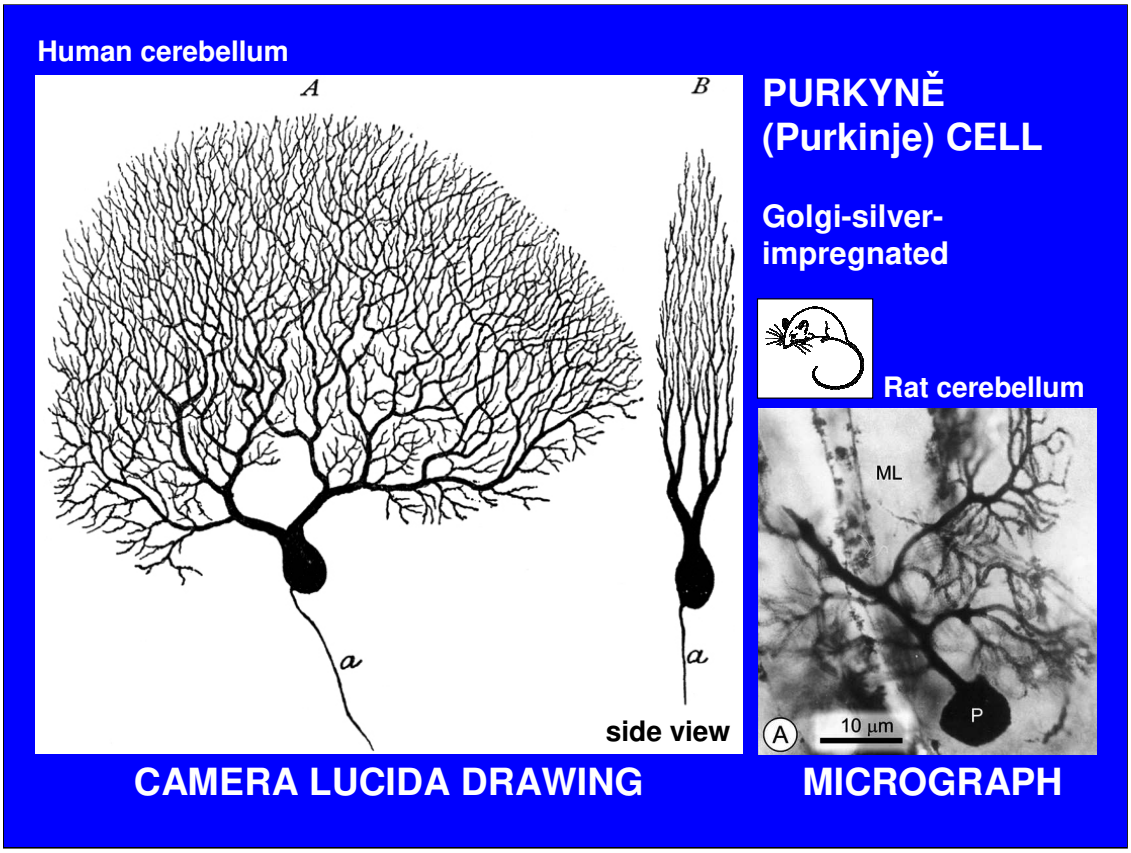


A …….. Fitting to Wild M20-EB microscope
B …….. Drawings of freshly isolated chick retina photoreceptor cells (cones) aligned by the outer limiting membrane (OLM). The colour spots are oil droplets acting as light filters aiding colour vision.

Camera lucida is a simple device that can be fitted between the oculars and objectives.

It makes it possible to simultaneously observe in the eyepieces the specimen and a piece of paper next to the microscope.

Cell shapes of interest can thus be reliably drawn.



Even nowadays, *camera lucida* drawings are often preferred over micrographs as relevant (important) structures can be highlighted, and redundant ones omitted (other cells, capillaries, debris etc).

Very often, the cell of interest is thicker than the depth of field (focus), i.e., not all its parts appear sharp in the micrograph.

In such case, several micrographs have to be acquired, each at a different focal plane.

To some extent, these micrographs can be combined electronically.

This is achieved by software that recognizes sharp areas in each image.

(e.g., “Extended Depth of Focus” by Leica, or “Extended Depth of Field“ by Olympus).

There are two alternatives to the above approach:

Option 1 (cheap but very laborious) requires cutting a series of very thin tissue sections (~1 µm), inspecting them individually, and making a 3D model from them.

