Biomedical optics

BIOENG-445; 3 credits

Life Sciences Engineering; Master 1&3
Microengineering; Master 1&3

Neuro-X; Master 1&3

Minors in: Neuro-X; Biomedical technologies; Photonics

Instructors: **Georges Wagnières**, MER; IPHYS, SB, EPFL
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(please make an appointment)
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Biomedical optics

- MEETING TIMES/DATES/LOCATION

  Classes on Monday, 08:15-10:00 in room CM 1 100

  Exercices: on Thursday 09:15-10:00 in room CM 1 100 (No session on 19/09/2024 !)

- MOODLE ACCESS FOR STUDENTS

  Webpage: https://moodle.epfl.ch/course/view.php?id=1291

  Slides; Forum; Course Recording (Previous years); other useful resources

Biomedical optics

Students list from IS-Academia (21.08.2024)

1	Al-Hussini Mohammed
2	Bargis Edoardo
3	Bodenstab Nina Shuxiang
4	Boiardi Pietro
5	Bonniot Charlotte Marguerite
6	Capacci Amandine Anna Marguerite
7	Chêne Lucie Gabrielle Iris
8	Defromont Iris Claire Thémis
9	Deprez Benjamin
10	Drouart Aurel Christian Alain
11	El Kaissi Tala
12	Fabbro Loris Alan
13	Flachaire De Roustan Ivalu
14	Forget Emma Marie Cécile
15	Frey Anaëlle Florence
16	Grandjean-Pierazzi Oriane Marthe
17	Huang Chih-Ying
18	Lacroix Théo Bastian
19	Lamouroux Lou-Anne Suzanne
20	Lattion Gilles
21	Montlahuc Louise Maryvonne Chantal
22	Nguyen Huyen Tran
23	Pouderoux Kilian Titouan Roger Pierre
24	Ramanoelina Iarantsoa Tahina
25	Rosinska Michaela
26	Somlo Stephanie Veronica

Biomedical optics

Teaching assistants

Supports GW for the exercises edition + correction + Moodle management + forum

Wei Cai, PhD student, LCBM / Laboratory of Biophysical Chemistry of Macromolecules.

Office hours: Thursday, 10:00-12:00, Room CH B3 494

(please make an appointment)

E-mail: wei.cai@epfl.ch

Biomedical optics

Teaching assistants, cont.

Supports GW for the course+ exercises sessions held on Thursday in room CM 1 100

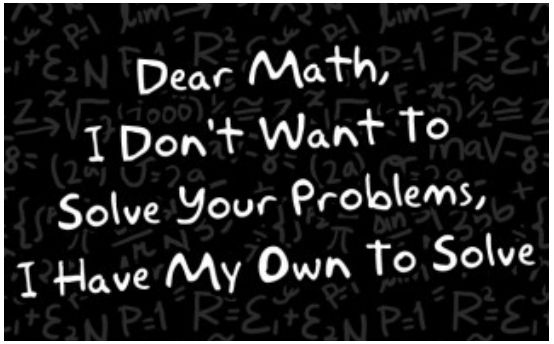
Aleksei Gaier, PhD student, HYLAB / Laboratory of Hybrid Photonics.

Office hours: Thursday, 10:00-12:00, Room BM 3137

(please make an appointment)

E-mail: aleksei.gaier@epfl.ch

Exercises



- This is a homework + preparation every Thursday!
- Personal work !

  (Please read the **Code of Honour** and **the Code of Ethics for Citing Information Sources:** available at «http://polylex.epfl.ch/ethics»).

Principle:

- You get the exercise (with hints, when applicable) during the class.
- Get support from TA (exercise sessions: Thursday 09:15-10:00 in room CM 1 100).
- The due date for each week's exercise submission is from Monday at noon (after the lecture) till the following Monday at 6 a.m. (before start of the next lecture)."
- Contact Wei, Aleksei or myself during the office hours if you need help/advices.

