# Biomedical Optics III

Tissue optical properties

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## Optical properties vs Optical measurements

- refractive index n
- absorption $\mu_a$
- scattering $\mu_s$
- anisotropy g
- reduced scattering $\mu_s(1-g)$

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- transmission T
- reflectance R

## Absorption

- In biomedical optics, *absorption* of photons is a most important event:

- Absorption is the primary event that allows a laser or other light source to cause a potentially therapeutic (or damaging) effect on a tissue.
  - Without absorption, there is no energy transfer to the tissue and the tissue is left unaffected by the light.
- Absorption of light provides a diagnostic role such as the spectroscopy of a tissue.
  - Absorption can provide a clue as to the chemical composition of a tissue, and serve as a mechanism of optical contrast during imaging.

$$dI = -\mu_a I dx$$

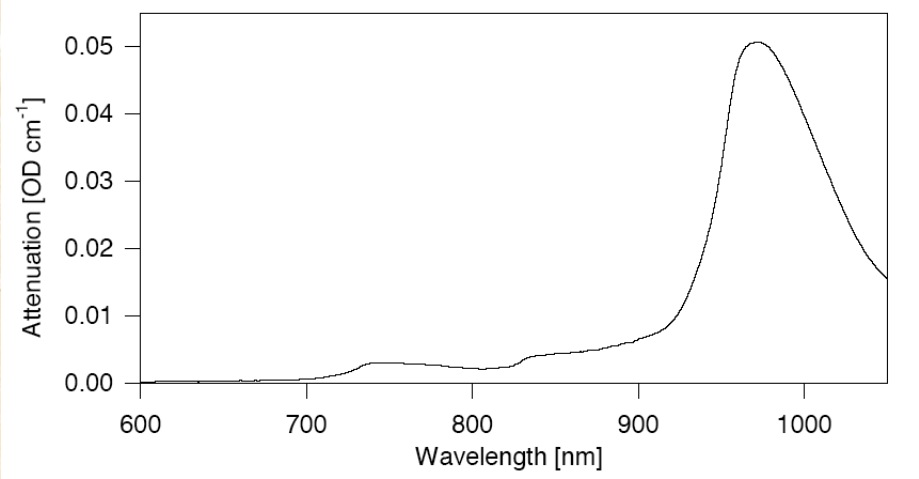
$$I = I_0 e^{-\mu_a x}$$

$$Beer - Lambert$$

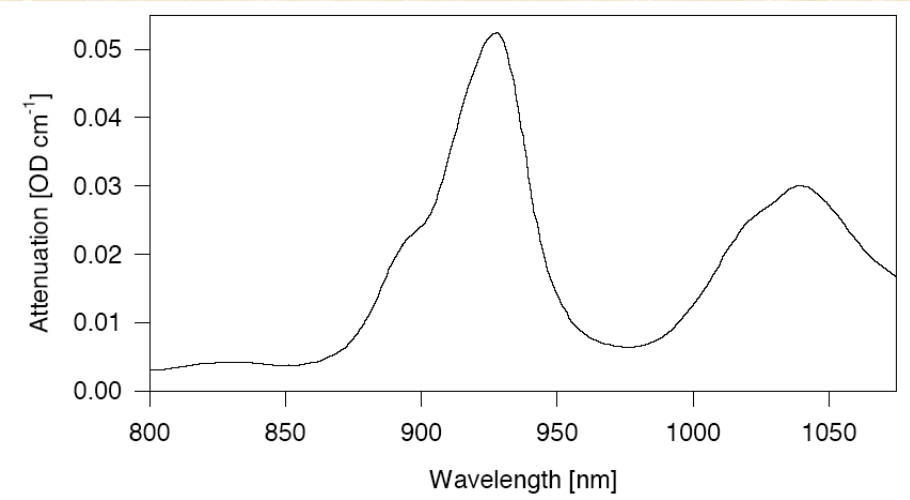
$$OD = \log_{10}(\frac{1}{T}) = -\log_{10}(\frac{I}{I_0}) = -\log_{10}(T)$$

