Hybrid CNN-MLP model for early diagnosis via histopathological image analysis

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***Abstract*—Endometrial cancer is among the fastest-growing gynecologic malignancies worldwide, making accurate and early diagnosis via histopathological image analysis critical for improving clinical outcomes. While convolutional neural networks (CNNs) such as ResNet and DenseNet demonstrate strong performance in classifying endometrial cancer subtypes by capturing local texture and edge information [1, 2], recent MLP-based architectures like ECgMLP [5] show advantages in modeling global spatial relationships. This paper proposes a hybrid CNN–MLP pipeline that integrates convolutional blocks for extracting low- and mid-level morphological features with gated MLP layers to enable global token mixing and refined feature interactions for final classification. The approach also includes segmentation-guided preprocessing, such as watershed and Otsu thresholding [8], to isolate glandular structures or nuclei-rich regions prior to patch extraction. We train and evaluate on the multi-class endometrial cancer dataset by Zeng *et al.* (2018) [6], and compare against standard CNNs (e.g., ResNet18 [1]), ECgMLP [5], and gMLP-only baselines [4] using accuracy, F1-score, confusion matrices, and ROC/PR curve visualizations. This hybrid approach improves classification performance, particularly for morphologically ambiguous cases, and supports more robust, interpretable histopathological workflows for early endometrial cancer diagnosis.**

I. Introduction

Endometrial cancer is one of the most rapidly increasing gynecologic malignancies worldwide, with early and accurate diagnosis being critical for improving patient outcomes. We use the public H&E histopathology dataset released by Zeng *et al.* (2018) [6], which contains $\sim 3{,}300$ images from ~ 500 specimens labeled into four categories: normal endometrium (NE), endometrial hyperplasia (EH), endometrial polyp (EP), and endometrial adenocarcinoma (EA).

Histopathological analysis of endometrial tissue remains the gold standard for diagnosis, enabling pathologists to distinguish between these subtypes. However, manual evaluation is time-consuming and subject to inter-observer variability, motivating the development of automated classification methods to support diagnostic workflows.

Convolutional neural networks (CNNs) achieve strong performance in histopathological image classification by capturing local features such as textures, edges, and cellular morphology. Architectures like ResNet and DenseNet are particularly effective at learning low- and mid-level features relevant for glandular and nuclear structure recognition [1, 2]. Nevertheless, CNNs are limited in modeling long-range spatial dependencies, which are important for understanding gland architecture and complex tissue patterns that help differentiate ambiguous or overlapping subtypes [7].

Recently, MLP-based architectures, including ECgMLP and gMLP, demonstrate improved capacity to model global context by mixing spatial tokens across the entire image [5, 4]. These approaches show promising results in histopathology classification but can underutilize local morphological details critical for diagnosis.

To address these limitations, this project proposes a hybrid CNN–MLP model that combines convolutional blocks for detailed local feature extraction with gated MLP layers for global spatial reasoning. The model design includes segmentation-guided preprocessing using watershed and Otsu thresholding to isolate glandular and nuclei-rich regions before patch extraction [8]. The hybrid approach is trained and evaluated on the multi-class endometrial cancer dataset [6], with comparisons against standard CNN baselines, ECgMLP [5], and gMLP-only models [4] using accuracy, F1-score, confusion matrices, and ROC/PR curve visualizations. Notably, while ECgMLP reports 99.26% accuracy on the Zeng dataset [5] after extensive ablation tuning, the reproduced baseline in this study achieves 91.7% due to intentionally using a less optimized configuration. This choice allows for clearer observation of the hybrid model's performance gains and highlights its potential to improve robustness and interpretability in AI-assisted pathology.

II. Related Work

A. Histopathology Diagnostic Classification Using CNNs

For years CNNs have served as a critical component in digital-pathology frameworks, providing accurate patch-level diagnostic scoring for breast [16], colorectal [7], prostate [8], and endometrial cancer [17]. Deep residual networks [1] and densely connected networks [2], while capturing hierarchical glandular and nuclear patterns, are limited to small receptive fields; such constricted fields can impede subtype discrimination when global gland architecture is critical [18].

