Slide-free MUSE Microscopy to H&E Histology Modality Conversion via Unpaired Image-to-Image Translation GAN Models

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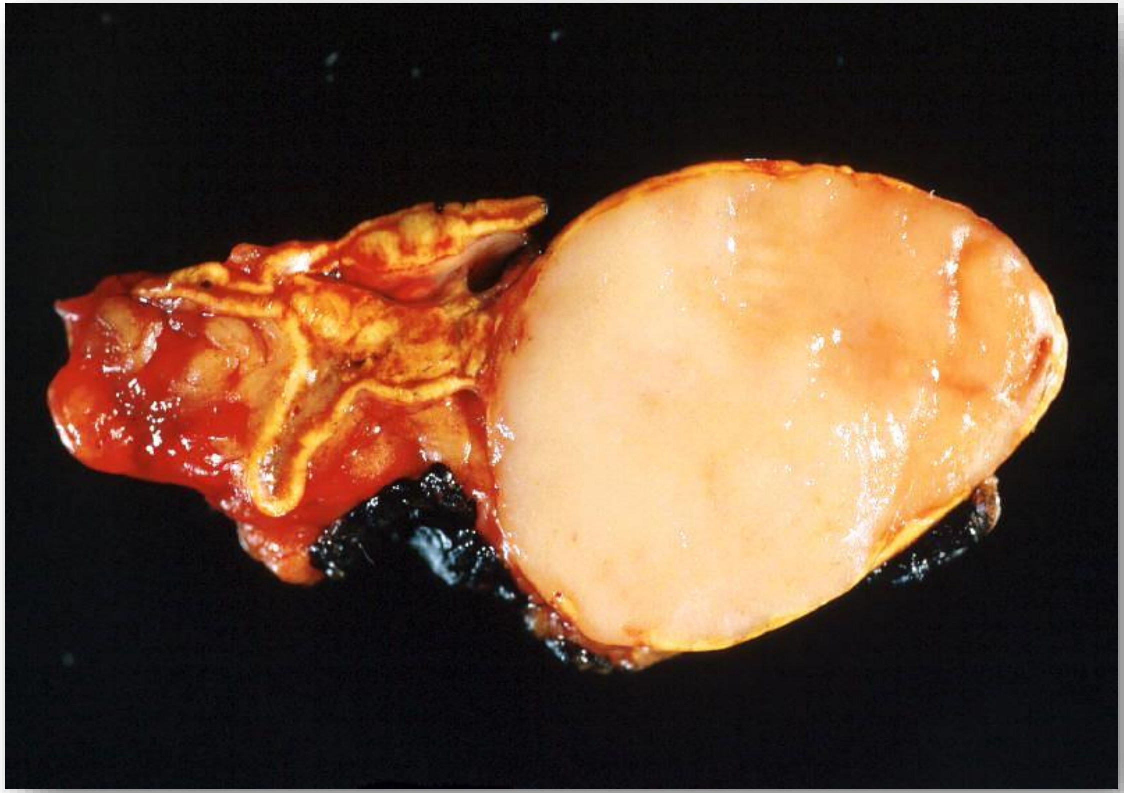
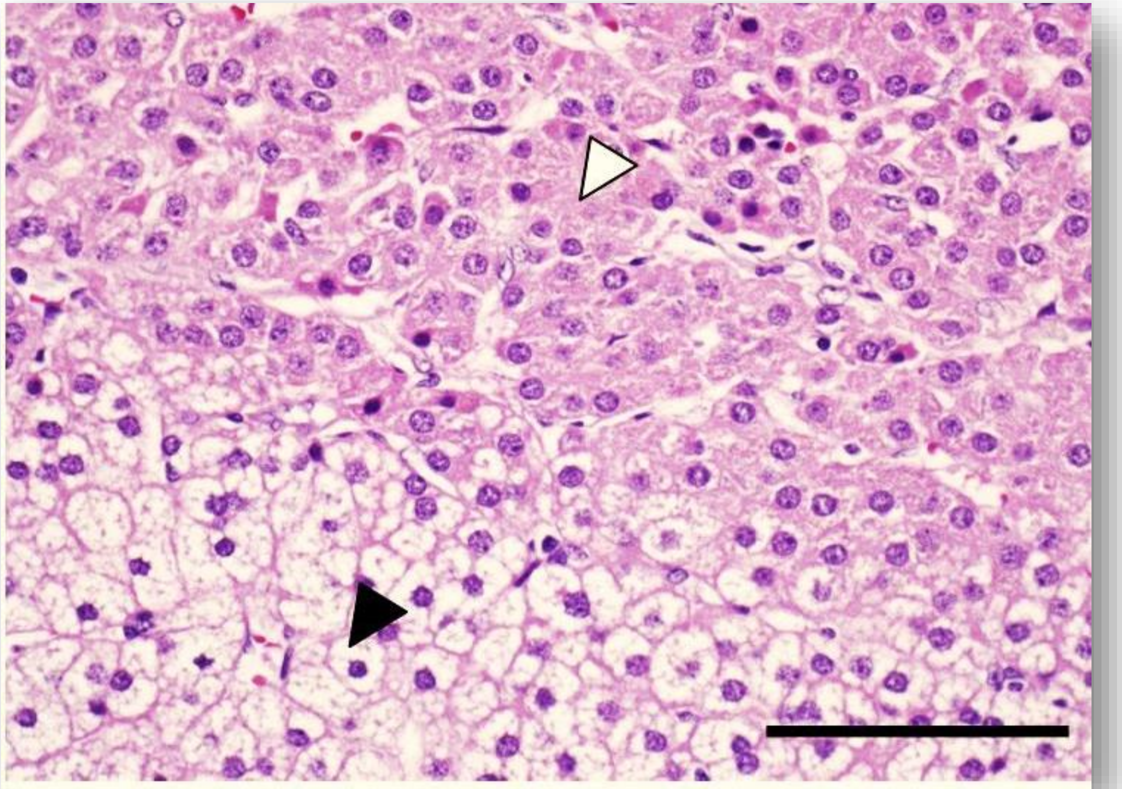
Background

Pathology

(Still the) gold-standard for diagnosis—and therapy guidance



Gross Anatomy



Histology …

Histology

The problem:

Hours to days

Procedure (or preclinical research)

