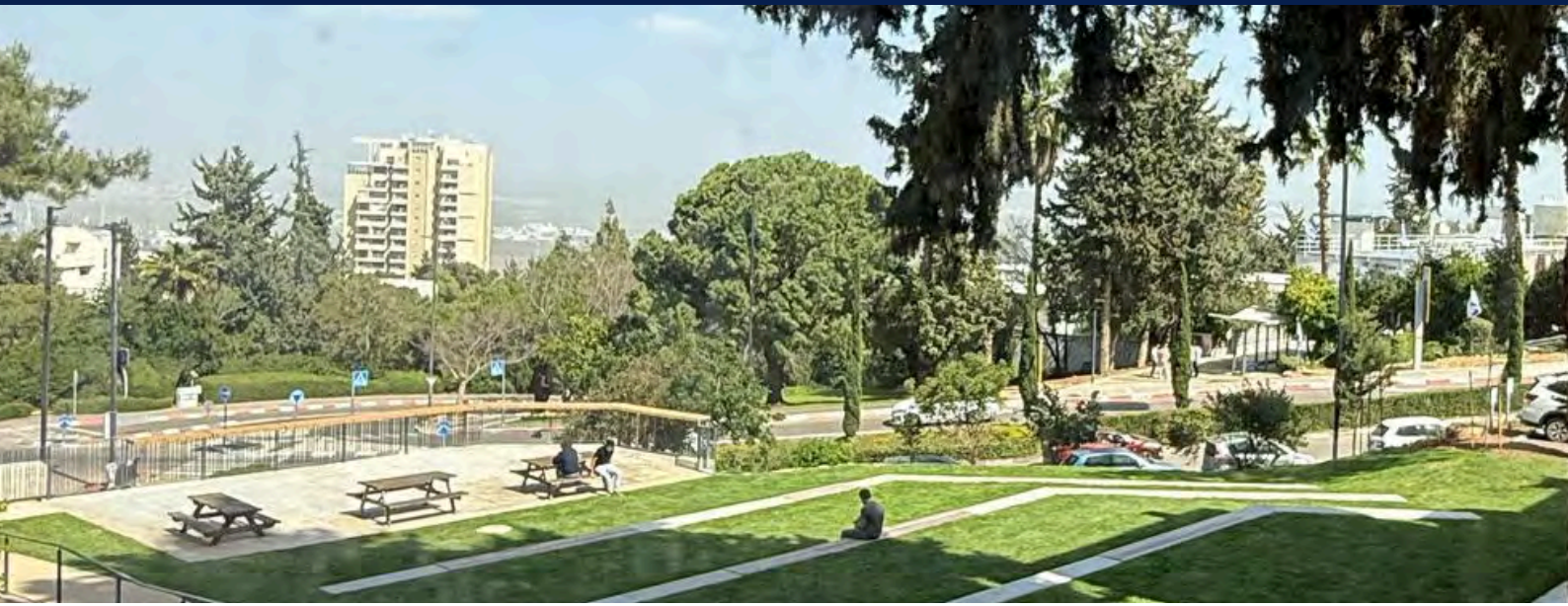
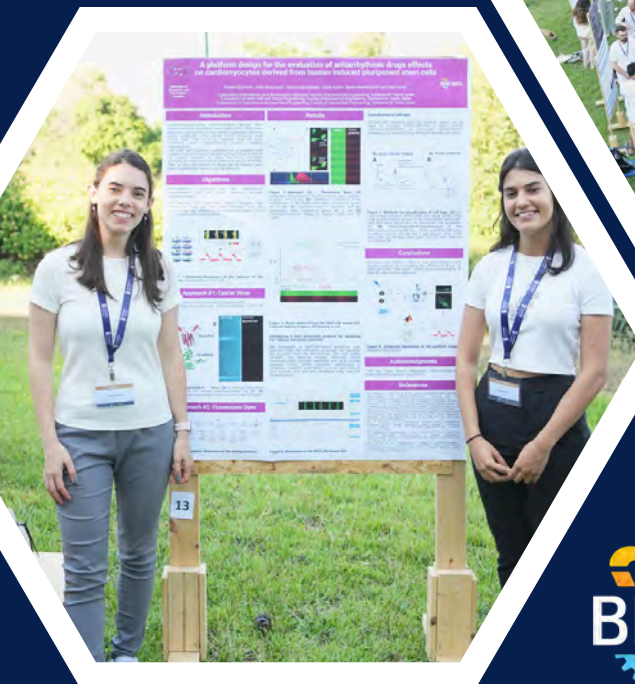




ABSTRACTS

ANNUAL PROJECT CONFERENCE 2025



Dear all,

We are proud and honored to welcome you to take part in the: ***Annual Project Presentation Conference 2025 of the Biomedical Engineering Faculty.***

This meeting culminates a yearlong research and development experience of our 4th year students. There is a say in Hebrew tradition: “אין חכם כבעל ניסיון”, meaning “Experience brings wisdom”. This, in a nutshell, is what the projects are all about.

During their project development experience, our students had to undergo through all the stages needed to make an idea come true. Starting with a medical problem which they had to tackle, they had to strain their imagination and think “out of the box” to come up with a plausible new solution. Then, they had to combine the knowledge they gained during their studies. This knowledge encompasses all the aspects of biomedical engineering, i.e. combining medical background with engineering skills and scientific knowledge. All this package had to be implemented to provide a real-world solution.

We believe that this hands-on experience exposed and prepared our graduates to the High-Tech biomedical industry and to a wide variety of biomedical research in a very strong way encouraging multidisciplinary work that is vital for the students’ future career, and in addition potentially fostering their entrepreneurship skills.

In this booklet the abstracts of all presented projects are displayed for your perusal. We are sure that the students are eager to present the outcome of their year-long projects. We wish all of them rewarding careers after graduation. We hope that very soon they will take an active part in similar projects as professional mentors from both industry and academia.

Kindest Regards,

Prof. Josué Sznitman, Faculty Dean

Assoc. Prof. Firas Mawase, Course Instructor

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Assessment of Stability Under Blood Flow Conditions

Reflexes in Neurology Toward Objective Neurological Assessment

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Introduction:

Examination of the patellar reflex response is a fundamental neurological test commonly used in clinical practice to assess neural pathways. However, traditional evaluation methods rely on subjective observation and lack quantitative metrics. In this study we aimed to develop objective, reproducible metrics for the patellar stretch reflex in healthy adults and to validate a straightforward video-analysis workflow that clinicians can apply across settings.

Methods:

Fifty healthy volunteers (26 males, 24 females; mean age 22.7 years) underwent bilateral patellar reflex testing using a custom-built reflex elicitation device (**Figure 1**). Each leg was tested up to five times. Reflexes were recorded using a standard smartphone camera filming at 60 frames-per-second, with markers placed according to standard kinematic analysis protocols. We quantified three parameters per trial using Kinovea software—delta angle, peak angular velocity, and reflex delay—then calculated each participant's median values. We assessed bilateral symmetry (Wilcoxon signed-rank), sex differences (Mann–Whitney U, post-hoc power), correlations with age/BMI (Spearman's ρ), inter-parameter associations (Pearson r and Spearman ρ), and measurement reliability (intra-rater, inter-limb, between-subject variability).

Results:

Reflex responses showed no bilateral asymmetry ($p > 0.5$) across all parameters, allowing to analyse the right and left legs together. Variability analysis demonstrated low intra-rater and inter-limb variability, confirming the repeatability and reliability of the measurement protocol. Reflex delay was significantly longer in males than in females (median: 43.17 ms vs. 38.75 ms, $p = 0.0119$); a post hoc power analysis ($d \approx 0.88$) yielded a power of 0.86, supporting the robustness of this finding. No significant differences were found in Delta angle and maximum angular velocity between the sexes. Delta angle and maximum angular velocity were highly correlated ($r = 0.841$, $\rho = 0.88$; $p < 0.0001$), highlighting them as interrelated components of reflex function, whereas delay remained independent (all $p > 0.26$). No significant correlations were found between reflex parameters and age or body mass index (all $|p| < 0.25$, $p > 0.08$).

Conclusions:

This study lays the foundation for a reliable, low-cost method for quantitatively assessing the patellar reflex using video-based motion analysis. The observed sex difference in reflex delay may reflect a physiological variation in neuromuscular response timing, calling for further investigation. The lack of correlations between the reflex parameters and age or body mass index, are likely due to the homogenic nature of the cohort. The tight coupling between delta angle and angular velocity—versus the independence of reflex delay—supports the distinct underlying physiological mechanisms involved in each. Together, these findings can be utilized for standardizing patellar reflex assessment in both clinical diagnostics and neuromuscular research.

Keywords:

patellar reflex, motion analysis, standardization



Figure 1 – The setup for the patellar reflex testing alongside Kinovea markers and angle-tracking overlays. Participants were seated with their lower legs hanging freely. The reflex hammer positioned at approximately 45° angle to strike the patellar tendon. A mounted phone camera recorded the leg movement.

Predictive Deep Learning Model of P63 Gene Expression Levels in Limbal Stem Cells

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Introduction:

Limbal Stem Cell Therapy is a medical treatment which involves the transplantation of donated stem cells to treat vision impairments caused by Limbal Stem Cell Deficiency and/or corneal damage. P-63 gene plays a critical role as a gatekeeper of epidermal morphogenesis and the development of epithelial tissues in the cornea. The success rates of Limbal Stem Cell Therapy correlate with the expression of P-63 transcription factor in the holoclone forming cells transplanted during the treatment. With 78% success rate in clinical treatments with cultures constituted of over 3% p63-bright cells, compared to 11% success rate of those under 3%. As of today, the ability to discover the expression levels of P-63 gene in stem-cells is limited to using cell staining techniques, a process that takes away parts of the culture meant for transplantation, takes time, and decreasing the “lifetime” of the stem-cells culture. By using a predictive model via deep learning machine, we could find the expression levels of the P-63 gene not only faster, but also without allowing the stem-cell culture to further grow and differentiate.

Methods:

Our dataset was collected from 2 cultures, in 4 different levels of differentiation, and is made up from Brightfield images of the cultures, DAPI stained images, and P63 stained images. We first performed automatic segmentation of cell nuclei using Cellpose model, then applied an image-processing pipeline to generate accurate ground truth for each patch. Next, we trained a ResNet50 network on Bright-Field images for binary classification of patches as “expressing” or “not expressing” P63. Additionally, we experimented with UNet++ for pixel-wise regression of expression maps. Finally, we developed a second ResNet50 model—also using Bright-Field inputs—to predict the median P63 expression level in each patch. We employed multiple strategies to address small and imbalanced data, including patch-based splitting, oversampling, smart loss functions, weighting, and hyperparameter optimization.

Results:

The Bright-Field binary classification model achieved a recall of 94% and a precision of 96%, demonstrating strong ability to distinguish patches with significant P63 expression.

The Bright-Field median-prediction ResNet50 model yielded a correlation of $R^2 = 0.4896$ between predicted and true median values, indicating a moderate yet meaningful agreement. Moreover, we saw stem-cells of high differentiation (and therefore lower rates of P63) getting lower predictions of values than those of low differentiation, showing the model manages to identify those differences in some capacity.

Conclusions:

Using Deep-Learning models can be used to predict levels of expression of the P63 gene in stem cells, and therefore possibly identify each cell's expression. That can be used to help doctors to use better cultures in transplantation, but might also be useful for research on stem cells. Due to the lack in optimization techniques, we believe further work could reach better accuracy.

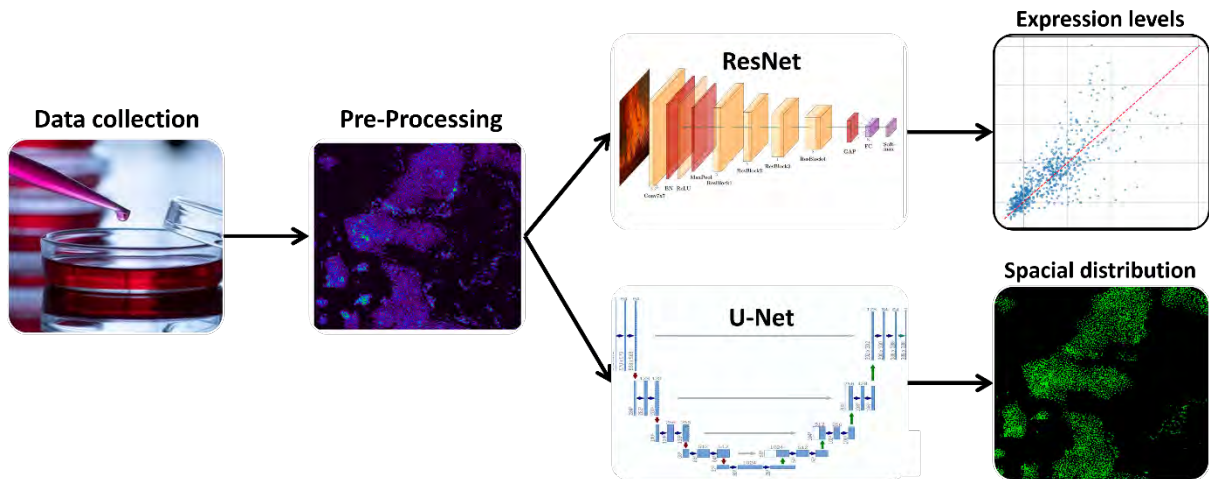


Figure 1: Model pipeline: Data harvested from cell culture is preprocessed and then used in training of two models; each Predicts levels of P63 expression in different ways.

Predictive Maintenance Using AI For CARTO Systems

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² Johnson & Johnson MedTech, Israel

Introduction:

CARTO™ 3 is a high-precision 3D navigation system used in cardiac electrophysiology procedures. These systems depend on synchronized hardware, telemetry sensors, and clinical workflows to ensure safe and effective operation. When system-related issues occur, support teams often rely on post-procedural logs and manual reviews to identify the source of failure. However, a significant portion of events remain unresolved due to the complexity and volume of data. This project presents an AI-powered pipeline for automated root cause analysis of CARTO 3 telemetry logs, aiming to simplify diagnosis, reduce device returns and "No Failure Found" (NFF) rate, and support engineering and clinical teams with actionable insights.

Methods:

The analysis pipeline developed in this project consists of three integrated stages. First, telemetry logs from CARTO™ 3 procedures are parsed and preprocessed to extract over 15 structured features, including spatial coordinates, force features, impedance readings, thermal features and diagnostic flags. The data is segmented around the time of failure and normalized to create synchronized event windows suitable for downstream analysis.

Second, a supervised machine learning model based on a Random Forest classifier is trained to identify the most likely root cause domain. The input vectors consist of telemetry features from the preprocessed data, and the model learns to differentiate between categories such as catheter hardware, connecting cable, system port and environmental interference. The classifier outputs feature importance values, which provide interpretability and indicate which features most affect classification.

Finally, the model's output is passed into an LLM based model, which produces a clear, human-readable explanation contextualized by the telemetry input. This diagnostic summary is then scored by a rules-based module that determines severity level and priority. The final product is a complete diagnostic report that is automatically routed to relevant stakeholders.

Results:

The Random Forest model was trained and evaluated on structured telemetry datasets. Performance was assessed using standard classification metrics including accuracy, precision, recall and F1 score. The model demonstrated strong predictive performance across multiple classes.

In addition, The model produced interpretable feature importance outputs, and the language model generated the report with explanations consistent with expert validation.

Conclusions:

The developed system introduces a scalable, data-driven approach to technical diagnostics in CARTO™ 3 workflows. By automating the interpretation of telemetry and generating root cause insights, the platform significantly reduces time-to-resolution, decreases the rate of unresolved device returns, and enhances operational clarity for both clinical and engineering teams. The system sets a new benchmark for AI-assisted diagnostics in electrophysiology and supports a transition toward proactive, insight-driven maintenance strategies across the ecosystem.

Keywords:

CARTO™ 3, Machine Learning, Large Language Model, Predictive Maintenance

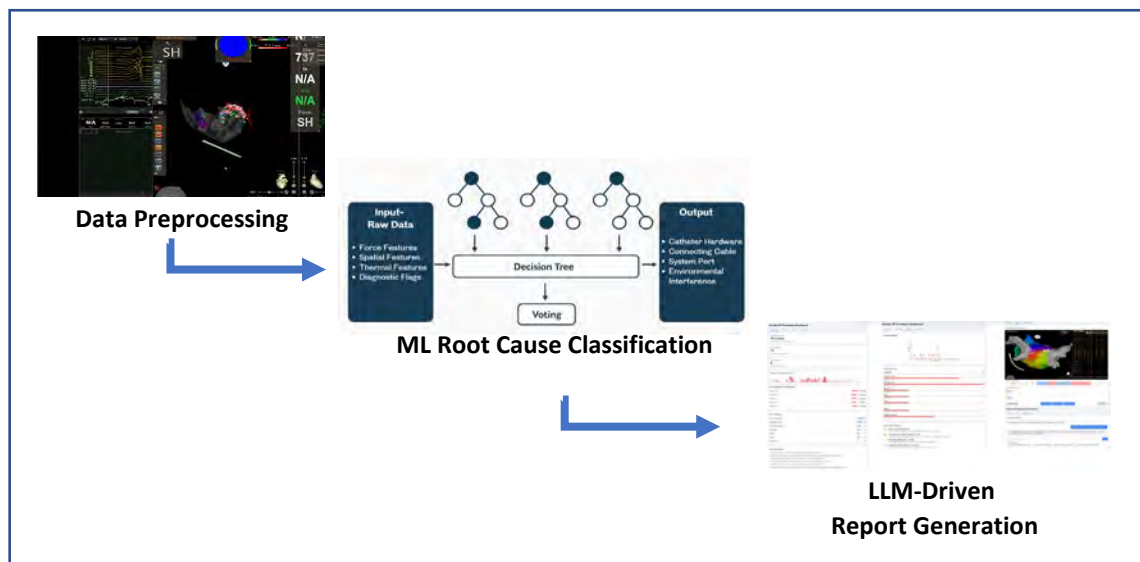


Figure 1: Multistage pipeline for AI-driven root cause analysis of CARTO™ 3 system events, leveraging telemetry data and automated reporting tools.

“Predicting Anxiety via HRV Analysis of PPG Signals Obtained from a Smartband”

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Introduction: Anxiety responses often go undetected until escalation, as subjective recognition typically occurs after the onset of physiological changes, limiting timely-intervention opportunities. Predicting anxiety before conscious awareness presents a unique challenge. Current tools detect anxiety only after onset or depend on contextual data unsuitable for continuous monitoring.

Heart Rate Variability (HRV) correlates to autonomic nervous system activity, and numerous studies have demonstrated its potential as a physiological biomarker for emotional and mental health conditions, including rising stress and anxiety disorders. While HRV is traditionally derived from ECG, we utilized non-invasive photoplethysmography (PPG) signals from wearable devices to assess feasibility of real-time prediction of anxiety onset.

Our findings suggest that rising anxiety levels can be detected using only HRV features derived from wrist-worn PPG sensors. Specifically, our model identified physiological changes associated with anxiety up to two minutes before participants consciously reported distress.

Methods: We conducted a controlled experiment with 31 participants, wearing a PPG-sensor equipped smartband. The protocol included pre-recorded instructions and timed, stress-inducing interruptions to ensure alignment between subjective reports and physiological stress responses.

A key challenge in studying anxiety is the reliance on subjective self-report, which can introduce variability and affect physiological measurements. To address this, we developed the AnxieClick button a real-time tagging device that allowed participants to self-report anxiety, without interrupting the task. To further reduce noise, we included events that occurred in the preparation phase or in proximity to interruptions during the presentation phase.

PPG signals were preprocessed with bandpass-filtration, segmented into 45-second windows with 15-second overlap, and processed using a validated peak detection algorithm. HRV features were extracted, with selection focused on short-term metrics suitable for capturing transient physiological responses within the short analysis windows. These labeled sequences were used to train the prediction model.

Results: We developed an integrated experimental framework that enables synchronized recording and labeling of subjective anxiety episodes. This included a pre-scripted protocol, wearable PPG monitoring, and a real-time tagging device. In addition, we developed a companion app for real-world integration. The model achieved an accuracy of 87% and an F1-

score of 0.86 for detecting pre-anxiety states. As shown in the ROC curve in Figure 1, it reliably distinguished between baseline and pre-anxiety patterns.

Conclusions: We present a complete pipeline for predicting anxiety using only PPG signals from a wearable smartband, validated on a student population under performance stress. This proof-of-concept demonstrates that real-time prediction of anxiety is feasible using non-invasive, consumer-grade sensors. For the first time, our approach enables preventive intervention before subjective awareness of stress, with the potential to reduce symptom escalation. Integrated into a mobile application, the model supports real-time tracking, personalized alerts, and future therapeutic use. Ongoing work focuses on clinical validation and deployment in broader populations.

Keywords: Anxiety prediction, Wearable monitoring, Heart Rate Variability (HRV), Photoplethysmography (PPG)

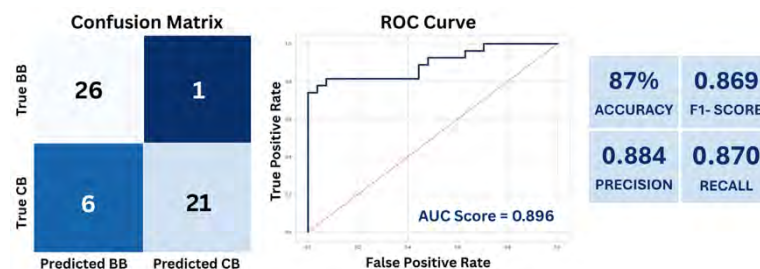


Figure 1 – Evaluation of model performance in distinguishing baseline from pre-anxiety states.

MRI Analysis and Biomechanics 1–1.5 Years After Anterior Cruciate Ligament Reconstruction Surgery

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Introduction: Anterior cruciate ligament reconstruction (ACLR) is among the most common orthopedic procedures, with about 400,000 surgeries annually in the U.S. However, up to 50% of patients develop knee osteoarthritis (OA) within 5–15 years post-surgery. Identifying early indicators of joint degeneration is critical. This study investigates whether biomechanical performance and patient-reported outcomes (PROs) collected near the time of surgery are associated with cartilage health as assessed by quantitative MRI 1.5 years after ACLR. Specifically, we examine correlations between joint kinematics, neuromuscular control, PROs, and UTE-T2* MRI biomarkers, aiming to identify early markers of long-term joint integrity.

Methods: This longitudinal study included five previously collected time points (pre-surgery and four post-surgery), with our project adding a sixth at 1.5 years post-ACLR. For biomechanical and PROs data, we analyzed only T1 (pre-surgery) for walking and T3 (three months post-surgery) for stairs. Assessments included strength and neuromuscular control using a hand-held dynamometer (peak force, rate of force development), electromyography (EMG) for muscle activation, and Xsens IMUs for joint kinematics. Participants performed walking at three speeds (normal, fast, slow) and stair climbing (ascending/descending) at a normal pace.

Knee function and psychological status were evaluated via validated questionnaires: the International Knee Documentation Committee (IKDC) for knee function, the Tampa Scale of Kinesiophobia for fear of movement, and the Generalized Anxiety Disorder (GAD) scale for anxiety severity. Group comparisons were made using the Mann–Whitney U test, and associations between biomechanical features and PROs were assessed using Pearson correlation.

MRI scans were acquired 1.5 years post-surgery using a UTE T2* protocol to assess early cartilage degeneration. Images were pre-processed before applying a pre-trained model to segment six regions of interest: femoral cartilage, medial/lateral tibial cartilage, patellar cartilage, and medial/lateral meniscus. T2* maps were generated via exponential fitting to reflect cartilage composition.

PyRadiomics was used to extract radiomic features from UTE-T2* scans obtained from the OAI dataset. Feature selection (ANOVA, mutual information, recursive feature elimination) reduced dimensionality. Multiple machine learning models were trained to classify OA status.

Results: Key biomechanical findings demonstrated clinical relevance reduced knee flexion at initial contact during fast walking in ACLR patients ($4.92^\circ \pm 3.93^\circ$) compared to healthy participants ($9.81^\circ \pm 3.12^\circ$; $p = 0.001$, $r = 0.48$). Ankle range of motion asymmetry during stair ascent was significantly greater in ACLR patients (47.45 ± 16.82) than in healthy controls (10.3 ± 6.28 ; $p < 0.000001$, $r = 0.82$) and strongly correlated with lower IKDC scores ($r = -0.77$, $p < 0.000001$).

MRI analysis identified 30 radiomic features using mutual information, with top predictors related to cartilage texture. A tuned Random Forest model achieved 85.2% accuracy and an Area Under the Curve (AUC) of 83.2 in classifying OA vs. non-OA.

Conclusions: These results support the potential utility of motion analysis and PROs as non-invasive indicators of long-term joint health. By integrating T2* mapping with biomechanical and PRO data into predictive models, future work may enable earlier detection of cartilage degeneration, risk stratification, and targeted rehabilitation strategies.

Keywords: Anterior Cruciate Ligament Reconstruction, Biomechanics, Machine Learning.

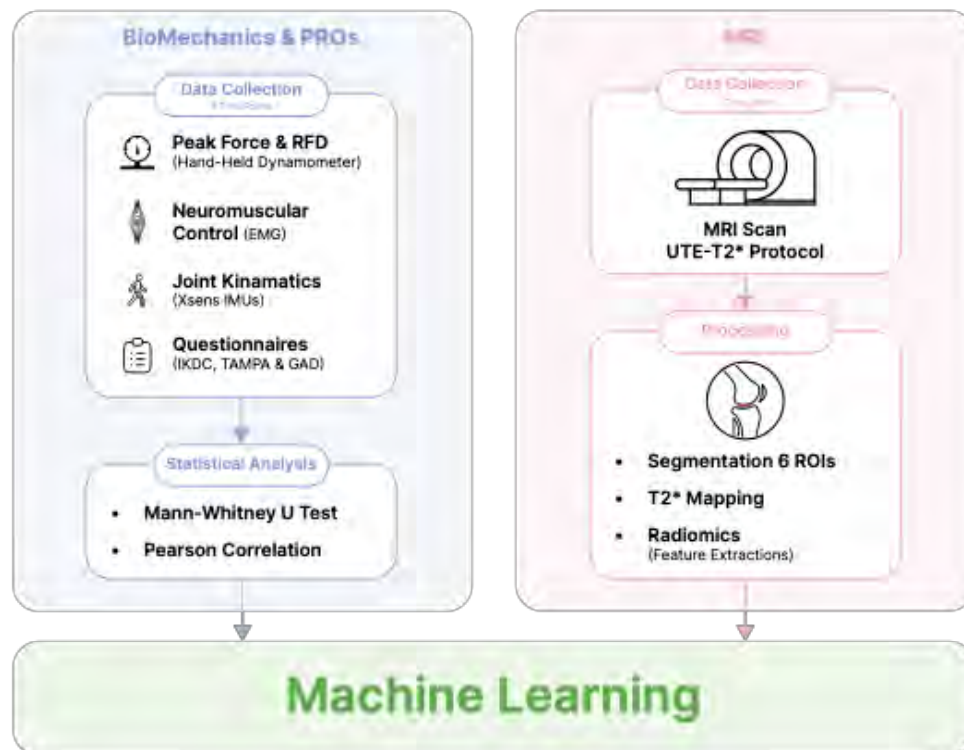


Figure 1. Study pipeline from data collection to cartilage health prediction using MRI, biomechanics, and PROs.