Exercises

Principle (Cont.):

- Exercises solutions must be submitted through the Moodle portal in PDF.
- Each week, there will be an “Exercise submission” icon where you can submit your file.
- Note:

1. **Scanning** of hand-written pages (please take good care of the shadows, handwriting readability and resolution) and **PDF** (preferred) prepared with MS Word / latex are **acceptable**.
2. Students should **avoid direct submission of MS Word documents** (compatibility issues might arise) or PDFs generated by iPad/Android/Windows tablet digital-pen scratches (as they are frequently ugly and unreadble).
3. There is **no specific formatting** requirements, as long as the procedures and the final results are clearly presented.
4. If you don't know how to solve the questions, **try writing some procedures**.
5. Sloppy handwritings, unreadable contents, and poor presentations will result in a **penalty of 5%** of the week's homework score. Instead, good presentations are **awarded 5%** of the total score. The final score of a week will not exceed 100/100.

What is Biomedical Optics ?

A multidisciplinary field employing theoretical and experimental methods from the ***optical* sciences*** *to characterize, quantify, process, modify and manipulate biological tissues, drugs and biomolecules for* ***biomedical applications****, as well as to detect, characterize or treat various conditions in the* ***clinic****.*

* Definitions according to the Cambridge Dictionary:

Optics: The study of light and instruments using light.

Light: The brightness that comes from a source that allows things to be seen.

!! Near infrared and near UV are also considered in biomedical optics !!

Main applications of biomedical optics

- Optical **diagnosis** (non-invasive/minimally invasive, high resolution)
- Light-based **therapies** (minimally invasive, novel treatments possible; e.g. photodynamic therapy, plastic surgery)
- Bioimaging / **biosensing** (non-invasive, highly sensitive/selective, remote sensing)
- Light **manipulations** of cells and **tissue engineering**.

…

Course Description and Objectives

- This course will provide students with an overview of current status and research in the most important fields of biomedical optics.
- Through ***lectures***, ***Exercises***, recent ***literature*** review papers, "classroom" ***discussion + oral presentation***, students should gain an understanding of the present status and major research directions in biomedical optics and develop the ability to critically evaluate works and technologies in the field.

Course Description and Objectives (*cont.*)

This course will also briefly review the basic principles of optics, optical spectroscopy and optical imaging as well as the most important applications of these techniques in biomedical optics.

Medical interests of biomedical optics

- Non-invasive, real-time **detection** and **measurements** of structures and functions in living systems *in situ*

- "Novel", minimally- or non-invasive **therapeutics**

- Enhanced sensing and spatial resolution **in biological microscopy** (focused lasers, multiphoton, near-field, …)

- Compatibility with other methods/technologies:
  - multi-modal: electrical, chemical, mechanical
  - fiber optics for minimally invasive therapy

Why Biomedical Optics !

Health care costs in 2019 in USA was 3.8 trillion $US, in Germany 390.6 billion €. Advanced photonic technology enables early detection of diseases and the development of minimal-invasive treatment leading to shorter hospitalization time. These changes will reduce health care cost considerably. Some estimates expect a reduction of up to 20%. This would result in an overall reduction of up to **1 trillion $US per annum worldwide**.

The market of **photonics** in **medtech** applications is growing fast: From US$ 5.95 billion in 2005 to US$ 20,4 billion in 2010 to US$ 38,3 billion in 2015.

Medical imaging contributed to a $ 710 million growth between 2015 and 2020

Source: Statistisches Bundesamt; "Towards a Bright Future for Europe Strategic Research Agenda in Photonics", Published by: European Technology Platform Photonics, www.forbes.com.; Photonics Spectra, 09/2017.

Why Biomedical Optics !