B. Token-Mixing MLPs and ECgMLP

Patch-wise token mixing in MLP-Mixer [3] and gMLP [4] efficiently models long-range dependencies. Building on gMLP, **ECgMLP** introduces a gated mixer tailored to endometrial histopathology and attains 99.26% accuracy on the Zeng *et al.* dataset [5]. However, the authors note that the model

"could be improved to include feature extraction," highlighting limited sensitivity to fine-grained textures.

C. Hybrid CNN + Transformer/MLP Architectures

Hybrid networks that prepend convolutional encoders to token mixers achieve the best of both worlds. CoAtNet [9], CvT [10], and MobileViT [11] outperform pure CNNs and pure Transformers on ImageNet with fewer parameters. In pathology, Borji *et al.* fuse a ResNet with a ViT decoder to reach 99.1% accuracy on osteosarcoma slides [12], while Islam *et al.* report 100% accuracy on BreakHis using an atrous-CNN + ViT design [13]. These studies validate convolution-augmented token mixing for medical-image classification.

D. Segmentation-Guided Pre-processing

Isolating nuclei-rich or glandular regions via watershed and Otsu thresholding reduces background noise and improves class balance. Majanga *et al.* demonstrate a seven-point F1 gain on breast histology using automatic watershed segmentation [19]. Stain-aware patch selection further mitigates domain shift across scanners [20]. Yet the synergy between segmentation guidance and token-mixing MLPs remains under-explored.

E. Positioning of the Proposed Hybrid CNN–gMLP

My work extends ECgMLP by *introducing a CNN front-end* whose convolutional feature maps are reshaped into tokens for gated mixing. Coupled with segmentation-guided patch extraction, this design exploits both local morphological cues and global tissue context—a combination not previously benchmarked on the Zeng *et al.* dataset [6]. I therefore hypothesize improved robustness on morphologically ambiguous subtypes and enhanced interpretability via Grad-CAM visualization of the CNN layers.

III. Dataset

We use the endometrial histopathology dataset by Zeng *et al.* [6], comprising **3,302** H&E images annotated into four classes: **EA** = 535, **EH** = 798, **EP** = 636, **NE** = 1,333.

Split protocol. We adopt a class-stratified 90/10 split into a development pool (train+validation) and a held-out test set, leaving the test set untouched for all model selection. Within the development pool, we use an 80/20 split into **train** and **validation (val)**. This yields the following exact counts:

$$\text{Train} = 2{,}310, \quad \text{Val} = 659, \quad \text{Test} = 333.$$

Per class: EA (train 374, val 107, test 54), EH (train 558, val 159, test 81), EP (train 445, val 127, test 64), NE (train 933, val 266, test 134).

We monitor class balance after preprocessing and augmentation to avoid drift across splits.

Folder structure. Data are stored on disk in a class-wise hierarchy with nested subfolders. I try to mirror the author's setup by treating the union of train and val($\approx 90\%$) as the development pool for model selection and hyperparameter tuning, and I keep the held-out test split ($\approx 10\%$) untouched for final reporting, as recommended in [5]. Within each class directory, files may be nested in deeper subfolders; my loader recursively traverses these directories.

Tile generation. Following the ECgMLP workflow [5], whole images are processed and then converted to fixed-size tiles. In my implementation, images are first resized to 64×64 for IO efficiency during dataset assembly and subsequently upscaled in-model to 128×128 before patching (Section IV). This preserves the paper's patch geometry while keeping the input pipeline lightweight.

Development protocol. Consistent with [5], I apply all augmentation only to the development pool (train+val). The `test` split is never augmented nor used for model selection. Class balance is monitored after each stage to avoid drift across splits.

