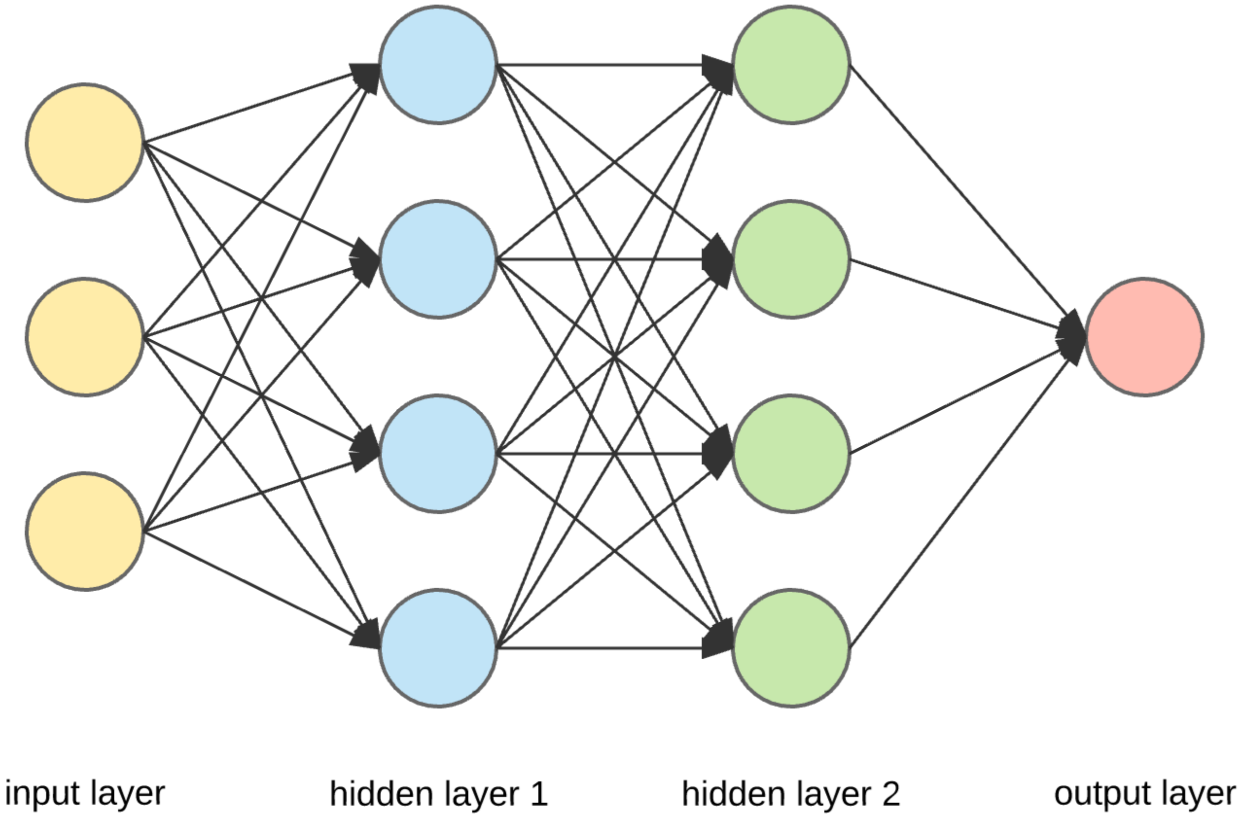
# Homework: CNN

# Neural Network (Q1)



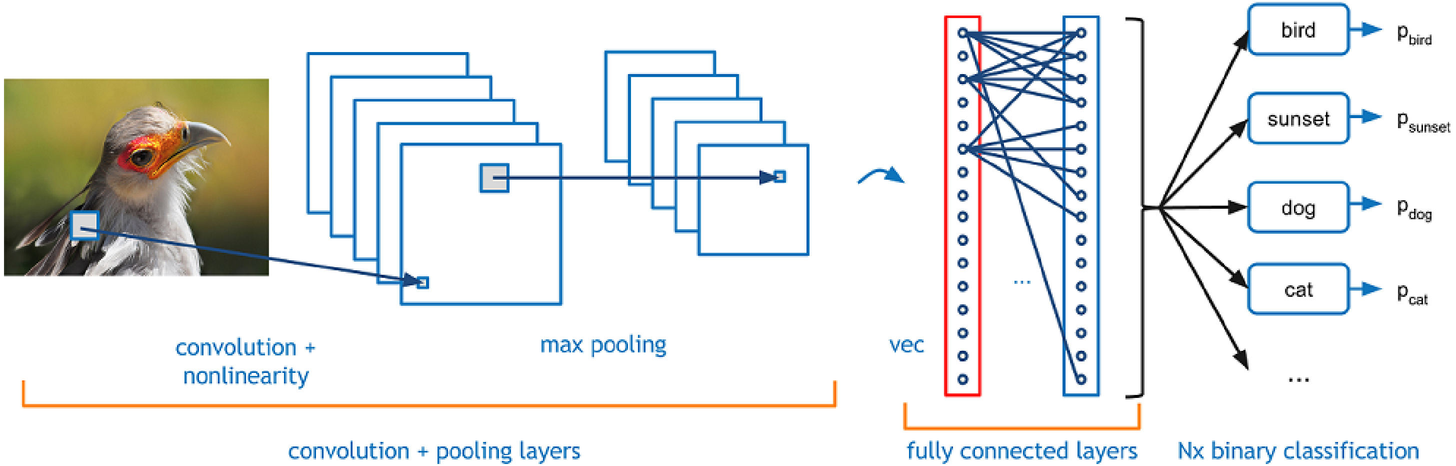
# Convolutional Neural Network (Q2)

