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A deep learning–based multi-level approach
for automatic detection of suspicious regions in
breast cancer histopathological images**Vemuri Nitin¹, Ravikumar Ch^{2*}, Satyanarayana Nimmala³, Naresh K⁴, Tedla Bhavani⁵, and Nagarjuna Dorthala⁶**¹Department of Computer Science and Applications, Koneru Lakshmaiah Education Foundation Bowrampet Campus, Hyderabad, Telangana, India²Department of Computer Science and Engineering, School of Engineering, Sreenidhi University, Hyderabad, Telangana, India³Department of Computer Science and Engineering (Data Science), CVR College of Engineering, Hyderabad, Telangana, India⁴Department of Computer Science and Engineering, Kommuri Pratap Reddy Institute of Technology, Hyderabad, Telangana, India⁵Department of Computer Science and Engineering, Maturi Venkata Subba Rao Engineering College, Hyderabad, Telangana, India⁶Populus Group, LLC, Troy, Michigan, United States of America***Corresponding author:**Ravikumar Ch
(Ravikumar.c@suh.edu.in)

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Abstract

Breast cancer is one of the most prevalent types of cancer, with high mortality rates all over the world. The disease is linked to uncontrolled growth of breast tissue, resulting in benign (not likely to spread) or malignant (able to spread) tumors. Malignant tumors are particularly dangerous due to their ability to spread. This study analyzes breast cancer histology images using deep learning methods to automatically detect and classify histology as benign or malignant. It used advanced models such as convolutional neural networks (CNNs) and long short-term memory (LSTM) models to account for the spatial and sequential aspects of the images. While CNNs detect textures and patterns that indicate malignancy, LSTM models effectively capture temporal and feature dependencies, making the representation complete. Our hybrid model (CNN combined with LSTM) outperformed single-scale approaches in accuracy and classification diversity. The hybrid model was independently tested on networks of Gated Recurrent Unit, Visual Geometry Group 16, and Residual Network 50. It achieved unprecedented scores of up to 96.21% accuracy, 95.21% sensitivity, and 98.23% F-score. The findings suggest that the proposed hybrid model could be invaluable for diagnosing breast cancer and assisting pathologists.

Keywords: Breast cancer; Deep learning; Convolutional neural network–long short-term memory hybrid model; Histopathological images; Automated detection

1. Introduction

Breast cancer has remained among the most dangerous health issues worldwide, impacting millions of women annually. It is the most common cancer in women and one of the most common causes of cancer-related mortality, with about 2.3 million new cases

being diagnosed and 685,000 reported deaths worldwide in 2020 (Nolan *et al.*, 2023). The incidence of breast cancer has been increasing significantly within the last five years, to almost 7.8 million cases, thus underlining the increasing burden of breast cancer on both healthcare systems and societies around the world. The most important causes of breast cancer are old age, inheritable mutations, and chronic exposure to environmental carcinogenic agents such as ionizing radiation and chemical agents. The mutagenic effects cause DNA damage and mitotic abnormalities, eventually resulting in abnormal cell proliferation (Onkar *et al.*, 2023). Although genetic factors are important, more recent studies show that non-genetic factors, such as hormonal imbalances, chronic exposure to industrial chemicals, and lifestyle habits including smoking, poor dietary habits, and obesity, are also major causes of the disease (Cardoso *et al.*, 2024). It is especially disturbing in developing countries such as India, where the incidence rate is growing rapidly, with one woman being diagnosed every four minutes, and preventive measures and early screening programs are urgently needed (Laws & Punglia, 2023).

In response to this global health crisis, the Global Breast Cancer Initiative (GBCI) has stressed early detection as a key measure to reduce mortality by 40% before 2040 (Loibl *et al.*, 2024). The program encourages full screening, early intervention, and extensive health education to raise awareness of preventive care. Early diagnosis is a revolutionary factor in patient survival because it enables medical care before the disease becomes widespread and untreatable. Different imaging modalities, such as mammography, magnetic resonance imaging (MRI), and ultrasound, have become essential tools for detecting breast abnormalities early. Nevertheless, traditional self-examinations, while useful in some situations, do not always detect minor structural or cellular anomalies, which have to be confirmed by medical imaging (Nicholson *et al.*, 2024).

Figure 1 illustrates representative histopathological

images from the Breast Cancer Histopathological Database (BreakHis) dataset at four magnification levels (40×, 100×, 200×, and 400×). The figure highlights variability in tissue appearance and the challenges of feature extraction across different image resolutions. These variations motivate the development of a robust multi-level convolutional neural network (CNN)–long short-term memory (LSTM) framework capable of learning discriminative features under heterogeneous imaging conditions.

Through the rapid changes in technology, ultrasound images and computer-aided diagnosis (CAD) systems have transformed the way breast cancer is diagnosed. These techniques have increased access and accuracy and enabled quicker interpretation of findings. Nonetheless, although clinical diagnostic methods are more reliable than self-examinations, they are also time-consuming and prone to human error. Specifically, dense breast tissue is problematic in mammography, as it usually creates false-negative outcomes and false biopsies (Koetzier *et al.*, 2023). To address these shortcomings, CAD systems provide automated feature extraction, segmentation, and pattern recognition to help identify anomalies radiologists might otherwise miss. They offer objective, non-judgmental decision support that improves accuracy, minimizes inter-observer variability, and speeds diagnosis (Boumaraf *et al.*, 2021). Moreover, CAD technology can greatly reduce clinicians' cognitive load, improve workflow efficiency, and minimize the risk of diagnostic oversight (Budak *et al.*, 2019).

