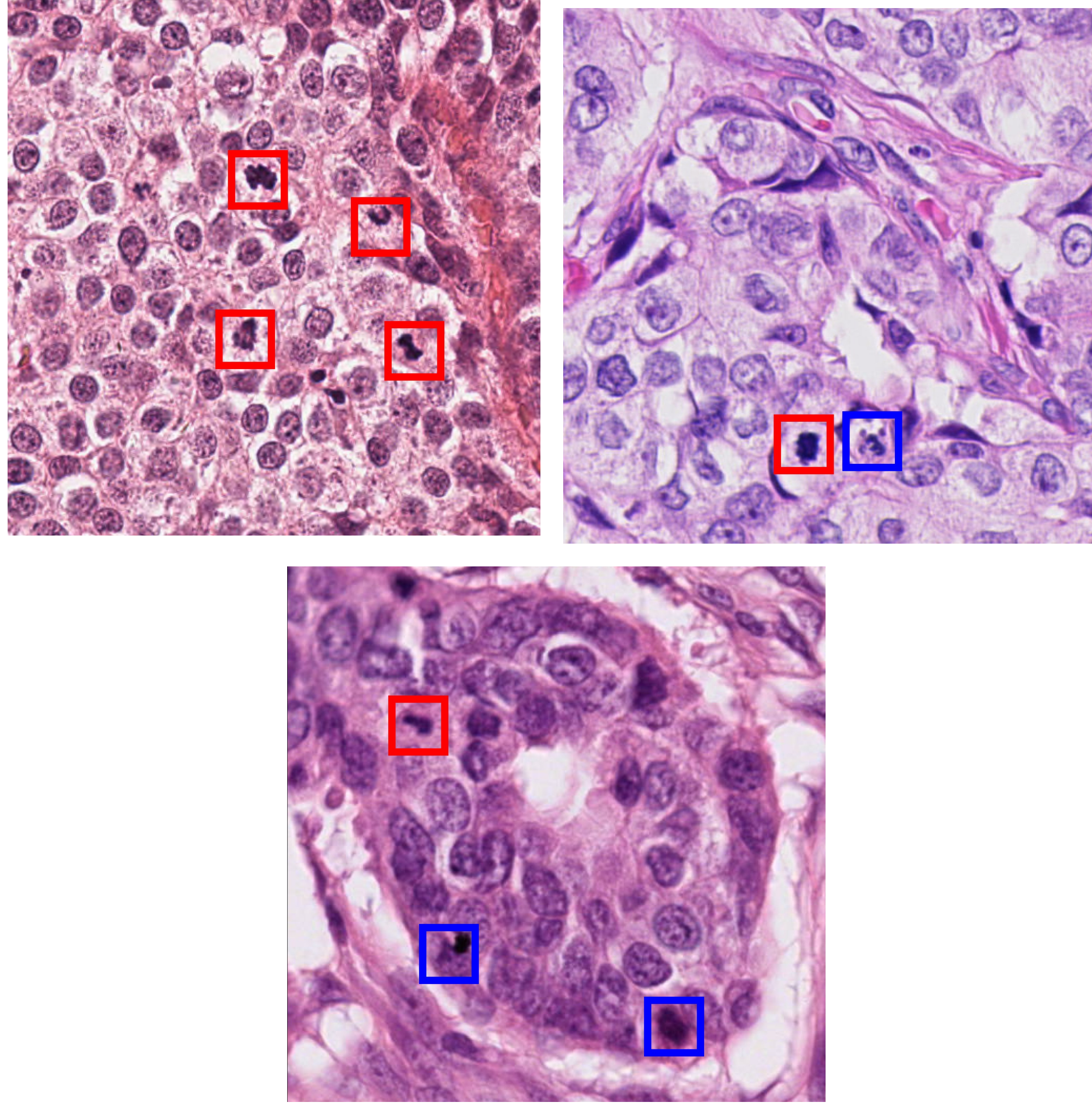


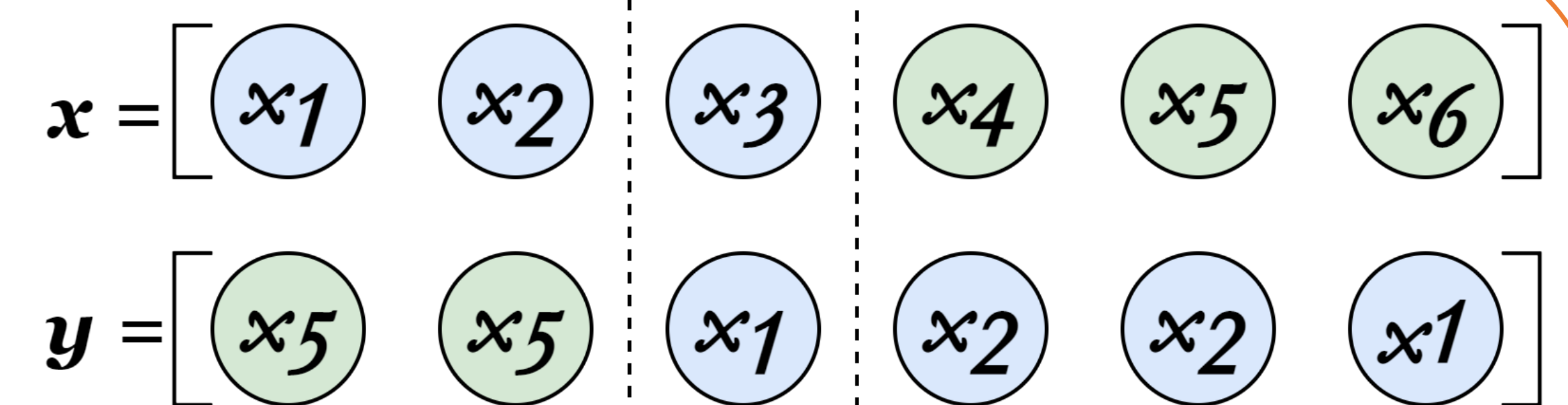
