Institute of Medical science and Technology

Development of Seamless Algorithm and Robust to Vignetting Artifact in Histological Images Obtained from Whole Slide Imaging Technique

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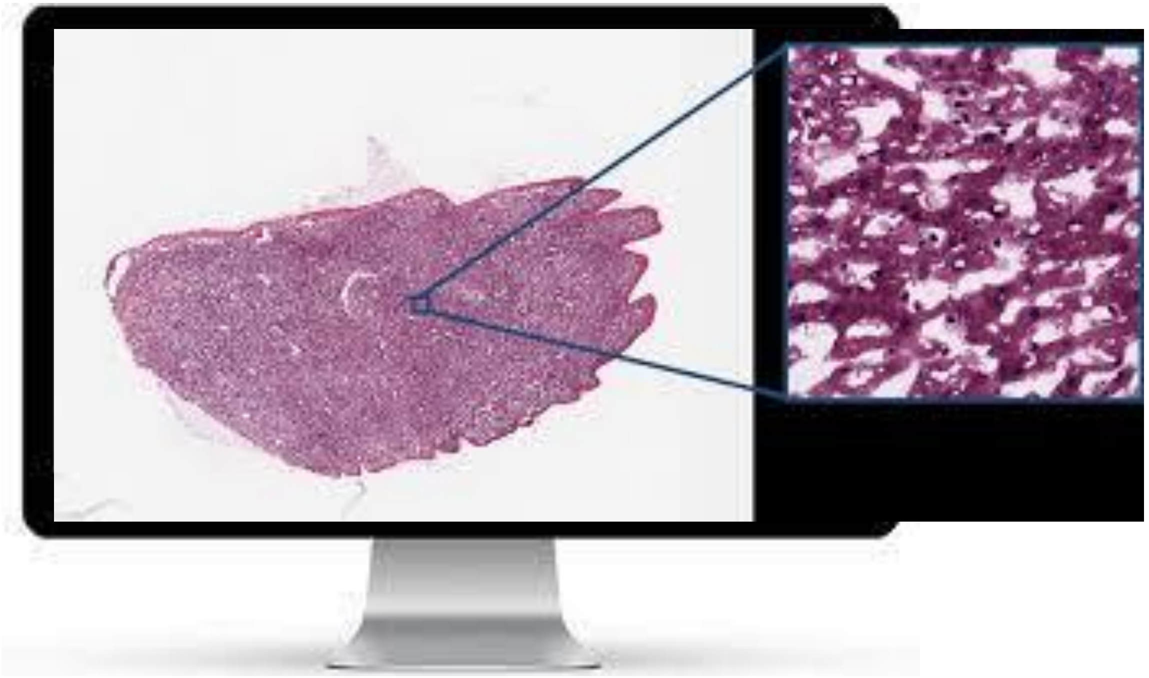
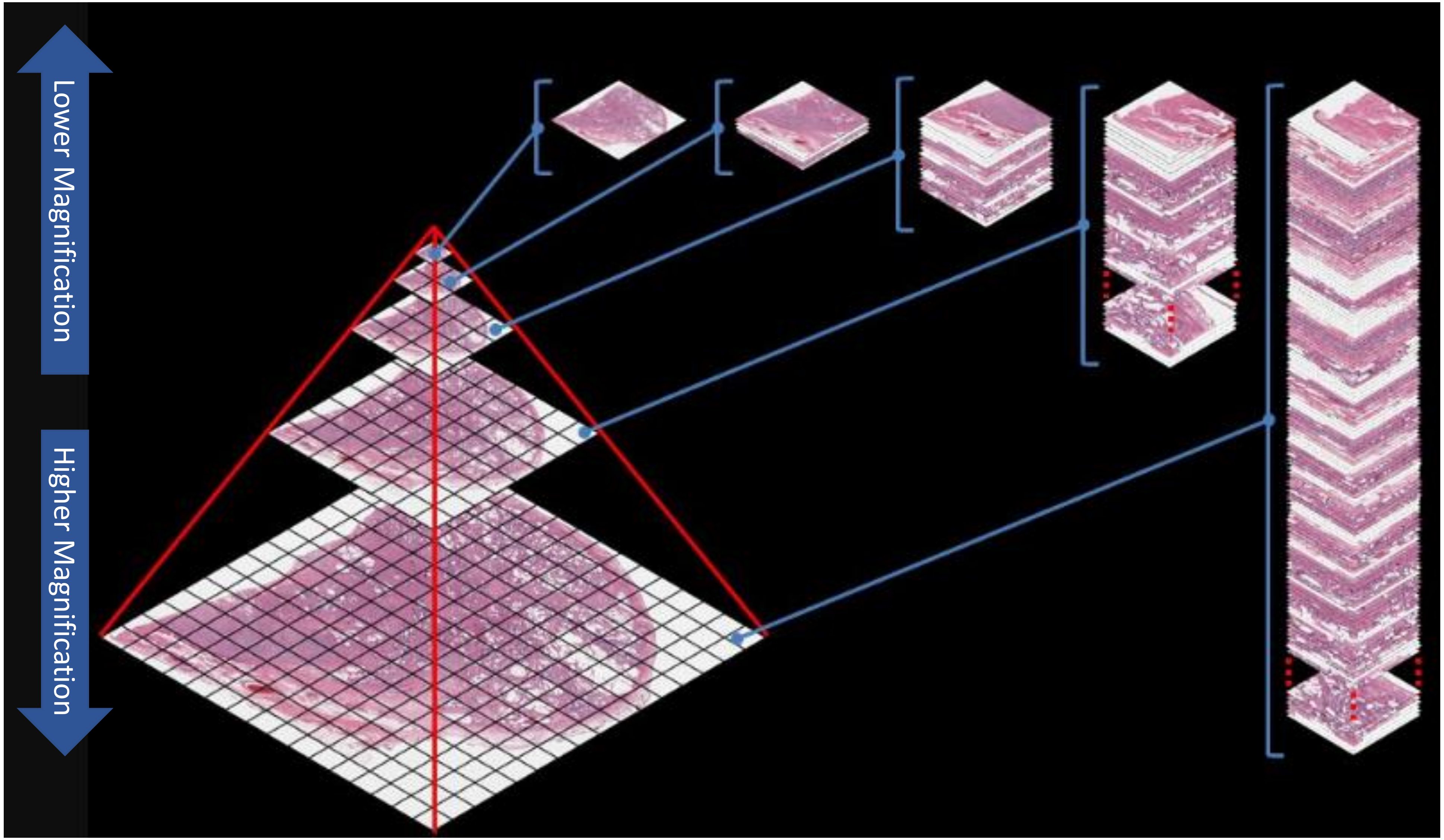
Whole Slide Imaging Technique

- Whole Slide Imaging (WSI) refers to **scanning a whole slide and creating a single high-resolution digital image**, is a relatively new technique that **solves the limited field of view (FOV) problem of traditional optical microscopes.**



Introduction



Introduction

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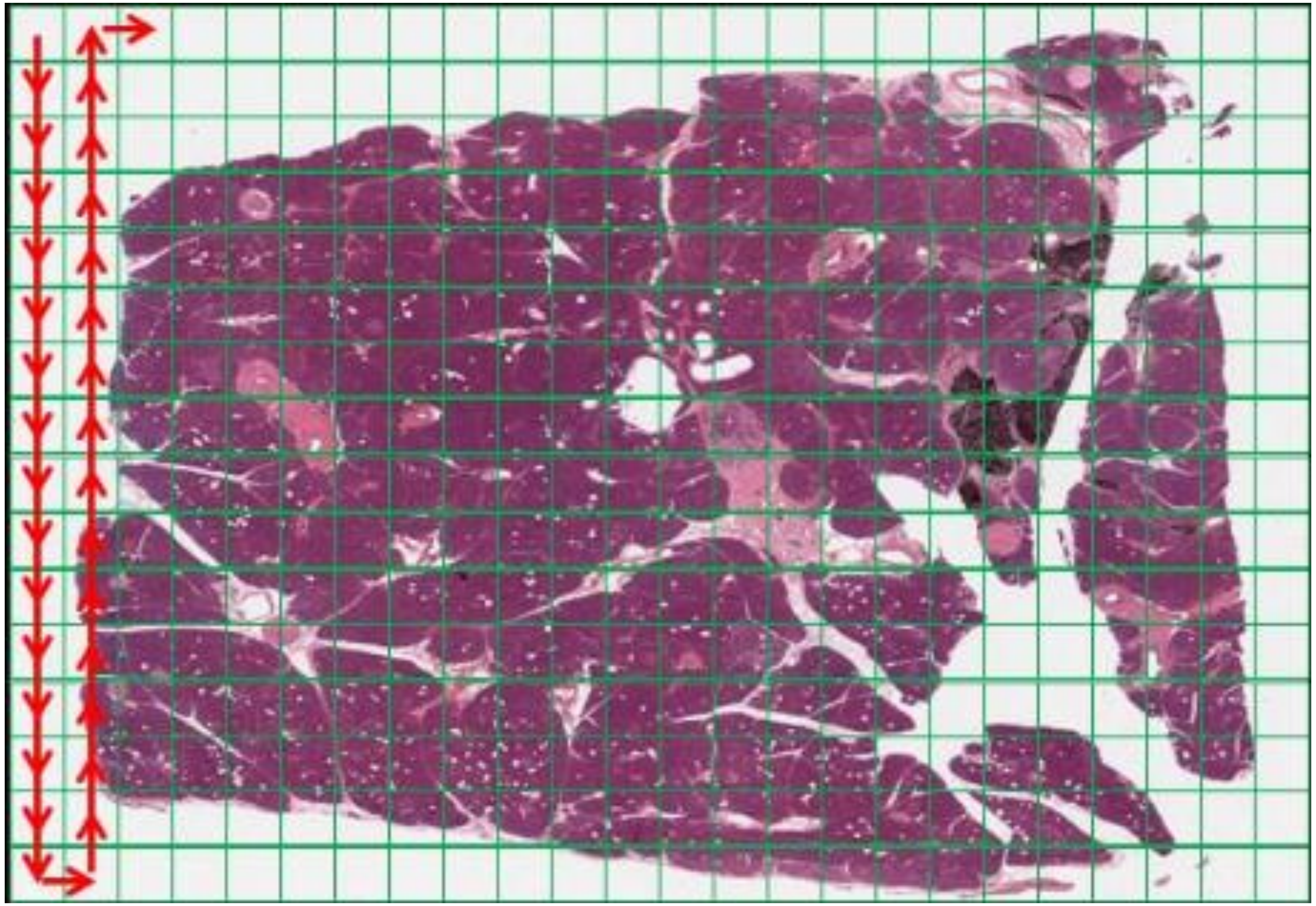
Stitching

