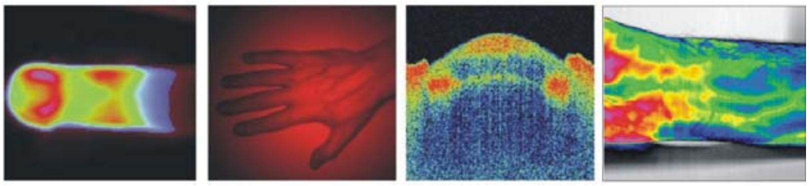
Applied Optoelectronics in Medicine

Aplikovaná optoelektronika v lékařství

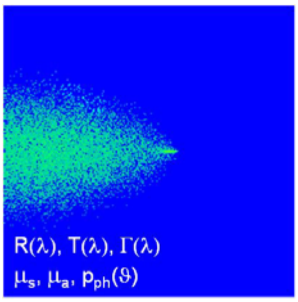
Interdisciplinary course at the CTU Prague (P317APL-E, W, 4 credits)

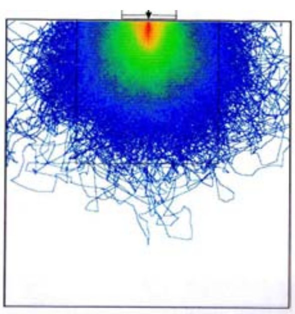


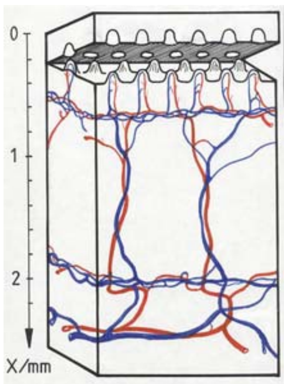
5. Tissue optics, parameters, describing light distribution in tissue
5. Optika lidské tkáně, parametry, popis rozptylu fotonů v tkáni

Learning aims of the fifth AOM lecture

- Strategies for assessment of photon penetration through the tissue
- Radiative transfer theory
- Kubelka-Munk theory
- Monte Carlo method, typical simulation results
- Optical model of the skin

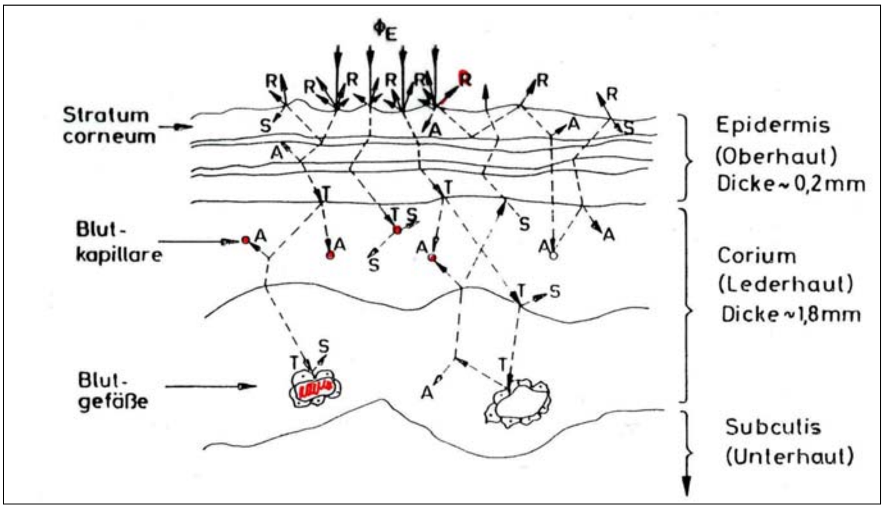






Simplified section through the human skin

with a schematic representation of the reflected, transmitted, absorbed and scattered radiation components

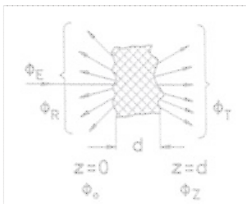


Terms and parameters of tissue optics - continuation

For the optical characterisation of the skin and other biological probes mainly the parameter reflection, transmission und extinction are used:

$$R(\lambda) = \frac{\Phi_R}{\Phi_E}, \quad T(\lambda) = \frac{\Phi_T}{\Phi_E}, \quad \Gamma(\lambda) = \frac{\Phi_\Gamma}{\Phi_E},$$

$$R(\lambda) + T(\lambda) + \Gamma(\lambda) = 1 .$$



Under the assumption of linear extinction the law of Lambert is valid:

$\Phi_z = \Phi_o \cdot e^{-\mu_t(\lambda) \cdot d}$ and after using of Φ_o and Φ_z $\dfrac{\Phi_E - \Phi_R - \Phi_\Gamma}{\Phi_E - \Phi_R} = e^{-\mu_t(\lambda) \cdot d}$.

Spectral extinction, absorption and scattering coefficient:

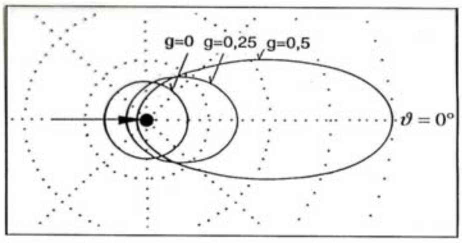
$$\mu_t = \mu_a + \mu_s = -\frac{\ln \dfrac{1 - R(\lambda) - \Gamma(\lambda)}{1 - R(\lambda)}}{d}$$

Phase function of the scattering process, anisotropy factor

The Henyey-Greenstein phase function has been proven in the description of scattering processes in biological samples, with scattering centers in the order of one or more wavelengths

$$p_{gh}(\vartheta) = \frac{1-g^2}{4\pi(1+g^2-2g\cdot\cos\vartheta)^{3/2}}$$

Der Parameter g ist der Anisotropiefaktor der Phasenfunktion ($|g| \le 1$), wobei g=1 reine Vorwärtsstreuung, g=0 isotrope Streuung und g=-1 reine Rückwärtsstreuung beschreibt.



