Predicting Chronic Phase Progression in Chikungunya Patients Using Machine Learning Models

Gabriel Masson Universidade de Pernambuco Caruaru, Brazil gabriel.masson@upe.br

Jamile Taniele-Silva Universidade Federal de Pernambuco Recife, Brazil jamile.taniele@ufpe.br Kaio Viana Universidade de Pernambuco Caruaru, Brazil kaio.viana@upe.br

Gabriela Cavalcanti Lima
Albuquerque
Universidade Federal de Pernambuco
Recife, Brazil
gabriela.cavalcantia@ufpe.br

Sebastião Rogerio da Silva Neto Universidade de Pernambuco Caruaru, Brazil srsn@ecomp.poli.br

Moacyr Jesus Barreto de Melo Rêgo Universidade Federal de Pernambuco Recife, Brazil moacyr.rego@ufpe.br

Raphael A. Dourado Universidade de Pernambuco Caruaru, Brazil raphael.dourado@upe.br Patricia Takako Endo Universidade de Pernambuco Caruaru, Brazil patricia.endo@upe.br

Abstract

Context: This research is set within the domain of neglected tropical diseases, specifically focusing on Chikungunya, a mosquitoborne viral disease. The study is motivated by the prevalence of Chikungunya in Brazil and the challenges associated with its chronic symptoms. Problem: The primary issue addressed is the difficulty in predicting which patients with acute Chikungunya will progress to the chronic phase. This progression leads to prolonged joint pain and other severe symptoms, affecting quality of life. Solution: We evaluate machine learning models, trained to predict the likelihood of acute Chikungunya cases progressing to the chronic phase. Theory of IS: The Information Processing Theory serves as the theoretical foundation, explaining how data is transformed into actionable insights. In this context, machine learning models act as information processors, learning from a real dataset how to produce predictions that can aid clinical decisions. Method: The methodology involves a quantitative analysis of different machine learning models, using documented data from Chikungunya diagnosed patients. The goal is to assess the models' performance in predicting disease progression. Summary of Results: Preliminary results show that the XGBoost model demonstrates 79.31% of recall and 74.19% of f1-score in distinguishing patients likely to develop chronic conditions. Contributions and impact on the field of IS: This study contributes to both information systems and healthcare by enhancing the process of decision-making for health professionals. The implications are significant for academic research and practical application (including SUS applicability), providing information that facilitate earlier and more targeted treatments, focusing on patient quality of life.

CCS Concepts

Computing methodologies → Machine learning;
 Applied computing → Health informatics; Life and medical sciences;
 Information systems → Decision support systems;
 Human-centered computing → Human-computer interaction.

Keywords

Chikungunya, Neglected Tropical Diseases, Machine Learning, Information Processing Theory, Data Analysis

1 Introduction

Arboviral diseases are emerging neglected tropical diseases (NTDs) transmitted by arthropods, that impact affected individuals and place a significant health burden on countries where they are incident. Some of the most well-known diseases include Dengue, Zika, and Chikungunya. According to the Pan American Health Organization (PAHO), arboviral diseases have a high incidence; and Brazil reporting highest prevalence of Chikungunya cases in the Americas, totaling around 391,754 reported cases by the third quarter of 2024 [1]. The Brazilian outbreak of the disease in September 2014 was associated with favorable conditions for vector proliferation, such as climate and high population density in urban conglomerates [2].

The Chikungunya virus (CHIKV) is transmitted by the *Aedes aegypti* and *Aedes albopictus* mosquitoes. Chikungunya presents symptoms very similar to Zika and Dengue, but its main distinguishing feature lies in the debilitating morbidity due to the involvement of the patient's musculoskeletal system [3]. Its main symptoms are high fever, intense arthralgia, myalgia, headache, rash and asthenia. The disease can be classified in three phases according to the duration of musculoskeletal symptoms: acute, subacute and chronic [4, 5]. Recent studies reported that chronic phase is characterized by the persistence of arthralgia beyond three months after CHIKV infection, which may extend for months or even years [3].

Currently, there are many challenges related to Chikungunya due to the lack of specific treatment and the absence of reliable biomarkers that indicate the progression of the disease [6, 7]. After a certain period following the onset of the acute phase, identifying patients at risk of progress to the chronic phase is crucial for mitigating the long-term effects post-Chikungunya, thereby enhancing overall quality of life.

