VSGD-Net:
Virtual **S**taining **G**uided Melanocyte **D**etection on Histopathological Images

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Outline

- Introduction
- Dataset
- Methodology
- Results and Discussions
  - Main Results
  - Ablation Study

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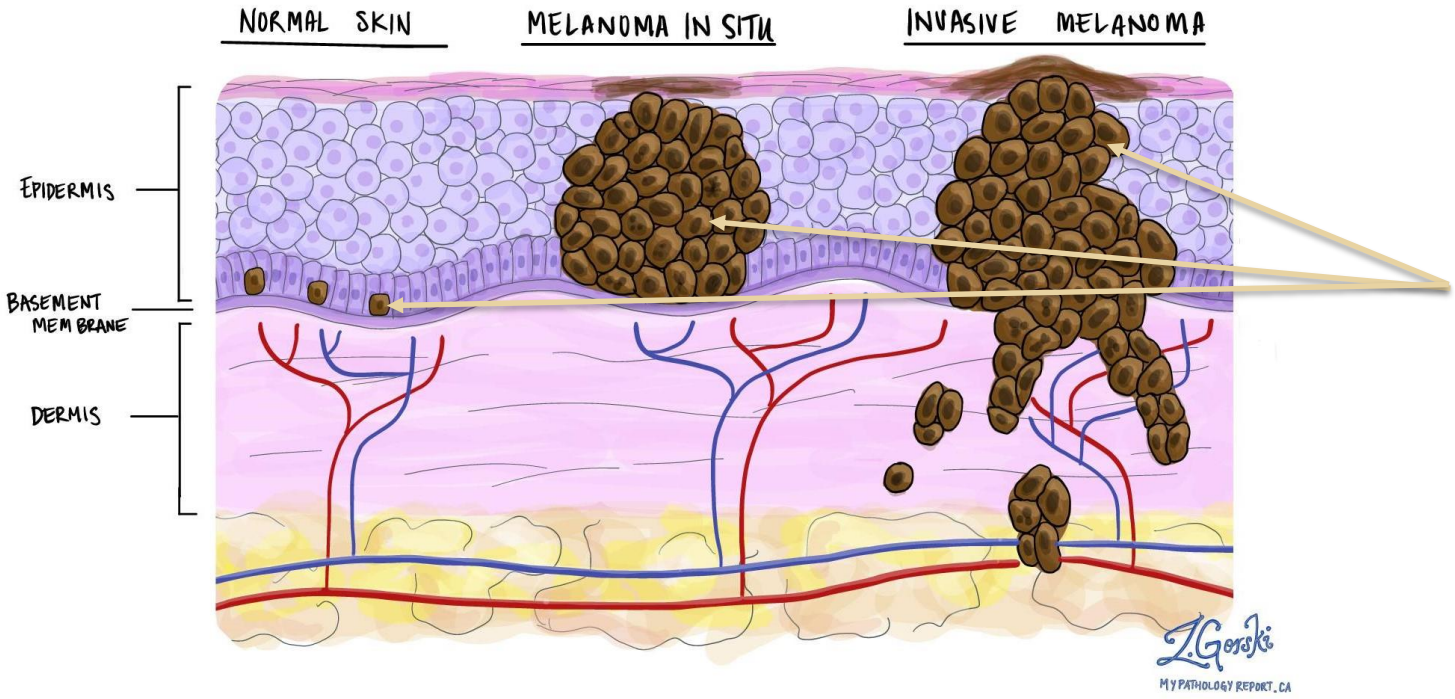
What is melanoma?

> Melanoma is the most serious type of skin cancer and is potentially fatal.

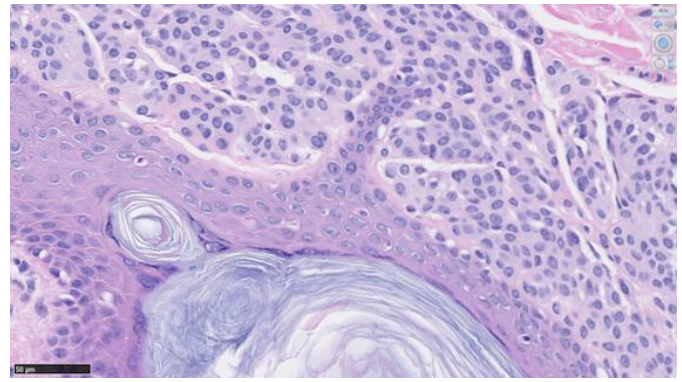
> Melanoma develops when melanocytes start to grow out of control.