Breast cancer may occur in milk ducts (ductal carcinoma) or in the lobules (lobular carcinoma); these are the two main structures that produce and transport milk. It is usually categorized as benign or malignant based on whether tumor cells invade neighboring tissues or metastasize to other organs. Benign tumors are localized and encapsulated, whereas malignant tumors show uncontrolled growth, infiltration, and spread (Burçak *et al.*, 2021). Proper histopathological analysis is the best way to differentiate between the two types. However, manual

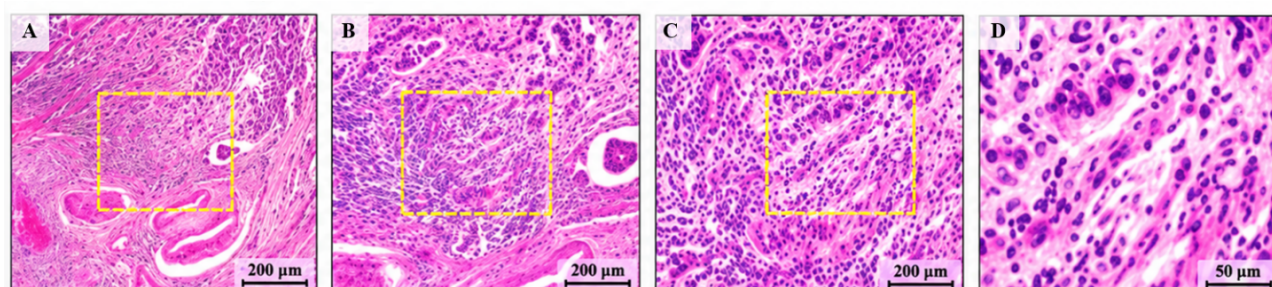


Figure 1. Breast histopathology images from the Breast Cancer Histopathological Database (BreakHis) at different magnification levels: (a) unknown magnification (scale bar: 200 μ m), (b) 100 $\times$ (scale bar: 200 μ m), (c) 200 $\times$ (scale bar: 200 μ m), and (d) 400 $\times$ (scale bar: 50 μ m)

analysis of tissue slides is time-consuming, subjective, and prone to interpretation errors. Under the microscope, malignant cells can sometimes resemble benign ones, which can lead to misdiagnosis and inadequate treatment (Azam *et al.*, 2021). To address this, superior computational techniques based on deep learning and artificial intelligence (AI) have been developed to improve the precision and reliability of breast cancer diagnosis (BabaAhmadi *et al.*, 2022).

Deep learning frameworks, especially those based on CNNs and LSTM networks, have become effective models in medical image analysis. CNNs can extract spatial features (shapes, textures, and edges) from histopathological data, and LSTMs can capture temporal or sequential dependencies (Bagchi *et al.*, 2023). A hybrid CNN-LSTM architecture can leverage both spatial and temporal features, improving classification performance and interpretability (Bejnordi *et al.*, 2017; Belsare, 2012). This integration not only improves the model's ability to capture complex image patterns but also ensures stable prediction outcomes across different magnification levels and image modalities. It has also been shown that deep learning models outperform conventional machine learning algorithms, especially in feature learning, segmentation, and anomaly detection, which are essential for detecting cancerous regions with high precision (Boumaraf *et al.*, 2021).

Furthermore, preprocessing methods such as noise elimination, image sharpening, and contrast enhancement have been incorporated to improve deep learning models, enabling more precise segmentation and localization of suspicious areas (Budak *et al.*, 2019). Segmentation accuracy directly affects the diagnostic reliability of the framework, as errors at this stage may carry through to later analyses. Despite these developments, challenges remain in ensuring data quality, generalization, and resistance to overfitting. Hence, regularization and model optimization are necessary to ensure that trained systems remain resilient on unseen data (Burçak *et al.*, 2021).

Against this backdrop, this paper proposes a multi-scale deep learning system for automated identification of abnormal regions in breast cancer histopathology images, addressing the trade-off between diagnostic performance and clinical interpretability. The proposed CNN-LSTM hybrid network preserves spatial and temporal characteristics, improving overall diagnostic accuracy and robustness. The model reduces overfitting and improves generalization and consistency through hyperparameter optimization, data augmentation, and stratified regularization. This framework aims to provide clinicians with an intelligent, reliable, and scalable diagnostic aid that can detect breast cancer faster and more accurately,

improving patient outcomes and advancing computational oncology (Cardoso *et al.*, 2024; Nolan *et al.*, 2023).

Although deep learning has advanced breast cancer detection, current research tends to focus on individual datasets and lacks robustness to changing imaging conditions. Further, little attention has been paid to modeling inter-feature dependencies in histopathological images and ensuring generalization across heterogeneous data. Thus, a common framework that can efficiently combine spatial and sequential learning while remaining robust and scalable across a wide range of clinical data is required.

Unlike traditional CNN-LSTM models, this research proposes a powerful multi-dataset assessment framework for breast cancer histopathological image recognition. Its main contributions are: (i) the combination of spatial and sequential feature learning to obtain better diagnostic performance, (ii) the large-scale cross-dataset validation on BreakHis, Breast Cancer Histology (BACH), and BreastMNIST datasets, and (iii) the robustness against noisy and heterogeneous imaging conditions. The work focuses on practical generalization and reliability rather than a totally novel architecture.

In this study, the term *multi-level approach* refers to the hierarchical learning strategy employed in the proposed CNN-LSTM framework. At the first level, CNNs extract low-level and high-level spatial characteristics, including textures, nuclei distributions, and tissue morphology. At the second level, the extracted feature maps are transformed into sequences and processed with LSTM layers to model inter-feature dependencies among spatial representations. Finally, the classification layer integrates these complementary representations to distinguish benign and malignant tissues. Through this multi-level feature learning mechanism, the proposed framework improves robustness and generalization across heterogeneous histopathological datasets.

The research question is: Can a hybrid CNN-LSTM framework improve classification accuracy and generalization across heterogeneous histopathological datasets while remaining robust to noise and variability?