Definitive answer

Traditional H&E (hematoxylin & eosin) histology workflow

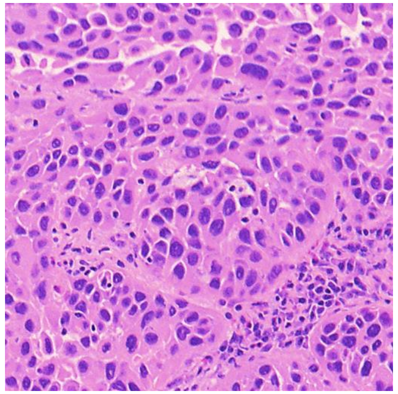
Biopsy

Fixation, paraffin embedding

Section tissue/slide prep

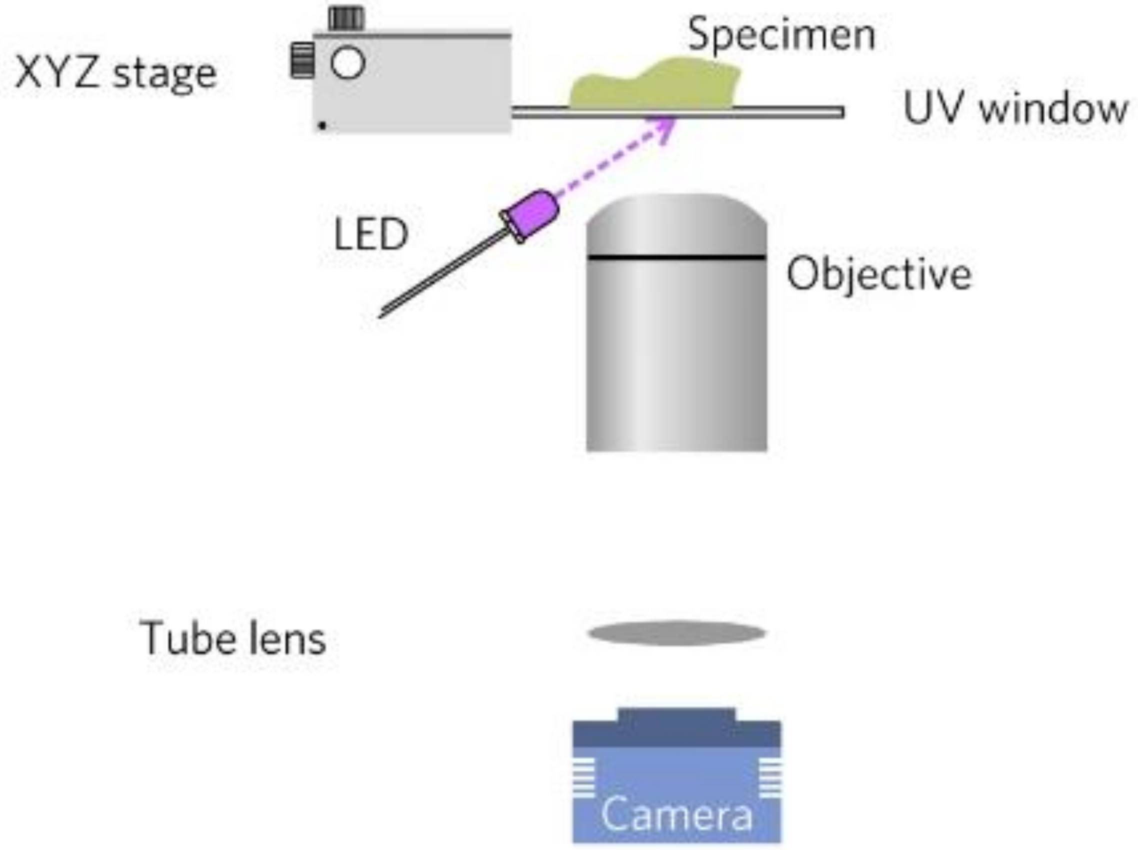
H&E staining

View in brightfield microscope



H&E brightfield image

<u>M</u>icroscopy with <u>U</u>ltraviolet <u>S</u>urface <u>E</u>xcitation (MUSE)

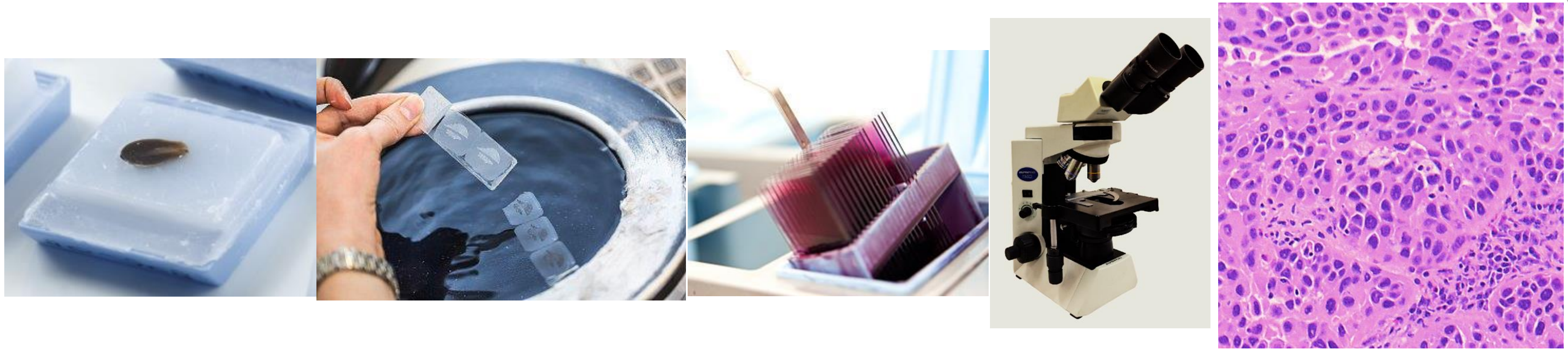


(Fereidouni et al. *Nat. Biomed. Eng.* 2017)

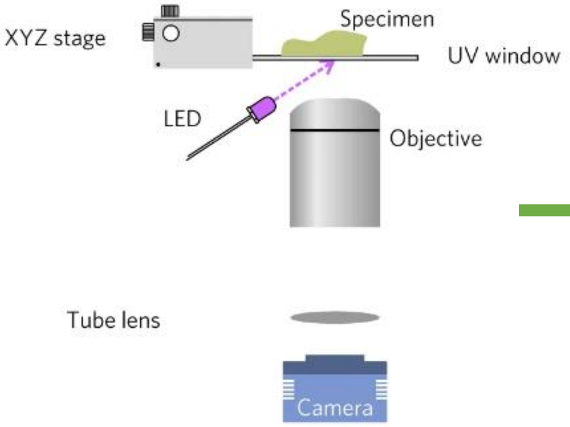
Comparison of the workflows

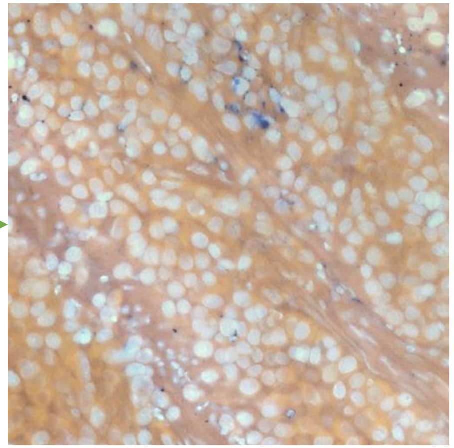
Sample

Traditional H&E histology workflow (8 hrs)



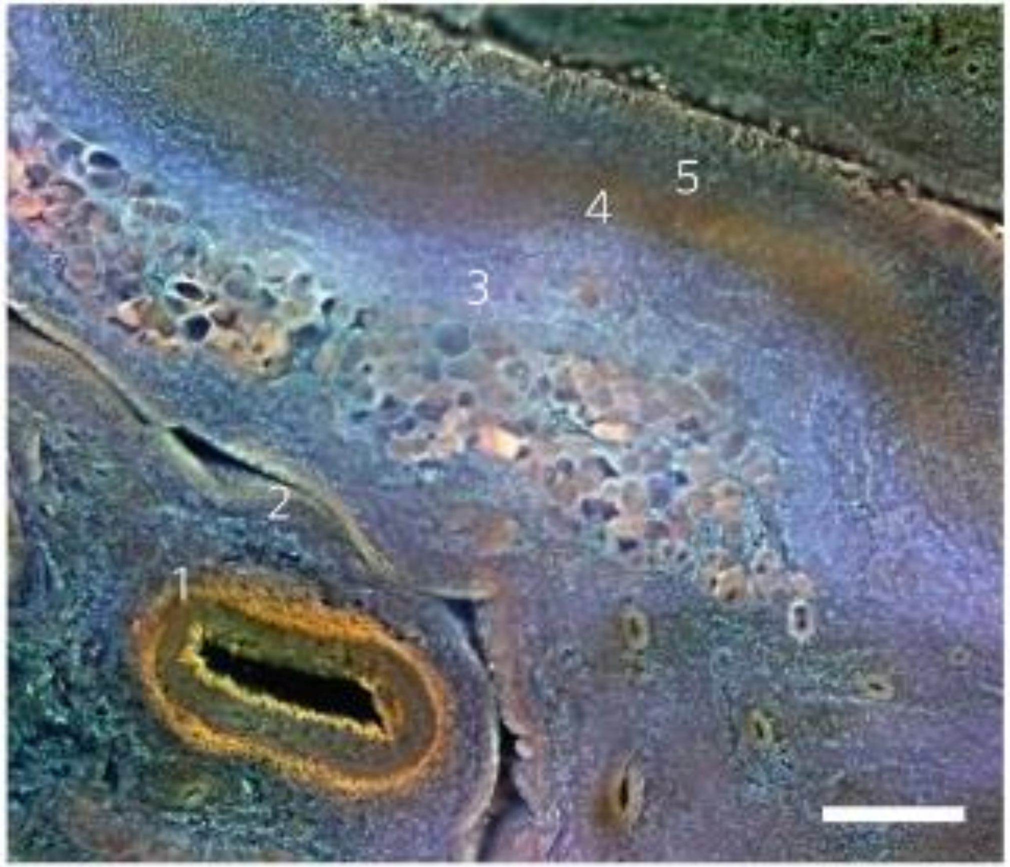
MUSE imaging workflow (5 min)