Reduziertzer Streukoeffizient: $\mu_s' := \mu_s(1-g)$

Albedo: $a := \mu_s / (\mu_a + \mu_s)$

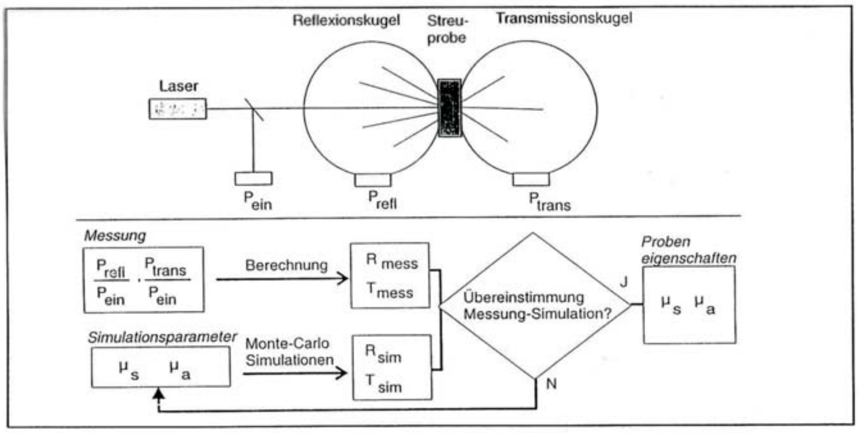
Mittlere freie Weglänge zwischen zwei Streuprozessen: $mfp := 1/\mu_s$

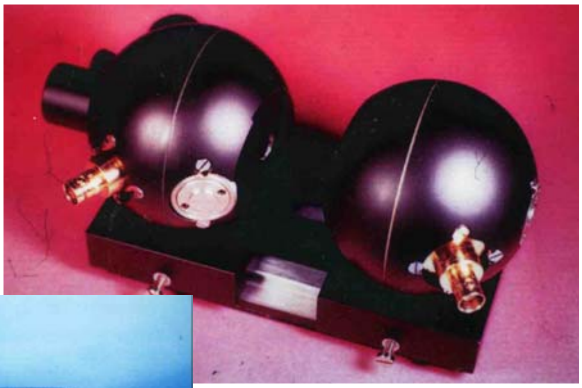
Eindringtiefe:
Die Kenntnis der optischen Eigenschaften ermöglicht auch die Bestimmung der Eindringtiefe des Lichtes in das betreffende Gewebe:

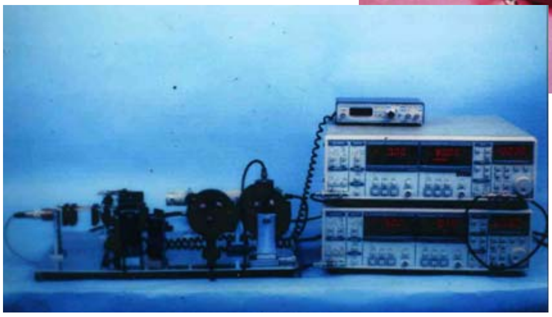
$$\delta = 1/\sqrt{3\mu_a(\mu_a + \mu_s(1-g))}$$

Spectro-photometric determination of scattering and absorption properties

The optical constant μa and μs cannot be determined directly by measurement. Therefore, we determine first the parameters R(λ) and T (λ) by spectrophotometry with a "double integrating sphere" sensor. Parallel we guess the optical coefficients and calculate the expected values R and T. Then we have to compare these values with the measured variables; to prove the calculated values.

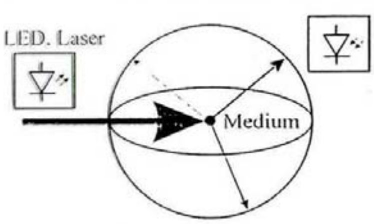






Determination of the scattering angle / of the scattering function with a goniometer measuring setup

A **goniometer** is an instrument that either measures an angle or allows an object to be rotated to a precise angular position. The term **goniometry** is derived from two Greek words, *gōnia*, meaning angle, and *metron*, meaning measure.

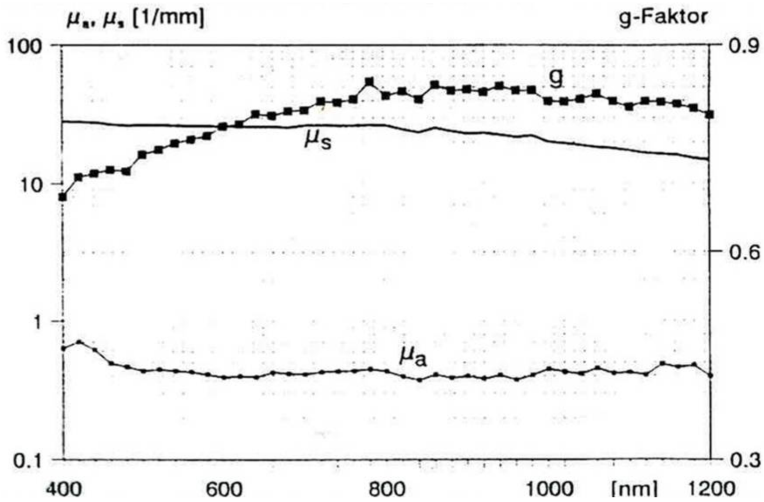


Example 1:
Typical optical properties of superficial skin layers
(at λ = 850 nm)

layer	μ_a, mm^{-1}	μ_s, mm^{-1}	g	n	d, µm
Epidermis	2.5	48.0	0.79	1.50	65
Upper dermis	0.27	18.7	0.82	1.40	565
Blood plexus	2.5	40.0	0.98	1.35	90
Lower dermis	0.27	18.7	0.82	1.40	565
Subcutaneous fat	0.02	2.0	0.80	1.37	610
Vessel wall	2.5	40.0	0.98	1.35	6380

