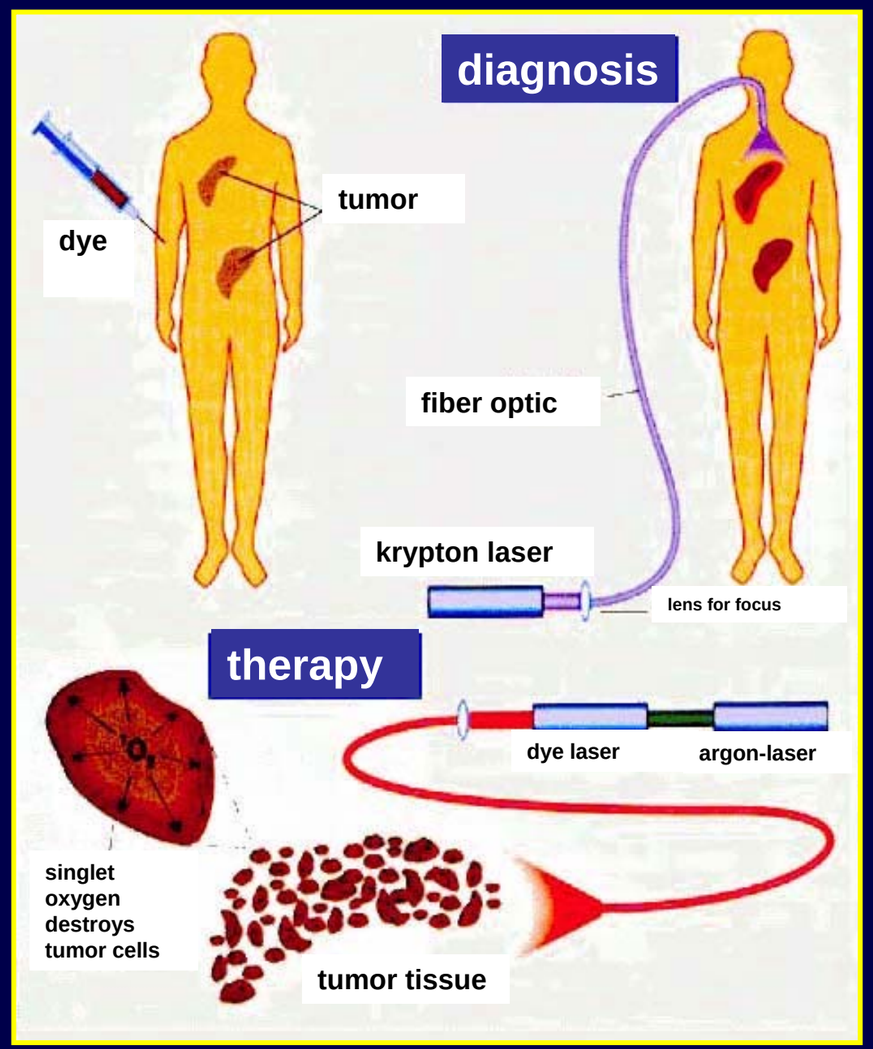
Photodynamic therapy and diagnosis



requirements

1) chemical components:
photosensitizer, e.g. porphyrin and O^2
2) selective uptake/ formation of the sensitizer in target tissue/ vessels
3) Selective irradiation with visible light

possible side effects

Light sensitivity of skin, nausea, vertigo; local pain with ALA-PDT

effects

after activation of the photosensitizer
1) fluorescence (for diagnosis)
2) chemical reaction with targets (for therapy), with the following sequence:
a) generation of singlet oxygen and ROS
b) oxidation of cell components
c) cell death or vessel shutdown
d) stimulation of the immune system

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PDT

- simple, useful, effective, cheap
- for malignant and non-malignant diseases
- minimally invasive, scar-free wound-healing, minor side effects
- applied with approval or due to failure of classical therapies or cross-resistance
- not tumorigenic, can be applied repeatedly and combined with other modalities

Application of the sensitizer via different routes: i.v., topically, orally, etc.

Irradiation at optimum sensitizer ratio in target-to-normal tissue

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Treatment of tumors at outer and inner surfaces (cavities) of the body:

ENT ➢ skin ➢ lung ➢ bladder ➢ oesophagus ➢ stomach ➢ cervix uteri ➢ brain ➢ pankreas ➢ prostate

licences e.g. in Canada, USA, Europe, Australia and Japan

Treatment of non-malignant diseases

➢ sterilisation of blood cells ➢ removal of bacteria and other microorganisms ➢ rheumatic arthritis ➢ arteriosclerosis ➢ macula-degeneration ➢ prophylaxis of restenosis after angioplastic ➢ caries ➢ dermatophytic fungi? ➢ malaria?

Indications in dermatology:

Morbus Bowen ➢ actinic keratosis ➢ basaloma ➢ Kaposi-sarkoma ➢ cutaneous metastases ➢ condyloma ➢ warts ➢ psoriasis ➢ acne ➢ skin rejuvenation. Excellent cosmetic results.

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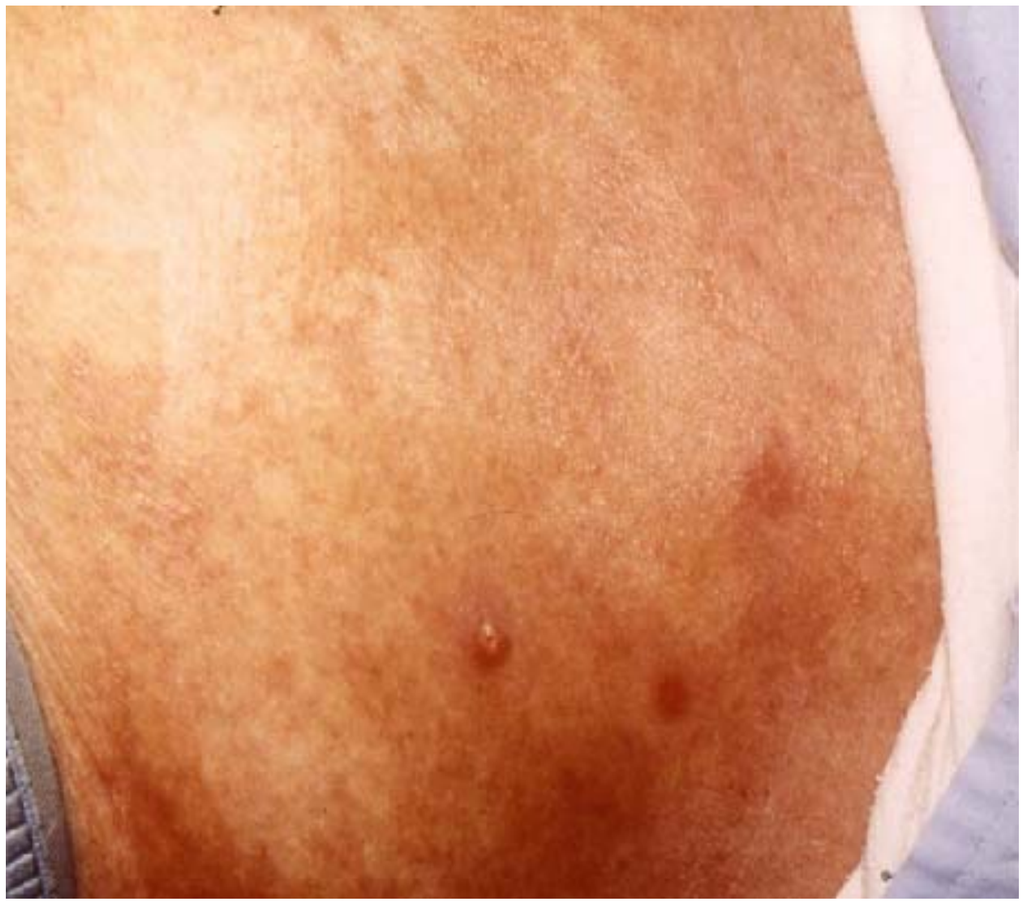
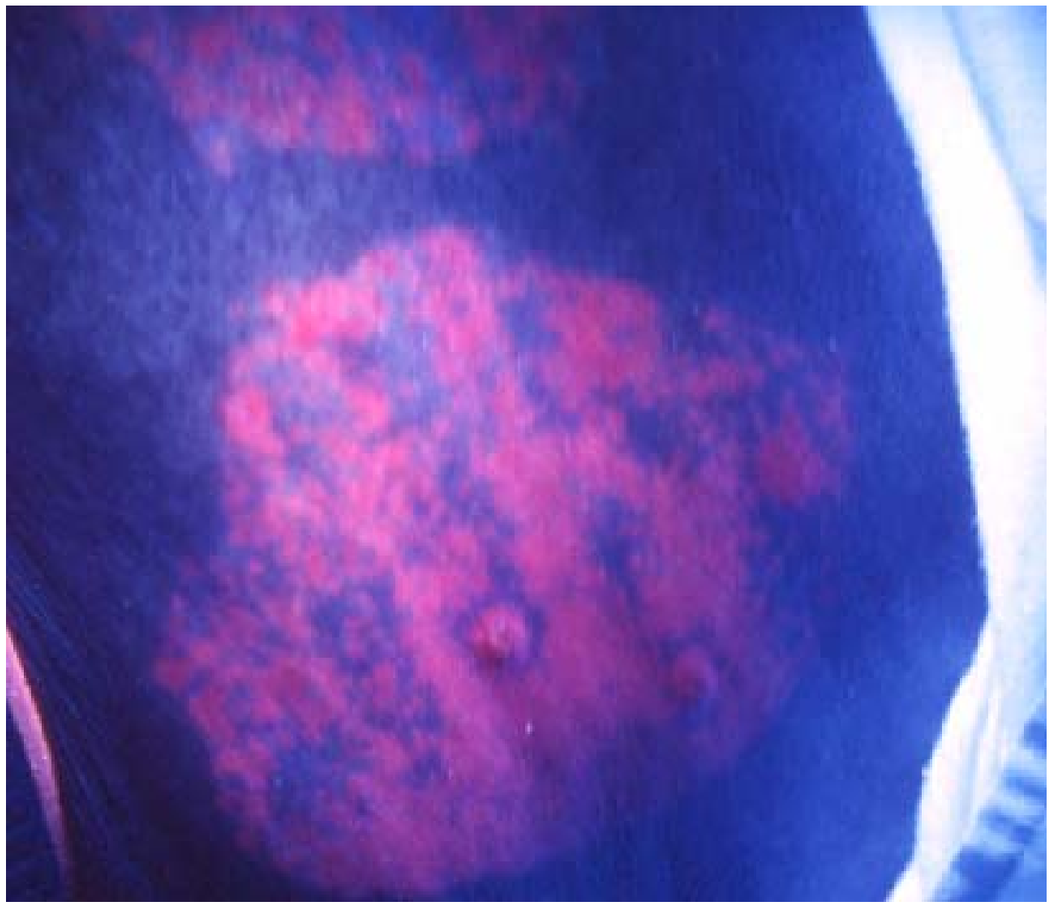
Several clinical examples, mainly about diagnosis:

Diagnosis with endogenous protoporphyrin

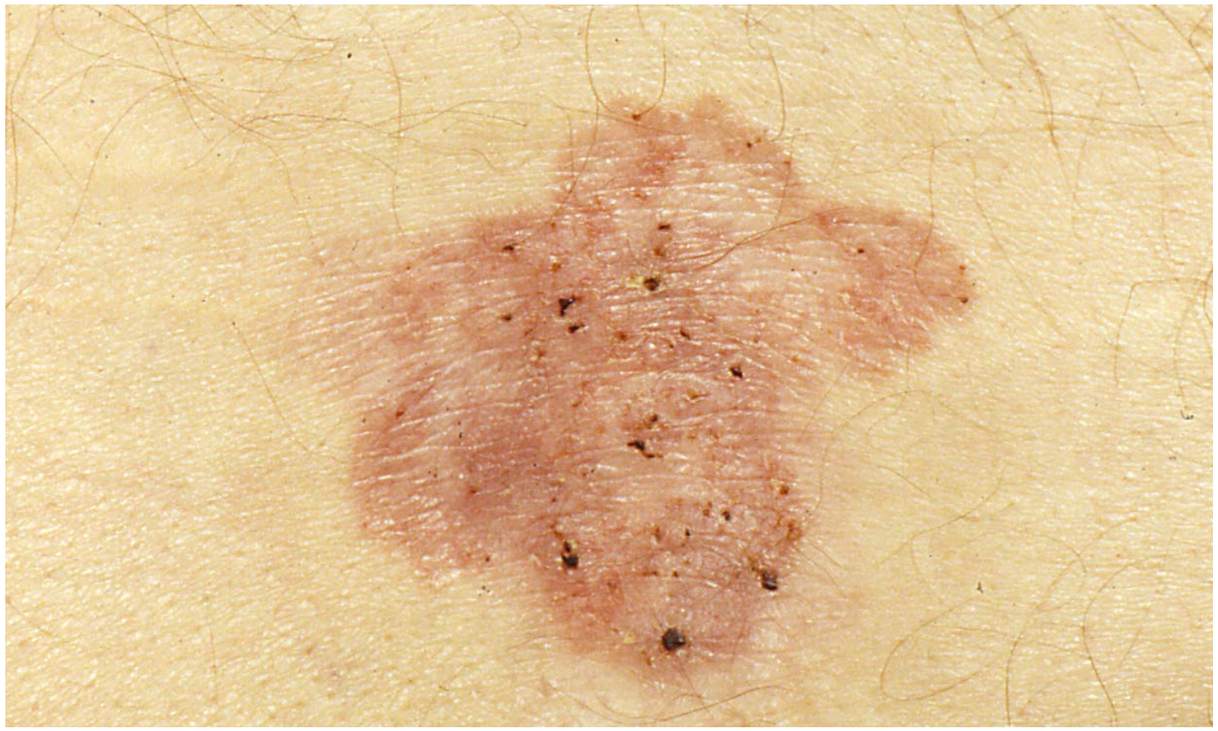
Cutaneous T cell lymphoma

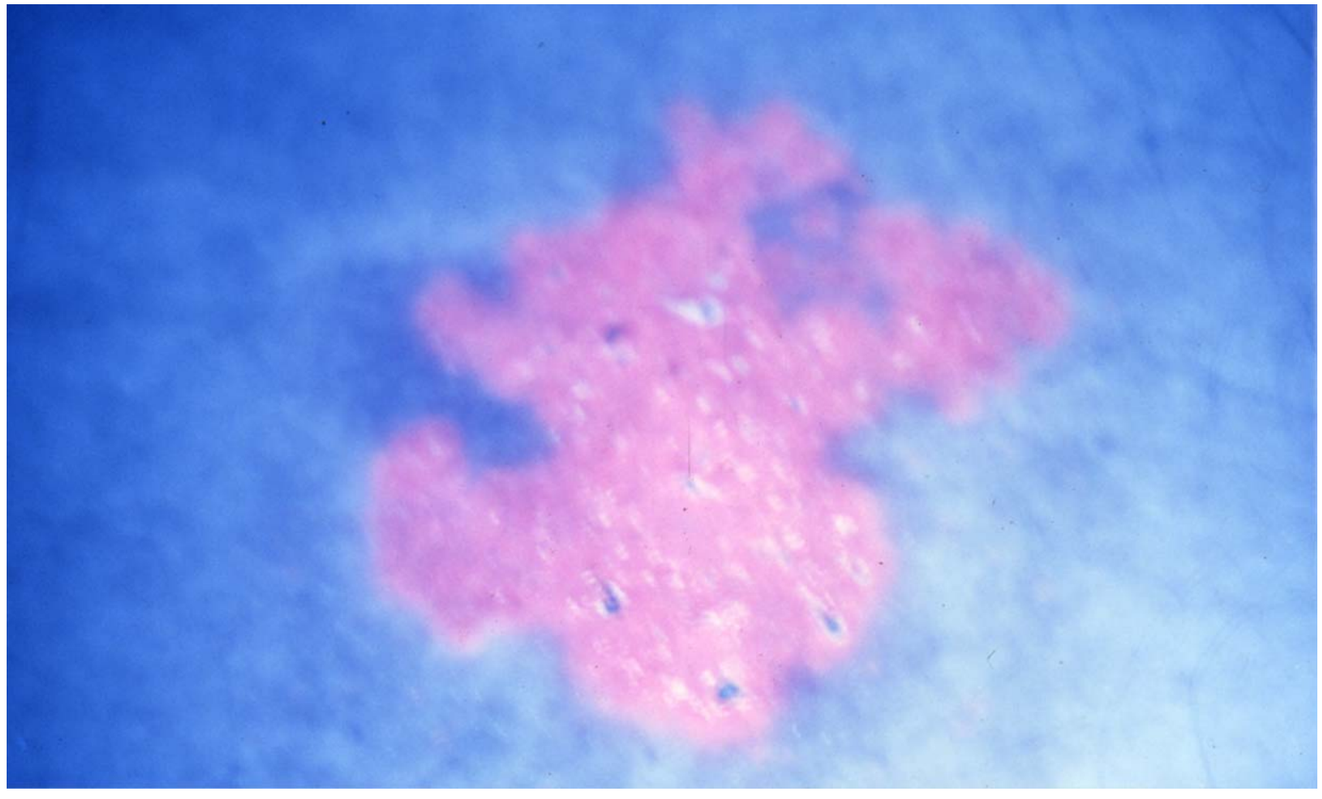




In: Introduction, J. C. Kennedy

Superficial basal cell carcinoma



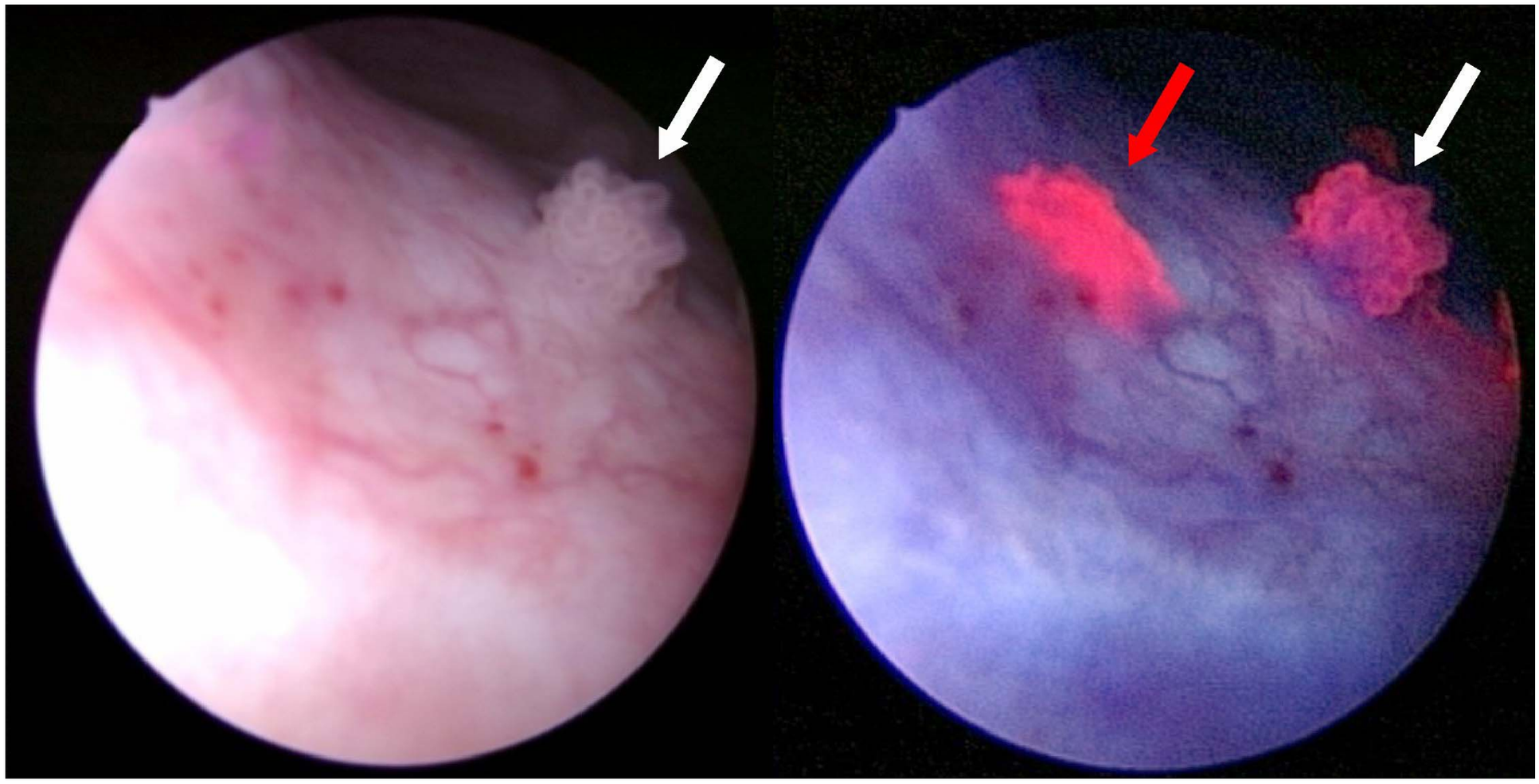


Note the lack of an exact correlation between the white light and the fluorescent photos

