

**DEVELOPMENT OF AN *IN SILICO*  
SURGICAL SIMULATION PLATFORM FOR  
BIOMECHANICAL ASSESSMENT OF BRAIN**

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**DEPARTMENT OF APPLIED MECHANICS  
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BIOMECHANICAL ASSESSMENT OF BRAIN**

by

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DEPARTMENT OF APPLIED MECHANICS

*Submitted*

*in fulfillment of requirements of the degree of Doctor of Philosophy*

*to the*



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*Dedicated to my loving parents*

# Certificate

This is to certify that the thesis titled “**Development of an *in silico* Surgical Simulation Platform for Biomechanical Assessment of Brain**”, submitted by **Abhilash Awasthi** to the Indian Institute of Technology Delhi, for the award of the degree of **Doctor of Philosophy**, is a record of the original, bona fide research work carried out by him under our supervision and guidance. The thesis has reached the standards fulfilling the requirements of the regulations related to the award of the degree.

The results contained in this thesis have not been submitted in part or in full to any other University or Institute for the award of any degree or diploma to the best of our knowledge.

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Abhilash Awasthi

# Abstract

Identifying the mechanisms underlying brain injury is essential for improving diagnostic precision, guiding surgical planning, and informing post-operative care. These mechanisms often manifest through observable pathological changes in brain tissue, and understanding their relationship can support more effective clinical decision-making. However, direct evidence linking injury mechanisms to tissue-level damage in humans remains limited, posing a challenge for establishing clinicopathological correlations. In this context, *in silico* modeling has emerged as a valuable and cost-effective tool for gaining deeper insights and uncovering new injury pathways. Physics- and machine learning-based models contribute to injury prevention and personalized treatment, mainly when patient-specific data is scarce. A key challenge is their context-independent nature, which can be addressed by developing subject-specific *in silico* models tailored to individual anatomy. Such models enable personalized assessment, treatment planning, and real-time clinical monitoring, supporting informed decision-making by clinicians.

This work aims to develop a patient-specific *in silico* modeling platform for neurosurgical interventions. An automated pipeline was developed to generate 3D computational brain models from raw MRI scans. The process includes segmentation, cortical surface reconstruction, and volumetric mesh generation to create anatomically detailed, personalized 3D models for biomechanical analysis of surgical procedures and trauma prevention. Further, to enable personalized simulations, *in-vivo* estimate of the material properties can be obtained through elastography. While not essential for all personalized simulations, such as those focused purely on image-guided navigation, incorporating *in-vivo* mechanical properties can significantly enhance the accuracy of biomechanical simulations involving tissue deformations during neurosurgical procedures.

Elastography, a non-invasive tool for subject-specific brain tissue characterization, requires solving a challenging inverse problem to obtain material parameters. To address this, an open-source MATLAB-based parallelized inverse finite element algorithm, also known as Non-Linear Inversion (MatNLI), was developed using BFGS and Levenberg-Marquardt optimization techniques. The efficacy of the MatNLI was demonstrated through case studies involving various isotropic and anisotropic material models, with the Adjoint method used for gradient computation.

Further, challenges with FE-based NLI frameworks, such as scalability and computational efficiency, and computation of various implicit expressions in the formulation when dealing with highly non-linear material models, were addressed using a *differentiable physics* framework using automatic differentiation. This framework automates iterative inversion processes like NLI, eliminating the need for human-derived sensitivities and improving computational efficiency. With the help of various 2D and 3D case studies, the proposed differentiable physics-based algorithm outperformed MatNLI through GPU acceleration.

Given the computational intensity of NLI, a data-driven Wavelet Neural Operator (WNO) was proposed as a surrogate model for inverse problems in elastography. Application of WNO to Ultrasound- and MRI-based *in-vivo* elastography data demonstrated feasibility in detecting stiff inclusions and accurately predicting stiffness distribution with a prediction error of less than 2% and a prediction time of just 6/100th of a second.

