Chapter 9

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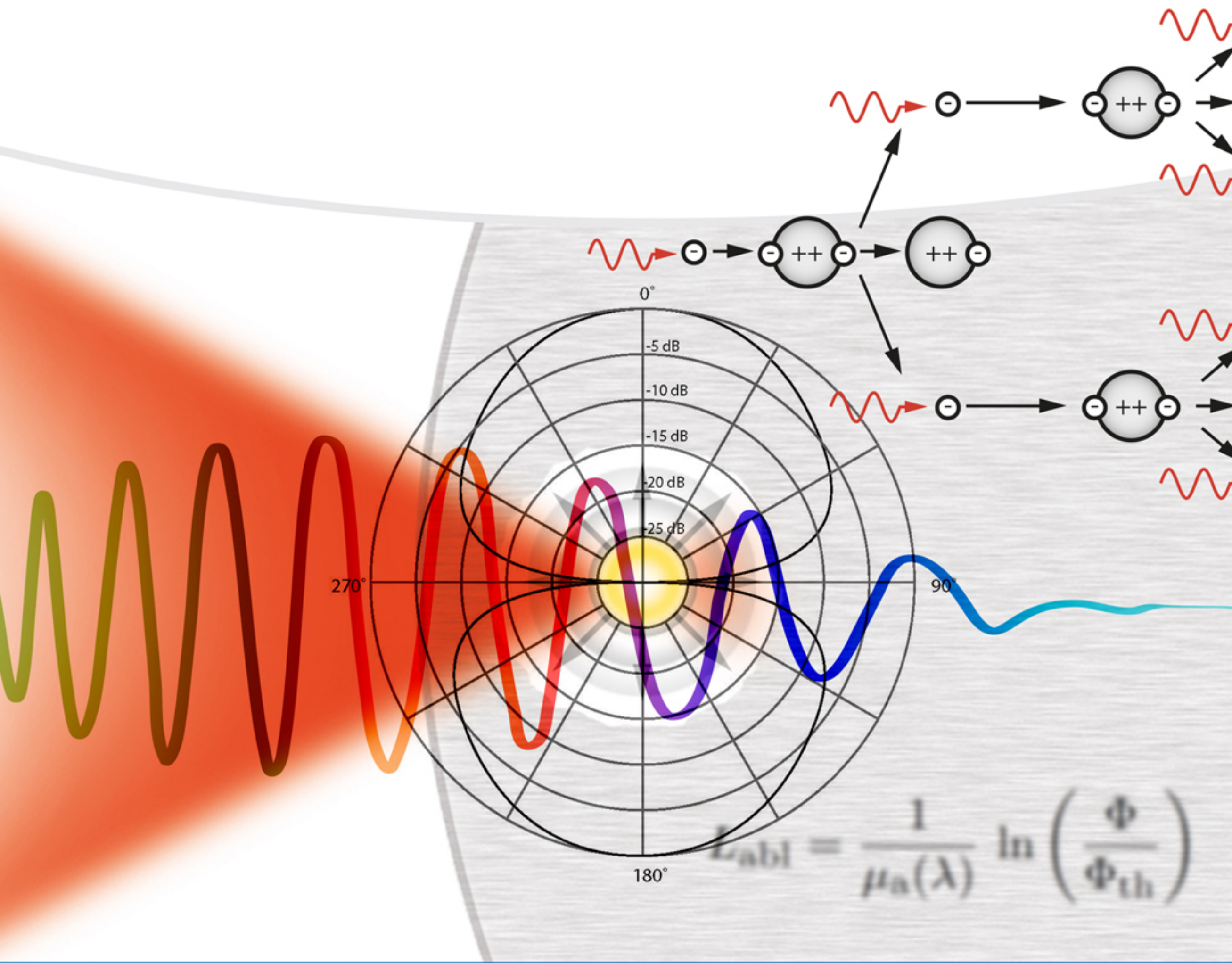
Laser-Tissue Interaction



Solutions to Problems in „Optical Devices in Ophthalmology and Optometry“

Contents

P9.1
Penetration depth of lasers

Calculate the penetration depths for the following lasers in water and in blood-rich tissue: Nd:YAG laser, Nd:YAG (frequency doubled), and ArF excimer laser.

Solution:

The penetration depth is given by

$$\delta_a = \frac{1}{\mu_a(\lambda)}$$

at which the intensity of incident light has dropped to $1/e = 37\%$.