Immunoassay Development for Quantification of Biomarkers in Serum of CAR-T Patients

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Introduction:

Chimeric Antigen Receptor (CAR) T-cell therapy is a highly effective treatment for hematologic malignancies but is frequently complicated by toxicities, notably Cytokine Release Syndrome (CRS) and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). These cytokine-driven complications can become life-threatening if not detected and managed early. Timely blood cytokine quantification allows for earlier risk assessment, yet current methods are limited by long assay times, complexity, and high cost. To overcome these limitations, a bead-based sandwich immunoassay was previously developed in Shechtman Lab for rapid, low-cost detection of interleukin-6 (IL-6), which has predictive value for such toxicities. Building on this platform, our project aimed to expand its diagnostic capabilities by identifying and integrating an additional biomarker, IL-15, to improve CRS and ICANS monitoring.

Methods:

IL-15 was selected as a complementary biomarker following a comparative review of over 20 cytokines. The detection procedure followed is outlined in Figure 1: magnetic beads conjugated with anti-IL-15 capture antibodies were incubated with recombinant IL-15 in diluted human serum. Detection was then achieved via fluorescently labeled antibodies, and samples were analyzed in flow. The resulting fluorescence intensity data was used to evaluate performance and guide system optimization. To support experimental design, a MATLAB model adapted from the literature (Chang et al., 2019) was used to simulate how key parameters influence assay sensitivity and specificity. Based on these simulations, we tested variables including shaking intensity, bead concentration, serum dilution factor, detection antibody concentration, and number of washes. For validation, a sensitivity assay was conducted using five IL-15 concentrations, and the final system was applied to a CAR-T patient serum sample.

Results:

IL-15 was selected due to its early serum elevation and high predictive value for CAR-T toxicities. Through experimental adaptation and parameter tuning, the assay showed improved sensitivity without compromising specificity. The final system produced a clear fluorescence signal that increased with IL-15 concentration across the tested range. Sensitivity testing confirmed a detection threshold of approximately 15 pg/mL. IL-15 levels in a CAR-T patient sample followed trends consistent with clinical reports.

Conclusions:

We successfully adapted and optimized the system for IL-15 detection, demonstrating its flexibility for new biomarkers. Compared to IL-6, the assay showed improved sensitivity, aligning with clinical levels. This was achieved through careful selection and tuning of key parameters. Sensitivity testing showed a reliable concentration-dependent signal, while patient sample analysis reflected expected IL-15 dynamics. Taken together, systems of this type may support early prediction of CAR-T toxicities and be adapted for broader clinical use.

Keywords:

CAR-T toxicity; IL-15; Immunoassay; Biomarker detection

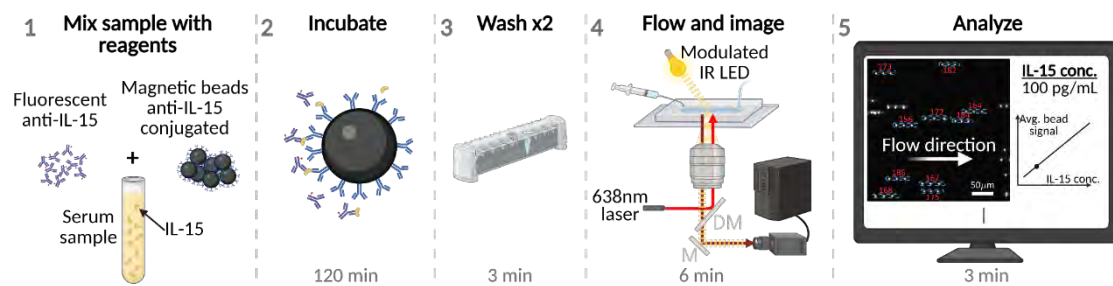


Figure 1: Workflow of IL-15 detection. (1) Beads, IL-15–spiked serum, and fluorescent antibodies are mixed. (2) Samples are incubated for 2 h at 1000 RPM. (3) Samples are washed twice to remove unbound components. (4) Samples are recorded for 6 min in flow. (5) Videos are analyzed and fluorescent signals are plotted vs. IL-15 concentration.

Personalized Physiotherapy: AI-Based Prediction of Treatment Plan Adjustments

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² WizeCare

Introduction: Physiotherapy services often face long waiting times, with delays of 2-4 months commonly reported in Israel. Since timely access to rehabilitation is crucial for optimal recovery, improving efficiency is essential. While digital tools have enabled home-based physiotherapy, the adaptation of treatment plans still relies heavily on manual clinical judgment, making the process inefficient and difficult to scale.

This project aims to develop an AI-based decision support tool to assist physiotherapists in updating home rehabilitation plans. By analyzing patterns in patient behavior and previous clinical decisions, the system predicts the type of adjustment likely to optimize outcomes, ultimately aiming to reduce clinician workload and enhance patient care.

Methods: We collaborated with WizeCare, a digital physiotherapy company, and used real world data from approximately 4,000 patients. After conducting a literature-based classification of exercises by clinical goals (e.g., flexibility, strength, pain reduction), we developed an algorithm to classify the type of treatment change class between consecutive plans, using a structured change scale we defined. Treatment modifications were grouped into eight distinct families, such as added or removed exercise categories, difficulty level adjustments, or shifts in training goals.

In parallel, we engineered patient level features, including adherence behavior, engagement, and self-reported scores from WizeCare's PRO system, such as perceived difficulty, safety, enjoyment, and pain levels. These features, together with treatment plan configurations, were used to train an XGBoost classifier to predict the treatment change class. To address class imbalance, SMOTE and undersampling techniques were applied.

Once trained, the model was integrated into a function that receives new patient data and provides a predicted treatment change along with supporting insights. The function highlights the key features that characterize the corresponding patient group, compares them to the patient's values, and identifies notable deviations. These structured insights, combined with clinician provided inputs (such as symptoms), are passed to an OpenAI GPT-based API that generates a personalized recommendation for the next treatment plan.

This enables physiotherapists to not only receive a data-driven suggestion but also understand the reasoning behind it- supporting clinical transparency, saving decision making time, and fostering trust in the system.

Results: The model achieved an overall accuracy of 82%, successfully classifying 6 out of 8 treatment change types. A clear correlation was observed between patient behaviors (e.g., high adherence, positive feedback) and types of treatment updates. These insights were reviewed and confirmed by clinicians as clinically meaningful.

Conclusions: This POC demonstrates that by analyzing adjustments made by physiotherapists to treatment plans, it is possible to model and approximate their clinical decision-making process. By combining expert-driven change patterns with patient behavior data, we present a scalable and explainable machine learning framework that supports the personalization of home-based rehabilitation programs.

Keywords: Physiotherapy Personalization, ML in Rehabilitation, WizeCare.

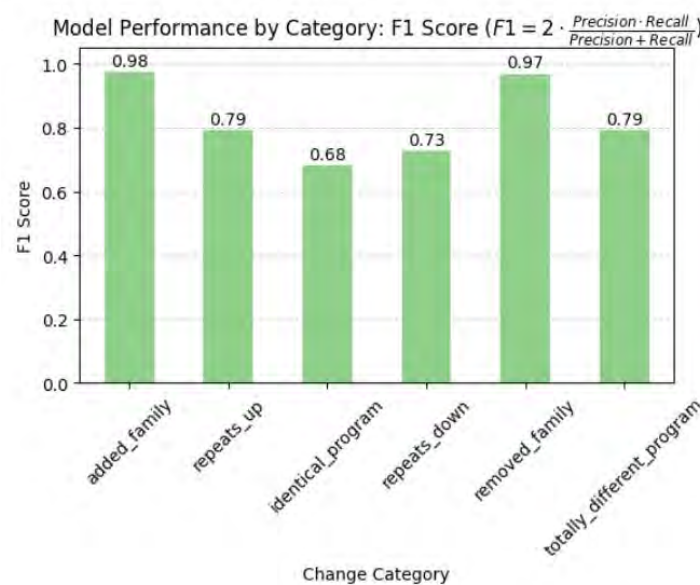


Figure 1: F1 score performance of the XGBoost classification model across treatment change categories.

Machine Learning-Based Personalization Tool for Acute Myeloid Leukemia (AML)

Noa Kopelman, Assaf Yassour

Supervised by: Dr. Shlomit Yehudai-Reshef, Prof. Tsila Zuckerman

CRIR - Clinical Research Institute at Rambam

Introduction:

Acute Myeloid Leukemia (AML) is a life-threatening malignancy characterized by the rapid proliferation of immature myeloid cells in the bone marrow. Despite initial treatment success, relapse remains a major clinical challenge, with most patients experiencing disease recurrence within the first two years. Alarming, approximately 70% of AML patients do not survive beyond five years from diagnosis, underscoring the urgent need for improved treatment strategies.

Recent studies highlight that subpopulations of hematopoietic stem and progenitor cells (HSPCs) in the bone marrow - including GMP, CMP, MLP, and HSC - exhibit resistance to standard chemotherapy and are therefore suspected to drive AML relapse.

In this project, we aim to develop a machine learning based approach capable of automatically identifying and classifying HSPC subpopulations from bone marrow microscopic images. By leveraging subtle morphological features, our method seeks to establish a tool for profiling individual patients. Such profiling could serve as a foundation for personalized treatment strategies aimed at preventing AML relapse and improving long-term outcomes.

Methods:

Microscopic images of patient-derived HSPC subpopulations were obtained using fluorescence staining, with each subpopulation labeled by a distinct fluorescent dye (yellow, green, blue, or red). Cells were cultured and stained according to standard biological protocols. Image segmentation was then performed using Mask R-CNN model, enabling identification of individual cells.

Quantitative features were extracted from each segmented cell and used to train a supervised machine learning model based on a Random Forest classifier. Model performance was evaluated using accuracy, recall, f1 score and confusion matrix. Feature importance analysis was conducted to identify the most discriminative parameters. To visualize class separability and validate the discriminative capacity of the extracted features, Linear Discriminant Analysis (LDA) was applied for dimensionality reduction.

Results:

The trained Random Forest model achieved a classification accuracy of 93% in distinguishing between the four HSPC subpopulations. Performance metrics indicated

high precision and recall across all classes. The confusion matrix revealed minimal misclassifications, primarily between morphologically similar classes. Analysis showed that the texture-based feature, LBP, contributed most to classification performance.

Conclusions:

The results demonstrate the feasibility of accurately classifying HSPC subpopulations using machine learning models trained on quantitative image-derived features. The high classification accuracy and clear group separability suggest that subtle morphological and texture differences can be effectively captured and leveraged for automated cell identification.

This approach may serve as a basis for developing a personalized HSPC patient profile, potentially contributing to the design of tailored therapeutic strategies in AML by improving relapse risk assessment and guiding chemotherapy treatments.

Keywords:

Leukemia, Machine Learning, Image-Based Classification, Microscopy.

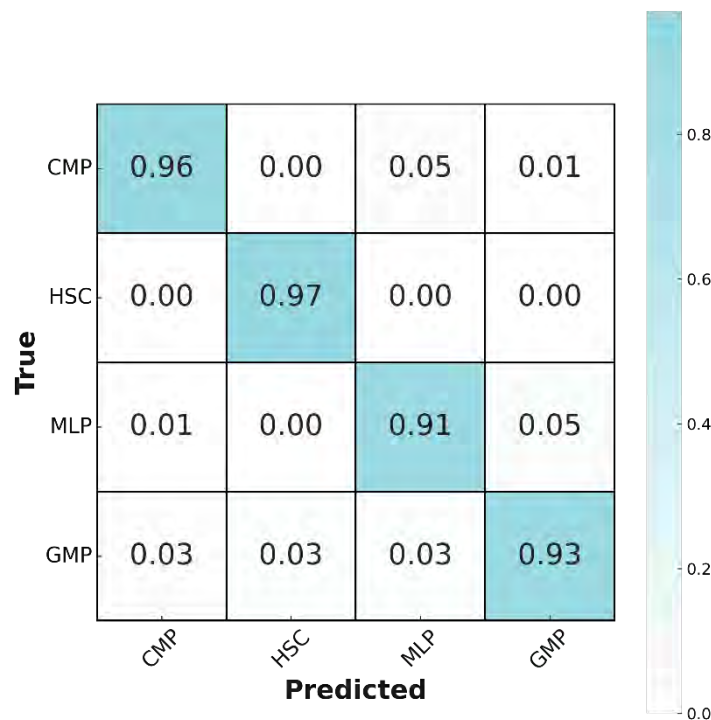


Figure 1: Confusion matrix of the tool's performance in classifying HSPC subpopulations, from microscopic images of bone marrow.

Retinal Vasculature Biomarkers for Stenosis Identification from Retinal Images

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Introduction:

Vascular stenosis is a pathological narrowing of blood vessels that may lead to serious cardiovascular complications. Early detection is essential but often depends on invasive or expensive diagnostic procedures. The retinal vasculature, visible in non-invasive fundus photography, provides a window into systemic vascular health. This project explores whether quantitative biomarkers extracted from retinal fundus images can distinguish between patients with stenosis and non-stenosis controls using machine learning techniques.

Methods:

Fundus images were segmented using a vessel segmentation application called lirot.ai to extract 28 quantitative vascular biomarkers, capturing geometric and caliber-related properties of arteries and veins. The dataset was divided into training and test sets while ensuring that no patient's images appeared in both. Feature selection was performed using the minimum redundancy maximum relevance (mRMR) method on the training set. Two classification models - logistic regression and random forest - were developed and evaluated using cross-validation and on a held-out test set. Permutation testing was used to assess statistical significance of model performance.

Results:

The logistic regression model achieved a test AUC of 0.738 and a permutation p-value of 0.031. The random forest model achieved a similar AUC of 0.744 with a p-value of 0.021. Statistical analysis revealed marked distributional differences in several biomarkers, including total arterial and venous area, between stenosis and control groups. Feature selection yielded a balanced set of artery and vein related features, suggesting that both vessel types carry diagnostic value.

Conclusions:

This study provides preliminary evidence that machine learning models trained on quantitative retinal vascular biomarkers may assist in distinguishing individuals with vascular stenosis from non-stenosis controls. The consistent selection of both arterial and venous features suggests that microvascular alterations captured in fundus images could reflect systemic vascular pathology. While these results are encouraging and support the potential of retinal imaging as a non-invasive diagnostic tool, they should be interpreted with caution due to the limited dataset size and scope. Additional research with larger, more diverse populations will be essential to confirm these findings and assess their generalizability in real-world clinical settings.

Keywords:

Fundus imaging, vascular stenosis, machine learning

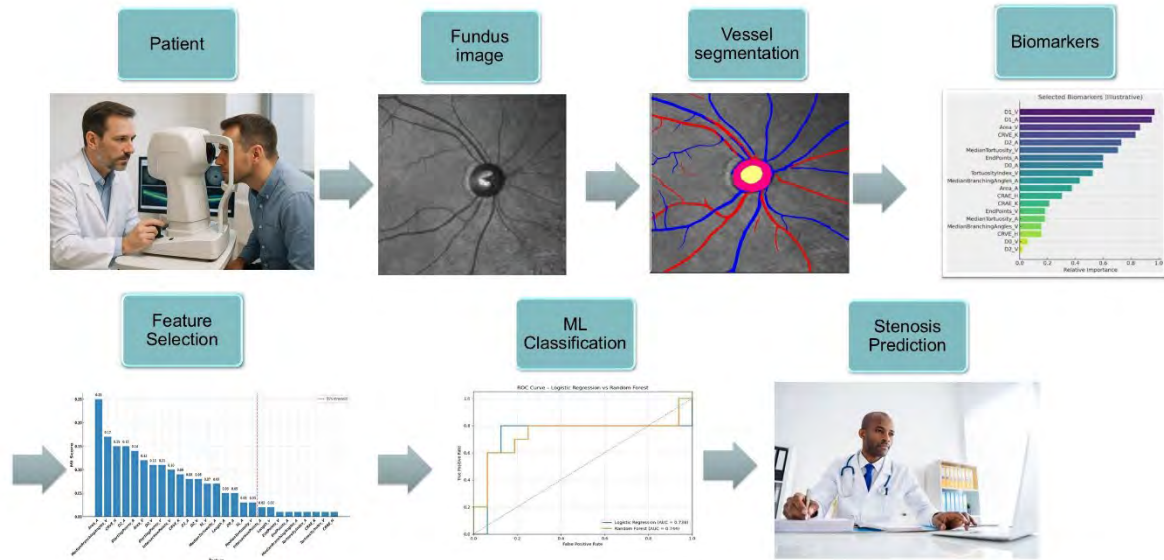


Figure 1. End-to-end pipeline for stenosis detection based on retinal images. Fundus photographs undergo vessel segmentation and biomarker extraction, followed by feature selection and machine learning classification to predict disease status.

Software Development for Automated Cardiac Motion Analysis in Larval Zebrafish

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Introduction:

Atrial fibrillation is an arrhythmia initiated by ectopic atrial foci which create rapid atrial activity, with variable ventricular response governed by atrioventricular node conduction. A novel approach of researching atrial fibrillation in-vivo has been developed and adapted, using zebrafish larvae; although the zebrafish heart is two-chambered, its electrical properties resemble those of humans. Moreover, the zebrafish embryo is transparent and allows direct observation of the heart rate and its variability. Progress in such approach necessitates detection tools tailored especially for in-vivo imaging of zebrafish larvae, both for pre-recorded data and live-imaging setting. With this motivation in hand, the objective outlined here is to develop a tool for detecting multiple, consecutive heart signals in situ from zebrafish larvae.

Methods:

Our analysis pipeline consists of four distinct stages, applied to each frame of the video recordings. First, individual zebrafish hearts are detected using a pre-trained, customized object detection model. Second, potential regions of interest are identified within each detected heart, using both analytic and supervised machine learning algorithms. Third, cardiac signals are extracted from each region of interest in the form of accumulated intensity per frame. Finally, the extracted signals undergo post-processing to compute heart rate variability metrics, and the resulting data is exported in both vector and video file formats. The analysis was implemented using the Python programming language, incorporating various specialized libraries.

Results:

The detection network demonstrates strong performance in identifying individual hearts within each frame. The object detection model achieved a mean average precision score of 0.844 for the “Heart” label, indicating high in-vivo accuracy. Extracted cardiac signals achieved signal to noise ratios of over 50dB across automated and manual region of interest selection. Accurate RR intervals and heart rate variability metrics were also successfully obtained.

Conclusions:

The study successfully developed software that detects zebrafish larvae hearts in both live and pre-recorded microscopic videos, while extracting cardiac signals and heart rate variability metrics from each larva. This platform offers a strong foundation for advancing atrial fibrillation research using zebrafish larvae.

Keywords:

Machine Learning, Live Imaging, Atrial Fibrillation, Image Analysis

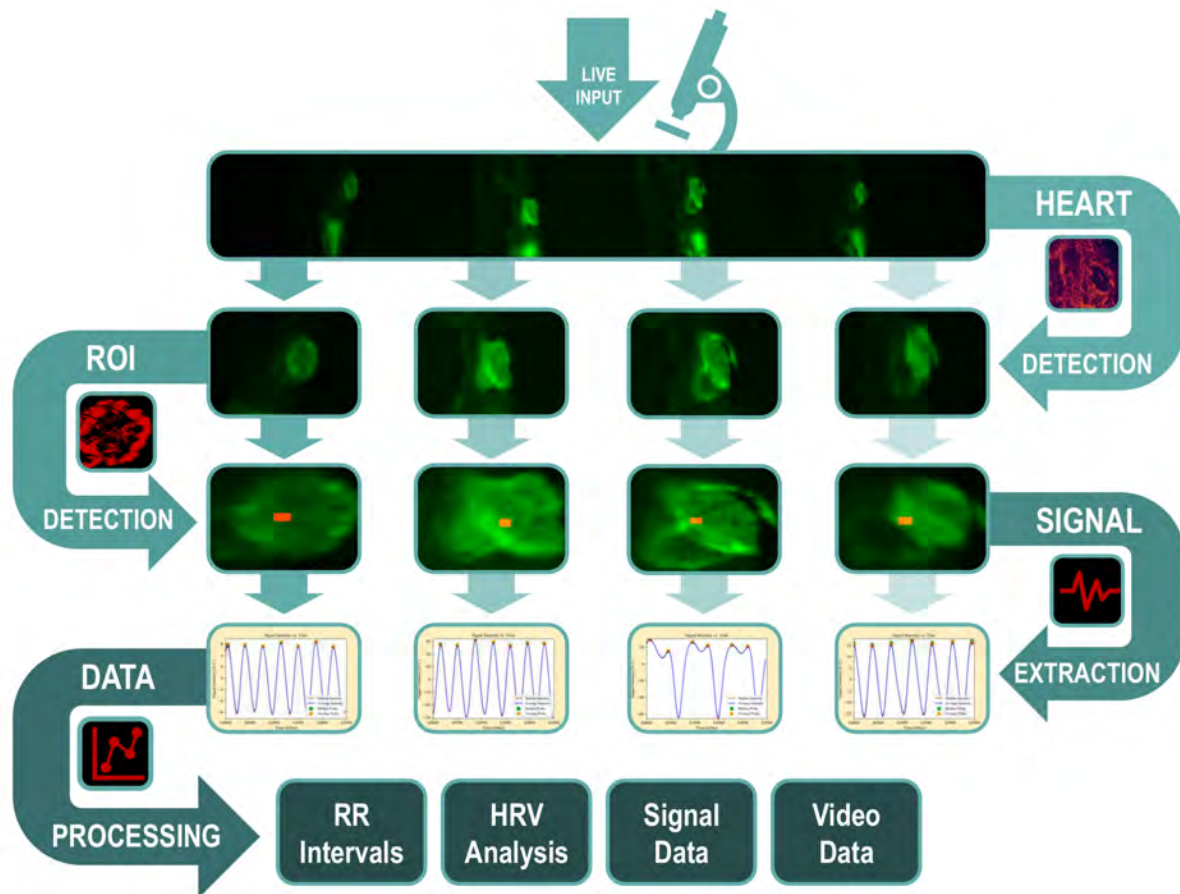


Figure 1: Schematic representation of the four-stage analysis pipeline applied to each video frame containing zebrafish larvae hearts, from top to bottom: (I) detection of individual hearts, (II) identification of regions of interest within each heart, (III) extraction of cardiac signals from each region of interest in the form of accumulated intensity per frame, and (IV) post-processing and analysis of the signals to derive heart rate variability metrics and export data in vector and video file formats.

Risk Prediction of Cardiovascular Diseases in Obstructive Sleep Apnea Patients Using Machine Learning

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Introduction:

Obstructive Sleep Apnea (OSA) is a disorder characterized by repeated breathing pauses during sleep. It affects nearly one billion adults worldwide and is often undiagnosed. Up to 80% of patients with heart failure, hypertension, or coronary artery disease also suffer from this condition. Early detection of cardiovascular disease (CVD) risk is particularly critical in these individuals, as their sleep-disordered breathing can silently increase heart damage over time. This project aims to develop a machine learning-based model to predict cardiovascular risk in patients with OSA.

Methods:

We applied a machine learning-based approach to assess the association between OSA and CVD risk, using the Sleep Heart Health Study (SHHS) dataset. The prediction target was defined as a composite outcome including four cardiovascular conditions: Myocardial Infarction, Stroke, Congestive Heart Failure, and CVD Death.

Features were grouped into three categories:

1. Sleep-related (e.g., Apnea-hypopnea index (AHI), total sleep time, daytime sleepiness, oxygen saturation).
2. Demographic (e.g., age, BMI, sex).
3. CVD-related (e.g., blood pressure, cholesterol, smoking status, hypertension).

During preprocessing, we performed statistical analysis, handled outliers, imputed missing values, and classified OSA severity based on the AHI. Feature selection was guided by clinical expertise and univariate Receiver Operating Characteristic Area Under the Curve (ROC-AUC) scores.

We initially trained 3 standard classification models: Logistic Regression, Random Forest, and Support Vector Machine (SVM). Hyperparameters were optimized using grid search and cross-validation, and class imbalance was addressed using weighting techniques. Model performance was evaluated using several metrics: accuracy, precision, sensitivity, F1-score, and ROC-AUC.

To enhance prediction performance, we tested additional strategies: Training separate models for each CVD outcome, stratifying patients based on OSA severity, model performance across different follow-up intervals, and applying Cox proportional hazards models to incorporate survival time into the analysis.

Due to the limitations of AHI as a severity metric, we engineered a physiological feature called Hypoxic Burden (HB). This measure captures the total depth and duration of oxygen desaturation events during sleep. It was incorporated into our models to represent the cumulative hypoxic stress induced by OSA. Model robustness was evaluated using bootstrapping technique.

Results:

Our final model achieved an AUC of approximately 0.83 in predicting CVD death among patients with moderate to severe OSA (Figure 1).

Conclusions:

Sleep features alone were insufficient for accurate CVD prediction. Non-linear models outperformed Logistic Regression, reflecting the data's non-linear nature. The AHI alone lacked detail, combining it with the HB feature improved model performance.

Keywords:

Obstructive Sleep Apnea, Apnea-Hypopnea Index, Hypoxic Burden, Cardiovascular Disease

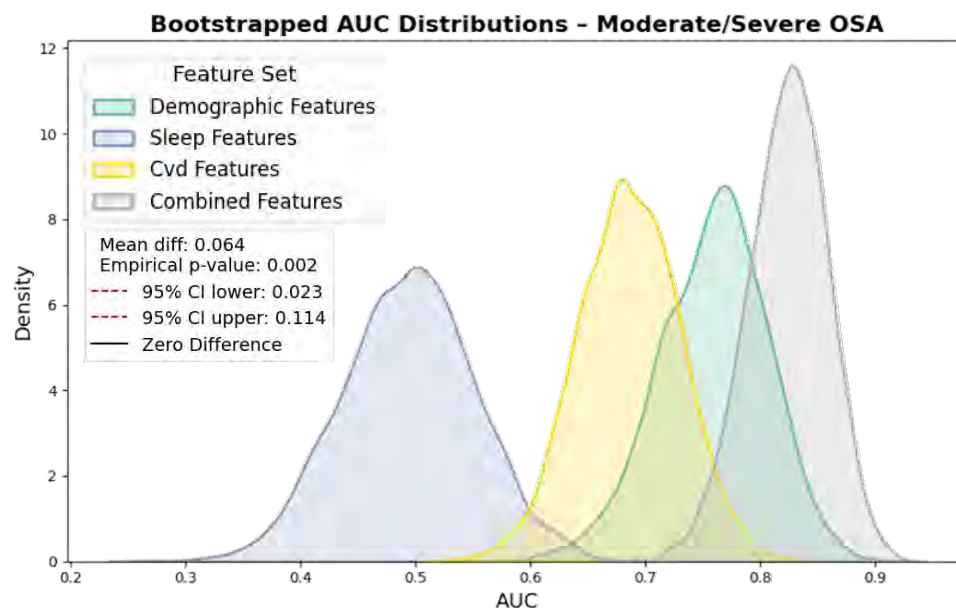


Figure 1: Predictive performance of Random Forest models evaluated with bootstrapping, using CVD Death as the prediction target.

The combined features model, tested on moderate to severe OSA group, achieved an AUC of ~0.83 and showed statistically significant improvement over the demographic features model.

A Programmable Optical-Pacing System for Chronic Pacing of Optogenetic hiPSC-Cardiomyocytes

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Introduction:

Cardiac arrhythmias - caused by abnormal electrical activity in the heart - are a major global health issue, affecting nearly one-third of the population. Studying arrhythmias and developing treatments require precise, long-term, and non-damaging pacing of cardiomyocytes. However, standard methods like electrical stimulation or fluorescent dyes can harm cells or limit experiment duration. To address these limitations, we developed a programmable system for chronic optical pacing of genetically engineered cardiomyocytes expressing a light-sensitive ion channel. The platform enables non-invasive stimulation across 24 wells inside an incubator and serves as a valuable tool for arrhythmia and cardiac electrophysiology research.

Methods:

Our approach combines software development, biological preparation, and optical mapping.

Software - We adapted the Light Plate Apparatus (LPA) to support two LEDs per well. The firmware was modified to allow cardiomyocyte pacing at millisecond resolution with control over frequency, illumination duration, and intensity. A custom graphical user interface (GUI) enables users to configure LED parameters across all wells and export protocols to the LPA.