in: Basic Principles, Krammer, Malik, Pottier and Stepp

Papillary malignant tumor of the urinary bladder

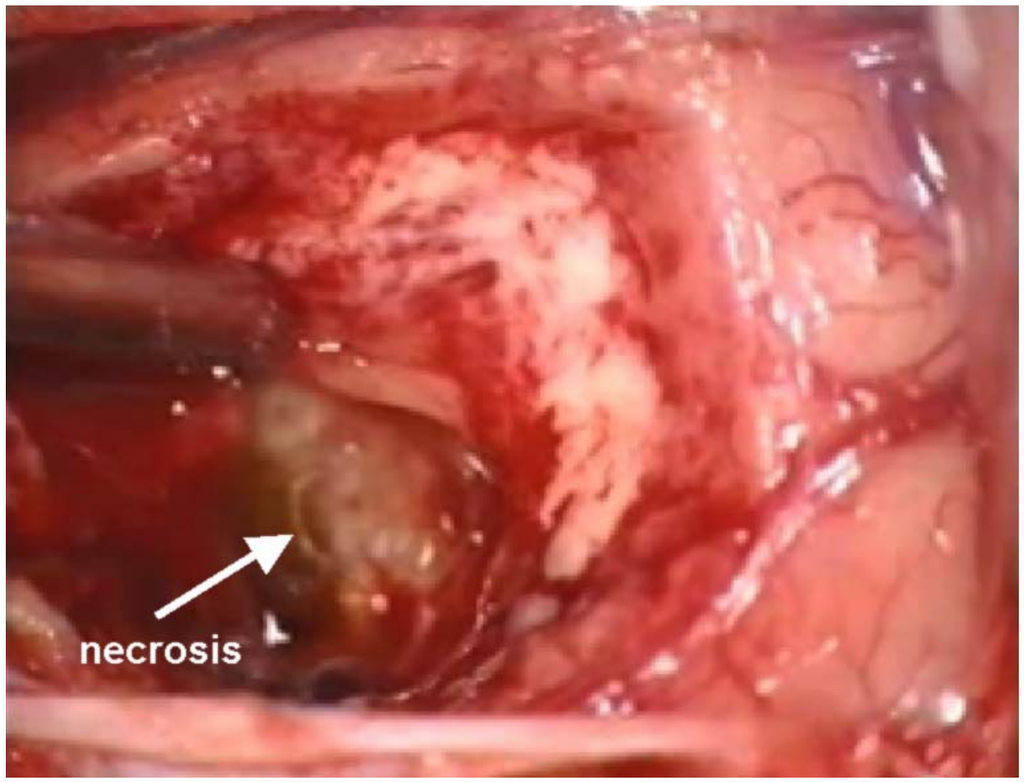
Left: white light endoscopy, right: fluorescence mode.
Distant from the tumor, an additional circumscribed area shows red fluorescence (red arrow): biopsy proved early stage malignant tumor

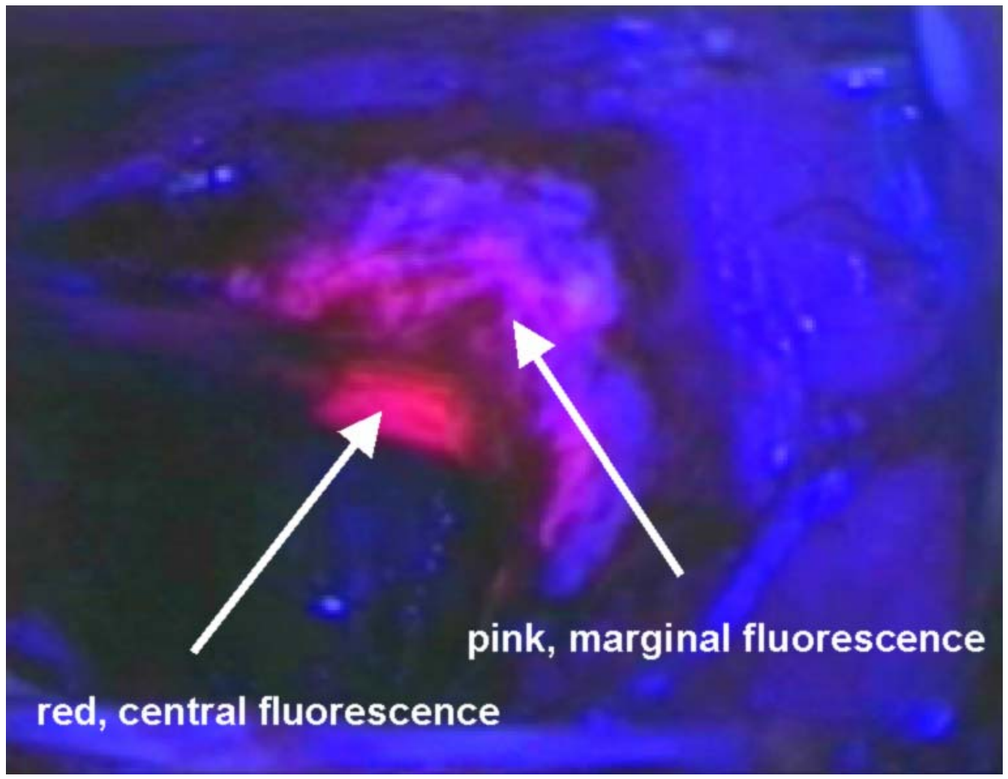


D. Zaak, in: Basic Principles

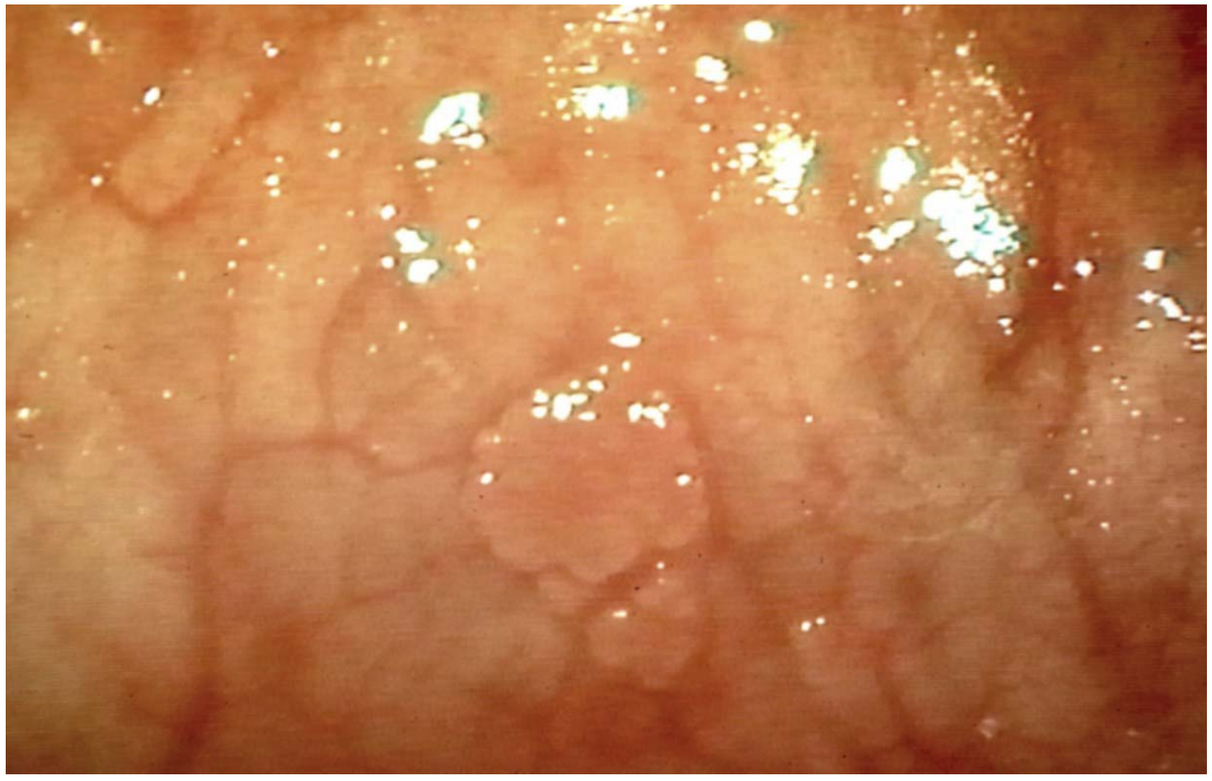
Malignant glioma

Left: microscope, right: fluorescence image.
Necrotic tumor shows no fluorescence accumulation. Adjacent tumor shows strong red fluorescence. This is surrounded by a margin of tissue with pink fluorescence

