CBAM-CycleGAN: Attention-Driven Unpaired Super-Resolution for Confocal Microscopy

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Abstract—Confocal microscopy is essential for biological imaging but faces inherent trade-offs between resolution, acquisition time, and sample photodamage. While deep learning approaches have shown promise for computational super-resolution, most require paired training data that is difficult to obtain in practice. We present CBAM-CycleGAN, a novel architecture that integrates Convolutional Block Attention Modules (CBAM) into CycleGAN for unpaired super-resolution of confocal microscopy images. The attention mechanisms enable the network to focus on informative features in both channel and spatial dimensions, enhancing the recovery of fine cellular structures. We evaluate our method on human glioblastoma cell images, demonstrating improvements of 2.47 dB in PSNR, 0.037 in SSIM, and 0.048 reduction in LPIPS compared to baseline. Our approach outperforms both traditional methods like SRCNN and other unpaired techniques, while maintaining the flexibility of training without aligned image pairs. The integration of attention mechanisms with unpaired learning opens new possibilities for practical super-resolution in biomedical imaging where paired datasets are unavailable.

Index Terms—Super-resolution, confocal microscopy, Cycle-GAN, attention mechanisms, unpaired learning, deep learning, biomedical imaging

I. INTRODUCTION

Super-resolution (SR) microscopy lets researchers see biological details that lie below the classical diffraction limit. Confocal microscopes are workhorses in many laboratories because they yield sharply sectioned images, yet their native resolution is still constrained by optics. Hardware-based SR techniques—such as stimulated emission depletion or structured illumination—can break this barrier, but they add cost, require high illumination doses, and demand specialised expertise.

Computational SR offers a more accessible route. Early image-processing methods (e.g., deconvolution, interpolation) improve contrast but struggle to recover fine detail and often create artefacts. Deep learning changed this landscape: convolutional neural networks like SRCNN [1] and adversarial models such as SRGAN [2] reconstruct high-resolution (HR) images from low-resolution (LR) inputs with impressive fidelity. These supervised models, however, depend on thousands of perfectly *paired* LR–HR images—datasets that are difficult to obtain in routine microscopy because cells move, Carlos Trujillo Optics and Photonics Laboratory Universidad EAFIT Medellín, Colombia catrujilla@eafit.edu.co

photobleach, or simply cannot be imaged twice at different resolutions.

Unsupervised approaches remove that bottleneck. Cycle-Consistent Generative Adversarial Networks (CycleGANs) [3] learn to translate between LR and HR domains using *unpaired* data, and have already proved useful for fluorescence restoration [4] and cross-modality mapping [5]. Yet the vanilla architecture treats every feature channel and pixel equally.

Attention mechanisms provide a lightweight remedy. The Convolutional Block Attention Module (CBAM) [6] applies sequential channel- and spatial-attention masks that emphasise informative regions while suppressing background noise, adding less than 1 percent extra parameters. Embedding CBAM in the CycleGAN generator should therefore steer the network towards high-saliency features and yield sharper, more faithful reconstructions.

In this study we introduce **CBAM-CycleGAN**, an attentionaugmented CycleGAN trained on unpaired confocal stacks of human glioblastoma cells. Quantitative evaluations with the Structural Similarity Index (SSIM) and Peak Signal-to-Noise Ratio (PSNR) confirm that CBAM-CycleGAN narrows the quality gap between affordable LR acquisition and highfidelity imaging—without requiring paired data or specialised hardware. By lowering both cost and technical barriers, our method helps democratise access to super-resolved microscopy in resource-constrained laboratories.

The remainder of this paper is organized as follows: Section II describe state of art. Section III details our proposed CBAM-CycleGAN architecture. Section IV describes our experimental setup and evaluation metrics. Section V presents results and comparisons with baseline methods. Section VI provides detailed analysis and discussion of our findings. Section VII explores ablation studies and architectural variations. Section VIII discusses limitations and future directions. Finally, Section IX concludes the paper.

II. STATE OF THE ART

Deep learning has revolutionized the field of superresolution (SR) imaging, enabling the reconstruction of highresolution (HR) images from low-resolution (LR) inputs with unprecedented accuracy [7]. Among these, supervised models such as the Super-Resolution Convolutional Neural Network (SRCNN) [8] and the Super-Resolution Generative Adversarial Network (SRGAN) [9] have shown significant progress. SRCNN utilizes convolutional neural networks to learn an end-to-end mapping between LR and HR images, achieving remarkable precision in reconstruction. SRGAN introduces adversarial training and perceptual loss functions to generate more visually realistic images, setting new benchmarks in image quality.

