Amplification of light
Laser

Medical Biophysics I. 6 November, 2024

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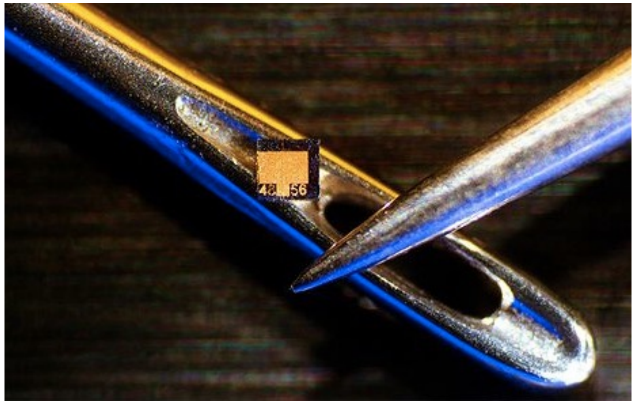
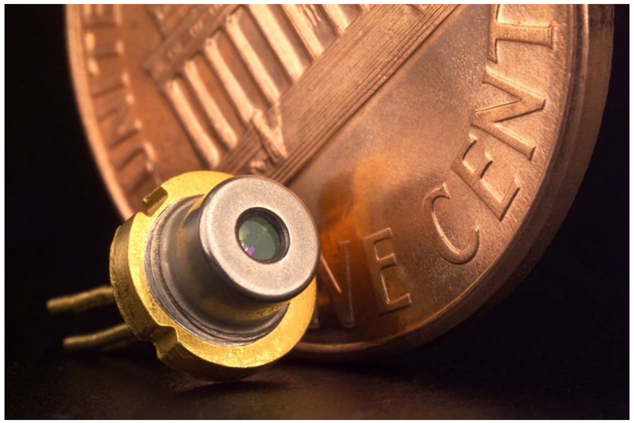
SEMMELWEIS
EGYETEM 1769

Lasers are everywhere

Laser: "Light Amplification by Stimulated Emission of Radiation"

Luminescent light source based on light amplification.





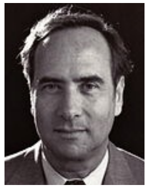
5 mW diode laser
few mms

Terawatt NOVA laser - Lawrence Livermore Laboratories
Size of a football field

Laser history in a nutshell

Albert Einstein
(1879-1955)

Arthur L. Schawlow
(1921-1999)



Theodore Maiman
(1927-2007)

Nikolay G. Basow
(1922-2001)

Charles H. Townes
(1915-)

Alexander M. Prokhorov
(1916-2002)

Steven Chu
(1948-)

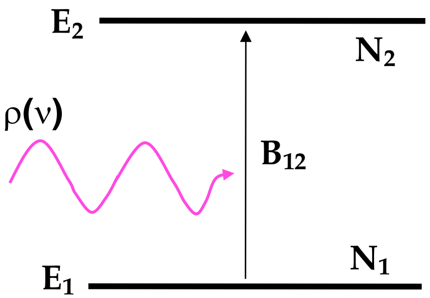
Dénes Gábor
(1900-1979)

Ferenc Krausz
(1962-)

- 1917 - Albert Einstein: theoretical prediction of stimulated emission.
- 1946 - G. Meyer-Schwickerather: first eye surgery with light.
- 1950 - Arthur Schawlow and Charles Townes: emitted photons may be in the visible range.
- 1954 - N.G. Basow, A.M. Prochorow, and C. Townes: ammonia maser
- 1960 - Theodore Maiman: first laser (ruby laser)
- 1964 - Basow, Prochorow, Townes (Nobel-prize): quantum electronics
- 1970 - Arthur Ashkin: laser tweezers
- 1971 - Dénes Gábor (Nobel-prize): holography
- 1997 - S. Chu, W.D. Phillips and C. Cohen-Tanoudji (Nobel-prize): atom cooling with laser.
- 2013, october 8: NIF (National Ignition Facility, USA): launching nuclear fusion with 192 laser beams, positive energy balance.
- 2017 - ELI (Extreme Light Infrastructure), Szeged, Hungary. generation of attosecond (10^{-18} s) light pulses.
- 2018 - Nobel-prize in physics: Arthur Ashkin (laser tweezers), Gérard Mourou and Donna Strickland (ultrashort laser pulses)
- 2023 – Nobel-prize in physics: Pierre Agostini, Ferenc Krausz, Anne L'Huillier, attosecond laser pulses.

Principles of laser I. stimulated emission

1. Absorption

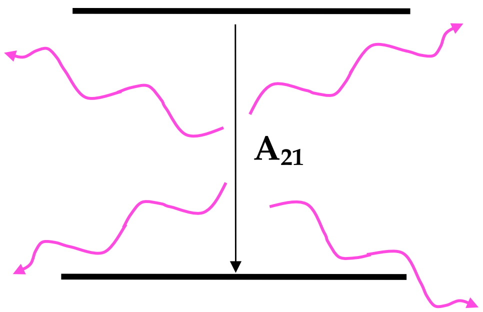


Frequency of transition:

$n_{12}=N_1 B_{12} \rho(\nu)$

$\Delta E= E_2-E_1=h\nu$
energy quantum is absorbed.

2. Spontaneous emission

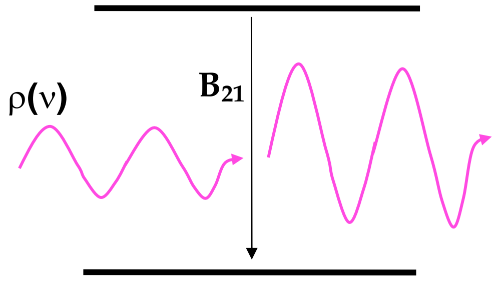


Frequency of transition:

$n_{21}=N_2 A_{21}$

E_2-E_1 photons
travel independently in all directions.

3. Stimulated emission



Frequency of transition:

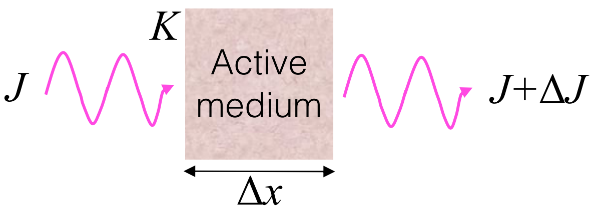
$n_{21}=N_2 B_{21} \rho(\nu)$

In the presence of exernal field.
Field energy is increased.
Phase, direction and frequency of emitted and external photons are identical.

Explanation: two-state atomic or molecular system.
E_1, E_2 : energy levels, $E_2>E_1$
$\rho(\nu)$: spectral energy density of external field.
N_1, N_2 : number of atoms or molecules on the given energy level.
B_{12}, A_{21}, B_{21}: transition probabilities (Einstein coefficients), $B_{12} = B_{21}$

Principles of laser II.
Population inversion

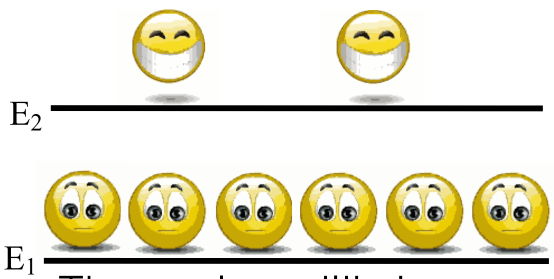
Light amplification depends on the relative population of energy levels.



