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Laser-Tissue Interactions

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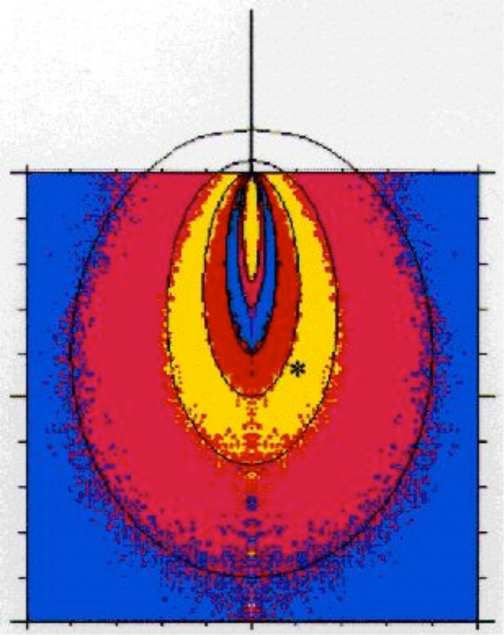

1. Introduction
2. Photochemical
3. Photothermal
4. Photomechanical

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OUTLINE

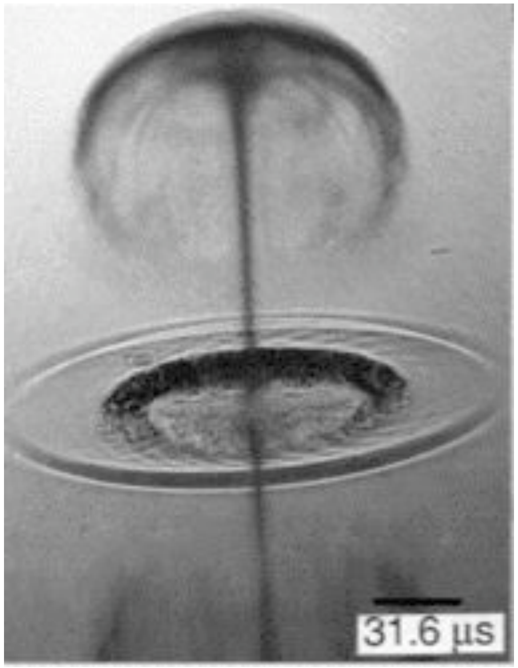
13:00 - 14:30	**Introduction**
	Photochemical
14:30 - 15:00	Coffee
15:00 - 16:30	**Photothermal**
	Photomechanical
16:30 - 16:45	break
16:45 - 17:30	**Discussion**

1. Where tissue affect photons...

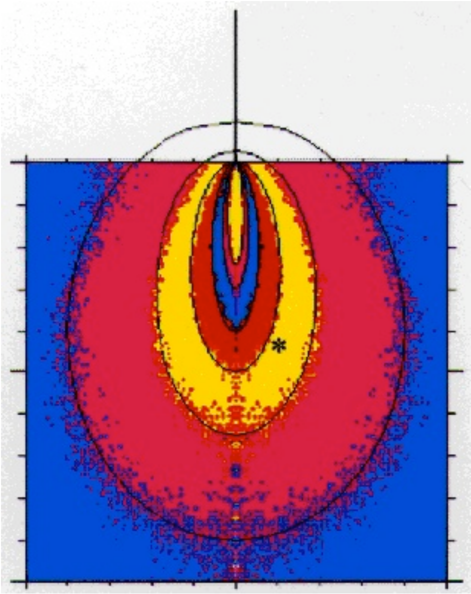
diagnostic sensing, imaging, and spectroscopy,

2. Where photons affect tissues….

surgical and therapeutic cutting, dissecting, machining, coagulating, welding and oxidizing

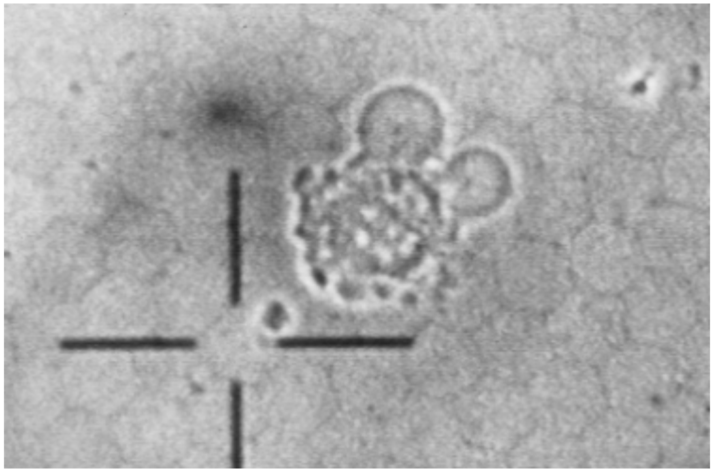


Micromachining with lasers

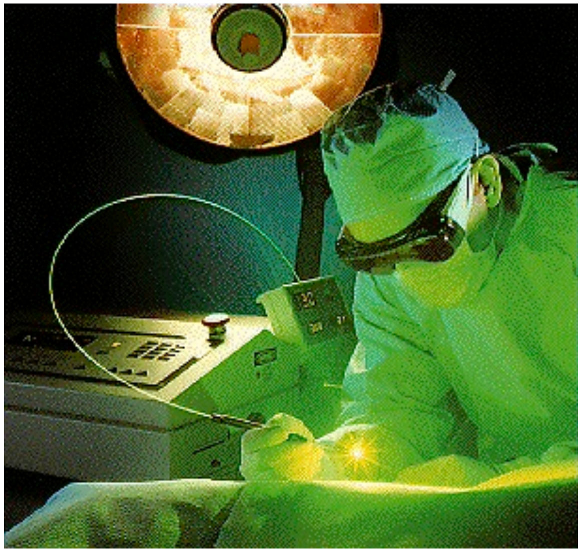


Computer simulations of laser effects in tissues

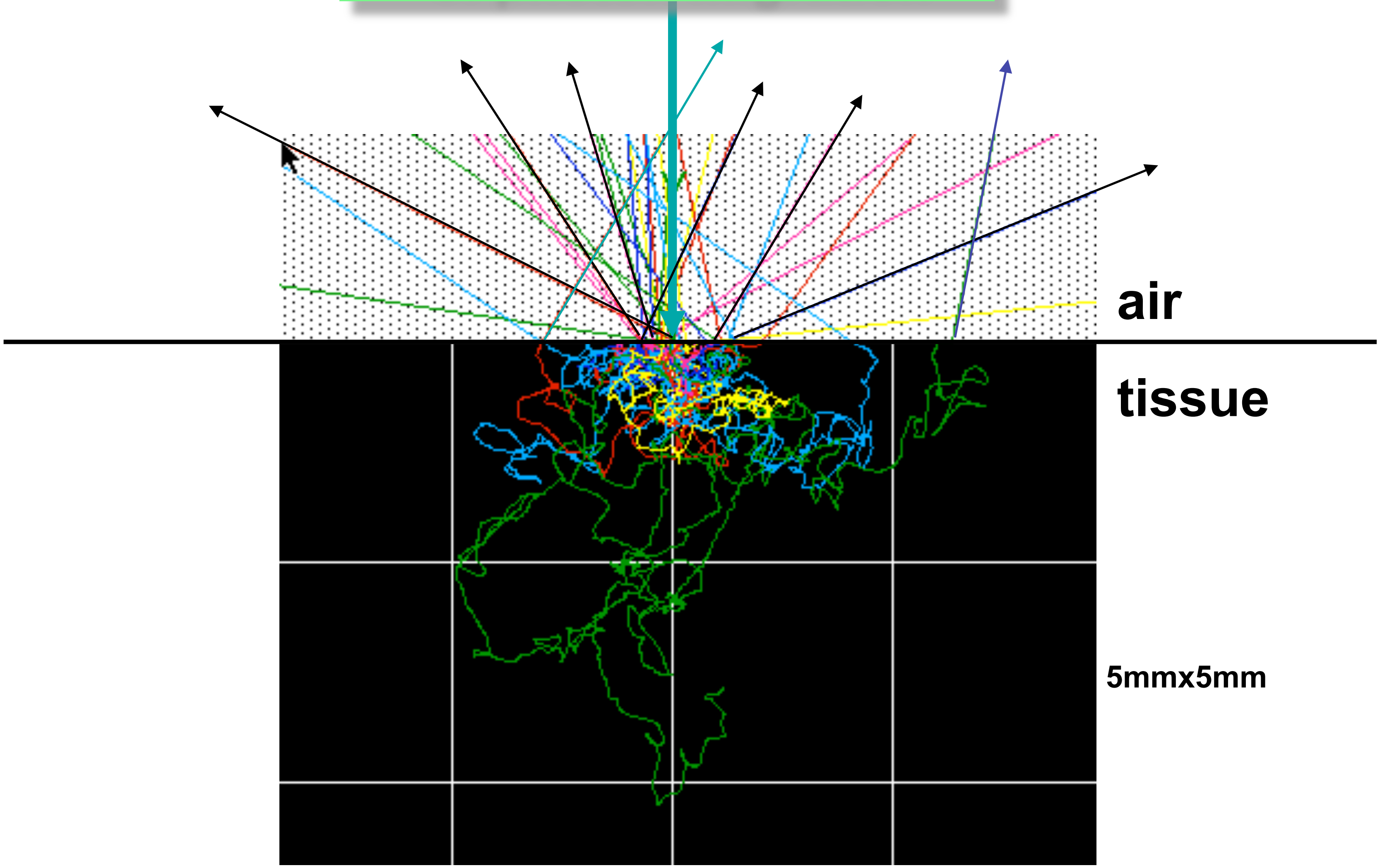
Photodynamic therapy of cancer



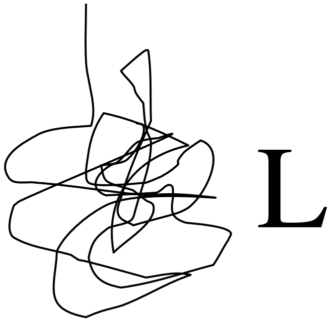
Laser surgery



Monte Carlo simulation of photon migration



esophagus @ 630 nm wavelength

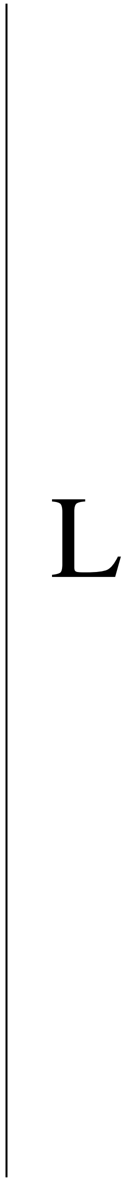


A photon's path is tortuous due to multiple scattering, *like a ball of string*.

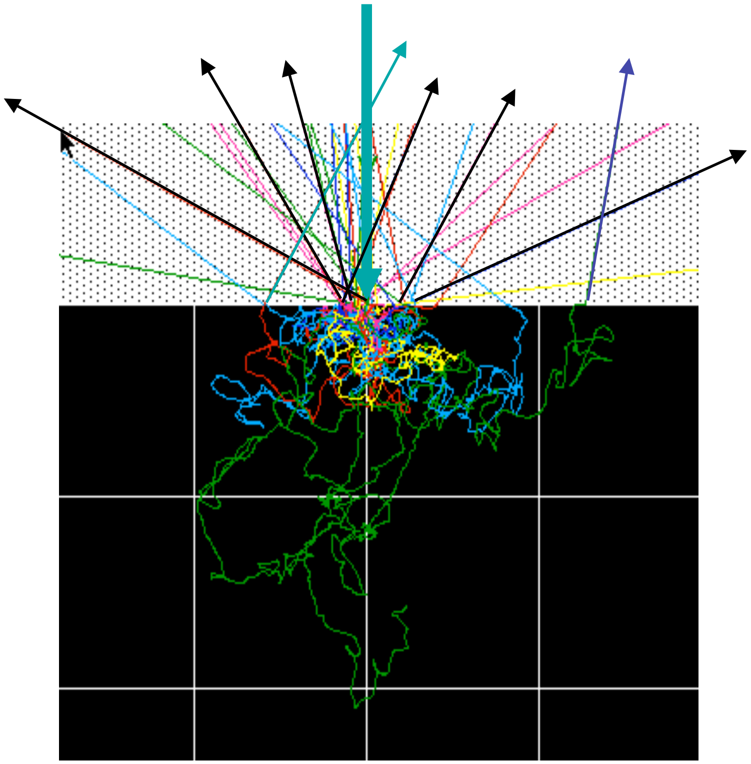
Nevertheless, there is a total pathlength L, *like the length of the string*.

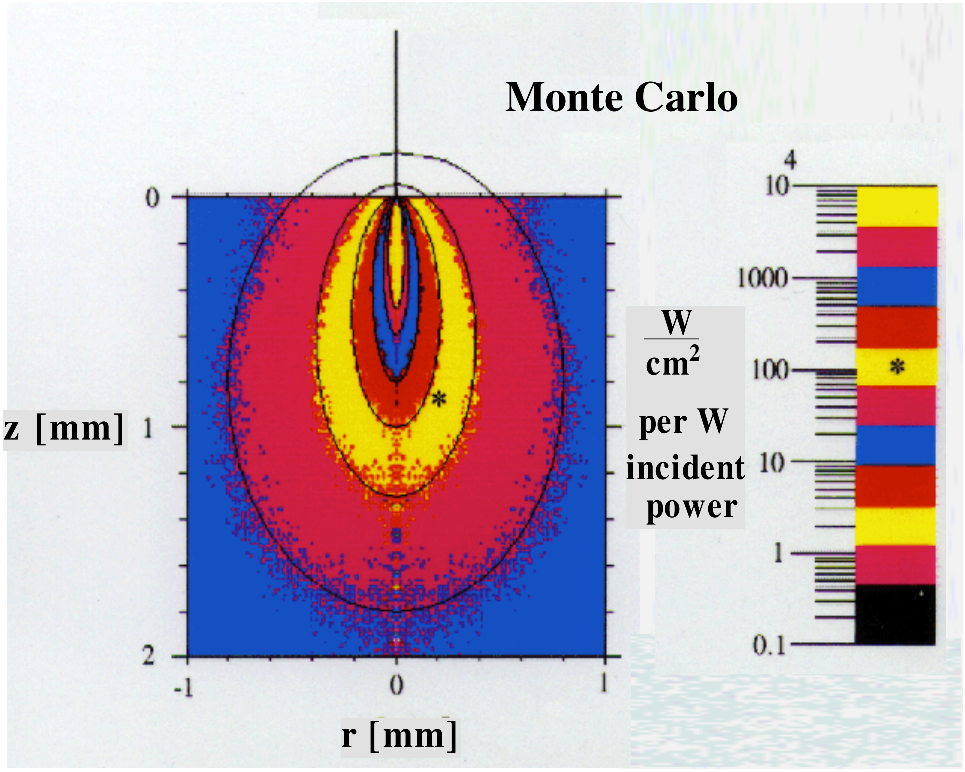
$$T = e^{-\mu_a L}$$

Mean free path = $1/\mu_a$



photon diffusion





Photochemical

Photothermal

Photomechanical

Concentration

Fluence rate [W/cm^2]

$$C = \frac{F}{c}$$

[J/cm^3]

Speed of light [cm/s]

Concentration

Fluence rate [W/cm^2]

$$C = \frac{F}{c}$$

[J/cm^3]

Speed of light [cm/s]

Number density of photons

[ph/J]

Wavelength [m]

$$C = \frac{F}{c}\,\frac{\lambda}{hc}$$

[#photons/cm^3]

Speed of light,[cm/s]

Planck's constant [J m]

$$1\ W/cm^3 = 1.1\times 10^{10}\ photons/cm^3$$

Concentration
of photons

[cm^3/liter]

$$C = \frac{F}{c}\,\frac{\lambda}{hc}\,\frac{1000}{N_{av}}$$

[moles/liter]

[1/mole]

$$\begin{aligned} 1\ W/cm^3 &= 1.1\times 10^{10}\ photons/cm^3 \\ &= 1.8\times 10^{-13}\ moles/liter \end{aligned}$$

Energy deposition

Fluence rate [W/cm^2]

time [s]

$$Q = \mu_a F t$$

[J/cm^3]

Absorption coefficient [1/cm]

Temperature rise

Fluence rate [W/cm²]

$$\Delta T = \mu_a F t \frac{1}{\rho C_p}$$

[°C]

specific heat [J/(g K)

density [g/cm³]

Absorption coefficient [1/cm]

photochemistry

(moles/liter)/(J/cm^3 absorbed)

J/cm^3 absorbed by photochemical reagent X

$$N = \mu_{a_x} F t \frac{\lambda}{hc} \frac{1000}{N_{av}} \Phi$$

# of photons participating in photochemistry

Absorption coefficient [1/cm]

of photochemical reagent X

Quantum efficiency

Stress, or pressure

Grüneisen coefficient
[dimensionless]

$$P = \mu_a F t \; \Gamma$$

$1\ [\mathrm{J/cm^3}] = 10$ bar

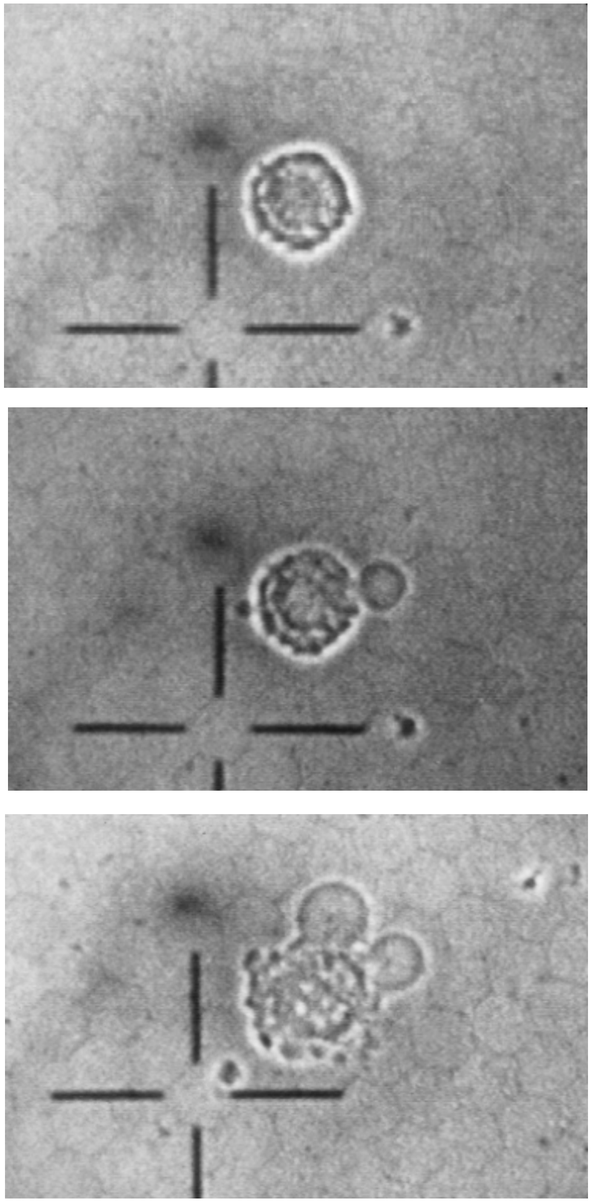
G = 0.12 at 25°C

--> 0.5 at higher temperatures

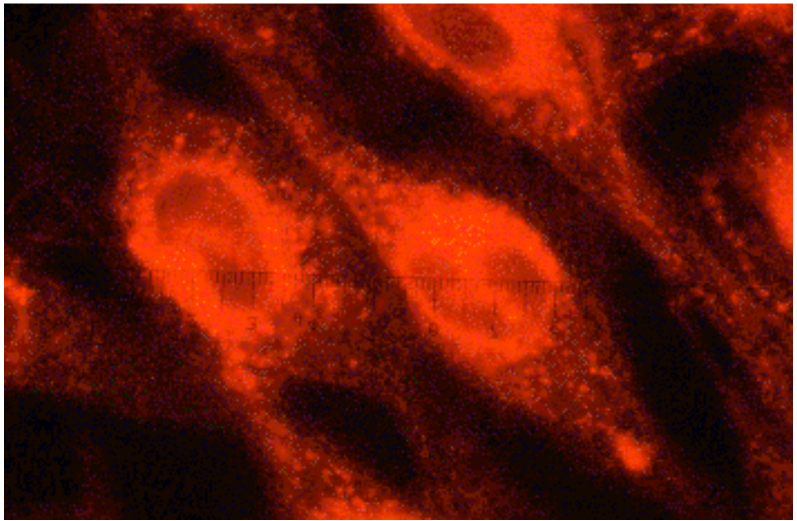
photochemical

$$N = \mu_{a_x} F t \frac{\lambda}{hc} \frac{1000}{N_{av}} \Phi$$

Photochemical effects …

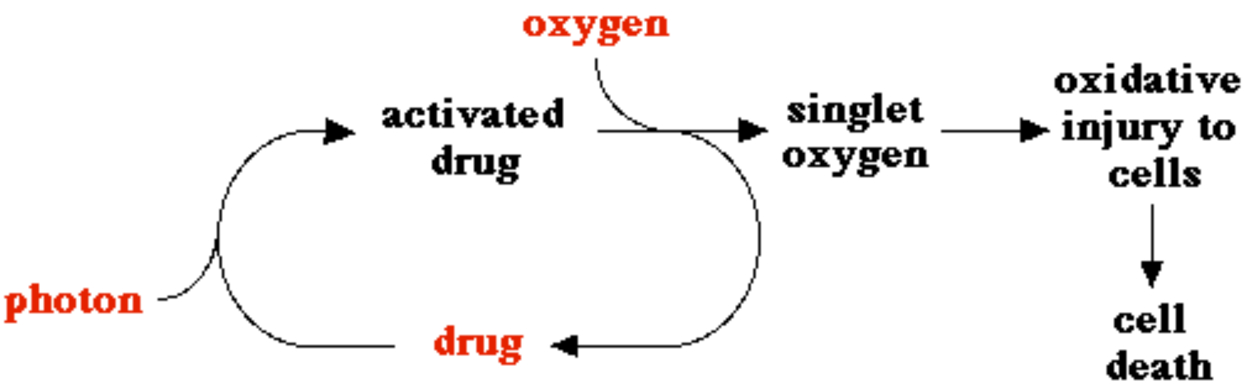


celulares de cáncer



celulares de cáncer con
fluorescent photosensitizer

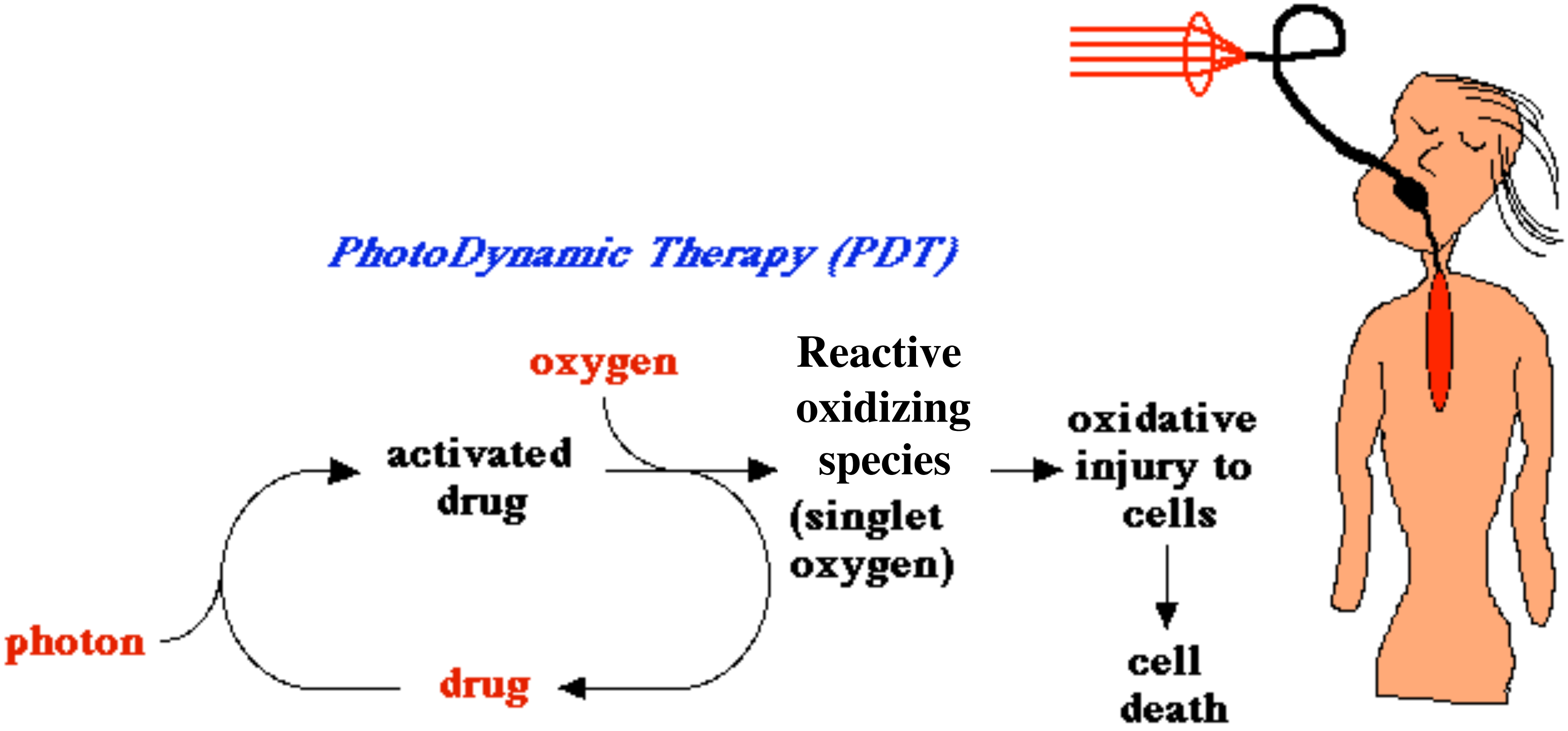
PhotoDynamic Therapy (PDT)



oxygen
activated drug
singlet oxygen
oxidative injury to cells
cell death
photon
drug

PDT

human treatment center



PDT

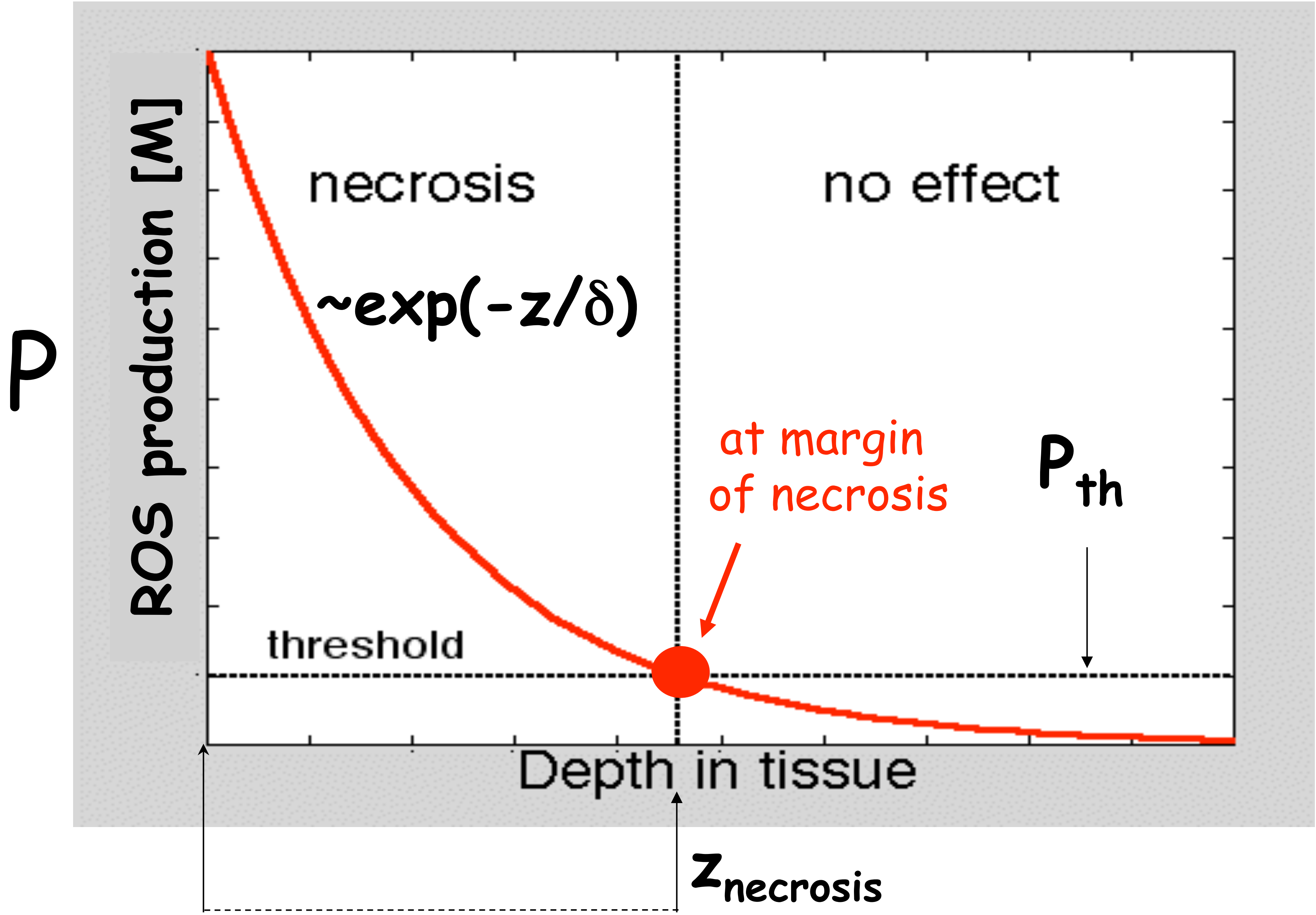
horse sarcoids

PDT

horse sarcoids

PDT

horse sarcoids

P
ROS production [M]
necrosis
no effect
~exp(-z/δ)
at margin of necrosis
P_{th}
threshold
Depth in tissue
$z_{necrosis}$

Production of oxidizing species

$$P_{th} = E \quad t \quad \varepsilon \quad C \quad \Phi \quad f_{kill} \quad e^{-z_{necrosis}/\delta}$$

Irradiance

Exposure time

Extinction coefficient of photosensitizer

Concentration of photosensitizer

Quantum yield of photosensitizer

Fraction of oxidizing species that attacks lethal sites

Light penetration

$$\boxed{P_{th} = E\ \ t\ \ \varepsilon\ \ C\ \ \Phi\ \ f_{kill}\ \ e^{-z_{necrosis}/\delta}}$$

$$\Downarrow$$

$$z_{necrosis} = \delta\left(-\log_e\left(\frac{E\ \ t\ \ \varepsilon\ \ C\ \ \Phi\ \ f_{kill}}{P_{th}}\right)\right)$$

