Adversarial learning of cancer tissue representations

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Abstract

- Deep generative models with representation learning properties provide an alternative path to further understand cancer tissue phenotypes, capturing tissue morphologies.
- We present an adversarial learning model to extract feature representations of cancer tissue, without the need for manual annotations.
- Here we show that these representations are able to identify a variety of morphological characteristics across three cancer types: breast, colon, and lung.

PathologyGAN Model
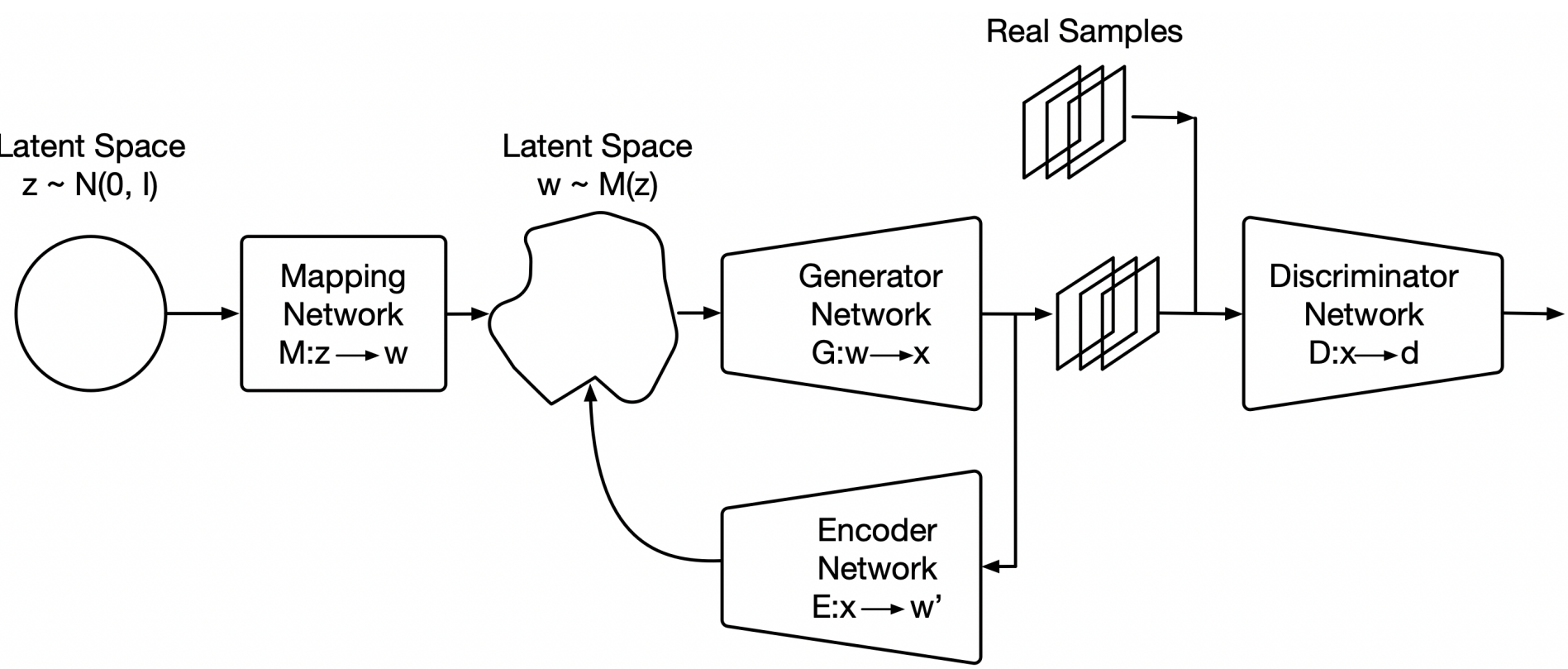
GAN Loss:
Relativistic Average Discriminator