Option 2 (elegant but costly) requires the use of a confocal microscope on tissue sections of normal size (~10 µm) or even thicker:

- Several images are acquired at different focal planes (an image stack).

- As every part of each of them is more-or-less sharp (“confocal“) the specimen becomes “optically sectioned“.

- Individual images (“optical sections“) are subsequently combined into a 3D image that can be viewed from any direction.

IMAGE SOURCES:

Drawing (human):

Piersol G.A. (1908) Human Anatomy. J. B. Lippincott, Philadelphia

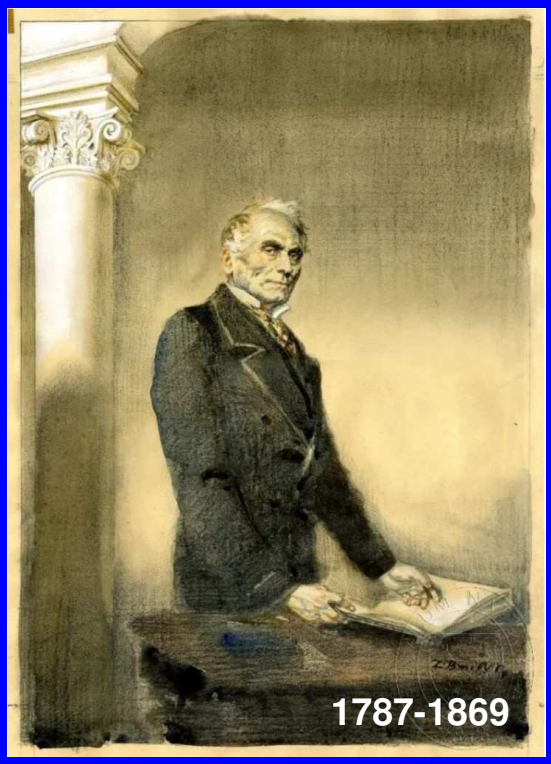
https://etc.usf.edu/clipart/53100/53184/53184_purkinje.htm

Micrograph (rat):

Neurohistology and Imaging Techniques, pp. 1-48.

https://doi.org/10.1007/978-1-0716-0428-1_1

(Fig. 9A)



Jan Evangelista Purkyně

Johann Purkinje,

Doctor der Medicin.

Prag, 1819.

In Commission bei Johann Gottfried Calve.

Johann Purkinje

NON-COMPULSORY CONTENTS.

Purkyně's surname was spelled "Purkinje" in German literature, to make sure it would be pronounced correctly.

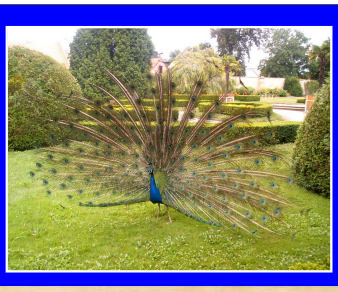
German language was more common in scientific literature than Czech or English at that time.

The odd legacy of this transliteration is the peculiar pronounciation of "Purkinje" by English speakers.

It sounds very different from the original (something like "Pakindži" in Czech).

Purkyně is often claimed to be "from Austria" as he was born in the Austro-Hungarian Empire.

LIBOCHOVICE CHÂTEAU



The birthplace of Jan Evangelista Purkyně + peacock residence

NON-COMPULSORY CONTENTS.

Coloured drawings had their counterpart in coloured photographs.

