Chapter 7

Summary

Diffusing photons can be used to detect, localize, and characterize optical and dynamical spatial inhomogeneities embedded in turbid media. Measurements of the intensity of diffuse photons reveals information about the optical properties of a system while speckle fluctuations carry information about the dynamical and optical properties. In this dissertation I have shown that simple diffusion theories can be used to accurately model the intensity signals and speckle correlation signals that diffuse through turbid media with spatially varying properties. This work is thus a unification of intensity and speckle probes of turbid media since the analogous theoretical models allow ideas and concepts developed for one probe to be easily applied to the other probe. I have also discussed possible biomedical applications for these techniques.

The photon diffusion equation has an interesting wave solution when the intensity of the light source is sinusoidally modulated. Under these conditions the diffusion equation reduces to a Helmholtz equation. For a point source in an infinite, homogeneous medium the solution is a scalar intensity wave that propagates spherically outwards from the source. The spherical wave has a complex wavenumber that depends on the optical properties and modulation frequency. This spherical wave has been observed and is called a diffuse photon density wave (DPDW).

The theoretical consequence of this solution is that we can neglect the details of the migration of individual photons and instead focus on the behavior of well understood classical, scalar waves. Classical wave theory indicates that waves refract at interfaces between media with different optical properties (e.g. scattering and absorption in this case and refractive index in the case of ray optics) and are diffracted by absorbing objects.

I experimentally demonstrated the refraction and diffraction of diffuse photon density waves and showed that standard refraction and diffraction models agreed well with observations. I also showed that the interaction of diffuse photon density waves with localized optical inhomogeneities can be treated as a standard scattering problem whereby the wave detected outside of the object is a superposition of the incident and scattered waves. The scattering solution for diffuse photon density waves is analogous to a scalar version of the Mie scattering theory for electromagentic waves and agrees well with experimental observation.

The photon diffusion equation is not valid if the absorption coefficient is larger than one tenth of the reduced scattering coefficient or if the DPDW modulation frequency approahces or exceeds the scattering frequency (i.e. $v\mu_s'$). I showed that higher order approximations to the radiative transport equation give better agreement with experimental observations under these conditions and that the solutions of these higher order approximations are still DPDW's, but with different functional forms for the wavenumber.

Because the scattering of diffuse photon density waves is understood, inverse scattering algorithms can be developed that permit optical inhomogeneities to be localized and characterized. Using realistic models for the intrinsic noise in a measurement, I performed a detailed signal-to-noise analysis which reveals the limits to the detection, localization, and characterization of optical inhomogeneities. I found that dominant sources of noise are shot noise and noise due to the uncertainties in the positions of the sources, detectors, and objects.

With best case estimates for these noise levels I found that optical inhomogeneities representing breast tumors (e.g. 300% contrast in absorption or 50% contrast in scattering) as small as 3 mm can be detected and localized, but that the size and optical properties of the "tumor" cannot be accurately characterized unless the diameter exceeds 1 cm. This signal-to-noise analysis can be used to determine the optimal measurement geometry for object characterization, such as determining the best measurement positions and frequencies. The best modulation frequencies are between 0 and 500 MHz. Scattering objects are better characterized with measurements at multiple frequencies while no such gain is obtained for absorbing objects. Measurements close to the object give the strongest object signature, but a spatially distributed set of measurements is required for full characterization.

The optimal spatial extent for the measurements depends in a detailed way on the system parameters and is best determined for each specific case. With full optimization it is possible in a best case scenario to characterize tumors as small as $\sim$7 mm embedded in 6 cm of breast tissue. Although this length scale cannot compete with magnetic resonance imaging (MRI) and x-ray mammography, it may still be clinically useful because of its potential for superior specification. Furthermore, there are applications for imaging large scale anomalies such as brain hematomas [15, 145, 146].

The correlation diffusion equation provides a simple framework for predicting and quantifying the speckle correlation functions that are measured on highly scattering systems with spatially varying dynamical and optical properties. Because the correlation diffusion equation is analogous to the photon diffusion equation, all concepts and ideas developed for DPDW's can be directly applied to the diffusion of correlation. I showed experimentally and with Monte Carlo simulations that the diffusion of correlation can be viewed as a correlation wave that propagates spherically outwards from the source and scatters from macroscopic spatial variations in dynamical and/or optical properties. I also demonstrated the utility of inverse scattering algorithms for reconstructing images of the spatially varying dynamical properties of a turbid media.

After laying the theoretical foundation for correlation diffusion, I illustrated its biomedical applicability with examples of monitoring blood flow and probing the depth of burned tissue. Combining diffuse photon and diffuse correlation methods to monitor non-invasively the behavior of blood during venous and arterial occlusion provides useful physiological information. In particular, we saw expected changes in blood volume, blood oxygen saturation, and blood flow, including hyperemia, during different stages of venous and arterial occlusion. The combination allows us to monitor oxygen delivery and metabolism non-invasively. This technique may be useful for the diagnosis of various vascular diseases such as thrombosis. Correlation diffusion may be used to quantify the depth of severely burned tissue. I demonstrated this application on phantom systems and in the clinic using a pig model. My results indicate that burn thicknesses differing by 100 μm can be distinguished both in phantoms and in the clinic. Furthermore, I found that the correlation diffusion equation accurately predicts experimental measurements on a layered burn model. This suggests that an inversion algorithm could be developed to quantify burn depth clinically. The realization of this goal will require the combined use of diffuse correlation and diffuse photon probes.

In this dissertation I have given a complete account of the theory behind photon diffusion and correlation diffusion, aimed to convince my audience that these diffusion models are accurate for systems with spatially varying properties, and exemplify the application of these diffuse probes to clinical problems. There are bound to be numerous clinical and industrial applications that are yet to be discovered, and I hope that this work stimulates and aids their development.