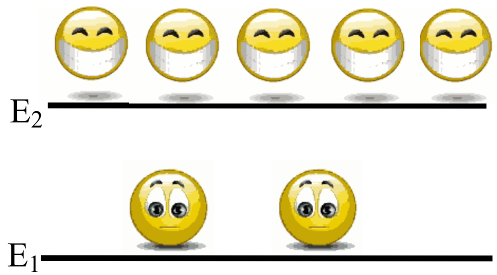
$$\Delta J = JK(N_2 - N_1)\Delta x$$

J = intensity
K = constant
x = distance travelled within medium
N_1, N_2 = number of atoms on the E level

N.B.: If ΔJ is positive, more light exits the medium, than has entered!

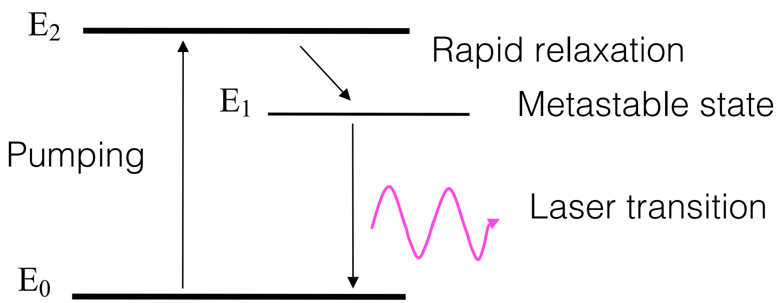


Thermal equilibrium

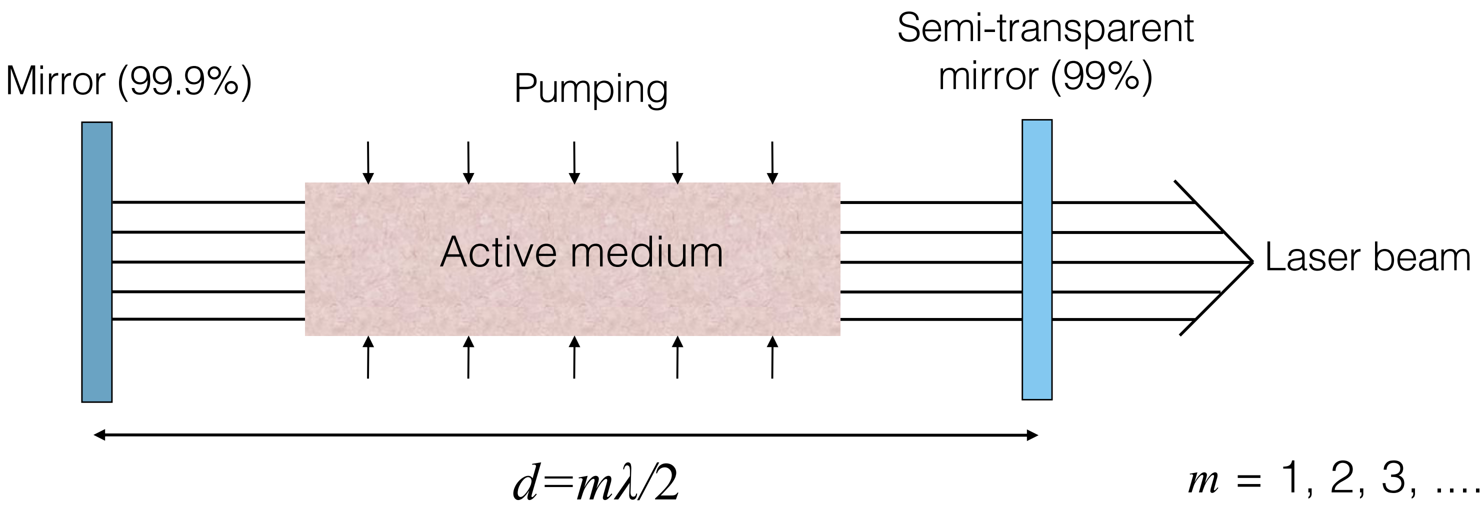


Population inversion

- Population inversion only in multiple-state systems!
- Pumping: electrical, optical, chemical energy



Principles of laser III.
Optical resonance



Resonator:

- two parallel (or concave) mirrors
- part of the exiting light is coupled back into the medium
- positive feedback -> self-excitation -> resonance

- Optical switch in the resonator: Q-switch, pulsed mode

Properties of laser light

1. Small divergence
   Parallel (collimated) beam

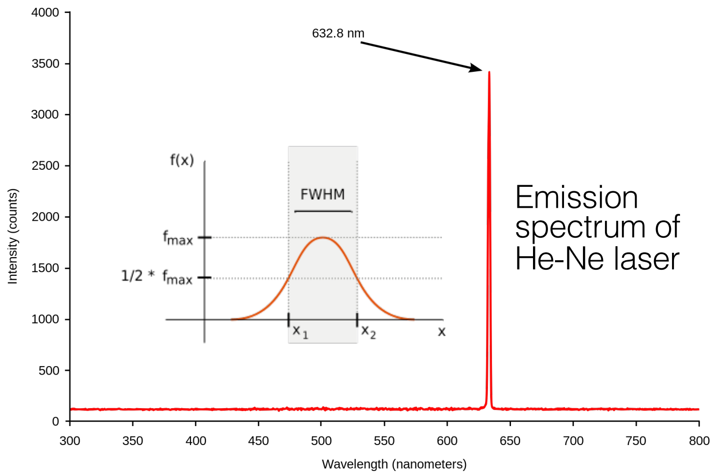
2. Large power
   In continuous (CW) mode, tens, hundreds of W (e.g., CO_2 laser)
   In Q-switched mode, momentary power is enormous (GW)
   Because of small divergence, large spatial power density.