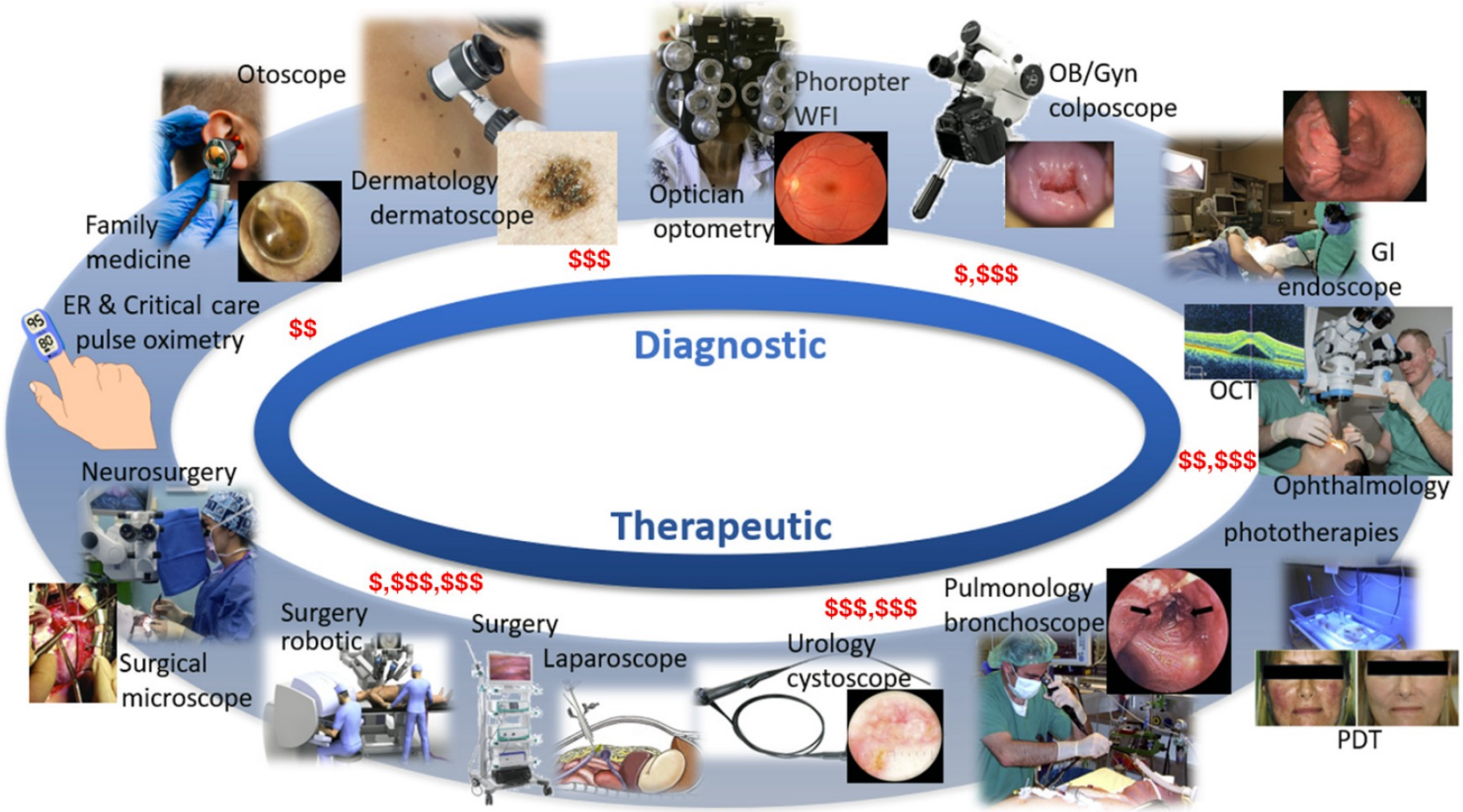


Fig. 2 Visual display of a range of many commonly adopted optical technologies used in medicine, broadly classified as diagnostic (top) and therapeutic (bottom), and roughly organized clockwise from lower system cost (top left) to higher system cost (bottom left), as noted by red dollar signs.

Source: B. Pogue, JBO, 2023

Why Biomedical Optics !

