Development of a Numerical Solver for Modeling Magnetic Hyperthermia

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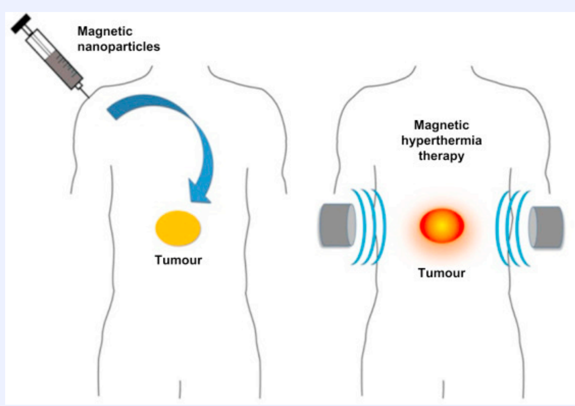
Abstract

Magnetic hyperthermia therapy is a novel cancer treatment that works by heating a tumor to kill the cancerous tissue. It is modeled using a differential equation that simulates how heat flows through the irregular interfaces and varied substances in the human body. In order to facilitate further development of this therapy, researchers require refined numerical approximations to how heat energy dissipates across the surface of a tumor, an irregularly shaped three-dimensional domain. Our team worked to develop a highly accurate numerical method that accounts for these irregularities and variations through corrected Taylor expansions, fictitious values, and an augmented system of equations. Solving this augmented system would require an impractical amount of computational time if we were to use traditional methods. Instead, we use a Fast Fourier Transform so that time consuming matrix operations can be done with simple multiplication. Numerical experiments in two and three dimensions demonstrate the accuracy and efficiency of this method, indicating that this is indeed a refined mathematical tool for studying these challenging biological problems.

Introduction

Magnetic Hyperthermia



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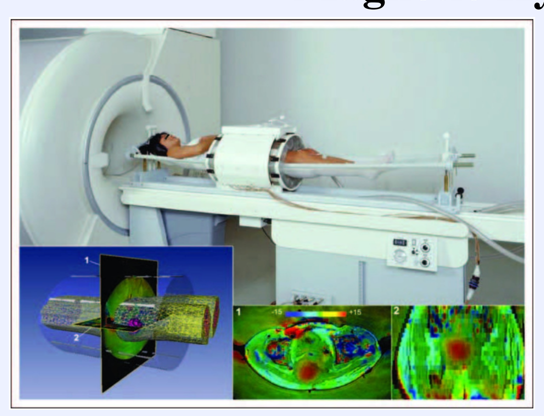

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- Magnetic nanoparticles injected into cancerous tumor
- Alternating magnetic field generates heat by nanoparticles
- Cancer cells die above 43°C
- Heat dissipation through blood flow is slower in cancer cells
- Cancer cells have lower specific heat than healthy tissue

[1]

Model

Initial Boundary Value Problem

Heat Equation

$$\Delta u = c\frac{\partial u}{\partial t} + f \quad \text{where } \alpha u + \beta\frac{\partial u}{\partial n} = \Phi$$

Boundary Value Problem

Poisson's Equation

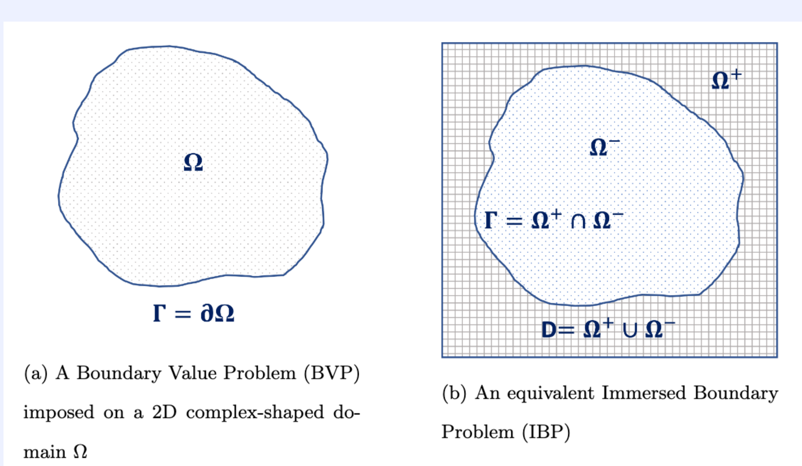
$$\Delta u = f \quad \text{where } \alpha u + \beta\frac{\partial u}{\partial n} = \Phi$$

