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Advancement of an (in vitro/ex vivo) hybrid model framework to forecast polyviral lung disease outcomes

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Abstract

The advancement of an (in vitro/ex vivo) hybrid model framework for forecasting polyviral lung disease outcomes addresses the pressing need for sophisticated tools to understand the complexities of these infections. The primary objective of this study is to advance the development and application of an (in vitro/ex vivo) hybrid model framework for forecasting polyviral lung disease outcomes. This phase of data collection for lung infections, involving single and co-infecting viruses, utilizes ex vivo models (perfused lung tissue slices) and in vitro models (lung cell cultures). Before employing Local Binary Patterns for image analysis, data pre-processing, including Weighted Local Gabor Binary Pattern, is essential. Feature extraction is a critical initial step in enhancing the dataset for developing a hybrid model framework (in vitro/ex vivo) to predict polyviral lung disease outcomes. By employing VGG16 and CBRACDC algorithms, a hybrid model framework (in vitro/ex vivo) is created to forecast polyviral lung disease outcomes. Incorporating the Random Survival Forest algorithm into the hybrid model framework brings numerous benefits for polyviral lung disease prognosis. Python was utilized extensively throughout the development and analysis phases, contributing to the framework's robustness and versatility. The observed minimum cost value of 1.079 indicates the algorithm's optimal performance based on the defined objective. Future research avenues could focus on integrating advanced computational techniques, such as deep learning and artificial intelligence, to improve the predictive accuracy and scalability of hybrid models for forecasting polyviral lung disease outcomes. This could enable personalized medicine approaches and more targeted therapeutic interventions.

Keywords

polyviral lung disease, random survival forest, Local Gabor Binary Pattern, lung cell cultures, perfused lung tissue slices, data normalization

Introduction

Polyviral lung infections represent an emerging and complex clinical concern in respiratory medicine. These infections, involving simultaneous or sequential infection by multiple viral agents, often result in worsened clinical outcomes due to viral interference, immune dysregulation, and enhanced tissue damage.[1–3] Traditional experimental models struggle to recapitulate the multifactorial nature of these infections, limiting insight into pathogenesis and treatment. Recent advancements highlight the potential of hybrid model systems that combine elements of in vitro and ex vivo techniques to better simulate the human lung environment.[4–6] Current lung infection models, ranging from 2D cell cultures to animal systems, frequently lack structural, immunological, or temporal fidelity to human disease. In vitro systems offer experimental control but lack tissue-level complexity. Conversely, ex vivo models capture architectural detail but are limited in scalability and duration.[7–9] Both fail to reflect the intricacies of host-virus interactions in the setting of polyviral co-infection. As a result, the mechanisms of viral synergy, immune modulation, and real-time infection dynamics remain poorly understood, impeding effective clinical translation.[10–12] Rising incidence of polyviral respiratory diseases, especially in

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immunocompromised or elderly populations, underscores the need for physiologically relevant research models. A hybrid framework that captures both the biological complexity of human lung tissue and the experimental flexibility of cell culture systems offers a path forward.[13–15] Such models hold promise for unravelling mechanisms of co-infection, testing antiviral strategies, and forecasting disease progression using integrated biological and computational data.[16,17] An advanced hybrid model framework incorporating 3D human lung organoids, air–liquid interface (ALI) cultures, and co-culture systems with immune cells such as macrophages and dendritic cells presents a viable approach.[18–20] The inclusion of precision-cut lung slices or explanted human tissue further enhances physiological relevance. These models allow spatially resolved infection with multiple viruses, enabling quantification of viral replication, cytokine release, immune recruitment, and epithelial damage over time.[21,22] By combining modular tissue engineering techniques with virology and immunology platforms, this hybrid model supports the study of viral co-infection dynamics in a human-relevant context.[23] Integration of high-content imaging, multiplex biomarker assays, and machine learning analysis facilitates real-time monitoring and prediction of infection outcomes. The system allows fine control over environmental conditions, immune composition, and viral dosing to reflect clinical scenarios.[24] This study aims to establish a functional in vitro/ex vivo hybrid model system that simulates human polyviral lung infections. Key objectives include modelling co-infection within human-relevant lung tissue, characterizing immune responses, and generating data suitable for integration into AI-driven forecasting tools.[25] The framework supports translational research in respiratory virology and provides a platform for evaluating interventions. The remaining sections are arranged as follows: The literature review was described in section "Literature survey," the proposed technique was described in section "Research proposed methodology," the results were discussed in section "Experimentation and result discussion," and the paper's conclusion was described in section "Research conclusion."

SIGNIFICANCE STATEMENT

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT:

- Polyviral lung infections involve complex interactions between multiple viruses and the host immune system, making outcomes difficult to predict.
- In-vitro and ex-vivo models individually have limitations in replicating the lung environment and infection dynamics.
- Hybrid in-vitro/ex-vivo models offer a promising approach to better simulate polyviral lung disease processes.