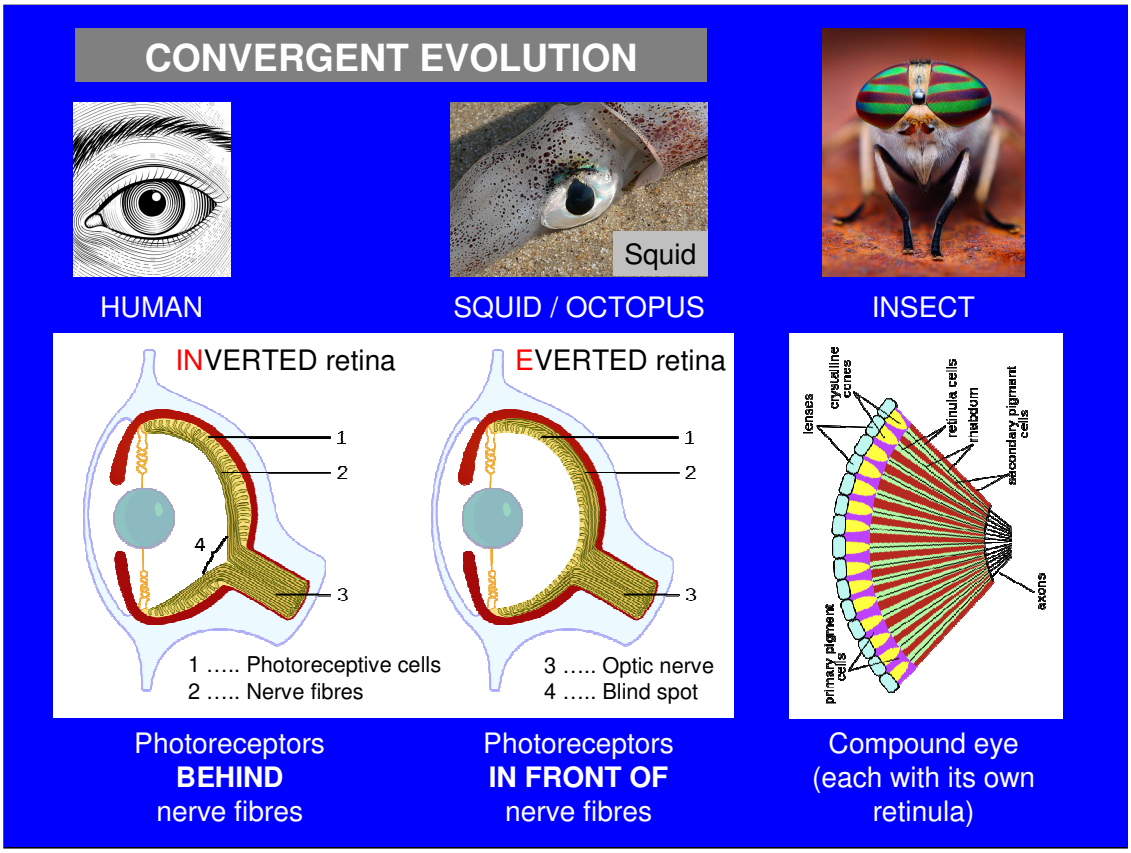
In the pre-digital age, colouring B&W photographs worked out cheaper than taking/developing colour photographs.

The Libochovice Château is the birthplace of Jan Evangelista Purkyně.

His father was not the château owner, he worked there as a caretaker.

Lecture #7
OPTICAL PROPERTIES of RETINAL GLIA and OTHER CELLS

NOBELISTS in OXFORD



It is not surprising that human eye is very different from squid/octopus eye.
However, the fact that human eye is very similar to squid/octopus eye is rather surprising.
This phenomenon is referred to as so-called convergent evolution.

Furthermore, human eye is designed less logically than squid/octopus eye:
In vertebrates, photoreceptive cells lie behind a light-scattering layer of neurons.
Vertebrates thus have a so-called inverted retina.

In squid/octopus, photoreceptive cells are placed in front of the layer of nerve fibres (ganglion cells).
This layout is referred to as so-called everted retina.