$$OD = \log_{10}(e)\mu_a x = \alpha c x$$

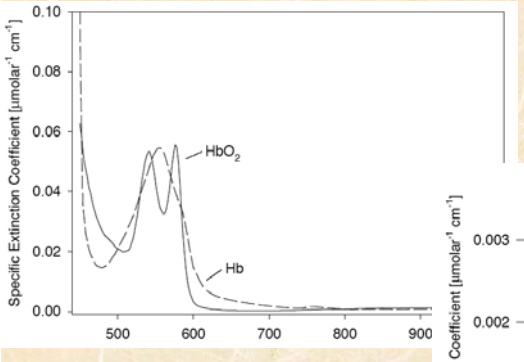
# Absorption spectrum of water

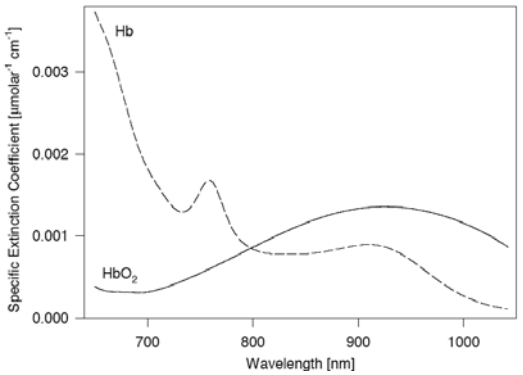


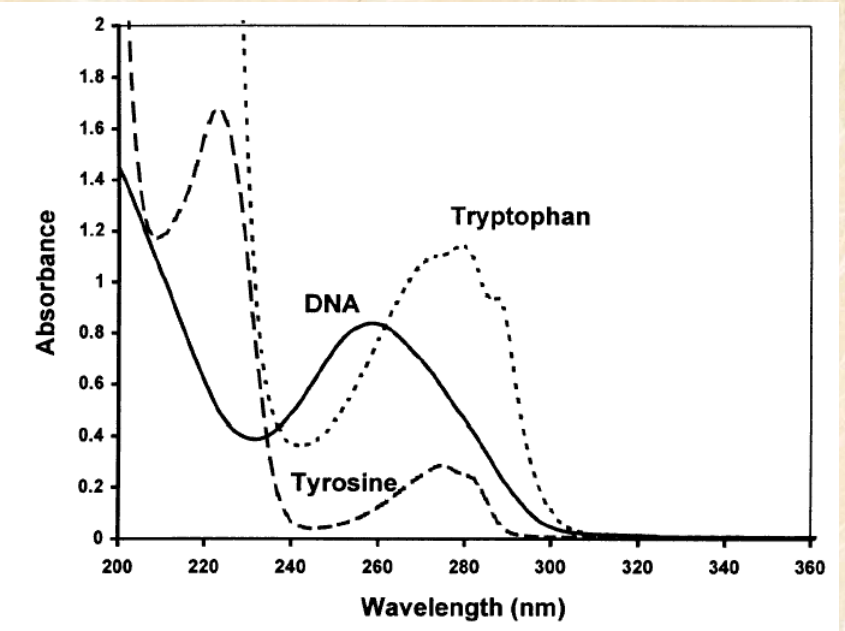

# Lipids




# Oxy and deoxy-heamoglobin



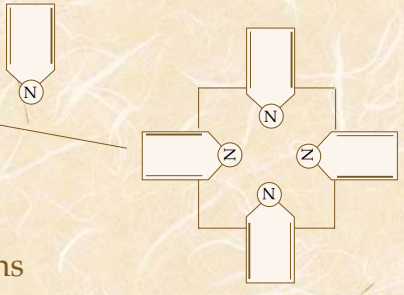



# Chromophores

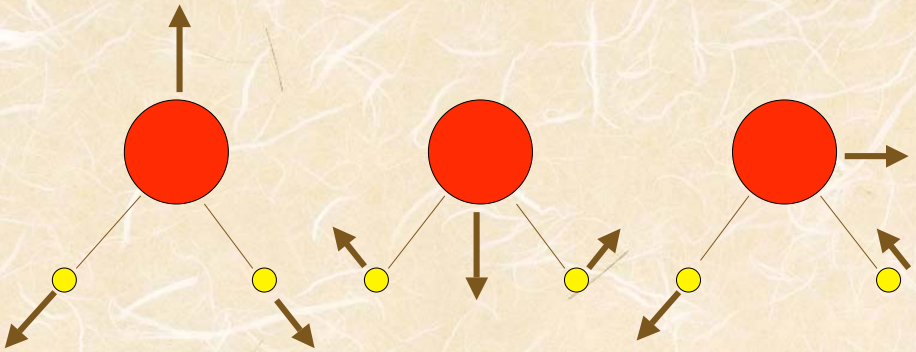
- Molecules that absorb light are called *chromophores*.
- There are two major types of chromophores:
  - electronic transitions
  - vibrational transitions

# Electronic transitions

pyroles
porphyrins
heme
chlorophyl
cytochromes
phycobiliproteins
carotenoids
ferredoxins
flavins
melanin




# Vibrational transistion



$\nu = 3652\ cm^{-1}$
$\lambda = 2.738\ \mu m$

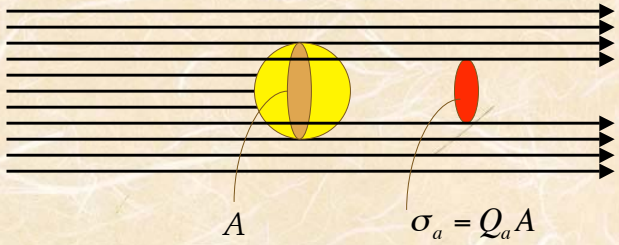
$\nu = 1595\ cm^{-1}$
$\lambda = 5.128\ \mu m$

$\nu = 3756\ cm^{-1}$
$\lambda = 2.662\ \mu m$

# absorption coefficient $\mu_a$

abs. cross-sectional area — $\sigma_a = Q_a A$ — geometrical area (efficiency)