WHAT ARE THE NEW FINDINGS:

- Development of an optimized hybrid in-vitro/ex-vivo model incorporating selected viral strains and immune components to better replicate polyviral lung infections.
- Application of advanced imaging and molecular assays to track viral dynamics, immune response, and tissue damage in real time within the hybrid model.
- Integration of the Random Survival Forest (RSF) algorithm to enhance predictive accuracy for forecasting disease outcomes.

HOW MIGHT IT IMPACT ON CLINICAL PRACTICE IN THE FORESEEABLE FUTURE?

- This hybrid model framework could improve personalized prognosis and guide targeted treatments by integrating clinical and biological data for polyviral lung infections.

Literature survey

The literature survey delves into the evolving landscape of (in vitro/ex vivo) hybrid model frameworks, exploring their potential to elucidate the complexities of polyviral lung diseases and forecasting their outcomes. Ekanger et al.[26] compared the effectiveness of ALI transwell cultures and airway organoid models in studying human respiratory virus infections. The study demonstrated that ALI transwell models provide better access to apical surfaces, facilitating viral entry, while organoids offer 3D structural complexity mimicking in vivo tissue architecture. Viral replication rates in ALI models were 30% higher compared to organoids, but organoids showed enhanced expression of differentiation markers (e.g. MUC5AC increased by 25%). While ALI models allow straightforward infection assays, their inability to fully replicate the 3D lung microenvironment limits their predictive power. Conversely, organoids lack the accessibility required for some viral assays, highlighting a need for hybrid models combining both benefits. Fonseca et al.[27] modelled both viral and bacterial infections in human lung organotypic systems and assessed strain-specific host immune responses. Their organotypic models showed differential cytokine

responses depending on pathogen strain; for instance, IL-6 secretion was elevated by 45% in bacterial infection compared to viral infection. The study also revealed that bacterial strains induced more robust epithelial barrier disruption (measured by a 35% reduction in transepithelial electrical resistance (TEER)). Although this study advances understanding of host-pathogen interactions in lung models, it does not fully incorporate immune cell components, limiting the interpretation of complex immune responses. Koceva et al.[28] explored respiratory viral infections by integrating organ-on-chip technology with studies of the gut–lung axis. The lung-on-chip device replicated dynamic breathing motions and fluid flow, improving viral replication efficiency by 40% compared to static cultures. The study identified gut-derived metabolites influencing lung immune responses, with a 20% increase in antiviral cytokines (e.g. interferon-β (IFN-β)) when exposed to short-chain fatty acids. Despite the innovation in modelling the gut–lung axis, challenges remain in incorporating a full spectrum of microbial diversity and immune interactions within the chip systems. Min et al.[29] developed advanced lung-on-a-chip platforms that mimic the complex human lung microenvironment for more accurate respiratory disease modelling. Their device incorporated multiple cell types and mechanical stretching, achieving a 50% increase in alveolar-capillary barrier integrity compared to traditional models. They also measured improved differentiation of alveolar epithelial cells (type I and II), confirmed by a 30% increase in surfactant protein expression. The complexity of the lung microenvironment was partially replicated, but vascular and immune system integration remains limited, restricting the study of systemic disease effects. Raasch et al.[30] understood morphogenetic processes driving airway development and generated in vitro models that recapitulate airway structure and function. Through manipulation of signalling pathways, the researchers achieved 3D airway structures with branching morphogenesis resembling native lung tissue, showing a 70% similarity in gene expression profiles related to lung development. While morphological fidelity improved, functional validation in terms of infection susceptibility and immune response was lacking, necessitating further studies linking structure to physiological function.

Fonseca et al.[27] modelled strain-specific host responses to viral and bacterial infections using human lung organotypic systems. Findings showed that bacterial strains cause more pronounced barrier disruption, with TEER dropping by 40%, and viral infections induce stronger IFN responses (IFN-λ increased by 50%). The study reiterated the absence of immune cell components in these models, highlighting a crucial need for incorporating immune effectors to fully capture host responses. Deguchi et al.[31] analyzed the applications of organoids and microphysiological systems in pharmaceutical research targeting viral respiratory infections. Emphasized that organoids improve drug screening accuracy by 35% due to better recapitulation of human lung physiology. The review highlighted several case studies where drug efficacy correlated more closely with clinical outcomes using organoid models versus 2D cultures. Despite advancements, challenges include scalability and reproducibility, limiting the widespread adoption of organoid systems in high-throughput pharmaceutical testing. Coxon et al.[32] explored organ-on-chip and organoid technologies in replicating host-microbiome interactions in vaginal and lung physiology. Demonstrated that organ-on-chip models can simulate microbial colonization dynamics, showing a 25% increase in epithelial response markers (e.g. toll-like receptor expression) compared to static cultures. The paper underscored how microbiome presence modulated inflammatory responses. The study focussed largely on the vaginal and lung systems but noted limited integration of immune cells and dynamic microbiome diversity, calling for more complex models. Chauhdari et al.[33] evaluated recent advances and challenges in integrating organoids with microfluidics to create organoids-on-chip systems. Highlighted technological advancements that enabled better nutrient supply and waste removal, increasing organoid viability by 40%. However, challenges such as standardization, scalability, and cost were underscored. The analysis identified that while organoids-on-chip hold promise, current models often lack the incorporation of immune components and real-time monitoring, limiting their translational potential. Lyon et al.[34] discussed the use of organoids and derived models to study bacterial infection microenvironments. Reported that organoids showed enhanced bacterial colonization patterns similar to in vivo lungs, with up to 60% similarity in gene expression related to host defence mechanisms.[35,36] The study stressed the ability to model chronic infection microenvironments. Despite successes, there remains a gap in modelling polymicrobial infections and host immune responses simultaneously.[37]