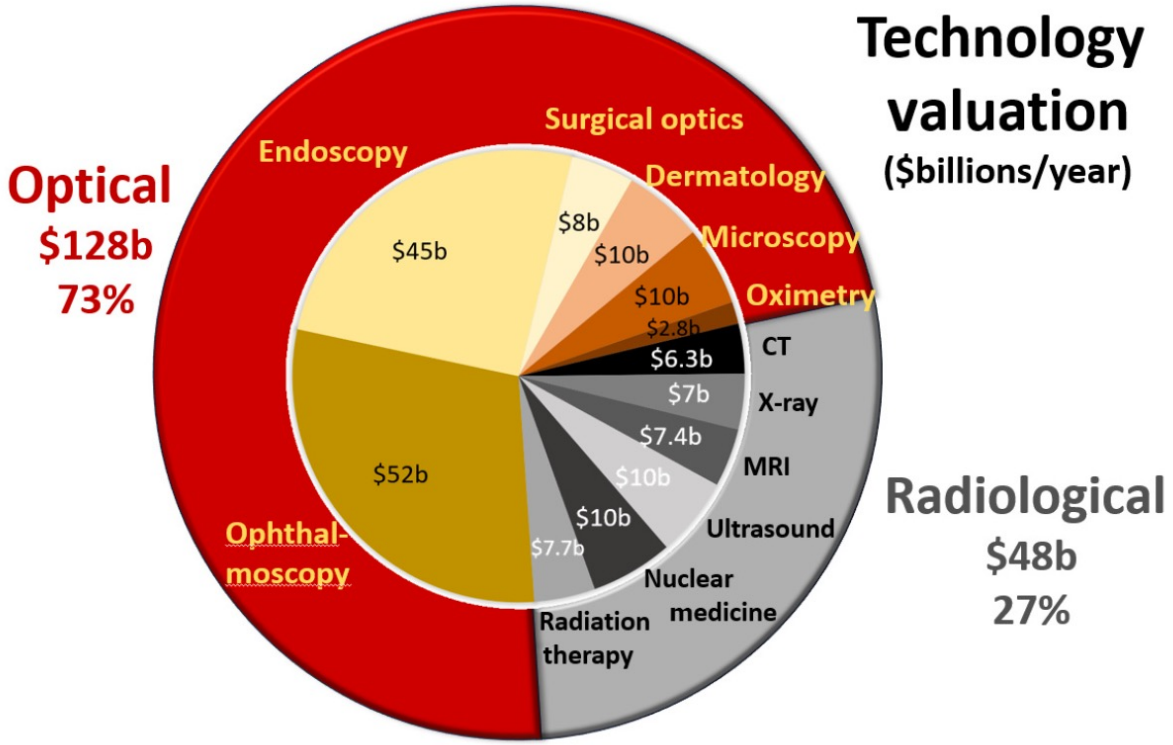


Fig. 3 Global market valuation of six radiological areas (CT, x-ray, MRI, ultrasound, nuclear medicine, and radiotherapy) is summarized above totaling $48 billion for 27% of the global device market. The optical technology areas that were largest are also summarized (ophthalmology, endoscopy, surgery, dermatology, microscopy, and pulse oximetry) totaling $128 billion/year for 73% market share.

Source: B. Pogue, JBO, 2023

Why Biomedical Optics !

Table 3 Strengths, weaknesses, opportunities & threats (SWOT) of the technology sector of medical optical imaging.

Strengths	Weaknesses
• Highly efficient economical imaging due to invention and advancement of CMOS cameras	• Largely limited to surface and cavity imaging, vision imaging, or near sub-surface sensing/imaging
• Enormous economy of scale with consumer optical devices, a $2.8 trillion industry	• Tissue imaging deeper than a few mm has never been commercially successful due to limited spatial resolution
• Large engineering workforce, largest technology sector in medicine	• Each application has specialized system, diffusing the overall view of optical imaging systems
• Primary tool for point-of-care and interventional vision	• Slow introduction of contrast agents
• Optical devices are core to many highly sensitive radiation detection systems	
• Synergy with advances in display technologies	
Opportunities	**Threats**
• Continuing explosion of consumer technologies that advance optical imaging capabilities	• Dearth of communication between academic and industrial biomedical optics research directions
• Advanced surgical, laparoscopic, endoscopic technologies that augment vision beyond just color imaging	• Limited NIH investment in optical tech despite being widely adopted in point-of-care exams
• Microscopic to macroscopic imaging in the same instruments	• Funding structures limit the ability to work with industry on collaborative development
• Scattering makes the signal more sensitive to the entire tissue volume, beyond vessels	• Lack of technical domain experts within the medical center to assist physician groups when deploying advanced medical optical systems
• Highest potential for molecular sensing of all imaging modalities due to numerous optical molecular probes	• Physician work overload minimizing use of advanced instruments
• Shifting healthcare toward wellness instead of healthcare, requiring monitoring technologies	
• Screening requires low-cost, low-risk systems	

