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PhD Thesis Summary

Interpretable Machine Learning Detection and Diagnosis Systems for Medical Data Analysis

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Abstract

Advancements in machine learning and the growing availability of medical data have enabled the construction of computer-aided detection (CAD) systems for analysis and classification. This thesis proposes interpretable machine learning models and self-explanatory deep learning models for medical data analysis, with a particular emphasis on breast cancer detection using digital mammograms. The primary objective is to enhance medical diagnostics with accurate and interpretable methods, ensuring trust and usability in clinical settings.

The research introduces novel CAD systems for critical medical applications, including breast cancer classification, prediction of nasal polyp recurrence, and Alzheimer's disease detection through functional magnetic resonance image (fMRI) analysis. Two primary methodological approaches are explored: traditional machine learning and deep learning. The former incorporates preprocessing, feature extraction, selection, and tree-based classifiers to address challenges in smaller datasets. The latter leverages self-explanatory deep learning models, such as convolutional neural networks, ensuring transparency in decision-making processes.

Comprehensive experiments are carried out utilizing publicly available datasets and real-world data. First, a CAD system is proposed for digital mammogram classification, combining texture- and shape-based features extracted from mammograms using traditional machine learning methods. Understanding the decision-making process of the systems utilized in healthcare is of utmost importance. Hence, self-explanatory deep learning models are evaluated for breast cancer detection to assess their effectiveness compared to traditional machine learning methods. The results show that traditional machine learning methods provide competitive accuracy while offering better interpretability compared to deep learning models. The findings highlight the efficiency and interpretability of traditional machine learning models, especially for smaller datasets. The proposed methods are also tested on real-world numerical medical data and other medical images related to psychology. The thesis contributes to the field of medical diagnostics by providing robust and interpretable methodologies for medical data analysis and classification.

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Chapter 1

Introduction

With advancements in machine learning, its application in computer-aided diagnosis and detection (CAD) systems has gained considerable interest. These systems assist healthcare professionals in the interpretation of medical images and data, aiming to improve diagnostic accuracy and efficiency. Medical data includes two main types: images and numerical data. Medical images capture the internal structure of the human body while numerical data includes demographic information on the patient, clinical history, and laboratory test results.

1.1 Motivation

Machine learning (ML) has been widely used in medical data analysis, with traditional approaches like Decision Trees (DTs) and Random Forests (RFs) proving effective in disease classification. Recently, deep learning (DL), particularly convolutional neural networks (CNNs), has shown success in image-based medical tasks. However, medical datasets often suffer from small sample sizes, high dimensionality, and class imbalance, making model development difficult.

Interpretability is crucial in healthcare applications. Traditional ML models, such as DTs and RFs, are inherently interpretable, providing a clear decision path. In contrast, DL models often function as black boxes, necessitating self-explanatory approaches for trust and transparency. This thesis aims to develop interpretable CAD systems combining traditional ML and self-explanatory DL for medical data analysis, focusing on breast cancer detection using digital mammograms.

1.2 Objectives

The thesis aims to develop and evaluate interpretable ML and DL models for medical data classification, with a primary focus on digital mammogram analysis.

The key objectives include:

1. Developing a CAD system for mammogram classification, distinguishing between normal, benign, and malignant cases using texture.

2. Developing a CAD system for mammogram classification, distinguishing between benign, and malignant cases using texture and shape-based features.

3. Exploring deep learning models for lesion classification, ensuring self-explanation via heatmaps highlighting relevant mammogram regions.

4. Analyzing real-world numerical medical data, applying ML techniques to classify diseases such as breast cancer and nasal polyp recurrence.

5. Extending methods to other medical applications, evaluating Alzheimer's disease detection using fMRI data.

1.3 Contributions

The thesis contributes to the field of computer-aided diagnosis and detection by developing ML and DL models for medical data analysis through the following innovations:

1. A *novel CAD system for digital mammogram classification* in three classes: (a) normal, (b) benign, and (c) malignant. The system uses texture features extracted from the Gray-Level Run-Length Matrix (GLRLM) along with traditional ML classification. The system is evaluated on the Mammographic Image Analysis Society (MIAS) dataset, demonstrating competitive performance in breast cancer classification.

   The results of this contribution are published in [BAC2021; Baj2021].

2. A *novel CAD system for lesion classification* in two classes: (a) benign, and (b) malignant. The system uses a novel feature extraction method *combining texture (GLRLM) and shape-based features* extracted from mammograms, providing a comprehensive view of mammograms, and leading to better classification performance. The system is evaluated on the Digital Database for Screening Mammography (DDSM) dataset, achieving competitive results. Additionally, the combination of features extracted from different perspectives of the mammogram is evaluated.

   The results of the contribution are published in [BAC2024; BC2025a].

