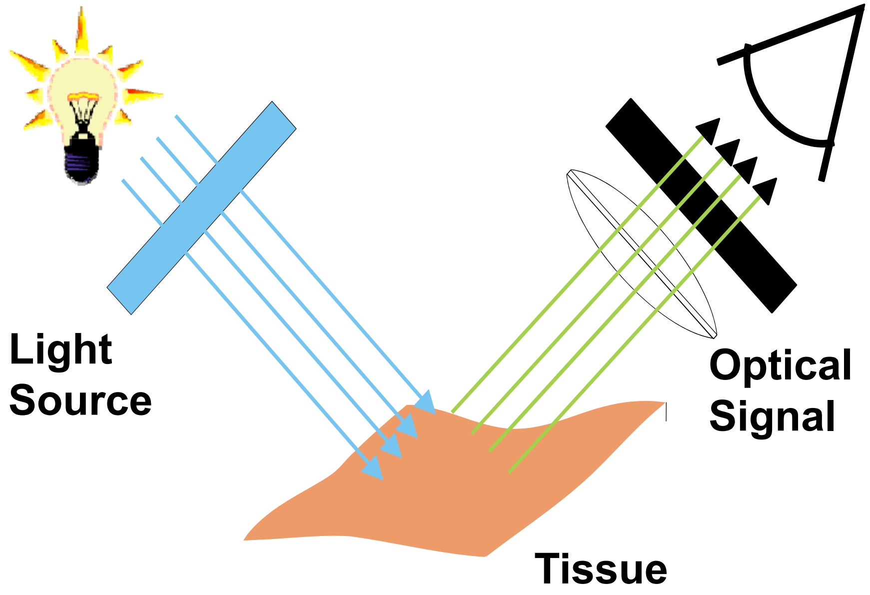
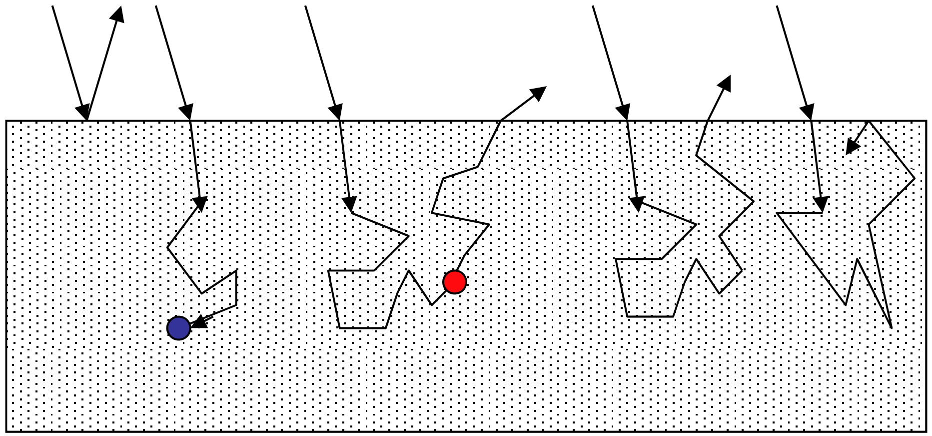
Tissue Optical Properties

Introduction

- **Interaction between Light and Tissue**
  - Reflection
  - Refraction
  - Absorption
  - Fluorescence
  - Scattering



- **Depends on**
  - Constituents of tissue
  - Optical properties of tissue
  - Propagation of light

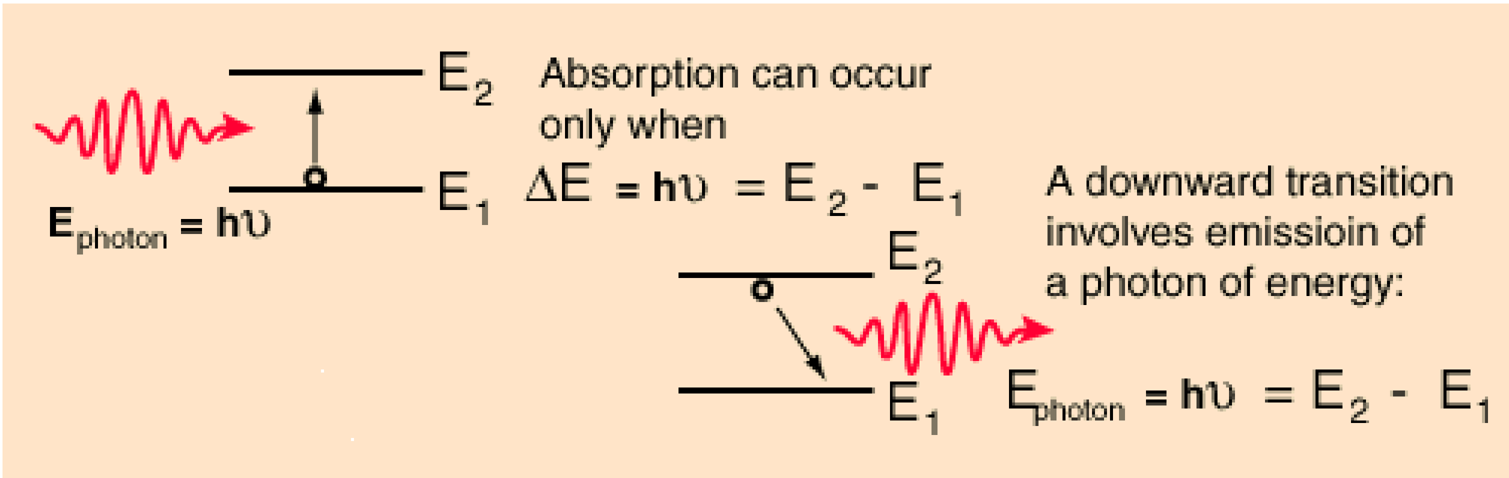


Absorption

- **Extraction of energy from light by a molecular species**
- **Diagnostic applications: Transitions between two energy levels of a molecule that are well defined at specific wavelengths could serve as spectral fingerprint of the molecule**
  - Various types of Chromophores (light absorbers) in Tissue
  - Wavelength-dependent absorption
  - Tumor detection and other physiological assessments (e.g. pulse-oximetry)
- **Therapeutic applications: Absorption of energy is the primary mechanism that allows light form a source (laser) to produce physical effects on tissue for treatment purpose**
  - Lasik (Laser Assisted in situ Keratomileusis) Eye Surgery, Tatoo Removal, PDT

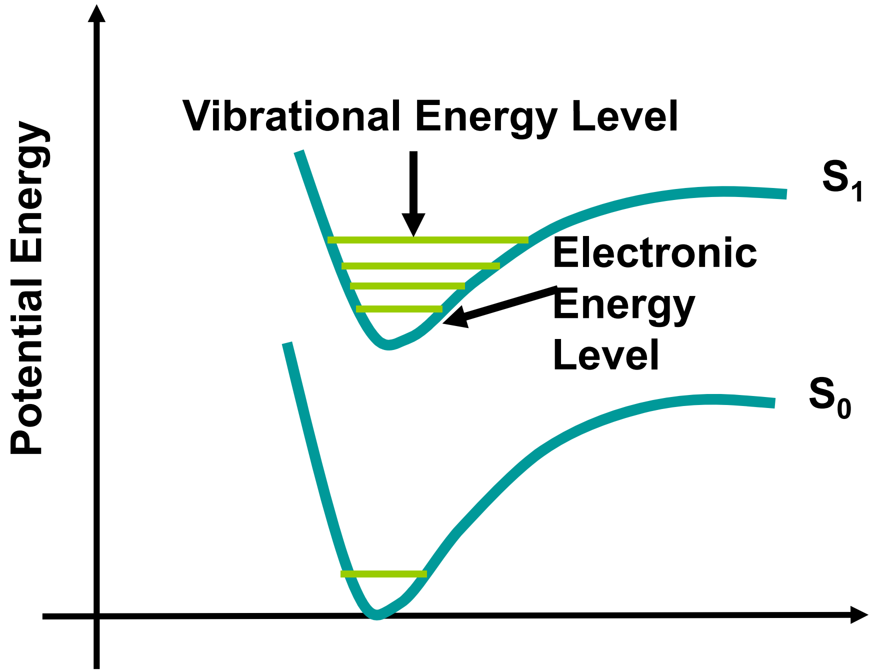
Absorption

- **Absorption occurs when the photon frequency matches the ‘frequency’ associated with the molecule’s energy transition**
  - Electrons absorb the energy of the light and transform it into vibrational motion
  - The absorption of a photon results in:
  - quantized change in charge separation
  - quantized excitation of vibrational modes
  - Electrons interact with neighboring atoms → convert vibrational energy into thermal energy



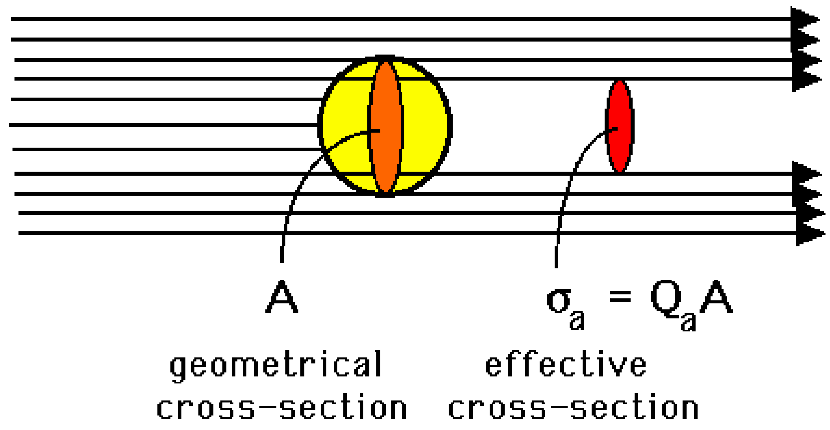
Absorption

- Each electronic energy levels is associated with many vibrational energy levels
- Absorption of UV and visible light promotes transition between electronic energy levels
- Absorption of infrared light promotes transitions between vibrational energy levels



