Optimized Neural Networks for Breast Cancer Classification Using Gene Expression Data

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Abstract. *This study aims to develop and evaluate optimized neural networks, including Multilayer Perceptrons (MLP) and Convolutional Neural Networks (CNN), by employing deep learning techniques to classify breast cancer subtypes, based on gene expression data. By implementing different neural network architectures and optimization strategies, this research seeks to determine the accuracy and efficiency of these classification methods. Data is sourced from The Cancer Genome Atlas (TCGA) repository and undergoes preprocessing, including dimensionality reduction, to prepare it for analysis. The contribution is to enhance diagnostic tools, as well as assess the predictive performance of the approaches. The comparison of networks performance presents a promising pathway to enhancing the precision of medical diagnostics and personalize treatment strategies in breast cancer.*

Resumo. *Este estudo tem como objetivo desenvolver e avaliar redes neurais otimizadas, incluindo Perceptrons Multicamadas (MLP) e Redes Neurais Convolucionais (CNN), empregando técnicas de aprendizagem profunda para classificar subtipos de câncer de mama, com base em dados de expressão gênica. Ao implementar diferentes arquiteturas de redes neurais e estratégias de otimização, este trabalho busca determinar a acurácia e a eficiência desses métodos de classificação. Os dados são provenientes do repositório Atlas do Genoma do Câncer (TCGA) e passam por pré-processamento, incluindo redução de dimensionalidade, a fim de prepará-los para análise. A contribuição é aprimorar as ferramentas de diagnóstico, bem como avaliar o desempenho preditivo das abordagens. A comparação dos resultados das redes apresenta um caminho promissor para aumentar a precisão dos diagnósticos médicos e personalizar as estratégias de tratamento do câncer de mama.*

1. Introduction

Breast cancer (BC) is a neoplastic condition characterized by the formation of a malignant tumor originating in breast cells. It is the most prevalent type of cancer among women. More than 2.3 million new cases of breast cancer are recorded annually, making it the most common type of cancer among adults. In 95% of countries, breast cancer ranks as the first or second leading cause of cancer-related deaths in women. However, breast cancer survival varies significantly between and within countries; approximately 80% of breast and cervical cancer deaths occur in low- and middle-income countries[World Health Organization 2023].

Early detection of BC can reduce both the financial burden on healthcare systems and families, as well as the mortality rate associated with the disease. Therefore, investing in early breast cancer screening and diagnosis, including mammography, ultrasound, magnetic resonance imaging, and biopsies, is ideal. Studies suggest that regular mammography screening programs can lead to a reduction in BC mortality rates. However, traditional breast cancer detection methods face challenges such as the complexity of mammographic images and the potential for false negatives due to difficulties in identifying patterns in the early stages of the disease [Ministério da Saúde 2024].

Recently, deep learning models have been explored for breast cancer detection, showing promising results. These models can learn complex hierarchical features, increasing the sensitivity and specificity of cancer detection, thereby aiding in early diagnosis. Additionally, the use of deep neural networks can reduce reliance on highly specialized professionals, allowing for the automation of part of the diagnostic process, for example [Sait and Nagaraj 2024]. Techniques such as transfer learning, which adapts pre-trained models to new tasks, have shown potential for improving diagnostic accuracy with limited resources.

In the literature, many studies have been adopting Neural Networks to classify BC [Turgut et al. 2018, Tewari et al. 2022, Rabiei et al. 2022, Wu and Hicks 2021, Iparraguirre-Villanueva et al. 2023, Sait and Nagaraj 2024]. In this context, this study employs MLP and CNNs to classify subtypes of breast cancer based on gene expression data. Although CNNs are traditionally used for image recognition tasks, they can be effectively adapted to handle high-dimensional biological data such as gene expression profiles [Lopez-Garcia et al. 2020].

