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MONOGRAPH

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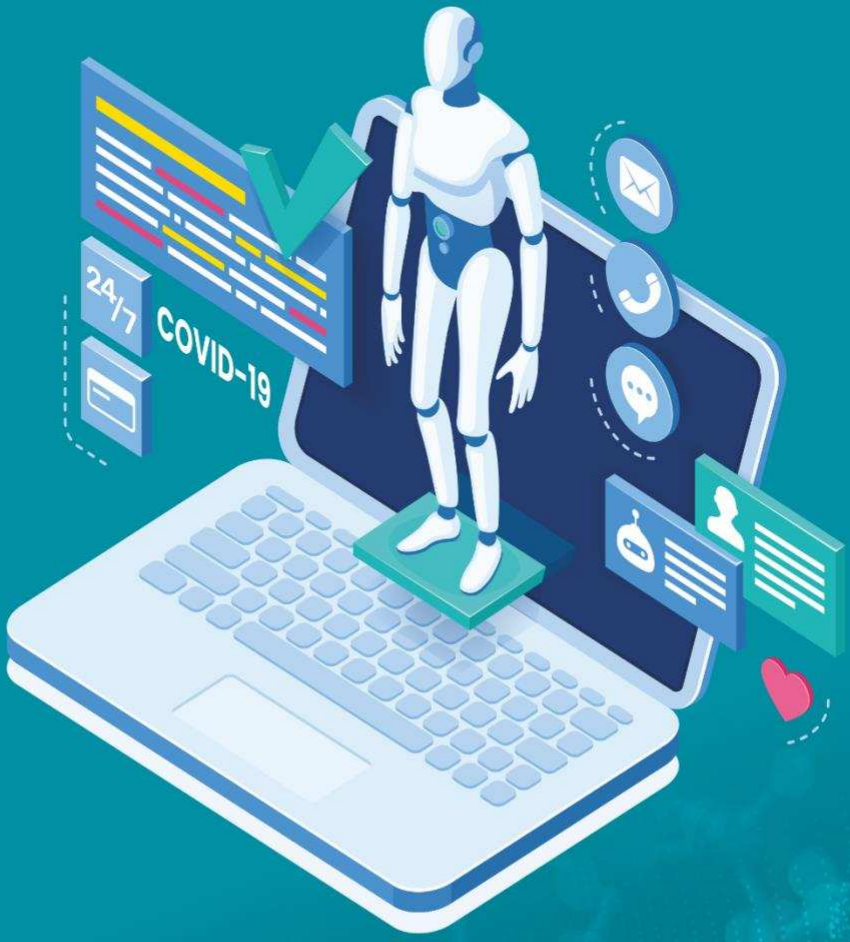
SMART AI-BASED

TELEMEDICINE SYSTEM FOR COVID-19



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Smart AI-Based Telemedicine System for COVID-19

Nunung Nurul Qomariyah, Ph.D
Dr. Dimitar Kazakov

CV. SYNTAX COMPUTAMA

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Preface

We are very grateful because this book could be resolved smoothly and various obstacles encountered can be resolved properly. This monograph aims to inform the readers about our valuable findings in the research of AI-based telemedicine for COVID-19. We expect that this book can provide insights and information that are useful for writers as well as for readers. As we know that, nowadays, we are in the middle of pandemic crisis which affect almost everyone in the world. The fight against this global pandemic, which is taking so many lives and challenging our societies, requires more efforts from many different roles worldwide. As a team with members from two different sides of the world, we also hope that our research will have a big contribution to the society, not only in the UK and Indonesia, but also in the other parts of the world.

This research is a part of collaboration work between Bina Nusantara University, Indonesia and the University of York, United Kingdom. We also partnered with a public hospital in Indonesia, Pasar Minggu Regional Hospital (*Rumah Sakit Umum Daerah Pasar Minggu*), Jakarta, which is one of the few designated hospitals for the treatment of COVID-19.

We would like to express our sincere gratitude to all the contributors of this research, our colleague, Ardimas Andi Purwita and Maria Seraphina Astriani, who involved directly in this project, also our under- graduate students, Arkaan, Fiqhy, Nicolas, Gardyan, Naufal, Elizabeth, Rachel, Clarissa, Aimee and Callista, from Binus University International. Special thanks to all colleagues in the department of Computer Science, Faculty of Computing and Media, Binus University International, Jakarta, Indonesia. We also thank to our medical consultant, dr. Sri Dhuny Atas Asri, S.P. for her invaluable time to provide advice. Gratitude should also go to Research Technological Transfer Office (RTTO) Binus University team for their help in supporting this research.

Jakarta, October 2021

Writer

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Consent and Ethical Clearance

The patients' medical records used in this study were collected by the data provider, including epidemiological, demographic, clinical, laboratory and mortality outcome information. This study has been approved by the Ethics Committee of the data provider, Pasar Minggu Regional Hospital Jakarta. The requirement for patient consent was waived as this was a secondary analysis of anonymized data.

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Acronyms

AI	Artificial Intelligence
API	Application Programming Interface
AST	Aspartate Aminotransferase
AUC	Area Under Curve
BCE	Binary Cross-Entropy
CART	Classification and Regression Tree
CBC	Complete Blood Count
CNN	Convolutional Neural Network
COVID-19	Coronavirus Disease 2019
CT	Computerized Tomography
CXR	Chest X-Ray
DNN	Deep Neural Network
eGFR	estimated Glomerular Filtration Rate
GGO	Ground-Glass Opacity
GPS	Global Positioning System
GRAD-CAM	Gradient-weighted Class Activation Mapping
HRV	Heart Rate Variability
hs-CRP	high-sensitivity C-Reactive Protein
INR	International Normalized Ratio
IoT	Internet of Things
IP	Intellectual Property Right
KNN	K-Nearest Neighbour
LDH	Lactic Dehydrogenase
LungVAE	Lung Variational Auto- Encoder
NLR	Neutrophil-to-lymphocyte
PPE	Personal Protective Equipment
PT	Prothrombin Time
REST	Representational State Transfer
ROC	Receiver Operating Characteristic
ROI	Region of Interests
RSUD PM	Sunday Market Area General Hospital
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SDLC	Software Development Life Cycle
SHAP	SHapley Additive exPlanations
SMOTE	Synthetic Minority Oversampling Technique
SMS	Short Message Service
TB	Tuberculosis
TL	Transfer Learning
t-SNE	t-distributed Stochastic Neighbor Embedding
VAE	Variational Auto-Encoder
WCC	White Cell Count
LC	Leucocyte Count
WHO	World Health Organization
XAI	Explainable AI
XGBoost	eXtreme Gradient Boosting

Chapter 1
Introduction

COVID-19 (Coronavirus Disease 2019) is a disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It is highly infectious and can spread easily through respiratory droplets when people sneeze or cough. The first identified case was in December 2019 in Wuhan, China, and since the beginning of 2020, the disease has spread all over the world. In Indonesia, the first two cases were confirmed on 2 March 2020 [1]. On 30 January 2020, The World Health Organization (WHO) upgraded the COVID-19 outbreak to a global pandemic. Researchers from various backgrounds are making joint efforts to combat this disease and are racing to develop means of its early detection to prevent wider transmission. Now, more than 18 months after the first case was identified, the number of critically ill patients with COVID-19 is still increasing, despite an active vaccination campaign taking place in several countries, including Indonesia. It is still hard to perform a differential diagnosis especially as reliable COVID-19- specific tests can be expensive, not universally accessible, and may require time to be carried out in practice.

1.1 Problem Analysis

COVID-19 condition requires health practitioners to be more restrictive and protective in dealing with infectious diseases. The lack of medical staff and Personal Protective Equipment (PPE) restricts the health service provider's capacity to manage the epidemic.

Research conducted by Mutambudzi et al. [2] using data from the UK Biobank study shows that healthcare workers had a more than seven-fold higher risk of severe COVID-19; those working in social care and transport occupations had a two-fold higher risk. This study also reinforces the need for adequate health and safety procedures, particularly in the healthcare sector, which can protect and support workers with an elevated risk of SARS-CoV-2 infection.

Another study by Ngunyen et al. [3] also shows a similar result. From the data of 2,135,190 people in the UK and USA collected by the COVID-19 Symptom Study app between March 24 and April 23, 2020, these authors found that front-line healthcare workers had at least a threefold increased risk of reporting a positive COVID-19 test and predicted COVID-19 infection, compared with the general community, even after accounting for other risk factors.

Indonesia, as the largest archipelago in the world which consists of five major islands and about 30 smaller groups, poses a special challenge to the efforts to fight the pandemic. There is a total number of 17,508 islands of which about 6,000 are inhabited. Geographically, there are people in rural areas who still do not have access to good

health facilities. This condition can also be an inhibiting factor in speeding up the handling of the COVID-19 pandemic.

1.2 Proposed Solution

In the health sector, caring for patients remotely has been offered since the 1950s, when the healthcare providers performed remote services over a landline telephone. This allows the patients to receive the services conve- niently, without having to leave their place. Nowadays, with the advancement of technology, telemedicine has enabled even easier communication between doctors and patients. It can be performed using several platforms, including website portals, mobile applications, video conferencing, and real-time chat with medical professionals. It offers the flexibility of being accessible anytime, anywhere without the hassle to wait for hours in line.

The existing telemedicine solutions in Indonesia, such as Halodoc [4], KlikDokter [5], Alodokter [6], Grab Health [7], have been around for four to five years. Until recently, those telemedicine applications have been used by medical doctors and nurses as individuals providing medical services based on their expertise, rather than with the backing of their institutions. Many major hospital operators now also try to launch their telemedicine platforms, a trend that has been further accelerated by the COVID-19 outbreak.

The emergence of telemedicine in Indonesia has been very helpful for society, especially as a way to reach the doctors and consult virtually when needed without the need to have to visit the hospital in person. In the current extremely restrictive situation concerning handling patients, telemedicine can help with a system for early diagnosis and patient monitoring to reduce the direct contact between the doctors and the COVID-19 patients.

Together with the advancement of telemedicine, Artificial Intelligence (AI) technology can work as a complement to the telemedicine system to contribute to the automation of epidemic modeling. Several AI learning algorithms can be implemented to learn about the epidemic behavior in general and the COVID-19 outbreak specifically. AI approaches, such as Machine Learning and Deep Learning – both mature research areas that aim to generate suitable models – can be used to better explain and put to good use the data collected via telemedicine.

We also propose the use of explainable AI which can allow a human interpretation of what is learned through machine learning. The proposed solution is not only building the intelligent telemedicine application but also allowing the medical experts to validate the resulting models, e.g. via suitable visualizations. This feature will become an advantage of our proposed solution when compared to the other existing telemedicine applications on the market.

1.3 Research Objective

The objectives of this research are:

1. Collect COVID-19 patients' health record data from primary and secondary sources;
2. Build machine learning models from three different types of datasets: chest X-Ray (CXR), Computerized Tomography (CT)-scans and blood samples;
3. Design a telemedicine system to be used by COVID-19 patients and their doctors.

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Chapter 2
Literature Review

The World Health Organization (WHO) has declared the COVID-19 outbreak as a global pandemic on 11 March 2020, with more than 10 million cases and 503,862 deaths across the world as of 30 June 2020 [1]. COVID-19 stands for Coronavirus Disease 2019 which is caused by severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2). This respiratory illness was responsible for the COVID-19 pandemic. The cure of this disease can be delayed due to some possible genetic mutations shown by the virus [2]. Researchers have been working on finding the best approach and solutions to cure the disease, limit the crisis, and help to prevent future such pandemics. In medical and virology domains, research about this virus has been conducted intensively, such as the one with a very high citation by Polack et al. [3] which has been studied on the safety and efficacy of the mRNA COVID-19 vaccine. On the other hand, scientists with technology backgrounds have also contributed to the fight against this disease by proposing a novel methodology with pattern recognition, early prediction, and risk reduction.

