On the Use of Transport Equations for Dose Calculation and Planning Optimization

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Facts & Figures

- **December 28, 1895:**
  X-rays discovered by Röntgen
- **January 12, 1896:**
  Used for cancer therapy by Grubbé
- **Year 2007:**
  11.3 million cancer cases
  Half of patients receive radiotherapy[a]

[a] WHO data

Clinical Radiotherapy

- **Radiotherapy:**
  Irradiation of tissue with photons (primary particles), electrons (secondary particles)

- **Future radiotherapy:**
  Protons / electrons / heavy ions as primary particles

- **Planning Goal:**
  Destroy cancer cells & minimize damage
  Treatment plan within 24 hours
  Fast simulation (2-3% error, $<$5 minutes)

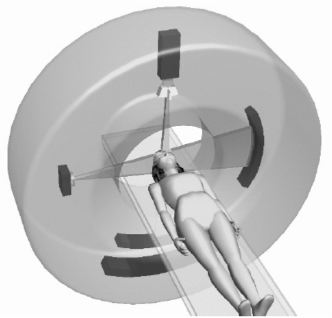
Trends in Radiotherapy

Current practice:

- Select 4-7 beams by hand & evaluate using dose calculation

Trends:

- IMRT: Intensity-modulated radiation therapy
- IGRT: Image-guided radiation therapy
- 4DRT: 4-dimensional radiation therapy



Why Transport Equations?

- **Pencil-Beam/Convolution-Superposition:**
  Green's function, semi-empirical
  Fast method, but limited accuracy
  Errors of up to 12% near inhomogeneties[1]
- **Monte-Carlo:**
  Models particle interactions directly
  Slow method, used as benchmark
- **Deterministic Transport Equations?**
  Exact modeling of particle interactions
  Computational effort comparable to Monte-Carlo[2]
  Starting point for simplified models, use structure for optimization

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[1] Krieger, Sauer, Phys. Med. Biol. 2005
[2] Börgers, Phys. Med. Biol. 1998

Literature Review

- **Computational methods:**
  Gifford et al., *Comparison of a finite-element multigroup discrete-ordinates code with Monte-Carlo for radiotherapy calculations*, Phys. Med. Biol. 51 (2006) 675.

- **Treatment planning based on transport equations:**
  Tervo et al., *Optimal control model for radiation therapy inverse planning applying the Boltzmann transport equation*, Lin. Alg. Appl. 428 (2008) 1230.

ELECTRON TRANSPORT IN TISSUE

Modeling of Particle Transport

Newton's laws of motion: $m_i\ddot{x}_i(t) = F_i(t, x(t), \dot{x}(t))$

$\downarrow$ Large number of particles $\downarrow$

Kinetic equations: $\partial_t f(t,x,v) + v\nabla f(t,x,v) = S(f)(t,x,v)$

$\downarrow$ Many collisions $\downarrow$

Macroscopic equations: $\partial_t E(t,x) + \nabla \frac{1}{3\kappa}\nabla E(t,x) = Q(E)(t,x)$

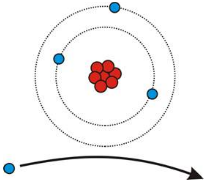
Particle Transport

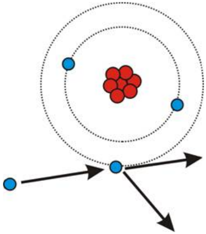
- **Model equation**

$$\Omega \cdot \nabla_x \psi(x, \epsilon, \Omega) = \int_{\epsilon}^{\infty} \int_{S^2} \sigma_s(x, \epsilon, \epsilon', \Omega \cdot \Omega') \psi(x, \epsilon', \Omega') d\Omega' d\epsilon' - \sigma_s^{(0)}(x, \epsilon) \psi(x, \epsilon, \Omega) + q(x, \epsilon, \Omega)$$

ψ is number of particles at $x \in \mathbb{R}^3$ with energy ϵ, direction $\Omega \in S^2$

Prescribe $\psi(x, \epsilon, \Omega) = \psi_b(x, \epsilon, \Omega)$ for $n(x) \cdot \Omega < 0$





