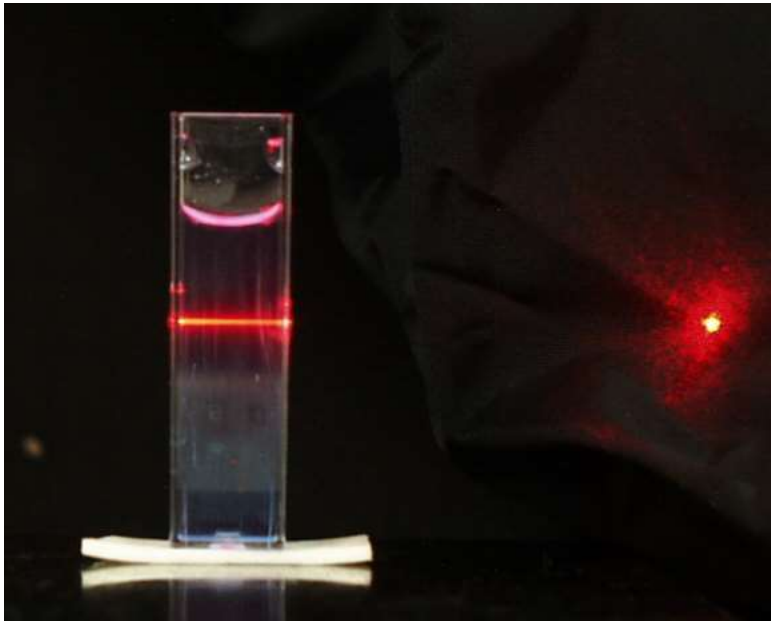
Turbid tissue optics I: Introduction

Andrew Berger

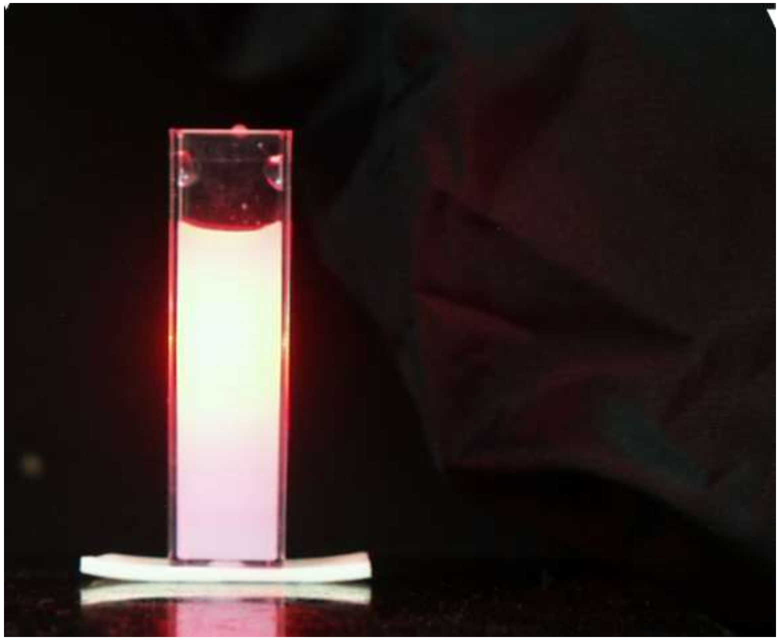
Abbe lecture #2

07.01.2014

Propagation of light in scattering vs. nonscattering media



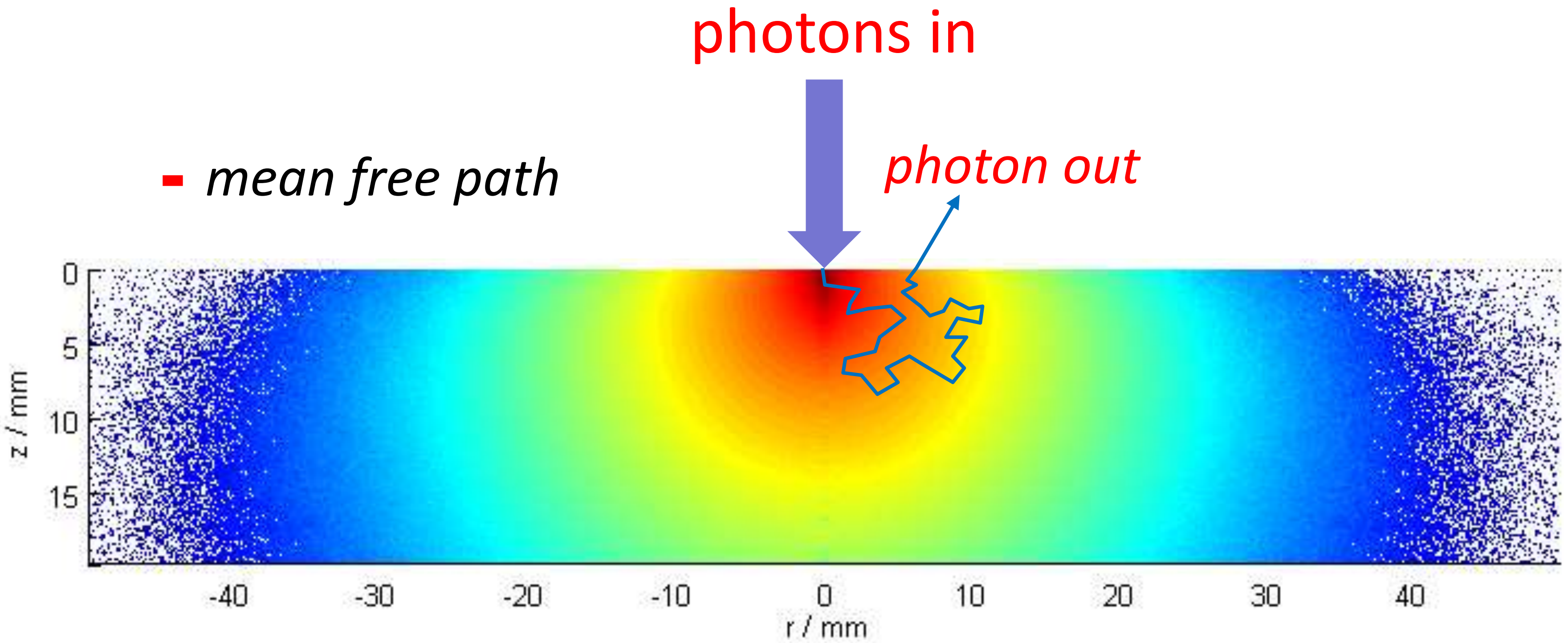
no scattering

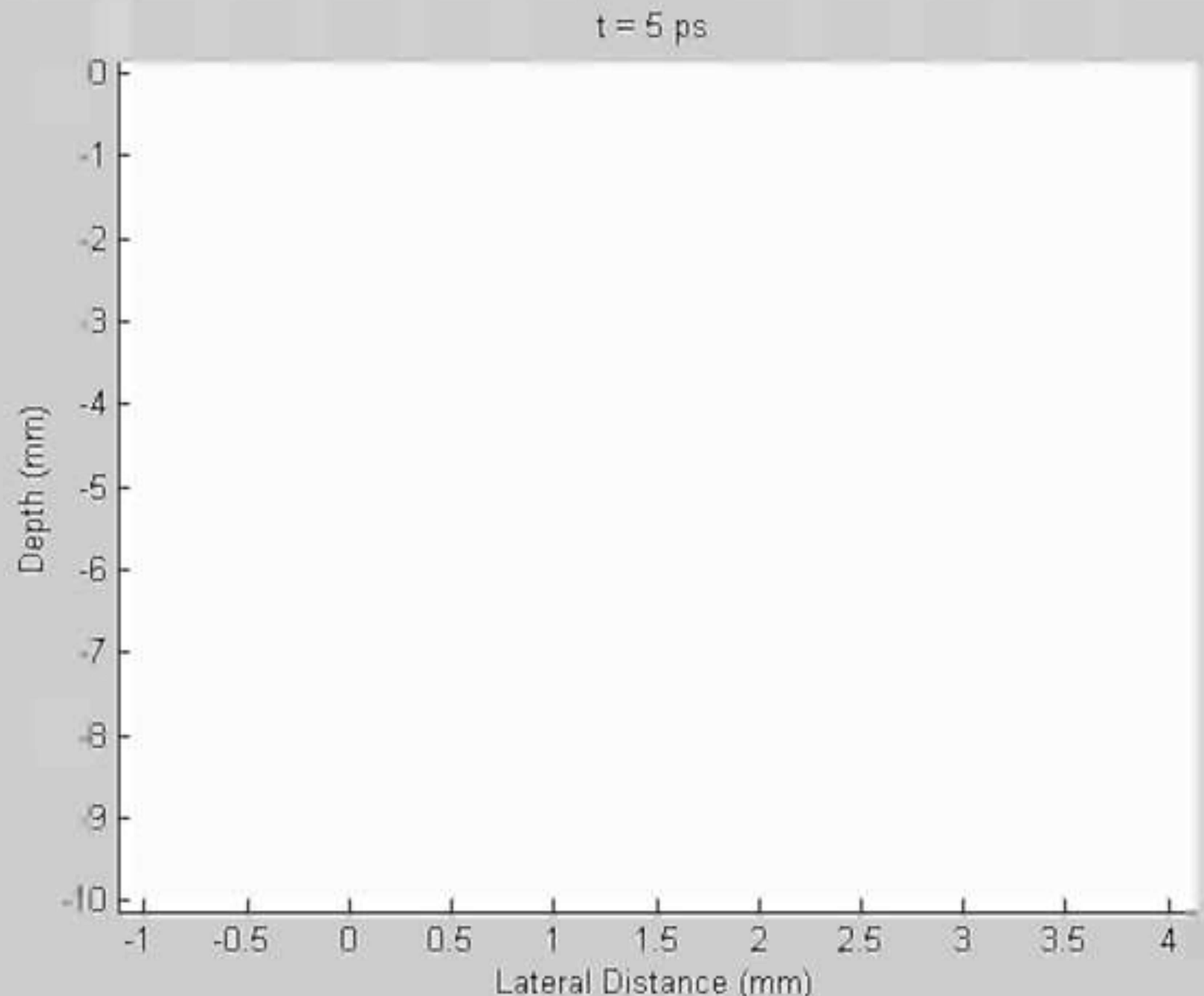


scattering

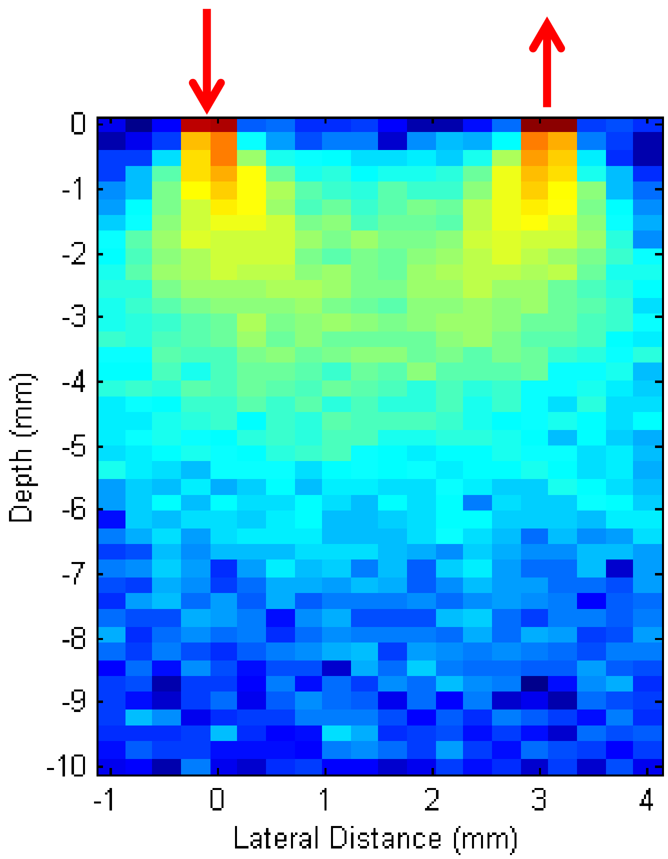
courtesy F. Bevilacqua

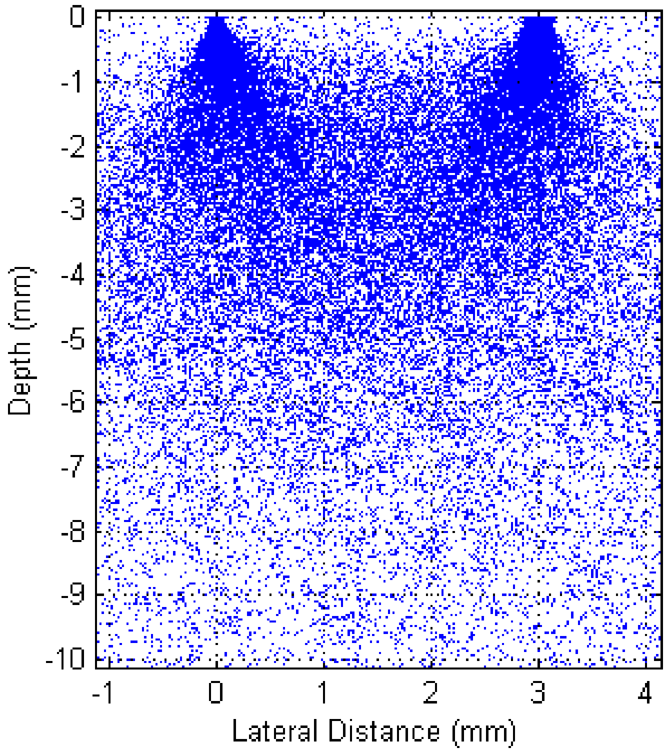
Photon diffusion




t = 5 ps
Depth (mm)
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
-1
-0.5
0
0.5
1
1.5
2
2.5
3
3.5
4
Lateral Distance (mm)

The biomedical optics "banana"!





Roadmap for today

μ_a	$\longleftrightarrow$	absorption
μ_s, μ_s'	$\longleftrightarrow$	scattering
L	$\longleftrightarrow$	radiance
ϕ	$\longleftrightarrow$	fluence (energy density)

radiative transport equation

diffusion equation

boundary conditions

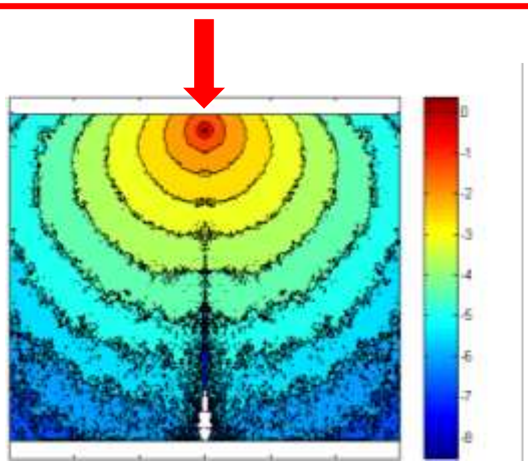
---

reflectance measurements in space and time

steady-state

pulsed

sinusoidally-modulated



Roadmap for today

μ_a ⟷ absorption

μ_s, μ_s' ⟷ scattering

L ⟷ radiance

ϕ ⟷ fluence (energy density)

radiative transport equation

diffusion equation

boundary conditions

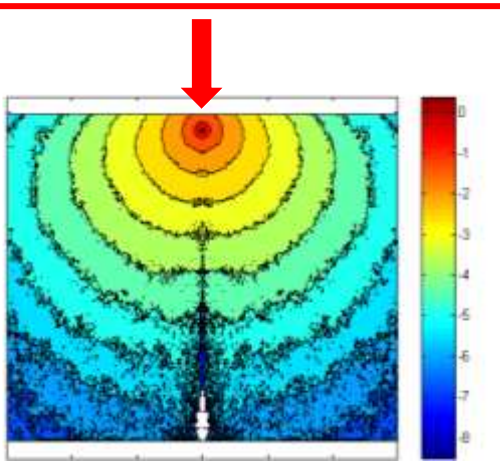
---

reflectance measurements in space and time

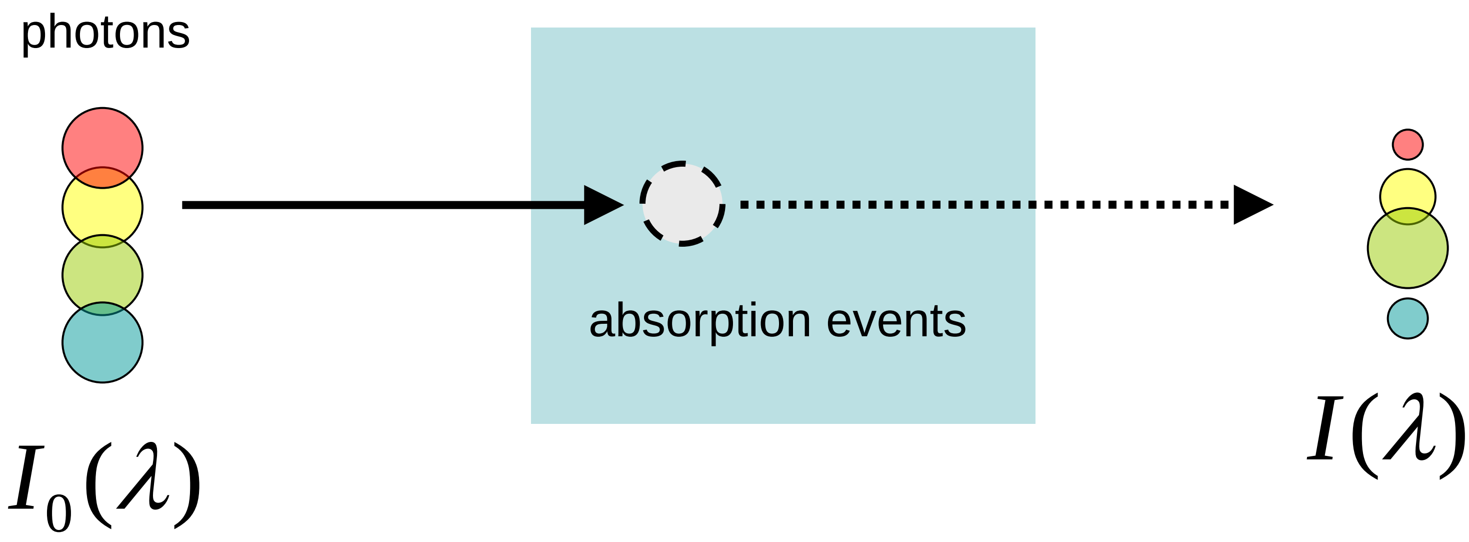
steady-state

pulsed

sinusoidally-modulated



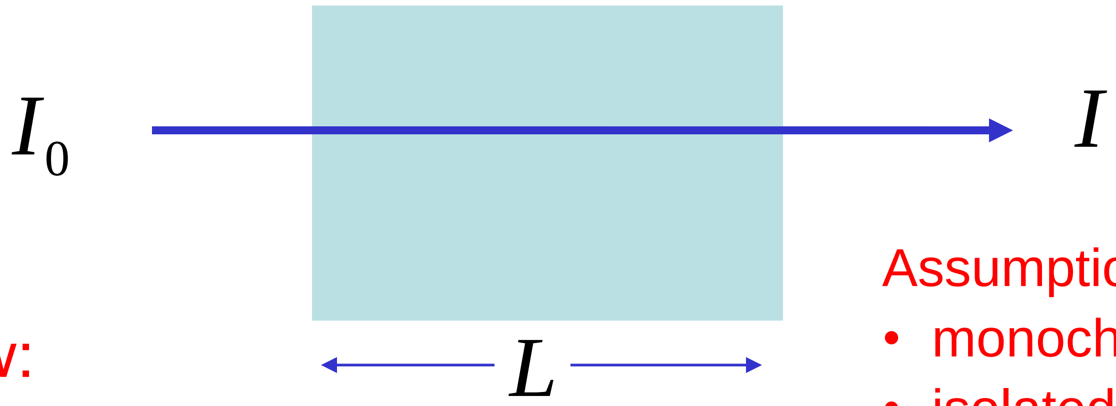
Introduction to biological absorption



Absorption = molecular transition between states

- electronic
- vibrational
- rotational
- (translational)

