Principles, types and medical applications of lasers

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28/10/2022

Laser

light amplification by stimulated emission of radiation
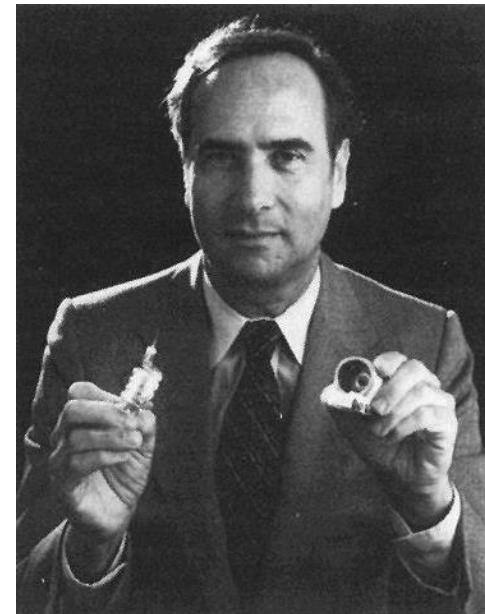
History of lasers in a nutshell…

1917 - *Albert Einstein:* theoretical prediction of stimulated emission

1954 - *N.G. Basow, A.M. Prochorow, C. Townes:* ammonia maser (**M**icrowave **A**mplification by **S**timulated **E**mission of **R**adiation)

1960 - *Theodore Maiman:* first laser in the visible spectral range (ruby laser)

a flashlamp-pumped synthetic ruby crystal to produce red laser light at 694 nm wavelength

Nobel prize in Physics 1964

for work in quantum electronics leading to lasers and masers

Alexander Prochorow   **Charles H. Townes**   **Nicolay Basow**

Nobel prize in Physics 1971

For invention of holography

XI. kerület, Magyar tudósok körútja 2.   **Gábor Dénes**

Steven Chu **William D. Phillips** **Claude Cohen-Tannoudji**

Nobel prize in Physics 1997
for development of methods to cool and trap
atoms with laser light

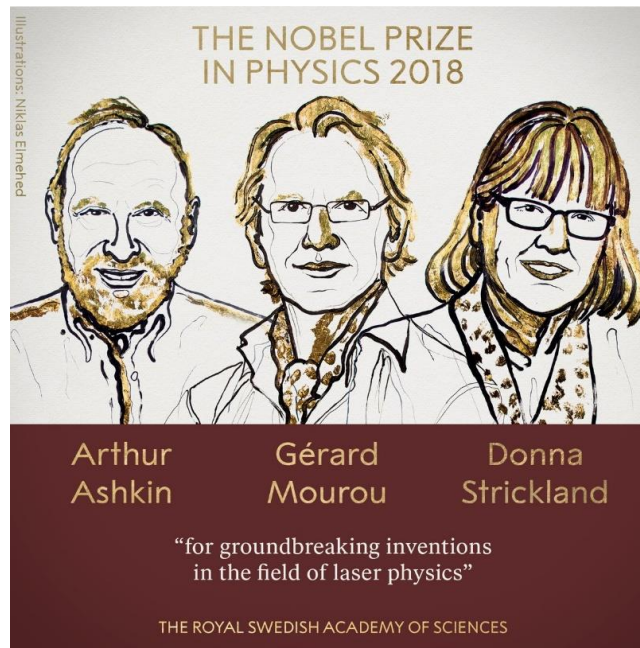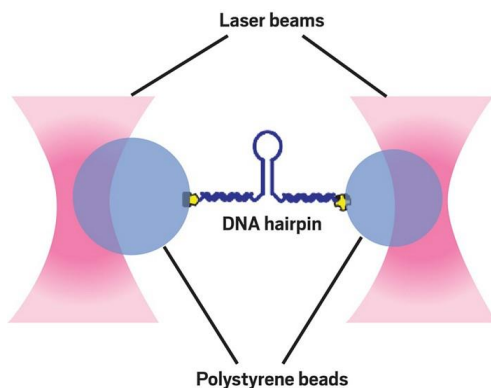**Zhores Ivanovich Alferov** **Herbert Kroemer**

Nobel prize in Physics 2000
Semiconducting laser diode

Nobel prize in Physics 2018
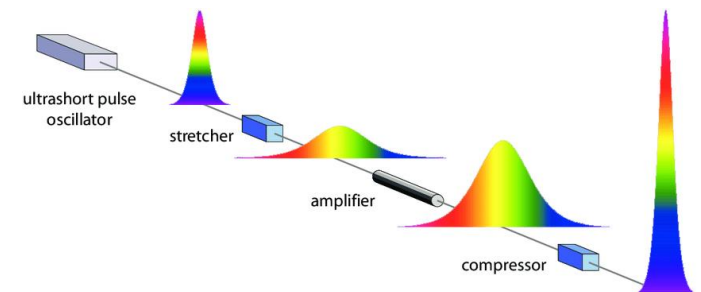## "for groundbreaking inventions in the field of laser physics"

Ashkin,

Arthur Ashkin invented optical tweezers that grab particles, atoms, molecules, and living cells with their laser beam fingers. The tweezers use laser light to push small particles towards the centre of the beam and to hold them there. In 1987, Ashkin succeeded in capturing living bacteria without harming them. Optical tweezers are now widely used to investigate biological systems.

THE NOBEL PRIZE IN PHYSICS 2018

Arthur Ashkin   Gérard Mourou   Donna Strickland

"for groundbreaking inventions in the field of laser physics"

THE ROYAL SWEDISH ACADEMY OF SCIENCES
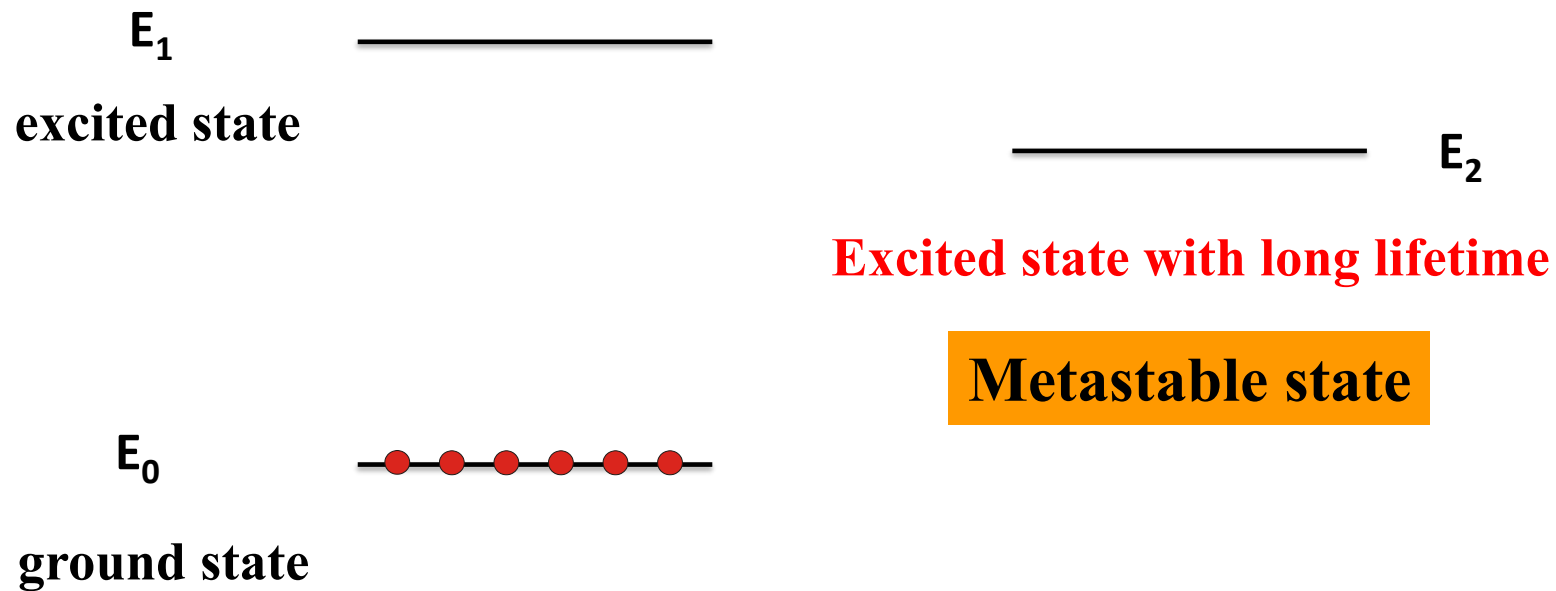
Mourou and Strickland

paved the way towards the shortest and most intense laser pulses ever created by mankind

