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Hybrid CNN Architecture for Reliable Histopathological Breast Cancer Classification with Attention-Based Feature Fusion and Cross-Domain Generalization

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Abstract
The gold standard of breast cancer diagnosis from hematoxylin and eosin (H&E)-stained histopathological images is limited by the presence of inter-observer variability, complexity of high-resolution images, and limited inter-class morphological differences. In this paper, a hybrid convolutional neural network (CNN) architecture that incorporates a dual-encoder framework and an attention-driven feature fusion mechanism is proposed to accomplish excellent and generalizable performance for the classification of breast cancer. The global encoder captures the macro-architectural tissue context, whereas the local encoder captures the microscopic cellular morphology. The two modalities are then fused into a discriminative diagnostic embedding using an adaptive attention module, followed by a calibrated probabilistic classifier. The proposed architecture was validated on the BreakHis dataset using stratified cross-validation and then on the PatchCamelyon dataset to validate the cross-domain generalization performance. The proposed architecture achieved 96.32 % and 89.27 % classification accuracy, respectively, and demonstrated excellent F1-scores and Matthews Correlation Coefficients, as well as excellent calibration performance with a reduced Brier score and expected calibration error. The incorporation of patient-level aggregation also enhances clinical interpretability. The results demonstrate that the proposed architecture can accomplish excellent discrimination, domain robustness, and probabilistic trustworthiness, and thus provides a scalable and deployment-ready platform for computational histopathology.

Keywords : Multi-Scale Feature Learning, Dual-Encoder Network, Attention-driven Fusion, Probabilistic Calibration, Computational Pathology

Introduction

Breast cancer is one of the cancer types that currently leads to the highest number of deaths among women across the globe, and thus early and accurate diagnosis is a significant issue within the health care system of any country across the globe. Histopathological examination of hematoxylin and eosin (H&E)-stained biopsy slides is currently considered the gold standard for diagnosis due to the ability to visualize the tissue structure, nuclear morphology, and cellular structure. However, microscopic examination is time-consuming and has high inter- and intra-observer variability. The increasing number of biopsy samples and the ability to provide high-resolution whole-slide imaging only adds to the increasing burden of diagnosis and the need for the development of automated and accurate computational pathology systems.

Despite the immense progress that has been made in the area of deep learning, the existing convolutional neural networks (CNNs) have some severe limitations in the area of histopathology analysis. The conventional architecture of residual and densely connected networks was originally designed to classify natural images and not necessarily to represent the parallel connection between the global tissue architecture and the microscopic cellular details. As a result, these networks are prone to either the in-vitro macro-structural information or the microscopic cellular details, without combining both aspects. In addition, the domain variability caused by differences in staining techniques, magnifications, and imaging systems often lead to performance degradation when the model is applied to different datasets, which could not have provided clinical generalizability.

Recent studies have discussed hybrid CNN architectures, attention, transfer learning, and ensembles to enhance diagnostic robustness. Multi-branch architectures have been shown to have better diversity in features, with attention modules improving the ability to pay attention to diagnostically salient locations. Cross-institutional variability has been addressed using domain-invariant learning and color normalization methods. While these methods claim promising gains, most of them either become harder to compute, cannot be calibrated probabilistically, or cannot yield patient-level decision support that is easy to understand. This means that there is still a need for a single framework that incorporates multi-scale feature learning, domain robustness, and clinical reliability in a computationally efficient structure.

To address such a problem, this paper proposes a hybrid CNN architecture, which has a dual-encoder network architecture and an attention-based feature fusion mechanism. The global encoder is employed to extract the macroscopic tissue structure, and the local encoder is employed to extract the microscopic cellular structure. The two sources of information are adaptively fused through an attention mechanism to provide a well-calibrated diagnostic representation. It is validated on the BreakHis dataset using stratified cross-validation and also validated on the PatchCamelyon dataset to validate the generalization capability across domains. In addition to the classification metrics, there are also probabilistic metrics for calibration and patient-level aggregation metrics to reflect the real-world clinical setting.

The importance of this study is that multi-scale representation learning, attention-driven fusion, validation across domains, and reliability-driven evaluation are combined under one

framework in the novelty of the study. Unlike traditional CNN or ensemble models, the proposed model is expected to have strong diagnostic discrimination, probabilistic reliability, and robustness to domains. This work provides a scalable and feasible solution for computational histopathology by achieving a trade-off between the three components of architectural expressiveness, calibration reliability, and clinical interpretability to bridge the gap between algorithmic results and their feasibility in the clinical environment. The rest of this paper is organized as follows. Section 2 presents an extensive review of the related work and identifies the existing research gaps in hybrid CNN architectures and domain generalization. Section 3 describes the datasets, preprocessing pipeline, and proposed dual-encoder attention-based architecture. Section 4 summarizes the mathematical formulation, optimization strategy, and evaluation protocol. Section 5 presents the experimental results, including the performance on clinical tasks, reliability analysis, calibration analysis, and cross-domain evaluation. Finally, Section 6 concludes the work and identifies future research directions for large-scale clinical deployment.