Biological - CoChR-expressing hiPSC-derived cardiomyocytes (CoChR-hiPSC-CMs) were seeded into 24-well glass-bottom plates to form cardiac cell sheets (CoChR-hiPSC-CCSs). Seeding methods were optimized for compatibility with the LPA. Multiple pacing protocols were applied using the GUI to evaluate performance.

Optical Mapping - A voltage-sensitive indicator was added to the medium to visualize electrical activity. The plate was mounted on the LPA, illuminated from above with red light, and imaged using a high-speed camera. Fluorescence changes corresponding to action potentials were captured and analyzed.

Results:

We applied optical pacing at 0.5, 1.0, 1.5, and 2.0 Hz with varying light intensities. Action potentials closely followed by programmed pacing rates, confirming reliable capture. Higher intensities produced diffuse activation, while lower intensities showed clear propagating wavefronts. Light-induced artifacts in raw signals were identified and corrected during signal analysis.

Conclusions:

We successfully developed a programmable optical pacing platform for cardiomyocyte studies. The GUI simplifies setup, and the system enables robust, repeatable pacing across multiple frequencies. Our findings highlight the value of low-intensity illumination for conduction mapping and the importance of artifact correction. This platform offers a scalable solution for arrhythmia research.

Keywords:

Optogenetic, hiPSC-CCSs, Optical Pacing, Arrhythmias.

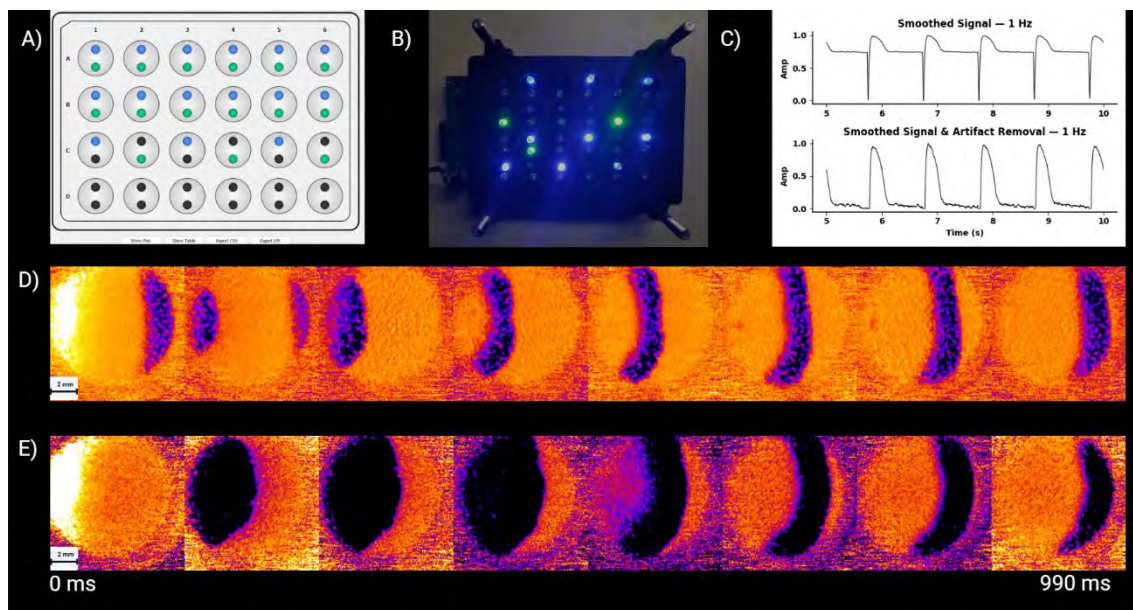


Figure1:

(A) GUI interface for LED configuration. (B) Assembled LPA system. (C) Fluorescence traces from CoChR-hiPSC-CCSs paced at 1 Hz, showing raw signals alongside processed data after artifact removal and smoothing. (D) APD map showing signal propagation under 10% light intensity for 990 [ms]. (E) APD map showing propagation under 30% light intensity for 990 [ms].

Real-time 3D Markerless Motion Tracking System using Neural Networks

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Introduction:

Understanding motor control and behavior in small animals, particularly mice, is fundamental to modern neuroscience and translational rehabilitation research. Traditional motion tracking systems often rely on physical markers, which interfere with natural movement and introduce experimental limitations. To address these limitations, our project aims to develop a real-time, three-dimensional markerless motion tracking system using deep neural networks (DNNs), with a particular emphasis on DeepLabCut. Our system is designed to provide accurate, scalable, and non-invasive kinematic analysis of freely moving mice, enabling new insights into motor learning and neurological functions.

Methods:

Our system integrates three synchronized high-resolution ALVIUM 1800U-240m cameras, to capture front and lateral views of a mouse on a split-belt treadmill. Cameras were mounted on a custom SolidWorks-designed bridge with socket joints—and later a pre-manufactured aluminum bridge—to enhance structural integrity. Optimal distances and angles for each view were set to target key anatomical landmarks. Videos are processed with DeepLabCut—a deep learning framework trained on manually labeled keypoints—for 2D pose estimation, then triangulated into 3D trajectories (using StreamPix and VimbaX SDK software). Checkerboard patterns enable accurate multi-camera calibration.

Results:

The pipeline was validated on six *pre-recorded top/side-view videos* from the *Engelhard Lab*. Key stages—frame extraction, manual labeling of 8 body parts, network training, evaluation, and pose estimation—were completed in DeepLabCut using a ResNet-50 network. Trained for ~200 epochs on 200 manually labeled frames (95% train- 5% test), using mean squared error (MSE) loss, achieving a 2.24-pixel error on training data and 7.22-pixel error on test data. The model then consistently detected 8 different body parts across variable lighting and motion speeds, demonstrating robust 2D keypoint tracking. Meanwhile, the split-belt treadmill, aluminum bridge, and three Alvium cameras are fully assembled and configured via VimbaX SDK and StreamPix, with infrastructure in place for immediate transition to full 3D reconstruction once live recordings are available.

Conclusions:

This project successfully develops a flexible, markerless motion-capture system by combining precision hardware (aluminum bridge and jointed mounts) with DeepLabCut neural-network tracking. Our 2D validation demonstrates robust, non-invasive keypoint detection in freely moving mice, replacing intrusive marker systems. With synchronized acquisition tools and calibration workflows in place, the system is ready for full 3D reconstruction to be performed in the near future. This framework paves the way for real-time studies in neurorehabilitation, behavioral neuroscience, and motor-disorder analysis.

Keywords:

3D Markerless Motion Capture, DeepLabCut, Neural Networks, Behavioral Neuroscience

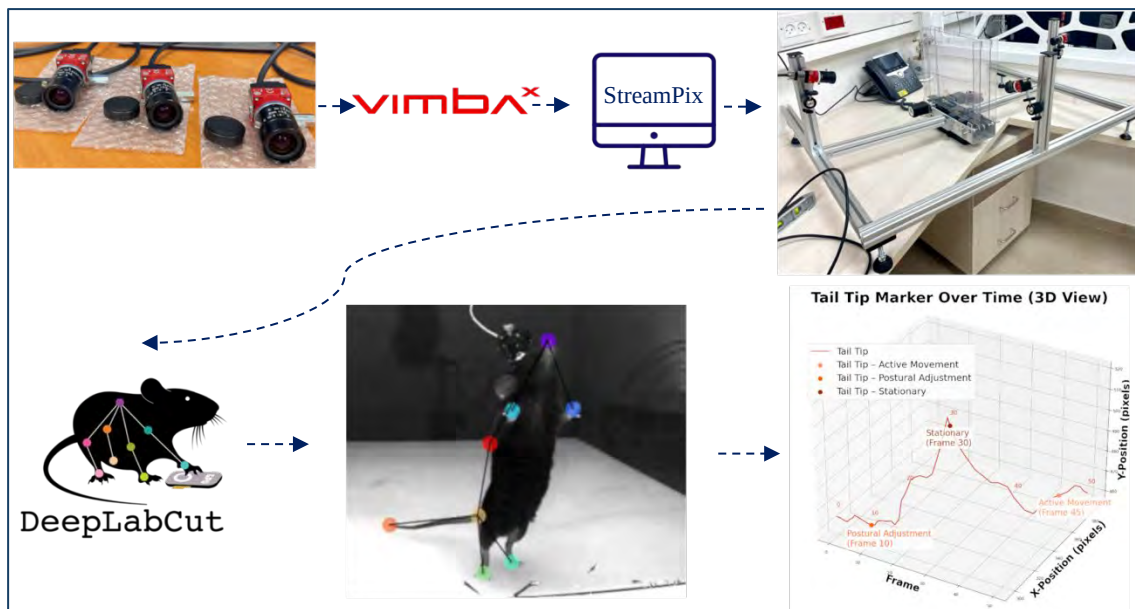


Figure 1: Schematic pipeline: three Alivum cameras mounted on the aluminum bridge capture synchronized videos (VimbaX SDK & StreamPix). Extracted frames are processed in DeepLabCut, producing 2D keypoints. The plot shows the tail tip's 3D trajectory of the marker over time, with three annotated movement phases.

Automated Interface for Metastatic Potential Analysis Using Nanoparticle Encapsulation

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Introduction:

Cancer metastasis remains the leading cause of cancer-related mortality worldwide yet current methods for assessing metastatic potential are labor-intensive, costly, and often lack accuracy and timeliness. This project aims to address these limitations by developing an automated, user-friendly graphical interface that applies advanced image processing techniques to assess the metastatic potential of cancer cells. By using nanoparticle encapsulation as a visible biomarker, our tool aspires to enable early detection and more personalized treatment decisions in oncology research and practice.

Methods:

Our methodology integrates fluorescent microscopy image acquisition, tailored preprocessing, adaptive segmentation, statistical correlation, and intuitive visualization in an integrated workflow. Tissue images stained for nuclei and nanoparticle encapsulation are acquired in CZI or TIFF formats. The graphical interface allows users to select tissue type and nanoparticle size. DAPI-stained and nanoparticle-labeled images are normalized to standardize pixel intensity. Preprocessing parameters such as contrast enhancement, gamma correction, denoising, and morphological thresholds are dynamically adjusted according to both particle size and cell type to enhance signal clarity. Segmentation includes adaptive thresholding, morphological operations such as closing, opening, and dilation, and background subtraction to isolate relevant cellular regions and suppress artifacts. In certain cases, clustering techniques refine the detection of nanoparticle regions. The relationship between nanoparticle encapsulation and nuclei is quantified using the Pearson Correlation Coefficient. An overlay process generates composite images to visually validate co-localization patterns. The graphical user interface supports batch file upload, automatic file renaming and grouping by channel, and real-time side-by-side visualization in a 2×2 grid for each image set. Users can instantly review Pearson correlation results and inspect distribution histograms and summary statistics. Final outputs can be exported as PDF reports and CSV files, providing a complete, standardized, and reproducible metastatic potential analysis pipeline.

Results:

Initial results demonstrated significant improvements in signal quality through dynamic preprocessing and adaptive segmentation. The combination of background subtraction and proximity masking with smaller nanoparticle sizes effectively isolated relevant regions of interest. Pearson correlation analysis revealed measurable co-localization patterns, supporting nanoparticle encapsulation as a promising biomarker for metastatic potential. The graphical

interface successfully handled multiple file formats, automated batch processing, and clear result visualization, demonstrating strong usability for both research and potential clinical applications.

Conclusions:

This project demonstrates the feasibility of an automated system for evaluating cancer cell metastatic potential using nanoparticle encapsulation as a biomarker. By combining robust preprocessing, adaptive segmentation, and intuitive statistical analysis within a graphical interface, the tool delivers fast, consistent, and accessible results. Future development will expand dataset diversity, refine feature detection using AI, and advance the tool toward real-world use in oncology research and clinical settings.

Keywords:

Metastatic Potential, Image Processing, Nanoparticle Biomarker, Graphical Interface.

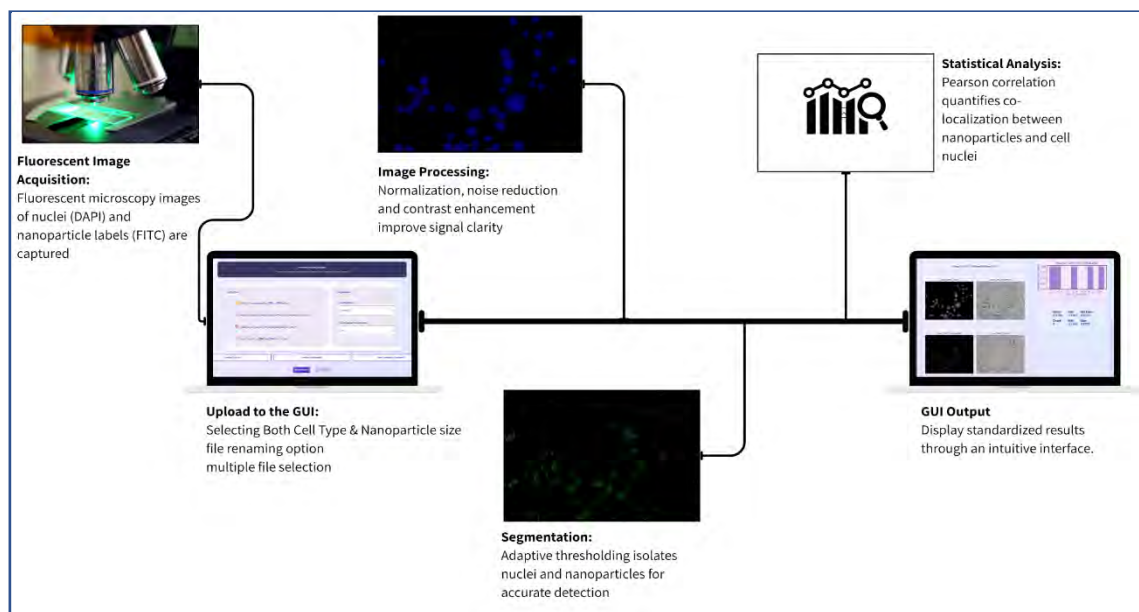


Figure 1: Schematic Workflow and Example Output of the Automated Interface for Metastatic Potential Analysis

Rigidity Assessment for DBS Surgery

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Introduction: Parkinson's Disease (PD) is a progressive neurodegenerative disorder caused by dopaminergic neuron loss in the substantia nigra, leading to tremor, bradykinesia, and rigidity. Rigidity, defined as increased resistance to passive movement, is associated with abnormal activity in the basal ganglia. As Parkinson's progresses, reduced drug efficacy often leads to surgical treatments like Deep Brain Stimulation (DBS). DBS involves implanting electrodes into deep brain regions, typically the subthalamic nucleus or globus pallidus internus, to deliver high-frequency stimulation and modulate motor circuits. The stimulation target is identified using medical imaging and confirmed with electrophysiological testing for precise electrode placement. To evaluate the clinical effect of stimulation in real time and guide electrode placement, rigidity is manually assessed intraoperatively through passive wrist movement at varying stimulation levels. This assessment relies on subjective clinical judgment and semi-quantitative scales such as the Unified Parkinson's Disease Rating Scale (UPDRS). Our goal is to develop an objective, standardized method to quantitatively assess muscle rigidity during Deep Brain Stimulation surgery, independent of surgeon variability.

Methods: We created a C++ algorithm integrated with a Phantom® Premium™ 1.5 haptic device robot (3D Systems, Inc.). The system simulates an active motor task where the subject moves the robot's stylus with the forearm secured by a strap, allowing only wrist movement. Two conditions were conducted: (1) repeated back-and-forth movement between two fixed virtual walls (free moving as a control trials), and (2) the same task with intermittent random walls introducing unexpected resistance (the interactions with these walls can be used as a measure of rigidity). Each participant performed four back-and-forth movements per simulation. Kinematic data (position and velocity) were collected in both conditions. In the second condition- contact force, wall penetration, and velocity decay were measured per wall encounter. The system was tested on five healthy individuals and on profiles mimicking Parkinsonian rigidity.

Results: Across both conditions (with and without random walls), clear differences emerged between healthy participants and those simulating Parkinsonian rigidity. Both experiments showed higher deviation errors in the rigidity group, especially in the simulation featuring random walls. The rigidity group also showed greater wall penetration and slower velocity decay during wall encounters.

Conclusions: The present findings highlight the potential of a robotic system as an objective tool for assessing motor rigidity. Kinematic parameters- trajectory consistency, peak wall penetration, and velocity decay demonstrated sensitivity to deviations associated with rigidity-like behavior. However, further validation on individuals diagnosed with Parkinson's disease

is necessary to establish the system's clinical relevance. Future developments should incorporate passive movement paradigms, where the robot initiates joint-based hand movements, enabling a more accurate and comprehensive evaluation of muscle tone and rigidity that better simulates the neurosurgeon's intraoperative assessment.

Keywords: Parkinson's Disease PD ,Deep Brain Stimulation (DBS), Rigidity, Haptic Robotics

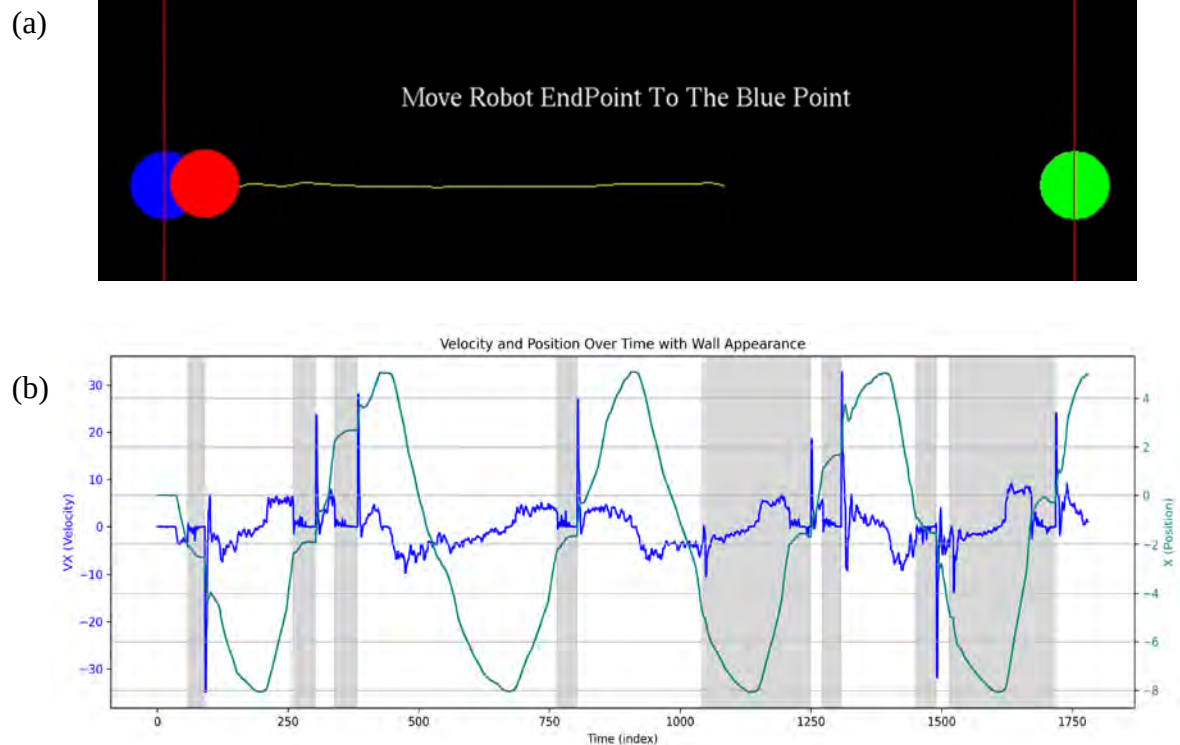


Figure 1: (a) Screen view of simulation, instructing the participant to move the robot's endpoint (red) from right to left, between the targets. (b) Graph showing participant position (green) and velocity (blue) along the x-axis over time. Gray regions indicate periods when random walls appeared during the simulation.

Developing a Tool for Storytelling Quality Assessment Using Acoustic Features

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Introduction:

Storytelling plays a central role in early childhood development, particularly when delivered in an interactive and expressive manner. Research has shown that dynamic reading styles engage brain regions associated with attention, imagination, and language processing. Despite this, most tools designed to assess storytelling quality still rely heavily on subjective observation. This project introduces an automated tool that analyzes storytelling recordings and assigns scores in three categories: Expressiveness (engagement and intonation), Clarity (pronunciation), and Naturalness (speech rhythm and flow), offering an automated way to evaluate acoustic delivery quality.

Methods:

A dataset of 69 Hebrew storytelling recordings was collected from three experimental sources, then filtered for quality. To increase data quantity and focus on adult speech, the recordings were segmented into shorter clips, resulting in 119 labeled audio samples. Each was manually rated on a 1-5 scale for expressiveness, clarity, and naturalness. After labeling, the data was preprocessed by removing long silences, resampling all recordings to a uniform sampling rate, and applying RMS-based volume normalization.

The analysis included two phases. In Phase 1, a lightweight GUI was built to extract and visualize simple acoustic features - pitch range, pitch change rate, formant dispersion, amplitude dynamics, and speech rate - against user-selected benchmark scores. Transcription via the Whisper library was optionally included to estimate speech rate or print text, though not used for scoring. In Phase 2, over 200 features were extracted, including MFCCs and other spectral descriptors. A Random Forest regression model with Leave-One-Out Cross-Validation was used to predict scores. Feature selection was applied to improve generalization by reducing dimensionality and addressing the imbalance between features and sample size.

Results:

Initial models trained on the full feature set produced low R^2 scores, likely due to overfitting. Performance improved significantly when low-importance features were removed, reaching its peak when 20–30 features were retained per label. This corresponded to about 15-25% of the training set size. Across all labels, pitch-related features—particularly pitch change rate—consistently emerged as the most informative. Some features showed low correlation with human scores but were ranked highly by the model, indicating the detection of nonlinear patterns beyond simple statistics.

Conclusions:

The project demonstrated the feasibility of using acoustic features to approximate subjective evaluations of storytelling quality. Through feature selection and cross-validation, the model achieved an R^2 score of approximately 0.3 for all three labels—an encouraging result, given the limited data and the inherently subjective nature of the task. In the behavioral and social sciences, where human perception and interpretation are central, R^2 values in the range of 0.2-0.4 are often considered meaningful, in contrast to the physical sciences, where higher thresholds are typically expected. These results suggest that machine learning can capture relevant patterns in expressive speech delivery, even when subjective ratings are used as ground truth. Further improvements in model performance are likely to come from expanding the dataset and refining the labeling process.

Keywords:

Machine Learning, Speech Signal Processing, Acoustic Feature Analysis, Storytelling Quality Assessment

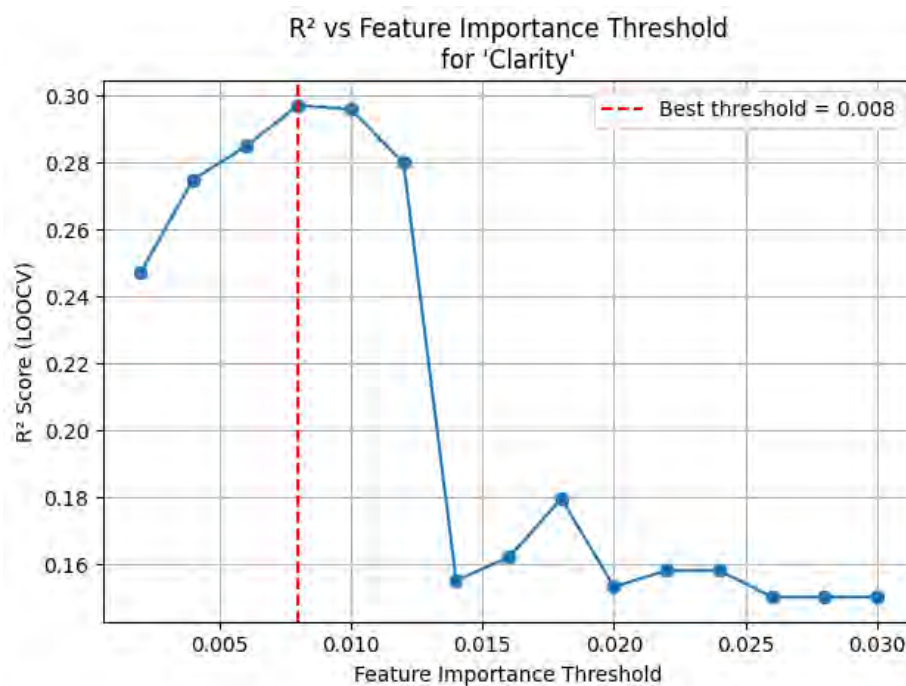


Figure 1: R^2 score vs. feature importance threshold for the Clarity label. A maximum score of ~ 0.3 was achieved using a small subset of high-importance features. Similar patterns were observed for all three labels, highlighting the effectiveness of targeted feature selection.

Development of Actuation and Sensing Capabilities for Robotic Catheter

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³ Spinodal

Introduction:

Cardiac catheterization procedures require precise navigation within the dynamic environment of the human heart. Current catheters- manual and robotic- often lack the fine control needed to perform complex interventions safely. This project aimed to study catheter behavior under internal and external forces to improve the accuracy of the catheter movement. Initially, we focused on understanding the relationship between injected volume and the catheter's bending and twisting angles. In the second phase, we examined how external forces affect catheter behavior to provide feedback about tissue contact during navigation.

Methods:

In the first phase, we injected fixed volumes into the catheter and measured resulting bending angles. We plotted angle versus volume, inverted the graph, and used MATLAB's curve fitting toolbox to model the inverse relationship. The angle was measured using the NDI system, which tracks the position of a sensor embedded in the catheter via a magnetic field. The injection was performed using a CETONI pump's system. We designed and 3D-printed stabilizing parts in SolidWorks for consistent experimental conditions. In the second phase, we conducted two experiments: one without external contact, and another applying external force via a force gauge. We recorded angle, pressure, injected volume, and force in both setups to identify patterns indicating tissue contact. To control the catheter, we developed an ARDUINO-based system for precise fluid injection, using the function found earlier. We used PYTHON scripts to interface with Arduino, allowing programmable control over injection parameters. We developed a GUI displaying real-time data on pressure, volume, and catheter angle, enabling physicians to monitor catheter behavior during operations.

Results:

The first study part yielded an exponential graph of angle versus injected volume, confirming angle increases more rapidly as it grows. We used the inverse function in our control code, observing smooth and consistent catheter movement.

In the second part of the study, we simulated tissue contact by pressing the catheter against a surface mimicking heart membrane resistance. We measured internal pressure with and without contact and used the difference to estimate the external force. Plotting the data revealed the relationship between volume and pressure, offering insight into tissue contact effects on catheter behavior.

Conclusions:

We conclude that catheter motion follows approximately exponential behavior, meaning that for equal increments of injected volume, the angle increases more rapidly as the cumulative volume rises. We recommend implementing a more precise calibration process for each catheter type and suggest developing an automatic calibration mechanism to improve future applications.

The second part of the study revealed a distinct point at which internal pressure rises, serving as an indicator for the physician that the catheter has made contact with tissue.