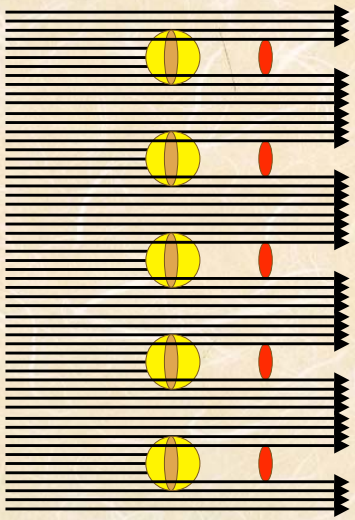
$$[cm^2] = [-][cm^2]$$




geometrical cross-section

effective cross-section

# absorption coefficient



$$\mu_a = \rho_a \sigma_a$$

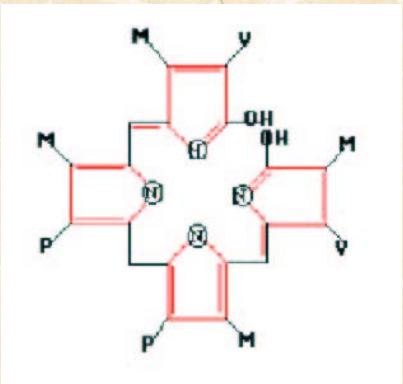
$\sigma_a$: abs. cross-sectional area

$\rho_a$: density

L is a photon's pathlength of travel.
The probability of survival (or transmission T) of the photon after a pathlength L is:

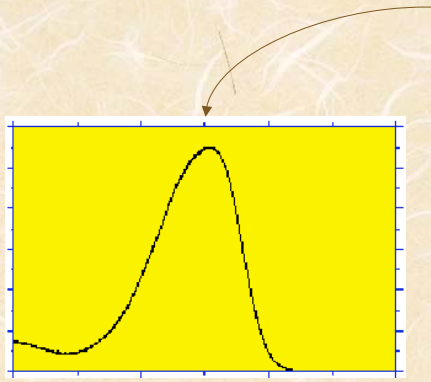
$$T = \exp[-\mu_a L]$$

# Bilirubin



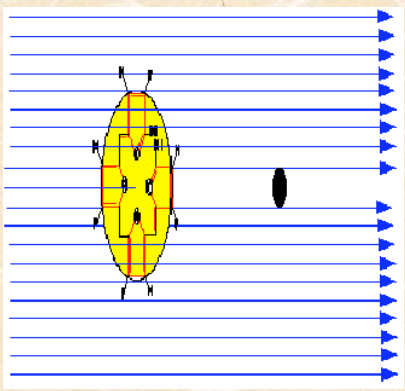
- The structure of bilirubin. The diameter is approximately 1nm.
- ⇒
- the geometrical area is $A = 4.5 \times 10^{-15}$ cm$^2$.

# Bilirubin spectrum



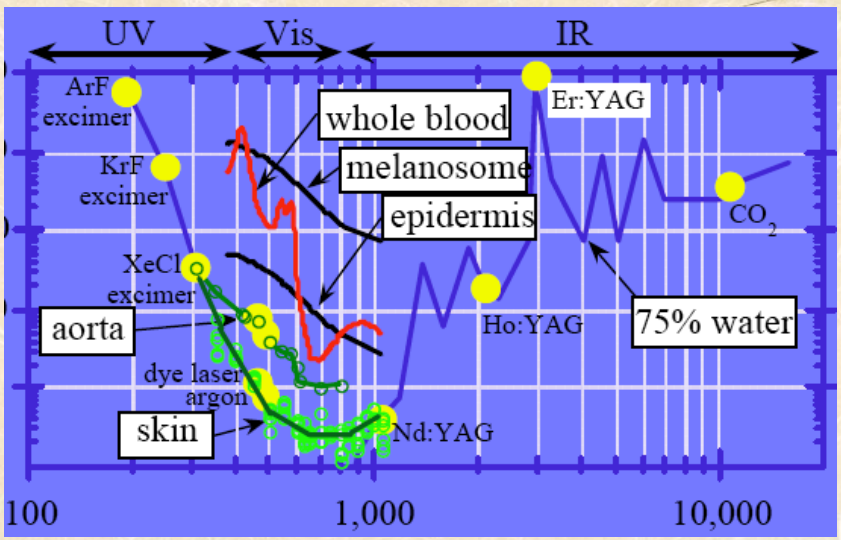

- At 460 nm, the extinction coefficient of bilirubin is $\varepsilon$ = 53,846 [cm$^{-1}$M$^{-1}$]
- If C is concentration [M] and L is pathlength [cm]. Therefore,
- $\mu_a = \varepsilon C \ln(10)$
- A typical jaundiced neonate might have a bilirubin concentration of 10 mg/dL, or (0.100 g/liter)/(574.65 g/mole) = $0.17 \times 10^{-3}$ M.
- The bilirubin absorption coefficient at 460 nm is roughly
- $\mu_a = \varepsilon C \ln(10)$ = (53846 [cm$^{-1}$M$^{-1}$])* ($0.17 \times 10^{-3}$ M)(2.3) = 21 cm$^{-1}$.