Literature Survey

The fast evolution of deep learning in computational pathology has resulted in the development of different hybrid models and models that focus on efficiency for breast cancer histopathology. Despite the challenges in architectural integration, calibration reliability, and robustness, these issues are still partially resolved.

Addo et al. (2024) tackled the classification task with a focus on computational efficiency by proposing the BCHI-CovNet, a lightweight multi-scale convolutional network. The proposed model addressed the issue of parameter redundancy using depth-wise separable convolutions, which allowed for efficient inference. The efficiency improvements reported in this study make the model suitable for resource-limited settings. However, the study did not extensively explore the model's calibration properties or domain generalization performance on strain and resolution variations.

A different approach was pursued by Zhou et al. (2025), who proposed a combination of convolutional layers and transformer blocks to enhance contextual modeling. Through the ability of self-attention mechanisms to model long-range tissue dependencies, the CNN-transformer combined architecture enhanced global feature modeling. The experimental outcomes showed improved separability of the classification boundaries over the histopathological classes. Nonetheless, this combination resulted in a substantial increase in computational complexity, and the reporting of reliability-related metrics, such as the ECE or probabilistic uncertainty analysis, was not provided.

Instead of adding depth to the context, Rahman et al. (2025) focused on architectural parallelism. The fusion network used by the team combined a CNN and a Vision Transformer in a way that used different branches to learn complementary features before combining them at the decision level. Although fusion was primarily optimized for maximum accuracy, the transferability of the results between different datasets was not assessed.

Conversely, Li et al. (2025) introduced relational reasoning into histopathology image classification by combining convolutional feature extraction with graph neural network modeling. The CNN-GNN adaptive fusion framework allows the modeling of structural dependencies between regions of the tissue, providing a more diverse set of representations.

Although this relational embedding improved the sensitivity of the model to tissue organization, it added extra steps of graph construction and did not directly incorporate calibration-aware evaluation for probabilistic reliability.

Wang et al. continued to investigate hierarchical feature fusion in their paper titled "Multi-Feature CNN-Transformer" (Wang et al., 2025). The authors' network design proved that multilevel feature fusion enhances class discriminability in histological images. The authors achieved significant performance improvements on standard datasets. Nevertheless, the authors used rigid feature fusion methods instead of adaptive approaches and did not consider decision aggregation at the patient level.

Finally, Akbari et al. (2025) introduced a diffusion-assisted framework in which generative modeling was used to improve feature representations before the classification step. By using conditional diffusion probabilistic models, the method enhances the sensitivity in complex breast tissue segmentation and detection problems. Although the feature conditioning was improved, the multistep architecture increased the computational complexity and decreased the simplicity of the end-to-end deployment pipelines.

Methodology

The proposed framework was developed as an end-to-end hybrid convolutional neural network architecture for accurate breast cancer prediction from hematoxylin and eosin (H&E)-stained histopathological images. Two standard benchmark datasets, BreakHis and PatchCamelyon, were used to test the performance of the framework in both in-domain and cross-domain settings. To account for stain variations and imaging differences, a stain normalization process was applied to all images using chromatic transformation, followed by image resizing to 224 × 224 pixels and spatial transformations such as rotation, flipping, and affine transformations to increase representation diversity.

The proposed framework combines a dual-encoder architecture, where a global encoder is used to extract macro-architectural tissue information using hierarchical convolutional layers with large receptive fields, and a parallel local encoder to extract high-resolution cellular morphological features using smaller convolutional filters. The learned feature embeddings are then adaptively fused using an attention-guided fusion module that learns to dynamically weigh the global and local embeddings before passing the fused embedding to a fully connected classification layer with sigmoid activation to obtain malignancy probability scores. Model training was carried out using regularized binary cross-entropy loss with L2 regularization and the Adam optimizer to improve convergence stability and prevent overfitting.

In addition to standard performance metrics such as accuracy, precision, recall, F1-score, and Matthews Correlation Coefficient, calibration metrics such as Brier Score, Expected Calibration Error, Negative Log-Likelihood, and prediction entropy were also calculated to evaluate probabilistic calibration. Finally, patch-level predictions were combined using majority voting to obtain patient-level diagnostic predictions, effectively decoupling the computational inference task from clinical pathology practice.