- The slide is scanned as a series of Rectangular tiles

- The tiles are stitched (Registration) into a WSI either concurrently or after the scanning is finished



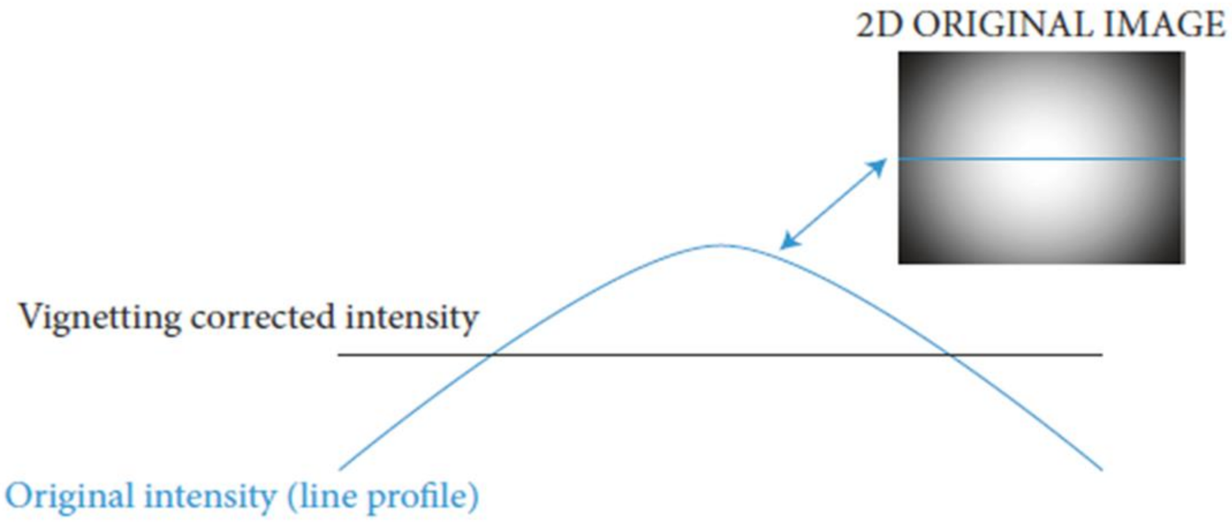
[1].Y.-O. Tak, A. Park, J. Choi, J. Eom, H.-S. Kwon, and J. B. Eom, "Simple Shading Correction Method for Brightfield Whole Slide Imaging," *Sensors*, vol. 20, no. 11, p. 3084, May 2020.
[2].Farahani N, Parwani A, Pantanowitz L. 11 June 2015. Whole slide imaging in pathology : advantages, limitations, and emerging perspectives. Pathology and Laboratory Medicine International, Volume 2015:7, Pages 23—33.

Introduction

- **Vignetting** is the lack of homogeneous intensity due to uneven background illumination, resulting in the usual darkening of the corners of the image [1].

- *Optical microscopy* data is often severely affected by vignetting (uneven illumination) or shading [2].

- If the illumination is not corrected, the **seams** in the stitched area will become obvious, which can mislead vision and lead to poor medical diagnostics and coming up processing such as registration, segmentation [3],[4].

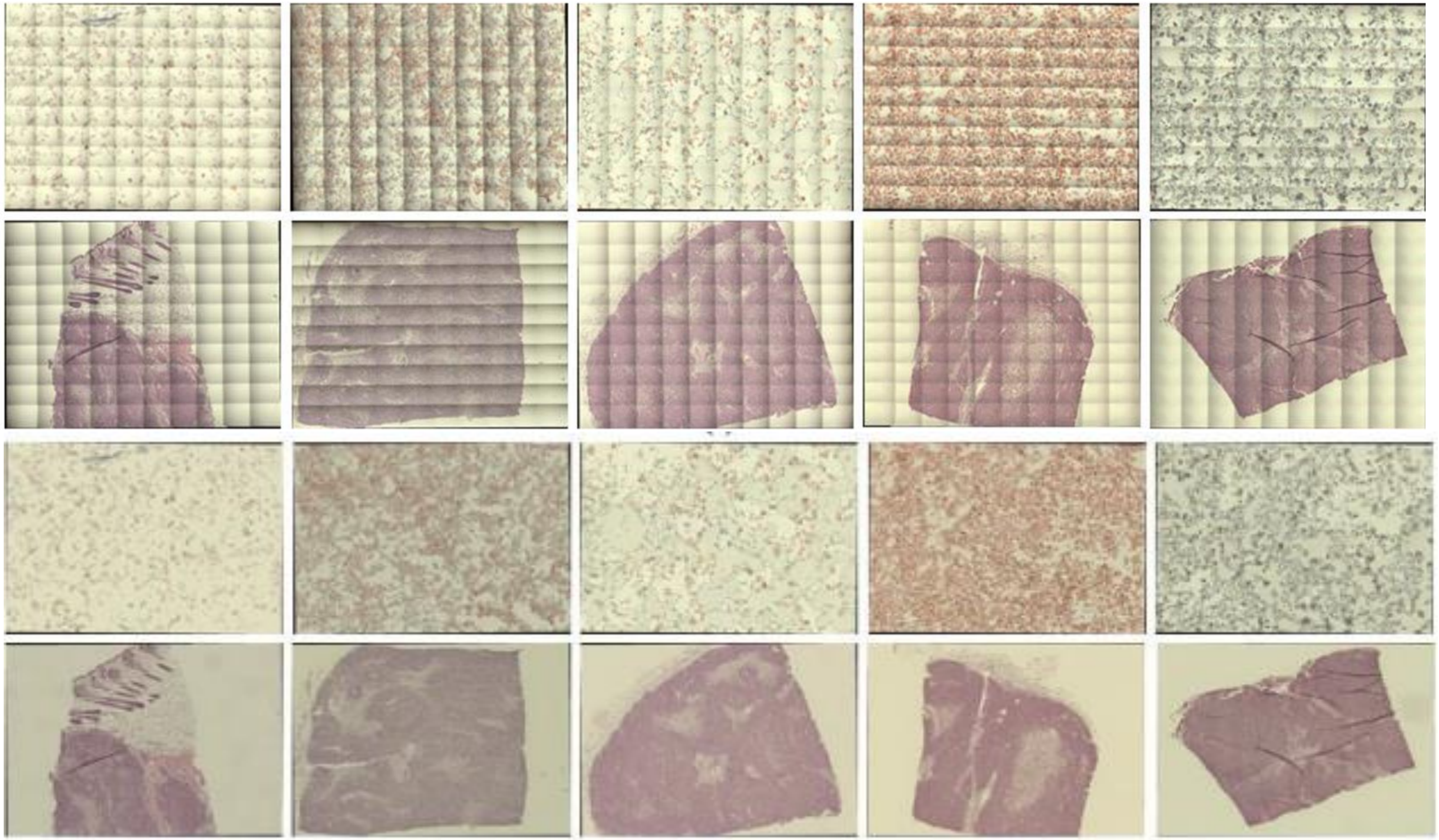


[1].Filippo Piccinini, Alessandro Bevilacqua, "Colour Vignetting Correction for Microscopy Image Mosaics Used for Quantitative Analyses", *BioMed Research International*, vol. 2018, Article ID 7082154, 15 pages, 2018.
[2]. Peng, Tingying, et al. "A BaSiC tool for background and shading correction of optical microscopy images." *Nature communications* 8.1 (2017): 1-7.
[3]. Tak, Yoon-Oh, et al. "Simple shading correction method for brightfield whole slide imaging." Sensors 20.11 (2020): 3084.
[4]. Wang, Jianhang, et al. "Correction of uneven illumination in color microscopic image based on fully convolutional network." *Optics Express* 29.18 (2021): 28503-28520.