In this context, this study aims to evaluate different machine learning models to classify the probability of patients progressing to the chronic phase and compare them with the neural network model. The model can serve as a tool to support healthcare professionals in clinical management, helping in identifying risk factors more effectively, thus potentially enabling earlier interventions and personalized treatment plans tailored to individual risk profiles.

2 Related work

In the systematic literature review conducted by Silva Neto et al. [8], studies on the classification of arboviruses using machine learning and deep learning techniques were analyzed. Out of a total of 963 papers, only 15 were considered relevant. The most commonly used machine learning technique was based on decision tree algorithms. Although 5 of these studies employed multiclass classification, none of them were focused on Chikungunya or progression of this disease.

As a related work, we can cite Silva Neto et al. [9], that had two main objectives: (1) classify patients between arboviral infections and other diseases; and (2) differentiate between Dengue and Chikungunya. The data used were sourced from the SINAN (Sistema de Informação de Agravos de Notificação) and the Open Data Portal of Recife. These datasets were combined, resulting in a total of 17,948 records for Dengue, 5,724 for Chikungunya, and 16,704 inconclusive cases, with 26 clinical attributes in total. Feature selection techniques based on the wrapper approach were applied, along with hyperparameter optimization through Grid Search. The Random Forest and XGBoost models demonstrated the best performance, achieving a recall over 80% for both Chikungunya and inconclusive cases.

Arrubla-Hoyos et al. [10], used a clinical dataset from Sincelejo, Colombia, containing 24 features and 150 records, with 89 cases of Zika, 52 of Dengue, and 9 of Chikungunya. Two tree-based algorithms were used: Decision Tree and Random Forest, aiming to distinguish between Dengue, Chikungunya, and Zika. The main differential of the study from [9] lies in the methodological approach used for data processing, which followed the 2022 PAHO Diagnostic Guide methodology for the differential classification of Dengue and Chikungunya [11]. Qualitative data were transformed into quantitative data based on the weights defined by the guide. The Random Forest model achieved accuracy of 99.70%; precision of 99.60%; recall of 99.40%; and f1-score of 99.50%, demonstrating its effectiveness as a model for differential diagnosis.

As shown, the current literature presents only few studies that apply machine learning to solve Chikungunya-related classification. The absence of relevant studies related to predicting chronic phase of Chikungunya allows us the exploration this area. Unlike previous studies, which primarily focus on classifying between Chikungunya, Dengue, and/or Zika, the present study is exclusively concentrated on Chikungunya. Based on the premise that patients have already been diagnosed with the disease, our goal is to predict whether the patient' condition will progress from the acute phase to the chronic phase using machine learning models.

3 Methods

This research follows a quantitative approach, employing data-driven analysis to evaluate machine learning models capable of predicting the progression from acute to chronic phase in Chikungunya patients. To achieve the objectives of this work, the Information Processing Theory [12] was applied, which helps to understand how information is collected, processed, and can be used in decision-making systems. This theory is particularly relevant here because it aligns with the way raw data on real Chikungunya cases is transformed into useful information for clinical decision process.

The research method used is experimental, where we systematically test and compare various machine learning algorithms to assess their efficacy in predicting disease progression. This study is explanatory, as its primary purpose is to elucidate factors associated with chronic Chikungunya progression, aiming to support early intervention and tailored treatment plans. Machine learning models receive patient tabular data and produce results that can assist health professionals in their clinical decisions. By improving both the efficiency and accuracy of patient data (such as signals and symptoms), models align with the principles of Information Processing Theory, providing healthcare professionals with predictions that can guide their interventions and improve patient outcomes (such as treatment).

The methodology steps are presented in Figure 1 and explained in the following sub-sections.

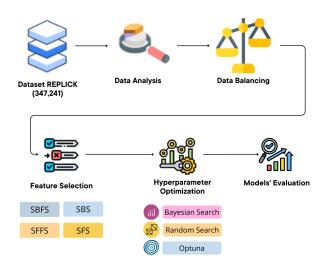


Figure 1: Methodology apply for models' configuration, training and test (image by author)

3.1 Dataset

The dataset used in this work comes from a clinical program, where patients with Chikungunya were monitored for up to 1,080 days [6]. During this period, laboratory and socioeconomic data were collected, allowing to record information about the patient and the disease.

The dataset contains 347 records and 579 variables. However, for the development of this work, health specialists filtered these variables, selecting the most relevant ones for the model's learning process based on their expertise, reducing to 241 variables (referred to as features in this study, hereafter).