How to talk about absorption



Assumptions:

- monochromatic light
- isolated absorbers
- collimated beam
- uniform pathlength
- homgeneous, nonscattering medium

Beer's Law:

$$\frac{I}{I_0} = 10^{-\varepsilon cL} = e^{-\mu_a L}$$

molar extinction

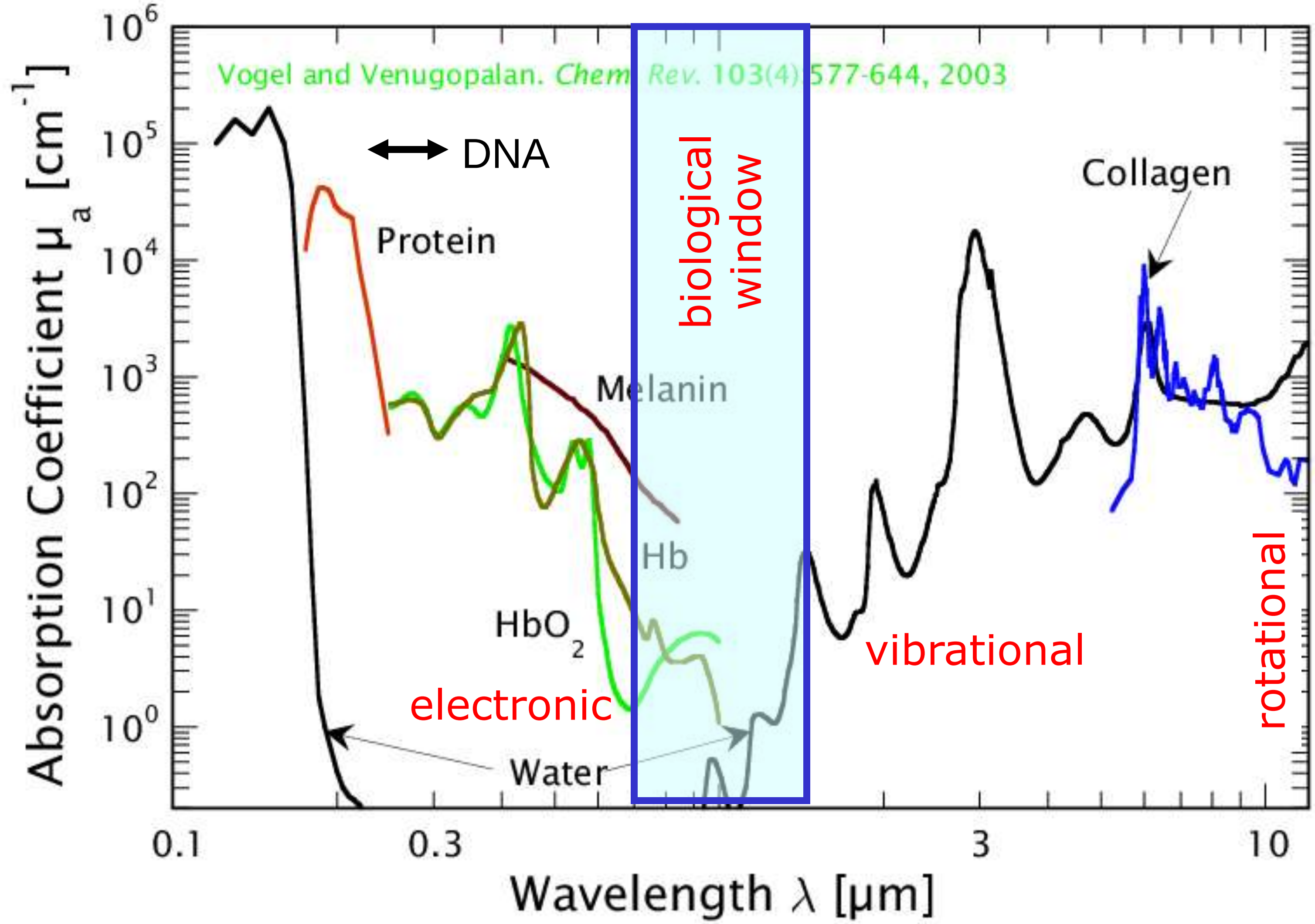
$$\left(\frac{1}{\text{length} \cdot \text{molarity}}\right)$$

concentration (molarity)

$$\mu_a \equiv \ln 10 \cdot \varepsilon c$$

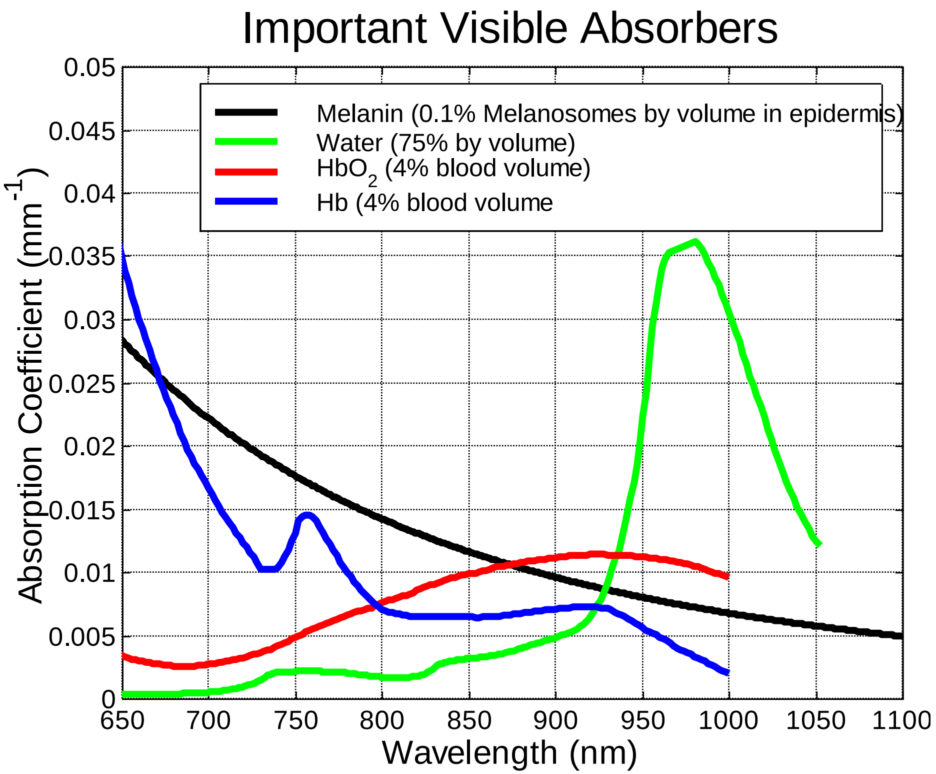
"absorption coefficient" [1/length]

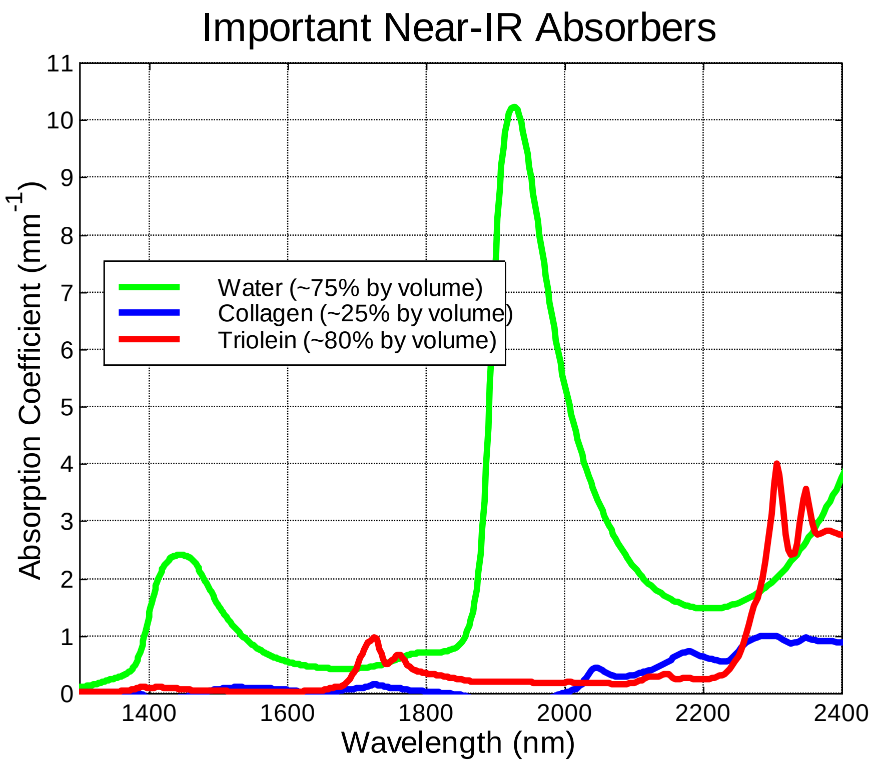
What's absorbing



courtesy V. Venugopalan, http://www.osa.org/meetings/archives/2004/BIOMED/program/#educ

Important tissue absorbers in the visible and near-infrared spectral regions: Skin

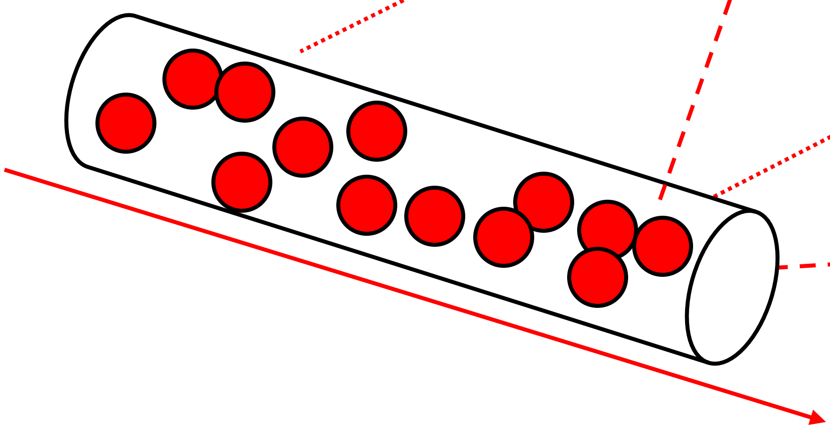




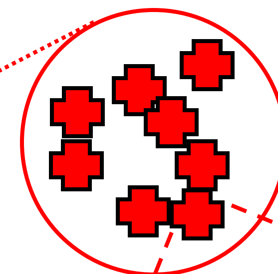
Typical tissue absorption!

adipose tissue ~ 1% blood
by volume

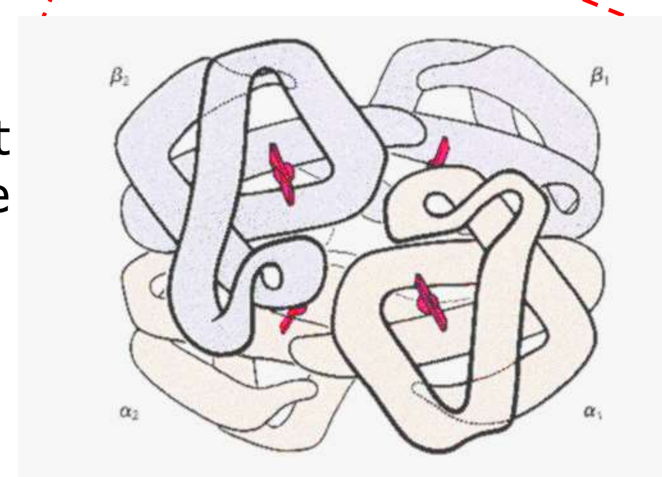
blood = 45% red
blood cells by volume



red blood cell =
1/3 hemoglobin
by weight

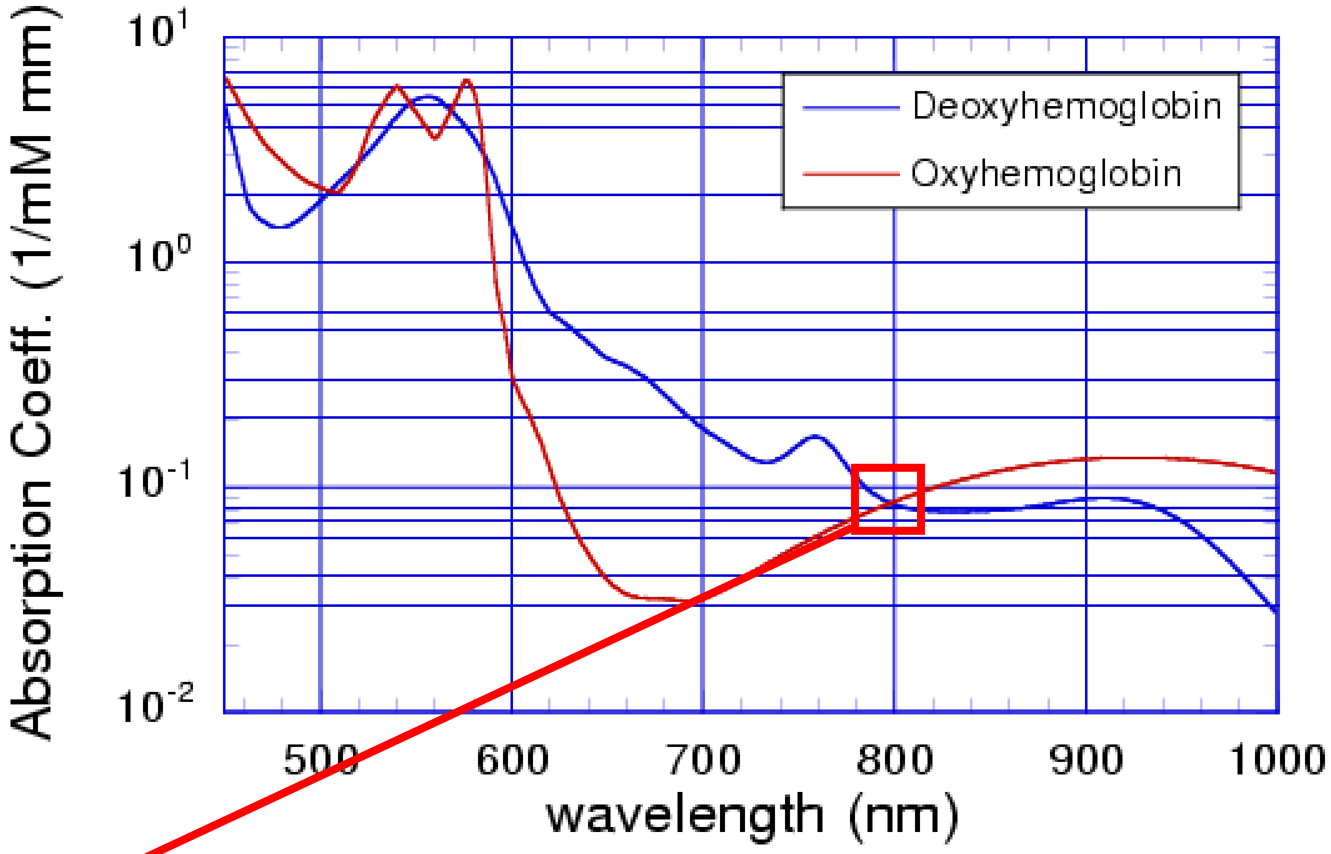


Hemoglobin molecular weight
= 65,000 mg/mmole



Hb concentration = 23 μM

Hemoglobin



at isosbestic point,

$$\mu_a = 0.023\,\mathrm{mM} \cdot 0.09\,\mathrm{mm}^{-1}/\mathrm{mM} = 0.002\,\mathrm{mm}^{-1}$$

Mean free absorption pathlength = 500 mm (!)

Hemodynamics calculations

single absorber :

$$\mu_a = \ln 10 \cdot \varepsilon c$$

two absorbers :

$$\begin{bmatrix} \mu_{a1} \\ \mu_{a2} \\ \vdots \end{bmatrix} = \ln 10 \cdot \begin{bmatrix} \varepsilon_1^{Hb} & \varepsilon_1^{HbO_2} \\ \varepsilon_2^{Hb} & \varepsilon_2^{HbO_2} \\ \vdots & \vdots \end{bmatrix} \begin{bmatrix} c^{Hb} \\ c^{HbO_2} \end{bmatrix}$$

measure the absorption coefficients

look up the molar extinction coefficients (e.g. http:/omlc.ogi.edu)

calculate the concentrations

parameters of interest :

oxygen saturation: $\dfrac{[HbO_2]}{[Hb]+[HbO_2]}$

total hemoglobin $[Hb]+[HbO_2]$

theory works for N>2 chromophores, too!

Roadmap for today

μ_a ⟷ absorption

μ_s, μ_s' ⟷ scattering

L ⟷ radiance

ϕ ⟷ fluence (energy density)

radiative transport equation

diffusion equation

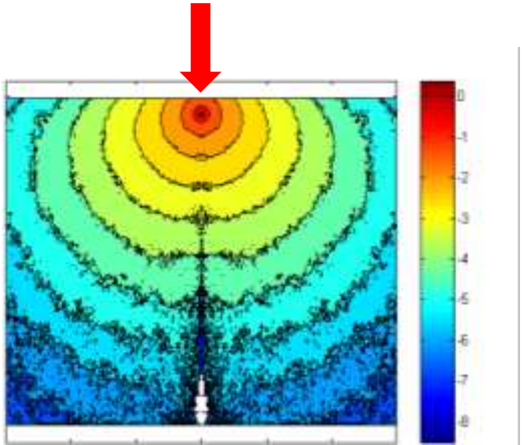
boundary conditions

reflectance measurements in space and time

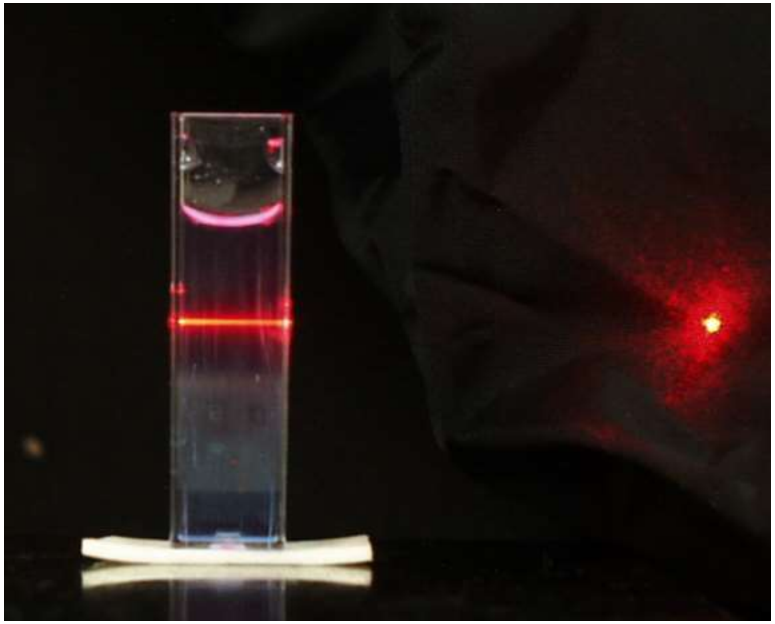
steady-state

pulsed

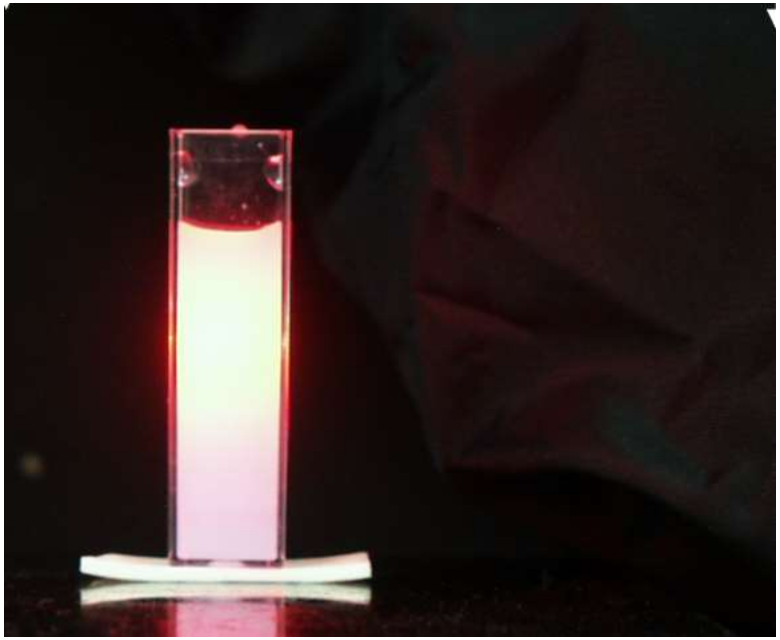
sinusoidally-modulated



Tissue is highly scattering!