3. Small spectral bandwidth
   "Monochromaticity"
   Large spectral energy density

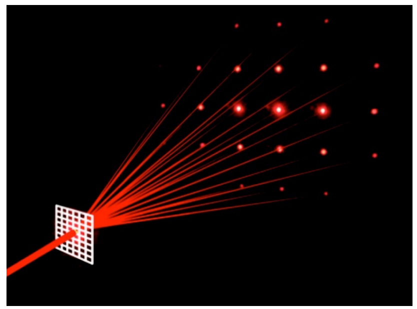
4. Often polarized

5. Possibility of extremely short pulses
   ps, fs

6. Coherence
   phase identity, interference tendency; temporal coherence (phase identity of photons emitted at different times); spatial coherence (phase identity across beam diameter). Application: holography, optical coherence tomography



Emission spectrum of He-Ne laser



Types of lasers

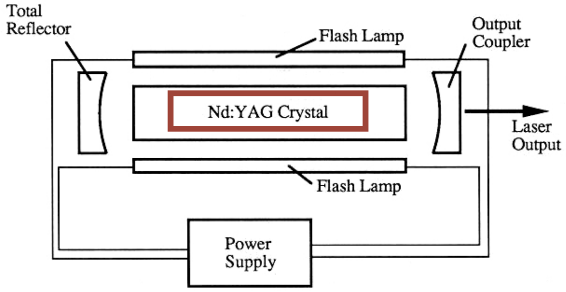
Based on **active medium**:

1. Solid state lasers
Metal doping in crystals or glasses; Ruby, Nd-YAG, Ti-sapphire
Red-infrared spectral range; CW, Q-switched mode, large power

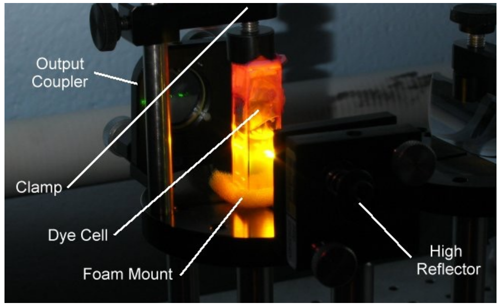
2. Gas lasers
Best known: He-Ne laser (10 He/Ne). Small energy, wide use
CO_2 laser: CO_2-N_2-He mixture; $\lambda \sim 10$ μm; Huge power (100 W)

3. Dye lasers
Dilute solution of organic dyes (e.g., rhodamine, coumarine);
Pumped by another laser.
Large power (Q-switched mode); Tunable

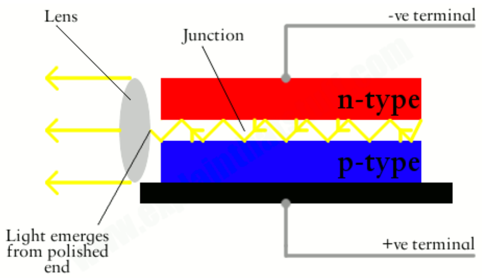
4. Semiconductor (diode) lasers
On the boundary of p- and n-type doped semiconductors.
No need for resonator mirrors (total internal reflection)
Red, IR spectral range. Huge CW power (up to 100W)
Beam characteristics are not very good. Wide use because of small size.



CO_2 laser (cutting a metal sheet)



Dye laser



Diode laser

Today: laser lines (wavelengths) are available from X-rays to infrared light!

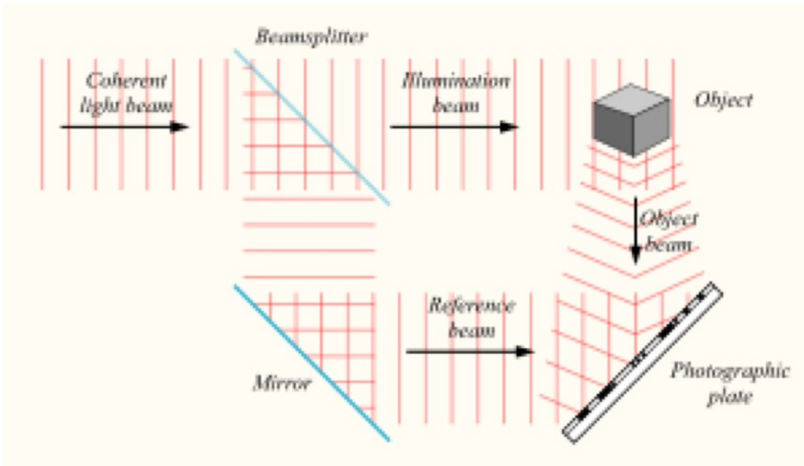
Factors to be considered in laser applications

- Steerability (small divergence)
- Monochromaticity/tunability
- Coherence
- Possibility of short pulses
- Power:
  - 5 mW – CD-ROM drive
  - 5–10 mW – DVD player or DVD-ROM drive
  - 100 mW – high-speed CD-RW writer
  - 250 mW – DVD-R writer
  - 1–20 W – solid-state laser for micromachining
  - 30–100 W – surgical CO_2 laser
  - 100–3000 W – industrial CO_2 laser (laser cutter)
  - 1 kW – 1 cm diode laser bar

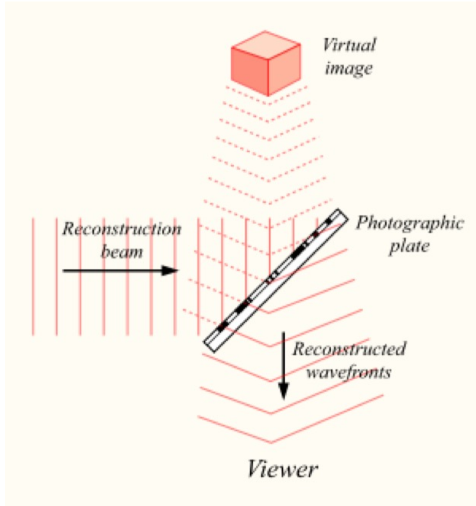
Holography

Laser property utilized: Coherence

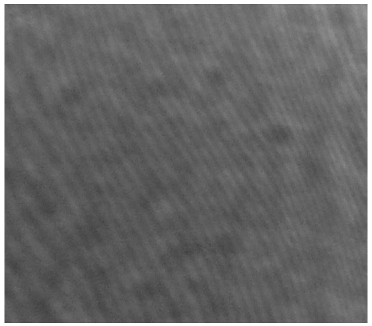
Dénes Gábor
(1900-1979)