The two most significant contributions in this area come from Artificial Intelligence (AI) community and epidemiologists as well as the mathematician community. The AI community's top contribution is on the automated detection from Computed Tomography (CT) scans and X-ray images, such as the one published by Wang et al. in 2020 [4]. Several datasets on this domain have also been published together with the novel methods. The other area of AI has worked on the prediction, such as the one published by Yan et al. in 2020 [5] which proposed a model to predict the mortality for COVID-19 patients based on their blood test results.

The second community, mathematicians and epidemiologists have also produced significant work in this area. The one published by Kucharski et al. in 2020 [6] developed a complex virus diffusion and transmission model to estimate the virus spread under several mobilities and social distancing scenarios. The other communities have also introduced several efforts to fight against COVID-19, such as an analysis conducted by Lopez et al. also in 2020 [7]. They performed a deep analysis of social and emotional behavior from social media. There is also a collection of the publicly available dataset which has been reported by Shuja et al. [8]. According to their study, the datasets for this domain are divided into three major categories: medical images (CT-scan and X-ray), textual (tweets, scholarly article, and COVID-19 case report), and speech (cough and breath). In this chapter, we discuss the literature review in three big focus areas: (1) study of COVID-19 from a blood test, (2) from radiology images, also (3) the

advancement of the Internet of Things (IoT) technology as the solution for COVID-19 telemedicine.

2.1 Blood Test Pattern Analysis

Several studies have reported the result of the experiment with a routine blood test to predict the mortality of COVID-19 patients which yielded a very high accuracy. The studies do not only show that machine learning can predict better and faster, but also suggest that in addition to the most common assessment method used to monitor the progress of common pulmonary disease such as X-ray and CT-scan images, the routine blood test can also be used as indicators of the COVID-19 severity level and predictors of the mortality.

A previous study by Yan et al. [5] in 2020 mentioned the three most prominent features found in the blood samples data which can predict the mortality of the COVID-19 patients, i.e., Lactic Dehydrogenase (LDH), Lymphocyte, and high-sensitivity C-Reactive Protein (hs-CRP). The training experiment was conducted by using 375 patient data from Tongji hospital in Wuhan, China. The model was tested to another 110 patients' data and the prediction result was claimed very accurately (over 90%). Although, this work recently received some counter statements from [9] and [10] regarding the clarity of how the blood test result was obtained and some possibilities of other complications in critically ill patients.

Another study by Habu et al. [11] reported a similar experiment with a blood sample in India. Based on their findings, they concluded that the most correlated factors with mortality were age, gender, and other complications such as diabetes mellitus and hypertension. The result of the experiment showed that the diabetes contributed as high as 53%, while hypertension shows as high as 33%. The other comorbidity such as cardiovascular, asthma and cerebrovascular disease were also found to be significant.

Similar study in Korea was conducted by Ko et al. [12]. They proposed EDRnet which was built based on deep neural network and random forest models. In their study, the model was trained on the blood test data which was obtained immediately within 24 hours after the patients being hospitalized. They claimed that their developed model can detect earlier than those which proposed earlier by Yan et al. [5]. The model was trained from the same data used in [5], and then tested to 106 other patient data from Korean hospitals. The accuracy result of the model reached 92%. The findings of the study were also supported by the other studies such as [13] which explain that the lower lymphocyte count was found in severe patients. This could be due to the infiltration and sequestration of CD4+/CD8+ T cells occurred in patients with poor outcome. Another study which also supported the finding was conducted by Kong et al. [14] which mentioned that the

Neutrophil-to-lymphocyte (NLR) in severe patients were found higher than the mild one. The COVID-19 disease mainly acts on lymphocytes, particularly T lymphocytes. This study also suggests that patients with high NLR should be admitted to an isolation ward as early as possible. With regard to the Platelet, many studies already confirmed that the lower count will increase the severity level of the patients [15]. This specifically related to COVID-19 because the decrease of immune system may lead to inappropriate platelet activation and consumption as well as impaired megakaryopoiesis as mentioned in [15].

Moreover, Sun et al. [16] proposed the model based on temporal deep learning to classify the COVID-19 progression. The model was also trained on the same data published in [5]. They also proposed four COVID- 19 stages definition which were never existed before. Based on their experiment, they found that low values of lymphocytes, eGFR (estimated Glomerular Filtration Rate), albumin and Serum Sodium, high values of LDH, hs-CRP, indirect bilirubin, creatinine and INR (International Normalized Ratio or also known as PT which stands for Prothrombin Time) were shown in the COVID-19 patients with critical condition. A similar result was found in the other study [17] which concluded that high-sensitivity C-reactive protein (hsCRP), Aspartate aminoTransferase (AST), and D-dimer were the indicators of COVID-19 mortality.

Another study by Kermali et al. [18] has collected the summary of most important biomarkers and describe their findings in critical patients. They found that C-reactive protein, Serum Amyloid A, Interleukin-6, Lactate Dehydrogenase (LDH), D-Dimer, Cardiac Troponin and Renal biomarker (Urea and Creatinin) have increased, while the White Cell Count (WCC) for NLR and Leucocyte Count (LC) have increased and decreased, respectively.

2.2 Radiology Images for COVID-19 Detection

The first signs of the onset of disease are still under investigation by many researchers. The symptoms cannot be easily recognized and can be different from one person to another. Such common symptoms like fever, dry cough and tiredness can always be misdiagnosed as common cold. Many infected patients are also asymptomatic which can increase the risk of transmitting the disease to other people without realizing it. In the early period of COVID-19 outbreak, some asymptomatic patients have been reported having a business meeting outside of Asia and it was when the disease started to spread out in another country as reported in [19].

Since the first wave of COVID-19 outbreak, several studies have been conducted on how to detect this disease by reading the patients' medical imaging. As has been stated in [20, 21], the studies showed a positive result towards the COVID-19 detection from radiological

images, such as chest CT scan and X-rays, which has strong evidence that the detection through radiological images was more accurate when compared to RT-PCR (Reverse-Transcriptase Polymerase Chain Reaction). Last year, radiologists have also published a finding which said that a deep learning model which was previously used to detect Tuberculosis (TB) disease from X-ray images could also be used to identify the abnormality pattern in the COVID-19 disease [22]. The development of learning model for COVID-19 automatic detection from radiology images is still in high demand. This is not only to detect the presence of the virus but also for the patient management, to automate the tedious job of interpreting the images so that the health care can focus on a more urgent task as well as to help the hospital management in predicting the bed capacity.

In the beginning era of Artificial Intelligence (AI), researchers have introduced intelligent systems which can perform decision making like a human without any fatigue and even better they can produce more consistent results faster. Some AI techniques have been emerged to solve many real-life problems. While the rising of different techniques in AI have been able to perform human tasks, people see a bigger risk to leave the machines work alone without a proper control on how the machines perform the calculation. There is always a possibility that a machine could make a miscalculation in every case. As mentioned in [23], for sensitive task involving human well-being or health, it is important to limit improper actions. This is where the emergence of Explainable AI (XAI) becomes inevitable. There is a need to validate the behaviour before deploying an AI system. XAI can be performed through dynamically generated graphs, textual descriptions or interpretable visual representations. In our problem, we want to employ XAI to show that the deep learning models can spot the problematic areas properly to be used for further investigation by the radiology experts. In this section, we collected research literature which aims to perform classification of problem on discriminating between general pulmonary disease and COVID-19.

Radiologists often look for the presence of features in the resulting scans including bilateral and peripheral predominant Ground-Glass Opacity (GGO) which is used as a marker to indicate the early stages of the COVID-19 infection. Due to the advancement of technology in the field of Computer Vision and Artificial Intelligence (AI), automated solutions are now available.

Deep learning is the most effective technology in medical research for precise diagnosis and prognosis of various diseases, due to the availability of adequately trained models to classify inputs into desired categories. Deep learning not only provides additional evaluation for whether or not AI systems will indeed enhance a patient's outcomes and survival, but it also plays an important role in the medical

field as medical image analysis provides a proving ground for human-AI interaction, which indicates the patient's receptivity to automated health-altering decisions [24]. Convolutional Neural Network (CNN), Transfer Learning (TL), and Gradient-weighted Class Activation Mapping (Grad-CAM) are all various deep learning architectures and are competent methods when it comes to differentiating CT scan images of patients infected with COVID-19 as positive or negative. This is accomplished through image processing, a technique in which developers and engineers can employ quantitative data or numerical data sets to alter the visual outcome of images in order to enhance and extract useful information.

The use of deep learning to learn image classification has been widely known to solve general problems such as handwriting recognition, object recognition, face recognition, license plate recognition, and many more. In solving a problem of COVID-19 classification from X-ray images, a study has been performed by Apostolopoulos and Mpesiana [25] which used transfer learning in multiclass classification problems on X-ray images with three class labels: common pneumonia, COVID-19, and normal. They chose to apply the transfer learning strategy to train the CNN model due to the fact that the COVID-19 dataset portion is considered very small (only 224 images) when compared to the whole dataset (1,427 images). With transfer learning, the learned knowledge from one task can be applied to learn another task. They showed a strong evidence that the transfer learning on VGG-19 [26] and MobileNet V2 [27] can learn well in a small COVID-19 dataset with the accuracy, sensitivity and specificity all above 90%.

Some other studies have also reported the use of deep learning techniques on detecting COVID-19 from CT and X-ray images, such as in [28, 29, 30, 31, 32, 33, 34].

The trend towards explainable AI (XAI) has also been utilized to solve similar problem in discriminating between a common pulmonary disease and COVID-19, as performed by Brunese et al. [35]. Their proposed method is not only able to detect the presence of the COVID-19 but also able to visually spot the symptomatic areas in the image. They employed VGG-16 architecture [26] to perform the classification task and Gradient- weighted Class Activation Mapping (Grad-CAM) algorithm [36] to visualize the symptomatic areas. The model has been evaluated on 6,523 X-ray images with 250 COVID-19, 2,753 other pulmonary disease, and 3,520 healthy cases. The model showed an accuracy of 97%.

The studies which utilized explainable deep learning to solve similar problems are still very limited, such as in [4, 37]. Wang et al. [4] introduced a deep learning framework, COVID-Net, which was developed for COVID-19 automatic detection from X-ray images. The

architecture was built upon a combination of a heterogeneous mix of convolution layers (ranging from 7x7 to 1x1 of kernel sizes), and different grouping configurations. COVID-Net is shown to be outperformed the other two architectures, VGG-19 [26] and ResNet-50 [38] in predicting multiclass classification problem with three classes, namely: Normal, Non-Covid-19 and COVID-19. The proposed architecture has also been audited by using GSInquire [39] to observe whether the resulting training model was able to spot the problematic area properly. It was shown that COVID-Net were relying on visually-indicated correct information to make the decisions.

A study by Alshazly et al. [37] used chest CT scan dataset and applied two visualisation approaches, namely t-distributed Stochastic Neighbor Embedding (t-SNE) [40] and Grad-CAM [36] for the explainability of the deep models. They evaluated 12 different deep learning architectures and they also proposed a transfer learning strategy. They proved that the proposed model can learn discriminative features very well on CT images.

2.3 Internet of Things (IoT) for Telemedicine Device

COVID-19 has many symptoms and one of the serious symptoms of COVID-19 is heart problems including the increase in heart rate and body temperature. The ZOE COVID Symptom Study app[1], a non-profit initiative collaboration between ZOE health science company and King's College London, has collected data from global contributors. As mentioned in [41], the researcher found that heart rate can also become an indicator whether a person is infected by the virus or not. It is also mentioned that a study conducted by Fitbit [42] has reported similar findings with the heart rate and claimed that the increased resting heart rate was an indicator of the disease. This finding is also supported by another study conducted by Hasty et al. [43], which also mentioned that the decrease of Heart Rate Variability (HRV) has the correlation with the worsening state of the COVID-19 patient. HRV focuses on the specific changes in time (variability) between the successive heart beats. In their study, the change of C-reactive protein (CRP) level in the patient's body was monitored which then compared with the change of HRV. The CRP is one indicator of inflammation in the body. The same claim was also stated in a study by Natarajan et al. [42], which confirmed that the heart rate and respiration rate of an infected patient were increasing while the HRV was decreasing. The data for their study was collected from 2,745 subjects diagnosed with COVID-19.