The document is structured as follows: Section 2 summarizes the relevant literature on using deep learning to detect breast cancer. Section 3 provides implementation details of the proposed multi-scale deep learning framework. Section 4 presents model results and performance evaluation, and Section 5 concludes the paper with model conclusions and future work.

2. Related work

Breast cancer is a significant health burden worldwide, and

there has been a lot of research on the creation of smart diagnostic frameworks that can accurately detect it in early stages. Machine learning and deep learning methods have been used to automatically classify breast lesions using histopathological and radiological images. These models distinguish between benign and malignant tissues and help clinicians make faster, more accurate diagnoses. CNNs, LSTM models, transfer learning strategies, and hybrid systems have been shown to improve diagnostic accuracy. As Laws and Punglia (2023) emphasized, early and accurate diagnosis is crucial to improving patient outcomes, and computational intelligence should supplement endocrine therapies in primary and secondary prevention. Likewise, Lee and Wu (2024) proposed a single-task meta-learning model that includes an auxiliary network for breast tumor tissue classification and achieved significant improvements in feature representation and classification accuracy across classes.

Modern CAD systems are based on deep learning. M. Liu *et al.* (2022) proposed a deep learning-based pathology image classification framework that proved more effective at extracting features to diagnose breast cancer tissues from histopathological images. Building on this idea, T. Liu *et al.* (2022) proposed a hybrid deep learning model that could combine multimodal data, including genomic and imaging data, to accurately predict molecular subtypes of breast cancer. The model showed higher diagnostic accuracy, demonstrating the potential of hybrid learning to gain insights into cancer heterogeneity. The European Society for Medical Oncology (ESMO) Clinical Practice Guideline by Loibl *et al.* (2024) further supports adopting advanced computational tools for early diagnosis, treatment, and follow-up to enhance clinical decision-making.

The diagnostic power of AI-based models has increased further with advances in segmentation and preprocessing methods. Michael *et al.* (2021) conducted a thorough review of existing breast cancer segmentation techniques and found deep learning-based segmentation to be the most promising approach, outperforming traditional methods such as thresholding and edge detection. Mohamed *et al.* (2022) showed that preprocessing measures, including normalization and ensemble learning, significantly affect model accuracy and reliability. Nicholson *et al.* (2024) highlighted the importance of such intelligent systems in supporting screening practices and suggested integrating machine learning-assisted systems into early breast cancer screening guidelines to minimize human error and enhance sensitivity. Furthermore, Nolan *et al.* (2023) showed how combining computational models with biological insights has reshaped clinical practice in deciphering tumor heterogeneity and improving personalized treatment plans.

Recent studies have also investigated new optimization and meta-learning methods to improve breast cancer image classification. Onkar *et al.* (2023) discussed the immune landscape of breast cancer subtypes and how it is used to model machine learning-based immune responses. Si *et al.* (2022) introduced a chimp optimization algorithm to dynamic contrast-enhanced MRI lesion segmentation, which is more accurate and robust than traditional algorithms. Their study showed that bio-inspired optimization can greatly improve image-segmentation accuracy for clinical diagnosis. Likewise, Ch *et al.* (2025) noted the growing popularity of deep learning in image processing, its challenges, and the importance of optimization methods in improving model robustness. Ch *et al.* (2024) also compared deep learning approaches to image forgery detection and showed that improved feature extraction and optimization algorithms can substantially increase classification accuracy, which also applies to breast cancer imaging.

C. Zhang *et al.* (2023) conducted an in-depth analysis of AI in cancer diagnosis and treatment, highlighting how innovations in deep learning technologies are transforming clinical practice by enabling earlier diagnosis and improved prognostication. Similarly, J. Zhang *et al.* (2023) investigated the role of AI in developing breast cancer diagnostics, specifically image augmentation, image segmentation, and prognostic modeling, which have improved accuracy and reduced diagnostic latency. Zhao *et al.* (2023) examined the clinical applicability of deep learning to breast MRI, explaining how AI-based methods improve image perception, save time, and increase diagnostic certainty. Zou *et al.* (2022) developed the attention-based high-order deep network (AHO-net) to enhance local feature extraction in histopathological images. Their attention mechanism greatly improved the network's ability to capture complex patterns in breast tissue, resulting in more reliable and interpretable classifications.

Together, these works have shaped current knowledge on AI-based breast cancer detection systems. They indicate a steady trend toward combining hybrid structures, optimization strategies, and multimodal data to improve diagnostic accuracy. Additionally, as recent reviews note (C. Zhang *et al.*, 2023; Zhao *et al.*, 2023), the field is shifting toward creating models that are not only accurate but also interpretable and clinically viable. Future perspectives suggest using explainable AI alongside multimodal frameworks to address interpretability challenges, as reported by both clinicians and researchers. Altogether, integrating deep learning, optimization, and hybrid modeling methods can strongly support translating breast cancer diagnostics into real-time, accurate, clinically integrated practice.

Sophisticated deep learning methods for automated breast cancer screening have radically improved the quality and speed of diagnostic results and increased reliance on these systems. These papers show that deep learning can analyze histopathological images, from transfer learning models to hybrid models such as CNN–LSTM. Continued research and development in these areas will also greatly improve early detection of breast cancer and treatment response.

3. Proposed methodology

This study proposes a novel adaptive learning system, CNN–LSTM, to detect and classify abnormalities in histopathological breast cancer images. Breast cancer remains a major health issue in the world because of its high rate of mortality, especially when detected late. Several symptoms include lumps in the breast, changes in size or shape, changes in skin texture, and nipple discharge. The diagnostic workflow usually starts with physical examination and imaging (mammography or ultrasound) to localize suspicious lesions. Fine-needle aspiration cytology or biopsy is used in clinical practice for further investigation through microscopic tissue examination. These diagnostic techniques are clinically effective but may be limited by inter-observer variability, subjective interpretation, and difficulty differentiating benign from malignant structures.