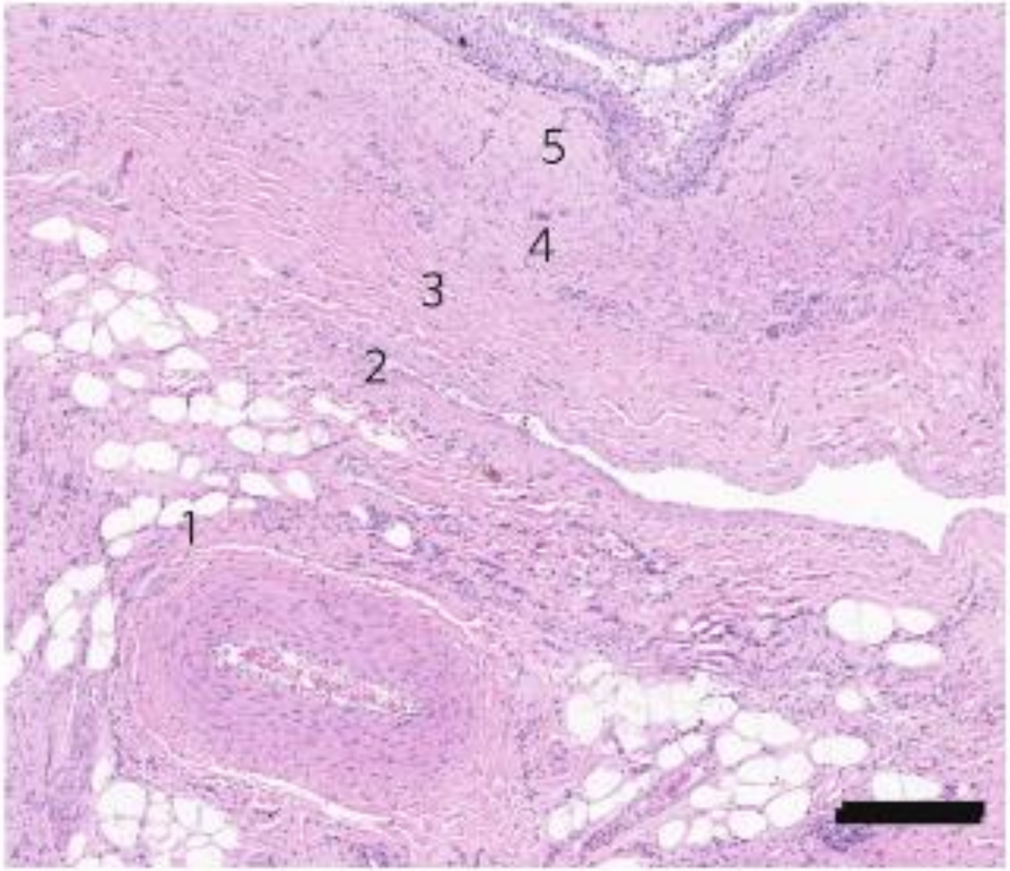


What’s the problem?

- The pathologists like H&E!
- Need to convert to “virtual” H&E



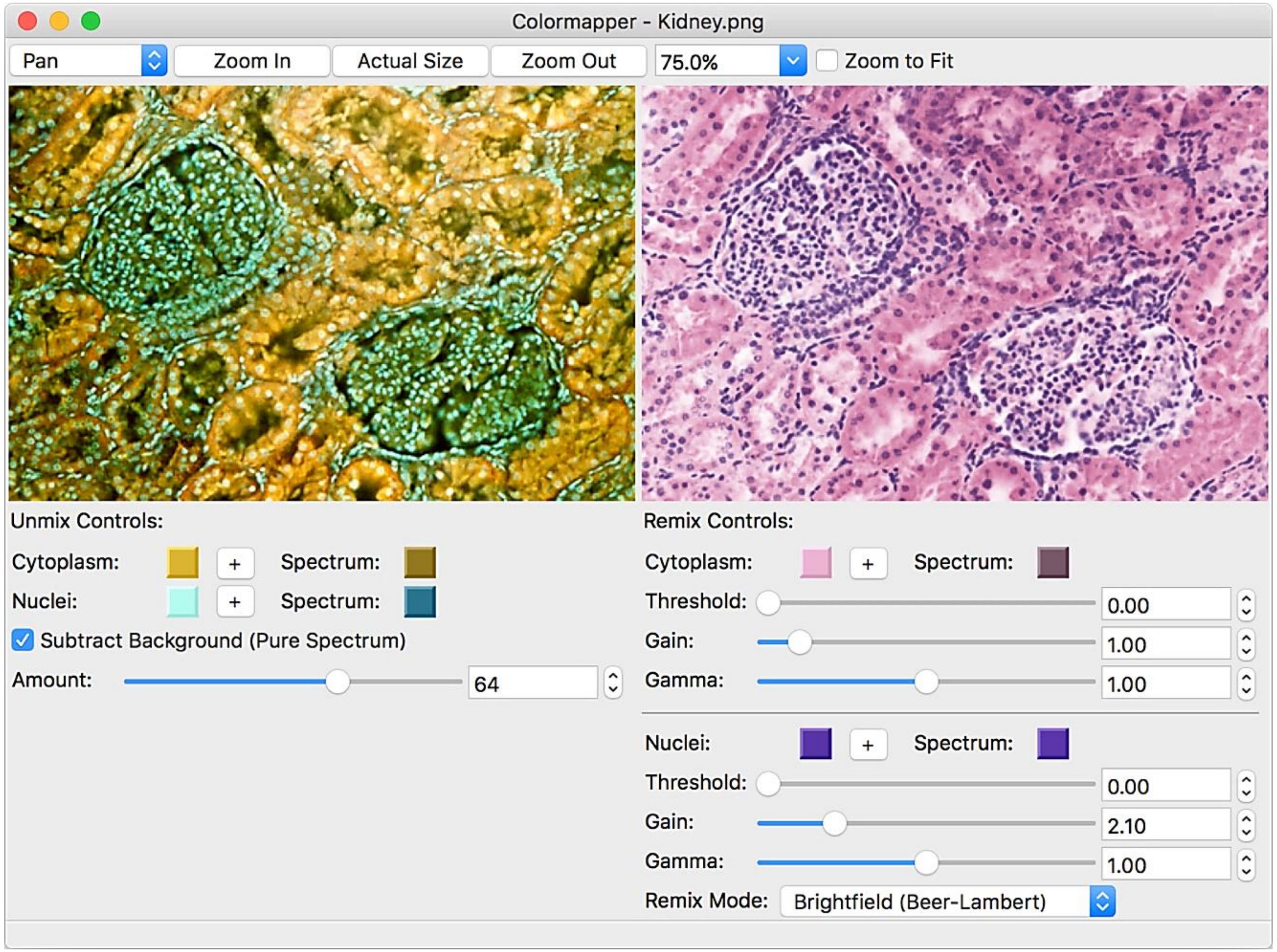
MUSE (porcine renal tissue)



H&E (porcine renal tissue)

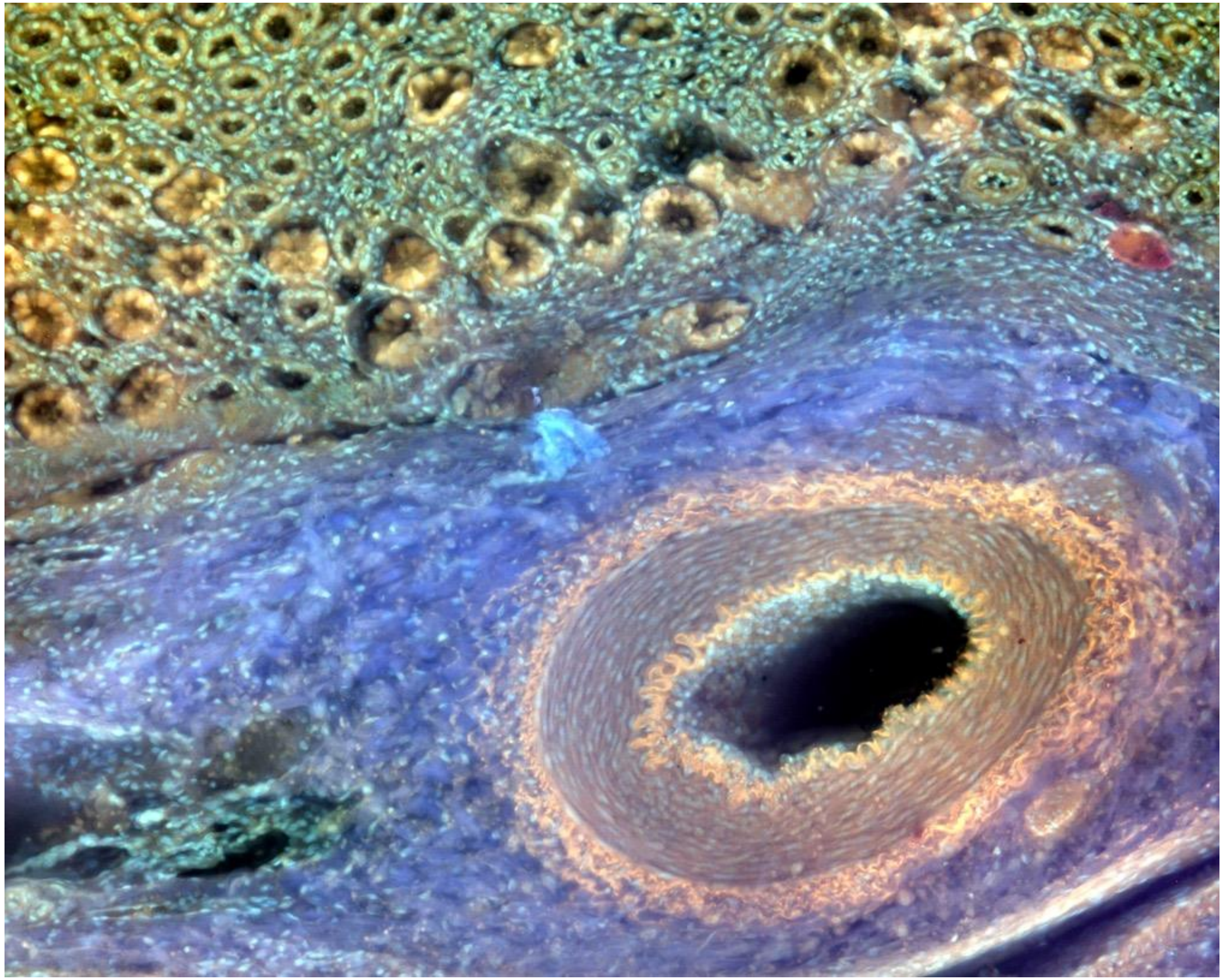
(Fereidouni et al. *Nat. Biomed. Eng.* 2017)