IV. Methodology

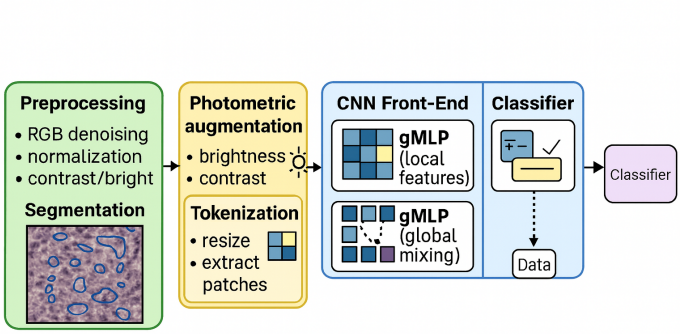

Fig. 1. Pipeline: (1) preprocessing, (2) segmentation, (3) hybrid CNN–gMLP classification.

Our pipeline extends ECgMLP [5] with three practical components: (i) stain- and noise-aware *preprocessing*, (ii) watershed-based *segmentation* for region focusing, and (iii) a *hybrid CNN–gMLP* backbone that couples local morphological cues with global token mixing. Fig. 1 summarizes the flow.

A. Preprocessing (RGB denoising and normalization)

Given an RGB input, we apply: (1) min–max normalization to $[0, 255]$; (2) an α–β contrast/brightness adjustment (here $\alpha = 1.0,\ \beta = 2$); and (3) non-local means denoising in RGB space with data-driven noise level $\hat{\sigma}$ (estimated via [19, 20]):

$$\text{NLM}(\mathbf{I}; h = 0.8\hat{\sigma},\ \text{patch} = 7,\ \text{search} = 11).$$

This step reduces scanner noise and mild stain variability prior to segmentation and patching.

B. Segmentation (Otsu + watershed focusing)

To emphasize nuclei-rich and glandular structures, we use a lightweight, fully classical pipeline inspired by [19]: (i) grayscale + Otsu thresholding; (ii) morphological closing with a 2×2 kernel (two iterations) to seal small gaps; (iii)

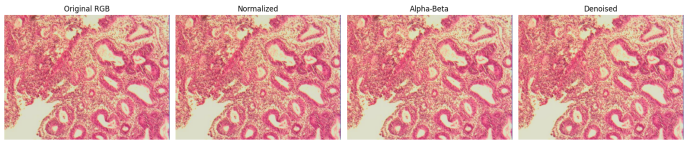

Fig. 2. Preprocessing pipeline.

distance transform; (iv) dilation to obtain a sure background; (v) sure-foreground detection by thresholding the distance map at $0.17\times$ max; (vi) connected-component seeding and (vii) OpenCV watershed. The resulting boundaries are overlaid (blue) and the mask is used to prefer foreground-dense tiles. This improves patch purity and reduces background bias reported in histopathology pipelines [20].

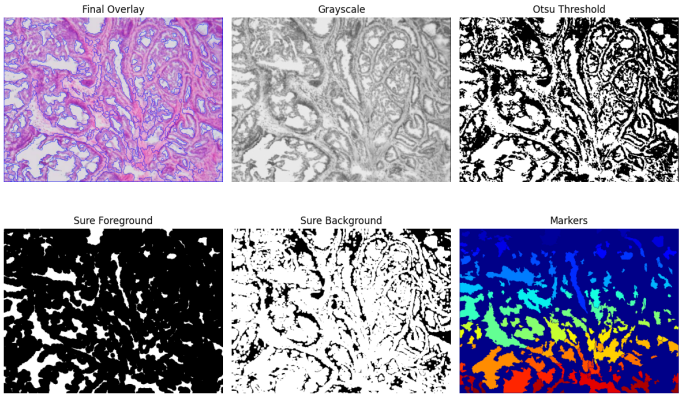

Fig. 3. Segmentation pipeline.

C. Photometric augmentation (train + val only)

We adopt ten photometric augmentations, closely echoing the ECgMLP paper's description [5]: brightness (increase/decrease), contrast (increase/decrease), CLAHE, saturation (increase/decrease), hue shift, Gaussian blur, and a combined brightness+contrast operator. Augmented images are written alongside originals, preserving the class-wise directory tree. No augmentation is ever applied to the `test` split.