In this context, the objective of this study is to develop and evaluate optimized neural networks, specifically MLP and CNNs, using deep learning techniques for the classification of breast cancer subtypes based on gene expression data. The study aims to enhance the accuracy and efficiency of subtype classification, contributing to the development of more precise diagnostic tools and personalized treatment approaches in breast cancer care. To this end, the advanced feature extraction capabilities offered by deep learning will be explored, with the application of the Optuna algorithm for model optimization, as well as a comparative analysis without the use of this method.

2. Materials and Methods

This section presents the methodology proposed in this study to perform the classification multiclass breast cancer, using gene expression data and neural networks modeling.

2.1. Methodological Path

The methodological path adopted for this study is presented in Figure 1. The raw data coming from the renowned TCGA[1] repository contains information such as the number of rows and columns, the classification type and class labels. The columns represent the features, that is, the input variables for the classification task.

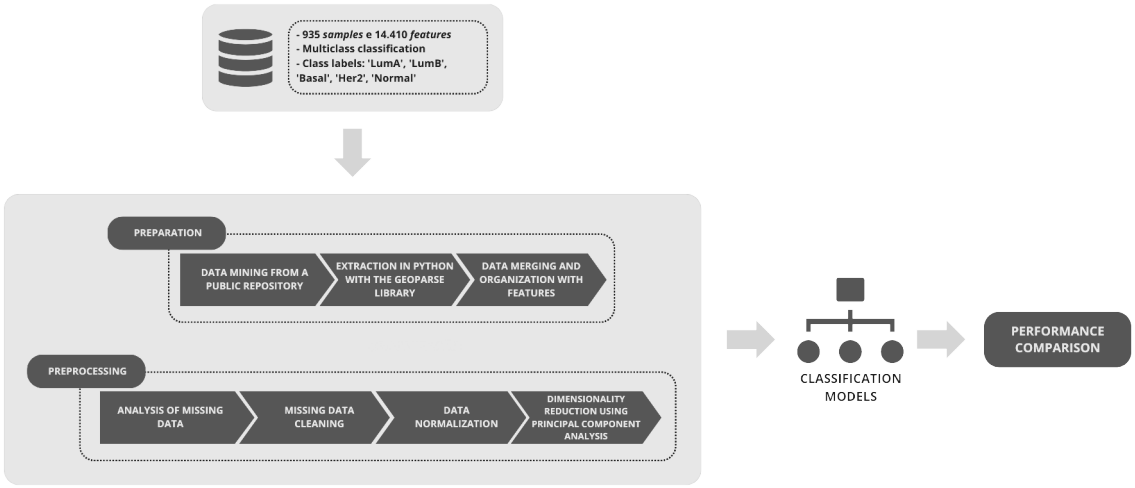

Figure 1. The methodological approach of the study.

The TCGA database consists of renowned repositories of gene expression data, where specific criteria are applied to identify breast cancer samples using the array expression profiling technique. The data generated is real and is publicly available to the scientific community. To extract the data, the "GEOparse" library in the Python language was used, followed by data merging and column organization. The database presents 935 samples (rows) and 14.410 features (colums). The last column contains 5 output classes, which represent the subtypes of breast cancer: Basal, Her2, LumA, LumB, and Normal (no cancer); therefore, this study presents a multiclass classification task.

After the data acquisition, the following step is the preprocessing. The missing data was treated and the cleaning process was executed, which resulted in the identification of outliers and values outside a certain scale, making data normalization necessary, using z-score [Kreyszig 2010]. This way, it is possible to prevent a characteristic with very high values from having a disproportionate weight or contribution in the analysis. The preprocessing step is essential to ensure that the dataset is ready for the modeling step.