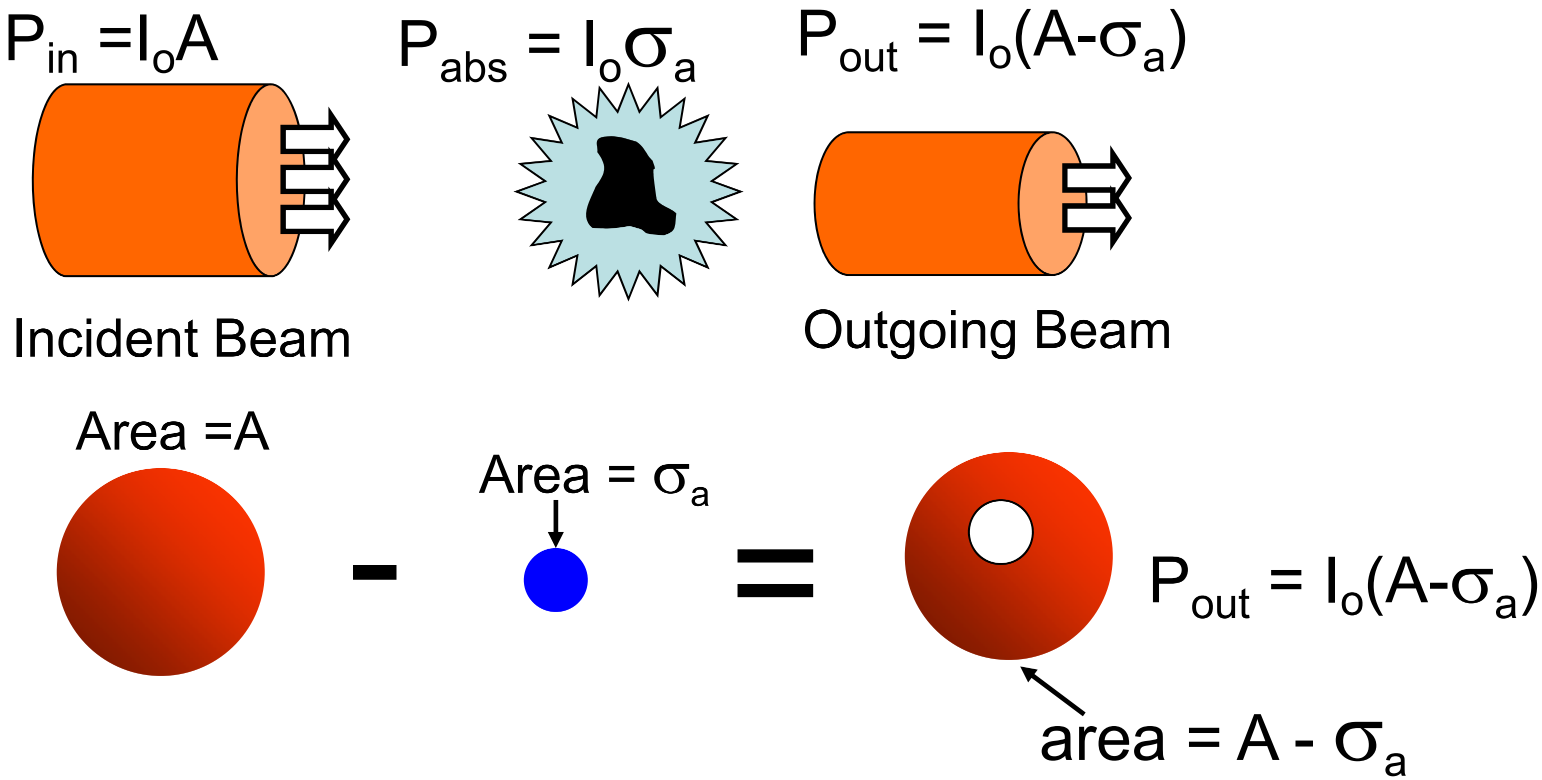
Absorption

- **Absorption Cross-section, σ [m^2]**
  - Consider a chromophore idealized as a sphere with a particular geometrical size.
  - Consider that this sphere blocks incident light and casts a shadow, which constitutes absorption.
  - The size of absorption shadow = absorption cross-section
  - Qa: absorption efficiency



$$\sigma_a = Q_a \cdot A$$

Absorption



$$\sigma_a = \frac{P_{abs}}{I_o}$$

Absorption

- **Assumptions**
  - Cross section is independent of relative orientation of the impinging light and absorber uniform distribution of N_a (molecules/cm^3) identical absorbing particles
- **Absorption Coefficient, ma [1/m]**

$$\mu_a = N_a \cdot \sigma_a$$

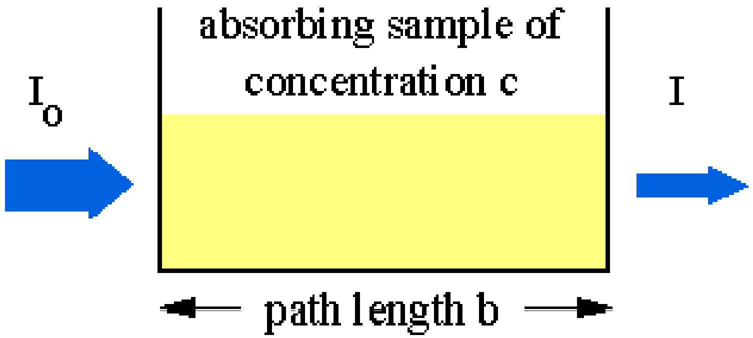
  - Absorption cross-sectional area per unit volume of medium
- **Absorption mean free path, la [m]**

$$l_a = \frac{1}{\mu_a}$$

  - Represents the average distance a photon travels before being absorbed

Absorption

- Transmission and Absorbance (macroscopic view)



- Transmission

$$T = \frac{I}{I_o}$$

- Absorbance (attenuation, or optical density)

$$A = -\log(T) = \log\left(\frac{I_o}{I}\right)$$

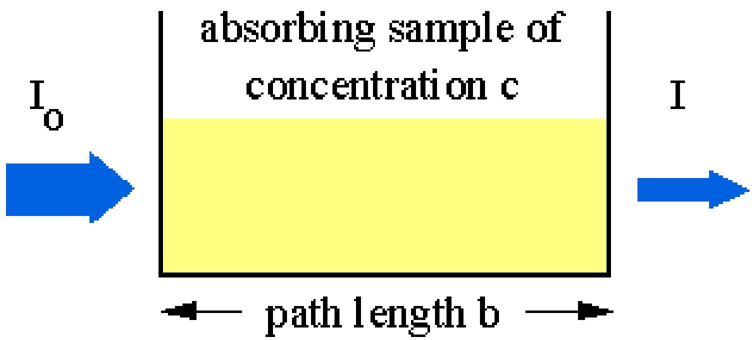
Absorption

- **Lambert – Beer Law:**
  - The linear relationship between absorbance and concentration of an absorbing species.
  - Relates μ_α, transmission, and absorbance

$$I = I_o e^{-\mu_a \cdot b}$$

$$\mu_a = N_a \cdot \sigma_a$$

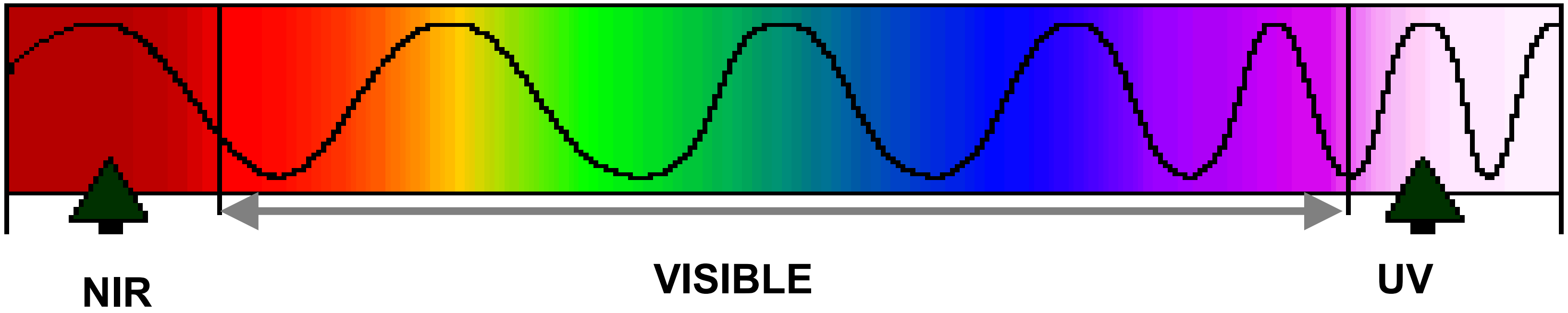
$$\sigma_a = \frac{P_{abs}}{I_O}$$



σ= absorption cross-sectional area [cm^2]
I_O = The intensity entering the sample at z = 0 [w/cm^2]
I = The intensity of light leaving the sample [w/cm^2]
b = pathlength traveled in the sample [cm]

Absorption

Absorbers in Tissue



- **NIR**
  - Hemoglobin
  - Lipids
  - Water

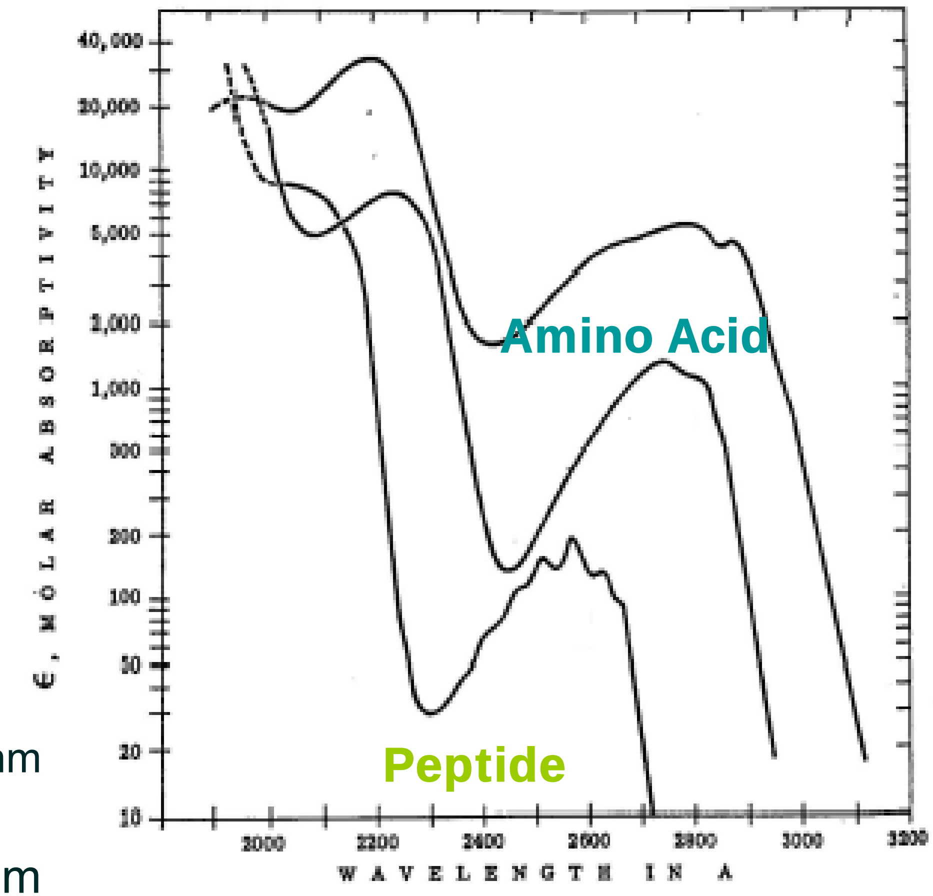
- **UV-VIS**
  - DNA
  - Hemoglobin
  - Lipids
  - Structural protein*
  - Electron carriers*
  - Amino acids*

* Absorbers that fluoresce when excited in the UV-VIS

Absorption

UV Absorption

- Protein, amino acid, fatty acid and DNA absorption dominate UV absorption
- Protein
  - Dominant 'non-water' constituent of all soft tissue, ~ 30%
  - Absorption properties determined by peptide bonds and amino acid residues
    - Peptide excitation about λ = 190 nm
    - Amino acids absorption at λ = 210 - 220 nm and 260 – 280 nm
- DNA
  - Absorbs radiation for λ ≤ 320 nm
- Large water absorption λ< 180 nm