# Example



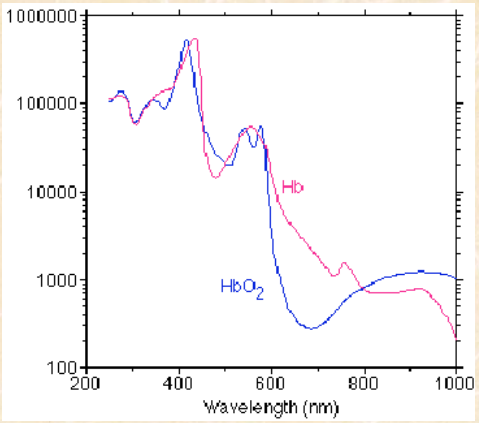
- If the concentration C is equivalent to $\rho_a$ =(0.17x10$^{-3}$ [moles/liter])* (6x1023 [mole$^{-1}$])/ (1000 cm$^3$/liter] = 1.02x1017 [cm$^{-3}$]
- The efficiency of absorption is estimated: $Q_a = \mu_a/(\rho_a A)$ = (21 [cm$^{-1}$])/((1.02x10$^{17}$ [cm$^{-3}$])* (A = 4.5x10$^{-15}$[cm$^2$])) = 0.046
- The effective cross-section is $\sigma_a = Q_a A$ = (0.046)(4.5x10$^{-15}$ [cm$^2$]) = 2.1x10$^{-16}$ [cm$^2$].
- Bilirubin's effective cross-sectional diameter is sqrt(.046) or 21% the size of its geometrical diameter.

# Example




# Most comman Hb-spectra

- If the hemoglobin molecule is bound to oxygen then one has oxy-hemoglobin or $Hb0_2$ [blue]
- If the hemoglobin molecule is bound to nothing then one has deoxy-hemoglobin or Hb [red]




# Less common spectra of blood

- If the hemoglobin molecule is bound to carbon monoxide then one has carboxy-hemoglobin or HbCO
- If the hemoglobin molecule has broken down then one has meta-hemoglobin.

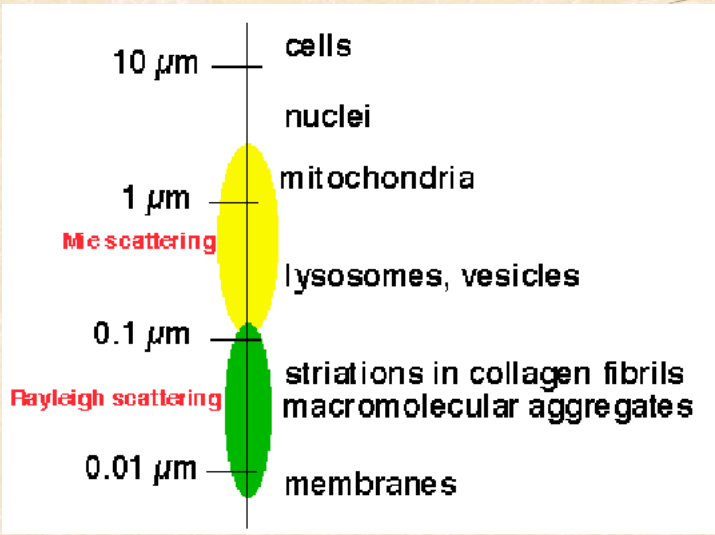
# Scattering

- The light scattered by a tissue has interacted with the ultrastructure of the tissue.
- Tissue ultrastructure extends from membranes to membrane aggregates to collagen fibers to nuclei to cells.
- Photons are most strongly scattered by those structures whose size matches the photon wavelength.

# Scattering possibilities

- Scattering provides feedback during **therapy**.
  - during laser coagulation of tissues, the onset of scattering is an observable endpoint
- Scattering has **diagnostic** value.
  - the density of lipid membranes in the cells, the size of nuclei, the presence of collagen fibers, the status of hydration in the tissue.