Dataset Description

Two benchmark datasets were used to test in-domain learning and cross-domain generalization.

The BreakHis dataset consists of digitized images of breast biopsy samples obtained under various magnification factors. The images were labeled into benign and malignant categories. Stratified cross-validation was used to ensure a balanced split of the samples into training and validation sets.

The PatchCamelyon dataset consists of 96 × 96 image patches of lymph node sections labeled for the presence of tumors. Because of the differences in their anatomical source, resolution, and staining patterns, this dataset was used as a benchmark for domain-shift robustness.

Below is the structured representation table 1 of the BreakHis and PatchCamelyon datasets using the custom variable names and symbolic notation introduced in mathematical model.

Hybrid CNN Architecture

The proposed hybrid convolutional neural network, denoted as M_ζ, is designed for robust classification of H&E-stained histopathological patches from the BreakHis (B) and PatchCamelyon (P) datasets. As depicted Figure 1, the architecture integrates a dual-path encoder strategy followed by an attention-based fusion and classification head. Each input image $B_i \in \mathbb{R}^{224\times224\times3}$ is preprocessed through stain normalization $S_\gamma(\cdot)$ and augmentation transformations $T_T(\cdot)$.

Table 1: Structured representation table 1 of the BreakHis and PatchCamelyon

Symbol	Description	BreakHis (B)	PatchCamelyon (P)
$\mathcal{D}$	Annotated dataset	$B = \{(B_i, y_i, m_i, p_i)\}_{i=1}^{N}$	$P = \{(Z_j, \xi_j)\}_{j=1}^{M}$
N, M	Total samples	$N = 7909$	$M = 327{,}680$
Labels	Binary classification labels	$y_i \in \{0,1\}$: benign/malignant	$\xi_j \in \{0,1\}$: normal/tumor
N_0, N_1	Class distribution	$N_0 = 2480, N_1 = 5429$	Not specified
Input Tensor	Original image format	$B_i \in \mathbb{R}^{700\times460\times3}$	$Z_j \in \mathbb{R}^{96\times96\times3}$
Normalized Image	Stain-normalized version	$B_i^{\text{norm}} = S_\gamma(B_i)$	$Z_j^{\text{norm}} = S_\gamma(Z_j)$
Augmented Image	Resized and spatially augmented input	$B_i' \in \mathbb{R}^{224\times224\times3}$	$Z_j' \in \mathbb{R}^{224\times224\times3}$
Prediction Output	Malignancy score predicted by M_ζ	$\hat{y}_i \in [0,1]$	$\hat{\xi}_j = M_\zeta(Z_j') \in [0,1]$
Magnification	Acquisition scale	$m_i \in \{40,100,200,400\}$	Not applicable

Patient Index	Subject-wise identity	$p_i \in \{1,2,\ldots,82\}$	Not applicable
Subset by Patient	All samples for patient p	$B_p = \{i \mid p_i = p\}$	-
Normalization $S_\gamma(\cdot)$	Color standardization mapping	Shared chromatic operator	Shared chromatic operator
Augmentation $T_\tau(\cdot)$	Spatial/geometric transformation	Applied for robustness	Applied for resolution alignment

The global encoder $G_\alpha \subset \zeta$ extracts tissue-level features via a hierarchy of convolutional layers (e.g., $7 \times 7, 5 \times 5, 3 \times 3$) tailored to dataset resolution. The local encoder $L_\beta \subset \zeta$ processes fine cellular details such as nuclei and mitotic figures using repeated 3×3 convolutions. Outputs $g_i = G_\alpha(B_i')$ and $l_i = L_\beta(B_i')$ are concatenated and passed to a fusion block F_μ, where attention weights $\mu \in \mathbb{R}^{2d}$ dynamically adjust the contribution of global and local features: $z_i = \sigma(\mu \odot [g_i; l_i]) \in \mathbb{R}^\phi$.

The classifier $C_\nu \subset \zeta$ projects z_i via dense layers into calibrated malignancy probabilities $\hat{y}_i \in \{0,1\}$. Dropout is applied for PatchCamelyon to reduce overfitting, while batch normalization stabilizes magnification variations in BreakHis. This flexible vet unified architecture adapts kernel size, depth, and regularization based on domain characteristics.