[1] https://covid.joinzoe.com/

In another study, the researcher found that 27.8% of 187 COVID-19 patients had heart problems leading to cardiac arrhythmia and heart failure [44]. Another similar conclusion was also stated in another study by Long et al. [45]. Based on 45 existing COVID-19 research articles, it can be ensured that doctors should be aware that the virus can cause "cardiovascular complications", such as an abnormal heart beat.

The other most common symptom of COVID-19 that can easily be observed is fever. Several studies shown evidence of the change of body temperature in the majority cases. This is due to the occurrence of the viral infection, which may trigger the alarm in the body in the form of the increasing body temperature. People all over the world are already aware with this symptom. We can see the body temperature check in the most of public place entrances. This effort is to ensure that a person with viral infection in his/her body will not be unnoticedly enter the place. Although, there are some people with the disease who have no symptoms at all, these two monitoring appliances: Heart rate and body temperature check, can still be useful to be included in our daily live to prevent further spread of the disease.

A study by Al Bassam et al. [46] proposed an IoT-based system with Global Positioning System (GPS) for self-isolation COVID-19 patients which can alert the authority if there is an indication that a person violates the quarantine procedure.

Mukhtar et al. [47] proposed an IoT framework for screening COVID-19 patients from real-time data. The medical sensors are integrated with Arduino and connected to smartphone applications. The sensors can read heart beat, cough, temperature and oxygen saturation. All the data received by the sensors will then be processed by a rule-based algorithm. They conducted an interview with the expert and classified the COVID-19 cases into four classes: (1) non-symptomatic, (2) mild symptoms, (3) moderate clinical symptoms, and (4) serious clinical symptoms.

A study by Mohammed et al. [48] contributed to the IoT for COVID-19 research domain by proposing the integrated IoT and facial recognition system developed in a smart helmet. This system is able to detect body temperature and it also uses face recognition technology to allow the users to detect pedestrian's body temperature automatically.

Another similar study in this area conducted by Hasan [49] which also proposed an IoT-based COVID- 19 automatic detection by identifying the fever symptoms. The developed system comprised of the use of (esp8266 (Node-MCU), RFID (RC522), ultrasonic (SR-04), human temperature body (MAX30205)), ThingSpeak IoT cloud, user monitoring tools, and IFTTT service. The system will generate an Short

Message Service (SMS) as a notification to the manager. ThingSpeak cloud was used to show the data received in graphical representation.

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Chapter 3
Research Methodology

Research method in this study is shown in the flowchart in Figure 3.1. It shows the general process of how this study will be conducted. Research on the development of AI-based telemedicine for COVID-19 patients is shown in Figure 3.1 and will be carried out in several stages as follows:

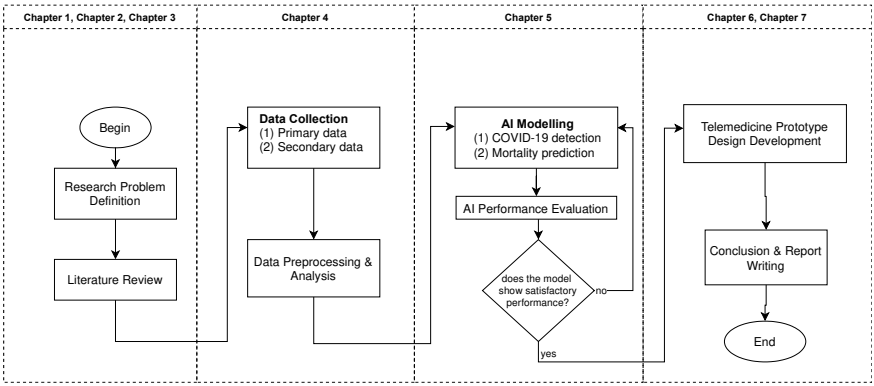

Figure 3.1: Research Method Flow Diagram

1. Research Problem Definition

The research has been initiated by defining the problem. We found and performed the analysis of the current situation of pandemics and proposed a solution. The result of our problem analysis is described in Chapter 1.

2. Literature Review

The next step was collecting a literature relevant to this study. We summarized the review from other related studies in Chapter 2.

3. Data collection

In this task, we collected primary data at our hospital partner, Pasar Minggu Regional Hospital (*Rumah Sakit Umum Daerah Pasar Minggu*), Jakarta, Indonesia, as one the Government's COVID-19 referral hospital. The collected data has been anonymized and the patients' identities have been redacted by the data provider, so that the patient's privacy is not violated. The researchers did not have the patients' identity in the data provided from the hospital. The data that were collected include: electronic patient medical record, triage data (such as prescribed medicines, given therapy), the doctor's and nurse's observation notes, and patient recovery status.

In addition to that, a secondary data has been collected to support the development of the model being made. Secondary data has been obtained from public datasets related to COVID-19 patients that have been published on sites such as Kagle.com, publications on some reputable journals and other sources. The detail about the data collection is explained in Chapter 4.

4. Data analysis

The data that has been collected has been preprocessed. It was then analyzed by the researchers with an AI expertise together with the medical expert in pulmonary disease from the Pasar Minggu Regional Hospital. The results of this analysis were used further to develop an AI model appropriate to the correct diagnostic procedure for the patient.

5. AI-based prediction model development

AI model development was carried out using several combinations of machine learning algorithms. We use a combination of classical machine learning and the deep learning method. This method was implemented and tested in a powerful computing machine in a laboratory. In this stage, the two AI models were proposed, each of which has the following advantages:

- An AI model that can automate diagnostic enforcement of COVID-19 patients with a fairly good level of accuracy, so that it can simplify the work of the health practitioners in treating the patients.
- An AI model that can predict a patient's recovery status automatically. So that health practitioners can easily observe the possibility of isolating the patients and take further actions for some particular patients.

6. Evaluation of the AI model

After the AI models were developed, the AI models were evaluated. The accuracy and other metrics of the models were measured and compared between one algorithm and another. The results of the experiments from this stage were also reported. Detailed implementation and evaluation result is explained in Chapter 5. Other matrices, such as time and space complexities of the proposed model that affect the performance during real-world deployment, were investigated. We performed the experiment with a high powerful machine and the appropriate suggestion for the best hardware specification to run the model properly were proposed.

7. Prototype of telemedicine system development

The work on the development of the telemedicine system has been carried out based on the outcome of the previous stage in which

a suitable AI model and data analysis has been proposed. The implementation of the system was following the Iterative prototyping method in Software Development Life Cycle (SDLC). Iterative prototyping method is an incremental model that focuses on the growth of the initial design and then follow the gradual change to a more complex design with some additional user specifications. It repeats the process in cycles. The cycle will end when a system that entirely meets the user's needs has been formed. Basically, an iterative model is an approach that classifies a large project into several small stages and deliverables. As the project continuity plan, we also plan to test the prototype and develop the software with the real users.

8. Conclusion and report writing

The research phase, as shown in the figure, will end with the reports writing and other desired outcomes, such as completing IPR (Intellectual Property Right/Hak Kekayaan Intelektual) documents, writing articles for scientific journals and documenting product prototypes that have been proposed. Although the flowchart in Figure 3.1 shows that the report writing is at the final stage of the research, the writing process was actually performed at any stage which allows us to publish some intermediate results of the study.

Chapter 4
Data Collection and Preprocessing

In this section, we explain the dataset collection and preprocessing step. This step is an important part in our study because no matter how good the AI model is, if we fail to preprocess the data accordingly, then the model will not yield a valid result. The dataset gathered from both primary and secondary sources were also explained in detail.

4.1 Primary Data

The dataset of routine blood sample test of 1,000 COVID-19 patients has been collected from our hospital partner, Pasar Minggu Regional Hospital, Jakarta, Indonesia from the period of March until December 2020. Due to the confidentiality and the permission to use the dataset, the content of the data will be made unavailable to the public by the authors but the sample structure of the dataset and column description are provided. This is done purposely so that the overall machine learning pipeline in this experiment can be clarified. Our original data consists of several blood tests which were performed by the hospital during the period from the first day they were admitted to hospital until they were discharged. Each patient has been represented with several rows in the dataset. Total entries in the COVID-19 dataset was 10,242 rows after duplicate data has been dropped. The data also contains demographics of the patients, including age and gender, but these were excluded in our study as we want to focus on finding the most prominent biomarkers to predict the patient outcome. The dataset contained 179 biomarker features which were then reduced by 28 features only to be used in this study. The features were selected based on the most common findings in the other related work and also based on the clinicians advice. The biomarker features which were used in our experiment is shown in Table 4.1.

We performed several steps in data preprocessing. First, the missing data were imputed with the latest data of the same patient with the combination of K-Nearest Neighbour (KNN) imputer method. The KNN imputer was only used if after the all data has been carried forward to fill the missing value, there were still missing values to be filled. KNN works by checking the value of the nearest k-neighbors. Two data points are considered close if the columns that neither is missing are similar (defined as close). Then one latest data of each patient was taken to be processed further.

The imputation step resulted in only 984 patient data records that were eligible to be used for further processing. The dataset was imbalanced with a total number of patients who survived of 893, while the non-survivors were only 92. Machine learning algorithms tend to

overfit if trained on imbalanced data. In our case, the positive class (non-survivors) is the minority class with a ratio of 1:10. We applied Synthetic Minority Oversampling Technique (SMOTE) [1] as one of the over-sampling methods for imbalanced datasets. In this study, we take a sampling size of 500 from each class to be trained.

Table 4.1: Biomarkers Used in Dataset

Biomarker	Feature code	Normal level (adult)	Unit
HEMATOLOGY			
Hemoglobin	HB	13.2 - 17.3	g/dL
Hematocrit	HCT	40 - 52	%
Leukocytes	LEKO	3.8 - 10.6	$10^3/\mu L$
Platelets	PLT	150 - 440	$10^3/\mu L$
Erythrocytes	ERI	4.40 - 5.90	$10^6/\mu L$
Red Cell Distribution Width	RDW	11.8 - 14.5	%
AVERAGE ERYTHROCYTE VALUE			
Mean Corpuscular Volume	MCV	80 - 100	fl
Mean Corpuscular Hemoglobin	MCH	27.5 - 33.2	pg
Mean Corpuscular Hemoglobin Concentration	MCHC	32 - 36	g/dL
COUNT TYPE			
Basophils	BASOFIL	0.0 - 1.0	%
Eosinophils	EOS	1.0 - 5.0	%
Stem Neutrophils	NEUTB	3.0 - 5.0	%
Segmented Neutrophils	SEGMEN	50 - 70	%
Lymphocytes	LIMFOSIT	25 - 50	%
Monocytes	MONOSIT	2.0 - 8.0	%
Neutrophil-Lymphocyte Ratio	NLR1	<3.12	
Erythrocyte Sedimentation Rate	LED	0 - 20	mm/hour
HEMOSTASIS			
D-Dimer	DDIMER	<0.5	µg/mL
prothrombin time	PTHSL	10.80 - 14.40	second
Activated Partial Thromboplastin Time	APTTHSL	25.00 - 35.00	second
BLOOD CHEMISTRY			
Arterial blood gas analysis			
Partial pressure of oxygen	PO2_N	71.0 - 104.0	mmHg
Oxygen saturation	O2S_N	94.0 - 100.0	%
Liver function			
Serum Glutamic Oxaloacetic Transaminase	SGOT	<50	U/L
Serum Glutamic Pyruvic Transaminase	SGPT	<50	U/L
Diabetes			
Random Plasma Glucose Test	GDSFULL	70 - 180	mg/dL
Kidney Function			

Urea	UREUM	<48	mg/dl
Creatinine	CREAT	0.70 - 1.30	mg/dL
Cardiac enzymes			
Lactate dehydrogenase	LDH	50 - 150	U/L

In addition, as the control data, we also collected a random sample of 1,000 inpatients with Pneumonia cases, and 1,000 inpatients with other diseases, in the period before March 2020. Each patient's blood test has been taken multiple times during their stay in the hospital. Each patient has been represented with several entries in the dataset. The original data entries count is shown in Table 4.2.