In machine learning problems focused on healthcare, usually the target class is the minority; however, in our problem, it is majority class with 247 records (chronic Chikungunya cases) and 100 records of recovered cases. This characteristic is due the focus of the clinical program that monitored patients for a long time, thus accompanying and minimizing the development of the disease.

3.2 Data balancing

The experiments were conducted considering two data balancing techniques: (a) hybridsampling and (b) undersampling. The hybridsampling technique combines two balancing methods simultaneously, based on a reference value, such as the average number of records per class. In this approach, the minority class is oversampled (using some synthetic data creation), while the majority class undergoes undersampling until the data are balanced according to the reference value [13].

Conversely, undersampling involves reducing the number of instances from the majority class in imbalanced datasets. The primary objective is to equalize or approximate the number of instances between classes, thereby preventing the majority class from disproportionately influencing the learning process of the machine learning model [14].

3.3 Feature selection

As the number of features grows larger, the dimensionality of the dataset increases, which also raises the complexity for machine learning learning. Feature selection techniques can be used to reduce the dimensionality of the original dataset by eliminating irrelevant, noisy, and/or redundant features [15].

In the literature, feature selection techniques are classified by their search strategy for the best set of features. There are three main approaches: filter, wrapper, and embedded [15]. In this study, the wrapper approach was used. The wrapper approach generates a subset of features to be used in a machine learning model, which acts as an evaluation function. For each candidate feature subset, the model is trained and then assessed. The feature subset selected by the wrapper method is the one that achieved the best performance in the evaluation model [16].

There are several approaches for selecting a subset of features, each functioning as an optimization function [16]. For this work, the Sequential Selection Strategies (SSS) approach was used, with four different methods: Sequential Forward Selection (SFS), Sequential Backward Selection (SBS), Sequential Forward Floating Selection (SFFS), and Sequential Backward Floating Selection (SBFS).

To apply feature selection, we have selected six algorithms due their ability for classification problems: Decision Tree (DT), Random Forest (RF), AdaBoost (ADA), Extreme Gradient Boost (XGB), Gradient Boost (GB), and Support Vector Machine (SVM).

3.4 Hyperparameter optimization techniques

Each machine learning model has a set of hyperparameters that impacts directly on their learning. Choosing the best combinations poses as a challenge, which is why there are specialized algorithms and frameworks designed to optimize hyperparameter search.

In this study, the optimizers Optuna, Random Search (RS), and Bayesian Search (BS) were applied to find the best hyperparameters. The search space used by the optimizers is described in Table 1.

- Optuna: Optuna is an open-source framework specialized in hyperparameter optimization. It allows users to create the search space dynamically. Optuna aims to minimize/maximize an objective function until it finds an optimal value. To ensure there is no overfitting, a regularization strategy called pruning is used [17].
- Random Search (RS): Within a defined search space, RS randomly searches for the best hyperparameter combinations. It is an efficient algorithm with low computational cost [18].
- Bayesian Search (BS): BS is an optimizer based on Bayes' theorem, which uses a sample selected through a Gaussian process to search for a global optimum within the search space [19].

3.5 Models' evaluation

For the models' testing, a portion of the data is allocated to evaluate the generalization ability of the models. To validate if models demonstrate satisfactory performance across the entire dataset (training and testing sets), a technique called cross-validation (CV) can be used, with the goal of using all available data from training and testing.

CV consists of a technique in which K-folds are defined, where the model is trained up to the K-th fold and evaluated based on a specific evaluation metric. The result of CV is given by the average performance of each trained model, allowing for the observation of the average performance and its variance [20]. In this study, we decided to use CV to train and test all models among all scenarios defined.

For a machine learning model, in a binary classification problem, its results are based on a threshold, where the classification above a given threshold will be the positive class. By changing this threshold, evaluation metrics are impacted, as this change affects the model's ability to differentiate one class from another [21] . The analysis of different values of threshold can be useful to discuss the trade-off in relation to precision and recall metrics.

After choosing the best model based on the presented metrics, the model's threshold was redefined ranging from 50% to 70%, representing the maximum level of confidence that the model can accept. A value below 50% will increase the prediction of patients who will progress to the chronic phase, while a value above 50% will increase the confidence that they will be considered chronic [22].

4 Results

4.1 Data analysis

In order to present an overview on the dataset we are working, we developed an interactive dashboard that can be found here https://abrir.link/EhJnK: Figure 2 shows the sociodemographic panel, in which about 77.52% of Chikungunya cases occur in women, mainly in women between 40 to 70 years old, similar to the results presented by Martins et al. [23]. The variables sex and age are associated with the progression and persistence of the disease in patients [24], being relevant factors for the training of our machine learning models and clinical decision-making.