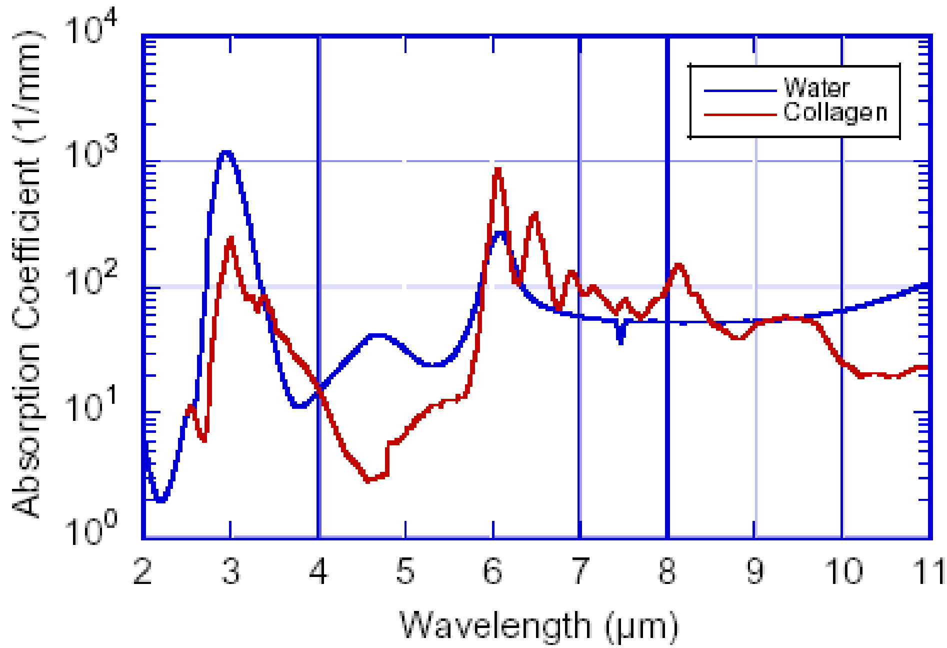


Absorption

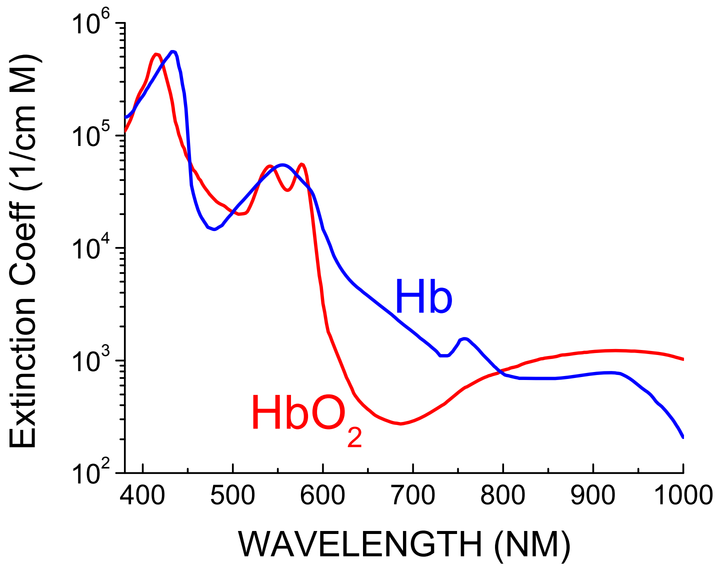
Infrared Absorption

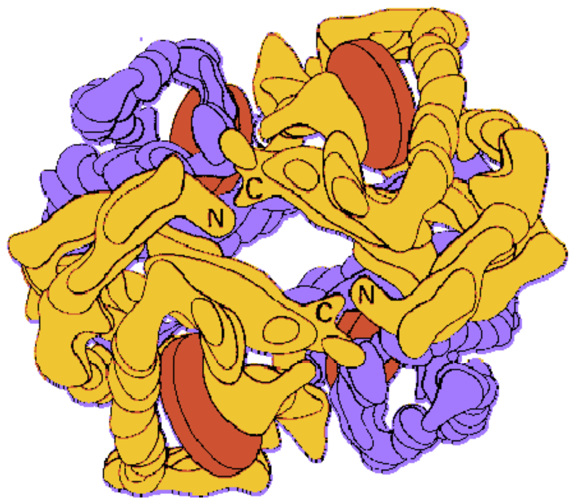
- Protein IR absorption peaks at 6.1, 6.45, and 8.3 μm due to amide excitation
- Absorption depth ≤ 10 μm in λ = 6-7 μm region

- **Water absorption peak at 0.96, 1.44, 1.95, 2.94 and 6.1 μm**
  - Absorption depth
    - ~ 500 mm at λ = 800 nm
    - <1 μm at λ=2.94 μm
    - ≤ 20 μm throughout λ ≥ 6 μm



Absorption





Main Absorbers at visible and NIR

- Hemoglobin
- Lipid

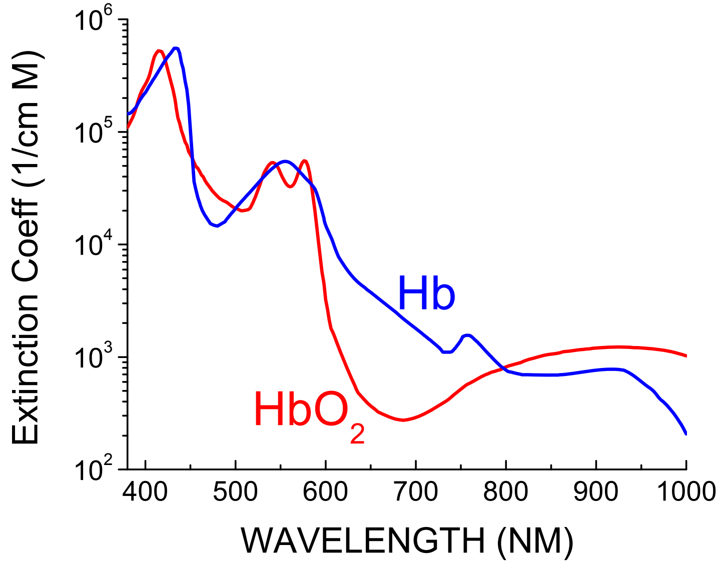
Hemoglobin

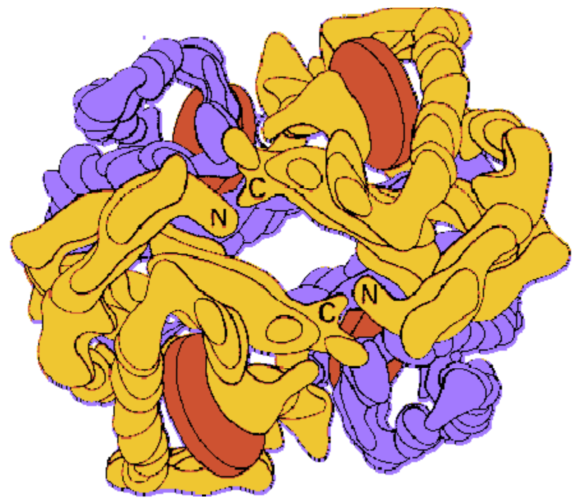
- Each hemoglobin has 4 heme (Fe^{2+}) sites to bind O_2
- Responsible for oxygen transport
- HbO_2 and Hb
- oxygen saturation is an indicator of oxygen delivery and utilization as well as metabolic activity

Absorption

Hemoglobin

- **Responsible for oxygen transport**
  - HbO2 and Hb
  - oxygen saturation is an indicator of oxygen delivery and utilization as well as metabolic activity
- **Deoxyhemoglobin has lower absorption than oxyhemoglobin in the blue and green**
  - Bright red arterial blood
  - Bluish venous blood
- **Absorption peaks for HbO_2**
  - 418, 542, 577, and 925 nm
- **Absorption peaks for Hb**
  - 550, 758, 910 nm
- **Isosbestic points**
  - 547, 569, 586, and 798 nm

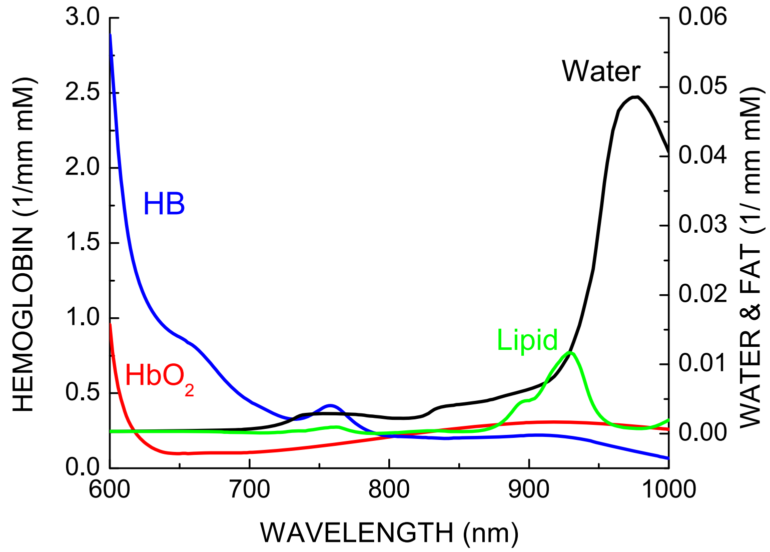




Absorption

Lipid (Fat)

- Important energy store in the body
- Site-specific measurements of body composition
- Monitoring of physiological changes in female breast tissue
- Tissue layer model