In addition, due to the nature of gene expression data (which generally has more columns than rows), it was necessary to apply a dimensionality reduction method, such as the Principal Component Analysis (PCA) technique [Rencher 2002, Timm 2002]. In PCA, principal components are created in such a way that they are uncorrelated each other and capture most of the variance present in the original data. They are used to identify and interpret dependencies between variables, in addition to examining relationships that may exist between individuals [Johnson and Wichern 2007]. In the context of this study, this technique also improves the performance of statistical modeling tasks and the classifiers

[1]https://www.cancer.gov/ccg/research/genome-sequencing/tcga

performance. Considering the preprocessing data executed, the next step, as illustrated in Figure 1, is the neural networks structures, described in Sections 2.2 and 2.3.

2.2. Multilayer Perceptron

In this study, a MLP model is employed to classify subtypes of breast cancer. The MLP is a type of feedforward artificial neural network consisting of an input layer, multiple hidden layers, and an output layer. Each neuron in a layer is connected to every neuron in the subsequent layer, creating a fully connected network [Aggarwal 2015]. The availability of a learning scheme is the backpropagation, which trains the entire network hierarchically. This architecture, shown in Figure 2.2 allows the model to learn complex patterns and relationships in the data, making it suitable for tasks such as multiclass classification.

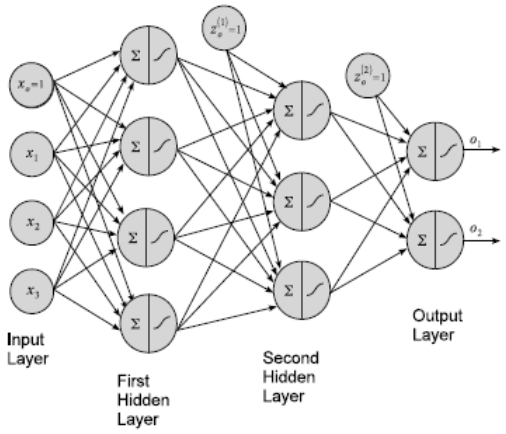

Figure 2. MLP Network Architecture for Classification [Aggarwal 2015]

The input layer consists of neurons that receive the raw gene expression data. Each neuron in this layer corresponds to a feature or gene from the dataset. MLPs have one or more hidden layers between the input and output layers. These layers consist of neurons that process the inputs from the previous layer. Each neuron applies a weighted sum of its inputs, followed by an activation function. The hidden layers capture complex patterns and interactions between genes that are relevant for classifying breast cancer subtypes. The number of hidden layers and the number of neurons per layer can vary and are chosen based on the complexity of the data and the problem.

Common activation functions used in MLPs include the ReLU (Rectified Linear Unit), sigmoid, and tanh functions. The output layer consists of neurons that provide the final classification result. In the case of breast cancer subtype classification. A softmax activation function is often used in the output layer to normalize the outputs into probabilities that sum to one, making it easier to interpret the results.

These elements work together to enable MLPs to learn and classify complex patterns in gene expression data, making them suitable for identifying breast cancer subtypes based on molecular characteristics.

2.3. Convolutional Neural Network

The CNN is a multilayer perceptron made of numerous layers where each layer is a nonlinear feature detector performing local processing of contiguous features within each

layer, leading to higher conceptual representation as information moves up to the output layer [Aggarwal 2015]. It is considered as the first successful implementation of a deep architecture that exploits prior knowledge [LeCun et al. 1995, LeCun et al. 1998].

The CNN's weight space is sparse as each unit in a layer only selectively takes input from a subset of contiguous neurons in the lower layers. By leveraging the local connectivity and weight-sharing properties of CNNs, the approach of this work aims to capture complex patterns and interactions among gene expressions that are indicative of different breast cancer subtypes.

Convolutional Layers are the core building blocks of CNNs. They apply a set of filters (or kernels) across the input data to extract features. The filters slide over the input, performing a dot product between the filter and patches of the input data. This operation results in a feature map that highlights specific patterns [LeCun et al. 1995, Chollet 2021].

