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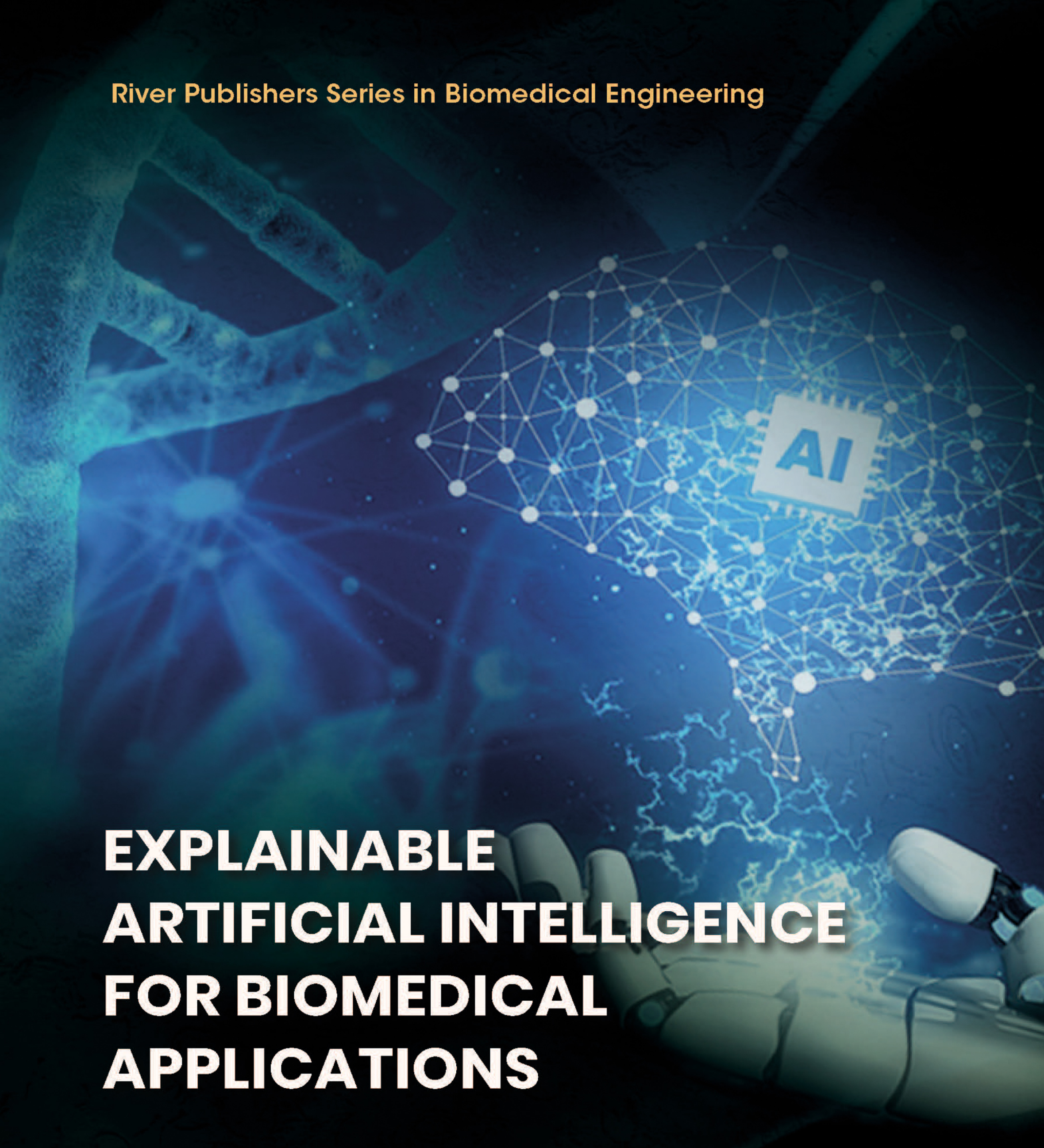

EXPLAINABLE ARTIFICIAL INTELLIGENCE FOR BIOMEDICAL APPLICATIONS

Editors:

Utku Kose
Deepak Gupta
Xi Chen

River Publishers

Explainable Artificial Intelligence for Biomedical Applications

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Explainable Artificial Intelligence for Biomedical Applications

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Preface

In the 21st century, so far, biomedical applications have been in a great momentum, thanks to the use of advanced technology. Here, the use of artificial intelligence models has a remarkable role to advance the outputs in terms of different tasks such as medical inferencing, diagnosis, and treatment planning. When it is evaluated from the variety of successful tasks, artificial intelligence is already an effective decision support tool for doctors, medical staff, and researchers. That situation is associated with intense developments, which are done often in the intersection of artificial intelligence and biomedical. Even early applications of intelligent systems were done for biomedical problems at first. So, more steps were taken for improving capabilities of artificial intelligence in analyzing biomedical data and solving the corresponding cases. As a result, current intelligent system applications are often associated with comparing machine and human limitations. It is known that today's intelligent systems ensure competitive findings when compared with human touches. Especially difficult tasks such as early diagnosis, prognosis, precision treatment, and drug design often receive revolutionary and promising results from the side of artificial intelligence.

Although technological developments are excellent for artificial intelligence usage in biomedical, there is the issue that today's intelligent systems go beyond the human capabilities. That means we are no longer able to track the mechanisms shaping the output results by analyzing the input variables. As long as deep learning models or hybrid machine learning formations require many parameters for success, it is almost impossible to have interpretable reasons for how these models can create a relation between input data and output decisions. At this point, it is not possible to detect failure and success points of intelligent systems. Being known as black box, such type of intelligent systems cannot be used directly without understanding their safety level. So, such black-box systems should not be accepted as trustworthy until some solutions may be used to solve the issue. Nowadays, explainable artificial intelligence (XAI) is a trendy solution to ensure explainability for black-box models, which are associated with especially deep learning. Of course, the interpretability in white-box machine learning techniques is now more important when alternative solutions for trustworthy intelligent systems are thought.