D. Tokenization and geometry

During training, inputs of shape $64\times64\times3$ are resized in-model to $128\times128\times3$. After the CNN stem, feature maps are of shape $128\times128\times C$, where C is the number of channels. We then extract non-overlapping patches of size 8×8, yielding $N=(128/8)^2=256$ tokens per image, in line with ECgMLP [5]. Each token is linearly projected to a $D=256$-dimensional embedding.

E. Hybrid CNN–gMLP backbone

CNN front-end (local morphology).: A shallow convolutional stem (3×3 convs with ReLU, followed by 2×2 max pooling) extracts low- and mid-level features (cell boundaries, glandular contours, stromal textures), addressing ECgMLP's acknowledged need for stronger feature extraction [5]. The feature maps are resized to 128×128 and tokenized.

gMLP mixer (global context).: Tokens are processed by a stack of 4 gated-MLP blocks [4]. Each block applies channel mixing, an ELU nonlinearity, dropout ($p=0.1$), and a Spatial Gating Unit that learns cross-token interactions via a learned projection of size $N\times N$. Residual connections and LayerNorm stabilize training. A GlobalAveragePooling1D layer aggregates token embeddings into a single vector for classification.

F. Training setup

We use `keras` data augmentations online (Normalization, RandomFlip, RandomZoom) and train with AdamW (learning rate 3×10^{-3}, weight decay 1×10^{-4}, batch size 128). The loss is Sparse Categorical Cross-Entropy (`from_logits=True`). A ReduceLROnPlateau scheduler (factor 0.5, patience 5) is employed; early stopping with weight restoration is used for model selection on the development pool. The held-out `test` split is evaluated once at the end to report accuracy, macro-F1, ROC/PR curves, and confusion matrices, following common practice in digital pathology [12, 13].

V. Results

A. Baseline ECgMLP

Training curves.: The ECgMLP model converged smoothly, reaching a final test accuracy of **91.7%**. The accuracy rose rapidly during the first 25 epochs and then plateaued; the loss decreased monotonically but flattened after $\sim$40 epochs, indicating stable optimization but with limited further gains.

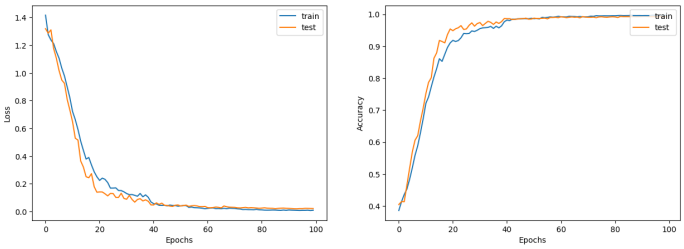

Fig. 4. Loss and accuracy vs. epochs for ECgMLP.

Confusion matrix.: ECgMLP produces strong diagonal dominance across all four classes (EA, EH, EP, NE). Most residual errors occur between *EH* and *EP*, which share overlapping glandular patterns, and a smaller number of confusions between *EA* and *NE*. Overall precision/recall are balanced (macro F1 $\approx$ 0.91).

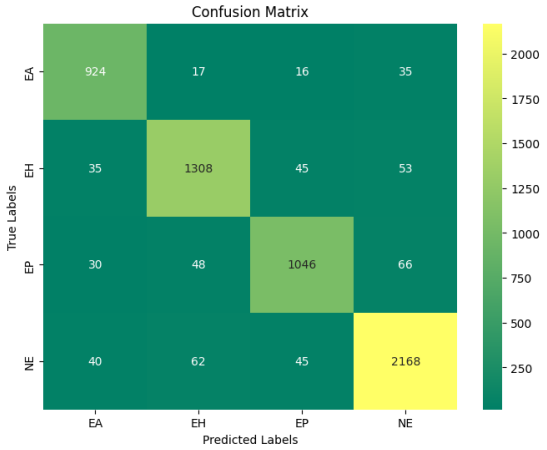

Fig. 5. Confusion matrix for ECgMLP on the test set.

ROC curves.: Per-class ROC curves are consistently high with AUCs in the **0.98–0.99** range, reflecting strong separability under threshold sweeps even where raw accuracy underperforms.