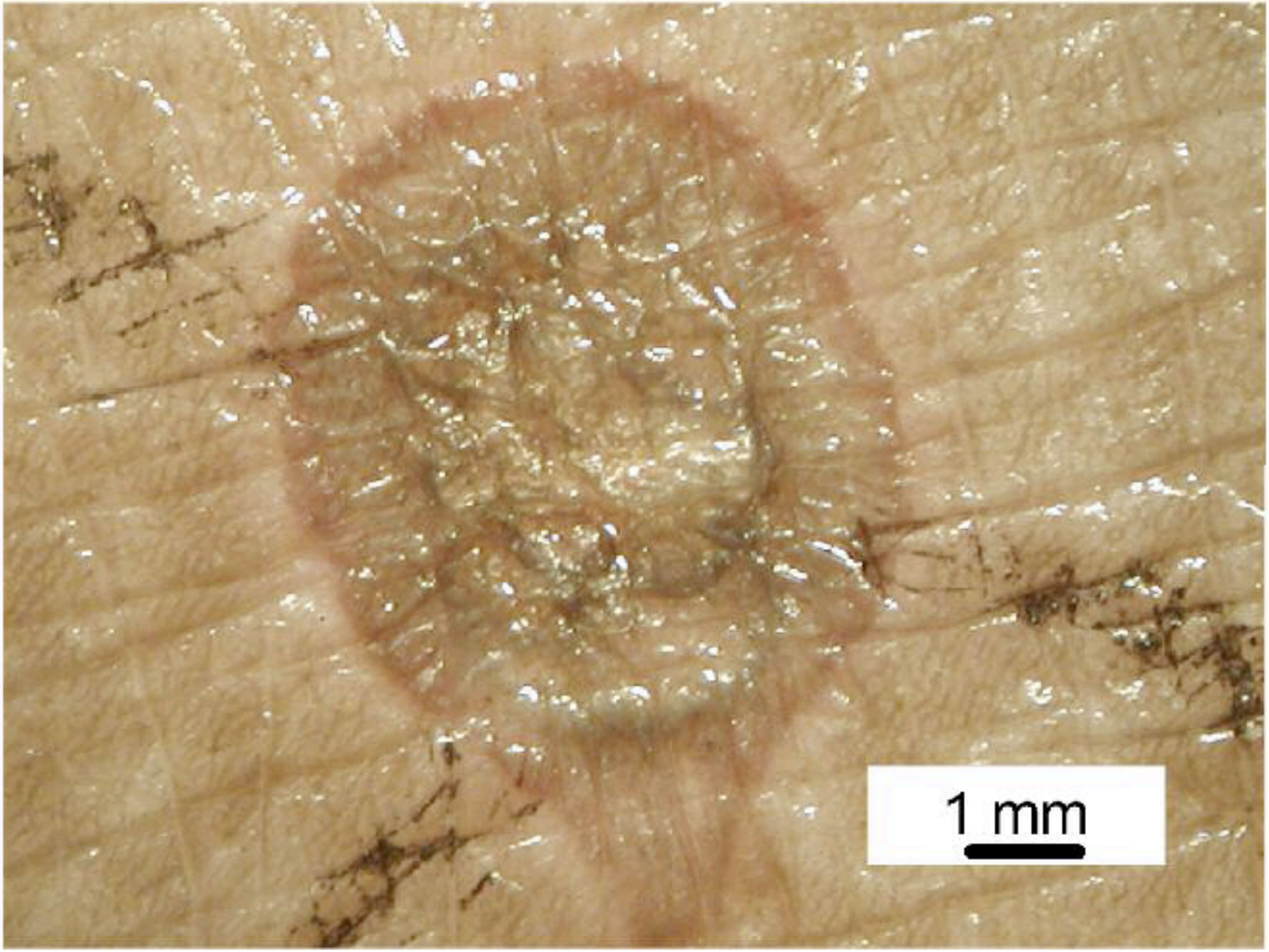
Optical
penetration depth

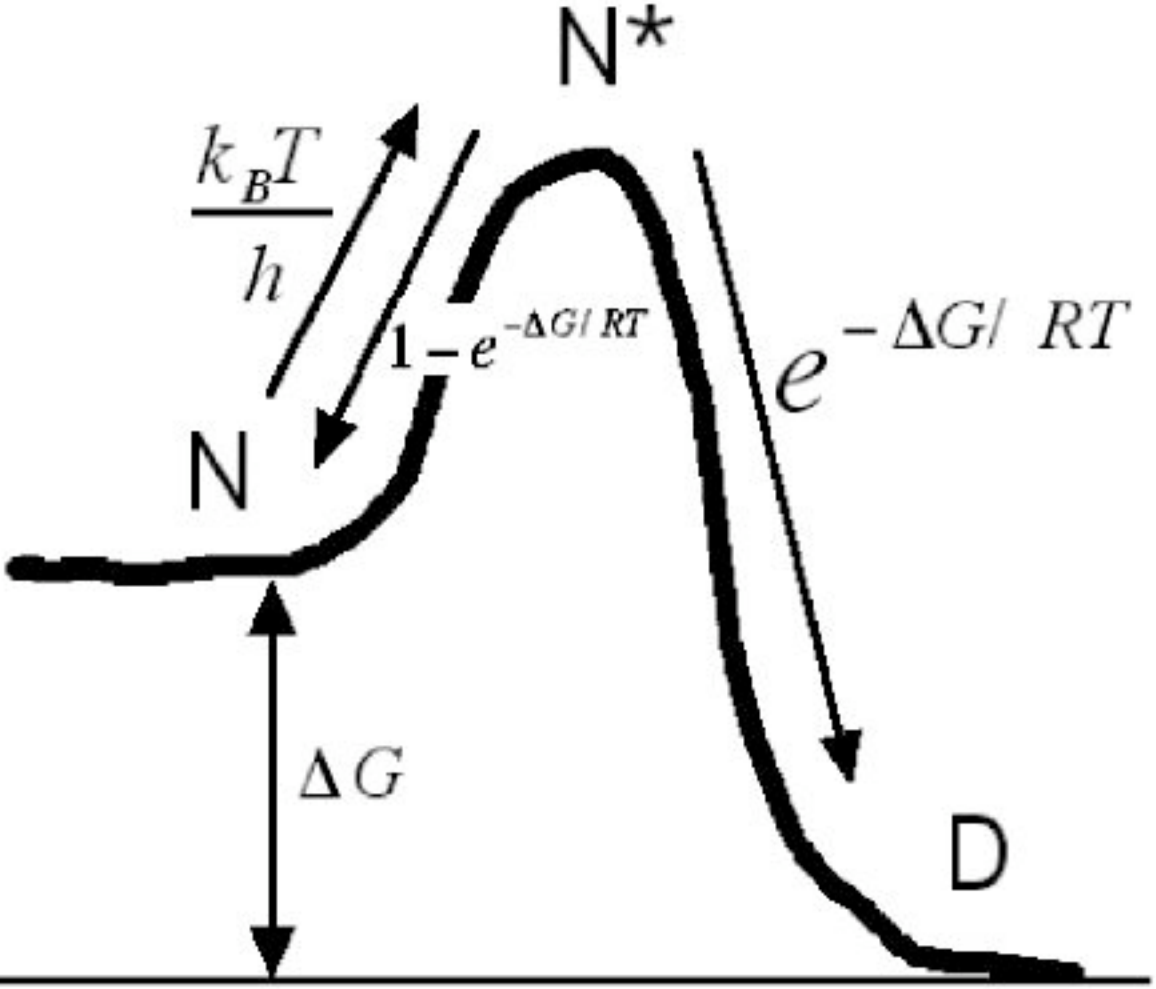
everything
else

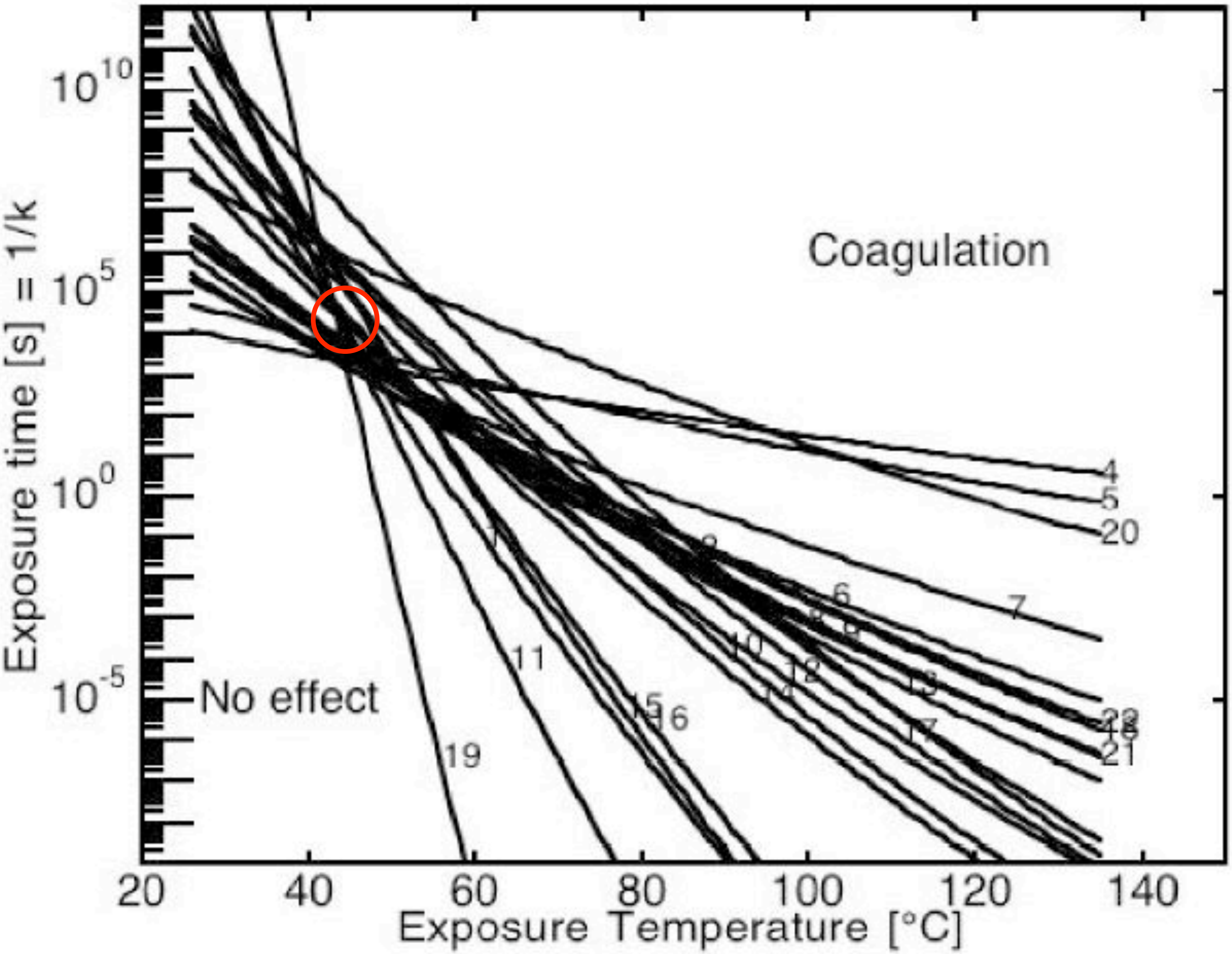
Depth of necrosis

phototermal

$$\Delta T = \mu_a F t \frac{1}{\rho C_p}$$


1 mm


N*
$\frac{k_B T}{h}$
$1 - e^{-\Delta G/RT}$
$e^{-\Delta G/RT}$
N
ΔG
D


Coagulation
No effect
Exposure time [s] = 1/k
Exposure Temperature [°C]
10^{10}
10^{5}
10^{0}
10^{-5}
20
40
60
80
100
120
140
1
3
4
5
6
7
8
9
10
11
12
13
14
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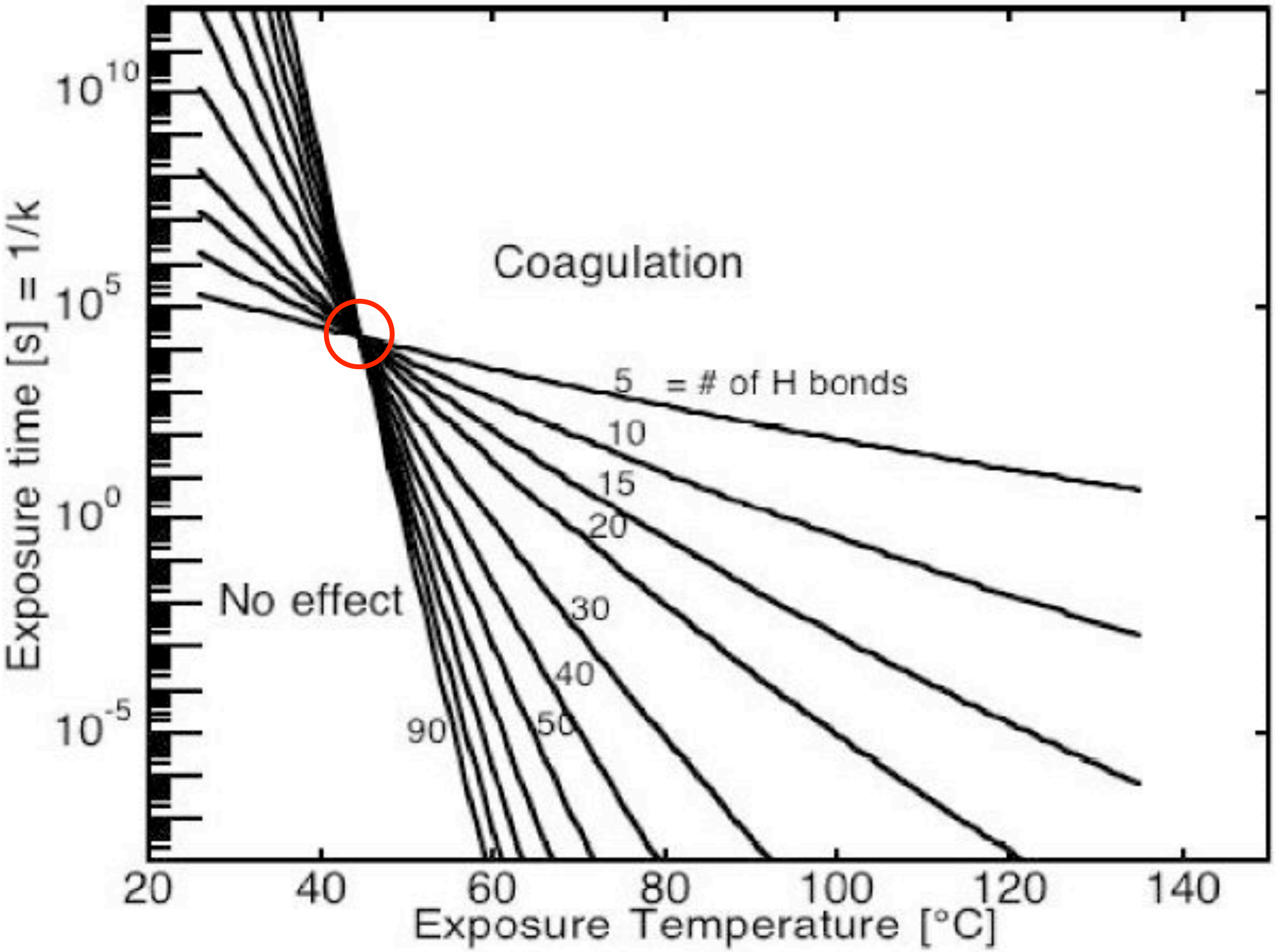
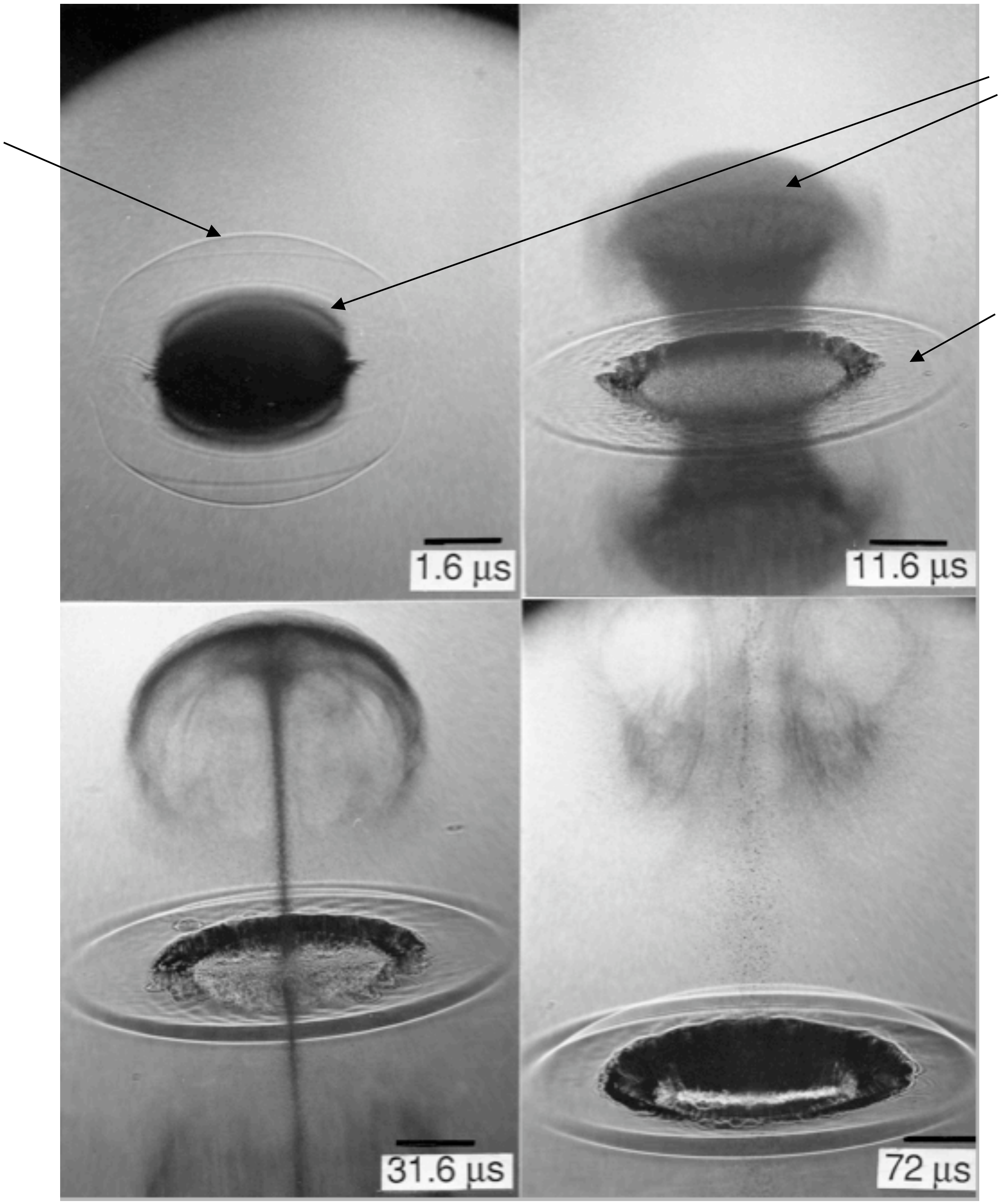
16
17
18
19
20
21
22



Exposure time [s] = 1/k
10^{10}
10^{5}
10^{0}
10^{-5}
Coagulation
No effect
5 = # of H bonds
10
15
20
30
40
50
90
20
40
60
80
100
120
140
Exposure Temperature [°C]

photomechanical

$$P = \mu_a F t \; \Gamma$$



Air pressure front

Explosive vaporization

Surface evaporation

Blow-off model

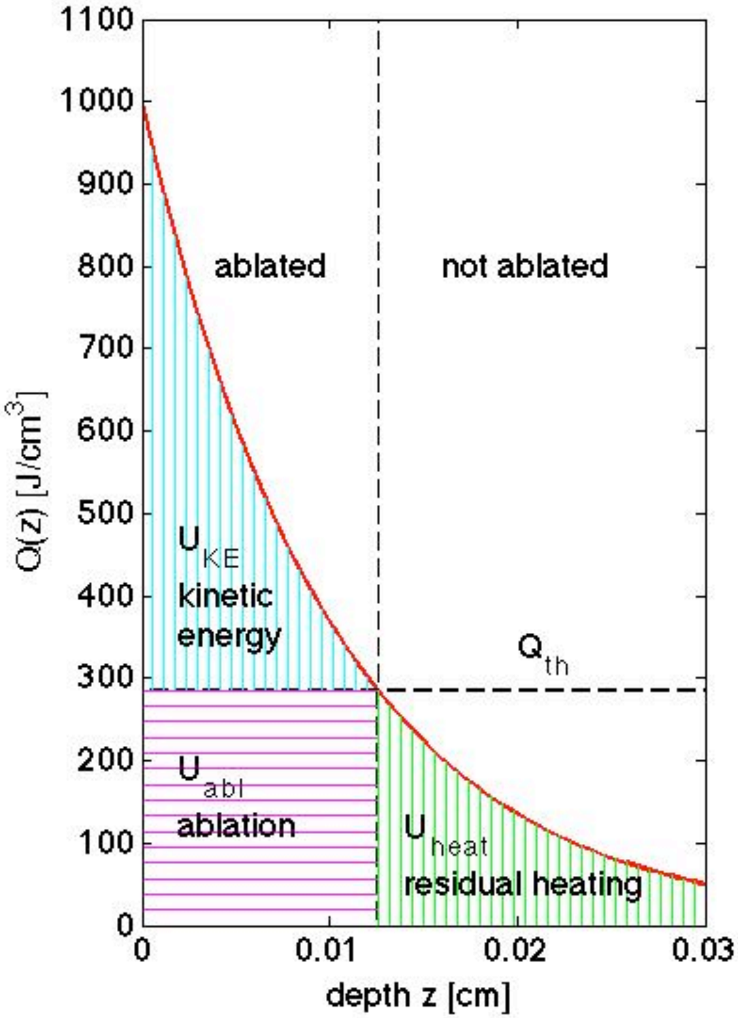
$$U_{KE} = U_p - U_{abl} - U_{heat}$$

$$U_{abl} = Q_{th} z_{abl}$$

$$U_{heat} = \frac{Q_{th}}{\mu_{a.eff}}$$

Energy
deposition
Q(z)

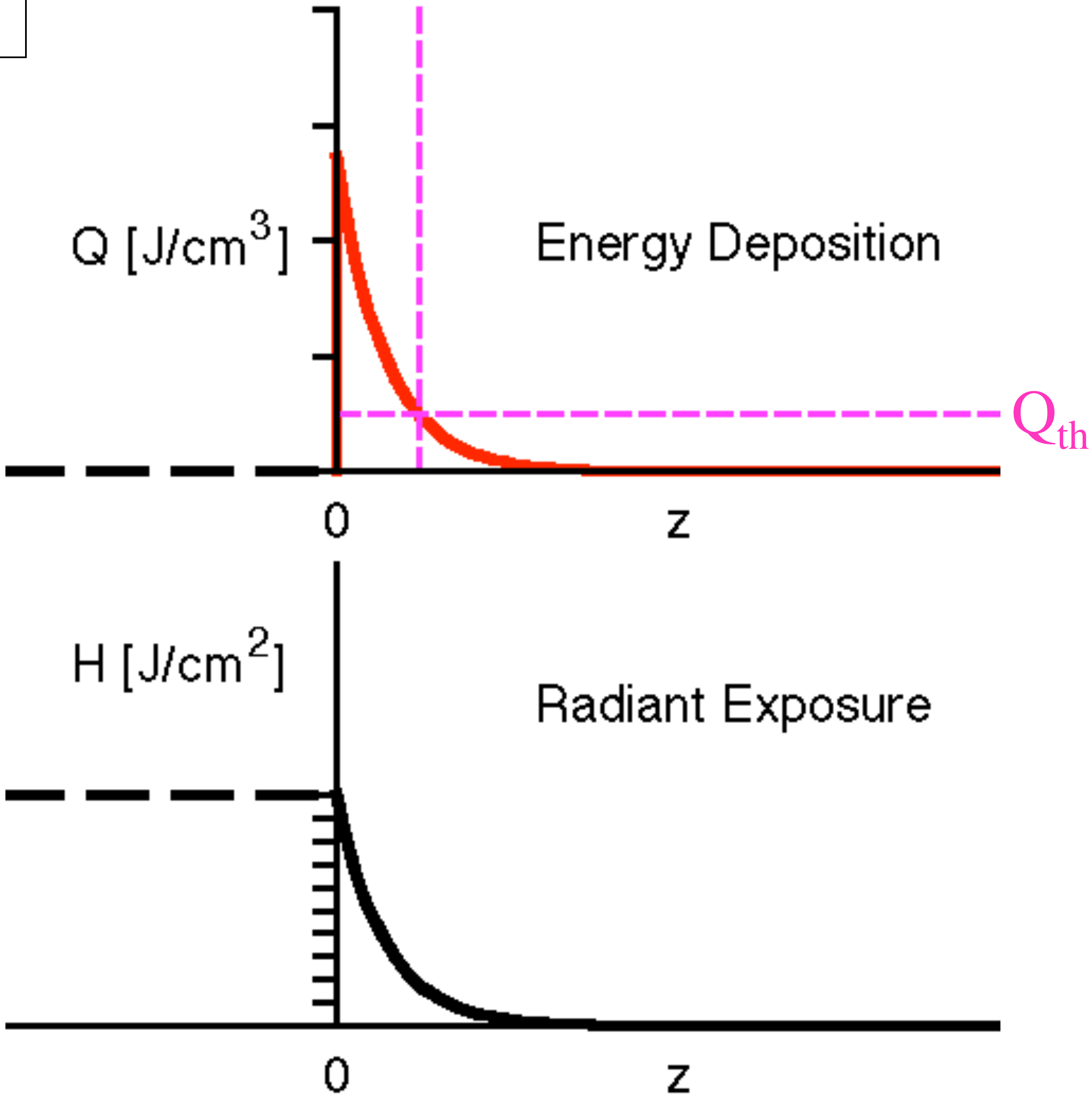
J/cm^3



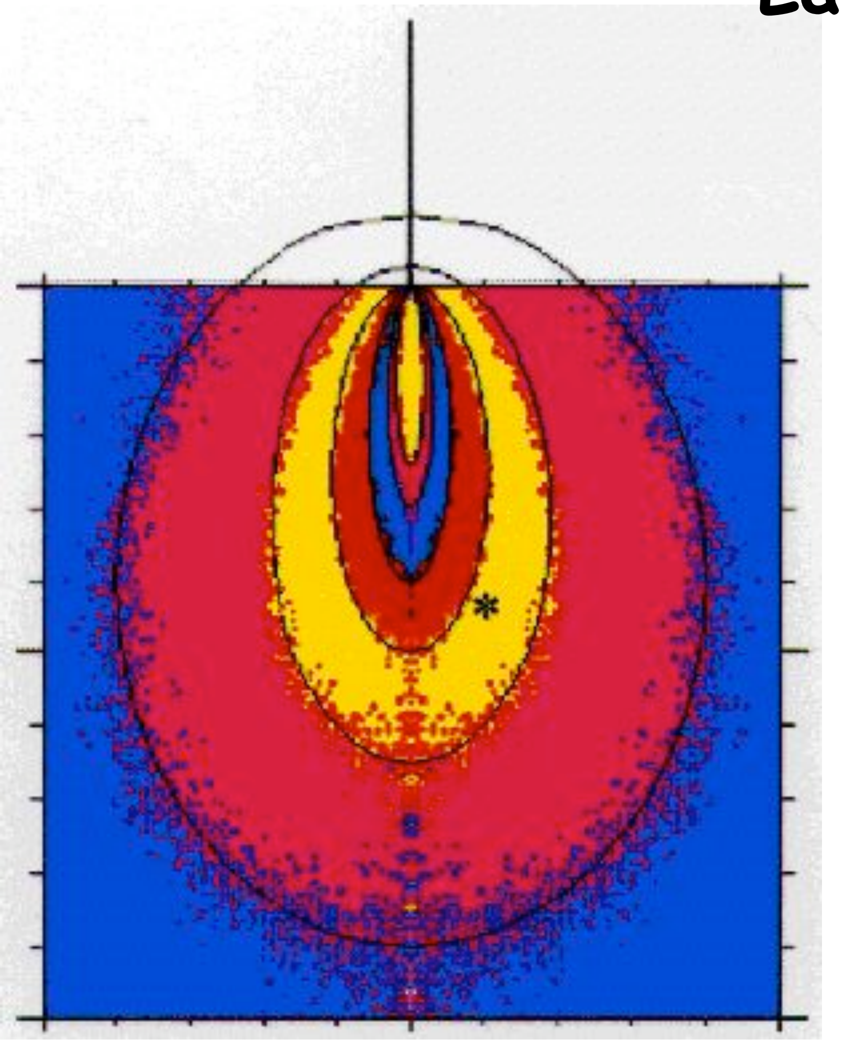
Depth in tissue, z [cm]

Blow-off model

$$Q = \mu_a H$$



Laser-Tissue Interactions



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photochemical

$$N = \mu_a F t \frac{\lambda}{hc} \frac{1000}{N_{av}} \boldsymbol{\Phi}$$

$$N_{abs} = \phi t \overset{\substack{\text{\# photons}\\ \downarrow}}{\frac{\lambda}{hc_0}} A \; \overset{\substack{\text{fraction absorbed}\\ \downarrow}}{(1-10^{-\varepsilon CL})}$$

ϕ = fluence rate [W/cm^2]

t = time of exposure [s]

c_0 = speed of light *in vacuum* 2.98x10^{10} [cm/s]

h = Planck's constant 6.626x10^{-34} [Js]

λ = wavelength [cm]

A = area illuminated by light [cm^2]

ε = extinction coefficient [cm^{-1}/M], M = moles/liter

C = concentration [M]

L = photon pathlength through medium [cm]

photons fraction absorbed

[W/cm^2] [s] [#/J] [cm^2] [cm^{-1}/M] [M] [cm]

$$N_{abs} = \boxed{\phi t \frac{\lambda}{h c_0} A} \left(1 - 10^{-\boxed{\varepsilon C L}}\right)$$

ϕ = fluence rate [W/cm^2]

t = time of exposure [s]

c_0 = speed of light *in vacuum* 2.98×10^{10} [cm/s]

h = Planck's constant 6.626×10^{-34} [Js]

λ = wavelength [cm]

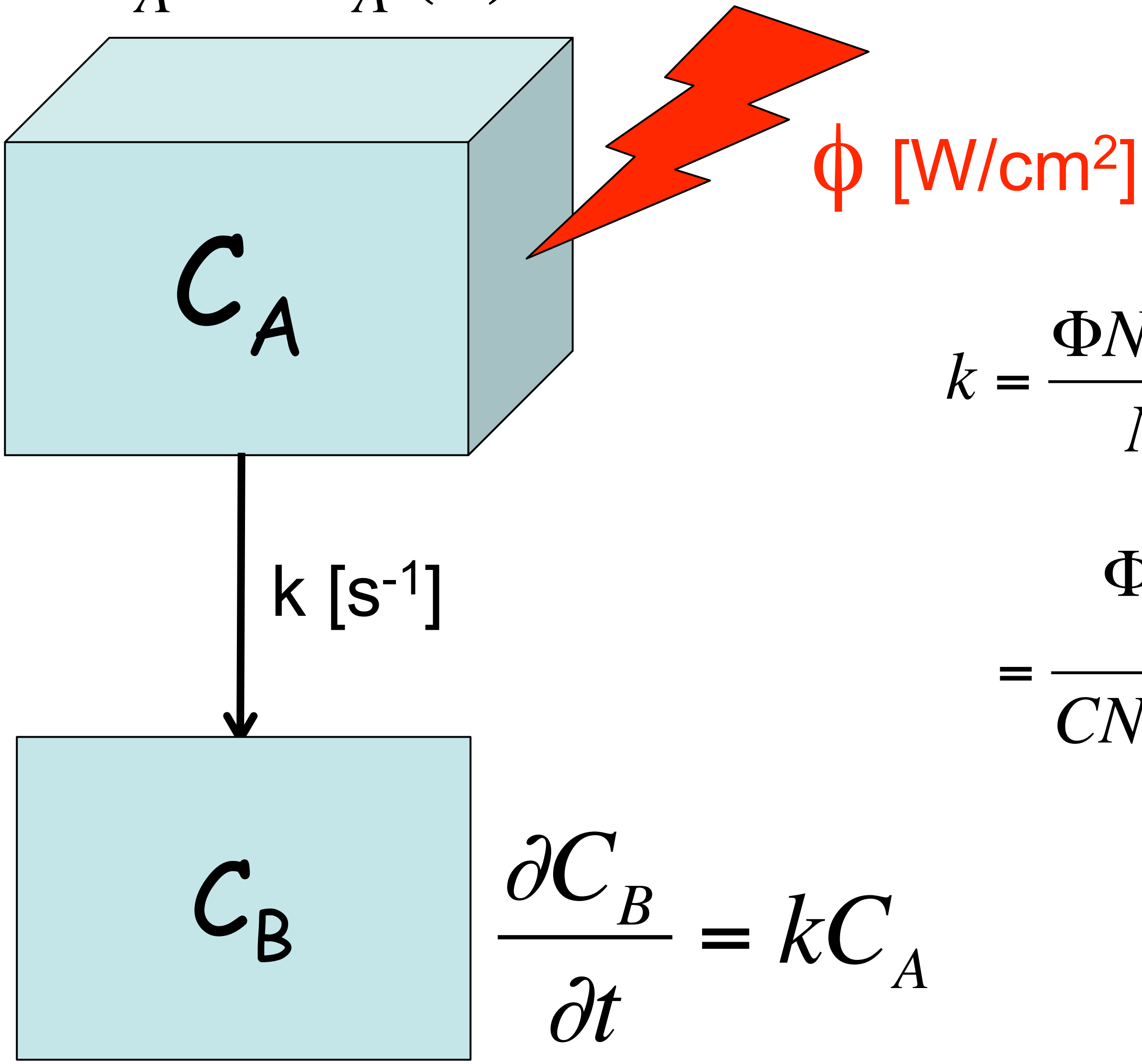
A = area illuminated by light [cm^2]

ε = extinction coefficient [cm^{-1}/M], M = moles/liter

C = concentration [M]

L = photon pathlength through medium [cm]

$$C_A = C_A(0)e^{-kt}$$



$$k = \frac{\Phi N_{abs}\ \ per\ \ s}{N_{molecules}}$$

$$= \frac{\Phi \phi \frac{\lambda}{hc_0} A\ (1-10^{-\varepsilon CL})}{C N_{Av} V / (1000 cm^3 / liter)}$$

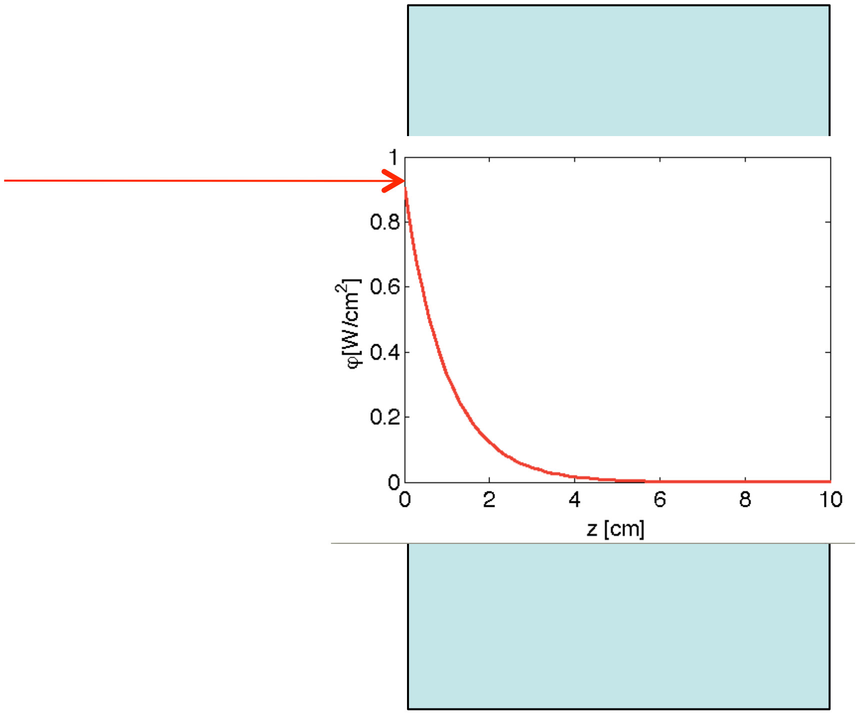
$$\frac{\partial C_B}{\partial t} = kC_A$$

$$C_A = C_A(0)e^{-kt}$$

$$= C_A(0)e^{-\phi t / H_{th}}$$

H_{th} = threshold dose [J/cm^2] for 1/e effect in the range of 10-100 J/cm^2 for many photochemical reactions

MATLAB
example



photolabile reagent
in non-scattering gel

how will the fluence
rate ϕ change as
reagent photobleaches?

Photochemical

Comparison of PDT efficiencies for photooxidation of substrate (NADPH) using a photosensitizer (Photofrin II).

PR Bargo, P Diagaradjane, SL Jacques

Proceedings of SPIE Vol. 3909 (2000)

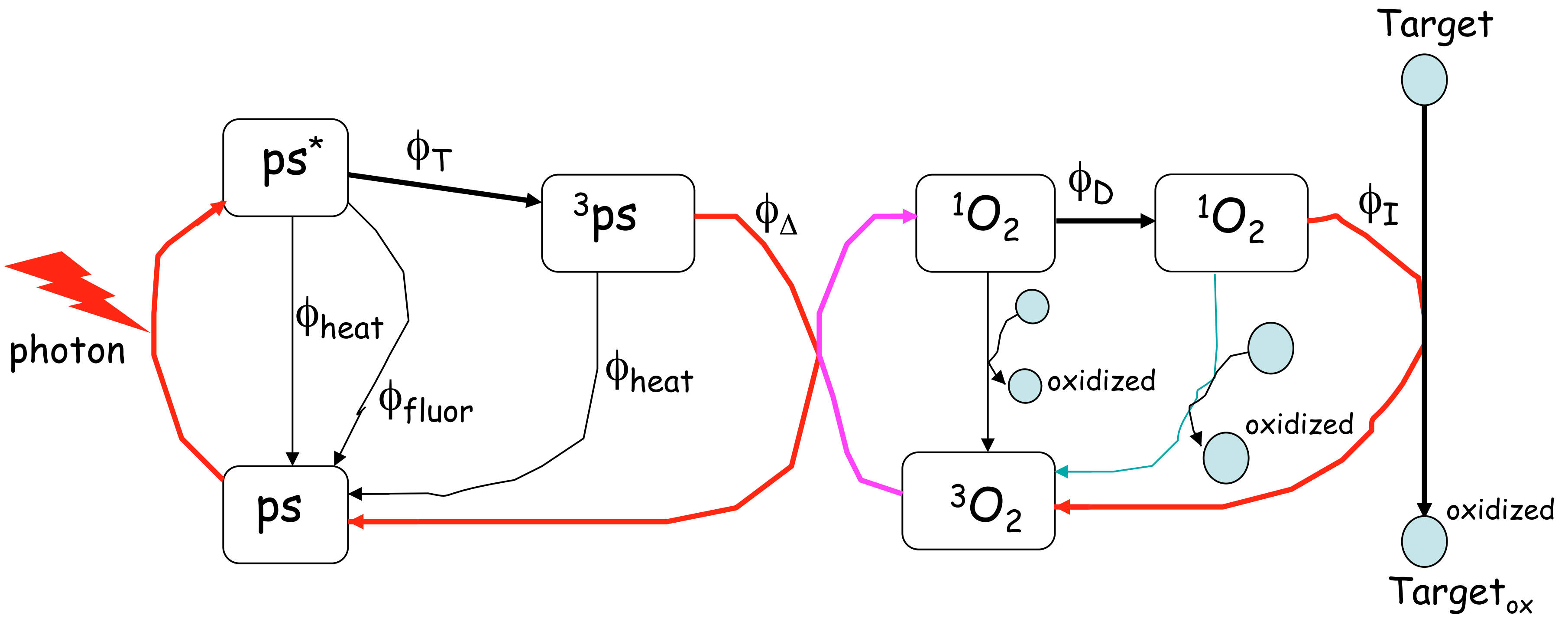
photoactivation

crossing to triplet state

transfer energy to singlet oxygen

diffusion to target

interaction with target



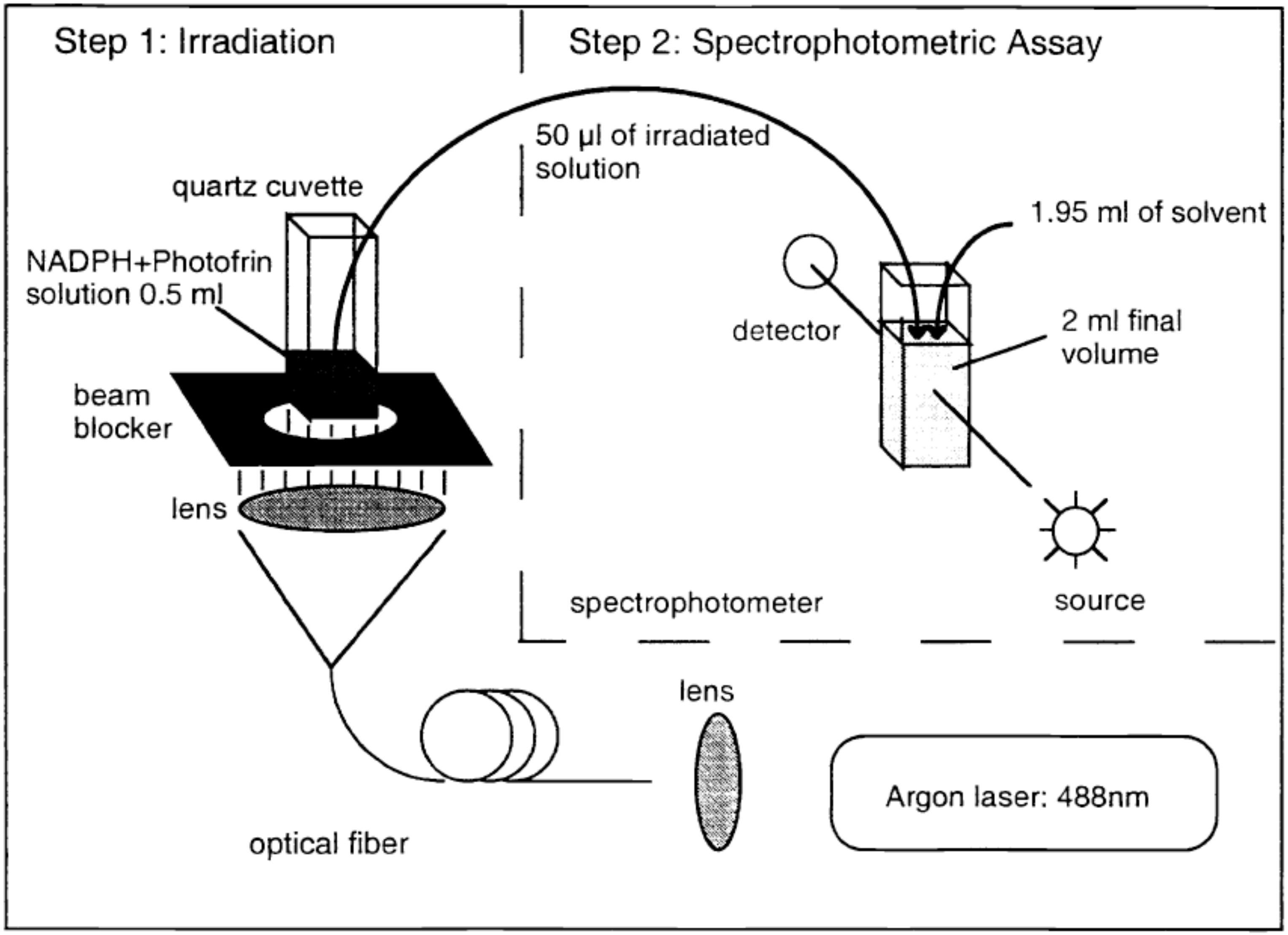


Figure 1 — Set-up for the irradiation and absorbance measurements. Samples were irradiated through the bottom of the cuvette with 488 nm light from an argon laser. Power delivered was 75 mW for exposure times ranging from 0 to 90 minutes. Aliquots of irradiated solution were diluted 1 :40 and absorbance spectra were.

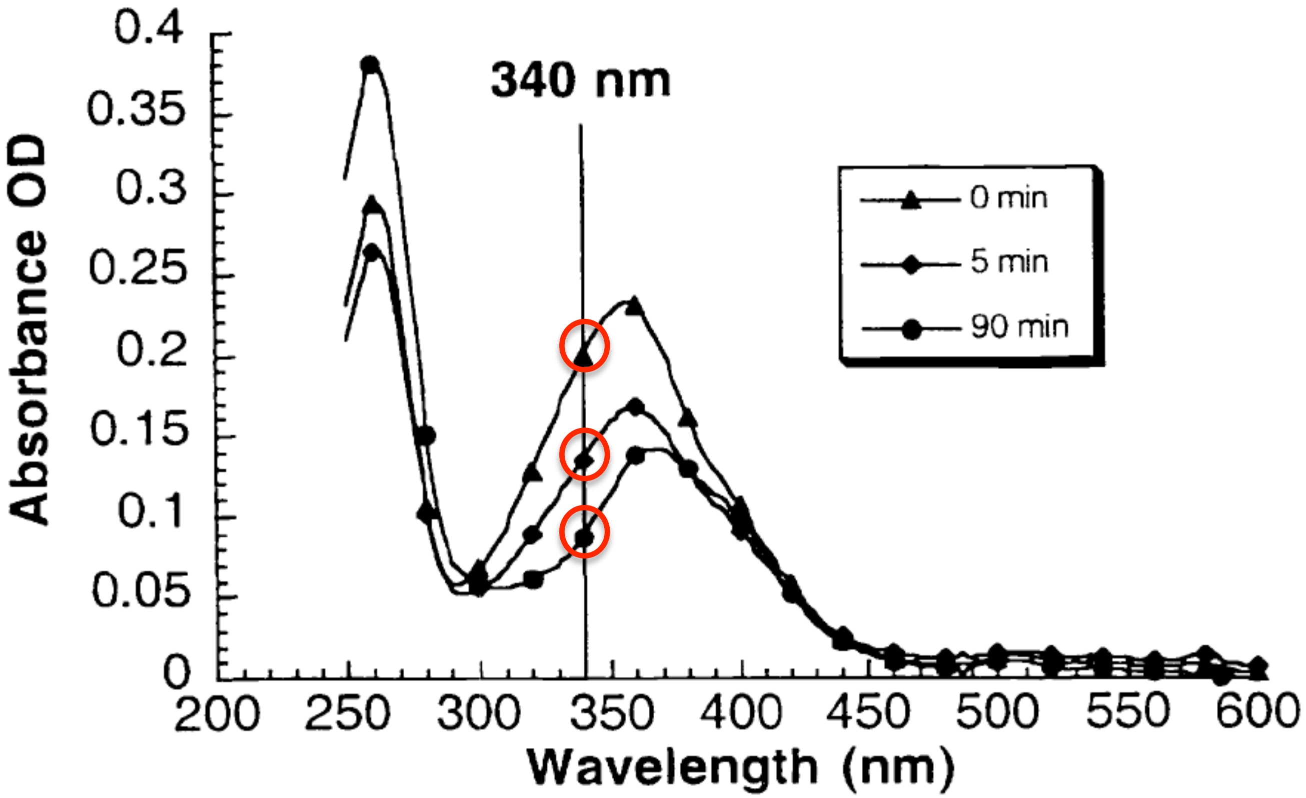


Figure 2: Absorbance spectra of NADPH (1 mM) + P11 (50 μg/ml) solution after different exposure times. Highlighted is the decay in the 340 nm peak after irradiation.

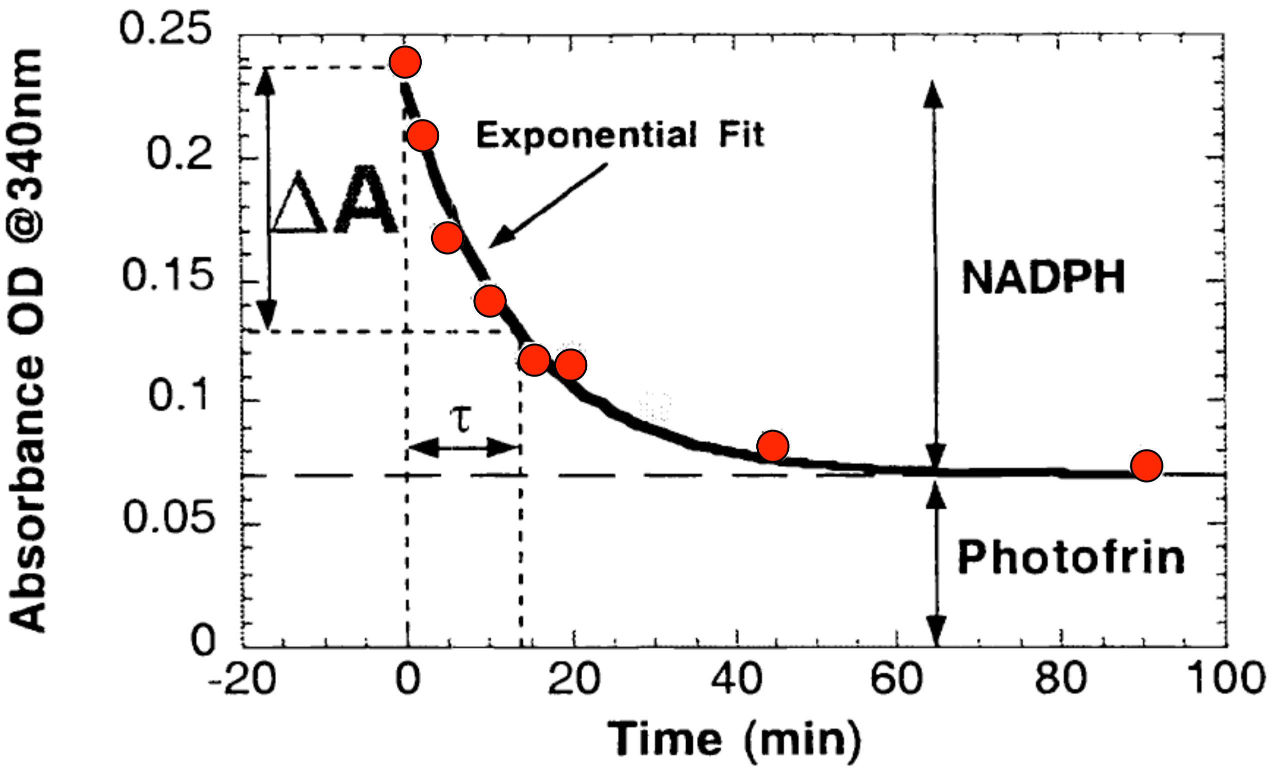
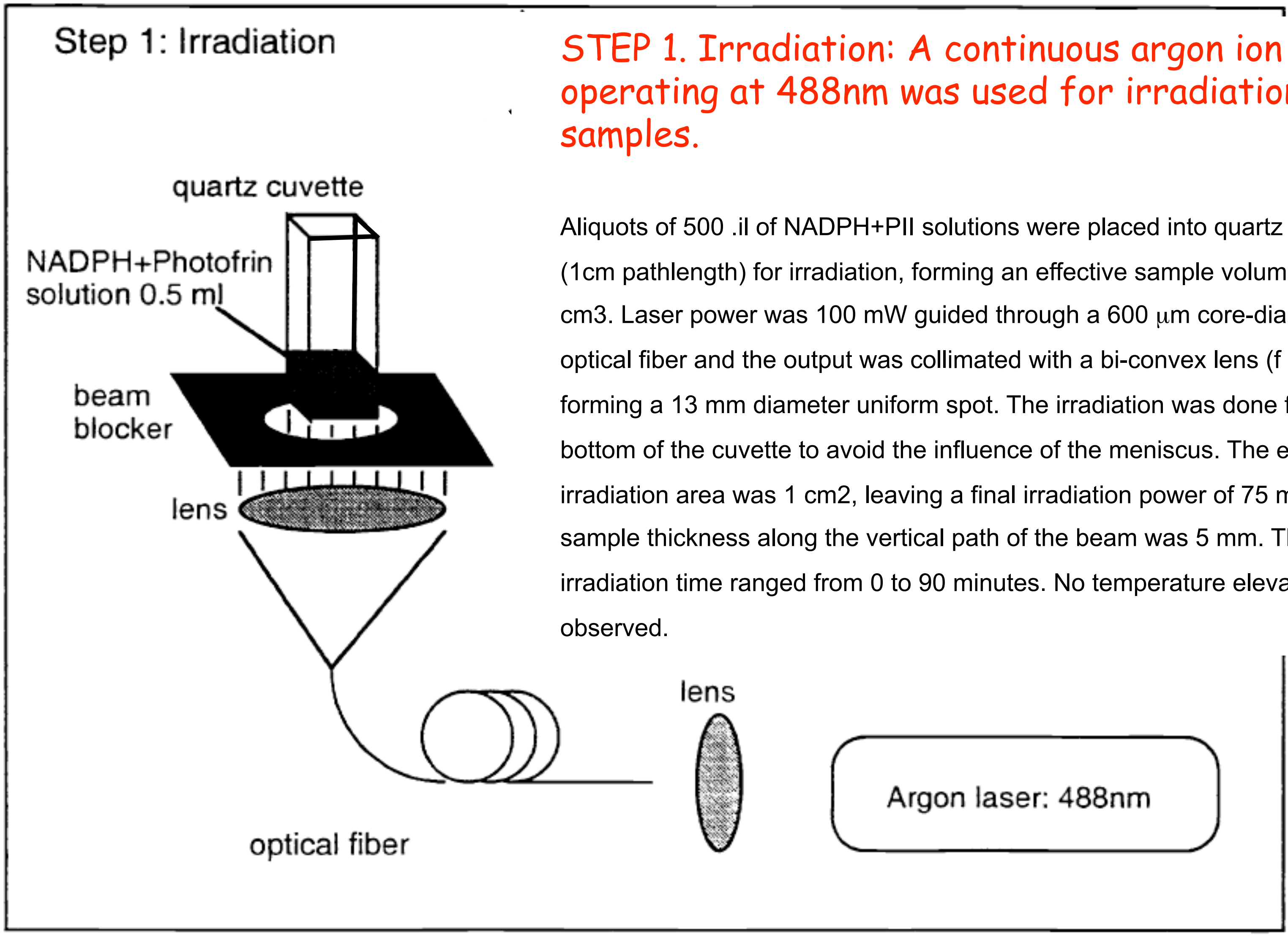


Figure 3: Typical decay in absorbance at 340 nm due to oxidation of NADPH. Data is fitted with a decayingexponential and the remaining offset is due to photofrin absorbance. ΔA and τ are used in equations 2 and 3.

STEP 1. Irradiation: A continuous argon ion laser operating at 488nm was used for irradiation of the samples.