The objective of this edited book is to provide the latest advancements in terms of XAI in biomedical applications. Intense consideration was given to employ the most recent research results by covering as much different topics as possible under the umbrella of biomedical field. A remarkable focus was also given to have alternative reviews for present and future state of XAI applications in the context of biomedical problems. Because there are also different solution methods for achieving explainability, the book had a careful selection for informing the audience about the variety of XAI methods. Not only including the XAI but also recalling the interpretable methods, the book hosts a total of 17 chapters targeting XAI use cases in specific problem areas. Contributions by each chapter are as follows.

Chapter 1 focuses on the diagnosis of gastric cancer by using a hybrid-network-based model. In detail, the exact mechanism of the model was analyzed, thanks to the SHAP analysis in the context of XAI research.

Chapter 2 considers another XAI method, LIME, to examine the disease diagnosis. It provides a general overview and examines the research flows in terms of applying and understanding the LIME method for diagnosis cases.

Chapter 3 ensures a review work by considering the XAI usage in veterinary and animal science field. It comes with a remarkable content by touching the animal sciences and showing the need for XAI from the veterinaries' perspective and the corresponding research topics.

Chapter 4 aims to examine a recent massive health issue: the corona virus. In this context, it provides an interpretable analysis for the potential impact of different versions of corona virus.

Chapter 5 comes with a deep review of XAI usage in biomedical applications. It hosts detailed explanations for different XAI methods and solutions with perspectives on present and future potentials.

Chapter 6 targets its research way in the survival of heart failure patients. As associated with the XAI, it considers the prediction capabilities of iterative learning by running factor analysis with the SHAP method.

Chapter 7 considers another important XAI method, CAM, for the research on deep learning for image-based data. In detail, it provides a general overview for the CAM usage and also discusses the use cases in alternative XAI solutions as well.

Chapter 8 provides a remarkable perspective on the usage of IoT in healthcare applications. The coverage of the chapter is with establishing the security with the XAI perspective.

Chapter 9 is another work associated with medical image data. It generally considers the chest disease identification from X-rays and focuses on the usage of deep learning.

Chapter 10 ensures another remarkable review of XAI, by considering dentistry as the target area. As it is critical to have the XAI touch in especially image data, the chapter achieves a timely theoretical examination for the literature of artificial intelligence applied in dentistry.

Chapter 11 hits a critical research topic, drug discovery, in the view of XAI solutions. In this context, it ensures a deep review of the research efforts for explainable drug discovery and design applications, which are supported by XAI.

Chapter 12 considers an automatic segmentation method for the spinal cord gray matter from MR image data. It employs the remarkable U-Net model for the problem solution.

Chapter 13 provides another review of drug discovery, by considering the XAI usage. It mostly considers alternative use cases of XAI for ensuring successful and trustworthy drug discovery efforts.

Chapter 14 considers a massive perspective in the context of smart healthcare services. At this point, it provides a recent view on XAI usage in the applications regarding the rural community.

Chapter 15 comes with an alternative review for XAI usage in drug discovery research. By giving an importance to the molecular inputs, it is another chapter to hit that critical research topic from the perspective of XAI.

Chapter 16 is based on research regarding classification of brain tumor images through a hybrid deep/machine learning model and alternative machine learning techniques. In detail, it considers the use of Grad-CAM for XAI purposes.

Chapter 17 recalls the IoT-based applications and focuses on the breast cancer diagnosis. In detail, it provides a remarkable comparative work.

As it may be seen, the book rises over different research orientations to understand more about the scope of XAI for better, trustworthy biomedical applications. We believe that all chapters will be useful for researchers, professionals, and degree students for understanding essentials of XAI, and the application ways for biomedical problems.

As the editors, we would like to thank all respectful authors for their valuable contributions. Our special thanks go to Prof. Omer Deperlioglu (from Afyon Kocatepe University, Turkey) for his kind foreword. Finally, we are grateful to the readers and looking forward to receiving their feedback for the book. In this context, any ideas for further projects are welcome, too.

Editors
Dr. Utku Kose
Dr. Deepak Gupta
Dr. Xi Chen

Foreword

In the field of biomedical, artificial intelligence has a great role in technological advancements. The use of intelligent algorithms allows us to improve known results and solve the most competitive problems associated with tasks such as diagnosis, treatment, and drug discovery. The latest research shows that the effective use of deep learning models achieves better findings when compared with humans. It is good to have automated solutions for saving time, saving costs, and building careful decision support for the human side. However, more advanced use of artificial intelligence causes them to be black box because we need more parameters to be optimized for better findings. That is a problem as we do not have any idea about inside mechanisms of such intelligent systems and we should still trust artificial intelligence in risky biomedical cases. Although there is a strong relation between artificial intelligence and biomedical, black-box state is a threating factor for the future advancements. As a chance, the scientific audience was not silent for this and XAI (explainable artificial intelligence) was introduced in order to integrate explainability components for tracking input–output relations.

According to me, XAI should be among essential requirements for building trustworthy intelligent systems. That is more critical when we think about using intelligent systems for biomedical cases. When we examine the literature, it may be seen that different medical data types can be analyzed through different methods such as CAM, LIME, and SHAP. As long as we take the support from mathematical and logical background for creating observable data relations, the XAI literature will host many alternative methods. That is just a matter of time according to human requirements for safe smart tools. So, there is a need for intense reviews of XAI-biomedical research, regarding the latest advancements and even future perspectives.