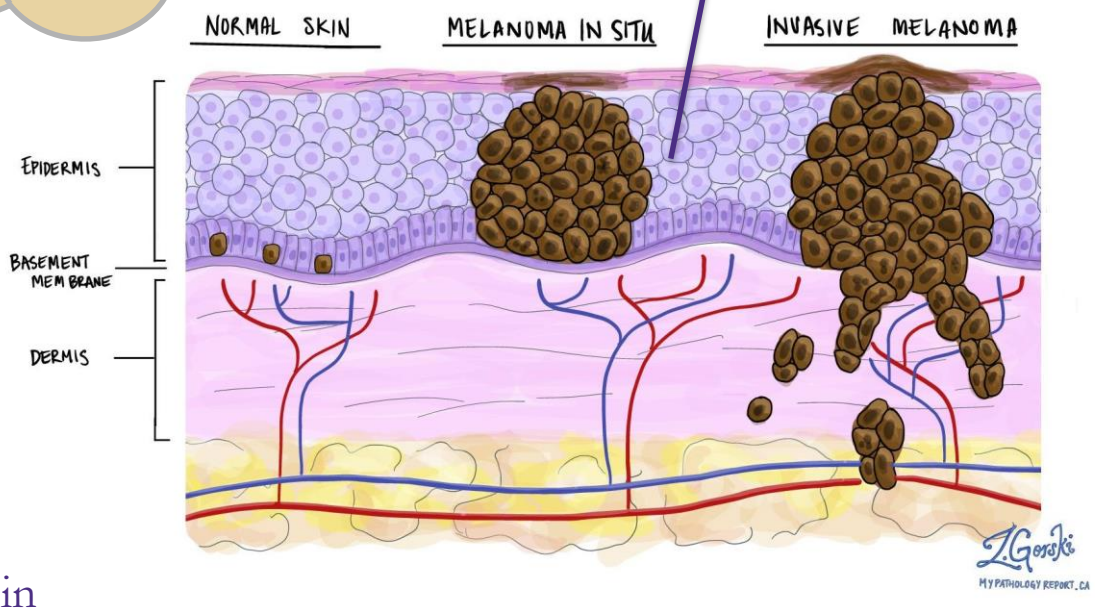


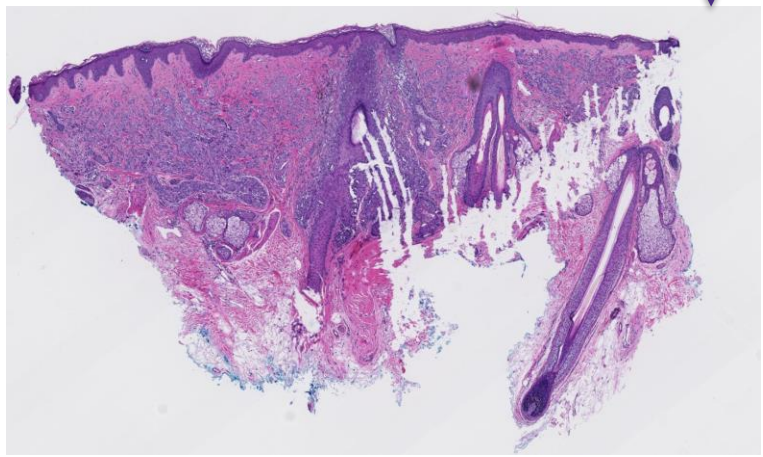
Melanocyte:
melanin-producing cell

How do pathologists diagnose melanoma?

Architectural growth patterns of melanocytes?