Introduction

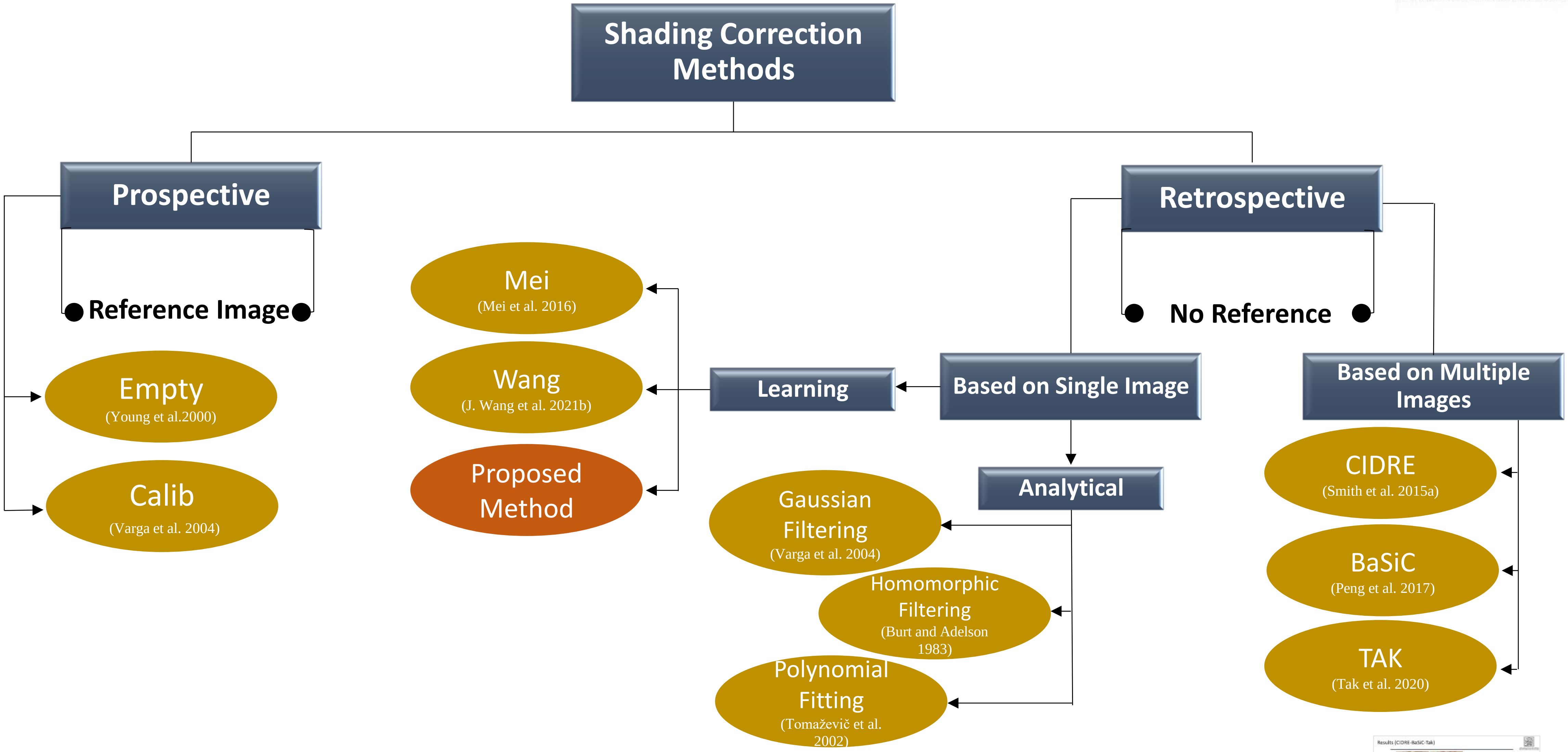
whole-slide images **before** shading correction

whole-slide images **after** shading correction

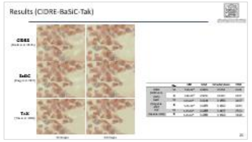


Tak, Yoon-Oh, et al. "Simple shading correction method for brightfield whole slide imaging." Sensors 20.11 (2020): 3084.

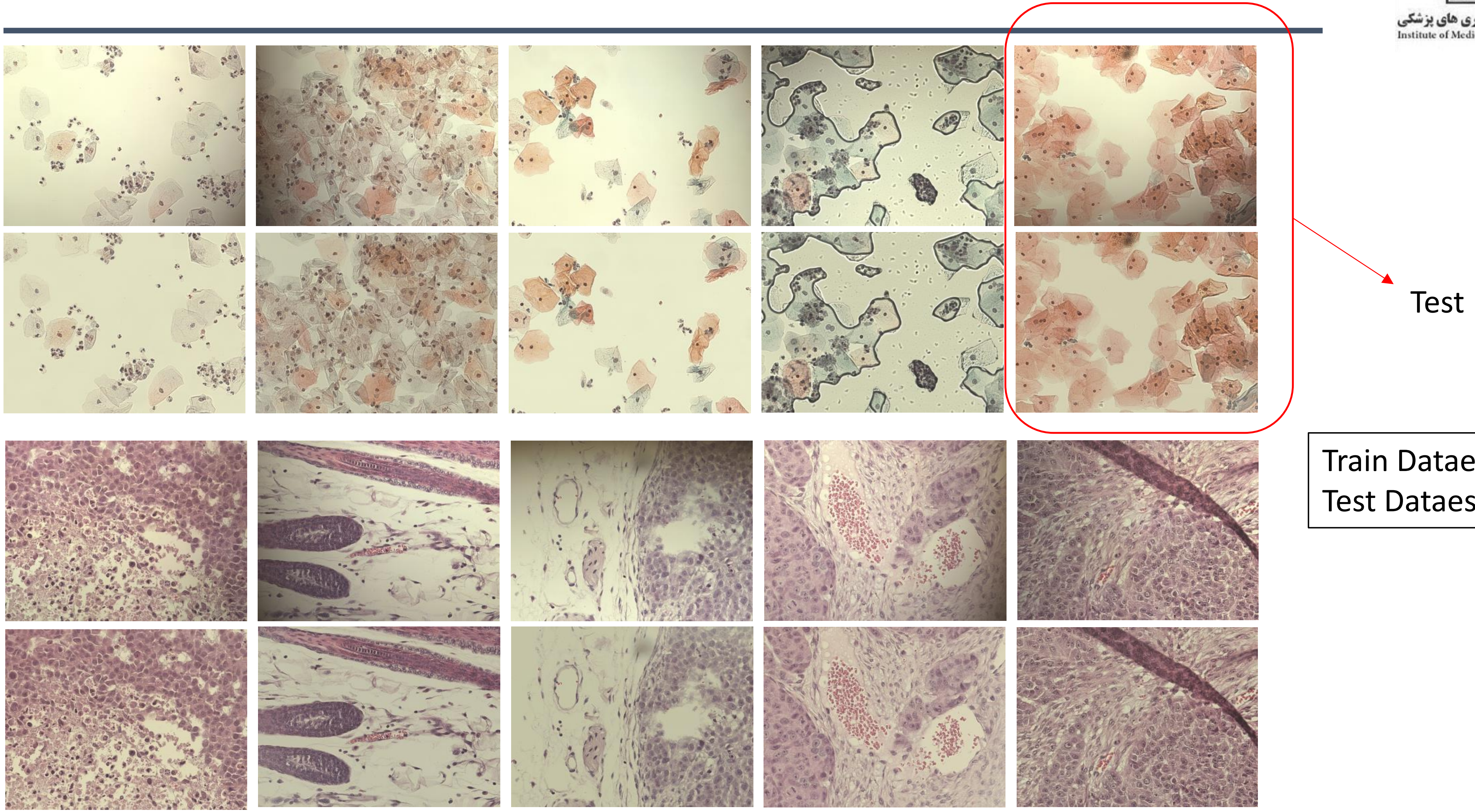
Methods



Shading Correction Methods
Prospective
Reference Image
Empty
(Young et al.2000)
Calib
(Varga et al. 2004)
Mei
(Mei et al. 2016)
Wang
(J. Wang et al. 2021b)
Proposed Method
Retrospective
No Reference
Learning
Based on Single Image
Based on Multiple Images
Analytical
Gaussian Filtering
(Varga et al. 2004)
Homomorphic Filtering
(Burt and Adelson 1983)
Polynomial Fitting
(Tomažević et al. 2002)
CIDRE
(Smith et al. 2015a)
BaSiC
(Peng et al. 2017)
TAK
(Tak et al. 2020)