This edited book titled as *Explainable Artificial Intelligence (XAI) for Biomedical Applications* is a timely contribution as the field of biomedical needs a direct focus on how we can run XAI in different biomedical topics. As we know, there is a great variety of research topics in the context of biomedical field. From that perspective, this book comes with a remarkable collection of 17 chapters including different solution tasks such as diagnosis, image analysis, and data discovery. It is great to see that the book also hosts critical reviews and targets specific problem areas such as dentistry, animal sciences, and IoT use cases. It is also nice to see that the chapters were carefully gathered to discuss different, recent XAI methods used in biomedical problem areas. Each chapter has pure language to reflect the necessary knowledge to the target audience. I believe the book will be a valuable reference for not only researchers but also degree students.

As my final words, I would like to express my sincere thanks to the valuable editors: Dr. Utku Kose, Dr. Deepak Gupta, and Dr. Xi Chen. Without their efforts, such a timely contribution would not be possible. All the best for a "healthy future" with safe employment of artificial intelligence!

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As the editors, we would like to thank all valuable River Publishers staff, and especially Junko Nakajima, Rajeev Prasad, and Nicki Dennis for their kind support for realizing such a timely book project.

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List of Abbreviations

ACA	Average classification accuracy
AD	Alzheimer's disease
Ada-WHIPS	Adaptive weighted high-importance path particles
ADMET	Absorption, distribution, metabolism, excretion, toxicity
ADT	Android development tools
AES	Advanced Encryption Standard
AF	Atrial fibrillation
AG	Atrophic gastritis
AI	Artificial intelligence
AIM	Artificial intelligence in medicine
ALS	Amyotrophic lateral sclerosis
ANFIS	Adaptive neuro fuzzy inference system
ANN	Artificial neural Networks
AUC	Area under the curve
BC	Block-chain
BPH	Benign prostatic hyperplasia
BPL	Below the poverty line
C	Convolutional layer
CAD	Computer-aided diagnostics
CAM	Class activation mapping
CART	Classification and regression tree
CASP	Computer-aided synthetic planning
CAV	Concept activation vector
CBCT	Cone beam computed tomography
CBN	Cannabinol
CEM	Contrastive explanation method
CFS	Correlation-based feature selection
CIA	Confidentiality integrity availability
CNN	Convolutional neural network
CNS	Central nervous system
COVID-19	Corona virus disease 2019
CPK	Creatinine phosphokinase

CSPs	Cloud service providers
CT	Computed tomography
DAE	Deep auto-encoder
DBNs	Deep belief networks
DeepLIFT	Deep learning important features
DL	Deep learning
DLM	Deep learning models
DMTA	Design-test-make-analyze
DNN	Deep neural network
DRL	Deep restoration learning
DSA	Digital signature algorithm
DSC	Dice similarity coefficient
DT	Decision tree
DVT	Dental volumetric tomography
ECFP	Extended connectivity fingerprints
ECG	Electrocardiogram
ECOC	Error-correcting output codes
ED	Erectile dysfunction
EF	Ejection fraction
EMR	Electronic medical record
ENT	Ear–nose–throat
ESPs	Edge service providers
f	Function in the proposed model
FCN	Fully convolutional neural
FDA	Food and Drug Administration
FI	Furcation involvement
FIS	Fuzzy inference system
FN	False negative
FOV	Field of view
FP	False positive
G.Grad-CAM	Guided Grad-CAM
GA	Genetic algorithm
GAN	Generative adversarial networks
GAP	Global average pooling
GBM	Gradient-boosting machine
GC	Gastric cancer
GCN	Graph convolutional network
GIB	Graph information bottleneck
GLM	Generalized linear model
GM	Gray matter

GMP	Global max pooling
GNN	Graph neural network
GNNExplainer	GNN explainer
GP	Gaussian process
GPU	Graphics processing units
Grad-CAM	Gradient-weighted class activation mapping
H & E	Hematoxylin-eosin
HIPAA	Health Insurance Portability and Accountability Act
ICTs	Information and communication technologies
IDE	Integrated development platform
IIoT	Industrial Internet of Things
IM	Intestinal metaplasia
In-Net	Inner network
IoMT	Internet of Medical Things
IoT	Internet of Things
JSI	Jaccard similarity index
KG	Knowledge graph
KNN	*K* nearest neighbors
***k*-NN**	*k*-nearest neighbor
LCs	Lightweight clients
LIMA	Local insights model agnostic
LIME	Local interpretable model-agnostic explanation
LR	Linear regression
LRP	Layer layer-wise relevance propagation
LSHTM	London school of hygiene and tropical medicine
LSTM	Long short-term memory
M	Max pool layer
MAE	mean absolute error
MF	Membership function
MIA	Medical image analysis
ML	Machine learning
MLP	Multilayer perceptron
MMP	Matched molecular pair
MR	Magnetic resonance
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
MSE	Mean squared error
MSN	Multi-scale network
N	Count of explanatory variables
NB –	Naive Bayes