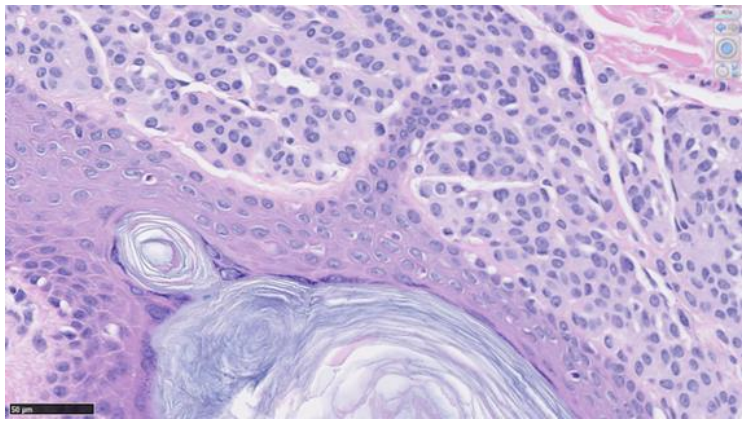




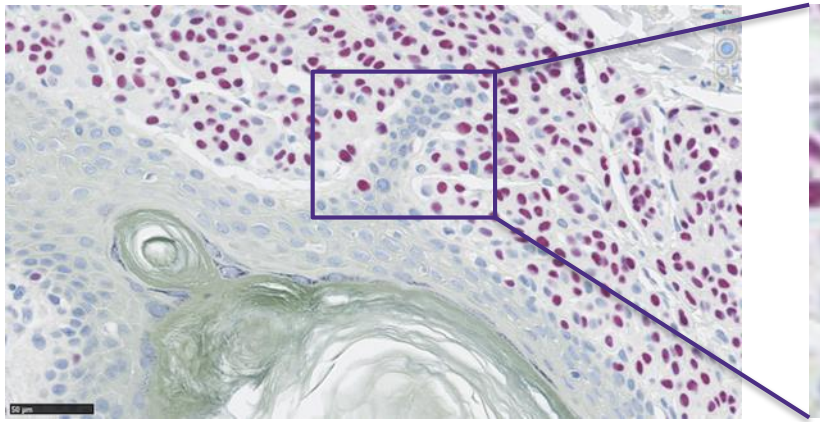
Hematoxylin and Eosin (H&E) stained skin biopsies

Supplemental Immunostaining

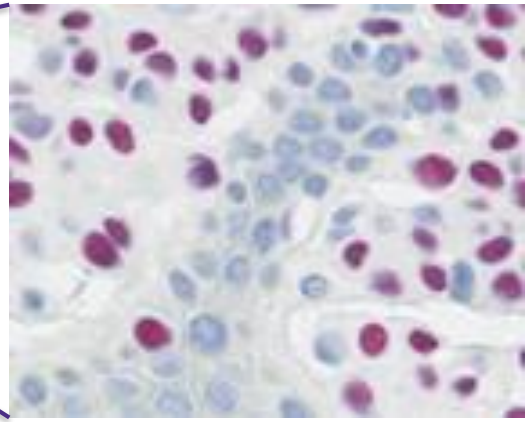
> Sox10 staining can highlight melanocytes, but it's not a routine procedure due to its **high cost**.