Keywords: Robotic Catheter, Cardiac Intervention, Micro-Flow Technology, Catheter Calibration

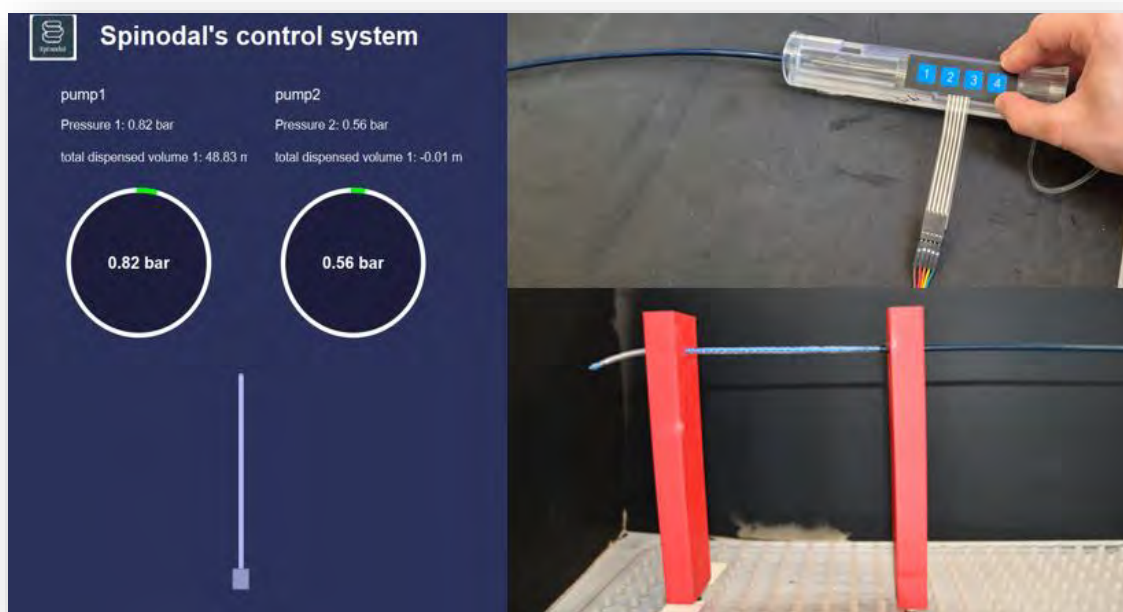


Figure 1- right down is the stabilized system we designed in SolidWorks with the catheter, right up is the Arduino system that control the catheter, and left is the Graphical user interface that we programmed in Python that gives the physician the ability to monitor the catheter and to gain information on Tissue's contact

PLEURAL EFFUSION DETECTION AND CLASSIFICATION USING A SMART STETHOSCOPE

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Introduction:

Pleural effusion, the accumulation of fluid in the pleural cavity, is a common clinical condition associated with heart failure, pneumonia, and malignancy. Early and repeated diagnosis is crucial but often relies on imaging tools such as ultrasound, X-ray, MRI or CT scans, which are expensive, not portable, and inaccessible in many settings. Our project aims to develop a non-invasive, low-cost, and accessible diagnostic method using the **Sanolla VoqX smart Stethoscope** combined with machine learning algorithms to detect and classify pleural effusion based on lung sound analysis.

Methods:

We collected 35 new clinical recordings from patients at Rambam Hospital alongside 110 previous recordings that were collected by previous students, using the VoqX digital stethoscope at 14 standardized thoracic points. The audio data underwent adaptive filtering and segmentation. Labeling was performed using Label Studio and breath cycle annotations. We focused on recordings from patients with one-sided effusion to highlight acoustic differences between the healthy and affected sides. Feature extraction was based on Mel-spectrograms and included spectral ratios, median energy, breathing rate, and time-to-peak. Several machine learning models were trained and evaluated, including Adaboost, bagged tree, logistic regression, and ensemble methods.

Results:

The AdaBoost model provided the best classification performance when applied to recordings from anatomical point 7, located at the lower right back, an area consistent with fluid accumulation in pleural effusion. The model achieved 93% accuracy in distinguishing effusion from non-effusion cases. In contrast, point 14, despite being anatomically similar and also positioned in the lower back, showed weaker performance. This may be due to patient fatigue by the time point 14 was recorded, affecting the quality of breath sounds. Combining data from multiple anatomical points led to lower performance, likely due to inter-point variability, environmental noise, and inconsistent breathing patterns. Logistic regression and bagged trees achieved moderate performance but lacked stability across different random splits. Feature analysis demonstrated distinct acoustic signatures in the lower thoracic region, especially in point 7, underscoring its diagnostic value. A comparison across multiple models and metrics confirmed that AdaBoost consistently outperformed others, not only in accuracy, but also in sensitivity, specificity, precision, F1 score, and AUC, demonstrating its robustness.

Conclusion:

Digital auscultation combined with machine learning demonstrates strong potential for non-invasive pleural effusion detection. Anatomical point 7 proved most informative, with features like average energy showing clear class separation. Among tested models, AdaBoost consistently outperformed others across all metrics. The Sanolla VoqX stethoscope's ability to detect infrasound enables AI to extract subtle diagnostic signals that may go unnoticed otherwise. These findings support integrating our approach into the VoqX system. Future work will focus on translating the algorithm into embedded C code and validating it through clinical trials, with potential to expand early detection in low-resource or remote settings.

Keywords:

Pleural Effusion, Digital Stethoscope, Machine Learning - AdaBoost, Acoustic Features.

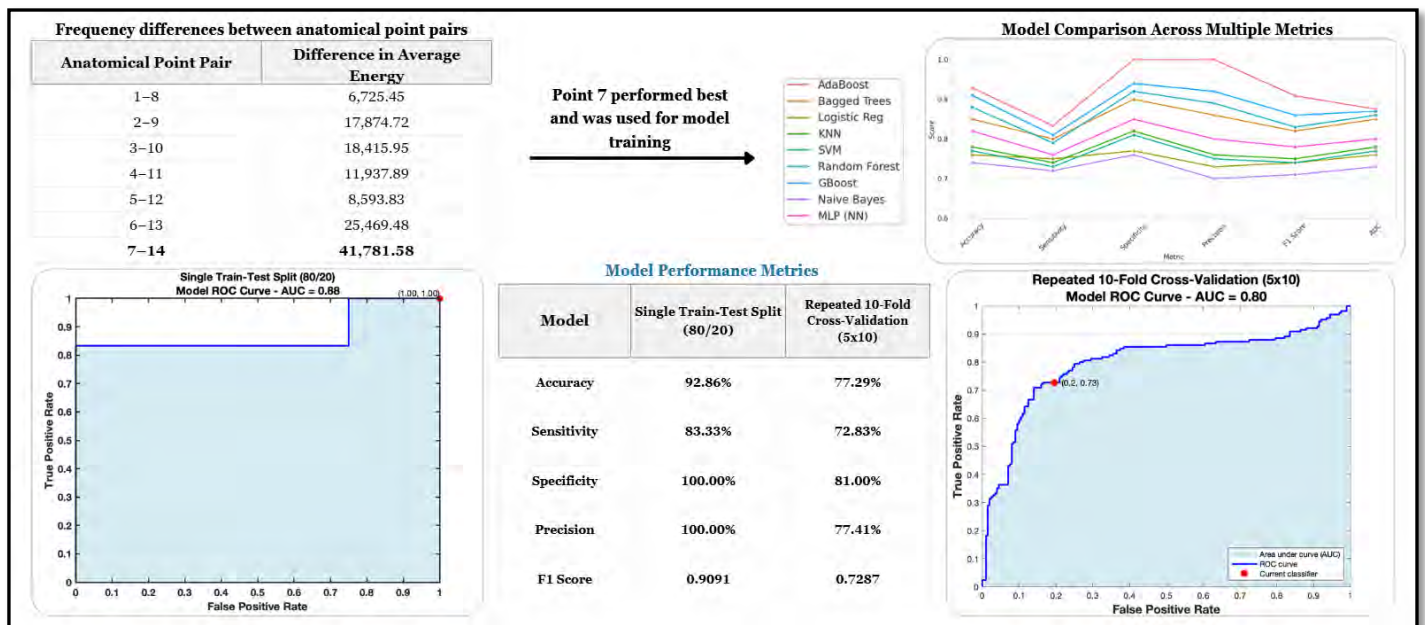


Figure 1: Model Selection and Performance Summary for Pleural Effusion Detection.

Digital Tools for Competitive Windsurfing Technique Analysis

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Introduction:

High-performance windsurfing involves rapid and dynamic maneuvers such as pumping, tacking, and jibing, all of which require a sophisticated combination of timing, body mechanics, and wind management. However, these maneuvers are often difficult to evaluate post-session due to a lack of objective, high-resolution feedback tools. Traditional coaching relies heavily on subjective observation, which is insufficient for identifying specific technique flaws.

To address this gap, we developed a suite of digital tools designed to automatically extract, classify, and evaluate critical windsurfing maneuvers using GPS and video data from sensors and mounted GoPro cameras. This toolchain supports automated detection and analysis of pumping events, turns (tacks/jibes), and their effectiveness, as well as generating synchronized video clips for visual performance review.

Methods:

We developed five distinct Python-based tools for capturing and analyzing windsurfing techniques:

1. GoPro Pump Detector:

This module identifies pumping events during windsurfing sessions using accelerometer and GPS data embedded in GoPro videos. After installing the necessary Python packages and FFmpeg, the user provides raw GoPro footage and a configuration file that includes thresholding parameters. The script processes the acceleration signal using a dual-stage moving average method, then applies threshold-based detection to flag pumping sequences. Detected pumping intervals are saved as CSV files and short video clips are automatically extracted using FFmpeg.

2. Turn Parser:

Turns are detected from GPS data exported from Sailmon devices. Users supply a Sailmon CSV file and a configuration file. The parser calculates heading changes and velocity thresholds to identify the start, peak, and end of each tack or jibe. Only turns above a minimum speed and angle threshold are included. The output is a turns.csv file containing time-stamped turn events, which serves as an input for downstream analysis.

3. Turn Analysis Tool:

Using the turns identified by the Turn Parser and the original Sailmon GPS file, this script quantitatively evaluates turn quality. By comparing the theoretical straight-line trajectory to the actual curved path during a turn, the tool estimates *lost distance*, *turn effectiveness*, and *turn exiting effectiveness*. Users can additionally visualize specific turns using plotTurn.py, which plots GPS paths, velocity made good, and wind alignment.

4. Turn Video Generator:

This tool bridges detected turn data and video analysis. Given GoPro footage and the corresponding turns.csv, the script extracts video clips of each turn using timestamp synchronization. Video clips are numbered and output, enabling athletes and coaches to visually review specific maneuvers alongside quantitative performance metrics.

5. Horizon Detection Algorithm:

The tool can be used to label and identify the horizon in any video footage. This tool goes frame by frame and utilizes OpenCV's image processing library to threshold and clean images, inspect pairs of points on the left and right of the image that lie on the threshold edge, construct a list of vectors between these pairs, then identify the most common direction among these pairs. By using this method, one can reliably extract the horizon line from pictures or videos. This can be used to identify pitch, roll, and yaw with a high level of accuracy.

Results:

The system successfully detected and extracted pumping events from over 2 hours of video footage and 100 turns across multiple windsurfing sessions. The Turn Analysis Tool revealed large variability in turn performance, with effectiveness scores ranging from 0.2 to 0.98. Negative/unrealistic effectiveness values were flagged and reviewed using the plotting tool, often revealing timing mismatches or poor exit trajectories. Pump detection clips aligned closely with acceleration spikes and demonstrated accurate temporal localization with a margin of error of less than 1 second of the ground truth. Turn video clips matched GPS-derived timestamps within an error margin of less than 1 second.

Conclusions:

We developed and validated a comprehensive toolchain for analyzing windsurfing technique through synchronized sensor data and video. The modular pipeline supports automated detection, quantitative assessment, and visual inspection of pumping and turning maneuvers. These tools enable athletes and coaches to objectively assess performance, isolate errors, and make data-driven improvements. Future work will involve extending these tools for real-time feedback, improving robustness to sensor dropout, and integrating machine learning for classification of performance patterns.

Keywords:

Windsurfing, Digital Signal Pipelines, Raw Sensor Data, Video Processing

SHARMA - SYSTEM FOR HOME BASED REMOVAL OF MALIGNANT ASCITES

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Introduction

Malignant ascites, characterized by fluid accumulation in the peritoneal cavity in late-stage cancers, leads to severe abdominal pain, respiratory distress, and malnutrition, significantly impacting quality of life. Current treatments - paracentesis, diuretics, and catheters, offer temporary relief with complications such as infection and patient dependency. There is a critical clinical need for a long-term, minimally invasive solution enabling patients to manage malignant ascites at home.

Methods

We developed a custom testing system, adapted for real malignant fluids, to evaluate membrane and pump components for an implantable drainage system. The setup includes an Arduino-based control unit with C++ time based code, KITA pressure sensors with dedicated calibration function and Sensirion low-flow sensors.

A testing run was conducted to compare different membrane structures, this test compared disks structure (2D) vs minichamber structure (3D)

A time controlled 3-channel Arduino system was built and used throughout the project run time, incorporating filter holders, vented biofluid, magnetic stirrer, KITA vacuum sensors and Sensirion low liquid flow sensors.

Experiments were conducted using both Deionized Water and patient-derived ascitic fluid, measuring flow rate, vacuum, membrane integrity, weight, permeability, specific gravity, and viscosity before and after tests.

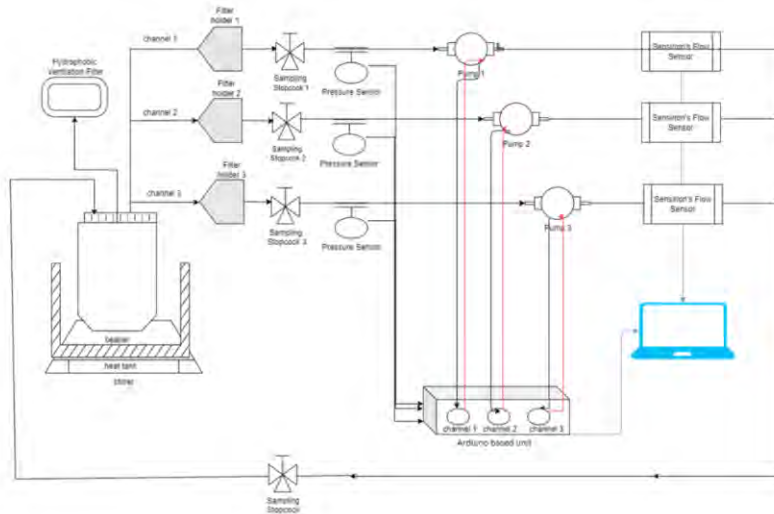


Figure 1: Diagram of SHARMA test setup showing 3-channel system and integrated sensors.

Results

Mid-run performance data and pre-/post-run weight measurements of the membranes were collected to evaluate changes in flow characteristics, fouling behavior, and material stability over time. These results provide insight into membrane efficiency under realistic malignant conditions. The results show that small-pore membranes often underperform under biological conditions, possibly due to clogging. The flow sensor integration was effective, but vacuum generation needs improvement. The ability to run biological fluid through the system demonstrates potential for clinical application with appropriate safety protocols.

Conclusions

We successfully built a membrane testing system and tested it with real biological fluids, identifying an ideal pore size range and several suitable materials.

We were able to identify a specific pore size range and materials for further testing and the company will continue the project using our results and protocols.

Key contributions include improvements to the FHFS protocol, integration of an Arduino-based pump testing setup and prototype building and development of a full 3D CAD model for the system for more consistent results.

The Relations Between Reading Fluency and Comprehension in Children with Benign Epilepsy: Behavioral and fMRI Findings

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Introduction:

Reading fluency plays a crucial role in supporting reading comprehension. However, children with benign epilepsy often struggle with both reading fluency and comprehension, despite having otherwise typical cognitive profiles. The specific neural mechanisms linking these two aspects of reading in this population remain poorly understood. This study examined how reading fluency relates to reading comprehension and the underlying brain network connectivity in children with benign epilepsy compared to typically developing peers.

Methods:

Fifty Hebrew-speaking, right-handed children aged 7 to 13 participated, including 31 typically developing readers and 19 children with benign epilepsy. All completed standardized assessments of reading fluency, phonological awareness, reading comprehension, and executive functions. Brain imaging was conducted using functional magnetic resonance imaging (fMRI) while participants performed a reading comprehension task. Functional connectivity was assessed within and between cognitive control networks (cingulo-opercular, frontoparietal, dorsal attention, and ventral attention) and sensory networks (auditory and visual). Independent t-tests and Pearson correlations examined group differences and brain–behavior relationships.

Results:

Children with epilepsy performed significantly lower in reading fluency and phonological awareness, especially in syllable omission and read-aloud tasks. Typically developing readers showed stronger connectivity within and between executive and visual networks. In contrast, the epilepsy group showed reduced modulation and integration. In typically developing children, reading fluency correlated positively with connectivity between control and attention networks. In children with epilepsy, reading fluency and comprehension were more related to auditory and visual network connectivity. Executive function performance in typically developing children was linked to frontoparietal and attention networks, while in children with epilepsy it was associated with sensory-attentional network activity, suggesting more reactive and less efficient control mechanisms.

Conclusions:

Children with benign epilepsy show altered brain connectivity during reading, with reduced engagement of executive networks and greater reliance on sensory pathways. These disruptions may underlie their reading and executive function difficulties. Interventions focused on

strengthening executive control and audiovisual integration may improve reading outcomes in this population.

Keywords:

Benign Epilepsy, Reading Fluency, Executive Functions, Functional Connectivity

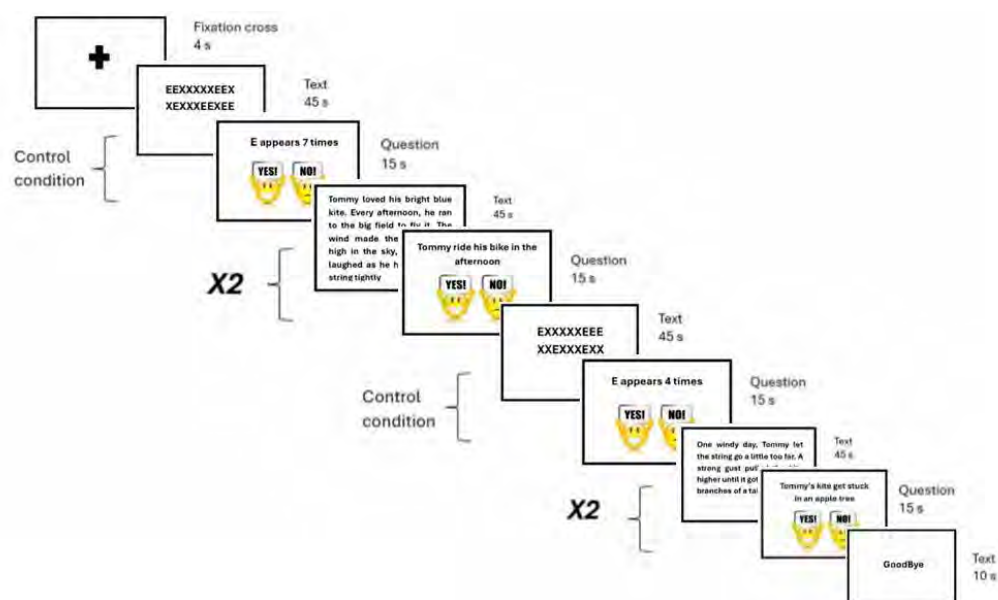


Figure 1. Schematic representation of the fMRI reading comprehension task.

The task included six alternating blocks: two control and four reading comprehension blocks. In control blocks, participants viewed sequences of the letters “X” and “E” for 45 seconds, followed by a 15-second yes/no question about the number of “E”s. In comprehension blocks, participants read short texts for 45 seconds and answered a yes/no comprehension question. Responses were given via button press (red for “yes,” blue for “no”). The entire task lasted 374 seconds and was performed inside the MRI scanner. To accommodate the pediatric population, child-friendly procedures and instructions were used to ensure comfort and reduce head motion during scanning.

Development of a Needle Guidance System for PCNL Surgery Based on Real-Time Surface Matching and CT Integration

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Introduction: Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure for kidney stone removal, requiring precise needle access to the renal collecting system. This step is technically challenging due to anatomical variability, organ motion, and limited intraoperative imaging. We present a novel laser-guided needle navigation system that integrates real-time surface matching with preoperative CT data, without the need for skin CT markers or expensive tracking equipment.

A structured-light 3D scanner captures the patient's skin surface intraoperatively and aligns it with a prior CT scan. A deep learning module enhances robustness against soft-tissue deformations. The resulting needle trajectory is projected onto the patient's body via a laser pointer, offering intuitive, real-time guidance.

Methods:

- The workflow begins with reconstructing the skin surface from a preoperative CT scan using an active contour algorithm. The surgeon defines the desired needle trajectory directly on the CT.
- "Intraoperatively", the patient's (CPR model in our POC project) surface is scanned using a structured-light 3D scanner (~30 seconds). A calibration cube is then detected using RANSAC to establish a spatial reference frame.
- Prior to registration, a preprocessing step enhances the overlap between CT and scanned surfaces by filtering and focusing on stable regions. Point-to-plane is then applied for accurate alignment.
- To account for posture-related deformations, a deep learning model predicts non-rigid corrections based on surface geometry, refining registration results.
- Finally, inverse kinematics computes the robotic arm configuration required to project the preplanned trajectory onto the patient's body using a laser.
- System performance was validated through a successful proof-of-concept experiment on a high-fidelity resuscitation mannikin.

Results: System performance was evaluated using realistic medical training CPR doll. The average cube detection error and the average relative positioning error were both 1.5 mm. The robotic arm positioning error was up to 4 mm. The resulting laser-guided trajectory achieved targeting accuracy within 1 cm of the target in our POC model, consistent with clinical requirements for PCNL.

Conclusions: We introduced an innovative, marker-less laser-guided navigation system for PCNL that combines CT-based trajectory planning with real-time surface scanning and registration. The system achieves clinically acceptable targeting accuracy, using only low-cost, accessible hardware. These results demonstrate strong potential for integration into clinical

workflows and pave the way for future validation under real-world anatomical variability and soft-tissue deformation.

Keywords: Needle navigation, skin reconstruction, registration, PCNL surgery.

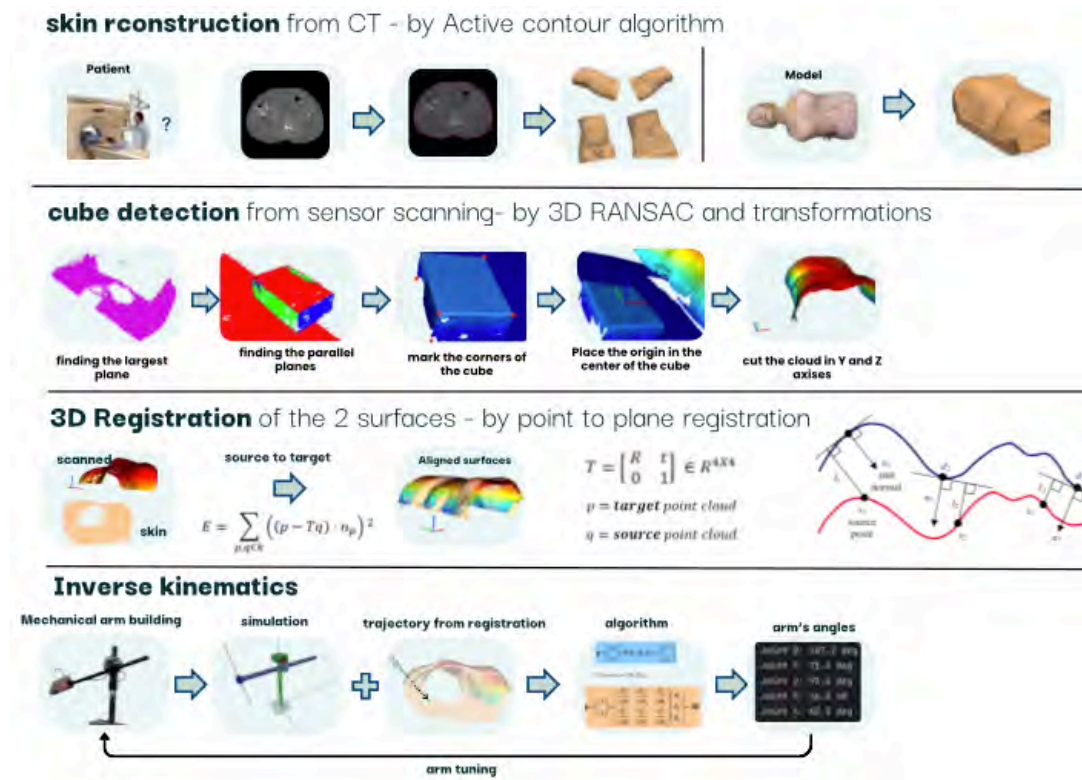


Figure 1 - illustration of the main pipeline of our system, detailing each stage of the algorithm from preoperative planning to intraoperative guidance. The process includes CT-based surface reconstruction, manual trajectory planning, real-time surface scanning, calibration, surface registration with optional deformation correction, and final laser-based needle projection. The pipeline reflects the integration of geometric processing and deep learning to enable accurate and marker-less navigation for PCNL procedures.

Surface EMG For Fecal Incontinence Biofeedback

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Introduction:

Fecal incontinence is a common condition involving involuntary stool leakage, which significantly affects quality of life. Continence relies on the coordinated activity of the anal sphincter muscles.

This project focuses on improving the detection and separation of electrical signals from the external anal sphincter using surface electromyography (sEMG) and advanced signal processing. The aim is to develop a non-invasive, patient-controlled biofeedback system to enhance muscle training and continence.

At this stage, we are investigating whether signal processing can reliably distinguish between muscle groups, particularly the anal sphincter, which could support more personalized and effective treatments.

Methods:

EMG signals were recorded from healthy participants in controlled experiments by Becario's company, using PALS 896230 surface electrodes (4×6.4 mm) placed around the anal sphincter and on the buttocks, sampled at 500 Hz. Recordings were performed during sitting and walking, focusing on voluntary anal sphincter contractions. Two setups were used: one with separate devices for buttocks and anal sphincter, and another with crossed recordings between left/right anus and opposite buttocks. Signals were filtered (20–249 Hz), rectified, smoothed, and segmented into bursts using dynamic thresholds. Each burst was analyzed in time and frequency domains (PSD), and coherence analysis assessed interactions between muscle groups.

Results:

During this study, we first tried to separate anal sphincter activity during sitting from buttocks muscle activity during walking using Independent Component Analysis (ICA), but clear separation wasn't achieved, likely due to method limitations under our experimental conditions.

We then performed spectral analysis by calculating the Power Spectral Density (PSD) for each contraction, separately for anal and buttocks signals. This showed that each muscle has a distinct spectral signature, potentially useful for future signal identification and separation.

Finally, coherence analysis between anal and buttocks signals revealed low values far from 1, indicating no significant overlap or dependency. This suggests that better separation of these

signals may be achievable in future studies, with possible diagnostic or signal-processing benefits.

Conclusions:

The analysis revealed no significant dependence between the activity of the buttocks muscles and the anal sphincter muscles, as evidenced by low coherence levels. These findings indicate that the muscles function independently and are not synchronized. Furthermore, each muscle exhibits a unique spectral signature (distinct PSD), allowing clear differentiation between them. These conclusions support the feasibility of separating muscle contractions, which is valuable for medical diagnostics or the development of advanced biofeedback systems. Additionally, there is potential for developing precise monitoring tools capable of detecting individual muscle activity, contributing to improved clinical accuracy and therapeutic outcomes.