Previous method – color mapper



(Fereidouni et al. *Nat. Biomed. Eng.* 2017)

Color conversion is hard if there are more than 2 colors…



…so we explored AI-based approaches

(Fereidouni et al. *Nat. Biomed. Eng.* 2017)

Similar approaches need context for color-mapping…

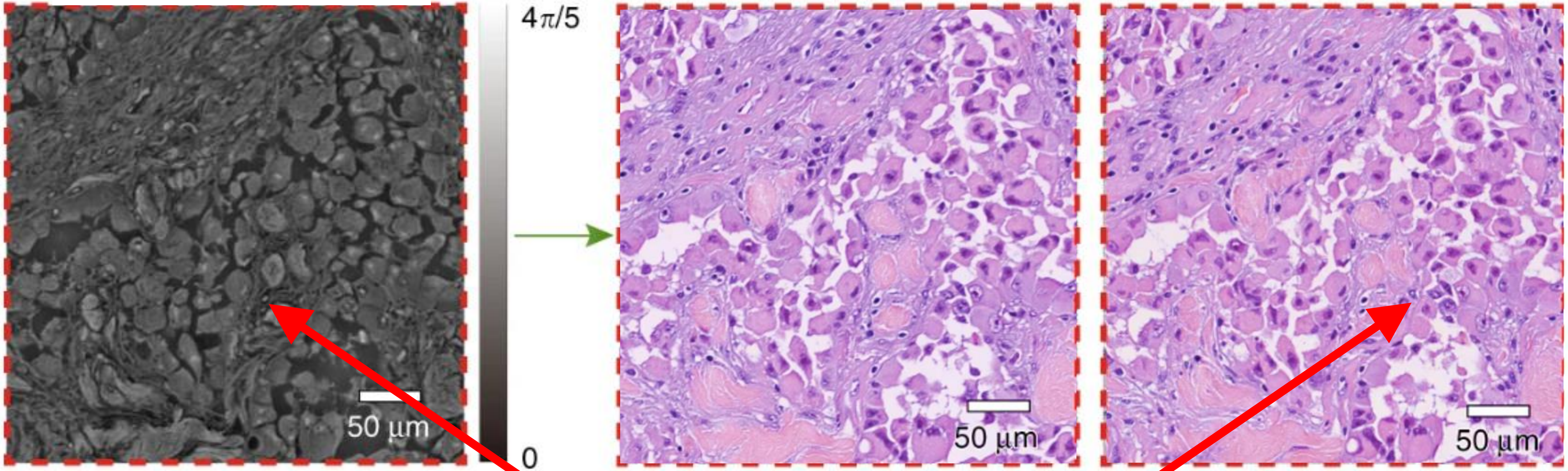
(Antic, 2018)

Microscopy modality conversion – prior work

QPI of unstained skin tissue section (zoom in)

Network output — digital H&E staining

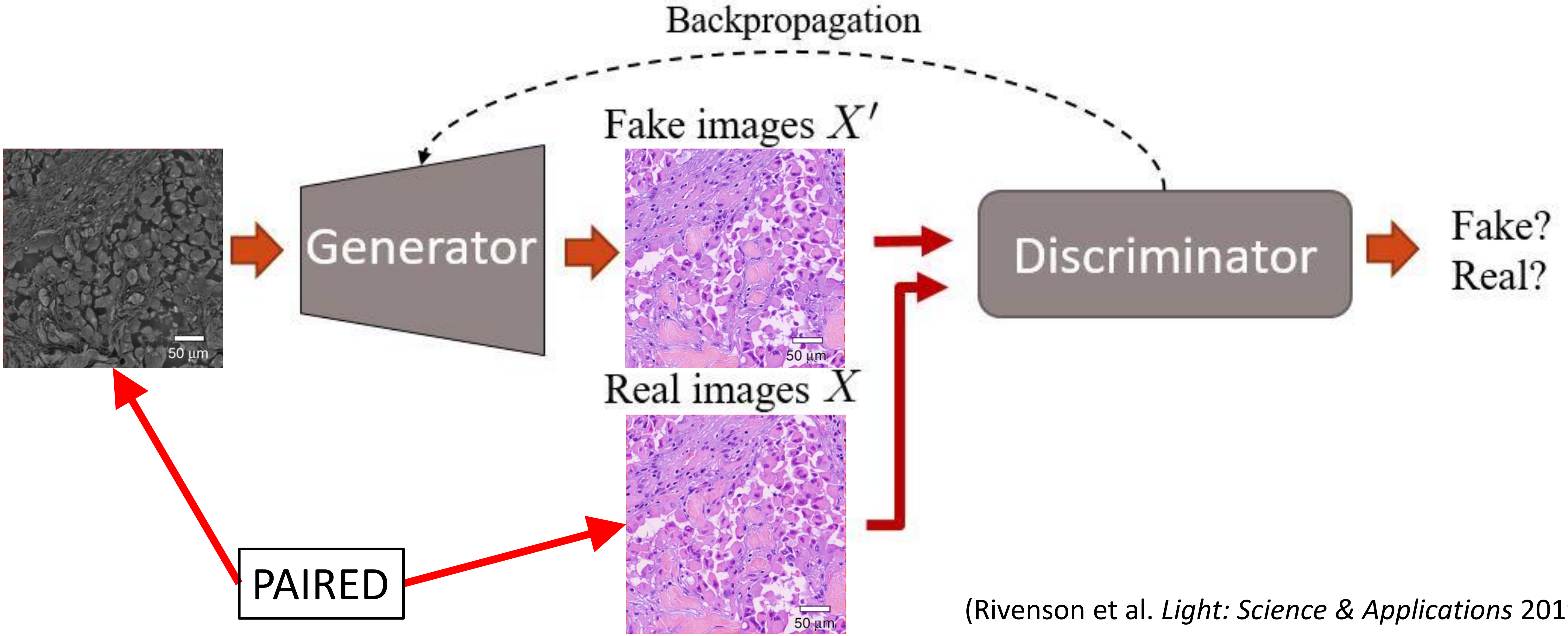
Brightfield image of the H&E histologically stained skin tissue (20×/0.75NA)



PAIRED!