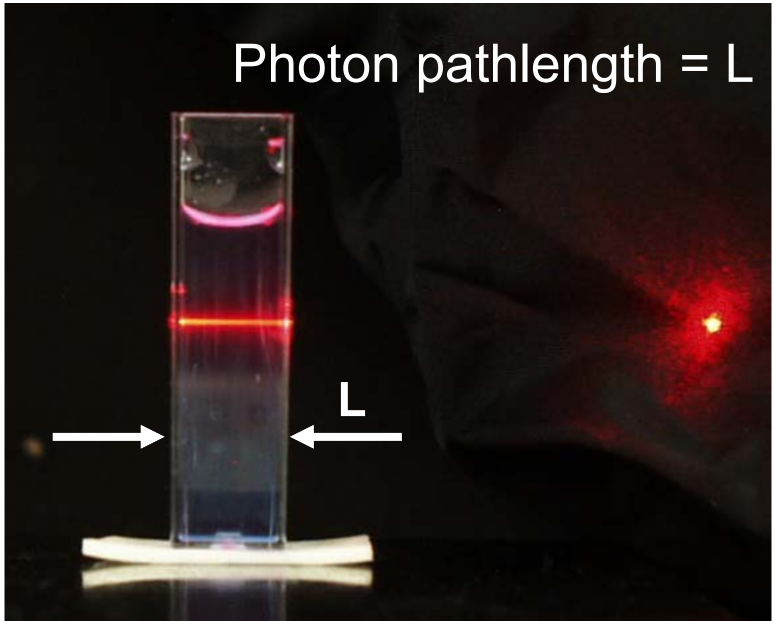


Scattering

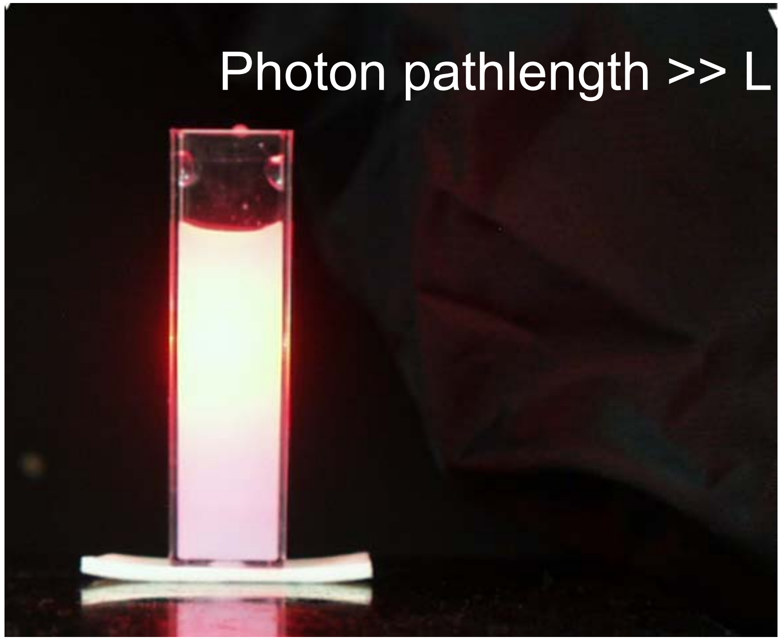
- Change of direction of propagation and/or energy of light by a molecular species
- Diagnostic applications: Scattering depends on the size, morphology, and structure of the components in tissues (e.g. lipid membrane, collagen fibers, nuclei).
  - Variations in these components due to disease would affect scattering properties, thus providing a means for diagnostic purpose
- Therapeutic applications: Scattering signals can be used to determine optimal light dosimetry and provide useful feedback during therapy

Scattering

Purely absorbing



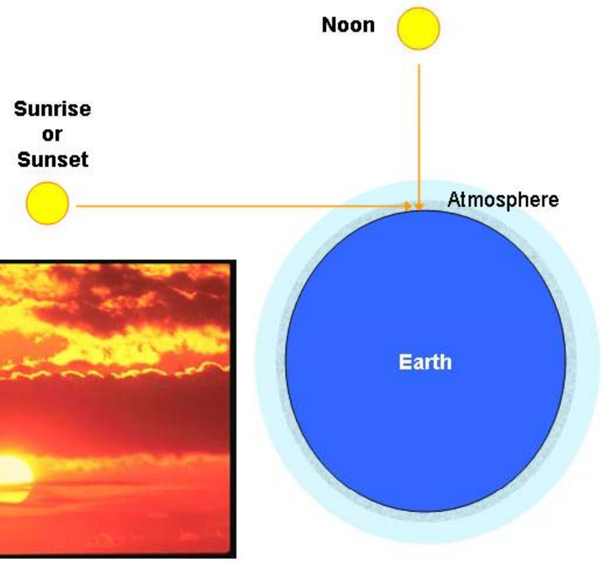
With Scattering



Lambert- Beer Law does not apply here!!!
Need to calculate true pathlength of light

Scattering

- **Why is the sky blue, clouds white, and sunsets red?**
  - Blue skies are produced due to scattering at shorter wavelengths
    - Visible light (violet & blue) are selectively scattered by O2 and N2 – much smaller than wavelengths of the light
    - violet and blue light has been scattered over and over again
  - When light encounters larger particles (cloud, fog), Mie scattering occurs
    - Mie scattering is not wavelength dependent – appears white
    - Cigarette smoke, too
  - At sunset
    - The light must travel over a longer path in the atmosphere
    - Blue/green is scattered away and only red/orange (scattered less) reaches your eyes



Scattering

- **Mechanism for Light Scattering**
  - Light scattering arises from the presence of heterogeneities within a bulk medium
    - Physical inclusions
    - Fluctuations in dielectric constant from random thermal motion
  - Heterogeneity/fluctuations → non-uniform temporal/spatial distribution of refractive index in the medium
    - Passage of an incident EM wave sets electric charges into oscillatory motion and can excite vibrational modes
    - Scattered light is re-radiated by acceleration of these charges and/or relaxation of vibrational transition

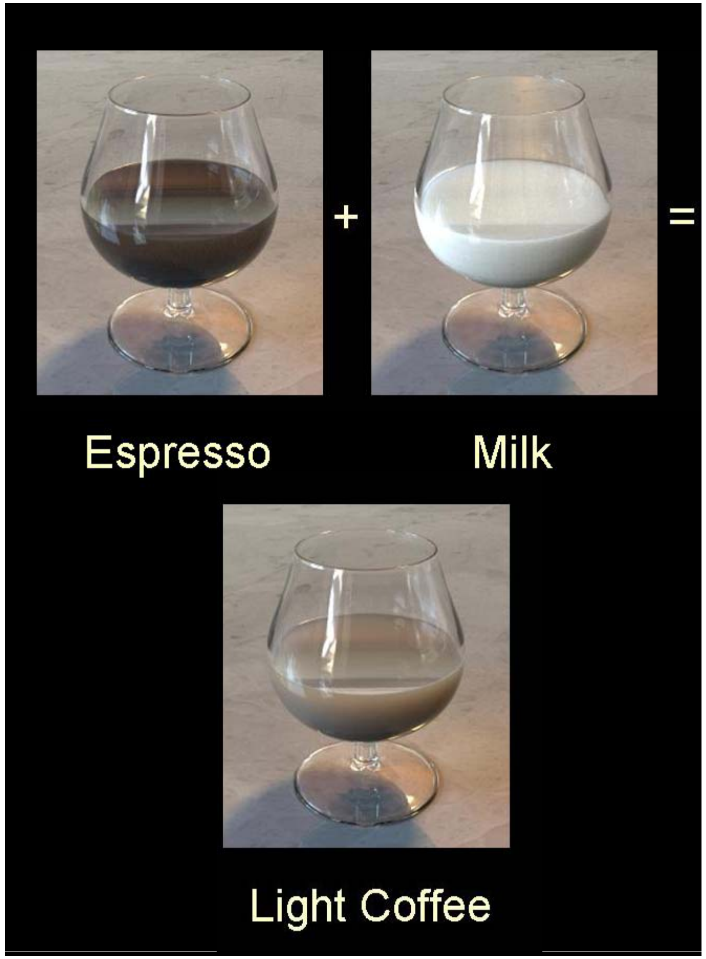
Scattering

- **Elastic scattering: no energy change**
  - Frequency of the scattered wave = frequency of incident wave
  - Probes static structure of material
  - Rayleigh and Mie scattering
- **Inelastic scattering: energy change**
  - Frequency of the scattered wave ≠ frequency of incident wave
  - Internal energy levels of atoms and molecules are excited
  - Probes vibrational bonds of the molecule
  - Raman scattering (stokes↓ and anti-stokes ↑)

Scattering

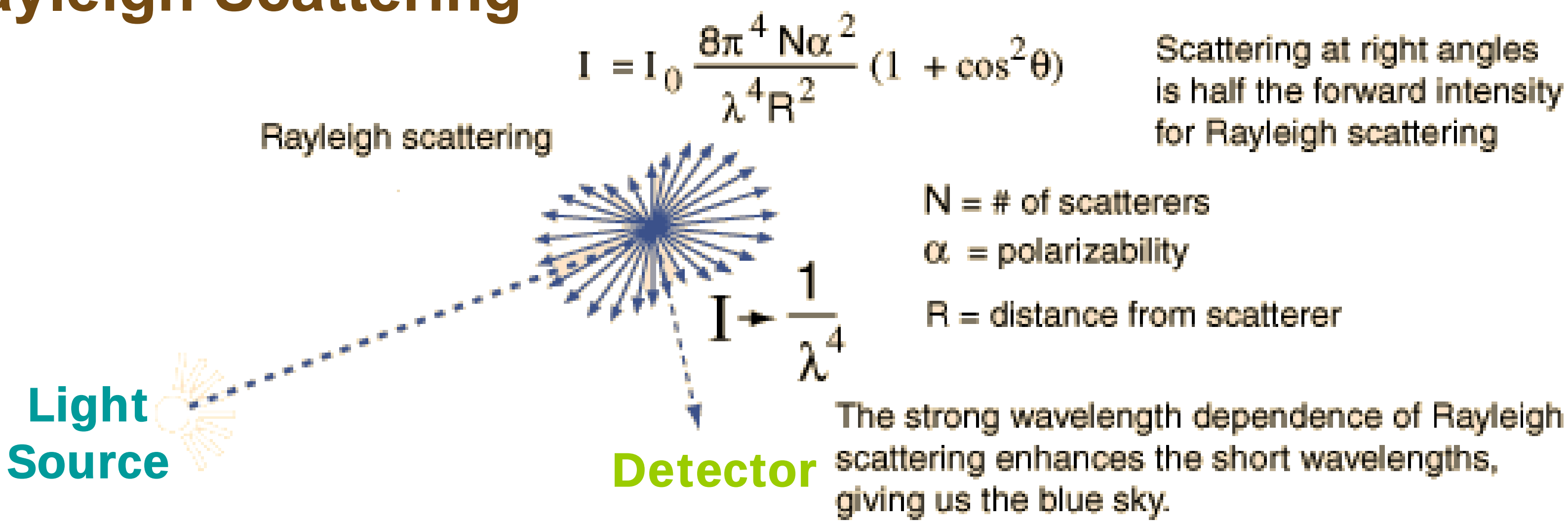
Elastic Scattering

- **The light scattered by a system has interacted with the inhomogeneities of the system**
- **Photons are mostly scattered by the structure whose size matches the wavelength**
- **Principal parameters that affect scattering**
  - Wavelength, λ
  - Relative refractive index
  - Particle radius
  - Shape and orientation
- **Two types of scattering: Rayleigh and Mie**



Scattering

Rayleigh Scattering



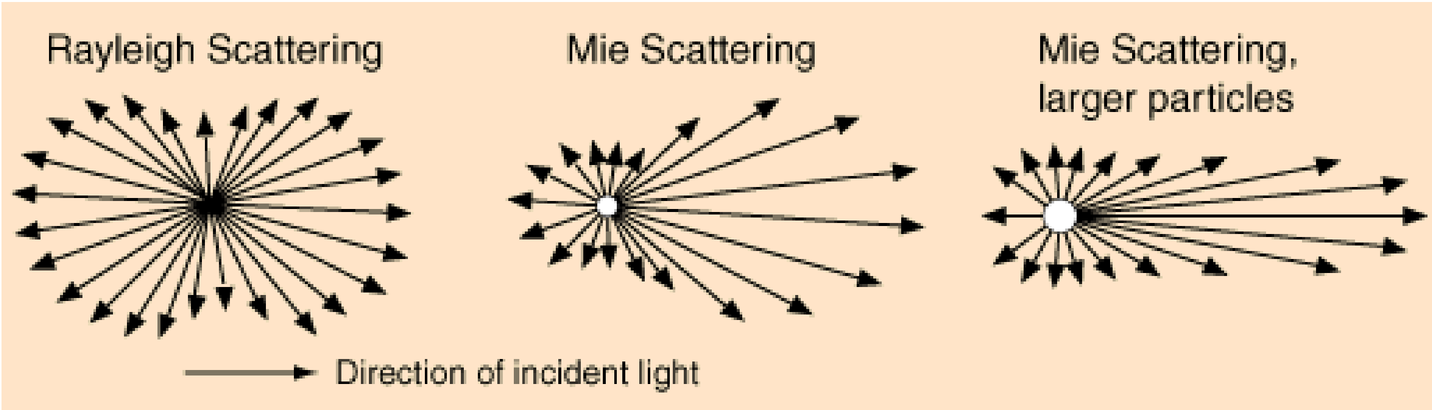
- Scattering from very small particles → ≤ λ/10
- Rayleigh scattering is inversely related to fourth power of the wavelength of the incident light

$$I \propto \frac{1}{\lambda^4}$$

λ is the wavelength of the incident light
I is the intensity of the scattered light