Aliquots of 500 .il of NADPH+PII solutions were placed into quartz cuvettes (1cm pathlength) for irradiation, forming an effective sample volume of IxIxO.5 cm3. Laser power was 100 mW guided through a 600 μm core-diameter optical fiber and the output was collimated with a bi-convex lens (f = 50 mm) forming a 13 mm diameter uniform spot. The irradiation was done from the bottom of the cuvette to avoid the influence of the meniscus. The effective irradiation area was 1 cm2, leaving a final irradiation power of 75 mW. The sample thickness along the vertical path of the beam was 5 mm. The irradiation time ranged from 0 to 90 minutes. No temperature elevation was observed.



$$\boxed{N_{abs} = P\ \ \tau\ \ b\ \ (1 - T_{488})}$$

P = Irradiated Power (0.075 Watts)

τ = Time constant (seconds) (Fig.3)

b = Conversion factor @488nm $b = \frac{\lambda}{hc} =$ (2.5x10^{18} photons/J)

$$(1 - T_{488}) = \left(1 - e^{-\mu_{a,488}^{PF} L_{irr}}\right)$$

$$\mu_{a,488}^{PF} = \ln(10)\varepsilon_{a,488}^{PF} C_{irr}$$

ε_{488}^{PII} = PII extinction coefficient (5.9 cm^{-1} (mg/ml)$^{-1}$)

C_{irr} = PII concentration (50 μg/ml)

L_{irr} = Irradiated pathlength (0.5 cm)

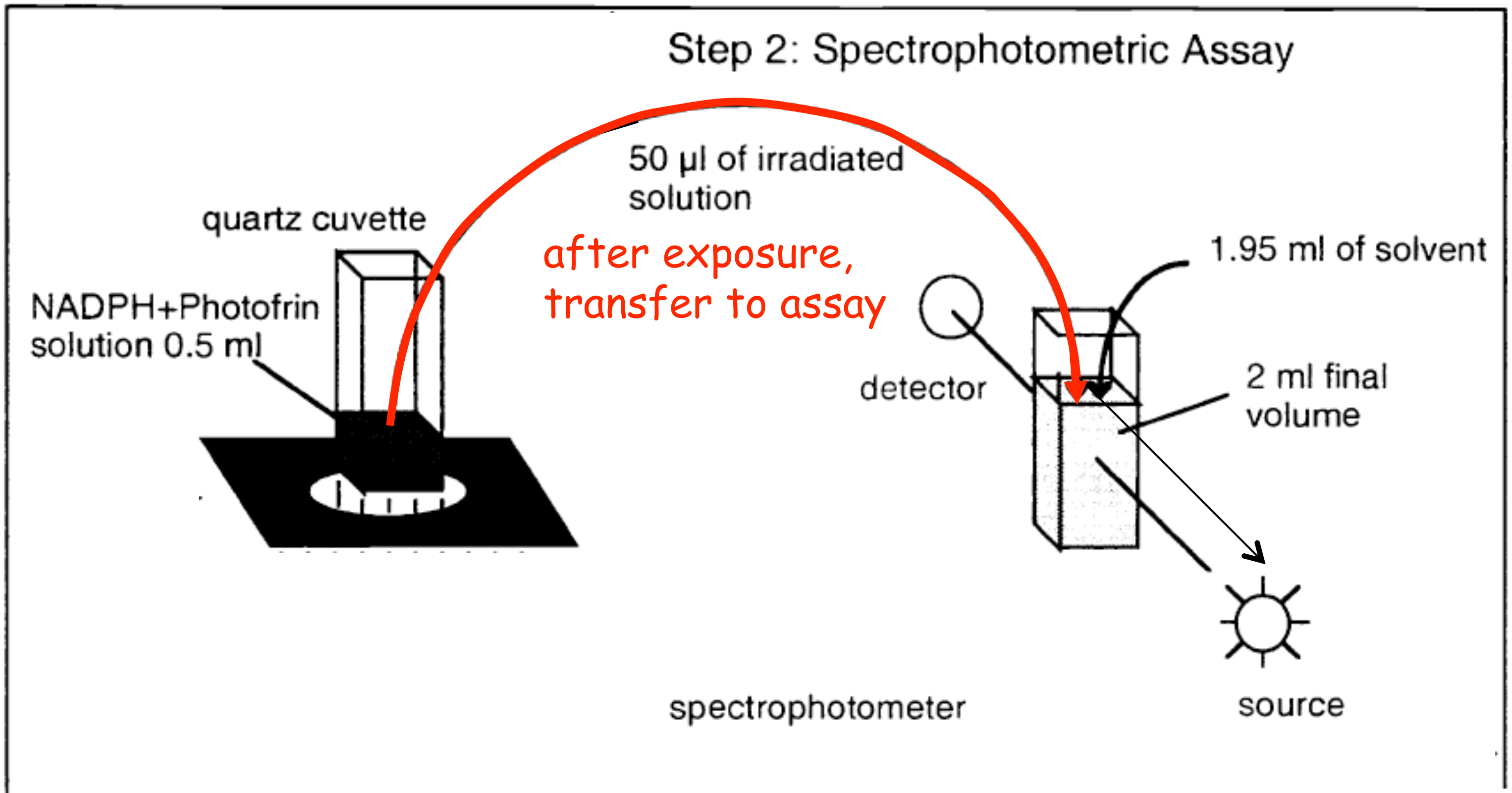
```
Cm       = 50e-3;   % mg/ml
epsilon  = 5.9;     % cm^-1 (mg/ml)^-1
L        = 0.5;     % cm

P        = 0.075;   % W
tau      = 14*60;   % s
b        = 2.5e18;  % ph/J

Apf      = Cm*epsilon*L        % [-]
Nabs     = P*tau*b*(1-10^-Apf) % # photons abs’d
```

RUN:

Nabs = 4.54e+19 photons absorbed



STEP 2. Spectrophotometric Assay: after exposure, transfer to assay

Absorbance measurements were taken in the 250-820 nm spectral range with a spectrophotometer (Hewlett Packard). Solutions were diluted 1:40 (50 μl of solution into 1.95 ml of Trizma) and placed into quartz cuvettes (1 cm pathlength). Spectra were recorded and absorbance at 340 nm was measured to assay the kinetics of NADPH oxidation. Measurements of the extinction coefficients of PIT at 488 nm (ε_{488}^{PII} = 5.9 [$cm^{-1}(mg/ml)^{-1}$] and NADPH at 340 nm (ε_{340}^{PII} = 5.1×10^3 [$cm^{-1}M^{-1}$]) were also measured.

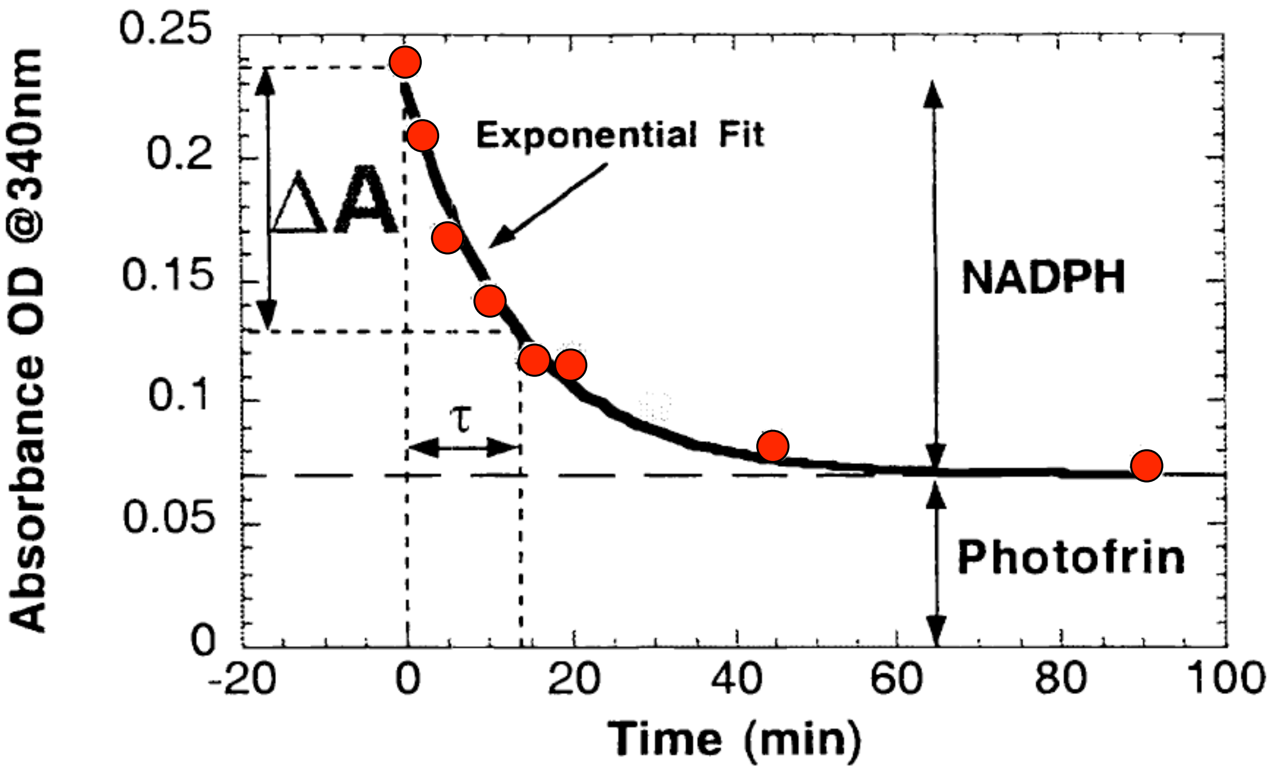


Figure 3: Typical decay in absorbance at 340 nm due to oxidation of NADPH. Data is fitted with a decayingexponential and the remaining offset is due to photofrin absorbance. ΔA and τ are used in equations 2 and 3.

$$N_{ox} = \frac{\Delta A \;\; N_{Av} \;\; V_{sp}}{\varepsilon_{340}^{NADPH} \, L_{sp}} \, \frac{1}{f}$$

ΔA = Decay in Absorbance @ 340nm	(Fig.3)
N_{av} = Avogrado's Number	(6.02×10^{23} molec/mol)
V_{sp} = Diluted Sample Volume in step 2	(2 ml)
$\varepsilon_{340}^{NADPH}$ = NADPH extinction coefficient @340nm	(5.1 cm^{-1} mM^{-1})
L_{sp} = Cuvette Path length for spectrophotometer	(1 cm)

$f = \frac{\text{Sample Volume}}{\text{Irradiated Volume}} = \frac{50\mu l}{500\mu l} = 0.1$ in step 1

```
dA = 0.25-0.13; % dOD after one time constant tau
Vsp = 2e-3;     % liters sample volume of assay, in step 2
epsilonNADPH = 5.1e3; % cm^-1 M^-1
L2 = 1;         % cm cuvette in step 2
f = 50/500;     % uL/uL, fraction of sample from step 1 assayed in step 2
Nav = 6.023e23; % Avagadro's number, #/mole

Nox = (dA/epsilonNADPH*L2)/f *Nav*Vsp
% [-]/([cm^-1 M^-1][cm])/[-] * [#/mole]*[2e-3 liter]
%            [M]             *  [#/M]     = # photons oxidized
```

Run:

Nox = 2.83e+17 photons oxidized

$$\boxed{\phi_{ox} = N_{ox} / N_{abs}}$$

```
phiox = Nox/Nabs
```

Run:

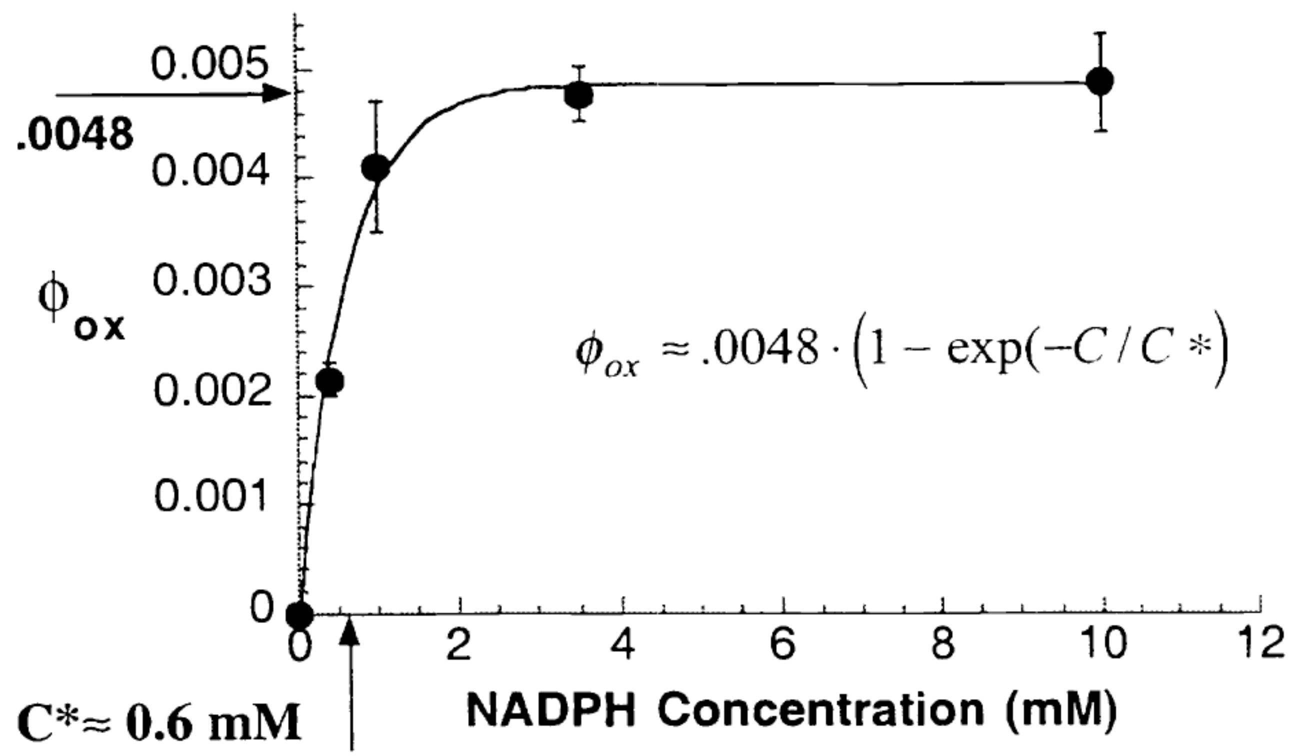
Nabs = 4.54e+19

Nox = 2.83e+17

phiox = 0.0062

Example calculation using figure.

All the experiments actually yielded saturated $\phi_{ox} \approx 0.0048$.



.0048

$$\phi_{ox} \approx .0048 \cdot \left(1 - \exp(-C / C^*)\right)$$

$C^* \approx 0.6$ mM

Triplet-crossing of activated sensitizer

Activation of oxygen to singlet oxygen

Oxidation of NADPH by singlet oxygen

$$\phi_{ox} = \phi_T \quad \phi_\Delta \quad \phi_R$$

$$= \phi_T \quad \phi_\Delta \quad \phi_D \quad \phi_I$$

Diffusion of singlet oxygen to NADPH

Interaction of singlet oxygen with NADPH

efficiency of singlet oxygen interaction with NADPH yielding oxidation

$$\phi_I = \frac{\phi_{ox}}{\phi_T \quad \phi_\Delta \quad \phi_D}$$

experiment

$$= \frac{0.0048}{0.63 \quad 0.32 \quad 1} = 0.024$$

literature

experiment, for $C_{NADPH} > C^*$

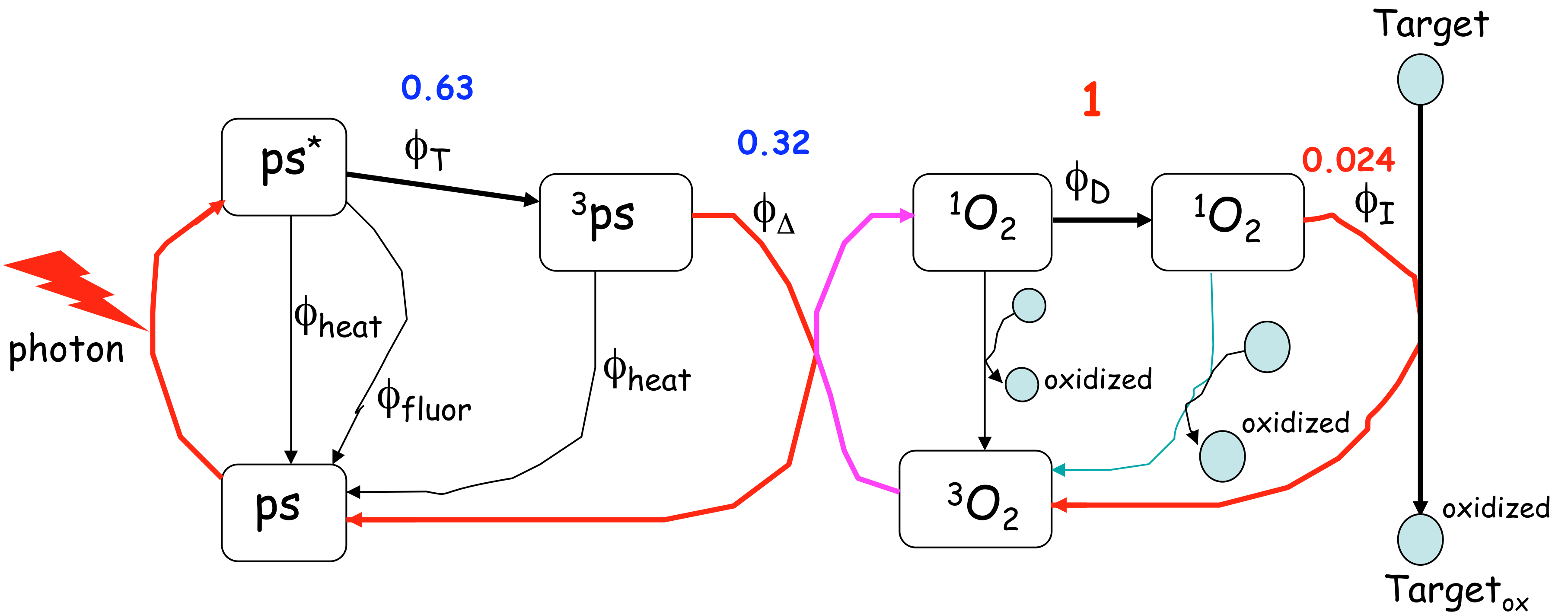
photoactivation

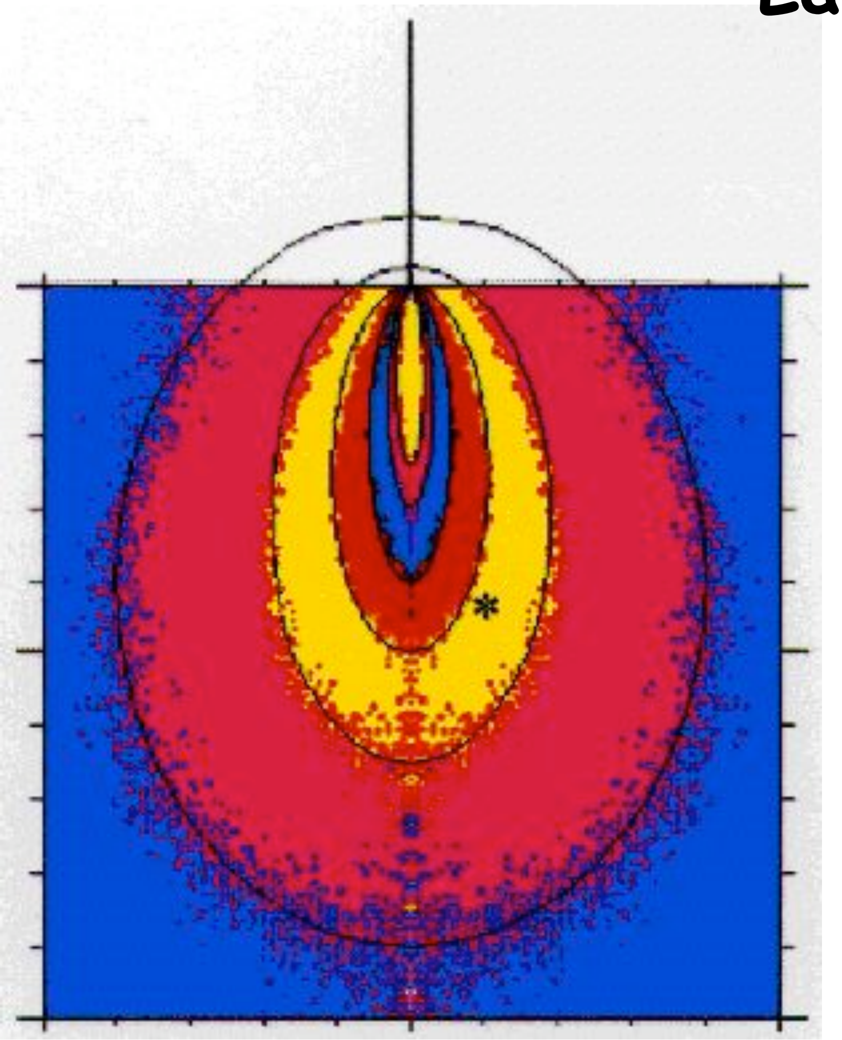
crossing to triplet state

transfer energy to singlet oxygen

diffusion to target

interaction with target





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http://omlc.ogi.edu

Depts. of Biomedical Engineering and Dermatology
Oregon Health & Science University,
Portland OR, USA

1. Introduction
2. Photochemical
3. Photothermal
4. Photomechanical

Temperature rise

Fluence rate [W/cm^2]

$$\Delta T = \mu_a F t \frac{1}{\rho C_p}$$

[°C]

specific heat [J/(g K)]

density [g/cm^3]

Absorption coefficient [1/cm]

Temperature source

Monte Carlo input file

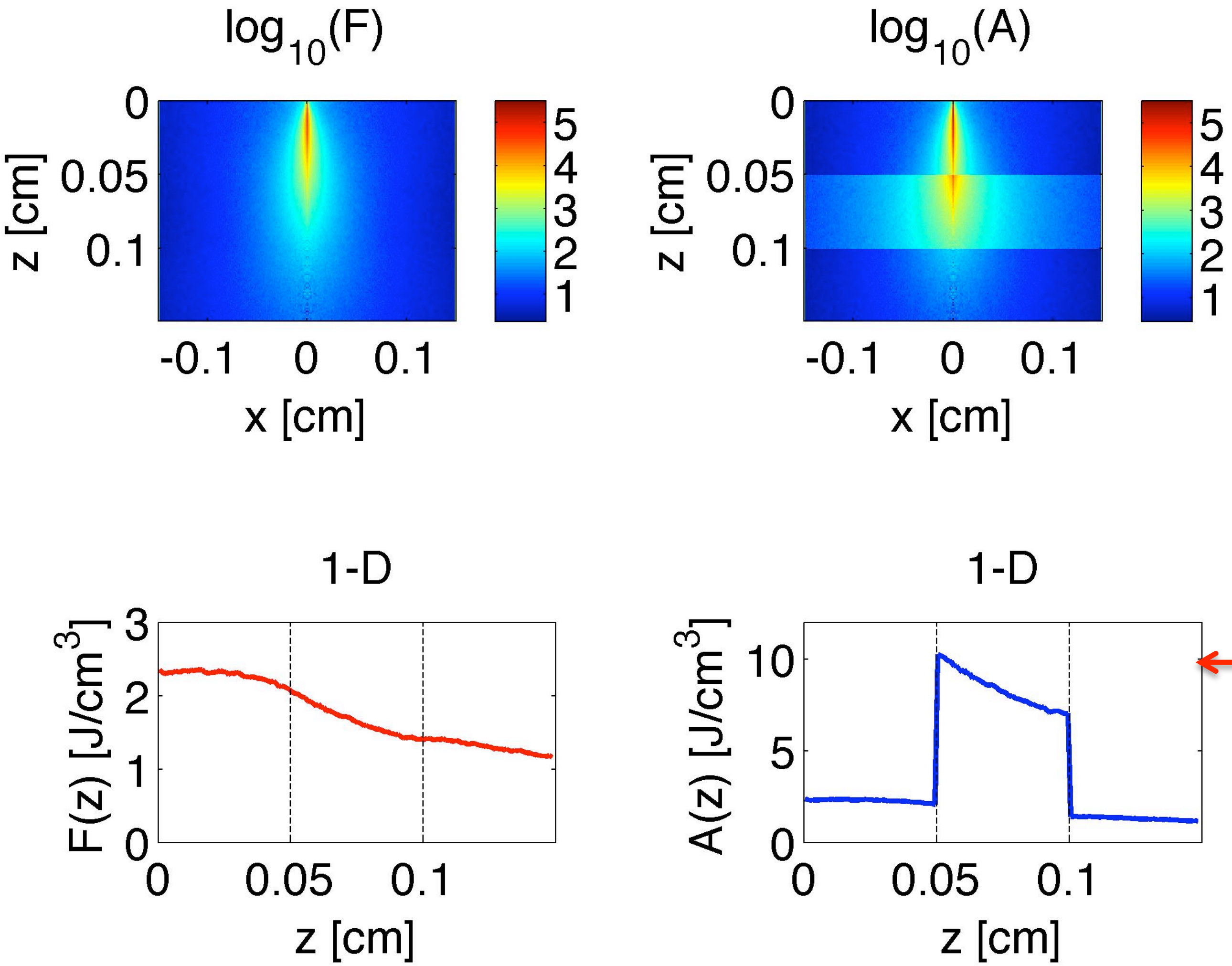
```
1.0                                                             # file version
1                                                               # number of runs


layersA.mco     A                                   # output filename, ASCII/Binary
100000                                                  # No. of photons
0.0010          0.0010                              # dz, dr for OUTPUT
150             150         1                       # No. of bins, Nz, Nr, Na for OUTPUT
3                                                               # No. of layers
# n             mua         mus       g       d                 # One line for each layer
1.00                                                            # n for medium above.
1.33            0.1         100       0.90    0.0500            # conjunctiva
1.33            0.5         100       0.90    0.0500            # conjunctiva
1.33            0.1         100       0.90    10.000            # conjunctiva
1.33                                                            # n for medium below.
```

Temperature source

fluence rate, F [J/cm^3] $= A/\mu_a$

absorption rate, A [J/cm^3] $= \mu_a F$



$\mu_a = 1$ cm^{-1}

$\mu_a = 5$ cm^{-1}

$\mu_a = 1$ cm^{-1}

for all 3 layers:
$\mu_s = 100$ cm^{-1}
$g = 0.90$

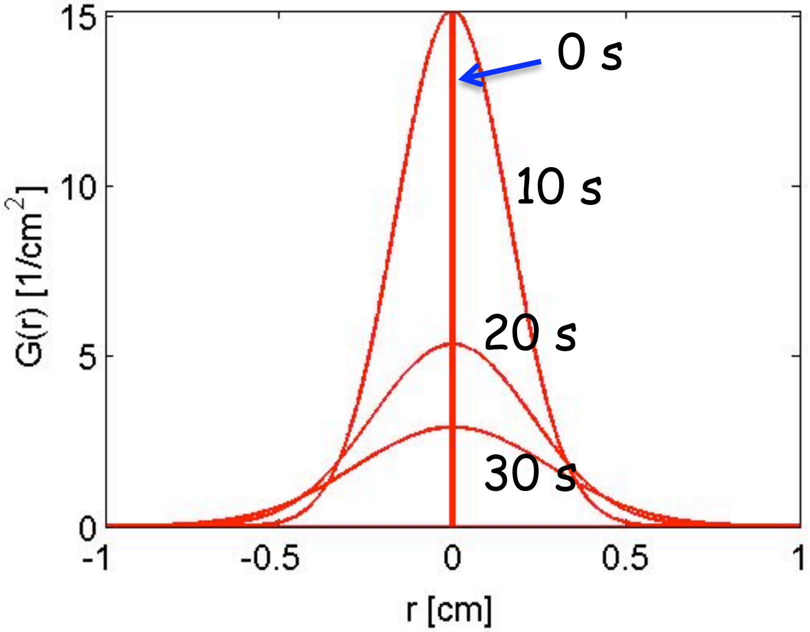
2.4°C ΔT
$= A/(4.18\ (\mathrm{J/cm^3})/°\mathrm{C})$
for water

Thermal diffusion

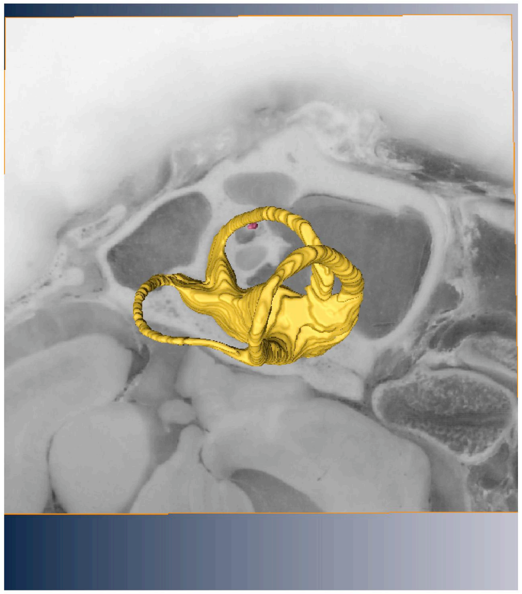
impulse response

$$\Delta T = \frac{U_p \mu_a T}{\rho C} G(x,t)$$

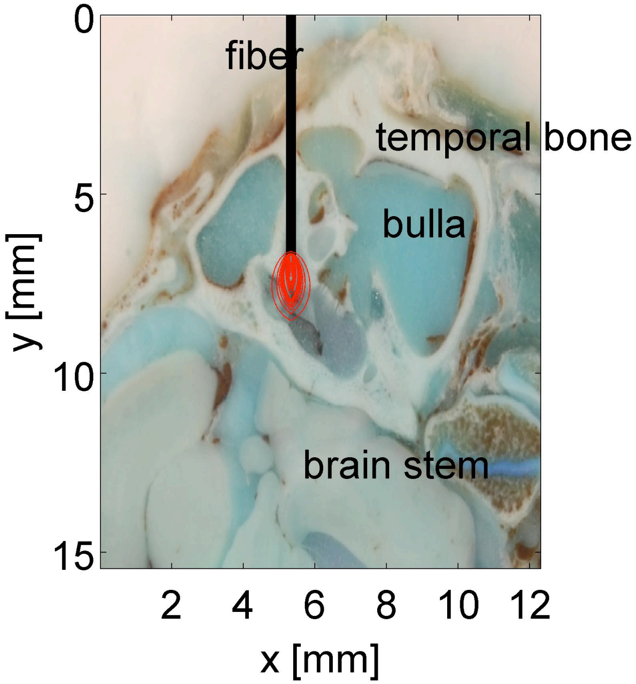
$$G(x,t) = \frac{e^{-x^2/(4\alpha t)}}{(4\pi\alpha t)^{3/2}}$$



Developing an optical nerve stimuator for vestibular system (chicken)



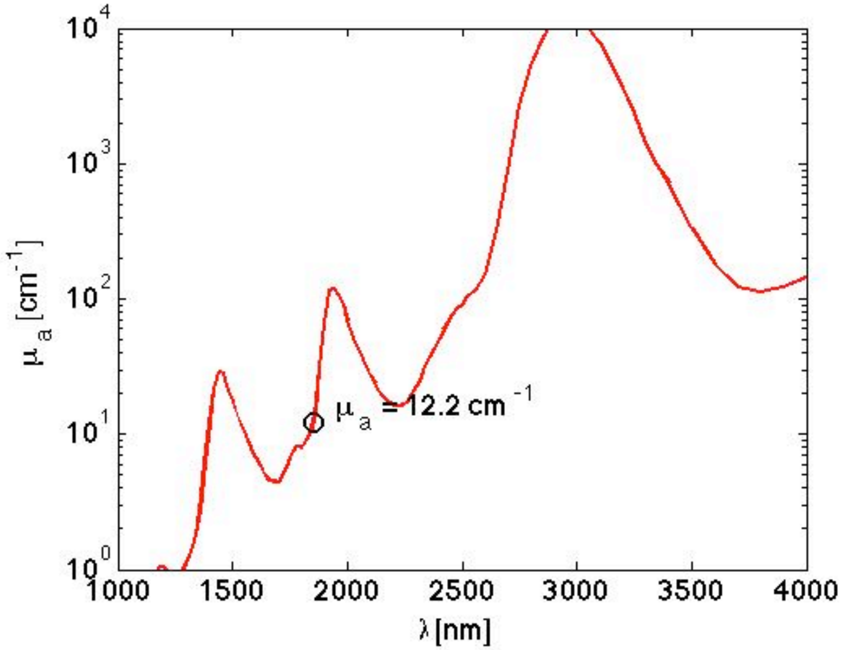
optical fiber delivers 1850 nm laser pulse to stimulate nerve