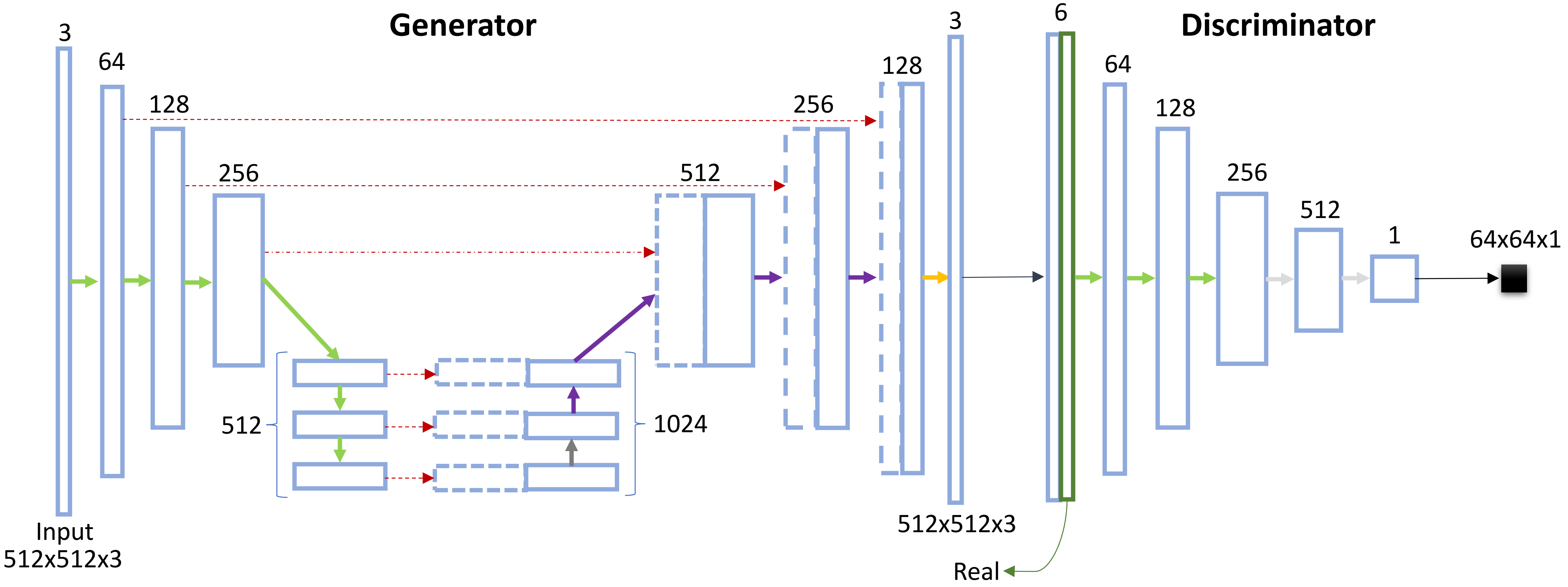
Data



Train Dataest: 900
Test Dataest: 94

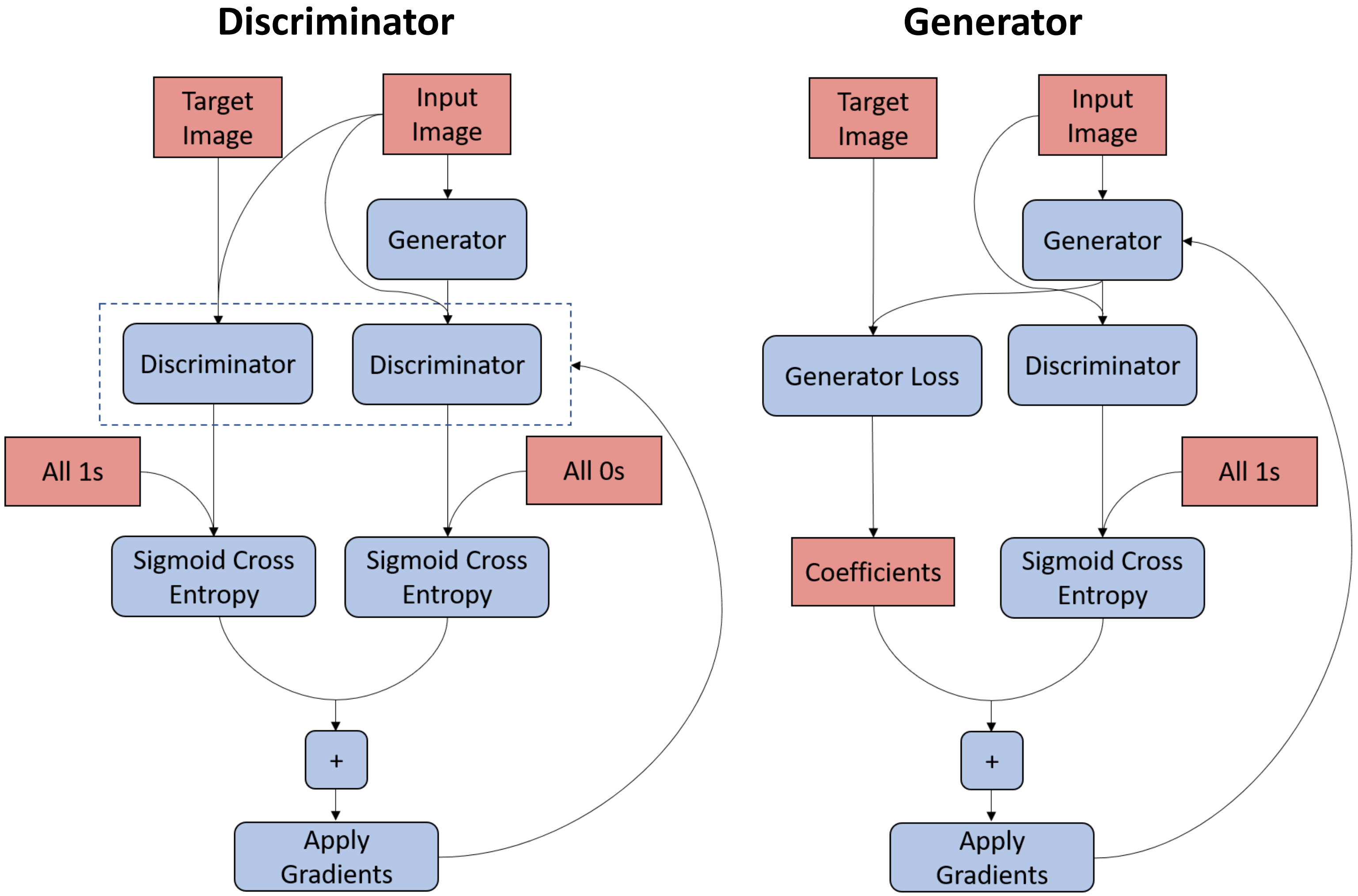
Tak, Yoon-Oh, et al. "Simple shading correction method for brightfield whole slide imaging." Sensors 20.11 (2020): 3084.

Proposed method based on Pix2Pix



- Convolution2D – BatchNorm – LeakyReLU – kernel size=3 – stride=2
- Convolution2D Transpose – BatchNorm - ReLU – kernel size=3 – stride=2
- Convolution2D Transpose – BatchNorm – ReLU – kernel size=3 – stride=2
- Convolution2D Transpose – tanh – kernel size=3 – stride=2
- Convolution2D – kernel size=3 – stride=1
- Concatenate

Training Process



[1]. Mirza, M., & Osindero, S. (2014). Conditional generative adversarial nets. *arXiv preprint arXiv:1411.1784*.
[2]. Isola, P., Zhu, J. Y., Zhou, T., & Efros, A. A. (2017). Image-to-image translation with conditional adversarial networks. In *Proceedings of the IEEE conference on computer vision and pattern recognition* (pp. 1125-1134).

Proposed method based on Pix2Pix

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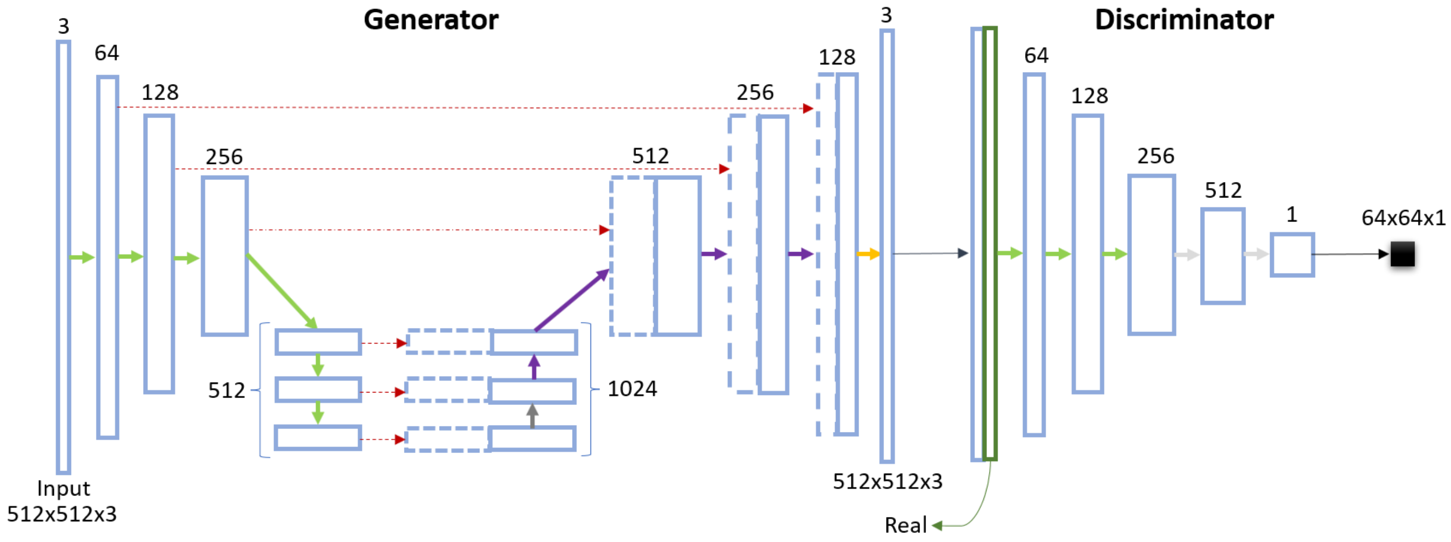


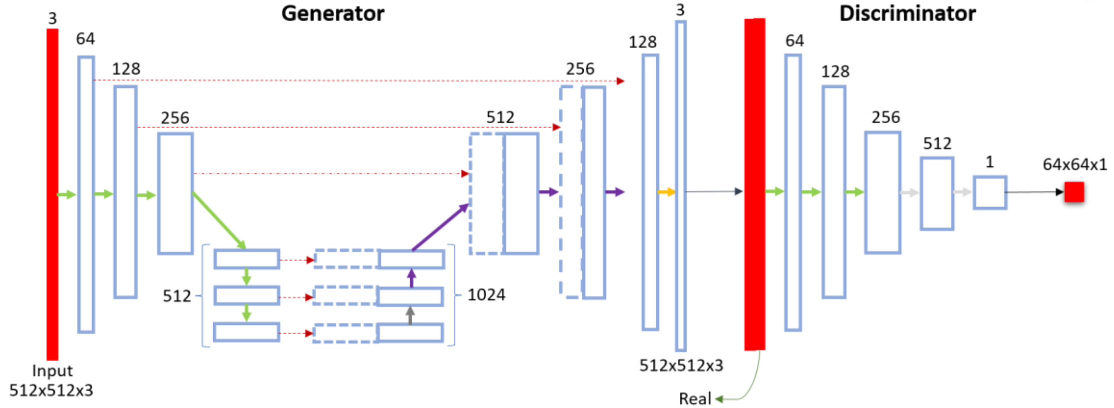
Variables

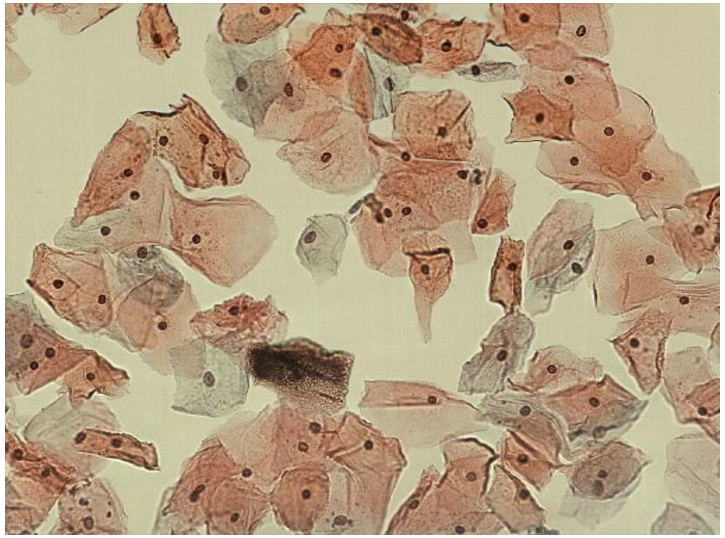
- **Input Image Size** → 512x512x3
- **Size of Generator Bottleneck** → 16x16
- **Generator Loss Function**
  1. Adversarial Loss + **40×MAE** + **20×SSIM** + **5×MSE**
  2. Adversarial Loss + **40×MAE** + **20×LPIPS**
- **Discriminator Loss Function** → Adversarial Loss + **10×**WGAN-GP