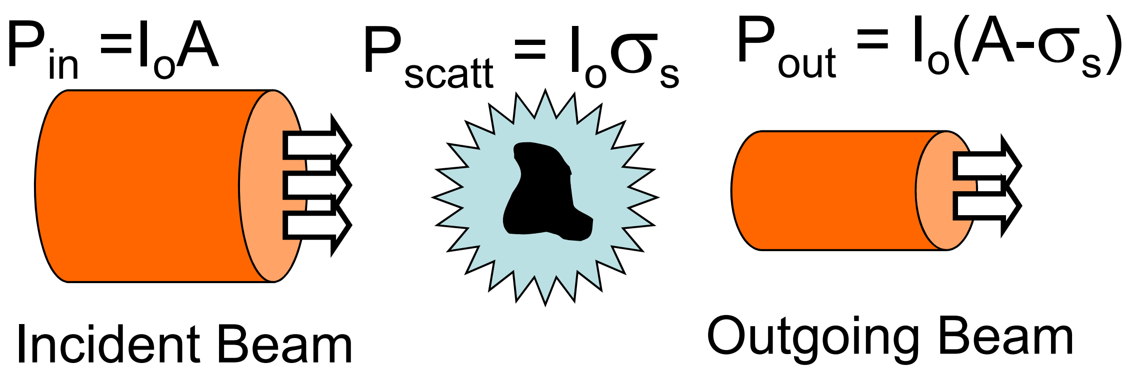
Scattering

Mie Scattering



- For scattering of particles comparable or larger than the wavelength, Mie scattering predominates
- Because of the relative particle size, Mie scattering is not strongly wavelength dependent
- Forward directional scattering

Scattering



- **Scattering Cross Section, σ_{scatt} [m^2]**
  - ‘area’ of an index-matched, perfectly absorbing disc necessary to produce
- **The measured reduction of light**

$$\sigma_{scatt} = Q_s * A_s$$

  - Q_s: Scattering efficiency (calculated by Mie theory); defined as the ratio of the scattering section to the projected area of the particle on the detector
  - A_s: Area of Scatterer [m2]

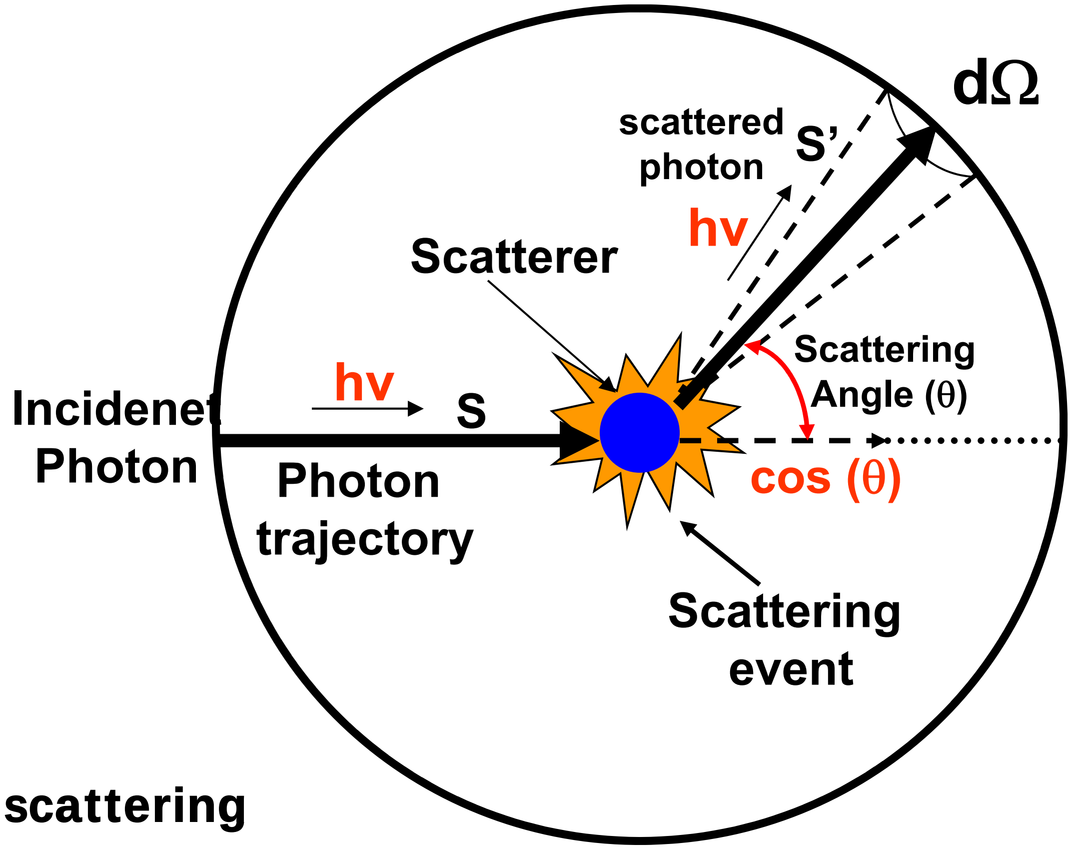
Scattering

- **Scattering Coefficient, μ_s [1/m]**
  - $\mu_s = N_s \sigma_s$,
    - N_s = the number density of scatterers
    - σ_s = scattering efficiency
  - Cross-sectional area for scattering per unit volume of medium
- **Scattering Mean Free Path, l_s**
  - Average distance a photon travels between scattering events

$$l_s = \frac{1}{\mu_s}$$

Scattering

- **Anisotropy, g**
  - Imagine that a photon is scattered by a particle so that its trajectory is deflected by an angle, θ
  - Then, component of a new trajectory aligned forward direction is cos(θ)
  - Anisotropy is a measure of forward direction retained after a single scattering event, < cos(θ)>



$$g = \begin{cases} -1 & \textbf{totally backward scattering} \\ 0 & \textbf{isotropic scattering} \\ 1 & \textbf{totally forward scattering} \end{cases}$$

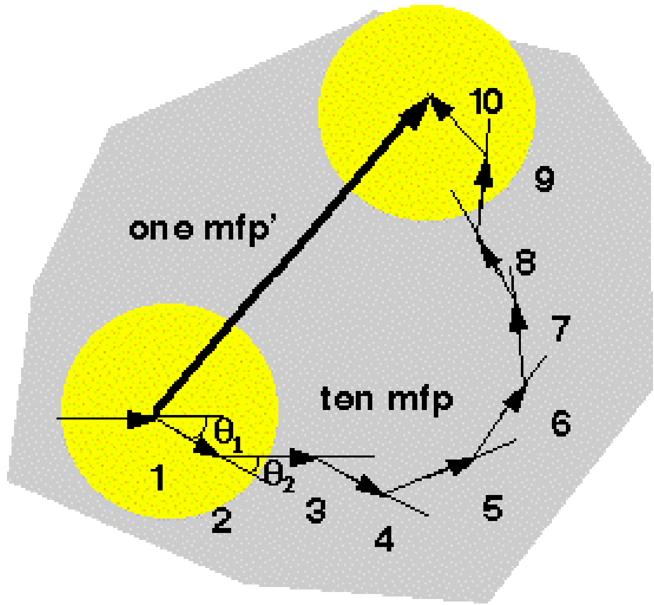
Biological Tissues:
0.65 < g <0.95

Scattering

- **Reduced Scattering Coefficient, μs' [1/m]**
  - μs' incorporates the scattering coefficient, μs and the anisotropy factor, g

    $$\mu_s' = (1 - g)\mu_s$$

  - μs' can be regarded as an **effective isotropic scattering** coefficient that represent the cumulative effect of several forward-scattering events
  - Special significant with respect to photon diffusion theory