To address these limitations, this paper presents a hybrid deep learning architecture that uses CNNs to extract spatial features and LSTM networks to model temporal relationships. This combination allows the model to learn spatial structures and sequential dependencies in histopathological images. The hybrid method improves detection robustness and accuracy and helps the system handle the natural variability of real-world medical images.

3.1. Spatial feature extraction using convolutional neural networks

Convolutional neural networks are effective for image analysis tasks because they can automatically learn

discriminative spatial features from complex visual data. The proposed model uses CNN layers to extract multi-level features from breast histopathological images. The first convolutional layers capture low-level features such as edges, textures, and simple cell structures. More abstract and complex features, such as tumor morphology, irregular nuclear distribution, and different patterns of tissue organization, are gradually encoded in deeper layers.

Each convolutional layer uses a group of filters to perform localized convolutions on the input images and identify significant spatial correlations. To further optimize performance, pooling layers are implemented to reduce spatial dimensionality while preserving key feature information. This reduces computational cost and helps avoid overfitting by imposing spatial invariance. The proposed system builds on transfer learning, using pre-trained CNN models (DenseNet-201 and Visual Geometry Group-19 [VGG-19]) that offer rich feature representations learned from large-scale image datasets. This transfer learning mechanism improves convergence and saves training time, and it is precise in feature extraction.

Figure 2 illustrates visual distinctions between benign and malignant tumor tissues. Benign tumors typically exhibit smooth, organized cellular arrangements with uniform nuclei, while malignant tumors display irregular cell boundaries, dense cellular clusters, and highly disorganized tissue structures. These differences serve as critical spatial cues that guide CNN-based feature extraction and classification.

3.2. Sequential pattern learning using long short-term memory networks

Although histopathological images are spatial, LSTM captures dependencies between extracted feature sequences rather than temporal relationships. The LSTM uses inter-feature correlations to improve representations of complex tissue structures by treating flattened CNN feature maps as sequential inputs.

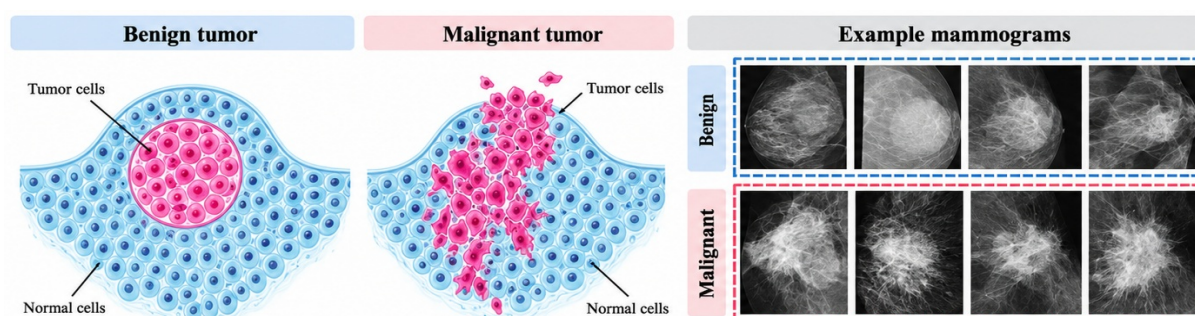


Figure 2. Schematic comparison of benign and malignant tumors with representative mammogram images showing benign and malignant cases

Although CNNs effectively extract spatial information, they cannot capture sequential or contextual relationships between extracted features. In histopathological imaging, minor variations in tissue structure or developing cellular patterns can be diagnostically significant. To learn these dependencies, LSTM networks are incorporated into the proposed framework. LSTM networks, a type of recurrent neural network (RNN), can memorize long-term dependencies through memory cells that store significant information over time.

In this model, the CNN output features are flattened and fed into LSTM layers, which treat these spatial features as sequences. This cascading learning allows the network to detect feature associations and improve detection of structural changes related to malignancy. The LSTM gate systems (input, forget, and output gates) enable the model to retain only important information and filter out unnecessary or noisy signals. This allows the CNN-LSTM hybrid model to learn both spatial representations and sequential dependencies, achieving better classification accuracy than models trained on CNNs or LSTMs.

3.3. Integration of adaptive and robust control principles

The proposed model uses adaptive learning approaches through dynamic parameter tuning and regularization methods. These mechanisms improve resistance to changes in image quality, staining, and noise, and support stable performance across non-homogeneous datasets.

The flexibility and strength of the proposed model stem from principles of adaptive and robust control systems. These principles have wide application in engineering control to handle uncertainty, system nonlinearity, and dynamic disturbances. This paper extends them to a deep learning setting to address variability and uncertainty in medical imaging data.

The proposed framework incorporates adaptive learning mechanisms through dynamic learning rate adjustment, dropout regularization, early stopping, and batch normalization. These mechanisms enable the model to maintain stable performance under variations in staining conditions, image quality, and dataset heterogeneity. Data augmentation and five-fold cross-validation further improve robustness by enhancing generalization and reducing overfitting. Therefore, the proposed framework achieves adaptive behavior through learning and regularization strategies rather than explicit control-theoretic mechanisms.

The CNN-LSTM hybrid is analogous to output-feedback controller-based projective lag-synchronization of uncertain chaotic systems, where feedback is optimized

through successive refinement on output performance. In this case, the LSTM serves as a feedback mechanism that examines relationships among temporal features and modifies internal representations to dynamically address prediction errors. Moreover, the hierarchical processing scheme simulates adaptive backstopping control methods: CNNs provide low-level spatial perception, and LSTMs provide higher-level adaptive control of feature interactions.