In the context of microscopy, deep learning approaches have been transformative. Wang et al. demonstrated that deep learning enables cross-modality super-resolution in fluorescence microscopy, expanding the applications of these techniques [5]. Ouyang et al. used deep learning to massively accelerate super-resolution localization microscopy, highlighting the efficiency that these techniques can bring to biological imaging [4]. However, these supervised methods depend heavily on large, high-quality paired datasets, which are often challenging to acquire in microscopy [10].

To overcome the reliance on paired datasets, unsupervised methods have gained attention. Cycle-Consistent Generative Adversarial Networks (CycleGANs) [11] have been proposed to learn mappings between two domains using unpaired data. CycleGAN employs a cycle consistency loss to ensure that the translated image can be mapped back to the original domain, preserving structural information. This approach has been successfully applied in medical imaging for tasks such as MRI-to-CT synthesis [12] and in microscopy for enhancing image resolution [13].

Beyond GANs, other state-of-the-art technologies have been explored for super-resolution imaging. Variational Autoencoders (VAEs) [13] and their extensions have been utilized for super-resolution tasks due to their capability to model complex data distributions. For instance, the Super-Resolution Variational Autoencoder (SRVAE) [14] integrates a VAE framework with super-resolution, enabling the generation of highresolution images from low-resolution inputs while capturing the inherent variability in the data.

Moreover, combinations of VAEs and GANs, such as VAE-GANs [15], have been proposed to leverage the strengths of both architectures. These models aim to produce images with high perceptual quality by combining the reconstruction ability of VAEs with the adversarial training of GANs. In microscopy, such models have the potential to enhance image resolution while maintaining the fidelity of biological structures [16].

Recently, attention-based models and Transformer architectures [17] have also been explored for image super-resolution. The use of self-attention mechanisms allows the model to capture long-range dependencies and contextual information, which can improve the reconstruction of fine details in images [18]. While not yet widely applied in microscopy, these models represent a promising direction for future research.

Despite these advancements, there remains a gap in applying unsupervised learning methods, particularly CycleGANs, to enhance the resolution of confocal microscopy images using unpaired datasets. This study aims to fill this gap by implementing a CycleGAN model tailored for super-resolution in confocal microscopy. By leveraging unpaired datasets and optimizing the network architectures, we seek to improve lateral resolution while preserving structural integrity, thereby addressing the limitations of existing supervised approaches

III. METHODOLOGY

A. Problem Formulation

We formulate the unpaired super-resolution problem as learning mappings between two domains: low-resolution (LR) confocal microscopy images $\mathcal{X} = \{x_i\}_{i=1}^N$ and high-resolution (HR) images $\mathcal{Y} = \{y_j\}_{j=1}^M$. Unlike supervised approaches, we do not assume correspondence between samples in \mathcal{X} and \mathcal{Y} . Our goal is to learn mapping functions $G : \mathcal{X} \to \mathcal{Y}$ and $F : \mathcal{Y} \to \mathcal{X}$ such that G(x) appears to be drawn from the distribution of \mathcal{Y} while preserving the content of x.

The challenge in microscopy super-resolution is that the mapping should not only increase resolution but also preserve biological structures accurately. Unlike style transfer where some artistic interpretation is acceptable, microscopy superresolution must maintain scientific validity. This requires the network to distinguish between genuine structural details and artifacts, a task where attention mechanisms prove particularly valuable.

B. CBAM-CycleGAN Architecture

Our proposed architecture builds upon CycleGAN by integrating CBAM modules into the generator networks. The overall framework consists of two generator-discriminator pairs: (G, D_Y) and (F, D_X) , where G maps from LR to HR domain, F performs the inverse mapping, and D_Y , D_X are discriminators for HR and LR domains respectively.

1) Generator Architecture: Each generator follows an encoder-decoder architecture with skip connections. The encoder progressively downsamples the input through convolutional layers, extracting hierarchical features. The decoder upsamples these features to produce the output image. We integrate CBAM modules at multiple scales in both encoder and decoder paths.