$$\langle \theta \rangle \approx 26^o$$

$$g = \langle \cos\theta \rangle = 0.90$$

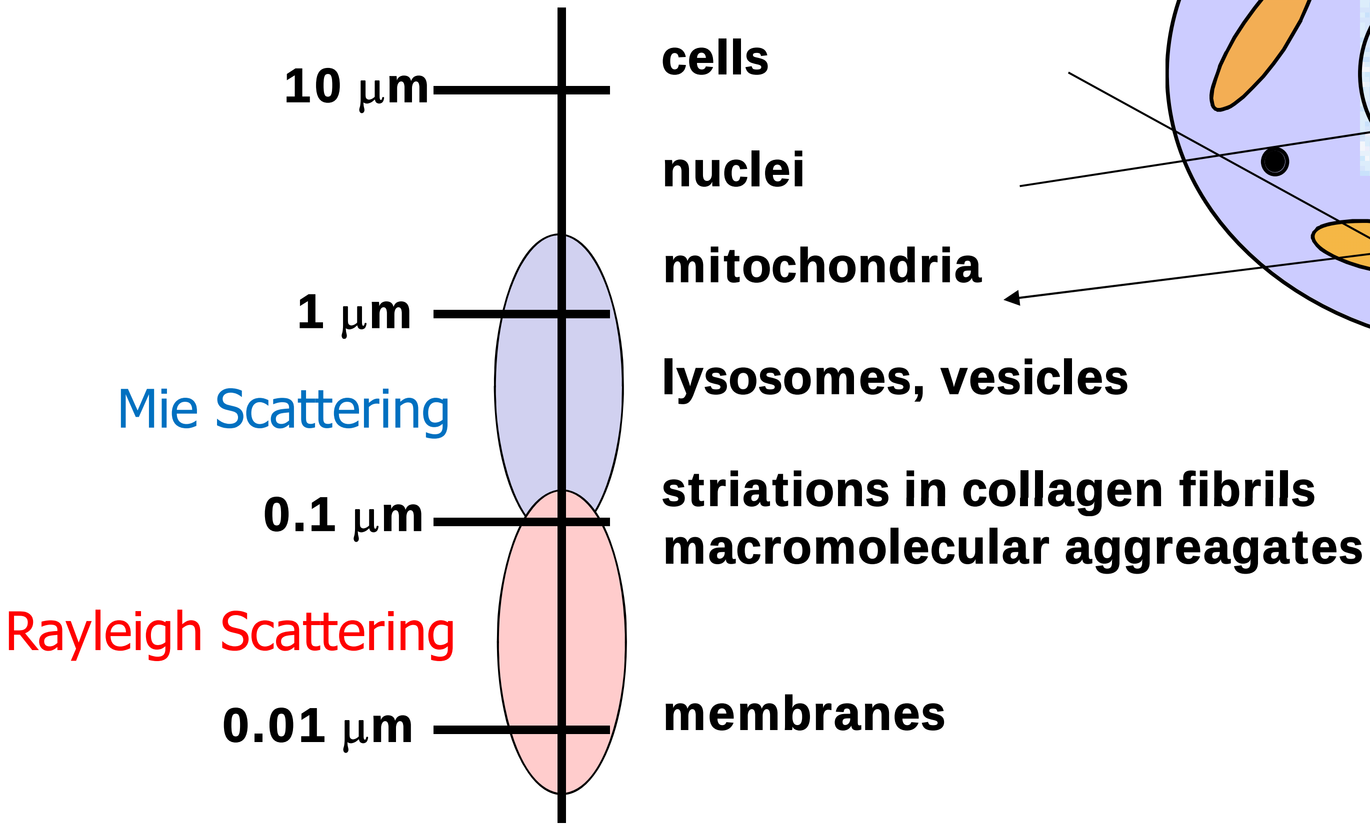
$$\mu_s' = (1 - g)\mu_s = 0.10\mu_s$$

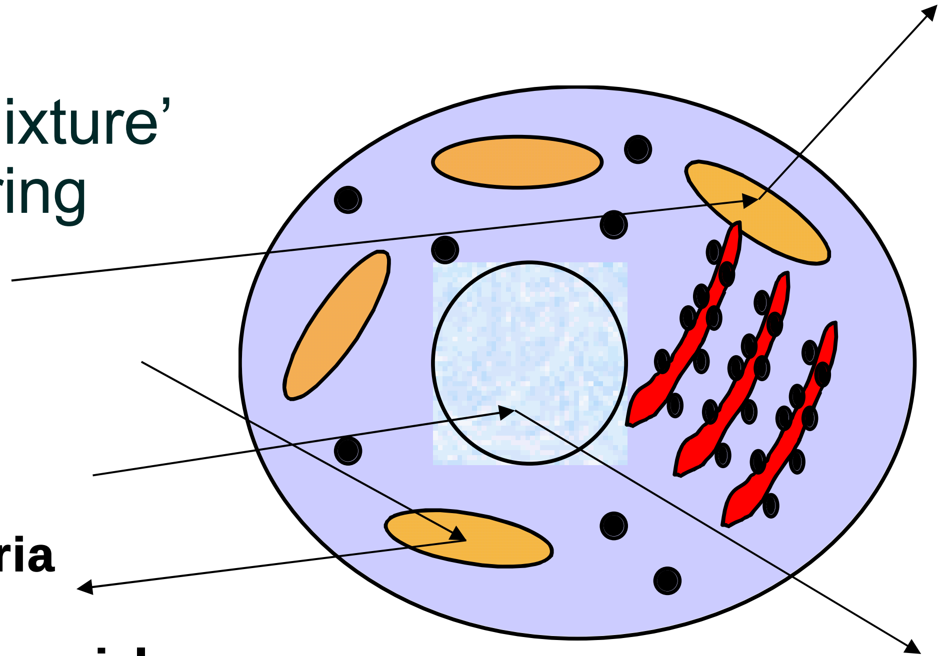
$$mpf = 1/\mu_s$$

$$mpf' = 1/\mu_s' = 10mpf = 10/\mu_s$$

Scattering

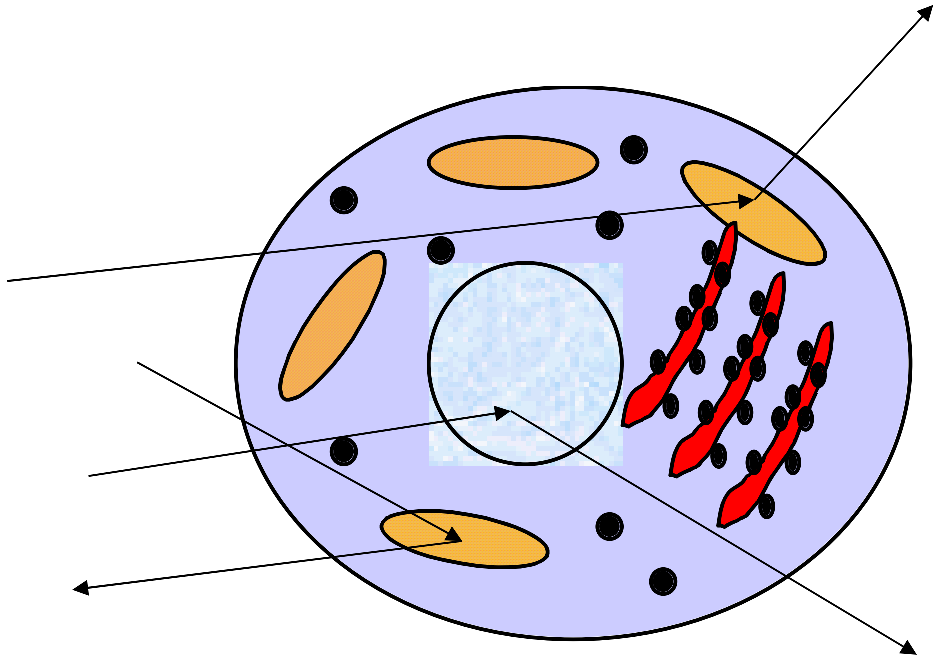
- **Scattering in Tissue**
  - Tissue is composed of a 'mixture' of Rayleigh and Mie scattering





Scattering

- **Scattering in Tissue**
  - Refractive index mismatch between lipid and surrounding aqueous medium
    - Soft tissues are dominated by lipid contents
    - Celluar membranes, membrane folds, and membraneous structure
  - Mitochondria, ~ 1μm
    - Intracelluar organelle composed of many folded membrane, cristae
  - Collegan fibers, 2 ~ 3μm
    - Collegan fibrils, 0.3 μm
    - Periodic fluctuation in collegan ultrastructure →source of Rayleigh scattering in UV and Visible range
  - Cells

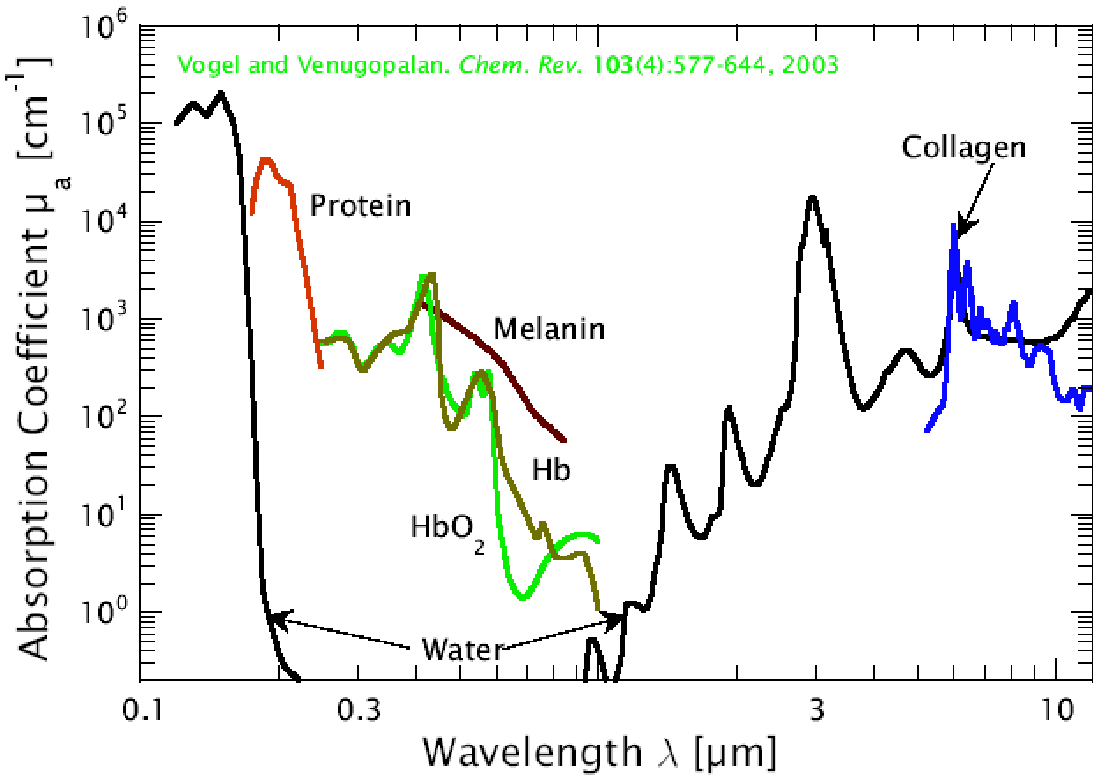


Light Transport in Tissue

- **Scattering and absorption occur simultaneously and are wavelength dependent**

$$\mu_t = \mu_s^{'} + \mu_a$$

- **Scattering monotonically decreases with wavelength**
- **Absorption is large in UV, near visible, and IR**
- **Absorption is low in red and NIR → Therapeutic window (600 ≤λ≤ 1000 nm)**

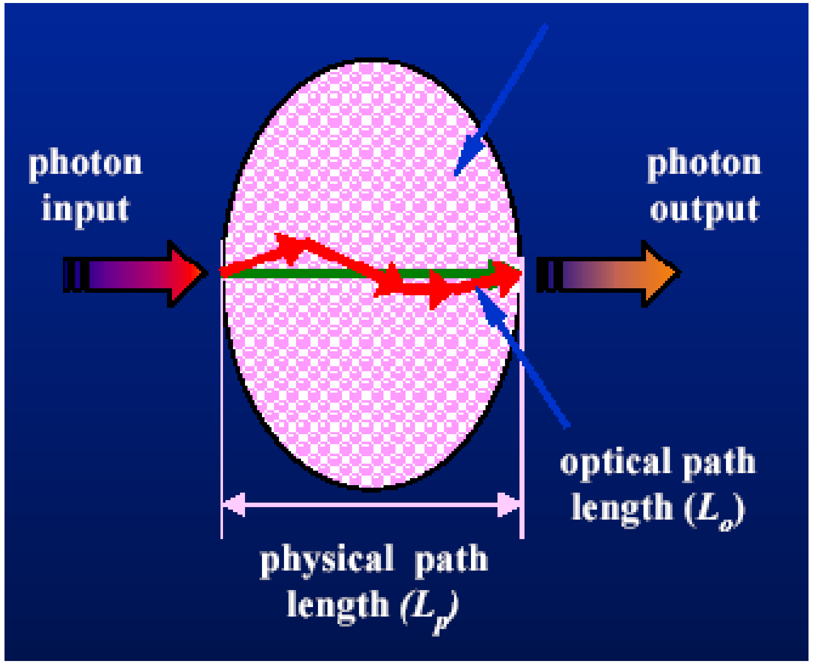


$$\mu_s' = A \cdot \lambda^{-b}$$

$$\mu_s' \sim \lambda^{-0.5} - \lambda^{-4}$$

Light Transport in Tissue

- **Modeling of light transport in tissues are often governed by the relative magnitudes of optical absorption and scattering**
  - μa >> μs' : Lambert-Beer Law (λ ≤300nm;λ≥2000nm)
  - μs' >> μa : Diffusion Approximation (600nm ~ 1000nm)
  - μs' ~ μa : Equation of Radiative Transfer, Monte Carlo (300nm ~ 600 nm; 1000nm ~ 2000nm)
- **Use Monte Carlo, Transport Theory, or Diffusion Theory**