Table 4.2: Dataset Count for Each Class

Class	Data Count	Missing Value Count
Other	2,634	48.12%
Pneumonia	3,136	44.36%
COVID-19	11,456	26.39%
Total Entries	17,226	32.99%

4.2 Secondary Data

4.2.1. Lung CT-Scan

In our research, we also collected secondary dataset from publicly available sources. These datasets include the Chest X-Ray (CXR) and lung CT-scan images of COVID-19 patients. The CT-scan data was collected from [2]. This large COVID-19 CT scan, sliced, a dataset consisting of 7,593 images of 466 patients with COVID-19 and 6,893 images of 604 normal patients from 13 different countries. This is a merged dataset gathered from public COVID-19 diagnosis literature made especially for deep learning applications.

To increase the diversity of data for training models, we performed data augmentation techniques. We augmented each training image by resizing and flipping the images. The main computational formulas are convolution, pooling, activation, and loss function. All images were resized to 256x256 before being used to train the AI model.

4.2.2. Chest X-ray

For the Chest X-ray dataset, we collected several radiology images sources as below:

- Cohen's dataset [3]
- Figure 1 COVID-19 Chest X-ray Dataset Initiative [4]
- Actualmed [5]

- Radiography [6]
- RSNA Pneumonia Detection [7]

4.2.3. Blood Test Data

The two publicly available COVID-19 blood test datasets for this research were gathered online from San Raffaele Hospital in Italy [8] and Albert Einstein Hospital in Brazil [9]. The first dataset consisted of 1,736 COVID-19 samples with 816 positives (47%) and the rest of the 920 samples were negatives (53%). The second dataset from Albert Einstein Hospital originally contained 5,644 samples with 558 (10%) COVID-19 positives. The second dataset used in this study is reduced to 599 samples with 81 positives and 518 negatives, as it focused on the Complete Blood Count (CBC) test-related features and had the least number of null values. Age values in the Brazilian dataset differ from the one in Italy, it is presented in the form of quantile ranging from 0 to 19 instead of the regular age number.

To allow the AI models to develop, all of the CBC test datasets were preprocessed using data imputation as the two datasets contained several missing values. We implemented two imputation techniques to the data, one of which is using the KNN algorithm. Another imputation is by replacing the null values using the calculated values based on each age group. Each age group is used to find the mean and the mode of all features.

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Chapter 5
Artificial Intelligence Model Development

In this chapter, the AI model development, including the performance evaluation and findings are explained in more detail. In this research, we performed several experiments in developing AI modules for the following tasks:

- COVID-19 detection:
  This task was solved through the use of three types of data: lung CT-scans, chest X-rays and blood tests.
- Mortality prediction:
  This task was solved by using blood test data only. This is due to the limitations of the available data with regards to COVID-19 mortality.

5.1 COVID-19 Detection

5.1.1 Model from Lung CT-Scan Images

Convolution neural network (CNN), also known as ConvNet, is a particular artificial neural network that analyzes data using perceptrons, a type of machine learning unit technique. It is often utilized for supervised learning and can be applied for image processing, natural language processing, and other cognitive tasks as well. In this case, a CNN approach is beneficial since the concept of dimensionality reduction accommodates a large number of parameters in an image, increasing its efficiency. Transfer learning, on the other hand, refers to the process of transferring knowledge extracted from a set of data to execute a separate yet related task where the volume of data available for the new task may be limited. We built CNN model by using two architectures: LeNet [1] and a pre-trained model of VGG-16 architecture [2]. Figure 5.1 shows the architecture of LeNet CNN. We have published the model in [3].

The VGG-16 architecture is used as our pre-trained model; Figure 5.2 shows the arrangement of 13 convolutional layers, 5 pool layers, and 3 dense layers that it follows consistently throughout the entire process. Our goal was to measure the performance of the pre-trained model and compare it with our LeNet CNN model. To build the last fully-connected layer of our model, we set our optimizer to 'Adam' and our loss function to 'categorical_crossentropy'. Following that is the training of the model, along with the implementation of early stopping as well as a model checkpoint to save the best results, at 10 steps per epoch and 32 validation steps. We also implemented Grad CAM [4] visualization to display parts of the input CT-scan that were identified as COVID-19 symptoms.

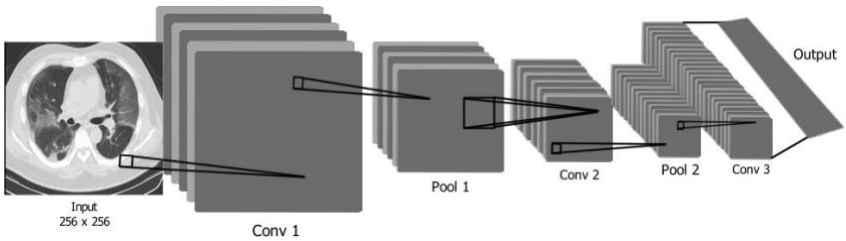


Figure 5.1: LeNet CNN Architecture [1]

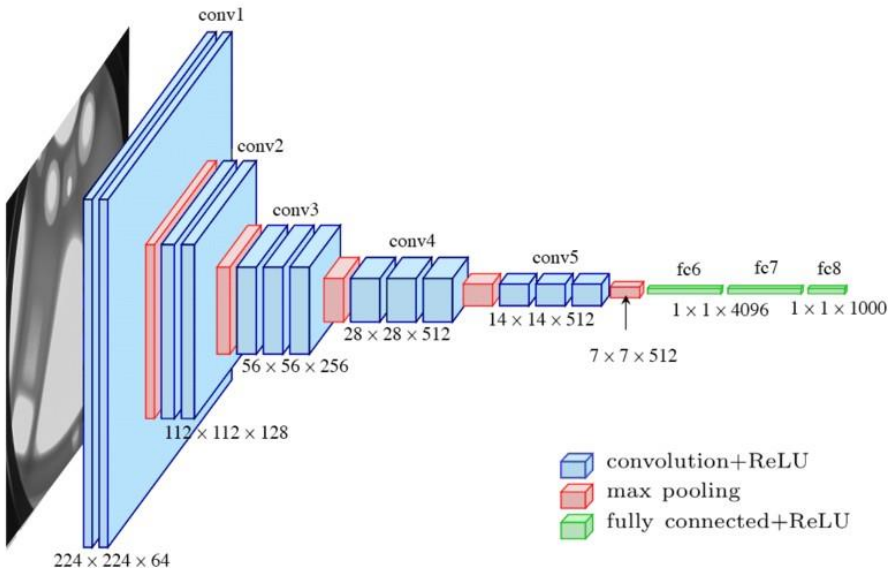
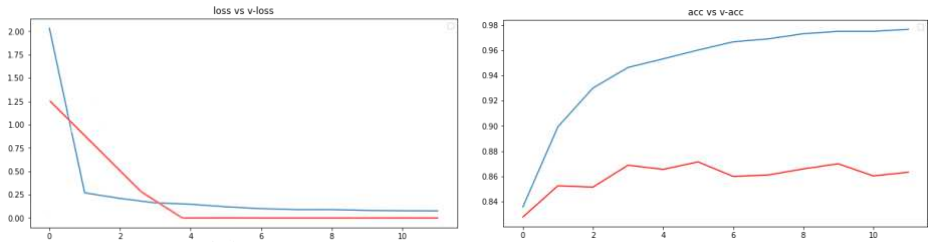


Fig. 5.2: VGG-16 Architecture [2]

We used the F1 measure, which is defined as the harmonic mean of the model's precision and recall, is a technique of combining the model's precision and recall. Merely calculating accuracy is not enough to indicate whether a model is doing its job properly, hence F-score is necessary to measure the balance between a model's precision and recall and when there is an uneven class distribution. The dataset was split into 80-20 proportions, where 80% is used for training and the 20% is used for validation.

The transfer learning approach was conducted on an AMD Ryzen 5 3600 64-bit Windows 10 OS with 16GB RAM, inputting 224 224 default image size for the VGG-16 model. In contrast, the LeNet CNN model was conducted on an AMD Ryzen 7 3700x 64-bit Windows 10 OS with 16GB RAM.



(a) Loss vs Epoch (b) Accuracy vs Epoch

Figure 5.3: Training Result of LeNet CNN
The red-colored line represents the measure on validation data, while the blue line shows the measure on training data.

The LeNet model received an accuracy of 97.10% from training data and 86.62% from validation data. In this case, the model predicted 2,372 accurately and 386 misdiagnoses. There was an overfit as shown in Figure 5.3. Meanwhile, transfer learning with VGG-16 shows the accuracy of 88.88% for training data and 87.88% for validation data, with the F1-score is 0.7308. The graph of loss and accuracy vs epoch from VGG-16 model is shown in Figure 5.5. As indicated by the figure, the accuracy curve shows our training accuracy with low overfitting due to its upwards direction towards a high accuracy value. On the other hand, the loss curve depicts a good learning rate as presented by its downwards direction towards a low loss value. Overall, the training and validation accuracy percentages are similar and quite high, hence the model is ready for testing.

In addition, we also show the sample during the validation phase in Figure 5.4 for model's result confirmation by the expert. In the testing stage, we used 60 images with the ratio (0.5, 0.5) for COVID- 19 and Normal conditions. We implemented Grad-CAM to show the GGO locations - or lack-thereof - presented on the CT-scan images, which indicates the significant features detected by the model. Figure 5.6 is an example of one of the test samples overlaid by the Grad-CAM heatmap, with the dark red spots within the lung area indicating the GGOs. Our implementation of Grad-CAM has allowed us to see parts of the CT-scan the model deems as GGOs. We provided a sample of COVID-19 and non-COVID-19 CT-scans, shown in Figure 5.6a and Figure 5.6b respectively. The CT-scan with a COVID-19 positive result has a 97.47% confidence level, whereas the COVID-19 negative result indicated a 49.90% assurance.