Conv

Pool

FC

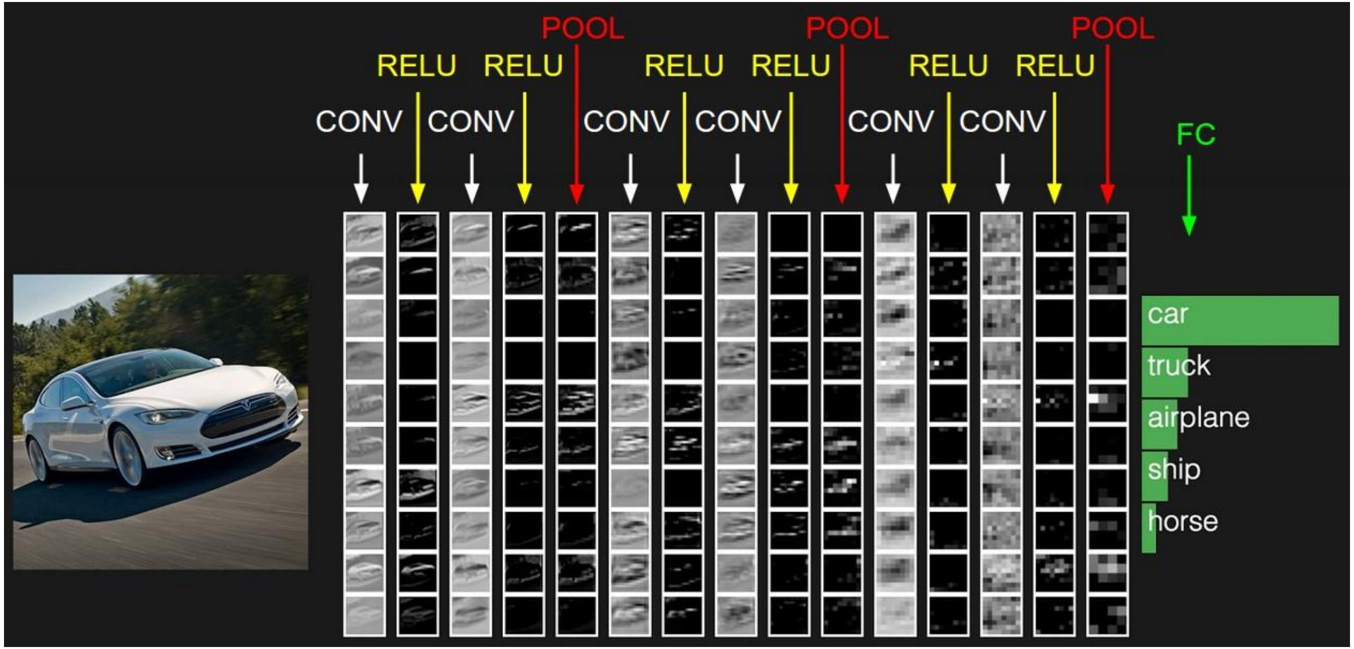
Cross Entropy



# Yellow or Blue?

# Color Normalization (Q3)

# Deep Convolutional Neural Network (Q4)



# Make the Design More Flexible

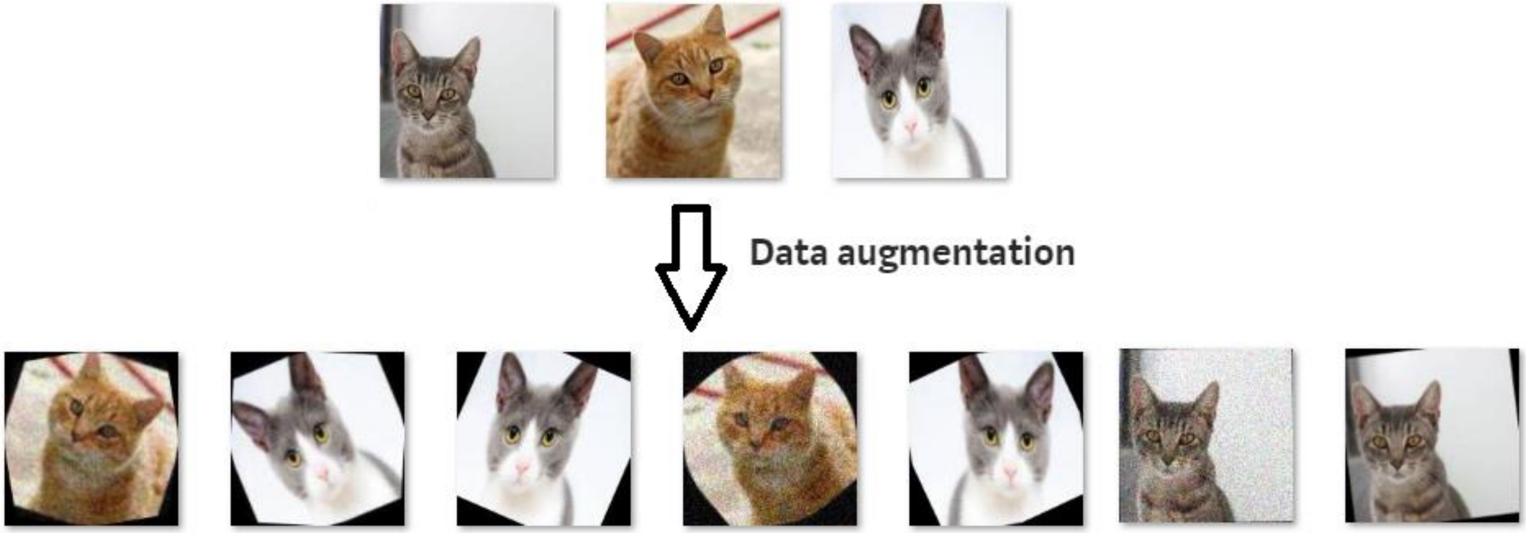
Input:

[8, 16, 32, "pool"]

| Layer | Output Size | Output Channels |
| --- | --- | --- |
| Input | 30 x 30 | 3 |
| Conv | 28 x 28 | 8 |
| ReLU | 28 x 28 | 8 |
| Conv | 26 x 26 | 16 |
| ReLU | 26 x 26 | 16 |
| Conv | 24 x 24 | 32 |
| ReLU | 24 x 24 | 32 |
| Max Pool | 12 x 12 | 32 |
| Linear | 5 | |

# Data Augmentation (Q5)

Random Affine Transformation



# VSGD-Net:
# Virtual Staining Guided Melanocyte Detection on Histopathological Images

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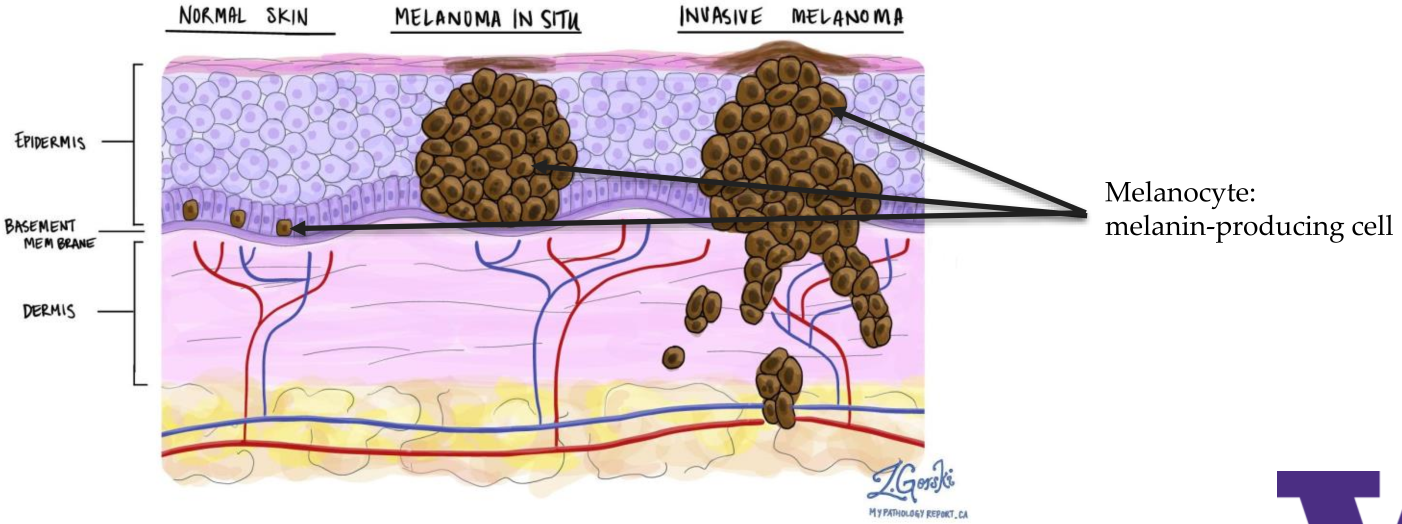
# Outline

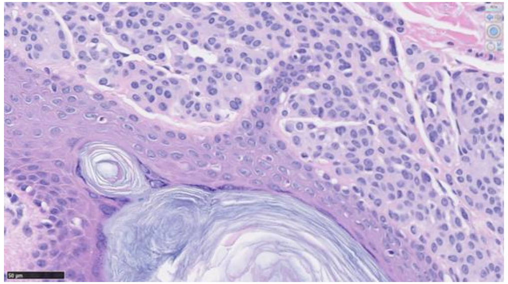
# What is melanoma?

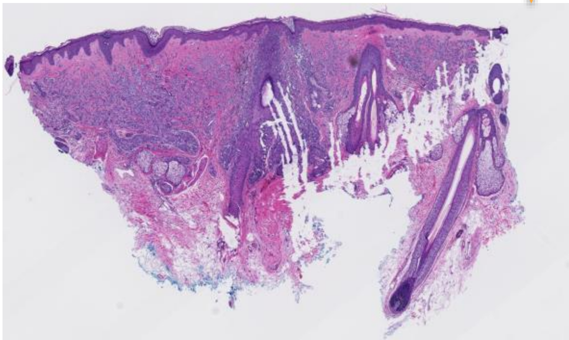
- Melanoma is the most serious type of skin cancer and is potentially fatal.
- Melanoma develops when melanocytes start to grow out of control.



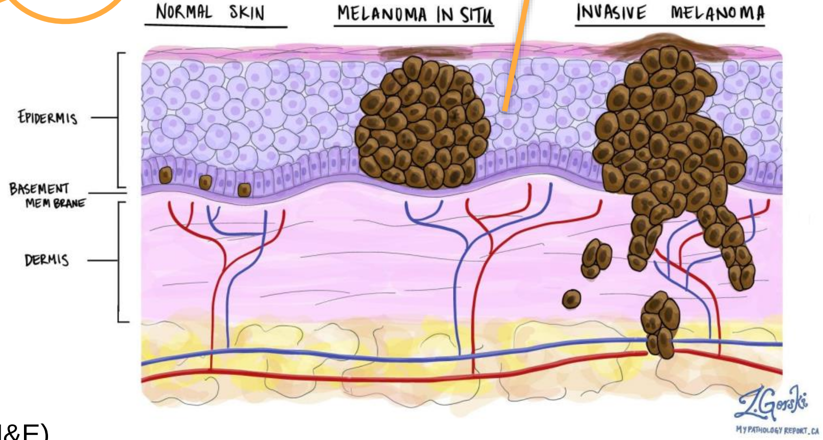
# How do pathologists diagnose melanoma?