From the Figure 9.3, the following calculations were performed for lasers in water and blood-rich (oxy- and deoxyhemoglobin) tissues:

Laser	Wavelength λ (nm)	Absorption coefficient of water $\mu_a(cm^{-1})$	Depth of penetration, δ_a (cm)
Nd: YAG	1064	0.5	2
Nd: YAG (frequency doubled)	532	0.0005	2000
ArF excimer	193	0.1	10

Laser	Wavelength λ (nm)	Absorption coefficient of oxyhemoglobin, $\mu_a(cm^{-1})$	Depth of penetration, δ_a (cm)
Nd: YAG	1064	6	0.167
Nd: YAG (frequency doubled)	532	200	0.005
ArF excimer	193	n/a [1)]	n/a

Laser	Wavelength λ (nm)	Absorption coefficient of deoxyhemoglobin $\mu_a(cm^{-1})$	Depth of penetration, δ_a (cm)
Nd: YAG	1064	2	0.5
Nd: YAG (frequency doubled)	532	300	0.003
ArF excimer	193	n/a	n/a

1) The absorption for ArF excimer lasers is entirely caused by water and protein absorption.

From these calculations it is evident that, for treatment of blood-rich tissues, lasers in the visible spectral range (particularly in the blue-green range) are well suited. Interventions in deeper tissue layers are better performed with near-infrared (NIR) laser light in the wavelength range of about 1 μm.

P9.2
Light–tissue interaction

1. Which light–tissue interaction can only be realized by the use of lasers? For which interaction mechanisms can conventional (thermal) light sources be used alternatively?
2. What are the primary reasons for laser usage in medical therapy?

Solution:

1. Light–tissue interactions such as plasma-induced ablation and photodisruption, which require very high light intensities and short exposure times, can only be realized in the focal region of short-pulse lasers. Other light–tissue interactions like the photothermal interaction and photochemical interaction can also be achieved by using conventional (thermal) light sources due to the requirement of low intensities and relatively long exposure times (Figure 9.4).

2. Due to high spatial and temporal coherence, they are extensively used in medical therapy. These properties make lasers precise and easy to manipulate according to the underlying medical condition. High spatial coherence ensures maximum transfer of energy to the interacting tissues and high temporal coherence which makes the laser source monochromatic or leads to a small bandwidth. Therefore, wavelength-specific tissue response can be achieved, since tissue properties determined by absorption and scattering coefficients depend on the wavelength of light.

P9.3
Intensity

1. Calculate the time average of the product of two trigonometric functions with equal frequencies. The time average is defined by

$$\langle a(t)b(t)\rangle = \frac{1}{T}\int_0^T a(t)b(t)\mathrm{d}t \tag{9.23}$$

in which

$$a(t) = \mathrm{Re}(Ae^{i\omega t)}, b(t) = \mathrm{Re}(Be^{i\omega t}) \tag{9.24}$$

and $T = \frac{2\pi}{\omega}$.

2. Show that the time average of the square of a function

$$a(t) = \mathrm{Re}(V(t)) = \mathrm{Re}\left(A_2 e^{i\omega t} + A_2 e^{i\omega t}\right) \tag{9.25}$$

is given by

$$\langle a^2(t)\rangle = \frac{1}{2}\{V(t)V^*(t)\} \ . \tag{9.26}$$

3. A red diode laser ($\lambda = 700$ nm) with 10 mW electrical power and 10% electrical efficiency is focused on an 100 m^2 spot. Which photon fluence (number of photons per time and area) does this correspond to?
4. Compare the result of 3 to the achievable intensity with a 20 W light bulb (assumed to be a Planck black body with 3000 K temperature), optical efficiency of 2% for a same spot size and a band-pass filter at 700 nm with bandwidth of $\Delta\lambda = 20$ nm. How would you design the collection optics? What electrical power would be needed to achieve the same spot intensity as in 3?

Solution:

1. We can write

$$a(t) = \mathrm{Re}(A\mathrm{e}^{i\omega t}) = A_\mathrm{R}\cos(\omega t) - A_\mathrm{I}\sin(\omega t) \ ,$$
$$b(t) = \mathrm{Re}(B\mathrm{e}^{i\omega t}) = B_\mathrm{R}\cos(\omega t) - B_\mathrm{I}\sin(\omega t) \ ,$$

with $A = A_\mathrm{R} + iA_\mathrm{I}$ and $B = B_\mathrm{R} + iB_\mathrm{I}$.