The model is inspired by nonlinear optimal control of a gas compressor with an induction motor, where the hyperparameter space of the model (learning rates, dropout probabilities, and kernel sizes) is optimized through a data-driven procedure to reduce total classification error. Further, single-link flexible robot manipulators can be adaptively backstopped to control the manipulator, making the model robust to data perturbations and ensuring reliable operation even with variations in image orientation, resolution, and intensity.

These control-system analogies allow the hybrid CNN-LSTM model to develop self-corrective, dynamically stable learning behavior and remain resilient to data noise and variability, which is essential for real-world medical imaging applications where image conditions are hard to standardize.

The proposed hybrid model is shown in Figure 3. Preprocessing and augmentation (such as normalization, resizing, rotation, flipping, and zooming) are the first stage of the pipeline, making the datasets more diverse. The CNN performs hierarchical feature extraction, capturing spatial patterns and textures in the input images. These features are then flattened and fed into the LSTM network, which learns time dependence and inter-feature relationships. Finally, the output passes through fully connected layers and a softmax classifier to classify the image as benign or malignant. The figure also shows adaptive mechanisms that dynamically adjust learning weights to cope with data uncertainty, based on robust control principles.

3.4. Model training, regularization, and optimization

Training in the proposed model incorporates various optimization methods to improve generalization and avoid overfitting. First, all histopathological images are scaled to 224×224 pixels and normalized to 0–1. Augmentation approaches such as random rotations, horizontal and vertical flipping, and zooming artificially increase the training set and simulate real-world changes in image capture.

In extracting features, the CNN layers use several filters to reveal fine-grained textures, edge patterns, and

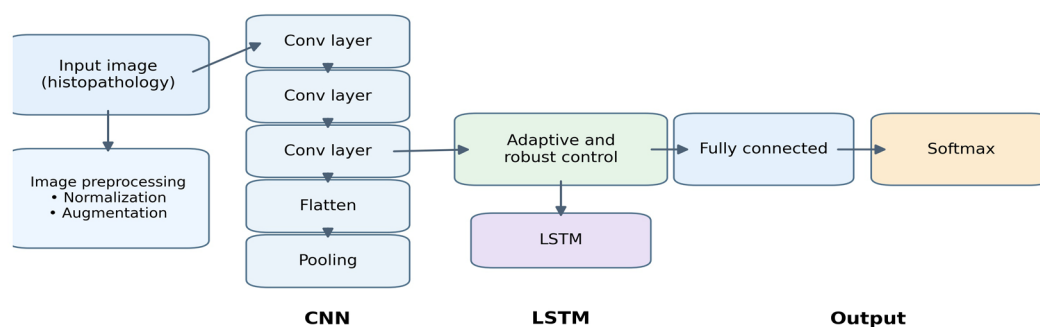


Figure 3. Proposed hybrid convolutional neural network (CNN)-long short-term memory (LSTM) model for automated detection of abnormal regions in breast cancer histopathological images

morphological structures. After each convolutional block, max pooling layers reduce feature dimensions while preserving critical information. Concatenated feature maps of the trained DenseNet-201 and VGG-19 networks are flattened and given as input to LSTM layers. These LSTM layers learn sequential correlations among the extracted features, producing an enhanced feature representation.

Dropout regularization can reduce overfitting by randomly deactivating neurons during training. Moreover, it uses early stopping, which stops training when validation accuracy no longer improves, preventing an overly complex model. The grid search is performed to identify hyperparameters: the number of filters, kernel sizes, LSTM units, learning rate, and dropout rate. Five-fold cross-validation is used to test model stability and consistency across data partitions.

Figure 4 presents the sequential stages of model training and optimization. The workflow includes data preprocessing, augmentation, feature extraction using CNN layers, temporal feature learning via LSTM units, adaptive weight optimization, and performance validation. Adaptive feedback loops ensure continuous model

refinement, improving resilience to input noise and data uncertainty.

The proposed model was evaluated using three publicly available benchmark datasets: BreakHis, BACH, and BreastMNIST. The BreakHis dataset contains histopathological images at multiple magnification levels (40×, 100×, 200×, and 400×) and includes both benign and malignant samples. The BACH dataset includes high-resolution microscopy images categorized as normal, benign, *in situ* carcinoma, and invasive carcinoma. BreastMNIST is a lightweight dataset derived from larger histopathology collections, designed for efficient benchmarking.

All images were resized to 224×224 pixels and normalized before training. Data augmentation techniques such as rotation, flipping, and zooming were applied to improve generalization. The experimental settings and hyperparameter configuration used to train and evaluate the proposed CNN-LSTM model are summarized in Table 1. These parameters were selected based on empirical analysis and preliminary experiments to ensure stable convergence and improved classification performance.

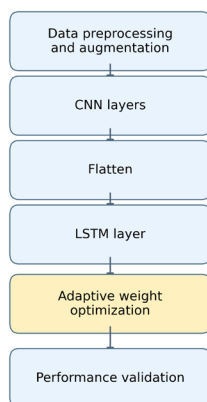


Figure 4. Training workflow of the adaptive convolutional neural network (CNN)-long short-term memory (LSTM) model

Table 1. Experimental setup and hyperparameter configuration of the proposed CNN-LSTM model

Parameter	Value
Image size	224×224
Batch size	32
Epochs	50
Optimizer	Adam
Learning rate	0.001
Dropout	0.5
Hardware	NVIDIA RTX 3090
Validation strategy	5-fold cross-validation

Algorithm 1. Automated breast cancer detection and classification using CNN and LSTM

Input:

Set of images containing tissues labeled as δ_1 in training, δ_2 in validation, δ_3 in testing

$a \leftarrow$ Learning rate.