After convolution operations, an activation function is applied element-wise to introduce non-linearity into the model. The most commonly used activation function in CNNs is the ReLU, which replaces all negative values in the feature map with zero, helping the model learn more complex patterns [LeCun et al. 1998].

Towards the end of the network, the high-level reasoning is performed by Dense layers. These layers take the flattened output of the previous layers and connect every neuron to every neuron in the previous layer. They help combine features learned by earlier layers to classify the input or make predictions [Chollet 2021].

Finally, the Output layer is typically a dense layer with a specific number of neurons that corresponds to the number of output classes. The softmax activation function is often used in the output layer to convert the raw output into probabilities, indicating the likelihood of each class.

2.4. Hyperparameter Optimization

Classification model hyperparameters have a significant effect on performance of learning algorithms, since hyperparameter tuning is a critical step in improving the performance of the classification models [Wu et al. 2019, Yang and Shami 2020]. In this way, a new set of design criteria for optimization frameworks, called "Optuna," is proposed [Akiba et al. 2019]. It is an open-source hyperparameter optimization framework that features define-by-run programming, which provides flexibility in the optimization process, efficient sampling algorithms and pruning that improve adaptability and a versatile, easy-to-configure architecture.

In this study, Optuna was employed to optimize the hyperparameters of MLP and CNN models. By systematically exploring the hyperparameter space, Optuna helps identify the optimal set of hyperparameters that lead to the best model performance.

Optuna uses a state-of-the-art optimization algorithm known as Tree-structured Parzen Estimator (TPE), which efficiently navigates the hyperparameter space by constructing probabilistic models of promising hyperparameter configurations. Optuna also supports pruning of unpromising trials, allowing faster convergence by halting trials that are unlikely to yield optimal results.

For the MLP model, the hyperparameters optimized by Optuna are: the number

of Hidden Layers (between 1 and 5), number of neurons in each hidden layer (from 32 to 256), learning rate (from 0.0001 to 0.1), batch size (from 16 to 128) and dropout rate (between 0.0 and 0.5, to prevent overfitting).

Similarly, for the CNN model, Optuna was used to optimize the number of convolutional layers (between 1 and 4), number of filters (from 32 to 256), Kernel size, learning rate (from 0.0001 to 0.1), batch size (from 16 to 128) and dropout rate (between 0.0 and 0.5).

Optuna conducted the optimization by running a certain number of trials and exploring different combinations of hyperparameters to identify those that maximize the model's performance. Optuna returns the best parameters found for each model. These parameters represent the settings that, within the 10 trials, provided the best average accuracy.

2.5. Evaluation Metrics

In order to train and test the performance of the models, the datasets were divided into training and testing sets, assigning 80% of the data to the training and 20% to the testing phase, according to Pareto distribution. After that, the cross-validation [Aggarwal 2015] was performed using k-fold method, with k=10 folds. The performance evaluation of the classification models was conducted by using well known statistical measures, confusion matrix, accuracy and cross-validation [Aggarwal 2015, Bishop 2006].

In this work, version 3.11 of Python was used as the programming language, due to its efficiency and performance. In all analyses, a fixed significance level of 5% was adopted. The Python scripts used for this study are available on GitHub. The repository can be accessed via the following link: `https://github.com/leonardocjr/ppgbioinfo`.

3. Results and Discussion

This section presents the findings of the study, highlighting the performance of MLP and CNN neural network architectures when applied to datasets from the TCGA repository. A comparative performance analysis is also provided, utilizing statistical metrics for evaluation.

The TCGA database originally consists of 935 rows and 14,408 columns. However, after applying the PCA technique, the size of the database was reduced to 935 rows and 184 columns, selecting the columns (genes) that have the greatest influence on the classification of breast cancer subtypes [Johnson and Wichern 2007].

