### The Corrected Diffusion Approximation

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# What I do I model light propagation in biological tissues for the purpose of locating early stage cancer cells.



What I do
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Why is it important?
Cancer!
Early detection



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What I do I model light propagation in biological tissues for the purpose of locating early stage cancer cells. Why is it important? Cancer! Early detection How it's done The Corrected Diffusion Approximation Something Awesome (Redacted)



What I do I model light propagation in biological tissues for the purpose of locating early stage cancer cells. Why is it important? Cancer! Early detection How it's done The Corrected Diffusion Approximation Something Awesome (Redacted) Results



### **Tissue Structure**



- a. Epithelial Layer
- b. Stromal Layer
- c. Smooth Muscle Layer



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# Setup

**Goal:** Model diffuse reflectance measurements of backscattered light by a turbid medium close to the source.



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- Use a thin continuous beam incident normally on the medium
- Represent medium by a semi-infinite half space
- Given constant scattering and absorption coefficients



#### Microscopic

# Maxwell's equations provide a rigorous model for EM wave propagation



# Light Propagation In Tissue

# Microscopic Maxwell's equations provide a rigorous model for EM wave propagation

#### Mesoscopic

The Radiative Transport equation provides a model for light propagation as transport of particles



## **Radiative Transport Equation**

# The Radiative Transport Equation is given by:

 $\hat{\mathbf{s}} \cdot \nabla I + \mu_a I + \mu_s \mathscr{L} I = 0$ 



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$$\mathscr{L}I = I - \int_{\mathbb{S}^2} p(\hat{\mathbf{s}} \cdot \hat{\mathbf{s}}') I(\hat{\mathbf{s}}', \mathbf{r}) d\hat{\mathbf{s}}'$$



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p defines the fraction of power scattered in direction  $\hat{\mathbf{s}}$  incident from direction  $\hat{\mathbf{s}}'.$ 

$$\int_{\mathbb{S}^2} p(\hat{\mathbf{s}} \cdot \hat{\mathbf{s}}') d\hat{\mathbf{s}}' = 1$$





# **Boundary Condition**

#### For a normally incident, Gaussian beam we consider

 $I(\mu, \varphi, x, y, 0) - r(\mu)I(-\mu, \varphi, x, y, 0) = \frac{\delta(\mu - 1)}{2\pi}f(x, y), \quad 0 < \mu \le 1$ 

$$f(x,y) = \frac{1}{2\pi w^2} e^{-\frac{x^2 + y^2}{2w^2}}$$



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#### and

 $I \to 0$  as  $z \to \infty$ 

In this,  $r(\mu)$  is the Fresnel reflection coefficient at the boundary.



# Light Propagation In Tissue

# Microscopic Maxwell's equations provide a rigorous model for EM wave propagation

- Mesoscopic
  - The Radiative Transport equation provides a model for light propagation as transport of particles

# Macroscopic The Diffusion Approximation is an approximation to the RTE.



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$$\nabla \cdot (D\nabla \Phi) - \mu_a \Phi = S.$$

in this,  $D = \frac{1}{3(\mu_a + \mu_s(1 - g))}$ , and S is the interior source term.



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in this,  $D = \frac{1}{3(\mu_a + \mu_s(1 - g))}$ , and *S* is the interior source term. **Problem:** This is known to be invalid close to the source.



Bridges the gap between Diffusion and RTE for tissues close to the boundary



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Compute Interior Solution (Diffusion,  $\Phi$ )



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- Compute Interior Solution (Diffusion,  $\Phi$ )
- Compute Boundary Layer Solution (RTE,  $\Psi$ )



Bridges the gap between Diffusion and RTE for tissues close to the boundary

- Compute Interior Solution (Diffusion,  $\Phi$ )
- Compute Boundary Layer Solution (RTE,  $\Psi$ )
- Combine results to satisfy original conditions

 $\overline{I(x, y, z, \hat{\mathbf{s}})} = \Phi(x, y, z) + \Psi(x, y, z, \hat{\mathbf{s}})$ 





# **Derivation of CDA: Rescaling**

Three length scales in our analysis ( $\ell_s \ll w \ll \ell_a$ ) Scattering mean free path,  $\ell_s = \frac{1}{\mu_s}$ Characteristic absorption length,  $\ell_a = \frac{1}{\mu_a}$ Beam width w