$$L_{Dis} = -\mathbb{E}_{x_r \sim \mathbb{P}}\left[\log\left(\tilde{D}\left(x_r\right)\right)\right] - \mathbb{E}_{x_f \sim \mathbb{Q}}\left[\log\left(1 - \tilde{D}\left(x_f\right)\right)\right],$$
$$L_{Gen} = -\mathbb{E}_{x_f \sim \mathbb{Q}}\left[\log\left(\tilde{D}\left(x_f\right)\right)\right] - \mathbb{E}_{x_r \sim \mathbb{P}}\left[\log\left(1 - \tilde{D}\left(x_r\right)\right)\right],$$
$$\tilde{D}\left(x_r\right) = \text{sigmoid}\left(C\left(x_r\right) - \mathbb{E}_{x_f \sim \mathbb{Q}}C\left(x_f\right)\right)\right),$$
$$\tilde{D}\left(x_f\right) = \text{sigmoid}\left(C\left(x_f\right) - \mathbb{E}_{x_r \sim \mathbb{P}}C\left(x_r\right)\right).$$

Encoder Loss:
MSE Reconstruction of Latent Vectors

$$L_{Enc} = \mathbb{E}_{z \sim P_z}\left[\frac{1}{n}\sum_{i=1}^{n}(w_i - w'_i)^2\right]$$
$$\text{where } n = dim(w), \ w' = E(G(w)), \ w = M(z).$$

Visualization of Latent Space and Tissue Classification
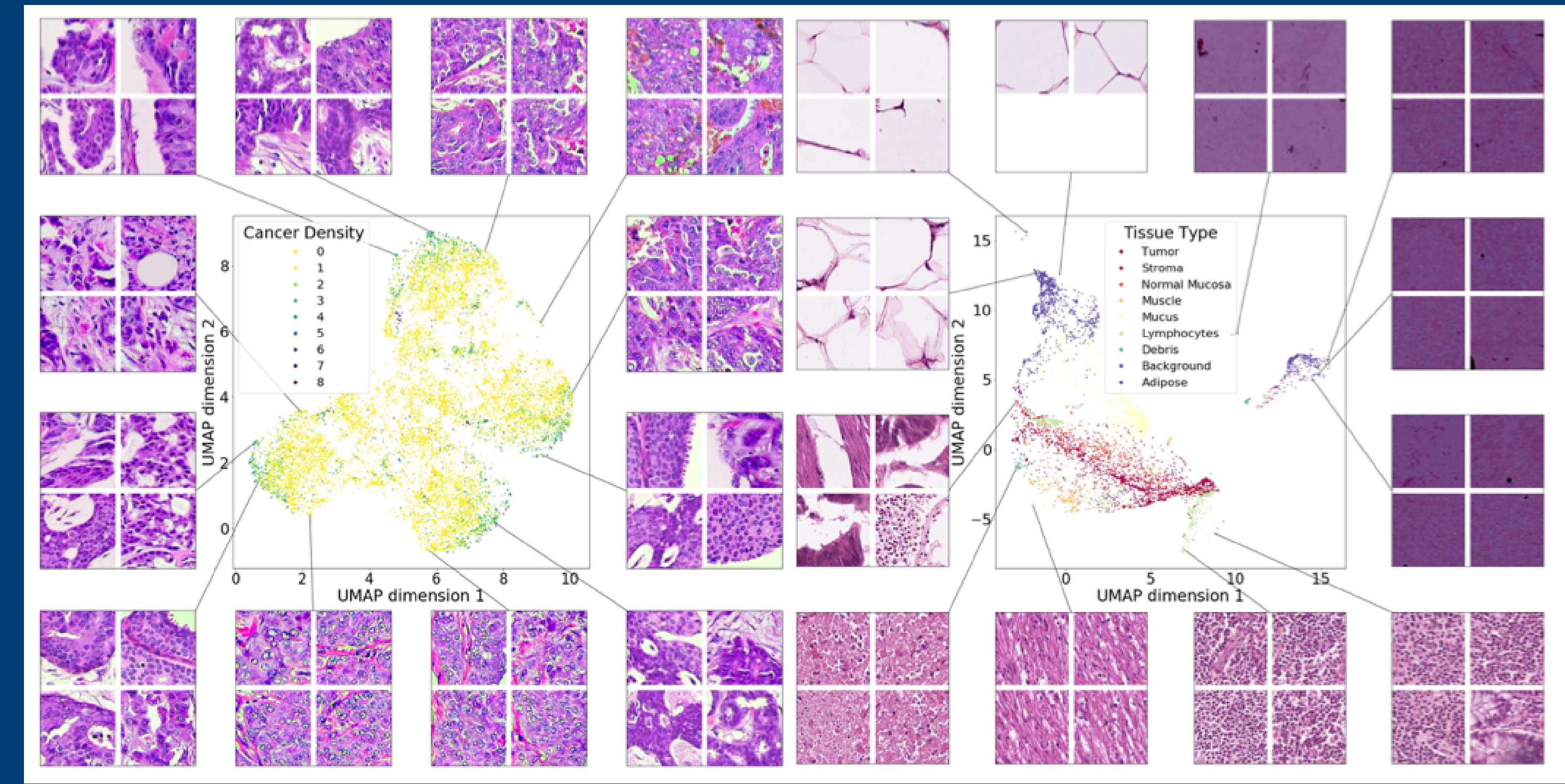
- **Visualizations:**
  - H&E breast cancer dataset (VGH/NKI) annotated with cancer cell density in tissue tiles.
  - H&E colorectal cancer dataset (NCT) annotated with tissue type: adipose, background, debris, lymphocytes, mucus, smooth muscle, normal colon mucosa, cancer-associated stroma, and colorectal adenocarcinoma.
- **Tissue Type Classification:**
  - Logistic regression trained over latent vectors.
  - Comparable to supervised approaches: Bayesian DNN [1] RBF-SVM [2].