Note that …

- $\Delta = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}$ in 2D
- $\Delta = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}$ in 3D
- We use general boundary conditions

Numerical Solution

Original Problem vs Immersed Problem



(a) A Boundary Value Problem (BVP) imposed on a 2D complex-shaped domain Ω

(b) An equivalent Immersed Boundary Problem (IBP)

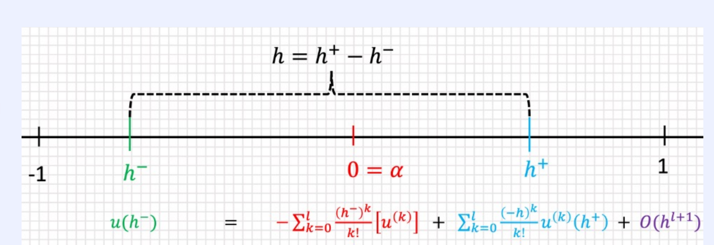
Standard 5-Point Central Difference Method

$$\frac{\partial^2}{\partial x^2}u(x_i) \approx \frac{1}{h_x^2}\left(-\frac{1}{12}u_{i-2} + \frac{4}{3}u_{i-1} - \frac{5}{2}u_i + \frac{4}{3}u_{i+1} - \frac{1}{12}u_{i+2}\right)$$

The Explicit-Jump Immersed Interface Method

$$u(h^-) = \sum_{k=0}^{l}\frac{(-h)^k}{k!}u^{(k)}(h^+) - \sum_{k=0}^{l}\frac{(h^-)^k}{k!}[u^{(k)}] + O(h^{l+1})$$

$$[u^{(k)}] = \lim_{x\to\alpha^+} u^{(k)}(x) - \lim_{x\to\alpha^-} u^{(k)}(x)$$



We will set $l = 3$ so that our method is $O(h^4)$

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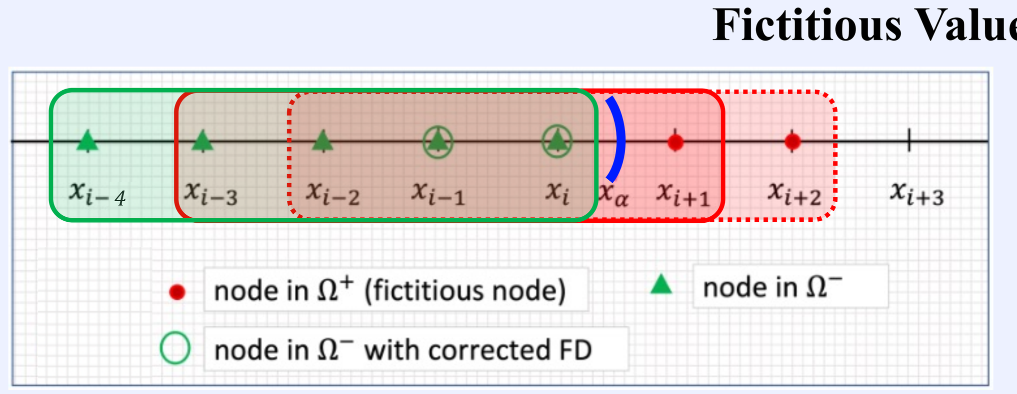
Fictitious Values and Unknown Jump Conditions