Finally, the subject-specific computational model and material parameters can be integrated to simulate surgical interventions and prevent brain tissue injuries. A boundary value problem for deep-brain retraction – a fundamental neurosurgical procedure – was developed using a viscohyperelastic framework. The 3D brain model accurately simulated brain deformations during retraction and indicated that intermittent retraction reduces injury risk compared to continuous retraction for the same extent of retraction. These biomechanical simulations align with clinical observations of brain retraction and offer a foundation for future research.

The proposed *in silico* framework holds promise for pre-surgical planning and intra-operative guidance, providing general ready-to-use tools for modeling various human organs. This work establishes a basis for constructing a digital twin of the human brain by integrating 3D model reconstruction, material parameter identification, and biomechanical simulations. This unified approach will enable personalized diagnosis and treatment strategies tailored to individual patients.

Keywords: *In silico* modeling, Non-linear inversion, *In-vivo* mechanical characterization, Magnetic Resonance Elastography, Brain injury, Scientific machine learning, Deep neural operators

## सार

मस्तिष्क की चोट के अंतर्निहित तंत्रों की पहचान करना निदान सटीकता में सुधार, शल्य चिकित्सा योजना का मार्गदर्शन करने और पश्चात-शल्य चिकित्सा की जानकारी देने के लिए आवश्यक है। ये तंत्र अक्सर मस्तिष्क के ऊतकों में देखे जा सकने वाले रोग संबंधी परिवर्तनों के माध्यम से प्रकट होते हैं, और उनके संबंध को समझना अधिक प्रभावी नैदानिक निर्णय लेने में सहायता कर सकता है। हालाँकि, मनुष्यों में ऊतक-स्तर की क्षति से चोट तंत्र को जोड़ने वाले प्रत्यक्ष साक्ष्य सीमित हैं, जो नैदानिक-विकृति संबंधी सहसंबंधों को स्थापित करने के लिए एक चुनौती पेश करते हैं। इस संदर्भ में, इन सिलिको प्रतिरूपण गहरी अंतर्दृष्टि प्राप्त करने और नई चोट के मार्गों को उजागर करने के लिए एक मूल्यवान और लागत प्रभावी उपकरण के रूप में उभरा है। भौतिकी और मशीन लर्निंग-आधारित मॉडल चोट की रोकथाम और व्यक्तिगत उपचार में योगदान करते हैं, मुख्य रूप से तब जब रोगी-विशिष्ट आँकड़े दुर्लभ होते हैं। एक प्रमुख चुनौती उनकी संदर्भ-स्वतंत्र प्रकृति है, जिसे व्यक्तिगत शारीरिक रचना के अनुरूप विषय-विशिष्ट इन सिलिको प्रतिरूप विकसित करके संबोधित किया जा सकता है। ऐसे प्रतिरूप व्यक्तिगत मूल्यांकन, उपचार योजना और वास्तविक समय नैदानिक निगरानी को सक्षम करते हैं, जो चिकित्सकों द्वारा सूचित निर्णय लेने का समर्थन करते हैं।

इस कार्य का उद्देश्य तंत्रिकाशल्यक हस्तक्षेपों के लिए रोगी-विशिष्ट इन सिलिको प्रतिरूपण मंच विकसित करना है। चुंबकीय अनुनाद प्रतिबिंबन से 3D संगणनात्मक मस्तिष्क प्रतिरूप बनाने के लिए एक स्वचालित आंकड़ा संसाधन विकसित की गई। इस प्रक्रिया में शल्य चिकित्सा प्रक्रियाओं और आघात की रोकथाम के जैवयांत्रिकी विश्लेषण के लिए शारीरिक रूप से विस्तृत, व्यक्तिगत 3D प्रतिरूप बनाने के लिए विभाजन, वल्कुटीय सतह पुनर्निर्माण और आयतनमितीय जाल उत्पादन शामिल है। इसके अलावा, व्यक्तिगत अनुकरण को सक्षम करने के लिए, इलास्टोग्राफी के माध्यम से सामग्री गुणों का जीव अनुमान प्राप्त किया जा सकता है। हालाँकि सभी व्यक्तिगत अनुकरण के लिए आवश्यक नहीं है, जैसे कि पूरी तरह से छवि-निर्देशित दिशाज्ञान पर केंद्रित, जीव यांत्रिक गुणों को शामिल करने से तंत्रिकाशल्यक प्रक्रियाओं के दौरान ऊतक विकृति से जुड़े जैवयांत्रिकी अनुकरण की सटीकता में काफी वृद्धि हो सकती है।