3. A *comprehensive analysis* evaluating the performance of traditional ML models, namely decision trees and random forests, in medical image analysis. The analysis includes the evaluation of (a) texture features (GLRLM), (b) shape-based features (defining the one-dimensional representation of a lesion) and (c) the combination of the features mentioned in (a) and (b). Lesion masks are necessary to extract shape-based features; hence, the DDSM dataset is used, as it provides a precise definition of the lesion boundaries.

   The results of the contribution are published in [BC2023; BCA2023].

4. A *novel and fully automated breast cancer classification system* that integrates interpretable methods for preprocessing, segmentation, feature extraction, feature selection, and classification. The preprocessing consists of defining the breast tissue using binary thresholding and enhancing it. The intermediary steps can be presented to the user to offer insight into the system's functioning. For segmentation Threshold-based GrowCut (ThGC) [Mor+2022] algorithm is employed. Being an iterative method, its results can be displayed at each iteration for deeper understanding of the segmentation process. From the segmented area easily understandable features – both texture- and shape-based – are extracted followed by feature selection to reduce the input size by empoying Principal Component Analysis. For classification, Decision Tree and Random Forest models are constructed. These models have an interpretable structure, facilitating the understanding of the decision-making process. The system is evaluated on the MIAS and DDSM datasets, obtaining comparable performance to systems presented in the literature.

   The results of the contribution is published in [Mor+2022; Mor+2025].

5. *A framework based on deep learning models*, evaluating ResNet-50, BagNet, and ProtoPNet, for the detection of breast cancer from digital mammograms. To improve the models' performance on medical datasets, transfer learning and data augmentation techniques are applied. Furthermore, ResNet-50 and ProtoPNet models are extended with additional dropout layers, which are separated by batch normalization to improve classification performance. Transparency is critical in systems integrated into medical decision-making. Hence, interpretability of the models is essential. BagNet and ProtoPNet are ResNet-50-based self-explanatory models with the ability to highlight the relevant regions of the mammogram used for the classification. The framework is evaluated on the MIAS and DDSM datasets.

   The results of the contribution is published in [BCS2025; Por+2024].

6. Two novel systems utilizing traditional machine learning methods for *numerical medical data analysis.*

(i) The first system is designed for breast cancer diagnosis using numerical medical data. The system is based on traditional ML models, using numerical data extracted from two biological fluids: blood (serum) and urine. The system shows high performance and emphasizes the use of this type of numerical analysis for breast cancer screening.

(ii) The second system aims to predict the recurrence of nasal polyps using numerical medical data. The system utilizes traditional ML models and achieves promising results, offering valuable insights. Its predictions assist healthcare professionals in developing tailored treatment plans for improved outcomes.

The development of the systems involves multiple iterations in cooperation with the field experts from the research group. The results are obtained on real-world data and evaluated both numerically and by medical experts. The achieved results demonstrate the effectiveness and robustness of the proposed systems.

The results of the contribution are published in [Gat+2024; Ian+2022].

7. *A system based on machine learning for functional-Magnetic Resonance Image (fMRI) analysis* with particular emphasizes on *Alzheimer's disease detection*. From the fMRI data three functional connectivity networks are extracted from 116 regions defined in the brain to detect disruptions in connectivity, namely (1) low-order topographical, (2) high-order topographical, and (3) associated high-order functional connectivity. For classification both traditional machine learning and deep learning models are used. The performance of the ML and DL models is compared with regard to the classification performance of fMRI showing the efficiency of traditional ML over DL models in data limited scenarios.

   The results of the contribution have been submitted for publication in [BC2025b].

1.4 List of publications

This section provides a list of publications that resulted from the research conducted in this thesis. Journal publications are categorized according to the Executive Unit for the Financing of Higher Education, Research, Development and Innovation (UEFISCDI)[1] based on their publishing year and article influence score. Conference papers are categorized according to Compute Research and Education (CORE)[2] rankings (categories A*, A, B, C, D) based on their publishing year.

[1] UEFISCDI: `https://uefiscdi.gov.ro/scientometrie-reviste`
[2] CORE Conference Portal: `https://portal.core.edu.au/conf-ranks`

1. **Adél Bajcsi**, and Camelia Chira, “Feature combination from different mammogram perspectives to improve lesion classification”. In: *Logic Journal of the IGPL* (2025). Accepted. [category C, 2 points]

2. **Adél Bajcsi**, Camelia Chira, and Annamária Szenkovits, “Evaluating ResNet-based Interpretable Models for Breast Lesion Classification”. In: *Proceedings of the 17th International Conference on Agents and Artificial Intelligence - Volume 3: ICAART2025*. SciTePress, 2025, pp. 288–295. ISBN: 978-989-758-737-5. DOI: 10.5220/0013121900003890. [category B, short paper, 2.67 points]