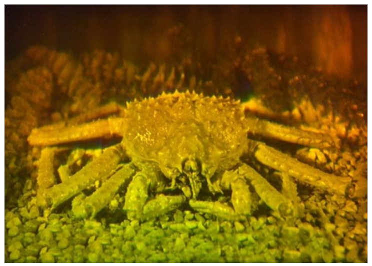
Recording a hologram

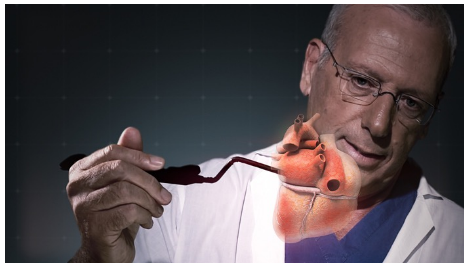


Visualization of a hologram



Surface of a hologram recording





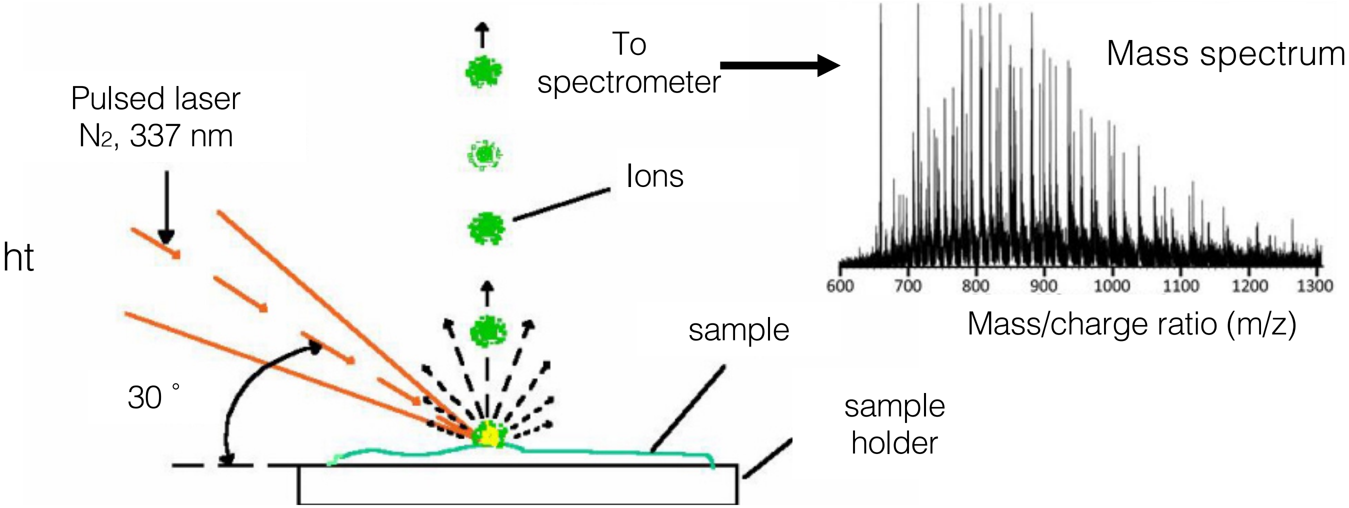
Holograms

Molecular analtics

MALDI-TOF mass spectrometry:

Matrix-Assisted Laser Desorption/Ionization Time Of Flight mass spectrometry

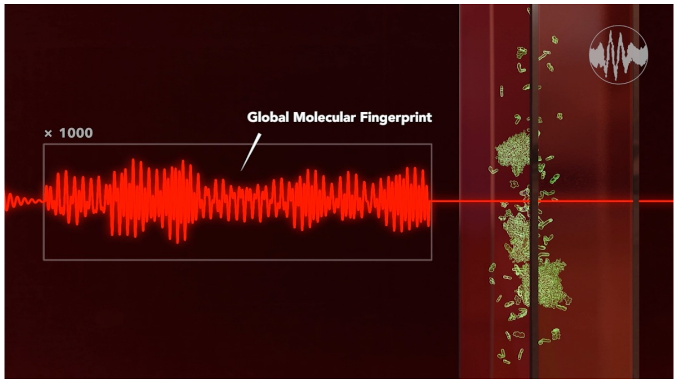
Power density

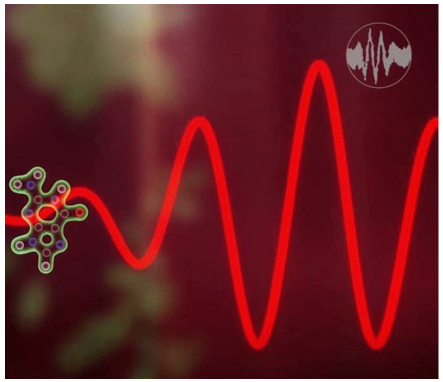


Molecular fingerprinting

Short pulses, tunability

Ferenc Krausz
(1962-)
Nobel-prize 2023





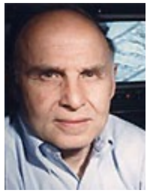
Laser pulse

Molecular and cellular manipulation

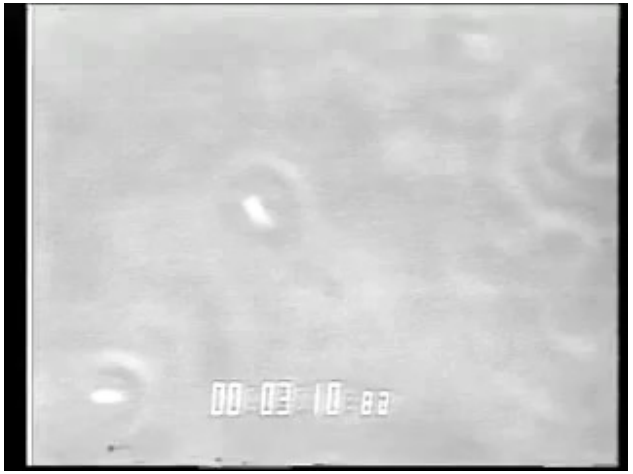
Optical tweezers

Power density,
steerability

Arthur Ashkin
(1922-2020)
Nobel-prize
2018

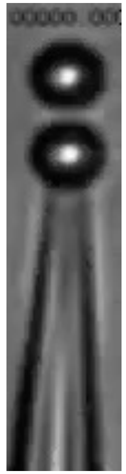


E.coli cells



Actin filament

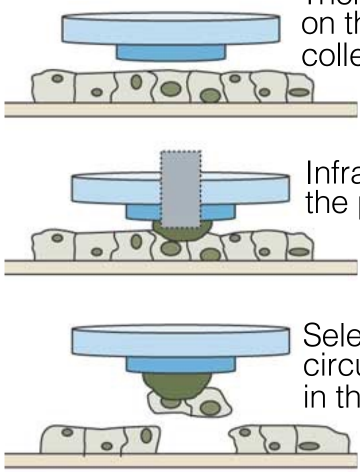
dsDNA



Molecular
force
measurement!

Laser capture microdissection

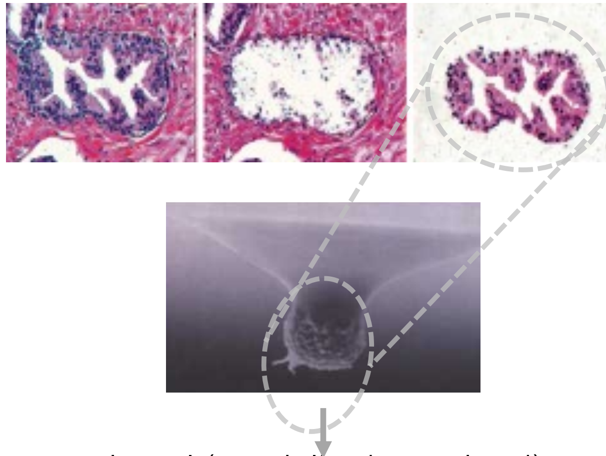
Power density,
steerability



Thermolabile polymer
on the bottom of
collector vial

Infrared laser melts
the polymer

Selected, laser-
circumscribed cells
in the polymer melt



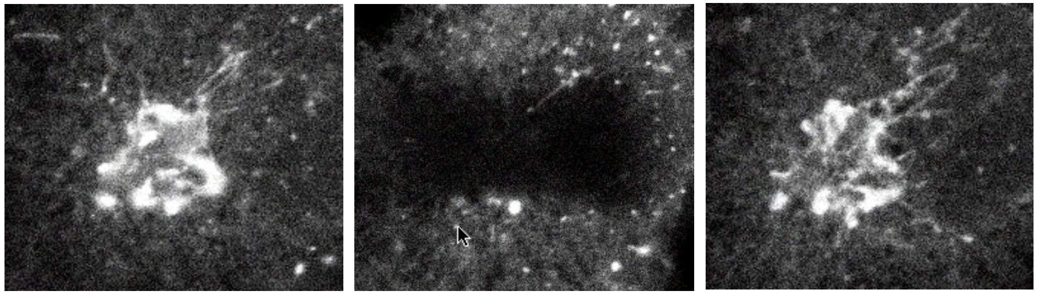
Local (spatially determined)
analytics (chemistry,
biochemistry, genetics)

