Physics In Modern Medicine

Fall 2009

Take-home Midterm Exam

Name_____Solution_____

Part	
Problem #1	/ 21
Problem #2	/ 28
Problem #3	/ 14
Problem #4	/ 21
Problem #5	/ 7
Problem #6	/ 14
Problem #7	/ 21
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Total	/140

Assigned: Friday, October 9, 2009 in class and in electronic format in email.
Due in electronic format: Wednesday, October 14, 2009, by Noon, EST. (This of course means that it should be in my inbox by 6am Hawaii Standard Time!)

Late exams will be penalized **10 points/half day.**

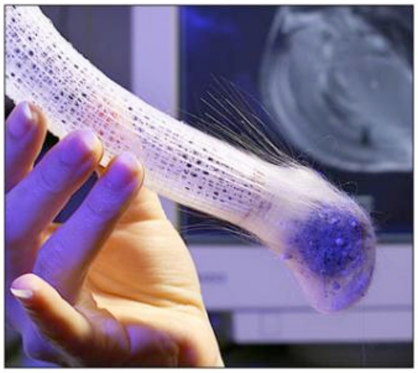
Ground rules: The total credit for the exam is 140 points with each subpart worth 7 points and there are 20 subparts. Be sure to start by reading all the questions carefully so you understand what you are being asked to do, and answer all parts. Explain your reasoning and show all of your work--don't simply write down numerical answers for the mathematical parts. This is crucial--failure to explain answers or show your reasoning will result in my inability to give you full credit, especially if you only write down a wrong numerical answer. Pay attention to the appropriate units, prefixes and powers of ten for full credit. You **must include units** for physical quantities. Even if you aren't sure about how to completely answer each part, put down as much work as you can, as clearly as possible, for partial credit. I will give partial credit for *everything relevant and correct* you have written down!

The exam is open book and open notes. You may only consult the textbooks by Kane and Wolbarst as well as any class notes or the class lecture slides. You may not communicate in any way with any other person during the exam, and you may not consult the web except for problem #8, which lists a web address. For those of you that know my exam style, doing so would be pointless anyway. You may, of course, use a calculator during the exam.

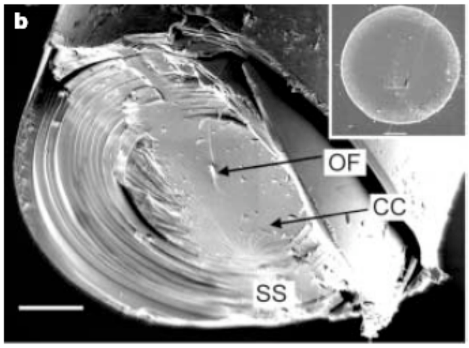
I will do my best to answer any questions that you may have up until Monday afternoon until about 11pm EST (my plane lands at 4:30 in Hawaii.) After Monday night, I will 6 hours behind you in time, so there may be a delay in the response. Be patient, if I'm able, I will respond as soon as I can.

1. Fiber optics

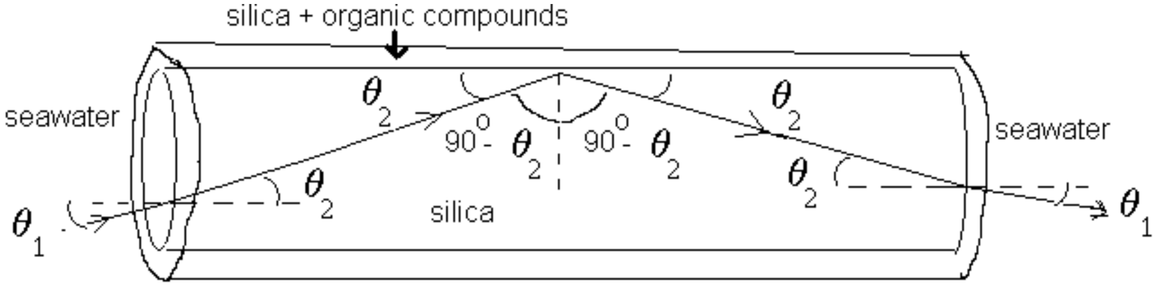
Sea sponges in the family Euplectella (Venus Flower Basket) have at their base long needle-like structures called spicules, made of a combination of the mineral silica and organic compounds. Scientists have investigated whether these spicules can act as optical fibers. Each spicule consist of an inner cylindrical core made of the mineral silica, surrounded by an outer cladding-like coating made of a mixture of silica and organic compounds. All this is illustrated in the images (A) through (C) below. In figure (C), SS is the outer coating while CC is the center core. The tough, flexible outer coating allows the spicules to bend into very small angles without cracking, unlike current optical fibers, so scientists are investigating whether they can help in designing more flexible optical fibers for medicine.



