Imaging in Highly Scattering Media

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Introduction

Research on developing 'imaging' methods for turbid media holds promise for applications in medicine and biology. Mammography in particular can benefit from an alternate diagnostic tool that does not involve either ionizing radiation or expensive measurement apparatus — particularly a method that holds promise of being able to differentiate between tissue types that x-ray mammography cannot.

The main area that requires innovation is the mathematics of reconstruction, and efficient computer implementation thereof. Little is known at the moment even about how well posed the inverse problem is, and what situations allow for reconstruction of the spatial distribution of optical absorption and scattering. A second area that needs work is the development of instrumentation, particularly detectors that can handle the extremely wide dynamic range encountered.

We have done preliminary work on mathematical modelling and algorithm development, as well as the measurement systems and are hoping to continue this work at an increased level.

Background

Some objects of interest in medicine and biology are translucent — some light penetrates, but light is scattered heavily within the object, making it impossible to image the interior of the object using traditional optical methods. We are exploring methods for recovering the distribution of absorbing and scattering material inside a volume using measurements of light transmission from many source points to many detectors on the surface of that volume.

We are using models for the interaction of light with the scattering and absorbing material to set up equations that allow simulation of light attenuation. The code for such a simulation solves the *forward* problem: given the distribution of absorption and scattering, what is the light flux detected at one point on the surface, when it is illuminated at another specified point?

We have also started to develop solutions to the *inverse* problem in certain simple cases. In the inverse problem one has a large number of measurements of source-to-detector signal attenuation and has to recover the internal distribution of absorbing and scattering material.

Such methods may find applications in medicine to imaging of the interior of translucent soft tissue volumes. One advantage of such a method over competing approaches is that it does not require use of ionizing radiation (as in CAT scanning). Another is that the instrumentation is smaller and cheaper than that of magnetic resonance imaging (MRI). It is also expected that tagging target molecules with pigments that selectively absorb certain wavelength of visible light will help differentiate between different types of growths.

Current indications are that the computational cost of methods for solving this problem are likely to be high. Fortunately, computation is one of the few areas where continuous advances are made in performance to cost ratio.

Applications of such methods to mammography should be apparent, but imaging of tumours in neonatal skulls, as well as testicles, and shallow structures like the thyroid may provide other opportunities.

Such methods may also play a role in imaging at high magnification, since most specimen of biological interest are not opaque under the microscope, yet heavily scatter light and so often yield hard-to-interpret images using traditional imaging methods.

Light in highly scattering media

In a medium where light transmission is dominated by scattering (i.e. where the scattering half length is much less than the thickness), the directionality of the incident light is rapidly lost and one can adequately represent the distribution by just the light flux — a scalar function of *position* within the object. This is a great simplification, since one does not need to represent light flux as a function of *direction* as well.

The light flux obeys a form of the diffusion equation which also applies to other physical systems such as current flow in resistive volumes, steady-state heat flow in a volume, deformation of elastic media, and neutron diffussion. Intuition about imaging in scattering media may be assisted by reasoning in analogy with these other, better understood, physical systems.

Comparison to optical imaging, CAT and MRI

To set the proposed new ‘imaging’ method in context, it may be well to review for a minute other imaging modalities.

(1) In ordinary optical imaging, one deals with opaque objects immersed in a transparent medium of constant refractive index. Light follows straight lines and does not interact with anything on its way from the surface of the object to the center of projection — and from there on to the image plane. Points on object surfaces map to points in the image. Both are two-dimensional manifolds (in the case of the image this is typically planar). Because of this, a great deal of information can typically be recovered from one image — or a small number of images. Imaging in this case is described by the perspective projection equation (geometry), and the image irradiance equation (radiometry) (see *Robot Vision*[3] and *Shape from Shading*[4])

(2) In tomography, one instead obtains line integrals of absorbing density (There may be a significant amount of scattering, but the scattered radiation is removed by collimators). It is possible in this case (and convenient) to work with two-dimensional ‘slices’ of the object. The line integrals taken with many source positions constitute the two dimensional Radon transform of the absorption density in this slice. Reconstruction algorihms for this problem are well developed (See ‘Density Reconstruction Using Arbitrary Ray Sampling Schemes’ [1] and ‘Fan-Beam Reconstruction Methods’ [2])

(3) In Magnetic Resonance Imaging, one instead obtains integrals of density over all planes. These integrals taken together over all magnetic field gradient directions constitute a three dimensional Radon transform. Again, reconstruction algorithms for this problem are well understood.

In each of the above cases, the observed signal depends on a spatially confined volume (point, line, and plane respectively). In the proposed new method each of the measurements will depend on all of the points in a *volume* of interest.

Competing Approaches

We are investigating an approach based on using the steady-state attenuation from source to detector, using many source positions and many detector positions. The instrumentation in relatively simple: lasers (possibly semiconductor lasers) and photo-detectors (most likely semiconductor diodes).

(1) An alternate approach is to use a streak camera to try and capture just the photons that have gone through without scattering, or minimal forward scattering. We don’t consider this a viable approach because with

the amount of scattering typical of biological tissues, virtually *no* photons will pass through without being scattered. Aside from this, the instrumentation is more complex.

(2) The incident light can be modulated at a high frequency (100 – 200 MHz). In this case, phase as well as amplitude can be measured in the detected signal. The equations governing the system in this case need to include a time derivative, which makes the system equivalent to a resistive network with distributed capacitive loading, or *non-steady state* heat-flow.