The MLP architecture employed in this study consists of one input layer, four hidden layers, and one output layer. The input layer size corresponds to the number of features in our dataset, which includes gene expression profiles relevant to breast cancer subtypes. The hidden layers are composed of 100, 75, 50, and 25 neurons, respectively, with each layer utilizing a ReLU activation function. The output layer contains a number of neurons equal to the number of breast cancer subtypes, with a softmax activation function to provide probabilities for each class.

The CNN used in this study consists of two convolutional layers with 32 and 64 filters, respectively. Each convolutional layer employs a 3x3 kernel size with a stride

of 1 and ‘same’ padding. After each convolutional layer, ReLU activation functions are applied. MaxPooling layers follow the convolutions to reduce dimensionality and capture important features. The model also includes a fully connected dense layer with 64 units and ReLU activation, followed by a dropout layer with a 50% rate to prevent overfitting. The final output layer applies a softmax activation function to provide class probabilities. Cross-validation with five folds is performed, and the model is trained with the Adam optimizer and sparse categorical cross-entropy as the loss function.

Table 1 presents the performance metrics of the MLP and CNN models before hyperparameter optimization using Optuna, providing a baseline for comparison.

Table 1. Performance of neural networks architectures: a) MLP b) CNN

Multilayer Perceptron without Optuna			
	Precision	Recall	F1-Score
Lum A	0.78	0.89	0.83
Lum B	0.64	0.51	0.57
Basal	0.75	0.77	0.76
Her 2	0.62	0.38	0.47
Normal	0.50	0.75	0.60
Accuracy (test)		0.7273	
Accuracy (cross-validation)		0.7498	

a)

Convolutional Neural Network without Optuna			
	Precision	Recall	F1-Score
Lum A	0.73	0.76	0.74
Lum B	0.37	0.47	0.41
Basal	0.83	0.83	0.83
Her 2	0.83	0.33	0.48
Normal	0.00	0.00	0.00
Accuracy (test)		0.6952	
Accuracy (cross-validation)		0.7046	

b)

In Table 1, it is important to highlight the values of the statistical measures that demonstrate the good performance of the multiclass classification for the considered breast cancer subtypes. For the MLP network architecture, the accuracy on the test set is 0.7273, and the accuracy using cross-validation is 0.7498. For the CNN architecture, the accuracy is 0.6952, and the accuracy using cross-validation is 0.7046. These results underline the effectiveness of the models in accurately classifying the breast cancer subtypes. The other statistical measures presented in the table further support this statement.

In order to better understand the classification performance, Figure 3 shows the confusion matrices for the MLP and CNN models without optimization. These matrices highlight the distribution of correct and incorrect predictions, indicating where the models may struggle.

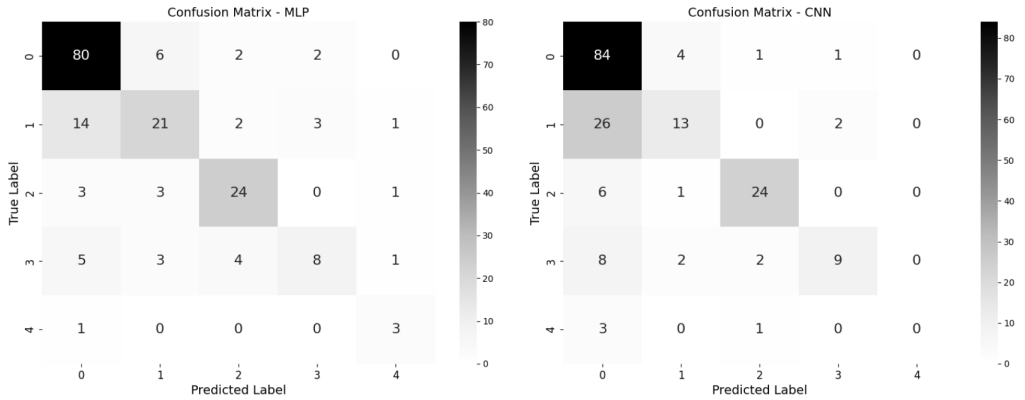

Figure 3. Confusion Matrix

A hyperparameter optimization method was used to fine-tune the MLP and CNN models, applying the Optuna library to determine the best parameters. For the CNN, the