NIH	National Institutes of Health
NLP	Natural language processing
NN	Neural network
NO	Nitric oxide
NYHA	New York Heart Association
OPS	Octopus poultry safe
OvA	One-vs-All
OvO	One-vs-One
OvR	One-vs-Rest
PAH	Pulmonary arterial hypertension
PCA	Principal component analysis
PDE	Phosphodiesterol type 5
PDP	Partial dependence plot
P-HNN	Progressive holistically nested network
PmHM	Public and medical health management
PPMI	Parkinson's progression markers initiative
PPV	Positive predictive value
PSC	Protein sequence composition
QSAR	Quantitative structure–activity relationship
RBF	Radial basis functions
RBM	Restricted Boltzmann machine
ReLU	Rectified linear unit
RF	Random forest
RFID	radio frequency identification
RMSE	Root mean squared error
RNN	Recurrent neural networks
ROC	Receiver operating characteristic curve
RSA	Rivest, Shamir, and Adleman
SACM	Secure access control mechanism
SCGMC	Spinal cord gray matter segmentation challenge
SC-Net	Slice-based classification
SGD	Stochastic gradient descent
SHAP	Shapley additive explanations
SIB	Swiss Institute of Bioinformatics
SIDU	Similarity distance and uniqueness
SIR	Susceptible infected recovered
SMILES	Simplified molecular input line entry systems
SNR	Signal-to-noise ratio
SVM	Support vector machine
TD3	Twin delayed deep deterministic

THC	Tetrahydrocannabinol
TN	True negative
TNR	True negative rate
TP	True positive
TPR	True positive rate
t-SNE	t-Distributed stochastic neighbor embedding
VADER	Valence aware dictionary and sentiment reasoner
WHO	World Health Organization
WLE	White light endoscopic
WM	White matter
x	The available variable
x'	The selected variable
XAI	Explainable artificial intelligence
XGBoost	Extreme gradient boosting

1

Gastric Cancer Detection using Hybrid-based Network and SHAP Analysis

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Abstract

Gastric cancer is one of the most widely reported problems in the world, causing high modality rates in recent times. Gastroscopy is an efficient method that is widely used to analyze gastric problems. The advent of deep learning helps doctors to detect gastric cancer in the early stages. The performance of the existing methods in detecting gastric cancer from the images is not accurate. This study proposes a novel deep-learning framework that can be used to detect gastric cancer from gastric slice images. The proposed method is based on a patch-based analysis of the given input image. Specifically, the model selects and extracts the features from the images in the training phase and evaluates the genuine risk of the patients. This is one of the novel contributions of the proposed work. The bag-of-features technique is applied to the extracted features in the proposed network for the selected patches for better analysis. Experimental results prove that the proposed framework can detect gastric cancer from the images effectively and efficiently. The model is robust enough to detect the minute lesions that can cause the gastric tumor in the further stages. The dataset used in this analysis is publicly available, and the results achieved by this model are higher than the other conventional models that use the same dataset. The proposed framework gives higher accuracy scores compared with existing frameworks.

1.1 Introduction

Stomach cancer, often known as gastric cancer (GC), is a type of cancer. When cells in the stomach's lining grow out of control, they develop into tumors that can infiltrate healthy tissues and spread to other body regions. Global data show that GC is the second most common cause of cancer-related fatalities and the fourth most prevalent malignancy worldwide [1]. Environmental and genetic factors, among others, play a complex role in the onset and development of GC, and their effects on these processes have not yet been fully understood. Even after receiving a full course of treatment that includes surgery, chemotherapy, and radiotherapy, the five-year survival percentage for advanced GC is still less than 30% [2], whereas the five-year survival rate for early GC can be over 90%, sometimes even having a curative impact [3]. The incidence and development of GC is a complicated process involving numerous mechanisms, steps, and stages. Several transitional phases include the precancerous state, namely "normal gastric mucosa – chronic non-atrophic gastritis – atrophic gastritis – intestinal metaplasia – dysplasia – gastric cancer," as per the observations of Correa's currently more widely accepted pattern of human GC [4]. Atrophic gastritis (AG) and intestinal metaplasia (IM) are two conditions that are thought to be precancerous lesions that are strongly linked to GC [5]. AG and IM are more likely to turn into GC if not treated promptly. Their early detection and prompt treatment have significant practical implications for the prevention and treatment of GC.

Examination of GC could be done with the help of various sources, namely imaging tests, pathological images, and endoscopy. To initiate, stomach cancer has to be detected successfully via endoscopy. The surface structure can be precisely analyzed by image-enhanced endoscopic techniques, including narrow-band imaging [6] and linked color imaging [7]. According to the studies, the precision of gastrointestinal tumor diagnosis [8] could be augmented by the deployment of endoscopic techniques. However, research states that even endoscopy examinations lead to still missed 10% of upper gastrointestinal malignancies [9]. Even if two experts participated, there would be missed diagnoses in an endoscopic unit [10]. The cause was that accurate gastroscopy image diagnosis requires years of practice to develop. Next, the gold standard for tumor diagnosis is histological image recognition. Diagnostic mistakes and a heavy workload for pathologists have been brought on by the dearth of pathologists [11]. Lastly, imaging tests are crucial in assessing the lymph node metastases of stomach cancer. An imaging evaluation's primary focus is on the lesions' morphological characteristics. For instance, the perigastric adipose tissue is so dense that it resembles lymph nodes. Doctors may make errors in diagnosis due to inexperience and missing diagnoses. The accuracy of the diagnosis will eventually decline, particularly in several cases [12].