Proposed method based on Pix2Pix

Variables

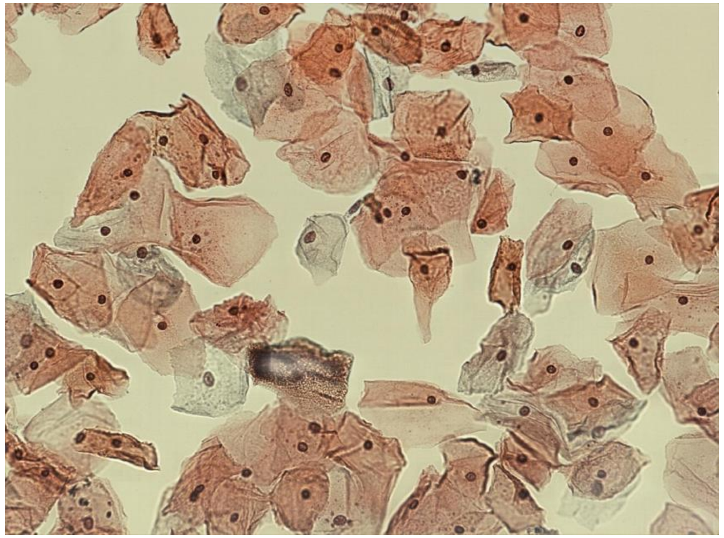
- Input Image Size





- **Input Image Size → 512x512x3**
- **Size of Generator Bottleneck → 16x16**
- **Generator Loss Function**

  Adversarial Loss + **40×MAE** + **20×SSIM** + **5×MSE**
- **Discriminator Loss Function →** Adversarial Loss + **10×**WGAN-GP



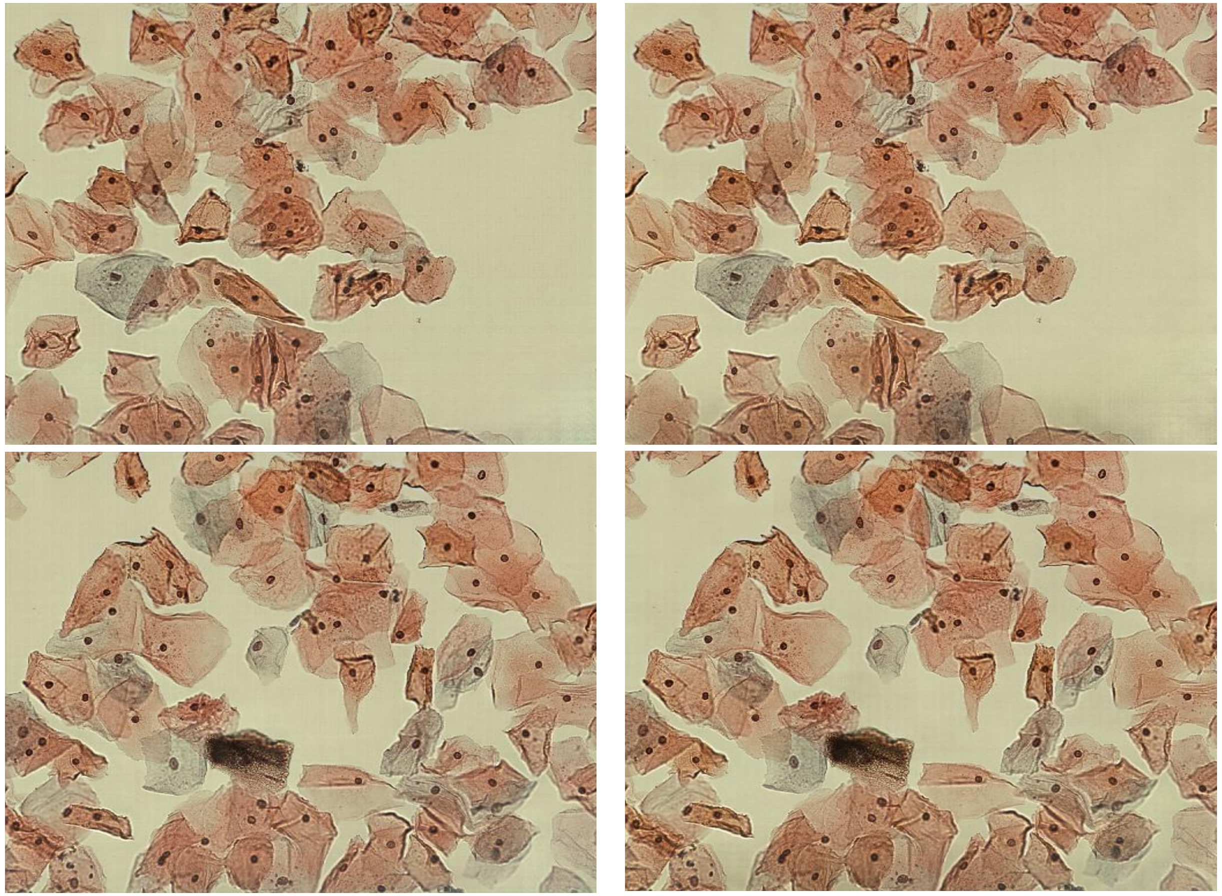
- **Input Image Size → 1600x1200x3**
- **Size of Generator Bottleneck → 100x75**
- **Generator Loss Function**

  Adversarial Loss + **40×MAE** + **20×SSIM** + **5×MSE**
- **Discriminator Loss Function →** Adversarial Loss + **10×**WGAN-GP

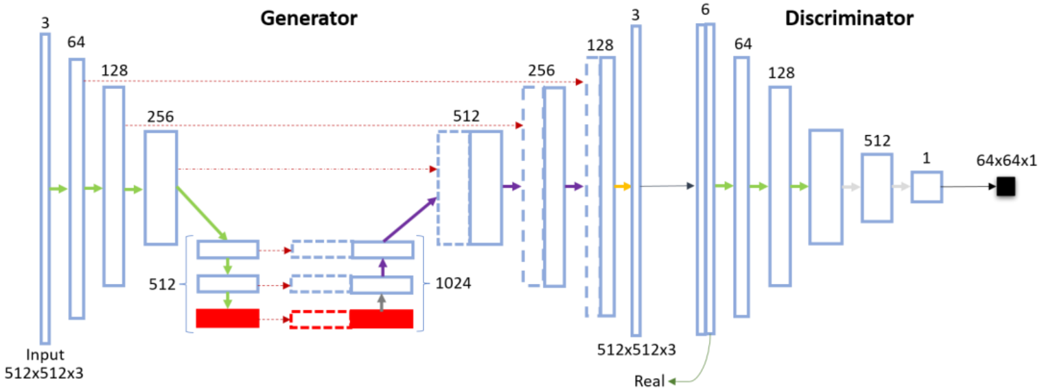
Proposed method based on Pix2Pix

Variables

➢ Generator Bottleneck Size



16x16 8x8

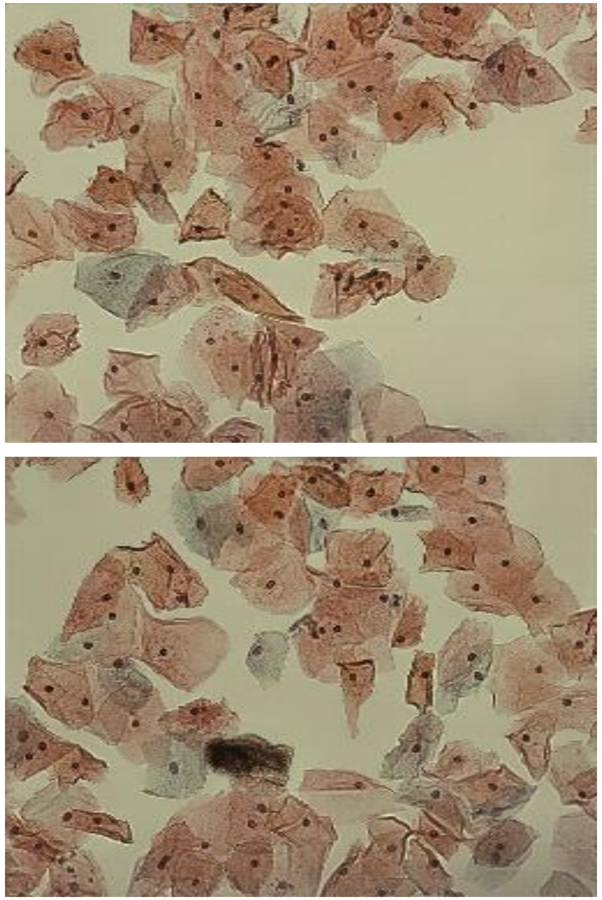


- **Input Image Size** → 512x512x3
- **Size of Generator Bottleneck** → 16x16 and 8x8
- **Generator Loss Function**
  Adversarial Loss + **40×MAE** + **20×SSIM** + **5×MSE**
- **Discriminator Loss Function** → Adversarial Loss + **10×**WGAN-GP