3. Cristiana Moroz-Dubenco, **Adél Bajcsi**, Anca Andreica, and Camelia Chira, “Towards an interpretable breast cancer detection and diagnosis system”. In: *Computers in Biology and Medicine* 185 (2025), p. 109520. ISSN: 0010-4825. DOI: 10.1016/j.compbiomed.2024.109520. [category A, 4 points]

4. **Adél Bajcsi**, Anca Andreica, and Camelia Chira, “Significance of Training Images and Feature Extraction in Lesion Classification”. In: *Proceedings of the 16th International Conference on Agents and Artificial Intelligence - Volume 3: ICAART2024*. SciTePress, 2024, pp. 117–124. ISBN: 978-989-758-680-4. DOI: 10.5220/0012308900003636. [category B, short paper, 2.67 points]

5. Anda Gata, Lajos Raduly, Liviuța Budișan, **Adél Bajcsi**, Teodora-Maria Ursu, Camelia Chira, Laura Dioșan, Ioana Berindan-Neagoe, and Silviu Albu, “Machine Learning Model Predicts Postoperative Outcomes in Chronic Rhinosinusitis With Nasal Polyps”. In: *Clinical Otolaryngology* 49.6 (Aug. 2024), pp. 776–784. ISSN: 1749-4486. DOI: 10.1111/coa.14208. [category B, 0.57 points]

6. Ábel Portik, **Adél Bajcsi**, Annamária Szekovits, and Zalán Bodó, “Exploring the Impact of Backbone Architecture on Explainable CNNs’ Interpretability”. In: *Acta Universitatis Sapientiae* 16 (1 2024), pp. 105–123. DOI: 10.2478/ausi-2024-0007. [category D, -]

7. **Adél Bajcsi**, and Camelia Chira, “Textural and Shape Features for Lesion Classification in Mammogram Analysis”. In: *Hybrid Artificial Intelligent Systems HAIS2023 (Lecture Notes in Computer Science)*. Vol. 14001. Springer Nature Switzerland, 2023, pp. 755–767. ISBN: 9783031407253. DOI: 10.1007/978-3-031-40725-3_64. [category C, 2 points]

8. **Adél Bajcsi**, Camelia Chira, and Anca Andreica, “Extended Mammogram Classification From Textural Features”. In: *Studia Universitatis Babeș-Bolyai Informatica* 67 (2 Feb. 2023), pp. 5–20. DOI: 10.24193/subbi.2022.2.01. [category D, 1 point]

9. Stefania D. Iancu, Ramona G. Cozan, Andrei Stefancu, Maria David, Tudor Moisoiu, Cristiana Moroz-Dubenco, **Adél Bajcsi**, Camelia Chira, Anca Andreica, Loredana F. Leopold, Daniela Eniu, Adelina Staicu, Iulian Goidescu, Carmen Socaciu, Dan T. Eniu, Laura Diosan, and Nicolae Leopold, "SERS liquid biopsy in breast cancer. What can we learn from SERS on serum and urine?" In: *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 273 (May 2022), p. 120992. ISSN: 1386-1425. DOI: `10.1016/j.saa.2022.120992`. [category B, 0.27 points]

10. Cristiana Moroz-Dubenco, **Adél Bajcsi**, Anca Andreica, and Camelia Chira, "An Unsupervised Threshold-based GrowCut Algorithm for Mammography Lesion Detection". In: *Knowledge-Based and Intelligent Information & Engineering Systems: Proceedings of the 26th International Conference KES2022*. Vol. 207. Elsevier BV, 2022, pp. 2096–2105. DOI: `10.1016/j.procs.2022.09.269`. [category B, 2 points]

11. **Adél Bajcsi**, "Towards a Support System for Digital Mammogram Classification". In: *Studia Universitatis Babeș-Bolyai Informatica* 66 (2 Dec. 2021), p. 19. ISSN: 2065-9601. DOI: `10.24193/subbi.2021.2.02`. [category D, 1 point]

12. **Adél Bajcsi**, Anca Andreica, and Camelia Chira, "Towards feature selection for digital mammogram classification". In: *Knowledge-Based and Intelligent Information & Engineering Systems: Proceedings of the 25th International Conference KES2021*. Vol. 192. Procedia Computer Science, 2021. DOI: `10.1016/j.procs.2021.08.065`. [category B, 4 points]

In addition, the following article has been submitted to the conference of *Artificial Intelligence in Medicine*:

Adél Bajcsi, and Camelia Chira, "fMRI Analysis for Alzheimer's Disease Detection: Traditional vs. Deep Learning Models". In: *Artificial Intelligence in Medicine AIME2025*. Submitted. 2025. [category B]

Chapter 2

Proposed Traditional Machine Learning System for Digital Mammogram Classification

Breast cancer is the most common cancer diagnosed in women. It also accounts for the highest number of cancer-related deaths in the European Union [EU 2023]. Early detection of abnormalities is crucial for a successful treatment. Digital mammography uses X-rays to capture the structure of breast tissue. Mammograms are frequently used for breast cancer screening and facilitate the development of CAD systems that assist doctors in making the diagnosis and choosing the proper treatment. This chapter presents the proposed traditional machine learning (ML) methods developed to address the problem of mammogram classification.