Cellular analytics

FRAP

(Fluorescence Recovery After Photobleaching)

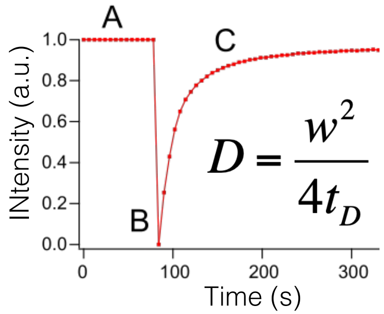
Power density, steerability



A. Prior to photobleaching

B. Right after laser illumination

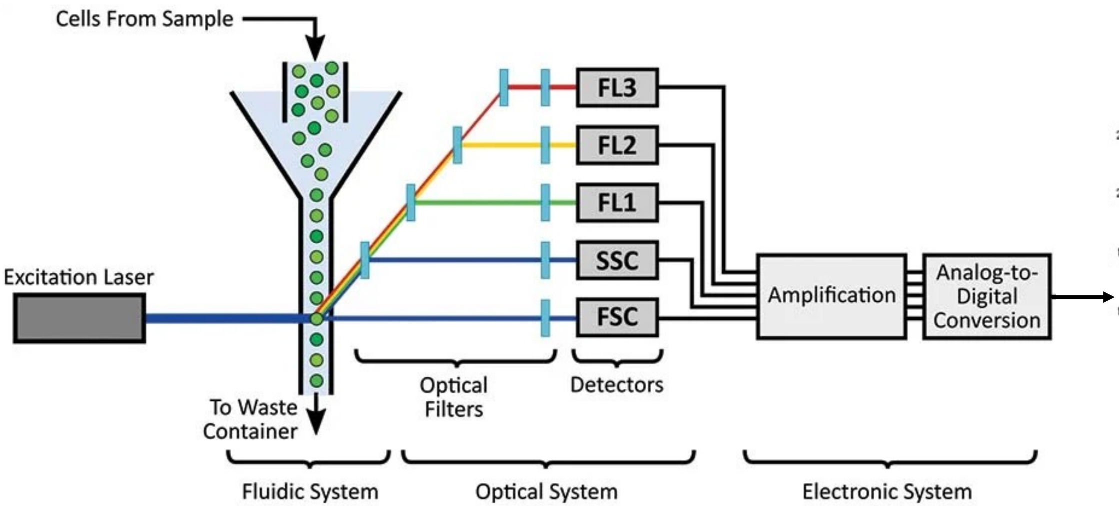
C. Recovered fluorescence

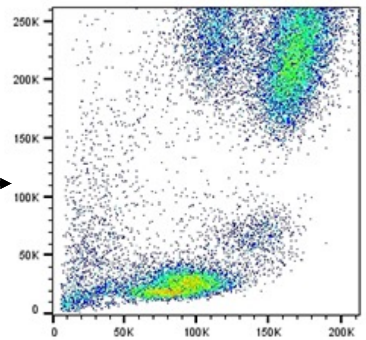


D = diffusion coefficient
w = diameter of bleached area
t_D = time constant

Flow cytometry

Monohromaticity





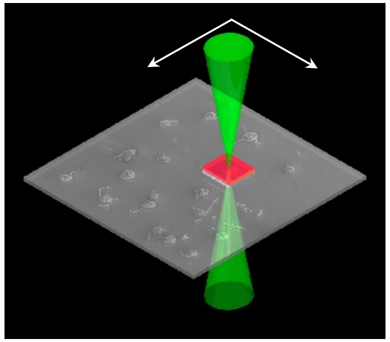
Analytics

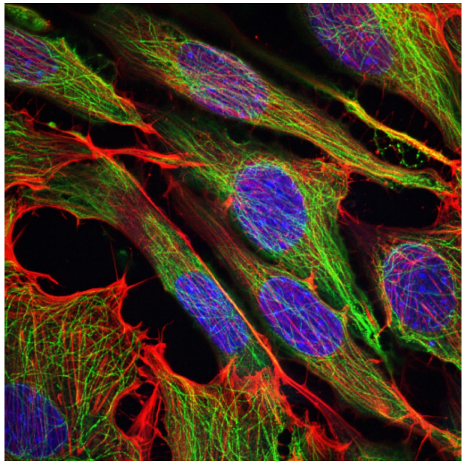
Microscopies

Problem: because of coherence, laser illumination requires special solutions!