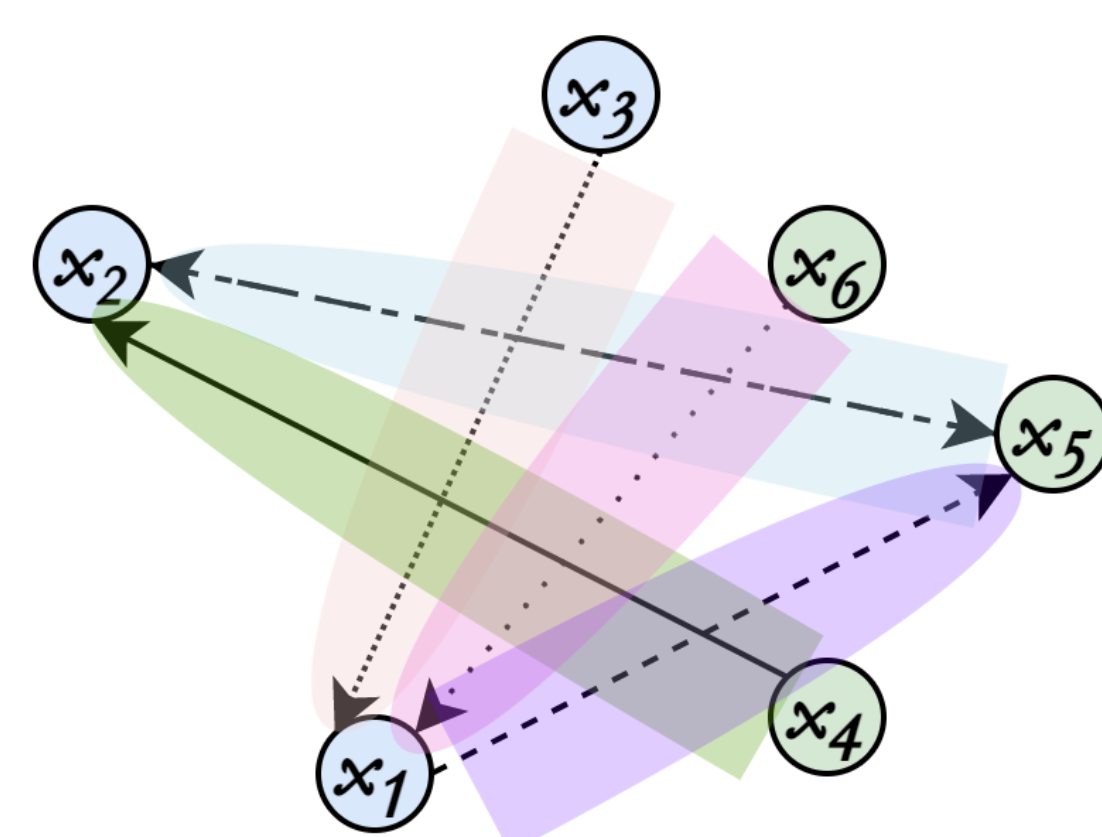
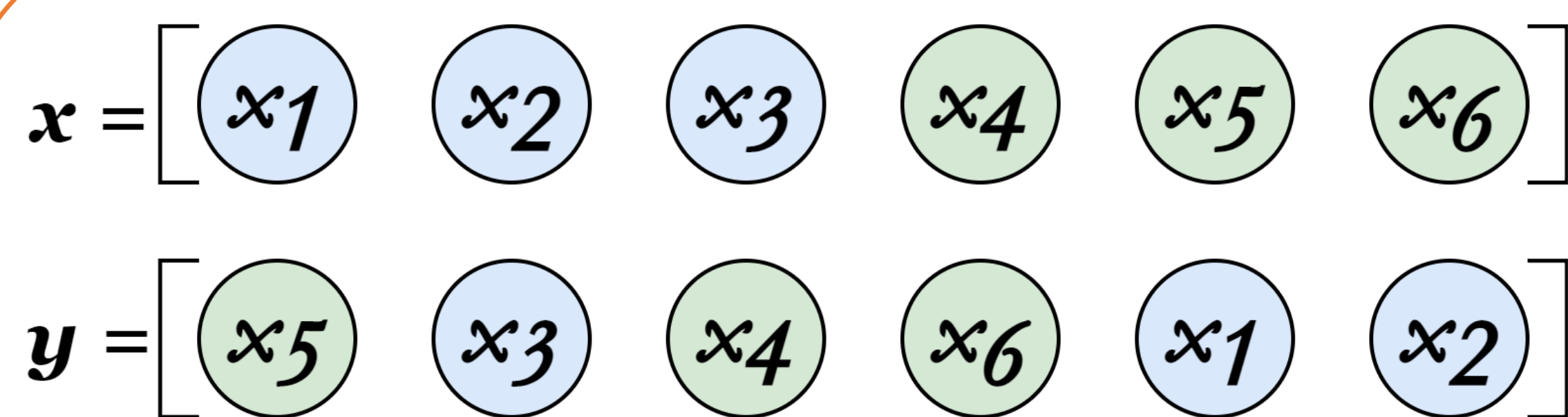
# Histopathological Image Analysis with Style-Augmented Feature Domain Mixing for Improved Generalization