(A)



(B)



(C)

(A) Photo of the sea sponge Euplectella. The fiber optic-like spicules are glass-like fibers projecting from the base.

(B) Cross-sectional image showing the central silica core and outer coating. (Joanna Aizenberg/Lucent Laboratories)

(C) Cartoon representation of a ray of light entering one end of the spicule's silica center core, reflecting from the interface with the outer coating and exiting the other end. (The angles shown are not necessarily realistic for these values of index of refraction.)

Here is some useful information about the optical properties of this system:

Medium	**Index of refraction**
Seawater	1.34
Silica (inner core of spicule)	1.46
Silica + organic compounds (outer layer of spicule)	1.43

a. Explain why a spicule can act as an optical fiber. Compute what its critical angle for total internal reflection would be. Explain your reasoning and show your calculations!

For both geometries we have the index of refraction in the central core (silica with index 1.46) having a larger index of refraction than its surroundings (either the coating, with 1.43 or seawater with 1.34), so total internal reflection can occur for some angles. To find which angles, we use Snell's Law:

$$\sin\theta_{\text{crit}} = \frac{n_2}{n_1}$$

$$\theta_{\text{crit}} = \sin^{-1}\left(\frac{n_2}{n_1}\right) = \sin^{-1}\left(\frac{1.43}{1.46}\right) = 78.4^o$$

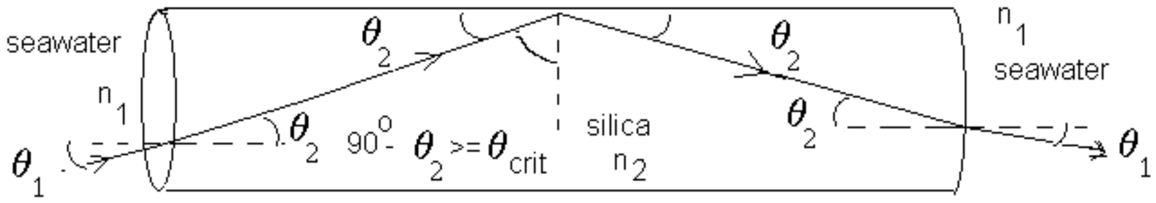
Also, the silica core must have the property of not absorbing visible light (that's it's highly transparent or translucent)

b. Would the spicules still work as an optical fiber if they did not have the outer layer of silica and organic compounds? (That is, if they consisted only of a fiber of pure silica surrounded by seawater along its entire length.) Explain your reasoning.

See part a.

c. Derive a value for the angle θ_2 using your calculation for the critical angle for total internal reflection from part (a) (just choose a value if you could not compute it), then compute the angle, θ_1, at which light *exits* the spicule. Use a drawing to explain clearly why your value for θ_1 is also the largest angle that can **enter** the spicule and still undergo total internal reflection. (Hint: you should show in your sketch the range of angles for light rays that will undergo total internal reflection.)

Break this into several parts: first make a sketch to see which angles correspond to total internal reflection vs. which angles are needed to compute refraction as the beam enters and leave the fiber; then compute θ_2, then finally compute θ_1 and argue why it's the same on either end. Now we need to observe that the angle in the cartoon, $90 - \theta_2$ is what we need to compare to the computed critical angle θ_{crit} from above. So long as $90 - \theta_2$ is greater than θ_{crit}, total internal reflection will occur. However, if θ_{crit} is greater than the value $90 - \theta_2$, then we cannot have total internal reflection. Here is a cartoon that shows all this:



We also have the same Snell's law relating θ_1, θ_2, n_1 and n_2 for both ends. Snell's law gives the same results in both cases, so once we have solved for q_1 in one case, we know the value of θ_1 in the other end. If the incident angle becomes greater than this value computed using the critical angle to derive, then θ_2 becomes larger. That means 90 - θ_2 becomes smaller than θ_{crit}, and violates the criterion for total internal reflection.