(a) H&E Staining



(b) Sox10 Staining – melanocytes are red



(c) Crop from Sox10

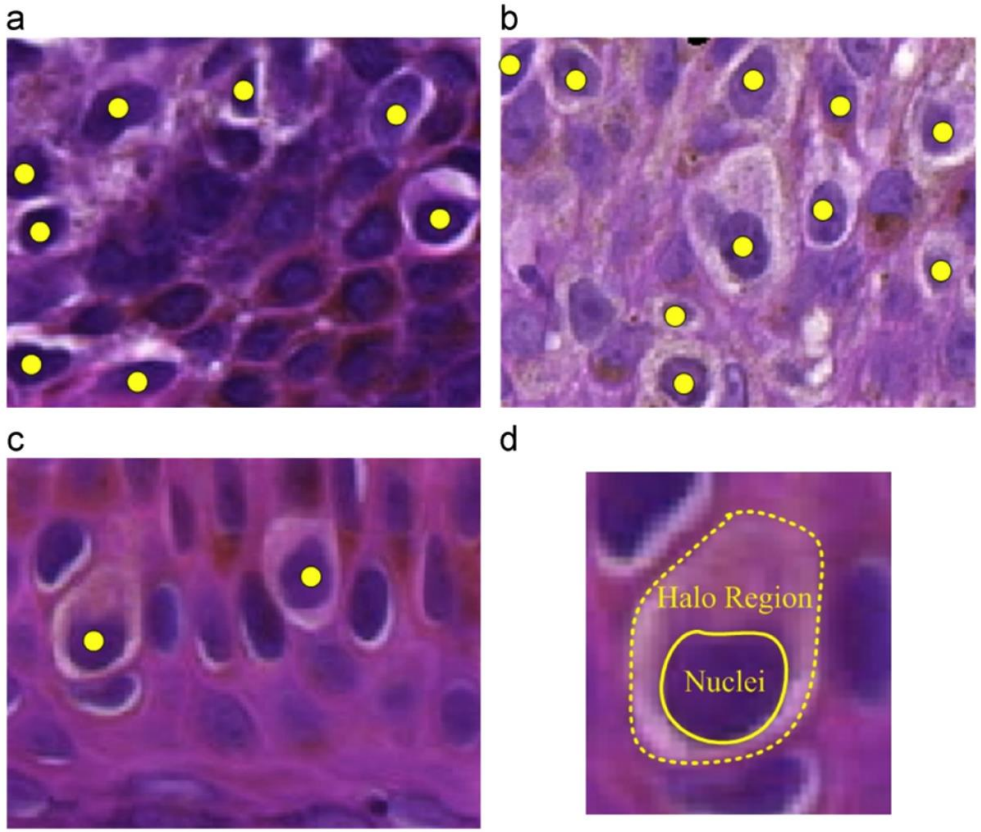
Study Goal

> Can we automatically **detect melanocytes** on **H&E** images?

1. Address the limitations:
   -- Visual similarity of melanocytes to other cells in H&E images
   -- High cost of Sox10 staining
2. Reduce the burden on pathologists
3. Aid in melanoma diagnosis in the future

Related Work

- **Melanocyte detection**
  - Radial Line Scanning [1] based on the "halo region" assumption.
  - Halo-regio /te detection.
- **Nuclei dete**
  - U-Net [2], [4], StarDist (a shape-guided CNN) [5], C etc.
  - Fail to inco
- **Tissues dete** AN [7]
  - Fail to expl e synthesis process.



Study Goal

> To automatically **detect melanocytes** on **H&E** stained images and leverage **the information from the two stainings** (H&E and Sox10), we propose **VSGD-Net (Virtual Staining Guided Detection Network).**

1. Address the limitations:
   -- Visual similarity of melanocytes to other cells in H&E images
   -- High cost of Sox10 staining
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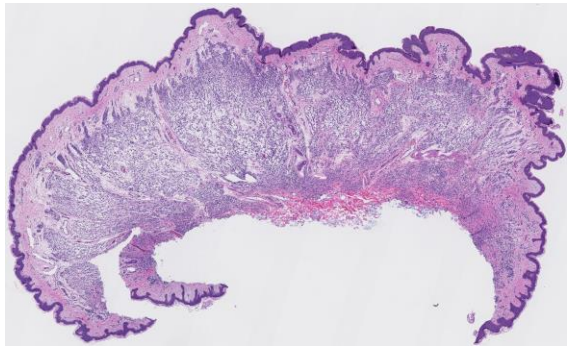
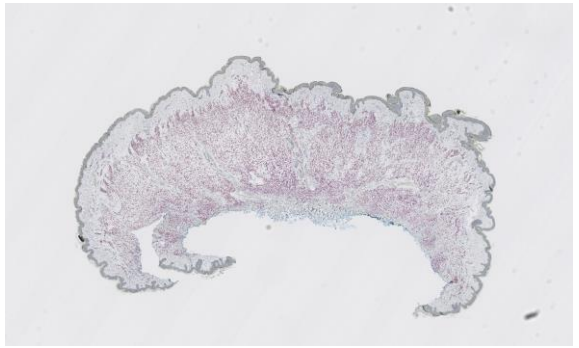
Dataset