Fornberg's method returns weights for interpolation formulas:

$$u_a = w_{i+1}\hat{u}_{i+1} + w_i u_i + w_{i-1}u_{i-1} + w_{i-2}u_{i-2} + w_{i-3}u_{i-3}$$

- $\hat{u}_{i+1}$ and $\hat{u}_{i+2}$ interpolation created using x_α and four interior grid points
- $[u^{(k)}]$ interpolation created using $\hat{u}_{i+1}, \hat{u}_{i+2}$, and three interior grid points
- Final weights found using substitution and algebraic manipulation

[3]

Augmented System Of Equations

$$\begin{pmatrix} A & B \\ C & I \end{pmatrix}\begin{pmatrix} U \\ Q \end{pmatrix} = \begin{pmatrix} F \\ \phi \end{pmatrix}$$

Known

Matrices

A = pentadiagonal matrix from standard 5 − point central difference method
B = coefficients of correction terms
C = coefficients to represent fictitious values
I = identity matrix

Vectors

F = source term evaluated at interior grid points
ϕ = known interface values

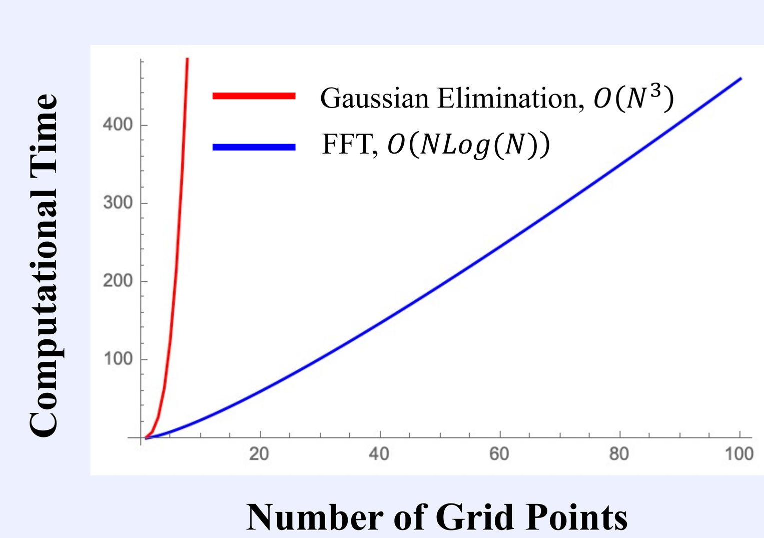
Unknown

Vectors

U = unknown values at interior points
Q = corrections at interfaces

[6]

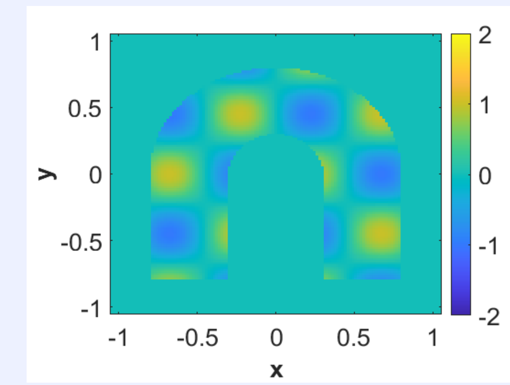
System Solved using Fast Fourier Transform (FFT)