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Use our length scales to define small parameters  $\alpha$  and  $\beta$ 





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Use our length scales to define small parameters  $\alpha$  and  $\beta$ 



Rescale (x, y, z) with respect to w which nondimensionalizes the problem Solve the rescaled, nondimensionalized equation using the fact that  $\alpha \ll \beta \ll 1$ 



#### **CDA: Rescaled Problem**

 $\beta \mu \partial_z I + \beta \sqrt{1 - \mu^2} (\cos \varphi \partial_x I + \sin \varphi \partial_y I) + \alpha I + \mathscr{L}I = 0$ 



# **CDA:** Rescaled Problem

$$\beta \mu \partial_z I + \beta \sqrt{1 - \mu^2} (\cos \varphi \partial_x I + \sin \varphi \partial_y I) + \alpha I + \mathscr{L}I = 0$$

Subject to boundary conditions

$$I(\mu,\varphi,x,y,0) = \frac{\delta(\mu-1)}{2\pi} f(x,y) + r(\mu)I(-\mu,\varphi,x,y,0), \quad 0 < \mu \le 1,$$
$$I \to 0 \quad \text{as} \quad z \to \infty.$$



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$$\begin{split} I(\mu,\varphi,x,y,0) &= \frac{\delta(\mu-1)}{2\pi} f(x,y) + r(\mu) I(-\mu,\varphi,x,y,0), \quad 0 < \mu \leq 1, \\ &\quad I \to 0 \quad \text{as} \quad z \to \infty. \end{split}$$

In these,  $r(\mu)$  is the Fresnel reflection coefficient at the boundary.

We represent I as the sum of an interior solution and a boundary layer solution as in a.

$$(I = \Phi + \Psi)$$

<sup>a</sup>S. B. Rohde and A. D. Kim, "Modeling the diffuse reflectance due to a narrow beam incident on a turbid medium," J. Opt. Soc. Am. A, **29**, 231-238 (2012).



# **Interior Solution**

In solving for  $\Phi$ , we find that  $\phi_0$  must satisfy the nondimensionalized diffusion equation

$$\nabla \cdot (\kappa \nabla \phi_0) - \frac{\alpha}{\beta^2} \phi_0 = 0.$$



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in this  $\kappa = \frac{1}{3(1-g)}$ , and we have a solution of the form

 $\Phi = \phi_0(\mathbf{r}) - \beta \hat{\mathbf{s}} \cdot [3\kappa \nabla \phi_0(\mathbf{r})] + O(\beta^2),$ 



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$$\Phi = \phi_0(\mathbf{r}) - \beta \hat{\mathbf{s}} \cdot [3\kappa \nabla \phi_0(\mathbf{r})] + O(\beta^2),$$

This solution alone cannot satisfy the boundary condition, and we apply a boundary layer solution



# **Boundary Layer Solution**

#### Introduce stretched variable $z = \beta Z$ , such that

 $\psi(\hat{\mathbf{s}}, x, y, Z) = \Psi(\hat{\mathbf{s}}, x, y, \beta Z),$ 



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# **Boundary Layer Solution**

#### Introduce stretched variable $z = \beta Z$ , such that

 $\psi(\hat{\mathbf{s}}, x, y, Z) = \Psi(\hat{\mathbf{s}}, x, y, \beta Z),$ 

substitute into the RTE

 $\mu\psi_Z + \beta\sqrt{1-\mu^2}(\cos\varphi\psi_x + \sin\varphi\psi_y) + \alpha\psi + \mathscr{L}\psi = 0$ 





# **Boundary Condition**

We apply the modified boundary condition for  $\psi = I - \Phi$ 

$$\begin{split} \psi(\mu,\varphi,x,y,0) &- r(\mu)\psi(-\mu,\varphi,x,y,0) = \\ \frac{\delta(\mu-1)}{2\pi}f(x,y) &- [1-r(\mu)]\phi_0(x,y,0) + 3\beta\kappa\mu[1+r(\mu)]\phi_{0,z}(x,y,0), \quad 0 < \mu \le 1 \end{split}$$