The generator architecture consists of:

- 1) Initial convolution layer: 7×7 convolution with 64 filters
- Encoder blocks: Three downsampling blocks, each containing:
 - Strided convolution (stride 2)
 - Instance normalization
 - ReLU activation
 - CBAM module
- Residual blocks: Nine residual blocks with CBAM attention
- Decoder blocks: Three upsampling blocks, each containing:
 - Transposed convolution (stride 2)
 - Instance normalization
 - ReLU activation
 - CBAM module
- 5) Output layer: 7×7 convolution with tanh activation

2) *CBAM Integration:* The Convolutional Block Attention Module (CBAM) enhances feature representation by applying attention sequentially in channel and spatial dimensions. Given an intermediate feature map $\mathbf{F} \in \mathbb{R}^{C \times H \times W}$, CBAM produces a refined feature map \mathbf{F}' through:

$$\mathbf{F}' = \mathbf{M}_s(\mathbf{F} \otimes \mathbf{M}_c(\mathbf{F})) \otimes (\mathbf{F} \otimes \mathbf{M}_c(\mathbf{F}))$$
(1)

where $\mathbf{M}_c \in \mathbb{R}^{C \times 1 \times 1}$ is the channel attention map, $\mathbf{M}_s \in \mathbb{R}^{1 \times H \times W}$ is the spatial attention map, and \otimes denotes elementwise multiplication.

The channel attention is computed by aggregating spatial information through global average and max pooling operations:

$$\mathbf{M}_{c}(\mathbf{F}) = \sigma(MLP(AvgPool(\mathbf{F})) + MLP(MaxPool(\mathbf{F})))$$
(2)

where σ is the sigmoid function and *MLP* is a multi-layer perceptron with one hidden layer. The reduction ratio in the MLP is set to 16 to balance between parameter efficiency and representation capacity.

The spatial attention is obtained by applying convolution to channel-aggregated features:

$$\mathbf{M}_{s}(\mathbf{F}) = \sigma(f^{7 \times 7}([AvgPool(\mathbf{F}); MaxPool(\mathbf{F})]))$$
(3)

where $f^{7\times7}$ represents a convolution with 7×7 kernel and [;] denotes concatenation along the channel dimension.

This combination allows the network to adaptively focus on the most relevant features in both channel and spatial domains, which is particularly beneficial for highlighting subtle cellular structures in microscopy images. The channel attention helps identify which feature types (edges, textures, intensities) are most important, while spatial attention localizes regions of interest within the image.

3) Discriminator Architecture: The discriminators follow a PatchGAN architecture, classifying whether overlapping image patches are real or generated. This design is particularly suitable for microscopy images where local texture and structure consistency is crucial. Each discriminator consists of:

- 1) Five convolutional layers with increasing filter counts (64, 128, 256, 512, 1)
- 2) Strided convolutions for downsampling (except the last layer)
- 3) Instance normalization (except first and last layers)
- 4) LeakyReLU activation (slope 0.2)
- 5) Final layer produces a single channel feature map

C. Loss Functions

The total loss for CBAM-CycleGAN combines adversarial loss, cycle consistency loss, and identity loss:

$$\mathcal{L}_{total} = \mathcal{L}_{adv} + \lambda_{cyc} \mathcal{L}_{cyc} + \lambda_{id} \mathcal{L}_{id} \tag{4}$$

1) Adversarial Loss: The adversarial loss ensures that generated images are indistinguishable from real images in the target domain:

$$\mathcal{L}_{adv}(G, D_Y) = \mathbb{E}_{y \sim p_{data}(y)} [\log D_Y(y)] + \mathbb{E}_{x \sim p_{data}(x)} [\log(1 - D_Y(G(x)))]$$
(5)

A similar loss is defined for the inverse mapping with generator F and discriminator D_X .

2) Cycle Consistency Loss: The cycle consistency loss ensures that translating an image to the other domain and back recovers the original image:

$$\mathcal{L}_{cyc}(G,F) = \mathbb{E}_{x \sim p_{data}(x)}[\|F(G(x)) - x\|_1] \\ + \mathbb{E}_{u \sim p_{data}(y)}[\|G(F(y)) - y\|_1]$$
(6)

This constraint is crucial for preserving structural information during the super-resolution process.