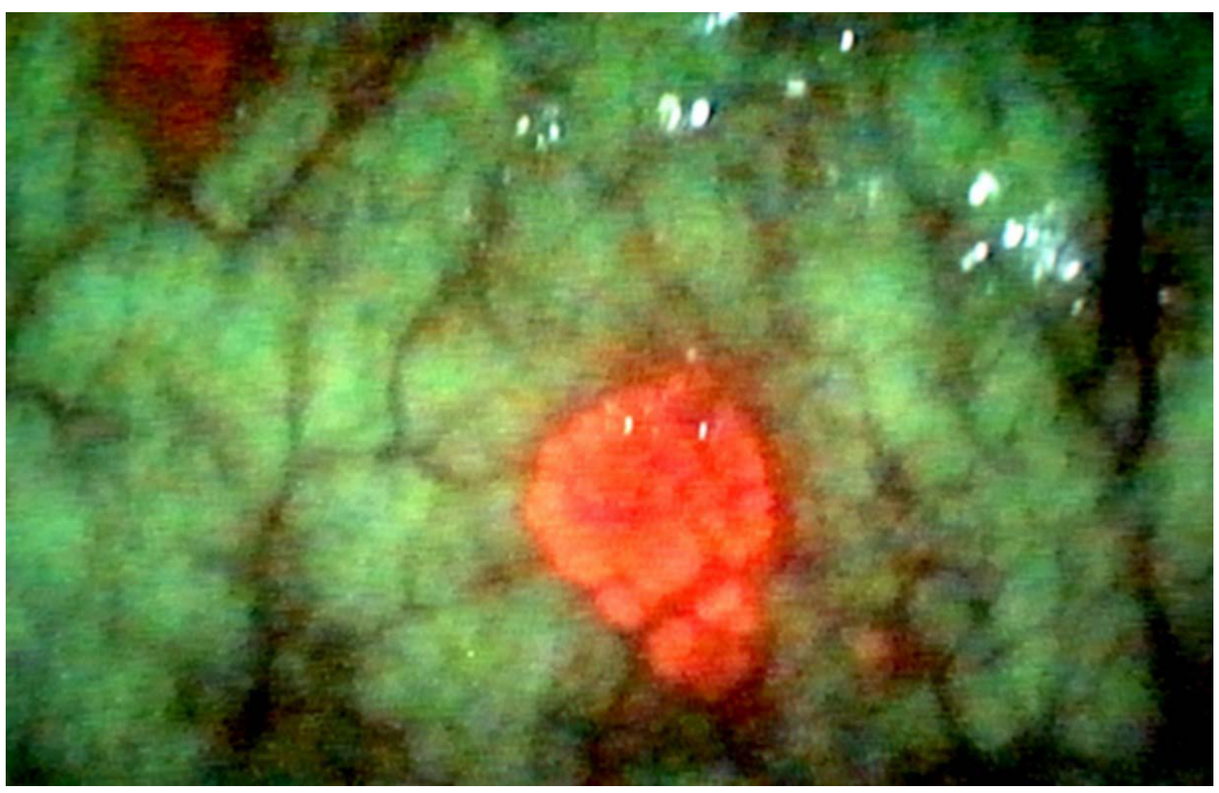




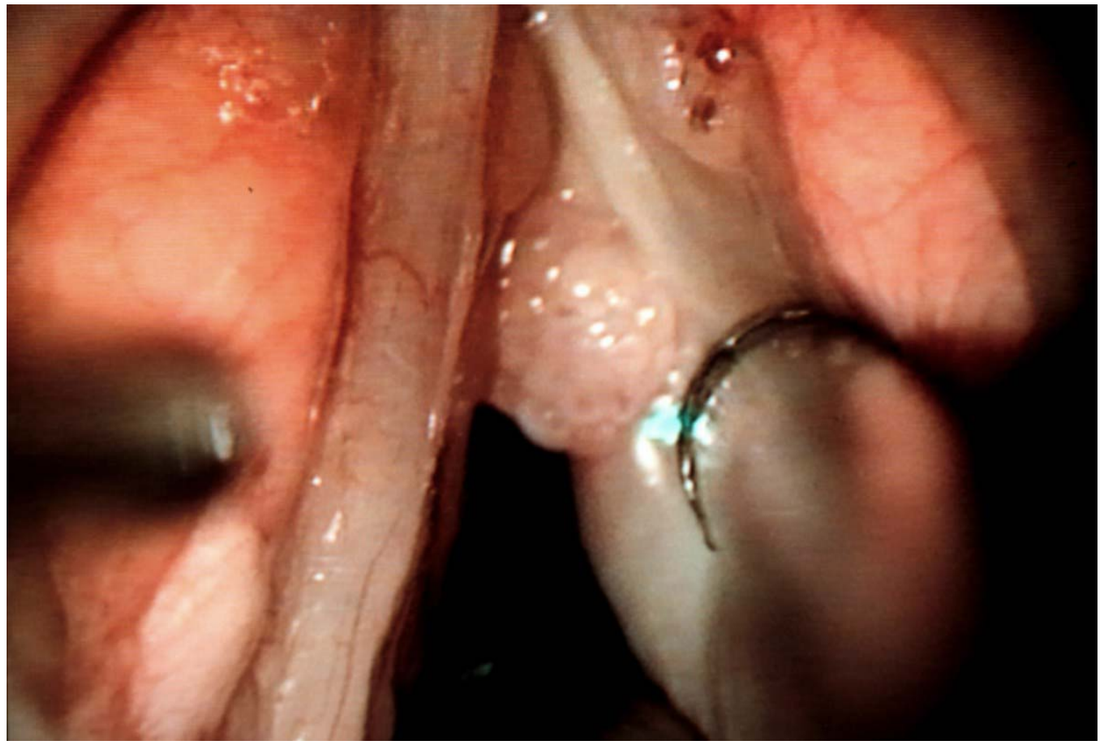
ALA-PDT and ALA-FD in the brain: Stummer, Baumgartner