# Scattering

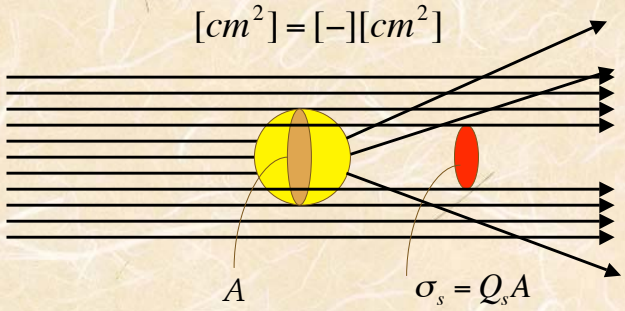



# Scattering coefficient $\mu_s$

abs. cross-sectional area — efficiency — geometrical area

$$\sigma_s = Q_s A$$

$$[cm^2] = [-][cm^2]$$




geometrical cross-section

effective cross-section

# Scattering coefficient $\mu_s$

$$\mu_s = \rho_s \sigma_s$$

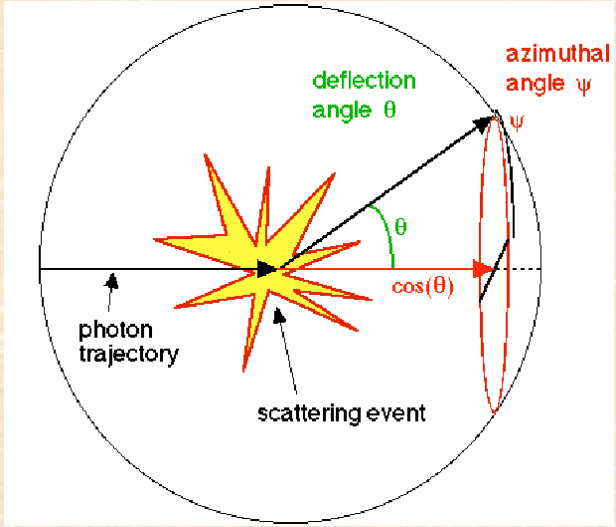
$\sigma_s$: scattering cross-sectional area

$\rho_s$: density

The probability of transmission T of the photon without redirection by scattering after a pathlength L is:

$$T = \exp[-\mu_s L]$$

# Anisotropy g




# Anisotropy definition

$$g = \int_0^{\pi} p(\theta)\cos\theta 2\pi\sin\theta d\theta = <\cos\theta>, \text{ where } \int_0^{\pi} p(\theta)2\pi\sin\theta d\theta = 1$$

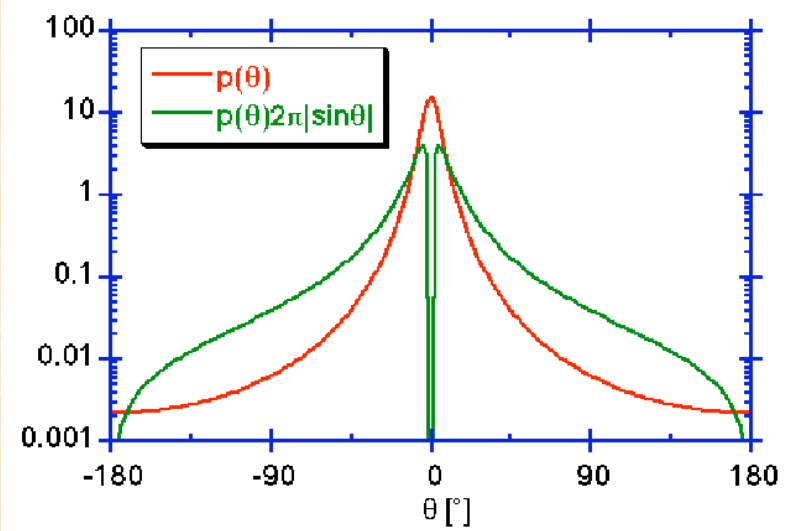
$$g = \int_{-1}^{1} p(\cos\theta)\cos\theta d(\cos\theta), \text{ where } \int_{-1}^{1} p(\cos\theta)d(\cos\theta) = 1$$

# Scattering function

- The angular dependence of scattering is called the scattering function, p(θ) which has units of [sr-1] and describes the probability of a photon scattering into a unit solid angle oriented at an angle relative to the photons original trajectory.

- Plotting p(θ) indicates how photons will scatter as a function of θ in a single plane of observation
- Plotting p(θ) 2πsinθ indicates how photons will scatter as a function of the deflection angle θ regardless of the azimuthal angle ψ, in other words integrating over all possible ψ in an azimuthal ring of width dθ and perimeter 2πsinθ at some given θ .

## Scattering functions




## Isotropic scattering

$$p(\theta) = \frac{1}{4\pi}, \text{ such that } \int_0^{\pi} p(\theta) 2\pi \sin\theta d\theta = 1$$