$$\theta_2 = 90^o - \theta_{crit} = 90^o - 78.4^o = 11.6^o$$

$$n_1 \sin\theta_1 = n_2 \sin\theta_2$$

$$\sin\theta_1 = \frac{n_2}{n_1}\sin\theta_2$$

$$\theta_1 = \sin^{-1}\left(\frac{n_2}{n_1}\sin\theta_2\right) = \sin^{-1}\left(\frac{1.46}{1.34}\sin 11.6^o\right) = 12.6^o$$

2. Laser surgery

A new titanium:sapphire laser has recently (September 2008) been approved for ophthalmological applications. In particular it provides a new treatment for glaucoma, a condition where a buildup of excess pressure in the eyeball can eventually damage the optic nerve. The procedure called *laser trabeculoplasty* relieves this pressure by creating a new drainage network of laser-induced holes in the eye's natural drainage structure, called the *trabecular meshwork*. Previously, argon ion lasers were one of the main lasers used for this procedure. Here are some typical specifications for each laser being considered. Use this information in answering the questions below.

Laser type	**Argon ion**	**Titanium:sapphire**
Wavelength	488 nm	790 nm
Type of laser	CW	Pulsed
	power = 1 watt	Energy / pulse = 30mJ
Pulse repetition rate	Continuous Wave	1 Hz
Pulse width	Continuous Wave	8.0 μs
Spot Diameter	100 microns	200 microns

a. What part of the spectrum does each laser's wavelength belong to? What is the energy per photon for each laser in eV and in Joules? What are the frequencies of each photon? Is either laser able to break chemical bonds through absorption of individual photons?

Argon ion: Blue-green; titanium:sapphire: near infrared. As a consequence neither should have energies per photon high enough to break a chemical bond.

Argon ion: $E = hc/\lambda = 4.14 \times 10^{-15}\ \text{eV-s}\ (3.00 \times 10^{8}\ \text{m/s}) / (488 \times 10^{-9}\ \text{m}) = \boldsymbol{2.55\ eV} = \boldsymbol{4.1 \text{x} 10^{-19} J}$; $f = c / \lambda = 3 \text{x} 10^{8} \text{m/s} / 488 \text{x} 10^{-9} \text{m} = \boldsymbol{6.2 \text{x} 10^{14}\ Hz}$

Titanium: sapphire: $E = hc/\lambda = 4.14 \times 10^{-15}\ \text{eV-s}\ (3.00 \times 10^{8}\ \text{m/s}) / (790 \times 10^{-9}\ \text{m}) = \boldsymbol{1.57\ eV = 2.5 \text{x} 10^{-19} J}$; $f = c / \lambda = 3 \text{x} 10^{8} \text{m/s} / 790 \text{x} 10^{-9} \text{m} = \boldsymbol{3.8 \text{x} 10^{14}\ Hz}$

b. Calculate the instantaneous and average *power* for each laser. What is each laser's average and instantaneous *power density*? (Answer using standard units for laser surgery in each case.)

For the ***argon ion****, its average and instantaneous power are identical and given already as* ***1 watt****. For the pulsed* ***titanium sapphire****, the values are:*
Instantaneous power $= 30 \times 10^{-3}\ J/(8 \times 10^{-6}\ \text{second}) = \mathbf{3750\ watts}$
Average power $= 30\ \text{milliJoule} \times 1\ Hz = 30 \times 10^{-3}\ J \times 1\ Hz = \mathbf{30 \times 10^{-3}\ watts}$

Power densities
Area for argon ion $= \pi (100\ \text{micron}/2)^2 = \pi (200 \times 10^{-4}\ \text{cm}/2)^2 = 7.85 \times 10^{-5}\ \text{cm}^2$

Area for titanium: sapphire laser = Area for argon ion $= \pi (200\ \text{micron}/2)^2 =$
$\pi (200 \times 10^{-4}\ \text{cm}/2)^2 = 3.14 \times 10^{-4}\ \text{cm}^2$

I = Power/Area
Argon ion*:* $I = (1\ \text{Watt}) / (7.85 \times 10^{-5}\ \text{cm}^2) = \mathbf{1.27 \times 10^{4}\ watts/\ cm^2}$