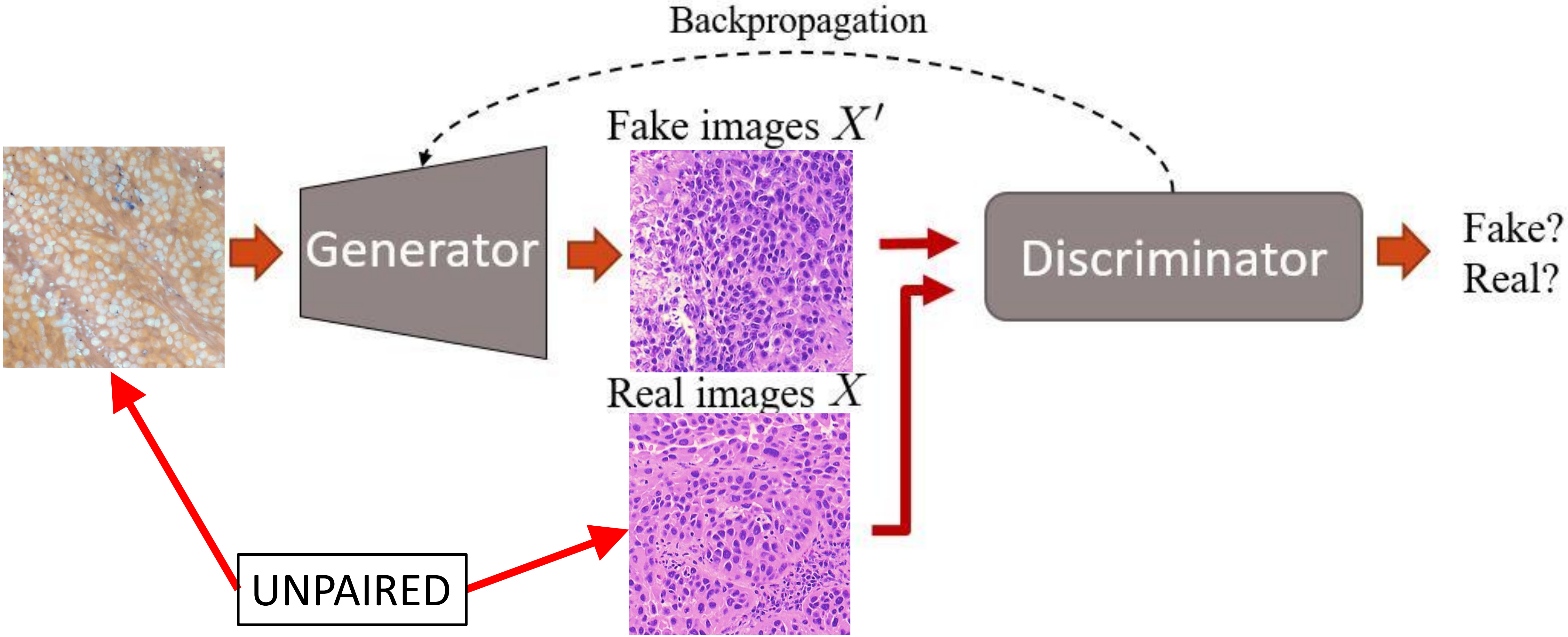
(Rivenson et al. *Light: Science & Applications* 2019)

Generative adversarial networks (GANs)



(Rivenson et al. *Light: Science & Applications* 2019)
(Guim Perarnau 2017)

GANs don't work with unpaired datasets

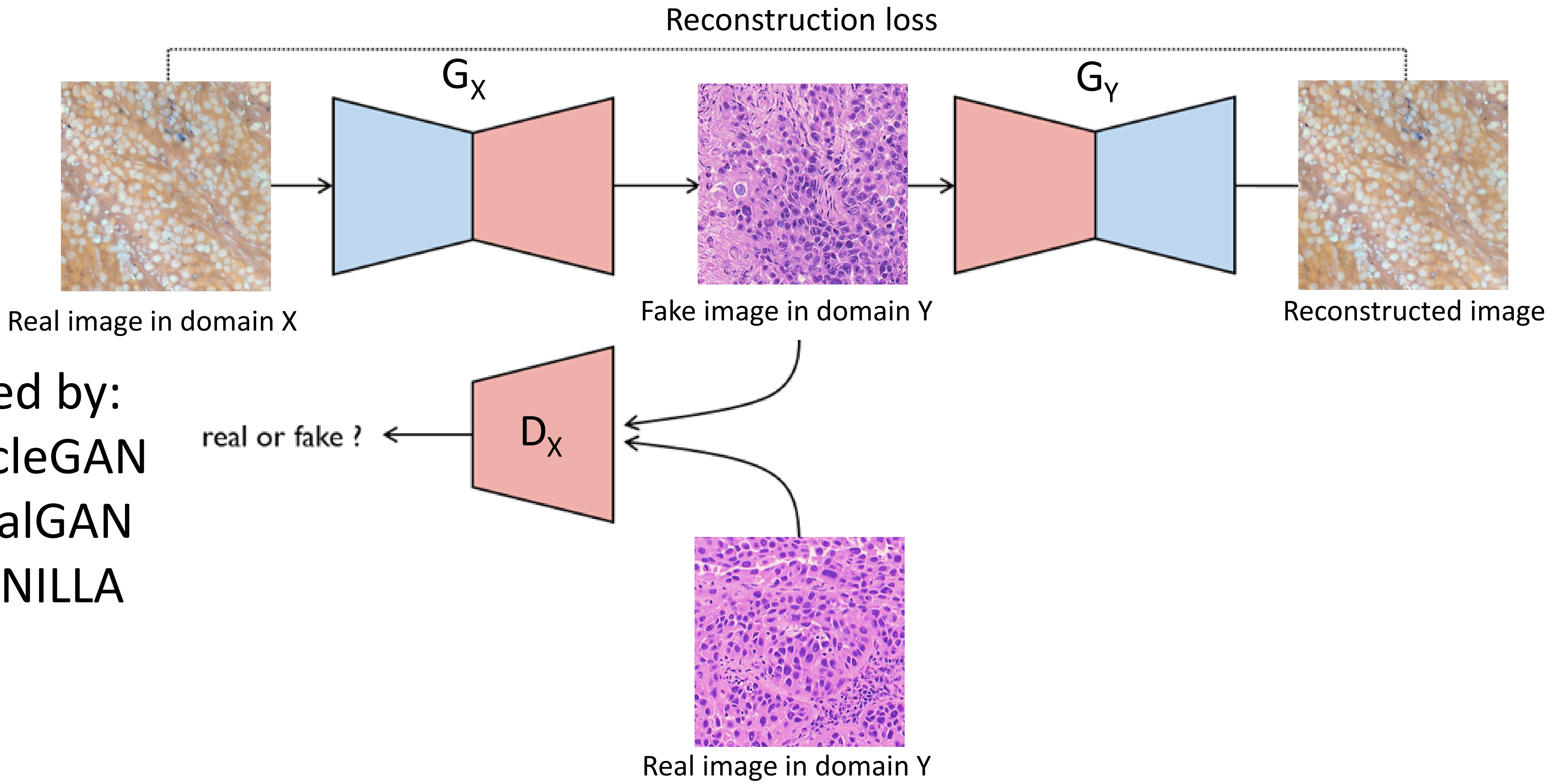


(Guim Perarnau 2017)

Unpaired image-to-image translation

[NVIDIA partner, Brighter AI]