Artificial intelligence (AI) is exploding in medicine due to the growing demand for detection, categorization, and segmentation or delineation of more accurate margins. After various findings in this recent scenario, the universal ground truth is that AI makes machines think like humans. One of the most crucial components of AI is machine learning. Deep learning is more accurate and flexible than standard machine learning techniques like support vector machines and Bayesian networks, and it is also easier to adapt to other fields and applications. Although AI-based technologies have shown impressive outcomes in the medical field, they have not been widely used in clinics. The main reasons are the black-box technique's unique feature and other factors, including high computing costs. It results from the inability to clearly represent the knowledge for a particular task carried out by a deep learning model, despite the underlying statistical principles. Simpler AI techniques, such as linear regression and decision trees, are self-explanatory since the model parameters allow one to visualize the classification decision border in a few dimensions. However, they do not possess the complexity needed for activities like classifying 3D and the majority of 2D medical images. Trust can be built among the patients only when the medical diagnosis done by the doctor is found to be open, clear, and explicable. It should ideally be able to fully explain the reasoning behind a certain choice to all parties concerned. Deploying deep learning models in the healthcare sector is challenging as the black box models need more interpretations. A model in AI needs to act as an aid for medical professionals, and, in addition, it should also permit the human expert to review the choices and exercise judgment. It has been understood from various articles that AI is used in various applications. This has drastically changed over the past 10 years due to advancements in machine learning (ML) and the broad industrial adoption of ML, which were made possible by more powerful machines, better learning algorithms, and easier access to enormous amounts of data [13]. Deep learning (DL) techniques [14] began to rule accuracy metrics around 2012, through which better results are obtained within the stipulated time. As a result, many real-world issues are now being solved using machine learning models in various industries, from fashion, education, and finance [15] to medicine and healthcare. Explainability is essential for the safe and trustworthy use of AI and a vital facilitator for its practical application.

By dispelling misconceptions about AI, end users can develop trust by seeing what a model considers while making a choice. For users who do not use deep learning, such as the majority of medical professionals, it is even

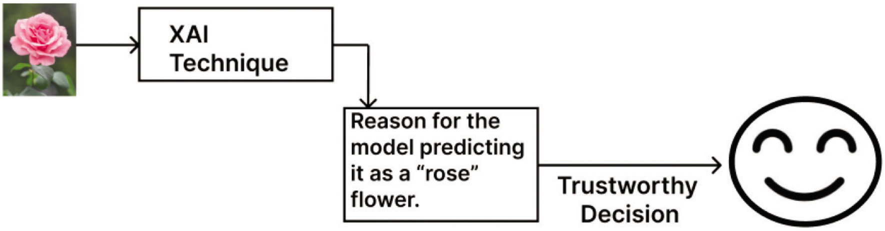

Figure 1.1 XAI model.

more crucial to display the domain-specific attributes used in conclusion. Machine learning algorithms' output and outcomes can now be understood and trusted by human users when those are obtained through a set of procedures and techniques known as explainable artificial intelligence (XAI). An AI model, its anticipated effects, and potential biases are all described in terms of explainable AI. It contributes to defining model correctness, fairness, transparency, and outcomes in decision-making supported by AI. A business must establish trust and confidence when putting AI models into production. A model to be established could adopt a suitable approach to AI development by deploying AI explainability.

Figure 1.1 depicts the way of working that XAI performs. An association could be made between explainability and uncertainty. Uncertainty is a key problem since deep learning classifiers typically cannot respond "I am not sure" in ambiguous situations and instead return the class with the highest probability, even if by a small margin. Recent research has examined uncertainty combined with the issue of explainability to highlight the instances where a model is unclear and, as a result, make the models more defensible to users unfamiliar with deep learning.

Understanding the deep learning models is complex as they are not transparent since it is impossible to gain knowledge directly from the neurons' weights. It has been shown in the study [16] that determining the significance of a neuron for a certain task is not solely dependent on the size, specificity, or influence of activations on networks. The researchers of an earlier study [17] thoroughly review explainable artificial intelligence (AI) terminology, ideas, and use scenarios. The next section describes the taxonomy of XAI approaches.

1.2 XAI Approaches

Figure 1.2 shows the taxonomy of XAI techniques that could be deployed. Various techniques, such as model agnostic versus model specific, a

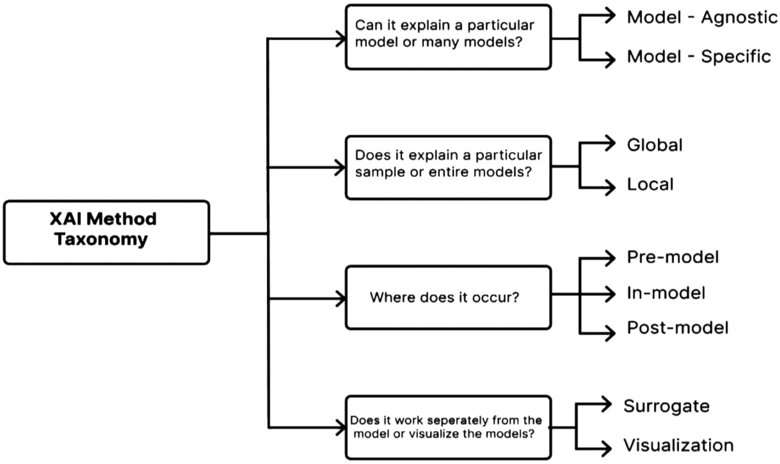

Figure 1.2 XAI taxonomy.

comparison of local and global methods, pre-model, in-model, and post-model specifications, and an overview of surrogate and visualization methods are discussed.

1.2.1 Model agnostic vs. model specific

Model-specific interpretation techniques are built around the exclusive model's parameters. Model agnostic approaches are not restricted to a certain model architecture and are typically applicable in *post-hoc* analysis. These techniques lack direct access to the structural or internal model weights.

1.2.2 Local and global methods

Local methods pertain to the single instance or single outcome of the model. Global approaches concentrate on the inside of a model by utilizing the whole understanding of model, training, and related data. It aims to provide a general explanation for the model's behavior. This strategy seeks to identify the features contributing much toward improving the model's performance. It is also known as feature engineering.

