Multiphysics Framework for Modeling of FUS/HIFU and Induced Effects

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Outline

• Introduction
• Part I: FUS/HIFU Multiphysics Framework
• Part II: Applications
• Part III: US & Thermal Modeling of tcMRgFUS
• Conclusions & Future Work
• Acknowledgements & Funding
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• Introduction
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• Part II: Applications
• Part III: US & Thermal Modeling of tcMRgFUS
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Introduction: MRgFUS & Applications

• advances in MR guided Focused Ultrasound (MRgFUS) allow use of US waves for therapeutic purposes

• modeling required for:
  - safety and efficacy assessment of ultrasonic devices (for therapeutic/diagnostic purposes)
  - device design and optimization
  - patient-specific treatment planning for acoustic therapies
  - outcome analysis & understanding of underlying mechanisms

• applications of interest to us:
  - evaluation and optimization of novel transducers/applicators for superficial and deep tumor ablation
  - modeling and treatment planning of FUS ablation (tumors and functional neurosurgery)
  - novel applications of FUS
Introduction: tcMRgFUS Neurosurgery

• clinical applications:
  - brain tumor ablation
  - functional neurosurgery:
    movement disorders (Parkinson’s, essential tremor, dystonia…), neuropathic pain treatment, epilepsy, OCD

• pre-clinical applications:
  - reversible BBB disruption (focal drug delivery and activation to counter CNS diseases)
  - thrombolysis
  - neural stimulation

• special issues:
  - large number of transducer elements
  - distortion and focusing
  - skull heating, hot-spots
Part I: FUS/HIFU Multiphysics Framework

- Framework
- Validation
- Conclusions & Future Work
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Framework: Overview

- simulation platform
  - 3D modeling, anatomical models
  - simulation setup (parameters, gridding, voxeling...)
  - scripting, visualization, post-processing

- segmentation platform
  - segmentation of MRI/CT image data

- solvers:
  - acoustic solver
  - μ-Bubble solver
  - thermal solver
  - flow solver
Framework: Image Segmentation

- custom software
- tool box with many, flexibly combinable segmentation methods
  - robust techniques ranging from:
    - highly interactive (e.g., live wire, interactive watershed transform, brush) ↔ highly automatic (e.g., improved k-means-based clustering, competitive fuzzy connectedness, competitive growing)
  - method specific user interactions paradigms
  - novel techniques (e.g., Gamma method based clustering, image based adaptation)
  - routines for noise reduction, hole/gap/island removal, smoothing, skin adding, connected component analysis
- live-wire based method for vascular tree extraction (vessel wall extraction to be improved)
- topologically flexible interpolation
  - not every slice has to be segmented
  - image based adaptation based on fuzzy logic
Framework: Virtual Population

- CAD models, >200 distinguished organs/tissues
- extensive literature-based tissue parameter database (online)
- pregnant women, animal models (dog, mice, rats, pig)
Framework: Posing / Morphing

- volume preserving influence region based deformation fields
- physics-based morphing
Framework: Acoustic Solver: Models

- selected numerical models:
  - linear propagation: linear acoustic pressure wave equation
    \[ \rho \nabla \frac{1}{\rho} \nabla p - \frac{1}{c^2} \frac{\partial^2 p}{\partial t^2} - \frac{\tilde{a}}{c^2} \frac{\partial p}{\partial t} = 0 \]

  - non-linear propagation: Westervelt-Lighthill equation:
    \[ \rho \nabla \frac{1}{\rho} \nabla p - \frac{1}{c_0^2} \frac{\partial^2 p}{\partial t^2} + \frac{\delta}{c_0^4} \frac{\partial^3 p}{\partial t^3} + \frac{\beta}{2 \rho_0 c_0^4} \frac{\partial^2 p^2}{\partial t^2} = 0 \]

  \( p \): pressure, \( c \): equilibrium speed of sound in medium, \( \rho \): equilibrium density of medium
  \( \alpha \): attenuation coefficient of medium, \( \delta \): diffusivity of medium, \( \beta \): nonlinearity parameter
Framework: Acoustic Solver