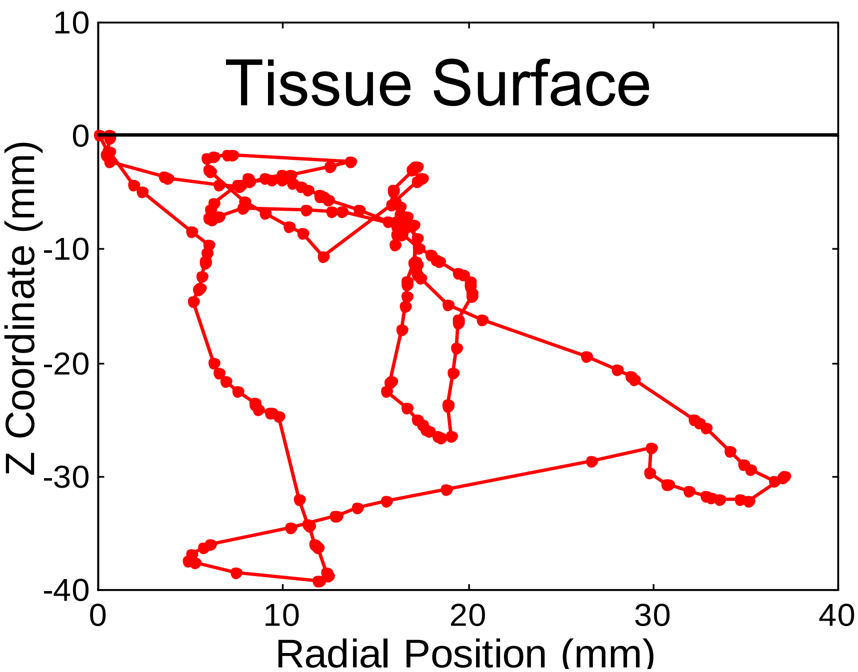
no scattering

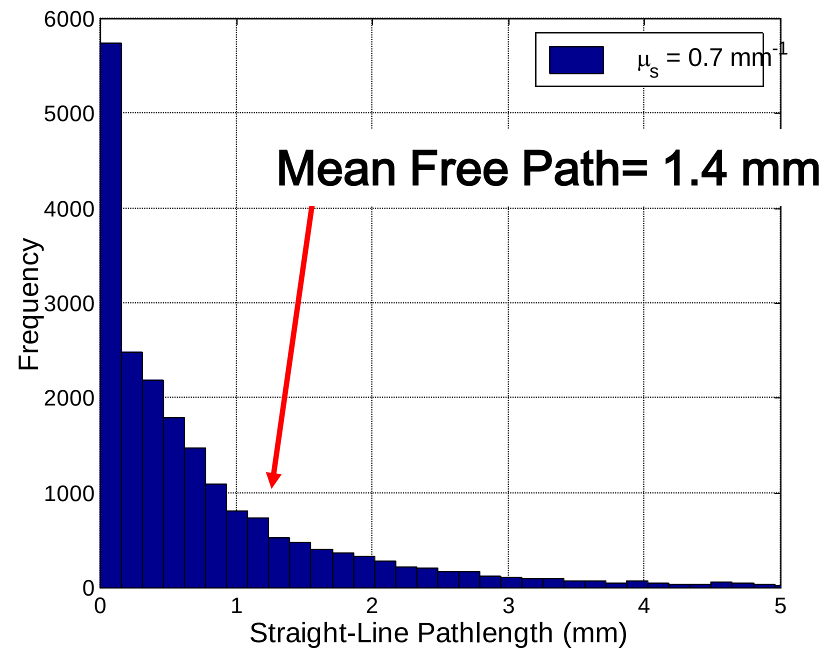


scattering

courtesy F. Bevilacqua

Scattering coefficient (μ_s): inverse of the average straight-line path a photon travels before scattering





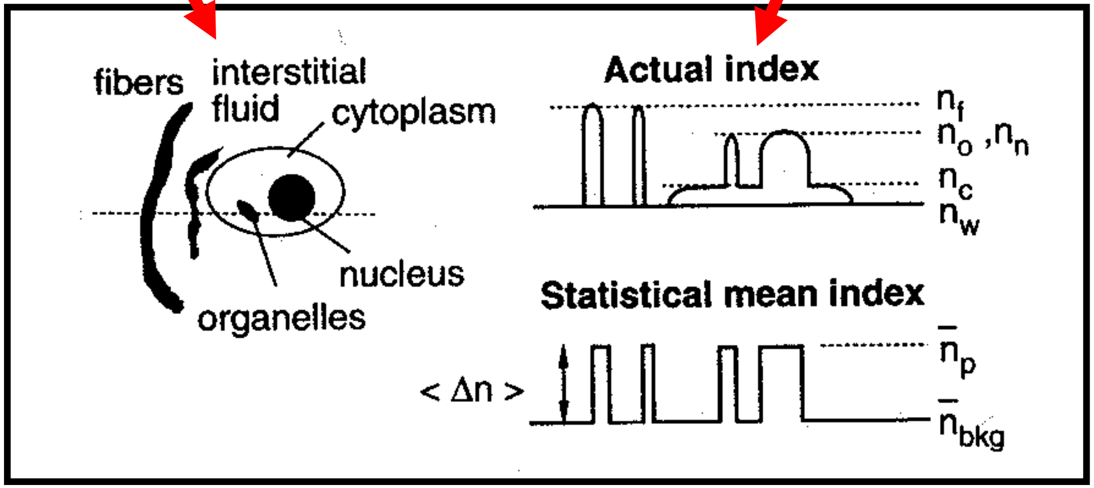
Monte Carlo simulation of a photon trajectory with ***μ_s* = 0.7 mm^{-1}**

Distribution of all straight-line path lengths for this simulation

Scattering of light is caused by index of refraction variations

Interfaces lead to reflection and refraction of light

Many refractive index changes as photon goes through tissue



J.M. Schmitt and G. Kumar, “Optical properties of soft tissue: a discrete particle model,” Appl. Opt. **37:**2788-2797 (1998)

Elastic scattering

- caused by variations in refractive index

component	*typical* n *in the vis/NIR*
extracellular fluid	1.35 – 1.36
cytoplasm	1.36 – 1.375
nucleus	1.38 – 1.41
mitochondria	1.38 – 1.41
water	1.33

Drezek et al., Appl. Opt. **38**:16, 3651-3661 (1999).

- various approaches to modeling:

full rigor	Maxwell's equations (e.g. Drezek above)
Mie theory	plane wave on homogeneous sphere (e.g., code at philiplaven.com)
van de Hulst	three-term approximation to Mie (larger spheres and modest n values)
Rayleigh scattering	very small particles (compared to λ)

Summary: Important sources of scattering in tissue

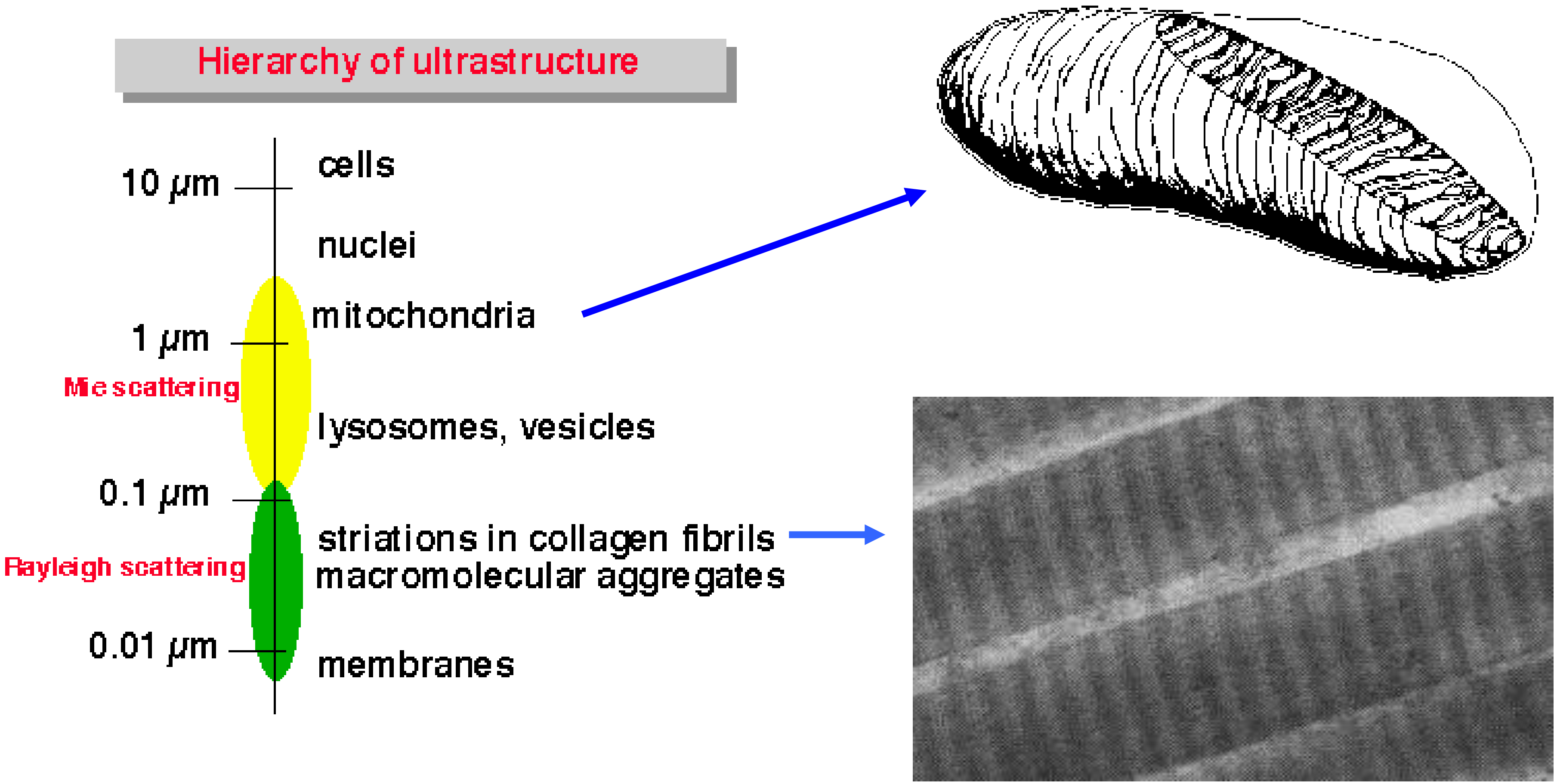
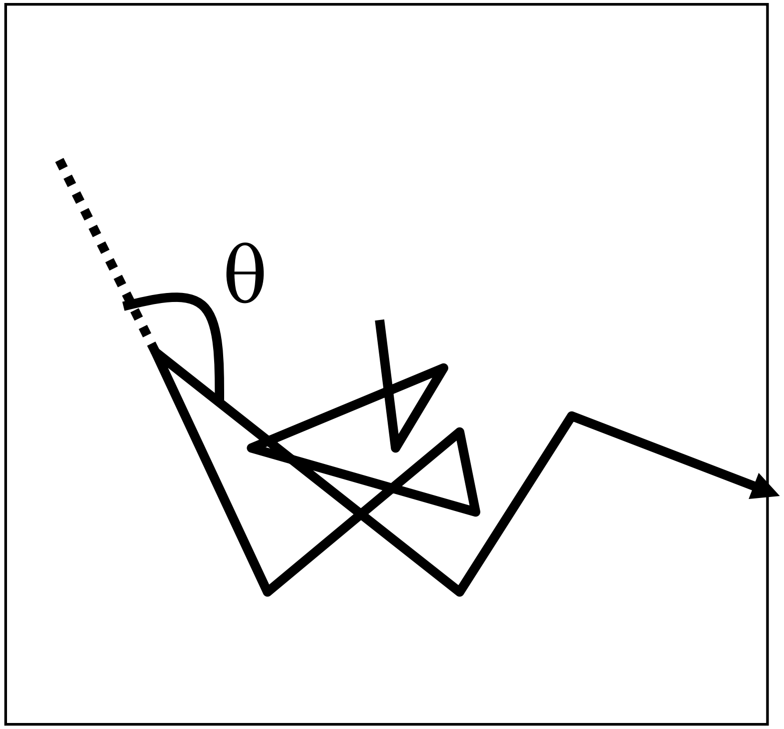


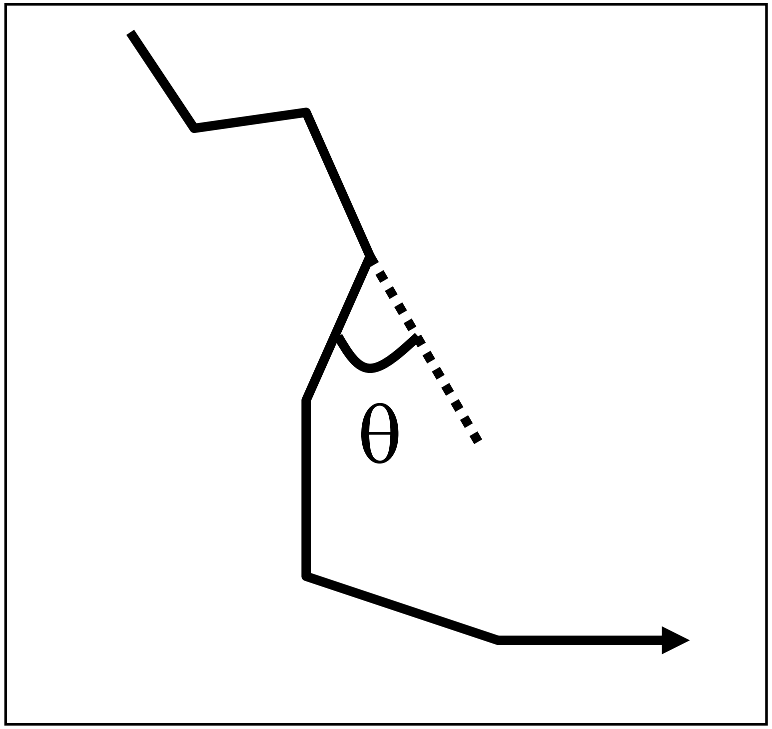
Figure by Steve Jacques,
Oregon Medical Laser Center
http://www.omlc.ogi.edu/classroom

The photon scattering angle is governed by the scattering phase function, p(θ)



Isotropic scattering phase function

$\overline{\cos(\theta)} = g = 0$

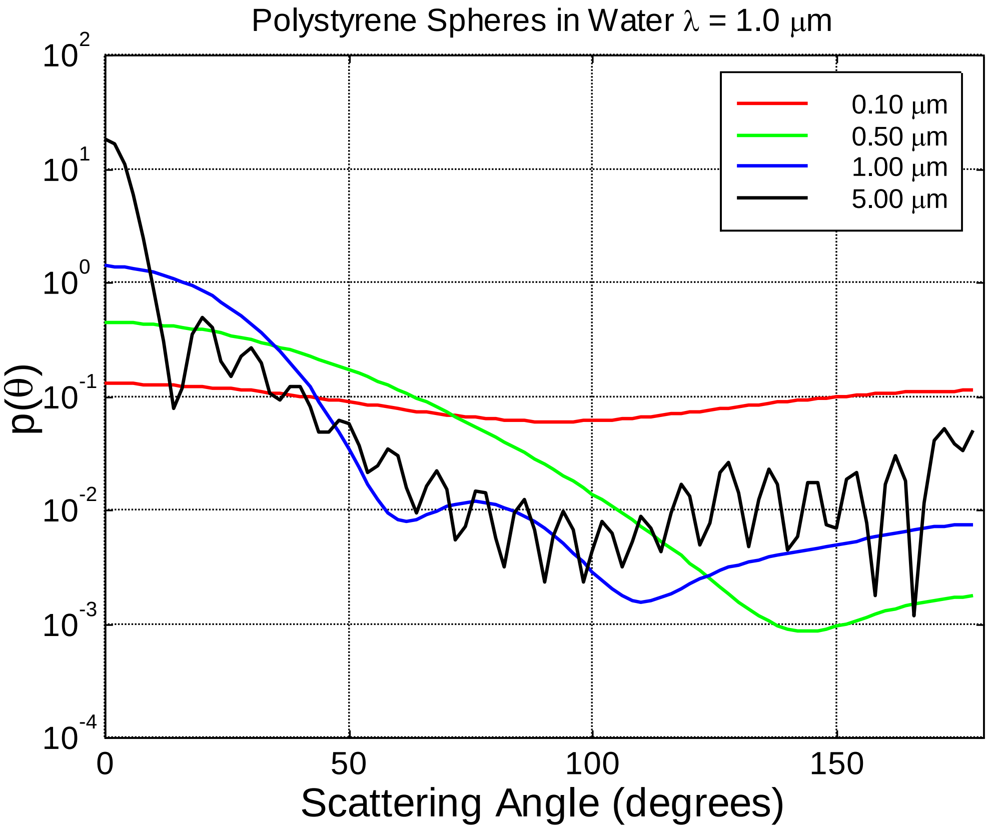


'Forward scattering' phase function (Typical of tissue)

$\overline{\cos(\theta)} = g = 0.9$

Mie scattering theory can be used to compute the phase function for spherical scatterers