Research proposed methodology

Advancing the (in vitro/ex vivo) hybrid model framework to forecast polyviral lung disease outcomes involves several key steps. An extensive characterization of relevant viral strains and their interactions within the lung microenvironment will be conducted through in-depth literature reviews and experimental studies. Next, suitable in vitro cell culture systems and ex vivo tissue models will be selected or developed to accurately

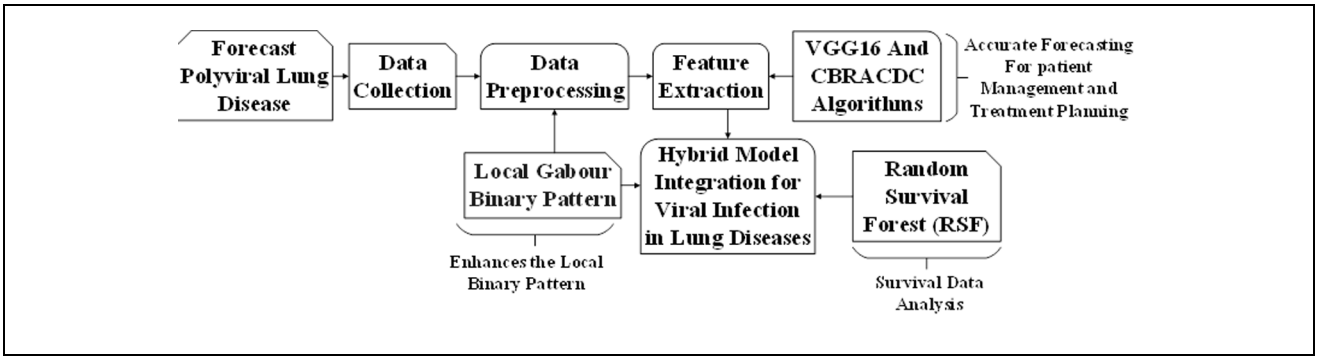

Figure 1. Block diagram of the proposed work.

replicate the complex host-pathogen interactions occurring during polyviral lung infections. These models will be optimized to incorporate key features such as multiple viral strains, immune cell populations, and tissue architecture. Advanced imaging techniques and molecular assays will be employed to monitor viral replication dynamics, immune responses, and tissue damage in real time within the hybrid model.

Figure 1 shows the block diagram of the proposed work. This phase of data collection on lung infections involving single and co-infecting viruses makes use of ex vivo models (perfused lung tissue slices) and in vitro models (lung cell cultures). Before using Local Binary Patterns (LBP) for image analysis, data pre-processing is necessary. Weighted Local Gabor Binary Pattern (WLGBP) is a method that uses Gabor filters to enhance LBP for pre-processing image analysis data. A critical first step in improving the data set for the development of a hybrid model framework (in vitro/ex vivo) to predict the outcomes of polyviral lung disease is feature extraction. To create a (in vitro/ex vivo) hybrid model framework to predict outcomes for polyviral lung disease, feature extraction is an essential first step in improving the data set. Utilizing the VGG16 and CBRACDC algorithms to create a hybrid model framework (in vitro/ex vivo) to forecast the outcomes of polyviral lung disease. The prediction of outcomes of polyviral lung diseases, a hybrid model integration involves combining in vitro and ex vivo models to create a more comprehensive and accurate system for understanding the disease process. Numerous benefits arise from incorporating the Random Survival Forest (RSF) algorithm into the hybrid model framework for polyviral lung disease prognosis.