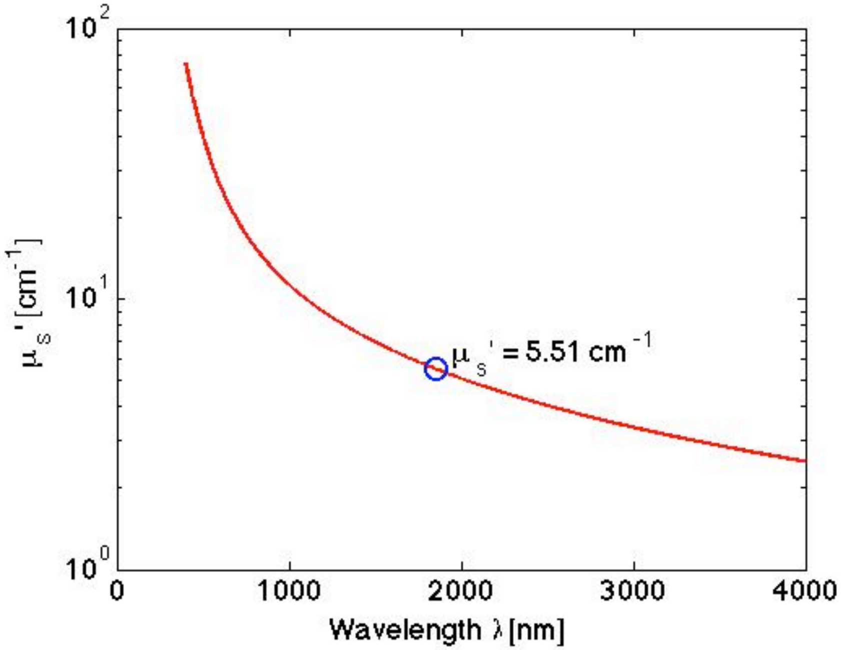


at 1850 nm wavlength

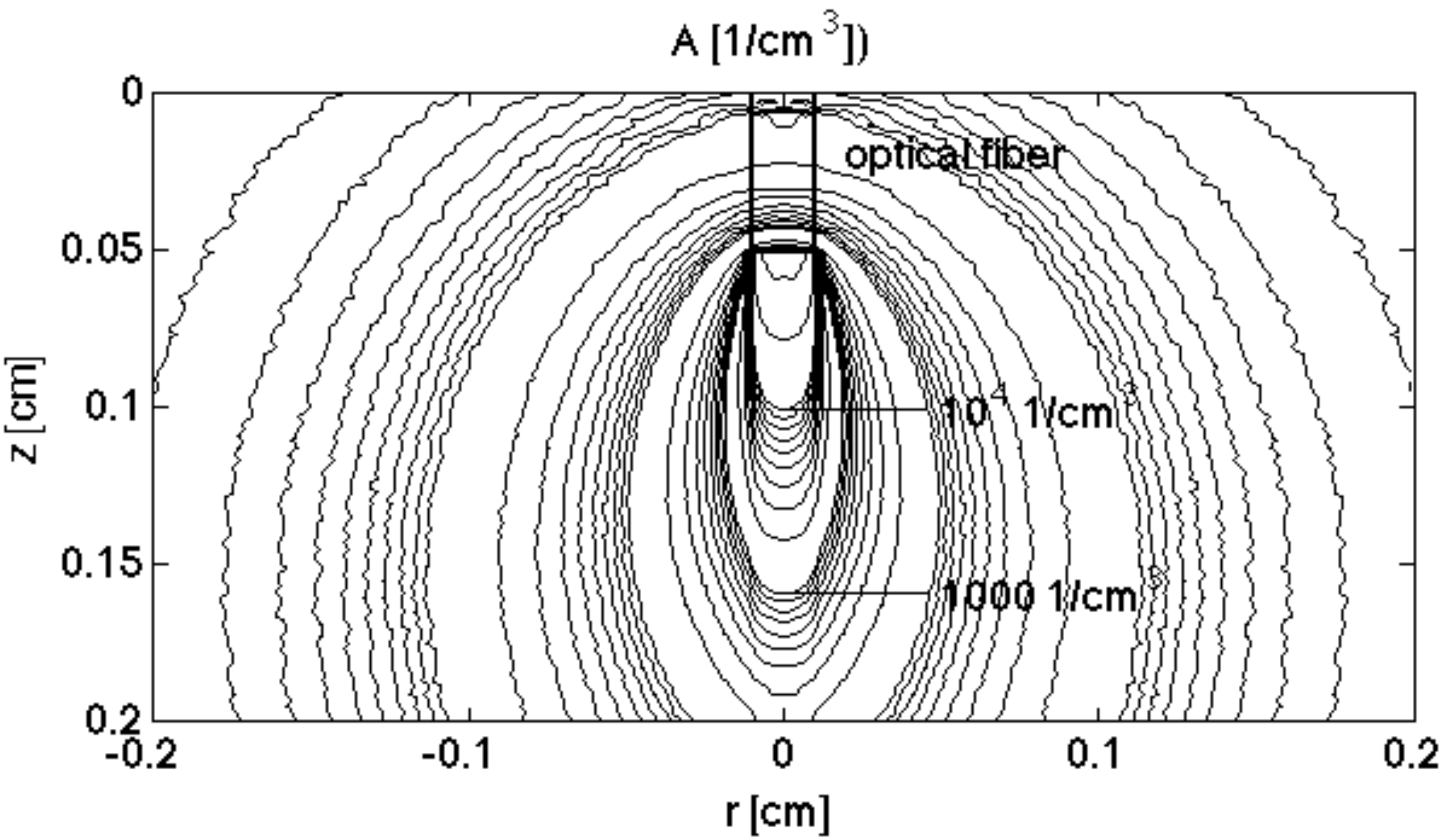
absorption

scattering

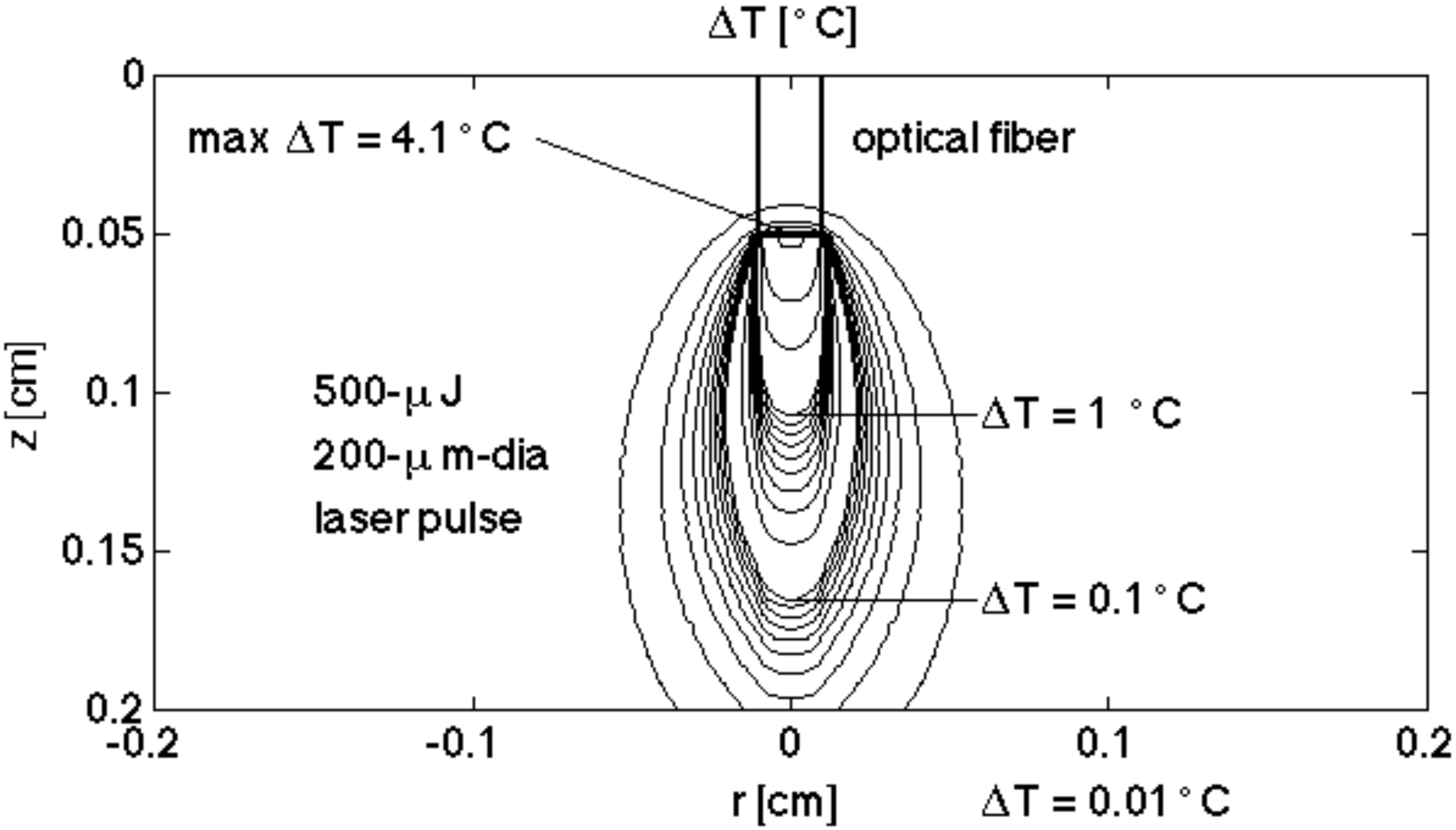


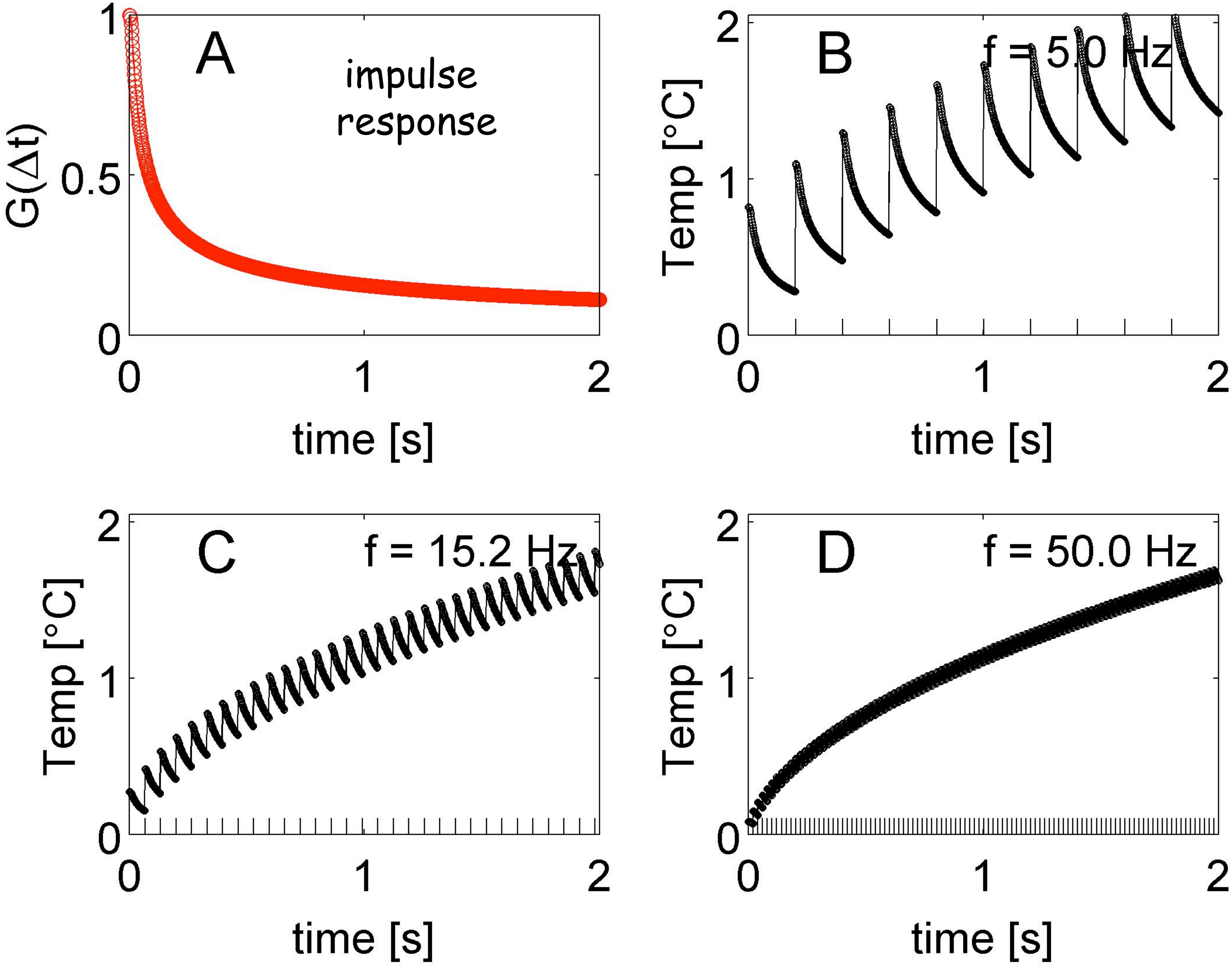


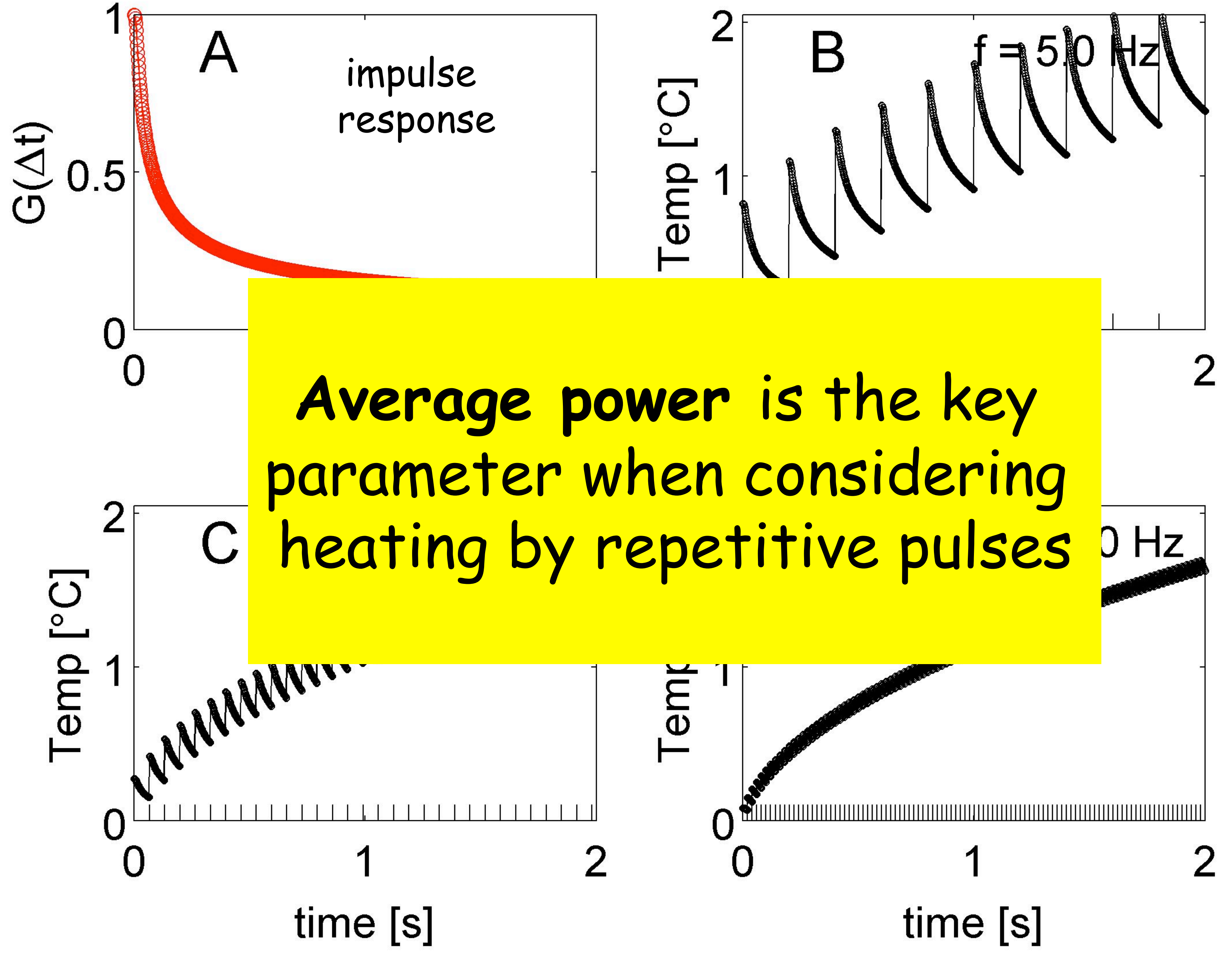
response to 1-J pulse



response to 0.00500-J pulse




A
impulse response
G(Δt)
1
0.5
0
time [s]
B
f = 5.0 Hz
Temp [°C]
2
1
0
time [s]
C
f = 15.2 Hz
Temp [°C]
D
f = 50.0 Hz
Temp [°C]
2
time [s]



Average power is the key parameter when considering heating by repetitive pulses

Thermal damage

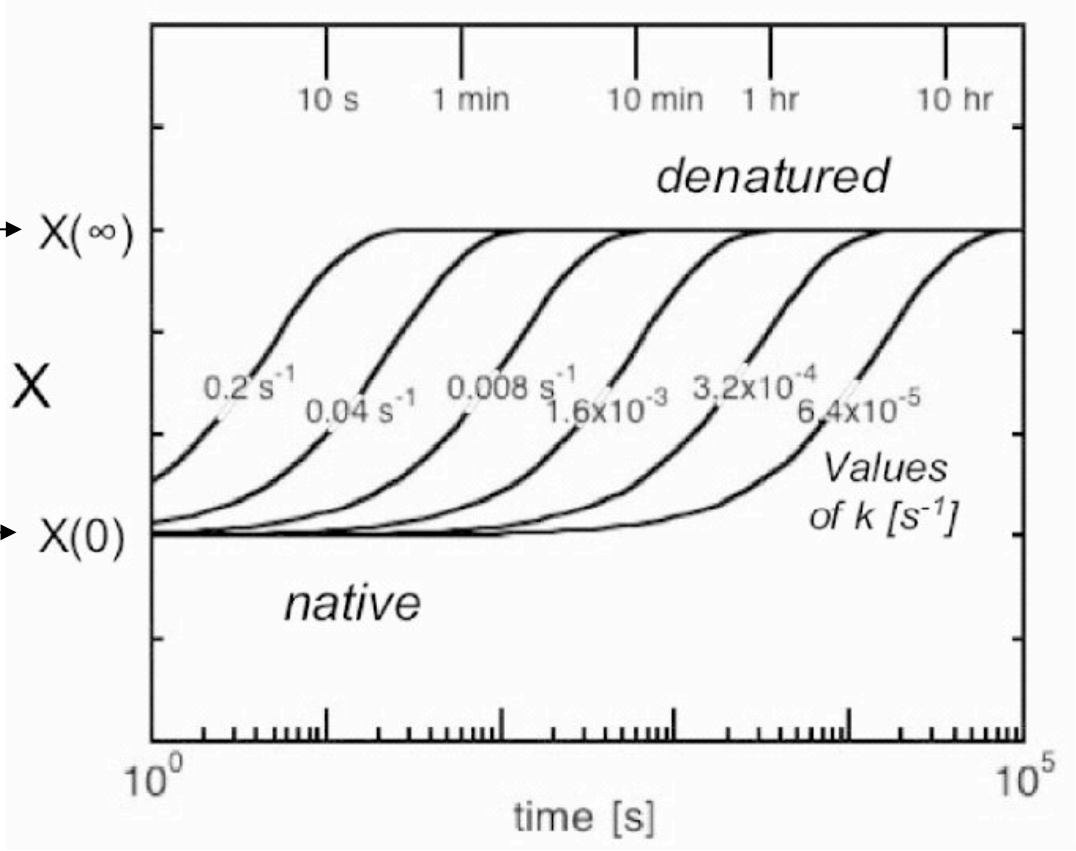
X(t) describes some tissue state that changes with denaturation

rate of denaturation

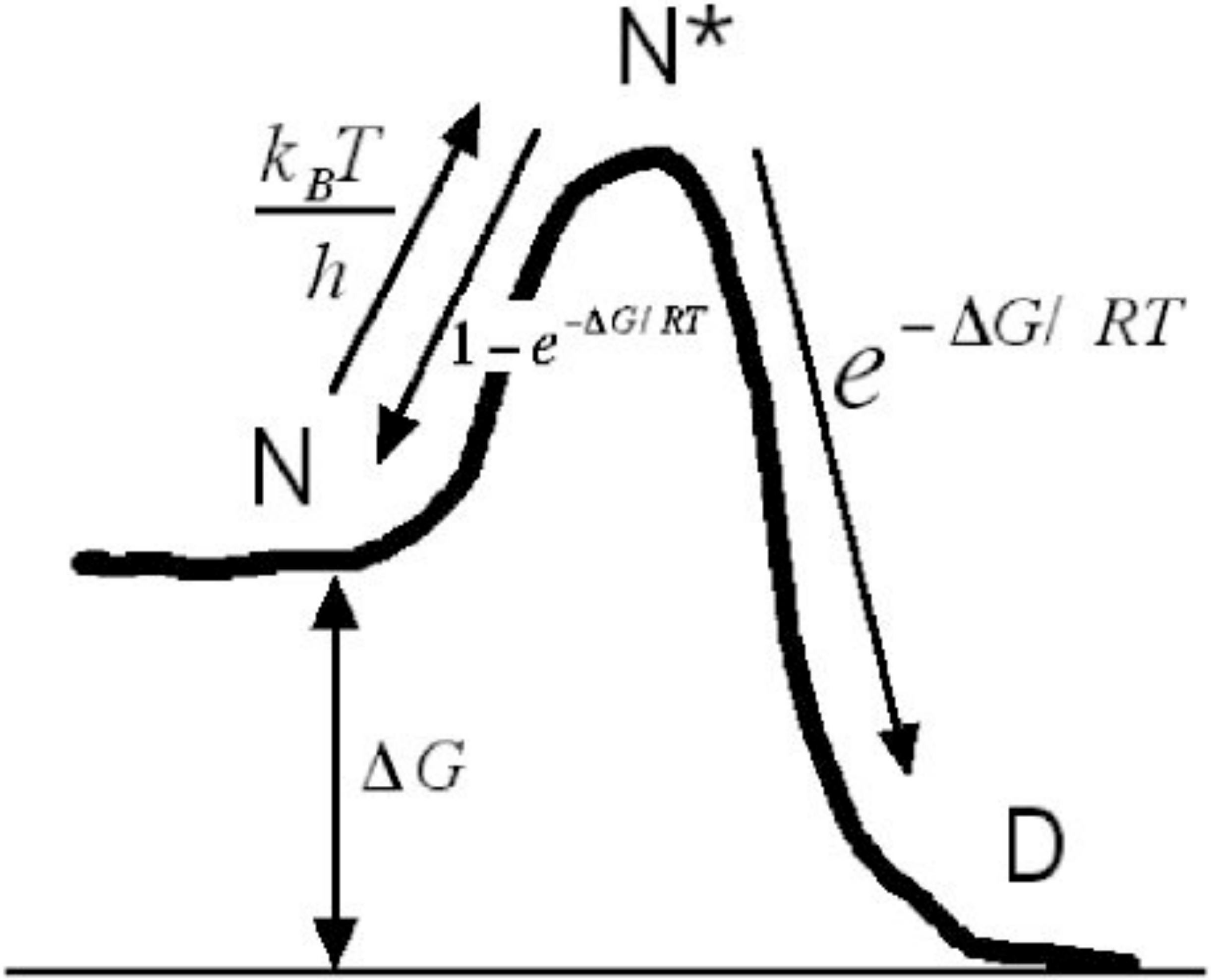
$$X(t) = X(0) + \left(X(\infty) - X(0)\right)\left(1 - e^{-kt}\right)$$

End point

Start point



Thermal damage



Thermal damage

$$k = \frac{k_B T}{h} e^{-\Delta G / RT}$$

where $$\Delta G = \Delta H - T\Delta S$$

Thermal damage

$6.2\text{x}10^{12}\ s^{-1}$
at room temperature

Entropy [J/(mole K)]

$$k = \boxed{\frac{k_B T}{h}} e^{\Delta S / R} \quad e^{-\Delta H / RT}$$

Enthalpy [J/mole]

where $$\Delta G = \Delta H - T\Delta S$$

Thermal damage

6.2x10^{12} s^{-1}
at room temperature

Entropy [J/(mole K)]

$$k = \boxed{\frac{k_B T}{h}} e^{\Delta S / R} \quad e^{-\Delta H / RT}$$

Enthalpy [J/mole]

where $$\Delta S = \frac{1}{T}\Delta H - \frac{1}{T}\Delta G$$

Thermal damage

$6.2\text{x}10^{12}\ \text{s}^{-1}$
at room temperature

Entropy [J/(mole K)]

$$k = \boxed{\frac{k_B T}{h}} e^{\Delta S / R} \quad e^{-\Delta H / RT}$$

Enthalpy [J/mole]

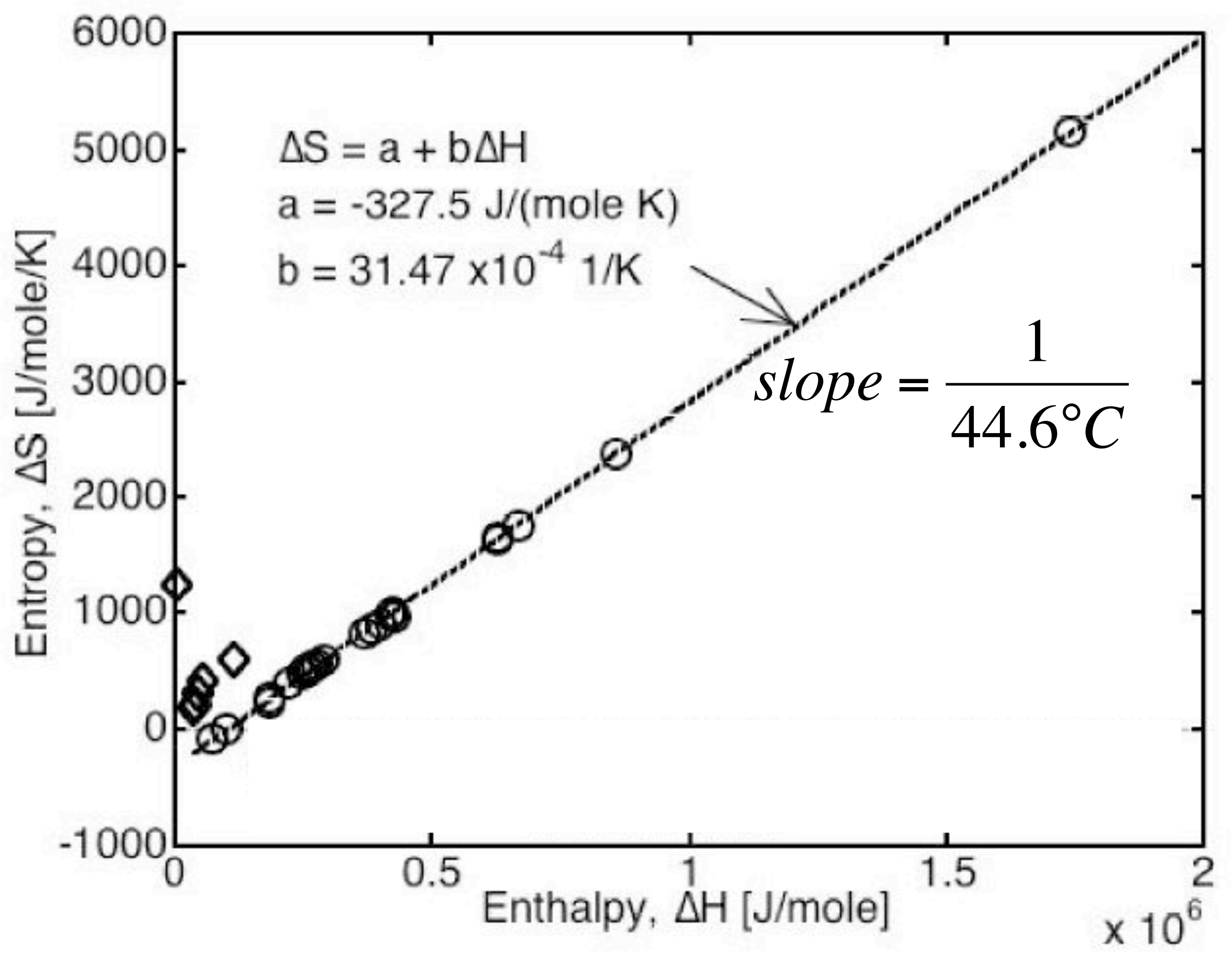
where $$\Delta S = \underbrace{\boxed{\frac{1}{T}}}_{\text{slope}} \Delta H - \underbrace{\boxed{\frac{1}{T} \Delta G}}_{\text{y-int}}$$

Thermal damage

Literature review

SL Jacques, _J. Biomed. Optics_ 11(4):041108, 2006

ΔS



$$slope = \frac{1}{44.6°C}$$

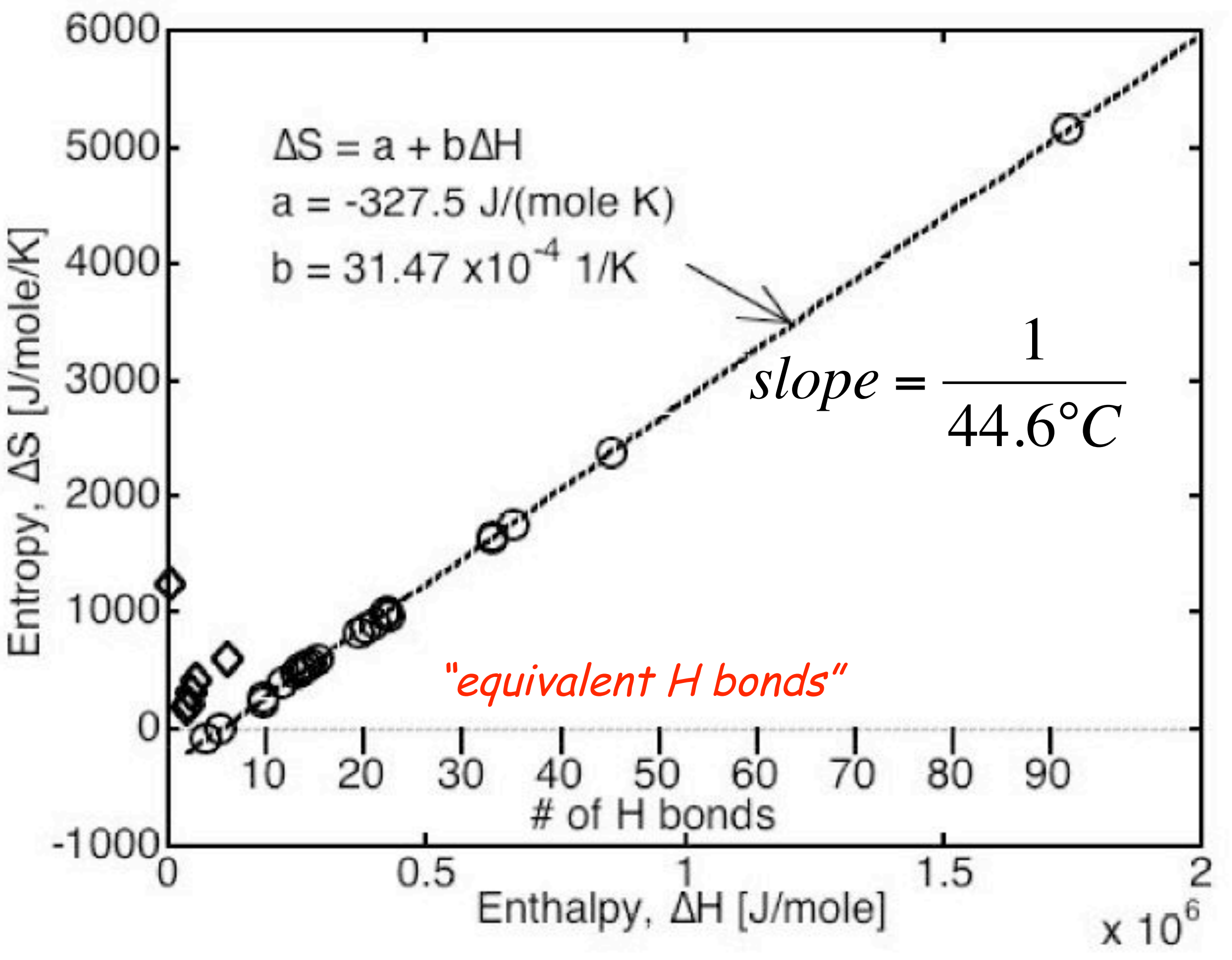
ΔH

Thermal damage

Literature review

SL Jacques, *J. Biomed. Optics* 11(4):041108, 2006

ΔS



$$slope = \frac{1}{44.6°C}$$

"equivalent H bonds"

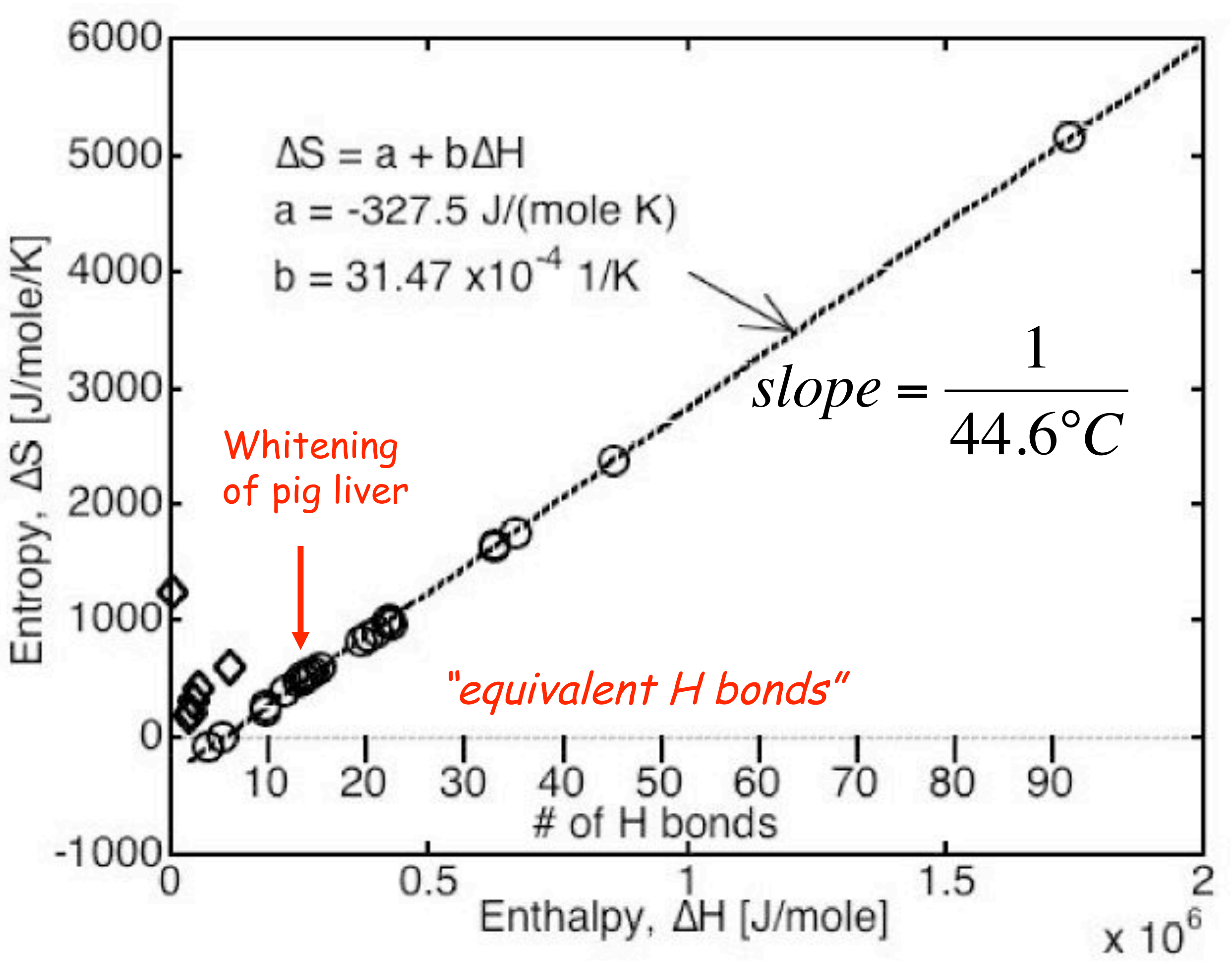
ΔH

Thermal damage

Literature review

SL Jacques, *J. Biomed. Optics* 11(4):041108, 2006

ΔS



$$slope = \frac{1}{44.6°C}$$

Whitening of pig liver

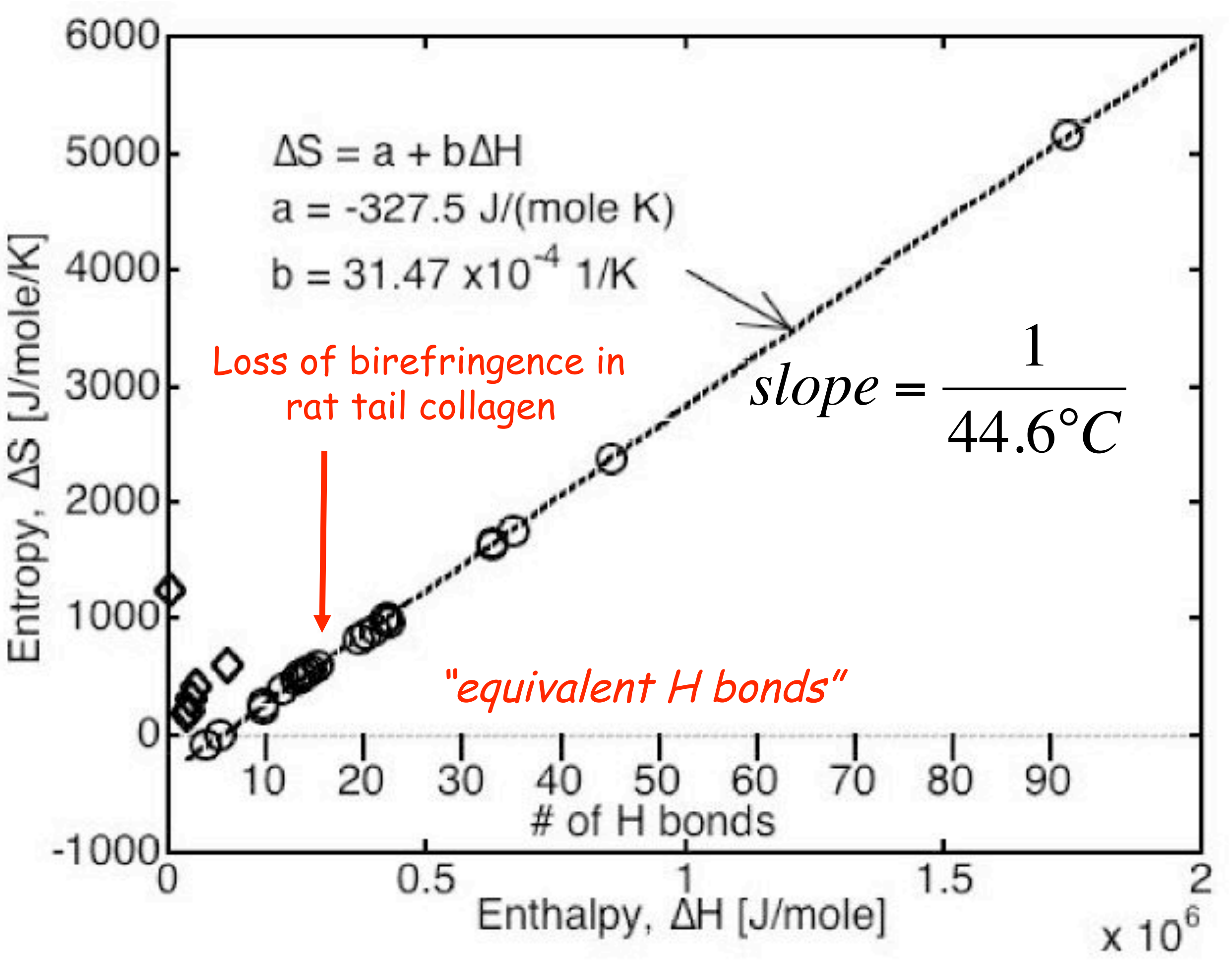
"equivalent H bonds"

ΔH

Thermal damage

Literature review

SL Jacques, *J. Biomed. Optics* 11(4):041108, 2006



Loss of birefringence in rat tail collagen

$$slope = \frac{1}{44.6°C}$$

"equivalent H bonds"

ΔS

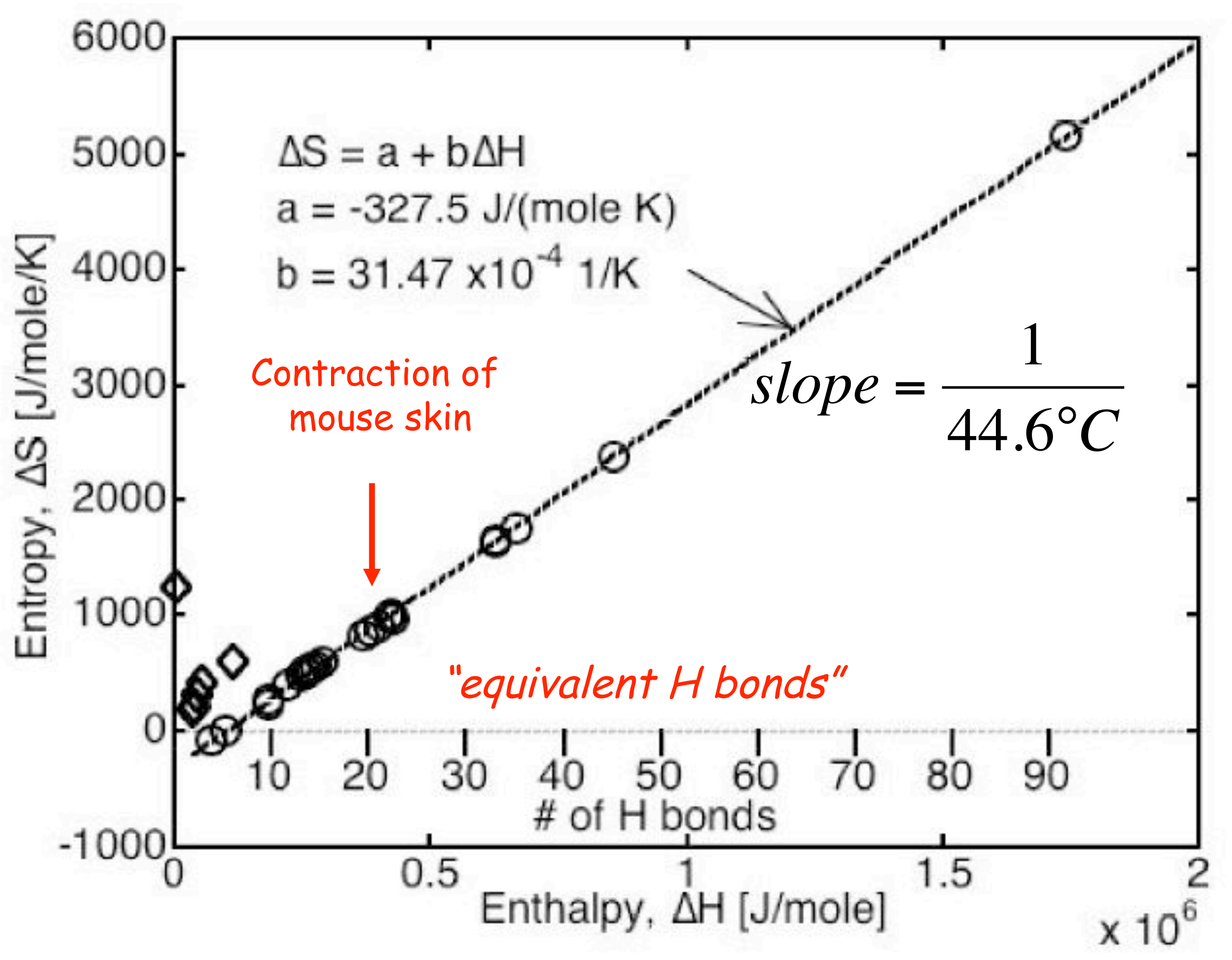
ΔH

Thermal damage

Literature review

SL Jacques, <u>*J. Biomed. Optics*</u> 11(4):041108, 2006

ΔS



Contraction of mouse skin

$$slope = \frac{1}{44.6°C}$$

"equivalent H bonds"