- acoustic Solvers:
  - 3D FDTD solvers for highly inhomogeneous anatomies (accounting for air-tissue and bone-tissue interfaces)
  - linear & non-linear variants
  - parallelization
    - CPU: OpenMP, up to 9x speed-up on 12 cores
    - GPU: CUDA, up to 36x speed-up on single GPU
  - Perfectly Matched Layer (PML) absorbing boundary conditions (allowing for domain truncation along inhomogeneous interfaces)
Framework: μ-Bubble Solver

- effect of μ-bubble sonication on BBB disruption (LTNT, ETH Zurich):
  - encapsulated μ-bubble in capillary
  - sonication by incident FUS field
  - cavitation
- implementation:
  - FVM simulation using FSI
  - bubble motion with modified Rayleigh-Plesset ODE accounting for confinement in vessel and viscoelastic lipid shell
- lumped parameter model:
  - UCA concentration -> modified effective tissue properties -> modified macroscopic pressure -> (shear) stresses on vessel wall
Framework: Thermal Solver I

- Pennes Bioheat Equation, widely used in thermal modeling:

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) + \rho Q_{\text{acoust.}} + \rho Q + \rho_b c_b \rho \omega (T_b - T) \quad \text{where} \quad Q_{\text{acoust.}} = \alpha \frac{p_{\text{ampl.}}^2}{c \cdot \rho}$$

- common caveats of most implementations
  - not accounting for directivity of blood flow
  - not accounting for the discreteness of vessels
  - assumption of local equilibrium between blood and environmental T (only true for small capillaries / arterial bleed-off)
  - not considering temperature dependence of tissue parameters

- sophisticated thermal solver modeling the complex thermal phenomena required to accurately simulation ablation
Framework: Thermal Solver II

- high performance explicit & implicit FD solvers
  - conformal schemes to reduce staircasing effects
  - thin structure models (accuracy & speed)

- temperature dependent tissue parameters
  - thermoregulation, vascular shut-down

- perfusion modeling
  - DIVA (Lagendijk), effective tensorial thermal conductivity, convection based on CFD simulation for major vessels
    - coupling of the 3D simulation to a pseudo-1D simulation of the vessel network
    - blood flow directivity (improved accuracy and over 100x acceleration)
  - support for MR perfusion maps

- thermal dose (CEM43) and tissue damage (Arrhenius) modeling
Framework: Flow Solver

- acoustic streaming
- microbubble concentration
- flow solver:
  - incompressible Navier-Stokes equation
  - coupled with the acoustics solver through Reynold stresses term
  - GMRES with a Schur complement preconditioning method
  - parallelized through MPI & PETSc
Part I: FUS/HIFU Multiphysics Framework

- Framework
- Validation
- Conclusions & Future Work
Validation: Approaches

- approaches
  - analytical validation (complete): comparison against analytically calculated fields
  - validation against software (complete): comparison against FOCUS simulations with the Gamma Dose Distribution (GDD) method
  - experimental (ongoing): 3D pressure field measurements of focused US transducer distorted by predefined obstacles
Validation: Measurement Setup

• components
  - plexiglass water-tank lined with acoustic absorbers
  - removable & adjustable sample holder with mounted transducer (550kHz, 80mm diameter)
  - acoustically characterized samples of different shapes and materials (delrin, polyurethane, RTV silicone) suspended with plexiglass rods in the beam path

• measurements
  - DASY52 NEO robot arm with a needle-type hydrophone and preamplifier
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- **measurements**
  - DASY52 NEO robot arm with a needle-type hydrophone and preamplifier
Validation: Results I

- empty water-tank (no sample) comparison
  - modified Gamma distribution comparison method
  - excellent agreement within given tolerances
  - dose criterion: 5% tolerance
  - distance criterion: $\lambda/2$
Validation: Results II

- **sample comparisons**
  - complex interference pattern
  - ongoing effort: need for registration/alignment, large positioning uncertainties
  - good visual agreement: reproduction of major field features, scale agreement

- **polyurethane cylinder**
  - speed of sound: 1700m/s
  - attenuation: 6dB/cm/MHz
  - density: 1130Kg/m³
Validation: Results III