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MedAGI



- Histopathological images are vital for medical diagnosis and treatment planning, providing microscopic insights into tissues and organs.
- Accurate interpretation is challenging due to variations in tissue preparation, staining, and imaging protocols, resulting in differences in image quality, tissue morphology, and staining intensity.
- Domain generalization in machine learning aims to address this challenge by enabling models to generalize to new domains or datasets.
- In histopathological images, domain generalization methods seek to enhance model generalizability by reducing dataset bias effects and increasing robustness to protocol variations.
- Style transfer-based data augmentation, exemplified by StainGAN, StainNet, and STRAP, transfers styles or textures between images, improving model generalization by diversifying training data. However, this approach has drawbacks, including time-consuming augmentation and potential collinearity issues between artistic styles.
- In contrast, the proposed method introduces feature domain style mixing, utilizing adaptive instance normalization to mix feature statistics from different images, saving time, reducing computation, and mitigating style dependencies.



A graphical illustration of FuseStyle. The shaded areas in (b) are the simulated points for augmentation. The domain label of each sample is colour-coded. There can be cases where the dot product (correlation) is the least within the domain as highlighted in the dotted rectangle in (c)

$$\gamma_i = \lambda_i \sigma(x_i) + (1 - \lambda_i) \sigma(y_i), \quad \beta_i = \lambda_i \mu(x_i) + (1 - \lambda_i) \mu(y_i)$$

$$\tilde{x}_i = \gamma_i \frac{x_i - \mu(x_i)}{\sigma(x_i)} + \beta_i$$

FEATURE MIXING

FuseStyle is applied between a layer,  $f_l$ , and  $f_{l+1}$ , and the output feature of the layer  $f_l$  is  $z_l \in \mathbb{R}^{B \times C \times W \times H}$ . Then, the correlation  $\rho \in \mathbb{R}^{B \times B}$  between different samples of the current batch can be computed by:

$$\rho = \hat{z}_l \odot \hat{z}_l^T$$

Here  $\odot$  represents the matrix multiplication,  $\{\hat{z}_l \in \mathbb{R}^{B \times C \times W \times H}\}$  is the vectorized version of the  $z_l$  and  $T$  represents the transpose operation. Next, we set  $i^{th}$  sample of the reference batch, that is,  $y_i$  to be  $x_j$ , where  $j = \arg \min_j \rho_{ij}$  and  $\rho_{ij} \in \mathbb{R}^B$  is the  $i^{th}$  row of the matrix  $\rho$ . Then, the  $i^{th}$  sample of the batch  $x$  is mixed with  $i^{th}$  sample of the batch  $y$  as mentioned get  $\tilde{x}_i$ .