First they stretched the laser pulses in time to reduce their peak power, then amplified them, and finally compressed them. If a pulse is compressed in time and becomes shorter, then more light is packed together in the same tiny space – the intensity of the pulse increases dramatically. The innumerable areas of application have not yet been completely explored…
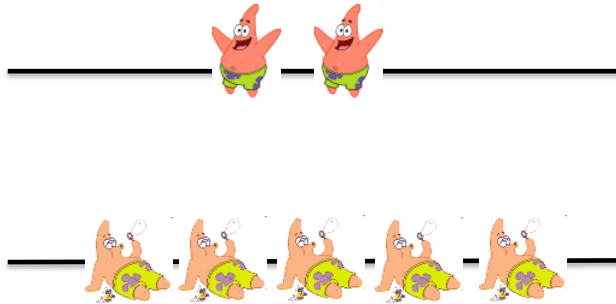
Fundamentals of laser operation

Special electronic energy states –
I. at least a three-state system

E_1

excited state

E_2

Excited state with long lifetime

Metastable state

E_0

ground state

Laser material: doped crystal, mixture of gases, solution of organic dyes

II: Occupancy in energy levels
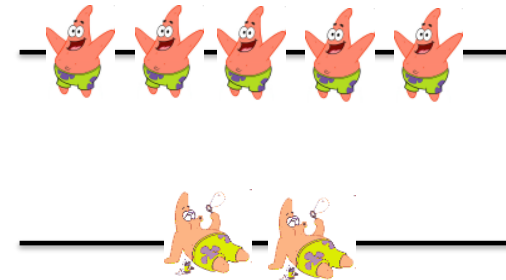# Population inversion

Thermal equilibrium

According to Boltzmann distribution

$$\frac{n_i}{n_0} = e^{-\frac{\varepsilon_i - \varepsilon_0}{k_B T}}$$
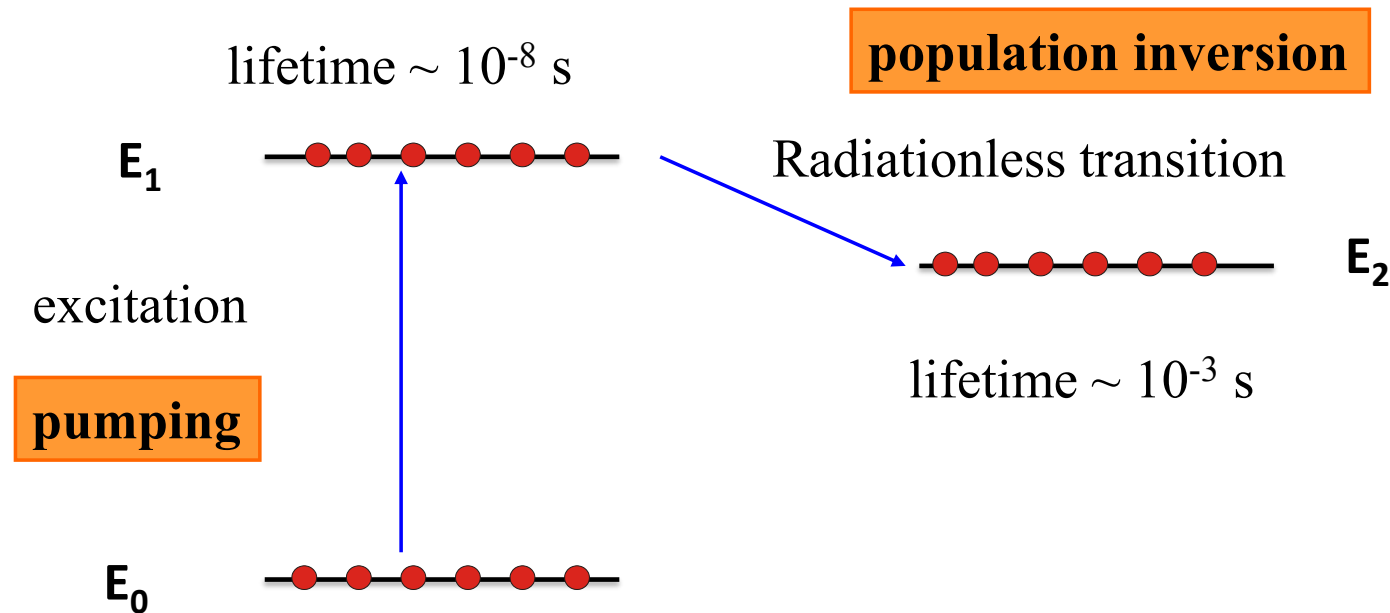
The number of atoms, **n**, at an energy level $\Delta\varepsilon$ higher than the ground level, if the number of atoms in the ground state is **n_0** in two energy levels separated by the energy difference.

Population inversion

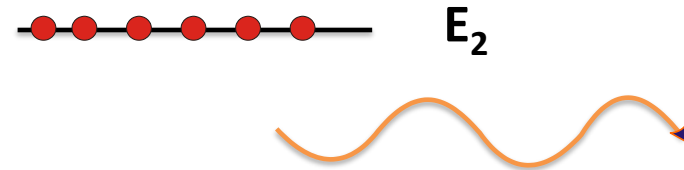"opposite" distribution – more electrons are in the excited state than in the ground state

III: Excitation
Optical pumping

lifetime $\sim 10^{-8}$ s

population inversion

E_1

Radiationless transition

E_2

excitation

pumping

lifetime $\sim 10^{-3}$ s

E_0

Optical pumping = energy input from an external source (electrical, optical, chemical energy)
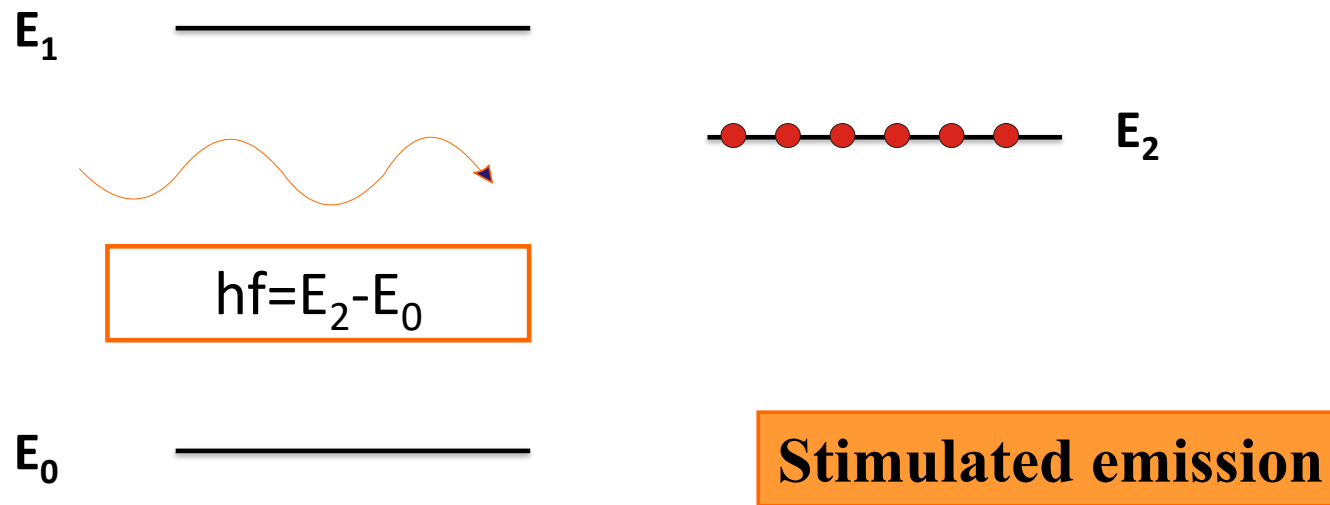
Spontaneous photon emission