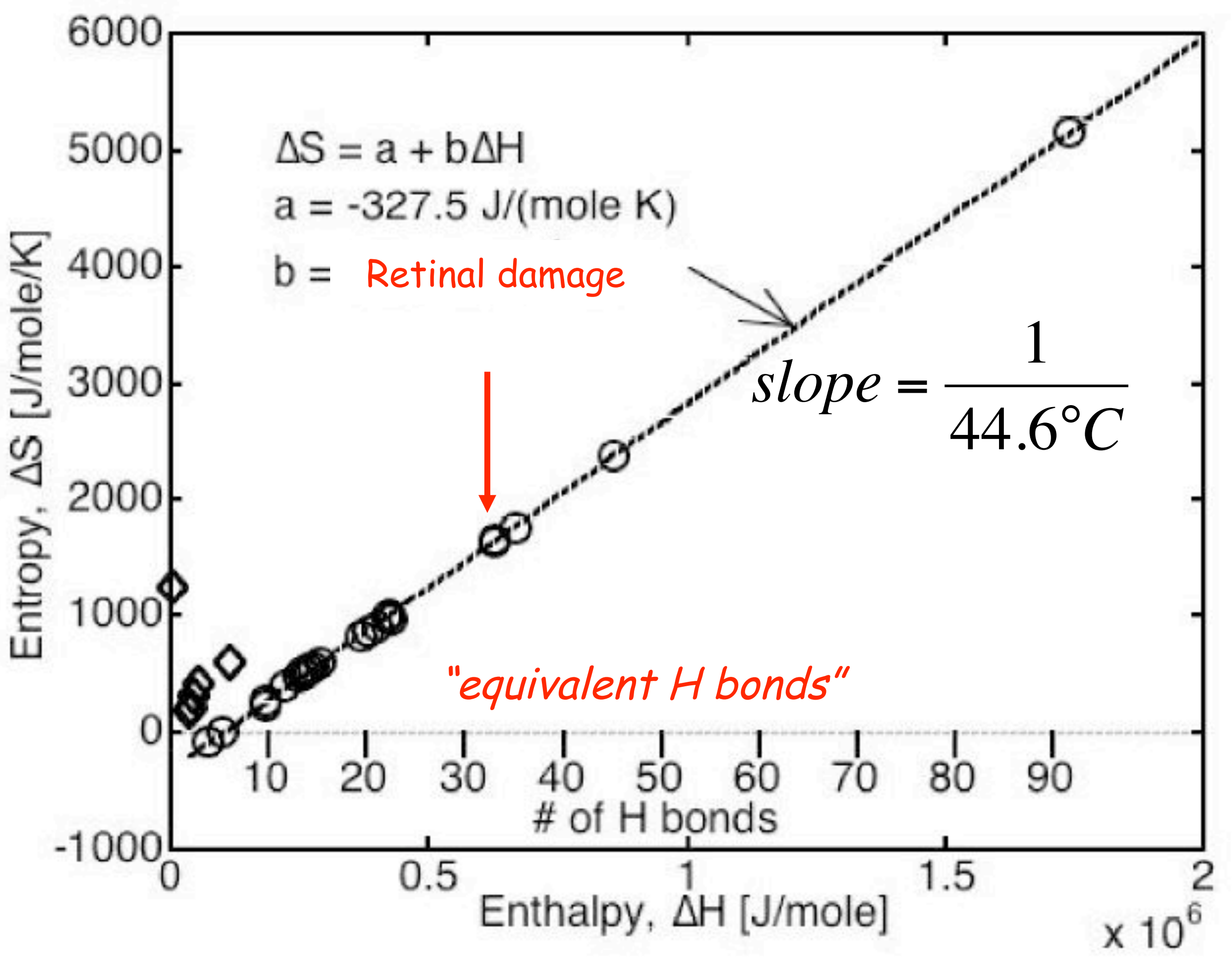
ΔH

Thermal damage

Literature review

SL Jacques, *J. Biomed. Optics* 11(4):041108, 2006

ΔS



$$slope = \frac{1}{44.6°C}$$

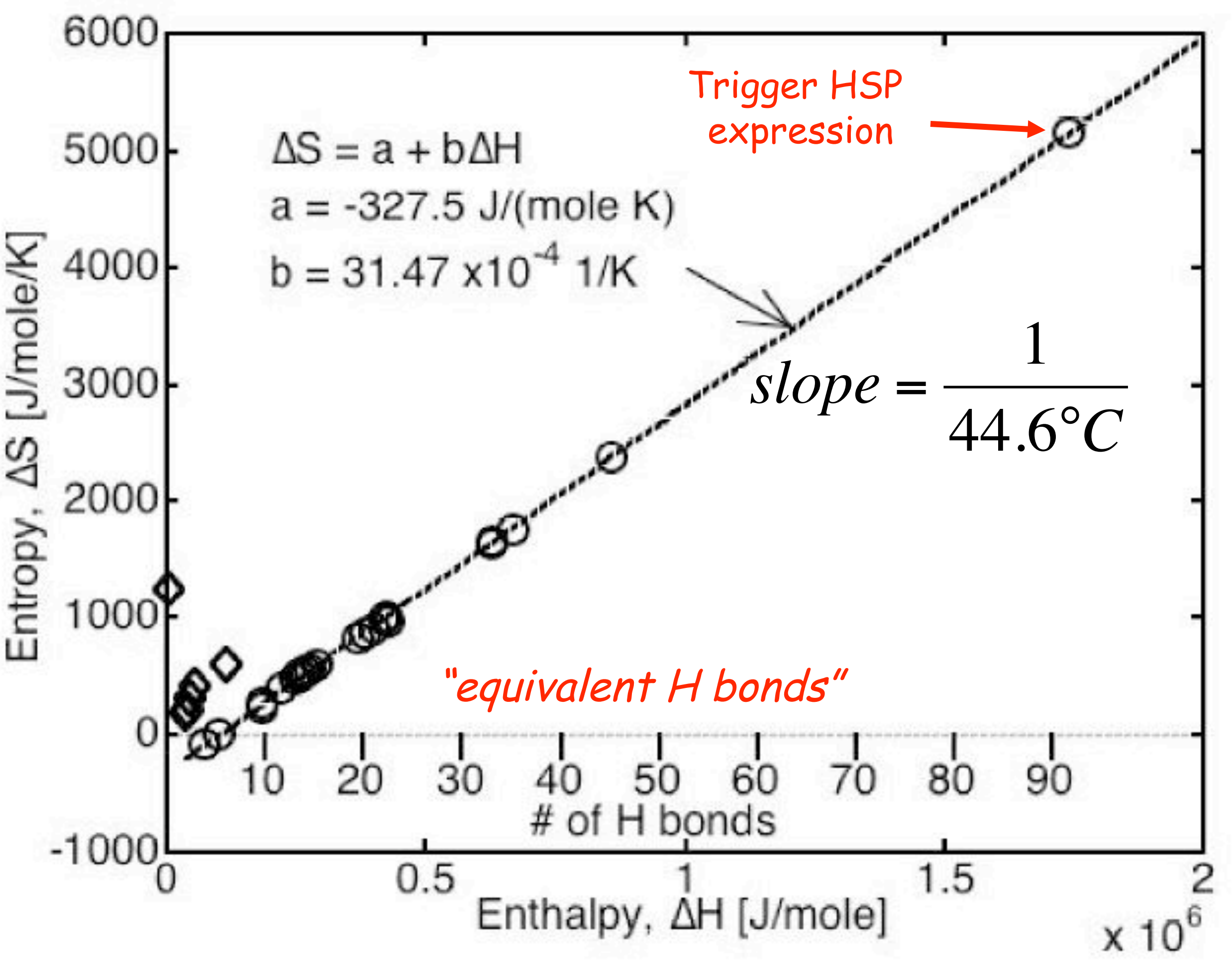
ΔH

Thermal damage

Literature review

SL Jacques, *J. Biomed. Optics* 11(4):041108, 2006

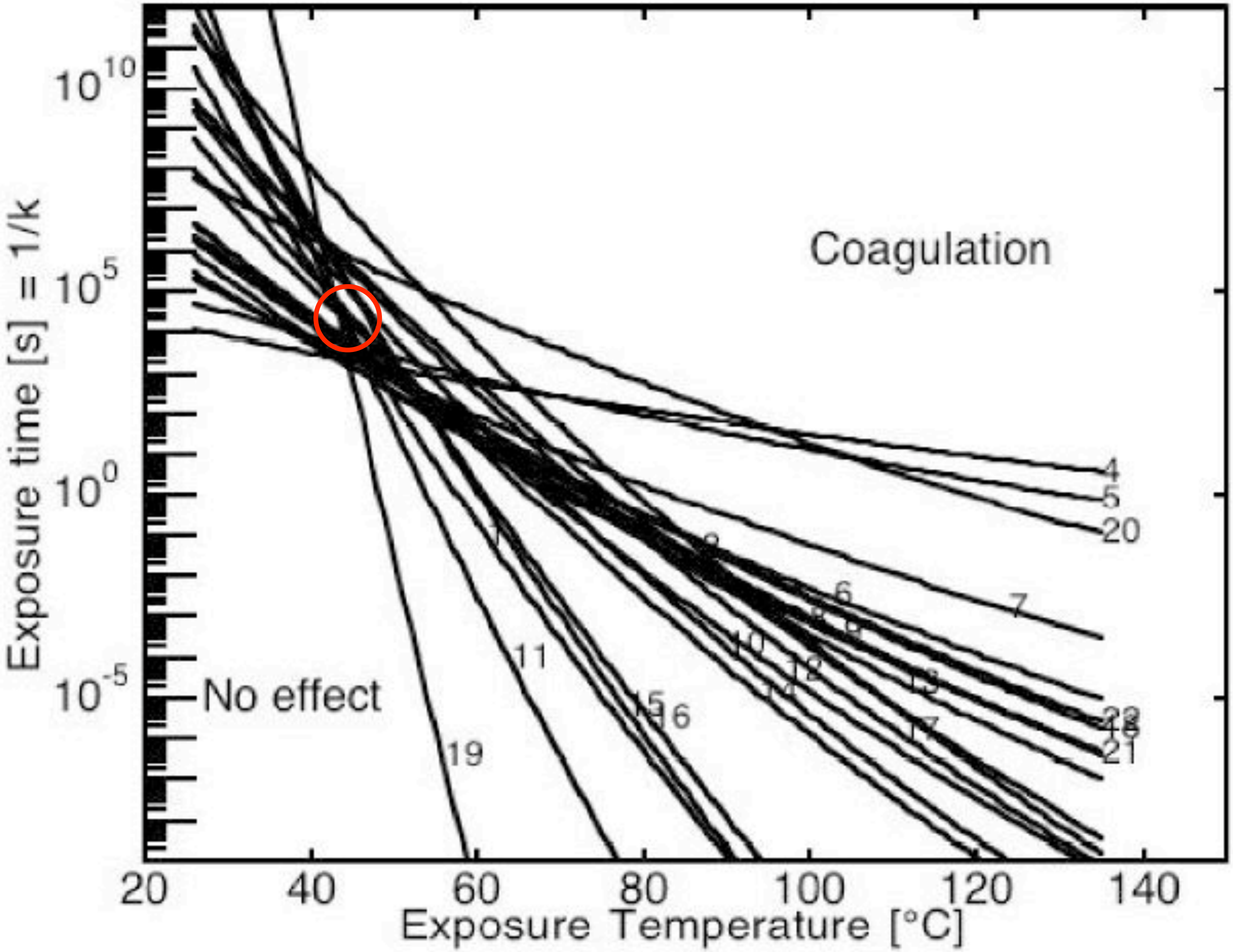
ΔS



$$slope = \frac{1}{44.6°C}$$

ΔH

Thermal damage

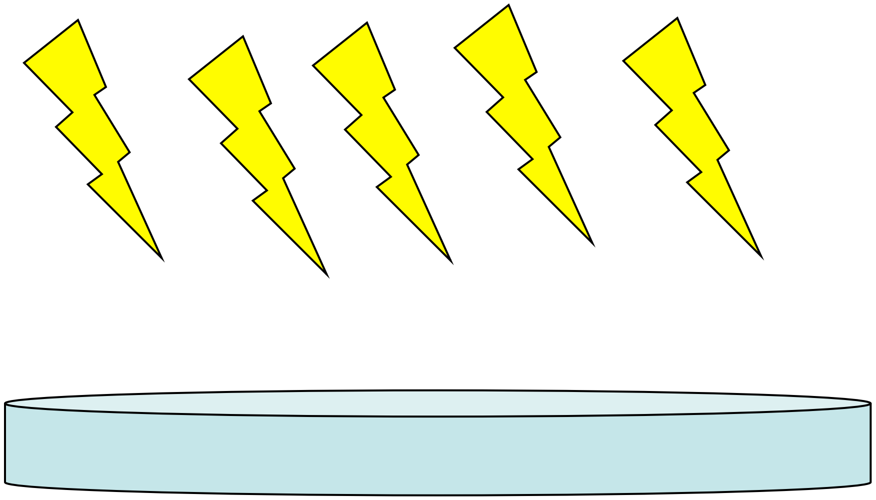


Thermal damage

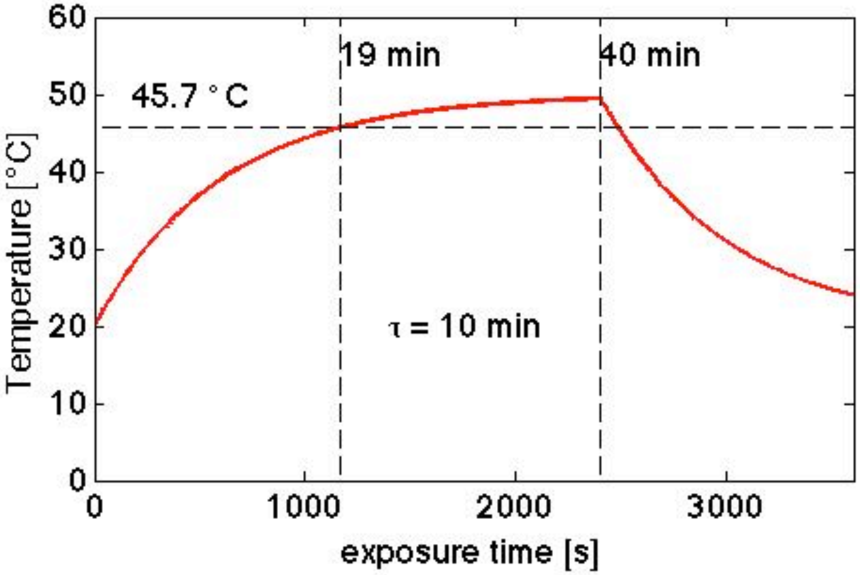
$$N(t) = N(0)e^{-\Omega}$$

$$\Omega = \int_0^t k(T(t))dt$$

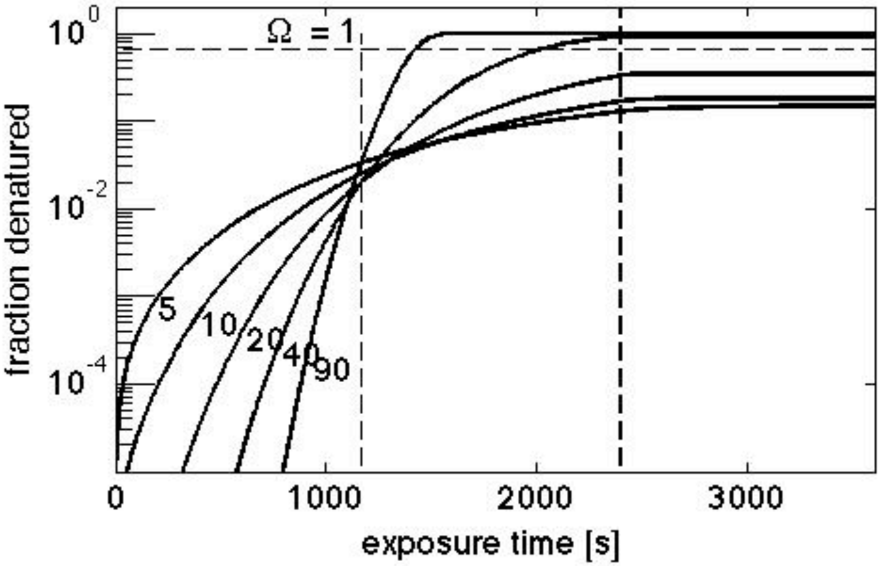
Solar heating ≈ 100 mW/cm^2



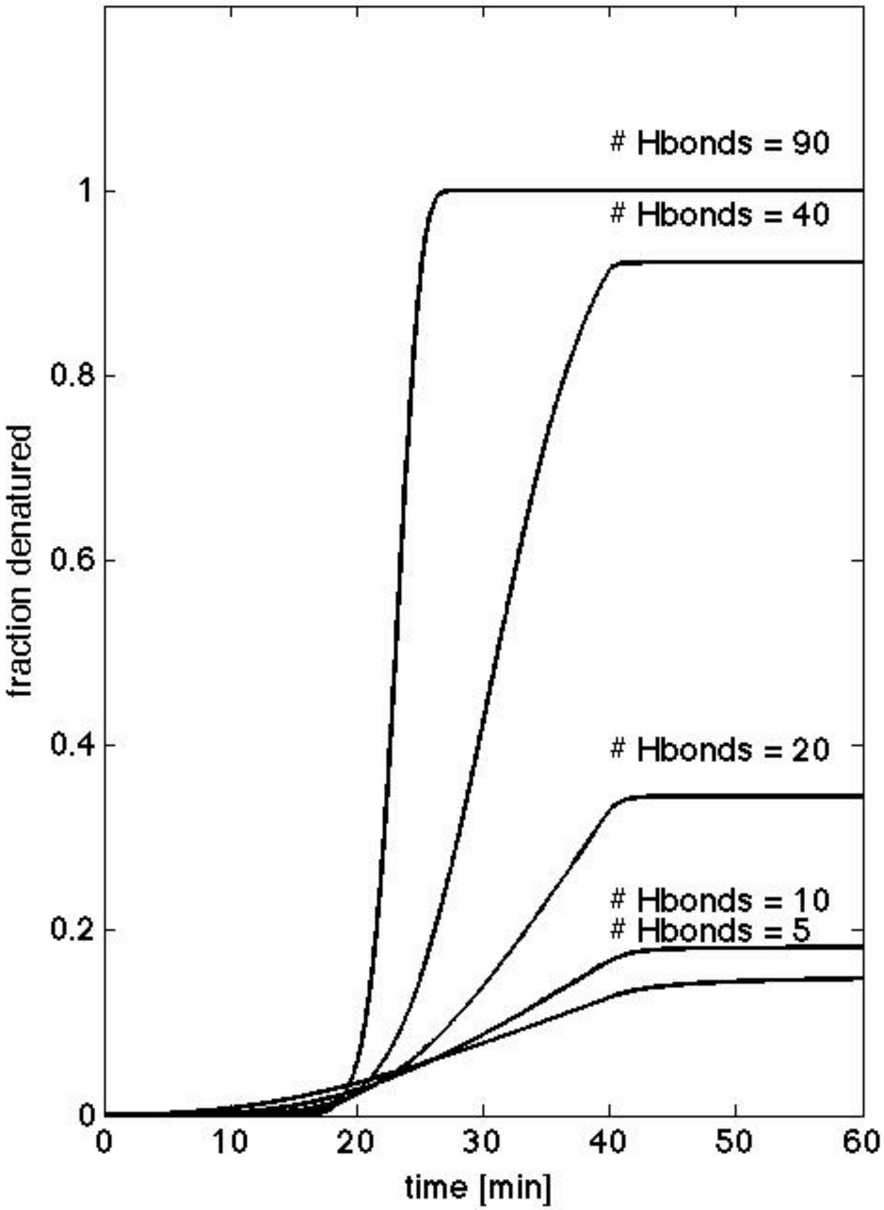
100 cm^2 x 1 cm =
1 liter



60
50
40
30
20
10
0
Temperature [°C]
45.7 °C
19 min
40 min
τ = 10 min
0
1000
2000
3000
exposure time [s]

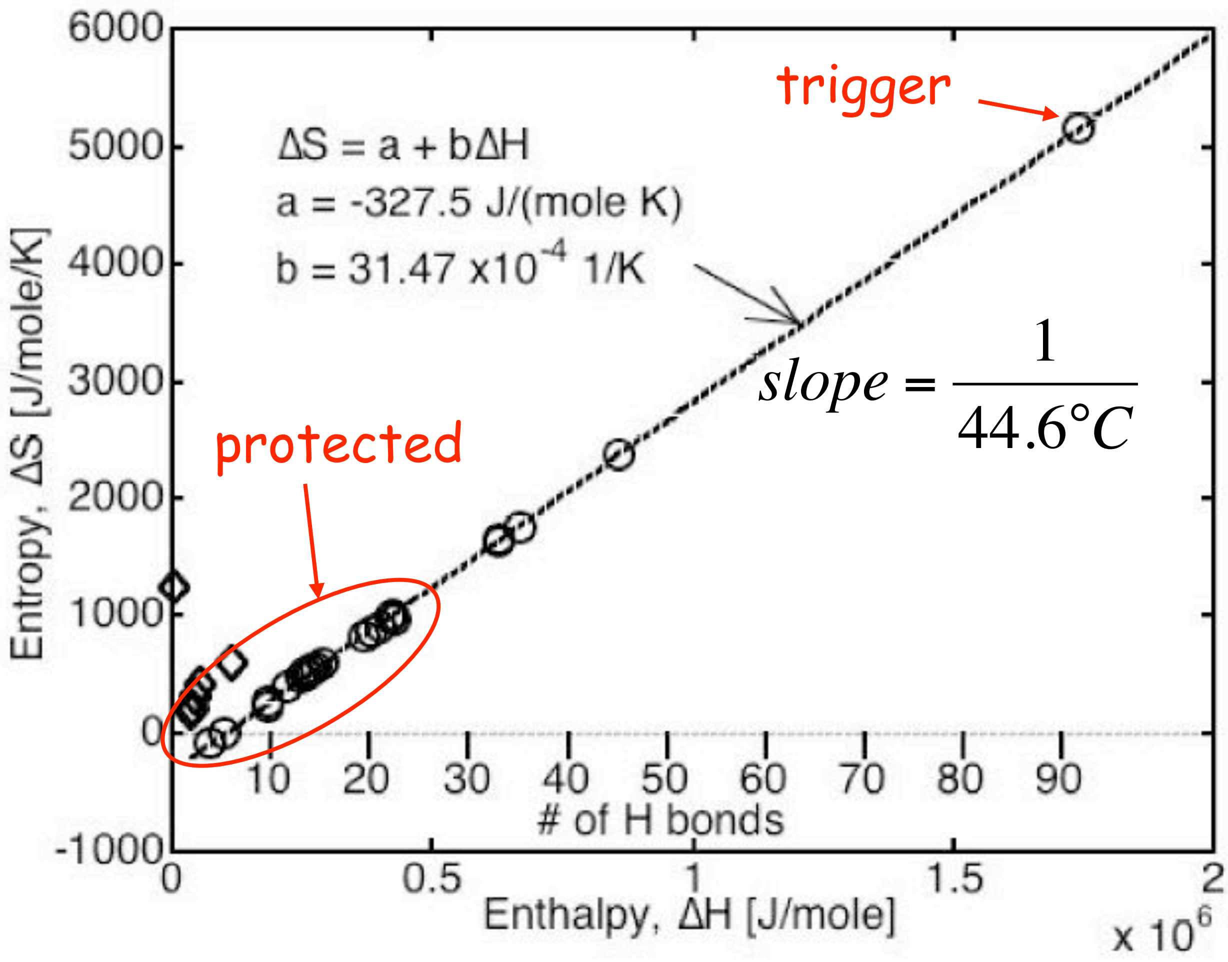


10^0
10^{-2}
10^{-4}
fraction denatured
Ω = 1
5
10
20
40
90
0
1000
2000
3000
exposure time [s]



Hbonds = 90
Hbonds = 40
Hbonds = 20
Hbonds = 10
Hbonds = 5
fraction denatured
0
0.2
0.4
0.6
0.8
1
0
10
20
30
40
50
60
time [min]

ΔS



trigger

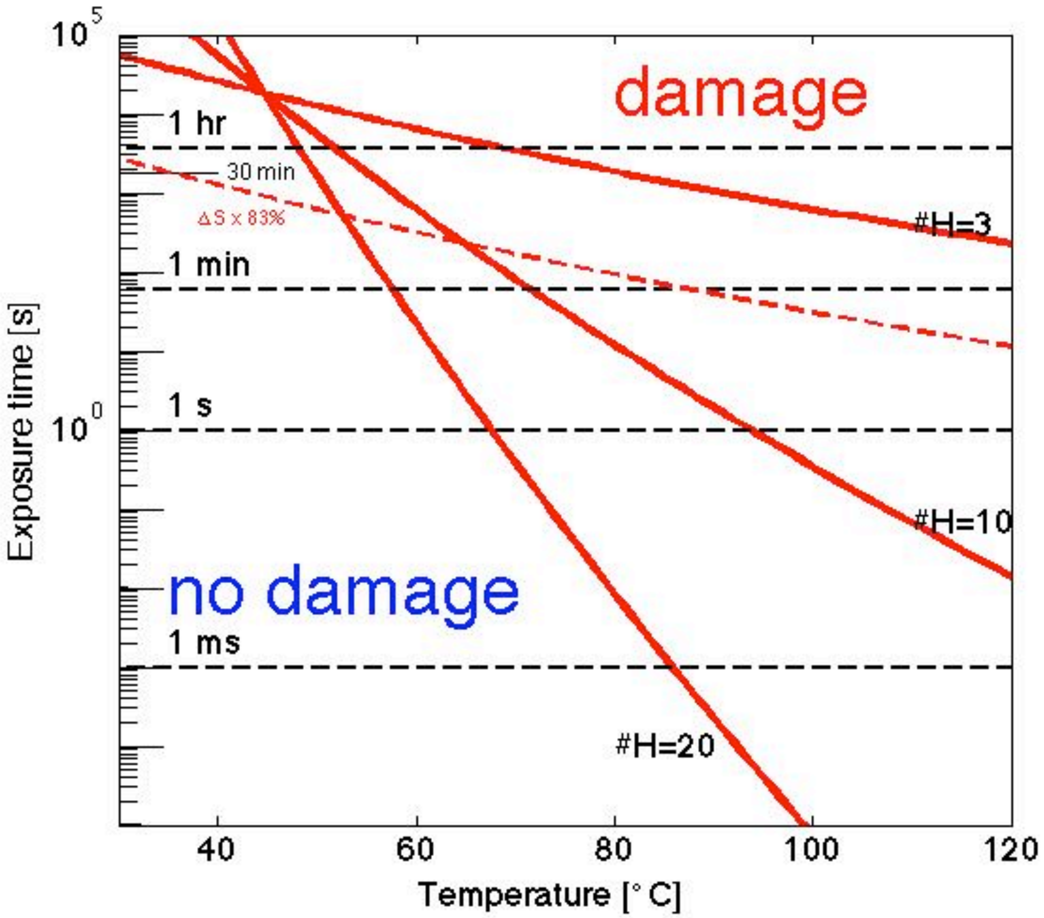
protected

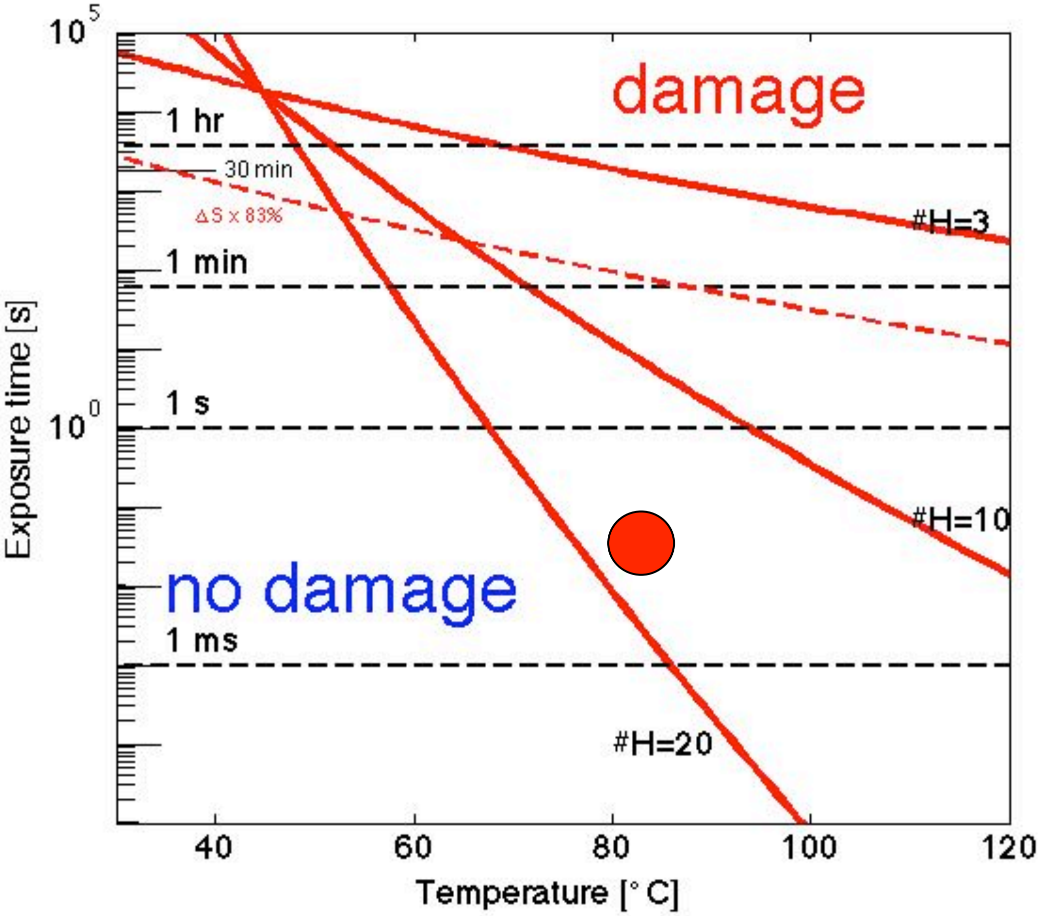
$$slope = \frac{1}{44.6°C}$$

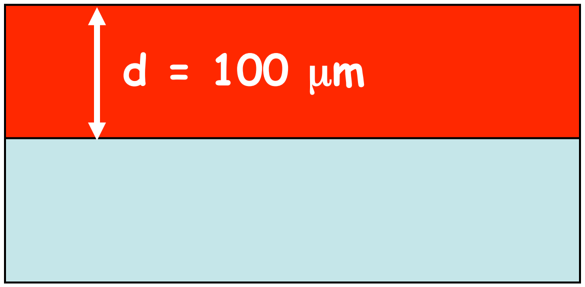
ΔH

…so how does this understanding of thermal injury impact the design of therapeutic protocols?

Time vs Temperature


10^5
10^0
damage
1 hr
30 min
ΔS x 83%
1 min
#H=3
1 s
#H=10
no damage
1 ms
#H=20
40
60
80
100
120
Exposure time [s]
Temperature [° C]





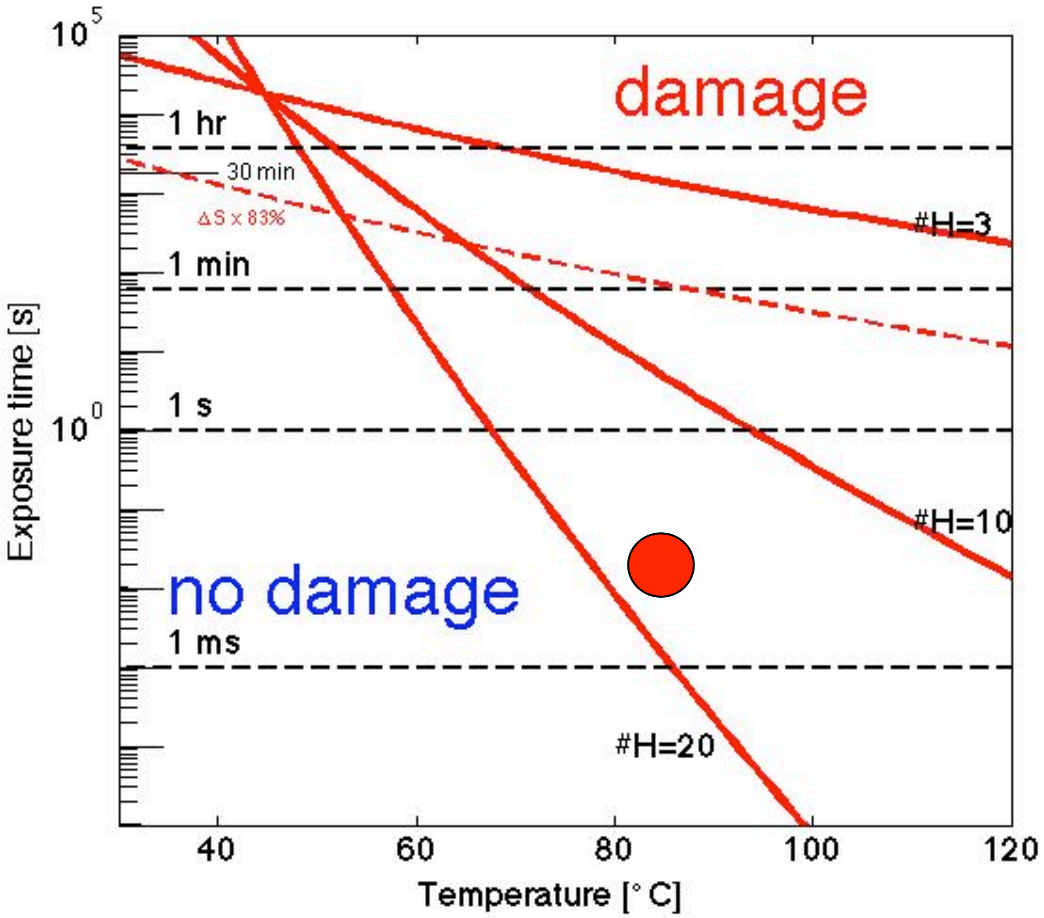
$$t_{relax} = \frac{(2d)^2}{4\alpha}$$

where

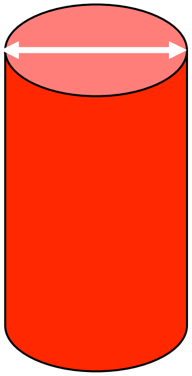
$$d = 100 \quad \mu m$$

$$\alpha = 1.3 \times 10^{-3} \quad cm^2/s$$

$$\boxed{t_{relax} = 77\ ms}$$



d = 100 µm



$$t_{relax} = \frac{d^2}{4\alpha}$$

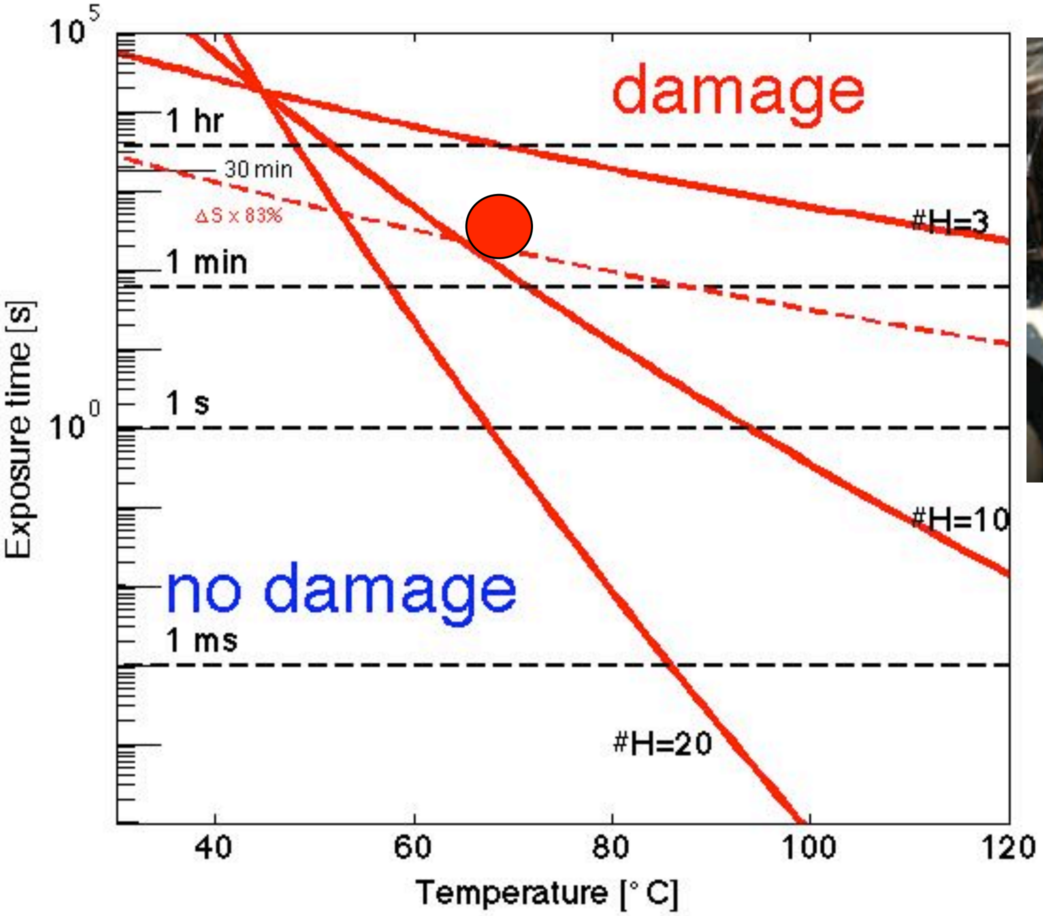
where

$$d = 100 \ \ \mu m$$

$$\alpha = 1.3 \times 10^{-3} \ \ cm^2/s$$

$$\boxed{t_{relax} = 19 \ ms}$$

Oral melanoma in veterinary care



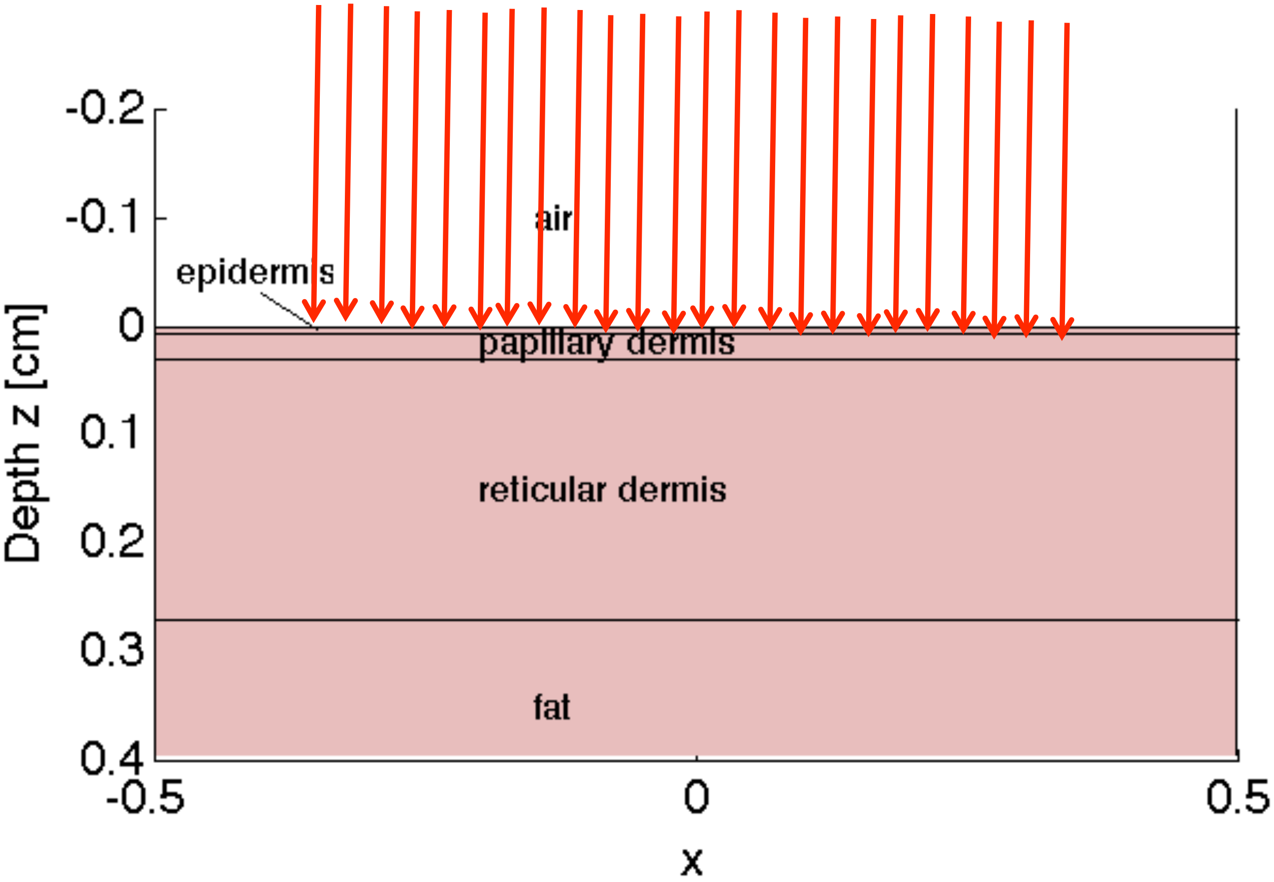
Oral melanoma in dog

Use diode laser at low power over several minutes to slowly heat,

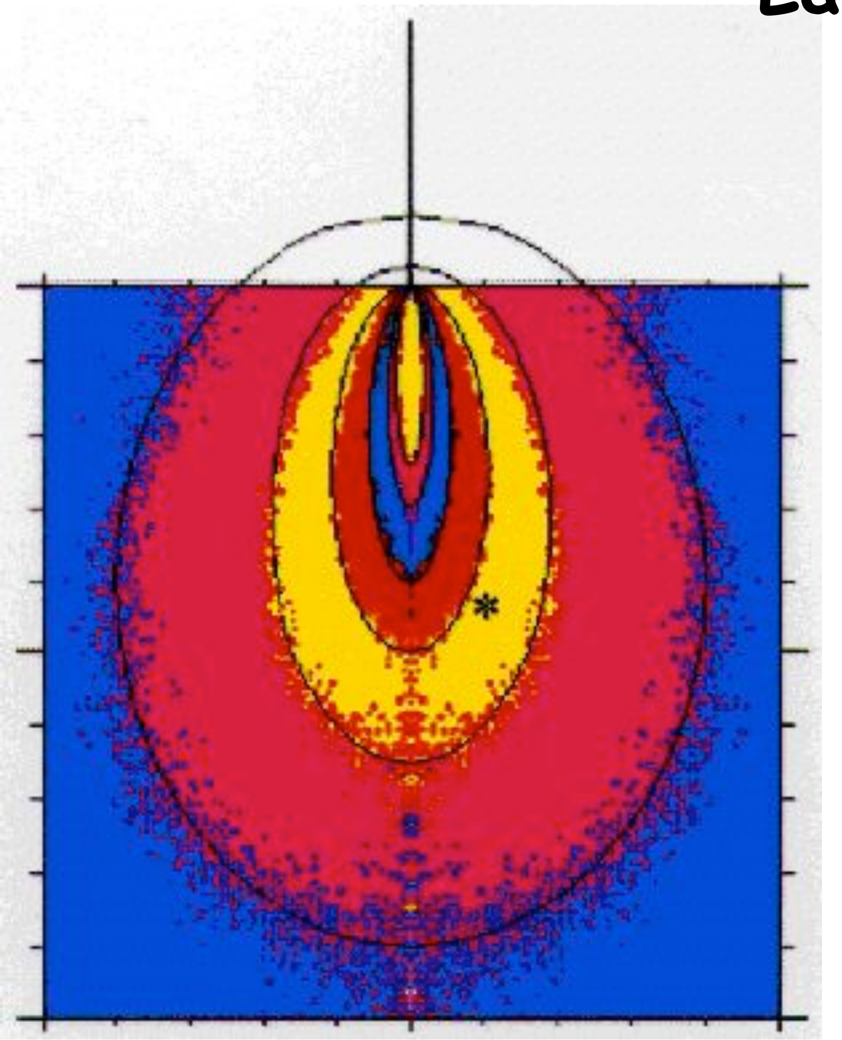
allowing thermal diffusion to bring heat to deeper layers,

avoid overheating and vaporizing surface

matlab example



Laser-Tissue Interactions



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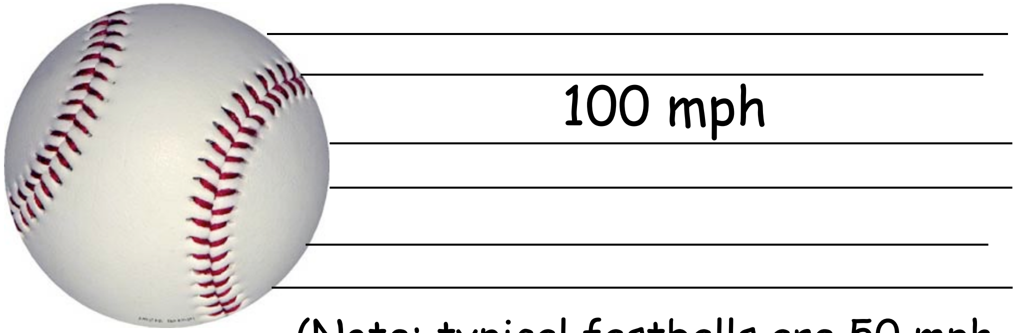
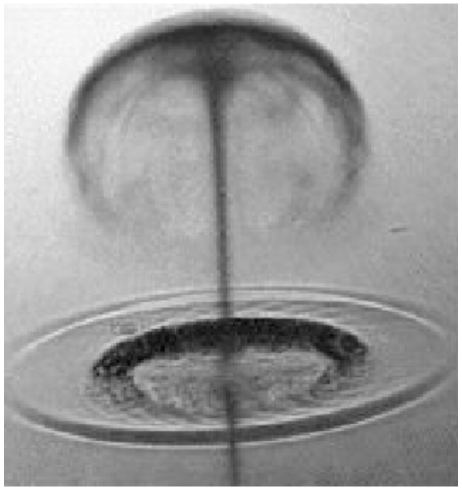
The physics of laser-induced concussive insult to peripheral nerves

Consider a 100 mph baseball thrown by a pitcher…

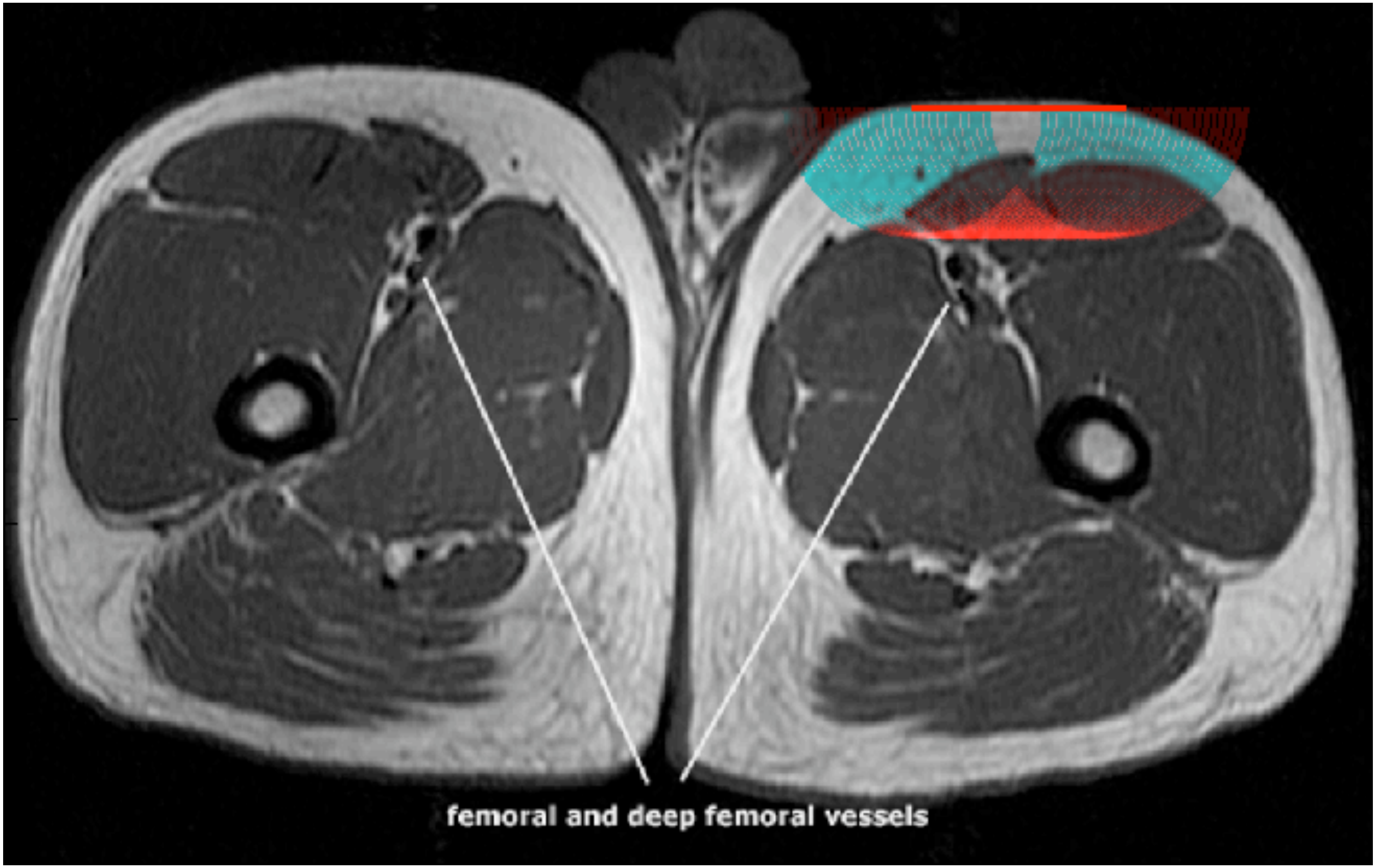


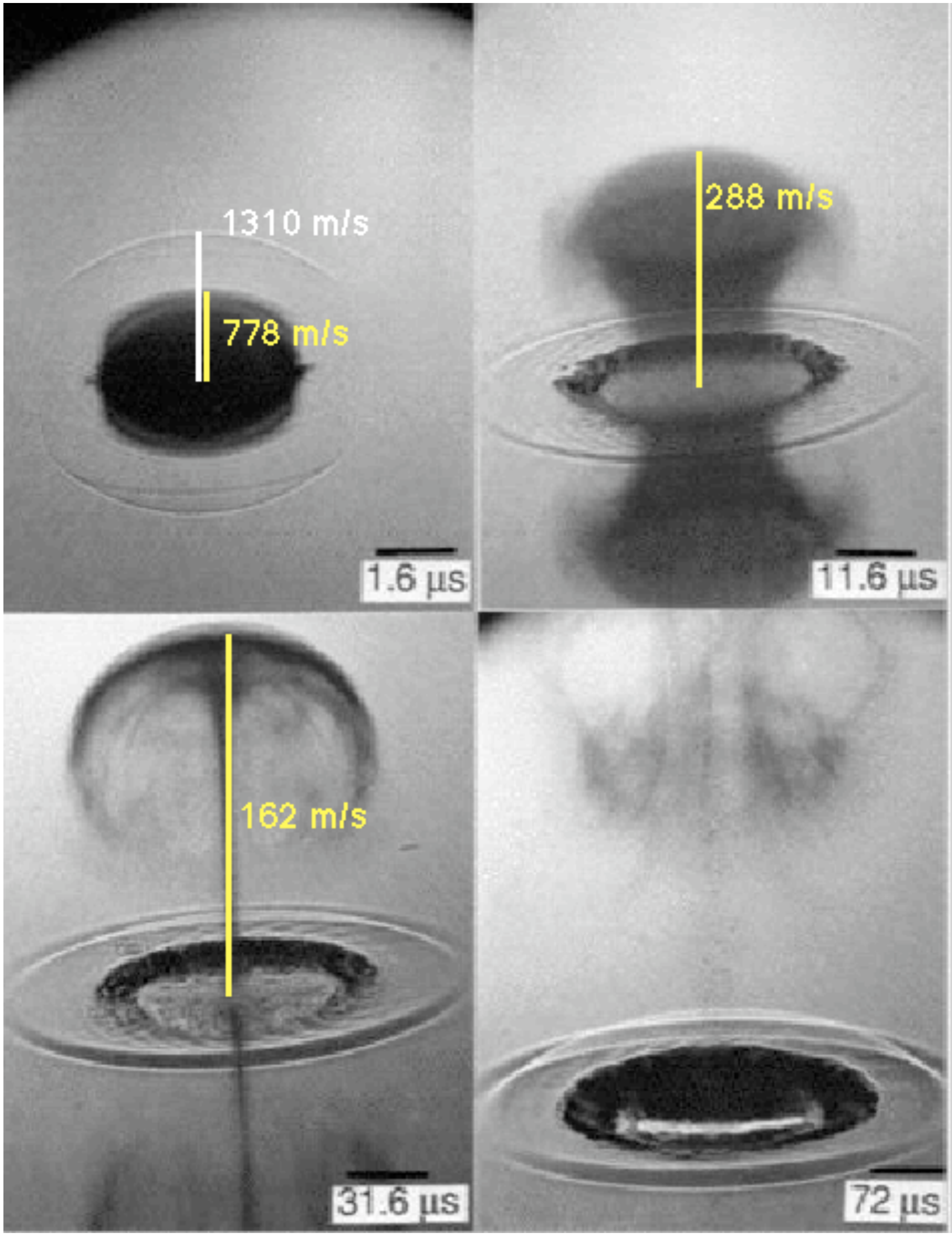
(Note: typical fastballs are 50 mph, but the fastest balls clocked are about 100 mph.)