Laser scanning confocal microscopy

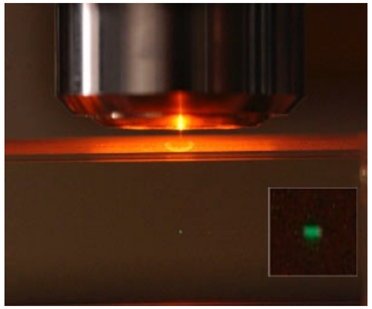
Monochromaticity, steerability

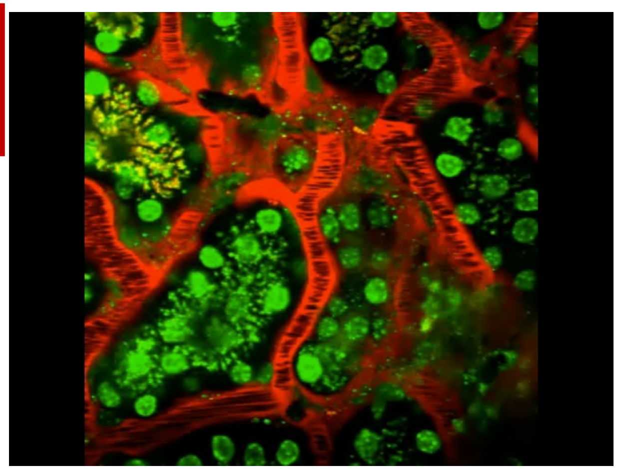




Multiphoton fluorescence microscopy

Monochromaticity, steerability, short pulses





Localization-based super-resolution microscopies

Monochromaticity, power density

E. Betzig

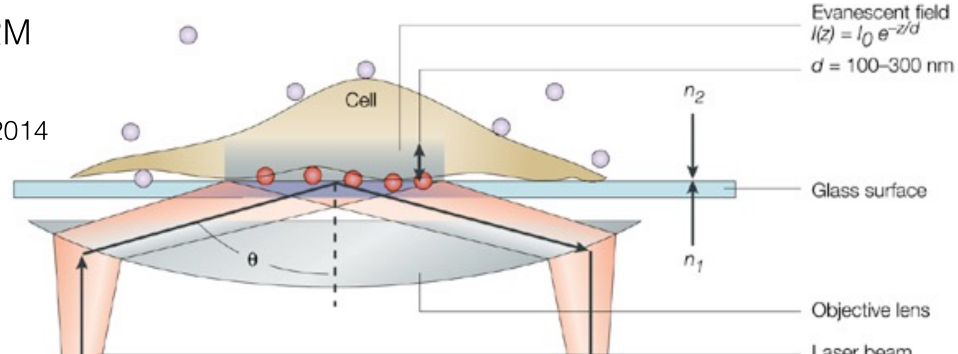
W.E.Moerner

STORM

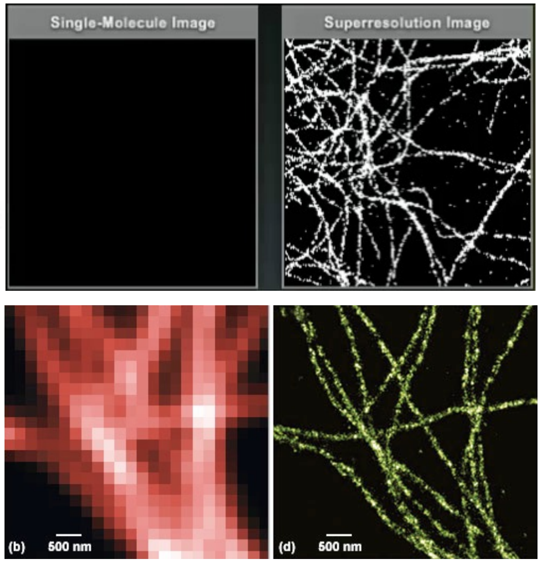
Nobel-prize, 2014

PALM

Xiaowei Zhuang



Total Internal Reflection

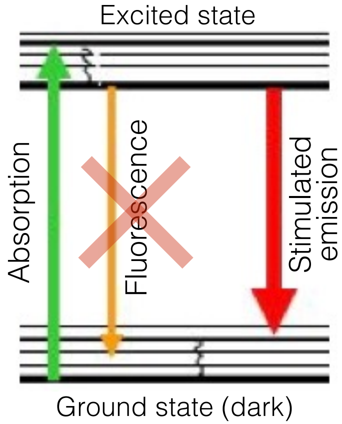


STED super-resolution miroscopy

(STimulated Emission Depletion)

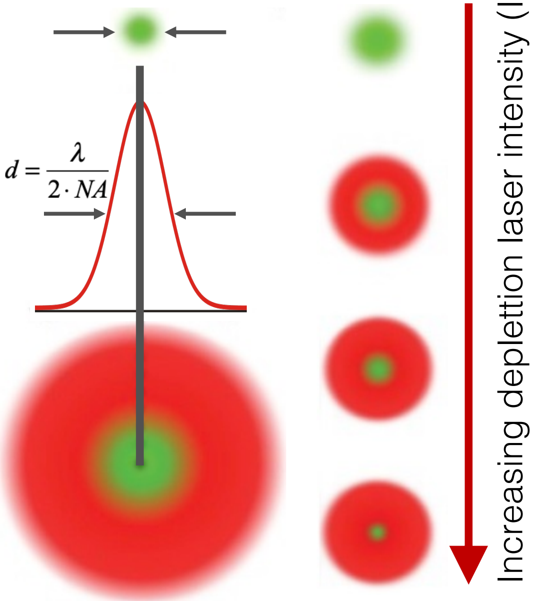
Fundamental laser process, monochromaticity, power density, steerability

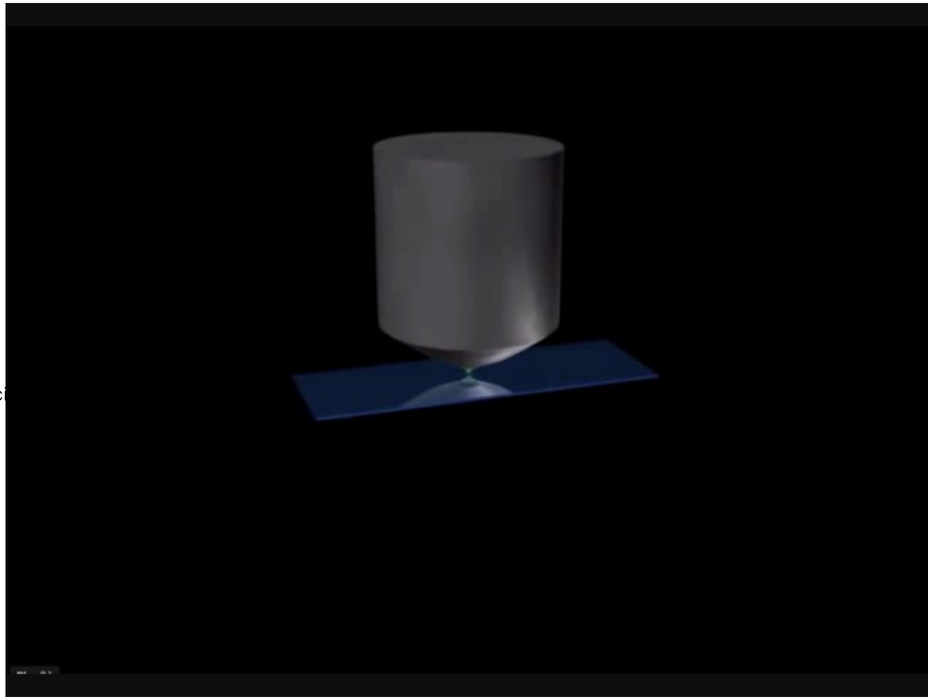
Stefan Hell (Nobel-prize 2014)