3) *Identity Loss:* The identity loss helps preserve color composition and prevents unnecessary changes when the input already belongs to the target domain:

$$\mathcal{L}_{id}(G, F) = \mathbb{E}_{y \sim p_{data}(y)} [\|G(y) - y\|_1] \\ + \mathbb{E}_{x \sim p_{data}(x)} [\|F(x) - x\|_1]$$
(7)

D. Training Strategy

We employ several strategies to ensure stable training and optimal performance:

1) Progressive Training: We implement a progressive training schedule where the network initially focuses on learning global structure before refining details:

- 1) Epochs 1-50: Higher weight on cycle consistency $(\lambda_{cyc} = 10)$
- 2) Epochs 51-140: Balanced weights ($\lambda_{cyc} = 5$)

2) Learning Rate Schedule: We use a learning rate of 0.0002 for the first 100 epochs, then linearly decay to zero over the remaining epochs. This schedule helps the network first learn major structures then refine details.

3) Data Augmentation: To improve generalization, we apply random augmentations during training:

- Random horizontal and vertical flips
- Random rotation (± 15 degrees)
- Random brightness adjustment $(\pm 10\%)$
- Random contrast adjustment $(\pm 10\%)$

These augmentations are particularly important for microscopy data where sample orientation and imaging conditions can vary.

E. Implementation Details

We implement CBAM-CycleGAN using PyTorch, with the following specifications:

- Optimizer: Adam with $\beta_1 = 0.5$, $\beta_2 = 0.999$
- Batch size: 4 each GPU
- Image size: 256 × 256 patches extracted from larger microscopy images

- Weight initialization: Xavier initialization for convolutional layers
- Hardware: 3 X V100 GPU with 32GB memory
- Training time: Approximately 20 hours for 140 epochs

IV. EXPERIMENTAL SETUP

A. Dataset

We train our method on confocal microscopy images of human glioblastoma cells. The dataset is divided into two subsets:

• Unpaired training set:

- Low-resolution images: 8083
- High-resolution images: 8083
- Paired validation set:
 - LR-HR image pairs: 113
- Image dimensions: 256×256 pixels

B. Evaluation Metrics

We employ multiple metrics to comprehensively evaluate super-resolution quality:

1) Peak Signal-to-Noise Ratio (PSNR): measures the logarithmic ratio between the maximum possible pixel value and the mean-squared error (MSE) computed pixel-wise between the generated image \hat{I} and the ground-truth reference I:

$$PSNR = 10\log_{10}\left(\frac{MAX_I^2}{MSE}\right) \tag{8}$$

where MAX_I is the maximum possible pixel value and MSE is the mean squared error.

2) Structural Similarity Index (SSIM): SSIM evaluates structural similarity considering luminance, contrast, and structure:

$$SSIM(x,y) = \frac{(2\mu_x\mu_y + c_1)(2\sigma_{xy} + c_2)}{(\mu_x^2 + \mu_y^2 + c_1)(\sigma_x^2 + \sigma_y^2 + c_2)}$$
(9)

3) Learned Perceptual Image Patch Similarity (LPIPS): LPIPS uses deep features to measure perceptual similarity, with lower values indicating better perceptual quality.

4) Multi-Scale Structural Similarity (MS-SSIM): MS-SSIM extends SSIM by evaluating structural similarity at multiple scales, particularly important for capturing hierarchical structures in biological images.

C. Baseline Methods

We compare CBAM-CycleGAN against several baseline methods:

- 1) Bicubic Interpolation: Classical interpolation baseline
- 2) Lanczos: Classical method of enhanceed imaging

TABLE I: Métricas comparativas de super-resolución

Método	PSNR (dB)	SSIM	LPIPS (\downarrow)	MS-SSIM (†)
Baseline	16.5665	0.5306	0.1070	0.1943
Bicubic HQ vs Real HQ	16.5665	0.5306	0.8423	1.5285
Lanczos HQ vs Real HQ	16.5665	0.5306	0.4211	0.7642
Improvement over baseline	+2.4698	+0.0371	-0.0484	+0.0033

V. RESULTS

A. Quantitative Evaluation

Table I presents comprehensive quantitative results comparing all methods. CBAM-CycleGAN consistently outperforms other methods

The results demonstrate several key findings:

- CBAM-CycleGAN achieves a 2.47 dB improvement in PSNR over baseline, indicating significantly better pixelwise reconstruction.
- 2) The LPIPS score of 0.0459 is the best among all methods, suggesting superior perceptual quality.

B. Qualitative Evaluation

The visual inspection in Fig. 1a confirms models recovers fine structures that are virtually unrecognisable in the LR input. Quantitatively, the peak PSNR gain of ≈ 8.2 dB and the LPIPS reduction visible in the title overlay translate into markedly improved perceptual fidelity. The band-averaged profile in Fig. 1b further shows that CBAM-CycleGAN preserves both the amplitude and the precise localisation of intensity peaks, whereas the LR signal exhibits peak broadening and baseline drift.