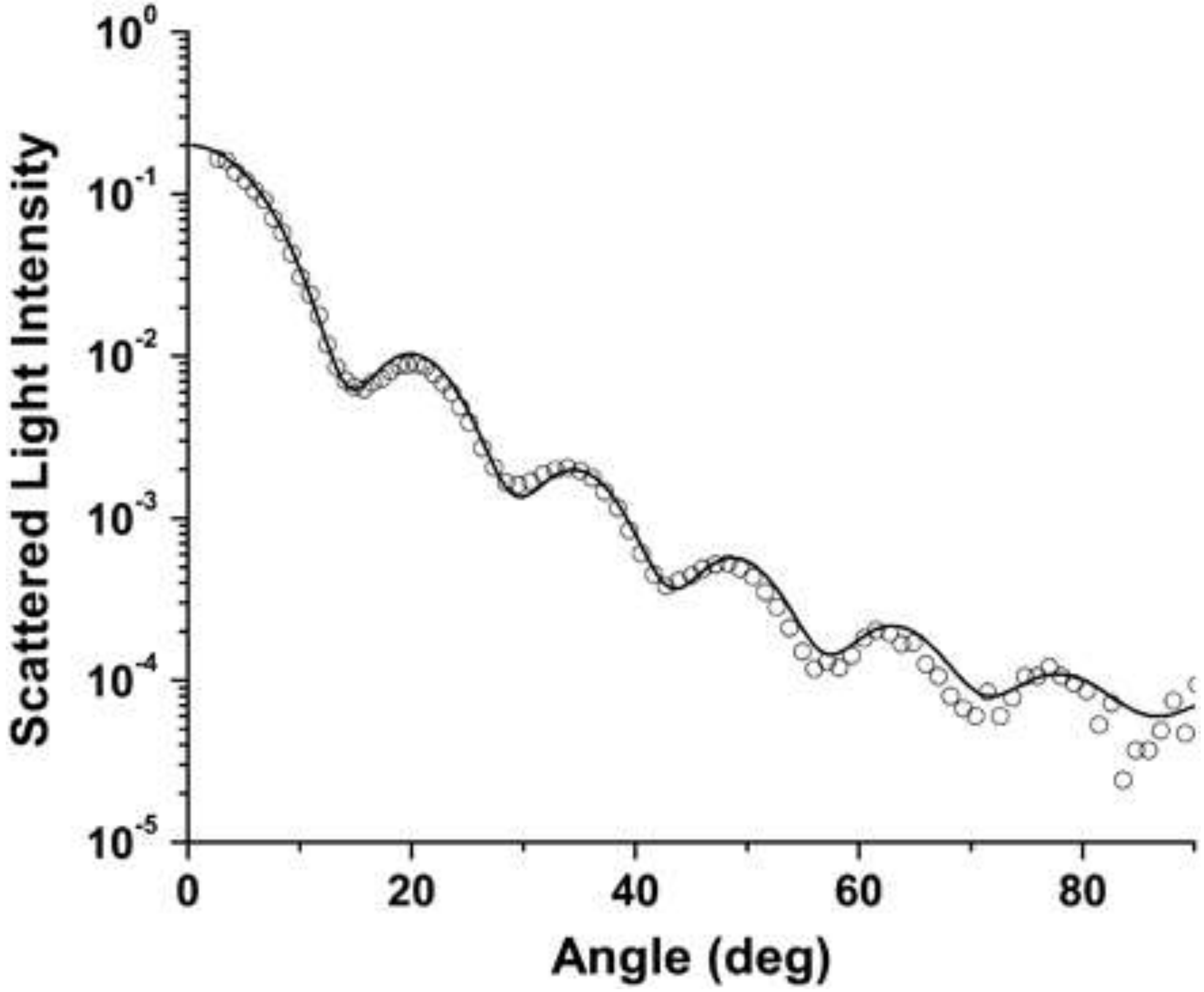
P(θ) for a variety of particle sizes



The shape of the phase function depends on a number of factors:

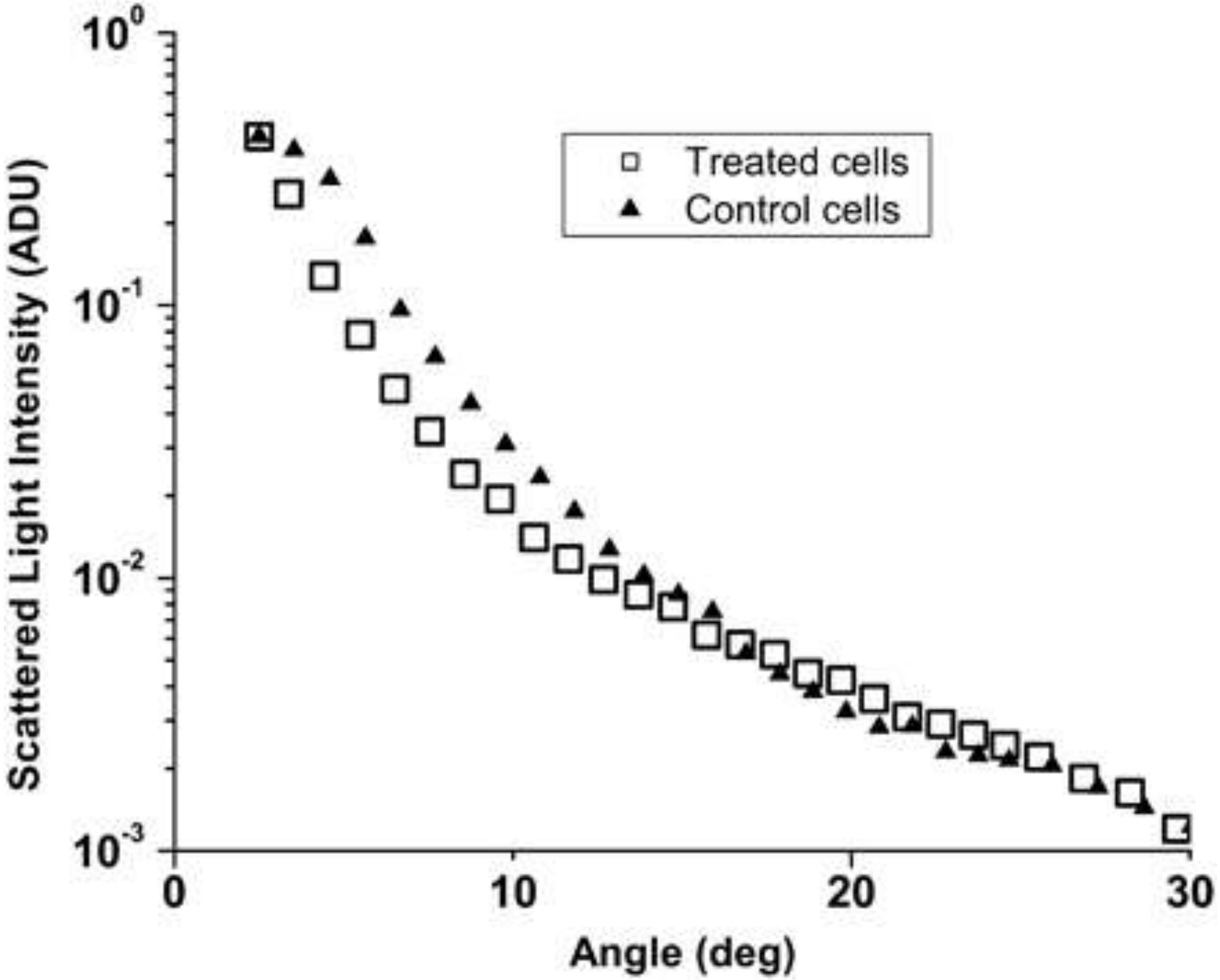
- Wavelength of light
- Size of scatterer
- Index of refraction mismatch
- Polarization state of the light

Angle-resolved light scattering from microspheres



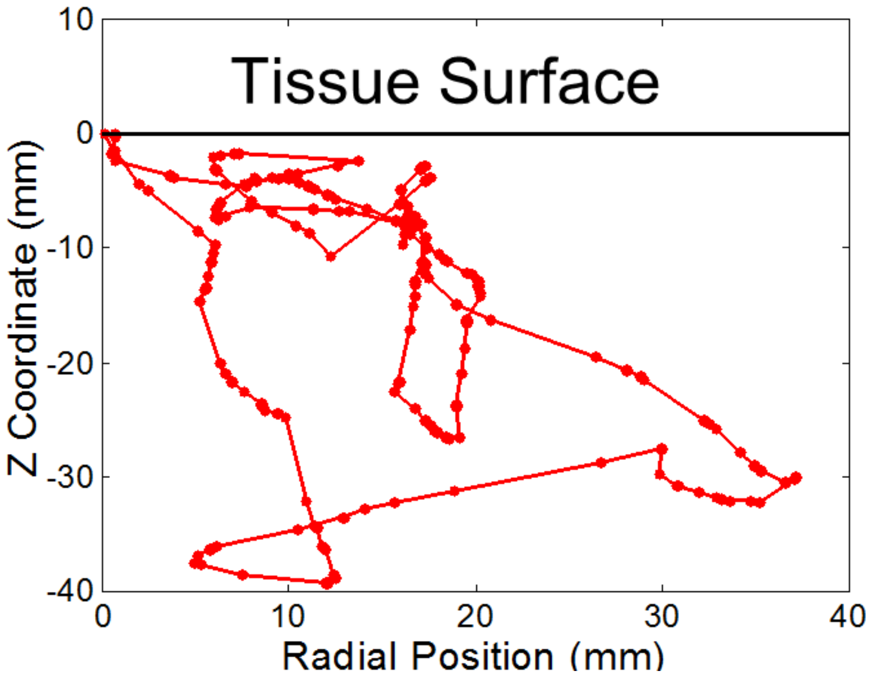
J. D. Wilson *et al.*, Biophysical Journal, 88(4), 2929 (2005).

Different cells = different scattering



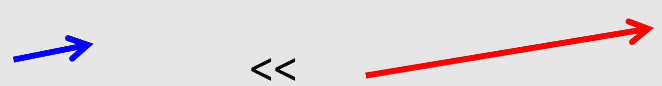
J. D. Wilson *et al.,* Biophysical Journal, 88(4), 2929 (2005).

Absorption vs. scattering in the near-infrared

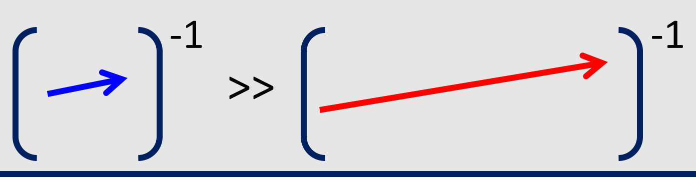


Many more scattering events than absorption events

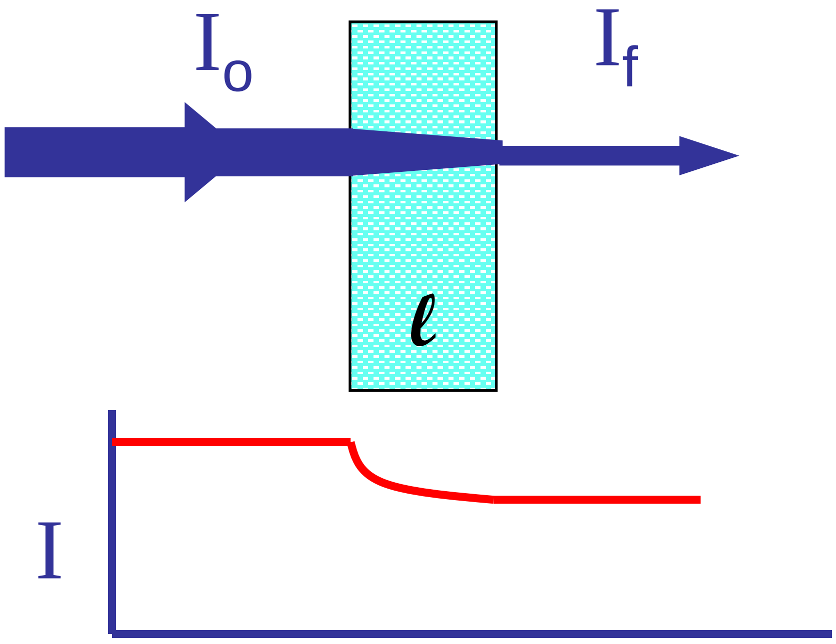
scattering length << absorption length

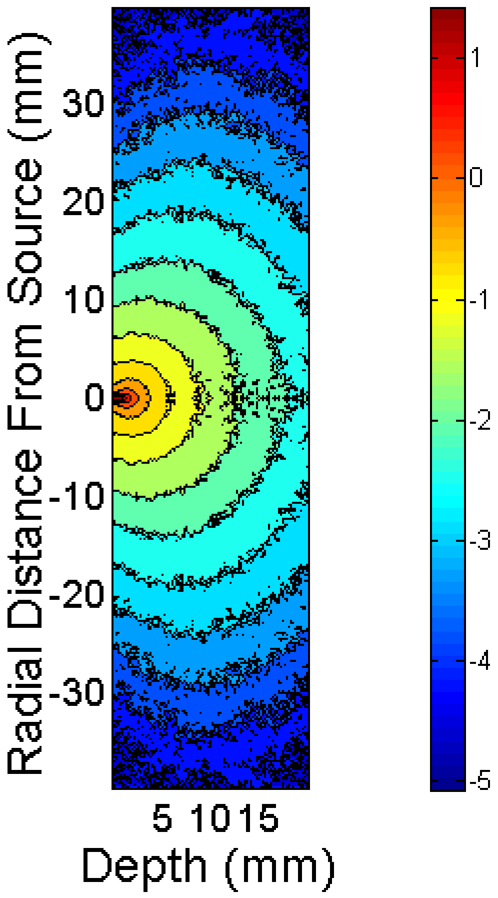


μ_s >> μ_a

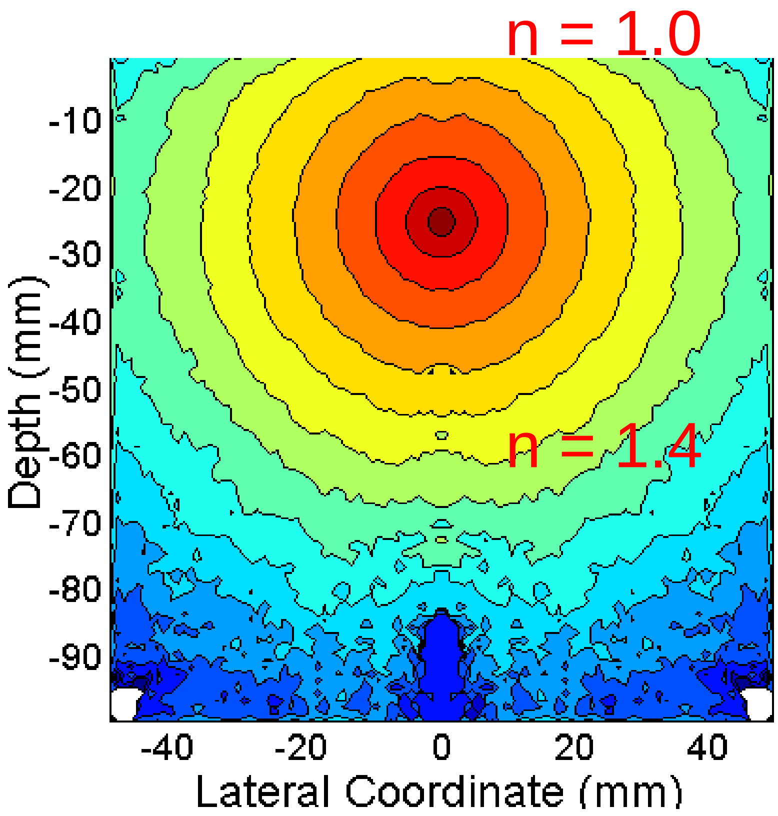


Separating the effects of absorption and scattering:
nicht einfach, aber nicht unmöglich!





Monte Carlo simulation of buried point source in a scattering and absorbing medium



- $\mu_s = 1.0\ mm^{-1}$
- $g=0.9$
- $\mu_a = 0.01\ mm^{-1}$
- $n_{rel} = 1.4$
- Isotropic emitter

Contours connect points of constant energy density

?? How to derive this mathematically??

Roadmap for today

μ_a $\longleftrightarrow$ absorption

μ_s, μ_s' $\longleftrightarrow$ scattering

L $\longleftrightarrow$ radiance

ϕ $\longleftrightarrow$ fluence (energy density)

radiative transport equation

diffusion equation

boundary conditions

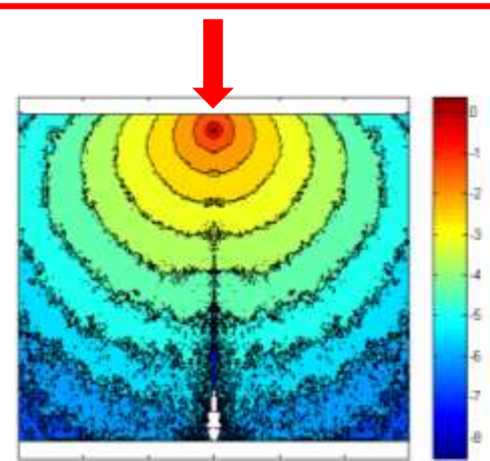
---

reflectance measurements in space and time

steady-state

pulsed

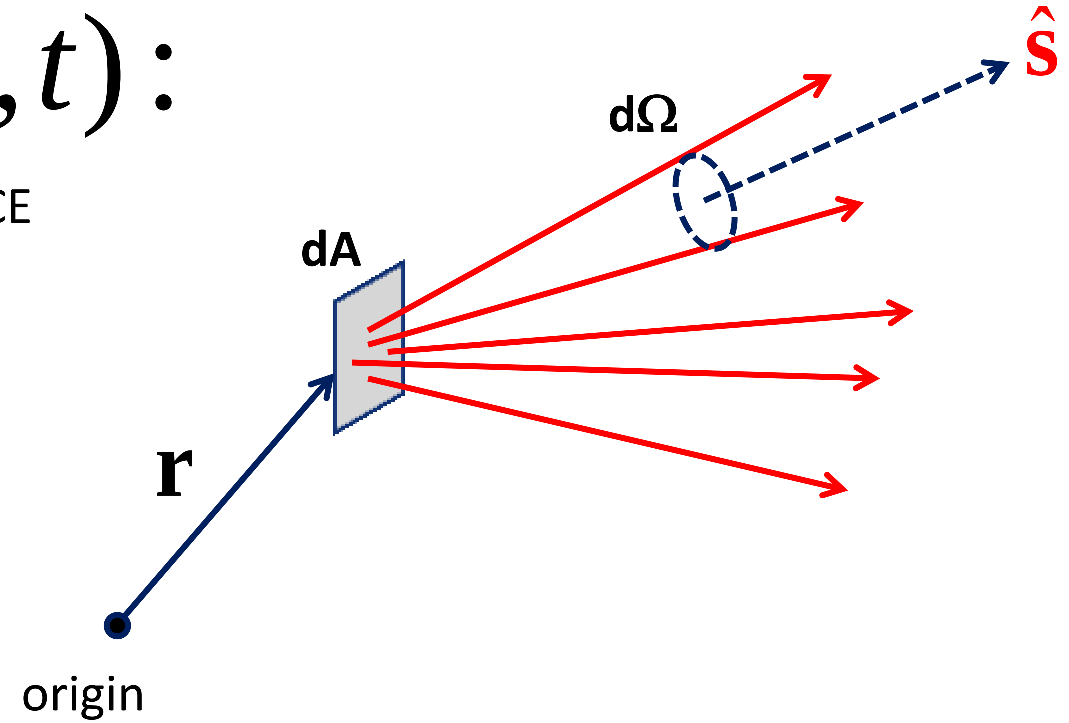
sinusoidally-modulated



Central quantity: RADIANCE

$$L(\mathbf{r},\hat{\mathbf{s}},t):$$

RADIANCE

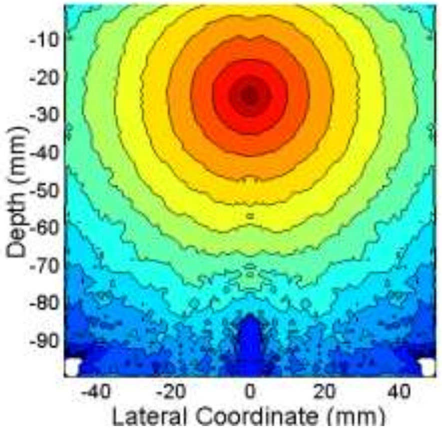


POWER per unit AREA, per unit SOLID ANGLE

W / m² / sr

Radiative Transport Equation: "conservation of radiance"