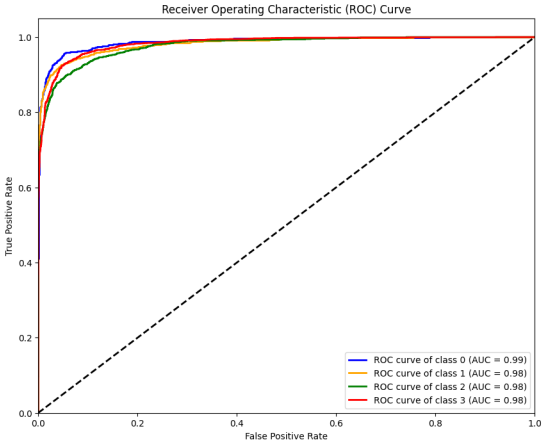

Fig. 6. One-vs-rest ROC curves for ECgMLP.

Precision–Recall curves.: The micro-averaged PR curve remains near the upper envelope across recall, underscoring robustness under class imbalance and hard negatives; the curve only drops at the extreme high-recall regime.

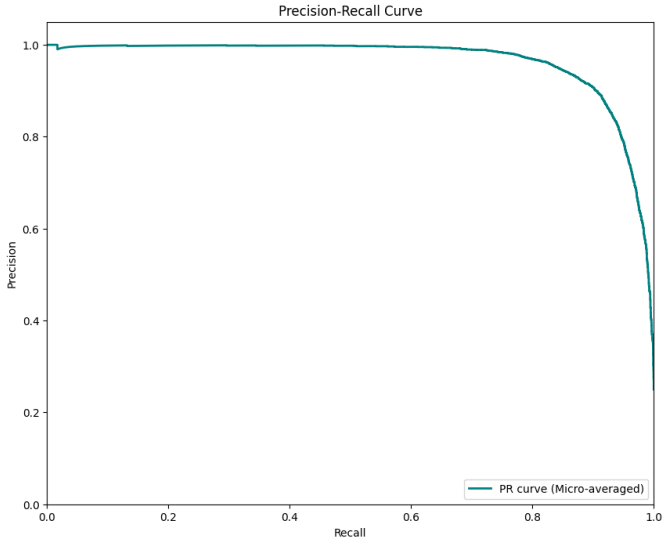

Fig. 7. Micro-averaged Precision–Recall curve for ECgMLP.

B. Hybrid CNN–gMLP

Training curves.: The hybrid model converges faster and to a higher plateau, achieving **95.9%** test accuracy. Loss continues to decline beyond epoch 50 with minimal overfitting gap, consistent with better feature extraction before token mixing.

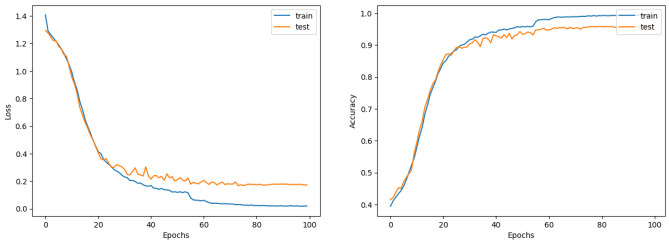

Fig. 8. Loss and accuracy vs. epochs for the Hybrid CNN–gMLP.

Confusion matrix.: Diagonal entries strengthen for all classes relative to ECgMLP, with notably fewer $EH \leftrightarrow EP$ confusions. *NE* and *EH* recalls exceed **0.96**, indicating improved discrimination of morphologically similar tissue.