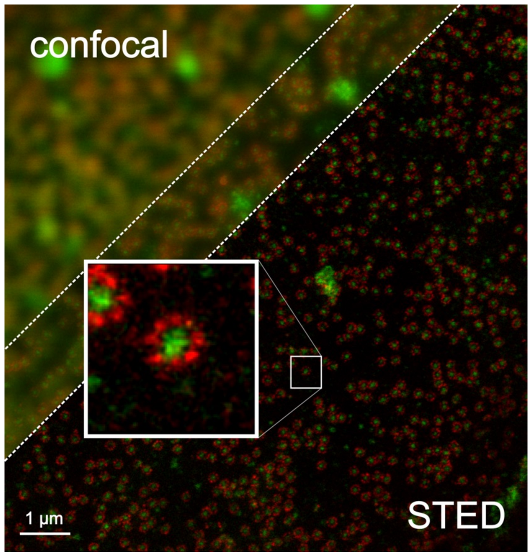


Hell: $d = \frac{\lambda}{2 \cdot NA\sqrt{1+I/I_s}}$

Abbé: $d = \frac{\lambda}{2 \cdot NA}$

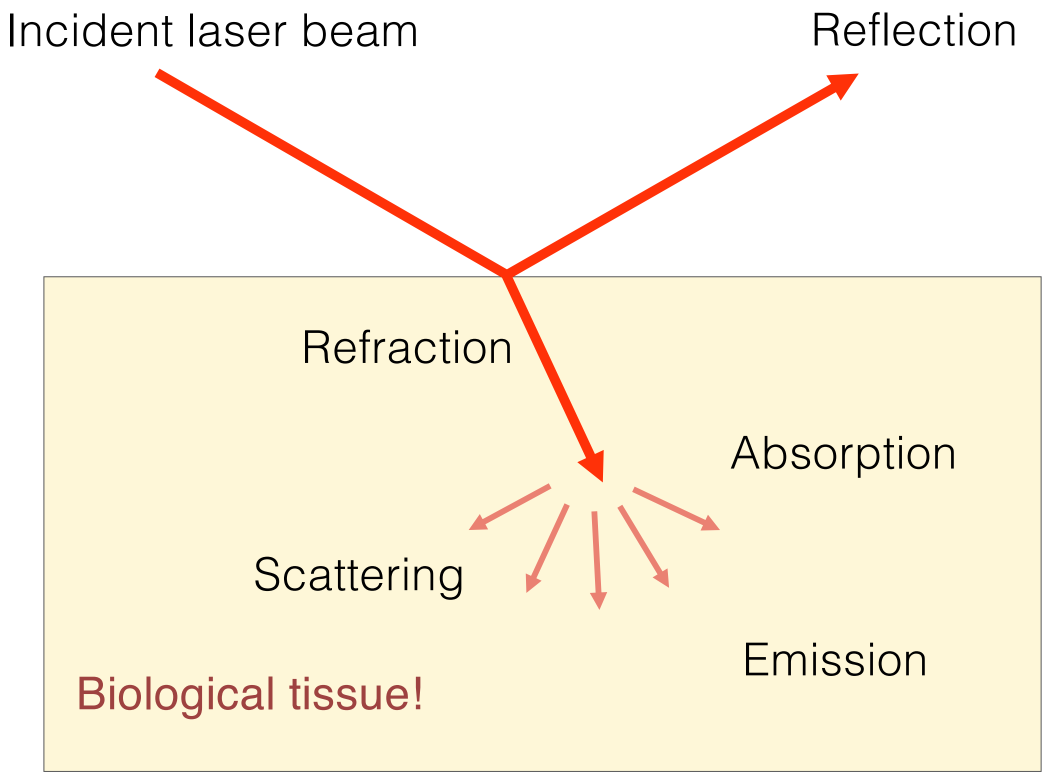






STED microscopic image of nuclear pore complexes

Medical applications of lasers



Laser properties to consider:

- Steerability (small divergence, surgeries)
- Power (surgical applications)
- Monochromaticity (tissue absorbance)
- Coherence (interference, image formation)

The effects depend not only on the properties of the laser, but also on those of the biological tissue: absorbance, transmittivity, light-induced reactions.

Dermatological applications

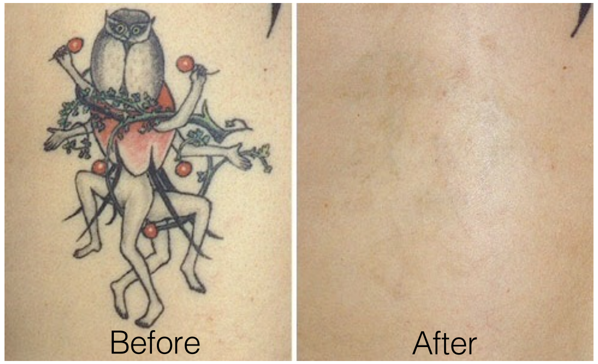
Hair removal, phototricholysis, photoepilation

Mechanism: selective photothermolysis, selective absorption by chromophores

Employed chromophores:

1. Carbon (exogenous, carbon or graphite-containing creams)
2. Hemoglobin (endogenous)
3. Melanin (endogenous)

Tattoo removal



Naevus removal

Removal of superficial blood vessels

Skin resurfacing

Wrinkle removal

Rhinophyma (sebaceous gland hypertrophy, fibrosis)

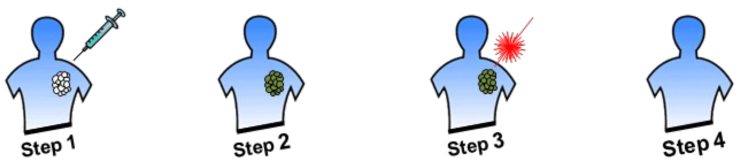
Oncological applications: Photodynamic therapy

Photodynamic therapy (PDT):
Roswell Park Cancer Institute 1970's.

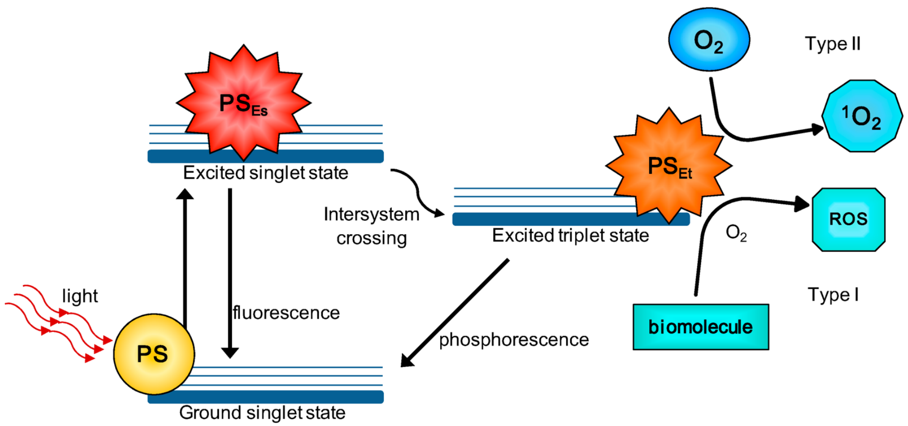
Three-component tumor therapeutic method:
1. Photosensitizing agent, 2. Light, 3. Oxygen.


Delivery of light into the patient: surface exposure, optical fiber

Steps:

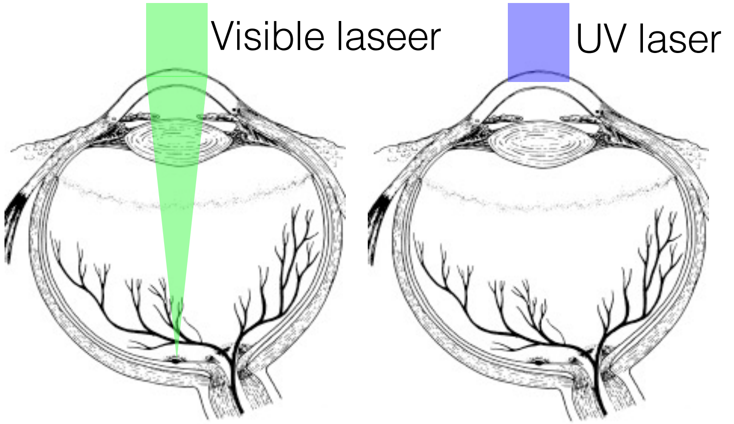


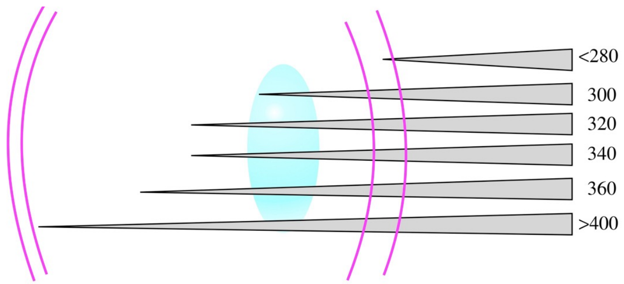
1. Administration of photosensitizing agent (aminolevulic acid, ALA).
2. Incubation for few hours. ALA is transformed into protoporhyrin IX.
3. Illumination of target area with diode laser (few minutes).
4. Protoporphyrin absorbs ➛ excited singlet state ➛ triplet state ➛ energy transfer with triplet oxygen ➛ excited, reactive oxygen ➛ tissue reaction. The illuminated area necrotizes in a few days.