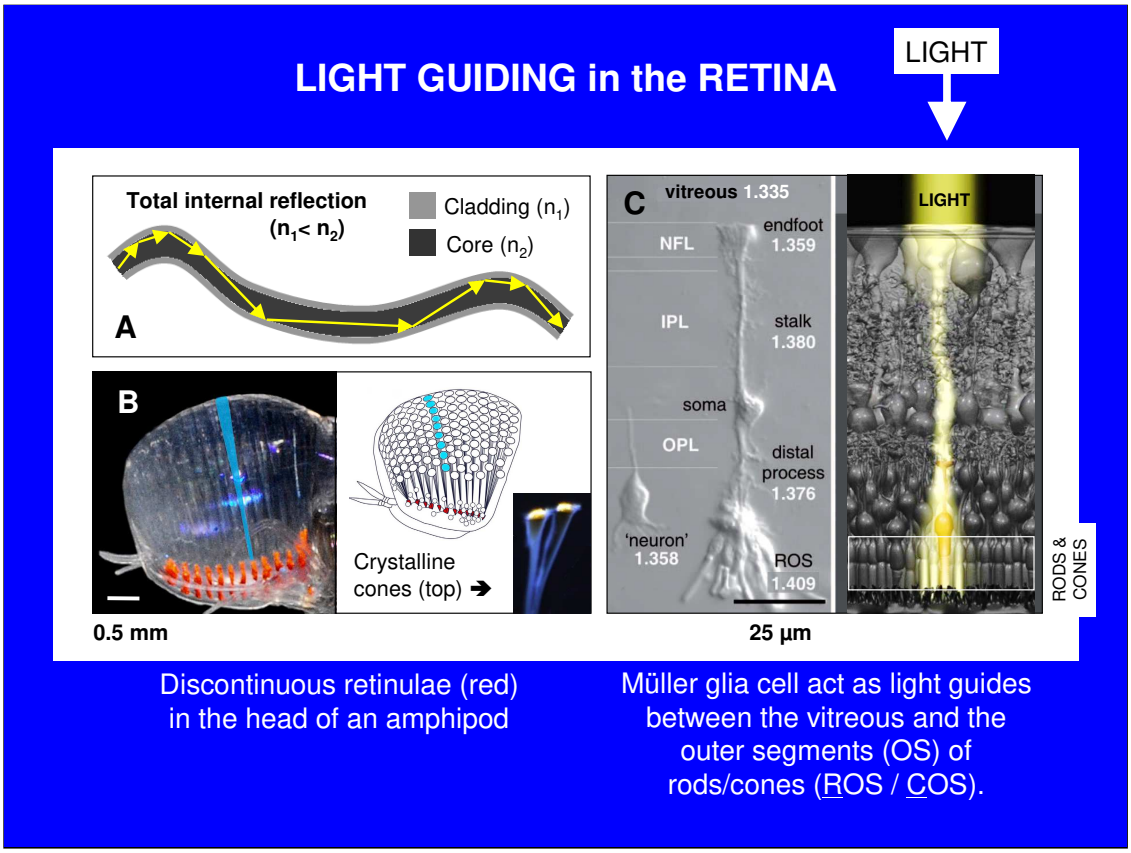
The reasons for such differences is unknown.
A possible explanation may be provided by comparative embryology (vertebrates vs. cephalopoda),
or by studying mutants lacking certain genes involved in eye development.

FURTHER READING:

Gehring W.J. (2014)
The evolution of vision.
WIREs Dev. Biol. 3 (1): 1-40.
https://doi.org/10.1002/wdev.96

Hanke F.D. & Kelber A. (2020)
The eye of the common octopus (Octopus vulgaris).
Frontiers in Physiology 10: 1637.
https://doi.org/10.3389/fphys.2019.01637

https://www.researchgate.net/publication/338574212 (PDF download)



Discontinuous retinulae (red) in the head of an amphipod

Müller glia cell act as light guides between the vitreous and the outer segments (OS) of rods/cones (ROS / COS).

A.

Total internal reflection is the underlying principle of light-guiding capability.

B.

Head of a near-transparent crustacean (an amphipod, *Paraphronima gracilis*) has numerous ommatidia acting as light guides.

These enable the incoming light (path highlighted in blue) to reach the discontinuous retina (red).

The front part of two of them (including so-called crystalline cones) is shown in dark-field illumination (inset).

Discontinuous retina is also found in insects.

C.

Müller glia cell of guinea pig retina, capable of acting as a light guide between the vitreous and the outer segments of photoreceptive cells.

LEFT: Refractive index values within a single Müller cell, rod outer segment (ROS), and an isolated retinal 'neuron' (bipolar cell).

RIGHT: Schematic illustration of Müller cell alone

NON-COMPULSORY CONTENTS:

(d) Diametre.