Titanium-sapphire*:* *average* $I = 30 \times 10^{-3}\ \text{watts} / (3.14 \times 10^{-4}\ \text{cm}^2) = \mathbf{95.5\ watts/\ cm^2}$
Instantaneous $I = 3750\ \text{watts} / (3.14 \times 10^{-4}\ \text{cm}^2) = \mathbf{1.19 \times 10^{7}\ watts/\ cm^2}$

So the titanium: sapphire laser's average power (and power density) is much lower but its instantaneous power and power density are much higher than those for argon ion lasers.

c. The newly approved laser uses *single* pulses to achieve its effects—that is, only a single pulse is used to create each drainage hole. Assume the argon ion laser employs a 1 second exposure time to create each hole. What is the energy used to create a hole in each procedure?

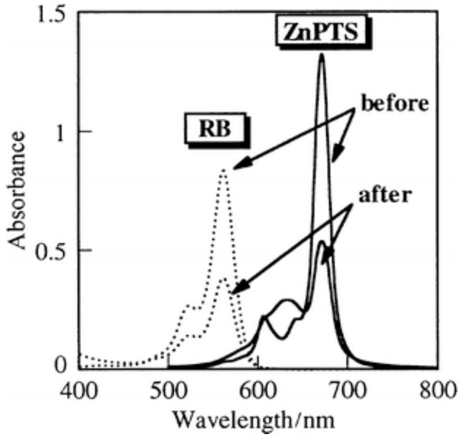
The energy for each is just
Argon ion: 1 watt × 1 second = 1 Joule
Titanium: sapphire = 30 milliJoule (already given)

d. Given the above information, what advantages would you expect the new titanium-sapphire laser to offer compared to the argon ion laser because of its different wavelength of operation—and why? (You may find it useful to know that the main pigment in the *trabecular meshwork* is melanin.)

You would expect less heat flow from the titanium:sapphire since it's light is delivered in highly intense pulses so fast that there is no time for any damage mechanism apart from photovaporization or ablation. However, it also have the advantage of penetrating more deeply because its wavelength is in the near-infrared, where all pigments (including melanin) are fairly low in their absorption compared to the blue-green light of the argon ion laser. "The titanium:sapphire laser's light penetrates deeper into the tissues and causes less thermal damage than currently used ophthalmological lasers", such as the argon ion laser.

3. Photodynamic therapy

Scientists and physicians are constantly working to identify new photosensitizers for photodynamic therapy (PDT) for ophthalmology, dermatology, cancer chemotherapy and other applications. Below we see an absorption spectrum for chemical compounds that are two new candidates for cancer therapy using PDT. We will call these two compounds just RB and ZnPTS. Reference this plot in answering the following questions. (The "before" curves correspond to absorption of each compound before laser light has been applied, while the "after" curves correspond to their absorption after each has been exposed to laser light.



a. What laser(s) would be the best match(es) (if any!) to use in performing PDT on using these two photosensitizers? Include any and all lasers that would be good matches. Be sure to provide both an answer and your reasoning, for each compound. Would either of these photosensitizers be good possibilities for PDT in treating tumors? Explain any assumptions that you make in answering this part. (You may assume that is it possible to decrease the power output of any laser if necessary by using special filters.)

Here the important point is absorption by other pigments in the body vs. absorption by the photosensitizer. Does its absorption overlap too much with melanin and hemoglobin, or is it distinct? We see that the RB compound has its absorption peaks (around 560 and 515 nm approximately) very close to those for hemoglobin (in the absorption spectra provided on the exam). However, the absorption spectrum for ZnPTS has a peak around 675 nm (approximately) that is at a wavelength where the absorption for hemoglobin has fallen off appreciably. Melanin has relatively low absorption at the peaks for both photosentizers. Thus if the only pigments present in the tissue are hemoglobin and melanin, then ZnPTS is a good possibility. It is better than HPD at avoiding the stronger absorption from hemoglobin and melanin as well. RB and HPD have peaks at similar regions, but without the advantage outlined for the other compound, so it does not appear a likely candidate where hemoglobin is present. The dye laser would cover both cases since it can produce any wavelength. Also, we see that the krypton laser would match well with the ZnPTS absorption peak at about 675 nm. Possibilities for the RB compound include the ND:YAG (frequency doubled to 532 nm)or the Argon ion (514 green line) or copper vapor (511 or 578 nm) lines, but these aren't as good a match as the other.

b. What else would you need to know about these two compounds to determine whether they would be effective photosensitizers? Be complete in your answer.