optimal configuration includes two convolutional layers with 55 filters in each layer, a kernel size of 4x4, and a pooling size of 2. The dense layer has 128 units, followed by a dropout rate of approximately 45%. The model was trained for 20 epochs. For the MLP, the best configuration found includes three hidden layers with 138, 97, and 25 neurons, respectively, all using ReLU activation. The model was trained with the Adam optimizer, an alpha value of 0.043, and an initial learning rate of 0.0074.

Table 2 shows the performance metrics for both neural networks architectures after applying Optuna optimization, demonstrating significant improvements compared to the baseline.

Table 2. Performance of neural networks architectures using Optuna: a) MLP b) CNN

Multilayer Perceptron with Optuna			
	Precision	Recall	F1-Score
Lum A	0.85	0.91	0.88
Lum B	0.68	0.63	0.66
Basal	0.93	0.87	0.90
Her 2	0.69	0.52	0.59
Normal	0.29	0.50	0.36
Accuracy (test)		0.7914	
Accuracy (cross-validation)		0.7794	

a)

Convolutional Neural Network with Optuna			
	Precision	Recall	F1-Score
Lum A	0.75	0.91	0.82
Lum B	0.68	0.51	0.58
Basal	0.88	0.94	0.91
Her 2	0.69	0.43	0.53
Normal	1.00	0.25	0.40
Accuracy (test)		0.7594	
Accuracy (cross-validation)		0.9253	

b)

Observing Table 2, it is important to highlight the values of the statistical measures that demonstrate the good performance of the multiclass classification for the breast cancer subtypes, using the Optuna hyperparameter optimizer. For the MLP network architecture with Optuna, the accuracy on the test set is 0.7914, and the accuracy using cross-validation is 0.7794. For the CNN architecture, the accuracy is 0.7594, and the accuracy using cross-validation is 0.9253. These results emphasize the enhanced performance of the models in accurately classifying the breast cancer subtypes, due to the use of the Optuna optimizer. As before, the additional statistical measures corroborate this statement.

To further evaluate the classification performance post-optimization, Figure 3 presents the confusion matrices for the optimized MLP and CNN models, illustrating the enhancements in prediction accuracy and the reduction of misclassified cases.

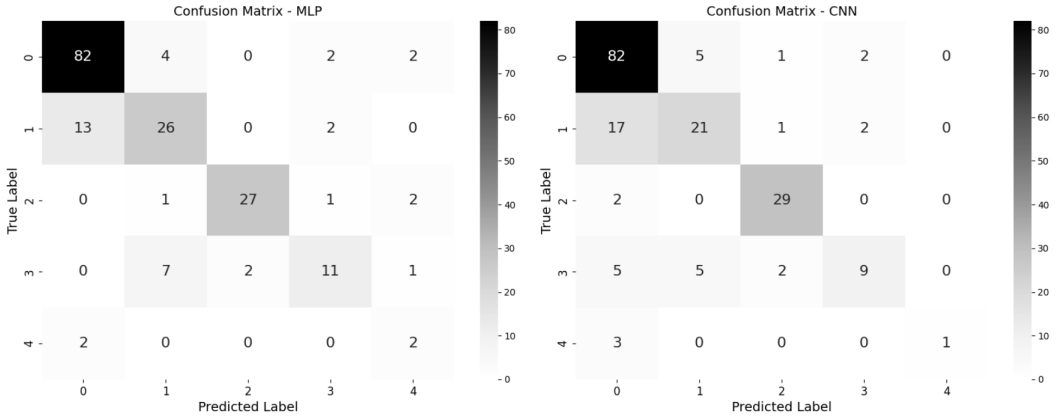

Figure 4. Confusion Matrix with Optuna

This study provides a detailed analysis of the performance of MLP and CNN architectures in the task of classifying breast cancer subtypes using data from the TCGA repository. The initial dimensionality reduction, performed using PCA, was crucial for selecting the most influential genes, reducing the number of features from 14,408 to 184. This preprocessing step was essential to improve model efficiency and focus on the most relevant features for classification.