Consider the recoil momentum due to pulse laser ablation of tissue…




femoral and deep femoral vessels


femoral and deep femoral vessels



Consider the recoil momentum due to pulse laser ablation of tissue.

A small scale example:

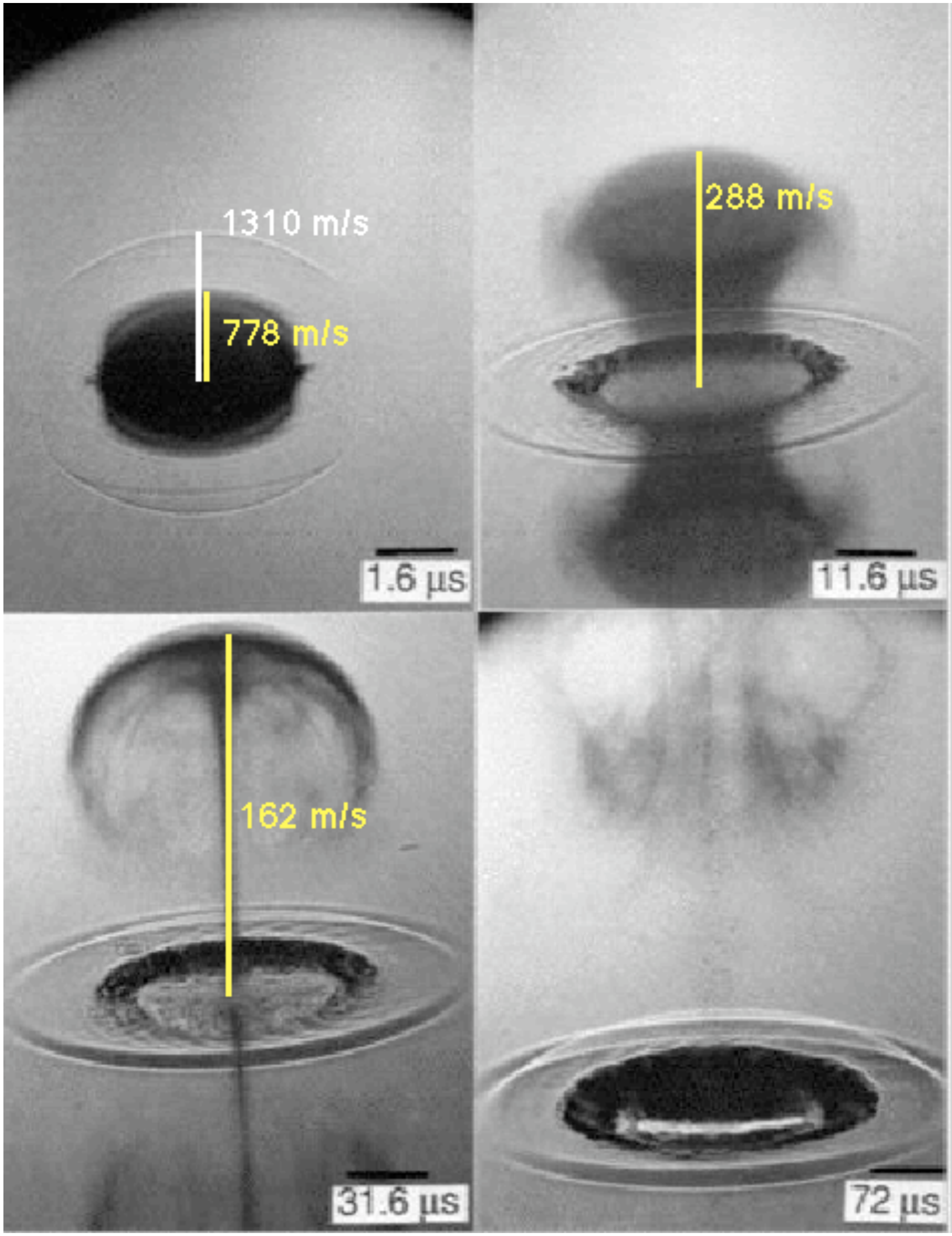
ErYAG laser ablation of water:

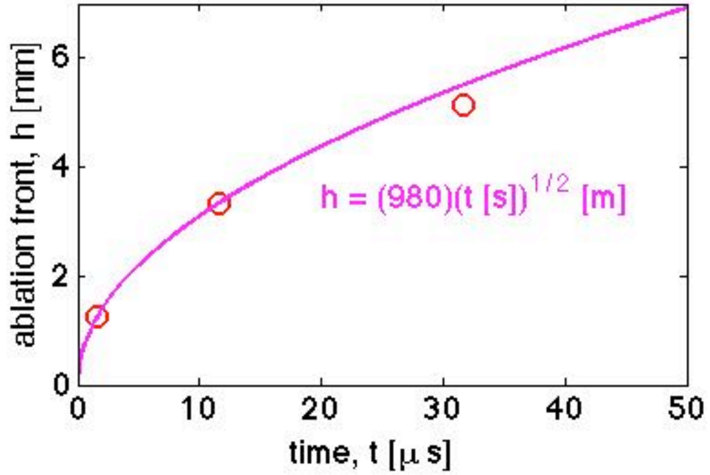
2.94 µm wavelength

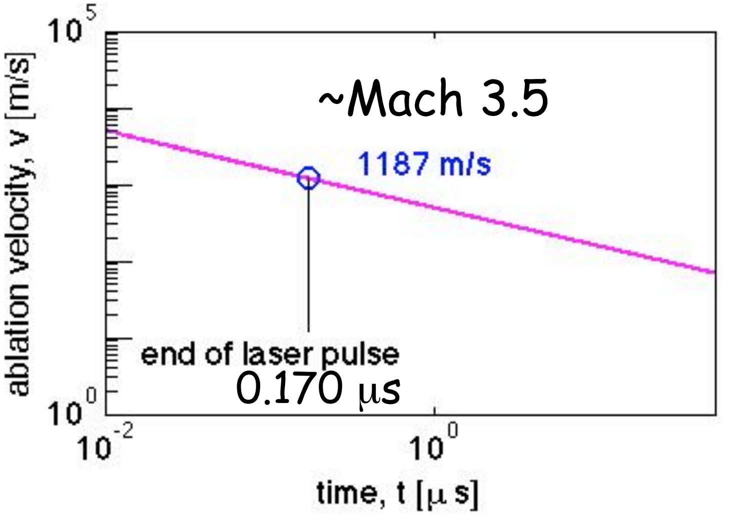
25 mJ pulse energy

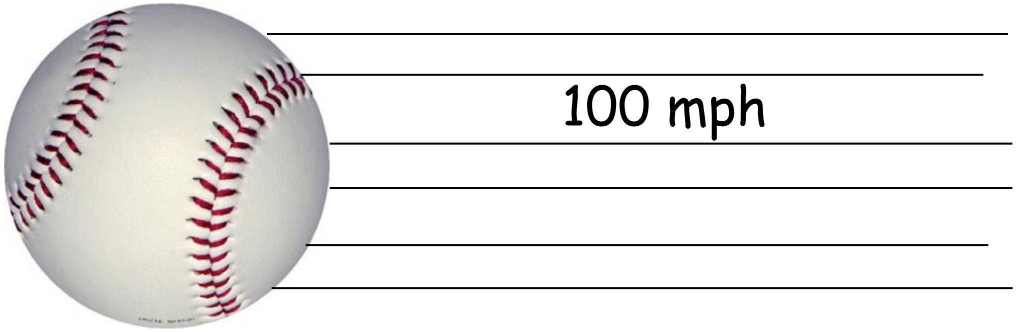
170 ns pulse duration

3.1 mm $1/e^2$ diameter for Gaussian beam


1310 m/s
778 m/s
1.6 µs
288 m/s
11.6 µs
162 m/s
31.6 µs
72 µs


ablation front, h [mm]
0
2
4
6
h = (980)(t [s])^1/2 [m]
0
10
20
30
40
50
time, t [µ s]


ablation velocity, v [m/s]
10^5
10^0
~Mach 3.5
1187 m/s
end of laser pulse
0.170 µs
10^-2
10^0
time, t [µ s]



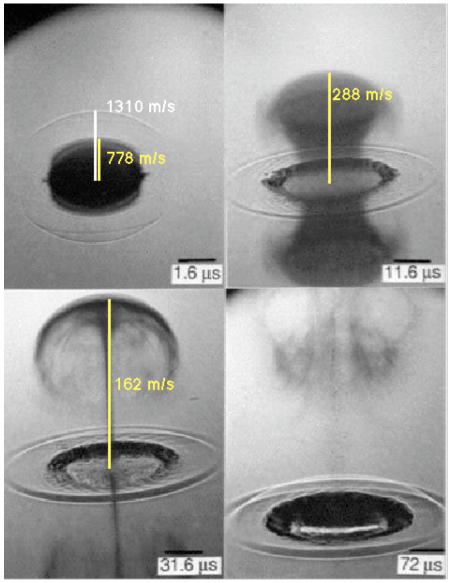
Consider a 100 mph baseball thrown by a pitcher:

The velocity is (100 mph)(1720 m/mile)/(3600 s/hr) = 48 m/s.

The mass of a baseball is 142.5 g (a standard Wilson$^{\text{TM}}$ baseball)

The momentum is (0.1425 kg)(48 m/s) = **6.8 [kg m/s].**

A baseball has a 9 inch (7.29 cm) diameter.



Consider the laser experiment:

The velocity of the ejected water ~ 1187 m/s, or Mach 3.5.

If the mass removal is 5.73 g,

(0.00573 kg)(1187 m/s) = **6.8 [kg m/s]**

5.73 g of mass corresponds to **729** µm over a 10-cm-dia. circular area.

Scale the problem

Momentum per unit area

Momentum of 100-mph baseball

$$\frac{6.8\ [\mathrm{kg\ m/s}]}{78.5\ \mathrm{cm}^2} = 0.087\ [(\mathrm{kg\ m/s})/\mathrm{cm}^2]$$

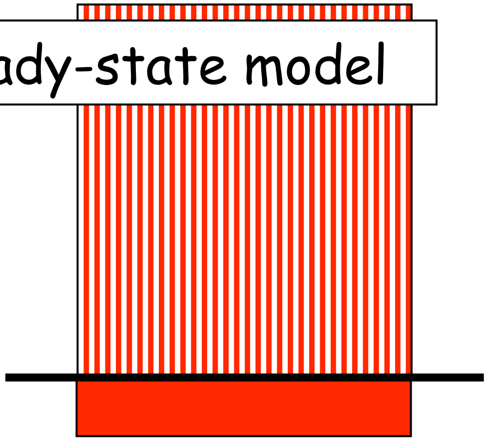
Area of 10-cm-dia. laser spot

Steady-state model

vs

Blow-off model

Steady-state model



Water explosively vaporizes away from surface during *long pulse* from laser

$$m = \rho \frac{U_p}{Q_{th}}$$

where

m = mass of tissue removed [g]

U_p = energy of laser pulse [J], $U_p = E\,t$,

E = irradiance [W/cm^2]

t = time of exposure [s]

ρ = density of tissue [g/cm^3]

Q_{th} = threshold energy density for ablation [J/cm^3]

Steady-state model

Water explosively vaporizes away from surface during *long pulse* from laser

$$m = \rho \frac{U_p}{Q_{th}}$$

where

m = mass of tissue removed [g]

U_p = energy of laser pulse [J], $U_p = E\,t$,

E = irradiance [W/cm^2]

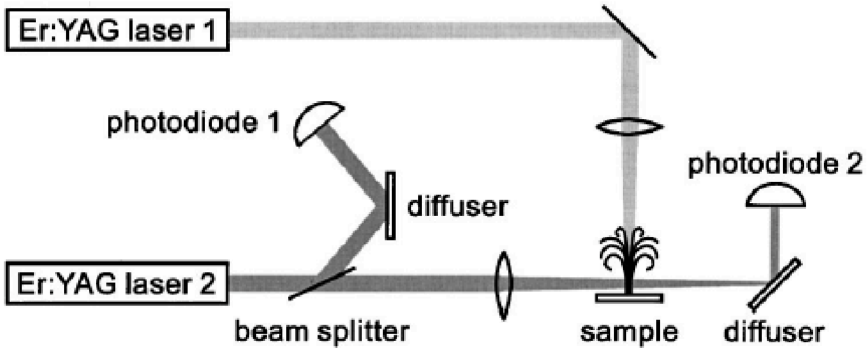
t = time of exposure [s]

ρ = density of tissue [g/cm^3]

Q_{th} = threshold energy density for ablation [J/cm^3]

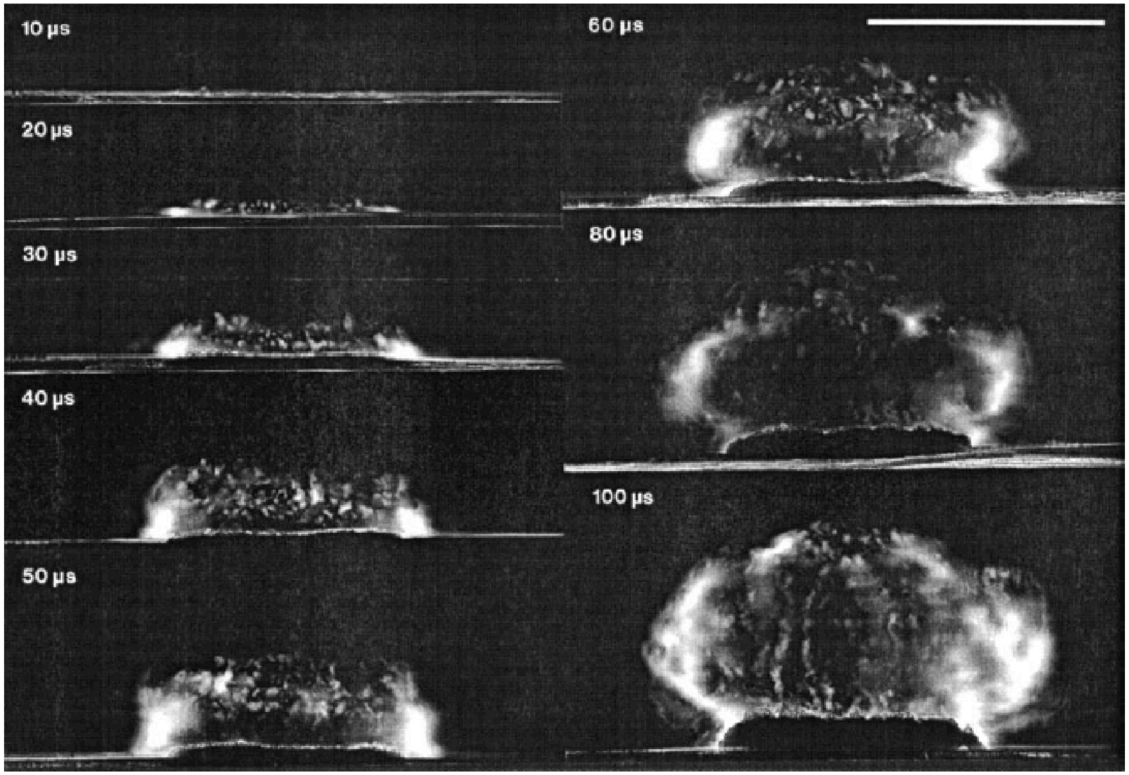
Steady-state model

Nahen and Vogel (2002)



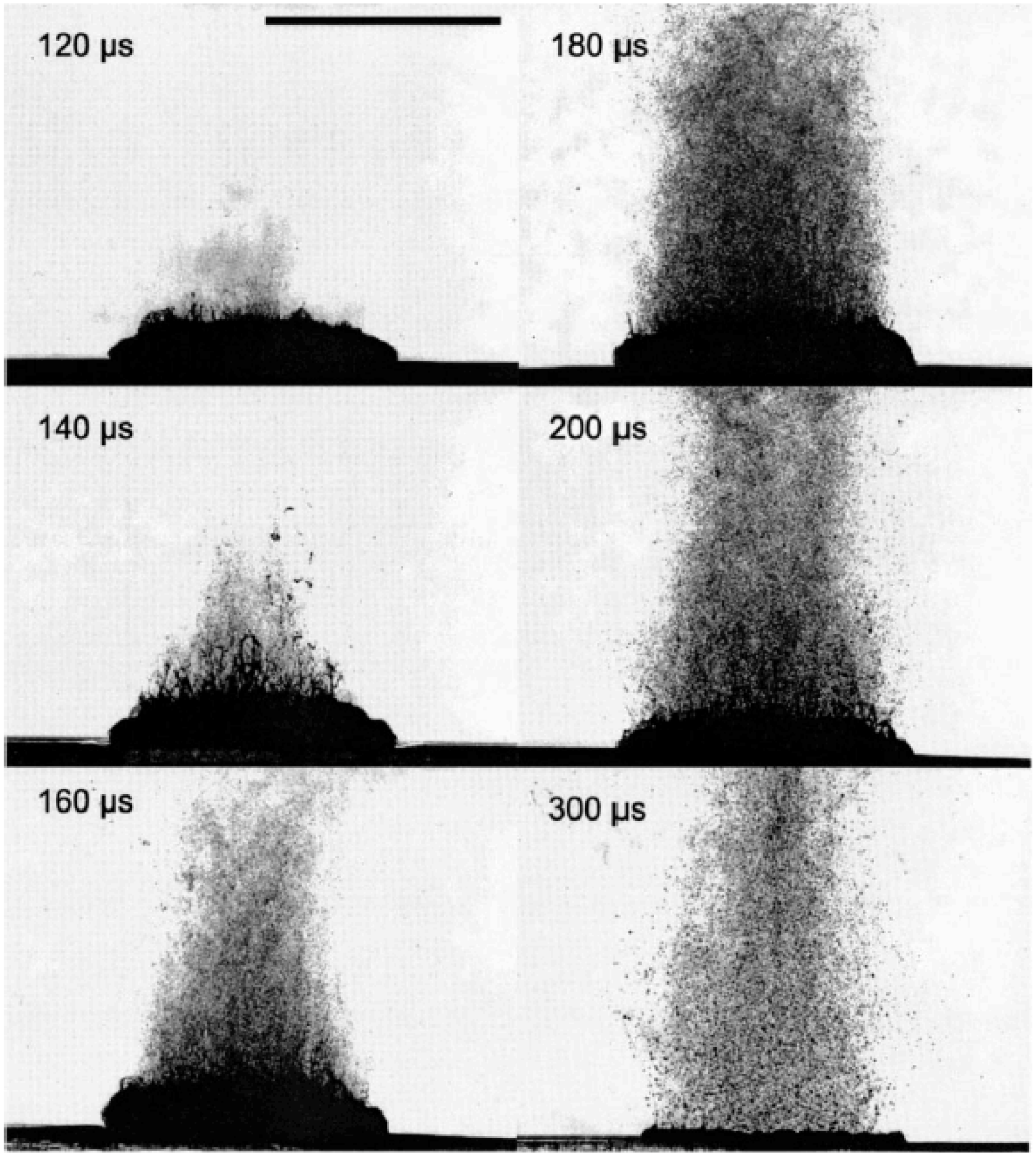
100 μs laser pulse

Four samples were tested:
1. 30% gelatin (70% water content)
2. 10% gelatin (90% water content)
3. water
4. skin



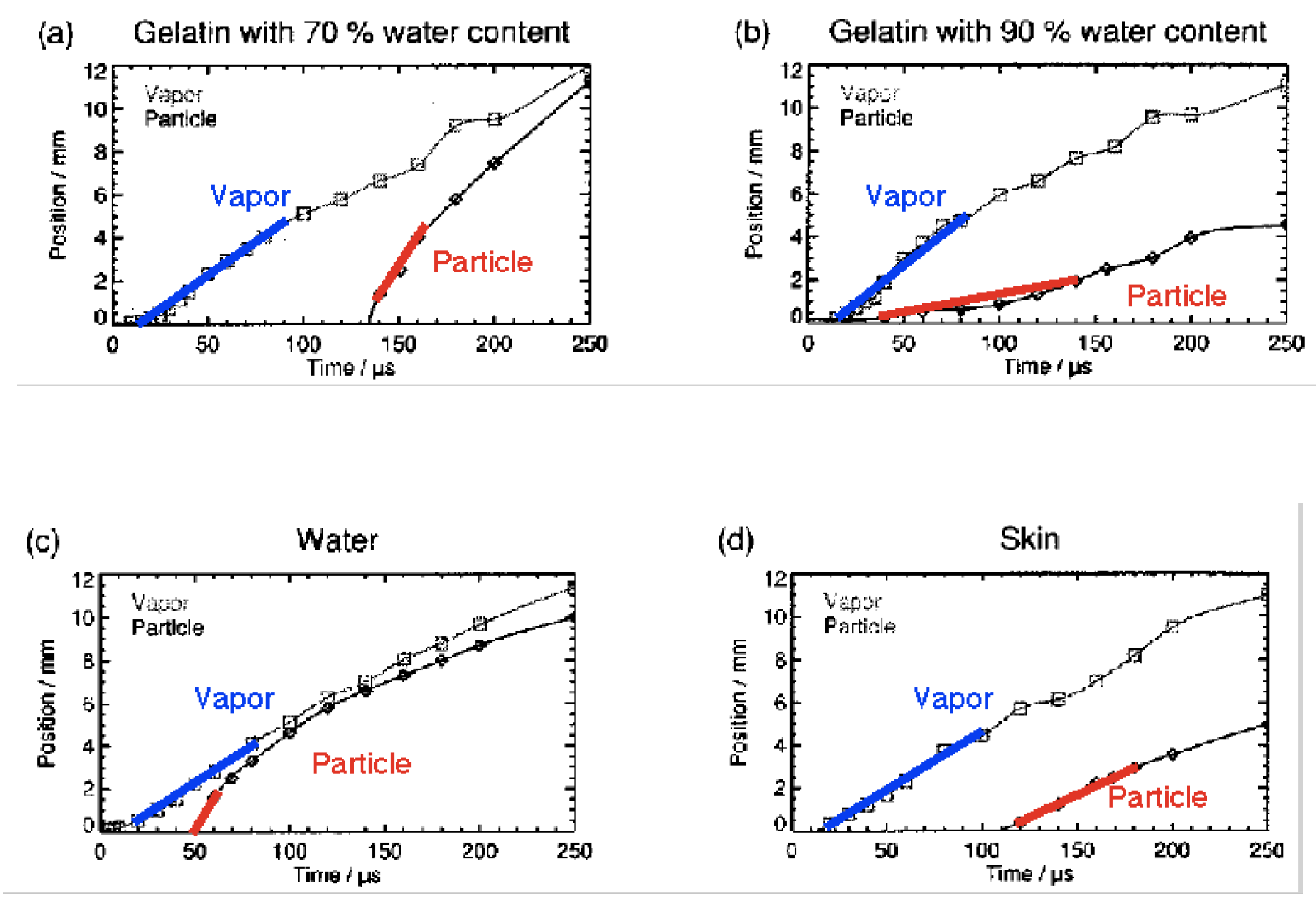
Steady-state model

Nahen and Vogel (2002)



Steady-state model

Nahen and Vogel (2002)



Steady-state model

based on data of Nahen and Vogel (2002)

Initial velocities during long-pulse laser ablation (200-µs Er:YAG laser), determined as the slope of the blue and red lines in previous figure.

sample	vapor	particle
30% gelatin	62 m/s	135 m/s
10% gelatin	71 m/s	16 m/s
water	58 m/s	143 m/s
skin	55 m/s	42 m/s

These velocities are roughly 10- to 100-fold lower than needed to achieve the *density of momentum* required for a **Concussive Insult**.

Steady-state
model

vs

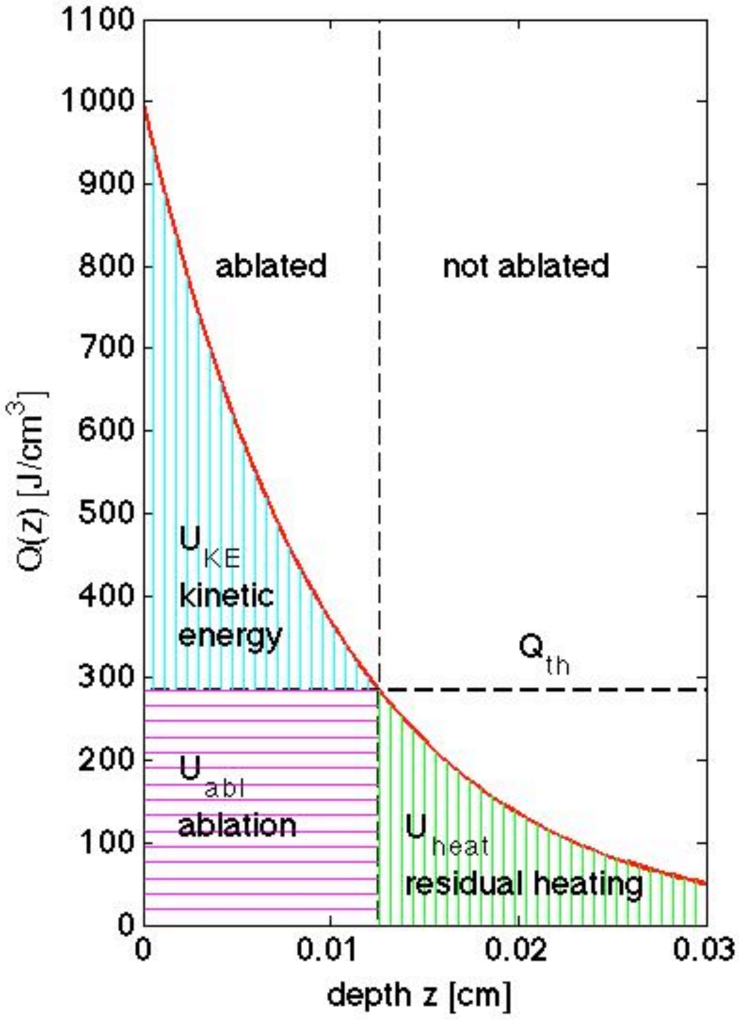
Blow-off model

Blow-off model

$$Q_{th} = \mu_a H_o e^{-\mu_a z_{abl}}$$

Energy deposition $Q(z)$

J/cm^3



Depth in tissue, z [cm]

$$U_{KE} = U_p - U_{abl} - U_{heat}$$

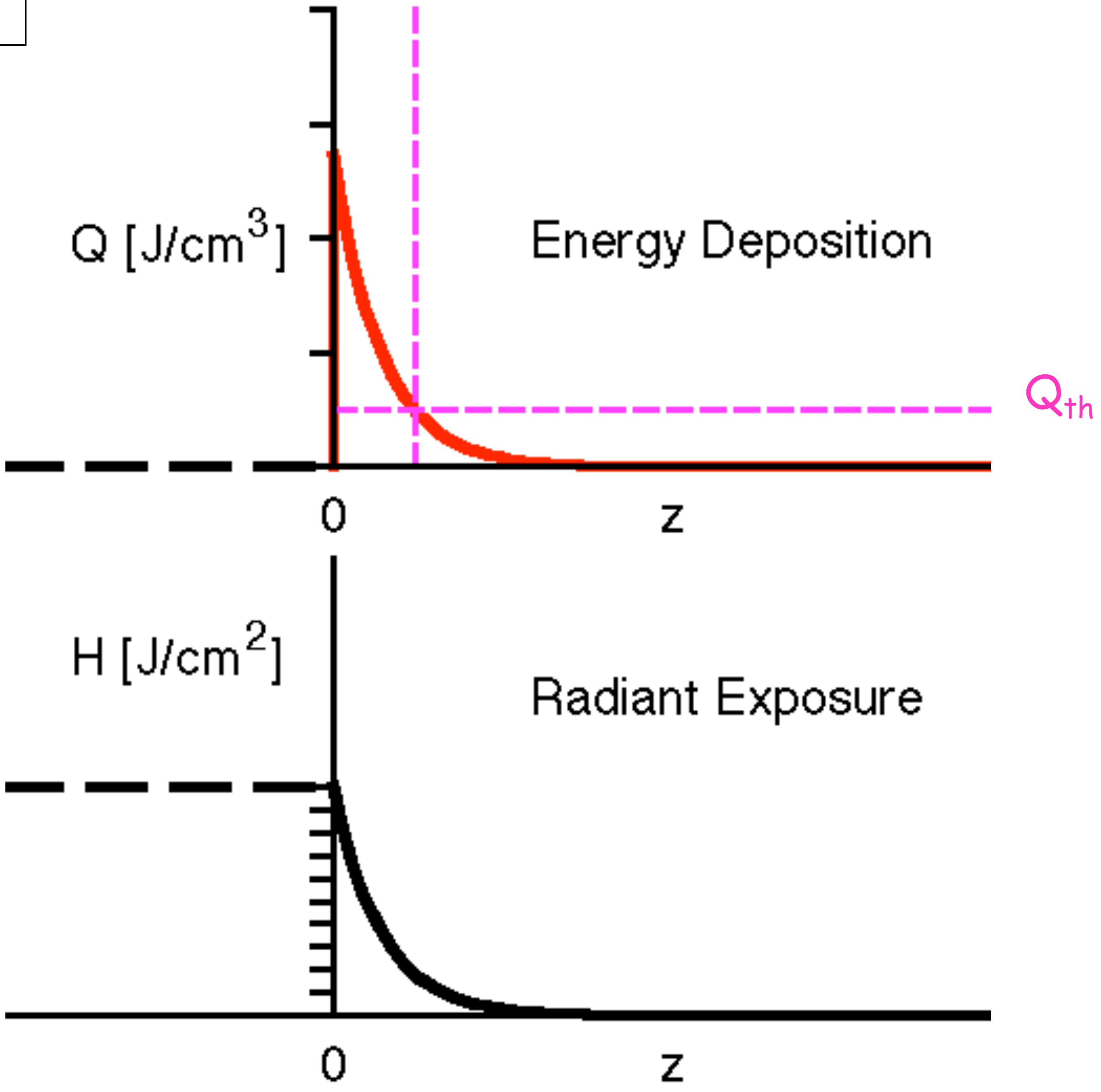
$$U_{abl} = Q_{th} z_{abl}$$

$$U_{heat} = \frac{Q_{th}}{m_{a.eff}}$$

Blow-off model

$$Q_{th} = \mu_a H_o e^{-\mu_a z_{abl}}$$

$$Q = \mu_a H$$



Thermal confinement:

Laser deposits faster than heat can diffuse away

$$t = \frac{d^2}{4\alpha} = \frac{1}{4\alpha\mu_a^2}$$

Stress confinement:

Laser deposits faster than pressure can progate away

$$t = \frac{d}{c_s} = \frac{1}{c_s\mu_a}$$

The ***mechanism of ablation*** underlying Q_{th}:

1. ***Explosive vaporization***:
   1. enthalpy of vaporization
   2. spinodal decomposition
   3. superheated fluid
   4. explosive ejection

~ 300°C

2. ***Thermoelastic expansion***:
   1. thermoelastic expansion
   2. inertia of the outward expansion
   3. Overcome breaking strength of the tissue
   4. ejection

~ 70°C

This mechanism was discussed by Dingus and Scammon (1991) as "spallation" and later discussed by Albagli et al. (1994) as "inertial confinement" in a review of ablation literature.

ΔT = 4°C --> ΔP = ± 10 bar --> cavitation of water

ΔT = 28°C --> ΔP = ± ~35 bar --> spallation of tissue

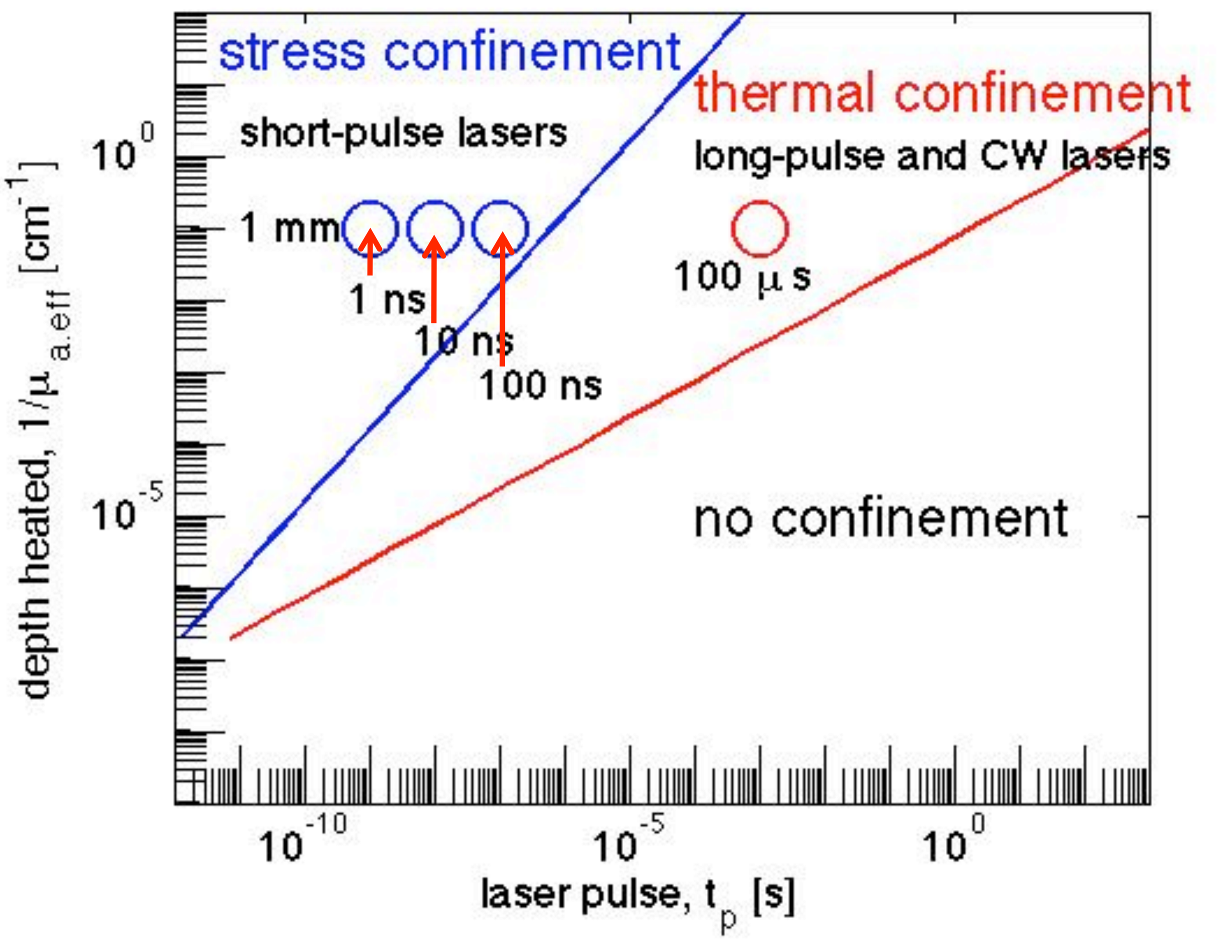
Reported threshold of ablation (Q_{th} [J/cm^3]) and equivalent temperature (T_{equiv} [°C]).

Laser	t_p	Q_{th}	T_{equiv}
ArF excimer ablation of skin	14 ns	397 J/cm^3	120 °C
Pulsed dye laser explosion of red blood cells	1 ms	392 J/cm^3	125 °C
Albagli's review (various tissues and lasers)	short pulses	285 J/cm^3	62 °C

… not 300°C !!