E_1 ————————

●●●●●● ———— E_2

Spontaneous light emission

E_0 ————————●

Low probability

Induction of atomic transition – relaxation of electrons from metastable state

E_1 ——————————

E_2 ●●●●●●——

$$hf = E_2 - E_0$$

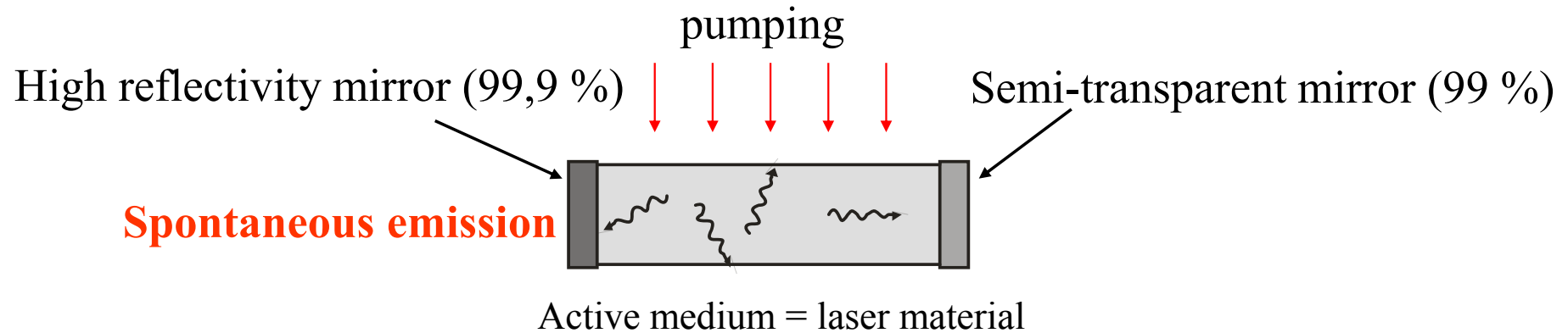E_0 ——————————

Stimulated emission

The incoming photon of hf = E_2-E_0 can interact with electrons on metastable state causing them to dorp to the lower energy level

Induction of atomic transition – relaxation of electrons from metastable state

E_1 ——————————

E_2

$$hf = E_2 - E_0$$
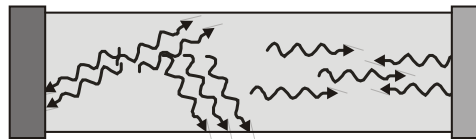
E_0 ● ● ● ● ● ●

Stimulated emission

Phase, frequency, polarization, and direction of the photons emitted with the stimulated emission are identical with that of induced the stimulation.
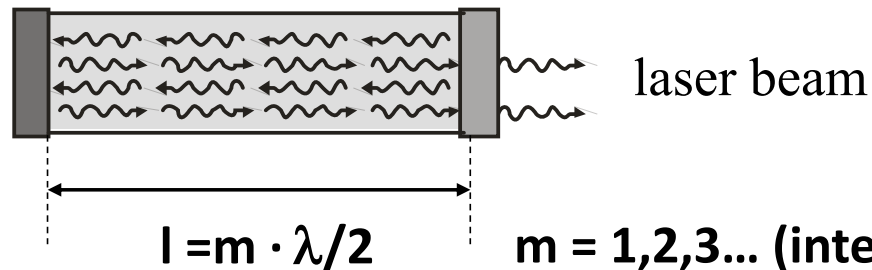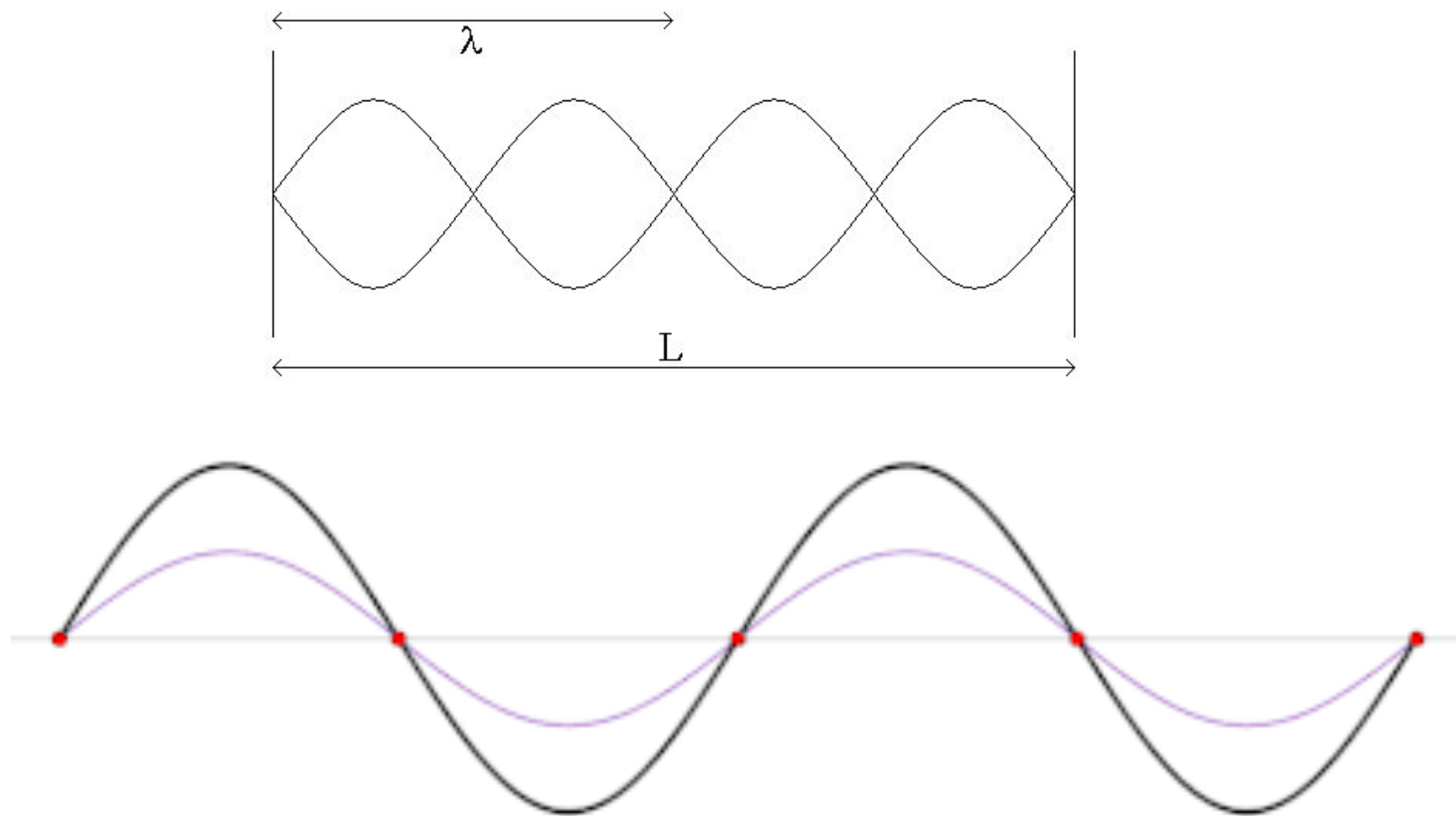
Optical resonator

pumping

High reflectivity mirror (99,9 %)　　　　Semi-transparent mirror (99 %)

Spontaneous emission

Active medium = laser material

Spontaneous and stimulated emission

Stimulated emission

laser beam

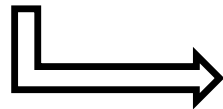$l = m \cdot \lambda / 2$　　　　$m = 1,2,3\ldots$ (integer number)

Standing wave in the optical resonator

General properties of laser light

Photons emitted by stimulated emission and the inducing photons are identical:
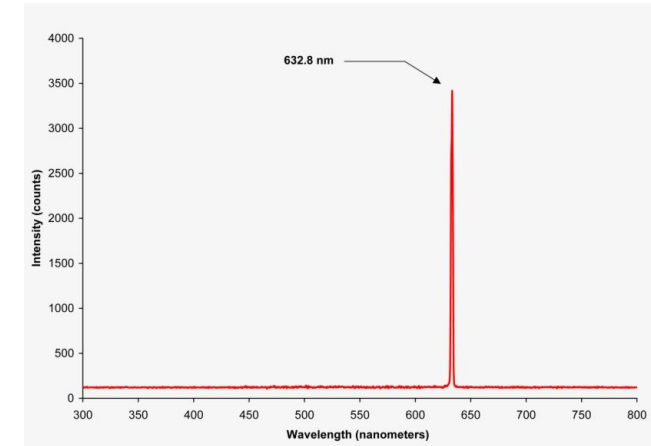
- energy
- phase
- polarization
- direction

↳⟹ **Consequently laser light is**

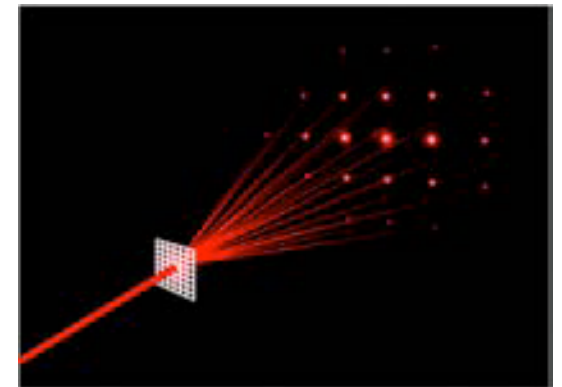
- monochromatic
- coherent
- polarized
- parallel beam