2.1 Three Class Classification: normal, benign and malignant

Digital mammogram datasets typically contain three classes: normal, benign, and malignant. The goal is to develop a classification system to distinguish between these classes.

Scanned mammograms often include artifacts (e.g., annotations) and the pectoral muscle, which are irrelevant for tumor detection. Artifacts are removed using binary classification, retaining the largest connected component as the breast mask. Two methods eliminate the pectoral muscle: a sliding window approach [Shr+2017] and a seeded region growing algorithm [MNB2012]. Contrast Limited Adaptive Histogram Equalization (CLAHE) enhances image texture.

Texture features, such as Gray-Level Run-Length Matrix (GLRLM) [CK2019], characterize tissue density. GLRLM captures spatial relationships by analyzing gray-level runs in four directions (horizontal, vertical, and diagonals). A total of 44 features are extracted from the mammogram images.

To reduce dimensionality, we employ Principal Component Analysis (PCA) [SGM2010] and a genetic algorithm (GA) [CK2019]. PCA transforms input features into orthogonal components ordered by variance explained, while GA identifies optimal feature subsets via classifier-based fitness evaluation.

To ensure interpretability, we use tree-based classifiers: Decision Tree (DT) and Random Forest (RF). These models provide transparency and feature importance insights, fostering trust in medical decision support systems.

2.2 Two Class Classification: benign and malignant

Selecting appropriate breast cancer treatment is challenging, as it depends on cancer type, stage, and patient health. We propose a binary classification system to differentiate benign from malignant tumors.

The lesion mask isolates the region of interest. A bounding box around the abnormality is expanded by 25 pixels to capture surrounding tissue and potential microcalcifications indicative of malignancy.

Malignant lesions exhibit irregular shapes, whereas benign lesions are more circular [Dav2022]. We extract shape features, including area, perimeter, and compactness. Additionally, contour-based features are computed by comparing the segmented lesion to an enclosing ellipse [Li+2017].

Mammograms are taken from two views: (1) mediolateral oblique (MLO) (side view) (2) craniocaudal (CC) (top-down view) Features from both views are concatenated into a single vector for improved classification.

We employ two feature selection methods (PCA, GA) and two classifiers (DT, RF), as described in Section 2.1, to classify mammograms as benign or malignant.

2.3 Computational Experiments

The proposed methods are evaluated using four metrics: accuracy, precision, recall, and F_1 score. These metrics are frequently used to assess imbalanced classification tasks.

The effectiveness of pectoral muscle removal methods is assessed using the MIAS dataset [SPD1994]. Since this dataset does not contain explicit pectoral muscle annotations, k-means clustering [Has+2021] is used to generate pectoral masks. The results indicate that the seeded region growing method performs better than the sliding window approach, achieving a precision of 95.72% and a recall of 70.14%.

The CAD system for distinguishing normal, benign, and malignant breast tissue is tested on the MIAS dataset. The system relies on GLRLM texture features extracted from mammograms. The best performance is obtained using PCA for feature selection and Random Forest for classification, resulting in an accuracy of 72.84%.

For binary classification of breast lesions, the system is evaluated on DDSM [Hea+1998; Hea+2001], which provides manual segmentation for each lesion. Preliminary experiments reveal that the assumption regarding lesion shape does not always hold, as some benign lesions appear irregular while some malignant lesions exhibit circular patterns. To address this, stratified subsets of the dataset are created based on lesion irregularity. The results demonstrate that shape features outperform texture features in distinguishing breast abnormalities. The highest accuracy, 96.12%, is achieved using Random Forest classification without feature selection on the subset excluding outliers. Additionally, an analysis of features extracted from different mammogram views indicates that those derived from the MLO view slightly outperform the combined features from both perspectives.

2.4 Conclusion

This chapter introduced a traditional machine learning-based CAD system for breast cancer classification using digital mammograms. The proposed system follows a structured pipeline: preprocessing, feature extraction, feature selection, and classification.

Experimental results demonstrate that Decision Trees (DTs) and Random Forests (RFs) achieve competitive classification performance while maintaining interpretability. Feature extraction methods based on texture (GLRLM) and shape features significantly contribute to accurate lesion classification. Additionally, feature selection techniques, such as Principal Component Analysis (PCA) and Genetic Algorithms (GA), enhance model efficiency by reducing dimensionality. The findings highlight the advantages of traditional ML over deep learning models in data-limited scenarios, proving that interpretable methods can achieve high accuracy while offering transparency in decision-making.