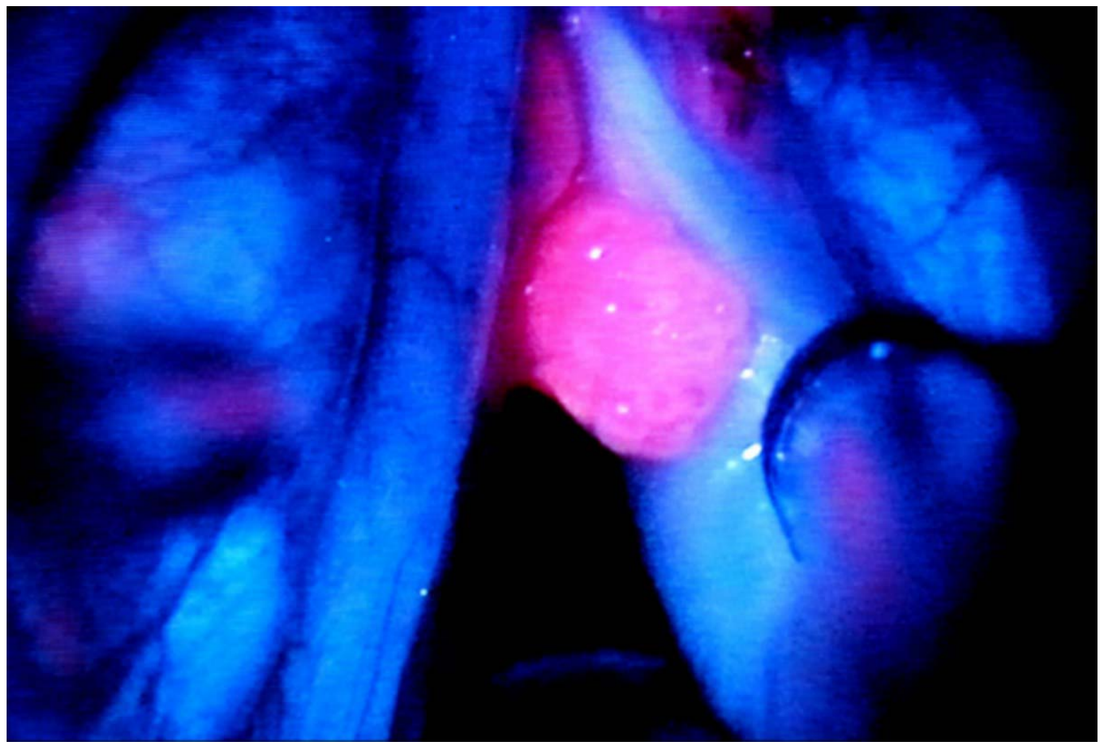


Tongue: papillomatous lesion



In: Otorhinolaryngology
C. S. Betz, A. Leunig





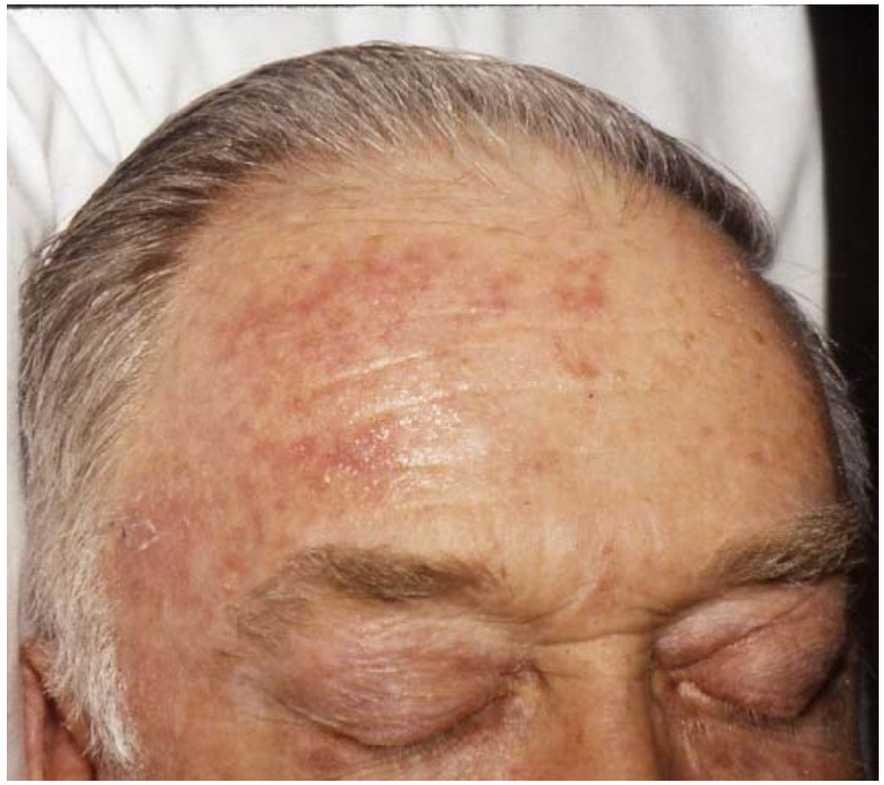
Laryngeal papillomatosis

In: Otorhinolaryngology
C. S. Betz, A. Leunig

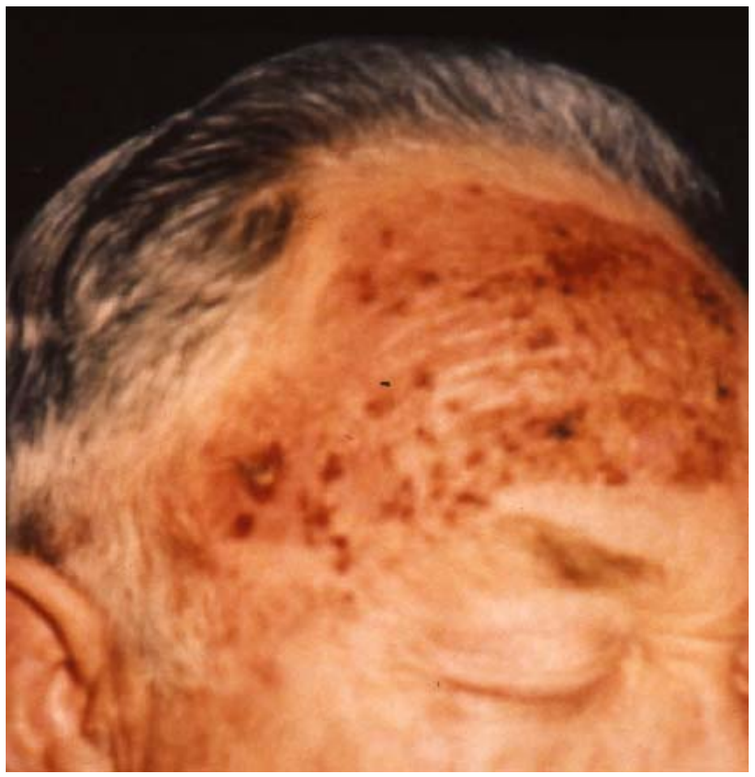
Therapy with endogenous protoporphyrin

Actinic keratosis

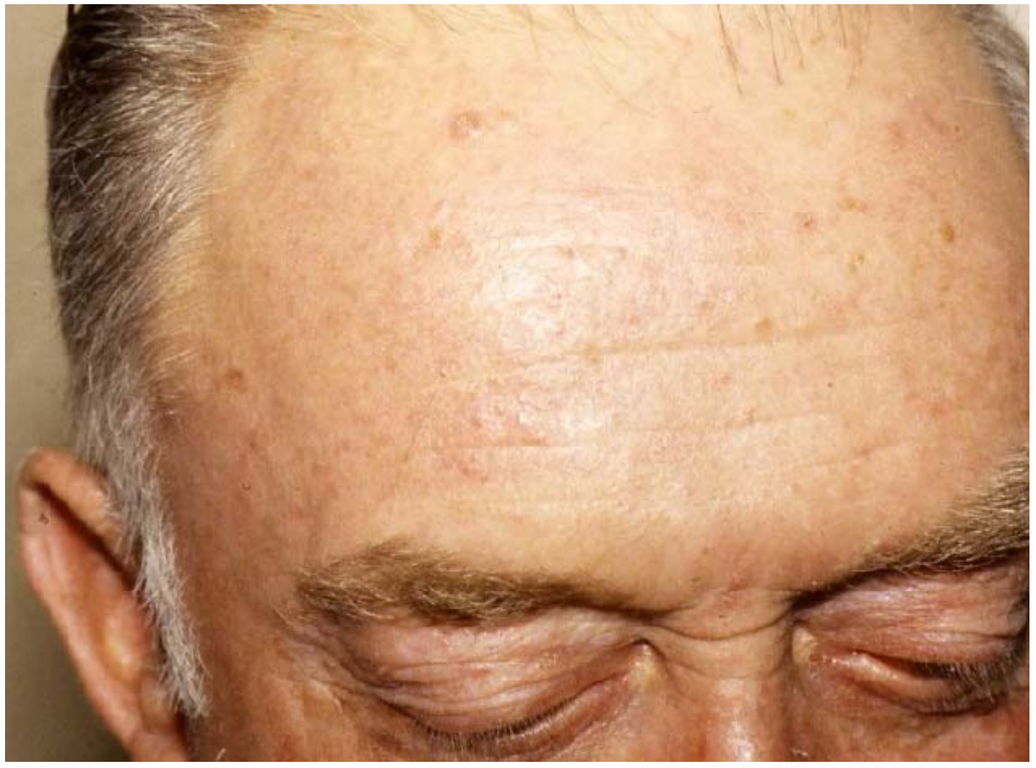
a) prior to treatment



b) 3 days after ALA-PDT



c) 30 days after ALA-PDT



In: Introduction, J. C. Kennedy

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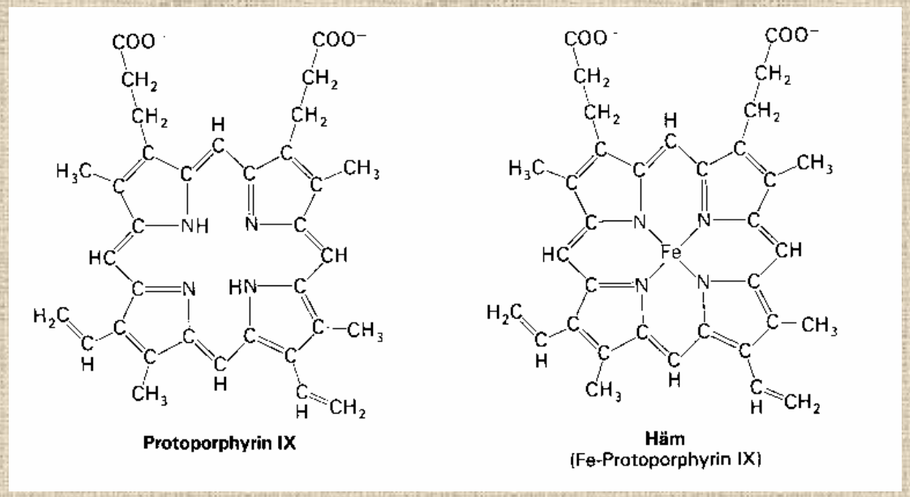
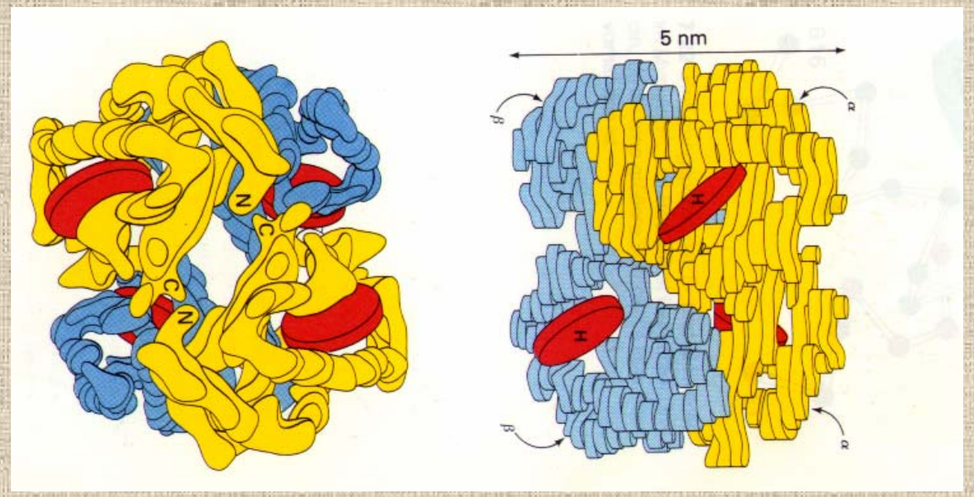
Photosensitizers

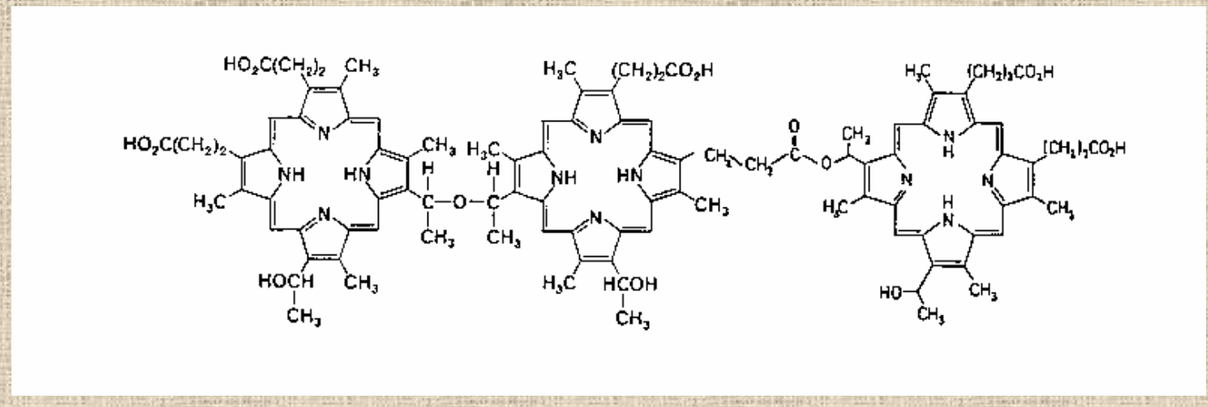


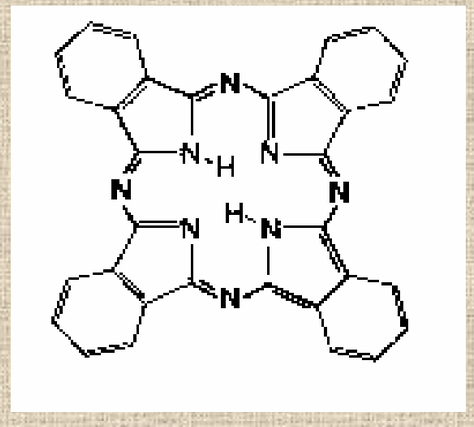
heme in hemoglobin (heme group: red)



ALA or MetVix® induced protoporphyrin IX as basis sensitizer and heme precursor

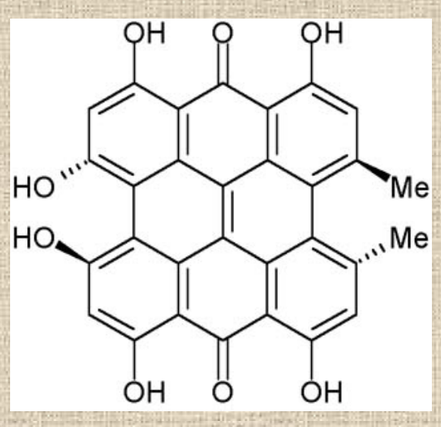
Hematoporphyrin derivative (~ Photofrin®)