It's also important to know that there is a laser that matches the absorption properties of each with the correct intensity and mode of operation (CW rather than pulsed) and that the absorption properties do not coincide entirely with that of pigments in the region of the body containing the tumor. Possible additional responses should include: is it toxic? Is it biocompatible and not cause allergic reactions, etc.? Does it cause a reaction that induces cell death when it absorbs laser light? Does it get preferentially taken up by and retained in malignant cells compared to normal cells? Does it clear from the body over a reasonable period of time? Can its action be taken advantage of in a reasonable treatment time?

4. Ultrasound Imaging

Consider the ultrasound scan shown below in answering the following questions. Assume the transducer is located at the top of the image, as shown with the figure. You do not need to know anything about the anatomy being portrayed here to answer these questions.

a. An ultrasound imaging device measures the following three times for echoes to return to the transducer in an imaging scan from the interfaces indicated: A: 1.5×10^{-5} seconds, B: 2.9×10^{-5} seconds and C: 5.2×10^{-5} seconds. How far below the transducer are each of the interfaces indicated? How far apart are interfaces B and C?

$$D = \frac{v_s \times t}{2}$$

$D_A = 1540\ m/s \times 1.2 \times 10^{-5}\ s / 2 = 0.012\ m = 1.2\ cm$

$D_B = 1540\ m/s \times 2.9 \times 10^{-5}\ s / 2 = 0.022\ m = 2.2\ cm$

$D_C = 1540\ m/s \times 5.2 \times 10^{-5}\ s / 2 = 0.040\ m = 4.0\ cm$

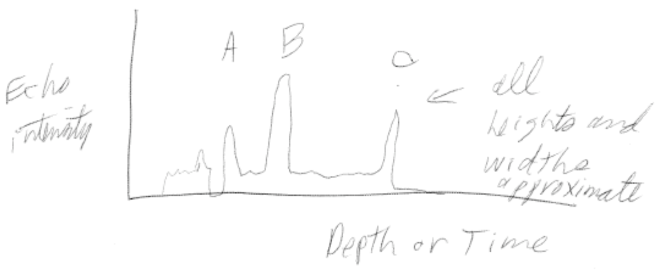
I have assumed an average value of the speed of sound in soft tissue.

B and C are $D_C - D_B = (4.0 - 2.2)\ cm = 1.8\ cm$ *apart.*

b. What would the A-mode intensity display (as a function of distance) along the white arrow look like? You will need to make a plot and assume an incident intensity of 1 W/m^2. What can you tell about the variation of acoustic impedance along this direction from your plot?

This shows that actual images have their echo intensities corrected for absorption, so your plot should not show a gradual falloff with depth (I did not take off for this, since you might have meant to plot the intensity before this correction, though.) All we know is the approximate change in acoustic impedance at each interface (divided by the summer acoustic impedances, but since these do not vary much in the body, most of the reflected intensity variation is due to differences.) There is no way to know whether the acoustic impedance increased or decreased, or its actual absolute value at any point in the scan.

sketch for Fig in 4 b)

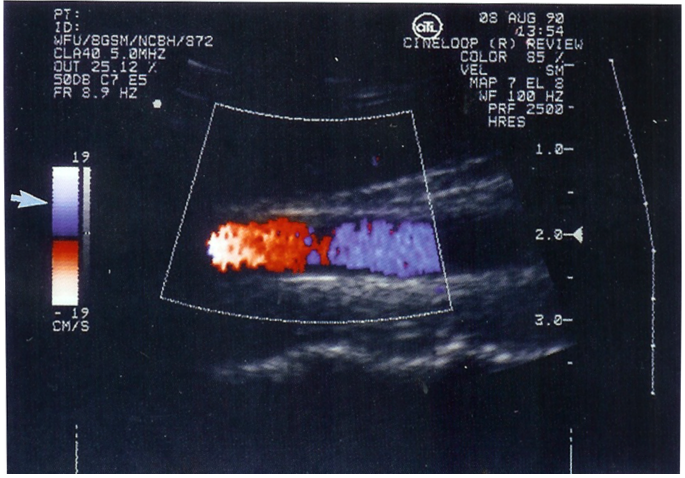


c. Assume this image was made with a 7.5 MHz transducer. Describe qualitatively at least two ways the image might change (and why) if it had instead been made with a transducer with a frequency of 3.5 MHz or 15 MHz.