The MLP, configured with four hidden layers, and the CNN, with two convolutional layers, demonstrated distinct performances in the initial evaluation. The MLP achieved an accuracy of 0.7498, while the CNN obtained 0.7046. These initial results suggest that, while both architectures are capable of capturing patterns in the data, the CNN may face additional challenges due to its high sensitivity to imbalanced data [Dablain et al. 2024] and the non-spatial nature of gene expression data.

The application of hyperparameter optimization using the Optuna method brought significant improvements to both models. The MLP's accuracy increased to 0.7794, while the CNN experienced a much more substantial increase, reaching an accuracy of 0.9253. This demonstrates that proper optimization can mitigate some of the initial limitations of the CNN, making it highly effective even in contexts where the nature of the data is not ideal for this architecture [Aggarwal 2015, Bishop 2006, Wu et al. 2019].

However, despite the improvements in accuracy, the optimized CNN may still be vulnerable to generalization issues when applied to unbalanced datasets [Dablain et al. 2024], as is often the case in gene expression studies. The robustness of the MLP, on the other hand, was less affected by the nature of the data, suggesting that this architecture may be more reliable in scenarios where the data are heterogeneous and lack a clear spatial structure.

Additionally, the confusion matrices after optimization reveal that, while the CNN achieved higher accuracy, it may still exhibit instability in certain misclassification cases. This can be attributed to the CNN's tendency to over-specialize in specific patterns, which can lead to overfitting, particularly in datasets with few representative samples for each class [Aggarwal 2015, Bishop 2006].

Therefore, when choosing between CNN and MLP for tasks involving the classification of gene expression data, it is important to consider the nature of the problem and the balance of the data. While the CNN can be extremely effective after optimization, its application should be accompanied by rigorous validations and strategies to address data unbalance. The MLP, with its greater flexibility and lower sensitivity to these issues, may offer a more stable and reliable solution in many cases.

These findings underscore the importance of a careful approach in selecting and optimizing learning models, particularly in fields such as bioinformatics, where the nature of the data can significantly influence the performance of network architectures.

4. Conclusion

This study compared the performance of two deep neural network architectures, MLP and CNN, applied to the classification of breast cancer subtypes using gene expression data from the TCGA repository. CNNs, which have ability to capture spatial patterns, proved unstable when applied to unstructured and unbalanced data, such as gene expression data.

MLPs, on the other hand, provided a more general and stable approach for this type of problem, using fully connected layers to capture complex relationships between genes.

Before hyperparameter optimization, both architectures exhibited limitations, highlighted in the confusion matrices, particularly in the performance of the CNN. Hyperparameter optimization using Optuna significantly improved the accuracy of both models. By defining an appropriate search space and selecting objective functions such as accuracy, Optuna iteratively refined the models' parameters, resulting in an optimized CNN with two convolutional layers and an MLP with three hidden layers that demonstrated improved performance.

Despite these improvements, the high sensitivity of the CNN in classifying unbalanced data underscores the need for careful analysis when applying this architecture to data that lacks clear spatial structure, such as gene expression data. The MLP, with its greater flexibility, proved to be a more robust alternative for this type of problem.

Therefore, the choice between CNN and MLP should be guided by the nature of the data. While the CNN can be optimized to perform well in specific contexts, the MLP has shown to be a more stable and effective solution for classifying breast cancer subtypes, particularly after applying hyperparameter optimization techniques like those offered by Optuna. These conclusions underscore the importance of an informed selection of network architecture and the careful application of optimization techniques to achieve superior performance in complex learning problems.