- sample comparisons
  - complex interference pattern
  - ongoing effort: need for registration/alignment, large positioning uncertainties
  - good visual agreement: reproduction of major field features, scale agreement

- delrin cylinder
  - speed of sound: 2430m/s
  - attenuation: 3dB/cm/MHz
  - density: 1430Kg/m³
Part I: FUS/HIFU Multiphysics Framework

- Framework
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Conclusions & Future Work

• next steps
  - coupling: flow solver, microbubble solver
  - validation: complete experimental validation

• conclusions
  - a comprehensive framework that allows for full wave propagation in complex anatomical models has been developed and validated
Part II: Applications

- Experimental BBB Disruption
- Neuropathic Pain Treatment
- Neck Tumor Ablation
- Renal & Hepatic Tumor Ablation
Experimental BBB Disruption

• experiment:
  - in-vivo experiments on live mice
  - combined use of FUS & UCA approach
  - assess efficacy of increasing the BBB permeability

• anatomical simulations:
  - simulation of animal stage with FUS sonication of the brain through the skull
Neuropathic Pain Treatment

- MRgFUS in tissue ablation:
  - non-invasive and precise tissue ablation
  - minimizes the risk of bleeding and infection,
  - avoids damage to non-targeted tissue
  - does not involve ionizing radiation

- neuropathic pain treatment:
  - micro-thalamotomy on live patients to treat chronic neuropathic pain with phased-array ultrasonic transducers
  - simulations will allow for patient-specific treatment planning and parameter exploration
Neck Tumor Ablation

• usage of the SonoKnife applicator to **ablate superficial tumors** in the head and neck region (tumor volume needs to be covered by scanning)

• simulations:
  - ablation of locally-advanced head and neck squamous cell carcinomas (HNSCC)
  - anatomically detailed model segmented from MRI data (Virtual Family)
  - model tailored to take into account tissue-air and tissue-bone interfaces
Renal & Hepatic Tumor Ablation I

- renal & hepatic tumor ablation (Salomir R, Petrusca L):
  - usage of MRgFUS to create lesions in the renal cortex and the liver is experimentally investigated on ex-vivo ovine kidneys and live sheep

- simulations:
  - segmented model of an ex-vivo kidney surrounded by fat and muscle tissue
  - segmented model of a live sheep including the ribcage and all major organs in the vicinity of the liver
  - understand unexpected focus shape
Renal & Hepatic Tumor Ablation II
Conclusions

- developed framework can be applied to investigate large range of relevant applications
  - tumor ablation
  - functional neurosurgery
  - reversible BBB opening
  - applicator development
Part III: US & Thermal Modeling of tcMRgFUS

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- US & Thermal Simulations
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Introduction: Simulations

• why simulations?
  - treatment planning (prediction & optimization of focus size, position & intensity)
  - risk assessment & reduction (standing waves, secondary foci → hemorrhages)
  - steering range increase (safely focus in currently unreachable areas)
  - prediction/prevention of skull heating
  - parameter sensitivity studies
  - technical optimization: applicator development

• requirements:
  - patient specific
  - fast & high-resolution
  - full-wave modeling (especially for applicators without principal propagation direction, e.g. ExAblate) in inhomogeneous anatomies
  - temperature and effect prediction (e.g. lesion size)
Part III: US & Thermal Modeling of tcMRgFUS

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Simulations: US Setup

- **applicator**: ExAblate4000
  - 1024 transducer elements
    - (area: $\sim1\text{cm}^2$)
  - 230kHz
  - focal depth: 150mm

- **head model**: Duke (Virtual Population)
  - segmented from hi-res MR data of 34yr male volunteer
  - 45 tissues distinguished in the head

- **simulation setup**:
  - target in the thalamus: $(0.0\text{mm}, -5.7\text{mm}, 22.8\text{mm})$ off geometric focus
Simulations: US Simulations

• inverse propagation simulation

• element phasors:
  - distance-based / simulation-based
  - normalized to 1kW total acoustic power