Mott and Møller Scattering for Water

- **Mott elastic scattering:**

$$\sigma(x,\epsilon,\epsilon',\mu) = \frac{\rho_c(x) Z^2(x) r_e^2 (1+\epsilon)^2}{4[\epsilon(\epsilon+2)]^2 (1+2\eta(x,\epsilon)-\mu)^2} \left[1 - \frac{\epsilon(\epsilon+2)}{2(1+\epsilon)^2}(1-\mu)^2\right] \delta(\epsilon,\epsilon')$$

  with screening parameter η

- **Møller inelastic scattering:**

$$\sigma(x,\epsilon,\epsilon',\mu) = \rho_e(x)\tilde{\sigma}(\epsilon',\epsilon)\frac{1}{2\pi}\delta(\mu,\mu')$$

$$\tilde{\sigma}(\epsilon',\epsilon) = \frac{2\pi r_e^2(\epsilon'+1)^2}{\epsilon'(\epsilon'+2)}\left[\frac{1}{\epsilon^2} + \frac{1}{(\epsilon'-\epsilon)^2} + \frac{1}{(\epsilon'+1)^2} - \frac{2\epsilon'+1}{(\epsilon'+1)^2\epsilon(\epsilon'-\epsilon)}\right]$$

  with $\epsilon' < \epsilon - \epsilon_B$

- Contain model parameters ρ_c, Z, ρ_e, ϵ_B

Continuous Slowing-Down

- Small energy loss & small deflection likely
- Asymptotic analysis for small energy loss
- Boltzmann continuous slowing-down (BCSD) approximation

$$\Omega \cdot \nabla_x \psi(x,\epsilon,\Omega) = \int_{S^2} \bar{\sigma}_s(x,\epsilon,\Omega\cdot\Omega')\psi(x,\epsilon,\Omega')d\Omega' - \sigma_s^{(0)}(x,\epsilon)\psi(x,\epsilon,\Omega) + \frac{\partial}{\partial\epsilon}(S(x,\epsilon)\psi(x,\epsilon,\Omega)) + q(x,\epsilon,\Omega)$$

  with stopping power S

- Dose

$$D(x) = \int_0^\infty \int_{S^2} S(x,\epsilon)\psi(x,\epsilon,\Omega)d\Omega d\epsilon$$

BCSD Initial Boundary Value Problem

- BCSD equation

$$-\frac{\partial}{\partial \epsilon}(S\psi) + \Omega \cdot \nabla_x \psi = \int_{S^2} \bar{\sigma}_s \psi d\Omega' - \sigma_s^{(0)} \psi + q$$

- Energy is mathematical time variable
- Solve by sweeping backward in energy with "initial value"

$$\psi(x, \infty, \Omega) = 0$$

- Prescribe ingoing radiation at spatial boundary

$$\psi(x, \epsilon, \Omega) = \psi_b(x, \epsilon, \Omega) \text{ on } \Gamma^- = \{(x, \epsilon, \Omega) : \ n(x) \cdot \Omega < 0\}$$

The Need For Approximate Models

Problem:

- Phase space density $\psi(x, \epsilon, \Omega)$ depends on 6 variables
- Direct discretization leads to very large system of equations

Idea:

- Try to derive fluid-dynamic-like macroscopic models
- Analogy: Navier-Stokes can be derived from Boltzmann
- Investigate hierarchies of approximations

MOMENT MODELS

Moments

- **Spherical harmonics:**
  Y_l tensor of spherical harmonics of order l

- **Moments:**

$$\psi_l(x,\epsilon) = \int_{S^2} \psi(x,\epsilon,\Omega) Y_l^*(\Omega) d\Omega$$

- **Moment equations:**
  Multiply BCSD equation with Y_l and integrate over S^2

Moment System

Moment system:

$$-\frac{\partial}{\partial \epsilon}(S\psi_l) + \nabla_x(B_{l,l-1}\psi_{l-1} + B_{l,l+1}\psi_{l+1}) = (\sigma_s^{(l)} - \sigma_s^{(0)})\psi_l + q_l$$

Closure problem:

- Model ψ_{N+1}
- P_N closure: $\psi_{N+1} = 0$
- Diffusion correction to P_N (Levermore)

$$\psi_{N+1} = -\frac{1}{\sigma_t}\frac{N+1}{2N+3}\partial_x\psi_N$$

- Other closures: simplified P_N, flux-limited diffusion, closure by optimal prediction