Keywords:

Surface Electromyography, Fecal Incontinence, Biofeedback, Signal Processing

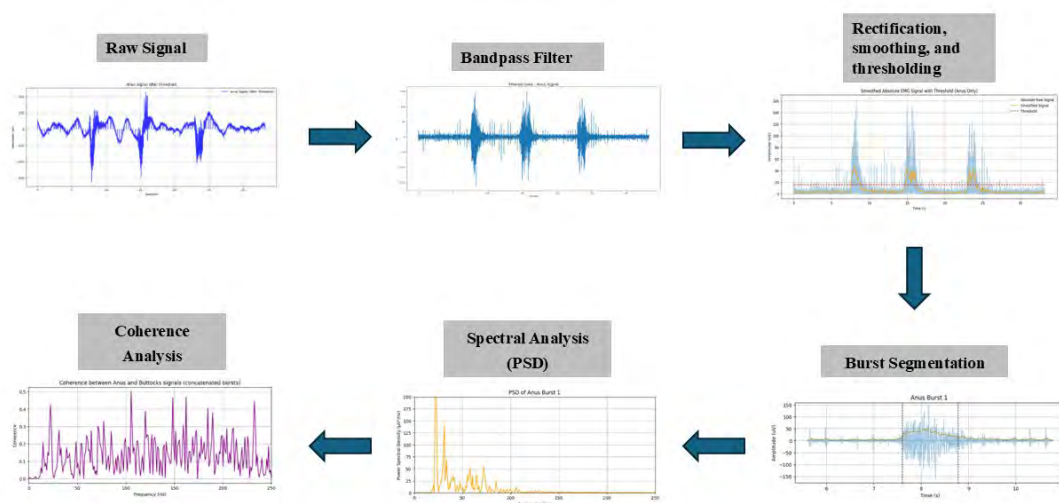


Figure 1. Workflow of EMG signal processing, including raw signal acquisition, bandpass filtering, rectification and smoothing, burst segmentation, spectral analysis (PSD), and coherence analysis.

VR Transformative Experience for PTSD Patients

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Introduction:

Post-Traumatic Stress Disorder (PTSD) is a chronic and disabling psychiatric condition that can emerge after exposure to traumatic events. Globally, it affects approximately 3.9% of the population, with rates rising sharply in conflict-affected regions. In Israel, recent data indicate that nearly 29.8% of individuals exhibited probable PTSD symptoms following the October 7, 2023 attacks.

Among emerging treatments, MDMA-assisted therapy has shown promising outcomes, particularly in reducing symptom severity and supporting psychological integration. However, its clinical use remains limited by pharmacological risks, regulatory barriers, and the need for medical supervision.

This project aims to develop a non-pharmacological alternative capable of offering the same transformative emotional impact as MDMA-assisted therapy, but through a controlled, immersive digital experience. Drawing on the structure and emotional dynamics of Near-Death Experiences (NDEs)—which often elicit long-lasting psychological effects—the intervention seeks to simulate key elements such as symbolic light, emotional release, and reconnection, within a safe and personalized therapeutic format.

Methods:

The development process focused on three key components:

- (1) A secure, trauma-aware data collection interface was created using a chatbot capable of gathering both clinical and emotional information, including visual and auditory preferences, in order to personalize the therapeutic experience.
- (2) A modular audio base was designed around a neutral, meditative script adaptable to each patient's preferred tone, rhythm, and atmosphere. Audio is generated using voice synthesis tools for scalability and personalization.
- (3) A visual framework was developed using calming symbolic environments into which personal elements, such as photos or meaningful scenes, can be integrated to enhance emotional relevance.

To evaluate its therapeutic potential, two assessment tools were selected:

- The PTSD Checklist for DSM-5 (PCL-5), to measure symptom severity.
- Heart Rate Variability (HRV) monitoring, to assess physiological stress regulation.

Results:

- (1) a trauma-informed chatbot enabling secure data collection,
 - (2) several 2D immersive video prototypes adaptable to individual needs
 - (3) initial automation of the audio generation process, improving delivery speed and scalability.
- A 3D version was explored but has not yet produced a prototype equivalent in quality to the 2D model.

Conclusion:

This project offers an innovative and scalable alternative to pharmacological PTSD treatments by reproducing the emotional depth of NDEs in a safe, digital format.

Future directions include clinical testing using validated tools (PCL-5, HRV), extension into 3D environments, and further automation. Broader applications may include anxiety, emotional regulation, or end-of-life support, confirming the model's potential as a flexible therapeutic solution.

Keyword:

Post-Traumatic Stress Disorder (PTSD), Digital Psychotherapy, Near-Death Experience, Virtual Reality (VR)

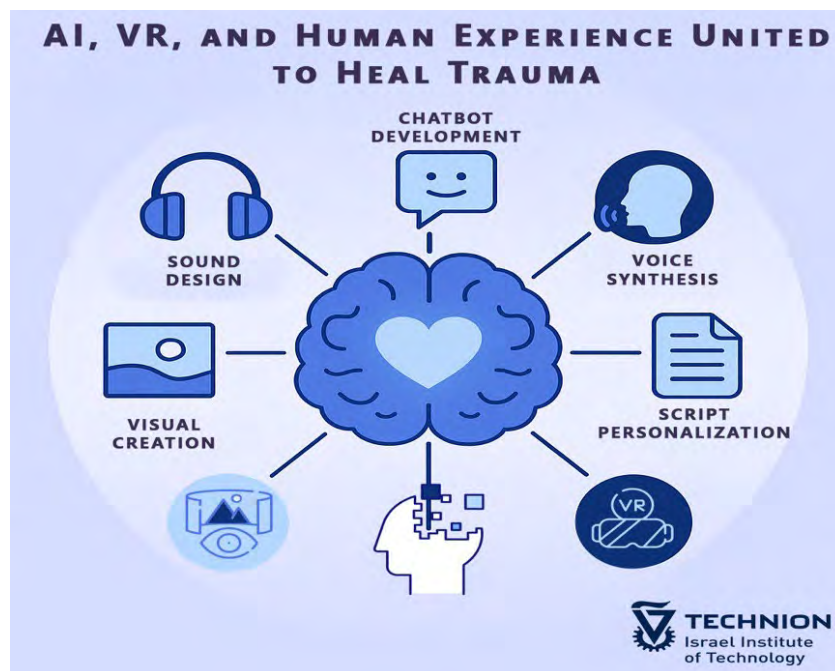


Figure 1. Conceptual representation of the therapeutic system combining AI, voice synthesis, personalized scriptwriting, and immersive visual design to deliver an emotionally adaptive experience for PTSD patients.

Deep Learning Techniques to Improve Diagnostic Accuracy for Crohn's Disease and Colitis

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Introduction:

Crohn's disease and ulcerative colitis (UC), collectively known as inflammatory bowel diseases (IBD), are chronic conditions requiring ongoing and reliable monitoring. Magnetic resonance enterography (MRE) offers a non-invasive imaging alternative to endoscopy, but manual segmentation of bowel structures is time-consuming, inconsistent, and unscalable. To address this challenge, we developed a deep learning model capable of automatically and accurately segmenting gastrointestinal (GI) anatomy, with the aim of supporting future diagnostic and treatment tools.

Methods:

We implemented an automated segmentation pipeline for MRE scans using the nnU-Net framework, which self-configures neural network architectures and training protocols for medical image analysis. We used the nnU-Net v2 3d full resolution configuration. Training was performed on MRE data manually annotated by expert radiologists, following a two-stage process: pretraining on public abdominal imaging datasets (91 scans) and fine-tuning on a curated institutional dataset (12 scans for training, 4 for validation, and 4 for testing). During the fine-tuning stage, the segmentation output layer was replaced to accommodate the new label set. We also reduced the initial learning rate from 0.01 to 0.001. A polynomial (Poly) learning rate schedule was used, along with a combined Dice and cross-entropy loss function and a stochastic gradient descent (SGD) optimizer with Nesterov momentum ($\mu = 0.99$). The model with the highest pseudo-Dice score on the validation set was selected. To improve anatomical precision, we focused on distinguishing clinically relevant, adjacent regions, particularly the jejunum and ileum, where previous models such as Zhong et al. (2025) fell short. We applied the standard nnU-Net data augmentations, including spatial transformations, Gaussian noise, and intensity variations, to improve generalizability.

Results:

Our model demonstrated high segmentation accuracy across gastrointestinal regions (mean Dice score: 0.645 ± 0.133) and was able to differentiate the jejunum from the ileum—something not achieved by previous models. It also partially segmented the ileocecal valve (ICV), expanding anatomical coverage beyond previous efforts. In practice, the model was deployed in the epi-IIRN Crohn's disease study to segment 703 MRE scans, enabling efficient, radiologist-independent extraction of bowel regions. These outputs were used to derive radiomic features that informed predictive models of inflammation severity, including bowel wall thickening and contrast enhancement patterns. The model's performance in this real-world context demonstrates its scalability and clinical relevance.

Conclusions:

We present a validated deep learning-based segmentation tool for MRE imaging that improves anatomical clarity and addresses key limitations of previous models. Its integration into large-scale research highlights its robustness, and its ability to distinguish subtle regional differences supports downstream radiomic analysis and diagnostic workflows. This tool forms a strong foundation for future AI-driven, non-invasive monitoring of IBD.

Keywords: Crohn's disease, deep learning, segmentation, inflammatory bowel disease.

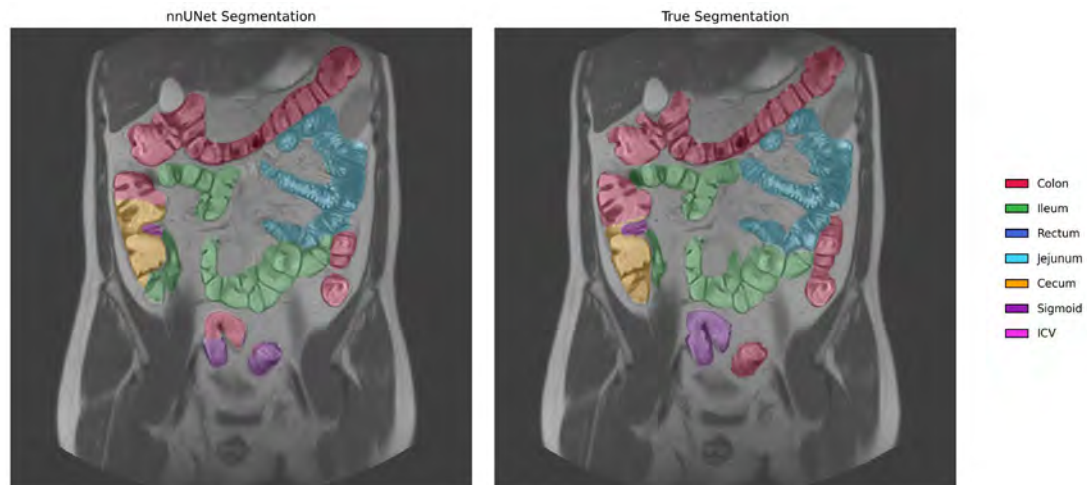


Figure 1: Automated segmentation of the colon, ileum, rectum, jejunum, cecum, sigmoid, and ileocecal valve (ICV) in MRE scans, demonstrating strong agreement with expert radiologist annotations.

Biopsy Cancer Detection Based on Spectral Imaging & Machine Learning Algorithms

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Introduction:

Cancer remains a leading cause of death worldwide and is considered a critical global health concern. Cancer diagnostics relies heavily on pathological examination of biopsy samples, a process traditionally performed using an optical microscope. This approach depends on highly skilled pathologists. It is often subjective and prone to errors, while the demand for biopsy tests is steadily increasing and outpacing available manpower.

To handle the high demand and the need for more objective diagnostics, digital and automated methods were developed. Most existing automated systems rely on three-channel colour information from hematoxylin and Eosin (H&E) stained biopsies.

We propose the use of a spectral imaging (SI) that acquires ~40 distinct wavelength bands, unlike standard RGB imaging that captures only 3 colour channels. SI offers significantly more information on the examined sample. SI was shown to provide a comprehensive view of nuclear behaviour by capturing subtle spectral differences that are often imperceptible to the human eye. By leveraging this high-dimensional information with machine learning (ML) techniques, we aim to develop a more accurate cancer diagnostic method.

Methods:

Biopsy slides from breast cancer tissues were scanned using a hyperspectral imaging system to acquire spectral images with ~40 wavelengths at each pixel and a 20X optical magnification. Previous studies revealed the importance of the nuclei of the cells, and therefore we focused on diagnostics of breast cancer that is based on the properties of the nuclei. First, nuclei were segmented using Spec-Net, a deep learning model trained on spectral data and subsequently corrected and labelled as cancerous or healthy using a custom MATLAB GUI. Tagged biopsies were provided by trained pathologists and were used for the learning phase.

We found four important features from each nucleus: 1. The average spectrum of all pixels in the nucleus (λ), 2. derived spectrum features (spec), 3. Geometric features (geo), and 4. RGB-based features. After data cleaning, a total of 5190 labelled nuclei were used for training and evaluation. Seven Support Vector Machine (SVM) models with RBF kernels were trained on different combinations of feature groups. Hyperparameter optimization was performed using nested cross-validation and the models were evaluated using F1 score, recall, and AUC, with F1 prioritized due to class imbalance.

Results:

Due to the highly imbalanced nature of the dataset, the F1 score was selected as the primary evaluation metric. The highest classification performance was achieved by Model “spec + geo” yielding an F1 score of 0.973 (Figure 1d). The next best Model was the “RGB + geo” with F1

score of 0.947. All models that excluded geometric features performed significantly worse, with RGB-only classification scoring the lowest F1 of 0.712.

Conclusions:

Combining spectral imaging with geometric features with AI analysis provided excellent diagnosis of breast cancer tissues. It outperformed other feature combinations for classification of cancerous nuclei. The geometric features are critical across all high-performing models. While spectral imaging offers 2.6% gain over RGB, it may still be justified in clinical scenarios where diagnostic accuracy is paramount and RGB features alone are insufficient for classification.

Keywords:

spectral imaging (SI), cancer detection, features engineering, biopsy.

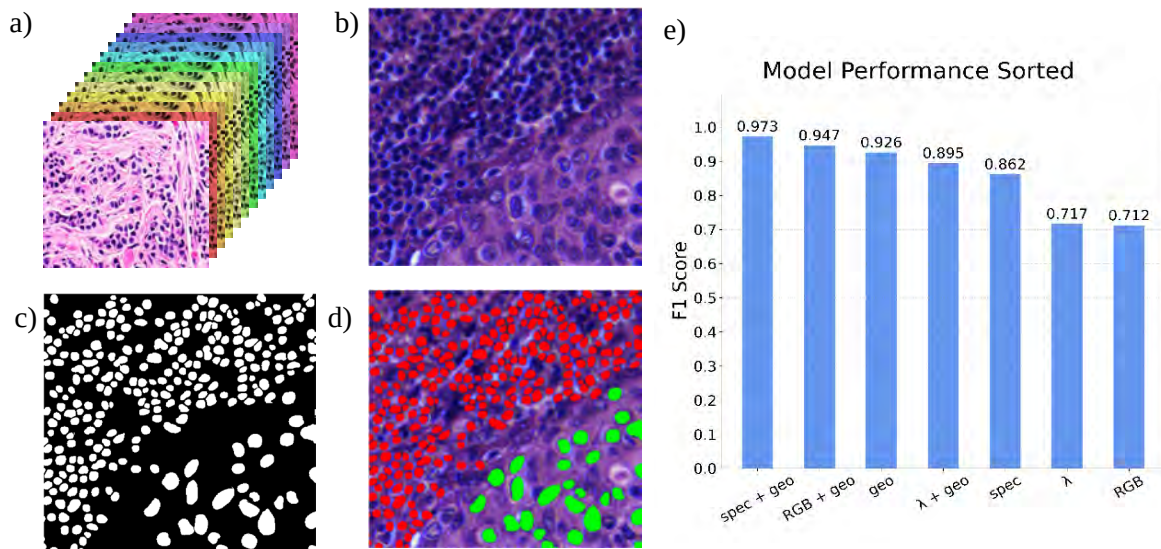


Figure 1: (a) Spectral biopsy image; (b) RGB image reconstructed from spectral data; (c) Nuclei mask by U-Net; (d) Labelled nuclei: cancerous (green), healthy (red); (e) F1 scores of all models.

A Benchmark for Deep Learning-Based Spatial Registration of Mouse Brain Slices

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Introduction: In basic neuroscience research, experiments often involve slicing animal brains, imaging the slices, and registering them to a volumetric atlas to localize structural, molecular, or functional changes. However, slice images are often degraded due to biological variability and laboratory conditions. Registration is typically performed manually using tools like QuickNII - a time-consuming, expertise-dependent process prone to human error. DeepSlice, a deep learning-based tool, automates this task but exhibits notable performance limitations. This project establishes a rigorous benchmark for automated brain slice registration and uses it to evaluate and improve modern deep learning models and training strategies.

Methods: We used the Allen Mouse Brain Atlas dataset from the Allen Institute, comprising over 500,000 images from 4,202 adult mouse brains, each with known three-dimensional spatial coordinates. Preprocessing involved removing unusable or mislabeled images, converting coordinate systems, and analyzing image type distributions. Initial models were based on UNet and ResNet architectures, trained using supervised learning in PyTorch. We tuned several training parameters, including batch size, number of epochs, optimizer, and loss function. Performance was compared to DeepSlice. To address observed limitations, we implemented advanced training protocols such as contrastive learning, supervised contrastive learning, BYOL, SimSiam, and DivideMix. We also evaluated various data augmentation strategies to improve model robustness to biologically or technically degraded slices.

Results: Model performance was assessed using the median Euclidean distance error between predicted and ground-truth slice locations, selected for its robustness to outliers. Our initial supervised learning approach yielded a clear improvement over the state-of-the-art. The UNet model achieved a median error of 364 μm (IQR: 281–480 μm), compared to 567 μm (IQR: 439–738 μm) for the best DeepSlice model across multiple tested configurations. To evaluate robustness, we tested models on curated datasets simulating common real-world image degradation, including randomly erased rectangles, rotated, and padded slices—artifacts reflecting challenges in laboratory image acquisition. Our models demonstrated substantial improvements in handling these corrupted inputs, indicating enhanced generalization under practical conditions.

Conclusions: This work establishes a comprehensive benchmark for automated brain slice registration, including a robust preprocessing pipeline, detailed dataset statistics, and standardized evaluation tools. These resources support reproducibility, enable fair comparison across methods, and lay critical groundwork for future research in computational neuroanatomy. Building on this foundation, we demonstrate that modern deep learning models can significantly outperform both manual registration and existing tools such as

DeepSlice. By leveraging advanced training protocols and strong data augmentation strategies, our approach not only improves accuracy and generalization but delivers even greater performance gains on experimentally acquired slices—where image degradation due to suboptimal acquisition conditions or human error is common. These results underscore the potential of deep learning to streamline neuroscience workflows and reduce reliance on manual effort.

Keywords: Neuroscience, Deep Learning, Benchmark

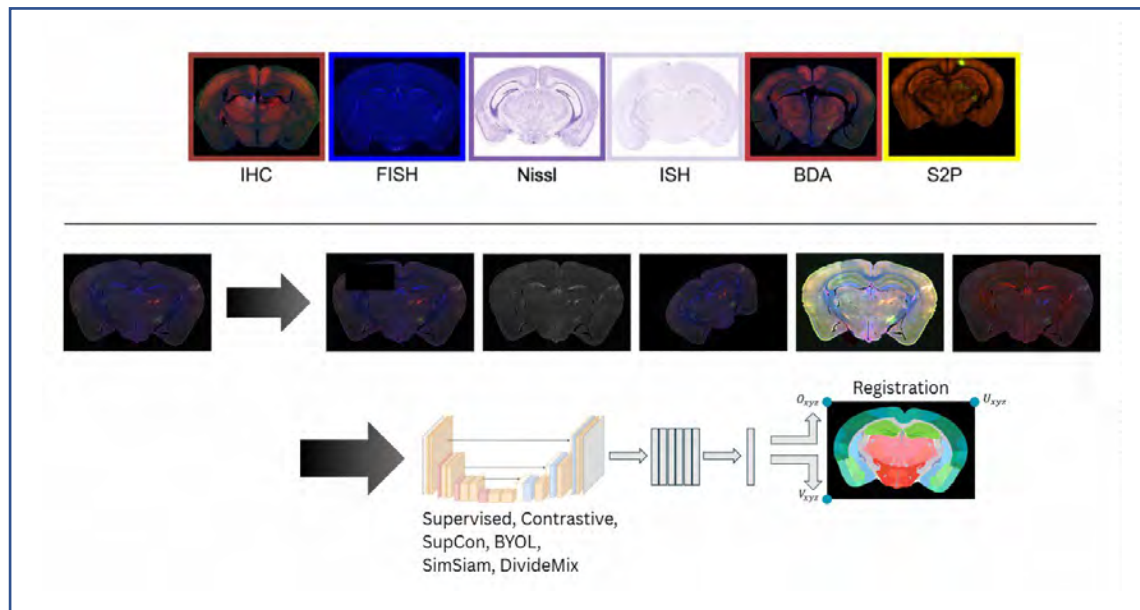


Figure 1: Our registration flow – acquisition of slice image, augmentations, varying models and training protocols, and the final result of spatial registration.

Investigation Of Photoelectric Responses in Silicon-Based Artificial Axons

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Introduction:

The central nervous system (CNS) relies on the rapid and coordinated conduction of electrical signals through myelinated axons. Disruptions in this process, such as in demyelinating diseases like multiple sclerosis (MS), lead to neurological impairments and a reduced quality of life. Existing biological models often fall short due to variability, ethical limitations, and poor reproducibility.

Artificial axons can model CNS disorders by mimicking the functional features of real axons. However, current models typically lack electrical responsiveness, a critical factor for mimicking axonal behavior. Silicon, with its semiconducting and photoelectric properties enabling light-induced electrical stimulation of artificial axons. This project aims to investigate the photoelectric properties of silicon in relation to its crystallographic orientation, surface treatment, and exposure to different light wavelengths. The goal is to identify the optimal combination that maximizes the photoelectric response, advancing the development of silicon-based artificial axons for neuroscience research and drug screening.

Methods:

To examine the photoelectric response of the silicon we tested two groups of samples: untreated silicon (control) and porous silicon, which was created by chemical etching using hydrofluoric and nitric acids to enhance photoelectric response. Each group included samples in three crystallographic orientations: (100), (110), and (111). For each orientation and treatment, three samples were prepared, and each was measured four times in different regions to reduce variability. We used a Patch Clamp system for measurements. Each sample was exposed to five light wavelengths: 455, 530, 625, 740, and 940 nm.

The data was processed using a dedicated Python script that extracted peak current values and normalized them by resistance and wavelength. Then we compared the different groups.

Results:

Each group (defined by orientation, treatment, and wavelength) yielded 12 peak values. Statistical methods removed outliers and verified whether parametric tests were suitable. While many groups met normality, unequal variances justified the use of the Tamhane post hoc test. A nonparametric approach was also applied, yielding the same top performing groups: silicon (100), porous, 530 nm; silicon (111), porous, 530 nm; and silicon (100), porous, 625 nm. The weakest responses were observed in untreated silicon (111) at 740 nm and 940 nm, and untreated silicon (110) at 740 nm.

Conclusions:

Crystallographic orientation and surface treatment both strongly influence silicon's photoelectric response. Porous treated samples, especially in the (100) orientation, showed the strongest performance. The best configuration: porous silicon (100) at 530 nm, offers potential for constructing electrically active artificial axons. These findings support the use of optimized silicon-based models in CNS research and applications such as drug screening for demyelinating diseases.

Keywords:

Artificial axons, Silicon photoelectric response, Crystallographic orientation, Patch Clamp

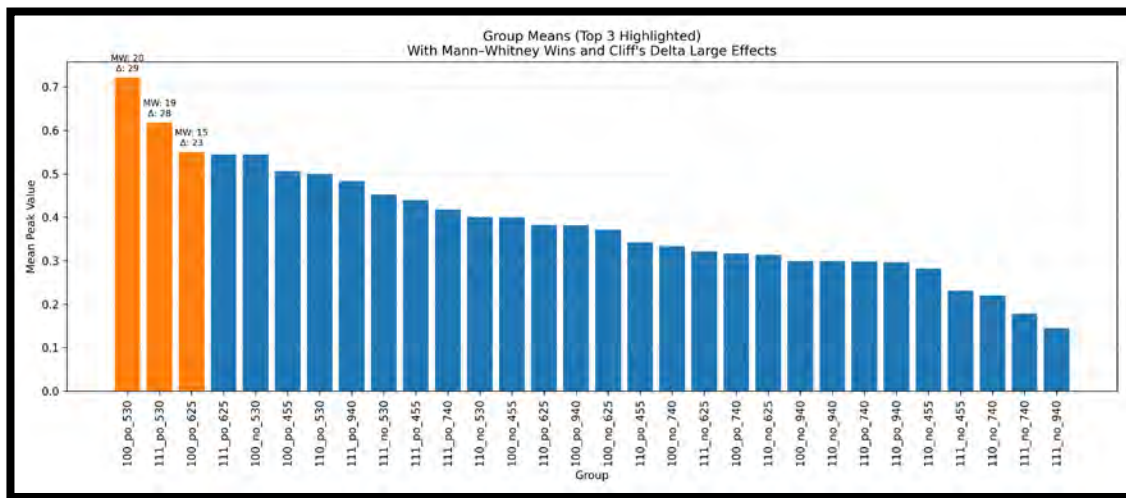


Figure 1: Bar plot showing mean peak values for all groups, with the top three groups highlighted in orange.

Each bar represents a group defined by silicon type, treatment condition (porous or no treatment), and wavelength. Annotations above the top three bars indicate how many groups each outperformed significantly ($p < 0.05$) based on the Mann-Whitney U test (MW), and how many large-effect size comparisons were found using Cliff's Delta ($\Delta > 0.474$). This visualization integrates statistical significance and effect size to highlight the most responsive conditions.

Impact of Anti-Epileptic Drugs on Post-Seizure Neural Mechanisms

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Introduction:

Epilepsy is one of the most common neurological disorders, affecting over 30 million people worldwide, yet its underlying mechanisms, and those of its main treatments, remain poorly understood. Research at the Freifeld Lab of Neuro-Engineering has shown that zebrafish larvae temporarily lose their intrinsic fight-or-flight response to external stimuli following seizure induction. This response is characterized by a sharp, rapid turn known as a “C-bend,” followed by an escape bend in the opposite direction and swimming away. This primitive reaction is hypothesized to be fundamentally conserved at the molecular level across vertebrates. This raises the question: how do commonly used anti-epileptic drugs influence this phenomenon? Using PTZ, a chemical that induces seizures in larvae, and valproic acid, a widely prescribed anti-epileptic drug, we aim to investigate this interaction to better understand the mechanisms of these drugs and why they do not fully control epilepsy in all patients.

Methods:

Zebrafish larvae were pre-exposed to 1 mM valproic acid for 24 hours. During the baseline phase, startle response rates of drug-treated and untreated larvae were compared. A calibrated weight delivered consistent mechanical taps to wells containing three larvae each at fixed intervals for 30 minutes. Responses were video recorded and analyzed using motion-tracking code to quantify short-latency C-start responses and overall reactivity. Seizures were then induced with 15 mM PTZ. Larvae were divided into four groups: PTZ only, PTZ + drug, drug only, and untreated controls. Seizure activity was recorded for 65 minutes in PTZ-exposed groups. Afterwards, the same tapping tests were repeated to assess post-seizure startle responses, and videos were analyzed again to quantify larval activity.

Results:

In larvae without anti-epileptic drug treatment, PTZ caused an ~75–80% decrease in startle response proportion, indicating a significant loss of the survival reflex. In contrast, larvae treated with AEDs showed no reduction in response rates after PTZ exposure, demonstrating complete protection against this effect. Notably, anti-epileptic drug-treated groups showed a ~30% lower baseline reactivity compared to untreated controls prior to any seizure activity.

Conclusion:

These findings suggest that while AEDs lower baseline reactivity, they fully protect the brain’s survival reflex from seizure-induced loss. This highlights their role in modulating neural excitability and preserving essential escape responses, which helps understand their mechanism of action better.