The majority of cases are concentrated in the Recife region, with 53.02% of patients identifying as mixed race, 27.08% as white, and 16.71% as Black. The most common diagnostic methods used are ELISA and Rapid Test, detecting 119 and 106 chronic cases, respectively.



Figure 2: Sociodemographic panel

Figure 3 shows the patient's pain scale on their first appointment (D0). The joint pain and fatigue are evaluated in a scale from 0 (no pain) to 10 (very pain). Here, we highlight that approximately 80.97% of patients who reported joint pain > 6 on D0, progressed to chronic cases. Furthermore, the distribution of the fatigue scale behaved similarly to joint pain, where 68.42% of patients who evolved to chronic cases reported fatigue > 4 on D0.

In Figure 4, the dashboard illustrates the distribution of pain intensity on a homunculus (a graphical representation of all the joints in the body to indicate pain points). Each joint is represented by a progress bar that uses four colors: green (no pain), yellow (mild pain), pink (moderate pain), and red (intense pain). The highest

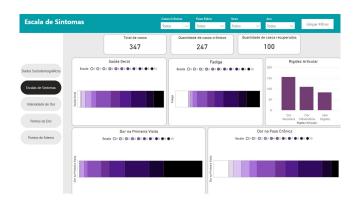


Figure 3: Symptom scale panel

incidence of pain is found in the hands, knees, ankles, and feet, aligning with the findings of Lazari et al. [25]. The lower limbs show a high frequency of pain, which may lead to physical incapacity and hinder the patient's ability to perform daily activities.

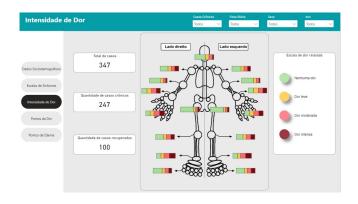


Figure 4: Pain intensity panel (image by author)

4.2 Models' performance

As presented in Section 3, for each machine learning model, were applied feature selection techniques (SFS, SBS, SFFS and SBFS), totaling 20 models with distinct features' subsets. In addiction, all 20 models passed for hyperparameters' optimization, using BS, RS and Optuna. Theses models were evaluated using the CV, with k=10, considering f1-score as metric. To facilitate the understanding, we

Algorithm	Search Space
DT	critério: gini, entropy; max_features: sqrt, log2; max_depth: 2-1000; min_samples_split: 2-10; min_samples_leaf: 2-10
RF	n_estimators: 10-1000; max_depth: 2-999; min_samples_split: 0.01-1.0; min_samples_leaf: 0.01-0.5; critério: gini, entropy
SVM	C: 1e-6 - 1e+6; kernel: linear, rbf, sigmoid; grau: 1, 5; gamma: 1e-6 - 1e+1
XGB	n_estimators: 10-999; learning_rate: 0.01-1.0; max_depth: 2-999; subsample: 0.01-1.0; colsample_bytree: 0.01-0.5
ADA	n_estimators: 10-600; learning_rate: 0.01-1.0; algoritmo: SAMME, SAMME.R
GB	n_estimators: 10-500; learning_rate: 0.01-1.0; max_depth: 2-999; min_samples_split: 0.01-1.0; min_samples_leaf: 0.01-0.5

Table 1: Search space for different algorithms

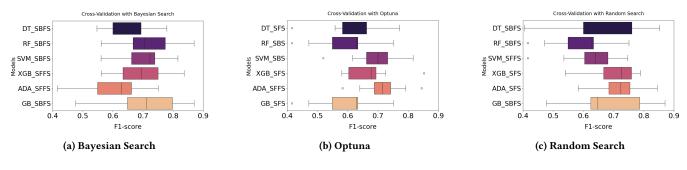


Figure 5: Models' F1-score performance when applying the hybridsampling technique

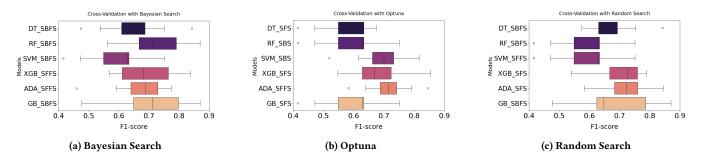


Figure 6: Models' F1-score performance when applying the undersampling technique

are using *MODEL_FS* that corresponds to the combination of a machine learning model and a feature selection technique.