Architectural growth patterns of melanocytes?



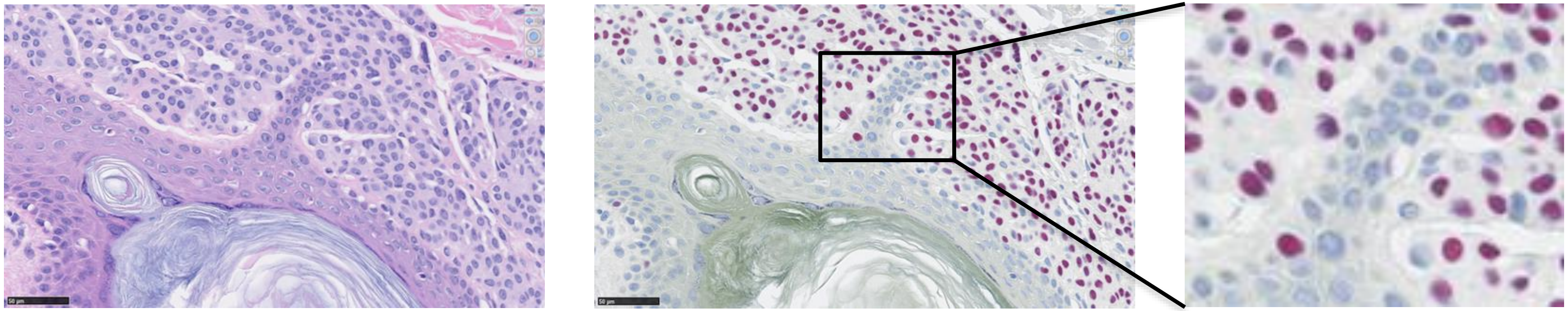


Hematoxylin and Eosin (H&E) stained skin biopsies



# Supplemental Immunostaining

> Sox10 staining can highlight melanocytes in red while keeping others in blue. 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

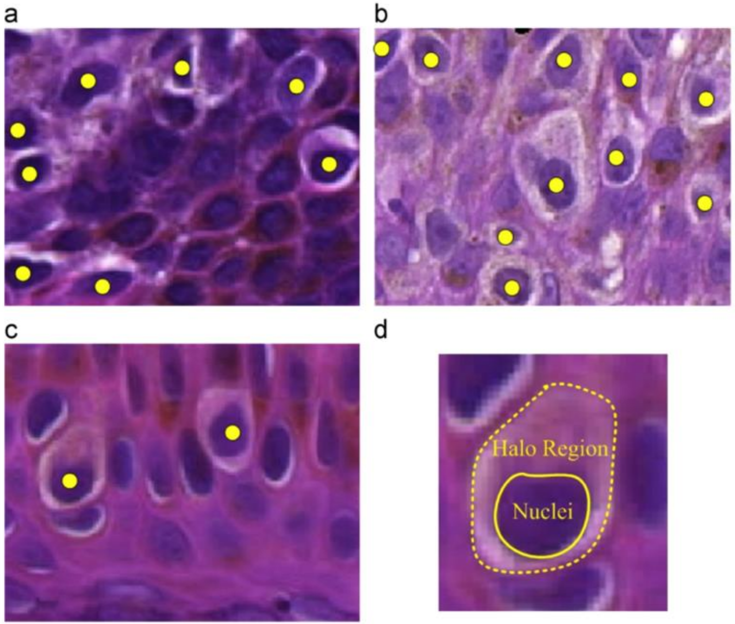
> Can we automatically **detect melanocytes** on **H&E** images?

1. Tackle the visual similarity between melanocytes and other cells in routine H&E images
2. Avoid the high cost of Sox10 staining
3. Reduce the burden on pathologists
4. Aid in melanoma diagnosis in the future

# Related Work

> **Melanocyte detection**

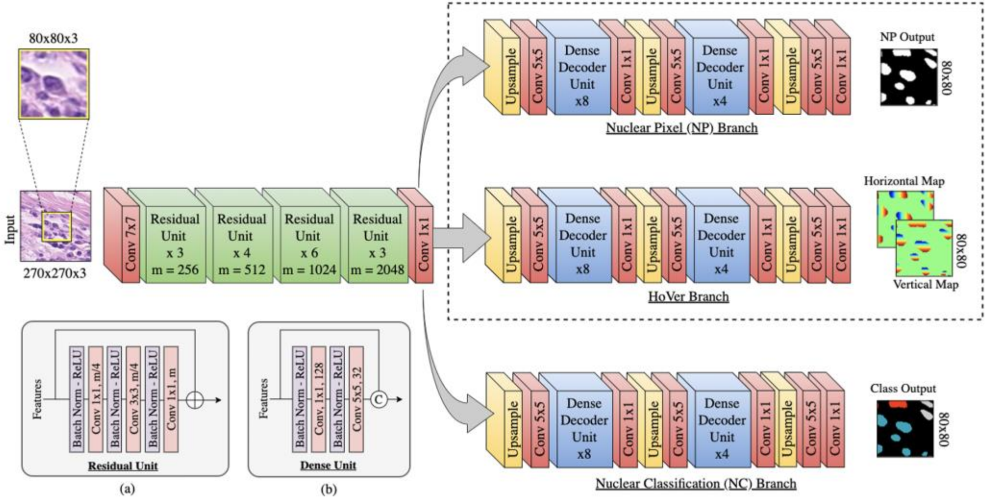
- Radial Line Scanning [1] based on the "halo region" assumption.



