Lecture 4: Modeling Diagnostic Signals
Lecture 4 Outline

• From Measurements to Diagnosis
• Influence of Boundary
• Measurement Design Considerations
• Spatially Resolved Diffuse Reflectance
• Time-Resolved Diffuse Reflectance
• Sensitivities in SDA and RTE Models
• Higher Order Approximations and RTE Similarity Theory
From Measurements to Diagnosis

Biomedical optics aims to utilize light collected at the surface for

• Diagnostics
• Imaging the tissue
• Guiding therapy
• Designing improved laser probes

Of key importance is prediction of optical property distributions from non-invasive measurements.

Much of the rest of this Workshop will be devoted to the technical issues that arise in making use of the RTE to model light-tissue interactions and to extract optical signatures from measurements made in the laboratory (real or virtual!), or the clinic.
From Measurements to Diagnosis

Light detected at the tissue surface must be used to infer the \textbf{distribution of optical properties} in the tissue that produced the measurements (inverse problem)

This depends on knowledge of the \textbf{detected light field} (photon “banana”), in contrast with the internal fluence distribution that was the focus of Lectures 1-3
Diagnostics: Technical/Computational Challenges

Noninvasive diagnosis creates computational challenges because

- Detected signals provide only sparse and indirect information about the radiance \( L(r, \Omega) \) throughout the tissue
- Detected signals are weak at locations distant from the source; this is an issue for MC simulations
- Refractive index mismatch at the tissue surface alters the light field detected at the surface and immediately below it and must be modeled accurately
Internal vs External Measurements: Sensitivities

The first GUI exercises were designed to gain familiarity with the impact of changes in optical properties, albedos and solver choices on the internal light field, as manifested by (integrals of) the forward RTE solution, $L(r,\Omega)$.

Now we switch our focus to the impact of these same changes on the detected light signals.

We investigate:

- How SDA and RTE models deal with boundary influence
- How to analyze sensitivities in the context of both SDA and RTE solvers
Boundary Influence

Moving from infinite to finite tissue means introducing boundary conditions involving Snell’s Law and the Fresnel relations (Lecture 3)

SDA relies on BC that is approximate (based on global conservation: integration over all angles)
MC implementation models the physics faithfully on a photon-by-photon basis; conservation is guaranteed for every exiting direction (using weighted MC)
Measurement Design Desiderata

Requirements for Effective Optical Measurements; e.g., to recover \((\mu_a, \mu'_s)\) or \((\mu_a, \mu_s, g)\)

1. At least **as many measurements** as optical properties
2. Measurements located in phase space (position, angle, time) to exhibit **sensitivity** to optical properties
3. Measurement **independence**; multiple measurements (in space or in time) sensitive to different tissue features
Spatially Resolved Diffuse Reflectance/Transmittance

The variables/parameters of interest to vary:
Distance \( \rho \) between source(s) & detector(s),
Number and locations of detectors

\[
R(\rho) = \int_{S^2^-} L(x, y, z = 0, \Omega) d\Omega
\]

where \( (\rho^2 = x^2 + y^2) \) and \( S^2^- \) designates the full hemisphere of exiting directions at the tissue surface, \( z = 0 \)

In practice, light is collected over reduced numerical apertures and small surface areas that include the desired values of \( \rho \); that is,

\[
R(\rho_\Delta, \Omega_\Delta) \approx \iiint_{\Delta \Omega \times \Delta \rho} L(x, y, z = 0, \Omega) d\Omega d\rho
\]
Time-Resolved Diffuse Reflectance

Time-resolved measurements depend on introduction of a pulsed light source and collection of light that arrives at each detector at different times (equivalently, distances traversed)

\[ R(\rho, \Omega_{\Delta}, t_{\Delta}) \approx \int \int L(x, y, z = 0, \Omega, t)d\Omega \]

For both spatially- and time-resolved measurements, avoiding redundancy requires intelligent placement of (neighboring) detectors
Representing Detection: Detector Functions

In Lecture 2 we saw that all metrics relevant to therapy and diagnostics are weighted integrals of the radiance

$$\iiint f(r,\Omega,t)L(r,\Omega,t)drd\Omega dt$$

where the function $f(r,\Omega,t)$, the “detector function”, restricts the light collection to specific locations $r$, orientations $\Omega$ and times $t$, either inside the tissue or on the tissue surface.
Diffuse Reflectance (Transmittance)

In other words, reflectance measurements can be expressed as multiple integrals

\[
\int \int \int L(x, y, z = 0, t) dt d \rho d \Omega
\]

which then defines the detector function \( f \) as

\[
f(r, \Omega, t) = \begin{cases} 
1 & \text{if } (x, y) \in \Delta \rho_j, \ \Omega \in \Delta \Omega_i, \ t \in \Delta t_k \\
0 & \text{otherwise}
\end{cases}
\]

This means that we can write, for large enough \( T_{\text{max}} \)

\[
\int \int \int L(x, y, z = 0, t) dt d \rho d \Omega = \int \int \int_0^{T_{\text{max}}} f(r, \Omega, \tau)L(r, \Omega, \tau) d \tau dr d \Omega
\]
Sensitivities: Analytic

SDA solvers rely on formulas $\varphi = \varphi(\mu_a, \mu_s, p(\mu),...)\) which can then be differentiated, either in closed form or numerically:

$$\frac{\partial \varphi}{\partial \mu_a} = \frac{\partial}{\partial \mu_a} \varphi(\mu_a, \mu_s, p(\mu),...)$$

$$\frac{\partial \varphi}{\partial \mu_a} \approx \frac{\Delta \varphi}{\Delta \mu_a} = \frac{\varphi(\mu_a + \Delta \mu_a, \mu_s, p(\mu),...) - \varphi(\mu_a, \mu_s, p(\mu),...)\)}{\Delta \mu_a}$$

The magnitudes of derivatives for various values of their arguments indicate where measurements are likely to do the most good.
Sensitivities: Stochastic

Stochastic (MC) solvers can also produce formula-based estimates of sensitivities, making use of weighted photon biographies (introduced in Lecture 2)

$$\xi(b) = \xi(P_0, P_1,...)$$

The weight $\xi$ of each photon contains information about the optical properties encountered throughout its random walk.