Minimum Entropy Closure

Idea:

- Describe system by limited information (finitely many moments)
- Most probable state minimizes/maximizes entropy[3]
- Rational Extended Thermodynamics[4]

Entropy :

- Maxwell-Boltzmann

$$H_R(\psi) = \int_{S^2} \psi \log \psi d\Omega$$

- Photons

$$H_R(\psi) = \int_0^\infty \int_{S^2} \frac{2k\nu^3}{c^2} (\tilde{\psi} \log \tilde{\psi} - (\tilde{\psi} + 1) \log(\tilde{\psi} + 1)) d\Omega d\nu$$

[3] Jaynes, Phys. Rev. 1957, Minerbo 1978

[4] Müller, Ruggeri 1998

Minimum Entropy Closure II

Entropy Minimization Principle:

- Determine ψ_{ME} as

$$\psi_{ME} = \text{argmin}_{\psi} H_R(\psi)$$

under the constraints

$$\int_{S^2} Y_l^* \psi_{ME} d\Omega = \psi_l \quad \text{for } l = 0, \ldots, N$$

Closure:

- Set

$$\psi_{N+1} = \int_{S^2} Y_{N+1}^* \psi_{ME} d\Omega$$

Mathematical Questions

Moment admissibility:

- Given sequence of ψ_l
- Existence of any ψ such that

$$\int_{S^2} Y_l^* \psi d\Omega = \psi_l$$

- Determinant criterion (a posteriori)

Existence & uniqueness of minimizer

- Existence & uniqueness of minimizer guaranteed for radiative transfer
- Issues for Boltzmann's equation[5]

[5] Hauck, Levermore, Tits, SIAM J. Control Optim. 2008

Computation of the Minimizer

- Unconstrained Problem

$$L(\psi, \alpha) = H_R(\psi) - \sum_{l=0}^{N} \alpha_l \left(\int_{S^2} Y_l^* \psi d\Omega - \psi_l \right)$$

- Minimizer (Maxwell-Boltzmann)

$$\psi_{ME} = \exp\left(\sum_{l=0}^{N} \alpha_l Y_l \right)$$

- Lagrange multipliers α_l determined by constraints

M_1 Minimum Entropy Closure

- Closure explicitly solvable for photons and $N = 1$
- M_1 minimum entropy[6]

$$-\frac{\partial}{\partial \epsilon}(S\psi_0) + \nabla_x \psi_1 = q_0$$
$$-\frac{\partial}{\partial \epsilon}(S\psi_1) + \nabla_x \left(\frac{1}{3}\psi_0 + \frac{2}{3}\psi_2\right) = (\sigma_s^{(1)} - \sigma_s^{(0)})\psi_1$$

- Eddington factor

$$\frac{1}{3}\psi_0 + \frac{2}{3}\psi_2 = \left(\frac{3\chi(\|N_1\|) - 1}{2} id - \frac{\chi(\|N_1\|)}{2} N_1 \otimes N_1\right)\psi_0,$$

where $N_1 = \psi_1/\psi_0$

[6] Minerbo, JQSRT 1978

Properties of the Minimum Entropy Closure

For standard radiative transfer:

- System dissipates entropy[7]

$$\partial_t H_R(\psi) \leq 0$$

- Symmetrizable (Lagrange multipliers as unknowns)
- Correct diffusion and free-streaming limit[8]
- Positivity of reconstructed distribution function
- Expect positivity of radiative energy & flux limitation

[7] Levermore, J. Stat. Phys. 1996

[8] Coulombel, Golse, Goudon, Asymptot. Anal. 2005

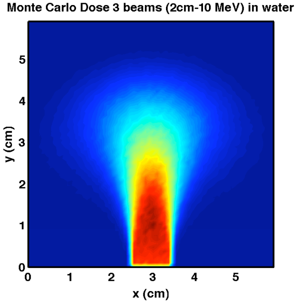
SIMULATION RESULTS

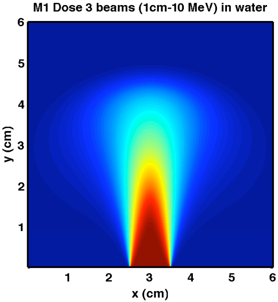
Comparisons

- Comparisons with PENELOPE 2008 Monte Carlo code package
- Monoenergetic electron beams approximated by narrow Gaussians in both energy and angle
- Stopping power S and transport coefficient $\sigma_s^{(1)} - \sigma_s^{(0)}$ from ICRU database
- Dose normalized to dose maximum