…supports the "spallation"
or "inertial confinement"
mechanism underlying Q_{th}

Target size



Time

etch depth

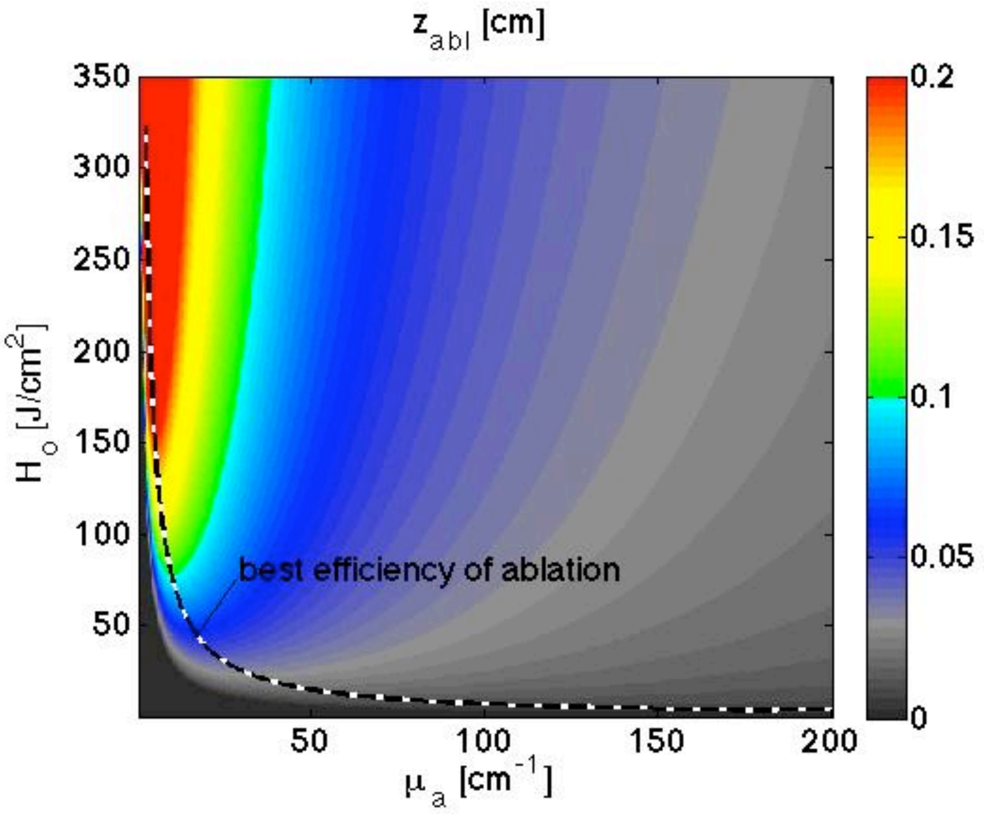
$$z_{abl} = \frac{1}{\mu_a}\log\left(\frac{\mu_a H_o}{Q_{th}}\right)$$

$$Q_{th} = \mu_a H_o e^{-\mu_a z_{abl}}$$

Radiant exposure

H_o

J/cm^2



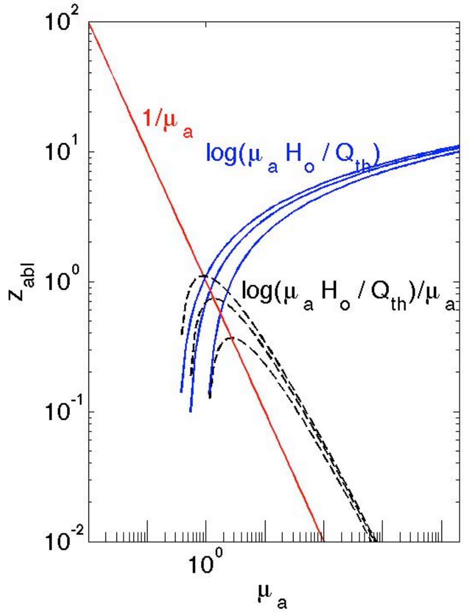
μ_a [cm^{-1}]

Absorption coefficient

etch depth

$$Q_{th} = \mu_a H_o e^{-\mu_a z_{abl}}$$

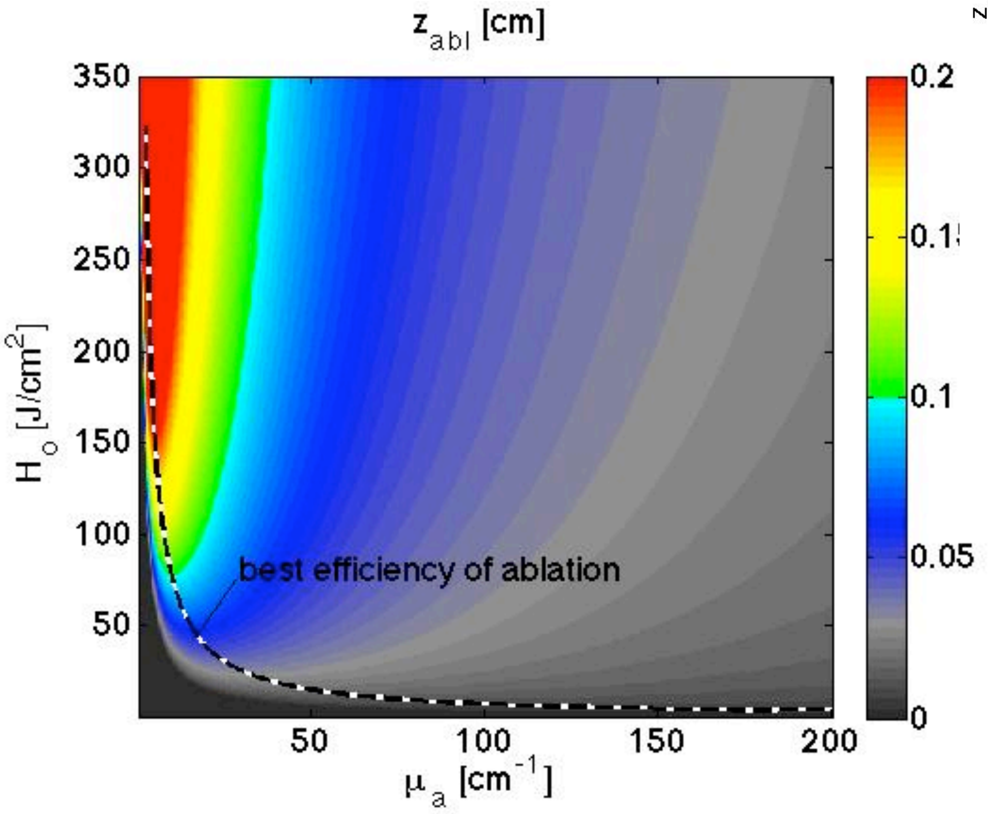
$$z_{abl} = \frac{1}{\mu_a} \log\left(\frac{\mu_a H_o}{Q_{th}}\right)$$



Radiant exposure

H_o

J/cm^2



μ_a [cm^{-1}]

Absorption coefficient

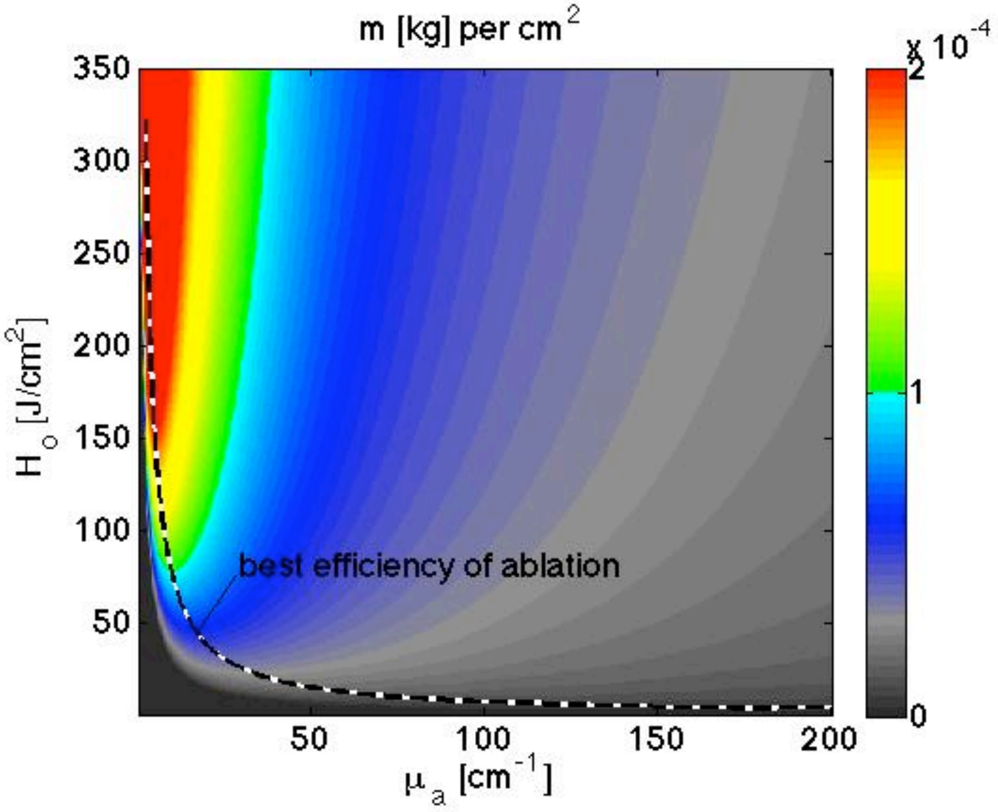
mass

$$m = \frac{\rho \ z_{abl}}{1000 \ \ g/kg}$$

Radiant exposure

H_o

J/cm^2



μ_a [cm^{-1}]

Absorption coefficient

Kinetic Energy

U_p = laser pulse

$$U_{KE} = U_p - U_{abl} - U_{heat}$$

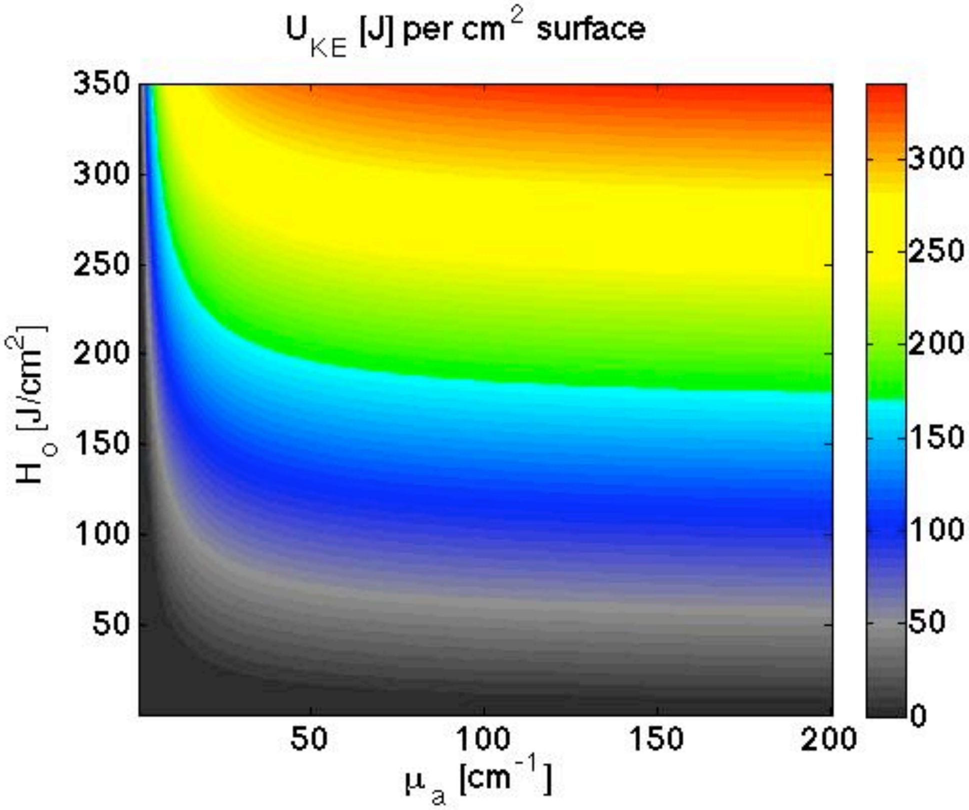
$$U_{abl} = Q_{th} z_{abl}$$

$$U_{heat} = \frac{Q_{th}}{\mu_{a.eff}}$$

Radiant exposure

H_o

J/cm^2



μ_a [cm^{-1}]

Absorption coefficient

velocity

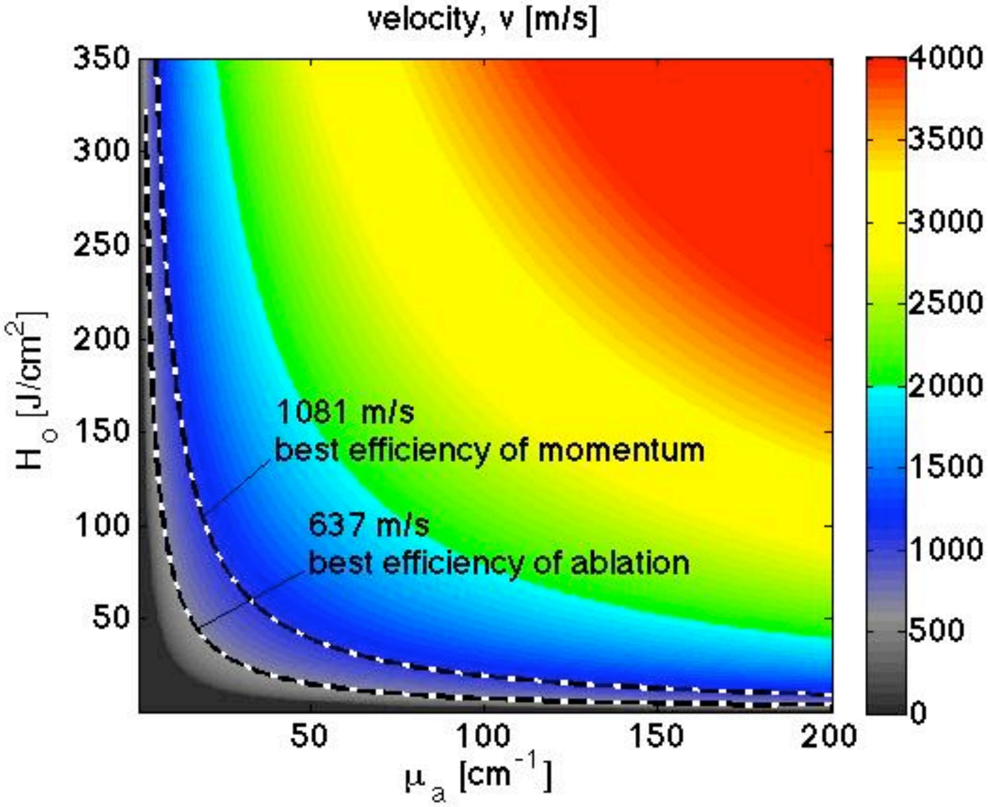
$$v = \sqrt{\frac{2\ U_{KE}}{m}}$$

$$U_{KE} = \tfrac{1}{2} m v^2$$

Radiant exposure

H_o

J/cm^2



μ_a [cm^{-1}]

Absorption coefficient

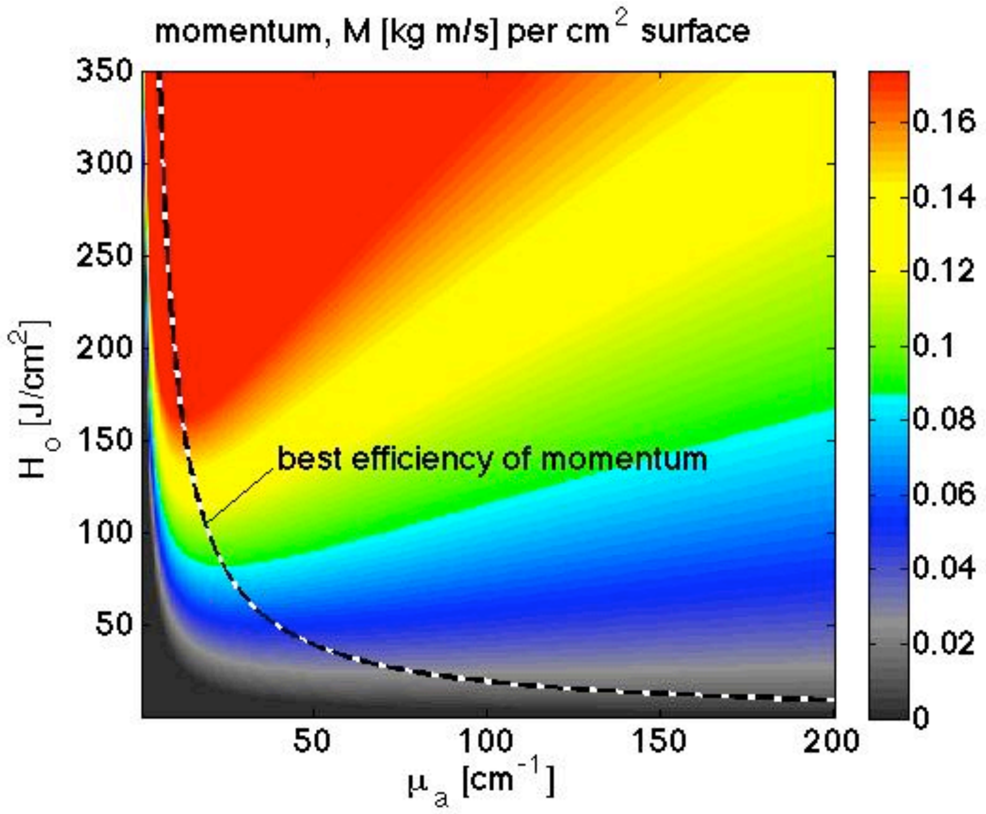
Momentum

$M = mv$

Radiant exposure

H_o

J/cm^2



μ_a [cm^{-1}]

Absorption coefficient

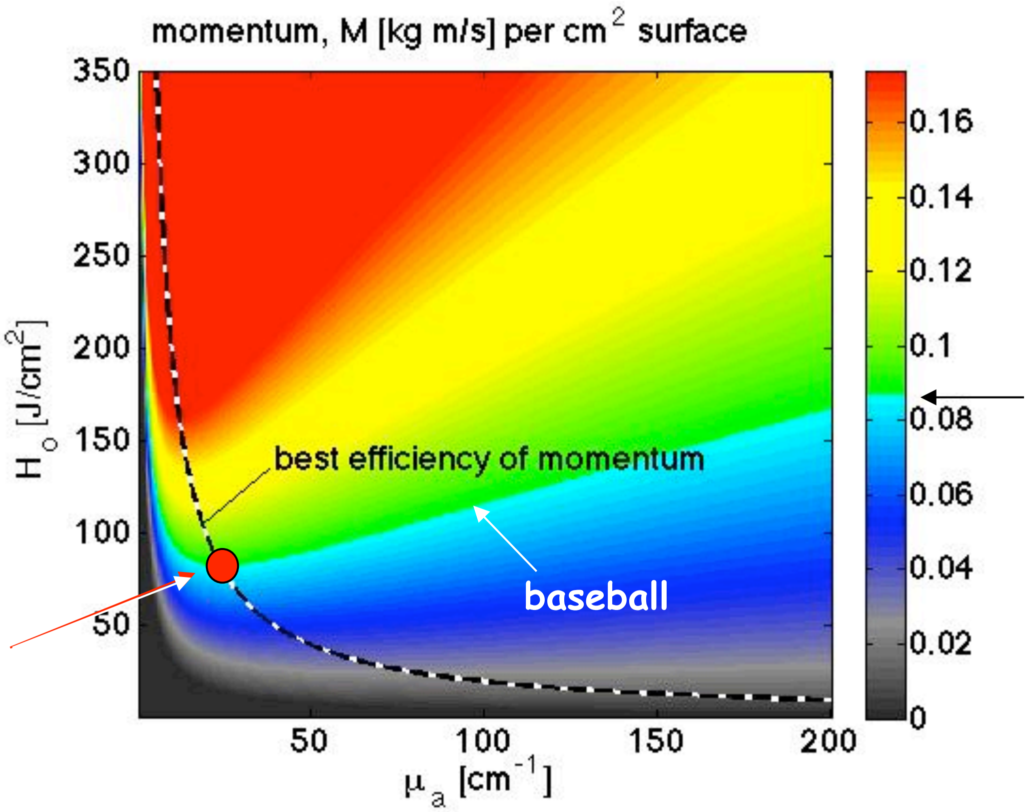
Momentum

$$M = mv$$

Radiant exposure

H_o

J/cm^2



Optimum laser

μ_a = 24.2 cm^{-1}

H_o = 82 J/cm^2

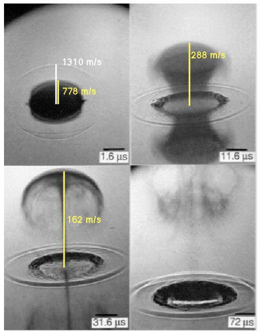
0.087 [(kg m/s)/cm^2]

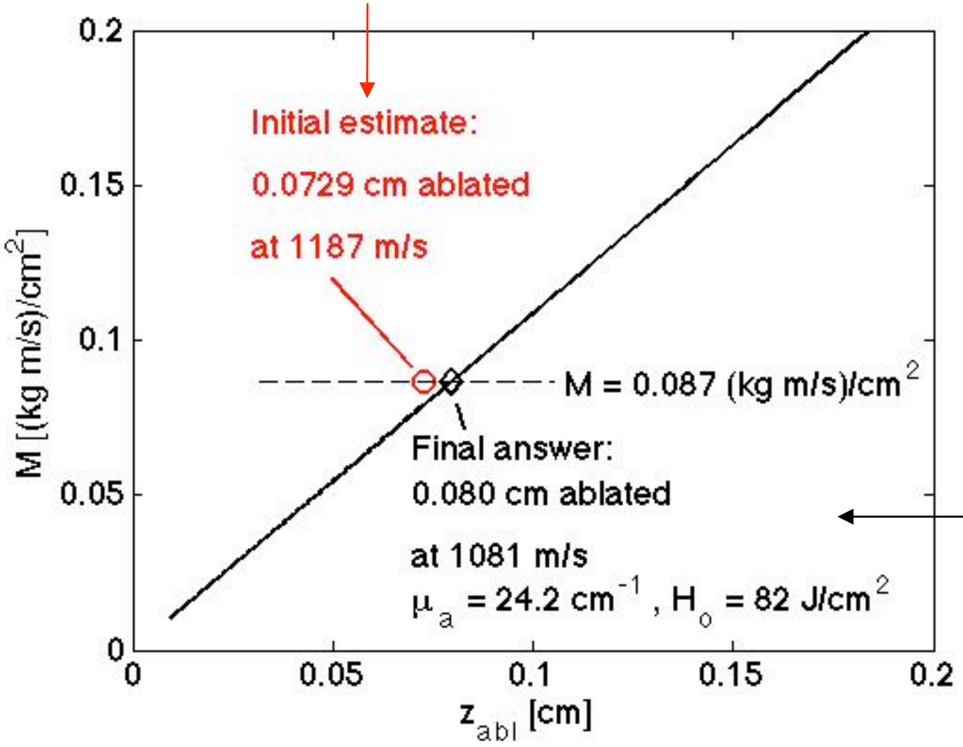
≈ 100-mph baseball

μ_a [cm^{-1}]

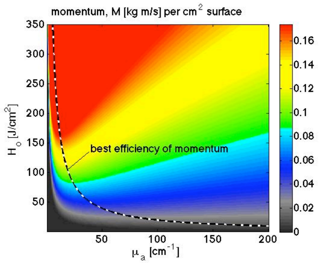
Absorption coefficient

… based on experiment





… based on Blow-off model



DIAGNOSTICS:

Photoacoustic Imaging

Stress, or pressure

Grüneisen coefficient
[dimensionless]

$$P = \mu_a F t \, \overset{\downarrow}{\Gamma}$$

1 [J/cm^3] = 10 bar

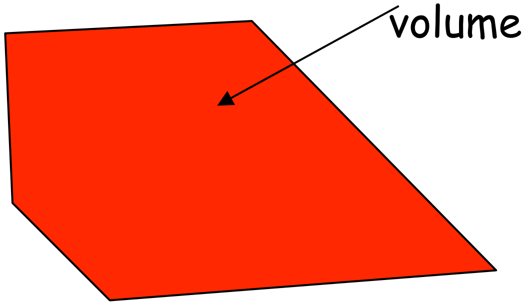
G = 0.12 at 25°C

--> 0.5 at higher temperatures

Photoacoustic imaging:

Initial thermoelastic expansion

$$P = \frac{M \beta}{\rho C_p} \mu_a H = \Gamma W$$


Energy deposition in volume, W [J/m^3]

energy deposition = $(\mu_a)(H) = W$ [J/m^3].

temperature rise = (energy deposition)/(ρC_p) [degree C].

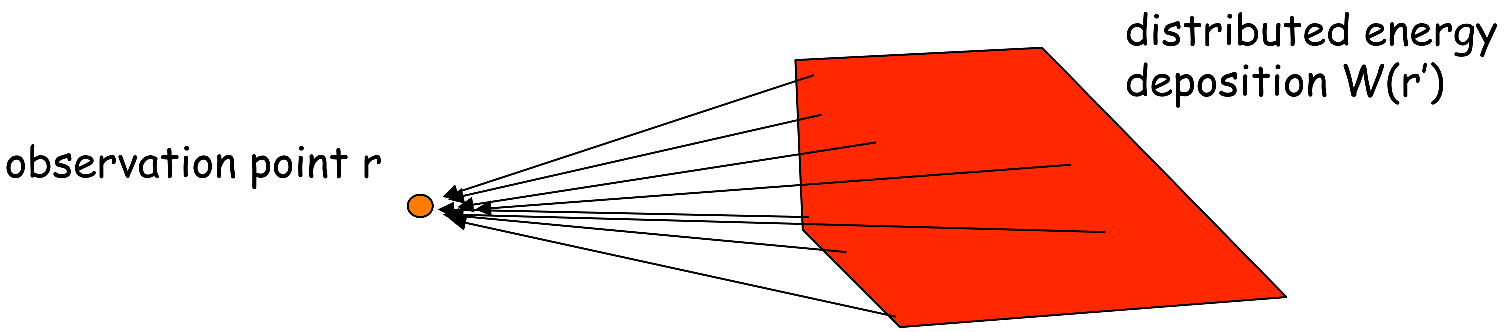
strain = (β)(temperature rise) [dimensionless].

pressure P = (M)(strain) [J/m^3] = [Pa].

1 J/m^3 = 1 Pa = 10^{-5} bar.

Photoacoustic imaging:

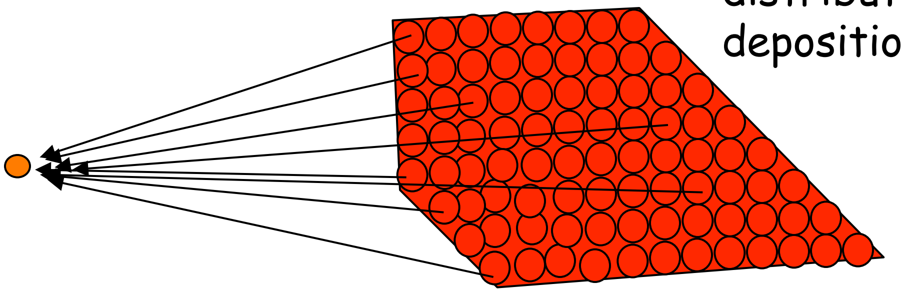
Velocity Potential related to energy deposition



$$\phi(\vec{r}_r, t) = -\frac{\beta}{4\pi\rho C_p} \oiiint \frac{W(\vec{r}\,')}{\left|\vec{r}\,' - \vec{r}_i\right|} \delta\left(t - \frac{\left|\vec{r}\,' - \vec{r}_i\right|}{c} \right) d^3 r'$$

Photoacoustic imaging:

Velocity Potential related to energy deposition



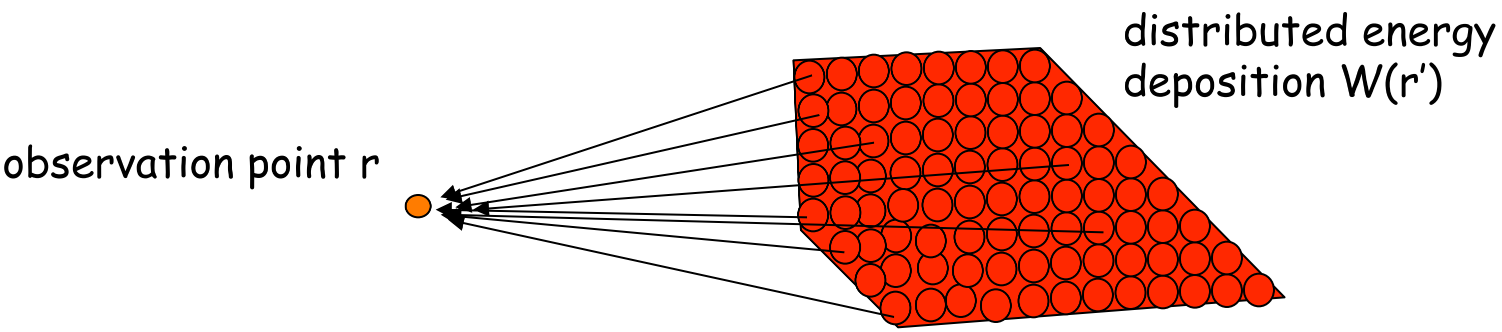
observation point r

distributed energy
deposition W(r′)

$$\phi(\vec{r}_r, t) = -\frac{\beta}{4\pi\rho C_p}\iiint \frac{W(\vec{r}\,')}{\left|\vec{r}\,' - \vec{r}_i\right|}\,\delta\!\left(t - \frac{\left|\vec{r}\,' - \vec{r}_i\right|}{c}\right) d^3 r'$$

Photoacoustic imaging:

Forward calculation



$$\phi[k] = -\frac{\beta}{4\pi\rho C_p}\frac{1}{\Delta t}\sum_j \frac{W[j]}{r[j]} V[j]$$

where k = round(r[j]/c_s/dt) is time index

and j is volume voxel index

Forward calculation called A:

$$\phi = A(W)$$

Photoacoustic imaging:

Pressure related to Velocity Potential

$$P(\vec{r},t) = -\rho \frac{\partial \phi(\vec{r},t)}{\partial t}$$

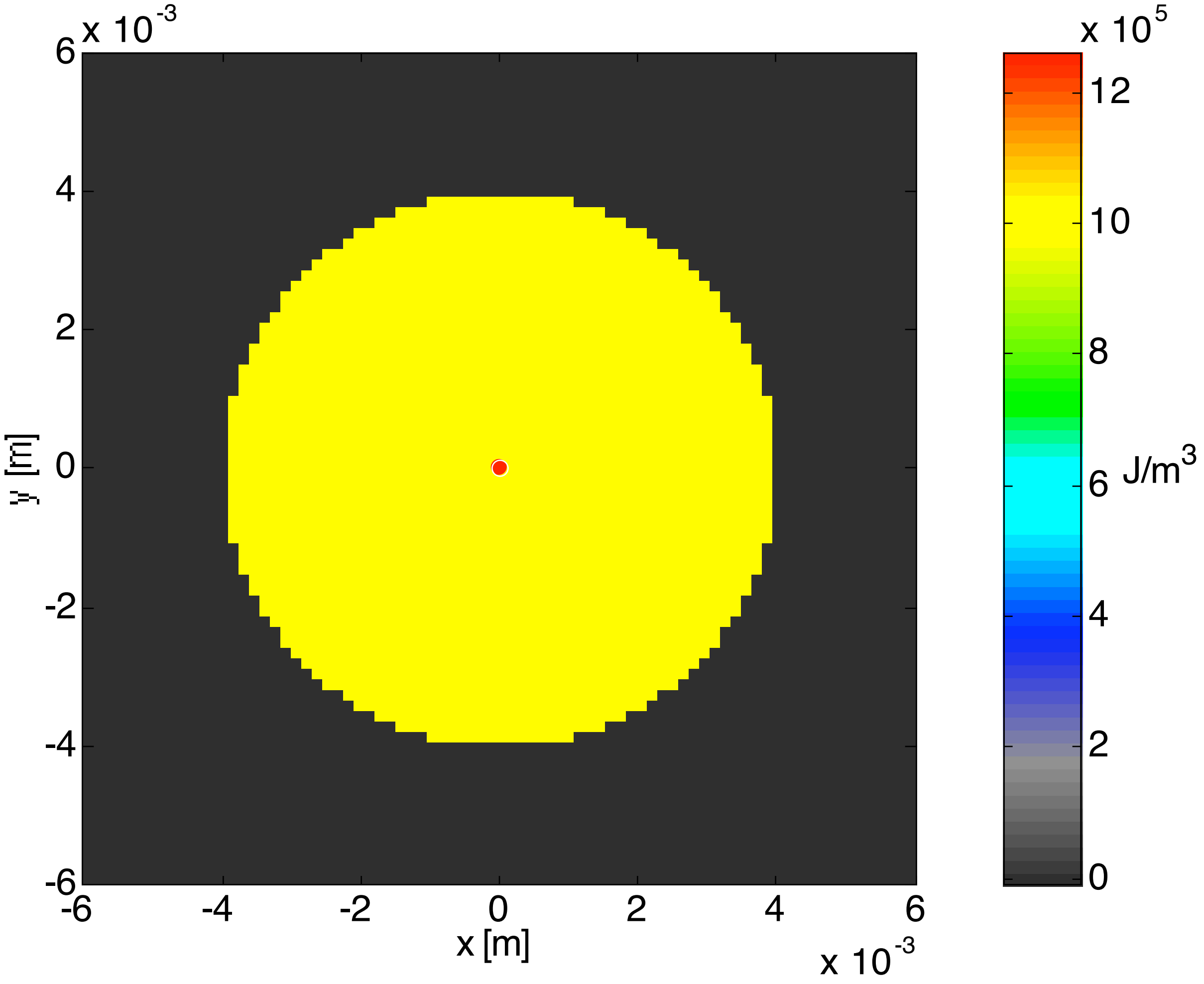
Pressure P   [J/m^3] or [Pa]

is related to

velocity potential ϕ [m^2/s]

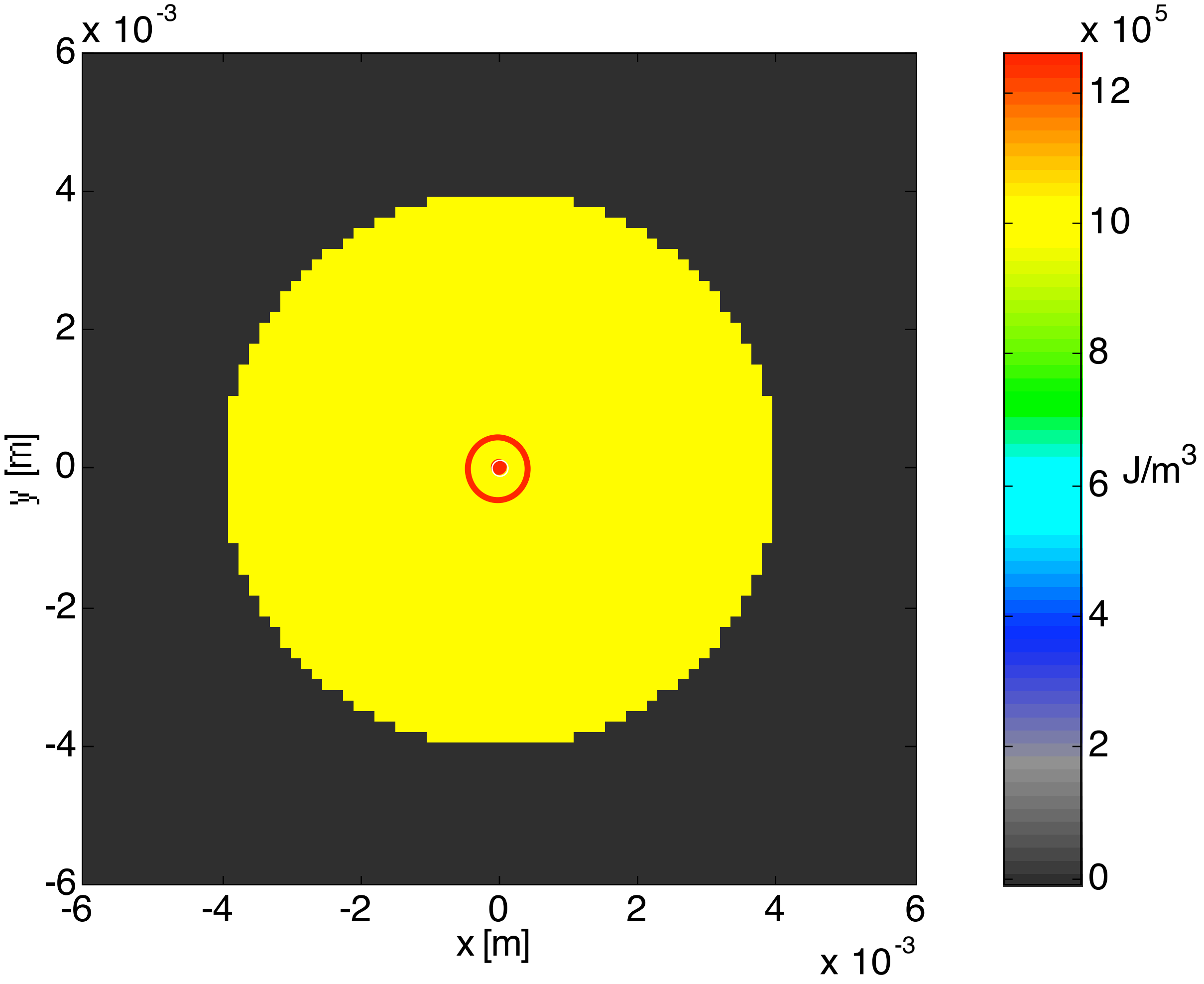
Energy deposition = 1 J/cm^3 = 10^6 J/m^3

....a 0.24°C temperature jump



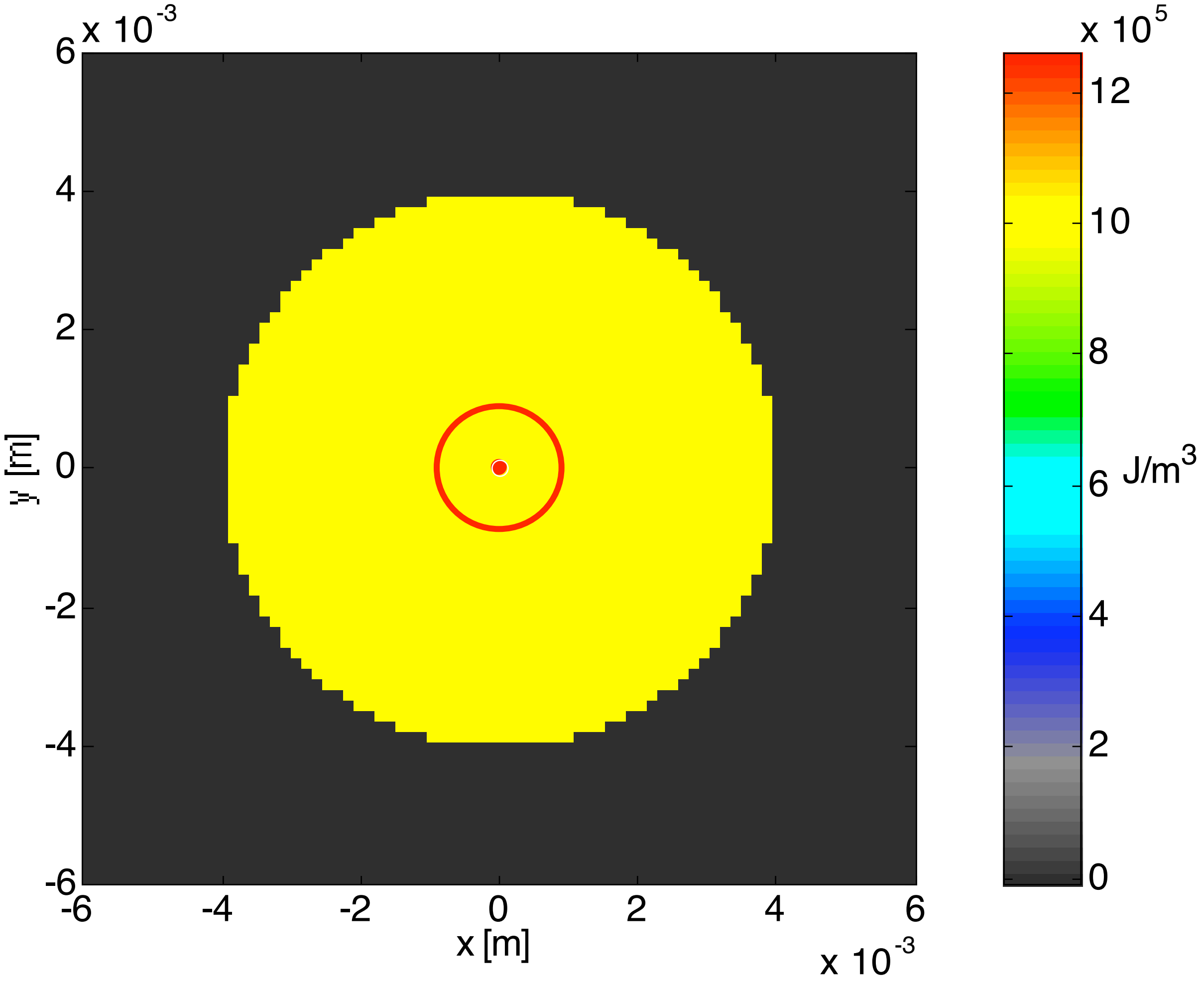
Energy deposition = 1 J/cm^3 = 10^6 J/m^3

....a 0.24°C temperature jump



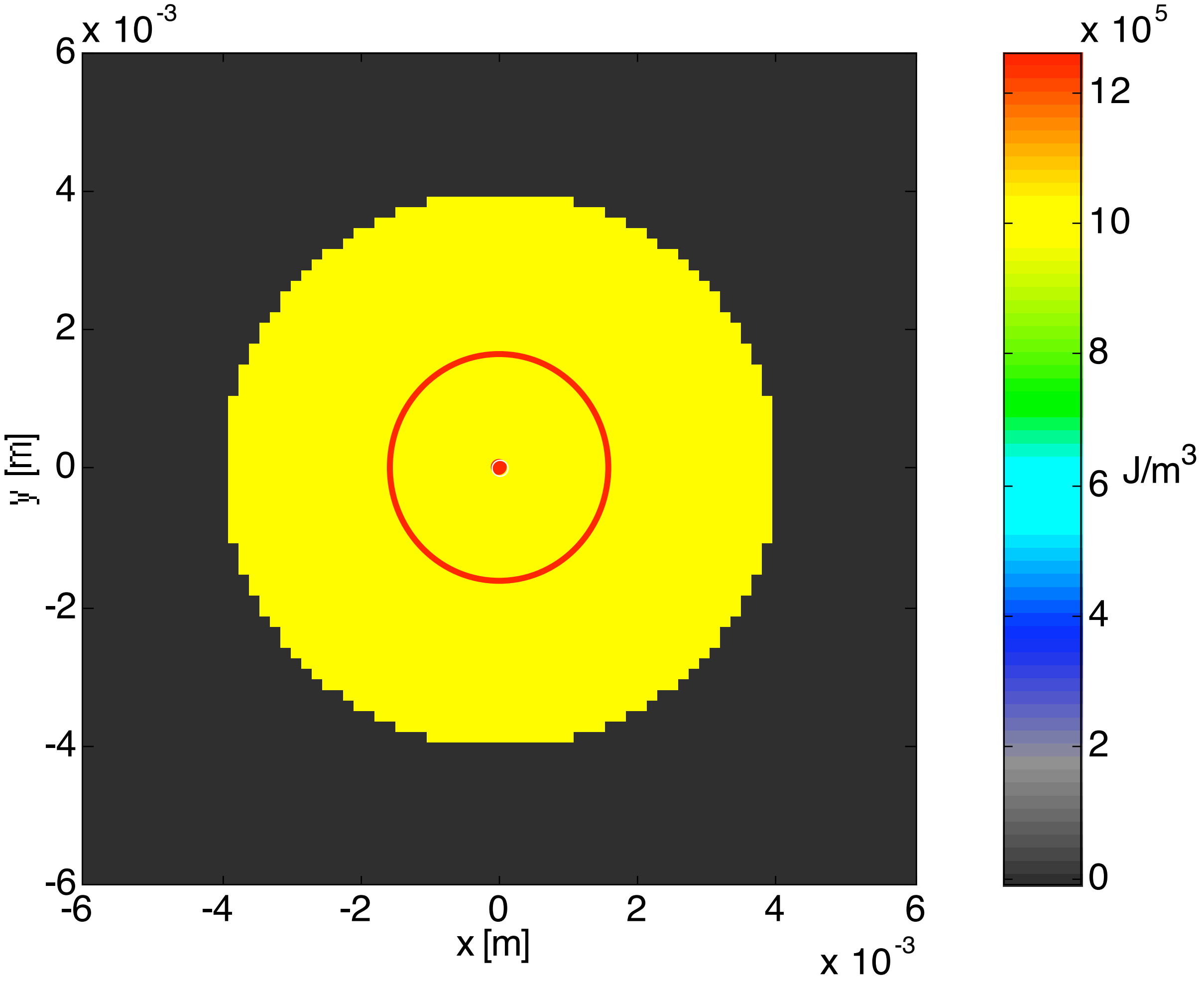
Energy deposition = 1 J/cm^3 = 10^6 J/m^3

....a 0.24°C temperature jump



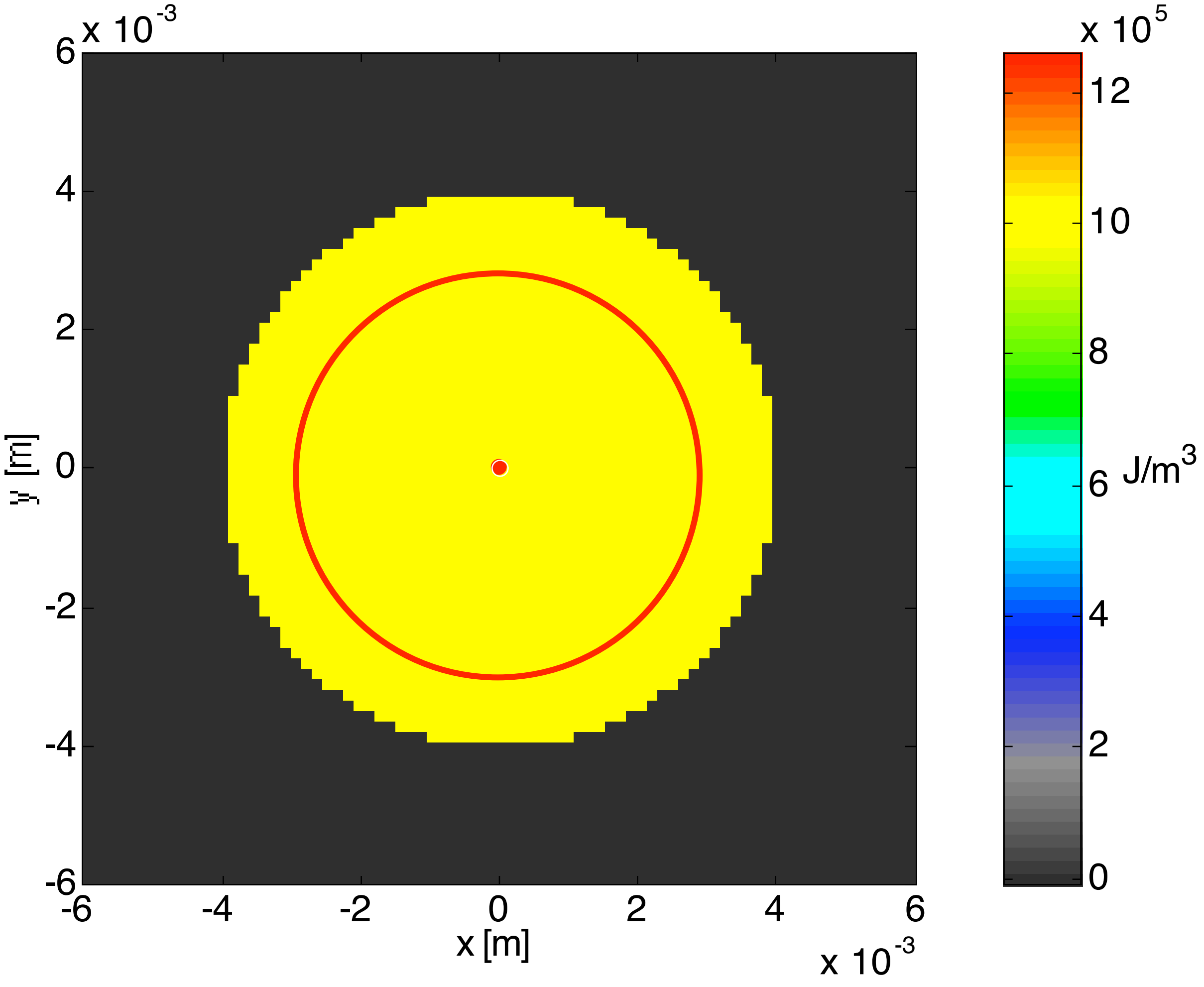
Energy deposition = 1 J/cm^3 = 10^6 J/m^3