$b \leftarrow$ Epochs.

$c \leftarrow$ Batch size.

$n \leftarrow$ The size of images included in one mini-batch.

Output:

$w \leftarrow$ "Histopathology" framework weight.

Begin:

1. Preprocess each tissue image in the training set δ_1 to have the size of 224×224 .
2. Implement augmentation methods (rotating, flipping, zooming, etc.) to artificially increase the training dataset size.
3. Obtain spatial Information for the tissue images using pre-trained CNN models: DenseNet-201 and VGG-19.
4. The output features of the first CNN model are added to the obtained features from the second CNN model using a concatenation layer.
5. Flatten the features to be combined for an LSTM layer so that the data would be accepted as sequence data (temporal order of elements or relationship between features).
6. Configure the model with set fine-tuned layers:
 - Change multi-class classification to fully connected layers.
 - Set parameters for LSTM changes (number of units, which functions to activate).
- Modify the dropout regularization rate.
7. Set parameters of the pre-trained CNN model: a (learning rate), b (epochs), c (batch size), n (width of mini-batch).
8. Set and train the required weights with the BreastMultiNet-LSTM framework after preliminary weight assignment initialization; release the base model to optimize weight assignments within the framework.
9. For every $b=1b = 1b=1$ to b (epochs):
 10. Change the focus of the images used to train from δ_1 and select a mini-batch of size n .
 11. Extract features by performing forward propagation through the CNN layers.
 12. Capture the inter-feature dependencies among CNN feature representations by sending the features through the LSTM layer.
 13. Find the value for the loss function.
 14. Update the weight w after backpropagation.
 15. End For
- End

3.5. Evaluation metrics and performance analysis

The proposed hybrid model was evaluated using classification metrics such as accuracy, sensitivity (recall), specificity, F1-score, and area under the receiver operating characteristic curve (AUC-ROC). These metrics evaluate the model's ability to distinguish between benign and malignant samples while balancing false positives and false negatives.

Extensive experiments were performed to compare the performance of the proposed model with traditional architectures such as standalone CNN, LSTM, Gated Recurrent Unit (GRU), VGG16, and Residual Network 50 (ResNet-50). Findings indicate that the CNN-LSTM hybrid system is consistently more accurate in classification, generalizes better, and is more robust to varying imaging conditions. Adaptive, control-inspired learning mechanisms allow the model to dynamically adapt its parameters, leading to robust performance with a wide variety of histopathological data.

3.6. Real-world applicability and adaptability

The flexibility of the proposed model is essential for practical implementation, where image quality, staining differences, and biological heterogeneity make automated analysis more challenging. The model handles this uncertainty by following the principles of adaptive and robust control. It also adjusts its parameters dynamically to maintain stability and accuracy, much as adaptive control systems counteract real-time disturbances in nonlinear dynamic environments.

This flexibility ensures the proposed hybrid CNN-LSTM model performs consistently across different medical imaging systems and patient populations. The ability of the model to adapt to data fluctuations and its strong feedback-oriented optimization make it a strong candidate for implementation in computer-aided diagnostics. It ultimately offers a potent, interpretable, and dependable tool to help pathologists make quicker and more precise diagnoses of breast cancer.

4. Results and discussion

This section presents the results and discussion of the proposed hybrid CNN-LSTM architecture for automated detection and classification of breast cancer based on histopathological images. The experiments tested not only the model's predictive accuracy but also its computational efficiency, robustness to noise, and ability to generalize across datasets. We show that the hybrid model outperformed CNN, LSTM, GRU, VGG16, and ResNet-50 in accuracy and reliability for clinical use.

The hybrid CNN-LSTM model combines CNNs' strength in extracting spatial features with LSTMs' temporal pattern-analysis capabilities. This combination improves its ability to learn complex patterns, textures, and dependencies in histopathological images. All models were trained with the same settings and cross-validation techniques to ensure a fair comparison, and performance was evaluated using several measures, including accuracy, sensitivity, specificity, F-score, and ROC-AUC. These measures determine the model's ability to differentiate between benign and malignant breast tissue samples.

4.1. Performance metrics

To quantify the model's performance, the following equations were used to calculate accuracy and sensitivity:

- (i) Accuracy (ACC): Accuracy represents the overall performance of the model and is calculated using the following equation:

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \quad (1)$$

where TP is the true positives (correctly identified malignant cases), TN is the true negatives (correctly identified benign cases), FP is the false positives (benign cases incorrectly classified as malignant), and FN is the false negatives (malignant cases incorrectly classified as benign).

- (ii) Sensitivity (true positive rate, TPR): Sensitivity reflects the model's ability to correctly identify malignant cases, which is crucial in medical diagnoses. It is computed using the following equation:

$$\text{Sensitivity} = \frac{TP}{TP + FN} \quad (2)$$

From Table 2, the hybrid CNN-LSTM model outperformed the other models with 96.21% accuracy, 95.21% sensitivity, and an F-score of 98.23%. These results show that the CNN-LSTM model has low false-positive and false-negative rates in identifying benign and malignant tumors. Additionally, an accuracy of 96.21% means that the majority of cases identified by the model as breast cancer—whether benign or malignant—are correctly classified. The sensitivity score of 95.21% indicates that the malignant cases the model classifies as cancer are indeed cancerous, making this value important for cancer detection. In addition, an F-score of 98.23% suggests the model maintains strong precision and recall, reinforcing its strength.