   For 3.5 MHz, the image will be blurred because of the lower spatial resolution, but features deeper into the body will be imaged because of the longer half-intensity length. The higher frequency scan will be at higher spatial resolution, so you might see additional details too blurred to resolve at 7.5 MHz. The features already imaged might be observed at higher resolution. However, the ultrasound is absorbed more rapidly near the surface, so the scan will not provide information as deep into the body.

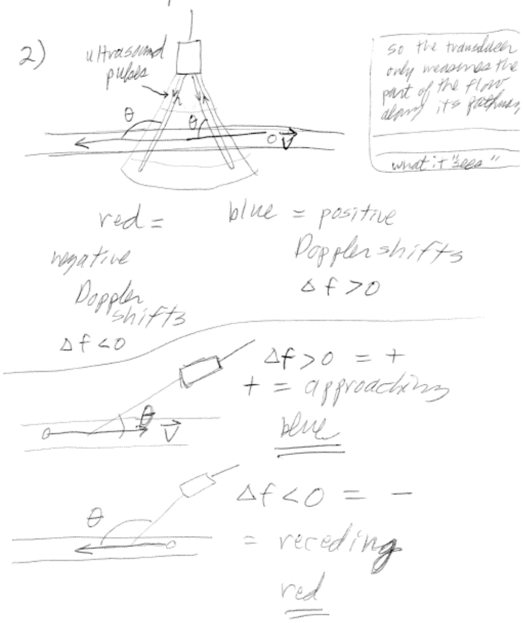
5. Doppler Ultrasound

The following image is a color flow Doppler ultrasound image described as flow in a straight line along a blood vessel. The source states, of the color map used: "In this map, blue and red are assigned to positive and negative Doppler shifts, respectively, progressing to white at the extremes." (That is, for the largest values of flow speed.) Explain how this color flow image could result from flow in a straight line along a blood vessel in this measurement geometry. Use a sketch, indicating the direction you have assumed for the pathway of the ultrasound beam at various times in the scan and the direction of flow of blood in the vessel at representative points along its length.



We know from the shape of the scan shown that the transducer is at the top of the image. This means the ultrasound pulses travel approximately up and down at each point on the image to measure the grayscale anatomical information as well as to measure the Doppler shifts. A positive Doppler shift (blue) means there is some component of the flow that is approaching the transducer, so $\Delta f > 0$ *and it is positive. A negative Doppler shift (red here) means there is some component of the flow that is receding from the transducer, so* $\Delta f < 0$ *and it is negative. In the middle, the transducer is oriented in a way such that the flow is perpendicular in the middle to the direction of the beam's travel, hence the colors become a bit* *dimmer, then reverse as the direction relative to the transducer reverses. The approximate directions are shown below.*

1) Transducer has to be at top



red = negative Doppler shifts Δf<0

blue = positive Doppler shifts Δf>0

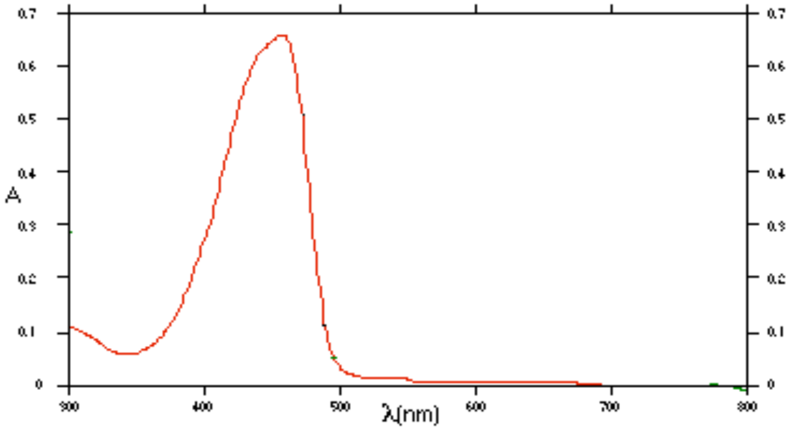
Δf>0 = +
+ = approaching
blue

Δf<0 = −
= receding
red

6. Phototherapy—More absorption of light

A light from a lamp is used to treat jaundice, or the condition that results when too much *bilirubin* is present in newborn babies. The absorption spectrum of *bilirubin* is shown below. The quantity A plotted along the y-axis is proportional to the Absorption at each wavelength, λ.