1.2.3 Pre-model, in-model, and post-model

Pre-model techniques are autonomous and can be applied to any model architecture. Some popular examples of these techniques include principal component analysis (PCA) [18] and t-distributed stochastic neighbor embedding (t-SNE) [19]. In-model methods are interpretability techniques that are built into the model itself. Some techniques are used after creating a model; hence, they are called post-model techniques. These techniques can produce insightful conclusions regarding a model's precise lessons acquired during training.

1.2.4 Visualization or surrogate methods

Surrogate methodologies use an ensemble of many models to examine other black-box models. Decisions that come out of the surrogate model are analyzed and compared with the decision obtained through the black-box model.

1.2.5 Approaches

Two well-known local explanation methods that can be used to explain any given black-box classifier are local interpretable model-agnostic explanation (LIME) and Shapley additive explanations (SHAP). These techniques learn a local interpretable model (like a linear model) around each prediction, explaining each prediction of every classifier in a comprehensible and accurate way. LIME and SHAP, in particular, estimate feature attributions on individual instances, which reflect each feature's contribution to the black box prediction. The next section describes in detail SHAP.

1.2.5.1 Shapley additive explanations (SHAP)

Among the popular model agnostic techniques available, Shapley additive explanations (SHAP) could be used to analyze the results. It explains how a machine learning model's predictions turned out. Shapley values are applied. The model characteristics are given weights known as Shapley values. It demonstrates how each feature affected the outcomes of the predictions. It establishes how features affect the outcomes of predictions. In the earlier study [20], researchers developed SHAP-a technique through the game theoretically ideal Shapley values to explain specific predictions. A popular strategy from cooperative game theory with desirable features is Shapley values. A data instance's feature values participate in a coalition as players. The average marginal contribution of a feature value overall potential coalition is known as the Shapley value. SHAP explanations guarantee a fair assessment of features and the contribution of output features as SHAP values [21]. In the financial industry, SHAP is frequently utilized for various projects, as mentioned in previous studies [22, 24]. Oikawa et al. [25]

proposed a multistage detection network to detect gastric cancer using pathological images. In the first stage of the network, handcrafted features were used as both pixel and geometric features. Support vector machine (SVM) is used in this study to differentiate the cancerous pathological images and non-cancerous images. The false-positive rate of this network is 18.7%. Xu et al. [26] presented a CNN (convolutional neural network) based approach to segment the histopathological images and classify them based on the epithelial and stromal regions of the input image. The images are separated into patches and analyzed. Wang et al. [27] predicted gastric cancer using advanced CNN methods based on lymph node images. However, this task is laborious and computationally expensive. Ueyama et al. [28] constructed a CNN-based network to detect gastric cancer from the narrow band histopathological images. This approach is high-speed, but the accuracy is comparatively low compared with other methods. Zheng et al. [29] designed a CNN model based on transfer learning with VGG-19 as primary architecture and achieved an accuracy of 91% in detecting gastric cancer based on white light endoscopic (WLE) images. Hirasawa et al. [30] curated a dataset of 3584 gastric cancer endoscopic images and built a database. The images in the data have 512 × 512 pixel resolution focused more on the affected area. The description of each image is also given. The whole dataset is made with 69 different patient data. Lee et al. [31] presented a dataset containing 367 ulcer patch images and 255 normal images for ulcer detection using white light endoscopy. Song et al. [32] introduced an AI-based system for predicting gastric cancer from histopathological images. The average specificity achieved by the model is 86%.

1.3 Materials and Methods

1.3.1 Data processing and augmentation

The dataset used for this study is taken from the King's Hospital, Oxford. The dataset is available for the public in the name of BOT gastric slice data. The dataset contains original gastric slice images of resolution 1024 × 1024. Since the dataset is in high-dimensional form, images have to reduce for the lower forms for better analysis. The images are scaled down to the resolution of 224 × 224 using random projection techniques. The features in the images are not lost in this process. These small patch images of 224 × 224 are split into training, testing, and validation data in the ratio of 70:20:10, respectively. The whole dataset contains 960 gastric cancer images and 571 non-cancerous images. The images are processed using the augmentation techniques like

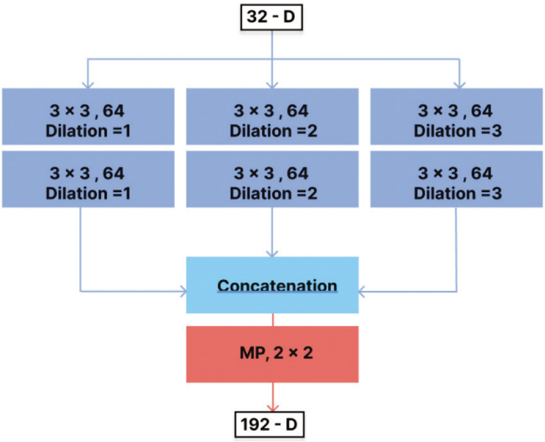

Figure 1.3 The architecture of the MSN module.

cropping, rotation, and shearing to increase the count of images. After the image augmentation, the images in the dataset are 14,581 cancerous images and 11,721 non-cancerous images.

1.3.2 Multi-scale network (MSN) module

For the shallow layers in the networks, a greater number of feature maps are present for the deep layers where object information at different scales is present. The single convolutional layer is unable to detect the multi-scale targets simultaneously. Hence, a multi-scale network is proposed in this study for the shallow layer to overcome the problem. The architecture of the proposed network is shown in Figure 1.3.

The dilated convolutional layer is adopted in the network to amplify the receptive field of the network. This enables the network to run simultaneously to extract the multi-scale features. The extracted features with various dilation rates are conjugated and max pooled for the adjacent layer.