A strategy for unpaired image-to-image translation

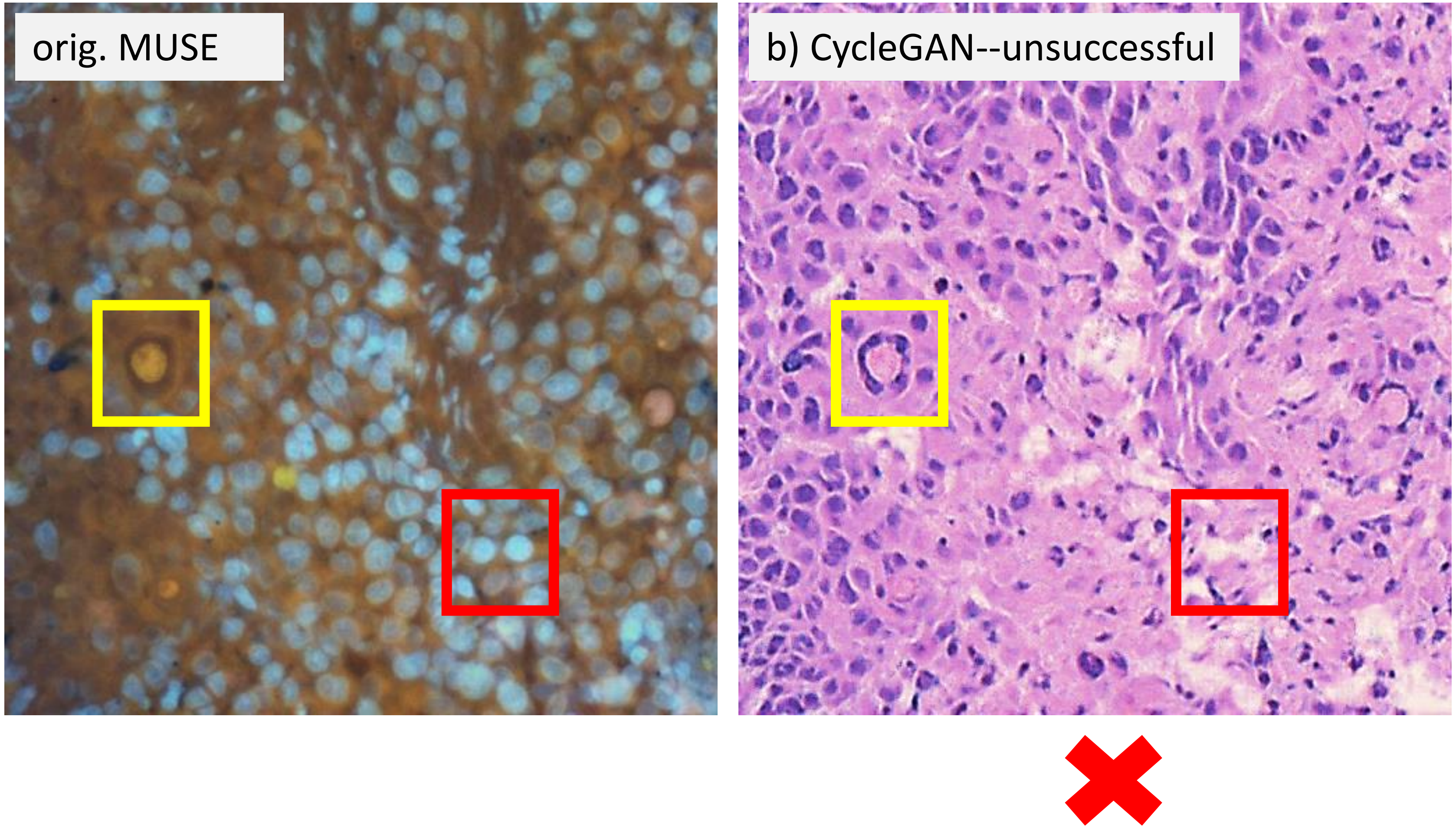


Shared by:

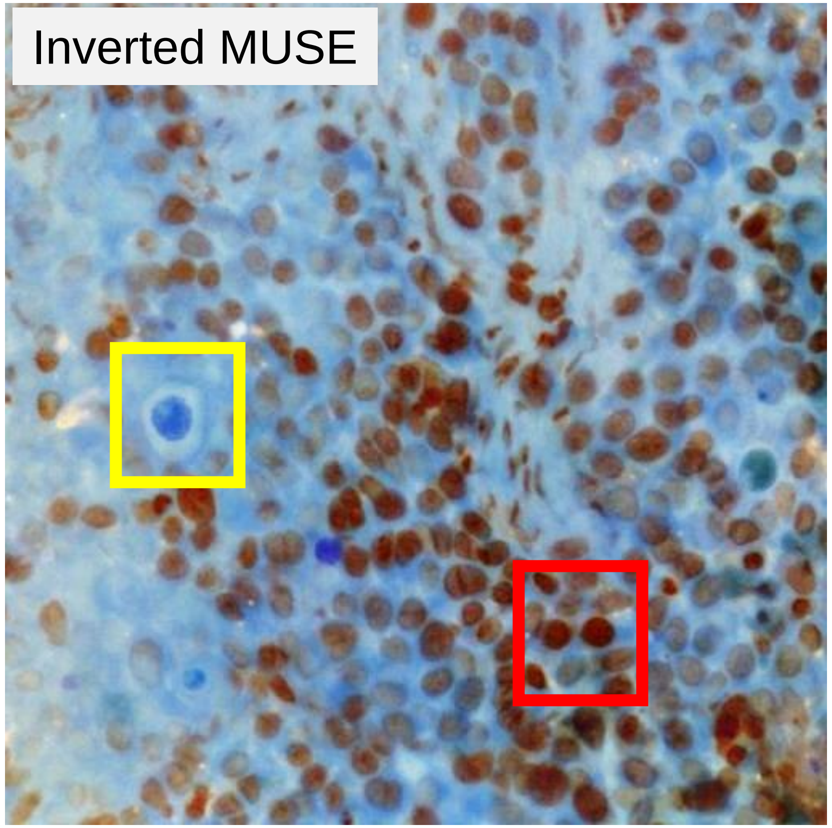
- CycleGAN
- DualGAN
- GANILLA

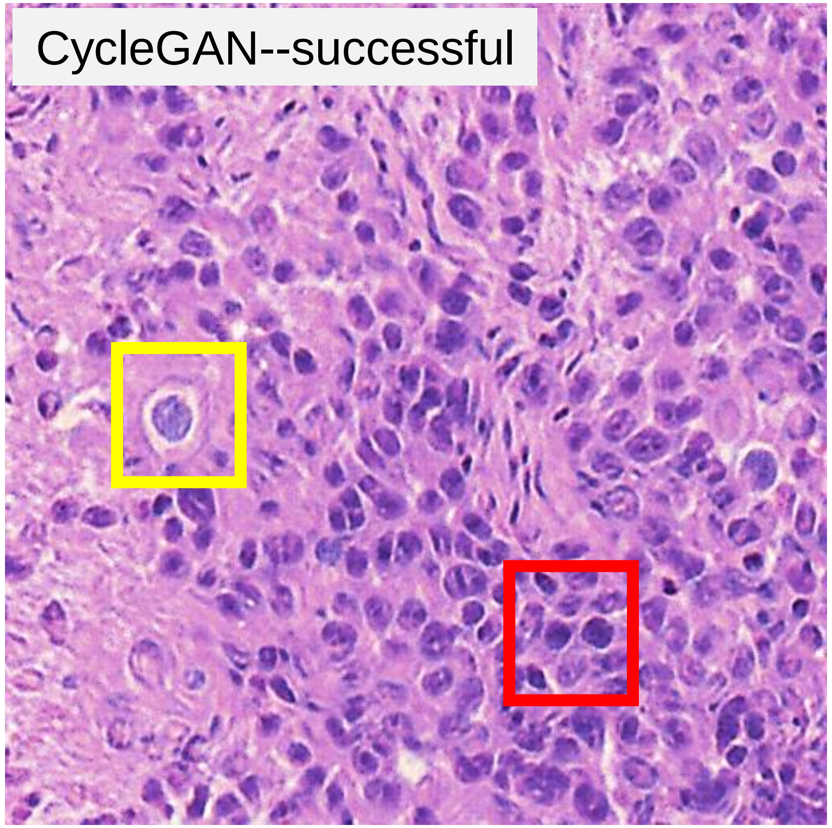
Results and Discussion

Training on original MUSE images fails



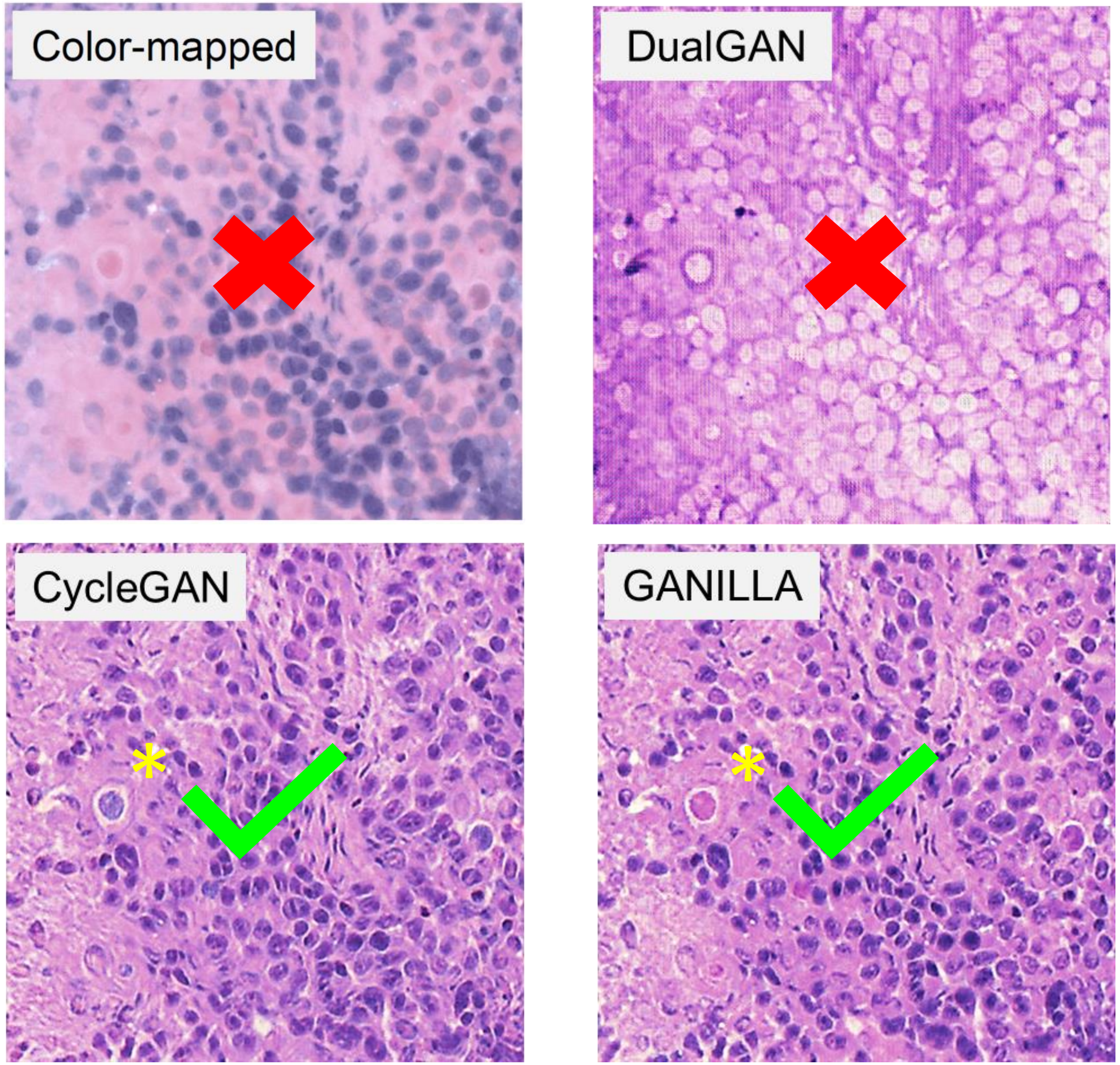
Training on inverted MUSE images succeeds



