Solving a non-linear partial differential equation for the simulation of tumour oxygenation

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Outline

1. Introduction
2. Theoretical Modelling
   • Mathematical Modelling
   • Tissue Generation
   • Discretisation
   • Numerics
3. Software Presentation
4. Results
   • Validation
   • Acute and Chronic Hypoxia
   • Memory Requirements
   • Application Example
5. Conclusion
Introduction
Tumour Oxygenation

**tumour micro-structure**
- non-regular vascular structure
- poor blood supply

**hypoxia**
- chronic hypoxia (diffusion limited)
- acute hypoxia (perfusion limited)

**importance for radiotherapy**
- radiosensitivity depends on oxygenation
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**Challenges**

**measurement methods**
- poor resolution
- small area
- influence oxygenation

**commercial software**
- not specialised
- high memory consumption
- only small domains

**theoretical modelling**

**design specialised software**
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- design specialised software
The Problem Equation

\[-D\Delta p + q(p) = 0\]

\[q(p) = q_{\text{max}} \frac{p}{p + k}\]

**Variable**
- partial oxygen pressure \( p \), \([p] = \text{mmHg}\)

**Parameters**
- diffusion coefficient \( D = 2 \cdot 10^3 \frac{\mu m^2}{s} \)
- maximum consumption rate \( q_{\text{max}} = 15 \frac{\text{mmHg}}{s} \)
- consumption at half pressure \( k = 2.5 \text{mmHg} \)
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Domain Description

properties

- two-dimensional, rectangular domain
- discoid blood vessels
Distribution Properties

vessel distribution

normal distribution of intervascular distances
characterised by mean $\mu$ and variance $\sigma^2$

Example

1. scattered grid
2. dart throwing
Scattered Grid

place vessels on equidistant grid

for each vessel do
    choose normally distributed distance
    choose uniformly distributed angle
    move vessel according to distance and angle
end for
Dart Throwing

while vessel fits in domain do
  choose normally distributed distance
  choose random coordinates
  place vessel at coordinates
  check distance
end while
Vessel Data Format

- Few vessels
- Easy to manipulate

Data structure

1. X-coordinate
2. Y-coordinate
3. Radius
4. Pressure
Vessel Discretisation

translate continuous into discrete information

- equidistant grid
- vessels serve as Dirichlet boundaries
- determine vessel points
- use efficient data structure

3 different discretisation methods
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Discretisation Methods

method 1
only points inside the vessel

method 2
points inside and adjacent points

method 3
points inside and close to the vessel boundary
Vessel Points Data Format

requirements

- many vessel points
- efficient data format needed
- consecutive data access for calculations

⇒ store information rowwise

data structure

1. leftmost vessel point
2. number of vessel
3. rightmost vessel point
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memory consumption increases linearly with resolution while number of vessel points increases quadratically
Vessel Points Data Format

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Discretisation of Laplacian

\[ -\Delta p_{i,j} \approx -p_{i-1,j} - p_{i,j-1} + 4p_{i,j} - p_{i,j+1} - p_{i+1,j} = -\Delta_h p_{i,j} \]

- second order accuracy
- results in a sparse symmetric positive definite matrix
- typical Laplacian matrix except for vessel boundary points
Non-linear System

\[ f(p) := D \cdot Ap + q(p) - D \cdot b = 0. \]

It is \( q(p) = 0 \) for all vessel points

\[ \implies \text{use Newton's algorithm (quadratic order of convergence)} \]

Application of Newton's algorithm leads to a linear system of equations

\[ f'(p_k) y_{k+1} = f(p_k) \quad \text{with} \quad f'(p) = D \cdot A + q'(p) \]

for each iteration \( k \)
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Linear System

requirements

- exploit matrix structure
- direct evaluation of matrix operations

⇒ use iterative methods like Conjugate Gradient or Conjugate Residual

implementation details

- class function pointers for matrix vector products
- interface for solvers
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Software Presentation

... and now a short example...
Results
Exact Solution of Simplified Problem

assumptions

- no consumption (linear problem)
- only one vessel in the center of quadratic domain
- exact solution as Dirichlet boundary condition

⇒ compare different discretisation methods
Comparison Between Discretisation Methods

- error occurs near vessel boundary
- method 3 gives best results
Comparison Between Discretisation Methods

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Comparison Between Discretisation Methods (2)

- method 3 gives best results
- linear order of convergence
Comparison Between Discretisation Methods (2)

- method 3 gives best results
- linear order of convergence
Modelling Chronic Hypoxia

\[ D = 2000 \text{ mmHg} \]

\[ D = 1000 \text{ mmHg} \]
Modelling Acute Hypoxia

25 % deleted

40 % deleted
Modelling Acute Hypoxia (2)

smaller diameter

smaller partial pressure
Memory Measurements

- discretisation memory increases linearly
- solver memory increases quadratically

⇒ almost no dependency on number of vessels
Large Domain Simulation
Conclusion
achievements

- new software developed
- resolved memory consumption problem
- simulation of real tumours possible

outlook

- extension to third dimension
- parallelisation of code
- implementation of other numerical methods
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Thank you for your attention!