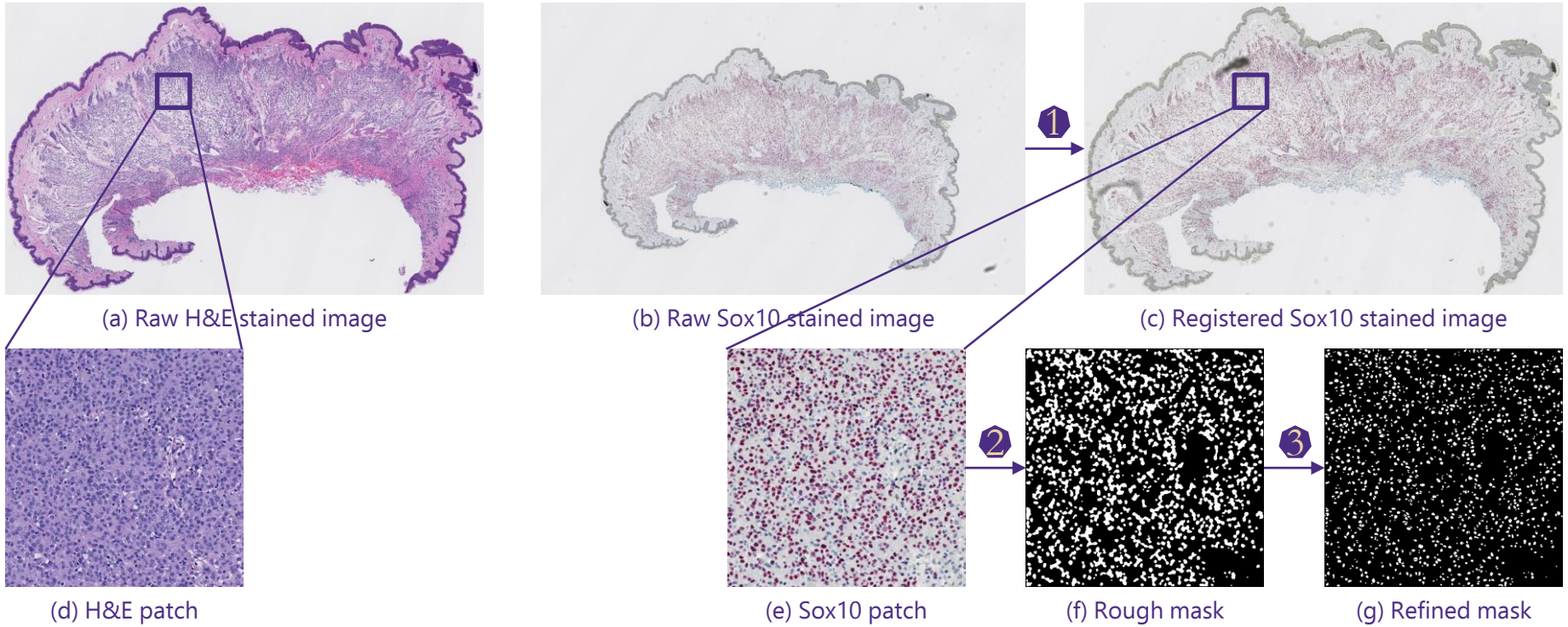
- Our dataset consists of skin tissues of 15 cases from a private dermatopathology lab, including 3 cases for each MPATH diagnostic category[1] [8].
- We stain each glass slide with H&E first, then de-stain and re-stain the same glass slide in Sox10.
- Each skin tissue is cut into multiple (4-6) thin slices for microscopic examination, resulting in **75 slices** at 20x magnification.





[1] Class 1-5: Benign mildly atypical nevi, Moderate dysplastic nevi, Melanoma in situ, Invasive melanoma T1a, and Invasive melanoma T1b.

Dataset - Preprocessing



(a) Raw H&E stained image (b) Raw Sox10 stained image (c) Registered Sox10 stained image

(d) H&E patch (e) Sox10 patch (f) Rough mask (g) Refined mask

Preprocessing steps: First, we register raw Sox10 images (b) into aligned Sox10 images (c) using template H&E images (a) with the Histokat software [9]. Then, we apply a Random Forest classifier to classify pixels into melanocyte or non-melanocyte. At last, the pretrained NuSeT [10] separates touching nuclei and refine the masks.

Dataset

> To fit images into memory as well as keep adequate information, we crop the registered paired images into 256x256 patches with 10x magnification and exclude the background patches, leaving 25,314 patches to use.