• forward propagation simulation:
  - distance-based phases, fixed (120kPa) amplitudes
  - simulation-based phases, fixed (120kPa) amplitudes
  - simulation-based phases, simulation-based (norm. to 120kPa) amplitudes:
    ‣ linear
    ‣ non-linear: base & 1st harmonic
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Simulations: Thermal Simulations

- heat source:
  \[ Q = \frac{a p^2}{\rho c} \]

- settings (all steering approaches):
  - 30’ without sonication to reach thermal equilibrium + 20” of sonication
  - convective boundary conditions for water (16°C) and air (25°C) cooling
  - impact of vascular shutdown on temperature increase
Part III: US & Thermal Modeling of tcMRgFUS

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Results: Temperatures & Lesion Sizes

<table>
<thead>
<tr>
<th>Focus Size [mm]</th>
<th>Temperature</th>
<th>FWHM</th>
<th>45°C</th>
<th>50°C</th>
<th>55°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance-Based Phases, Fixed (120kPa) Amplitudes</td>
<td>Max</td>
<td>dX</td>
<td>dY</td>
<td>dZ</td>
<td>dX</td>
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<td></td>
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<td>3.8</td>
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<td>Simulation-Based Phases, Fixed (120kPa) Amplitudes</td>
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<tr>
<td></td>
<td>55.9</td>
<td>4</td>
<td>4.1</td>
<td>4.6</td>
<td>4.7</td>
</tr>
<tr>
<td>Simulation-Based Phases, Simulation-Based (Normalized to 120kPa) Amplitudes</td>
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<tr>
<td></td>
<td>58.88</td>
<td>4</td>
<td>4.1</td>
<td>4.5</td>
<td>5.2</td>
</tr>
</tbody>
</table>
Results: Temperature Iso-Surfaces: 45°C

Distance-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Simulation-Based (Normalized to 120kPa)
Results: Temperature Iso-Surfaces: 50°C

Distance-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Simulation-Based (Normalized to 120kPa)
Results: Temperature Iso-Surfaces: 55°C

Distance-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Fixed (120kPa) Amplitudes

Simulation-Based Phases, Simulation-Based (Normalized to 120kPa)
Results: Non-linearity & Vascular Shutdown

- non-linear US propagation
  - performed for 3rd steering approach
  - negligible impact on pressure & temperature results
  - pressure amplitude & frequency not high enough to induce strong harmonics/energy deposition

- vascular shutdown
  - complete shutdown assumed between 50°C and 51°C
  - +1°C temperature in focus area
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Conclusions

• application to tissue ablation in the brain with ExAblate (quantitative)
  - full-wave, HPC enabled (~5’ for linear) US simulations with high anatomical and physical complexity
  - could help improve efficiency, increase attainable focus locations, reduce treatment time and risk

• examined
  - impact of focusing strategy & focus shifting
  - temperature increase
  - lesion shape & size
  - impact of non-linear US propagation
  - Impact of vascular shutdown
Future Work

• apply this approach to the 650KHz system

• extended validation
  - ultimate goal: ex-vivo/in-vivo MR thermometry validation

• optimization
  - alternative steering approaches
  - hot-spot reduction
  - time-modulated steering
  - goal weighting
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Conclusions

- **comprehensive framework** for modeling of FUS and induced effects has been developed
  - full-wave acoustic solver ideally suited for complex wave propagation in inhomogeneous anatomical models
  - cavitation modeling
  - induced heating and tissue damage
  - integrated into multi-physics framework (flow, EM, CRD, mechanics…)
  - HPC enabled, high resolution

- **realism** in simulations
  - detailed anatomical models & segmentation platform for model creation
  - comprehensive tissue parameter databases, towards personalized tissue properties and dynamic tissue models
  - sophisticated thermal models (perfusion/thermoregulation tissue damage, dose)

- framework has been applied to **wide range of relevant applications**
Conclusions

- can be used for quantitative assessments and investigation of mechanisms / parameter studies (example: tcFUS)
- goal: patient specific treatment optimization

future work:
- importance of validation of software and models; ongoing
- optimization of steering
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