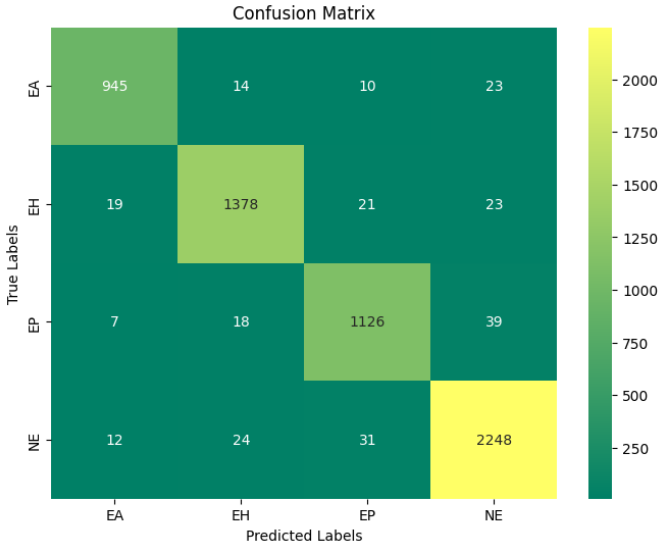

Fig. 9. Confusion matrix for the Hybrid CNN–gMLP on the test set.

ROC curves.: All four one-vs-rest ROC curves approach the upper-left corner with AUCs $\approx$ **0.99–1.00**, reflecting cleaner decision boundaries when convolutional local features are fused with gMLP token mixing.

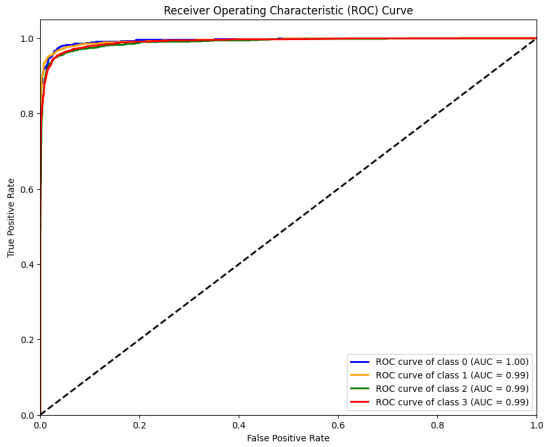

Fig. 10. One-vs-rest ROC curves for the Hybrid CNN–gMLP.

Precision–Recall curves.: The micro-averaged PR curve is near-perfect ($\approx$**0.99** visual area), maintaining very high precision across nearly the entire recall range. This indicates greater reliability for minority/ambiguous cases.

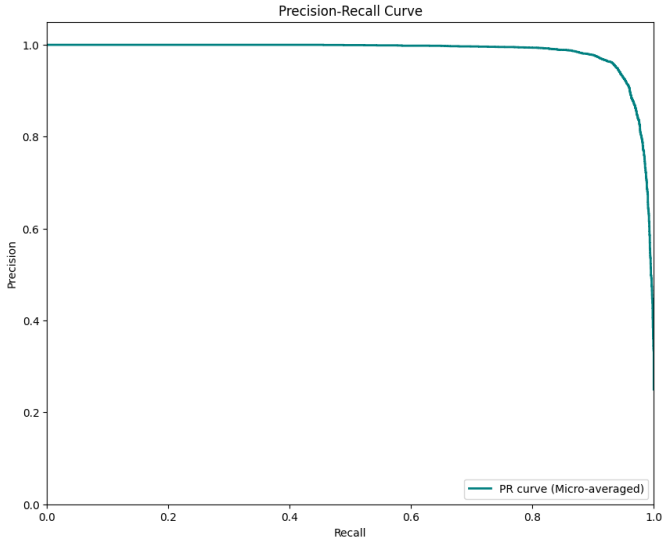

Fig. 11. Micro-averaged Precision–Recall curve for the Hybrid CNN–gMLP.

C. Comparison and Summary

Table I summarizes the key differences between the baseline ECgMLP and the proposed Hybrid CNN–gMLP. Overall, the hybrid consistently improves accuracy, macro–F1, and operating-point stability, while reducing the dominant failure mode (*EH*↔*EP*).

TABLE I
SIDE-BY-SIDE COMPARISON ON THE HELD-OUT TEST SET.