In Figures 5 and 6, we present the combinations of model and features selection that performed the best F1-score when using undersampling and hybridsampling, respectively.

When conducting the analysis using CV, a high variance in the f1-score is observed in all the models, as demonstrated in Figures 5 and 6. It can be observed that the SVM_SBFS and XGB_SFFS models show f1-scores ranging from 55% to 85%, while in Figure 5a, the RF_SBFS and SVM_SFFS models range from 50% to 75%. On the other hand, the models in Fig 5c such as XGB_SFS and ADA_SFS achieved the highest median among all models with 73%. Although in Fig 5c the ADA algorithm achieved the highest median, in Fig 5a the ADA_SFFS model achieved the lowest value with 63%.

In Figures 8 and 9, the considerations for each model used in this work are presented. In Figure 8b, the ADA_SFFS model obtained a recall of 85%, specificity of 60% and precision of 54%. In Figure 8c, the XGB_SFS obtained 79% recall, 70% precision and specificity. Furthermore, we can observe that RF produced similar results for both Optuna and Random Search, achieving a specificity and precision of 100% and recall of 0%, accuracy and AUC of 40%, despite being subjected to the same evaluation conditions. XGB stood out in the metrics, achieving 8% recall, 75% precision and 79% f1 score, keeping its metrics within the same range in all scenarios. Another model that stood out was ADA, with 73% recall, 70% precision and 75% f1-score.

The XGB_SFS_RS_hybrid was chosen for threshold analysis because it stands out in its performance in the evaluation metrics in relation to others, as shown in table 3.The initial value of 0.5 was chosen because it is a common standard, while the upper limit of

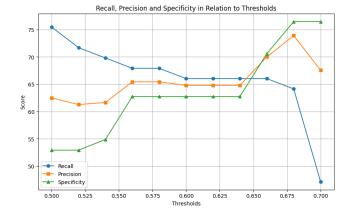


Figure 7: Threshold analysis

0.7 was predicted to avoid bias in the model. Observing Figure 7, as the threshold increases, the trade-off between recall and precision decreases. After the threshold of 0.64, precision and specificity exceed recall, although recall remains constant.

However, when exceeding the threshold of 0.66, the model presents an inversion in the metrics: while recall decreases, precision and specificity increase. This inversion implies that the higher the threshold, the greater the chance of bias occurring for one of the classes. However, this proves to be a technique that contributes to minimizing the trade-off between precision, recall and specificity.

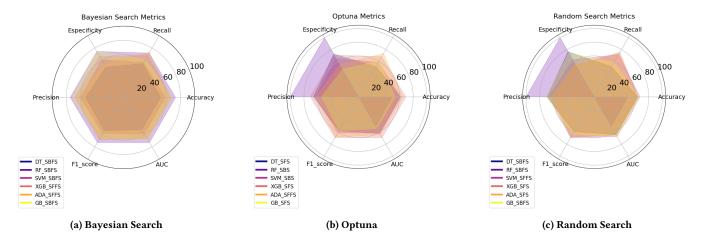


Figure 8: Evaluation of models with hybridsampling

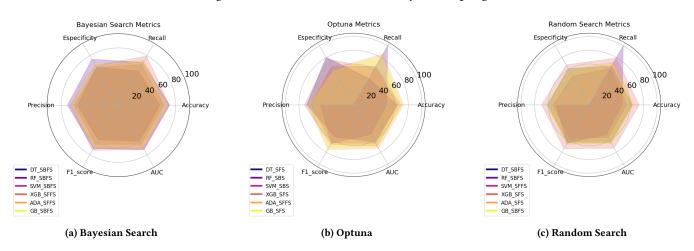


Figure 9: Evaluation of models with undersampling

4.3 Discussions

Balancing techniques are very important for pre-processing data that impacts model learning. However, the balancing techniques did not show a significant difference in the final evaluation of the models due to the limitation of the dataset, which contains few records.

Figures 8b and 8c demonstrated that RF_SBS and RF_SBFS reached 0% for the recall and f1-score metrics and 100% for specificity and precision, both with different hyperparameters and features. In Figures 9b and 9c, only specificity reached 0%, while recall reached 100%. An improvement in some metrics was expected due to the increased/decreased representation of a class, but there was a bias towards one class, preventing the RF from identifying the progression of chikungunya. The hyperparameters selected for each model can be found in Table 2.