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

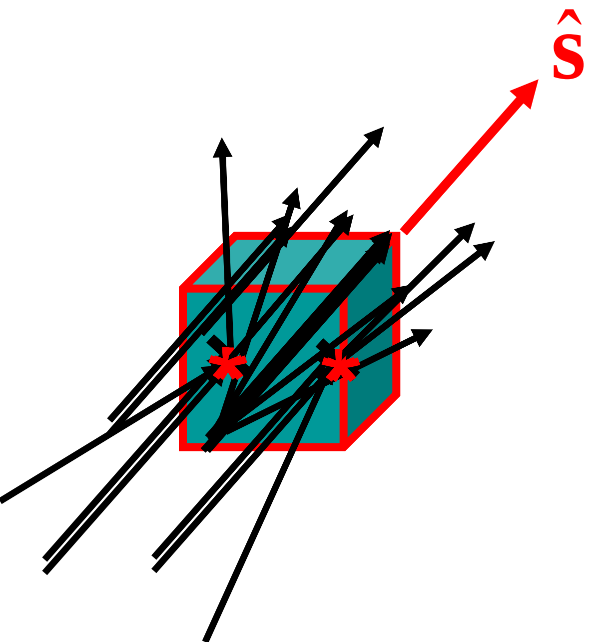


- **L = radiance [W mm^{-2} sr^{-1}]**
- **μ_t = total interaction coefficient = μ_a + μ_s [mm^{-1}]**
- **$\hat{s}$ = observation direction**
- **p(θ) = scattering phase function [-]**
- **S = contribution from sources [W mm^{-3} sr^{-1}]**

Radiative Transport Equation: "conservation of radiance"

$$\frac{1}{c}\frac{\partial L(\mathbf{r},\hat{\mathbf{s}},t)}{\partial t} = -\nabla \cdot L(\mathbf{r},\hat{\mathbf{s}},t)\hat{\mathbf{s}} - (\mu_a + \mu_s)L(\mathbf{r},\hat{\mathbf{s}},t)$$

$$+\mu_s \int_{4\pi} L(\mathbf{r},\hat{\mathbf{s}},t)\, p(\cos^{-1}(\hat{\mathbf{s}}\cdot\hat{\mathbf{s}}'))\, d\Omega + S(\mathbf{r},\hat{\mathbf{s}},t)$$



The rate of change of the radiance is governed by

- **Losses from divergence (spreading out) within d^3x**
- **Losses from absorption in element d^3x**
- **Losses from scattering out of d^3x**
- **Gains from scattering into d^3x**
- **Gains from sources**

Roadmap for today

μ_a $\longleftrightarrow$ absorption

μ_s, μ_s' $\longleftrightarrow$ scattering

L $\longleftrightarrow$ radiance

ϕ $\longleftrightarrow$ fluence (energy density)

radiative transport equation

diffusion equation

boundary conditions

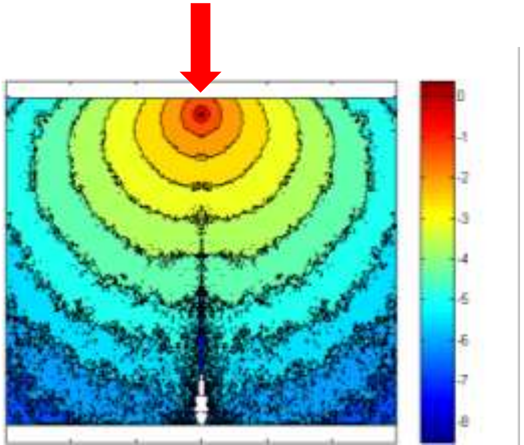
---

reflectance measurements in space and time

steady-state

pulsed

sinusoidally-modulated



Getting to a diffusion equation

Define "fluence" as radiance integrated over all directions $\hat{s}$:

$$\phi(\mathbf{r},t) = \int_{4\pi} L(\mathbf{r},\hat{\mathbf{s}},t)\,d\Omega$$

[units are power/area]

$[\phi/c = \text{energy density}]$

When we integrate the radiative transfer equation over all directions…

$$\frac{1}{c}\frac{\partial L(\mathbf{r},\hat{\mathbf{s}},t)}{\partial t} = -\nabla\cdot L(\mathbf{r},\hat{\mathbf{s}},t)\hat{\mathbf{s}}$$

divergence of the fluence
(more divergent = more loss)

rate of increase of
the local fluence

$$-(\mu_a+\mu_s)L(\mathbf{r},\hat{\mathbf{s}},t)$$

$$+\mu_s\int_{4\pi} L(\mathbf{r},\hat{\mathbf{s}},t)\,p(\cos^{-1}(\hat{\mathbf{s}}\cdot\hat{\mathbf{s}}'))\,d\Omega$$

net absorption, in-scatter,
and out-scatter from
all directions

$$+S(\mathbf{r},\hat{\mathbf{s}},t)$$

total contribution
from sources

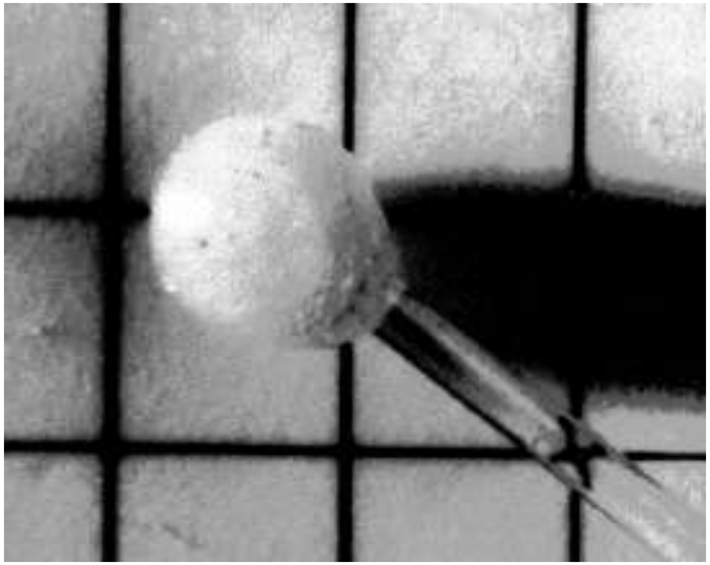
Result: the time-dependent diffusion equation

$$\frac{1}{c}\frac{\partial}{\partial t}\Phi(\mathbf{r},t) = D\nabla^2\Phi(\mathbf{r},t) - \mu_a\Phi(\mathbf{r},t) + S(\mathbf{r},t)$$

- D = Diffusion coefficient [mm] (to be defined soon)
- Φ = Optical 'fluence' (integration of radiance)
- S = Source term [W mm^{-3}] (integration of emission sources; isotropic emission assumed)

How did those integrals in the previous slide get simplified so much?

A "4π" detector samples the optical fluence

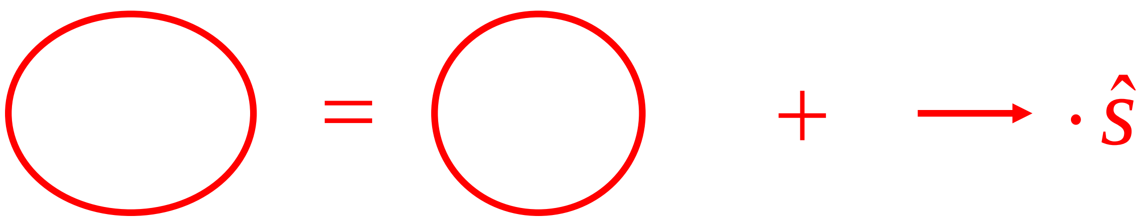


Assumption 1: radiance and source terms are the sum of an isotropic term and a (weak) cosine term

fluence

gradient of fluence
(formula to follow)

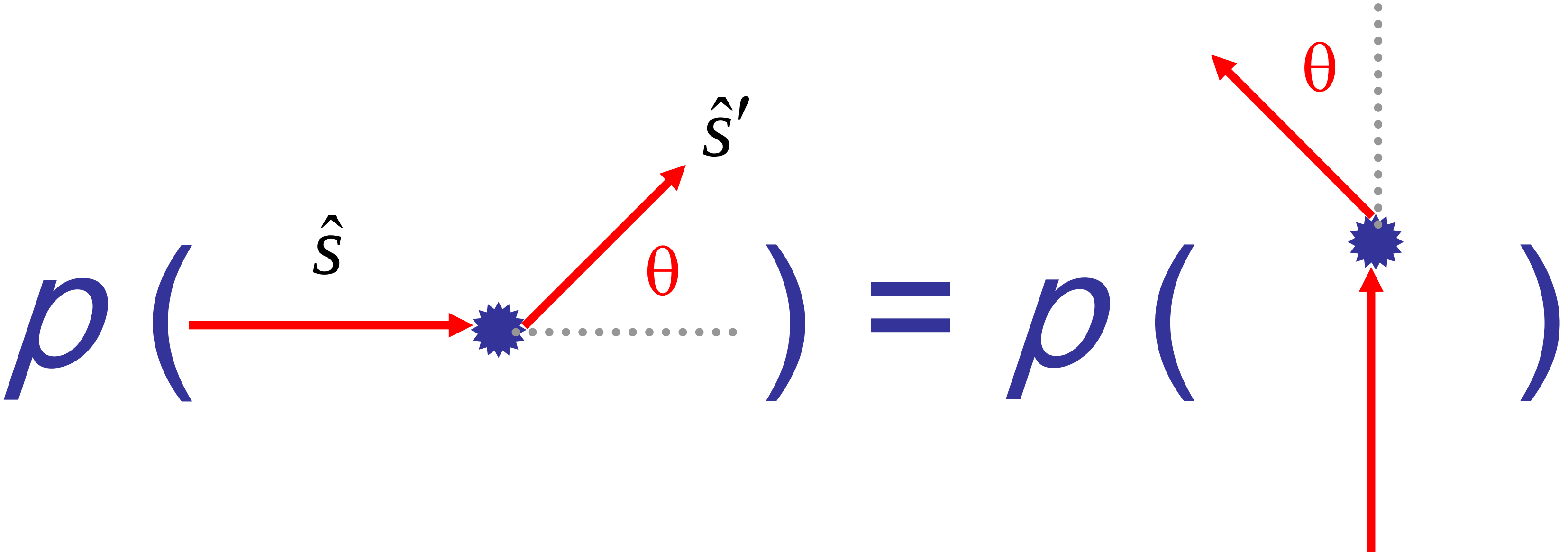
$$L(\mathbf{r},\hat{s},t)=\frac{1}{4\pi}\Phi(\mathbf{r},t)+\frac{3}{4\pi}\mathbf{j}(\mathbf{r},t)\cdot\hat{s}$$



Mathematically: Taylor expansions for *L* and *S*, truncated after two terms.

$$S(\mathbf{r},\hat{s},t)=\frac{1}{4\pi}S_0(\mathbf{r},t)+\frac{3}{4\pi}\mathbf{S}_1(\mathbf{r},t)\cdot\hat{s}$$

Assumption 2: simplified scattering-angle probability distribution



$$p(\hat{s},\hat{s}') = p(\hat{s}\cdot\hat{s}')$$

$$\approx \frac{1}{4\pi} + \frac{3}{4\pi} g\cos(\theta) + \ldots$$

What happens when we integrate

Define "fluence" as radiance integrated over all directions $\hat{s}$:

$$\phi(\mathbf{r},t) = \int_{4\pi} L(\mathbf{r},\hat{\mathbf{s}},t)\,d\Omega$$

[units are power/area]

[ϕ/c = energy density]

When we integrate the radiative transfer equation over all directions…

$$\frac{1}{c}\frac{\partial L(\mathbf{r},\hat{\mathbf{s}},t)}{\partial t} = -\nabla\cdot L(\mathbf{r},\hat{\mathbf{s}},t)\hat{\mathbf{s}} \rightarrow D\nabla^2\Phi(\mathbf{r},t)$$

$$\frac{1}{c}\frac{\partial}{\partial t}\Phi(\mathbf{r},t)$$

(and other terms)

$$-(\mu_a+\mu_s)L(\mathbf{r},\hat{\mathbf{s}},t)$$

$$-\mu_a\Phi(\mathbf{r},t)$$

$$+\mu_s\int_{4\pi} L(\mathbf{r},\hat{\mathbf{s}},t)\,p(\cos^{-1}(\hat{\mathbf{s}}\cdot\hat{\mathbf{s}}'))\,d\Omega$$

$$+S(\mathbf{r},\hat{\mathbf{s}},t) \rightarrow$$

various source terms

(nicht sehr wichtig)

Don’t read this slide too closely

The full equation becomes

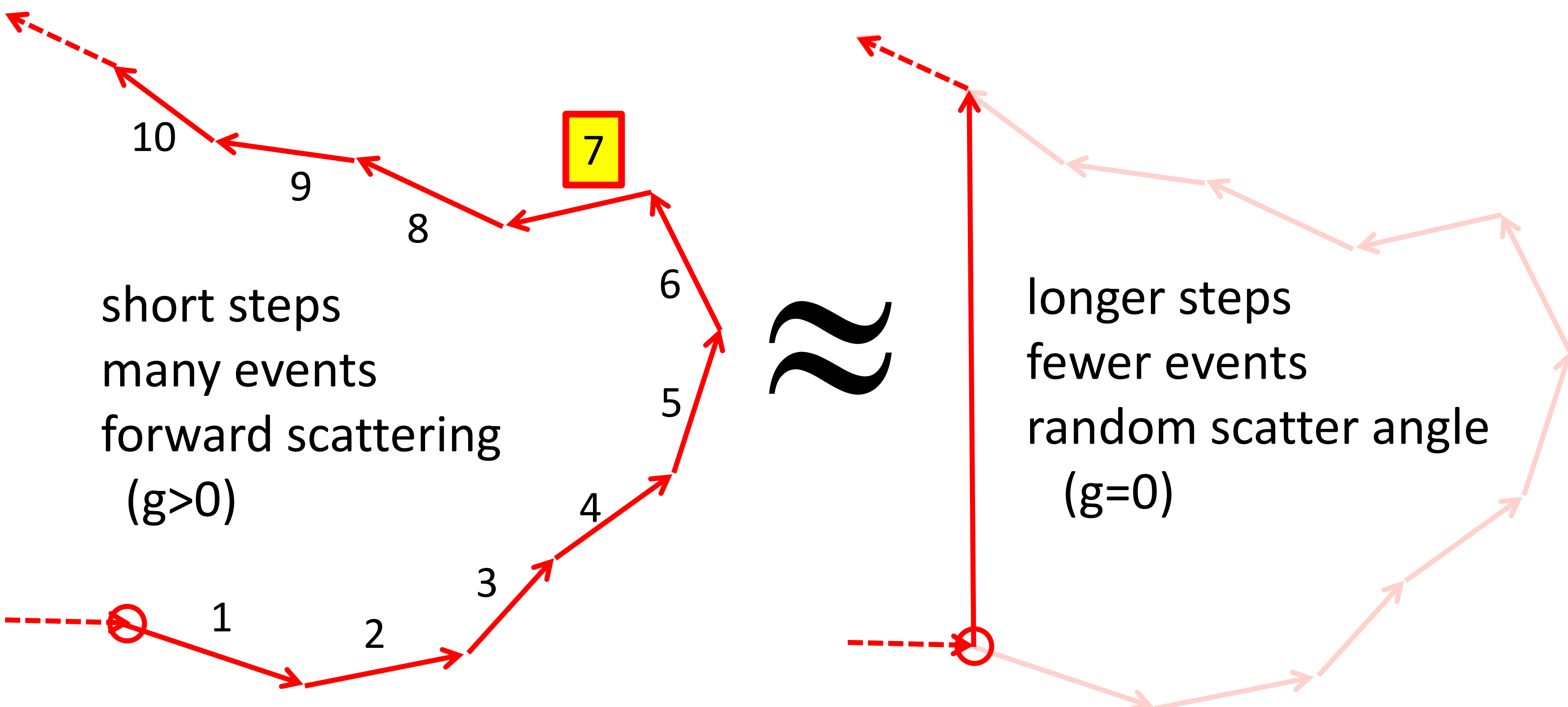
$$-D\nabla^2\Phi(\mathbf{r},t)+\mu_a\Phi(\mathbf{r},t)+\frac{1}{c}\frac{\partial\Phi(\mathbf{r},t)}{\partial t}+\frac{3D}{c}\left[\mu_a\frac{\partial\Phi}{\partial t}+\frac{1}{c}\frac{\partial^2\Phi}{\partial t^2}\right]=$$

$$S_0(\mathbf{r},t)-3D\nabla\cdot\mathbf{S_1}(\mathbf{r},t)+\frac{3D}{c}\frac{\partial S_0(\mathbf{r},t)}{\partial t},$$

where D is the optical diffusion coefficient,

$$D=\frac{1}{3(\mu_a+\boxed{\mu_s(1-g)})}$$

"Reduced scattering" substitution



Reduced-scattering coefficient: $\boxed{\mu_s'} \equiv \mu_s(1-g)$

Time-dependent diffusion equation

$$-D\nabla^2\Phi(\mathbf{r},t)+\mu_a\Phi(\mathbf{r},t)+\frac{1}{c}\frac{\partial\Phi(\mathbf{r},t)}{\partial t}+\frac{3D}{c}\left[\mu_a\frac{\partial\Phi}{\partial t}+\frac{1}{c}\frac{\partial^2\Phi}{\partial t^2}\right]=$$

$$S_0(\mathbf{r},t)-3D\nabla\cdot\mathbf{S_1}(\mathbf{r},t)+\frac{3D}{c}\frac{\partial S_0(\mathbf{r},t)}{\partial t}.$$

If circled terms are ignored (discussion to follow), then we get

$$-D\nabla^2\Phi(\mathbf{r},t)+\mu_a\Phi(\mathbf{r},t)+\frac{1}{c}\frac{\partial\Phi(\mathbf{r},t)}{\partial t}=$$

$$S_0(\mathbf{r},t)-3D\nabla\cdot\mathbf{S_1}(\mathbf{r},t)$$

directionality of emission; vanishes for isotropic emission

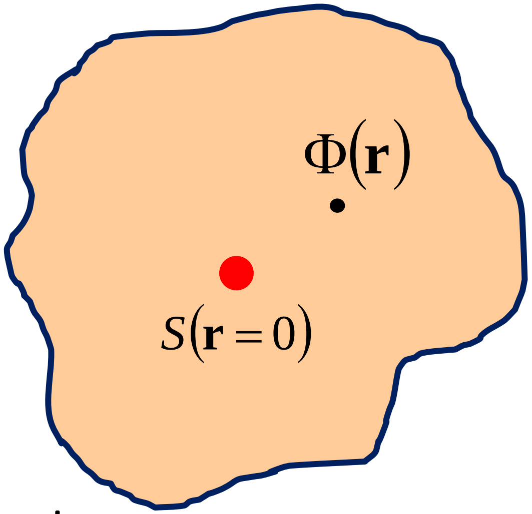
J. B. Fishkin et al., "Gigahertz photon density waves in a turbid medium: Theory and experiments," *Phys. Rev. E* **53:** 2307-2319 (1996).