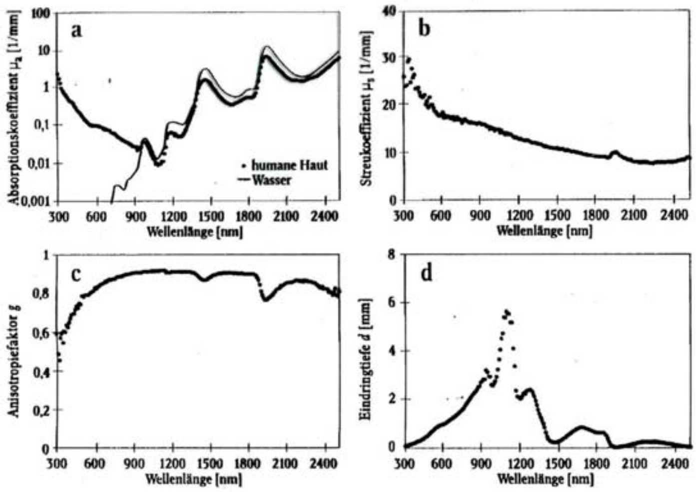
Example 2:

Optical properties of brain tissue (white substance)



Example 3:

Optical properties of human skin in vivo (Type II according Filzpatrick)



a) Absorption coefficient, b) scattering coeggicient, c) anisotropy factor, d) photon penetration depth

Calculation methods of light propagation in biological tissue

- Application of Maxwell's equations
- Radiative transfer theory
- Kubelka-Munk theory
- Monte Carlo simulation method

Analytical method / application of Maxwell's equations

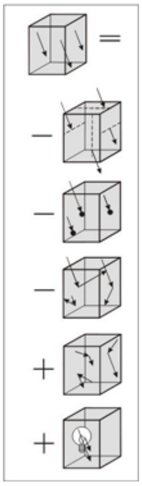
Very comprehensive approach for determining the photon flux in a medium. Definition of material properties, geometry, boundary conditions and the excitation gives us a boundary value problem, which solutions leads to a determination of fields in the medium. From the field distribution we can theoretically calculate the transport of energy and thus the photon flux.

Radiative transfer theory (RTT)

Describes the energy balance, or the spatial changes of the irradiance L for an infinitesimal area at the point r respectively.

$$\frac{1}{c}\cdot\frac{\partial L(\vec{r},s,t)}{\partial t} = -s\cdot\nabla L(\vec{r},s,t) - \mu_t L(\vec{r},s,t) + \mu_s \int_{4\pi} p(s',s)\cdot L(\vec{r},s',t)\,d\Omega' + \varepsilon(\vec{r},s,t)$$

The radiance density is attenuated by scattering and absorption; but at the same time, it is increased by light scattered back to the original direction s or regenerated in the medium (e.g. fluorescence):



$$\frac{1}{c}\int_V \frac{\partial L(\vec{r},s,t)}{\partial t}\cdot dV =$$

$$-\int_S L(\vec{r},s,t)s\cdot ds = -\int_V \nabla\cdot(L(\vec{r},s,t)s)\cdot dV =$$

$$= -\int_V s\cdot\nabla L(\vec{r},s,t)\cdot dV$$

$$-\int_V \mu_a L(\vec{r},s,t)\cdot dV$$

$$-\int_V \mu_s L(\vec{r},s,t)\cdot dV$$

$$+\int_V \mu_s \int_{4\pi} p(s',s)\cdot L(\vec{r},s,t)\cdot d\Omega'\cdot dV$$

$$+\int_V \varepsilon(\vec{r},s,t)\cdot dV$$

Kubelka-Munk theory *

An approximate method for describing the optical flow in scattering media by a "Two-flow model".

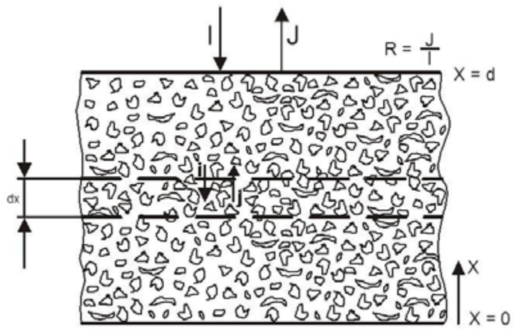
It considers the forward (I) and reverse scattering (J) only, with the aim to determine the scattering ratio absorption/scattering (K / S).

The flow I, in the direction x, in distance x opposite to the illuminated side (x=0), in a differential layer of thickness dx, is attenuated by backscattering (coefficient S) and absorption (coefficient K):

$$-di = (S+K)i(dx)$$

The same happens to flux J in the opposite direction:

$$dj = (S+K)j(dx)$$



* Kubelka, P., Munk. F.: Ein Beitrag zur Optik der Farbanstriche. Z. techn. Phys. 11a (1931), 593

It gives the basic differential equations:

$$-dj/dx = -(S+K)i + Sj \qquad dj/dx = -(S+K)j + Si$$ resp.

$$\frac{1}{S}\left(\frac{dj}{jdx} - \frac{di}{idx}\right) = -2a + r + \frac{1}{r}$$

with $S = 2\mu_s$; $K = 2\mu_a$; $a = (S+K)S$ und $r = j/i$.

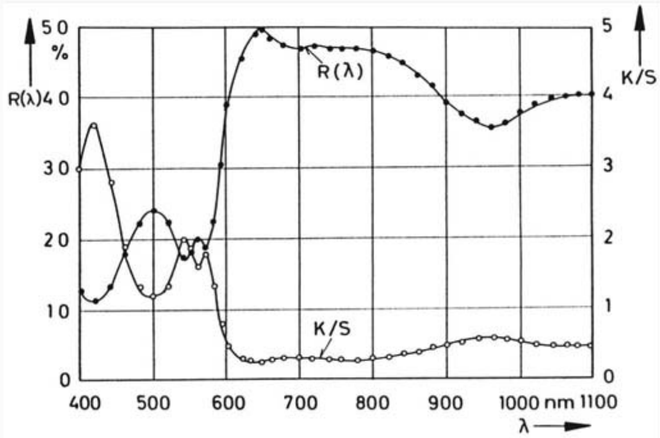
A general solution of the differential equation for the reflection coefficient r (x) at any location $0 \le x \le d$:

$$r(x) = \frac{1 - r_g(a-b)\cdot\coth(Sbx)}{a + b\cdot\coth(Sbd) - r_g}$$ mit $b = \sqrt{a^2 - 1}$; r_g ... Reflection coefficient of the substrate. .

x = d gives the ratio R of the direct to the reflected flux at the surface of the sample, the Reflection coefficient. For r_g = 0 and d -> ∞ is:

$$r_\infty = 1/(a+b)$$ resp. $$a = 0{,}5((1/r_\infty) + r_\infty) = 1 + (K/S)$$.