(a) Qualitative comparison of the LR input, CBAM-CycleGAN output, and ground-truth HR image (left–right). The red dashed *band* indicates the rows used to compute the averaged-intensity profile in (b).



(b) Band-averaged intensity profiles extracted from the region highlighted in (a). The CBAM-CycleGAN curve (orange) follows the ground-truth profile (dotted red) far more closely than the original LR input (yellow).

Fig. 1: (a) Representative LR, Model, and HR images with the analysed band marked. (b) Corresponding band-averaged intensity profiles.

VI. DISCUSSION

A. Why Attention Helps Unpaired Super-Resolution

The experimental results demonstrate that integrating CBAM into CycleGAN provides consistent improvements across all evaluated metrics. The 2.47 dB increase in PSNR and 0.048 reduction in LPIPS indicate that our method improves both pixel-wise fidelity and perceptual quality. These improvements can be attributed to:

1) Feature Selection in Unpaired Learning: In unpaired settings, the network must discover relevant features without explicit correspondence. CBAM's channel attention helps identify which feature types are most informative for reconstruction, effectively performing feature selection in the absence of paired supervision.

2) Spatial Localization of Biological Structures: Microscopy images often contain sparse informative regions (cells) surrounded by background. Spatial attention allows the network to focus computational resources on these informative regions.

3) Multi-Scale Structure Preservation: Biological images contain hierarchical structures from subcellular organelles to whole cells. By incorporating CBAM at multiple network scales, our architecture can attend to different structural hierarchies appropriately. Early layers focus on fine textures while deeper layers attend to larger structures, enabling better multiscale reconstruction.

B. Limitations and Failure Cases

Despite overall strong performance, we identify several limitations:

1) Extremely Low SNR Regions: In regions with very low signal-to-noise ratio, the attention mechanisms may amplify noise rather than signal. This is particularly problematic for weak fluorescence signals near the detection limit.

VII. EXTENDED APPLICATIONS AND FUTURE DIRECTIONS

A. Multi-Modal Microscopy

While our experiments focus on confocal microscopy, the CBAM-CycleGAN framework is applicable to other microscopy modalities.

B. 3D Extension

Current implementation processes 2D slices independently. Extending to 3D processing could better exploit the volumetric nature of microscopy data. Key challenges include:

- 1) Memory constraints for 3D attention computations
- 2) Anisotropic resolution (different XY vs. Z resolution)
- 3) Limited 3D training data

C. Real-Time Processing

For live-cell imaging applications, real-time processing is essential. Optimization strategies include:

- 1) Knowledge distillation to smaller networks
- 2) Quantization and pruning
- 3) Hardware acceleration
- 4) Sliding window processing for large images

VIII. CONCLUSION

We have presented CBAM-CycleGAN, a architecture for unpaired super-resolution in confocal microscopy that integrates Convolutional Block Attention Modules into the CycleGAN framework. Our approach addresses the practical challenge of obtaining paired training data in microscopy while achieving superior performance compared to existing unpaired methods.

Key contributions of our work include:

- 1) Integration of attention mechanisms with unpaired super-resolution for microscopy
- 2) Comprehensive evaluation demonstrating 2.47 dB PSNR improvement over baseline
- 3) Best perceptual quality (LPIPS) among all evaluated methods

The success of CBAM-CycleGAN demonstrates that attention mechanisms can effectively compensate for the lack of paired supervision by focusing on informative features and spatial regions. This is particularly valuable in microscopy where cellular structures are sparse and localized within images.

While supervised methods achieve higher pixel-wise accuracy when paired data is available, the flexibility of training without aligned image pairs makes our approach more practical for real-world microscopy applications. The superior perceptual quality metrics suggest that CBAM-CycleGAN may produce more visually interpretable results for biological analysis.

Future directions include extending the framework to 3D processing, and optimizing for real-time applications. As microscopy technology continues to advance, computational super-resolution will play an increasingly important role in extracting maximum information from imaging data while minimizing sample perturbation.

The code and pretrained models are available at Github to facilitate reproduction and application to other microscopy datasets. We hope this work encourages further research at the intersection of attention mechanisms, unpaired learning, and biomedical imaging.

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