## Henyey-Greenstein scattering function

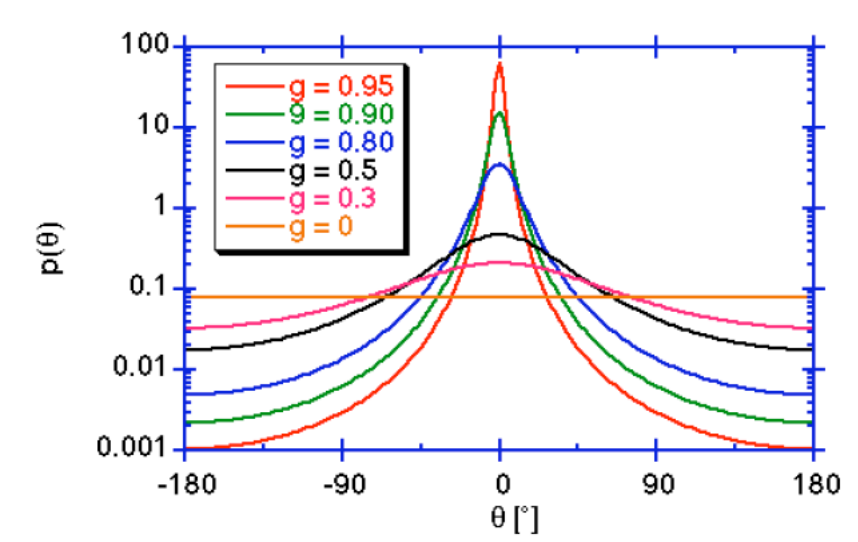
$$p(\theta) = \frac{1}{4\pi} \frac{1-g^2}{(1+g^2-2g\cos\theta)^{3/2}}, \text{ such that } \int_0^{\pi} p(\theta) 2\pi \sin\theta d\theta = 1$$

$$\text{and } \int_0^{\pi} p(\cos\theta) d(\cos\theta) = 1$$

$$p(\theta) = \frac{1}{2} \frac{1-g^2}{(1+g^2-2g\cos\theta)^{3/2}}, \text{ such that } \int_0^{\pi} p(\cos\theta) d(\cos\theta) = 1$$

$$\text{and } \int_0^{\pi} p(\theta) 2\pi \sin\theta d\theta = 1$$

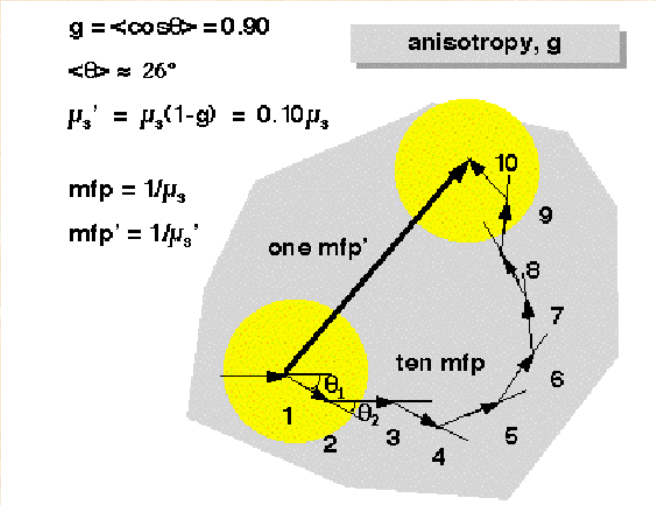
## Different anisotropy values



# Reduced scattering coefficient

- $\mu_{s'} = \mu_s(1 - g)$ [$cm^{-1}$]
- The purpose of $\mu_{s'}$ is to describe the diffusion of photons in a random walk of step size of $1/\mu_{s'}$ [cm] where each step involves isotropic scattering.
- This occurs if there are many scattering events before an absorption event, i.e., $\mu_a << \mu_{s'}$.
- This situation of scattering-dominated light transport is called the diffusion regime and $\mu_{s'}$ is useful in the diffusion regime which is commonly encountered when treating how visible and near-infrared light propagates through biological tissues.

# Example




# Summary

- **Optically tissue may be characterized by its**
  - scattering, refractive index, and absorption.
- **The scattering arises from**
  - cell membranes, cell nuclei, capillary walls, hair follicles...
- **The absorption arises from**
  - visible and NIR wavelengths (400 nm - 800 nm);
    - *» hemoglobin and melanin,*
  - IR wavelengths;
    - *» water and molecular vibrational/ rotational states.*

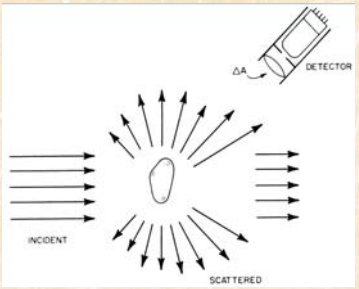
# Importance of light scattering

- **Important because**
  - light propagation is affected by the tissue *optical properties*,
  - the *physiological condition* or state of single cells or tissues is expressed through (but not exclusively) changes in cell size or refractive index,
  - changes in refractive index or cell size influence the *optical properties*.

*Therefore measurements or analysis of scattering provide information about the tissue.*

# Characteristic quantities

- Four important properties
- Cross section
  - absorption
  - scattering
  - extinction
- Angular dependence
  - scattering phase function




# Cross sections

Scattering cross section

$$\sigma_s = \int_{4\pi} \sigma_d \, d\omega = \frac{\sigma_t}{4\pi} \int_{4\pi} p(\mathbf{s},\mathbf{i}) \, d\omega$$