Kubelka-Munk theory - typical results

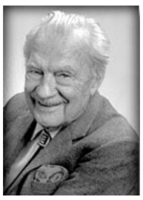


Remember:

From a single measurement of the reflection coefficient at infinitely large probe thickness the absorption/scattering ratio can be approximately calculated using the Kubelka-Munk method

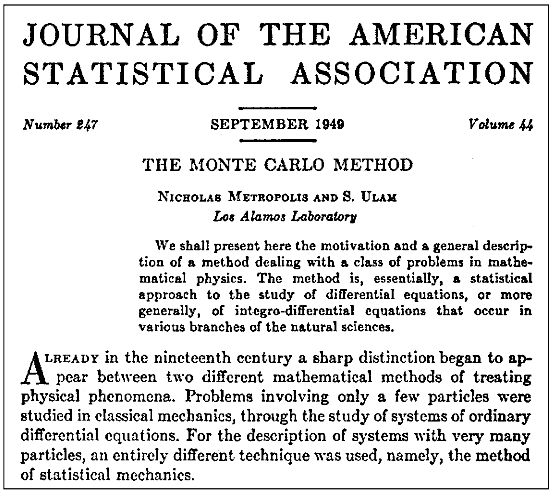
Simulation of photon propagation in scattering media by means of Monte Carlo method

The name Monte Carlo method was given by Metropolis and Ulam in 1949. They studied Simulation of diffusion processes in radioactive material.



Nicholas METROPOLIS
(1915 – 1999)

Stanislaw ULAM
(1909 – 1986)



JOURNAL OF THE AMERICAN STATISTICAL ASSOCIATION

Number 247 SEPTEMBER 1949 *Volume 44*

THE MONTE CARLO METHOD

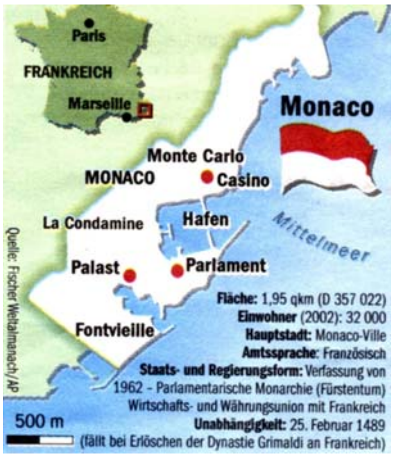
Nicholas Metropolis and S. Ulam
Los Alamos Laboratory

We shall present here the motivation and a general description of a method dealing with a class of problems in mathematical physics. The method is, essentially, a statistical approach to the study of differential equations, or more generally, of integro-differential equations that occur in various branches of the natural sciences.

Already in the nineteenth century a sharp distinction began to appear between two different mathematical methods of treating physical phenomena. Problems involving only a few particles were studied in classical mechanics, through the study of systems of ordinary differential equations. For the description of systems with very many particles, an entirely different technique was used, namely, the method of statistical mechanics.

Why Monte Carlo ...?

Metropolis and Ulam were inspired by the first tables of random numbers based on the results from the Casino of Monte Carlo




Kaiser KARL IV. (1316 - 1379)

* HENGARTNER, W.: THEODORESCU, R.: Einführung in die Monte-Carlo-Methode. Hanser Verlag, München 1978

Simulation of photon propagation in scattering media by means of Monte Carlo method

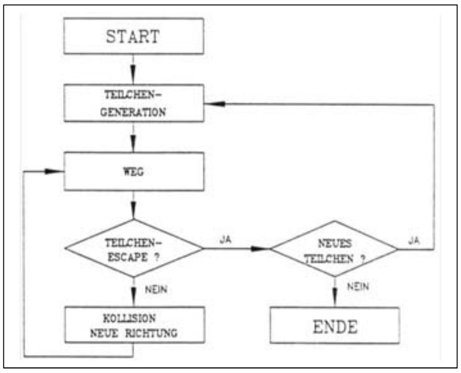
MC simulation is a stochastic method, based very often on coincidence experiments.
With the help of probability theory, it attempts, in mathematical context, to solve analytically intractable problems numerically, based on these coincidence results. Justification is mainly the law of large numbers.
The coincidence experiments can be either performed in reality, such throwing dice (cube), or through the generation of random numbers.
Nowadays, computers generate random processes in almost any large scale.

The Monte Carlo simulation can simulate uncertainties and statistical behavior such as:
If you do not know how rain falls, than simulate the path of a drop with randomly distributed other drops and collisions. After the simulation of several drops it gives you a statement about the average droplet size and dependent on temperature and density of droplets about possible snow or hail.

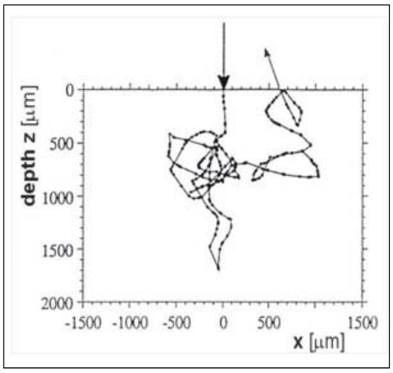
Important for realistic simulation results:

- good random number generator;
- high number of simulated events (here large number of photons N);
- valid for estimating the error of the simulation: $err = 1/\sqrt{N}$

Program structure for Monte Carlo simulation of photon propagation in tissue
(μ_s = 15/cm, g = 0.9)
(Mühl, PhD thesis, RWTH Aachen Univ., 1988)



Typical Photon trajectory in a homogeneous scattering sample
two dimensional projection (μ_a = 0.5/cm)
(Wang et al., 1992)