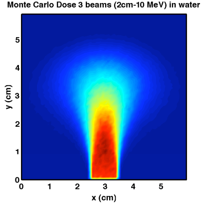
- Computation times (laptop)
  - Penelope with 15 million particles: 2.5 hours
  - M1 in 2D on 200×200×450 grid: 40 seconds

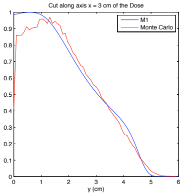
10 MeV Electrons on Water

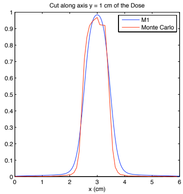


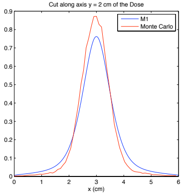


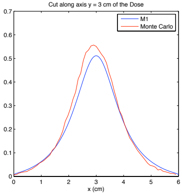
10 MeV Electrons on Water II

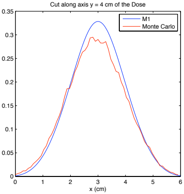




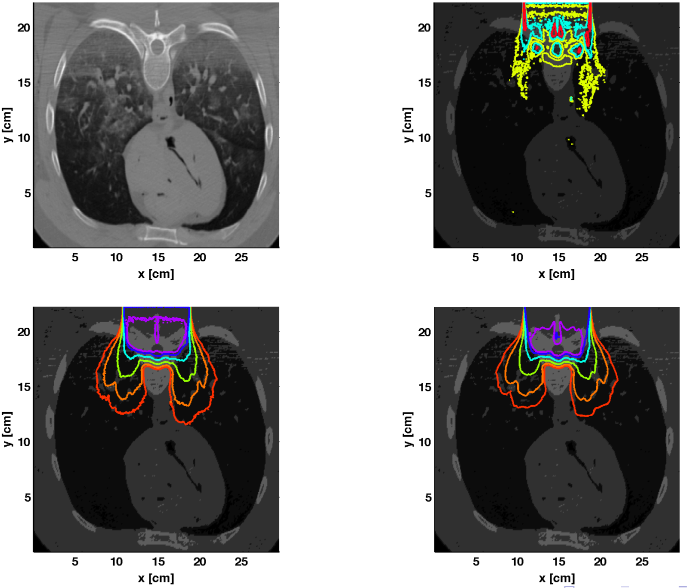








15 MeV Electrons on Vertebral Column



OPTIMAL TREATMENT PLANNING

Planning Goal

- **Planning goal:**
  Destroy cancer cells
  Minimize dose in healthy tissue
  Spare regions at risk
- **Many biological models for radiation effect**
- **Minimize tracking-type functional:**[9]

$$J(\psi) = \frac{\alpha_T}{2}\int_{Z_T}(D-\bar{D})^2 dx + \frac{\alpha_R}{2}\int_{Z_R}(D-\bar{D})^2 dx + \frac{\alpha_N}{2}\int_{Z_N}(D-\bar{D})^2 dx$$

where $D(x) = \int_0^\infty \int_{S^2} S(x,\epsilon)\psi(x,\epsilon,\Omega)\,d\Omega\,d\epsilon$.

[9] Shepard et al., *Optimizing the delivery of radiation therapy to cancer patients*, SIAM Rev. 41 (1999) 721.