In the CV analysis, ADA demonstrated an average f1-score of 71% across four scenarios, demonstrating little variability; however, the model presented a trade-off, with recall of 73.58%, specificity of 54.90% and precision of 62.90%. Although CV is an important

evaluation technique, considering it in isolation when choosing a model can mask problems in other metrics.

Table 3 presents the results of the models that performed best according to CV. Among all models, XGB_SFS_RS_hybrid showed superior performance in accuracy metrics with 73.33%, recall of 79.31%, f1-score of 74.19% and AUC of 73.53% in addiction, other RF_SBFS_BS_hybrid excelled in specificity with 74.19% and precision of 71.43%. Thus, the more performative model to classify the likelihood of patients progressing to the chronic phase was XGB_SFS_RS_hybrid.

This work presented the evaluation of machine learning models to classify the likelihood of patients progressing to the chronic phase of Chikungunya. Although the models showed high variance, XGB_SFS_RS_hybrid stood out among the rest with its superior metrics, being able to identify potential patients at risk of progressing to the chronic phase. A limitation of this work arise due to the small number of records and the high dimensionality of the dataset, which made it difficult for the models to learn. Furthermore, the use of k=10 cross-validation may have impacted the evaluation of

Hyperparameters			
criterion:'entropy', max_depth: 79, max_features:'log2',			
min_samples_leaf: 9, min_samples_split: 7			
criterion: 'gini', n_estimators: 974, max_depth: 1000,			
min_samples_split: 0.01, min_samples_leaf: 0.01			
kernel: 'linear', degree: 2,			
gamma: 4.2594025, C: 0.010007202			
colsample_bytree: 0.239900212, learning_rate: 0.068163796, max_depth: 780			
n_estimators: 699, subsample: 0.067780561			
n_estimators: 502, learning_rate: 0.2607703, algorithm: "SAMME"			
n_estimators: 288, learning_rate: 0.0182112977748381, max_depth: 999,			
min_samples_split: 0.01, min_samples_leaf: 0.403862979577575,			

Table 2: Hyperparameters selected for each model

Models	Accuracy	Recall	Specificity	Precision	F1_score	AUC
DT_SBFS_RS_under	63.33%	65.52%	61.29%	61.29%	63.33%	63.40%
RF_SBFS_BS_hybrid	71.67%	68.97%	74.19%	71.43%	70.18%	71.08%
SVM_SBS_Optuna_hybrid	61.54%	58.49%	64.71%	63.27%	60.78%	58.69%
XGB_SFS_RS_hybrid	73.33%	79.31%	67.74%	69.70%	74.19%	73.53%
ADA_SFFS_Optuna_hybrid	64.42%	73.58%	54.90%	62.90%	67.83%	64.24%
GB_SBFS_BS_hybrid	68.33%	68.97%	67.74%	66.67%	67.80%	68.39%

Table 3: Performance metrics for each model

the models, the use of a smaller k can contribute to a more accurate analysis due to the few records from dataset.

However, Arrubla's work [10] presents limitations similar to ours, such as the number of Chikungunya records in the dataset. This is a problem that goes beyond computing, as it involves the culture of data appreciation and public policies that contribute to data collection and processing. Therefore, to overcome these problems, the use of different pre-processing approaches such as [11], the use of hybrid systems [26] or the use of deep learning [27], can contribute to a model that serves healthcare professionals with excellence.

Finally, a limitation of our work is the lack of rigorous statistical analysis to assess the significance of the models and identify the best ones; we used only cross-validation and evaluation metrics. Furthermore, in feature selection, we used exclusively computational techniques, without expert evaluation of the selected attributes, which impacts the interpretability of the model. For future work, relying on expert support and following the guidelines of the PAHO "Guidelines for the Clinical Diagnosis and Treatment of Dengue,

Chikungunya, and Zika" [28] may help to overcome this limitation and improve the performance of the models.

5 Conclusions and future works

Our study addressed significant challenges identified in both SBSI 2025 and the Grand Challenges of Information Systems Research in Brazil, which emphasize the importance of integrating and advancing data analysis across various sectors, including healthcare.

The topics of interest highlighted by SBSI 2025 emphasize the relevance of adaptive and robust information systems capable of handling data interoperability and practical applications of advanced analytical models. Our study aligns directly with these interests by evaluating machine learning models capable of predicting health outcomes, representing a direct application of information systems principles in a practical context.