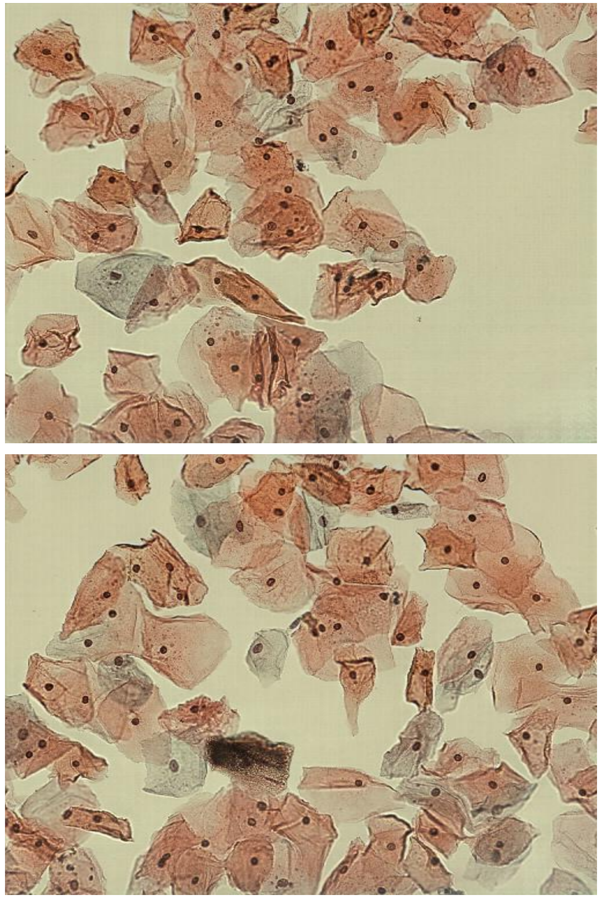
Proposed method based on Pix2Pix

Variables

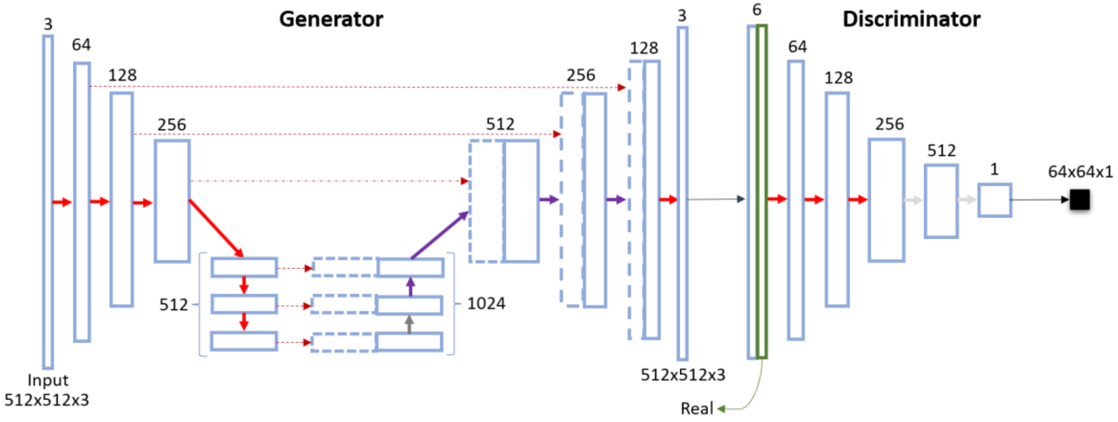
➢ Layer Activation Function



ReLU



Leaky ReLU



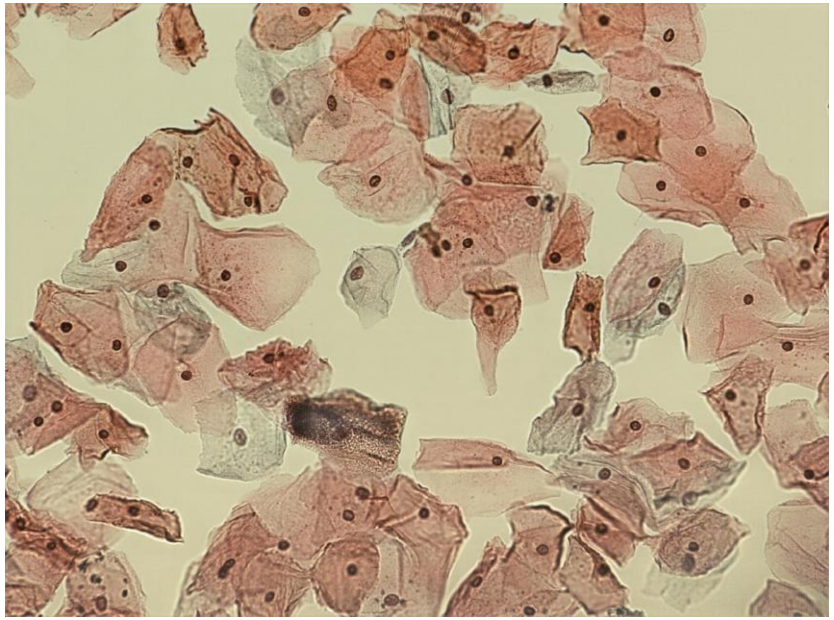
- **Input Image Size →** 512x512x3
- **Size of Generator Bottleneck →** 16x16
- **Generator Loss Function**
  Adversarial Loss + **40×MAE** + **20×SSIM** + **5×MSE**
- **Discriminator Loss Function →** Adversarial Loss + **10×**WGAN-GP

Proposed method based on Pix2Pix

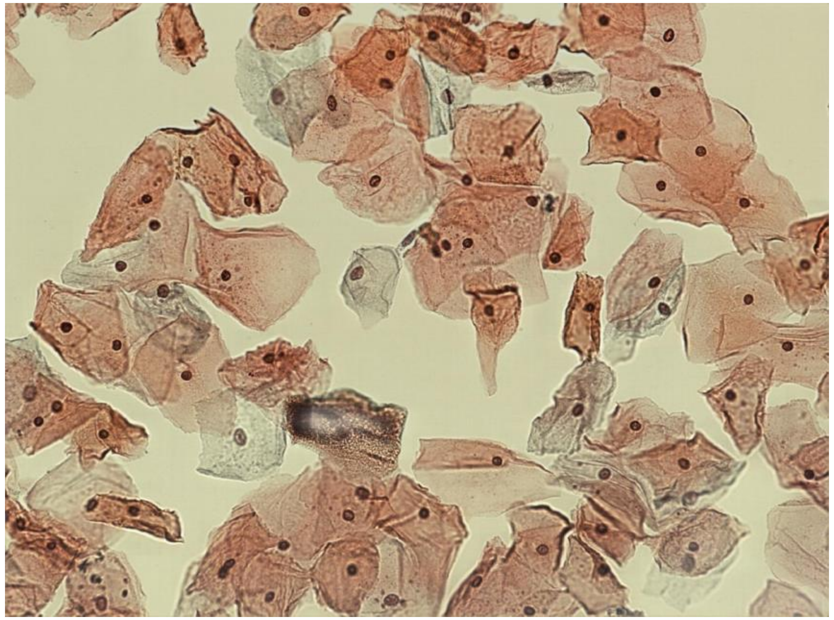
Variables

- ➢ Generator Loss Function Coefficients

- **Generator Loss Function**
  Adversarial Loss + **40×MAE** + **20×SSIM** + **5×MSE**
  Adversarial Loss + **40×MAE** + **20×LPIPS**
- **Discriminator Loss Function** → Adversarial Loss + **10×**WGAN-GP



20xMAE



80xMAE

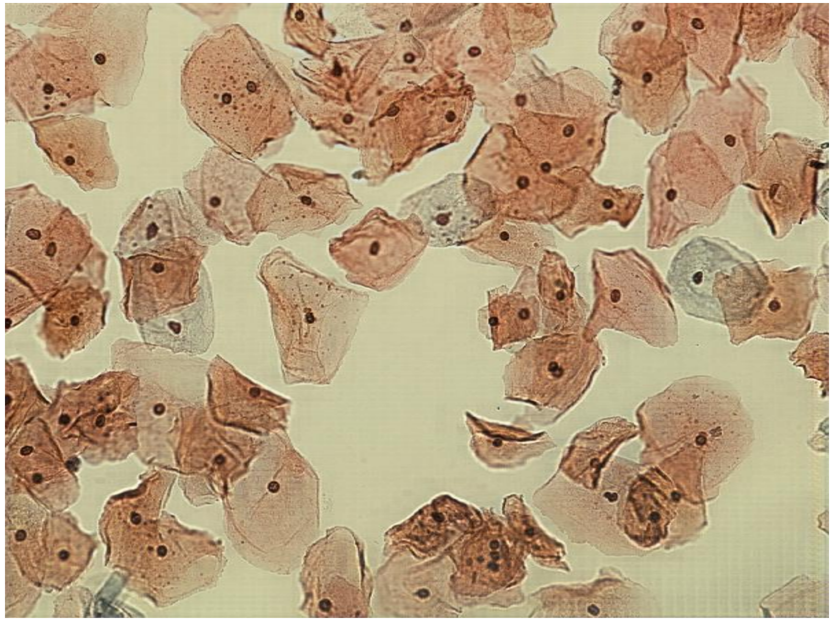
Less L1 → Better restoration for dark object

Proposed method based on Pix2Pix

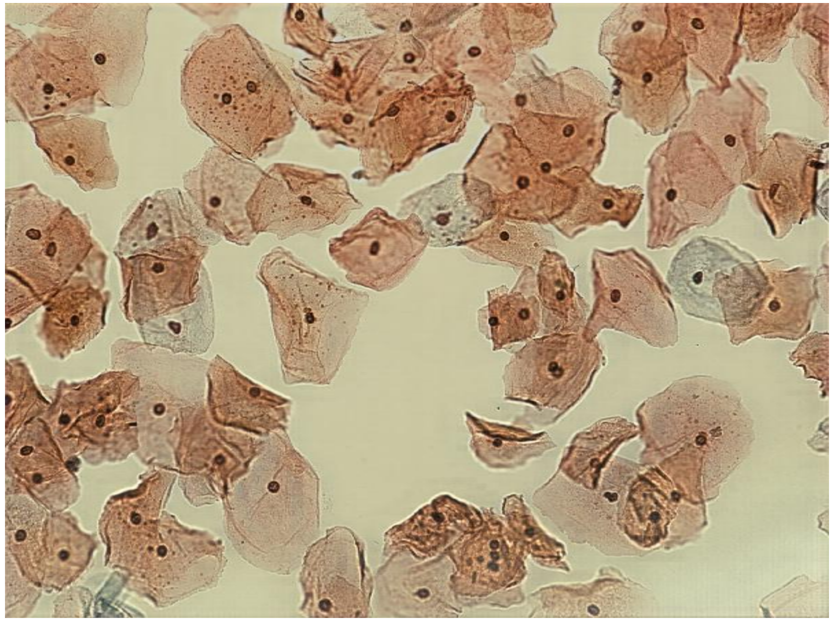
Variables

➢ Generator Loss Function Coefficients

- **Generator Loss Function**
  Adversarial Loss + **40×MAE** + **20×SSIM + 5×MSE**
- **Discriminator Loss Function →** Adversarial Loss + **10**×WGAN-GP