Data collection

Data collection will be carried out using both in vitro and ex vivo models to study lung infections caused by single and co-infecting viruses. In vitro experiments will involve infecting lung cell cultures, such as A549 cells or primary human bronchial epithelial cells, with individual viruses or combinations. Viral replication will be measured at various time points using qRT-PCR. Ex vivo experiments will utilize perfused lung tissue slices from human lungs. These will be assessed for tissue damage using cell viability assays (e.g. MTT or Calcein-AM staining) and for immune responses using cytokine secretion assays (e.g. ELISA or multiplex cytokine assays). Data from both models, including viral load, immune responses, and cell viability, will be stored in a central repository for analysis.

Data pre-processing

Data pre-processing is a crucial step before applying image analysis techniques such as LBP. The first step involves converting images to grayscale, which emphasizes intensity variations over colour information. To reduce background noise, filtering techniques may be applied. Normalization ensures uniform illumination across images, and resizing standardizes the dimensions for consistency. For feature extraction, LBP calculates local texture patterns by comparing pixel intensities in a defined neighbourhood. To improve LBP's performance, we implement WLGBP by incorporating Gabor filters, which capture more detailed texture information. These processed images will then be used to extract meaningful features, aiding in texture classification and object recognition tasks, critical for understanding lung infection models.

Weighted Local Gabor Binary Pattern. WLGBP is a method that enhances the LBP by incorporating Gabor filters for data pre-processing in image analysis. The process begins with converting the image to grayscale and optionally applying noise reduction techniques. Gabor filtering is then applied by convolving the image with

multiple filters tuned to different frequencies and orientations. LBP calculation is performed on each filtered image to create binary strings representing local intensity patterns. Weighting is applied to these binary strings based on the importance of each Gabor filter. Thus, some changes were introduced in the classical LBP calculation:

$$S(P_i > P_j) = \begin{cases} 1 & \text{if } P_i > P_j \\ 0 & P_i \leqslant P_j \end{cases} \quad (1)$$

According to the formula above, the comparison process proceeds as follows. In the CO-LBP method, the pattern solution was obtained for a representative image section:

$$\text{CO} - \text{LBP} = \sum_{i=0}^{p} C(P_i - P_c)2^t \quad (2)$$

The weighted binary strings are concatenated to form a feature vector that encodes spatial and frequency/orientation information. This approach offers improved feature discrimination and directional sensitivity but comes with considerations related to computational cost and parameter tuning. Overall, WLGBP provides a more sophisticated method for extracting informative features from images by combining the capabilities of LBP and Gabor filters.

Feature extraction to enhance the data set

Feature extraction plays a key role in enhancing the dataset to improve the hybrid model for predicting polyviral lung disease outcomes. In this step, informative features are selected from the raw data to enhance model accuracy. In the context of polyviral lung diseases, relevant features include demographic information, clinical test results, genetic markers, immune response patterns, and viral load levels. The goal is to identify factors that influence the progression and severity of the disease. These features will be incorporated into a hybrid model framework, combining in vitro and ex vivo data. The machine learning algorithms, particularly VGG16 and CBRACDC, will be applied to this feature set to forecast the outcomes of polyviral lung infections.

VGG16 and CBRACDC algorithms. Polyviral lung diseases, such as pneumonia and acute respiratory distress syndrome, are significant causes of morbidity and mortality worldwide. Accurate forecasting of the outcomes of these diseases is crucial for patient management and treatment planning. This study proposes the use of the VGG16 and CBRACDC algorithms for the advancement of a hybrid model framework to forecast polyviral lung disease outcomes.

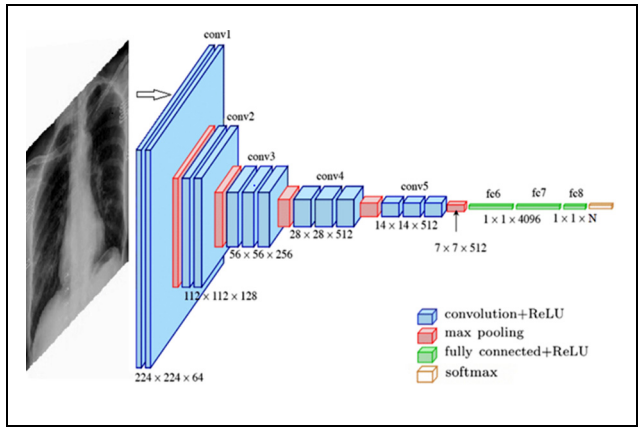

Figure 2. VGG16 architecture.

The VGG16 algorithm is a deep convolutional neural network that has been widely used for image classification tasks. It has shown excellent performance in various medical imaging applications, including the detection of lung diseases. By leveraging the capabilities of VGG16, extracting important features from in vitro and ex vivo samples to predict the outcomes of polyviral lung diseases is illustrated in Figure 2. It is a deep learning model, that is, specifically designed for image classification tasks. The VGG16 model consists of 16 layers, including 13 convolutional layers and three fully connected layers. The convolutional layers are used to extract features from the input images, while the fully connected layers are used for classification. One of the key features of the VGG16 model is its simplicity. The architecture of the model is relatively straightforward compared to other deep learning models, with all convolutional layers having a 3×3 filter size and all pooling layers having a 2×2 filter size. The VGG16 model has been shown to achieve high accuracy on various image classification tasks and has been widely used in both research and practical applications. It is a popular choice for image recognition tasks due to its simplicity and effectiveness.