इलास्टोग्राफी, विषय-विशिष्ट मस्तिष्क ऊतक लक्षण वर्णन के लिए एक गैर-आक्रामक उपकरण है, जिसके लिए भौतिक मापदण्ड प्राप्त करने के लिए एक चुनौतीपूर्ण व्युत्क्रम समस्या को हल करने की आवश्यकता होती है। इसे संबोधित करने के लिए, एक खुले स्रोत, MATLAB-आधारित समानांतर

व्युत्क्रम परिमित तत्व नियमों की प्रणाली, जिसे गैर-रैखिक व्युत्क्रम (MatNLI) के रूप में भी जाना जाता है, BFGS और लेवेनबर्ग-मार्वार्ड इष्टतमीकरण तकनीकों का उपयोग करके विकसित किया गया। MatNLI की प्रभावकारिता विभिन्न समदैशिक और विषमदैशिक भौतिक प्रतिरूप से जुड़े मामलों के अध्ययन के माध्यम से प्रदर्शित की गई, जिसमें ढलान गणना के लिए एडजॉइंट विधि का उपयोग किया गया है।

इसके अलावा, परिमित तत्व विधि-आधारित NLI संरचना की चुनौतियों, जैसे कि मापनीयता और संगणनात्मक दक्षता, और अत्यधिक गैर-रैखिक भौतिक प्रतिरूप से निपटने के दौरान सूत्रीकरण में विभिन्न अंतर्निहित अभिव्यक्तियों की गणना, स्वचालित विभेदन का उपयोग करके एक विभेदक भौतिकी फ्रेमवर्क का उपयोग करके संबोधित की गई। यह संरचना NLI जैसी पुनरावृत्त व्युत्क्रम प्रक्रियाओं को स्वचालित करता है, मानव-व्युत्पन्न संवेदनशीलता की आवश्यकता को समाप्त करता है और संगणनात्मक दक्षता में सुधार करता है। विभिन्न 2D और 3D मामलों के अध्ययन से, प्रस्तावित विभेदक भौतिकी-आधारित नियमों की प्रणाली ने GPU त्वरण के माध्यम से MatNLI को बेहतर प्रदर्शन किया।

NLI की संगणनात्मक तीव्रता को देखते हुए, इलास्टोग्राफी में व्युत्क्रम समस्याओं के लिए एक प्रतिनियुक्त मॉडल के रूप में आंकड़ा-संचालित वेवलेट न्यूरल ऑपरेटर (WNO) का प्रस्ताव रखा गया है। पराध्वनिक चित्रण और चुंबकीय अनुनाद प्रतिबिंबन-आधारित इलास्टोग्राफी आंकड़ों पर WNO के अनुप्रयोग ने कठोर समावेशन का पता लगाने और 2% से कम की भविष्यवाणी त्रुटि और केवल 6/100 सेकंड के पूर्वानुमान समय के साथ कठोरता वितरण का सटीक अनुमान लगाने में व्यवहार्यता प्रदर्शित की।

अंत में, विषय-विशिष्ट संगणनात्मक प्रतिरूप और सामग्री मापदंडों को शल्य चिकित्सा हस्तक्षेपों का अनुकरण करने और मस्तिष्क ऊतक की चोटों को रोकने के लिए एकीकृत किया जा सकता है। गहरा-मस्तिष्क प्रत्याहार - एक मौलिक तंत्रिकाशल्यक प्रक्रिया - के लिए एक सीमा मूल्य समस्या को श्यान अतिप्रत्यास्थ संरचना का उपयोग करके विकसित किया गया है। 3D मस्तिष्क प्रतिरूप ने प्रत्याहार के दौरान मस्तिष्क की विकृतियों का सटीक रूप से अनुकरण किया और संकेत दिया कि प्रत्याहार की समान सीमा के लिए निरंतर प्रत्याहार की तुलना में आंतरायिक प्रत्याहार चोट के जोखिम को कम करता है। ये जैवयांत्रिकी अनुकरण मस्तिष्क प्रत्याहार के नैदानिक अवलोकनों के साथ संरेखित होते हैं और भविष्य के शोध के लिए एक आधार प्रदान करते हैं।