Furthermore, the research contributes to the Grand Challenges of Information Systems Research in Brazil, which include promoting innovation in healthcare through information technology and developing data infrastructures that support clinical decisions and public

health policies. By developing models that can predict Chikungunya progression, our study provides a valuable contribution to the development of our Brazilian health information system.

As future works, we plan to improve our models' performance, bringing more attributes and also applying other pre-processing techniques before the training phase. We also plan to develop a dashboard to visualize all data available, focusing on visualizing the primary joint pain areas and their severity over time. This visualization will allow healthcare professionals to identify patterns and trends in symptom progression, enabling more personalized patient care. By highlighting these key areas, the dashboard can facilitate quicker and more effective treatment decisions, ultimately benefiting patient outcomes by potentially reducing the duration and intensity of chronic symptoms.

Acknowledgements

This work was funded by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Universidade de Pernambuco (UPE). The work was carried out in collaboration with the Rede de Pesquisa Clínica e Aplicada em Chikungunya (Replick), which contributed to the execuation and validation of this work.

References

- Pan American Health Organization. n.d. Chikungunya paho/who data weekly cases. https://www3.paho.org/data/index.php/en/mnu-topics/c hikv-en/550-chikv-weekly-en.html. Accessed: September 18, 2024. (n.d.).
- [2] Ministério da Saúde. 2022. Serviço de Vigilância Epidemiológica Boletim Epidemiológico: Monitoramento dos casos de arboviroses urbanas causados por vírus transmitidos pelo mosquito Aedes (dengue, chikungunya e zika), semanas epidemiológicas 1 a 52, 2021. Tech. rep. 53. n48. https://www.gov.br/s aude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/edic oes/2021/boletim-epidemiologico-vol-52-no-48.pdf/view.
- [3] WM de Souza et al. 2024. Chikungunya: a decade of burden in the americas. The Lancet Regional Health - Americas, 30, 100673. DOI: 10.1016/j.lana.2023.100673.
- [4] SC Weaver and M Lecuit. 2015. Chikungunya virus and the global spread of a mosquito-borne disease. The New England Journal of Medicine, 372, 13, 1231– 1239. DOI: 10.1056/NEJMra1406035.
- [5] Ministério da Saúde. 2017. Chikungunya: manejo clínico. Disponível em: http://bvsms.saude.gov.br/bvs/publicacoes/chikungunya_manejo_clinico_1ed.pdf. Ministério da Saúde, Brasília. ISBN: 978-85-334-2494-4.
- [6] Giovanny da Silva Duarte, Adrian D Jones, Lydiana P de Goes Cavalcanti, et al. 2023. Multicenter study of the natural history and therapeutic responses of patients with chikungunya, focusing on acute and chronic musculoskeletal manifestations – a study protocol from the clinical and applied research in chikungunya (replick network). BMC Infectious Diseases, 23, 1, 499. DOI: 10.118 6/s12879-023-08292-v.
- [7] RMM Brito, MF de Melo, JV Fernandes, JG Valverde, PM Matta Guedes, JMG de Araújo, and MSL Nascimento. 2024. Acute chikungunya virus infection triggers a diverse range of t helper lymphocyte profiles. Viruses, 16, 9, 1387. DOI: 10.3390/v16091387.
- [8] S. R. Da Silva Neto, T. Tabosa Oliveira, I. V. Teixeira, S. B. Aguiar de Oliveira, V. Souza Sampaio, T. Lynn, and P. T. Endo. 2022. Machine learning and deep learning techniques to support clinical diagnosis of arboviral diseases: a systematic review. PLoS Neglected Tropical Diseases, 16, 1, e0010061.
- [9] S. R. Da Silva Neto, T. Talosa, L. Medeiros Neto, I. V. Teixeira, S. Sadok, V. De Souza Sampaio, and P. T. Endo. 2023. Binary models for arboviruses classification using machine learning: a benchmarking evaluation.
- [10] W. Arrubla-Hoyos, J.G. Gómez, and E. De-La-Hoz-Franco. 2024. Differential classification of dengue, zika, and chikungunya using machine learning—random forest and decision tree techniques. *Informatics*, 11, 69. DOI: 10.33 90/informatics11030069.
- [11] W. Arrubla-Hoyos, J.G. Gómez, and E. De-La-Hoz-Franco. 2024. Methodology for the differential classification of dengue and chikungunya according to the paho 2022 diagnostic guide. Viruses, 16, 7, (July 2024), 1088. DOI: 10.3390/v1607 1088.
- [12] Mariano Pimentel and Hugo Funks. 2012. Sistemas Colaborativo. Elsevier Editora Ltda, Rio de Janeiro, RJ, Brazil. ISBN: 978-85-352-4669-6.
- [13] W. A. Kusuma, A. S. Rahmi, and R. Heryanto. 2019. Implementation of hybrid sampling technique for predicting active compound and protein interaction