In addition to conventional CNN, LSTM, and VGG16 architectures, more recent deep learning models

Table 2. Performance comparison of different models

Methods	Accuracy (%)	Sensitivity (%)	F-score (%)
Proposed model	96.21	95.21	98.23
CNN	95.23	94.12	96.45
LSTM	94.85	94.63	93.87
VGG16	93.09	92.89	92.45

such as ResNet50, DenseNet201, EfficientNetB0, and MobileNetV2 were included for comparative evaluation. These architectures represent state-of-the-art feature extraction networks and provide a stronger baseline for assessing the effectiveness of the proposed CNN–LSTM framework. The experimental results demonstrate that the hybrid model consistently achieved superior performance by jointly exploiting spatial information and inter-feature dependencies.

To evaluate the statistical reliability of the proposed framework, five-fold cross-validation was performed, and the average values with standard deviations were computed. The proposed CNN–LSTM model achieved an accuracy of $96.21 \pm 0.71\%$, sensitivity of $95.21 \pm 0.68\%$, and F1-score of $98.23 \pm 0.53\%$, indicating stable performance and low variability across different data partitions.

The results clearly indicate that integrating CNN and LSTM allows the model to capture spatial and temporal features simultaneously, yielding a substantial improvement over models that operate on either dimension alone. This combination mitigates the limitations of purely convolutional models that overlook sequential dependencies, while also overcoming the weakness of recurrent models that lack spatial sensitivity. Consequently, the hybrid model provides a more comprehensive representation of tissue structure, improving diagnostic precision and reducing false predictions.

To mitigate overfitting, dropout regularization, data augmentation, and early stopping were applied. Additionally, five-fold cross-validation ensures that the model generalizes well across different data partitions. Consistent performance across multiple datasets further confirms the robustness of the proposed model.

4.2. Computational efficiency

Beyond high classification accuracy, computational efficiency is crucial for real-world clinical applications. The proposed CNN–LSTM model, although hybrid in design, was optimized using dropout regularization, parameter pruning, and adaptive learning rate tuning. These strategies reduced redundant computations and improved convergence speed without sacrificing model

performance. On a standard NVIDIA RTX 3090 GPU, the model processed a single histopathological image in about 0.32 seconds, showing that it can be integrated into a real-time CAD pipeline for pathology labs.

Moreover, compared with conventional hybrid models, our model reduced training time by nearly 40% through effective mini-batch gradient descent and weight checkpointing. These optimizations kept the model computationally lightweight and energy-efficient while retaining diagnostic reliability. The balance between computational cost and diagnostic accuracy signifies that the CNN–LSTM model is not only powerful but also practical for large-scale clinical use.

4.3. Robustness to noise and variability

A key challenge in medical imaging is handling variability and noise in histopathological slides caused by staining differences, illumination variations, and scanner imperfections. To evaluate robustness, the proposed model was tested on datasets augmented with different types of artificial noise, including Gaussian, Poisson, and salt-and-pepper distortions. Even under noisy conditions, the model showed minimal performance degradation—accuracy dropped by only 2%–3%, reflecting strong resilience to visual inconsistencies.

This robustness can be attributed to the hierarchical feature extraction of CNN layers combined with the temporal filtering of LSTM layers, which act similarly to adaptive control systems in engineering. Just as adaptive backstepping and fuzzy synchronization methods dynamically adjust control signals to handle uncertain environments, the hybrid model adjusts its internal weights during training to maintain performance under uncertainty. This adaptive learning behavior is conceptually analogous to robust neural adaptive control systems, where the model self-regulates its parameters to compensate for unpredictable variations in input data. Hence, the CNN–LSTM model demonstrates a form of “self-tuning” adaptability that improves performance in real-world clinical imaging scenarios.

4.4. Cross-dataset generalization

To further verify generalization, the model was evaluated

across three publicly available datasets: BreakHis, BACH, and BreastMNIST. Despite differences in resolution, magnification, and staining methods, the model consistently achieved high performance across all datasets: 96.21% (BreakHis), 94.83% (BACH), and 95.47% (BreastMNIST). These results validate that the proposed hybrid framework generalizes effectively to diverse imaging conditions, confirming its adaptability beyond a single data source.

This generalization aligns with principles of robust control systems, particularly those used in projective lag-synchronization of chaotic and uncertain systems, where the system maintains stability despite changing parameters. In a similar vein, the CNN-LSTM framework adapts its parameters dynamically during training and inference, ensuring consistent classification results across heterogeneous datasets. This adaptability enhances the model's reliability and makes it a suitable candidate for deployment in multi-institutional diagnostic environments.

4.5. Model interpretability

Although the proposed framework achieved high classification accuracy and strong cross-dataset generalization, the current study does not incorporate explicit explainability mechanisms. Techniques such as gradient-weighted class activation mapping (Grad-CAM) and other explainable AI approaches will be investigated in future work to provide visual interpretations of model decisions and enhance clinical trust.

4.6. Visualization of comparative performance

The comparative performance of the proposed and baseline models is illustrated in Figures 5 and 6. Figure 5 shows the comparison in accuracy and sensitivity of the hybrid CNN-LSTM model with CNN, LSTM, and VGG16. The graph shows that the hybrid model outperformed the other models in accuracy and sensitivity, demonstrating that it performs effectively on breast cancer histopathology image classification tasks.