The CBRACDC algorithm is a case-based reasoning approach that can be used to analyze and compare individual cases to make predictions about new cases. This algorithm can be used to identify patterns in the data and make predictions based on similarities between cases. By combining the strengths of the VGG16 and CBRACDC algorithms, the study can create a powerful hybrid model framework that leverages the strengths of both approaches to accurately forecast the outcomes of polyviral lung diseases:

$$\text{New}_{\text{value}} = \frac{(a - \lambda)}{\sigma} \quad (3)$$

where a is the real value, λ is the data mean, and σ is SD.

$$M_{K+1} = \cos\left(0.5\cos^{-1}M_K\right) \tag{4}$$

where, xx_i is the weight function estimated using the map in equation (5):

$$\mathrm{MH}(m,n) = \left|\mathcal{Q}_1 - \mathcal{Q}_2 \mid + \left|R_1 - R^2\right|\right. \tag{5}$$

Manhattan distance (MH) among sample $\mathcal{Q}$ and R was computed as per the formula:

$$W = (\mathcal{Q} \otimes L)\ \mathrm{MH} + R \otimes (1-L)) \times xx_1 \tag{6}$$

Apply the Kronecker product merging, then save the results in equation, where is the damaged soldier location in a dimension, which is a randomized value. As per the proposed logic, randomization is evaluated using the logistic map function given in equation (7):

$$B_{l+1} = 4B_l(1.B_l) \tag{7}$$

The classification accuracy is highly reliant on the minimization of error, that is, the error between actual and predicted values. As per the work, the error minimization is fixed as the objective while tuning the optimal weights as depicted in the figure:

$$oB_j = \min(\text{error}) \tag{8}$$

The rectification layer is said to be a layer ll. Subsequently, its input consists of O_1^{ll-1} feature maps with a size of $O_2^{ll-1} \times O_3^{ll-1}$:

$$P_i^{ll} = \left|P_i^{ll}\right| \tag{9}$$

Typically, the last layer of Convolutional Neural Network (CNN) architecture is made up of Fully Connected (FC) layers, where each layer's neurons are linked to those of the layer before it. The CNN design uses the final FC layer as the output layer. Layer ll is said to be an FC layer. The i^{th} unit in layer ll is generated according to the equation.

$$P_i^{ll} = h\left(c_i^{ll}\right) \tag{10}$$

Overall, the proposed framework has the potential to revolutionize the field of predictive medicine by providing healthcare providers with a powerful tool for predicting the outcomes of polyviral lung diseases. By accurately forecasting these outcomes, healthcare providers can make more informed decisions about patient care and improve outcomes for patients with these challenging diseases.

Table 1 illustrates that the feature extraction process for the hybrid model framework involves data collection, pre-processing, feature selection, and extraction of clinical, demographic, and laboratory features. Advanced techniques, such as dimensionality reduction and feature engineering, are used to extract meaningful information. The hybrid model framework combines in vitro and ex vivo data, implements machine learning and deep learning algorithms, and incorporates extracted features to improve predictive accuracy. Evaluation and validation are conducted to assess the model's performance, and continuous improvement involves fine-tuning and updating the model with new data and insights for enhanced predictive capabilities. This enhanced dataset allows for a better understanding of the disease mechanisms and can aid in developing

Table 1. CBRACDC algorithm.

Algorithm 1: Customized Battle Royale Algorithm with Canberra Distance Calculation (CBRACDC)

Begin
Initialize entire parameters
$shrink = ceil(log_{10}(Max\_Cicle)))$
$\nabla = round(Max\_Cicle \ / \ shrink))$
$iter = 0;$
While the termination condition is not reached do
$iter = iter + 1$
For $i = 1 : pop^{size}$
$dmg = j$
$vic = i$
If $(Y_i) < w(Y_j)$
$dmg = i$
$vic = j$
end if
if
$x_{dmg}.damage < Threshold$
for $d = 1 : Dimension$
A damaged soldier's position will be changed depending on:
$Y_{dmg,f} = h\left(max\left(Y_{dmg,f}, Y_{best,f}\right) - min\left(Y_{dmg,f}, Y_{best,f}\right)\right)$
$+ max\left(Y_{dmg,f}, Y_{best,f}\right)$

According to the proposed CBRACDC approach randomness h is estimated using the Logistic map function.
end for $fY_{dmg}.damage = Y_i.damage + 1Y_{vic}.damage = 0$
else
for $f = 1$: Dimension
The position update of a soldier is calculated according to the proposed CBRACDC approach.
End for f
Update $w\left(Y_{dmg}\right)\ Y_{dmg}.damage = 0$
end for i
if $iter >= \nabla$
update $(Up - Lw)$ depending on $\nabla = \nabla + round\left(\frac{\nabla}{2}\right)$
end if
if the $Lw_f \ / \ Up_f$ extends actual $lower/\ upper$ bound then sets it to real $Lw_f \ / \ Up_f$
end if
end while

more effective treatment strategies. Overall, feature extraction plays a crucial role in improving the predictive power of the hybrid model framework and ultimately contributes to the advancement of personalized medicine in the management of polyviral lung diseases.