Keywords:

Zebrafish, Seizure, Anti-Epileptic Drugs, Fight-or-Flight

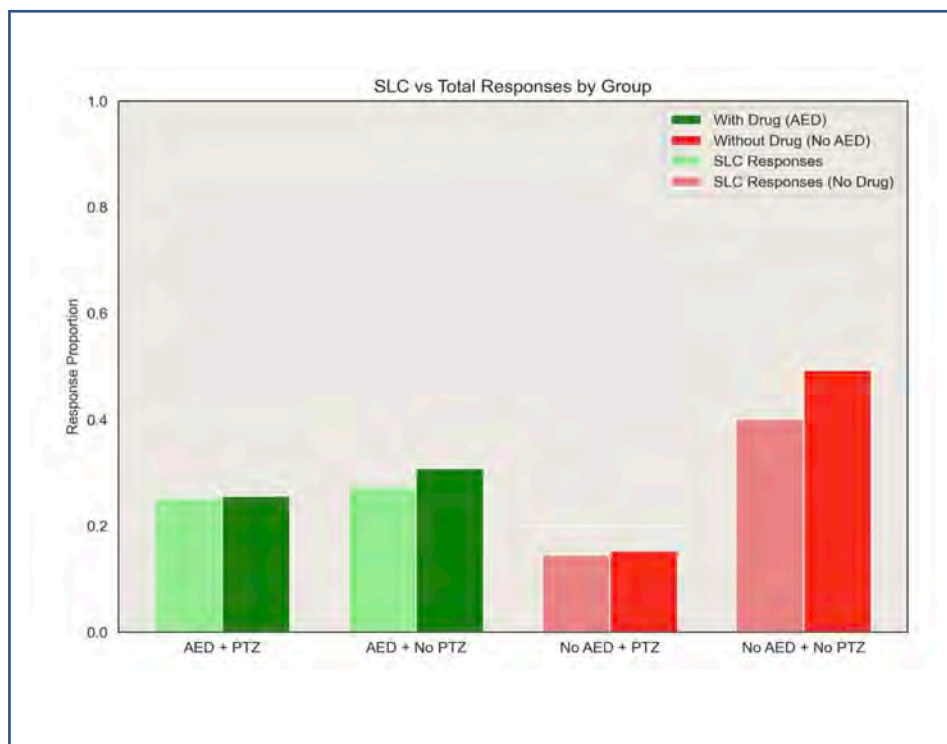


Figure 1: Response proportions with and without AEDs and PTZ, Short- Latency C-bend responses (light) and total responses (dark) for each group

A Novel Method for Fast Detection of Diastolic Heart Failure Using Echocardiography

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Introduction:

Heart failure (HF) is a leading global cause of death. Diastolic heart failure (DHF) accounts for half of all HF cases and is characterized by impaired ventricular compliance. Unlike systolic HF, DHF's nonspecific symptoms and preserved ejection fraction make it challenging to diagnose conventionally. Cardiologists currently diagnose DHF using a complex echocardiographic algorithm, incorporating mitral valve inflow and annular tissue velocities, along with flow velocity and volume indices. This diagnosis typically takes hours to days, depending on case complexity and tests used.

The cardiac cycle consists of distinct phases, with particular interest in the isovolumetric phases. The duration of the isovolumetric relaxation phase (IVRT) was suggested to be a valuable indicator for diagnosing DHF or diastolic dysfunction (DD). In previous studies, researchers have utilized color tissue Doppler and tissue Doppler imaging to extract IVRT values noninvasively, which can be imprecise and highly operator dependent.

Our work aims to develop an automated novel method, using short axis ultrasound cines instead of Doppler imaging, for accurate IVRT measurement. Our method will allow fast DHF detection to be utilized in intensive care units.

Methods:

Echocardiographic cines from 16 patients were used, focusing on Short Axis cines for extracting IVRT. Using the short axis cines, "Difference Echo cines" were produced by subtracting consecutive frames, such that previous locations are colored in blue, and current locations in red. Each cardiac phase has a unique endocardium and epicardium color pattern shown in the Difference cines. Manual observation of the change in motion of the cardiac walls allowed us to extract the IVRT for each patient, such that blue colored epicardium and endocardium represent the IVR phase. We then statistically correlated IVRT with cardiologists' DD diagnoses, assessing the p-value on the linear regression slope and the coefficient of determination.

We developed an automatic image instance segmentation algorithm to detect the endocardium and epicardium by processing Difference Echo cines. We then determined the cardiac phase according to the walls' colors. The segmentation algorithm was optimized using the best quality cine, since most of the patients' cines were somewhat noisy and had low quality.

Results:

A significant correlation between IVRT and DD diagnosis was observed ($p=0.01$). The image processing algorithm successfully detected the epicardium in 50% (7/14 frames) and endocardium in 79% (11/14 frames) of IVR images from the best quality cine. Figure 1 shows ejection phase detection using our algorithm.

Conclusions:

The strong correlation between IVRT and DD metrics supports the clinical relevance of IVRT as an indicator of DHF. While the image processing algorithm was able to detect the epicardium and endocardium with reasonable accuracy, its shortcomings currently prevent precise IVRT extraction and further improvements to the algorithm are needed.

Keywords:

Heart Failure, Isovolumetric Relaxation, Diastolic Dysfunction

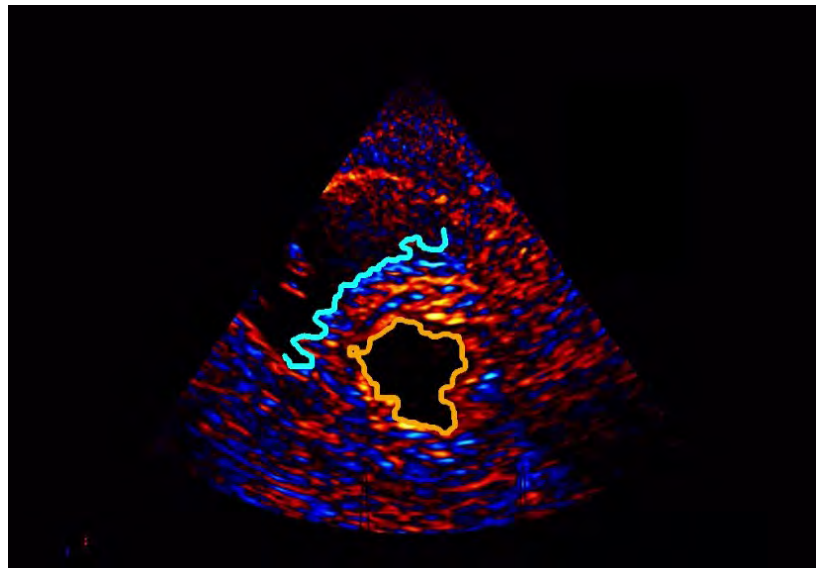


Figure 1: Difference frame taken from short axis cine of ejection phase after image processing. Red pixels represent current locations, and blue represents the previous locations. Orange and cyan contours represent the endocardium and epicardium respectively as detected by our algorithm.

Integrating AI, Pathomics and Genomics for Enhanced Met Associated Breast Cancer Prognostics

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Introduction:

The objective of this project is to develop and implement an advanced computational pipeline for analyzing digitized histopathology Hematoxylin and Eosin whole slide images (WSI) using a pathomics approach. The main goal is to extract, cluster, and interpret morphological features from WSI to enable detailed characterization of tissue architecture in breast tumors. By leveraging on recent advances in foundation models (FM) for pathomics, the project aims to provide a scalable, standardized workflow for large-scale analysis of WSI data for basic and clinical research.

Methods:

The pipeline begins with WSIs that are standardized through a trained color normalization model. This normalization reduces staining variability across the dataset. Following normalization, tissue segmentation and patching are performed using the TRIDENT framework. Slides are divided into high-resolution image patches, and deep learning models are applied to segment tissue ROIs and extract patch-level feature embeddings that capture local morphological characteristics. These patch-level features serve as inputs to the PANTHER pipeline, which employs a Gaussian mixture model for clustering. The clustering process identifies morphological prototypes that correspond to biologically meaningful tissue components, such as tumor epithelium, stromal regions, inflammatory infiltrates. The distribution of these clusters across patches is used to construct WSI representations. Dimensionality reduction techniques, such as principal component analysis and clustering methods like K-means, are applied to produce interpretable, compact embeddings that summarize the morphological composition of entire slides. The final outputs are structured datasets of patch-level clusters and slide-level embeddings suitable for downstream analyses.

Results:

The computational pipeline successfully processed WSI from initial normalization through segmentation, patching, feature extraction, clustering, and embedding generation. The normalization step produced visually consistent slides across diverse staining conditions, facilitating robust downstream analysis. The TRIDENT-based segmentation and patch extraction steps yielded high-quality patches that preserved tissue detail, while feature extraction captured discriminative morphological patterns at the patch level. Clustering using the PANTHER pipeline identified distinct morphological prototypes, enabling clear differentiation of tissue components within slides. The resulting prototypes reflected

interpretable biological structures and allowed for quantification of their prevalence in individual samples. Slide-level embeddings constructed from these clustered features demonstrated meaningful variation across the dataset, with clear separation of morphological patterns observed in exploratory analyses. These embeddings provide a standardized, scalable representation of tissue heterogeneity that can be used for hypothesis generation and integrated with other molecular (such as MET mutation) and clinical data in future studies.

Conclusions:

This project demonstrates the feasibility and utility of a FM-based pathomics pipeline for unsupervised morphological profiling of breast tumor samples that produce interpretable morphological prototypes and compact slide-level representations. The pipeline offers a scalable, standardized framework for large-scale analysis of WSIs data, enabling systematic characterization of tissue architecture and supporting future research into genomics, disease mechanisms and potential biomarkers generation.

Keywords:

Pathomics, Morphological Clustering, MET Mutation

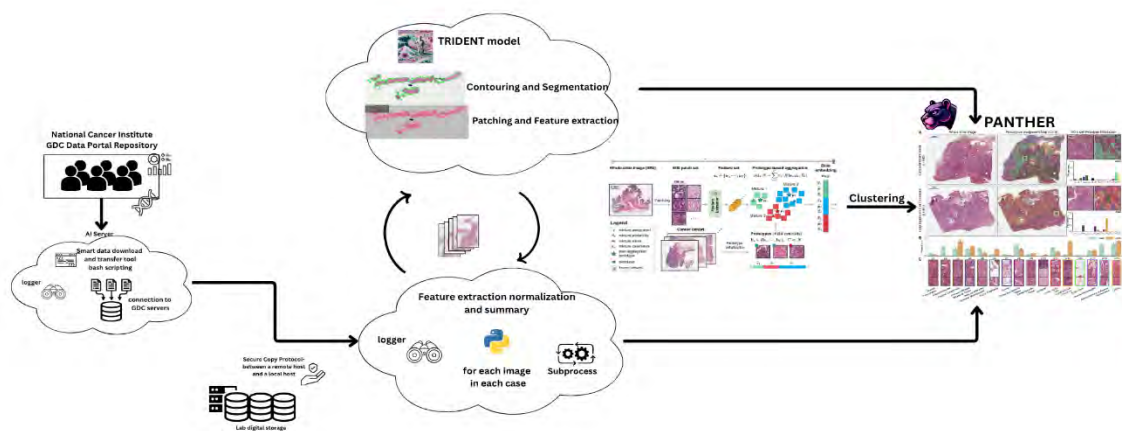


Figure 1: WSI analysis workflow, showing data acquisition, normalization, TRIDENT-based segmentation, feature extraction, and PANTHER clustering FMs to generate interpretable morphological profiles.

Physically Primed T2 Relaxometry for Pancreatic MRI: Model Validation and Glucose Response Assessment in Type 1 Diabetes

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Introduction:

Type 1 diabetes mellitus (T1DM) is an autoimmune disease marked by beta-cell destruction and insulin deficiency. Diagnosis commonly relies on blood glucose and autoantibody tests, which may miss early disease. MRI is non-invasive and offers anatomical detail; conventional T_2 -weighted images reflect water content and microstructure qualitatively. Quantitative MRI (qMRI) decomposes signals into multiple T_2 components, revealing water compartments and microstructural changes, and may detect fat infiltration and inflammation in T1DM. We evaluate the robustness of the Physically Primed T2 (P2T2) model and its bootstrapped variant for abdominal T_2 mapping and assess glucose-induced changes in pancreatic T_2 distributions in T1DM, combining model validation with clinical investigation using anatomical and T_2 -weighted scans.

Methods:

Anatomical and multi-echo T_2 -weighted abdominal MRI scans were acquired. For test–retest, seven healthy subjects were scanned twice, ten minutes apart; For the T1DM analysis two healthy and two T2D participants were scanned before and after glucose intake. We manually segmented the pancreas into head, body, and tail. Then projected the masks onto the multi-echo data for region alignment. Voxel-wise T_2 distributions were estimated using three models (MIML, P2T2, Bootstrapped-P2T2) and fit as a sum of two Gaussian components. The resulting probability curves for each segmentation were compared between paired scans using the Wasserstein distance, and mean tissue fractions for each Gaussian component quantified test–retest variability and glucose-induced changes.

Results:

(a) Test Retest

In test–retest analysis, the bootstrapped P2T2 model produced the lowest Wasserstein distance (Fig 1a), reflecting superior stability and reliability of T_2 -distribution estimates across repeated scans. Variability was greatest in the pancreatic head, while focusing on the body and tail improved inter-scan consistency and reproducibility.

(b) T1DM

Among T1DM subjects, the Wasserstein distance was consistently larger across full pancreas masks (Fig 1b), suggesting greater variation in T_2 distributions following glucose intake. When analyzing individual pancreatic sections, the most pronounced differences occurred in the body and tail, with distance increases versus controls achieving statistical significance. Additionally, prior to glucose intake, the first component of the T_2 distribution was consistently reduced in T1DM subjects across all pancreatic regions.

Test-retest: Wasserstein distance as calculated in each model T1DM vs Control: Before and after Glucose

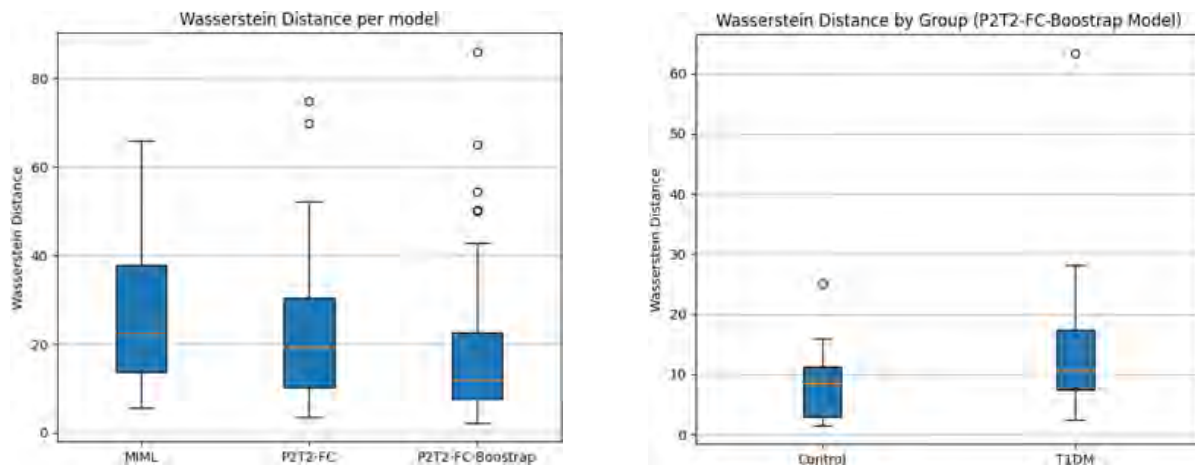


Figure 1: Comparison of distribution differences.
(A) Test-retest reliability. (B) Group differences between T1DM and controls.

Conclusions:

Two distinct water components were identified in the pancreas, corresponding to different tissue characteristics. Among the models tested, the P2T2 model proved most robust for analyzing pancreatic T_2 distributions. Our analysis confirmed that when combining all pancreas masks, T1DM subjects showed a consistently larger Wasserstein distance, indicating altered tissue composition versus healthy controls. Notably, the body and tail regions exhibited stable patterns, supporting greater endocrine-region involvement in T1DM, whereas head results were less consistent, likely due to limited scan coverage. The first component before glucose intake is smaller in T1DM subjects, supporting the hypothesis of a baseline difference in pancreatic tissue composition between diabetic and healthy individuals.

Keywords:

Type 1 Diabetes; Quantitative MRI; T2 Relaxometry; Deep Learning; Microstructure Analysis; Test-Retest Reliability

Audiovisual Integration During Early Mathematical Task: The Role of Fluency in Math Acquisition

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Introduction:

Fluent math perception—the ability to automatically evaluate differences in quantity or size—is a strong predictor of later academic achievement. While audiovisual integration and cognitive control have been extensively studied in relation to reading fluency, their role in early math acquisition remains poorly understood. To address this gap, the present study aimed to examine the contribution of audiovisual integration and cognitive control to early mathematical performance. We investigated the neurocognitive basis of math perception through both behavioural measures and EEG data in typically developing preschool children.

Methods:

51 typically developing children aged 4–6 completed behavioural assessments of language, literacy, and executive function during the same year as EEG recordings. EEG data were preprocessed in EEGLAB, including band-pass and notch filtering, followed by Independent Component Analysis to remove artifacts. EEG signals were segmented based on stimulus timing, and synchronization between electrodes associated with audiovisual and frontal regions was assessed using circular correlation analysis. Correlation coefficients were converted using Fisher's Z-transform prior to statistical comparison. Correlation matrices were compared across conditions using paired t-tests at both the electrode-pair and electrode-group levels. Finally, Pearson correlations were used to examine the relationship between neural synchronization and behavioural performance, with a particular focus on naming ability, a foundational skill for early reading fluency.

Results:

Children showed comparable accuracy and automaticity across conditions. Although electrode-pair differences did not reach significance after False Discovery Rate correction, group-level analysis revealed a significant condition-related difference in audiovisual integration. A significant negative correlation was observed between frontal-region synchronization and naming performance ($r = -0.324$, $p = 0.032$), suggesting that greater frontal engagement was associated with slower naming. A negative trend between audiovisual integration and naming was noted ($r = -0.263$, $p = 0.085$).

Conclusions:

Greater audiovisual integration supports math fluency in easier tasks. Increased frontal and audiovisual synchronization during congruent conditions relates to slower naming, suggesting children with lower language fluency exert more cognitive effort.

Keywords:

Audio-visual integration, cognitive control, Math perception, EEG.

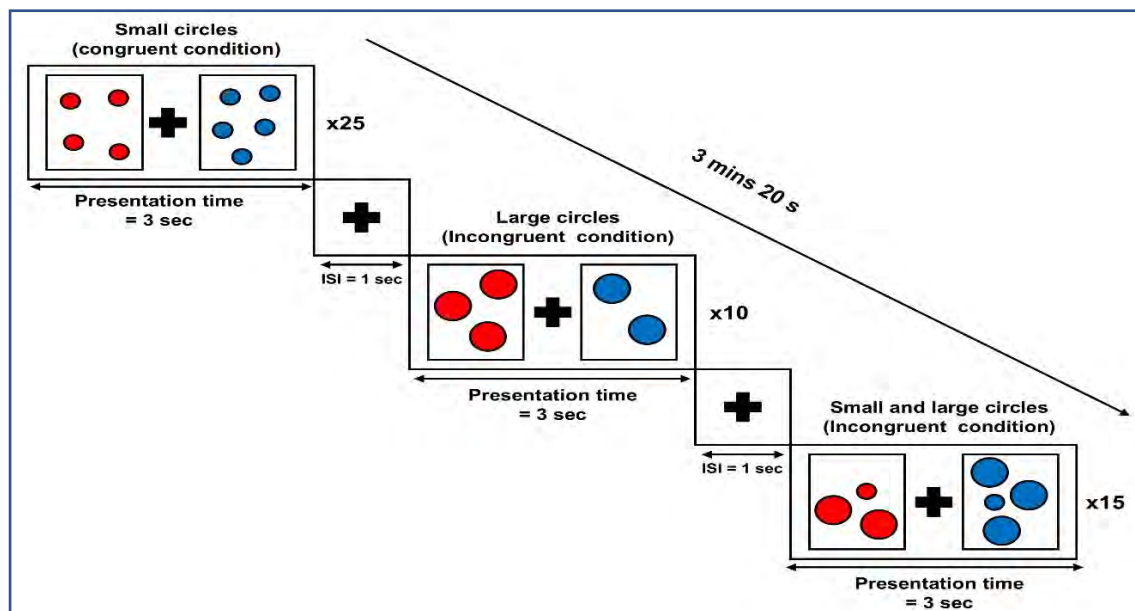


Figure 1. EEG Task: Children identified the side with more circles (red or blue). Trials were either congruent (all small circles) or incongruent (included large circles, introducing visual conflict).

Encapsulation of Nanoparticles of Different Sizes as a Potential Marker for Metastasis

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Introduction:

Metastasis, the process by which cancer cells spread from the primary tumor to distant sites, is a major cause of morbidity and mortality in cancer patients. Cancers such as pancreatic and colorectal cancer are frequently diagnosed at advanced stages, often after metastasis has occurred, leading to significantly poorer prognosis. Early, accurate prediction of metastatic potential is critical for treatment, highlighting a pressing need for innovative diagnostic tools to differentiate aggressive tumor cells.

Nanotechnology offers a promising approach for advanced diagnostics, utilizing nanomaterials' unique properties, including size-dependent biological interactions. Engineered nanoparticles, with specific cellular uptake, are ideal for oncological imaging and diagnosis. While prior research shows their cancer detection potential, the precise influence of nanoparticle size on cellular uptake dynamics, particularly in distinguishing varying cancer aggressiveness, remains an area requiring further investigation. This project aims to investigate the potential of using optimized nanoparticle size to differentiate aggressive from non-aggressive colorectal cancer cells.

Methods:

To explore how nanoparticle uptake correlates with cancer cell aggressiveness, we conducted in vitro experiments using multiple cell lines: J774 macrophages, HNDF fibroblasts, and human pancreatic and colorectal cancer cells - SW480 (less aggressive) and SW620 (more aggressive). Cells were cultured under sterile conditions and seeded into 96-well plates to ensure consistent distribution. Fluorescently labeled carboxylate-modified polystyrene nanoparticles were prepared in three size groups: 30 nm, 200 nm, and 1000 nm. Once the cultured cells were stabilized, nanoparticles were added to the cells, and fluorescence microscopy was used to visualize particle internalization. Images were analyzed using ImageJ software to quantify uptake levels. Cell morphology was observed throughout the process, and three independent biological replicates were performed for each experimental condition to ensure data reliability and reproducibility.

Results:

Our findings indicate that nanoparticle uptake was size-dependent. SW620 cells showed significantly higher uptake than SW480 for both 200 nm and 1000 nm particles. For 30 nm particles, uptake was minimal in both cell lines. These trends were consistent across three biological replicates and supported by quantitative image analysis.

Conclusions:

Our results suggest that both the size of the nanoparticles and the aggressiveness of the cancer cells affect how efficiently the particles are internalized. Interestingly, the more aggressive cancer cells tend to take up more nanoparticles than the less aggressive cells. This could point to a potential way to use nanoparticles not just for treatment delivery, but also to help distinguish between different cancer subtypes. While more research is needed, these findings open the door to future diagnostic applications using nanotechnology in cancer.

Keywords: Cancer Metastasis, Early Diagnosis, Nanoparticles Size, Cell Internalization

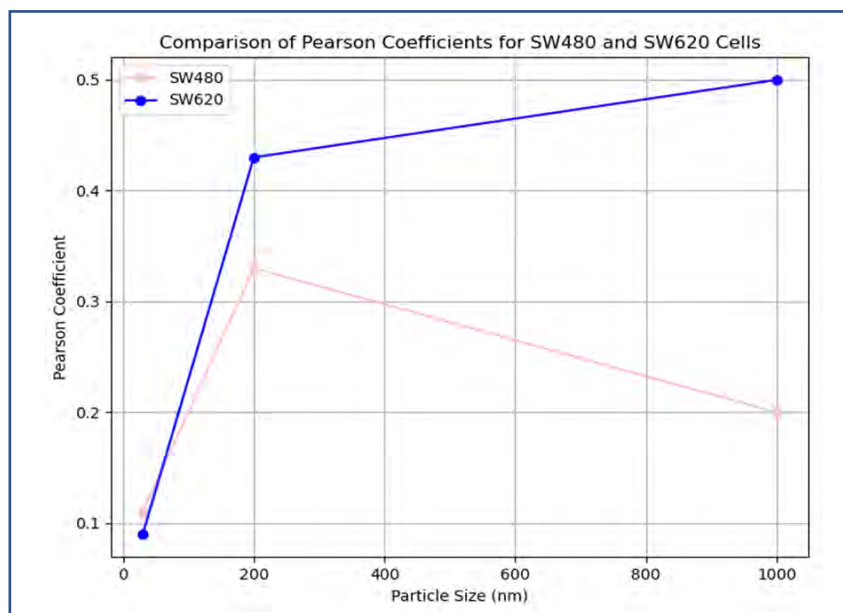


Figure 1 : Illustrates size-dependent differential nanoparticle uptake by SW480 (less aggressive) and SW620 (more aggressive) colorectal cancer cells, highlighting its potential for differentiating metastatic potential.

Distinguishing Between Different Cell lines Based on mtDNA Nanopore Analysis

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Introduction:

Solid State Nanopore sensing is an advanced analytical technique capable of detecting single molecules without the need for labeling, relying on ion current signals generated as molecules translocate through the nanopore. Mitochondrial DNA (mtDNA), a circular DNA molecule located within mitochondria, has been shown in previous studies to produce distinct ion current signatures characterized by unique fluctuations, thereby allowing the detection and quantification of endogenous mtDNA molecules over the background of fragmented genomic DNA (gDNA) from human cell lines and blood cells. We aimed to leverage on this finding to test whether nanopore sensing combined with machine learning would enable the differentiation between disease status or cancer stages using three different human colon cancer cell lines. This proof-of-concept study could, in principle, lead to precise real-time disease stage monitoring, and support the development of personalized therapeutic strategies. Furthermore, we included in the study a fourth cell line originating from mouse muscle cells, to determine whether the mtDNA signature is conserved between species.

Methods:

A three-step methodological strategy was implemented. First, SW480 and SW620 isogenic cell lines, taken from the same colon cancer patient from primary and metastatic tumors, were cultured under standardized laboratory conditions. Total DNA was extracted from these two cell lines, as well as from additional cell lines: human cancer and muscle cell line from mouse, HCT116 and C2C12, respectively, which were provided by the lab. Extracted total DNA samples were subjected to subsequent enzymatic treatments, finally resulting in fragmented gDNAs and linearized mtDNAs molecules.

Second, nanopores were fabricated on silicon chips by applying voltage pulses. Each of the four different samples was translocated through these nanopores by applying a negative potential to the chamber containing the sample and a positive potential to the opposite side of the membrane. The resulting ion current signals were recorded.

Third, these signals were analyzed statistically to extract key parameters, including blockage current (IB), dwell time (td), log-transformed dwell time (ltd), and RMS current (IRMS). These parameters were visualized using scatter plots and histograms. Finally, the extracted parameters, ion current signals, and cell type labels were used to

train and evaluate a supported vector machine (SVM) model, enabling the classification and differentiation of the four different cell lines based on their unique mtDNA ion current signatures.

Results:

By comparing mtDNA translocation signals from mouse and human cell lines, the mtDNA signature was found to be conserved among these two species. As for the three human colon cancer cell lines, by examining only the scatter plots and histograms, no clear visual differences were found. Nonetheless, following the SVM analysis, the confusion matrix indicated a good classification performance, with SW480 cells achieving 76.83% accuracy, SW620 cells 96%, and HCT116 cells 80.36%.