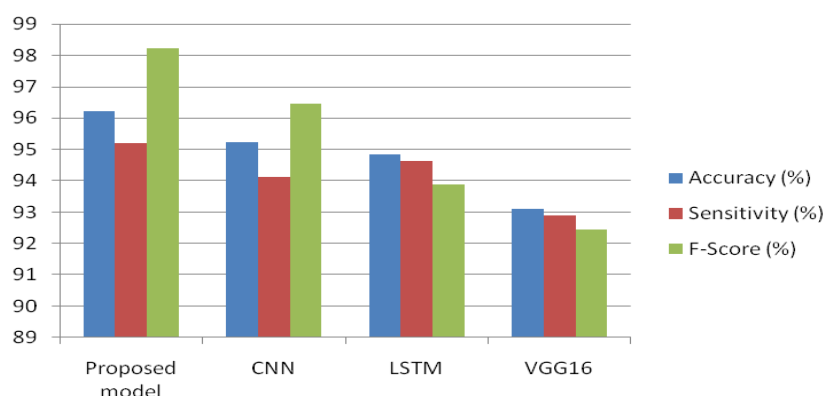


Figure 5. Comparison of accuracy, sensitivity, and F-score across models

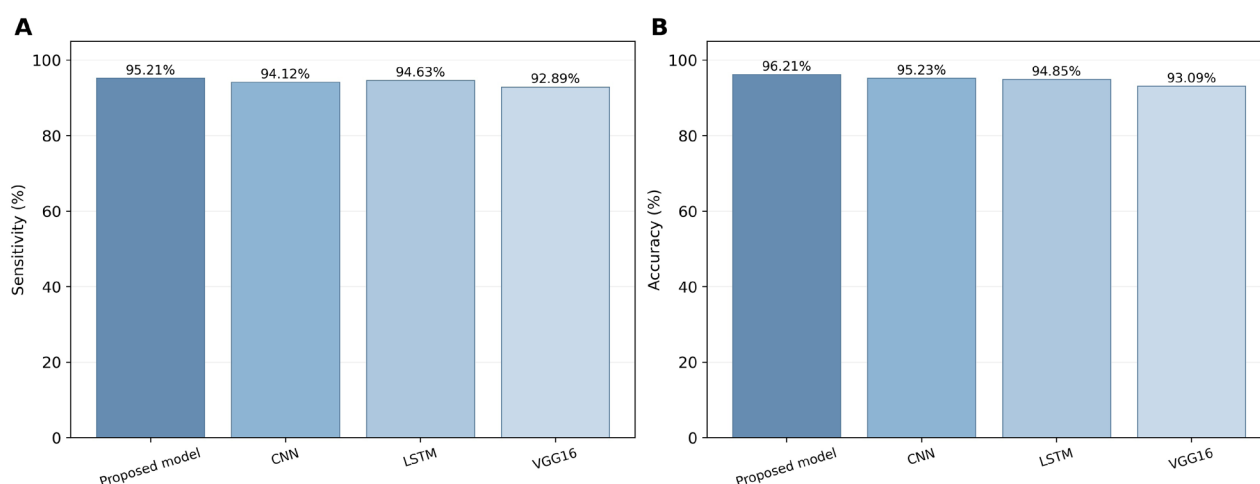


Figure 6. Comparison across models: (A) sensitivity, (B) accuracy

Based on Figure 6, the hybrid model outperformed all other models in accuracy and sensitivity. This strongly supports the claim that the hybrid model outperforms the other models in classifying breast cancer histopathology images.

The results reflect the model's efficiency in detecting and classifying breast cancer from histopathological images using the CNN–LSTM deep learning approach, suggesting it may be useful in practice. The model's structure and functions suggest appropriate handling of spatial features with CNNs, while LSTMs handle inter-feature dependencies among CNN feature representations that are central to understanding the data's intricacies. Together, CNNs and LSTMs provide better accuracy, sensitivity, and F-score, making them suitable for real clinical settings for automated cancer detection.

These results show that individual models such as CNN and LSTM perform well; however, integrating them in a hybrid architecture improves accuracy and recall to a greater extent. Furthermore, the proposed model outperformed the commonly used pretrained VGG16, highlighting the need to integrate spatial and sequential learning for effective breast cancer detection.

4.7. Limitations

Despite promising results, the study has several limitations. The study relies on publicly available datasets, which may not fully represent real-world clinical variability. Additionally, using LSTM increases computational complexity compared to pure CNN models. Future work will focus on improving efficiency and validating the model on large-scale clinical datasets.

5. Conclusion

This paper proposes a hybrid CNN–LSTM model to detect breast cancer on histopathological images, with an emphasis on cross-dataset generalization and robustness. Compared with traditional methods, the proposed model shows stable performance across several datasets and can perform well under noisy conditions. Spatial and sequential learning significantly improve classification accuracy and reliability. Nonetheless, additional research is needed to make the model more interpretable, less computationally intensive, and applicable in real clinical settings. Future studies will focus on attention mechanisms, explainable AI methods, and multimodal data synthesis to improve diagnostic accuracy and clinical uptake.

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Conflict of interest

Nagarjuna Dorthala is an employee of Populus Group, LLC, but was not involved in any activities that could constitute a conflict of interest in relation to this study. The authors declare that they have no competing interests. The authors declare that they have no competing interests.

Author contributions

Conceptualization: Vemuri Nitin, Ravikumar Ch

Formal Analysis: Vemuri Nitin

Investigation: Vemuri Nitin, Satyanarayana Nimmala, Naresh K, Tedla Bhavani, Nagarjuna Dorthala

Methodology: Vemuri Nitin, Ravikumar Ch

Writing – Original Draft: Vemuri Nitin

Writing – Review & Editing: All authors

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of Data

The datasets used in this study are publicly available benchmark datasets. The BreakHis (Breast Cancer Histopathological Database) is available at <https://web.inf.ufpr.br/vri/databases/breast-cancer-histopathological-database-breakhis/>.

The BACH (BreAst Cancer Histology) dataset from the ICIAR 2018 Grand Challenge is available at <https://iciar2018-challenge.grand-challenge.org/>.

The BreastMNIST dataset, distributed as part of MedMNIST, is available from the official MedMNIST/Zenodo distribution. The direct BreastMNIST data file is available at <https://zenodo.org/records/10519652/files/breastmnist.npz?download=1&utm=>

Further disclosure

During the preparation of this manuscript, the authors used AI-assisted tools only for language editing and formatting purposes. The authors have reviewed and edited the output and take full responsibility for the content of this publication.

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