प्रस्तावित इन सिलिको संरचना पूर्व-शल्यक योजना और शस्त्रकर्मकालीन मार्गदर्शन के लिए आशाजनक है, जो विभिन्न मानव अंगों के प्रतिरूपण के लिए सामान्य तैयार-से-उपयोग उपकरण प्रदान करता है। यह कार्य 3D प्रतिरूप पुनर्निर्माण, भौतिक मापदण्ड पहचान और जैवयांत्रिकी अनुकरण को एकीकृत करके मानव मस्तिष्क के अंकीय प्रतिरूप के निर्माण के लिए एक आधार स्थापित करता है। यह एकीकृत दृष्टिकोण व्यक्तिगत रोगियों के अनुरूप व्यक्तिगत निदान और उपचार रणनीतियों को सक्षम करेगा।

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# Symbols

$\Omega_R$	Reference or stress-free configuration
$\Omega$	Current or deformed configuration
$\nabla$	Gradient with respect to material point $\mathbf{X}$
Div	Divergence with respect to material point $\mathbf{X}$
$\det(\mathbf{M})$	Determinant of second order tensor $\mathbf{M}$
$\mathbf{M}^T$	Transpose of second order tensor $\mathbf{M}$
$\mathbf{M} : \mathbf{N}$	Inner product between two $2^{nd}$ order tensors $\mathbf{M}$ and $\mathbf{N}$
$\mathbf{F}$	Deformation gradient tensor
$\mathbf{B}$	Left Cauchy-Green deformation tensor
$\mathbf{C}$	Right Cauchy-Green deformation tensor
$\mathbf{t}_R$	Surface traction in reference configuration
$\mathbf{b}_R$	Body force per unit reference volume ( $V$ )
$\mathbf{P}$	First Piola-Kirchhoff stress tensor
$\mathbf{T}$	Cauchy stress tensor
$J$	$\det(\mathbf{F}) > 0$ , Ratio of deformed volume ( $v$ ) to reference volume ( $V$ )
$W$	Strain energy density function per unit reference volume ( $V$ )
$\lambda$	Stretch ratio (ratio of final to initial lengths)
$\tau_k$	Characteristic times
$C_{ij\infty}$	Long-term strain dependent relaxation moduli
$C_{ij0}$	Instantaneous relaxation moduli
$\mathbf{u}_c$	Model computed displacement field vector
$\mathbf{u}_m$	Experimentally observed displacement field vector
$\mathcal{C}$	Constraint function
$\Pi$	Objective function
$\Gamma$	Smooth boundary of solid domain $\Omega$
$\Gamma_D$	Dirichlet part of the boundary $\Gamma$

$\Gamma_N$	Neumann part of the boundary $\Gamma$
$\dot{\delta}$	Loading rate
$\mathbf{b}$	Body force vector per unit volume
$\rho$	Material density
$\mathbf{R}$	Global residual vector
$\mathbf{C}$	Fourth order elasticity tensor
$\mathbf{K}$	Stiffness matrix
$\mathbf{N}$	Finite element basis functions
$\boldsymbol{\lambda}$	Vector of adjoint variables
$v$	Velocity of a particle relative to reference configuration
$\bar{I}$	Invariant of left Cauchy-Green strain tensor ( $\mathbf{B}$ )
$I$	Invariant of right Cauchy-Green strain tensor ( $\mathbf{C}$ )
$t$	Current time
$\text{tr}(\mathbf{M})$	Trace of a second order tensor $\mathbf{M}$
$G^*$	Complex shear modulus
$G'$	$\text{Re}\{G^*\}$ – Storage modulus
$G''$	$\text{Im}\{G^*\}$ – Loss modulus
$\gamma$	Boundary of Lipschitz domain $\Omega$
$\gamma_D$	Dirichlet part of boundary
$\gamma_N$	Neumann part of boundary
$\omega$	Excitation frequency (in radians)
$\boldsymbol{\varepsilon}$	Linear strain tensor
$\boldsymbol{\sigma}$	Linear stress tensor
$\mathbf{I}$	Identity tensor
$p$	Hydrostatic pressure
$K$	Bulk modulus
$\boldsymbol{\theta}$	Material parameter vector