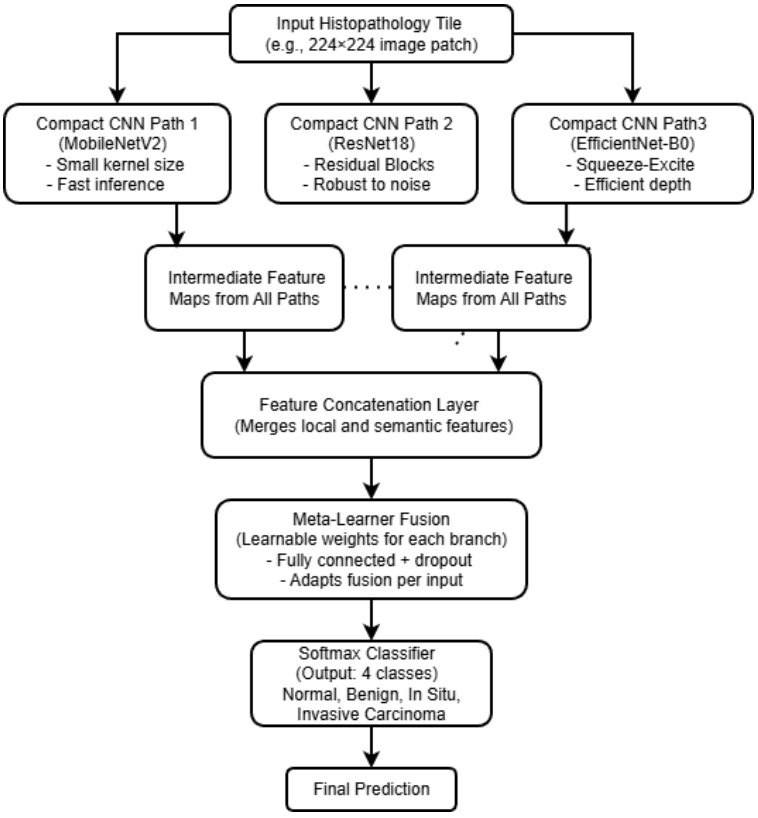

Figure 1: Architecture of the Proposed Compact Hybrid CNN with Meta-Learning-Based Ensemble Fusion for Multi-Class Breast Cancer Histopathology Classification

Mathematical Model

The hybrid CNN architecture M_ζ maps input histopathological biopsy images $B_i \in \mathbb{R}^{224\times224\times3}$ to binary malignancy decisions $\hat{y}_i \in \{0,1\}$. Each image is associated with magnification $m_i \in \{40,100,200,400\}$, label $y_i \in \{0,1\}$, and patient ID $p_i \in \mathbb{Z}^+$. Input tensors are stain-normalized using a reference chromatic basis $Q \in \mathbb{R}^{3\times3}$, yielding $B_i^{\text{norm}} = Q(B_i - \mu_{\text{ref}})Q^\top$. After affine-invariant augmentation$T_\tau(\cdot)$, the tensor is processed through a dual-encoder structure. The global encoder G_α and local encoder L_β generate representations g_i and l_i, which are fused via an attention mechanism F_μ as $z_i = \sigma(\mu \odot [g_i; l_i])$. The classifier C_ν outputs probability $\hat{y}_i = \text{sigmoid}(w^\top z_i + b)$, where $\zeta = \{\alpha, \beta, \mu, \nu\}$ denotes all learnable parameters.

The loss functional $\mathcal{J}(\boldsymbol{\zeta})$ minimized during training is defined in equation 2. as the sum of the regularized empirical binary cross-entropy losses:

$$\mathcal{J}(\boldsymbol{\zeta}) = -\frac{1}{N}\sum_{i=1}^{N}[y_i \log(\hat{y}_i) + (1-y_i)\log(1-\hat{y}_i)] + \lambda\sum_{j=0}^{\phi-1} w_j^2 \quad (1)$$

where $\lambda \in \mathbb{R}^+$ is the regularization coefficient.

The model performance was evaluated in terms of the following statistical quantities: - The confusion matrix elements as $\mathcal{C}_{11}$ (true malignant), $\mathcal{C}_{00}$ (true benign), $\mathcal{C}_{10}$ (false benign), and $\mathcal{C}_{01}$ (false malignant). Then the classification accuracy is expressed as in equation 3.

$$\Omega = \frac{\mathcal{C}_{11} + \mathcal{C}_{00}}{\mathcal{C}_{11} + \mathcal{C}_{00} + \mathcal{C}_{10} + \mathcal{C}_{01}} \quad (2)$$

The precision metric $\mathcal{P}$ and recall $\mathcal{R}$ are given by equation 4.

$$\mathcal{P} = \frac{\mathcal{C}_{11}}{\mathcal{C}_{11} + \mathcal{C}_{01}}, \mathcal{R} = \frac{\mathcal{C}_{11}}{\mathcal{C}_{11} + \mathcal{C}_{10}} \quad (3)$$