Chapter 3

Proposed Explainable Deep Learning System for Digital Mammograms Classification

Deep learning models are frequently used for image classification tasks. In general, constructing a deep neural network model involves a considerable amount of data due to the large number of parameters optimized during training. Medical datasets usually contain a few thousand records (at most) due to the limited number of subjects and data privacy concerns. Consequently, data augmentation has emerged as a crucial technique to artificially expand the size and variance of these datasets.

In critical field, such as healthcare, the transparency of the model is essential. The explainability of the model is crucial for the acceptance of the model by medical professionals. Hence, in this chapter, we investigate two explainable models, namely ProtoPNet [Che+2018] and BagNet [BB2019].

3.1 Proposed Methods

The images are preprocessed similarly to Section 2.2. In addition, the images are normalized to have zero mean and unit variance and resized to 224×224.

In the experiments, three models are included: ResNet-50 [He+2015], BagNet [BB2019], and ProtoPNet [Che+2018]. ResNet-50 [He+2015] serves as the backbone for both BagNet and ProtoPNet. It is a widely used black-box model designed to mitigate vanishing gradients through residual blocks. To enhance performance, additional dropout layers are inserted before the fully connected layer, combined with batch normalization and ReLU activation.

BagNet [BB2019] modifies the structure of the ResNet-50 model by: (1) replacing the initial 7×7 convolution with a 3×3 convolution, and (2) reducing the number of 3×3 convolutions by leaving only the first bottleneck block of a residual block 3×3 convolution, and the rest is decreased to 1×1 convolutions.

ProtoPNet [Che+2018] consists of three modules: (1) feature extraction, (2) prototype generation, and (3) classification. To ensure comparability, feature extraction is performed using a ResNet-50 model. Similar to the other models, ProtoPNet is extended with batch normalization and dropout layers before the fully connected layer.

3.2 Computational Experiments

To evaluate the proposed deep learning-based CAD system, multiple experiments were conducted on publicly available mammogram datasets (MIAS [SPD1994] and DDSM [Hea+1998; Hea+2001]). The experiments assess the effectiveness of ResNet-50, BagNet, and ProtoPNet, focusing on classification accuracy and interpretability (by visual evaluation).

Given the limited size of medical datasets, data augmentation (e.g., rotation, flipping, contrast adjustments) was applied to improve model generalization. Transfer learning was used by fine-tuning pre-trained models to leverage knowledge from larger datasets.

The results showed that BagNet and ProtoPNet improved interpretability by generating heatmaps that highlighted relevant regions in mammograms, while ResNet-50 achieved high accuracy but lacked transparency. When comparing traditional machine learning with deep learning models, deep learning methods provided strong classification performance, but traditional ML approaches remained competitive, particularly for smaller datasets where interpretability plays a crucial role.

3.3 Conclusions

This chapter presented a deep learning-based CAD system for breast cancer classification, focusing on self-explanatory models to enhance interpretability. Three architectures were evaluated: ResNet-50, BagNet, and ProtoPNet. Results show that self-explanatory deep learning models provide insights into decision-making by highlighting relevant mammogram regions. While deep learning achieves high accuracy, it remains more complex and less interpretable compared to traditional ML models. BagNet and ProtoPNet offer better transparency by enabling heatmap generation, making them more suitable for medical applications requiring explainability.

Chapter 4

Proposed Systems for Cancer Detection from Numerical Medical Data Analysis

This chapter focuses on the development of traditional machine learning CAD systems based on numerical data analysis. First, surface-enhanced Raman scattering analysis of biofluids is used for the prediction of breast cancer, followed by the classification of tissue analysis reports to predict the relapse of nasal polyps. Both research studies are the result of a collaboration with medical experts, and are conducted on real-world data.

4.1 Prediction of Breast Cancer based on Numerical Data Analysis

Breast cancer detection using numerical medical data presents a valuable alternative to image-based approaches. Among these, surface-enhanced Raman scattering (SERS) has attracted considerable interest as a promising technique. With the development of artificial intelligence, CAD systems that utilize machine learning methods have been widely investigated. This section presents the results of a collaboration with a multidisciplinary group of researchers.

4.1.1 Proposed Methods

The first step of the system is the preprocessing of the SERS spectra. To reduce the noice, filtering and rubberband baseline subtraction are employed. The spectra are further normalized and smoothed.

We propose the use of five machine learning methods (Linear Discriminant Analysis – LDA [Zha+2024], Decision Tree – DT [Bur2019], Random Forest – RF [Bur2019], Gaussian Naïve Bayes – GNB [Rah+2021], and Support Vector Machine – SVM [An+2023]) for the classification of SERS information resulting from the analysis of different biological specimens. The purpose of these models is to distinguish patients in the control group from those with breast cancer.