Absorption cross section

$$\sigma_a$$

Back-scatter cross section

$$\sigma_b = 4\pi\sigma_d(-\mathbf{i},\mathbf{i})$$

Extinction cross section

$$\sigma_t = \sigma_s + \sigma_a$$

Albedo

$$W_0 = \frac{\sigma_s}{\sigma_s + \sigma_a} = \frac{\sigma_s}{\sigma_t}$$

Note: $W_0$ is close to zero for most tissues

$\sigma_b$ = differential scattering cross section

# Scattering cases

- Size parameter $x = 2\pi a / (\lambda / n_{med})$
- Refractive index ratio $n_r = n_p / n_{med}$
- Rayleigh approximation
  - the particle a dipole, strength related to its volume
  - valid if $a << 1$ or until a is 5% of $\lambda$
  - proportional to $\lambda^{-4}$

# Rayleigh scattering

- Scattered intensity

$$I_s = \frac{8\pi^4 N r^6}{\lambda^4 R^2} \left| \frac{n_r^{\,2} - 1}{n_r^{\,2} + 1} \right| (1 + \cos^2\theta) I_i$$

- where r=radius and $n_r = n_p / n_{med}$

## Mie theory model for tissue optical properties

- Mie theory describes the scattering of light by particles, with refractive index ($n_p$) that differs from the refractive index of its surroundings ($n_{med}$).
- The dipole re-radiation pattern from oscillating electrons in the molecules of such particles superimpose to yield a strong net source of scattered radiation.
- Also, the re-radiation patterns from all the dipoles do not cancel in all but the forward direction of the incident light as is true for homogeneous medium, but rather interfere both constructively and destructively in a radiation pattern.
- Hence, particles "scatter" light in various directions with varying efficiency.

## Mie

- Mie's classical solution is described in terms of two parameters, $\mathbf{n_r}$ and $\mathbf{x}$:
  - *the magnitude of refractive index mismatch between particle and medium expressed as the ratio of the n for particle and medium,*

    $n_r = n_p/n_{med}$

    a
  - *the size of the surface of refractive index mismatch which is the "antenna" for reradiation of electromagnetic energy, expressed as a size parameter (x) which is the ratio of the meridional circumference of the sphere ($2\pi a$, where radius = a) to the wavelength ($\lambda/n_{med}$) of light in the medium,*

    $x = 2\pi a / (\lambda/n_{med})$

## Mie calculations

- A Mie theory calculation will yield the efficiency of scattering which relates the cross-sectional area of scattering, $\sigma_s$ to the true geometrical cross-sectional area of the particle, $A = \pi a^2$
- $\sigma_s = Q_s A$
- Finally, the scattering coefficient is related to the product of scatterer number density, $\rho_s$, and the cross-sectional area of scattering, $\sigma_s$

  $\mu_s = \rho_s \sigma_s$

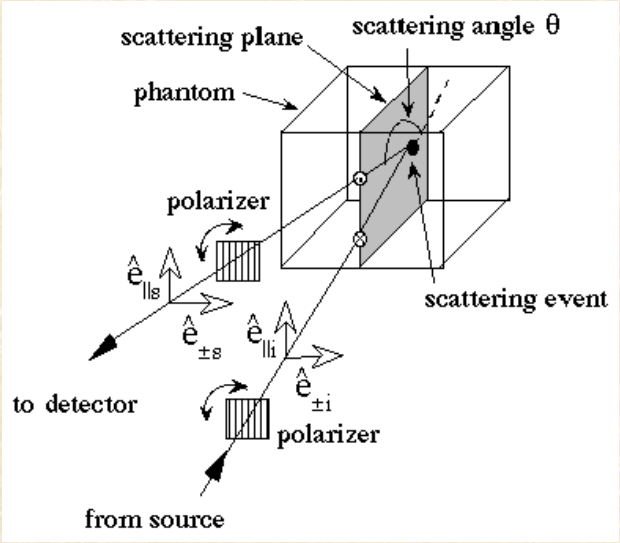
## MIE scattering

$$\{Q_s, p(\theta)\} = \text{Mie}\left(\frac{n_p}{n_{med}}, \frac{2\pi a}{\lambda / n_{med}}\right)$$

$$\sigma_s = Q_s \pi a^2$$

$$g = \frac{\int_0^{\pi} p(\theta)\cos\theta \cdot 2\pi \sin\theta d\theta}{\int_0^{\pi} p(\theta) \cdot 2\pi \sin\theta d\theta}$$

# The math of Mie scattering




# Scattering matrix

- Describes the relationship between incident and scattered electric field components perpendicular and parallel to the scattering plane as observed in the "far-field"

$$\begin{bmatrix} E_{lls} \\ E_{\perp s} \end{bmatrix} = \frac{\exp(-ik(\mathbf{r}-\mathbf{z}))}{ik\mathbf{r}} \begin{bmatrix} S_2 & S_3 \\ S_4 & S_1 \end{bmatrix} \begin{bmatrix} E_{lli} \\ E_{\perp i} \end{bmatrix}$$

- The total field ($E_{tot}$) depends on the incident field ($E_i$), the scattered field ($E_s$) , and the interaction of these fields ($E_{int}$). If one observes the scattering from a position which avoids Ei, then both $E_i$ and $E_{int}$ are zero and only $E_s$ is observed.