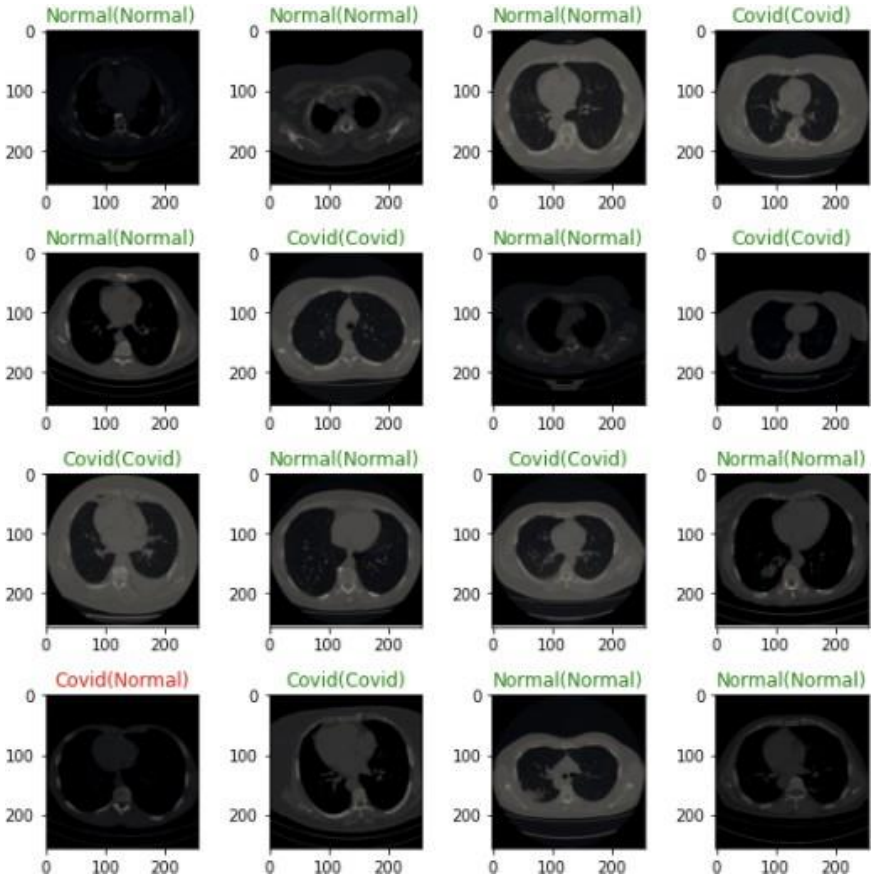
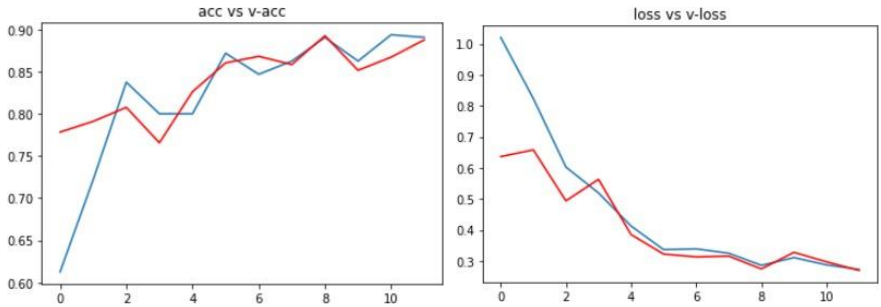


Figure 5.4: LeNet Model Prediction Sample
The text inside the bracket shows the true label of the image.

5.1.2 Model from Chest X-Rays (CXR)

As suggested in the paper conducted by López-Cabrera, et al. [5], pre-processing the dataset before using it to train the machine learning model can be used to mitigate the problems of bias in the datasets. Pre-processing the CXR images by segmenting the lung portion of the CXR image can be used to mitigate biases such as corner titles and annotations outside of the lung region of the image.

Image segmentation is used to generate the segmented dataset. The CXR images are segmented to extract the lung Region of Interest (ROI). The ROI is extracted by using an existing deep generative model called LungVAE, which generates a ROI mask from a given CXR image as illustrated in Figure 4.2.



(a) Loss vs Epoch (b) Accuracy vs Epoch

Figure 5.5: Training Result of VGG-16 Transfer Learning
The red-colored line represents the measure on validation data, while the blue line shows the measure on training data.

(a) Heatmap showing Positive COVID-19 (b) Heatmap showing Negative COVID-19

Figure 5.6: GradCAM Result of VGG-16 Transfer Learning

LungVAE is a Variational Auto-Encoder (VAE), which is a type of Auto-Encoder designed as a generative model [6]. LungVAE is designed to generate lung segmentation masks from CXR images. It is specialized in segmenting CXR images that contain abnormalities such as CXR images with high opacity regions. It is focused on segmenting abnormal CXR images caused by respiratory ailments such as COVID-19. LungVAE generates a mask image of the lung ROI illustrated in Figure 4.3. (b) from the original CXR image illustrated in Figure 5.7a. The mask of the lung ROI is then used in a bitwise-and operation on the original image (Figure 5.7b), which generates the segmented lung CXR image in Figure 5.7c.

(a) Original CXR image (b) Lung mask generated by LungVAE (c) Segmented lung ROI

Figure 5.7: Lung ROI Masking with LungVAE

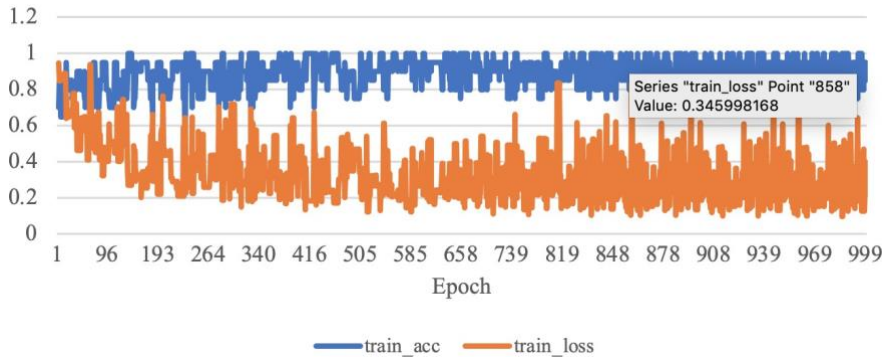
The 3,120 CXR images are divided into three classifications: COVID-19, Normal, Pneumonia, where each classification contains 1,040 CXR images. The testing batch contains 390 CXR images for each dataset, which is also divided into the three classifications resulting in 130 CXR images for each classification.

We used an existing pre-trained Torch XRV DenseNet model that is specialized for processing CXR images published in [7]. The DenseNet model is re-trained using the transfer learning method, where only the classifier portion of the model is trained, while the feature learning portion is not re-trained. The feature learning portion of the pre-trained DenseNet model is not re-trained since the model is already trained to process features of CXR images. We trained the Torch XRV DenseNet model up to epoch 1,000. The graph of the model's performance during the training process for each epoch is shown in Figure 5.8. The result of the evaluation on the test data is shown in Table 5.1.

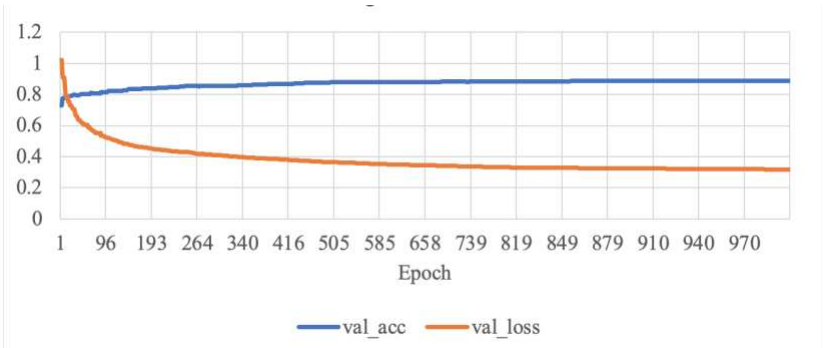
The results of the model testing were summarised using confusion matrices and the values derived from them: recall, precision, and F1-scores. Grad-CAM was also used to give better insight on the activations of the model when processing a given CXR image. Each CXR image tested was used to generate an activation heatmap using Grad-CAM, such as the one illustrated in Figure 5.9b where the heatmap is produced as the result of model's training. The heatmap is then superimposed on the sample CXR image (Figure 5.9a) as illustrated in Figure 5.9c to visualise the activation regions.

Table 5.1: Model's Evaluation Result

Class	Precision	Recall	F1-Score	Accuracy
COVID-19	0.97	0.85	0.91	0.88
Normal	0.81	0.95	0.88	
Pneumonia	0.88	0.84	0.86	

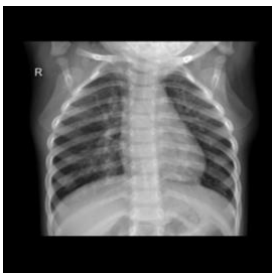


(a) Loss and accuracy in training data

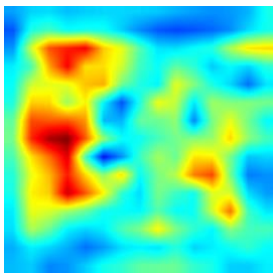


(b) Loss and accuracy in validation data

Figure 5.8: Torch XRV DenseNet Model on Training and Validation Set



(a) Sample CXR image



(b) Grad-CAM heatmap representing activation regions

(c) Sample CXR image superimposed with the Grad-CAM heatmap

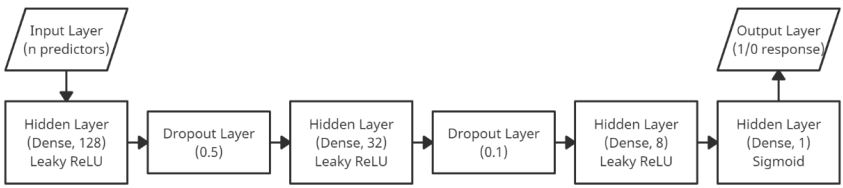
Figure 5.9: Grad-CAM on a CXR Image

5.1.3 Model from Blood Test Data

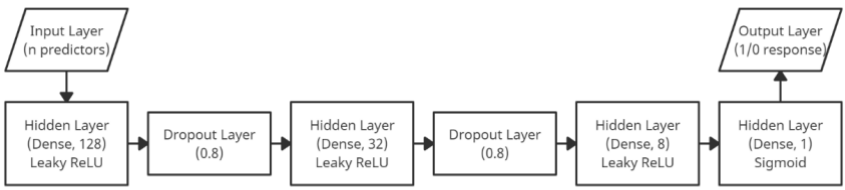
In building COVID-19 detection model from blood test data, we used the deep learning approach. The deep learning approach works best with very large data. We utilized deep learning to anticipate the possibility of the COVID-19 data to grow exponentially in the pandemic situation. Research on deep learning for tabular data is still very limited. We already mentioned in the literature review that similar studies have been found on detecting the presence of COVID-19 from blood tests by using classical machine learning algorithms. In this task, we want to explore the advantage of deep learning in our dataset.

Two deep neural network (DNN) architectures were used in the experiment. We developed a simple deep neural network architecture and compared it to the TabNet architecture [8], which were designed specifically to handle the tabular data. We also evaluated the performance from both architectures.

Our developed neural network architecture model is shown in Figure 5.10. As the datasets used had different characteristics (the imbalanced class and missing values), we need to adjust a little bit in the dropout layer. We used Binary Cross-Entropy (BCE) loss function to predict binary class outputs (i.e. COVID-19 and Non-COVID-19) and Adam optimizer to adjust the parameter during the training. Learning rate of both architectures were set to 0.001 and the batch size was 8 with hundred training epochs.



(a) Neural network architecture for San Raphael and Pasar Minggu Hospital dataset



(b) Neural network architecture for the Albert Einstein Hospital dataset

Figure 5.10: Neural Network Architecture

In addition, we also observed the important features from the three datasets. The summary of important features is shown in Table 5.2. The table shows several common features in the datasets, and the top three were always found prominent, which are eosinophils,

leukocytes and platelets. However, the summary cannot be generalized for the other dataset, because the dataset we used has several limitations, such as several missing values and imbalanced class problems.

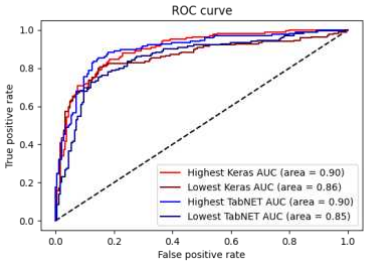
Table 5.2: Summary of Top Important Features from Three Datasets

Blood Biomarker	Hospital Dataset		
	San Raphael	Albert Einstein	Pasar Minggu
Eosinophils	v	v	v
Leukocytes	v	v	v
Platelets	v	v	v
Mean corpuscular hemoglobin concentration		v	v
Monocytes		v	v
Neutrophils	v		v
Segmented Neutrophils			v
Urea		v	v
C-reactive protein	v	v	
Haematocrit	v	v	
Blood sugar (blood glucose)			v
Erythrocyte sedimentation rate			v
Lymphocytes			v
Mean Corpuscular Volume			v
Basophils		v	
Haemoglobin		v	
B-cells inflammatory		v	
Red cell distribution width		v	
Alkaline phosphatase	v		
Alanine aminotransferase	v		
Creatine kinase	v		
Lactate dehydrogenase	v		

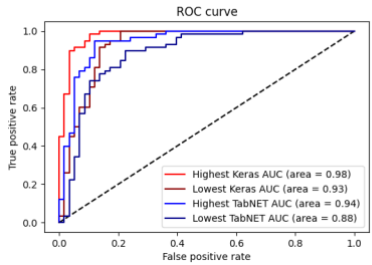
The experiment was repeated 10 times to examine whether the models show robust performance and eliminate chance results. We used Area Under the ROC (Receiver Operating Characteristic) Curve (AUC) as the main evaluation metric. This was done to measure the performance of the model in many different threshold settings. The AUC is shown in Table 5.3 and the ROC curve is shown in Figure 5.11. As previously explained in Chapter 4, we performed two different imputation methods in the datasets, namely age-based imputer and KNN. We also examine and compare both to see whether the different imputation techniques affect the model's performance.