Conclusion:

The results demonstrate promising classification accuracies, indicating that it is possible to differentiate between the examined cell lines based on their mtDNA ion current signatures. In particular, successful separation was achieved even between the isogenic cell lines SW480 and SW620. Nevertheless, further repeated experiments are needed to improve model training and to validate the reliability and robustness of these findings.

Keywords:

Solid State Nanopores, mtDNA Sensing, SVM model, Neural Network

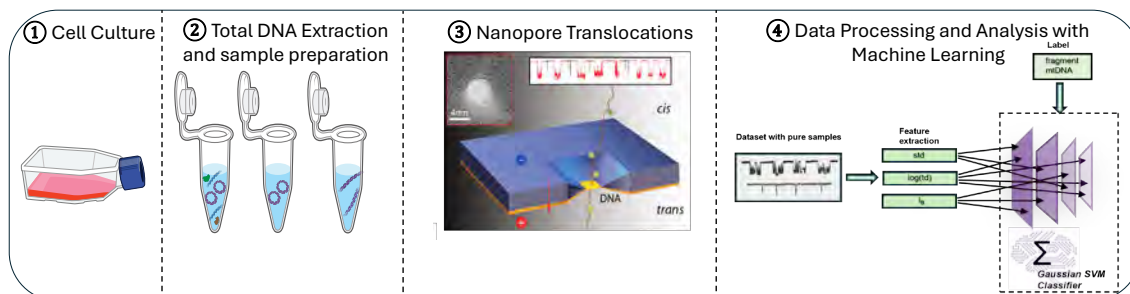


Figure 1 - The study included four main methodological steps. First, culturing the SW480 and SW620 cell lines. Second, extracting DNA and preparing mtDNA samples from SW480, SW620, HCT116, and C2C12 cells. Third, recording nanopore translocation events. Finally, processing the data through statistical analysis and applying an SVM model for classification.

Delineating the Source of mtDNA's Signature in Nanopores

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Introduction:

Mitochondrial DNA (mtDNA) is structurally and functionally distinct from genomic DNA, notably in its circular form and maternal inheritance. Current methods rely on mtDNA amplification for its analysis, thereby losing important information. In previous research, the Meller lab used nanopores to detect and quantify endogenous mtDNA. Specifically, they found that mtDNA exhibited a unique electrical signature with ion current fluctuations during nanopore translocation experiments. Our project aims to identify the factor responsible for this signature, focusing on two hypotheses: (1) It originates from an mtDNA sequence which forms a D-loop structure or (2) Transcription Factor A, Mitochondrial (TFAM) packaging proteins are bound to mtDNA, resulting in ion current fluctuations during nanopore translocations. Unravelling the source of the unique ion current fluctuations could support the development of new diagnostic approaches for mitochondrial disorders.

Methods:

A series of biochemical treatments were performed on mtDNA extracted from human placenta, including Exonuclease V digestion, restriction enzyme cleavage, and incubation with Proteinase K for protein degradation. The samples were then subjected to further treatments to either attempt to remove TFAM proteins from the mtDNA or achieve D-Loop cleavage. Solid-state SiO₂ nanopores were fabricated and drilled to achieve optimal conductance and diameter parameters. Control samples were also prepared using synthetic 'NoLimits' DNA. Samples were validated using gel electrophoresis and analyzed using nanopore sensing experiments. Event data was collected using the Axon software, with a focus on dwell time and current blockage parameters.

Results:

Sample preparations were confirmed using gel electrophoresis. Heatmaps and tracers extracted from the statistical analysis showed that: (1) Treatment with Proteinase K overnight resulted in increased dwell time in comparison to treatment for 1 hour. (2) The signal for overnight Proteinase K treatment retained ion current fluctuations, indicating incomplete removal of TFAM proteins. (3) D-loop cleavage samples show two populations, as expected. (4) SDS treated samples show shallow and long translocations, indicating formation of SDS micelles.

Conclusions:

In this project, we aimed to identify which factor of mtDNA contributes to mtDNA's distinct signature, observed as ion current fluctuations during nanopore translocations. We designed and implemented an experimental framework to test two hypotheses: whether the observed signal arises from mtDNA-bound TFAM proteins, or the D-loop region. Statistical analysis showed that none of the treatments completely abolished current fluctuations, which leads us to believe that Proteinase K cleaves TFAM proteins but does not remove them entirely from the mtDNA. With additional time, we would optimize and repeat the treatments using new mtDNA samples and explore alternative protein removal techniques to isolate the source of the signature more precisely.

Keywords:

Mitochondrial DNA (mtDNA), Nanopore Translocation, TFAM, D-loop

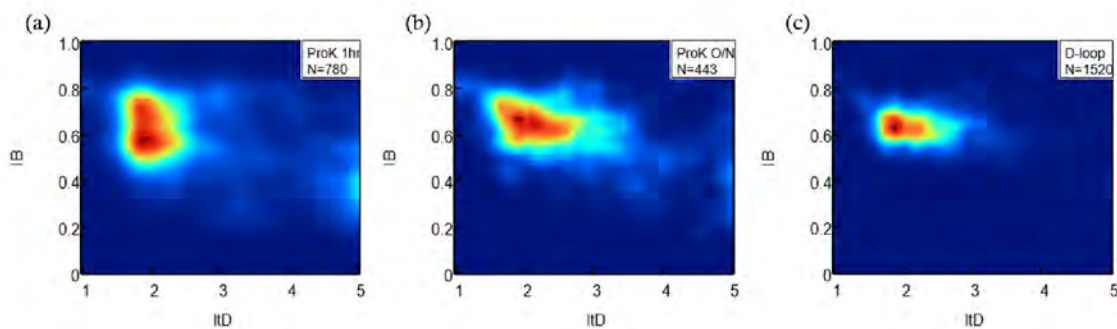


Figure 1: Representative heatmaps showing blocked pore current versus dwell time of samples treated with: (a) incubation with Proteinase K for 1 hour (no additional treatment), (b) incubation with Proteinase K overnight and (c) D-Loop restriction using *XhoI*.

DNA origami for DNA-protein interaction

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Introduction:

DNA origami is a technique that enables the construction of precise nanostructures by folding a long single-stranded DNA scaffold into predefined shapes using short staple strands. These staples hybridize with specific regions on the scaffold, guiding its folding through sequence complementarity. This approach has broad applications in the biomedical field. In this project, we aimed to assemble a DNA origami structure, with the primary goal of investigating the binding of Lamin A—a crucial protein in the cell nucleus—to DNA at the single-molecule level.

Methods:

We used a pre-designed DNA origami model of a rectangular frame with a central hole. Staple strands were received in powder form and reconstituted in buffer. Stocks were prepared for different groups of staples, and the final folding mixture included the stocks, scaffold DNA, MgCl_2 , and buffer.

Folding was performed using a thermal annealing protocol: the mixture was heated and then slowly cooled down. This step allows the strands to bind accurately to the scaffold and form the desired structure. After folding, excess short DNA strands were removed using Amicon filtration, and samples were prepared on freshly cleaved mica with Mg^{2+} -containing buffer for imaging by Atomic Force Microscopy (AFM).

Results:

Initial AFM imaging failed to reveal DNA origami structures, prompting systematic troubleshooting. DNA concentrations were verified using Nanodrop, and repeated AFM scans under varying magnesium concentrations showed no improvement.

To investigate further, we prepared 14 samples reflecting different folding conditions and stock components. Gel electrophoresis revealed scaffold absence in filtered samples, and possible aggregation in some unfiltered samples with high magnesium. While scaffold and main stocks were visible, several functional strands showed no bands, possibly due to degradation or low concentration.

Conclusions:

The absence of detectable DNA origami structures in the AFM images does not necessarily indicate a complete failure but may instead reflect partial or unstable folding. However, our main conclusion is that the consistent absence of scaffold in most of the gel lanes is likely the key reason for the lack of structure formation, since the scaffold is essential for DNA origami

assembly. Although a scaffold was added to all samples, the results suggest it may have degraded, been filtered out, or otherwise lost during preparation. This highlights the method's high sensitivity to experimental conditions and the importance of validating each component throughout the process.

Keywords: DNA origami, Scaffold, AFM imaging, Gel electrophoresis

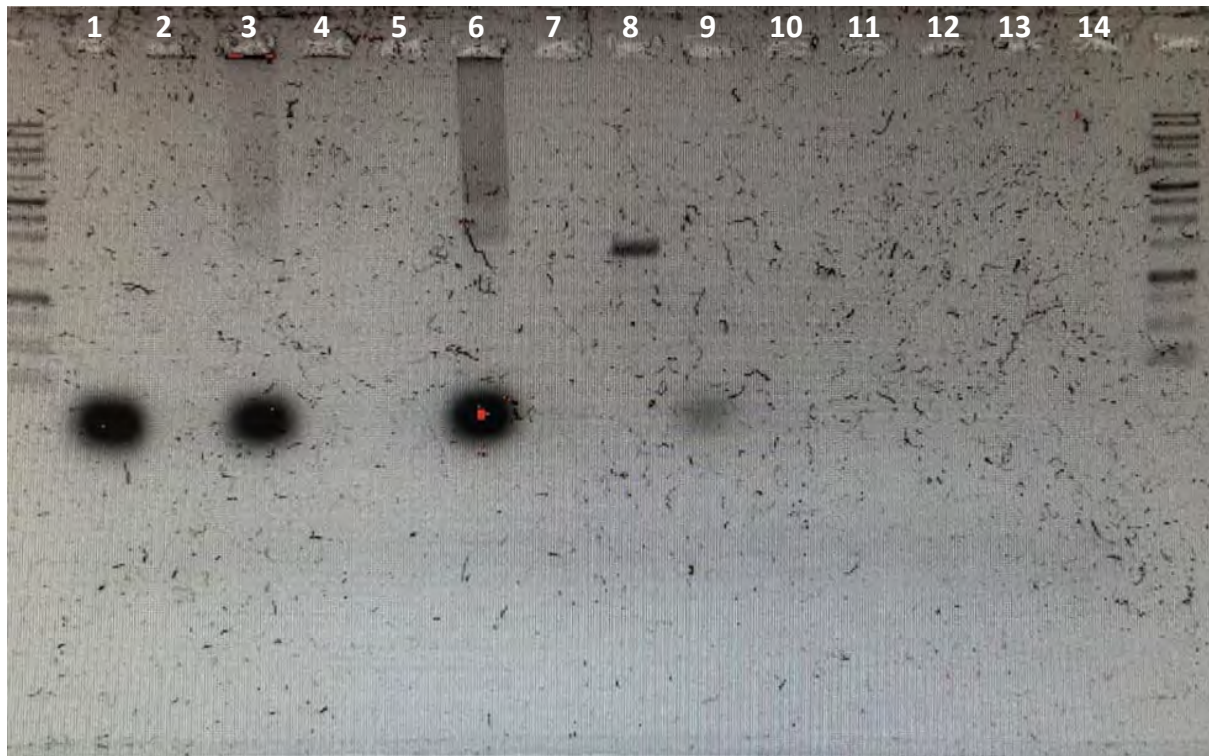


Figure 1: Gel electrophoresis of 14 DNA origami samples.

Lanes 1, 3, and 6: unfiltered samples showing free DNA at the bottom-no structure formed.

Lanes 2, 4, 5, and 7: filtered samples with empty lanes-unfolded material was removed, but folding failed.

Lanes 8 and 9: scaffold and main strand stocks with clear bands.

Lanes 10–14: functional strands with no visible bands, likely due to degradation or low concentration.

T1 MAPPING OF NORMAL LIVER TISSUE USING OPEN MOLLI MRI PULSE SEQUENCE

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Introduction: Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD) and its progressive form MASH, affects a large portion of the population. Early diagnosis is essential, yet current tools are limited: biopsy is invasive, and non-invasive alternatives often lack sensitivity to early inflammation. MRI-based T1 mapping offers a promising quantitative approach by measuring tissue-specific relaxation times. Although widely used in cardiac imaging, its application to liver assessment remains underdeveloped. This project aims to develop and optimize a liver-specific T1 mapping protocol using Open-MOLLI sequence to accurately assess normal liver tissue and support pathological detection.

Methods: (1) Sequence development for liver T1 mapping, (2) MRI data acquisition, (3) Image reconstruction (4) ROI-based T1 maps analysis. An open-MOLLI sequence was adapted for liver imaging. Scans were performed during breath-holds without ECG triggering. Key parameters included ADC duration (determines repetition time-TR), flip angle, and inversion time (TI) vector. Parameters were optimized iteratively based on literature and experimental findings.

MRI was performed on a 3T Siemens scanner using *ex-vivo* (fat–water phantoms and an animal liver), followed by *in vivo* human scans (n=14). Initial scans (n = 6) assessed how different parameter configurations affect image quality. Based on the results, eight additional subjects were scanned with focus on TR optimization. Additional adjustments included field of view (FOV), slice thickness, and localized shimming over the liver to reduce artifacts and improve map quality.

Image reconstruction and T1 map generation and analysis were performed using a MATLAB-based pipeline. PSIR signals were used for curve fitting. Regions of interest were manually segmented, excluding blood vessels. Analysis included histograms, visualizations of signal curve fitting and statistical summaries of fitted values.

Results: *Ex-vivo* phantom scans revealed PSIR inconsistent behavior due to partial volume effects, while animal liver scans produced continuous, artifact-free T1 maps. *In-vivo* initial human scans (n=6), using ADC = 4500/2 ms and flip angle = 38° provided high-quality T1 maps with limited artifacts. However, ROI-based analysis revealed phase opposition between fat and water that led to distorted signal recovery and inaccurate T1 estimation. New hypothesis based on literature suggested that TR values between 4.6-4.76 ms lead to in-phase and minimize interference.

Further human scans (n=8) within the TR range suggested improved T1 estimation accuracy and consistency at ~4.6-4.65 ms compared to values near 4.76 ms. These findings highlight a

narrow TR window where fat-water phase coherence supports reliable mapping, however require further validation.

Conclusions: The developed protocol forms a basis for normal liver T1 mapping. The findings highlight the importance of TR in preserving phase coherence and modeling accuracy in liver T1 mapping. Parameters' optimization must align with physical assumptions. Future studies require TR refinement, test–retest reliability assessment, advanced fitting models, and improved segmentation strategies.

Keywords: T1 mapping, Liver Quantitative MRI, Open-MOLLI, Fat–Water Interference

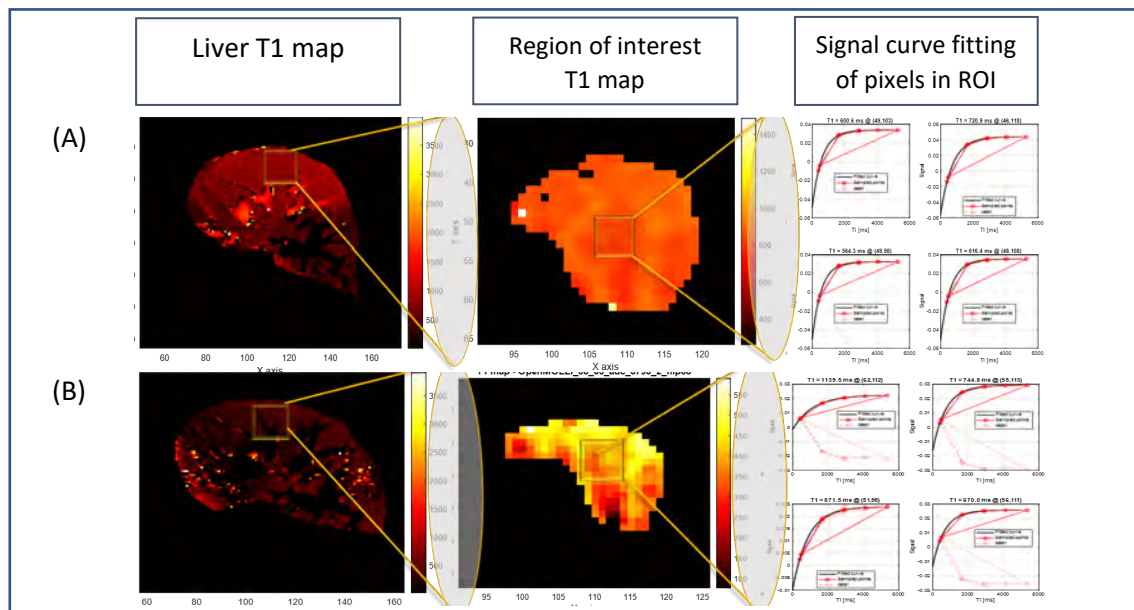


Figure 1: Two TR values within the in-phase range. (A) $TR = 4.64$ ms shows a continuous T1 map with physically expected behavior and increasing signal. (B) $TR = 4.75$ ms, results in a less continuous map with significant amount of decaying signals,

Lamin A Expression Effect on Chromatin Dynamics in the Cell Nucleus

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Introduction:

The eukaryotic cell nucleus houses tens of thousands of genes arranged in a remarkably ordered yet dynamic architecture. Within this confined space, chromosomes occupy distinct regions known as chromosome territories, and chromatin organizes itself without the aid of sub-membranes or a nuclear cytoskeleton. The spatial organization of chromatin has been linked to essential cellular processes such as gene regulation and mitotic fidelity, yet the mechanisms controlling this organization remain incompletely understood. Key nuclear components such as nuclear lamina have been identified as influential organizers. It has been shown that the protein lamin A reduces chromatin mobility, thereby contributing to nuclear integrity and chromatin structure.

Although Lamin A is linked to chromatin dynamics, it is unclear whether it affects chromosome organization directly through chromatin interactions or indirectly via other nuclear factors such as chromatin density and distribution. In this project, we aim to take a step closer to understanding these integral processes and to gain deeper insights into the organization mechanisms of the cell nucleus.

Methods:

Two mouse embryonic fibroblast (MEF) cell-lines were used in this study, one is wild-type (WT) MEF the other is knocked-out (KO) of the gene LMNA that encodes the proteins lamin A/C. To visualize nuclear structures and chromatin dynamics, cells were transfected with H2B-GFP to label the histones, indirectly labeling the whole chromatin, and DS-Red-TRF1 to mark telomeres. Telomere dynamics were recorded using a Nikon spinning disk confocal microscope over two-minute videos at a frame rate of 20Hz.

Data extraction was performed using single particle tracking (SPT), achieved by Imaris image analysis software, for locating coordinates of labelled telomeres as well as the mean H2B-GFP intensity within a $1\mu m$ diameter around each particle throughout the video. In addition, general GFP intensity was measured for each cell to allow normalization. We used custom made MATLAB scripts for further SPT and intensity analysis. We applied quantificational analysis of the chromatin dynamics and density distribution such as Convex Hull algorithm for the area covered by each particle during its motion, mean squared displacement (MSD) calculations, and estimation of the diffusion parameters α and D_α according to the equation $\langle r^2(\tau) \rangle = 4D_\alpha \tau^\alpha$. We performed comparison analysis of the relationship between local chromatin intensity, telomere motion area and the diffusion parameters.

Results:

Our results showed that absence of lamin A in the KO cells led to increased chromatin mobility compared to WT cells. Furthermore, chromatin density seemed to influence telomere dynamics

primarily in WT cells, with little to no effect observed in KO cells. This was evidenced by clearer correlations between local chromatin density and the estimated dynamic parameters.

Conclusions:

Our results suggest that lamin A plays a crucial role in regulating chromatin dynamics through a direct effect that outweighs the influence of chromatin density alone in restricting chromatin motion. These findings take us a step closer to supporting the idea that lamin A affects chromatin dynamics by directly binding to chromatin sites and help to unravel the key biological and biophysical mechanisms involved in gene regulation and nuclear function.

Keywords:

Lamin A, Chromatin Dynamics, Chromatin Density, Cell Nucleus

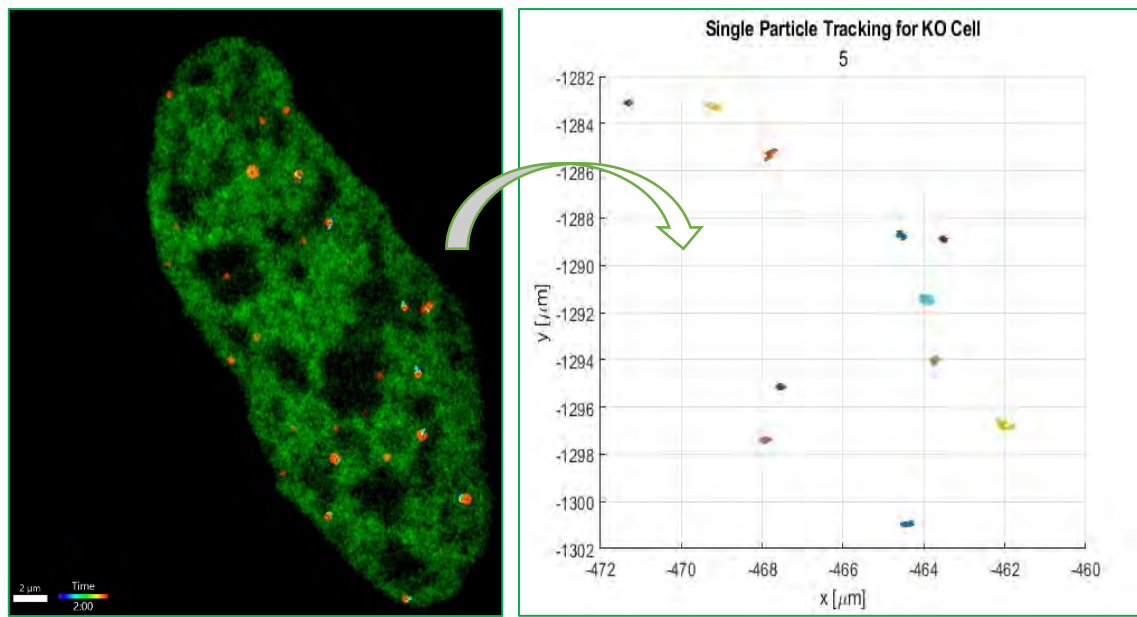


Figure 1: (A) Microscopic image of a KO cell showing histone H2B in green (GFP) as an indicator of chromatin distribution and location, and telomeres in red (DsRed). (B) SPT plots from MATLAB on the right demonstrate the increased telomere movement observed in KO cells

Efficacy of Growth Factor TGF- β 3 on Fibroblasts and Keratinocytes in an *In Vitro* Model

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Introduction:

Skin regeneration following injury differs significantly between fetal and adult tissues. While fetal wounds heal without scarring, adult wounds often result in fibrosis. A key difference is the growth factor profile—specifically, fetal wounds express high levels of Transforming Growth Factor Beta-3 (TGF- β 3), associated with regenerative healing. This project evaluates the effects of TGF- β 3, in both active and latent forms, on fibroblast and keratinocyte behavior using *in vitro* models. A two-dimensional (2D) scratch assay examined fibroblast migration, while a three-dimensional (3D) gel-in-gel model representing tissue structure assessed both fibroblast and keratinocyte migration and proliferation. These models aim to determine the therapeutic potential of TGF- β 3 in promoting regeneration, implicating improved wound healing and reduced scarring.

Methods:

Two models were used: a 2D scratch assay and a 3D gel-in-gel system. Treatment groups received media containing 1% fetal bovine serum (FBS) and were exposed to active or latent TGF- β 3 at 50, 100, or 500 ng/mL. Controls received media containing 0%, 1%, or 10% FBS without protein.

In the 2D assay, normal human dermal fibroblasts expressing green fluorescent protein (NHDF-GFP) were cultured and scratched using standardized force. Treatment-specific media was then applied. Wound closure was imaged at 0, 6, 12, and 18 hours and analyzed by direct cell counting and confluency analysis normalized to side regions, with custom MATLAB scripts.

In the 3D model, circular polyethylene glycol (PEG)-fibrinogen hydrogels containing NHDF or human adult keratinocyte (HaCaT) cells were embedded within acellular hydrogels and inserted into outer hydrogels. Outer hydrogels for treatment groups contained protein. Images were taken on days 0, 1, and 3. Outgrowth was quantified by measuring radial extension beyond hydrogel edge in MATLAB.

Results:

In the 3D model, both fibroblasts and keratinocytes showed enhanced outgrowth with TGF- β 3, indicating migration and proliferation. For fibroblasts, all concentrations of both active and latent forms led to significant outgrowth compared to 1% FBS control, with strongest effects on day 3. No significant difference was observed between active and latent forms at same doses.

Keratinocytes showed a similar trend, with 500 ng/mL yielding the greatest effect. As with fibroblasts, no significant difference was found between active and latent forms,

though active TGF- β 3 had slightly higher values. The increase from day 1 to day 3 suggests a proliferative response.

In the 2D assay, absolute cell count showed dose- and time-dependent increases. At 12 hours, 100 and 500 ng/mL of active TGF- β 3 and 500 ng/mL of latent TGF- β 3 significantly increased cell numbers. By 18 hours, all active and higher latent doses showed significant effects.

Confluency analysis showed no significant differences from 1% FBS control, likely due to similar cell behavior within surrounding regions.

Conclusions:

TGF- β 3 enhances fibroblast migration in 2D and fibroblast and keratinocyte migration and proliferation in 3D *in vitro* models. The most effective concentration was 500 ng/mL. While active TGF- β 3 performed best, latent TGF- β 3 also showed strong efficacy and is more cost-effective and lab-producible. These findings highlight the therapeutic potential of TGF- β 3 for wound healing and support further exploration of its sustained delivery using hydrogels.

Keywords:

TGF- β 3, wound healing, *in vitro* model, cell migration and proliferation

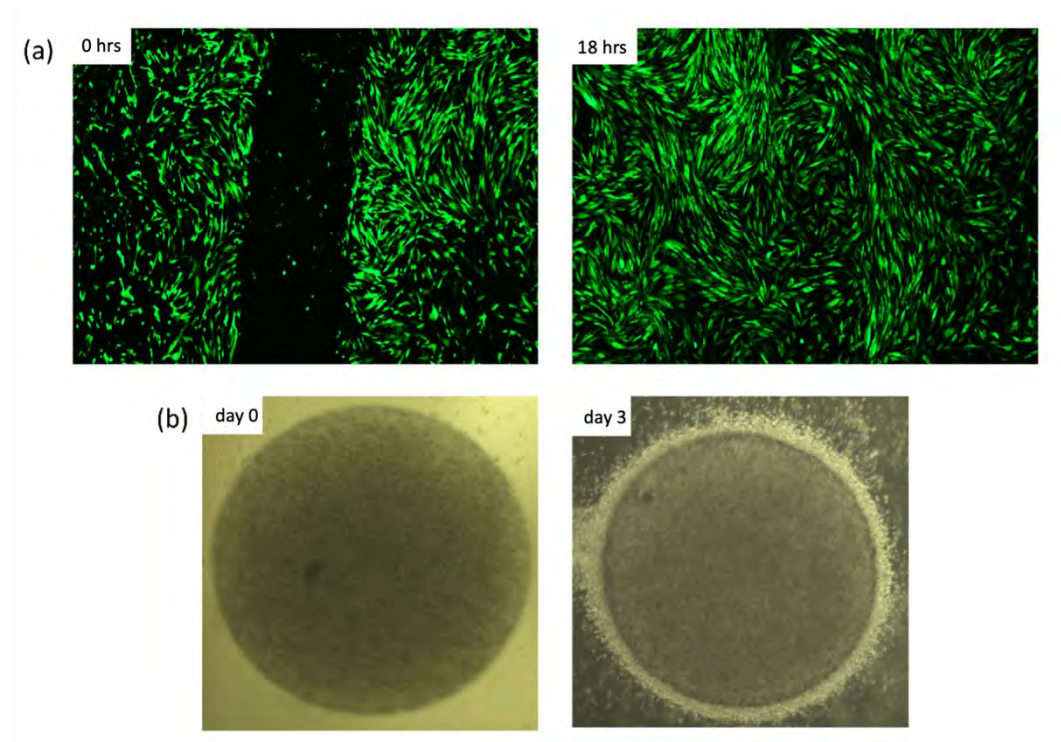


Figure 1: Representative biological results from each *in vitro* model. (a) Fibroblast migration in the 2D scratch assay shown at 0 and 18 hours, illustrating wound closure over time. (b) Gel-in-gel 3D model showing keratinocyte/fibroblast outgrowth from cell-laden hydrogel into the surrounding gel between day 0 and day 3.