Ophthalmologic applications I.

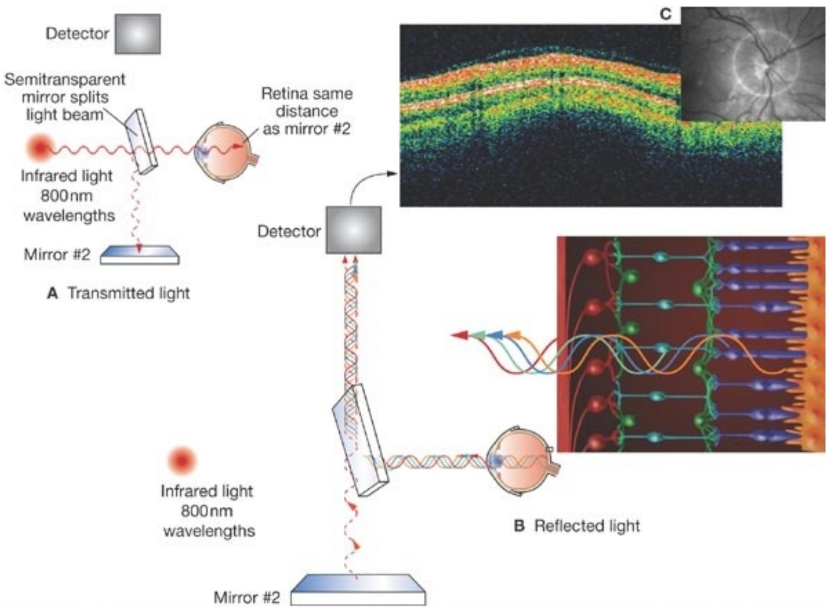
Principle: transmittivity of optical media is wavelength-dependent

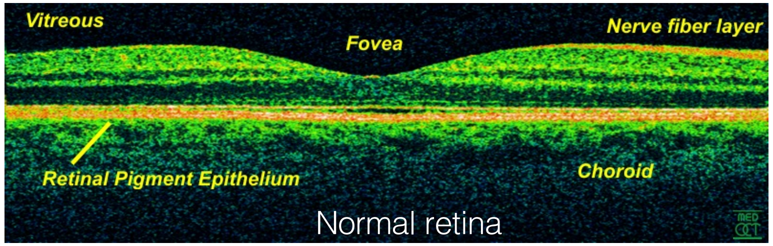


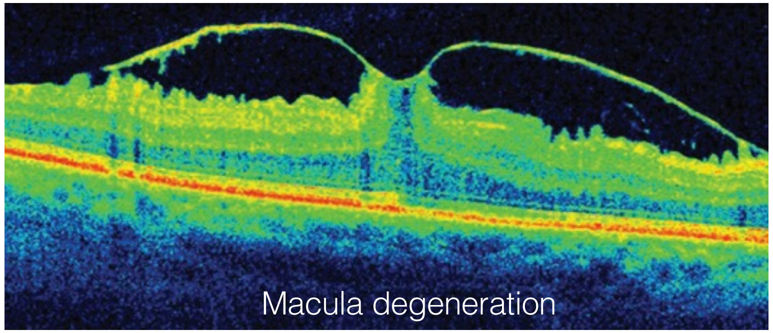


Diagnostics: Optical Coherence Tomography (OCT)

- Non-invasive
- Contrast-agent free
- Near microscopic resolution
- light rays reflected in deeper tissue layers can be separated from scatter by using interferometry.
- The spatial position of the reflecting layers can be determined.
- The structure of the illuminated sample can be resolved within 1-2 mm depth.





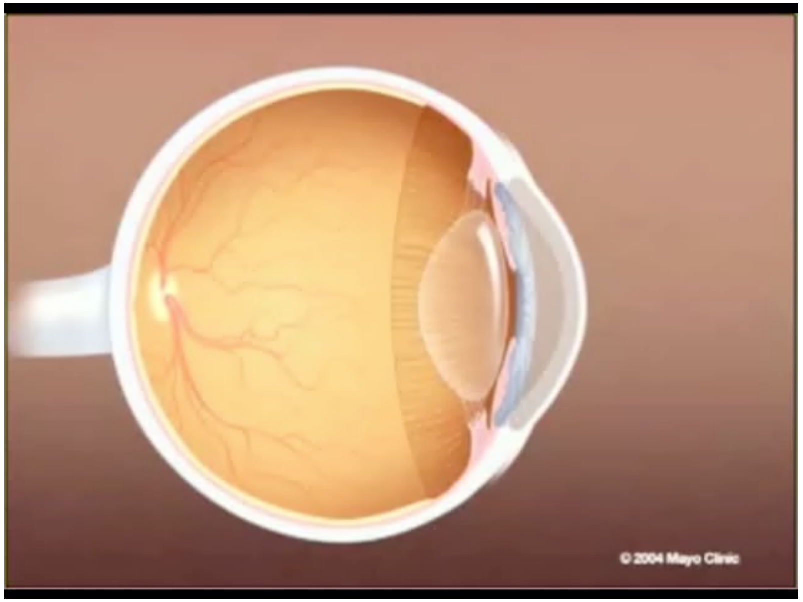


Ophthalmologic applications II.
Therapeutics:LASIK

“Laser-assisted In Situ Keratomileusis”
A type of refractive laser eye surgery

History:
Jose Barraquer, 1970: construction of a microkeratome, with which he was able to cut lines and lobes in the cornea with laser (keratomileusis).
Lucio Buratto (Italian) and Ioannis Pallikaris (Greek), 1990: combination of keratomileusis photorefractive keratectomy.
Thomas and Tobias Neuhann (Germany), 1991: automated microkeratome.

Steps:
1. Removal of contact lens (7-10 days prior to treatment)
2. Scanning the topography of the cornea with low-power laser.
3. Cutting and lifting a layer of the cornea with femtosecond laser.
4. Removal of material from the corneal stroma (few tens of microns). Excimer laser (193 nm).



Feedback

https://feedback.semmelweis.hu/feedback/pre-show-qr.php?type=feedback&qr=GZNYB9LC68CNXPMA