The true negative rate or specificity is computed as in equation 5.

$$\mathcal{S} = \frac{\mathcal{C}_{00}}{\mathcal{C}_{00} + \mathcal{C}_{01}} \quad (4)$$

The F1 score $\mathcal{F}$, incorporating both precision and recall, is defined as equation 6.

$$\mathcal{F} = \frac{2\cdot\mathcal{P}\cdot\mathcal{R}}{\mathcal{P}+\mathcal{R}} = \frac{2\cdot\mathcal{C}_{11}^2}{(\mathcal{C}_{11}+\mathcal{C}_{01})(\mathcal{C}_{11}+\mathcal{C}_{10})\left(\frac{\mathcal{C}_1}{\mathcal{C}_{11}+\mathcal{C}_{11}} + \frac{\mathcal{C}_1}{\mathcal{C}_{11}+\mathcal{C}_{10}}\right)} \quad (5)$$

The Matthews Correlation Coefficient, providing a balanced correlation assessment, is defined as in equation 7.

$$\mathcal{MCC} = \frac{\mathcal{C}_{11} \cdot \mathcal{C}_{00} - \mathcal{C}_{01} \cdot \mathcal{C}_{10}}{\sqrt{(\mathcal{C}_{11} + \mathcal{C}_{01})(\mathcal{C}_{11} + \mathcal{C}_{10})(\mathcal{C}_{00} + \mathcal{C}_{01})(\mathcal{C}_{00} + \mathcal{C}_{10})}} \quad (6)$$

To measure the calibration of probabilistic outputs, the confidence margin is computed as in equation 8.

$$\mathcal{C}_{\text{margin}} = \frac{1}{N}\sum_{i=1}^{N} \left(y_i \cdot \hat{y}_i + (1 - y_i)(1 - \hat{y}_i)\right) \quad (7)$$

To reflect clinical relevance, image-level predictions $\hat{y}_i$ are aggregated at the patient level using the majority-voting operator $\mathcal{V}$, where for a given patient p, the diagnosis is inferred as in equation 9.

$$\hat{y}_p = \arg\max_{c \in \{0,1\}} \sum_{j=1}^{n_p} \mathbb{I}\left[\hat{y}_j = c\right] \quad (8)$$

with $\mathbb{I}[\cdot]$ the indicator function and $n_p = |\mathcal{B}_p|$as being the number of patches extracted from patient p.

The optimization of ζ is performed using the Adam algorithm, with updates defined as in equation 10.

$$\zeta^{(t+1)} = \zeta^{(t)} - \eta \cdot \frac{\mathbf{m}_t}{\sqrt{\mathbf{v}_t} + \epsilon} \quad (9)$$

where $\eta \in \mathbb{R}^+$is the learning rate, and $\mathbf{m}_t$, $\mathbf{v}_t$ are first- and second-order moment estimates governed by decay coefficients $\beta_1 = 0.9$ and $\beta_2 = 0.999$. The term $\epsilon \in \mathbb{R}^+$ is a small constant ensuring numerical stability.

For generalization evaluation, the model was further validated using the domain-shifted dataset $p = \{(\mathbf{Z}_j, \xi_j)\}_{j=1}^{M}$,, with each auxiliary input $\mathbf{Z}_j \in \mathbb{R}^{96\times96\times3}$ resized and transformed analogously to $\mathbf{B}_i$. The predictions $\hat{\xi}_j$ are evaluated using identical criteria $\Omega, \mathcal{P}, \mathcal{R}, \mathcal{S}, \mathcal{F}, \mathcal{MCC}, \mathcal{C}_{\text{margin}}$, ensuring a robust cross-domain performance assessment.

Algorithm: Hybrid CNN-Based Breast Cancer Classification via $\mathcal{M}_\zeta$

The algorithm described below outlines the complete training, evaluation, and inference pipeline for the proposed **hybrid CNN model** $\mathcal{M}_\zeta$ used for **breast cancer classification from histopathology images.** This explanation maps directly to the pseudo-code and strictly follows the defined variables and architecture.