Where  $\psi = \psi_0 + \beta \psi_1$ 



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Where  $\psi = \psi_0 + \beta \psi_1$ , and  $\psi_0$  satisfies the 1-D RTE

$$\mu\psi_{0,Z} + \mathscr{L}\psi_0 = 0.$$

 $\psi_1$  satisfies

$$\mu\psi_{1,Z} + \mathscr{L}\psi_1 = -\sqrt{1-\mu^2}(\cos\varphi\psi_{0,x} + \sin\varphi\psi_{0,y})$$



The 1-D RTE in  $\psi$  can be solved as a constant



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We ensure that the constant solution is zero to satisfy  $\psi \to 0$  as  $Z \to \infty$ 



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This returns the boundary condition for the diffusion approximation

$$a_0\phi_0 - b_0\phi_{0,z} = f_0f(x,y), \quad z = 0$$



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$$a_0\phi_0 - b_0\phi_{0,z} = f_0f(x,y), \quad z = 0$$

 $a_0$ ,  $b_0$ , and  $f_0$  are determined numerically using the boundary condition for  $\psi$  and a numerically calculated Green's function for the 1-D RTE



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 $a_0$ ,  $b_0$ , and  $f_0$  are determined numerically using the boundary condition for  $\psi$  and a numerically calculated Green's function for the 1-D RTE We next solve for  $\phi$  and then apply the full boundary condition with the numerically calculated Green's function to determine  $\psi$ 



# Interior Solution: Diffusion Approximation Solution

We can now solve

$$\nabla \cdot (\kappa \nabla \phi) - \alpha \phi = 0,$$

$$a_0\phi - b_0\phi_z = f_0f(xy), \text{ at } z = 0.$$



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Using Fourier Transforms  $(x, y) \rightarrow (\xi, \eta)$ 

$$-\xi^2 \kappa \hat{\phi} - \eta^2 \kappa \hat{\phi} + \kappa \partial_z^2 \hat{\phi} - \alpha \hat{\phi} = 0,$$



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$$-\xi^2 \kappa \hat{\phi} - \eta^2 \kappa \hat{\phi} + \kappa \partial_z^2 \hat{\phi} - \alpha \hat{\phi} = 0,$$

Since  $\phi$  decays exponentially in z we set  $\gamma(\xi, \eta) = -\sqrt{\alpha/\kappa + \xi^2 + \eta^2}$ . Substituting this into the BC we find

$$\hat{\phi} = \frac{f_0 \hat{f}(\xi, \eta)}{a_0 + b_0 \gamma}, \quad z = 0.$$



Solve 1D RTE with Plane Wave Solutions



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# Solve 1D RTE with Plane Wave Solutions

**Build Greens Function numerically** 



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- Solve 1D RTE with Plane Wave Solutions
- **Build Greens Function numerically**
- Integrate with our source terms to solve for  $\Psi$  and  $\Phi$ ,  $I = \Psi + \Phi$



Solve 1D RTE with Plane Wave Solutions <sup>b</sup>

**Build Greens Function numerically** 

Integrate with our source terms to solve for  $\Psi$  and  $\Phi$ ,  $I = \Psi + \Phi$ 

Integrate over the range of angles exiting the medium to determine reflectance at the boundary

$$R(x,y) = -\iint_{NA} I(\mathbf{r},\hat{\mathbf{s}})\hat{\mathbf{s}} \cdot \hat{\mathbf{z}}d\hat{\mathbf{s}}.$$



<sup>&</sup>lt;sup>b</sup>A. D. Kim, "Correcting the diffusion approximation at the boundary," J. Opt. Soc. Am. A **28**, 1007-1015 (2011).

0.5

0L 0

0.5





1.5

Rho

1

2

2.5

3



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1.5

Rho

1

2

2.5

3

0L 0

0.5



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Reflectance Error





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# **Conclusions and Acknowledgements**

We constructed a forward model for accurate reflectance measurements close to the source

We have extended it to include Fresnel reflection, layered tissues, and oblique incidence

These models give us an option for modeling epithelial tissue specifically in an effort to locate early stage cancer cells, as well as an effective and invertible model for calculating optical properties of tissue



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#### To Do:

Inverse problem

Spatial frequency domain problem



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#### Acknowledgements:

- Arnold D. Kim
- BLI team for the use of their Monte Carlo Virtual Tissue Simulator software
- A. D. Kim and S. Rohde acknowledge support from the National Science Foundation
  - (NSF) for the work done on CDA.





Thank you!



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