For the time average given in Eq. (9.23), we can write

$$\begin{aligned}\langle a(t)b(t)\rangle &= \frac{1}{T}\int_0^T a(t)\cdot b(t)\,\mathrm{d}t\\ &= \frac{1}{T}\int_0^T [A_\mathrm{R}\cos(\omega t) - A_\mathrm{I}\sin(\omega t)]\cdot[B_\mathrm{R}\cos(\omega t) - B_\mathrm{I}\sin(\omega t)]\,\mathrm{d}t\\ &= \frac{1}{T}\int_0^T [B_\mathrm{R}\cos(\omega t)A_\mathrm{R}\cos(\omega t) + B_\mathrm{I}\sin(\omega t)A_\mathrm{I}\sin(\omega t)]\,\mathrm{d}t\\ &- \frac{1}{T}\int_0^T [A_\mathrm{R}\cos(\omega t)B_\mathrm{I}\sin(\omega t) + A_\mathrm{I}\sin(\omega t)B_\mathrm{R}\cos(\omega t)]\,\mathrm{d}t\ .\end{aligned}\tag{S9.1}$$

With the integrals

$$\frac{1}{T}\int_0^T \cos(\omega t)\,\mathrm{d}t = 0,\ \frac{1}{T}\int_0^T \sin(\omega t)\,\mathrm{d}t = 0\ ,$$

$$\frac{1}{T}\int_0^T \sin(\omega t)\cos(\omega t)\,\mathrm{d}t = \frac{1}{2T}\int_0^T \sin(2\omega t)\,\mathrm{d}t = 0\ ,$$

$$\int_0^T \sin^2(\omega t)\,\mathrm{d}t = \frac{t}{2} - \frac{1}{4\omega}\sin(2\omega t)\Big|_0^T = \frac{T}{2}\ ,$$

$$\int_0^T \cos^2(\omega t)\,\mathrm{d}t = \frac{t}{2} + \frac{1}{4\omega}\sin(2\omega t)\Big|_0^T = \frac{T}{2}\ ,$$

the last row of Eq. (S9.1) vanishes, and we obtain for the time average

$$\begin{aligned}\langle a(t)b(t)\rangle &= \frac{1}{T}\int_0^T [A_\mathrm{R}B_\mathrm{R}\cos^2(\omega t) + A_\mathrm{I}B_\mathrm{I}\sin^2(\omega t)]\,\mathrm{d}t\\ &= \frac{1}{2}(A_\mathrm{R}B_\mathrm{R} + A_\mathrm{I}B_\mathrm{I}) = \frac{1}{2}\mathrm{Re}(AB^*)\ .\end{aligned}$$

For A = B as a special case, we calculate

$$\langle a(t)b(t)\rangle = \frac{1}{2}\mathrm{Re}(AA^*) = \frac{1}{2}|A|^2\ .$$

2. We can write

$$\begin{aligned}a(t) &= \mathrm{Re}(V) = \frac{V+V^*}{2}\\ a^2(t) &= \mathrm{Re}(V)\mathrm{Re}(V) = \left(\frac{V+V^*}{2}\right)\left(\frac{V+V^*}{2}\right)\\ &= \frac{1}{4}(V^2 + V^{*2}) + \frac{1}{2}VV^*\ .\end{aligned}\tag{S9.2}$$

For the time average, we obtain

$$V(t) = A_1 \mathrm{e}^{i\omega_1 t} + A_2 \mathrm{e}^{i\omega_2 t}$$
$$\left\langle a^2(t) \right\rangle = \frac{1}{4}\left\langle V^2 \right\rangle + \frac{1}{4}\left\langle V^{*2} \right\rangle + \frac{1}{2}\left\langle VV^* \right\rangle$$

and for the first two terms

$$\left\langle V^2(t) \right\rangle = A_1^2 \left\langle \mathrm{e}^{2i\omega_1 t} \right\rangle + 2A_1A_2 \left\langle e^{i(\omega_1+\omega_2)t} \right\rangle + A_2^2 \left\langle e^{2i\omega_2 t} \right\rangle = 0$$
$$\left\langle V^{*2}(t) \right\rangle = A_1^2 \left\langle \mathrm{e}^{-2i\omega_1 t} \right\rangle + 2A_1A_2 \left\langle e^{-i(\omega_1+\omega_2)t} \right\rangle + A_2^2 \left\langle e^{-2i\omega_2 t} \right\rangle = 0$$

because of

$$\lim_{T\to\infty} \frac{1}{T} \int_0^T \mathrm{e}^{2i\omega t} \mathrm{d}t = 0 \ .$$