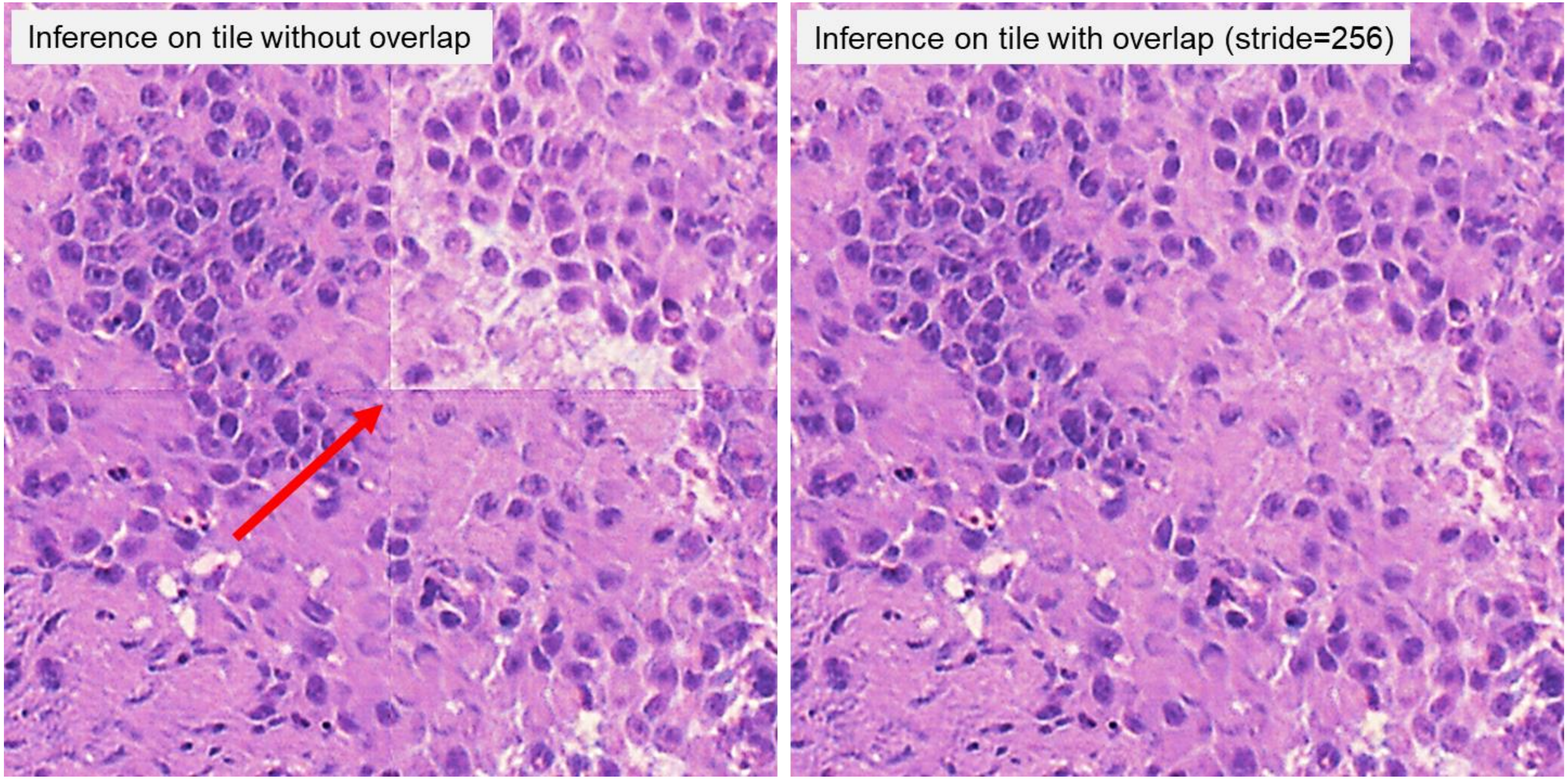


Even with image inversion, not all GANs succeed

Not a GAN

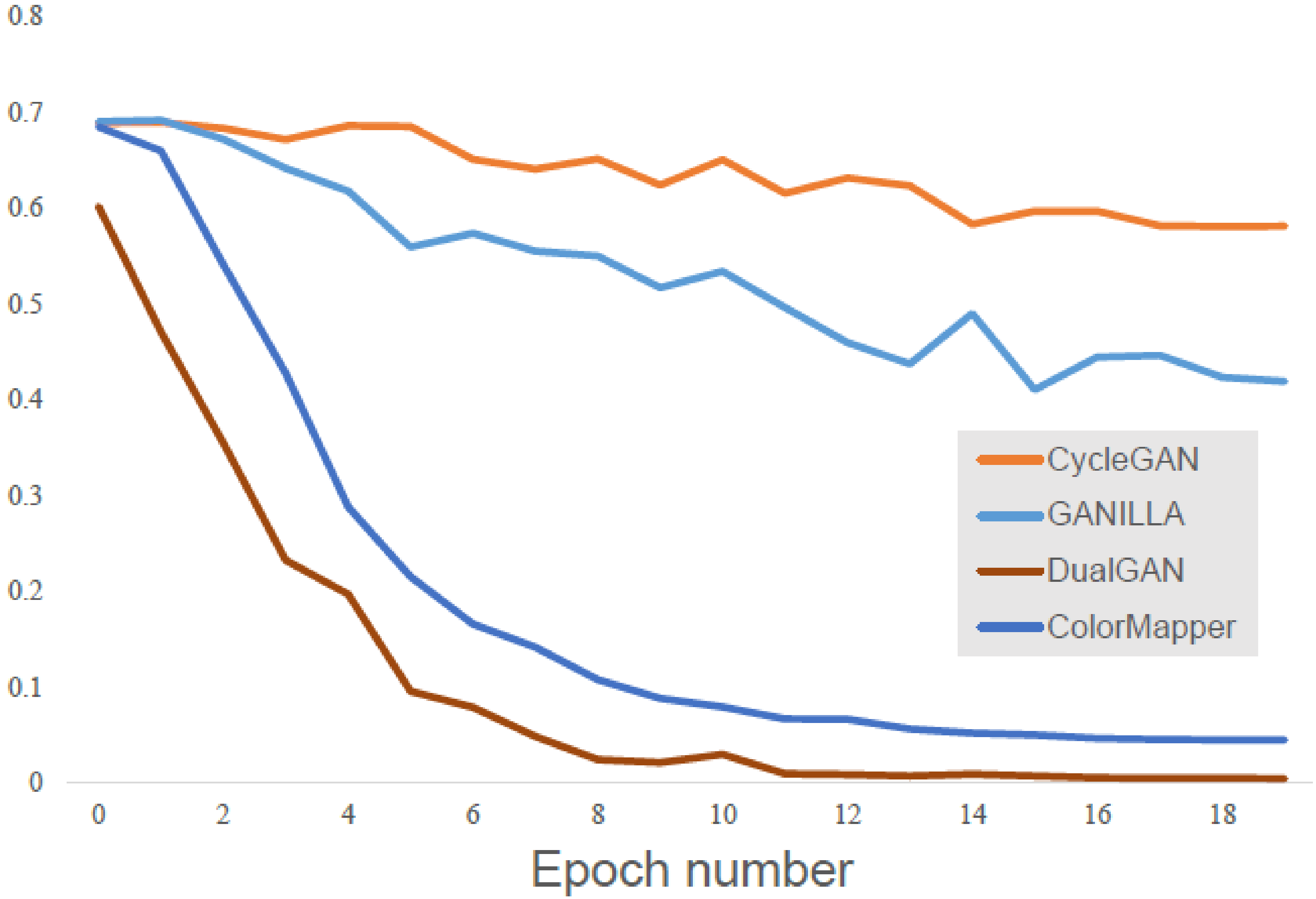


Tiling artifacts are solvable for image montages



“Quantitative” evaluation

- Training separate classifier to classify real & generated H&E images
- External critic score (higher is better):