Steady-state diffusion equation

Dropping time-dependent terms and assuming an isotropic source yields:

$$-D\nabla^2\Phi(\mathbf{r},t)+\mu_a\Phi(\mathbf{r},t)=S_0(\mathbf{r},t)$$

where $D=1/\left[3(\mu_a+\mu_s')\right]$



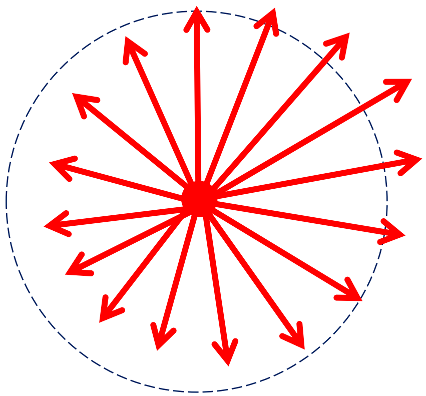
The Green's function for this equation is

$$\Phi_G=\frac{1}{4\pi D}\frac{e^{-\mu_{eff}r}}{r}$$

where μ_{eff} is the 'effective attenuation coefficient':

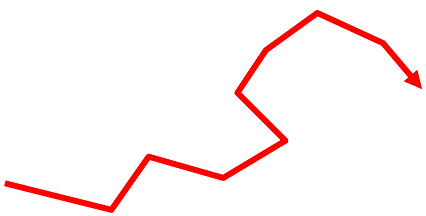
$$\mu_{eff}=\left[3\mu_a(\mu_a+\mu_s')\right]^{1/2}$$

Review of assumptions in the derivation of the photo-diffusion equation



Radiance is only mildly anisotropic

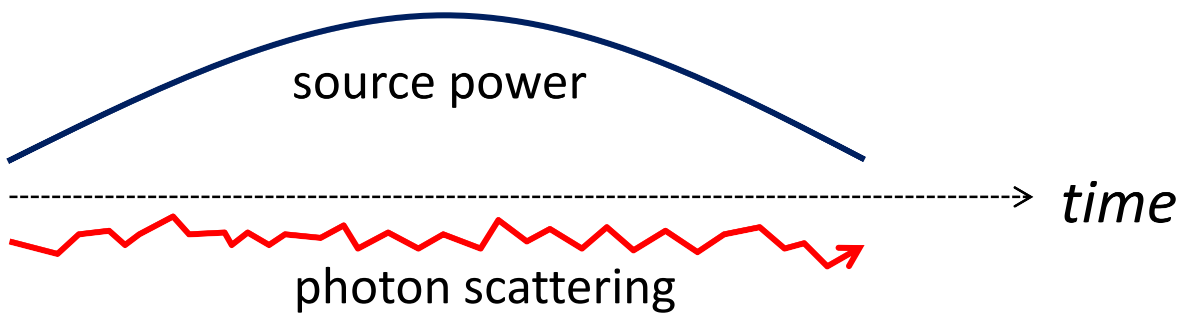
problem near boundaries and sources!



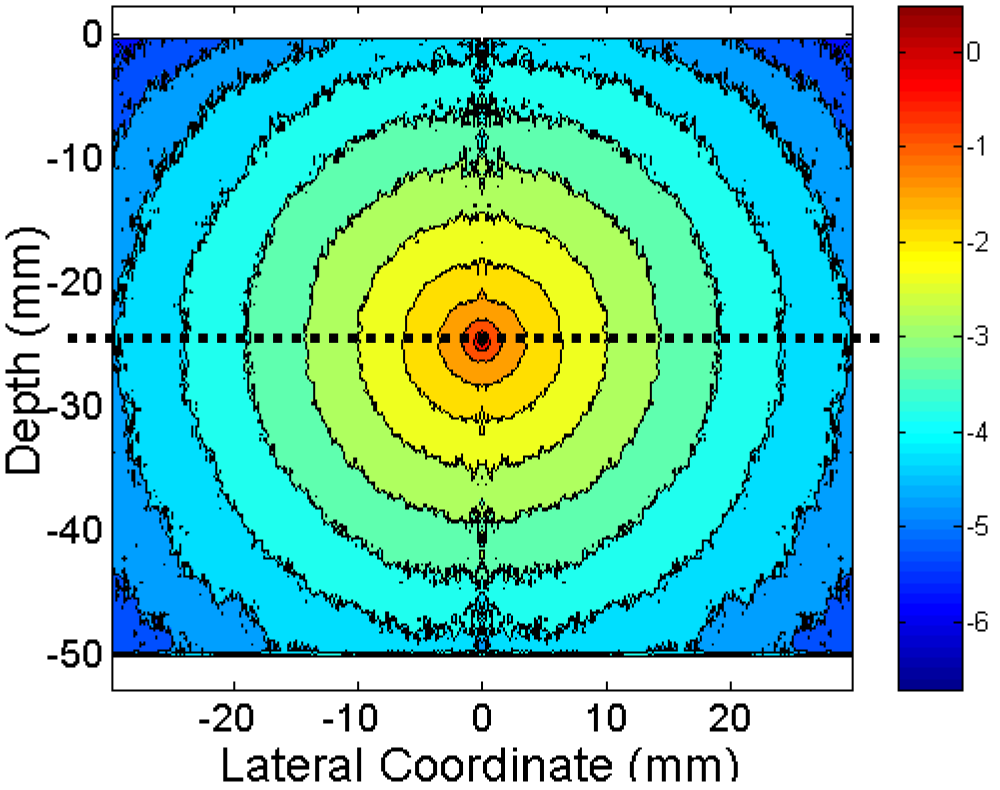
Scattering dominates absorption

$\mu_s' >> \mu_a$

"Scattering frequency" >> source modulation frequency

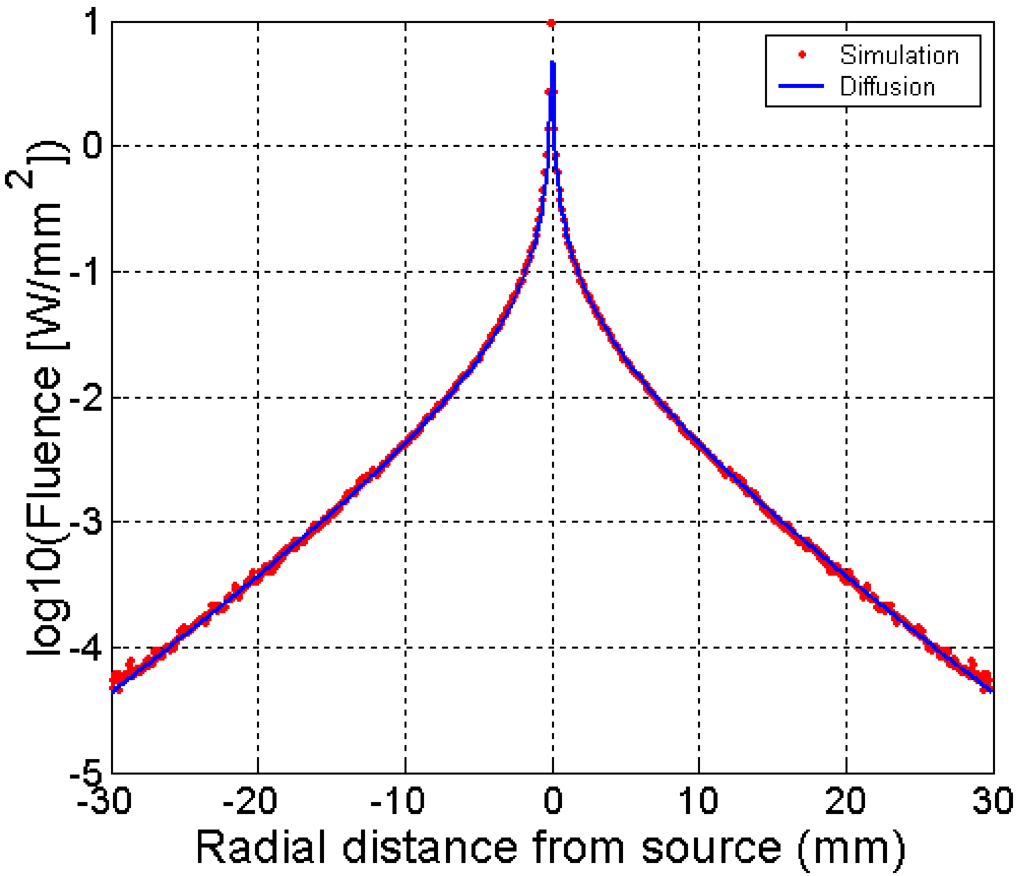


Fluence from an isotropic point source: Theoretical vs. Monte Carlo simulation



- **μ_a = 0.01 mm^{-1}**
- μ_s = 10.0 mm^{-1}
- g=0.9
- n_{rel} = 1.4
- Isotropic emitter, z = 24.75

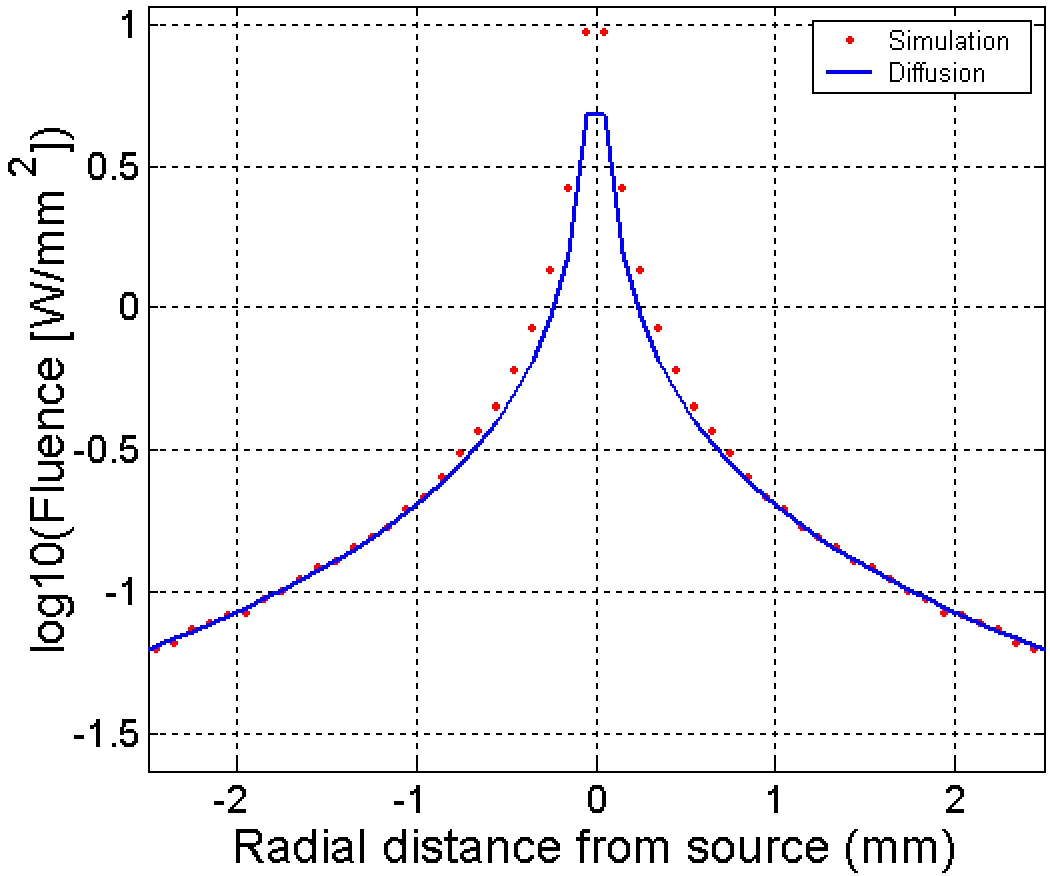
Fluence from an isotropic point source: Theoretical vs. Monte Carlo simulation (cut-through of previous slide)



- **μ_a = 0.01 mm^{-1}**
- μ_s = 10.0 mm^{-1}
- g=0.9
- n_{rel} = 1.4
- Isotropic emitter, z = 24.75

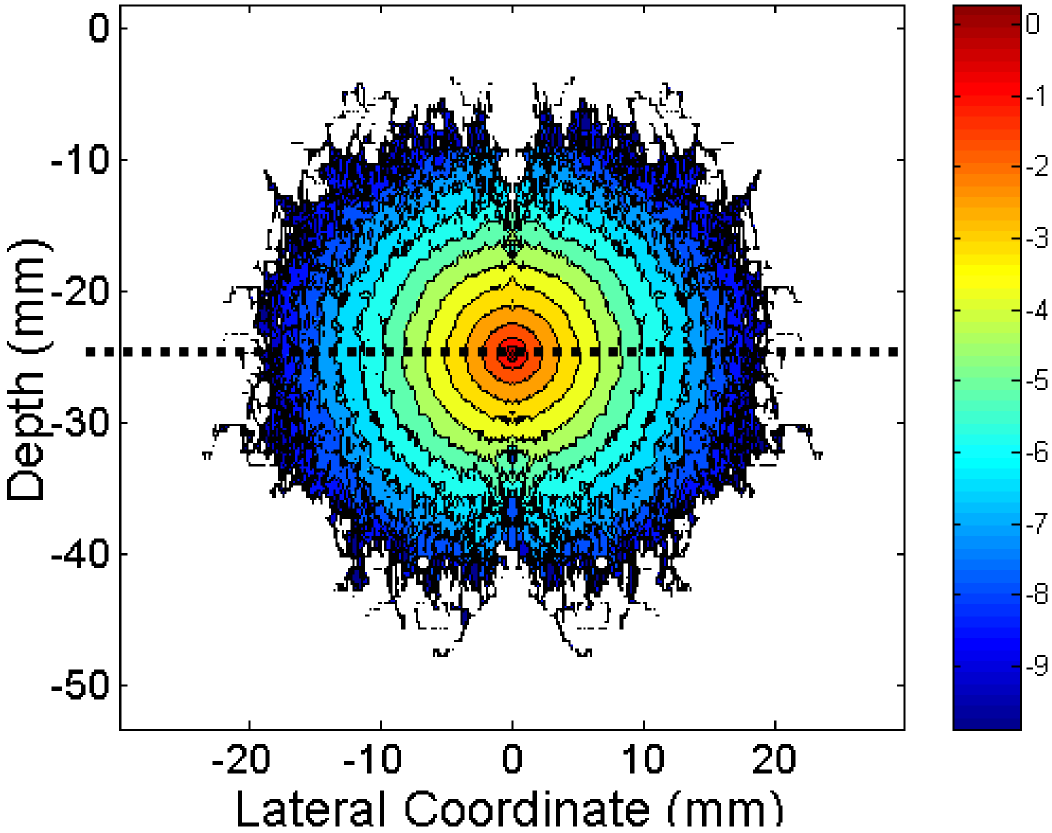
Fluence from an isotropic point source: Theoretical vs. Monte Carlo simulation (zoomed in)

disagreement near the source



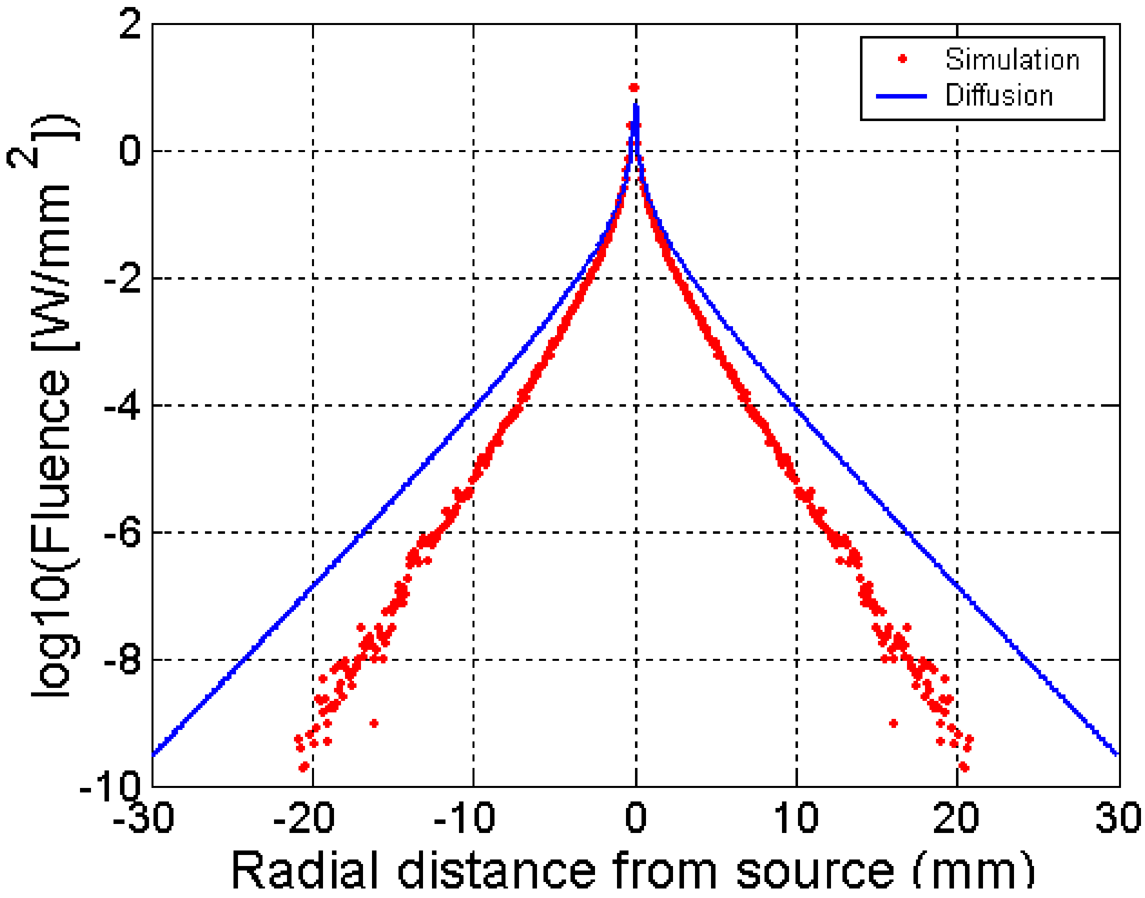
- **μ_a = 0.01 mm^{-1}**
- μ_s = 10.0 mm^{-1}
- g=0.9
- n_{rel} = 1.4
- Isotropic emitter, z = 24.75

Fluence from an isotropic point source: Theoretical vs. Monte Carlo simulation



- **$\mu_a = 0.2\ mm^{-1}$**
- $\mu_s = 10.0\ mm^{-1}$
- g=0.9
- $n_{rel} = 1.4$
- Isotropic emitter, z = 24.75 mm

Fluence from an isotropic point source: Theoretical vs. Monte Carlo simulation



- **μ_a = 0.2 mm^{-1}**
- μ_s = 10.0 mm^{-1}
- g=0.9
- n_{rel} = 1.4
- Isotropic emitter, z = 24.75