For the remaining third term of (S9.2), we then have

$$\left\langle a^2(t) \right\rangle = \frac{1}{2} \left\langle V(t) V^*(t) \right\rangle \ .$$

3. The energy of a single photon is

$$E_{\mathrm{ph}} = h\nu = \frac{hc}{\lambda} \ .$$

The intensity is given by

$$I = \frac{P}{A} = \frac{E}{At} = \frac{10^{-3}\ \mathrm{W}}{100 \times 10^{-12}\ \mathrm{m}^2} = 10^7 \frac{\mathrm{W}}{\mathrm{m}^2} = 10^3 \frac{\mathrm{W}}{\mathrm{cm}^2}$$

with the power P, the energy E, and the spot area A.

The photon fluence then is given by

$$\Phi = \frac{N}{At} = \frac{E/E_{\mathrm{ph}}}{At} = \frac{P}{AE_{\mathrm{ph}}} = \frac{P\lambda}{A \cdot hc}$$

with N being the number of photons. With $\lambda = 700$ nm, $P = 1$ mW, $c = 3 \times 10^8$ m/s, $h = 6.63 \times 10^{-34}$ Js, and $A = 100\ \mu\mathrm{m}^2$, we obtain

$$\Phi = \frac{(10^{-3}\mathrm{W})(7 \times 10^{-7}\ \mathrm{m})}{100\ \mu\mathrm{m}^2 \cdot 6.63 \times 10^{-34}\ \mathrm{Ws}^2 \cdot 3 \times 10^8\ \mathrm{m/s}} = 3.5 \times 10^{21}\ \mathrm{cm}^{-2}\ \mathrm{s}^{-1} \ .$$

4. As given in the text, we assume a Planck black body with a temperature of 3000 K. The spectral radiance $L_{\mathrm{e,h}}(\lambda, T)$ is then given by (see Problem P8.2)

$$L_{\mathrm{e},\lambda}(\lambda, T) = \frac{2hc^2}{\lambda^5} \cdot \frac{1}{\exp\left(\frac{hc}{\lambda\, k_B T}\right) - 1} \qquad \text{(S9.3)}$$

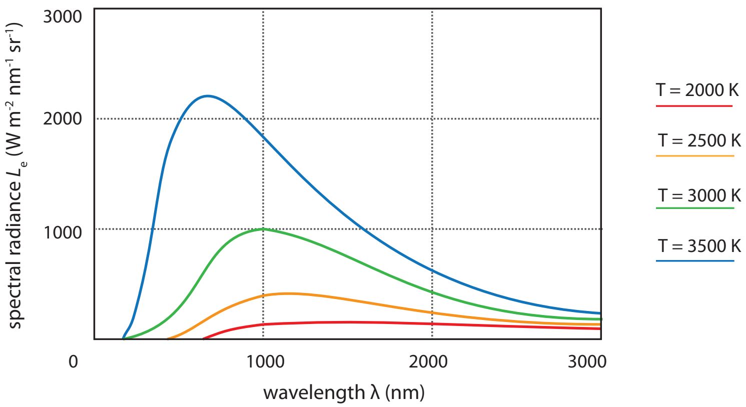


Figure S9.1. Spectral radiance of black body radiation for various temperatures over wavelength (in nm) in units of $\mathrm{Wm^{-2}\ nm^{-1}\ sr^{-1}}$.

in units of $\mathrm{W/(sr \cdot m^3)}$.