Physical experiments that we conducted based on this approach were not very promising: obtaining accurate phase measurements at these frequencies given the high attenuation in the medium was not easy, and the effect on phase of the insertion of extra localized absorbing material was not profound (the order of 1 degree phase shift only). Also, the model for this situation is more complex and requires much more computation.

(3) Yet another approach is based on the average time delay of the pulse of light exiting the volume. This requires considerably more complex instrumentation, since semiconductor sensors do not have the required time resolution (tens of pico-seconds), but it is felt by some researchers (Simon R. Arridge, private communication) to add information that is not available just from the 'DC' measurement of attenuation. Since this time domain measurement is related to the phase measurement described above, we are not convinced that the extra complexity both of instrumentation and reconstruction algorithms is warranted.

Some Additional Issues of Concern

The overall attenuation from source to detector is largely governed by the geometric mean of average scattering and average absorption coefficients. For biological tissues the overall attentuation is many orders of magnitude — possibly more than ten or twelve orders of magnitude in some situations of practical interest. This means that the detectors need to be very sensitive, yet have a very wide dynamic range (since they will be used both far from, as well as near the source). Superb shielding is also required to prevent stray light from the source from reaching the detector. The effects of light from other extraneous sources can be greatly ameliorated though by modulating the source at some low frequency (1 kHz say) and demodulating the sensor signal.

Boundary conditions on the volume of interest are important. That is, we need to be aware of what happens to photons that exit. Conversely we may gain some advantage by controlling what happens to them. One extreme boundary conditions is: all light leaving the volume is lost (either because the volume is in a large dark room or because the surface is covered with highly absorbing material). The opposite extreme is where all light is reflected back into the volume right where it exits (the surface is covered with a highly reflective material such as white paint, or powder). The ability to reconstruct the distribution of absorption density in the interior of the volume will depend on the boundary conditions.

Our main focus is on situations where scattering can be assumed approximately constant within the volume of interest, while the quantity to be recovered is the spatialy varying absorption density. In some cases — such the neonatal skull — this may not be a good assumption since scattering in the skull is significantly stronger than in white or grey matter. But in the other applications sited, variations in scattering are less likely to be of overwhelming significance. It is possible to introduce scattering as another unknown spatial distribution, but this doubles the number of unknowns and hence makes the problem less well posed.

The contrast between certain tissue — such as a particular type of tumour — and the 'background' can be greatly enhanced by attaching 'micro-bubbles' carrying strongly absorbing pigment to cells of that tissue type. We expect that this will greatly aid detection, and that without such techniques, the detection may be limited to near-surface layers. A particularly useful technique in this regard will be sensing at two wavelengths, one where the pigment absorbs strongly and one at a wavelength where it does not.

Current status of algorithm exploration

We have developed code for the forward problem in some simple two-dimensional geometries. This has allowed us to get a feeling for how much the source to detector attenuation depends on the distribution of absorbing material.

We have also developed linearized mathematical models that allow prediction of changes in output when localized changes in absorption are made.

In some simple geometries (with relatively few resolution elements), we have developed methods for solving the inverse problem in an iterative fashion, using the linearized model.

A particularly simple model is one where the unknown absorbing density distribution is only a function of one variable and where the measurements are also a function of one variable. In this 'one-d to one-d' problem we have developed a preliminary feel for the circumstances when the reconstruction problem is not well posed.

A slightly surprising result is that — for given scattering — the problem becomes *better* posed when the average absorption is higher (although the signal is decreased, of course).

Another slightly surprising result is that the problem is better posed when the surface of the volume is covered with fully absorbing material as opposed to fully reflecting material.

Planned Work

We need to develop a better understanding for the geometries, scattering and absorption distribution which can potentially lead to stable solutions. This means building numerical models for more realistic geometries, developing faster simulation algorithms, and doing more experiments.

The reconstruction algorithms currently used are relatively brute force methods that are computationally very expensive. We need to develop the mathematics of reconstruction, and improve the implementation of the algorithms.

A large part of the planned work done lies in the area of algorithms, both the underlying math as well as practical implementation. We also want to look more carefully at design of the required instrumentation, and perform some mroe experiments with phantoms.

The Team

A inter-disciplinary group of people from MIT, Harvard MIT Health Science program and University of Massachusetts Worcester Medical School (primarily Frederick H. Bowman, Aaron B. Brill, Berthold K.P. Horn, Richard C. Lanza, Charles G. Sodini) has been meeting regularly to discuss this 'diaphanography' problem. We have been discussing the literature on this subject [9–30], attenting talks by invited speakers, but focusing largely on developing our own methods.

Several undergraduate student projects (UROP), a Bachelor's thesis [5], and a Masters thesis [6] have sprung from this effort so far, as have conference papers [7,8]. We have some simulation results on simple geometries, and some measurements using both 'DC' and high frequency (100 MHz) modulated light.

Support requested

It has become clear that the focus should be on the mathematical analysis and reconstruction algorithms. This will tell us the physical circumstances (wavelength, thickness, absorption and scattering coefficients, imaging geometry, number of sources and number of detectors) under which we can expect the reconstruction to be stable. Also developing the mathematical foundation and the algorithm will allows us to predict what spatial resolution can be achieved, and what the smallest increment in absorption is that can be detected over a given volume. We will also discover what measurment geometry — position and number of sources and detectors — are required.

We also need to develop the actual instrumentation to make the measurements. Sources and sensors can then be applied to phantoms constructed to simulate tissue. This will allow us to gather data that will then be used to test algorithms.

We are looking for support of at least one student working on the mathematical analysis and algorithm development and implementation. We are also looking for support of one student to work on the instrumentation — mostly development of the high dynamic range detector electronics. Some electronics will need to be acquired as well.

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