Table 5.3: AUC of the three datasets used in the experiment

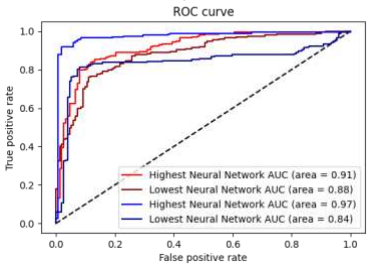
Dataset	AUC score (mean ± std)
San Raphael Hospital	0.87 ± 0.014
Albert Einstein Hospital	0.90 ± 0.057
Pasar Minggu Hospital	0.88 ± 0.024



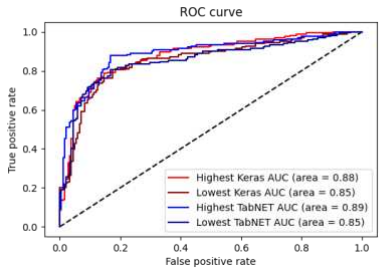
(a) San Raphael Hospital with KNN imputer



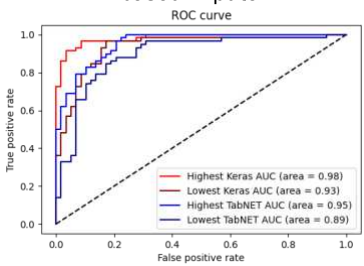
(b) Albert Einstein Hospital with KNN imputer



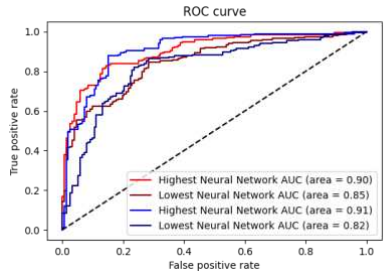
(c) Pasar Minggu Hospital with KNN-based imputer



(d) San Raphael Hospital with age-based imputer



(e) Albert Einstein Hospital with age-based imputer



(f) Pasar Minggu Hospital with age-based imputer

Fig. 5.11: ROC Curve of Three Deep Neural Network Models

5.2 Mortality Prediction

We have published the work in mortality prediction by using decision-tree based algorithms in [9]. In predicting the survivor/mortality case, we used blood test data. We selected a tree-based model to benefit from their white-box approach advantage which allows us to see the model of the learning algorithm. With this approach, the model can be easily analyzed by the human expert. We used three algorithms in this study: CART Decision Tree, (2) Random Forest, and (3) eXtreme Gradient Boosting (XGBoost).

CART stands for Classification and Regression Tree algorithm which is a term introduced by Breiman et al. [10]. It is a decision tree algorithm which can be used for both classification and regression problems. In the CART algorithm, the data is represented in a single binary tree with the node representing the feature and the leaf representing the class decision. This algorithm is commonly used in data mining and considered simple and good enough to explain the data. Decision tree is non-parametric and can also deal with a large dataset with simplified tree-based model explanation.

Random Forest algorithm uses more than a single tree to model the data. It can be said that a random forest is a collection of decision trees. It takes votes on several decisions made from more than one tree and return the majority. The more diversity of the tree is attached the better the prediction. When compared to the classical decision tree, this algorithm performs slower but the accuracy is higher. The high accuracy in this algorithm is due to the random features which are chosen during the training process. It does not depend highly on any single or a set of features. With this method, a random forest can generalize data better than the decision tree.

XGBoost is short for Extreme Gradient Boosting Algorithm which works by building up many decision trees. It uses a gradient descent algorithm to optimize the search. It always tries to correct the model from previous mistakes, so the next step is an improvement. The process is continued until there is no further improvement. It is a fast algorithm and can handle large data very well. XGboost can also perform well on data with an imbalanced class. The main difference with the previously mentioned algorithm is that the way it builds the tree in additive, one tree at a time. This is done in a forward stage-wise process. Both algorithms also differ in the way they combine the results. Gradient boosting combines the results along the process.

We used the implementation of the three algorithms in Python Languange. For the first two algorithms, we used the implementation from Scikit learn library[1], and for the last algorithm, we used the implementation package called xgboost[2]. The hyperparameter setting of each model is shown in Table 5.4.

5.2.1 Evaluation Technique

In this study, we used standard classification evaluation techniques by measuring the precision, recall, F1- score, and accuracy of the model. The dataset was divided into two parts randomly with the ratio of 70% training data and 30% testing data. We used stratified sampling when dividing the dataset to avoid overfitting. Due to the stochastic nature of the algorithms, the experiments were repeated several times and the average.

Table 5.4: Setting of the Model's Hyperparameters

Algorithm	Setting
Decision Tree	min_samples_leaf=50
	criterion=gini
Random Forest	max_depth=5
	n_estimators=10
	class_weight=balanced_subsample
	min_samples_split=15
XGBoost	max_depth = 5
	min_child_weight = 1
	eval_metric=logloss

Result were reported. The tree generated from each algorithm was selected based on the highest accuracy of the model. All the models were run on the same random state of the data splitting, so there was no bias, they were all observing the same data point. For a deeper analysis, we also reported the feature importance found by the decision tree. We used SHAP (SHapley Additive exPlanations) value for explaining random forest and XGBoost models. The SHAP values express how big is the contribution of each feature to the predictive power of the model.

5.2.2 Result and Analysis

The feature importance of each model is shown in Figure 5.12. We show only eleven most prominent features in the dataset. From the figure we can see that those three algorithms show similar results and this can be easily interpreted by the clinicians. The SHAP value explains how each feature contributes to the model prediction. The top 11 features and the trend found in the dataset with regard to each class are shown in Table 5.5. The findings are in line with the literature shown in the previous section. As mentioned in [11], the changes in lymphocytes, neutrophils, monocytes, eosinophils, and platelets are related to viral replication and hyperinflammation in COVID-19 cases. The platelet decrease, called thrombocytopenia, has been associated with severity of COVID-19. It is a common condition of patient with COVID-19. The possible cause of the platelet decrease in the blood are

(1) direct infection of bone marrow cell by the virus, (2) body's immune system attacking and destroying the platelets, and (3) the aggregation of the platelet in the lungs, which caused microthrombi and platelet consumption [12].

Arterial blood gas biomarker was also shown to be an important feature, as expected. The partial pressure of oxygen (PO2_N), also known as PaO2, measures the oxygen pressure in the arterial blood, which reflects how well the oxygen circulates. We were also expecting the oxygen saturation level to be the most important feature, but since we have limited the model to focus on showing the top 11 features to increase the model readability, the oxygen saturation was not captured here.

Other disease indicators, such as hyperglycemia (the increase of blood sugar level), chronic renal (shown by the increase of urea level), and liver damage (shown by the increase of SGOT/SGPT level) were also captured in the top 11 features. The common biomarkers associated with coagulation index, including D-Dimer, prothrombin time (PT), activated partial thromboplastin time (APTT), which could sensitively reflect the blood clotting state [13], were also shown significant in the result.

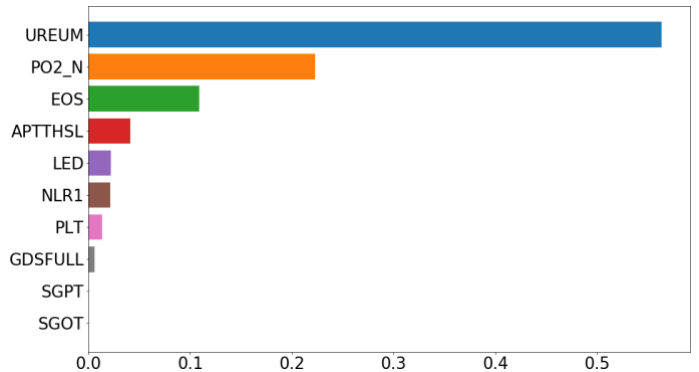
The performance of each model is shown in Table 5.6. It is shown that XGBoost performs better than the other two tree-based algorithms, as expected, with reasonably fast execution time. In this paper, our aim is to explore the important biomarkers in our dataset, while we can also observe the classification performance of each model.

Table 5.5: The Top 11 Features Trends

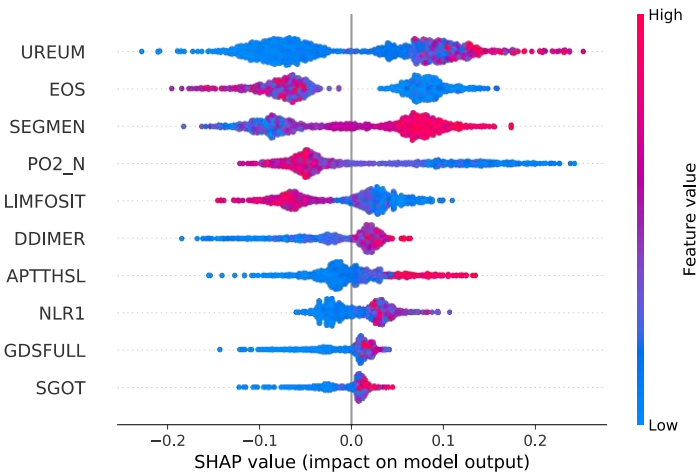
Feature	Found in the class of	
	survive	dead
UREUM	decrease	increase
PO2_N	increase	decrease
EOS	increase	decrease
APPTHSL	decrease	increase
LED	decrease	increase
DDIMER	decrease	increase
GDSFULL	decrease	increase
SGOT/SGPT	decrease	increase
PLT	increase	decrease
LIMFOSIT	increase	decrease
SEGMEN	decrease	increase

Table 5.6: Model Performance

Algorithm	Class	Prec.	Recall	F1-score	Accuracy	Execution Time (sec)
Decision Tree	survive	0.88	0.92	0.90	0.90	0.03
	dead	0.91	0.87	0.89		
Random Forest	survive	0.94	0.91	0.92	0.92	10.71
	dead	0.91	0.94	0.92		
XGBoost	survive	0.99	0.96	0.98	0.98	1.03
	dead	0.96	0.99	0.98		



(a) Decision Tree Feature Importance



(b) Random Forest

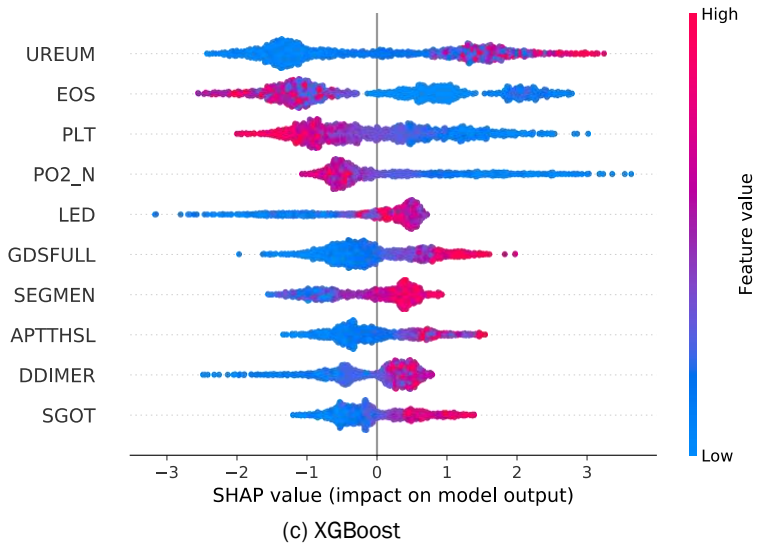


Figure 5.12: Feature Importance and SHAP Summary

The tree produced by each model is shown in Figure 5.13, 5.14 and 5.15. Figure 5.13 shows the decision tree result after being trained on the dataset. One possible interpretation can be: if the D-Dimer of a patient was less than or equal to 1.568 µg/mL (the normal level < 0.5 µg/mL), then the patient would be more likely to survive. If it is not the case, then we need to check on other conditions. In Figure 5.14, we can see that the tree produced by random forest was quite similar with the single decision tree. This is due to this method using the same approach with multiple trees. We select randomly a subtree to be shown here as an example. Figure 5.15 shows a subtree of xgboost model which can explain the data explicitly. One can interpret and read the subtree as if a patient found to have a high LED (Erythrocyte Sedimentation Rate) and D-Dimer was also found to be higher than normal value, while the PLT (platelet counts) lower than 404 10^3/µL (normal level 150 - 440 10^3/µL), then this patient will have a higher chance to die than survive, with the probability of 0.629 (σ(0.534)).