We know that the total (optical-visible) efficiency of the bulb is 2% of the electrical input. It thus follows that

$$\eta = \frac{P_{\mathrm{vis}}}{P_{\mathrm{el}}} = \frac{1}{P_{\mathrm{el}}} \iiint\limits_{380\ \mathrm{nm}}^{780\ \mathrm{nm}} L_{\mathrm{e}}(\lambda)\ \mathrm{d}A\mathrm{d}\Omega\mathrm{d}\lambda = 2\% \quad .$$

From this, we obtain

$$P_{\mathrm{vis}} = \iiint\limits_{380\ \mathrm{nm}}^{780\ \mathrm{nm}} L_{\mathrm{e}}(\lambda)\ \mathrm{d}A\mathrm{d}\Omega\mathrm{d}\lambda = 0.4\ \mathrm{W} \quad .$$

The total power after the filter then is (assuming a total enclosure by the band filter)

$$P_{\mathrm{BW}} = \iiint\limits_{690\ \mathrm{nm}}^{710\ \mathrm{nm}} L_{\mathrm{e}}(\lambda)\ \mathrm{d}A\mathrm{d}\Omega\mathrm{d}\lambda \quad .$$

For a center wavelength of $\lambda_0 = 700\,\mathrm{nm}$ and a filter bandwidth of $\Delta\lambda = 20\,\mathrm{nm}$, we can calculate the radiance (emitted power per surface area and solid angle, see Problem P8.2) using Eq. (S9.3) to

$$L_{\mathrm{e}}(\lambda_0, T) = \int\limits_{\lambda_0-\Delta\lambda/2}^{\lambda_0+\Delta\lambda/2} L_{\mathrm{e},\lambda}(\lambda, T)\ \mathrm{d}\lambda \approx L_{\mathrm{e},\lambda}(\lambda_0, T) \cdot \Delta\lambda$$

$$= \frac{2hc^2}{\lambda_0^5} \cdot \frac{\Delta\lambda}{\exp\left(\frac{hc}{\lambda_0\, k_B T}\right) - 1} = 1.47 \times 10^4\ \mathrm{Wm^{-2}\ sr^{-1}} \qquad \text{(S9.4)}$$

Assuming the characteristics (per unit area and solid angle) for all wavelengths of the Planck black body, we can write

$$P_{\text{vis}} = \int_{380\ \text{nm}}^{780\ \text{nm}} L_{\text{e},\lambda}(\lambda, T = 3000\ \text{K})\ \text{d}\lambda \cdot \iint \text{d}A\text{d}\Omega = 0.4\ \text{W} \quad . \tag{S9.5}$$

Numerical integration yields

$$P_{\text{vis}} = 1.814 \times 10^5\ \text{Wm}^{-2}\ \text{sr}^{-1} \cdot \iint \text{d}A\text{d}\Omega = 0.4\ \text{W} \quad ,$$

from which we obtain

$$\iint \text{d}A\text{d}\Omega = \frac{0.4\ \text{W}}{1.814 \times 10^5\ \text{Wm}^{-2}\ \text{sr}^{-1}} = 2.2 \times 10^{-6}\ \text{m}^2\text{sr} \quad .$$

Using Eqs. (S9.4) and (S9.6), we find for the power transmitted through the filter

$$\begin{aligned} P_{\text{BW}} &= \iint L_{\text{e}}(\lambda_0, T)\ \text{d}A\text{d}\Omega \\ &= 2.2 \times 10^{-6}\ \text{m}^2\text{sr} \cdot 1.47 \times 10^4\ \text{W m}^{-2}\ \text{sr}^{-1} = 0.033\ \text{W} \quad . \end{aligned}$$

This power would be distributed into the entire solid angle for a point source, that is, $\Omega = 4\pi$. In the case of a light bulb, we have the emission characteristics as shown in Figure S9.2, so we estimate the power to be emitted into a solid angle of about 3π.

In order to collect as much as possible light, collectors are being used which typically have a large numerical-aperture. In our case, color correction does not matter (because of the small bandwidth). Hence, a large NA $= n\sin(\theta) = 0.8$ with $f = 15$ mm can be used [2] from which we derive a collector angle of $\theta \approx 53°$. The collector efficiency can then be estimated to

$$\int_{-\theta}^{\theta} \text{d}\phi \int_{0}^{\frac{\pi}{2}+\theta} \sin\vartheta \text{d}\vartheta \approx 1.05\,\pi \quad ,$$

which means that the collector collects about a third of the total filtered power, that is, 0.01 W. As the light bulb is not a point source, we have quite some divergence after the collector in the collected light which can be estimated by using the lateral extension of the bulb filament d_{bulb}:

$$\varepsilon \approx \frac{d_{\text{bulb}}}{f} \approx \frac{2\ \text{mm}}{15\text{mm}} = 0.13\ \text{rad} \quad .$$

From Figure (A.37) and Eq. (A96), we conclude that

$$2w'_{\text{F}} \approx 2f \cdot \varepsilon = 15\ \text{mm} \cdot 0.13 = 1.95\ \text{mm} \quad .$$

2) see also Gross, H. (2008) *Handbook of Optical Systems – Survey of Optical Instruments*, vol. 4, John Wiley & Sons.