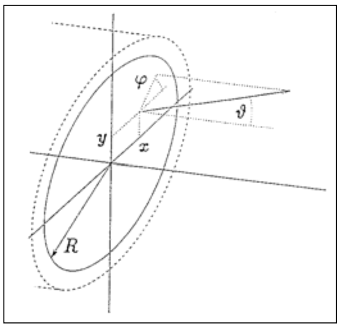
Monte Carlo simulation of photon trajectory in highly scattering tissue:
1) Modeling of the photon generation

Starting point of the photon injection:

$$x = (1-2\xi_1)\cdot R$$
$$y = (1-2\xi_2)\cdot R$$
$$\vartheta = \xi_3 \vartheta_{\max} \cdot (\vartheta_{\max} \le \pi)$$
$$\varphi = 2\pi\xi_4$$

R … Radius of the fiber core

ξ_i … Uniformly distributed random number in the interval (0,1)



Probability of the photon flux in a given direction by their distribution density function:

$$W(x,y,\vartheta,\varphi) = \frac{\left|\vec{\Phi}(x,y)\right|}{\int_{-R}^{R}\int_{-R}^{R}\left|\vec{\Phi}(x',y')\right|\cdot d_x \cdot d_y}\cdot p(x,y,\vartheta,\varphi)$$

Monte Carlo simulation of photon trajectory in highly scattering tissue:
2) Modeling of photon scattering and absorption

Scattering and absorption probability in homogeneous medium are constant.
This results in an exponentially decaying probability density function of the free path length s between two successive photon collisions in the tissue:

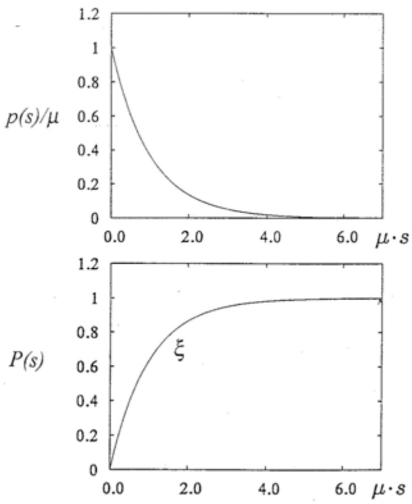
$$p(s) = \mu \cdot e^{-\mu . s}$$

By integration we obtain the distribution
Function of the mean free path s:

$$P(s) = (1 - e^{-\mu . s})$$

Determination of an exponentially distributed path-length:

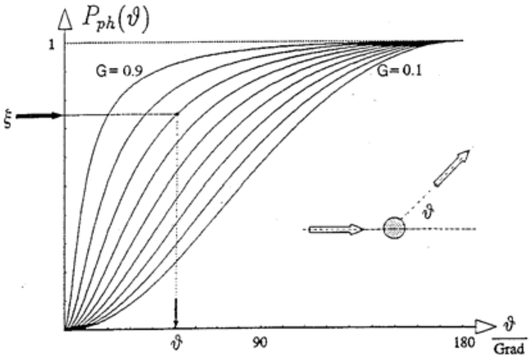
$$s_\xi = -1/\mu \cdot \ln(1-\xi)$$



Monte Carlo simulation of photon trajectory in highly scattering tissue:
3) Modeling of the flight direction after scattering

The starting point is the Henyey-Greenstein phase function
Integrating over the polar scattering angle gives the distribution function of different anisotropy factor g:

$$P_{ph}(\vartheta) = \int_0^{\vartheta} p_{ph}(\vartheta') \cdot 2\pi \sin\vartheta' d\vartheta =$$
$$= \frac{1-g^2}{2g}\left(\frac{1}{1-g} - \frac{1}{\sqrt{1+g^2-2g\cdot\cos\vartheta}}\right)$$



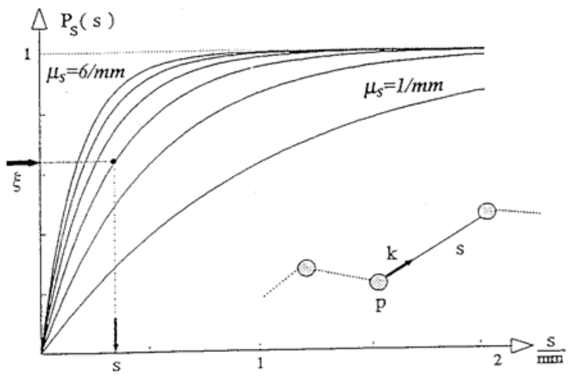
Monte Carlo simulation of photon trajectory in highly scattering tissue:
4) Free flight path between two collisions for various scattering coefficients

Probability of scattering along the n-th path:

$$P_s(n\cdot ds) - P_s((n-1)ds) =$$
$$= (1 - P_s((n-1)ds)) \cdot (1 - e^{-\mu_{s,n}} \cdot ds)$$

Total probability of scattering at the point s = nds:

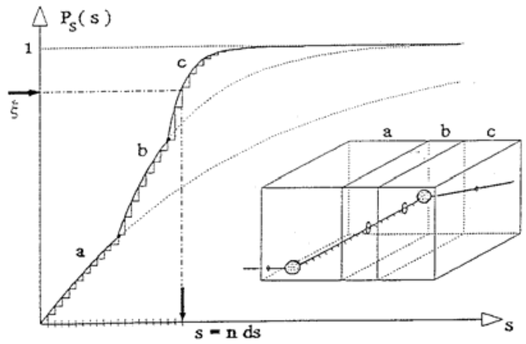
$$P_s(n\cdot ds) = 1 - e^{-\sum_{i=0}^{n}(\mu_{s,i}\cdot ds)}$$



Monte Carlo simulation of photon trajectory in highly scattering tissue:

4) Free flight path between two collisions for various scattering coefficients

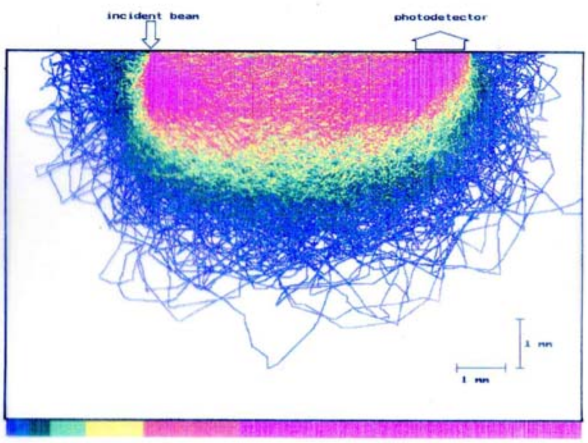
Expansion of the distribution function for layered media



Remember: *Random variables of the process (used to determine the solution of the process) are simulated by generation of random numbers with corresponding distribution functions.*

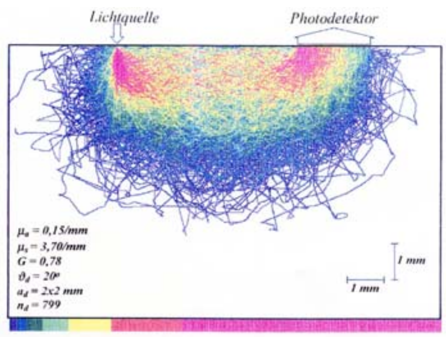
Light distribution in biotissue:

typical Monte Carlo simulation results

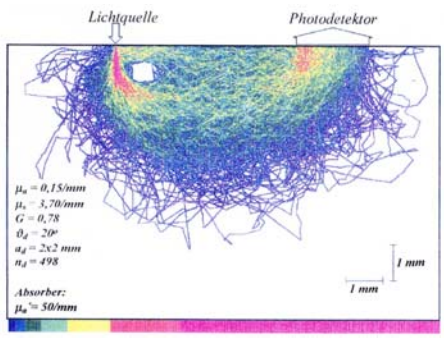


Shadow projection (y = 0) of the detected photon trajectories (1516 from 3.10 ^{6})
z = 6 mm, α_d = 60°
Longest trajectory 20mm. CPU time: 11.5 h

Light distribution in biotissue:
typical Monte Carlo simulation results

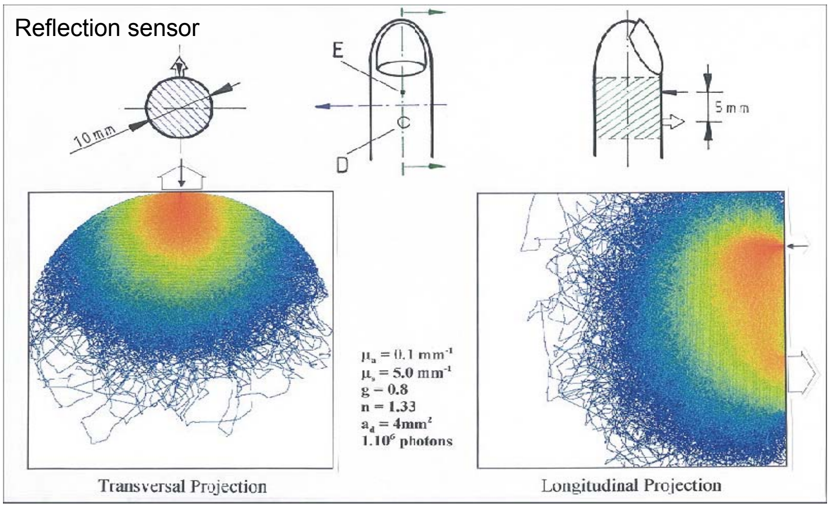


Homogeneous skin model



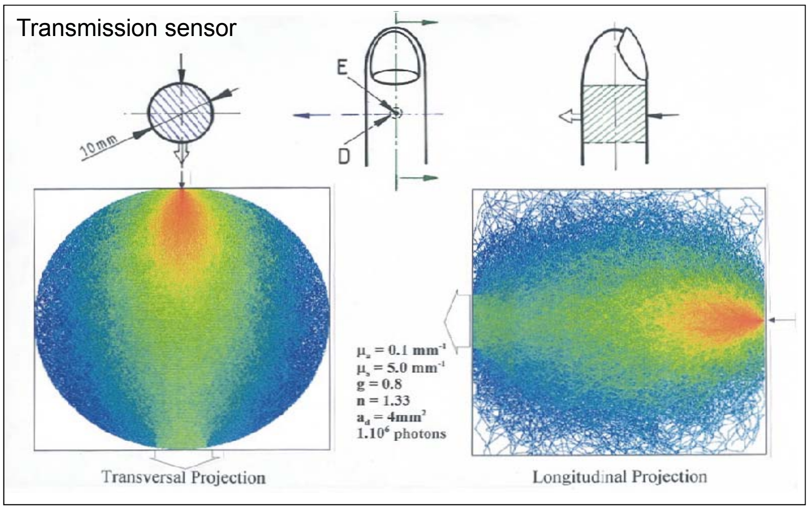
Skin model with a singular, strongly absorbing structure

Monte Carlo simulation of photon paths in highly scattering tissue
Homogeneous scenario, typical results



Monte Carlo simulation of photon paths in highly scattering tissue

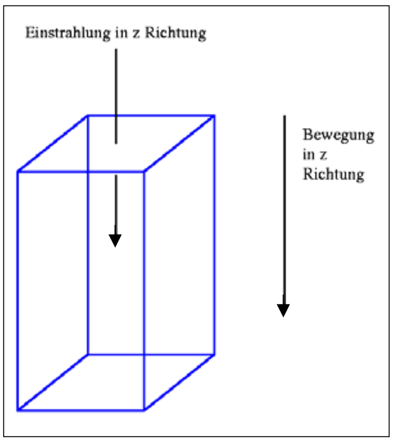
Homogeneous scenario, typical results

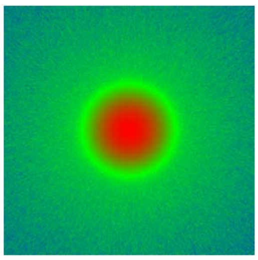


Monte Carlo simulation of photon paths in highly scattering tissue

Homogeneous scenario, typical results

The simulation domain is running toward the light source. The animation illustrates the spatial distribution. A temporal resolution of the photon motion is not carried out.