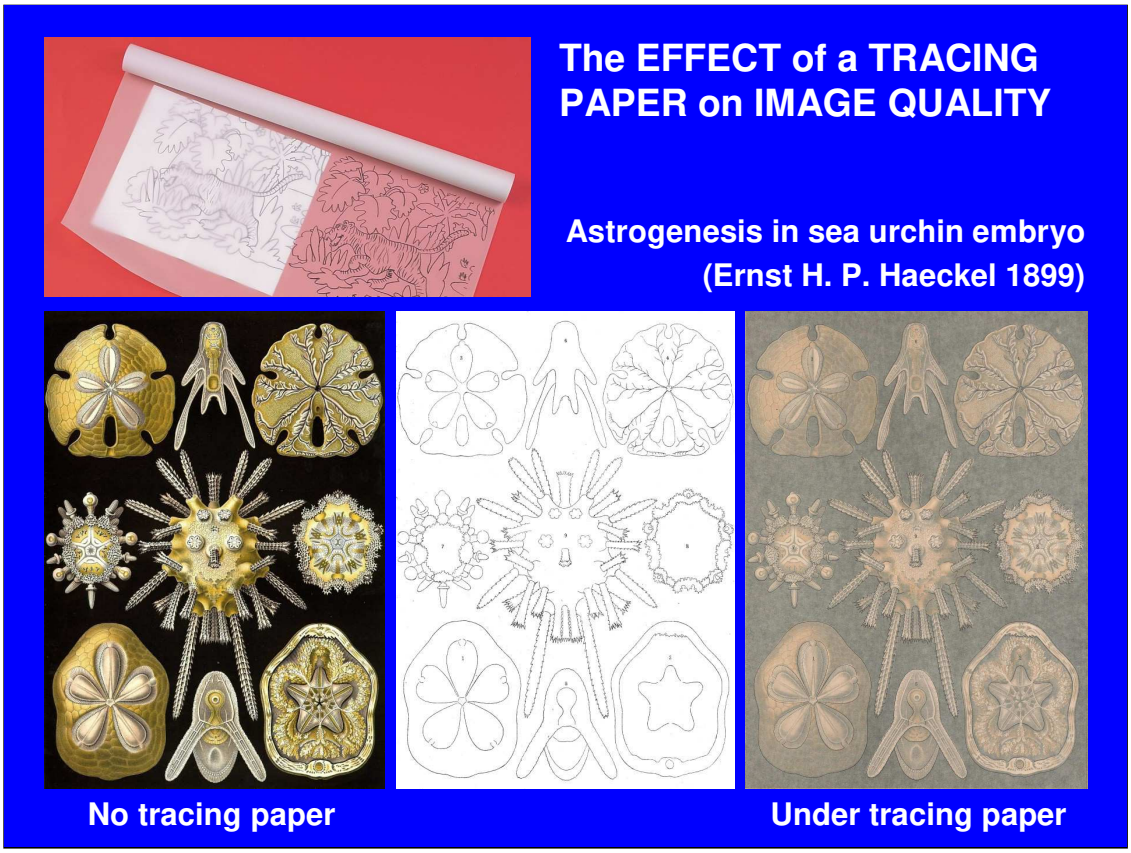
(IPL) Inner plexiform layer.

(NFL) Nerve fiber layer.

(OPL) Outer plexiform layer.

(V) Waveguide characteristic frequency as a parameter of light-guiding capability.

The "V" values are shown for wavelengths of 500 nm (cyan) and 700 nm (red)



Without the Müller glia cells, our vision would probably be degraded, as if looking through a tracing paper.

Its thickness is approximately the same as the thickness of retina between the inner and outer limiting membrane (ca 150 µm).

These beautiful drawings were prepared by Ernst Haeckel, a prominent embryologist in Jena (Germany).

He is the original author of the Biogenic Law, i.e., that an observation that ontogeny is a repeat of phylogeny

("ontogeny ontogeny recapitulates phylogeny") [1, 2].

E.g., up to a certain point in time, chick embryo looks the same as human embryo.

You can visit his museum there, and the house where he lived is also open to public.

The first modern microscopes in the world started to be made in Jena as well, by a company called Carl Zeiss.

Their own museum dedicated to the history of microscopy is also worth visiting.