Sub-dataset	From ? cases	# Patches
Train	10 cases	14,630
Validation		1,032
Test	5 cases	9,652

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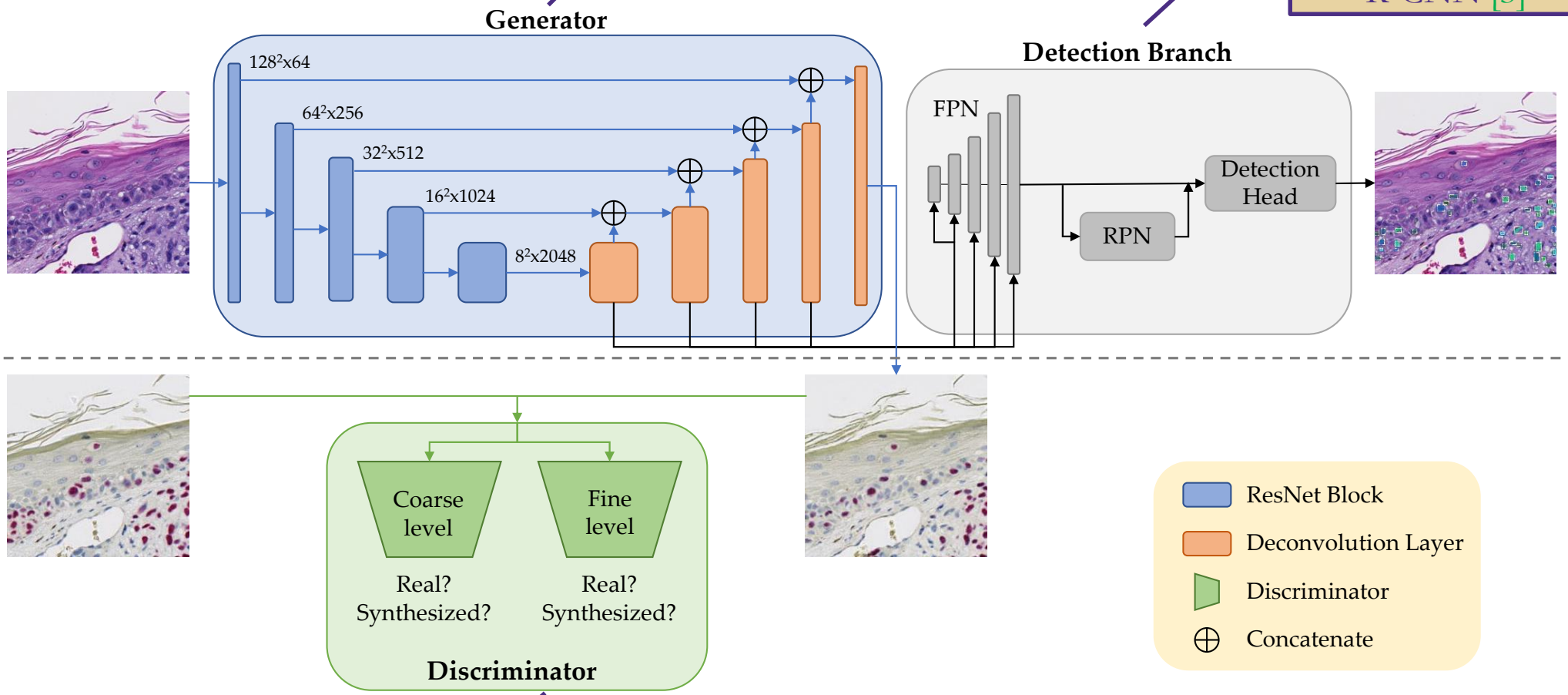
VSGD-Net