Light generated by stimulated emission

1. monochromatic – narrow spectral width

2. coherent – phase identity
   temporal coherence: (phase identity of photons emitted at different times)
   spatial coherence: (phase identity across beam diameter)

3. Small divergence: parallel beam

4. Polarized: electric field vector oscillates in a single plane

5. Extremely short pulses: fs, ps, as

6. High power (kW-GW): large spatial power density,
   e.g.: Nd-YAG laser pulse energy 2 J, 20 ns, 10 Hz –> emitted average power:
   2 J/0,1 s = 20 W, power of single pulse: 2 J/20 ns = 10^8 W

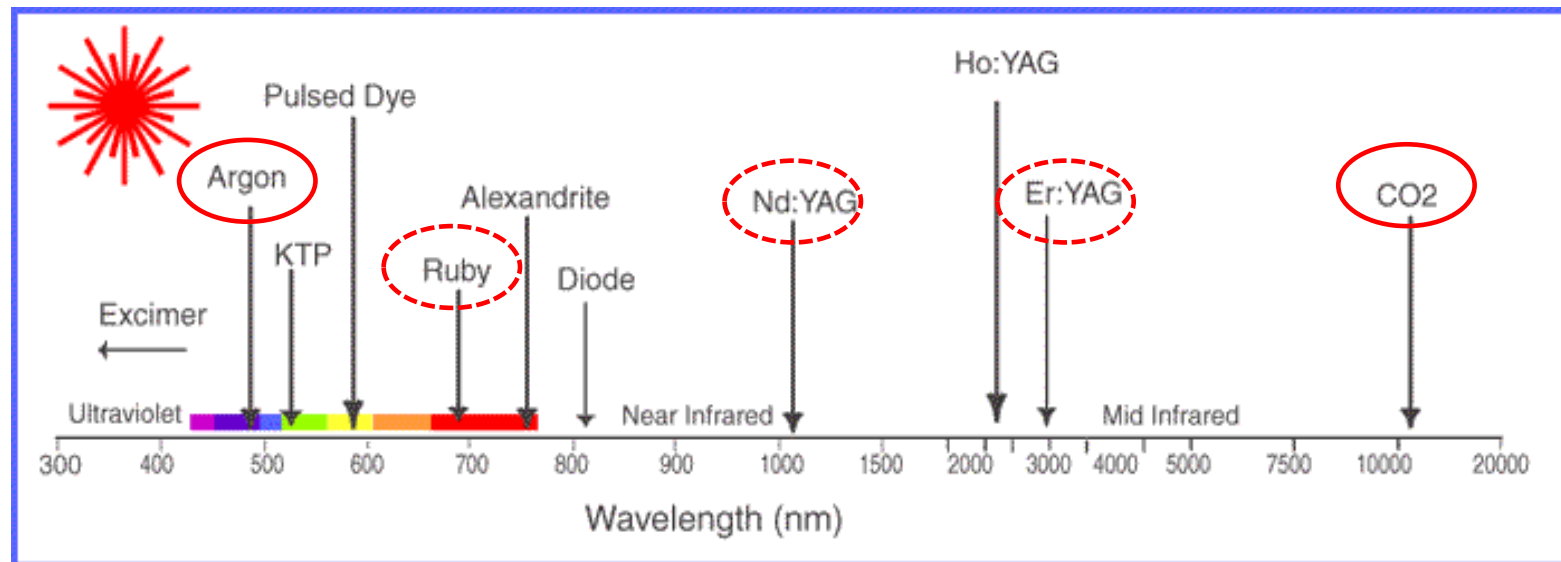7. Continous wave or pulsed lasers

He-Ne laser emission spectrum

Interference pattern of laser beam

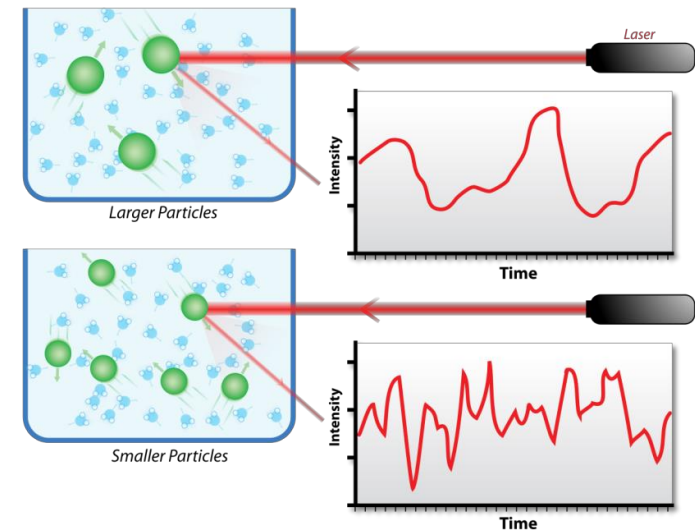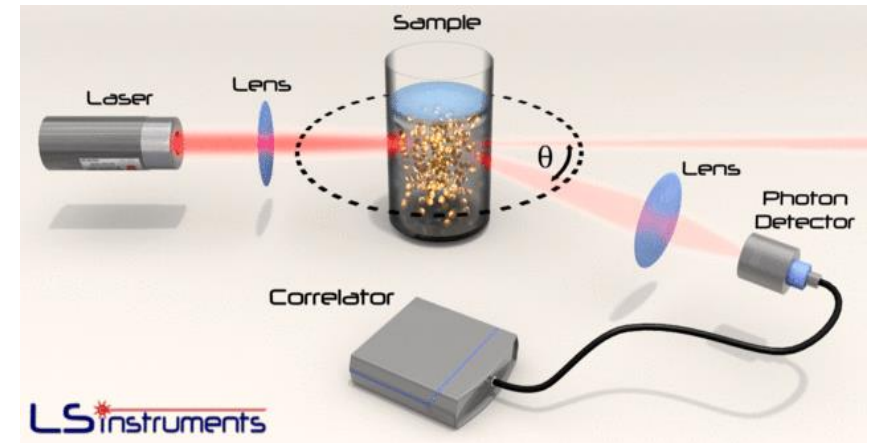# Types of lasers – *based on material (active medium)*

1. Solid state lasers: Metal dopoing crystals (Ruby, Nd-YAG ittrium-aluminium-garnet, Ti-sapphire)

2. Gas lasers: He-Ne, CO_2, Ar, Kr

3. Dye lasers: dilute solution of organic dyes (rhodamine, coumarin)

4. Semiconductor (diode) lasers: combination of p- and n-type dopes semiconductors

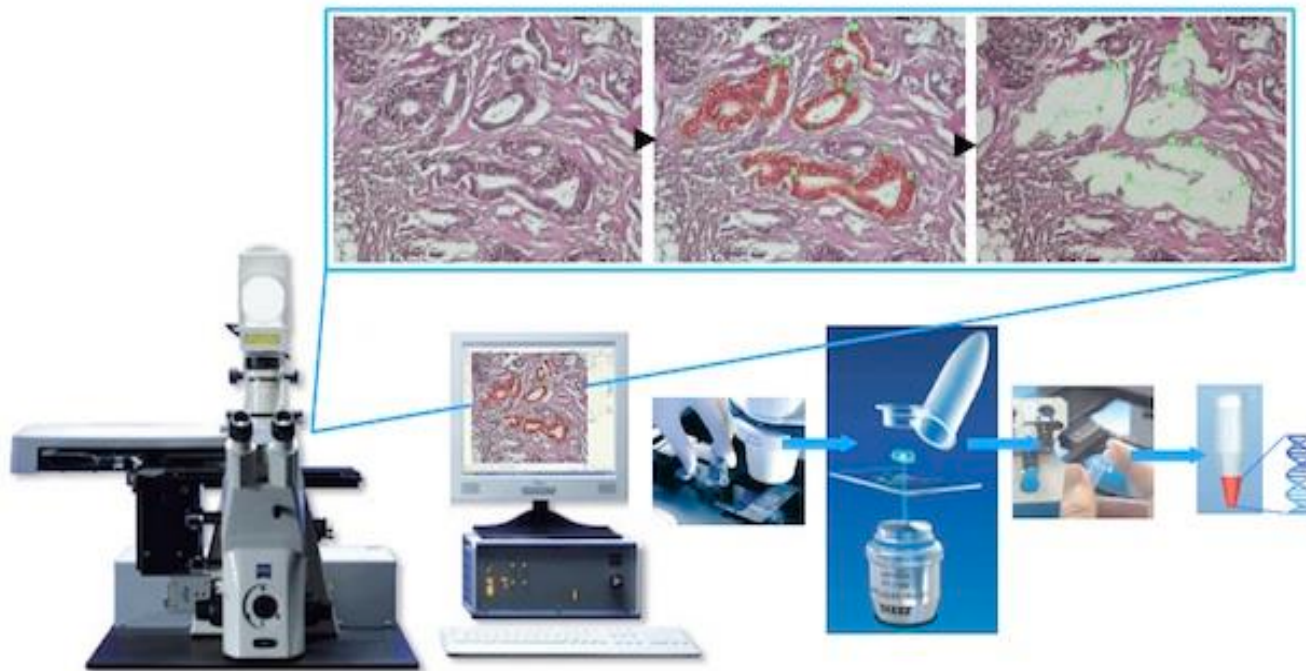# Application of lasers – laboratory techniques