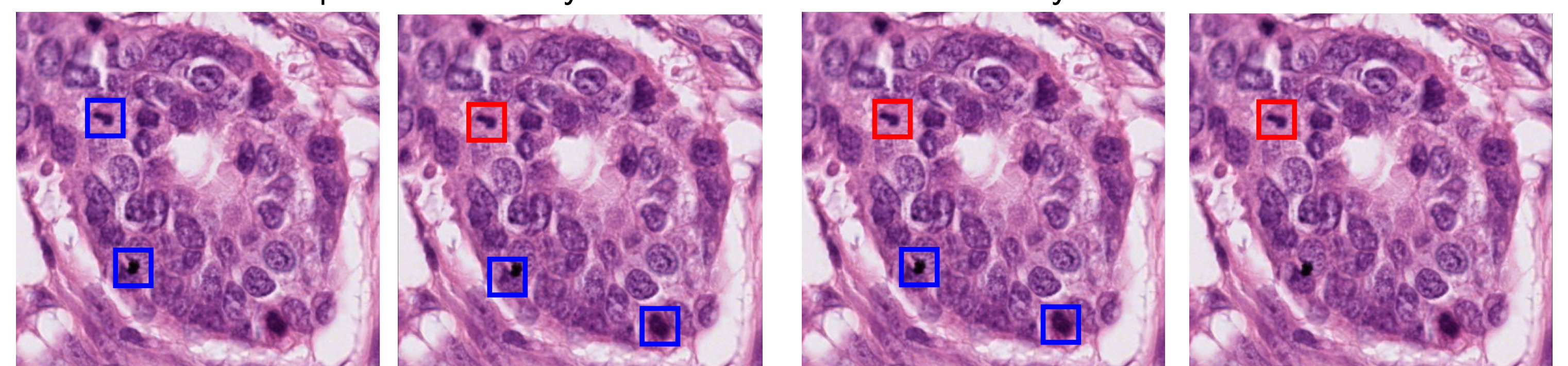
OUR PROPOSAL

Network	Methods	XR	S360	CS	Time/epoch (sec)
Train:	M1	76.42	89.45	88.76	08
	RA	<b>77.56</b>	<b>91.07</b>	<b>90.46</b>	08
	M2	67.05	88.64	90.29	08
Test:	M3	74.43	87.18	88.76	111
	RA	84.09	71.59	85.18	08
	M2	90.06	75.16	<b>92.16</b>	08
XR & CS	M3	<b>90.34</b>	75.65	91.65	08
	S360	83.07	<b>78.90</b>	89.95	111
	M1	<b>88.64</b>	89.45	72.40	08
XR & S360	RA	86.65	88.96	74.10	08
	M2	87.78	<b>90.91</b>	76.32	08
	M3	86.34	87.34	<b>78.02</b>	111

Ablation of Sample Selection Strategy using MIDOG'21 and MIDOG'22 dataset

Methods	STRAP	FuseStyle	LISA	Fish	ERM	V-REx	DomainMix	IB-IRM	GroupDRO
Test Accuracy	93.7%	90.49%	77.1%	74.7%	70.3%	71.5%	69.7%	68.9%	68.4%

Comparison of FuseStyle with SoTA methods on Camelyon17-WILDS



Mitotic figure detection by different methods in S360 image with model trained on XR & CS,

References:

- Aubreville, M., Bertram, C., Breininger, K., Jabari, S., Stathonikos, N., Veta, M.: Mitosis domain generalization challenge 2022 (Mar 2022). <https://doi.org/10.5281/zenodo.6362337>, <https://doi.org/10.5281/zenodo.6362337>
- Yamashita, R., Long, J., Banda, S., Shen, J., Rubin, D.L.: Learning domain agnostic visual representation for computational pathology using medically irrelevant style transfer augmentation. IEEE Transactions on Medical Imaging 40(12), 3945–3954 (2021). <https://doi.org/10.1109/TMI.2021.3101985>
- Koh, P.W., Sagawa, S., Marklund, H., Xie, S.M., Zhang, M., Balsubramani, A.Hu, W., Yasunaga, M., Phillips, R.L., Gao, L., et al.: Wilds: A benchmark of in-the-wild distribution shifts. In: International Conference on Machine Learning, pp. 5637–5664. PMLR (2021)

Experimental Details:

Object Detection: Dataset—MIDOG'21 and MIDOG'22, Backbone—Retina Net

Classification : Dataset—Camelyon17 WILDS, MIDOG'21, Backbone—ResNet50

Networks {Train, Test}	STRAP Test Accuracy(%)			FuseStyle Test Accuracy(%)		
	XR	S360	CS	XR	S360	CS
{S360+CS, XR}	67.33	87.99	84.67	<b>77.56</b>	<b>91.07</b>	<b>90.46</b>
{XR+CS, S360}	88.35	<b>76.78</b>	91.14	<b>90.06</b>	75.16	<b>92.16</b>
{XR+S360, CS}	<b>88.92</b>	<b>92.70</b>	<b>74.28</b>	86.65	88.96	74.10

Classification using FuseStyle and STRAP on MIDOG'21 Dataset

Network	Precision			Recall			F1 Score		
	XR	S360	CS	XR	S360	CS	XR	S360	CS
RetinaNet	0.91	0.93	0.93	0.76	0.3	0.76	0.83	0.45	0.84
STRAP	0.85	0.91	0.88	0.88	0.70	0.95	0.87	0.79	0.92
FuseStyle	0.82	0.92	0.90	0.92	0.76	0.90	0.87	0.83	0.90

Mitotic Figure Detection Analysis on MIDOG'21 Challenge Dataset.