# Abbreviations

<b>2D</b>	<b>Two-Dimensional</b>
<b>3D</b>	<b>Three-Dimensional</b>
<b>AD</b>	<b>Automatic Differentiation</b>
<b>AzD</b>	<b>Alzheimer’s Disease</b>
<b>AR</b>	<b>Augmented Reality</b>
<b>BBB</b>	<b>Blood-Brain Barrier</b>
<b>BFGS</b>	<b>Broyden-Fletcher-Goldfarb-Shanno</b>
<b>BRP</b>	<b>Brain Retraction Pressure</b>
<b>BVP</b>	<b>Boundary Value Problem</b>
<b>CNN</b>	<b>Convolution Neural Network</b>
<b>CNS</b>	<b>Central Nervous System</b>
<b>CSF</b>	<b>Cerebrospinal Fluid</b>
<b>CT</b>	<b>Computed Tomography</b>
<b>DAI</b>	<b>Diffuse Axonal Injury</b>
<b>DBC</b>	<b>Dirichlet Boundary Conditions</b>
<b>DI</b>	<b>Direct Inversion</b>
<b>DWT</b>	<b>Discrete Wavelet Transform</b>
<b>FEM</b>	<b>Finite Element Method</b>
<b>FFT</b>	<b>Fast Fourier Transform</b>
<b>GAN</b>	<b>Generative Adversarial Network</b>
<b>GM</b>	<b>Grey Matter</b>
<b>ICP</b>	<b>Intracranial Pressure</b>
<b>IDWT</b>	<b>Inverse Discrete Wavelet Transform</b>
<b>JIT</b>	<b>Just In Time</b>
<b>JVP</b>	<b>Jacobian Vector Product</b>
<b>L-BFGS</b>	<b>Limited-memory Broyden-Fletcher-Goldfarb-Shanno</b>
<b>LFE</b>	<b>Local Frequency Estimation</b>

<b>LM</b>	<b>L</b> evenberg <b>M</b> arquardt
<b>ML</b>	<b>M</b> achine <b>L</b> earning
<b>MLS</b>	<b>M</b> oving <b>L</b> east <b>S</b> quare
<b>MRE</b>	<b>M</b> agnetic <b>R</b> esonance <b>E</b> lastography
<b>MRI</b>	<b>M</b> agnetic <b>R</b> esonance <b>I</b> maging
<b>NBC</b>	<b>N</b> eumann <b>B</b> oundary <b>C</b> onditions
<b>NLI</b>	<b>N</b> on- <b>L</b> inear <b>I</b> nversion
<b>OSS</b>	<b>O</b> ctahedral <b>S</b> hear <b>S</b> train
<b>PD</b>	<b>P</b> arkinson's <b>D</b> isease
<b>PDE</b>	<b>P</b> artial <b>D</b> ifferential <b>E</b> quations
<b>SBI</b>	<b>S</b> urgical <b>B</b> rain <b>I</b> njuries
<b>SNR</b>	<b>S</b> ignal-to- <b>N</b> oise <b>R</b> atio
<b>TBI</b>	<b>T</b> raumatic <b>B</b> rain <b>I</b> njury
<b>TI</b>	<b>T</b> ransversely <b>I</b> sotropic
<b>US</b>	<b>U</b> ltrasound
<b>VJP</b>	<b>V</b> ector <b>J</b> acobian <b>P</b> roduct
<b>VR</b>	<b>V</b> irtual <b>R</b> eality
<b>WM</b>	<b>W</b> hite <b>M</b> atter
<b>WNO</b>	<b>W</b> avelet <b>N</b> eural <b>O</b> perator