Dynamics Light Scattering (DLS)

- nm-sized diffusing particles
- particles in suspension scatter the light
- the intensity of scattered light fluctuate in time
- related to the size of particles
- diffusion coefficient can be deduced
- radius of particle can be calculated
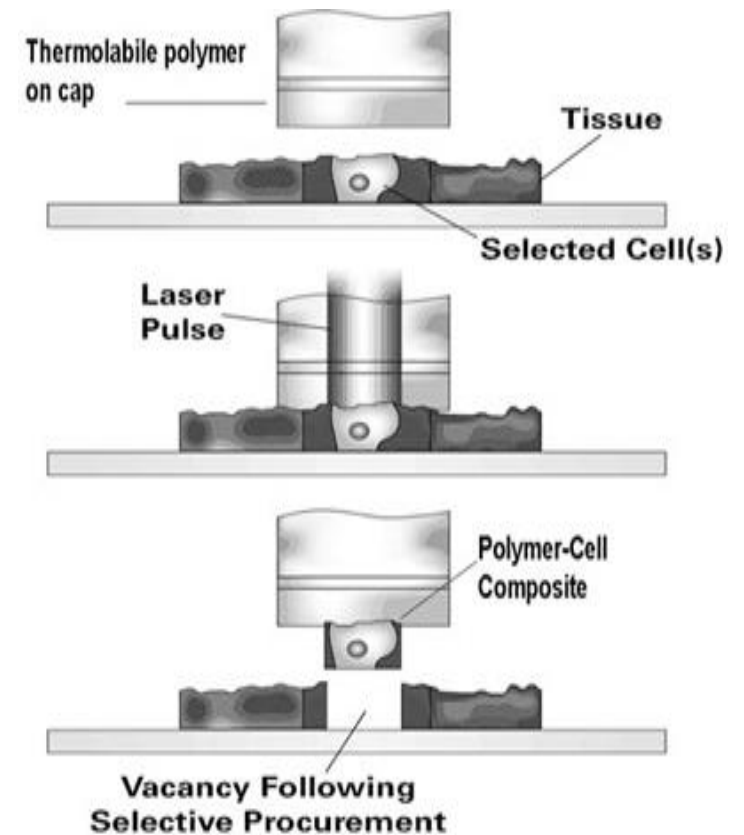- viruses, vesicles, nanoparticles, liposomes

$$D = \frac{k_B T}{6\pi\eta r}$$

Laser capture microdissection (LCM)

Local genetics/proteomics: KRAS somatic mutation, important diagnostic tumor marker in colon cancer, DNA from cancer cells can be tested, mixture of healthy and cancerous cells – false negative, improving selectivity/sensitivity
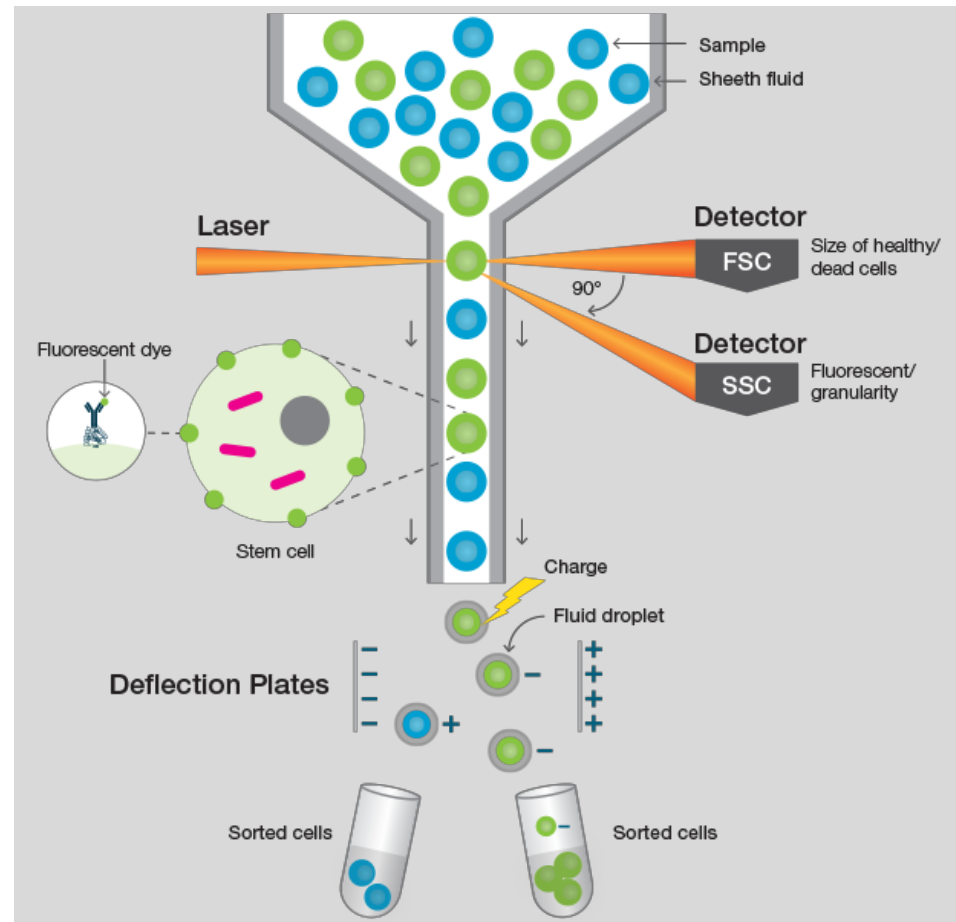
UV laser – cut
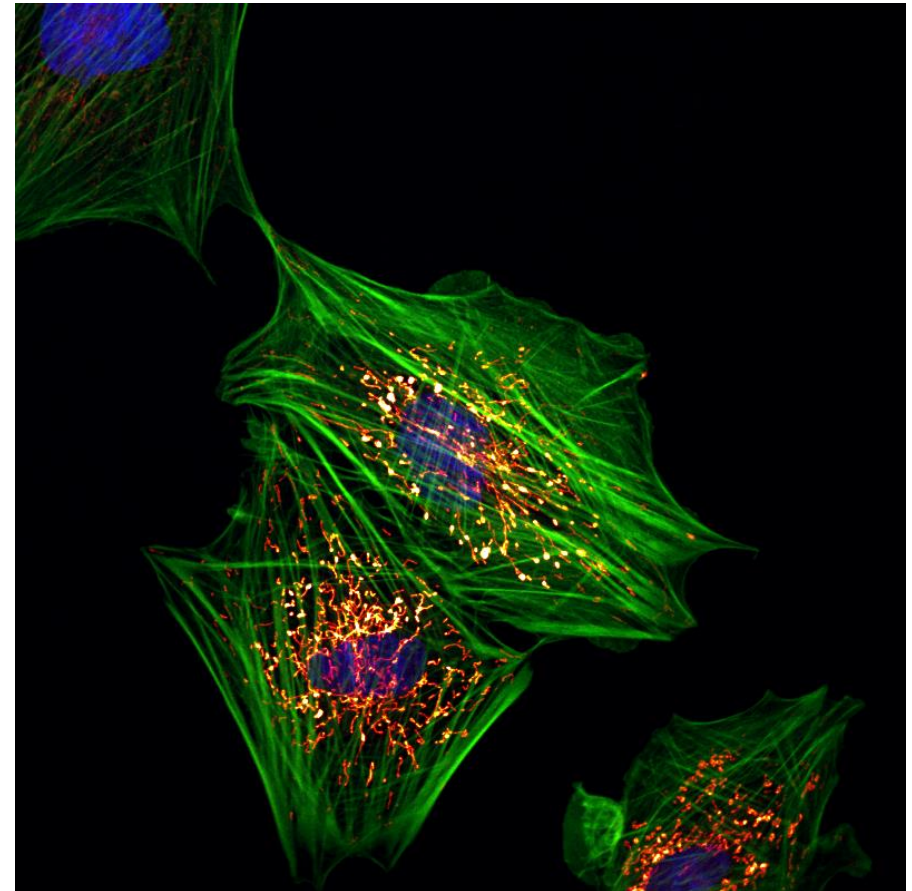IR laser – heating the polymer cap

FACS (Fluorescence activated cell sorter)

- counting, sorting, isolation of living cell population

- Fluorescent labeling of cells (specific antibodies)

- Hydrodinamic focusing = cells are separated in a laminar flow

- One cell at a time passes through a perpendicular laser beam

- Cells can be sorted by the emitted fluorescent wavelenght

- Immunology, cell biology

Laser scanning confocal microscopy (spoiler alert!)