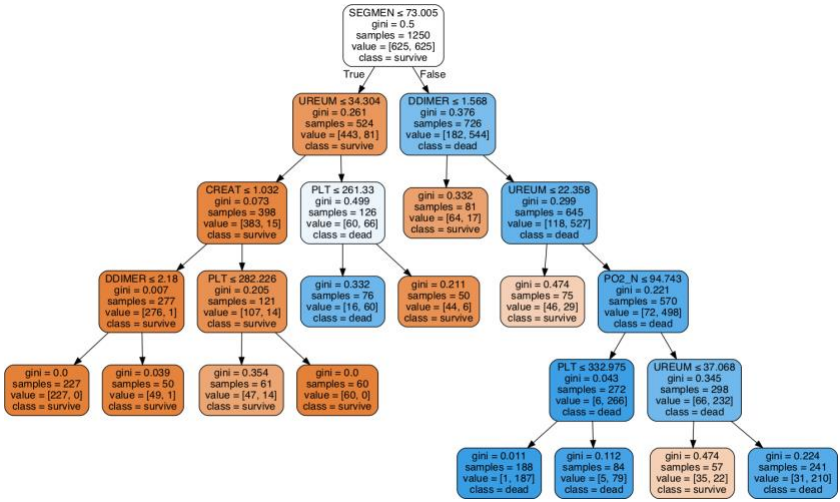


Figure 5.13: Decision Tree

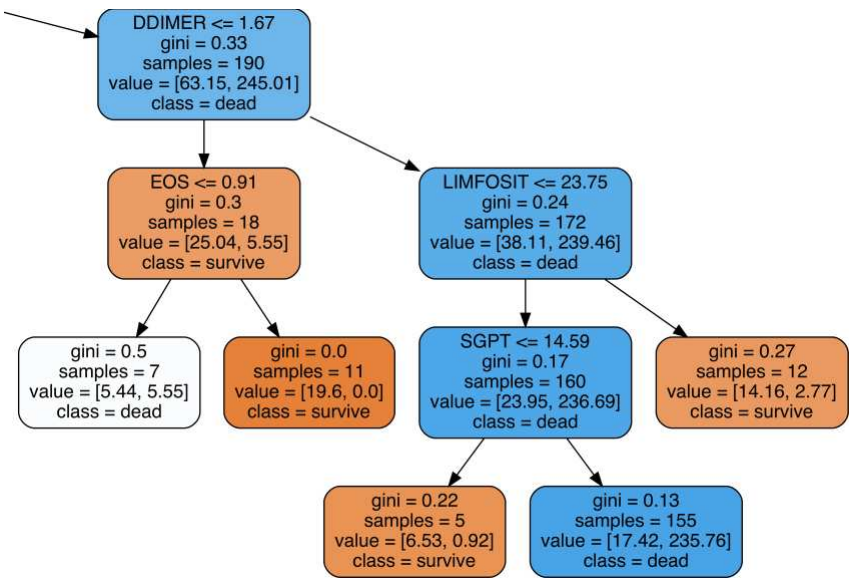


Figure 5.14: Random Forest Subtree

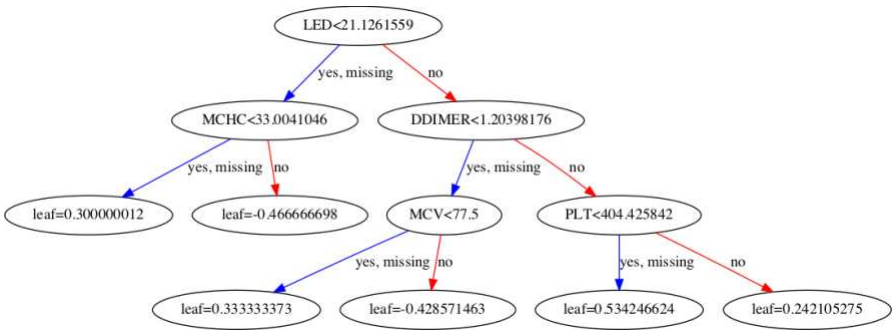


Figure 5.15: XGBoost Subtree

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Chapter 6
Telemedicine System Design

6.1 Software Specification

In this section, the software specifications will be discussed in detail by using diagrams, i.e. concept, architecture, data flow, and use case diagrams, respectively. In this document, we will introduce our system, NuMed: A New AI-based Telemedicine for COVID-19 Detection.

6.1.1. Concept Diagram

Figure 6.1 depicts our concept diagram. As previously mentioned, the COVID-19 pandemic is still happening, and more tests are required. Hence, some alternatives other than RT-PCR and the rapid antigen test are needed in order to improve early diagnosis tests, which further helps to reduce, for example, workloads in hospitals. Existing solutions resort to manual tests, e.g., COVID-19 test kits are given, and the kits are sent back to medical institutions for inspections. Another example is that trained medical practitioners need to visit patients' houses and conduct the tests there. In addition, there are still few existing telemedicine applications that can support COVID-19 detections. This is where NuMed comes into play. NuMed provides an automatic tool where users can submit their medical data, and immediate results can then be obtained by using XAI. The current proposal envisions such that users can upload their CXR, lung CT-scan, and blood sample data themselves. Then, predictions as well as confidence probabilities whether a user has been infected by COVID-19 virus are given.

6.1.2. Architecture Diagram

Our implementation comprises four parts, i.e., a mobile application as the frontend, a reverse proxy, an authentication and authorization service, and backend services that handle each medical data as shown in Figure 6.2. We plan to use a low-code software platform from Mendix to implement the user interface for the mobile application. Then, a reverse proxy is used to proxy users' requests to corresponding server-side services. The reverse proxy can also later be used as a load balancer. First, the user needs to request a token from the authentication and authorization service. Each medical data, i.e., CXR images, lung CT-scan images, or blood sample data, is then sent to the corresponding machine learning model over a representational state transfer (REST) application programming interface (API). Note that these requests should be accompanied by the token received by the authentication and authorization service. Results are then each recorded in a database.

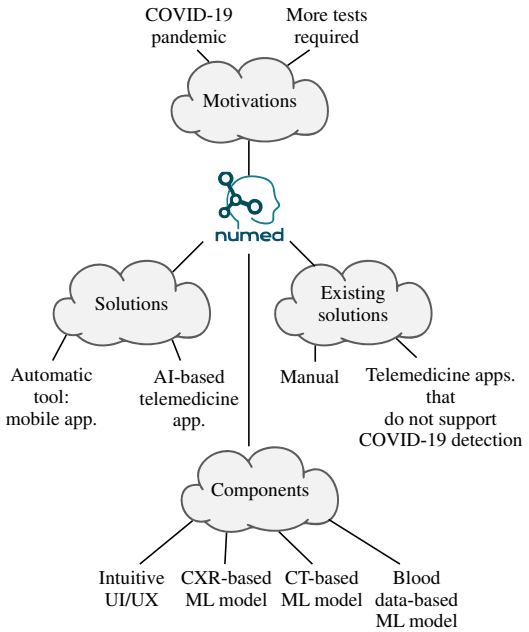


Figure 6.1: NuMed's Concept Diagram

6.1.3. Data Flow Diagram

Figure 6.3 shows our data flow diagram where users first uploaded their medical data into NuMed. For example, a CXR image is uploaded to the CXR-based COVID-19 detection service. It is worth noting here that we assume users already get their copied medical data from their hospitals so that they can conduct the COVID-19 test themselves. Then, prediction results are shown to the user and also stored in a database as a record.

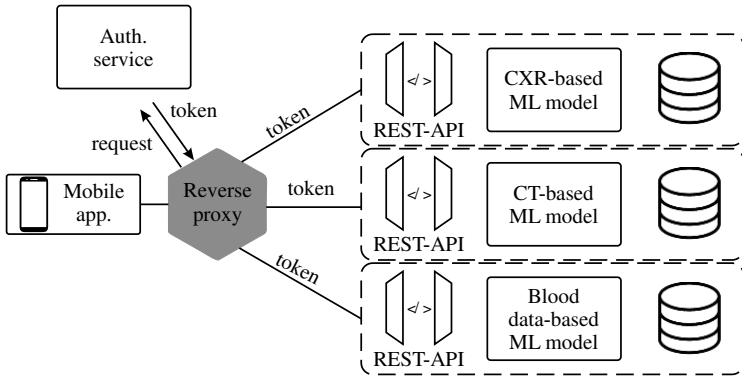


Figure 6.2: NuMed's Architecture Diagram

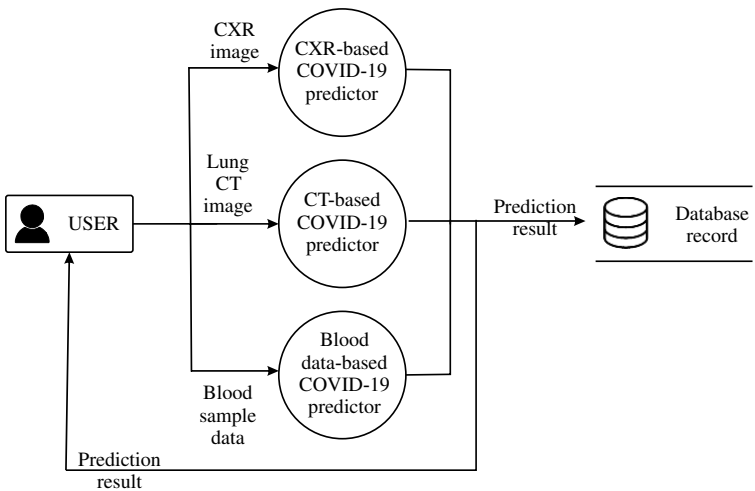


Figure 6.3: NuMed's Data Flow Diagram

6.1.4. Use Case Diagram

NuMed's use case diagram is depicted in Figure 6.4. Users can interact with NuMed in multiple ways. Generally, users can register and login. Also, if users forget their passwords, they can reset it. Once they are logged in, they can perform COVID-19 tests by uploading their medical data, and then they can see the prediction results. Users can also call the nearest hospital where they are registered. This information is inputted during registration and can be seen in users' profile page.