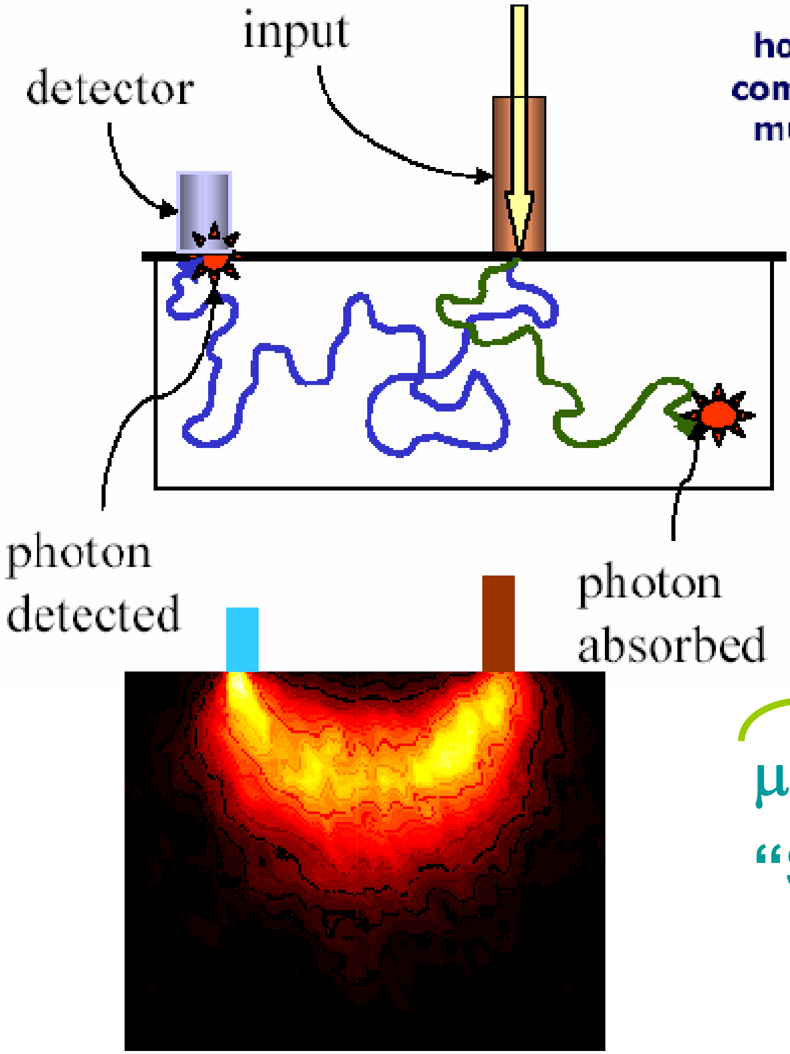


Physical Pathlength: L_p
Optical Pathlength: L_o

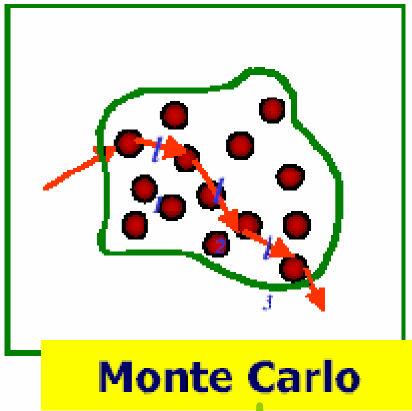
Biological Tissue
L_o/L_p = 4 or ↑

Light Transport in Tissue

- **Modeling Photon Propagation**



Random Walk depiction of photon propagation in a homogeneous medium. This comprises of combinations of multiple-scatter, absorption and detection.



μ_a, μ_s, g, phase function S

"Stochastic" Description

Light Transport in Tissue

• Radiative Transport Theory

- The direct application of EM theory is complicated
- RTT deals with the transport of light energy
- RTT ignores wave phenomena (polarization, interference) of EMT

Steady State Radiative Transport Equation

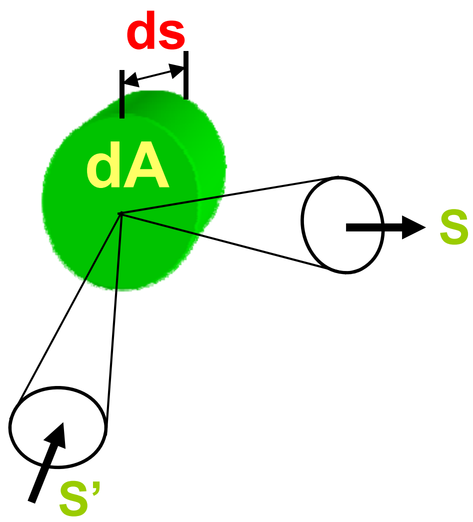
$$\frac{\partial L(\vec{r},\hat{\Omega})}{\partial s} = -(\mu_a + \mu_s)L(\vec{r},\hat{s}) + \mu_s \int_{4\pi} p(\hat{s},\hat{s}')L(\vec{r},\hat{s})d\hat{s}' + S(\vec{r},\hat{s})$$

Loss due to scatt and abs

Overall Energy balance at position r and direction s

gain due to scattering from s’ to s at r

Source term



L = radiance [W/m² sr], propagation of photon power
P(s, s’) = phase (scattering) function
s, s’ = directional vectors of photon propagation

Light Transport in Tissue

- **Diffusion Approximation**
  - Simplified form of RTT at “diffusion limit”
  - μs’ >> μa
    - the number of photon undergoing the random walk is large

$$\partial j(\vec{r},t)/\partial t << c(\mu_a + \mu_s') = c\mu_t'$$

$$L(\vec{r},\hat{s},t) \approx \frac{1}{4\pi}\phi(\vec{r},t) + \frac{3}{4\pi}\vec{j}(\vec{r},t)\cdot\hat{s}$$

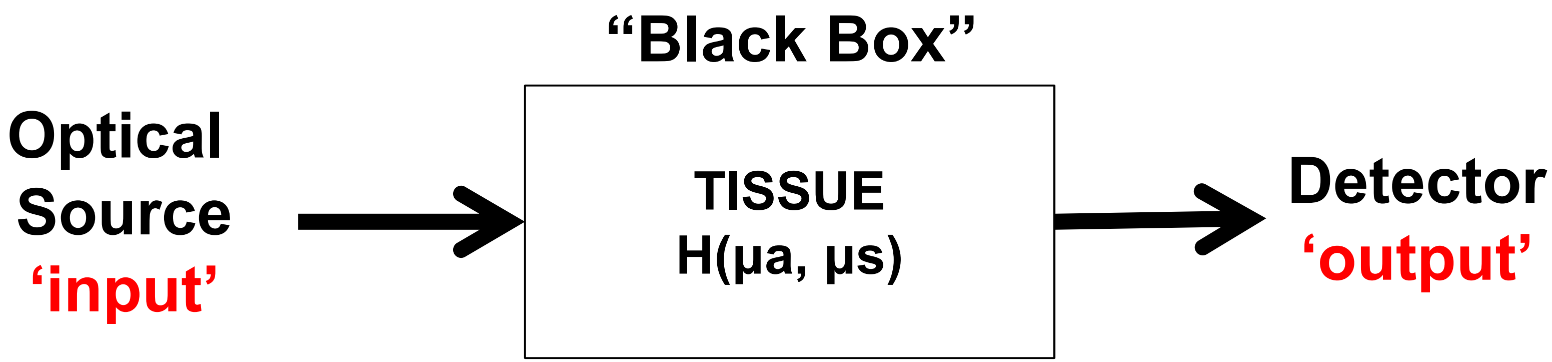
  - Isotropic source beyond 1/μt’
    - ~10/μt’ (~ 1mm in biological tissue)
    - far from sources & boundaries
    - assume tissue is “macroscopically homogeneous”

$$\frac{1}{c}\frac{\partial\phi(\vec{r},t)}{\partial t} - \nabla\cdot D(\vec{r})\nabla\phi(\vec{r}) - \mu_a\phi(\vec{r},t) = S(\vec{r},t)$$

$$\text{where } D(\vec{r}) = 1/3\left[\mu_a(\vec{r}) + \mu_s(\vec{r})\right]$$

Tissue Optical Properties

- **Measurement Strategies**



H: System Function

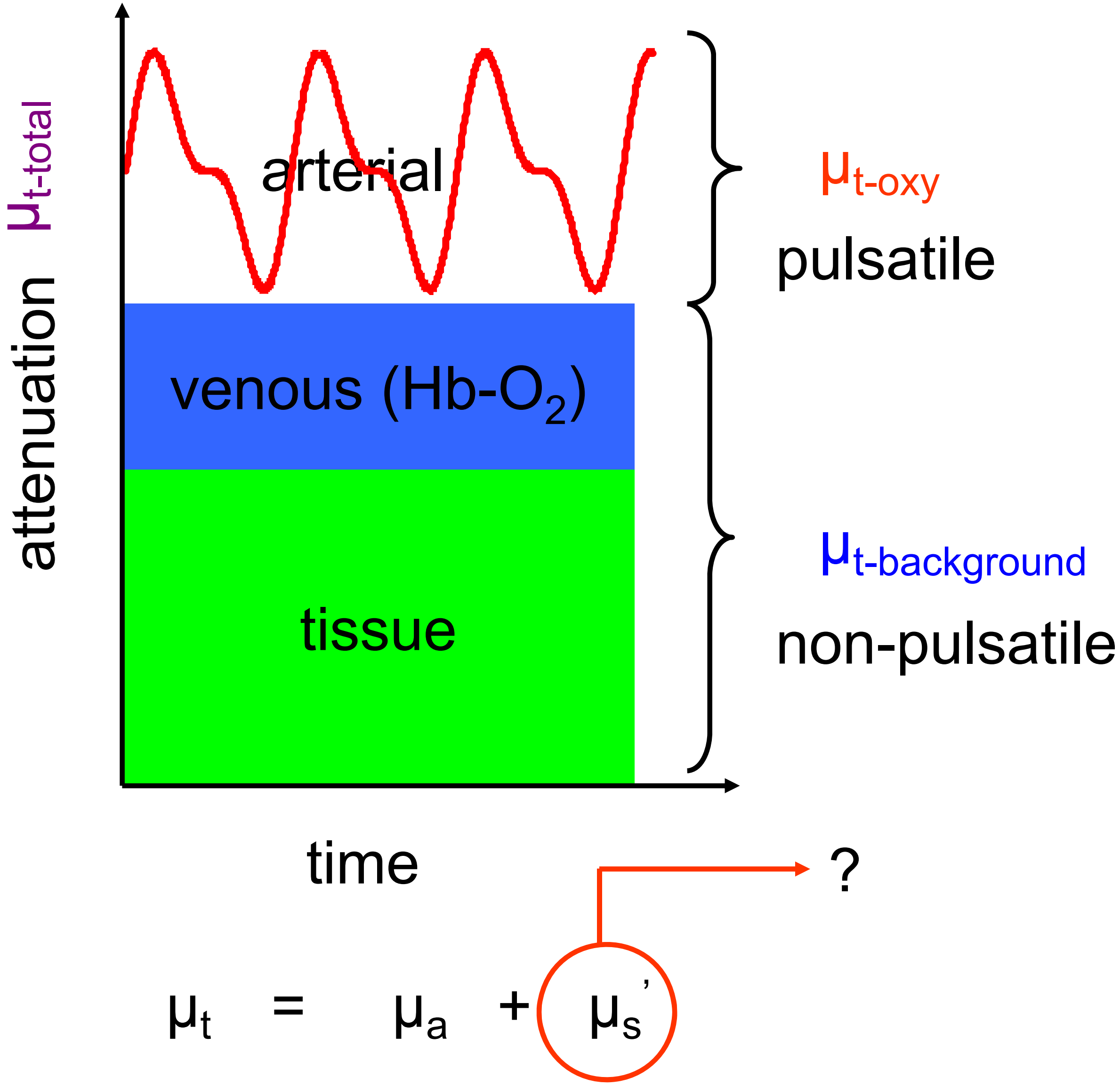
- Goal: To find out H(μa, μs)
- Requires Non-Static system → Perturbations in either optical source or tissue