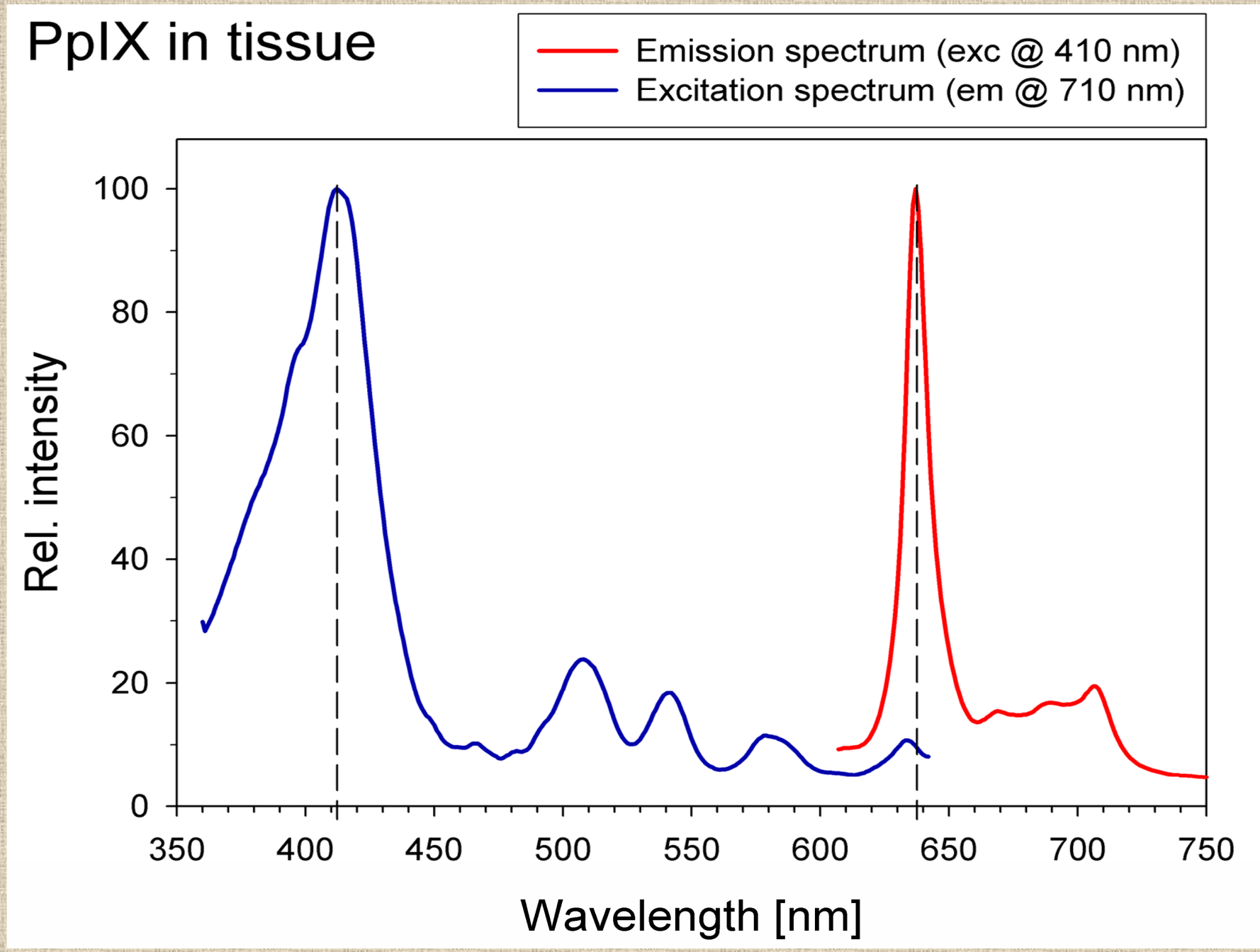
phthalocyanine: artificial sensitizer

hypericin from St. John‘s wort



Visudyne® , Foscan®
Lutetium-Texaphyrin
Tin-Etiopurpurin
Pheophorbide a
Chlorin e6, etc.

Absorption spectrum



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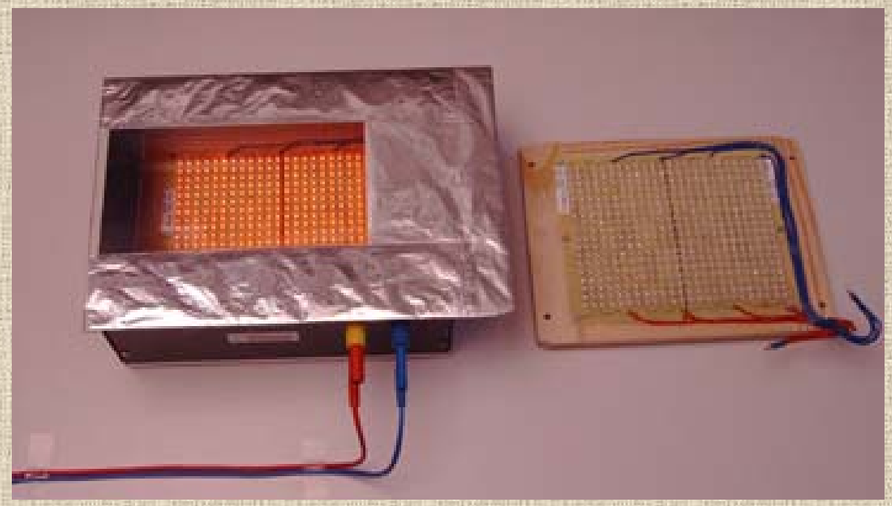
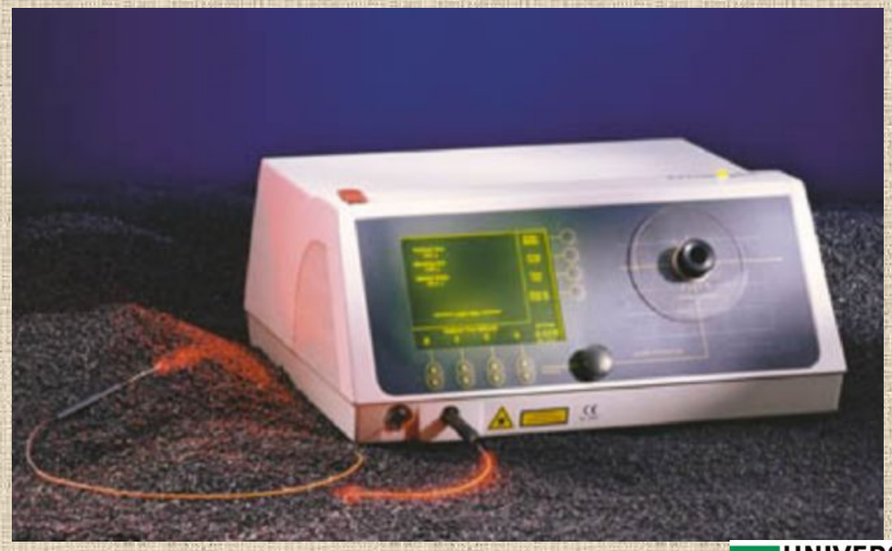
Irradiation devices

Halogen array & cut-off-Filter < 600nm

LED Array, constructed by our workgroup



Diode laser system with fiber-based applicators. Ceralas PDT (www.biolitec-us.com).



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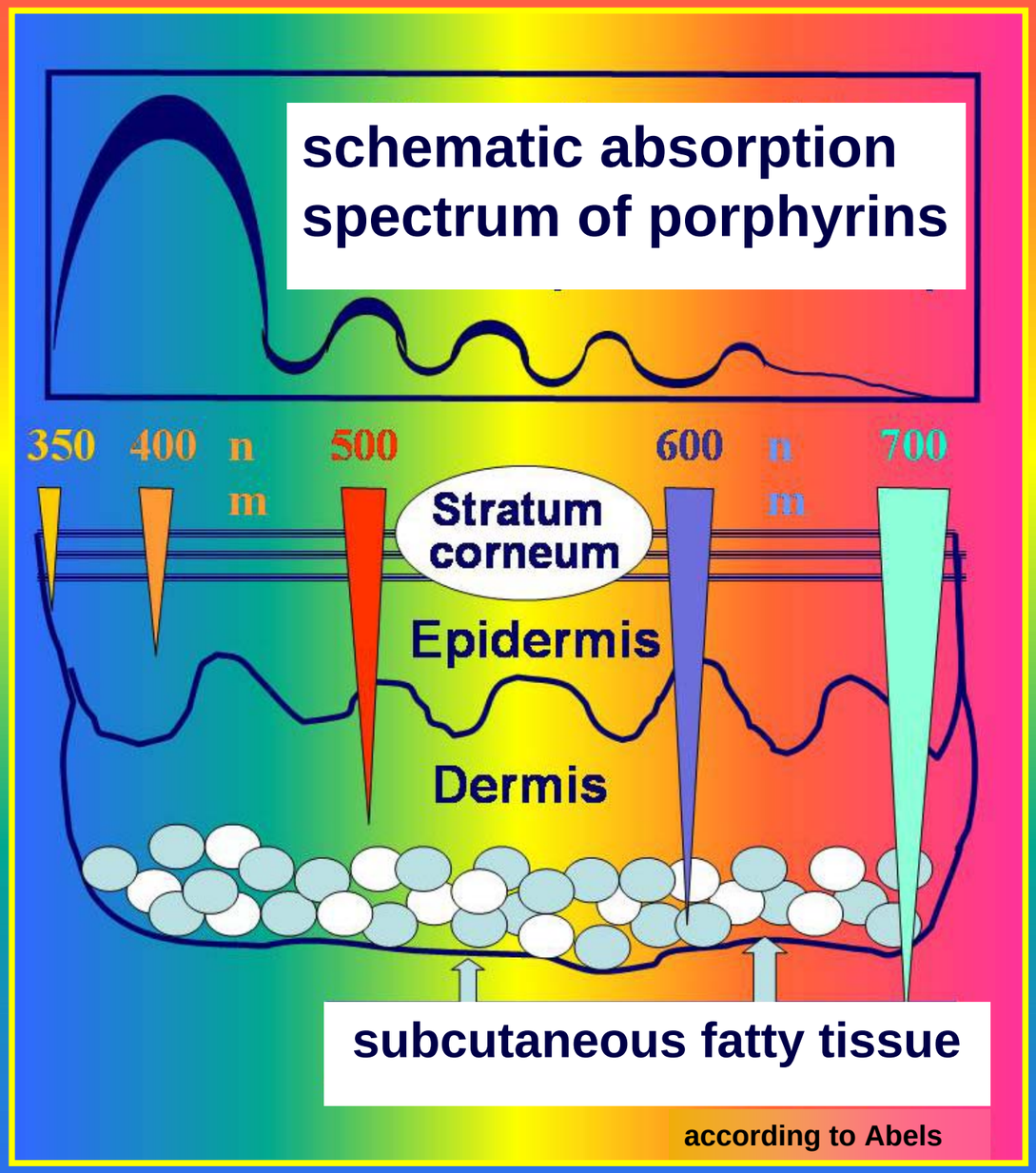
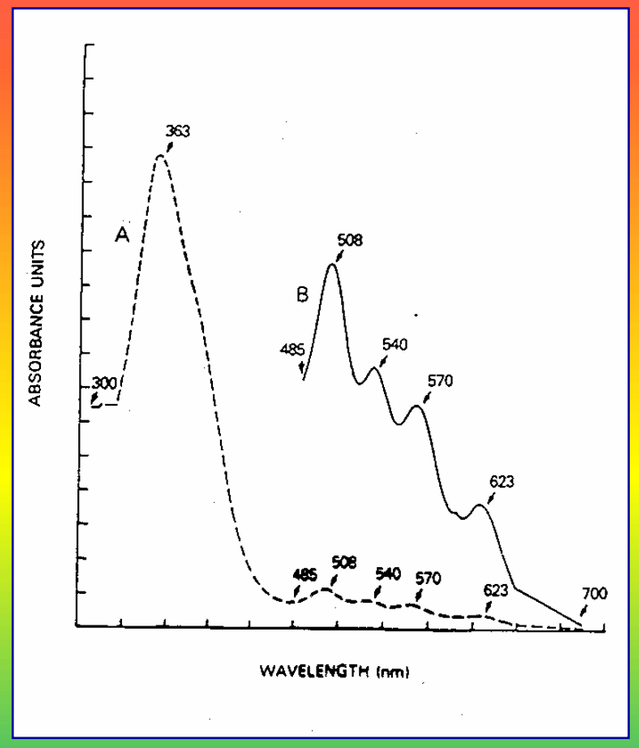
Penetration depth of light in skin, correlated with the wavelength