Source: B. Pogue, JBO, 2023

Biomedical optics: motivation / interest

- One of the dominant technology for this new century!
- It is multidisciplinary!
  (major technology breakthroughs frequently occur at the interfaces of disciplines)

- **Opportunities for engineers:**
  - Optical engineering for noninvasive diagnostic technologies (imaging, "point" measurements).
  - Optical BioMEMS (micro-electro-mechanical system) for bioimaging and biosensing.
  - Device miniaturization, integration, automation, and robotic control.

Biomedical optics: motivation / interest (cont.)

- **Opportunities for engineers** (continued):
  - New chemicals: Photosensitizers or probes for analyte detection, biosensing and treatments.
  - Bioimaging to probe molecular, cellular, and tissue functions.
  - Real time monitoring of drug delivery and action

…

Biomedical optics: motivation / interest (cont.)

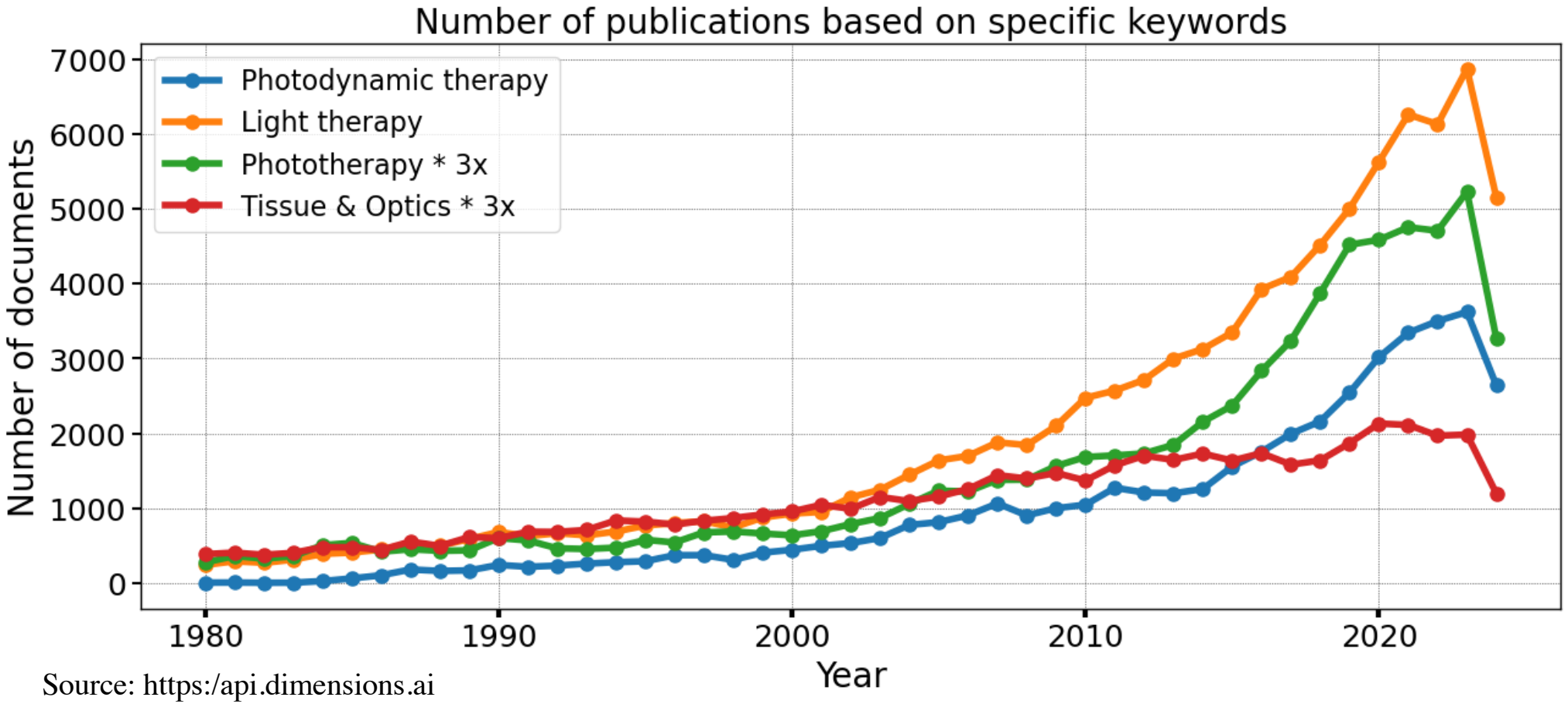
Emerging developments in optical science…