Tissue Optical Properties

Measurement Schemes

- **CW (Continuous Wave) Measurement**
  - Simplest form of measurement
  - Static, continuous wave input
  - requires dynamic tissue property changes
  - E.g. pulse oximetery
- **Time-Resolved Measurements**
  - Temporal changes in optical sources
  - Time Domain Photon Migration (TDPM)
  - Frequency Domain Photon Migration (FDPM)
- **Spatially-Resolved Measurement**
  - Spatial changes in optical path

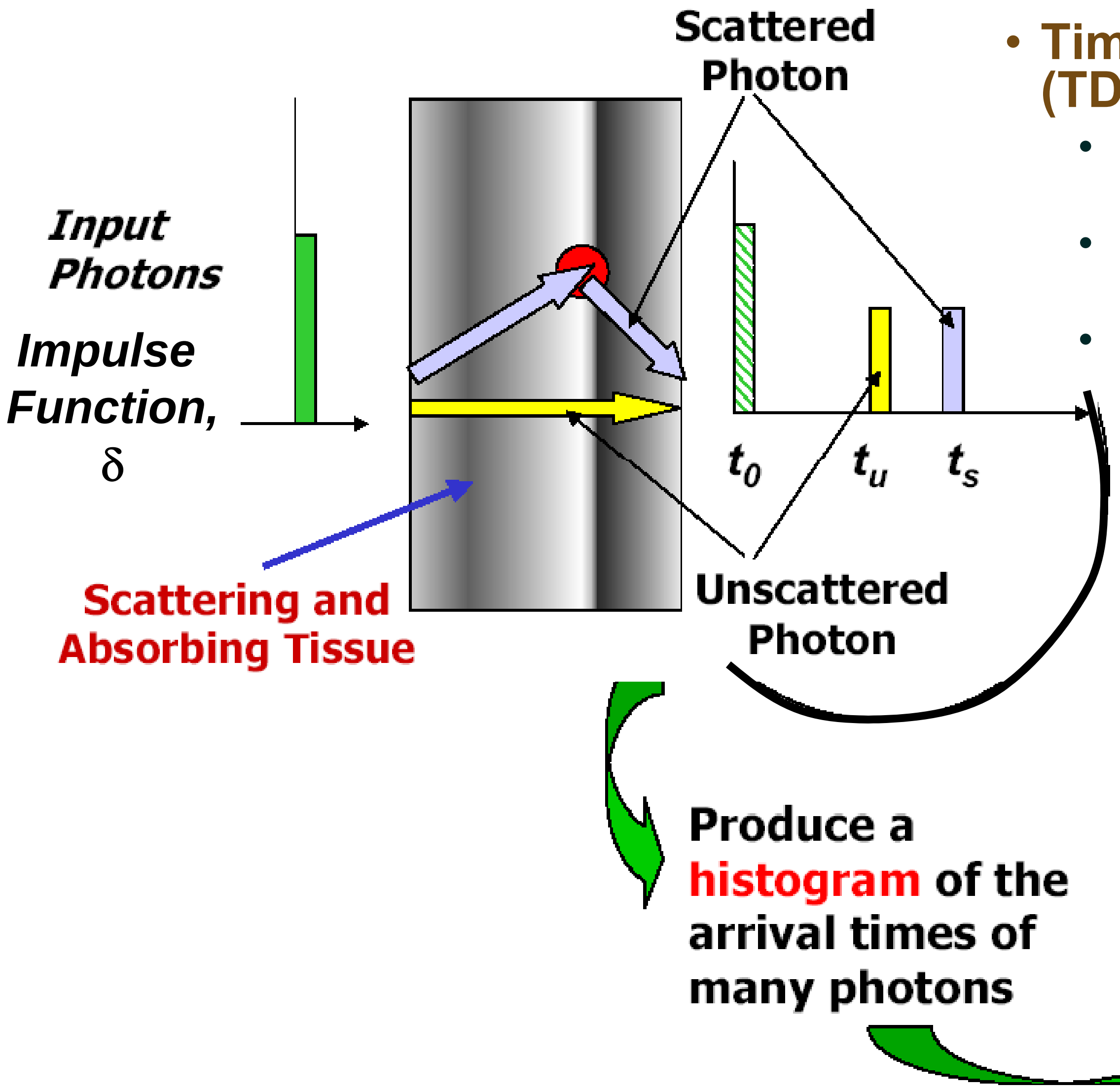
Tissue Optical Properties

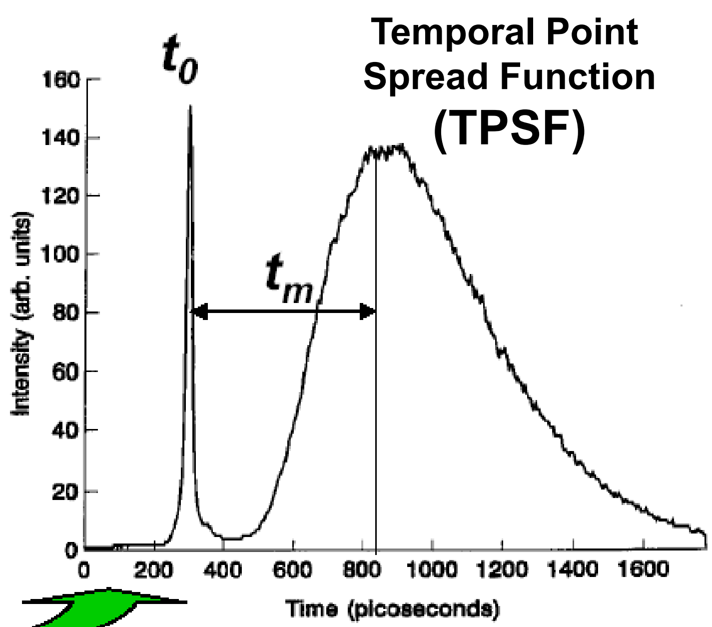


- **CW (continuous wave)**
  - pulse oximetry locks into pulse
  - healthy adult calibration accounts for tissue scatter (ms')
  - typically at 2 wavelengths (660, 940 nm)

Tissue Optical Properties

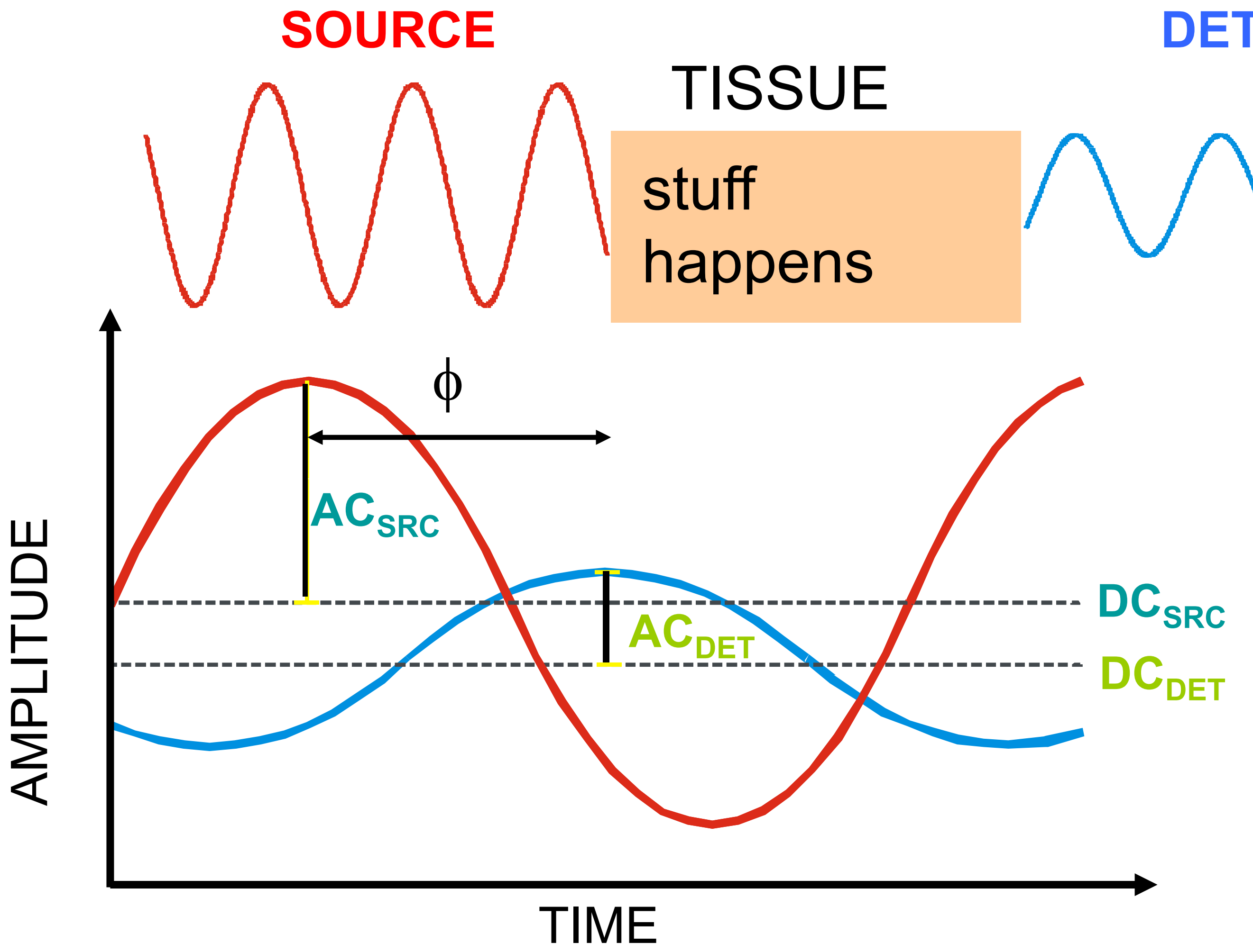
- **Time Domain Photon Migration (TDPM)**
  - Directly measure ma and ms from TPSF using Diffusion Equation
  - Complicated and expensive detection system
  - rather low SNR





Tissue Optical Properties

- **Frequency Domain Photon Migration (FDPM)**



ϕ ~ TIME

M = AC/DC