....a 0.24°C temperature jump



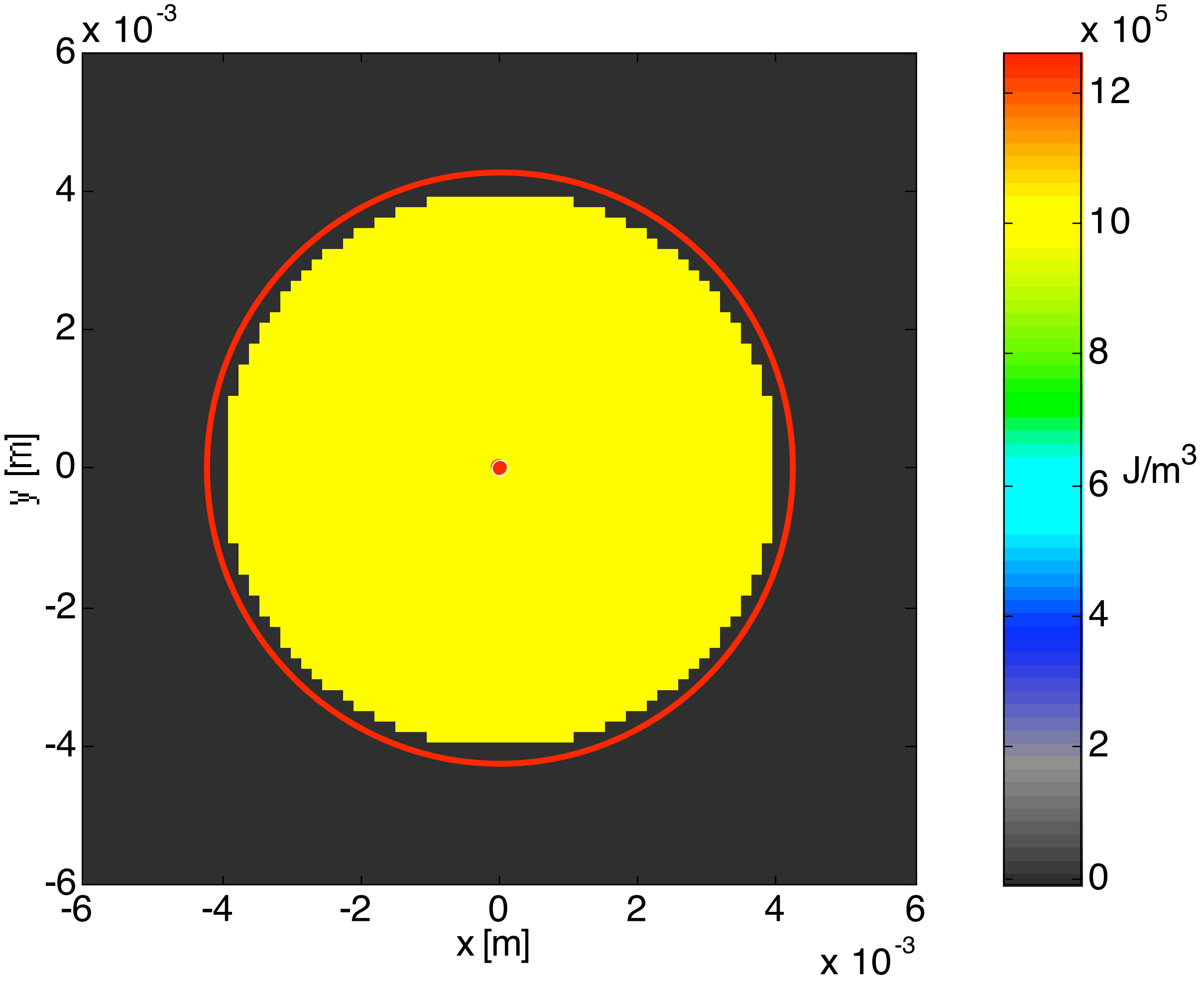
Energy deposition = 1 J/cm^3 = 10^6 J/m^3

....a 0.24°C temperature jump



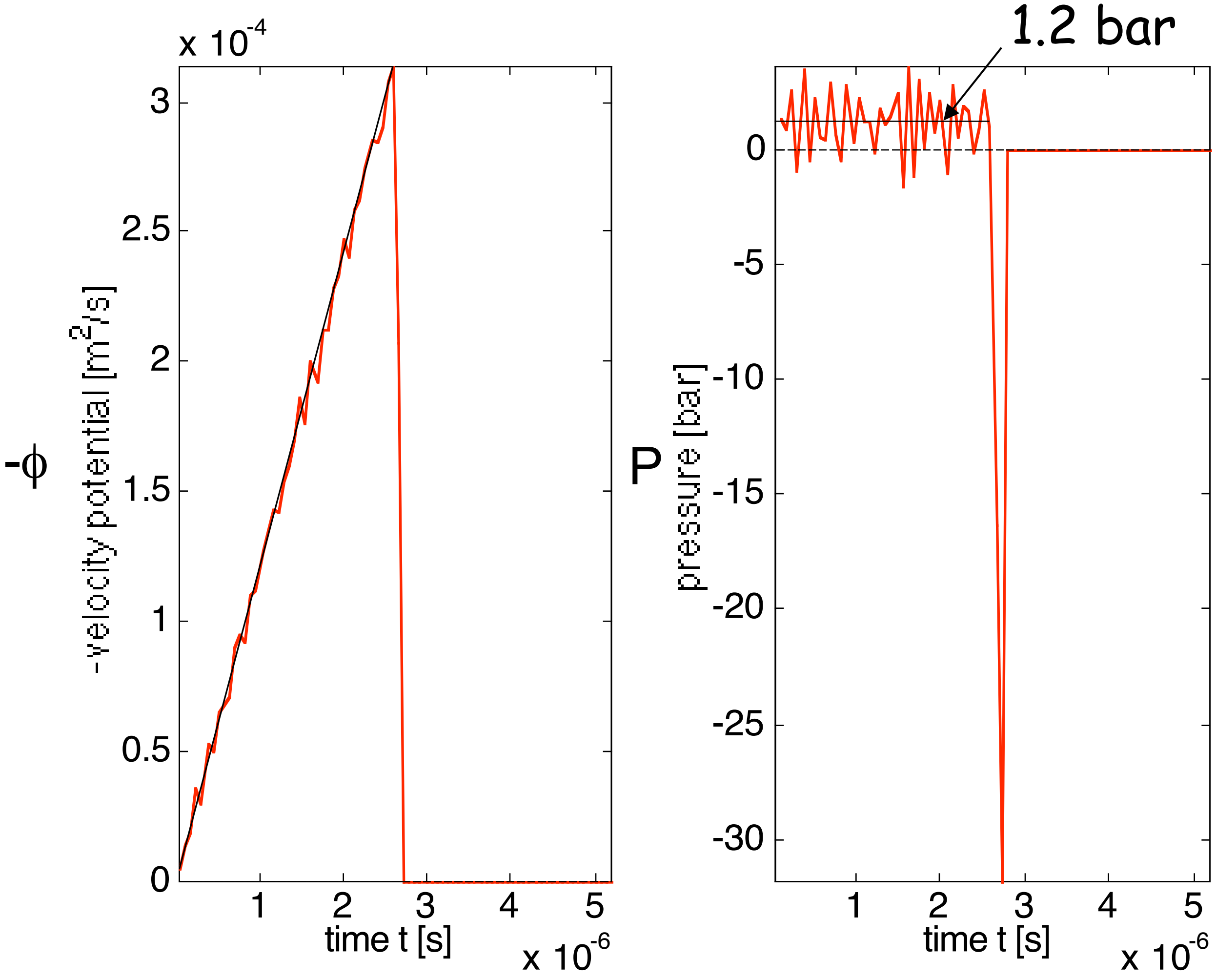
Energy deposition = 1 J/cm^3 = 10^6 J/m^3

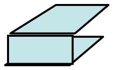
....a 0.24°C temperature jump

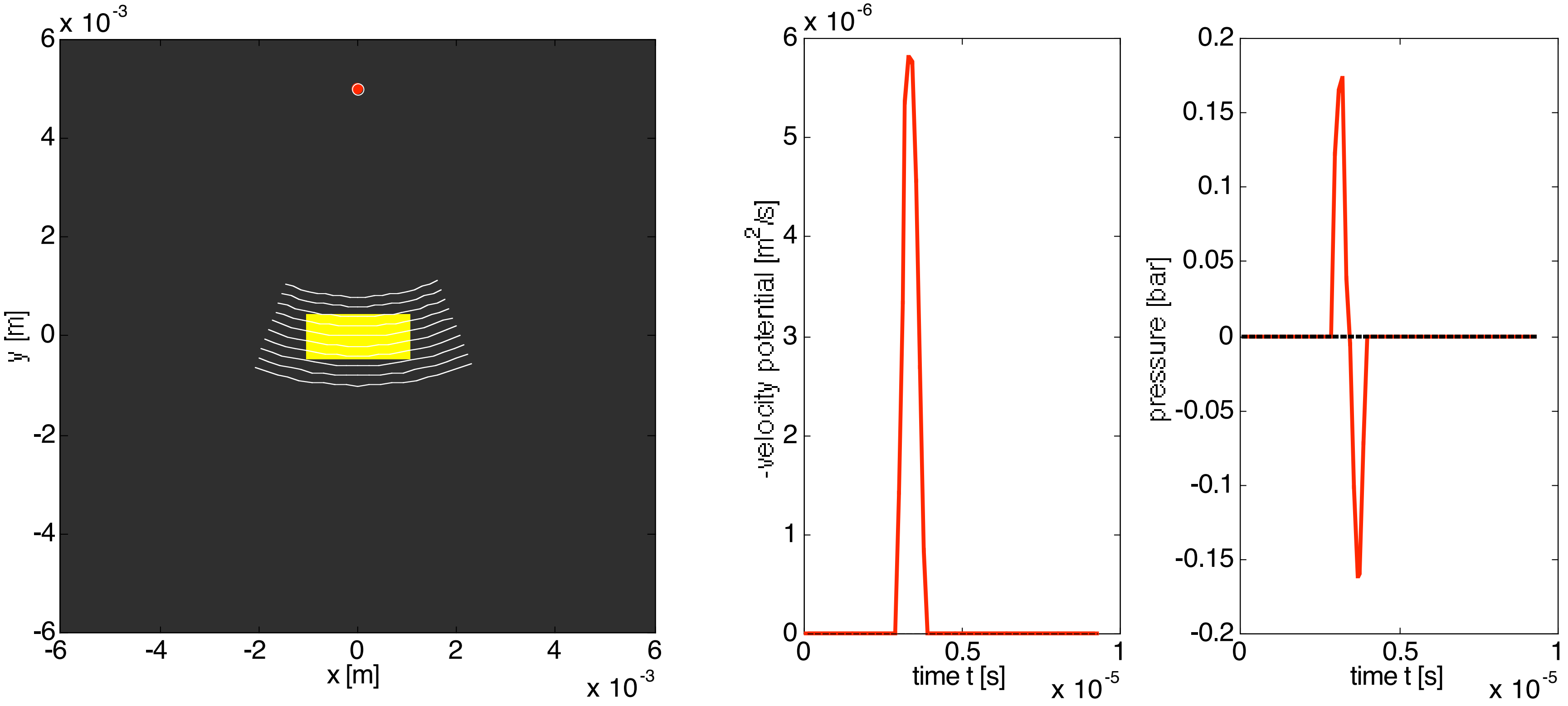


for 10^6 J/m^3 deposition

$$P = -\rho\, \partial\phi/\partial t$$

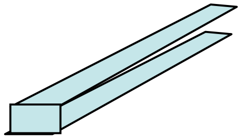


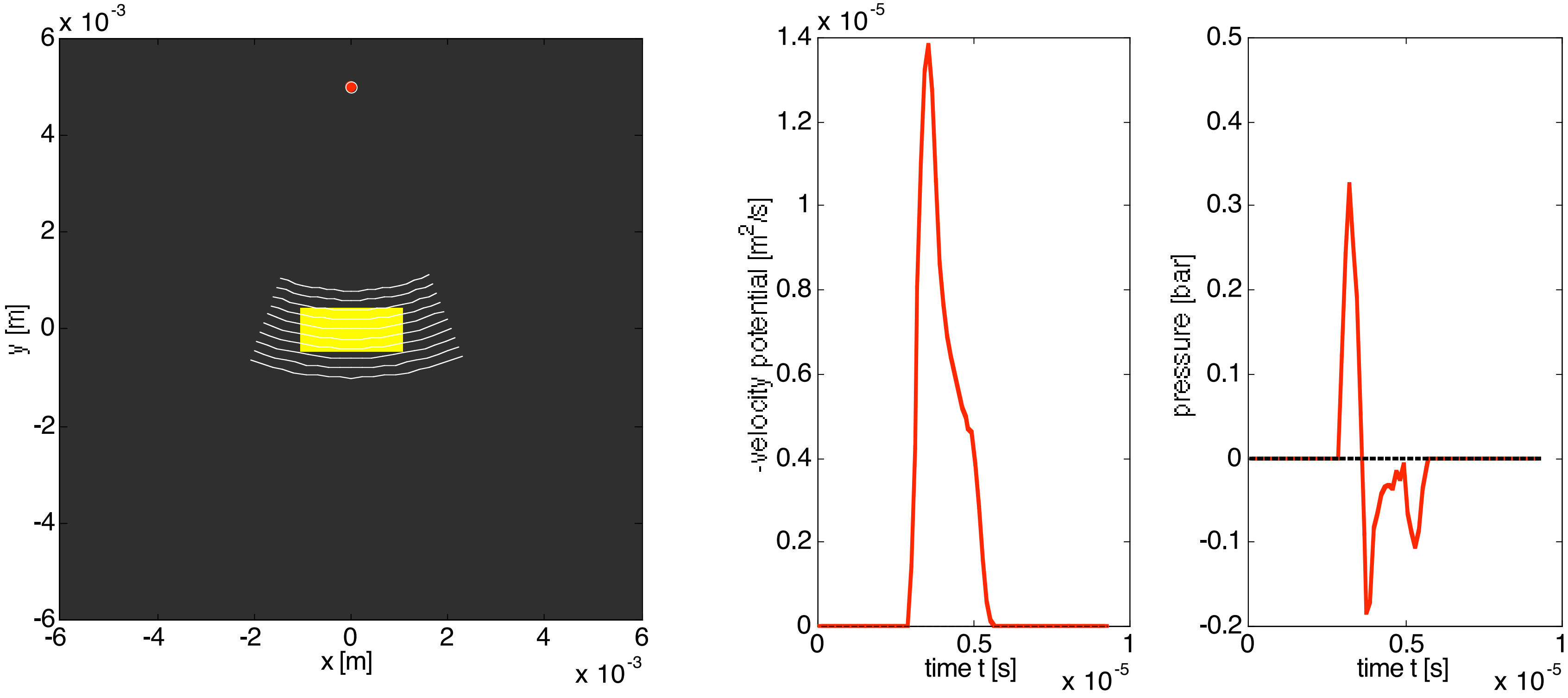




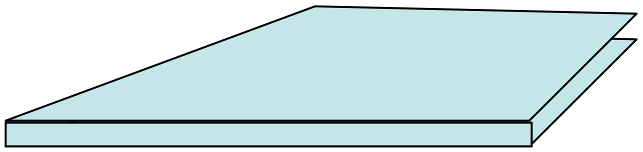
1mm x 2mm x 2mm block of deposition

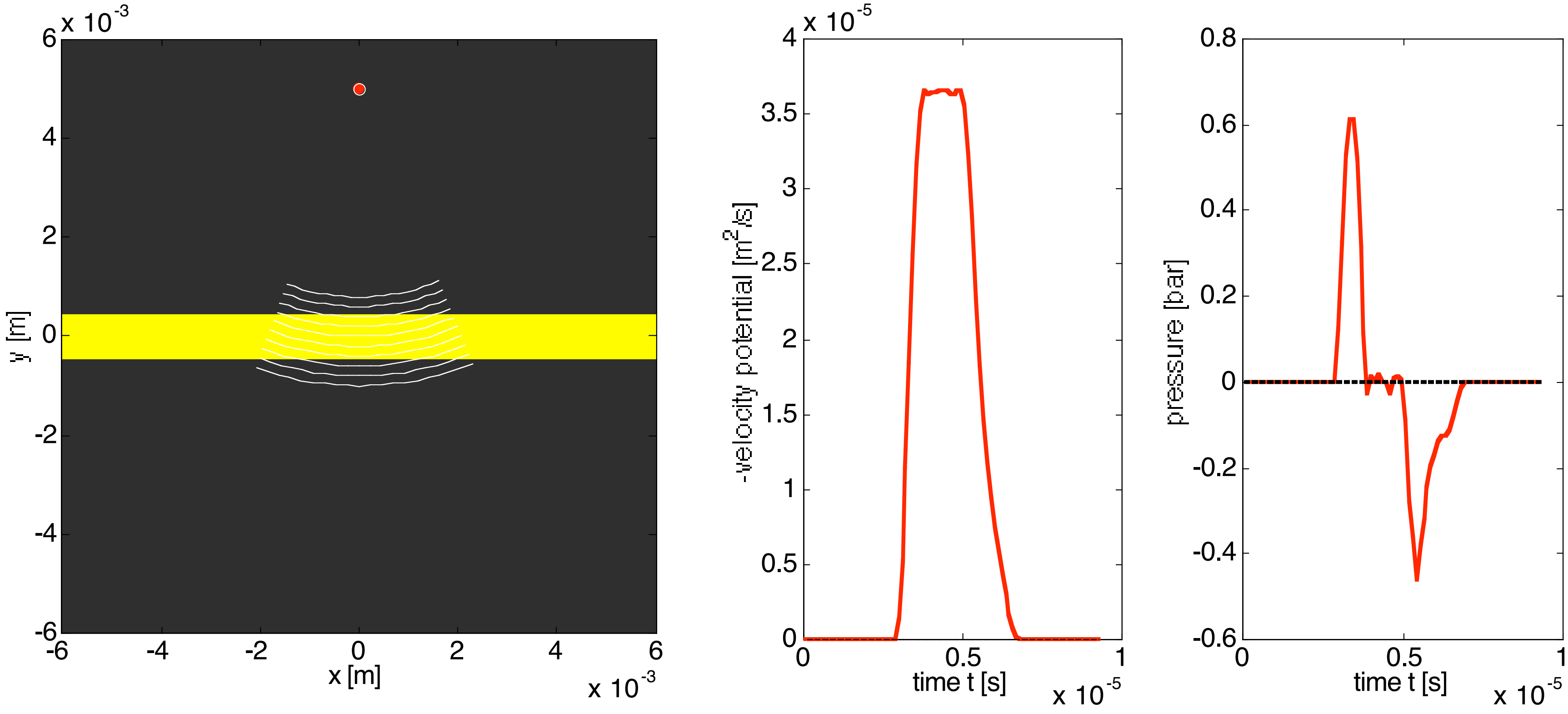
(figure extends ± 1 mm along z direction)



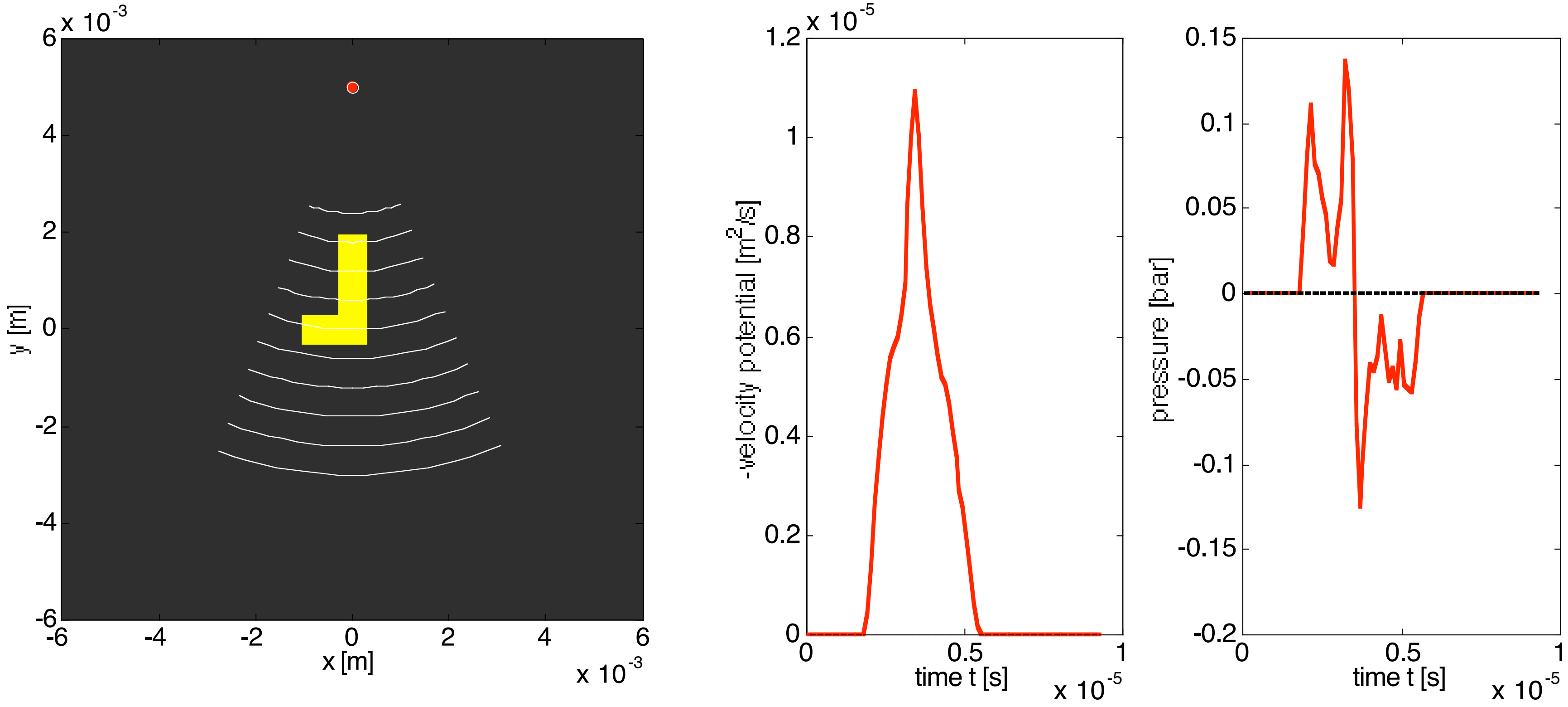


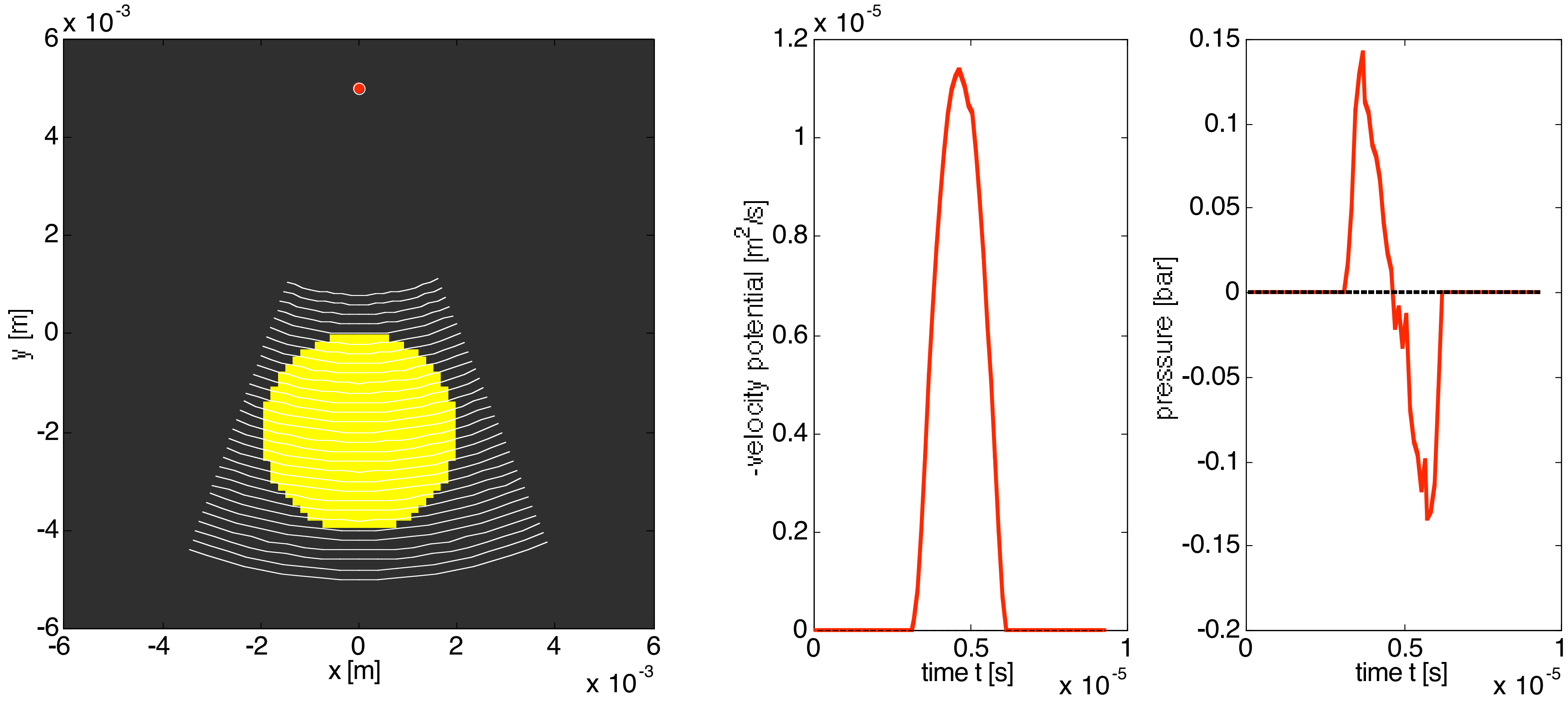
1mm x 2mm x 12mm bar of deposition
(figure extends ± 6 mm along z direction)





12mm x 12mm x 12mm plane of deposition
(figure extends ± 6 mm along z direction)


x 10^-3
6
4
2
0
-2
-4
-6
y [m]
-6
-4
-2
0
2
4
6
x [m]
x 10^-3
x 10^-5
1.2
1
0.8
0.6
0.4
0.2
0
-velocity potential [m^2/s]
0
0.5
1
time t [s]
x 10^-5
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
pressure [bar]
0
0.5
1
time t [s]
x 10^-5


x 10^-3
6
4
2
0
-2
-4
-6
y [m]
-6
-4
-2
0
2
4
6
x [m]
x 10^-3
x 10^-5
1.2
1
0.8
0.6
0.4
0.2
0
-velocity potential [m^2/s]
0
0.5
1
time t [s]
x 10^-5
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
pressure [bar]
0
0.5
1
time t [s]
x 10^-5

Photoacoustic imaging:
Inverse Problem

measure ϕ by integrating pressure detector
backproject W = source of energy deposition

for one detector:

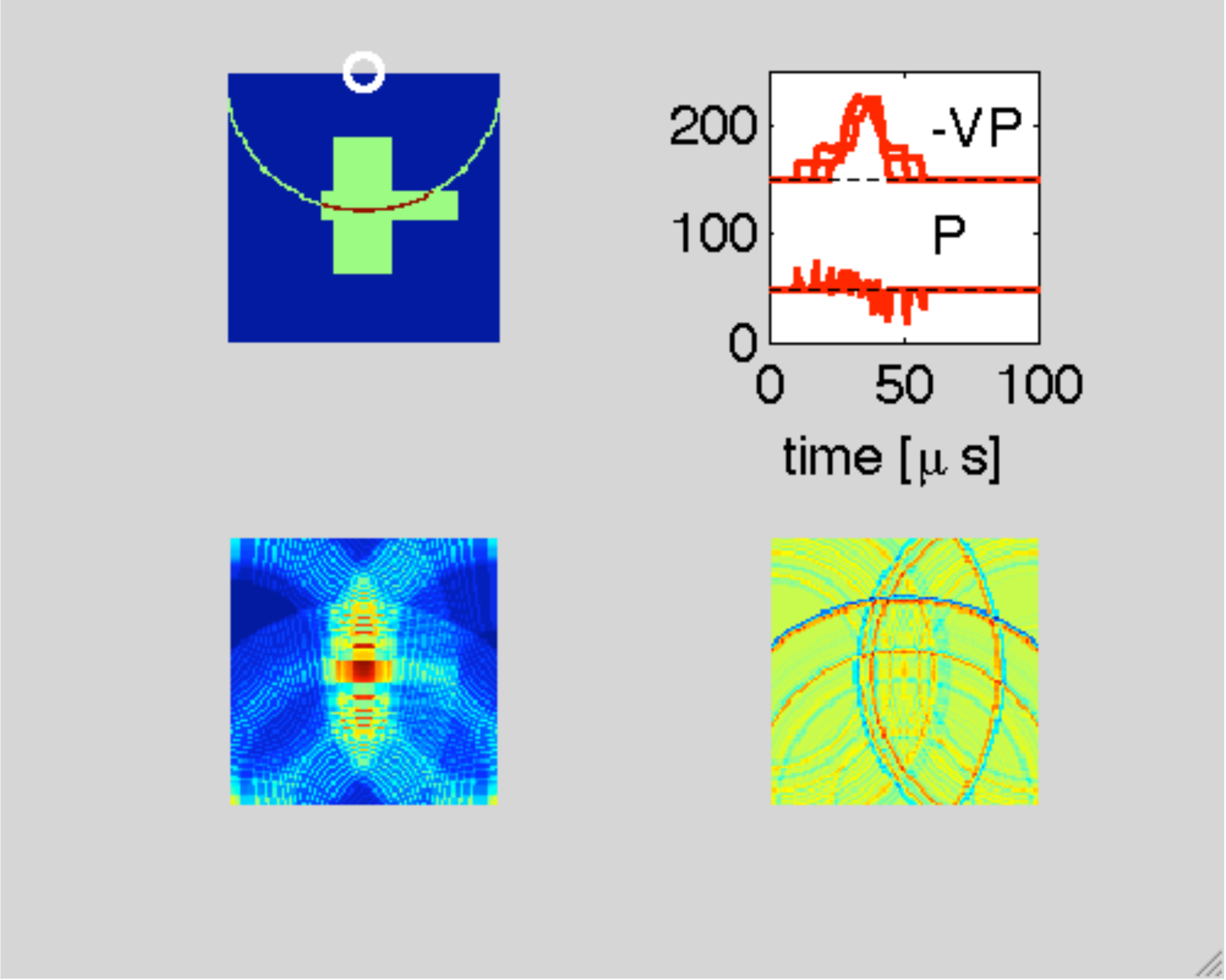
$$W[j] = \left(- \frac{4\pi\rho C_p}{\beta} \right) dt \sum_{k=1}^{N_t} \frac{\phi[k]\, r}{V_{\mathrm{shell}}} (r - c_s k dt < dr)$$

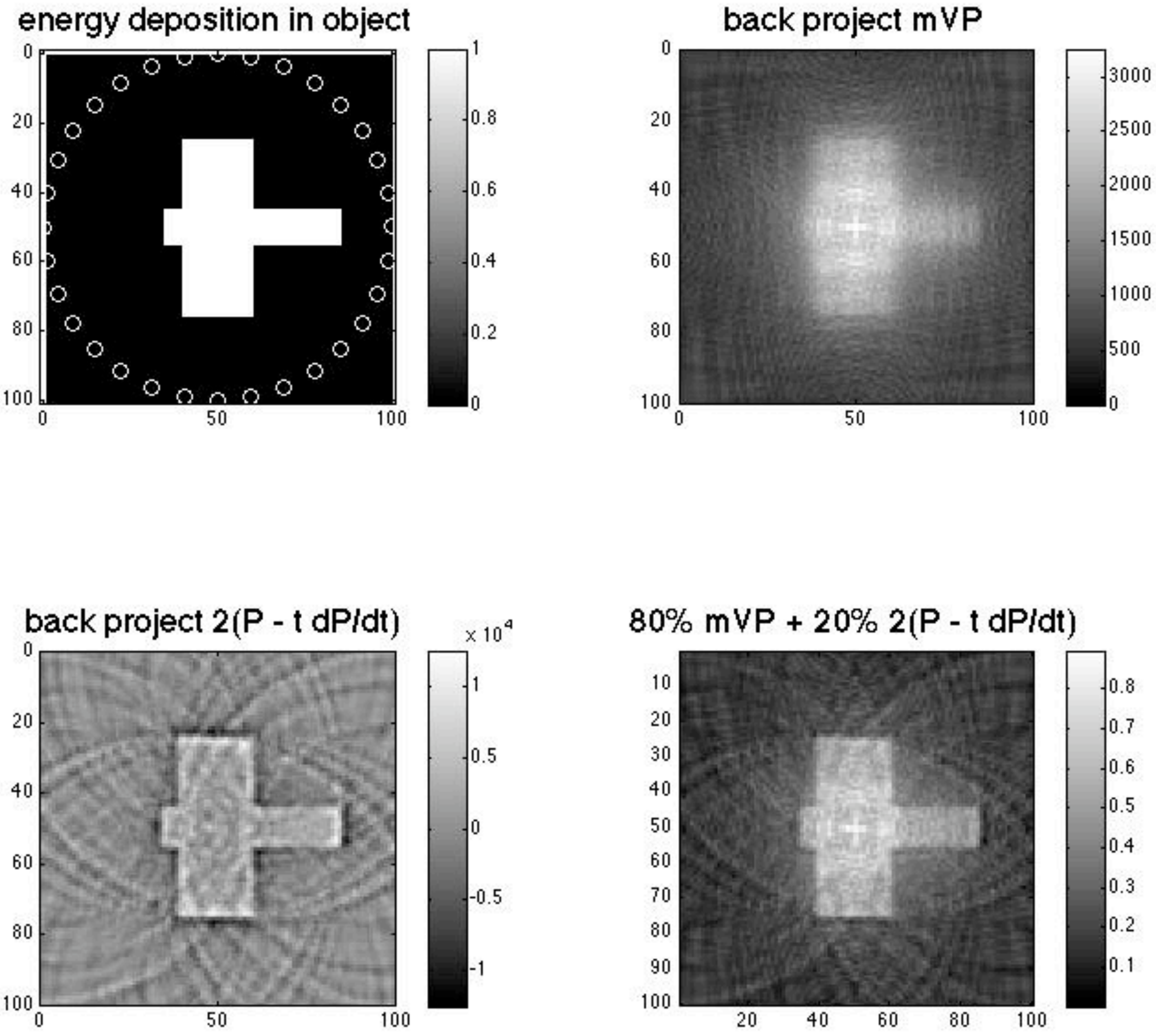
for all j voxels where $r[j] - c_s k dt < dr$

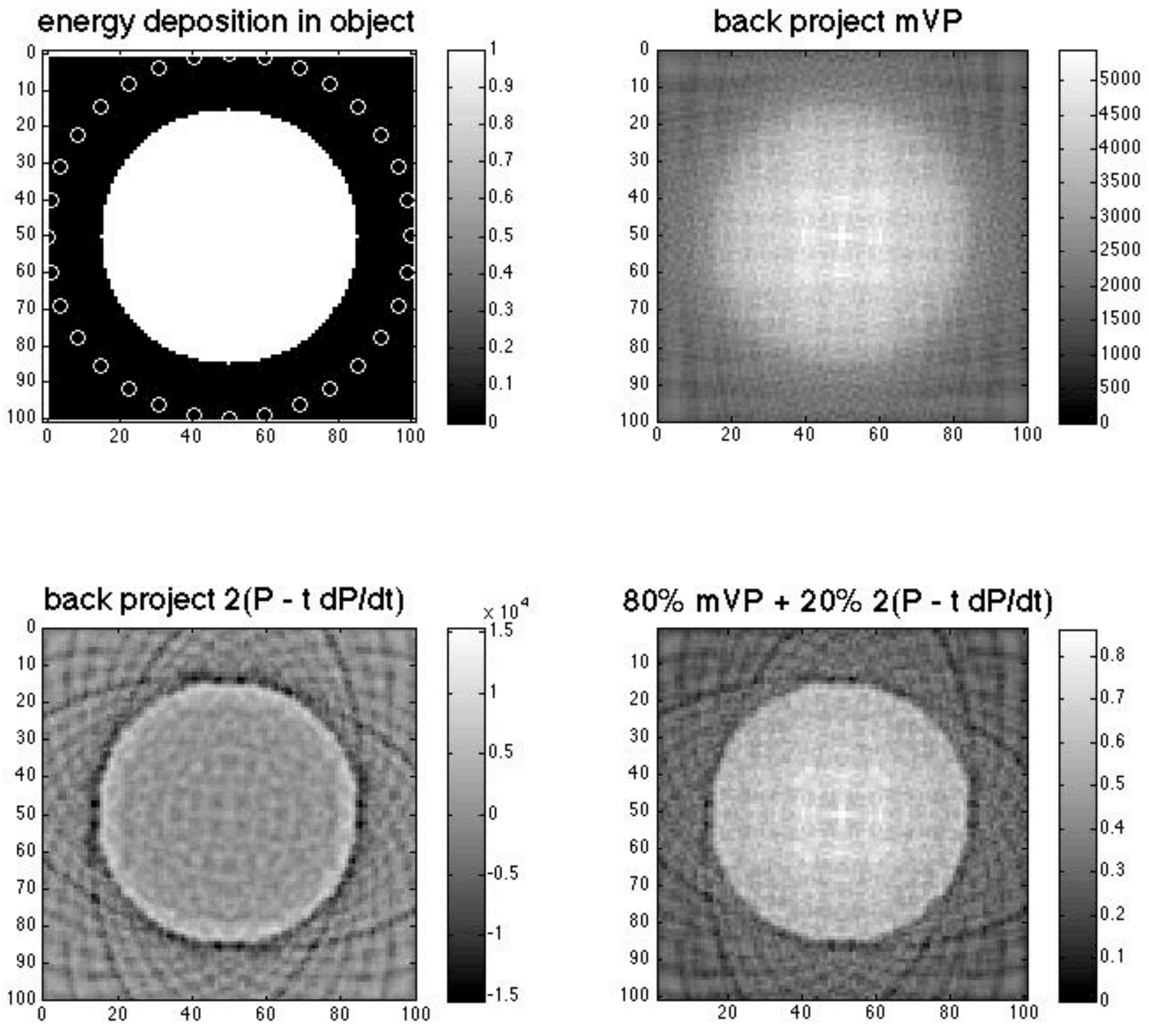
where $$V_{\mathrm{shell}} = \sum_j V[j]\, (r[j] - c_s k dt < dr)$$

Inverse calculation called B:

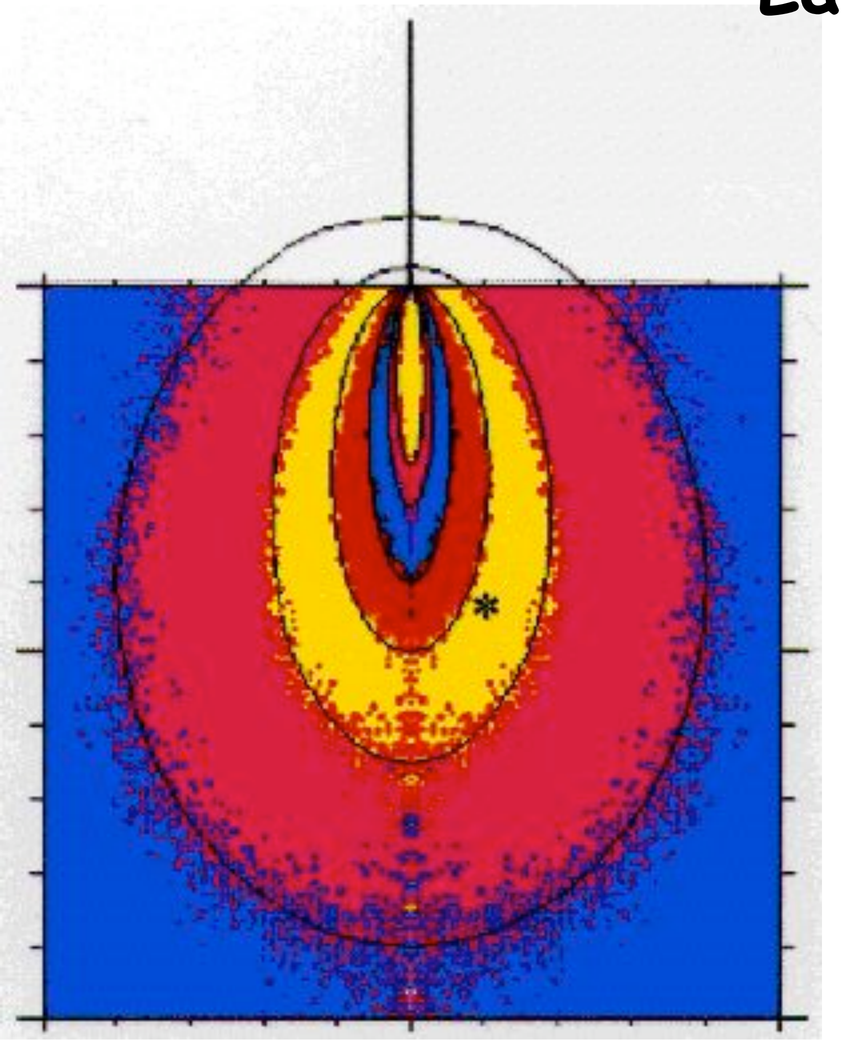
$$W = B(\phi)$$


200
100
0
-VP
P
0
50
100
time [μ s]


energy deposition in object
back project mVP
back project 2(P - t dP/dt)
80% mVP + 20% 2(P - t dP/dt)
0
20
40
60
80
100
0
50
100
1
0.8
0.6
0.4
0.2
0
3000
2500
2000
1500
1000
500
× 10^4
1
0.5
-0.5
-1
10
30
50
70
90
0.7
0.5
0.3
0.1


energy deposition in object
back project mVP
back project 2(P - t dP/dt)
80% mVP + 20% 2(P - t dP/dt)
0
10
20
30
40
50
60
70
80
90
100
0
20
40
60
80
100
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
x 10^4
1.5
1
0.5
0
-0.5
-1
-1.5
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0

Laser-Tissue Interactions



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Portland OR, USA

1. Introduction
2. Photochemical
3. Photothermal
4. Photomechanical