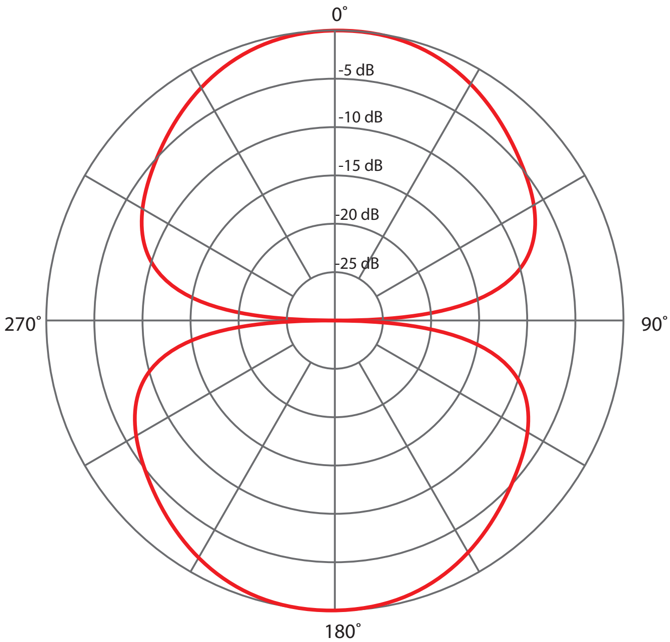


Figure S9.2 Emission characteristic of a light bulb. Taken from https://de.wikipedia.org/wiki/Strahlungsdiagramm

Obviously, the light from the bulb cannot be focused to the extend the laser beam can. If we compare the light intensities in the focus spot, we find for a laser beam with a power of 1 mW, $\lambda = 700$ nm, and a spot area of $100\ \mu\text{m}^2$ an intensity of

$$I = \frac{P}{A} = \frac{1\ \text{mW}}{100\ \mu\text{m}^2} = 10^3 \frac{\text{W}}{\text{cm}^2} \quad .$$

For a light bulb with a power of 20 W, $\lambda = 700$ nm, a bandwidth of $\Delta\lambda = 20$ nm, a collector aperture of $\text{NA} = 0.8$, and a focusing lens with $f = 15$ mm, we find an intensity of

$$I = \frac{P}{A} = \frac{0.01\ \text{W}}{\pi w_{\text{F}}'^2} = \frac{0.01\ \text{W}}{0.03\ \text{cm}^2} = 0.33\ \frac{\text{W}}{\text{cm}^2} \quad .$$

The advantages of the laser beam are obvious. To achieve the same spot intensity with the light bulb as with the 1 mW laser in part 3 of this problem, an electrical power of approximately 60 kW would be required!

P9.4
Photocoagulation

Suppose you cook an egg in the pan. Why does the egg white turn from transparent to white?

Solution:

Egg white primarily consists of 90% water and 10% proteins. At this stage, scattering due to the protein molecules is negligible so that it appears transparent. When heated, proteins undergo denaturation[3] which leads to coagulation. The coagulated molecules are highly scattering in nature which is responsible for the white appearance.

P9.5
Photoablation and photodisruption

Plasma-induced ablation and photodisruption are two kind of a laser–tissue interaction occurring at short irradiation times and high intensities. What do they have in common and what is different in the two processes?

Solution:

Similarities:

- Due to the short irradiation times and high intensities at the focal spot, optical breakdown occurs by means of multi-photon ionization and avalanche ionization.
- The laser-induced optical breakdown leads to the formation of a plasma bubble at the focal spot.
- Due to the high absorption coefficient of the laser-induced plasma, light energy can be transferred to the biological tissue, which is otherwise transparent for the laser wavelength at low intensities.
- Within the plasma volume, the tissue is ionized (plasma-induced tissue ionization).
- Further energy deposition into the plasma leads to explosion-like expansion by which shock waves and cavitation bubbles are formed, which can also lead to tissue fragmentation outside the focal volume (plasma-induced mechanical tissue fragmentation)

3) Process due to which proteins lose their structure in native stage by application of external stress like heat or compounds