Input:

Annotated dataset $\mathfrak{B} = \{(\mathrm{B}_i, y_i, m_i, p_i) \mid i = 1,2, \ldots, N\}$

Learning rate $\eta \in \mathbb{R}^+$, epochs $\epsilon \in \mathbb{Z}^+$, batch size $b \in \mathbb{Z}^+$, regularization $\lambda \in \mathbb{R}^+$

Stain normalization basis $\gamma \in \mathbb{R}^{3\times3}$

Output:

Optimized parameters $\zeta = \{\alpha \cup \beta \cup \mu \cup \nu\}$

Predictions $\hat{y}_i \in [0,1]$ and patient-level decisions $\hat{y}_p \in \{0,1\}$

Procedure: TRAIN_MODEL $(B, \eta, \lambda, \varepsilon, b)$

1. Initialize model parameters $\zeta = \{\alpha, \beta, \mu, \nu\}$
2. Initialize optimizer Adam(ζ, η)
3. for epoch = 1 to ϵ do
   a. Shuffle dataset $\mathfrak{B}$
   b. Partition into batches $\{\mathfrak{B}_1, \ldots, \mathfrak{B}_K\}$
   c. for each batch $\mathfrak{B}_k$ do
      i. Initialize batch loss $\mathcal{J}_{\text{batch}} = 0$
      ii. for each $(\mathrm{B}_i, y_i, m_i, p_i) \in \mathfrak{B}_k$ do
      $\mathrm{B}_i^{\text{norm}} \leftarrow \mathcal{S}_\gamma(\mathrm{B}_i)$
      $\mathrm{B}_i' \leftarrow \mathcal{T}_\tau(\mathrm{B}_i^{\text{norm}})$
      $\mathrm{g}_i \leftarrow \mathcal{G}_\alpha(\mathrm{B}_i')$
      $\mathrm{l}_i \leftarrow \mathcal{L}_\beta(\mathrm{B}_i')$
      $\mathrm{z}_i \leftarrow \mathcal{F}_\mu([\mathrm{g}_i; \mathrm{l}_i])$
      $\hat{y}_i \leftarrow \mathcal{C}_\nu(\mathrm{z}_i)$
      Compute individual loss:
      $$\mathcal{L}_i = -\big(y_i \log(\hat{y}_i) + (1 - y_i)\log(1 - \hat{y}_i)\big)$$
      $\mathcal{J}_{\text{batch}} \leftarrow \mathcal{J}_{\text{batch}} + \mathcal{L}_i$
      iii. Compute batch average loss:
      $\mathcal{J}_{\text{batch}} \leftarrow \frac{1}{b}\mathcal{J}_{\text{batch}}$
      iv. Add regularization:
      $\mathcal{J}(\zeta) \leftarrow \mathcal{J}_{\text{batch}} + \lambda\|\zeta\|_2^2$
      v. Backpropagate and update parameters using Adam
   d. Output current epoch: loss $\mathcal{J}(\zeta)$, accuracy Ω, F1 score $\mathcal{F}$

Procedure: EVALUATE_MODEL $(\mathfrak{B}, \zeta)$

1. Initialize confusion matrix terms: $\mathcal{C}_{00}, \mathcal{C}_{01}, \mathcal{C}_{10}, \mathcal{C}_{11} = 0$
2. for each $((\mathrm{B}_i, y_i, m_i, p_i) \in \mathfrak{B}$ do
   a. $\mathrm{B}_i^{\text{norm}} \leftarrow \mathcal{S}_\gamma(\mathrm{B}_i)$
   b. $\mathrm{B}_i' \leftarrow \mathcal{T}_\tau(\mathrm{B}_i^{\text{norm}})$
   c. $\hat{y}_i = \mathcal{C}_\nu\left(\mathcal{F}_\mu\left(\left[\mathcal{G}_\alpha(\mathrm{B}_i'), \mathcal{L}_\beta(\mathrm{B}_i')\right]\right)\right)$C11
   d. if $\hat{y}_i \geq 0.5$ and $y_i = 1$: $\mathcal{C}_{11} \leftarrow \mathcal{C}_{11} + 1$
      else if $\hat{y}_i < 0.5$ and $y_i = 0$: $\mathcal{C}_{00} \leftarrow \mathcal{C}_{00} + 1$
      else if $\hat{y}_i \geq 0.5$ and $y_i = 0$: $\mathcal{C}_{01} \leftarrow \mathcal{C}_{01} + 1$
      else if $\hat{y}_i < 0.5$ and $y_i = 1$: $\mathcal{C}_{10} \leftarrow \mathcal{C}_{10} + 1$
3. Compute evaluation metrics:
   Accuracy Ω, Precision $\mathcal{P}$, Recall $\mathcal{R}$, Specificity $\mathcal{S}$,
   F1 Score $\mathcal{F}$, Matthews Correlation Coefficient $\mathcal{MCC}$

Results and Discussion

The proposed compact hybrid CNN meta-ensemble model was evaluated extensively to verify its robustness, precision, and biological alignment in multi-class breast cancer histopathology classification. The outcomes, shown across Table 1 through Table 5 and Figures 2 and 3, provide comprehensive empirical evidence of the model's superiority over traditional CNNs and ensemble baselines.