Fluorescent labeling of fibroblast cells: blue – nucleus, green – microtubules, red - mitochondria

Medical applications of lasers – interactions…

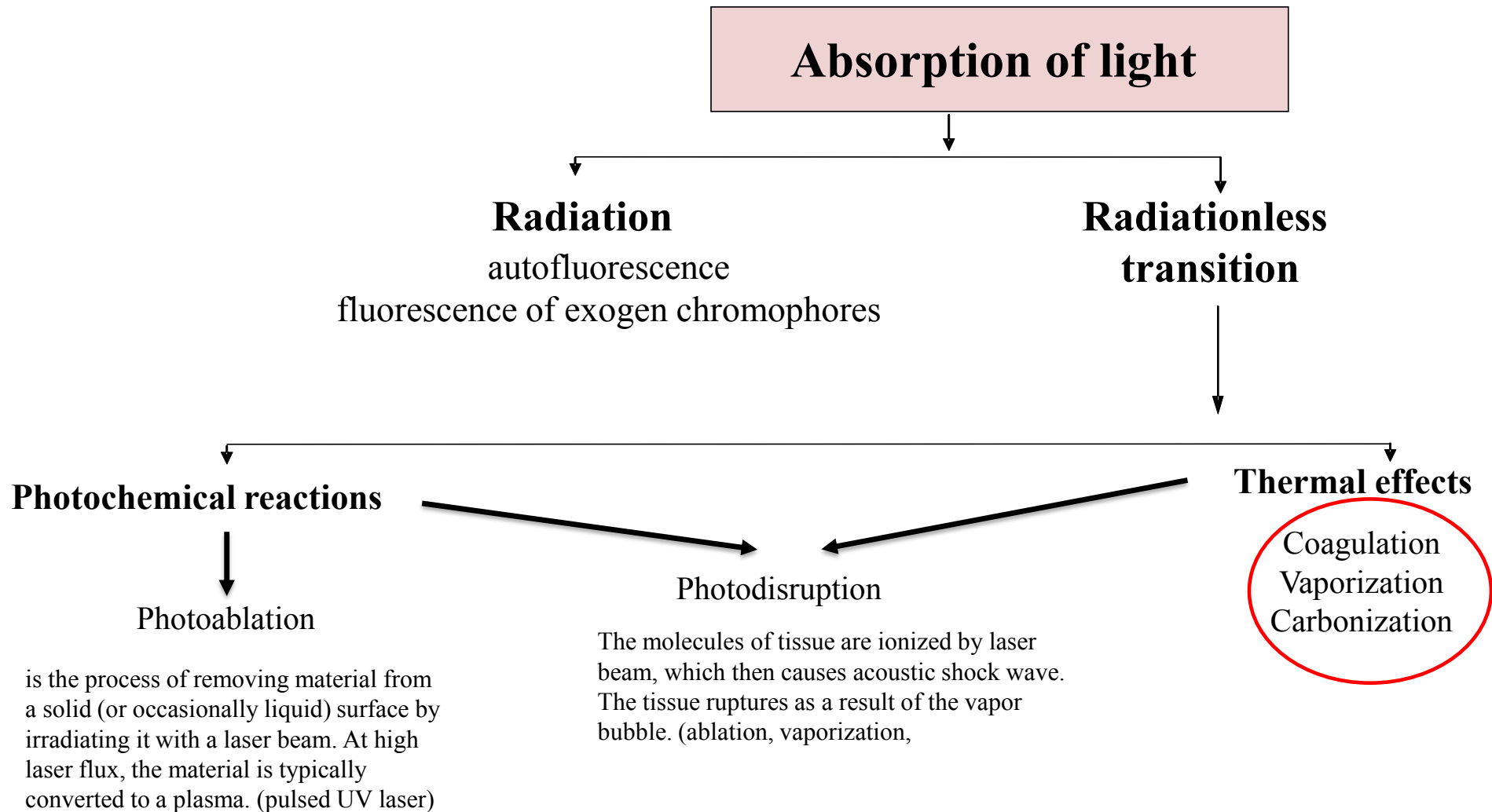**Absorption of light**

Radiation
autofluorescence
fluorescence of exogen chromophores

Radiationless transition

Photochemical reactions

Thermal effects

Coagulation
Vaporization
Carbonization

Photoablation

is the process of removing material from a solid (or occasionally liquid) surface by irradiating it with a laser beam. At high laser flux, the material is typically converted to a plasma. (pulsed UV laser)

Photodisruption

The molecules of tissue are ionized by laser beam, which then causes acoustic shock wave. The tissue ruptures as a result of the vapor bubble. (ablation, vaporization,

Thermal effects

biostimulation

coagulation

carbonization

vaporization

40 °C 60 °C 100°C 300 °C

Orthopedics

Oral Diagnosis
Herpes Treatment

48 Hours Later
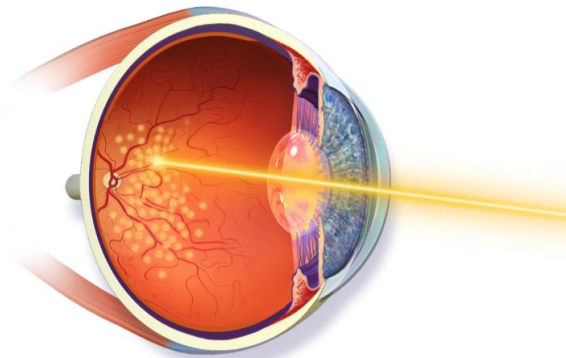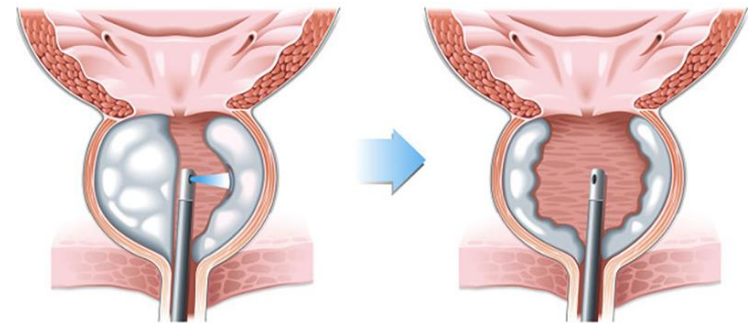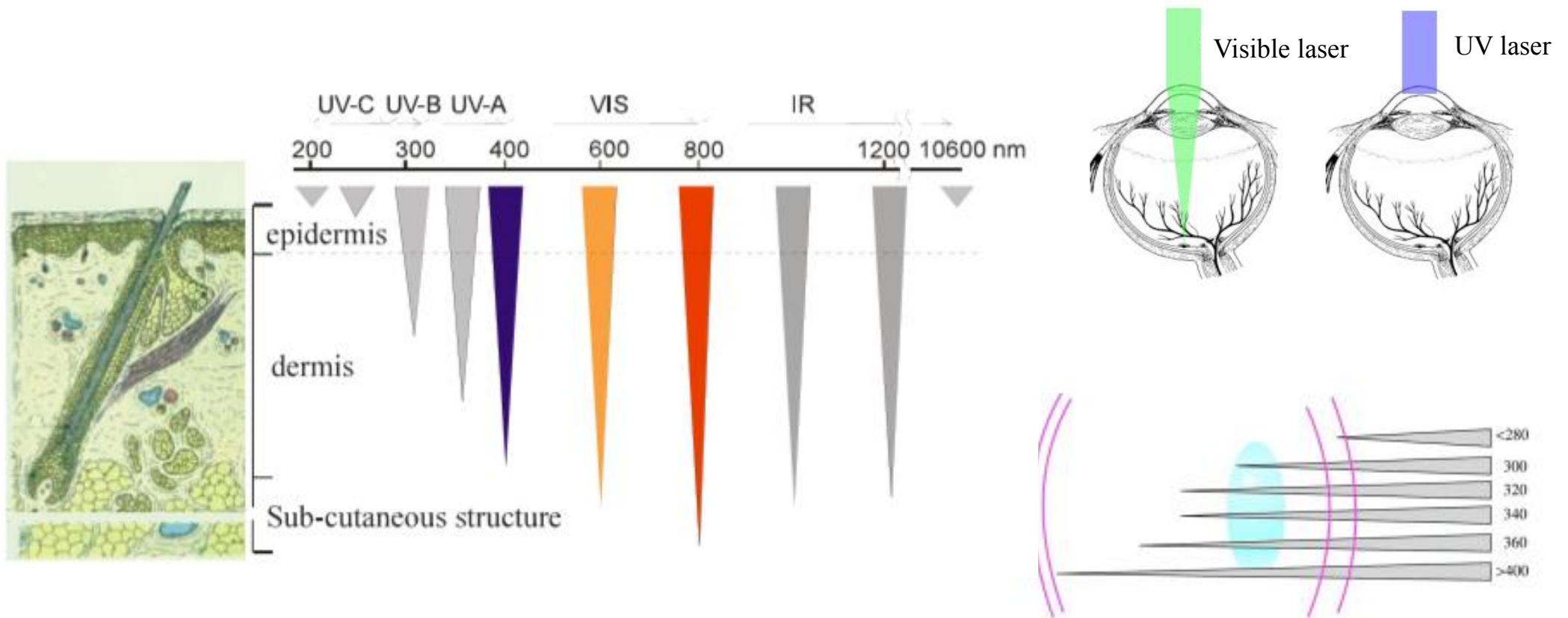
Retina treatment