Hybrid model integration for viral infection in lung diseases

The hybrid model integration for predicting outcomes of polyviral lung diseases will combine data from both in vitro and ex vivo models. In vitro models involve infecting lung cells, such as A549 cells or lung organoids, with viruses. These models will allow the study of viral replication and immune responses at the cellular level. Ex vivo models will use perfused lung tissue slices to assess tissue-level responses to viral infections, including cell viability and immune activation. The integration of these data types will provide a more comprehensive understanding of polyviral infection. The model will also incorporate machine learning algorithms to predict disease progression, ultimately improving diagnosis, treatment strategies, and patient outcomes in polyviral lung infections.

Random Survival Forest. The integration of the RSF algorithm within the hybrid model framework for predicting outcomes of polyviral lung diseases offers several advantages. RSF, an ensemble method that combines multiple decision trees, is specifically designed for survival data analysis. By utilizing features from in vitro and ex vivo studies, the RSF model can be trained on data from patients with polyviral lung diseases to predict specific outcomes such as time to recovery or lung failure, which maximizes the survival difference between daughter nodes, and was used for each survival tree in the forest. In traditional RSF, each survival tree is grown to full size under the constraint that a terminal node should have no fewer than $d_0 > 0$ unique deaths. However, the log-rank test was shown to be asymptotically optimal under the proportional hazards alternative because of an equal censoring pattern hypothesis in the two groups. In addition, the stopping criterion is arbitrary and demonstrates a bias toward predictors with a larger population. This is because it is difficult for predictors with a smaller population to satisfy the criterion, especially when d_0 is large.

Therefore, an improved RSF with a novel split rule and stopping criterion for identifying more accurate predictors that can separate survivors and non-survivors and thus improve discrimination ability can be applied to non-proportional hazard situations to improve the test for a range of alternative hypotheses. Study let $d(t)$ be the number of deaths, $Y(t)$ be the individuals at risk, and t be time. The hazard function estimate $H(t)$ at a time t with the Nelson–Aalen estimator can be expressed as:

$$H(t) = \frac{d(t)}{Y(t)},\ t \leqslant < = \tau_0 \tag{11}$$

where $\tau_0 = 365$ in the study. The model proposed in equation (11) can be used in this study and expressed as:

$$H_R(T) = \frac{\theta_1 \theta_2}{\theta_1 + (\theta_2 - \theta_1 Y_{L(t)})} H_L(t) \tag{12}$$

where $H_R(T)$ and $H_L(t)$ are the respective hazard functions of the right branch and left branch of a grown tree $Y_R(T)$ and $Y_L(T)$ are the respective survival functions of the right branch and left branch, $.\theta_1 =$ limt $\downarrow$ 0 $H_R(T)/H_L(t)$, and θ_2 = limt $\uparrow \tau 0$ $H_R(T)/H_L(t)$. $A\chi 2$ test using the two estimating functions of the right and left branches was used by (Fábio and Vinícius 2021)[38] to test the hypothesis of a significant difference. This study let $t_{1,h} \leqslant < = t \leqslant < = t_{N(h)h}$ be the $N(h)$ distinct event times in a node of the grown tree. The cumulative hazard function can be expressed as $\mathrm{CH}(t) = H(t)$. $\mathrm{CH}_R(t)$ and $\mathrm{CH}_L(t)$ are cumulative hazard functions of the right branch and left branch. The relative cumulative hazard function at each distinct event time can be computed using:

$$\mathrm{RH}(t) = \mathrm{abs}(\log \frac{\mathrm{CH}_R(t)}{\mathrm{CH}_L(t)},\quad t_{1,h} \leqslant t \leqslant t_{N(h)} \tag{13}$$

To identify the predictors that can discriminate low risk (with a small cumulative hazard function) and high risk (with a large cumulative hazard function), combined with the fact that high-risk populations have high mortality rates in the short term, the split function was defined as follows in equation (14):

$$\mathrm{spiltfun} = \sum\nolimits_{t_{1,h} \leqslant t \leqslant t_{N(h)}} \frac{r(H)t}{t} t_{N,h} \tag{14}$$

The stopping criterion is defined as the split function decreasing. The benefits of using RSF include its ability to handle complex relationships, improved prediction accuracy through ensemble learning, and the potential for interpretability by identifying influential features. Overall, incorporating RSF within the hybrid model framework provides a robust approach to analyzing data and making accurate predictions for patients with polyviral lung infections.