# Related Work

## > Nuclei detection with CNN

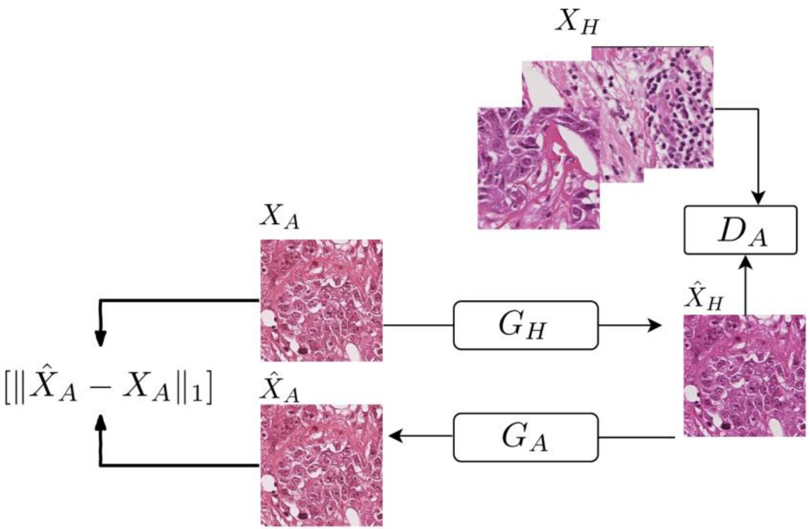
- U-Net [2], Mask R-CNN [3], Hover-Net (deep CNN) [4], StarDist (a shape-guided CNN) [5], CHR-Net (a high resolution network) [6], etc.



# Related Work

> **Image-to-Image translation**

- Tissues detection on images synthesized by GAN [7]



# Related Work

> **Melanocyte detection**

- Radial Line Scanning [1] based on the "halo region" assumption.
- Halo-regions are not the gold standard of melanocyte detection.

> **Nuclei detection with CNN**

- U-Net [2], Mask R-CNN [3], Hover-Net (deep CNN) [4], StarDist (a shape-guided CNN) [5], CHR-Net (a high resolution network) [6], etc.
- Fail to differentiate various classes of cells due to the inter-class visual similarity.

> **Image-to-Image translation**

- **Tissues detection on images synthesized by GAN [7]**
- Fail to exploit the intermediate features from the image synthesis process.

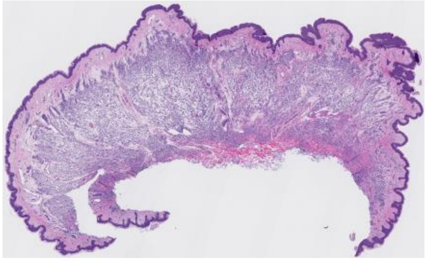
# Study Goal

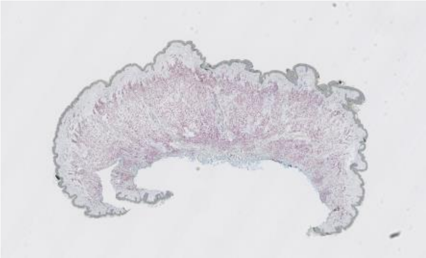
> To automatically **detect melanocytes** on **H&E** stained images and leverage **the information from the two stainings** (H&E and Sox10), we propose **VSGD-Net (Virtual Staining Guided Detection Network).**

1. Tackle the visual similarity between melanocytes and other cells in routine H&E images
2. Avoid the high cost of Sox10 staining
3. Reduce the burden on pathologists
4. Aid in melanoma diagnosis in the future

# Dataset

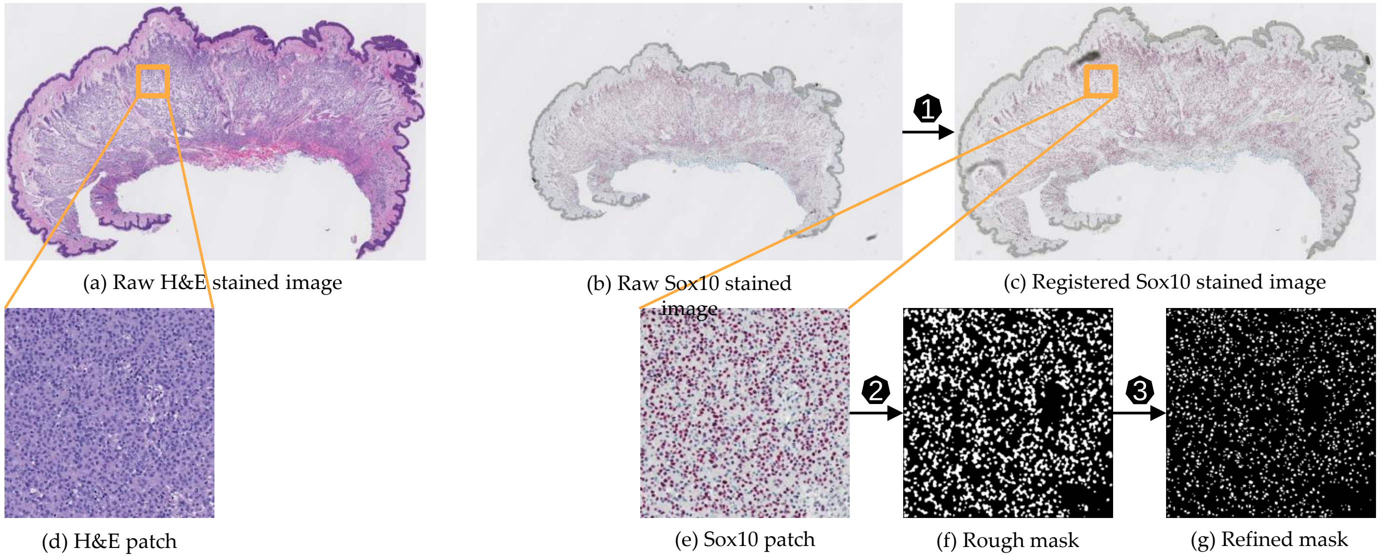
- Our dataset consists of skin tissues of 15 cases from a private dermatopathology lab, including 3 cases for each MPATH diagnostic category[1] [8].
- We stain each glass slide with H&E first, then de-stain and re-stain the same glass slide in Sox10.
- Each skin tissue is cut into multiple (4-6) thin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




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.