U-Net [2] with ResNet50

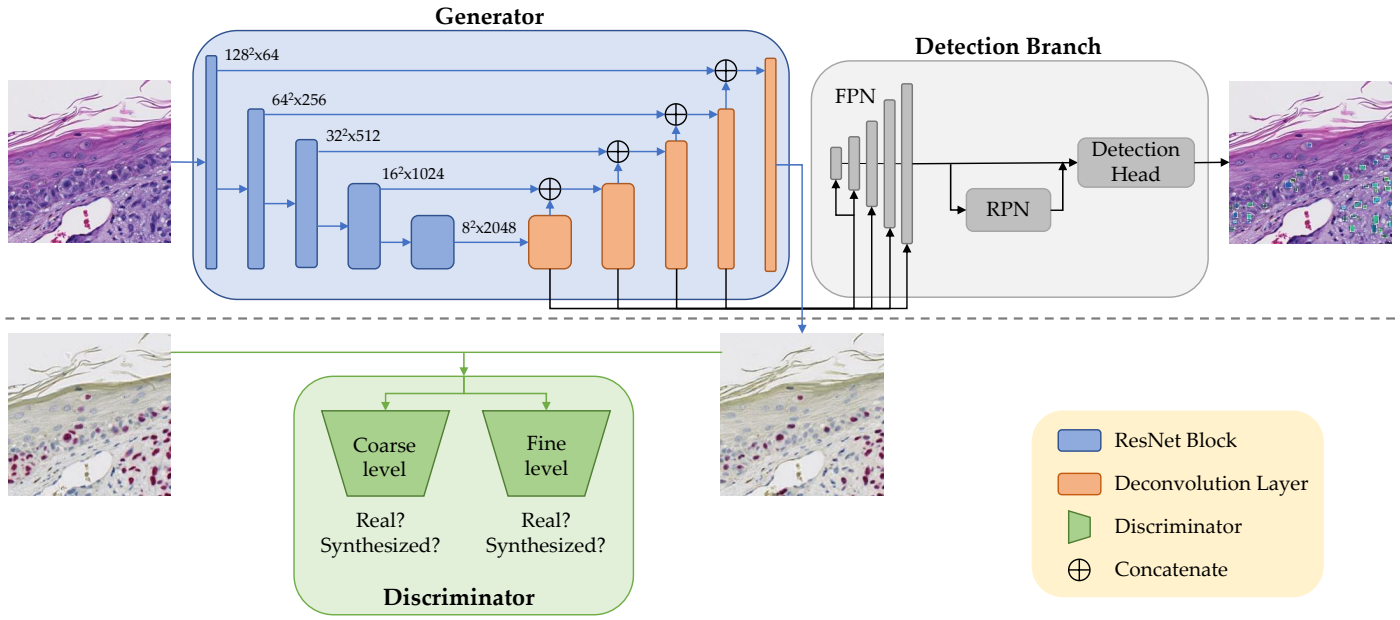
Inspired by Mask R-CNN [3]