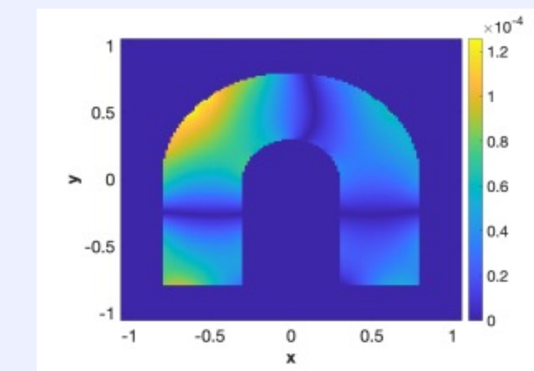
Numerical Experiments

Two Dimensional Experiments

Arch

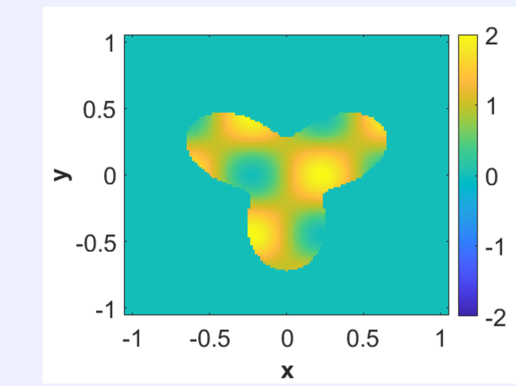


Solution at $t = 6.284$

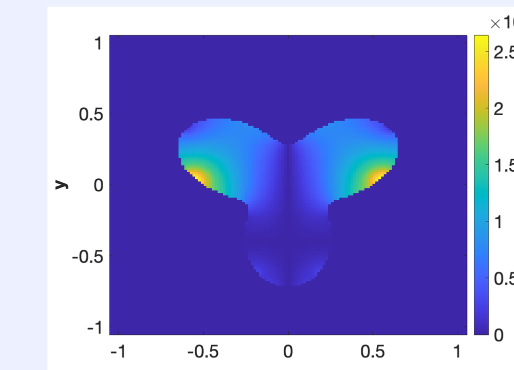


Error at $t = 6.284$

Three Point Star



Solution at $t = 6.284$

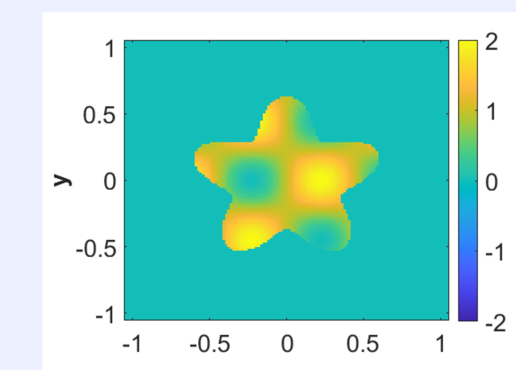


Error at $t = 6.284$

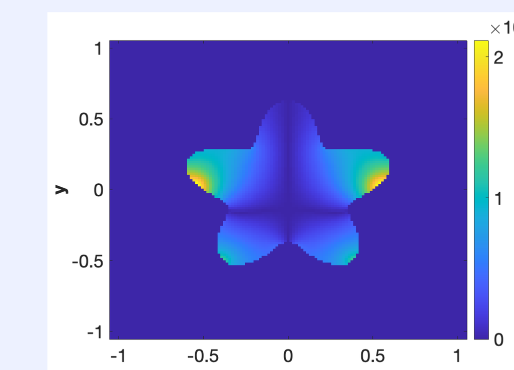
Spatial Convergence

$[N_x, N_y]$	L^∞ error	L^∞ order	L^2 error	L^2 order
[65, 65]	1.61E-03		5.00E-04	
[129, 129]	7.53E-05	4.41	2.81E-05	4.16
[257, 257]	4.24E-06	4.15	1.60E-06	4.14
[513, 513]	3.53E-07	3.59	9.77E-08	4.03
[1025, 1025]	3.14E-08	3.49	6.90E-09	3.82