Total AUC: 0.976								
Tumor	Simple Stroma	Mucosa	Mucus	Lymph.	Debris	Back.	Adipose
0.974	0.929	0.964	0.997	0.994	0.959	1.0	0.998

Total Accuracy: 85.43%								
Tumor	Simple Stroma	Mucosa	Mucus	Lymph.	Debris	Back.	Adipose
89%	71%	68%	91%	83%	63%	100%	96%

Model	AUC	Accuracy
Ours	0.976	85.43%
BayesianDNN	**0.995**	**99.2%**
RBF-SVM	0.976	87.4%

# Multiple Instance Learning over Latent Representations

- We use the attention-based deep MIL [1] over latent representations in TCGA Lung cancer WSIs.
- We highlight images and representations of the top weighted representations for the tumor outcome prediction.
- MIL model focuses on regions of the latent space with tumor tissue.

Model	AUC	Accuracy
Ours	0.980	94.0%
Coudray et al [3]	**0.993**	**97.5%**
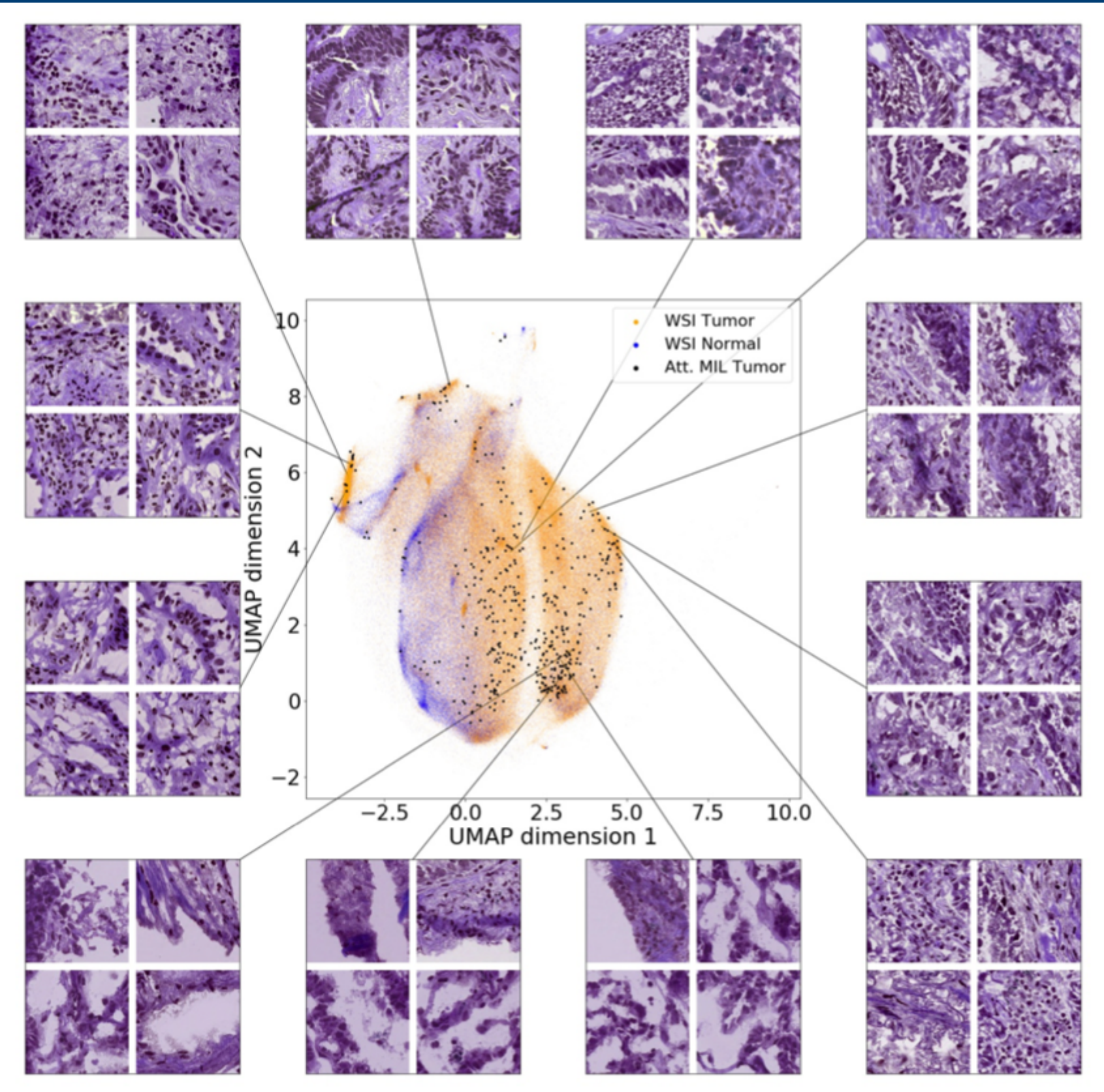
Real Tissue Reconstructions