a. Explain what color of light you would expect to use for phototherapy for jaundice and JUSTIFY YOUR ANSWER FULLY based on the absorption spectrum. Just stating a color or colors isn't enough—to get credit you need to explain why this is determined by the absorption spectrum!



Since the absorption spectrum is greatest where the molecule most strongly absorbs light, you want light which has a wavelength composition which matchest the strong bilirubin absorption over the range 400 to around 480 nm, peaking at approximately 450 nm (values are approximate and estimates are OK). This corresponds to the blue part of the visible spectrum.

b. Imagine you are an FDA investigator looking into a firm that has begun to market light emitting diodes (LED's) for photodynamic therapy of various kinds. Explain why you would or would not consider the following system an appropriate choice for phototherapy for jaundice, based on an evaluation of each of their claims as follows: "Our Bili-LED system has a peak emitted wavelength between 450 and 475 nm. Our unit has the advantage that it offers high intensity light with little emission in the ultraviolet and infrared compared to conventional lamp sources for jaundice therapy on the market."

Here are some possible comments: You want to optimize emission at the wavelengths best absorbed by the bilirubin: their emission peak of 450 to 475 nm is right on target. You never want emission at wavelengths that will not be significantly absorbed by your molecule of interest (here, that's bilirubin) if other body tissues also absorb the light and that can cause damage. Infrared light is emitted by lamps as is ultraviolet light, to some extent (see for example Fig. 3.18 in the textbook), and the LED manufacturers state that their product has less emission at these undesirable wavelengths which can cause heating (IR) or chemical damage (UV) light so that's a good thing. Given the last statement, the high intensity is desirable because it is all concentrated at the correct blue wavelengths best absorbed and most likely to cause the desired effect for shorter exposures.

7. Lasers in medicine

In *laser lithotripsy*, extremely high power densities are used to disrupt kidney stones and other painful mineralized deposits. High power pulsed holmium-YAG laser systems can be used in this application.

a. A laser used for lithotripsy is transmitted into the kidneys laparoscopically using an optical fiber. When laser light exits the optical fiber, the intense laser beam instantly vaporizes the water at the very tip of the optical fiber, creating a shock wave that destroys the stone. (No focusing of the laser is needed for the high instantaneous intensities used.) To achieve this result, power densities of 10^{10} watts/cm^2 are required. Use as your effective laser spot size the diameter of the optical fiber, 1000 microns. What must the instantaneous laser power be in order to achieve the necessary power density required to generate the shock waves needed to break up kidney stones?

Here we need to compute the instantaneous power using: $P = I \times A$ *where* A *= area of circular optical fiber with diameter 1000 microns =* πR^2 *and* R *= (1000*

microns/2) × 10^{-4} microns/cm = 0.05 cm. We also are told we need to have: I = power density = 10^{10} watts/cm^2
This gives a required instantaneous power of P = (10^{10} watts/cm^2) π (0.05 cm)^2 = ***78.6 × 10^6 watts= 78.5 megawatts****.*

b. Each pulse lasts 1.0ns long and the optical fiber can carry up to 100mJ without melting. How much energy is emitted per pulse? Will it melt the optical fiber?

   We have from part (a) instantaneous power of P =78.6 × 10^6 watts and the energy deposited in a 1 nanosecond pulse is equal to: E = P t_{pulse} = 78.6 × 10^6 watts × 1 nanosecond × 10^{-9} seconds/nanosecond = ***0.0785 Joules****. 100 milliJoules = 0.100 Joules, so it will not melt the fiber.*

c. One source lists a fluence of 100 J/cm^2 for this technique. How long must the laser be turned on in order to achieve this value if the pulse repetition rate is 20 Hz?