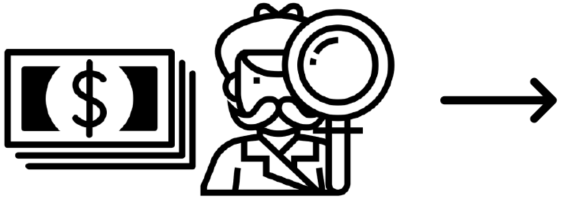
| Sub-dataset | From ? cases | # Patches |
|---|---|---|
| Train | 10 cases | 14,630 |
| Validation | | 1,032 |
| Test | 5 cases | 9,652 |

# Intro to GAN

**Generator** (Counterfeiter): Creates fake data from random input

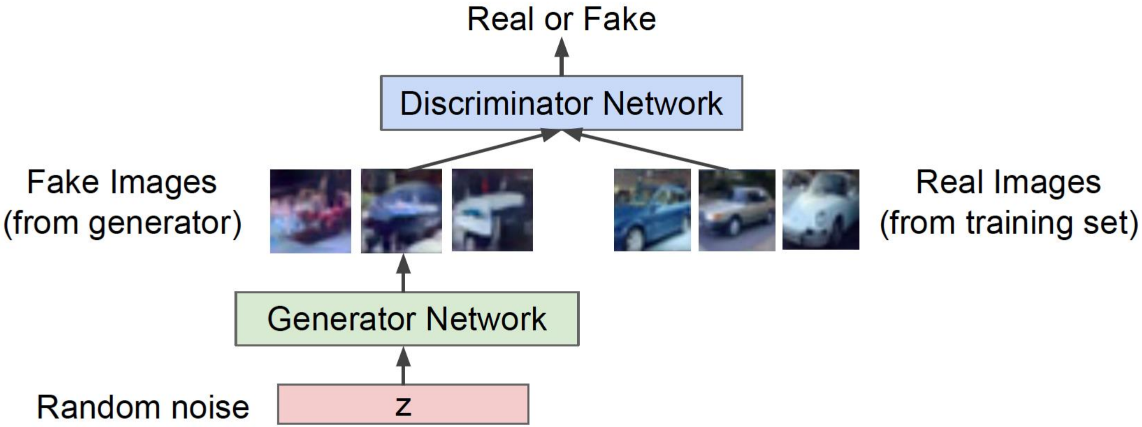
**Discriminator** (Detective): Distinguish real data from fake data

Looks Fake!



Looks Real!

# Intro to GAN



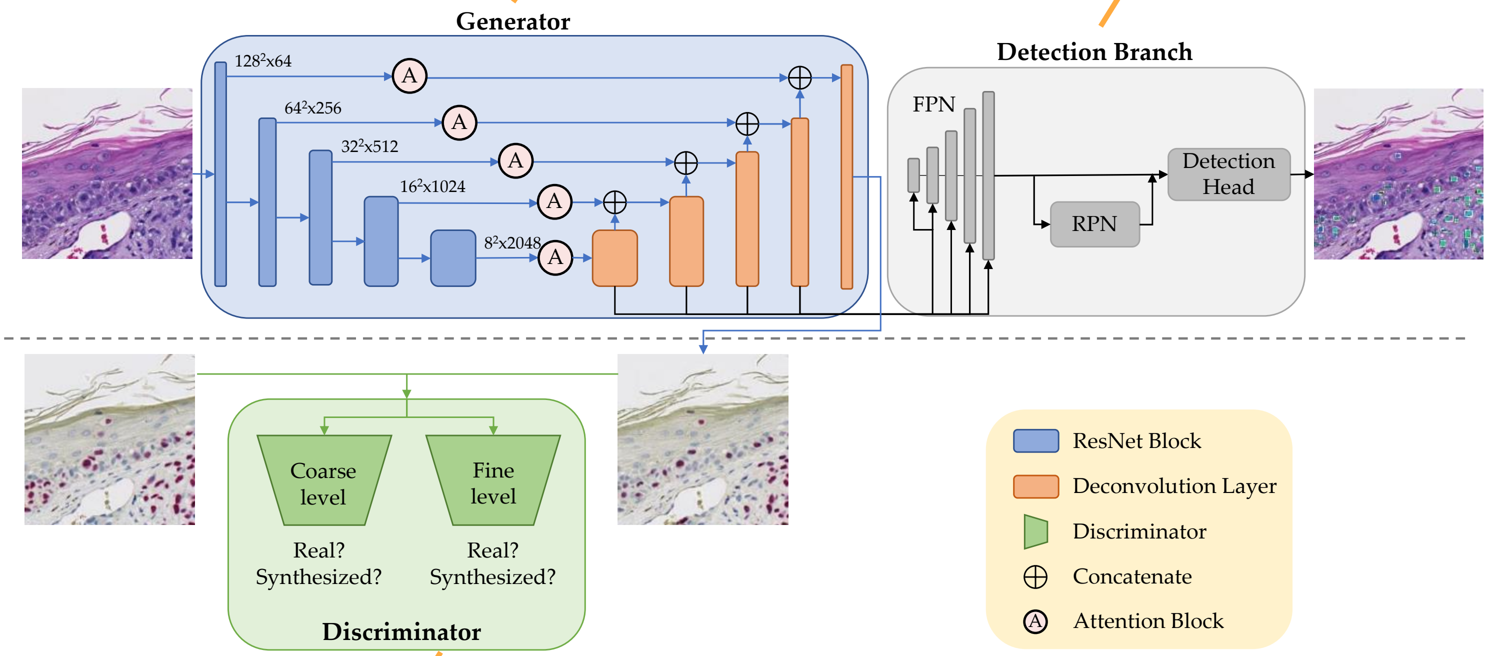

Minimax objective function:

$$\min_{\theta_g}\max_{\theta_d}\left[\mathbb{E}_{x\sim p_{data}}\log \underbrace{D_{\theta_d}(x)}_{\substack{\text{Discriminator output}\\ \text{for real data x}}} + \mathbb{E}_{z\sim p(z)}\log(1-\underbrace{D_{\theta_d}(G_{\theta_g}(z))}_{\substack{\text{Discriminator output for}\\ \text{generated fake data G(z)}}})\right]$$

# VSGD-Net

U-Net [2] with ResNet50

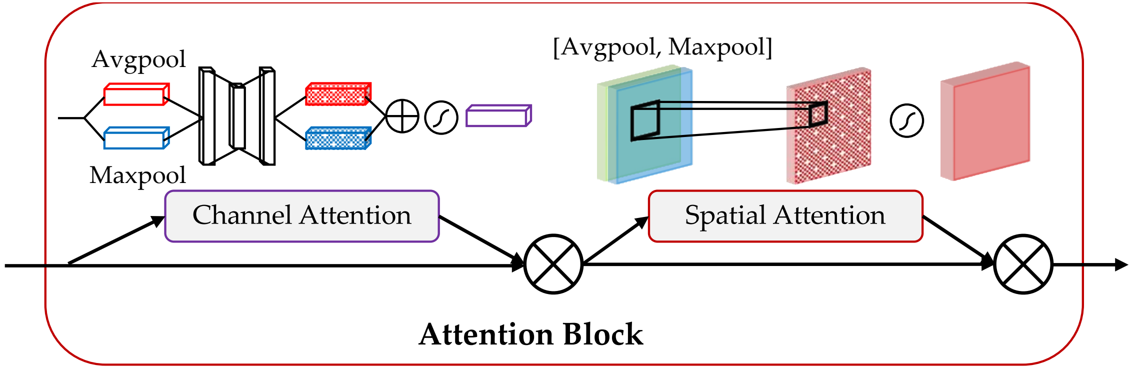
Inspired by Mask R-CNN [3]




Multi-scale discriminator

# Attention module

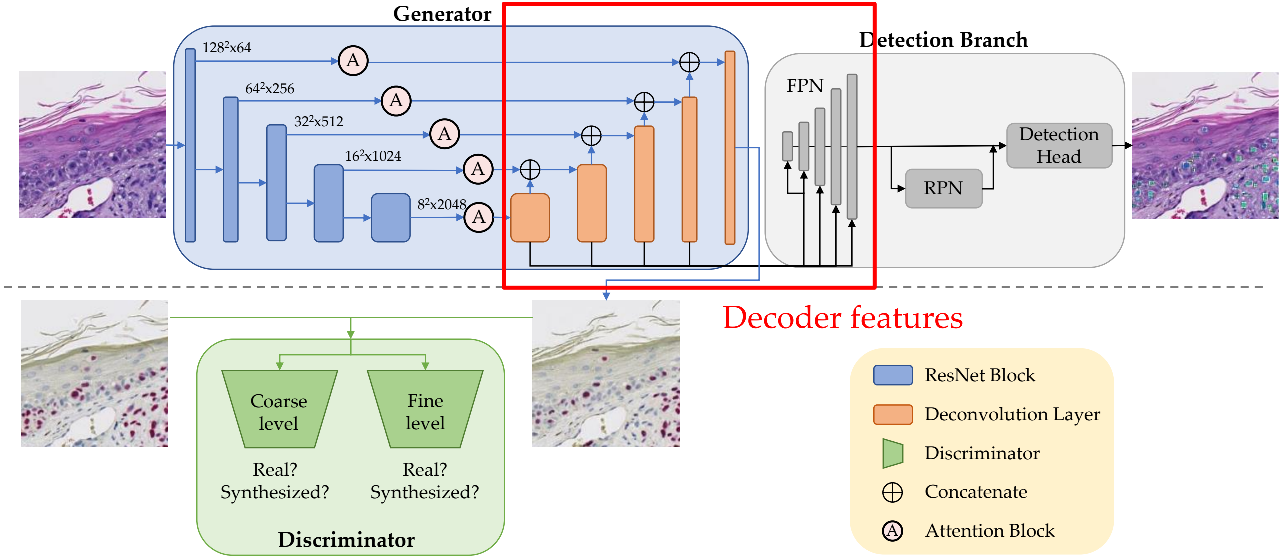
Channel attention and spatial attention are consecutively computed to refine the features[12].