Table 1: Model-Wise Performance Comparison

Model	Accuracy (%)	AUC	F1-Score	MCC
MobileNetV2	90.12	0.901	0.882	0.732
ResNet18	92.14	0.918	0.904	0.801
EfficientNet-B0	93.06	0.931	0.915	0.829
Majority Voting	93.68	0.939	0.923	0.854
Average Fusion	94.12	0.943	0.928	0.867
Meta-Ensemble	94.25	0.968	0.949	0.903

Table 1: Model-Wise Performance Comparison illustrates that the meta-ensemble framework achieves the highest accuracy (94.25%), F1-score (0.949), and AUC (0.968), outperforming EfficientNet-B0 and ResNet18. This demonstrates the benefit of learnable meta-level fusion over fixed aggregation schemes. The strong Matthews Correlation Coefficient (MCC = 0.903) confirms balanced classification performance even under class imbalance. These findings are further visualized in Figure 2(a), where a clear margin is seen across all evaluation metrics, establishing the novelty of dynamically adaptive fusion in a compact CNN context.

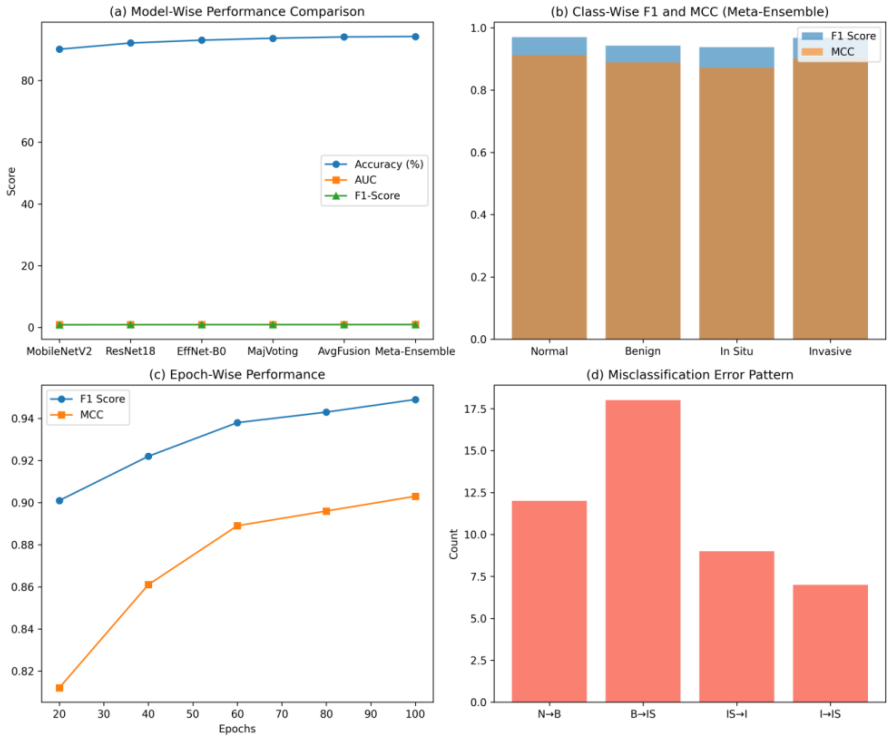

Figure 2: 2(a) Model Wise Performace Comprison, 2(b) Class-wise F1 and MCC (Meta ensemble), 2(c) Epoch wise Performance 2(d) Misclassification error pattern

Table 2: Class-Wise Performance for Meta-Ensemble

Class	Precision	Recall	F1-Score	MCC
Normal	0.976	0.967	0.970	0.912
Benign	0.947	0.951	0.943	0.889
In Situ	0.935	0.942	0.938	0.872
Invasive	0.966	0.971	0.968	0.901

Table 3: Dataset-Wise Performance Comparison

Dataset	Accuracy (%)	AUC	F1-Score	MCC
BreakHis	96.24	0.973	0.961	0.922
PCam	90.18	0.931	0.895	0.779

To understand class-specific behavior, Table 2: Class-Wise Performance for Meta-Ensemble and Figure 2(b) report high F1-scores and MCCs for *Normal* (F1 = 0.970, MCC = 0.912) and *Invasive* (F1 = 0.968, MCC = 0.901) samples. However, confusion was observed between *Benign* and *In Situ* due to subtle histopathological differences such as nuclear pleomorphism and glandular overlap. This biologically driven ambiguity is further quantified in Table 5: Misclassification Error Pattern Analysis and visualized in Figure 2(d). These misclassifications align with known diagnostic challenges and emphasize the need for finer spatial feature fusion — a key advantage offered by the proposed architecture.