80xMAE + **20**xMSE



80xMAE + **20**xSSIM

Less MSE and more SSIM

Proposed method based on Pix2Pix

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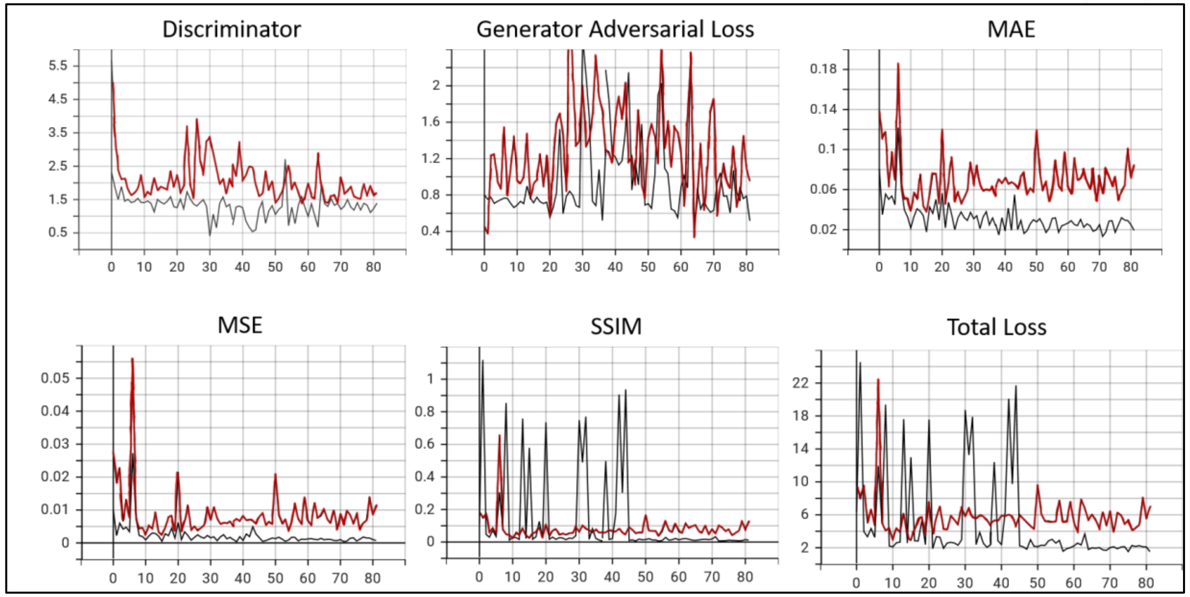
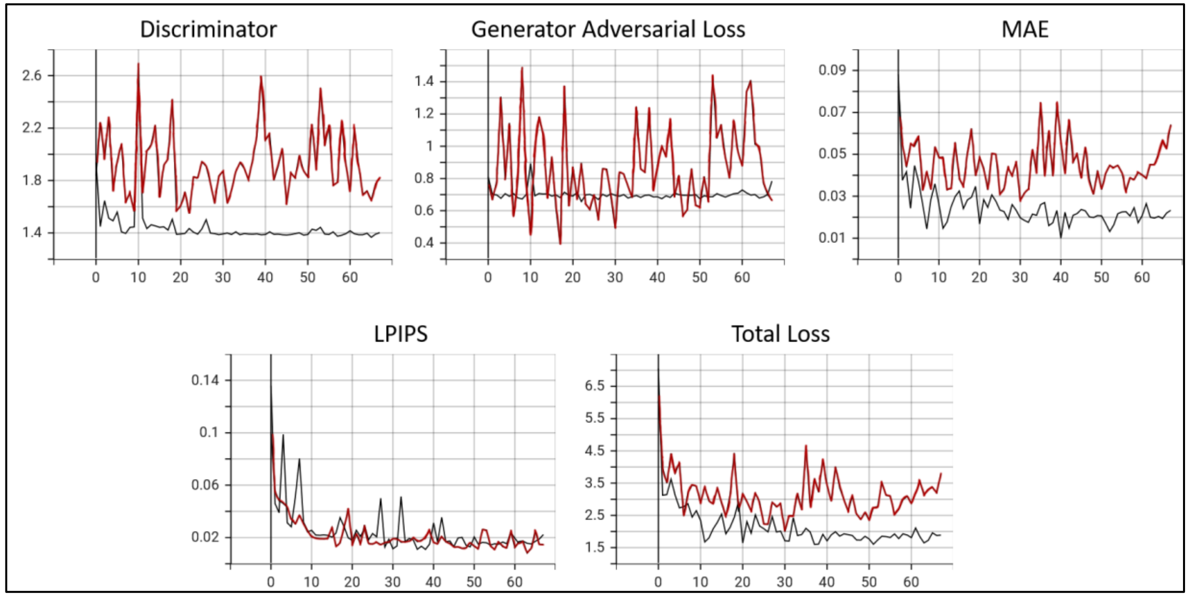


- **Input Image Size** → 512x512x3
- **Size of Generator Bottleneck** → 16x16
- **Generator Loss Function**
  Adversarial Loss + **40**×**MAE** + **20**×**SSIM** + **5**×**MSE**
- **Discriminator Loss Function** → Adversarial Loss + **10**×WGAN-GP



- **Input Image Size** → 512x512x3
- **Size of Generator Bottleneck** → 16x16
- **Generator Loss Function**
  Adversarial Loss + **40**×**MAE** + **20**×**LPIPS**
- **Discriminator Loss Function** → Adversarial Loss + **10**×WGAN-GP

Results: Quantitative

Method	MSE	SSIM	PSNR	Entropy	Correction Score	NIQE	PIQE	BRISQUE
Proposed Method (40xMAE+20xSSIM+5xMSE)	5.00×10^{-3}	0.9636	23.08	6.8346	0.2735	3.7391	36.72	**19.14**
Proposed Method (40xMAE+20xLPIPS)	6.50×10^{-3}	0.9590	21.93	6.8720	**0.2542**	3.7080	36.37	20.72
BaSiC (#image=94)	6.45×10^{-4}	0.9850	31.91	6.6856	0.5537	3.6163	25.02	22.86
BaSiC (#image=10)	1.30×10^{-3}	0.9701	28.87	6.8645	0.5775	3.6021	**23.50**	21.14
CIDRE (#image=94)	7.90×10^{-4}	0.9818	31.04	6.7273	0.5718	3.5007	25.57	20.38
CIDRE (#image=10)	1.40×10^{-3}	0.9656	28.57	6.7506	0.6167	**3.4943**	24.11	20.67
Tak (#image=94)	**4.59×10^{-4}**	**0.9894**	**33.41**	**6.3140**	0.5704	4.1448	25.93	33.12
Tak (#image=10)	8.77×10^{-4}	0.9796	30.57	6.6052	0.5759	3.5293	24.77	24.55

Results: Qualitative

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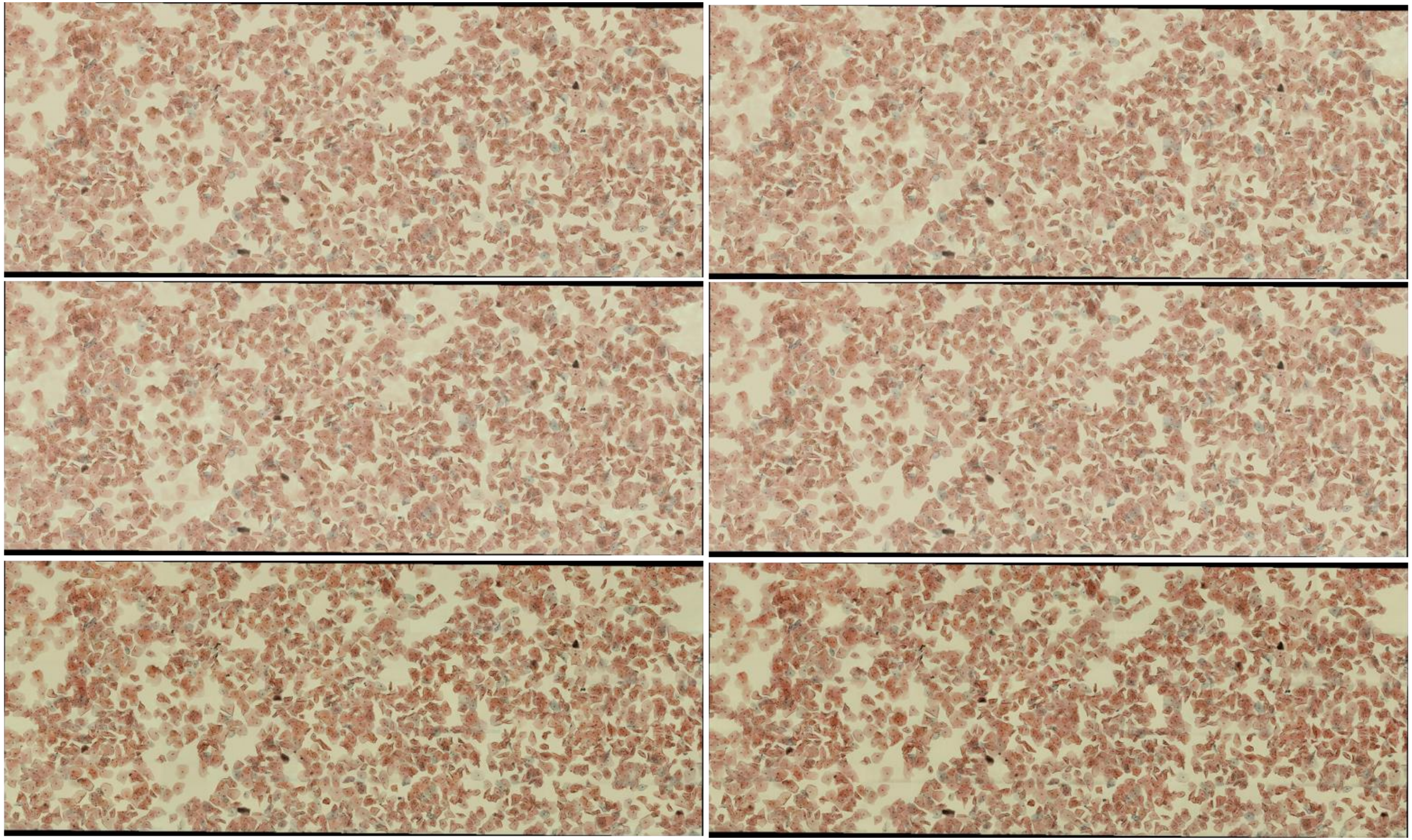