Constrained Optimization Problem

- **Find boundary value $\psi_b \geq 0$ that minimizes:**

$$J(\psi,\psi_b) = \frac{\alpha_T}{2}\int_{Z_T}(D-\bar{D})^2dx + \frac{\alpha_R}{2}\int_{Z_R}(D-\bar{D})^2dx + \frac{\alpha_N}{2}\int_{Z_N}(D-\bar{D})^2dx + \frac{\alpha_C}{2}\int_{\Gamma^-}(n\cdot\Omega)(\psi_b-\bar{\psi}_b)^2dxd\Omega$$

- **Constrained by integro-diffferential equation:**

$$-\frac{\partial}{\partial\epsilon}(S\psi) + \Omega\cdot\nabla_x\psi = \int_{S^2}\bar{\sigma}_s\psi d\Omega' - \sigma_s^{(0)}\psi$$

with boundary condition $\psi = \psi_b$ on Γ^- and $\psi(x,\infty,\Omega) = 0$

Adjoint Calculus

- **Lagrangian:** $L(\psi_b, \psi, \lambda) = J(\psi_b, \psi) - \langle \lambda, E(\psi, \psi_b) \rangle$ where

$$
\begin{aligned}
&\langle \lambda, E(\psi, \psi_b) \rangle \\
&= \int_Z \int_0^\infty \int_{S^2} \lambda \left(-\partial_\epsilon (S\psi) + \Omega \cdot \nabla_x \psi - \int_{S^2} \bar{\sigma}_s \psi d\Omega' + \sigma_s^{(0)} \psi \right) d\Omega d\epsilon dx \\
&= \int_Z \int_0^\infty \int_{S^2} \psi \left(S\partial_\epsilon \lambda - \Omega \cdot \nabla_x \lambda - \int_{S^2} \bar{\sigma}_s \lambda d\Omega' + \sigma_s^{(0)} \lambda \right) d\Omega d\epsilon dx \\
&\quad - \int_Z \int_{S^2} S\lambda\psi|_{\epsilon=0}^{\infty} d\Omega dx + \int_{\partial Z} \int_0^\infty \int_{S^2} (n \cdot \Omega) \lambda \psi d\Omega d\epsilon dx
\end{aligned}
$$

- Take functional derivatives with respect to ψ_b, ψ, λ to obtain optimality conditions

First-order optimality conditions:

- **Forward equation**

$$-\partial_\epsilon(S\psi) + \Omega \cdot \nabla_x \psi - \int_{S^2} \bar{\sigma}_s \psi d\Omega' + \sigma_s^{(0)} \psi = 0$$

with $\psi = \psi_b$ on Γ^- and $\psi(x, \infty, \Omega) = 0$

- **Adjoint equation**

$$S\partial_\epsilon \lambda - \Omega \cdot \nabla_x \lambda - \int_{S^2} \bar{\sigma}_s \lambda d\Omega' + \sigma_s^{(0)} \lambda = \alpha(D - \bar{D})$$

with $\lambda = 0$ on Γ^+ and $\lambda(x, 0, \Omega) = 0$

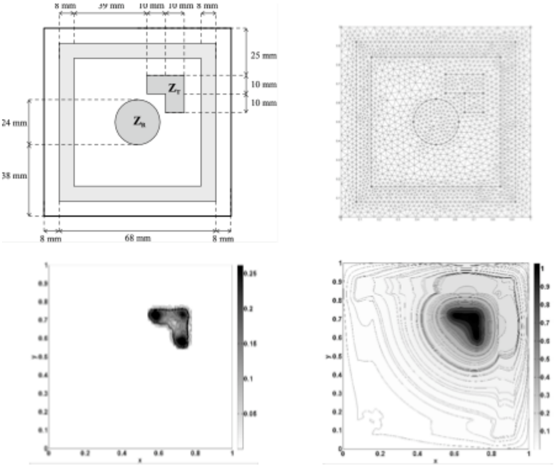
- **Update for control**

$$\alpha_C(\psi_b - \bar{\psi}_b) - \lambda = 0$$

Optimization Method

- Use update for control as gradient information in optimization algorithm
- **Advantage of adjoints:**
  Obtain gradient independent of the discretization
- **Adjoints vs black-box optimization in 1D example:**
  Distributed control in 100 points
  `fmincon`: 17 iterations, 1818 function evaluations
  `fmincon` with adjoint: 30 iterations, 647 function evaluations

Example (Pn Discretization in 2D)



Conclusions & Future Work

- Deterministic approach suitable for dose calculation
- Investigate different approximations to radiative transfer from a general point of view and select best for radiotherapy
- Consider optimization problems constrained by integro-differential equation
- Many open questions in treatment planning, where computational scientists can contribute