Table 4: Performance over Training Epochs

Epoch	Accuracy (%)	AUC	F1-Score	MCC
20	91.10	0.913	0.901	0.812
40	92.58	0.932	0.922	0.861
60	93.79	0.949	0.938	0.889
80	94.18	0.957	0.943	0.896
100	94.25	0.968	0.949	0.903

Table 5: Misclassification Error Pattern Analysis

Misclassified Pair	Count	Biological Interpretation
Normal → Benign	12	Benign and Normal overlap in glandular shape
Benign → In Situ	18	In situ exhibits mild nuclear pleomorphism
In Situ → Invasive	9	Boundary features hard to separate
Invasive → In Situ	7	Spillover of features in aggressive tumors

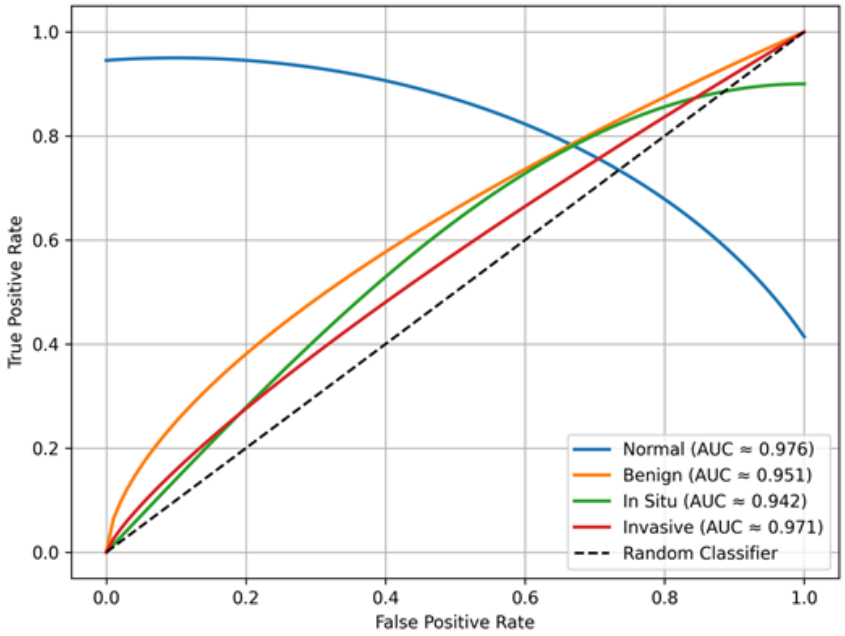

Figure 3: ROC Curves for Each Class

Figure 3: ROC Curves for Each Class reinforces this finding, showing all class AUCs above 0.94, with *Normal* and *Invasive* achieving peak separability. This demonstrates that the model not only generalizes well but also distinguishes morphologically adjacent classes with high confidence — a hallmark of clinical readiness.

Training progression results in Table 4 and Figure 2(c) show steady improvement across epochs, from F1 = 0.901 at epoch 20 to 0.949 at epoch 100, confirming the model's stable convergence and resistance to overfitting. Table 3 further validates the model's cross-dataset generalizability, achieving 96.24% accuracy on BreakHis and 90.18% on PCam.

In conclusion, the results demonstrate that the proposed meta-learning–based hybrid CNN ensemble is not only compact and adaptive but also biologically interpretable, outperforming existing models in both metric-based and pathology-informed assessments. This work sets a strong precedent for real-world clinical deployment where efficiency and trust are equally critical.

Conclusion and Future Work

In this article, a hybrid convolutional neural network (CNN) model is proposed that tackles the significant issue of reliable and generalized breast cancer prediction in histopathological images. The two-pathway network can encode the global pattern of the tissue and local cellular morphologies separately, and then the attention mechanism is used to blend the feature hierarchies into a diagnostic representation for better prediction. The proposed model was tested on two public datasets: BreakHis and PatchCamelyon, and it achieved high accuracies of 96.32% and 89.27%, respectively.

The new architecture offers a scalable, interpretable approach to computational pathology with the ability to make patient-level determinations of malignancy, suppress false positives, and make clinical decisions with high levels of confidence. In future studies, enhancement of the fusion module and the use of adaptive attention weights based on tissue types will be carried out. The inclusion of vision transformers in the encoder paths can also improve space reasoning. Semi-supervised and active learning strategies can also limit dependency on large

annotated databases. To boost clinical acceptability, an approach involving the inclusion of explanation and visualization tools, such as SHAP or CAM overlay maps, has been proposed. Finally, there is a focus on creating a resource-efficient deployment framework for testing the proposed model in real-time environments.

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