1.3.3 Inner network (In-Net) module

A recent study shows that the densely connected networks improve the feature extraction and performance of the network. The features extracted by the three different MSN modules are conjected for longer features in the deeper layers. The main focus of the In-Net module is to perform a better fusion of the extracted features at the deeper layers. The pipeline of the In-Net module

Table 1.1 Pipeline of the In-Net module.

Layer	Type	Dilation rate	Kernel size, number
1	C	2	3 × 3, 1024
2	C	2	1 × 1, 512
3	C	2	3 × 3, 1024
4	M	–	2 × 2
5	C	1	3 × 3, 1024
6	C	1	1 × 1, 512
7	C	1	3 × 3, 1024

is given in Table 1.1. In contrast to the shallow layers, the feature maps at the deeper layers are small. Therefore, a single convolutional layer is capable of feature extraction. For feature fusion, a 1 × 1 kernel-sized convolutional layer in between two 3 × 3 kernel-sized convolutional layers is placed.

1.3.4 Slice-based classification (SC-Net) module

The proposed deep learning framework is based on image patches. The SC-Net module is built to classify the gastric slice image by probabilistic determination. For testing the proposed method, each gastric slice image is cropped to 81 smaller pieces of 224 × 224 pixels as the input image for the deep learning network. The result of patch-based classification is exemplified by the heat map shown in Figure 1.4. The colors of the heat map in Figure 1.4 represent the possibility of the gastric image being normal or cancerous. The lower the color value in the image is, the higher the chance of gastric cancer. The results may not be accurate if the whole image is taken and analyzed. The analysis performed is on the pixel level. The features selected and extracted at the training are observed at the pixels. The pixel-level classification gives an accurate analysis of gastric slice images. The lowest 10 scores are used for possibility calculation to attenuate the proposed framework. The label of the image (gastric/non-gastric) is determined by comparing the possibility with the pre-defined threshold value. In this study, the threshold value is set to 0.34.

1.3.5 Implementation of the proposed network

The proposed network is developed using the PyTorch and Keras toolboxes. The model is trained on the five different GPUS (GeoForce FTX 3500 X, 12 GB RAM) with a batch size of 128 and a learning rate of 0.001. Adam is used in support of the stochastic gradient descent with 100 epochs at training. The framework integrated with all the modules is given in Figure 1.5.

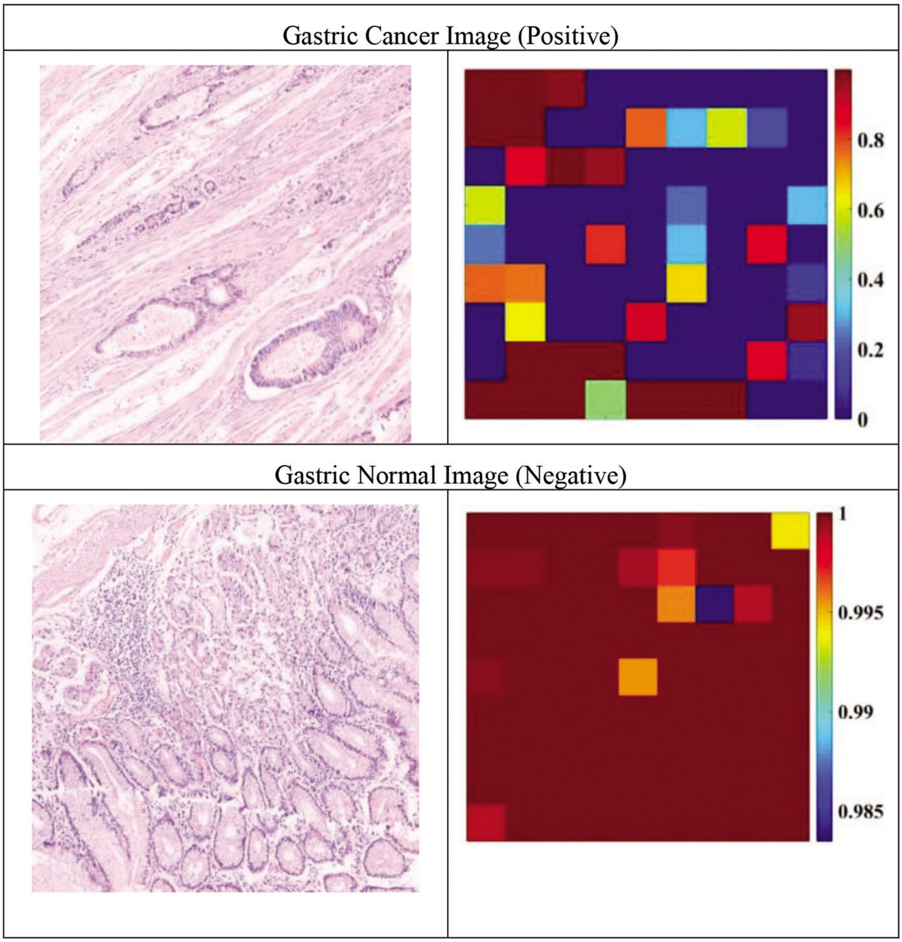

Figure 1.4 The gastric images and non-gastric cancer images, along with the corresponding generated heat maps.

1.4 Experiments and Results

1.4.1 BOT gastric dataset

The dataset is curated by the King's Hospital, Oxford. This dataset is properly used in this study after processing and augmentation. The gastric slice images in the dataset are the hematoxylin–eosin (H&E) stained with a magnification factor of 0.3×. Gastric cancer-affected areas are partly provided in the dataset with a description. The predicted pixel positions are manually compared with the given description giving accurate results.