- laser sources
- optoelectronic devices (LEDs)
- fiber optics
- physical and chemical sensors
- spectroscopy and imaging
- MEMS

…are being applied to photomedicine and biomedical optics.

Many of them are versatile, robust and inexpensive, and are being developed at an increasing rate!

Web of Science records for specific topics
(1980 to 2024)



Source: https:/api.dimensions.ai

Tentative Syllabus

1. **Introduction**
2. **History**
3. **Radiometry / photometry**
4. **Optics review**
   - Ray optics
   - Electromagnetic / wave optics
   - Quantum description of light
   - Wave-particle duality

Tentative Syllabus *cont.*

5. **Tissue optics**
   - Tissue optical parameters
   - The radiative transport equation (RTE)
   - Approximation of the RTE
   - Measurement methods
6. **Light dosimetry in tissues**
7. **Applications of Absorption, fluorescence and Raman spectroscopies and imaging in photomedicine**
8. **Dyes, luminophores and photosensitizers**

Tentative Syllabus *cont.*

9. Intruments

Light sources

Dispersive devices

Detectors for optical spectroscopy and imaging

10. Selected applications (in part students' presentations)

Oxymetry

Angiography

Laser-tissue interactions

Phototherapy and Photodynamic therapy

Photodetection of early cancers

Optical coherence tomography

…

Class presentation

- On a topic of major interest to you, you will review relevant literature.

- This could be a general review paper, or a critical evaluation/description of a particular phenomenon, study, method, or technology.

- In order to benefit the entire class and provide you with valuable feedback, you will give an oral, in-class presentation (about 15 + 5 minutes) on your topic.

Class presentation

Examples of topics

Final selections of the topics must be approved by the instructor.
I encourage you to discuss your ideas with GW as soon as possible.

- Molecular probes/markers/contrast agents used in photomedicine.
- Photosensitizers used in photodynamic therapy.
- Optical Instrumentation: light (laser) sources; optical waveguides; detectors; time-domain vs. frequency-domain methods; safety considerations; …
- Tissue Optics.
- Computational approaches to model the light propagation in tissues.

Class presentation

Examples of topics *cont*.

Final selections of the topics must be approved by the instructor.
I encourage you to discuss your ideas with GW as soon as possible.

- Optical Diagnostics: Clinical Spectroscopy and Imaging: elastic scattering; diffuse reflectance; laser-induced fluorescence; Raman; endogenous and exogenous contrast agents; optical coherence tomography; low coherence interferometry; …

- Biomedical Microscopy: fluorescence wide-field; fluorescence lifetime; confocal sectioning; multi-photon excitation; second-harmonic generation; near-field ...

Class presentation

Examples of topics *cont*.

Final selections of the topics must be approved by the instructor.
I encourage you to discuss your ideas with GW as soon as possible.

- Light/laser-based Therapy: photothermal; photomechanical; photochemical; photodynamic therapy; tissue engineering ...

- Biophotonic Technology: optical biosensors; microarray technology; flow cytometry; laser tweezers; laser scissors; laser capture microdissection; bionanophotonics; biomaterials for photonics ...

Class presentation

Examples of topics *cont*.

Final selections of the topics must be approved by the instructor.
I encourage you to discuss your ideas with GW as soon as possible.

- Why do sub-dermal blood vessels look blue ?
  Tissue optics is complex. One particular observation that is not completely obvious is why sub-dermal blood vessels look blue and not red, as one might have suspected. An understanding of this problem is of interest for laser treatments of hyper-vascularised lesions, such as port wine stains.