# VSGD-Net

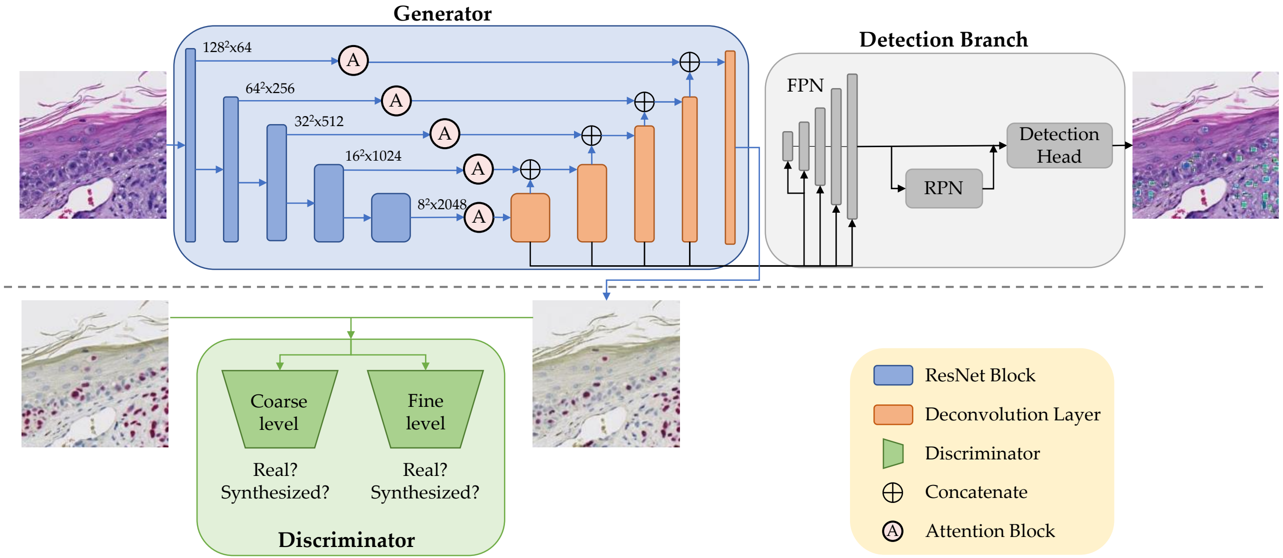
> Features input to the detection branch?

- We assume decoder layers have higher correlation with the Sox10 than encoder layers.
- The ablation study validates this design.



# VSGD-Net

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



# Evaluation Metrics

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

# Melanocyte Detection Results

Comparison with nuclei detection methods

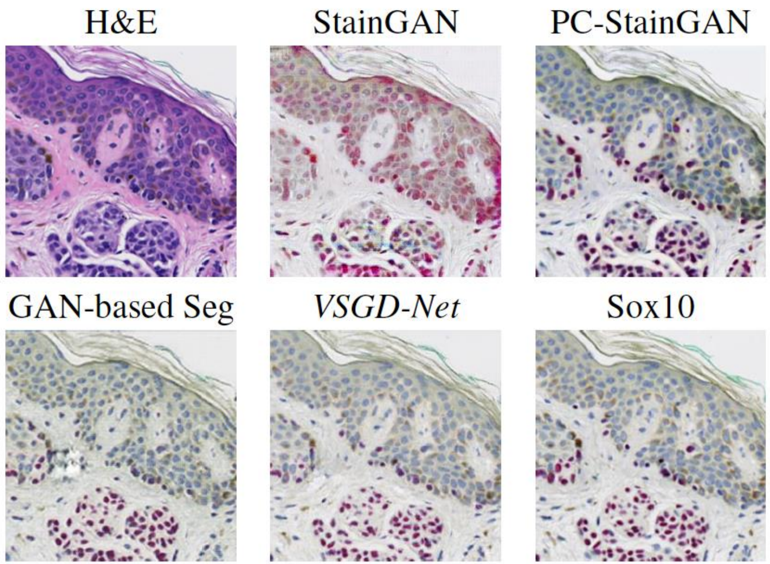
| Method | P | R | $F_1$ | Jaccard |
|---|---|---|---|---|
| RLS [24] | 0.443 | 0.570 | 0.499 | 0.332 |
| Nuclei Classification | 0.693 | 0.506 | 0.585 | 0.413 |
| Mask R-CNN [9] | 0.735 | 0.514 | 0.605 | 0.434 |
| U-Net [36] | 0.630 | 0.639 | 0.635 | 0.465 |
| StarDist[37] | **0.745** | 0.426 | 0.542 | 0.372 |
| HoverNet[8] | 0.729 | 0.499 | 0.592 | 0.421 |
| CHR-Net [5] | 0.607 | 0.688 | 0.645 | 0.476 |
| **Ours** | 0.660 | **0.710** | **0.684** | **0.520** |

Comparison with GAN-based methods

| Method | P | R | $F_1$ | Jaccard |
|---|---|---|---|---|
| StainGAN [39] | 0.476 | 0.299 | 0.367 | 0.225 |
| PC-StainGAN [20] | 0.591 | 0.343 | 0.434 | 0.277 |
| GAN-based Segmentation | 0.569 | **0.719** | 0.636 | 0.466 |
| **Ours** | **0.660** | 0.710 | **0.684** | **0.520** |

# Image Synthesis Evaluation

| Method | PSNR(dB) | SSIM |
|---|---|---|
| StainGAN [39] | 19.010 | 0.577 |
| PC-StainGAN [20] | 19.344 | **0.618** |
| GAN-based Segmentation | 19.583 | 0.569 |
| **Ours** | **19.815** | 0.611 |



# Ablation Study

> Our VSGD-Net learning scheme can achieve comparable results even with the simpler generator.
> Decoder layers have higher correlation with the Sox10 than encoder layers.
> The attention module refines the intermediate features.

Table 4. Ablation results.

| Generator | Features From | Atten. | $F_1$ | Jaccard |
|---|---|---|---|---|
| Pix2pixHD | Decoder | - | 0.654 | 0.486 |
| Ours | Encoder | ✗ | 0.641 | 0.472 |
| Ours | Decoder | ✗ | 0.674 | 0.508 |
| Ours | Encoder | ✓ | 0.660 | 0.492 |
| Ours | Decoder | ✓ | **0.684** | **0.520** |

# Conclusion

> We propose a novel instance detection scheme that investigate the detection task using image synthesis features between two stainings.
> During inference, the model can produce promising results from only the routine staining.
> We anticipate that the proposed method can adapt to a broad category of diseases.

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# Thanks!