Targeted Magnetic Particles Inhalation Therapy

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Introduction:

Conventional inhalation therapies struggle to achieve targeted aerosol deposition in specific lung regions, particularly in diseases like lung cancer. As a result, most drugs diffuse broadly across the pulmonary tract, leading to low treatment efficiency and systemic side effects. To address this challenge, we propose an inhalation protocol that uses magnetic fields to direct superparamagnetic iron oxide nanoparticles (SPIONs) to targeted lung tissue. By integrating a breath-hold (BH) period, we aim to enhance deposition by eliminating drag forces, allowing magnetic forces to dominate.

Methods:

The project employs ex-vivo porcine lungs connected to a pressurized inhalation system delivering SPION-laden aerosols during controlled BH periods. The system and code were based on Arduino. Magnetic fields were applied externally at various positions, and particle deposition was evaluated using fluorescence tagging (fluorescein) and analysis. Tissue samples were dissected post-experiment for region-specific concentration analysis. The analysis is done utilizing the Odyssey M imaging to analyze whole-lung section fluorescence distribution.

Results:

Odyssey M fluorescence imaging revealed targeted SPION deposition in lobes exposed to magnetic force. Using three small magnets, we observed concentrated fluorescence in the cranial and cardial lobes, and a clear deposition gradient in the bialobed lobe. With a single large magnet (~10× stronger), broader and more intense deposition was observed across the bialobed lobe, highlighting the effect of field strength on particle accumulation. In contrast, the control caudal lobe, located far from the magnet, showed negligible fluorescence, confirming that deposition depends on proximity to an active magnetic field.

Conclusions:

These findings confirm that external magnetic fields can significantly enhance targeted aerosol deposition in ex-vivo lungs. The deposition pattern is influenced by both magnet configuration and anatomical airway structure, including bronchial bifurcation. Importantly, increased magnetic strength correlates with greater deposition, as demonstrated by the comparison between weak and strong magnet setups. This approach holds strong potential for lobe-specific drug delivery during inhalation therapy. Future work will explore optimal magnet placement and anatomical accessibility across different lung lobes.

Keywords: inhalation therapy, magnetic nanoparticles, SPIONs, targeted drug delivery

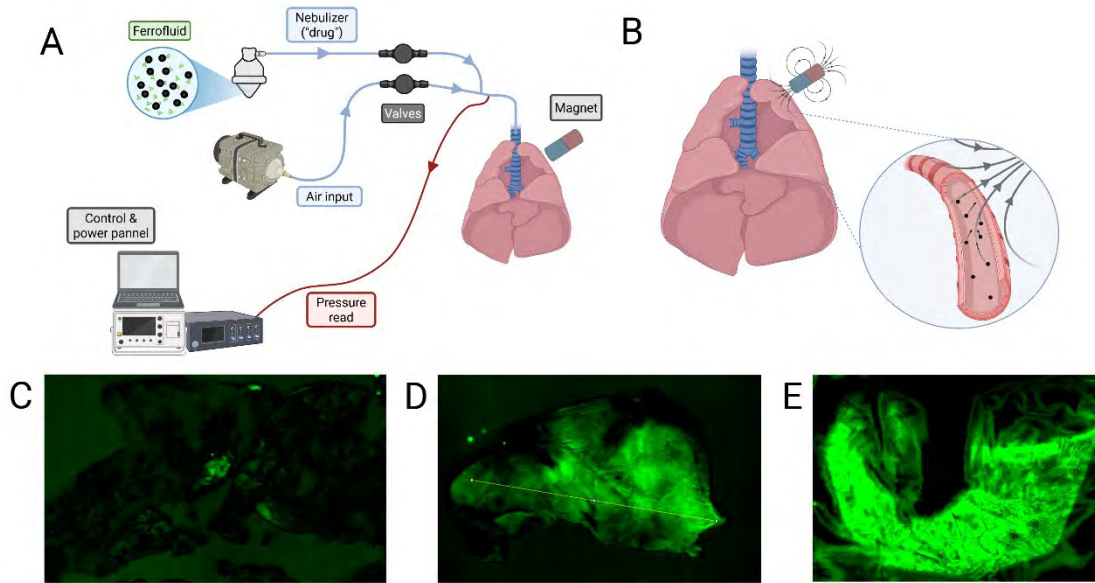


Figure 1: Magnetic targeting of SPION aerosols in ex-vivo pig lungs. (A) Schematic of the experimental system: a SPION-based ferrofluid is aerosolized via a nebulizer and delivered to an ex-vivo pig lung during a controlled breath-hold, with external magnets positioned to guide particle deposition. (B) Illustration of magnetic particle attraction toward airway walls during breath-hold. (C–E) Representative Odyssey M fluorescence images show SPION deposition in different lobes. (C) Localized deposition in the cranial/cardial lobes with small magnets. (D) Gradient pattern in the bialobed lobe, influenced by magnetic field direction and airway bifurcation. (E) Widespread deposition with a single strong magnet positioned beneath the lobe. Created in <https://BioRender.com>

Engineering A Multi-Layered Large Artificial Blood Vessel with Elastic Properties of Natural Tissue

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Introduction:

Vascular diseases are a leading cause of death worldwide, often requiring treatment with vascular grafts. Autologous grafts are biocompatible but can cause donor site morbidity, and sometimes there is a lack of suitable vessels. Synthetic grafts, on the other hand, often lack compliance matching, leading to abnormal hemodynamics. This project aims to engineer a multi-layered artificial blood vessel that mimics the elasticity and mechanical behavior of native vessels to overcome these limitations.

Methods:

A multi-layer vascular scaffold was designed to replicate the compliance and structural features of natural arteries. A supporting scaffold was designed and fabricated, then implemented into a mold. Next, multiple-step molding techniques were applied to construct the layers of the artery. To design the supporting scaffold, CAD models were created using SolidWorks and analysed using finite element analysis (FEA) in ANSYS. The CAD file was then printed using a 3D-printer (Formlabs B4, Grey Resin V5). After printing, mechanical testing- the ring test, was performed to assess its elasticity and durability. To fabricate the vessel walls made of PEGDA, a negative mold technique was used. A temporary Butenediol Vinyl Alcohol Copolymer (BVOH) mold was 3D-printed (Bambulab Carbon X1). By filling the BVOH with polydimethylsiloxane (PDMS), a soft mold was fabricated, enabling easy extraction of the final product without damage. After the PDMS cured, the BVOH mold was put in a DW beaker, allowing for BVOH elimination as it dissolves in water. The PDMS mold was then filled with Polyethylene Glycol Diacrylate (PEGDA) hydrogel, forming the soft hydrogel component of the vessel wall. Finally, the supporting scaffold was inserted inside the PEGDA, in addition to a needle placed in the center to form a lumen. Afterwards, the PEGDA was crosslinked under UV light, and the whole structure was extracted, forming the final model.

Results:

Finite element analysis (FEA) showed that the scaffold had a compliance of $3.9 \times 10^{-3} \text{ mm}^2/\text{mmHg}$, which is within the compliance target range of large rat arteries (2.13×10^{-3} to $0.013 \text{ mm}^2/\text{mmHg}$). In addition, the highest stress was below the material's failure point, and the calculated safety factor was 2.9. The ring test showed a compliance range from 3.9×10^{-3} to $4.4 \times 10^{-3} \text{ mm}^2/\text{mmHg}$, which fits within the target range. It also demonstrated that the scaffold withstood physiological pressures without failure. After fabrication, red dye was injected through the lumen to confirm it stayed unobstructed.

Conclusions:

This study shows proof of concept for a multi-layered, 3D-printed artificial blood vessel with mechanical properties like natural large arteries. The vessel operates safely within the physiological range, which is well below the model's failure point, showing its potential for future use in vascular grafts. Repeating the fabrication step enables the assembly of a multi-layered vascular construct, demonstrating the method's feasibility. In the future, we plan to use biocompatible materials (ColMA, Biomed Black resin) to support possible integration with living tissue.

Keywords:

Artificial Blood Vessel, Compliance Matching, Vascular Tissue Engineering, 3D Printing.

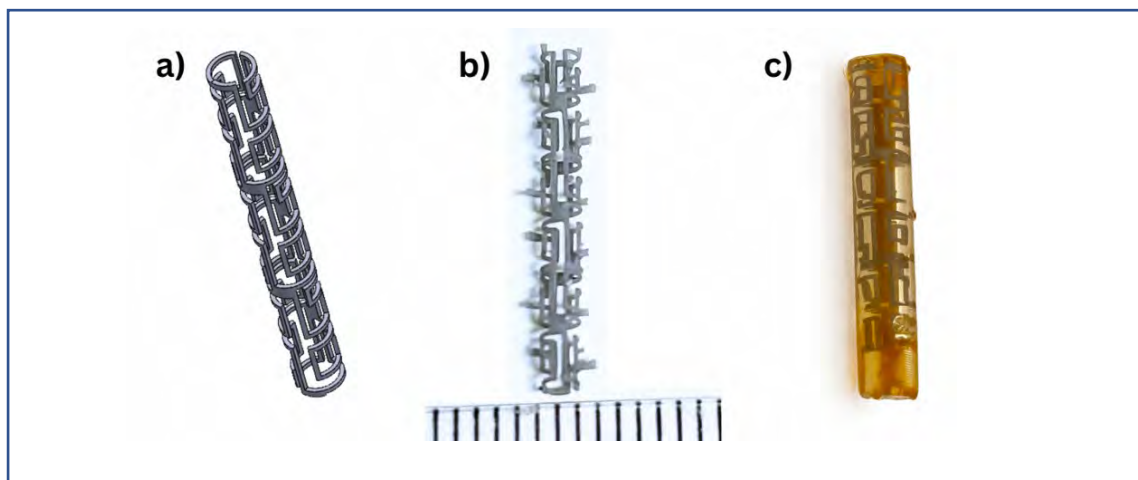
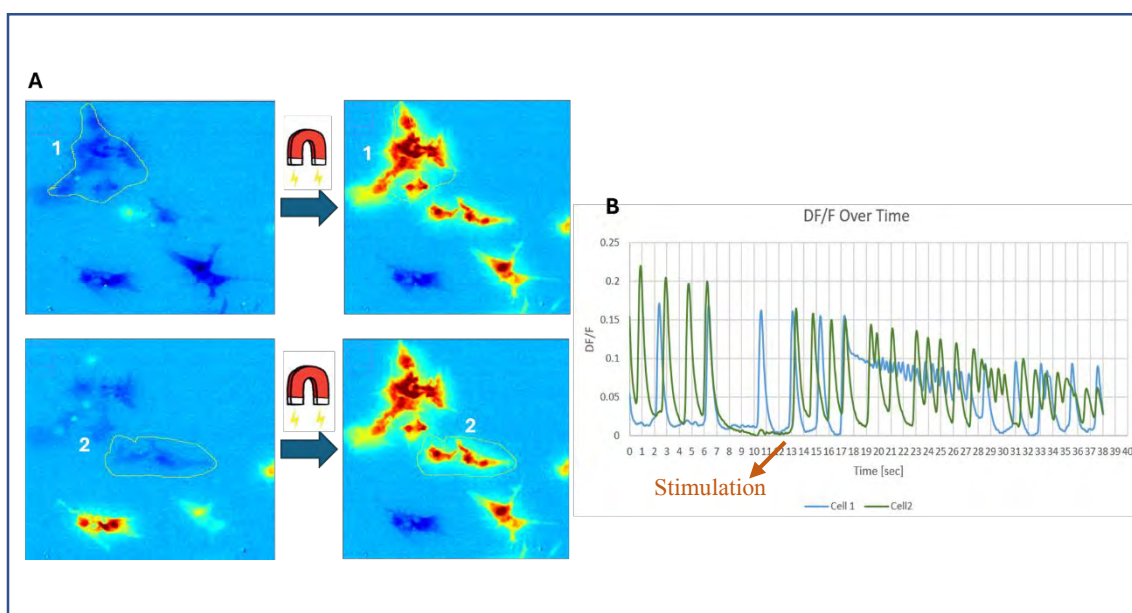


Figure 1: The Supporting Scaffold Prototype. a) CAD model designed using SolidWorks. b) 3D-printed scaffold c) Final stage of fabrication: the construct includes the inserted scaffold and crosslinked PEGDA. The red dye was injected to visualize the lumen.

vivo

ex vivo *in*



Development of a 3D In Vitro Bone Model and Image-Based Computational Analysis Pipeline

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Introduction: Bone is a dynamic, living tissue that continuously remodels itself to maintain strength, support movement, and aid in mineral homeostasis. Bone diseases may develop when the delicate balance between bone formation and resorption is disrupted. This process is governed by the coordinated activity of osteoblasts, which build new bone tissue, and osteoclasts, which break down old or damaged bones. Factors such as aging, hormonal shifts, inflammation, or genetic alterations can disturb this balance—ultimately compromising bone strength and repair. In some cases, such as compound fractures, trauma, osteoporotic fractures or cancer, critical size defects can occur inhibiting normal bone repair leaving the patient with a large gap between both bone ends that cannot be repaired naturally.

The main goal of the research is designing personalized scaffolds coated with molecules that enhance cell migration and accelerate osteoblast differentiation, ultimately promoting faster and more effective bone regeneration.

Our project aims to explore the cellular and molecular differences between healthy and diseased bone environments using advanced 3D cultures that closely mimic native bone tissue, aiming to characterize how the body responds to critical-size defects in each condition. Our findings may help identify key proteins that can be used to coat scaffolds and enhance their biological performance in bone regeneration.

Methods: using salt leach method to create porous 3D scaffolds, seeding scaffolds with MSCs and endothelial cells under differentiation medium to allow bone and vessel formation. During the experiment, we applied key cell culture techniques: cell seeding to establish optimal density, changing medium to maintain a healthy environment for the cells, cell splitting and counting to control growth, and cell fixation to preserve morphology for imaging. The 3D cultures included adipose-derived mesenchymal stem cells (ADMSCs) and human umbilical vein endothelial cells (HUVECs) to better mimic the native bone microenvironment. Image processing code will be implemented to support future analyses and reduce analysis time.

Results: We developed a custom Python script that performs rapid analysis across multiple images, saving time and reducing the need for lengthy manual quantification of RUNX2 expression in immunofluorescence-stained 3D cultures.

Our experimental results demonstrated that co-culturing HUVECs with ADMSCs significantly enhanced the formation of vascular-like structures. The ADMSCs contributed to this process

by secreting growth factors that promoted HUVEC proliferation, migration, and organization into tube-like formations resembling early-stage blood vessels.

Conclusions: Our study successfully highlighted the synergistic role of ADMSCs and HUVECs in promoting vascularization, a key factor for effective bone regeneration. This co-culture approach more accurately mimics the native bone environment in 3D culture, allowing for more precise and realistic characterization of cellular behavior in both healthy and bone disease conditions.

combined with a computational analysis tool for image-based quantification. The image analysis code we developed will serve as a significant time-saving tool in future analyses of bone research at the molecular level. These findings support the potential of designing biofunctionalized scaffolds tailored to enhance bone healing in both healthy and diseased environments.

Keywords: bone regeneration, salt leaching, 3D co-culturing, osteoblast differentiation, Image analysis

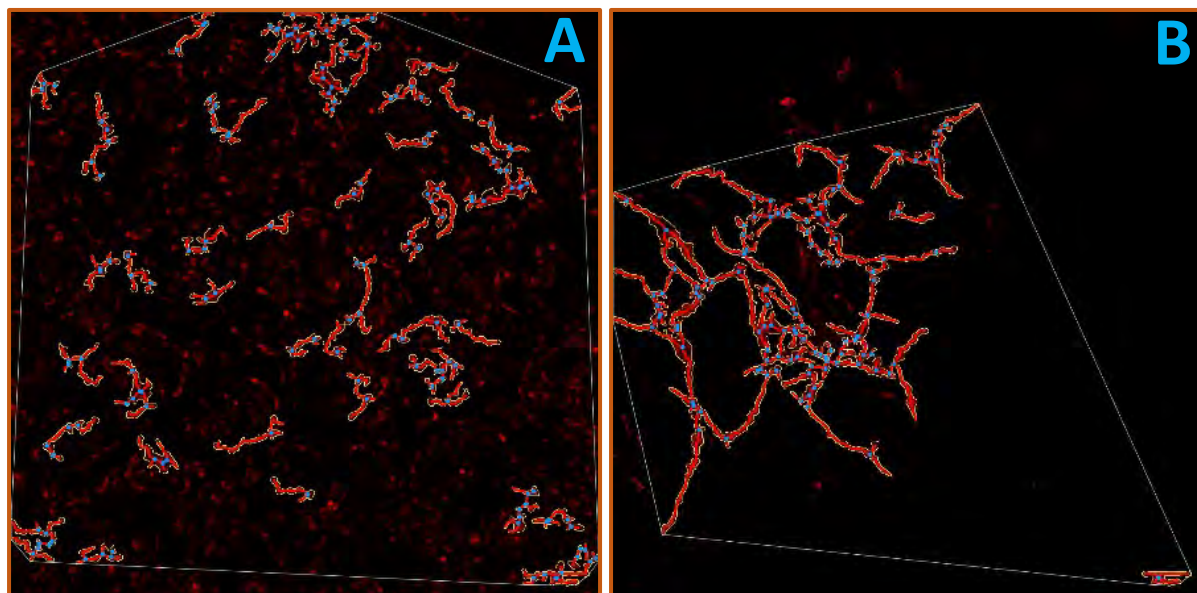


Figure 1. 3D models of healthy lining cell tissue were developed to evaluate the effect of co-culturing cells on enhancing the imitation of native bone tissue. (A) 3D culture of HUVECs alone at 5× magnification. (B) 3D co-culture of HUVECs with MSCs at 5× magnification. Co-culturing HUVECs with ADMSCs significantly enhanced the formation of vascular-like structures.

Development Of Bio-Electrodes Using Live Cells

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Introduction:

Pacemakers are widely used to regulate heart rhythm, but their metal electrodes can cause problems over time, such as tissue damage, inflammation, and reduced signal efficiency. These issues are mainly due to the difference in stiffness between the rigid electrode and the soft heart tissue. In this project, we aimed to develop a new kind of pacemaker electrode made from a soft, biocompatible hydrogel that contains living heart cells. The idea is to use a fibrin-thrombin hydrogel as a base and embed cardiomyocytes inside it so that they can help transmit the electrical signals from the pacemaker to the heart tissue. Our goal was to create an electrode that better integrates with the heart, reduces unwanted reactions.

Methods:

Stock solutions of fibrinogen (10 mg/mL) and thrombin (2 U/mL) were prepared in PBS and mixed using a dual-syringe system, then injected into straight-line molds (0.7 mm and 1 mm diameters). After incubation at 37 °C for 10 minutes to achieve complete cross-linking, the hydrogels were gently released by scraping and PBS flushing, then transferred into fresh PBS for stabilization. For biocompatibility testing, two setups were used. First, flat hydrogel layers were cast in culture plates and seeded with HNDF cells on the surface. Samples were incubated in cell culture medium, and cell attachment and morphology were evaluated using light microscopy after 3 days. In the second setup, HNDF cells were mixed directly into the Fibrinogen solution before gelation for 3D encapsulation. Cell-loaded gels were tested as droplets in a dish and as shaped lines. After 3 days, cell viability was assessed using live/dead staining and confocal microscopy.

Results:

The dual-syringe system enabled uniform mixing, and the hydrogel was successfully shaped using molds of defined diameters. The structures remained stable after incubation and transfer. In 2D seeding, HNDF cells adhered well to the flat hydrogel, remained viable, and showed healthy, elongated shapes. Similarly, 3D-encapsulated cells in hydrogel droplets remained alive and spread. In contrast, cells embedded in line-shaped hydrogels were also viable but appeared rounded, suggesting a different cellular response in the shaped structure.

Conclusions:

This project presents a promising approach for fabricating soft, fibrin–thrombin hydrogels in well-defined shapes, offering potential as a biocompatible electrode platform. Initial experiments demonstrated that the material could support cell viability in both 2D and 3D configurations. Future work will focus on testing the shaped constructs with HNDF and

cardiomyocytes to evaluate its potential as an injectable bioelectrode for pacemaker applications.

Keywords:

Bioelectrodes, Hydrogel-based implants, Pacemaker technology, Conductive biomaterials.

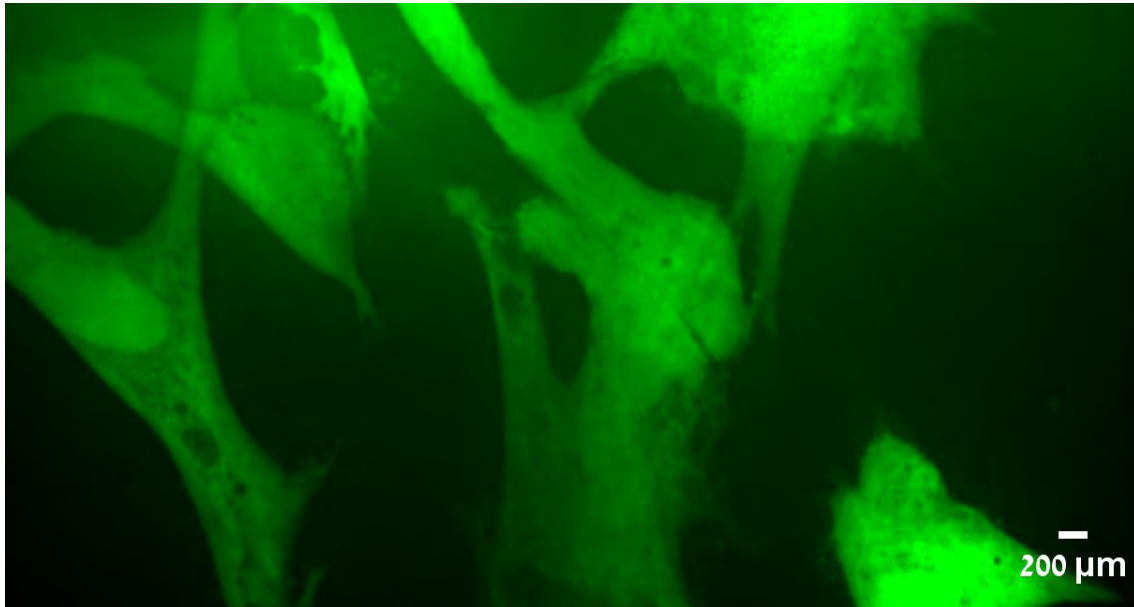


Figure 1 - Confocal image of HNDF cells embedded in a 3D fibrin-thrombin hydrogel (plate format), stained for viability. Cells remained alive and spread throughout the gel after 3 days in culture, demonstrating good compatibility and integration in a 3D environment. Scale bar = 200 μm.

Numerical Analysis and Design of an Intravascular Aneurysm Isolation Device

Assessment of Stability Under Blood Flow Conditions

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Introduction:

Cerebral aneurysms, which affect approximately 5% of the population, represent a significant health risk due to their high mortality rate associated with rupture, reaching around 50%. Current treatment options, including clipping, coiling, and flow diverters, have limitations such as migration, recurrence, and compaction. This project focuses on a fluid mechanics numerical analysis of an intravascular device designed to isolate cerebral aneurysms using an immiscible phase (IMP) fluid layer positioned at its outer surface, while allowing blood to continue its normal physiological flow through the device's inner hollow section. The goal is to assess the stability and performance of both the device and the surrounding IMP through computational simulations.

Methods:

The study was conducted using multiphase flow simulations in ANSYS Fluent®, modeling the interaction between blood and a pre-injected IMP surrounding the isolating device (Figure 1). The simulations accounted for multi-scale flow behavior, with blood flow modeled at the millimeter scale and the immiscible phase at the micrometer scale. Parameters tested included flow rate (10 and 100 mL/min), surface contact angle (30° and 150°), and geometry shape (sharp vs. smoothed device's edge configuration).

Results:

Flow rate had a substantial effect on the behavior of the immiscible phase. Under high flow conditions (100 mL/min), the IMP was rapidly washed away when a neutral contact angle (90°) was used. In contrast, under low flow conditions (10 mL/min), it remained considerably more stable. The stability of the IMP improved further when the edge of the device closest to the inlet was modified from a sharp to a smoother configuration. Importantly, a hydrophobic outer surface of the device, exhibiting a high contact angle relative to blood (150°), produced the most stable outcomes, with the IMP remaining intact and resisting deformation or migration even under high flow. In contrast, a hydrophilic surface (30°) led to substantial displacement and instability of the injected material.

Conclusions:

To enhance the stability of IMP under physiological blood flow, geometrical smoothing must be applied to prevent large stagnation regions in contact with the device. The most critical aspect to consider is the device's surface treatment, as a hydrophobic surface leads to higher adhesion to the device. These insights contribute to the design of future isolating devices that rely on surface tension to enable localized targeting of diseased tissues.

Keywords:

cerebral aneurysm, multiphase flow, embolization device, fluid dynamics.

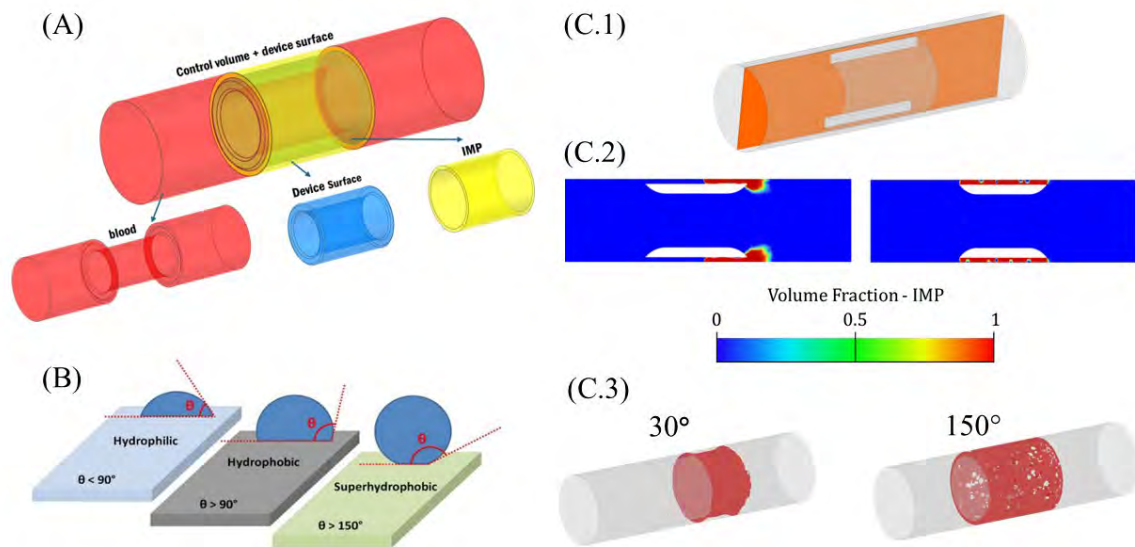


Figure 1: Computational fluid dynamics (CFD) simulation of the models tested in the project.

(A) Schematic of the control volume used in the flow model. (B) Schematic representation of contact angles. (C) Results of the CFD simulations. (C.1) Symmetry plane used for analysis. (C.2) Volume fraction contours of hydrophilic (30° – left) and hydrophobic (150° – right) contact angles on the outer surface of the device at the symmetry plane at a specific time point. (C.3) Iso-volume surfaces of the immiscible phase (IMP) surrounding the device at a specific time point.