- in unbalanced dataset. IOP Conference Series: Earth and Environmental Science, 335, 012005. DOI: 10.1088/1755-1315/335/1/012005.
- [14] A. Ali, S. M. Shamsuddin, and A. L. Ralescu. 2015. Classification with class imbalance problem: a review. *International Journal of Advanced Soft Computing* and its Applications, 7, 3, 176–204.
- [15] Jie Miao and Liyuan Niu. 2016. A survey on feature selection. Procedia Computer Science, 91, 919–926. DOI: 10.1016/j.procs.2016.07.111.
- [16] Naoual El Aboudi and Laila Benhlima. 2016. Review on wrapper feature selection approaches. In 2016 International Conference on Engineering & MIS (ICEMIS). IEEE, 1–5. DOI: 10.1109/ICEMIS.2016.7745366.
- [17] Takuya Akiba, Shotaro Sano, Toshihiko Yanase, Takeru Ohta, and Masanori Koyama. 2019. Optuna: a next-generation hyperparameter optimization framework. In Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining. ACM, 2623–2631. DOI: 10.1145/3292500.3 330701.
- [18] James Bergstra and Yoshua Bengio. 2012. Random search for hyper-parameter optimization. Journal of Machine Learning Research, 13, 2, 281–305.
- [19] Jia Wu, Xiaojun Zhu, Zhipeng Lin, and Weiqing Ma. 2019. Hyperparameter optimization for machine learning models based on bayesian optimization. *Journal of Electronic Science and Technology*, 17, 1, 26–40. DOI: 10.11989/JEST.1 674-862X.80904120.
- [20] Daniel Berrar. 2019. Cross-validation. Encyclopedia of Bioinformatics and Computational Biology, 1, April, 542–545.
- [21] Quan Zou and et al. 2016. Finding the best classification threshold in imbalanced classification. *Big Data Research*, 5, 2–8. DOI: 10.1016/j.bdr.2015.12.001.
- [22] C. Esposito, G. A. Landrum, N. Schneider, N. Stiefl, and S. Riniker. 2021. GHOST: Adjusting the Decision Threshold to Handle Imbalanced Data in Machine Learning. Journal of Chemical Information and Modeling, 61, 6, 2623–2640. DOI: 10.1021/acs.jcim.1c00160.
- [23] E. B. Martins, M. S. Quintana, M. F. Silva, F. de Bruycker-Nogueira, I. C. Moraes, C. D. Rodrigues, and G. A. Calvet. 2023. Predictors of chronic joint pain after chikungunya virus infection in the inovachik prospective cohort study. *Journal* of Clinical Virology, 169, 105610. DOI: 10.1016/j.jcv.2023.105610.
- [24] L. de Moraes, T. Čerqueira-Silva, V. Nobrega, K. Akrami, L.A. Santos, C. Orge, et al. 2020. A clinical scoring system to predict long-term arthralgia in chikungunya disease: a cohort study. PLOS Neglected Tropical Diseases, 14, 7, e0008467. DOI: 10.1371/journal.pntd.0008467.
- [25] CDS Lázari et al. 2023. Clinical markers of post-chikungunya chronic inflammatory joint disease: a brazilian cohort. PLoS Neglected Tropical Diseases, 17, 1, e0011037. DOI: 10.1371/journal.pntd.0011037.
- [26] S.G. Shaikh, B.S. Kumar, G. Narang, and N.N. Pachpor. 2024. Hybrid machine learning method for classification and recommendation of vector-borne disease. J. Auton. Intell., 7, 1–14. DOI: 10.32629/jai.v7i2.797.
- [27] L. M. Neto, S. Rogerio da S. Neto, and P. T. Endo. 2023. A comparative analysis of converters of tabular data into image for the classification of arboviruses using convolutional neural networks. PLOS ONE, 18, 12, e0295598. DOI: 10.137 1/journal.pone.0295598.
- [28] Pan American Health Organization. 2022. Guidelines for the clinical diagnosis and treatment of dengue, chikungunya, and zika. Pan American Health Organization (PAHO). ISBN: 978-92-75-12488-8.