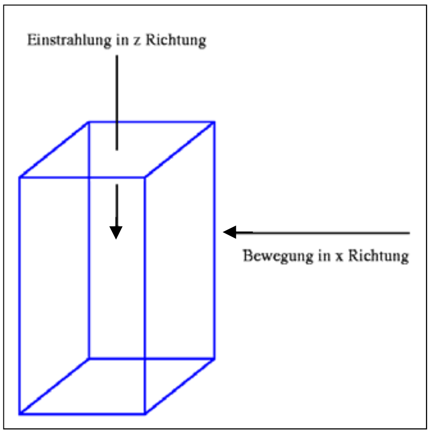




Monte Carlo simulation of photon paths in highly scattering tissue

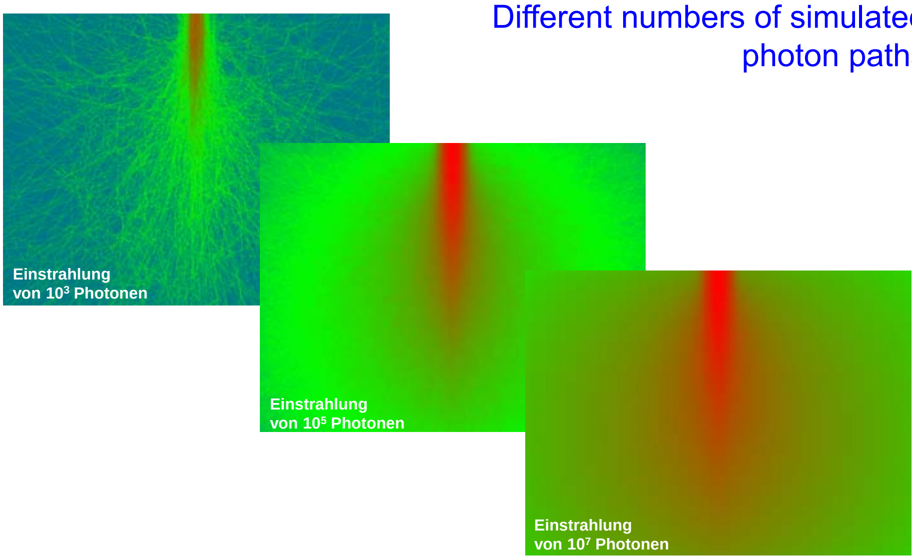
Homogeneous scenario, typical results

The simulation domain is running transversally to the light source. The animation illustrates the spatial distribution. A temporal resolution of the photon motion is not carried out.



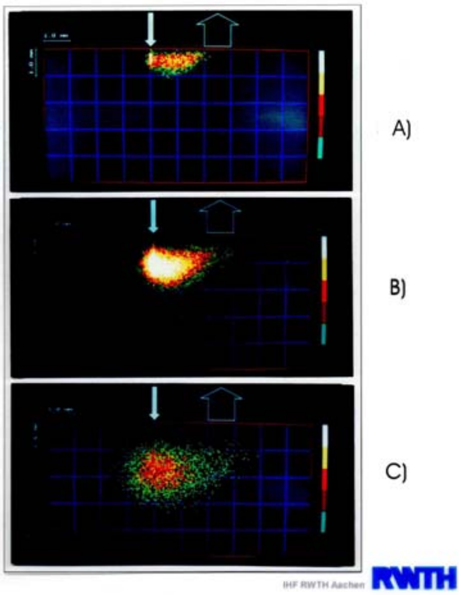
Monte Carlo simulation of photon paths in highly scattering tissue

Different numbers of simulated photon paths

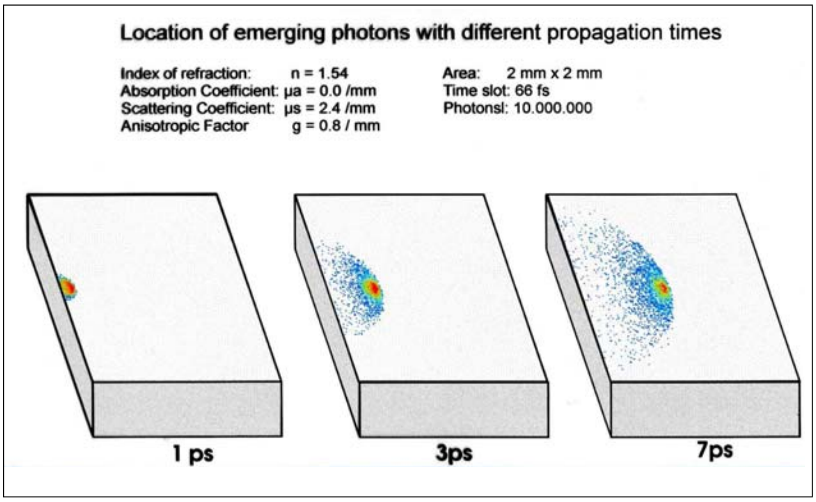


Temporal selective Monte Carlo simulation

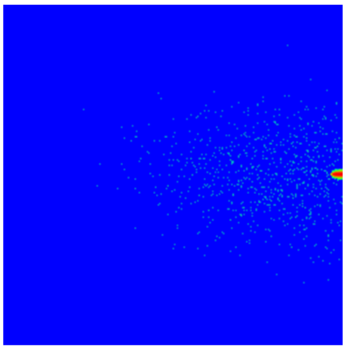
A) Time of photon flight: 9 - 13 ps
B) Time of photon flight: 18 - 22 ps
C) Time of photon flight: 32 - 36 ps



Temporal selective Monte Carlo simulation

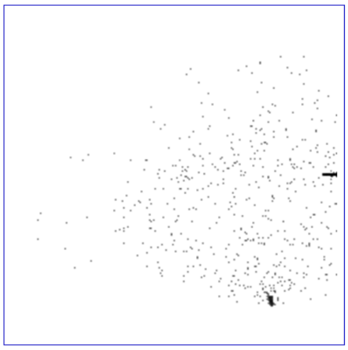


Temporal selective Monte Carlo simulation



Simulation parameters:

Scattering coefficient:	μ_s = 1.0/mm
Absorption coefficient:	μ_a = 0.1/mm
Anisotropy factor:	g = 0,9
Refractive index:	n = 1.33
Photon number:	100.000 per image
Image section:	10x10 mm^2
Gradually:	1mm photon way



Inhomogeneity with increased scattering coefficient and refractive index

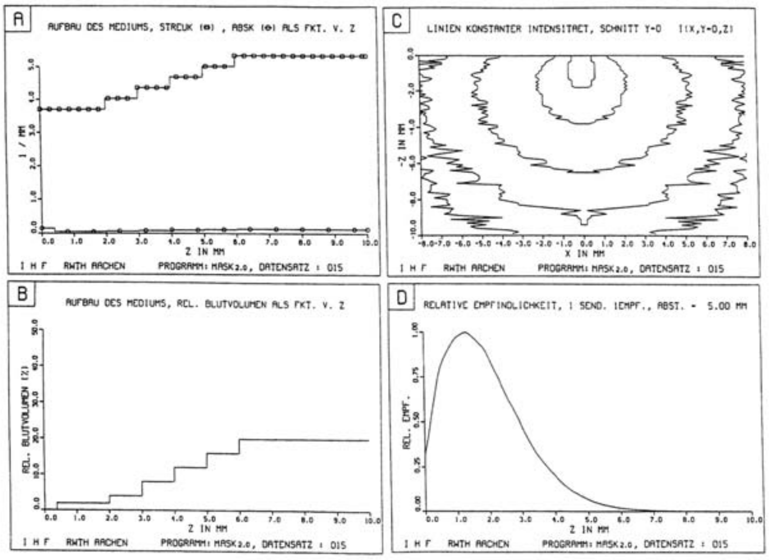
Monte Carlo simulation of light distribution in a 6-layer skin phantom

With this differentiated skin model that takes into account local blood volume fluctuations and consider realistic geometry assumptions of skin structures and variable absorption and scattering coefficients. It is possible, among others, to conduct optimization of the skin attached optoelectronic sensors for hemodynamic studies.

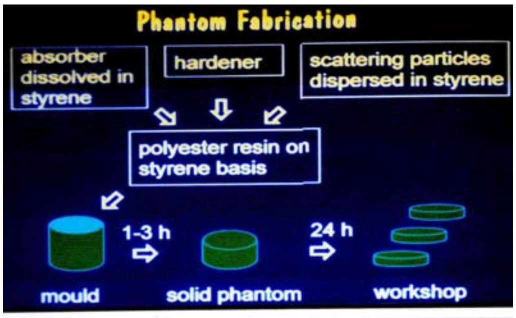
Model of skin / vessel phantom:

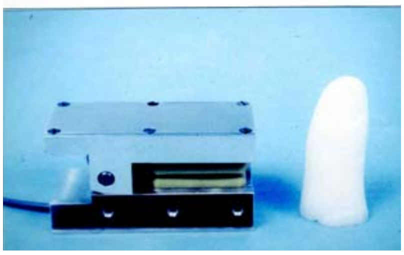
	z /mm	μ_a /mm^{-1}	μ_s /mm^{-1}	c_b
Epidermis	0.0-0.2	0.150	3.70	0.00
Plexus capillaries	0.2-0.4	0.068	4.03	0.04
Plexus superficialis	0.4-0.6	0.095	4.53	0.10
Vasa communicantia	0.6-1.5	0.073	4.12	0.05
Plexus profundus	1.5-2.0	0.118	4.93	0.15
Subcutis	>2.0	0.068	4.03	0.04

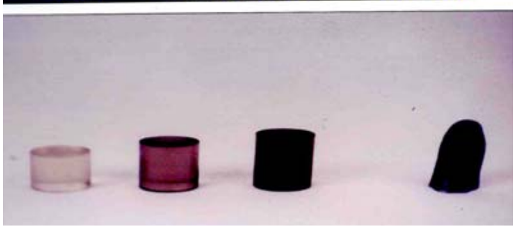
Monte Carlo simulation of light distribution in a 6-layer skin phantom



How is a tissue phantom to define and generate?



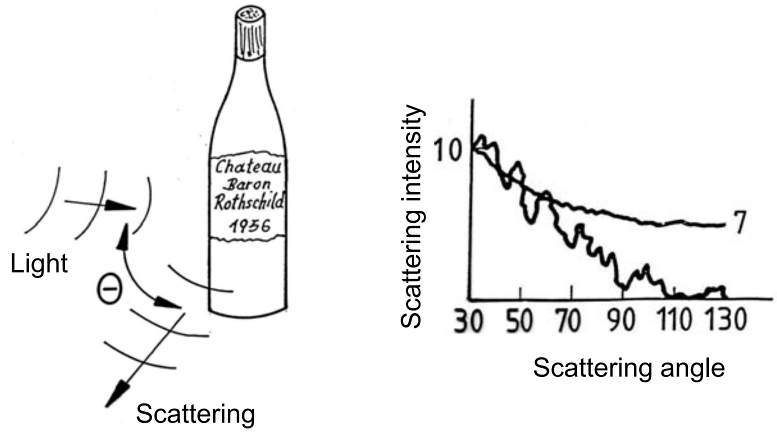




Related publication, recommended for further study:
D.J. Smithies and P.H. Butler

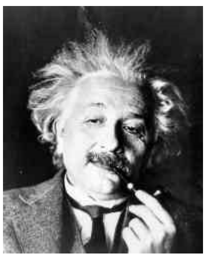
Modelling the distribution of laser light in port-wine stains with the Monte Carlo method

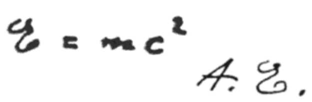
Phys. Med. Biol. 40,5 (1995), pp. 701-731



Citát pro pátou přednášku / Quotation of the lecture 5:

„Education is what is remaining, when we forgot everything, what we learned in the school“





Albert EINSTEIN (1879 - 1955)
Creator of the description as „light quant“
Nobel price 1921