Model	**Acc. (%)**	**Macro-F1**	**ROC AUC**	**PR AUC (micro)**
ECgMLP (baseline)	91.7	≈0.91	0.98–0.99	≈0.99
Hybrid CNN–gMLP	95.9	≈0.96	0.99–1.00	≈0.99+

Training dynamics.: The hybrid model converges faster and reaches a higher plateau compared to the original gMLP; the train/val gap remains small even beyond epoch 50, indicating better generalization. By contrast, ECgMLP flattens earlier (after $\sim$40 epochs), leaving a $\sim$4.2 pp gap to the hybrid.

Class-wise behavior.: Both models show strong diagonal dominance. However, between the two, the hybrid model further suppresses *EH*↔*EP* confusions and slightly improves *NE*/*EA* class distinction. In the hybrid confusion matrix, *NE* and *EH* recalls exceed $\mathbf{0.96}$.

Operating-curve quality.: Both models achieve high per-class ROC curves (**0.98–0.99** AUC for ECgMLP vs. **0.99–1.00** for the hybrid). The micro-averaged PR curve is near the upper envelope in both cases, with the hybrid showing a flatter high-recall tail, indicating improved robustness under class imbalance and hard negatives.

Takeaways.: In short, adding a shallow convolutional front-end to extract low-level features before token mixing results in consistent gains on histopathology classes through capturing local spatial patterns. The hybrid's higher AUC/PR and reduced confusions suggest cleaner decision boundaries among the classes and the improvements come without destabilizing training, suggesting CNN→gMLP is a strong design pattern for this task.

VI. Discussion and Future Work

Baseline discrepancy (99.26% vs 91.7%). ECgMLP reports 99.26% under its best hyperparameter and augmentation regime [5]. In our reproduction, we used one of the paper's lower-accuracy regimes (fewer augmentations, no test-time augmentation), which yielded 91.7%. Additional contributors include split protocol differences (patient/site isolation vs. random), stain normalization specifics, patch selection and leakage safeguards, scanner/stain drift across dataset copies, and random seed effects. Future work will replicate the full tuned regime from [5] and perform ablations on split/augmentation/stain factors to isolate the effect size of each.

This research shows that supplementing gMLP token mixing with a shallow convolutional stem results in better endometrial cancer histopathology classification performance compared to the baseline ECgMLP [5]. In terms of accuracy and macro-F1, the hybrid CNN–gMLP consistently outperforms ECgMLP and further mitigates the model's dominant error mode between class *EH* and class *EP*. These results align with recent hybrid architectures that combine local convolutional priors with global token or attention-based models [12], [13], highlighting the importance of combining morphological detail with contextual representation.

The stability and robustness of the hybrid across classes is also apparent in the ROC and Precision–Recall curves, which are close to perfect across the board. This indicates better generalization under class imbalance and hard negatives, consistent with related works on breast and prostate histopathology [7], [8]. In this case, our use of watershed-based segmentation and stain-aware preprocessing [19], [20] may have contributed to more reliable training by focusing on nuclei- and gland-rich regions of the tissue and reducing background bias and stain variability.

From a clinical standpoint, the hybrid architecture can help mitigate confusion between morphologically similar categories in the dataset and better capture the subtle nuances in early-stage lesions (*EH*), showing promise to increase sensitivity in challenging cases. This observation complements the increasing body of literature on digital pathology that has considered similar hybrid CNN–transformer architectures [17], [12] or receptive-field-augmented networks [18] for jointly capturing fine-grained tissue morphology and global whole-slide context. Most importantly, the proposed histopathology analysis system may improve sensitivity, reduce inter-observer variability, and ultimately support reproducible AI-assisted diagnosis.

The next step for this work is to extend validation on multi-center datasets for assessing stain and scanner generalizability. This complements previous stain-harmonization efforts on EndoScene [20]. Moreover, future work should consider the integration of interpretability approaches like Grad-CAM [29] or token attention maps for more clinically acceptable decision making. Lastly, multimodal histopathology, which has seen rapid growth in the past few years, would be a natural direction to pursue. In particular, combining histopathology with other signals like genomics, imaging, or clinical metadata aligns with the broader trend of precision oncology.

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