Roadmap for today

μ_a $\longleftrightarrow$ absorption

μ_s, μ_s' $\longleftrightarrow$ scattering

L $\longleftrightarrow$ radiance

ϕ $\longleftrightarrow$ fluence (energy density)

radiative transport equation

diffusion equation

$\Rightarrow$ *boundary conditions*

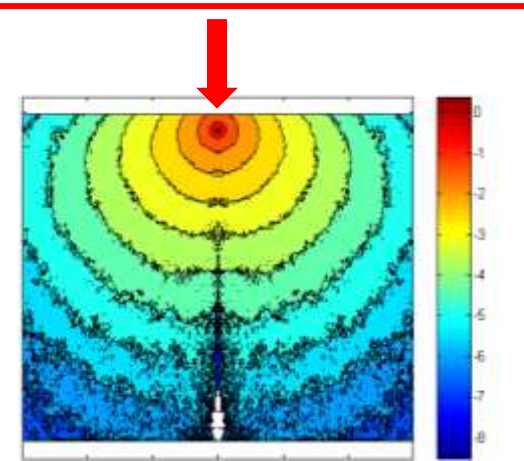
---

reflectance measurements in space and time

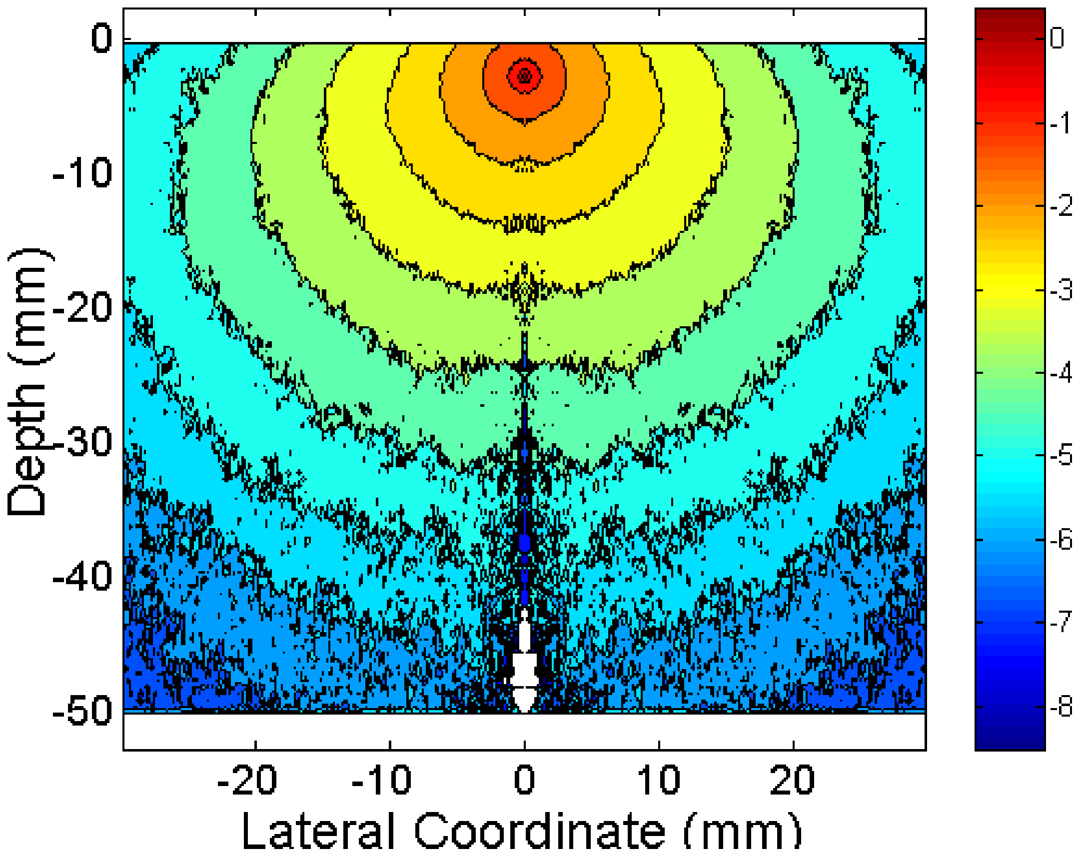
steady-state

pulsed

sinusoidally-modulated



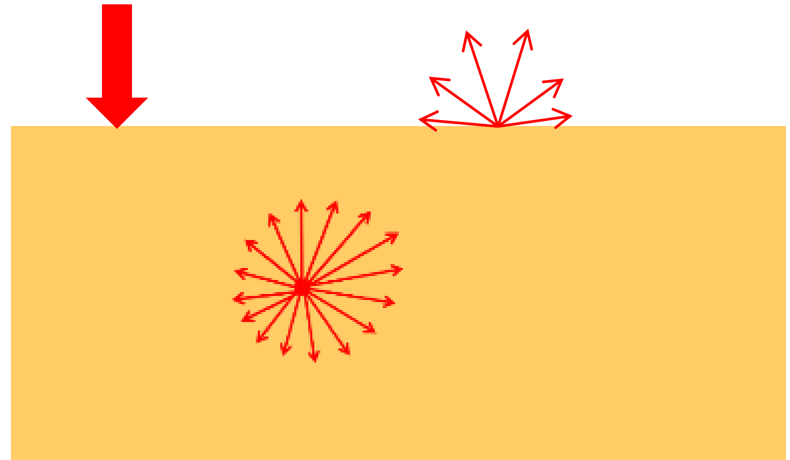
Fluence from an isotropic point source: Theoretical vs. Monte Carlo simulation



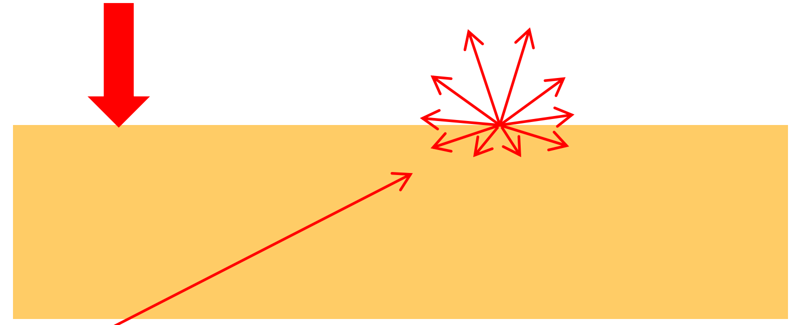
- **μ_a = 0.01 mm^{-1}**
- μ_s = 10.0 mm^{-1}
- g=0.9
- n_{rel} = 1.4
- Isotropic emitter, z=2.75 mm

Exact boundary condition for the photo-diffusion equation

index-matched:
no light heading downward at boundary



index-mismatched:
downward irradiance from Fresnel reflections



But highly anisotopic!

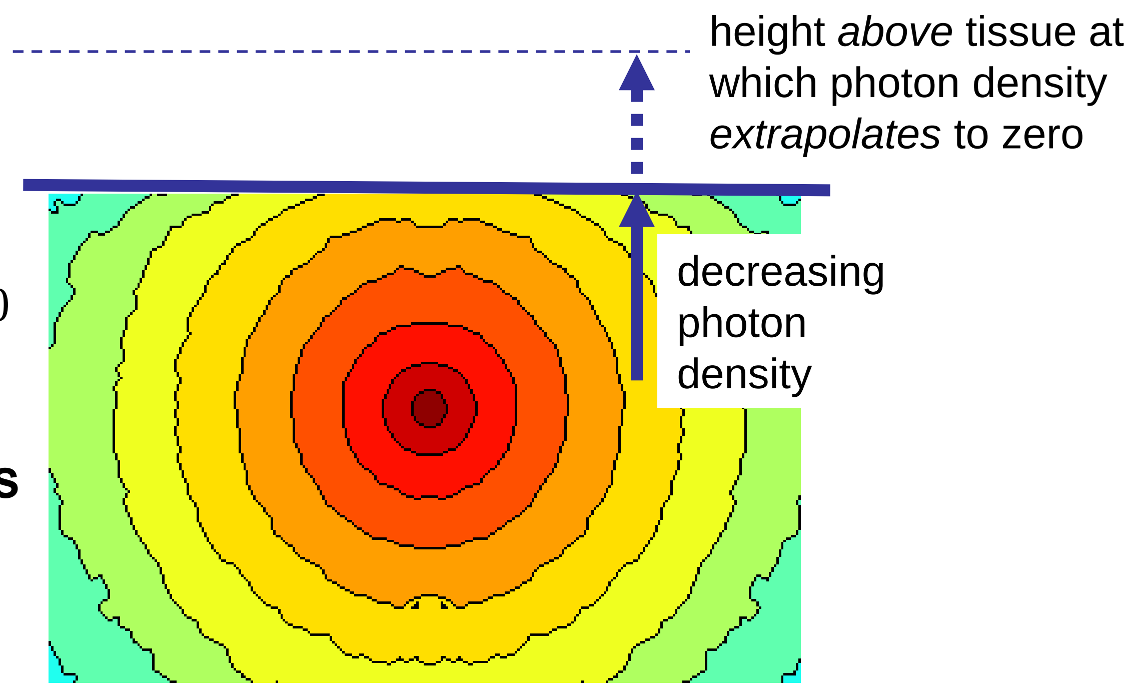
Compromise with diffusion approximation, and get…

How to write the boundary condition: options

Partial-Current BC:

$$\left.\frac{\partial \Phi}{\partial z}\right|_{z=0} = \frac{1}{2AD} \left.\Phi\right|_{z=0}$$

Where A (dimensionless) is the 'internal reflection coefficient'

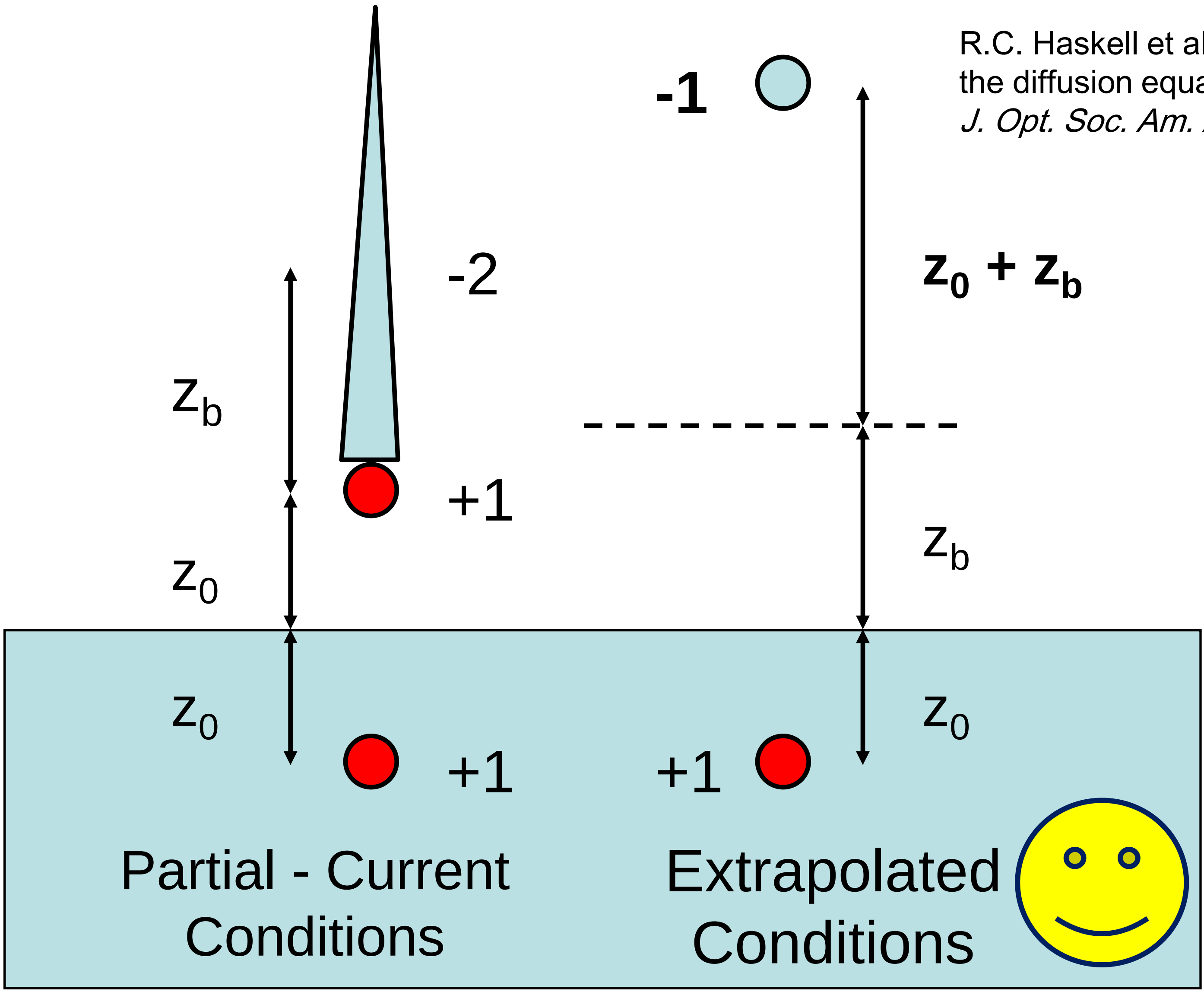


This motivates the "extrapolated-boundary" condition:

Extrapolated BC: $$\left.\Phi\right|_{z=-2AD} = 0$$

Image solutions for the partial-current and extrapolated boundary conditions

R.C. Haskell et al., "Boundary conditions for the diffusion equation in radiative transfer," *J. Opt. Soc. Am. A,* **11:**2727-2741 (1994).

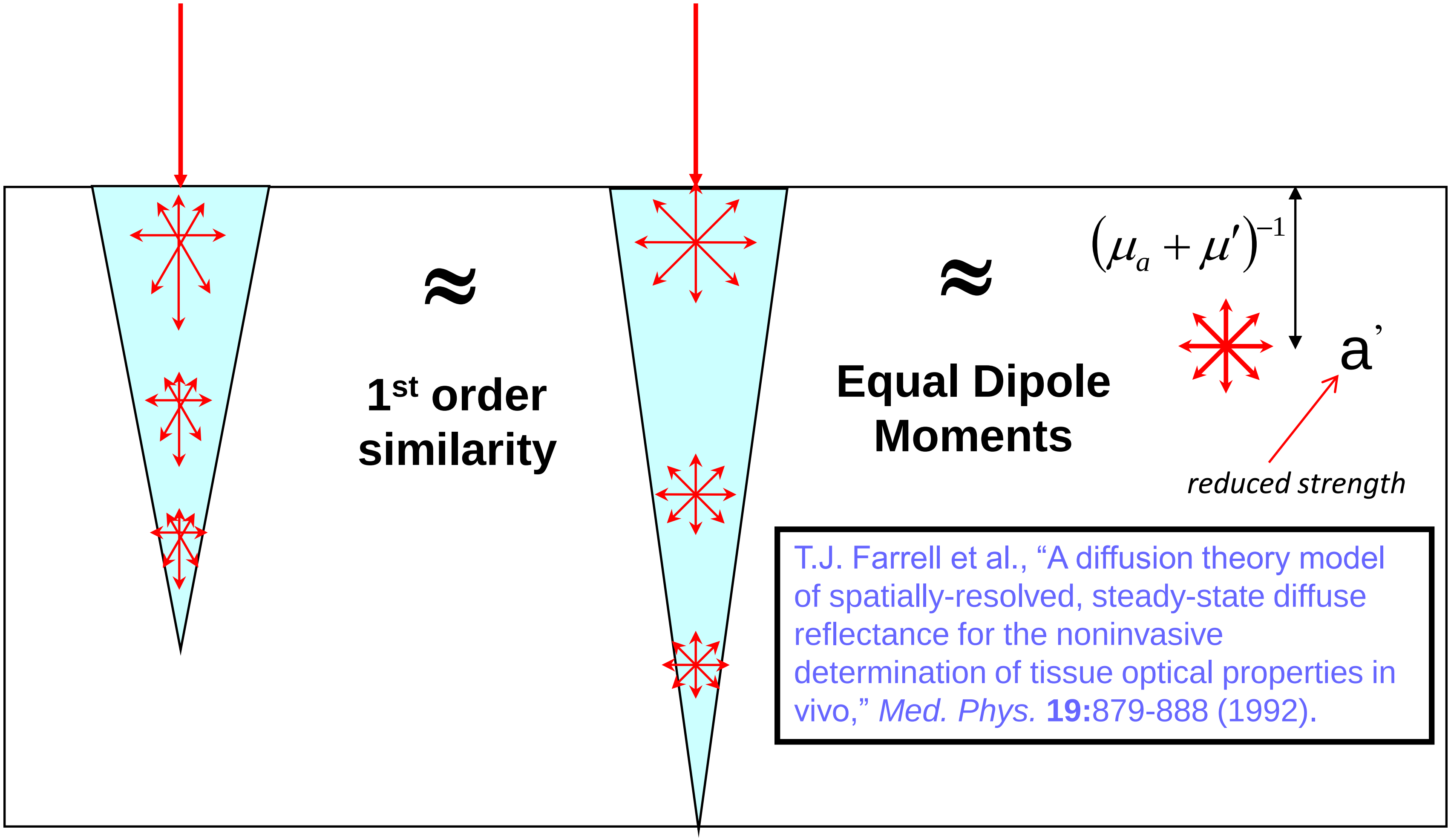


How to model an incident laser beam

$$I_{unatten} = I_0 e^{-(\mu_a + \mu_s) z}$$

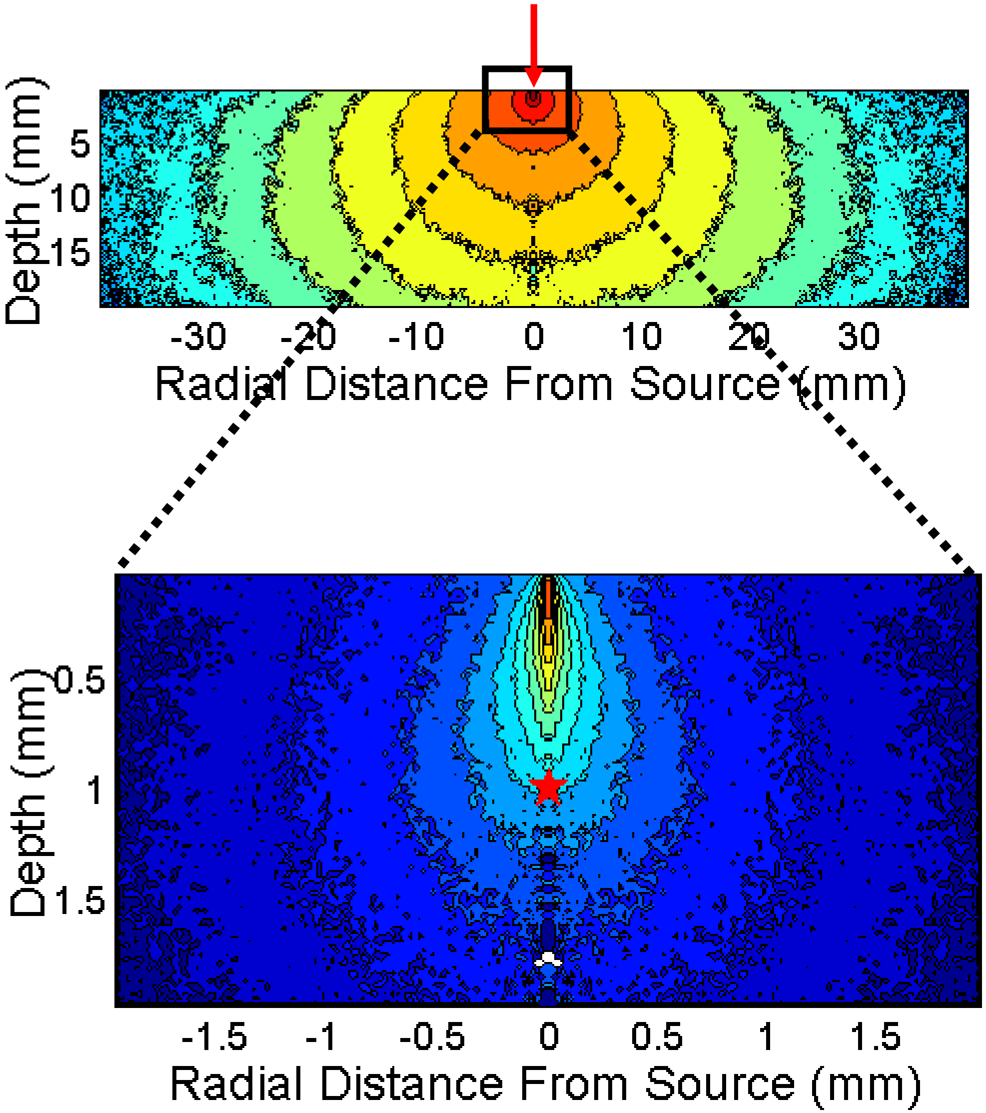
$$I_{unatten} = I_0 e^{-(\mu_a + \mu_s') z}$$

buried point source



T.J. Farrell et al., "A diffusion theory model of spatially-resolved, steady-state diffuse reflectance for the noninvasive determination of tissue optical properties in vivo," *Med. Phys.* **19:**879-888 (1992).