- Real tissue images (a) and their reconstructions (b), images are paired by columns.
- We show examples of Breast and Colorectal cancer tissue.
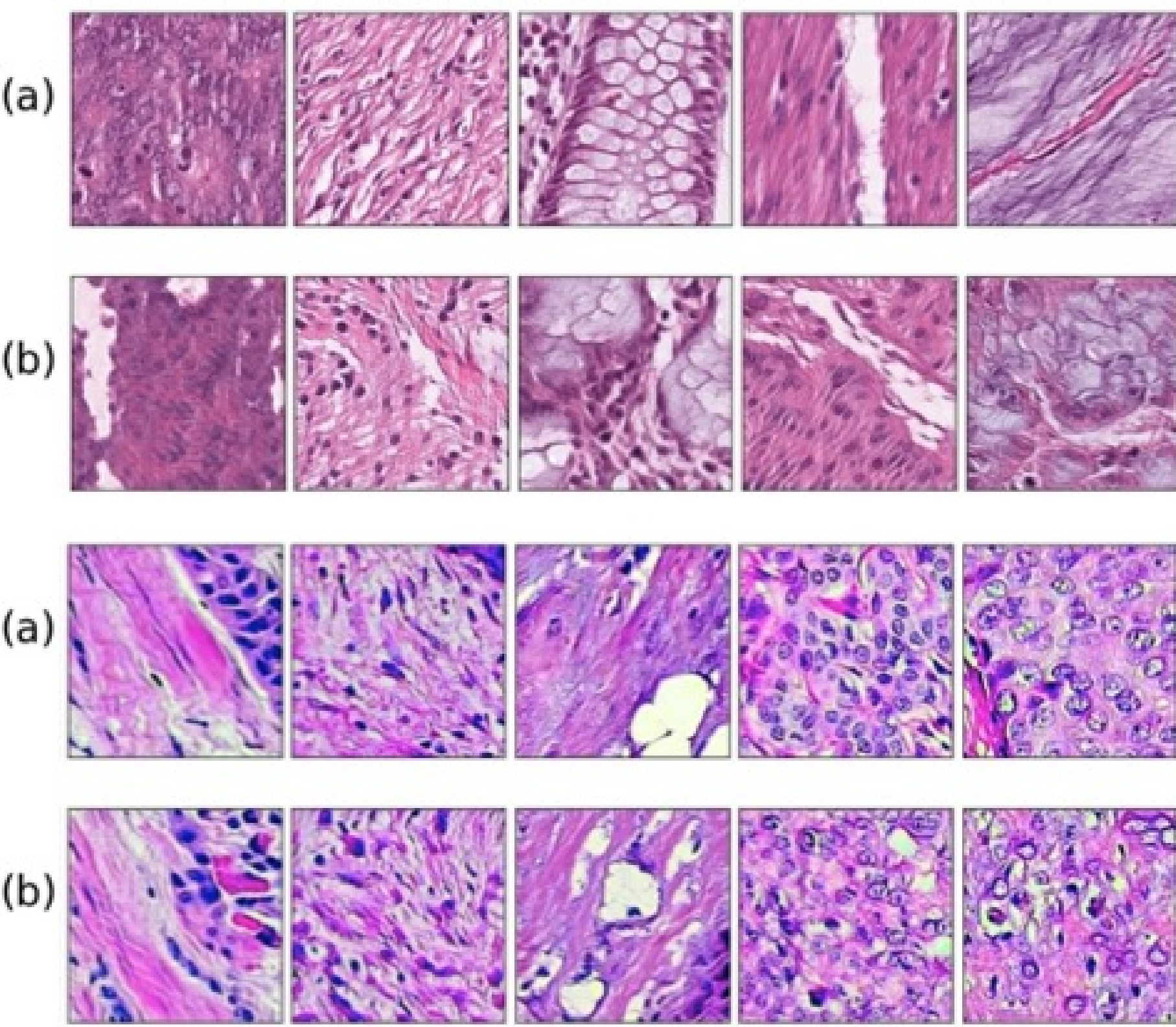
Contributions

PathologyGAN[3] captures distinct phenotype characteristics of cancer tissue. We tested the applicability of our representations in three different settings:
1. Latent space visualization.
2. Tissue type classification over latent representations.
3. Tumor WSI prediction with Multiple Instance Learning.

References

[1] Raczkowski, L. et al. Ara: accurate, reliable and active histopathological image classification framework with bayesian deep learning. Scientific Reports. 2019.

[2] Kather, J.N. et al.: Multi-class texture analysis in colorectal cancer histology. Scientific Reports. 2016.

[3] Coudray, N. et al. Classification and mutation prediction from non−small cell lung cancer histopathology images using deep learning. Nature Medicine. 2018

[4] Quiros, A.C. et al. Pathologygan: Learning deep representations of cancer tissue. MIDL 2020.

Acknowlegments

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