Ground Truth

CIDRE
(Smith et al.2015)

BaSiC
(Peng et al.2017)

Tak
(Tak et al.2020)

Proposed Method
(40MAE+20SSIM+5MSE)

Proposed Method
(40MAE+20LPIPS)

Results: Qualitative

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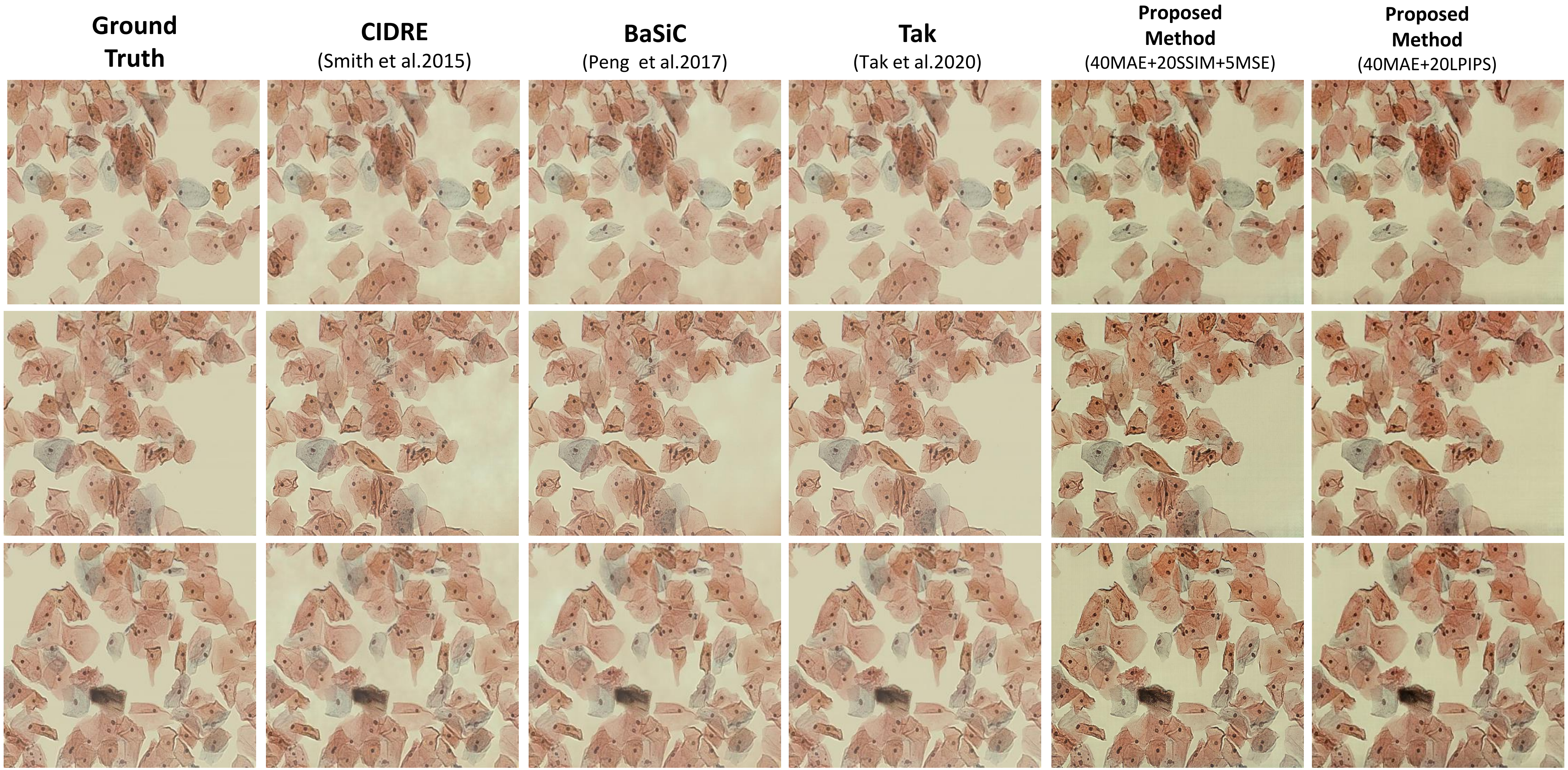

Conclusion

In this research, we have shown that:

- Conditional Generative Adversarial Network of image-to-image translation type is a proper choice to remove shading pattern from microscopic images obtained from bright-field devices.

- By using the proposed network, the images can be modified instantly and independently.

- The output images of proposed network have *higher resolution* even than the ground-truth images.

- The results of the proposed method have been the best compared to retrospective methods based on quantitative criteria *Correction Score* and *BRISQUE*.

Future Works

- More investigation on Discriminator and the impact of PatchGAN size

- Replace MAE with Smooth L1

- Replace Least Square GAN with WGAN-GP


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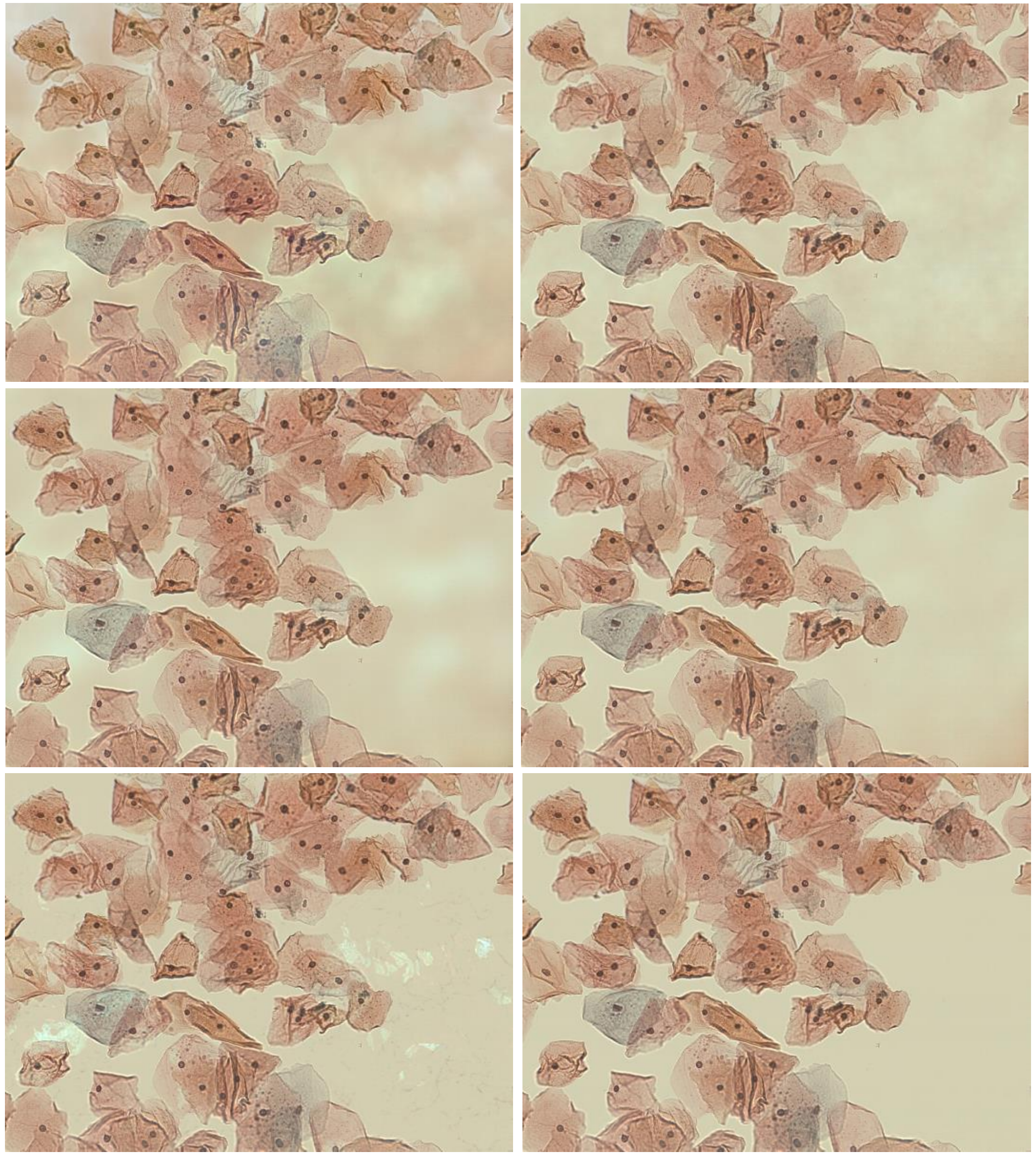
Results (CIDRE-BaSiC-Tak)

CIDRE
(Smith et al. 2015a)

BaSiC
(Peng et al. 2017)

TAK
(Tak et al. 2020)



10 Images   94 Images

	No.	MSE	SSIM	Correction Score	PSNR
CIDRE (Smith et al. 2015)	94	7.90×10^{-4}	0.9818	0.5718	31.04
	10	1.40×10^{-3}	0.9656	0.6167	28.57
BaSiC (Peng et al. 2017)	94	3.91×10^{-4}	0.9911	0.1553	34.07
	10	5.47×10^{-4}	0.9876	0.1802	32.63
TAK (Tak et al. 2020)	94	1.97×10^{-4}	0.9955	0.1137	37.03
	10	6.35×10^{-4}	0.9856	0.1690	31.96