DT and RF have been chosen for their ability to handle high-dimensional data and their interpretability. LDA is a linear classifier that is widely used in the field of medical diagnostics. GNB is a simple probabilistic classifier that is easy to implement and computationally efficient. SVM is a powerful classifier that can handle high-dimensional data and is widely used in medical diagnostics.

4.1.2 Computational Experiments

The system is evaluated on a real-world dataset collected from patients with breast cancer and control subjects. The dataset consists of SERS spectra extracted from serum and urine samples.

The performance of the system is evaluated using the following metrics: accuracy, precision, recall, and F_1 score. Using the spectra extracted from serum achieves the best performance with an accuracy of 83.33% and an F_1 score of 88% using the LDA classifier. On the other hand, using the spectra extracted from urine produces the best performance with an accuracy of 83.33%, a correctness of 84.62%, a completeness of 91.67%, and an F_1 score of 88% using the LDA classifier. On the other hand, the best-performing model using urine SERS data is the DT classifier, with an accuracy of 88.89%, a correctness, completeness and an F_1 score of 91.67%. The results show that the SERS spectra extracted from urine and serum contain different information, which can lead to better classification performance. The combination of serum and urine SERS spectra is also investigated, showing similar performance to the classification using serum SERS data.

The effect of feature selection (PCA) is also investigated, showing that the performance of the models is not significantly improved by reducing the dimensionality of the data. The results suggest that the SERS spectra contain valuable information for the classification of breast cancer patients and control subjects.

In addition to the numerical evaluation, the results are also evaluated by the medical experts of the research group.

4.1.3 Conclusions

In this section, we proposed a computer-aided detection system for breast cancer detection using SERS spectra. The system uses five different classifiers (Linear Discriminant Analysis, Decision Tree, Random Forest, Gaussian Naïve Bayes, and

Support Vector Machine) to distinguish breast cancer patients from control subjects based on SERS spectra extracted from serum and urine. Slightly higher classification accuracies are achieved using urine samples compared to serum samples, despite the higher variability in the urine SERS spectra. The effect of combining the SERS data extracted from serum and urine is also investigated, showing a similar performance to that of the classification using SERS data extracted from serum.

4.2 Prediction of Nasal Polyps Recurrence After Endoscopic Sinus Surgery

Endoscopic Sinus Surgery is the most frequently used treatment for chronic rhinosinusitis with nasal polyps when medical treatments are not effective enough [Tao+2018]. The recurrence rate of polyps is concerning, emerging the development of a CAD system that predicts the likelihood of relapse and assists doctors in selecting the most appropriate treatment. The experiments presented in this section are the result of a collaboration with medical experts, who collected real-world data.

4.2.1 Proposed Methods

In this section, we propose a CAD system for predicting the relapse of nasal polyps from two types of data: (1) noninvasive, and (2) invasive. The data is normalized, and the correlation between the features is analyzed.

The aim of the system is to predict three classes: (1) control, (2) partial control, and (3) relapse. The interpretability of the models is crucial in medical applications, and tree-based classifiers are used for their inherent interpretability and promising results in medical data analysis. Decision Trees (DTs) are simple classifiers that make decisions by evaluating a series of conditions. These conditions are applied at each node of the tree, leading to a classification decision at the leaves, which makes DTs highly interpretable and useful for understanding how specific features influence predictions. Random Forests (RFs) are ensemble models composed of a given number of DTs. The final label is determined through a majority vote, improving accuracy and capturing a wider range of decision patterns, thus enhancing robustness and reducing overfitting.

4.2.2 Computational Experiments

The system is evaluated on a real-world dataset consisting of an 18-month follow-up period, with semiannual evaluations of patients who underwent endoscopic sinus surgery. The aim of the system is to predict the state of the patient 18 months after the surgery. First, the performance of the classifiers is evaluated for predicting relapse state at each follow-up visit. The results show that Random Forest classifiers achieve higher results.

In recent years, the use of microRNA has gained attention as a possible biomarker for chronic rhinosinusitis [Son+2022]. The dataset contains two microRNA types: microRNA 125b and microRNA 203a-3p, extracted from tissue samples retained during surgery. The effect of different microRNA combinations on the prediction performance is analyzed. The results show that the use of microRNA 125b improves the performance of the classifiers, achieving 84.62%, 87.28%, 84.62%, and 83.79% accuracy, precision, recall, and F_1 score, respectively.

The use of Random Forest classifier enables the analysis of features importance, providing valuable insight into the relevance of the features for the prediction task. The results show that microRNA 125b is the most important feature for the prediction of nasal polyps relapse.