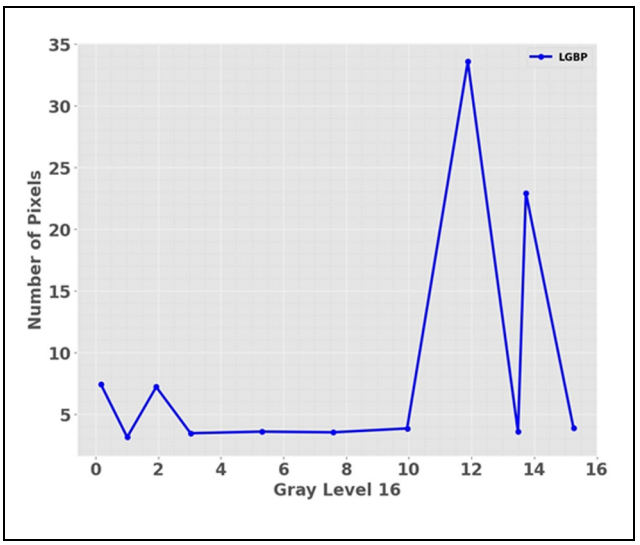

Figure 3. Distribution of grey levels and number of pixels.

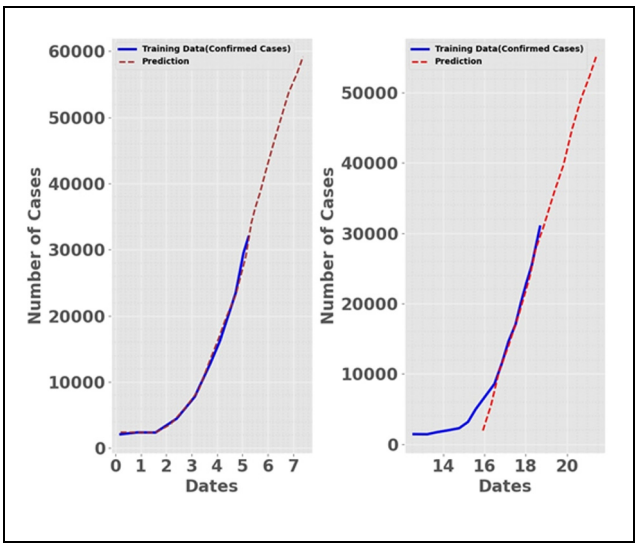

Figure 4. Temporal progression of COVID-19 cases.

Experimentation and result discussion

In medical research, the advancement of an (in vitro/ex vivo) hybrid model framework holds immense promise for forecasting outcomes in polyviral lung diseases. By integrating computational techniques and experimental data, this approach aims to provide a more comprehensive understanding of disease progression and treatment responses. The Python programming language facilitates the implementation of sophisticated algorithms and analysis tools, further enhancing the framework's capabilities in data processing and prediction accuracy. The simulations were conducted using Python Jupiter version 3.8.0 on an Ubuntu operating system. The system had a memory capacity of 4 GB DDR3 and was powered by an Intel Core i5 processor clocked at 3.5 GHz.

Figure 3 illustrates the Local Grey-Level Binary Patterns (LGBP) with 34 patterns, demonstrating the relationship between grey levels and the number of pixels in an image. LGBP is an extension of the LBP, which captures texture information by comparing the grey-level intensity of each pixel with its neighbouring pixels. This comparison is encoded into binary patterns that help characterize the texture of an image. With 16 grey levels, each representing a unique intensity level, the distribution of these grey levels across the pixels provides crucial insight into the image's texture. By enhancing spatial relationships, LGBP with 34 patterns improves upon LBP, allowing it to better capture more complex textures. This capability enhances its effectiveness in image analysis, particularly in applications requiring detailed texture classification or object recognition.

Figure 4 shows the temporal progression of COVID-19 cases, represented by a dataset with 30,020 entries for training and 5070 entries for prediction. This dataset tracks the change in COVID-19 cases over time, offering valuable insights into the pandemic's dynamics. The training data is used to build predictive models that estimate the future trajectory of the virus. By analyzing historical data, patterns are identified, and predictions are made for future case numbers. These predictions assist public health professionals and policymakers in making informed decisions regarding interventions and mitigation strategies. The dataset's size ensures a robust model, and the prediction subset helps project trends beyond the training period. This makes the dataset an invaluable resource for managing and controlling COVID-19 outbreaks through data-driven decision-making.