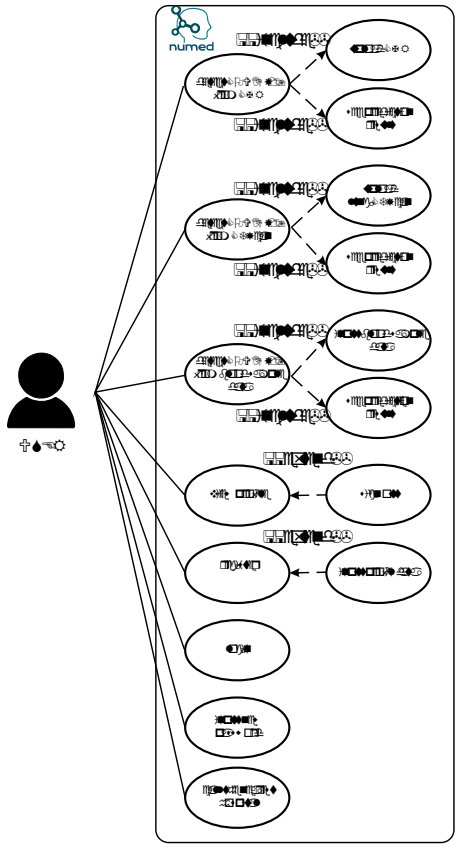
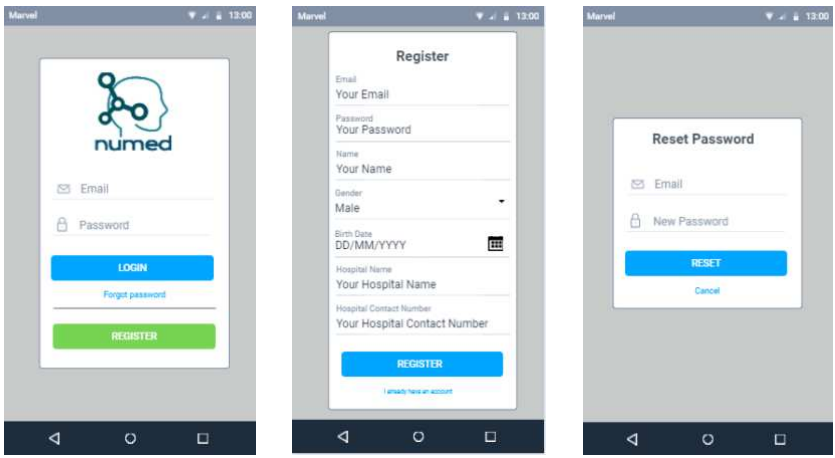


Figure 6.4: NuMed's Use Case Diagram

6.2. Mock Up Design of the Solution

When the user opens the app for the first time, they will be greeted with a login page for them to enter their credentials. They can also register and reset their password in the respective pages as depicted in Figure 6.5.

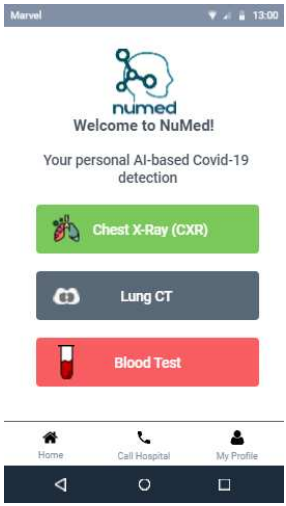


(a) Login page (b) Register page (c) Reset password page

Figure 6.5: NuMed's Mock Up: User Authentication Pages

The landing page (or home page) is accessible after the user fills in their credentials. Here they can tap on any of the three buttons to perform COVID-19 detection via chest x-ray, lung CT scan, or blood test result. Additionally, tapping on the "Call Hospital" button on the bottom navigation bar will call their registered hospital and "My Profile" will open the user's profile page (Figure 6.6).

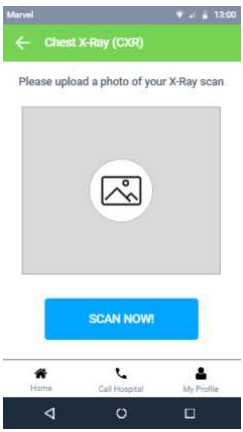
Additionally, tapping on the "Call Hospital" button will call the user's registered hospital. Working under the assumption that the hospital has access to the system database and can fetch the user's data, they will be asked to provide their credentials to identify them, such as their name or UID. This information can be viewed in the user's profile page as seen in Figure 6.6b. The CXR page allows the user to upload an image of their chest x-ray. Tapping on the "Scan Now!" button processes their image and shows the user the probability of them having COVID-19 as seen in figure 6.7c. The lung CT page does the same thing as CXR, except the user uploads an image of their lung CT-scan. The blood test page is where the user fills in a form with information regarding their blood test results. The app will use this data to return the probability of the user being positive with the COVID-19 virus.



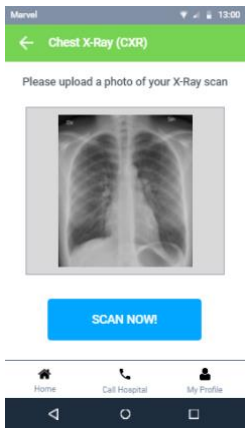
(a) Landing page

(b) Profile page

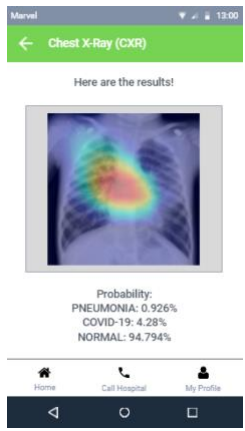
Figure 6.6: NuMed's Mock Up: General Pages



(a) CXR page

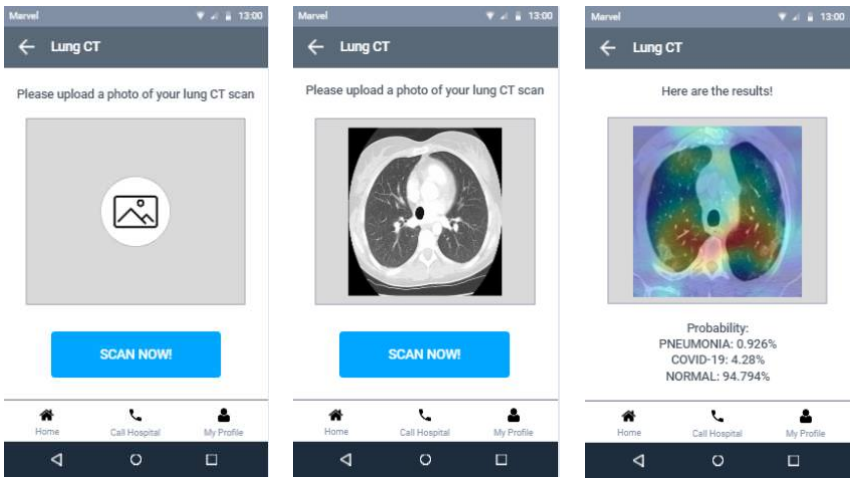


(b) CXR page (image uploaded)



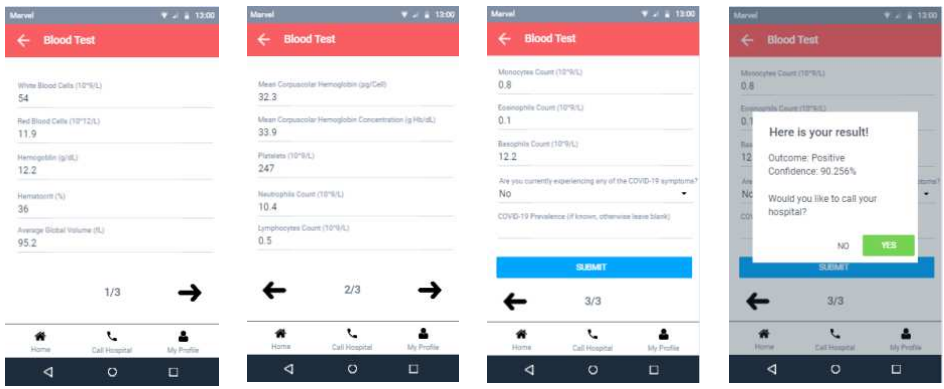
(c) CXR result page

Figure 6.7: NuMed's Mock Up: CXR Pages



(a) CT page (b) CT page (image uploaded) (c) CT result page

Figure 6.8: NuMed's Mock Up: CT Pages



(a) Blood test page (1/3) (b) Blood test page (2/3) (c) Blood test page (3/3) (d) Blood test result

Figure 6.9: NuMed's Mock Up: Blood Test Pages

Chapter 7
Conclusion and Future Work

COVID-19 is attacking people all over the world. It has been more than a year we have to deal with this pandemic situation and it is not over yet. In this study, we have successfully developed several AI models in which we integrated to a new telemedicine system. The experiments on the AI modules has shown a satisfactory result and we were able to perform the disease detection by using three different datasets, CT-scan, Chest X-ray and blood test. While mortality cases can also be predicted by using the blood test.

As we all know that nowadays, the gold standard of detecting COVID-19 is using RT-PCR testing, but from the research result, we have shown that we can also perform the test and predict the presence of the disease by looking at the pattern from CT-scan, Chest X-ray and blood test. These methods can provide alternatives for people who lack of access to the facilities. These alternatives can be also useful especially in the developing countries where the health facilities for COVID-19 were still inadequate when compared to the infected patients.

Finally, we also proposed a system design of telemedicine application which uses an explainable AI system to predict the disease remotely. The application will also allow the doctors to verify the result generated by the AI before performing online consultation with the patients.

In the future, we plan to also include the IoT technology in our telemedicine system to make it possible to conduct the patient monitoring remotely. We will also improve our AI model by collecting more data from different countries. In the future, we can also explore the time dimension of the data and observe whether the current finding is still valid and can be used to detect both mortality and the presence of the disease earlier. In addition to the blood sample data, we plan to also add clinicians observation reports of the patients during the hospitalization. This report which is usually created in freetext format can be handled by employing some Natural Language Processing methods. We also want to explore the treatments given to the patients with the effect of patient outcome.

In the image processing area, it is also interesting to have a larger size of radiology image dataset with precise locations of GGO from many radiologists. Comparing the model with the diagnosis of radiologists can benefit our community to realize more reliable AI-based diagnostic tools that can be used for clinical purposes.

Even though the AI-based detection, as an alternative method, cannot be as accurate as the RT-PCR test, and unreliable to be used as a primary method, but the system can become a good indicator for

further investigation by the health workers. Based on the WHO research, it was mentioned that the health workers who are particularly in contact with the COVID-19 patients are at higher risk of being infected with COVID-19. Not only because of the number of the health workers which are limited, but also because of the higher risk of being in contact with the infectious patients that could allow them to benefit from our proposed AI-based telemedicine system. More than that, our proposed solution will also have a larger reach not only for health workers and the patient, but also for the society from any different places.

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- Numed Telemedicine for COVID-19, Registered under DIRJEN KI Indonesia No. 000305382, 14 July 2021

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MONOGRAPH

SMART AI-BASED

TELEMEDICINE SYSTEM FOR COVID-19

COVID-19 is a disease that attacks the human respiratory system. The outbreak of this disease has been declared as a pandemic by the World Health Organization (WHO) since 2020. COVID-19 condition requires the health practitioners to be more restrictive and protective in handling the infected patients. The lack of medical staff and Personal Protective Equipment (PPE) restricts the health service provider's capacity to manage the epidemic. Indonesia as the largest archipelagic country in the world has its own challenges in fighting the pandemic. Some people in rural areas still have difficulty accessing good health facilities. This condition can also be an inhibiting factor in accelerating the handling of the COVID-19 pandemic.

In this book, we demonstrate our research proposing an AI-based telemedicine system to fight COVID-19. This system can reduce direct contact between the health workers and the patients. The telemedicine system also allows two-way communication between the patients and the doctors from a distance. The telemedicine system is equipped with an AI-based module that can help the doctors to gather an initial description of the patient's condition. We focus on the explainable AI which is able to allow a human interpretation of what is learned through machine learning. The proposed solution is not only building the intelligent telemedicine application but also allowing the medical experts to validate the resulting models, e.g. via suitable visualizations. This feature will become an advantage of our proposed solution when compared to the other existing telemedicine applications on the market.

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