[1] https://thebrain.mcgill.ca/flash/capsules/outil_bleu12.html

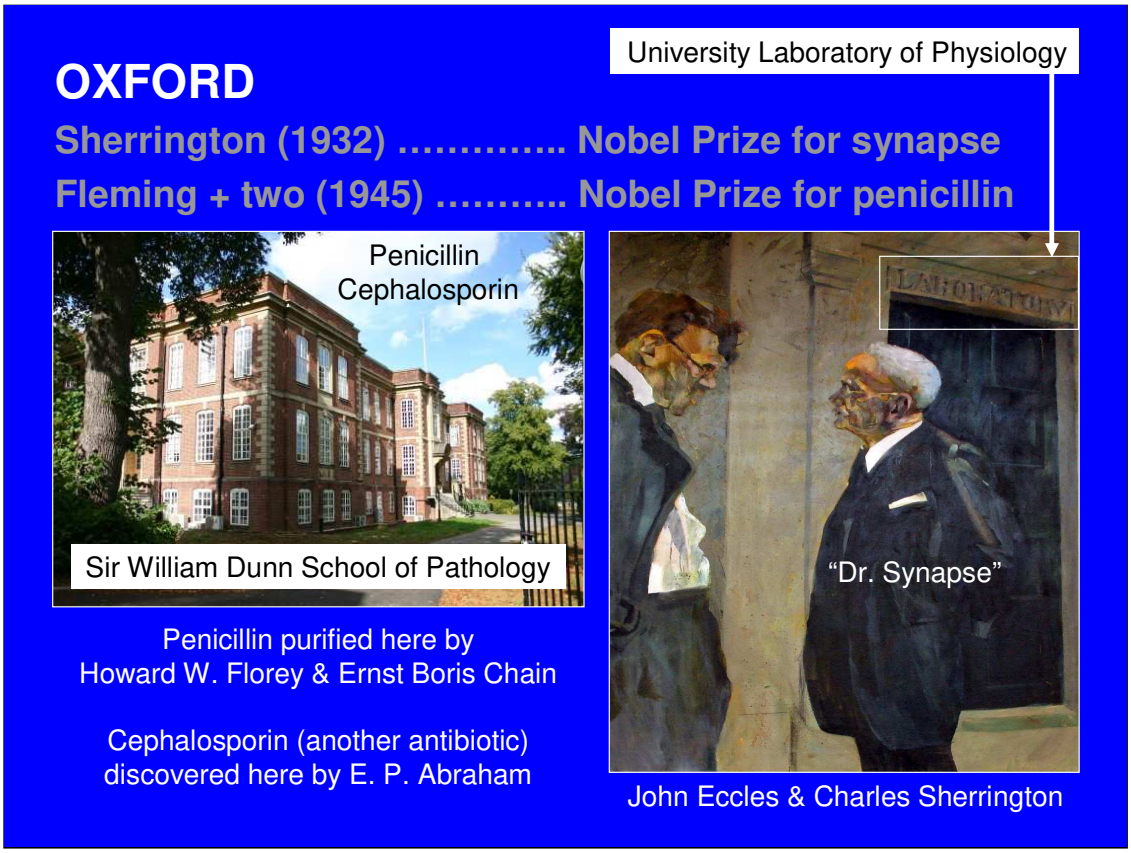
[2] https://embryo.asu.edu/pages/ernst-haeckels-biogenetic-law-1866

IMAGE SOURCES:

Haeckel E. (1899/1904)

Kunstformen der Natur (1st/3rd ed.).

A VIRTUAL TOUR OF OXFORD UNIVERSITY



Burdon-Sanderson discovered antibacterial properties of fungi 60 years before Fleming [1].

Fleming's original 1929 paper [2] on antibacterial properties of fungi was initially 'forgotten' for about 10 years.

Fleming himself lost interest in penicillin as it was difficult to isolate and purify.

He also studied antibacterial properties of lysosyme, and initially believed that penicillin is also an enzyme.

Chain & Florey purified penicillin so that it could be produced at mass scale to treat infections during the war [3].

They probably did more work on penicillin than Fleming but unlike him, they were introverts 'hiding' in their laboratories.

Fleming, on the other hand, was keen to give interviews.

All three of them jointly received the Nobel Prize.

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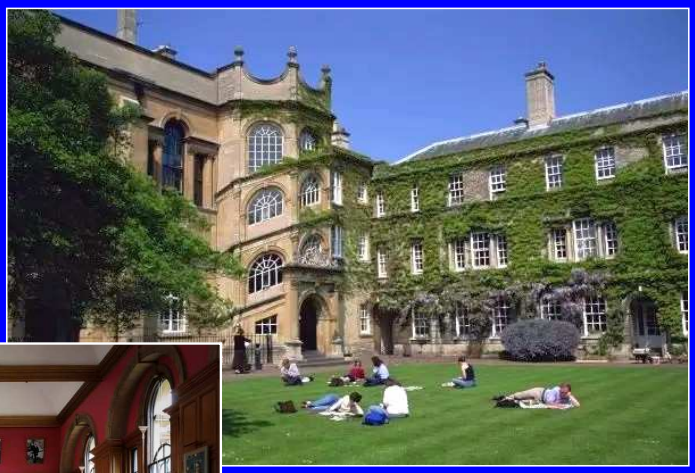
[1] https://www.bbvaopenmind.com/en/science/bioscience/fleming-and-the-difficult-beginnings-of-penicillin-myth-and-reality/