   Here you need to think through two steps. Since the laser is pulsed, its instantaneous power is only present during pulses. So you can compute the exposure time in more than one way. Here is one possibility. Compute the average power corresponding to the energy per pulse from (b) and the repetition rate given:
   P_{ave} = (0.0785 Joules) 20 Hz. Then use this power to compute the average intensity: I_{ave} = P_{ave}/A, and use it to find the exposure time, T_E from F = I_{ave} × T_E = 100 J/cm^2. Then, the exposure time is found from: T_E =F/ I_{ave} = (0.0785 Joules) 20 Hz × A = (0.0785 Joules) 20 Hz × π (0.05 cm)^2 = ***0.5 seconds****.*

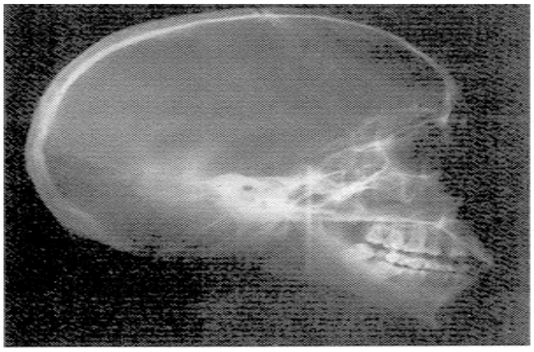
8. X-ray imaging

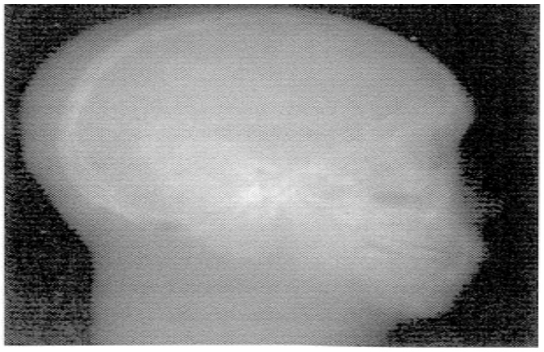
Suppose that you want to use copper x-rays for imaging. You wouldn't really want to use Cu x-rays since x-rays below 10keV do not penetrate far into the body. Copper x-rays have a wavelength of $1.54x10^{-10}m$ and a density $\rho = 8.92\ g/cm^3$.

a. What is the *HVL* for the copper x-rays and if the beam has an intensity of *1 W/m^2* incident in a material, what percent of the x-rays are transmitted? You will need the attenuation coefficient for Cu x-rays, which can be found at http://physics.nist.gov/PhysRefData/XrayMassCoef/ElemTab/z29.html. (Hint: The mass attenuation coefficients are energy dependent.)

   The half layer value is given as
   $x_{\frac{1}{2}} = \dfrac{0.693}{\mu} = \dfrac{0.693}{52.55\frac{cm^2}{g} \times 8.92\frac{g}{cm^3}} = 0.0015cm = 0.015mm$, where the energy (used to determine the attenuation coefficient) is given by
   $E = \dfrac{hc}{\lambda} = \dfrac{6.63\times10^{-34} Js \times 3\times10^{8} \frac{m}{s}}{1.54\times10^{-10} m} \times \dfrac{1eV}{1.6\times10^{-19} J} = 8072eV = 8.0keV$. The percent of the x-rays transmitted is given by $\dfrac{I_T}{I_0} = e^{-0.693} = 0.5 = 50\%$.

b. The following radiography images were made with x-ray sources, not necessarily Cu (and probably not copper), of different average energies. Which image was made with the higher and which with the lower x-ray energy? Explain your reasoning.





Since x-rays lower than 10 keV aren't used for imaging, since they are insufficiently penetrating, we must consider only x-rays above 10 keV. For that range, there is significant contrast between bone, fat, muscle and other soft tissues for the lower x-ray energies (more photoelectric absorption). As x-ray energy increases, contrast decreases (more Compton scattering) and beam hardening makes the x-rays all transmit with the same relative energy and thus there is little contrast. Therefore, the left-hand image must be the lower x-ray energy.

These questions are not for credit and do not have to be turned in with the exam. I will be looking for answers to these questions when I return. Please type your answers below and print them out then give them to me when class resumes. These can be anonymous if you prefer, or you may put your name on them if you'd like.

1. What is your impression of the course so far?

2. What are the topics that you like/dislike and why?

3. What could be done to improve the quality of the remainder of the course?

4. Are there any questions, comments or complaints that you would like me to address?