Laser surgery of benign
prostatic hyperplasia

Penetration ability of light in tissue highly depends on its wavelenght!

Medical applications of lasers – DENTISTRY
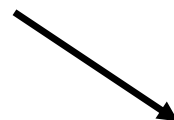
Soft laser therapy (SLT)

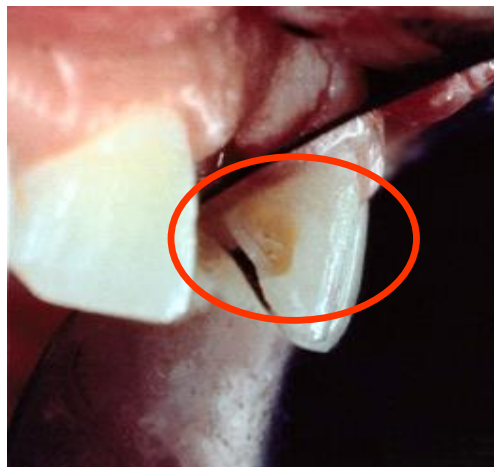- Biostimulation

- Low power: 100-150 mW

- Two wavelenght ranges applied:
  650-660 nm – 3 cm depth
  780-980 nm – 8-10 cm depth

- Faster wound healing

- Antimicrobial effect

- Bone restoring, implantology

Caries removal

- Vaporization and mechanical shockwave

- ErYAG

- 2940 nm

- Absorption in water and hydroxyapatite

- No carbonization, no heat formation

- Superficial layer is treated

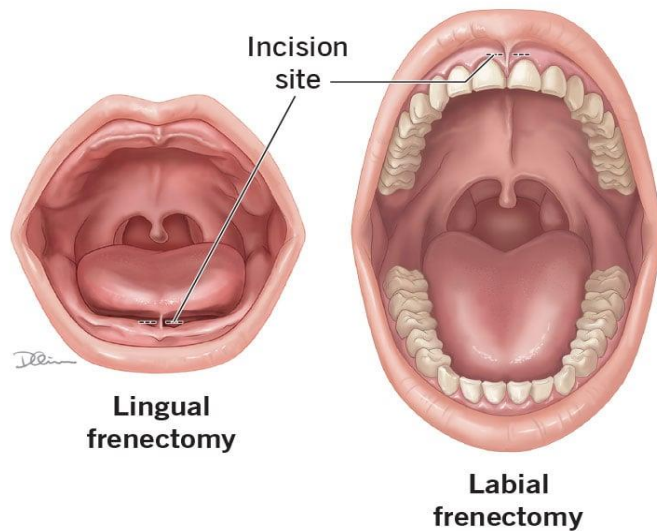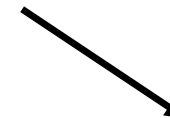caries removal

Oral surgery

Nd:YAP* laser
1340 nm

frenectomy

gingivectomy

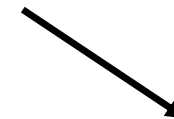*YAlO$_3$:Nd Neodymium doped yttrium aluminium perovskite

Teeth whitening

- Argon laser
- 488 nm

Ad of whitening pen…

https://www.youtube.com/watch?v=NW6XI5JvGsE

Medical applications of lasers – DERMATOLOGY

Laser type	Wavelength	Cutaneous application
Copper vapor/bromide (quasi-CW)	510nm	Pigment
	578nm	Vascular lesions
Pulsed dye	510nm	Superficial pigment, red/yellow/orange tattoos
	585nm	Vascular lesions, warts, hypertrophic scars, striae
Potassium titanyl phosphate (KTP)	532nm	Pigmented/vascular lesions
Neodymium:yttrium-aluminium-garnet (Nd:YAG) [frequency-doubled]	532nm	Superficial pigment, red/orange/yellow tattoos
Tunable dye argon (quasi-CW)	577/585nm	Vascular lesions
Ruby	694nm	
Q-switched		Pigment, blue/black/green tattoos
Normal mode		Hair
Alexandrite	755nm	
Q-switched		Pigment, blue/black/green tattoos
Long-pulsed		Hair
Nd:YAG	1064nm	
Q-switched		Pigment, blue-black tattoos
Long-pulsed		Hair (darker skin phototypes)
Nd:YAG	1320nm	Nonablative skin resurfacing
Erbium:YAG (pulsed)	2940nm	Skin resurfacing, epidermal lesions
Carbon dioxide (CO_2)[CW]	10 600nm	Actinic cheilitis, verrucae, rhinophyma
CO_2 (high-energy, pulsed)	10 600nm	Skin resurfacing, epidermal/dermal lesions

CW = continuous wave; **Q-switched** = quality-switched.

American Journal of Clinical Dermatology 2001, Lasers in Dermatology, T. Alster, J. Lupton

Er:YAG laser

or

CO$_2$ laser

2940 nm

10600 nm

„skin resurfacing" – photoablative technique

Wrinkles, scars, acne treatment

Dr. Varjú Gábor, Lézerek az esztétikai bőrgyógyászatban: a rejuvenáció módszerei, BŐRGYÓGYÁSZATI ÉS VENEROLÓGIAI SZEMLE • 2020 • 96. ÉVF.4. 163–181.

Removal of superficial blood vessels, veins

Nd:YAG laser

1064 nm

chromophore: oxyhemoglobin with 418, 542 and 577 nm absorption maxima
BUT! Depth of vessels, thickness, skin phototype, avoid: melanocytes, hair follicules

Photocoagulation based correction of veins

Nd:YAG laser
1064 nm

chromophore: oxyhemoglobin with 418, 542 and 577 nm absorption maxima
BUT! Depth of vessels, thickness, skin phototype, avoid: melanocytes, hair follicules
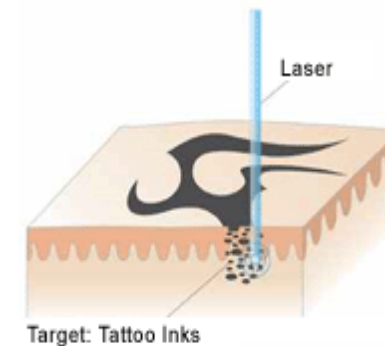
Aesthetic applications: hair, tattoo removal

DOES YOUR CAT NEED LASER HAIR REMOVAL?