The derivatives

$$\frac{\partial \xi}{\partial \mu_a} = \frac{\partial}{\partial \mu_a} \xi(P_0, P_1,...)$$
$$\frac{\partial \xi}{\partial \mu_s} = \frac{\partial}{\partial \mu_s} \xi(P_0, P_1,...)$$

of the weights have been shown to provide stochastic estimates of sensitivities that converge to the correct RTE sensitivities. C.K. Hayakawa, “Perturbation Monte Carlo Methods for the Solution of Inverse Problems”, Ph.D. dissertation, Claremont Graduate University, 2002
Illustration: Continuous Absorption Weighting

In homogeneous tissue:

suppose a photon biography $b$ is reflected after traveling distance $D$ in the tissue; with continuous absorption weighting, such a biography tallies $\exp(-\mu_a D)$

Heterogeneous tissue with different scattering $\mu^*_{s}$, say, in some sub-region (e.g., tumor) may be faithfully modeled by using the tally

$$
\xi(b) = \exp(\mu_aD) \left( \frac{\mu^*_{s}}{\mu_s} \right)^j \exp[-(\mu^*_{s} - \mu_s)S]
$$

$j =$ number of collisions in the tumor

$S =$ total path length in the tumor

Differentiation of $\xi$ provides valid RTE sensitivity estimates
Recall: From the SDA derivations

\[
\frac{dL_1(x)}{dx} + (\mu_t - \mu_s p_0)L_0(x) = Q_0(x) \quad \frac{dL_0(x)}{dx} + 3(\mu_t - \mu_s p_1)L_1(x) = 3Q_1(x)
\]

For fixed \(\mu_a\), all \((\mu_s, g)\) \textit{pairs} with identical \(\mu_s'\) values give rise to \textit{identical} SDA solutions.

This principle can be generalized by carrying out the Legendre expansions to any number \(N\) of terms and truncating. Starting with the RTE

\[
\Omega \cdot \nabla L(r, \Omega) + \mu_t(r)L(r, \Omega) = \mu_s(r) \int_{4\pi} L(r, \Omega') p(r, \Omega' \rightarrow \Omega) d\Omega' + Q(r, \Omega)
\]
Sensitivity & Inverse Problems

Introduce a time-like parameter, $s$, that measures the distance traveled along the ray between $r'$ and $r$

\[
\frac{\partial}{\partial s} L(r, \Omega, s) + \omega \cdot \nabla L(r, \Omega, s) + \mu_s L(r, \Omega, s)
\]

\[
= \mu_s \int L(r, \Omega', s) \rho(r, \Omega' \rightarrow \Omega) d\Omega'
\]

Specialize to an infinite homogeneous slab geometry:

\[
(n+1) dL_{n+1}(x)/dx + n \ L_{n-1}(x) + (2n+1)(\mu_t - \mu_s \rho_n) \ L_n(x)
\]

\[
= (2n+1) \ q_n(x) \text{ for } n = 0, 1, \ldots \text{ with } L_{-1}(x) = 0.
\]
Note the occurrence of the combinations $\mu_t - \mu_s p_n$
Define **optical invariants**: $I_n = \mu_t - \mu_s p_n$

It has been shown that the $(n,m)$th order space-angle moment, $L_{m,n}$ of the solution $L(s)$

$$L_{m,n}(s) = \int_{-\infty}^{\infty} \int_{-1}^{1} x^n \mu^m L(x, \mu, s) d\mu dx$$

depends only on $s$ and the optical invariants

$$I_n = \mu_t - \mu_s p_n$$

RTE Similarity Theory

Restating this result, it means that if the original RTE is replaced by one with different optical properties $\mu^*_t, \mu^*_s$ and a different phase function $p^*$ so that

$$I_n = \mu_t - \mu_s g_n = I_n^* = \mu_t^* - \mu_s^* g_n^*$$

the corresponding solutions $L(r, \Omega, s), L^*(r, \Omega, s)$ must be \textit{identical}

►► One can control approximation accuracy through the number of optical invariants preserved
Additional Comments

1. As \( N \to \infty \), the RTE solution is recovered (uniqueness)
2. For \( N \) finite, inverse problem will be ill-conditioned
3. For \( N > 1 \) closed form solutions are much harder to obtain (e.g., need \( N \) boundary conditions)
4. Both deterministic and stochastic \( P_N \) methods provide useful higher order solvers
Summary and Take Home Messages

1. Presence of boundaries complicates RTE formulations
2. Care is needed in designing optical measurements
3. Sensitivities provides key information
4. Ill-conditioned inverse problems should be anticipated
GUI Interaction C – Spatially- and Temporally-Resolved Diffuse Reflectance

The next GUI exercise asks you to examine differences in spatially - resolved and time - resolved reflectance plots for different source configurations and ratios of scattering to absorption.

This exercise is designed to stimulate thinking about how changes in optical properties influence reflectance for both SDA and RTE solvers.