Differences:

- In plasma-induced ablation, the local ionization of tissue in the focal volume is the main effect. The energy density of the plasma in plasma-induced ablation is relatively low due to the low optical breakdown threshold. Therefore, plasma-induced *mechanical* effects can be neglected. The ablated region is confined to the optical breakdown region and shows little thermal or mechanical side-effects. Thus, an extremely precise tissue manipulation is possible.
- In photodisruption, the energy density of plasma is higher due to the higher threshold exposure and thus higher energy deposition. Plasma-induced mechanical effects dominate and are characterized by the shock waves and cavitation. The damaged tissue volume is determined by the effect of shock waves and cavitation bubbles. In photodisruption, because the plasma-induced mechanical tissue fragmentation is the major effect, the affected volume is bigger than the focal volume.
- We find plasma-induced ablation predominantly when fs and sub-ps pulses are used, whereas photodisruption will also be observed with ps- and ns-pulses.

P9.6
Laser safety

Verify the nominal ocular hazard distance safety analysis depicted in Figure 9.15 for an unintended look into a laser beam with a power of 1 W, a wavelength of 532 nm, and a beam diameter of $2w = 2$ mm for a
1. direct laser beam with a beam divergence of 2.5 mrad and a
2. laser beam focused by a lens with a focal length of 50 mm.

Solution:

1. The irradiance $I(z)$ at a distance z from the laser source is given by

$$I(z) = \frac{P}{\pi \cdot w^2(z)} \tag{S9.6}$$

with

$$w(z) = w(0) + \varepsilon z,$$

where P is the laser beam power ($P = 1$ W), $w(0)$ the beam radius at the laser source ($w(0) = 1$ mm), ε the laser beam divergence ($\varepsilon = 2.5$ mrad), and z the distance from the laser source.

The distance, in which the maximum permissible exposure (MPE) values for eyes is exceeded, is referred to as the nominal ocular hazard distance (z_{NOHD}). Therefore,

$$I(z_{\mathrm{NOHD}}) = \mathrm{MPE} \ .$$

As visible laser light with a wavelength of 532 nm is used, the eyelid closure reflex limits the exposure time to 0.25 s. In this case, we obtain an MPE value of

$25.5\ \mathrm{W/m^2}$ for the unintendend look into the laser according to Section 9.6.2. From Eq. (S9.6), z_{NOHD} can be calculated via

$$w(0) + \varepsilon \cdot z_{\mathrm{NOHD}} = \sqrt{\frac{P}{\pi \cdot \mathrm{MPE}}}$$

or

$$z_{\mathrm{NOHD}} = \frac{1}{\varepsilon}\left(\sqrt{\frac{P}{\pi \cdot \mathrm{MPE}}} - w(0)\right) \ .$$

With the given values, we finally obtain

$$z_{\mathrm{NOHD}} = \frac{10^3}{2.5} \cdot \left(\sqrt{\frac{1\ \mathrm{Wm}^2}{\pi \cdot 25.5\ \mathrm{W}}} - 10^{-3}\mathrm{m}\right) = 44.7\ \mathrm{m} \approx 45\ \mathrm{m} \ .$$

2. According to Figure 10.5 and Eq. (10.5) the angle of convergence of a focused laser beam and the corresponding divergence is given by

$$\varepsilon_{\mathrm{L}} = \arctan\left(\frac{w_{\mathrm{L}}}{f}\right) \ ,$$

in which w_{L} is the beam radius on and f the focal length of the lens. Under the assumption that the distance between focusing lens and laser is small, we can approximate

$$w_{\mathrm{L}} \approx w(0)$$

and, because of $f \gg w(0)$, we find

$$\varepsilon_{\mathrm{L}} = \arctan\left(\frac{w(0)}{f}\right) \approx \frac{w(0)}{f} = \frac{1}{50} = 0.02\ \mathrm{rad} = 20\ \mathrm{mrad} \ .$$

The focused laser beam divergence ε_{L} is thus about $8\times$ larger than the beam divergence of case 1). Thus, the nominal ocular hazard distance $z_{\mathrm{NOHD,L}}$ is smaller by the same factor. As a consequence, we get

$$z_{\mathrm{NOHD,L}} = \frac{z_{\mathrm{NOHD}}}{8} \approx \frac{45}{8}\ \mathrm{m} \approx 5.6\ \mathrm{m} \ .$$