BEFORE — AFTER

before   after

Hair removal
Ruby: 694 nm
Alexandrite (BeAl$_2$O$_4$): : 755 nm
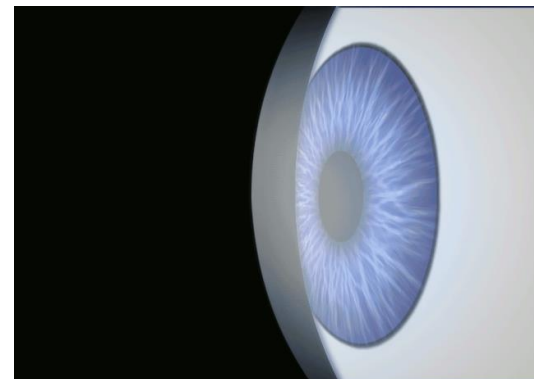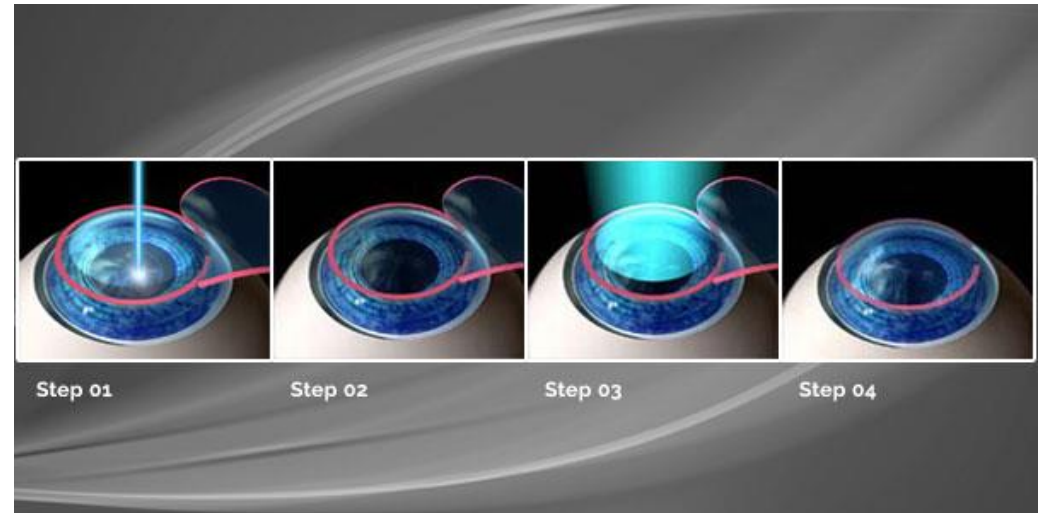NdYAG: 1064 nm

Laser

Target: Tattoo Inks

ruby laser (694 nm) is specifically absorbed by the color
pigments in the tattoo - vaporization

Medical applications of lasers – OPTHALMOLOGY

FEMTO-LASIK – Femtosecond-assisted Laser In Situ Keratomileusis

- is used to reshape the cornea of the eye
- correct refractive disorders
- femto laser – to create the corneal flap
- removal of material from the corneal stroma (few tens of μm)
- excimer laser (193 nm) (noble gases or the mixture of noble gas and halogen)
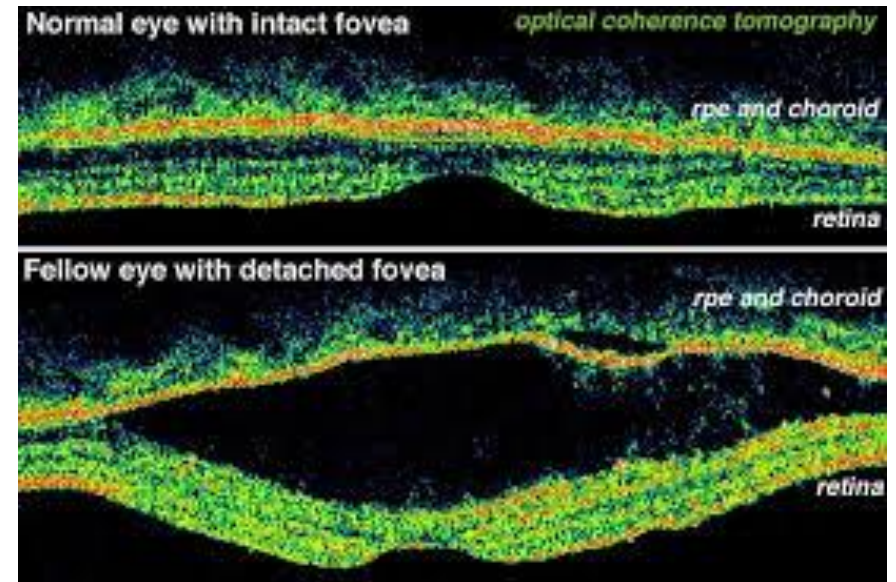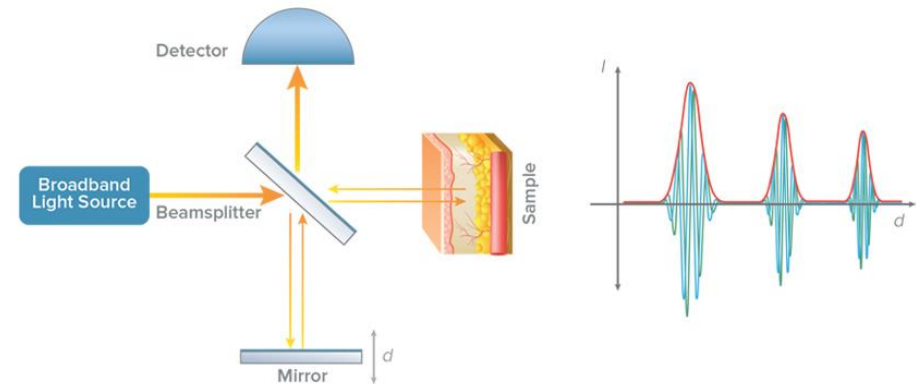- after surgery, the flap can be replaced without sutures, allowing for quicker healing

Step 01   Step 02   Step 03   Step 04

OCT – Optical coherence tomography

- diagnostic method in opthalmology
- show cross-sections of retina layers with micrometer resolution
- glaucoma, macular degeneration, diabetic macular oedema, multiple sclerosis

Principles:
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.
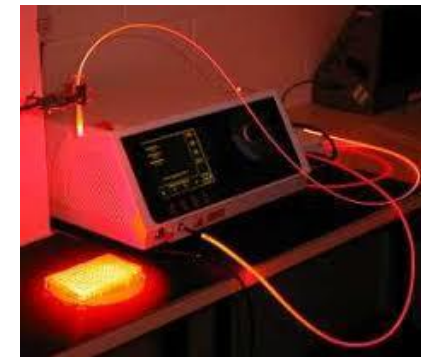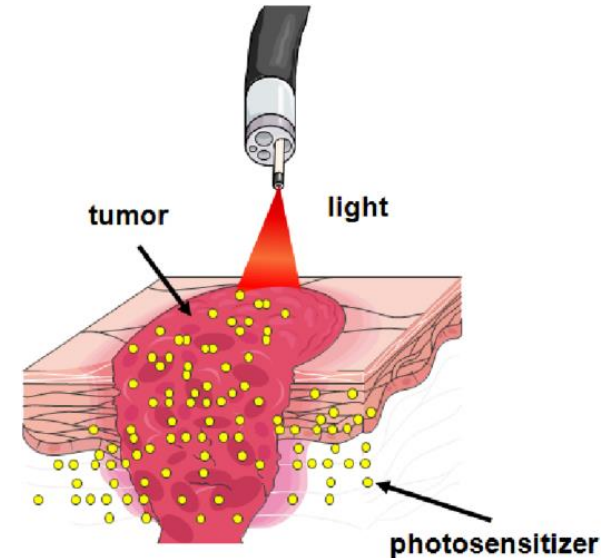
Medical applications of lasers – ONCOLOGY

PDT – Photodynamic therapy

1. administration of photosensitizing agent
   (porphyrins or 5-aminolaevulinic acid)
2. the photosensitiser concentrated in cancer tissue
3. activation of photosensitiser with light
4. the excited photosensitizer produces free radicals
   and reactive oxygen species (ROS)
5. tissue reaction
6. neighbouring healthy tissues remain intact

superficial skin cancers, tumor of cavity organs - oesophagus,
bronchus, ureters, bladder

Laser types:
Ar, NdYAG, TiS
310-1285 nm-tunable

Checklist

- Requirements of laser operation

    - 3 energy levels (metastable)

    - Population inversion (pumping)

    - Stimulated emission

- Optical resonator

- Properties of laser light (coherence, polarized, monochromatic, high power, parallel beam)

- Types of lasers

- Laboratory and medical applications

    - Absorption in tissue

    - Thermal effects

    - Penetration depth in tissues

Related chapters:

Damjanovich, Fidy, Szöllősi: Medical Biophysics

II. 2.2

        2.2.5

        2.2.7

        2.2.8

IX. 1.1

IX. 1.2