Five Point Star



Solution at $t = 6.284$

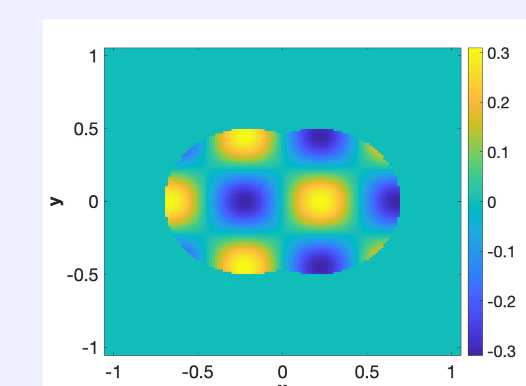


Error at $t = 6.284$

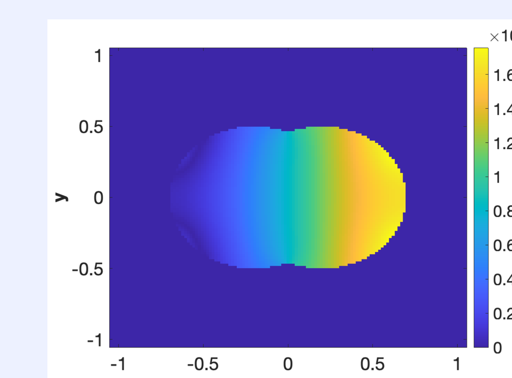
Temporal Convergence

N_t	L^∞ error	L^∞ order	L^2 error	L^2 order
2	4.06E-04		2.00E-04	
4	9.86E-05	2.04	4.85E-05	2.05
8	2.45E-05	2.01	1.20E-05	2.01
16	6.14E-06	2.00	3.00E-06	2.00
32	1.56E-06	1.98	7.47E-07	2.01
64	4.13E-07	1.92	1.84E-07	2.02
128	1.27E-07	1.70	4.69E-08	1.97

Union of Two Circles



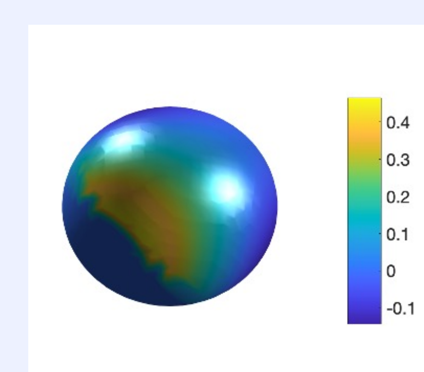
Solution at $t = 6.284$



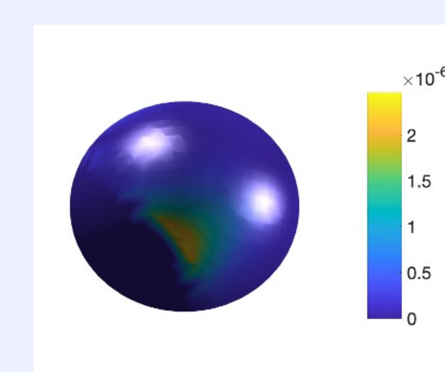
Error at $t = 6.284$

Three Dimensional Experiments

Sphere



Solution at $t = 10^{-2}$



Error at $t = 10^{-2}$

$[N_x, N_y, N_z]$	L^∞ error	L^∞ order	L^2 error	L^2 order	Wall Clock (s)
[33, 33, 33]	1.19E-03		7.61E-05		121
[65, 65, 65]	1.21E-04	3.29	5.20E-06	3.87	1341
[129, 129, 129]	8.12E-06	3.90	3.58E-07	3.86	12058
[257, 257, 257]	4.00E-07	4.34	1.86E-08	4.27	107094

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Conclusion and Summary

In conclusion, we find that this method is indeed as accurate and efficient as predicted. Numerical experiments confirm that this method can handle an irregularly shaped boundary and different boundary conditions while achieving fourth order accuracy in both two and three dimensions. The Fast Fourier Transform allows us to use a fine grid even in three dimensions, something that is not feasible using more traditional methods for solving systems of equations because of the impractically large computation time. These findings indicate that this method could aid greatly in the progress of magnetic hyperthermia by providing cancer researchers with the information they need to refine their treatment methods.

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