4.2.3 Conclusions

In this section, the results of a collaboration with medical experts from the Department of Otorhinolaryngology of the University of Medicine and Pharmacy "Iuliu Hațieganu" are presented to predict the reformation of the nasal polyp after surgery. Tree-based models are proposed for the classification of real-world data collected at the Clinical Hospital CF Cluj-Napoca, to predict the postoperative severity of nasal polyps. Our research shows the relevance of microRNA, especially microRNA 125a, for the prediction of disease recurrence. In addition, Random Forest achieves the highest performance, with 84.62% accuracy and 85.93% F_1 score. Since Random Forest is inherently interpretable, it provides valuable insight into the feature importance, allowing for better understanding and transparency in medical decision-making process.

Chapter 5

Machine Learning Approaches to fMRI Analysis for Alzheimer's Disease Detection

Medical images are widely used and are interdisciplinary. For example, analysis of functional Magnetic Resonance Images (fMRIs) can assist psychologists predict the effect of a trauma or help neurologists predict the stage of dementia. The aim of this chapter is to explore the performance of methods proposed previously for fMRI analysis for Alzheimer's disease.

In the present thesis, we propose a CAD system using machine learning for fMRI data analysis and classification. fMRIs are widely used for detecting Alzheimer's by recording blood oxygen levels, enabling the analysis of brain connectivity.

5.1 Proposed Methods

Resting-state FMRI (rs-FMRI) is the most frequently used imaging modality for Alzheimer's detection. rs-FMRI are four-dimensional images: the volume of the brain is recorded over a period of time. The images capture the blood oxygen level of the brain representing the activity of the respective region. By extracting and analyzing the signals from these images, we can infer the connectivity between different regions of the brain. The connectivity matrix is then used to train a machine learning model for classification.

The preprocessing of the rs-FMRI data begins with the removal of the first 10 volumes to ensure the stabilization of the magnetic field. The data is then corrected for the slice timing and motion artifacts. The images are co-registered to the anatomical images and normalized to the MNI template. The data is then smoothed and band-pass filtered to remove noise. The regions of interest (ROIs) of the brain are determined using the AAL atlas. The mean signal from each ROI is extracted and used to calculate the connectivity matrix.

We propose the use of three functional connectivity networks (FC): (1) low-order, (2) topographical high-order, and (3) associated high-order. Low-order FC represents the correlation between the ROIs creating a subnetwork. The topographical high-order FC represents the correlation between subnetworks. The associated high-order FC represents the correlation between ROIs and subnetworks. Using a sliding window, we can split the signal into smaller parts and use them to compute the aforementioned FC networks to achieve dynamic features. Based on the experiments presented in [Zha+2017], the window length is set to 70 and the stride is set to 1, resulting in 61 sub-series. In addition, static features are also defined using a window length equal to the length of the signal.

To classify the extracted features, both traditional machine learning algorithms and deep learning models are used. Traditional machine learning algorithms include: Support Vector Machine (SVM), Decision Tree (DT), Random Forest (RF), and k-Nearest Neighbors (kNN). The deep learning models include: ResNet-18 and ResNet-50. DT, RF and SVM have been presented in Section 4.1. kNN is a simple and effective algorithm that classifies data based on the majority of the k nearest neighbors. ResNet-18 and ResNet-50 are widely used for image classification tasks differing in model complexity, which is determined by the number of layers.

5.2 Computational Experiments

To evaluate the performance of the proposed methods, we conducted experiments on the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset [ADNI2024]. The dataset comprises a vast collection of clinical and neuroimaging data, particularly focusing on AD and its early stages. For the current experiments, we select individuals labeled as CN or AD patients who have structural MRI and resting-state fMRI scans. We also consider the balanced distribution of cases and a similar average age (around 75). As a result, 93 cases are selected from each class, 186 cases in total.

First, the best filtering is selected for fMRI analysis. We compare the performance of the traditional machine learning algorithms using the following filters: (1) slow5 (0.01 Hz – 0.027 Hz), (2) slow4 (0.027 Hz – 0.08 Hz), and (3) full-band (0.01 Hz – 0.08 Hz). In general, classifiers perform better with the slow5 filter. We also compare the performance of the traditional machine learning algorithms with the deep learning models. The traditional machine learning methods outperform the deep learning models, which may be due to the small size of the dataset. The best results achieved by traditional machine learning are with SVM, reaching a test accuracy 97.37%, while the best results achieved by deep learning are with

ResNet-18, reaching a test accuracy of 71.05%. ResNet-18 achieves the best test performance when trained on dynamic FC by 71.05%. ResNet-50 is less effective than ResNet-18. This could be attributed to the higher number of parameters in ResNet-50 and the limited number of training data.