Figure 5 displays a time versus survival analysis, with peak VO_2 levels highlighted at 0.990. This plot illustrates the relationship between oxygen consumption (VO_2) during peak exercise and survival rates over time. A peak VO_2 value of 0.990 is associated with high levels of cardiovascular fitness and is often a significant indicator of overall health. By examining survival trends over time for individuals with this peak VO_2 level, clinicians can gain insights into the prognostic significance of VO_2 in predicting long-term patient outcomes. This analysis helps identify individuals who may require intervention or more focussed treatment strategies, ultimately improving clinical decision-making. The data underscores the importance of aerobic capacity in predicting survival rates, thereby guiding healthcare

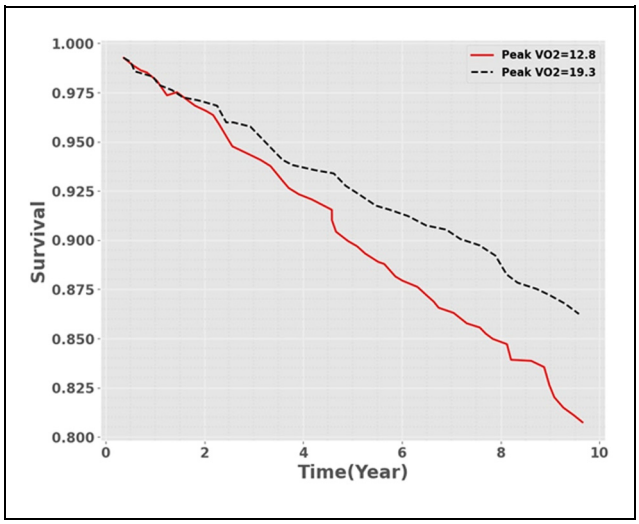

Figure 5. Time versus survival analysis.

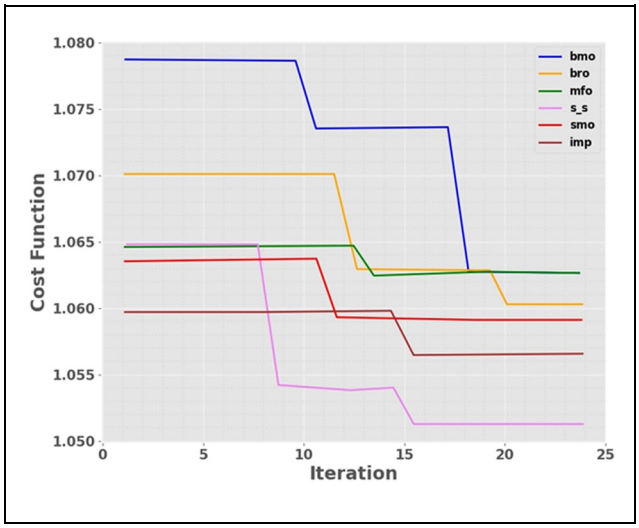

Figure 6. Convergence analysis of optimization algorithm.

professionals in making more informed decisions about patient care and treatment plans.

Figure 6 presents the convergence analysis of an optimization algorithm, where the relationship between the iteration number and the cost function is plotted, revealing a minimum value of 1.079. This figure is pivotal in evaluating the efficiency of the optimization process, as the decreasing trend of the cost function over iterations indicates that the algorithm is steadily progressing towards the optimal solution. The minimum value of 1.079 marks the point where the algorithm has found the best possible solution according to the defined objective. Various optimization techniques are depicted in this figure, including Bee Migration Optimization, inspired by the migratory behaviour of bees; Bat-inspired Algorithm, which mimics bat echolocation; Moth-Flame Optimization, modelled after moth navigation towards light; Spotted Hyena Optimization, based on cooperative hunting strategies; Simulated Annealing, designed for global optimization; and the Improvised Method, a refinement of traditional algorithms. This variety of techniques highlights different approaches to optimizing solutions in complex problem spaces.

Research conclusion

The advancement of an (in vitro/ex vivo) hybrid model framework for forecasting polyviral lung disease outcomes represents a significant step forward in predictive healthcare analytics. Through the integration of both in vitro and ex vivo experimental data with computational modelling techniques, this hybrid framework offers a comprehensive approach to predicting disease progression and treatment response. The findings indicate that the observed minimum cost value of 1.079 signifies the point at which the algorithm achieves the best possible outcome according to the defined objective. Further research could explore the integration of advanced computational techniques, such as deep learning and artificial intelligence, to enhance the predictive accuracy and scalability of hybrid models for forecasting polyviral lung disease outcomes, paving the way for personalized medicine approaches and targeted therapeutic interventions. Python-based implementations of these models provide a flexible and efficient platform for analyzing complex biological data and developing predictive algorithms, further enhancing the utility of this research in clinical practice and public health decision-making. A potential future direction for the advancement of the hybrid model framework to forecast polyviral lung disease outcomes could involve integrating real-time patient data streams and incorporating machine learning algorithms to enhance predictive accuracy and enable personalized treatment strategies.

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