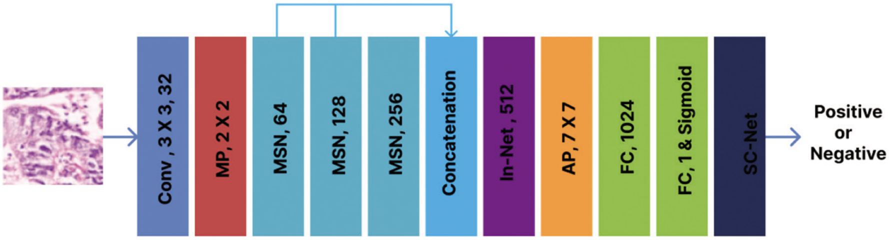

Figure 1.5 The architectural framework of the proposed deep learning model.

Table 1.2 Comparison of the patch-based ACA in various models.

Model	ACA
AlexNet []	92.36%
ResNet []	91.51%
DenseNet	91.34%
VGG-19	90.97%
Inception	90.59%
Proposed model (this work)	**97.43%**

1.4.2 Results

The average classification accuracy (ACA) of the testing images is considered the evaluation metric. The existing works are compared with the proposed model.

1.4.2.1 Patch-based classification

In this section, the proposed model is compared with existing works like AlexNet [12], ResNet [13], DenseNet [14], VGG-19 [15], and Inception [16] on slice-based testing datasets. The obtained results are given in Table 1.2. The results show that the proposed network achieves high performance, i.e., an accuracy of 97.43%. This is 5% more than the high-performance network. The proposed network has fewer layers when compared to the existing networks. The existing methods alleviate the problem of overfitting, which is not there in the proposed network.

1.4.2.2 Slice-based classification

The gastric slice images are tested with 2945 cancerous images and 1349 non-cancerous images. The proposed SC-Net module in the proposed model is compared with other benchmarking networks, and the results are presented in Table 1.3. The slice-based classification accuracy of the proposed network is significantly higher than the existing methods.

Table 1.3 Comparison of the slice-based ACA in various models.

Model	ACA
AlexNet []	95.45%
ResNet []	95.72%
DenseNet	96.43%
VGG-19	97.27%
Inception	98.65%
Proposed model	**99.82%**

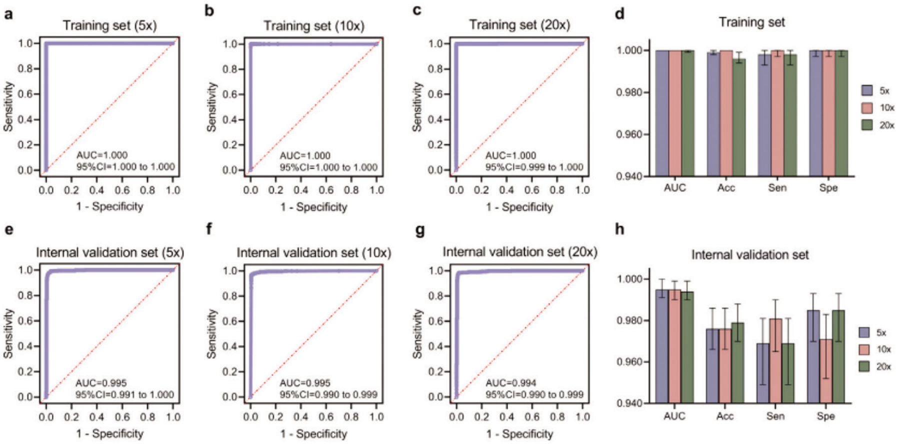

Figure 1.6 Diagnostic performance of the proposed model at various magnification rates in training and validation phases.

Internal validation of the model achieved the AUC score of 0.995. The AUC score of the model highly relies on the magnification rate of the images. The differences in the accuracy at different magnification rates were statically significant. The results are given in Figure 1.6.

1.4.2.3 SHAP analysis

The (Shapley additive explanation) SHAP analysis framework is adopted in the proposed framework because of its diversified properties. In this framework, the prediction variability is distributed among available covariates. The contribution of explanatory variable prediction at each point is assessed as the underlying model. The SHAP analysis results in the Shapley values demonstrating the model predictions as the binary variable linear combination that describes the presence of the covariate in the proposed model or not. The SHAP algorithm estimates the prediction $p(x)$ linear function of binary variables where z belongs to $\{0,1\}^N$ and the quantities belong to a real number, defined in eqn (1.1).

$$p(N') = \varphi_0 + \sum_{i=1}^{N} \varphi_i N_i' \qquad (1.1)$$

where N is the count of explanatory variables.

Eqn (1.2) shows the properties of the local accuracy, consistency, and missingness obtained at each variable:

$$\varphi_i(p,x) = \sum_{z'x'} \frac{|N'||(M - |x'| - 1)|}{N!} |p(x') - (z')|. \qquad (1.2)$$

In the function f in the proposed model, x is the available variable and x' will be the selected variable. The Shapley variables differ in the mean at the ith variable.

1.5 Conclusion

In this study, a novel deep-learning framework is presented for detecting gastric cancer. In this framework, different architectures were adopted at shallow and deep layers, i.e., MSN-module and In-Net module. The proposed framework is evaluated on BOT gastric dataset, and the results show that the model is robust and effective. The model also outperforms well-existed frameworks with fewer layers. The average classification accuracy of the model at the pixel level is 99.82%. This work can be improved further by integrating white light endoscopic images based prediction and the H&E-stained images for finer and early predictions at the root levels of the tumor.

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