Monte Carlo simulation of normally-incident beam



- **μ_a = 0.01 mm^{-1}**
- μ_s = 1.0 mm^{-1}
- g=0.9
- n_{rel} = 1.4

star indicates depth of "equivalent" point source from previous slide

Roadmap for today

μ_a $\longleftrightarrow$ absorption

μ_s, μ_s' $\longleftrightarrow$ scattering

L $\longleftrightarrow$ radiance

ϕ $\longleftrightarrow$ fluence (energy density)

radiative transport equation

diffusion equation

boundary conditions

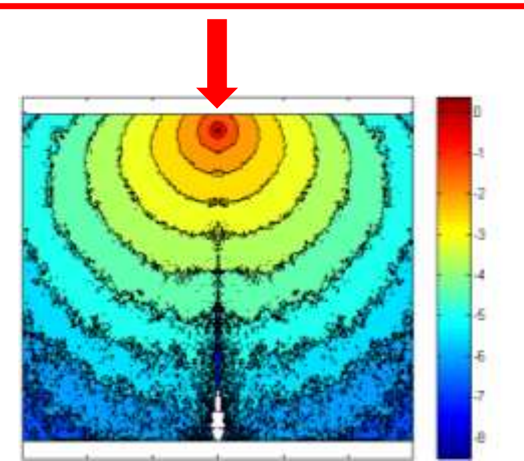
---

reflectance measurements in space and time

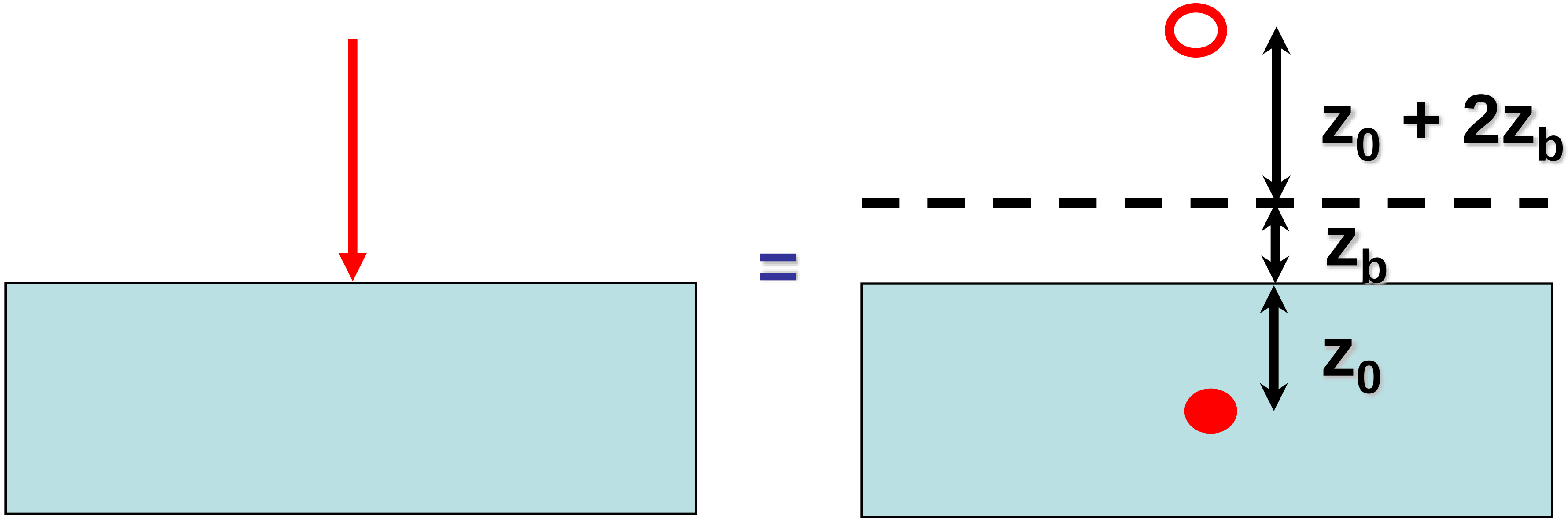
steady-state

pulsed

sinusoidally-modulated



Diffusion theory can be used to perform quantitative, noninvasive tissue spectroscopy

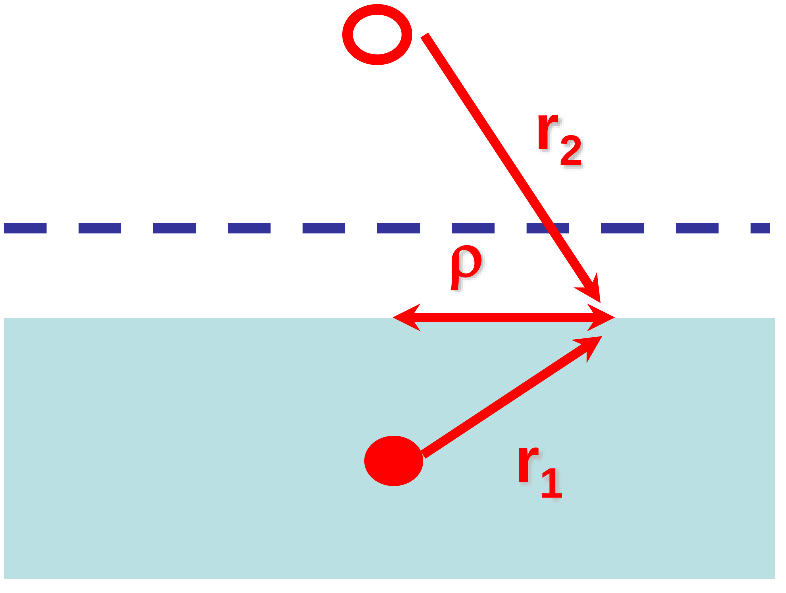


$$\Phi_{in} = \Phi_{source} + \Phi_{image}$$

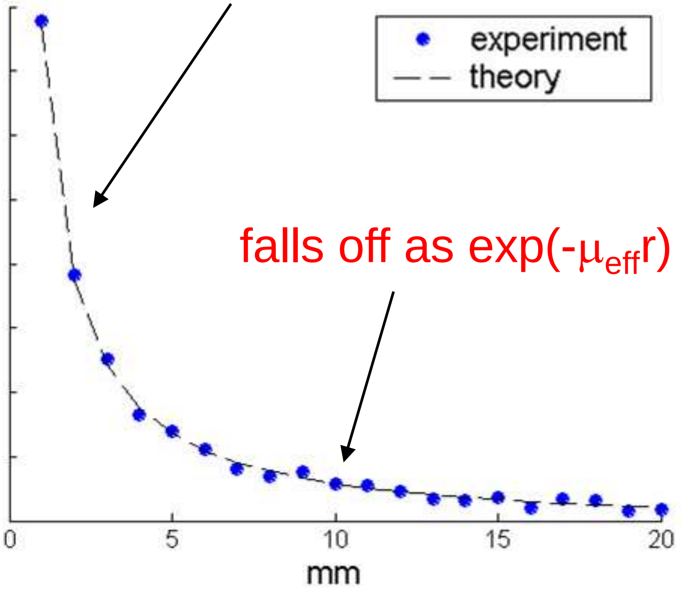
$$= \frac{1}{4\pi D}\left(\frac{\exp(-\mu_{eff} r_{source})}{r_{source}} - \frac{\exp(-\mu_{eff} r_{image})}{r_{image}}\right)$$

infinite-boundary Green's function

Spatially-resolved diffuse reflectance yields estimates of scattering and absorption coefficients



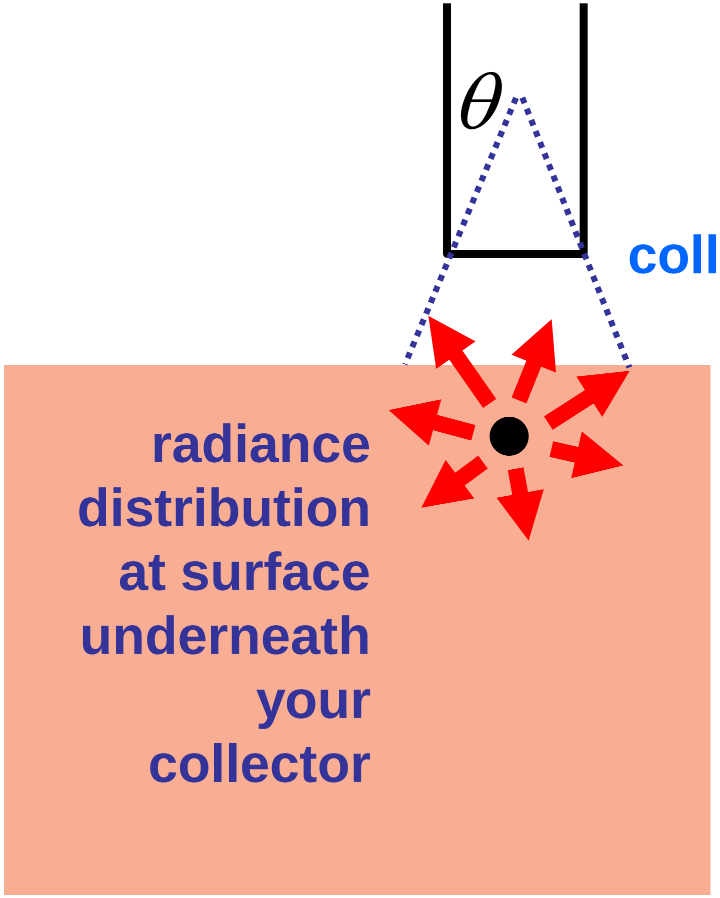
dominated by scattering (1/Dr)



falls off as exp(-μ_{eff}r)

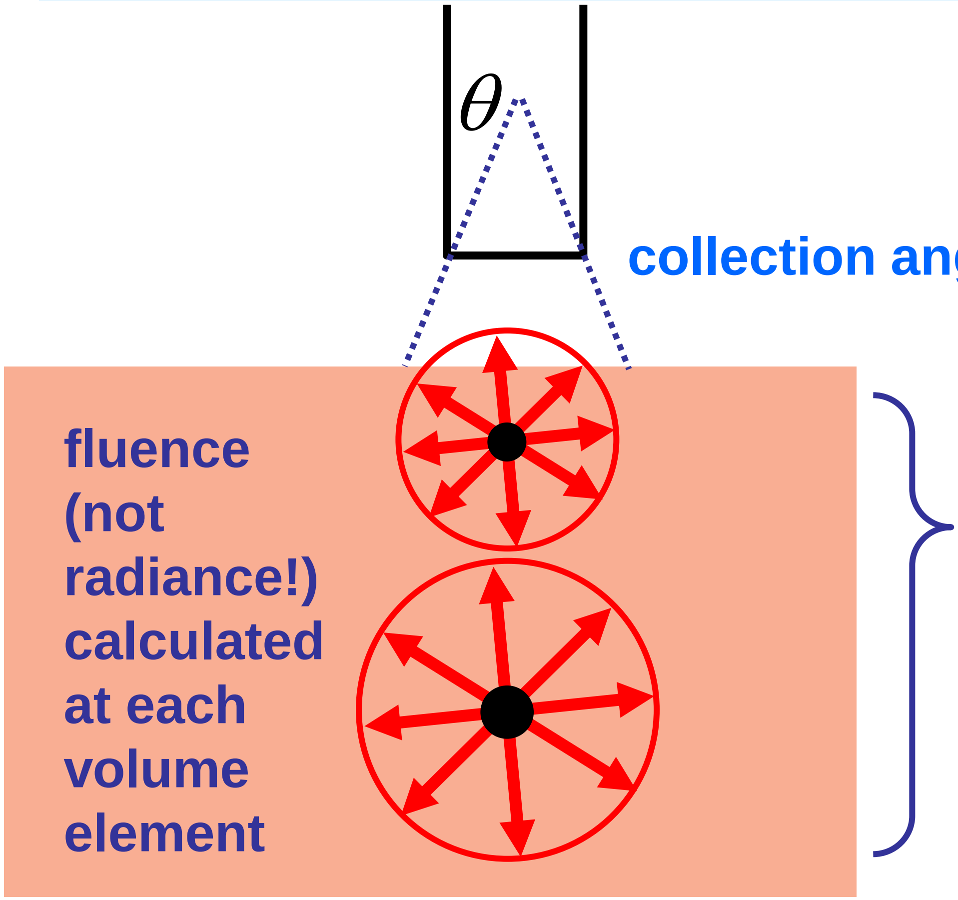
$$\Phi(\rho) = \frac{1}{4\pi D}\left(\frac{\exp(-\mu_{eff}\, r_1(\rho))}{r_1(\rho)} - \frac{\exp(-\mu_{eff}\, r_2(\rho))}{r_2(\rho)}\right)$$

What do you actually detect?
Part I: What is truly happening



$$E_{out} = \int_{\hat{\mathbf{s}}\cdot\hat{\mathbf{n}}\geq\cos\theta} T_{Fresnel}(\hat{\mathbf{s}})L(\mathbf{r},\hat{\mathbf{s}})(\hat{\mathbf{s}}\cdot\hat{\mathbf{n}})\,d\Omega$$

What do you actually detect?
Part II: What you can model using diffusion theory



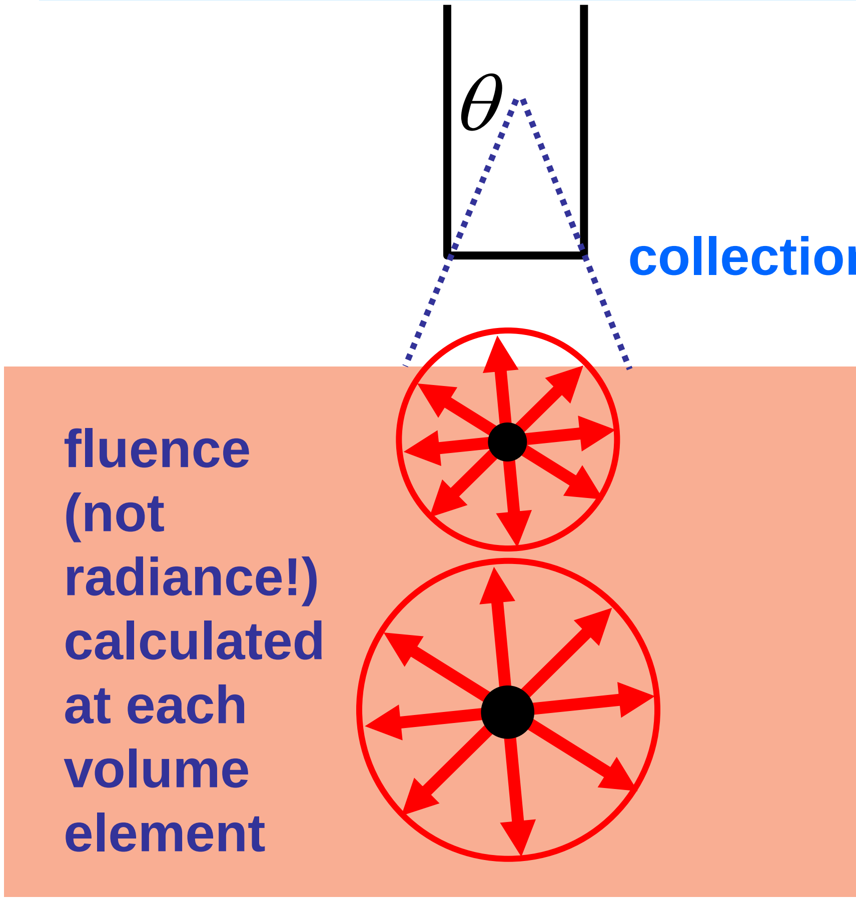
gradient of fluence indicates net photon flow direction:

$$\mathbf{j}(\mathbf{r}) = -D\nabla\Phi(\mathbf{r})$$

Fick's Law for optical diffusion

- Detected signal usually assumed proportional to fluence, flux, or some linear combination
- Usually only a relative measurement (to other locations or times)

One example of a formula



collection angle θ

Formula for measured reflectance (particular case of index mismatch 1.0/1.4, fiber with NA of about 0.22):

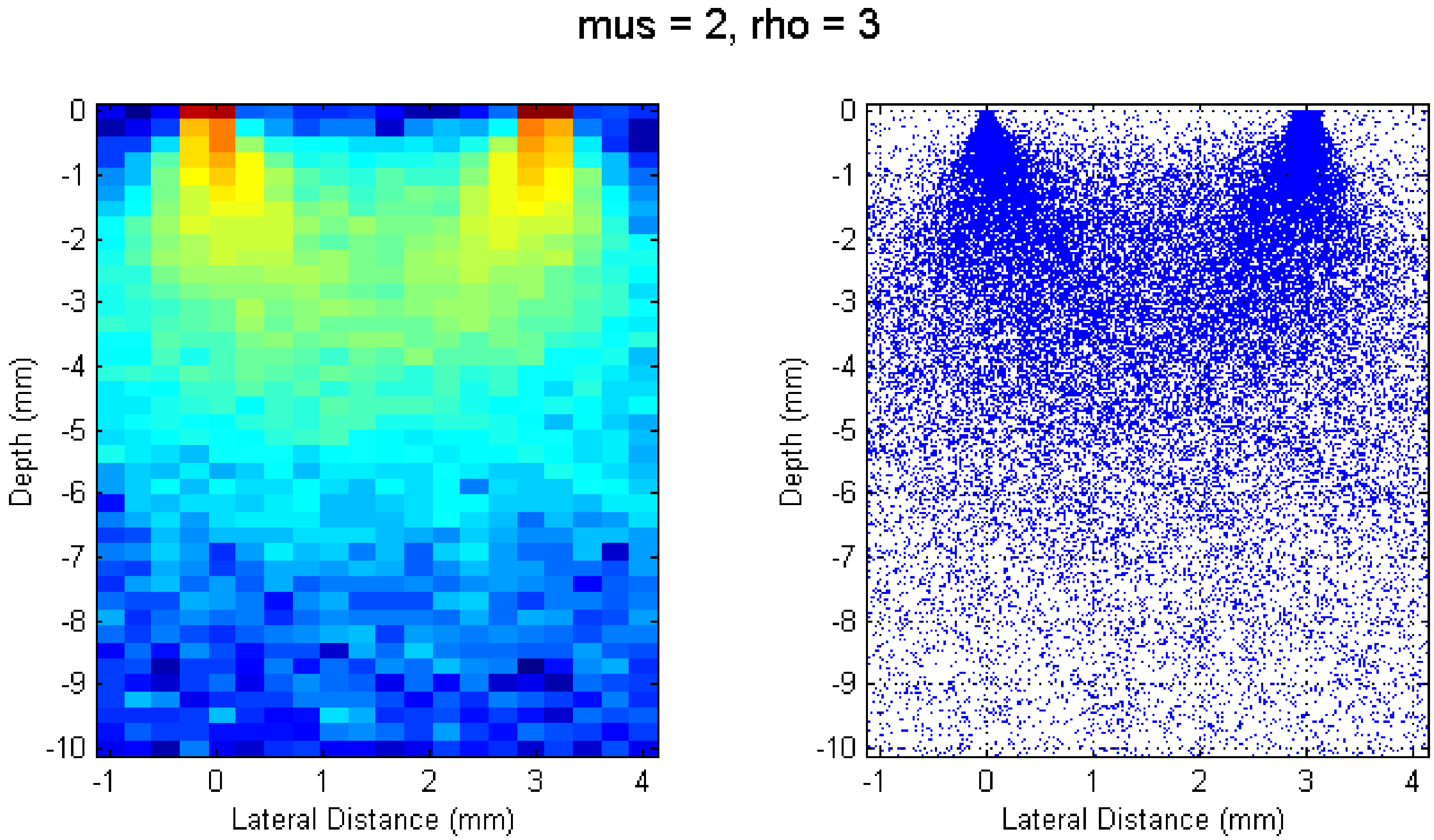
$$R = 0.118\Phi + 0.306 R_f$$

fluence term

flux term

A. Kienle and M. S. Patterson, “Improved solutions of the steady-state and the time-resolved diffusion equations for reflectance from a semi-infinite turbid medium,” JOSA A 14(1), 246-254 (1997).
R. C. Haskell et al., “Boundary conditions for the diffusion equation in radiative transfer,” JOSA A 11(10), 2727-2741 (1994).

Optical fibers preferentially collect photons that have interrogated specific tissue regions



- $\mu_a = 0.01\ mm^{-1}$
- $\mu_s = 2.0\ mm^{-1}$
- g=0.9

Alternatives to diffusion theory

- More refined mathematical models
  - More terms (higher angular dependence) retained in the expansion of the transport equation
  - Numerical solution of the transport equation
  - Exact solutions to Maxwell's equations (preserves coherence, polarization)
- Simulation
  - Monte Carlo methods -> 'Lookup tables'
- Empirical relationships between light distributions and known conditions (i.e., calibration)
  - Multivariate methods, neural networks