5.3 Conclusions

Alzheimer's disease affects the lives of millions of people worldwide. Timely detection of the disease, and proper treatment, can slow down the course of dementia. In this chapter, we presented a system based on the analysis of resting-state fMRI using the previously proposed machine learning models to detect Alzheimer's disease. After preprocessing and extracting functional connectivity, we built four traditional machine learning models (DT, RF, kNN, and SVM) and two deep learning models (ResNet-18 and ResNet-50). The results show that SVM has the best performance among traditional machine learning methods, achieving 97.37% test accuracy. We also conclude that ResNet-18 outperforms ResNet-50, achieving 71.05% test accuracy. The performance difference could be due to the limited number of data available to train deep learning models.

In future work, we aim to investigate the effect of data augmentation and add-on layers using batch normalization and dropout to enhance the performance of deep learning. We will also extend our analysis to other deep learning models as well. Furthermore, in future experiments, we will include intermediate states of AD, such as mild cognitive impairment (MCI), and we will assess the performance of the proposed models with regard to (1) binary classification (CN vs. MCI, MCI vs. AD) and (2) multiclass classification.

Chapter 6

Conclusions and Future Work

This thesis explored the development and evaluation of interpretable machine learning and computer-aided detection (CAD) systems for medical data analysis and classification, with a particular emphasis on breast cancer detection using digital mammograms, among other applications. The primary objective was to advance methodologies in medical diagnostics, ensuring both accuracy and interpretability to enhance trust and usability in clinical settings.

6.1 Main Results and Contributions

The thesis contributes to the field of digital mammogram classification by proposing a novel CAD system that combines texture and shape features extracted from mammograms using traditional machine learning (ML) approach. The system was evaluated on the Digital Database for Screening Mammography (DDSM). The system successfully classified lesions in mammograms into two classes: benign and malignant, with an accuracy of 96.12% on the DDSM dataset. Furthermore, we have proposed a fully automated breast cancer classification system that integrates interpretable methods. The system was evaluated on the Mammogramphic Image Analysis Society (MIAS) and DDSM datasets, and achieved an accuracy of 95%, and 97%, respectively, for breast cancer classification, highlighting the robustness of the approach. The proposed systems emphasize the efficiency and interpretability of traditional ML models, particularly for smaller datasets.

The research emphasized the importance of model explainability in healthcare. We proposed the use of self-explanatory deep learning (DL) models for breast cancer detection, which are essential to build trust in the system and understand the decision-making process. We evaluated three deep learning models: ResNet-50, BagNet, and ProtoPNet, on the MIAS and DDSM datasets. To address the limitations of medical datasets, techniques such as transfer learning and data augmentation were employed effectively, significantly improving model performance while preserving diagnostic integrity. The models successfully distinguished lesions, with an accuracy of 93.38%, 92.39%, and 78.11% on the MIAS, and 95.26%, 95.25%, and 91.23% on the DDSM dataset, respectively, using ResNet-50, BagNet, and ProtoPNet models.

The methodologies were applied to breast cancer detection, nasal polyp recurrence prediction, and Alzheimer's disease detection using fMRI data through collaboration with experts. The diversity of applications demonstrates the flexibility and robustness of the proposed methods. In addition to mammogram analysis, a breast cancer detection system was developed using numerical medical data (SERS liquid biopsy). The system achieves an accuracy of 88.89% and an F_1 score of 91.67% using Decision Tree classifier. For the prediction of nasal polyp reformation, real-world numerical data was used and the performance of tree-based classifiers were evaluated. The results show the efficiency of the Random Forest over Decision Tree. For fMRI analysis, the ML and DL approaches were compared. The best-performing ML model (SVM) achieved 97.37%, while the best-performing DL model (ResNet-18) achieved 71.05% accuracy. The results highlight the advantage of ML compared to DL when the data is limited.

6.2 Directions for Future Work

An interdisciplinary collaboration with radiologists and oncologists from "Ion Chiricuță" Oncologic Institute in Cluj-Napoca, Romania, is working on the collection and annotation of the new digital mammogram dataset. In the future, we will apply the proposed methodologies to the new dataset to evaluate the performance of the systems on dense breast tissue.

A promising research direction for breast cancer classification would be the extension of the system into a multimodal one, combining mammogram images with demographic details of the patient and medical background. This would provide a more comprehensive view of the patient's health status, leading to more accurate and personalized diagnosis. However, to the best of our knowledge, no such dataset currently exists.

In future work, we aim to conduct a comprehensive user study to evaluate the usability and effectiveness of the proposed systems in clinical settings. The study will involve radiologists, oncologists, and other healthcare professionals to assess the interpretability and trustworthiness of the proposed systems. Feedback from the study will be used to further refine the systems. Additionally, post hoc interpretability approaches, such as Grad-CAM [Sel+2019], SHAP [LL2017] and LIME [RSG2016] will be explored to provide more detailed insights into the decision-making process of the deep learning models.

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