References

Aggarwal, C. C. (2015). *Data Classification*. CRC Press, Florida - USA.

Akiba, T., Sano, S., Yanase, T., Ohta, T., and Koyama, M. (2019). Optuna: A next-generation hyperparameter optimization framework. *CoRR*, abs/1907.10902.

Bishop, C. M. (2006). *Pattern recognition and machine learning*, volume 2. Springer.

Chollet, F. (2021). *Deep Learning with Python*. New York: Manning Publication, second edition.

Dablain, D., Jacobson, K. N., Bellinger, C., Roberts, M., and Chawla, N. V. (2024). Understanding cnn fragility when learning with imbalanced data. *Machine Learning*, 113(7):4785–4810.

Iparraguirre-Villanueva, O., Epifanía-Huerta, A., Torres-Ceclén, C., Ruiz-Alvarado, J., and Cabanillas-Carbonell, M. (2023). Breast cancer prediction using machine learning models. *International Journal of Advanced Computer Science and Applications*, 14(2):610–620.

Johnson, R. A. and Wichern, D. W. (2007). *Applied Multivariate Statistical Analysis*, volume 6. Pearson Education.

Kreyszig, E. (2010). *Advanced Engineering Mathematics*. John Wiley & Sons, New York, 10 edition.

LeCun, Y., Bengio, Y., et al. (1995). Convolutional networks for images, speech, and time series. *The handbook of brain theory and neural networks*, 3361(10):1995.

LeCun, Y., Bottou, L., Bengio, Y., and Haffner, P. (1998). Gradient-based learning applied to document recognition. *Proceedings of the IEEE*, 86(11):2278–2324.

Lopez-Garcia, G., Jerez, J. M., Franco, L., and Veredas, F. J. (2020). Transfer learning with convolutional neural networks for cancer survival prediction using gene-expression data. *PloS one*, 15(3):e0230536.

Ministério da Saúde (2024). Câncer de mama. `https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/c/cancer-de-mama`. Accessed: 2024-08-26.

Rabiei, R., M., A. S., Sohrabei, S., Esmaeili, M., and Atashi, A. (2022). Prediction of breast cancer using machine learning approaches. *J Biomed Phys Eng*, 12(3):297–308.

Rencher, A. (2002). *Methods of Multivariate Analysis*. Wiley series in probability and mathematical statistics. Wiley.

Sait, A. R. W. and Nagaraj, R. (2024). An enhanced lightgbm-based breast cancer detection technique using mammography images. *Diagnostics*, 14(2):227.

Tewari, Y., Ujjwal, E., and Kumar, L. (2022). Breast cancer classification using machine learning. In *2022 2nd International Conference on Advance Computing and Innovative Technologies in Engineering (ICACITE)*.

Timm, N. (2002). *Applied Multivariate Analysis*. Springer Texts in Statistics. Springer New York.

Turgut, S., Dağtekin, M., and Ensari, T. (2018). Microarray breast cancer data classification using machine learning methods. In *2018 Electric Electronics, Computer Science, Biomedical Engineerings' Meeting (EBBT)*.

World Health Organization (2023). Who launches new roadmap on breast cancer. `https://www.who.int/news/item/03-02-2023-who-launches-new-roadmap-on-breast-cancer`. Accessed: 2024-08-26.

Wu, J., Chen, X.-Y., Zhang, H., Xiong, L.-D., Lei, H., and Deng, S.-H. (2019). Hyperparameter optimization for machine learning models based on bayesian optimizationb. *Journal of Electronic Science and Technology*, 17(1):26–40.

Wu, J. and Hicks, C. (2021). Breast cancer type classification using machine learning. *Journal of Personalized Medicine*, 11(61).

Yang, L. and Shami, A. (2020). On hyperparameter optimization of machine learning algorithms: Theory and practice. *Neurocomputing*, 415:295–316.