Class presentation

- This is a personal work !

  (Please read the polylex **Honor Code** and **the Code of Ethics for Citing Information Sources**).

Exams

Grading

Your grade will be determined as follows:

-	Oral exam	1/2
-	Class presentation	3/8
-	Exercises	1/8

Recommended readings

General Reference Texts:

- *Quantitative Biomedical Optics*
  I. Bigio and S. Fantini (Cambridge Uni. Press, 2016)
- *Fundamentals of Biomedical Optics*
  C. Boudoux (Pollux, 2016)
- *Handbook of Photomedicine*
  M. Hamblin, Y-Y. Huang (CRC Press, 2014)
- *Optics*
  E. Hecht (Addison Wesley, 2000)
- *An introduction to Biomedical Optics*
  – R. Splinter & B.A. Hooper (Taylor&Francis,2007)

Recommended readings *cont.*

Specialized Texts:

- *Handbook of Biomedical Fluorescence*
  M.-A. Mycek & B.W. Pogue (Dekker, 2003)
  http://www.crcnetbase.com/isbn/9780824709556

- *Optical-Thermal Response of Laser Irradiated Tissue*
  A.J. Welch & M.J.C. van Gemert (Plenum, 1995)

- *Principles of Fluorescence Spectroscopy*
  J.R. Lakowicz (Kluwer, 1999)

References *cont.*

(Other useful resources)

- ***Biophotonics***
  - free subscription at: https://www.photonics.com/BioPhotonics/p1
- ***The Virtual Journal for Biomedical Optics***
  - http://www.opticsinfobase.org/vjbo/virtual_issue.cfm
- **Newport** has very good optics tutorials
  - https://www.newport.com/resourceListing/tutorials
- **http://www.photobiology.info** is a very good site in the field of photobiological sciences

Glossaries

Optics https://www.plasticoptics.com/glossary.pdf

Optical fibers https://focenter.com/foc-glossary

Medicine http://alexabe.pbworks.com/f/Dictionary+of+Medical+Terms+4th+Ed.-+(Malestrom).pdf

Available on Moodle !

Photochemistry

GLOSSARY OF TERMS USED IN PHOTOCHEMISTRY
INTERNATIONAL UNION OF PURE
AND APPLIED CHEMISTRY
ORGANIC CHEMISTRY DIVISION
COMMISSION ON PHOTOCHEMISTRY
S.E. Braslavsky Pure and Applied Chemistry Vol. 79, No. 3, pp. 293-465, 2007

Available on Moodle !

Thanks !

GW would like to acknowledge and heartily thank the people who Helped him to create this course.
In particular, I am deeply indebted to:

- Prof. Jianan Qu, Hong-Kong University
- Prof. Mary-Ann Mycek, Univertity of Michigan
- Prof. Stefan Andersson-Engels, Lund Institute of Technology
- Dr. Geneviève Bourg-Heckly, Université Pierre et Marie Curie, Paris
- Dr. Dietrich Schweitzer, University of Jena
- Prof. Bruce Tromberg, University of California, Irvine
- Prof. Urs Utzinger, University of Arizona
- Prof. Pavol Miskovsky, J. Safarik University, Kosice, Slovakia
- Prof. Céline Frochot, University of Lorraine, Nancy, France

For sending their lecture materials

Exercise for Week 1 (09.09.2024)

1) What is the portion of the electromagnetic spectrum considered in biomedical optics?
2) Explain why the market valuation of technologies related to medical imaging is much more important for optical systems than for radiologic ones, although the cost/unit is much more important for the latter.
3) Give a list of the enabling technologies playing a key role in biomedical optics.
4) Identify the advantages of using light for diagnostic and therapeutic applications
5) Identify and discuss the reasons/factors that are at the origin of the fast development of these fields.
6) Give two examples, one in biology and one in medicine, of applications illustrating your statements and identify their specific features corresponding to the reasons/factors mentioned above.
7) Can you identify factors preventing the clinical use of technologies related to biomedical optics?

Typical length of your response: between ½ and one page