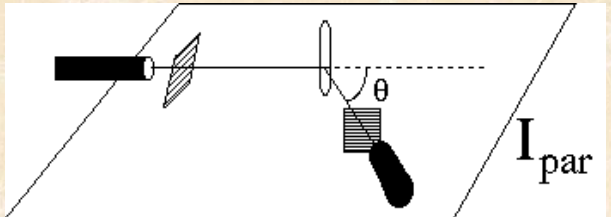
# Measured scattering matrix

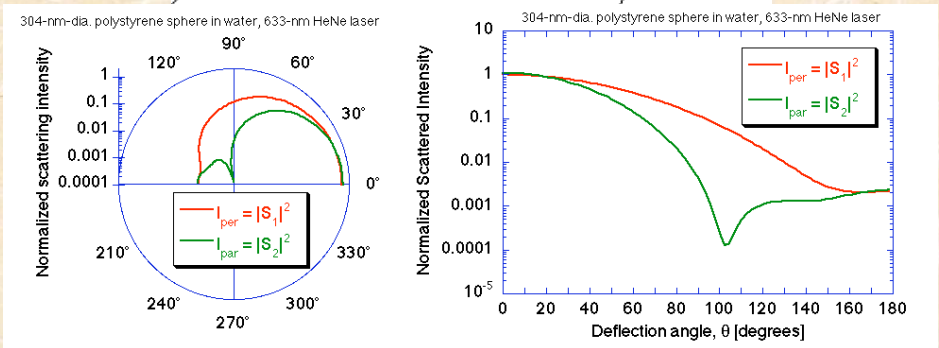
$$I = < EE^* > = (1/2)a^2, where\ E = a\exp(-i\delta)$$

$$\begin{bmatrix} I_{lls} \\ I_{\perp s} \end{bmatrix} = constant \begin{bmatrix} |S_2|^2 & 0 \\ 0 & |S_1|^2 \end{bmatrix} \begin{bmatrix} I_{lli} \\ I_{\perp i} \end{bmatrix}$$

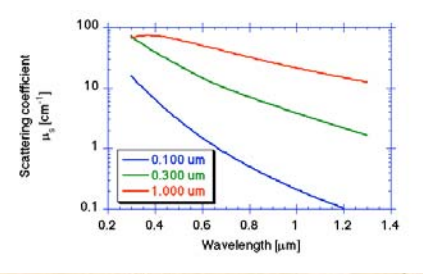
Stokes vector

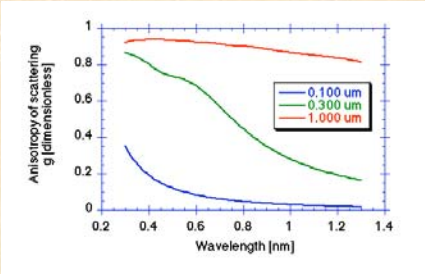
# Angular scattering pattern of polarized light

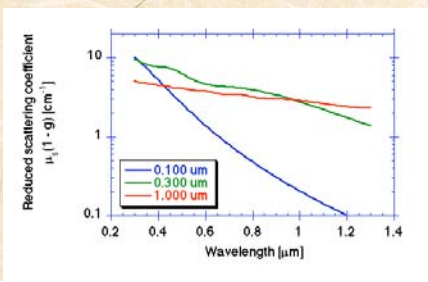


# Scattering vs wavelength




# Summary Mie

- Mie theory
  - direct solution to maxwell's equations with proper boundary conditions,
  - only a few, simple cases with analyticl solutions.
- Scattering from sphere may be calculated exactly from Mie theory
  - solved in spherical coordinates,
  - assumes plane wave incidence

# Mie scattering from cellular structures

- Soft tissue optics are dominated by the lipid content of the tissues.
- Mie theory provides a simple first approximation to the scattering of soft tissues
- The approximation involves a few assumptions:
  - Assume the refractive index of the lipid membranes of cells is 1.46, based on the reported
  - Assume the refractive index of the cytosol of cells is 1.35, based on the reported value for cellular cytoplasms
  - Assume the lipid content of soft tissue is about 1-10% (fv = 0.02-0.10).
  - Let's choose fv = 0.02 for this example to match the value for several typical soft tissues such as lungs, spleen, prostate, ovary, intestine, liver, arteries, to name a few.
  - Assume all the lipid is packaged as small spheres of various sizes whose number density maintains a constant volume fraction fv.
  - Ignore the interference of scattered fields from particles which can alter the apparent scattering properties based on isolated particles.

# Summary optical properties

- A survey of all tissue types has not been completed.
  - A survey would only be a guideline since subject to subject variation and normal vs diseased variation apparently are sufficiently significant to warrant ad hoc measurements on any particular tissue site of interest.Other tissues may present different types of scattering than just the simple "soft tissue" and "dermis" models.
- Muscles have myoglobin and actin-myosin fibers.
- Brain has myelin sheaths around nerves.
- Fatty tissues are distinct in their properties. The scattering by the nucleus has been ignored here, but is a potential scattering site of clinical importance.