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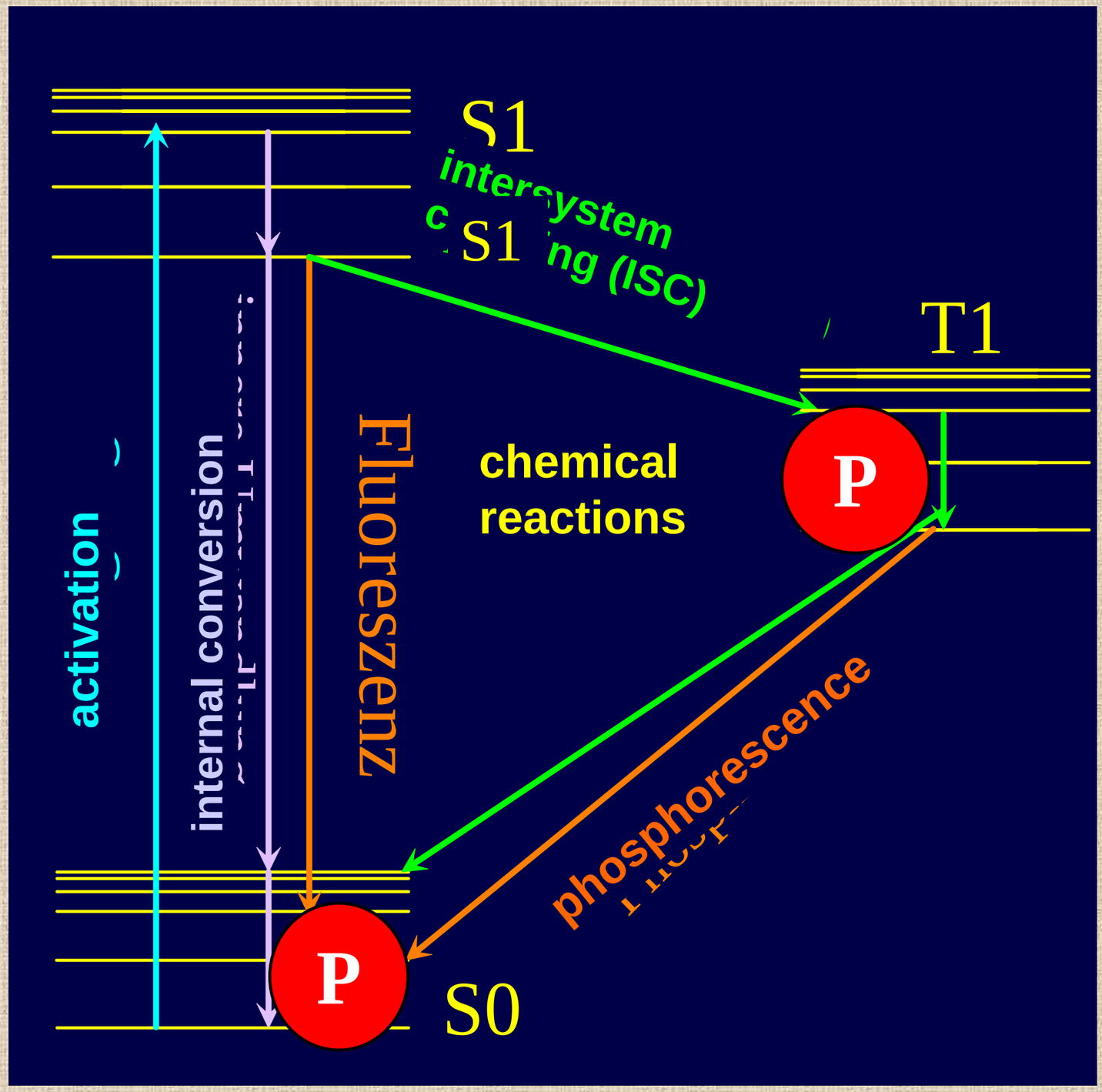
Jablonski diagram



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Reaction levels following irradiation

physico-chemical level:

energy transfer ⇨ singlet oxygen

electron transfer ⇨ radical formation of sensitizer and target

biochemical level:

oxidation of cells and tissue ⇨

Inactivation of proteins and lipid peroxidation

biological level:

cytotoxic effects

immunological effects

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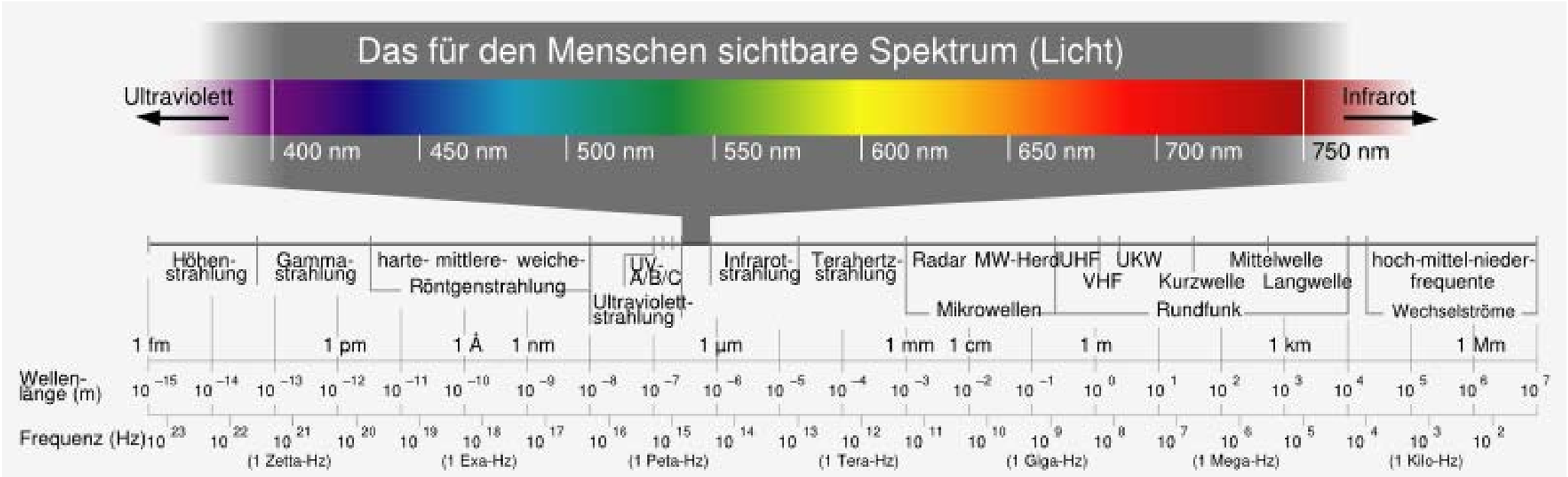
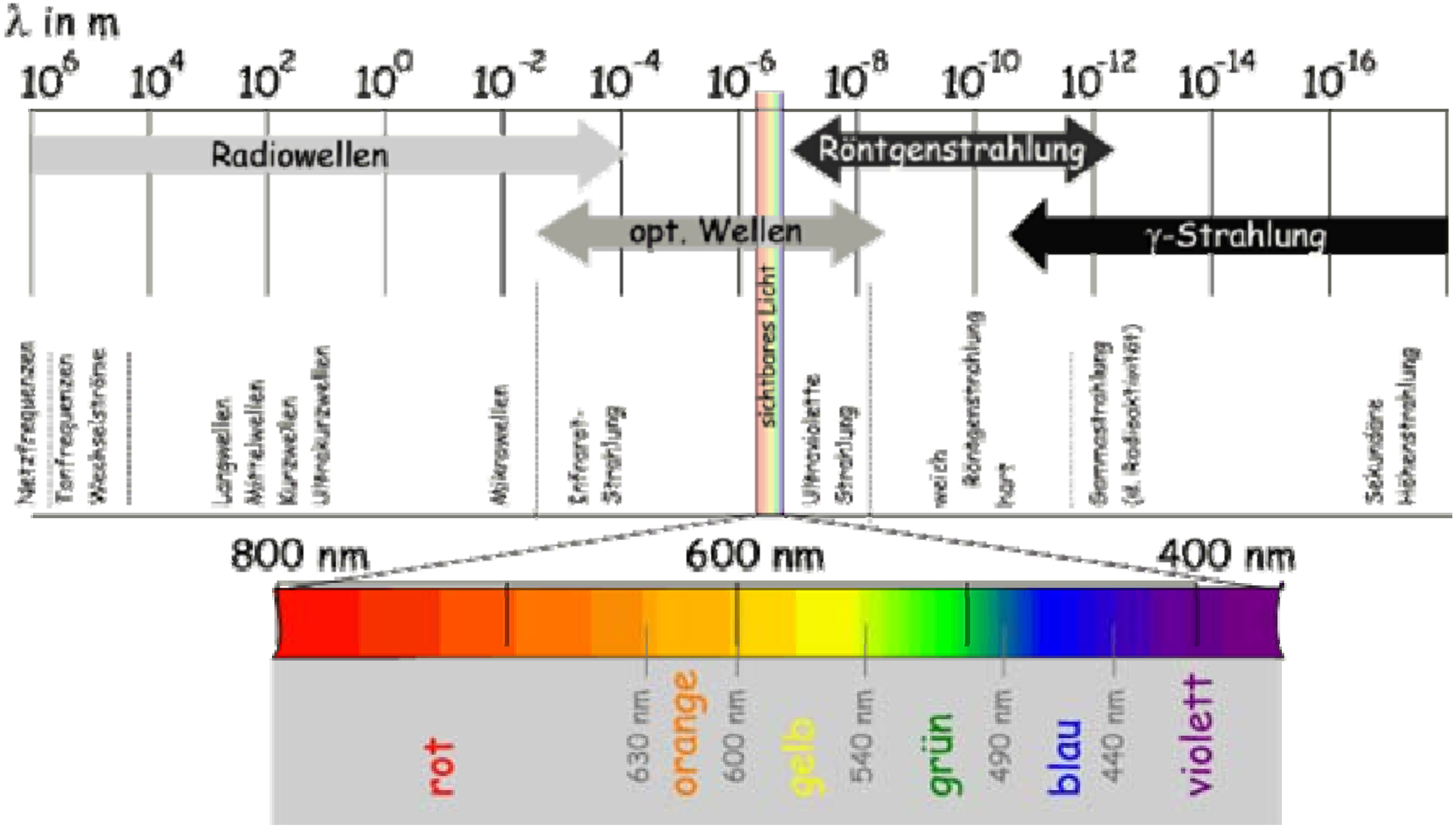
Elektromagnetisches Spektrum