[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2048009/

[3] https://www.sciencehistory.org/historical-profile/howard-walter-florey-and-ernst-boris-chain

Arriving @ Oxford from London

HERTFORD COLLEGE



FROM COLLEGE RECORDS:

"As recently as 1805, Hertford College (est. 1284) was a mere ruin, and all students have run away. Only two scholars remained, one of them mad."

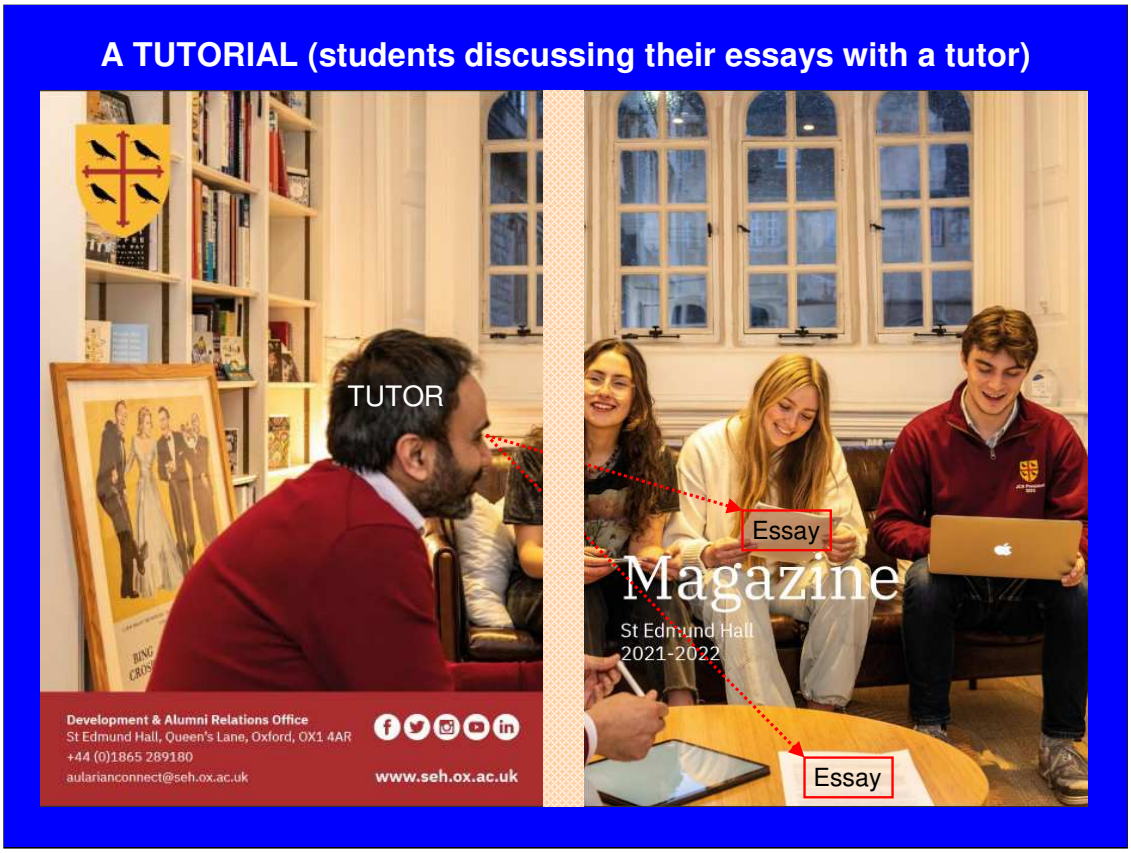
NON-COMPULSORY CONTENTS

Hertford College is one of the oldest at Oxford.

It has not always looked as great as now.

In fact, it almost disappeared due to lack of endowment …

St EDMUND HALL LIBRARY
St Peter-in-the-East church



NON-COMPULSORY CONTENTS

GAME OVER

You are welcome to visit the labs

Institute of Biochemistry

The cure against HIV-AIDS and hepatitis-B has been discovered here by Antonín Holý