Discussion

- Challenges and future work:
  - Inversion effect – additional loss constraints
  - Lack of quantitative metrics – pathologist evaluation
  - Preservation of content (prevention of hallucinations) – additional loss constraints?
  - Slow model inference – GAN compression

Conclusion

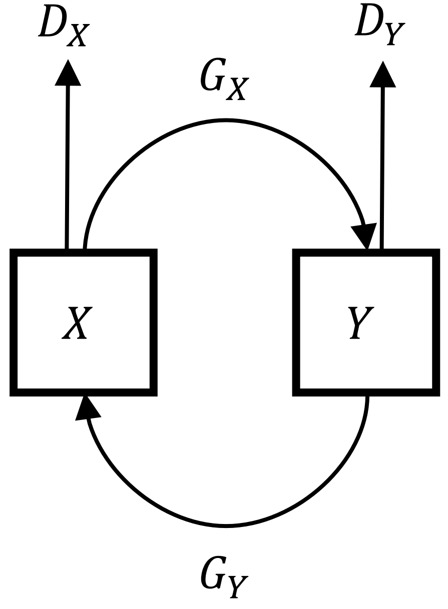
- Successful MUSE-to-H&E modality conversion with unpaired image-to-image translation

- Slide-free microscopy may see widespread adoption!

Appendix (Methods)

Method details

- Dataset - Urothelial Cell Carcinoma in Human Kidney
- Converting from MUSE (X) to H&E (Y) and back to MUSE (X)
- Discriminator (D_Y) that classifies between real and generated H&E images
- Generator (G_X) trained to fool the discriminator
- Generators (G_X and G_Y) trained to reconstruct MUSE image

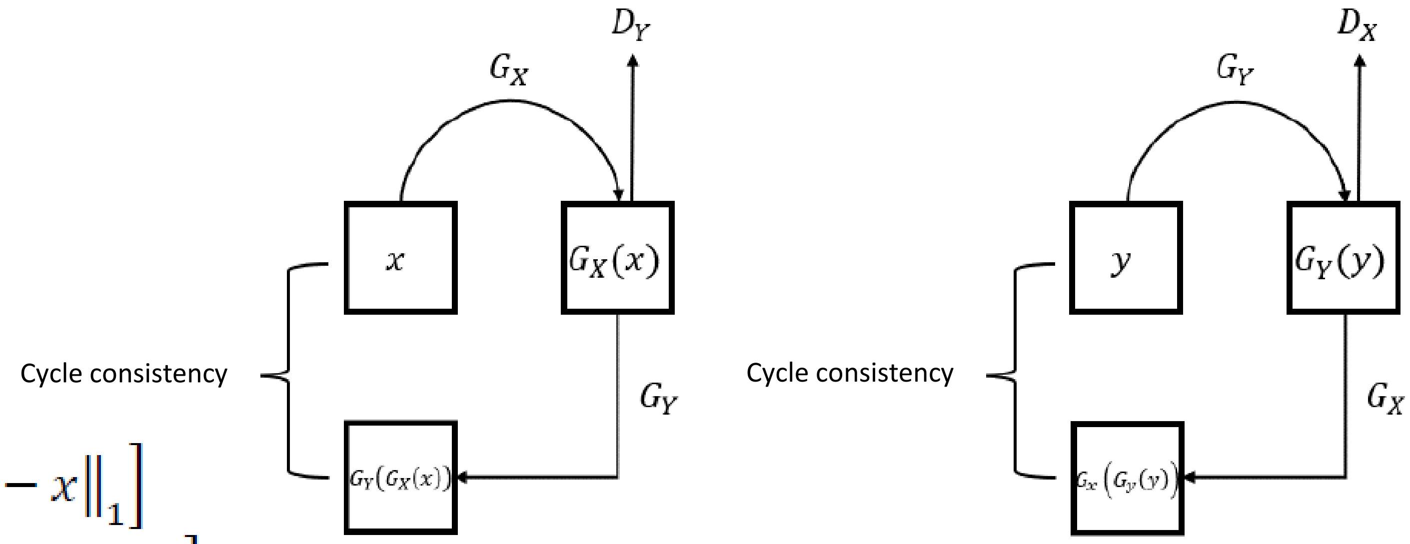


Tested techniques:

- All methods use GAN adversarial loss:

$$\mathcal{L}_{GAN}(G_X, D_Y, X, Y) \\ = \mathbb{E}_{y \sim p_{data}(y)}[\log D_Y(y)] \\ + \mathbb{E}_{x \sim p_{data}(x)}\left[\log\left(1 - D_Y\left(G_X(x)\right)\right)\right]$$

CycleGAN model:



- Cycle-consistency loss:

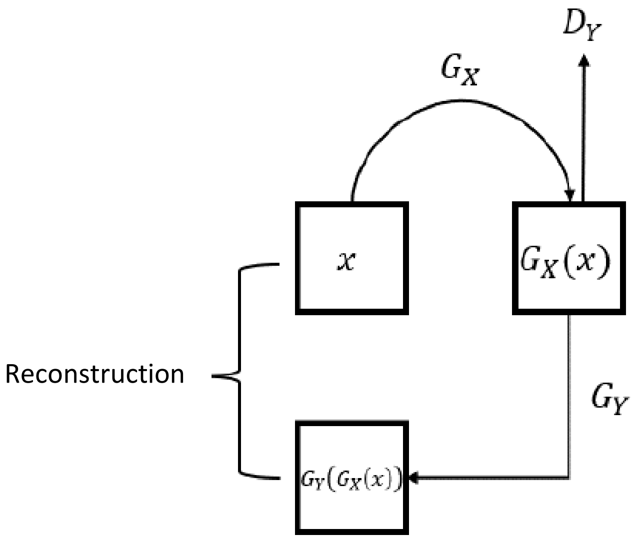
$$\mathcal{L}_{cycle}(G_X, G_Y) = \mathbb{E}_{x\sim p_{data}(x)}\left[\|G_Y(G_X(x)) - x\|_1\right] + \mathbb{E}_{y\sim p_{data}(y)}\left[\|G_X(G_Y(y)) - y\|_1\right]$$

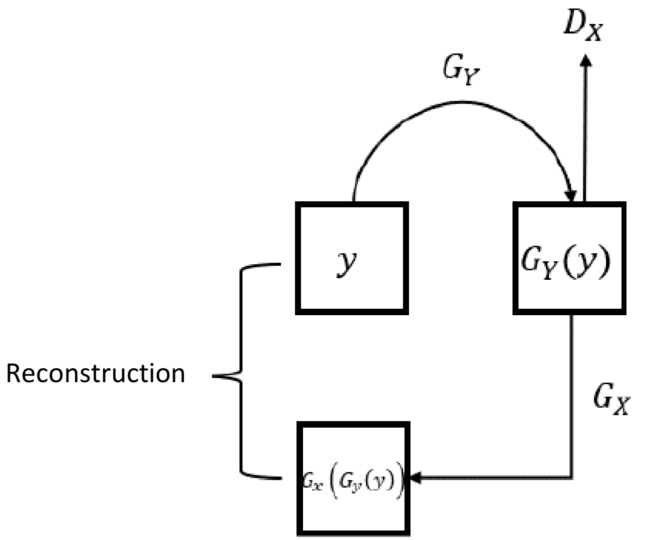
- Identity loss (regularization):

$$\mathcal{L}_{identity}(G_X, G_Y) = \mathbb{E}_{y\sim p_{data}(y)}[\|G_X(y) - y\|_1] + \mathbb{E}_{x\sim p_{data}(x)}[\|G_Y(x) - x\|_1]$$

- Generator: Residual block-based network in Johnson et al.
- Discriminator: 70x70 PatchGAN

DualGAN model:





- Reconstruction loss:

$$\mathcal{L}_G(G_X, G_Y) = \lambda_X \|x - G_Y(G_X(x))\|_1 + \lambda_Y \|y - G_X(G_Y(y))\|_1 - D_X(G_Y(y)) - D_Y(G_X(x))$$

- Discriminator loss:

$$\mathcal{L}_D(G_X, D_Y, X, Y) = D_Y(G_X(x)) - D_Y(y)$$

- Generator: U-net
- Discriminator: 70x70 PatchGAN
- WGAN training procedure

GANILLA

- Same as CycleGAN, different generator!
- Aim to preserve content