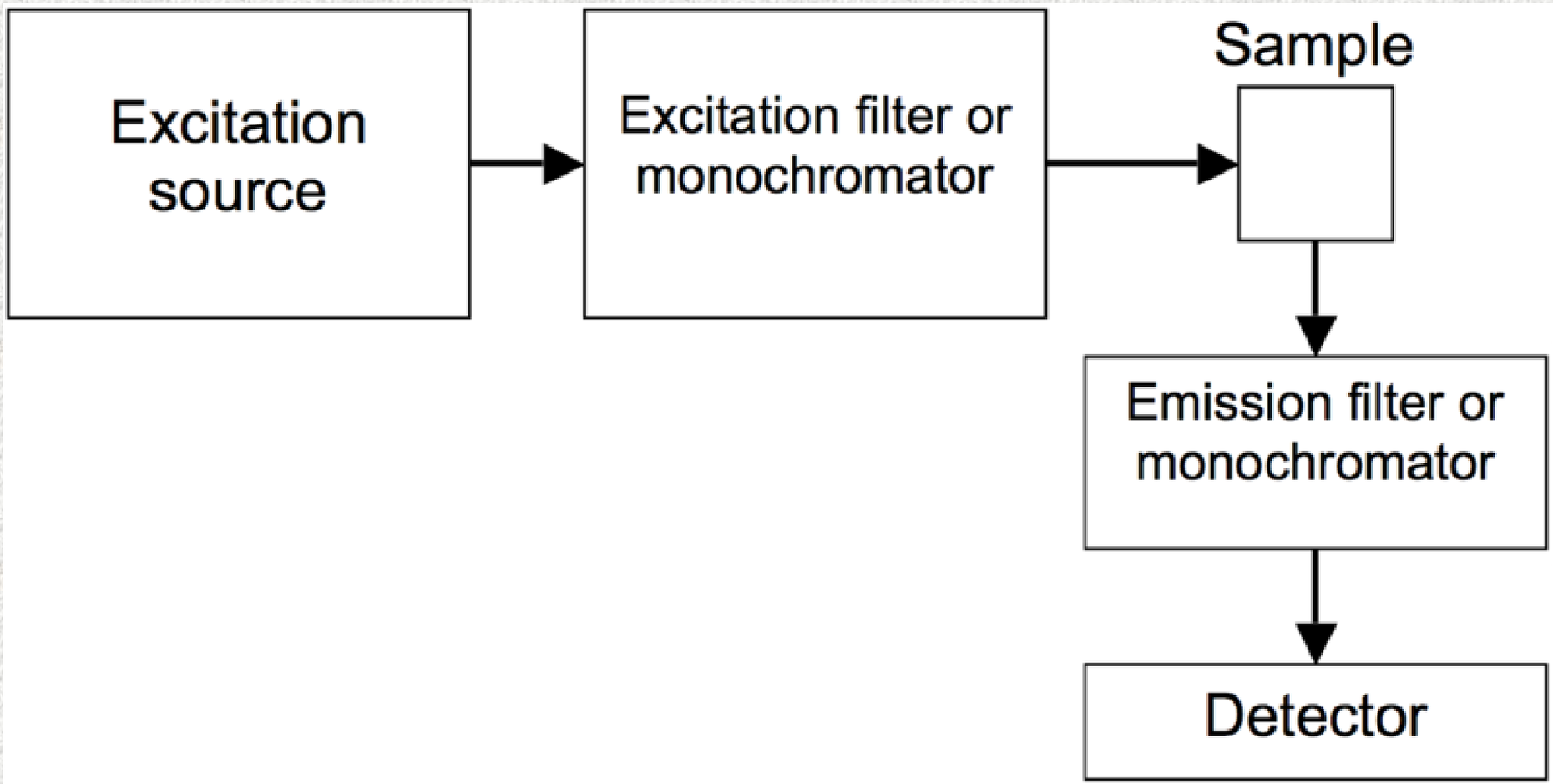


Elektromagnetisches Spektrum



www.roro-seiten.de/physik/lk12/emwellen/**elektromagnetisches_spektrum**.html

Fluoreszenzspektrophotometer



Warum kann Fluoreszenz nicht in absoluten Werten ausgedrückt werden wie Absorption?

Es können viele komplexe Faktoren die Fluoreszenz beeinflussen:
1. Photodegradierung und „bleaching“
Innerer Filtereffekt:
2. Reabsorption der emittierten Photonen durch andere Substanzen.
3. Zu hohe Konzentrationen der absorbierenden Moleküle.

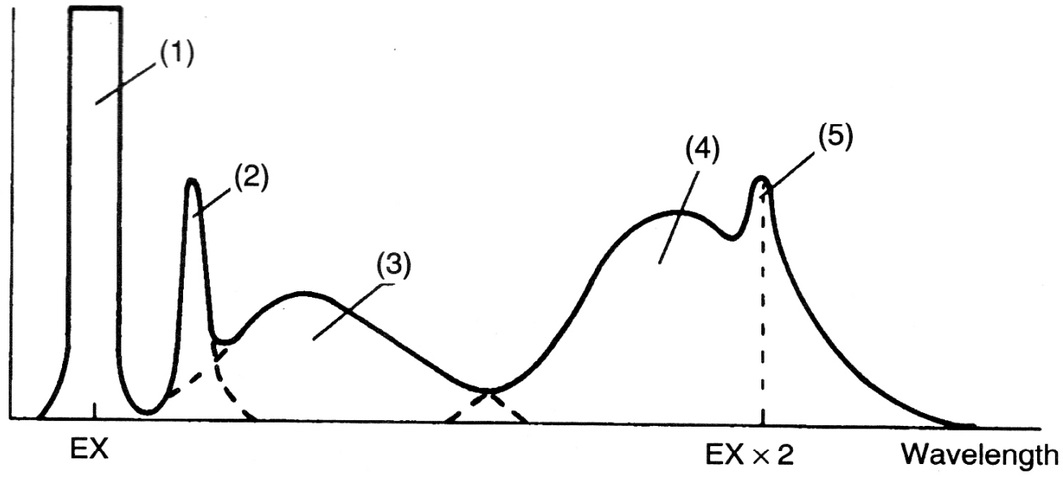
Im Spektrum treten mehrere Peaks auf:

Streulicht: Rayleigh and Raman Streuung. Rayleigh Streulicht hat die gleiche Wellenlänge wie das einfallende Licht, Raman Streulicht hat höhere, die mit der Wellenlänge zunehmen.

(Raman scattering is the result of a virtual electronic state induced by the excitation light. From this virtual state, the molecules may relax back to a vibrational level other than the vibrational ground state. In fluorescence spectra, it is always seen at a constant wavenumber difference relative to the excitation wavenumber e.g. the peak appears at a wavenumber 3600 cm−1 lower than the excitation light in water.)

E.3.7 Measurement Example of Fluorescence Spectrum

Figure E-7 shows a measurement example of fluorescence spectrum.



(1) Scattering of exciting radiation
(2) Raman spectrum of solvent
(3) Fluorescence of impurities, solvent, etc.
(4) Fluorescence of sample
(5) Second-order spectrum of exciting radiation

Fig. E-7 Measurement Example of Fluorescence Spectrum

As shown in Figure E-7, other peaks than a fluorescence peak of sample appear in fluorescence spectral measurement.
With reference to this example, it is necessary to identify a fluorescence peal of sample.

Quantitative Messung der Fluoreszenzspektren von

1) PI (Propodium Iodide) 20 µM in Wasser (toxisch!)

2) DiOC6 (3,3'-dihexyloxacarbocyanine iodide) 200µM in DMSO

3) Hypericin 25 und 12.5 µM in DMSO

4) Pc (tetrasulfoniertes Phthalocyanin) 25 µM in Wasser

5) Wasser

Eichreihe mit DiOC6:

10 Werte zur Demo

5 untere Werte für Eichgerade

Übertragung der Werte ins Excel und weitere Bearbeitung