Multi-scale discriminator

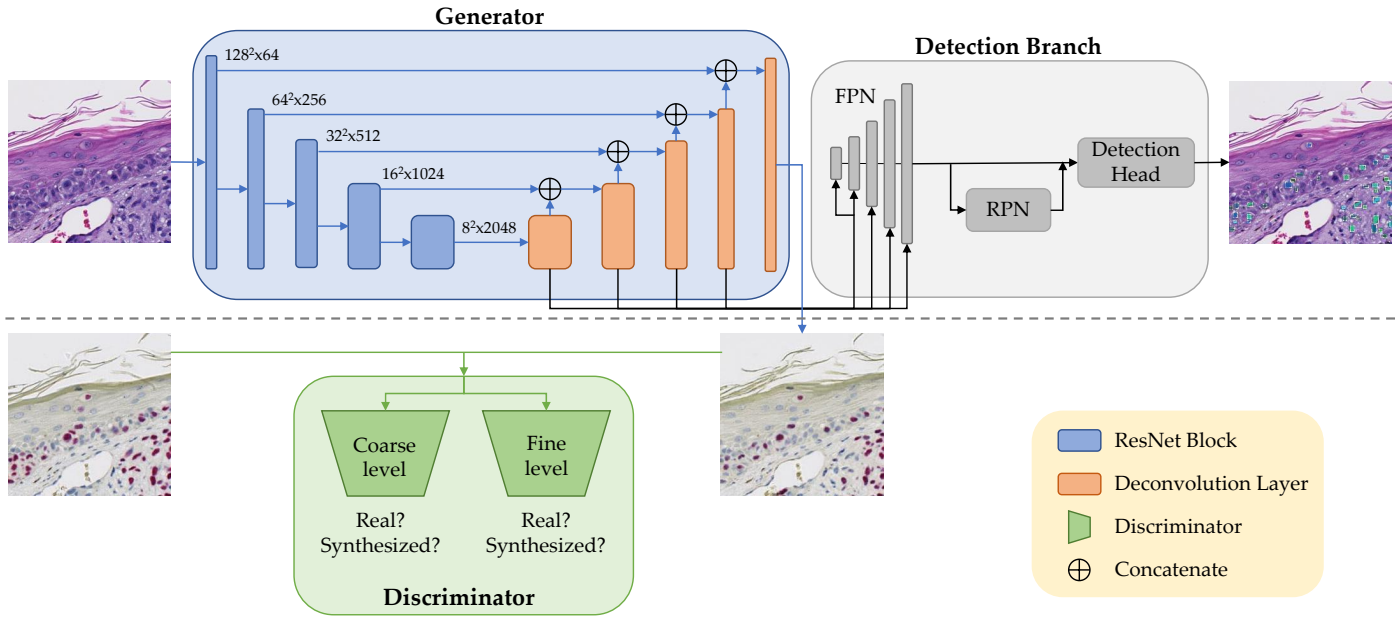
VSGD-Net

- Features input to the detection branch?
  - We assume decoder layers have higher correlation with the Sox10 than encoder layers.
  - The ablation study validates this design.



VSGD-Net

$$L = \underbrace{\sum_{i=1,2} \left(\log(D_i (X_s)) + \log(1 - D_i (G (X_h))) \right)}_{L_{GAN}} + \underbrace{L_{rpn} + L_{box_c} + L_{box_r} + L_{seg}}_{L_{DET}}$$



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Evaluation Metrics

- Precision = TP / (TP + FP)
- Recall = TP / (TP + FN)
- F1-score = $2 \times \frac{(\text{Precision} \times \text{Recall})}{\text{Precision} + \text{Recall}}$
- Jaccard Index = TP / (TP + FN + FP)

Baseline Methods

- **Radial Line Scanning** [1]: detects melanocytes through the halo regions
- **Mask R-CNN** [3]
- **U-Net** [2]
- **StarDist** [5]: guided by nuclei shape
- **HoverNet** [4]: leverages the distance maps from pixels to nuclear center
- **CHR-Net** [6]: leverages high-resolution feature extractors
- **Nuclei Classification**: train ESPNetv2 [11] to classify predicted nuclei patches into melanocytes or non-melanocytes.

Main Results

Table 1: Results of different methods.

Method	Precision	Recall	F_1	Jaccard
RLS [16]	0.443	0.570	0.499	0.332
Nuclei Classification	0.693	0.506	0.585	0.413
Mask R-CNN [7] (w/o image resize)	0.698	0.500	0.583	0.411
Mask R-CNN [7] (w image resize)	0.735	0.514	0.605	0.434
U-Net [21]	0.630	0.639	0.635	0.465
StarDist [22]	**0.745**	0.426	0.542	0.372
HoverNet [6]	0.729	0.499	0.592	0.421
CHR-Net [3]	0.607	0.688	0.645	0.476
Ours (w Pix2PixHD [27] generator)	0.663	0.645	0.654	0.486
Ours	0.623	**0.733**	**0.674**	**0.508**

Lack generalizability

High precision but Low recall

Fails due to the similarity between melanocytes and other cells

Benefit from skip connections

Fewer Conv layers & no skip connection

Ablation Study

> Decoder layers have higher correlation with the Sox10 than encoder layers.

Table 2: Ablation results for the skip connection and the input features of the detection branch.

Skip Connections	Features for Detection	Precision	Recall	F_1	Jaccard
No	Encoder	0.586	0.713	0.644	0.474
No	Decoder	0.600	0.624	0.618	0.441
Yes	Encoder	0.618	0.667	0.641	0.472
Yes	Decoder	**0.623**	**0.733**	**0.674**	**0.508**

Limitations

- Pseudo ground-truth labels
  - It's not feasible to manually label melanocytes for training.
- Generator structure
  - Synthesis features can be improved by SOTA GAN models.

Future Work

- Build a computer-aided system (CAD) to analyze the growth patterns of melanocytes and expand it to a diagnosis framework.
- Apple VSGD-Net to more multi-modality medical imaging fields, such as CT-MRI [12], PET-MRI [13], etc.

Conclusion

> We present a novel virtual staining guided detection network, VSGD-Net.

> During inference, the model can produce promising results from only the routine H&E staining.

> We anticipate that the proposed method can adapt to a broad category of diseases.

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Thank you for your attention.